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ORIGINAL ARTICLE

Application of hip capsule peripheral nerve block in early analgesia in elderly patients with hip fracture

Aplicación del bloqueo del nervio periférico de la cápsula de la cadera en analgesia temprana en pacientes ancianos con fractura de cadera

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Abstract

Objective: *The objective of the study is to investigate the effect of pericapsular nerve group (PENG) block in early analgesia in elderly patients with hip fracture.* **Methods:** *A total of 44 elderly patients with hip fracture admitted to our hospital from August 2021 to December 2022 were selected and divided into 2 groups according to different analgesia programs.* **Results:** *At T_1~T_4, the resting and active visual analog scale (VAS) scores in group P were lower than group F ($p < 0.05$). The resting and active VAS scores at T_5 in both groups were no visible differences ($p > 0.05$). After 30 min of block, systolic blood pressure, diastolic blood pressure, and heart rate were decreased in both groups ($p < 0.05$), but no obvious difference was found in the two groups ($p > 0.05$). Before surgery, Pittsburgh Sleep Quality Index (PSQI) and mini–mental state scale (MMSE) scores in both groups were reduced, and PSQI score in group P was lower than that in group F and MMSE score was higher than group F ($p < 0.05$).* **Conclusions:** *PENG technology is safe and effective in the early analgesia of elderly hip fractures. It can effectively block physiological stress response caused by acute trauma, improve pre-operative sleep quality, and reduce the incidence of cognitive dysfunction.*

Keywords: *Hip fracture. Pericapsular nerve group block. Fascia iliaca compartment block. Early analgesia. Security.*

Resumen

Objetivo: *Investigar el efecto del bloqueo del grupo del nervio pericapsular en analgesia temprana en pacientes ancianos con fractura de cadera.* **Métodos:** *Se seleccionaron 44 pacientes ancianos con fractura de cadera ingresados en nuestro hospital entre agosto de 2021 y diciembre de 2022, divididos en dos grupos según diferentes programas de analgesia.* **Resultados:** *En T1~T4, los valores de la escala visual análoga (EVA) en reposo y con actividad en el grupo P fueron menores que en el grupo F ($p < 0.05$). Los puntajes de la EVA en reposo y en actividad en T5 en ambos grupos no mostraron diferencias visibles ($p > 0.05$). Después de 30 minutos de bloqueo, la presión arterial sistólica y diastólica, y la frecuencia cardiaca, disminuyeron en ambos grupos ($p < 0.05$), pero no se encontró una diferencia obvia entre ellos ($p > 0.05$). Antes de la cirugía, las puntuaciones del Pittsburgh Sleep Quality Index (PSQI) y de la Mini-Mental State Scale (MMSE) en ambos grupos eran reducidas, y la puntuación del PSQI en el grupo P fue menor que en el grupo F, y la puntuación del MMSE fue mayor que en el grupo F ($p < 0.05$).* **Conclusiones:** *La técnica de bloqueo del grupo del nervio pericapsular es segura y efectiva en la analgesia temprana de fracturas de cadera en ancianos. Puede bloquear eficazmente la respuesta al estrés fisiológico causado por un trauma agudo, mejorar la calidad del sueño preoperatorio y reducir la incidencia de disfunción cognitiva.*

Palabras clave: *Fractura de cadera. Bloqueo del grupo del nervio pericapsular. Bloqueo de la fascia iliaca. Analgesia temprana. Seguridad.*

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Introduction

With the rapid development of our economy and society, the problem of aging population and prevention of related diseases have become a hot topic. As one of the emergencies in elderly population, hip fracture can lead to severe pain, especially during the early position change and moving examination, which can cause the excitation of the sympathetic adrenal medulla axis, leading to a series of stress reactions[1,2]. For elderly patients, trauma and pain stimulation have more severe effects on the whole body. Pain may affect the secretion of hormones by changing the patients' sleep rhythm, thus leading to the occurrence of delirium[3]. Post-operative delirium and cognitive dysfunction are highly common in elderly orthopedic patients. Studies have shown that the incidence of post-operative delirium in elderly orthopedic surgery patients ranges from 25% to 48%, which may even cause permanent cognitive dysfunction and seriously affect brain function and prognosis[4,5]. At present, studies on pain control in elderly patients with hip fracture tend to focus on post-operative pain management and pay insufficient attention to the period from the occurrence of trauma to the start of surgery. Previous clinical studies have shown that non-steroidal anti-inflammatory drugs (NSAIDs) given in acute pain can significantly improve the prognosis of patients, but such drugs may increase the risk of cardiovascular adverse events, coagulation disorders, and peptic ulcers[6]. Opioids are another method for pre-operative pain management, but they can be accompanied by side effects such as nausea, vomiting, dizziness and respiratory depression, and their application is limited, especially for elderly patients with many complications[7]. Moreover, improper use of opioids can increase the occurrence of adverse events such as delirium and may even lead to death[8]. The sensory fibers of the hip joint are mainly distributed in the front of the hip capsule, and the innervation mainly comes from the branches of the lumbar plexus. Studies have reported that fascia iliaca compartment block (FICB) is better than fentanyl and non-steroidal analgesics in the early analgesia of patients with hip fractures, but it has some defects such as large local anesthetic volume and total dose and excessive poisoning risk for elderly patients[9,10]. Therefore, finding safe and effective early analgesic methods for elderly patients with hip fracture are still an urgent clinical problem.

Pericapsular nerve group block (PENG) as a new block technique, which uses ultrasound-guided puncture technology and in-plane injection method to attach the nerve block needle to the anterior inferior iliac spine, accurately inject local anesthetics into the acetabular bone surface, block the femoral nerve and obturator nerve distributed in front of the hip capsule at the same time, and can quickly and effectively relieve the pain after hip fracture[11,12]. In addition, the PENG has a wide range of clinical application prospects for the simple implementation, short operation time, rapid onset, and low incidence of adverse reactions. However, there are few reports of early analgesia with PENG in elderly patients with hip fracture. Therefore, this study compared the early analgesia efficacy of PENG and FICB in elderly patients with hip fracture.

Materials and methods

Ethical approval of the research protocol

This study was approved by the hospital Ethics Committee. All patients signed an informed consent form agreeing to participate in the clinical study.

Patients

The elderly with hip fracture treated in our hospital were included in the study. Inclusion criteria: age 65 years old or above, expected to undergo surgery within 72 h, visual analog scale (VAS) score > 4, no serious heart, liver, kidney diseases. Exclusion criteria: history of scar, infection and local anesthetics at the puncture site, refusing a nerve block, inability to coordinate and communicate well with doctors. A total of 44 patients were divided into PENG group (group P) and FICB group (group F) according to the different analgesia programs. There were 24 cases in Group P and 20 cases in Group F. Moreover, anesthesia was performed by the same neurosurgeon with over 15 years of resident experience.

Analgesia method

Group P received ultrasound-guided PNGB analgesia regimen: the patients were placed in supine position, routinely disinfected and covered, and the portable two-dimensional ultrasound instrument (Sonosite, USA) was used for detection. The linear array

probe of 10~13 MHz was placed on the joint line between the anterior superior iliac spine and the pubic bone, and then, the probe was shifted toward the tail end and slightly toward the head end when the image of the femoral head appeared under ultrasound. At this time, the image of the femoral head disappeared. The presence of a high-echo bright line is the iliopubic process, the medial side is the ramus of the pubis, the lateral side is the anterior inferior iliac spine, the superficial side of the bone surface is the iliopsoas muscle, and the medial side is the femoral artery. The in-plane injection method was adopted, and 22G local anesthesia needle was used to puncture the anterior inferior iliac spine to the acetabular bone surface from the outside to the inside. When no blood was drawn back, the 15 mL 0.25% ropivacaine was injected. The ultrasonography images in figure 1 show the anatomical structure of puncture site.

Group F received ultrasound-guided FICB analgesia regimen: the patients were placed in supine position, routinely disinfected and covered, and a portable two-dimensional ultrasound instrument (Sonosite, USA) was used. The puncture point was set at the junction of the middle 1/3 of the line between the anterior superior iliac spine and the pubic tuberous node, opening 1.5 cm to the caudal side. The linear array probe of 10~13 MHz was placed parallel to the inguinal fold. The fascia lata, iliac fascia, and iliopsoas muscle on the ultrasound image were confirmed. The injection was performed from the outside to the inside by in-plane technique. After experiencing two breakthrough sensations, no blood was extracted and 15 mL 0.25% ropivacaine was injected. Then, the probe was placed parallel to the inner thigh along the extended line of the inguinal fold, and the space between the adductor longus, adductor brevity, and adductor magnus was identified by ultrasonic development. Subfascia obturator nerve block was used, and 5 mL 0.25% ropivacaine hydrochloride was injected. The ultrasonography images in figure 2 show the anatomical structure of puncture site.

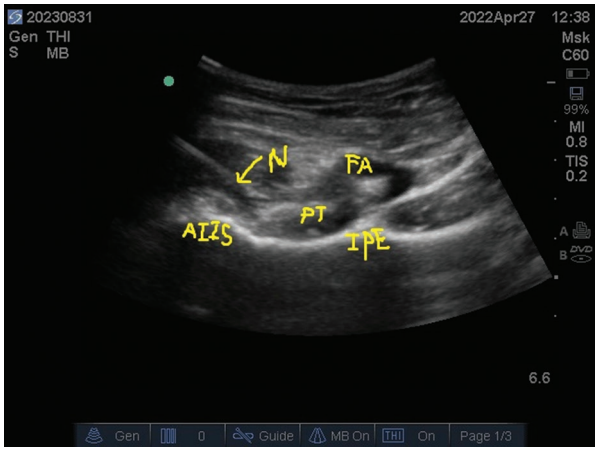

Figure 1. *PENG block. AIIS: anterior inferior iliac spine; FA: femoral artery; IPE: iliopubic eminence; PT: psoas tendon; N: needle.*

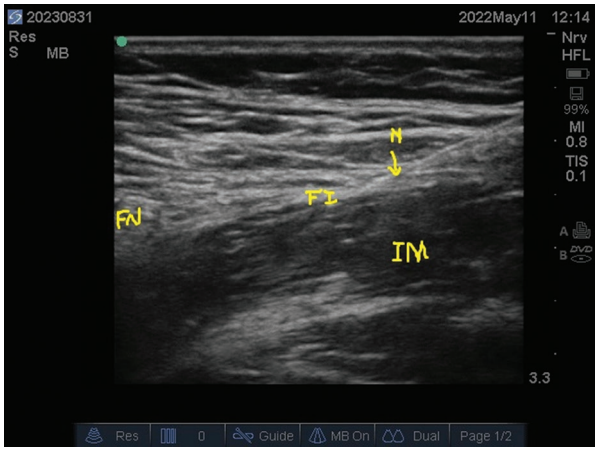

Figure 2. *Fascia iliaca block. FI: fascia iliaca; FN: femoral nerve; IM: iliacus muscle; N: needle.*

Outcome measures

The scores of resting and active VAS were evaluated before block (T_0), block for 5 min (T_1), 10 min (T_2), 20 min (T_3), 30 min (T_4), and the next morning after hospitalization (T_5). The vital signs of the two groups were evaluated, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) changes before and 30 min after the block. The sleep quality and cognitive function status of the two groups were evaluated at admission and before the surgery. The time from admission to operation and the situation of analgesic drugs within 24 h after operation were recorded in both groups, and the safety of the two groups was assessed.

Statistical analyses

SPSS 22.0 statistical software was used to analyze research data. Normally distributed continuous variables including VAS score, SBP, DBP, HR, PSQI, and MMSE scores were presented as the mean ± standard deviation, and comparison between groups was performed by independent sample t-test. Categorical

Table 1. Clinical characteristics of patients in the two groups

Variable	Group P (n = 24)	Group F (n = 20)	χ^2/t-values	p-values
Sex (male/female)	11/13	10/10	0.076	0.783
Age (years)	78.33 ± 7.75	79.25 ± 8.43	0.377	0.708
BMI (kg/m^2)	20.67 ± 2.85	21.20 ± 3.59	0.546	0.588
ASA grading (II/III)	13/11	11/9	0.003	0.956

BMI: body mass index; ASA: American Society of Anesthesiologists.

Table 2. Comparison of analgesic indexes between two groups

States	Groups	T_0	T_1	T_2	T_3	T_4	T_5
Resting state	Group P (n = 24)	4.88 ± 0.99	4.13 ± 1.19*	2.67 ± 1.13*	1.83 ± 0.92*	1.46 ± 0.51*	1.54 ± 0.88*
	Group F (n = 20)	5.00 ± 1.08	5.00 ± 1.08	4.15 ± 0.99*	3.35 ± 1.31*	1.95 ± 0.94*	1.70 ± 0.80*
	t-values	0.384	2.517	4.573	4.509	2.198	0.626
	p-values	0.703	0.016	0.000	0.000	0.034	0.535
Active state	Group P (n = 24)	6.69 ± 1.42	5.88 ± 0.90*	4.08 ± 1.41*	2.21 ± 1.18*	1.88 ± 0.90*	2.75 ± 0.90*
	Group F (n = 20)	6.76 ± 1.08	6.65 ± 1.39	5.65 ± 1.57*	3.50 ± 1.43*	2.40 ± 0.75*	2.80 ± 0.77*
	t-values	0.181	2.216	3.493	3.280	2.056	0.196
	p-values	0.857	0.032	0.001	0.002	0.046	0.846

*$p < 0.05$ versus T_0.

data were expressed as frequencies and percentages and analyzed using Chi-squared tests if appropriate. $p < 0.05$ was considered significant.

Results

Baseline characteristics

The gender, age, BMI, and ASA grading in two groups were no obvious differences ($p > 0.05$), as shown in table 1.

Analgesic indexes

At T_0, T_5, the VAS scores at resting and active state were all no visible differences among both groups ($p > 0.05$). At T_1~T_4, the VAS scores at resting and active state in group P were obviously decreased than those in group F ($p < 0.05$); the VAS scores at resting and active state in group P started decreasing from T_1, while those in group F were decreased from T_2, seen from table 2.

Stress response indexes

After blocking for 30 min, SBP, DBP, and HR were decreased in both groups ($p < 0.05$), but there was no obvious difference between two groups ($p > 0.05$), seen from table 3.

Sleep quality and cognitive function

At admission, PSQI and MMSE scores in two groups were no evident difference ($p > 0.05$). Before surgery, PSQI and MMSE scores were decreased in both groups, and PSQI score in group P was lower than that in group F and MMSE score in group P was higher than that in group F ($p < 0.05$), seen from table 4.

Time from admission to operation

The time from admission to operation in group P was (35.22 ± 6.78) hours, which was shorter than (48.45 ± 8.29) hours in group F (t = 5.825, $p < 0.05$).

Table 3. Comparison of SBP, DBP, and HR between the two groups before and 30 min after the block

Groups	SBP (mmHg)		DBP (mmHg)		HR (time/min)	
	Before block	30 min after the block	Before block	Block for 30 min	Before block	Block for 30 min
Group P (n = 24)	161.63 ± 24.17	139.46 ± 14.27*	91.67 ± 14.47	80.58 ± 11.58*	88.96 ± 16.69	75.79 ± 11.40*
Group F (n = 20)	152.90 ± 23.04	138.40 ± 16.92*	91.20 ± 10.85	79.50 ± 10.51*	86.80 ± 15.85	78.40 ± 11.60*
t-values	1.218	0.223	0.120	0.321	0.437	0.750
p-values	0.230	0.823	0.905	0.750	0.664	0.457

*$p < 0.05$ versus before block.
SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate

Table 4. Comparison of sleep quality and cognitive function between the two groups at admission and before operation

Groups	PSQI		MMSE	
	At admission	Before the surgery	At admission	Before the surgery
Group P (n = 24)	5.33 ± 1.38	4.09 ± 1.08*	26.19 ± 3.06	24.22 ± 3.15*
Group F (n = 20)	5.46 ± 1.44	4.85 ± 1.11*	26.49 ± 2.35	22.16 ± 3.22*
t-values	0.305	2.295	0.359	2.138
p-values	0.762	0.027	0.722	0.038

*$p < 0.05$ versus admission; PSQI: Pittsburgh Sleep Quality Index; MMSE: mini–mental state scale.

The situation of analgesic drugs within 24 h after surgery and adverse reactions

Group P was not treated with analgesic drug supplement after operation, and no adverse reactions occurred, while 3 cases in group F were given analgesic drug supplementation and 4 cases occurred nausea, vomiting, vertigo, and other adverse reactions (χ^2 = 3.863, 5.280, $p < 0.05$).

Discussion

The preferred treatment method for the elderly with hip fracture is surgery. Most elderly patients are physically weak, and the pain and stimulation caused by fracture will cause the body stress response, seriously affect the sleep quality of elderly patients, and further aggravate the weakness, which is not conducive to the control of patients' underlying diseases and may lead to the delay of surgical treatment[13]. With the popularization of the concept of accelerated rehabilitation, pre-operative analgesia has been paid more and more attention in clinic. In the past, drug analgesia was mainly used in clinical practice, but there were shortcomings such as incomplete analgesia and many adverse reactions[14]. At present, with the wide clinical application of ultrasound technology, perioperative analgesia, which is mainly based on nerve block and analgesia technology in affected area, has become a hot spot in clinical research[15].

Iliac fascia space nerve block is a commonly used nerve block technique in clinical practice. Theoretically, it can block femoral nerve and obturator nerve at the same time, and its effect in pre-operative analgesia is better than traditional drug analgesia. However, this technique has defects such as large dose, high risk of poisoning, and slow onset in elderly patients[16]. PENG block is a new type of block proposed based on hip innervation, which belongs to myofascial plane block. It is easy to master under the guidance of ultrasound, has a high success rate, and is suitable for continuous block and analgesia with catheterization[17]. Hence, this study investigated the effects of PENG block on analgesia, stress response, sleep quality, and cognitive function in elderly patients with hip fracture during pre-operative hospitalization and evaluated the safety of PENG block for elderly patients with hip fracture.

In this study, we compared the early analgesic efficacy of two block techniques in elderly patients with hip

fractures. The results showed that the VAS scores at resting and active state in group P at T_1~T_4 were obviously decreased than those in group F, and the VAS scores at resting and active state in group P started decreasing from T_1, while those in group F were decreased from T_2, suggesting PENG block technique is more effective and faster than FICB technique in early analgesia for elderly patients with hip fracture. The reason may be that the anterior capsule of the hip joint is innervated by obturator nerve, the accessory obturator nerve, and the femoral nerve, and it is the most abundant part of the hip joint nerve innervation. The hip joint branch of the femoral nerve and the accessory obturator nerve is always located between the anterior inferior iliac spine and the iliopubic uplift. Therefore, local anesthetic injection into the plane between them for nerve block is more targeted for hip fracture analgesia[18]. The results showed when blocking for 30 min, the SBP, DBP, and HR decreased in both groups, but there was no prominent difference between two groups, indicating the both blocks could effectively reduce the physiological stress response of elderly patients with hip fracture. Previous studies have shown that pain affects not only sleep but also cognitive function[19]. In the study, after blocking, PSQI and MMSE scores decreased in both groups, and PSQI score in group P was lower than that in group F, MMSE score in group P was higher than group F, revealing that the both blocks could improve the sleep quality of the elderly and play a certain protective effect on their neurological function, but the effect of PENG block was more significant. The possible mechanisms of the protective effect of nerve block on cognitive function are as follows: regional block can significantly reduce the dosage of general anesthesia drugs, reduce the concentration of inhaled anesthesia drugs, and thus, reduce the neurotoxic effects of general anesthesia drugs; regional block can reduce the stress of surgical trauma and pain on the whole body, inhibit the inflammatory response of the central nervous system, reduce the damage of the central nervous system, and thus protect the cognitive function[20].

In addition, the time from admission to operation in group P was shorter than that in group F, indicating the PENG block can shorten the pre-operative waiting time of patients. Moreover, Group P was not treated with analgesic drug supplement after operation, and no adverse reactions occurred, while 3 cases in group F were given analgesic drug supplementation and 4 cases occurred nausea, vomiting, vertigo, and other adverse reactions, further demonstrating the safety of PENG block in early analgesia in elderly patients with hip fracture.

Conclusions

The early analgesic effect of PENG block on elderly patients with hip fracture is significant, and the analgesic effect is fast. It can shorten the pre-operative waiting time of patients, create a good opportunity for surgery, reduce pain stimulation, improve the sleep quality of patients, further protect the cognitive function, and contribute to the rapid recovery of elderly patients with hip fracture. However, this study still shows some shortcomings. For example, this study has a limited sample size and a single source of cases, so the conclusions still need to be confirmed by a large number of large sample and multi-center studies.

Funding

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Conflicts of interest

All authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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ORIGINAL ARTICLE

From medical imaging to 3D printed anatomical models: a low-cost, affordable 3D printing approach

De imágenes médicas a modelos anatómicos impresos en 3D: un enfoque de impresión 3D asequible y de bajo costo

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Abstract

Objective: *To share our experience in creating precise anatomical models using available open-source software.* **Methods:** *An affordable method is presented, where from a DICOM format of a computed tomography, a segmentation of the region of interest is achieved. The image is then processed for surface improvement and the DICOM format is converted to STL. Error correction is achieved and the model is optimized to be printed by stereolithography with a desktop 3D printer.* ***Results:*** *Precise measurements of the dimensions of the DICOM file (CT), the STL file, and the printed model (3D) were carried out. For the C6 vertebra, the dimensions of the horizontal axis were 55.3 mm (CT), 55.337 mm (STL), and 55.3183 mm (3D). The dimensions of the vertebral body were 14.2 mm (CT), 14.551 mm (STL), and 14.8159 mm (3D). The length of the spinous process was 18.2 mm (CT), 18.283 mm (STL), and 18.2266 mm (3D), while its width was 8.5 mm (CT), 8.3644 mm (STL), and 8.3226 mm (3D). For the C7 vertebra, the dimensions of the horizontal axis were 58.6 mm (CT), 58.739 mm (STL), and 58.7144 mm (3D). The dimensions of the vertebral body were 14 mm (CT), 14.0255 mm (STL), and 14.2312 mm (3D). The length of the spinous process was 18.7 mm (CT), 18.79 mm (STL), and 18.6458 mm (3D), and its width was 8.9 mm (CT), 8.988 mm (STL), and 8.9760 mm (3D).* ***Conclusion:*** *The printing of a 3D model of bone tissue using this algorithm is a viable, useful option with high precision.*

Keywords: *3D printing. Virtual planning. Surgical planning. Mandibular reconstruction. Stereolithography.*

Resumen

Objetivo: *Compartir nuestra experiencia para crear modelos anatómicos precisos utilizando software con licencia abierta disponibles.* ***Métodos:*** *Se presenta un método asequible, en donde a partir de un formato DICOM de una tomografía computarizada se logra una segmentación de la región de interés. Posteriormente se procesa la imagen para una mejora de superficie y se realiza la conversión de formato DICOM a STL. Se logra la corrección de errores y se optimiza el modelo para luego ser impreso por medio de estereolitografía con una impresora 3D de escritorio.* ***Resultados:*** *Se efectuaron mediciones precisas de las dimensiones del archivo DICOM (TC), del archivo STL y del modelo impreso (3D). Para la vértebra C6, las dimensiones del eje horizontal fueron 55.3 mm (TC), 55.337 mm (STL) y 55.3183 mm (3D). Las dimensiones del cuerpo*

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vertebral fueron 14.2 mm (TC), 14.551 mm (STL) y 14.8159 mm (3D). La longitud de la apófisis espinosa fue de 18.2 mm (TC), 18.283 mm (STL) y 18.2266 mm (3D), mientras que su ancho fue de 8.5 mm (TC), 8.3644 mm (STL) y 8.3226 mm (3D). Para la vértebra C7, las dimensiones del eje horizontal fueron 58.6 mm (TC), 58.739 mm (STL) y 58.7144 mm (3D). Las dimensiones del cuerpo vertebral fueron 14 mm (TC), 14.0255 mm (STL) y 14.2312 mm (3D). La longitud de la apófisis espinosa fue de 18.7 mm (TC), 18.79 mm (STL) y 18.6458 mm (3D), y su ancho fue de 8.9 mm (TC), 8.988 mm (STL) y 8.9760 mm (3D). ***Conclusión:*** *La impresión de un modelo en 3D de tejido óseo mediante este algoritmo resulta una opción viable, útil y con una alta precisión.*

Palabras clave: *Impresión 3D. Planificación virtual. Planificación quirúrgica. Reconstrucción mandibular. Estereolitografía.*

Introduction

The application of 3D printing technology in the medical field is not new. As interest among surgical professionals and the availability of low-cost 3D printers have increased, biomedical advances and benefits in medicine through rapid prototyping have been achieved. 3D printing has expanded in the medical field for various applications, including prosthetics, implants, and customized models, as well as in medical education, among other areas. These applications have generated valuable benefits in terms of the customization of medical equipment and patient care[1]. One could think that implementing this technology involves high costs and requires a high level of expertise and specialization, making it unfeasible in certain hospitals, and, therefore, outsourcing services is often a possible alternative. Various companies offer 3D printing services, but in many cases, the costs associated with these services are not affordable for patients[2,3]. This article evaluates the feasibility of using free-licensed software, along with a desktop printer, for the design, fabrication, and application of patient-specific anatomical bone models, which provide extensive and detailed information for the preoperative planning of complex fractures, deformities, and bone tumors, among others. These models have potential uses in preoperative planning, enhancing patient understanding of their pathology and the procedure, improving doctor-patient communication, and supporting training personnel by facilitating knowledge acquisition through haptic feedback[4].

Method

With the patient's prior consent, neck images were obtained from a 16-slice multidetector computed tomography scanner (Brilliance 16; Philips Medical), acquiring images of the cervical spine to create a model of 2 vertebral bodies (C6 and C7), which represent bone tissue with a complex surface, unlike a long bone, to simulate a clinical situation where spinal surgery planning would be performed. Volumetric data were acquired (1 mm slice thickness, 140 kVp, 103 mA). The next step involves obtaining a format that allows for 3D printing, using a file with STL (stereolithography) extension so that the printer can execute the commands in millimeter coordinates on the x, y, and z axes.

To outline the boundaries of the tissues or organs of interest and generate a 3D reconstruction for further analysis, a segmentation process is performed. Image segmentation is a technique used in digital imaging to organize scanned volumes into connected, non-overlapping, discrete, homogeneous, and semantically meaningful regions. Each of these partitions consists of sets of pixels or voxels, and the differences between each voxel in intensity (densities) or texture represent an opportunity from which this partition is made. This process can be manual, adjusting the contours of the selected volume manually, which can be time-consuming and exhausting, or automatic through multiple tools with algorithms that divide into regions with similar intensity or texture characteristics. Due to their particular nature, these algorithms have no proper rule for validating the obtained segmentation results, nor do they guarantee a feasible model for 3D printing; therefore, a semi-automatic approach was adapted.

During our process, the radiology team supervised and supported the development of the segmentation. The Slicer program, in the segment editor module, has multiple tools for segmentation. We used thresholding, which allows manual adjustment of threshold ranges, to select the Hounsfield units that cover the region of interest with little or no mottling of other structures. The ranges were adjusted to ensure that the largest bone structure of interest was selected. To ensure accuracy in volume segmentation, each of the CT scans was reviewed to reinforce scrupulousness and precision. With the paint and draw options, details were refined by manually removing "undesired volume" and adding "missing volume." Next, structures within the selected threshold

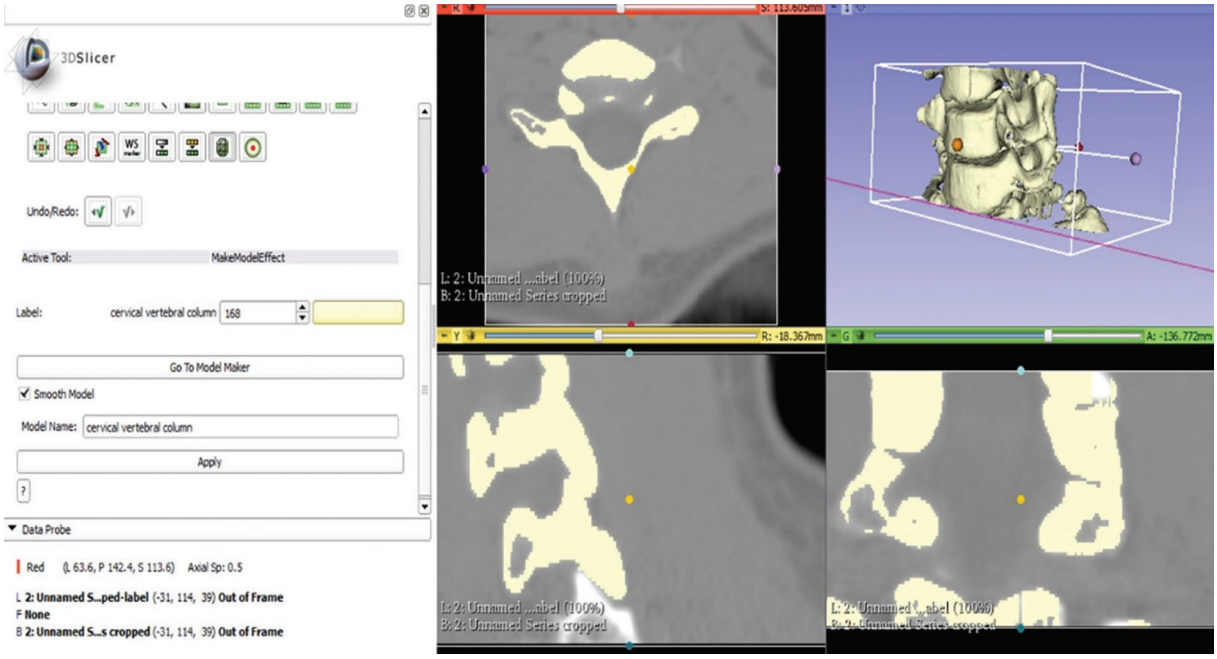

Figure 1. *Model during processing in 3D Slicer. Segmentation and refinements are performed, non-interesting regions are removed, and "Create Surface" is selected to visualize our structure in a 3D reconstruction.*

that were not part of the region of interest were removed; this was facilitated by cropping the workspace with the crop option, then selecting the structure of interest with the “keep selected island” option and using scissors to manually and meticulously surround the volume of interest, selecting “erase outside.” Afterwards, the create surface option was selected to visualize our structure in a 3D reconstruction (Fig. 1).

The volume saved in STL format was loaded into Blender software to optimize the model and prepare it for printing. The mesh was created in the model using the Edit Mode option, which generates the mesh in the 3D model. Afterwards, one of the vertices of the exterior mesh was selected, and the linked option was used to select everything linked to that vertex, which is the entire exterior mesh of the vertebrae. Following this, the Inverse option was used to select all the internal meshes that had been generated within the model internal cavity, which are vertices and edges decoupled from the rest of the object. Having selected them, any geometry was deleted with the delete option to clean the model and improve the printing process; subsequently, gaps were filled, and the surface was smoothed (Figs. 2 and 3).

The file was re-exported in STL format and printed on a Formlabs Form 1 3D printer that uses SLA (stereolithography) technology with UV light to solidify a photopolymer resin according to the STL format commands. Using this type of printer provides great precision and detail to the 3D model, as the layer thickness is 25 to 200 μm (Fig. 4).

Figure 5 illustrates the methodology used to create the printed model.

To assess the feasibility and accuracy of the printed model, measurements were taken on the tomography (Philips multi-modality DICOM Viewer R3.0 SP15, Philips Medical Systems), on the STL format model before printing (Blender), and on the printed model, which were performed on a Keyence IM-7020 measurement system (Keyence, Mexico).

Results

Table 1 illustrates the main characteristics of the printed model.

Measurements were taken of the dimensions of the DICOM file, as well as of the STL file, and subsequently measurements of the printed model. The radiology, engineering, and medical teams were involved in all measurements. The largest horizontal axis of the transverse apophysis to the transverse apophysis, the largest anteroposterior axis of the vertebral body, the largest anteroposterior axis of the spinous process,

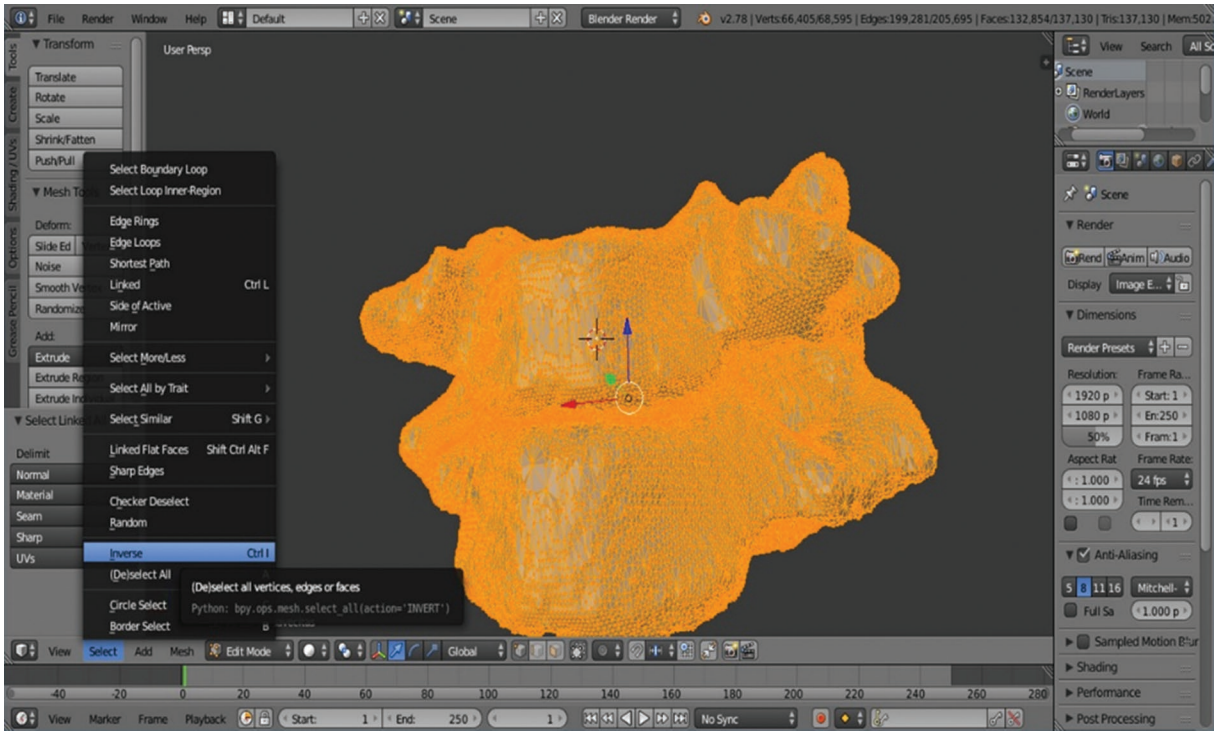

Figure 2. *The volume saved in STL format is loaded into Blender software, where model cleaning and enhancement begin. A mesh is created, and disconnected vertices and edges are removed to improve the printing process.*

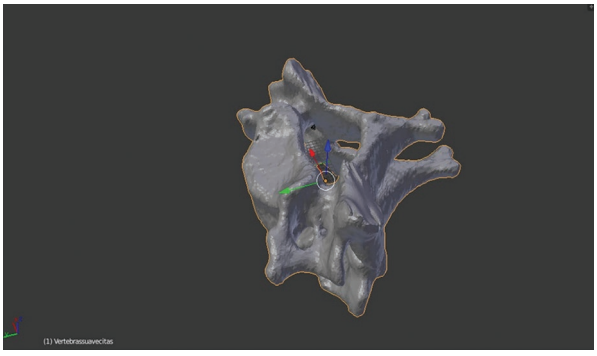

Figure 3. *In Blender, once the model is optimized, gaps are filled, and the surface is smoothed.*

Figure 4. *3D printed model.*

and the largest laterolateral axis of the spinous process were measured (Fig. 6). Comparisons were made between the CT image and the STL file, as well as between the printed model and the CT image. Table 2 illustrats the results of the measurements obtained.

Discussion

The advancement of 3D printing technology has enabled the creation of representative physical 3D models using a printer. This has significantly benefited the medical field with numerous applications in surgery, primarily in traumatology and orthopedics, maxillofacial, plastic, vascular, and neurosurgery, among others, revolutionizing the dynamics of medicine and biomedical engineering in patient treatment in an era increasingly focused on personalized medicine[5,6]. The applications of 3D printing in health care are not limited to surgical planning; they extend from educating

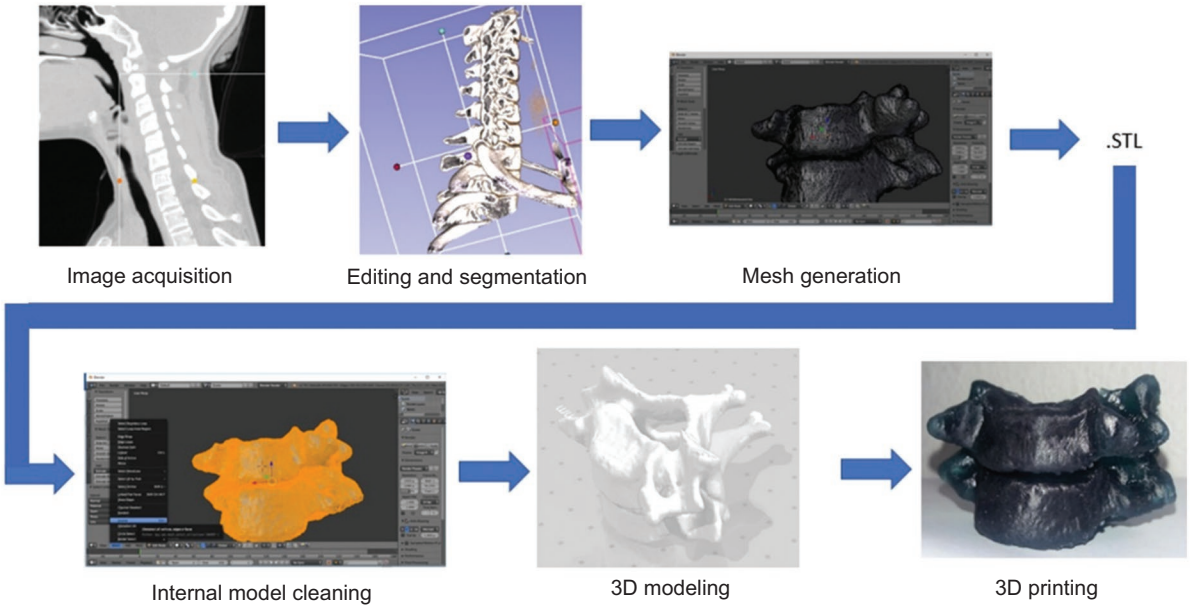

Figure 5. *Summary of the workflow for creating a 3D printed model.*

Table 1. Summary of the main characteristics of the printed model

Formlabs Form 1 (Formlabs, Boston, United States)	
Vertices	66.405
Faces	132.854
Printing and Resin Curing Time	10.5 hours
Printing Cost (UACJ Rapid Prototyping Lab)	231 mexican

patients and students to creating customized tools and prosthetics for each case[1,7].

There are various software options available to process medical images and generate 3D models for printing, some of which are free of charge, while others are paid. Free options include 3D Slicer and MeshLab, which offer a wide range of tools and functionalities for processing medical images and creating 3D models. However, these alternatives may have limitations in terms of technical support and updates, though they present a cost advantage for institutions with limited resources[8].

Philips IntelliSpace Portal[10] and Materialise Mimics are prominent options in the market but have the drawback of being paid software. To utilize these platforms and access their extensive advanced functionalities, analysis tools, and specialized technical support, it is necessary to acquire the corresponding license[9,10].

Nevertheless, when using these software options, additional programs are also required for mesh editing, which are used to refine and adjust the 3D models generated by both free and paid software. These programs are particularly important when using free solutions like 3D Slicer, as the resulting 3D models may have imperfections and require minor adjustments. The functionalities of these editing programs include scaling, moving, and rotating the piece, removing undesired areas through imperfect segmentation, closing gaps, smoothing areas with deformities, modifying the geometry of specific areas, and cutting the piece to create different sections[11].

The vertebral anatomical model used in this review was characterized by its low cost, making it a financially viable alternative. This model was designed as an educational resource for both students and patients undergoing surgical procedures. It was developed using the free software 3D Slicer and refined through the program Blender, known for being an open-source, free 3D creation platform. This approach to model creation demonstrates an efficient strategy based on the accessibility of cutting-edge technologies. The printing was done using the Form 1 desktop SLA printer (FormLabs, United States) from the rapid prototyping lab at University Autónoma de Ciudad Juárez, which is available to the general public. A final

Table 2. Measurement results of the 3D printed model, STL formats, and CT scan

	C6 CT	C6 STL	C6 3D	C7 CT	C7 STL	C7 3D
Largest horizontal axis	55.3 mm	55.337 mm	55.3183 mm	58.6 mm	58.739 mm	58.7144 mm
Vertebral body	14.2 mm	14.551 mm	14.8159 mm	14.1 mm	14.025 mm	14.2312 mm
Spinous process length	18.2 mm	18.283 mm	18.2266 mm	18.7 mm	18.790 mm	18.6458 mm
Spinous process width	8.5 mm	8.364 mm	8.3226 mm	8.9 mm	8.988 mm	8.9760 mm

3D: 3D printed model; STL: Model in STL format in Slicer; CT: Model in computed tomography (CT) scan.

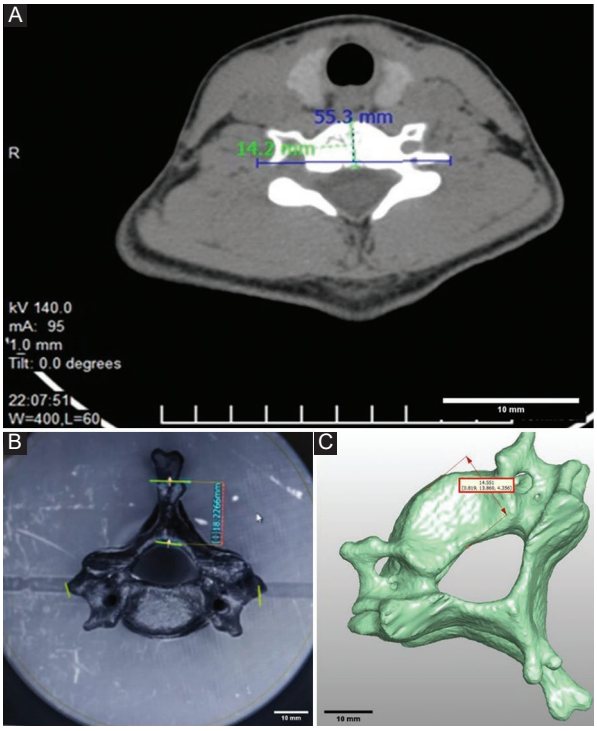

Figure 6. A: *measurement of the anteroposterior axis of the vertebral body using 3D Slicer software.* **B:** *measurement of the anteroposterior axis of the spinous apophysis on the 3D printed model using the Keyence IM-7020 measurement system (Keyence, Mexico).* **C:** *measurement of the horizontal axis from transverse apophysis to transverse apophysis in CT scan images.*

model of high precision and quality was obtained for approximately 200 Mexican pesos or 9 US dollars. The time taken to create this model, from obtaining the CT scan to the complete printing of the model, was approximately 15 hours.

The time needed to print a 3D medical model can vary depending on several factors, including the desired level of detail and the layer thickness used for printing. Thinner layers can capture finer details, but at the expense of longer printing times; for example, a sample piece printed with a layer thickness of 100 μm in standard resin takes approximately 2 hours to print. However, printing the same piece at 50 μm would take about twice as long, and printing it at 25 μm would require nearly 7 hours. The printing time can also affect production costs, as longer printing times may result in higher material costs and prolonged use of the printing equipment. Therefore, it is essential to consider the balance between printing time and the level of detail required when generating 3D medical models[12-14].

The level of precision and fineness that can be achieved in 3D printing depends on several factors, including the printing technology used, the resolution of the printer, the quality of the materials, and the complexity of the model. In general, stereolithography (SLA) and fused deposition modeling (FDM) are popular 3D printing technologies that can achieve high precision and fineness in printed models. SLA uses a high-precision laser to solidify liquid resin layer by layer, allowing for extremely fine print resolutions, up to 25 microns or even less in some cases. FDM uses a thermoplastic filament to build the model layer by layer and print quality can vary depending on the printer resolution and quality of the filament used. Most modern 3D printers have a print accuracy ranging from 0.1 mm up to 0.3 mm, and some high-end printers can achieve an accuracy of up to 0.02 mm or even less[12-15].

To implement this, the software and hardware requirements will largely depend on the goals of the 3D printing center; for example, the resolution and material requirements for creating a preoperative educational model for patients or medical students will be much lower than those for a preoperative model intended for a pediatric cardiothoracic surgeon to simulate the intraoperative environment of a complex congenital heart defect. 3D Slicer provides high resolution and an intuitive interface for free, primarily when there are significant Hounsfield unit differences between adjacent structures, such as bone and

contrast-enhanced structures like vascular structures in angiograms, to name a few. Werz et al.[16] described in a study that the creation of maxillary models using a desktop 3D printer for maxillofacial surgery practice by students and residents was more cost-effective than obtaining maxillary models from third parties, and categorized these models as "good" for simulating and practicing certain surgical procedures[16,17].

The required model size will also help determine the necessary hardware; for example, a pediatric heart model is small enough to fit within the popular Form 1 or Form 2 desktop SLA printer (FormLabs, United States), but a full-size adult pelvis is not, and it would need to be printed in parts or use a larger capacity printer.

In the realm of 3D printing, various materials can be used depending on the printing technology used and the type of object to be printed. Common materials include polymers, such as polycarbonate (PC), polylactic acid (PLA), polyether ether ketone (PEEK), and polycarbonate urethane (PCU), which are also biocompatible[18,19]. Resins, on the other hand, are used in stereolithography (SLA) and digital light processing (DLP) printing technologies, with polyethylene glycol (PEG), poly(D, L-lactide) (PDLLA), poly-ε-caprolactone (PCL), and poly(propylene fumarate) (PPF) being some of the most widely used, and they are also biocompatible[18,20]. Additionally, 3D printing with metals, such as titanium, stainless steel, aluminum, copper, and gold has become popular, with titanium being the most used for 3D printing implants and customized prostheses[21-25]. Bioinert ceramics, such as alumina and zirconia offer high chemical stability, providing promising advantages for their use as implants in patients[26].

It is crucial to note that not all materials used in the 3D printing process are safe; even if not used as implants, handling models that generate resin residues or powders can pose a health risk if the necessary precautions and safety measures are not taken during the handling of these materials[27].

Regarding the Formlabs Form 1 3D printer, it employs an exclusive liquid photopolymer resin known as Formlabs Standard Resin, specifically formulated for use with the stereolithography (SLA) technology used in the above-mentioned printer. Its curing process is performed using a high-precision laser, resulting in the creation of parts with superior quality and resolution. Formlabs Standard Resin offers a combination of strength, rigidity, and durability, and there are other specialized resin varieties available for the Form 1 printer, such as flexible resins, transparent resins, and high-temperature resins[28,29]. In addition to its application in printing 3D models for educational purposes[30] and improving communication with patients, the use of 3D prints is experiencing significant growth in its use as tools for preoperative planning and the fabrication of prostheses, particularly in the fields of orthopedic and maxillofacial surgery. The utility of 3D printing has been demonstrated in total knee arthroplasty; current literature suggests that satisfactory clinical and radiological outcomes could be achieved with the help of 3D printing, even demonstrating greater precision in implanting an articular prosthesis[31-33]. In total hip arthroplasty, 3D printing technology has been shown to improve surgical efficiency, shorten surgical times, and reduce radiation exposure. This technology also offers new potential for the treatment of complex hip joint diseases, indicating that 3D printing has enormous potential in this area[3,34-38]. In hand surgery, its utility has been demonstrated in constructing patient-specific models for preoperative planning, designing patient-specific orthopedic and prosthetic devices, generating patient-specific hardware and prostheses, and applications in resident and student education[39]. In spinal surgery, it has shown practical value and has become popular as a reference for clinical education and diagnostic aid, as well as for improving communication between physician and patient and in the planning of surgical approaches, in addition to its utility as a reference for complex surgeries[40-45]. In maxillofacial surgery, it allows for better planning and preoperative training for procedures and pre-molding of plates[46,47]. Additionally, the use of 3D printing methods in orthognathic surgery offers the benefit of optimal functional and aesthetic outcomes, patient satisfaction, and precise translation of the treatment plan to the patient[48].

The use of 3D-printed models in plastic surgery is a new field, experiencing significant growth, particularly in the area of reconstructive surgery, with promising results in precise anatomic biomodels, surgical cutting guides for reconstruction, and the fabrication of patient-specific implants, which have a potentially immense future impact on the reconstruction of traumatic injuries, the development of facial and limb prostheses, as well as advancements in biological and synthetic implants[49–55].

In a review conducted by Tack et al., it was reported that most branches of reported studies are in orthopedic surgery, accounting for 45.1%, with knee surgery representing 30.7%, hip surgery 8.3%, shoulder

surgery 2.1%, and hand surgery 1.7%. Maxillofacial surgery accounts for a significant proportion, at 24.1%, followed by cranial surgery and spinal surgery, representing 12.7% and 7.4%, respectively[4].

When approaching a surgical patient, the surgeon is faced daily with the challenge of interpreting and working with two-dimensional images, from which they must diagnose, plan, and make surgical decisions, often requiring considerable skill and experience, especially with unique or complex diseases. Although the objective is usually achieved, communication within the surgical team can be inefficient, as this skill is not always shared by all members, particularly the less experienced ones. Three-dimensionally-printed anatomical models are a useful tool for studying complex cases and planning preoperative strategies, such as tool selection and surgical approach organization. Additionally, they can serve as surgical guides and for preoperative training of residents, as well as for preoperative education of the patient and their family. The visual feedback provided by these models can also improve effective communication with patients and their families, which is especially important when personalized prostheses are required to repair anatomical defects with the greatest precision possible[30,56].

In the plastic and reconstructive surgery service, as well as in the maxillofacial surgery service, we have used this algorithm over the past few years for the planning and execution of reconstructive surgeries, particularly in head and neck reconstruction (Fig. 7), where the implementation of a 3D-printed model of the patient's bone structure for pre- and intraoperative planning of a free fibula flap has reduced risks and costs in our center. Another illustrative example of a model prepared for subsequent 3D printing is shown in figure 8. Through the use of multiple tools available in Blender, it is possible not only to segment and isolate specific bone structures but also to select a preferred bone segment for subsequent three-dimensional printing. This approach allows for greater customization and adaptability in the generation of anatomical models, thereby optimizing the surgical planning process and the production of personalized prostheses.

Given the growing popularity of 3D printing in the medical field, question arises as to whether this technology truly provides added value, or superior benefits vs conventional imaging or computer simulation during the surgical process. In a review[4], considering all applications of 3D printing, it was found that it reduced surgical time in 46% of studies. In 76% of reports, it

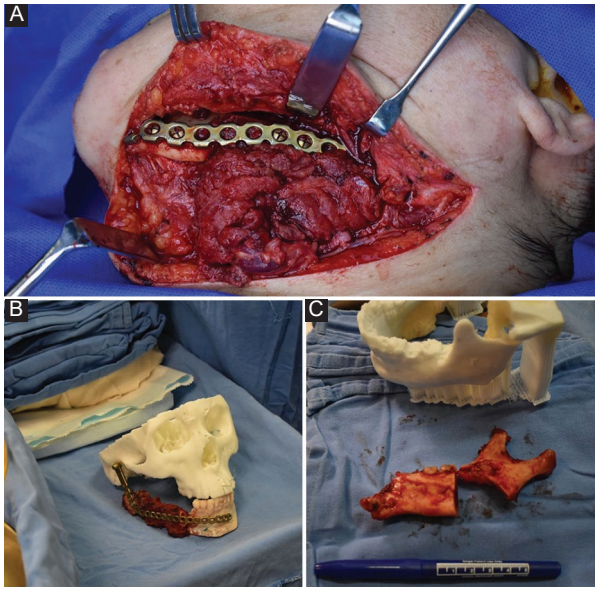

Figure 7. A: *3D printed model of the facial skeleton for pre- and intraoperative planning during patient reconstruction using a free fibula flap and a reconstruction plate.* **B:** *free fibula flap with reconstruction plate after placement and fixation in the patient's mandibular defect.* **C:** *3D printed model used for planning the partial resection of the mandible, as well as for pre-contouring the reconstruction plate. The model high precision is evident vs the resected piece.*

is mentioned that printing had good accuracy, and 72% reported improvement in outcomes. Studies demonstrate a reduction in surgical time when 3D prints are used for implant modeling, preoperative planning, creation of personalized implants, and as surgical guides. Additionally, shorter fluoroscopy times have been reported in thoracic spine surgery, and reduced use of contrast media and fluoroscopy in abdominal aortic aneurysm repair and cardiovascular surgery in cohorts where 3D-printed anatomical models were used as preoperative preparation[56–58]. However, the use of this technology in medicine involves high costs: 33% of the articles report that this technology is more expensive[4]. Depending on the existing infrastructure, creating an in-house center can be very costly and requires expertise that is difficult to find, often making it an unviable initial option for small medical centers.

Except for image acquisition, outsourcing is an option for the remaining steps of the 3D printing workflow. Currently, there is no software available that can integrate all the necessary processes for creating 3D models from medical images. Although various specialized tools exist for each stage of the process, their integration has been limited by the lack of a comprehensive solution. Nonetheless, some companies

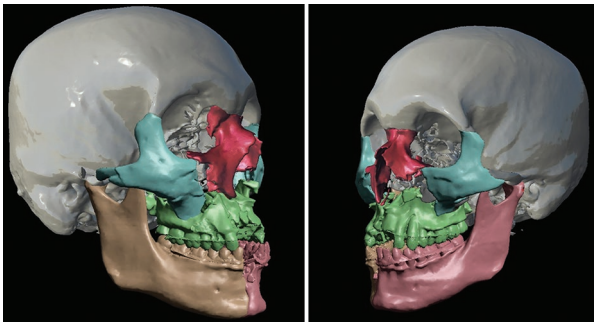

Figure 8. *Anatomical model specifically prepared for 3D printing, representing a patient with panfacial fractures. This model has been generated for use in the surgical planning of these fractures. It will facilitate spatial visualization and understanding of anatomical complexity, which is crucial for precise surgical intervention planning.*

offer services that allow for all processes, from obtaining medical images to printing the final model, to be performed. Examples include 3D Systems (United States) and Materialise (Belgium), which offer these services at a medical grade, including DICOM conversion, segmentation, and printing all in one, though their cost often reaches several thousand dollars[3,12]. Moreover, outsourcing services adds complexity to project management. The transfer of data and sensitive medical information can also pose challenges related to patient safety and privacy.

Despite this, the use of 3D models in certain surgical scenarios reduces surgery times and could imply a financial benefit that justifies the investment in a printing center, for which prospective studies are needed to estimate these figures more clearly[5,8].

Conclusion

The proposed method allows for the fabrication of 1:1 scale models of bone structures with high precision and detail. Using a computed tomography scan and the patient's anatomy, we designed and manufactured a 3D-printed model. The methodology is low-cost and very easy to perform. This study is valuable on multiple levels, as it not only documents feasibility and accuracy but also inspires other researchers in terms of study design and technique by establishing tangible workflows.

Based on the parameters obtained in the results analysis, the design of a 3D-printed model from anatomical images of bone tissue using available web software represents a viable option for preoperative use, especially in selected cases such as complex, rare, and high-risk surgeries, in which the cost-benefit of adding 3D printing is truly feasible and cost-effective. Technological advancements have driven exponential development in the field and a significant reduction in costs. Applications in medicine have been largely described in case reports; although more complex studies continue to emerge, further research focusing on clinical benefits is needed to design guidelines.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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ORIGINAL ARTICLE

Elastofibroma Dorsi: experience of a single center

Elastofibroma dorsi: experiencia en un centro

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Abstract

Objective: *Elastofibroma dorsi (ED) is a rare benign tumor located in the subscapular region. The aim of this study was to evaluate our clinical findings, surgical approach, and management of ED patients based on single-center data with the relevant literature.* **Method:** *A retrospective evaluation was conducted on 20 patients who were operated on for ED.* **Results:** *Of the 16 (80%) female patients and 4 (20%) male patients, the main complaint was swelling (80%), and 10 cases (50%) had unilateral involvement. All patients were operated on using standard surgical procedures. Despite a long follow-up period (6-53 months, mean of 26.6 months), no recurrences were observed. Two patients (10%) required simple needle aspiration due to post-operative seroma, and one patient, due to infection, required evacuation (5%).* **Conclusion:** *Although rare, ED should not be overlooked in patients with swelling in the back region. Our data suggests that surgery can be safely performed in such patients after a clinical and radiological diagnosis of ED has been established.*

Keywords: *Elastofibroma dorsi. Clinical presentation. Diagnosis. Follow-up. Treatment.*

Resumen

Objetivo: *Evaluar los hallazgos clínicos, el enfoque quirúrgico y el manejo de los pacientes con urgencias a partir de los datos de un solo centro y la literatura relevante.* **Método:** *Se realizó una evaluación retrospectiva de 20 pacientes que fueron operados de ED.* **Resultados:** *En los 16 (80%), pacientes del sexo femenino y cuatro (20%) del sexo masculino, la queja principal fue la tumefacción (80%) y 10 casos (50%) tuvieron afectación unilateral. Todos los pacientes fueron operados utilizando procedimientos quirúrgicos estándar. Con un largo periodo de seguimiento (6-53 meses, media de 26.6 meses), no se observaron recurrencias. Dos pacientes (10%) requirieron aspiración con aguja simple por seroma posoperatorio y un paciente (5%) requirió evacuación por infección.* **Conclusiones:** *Aunque es raro, el ED no debe pasarse por alto en pacientes con hinchazón en la región de la espalda. Nuestros datos sugieren que la cirugía se puede realizar de manera segura en estos pacientes después de haber establecido el diagnóstico clínico y radiológico de ED.*

Palabras clave: *Elastofibroma dorsi. Presentación clínica. Diagnóstico. Seguimiento. Tratamiento.*

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Introduction

Elastofibroma dorsi (ED) is a benign lesion of unknown pathogenesis that is most often located in the subscapular or pericapsular region but has also been reported in rare regions such as the deltoid, ischial, olecranon, gluteus maximus muscle, stomach, mediastinum, omentum, and tricuspid valve[1,2]. Although ED is usually slow-growing and asymptomatic, the diagnosis of ED is important because it may mimic malignant tumors of the thoracic wall[1]. Some patients may experience back pain and limited shoulder mobility[1,3]. ED etiology is thought to include tissue responses to trauma or vascular damage, ultimately leading to the formation of a mass characterized by infiltration of adipocytes and deposition of abnormal collagen and elastic fibers.

The common approach for ED is surgical excision when the tumor is < 5 cm or symptomatic[4,5]. However, due to the lack of a comprehensive series examining the diagnosis and treatment of ED, opinions vary on how to manage the disease. In this study, we present and discuss the clinical, radiological, and surgical findings of ED patients who underwent surgery at our clinic in light of current literature.

Material and methods

The study was approved by the Clinical Studies Ethics Committee of Tokat Gaziosmanpasa University Faculty of Medicine (Approval No. 22-KAEK-097), and all steps were carried out in compliance with the Declaration of Helsinki. Twenty patients who were diagnosed with ED at Tokat State Hospital and underwent surgery at our clinic between 2007 and 2022 were included in the study. Data from these patients were retrospectively evaluated in relation to demographic information, profession, complaints, presence of local recurrences, and follow-up and post-operative observations.

Patients with signs of swelling in the subscapular region underwent a physical examination followed by a magnetic resonance image (MRI) to evaluate the tumor's position and its relationship with surrounding tissue (Fig. 1A and B). No diagnostic biopsies were performed before surgery. Any post-operative recurrences or other anomalies were evaluated using ultrasonography.

All patients underwent marginal resections of their tumors under general anesthesia. In the prone position, an incision was made along the border of the scapula, and the mass was meticulously resected from the thoracic cage and subscapular area by blunt and sharp dissection. Bilateral cases were operated on in a single session. Immobilization of the shoulder, hemovac drainage, and garments (elastic bondage) were used in all patients. Hemovac drains were removed on the 3rd post-operative day.

For the evaluation of pre-operative and post-operative pain, the Numerical Rating Scale (NRS) was used. NRS is an assessment in which patients rate their pain on a scale of 0 to 10, with 0 being no pain and 10 being the worst pain. This scale is applied by the patient verbally or in writing.

Results

Sixteen of the study patients (80%) were female, and 4 (20%) were male. Swelling and back pain were the main complaints in 80% of patients, and a visual mass was observed in all patients in the subscapular region during anterior flexion of the arm (Fig. 1B). Limited shoulder mobility was observed in twelve patients (30%), and four (20%) were asymptomatic. An opening snap was observed in two patients (10%). The mean age was 61 years (with an overall age range of 41-74). Bilateral tumors were present in ten patients (50%), and unilateral lesions were more common on the right side (60%) (Table 1). Excisional surgery was performed on all patients, and tumors were completely removed (Figs. 2A and B).

Although the follow-up period was lengthy (6-53 months, mean of 26.6 months), no recurrences were observed. Two (10%) patients required simple needle aspiration of post-operative seroma, and 1 patient (5%) needed evacuation due to infection.

Discussion

ED was first described in 1959 by Jarvi and Saxen and has since been reported in 1961[6,7]. ED is a rare and benign soft-tissue tumor that typically occurs between the latissimus dorsi and serratus anterior muscle groups in the subscapular region. The tumor is firmly attached to the thoracic wall between the sixth rib and the eighth[8]. It is controversial whether ED is a true tumor, and its etiology is considered to be multifactorial. Recent studies suggest that the incidence of ED may be higher in individuals who engage in

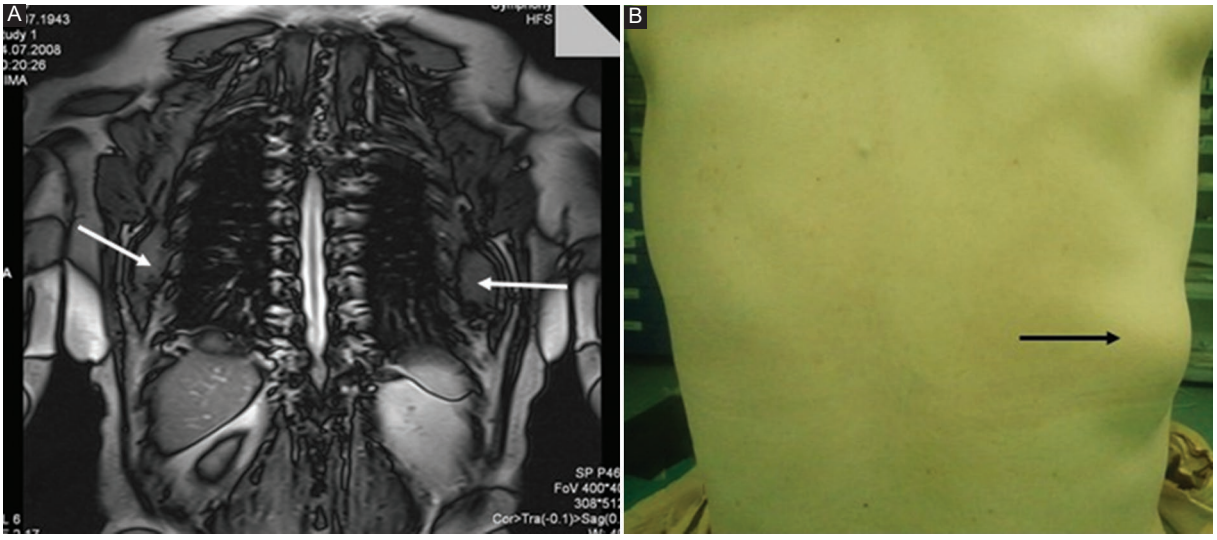

Figure 1. A: *T1-weighted coronal magnetic resonance image of ED in a case with bilateral involvement (white arrows).* **B:** *view of ED in the lower corner of the scapula (clearly visual with anterior flexion of arm black arrow).*

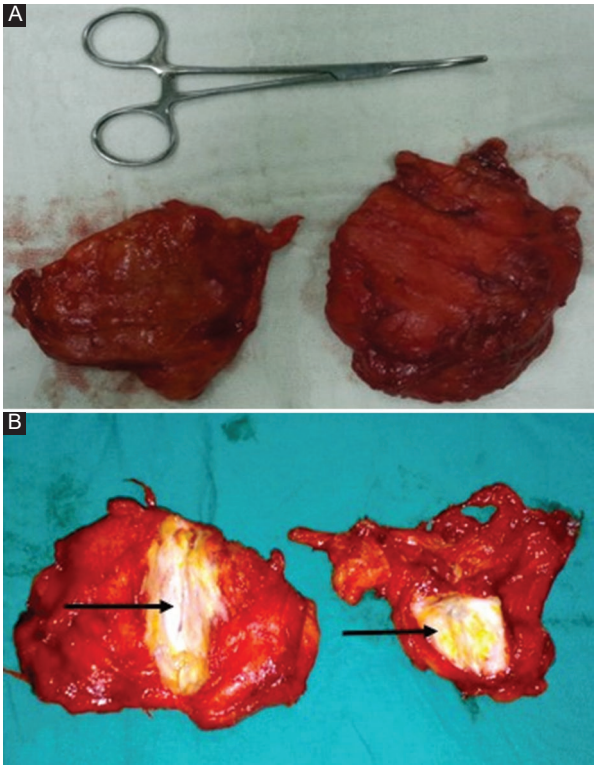

Figure 2. A: *macroscopic view of bilaterally excised ED tumor; rubbery solid mass with undefined borders.* **B:** *cut surface of tumor; white-gray rubbery tissue containing yellow fatty islands (black arrows).*

physical work that involves trauma to this area, but it has been reported in such regions as mediastinum and omentum, seemingly contradicting this theory[1]. Genetic anomalies, including mutations in the Xq12-q22 region and chromosome 19, may play a role in the development of ED, as some have suggested[9]. As was true in our study, ED is known to be more common in females, especially those over 55 years of age[10]. In elderly females, reactive fibromatosis and secondary degeneration of elastic fibers due to vascular insufficiency have been proposed as another theory for etiology, but it has also been reported in young individuals[11].

ED is typically asymptomatic. However, when symptoms do occur, patients can experience swelling and pain in the subscapular region and limited shoulder mobility, such as friction, stiffness, and an opening snap. Due to the diverse symptomatology of ED, as a differential diagnosis, cervical lesions and rotator cuff tears must be kept in mind[12]. In our study, visual mass from anterior flexion of the arm and back pain in the subscapular region were the main symptoms. The suggested association between ED and physical activity, along with more frequent involvement of the dominant limb, may explain the observation that ED arises more often on the right side. ED has commonly been reported as unilateral. However, half of the patients in our study had bilateral involvement, and there have also been reports of bilateral involvement up to 66% due to the asynchronous development of tumors[13].

The diagnosis of ED is usually based on clinical examination and radiological imaging. The mass can be more easily palpated when the arm is flexed anteriorly[13,14]. MRI is the preferred imaging modality as it can accurately determine the size of the tumor, its

Table 1. Clinic details of 20 patients operated on for elastofibroma dorsi

AGE	G	BP	Swelling	OP	LSM	Site	Profession	NRS (Pre-post)
74	F	+	+	+	+	B	Housewife	6-2
41	M	+	-	-	-	R-U	Policeman	4-0
68	F	+	+	-	+	B	Housewife	5-1
60	F	+	+	-	+	B	Housewife	7-2
50	F	+	+	-	-	B	Lawyer	4-0
54	F	+	+	-	+	R-U	Tailer	5-1
60	M	+	+	-	+	B	Officer	4-0
62	F	+	+	-	+	B	Housewife	7-2
59	M	-	+	-	-	L-U	Officer	0-0
66	F	+	+	-	+	R-U	Engineer	4-0
64	F	+	+	+	+	L-U	Teacher	5-1
66	F	-	+	-	-	B	Housewife	0-0
64	F	+	-	-	+	R-U	Housewife	7-2
66	F	-	-	-	-	R-U	Housewife	0-0
57	M	+	+	-	+	L-U	Barber	4-0
55	F	-	-	-	-	L-U	Nurse	0-0
64	F	+	+	-	-	B	Housewife	8-1
64	F	+	+	-	+	B	Housewife	6-1
60	F	+	+	-	-	R-U	Housewife	7-1
66	F	+	+	-	+	B	Housewife	8-2

BP: back pain; OP: opening snap; LSM: limited shoulder mobility; R: right; L: left; B: bilateral; U: unilateral; NRS: numerical rating scale (preoperative-post-operative).

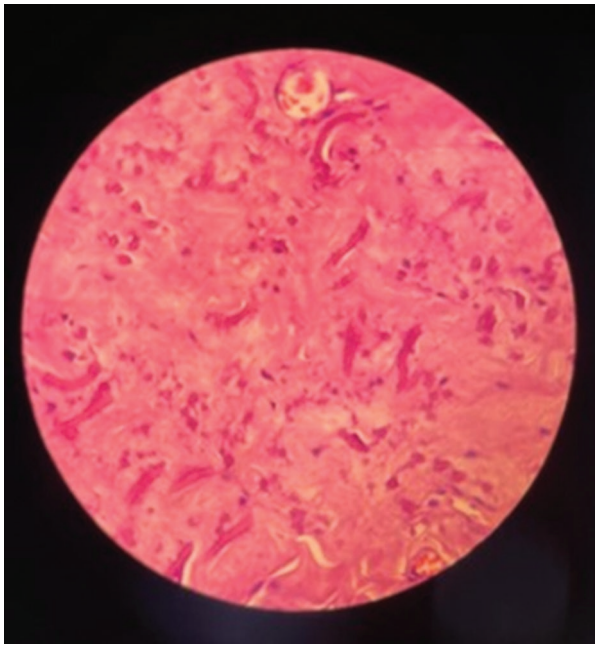

Figure 3. *Collegenius tissue with fragmented elastic fibers (H&E 100).*

borders, and its relationship with the surrounding tissue[8,15]. In a typical ED MRI, the interposed areas of decreased signal intensity also appear as low signal intensity on T2-weighted sequences[16].

The data regarding the value of diagnostic biopsies are not conclusive. Although some authors suggest that a fine needle or open biopsy may be useful in supporting the diagnosis, others argue that a basic clinical examination and radiological findings are sufficient[13]. In our study, patients were diagnosed based on physical examinations and typical MRI results, with no indication of suspected malignancy. Therefore, no biopsies were performed, as a complete resection of the tumors was proposed as the treatment approach. Some authors have also suggested surgery in asymptomatic patients to confirm the diagnosis or address possible malignant pathology[17,18]. All our asymptomatic patients (20%) refused follow-up and preferred surgery because of fear of cancer and cosmetic reasons. NRS is reliable in evaluating pain improvements in elderly patients[19].

The macroscopic appearance of tumors is typically poorly defined as a non-encapsulated mass with a rubbery consistency and a cut-surface containing white and yellow areas due to fibrous and fatty tissue. Histological examination has demonstrated it to be a collagenous tissue mixed with eosinophilic fragmented elastic fibers (Fig. 3).

Seromas and hematomas are the most common post-operative problems after ED resection, as they result from the dead space introduced during surgery and damaged adherent surrounding tissue while separating from the mass[5]. Measures such as bleeding control, placement of appropriate drains without suturing the skin, shoulder immobilization, and bandaging after the procedure can minimize these problems. Our post-operative complication rates were 10% for seroma and 5% for infection, which is in accordance with statistics from the literature[1]. In different series, seroma has been reported at 10-40%, which is probably due to tumor size leading to dead space[5,8]. Some authors suggest talc insufflation when drainage is over 50 cc. and persistence after 3 days[5]. Overall, our findings suggest that surgical resection is a safe and appropriate therapeutic approach for ED following a diagnosis based on physical examination and MRI.

Conclusion

ED is a subscapular pathology that pre-dominantly affects elderly females. While the diagnosis can be made based on clinical and radiological data, a biopsy or surgical excision may be advised if there is a suspicion of malignancy. Our findings suggest that marginal resection of the tumor is a safe treatment option with minimal morbidity that may be best suited for symptomatic patients or when malignancy is suspected.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for the analysis and publication of routinely acquired clinical data, and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they haven't used generative artificial intelligence, specifically, in the writing of this manuscript and/or in the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

The relationship between heart failure and smoking, and development of urethral stricture

Relación entre insuficiencia cardiaca, tabaquismo y desarrollo de estenosis uretral

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Abstract

Objective: *To evaluate the relationship between heart failure (HF), chronic obstructive pulmonary disease (COPD), and smoking with the development of urethral stricture (US) by examining the patients who underwent transurethral prostate resection procedure, with and without the development of US in their follow-ups.* **Methods:** *Among the patients who underwent transurethral resection of the prostate, 50 patients who developed US during their follow-ups formed group 1, while a total of 50 patients who did not develop US and were selected by lot formed group 2. The relationship between the patients' data on HF, COPD and smoking status and the development of US was investigated.* **Results:** *The mean number of cigarettes smoked was statistically significantly high in the group with stricture ($p = 0.007$). Furthermore, pulmonary function test parameters of patients such as forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC were found to be statistically significantly higher in Group 2 ($p < 0.001$, $p < 0.001$, and $p = 0.008$, respectively). In the logistic regression analysis, being a smoker was found to be the strongest predictor ($p = 0.032$).* **Conclusions:** *Our study concluded that smoking, HF, and COPD significantly increase the risk of developing stricture after transurethral resection of the prostate.*

Keywords: *Urethral stricture. Transurethral prostate resection. Smoking. Chronic obstructive pulmonary disease. Heart failure.*

Resumen

Objetivo: *Evaluar la relación de la insuficiencia cardiaca, la enfermedad pulmonar obstructiva crónica y el tabaquismo con el desarrollo de estenosis de uretra en pacientes sometidos a resección transuretral de próstata con y sin desarrollo de estenosis de uretra en su seguimiento.* **Métodos:** *Cincuenta pacientes que desarrollaron estenosis de uretra durante su seguimiento formaron el grupo 1, y 50 pacientes que no desarrollaron estenosis de uretra y fueron seleccionados por lote formaron el grupo 2. Se investigó la relación de los datos de los pacientes sobre insuficiencia cardiaca, enfermedad pulmonar obstructiva crónica y tabaquismo con el desarrollo de estenosis uretral.* **Resultados:** *La media de cigarrillos fumados fue significativamente más alta en el grupo con estenosis ($p = 0.007$). Además, se encontró que los parámetros de las pruebas de función pulmonar de los pacientes, como FEV1, FVC y FEV1/FVC, eran significativamente más altos en el grupo 2 ($p < 0.001$, $p < 0.001$ y $p = 0.008$, respectivamente).* **Conclusiones:** *El tabaquismo, la insuficiencia cardiaca y la enfermedad pulmonar obstructiva crónica aumentan significativamente el riesgo de desarrollar estenosis después de una resección transuretral de próstata.*

Palabras clave: *Estenosis uretral. Resección transuretral de prostata. Tabaquismo. Enfermedad pulmonar obstructiva crónica. Insuficiencia cardiaca.*

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Introduction

The incidence of urethral stricture (US) is estimated to be 0.3%, and it is more common in men over 55 years of age[1,2]. The development of iatrogenic US took the first place with a high rate of 45% as a result of the increase and widespread use of diagnostic and therapeutic endourological approaches to urological diseases in recent years[3].

Transurethral prostate resection (TURP) is the most important of these endoscopic urethral approaches. TURP is the most well-known, common, and gold-standard surgical treatment of benign prostatic hyperplasia[4]. US is one of the most common late complications of TURP, and its incidence has been reported as 13% in the literature[5]. According to the results of the patient follow-ups in the studies, most of the patients who developed US after transurethral surgery were observed to make a visit within the first 6 months, and the localization of the stricture was generally reported as the bulbar urethra[6,7].

When we look at the pathogenesis of stricture, leakage of urine into the subepithelial area after damage to the urethral epithelium for any reason has prognostic importance. Urine leaking into the subepithelial area triggers fibrotic processes through corpus spongiosum sinusoids and dense connective tissue intermediates[8].

Oxygen is required as a precursor in all stages of wound healing. Moreover, the hypoxic state is a factor that plays a role in the execution of all of these processes through the hypoxia-inducible factor-1 (HIF-1) signaling pathway[9]. Abnormal wound healing caused by excessive accumulation of extracellular matrix elements by fibroblasts and myofibroblasts in the wound area is called fibrosis. In tissues where fibrotic healing begins to be observed, the tissue becomes hypoxic as a result of decreased vascular density. Studies indicate that the development and progression of fibrosis are associated with hypoxia, that is, profibrotic genes activated by HIF-1α[10,11].

There should be a balance between the need for oxygen and its transmission to maintain physiological events in the body. The two main organ systems responsible for the delivery of oxygen to the body and maintaining homeostasis are the respiratory and the cardiovascular systems. Abnormal functions of either of these two would lead to the development of hypoxemia and its harmful consequences[12].

Heart failure (HF), chronic obstructive pulmonary disease (COPD), and smoking are comorbidities that cause ventilation/perfusion mismatch systemically. These conditions can cause hypoxemia in systemic arterial blood and microvascular areas. The negative effects of smoking on wound healing were first shown in a study conducted in 1977[13]. In a retrospective study in which 3500 cases were examined, COPD has been emphasized to be a potential risk factor for wound dehiscence[14]. Especially in the older adult patient population, HF is considered responsible for the development of complicated wounds[15].

US which develops in patients who underwent TURP for bladder outlet obstruction is an important complication. We could not come across any study in the literature drawing attention to the relationship between this condition and HF, COPD, and smoking. However, studies show that smoking after surgeries such as radical prostatectomy and urethroplasty is a factor that leads up to the development of stricture[16,17]. Similarly, COPD and cardiac pathologies were shown to increase the relapse rate of it after internal urethrotomy[18].

Based on all this information, it was aimed to evaluate the relationship between HF, COPD, and smoking with the development of US by examining the patients who underwent TURP procedure, with and without the development of US in their follow-ups.

Materials and methods

Study population

This study was conducted in the urology and chest diseases department of Afyonkarahisar Health Sciences University Hospital between February 2021 and August 2021. The study data were collected retrospectively after obtaining the ethical approval (2011-KAEK-2 2021/2) for the study from the Clinical Research Ethics Committee of Afyonkarahisar Health Sciences University. It was conducted in accordance with the principles of the Declaration of Helsinki. The purpose and the study process were explained to the patients in detail, and then written informed consent was obtained from each patient.

Among the 834 patients who underwent TUR-P between 2017 and 2021, 102 patients did not attend their follow-up visits for at least 6 months after the operation. Seventy-eight patients were excluded from the study considering the stated exclusion criteria. During

the follow-up, 32 patients who underwent traumatic catheterization due to urinary retention or severe low urinary tract symptoms (LUTS), urethra dilatation, percutaneous cystostomy, complicated urethral stenosis, and prostatic urethra or meatus stenosis were excluded from the study. Among the remaining 622 patients, penile or bulbar urethral stenosis was detected in 63 patients as a result of diagnostic evaluations performed with cystoscopy during their follow-up. Our stenosis rate was found to be 10.1% in patients who had regular check-ups and had a known medical history. Among these patients, 50 patients were selected using the randomizer.org system. Among the remaining 559 patients, 50 patients were randomly selected as the control group, again using the randomizer.org system.

History of following conditions as pelvic radiotherapy, neurogenic bladder, bladder cancer, US before TURP, bladder stones, urethritis with a definitive diagnosis, lichen sclerosus, high-energy pelvic trauma/fracture and urethral anomaly (Hipospadias etc.), and malignancy in TURP pathology and diagnosis of prostate cancer were the exclusion criteria.

Application

Anamnesis, detailed physical examination, DRM, UFM, PVR and prostate volume measurement with transabdominal ultrasonography, serum PSA, TIT, urine culture, chest X-ray, electrocardiography, complete blood count, blood biochemistry analysis, coagulation tests, and viral marker tests were evaluated preoperatively for all patients who underwent transurethral resection of the prostate. Anaesthesia, cardiology, and pulmonology consultation reports in which patients were consulted for pre-operative evaluation purposes were noted.

Name-surname, age, height, weight, smoking status (packs/year), pre-operative UFM data, IPSS and QoL data for symptom severity, PVR, and prostate volumes (cm^3) evaluated by transabdominal USG of the participants were recorded in the individual files of the patients. Furthermore, ACC/AHA stage, scores of mMRC scale, and COPD CAT were created in line with the verbal responses from the patient used to predict the level of comorbidities such as HF and COPD and information obtained from cardiology and chest diseases department consultation reports preoperatively. Pulmonary function testing (spirometry) and clinical evaluation results carried out by a pulmonologist were recorded.

All patients were selected from cases operated by three urologists, each with more than 100 TURP case experiences. In all operations, resection was routinely performed with an Olympus 26-Fr permanent current resectoscope and standard electrode (Olympus Winter and Ibe GmbH, Germany) under irrigation of saline (0.9% sodium chloride), and a bipolar plasma kinetic energy source was used. After the operation, a 22-Fr 3-way Rüsch brand catheter was inserted in all patients, and continuous bladder irrigation, started immediately with saline (0.9% sodium chloride) in a way that the urine color was clear, and was routinely continued until the morning of the 1st post-operative day. The catheters of the patients were removed between 3 to 6 days.

Patients' data on post-operative follow-up, infection status, storage symptoms, US status, UFM, PVR, and IPSS-QoL were recorded on their files. Internal urethrotomy was performed using a cold knife with a Storz 21-Fr Sacshe model optical urethrotome as a standard on patients who were found to have penile or bulbar US according to the diagnostic evaluations during their follow-ups. All patients evaluated in the stenosis group in the study had stenoses shorter than 2 cm and uncomplicated.

While 50 patients in whom penile or bulbar US was detected at least once in their follow-ups after the TURP operation formed Study Group 1, 50 patients selected by lot among the patients in whom no stricture was detected formed Study Group 2.

Statistical analysis

Statistical analysis of the study data was performed using the IBM Statistical Package for the Social Sciences version 15.0 program. The Kolmogorov–Smirnov test was used to check whether the variables had a normal distribution. In the comparison of paired groups, Student's t-test was used for normally distributed parameters and the Mann–Whitney U-test was used for the parameters which did not have normal distribution parameters. The Chi-square test or Fisher's Exact test was used for the evaluation of multi-well crosstabs. In multivariate analysis, independent predictors of stricture development were examined with the enter method and binary logistic regression analysis using possible factors identified in previous analyzes. The Hosmer–Lemeshow test was used for model fit. Results with a type 1 error level of $p < 0.05$ were considered statistically significant.

Results

The quantitative parameters of the patients such as age, body mass index (BMI), and number of cigarettes smoked (packs/year) evaluated before the operation was given as mean and standard deviation, and were compared for Group 1 and Group 2, and the results are presented in Table. No statistically significant difference was found between the ages of the patients in both groups (p = 0.368). While the mean BMI value of the patients in group 1 was 27.43 ± 3.17 kg/m^2, it was 25.95 ± 2.78 kg/m^2 in group 2, and the mean BMI value was found to be statistically significantly higher in the group with stricture. Similarly, while the mean number of cigarettes smoked in group 1 was 23.78 ± 18.2 packs/year, it was 13.94 ± 19.94 packs/year in group 2 and the mean number of cigarettes smoked was found to be statistically significantly higher in the group with stricture (p = 0.007) (Table 1).

Data that are considered to be predictors of LUTS such as prostate volume, Qmax, PVR, IPSS, and QoL evaluated preoperatively, and surgery-related variables such as duration of operation and duration post-operative catheter stay were given as mean and standard deviation and were compared for Group 1 and Group 2, and the results are presented in the Table. When the table is examined, there was no statistically significant difference between the two groups in terms of prostate volume, Qmax, IPSS, QoL, duration of operation, and post-operative catheter stay parameters (p = 0.126, p = 0.059, p = 0.102, p = 0.555, p = 0.102, and p = 0.571, respectively). The PVR value measured before the operation in group 1 was found to be significantly higher than in group 2 (p = 0.007) (Table 1).

The staging of patients in terms of HF was performed according to the ACC/AHA system, a classification based mainly on symptoms and exercise capacity. Eighteen patients with no abnormality in their cardiac structures and no risk factors for the development of HF were not included in this classification (Table 2). While Stage A and Stage B patients were asymptomatic patients in terms of HF, with 18 patients not included in this classification, HF symptoms were observed in Stage C and Stage D patients. Symptomatic and asymptomatic patient groups in terms of HF were examined in the crosstabs with Group 1 and Group 2. While the rate of symptomatic HF was 56% in Group 1, it was 26% in Group 2. The patients with symptomatic HF were determined to have a statistically significantly higher rate of stricture development, which was found with the Chi-square test (p = 0.002) (Table 3). The data obtained from the mMRC scale and CAT scores, which evaluate the pulmonary functions of the patients before the operation, and the pulmonary function testing parameters such as forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC

Table 1. Comparison of pre-operative and intraoperative data between groups

Patient data	Group 1 (n = 50)	Group 2 (n = 50)	p-value
	Mean ± SD	Mean ± SD	
Age (years)	67.94 ± 8.07	66.62 ± 8.16	0.368
BMI (kg/m^2)	27.43 ± 3.17	25.95 ± 2.78	0.015
Number of cigarettes (packs/year)	23.78 ± 18.2	13.94 ± 19.94	0.007
Prostate volume (cm^3)	63.68 ± 23.78	56.42 ± 23.19	0.126
Qmax (ml/sec)	7.88 ± 3.22	6.72 ± 2.75	0.059
PVR(cm^3)	152.06 ± 83.51	112.78 ± 66.94	0.007
IPSS	20.4 ± 5.22	22.04 ± 4.7	0.102
QoL	3.5 ± 0.99	3.66 ± 0.87	0.555
Duration of operation (min)	49 ± 17.78	43 ± 17.14	0.102
Duration of catheter stay (days)	3.76 ± 0.79	3.66 ± 0.71	0.571

BMI: body mass ındex; Qmax: maximum urine flow rate; PVR: post-void residual; IPSS: ınternational prostate symptom score; QoL: quality of life; Mean ± SD: mean ± standard deviation.

Table 2. ACC/AHA staging of patients

Number of Patients	None	Stage A	Stage B	Stage C	Stage D	Total
Number of Patients	18	26	15	32	9	100

Table 3. Distribution of two groups according to HF symptom status and Chi-square test

HF symptom status	Group 1 (n = 50)	Group 2 (n = 50)	Total	p-value
No symptoms	22	37	59	0.002
With symptoms	28	13	41	
Total	50	50	100	

HF: heart failure.

were given as mean and standard deviation and were compared for Group 1 and Group 2, and the results are presented in the Table. The mean mMRC scale and CAT scores of the patients in group 1 were found to be statistically significantly higher than those in group 2 (p = 0.003, p = 0.002, respectively). FEV1, FVC, and FEV1/FVC values, on the other hand, were found to be statistically significantly lower in Group 1 compared to Group 2 (p < 0.001, p < 0.001, p = 0.008, respectively) (Table 4).

When the PFT results were evaluated, 35 out of 100 patients were considered to have COPD due to the detection of FEV1/FVC <70% after bronchodilator. Groups of patients with and without COPD were examined in crosstabs with Group 1 and Group 2. While the rate of COPD was 48% in Group 1, it was 22% in Group 2. The patients with COPD were determined to have a statistically significantly higher rate of stricture development, which was found with the Chi-square test (p = 0.006) (Table 5).

When the group that developed stricture in the post-operative follow-up was examined, the mean time to develop stricture was found to be 7.04 ± 3.75 months. When the relationship between being a smoker, HF symptom status, and the status of having COPD and the duration of stricture development was evaluated, no statistically significant finding was found.

Binary logistic regression analysis was used to identify the possible independent predictors of stricture development that contributed the most to the outcome. Being a smoker, the number of cigarettes smoked, BMI value, pre-operative PVR, symptomatic HF, scores of mMRC scale and CAT, FEV1/FVC, and COPD status were used as predictors. The model predicting the development of stricture was significant ($\chi 2(8) = 4.26$, p = 0.832) and explained 32.7% of the variance (Nagelkerke R2 = 0.327). The model correctly predicted 70% of non-relapsed and 72% of relapsed (71% overall). Smoking, the number of cigarettes smoked, and the pre-operative PVR value were important predictors for the development of stricture. Being a smoker was found to be the strongest predictor among these parameters in the model (p = 0.032). One unit increase in the number of cigarettes smoked increased the risk of stricture by 2 units (Table 6).

Table 4. Comparison of data evaluating patients' respiratory functions

Respiratory function data	Group 1 (n = 50)	Group 2 (n = 50)	p-value
	Mean ± SD	Mean ±SD	
mMRC	1.07 ± 1.54	0.68 ± 1.25	0.003
CAT	14.6 ± 10.06	8.66 ± 7.98	0.002
FEV1 (%)	71.02 ± 22.69	87.36 ± 15.19	<0.001
FVC (%)	83.18 ± 16.31	95.84 ± 10.14	<0.001
FEV1/FVC (%)	66.6 ± 10.84	72.5 ± 6.69	0.008

mMRC: modified medical research council; CAT: COPD assessment test; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; Mean ± SD: mean ± standard deviation.

Table 5. Distribution of two groups according to COPD status and Chi-square test

COPD status	Group 1 (n = 50)	Group 2 (n = 50)	Total	p-value
No COPD	26	39	65	0.006
With COPD	24	11	35	
Total	50	50	100	

COPD: chronic obstructive pulmonary disease.

Table 6. Predictors for the development of stricture

Risk factor	Development of stricture	
	RR (95% CI)	p-value
Smoking	7.39 (1.18-46.18)	0.032
Number of cigarettes	0.94 (0.88-0.99)	0.042
BMI	1.18 (0.99-1.39)	0.052
PVR	1.00(1.00-1.01)	0.042
Symptomatic HF	4.66 (0.39-54.58)	0.220
mMRC	0.79 (0.29-2.10)	0.638
CAT	1.06 (0.93-1.21)	0.335
FEV1/FVC	0.95 (0.85-1.06)	0.377
COPD	1.11 (0.15-7.97)	0.918

BMI: body mass ındex; PVR: post-void residual; HF: heart failure; mMRC: modified medical research council; CAT: COPD assessment test; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; COPD: chronic obstructive pulmonary disease.

Discussion

The development of US after TURP has been reported in the literature in recent years, in the range of approximately 9.8-13%[5,19]. Prevention of stricture development after diagnostic or therapeutic endourological procedures or reduction of high relapse rates after transurethral treatments such as internal urethrotomy carried out on advanced US is the main

goal of the US approach, considering the high treatment costs[20].

Both adequate oxygenation of tissue and hypoxia are necessary factors for normal wound healing[21]. The hypoxic environment at the beginning of wound healing plays an early stimulating role in tissue repair and angiogenesis through HIF-1[9,21]. However, the finding that the proliferative rate of fibroblasts increases by 71% if the hypoxic environment lasts for more than 72 h is thought-provoking for fibrotic pathologies[22]. Recent studies have shown that profibrotic genes associated with HIF-1a, that is, hypoxia-induced, are effective in the development of fibrosis[23]. More studies are being conducted on HIF-1α inhibition for the treatment and prevention of fibrotic diseases[24].

Hypoxia and hypoxemia describe different conditions. Hypoxemia refers to a decrease in partial oxygen pressure in the blood, while hypoxia refers to decreased tissue oxygenation. Hypoxemia might lead to hypoxia as a result. The most common cause of hypoxemia is ventilation/perfusion mismatch and it benefits from complementary oxygen therapies[12,25].

Based on these considerations, in our study, we aimed to evaluate the relationship between HF, COPD, and smoking with the development of US by making a comparison between the patients with US development in their follow-ups after the TURP operation and those without. HF, COPD, and smoking are comorbidities that cause ventilation/perfusion mismatch systemically. These conditions can cause hypoxemia in systemic arterial blood and microvascular areas and thus hypoxia at the tissue level.

There are studies on medical treatment options that can prevent the development of US in the literature. However, there is no method that was accepted and included in the treatment routine yet.

In their study in 2014, Ateş et al. evaluated the effectiveness of hyperbaric oxygen therapy (HBOT) on hypospadias cases that they treated with the help of a buccal mucosal graft. The success rate was found to be significantly higher in the patient groups who were given HBOT after both the first surgery and the second surgery stages. They reported in their conclusion that HBOT can be used as an alternative method to increase the success of the procedure in these patients[26].

In an experimental study conducted in Ankara, Turkiye, the early administration of dexpanthenol to rats with urethral damage has been shown to significantly reduce inflammation and spongiofibrosis and it was suggested that it would be beneficial in preventing the development of US after urethral damage[27].

A US-based study suggested that the mechanism responsible for the development of US was urethral fibrosis resulting from altered or increased fibroblast activity within the tissue. In this study, the application of an antifibrotic agent mitomycin C in addition to internal urethrotomy was compared and it was resented as an alternative option for poor open surgery candidates and patients who require repeated multiple internal urethrotomy[28].

In the study conducted by Dalkılınç et al. in 2018, the effect of low molecular weight heparin (LMWH), which is mainly used as an anticoagulant, on the incidence of US in patients who underwent TURP operation was investigated since it was presented to have antifibrotic effects. Given the relapse and urethroplasty rates, the incidence of developing severe US was concluded to be less in those receiving anticoagulant therapy with LMWH[29].

In the literature review conducted, we did not come across any study that found a direct relationship between the development of US after TURP and smoking. In their study in which a total of 467 patients who underwent radical prostatectomy have been reviewed retrospectively, Borboroglu et al. indicated that smoking significantly increased the risk of vesico US development[17].

There are studies with different opinions about smoking among studies evaluating which factors could be associated with stricture relapse after urethroplasty. Some studies suggest that smoking increases the rate of stricture relapse after urethroplasty[16]. One of the important studies is the study by Whitson et al. in 2008. They, in their study, concluded that smoking was a predictor of failure in patients who underwent fasciocutaneous flap urethroplasty[30]. On the other hand, many studies, especially Kinnaird et al.'s study in which they evaluated 604 urethroplasty cases retrospectively, state that smoking is not associated with relapse[31].

There is also a similar difference of opinion on the relationship between relapse after internal urethrotomy and smoking. Aydemir et al., as a result of the retrospective analysis of the data of 94 patients, suggested that smoking increases relapse after internal urethrotomy[32]. On the contrary, Redon-Galvez et al. argued in a similar study that age, weight, smoking status, and cardiovascular risk factors did not have a significant effect on relapse after internal urethrotomy[33].

The mean number of cigarettes smoked in the group with stricture was statistically significantly higher than the control group in our study ($p = 0.007$). In the logistic regression analysis carried out to identify the possible

independent predictors of stricture development that contributed the most to the outcome, smoking was found to be the strongest predictor in the model (p = 0.032). One unit increase in the number of cigarettes smoked increased the risk of stricture by 2 units. The number of cigarettes smoked was also found to be high in patients with stricture who had a relapse after internal urethrotomy, but this difference was not statistically significant (p = 0.732).

Sinanoglu et al. suggested in their retrospective review of TURP data of 317 patients with different comorbidities that COPD was not a risk factor for the development of post-operative stricture[34]. In another study with a similar design, the minimum triple combinations of diabetes mellitus (DM), hypertension, coronary artery disease (CAD), and COPD comorbidities were determined to pose a risk in the development of stricture after internal urethrotomy[18]. The erectile dysfunction status of 41 patients with COPD was investigated in another study in which the severity of erectile dysfunction was observed to increase as the pulmonary function test parameters FEV1, FVC, and FEV1/FVC levels decreased[35]. Given that the penis and urethra are both supplied with blood by the internal pudendal artery, it was thought that there may be a connection between erectile perfusion and urethral ischemia.

In our study, COPD, as an independent comorbidity, was found in a higher number of patients in the group with stricture, which was statistically significant (p = 0.006). The mMRC scale and CAT test results evaluating the patients in terms of respiratory symptoms and severity of dyspnea were significantly higher in the stricture group (p = 0.003, p = 0.002, respectively). Levels of the pulmonary function test parameters FEV1, FVC, and FEV1/FVC levels were significantly lower in the stricture group (p < 0.001, p < 0.001, p = 0.008, respectively).

Sinanoglu et al. concluded in their study that comorbidities such as HT, DM, and CAD (Congenital Adrenal Hyperplasia) are risk factors for the development of US, especially in patients who underwent plasma kinetic TURP[34]. There are also studies showing that the same comorbidities are associated with the development of stricture after radical prostatectomy[17,18,32] and relapse after internal urethrotomy. In a study conducted by Ruutu et al., among the patients who underwent open heart surgery and had a short-term urethral catheter and did not develop mortality in their 1-year follow-ups, 16.6% of them were found to have US developed[36]. In another study, the severity of CAD has been found to be associated with the US development in patients who underwent cardiac angiography for acute coronary syndrome and had a urethral catheter placed[37].

In our study, patients were evaluated for HF using the ACC/AHA classification. After that, they were grouped as asymptomatic and symptomatic patients in terms of HF. The reason for this is that the hypoxemia picture, considered responsible for the pathogenesis in our study, was encountered only in symptomatic HF patients. When evaluated in this way, it was observed that there were many symptomatic HF patients at a statistically significant level in the group that developed stricture (p = 0.002).

In the literature, US has been observed to be detected in the first 6 months on average after TURP[6]. This period was 7.04 months in our study on average and was similar to the literature. There was no significant relationship between HF, COPD, smoking, and duration of stricture development.

Our study has some limitations. These include; the retrospective design of the study and the inability to perform histological examination because urethral tissue was not taken. In addition, smoking, COPD, and HF were evaluated using scales. Comorbidity studies detailed with physiometric and radiological imaging may contribute to the literature.

Conclusion

In our study, we concluded that smoking, HF, and COPD significantly increase the risk of stricture development after TURP. The symptom scores and each of the pulmonary function test parameters used in the diagnosis of COPD were determined to have a statistically significant relationship with stricture development. Among the possible independent predictors for stricture development, smoking was found to be the strongest predictor in the model.

Given these conclusions, it is believed that the hypoxemic picture should be closely monitored in the pre-operative, intraoperative, and post-operative periods in patients who would undergo TURP operation and remedial treatments and measures should be taken to reduce the rate of US development. Furthermore, patients who are planned for TURP and who are at high risk of developing US considering these factors can be provided more detailed information about the complications that might develop before the procedure, and they could be informed that they have a higher risk for this condition. Thus, despite the complications that might occur in the post-operative

period, higher patient satisfaction and a conscious patient profile can be achieved.

The implications of our study need to be supported by more randomized controlled studies and meta-analyses as required by evidence-based science.

Authors' contributions

K.T, A.D, O.G., and I.K. designed the study; K.T, K.U, A.B, and M.K. recruited the participants and collected the data; K.T, O.G., and I.K. performed the statistical analysis; K.T, A.D, and A.B interpreted the data; K.T. drafted the first manuscript; and all authors critically reviewed the paper.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study. This study was approved by the Local Ethics Committee (AFSU 2011-KAEK-2/2021/2) and was conducted in accordance with the ethical standards of the Declaration of Helsinki.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

Surgical resection and survival of clear cell renal cancer metastases to the pancreas

Resección quirúrgica y sobrevida de metástasis de cáncer renal de células claras a páncreas

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Abstract

Introduction: *Pancreas is considered one of the organs most frequently affected by recurrence after nephrectomy secondary to renal cell carcinoma reporting an incidence of 20%, 85% of these occur within the first 3 years.* **Objective:** *The objective of the study is to evaluate overall survival and disease-free survival in patients with renal cancer and pancreatic metastases who underwent surgical treatment.* **Methods:** *A retrospective cross-sectional study of patients with histological diagnosis of renal cancer associated with pancreatic metastasis was performed and included those treated by pancreatoduodenectomy or distal pancreatectomy during the period 1987-2020.* **Results:** *14 patients with pancreatic metastasis were included. Two groups of patients were obtained: those who underwent pancreatic surgery for metastasis and those who did not undergo surgical procedure. According to the location of the metastasis, 71.4% corresponded to a single location and 28.6% to multiple locations. 57.1% underwent Whipple and 42.9% distal pancreatectomy. Survival after the surgical procedure was 1150 days versus 499 days in non-operated patients.* **Conclusion:** *Pancreatic metastases due to RCC can be curable, improve morbidity, and increase disease-free survival with surgical treatment.*

Keywords: *Renal cancer. Metastasis. Whipple. Pancreas. Survival. Distal pancreatectomy.*

Resumen

Introducción: *El páncreas es considerado de los órganos más frecuentemente afectados por recurrencia después de la nefrectomía secundaria a carcinoma de células renales notificándose una incidencia de 20%, 85% de estas ocurren dentro de los primeros 3 años.* **Objetivo:** *Evaluar la sobrevida general y sobrevida libre de enfermedad en pacientes con cáncer renal y metástasis pancreáticas sometidos a tratamiento quirúrgico.* **Métodos:** *Se realizó un estudio retrospectivo transversal de pacientes con diagnóstico histológico de cáncer renal asociado a metástasis pancreática y se incluyeron aquellos tratados mediante cirugía de tipo pancreatoduodenectomía o pancreatectomía distal durante el periodo de tiempo 1987-2020.* **Resultados:** *Se incluyeron 14 pacientes con metástasis a páncreas. Se obtuvieron dos grupos de pacientes: sometidos a cirugía pancreática por metástasis y aquellos que no se les realizó procedimiento quirúrgico. De acuerdo a la localización de la metástasis 71.4% correspondía a ubicación única y 28.6% a ubicación múltiple. Al 57.1% se les realizó Whipple y 42.9% pancreatectomía distal. La sobrevida tras el procedimiento quirúrgico, fue de 1150 días vs. 499 días en no operados.* **Conclusión:** *Las metástasis a páncreas por CCR pueden ser curables, mejorar la morbilidad y aumentar la sobrevida libre de enfermedad con tratamiento quirúrgico.*

Palabras clave: *Cáncer renal, metástasis. Whipple. Páncreas. Sobrevida. Pancreatectomía distal.*

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Introduction

Metastases that commonly affect the pancreas correspond to renal cell carcinoma (RCC), melanoma, colorectal carcinomas, mammary carcinomas, and sarcomas[1].

RCC accounts for 90% of the different types of cancers that originate in the kidney, encompassing 10 different subtypes, of which clear cell renal cell carcinoma (CCRCC) is the most common and is associated with the highest mortality[2].

Metastasis of RCC is common, it is present in approximately 25% of patients[3], it can extend directly to the ipsilateral adrenal gland or to the adjacent musculature and, not often, to the liver, spleen, colon, and pancreas[4]. Focusing attention on the latter, clinically, secondary neoplasms affecting the pancreas are uncommon, representing 2-5%[1,5]. It is considered the seventh most common cancer in men and the ninth most common cancer in women worldwide, usually presenting at an average age of 65 years. It is important to diagnose RCC metastasis because it can manifest itself more than a decade after its initial presentation and diagnosis[1,5]. The pancreas is considered one of the organs most frequently affected by recurrence after nephrectomy secondary to RCC, with an incidence of 20-30%, 85% of which occur within the first 3 years after nephrectomy[1].

As for the clinical presentation, if the lesion is smaller than 2 cm and is well localized in the pancreas, it does not show clinical features that could be suspicious of metastasis to the pancreas. If the lesion is larger, the clinical manifestations are jaundice, weight loss, and pain[6]. Pancreatic lesions are localized after ultrasound, computed tomography (the most important method for making the pre-operative decision, usually a hyperdense lesion), routine magnetic resonance imaging, or positron emission tomography[7].

The diagnosis of certainty for CCRCC will be by nephrectomy or cytology, for which a fine needle aspiration biopsy guided by endoscopic ultrasound should be performed; often it is not necessary before surgery since the diagnosis is made with imaging studies and clinical history[7,8]. Histopathologically, CCRCC cells appear as large polygonal cells in clusters or single cells with abundant vacuolated or granular cytoplasm (glycogen and lipids in vacuoles) giving the appearance of “empty” or “clear,” nucleus with mild to moderate pleomorphism, prominent nucleolus and a thin capillary network. Immunohistochemically, it is positive for EMA, PAX-8 CD10, RCC, CD12, CD15, and MUC-1[9].

The current approaches for the treatment of metastatic CCRCC include immunotherapy with interferon-α, targeted therapy, or one of these therapies combined with metastasectomy[10], within the techniques used are pancreatoduodenectomy, distal pancreatectomy, total pancreatectomy, etc. The surgical strategy for metastatic pancreatic tumor has not been established[11], a decision must be made to achieve clear resection margins depending on the location of the tumor within the pancreas. Regardless of the site of recurrence, several reports have shown that complete metastatic clearance is the key to prolonged survival[12].

A median survival of 72 months has been reported for surgically treated patients, whereas those who did not undergo pancreatic resection had a median survival of only 10 months[13].

According to the literature, renal cancer occurs in very low proportion in the population, and even more so metastases to the pancreas from renal cancer. There are few case reports, as well as a series of studies at international level of metastasis of renal carcinoma to pancreas as well as the surgical treatment given to them. In the Mexican population, the evidence is null, which is why the study of our population is relevant. The aim of the present study is to evaluate overall survival and disease-free survival in patients with renal cancer and pancreatic metastases undergoing surgical treatment.

Methods

A retrospective cross-sectional study of patients with histological diagnosis of clear cell renal cancer associated with pancreatic metastasis was performed and included those who were treated by pancreatoduodenectomy or distal pancreatectomy type surgery during the time period 1987-2020 at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán.

Electronic and physical records were reviewed, as well as the clinical evolution registry (overall survival and disease-free survival) in all patients who underwent surgery for pancreatic metastasis due to clear cell renal cancer. Descriptive statistics were used including mean and ranges for quantitative variables as well as frequency and percentage for qualitative variables.

Table 1. Characteristics of the patients with renal cell carcinoma and pancreatic metastasis

Case	Age/Sex	Primary tumor	Treatment for the primary tumor	Interval (days)	Location of pancreatic metastases	Operative procedure	Outcome
1	69-F	Clear cell RCC	Nephrectomy	7270	Head	Whipple	Die
2	34-F	Clear cell RCC	Nephrectomy	5878	Periampullary	Whipple	Alive
3	84-F	Clear cell RCC	Nephrectomy	3649	Periampullary	Whipple	Alive
4	50-M	Clear cell RCC	Nephrectomy	1244	Head and body	Whipple	Alive
5	45-F	Clear cell RCC	Nephrectomy	4630	Head and body	Whipple	Alive
6	65-F	Clear cell RCC	Nephrectomy	5492	Head	Whipple	Alive
7	64-F	Clear cell RCC	Nephrectomy	2418	Head	Whipple	Alive
8	43-M	Clear cell RCC	Surveillance	0	Head	Whipple	Alive
9	77-M	Clear cell RCC	Nephrectomy	1986	Body	DP	Alive
10	65-M	Clear cell RCC	Nephrectomy	121	Head and tail	DP	Alive
11	40-F	Clear cell RCC	Nephrectomy	5	Head and tail	DP	Alive
12	53-M	Clear cell RCC	Nephrectomy	366	Peripancreatic	DP	Alive
13	45-M	Clear cell RCC	Nephrectomy	4468	Tail	DP	Alive
14	60-F	Clear cell RCC	Nephrectomy	4063	Body	DP	Alive

Interval days from diagnosis of primary tumor to diagnosis of pancreatic metastases. M: male; F: female; RCC: renal cell carcinoma; DP: distal pancreatectomy.

Results

According to the analysis, 302 patients with CCRCC were analyzed, of which only 14 patients had pancreatic metastasis (4.2%). Two groups of patients were obtained: those who underwent pancreatic surgery for metastasis (n = 14) and those who did not undergo pancreatic surgery (n = 6) table 1.

Of the group of operated patients, there is a slight difference in relation to sex, 57.1% corresponds to the female sex (n = 8) and 42.9% to the male sex (n = 6). In relation to the clinical stage of CCRCC, clinical stage 4 (A and B) was found most frequently in 42.8% (n = 6), although in 42.8% (n = 6) the clinical stage at diagnosis could not be obtained as it was not reported in the file. 78.6% (n = 11) had no metastases at diagnosis, 21.4% (n = 3) were diagnosed with metastases to pancreas along with CCRCC. Only 14.3% (n = 2) received radiotherapy prior to pancreatic surgery. According to the location of the metastasis 71.4% corresponded to single location, being in order of frequency head, body, tail, periampullary and peripancreatic fat (21.4%, 14.3% 14.3%, 14.3% 7.1%, respectively) and 28.6% to multiple location corresponding to head-body, head-tail, body-tail (14.3%, 7.1% 7.1%, respectively). Regarding the surgical procedure, 57.1% (n = 8) underwent Whipple and 42.9% (n = 6) distal pancreatectomy.

The average size of the metastatic lesion to the pancreas was 2.9 cm (0.9-6 cm range) (Table 2) Only one of the operated patients presented extrapancreatic metastasis, located in the stomach. Two of the non-operated patients had extrapancreatic lesions in the liver and lung.

Regarding survival after the diagnosis of metastasis, after the surgical procedure, it was 1150 days on average. In contrast to those who did not undergo surgery, survival after diagnosis of metastasis was 499 days.

Post-operative complications presented by the patients were mainly: 42.8% abdominal sepsis (n = 6), 14.28% (n = 2) pancreatic fistula, and 7.14% (n = 1) delayed emptying. There were no in-hospital deaths.

Of the patients who did not undergo surgery, 50% (n = 3) received management with ERCP and stent placement, 33.3% (n = 2) underwent biliodigestive bypass and one was a candidate for cycles of Soratenib.

Discussion

Secondary neoplasms affecting the pancreas are rare, accounting for 2-5% of all malignant neoplasms

Table 2. Surgical characteristics of pancreatic metastases

Case	Size (cm)	Operative time (min)	Operative bleeding (ml)	Post-operative complication	Clavien-Dindo
1	3.5 × 2.5	-	-	Sepsis DGE	IIIa II
2	5	350	400	None	-
3	4.9 × 4	300	450	None	-
4	2.1 × 1.3 (head) and 0.9 × 0.9 (body)	300	200	None	-
5	2.1 × 1.3 (head) and 0.9 × 0.9 (body)	300	200	Sepsis	IIIa
6	2.1 × 1.5	350	550	Sepsis POPF	IIIa II
7	1.9 × 1.4	210	200	None	-
8	6 × 4.5 × 3.5	600	5000	Sepsis	IIIa
9	1.4 × 1.4	240	300	Intra-abdominal collections	II
10	5.5 × 4.5 × 4	315	450	None	-
11	1.3 × 0.5 × 0.4	445	3000	Pneumothorax Sepsis Dehiscence of anastomosis	I II IIIb
12	6 × 4	300	500	None	-
13	2 × 1.4	230	350	Intestinal occlusion POPF Sepsis	IIIb II III
14	4 × 2.7	180	600	Atelectasis	I

cm: centimeters; mL: milliliters; min: minutes; DGE: delayed gastric emptying; POPF: post-operative pancreatic fistula.

of the pancreas[1,14] which agrees with the analysis of this study since it was recorded at 4.2%. Our hospital, being a referral center for patients diagnosed with renal and pancreatic cancer considered as a high level in specialized hepatopancreaticobiliary surgery, confirms the rarity of this type of metastasis for clear cell renal cancer. In this study, they only found 14 patients with clear cell renal cancer metastasis in pancreas.

It is suggested that metastases to the pancreas due to CCRCC occur within the 1st year, from 5 to 10 years according to the literature[3,10], in this study, it was found that the average time between nephrectomy and the diagnosis of recurrence to the pancreas was 8.3 years (3033 days), being 19.9 years (7270 days) the longest time in which the metastasis was detected.

Survival from CCRCC diagnosis obtained in our case series within our tertiary care center averaged 4167 days to last follow-up (range 803-8327 days) in patients who had pancreatic surgery while in patients who it was decided not to operate for metastasis, it was 4063 days (range 71-8751 days).

According to the results of this study, surgery is probably the best treatment option for pancreatic metastasis[3,15], since the survival from the diagnosis of metastasis to the last follow-up in patients who underwent surgery was 1150 days (range 104-3068 days), while those who did not undergo surgery had a survival of 499 days (range 3-1201 days).

Survival at 1, 3, and 5 years of patients with pancreatic metastasis due to CCRCC who underwent surgery was 92.85%, 50%, and 35.71%, respectively, compared with the survival after diagnosis of pancreatic recurrence of those who did not undergo surgery, which was 28.57% at 1 year, 14.28% at 3 years and no survival at 5 years, which coincides in its majority with international literature[9,11,13] and favors the surgical management of metastasis. Only one of the operated patients died in the 1st year after pancreatic surgery, with a follow-up of less than 6 months (163 days), due to age and post-surgical complications.

Conclusion

Pancreatic metastases due to CCRCC can be curable, improve morbidity, and increase disease-free survival with surgical treatment. The fact is that they can be diagnosed in time, since their growth is slow, the appearance of symptoms is not frequent and they take years to recur after nephrectomy for the primary tumor. Despite the poor data that exist in Latin American centers about this condition, the patients in this study saw a greater survival at 1, 3, and 5 years after pancreatic surgery. Despite this finding, a larger case series with longer follow-up is needed to further clarify the role of pancreatic metastases and also to know which patients benefit most from surgical management.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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ORIGINAL ARTICLE

Radiofrequency ablation therapy for knee osteoarthritis: a systematic review and meta-analysis

Terapia de ablación por radiofrecuencia para la osteoartritis de rodilla: revisión sistemática y metaanálisis

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Abstract

Objective: *The objective of the study is to systematically analyze the safety and efficacy of radiofrequency ablation (RFA) therapy for the treatment of patients with knee osteoarthritis (KOA) and to assess the methodological quality of the published studies.* **Method:** *By searching the PubMed, Embase, and CENTRAL databases, we retrieved and collected relevant randomized controlled trials (RCTs) published up to June 26, 2023.* **Results:** *We included 13 RCTs, involving a total of 865 patients. Compared with the control group, the RFA group had significantly reduced pain scores at 1-2 weeks, 4 weeks, 12 weeks, and 24 weeks post-treatment, with standardized mean differences of −1.24 (95% confidence interval [CI]: −1.99-−0.49; p = 0.001; I^2 = 91%), −0.76 (95% CI: −1.27-−0.26; p = 0.003; I^2 = 76%), −1.70 (95% CI: −2.56-−0.83; p = 0.0001; I^2 = 94%), and −2.26 (95% CI: −3.49-−1.04; p = 0.0003; I^2 = 95%).* **Conclusions:** *RFA, as an adjunctive treatment modality, demonstrates potential in the treatment of patients with KOA. This method may become a primary treatment strategy for these patients.*

Keywords: *Osteoarthritis. Radiofrequency ablation. Knee. Meta-analysis.*

Resumen

Objetivo: *Analizar sistemáticamente la seguridad y la eficacia de la ablación por radiofrecuencia en pacientes con osteoartritis de rodilla y evaluar la calidad metodológica de los estudios publicados.* **Método:** *Mediante una búsqueda en las bases de datos PubMed, EMBASE y CENTRAL, recuperamos y recopilamos los ensayos aleatorizados controlados relevantes publicados hasta el 26 de junio de 2023.* **Resultados:** *Se incluyeron 13 ensayos aleatorizados controlados que involucraron a 865 pacientes. En comparación con el grupo control, el grupo de ablación por radiofrecuencia registró una reducción significativa en la puntuación de dolor a 1-2 semanas, 4 semanas, 12 semanas y 24 semanas del tratamiento, con una diferencia media estandarizada de −1.24 (intervalo de confianza del 95% [IC95%]: −1.99 a −0.49; p = 0.001; I2 = 91%), de −0.76 (IC95%: −1.27 a −0.26; p = 0.003; I2 = 76%), de −1.70 (IC95%: −2.56 a − 0.83; p = 0.0001%; I2 = 2.94%) y de – 2.26 (IC95%: −3.49 a −1.04; p = 0.0003; I2 = 95%), respectivamente.* **Conclusiones:** *La ablación por radiofrecuencia como tratamiento adyuvante muestra potencial en el tratamiento de pacientes con osteoartritis de rodilla. Este método puede convertirse en la principal estrategia terapéutica para estos pacientes.*

Palabras clave: *Osteoartritis. Ablación por radiofrecuencia. Rodilla. Metaanálisis.*

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Introduction

Knee osteoarthritis (KOA) is a common chronic degenerative joint disease that mainly affects middle-aged and elderly populations, particularly those over 50 years old[1]. Statistics show that KOA has become one of the leading causes of disability and health impairment, affecting tens of millions of lives globally[2]. Its incidence continues to rise with population aging, and it is predicted that the burden of this disease will continue to grow in the coming decades[3]. Beyond its significant impact on individual health, KOA also places a considerable burden on socioeconomic aspects, including health-care resource utilization and diminished work productivity[4].

KOA is the primary cause of joint pain and disability in the elderly, which seriously affects the quality of life of the elderly. Identifying the source and mechanism of pain in KOA is important, and understanding the cause of pain may help to better target appropriate treatment to affected patients and may also help to identify alternatives that can help reduce symptoms and improve function. Studies have shown that the peripheral and/or central nervous system plays an important role in the occurrence and development mechanism of KOA-related pain. Peripheral pain mechanisms include direct activation and/or sensitization of nociceptors by stimuli such as joint inflammation and/or structural damage[5]. The inflammation was mainly synovial inflammation, and the structural damage was mainly the bone marrow lesion and cartilage loss. In KOA, inflammatory lesions, namely synovitis and bone marrow lesions, have always been the main pathological damage related to pain[6]. Although cartilage loss is an important structural feature, it is not neurogenic and therefore cannot be a direct source of pain in mild-to-moderate disease. Loss, inactivation, or overactivation of nociceptive regulatory mechanisms in the central nervous system can lead to hyperalgesia and hypersensitivity, and their altered sensitivity may explain more persistent pain in KOA[7]. At present, the treatment of KOA primarily aims to alleviate patients' pain and improve joint function. Common treatments include non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, orthopedic braces, and intra-articular injections[8,9]. NSAIDs are prescribed when the patient presents with exacerbation of pain and a swollen knee. These agents act by blocking the pro-inflammatory agents such as prostaglandins and leukotrienes by reversibly blocking the cyclooxygenase and lipoxygenase pathway. Long-term use of drugs such as NSAIDs can also cause adverse gastrointestinal reactions and cardiovascular risks, imposing an additional health burden on patients[1]. Physiotherapy is good quality evidence that muscle strengthening and an aerobic exercise program are beneficial in the management of KOA[10]. Range-of-motion exercises help to prevent the development of contractures. Periarticular muscle strengthening exercises tend to stabilize the knee and improve symptoms. The aim of an orthosis is to reduce pain and improve function. The ideal candidate for an orthosis is a patient with passively correctable unicompartmental arthritis. A brace may function by improving the biomechanical axis of the deformity thereby unloading the compartment or by improving the perception of instability. Injectable hyaluronate therapy has a theoretical advantage in KOA as a result of its viscoelastic, analgesic, anti-inflammatory, and chondroprotective properties. A review revealed up to 5-13 weeks of improvement in pain and function post-injection following the use of the hyaluronate group of products[11]. However, although these methods can alleviate patients' pain and inflammation to some extent, they cannot fundamentally prevent the progression of the disease and the degradation of the cartilage[12]. Radiofrequency ablation (RFA) therapy, as an emerging interventional treatment, has received widespread attention in recent years. The principle is to apply radiofrequency energy to the disease site, relieving pain by disrupting nerve endings conduction[13]. For KOA, RFA is considered a promising treatment option that can improve pain and restore joint function by alleviating inflammatory reactions and abnormal nerve conduction[14].

While several studies have delved into the application of RFA in KOA, debates persist regarding its safety and efficacy[15]. Previous meta-analyses have presented partial evidence, yet they included non-SCI indexed literature of lower methodological quality and incomplete systematic retrieval, while new research findings continue to emerge[16,17]. Therefore, we conducted this updated systematic review and meta-analysis to more comprehensively assess the efficacy and safety of RFA in the treatment of KOA, citing the latest research evidence to provide a more reliable basis for clinical decision-making.

Materials and methods

We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

recommended by the Cochrane Collaboration for this systematic review and meta-analysis[18]. We searched three electronic databases: PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL), from their inception to June 26, 2023, and limited the language to English. Our search strategy combined MeSH/Emtree terms and free text, with keywords mainly including "knee," "osteoarthritis," "radiofrequency ablation," "randomized controlled trial," etc., set to search in the title and abstract. Two researchers independently screened electronic records and retrieved publications based on the inclusion and exclusion criteria. During the screening process, any discrepancies were resolved by mutual discussion and full-text review. In cases where a consensus could not be reached, a decision was made by a senior researcher.

In this study, we established the following inclusion criteria: (1) Patients diagnosed with KOA; (2) Patients in the intervention group received RFA treatment; (3) A control group was established, receiving sham surgery or other therapeutic methods such as drugs; (4) Relevant outcomes such as post-operative Visual Analog Scale (VAS), numerical rating scale (NRS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score (OKS), Global Perceived Effect (GPE) scale, adverse reactions, etc.; and (5) Only randomized controlled trials (RCTs) were included. Our exclusion criteria primarily included the following: (1) Duplicate data, extended studies, or the same study; (2) Types of studies irrelevant to the topic, such as animal studies, case reports, literature reviews, or conference abstracts; (3) Studies with incomplete data or unreported established outcomes, such as using a self-control group; and (4) Studies using other interventions or controls.

After excluding irrelevant studies, two researchers independently extracted the features and data of the included studies. In accordance with the suggestions of the Cochrane Reviewers' Handbook 5.1, two researchers independently assessed the risk of bias in the included studies.

We conducted a meta-analysis using RevMan 5.3 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark). For continuous variables, we used standardized mean differences (SMD) and 95% confidence intervals (CI) as the statistical analysis indicators of effect size. For categorical variables, we used risk difference (RD) as the statistical analysis indicator of effect size. We used the Cochran Q test in conjunction with the I^2 statistic to assess the degree of heterogeneity among the results of the included studies. When the statistical heterogeneity of the results of the included studies was low ($p > 0.1$ or $I^2 < 50\%$), we used a fixed-effect model for analysis; when there was statistical heterogeneity among the results of the included studies ($p < 0.1$ or $I^2 \geq 50\%$), and we used a random-effects model for meta-analysis. We set the significance level of the meta-analysis at $\alpha = 0.05$. We evaluated the presence of publication bias by plotting a funnel plot. To assess the impact of individual studies on the overall effect, we conducted a sensitivity analysis, observing the changes in effect size after excluding individual studies. In addition, we also conducted subgroup analyses to examine the changes in the treatment effects of RFA in different situations for patients with KOA.

Results

According to the search strategy, a total of 147 electronic records were retrieved, including 49 from PubMed, 57 from Embase, and 41 from Cochrane. After using Endnote X9 software and manually removing 44 duplicate records, 79 irrelevant papers were excluded by browsing titles and abstracts. By reading the full text, 11 papers with irrelevant outcome indicators, unrelated comparison strategies, incomplete data, or extended similar studies were removed. Finally, 13 papers were included in the meta-analysis, and the results of the literature screening process are shown in figure 1.

This study included 13 articles and 865 patients[19-31]. The basic characteristics of the included literature in this study are shown in table 1. There were 6 studies conducted in Asia. The majority of the studies' design (84.6%) were single-center RCTs, 4 studies used a double-blind experiment, 3 studies adopted a single-blind setting, and 6 studies used an open-label setting. The included studies employed various types of RFA procedures, such as pulsed RFA and cooled RFA. The settings of the control groups were diverse, including placebo surgery groups, intra-articular injections of sodium hyaluronate, local anesthetic injections, steroid injections, and oral administration of NSAIDs. The stimulation sites and intervention parameters of RFA varied due to different study designs, but most studies focused on the knee joint nerves as the treatment target. The intervention parameters used were quite varied, and the observed scores were primarily the NRS and VAS for pain, as well as the WOMAC, GPE, and OKS.

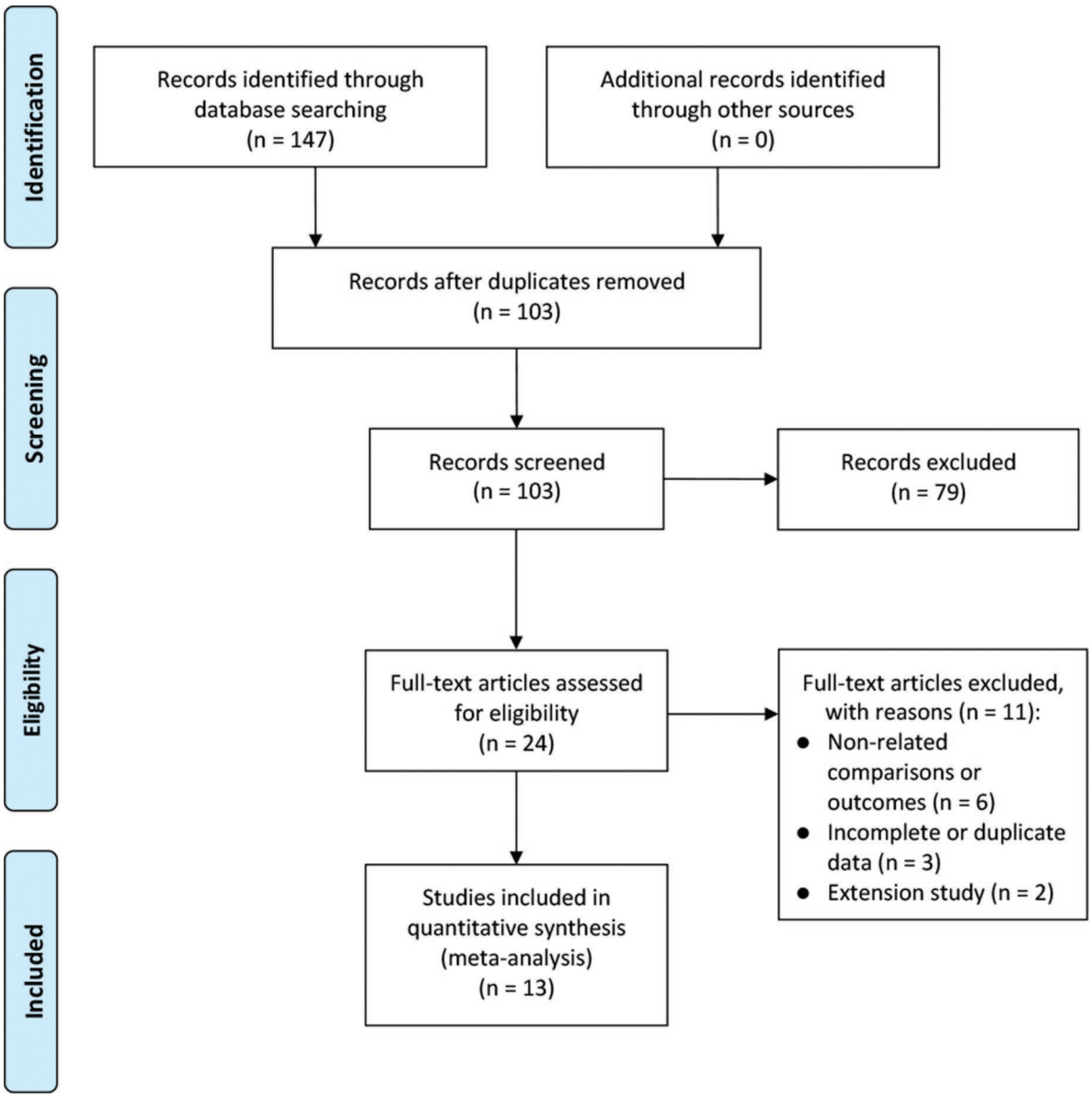

Figure 1. *Flow diagram of the study selection process.*

In addition, the patient characteristics of the included studies are shown in table 2. The total proportion of males in the RFA group and the control group were 140/434 (32.3%) and 145/431 (33.6%), respectively. The average age range for the RFA group and the control group were 56.5-70.37 years and 56.87-71.08 years, respectively. The average body mass index ranges for the RFA group and the control group were 23.51-32.2 and 25.8-30.5 kg/m^2, respectively. The average disease duration for the RFA group and the control group were 5.6-90 months and 4.3-60 months, respectively. The average pain scores for the RFA group and the control group were 5.9-8.25 and 5.6-8, respectively.

Detailed information about the risk of bias is shown in figure 2. Quality assessment of the literature was conducted using the cochrane collaboration tool. All studies clearly reported methods of random sequence generation, and most studies (61.5%) described allocation concealment methods. Some trials obtained unclear or high-risk bias due to open-label or single-blind measures for participants and executors, only four studies explicitly mentioned conducting double-blind research, and many studies did not provide explicit descriptions for outcome indicator blinding. All RCTs did not have incomplete outcome data, apparent selective reporting, or other biases.

Table 1. Basic Characteristics of Included Studies

Authors	Year	Country	Design	Blinding	Intervention Group	Control Group	Treatment Target	Intervention Parameters	Observation Score	Longest Follow-up Time (Weeks)
Carpenedo et al.[20]	2021	Italy	Single-center	Double-blind	PRF	Sham	IA	42°C, 120s	NRS, OKS	24
Chen et al.[21]	2020	America	Multi-center	Open-label	CRF	IA HA	IA	60°C, 150s	GPE, WOMAC	24
Choi et al.[22]	2011	Korea	Single-center	Double-blind	RFA	Sham	GN	70°C, 90s	VAS, GPE, OKS	12
Davis et al.[23]	2019	America	Multi-center	Open-label	CRF	IA steroids	GN	60°C, 150s	NRS, OKS	24
El-Hakeim et al.[24]	2018	Egypt	Single-center	Single-blind	RFA	Oral NSAIDs	GN	80°C, 270s	VAS, WOMAC	24
Hong et al.[25]	2020	China	Single-center	Single-blind	RFT	IA steroids	GN	70°C, 120s	GPE	24
Kumaran and Watson[26]	2019	UK	Single-center	Single-blind	CRMRF	Sham	IA	15 min	VAS	12
Qudsi-Sinclair et al.[27]	2018	Spain	Single-center	Double-blind	RFA	IA steroids	GN	80°C, 90s	NRS, OKS, KSS, SF-36, PGI-I	48
Rahimzadeh et al.[28]	2014	Iran	Single-center	Double-blind	PRF	IA dextrose	IA	42°C, 15 min	VAS	12
Sari et al.[29]	2018	Turkey	Single-center	Open-label	RFA	IA analgesics	GN	80°C, 90s	VAS, WOMAC	12
Shen et al.[30]	2017	China	Single-center	Open-label	RFT	IA PRP+HA	IA	70°C, 120s	VAS, SF-36, AKSS	12
Xiao et al.[31]	2018	China	Single-center	Open-label	RFA	IA HA	GN	60, 70, and 80°C, 90 s	VAS	24
Yuan et al.[32]	2016	China	Single-center	Open-label	PRF	IA analgesics	IA	42°C, 6 min	VAS, WOMAC	24

PRF: pulsed radiofrequency ablation; NRS: numerical rating scale; OKS: Oxford Knee Scores; CRF: cooled radiofrequency ablation; IA: intra-articular; HA: hyaluronic acid; GPE: global perceived effect; WOMAC: Western Ontario and McMaster's Universities Osteoarthritis; GN: genicular nerve; VAS: Visual Analog Score; RFA: radiofrequency ablation; NSAIDs: non-steroidal anti-inflammatory drugs; RFT: radiofrequency thermocoagulation; CRMRF: capacitive resistive monopolar radiofrequency; KSS: knee society score; SF-36: 36-Item Short Form Health Survey; PGI-I: Patient Global Impression Scale of Improvement; AKSS: American K.

All 13 studies reported post-treatment pain scores. Among them, 9 studies reported pain scores 1-2 weeks after treatment, 7 studies reported pain scores 4 weeks after treatment, 10 studies reported pain scores 12 weeks after treatment, and 6 studies reported pain scores 24 weeks after treatment. Compared with the control group, the pain scores of the patients in the RFA group significantly reduced at 1-2 weeks, 4 weeks, 12 weeks, and 24 weeks after treatment, with SMDs of –1.24 (95% CI: –1.99-–0.49; $p = 0.001$; $I^2 = 91\%$), –0.76 (95% CI: –1.27-–0.26; $p = 0.003$; $I^2 = 76\%$), –1.70 (95% CI: –2.56-–0.83; $p = 0.0001$; $I^2 = 94\%$), and –2.26 (95% CI: –3.49-–1.04; $p = 0.0003$; $I^2 = 95\%$), respectively (Fig. 3).

Three, four, and three studies, respectively, evaluated the changes in the WOMAC index at 4 weeks, 12 weeks, and 24 weeks after treatment. The results showed that compared with the control group, the WOMAC index of the RFA group was lower. The pooled SMDs were –0.65 (95% CI: –1.07-–0.23; $p = 0.002$; $I^2 = 60\%$), –1.26 (95% CI: –2.33-–0.19; $p = 0.02$; $I^2 = 94\%$), and –1.58 (95% CI: –2.89-–0.26; $p = 0.02$; $I^2 = 94\%$), respectively (Fig. 4).

Three studies each reported the comparison of the GPE scores of the two groups of patients after treatment. Compared with the control group, RFA significantly improved patient satisfaction 12 weeks after treatment, but there was no significant difference

Table 2. Basic characteristics of the included population

Authors	Sample size (RF/Con)	Male count (RF/Con)	Intervention group age (years)	Control group age (years)	Average BMI (RF/Con)	Average disease duration (months) (RF/Con)	Baseline pain score of intervention group	Baseline pain score of control group
Carpenedo et al.[20]	8/8	2/3	70.37 ± 7.36	70.87 ± 11.81	29.48/29.62	9.62/10.37	8.25 ± 0.70	8 ± 1.19
Chen et al.[21]	89/88	37/34	63.3 ± 10.7	63.1 ± 9.7	32.2/30.5	90/106	NA	NA
Choi et al.[22]	17/18	2/3	67.9 ± 7.1	66.5 ± 4.8	26.2/26.5	75.6/88.8	7.82 ± 1.38	7.72 ± 0.75
Davis et al.[23]	76/75	26/26	63 ± 12	66 ± 13	30.6/30.4	10.7/8.6	7.3 ± 1.2	7.2 ± 1.0
El-Hakeim et al.[24]	30/30	9/12	62 ± 7.37	56.87 ± 6.53	32.02/30.21	7.6/5.7	7.07 ± 0.2	7.07 ± 0.2
Hong et al.[25]	26/27	10/12	59.46 ± 5.81	60.93 ± 7.50	24.6/25.8	32.54/34.67	6.46 ± 1.14	6.37 ± 0.93
Kumaran and Watson[26]	15/15	6/6	63 ± 10	63 ± 10	31/31	5.6/4.3	6.3 ± 1.2	5.8 ± 1.2
Qudsi-Sinclair et al.[27]	14/14	4/3	67.4 ± 7.2	71.08 ± 9.4	NA	42/31	7.07 ± 1.06	6.43 ± 1.56
Rahimzadeh et al.[28]	24/26	11/10	56.95 ± 8.31	60.57 ± 7.47	NA	NA	7.08 ± 1.41	7.11 ± 1.03
Sari et al.[29]	37/36	7/9	64 ± 8	64 ± 10	23.51/22.89	60/60	NA	NA
Shen et al.[30]	27/27	7/9	62.24 ± 10.35	62.35 ± 9.70	NA	60.12/59.52	7.12 ± 1.08	7.14 ± 1.03
Xiao et al.[31]	49/47	12/11	56.5 ± 9.5	61.5 ± 8.5	NA	36.5/35.5	7.48 ± 1.24	7.53 ± 1.27
Yuan et al.[32]	22/20	7/7	69.9 ± 11.1	67.4 ± 10.3	NA	41.6/38.3	5.9 ± 1.1	5.6 ± 1.4

RF: radiofrequency group; Con: control group; BMI: body mass index; NA: non-applicable.

4 weeks after treatment. The pooled SMDs were 1.29 (95% CI: 0.52-2.06; p = 0.001; I^2 = 82%) and 0.66 (95% CI: −0.20-1.52; p = 0.13; I^2 = 88%), respectively (Fig. 5).

Ten RCTs reported on side effects after using RFA. Compared to the control group, the risk of adverse events in patients using RFA did not change. The pooled RD was 0.01 (95% CI: −0.02-0.04; p = 0.52; I^2 = 0%) (Fig. 6).

We also conducted a subgroup analysis to assess the impact of different factors on the pooled results and heterogeneity of pain scores at the 12-week follow-up, as shown in Table 3. The results show that whether the studies were conducted in Asia or other regions, RFA is indicated to improve patient pain scores. The effect is better when targeting the nerves of the knee joint, whereas the intra-articular approach has achieved a marginal effect (p = 0.05). In addition, both traditional RFA and other RFA methods have achieved improvements. It is worth noting that heterogeneity did not significantly change in the subgroup analysis, suggesting that it may come from other sources.

We performed a funnel plot analysis on post-operative pain scores. The funnel plots show that the results are approximately symmetrically distributed at any follow-up period, indicating no apparent publication bias (Fig. S1). Moreover, we performed a sensitivity analysis on the post-operative pain scores. The results did not significantly change after excluding each study, suggesting that individual studies have a limited impact on the overall results, but the heterogeneity among studies remains high.

Discussion

This meta-analysis systematically evaluates the efficacy and safety of RFA as a treatment for patients with KOA, and a methodological quality assessment was carried out on the included studies. The primary findings of this study are as follows: (1) Compared to the control group, patients undergoing RFA showed significant decreases in pain scores at 1-2 weeks, 4 weeks, 12 weeks, and 24 weeks post-treatment, although no significant differences were observed in the VAS scores at 48 h post-operation between the two groups; (2) RFA helps to reduce the WOMAC scores of patients at 4 weeks, 12 weeks, and 24 weeks; (3) RFA significantly improves patient satisfaction at 12 weeks post-treatment, but no significant difference

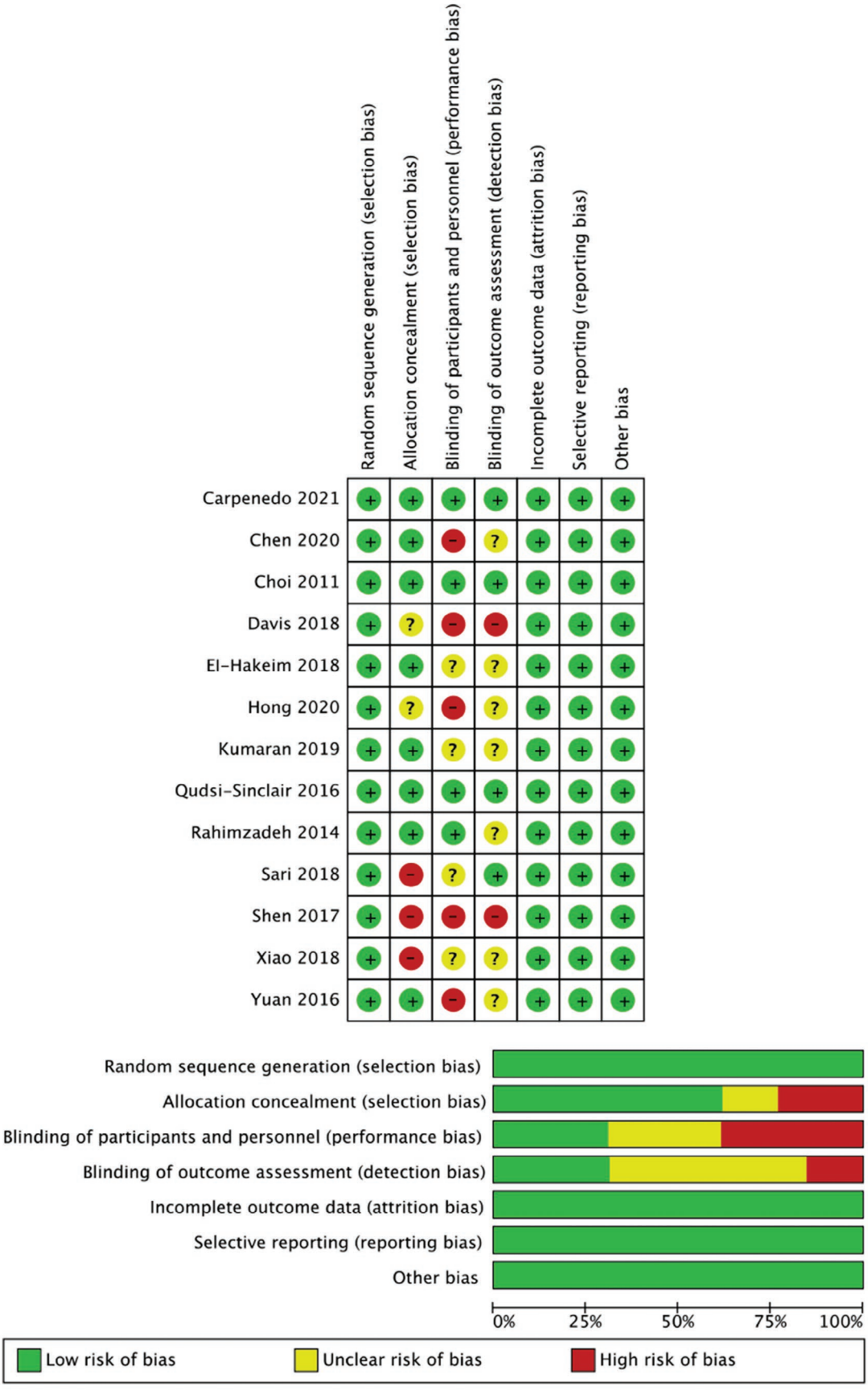

Figure 2. *Summary of bias and quality assessment of the included studies.*

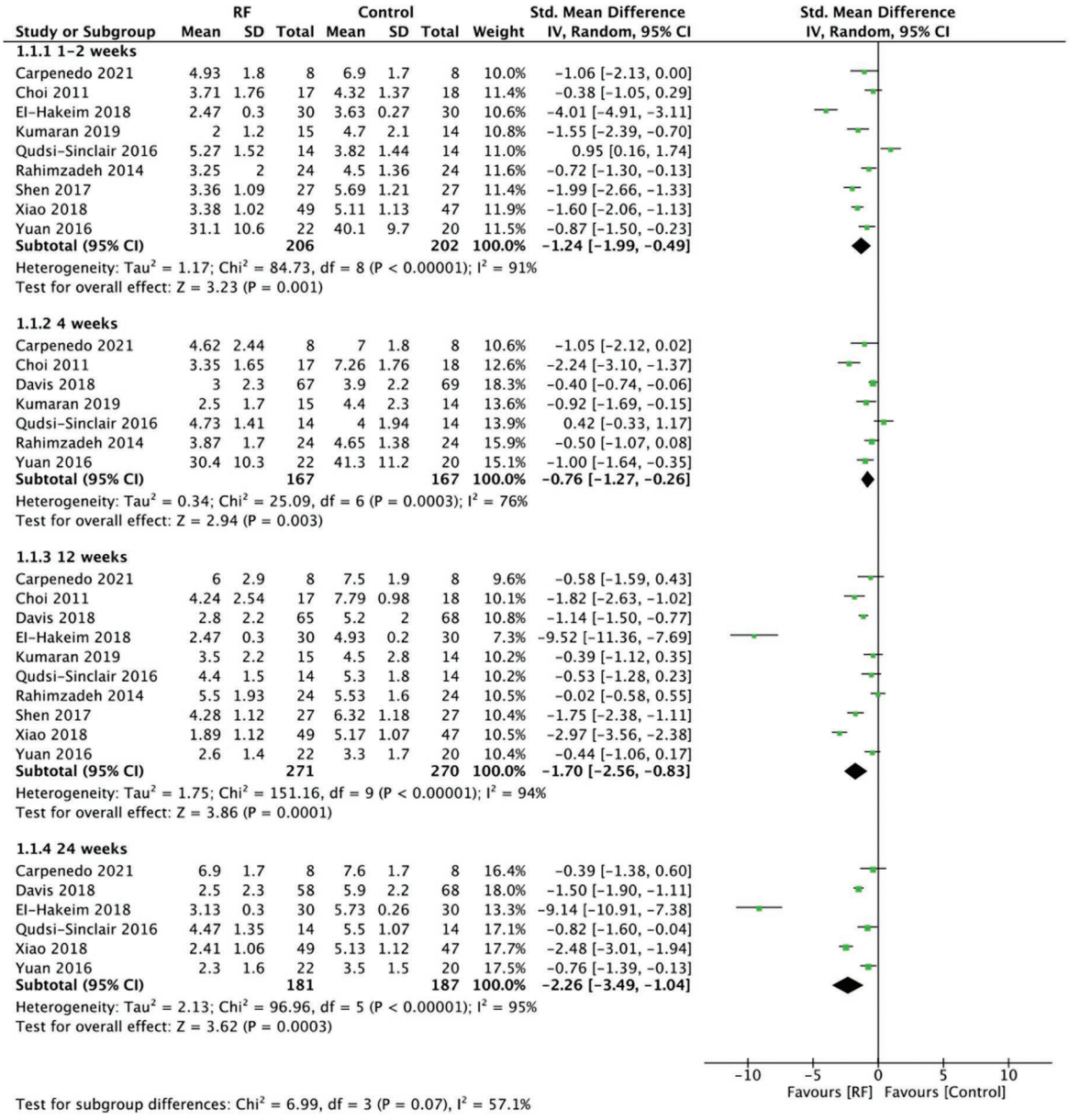

Figure 3. *Forest plot comparing pain scores between the RF group and the control group. RF: radiofrequency; M-H: Mantel-Haenszel; SD: standard deviation; IV: inverse variance.*

was noted at 4-week post-treatment; and (4) Compared to the control group, RFA does not increase the risk of adverse events in patients. This study hopes to provide evidence-based medical justification for the clinical use of RFA as a pain relief method in treating patients with KOA and offer a reference for improving patient satisfaction and preventing adverse events.

Osteoarthritis is a chronic degenerative joint disease, the progression of which involves several pathological changes[32,33]. First, the damage and degeneration of articular cartilage are the core features of osteoarthritis. The degeneration of cartilage leads to irregularities on the joint surface, resulting in joint friction and wear. Second, the inflammatory response around the joint and changes in synovial fluid are also important characteristics of osteoarthritis. The inflammatory response leads to synovial membrane thickening and an increase in joint fluid production, further exacerbating the pathological changes of the disease. Finally, osteophyte formation is a late-stage manifestation of osteoarthritis. It may represent the body's self-repair mechanism in response to joint damage, but it may also cause joint

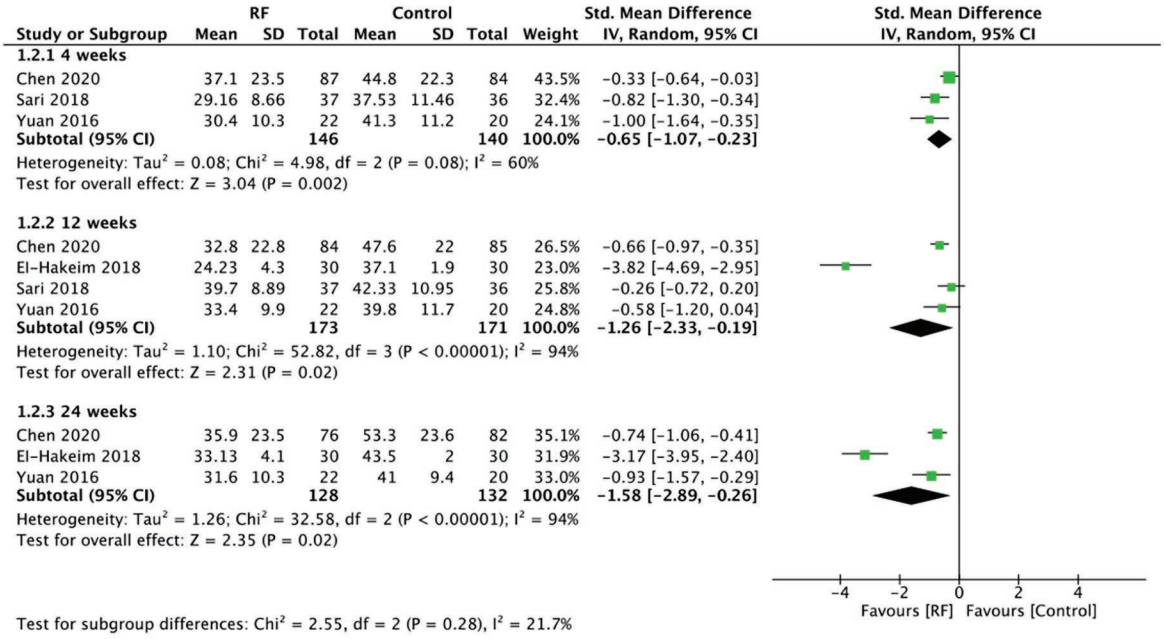

Figure 4. *Forest plot comparing WOMAC index between the RF group and the control group. WOMAC: Western Ontario and McMaster's Universities Osteoarthritis; RF: radiofrequency; M-H: Mantel-Haenszel; SD: standard deviation; IV: inverse variance.*

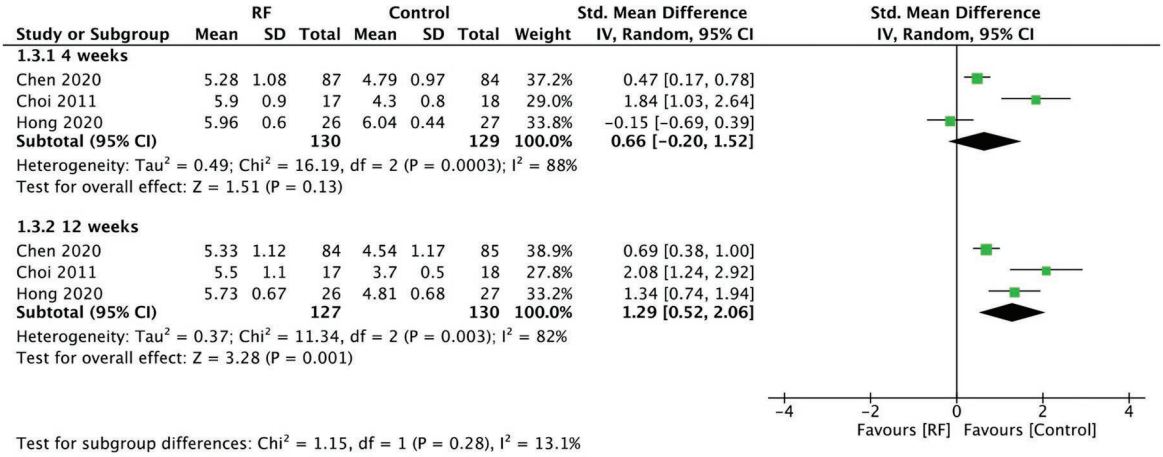

Figure 5. *Forest Plot Comparing GPE Scores between the RF Group and the Control Group; GPE: Global Perceived Effect; RF: radiofrequency. M-H: Mantel-Haenszel; SD: standard deviation; IV: inverse variance.*

deformity and functional impairment. Pain is one of the most common and primary symptoms among osteoarthritis patients. The occurrence of pain is related to several factors[34]. First, the destruction and degeneration of articular cartilage cause irregularities on the joint surface, increasing joint friction and pressure, and leading to inflammation and pain. Second, the inflammatory response around the joint and changes in the synovial fluid lead to congestion of the synovial membrane and increased sensitivity of nerve endings, further triggering pain. Furthermore, a decrease in joint stability and a decline in muscle strength can also increase joint load and the perception of pain. At present, the therapeutic management of osteoarthritic pain mainly includes two aspects: Pharmacological and non-pharmacological treatments. Commonly used pharmacological treatments include NSAIDs and corticosteroids. NSAIDs have anti-inflammatory and analgesic effects and can

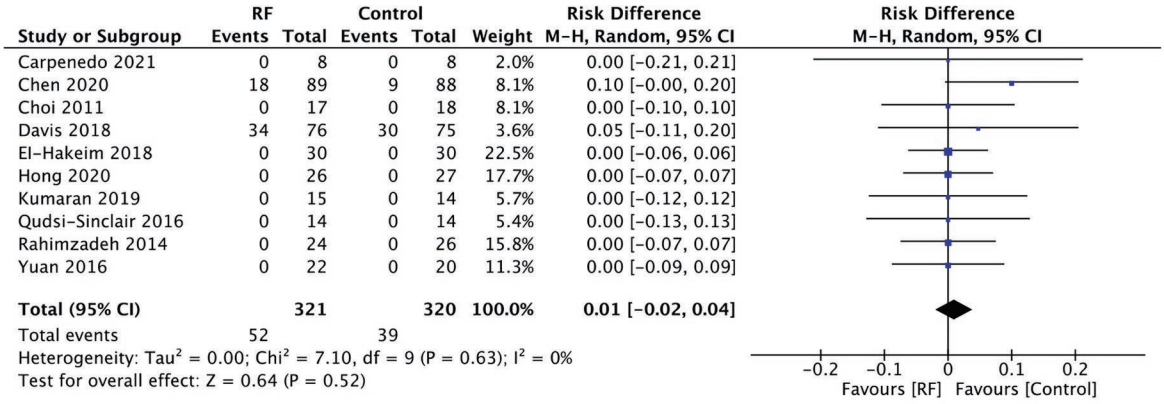

Figure 6. *Forest plot comparing adverse reactions between the RF group and the control group; RF: radiofrequency; M-H: Mantel-Haenszel; SD: standard deviation; IV: inverse variance.*

Table 3. Subgroup analysis of patient pain score at 12 weeks post-treatment

Group	Number of studies	Pooled SMD (95% CI)	Z-value	p-value	Heterogeneity	
					I^2 (%)	p-value
Geographic Location						
Asia	5	−1.40 (−2.51-−0.29)	2.46	0.01	94	< 0.001
Other	5	−2.16 (−3.75-−0.57)	2.66	0.008	95	0.008
RFA Target						
GN	5	−2.93 (−4.50-−1.36)	3.66	< 0.001	96	< 0.001
IA	5	−0.63 (−1.27-0.00)	1.95	0.05	77	0.002
Type of RFA						
RFA	4	−3.53 (−5.79-−1.26)	3.05	0.002	97	< 0.001
Other	6	−0.74 (−1.26-−0.22)	2.78	0.005	77	< 0.001

SMD: standard mean difference; CI: confidence interval; GN: genicular nerve; IA: intra-articular; RFA: radiofrequency ablation.

effectively alleviate the pain and inflammatory response of osteoarthritis. In addition, topical NSAIDs also offer a choice for local pain relief[6]. The OARSI guidelines recommend that NSAIDs should be given in conservative doses and durations, as there is concern regarding an increasing risk of gastrointestinal disturbance and multi-organ failure[35]. So, caution and attention must be focused on avoiding excessive use of these medications. In addition, consideration of all known safety information and individual patient comorbidities is imperative when the health-care practitioner is selecting any of these medications for a patient. Non-pharmacological treatments include physical therapies (such as hot compress, cold compress, and rehabilitative exercise) and rehabilitation therapies[36]. These therapeutic methods aim to improve joint function, alleviate pain, and enhance the patient's quality of life.

RFA is an interventional treatment method that uses the effects of radiofrequency current to destroy disease-related tissue or nerve conduction pathways to achieve pain relief. This technique is based on the high-frequency oscillation and thermal effects of radiofrequency current, which can precisely target specific areas for tissue ablation[37]. The principle of RFA is based on the resistive heating effect of tissues. Under the influence of radiofrequency current, friction between positive and negative charges within tissues generates heat. This high-temperature effect can destroy nerve conduction pathways in the diseased tissue, thus blocking the transmission of pain signals[38]. RFA has adjustable power and time settings, allowing for personalized treatment according to specific conditions. The application of RFA in disease treatment has a multi-year developmental trajectory. Initially, RFA was primarily used in the field of cardiology, for

treating diseases such as arrhythmias[39]. With continuous technological advancement and accumulated clinical practice, RFA has gradually found applications in other areas, such as tumor treatment, pain management, and more[40]. RFA has become one of the major means in the field of interventional treatment. In disease therapy, significant advancements have been made in the pain relief applications of RFA. This technique is extensively utilized to treat chronic pain conditions, such as back pain, neck pain, and arthritis[41]. Compared to traditional pharmacological treatments, RFA provides durable analgesic effects and can reduce drug usage, thus lowering the occurrence of adverse reactions[42]. Therefore, RFA is widely recognized as a safe and effective pain management method. The application of RFA in the treatment of osteoarthritis has also received much attention. As a minimally invasive interventional treatment modality with quick recovery, RFA demonstrates the potential in relieving osteoarthritic pain. It can improve patients' symptoms and quality of life by precisely destroying pain sources, thereby alleviating arthritic inflammation and transmission of pain signals[43].

The results of this study are consistent with previous meta-analyses and relevant research, supporting the efficacy and safety of RFA in the treatment of pain in patients with KOA[17,18]. This meta-analysis has several advantages, highlighting the importance of updated clinical evidence, the inclusion of more studies, and the exclusion of low-quality research. First, a crucial advantage of this meta-analysis lies in its updated clinical evidence. The latest research outcomes were included in this meta-analysis to provide more accurate and reliable conclusions. By including the latest studies, we can better understand the safety and efficacy of RFA therapy in treating KOA. Second, this meta-analysis incorporated more studies. By extensively searching multiple databases and academic journals, we endeavored to access as many relevant studies as possible and included them in the analysis. The advantage of doing this is the increase in the sample size, thereby enhancing the statistical power of the analysis, which allows for a more accurate assessment of the effects of RFA therapy. Including more studies can also enhance the consistency and stability of the results, making the conclusions more universally applicable and can be generated for other studies. Compared to previous meta-analyses, we also searched for studies that had been overlooked before and incorporated them into this analysis. Third, this meta-analysis excluded low-quality research. Through a rigorous screening and evaluation process, we excluded lower-quality non-SCI included studies previously incorporated by Liu et al.[18]. By doing so, we intend to ensure the reliability and accuracy of the analysis, avoiding the introduction of bias from low-quality research that could adversely affect the results. By excluding low-quality research, we can draw more reliable and trustworthy conclusions, providing more meaningful guidance for clinical practice. Due to the low incidence rate, and for a more systematic evaluation of the effects of RFA, this study combined all the reported data on the incidence of adverse reactions from all the studies and used RD for analysis, instead of classifying adverse reactions for quantitative analysis. The results found that the use of RFA did not increase the risk of adverse reactions, which is also consistent with previous research. Subgroup analysis found that the geographical area of the study, the target location, and the type of RFA did not significantly affect the consolidated results after 12 weeks, to some extent supporting the therapeutic effect of RFA for pain relief in KOA. However, it is worth noting that the source of heterogeneity is not yet determined; this might come from the design of the control group therapy, different blind method settings, etc., suggesting the need for more high-quality evidence in the future, and the strengthening of the classification and screening of the included research data.

RFA has recently gained popularity as an intervention for chronic knee pain in patients. Long-term efficacy and adverse events are still largely unknown. Although vascular injuries after genicular nerve RFA have not been reported, genicular vascular complications are well documented in the surgical literature. The systematic review of RFA showed that among the 27 patients analyzed, the superior lateral genicular artery was involved in 25.9% (7/27), the superior medial genicular artery was involved in 40.7% (11/27), and the inferior medial genicular artery was involved in 33.3% (9/27)[44]. Most often, these vascular injuries result in the formation of a pseudoaneurysm, arteriovenous fistula (AVF), hemarthrosis, and/or osteonecrosis of the patella. Based on the detailed dissections and review of the literature, our investigation suggests that vascular injury is a possible risk of genicular RFA. Therefore, the interventionist must exercise great care while performing RFA of genicular nerves to avoid inadvertently injuring nearby structures, especially vascular structures, leading to iatrogenic complications. We should also consider the sink effect of blood

vessels in proximity to the RFA targets. Due to constant blood flow, the temperature of the targeted area is attenuated[45]. Perhaps, this reduction in temperature may lead to a better coagulation effect than if it were by direct needle trauma, and thus, vascular injury can be avoided. The longest follow-up period of the 13 included studies was only 48 weeks, and none of them involved adverse events of osteonecrosis in RFA, so our study did not address the long-term theoretical risks associated with RFA in the knee, including the possibility of vascular injury leading to osteonecrosis. However, these potential complications have not been observed in long-term RFA studies[46,47], and our subjects did not develop any early symptoms of these complications. We conclude that RFA is unlikely to result in these types of complications when performed by a fully trained and experienced physician. In the future, we will pay attention to studies with long-term follow-up results to analyze whether there are adverse reactions such as osteonecrosis in the treatment of KOA with RFA.

There are some limitations to this study that requires discussion. First, even though this analysis only included RCTs, significant heterogeneity could lead to biased results. Therefore, more high-quality RCTs are required in the future to further investigate this issue. Second, the current studies mainly focus on the short-term impact of RFA on patients, with a lack of research into long-term follow-up results, and the indicators of attention to adverse reactions from RFA are not sufficiently detailed. Furthermore, the results of this study rely solely on data reported in published studies. For some critical details or specific subgroup analyses, there may be situations where data are incomplete or unobtainable. This may impact the reliability and accuracy of certain conclusions. Lastly, despite excluding low-quality studies, some of the included studies still demonstrate poor research quality. This might have some effect on the final results. In addition, due to potential variances in methodologies and standards across different studies, heterogeneity might present certain challenges.

Conclusions

In summary, RFA, as a surgical approach, when compared to conventional treatment or sham surgery, helps enhance analgesic effects, improves joint symptoms, and increases patient satisfaction, without increasing the incidence rate of side effects. It has the potential to become a new therapeutic strategy for pain management in patients with KOA. However, due to the rather significant heterogeneity and the lack of studies on long-term follow-up results in this analysis, more high-quality research is needed in the future to delve deeper into these aspects of the results.

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Conflicts of interest

All of the authors had no personal, financial, commercial, or academic conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for the analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Supplementary data

Supplementary data are available at DOI: 10.24875/CIRUE.M23000723. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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ORIGINAL ARTICLE

Morbidity and mortality of emergency surgery in octogenarian patient

Morbimortalidad de la cirugía de urgencia en el paciente octogenario

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Abstract

Objective: *To evaluate the health outcomes (postoperative morbidity and mortality) and the functional status at discharge of elderly patients older than 80 years who underwent emergency surgery.* **Method:** *Patients > 80 years of age who underwent emergency surgery during one year at the Marqués de Valdecilla University Hospital, Santander, Spain. Preoperative data (age, sex, type of surgery, comorbidity) and postoperative data (complications) were evaluated, as well as in-hospital mortal- ity, at 30 days and 6 months after surgery.* **Results:** *Five-hundred-sixty-eight patients underwent emergency surgery between 2018 and 2019. After the review, 407 patients were included in the study. Average age: 86.9 years. Women 61.7%. Mean hospital stay: 10.4 days. Traumatic interventions 41.3%, vascular surgery 19.7%, general-digestive surgery 25.3%. Medium ASA risk: 2.88. Functional status at discharge: 3.15. Postoperative complications: Clavien-Dindo I 40.8%, II 40.3%, IIIA 3.4%, IIIB 2.5%, IVA 3.9%, IVB 2.0% and V 7.1%. Hospital mortality 7.1%, 30-day mortality 10.3%, mortality at 6 months 24.6%.* **Conclusions:** *Patients > 80 years of age undergoing urgent surgery have high preoperative comorbidity, postoperative complications, and high mortality at 30 days and 6 months after surgery. This mortality is more significant in those ASA IV, nonagenarians and those undergoing high-risk surgery.*

Keywords: *Elderly patient. Octogenarian. Emergency surgery. Morbidity. Mortality.*

Resumen

Objetivo: *Evaluar los resultados en salud (morbilidad y mortalidad posoperatorias) y el estado funcional al alta de los paci- entes mayores de 80 años sometidos a cirugía de urgencia.* **Método:** *Pacientes de edad > 80 años sometidos a cirugía de urgencia durante 1 año en el Hospital Universitario Marqués de Valdecilla, Santander, España. Se evaluaron datos preopera- torios (edad, sexo, tipo de cirugía, comorbilidad) y posoperatorios (complicaciones), así como mortalidad hospitalaria, a los 30 días y a los 6 meses de la cirugía.* **Resultados:** *En 2018-2019 fueron operados de urgencia 568 pacientes, de los cuales 407 fueron incluidos en el estudio. Edad media: 86.9 años. El 61.7% fueron mujeres. Estancia media hospitalaria: 10.4 días. El 41.3% fueron intervenciones traumatológicas, el 19.7% cirugía vascular, el 25.3% cirugía general-digestiva. Riesgo ASA me- dio: 2.88. Estado funcional al alta: 3.15. Complicaciones posoperatorias: Clavien-Dindo I 40.8%, II 40.3%, IIIA 3.4%, IIIB 2.5%,*

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IVA 3.9%, IVB 2.0% y V 7.1%. Mortalidad: hospitalaria 7.1%, a los 30 días 10.3% y a los 6 meses 24.6%. **Conclusiones:** *Los pacientes > 80 años sometidos a cirugía urgente presentan elevada comorbilidad preoperatoria, compli- caciones posoperatorias y elevada mortalidad a 30 días y 6 meses de la cirugía. Esta mortalidad es más significativa en los ASA IV, nonagenarios y sometidos a cirugía de alto riesgo.*

Palabras clave: *Paciente anciano. Octogenario. Cirugía de urgencia. Morbilidad. Mortalidad.*

Introduction

For the first time in history, the number of people aged 65 and older exceeds the number of people aged 65 and younger worldwide. Aging is the result of socioeconomic development and improvements in healthcare systems over recent decades.

Life expectancy in Spain is among the highest in the world. According to the World Health Organization, Spain ranks third in life expectancy (83.1 years on average; 80.3 years for men and 85.7 years for women), behind Switzerland (83.3 years) and Japan (84.2 years). Currently, 20% of Spanish society is older than 65 years, and it is estimated that by 2050 this figure will rise to more than 30%. The number of older individuals will increase dramatically in the coming decades, with population projections for 2055 indicating a 66% increase in the 65 to 74-year age group[1]. Aging is associated with a decline in the functional reserve of all organs. Our hypothesis is that patients older than 80 undergoing emergency surgery present high morbidity and mortality, both of which are proportional to their pre-existing comorbidities or frailty.

The aim of this research was to study a cohort of elderly patients undergoing emergency surgery to assess their preoperative functional status, comorbidities, and health outcomes following surgery in terms of postoperative complications, morbidity, and hospital mortality, at 30 days and 6 months.

Method

The Admission and Clinical Documentation Service (SADC) of Hospital Universitario Marqués de Valdecilla (HUMV), in Santander, Spain, was requested to provide a list of all patients older than 80 years who underwent emergency surgery between October 2018 and October 2019, from any surgical specialty offered in HUMV service portfolio. Clinical data were obtained from each patient's individual health history, the Altamira electronic health record, and the Visor Medical Record system. The following variables were recorded for all patients: age, sex, surgical specialty, length of stay, surgical risk[2], type of anesthesia, pathological history, hypertension, atrial fibrillation, heart failure, chronic kidney disease, chronic obstructive pulmonary disease, ischemic heart disease, diabetes mellitus, stroke, anemia, and cognitive impairment. In cases requiring surgery due to traumatic disease, it was noted whether it was a hip fracture; if surgery was required for general-digestive disease, it was noted whether the clinical picture was compatible with acute abdomen.

Postoperative complications occurring from the first day after surgery until discharge or death were recorded: respiratory failure, acute renal failure, atrial fibrillation, pneumonia, atelectasis, deep vein thrombosis, pulmonary embolism, mechanical ventilation, acute myocardial infarction, stroke, urinary tract infection, sepsis, bacteremia, suture dehiscence, surgical site infection, cognitive impairment or worsening at discharge, delirium, and need for blood transfusion. Preoperative risk values were recorded according to the ASA (American Society of Anesthesiologists) classification and complication classes according to the Clavien-Dindo classification[3]. Functional status at discharge was assessed using a simplified system created by the authors based on walking ability. Finally, hospital mortality, mortality at 1 month, and mortality at 6 months after discharge were recorded.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS®; IBM, Armonk, NY, United States). Descriptive (means, frequencies) and bivariate analyses (analysis of variance, ANOVA, and Student t-test) were used to obtain results, along with regression analysis and factors if deemed necessary. A p-value < 0.05 was considered statistically significant.

Results

According to the HUMV SADC, a total 568 patients older than 80 years old underwent surgery from October 2018 through October 2019. After review, a total

of 407 patients were included in the study (Fig. 1). The reasons for excluding the remaining 161 patients were: reoperation by the same service (118), recording only the first intervention (generally vascular surgery), or being registered as urgent (43) when in fact they were scheduled surgeries (mostly intracranial pressure recordings).

The patients' mean age was 86.9 ± 4.3 years, with the following age groups: 40.5% were 80-85 years, 38.4% were 86-90 years, 17.2% were 91-95 years, and 3.9% were older than 95 years. In terms of sex distribution, 61.7% (n = 251) were women and 38.3% (n = 156), men. The mean length of stay was 10.4 ± 12.5 days, and the mean length of ICU stay was 0.5 ± 2.1 days. Regarding surgical specialties, 41.3% of all interventions were associated with traumatology, 19.7% with vascular surgery, 25.3% with general-digestive surgery, 5.7% with neurosurgery, 3.9% with urology, 1.7% with ophthalmology, 0.7% with gynecology, 0.7% with maxillofacial surgery, 0.5% with thoracic surgery, 0.2% with plastic surgery, and 0.2% with cardiac surgery. The mean ASA risk was 2.8 ± 0.7, with the following distribution: ASA I 2%, ASA II 26.8%, ASA III 52%, and ASA IV 19.2%.

Functional status at discharge was 3.1 ± 1.2. Postoperative complications were as follows: Clavien-Dindo I, 40.8%; Clavien-Dindo II, 40.3%; Clavien-Dindo IIIA, 3.4%; Clavien-Dindo IIIB, 2.5%; Clavien-Dindo IVA, 3.9%; Clavien-Dindo, IVB 2.0%; and Clavien-Dindo V, 7.1%. It should be noted that many of the urgently reoperated patients (category IIIA/B) may have required admission to the ICU due to isolated organ failure or multiple organ failure, thus shifting them to category IV, which may have slightly affected the actual distribution of reoperated patients. Regarding mortality, it was distributed as follows: hospital mortality, 7.1%; 30-day mortality, 10.3%; and 6-month mortality, 24.6%. Six-month mortality rate according to surgical specialty, age range, ASA risk, and presence of hip fracture or acute abdomen is shown in table 1. Postoperative complications and their Clavien-Dindo classification by surgical specialties are shown in table 2, and by surgical risk in table 3. Postoperative complications occurring up to discharge are outlined in table 4.

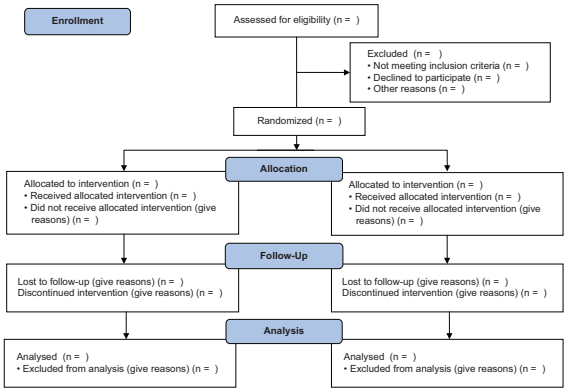

Figure 1. *Flowchart of patient inclusion.*

Discussion

It is estimated that by 2040 more than 40% of the population will be older than 65 years old. This rapid increase in aging requires studying its pathological characteristics, care needs, and recovery possibilities following emergency surgery. With current longevity prospects, a considerable number of elderly patients are expected to continue living with good function and excellent quality of life after surgery. However, the mortality rate for emergency surgery can reach 15% up to 30%, double if complications are associated, and is notably higher in patients aged 75-80 years.

Our study highlights that most patients older than 80 years have comorbidities, with more than 70% having an ASA III or IV risk. In-hospital mortality was relatively low (7%) vs other studies[4] reporting a mean of 14.7% in patients undergoing emergency general surgery, going up to 33% in nonagenarians. For the same type of surgery, our study reported an in-hospital mortality rate of 8%.

The ASA score, described by Saklad5, is a subjective assessment of a patient's overall health that considers 4 classes (I to IV), and is used as a tool to predict short- and mid-term outcomes in surgical patients. It has also proven to be a good predictor of mortality and postoperative complication rates[6].

In the present study, the mean ASA score was 2.9, and more than 70% of patients were ASA III/IV. Since there were only 8 cases of ASA I (with 3 deaths), the rest of ASA II to IV determined a direct relationship between their value and 6-month mortality (from 11.9% up to 44.8%), that is, nearly half of ASA IV patients died at 6 months. The study by Merani et al.[4] in patients undergoing general surgery with ASA IV found an in-hospital mortality rate > 30%, and while it did not assess the 6-month mortality rate, it is likely to approximate or exceed the rates found in our study.

Table 1. In-hospital mortality, mortality at 30 days, and mortality at 6 months, by disease, age range, surgical risk, and surgical specialty

Criteria	In-hospital Mortality	30-day mortality rate	6-month mortality rate
All (%)	7.1	10.3	24.6
Hip Fracture			
81-85 years	5.2	7.3	32.7[a]
86-90 years	9.4	32.7	20.1
> 90 years	5.8	20.1	
Acute abdomen			
81-85 years	8.3	29.6[c]	
86-90 years	11.1	40[c]	
> 90 years	17.9	25[b]	
Surgical risk			
Low			
Intermediate			
High	20.05	22.9	36.5%[d]
ASA			
I	37.5[e]		
II	11.9	23.1	
III	23.1	44.8[f]	
IV	44.8[f]		
Surgical Specialty			
Traumatology	20.2		
Cardiac	100		
Vascular	30		
Neurosurgery	13		
General	28.1		
Urology	31.2		
Plastic	0		
Thoracic	0		
Ophthalmologic	28.5		

[a]p < 0.001 vs other age groups.
[b]p < 0.001 vs hip fracture.
[c]p < 0.001 between age ranges.
[d]p < 0.001 vs low and intermediate surgical risk.
[e]Only 8 ASA I patients, with 3 deaths.
[f]p < 0.001 vs ASA II-III.

Table 2. Clavien-Dindo classification of postoperative complications by surgical specialty

Surgical specialty	Clavien-Dindo score
Traumatology	1.88
Neurosurgery	1.95
General surgery	2.65
Cardiac surgery	5.00
Maxillofacial surgery	1.33
Plastic surgery	1.00
Gynecology	3.33
Urology	2.81
Thoracic surgery	3.50

Table 3. Clavien-Dindo classification of postoperative surgical complications by surgical risk

Surgical risk	Clavien-Dindo score
Low Risk	1.67
Intermediate Risk	2.02
High Risk	3.92

p < 0.005 between risk levels.

Table 4. Postoperative complications until discharge

Complication	Incidence rate (%)
Respiratory failure	9.1
Pulmonary embolism	0.2
Postoperative mechanical ventilation	4.9
Heart failure	8.6
Atrial fibrillation	3.4
Surgical wound infection	11.1
Sepsis	6.1
Acute renal failure	11.5
Transfusion of 1 red blood cell concentrate	32.7
Pneumonia	6.4
Atelectasis	2.5
Acute myocardial infarction	0.7
Transient or established ischemic stroke	1.0
Wound dehiscence	3.9
Bacteremia	7.6
Urinary tract infection	7.6
Delirium	17.2
Transfusion of 2 or more red blood cell concentrates	21.6

Total respiratory complications: 18%
Total cardiovascular complications: 13.7%

The most involved surgical specialties in emergency care for the elderly are consistent in such studies: traumatology (mainly hip fractures), vascular surgery (related to lower limb ischemia), and general surgery (usually for acute abdomen processes). Hip fractures are highly prevalent (almost 1 million cases annually in the United Kingdom), considered a "fragility fracture," along with osteoporosis, osteopenia, and other comorbidities. After surgery, up to one-third of patients die within 12 months, more than 20% of

survivors become more dependent, and many require institutionalization[7].

In our study, the in-hospital mortality for patients with hip fractures can be considered low (5%), with a 6-month mortality rate of 20%, which is consistent with the literature. In younger patients (mean age, 81 years), Krishnan et al.[8] found a 30-day mortality rate of 10.5% (9.3% in our cohort), and Patel et al.[9] reported a 1-year mortality rate of 20.5% in a cohort also younger than ours (mean age, 81.5 years). It is recommended that the best way to reduce mortality in this disease is through a multidisciplinary approach with significant geriatric oversight, including early surgery, early mobilization, and avoiding polypharmacy.

The second group consists of vascular surgery for lower limb ischemia. Atherosclerosis and atrial fibrillation are very common in the elderly, as are other vascular risk factors (heart failure, diabetes mellitus, etc.). Therefore, vascular ischemia due to embolic or terminal ischemia is a common finding. In a 1998 study[10], in-hospital mortality in elderly patients undergoing vascular surgery approached 40%, with a 5% rate of amputations. More recent studies show no improvement in outcomes, with mortality around 25% and an amputation rate of 12%[11,12].

General surgery is another area of urgent surgical intervention in the elderly, with a wide range of pathology severity, from simple appendicitis to intestinal ischemia, including intermediate conditions, such as cholecystitis, incarcerated hernias, or intestinal perforations or obstructions. For appendicitis, its incidence over 60 years is 10%, yet the incidence of morbidity is high in this age group, generally due to delayed diagnosis, with a high rate of complications[13]. Regarding cholecystitis, it is noteworthy that up to 50% of the population older than 65 years has cholelithiasis, and like appendicitis, it often presents silently, leading to late diagnoses, with a 10% mortality rate in elderly patients[14]. Intestinal disease is highly variable (obstruction, perforation, volvulus), requiring emergency surgery in any case, and up to 20% of colon cancers present urgently. Except for cases of associated peritonitis, outcomes are not much worse in the elderly population, yet the stoma rate is significantly higher[15].

Another aspect that should be taken into consideration is chronological age as a determinant of mortality. Although it seems logical that comorbidity, and specifically frailty, are the determining factors for outcomes, we found a direct relationship between 6-month mortality and age in our cohort of patients older than 80 years. This was evident in patients undergoing surgery for both hip fractures and acute abdomen.

Previous comorbidity and the lack of adequate preparation in the context of emergency surgery resulted in an increase in postoperative complications. Among these, there was a high incidence of delirium, respiratory and cardiovascular complications, and need for transfusion. The study by Merani et al.[4] found a 16% incidence of respiratory complications, which is very similar to our study. Naturally, there was a direct relationship between mortality and surgical risk, with high-risk surgery nearly doubling the 6-month mortality vs low-risk surgery. Our study highlights a high rate of surgical complications in elderly patients, significantly higher in high-risk surgeries and specialties such as gynecology, thoracic surgery, and general surgery.

This study is limited by its retrospective nature and being conducted in a single hospital center. It is evident that many other patients with acute surgical diseases went to the ER and were managed non-interventionally, or simply approached from a palliative perspective due to their diminished functional status and null survival chances.

In conclusion, deciding to undertake surgical treatment in an emergency situation for the elderly is challenging. Patients older than 80 undergoing emergency surgery present preoperative comorbidity, postoperative complications, and a high mortality rate at 30 days and 6 months after surgery. This mortality is more significant in those with ASA IV, nonagenarians, and those undergoing high-risk surgery, with a 6-month mortality approaching 50%, and in cases of survival, a high degree of dependence measured by walking ability. Regardless of this, as a cohort of patients aged > 80 years, most patients in this study had severe functional limitations at discharge (bed-to-chair life or requiring care for ambulation at home). Further studies are needed to define the therapeutic benefit of emergency surgery in elderly patients, allowing both families and the surgical team to make decisions from a realistic perspective with appropriate end-of-life care considerations.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

Bariatric and general surgical procedures in obese patients with a history of venous thromboembolism and concurrent anticoagulation therapy

Cirugía general y bariátrica en pacientes obesos con antecedentes de tromboembolia venosa y tratamiento anticoagulante concomitante

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Abstract

Objective: *The objective of this study was to examine the use and outcomes of perioperative anticoagulation (AC) in obese patients with a known history of venous thromboembolism event (VTE).* **Method:** *A retrospective review of a prospective database for patients with a VTE history undergoing bariatric and general surgery at a single center (1/2008-12/2017) was performed. Factors assessed included demographics, surgical details, and outcomes.* **Results:** *Sixty-five patients underwent 76 procedures: 46 females (71%); mean age 51 years (range 26-73), mean weight 284 pounds (range 110-558), mean body mass index 45 (range 19-87). Comorbidities include hypertension (60%), gastroesophageal reflux disease (54%), osteoarthritis (49%), obstructive sleep apnea (45%), and diabetes (37%). Operations: 22 general surgeries (29%), 20 sleeve gastrectomies (26%), 12 revisions/conversions (16%), 12 Roux-en-Y gastric bypasses (16%), and 10 gastric bands (13%). Modalities: 67% laparoscopic, 28% robotic, and 5% open. Twenty-two patients (34%) had a pre-operative inferior vena cava filter placed with no complications. The mean length of stay was 4.4 days (range 1-31). Complications: seven 30-day readmissions (9%), one 30-day reoperation (1%), and two 90-day VTEs (3%). Thirty-day readmissions: four for inability to tolerate PO, two for small bowel obstruction, and one for symptomatic anastomotic ulcer.* **Conclusions:** *In our patients, post-operative AC could be started without an increased risk of bleeding in patients with a history of VTE undergoing bariatric surgery.*

Keywords: *Anticoagulation. Bariatric surgery. Deep vein thrombosis. Morbid obesity. Pulmonary embolism.*

Resumen

Objetivo: *Examinar el uso y los resultados de la anticoagulación perioperatoria en pacientes bariátricos con antecedentes de tromboembolia venosa (TEV).* **Método:** *Revisión retrospectiva (base de datos prospectiva) de pacientes sometidos a cirugía general y bariátrica (1/2008-12/2017). Se evaluaron datos demográficos, detalles quirúrgicos y resultados.* **Resultados:** *Sesenta y cinco pacientes se sometieron a 76 procedimientos: 46 mujeres (71%), edad media 51 años (rango: 26-73), peso medio 284 libras (rango: 110-558), índice de masa corporal medio 45 (rango: 19-87). Comorbilidad: hipertensión (60%), enfermedad por reflujo gastroesofágico (54%), osteoartritis (49%), apnea obstructiva del sueño (45%), diabetes (37%). Operaciones: 22 cirugía general (29%), 20 gastrectomías en manga (26%), 12 revisiones/conversiones (16%), 12 Y-de-Roux (16%),*

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10 bandas gástricas (13%). Modalidades: 67% laparoscópica, 28% robótica, 5% abierta. A 22 pacientes (34%) se les colocó un filtro de vena cava inferior preoperatorio sin complicaciones. La estancia media fue de 4.4 días (rango: 1-31). Complicaciones: 7 reingresos a los 30 días (9%), 1 reoperación a los 30 días (1%), 2 TEV a los 90 días (3%). Reingresos a los 30 días: 4 por incapacidad para tolerar la vía oral, 2 obstrucciones de intestino delgado y 1 úlcera anastomótica sintomática. **Conclusiones:** *En nuestros casos, la anticoagulación posoperatoria pudo iniciarse sin aumento del riesgo de sangrado en pacientes con antecedentes de TVE sometidos a cirugía bariátrica.*

Palabras clave: *Anticoagulación. Cirugía bariátrica. Trombosis venosa profunda. Obesidad mórbida. Embolia pulmonar.*

Introduction

Bariatric patients are at an increased risk of venous thromboembolism events (VTE) due to a combination of factors, such as high body mass index (BMI), immobility, weight-related ventilation disorders (i.e., obstructive sleep apnea [OSA] and obesity hypoventilation syndrome), and venous stasis disease[1,2]. The dilemma is with respect to the concurrent prevention of VTE while avoiding bleeding events for bariatric patients undergoing major operations. Current literature reports the incidence of 30-day post-operative, symptomatic VTE in the bariatric population as 0.4% and 0.42% in the 90-day post-operative period[3,4]. Furthermore, VTE incidence following bariatric procedures ranges from 1% to 5.4% and < 1% for laparoscopic procedures[1]. Despite a low incidence of VTE following bariatric procedures, autopsies performed on 10 post-bariatric patients revealed pulmonary embolism (PE) as the cause of death in 30% of the patients[5]. While no exact epidemiological data are available, the incidence of PE is estimated at 60-70/100,000, and that venous thrombosis is approximately 124/100,000 of the general population[6], emphasizing the high prevalence of both fatal and non-fatal VTEs. A 2018 study reviewing the impact of bariatric surgery complications on clinical outcomes suggests that initiatives focused on reducing post-operative VTE have the greatest potential to lower mortality and readmission after bariatric surgery[7].

Chemoprophylaxis of VTE must be balanced with the inhibition of hemorrhagic events. A recent article reviewing patients with chronic anticoagulation (AC) undergoing bariatric procedures found patients to be at higher than average risk for post-operative complications and readmissions[8]. The authors state that attention to AC protocols and operative technique is necessary to decrease perioperative risk in this population. A meta-analysis of 19 studies found a weighted mean incidence of major bleeding in 2% with weight-adjusted, prophylactic heparin[9]. Optimal perioperative AC and the resulting occurrence of post-operative bleeding events or acute thrombotic events in patients with a known history of VTE have not been well-established. We hypothesize that there is a very low risk of bleeding complications in bariatric patients with a history of VTE. Therefore, the goal of this study was to examine the use and outcomes of perioperative AC in obese patients with a known history of VTE, undergoing bariatric and general surgical procedures at a Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program Center of Excellence.

Material and methods

After approval of our Institutional Review Board approval was obtained, our prospective database was retrospectively reviewed for patients with a VTE history who underwent primary and secondary bariatric and non-bariatric procedures from January 2008 through December 2017. Independent demographic variables included age, gender, weight, and BMI. Examined comorbidities included diabetes, hypertension (HTN), gastroesophageal reflux disease (GERD), osteoarthritis (OA), and OSA. The surgical details include procedure type, modality, presence of inferior vena cava filter (IVCF), and perioperative AC. Outcomes were reported as the length of stay (LOS), 30-day readmission, 30-day reoperation, 30-day and 90-day VTE, bleeding events, and mortality.

The prophylactic protocol used at this institution included the use of 5000 units of low molecular weight heparin (LMWH) given subcutaneously preoperatively in combination with bilateral lower-extremity intermittent pneumatic compression unless the patient had a contraindication such as lymphedema. Patients were encouraged to ambulate 3-4 h following extubation and every 3-4 h while admitted. Patients with a BMI > 50 kg/m^2 were also discharged with 40 mg subcutaneous post-operative enoxaparin sodium twice daily for 14 days. If a patient was taking therapeutic doses of AC, for example, warfarin or apixaban, discussions with the prescribing physician and recommendations for

perioperative AC were made. The patients were instructed to discontinue the use of home AC preoperatively for a pre-determined number of days (e.g., clopidogrel held 10 days before surgery) and use subcutaneous enoxaparin sodium until the morning of surgery. Postoperatively, full AC with subcutaneous enoxaparin sodium based on weight was resumed after 48 h to a maximum of 100 mg/kg. This was continued until the recommencement of the patient's home medication. For patients with a BMI > 60 kg/m^2, vascular surgery consultation was obtained for the evaluation of potential placement of a prophylactic IVCF. Patients who refused IVCF were treated with AC through enoxaparin sodium as noted above. Oral contraceptive pills were held 1 month before and 1 month following surgery. Smoking cessation was required for 6 weeks before primary bariatric procedures and confirmatory testing was performed using carboxyhemoglobin and nicotine levels. Patients with a known hypercoagulable state were referred to hematology for evaluation and recommendations before surgery. Non-compliant patients did not undergo elective operations.

Statistical analysis

Descriptive statistics were calculated for the overall sample. Data are reported as mean ± SD (range) for continuous variables and frequency (%) for categorical variables.

Results

Patient demographics

Sixty-five patients underwent 76 surgical procedures over the 10-year period. Table 1 shows the baseline demographic data of patients who underwent primary and secondary bariatric procedures between 2008 and 2017. Of these, the majority were female (71%) and the mean age for all patients was 51 years (range 26-73 years). The average BMI was 44.8 kg/m^2 (range 20.0-87.0 kg/m^2), and the average weight in pounds was 284 with a range of 110-558. Most patients were noted to have class III obesity, with a BMI > 40.0 kg/m^2. The following co-morbidities were identified: HTN (n = 39; 60%), GERD (n = 35; 53.8%), OA (n = 32; 49.2%), OSA (n = 29; 44.6%), and diabetes mellitus (n = 24; 36.9%). Of the 54 patients who underwent bariatric procedures, 22 (41%) had pre-operative IVCF in place. The range in time of placement before the surgery spanned from 16 years (for a remote history of VTE) up to 5 days preoperatively. Six were placed specifically for VTE prophylaxis before surgery (mean 17-day preoperatively). Fifteen patients (23%) were on therapeutic pre-operative AC; agents included warfarin, rivaroxaban, enoxaparin sodium, and apixaban.

Table 1. Patient demographics

Variable	n = 65 (%)
Gender	
Female	46 (71)
Male	19 (29)
Age, years	51.0 ± 12.2* (26-73)
Caucasian	160 (76.9)
BMI	44.6 ± 11.6* (20-87)
< 30.0	6 (9.2)
30.0-39.9	13 (20)
40.0-49.9	28 (43.1)
50.0-59.9	12 (18.5)
≥ 60.0	6 (9.2)
Weight, pounds	284.0 ± 89.2* (110-558)
Therapeutic AC†	15.0 (23.1)
Co-morbidities	
OSA	29 (45)
HTN	39 (60)
GERD	35 (54)
OA	32 (49)
DM	24 (37)
IVCF‡	22 (33.8)

*Data are reported as mean ± SD (range) for continuous and frequency (%) for categorical measures. †AC: anticoagulation; includes warfarin, rivaroxaban, enoxaparin sodium, and apixaban. ‡ICVF: inferior vena cava filter; pre-operative; BMI: body mass index; OSA: obstructive sleep apnea; HTN: hypertension; GERD: gastroesophageal reflux disease; OA: osteoarthritis; DM: diabetes mellitus.

Operative details

Overall patients underwent procedures that included herniorrhaphy (hiatal, internal, umbilical, ventral, and incisional), adhesiolysis, cholecystectomy, repair of intestinal perforation, and colon resection (total n = 76). Table 2 illustrates the operative details of the 76 cases performed.

A minimally invasive approach was used in 95% of the cases with no conversions to open. The mean LOS was 4.4 days (1-31 days). The data were further stratified into patients who underwent bariatric procedures (n = 65). Of the 42 primary bariatric procedures performed, 15 patients had a pre-operative IVCF in place,

Table 2. Operative details of the studied cohort

Variable	n = 76 (%)
General Surgery	22 (29)
Gastric Band	10 (13)
Sleeve Gastrectomy	20 (26)
Roux-en-Y Bypass	12 (16)
Revision/Conversion	12 (16)
Modality	
Laparoscopic	51 (67)
Robot-assisted	21 (28)
Open	4 (5)

Table 3. Post-operative outcomes of the studied cohort

Variable	n = 76 (%)
LOS (day)	4.4 ± 7.1* (1-31)
	n (%)
VTE	
30-day	0 (0)
90-day	2 (2.6)
30-day readmissions	7 (9)
30-day reoperations	1 (1)
Conversion to open	0 (0)
Bleeding event	0 (0)
Mortality	0 (0)

LOS: length of stay; VTE: venous thromboembolism event.

with six placed specifically for VTE prophylaxis before surgery (mean 17-day preoperatively). No IVCF-related complications occurred. Thirty-day complications included seven readmissions (9%). Four readmissions were for inability to tolerate oral (PO) intake, two were for small bowel obstruction, and one was for a symptomatic anastomotic ulcer evidenced by syncope secondary to anemia. The patient with a symptomatic ulcer had a suspected bleeding event but was never confirmed during the workup. There were no other bleeding events that occurred. All readmitted cases were managed nonoperatively with esophagogastroduodenoscopy or placement of a nasogastric tube as indicated. No mortalities or reoperations occurred. All bariatric patients who had a pre-operative IVCF received preoperative heparin and those who were started on postoperative enoxaparin sodium within 24 h, were discharged on it with no bleeding complications or readmissions. Of the 15 patients that were on home AC, 11 (73%) received post-operative enoxaparin or heparin and were discharged on the former, while the remainder were discharged on their prior home regimen. No readmissions or bleeding events were noted in this group.

Of the 76 patients in the cohort, the occurrence of 30- and 90-day clinically significant VTEs was zero and two (2.6%), respectively. Of the two patients readmitted for 90-day VTE, both were bariatric cases. One was a laparoscopic Roux-en-Y and the second was a laparoscopic gastric banding procedure (Table 3). Both patients were Caucasian; the former was a 63-year-old female, with a BMI of 54 kg/m^2 and the second patient was a 61-year-old male, with a BMI of 37 kg/m^2. One patient had an IVCF placed preoperatively secondary to her habitus, and the second patient had an IVCF placed after thrombectomy for the DVT in the lower extremity on readmission. The female patient had a history of a DVT and received pre-operative heparin per institution protocol but to our knowledge was not on any home AC. Both patients received post-operative enoxaparin sodium.

Discussion

While the incidence is low, PE is the most common cause of post-discharge mortality after bariatric surgery and is a feared complication[10]. Bariatric surgery patients are at least at moderate risk of thromboembolism and ideally should be started on combined mechanical and pharmacological prophylaxis[11]. This study aimed to evaluate the incidence of VTE in a single institution population cohort to better assess the optimal timing of AC treatment in patients with a history of VTE and the risk of occurrence of postoperative hemorrhagic events. Several risk factors must be taken into account when planning the ideal perioperative VTE prophylaxis, including a history of prior VTE[2]. The American Society for Metabolic and Bariatric Surgery (ASMBS) released an updated statement on VTE prophylaxis in the bariatric surgery population, which states the lack of class I evidence to provide guidance[2]. However, nine recommendations were given which include mechanical prophylaxis and early ambulation for all bariatric surgery patients; a combination of mechanical and chemoprophylaxis based on clinical judgment and bleeding risk; LMWH may offer better VTE prophylaxis than unfractionated heparin without increasing bleeding risk – though the evidence is conflicting; the use of IVCFs should be used in conjunction with chemical and mechanical prophylaxis in select high-risk patients. The authors

also stated that most VTE events occur in the first 30 days after discharge. However, there was not enough evidence to recommend a specific duration of prophylaxis extension. The ASMBS also states that individual practices developed and adhered to prophylactic protocols show a reduction in the incidence of VTE complications.

In 2012, the American College of Chest Physicians released evidence-based clinical practice guidelines with respect to the prevention of VTE in non-orthopedic surgical patients[12]. Recommendations for mechanical or chemical prophylaxis for patients undergoing bariatric surgery were stratified by the patients' risk of thrombotic events. Virtually all bariatric patients are categorized as moderate risk and some even high depending on other co-morbidities. Moderate-risk patients are placed on either LMWH or mechanical prophylaxis. High-risk patients without a high risk of bleeding are placed on either AC in addition to mechanical prophylaxis. If there is a significant risk of major bleeding complications, mechanical prophylaxis is preferred until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated. The use of IVCF as a primary VTE prophylaxis was not recommended. No level 1 evidence was provided for optimal perioperative AC bridging for patients on prior therapeutic AC. In essence, the choice of prophylaxis should be determined based on the provider's individual risk assessment of the patient.

A 2013 study evaluated the prevalence of in-hospital VTE among post-bariatric surgery patients[13]. PE was diagnosed in 0.9% and DVT without PE was found in 1.3% of patients. IVCF was placed in 0.3% of all patients who underwent bariatric procedures and in 10.5% of patients with a VTE. The authors were unable to determine if the filters were placed before or after the development of the VTE. Of note, the in-hospital mortality of patients with a PE and an IVCF was 3.9% compared to 2.7% of those with a PE and no filter (not a statistically significant difference). Conversely, of patients with a DVT, in-hospital mortality was 0% with a filter and 1.3% without ($p = 0.009$), suggesting a potential propensity for patients with DVT. In comparison, a 2010 study found that IVCF did not reduce the incidence of post-operative VTE or mortality and that 57% of patients with an IVCF place experienced a fatal PE or complication related to the filter itself[14]. However, due to the relatively rare incidence of post-operative VTE, the lack of statistical power to demonstrate significant harm related to IVCF is a confounding variable.

Prophylactic planning in obese patients remains unstandardized. A single academic institution demonstrated effective risk reduction with the implementation of VTE prophylactic protocols for patients who underwent bariatric surgery[15]. Before the protocol, VTE and bleeding occurred in 1.6%, respectively. After protocol initiation, the incidence of VTE decreased to zero. Post-operative bleeding events increased to 2.7%; however, the incidence of severe bleeding, defined as requiring blood transfusion or re-operation, only occurred in 1.6% of the post-protocol group, which was no different than the pre-protocol incidence.

At our institution, VTE incidence was 2.6% ($n = 2$), which is higher than the stated literature. Given the small sample size, an overestimate of the magnitude is not unexpected. We also assume the degree of adherence to VTE prophylaxis is consistent but can contribute to increased incidence. Aminian et al.[16] aimed to generate a risk calculator for post-discharge VTE events in patients undergoing primary and revisional bariatric surgery. The study found that patients who developed post-discharge VTE as compared to those with no VTE were black, male, had higher BMI, increased age, and had a high prevalence of the following medical conditions at baseline: congestive heart failure, peripheral vascular diseases, paraplegia, and chronic obstructive pulmonary disease. Both of our patients had factors that placed them at higher risk including age > 60 years, male sex, and super-obesity (BMI $\geq 50 kg/m^2$). Bariatric centers can decide whether to be conservative or aggressive when considering extended pharmaco-prophylaxis in the setting of patients with a history of VTE, keeping in mind the potential benefits and complications of the available medication options. The question of choosing a stop point on estimated post-discharge VTE to guide extended pharmaco-prophylaxis should be considered. Particularly, patients with a prior history of VTE are at higher risk of reoccurrence and may warrant extended therapy.

The next question begs how to adequately carry out which AC for the bariatric patient. A large literature review by Huo and Muntz showed that LMWH was efficacious and associated with lower rates of clinically relevant bleeding complications[17]. LMWH has a longer half-life, carries less risk for heparin-induced thrombocytopenia, and has similar rates of post-operative hemorrhage when compared to unfractionated heparin (1.6%)[18]. Our study results support this; most patients were started on post-operative AC within 12 h

or bridged to their home reagent. There were no clinically significant bleeding events.

Post-discharge VTE in bariatric patients need prophylaxis. It is reasonable to consider a pre-operative risk assessment and stratify patients based on a calculated VTE risk. The likelihood of post-operative bleeding should be taken into consideration; from our study results, we support the resumption of full AC. Those with a prior VTE and other subset higher risk populations may benefit from extension pharmaco-prophylaxis.

Conclusions

Obese patients with a history of VTE can undergo bariatric and general surgical procedures with a low incidence of post-operative VTE or bleeding events. While the overall incidence rate is low, clinically fatal VTE is a single cause of mortality easily amenable to reduction by a systematic change in practice. Therefore, each institution should implement a VTE prophylaxis protocol to decrease the occurrence of clinically significant DVT and PE. The choice of prophylaxis should be based on the specific assessment of each patient's risk for VTE or bleeding; however, LMWH has generally been shown to be superior. Post-operative AC can be started within 12 h of surgery and patients at high risk should be considered for extension pharmaco-prophylaxis. Further prospective studies are needed to consider the optimal dose, time, and frequency of VTE post-discharge prophylaxis.

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The authors declare to have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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ORIGINAL ARTICLE

Preoperative neutrophil-to-C-reactive protein ratio as a predictor of post-operative complications of pancreas cancer

Relación preoperatoria de neutrófilos a proteína C reactiva como predictor de complicaciones posoperatorias del cáncer de pancreas

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Abstract

Objective: *We would like to investigate the prognostic utility of the previously described factors and offer a new parameter called neutrophil-to-C-reactive protein ratio (NCR) as a predictor of post-operative complications of pancreas cancer.* **Methods:** *92 patients underwent pancreaticoduodenectomy for the pancreatic head tumor were enrolled in this study. Receiver operating curve analysis was performed to detect the cutoff values, and logistic regression analyses were performed to identify the independent risk factors of complications.* **Results:** *In univariate analysis, complications were observed in lymphocyte-to-C-reactive protein ratio levels below 0.06 (Odds Ratio [OR]: 3.92, 95% confidence interval [CI] = 1.08-14.21, p = 0.037). In multivariate analysis, albumin < 3.6 (OR: 3.25, 95% CI: 1.16-9.06, p = 0.024) and NCR < 0.28 (OR: 2.81, 95 % CI: 1.07-7.63, p = 0.042) were the independent and significant predictors of the overall survival.* **Discussion:** *Quantification of preoperative NCR and albumin may help surgeons to settle an effective perioperative management, take extra caution, and be aware of post-operative complications of pancreatic cancer patients.*

Keywords: *Pancreas cancer. Postoperative complication. Neutrophil-to-C-reactive protein ratio.*

Resumen

Objetivo: *Se investigó la proporción de neutrófilos a proteína C reactiva (NCR) como predictor de complicaciones posoperatorias del cáncer de páncreas.* **Material y Métodos:** *92 pacientes fueron sometidos a pancreaticoduodenectomía (PD) por el tumor de la cabeza del páncreas incluidos en este estudio. Se realizaron análisis de curva operativa del receptor (ROC) y análisis de regresión logística para detectar los valores de corte y los factores de riesgo independientes de complicaciones.* **Resultados:** *En análisis univariado; se observaron complicaciones en niveles de LCR por debajo de 0,06 (OR: 3.92, IC 95%: 1.08-14.21, p = 0.037). En análisis multivariado; albúmina < 3.6 (OR: 3.25, IC 95 %: 1.16-9.06, p = 0.024), NCR < 0.28 (OR: 2.81, IC 95 %: 1.07-7.63, p = 0.042) fueron los predictores independientes y significativos de la supervivencia.* **Conclusión:** *La cuantificación de la NCR y la albúmina preoperatorias puede ayudar a los cirujanos a establecer un manejo perioperatorio efectivo, tomar precauciones adicionales y estar atentos a las complicaciones posoperatorias.*

Palabras clave: *Cáncer de páncreas. Complicación postoperatoria. Proporción de neutrófilos a proteína C reactiva.*

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Introduction

Pancreatic cancer is one of the most lethal cancers, and the 5-year survival rate is about 10%. Because of anatomical localization of the pancreas, cancer is mostly diagnosed at an advanced stage. The standard treatment is pancreaticoduodenectomy (PD) followed by complex reconstruction which may lead to early postoperative complications[1-3]. Because to the challenging status of surgery and post-operative care difficulties, researchers try describing some parameters that predict post-operative complications before surgery and attempted to identify critical patients who need extra care. In some papers, patient-related inflammatory and immunonutritional markers, such as the prognostic C-reactive protein (CRP), albumin, prognostic nutritional index (PNI), modified Glasgow prognostic score, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-C-reactive protein ratio (LCR) are reported to be prognostic factors for the early postoperative complications, the survival of patients who have gastrointestinal cancer[4-6].

In this study, we would like to reveal the prognostic utility of the previously described factors and offer a new parameter called neutrophil to C-reactive protein ratio (NCR) for patients who underwent resection for pancreatic head tumors.

Methods

Sample

From January 2016 to December 2021, 92 patients underwent PD for the pancreatic head tumors in the department of general surgery of a tertiary hospital. All patients were admitted to surgery, and no one received neoadjuvant chemotherapy. Patients who underwent additional hepatic resection for metastases which is not detected previously and the ones who had cholangitis were excluded from the study. Patient data including age, sex, underlying disease, blood levels of hemogram parameters such as hemoglobin, neutrophil, lymphocyte and platelet levels, serum levels of albumin, bilirubin (total and direct), CRP and additional organ resection, post-operative complications according to Clavien Dindo classification, post-operative hospital stay, intensive care requirements, mortality, and pathology results were collected retrospectively. PNI, NLR, LCR, and NCR were also calculated. PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3). After initial analysis, patients were divided into two groups whether there were complications or not. Group one who had complications and group two who had discharged without any significant complications. The post-operative complications were classified according to the Clavien-Dindo[7]. Some demographic data and laboratory parameters were checked for difference if it existed between the groups. The receiver operating curve (ROC) analysis was performed between groups and detects the cutoff levels of PNI, NLR, CRP, albumin, LCR, and NCR. Univariate and multivariate logistic regression analyses were performed to identify the independent risk factors of complications. The study was approved by the local ethical committee of the University of Health Sciences, Antalya Education and Research Hospital.

Statistical analysis

All statistical analysis was carried out using JMP version 15.1 (SAS Institute Inc., Cary, NC, 1989-2019). Normality analysis of the data was tested using Shapiro–Wilk test. As the continuous variables were normally distributed, descriptive statistics are shown mean ± standard deviation standard error of mean and for variables that were not normally distributed are shown as median interquartile range. Categorical variables were displayed using numbers (n) and percentages (%). A Chi-square test was performed for sex, additional comorbidity, complication status, pathology, whether it is malign or benign, and mortality status. Independent samples tests were performed for parametric and normally distributed variables such as albumin and PNI, Mann-Whitney U-test was used for non-parametric variables or were not normally distributed; such as age, length of hospital stay (days), neutrophil count, lymphocyte count, CRP, NLR, NCR, and LCR. ROC analysis was performed to determine the cutoff value of the PNI, NLR, NCR, and albumin between groups. The area under the curve and 95% confidence intervals (CI) were calculated. The Youden index is used for determining the best cutoff points in the ROC analysis. Univariate and multivariate logistic regression analyses were performed to determine independent factors affecting post-operative complications. A $p < 0.05$ was set as statistically significant.

Results

The detailed demographic data of the patients are given in table 1. The study was composed of

Table 1. Demographic data of patients (n = 92)

Age, median (IQR) year	67 (60.25-75)
Sex, Male/Female, n (%)	56 (61) / 36 (39)
Co-morbidity, n (%)	69 (75)
PNI, mean ± SD (SEM)	42.3 ± 8.27 (0.86)
Albumin, mean ± SD (SEM)	3.33 ± 0.57 (0.05)
LCR, median (IQR)	0.13 (0.01-0.39)
NCR, median (IQR)	0.32 (0.15-0.86)
Lymphocytes/CRP, median (IQR)	0.12 (0.32-0.38)
Complications, n	57
Clavien Dindo	
I-II	25 (43.9)
III-IV-V	32 (56.1)
Hospital stay, median (IQR), days	13.5 (8-21.75)
Pathology, n (%),	
Benign	11 (12)
Malignant	81 (88)
Mortality, n (%)	16 (17)

IQR: interquartile range; CRP: c-reactive protein; LCR: lymphocyte-to-c-reactive protein ratio; NCR: neutrophil-to-c-reactive protein ratio; PNI: prognostic nutritional index; IQR: interquartile range; SEM: standard error of mean; SD: standard deviation.

92 patients with a median age of 67 years, and 56 (61%) patients were male. Up to 75% of patients had comorbidities such as diabetes, coronary artery disease, hypertension, and chronic obstructive pulmonary disease. Post-operative complications were observed in 57 patients according to Clavien Dindo. 25 of them were Grade I-II and 32 of them were Grade III-IV and V. Median hospital stay was 13.5 days. Post-operative pathology results revealed 88% malignity.

A comparison of demographic characteristics and laboratory parameters of the groups is presented in table 2. Age, albumin, CRP levels, and NCR were statistically significant between the groups. The median age was 69 in the Group 1, the mean albumin level was 3.21 and the median CRP level was detected at 17 in the complication group. The median NCR was 0.25 and 0.46, respectively, in Groups 1 and 2.

ROC analysis confirmed the cutoff values of the patient-related inflammatory and immunonutritional parameters between the groups which are given in table 3. Cutoff values for NCR and albumin were 0.28 and 3.6, respectively. High-sensitivity levels were observed in albumin and LCR, and high specificity was observed in NCR with a $p < 0.05$.

With the help of ROC analysis, patients were divided into two groups based on the cutoff levels of NCR (0.28) and data are given in table 4. Mortality and complications were found to be statistically significant below the cutoff value of 0.28. ($p = 0.007$, $p = 0.02$ respectively)

Univariate and multivariate logistic regression analyses were performed to determine independent factors affecting complications. In univariate analysis, complications were observed at LCR levels below 0.06 (Odds Ratio [OR]: 3.92, 95% CI: 1.08-14.21, $p = 0.037$). In multivariate analysis, albumin < 3.6 (OR: 3.25, 95 % CI: 1.16-9.06, $p = 0.024$) and NCR < 0.28 (OR: 2.81, 95% CI: 1.07-7.63, $p = 0.042$) were the independent and significant predictors of the overall survival (Table 5).

Discussion

The nutritional status of patients with cancer is important that cannot be ignored as there is a correlation between nutritional status and post-operative complications and outcomes. Plenty of studies published for predicting the post-operative early and long-term results for gastrointestinal malignities[8,9]. Serum albumin and CRP levels are well-known parameters that provide valuable data about post-operative morbidity and long-term mortality. Albumin is synthesized in the liver and is known as a negative acute phase reactant. Malnutrition, underlying liver disease, malignancy, acute trauma, and surgery may alter the levels of serum albumin levels. Low levels of albumin were correlated with the worse post-operative outcome[10].

CRP is also synthesized in liver as a positive acute phase reactant induced by pro-inflammatory cytokines, especially IL-6. In pancreatic cancer, peripheral blood mononuclear cells may also produce IL-6, which may lead increase in CRP levels[11]. In our recent study, mean albumin level was 3.21 ($p = 0.01$) and CRP level was 17 ($p = 0.02$) in the complication group.

PNI is a widely investigated predictor of gastrointestinal and pancreatic cancer to predict post-operative outcomes that was initially identified in 1980 by Buzby et al.[12] Albumin and lymphocyte levels are important to calculate the PNI level, and PNI can give us a fast and sufficient information for the postoperative course. A PNI level of around 45 is mostly set as a cutoff value and values > 45 are better for convincing outcomes following surgery[13,14]. The cutoff value for PNI was 44 in our study. Although there was a difference between the groups, there was no significance in logistic regression analysis.

Table 2. Comparison of demographic characteristics and laboratory parameters of groups (n = 92)

Variables	Group 1-complication (n = 57)	Group 2- no complication (n = 35)	p-value
Age, median (IQR range) year	69 (62.5-76.5)	63 (55-73)	0.01
Sex, Male/Female, n (%)	38 / 19 (66.7 / 33.3)	18/17 (51.4/48.6)	0.14
Co-morbidities, n (%)	45 (65.2)	24 (34.8	0.26
Albumin, mean ± SD (SEM)	3.21 ± 0.55 (0.07)	3.53 ± 0.55 (0.09)	< 0,01
CRP median (IQR)	17 (7-43)	10 (3-21)	0.02
Bilirubin, median (IQR)	3.1 (0.75-10.6)	1.9 (0.7-10.5)	0.5
PNI, mean ± SD (SEM)	41.18 ± 8.48 (1.12)	44.2 ± 7.67 (1.29)	0.08
NCR, median (IQR)	0.25 (0.12-0.64)	0.46 (0.27-1.61)	0.03
NLR, median (IQR) ($\times 10^3/mm^3$)	3.06 (1.79-4.81)	2.68 (1.95-3.89)	0.57
LCR median (IQR)	0.1 (0.03-0.34)	0.18 (0.07-0.62)	0.1

CRP: c-reactive protein; LCR: lymphocyte-to-c-reactive protein ratio; NCR: neutrophil-to-c-reactive protein ratio; AUC: area under curve; CI: confidence interval; PNI: prognostic nutritional index; IQR: interquartile range; SEM: standard error of mean; SD: standard deviation.

Table 3. Receiver operating characteristics analysis of parameters for complication cases

Variables	Value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	p-value
PNI	44	0.60 (0.48-0.72)	57.1	65	0.08
NLR ($\times 10^3/mm^3$)	2.88	0.52 (0.4-0.64)	62.8	54.4	0,65
CRP (mg/dL)	16	0.64 (0.52-0.75)	54,2	71.5	0,03
Albumin (mg/dL)	3,6	0.65 (0.53-0.76)	82.4	45.8	0.02
LCR ($\times 10^3/mm^3$)	0.06	0.62 (0.5-0.74)	82.8	45.7	0.048
NCR ($\times 10^3/mm^3$)	0.28	0.65 (0.53-0.76)	52,54	77.2	0.02

CRP: c-reactive protein; LCR: lymphocyte to c-reactive protein ratio; NCR: neutrophil-to-c-reactive protein ratio; AUC: area under curve; CI: confidence interval; PNI: prognostic nutritional index; IQR: interquartile range; SEM: standard error of mean; SD: standard deviation.

NLR reflects online dynamic relationship between innate (neutrophils) and adaptive cellular immune response (lymphocytes) during illness and various pathological states[15]. NLR is also a well-known parameter correlated with many other gastrointestinal cancer outcomes. In a meta-analysis conducted by Yang et al. including eleven studies with 1804 patients, NLR was found to be a poor prognostic factor for pancreatic cancer patients' overall survival[16]. In another study, NLR and blood loss volume were associated with post‐operative complications[17]. We could not find strong correlation between NLR and post-operative complications.

Recently, LCR is another marker shown to be a predictive factor for some various cancer types. In patients with colorectal, gastric, and hepatocellular cancer, LCR levels were found to be a prognostic factor for short-term and long-term outcomes[5,8,18]. To our knowledge, this study could be the early ones of the study that LCR was found to be an independent prognostic factor in the univariate analysis of early post-operative complications in patients with pancreatic cancer (p = 0.037).

Neutrophils occupy 50-70% of all leukocytes, which are the most abundant immune cell population. Patients with various cancer types, not limited to breast, lung, and colorectal cancer, often express increased numbers of circulating neutrophils[19]. In a recent study, we also evaluated the correlation between NCR and postoperative complications. NCR was described as a prognostic factor of bowel resection in incarcerated inguinal hernia. A level of 0.45 was the cutoff value for prediction resection of bowel[20]. In another study, NCR and LCR used for prediction the severity of acute appendicitis[21]. In both univariate and multivariate

Table 4. Clinicopathological data of patients according to cutoff values of neutrophil to CRP ratio (n = 92)

Variables	NCR < 0.28	NCR > 0.28	p-value
Age, median (IQR) year	68.5 (64.25-75.75)	65 (57.25-74.75)	0.04
Sex, Male/Female, n (%)	31 (55.4) / 25 (44.6)	9 (25) / 27 (75)	0.004
Comorbidity, n (%)	32 (46.4)	37 (53.6)	0,3
Complications, n (%)	31 (54.4)	26 (45.6)	0.007
Clavien dindo, n (%)			0,4
I-II	12 (38.7)	19 (61.3)	
III-IV-V	13 (50)	13 (50)	
Hospital stay, median (IQR), days	15.5 (8.25-22.75)	12.5 (8-20)	0.4
Pathology, n (%),			0.6
Benign	4 (36.4)	7 (63.6)	
Malignant	36 (44.4)	45 (55.6)	
Mortality, n (%)	11 (68.8)	5 (31.2	0.02

IQR: inter quartile range.

Table 5. Logistic regression analysis of the independent predictors of complications in periampullary tumor surgery

Variable	Univariate analysis		Multivariate analysis	
	OR (CI 95%)	p-value	OR (CI 95%)	p-value
Age	0.218 (0.4-1.19)	0.079		
PNI	1.95 (0.83-4.61)	0.124		
NLR ($\times 10^3/mm^3$)	0.55 (0.23-1.31)	0.182		
CRP (mg/dL)	0.4 (0.11-1.32)	0.132		
Albumin (mg/dL)	3.96 (1.52-10.26)	0.005	3.25 (1.16-9.06)	0.024
LCR ($\times 10^3/mm^3$)	3.92 (1.08-14.21)	0.037	1.56 (0.37-6.66)	0.545
NCR ($\times 10^3/mm^3$)	3.44 (1.37-8.64)	0.008	2.81 (1.07-7.63)	0.042

CRP: c-reactive protein; LCR: lymphocyte-to-c-reactive protein ratio; NCR: neutrophil-to-c-reactive protein ratio; CI: confidence interval; PNI: prognostic nutritional index; OR: odds ratio.

logistic regression analyses, an NCR level of 0.28 was found to be an independent parameter of post-operative complications. To the best of our knowledge, this is the only study that has evaluated the effect of NCR on post-operative complications of PD.

Learning points

Complications after PD are a challenging issue.

Several biomarkers such as PNI, NLR, and CRP have been studied to predict the better postoperative outcome.

The LCR and NCR could be valuable parameters in predicting the postoperative course.

To the best of our knowledge, there is no report on the use of NCR in the prediction of post-operative complications of PD.

Limitations of the study

Since this is a retrospectively designed study, we have some limitations. Data were collected from the database of our hospital and there may be some missing values due to coding errors. Even though the study was conducted in a tertiary hospital, it is a single-centered study.

Conclusion

Pancreatic cancer is one of the most lethal cancers in the world and post-operative complications are important issues to deal with. According to both univariate and multivariate logistic regression analyses, our results confirm that albumin and NCR can be used to predict post-operative complications of pancreatic cancer. Quantification of pre-operative NCR and albumin may help surgeons design more effective perioperative management, take extra caution, and be aware of post-operative complications of pancreatic cancer patients.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the ethics committee for analysis and publication of routinely acquired clinical data, and informed consent was not required for this retrospective observational study.

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ORIGINAL ARTICLE

Determining the need for surgery in small bowel obstructions based on clinical, laboratory, and radiological parameters

Determinación de la necesidad de cirugía en obstrucciones del intestino delgado según parámetros clínicos, de laboratorio y radiológicos

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Abstract

Objective: *Small bowel obstruction (SBO) is a common and important surgical emergency. Our aim in this study is to describe the clinical, laboratory, and computed tomography (CT) findings to facilitate the objective identification of SBO patients in need of operative treatment in this patient population.* **Method:** *This retrospective study included 340 patients hospitalized due to a preliminary diagnosis of ileus. Retrieved data of patients included age, gender, comorbidities, previous hospitalization due to ileus, surgical history, physical examination findings, complete blood count and biochemistry test results, and CT findings at admission.* **Results:** *The study included 180 (52.9%) male and 160 (47.1%) female patients. Treatment was conservative in 216 patients and surgery in 124 patients. Of the patients included in the study, 36.4% needed surgery. Of the female patients, 38.90% received conservative treatment and 61.30% underwent surgery. Adhesions were the most common cause of obstruction in operated patients (43.50%).* **Conclusions:** *We have found that female gender, vomiting, guarding, rebound, C-reactive protein levels above 75 mg/L, increased bowel diameter, and a transition zone on CT images indicate a strong need for surgery, but a history of previous hospitalization for ileus may show that surgery may not be the best option.*

Keywords: *Surgical treatment. Ileus. Small bowel obstruction. Conservative approach.*

Resumen

Objetivo: *Describir los hallazgos clínicos, de laboratorio y de tomografía computarizada (TC) para facilitar la identificación objetiva de los pacientes con obstrucción del intestino delgado que necesitan tratamiento quirúrgico.* **Método:** *Este estudio incluyó 340 pacientes. Los datos obtenidos fueron edad, sexo, comorbilidad, hospitalización previa debida a íleo, historia quirúrgica, hallazgos de la exploración física, hemograma completo y resultados de las pruebas bioquímicas, y hallazgos de la TC al ingreso.* **Resultados:** *El estudio incluyó 180 (52.9%) varones y 160 (47.1%) mujeres. El tratamiento fue conservador en 216 pacientes y quirúrgico en 124 pacientes. De los pacientes incluidos en el estudio, el 36.4% necesitaron cirugía. De las mujeres, el 38.90% recibieron tratamiento conservador y el 61.30% se sometieron a cirugía.* **Conclusiones:** *Encontramos que el sexo femenino, los vómitos, la guardia, el rebote, los niveles de proteína C reactiva superiores a 75 mg/l, el aumento del diámetro intestinal y una zona de transición en las imágenes de TC indican una fuerte necesidad de cirugía.*

Palabras clave: *Tratamiento quirúrgico. Íleo. Obstrucción del intestino delgado. Enfoque conservador.*

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Introduction

Small bowel obstructions (SBOs) account for approximately 3% of all laparotomies[1]. A precise diagnosis of SBO may be difficult with the decision-making process for surgery mainly based on clinical findings. Clinical findings of SBO include signs of peritoneal irritation, abdominal pain, abnormal bowel sounds, and a history of previous abdominal surgery. The underlying cause of such symptoms needs to be identified for timely and appropriate intervention with reductions in morbidity and mortality. Adhesions are the potential complications of abdominal surgery and the leading cause of SBO[2].

Strangulated SBO (SSBO) may require immediate surgical intervention. Studies report 2-10 times higher mortality rates in patients with SSBO compared to those without[3]. The time from the onset of complaints to surgery has been identified as a risk factor for strangulation and surgical site complications[4]. Therefore, there is a need for the rapid identification of the characteristic findings of SBO to prevent potential strangulation and bowel necrosis and reduce morbidity and mortality rates[5]. Studies are available in the literature showing that a large number of SBO cases without strangulation can be successfully managed through conservative treatment[5-7]. This requires the identification of patients without SSBO to avoid the risk of immediate surgery and to start standard conservative treatment, which includes fluid and electrolyte resuscitation, nasogastric (NG) decompression, and fasting. Standard conservative treatment is most successful (80%) in patients with partial obstruction[8,9]. The maximum duration of allowed conservative treatment usually ranges from 3 to 5 days, depending on the surgeon and the institution[10]. Close monitoring of persisting and progressing symptoms and appropriate clinical management is necessary to avoid late recognition of strangulation associated with increased morbidity and mortality. In this study, accordingly, we aimed to develop an objective approach based on clinical, laboratory, and radiological data to predict the need for operative intervention in SBO.

Materials and methods

This retrospective study included data from 340 patients, who were hospitalized due to a preliminary diagnosis of ileus in our clinic, the General Surgery Clinic of Bursa Yüksek İhtisas Training and Research Hospital of Health Sciences University, during the period between January 01, 2018, and December 31, 2021. Before starting the study, approval was obtained from the Clinical Research Ethics Committee of the Hospital with the decision number 2011-KAEK-25 2021/12-06 on December 15, 2021.

During the planning phase of our study, we performed a power analysis based on similar studies and calculated a sample size of 304 patients. Patients, who were hospitalized due to the diagnosis of ileus and received medical/surgical treatment, were included in our study. We retrieved patients' medical information from the patient information-processing system and medical files. We included clinical and laboratory findings and computed tomography (CT) images obtained in the emergency setting after admission. The recorded medical data of eligible patients for the study included age, gender, the history of previous hospitalization due to ileus, surgical history, physical examination findings, complete blood count and laboratory test results (leukocyte [white blood cell], neutrophil, platelet counts; hemoglobin levels, neutrophil-lymphocyte ratios, and sodium [Na], aspartate aminotransferase [AST], alanine aminotransferase [ALT], blood urea nitrogen, creatinine, and C-reactive protein [CRP] levels), and CT findings (intraperitoneal fluid volume, small bowel diameter, small bowel wall thickness, transition zone). An assigned physician reviewed CT findings. Intraperitoneal fluid volumes on CT images were measured according to the method described by Oriuchi et al.[11]. We used these recorded data for comparisons to examine the need for surgery and small bowel resection. Patients under the age of 18, patients with colonic obstruction, and missing data in medical records were excluded from the study.

Surgery or conservative treatment was decided based on clinical judgment by the current on-duty physician. Patients with suspected simple obstruction received conservative treatment with bowel rest, NG decompression, and intravenous fluid supply. Patients with suspected complicated SBO underwent emergency laparotomy. The diagnosis of complicated obstruction was made at laparotomy with macroscopic evidence of intestinal ischemia requiring small bowel resection.

We performed the statistical analyses of the study using the SPSS program (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). We tested the conformity of continuous variables to a normal distribution by the Shapiro–Wilk test. We summarized continuous

variables conforming to a normal distribution as mean ± standard deviation and those not as median (minimum: maximum). We summarized categorical variables as numbers and percentages. We performed the intergroup comparisons of normally distributed continuous variables using the independent double-sample t-test. We used the Mann–Whitney U test to perform intergroup comparisons of continuous variables not conforming to a normal distribution. We used the χ^2, Fisher's exact χ^2, and Fisher–Freeman–Halton tests to compare categorical variables between groups. We performed a logistic regression analysis to investigate potential risk factors favoring the decision for surgery. We accepted a type I error rate of 5% in statistical comparisons.

Results

This study included 340 patients, who were admitted to the hospital due to SBO. Of these patients, 216 received conservative treatment and 124 underwent surgery. Of the patients, who underwent surgery, 93 underwent resection and 31 did not. Table 1 shows the causes of SBO in study patients. The most common cause of SBO was adhesion in patients, who underwent surgery because of the clinical signs and symptoms of SBO. Figures 1 and 2 show a case of SBO due to intussusception and adhesive tape.

Table 2 shows the comparison of the demographic, clinical, laboratory, and radiological characteristics of patients between the conservative treatment and surgical intervention groups.

There were significant differences in gender distribution, length of hospital stay, and mortality rates between the groups ($p < 0.001$). The median length of hospital stay was longer (9.50 days) in the surgical group compared to that found in the conservative treatment group (4 days). Women accounted for 38.90% and 61.30% of the patients in the conservative and surgical treatment groups, respectively.

The presence of vomiting ($p = 0.012$) and peritoneal irritation findings (tenderness [$p = 0.015$], guarding [$p < 0.001$], and rebound [$p < 0.001$]) were significantly different between the groups, occurring more commonly in the surgical group. When we examined the patient distribution under the CRP < 75 mg/L and CRP ≥ 75 mg/L categories, we observed that the patients with CRP ≥ 75 mg/L were more common in the surgical group ($p < 0.001$).

The median bowel diameter and the rate of patients with a transition zone were higher in the surgical intervention group compared to the conservative treatment group ($p = 0.001$ and $p < 0.001$, respectively) (Figs. 3 and 4). The wall thickness was not different between the groups. Elimination of the cause (adhesiolysis, inguinal hernia repair, etc.) was sufficient for the treatment of the obstruction in patients with no intraoperative complications such as strangulation, necrosis, or perforation.

In the surgical group, when we compared demographic, clinical, laboratory, and CT findings between

Table 1. Distribution of patients according to the cause of SBO in the surgical group

Cause of SBO	(n = 124) (%)
Adhesion	54 (43.50)
Inguinal hernia	16 (12.90)
Incisional hernia	12 (9.70)
Bezoar	9 (7.30)
Femoral hernia	8 (6.50)
Internal Herniation	8 (6.50)
Malignancy	8 (6.50)
Invagination	5 (4.0)
Umbilical hernia	3 (2.40)

SBO: small bowel obstruction.

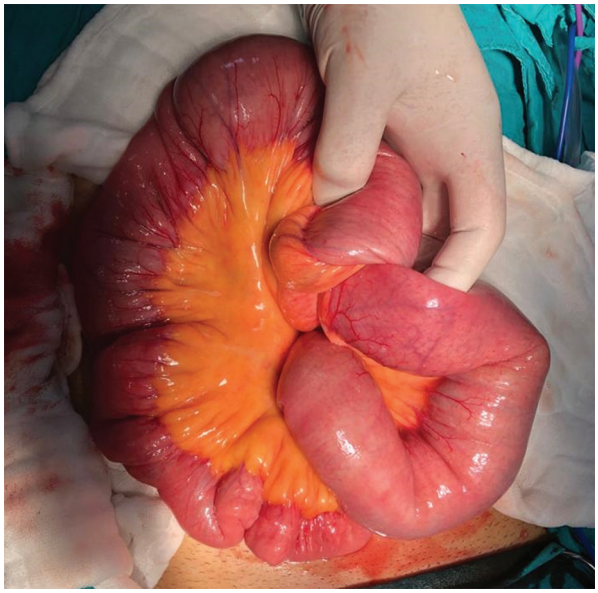

Figure 1. *Small bowel obstruction due to invagination, intraoperative image.*

Table 2. Comparison of the demographic, clinical, laboratory, and radiological findings between the conservative treatment and surgical intervention groups

Variables	Conservative treatment (n = 216)	Surgery (n = 124)	p-value
Age (Years)*	61 (19-95)	63.50 (19-95)	0.068[a]
Gender (%)			
Female	84 (38.90)	76 (61.30)	< 0.001[b]
Male	132 (61.10)	48 (38.70)	
Length of hospital stay (Days)*	4 (1-24)	9.50 (1-60)	< 0.001[a]
Outcome (%)			
Hospital discharge	215 (99.50)	112 (90.30)	< 0.001[c]
Death	1 (0.50)	12 (9.70)	
Pain duration (Days) (%)			
1-3	179 (82.90)	94 (75.80)	0.143[d]
4-7	35 (16.20)	26 (21.0)	
> 7	2 (0.90)	4 (3.20)	
Vomiting (%)	118 (54.60)	85 (68.50)	0.012[b]
Tenderness (%)	144 (66.70)	98 (79)	0.015[b]
Guarding (%)	3 (1.40)	17 (13.70)	< 0.001[b]
Rebound (%)	1 (0.50)	11 (8.90)	< 0.001[c]
Distention (%)	81 (37.50)	59 (47.60)	0.069[b]
Previous abdominal surgery (%)			
Major	96 (44.40)	43 (34.70)	0.175[b]
Minor	57 (26.40)	42 (33.90)	
None	63 (29.20)	39 (31.50)	
Previous hospitalization for ileus (%)	46 (21.30)	18 (14.50)	0.124[b]
History of radiation exposure (%)	10 (4.60)	2 (1.60)	0.223[c]
WBC (10^3/ml)*	12.63 (3.87-48.14)	11.49 (2.20-28.80)	0.077[a]
NLR*	7.07 (0.51-50.26)	6.43 (1.43-42.83)	0.810[a]
PLT (10^3/mL)*	285 (103-738)	298.50 (101-632)	0.217[a]
Hgb (g/dL)*	14.20 (7.80-18.60)	13.45 (8.20-17.70)	0.024[a]
CRP (mg/L)*	16.85 (2.86-434)	38 (2.86-349)	< 0.001[a]
CRP (mg/l) (%)			
< 75	176 (81.50)	76 (61.30)	< 0.001[b]
≥ 75	40 (18.50)	48 (38.70)	
Sodium (mmol/L)*	137 (122-151)	136 (125-145)	0.022[a]
AST (u/L)*	21 (6-174)	24 (12-87)	0.030[a]
ALT (u/L)*	15 (4-309)	17 (5-107)	0.122[a]
BUN (mg/dL)*	17.48 (5.37-76.31)	20.77 (4.44-154.70)	0.011[a]
Creatinine (mg/dL)*	0.91 (0.46-6.88)	0.89 (0.53-6.01)	0.434[a]
DRR	1.45 (0.21:5.40)	1,42 (0,39:6,20)	0.951[a]
CT: Presence of intraperitoneal fluid (%)	31 (14.40)	26 (21.0)	0.116[b]
CT: Bowel diameter (mm)*	38.50 (18-60)	40.50 (26-75)	0.001[a]
CT: Wall thickness (mm)*	3 (1.50-7)	2.70 (1.50-7)	0.413[a]
CT: Presence of a transition zone (%)	52 (24.10)	85 (68.50)	< 0.001[b]

*Data are expressed as median (minimum-maximum) and numbers and percentages. [a]Mann–Whitney U Test, [b]χ^2 test, [c]Fisher's exact χ^2 test, [d]Fisher–Freeman–Halton test.
WBC: white blood cell leukocyte count; NLR: neutrophil–to–leukocyte ratio; PLT: platelet count; HgB: hemoglobin; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen; DRR: De Ritis ratio; CT: computed tomography.

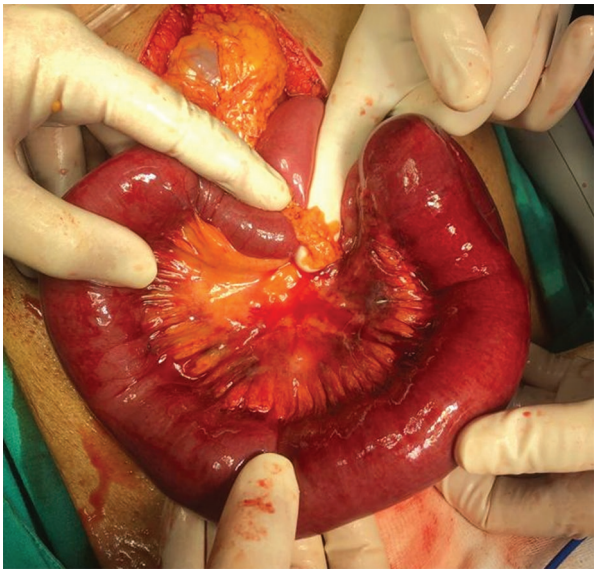

Figure 2. *Small bowel obstruction due to adhesive tape and disruption of intestinal blood flow.*

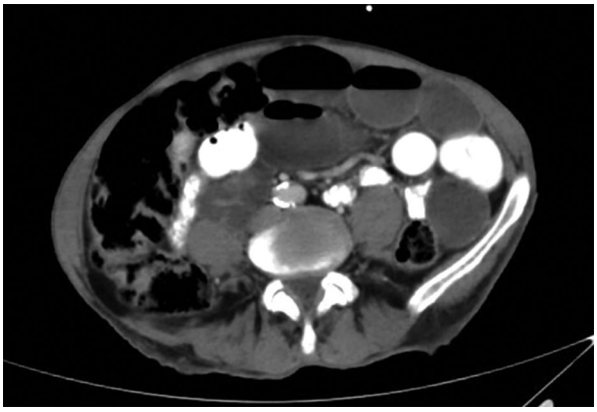

Figure 3. *Computed tomography of the abdomen shows dilated small intestines.*

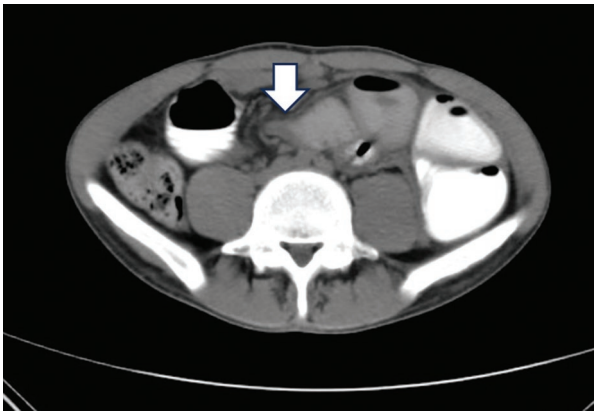

Figure 4. *Abdominal computed tomography showing the transition zone (arrow).*

the resection and non-resection groups, we found no significant differences in demographic data and clinical findings. However, in laboratory tests, we found a significant difference in the percentage of neutrophils and sodium levels between the resection and non-resection groups. The percentage of neutrophils and sodium levels were higher in patients, who underwent resection ($p = 0.026$ for both). Receiver operator characteristics curve (ROC) analysis was conducted to establish the cutoff point for neutrophil percentage in predicting the presence of resection in the patients included in the study (Fig. 5). If the neutrophil percentage was > 81.6, the area under the ROC curve was calculated as 0.63 (sensitivity 52.69%, specificity 74.19%, $p = 0.016$). It was concluded that a neutrophil percentage exceeding 81.6% was associated with the presence of resection. The comparison of CT findings between the resection and non-resection groups revealed that the intestinal wall thickness was higher in patients, who did not undergo resection ($p = 0.037$). No significant differences were found in other parameters between the resection and non-resection groups (Table 3).

We performed the logistic regression analysis method to examine the factors leading to the patient's referral for surgical intervention. First, we examined the variables in table 2 by univariate logistic regression analysis. Then, we included the variables that met the $p < 0.25$ condition in the multivariate logistic regression analysis. In the multivariate logistic regression analysis, we performed a variable selection process using the forward elimination method. Table 4 shows the findings obtained by the model in the final step.

The logistic regression model obtained in the final step of the logistic regression analysis was significant ($p < 0.001$) and the regression model fitted the data set ($p = 0.625$). Gender was a risk factor for surgery, and the rate of surgery was 2.66 times higher in women than in men. The rate of referral to surgery was 2.59 times higher in patients with vomiting compared to those with no vomiting. Patients with guarding and rebound were 6.16 and 29.31 times more likely to be referred to surgery, respectively, compared to patients without. In the patient group with a history of previous hospitalization for ileus, the rate of surgical intervention was 60% lower compared to patients with no such history. The rate of referral to surgery was 2.83 times higher in the patient group with CRP levels of ≥ 75 mg/L compared to the patient group with CRP levels of < 75 mg/L. A one-unit increase in the bowel diameter increased the rate of referral to surgery by

Table 3. Comparison of patients, who underwent small bowel resection, to those, who underwent surgery but no small bowel resection

Variables	Resection (n = 93)	No resection (n = 31)	p-value
Neutrophil %	82 (50.20-94)	77.30 (56.70-91.7)	0.026[a]
Sodium (mmol/L)	137 (125-145)	136 (127-144)	0.026[a]
CT: Wall Thickness (mm)	2.50 (1.50-7)	3 (2-7)	0.037[a]
DRR	1.40 (0.39:4.25)	1.50 (0.52:6.20)	0.427[a]

Data are expressed as median (minimum-maximum) and numbers and percentages.
a: Mann–Whitney U test; CT: computed tomography; DRR: de Ritis ratio.

Table 4. Risk factors acting on the decision of the patient's referral for surgery

Variables	Wald	p-value	OR	%95 (CI)	
				Lower	Upper
Gender (Female)	10.67	0.001	2.66	1.48	4.79
Vomiting	9.04	0.003	2.59	1.39	4.82
Guarding	5.17	0.023	6.16	1.28	29.58
Rebound	6.48	0.011	29.31	2.17	395.04
Previous hospitalization for ileus	4.94	0.026	0.40	0.18	0.90
CRP Level (≥ 75) (mg/L)	9.63	0.002	2.83	1.47	5.44
Bowel diameter (mm)	4.85	0.028	1.05	1.01	1.10
Presence of a transition zone	43.17	< 0.001	7.49	4.11	13.65
Model χ^2 = 114.68; p < 0.001					

Hosmer and Lemeshow test: *P* = 0.625; OR: odds ratio; CI: confidence interval; CRP: C-reactive protein.

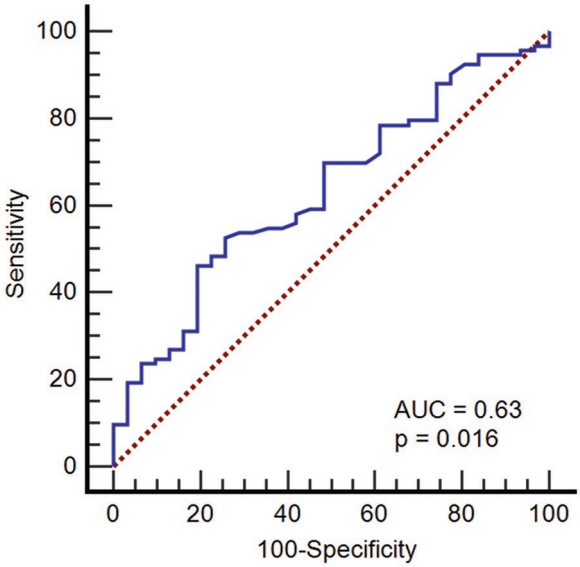

Figure 5. *Receiver operator characteristics analysis for neutrophil percentage.*

1.05 times. When there was a transition zone, the rate of referral to surgery was 7.49 times higher compared to the patients without a transition zone on CT images.

Discussion

Intestinal obstruction is the partial or complete inhibition of the distal passage of intestinal contents in the gastrointestinal tract[12]. The decision to operate on a patient with suspected SBO is based on physicians' clinical evaluation. The lack of widely accepted guidelines encouraged us to evaluate the accuracy of the clinical diagnosis of SBO. Timely and appropriate operative treatment of SBO should improve morbidity and mortality rates; however, it may be difficult to accurately identify patients in need of surgery during their hospital stay[13].

To this end, several attempts have been made to construct a predictive model to help guide the provision of appropriate treatment for SBO, but these studies used data from selected parts of the entire clinical scenario[14-16]. Instead, we examined all clinical parameters routinely tested during a hospital stay due to SBO, including history, physical examination, laboratory, and CT findings.

It is reported that 20-30% of patients with SBO need surgery[2]. This rate was 36.4% in our study. SBO is caused by adhesion, hernia, or malignancy in 90% of cases[17]. In our study, the most common cause of obstruction in operated patients was adhesion (43.50%), and the second most common cause was incarcerated inguinal hernia (12.90%).

Non-surgical follow-up is possible for most patients with intestinal bowel obstruction with no indication for emergency surgery. In many patients with SBO, non-surgical treatment improves symptoms, but success rates depend on the etiology. In adhesive SBOs, non-surgical management is usually successful in 65-80% of patients[18-21]. However, non-surgical management of adhesive SBO is associated with higher recurrence rates and shorter disease-free intervals compared to surgical management[2,7]. While approximately 40% of cases with complete obstruction can be managed conservatively, the need for bowel resection is high

(30%) in patients with unsuccessful conservative treatment outcomes[8,9]. In our study, on 340 patients, 216 patients received conservative treatment and 124 patients underwent surgery. Patients receiving conservative treatment in our study received fluid resuscitation, underwent NG decompression, and fasted during an appropriate period depending on their clinical condition.

Peritoneal irritation findings are vital findings favoring an emergency surgery decision. When similar studies in the literature are reviewed, peritoneal irritation findings come to the forefront in determining the need for surgery[22-24]. In our study, the rate of peritoneal irritation findings (tenderness, guarding, and rebound) was higher in the surgical group compared to the conservative treatment group. Tenderness occurred in 79% and 66.7%, guarding in 13.7% and 1.4%, and rebound occurred in 8.9% and 0.5% of the patients in the surgical and conservative treatment groups, respectively.

Animal experiments have shown that CRP levels are associated with the severity of bacterial translocation in acute intestinal obstruction[3]. In our study, we obtained findings consistent with the literature on this subject matter. When we grouped the patients under the CRP < 75 mg/L and CRP ≥ 75 mg/L categories, we observed that the patients with CRP ≥ 75 mg/L were more common in the surgical group ($p < 0.001$).

In clinical situations such as intestinal ischemia, hepatocyte damage may occur and AST and ALT ratios measured in blood may change. In one study, the De Ritis ratio was found to be a significant marker in predicting small bowel necrosis[25]. In our study, no significant difference was detected between the groups.

One study reported some inherent limitations of using CT alone to diagnose SBO and suggested that a combination of clinical and CT findings could improve diagnosis[26]. Two prospective studies examining the benefits of CT in the diagnosis of SBO showed an accuracy rate of 83-94% in differentiating obstruction from non-obstruction[27,28]. In a retrospective study on SBO patients, Jones et al. tested the correlation between CT scores and actual treatment and reported that images of dilated small bowel or free fluid on CT predicted SBO[29].

The transition zone is defined as the region between the small bowel loops proximal and distal to the obstruction. When the diameter difference between the dilated proximal and collapsed distal small bowel segments is small, it is difficult to identify the transition zone and the level of obstruction. Therefore, it is not as much as easy to detect the transition zone in patients with adhesions compared to tumors and hernias. In their study, Fukuya et al. reported an increased diagnostic value by the use of oral contrast material in cases with unclear transition zones on CT images[30]. Gazelle et al. reported in their study that the presence of the transition zone on CT was a statistically significant parameter to make the diagnosis of SBO[31]. In our study, the rate of patients with a transition zone was higher in the surgical group ($p < 0.001$).

Similar studies reported the presence of intraperitoneal fluid as the most important factor in the diagnosis of SBO[29,32]. In our study, we found that the rates of patients with intraperitoneal fluid did not differ statistically between the surgical and conservative treatment groups ($p = 0.116$). However, there was a difference between the groups by the bowel diameter. The median bowel diameter was statistically significantly higher in the surgical group compared to the conservative treatment group ($p = 0.001$).

Vomiting is a common symptom in patients with SBO. In the study by Zielinski et al., patients with vomiting were 4.7 times more likely to undergo surgery[32]. In our study, the need for surgery was 2.59 times more in patients with vomiting than in patients without.

Our study has some limitations: it is a retrospective study and our data are based on the existing records in our hospital's database. Because it is a single-center study, our results require further validation. Larger-scale and well-designed studies are needed.

Conclusion

Overall, our study on patients with symptoms and signs of SBO has shown that being a woman and having the following symptoms and signs including vomiting, guarding, rebound, CRP levels of ≥ 75 mg/L, increased bowel diameter, and a transition zone on CT increase the need for surgery. However, having a history of previous hospitalization due to ileus is associated with a reduced rate of surgery. The statistically significant results in our study are comparable with similar studies in the literature.

In light of the data obtained from our study, we have concluded that a comprehensive evaluation based on clinical, laboratory, and radiological parameters is necessary to determine the need for surgery in cases with SBO. Our statistically significant results can be used as objective findings to guide surgical decision-making in the management of patients with SBO.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

Assessment of quality of life in patients with neurogenic bladders who undergone urinary system reconstruction (Mitrofanoff)

Evaluación de la calidad de vida en pacientes con vejiga neurogénica que se sometieron a reconstrucción del sistema urinario (Mitrofanoff)

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Abstract

Objective: *The purpose of this study was to evaluate the additional contribution of the Mitrofanoff channel to health-related quality of life (HRQoL).* **Method:** *Between 2005 and 2009, we conducted a retrospective study on 10 pediatric patients who underwent Mitrofanoff surgery for neurogenic bladder and 11 control patients using urethral catheterization. We evaluated HRQoL using questionnaires tailored for various age groups, with higher scores indicating better QoL.* **Results:** *The mean age in the patient group was 12.8 years and 10.7 years in the control group (p = 0.103). Shunt use and wheelchair dependency were similar between groups (p = 0.217 and p = 0.505, respectively). Diaper use showed no significant difference (p = 0.256). Notably, 50% of the patient group performed self-catheterization compared to 9.1% in the control group, a significant difference (p = 0.038). Prophylaxis application was significantly higher in the control group (p = 0.049). HRQoL scores were not significantly different between surgery and control groups in children (p = 0.251) and adolescents (p = 0.831), with Cronbach's α values indicating high reliability of the HRQoL scale.* **Conclusions:** *Although the procedure shows potential in enhancing independence, particularly in self-catheterization, the impact on overall HRQoL is not significantly different from the control group.*

Keywords: *Mitrofanoff. Quality of life. Neurogenic bladders. Urinary system reconstruction.*

Resumen

Objetivo: *Evaluar la contribución adicional del canal de Mitrofanoff a la calidad de vida relacionada con la salud (CVRS).* **Método:** *Evaluamos la CVRS utilizando cuestionarios adaptados para varios grupos de edad, con puntuaciones más altas indicando una mejor calidad.* **Resultados:** *La edad media de los pacientes fue de 12.8 años y la del grupo control fue de 10.7 años (p = 0.103). El uso de derivaciones y la dependencia de silla de ruedas fueron similares entre los grupos (p = 0.217 y p = 0.505, respectivamente). Es notable que el 50% del grupo de pacientes realizaron autocateterización, en comparación con el 9.1% del grupo control (diferencia significativa, p = 0.038). La aplicación de profilaxis fue significativamente mayor en el grupo control (p = 0.049). Las puntuaciones de CVRS no fueron significativamente diferentes entre los grupos de cirugía y control en niños (p = 0.251) y adolescentes (p = 0.831), con valores alfa de Cronbach indicando una alta fiabilidad de la escala de CVRS.* **Conclusiones:** *Aunque el procedimiento muestra potencial en mejorar la independencia, en particular en la autocateterización, el impacto en la CVRS general no es significativamente diferente del grupo de control.*

Palabras clave: *Mitrofanoff. Calidad de vida. Vejiga neurógena. Reconstrucción del sistema urinario.*

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Introduction

In the United States, spinal dysraphism, particularly myelomeningocele, is one of the most common birth defects causing permanent disability, occurring in about 30 cases/100,000 live births[1-3]. More than 90% of patients with spina bifida develop neuropathic bladder dysfunction as a result; this can manifest as urinary incontinence, recurrent urinary tract infections, and, in the most severe cases, upper urinary system damage[4,5]. Unfortunately, up to 30% of adolescents in this condition experience some degree of kidney dysfunction.

Patients with neurogenic bladders often require minor or major surgical interventions to address urinary incontinence issues. Due to their inability to control urination, these children, often carrying the odor of urine and ostracized by their peers during childhood, experience a lack of self-confidence[6]. As adults, they continue to face similar challenges in finding and maintaining employment. In addressing this condition, the primary focus of assistance should be questioned: should it be on preserving the upper urinary tracts, or ensuring that the child remains dry? Both objectives are important, but the choice of focus can significantly impact the treatment approach and the patient's quality of life (QoL).

The QoL for patients with neurogenic bladders has significantly improved since the early 1970s with the introduction of the clean ıntermittent catheterization (CIC) method proposed by Lapides[7]. This method is considered a revolution in the treatment and management of neurogenic bladder. However, in some of these patients, despite having adequate bladder outlet resistance, bladder compliance and capacity may be low. Therefore, due to limited storage capacity, frequent CIC may be necessary to stay dry, which can complicate social life[7,8]. This highlights the complexity of managing neurogenic bladder conditions, where balancing medical needs with the impact on daily life is a critical part of treatment and care.

Patients who have undergone augmentation cystoplasty, as well as those who have not, often require lifelong CIC[9]. Due to this, they may need a continent-catheterizable channel, which facilitates easier catheterization than the urethra. For patients who have difficulty with urethral catheterization due to physical or anatomical reasons, or simply for ease of use, a tube can be created from various tissues such as the appendix, narrowed ileum, segments of the colon, distal ureter, bladder wall, or even fallopian tubes[10]. This tube is then implanted into the bladder wall using an anti-reflux method. Such a construction allows the patient to self-catheterize without assistance, greatly enhancing independence, and ease of living with their condition. This approach plays a significant role in improving the QoL for these patients by offering a more manageable and less invasive means of bladder management.

In our study, we conducted a QoL survey among patients with neurogenic bladders who underwent bladder augmentation and the Mitrofanoff procedure and subsequently performed CIC through this method. In addition, we surveyed patients with neurogenic bladders who performed CIC through the urethral route. The purpose of this study was to evaluate the additional contribution of the Mitrofanoff channel to HRQoL.

Materials and methods

Patients and design

Between 2005 and 2009, a retrospective study was conducted at the Pediatric Surgery Clinic and Pediatric Nephrology Outpatient Clinic of Şişli Etfal Hospital. It involved 10 patients between the ages of 5 and 20, who had undergone the Mitrofanoff operation due to neurogenic bladder. In addition, as a control group, 11 patients who performed CIC through the urethral route for the same reason were also included in the study. For evaluation purposes, these patients were asked to fill out a questionnaire.

The HRQoL developed by Parkin et al. evaluates patients across 10 fundamental life domains including social, emotional, mental, financial, medical, independence, environmental, physical, and occupational aspects. In practice, parents of children aged 5-12 were asked to complete a 44-item questionnaire, whereas patients aged 13-20 were given a 47-item questionnaire[11]. For patients with insufficient mental capacity, their parents completed the survey. Those who were unable to visit the hospital were surveyed over the phone. Higher scores obtained in the survey were interpreted as indicative of a higher health-related quality of life (HRQoL) (Tables 1 and 2).

In this study, higher scores obtained from the survey were indicative of a higher HRQoL. This survey aimed to provide detailed insights into the patients' perceptions of their continence post-surgery, a crucial aspect of their overall well-being and QoL.

Table 1. The health-related quality of life survey for children

Question no.	Question description
1	Is treated with respect + dignity by others?
2	Feels good about her/himself?
3	Is able to do some things as independently as possible?
4	Is able to get into the houses of his/her friends?
5	Accepts his/her physical limitations?
6	Will be able to choose a career of his/her own?
7	Has a chance to continue to study things in which he/she is interested?
8	Has a chance to learn to swim?
9	Participates in the same recreational activities as other children?
10	Has an opportunity to play indoors?
11	Has an opportunity to play outdoors?
12	Participates in games at recess?
13	Feels capable or skillful in some sport, hobby, or other activity?
14	Is stared at by others?
15	Is treated as if he/she were different?
16	Is healthy?
17	Is integrated into the school system?
18	Is able to use public washrooms that are accessible and private?
19	Has access to the community through ramps and elevators?
20	Is accepted and valued in our society?
21	Attends school that has a positive attitude toward children with disabilities?
22	Is in an environment that does not contain a lot of obstacles?
23	Has someone to confide in outside immediate family?
24	Has friends?
25	Has a supportive family?
26	Feels welcome in other children's homes?
27	Receives praise for things that he/she is able to do?
28	Feels important?
29	Is treated with respect by others?
30	Feels that she/he can accomplish her/his plans?
31	Expresses her/his emotions?
32	Has an opportunity to do everything other children do in school?
33	Is able to learn well in an environment that is favorable to children with disabilities?
34	Is motivated to learn?
35	Is able to attend camp for children with disabilities?
36	Feels that examinations and treatments at a hospital or clinic are respectful?
37	Feels that examinations and treatments at a hospital or clinic are private?
38	Feels related to as a whole person by a doctor?
39	Is able to deal well with being in the hospital?
40	Feels in control of the situation in medical appointments and treatments?
41	Is learning to deal positively with his/her disability?
42	Is becoming appropriately independent in areas of self-care, mobility, and self-catheterization?
43	Will be able to live independently in the future?
44	Possesses self-confidence?

*Patients were required to score from 1—a little to 5—a lot.

Eligibility criteria

Patients who opted not to participate in our study were excluded. Only those who completed the questionnaire and provided complete data were included in the study. Patients over the age of 20 were not considered within the scope of the study.

Surgical procedure

In many pediatric patients, a lower midline or transverse incision is made. A deep space is prepared on the right side of the bladder without opening the peritoneum. During this process, the umbilical artery remnant is ligated and cut, and the vas deferens are isolated and protected. Subsequently, the peritoneal cavity is entered, and the cecum and appendix are mobilized[12] (Fig. 1).

Sometimes, the cecum may be positioned high in the abdomen. Mobilization of the ascending colon along the Toldt line may be necessary to facilitate the mobilization of the appendix and its mesentery. An appendectomy is performed, preserving the vascular pedicle and including a portion of the cecal wall

Table 2. The health-related quality of life survey for adolescent

Question no.	Question description
1	That you are treated the same as everyone else?
2	That you have a supportive family?
3	That you are accepted just as you are?
4	That you are able to talk to 1 or both of your parents?
5	That people enjoy being with you?
6	That you are happy with yourself?
7	That you are able to speak up for yourself?
8	That there is hope for the future?
9	Positive about yourself?
10	That other people respect you?
11	Satisfied with your school program?
12	Able to participate in group activities?
13	That you are able to have a special friend?
14	Like you are treated the same as other kids?
15	That you are able to take care of yourself, for example brushing your hair & teeth?
16	That you are able to feed yourself?
17	That you are able to help with some or all of your catheterization?
18	That you are able to participate in some or all of your own bathing?
19	That you have a lot of pain?
20	That you can stand up for your rights?
21	That you can make your own choices and decisions?
22	That you are as independent as you are able to be?
23	That you can use the telephone?
24	That people listen to your opinions?
25	That you are treated with respect and dignity at your medical appointments?
26	That you have say in your medical treatment?
27	That you understand what your medical condition will be like in the future?
28	That you are getting good care at your spina bifida clinic?
29	That your doctors, nurses+others who treat you know about spina bifida?
30	That people see you + not only your disability?
31	That you will have a suitable home in the future?
32	That you have privacy + accessibility in public washrooms?
33	That you are able to use kitchen at home?
34	That your present washroom is suitable for you?
35	That you are able to participate in outdoor activities?
36	That you have the physical strength to do sports such as swimming and skiing?
37	You are able to go out on dates + to parties?
38	Challenged and encouraged through sports?
39	Successful or skilled in some sport or other activity you like?
40	That there will be job opportunities for you in the future?
41	You are able to get an education for a job that interests you?
42	That you have a career goal in mind?
43	Able to hold down a part-time job?
44	That you will be able to have children in the future?
45	That you will marry?
46	That you have somebody with spina bifida to look up to + to have as
47	That you have a close friend who is like you in many ways?

*Patients were required to score from 1—a little to 5—a lot.

making the stomal anastomosis easier and reducing the risk of stenosis. If the appendix is short, a portion of the cecal wall can be tubularized with the appendix. The defect in the cecum is closed, and the appendix, with its vascular pedicle, is transferred through the right mesocolon to the right side of the bladder. The peritoneum is then closed. The subsequent stages of the surgery continue extraperitoneally[12,13].

The bladder is opened in a vertical direction along the midline. If the bladder neck is to be closed, the incision is extended to the bladder neck, detached from the urethra, and the urethra is then closed. The closed end of the appendix is opened, and this end is implanted through an oblique or transverse submucosal tunnel in the trigone. The tunnel should be 3-4 cm in length (to maintain a 5:1 ratio). A Penrose drain is placed in the perivesical space to remain for several days[14,15] (Fig. 2).

The cecal end of the appendix is anastomosed to the abdominal wall in the right lower quadrant or

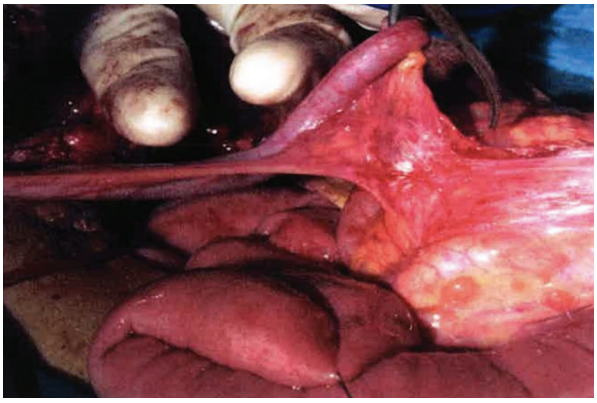

Figure 1. *Appendectomy for Mitrofanoff (schematic and operation image).*

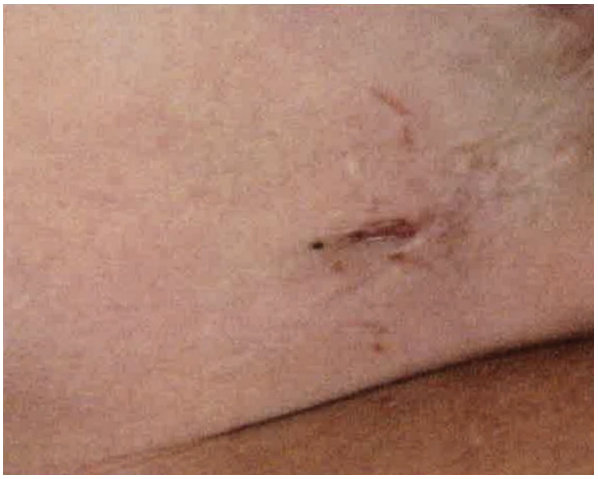

Figure 3. *A view of Mitrofannoff in post-operative period.*

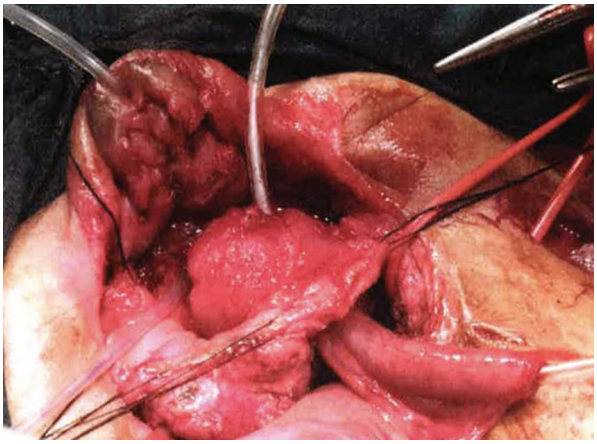

Figure 2. *Mitrofanoff's anastomosis to the bladder (operation image).*

umbilical pit, ensuring no tension is present at the site suitable for the patient. During this stage, care must be taken to ensure that the appendix and its mesentery pass through the anterior abdominal wall without kinking or angulation. To prevent kinking and problems with catheterization, a conduit as short as possible is recommended. Fixing the appendix and bladder wall beneath the fascia to the peritoneum helps reduce the problem of conduit angulation with bladder filling. Concealing the stoma at the skin level with the help of some flaps provides a more cosmetic result (Fig. 3). The catheter passing through the appendix is kept in place for at least 2 weeks[15].

Statistical analysis

This study's statistical analyses were conducted using NCSS 2007 software. The Cronbach's α coefficient was chosen to determine the reliability of the HRQoL scale. In the analysis of the data, descriptive statistical methods (mean and standard deviation), the Mann–Whitney U-test for binary group comparisons, and the χ^2 test for qualitative data comparisons were used. A one-way analysis of variance was conducted to compare the study groups of Parkin and Mac Neily with the groups in this study. The results were evaluated at a significance level of $p < 0.05$.

Results

A total of 21 patients were included in this study. Table 3 presents demographic and medical information for 10 patients with various medical conditions and 11 control patients. While the ages of the patients ranged from 8 to 18, the gender distribution was equal between males and females. In the surgery group, there were six patients with meningomyelocele, one patient with both meningomyelocele and high-type anorectal malformation, one patient with caudal regression syndrome, and two patients who underwent surgery due to exstrophy of the bladder. The patients' age at surgery ranged from 6 to 16, and the post-operative follow-up period varied between 14 and 73 months.

The study was conducted on two different groups consisting of a total of 21 participants. When examining the age distribution between the patient group (n = 10) and the control group (n = 11), the mean age of the patient group was found to be 12.8 ± 3.03 years, whereas the mean age of the control group was 10.7 ± 2.45 years. The age difference between the two

Table 3. Demographic characteristics of patients undergoing Mitrofanoff procedure

Patient no.	Age	Gender	Etiology	Operation age (year)	Post-operative follow-up (months)
1	17	Male	Meningomyelocele	11	73
2	13	Female	Meningomyelocele	7	73
3	12	Male	Meningomyelocele and high-type anorectal malformation	9	34
4	18	Female	Operated exstrophy of the bladder	16	29
5	14	Female	Caudal regression	12	29
6	13	Female	Meningomyelocele	11	29
7	9	Female	Meningomyelocele	6	35
8	12	Male	Meningomyelocele	9	49
9	12	Male	Meningomyelocele	9	47
10	8	Female	Operated exstrophy of the bladder	7	14

groups was not statistically significant (p = 0.103). In terms of gender distribution, 60% of the patient group were female and 40% were male, whereas in the control group, 45.5% were female and 54.5% were male (p = 0.505). The use of shunts was found to be 20% in the patient group and 45.5% in the control group, and the difference between the groups was not statistically significant (p = 0.217). Regarding dependency on a wheelchair, 40% of the patient group and 54.5% of the control group used wheelchairs (p = 0.505). Diaper use showed no significant difference between groups (p = 0.256). When the frequency of urinary bladder catheterization was examined, it was observed that there was no prophylaxis applied by some participants in the patient group, whereas, in the control group, frequencies of 2 × 1, 3 × 1, 4 × 1, 5 × 1, and 6 × 1 were observed. Due to inconsistency among these frequencies, statistical analysis could not be conducted. However, the number of patients who performed self-catheterization was 50% in the patient group, whereas it was 9.1% in the control group, and this difference was statistically significant (p = 0.038). Furthermore, when looking at the prophylaxis application status, 30% of the patient group applied prophylaxis, whereas 72.7% of the control group applied prophylaxis, and this difference was statistically significant (p = 0.049) (Table 4).

Table 5, patients who underwent surgery in terms of the intestine segment used for augmentation, whether anti-reflux surgery was performed, whether bladder neck repair was done, and if done, the method used, the preferred organ for the Mitrofanoff procedure, and the indications for surgical intervention are summarized.

The internal consistency of the scale used to assess HRQoL in the study was evaluated, and the Cronbach's α value was calculated as 0.964 for the adolescent surgery group, 0.909 for the control group, 0.864 for the child surgery group, and 0.950 for the child control group. When looking at HRQoL scores, in children, patients who underwent surgery had a score of 180, whereas the control group had a score of 153, and the difference between them was not statistically significant (p = 0.251). However, although the difference may not be significant, a higher and better QoL score was obtained in the surgery group. On the other hand, when looking at HRQoL scores in adolescents, patients who underwent surgery had a score of 188, whereas the control group had a score of 190, and the difference between them was not statistically significant (p = 0.831) (Table 6 and Fig. 4).

Discussion

In this study, the effect of the Mitrofanoff procedure on HRQoL in patients with neurogenic bladder dysfunction was evaluated. Spinal dysraphism, especially myelomeningocele, is one of the most common birth defects in the United States, leading to permanent disability, and over 90% of spina bifida patients with neurogenic bladder dysfunction experience problems such as urinary incontinence, recurrent urinary tract

Table 4. Comparison of the groups

Patients' characteristics	Patients group (n = 10)	Control group (n = 11)	p-value
Current age (year)	12.8 ± 3.03	10.7 ± 2.45	0.103
Age at operation (year)			
Gender			0.505
Male	4 (40%)	6 (54.5%)	
Female	6 (60%)	5 (45.5%)	
Shunt			0.217
Yes	2 (20%)	5 (45.5%)	
No	8 (80%)	6 (54.5%)	
Wheelchair dependency			0.505
Yes	4 (40%)	6 (54.5%)	
No	6 (60%)	5 (45.5%)	
Diaper use			0.256
Yes	3 (30%)	6 (54.5%)	
No	7 (70%)	5 (45.5%)	
Clean intermittent catheter frequency			N/A
None	2 (20%)		
2 × 1		2 (18.2%)	
3 × 1		1 (9.1%)	
4 × 1		3 (27.3%)	
5 × 1	5 (50%)	2 (18.2%)	
6 × 1	3 (30%)	3 (27.3%)	
Self-catheterization	5 (50%)	1 (9.1%)	0.038
Profilaxis			0.049
Yes	3 (30%)	8 (72.7%)	
No	7 (70%)	3 (27.3%)	

Table 5. Detailed data of patients who underwent surgery

No	Segment of intestine used for augmentation	Anti-reflux procedure	Bladder neck repair	Organ used for Mitrofanoff	Indication for surgery
1	Ileum	No	No	Appendix	Upper urinary tract disruption and incontinence despite medical treatment
2	Ileum	No	No	Appendix	Upper urinary tract disruption despite medical treatment
3	Ileum	Politano Lead Better	Bladder neck sling with detrusor flap	Ileum	Upper urinary tract disruption and incontinence despite medical treatment
4	Ileum	Cohen	No	Appendix	Upper urinary tract disruption despite medical treatment
5	Ileum	Politano Lead Better	Young-Dees	Ileum	Upper urinary tract disruption and incontinence despite medical treatment
6	Ileum	No	Young-Dees	Ileum	Urinary incontinence
7	Ileum	Politano Lead Better	Young-Dees	Appendix	Urinary incontinence
8	Ileum	No	Young-Dees	Appendix	Urinary incontinence
9	Ileum	Cohen	Young-Dees	Appendix	Urinary incontinence
10	Ileum	Politano Lead Better	No	Appendix	Upper urinary tract disruption despite medical treatment

Table 6. Comparison of the HRQoL between groups

HRQoL domains	HRQoL		p-value
	Patients (n = 10)	Controls (n = 11)	
Children (< 12 years)	180.75 ± 22	153.43 ± 36	0.251
Adolescent (> 12 years)	188.67 ± 35	190 ± 26	0.831

HRQoL: health-related quality of life.

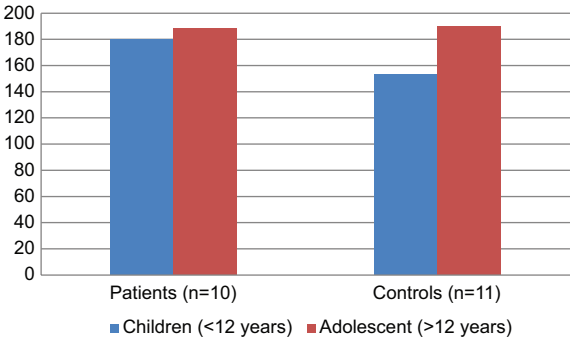

Figure 4. *Graph of health-related quality of life between groups.*

infections, and in the most severe cases, upper urinary tract damage[1,2]. This study examined the impact of this condition requiring surgical intervention and the addition of the Mitrofanoff channel on the QoL of these patients.

Although the success of surgical interventions in childhood incontinence has been extensively examined in many reports, there are few studies that evaluate the impact of such interventions on HRQoL. In recent years, there has been an increased interest in measuring HRQoL in adult urology. Criteria have been developed for benign prostatic hyperplasia, prostate cancer, bladder cancer, and overactive bladder[16-18]. In chronic diseases such as spina bifida, which make up a significant portion of the patients in this study, treatment success will increase not only through the eradication of the disease but also through the improvement of QoL.

The attainment of social continence marks a pivotal point in the lives of patients with these conditions. Being a continent is a socially expected norm[19]. It is widely believed that incontinence adversely affects the development of self-confidence and self-esteem in children. However, the challenges faced by these patients extend beyond the surgical procedure. Surgeons should recognize that although the surgery successfully achieves "dryness," the lifelong commitment to intermittent catheterization could potentially be seen as substituting one issue for another[20]. This situation often extends its impact to include family members or caregivers, who not only accompany patients during their treatment but are also responsible for managing the intricacies of the procedure.

Lima et al. conducted an assessment of QoL in individuals with neurogenic bladder who underwent urological reconstructive procedures. They utilized the SF-36 Health Survey and the Qualiveen questionnaire to measure patient-reported outcomes and found notable enhancements across all domains, which were statistically significant[21].

In the study conducted by Macneil et al., the postoperative average HRQoL scores of patients with neurogenic bladder problems due to spina bifida were not found to be higher than those of the control group[22]. Similarly, in a study conducted by Parkin and colleagues in 1997, they assessed the QoL of spina bifida patients and did not find that patients with neurogenic bladder problems had higher HRQoL[12]. In our study, when assessing the internal consistency of the scale used to evaluate HRQoL, the Cronbach's α value was calculated as 0.964 for the adolescent surgery group, 0.909 for the control group, 0.864 for the child surgery group, and 0.950 for the child control group. When looking at the HRQoL scores, in children, patients who underwent surgery had a score of 180, whereas the control group had a score of 153, and the difference between them was not statistically significant ($p = 0.251$). However, even though the difference may not be statistically significant, a higher and better QoL score was obtained in the surgery group. Particularly, the significant difference in the proportion of patients who can self-catheterize suggests that surgical intervention may increase the independence levels of patients. These findings emphasize the importance of surgical interventions in the management of neurogenic bladder dysfunction. Furthermore, the lower rates of prophylaxis application in the surgical group compared to the control group also indicate that this group requires less medical intervention. In this regard, looking at the patients who underwent the Mitrofanoff procedure, their ability to perform CIC on their own and their independence in this regard, as well as their advantages in various aspects, including prophylaxis, are evident.

The limitations of our study with a total of 21 patients, the sample size is relatively small. This small cohort may not fully represent the broader population

of patients with neurogenic bladders, potentially affecting the generalizability of our findings. Addressing these limitations in future research would significantly enhance the understanding of the impact of the Mitrofanoff procedure on the QoL of patients with neurogenic bladders.

Conclusions

Our study, assessing the HRQoL in patients with neurogenic bladders post-Mitrofanoff procedure, reveals nuanced insights. Although the procedure shows potential in enhancing independence, particularly in self-catheterization, the impact on overall HRQoL is not significantly different from the control group. This suggests that while surgical advancements such as the Mitrofanoff procedure offer technical benefits, their holistic impact on patient QoL remains complex and multifaceted. Future research, addressing the limitations of our small-scale, retrospective study, is crucial to deepen understanding in this vital area of patient care.

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Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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ORIGINAL ARTICLE

Internet addiction and depression: a study among adolescents

Adicción a internet y depresión: un estudio en adolescentes

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Abstract

Objective: *The goal of our study is to determine the level of Internet addiction (IA) in adolescents by utilizing the IA scale.* **Method:** *We employed two tools: the IA test (IAT) and the beck depression inventory (BDI), complemented by a sociodemographic information form, to assess IA and depression levels.* **Results:** *A total of 201 participants were included. A positive correlation was found between daily Internet usage time and IAT scores ($r = 0.388$, $p < 0.001$) and between BDI scores and IAT scores ($r = 0.161$, $p = 0.013$). Females had a lower mean IAT score (63.56 ± 28.08) ($p < 0.001$). The BDI scores varied significantly across the groups ($p = 0.004$). The mean BDI scores were higher in the severe addiction group (13.53 ± 7.15) compared to the moderate (11.04 ± 6.62), mild (10.11 ± 5.38), and normal usage groups (9.28 ± 5.54). A significant difference was found in gender distribution across the groups ($p = 0.001$). The presence of suicidal ideation differed significantly across the groups ($p = 0.002$). The presence of depression showed a significant difference ($p = 0.038$).* **Conclusions:** *Our study reveals a significant correlation between increased Internet usage and heightened levels of IA and depression among adolescents, with notable gender differences in IA severity.*

Keywords: *Internet addiction. Depression. Adolescents. Students.*

Resumen

Objetivo: *Determinar el nivel de adicción a internet en adolescentes utilizando una escala de adicción a internet.* **Método:** *Nuestro estudio involucró a 201 estudiantes con adicción a internet. Empleamos dos herramientas, la IAT (internet addiction test) y el BDI (beck depression inventory), que se complementaron con un formulario de información sociodemográfica, para evaluar los niveles de adicción a internet y de depresión.* **Resultados:** *Se encontró una correlación positiva entre el tiempo diario de uso de internet y las puntuaciones del IAT ($r = 0.388$; $p < 0.001$), así como entre las puntuaciones del BDI y del IAT ($r = 0.161$; $p = 0.013$). Las mujeres tuvieron una puntuación media más baja en el IAT ($p < 0.001$). Las puntuaciones del BDI variaron significativamente entre los grupos ($p = 0.004$). Las puntuaciones medias del BDI fueron más altas en el grupo de adicción grave en comparación con los grupos de adicción moderada y de uso normal. Se encontró una diferencia significativa en la distribución por sexo entre los grupos ($p = 0.001$). La presencia de ideación suicida difirió significativamente entre los grupos ($p = 0.002$). La presencia de depresión mostró una diferencia significativa ($p = 0.038$).* **Conclusiones:** *Nuestro estudio revela una correlación significativa entre mayor uso de internet y niveles elevados de adicción y depresión en adolescentes, con diferencias de sexo notables en la gravedad de la adicción.*

Palabras clave: *Adicción a internet. Depresión. Adolescentes. Estudiantes.*

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Introduction

The advent of the Internet has revolutionized the way we communicate, learn, work, and entertain ourselves. This transformation became even more pronounced with the onset of COVID-19 restrictions, leading to a surge in the global Internet user base from 738 million in 2000 to 4.9 billion in 2021, marking a staggering 5 times growth within two decades[1-3]. Data from the Internet World Stats reveal that by 2019, approximately 4.5 billion people, representing 58.8% of the world's population, were actively using the Internet. This significant statistic underscores that over half of the world's population engaged in online activities during this period. The proliferation of affordable mobile technology has further facilitated Internet access, with the number of smartphone users worldwide reaching 3.8 billion in 2021, a notable increase from just over 1 billion in 2013[3]. The prevalence of Internet access among children is now widespread. Data from the American Community Survey highlight this trend, revealing that 95% of children aged 3-18 in the United States has access to the Internet at home. The majority of these children are using computers, while a smaller proportion utilizes smartphones for Internet access. Amidst this growing digital engagement, concerns regarding Internet addiction (IA) have intensified over the past two decades, prompting researchers to delve deeper into understanding and defining this phenomenon, alternately referred to as IA, problematic Internet use (PIU), or IA disorder (IAD)[4].

With digital technologies advancing rapidly and more individuals turning to the Internet, new forms of addiction-related behaviors have emerged. IA is characterized by excessive or compulsive Internet usage that leads to distress or impairment. A specific subset of this behavior, Internet gaming disorder (IGD), has gained recognition in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5)[5], and gaming disorder (GD) is acknowledged in the International Classification of Diseases by the World Health Organization[6]. These developments indicate a broader understanding of the various subtypes of IA, including compulsive gaming, sexual preoccupations, and excessive email/text messaging. However, further research is necessary to delineate the nuances across these subtypes[7].

The relationship between IA and risky behaviors in adolescents and young adults, such as drinking, smoking, suicidal behavior, gambling, and drug abuse, is a growing concern[8,9]. Studies have indicated a positive correlation between IAD and these risky behaviors[10,11]. Investigations have revealed associations between levels of Internet dependence and heightened risks of suicidal behavior, while time spent on Internet gaming has been linked to increased alcohol consumption[12,13]. However, not all studies have found significant correlations between these behaviors[14]. For instance, smoking has been suggested as a potential facilitator for developing IAD[15,16]. Research involving Chinese adolescents has shown that those with IAD or IGD may engage in more risky activities, highlighting the need for further examination in this area[17].

IA, particularly among adolescents, has increasingly been recognized as a significant mental health concern. Excessive Internet use can lead to a host of negative mental health outcomes, including insomnia, anxiety, depression, low self-esteem, impulsiveness, mood disorders, strained family relationships, self-harm, and suicidal tendencies[18-20]. The widespread availability of mobile devices has perpetuated constant Internet connectivity among young people, often serving as a primary communication tool and an escape mechanism. However, when the Internet becomes the main coping strategy for stress, it can lead to numerous adverse effects[21].

The goal of our study is to determine the level of IA in adolescents by utilizing the IA scale.

Materials and methods

The study sample consisted of 201 adolescents (students) from Diyarbakir City Center who voluntarily agreed to participate in the study. Information about the study was provided to all students, and consent was obtained from those who agreed to participate. The sociodemographic information form and scales were distributed to the students. Ethical approval was obtained from Dicle University non-interventional local ethical committee (number: 222).

IA test (IAT)

This questionnaire is composed of 20 statements. Please read each statement with attention and, using the 5-point Likert scale, choose the response (0, 1, 2, 3, 4, or 5) that most accurately reflects your experiences. If you find two options equally applicable, select the one that best describes your typical behavior over the past month. It is important to consider each statement thoroughly before making a decision. These statements generally pertain to offline behaviors and

situations unless specified otherwise. The total score on the IAT is calculated by adding up your ratings for each of the 20 items. Each item is scored on a 5-point scale, ranging from 0 to 5. The highest possible score is 100. A higher score indicates greater severity of the issue. Scores from 0 to 30 suggest a normal level of Internet usage. Scores between 31 and 49 indicate a mild level of IA, while scores from 50 to 79 suggest a moderate level. Scores range from 80 to 100 point toward severe Internet dependence[22].

Beck depression inventory (BDI)

The BDI was employed to assess depression levels. It features 21 questions, each offering four possible answers. These questions are designed to evaluate the physical, behavioral, and cognitive symptoms of depression, as well as to gauge the severity of depression, which can range from mild to severe. Responses are rated on a scale from 0 to 3, leading to a maximum possible score of 63 and a minimum of 0. The scoring categories are as follows: scores under 14 indicate minimal depression; scores between 14 and 19 suggest mild depression; scores from 20 to 28 denote moderate depression; and scores between 29 and 63 are indicative of severe depression[23].

Statistical analysis

In the analysis, SPSS version 26.00 software served as the primary tool. Results were presented as mean ± standard deviation (SD), n (%), or median (Q1-Q3). For comparing normally distributed variables across independent groups, we utilized the Student's t-test. When dealing with non-parametric or ordinal variables, the Mann–Whitney U test was employed. To assess the correlation coefficients and determine the statistical significance of normally distributed variables, Pearson's test was applied. Conversely, Spearman's test was used for evaluating variables that were not normally distributed. The χ^2 test was utilized for the comparisons of the categorical variables. A $p < 0.05$ was deemed indicative of statistical significance.

Results

A total of 201 participants were included, 47.7% of them were female (n = 96) and 52.3% (n = 105) of them were male. The sociodemographic data and scale scores of the participants are summarized in table 1.

Table 1. Sociodemographic data and scale scores

Characteristics	Mean	SD	Minimum	Maximum
Age	13	1.88	9	18
Mother age	39.19	6.53	26	58
Father age	43.28	6.66	29	63
Number of siblings	5.35	2.45	2	13
IAT scores	72.28	25.78	35	100
BDI scores	11.99	7.17	0	38

*IAT: internet addiction test; BDI: beck depression inventory; SD: standard deviation.

The average age of the participants was found to be 13 ± 1.88 years. Participants had 5.35 ± 2.45 siblings. Regarding the scale scores, the IAT scores were 72.28 ± 25.78. BDI scores averaged at 11.99 ± 7.17.

The correlation between various sociodemographic factors and IAT scores is detailed in table 2. A notable finding was the positive correlation between daily Internet usage time and IAT scores. This correlation was moderate ($r = 0.388$) and highly significant ($p < 0.001$). In addition, a significant but relatively weak positive correlation was observed between the BDI scores and IAT scores ($r = 0.161$, $p = 0.013$). This indicates a relationship between higher levels of depressive symptoms and greater IA tendencies.

The comparative analysis of IAT scores across different demographic and behavioral variables is presented in table 3. The results showed significant differences in IAT scores based on several factors. A significant difference was observed in the mean IAT scores between females and males. Females had a lower mean score (63.56 ± 28.08), while males exhibited a higher mean score (81.15 ± 34.89) ($p < 0.001$). The analysis of IAT scores based on school success (categorized as poor, moderate, and good) did not reveal a statistically significant difference ($p = 0.318$). There was a statistically significant difference in IAT scores between individuals who smoke and those who do not ($p = 0.008$). Smokers had a higher mean score (81.29 ± 36.48) compared to non-smokers (67.89 ± 29.97). Participants with Internet access at home had a higher mean score (86.15 ± 30.98) compared to those without (66.01 ± 31.79) ($p < 0.001$). Similar to home access, having Internet access in one's own room was associated with higher IAT scores. Those with personal room access had a mean score of 87.42 ± 35.68, whereas those without had a score of 70.58 ± 31.87, and this difference was statistically significant ($p = 0.009$).

Table 2. Correlation to Internet addiction test score

Characteristics	r	p
Age	0.019	0.772
Mother age	−0.051	0.514
Father age	−0.106	0.169
Number of siblings	−0.047	0.462
Internet usage time (h/day)	0.388	0.000
BDI scores	0.161	0.013

*BDI: Beck Depression Inventory.

Table 3. Comparisons in terms of Internet addiction test score

Characteristics	Mean ± SD	p-values
Gender		0.000
Female	63.56 ± 28.08	
Male	81.15 ± 34.89	
School success		0.318
Poor	76.37 ± 35.55	
Moderate	68.29 ± 28.96	
Good	68.89 ± 31.60	
Smoking		0.008
Yes	81.29 ± 36.48	
No	67.89 ± 29.97	
Internet access at home		0.000
Yes	86.15 ± 30.98	
No	66.01 ± 31.79	
Internet access in her/his room		0.009
Yes	87.42 ± 35.68	
No	70.58 ± 31.87	

*SD: standard deviation.

Table 4 presents a subgroup analysis of IAT scores, categorizing participants into four groups: severe addiction, moderate addiction, mild addiction, and normal usage. The analysis examined various factors across these groups. The mean age across the groups did not show a significant difference (p = 0.501). The BDI scores varied significantly across the groups (p = 0.004). The mean scores were higher in the severe addiction group (13.53 ± 7.15) compared to the moderate (11.04 ± 6.62), mild (10.11 ± 5.38), and normal usage groups (9.28 ± 5.54). A significant difference was found in gender distribution across the groups (p = 0.001). Smoking status showed no significance (p = 0.067). The presence of suicidal ideation differed significantly across the groups (p = 0.002). It was more prevalent in the severe addiction group (n = 12) compared to the other groups. The presence of depression also showed a significant difference (p = 0.038), being higher in the severe addiction group (n = 22) compared to others. There was a significant difference based on home Internet access (p = 0.017). No significant difference was observed in terms of personal room Internet access across the groups (p = 0.341).

Discussion

In our study, we have identified significant findings that contribute to the understanding of Internet usage and its psychological impacts. The results indicate a positive correlation between Internet usage time and scores on the IAT, as well as between BDI scores. Notably, male participants exhibited higher IAT scores, suggesting a greater tendency toward IA in this demographic. Our findings also reveal a nuanced relationship between increased Internet accessibility and various psychological and behavioral aspects. While enhanced Internet access correlates with higher rates of smoking, elevated depression levels, and an increase in suicidal thoughts, it interestingly does not appear to impact school success performance.

IA is increasingly recognized in the literature as a new form of addiction, drawing significant attention from both psychologists and clinicians. It is particularly impactful on adolescents, bringing with it a range of psychological, sociological, and physiological adversities[5,7,10]. This assertion is supported by various studies[2,24,25]. Diagnosing individuals with IA is a process that cannot be arbitrary nor solely based on observation. Similar to chemical dependencies, IA follows criteria outlined in the DSM[5]. Due to its nature as a behavior-based addiction, the diagnosis of IA relies on tools and techniques such as tests, scales, criteria, and checklists. In addition, reliable diagnoses can be further enhanced by gathering data through observations and interviews with the individual's family and social circle[5,22].

Recent epidemiological research has consistently shown a year-on-year increase in the global prevalence of IA and depression, as highlighted in studies by Shorey et al. and Xin et al.[26,27]. However, an intriguing observation emerges from Ye et al.'s meta-analysis, which indicates a reduced risk of depression in studies conducted during 2021-2022[28]. This unexpected trend may stem from a range of factors, such as the limited scope of research data included, the diversity of measurement tools used, and the variation in age groups studied.

Table 4. Comparisons in terms of Internet addiction test score (subgroup analysis)

Characteristics	Severe addiction (n = 90)	Moderate addiction (n = 50)	Mild addiction (n = 18)	Normal usage (n = 43)	p-value
Age	12.87 ± 1.63	13.4 ± 2.07	13.14 ± 2.15	12.84 ± 1.82	0.501
BDI scores	13.53 ± 7.15	11.04 ± 6.62	10.11 ± 5.38	9.28 ± 5.54	0.004
Gender					
Female	29 (32.2%)	31 (62%)	10 (55.5%)	26 (60.5%)	0.001
Male	61 (67.8%)	19 (38%)	8 (44.5%)	17 (39.5%)	
Smoking					
Yes	39 (43.3%)	15 (30%)	4 (22.2%)	10 (23.2%)	0.067
No	51 (56.7%)	35 (70%)	14 (77.8%)	33 (76.8%)	
Suicidal ideation					
Yes	12 (13.3%)	14 (28%)	2 (11.1%)	0 (0%)	0.002
No	78 (86.7%)	36 (72%)	15 (83.3%)	42 (97.7%)	
Depression					
Yes	22 (24.4%)	6 (12%)	1 (5.5%)	4 (9.3%)	0.038
No	66 (73.3%)	44 (88%)	17 (94.5%)	39 (90.7%)	
Internet access at home					
Yes	42 (46.6%)	19 (38%)	8 (44.5%)	8 (18.6%)	0.017
No	46 (51.2%)	30 (60%)	9 (50%)	34 (79.1%)	
Internet access in her/his room					
Yes	17 (18.8%)	7 (14%)	3 (16.7%)	3 (6.9%)	0.341
No	71 (78.8%)	42 (84%)	14 (77.8%)	39 (90.7%)	

*BDI: Beck Depression Inventory.

Research from Finland by Tóth-Király indicates that depression significantly elevates the risk of IA[29]. This finding aligns with Shensa et al. who note that individuals with depressive symptoms may be as prone to IA as to other behavioral addictions, such as gambling and eating disorders[30]. Complementing this, Geng et al. suggest that excessive Internet use can, in turn, increase the likelihood of depression[31]. This cycle is particularly evident in adolescents, where heightened IA may lead to a neglect of constructive activities and reduced face-to-face social interactions, factors that can exacerbate depression, as discussed by Al Mukhaini et al.[32]. Our study's findings align with existing literature, presenting a significant observation: a positive correlation between daily Internet usage time and IAT scores. Furthermore, we noted a positive correlation between BDI scores and IAT scores ($r = 0.161$, $p = 0.013$), suggesting a link between increased depressive symptoms and heightened tendencies toward IA.

Moreover, the impact of IA on depression appears to be more pronounced than the reverse, highlighting a need for more in-depth future research to explore this dynamic further. An intriguing aspect of this relationship was uncovered in a Chinese longitudinal study by Zhang et al. which found that the link between IA and depression was specific to the female adolescent population[33]. Conversely, our study revealed higher IAT scores among males. A significant difference was observed in the mean IAT scores between females and males. Females had a lower mean score (63.56 ± 28.08), while males exhibited a higher mean score (81.15 ± 34.89) ($p < 0.001$).

Our study, focusing on IA, depression, and their interplay with various sociodemographic factors, offers important insights but also faces several limitations. Conducted with 201 adolescents from Diyarbakir City Center, the findings might not be widely generalizable due to the unique cultural, social, and economic backdrop of this group. The study's cross-sectional design limits us to observing correlations, not establishing causality between Internet usage, IA, and depression. Utilizing self-report measures such as the IAT and the BDI introduces potential biases, as participants may underreport or overreport symptoms. Crucially, our study did not control for factors such as socioeconomic status, family dynamics, or other health conditions, which might influence both Internet habits and mental health. The evolving criteria for diagnosing IA, along with rapid

technological changes, pose challenges in maintaining the relevance and comparability of our results.

Conclusions

Our study reveals a significant correlation between increased Internet usage and heightened levels of IA and depression among adolescents, with notable gender differences in IA severity. These insights contribute to the broader understanding of IA as a growing mental health concern, particularly in the context of the digital age's rapid evolution.

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Ethical disclosures

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Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

Effects of different indications on electroconvulsive therapy

Efectos de las diferentes indicaciones sobre la terapia electroconvulsiva

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Abstract

Objective: *The objective of the study is to evaluate how electroconvulsive therapy (ECT) affects treatment-resistant depression, bipolar and schizophrenic patient groups, and suicide attempt histories and to evaluate the relationship between treatment variables and patient outcomes.* **Method:** *In a retrospective cohort study at the inpatient psychiatry clinic of Çam and Sakura City Hospital between January, 2021, and February, 2023, 103 patients receiving ECT were analyzed. They were categorized into two groups according to indications that suicide risk (n = 76) and resistance to pharmacotherapy (n = 27).* **Results:** *The analysis revealed no significant age (p = 0.374) or gender (p = 0.304) differences between groups. However, significant differences emerged in diagnostic distribution (p = 0.027), with the suicide risk group receiving more ECT sessions (13.6 ± 11.2, p = 0.025) and experiencing longer total seizure times (427 ± 325 s, p = 0.023) compared to the treatment-resistant group (8.5 ± 4.7 sessions and 279 ± 115 s, respectively).* **Conclusions:** *ECT's therapeutic application does not differ from demographic variables but is influenced by clinical diagnosis, with suicide risk patients receiving more intensive treatment. These findings highlight the necessity of individualized ECT protocols and suggest that diagnostic considerations are critical in optimizing ECT treatment strategies. Despite its retrospective design, the study underscores the importance of personalized ECT regimens and calls for further prospective research to validate these findings.*

Keywords: *Electroconvulsive therapy. Suicide. Resistant to pharmacotherapy. Schizophrenia. Bipolar disorder. Depression.*

Resumen

Objetivo: *Evaluar cómo la terapia electroconvulsiva afecta a grupos de pacientes con depresión resistente al tratamiento, trastorno bipolar, esquizofrenia y antecedentes de intentos suicidio, y evaluar la relación entre variables de tratamiento y resultados.* **Método:** *En una cohorte retrospectiva en la clínica de psiquiatría para pacientes internados del Çam and Sakura City Hospital, entre el 01/2021 y el 03/2023, se analizaron 103 pacientes que recibieron terapia electroconvulsiva. Estos se clasificaron en dos grupos según los indicios de riesgo de suicidio (n = 76) y de resistencia a la farmacoterapia (n = 27).* **Resultados:** *El análisis no mostró diferencias significativas en cuanto a edad (p = 0.374) y sexo (p = 0.304) entre los grupos. Sin embargo, hubo diferencias significativas en la distribución diagnóstica (p = 0.027), con el grupo de riesgo de suicidio recibiendo más sesiones de terapia electroconvulsiva (13.6 ± 11.2; p = 0.025) y experimentando tiempos totales de convulsión más largos (427 ± 325 segundos; p = 0.023) en comparación con el grupo resistente al tratamiento (8.5 ± 4.7 sesiones y 279 ± 115 segundos, respectivamente).* **Conclusiones:** *La aplicación terapéutica de la terapia electroconvulsiva no difiere según las variables demográficas, pero sí se ve influenciada por el diagnóstico clínico, recibiendo los pacientes de riesgo de suicidio un tratamiento más intensivo.*

Palabras clave: *Terapia electroconvulsiva. Suicidio. Resistencia a la farmacoterapia. Esquizofrenia. Trastorno bipolar. Depresión.*

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Introduction

Electroconvulsive therapy (ECT), a medical treatment that's been available since the 1930s, has been both hailed as a lifesaver and condemned as controversial in the field of psychiatry. Administered under intravenous sedation or general anesthesia, ECT works by inducing a generalized cerebral seizure with an electric current, an approach that has evolved considerably over the decades with refinements such as the introduction of muscle relaxants and advancements in anesthesia[1]. Despite its long history, ECT continues to polarize opinion; some experts regard it as the most effective psychiatric treatment and entirely safe, while others raise concerns about its efficacy and potential for causing brain damage[2].

This complex intervention is not a one-size-fits-all remedy; its outcomes are influenced by various factors, including electrode placement, electrical stimulus dosage and waveform, and treatment frequency. ECT can be considered as the first-line treatment option in cases such as depressive stupor, severe psychomotor retardation, refusal to eat or drink, high risk of suicide, severe excitement, neuroleptic malignant syndrome, some systemic diseases, and psychiatric disorders of the perinatal period. In addition, treatment-resistant cases constitute the most common indication for ECT[3].

Treatment resistance affects 20–60% of patients with psychiatric disorders and is associated with increased health-care burden and costs up to ten-fold higher relative to patients in general. Treatment resistance is recognized across a range of psychiatric disorders, including schizophrenia, major depressive disorder, and bipolar disorder. Guidelines highlight three core components required to establish the definition of treatment resistance seen across disorders; these are that the correct diagnosis has been made, that adequate treatment has been given, and that there has been inadequate response. However, there are still significant differences in details between the guides. In general, lack of adequate response despite adequate use of at least two drugs defines treatment resistance[4].

The global suicide mortality rate amounts to 1.4% of all deaths worldwide. Most suicides are related to psychiatric disease, and almost all psychiatric disorders are correlated with increased suicide risk. A rough estimate is that suicide attempts are 10 times more likely than completed suicides, and suicide plans are 10 times more likely than attempts[5]. When viewed from this perspective, the devastation caused by suicide and the importance of its treatment can be seen better[6,7].

As the utility of ECT continues to be a subject of clinical interest, particularly in its application for severe psychiatric disorders, this study is predicated on the hypothesis that distinct patient populations those with a history of suicide attempts and those who are treatment-resistant may exhibit differing responses to ECT in terms of clinical outcomes and treatment course[8-10]. We posit that the intensity and frequency of ECT sessions, as well as the duration of induced seizures, may correlate with the diagnostic category and severity of the psychiatric condition.

In this study, we aimed to evaluate how ECT affects treatment-resistant depression, bipolar and schizophrenic patient groups, and suicide attempt histories and to evaluate the relationship between treatment variables and patient outcomes.

Materials and methods

Design of the study

This research conducted a comparative retrospective analysis, centering on two groups of patients between January 2021 and March 2023. A total of 103 patients were included. Patients receiving ECT were divided into two groups based on their indications for undergoing ECT. Group 1 (n = 76) consisted of patients who received ECT due to suicidal attempts, and Group 2 (n = 27) consisted of patients who were resistant to pharmacotherapy. Both groups had undergone ECT at our institution. We compared age, gender, distribution of the diagnosis, neutrophil counts, lymphocyte counts, neutrophil-to-lymphocyte ratio (NLR), number of applied ECT, and total seizure time.

Inclusion criteria

Our study included patients over the age of 18 who had been diagnosed with bipolar disorder, schizophrenia, and depression according to DSM-5-TR diagnostic criteria. The study was single-centered, encompassing patients who presented to the psychiatric department of Çam and Sakura City Hospital and underwent inpatient treatment, including the administration of ECT.

Exclusion criteria

Patients were excluded if they had a history of neurological disorders, substance abuse within 6 months before ECT, or incomplete medical records. Those who received < 4 sessions of ECT were excluded from the study, assuming they still needed to complete treatment. Pregnant cases were excluded because we classified our cases according to indication, and pregnancy could create a different indication, such as reducing drug exposure. Furthermore, cases that could fall into both suicidality and treatment resistance groups were excluded.

ECT procedure

Patients in our study received bilateral ECT treatments twice to 5 times a week with Thymatron® DGxTM (Somatics, LLC). Doses for the first ECT sessions were calculated through the half-age rule. Efforts are being made to find an ECT dosing approach that minimizes the occurrence and intensity of neurocognitive deficits linked to the treatment while preserving its therapeutic advantages. In employing this method, individuals adjust the "percent energy dial" to half the patient's chronological age or round it up to the nearest higher available setting[11]. Throughout the ECT series, doses were progressively increased to ensure seizure durations met or exceeded the 20-s minimum. Physiological parameters were continuously monitored using pulse oximetry, noninvasive blood pressure, electrocardiography, and electroencephalography. ECT was administered until the patient achieved full remission[10].

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Başakşehir Çam and Sakura Training and Research Hospital (Approval number: [2023-347]). Informed consent was waived due to the retrospective nature of the study.

Statistical analysis

Data were analyzed using the JAMOVI software, version 2.4. Continuous variables were expressed as means ± standard deviation and compared using the t-test or the Mann–Whitney U test, as appropriate. Categorical variables were compared using the X^2 test or Fisher's exact test. A $p < 0.05$ was considered statistically significant.

Results

The average age of patients in the suicide group was 33.4 ± 12.1 years, while the treatment resistance group averaged 35.8 ± 12.7 years; this age difference was not statistically significant (p = 0.374). Gender distribution among the groups showed that 63% (n = 48) of the suicide group were male compared to 74% (n = 20) in the treatment resistance group, which was not a significant difference (p = 0.304). The diagnostic composition between the groups revealed significant differences (p = 0.027). Within the suicide group, 17% (n = 13) were diagnosed with bipolar disorder, 63% (n = 48) with schizophrenia, and 19% (n = 15) with major depression. Conversely, the treatment resistance group had a higher proportion of bipolar disorder at 40% (n = 11), while schizophrenia and major depression were represented at 37% (n = 10) and 22% (n = 6), respectively (Fig. 1C). The mean neutrophil count was 5.9 ± 2.3 for the suicide group and 5.2 ± 2.2 for the treatment resistance group, which did not differ significantly (p = 0.202). Lymphocyte counts were also similar between the two groups (suicide: 2.3 ± 0.7; treatment resistance: 2.3 ± 0.9) (p = 0.763), as were the NLR measurements (suicide: 2.9 ± 2.2; treatment resistance: 2.7 ± 1.9; p = 0.674).

However, the number of ECT sessions applied varied significantly between groups, with the suicide group receiving a higher number of treatments (13.6 ± 11.2) compared to the treatment resistance group (8.5 ± 4.7) (p = 0.025) (Fig. 1A). In addition, the total seizure time was significantly longer in the suicide group (427 ± 325 s) than in the treatment resistance group (279 ± 115 s) (p = 0.023) (Table 1 and Fig. 1B). The differences of the number of applied ECT and total seizure times in terms of indications were shown in figure 2A and B. figure 3 illustrates the scatter plot of number of applied ECT, total seizure time, and diagnosis.

Discussion

This study provides an in-depth analysis of ECT as a treatment method for two specific groups: individuals with suicide risk and those showing resistance to pharmacological treatments. Our findings contribute to the nuanced understanding of ECT's clinical outcomes and demographic correlations, underpinning its application in psychiatric treatment strategies.

ECT maintains its essential place in the treatment of psychiatric patients, although stigmatization problems persist. Many large-scale studies reveal the characteristics of

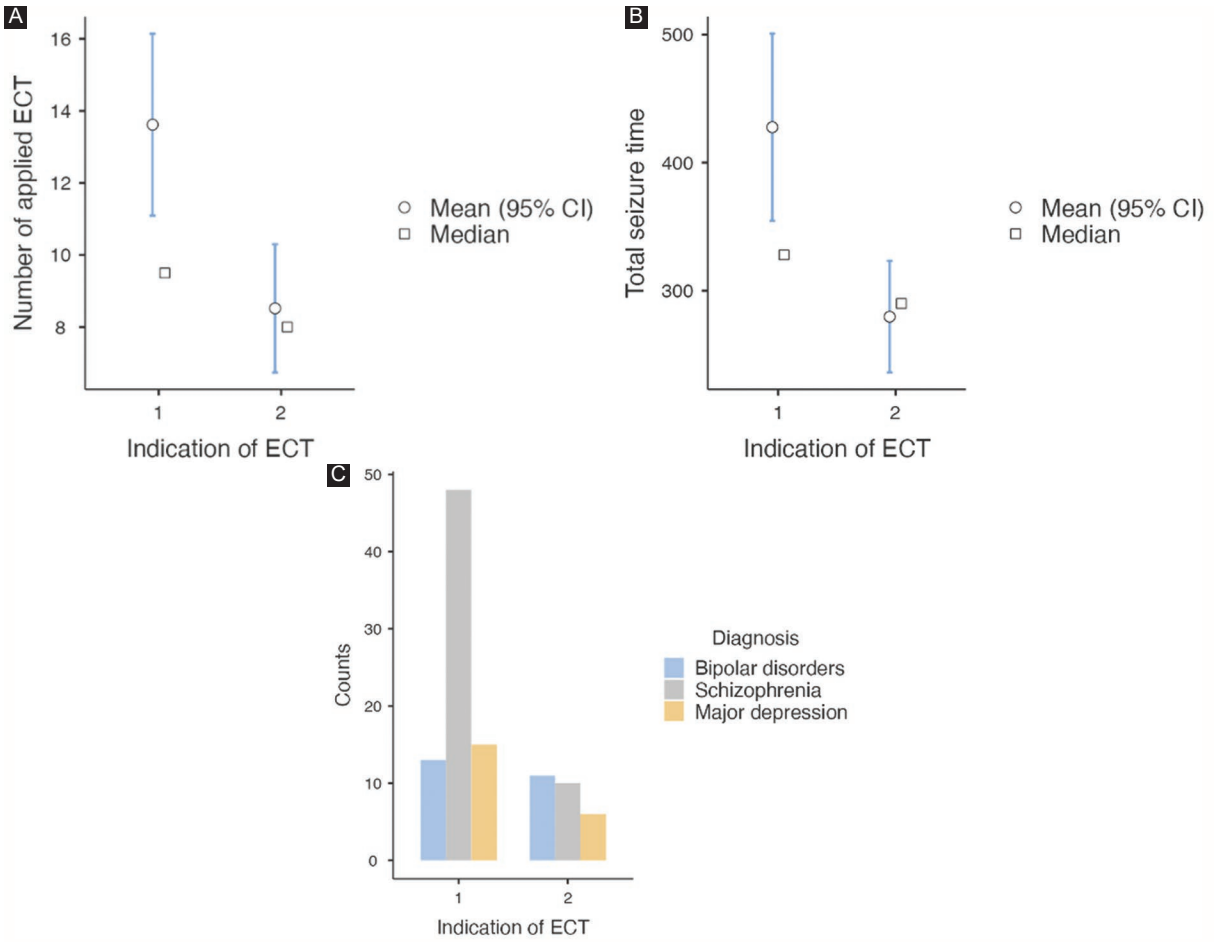

Figure 1. A: *the number of applied electroconvulsive therapy.* **B:** *total seizure time.* **C:** *indication and diagnosis. Group 1 = suiside group; Group 2 = treatment resistant group.*

Table 1. Demographic and comparisons

Variables	Suicide (n = 76) (%)	Treatment resistance (n = 27) (%)	p-value
Age	33.4 ± 12.1	35.8 ± 12.7	0.374
Gender (M)	48 (63)	20 (74)	0.304
Diagnosis			0.027
Bipolar disorder	13 (17)	11 (40)	
Schizophrenia	48 (63)	10 (37)	
Major depression	15 (19)	6 (22)	
Neutrophil	5.9 ± 2.3	5.2 ± 2.2	0.202
Lymphocyte	2.3 ± 0.7	2.3 ± 0.9	0.763
NLR	2.9 ± 2.2	2.7 ± 1.9	0.674
Number of applied ECT	13.6 ± 11.2	8.5 ± 4.7	0.025
Total seizure time (sec)	427 ± 325	279 ± 115	0.023

*ECT: electroconvulsive treatment; NLR: neutrophil-to-lymphocyte ratio.

patients receiving ECT and the effectiveness of the treatment[7,8,10]. There are also studies comparing the effectiveness of ECT on a diagnostic basis and the prominent features in different groups[7,8,12]. However, there are a limited number of studies comparing ECT according to indications. In this respect, our study is one of the first steps in filling a significant gap.

The most common indication of 176 ECT treatments performed for 5 years in a hospital located in another province in Turkey was suicidality, followed by treatment resistance. The order of the indications is similar to our study[13]. However, in the study conducted by Tor et al. in Singapore, unlike our study, the indication for treatment resistance was significantly higher than suicidality[8]. The fact that all three studies were single-centered suggests that the different characteristics of the centers may affect the rates. Similar rates in two Turkey-based studies, our study and the study of Bolu et al., may indicate the relationship between diseases and sociocultural or genetic structure[13].

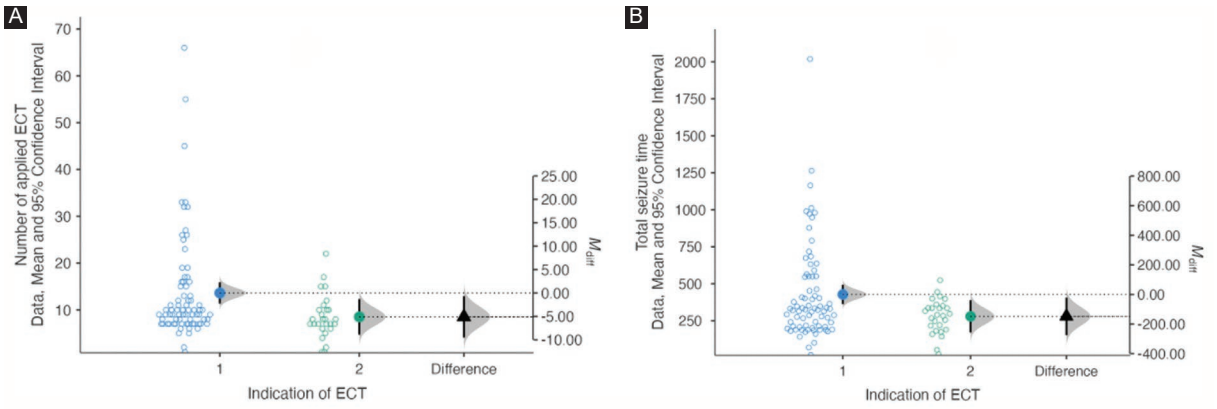

Figure 2. *Differences between groups.* **A:** *number of applied electroconvulsive therapy.* **B:** *total seizure time. Group 1 = suicide group, Group 2 = treatment resistant group.*

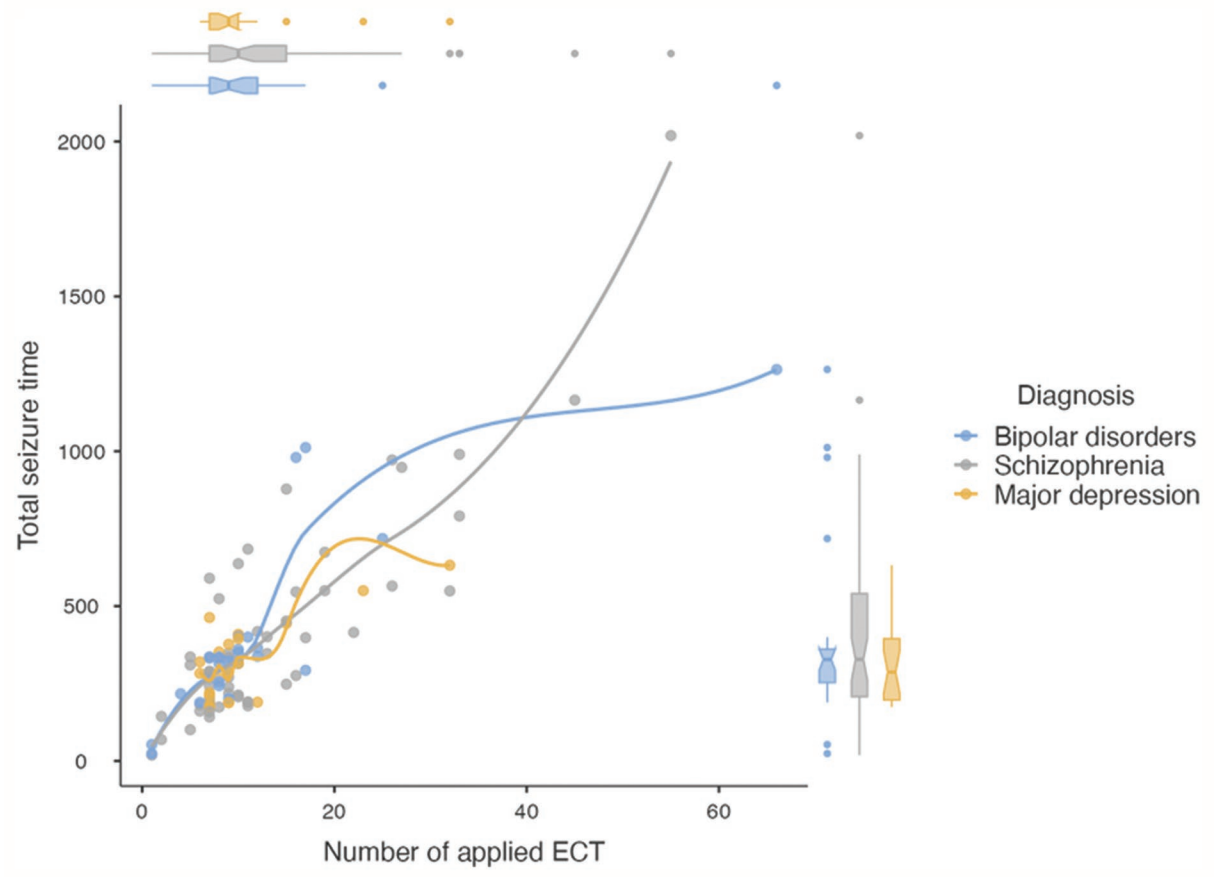

Figure 3. *A scatter plot of diagnosis, number of applied electroconvulsive therapy, and total seizure time.*

Demographic analysis in our study revealed no significant age differences between the suicidal and treatment-resistant groups; this suggests that the therapeutic decision for ECT transcends the age factor in the context of these two conditions. Similarly, the gender distribution did not show a significant difference, implying that the decision for ECT application is primarily driven by clinical indications rather than gender. This is consistent with the non-discriminatory application of ECT across different demographic groups, reflecting its broad acceptability in psychiatric practice[13].

Our study showed a significant difference in diagnoses in the suicidality and treatment resistance indication groups. While schizophrenia patients were predominant in the suicidality group (68%), there was a relatively balanced distribution in the treatment-resistance group. In the study of Tor et al., positive psychotic symptoms dominated the treatment resistance group, followed by mania, depression, and psychotic depression, respectively[8]. The different diagnostic distinctions make it difficult to compare the two studies. The limited number of people who received ECT due to the risk of suicide (n: 8) also does not allow comparison. It was interesting and surprising that the number of schizophrenia patients was higher than depression in the suicidality group. It points out the importance of assessment of suicide risk in addition to the positive and negative symptoms of schizophrenia.

Mean neutrophil-to-lymphocyte counts and NLR are essential biomarkers. Many studies have shown that it is increased in psychiatric conditions such as depression and schizophrenia or first-episode psychosis, and a smaller number of studies have shown that it is increased in bipolar disorder[14-16]. Studies are showing the relationship between NLR and the presence and severity of suicidal behavior[17,18]. High NLR rates are also associated with treatment-resistant depression and schizophrenia[19]. Our study detected no difference between the two groups regarding neutrophils, lymphocyte counts, and NLR before ECT. Since the NLR will be high in both suicidality and treatment resistance, it can be interpreted that the high NLR does not make a difference between the two groups. Furthermore, our results appear to be consistent with a large-scale study claiming that a high NLR rate is a transdiagnostic marker in psychiatric diseases[20]. However, our study's need for a healthy control group limits our interpretations.

The significant difference in the number of ECT sessions and total seizure time between the groups is a critical finding. Patients with suicide risk received more ECT sessions and had longer total seizure durations, indicating a more intensive treatment course. According to the study of İzci et al.,[21] in which patients diagnosed with major depression receiving ECT were grouped into suicidality and treatment resistance, similar to our study, no difference was found between the number and total duration of ECTs in these two groups. This result contradicts ours in the context of depression. Tor et al. in a study evaluating ECT indications according to diagnoses also classified them according to the actual reasons for ECT[8]. According to this study, ECT was applied to 55% of the participants (n: 386) due to lack of response to medical treatment and 1.2% (n: 8) due to a high risk of suicide. The average duration of ECT was found mainly in the treatment of positive psychotic symptoms, followed by catatonia, mania, psychotic depression, and depression. Although the study design does not allow comparison with our study, the significant difference in session durations in different indications is a finding that overlaps with our study. According to the Royal Australian and New Zealand guidelines, catatonia generally responds more quickly to ECT treatment than depression and treatment-resistant schizophrenia and mania[22]. Another study comparing the number of ECT sessions did not find a significant difference in the number of sessions between diagnoses[23]. The study shows that only people over 65 receive more ECT sessions. Another study conducted in Turkey did not find a significant difference in the number of sessions between different diagnoses[24]. However, these two studies differ from our study because they evaluate the indication diagnostically. The number of studies examining the effects of different indications on the number and duration of ECT is limited in the literature, and conflicting results indicate that more extensive studies are needed on this subject.

Furthermore, our research has important implications for the patient management pathway, including the need for robust post-ECT follow-up, particularly for those with severe psychiatric presentations. The necessity for a personalized approach to ECT, considering the individual's diagnostic profile and previous treatment responses, is underscored by the variation in treatment regimens observed.

However, this study is not without limitations. The retrospective design inherently carries the potential for selection and information bias. The exclusion of patients due to incomplete medical records may also have led to an underrepresentation of the true clinical picture. The sample size, particularly of the treatment-resistant group, is small, which may limit the statistical power to detect differences and may not fully represent the broader population undergoing ECT.

Conclusion

The study affirms the role of ECT as a valuable treatment option for both suicidal and treatment-resistant patients, with specific clinical and demographic profiles associated with each group. The findings call for a tailored approach to ECT administration, considering the patient's diagnostic background and severity

of presentation. Prospective, larger-scale studies are required to further elucidate the intricacies of ECT outcomes, optimally inform clinical protocols, and ensure the best possible patient care.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the approval of the Ethics Committee for the analysis and publication of clinical data obtained routinely. The informed consent of the patients was not required because it was a retrospective observational study

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

Anxiety and e-health literacy levels of patients scheduled for thoracic surgery

Ansiedad y alfabetización en salud electrónica de pacientes que se someterán a cirugía torácica

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Abstract

Objective: *This study was conducted to examine the relationship between the pre-operative anxiety levels of patients scheduled for thoracic surgery and their e-health literacy levels pertaining to skills such as finding and evaluating electronic health information about health problems.* **Methods:** *This study was a descriptive and correlational study. One hundred and two patients scheduled for thoracic surgery were interviewed in İzmir. The Amsterdam pre-operative anxiety and information scale (APAIS), the Visual Analog Scale for anxiety (VAS-A), the eHealth literacy scale (eHEALS), and a patient information form were used to collect data.* **Results:** *The mean VAS-A score of the patients was 6.02 ± 2.51, their mean APAIS score was 18.73 ± 5.85, and their mean eHEALS score was 24.84 ± 9.21. There was no significant relationship between the anxiety and e-health literacy levels of the patients. Significant differences were found in the e-health literacy levels of the patients according to their ages and reasons for surgery.* **Conclusions:** *Patients scheduled for thoracic surgery were determined to experience moderate anxiety and need moderate levels of information. The patients were also found to have moderate e-health literacy levels. There was no significant relationship between the anxiety and e-health literacy levels of the patients.*

Keywords: *Thoracic surgery. E-health literacy. Pre-operative anxiety.*

Resumen

Objetivo: *Examinar la relación entre los niveles de ansiedad pre-operatoria de los pacientes que se someterán a una cirugía torácica y la alfabetización en salud electrónica, como encontrar y evaluar información de salud electrónica sobre problemas de salud.* **Métodos:** *Estudio descriptivo y relacional. Para recopilar datos se utilizaron la Escala de Ansiedad e Información Pre-operatoria de Amsterdam (APAIS), la Escala de Ansiedad Analógica Visual (EVA-A) y la Escala de Alfabetización en E-salud, y un formulario de información descriptiva del paciente.* **Resultados:** *Según la EVA-A, los niveles de ansiedad de los pacientes fueron de 6.02 ± 2.51. La puntuación APAIS fue de 18.73 ± 5.85. La puntuación de la escala de alfabetización en salud electrónica de los pacientes fue de 24.84 ± 9.21. No hubo una relación significativa entre los niveles de ansiedad de los pacientes y su alfabetización en salud electrónica. Se encontró una diferencia significativa entre los niveles de alfabetización en salud electrónica de los pacientes según su edad y el motive de la cirugía.* **Conclusiones:** *Los pacientes que serán sometidos a cirugía torácica experimentan ansiedad moderada y se determinó que necesitan información moderada. También se descubrió que los pacientes tenían niveles moderados de conocimientos sobre cibersalud. No hubo una relación significativa entre la ansiedad y los niveles de alfabetización en salud electrónica de los pacientes.*

Palabras clave: *Cirugía torácica. Alfabetización en salud electronica. Ansiedad pre-operatoria.*

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Introduction

Anxiety is an emotional response to stimuli that people perceive as threatening[1]. It is one of the most common psychological reactions in patients undergoing surgery and is seen in 80% of patients scheduled for high-risk surgery[2]. In the pre-operative period, patients face various situations that trigger anxiety[3]. Pre-operative anxiety seems to be due to reasons such as a lack of knowledge about surgery and anesthesia, complications that may develop due to surgery and anesthesia, and dependency on others after surgery. For these reasons, the pre-operative, intraoperative, and post-operative periods are worrisome for most patients and create pre-operative anxiety[4,5]. In a study examining the thoughts and wishes of patients who would undergo surgery, it was found that 91.5% of the patients experienced anxiety before their surgery[6]. It was reported that the presence of anxiety in patients before surgery caused an increase in the usage of doses of anesthesia, post-operative pain, prolonged hospitalizations, and patient dissatisfaction[3,7]. It was shown that providing educational information about the entire surgical process was effective in reducing the anxiety of patients in the pre-operative period[4]. Patients can also obtain information from the internet to meet their information needs. E-health literacy skills are important for patients to obtain information from electronic environments. E-health literacy is a tool that enables people to access necessary health-related information from electronic sources and make decisions about their health. In a study on the access of surgical patients to health-related information, 46.1% of the patients were found to use the internet, and 97.1% were using it to conduct online research about health[8]. In a study conducted with cancer patients, it was stated that 70.8% of the patients received information about their disease from the internet[9]. It was reported that 69.6% of individuals using the internet in Turkey had used it in the last 3 months to search for health-related information (e.g., injuries, diseases, nutrition, improving health)[10]. Studies have demonstrated that patients use electronic media such as the internet to obtain information.

Anxiety is common in patients after lung cancer surgery[11]. In a study examining the anxiety levels of 278 patients who underwent curative surgical resection for lung cancer, the prevalence of pre-operative anxiety was found to be 8%[7]. To the best of our knowledge, in the relevant literature, there exists no study examining the relationship between the pre-operative anxiety levels of patients scheduled for thoracic surgery and their e-health literacy, referring to their abilities of searching and obtaining information about their health using electronic media or the internet. In this study, it was aimed to examine the relationship between pre-operative anxiety and e-health literacy levels of patients scheduled for thoracic surgery. The results of this study will help show the tendency of patients to use e-health applications to reduce their anxiety.

Materials and methods

Aim

The aim of this study was to examine the relationship between pre-operative anxiety and e-health literacy in patients scheduled for thoracic surgery.

Design

This study was performed with a descriptive and correlational design.

Settings

The study was carried out in the thoracic surgery clinic of a university hospital in İzmir, Turkey. There are a total of 18 patient beds in this clinic, and patients were interviewed before their surgeries. Data were collected between April and October 2022.

Sample

All patients who were planned to undergo thoracic surgery in the thoracic surgery clinic of the University Hospital formed the population of the study. To identify the sample size required to conduct the study, the G*Power 3.0 program was used for the power analysis, and it was found that at least 90 patients in a single group needed to be included in the sample at a significance level of 0.5, with a medium effect size of 0.01, and a power of 0.95. Considering potential data losses, a total of 102 patients were interviewed.

The sample consisted of 102 patients > 18 years of age who were going to have their first thoracic surgery, had no hearing or vision problems, were internet users (at home, at work, or on mobile devices), and agreed to participate in the study. Patients who did not have internet access at home or on their mobile devices were excluded from the sample. Verbal and written consent was obtained from each patient.

Implementation

A patient information form was used to determine the sociodemographic and clinical characteristics of the patients. The Amsterdam pre-operative anxiety and information scale (APAIS) was used to assess the pre-operative anxiety levels of the patients and their need for information, the visual analog scale for anxiety (VAS-A) was used to assess the anxiety experienced by the patients before surgery, and the eHealth literacy scale (eHEALS) was used to determine their e-health literacy levels. The data were collected by the researchers in face-to-face interviews held with the patients before surgery.

Patient information form

The form, which was created by the researchers based on the relevant literature, included questions about the sociodemographic and clinical characteristics of the patients[6,8].

APAIS

This scale was developed by Moerman et al. in 1996 to determine the pre-operative anxiety levels of patients and assess their need for information[12]. APAIS is a 5-point Likert-type scale consisting of 6 items[12].

Four items of the scale, constituting APAIS-A, assess anesthesia anxiety (items 1 and 2) and surgical procedure anxiety (items 4 and 5) (Cronbach's alpha 0.86). Two items, constituting APAIS-B (items 3 and 6), identify the need of the patient for information (Cronbach's alpha 0.72)[12]. The range of possible scores on APAIS-A, the anxiety subscale, is 4-20, while the range of possible scores on APAIS-B, the need for information subscale, is 2-10. Total scale scores vary between 6 and 30. High scores are associated with high levels of anxiety and need for information[12]. Çetinkaya et al. found $\alpha = 0.89$ for APAIS-A and $\alpha = 0.78$ for APAIS-B in their and showed that the scale had high reliability for the Turkish population[13].

VAS-A

The VAS-A is a scale that has been implemented and accepted all over the world for a long time. The scale has no language and is easy to implement[14]. Since it is quick and simple, it is a more global and multidimensional tool for assessing anxiety[15]. A strong positive correlation ($r = 0.686$; $p = 0.000$) was reported between VAS-A and the state-trait anxiety inventory[16]. In VAS-A, patients are asked to indicate their pre-operative anxiety level using a 10 cm horizontal line (values ranging from 0 to 10), measured from the left to the right. This scale was used to assess the self-evaluations of the patients about their anxiety levels experienced before surgery.

eHEALS

This scale was developed by Norman and Skinner in 2006 to measure the perceived skills of individuals in finding, evaluating, and applying electronic health information regarding health problems[17]. It is a 5-point Likert-type scale consisting of two items on internet use and eight items on internet attitudes. The first two items of the scale are evaluated separately. The minimum and maximum scores on the scale are 8 and 40. The Cronbach alpha has been found to be 0.88 and a high agreement[17]. A higher scale score indicates an increase in e-health literacy levels.

Data analysis

Frequency, percentage, and mean values were used in the analyses of the data. The data were analyzed in the SPSS 26 program. The one-way analysis of variance test was performed on the APAIS and VAS-A scores of the patients according to their reasons for undergoing surgery. Pearson's correlation analyses were carried out to identify relationships between the APAIS, VAS-A, and eHEALS scores of the patients. Linear regression analysis was performed to identify the independent variables (age, reason for surgery) predicting the e-health literacy levels of the patients.

Ethical dimension

Ethics committee approval (no: 2022/12-02) and institutional permission (no: E-43940943-100-198235) from the institution where the study would be conducted were obtained before starting to collect data. The purpose of the study was explained to the patients, and written informed consent was obtained from the patients who agreed to participate in the study. This study was descriptive. No invasive intervention was performed in the study. Therefore, no

harm was caused to the patients during the study process. No fee was paid to the patients in exchange for their participation. It was explained to the patients that they could leave the study at any time during the research process. This study was conducted in accordance with the principles of the Declaration of Helsinki, as well as research and publication ethics.

Results

The mean age of the patients was 53.29 ± 19.35 years. While 34.3% of the patients were > 65 years old, 64.7% (n = 66) were male, 71.6% would undergo surgery due to a lung mass, and 85.3% stated that they needed pre-operative information (Table 1).

According to the pre-operative measurements, the mean VAS-A score of the patients was 6.02 ± 2.51, and their mean APAIS-A score was 11.56 ± 3.89 (min: 4 - max: 20) (Table 2). The patients were found to experience moderate anxiety. In the evaluations made based on the surgical indications of the patients, the mean VAS-A score of the patients with lung masses was found as 6.26 ± 2.46, the mean VAS-A score of those with chest trauma was 5.90 ± 3.24, and the mean VAS-A score of those who had chest deformities was 5.21 ± 2.25. There was no significant difference in the VAS-A scores of the patients according to their reasons for undergoing surgery (F: 1.33 p = 0.267, p > 0.05).

According to their APAIS scores, 39.2% of the patients needed vast amounts of information about the surgical procedure. The mean APAIS-B score of the patients was 6.85 ± 2.38. It was determined that the patients had moderate levels of need for information in general. The mean total APAIS score of the patients was 18.73 ± 5.85 (Table 2). In the evaluations made based on the surgical indications of the patients, the mean total APAIS score of the patients who had lung masses was 18.42 ± 5.89, the mean total APAIS score of those with chest trauma was 21.2 ± 8.20, and the mean total APAIS score of those who had chest deformities was 16.68 ± 5.57. There was no significant difference in the mean total APAIS scores of the patients based on their reasons for undergoing surgery (F: 1.99, p = 0.141).

The mean eHEALS score of the patients was 24.84 ± 9.21 (min: 8 - max: 40) (Table 2). While 41.2% of the patients stated that it is important to access health resources on the internet, 52% stated that the internet is useful when making decisions about their health.

Table 1. Sociodemographic and clinical characteristics of the patients (n = 102)

Sociodemographic and clinical features	X ± sd (min-max)	
Age	53.29 ± 19.35 (18-91)	
	n	**%**
Sex		
Famale	36	35.4
Male	66	64.7
Age		
65 or younger	67	65.7
66 or older	32	34.3
Reason for surgery		
Cancer (n = 73)	73	71.6
Chest trauma (n = 10)	10	9.8
Chest deformities (n = 19)	19	18.6
First feeling after the decision to undergo surgery		
Anger	6	5.9
Anxiety	26	25.5
Fear	39	38.2
Sadness	4	3.9
Calmness	27	26.5
Needs information about the surgery		
Yes	87	85.3
No	15	14.7

n: total number; %: percentage; x ± sd: mean and standard deviation.

Table 2. Total VAS-A, APAIS, and eHEALS scores of the patients

Scales	x ± sd (min-max)
VAS-A	6.02 ± 2.51 (0-10)
APAIS-A	11.56 ± 3.89 (4-20)
APAIS-B	6.85 ± 2.38 (2-10)
APAIS total	18.73 ± 5.85 (6-30)
eHEALS	24.84 ± 9.21 (8-40)

x ± sd: mean and standard deviation; VAS-A: visual analog scale for anxiety; APAIS-A: APAIS A, anesthesia anxiety (items 1 and 2) and surgical procedure anxiety (items 4 and 5); APAIS-B: APAIS-B, (items 3 and 6) information needs; eHEALS: eHealth literacy scale.

There was a statistically significant relationship between the total eHEALS scores of the patients and their age (t: 2.896, p < 0.05). High e-health literacy levels were found in patients under 65 years of age (Table 3). The correlation between the ages of the patients and their total eHEALS scores was negative, moderate, and statistically significant (r = −0.409, p = 0.001). As the ages of the patients decreased, their e-health literacy levels increased. In other words, younger patients had higher eHEALS scores.

Table 3. Effects of sex, age, and reason for surgery on e-health literacy

Variables	X ± SD	t/F p
Age		
65 years and under	26.68 ± 8.78	t = 2.896
66 years and older	21.31 ± 9.10	p = 0.005
Sex		
Famale	26.00 ± 10.0	t = 0.936
Male	24.21 ± 8.76	p = 0.352
Reason for surgery		
Cancer (n = 73)	23.31 ± 9.33	F = 4.087
Chest trauma (n = 10)	26.80 ± 8.20	p = 0.020
Chest deformities (n = 19)	29.68 ± 7.63	

N: frequency; X: mean; SD: standard deviation; t: independent-samples t-test; p < 0.05 F: analysis of variance (ANOVA).

Table 4. Relationships between pre-operative anxiety and e-health literacy

Scales	eHEALS total	
	r	p
VAS-A	–0.090	0.371
APAIS- A (anxiety)	0.009	0.925
APAIS- B (need for information)	–0.063	0.530
APAIS total	–0.041	0.679

r: Pearson correlation, p < 0.05.

Table 5. Linear regression analysis of variables potentially predicting e-health literacy

Variables	Model				
	B	SH	B	T	p
Constant	35.667	5.043		7.073	0.000
Age	–0.199	0.060	–0.418	–3.294	0.001
Reason for surgery	–0.153	1.476	–0.013	–0.104	0.918
R	0.409				
R^2	0.167				
F	9.955				
p	0.000				
DW (1.5-2.5)	1.875				

p < 0.050; B: estimation equation; SH: standard error; β: beta; R2: coefficient of determination; DW: Durbin-Watson.

There was no statistically significant relationship between the total eHEALS scores of the patients and their sex (t: 0.936 p > 0.05). A significant relationship was found between the e-health literacy levels of the patients and their reasons for undergoing surgery (F: 4.087, p < 0.05). The total eHEALS scores of the patients who were scheduled to undergo surgery due to chest deformities were high (Table 3).

In the examination of the relationship between the pre-operative anxiety and e-health literacy levels of the patients based on their VAS-A and APAIS scores, no significant correlation was found between these two variables (Table 4).

In the logistic regression analysis of the variables related to the total e-health literacy levels of the patients, the predictive role of the ages of the patients and their reasons for undergoing surgery was examined. It was determined that the ages of the patients (β: –0.436 p = 0.001) significantly predicted their e-health literacy levels. According to the model, a one-unit decrease in age increased the total eHEALS score by 0.19. According to the model, these variables explained 16% of the total variance in e-health literacy (Table 5).

Discussion

In this study, the relationship between the pre-operative anxiety and e-health literacy levels of patients scheduled for thoracic surgery was examined.

The mean VAS-A and APAIS-A scores of the patients, indicating their pre-operative anxiety levels, were 6.02 ± 2.51 and 11.56 ± 3.89, respectively. The mean total APAIS score of the patients was 18.73 ± 5.85. There was no significant difference in the pre-operative anxiety levels of the patients measured by APAIS and VAS-A based on their reasons for undergoing surgery. The patients had moderate anxiety levels in general, regardless of their reasons for undergoing surgery. In a study investigating pre-operative anxiety with APAIS, 3087 patients were interviewed. In the study, 92.6% of the patients reported that they experienced pre-operative anxiety, and 40.5% stated that they experienced high levels of anxiety[18]. In our study, 85.3% of the patients stated that they needed pre-operative information. In addition, according to their APAIS scores, 39.2% of the patients wanted to receive vast amounts of information about the surgical procedure, while the overall level of need for information among all patients was moderate. It was shown that education given to patients before surgery had a positive effect in reducing their anxiety levels[19]. Therefore, pre-operative patients may experience moderate anxiety due to their need for information on various matters.

In this study, 41.2% of the patients stated that it is important to access health resources on the internet, and 52% stated that the internet is useful when making decisions about their health. In a study on the e-health literacy of patients with lung cancer, 29.3% of the patients stated that it is important to access health resources on the internet, and 53.7% stated that the internet is useful when making decisions about their health[20]. In the pre-operative period, patients may need information in accordance with their needs or because they are not informed adequately. In cases where patients cannot get answers from the healthcare team on matters related to their health, or when the healthcare team's answers do not comfort them, they may look for information on the internet.

The patients who participated in this study were found to have moderate e-health literacy levels. A study on the e-health literacy of patients with lung cancer found low levels of e-health literacy[20]. In studies conducted with cancer patients, it has been stated that the e-health literacy levels of these patients are moderate[21-23]. The moderate e-health literacy levels of the patients in our study may be associated with their limited knowledge and skills about how to use the internet to obtain information.

In our study, it was determined that the e-health literacy levels of the patients under the age of 65 were high (t: 2.896, $p < 0.05$). A statistically significant moderate correlation was found between the ages of the patients and their e-health literacy levels ($r = -0.409$, $p = 0.001$). As the ages of the patients decreased, their e-health literacy levels increased. In other words, younger patients had higher total eHEALS scores. Other studies have shown that being young affects the e-health literacy levels of individuals[21,23-25]. In another study conducted with lung cancer patients, no significant relationship was found between e-health literacy and age[20]. A study evaluating cancer-related internet usage patterns in adolescents and young adults (18-39 years) and adult cancer patients (40+ years) revealed that adolescent and young adult (18-39 years) cancer patients ran significantly more searches on the internet per day[26]. We think the high internet use rates of patients under the age of 65 affect their e-health literacy levels positively.

There was no statistically significant difference in the total eHEALS scores of the patients based on their sex (t: 0.93 $p > 0.05$). In one study, it was found that female patients had higher e-health literacy levels than male patients[22]. In another study, the e-health literacy levels of immigrant female patients were found to be lower than the levels of male patients[27]. Another study showed no significant relationship between e-health literacy and sex[28]. No clear results have yet been found regarding the relationship between e-health literacy and sex. The e-health literacy levels of men and women may be similar due to their similar levels of access to and usage of e-health applications.

A significant relationship was found between the e-health literacy levels of the patients included in our study and their reasons for undergoing surgery (F: 4.087, $p < 0.05$). The total eHEALS scores of the patients who were going to undergo surgery due to chest wall deformities were high. In the relevant literature, another study on the e-health literacy levels of patients scheduled for thoracic surgery could not be found. Patients with chest wall deformities are young patients. Young patients have higher rates of internet and social media usage[26]. Therefore, patients who will undergo surgery for chest wall deformities may have higher e-health literacy levels.

No significant correlation was found between the anxiety and e-health literacy levels of the patients in our study. Organized results of a study examining anxiety and health literacy in patients undergoing same-day surgery have not yet been published[29]. Likewise, studies examining the relationship between pre-operative anxiety and e-health literacy could not be found. The absence of a significant relationship between e-health literacy and pre-operative anxiety in the context of efforts to reduce the anxiety levels of surgical patients may be explained by the possibility that these patients obtain health-related information from other sources such as doctors, nurses, other patients, and patient relatives to inform their decisions about their health, rather than getting information from electronic sources.

In our study, the predictive effects of two variables (age and reason for surgery) on the e-health literacy levels of the patients were examined by logistic regression analysis. The variables that were found significantly correlated with e-health literacy were included in the regression model. The age variable was a significant and negative predictor of the e-health literacy levels of the patients (β: −0.418 $p = 0.001$). The e-health literacy levels of the patients increased as their age decreased. In a study examining the factors affecting the e-health literacy levels of patients with lung cancer, a significant relationship was found between e-health literacy and age ($p < 0.005$)[20]. In other studies examining the factors affecting e-health literacy, significant relationships

have been identified between e-health literacy and age ($p < 0.005$)[21,26,30,31]. Internet use, especially health-related internet use, is more prevalent among young adults compared to older adults[32]. This may affect the e-health literacy levels of patients because young patients already use the internet in many areas of their lives, and they are likely to use it to find answers to their questions about health.

Conclusion

Patients who were scheduled for thoracic surgery were determined to need information regarding the surgical process. They had moderate anxiety levels because of their information needs. The patients were also found to have moderate e-health literacy levels. There was no significant relationship between the preoperative anxiety and e-health literacy levels of the patients. A significant relationship was found between the e-health literacy levels of the patients and their ages, and the patients under the age of 65 had higher levels of e-health literacy. Although the e-health literacy levels of young patients are high, it is recommended that healthcare professionals use educational materials that can be easily used by patients in training programs to be given to all patients, especially patients aged 65 or older, and develop easy-to-use, attractive, and highly accessible online platforms and mobile applications for patients using e-health applications. Healthcare professionals need to focus on the information-related needs and information-seeking behaviors of patients. This study will provide nurses with information about the health literacy status of patients who are scheduled for surgery.

Limitations

In our study, there were patients who were scheduled for thoracic surgery for different reasons. For example, patients with chest deformities had higher e-health literacy levels, and this group was also younger. The small number of patients in this group was a limitation. The e-health literacy levels of the patients who would undergo surgery due to cancer were lower than the levels of other patients. It was found that cancer patients trust online health information less[33]. Other studies showed that cancer patients face several challenges when searching for health-related information and using the internet to solve health problems. In particular, it was observed that they often had problems identifying websites with reliable health information[34,35]. This study did not focus on the information needs and information-seeking behaviors of cancer patients. Another limitation was that e-health literacy was measured once in a clinical setting before surgery. Patients who had thoracic surgery for different reasons can be evaluated in different studies and with larger samples.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

The advantages of using tranexamic acid in anterior cruciate ligament reconstruction: a randomized controlled trial

Las ventajas del uso de ácido tranexámico en la reconstrucción del ligamento cruzado anterior: un ensayo controlado aleatorizado

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Abstract

Objective: *The number of participants in sports or some form of recreation globally has led to an increase in the incidence of anterior cruciate ligament (ACL) injuries and the number of surgeries performed. Although it does not belong to risky surgical interventions, this operation is accompanied by complications that slow down post-operative rehabilitation. The objective is to analyze the effects of intra-articular (IA) injection of tranexamic acid (TXA) on the reduction of post-operative drained blood volume, pain intensity, and incidence of hemarthrosis after ACL reconstruction.* **Method:** *This prospective research included 124 patients undergoing ACL reconstruction surgery, randomly divided into two groups. The TXA group received IA TXA, whereas an equal amount of placebo was administered using the same route in the control group.* **Results:** *The research has shown that IA injection of TXA effectively reduces post-operative blood loss (TXA group 71.29 ± 40.76 vs. control group 154.35 ± 81.45), reducing the intensity of post-operative pain ($p < 0.001$) and the incidence of hemarthrosis.* **Conclusion:** *The application of TXA significantly reduced post-operative bleeding and pain intensity, which accelerated the post-operative period.*

Keywords: *Tranexamic acid. Anterior cruciate ligament reconstruction. Hemarthrosis. Intra-articular administration.*

Resumen

Objetivo: *El mayor número de participantes en deportes o alguna forma de recreación en todo el mundo ha llevado a un aumento en la incidencia de lesiones del ligamento cruzado anterior (LCA) y de las cirugías realizadas. Aunque no es una intervención quirúrgica de riesgo, esta operación va acompañada de complicaciones que ralentizan la rehabilitación posoperatoria. El objetivo es analizar los efectos de la inyección intraarticular de ácido tranexámico (TXA) sobre la reducción del volumen sanguíneo drenado posoperatorio, la intensidad del dolor y la incidencia de hemartrosis tras la reconstrucción del LCA.* **Método:** *Esta investigación prospectiva incluyó 124 pacientes sometidos a cirugía de reconstrucción del LCA, divididos aleatoriamente en dos grupos: uno recibió TXA intraarticular y otro (grupo de control) una cantidad igual de placebo por la misma vía.* **Resultados:** *La investigación ha demostrado que la inyección intraarticular de TXA reduce efectivamente la pérdida de sangre posoperatoria (grupo TXA 71.29 ± 40.76 vs. grupo control 154.35 ± 81.45), reduciendo la intensidad del dolor posoperatorio ($p < 0.001$) y la incidencia de hemartrosis.* **Conclusiones:** *La aplicación de TXA redujo significativamente el sangrado posoperatorio y la intensidad del dolor, lo que aceleró el posoperatorio.*

***Palabras clave*:** *Ácido tranexámico. Reconstrucción del ligamento cruzado anterior. Hemartrosis. Administración intraarticular.*

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Introduction

The global increase in sports and recreational activities has resulted in a rise in the number of anterior cruciate ligament (ACL) injuries. ACL injuries are a significant problem, particularly because they occur more frequently in young and working-age individuals[1].

In Vojvodina, a region in the Republic of Serbia with a population of around two million, there are approximately 400 ACL reconstructions performed each year[2,3]. Although ACL reconstruction is considered a minimally invasive and safe procedure with minimal blood loss, even small amounts of bleeding can have negative effects on the knee joint structures[4]. The most common complications associated with ACL reconstruction are hemarthrosis, movement deficits, and infections[5]. Hemarthrosis causes post-operative pain, knee swelling, and a loss of knee joint range of motion, which can lead to limited mobility and poor functional outcomes[6]. In addition, hemarthrosis can be toxic to the articular cartilage and increase the risk of infection[5]. Slow post-operative recovery and prolonged rehabilitation can lead to increased morbidity, poor short-term and medium-term results, and higher costs for both individuals and the health-care system[4,6].

Several studies have been conducted to reduce the risk of post-operative hemarthrosis after ACL reconstruction. These studies examined the effects of intravenous (IV) tranexamic acid (TXA) which requires careful consideration of the patient's health condition and constant monitoring by the anesthesiologist and surgeon. Although previous research has shown encouraging results, there are inconsistent opinions among authors about the dosage regimen[7-10]. Due to the complexities of IV administration, there have been studies on the clinical benefits of intra-articular (IA) administration of TXA during ACL reconstruction. However, there is still no unified opinion among researchers for its routine application[10-12].

Our study aims to evaluate the effect of IA administration of TXA after ACL reconstruction on post-operative bleeding, frequency of complications, occurrence of hemarthrosis, and pain intensity during six post-operative weeks.

Methods

The clinical research included 124 patients with a diagnosis of an ACL rupture and an indication for operative treatment. The study included patients who were 18 years or older and underwent arthroscopically assisted ACL reconstruction for the 1st time. Exclusion criteria used in the study included: A history of previous surgery on the same knee joint, kidney dysfunction, coagulation parameters showing pathological values, thrombophilia, treatment with drugs interfering with coagulation or TXA clearance, and history of previous allergic reaction to TXA (Fig. 1. Flowchart of case selection). Knee ACL reconstruction was performed according to the appropriate surgical protocol (modified clancy technique) for all patients. After the ACL reconstruction is completed, and after checking its isometry and stability in the knee joint, a drainage drain with a graduated vacuum bottle (redon-vacuum aspirator safe 500 mL OP-system) is placed, to monitor the amount of blood loss. A pneumatic surgical tourniquet was used routinely in all patients. All operations were performed by the same surgical team led by the same orthopedic surgeon, and the duration of the operation was recorded in the protocol.

For this research, we designed a randomizer to select and categorize our research sample with complete objectivity. On the day of surgery, we decisively divided the participants into two groups: The TXA group and the control group. Allocation was performed by computer-generated randomization by a non-involved contributor, leaving no room for any potential bias in the selection process. The surgeon, anesthetist, and patients were blinded regarding the use of TXA. Immediately before releasing the pneumatic surgical tourniquet, a 20 mL solution of TXA (5 mg/mL) was applied IA to the examined group of patients, while the patients in the control group were treated in the same way with an equivalent amount of sterile solution (normal saline). The drain was clamped for 30 min after the operation was completed, and then it was opened. On the 1st day after surgery, the patient's drain was removed. The volume of blood drained in the graduated vacuum bottle was recorded in their medical records. During the immediate preoperative preparation of the patient, 30 min immediately before the procedure, antibiotic protection was applied. During the post-operative period, the analgesia regimen included IV administration of a non-steroidal anti-inflammatory drug, according to the standard protocol of the clinic and the manufacturer's recommendation.

Our research uses a Visual Analog Scale (VAS) to measure pain intensity. The VAS is a widely used subjective measurement scale in clinical practice,

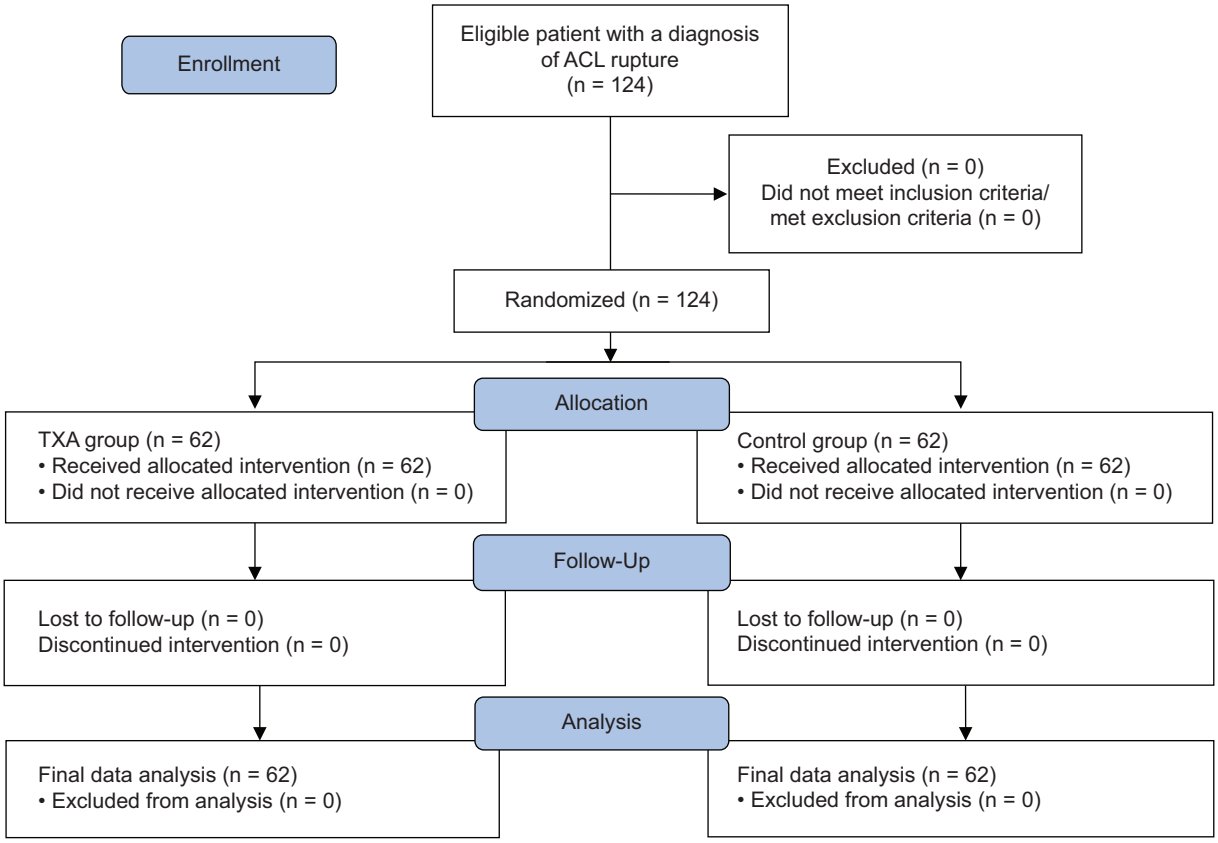

Figure 1. *Consolidated standards of reporting trials flow diagram. ACL: anterior cruciate ligament; TXA: tranexamic acid.*

research studies, and clinical trials to assess pain intensity in a variety of settings, including acute and chronic pain conditions, post-operative pain, cancer pain, and more. Individuals can express their pain intensity by marking a point along a continuous line from 0 to 10, with 0 representing no pain and 10 representing the worst possible pain. During the post-operative phase, patients were requested to assess their pain intensity using a VAS at different time intervals, including 3, 6, 12, and 24 h, and for the following 7 days. The patients were followed up to 6 weeks after surgery, during which the presence of swelling, degree of hemarthrosis, and hematoma were evaluated. From the 1st post-operative day, the patients were put on an established protocol of early rehabilitation and performed exercises involving passive bending of the operated knee joint with the aid of a device for continuous passive mobilization (Kinetic-device) during their hospital stay. After 2 weeks of surgery, partial support was allowed on the operated limb, and full support was allowed after 6 weeks. All patients were put through the same rehabilitation program, which included a set of kinetic exercises to strengthen and restore the strength of the muscles of the front and back of the upper leg, immediately after the end of anesthesia. The duration of hospitalization was the same for all patients in both groups, and all patients completed the study.

The ethics and investigation committee of our institution approved the study design. All patients provided written informed consent.

Statistics

The IBM Statistical Package for the Social Sciences (SPSS) Statistics 21.0 package was used for data analysis. Numerical characteristics were measured using mean values and measures of variability, whereas attributive characteristics were measured using frequencies and percentages. The χ^2 test was used to evaluate differences in frequency distribution for attributive features. To compare the average values of numerical features between two groups of data, the Student's t-test was used for parametric data, while the Mann–Whitney test was used for non-parametric data. The analysis of variance (ANOVA) test was used

for repeated measurements to compare the values of three or more dependent samples with a measurement scale. For values with an ordinal measurement scale, the Friedman two-way ANOVA was used. Further mutual comparison was done using the Wilcoxon test of equivalent pairs. To determine the sample size, a significance level of $\alpha = 0.05$, a power of the test of $1\text{-}\beta = 0.80$, and an effect size of d = 0.62 were used. The estimated significant difference between the average amount of drained blood in the TXA and control groups was 50 mL (standard deviation = 80 mL), which was used to define the size of the effect. Based on this data, the minimum sample size for the study and control groups was 40. Oversampling of patients in each group was done due to potential withdrawals and losses. All tests used are two-sided, and a significance level of $p < 0.05$ is considered statistically significant.

Results

Out of the 124 patients who took part in this study, 102 (82.3%) were male, and 22 (17.7%) were female. Their average age was 31.0 ± 8.1 years. All the patients who were randomized for the study were accounted for. In both groups, there was a proper distribution of gender with 51 men and 11 women. Both groups were similar in all variables (Age, body mass index, American Society of Anesthesiologists, and type of anesthesia), except for the duration of the surgical intervention. In the TXA group, operative procedures were on average shorter (TXA group 79.35 ± 20.56 vs. control group 86.94 ± 21.45, p = 0.047) (Table 1).

The data in table 2 illustrate the difference in the amount of blood drainage after ACL reconstruction and the occurrence of hemarthrosis relative to IA injection of TXA. The average amount of post-operative bleeding in the examined group was 71.29 ± 40.76 mL, while in the control group, it was 154.35 ± 81.45 mL. The difference in post-operative blood loss between the groups was statistically significant ($p < 0.001$). After comparing the control group and the tested group of patients, it was found that the patients in the tested group had significantly lower pain intensity scores 3 h (p = 0.030) and 12 h (p = 0.039) after surgery. There was no significant difference in pain intensity score between the two groups 6 h and 24 h after surgery (p = 0.092, p = 0.051) (Table 2). During the 6 weeks following surgery, there were no instances of DVT or infections within the observed

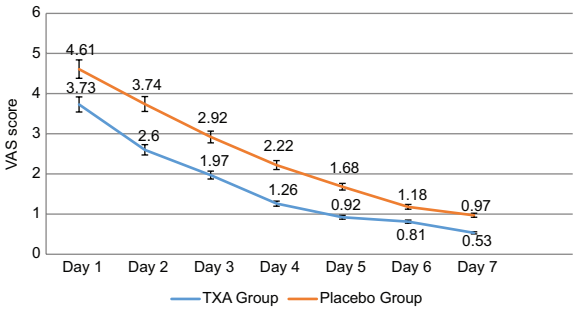

Figure 2. *Visual Analog Scale during 1-7 post-operative days.*

groups. In the TXA group, we have two patients who had aspiration. During the 3rd post-operative week, one patient had hemarthrosis (40 mL), and after the sixth post-operative week, another patient had hemarthrosis (60 mL). In the control group, two patients experienced hemarthrosis in the 6th post-operative week. In both cases, 60 mL of blood was aspirated (Table 2).

A comparison was made between the group that received TXA and the control group. The study found a significant difference in the intensity of pain experienced by the two groups on the 2nd day after surgery (p = 0.003), 3rd day (p = 0.003), 4th day ($p < 0.001$), 5th day (p = 0.001), and on the 7th day ($p < 0.001$). No significant difference in pain intensity was found between the two groups on the 1st day after surgery (p = 0.051) and the 6th day after surgery (p = 0.069) (Fig. 2).

Discussion

Our research found that the IA of TXA effectively reduces bleeding and pain following ACL reconstruction surgery, without complications such as DVT or infections.

Chiang et al. also reported similar findings in their research. They confirmed that IA administration of 10 mL of TXA (100 mg/mL) significantly reduced the amount of post-operative bleeding in the drain[10]. The research conducted by Karaaslan et al. provides compelling evidence that the administration of TXA can have a beneficial impact on both the early post-operative period and functional outcomes[7]. The results of their research indicate reduced post-operative drainage after IV application (TXA group 60 mL; Control group 150 mL), reduced post-operative hemarthrosis, and reduced need for knee aspiration[7].

Table 1. Socio-demographic and perioperative data of patients

Variables	Category	TXA group (n = 62)	Control group (n = 62)	p
Sex, n (%)	Male	51 (82)	51 (82)	> 0.05
	Female	11 (18)	11 (18)	
Age, year		29.37 ± 7.93	26.76 ± 7.93	0.069[ns]
BMI, kg/m^2		25.80 ± 3.48	24.68 ± 3.21	0.064[ns]
ASA	I	38 (61.3)	46 (74.2)	0.147[ns]
	II	24 (38.7)	15 (24.2)	
	III	0 (0)	1 (1.6)	
Type of anesthesia, n (%)	General	27 (43.5)	23 (37.1)	0.667[ns]
	Spinal	34 (54.8)	34 (54.8)	
	Combined	1 (1.6)	4 (6.5)	
	Femoral nerve bloc	0	1 (1.6)	
Operative time (min)		79.35 ± 20.56	86.94 ± 21.45	0.047

ns: non-significance; BMI: body mass index; ASA: American Society of Anesthesiologists.

Table 2. Early post-operative outcomes

Variables	Category	TXA group (n = 62)	Control group (n = 62)	p
Post-operative bleeding (mL)		71.29 ± 40.76	154.35 ± 81.45	< 0.001
VAS score	3 h	3.98 ± 3.31	5.26 ± 3.15	0.030
	6 h	4.81 ± 2.91	5.65 ± 2.58	0.092[ns]
	12 h	4.71 ± 3.25	5.92 ± 3.22	0.039
	24 h	3.73 ± 2.66	4.61 ± 2.36	0.051[ns]
Post-operative week 1	VAS	0.53 ± 1.02	0.97 ± 0.97	0.018
	Hemarthrosis, n (mL)	-	-	-
Post-operative week 3	VAS	0.0 ± 0.0	0.18 ± 0.39	< 0.001
	Hemarthrosis, n (mL)	1 (40 mL)	-	-
Post-operative week 6	VAS	0.0 ± 0.0	0.05 ± 0.22	0.073
	Hemarthrosis, n (mL)	1 (60 mL)	2 (60/60 mL)	-

ns: non-significance; VAS: Visual Analog Scale.

This reinforces the importance of considering TXA as a treatment option in relevant cases. Reduced post-operative bleeding was also reported in the study by Felli et al.[6] (TXA group 59.3 ± 29.5; control group 133.3 ± 56.1), but also in Pande and Bhaskarwar research[8], which reports positive outcomes of TXA application, even though no drain was placed. The placement of the drain is still a topic of dispute for many authors. While some authors place a drain routinely, others associate it with the onset of infection[13]. IA drainage was inserted in our study, to monitor blood loss more precisely. During the 6th week of follow-up, we did not have any recorded complications in any group of patients, which we could relate to the placement of the drain.

Contrary to these results, Lee et al.[11] found no significant difference in post-operative bleeding after IA application of 30 mg/mL TXA (control group 558 ± 236 [136-1088 mL]; TXA group 467 ± 242 [179-1127 mL]). However, they did not place a drain, so the estimated blood loss was controlled by the indirect method, which is also stated as a limitation of their study.

According to the research by Valkering et al.[14], the first two post-operative days after the reconstruction of the ACL are the most painful, which was also confirmed by our research, whereas the TXA group had lower VAS score values. We noted that respondents in the TXA group showed a lower pain score at the third and twelfth post-operative hour, which can be related to the effect of an early IA injection of TXA,

which is in accordance with the available literature[15]. During the 6th h and the first 24 h of the post-operative course, no significant difference was found between groups, although the pain intensity scores were lower in the test group at these times, as well. Moreover, a significant difference in pain intensity was observed between the test groups, on every subsequent day, except for the 6th day when the difference in pain intensity was in favor of the TXA group, although small. In our research, the assessment of pain intensity confirms a significant difference based on pain intensity on the 1st and 3rd week after surgery, but on the 6th week, no significant difference in pain intensity was found between the groups. In contrast to our research, Chiang et al.[10] monitored the VAS scale score 2 times: on the 3rd day and the 4th week postoperatively, documenting a significantly lower intensity of pain on the 3rd day, while in the 4th week, they reported minimal differences in the VAS score between the groups[10]. Ma et al.[12] reported a lower VAS scale in 1st and 2 weeks, but there was no reported difference in the VAS scale in 4th week between groups. Contrary to these studies, Lee et al.[11] report no significant differences in pain intensity between groups, at all. Comparison of the VAS scale among the available studies should be viewed with a dose of caution, given that different anesthesia protocols, analgesia, and surgical techniques were used.

In the case of hemarthrosis, the patient usually needs aspiration (arthrocentesis). This is a procedure that causes discomfort to the patient and a potential cause of infection. Unlike the study by Chiang et al.[10] who did not report the occurrence of hemarthrosis and Lee et al.[11] who did not observe a statistically significant difference between the groups regarding the occurrence of hemarthrosis, in our study patients from both groups required knee aspiration at week 3 (n = 1 TXA group), that is, in the 6th week (n = 1 TXA group; n = 2 control group). According to the available data, three authors report the need for aspiration in patients who received TXA IV. Karaaslan et al.[7] state the need for aspiration in 23 patients (four TXA group and 19 control group), Pande and Bhaskarwar[8] in a total of 10 patients (three TXA group and seven control group), while Fried et al.[9] performed aspiration in 49 patients (23 TXA group and 26 control group).

In conclusion, the meta-analysis conducted by Johns et al.[15], it was found that IV use of TXA is preferable over IA administration. Their analysis included only one study where TXA was administered IA[15]. Considering previous research, the conclusions of two meta-analyses suggest that the use of TXA in ACL reconstruction reduces drainage output and knee swelling, pain intensity, incidence of hemarthrosis, and the need for aspiration in the post-operative period. Given that there were no reported complications, the use of TXA could be useful in arthroscopic surgery[16,17].

In our study, it was proven that the bleeding in the knee joint was reduced, as well as the low intensity of pain during the entire monitoring period. Thus, IA administration of TXA could be considered a safe solution to reduce post-operative bleeding and pain after ACL reconstruction. Due to the need for aspiration of the knee joint that occurred in both groups of patients in our study, additional research would be useful to confirm the late effect of IA TXA administration on the occurrence of hemarthrosis. The studies available so far differed in the way and doses of TXA applied, not only in ACL reconstruction but also in orthopedic prosthetic surgery. Studies comparing the same route of administration at different doses in the same study group may be of great importance[18]. It would certainly be important to conduct extensive research on the assessment of the optimal dose and time of exposure of the knee joint structures to the effect of TXA, to take a common position on the IA application of TXA during ACL reconstruction.

Study limitations

Our study has some limitations that need to be addressed. Firstly, the sample we examined consisted of professional athletes whose previous physical fitness and self-discipline may differ from those who engage in sports only recreationally or not at all. This difference could have affected the extent of pain tolerance and changes in the VAS scale. In addition, we did not consider the difference in time between injury and surgery. Finally, due to the low representation of female subjects, we were unable to confirm with certainty whether IA injection of TXA has been linked to post-operative bleeding, VAS scale values, and the incidence of hemarthrosis in patients of both genders.

Conclusion

Based on our research, applying TXA in the joint effectively reduces post-operative bleeding in the first 24 h, minimizes hemarthrosis occurrence in the early period, and reduces pain intensity during the 1st week. The group of patients who underwent the IA application didn't experience any systemic side effects during

the follow-up period. Although we have some knowledge regarding the benefits of using TXA in ACL reconstruction, we believe that more research is necessary to collect data on the relationship between TXA effectiveness and different methods of administration, dosage, duration of exposure, and the impact of TXA use on long-term functional outcomes.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the code of ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

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ORIGINAL ARTICLE

Epithelioid hemangioendothelioma as a cause of intestinal intussusception in an adult female patient: case report

Hemangioendotelioma epitelioide como causa de intususcepción intestinal en una paciente adulta: caso clínico

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Abstract

Introduction: *Epithelioid hemangioendothelioma is a rare vascular tumor with an epithelioid and histiocytoid appearance. Intestinal intussusception can manifest as chronic abdominal pain, representing only 1-5% of intestinal obstructions in adults.* **Case report:** *65-year-old female who is attended with chronic abdominal pain. We performed a computed tomography showing the incursion of the ileum into the right colon. She was taken to the operating table, with the finding of ileo-colic intestinal intussusception due to small bowel tumor, with subsequent anatomopathological results of epithelioid hemangioendothelioma.* **Conclusions:** *The diagnosis and management process with an appropriate postoperative outcome is described.*

Keywords: *Hemangioendothelioma. Vascular tissue neoplasm. Abdominal pain. Intussusception. Intestinal invagination.*

Resumen

Introducción: *El hemangioendotelioma epitelioide es un tumor vascular poco frecuente de aspecto epitelioide e histiocitoide. La intususcepción intestinal suele ser causa de dolor abdominal crónico y corresponde al 1-5% de las obstrucciones intestinales en el adulto.* **Caso clínico:** *Mujer de 65 años que acude con dolor abdominal crónico. Se realiza tomografía computarizada y se observa incursión del íleon en el colon derecho. Es llevada a mesa operatoria con hallazgo de intususcepción intestinal ileocólica por tumoración de intestino delgado, con resultado anatomopatológico de hemangioendotelioma epitelioide.* **Conclusiones:** *Se describe el proceso de diagnóstico y manejo, con apropiado desenlace posoperatorio.*

Palabras clave: *Hemangioendotelioma. Neoplasias de tejido vascular. Dolor abdominal. Intususcepción. Invaginación intestinal.*

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Introduction

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor of an epithelioid and histiocytoid appearance originating from endothelial or pre-endothelial vascular cells[1]. It represents < 1% of vascular tumors and was first described in 1975 by Dail and Liebow as pulmonary EHE; the term "epithelioid hemangioendothelioma" was first introduced back in 1982 by Weiss and Enzinger to describe a vascular tumor of the bone and soft tissue with characteristics between hemangioma and angiosarcoma[2]. The estimated prevalence is < 1 case per million inhabitants[3]. It is usually diagnosed in women in the 6th decade of life, showing as abdominal pain and iron deficiency anemia when located in the small intestine, and weight loss, painful hepatomegaly, portal hypertension, or platelet sequestration (Kasabach-Merritt syndrome) when located in the liver[4].

Nonspecific abdominal pain is the most common cause of acute surgical admission for abdominal pain. Its etiology cannot be established in up to 40%-65% of patients, which can lead to a chronic course of the disease[5]. In acute abdominal pain, studies often focus on excluding conditions such as acute appendicitis, intestinal obstruction, and similar ailments; in chronic pain, the main focus is on malignant diseases, inflammatory bowel disease, acid-peptic disease, gynecological diseases, and hepatobiliary disease[5].

Intestinal intussusception is a rare type of intestinal obstruction, defined as the introduction of a proximal intestinal loop (intussusceptum) into a distal loop (intussuscipiens), resulting in the obliteration of its lumen. Although it is a common cause of intestinal obstruction in children, intestinal intussusception in adults is quite rare, with an estimated incidence of 2 cases per million inhabitants per year[6]. Of all intussusception cases, only 5% occur in adults, and they represent only 1% up to 5% of all intestinal obstructions in adults[7]. The most common locations are the junctions between segments of the intestine that can move freely and the segments of the intestine that are adhered or fixed to the retroperitoneum[8].

The clinical presentation of intestinal intussusception in adults is usually nonspecific. The classic triad of abdominal pain, vomiting, and "currant jelly" stools is rarely evident, which is more common in children, leading to delays in diagnosis. However, intestinal intussusception is an important differential diagnosis to consider because most cases in adults are caused by structural lesions, commonly malignant neoplasms[9]. The use of computed tomography as a preoperative diagnostic method has been widely developed in recent years for this type of pathology[10].

Case report

A 65-year-old woman, originally from Mérida, Venezuela, with a surgical history of open appendectomy, presents with a current illness of 4 months characterized by insidious onset and a 3-month history of mild, sharp abdominal pain, initially generalized but later localized to the right iliac fossa, for which she consulted a physician, who prescribed medical therapy with partial improvement of the condition. As symptoms persisted and a palpable mass appeared in the right iliac fossa, she visited the gastroenterology department of our center, where a colonoscopy revealed the presence of a subepithelial tumor in the cecal region.

She also presented with altered bowel habits, alternating between periods of constipation and diarrhea, recent onset of fever (15 days), and intolerance to oral intake (solids), for which she was referred to the general surgery department.

On physical examination, she was found to be in stable clinical condition, afebrile, hydrated, with adequate skin and mucosal coloration; abdominal examination revealed a flat abdomen, present bowel sounds, soft and depressible, with a palpable 5 cm × 5 cm painful mass in the right iliac fossa, without any signs of peritoneal irritation; rectal examination revealed a normal anus, preserved sphincter tone, smooth rectal walls with no palpable tumors, and scant soft stools inside; gynecological examination showed no abnormalities; the rest of the physical examination was unremarkable.

A computed tomography scan with double contrast (oral and intravenous) was requested, showing loss of the usual configuration in the ileocecal region with significant enlargement of the cecum, and the ileum was observed to protrude into the right colon along a long tract from the transverse colon to the splenic flexure (Fig. 1), where a sac-like formation filled with oral contrast was observed. During the arterial phase, the cecal region showed no changes in density, and vascular pathways were observed throughout the colon along with adipose tissue, but double enhancement was evident in the region of the splenic flexure of the transverse colon. Findings were suggestive of intussusception secondary to neoplasm.

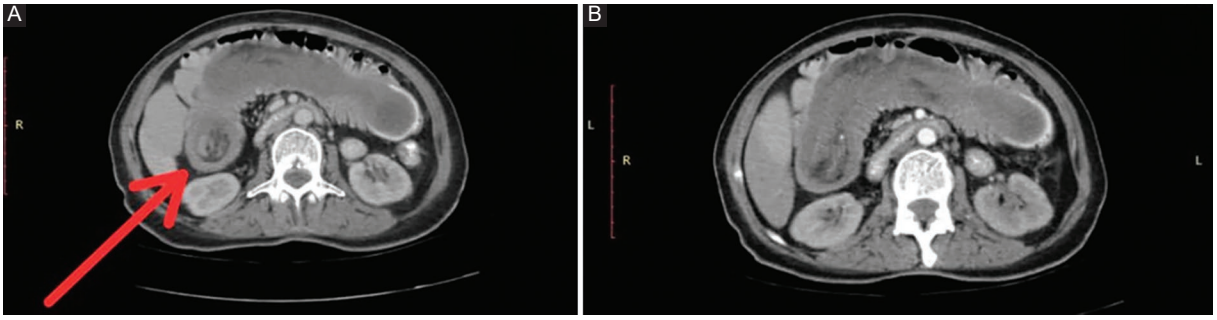

Figure 1. A: *loss of usual configuration of the ileocecal region (arrow).* **B:** *incursion of the ileum into the right colon across a long tract extending from the transverse colon to the splenic flexure.*

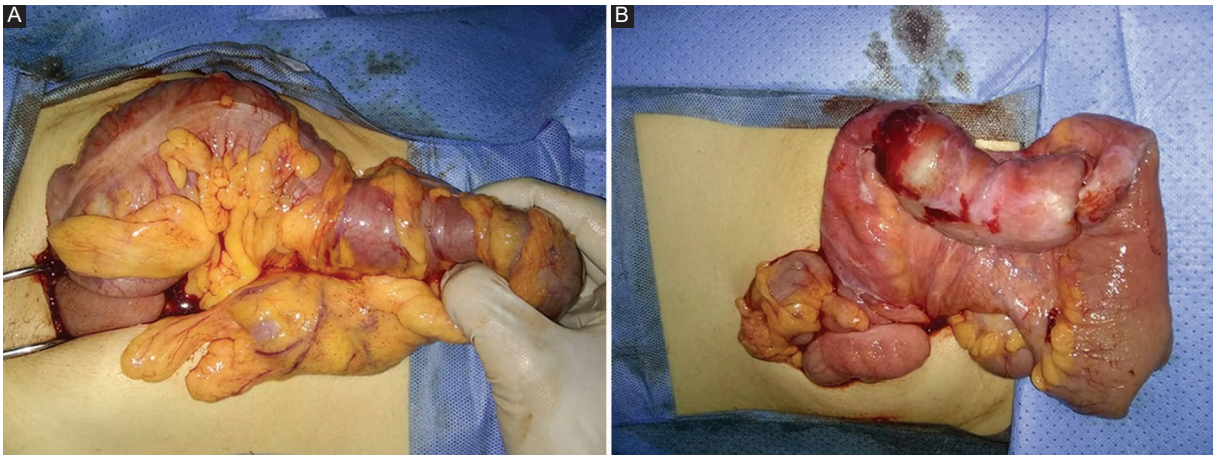

Figure 2. A: *ileo-colic intussusception up to the hepatic flexure of the transverse colon.* **B:** *tumor found 10 cm away from the ileocecal valve, and 10 cm in length found in the small intestine, invading up to the indurated serosa and compromising the intestinal lumen.*

Given the tomographic findings and physical examination, the patient was taken to the operating room, where a small amount of free serous fluid was found in the abdominal cavity. Ileocolic intussusception was evident up to the hepatic flexure of the transverse colon (Fig. 2A). Upon reducing the intussusception, a 10 cm tumor was observed 10 cm from the ileocecal valve in the small intestine, invading up to the serosa, indurated, and compromising the intestinal lumen (Fig. 2B), with multiple mesenteric lymph nodes of varying sizes (no > 2 cm) in the right colon mesentery, without evidence of liver lesions. The Cattell-Braasch maneuver was performed, right hemicolectomy up to the emergence of the right colic artery, closure of the transverse colon stump, and construction of a side-to-side ileotransverse anastomosis, washing and drainage of the cavity, and layered closure of the abdominal cavity. The surgical act ended uneventfully, and the patient had a favorable clinical course. Oral intake was started 48 hours postoperatively. She was discharged 5 days postoperatively, the drain was removed at 10 days, and the patient continued follow-up in the general surgery department without any complications.

The studied sample showed a neoplastic lesion characterized by the proliferation of tubular structures with endothelial-like lining exhibiting eosinophilic cytoplasm, vesicular nuclei without nucleoli, intracytoplasmic vacuoles, presenting endothelial lumens, some with erythrocytes, and isolated mitoses (3 in 40 high-power fields). This area showed an increase in fibrous connective tissue. At the periphery, a significant polymorphonuclear neutrophil and lymphocytic inflammatory infiltrate with necrosis, cellular debris, and extravasated erythrocytes was observed. Special stains of PAS (Periodic Acid-Schiff) and Gomori's trichrome showed the presence of fibrous connective tissue around the described neoplastic lesion areas;

sections of the large intestine with mucosal lining showed no significant alterations, as did the mesentery. Findings in the small intestine were consistent with EHE of intermediate malignancy.

Discussion

Intussusception is classified, according to its location, into 4 different categories:

– Entero-enteric: confined to the small intestine.
– Colo-colonic: affects only the large intestine.
– Ileo-colic: defined as the introduction of the terminal ileum into the ascending colon.
– Ileo-cecal: the ileocecal valve is the main point of the intussusception and is somewhat difficult to distinguish from the ileo-colic variant[11].

We present the case of an adult patient with ileocolic intussusception, which is very uncommon in this age group. The exact pathophysiology of intestinal intussusception (primary or idiopathic) is currently unknown in 8% up to 20% of cases, being more likely to occur in the small intestine[7]. In this case, it was due to an EHE, a very rare tumor representing only 1% up to 3% of all malignant gastrointestinal neoplasms[12], while the most common malignant tumors in the gastrointestinal tract are adenocarcinomas (40%), carcinoids (25% up to 30%), lymphomas (15% up to 20%), sarcomas (12%), and metastases[13].

EHE is a rare and locally aggressive tumor described in the small intestine as a cause of upper GI bleeding[4]. Although we conducted an extensive literature review, we did not find any described cases as a cause of intestinal intussusception in adult or pediatric patients. There are 4 different histological types of hemangioendothelioma: epithelioid, spindle cell, Kaposiform, and malignant papillary intravascular or Dabska tumor[4]. In descending order of frequency, their location is usually the skin, liver, spleen, the GI tract (mainly the jejunum and ileum), bone, lung, and head and neck. Approximately 50% of patients with internal organ involvement present with associated skin lesions. In adults, the spindle cell and epithelioid variants are the most common, affecting one or several organs nodularly or diffusely[4].

The patient underwent successive follow-up using other imaging methods (abdominal ultrasound and chest X-ray), without evidence of tumors in other organs or skin involvement, concluding that the localized EHE was a primary tumor affecting only 1 organ. The abdominal pain presented can be attributed to the intussusception, which showed an atypical clinical expression.

Conclusions

Untreated intestinal intussusception can be life-threatening, causing progressive intestinal distension resulting in increased intraluminal pressure, which can lead to microvascular ischemia, tissue necrosis with intestinal perforation, and subsequently peritonitis[14]. Distant metastases of EHE have been described by hematogenous dissemination; they primarily invade the liver, but also the skin, serous membranes, spleen, tonsils, retroperitoneum, and kidneys, and exceptionally colonic metastases have been described[15].

When lesions are small and limited in number, some authors recommend surgical resection or a preventive approach in asymptomatic patients. Although successful curative resection achieves good results, the role of adjuvant chemotherapy and radiotherapy is ambiguous. Radiotherapy is generally chosen after surgical resection of localized EHE to control residual disease, while chemotherapy is preferred in cases of disseminated disease, but its beneficial effect is not yet confirmed[1].

In this patient, early diagnosis based on presumption, coupled with more specific diagnostic imaging modalities (computed tomography) led to early surgical resolution, correcting not only the intussusception but also resecting a tumor of intermediate malignancy.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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CASO CLÍNICO

Calcified clumped neodymium magnetic spheres as an intravesical foreign body: case report and literature review

Esferas magnéticas de neodimio agrupadas calcificadas como un cuerpo extraño intravesical: reporte de un caso y revisión de la literatura

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Abstract

Foreign bodies in the bladder can occur by self-insertion, and patients often hide the symptoms owing to embarrassment. The foreign bodies act as a nidus for calculus formation when not detected for a long time. Foreign bodies can declare symptoms such as frequency, dysuria, nocturia, hematuria, urethrorrhagia, obstruction, or retention. This case spotlights self-inserted intravesical neodymium magnetic spheres clumped and calcified due to delayed presentation which were removed by open cystotomy after a cystoscopic failure.

Keywords: *Exploratory behavior. Foreign bodies. Magnets. Neodymium. Urinary bladder.*

Resumen

Los cuerpos extraños en la vejiga pueden ocurrir por autoinserción y los pacientes a menudo ocultan los síntomas por vergüenza. Los cuerpos extraños actúan como un nido para la formación de cálculos cuando no se detectan durante mucho tiempo. Los cuerpos extraños pueden manifestar síntomas como polaquiuria, disuria, nicturia, hematuria, uretrorragia, obstrucción o retención. Este caso destaca esferas magnéticas de neodimio intravesicales autoinsertadas, agrupadas y calcificadas debido a una presentación tardía que se extrajeron mediante cistotomía abierta después de una falla cistoscópica.

Palabras clave: *Adolescente. Comportamiento exploratorio. Cuerpos extraños. Imanes. Neodimio. Vejiga urinaria.*

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Introduction

A great variety of self-inserted foreign bodies in the bladder have been described. The reason is usually eroticism or curiosity. Self-inserted foreign bodies cases in the bladder are infrequent in adolescents. Depending on the nature of the foreign body, the diagnosis and management might be challenging. Diagnosis is always difficult because the insertion is hidden. Our presentation aims to report a case of an unusual self-inserted intravesical foreign body with calcification as a first-reported complication and briefly discuss the diagnostic and therapeutic implications in this challenging situation.

Case presentation

A 15-year-old healthy male adolescent applied to a urologist immediately after seeing blood in his urine. He has also confessed to groin pain, dysuria, and foul-smelling urine for 6 months. Vital signs and physical examination were insignificant other than a mild suprapubic tenderness to palpation. Laboratory blood test results were normal. The urinary sediment showed > 80 white blood cells/μL and > 5 red blood cells/μL. X-ray, ultrasonography (USG), and computed tomography (CT) were performed, respectively (Figs. 1-3) (supplementary material 1). Cystoscopy was planned for the optimal diagnosis and treatment. Under general anesthesia, a cystoscope with a 20 Fr sheath was introduced into the urethra, and a bladder stone was identified in the bladder trigone. After the holmium laser process was started, as the superficial stone layer was removed, a deeply colored core consisting of spheres appeared (Fig. 4) (supplementary material 2).. The superficial stone layer was easily fragmented, but the colorful inner layer was resistant, even though fragmented, the pieces were being reunited. The fragments of the outer stone layer were cleared through the cystoscope, but since the beads and metallic fragments were not split due to the magnetic attraction, withdrawal through the cystoscope or using forceps was impossible. Hence, a small cystotomy was performed through a Pfannenstiel incision, and all the 64 magnetic spheres were removed, some of which were partially fragmented by holmium laser, and the bladder was cleared completely (Fig. 5). The patient's course in the postoperative period was stable. A preliminary psychological evaluation was administered on the 1st post-operative day. The patient volunteered his story about the magnetic spheres; 9 months ago, out of curiosity, he had sent one sphere through the urethra and used the second one to pick the first one up, thus inserting all 64 beads into the urethra. On the 3rd postoperative day, the drain was removed, and the patient was discharged with a urethral catheter. The catheter was removed on the 1-week follow-up after a cystogram was performed which revealed neither leakage nor any residual contrast (supplementary material 3). The patient recovered without complications.

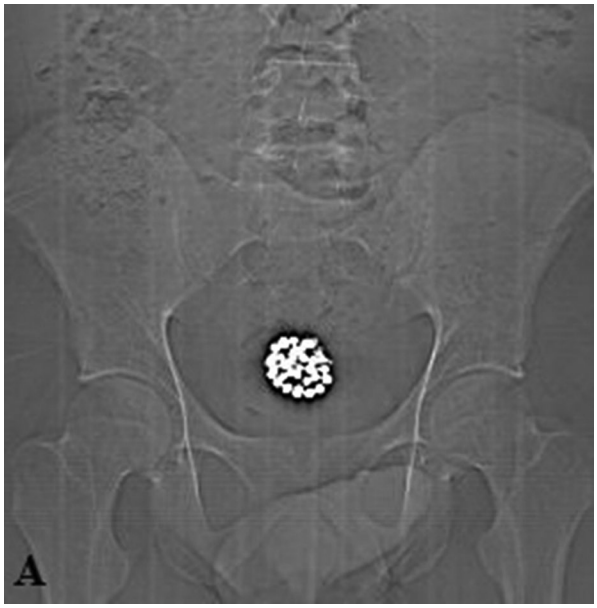

Figure 1. *X-ray of pelvis demonstrating metallic balls in the bladder region.*

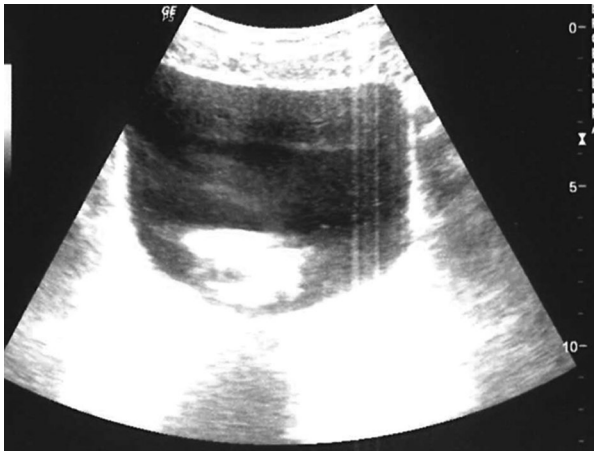

Figure 2. *Ultrasonography reporting a stone of 35 mm × 39 mm and emphasizing a strong acoustic shadow.*

Table 1. Self-inserted magnetic spheres cases in the available literature are listed in the table. Cases are always male, usually without psychiatric disorders, on their first attempt, confessing the self-insertion and used spheres 5-mm in diameter. Exceptional information is given in the symptoms column

Author	Age	Symptoms (additional information, if any)	#	Retrieval method
Gurpriya et al.[3]	19	Dysuria, inability to pass urine	51	Extraperitoneal laparoscopy after a cystoscopic failure
Alyami et al.[7]	19	Dysuria, voiding difficulty (with documented psychiatric illness)		Cystotomy after a cystoscopic failure
Brooks et al.[11]	26	Dysuria, decreased urinary output for three days,	42	Cystoscopy using basket and three-pronged grasper
Ellimoottil et al.[5]	11	Acute onset of gross hematuria and difficulty voiding	24	Cystoscopy using basket and grasper
Graziottin et al.[14]	22	Urethral bleeding and dysuria (with panic disorder)	29	Cystoscopy using forceps
Hedgepeth[15]	23	Urgency, frequency, hematuria	62	Cystotomy after a cystoscopic failure
Levine and Evans[16]	42	Applied with confessing the insertion	18	Cystotomy after a cystoscopic failure
	43	Applied with confessing the insertion	55	Cystotomy after a cystoscopic failure
	30	Urinary retention (has previous insertion history)	50	First-line cystotomy
Song et al.[9]	41	Hematuria, urinary retention, dysuria	82	Cystoscopy using grasper
Pieretti[4]	16	Mild hematuria	25	Cystotomy after a cystoscopic failure
Robey et al.[17]	12	Applied with confessing the insertion	30	Percutaneous cystostomy due to cystoscopy is time-demanding
Zeng et al.[10]	21	Gross hematuria, frequency, acute lower abdominal pain (has previous insertion history) (3-mm diameter spheres)	125	Cystoscopy using a self-invented magnetic sheath
Li et al.[2]	50	Lower abdominal pain dysuria	57	Cystoscopy
Gibson et al.[6]	11	New onset hematuria (with attention hyperactivity disorder)	16	Cystotomy after a cystoscopic failure
	18	Dysuria, gross hematuria (with autism spectrum disorder)	52	Cystotomy after a cystoscopic failure
Lindsay[12]	18	Applied with confessing the insertion	60	Cystoscopy using grasper
Liu et al.[13]	28	Applied with confessing the insertion	159	Nephroscope and its forceps through the cystoscope
Tang and Tsai[8]	17	Gross hematuria, frequency, dysuria (never confessed the insertion)	74	Cystoscopy using grasper
Zhang et al.[1]	11	Lower abdominal pain, urethral bleeding, dysuria	38	Pneumovesicoscopy after a cystoscopic failure

#number of the magnetic spheres.

Discussion

Intravesical foreign bodies are not rare cases[1]. Ingress of foreign bodies into the bladder may be by self-insertion, migration from neighbor organs, traumatic, and iatrogenic[2]. A variety of intravesical foreign bodies has been documented, including thermometers, electrical wires, needles, batteries, and so on[3]. Foreign bodies also vary according to changing eras. Neodymium spheres with high magnetic power, with the smallest diameter of three millimeters, which are marketed as toys, have also recently started to appear as a foreign body in the bladder (Fig. 6)[4]. The cases documented in the available literature regarding self-inserted neodymium magnetic spheres are compiled in table 1. Self-insertion of foreign bodies is rarely seen in the childhood age[5]. Usually, they are initially sighted at the beginning of puberty[6]. The reasons for the insertion of foreign bodies into the genitourinary tract could be sexual gratification, psychiatric, accidental, curiosity, especially among children, or therapeutic[7]. Most patients delay referring to a health professional due to embarrassment causing serious short and/or long-term complications[8]. In this article, calcified magnetic

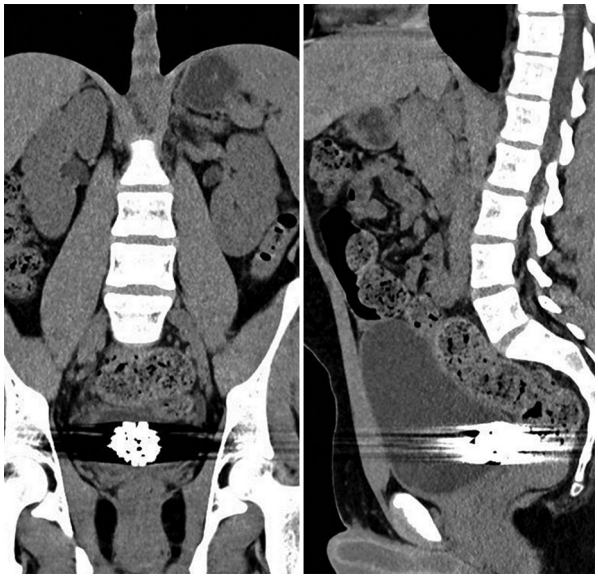

Figure 3. *Coronal and sagittal computed tomography sections revealing a 31 mm diameter globe-shaped hyperdense image in the bladder with a marked metallic artifact.*

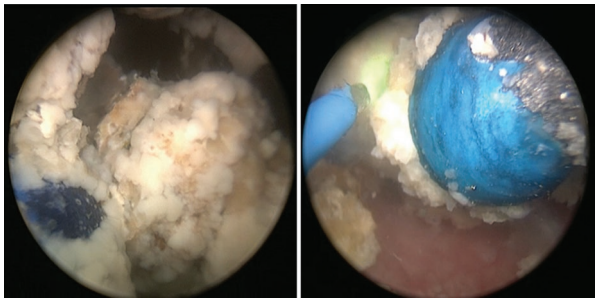

Figure 4. *Cystoscopic view of calcified magnetic ball mass and one of the magnetic balls after the calcific layer was removed peeling.*

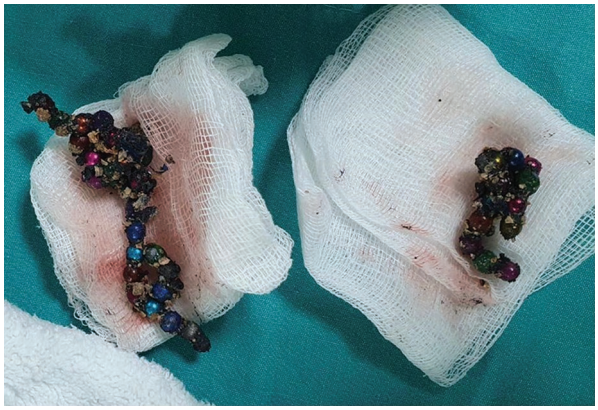

Figure 5. *Magnetic spheres removed from the bladder by open approach.*

Figure 6. *Neodymium magnetic speheres.*

spheres were highlighted for the 1st time in the literature, due to delayed presentation. The consequences usually include symptoms such as frequency, dysuria, nocturia, hematuria, urethrorrhagia, obstruction, or retention[9]. Physical examination may reveal suprapubic tenderness and external genital organ swelling. Urinalysis may represent erythrocyturia or leukocyturia. After taking a detailed history, ideal imaging (X-ray-USG-CT) is essential in diagnosis[10]. X-ray is useful for radiopaque foreign bodies only, as the USG is helpful for both radiopaque and radiolucent foreign bodies. In our case, the uniform clustering of magnetic spheres led to the diagnosis of bladder stones with the help of stone formation in the outer layer making them appear blurred in the X-ray. Cystoscopic visualization is a precise method to verify the presence of intravesical foreign bodies[11]. In the majority of cases, cystoscopic removal is presumed optimal, usually working with balloon-wire snares, endoscopic forceps, and stone-retrieving baskets[12]. The studies that subject self-inserted and iatrogenic foreign bodies claim that cystoscopic retrieval is possible in approximately half of the cases[13]. Objects introduced through the urethra have a higher cystoscopic retrieval rate since their sizes are limited by urethral diameter[14]. Suprapubic cystostomy or open surgery may be performed unless cystoscopic intervention is successful in removing foreign bodies[15]. The up-to-date reports suggest prioritizing the open method in magnetic spheres[16]. An

immediate proper treatment option is recommended to reduce complications. One of the most common complications in delayed presented cases is stone formation since all the foreign bodies when left for long behave as a nidus for stone formation. It is suggested that a psychiatric evaluation should be recommended to discover any underlying mental health disorders, thus reducing the risk of recurrence[17].

Conclusion

The physician should keep the presence of foreign bodies in mind in patients presenting with frequency, dysuria, nocturia, and hematuria. The presentation of these cases is usually delayed due to the fear of embarrassment. Imaging techniques are crucial to identify the number, exact size, and nature of the foreign bodies. The best approach for the removal of the foreign bodies depends directly on foreign bodies' location, nature, and size and patients' age, as well as surgical expertise and accessible equipment. However, most foreign bodies can be retrieved utilizing cystoscopic techniques, according to the literature. Open surgical removal is usually reserved for those in whom cystoscopic techniques are unsuitable or have failed.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Supplementary data

Supplementary data are available at DOI: 10.24875/CIRUE.M22000699. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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CLINICAL CASE

Intracranial Rosai Dorfman disease - A rare differential diagnosis of multiple meningiomas: case report

Enfermedad de Rosai Dorfman intracraneal - Un diagnóstico diferencial poco frecuente de meningiomas múltiples: informe de un caso

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Abstract

Rosai Dorfman Destombes (RDD) disease is a non-Langerhans histiocytosis. The central nervous system is affected in < 5% of cases. We report the case of a 59-year-old man, who began 8 months before admission with headache, diminished visual acuity in the temporal hemifields, hyposmia, and seizures. Magnetic resonance imaging showed three midline skull-base lesions in anterior, media, and posterior fossae. We performed a complete resection of symptomatic lesions using a bifrontal craniotomy. The histopathological analysis determined RDD, therefore, we started steroid treatment. Our case description is due to the diagnosis and location, one of the rarest reported to date in the literature.

Keywords: *Intracranial. Multiple meningiomas. Rosai Dorfman disease. Sinus histiocytosis.*

Resumen

La enfermedad de Rosai-Dorfman-Destombes (RDD) es una histiocitosis no Langerhans. El SNC se ve afectado en menos del 5% de los casos. Presentamos el caso de un hombre de 59 años quien inició ocho meses previos al ingreso con cefalea, hemianopsia bitemporal, hiposmia y convulsiones. La resonancia magnética mostró tres lesiones de la base del cráneo en las fosas anterior, media y posterior. Realizamos una resección completa de las lesiones sintomáticas mediante una craneotomía bifrontal. El análisis histopatológico determinó RDD. Nuestro caso es debido al diagnóstico y localización, uno de los más raros reportados hasta la fecha en la literatura.

***Palabras clave*:** *Intracraneal. Enfermedad de Rosai Dorfman. Meningiomas múltiples. Histiocitosis sinusal.*

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Introduction

Histiocytosis includes a group of rare diseases characterized by the accumulation of cells derived from macrophages or dendritic cells[1,2]. Although most of them are considered systemic diseases, only a few affect the central nervous system (CNS), the main ones: Erdheim Chester disease, Rosai Dorfman Destombes disease (RDD), Langerhans cell histiocytosis, histiocytic sarcoma, and juvenile xanthogranuloma[3]. Sinus histiocytosis with massive lymphadenopathy or Rosai Dorfman Destombes disease (RDD) is a non-Langerhans histiocytosis first described in 1965 by pathologist Pierre Paul Destombes and then characterized in 1969 by Juan Rosai and Ronald Dorfman[4,5]. Clinically, it presents as painless bilateral cervical lymphadenopathy associated with fever, fatigue, and weight loss. Extranodal involvement occurs in 43% of cases, mostly in the skin, nasal cavity, bone, soft tissues, and orbits[1]. CNS is affected in < 5% of cases and it can exist in the context of a systemic disease or as an isolated entity[1]. There are < 200 reported isolated RDD cases (75% intracranial and 25% spinal); of these, only 21 as multiple isolated intracranial lesions[6,7].

This report aims to report the case of a patient with multiple intracranial lesions, with symptoms and radiographic characteristics of meningiomas, but histopathological characteristics of RDD.

Case presentation

A 59-year-old man without known prior illnesses was referred to our institution complaining of intense morning holocranial headache without accompanying symptoms in the past 8 months. Two months after the initial symptom, he noticed diminished visual acuity in the temporal hemifields and hyposmia. Finally, 1 month before hospitalization, he presented two episodes of generalized tonic-clonic seizures with an approximate duration of 1 min.

The neurological exam demonstrated preserved cognitive functions, hyposmia, and bitemporal hemianopsia despite normal visual acuity. Fundoscopy showed edema of the papilla in the left eye and slight pallor of the papilla in the right eye. The complementary lab tests were normal, the electroencephalogram reported abnormal bifrontal activity, and the computed campimetry corroborated both temporal fields' affection. The computed tomography (CT)-scan reported three lesions: (1) midline in the floor of the anterior fossa in the crista Galli and cribriform plate (2) in the sphenoidal plane with extension to the tuberculum sellae, and (3) on the middle and lower portion of clivus. The three lesions presented the same characteristics; they were isodense with homogeneous and intense contrast enhancement. Magnetic resonance imaging (MRI) revealed isointense lesions with peritumoral edema in T1, T2, and fluid attenuation inversion recovery (FLAIR), with intense and homogeneous gadolinium-enhancement demonstrating a dural attachment (Fig. 1).

We established the diagnosis of multiple meningiomas. According to the evidence and our previous experience, we decided to resect the symptomatic lesions: olfactory groove and tuberculum sellae. We made a bicoronal incision to perform a bifrontal craniotomy and a sub-frontal approach. Debulking was possible using an ultrasonic aspirator for the first lesion, provided that it showed low vascularity. According to skull-base meningioma surgery principles, we performed anterior fossa drilling to reduce the recurrence probability. On removal of the first lesion, a wide corridor was formed through which it was possible to excise the second lesion of the tuberculum sellae. We used the ultrasonic aspirator to debulk this second lesion as it adhered to the optic chiasm. We achieved to resect both lesions through the same craniotomy completely (Fig. 2). Immediately post-operative, the patient remained without complications and was discharged 5 days after surgery.

In the histopathological analysis, a mixed inflammatory infiltrate with plasma cells, lymphocytes, and macrophages was found with H and E staining, with no evidence of meningothelial cells. Immunohistochemical profile reported positive expression of CD68 (macrophages), CD20 (B lymphocytes), CD2 (T lymphocytes), and PS100, in which lymphagocytosis was observed. IgG and IgG4 positivity were also identified. A negative expression for CD30 and CD15 (reed Stenberg cells), and Cd1A (Langerhans cells) was observed. With these findings, the diagnosis of RDD was established (Fig. 3).

In the subsequent follow-up, extension studies were carried out to identify the presence of infiltrates in other organs, which were ruled out with a thoracic and abdomen-pelvic CT. Treatment with prednisone 50 mg/day was indicated, with well adherence and tolerability by the patient, thus remaining asymptomatic and without the clivus lesion's growth at 8-month follow-up.

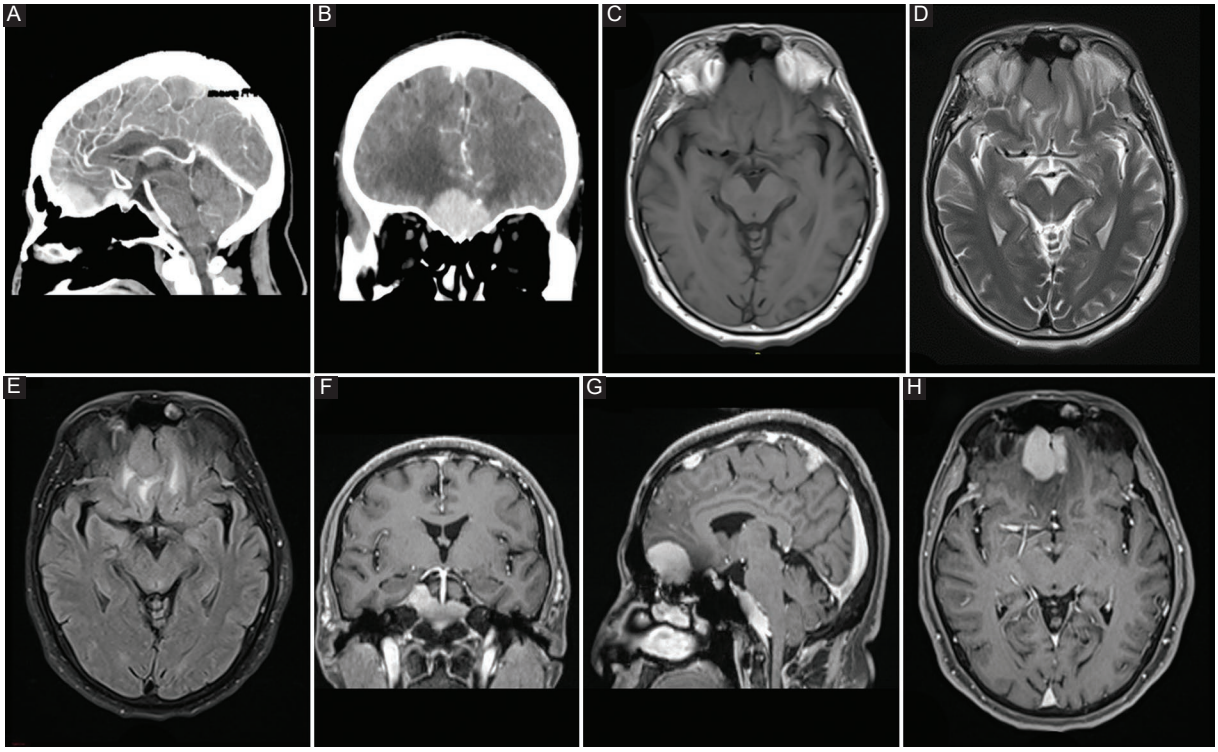

Figure 1. *Neuroimaging studies. Enhanced sagittal head computed tomography-scan with an olfactory groove, tuberculum sellae, and clival lesion in* **(A)** *sagittal and* **(B)** *coronal sections (arrows). Olfactory groove lesion was isointense on magnetic resonance imaging in the* **(C)** *T1-weighted,* **(D)** *T2-weighted, and* **(E)** *fluid attenuation inversion recovery, demonstrated peritumoral edema. Homogeneous gadolinium-enhancement is shown in the* **(F)** *coronal,* **(G)** *sagittal,* **(H)** *and axial sections (arrows). Dural attachment was visible in the three lesions.*

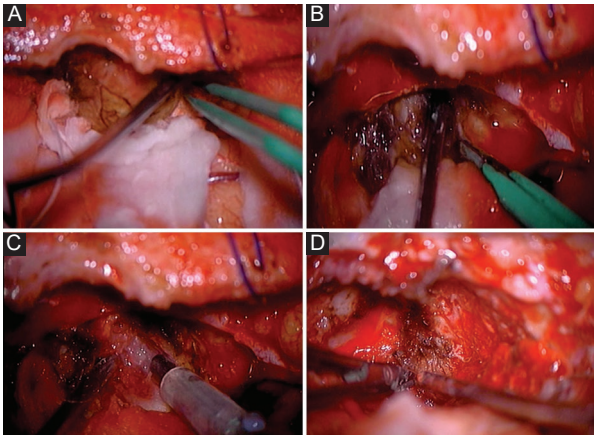

Figure 2. *Approach to the anterior fossa lesion. Perimeter dissection of the anterior cranial fossa lesion is shown* **(A-B)**. *Debulking with ultrasonic aspiration* **(C)** *and complete resection of olfactory groove* **(D)** *is demonstrated.*

Discussion

This paper presents a case of RDD, an entity described as a benign proliferative process with unknown pathophysiology[1,8]. Various theories have been proposed to explain the pathogenesis of the disease and multiple associations have been found with viral diseases such as herpes virus, Epstein-Barr virus, cytomegalovirus, and HIV[1,2]. It has also been associated with immunological disorders such as IgG4 disease, systemic lupus erythematosus, and juvenile idiopathic arthritis[7], and malignancies Hodgkin and non-Hodgkin lymphoma[7,9]. Given its multiple associations, it is currently postulated as a disease with multiple triggers[1,7,10,11]. For this reason, in the post-diagnosis approach to intracranial RDD, all these diseases should be ruled out[1].

As previously mentioned, the classic form of RDD occurs in young patients in the second or third decade of life with constitutional symptoms and bilateral cervical lymphatic infiltration[1]. However, in our case, similar to that previously described in other reports, isolated intracranial affection is usually found in patients in the fifth and sixth decades of life that manifests headache, seizures, and focal neurological deficit associated with the mass effect of the lesions without constitutional symptoms[9,12]. This clinical and radiological presentation is similar to the presentation of meningiomas, lesions that, due to their

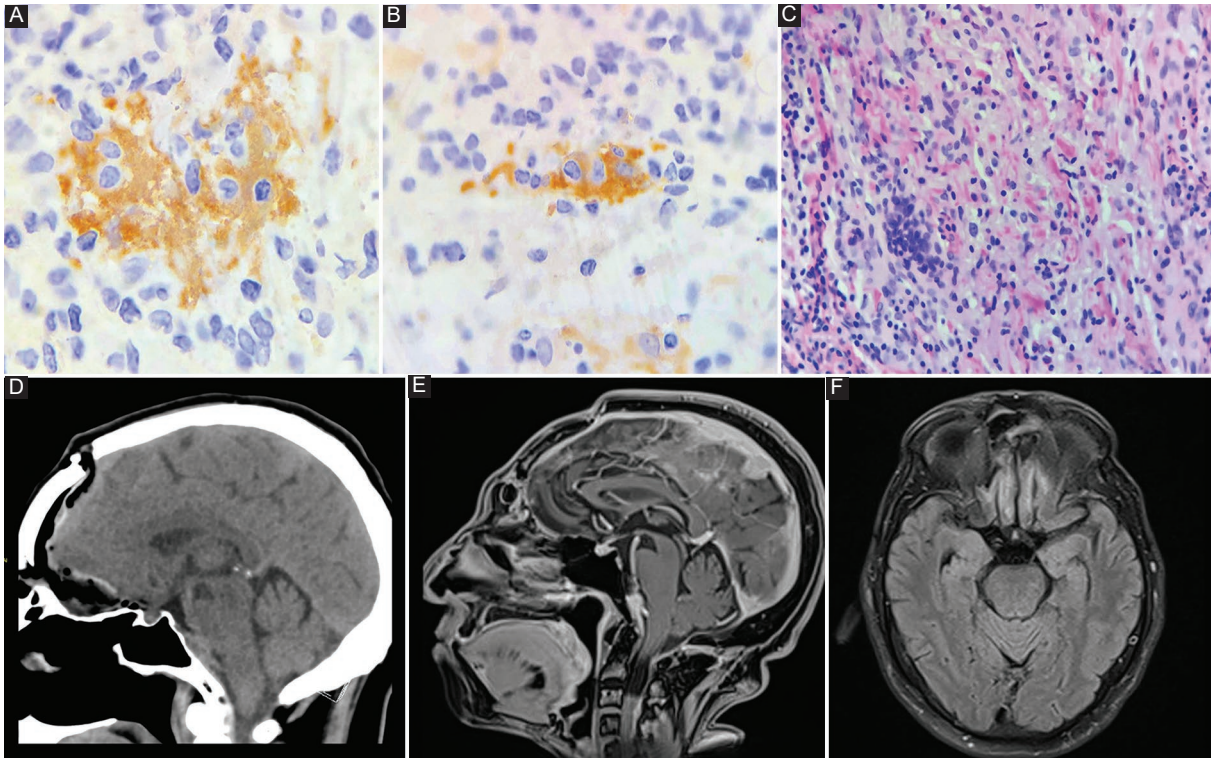

Figure 3. *Histopathological findings.* **(A-B)** *Positive immunohistochemistry to PS100 where emperipolesis is observed (arrows). H and E staining with an extended mixed inflammatory infiltrate with plasma cells, lymphocytes, and macrophages* **(C)**. *Sagittal section of post-operative computed tomography* **(D)**. *Enhanced sagittal T1* **(E)**, *and axial FLAIR* **(F)** *with complete resection of anterior and middle fossa lesions.*

extra-axial location, compress the cerebral cortex, causing headache and seizures in this age group, although, unlike RDD, they occur mainly in women[7,8].

In the review of the radiologic findings, CT shows iso or hyperdense lesions with homogeneous contrast enhancement and vasogenic edema around the tumor and may even show bone erosion[9]. MRI usually shows extra-axial, dural based, and well-circumscribed, it is usually isointense in T1, iso, or hypointense in T2 with edema surrounding the tumor and homogeneous contrast-enhancement[3,9]. In a review of 10 cases, a dural tail was found in all cases, so RDD is also a differential diagnosis of meningiomas[13]. In this review, Zhu et al. concluded that unlike meningiomas, a typical hypointensity non-related to calcification on T2-weighted or FLAIR images could suggest the RDD diagnosis[13]. Despite MRI enhancement, in angiography, they are avascular lesions[8]. In our case, the imaging findings were similar to that reported, and a dural tail was identified in the three lesions, so the preoperative diagnosis coincided with the clinic of multiple meningiomas.

Histopathological analysis classically found a polymorphic infiltrate of histiocytes, lymphocytes, and plasma cells. In the immunophenotype, histiocytes are usually of two main types: (1) large histiocytes with emperipolesis or lymphagocytosis (lymphocytes intact within phagocytic vacuoles of macrophages) and positive for S100 and CD68, which is considered characteristic of RDD and (2) histiocytes of average size in S100 negative differentiation. Routine Cd1a should be performed to rule out Langerhans histiocytes[1,7,8,14].

Regarding treatment, the literature concurs that total surgical resection is the best approach, at least for symptomatic intracranial lesions, since a low recurrence rate (14%) has been observed during follow-up. In cases where biopsy-alone was performed, no remission of symptoms despite medical treatment[1,8,9,14]. In the case of residual intracranial lesions, different treatment modalities have been tried, from radiotherapy (2000-4500 cGy), chemotherapy (MTX and 6-MP), and steroids (prednisone 40-70 mg/day)[1,9]. Although no studies compare these treatment strategies, case-series seem to favor using steroids; nevertheless, each case must be evaluated separately[1,9].

Regarding our patient's perspective, in the follow-up, he has stated that he agrees with the treatment, given that he has been able to return to his professional

activity. However, he concerns the adverse effects of steroids (especially regarding weight gain) and the evolution that the clivus lesion could eventually have. Finally, he thinks that although he has not gotten used to hyposmia, it is a lesser concern.

Conclusion

Our case is due to the diagnosis and location, one of the rarest reported to date in the literature. RDD should be considered the differential diagnosis of multiple meningiomas, with the latter is the best diagnostic and therapeutic approach to improve symptoms and obtain a diagnosis. Since the behavior of RDD is unknown, patients should have close surveillance.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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REVIEW ARTICLE

Pancreas transplantation: review

Trasplante de páncreas: revisión

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Abstract

Pancreas transplant (PTx) is the only treatment that establishes normal glucose levels for patients diagnosed with diabetes types 1 and 2. The paper aims to review and analyze graft survival, patient survival, and the impact on diabetic complications. We describe that the graft survival was 82-98% at 1 year, 90% at 5 years, and 75-54% at 10 years for simultaneous pancreas-kidney recipient; 71% pancreas after kidney (PAK), and 62% PTx alone at 1 year. Patient survival: At 1 year for recipients was 96.9% simultaneous pancreas-kidney transplantation (SPK); for PAK transplantation recipients, 96.3%; and for PTx alone recipients, 98.3%. In general, the pancreas transplantation improves and reverses diabetic complications. Finally, the pancreatic transplant is a morbid procedure and emerges as a significant alternative in diabetes management, directly competing with conventional insulin therapies. Results so far suggest that the most effective transplant model is the SPK. While more patients could benefit from this procedure, surgical complications and the need for immunosuppression pose significant challenges.

Keywords: *Pancreas transplantation. Diabetes mellitus. Pancreas donor selection. Surgical technique. Outcomes.*

Resumen

El trasplante de páncreas es el único tratamiento que estabiliza los niveles normales de glucosa en los pacientes diagnosticados con diabetes tipo 1 o tipo 2. En esta revisión se analizan la supervivencia del injerto, la supervivencia del paciente y el impacto en las complicaciones diabéticas. Se describe la supervivencia del injerto: 82-98% al año para los receptores de trasplante simultáneo de páncreas y riñón, 71% para trasplante páncreas después de riñón y 62% para trasplante de páncreas solitario al año. Supervivencia de los pacientes a 1 año: 96.9% para los receptores de trasplante simultáneo de páncreas y riñón, 96.3% para los receptores de trasplante de páncreas después de riñón y 98.3% para los receptores de páncreas solitario. En general, el trasplante de páncreas mejora y revierte las complicaciones diabéticas. Finalmente, el trasplante de páncreas, un procedimiento mórbido, surge como una alternativa significativa en el manejo de la diabetes, compitiendo directamente con las terapias convencionales de insulina. Hasta ahora, los resultados indican que el modelo de trasplante más efectivo es el simultáneo de páncreas y riñón. Aunque más pacientes podrían beneficiarse de este procedimiento, las complicaciones quirúrgicas y la necesidad de inmunosupresión plantean desafíos significativos.

Palabras clave: *Trasplante de páncreas. Diabetes mellitus. Selección de donante de páncreas. Técnica quirúrgica. Resultados.*

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Introduction

The first report of a human pancreas transplant (PTx) was a simultaneous pancreas-kidney procedure performed in 1966 by Drs Richard Lillehei and William Kelly[1]. In Mexico, the current evidence is limited to a case report of simultaneous pancreas-kidney (SPK) transplantation[2]. The evolution of pancreatic transplant was determined by the advancement of technology as to surgical technique, preservation of organs, and immunosuppression[3]. Transplantation of the pancreas is the only near-cure treatment for type 1 diabetic patients[4]. Diabetes is the leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide[5]. Successful pancreas transplantation provides durable insulin independence, preventing worsening of diabetic complications (microvascular and macrovascular systems, causing multiple complications in the cardiovascular, renal, ophthalmic, and nervous system), and improving quality of life[1,6].

Materials and methods

A bibliographic search was implemented in PubMed/Medline, Clinical Key, ScienceDirect, and Index Medicus with MESH terms, from the year 1967 to 2024. The detailed data retrieval strategies and inclusion procedure of this study are shown in figure 1.

Objectives

Transplantation of a whole pancreas is being offered for the treatment of diabetes, the goals of the pancreas transplantation program should include:

- Surgical procedure with overall low morbidity and mortality
- Progressive elimination of the insulin requirements and close blood glucose monitoring with the creation of a euglycemic state, the HbA1c levels should be comparable to those non-diabetic populations
- Eliminate the occurrence of significant hypoglycemic events
- Improved glucose control reduced the long-term complications of insulin-dependent diabetes[3,7,8].

Epidemiology

According to data from the International Diabetes Federation, there were 536.6 million people between the ages of 20 and 79 with diabetes worldwide in 2021. Mexico ranks seventh in terms of cases, with an approximate estimate of 14.1 million people with diabetes in 2021. However, Encuesta Nacional de Salud y Nutrición (Ensanut) 2021 indicates that 12.4 million people have diabetes. It has been roughly estimated that only about 1% of the reported cases of diabetes correspond to type 1 diabetes (T1D) with greater prevalence among children and young adults; the incidence overall annual increase of approximately 3%[9]. At present, 6.2 million Mexicans with diabetes are experiencing varying stages of renal insufficiency[10].

Diabetes is the second leading cause of death in Mexico, following cardiovascular diseases. According to the most recent numbers released by the Instituto Nacional de Estadísticas y Geografía, the deaths due to this disease in the previous year were 140,729 which represents 13% of the total in 2021; of those who died from Diabetes 105,395 (74.9%), or three out of every four, were not insulin-dependent, meaning they did not require insulin administration; while 3,109 (2.2%) were[11].

Pancreas transplantation for type 2 diabetes (T2D) accounts for 18.4-20.6% of all PTxs performed annually[12].

Most recipients with T2D require an SPK transplant due to the additional ESRD. Between 2016 and 2020, 19% of SPKs, 12% of pancreas after kidney (PAK), and only 2% of pancreas transplant alone (PTA) were performed in patients with T2D, the rest (77%) were due to T1D[13].

Types of transplantation[4,8,14-17]

- SPK transplant is the most common type of PTx. SPK is a well-established treatment modality for patients with severe metabolic complications and ESRD. Both organs are procured from a single deceased organ donor[14]. SPK performed before dialysis (i.e., preemptive SPK) is associated with improved results[18,19].
- PAK transplantation is offered to diabetic patients who have had a kidney transplant. PAK sequence in patients who have a viable living kidney donor identified, because the waiting time for a pancreas alone is much shorter than for a kidney-pancreas, transplantation should be performed < 1 year after kidney transplantation[18,19].
- PTA considered for recipients with eGFR > 60 mL/min/1.73 m^2 is offered to candidates with frequent, acute, and potentially life-threatening

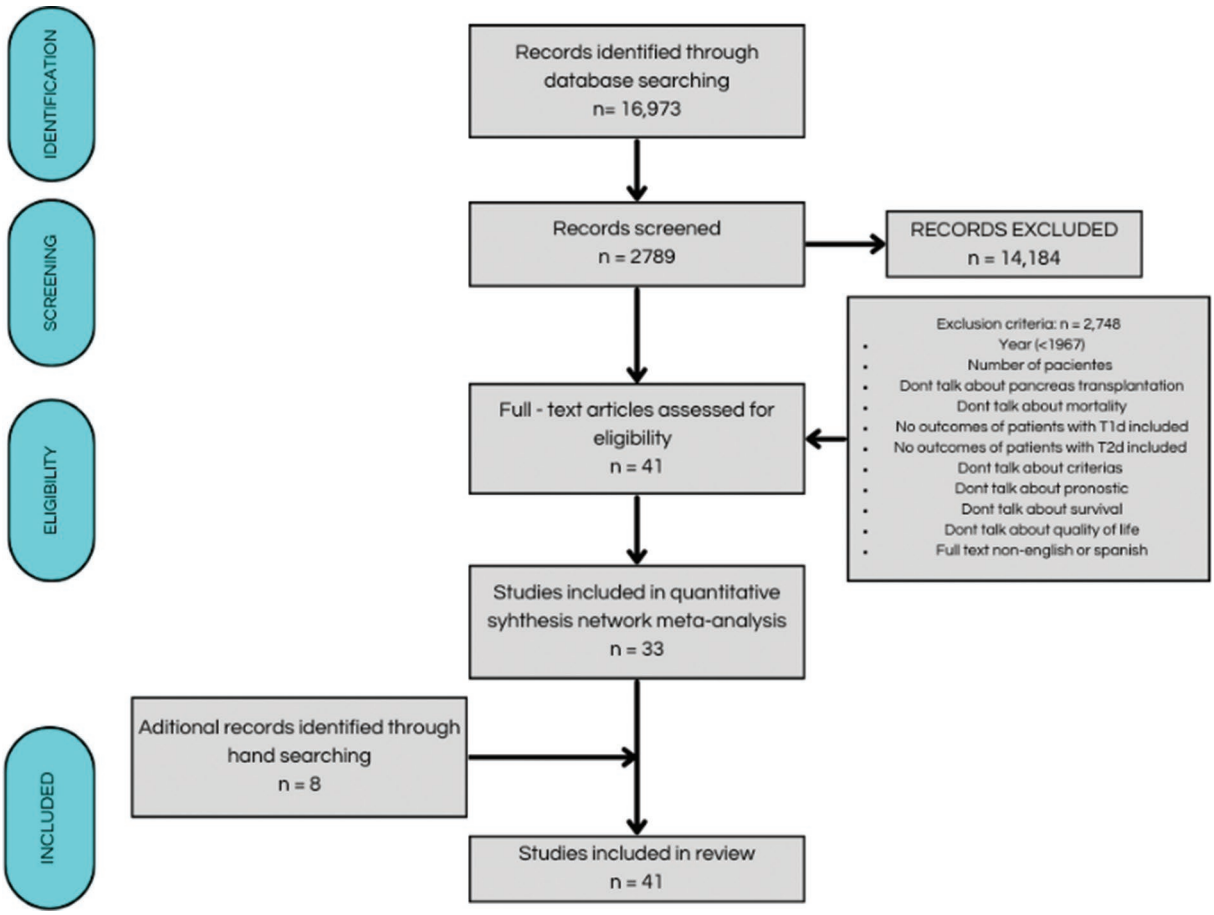

Figure 1. *Data retrieval strategies and inclusion procedure of this study.*

complications of diabetes such as ketoacidosis, hypoglycemia unawareness, and incapacitating problems with insulin therapy is suitable for this type of transplantation. For this patient group, PTx can be lifesaving but must be weighed against the risks of lifelong immunosuppression, and also have stable renal function to tolerate potential calcineurin nephrotoxicity[19,20].

- Living donor segmental pancreas grafts have been described, with or without concurrent living donor kidney transplantation, but are not common[19,20].
- Islet cell transplantation is an appealing alternative to whole pancreas transplantation and it is frequently recommended after total pancreatectomy for benign disease to avoid the insulin-dependent state of these procedure[19,20].

Criteria for waiting list

Patients are listed for PTx after meeting the following United Network for Organ Sharing (UNOS) criteria:

- Insulin therapy and absolute deficiency of endogenous insulin demonstrated by a C-peptide ≤ 2 ng/mL; or
- Insulin with a c-peptide > 2 ng/mL and have a body mass index (BMI) ≤ 28[14].

Other authors establish different criteria, which are listed in table 1.

Contraindications

Absolute contraindications (Table 2) and relative contraindications are shown in table 3.

T2D receptor

Originally considered exclusively for patients with TID, improving outcomes has resulted in an expansion of SPKT to selected patients with T2D as well.

Conceptually, the TID terminology is used to describe patients with diabetes who do not produce sufficient insulin, whereas T2D terminology is reserved

Table 1. Criteria for waiting list

Diabetic patients with imminent or established ESRD who have had or plan to have a kidney transplant[17,35].
A history of frequent, acute, and severe metabolic complications (hypoglycemia, hyperglycemia, ketoacidosis) requiring medical attention[16,36].
Incapacitating problems with exogenous insulin therapy16,36.
Consistent failure of insulin-based management to prevent acute complications[14].
High risk of secondary chronic complications of diabetes (e.g., nephropathy, retinopathy, neuropathy) is judged to be fit enough to survive the operation[7].
A small number of pancreas transplants are also performed for chronic pancreatitis and malignancy requiring pancreatectomy[14,16].

ESRD: end-stage renal disease.

Table 2. Absolute contraindications for PTx[4]

Age over 65
Noninsulin requiring diabetes with the absence of glucose hypermobility or progressive diabetic complications
Significant cardiovascular disease (with severe, non-correctable coronary artery disease, recent myocardial infarction, left ventricular ejection fraction < 50%)
Pulmonary artery systolic pressure over 50 mmHg
Presence of severe peripheral vascular (aortoiliac) disease
Incurable malignancy except localized skin cancer
Active sepsis or peptic ulcer
Inadequate psychosocial support and financial resources
Poor overall functional and performance status (severe deconditioning or malnutrition, frailty, sarcopenia, dementia, wheelchair-bound, need for chronic oxygen therapy)
A major psychiatric history which can result in non-adherence to the treatment
Inability to withstand surgery
Positive crossmatch with a specific donor

Table 3. Relative contraindications for PTx[6]

Excessive need for insulin > 1.5 U/kg/d
Cerebrovascular event with long-standing impairment
Hepatitis B or C viruses (HCV)
Human immunodeficiency viral infection
Peritoneal dialysis with multiple episodes of peritonitis; multiple previous laparotomies; previous intra-abdominal/pelvic irradiation or multiple surgical procedures
BMI > 30 kg/m
Extensive vascular, aortic, and renal artery disease
Presence of an ostomy, feeding tube, or chronic bladder drainage catheter
Limited social support (lives alone, relies, on public transportation) or financial resources
Continuous use of alcohol, smoking, and other drugs.

BMI: body mass index.

Table 4. Pancreas transplantation in patients with T2D[5,15,27,34]

Age < 60 years
BMI < 30 kg/m^2
Fasting a C-peptide level 10 mg/mL or less
Total daily insulin dose < 1.5 U/kg/day and < 100 U/day
Insulin requiring for minimum of 3-5 years
Presence of complicated diabetes including glucose hypermobility
Absence of smoking, major amputation, severe cardiac, or vascular disease
No recent history of dietary and medication non-compliance
Adequate psychosocial and financial support

BMI: body mass index.

for those that are "insulin resistant." TID continues to produce some insulin but in insufficient quantities. Alternatively, T2D stops producing insulin entirely. For this reason, defining the type of diabetes by C-peptide levels alone is inadequate (Table 4)[16].

PTx was uncommon among recipients aged over 60 years. This practice is changing and in 2016, almost one-fourth of pancreas recipients were aged > 60 years at the time of transplant; reports suggest that these older recipients had similar patient survival compared with younger recipients, although more cardiovascular events occurred in the older recipients[21].

PTx versus insulin

Insulin therapy achieves good glycemic control but does not allow the restoration of damaged β-cells or prevent vascular complications resulting in irreversible organic damage is inevitable in most patients. Sometimes, even in the case of correct administration, episodes of hyperglycemia can occur and if persistent can lead to irreversible complications systemically.

Therefore, the development of pancreas transplantation is not only a research challenge but also a necessity for the entire population[15,18].

Donor selection

The ideal pancreas donor is, as with most other solid organ transplants, a young healthy heart-beating donor aged < 60 y and with a normal BMI. Donors with a BMI (kg/m^2) of > 30 are not routinely used for whole PTx due to concern for fatty infiltration and a higher risk of graft pancreatitis. Donors > 60 years of age have a higher risk of atherosclerosis and islet depletion and are also rarely used[3,14,16].

Since 2009, the Eurotransplant Pancreas Advisory Committee designed the pre-procurement pancreas suitability score (P-PASS) and was introduced to support clinical decision-making and ultimately expand the currently insufficient pancreas donor pool which is a calculated score based on nine donor-specific clinical parameters. Including patient age, BMI, the occurrence of cardiac arrest, serum levels of sodium, amylase, lipase, vasopressor substances (adrenaline or dopamine), and the length of stay in the intensive care unit[22], however, the predictive value remains controversial.

Furthermore, the pancreas donor risk index (pDRI) is a measure of allograft quality that predicts the risk of allograft failure at 1 year. The pDRI consists of the specific donor characteristics that include gender, BMI, serum creatinine, age, race, cause of death, donor after cardiac death, and the parameter of pancreas preservation time[23]. P-PASS and pDRI are used to know whether or not an organ is acceptable for transplantation. The eurotransplant now recommends that pancreas grafts from donors with a P-PASS score of < 17 should be considered for organ transplantation because they have a 3-times higher acceptance rate as compared to grafts with a P-PASS score of ≥ 17[22].

Donor contraindications

The donor selection criteria are more strict for pancreas transplantation as compared to other organs, thus limiting potential donors. The donor organ may be rejected due to alcohol intake or a family history of diabetes, pancreatic disease, malignant tumor, prior surgery of the duodenum, pancreas, or splenectomy, positive serology for infectious diseases (human immunodeficiency viral infection, Hepatitis C viruses, Hepatitis B viruses), chronic liver disease, and BMI > 30 kg/m^2.

Macroscopic evaluation of the pancreas considers the presence of signs of acute pancreatitis, glandular edema, hematoma, fatty infiltration (associated with severe reperfusion pancreatitis), and/or hardened consistency since such factors increase the risk of post-transplant complications, and under these conditions, the grafts should be discarded[12].

Surgical technique

The PTx is preferentially done in the right iliac fossa of the recipient as the right iliac vessels are more accessible. The native pancreas and kidneys are left in place[4,6].

Ideally, preservation time should not exceed 12 h, but preservation times up to 24 h can still be accepted[19,20].

- Donor: Procurement of the pancreatic graft is generally part of the removal of multiple intra-abdominal organs[12]. The pancreatic graft is removed *en bloc*, along with the duodenum and spleen, preserving the vascular stumps of the superior mesenteric and splenic arteries, and of the portal vein[3].
- Graft: On back table surgery, the pancreatoduodenal graft is prepared basically by removing the spleen, shortening the duodenal segment, suture, and invagination of the duodenal borders, mobilization of the portal vein, and vascular Y graft reconstruction (iliac arteries from the donor with the pancreatic graft superior mesenteric artery and splenic artery)[3].
- Recipient: The blood vessels of the new pancreas are connected to the external iliac vessels. The pancreas has two arterial supplies, so a "Y" graft from the donor iliac artery sutured onto the donor superior mesenteric and splenic arteries[4,6,7], which allows both to be supplied from a single arterial anastomosis.
- Drainage: The implant of the pancreas can be done by drainage of systemic or portal venous blood. Drainage of pancreatic exocrine secretion of the graft can be enteric (side-to-side duodenojejunal anastomosis) or vesical (side-to-side duodenovesical anastomosis)[3].

With the technique used, there are advantages and disadvantages, as in any procedure. Next, we will discuss the different types of exocrine drainage.

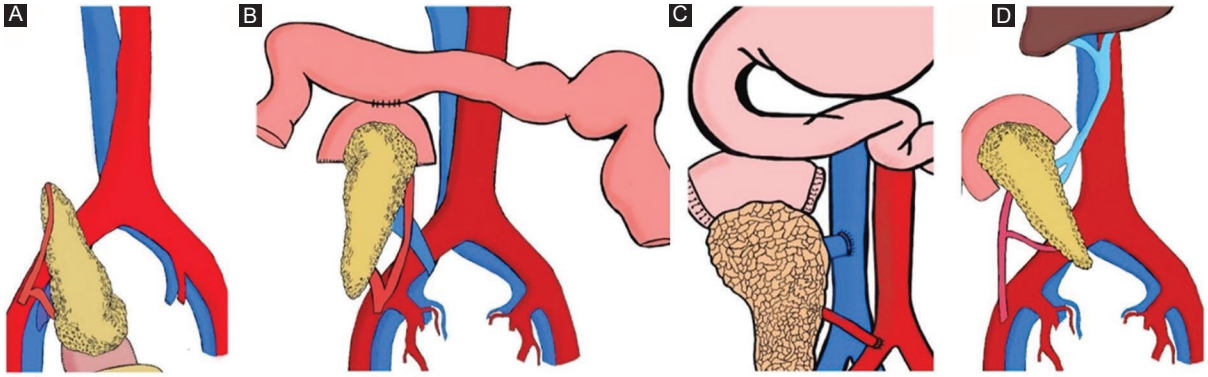

Figure 2. *Types of drainage.* **A:** *bladder exocrine drainage and systemic venous endocrine drainage.* **B:** *enteric exocrine drainage and systemic venous endocrine drainage.* **C:** *duodenal exocrine drainage and systemic venous endocrine drainage.* **D:** *enteric exocrine drainage and portal venous endocrine drainage.*

- Exocrine (enteric vs. bladder) drainage:
  - Bladder drainage (Fig. 2A). Some advantages include that pancreatic dysfunction can be detected early by changes of urinary amylase, easily accessible for biopsy, and reduced rate of infection due to the relative sterility of the lower urinary tract. It has many technical advantages: bladder vasculature promotes healing anastomosis, bladder mobilization permits tension-free anastomosis, multilayer anastomosis, and control of anastomotic leakage can be achieved by bladder catheter. Some of the disadvantages include fluid and electrolyte imbalance and metabolic acidosis. Local effects include chemical cystitis, hematuria, urethritis and urethral stricture, bladder leak, and reflux pancreatitis; lower urinary tract infection and stone formation; in male effects are epididymitis, prostatitis, and prostatic abscess[8]. Up to 25% of patients with bladder drainage will need a conversion to enteric drainage within 10 years[7].
  - Enteric drainage (Fig. 2B)[1]. Lillehei described that enteric drainage is more physiological and avoids urologic complications. Some disadvantages include a higher incidence of pancreatitis, leakage of pancreatic enzymes, and peripancreatic fluid collections, more risk of anastomotic leakage, peritonitis, intra-abdominal collection and sepsis[24], inability to measure exocrine secretions for early detection of graft dysfunction and allograft biopsy is more challenging.
  - Duodenal drainage (Fig. 2C). A modification of enteric exocrine drainage with additional benefits in the form of improved accessibility for biopsy through endoscopy, it expands the options for exocrine drainage sites, especially in cases of pancreas retransplantation. Same disadvantages mentioned above with enteric drainage except for relatively easily accessible allograft.

Experts confirmed that enteric drainage should be preferred over bladder drainage with respect to infectious, metabolic, and urinary tract complications[6,20].

- Endocrine (systemic venous vs. portal venous) drainage:
  - Systemic venous drainage (Fig. 2A). Some disadvantages include hyperinsulinemia (predisposes to accelerated atherosclerosis) and hiperlipoproteinemia[25].
  - Portal venous drainage (Fig. 2D). Some advantages include[26] avoiding the risk of postprandial hypoglycemia, better lipoprotein metabolism, and allowing physiological passage of insulin through the liver in which it undergoes 50% first-pass metabolism. Some disadvantages are mentioned above in addition to a higher risk of vascular thrombosis.

Portal venous drainage provides better results than system venous drainage[6,20].

Complications

In general, the primary complication related to pancreatic graft loss is technical failure (loss of the graft in the first 3 months of a transplant), followed by acute or chronic rejection. The risk factors for surgical complications are donor or recipient having a BMI > 30 kg/m^2 for donor or recipient age over 45 years, prolonged preservation time (> 24 h), cerebrovascular disease as a cause of donor death, retransplantation, and prior

abdominal surgery. Infectious complications are the primary causes of morbidity and mortality in pancreas transplantation[4].

Without any risk factors, the risk of technical failure is 7.3%; with one risk factor, it is 12.8%; with two, it rises to 26.7%; and with three or more, it reaches 42.9%. These factors have an impact on graft survival. With just one risk factor, graft survival is 92.5%, but with two, it decreases to 75.9% and with three factors, survival is only 57.1% at 1 year[27].

PTxs are particularly susceptible to graft rejection, with an incidence of 15-21% at 1 year and 27-30% at 5 years. The rejection rate is lower in older than in younger recipients but those > 50 years have an increased rate of post-operative complications that should be taken into account when the benefits and risks are assessed[7].

The complications of PTx can be divided into surgical (early and late), medical, and immunologic (acute and chronic).

Some examples of early surgical complications are infection (incidence 18%), anastomotic leaks (urinary: 5-18% and enteric 4-9%), venous or arterial graft thrombosis (5-15%), hemorrhage intraabdominal, gastrointestinal or bladder (10%), pancreatic-enteric fistula (4-6%), and graft acute pancreatitis (3%).

Some examples of late surgical complications are infection (38%), venous or arterial graft thrombosis (7-20%), peripancreatic collection (20%), pseudoaneurysm (8-16%), wound dehiscence (14%), pancreas retransplant (5.9%), hemorrhage intraabdominal, gastrointestinal or bladder (5%), post-transplant pancreatectomy (4.5%), bowel obstruction (3%), graft pancreatitis (2.5%), incisional hernia (2.5%), and pseudocyst pancreatic (< 1%).

Some examples of medical complications are cytomegalovirus infection (10-42%), acute tubular necrosis (5-30%), and BK virus nephropathy (2.9-7.5%).

Some examples of immunologic complications are acute rejection (15-21%) and chronic rejection (27-30%)[13,27].

Outcomes

Graft survival

Graft survival (defined as total freedom from insulin therapy, normal fasting blood glucose concentrations, and normal or only slightly elevated HbA1c) was 82-98% at 1 year, 90% at 5 years, and 75-54% at 10 years for SPK recipient[6,13,14,28]; 71% PAK, and 62% PTA at 1 year[13].

The best survival of the pancreatic and renal grafts in the first post-transplant year is 86% and 93%, respectively, in the SPK category. Graft loss due to immunological rejection in the first post-transplant year for SPK, PAK, and PTA was, respectively, 1.8%, 3.7%, and 6%[3].

Boggi et al., report 10-y outcomes following PTA in 66 patients with T1D and low BMI (< 30 kg/m^2). At 10-y follow-up, overall mortality was low (7.6%), good or excellent pancreas allograft function (death-censored) was 60% (57% insulin free), and the incidence of progression to stage 4/5 CKD was 10%[24,29].

The longest surviving graft was recorded as SPK transplant 26 years, 24 years pancreas after a kidney, and 23 years for PTx alone[4,19,20].

The most common causes of graft loss after 10 years are death of the recipient (53%) and chronic rejection (33%)[19]. PTx is associated with an all-cause mortality rate of 4% at 1 year and 9% at 5 years. The single most common cause of death is cardiovascular[14].

Patient survival

The patient survival rate after primary deceased donor PTxs at 1 year for SPK recipients was 96.9% in 2016-2020 versus initially 58.3% in 1966-1985; for PAK recipients, 96.3% versus 81.4%; and for PTA recipients, 98.3% versus 75.2%[30].

Fifteen year actuarial patient survival is 56% (pancreas graft success 36%) for SPK, 42% (18%) for PAK, and 59% (16%) for PTA[7].

With the improvement in outcome, long-term survival is dependent on the length of possible follow-up. Long-term patient survival rates have paralleled short-term outcomes: the 5-year patient survival rate has reached over 90% and the 10-year survival rate over 70% in all three recipient categories. At 20 years, after a successful SPK or PTA transplant > 30% of SPK recipients and 25% of PAK recipients were alive.

PTA does not increase the long-term risk of mortality when compared to continued insulin therapy and could be actually associated with a survival advantage, especially in patients who have impaired hypoglycemia awareness[14,19,20].

They found that mortality for PTx and PTA recipients is not higher than for patients on the waiting list and managed by insulin[31].

Therefore, pancreas transplantation is justified on the basis of the data for survival, and the most important factor for long-term survival is the preservation of the pancreas graft[17].

Effect on diabetic complications

- Nephropathy: diabetic Kidney Disease, often referred to as diabetic nephropathy, is a progressive disorder defined by reduced renal function due to hyperglycemia, often co-occurring with albuminuria. Individuals with diabetes can also present with non-specific kidney disease in which their reduced renal function is a result of risk factors independent of or indirectly related to their diabetes, such as hypertension, obesity, or dyslipidemia
- Neuropathy: diabetes is a leading cause of nerve damage, particularly for the longer peripheral nerves that innervate the lower limbs. In general, diabetic neuropathies can be divided into several subtypes, including the most common form, distal symmetric polyneuropathy (a type of peripheral neuropathy), autonomic neuropathies, atypical neuropathies and also non-diabetic neuropathies common in diabetes. On top of excess pain and decreased quality of life associated with diabetic neuropathy, individuals with diabetes have a 15–25% lifetime risk of foot ulcerations and a 15-fold increased risk of lower-extremity amputation compared with individuals without diabetes[32].
- Retinopathy: hyperglycemia can induce progressive damage to the blood vessels in the retina, which can lead to hemorrhage, retinal detachment, and blindness. Diabetic retinopathy can be classified as an early, more common non-proliferative diabetic retinopathy (PDR) form, characterized by weakened blood vessels, and as the more severe, late-stage PDR form, characterized by the growth of new fragile and leaky blood vessels throughout the retina and into the vitreous. Diabetic retinopathy is the most common diabetes complication and is the most frequent cause of new cases of blindness among adults aged 20-74 years in developed countries.
- Atherosclerotic cardiovascular disease: Defined as coronary heart disease, cerebrovascular disease, or peripheral artery disease presumed to be of atherosclerotic origin[33].

In table 5, chronic complications are listed along with the effect provided by the PTx.

Table 5. Effect on diabetic complications

Complication	Effect
Glycemic control	Lowers Hb1Ac levels; restores glucagon secretion; improves the counter regulatory responses to hypoglycemia[14,13]
Nephropathy	Improvement in glomerular, tubular basement membrane thickening; proteinuria decreased[5,6,13,14,17,19,20,29,37]
Neuropathy	Stabilization and improvement of motor and sensory nerve conduction[5,13,14,17,19,20,37,38.]
Retinopathy	Can deteriorate in 10-35% of patients with unstable eye disease immediately after PTx, however, the benefits become apparent after a few years. Cataracts may worsen due to treatment with calcineurin inhibitors and steroids[7,14].
Cardiovascular disease	Regression of coronary atherosclerosis in 40%, lower incidence of myocardial infarction, left ventricular ejection fraction was higher; control of blood pressure[5,7,13,14,17,19,39,40]
Cerebrovascular disease	Carotid intimal thickness has been seen to improve within 2-y[7,13]

Discussion

Diabetes is a healthcare and social pandemic pathology whose treatment poses several challenges to health professionals and determines a conspicuous health-care expenditure globally[9]. The number of patients with type 1 and T2D is rapidly growing worldwide. Diabetes mellitus is a health care and social pandemic that presents a multitude of a serious challenge for developed as well as for developing countries. Even with improvements in new technologies, for some patients, a successful PTx will remain the best option for an insulin-free life[13].

The complications of chronic diseases also affect health care by increasing the number of hospitalizations, the length of hospital stays, and health management costs[19].

PT recipients are older and the rate of recipients with T2Ds has significantly increased. Over the past years, indications for pancreas transplantation have changed considerably. PTx recipients are older and the rate of recipients with T2Ds has significantly increased. In countries such as China and India, where T2Ds is now endemic and rates are increasing, over 80% of PTx recipients have T2Ds and are primarily patients with ESRD who do require both kidney and pancreas grafts. This trend will continue in the rest of

the world, also in part due to the growing obesity pandemic. In addition, pancreas transplantation is increasingly offered to Black, Hispanic, and Asian recipients, who are no longer considered to be high-risk patients. Initially, pancreas transplantation was developed for young recipients with brittle diabetes and rapidly developing secondary complications[13].

Originally developed as a therapeutic modality to reestablish endogenous insulin secretion responsive to normal feedback controls, vascularized whole organ PTx has evolved into a method of complete β-cell replacement that frees the patient with diabetes from the need to monitor serum glucose concentrations with finger sticks and from dependence on exogenous insulin administration, and hypoglycemic unawareness is no longer a problem. Unfortunately, PTx entails a major surgical procedure, a limited number of donor organs, and the necessity for long-term immunosuppression, which means that despite the high likelihood of rendering patients ex-diabetic, it is considered a treatment rather than a cure. A successful PTx is currently the only definitive long-term treatment that restores normal glucose homeostasis and may prevent, stabilize, or even reverse progressive diabetic complications[16].

Outcome after PTxs significantly improved over the past 50 years in all recipient categories (transplant techniques, immunosuppression therapies, and post-transplant monitoring of graft function and rejection)[8]. As a result of this success, the number of PTxs performed worldwide continues to grow, as does the number of PTx centers around the world. Patient survival during the last decade of the 20th century improved to the point that a PTx, regardless of the recipient category, became not only a viable option but also a desirable option[13].

SPK has been shown to have beneficial outcomes compared to kidney transplant alone with regards to prolonged kidney allograft function, patient survival, quality of life, and delayed progression of diabetic complications.

Clearly, while outcomes of SPK transplantation are equivalent T1DM and T2DM recipients, the recipient profiles are not. Randomized trials will continue to be lacking, and the debate regarding BMI and C-peptide cutoffs remains. Randomized trials are needed to compare different modalities for treating T2DM CKD patients. Despite current UNOS regulations restricting patients with high C-peptide and high BMI from receiving an SPK transplant, the existing medical evidence does not support using BMI or C-peptide for determining SPK candidacy. Insulin-dependent patients with ESRD should be evaluated for pancreas transplantation (SPK or PAK) based on their predicted ability to tolerate the morbidity of the surgical procedure and immunosuppression. PTA transplantation in T2DM will remain reserved for those with severe metabolic disturbances and incapacitating clinical and emotional problems with exogenous insulin therapy, which is generally rare amongst T2DM patients. We currently believe that centers should decide on a case-to-case basis whether to accept a patient for transplantation or not. As national UNOS-mandated BMI thresholds do not exist for other organs such as kidney and liver, we believe they should not exist for pancreas transplantation[34].

Transplantation of a pancreas, unlike the liver, lung, and heart, is not a life-saving operation but it improves quality of life. The long-term advantages of this surgical procedure have to be balanced against the potential morbidity and mortality associated with it, and the side effects from the long-term immunosuppression that is needed to prevent alloimmunity and autoimmune recurrence[7].

Conclusion

The pancreatic transplant, is a morbid procedure, emerges as a significant alternative in diabetes management, directly competing with conventional insulin therapies. Although the latter have been fundamental pillars in diabetes treatment, pancreatic transplantation stands out for its ability to prevent or even reverse late complications associated with this chronic disease. Results so far suggest that the most effective transplant model is the SPK, providing a comprehensive solution to address both pancreatic dysfunction and renal complications. While more patients could benefit from this procedure, surgical complications and the need for immunosuppression pose significant challenges.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

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LETTER TO THE EDITOR

Modified Klingler technique: a universal tool for surgical training in neurosurgery residents and specialists

Técnica de Klingler modificada: una herramienta universal para el adiestramiento quirúrgico en residentes y especialistas de neurocirugía

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Dear Editor,

The neurosurgical training of residents and neurosurgery specialists in our country, and the rest of the world, is through dissection in cadavers fixed with formaldehyde, and human brains preserved with the Klingler technique, a technique that in recent years has become a fundamental tool in neurosurgical teaching. In the same way, this technique allows dissection, investigation, and exposure of white matter fibers; such as association fibers, projection fibers, and commissural fibers belonging to the corpus callosum and other commissures. The Klingler technique was created by the German neuroanatomist Joseph Klingler in 1935 as a unique method for the preservation and dissection of white matter fibers, nuclei, and brain stem[1]. This method consists of 5 stages. Obtaining human brains without alterations in the parenchyma and, with a post-mortem between 24 and 48 h; fixation with 10% formaldehyde for a minimum period of 60 days; dissection of arachnoids and vascular elements with the help of forceps and microdissection scissors; the freezing process for 10 days at a temperature between 15 and 18 degrees; and finally the thawing process for 24 h at room temperature[2,3] (Fig. 1). About 10% formaldehyde perfectly penetrates the gray matter, which when frozen forms microcrystals that separate both substances, allowing easy dissection using a wooden spatula[2-4]. On the other hand, the dissection of white matter fibers using the Klingler technique is not a new technique, its study and understanding are still extremely useful since it gives us the possibility of better understanding and manipulating the internal configuration of the brain, obtaining better neurosurgical training.

Without forgetting that to achieve optimal results, a minimum of three fundamentals are needed: (1) possess extensive knowledge of neuroanatomy, (2) possess excellent training and manual dexterity, and (3) patience and perseverance[1].

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Conflicts of interest

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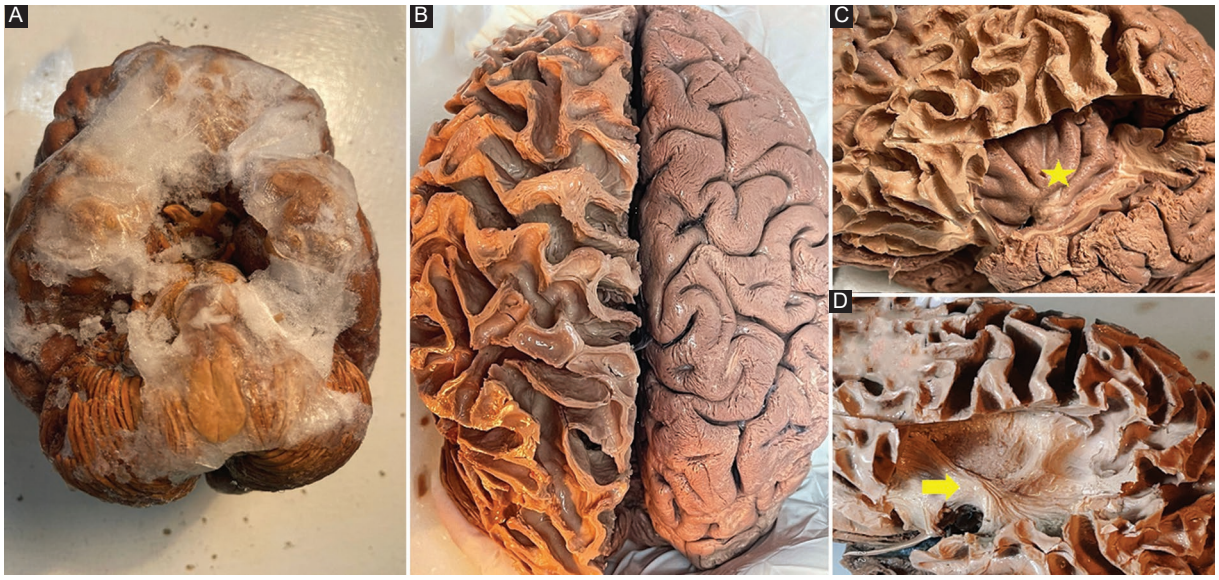

Figure 1. A: *ventral side of the brain, previously fixed with 10% formaldehyde and frozen.* **B:** *dorsal side of the brain, left hemisphere decorticated and exposing white matter fibers of short association.* **C:** *lateral view of the brain, exposing the lobe of the insula (yellow star).* **D:** *dissection of the lateral aspect of the brain, exposing the uncinate fasciculus (yellow arrow).*

Ethical responsibilities

Protection of humans and animals. The authors declare that no experiments on humans or animals have been performed for this research.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

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