

Laparoscopic retroperitoneal lymph node dissection in testicular cancer: feasibility and safety at a tertiary center

Linfadenectomía retroperitoneal laparoscópica en cáncer de testículo: factibilidad y seguridad en un centro de tercer nivel

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Abstract

Objective: To bear the evidence that laparoscopy is the possible new treatment of choice in the management of retroperitoneal disease in patients with testicular cancer. The surgical management of retroperitoneal lymph nodes is a crucial step in the multidisciplinary treatment of testicular germ cell tumors. Laparoscopic retroperitoneal approach poses technical challenges in urologic oncology. This study reports on the safety, efficacy, and short-term oncological outcomes of laparoscopic retroperitoneal lymph node dissection at a tertiary referral hospital. **Method:** Prospective, observational, descriptive study conducted from 2021 to 2023, including 83 patients who underwent laparoscopic retroperitoneal lymph node dissection. **Results:** Eleven cases of primary laparoscopic retroperitoneal lymph node dissection (13.3%), 36 standard (43.3%), 22 salvage (26.5%), 11 desperation (13.3%), and 3 redo cases (3.6%) were performed. In primary cases, 81.9% of patients had positive nodes (pN1-3). The conversion rate to open surgery was 6%. Bleeding, lymph node volume, pre-lymphadenectomy markers, chemotherapy, initial histology, and lymph node histology were not risk factors for conversion = Mean surgical time was 250 minutes. There were no major complications (organ injury, vascular injury) or need for blood transfusion = Mean blood loss was 60 mL. Recurrence rate was 9.6%, with recurrence-free survival of 36.7 months. **Conclusions:** The reported experience demonstrated the safety and efficacy of primary laparoscopic retroperitoneal lymph node dissection, as well as post-chemotherapy cases. Laparoscopic approach allows for early patient recovery without compromising oncological outcomes. It is advisable to perform this surgery in high-volume centers with experienced surgeons in retroperitoneal surgery.

Keywords: Testicular cancer. Retroperitoneal lymphadenectomy. Minimally invasive surgery.

Resumen

Objetivo: Apoyar la evidencia de que la laparoscopia es el posible nuevo tratamiento de elección en el control de la enfermedad retroperitoneal en pacientes con cáncer de testículo. El manejo quirúrgico de los ganglios retroperitoneales es un paso fundamental en el tratamiento multidisciplinario de los tumores testiculares de células germinales. El abordaje laparoscópico del retroperitoneo es un desafío técnico en la urología oncológica. En el siguiente trabajo reportamos la seguridad, la eficacia y los resultados oncológicos a corto plazo de la linfadenectomía retroperitoneal laparoscópica en un instituto de referencia de tercer nivel. **Método:** Estudio prospectivo, observacional, descriptivo, de enero de 2021 a septiembre de 2023, que incluyó 83 pacientes sometidos a linfadenectomía retroperitoneal laparoscópica. **Resultados:** Se realizaron 11 procedimientos de linfadenectomía retroperitoneal laparoscópica primaria (13.3%), 36 (43.3%) estándar, 22 (26.5%) de salvamento, 11 (13.3%) de desesperación y 3 (3.6%) redo. En los casos de linfadenectomía primaria, el 81.9% de los pacientes tuvieron ganglios positivos

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Date of reception: 29-06-2024

Date of acceptance: 16-05-2025

DOI: 10.24875/CIRUE.M25000928

Cir Cir (Eng). 2026;94(2):146-152

Contents available at PubMed

www.cirugiaycirujanos.com

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(pN1-3). La tasa de conversión a cirugía abierta fue del 6%. El sangrado, el volumen ganglionar, los marcadores prelinfadenectomía, la quimioterapia, la histología inicial y la histología de los ganglios no fueron factores de riesgo para conversión = El tiempo quirúrgico medio fue de 250 minutos. No hubo complicaciones mayores (lesiones a órganos o lesiones vasculares) ni necesidad de transfusión hemática. El sangrado medio fue de 60 ml. El 9.6% de los pacientes tuvieron recurrencia; la sobrevida libre de recurrencia fue de 36.7 meses. **Conclusiones:** La experiencia reportada demuestra la seguridad y la eficacia de la linfadenectomía retroperitoneal laparoscópica primaria, así como en tumores residuales tras quimioterapia. El abordaje laparoscópico permite una pronta recuperación de los pacientes sin afectar los resultados oncológicos. Es recomendable realizar este tipo de cirugía en centros de alto volumen y en manos de cirujanos experimentados en cirugía retroperitoneal.

Palabras clave: Cáncer de testículo. Linfadenectomía retroperitoneal. Cirugía mínimamente invasiva.

Introduction

The multidisciplinary approach to testicular cancer is essential to achieve a survival rate > 90%. Retroperitoneal surgery is a fundamental step in these patients and may be primary or performed after chemotherapy. Primary retroperitoneal lymph node dissection has several objectives:

- To correctly stage patients; 20-30% of tumors classified as clinical stage I by imaging methods are restaged after surgery as clinical stage II with positive lymph nodes.¹
- To avoid the 70% probability of retroperitoneal recurrence in clinical stage I nonseminomatous germ cell tumors with lymphovascular invasion or the presence of embryonal carcinoma in the testis.²
- After chemotherapy, in nonseminomatous germ cell tumors, it is performed in residual masses > 1 cm in order to treat the 30% of residual masses that may contain viable tumor or teratoma.³ In clinical stage II-III seminomas, it may be considered in residual masses > 3 cm that show uptake on positron emission tomography; in these cases, resections are usually more complex, and it is recommended that they be performed at an experienced, high-volume center.³

Minimally invasive surgery, laparoscopic or robot-assisted, in the management of the retroperitoneum in patients with testicular cancer has gained popularity in recent decades. Initially, the first successful cases of laparoscopic treatment were described in patients with clinical stage I disease.^{4,5} In the postchemotherapy setting, minimally invasive surgery may produce outcomes comparable to open procedures in selected cases, with low-volume residual disease and when performed by highly experienced surgeons.³ In cases in which bilateral templates must be performed, laparoscopic retroperitoneal surgery has been shown to

be inferior to open surgery in terms of operative time, bleeding, and conversion rate.⁶ The efficacy, feasibility, and ideal approach for postchemotherapy retroperitoneal dissection remain controversial.

In the present study, we examined our perioperative and oncological outcomes after primary and postchemotherapy laparoscopic retroperitoneal lymph node dissection (L-RPLND), to support the evidence that laparoscopy may be the new treatment of choice in the management of retroperitoneal disease in patients with testicular cancer.

Method

After approval by the Research and Ethics Committee of *Instituto Nacional de Cancerología* (number 023/006/URI), data were prospectively and consecutively collected from patients who underwent L-RPLND for testicular cancer at *Instituto Nacional de Cancerología* from January 2021 through September 2023.

The following data were considered: primary tumor histology, clinical stage according to the Union for International Cancer Control classification (UICC 2016, 8th ed.), and tumor marker levels, including alpha-fetoprotein, beta-human chorionic gonadotropin, and lactate dehydrogenase, before and after orchiectomy and after chemotherapy. Patients received bleomycin, etoposide, and platinum (BEP) or etoposide and platinum (EP), and, as second-line treatment, paclitaxel, ifosfamide, and platinum (TIP).

L-RPLND is categorized as primary, when performed in patients who do not receive chemotherapy, for pathological stratification or as primary treatment, or postchemotherapy. The latter is subclassified into 4 types: standard, performed for residual tumors after one line of chemotherapy in the presence of negative tumor markers; salvage, after 2 lines of chemotherapy or after primary lymph node dissection or incomplete tumor resection, with negative tumor markers; desperation, performed after 2 lines of chemotherapy and

in the presence of positive tumor markers; and “redo,” in cases of recurrence within the primary dissection field. The indication for postchemotherapy retroperitoneal lymph node dissection depends mainly on the histology of the primary tumor and on the presence and size of residual masses, according to international clinical practice guidelines.^{3,7}

The inclusion criteria for the study were as follows: patients who were eligible for primary lymph node dissection; nonseminomatous germ cell tumors with residual mass > 1 cm after chemotherapy and < 8 cm; and patients with retroperitoneal seminoma between 3 cm and 8 cm. Patients with bulky postchemotherapy masses, large tumors with compression of the vena cava or aorta, were not considered candidates for laparoscopy.

Intraoperative outcomes, including bleeding, operative time, conversion rate, length of stay (in days), and complications according to the Clavien-Dindo classification, and postoperative oncological outcomes, including tumor histology, need for salvage chemotherapy, cases of recurrence, defined as radiological evidence of new lesions in the lung, abdomen, or pelvis, or increased tumor markers, and recurrence-free survival calculated from the date of lymph node dissection to the date of recurrence, were reported. Follow-up was calculated from the date of initial diagnosis to the last consultation.

Statistical analysis was performed using SPSS, version 25. The mean and SD, median and IQR, and frequency of the sample characteristics were reported according to the type of variable. Comparison between the conversion and nonconversion groups was performed using Pearson's chi-square test or Fisher's exact test for qualitative variables; the Mann-Whitney U test or Mann/Wilcoxon test was used to compare variables in 2 independent samples, and the Kruskal-Wallis test was applied for three independent samples. Recurrence-free survival was estimated using the Kaplan-Meier method. Comparison of this time according to selected variables was performed using the log-rank test. In all cases, a value of $p < 0.05$ was considered statistically significant.

Surgical techniques

In cases in which a bilateral template was performed, patients were placed in the supine position, and in those with a modified unilateral template, they were placed in the lateral decubitus position. Access was obtained using the Hasson technique. Five

trocars were used for bilateral templates, three 12-mm and two 5-mm trocars, and four trocars were used for unilateral templates. The optical trocar was placed in the periumbilical area, and the remaining trocars were placed along the vertical flank lines or in the iliac fossae. For the right side, a 5-mm trocar was placed in the epigastrium to retract the liver from the renal hilum. The approach of choice was transperitoneal; an extraperitoneal approach was not performed in any case. The templates were modified bilateral or unilateral templates. The right-sided template has the renal vessels as its superior limits, inferiorly the right ureter at the level of its crossing with the iliac vessels, and medially the inferior mesenteric artery; the lymph nodes included are the paracaval, laterocaval, retrocaval, interaortocaval, and right gonadal nodes. For the left-sided template, the dissection limits are the mirror image of the contralateral side, and the para-aortic, preaortic, interaortocaval, retroaortic, left iliac, and left gonadal lymph nodes are removed. As suggested by the Indiana school, in the modified templates, dissection of contralateral tissue below the inferior mesenteric artery was omitted, thereby avoiding the lumbosacral sympathetic nerves, postsympathetic efferent nerves, and hypogastric sympathetic plexus. Furthermore, suprahilal dissection was omitted, since the relapse rate in pathological stage II is equivalent when the suprahilal areas are included.⁸ Polymer clips were used to close all lymphatic channels, taking care to avoid transecting the lymph nodes.

Results

A total of 83 cases of L-RPLND performed during the study period were analyzed. The median age was 27.60 years (IQR, 8). Blood transfusion was not necessary in any case. The clinical and pathological characteristics of the cohort at the time of prelymphadenectomy diagnosis are summarized in table 1. Orchiectomy was performed in a delayed manner in four cases (4.8%) because of disease extension into the spermatic cord or because of the patients' critical condition; in these cases of postchemotherapy orchiectomy, there was no evidence of viable tumor in the testis, only fibrosis. In the laparoscopic retroperitoneal resection of the delayed-orchiectomy cases, residual teratoma was reported in only 1 case; in the others, fibrosis was reported. In 3 of the 4 patients (3.6%) who underwent delayed orchiectomy, the laparoscopic retroperitoneal approach was performed simultaneously.

There were 2 cases of L-RPLND in primary extragonadal germ cell tumors. In cases of postpubertal teratoma at the initial diagnosis ($n = 5$), primary lymphadenectomy was performed in two cases and postchemotherapy lymphadenectomy in three.

Eleven cases (13.3%) of primary L-RPLND were performed: 36 (43.3%) standard, 22 (26.5%) salvage, 11 (13.3%) desperation, and 3 (3.6%) redo. In the primary lymphadenectomy cases, 81.9% ($n = 9$) of the patients had positive lymph nodes (pN1-3), with the presence of viable tumor and teratoma. There was a statistically significant difference ($p = 0.05$, Pearson's chi-square test) between clinical staging (cN) and pathological staging (pN). Intra- and postoperative outcomes are summarized in tables 2 and 3. Lymph node resection was achieved in 89.2% ($n = 74$) of cases; incomplete resection ($n = 9$) was due to the presence of postchemotherapy desmoplastic tissue reaction.

The conversion rate to open surgery was 6% ($n = 5$). There was no difference in bleeding, lymph node volume, prelymphadenectomy markers, prelymphadenectomy chemotherapy, initial histology, type of lymphadenectomy, primary or postchemotherapy, templates, or lymph node histology between patients with and without conversion to open surgery (Table 4). No risk factors for conversion to open surgery were identified; however, there was a higher risk of conversion in the presence of fibrosis (RR, 1.282; 95% CI, 0.429-3.833) compared with the presence of viable tumor/teratoma (RR, 0.812; 95% CI, 0.383-1.721).

Blood transfusion was not necessary in any patient. There were no cases of vascular injury. The only intraoperative complication was a ureteral injury in a patient with a JJ ureteral stent, which was repaired with 3-0 Monocryl suture. Two patients had lymphoceles at the 3-month follow-up; one of them, with a 5 cm × 5 cm lymphocele, required computed tomography-guided radiological puncture, with evacuation of 80 mL of citrine fluid. Four cases (5%) of anejaculation were reported.

There was no difference in surgical time across the various types of lymphadenectomy ($p = 0.719$) or across surgical templates ($p = 0.463$; Kruskal-Wallis test). Recurrence occurred in 8.4% ($n = 7$) of patients; of these, 2 had undergone primary lymphadenectomy and 5 postchemotherapy lymphadenectomy, and all except one had viable tumor or teratoma on retroperitoneal histology. Of the cases that presented

Table 1. Clinical characteristics of the patients ($n = 83$) before lymphadenectomy

Variables	n (%)
Orchiectomy	
Left	39 (47)
Right	42 (50.6)
Extragenadal	2 (2.4)
Pathology at diagnosis	
Seminoma	6 (7.2)
Mixed nonseminomatous germ cell tumor	58 (69.9)
Postpubertal teratoma	5 (6)
Embryonal carcinoma	6 (7.2)
Yolk sac tumor	1 (1.2)
Fibrosis	4 (4.8)
Extragenadal	2 (2.4)
Unknown	1 (1.2)
Preorchiectomy tumor markers	
Negative	2 (2.4)
Positive	59 (71.1)
Unknown value	20 (24.1)
Postorchiectomy tumor markers	
Negative	23 (27.7)
Positive	58 (69.9)
Unknown value	2 (2.4)
Prognostic group (IGCCC)	
Good	40 (48.2)
Intermediate	22 (26.5)
Poor	21 (25.3)
Clinical stage	
IS	3 (3.6)
IA	5 (6)
IB	3 (3.6)
IIA	11 (13.3)
IIB	10 (12)
IIC	7 (8.4)
IIIA	10 (12)
IIIB	11 (13.3)
IIIC	19 (22.9)
Unknown	4 (4.8)
Chemotherapy	
No	11 (13.3)
1BEP	1 (1.2)
2BEP	1 (1.2)
3-4 BEP	28 (33.7)
2 EP	1 (1.2)
4 EP	24 (28.9)
TIP	17 (20.5)
Preliminary lymphadenectomy tumor markers	
Negative	72 (86.7)
Positive	11 (13.3)
Preliminary lymphadenectomy cN	
cN0	10 (12)
cN1	16 (19.3)
cN2	24 (28.9)
cN3	30 (36.1)
cNx	3 (3.6)

BEP: bleomycin, etoposide, and platinum; EP: etoposide and platinum; IGCCC: International Germ Cell Cancer Collaborative Group classification; TIP: paclitaxel, ifosfamide, and platinum.

Table 2. Intraoperative and postlymphadenectomy findings

Variables	Median (IQR), range, IQR, frequency
Residual tumor diameter by imaging study, largest diameter, mm	62.0 (16-175; 44)
Residual tumor size, pathology, mm	58.4 (7.0-150; 30)
Surgical template	
Right	34 (41%)
Left	45 (54.2%)
Bilateral	4 (4.8%)
Operative time, median, min	250 (60-495; 130)
Bleeding, median, mL	60 (10-600; 120)
Days of hospitalization	1.35 (1-4; 1)

IQR: interquartile range.

Table 3. Pathology results

Variables	n (%)
Lymphadenectomy histology	
Viable tumor	11 (13.3)
Teratoma	30 (36.1)
Fibrosis	36 (43.4)
Hyperplasia	6 (7.2)
Number of lymph nodes	3.4 (range: 1-24; 3)
Number of positive lymph nodes	41 (49.4)
Adjuvant chemotherapy in pN+, salvage	
No	32 (46.4)
Yes	5 (35.7)

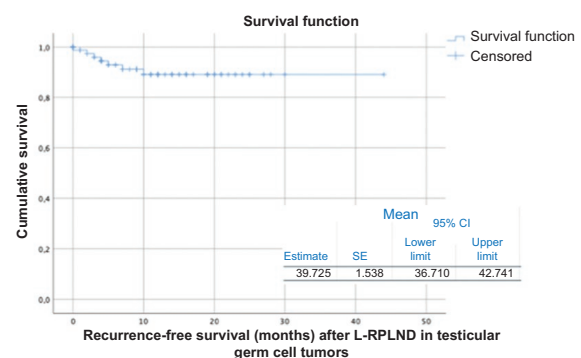
recurrence, 3 underwent a new laparoscopic resection (redo), and 2 cases of viable tumor received a second line of chemotherapy.

Recurrence-free survival was 39.7 months (IQR, 12) (Fig. 1). The recurrence sites were the retroperitoneum, subdiaphragmatic area, and inguinal canal. Two recurrence cases showed somatic transformation to neurogenic carcinoma and rhabdomyosarcoma in the testis. A difference in progression-free survival was observed between viable tumor/teratoma and fibrosis (log-rank: 0.04) (Fig. 2). Disease persistence was observed in 21 patients (25.3%) at extraretroperitoneal sites. A total of 13.3% (n = 11) progressed to the lung, liver, and retroperitoneum; the cases that progressed had undergone standard lymphadenectomy (n = 4), salvage lymphadenectomy (n = 4), or desperation lymphadenectomy (n = 3). The mean follow-up time was 40 months. After a median follow-up of 12 months (IQR, 12), three patients died from the disease.

Table 4. Risk factors for conversion to open surgery

Variables	p*
Bleeding	0.289
Lymph node volume, mm	0.385
Preliminary lymphadenectomy markers	0.298
Preliminary lymphadenectomy chemotherapy	0.354
Histology at diagnosis	0.484
pN histology	0.627
Operative time	0.875
Type of lymphadenectomy, primary or postchemotherapy	0.609
Template, unilateral or bilateral	0.241

*Mann-Whitney test.

**Figure 1.** Recurrence-free survival after L-RPLND in patients with testicular germ cell tumors.

Discussion

The series reported is the largest from a tertiary referral center in Mexico for multidisciplinary treatment of germ cell tumors of testicular cancer.

Most reported cases of L-RPLND were performed after chemotherapy. Postchemotherapy L-RPLND is challenging compared with primary L-RPLND because of the presence of desmoplastic reactions and scar tissue caused by chemotherapy agents. In our series, from a high-volume center in the management of conventional retroperitoneal surgery, we observed that the presence of fibrosis in the residual tumor could be a reason for conversion to open surgery. However, minimally invasive surgery itself may facilitate dissection of residual masses because of optical tissue magnification and better visualization of the vascular supply; carbon dioxide itself may help with resectability of planes that are strongly adherent because of the

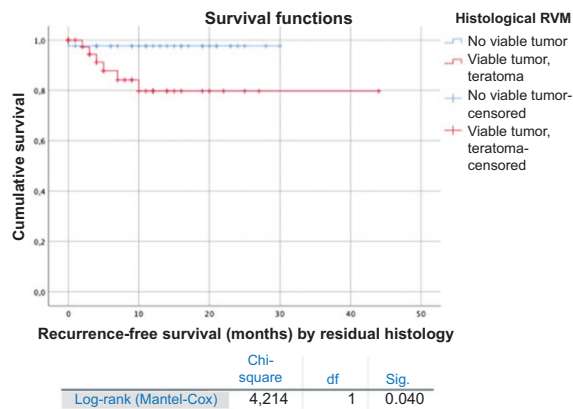


Figure 2. Recurrence-free survival by residual histology.

tissue reaction caused by chemotherapy. We were unable to identify factors that could predict conversion to open surgery, despite the fact that most were complex cases performed after chemotherapy.

Despite the indisputable advantages of minimally invasive surgery over retroperitoneal surgery, such as lower blood loss, shorter lengths of stay, and reduced postoperative complications and recurrence rate, conventional open surgery remains the reference standard for residual or recurrent retroperitoneal masses after chemotherapy.³ Fortunately, several studies have shown that laparoscopic techniques appear to offset the shortcomings of open surgery. The laparoscopic approach to the retroperitoneum reduces postoperative complications and the recurrence rate,⁹⁻¹¹ and is superior to open surgery in terms of fewer complications, fewer days of hospital stay, and lower blood loss.¹⁰

Our study supports an acceptable morbidity profile and suggests the short-term oncological efficacy of L-RPLND in a high-volume national referral center. The cases of early recurrence that we observed were due to the fact that, from the outset, the patients presented with poor- or intermediate-risk disease, and therefore retroperitoneal surgery was part of multimodal treatment.

Our perioperative outcomes were similar to those of the open series reported in the literature. We had a longer surgical time when performing a bilateral template, in agreement with other series.⁹⁻¹¹ The mean surgical time is consistent with that of open series, robotic: 235 minutes; open: 188-270 minutes; however, L-RPLND was associated with lower blood loss, 60 mL vs 184-450 mL, and shorter hospitalization, 1 day vs 4-6 days.¹²⁻¹⁸ In a series of 151 patients undergoing retroperitoneal lymph node dissection for metastatic

nonseminomatous germ cell tumors, the presence of fibrotic tissue and larger tumor volume were shown to be risk factors for longer surgical time and conversion to open surgery.¹⁹ Our conversion rate to open surgery was lower than that reported in another series.¹⁹

Preliminary results of minimally invasive primary retroperitoneal lymph node dissection in clinical stage II seminoma indicate that it is effective and low risk; therefore, the option of choosing surgery instead of chemotherapy or radiotherapy could reduce the long-term toxicity of the latter two options.¹⁶⁻¹⁸ In our series, we only performed primary lymphadenectomy in nonseminomatous germ cell tumors.

In our own experience, the recurrence rate and recurrence-free survival are comparable to those reported in other series. To achieve recurrence-free survival, complete lymph node resection is essential.²⁰ There is evidence that recurrence rates with conventional open surgery and minimally invasive surgery are comparable.^{10,21,22}

Minimally invasive surgery has gained considerable popularity in recent decades because of its potential benefits. Laparoscopic surgery is a more economical alternative to robotic surgery in patients with testicular cancer. Given the young age of most patients with testicular cancer, quality of life and morbidity must be preserved in the surgical approach to the retroperitoneum; these objectives are fully achieved with minimally invasive surgery compared with open surgery. Patients may achieve an easier recovery and return to their daily life or continue chemotherapy treatments more quickly when they undergo laparoscopic surgery.

Some important considerations should be made. First, L-RPLND is as effective as open surgery for clearing the retroperitoneum. Second, postchemotherapy L-RPLND maintains the expected benefits in terms of tolerability, as was already known in the case of primary lymphadenectomy.²³ Intraoperative complications are minimal, lower than in open surgery, with shorter hospitalization and fewer complications, very few grade > 2 vs its open counterpart.^{9,22,24,25}

Our study is not without limitations. The mean follow-up duration is 12 months, which prevents us from offering long-term outcomes. Nevertheless, it should be taken into consideration that most relapses of testicular tumors usually occur within the first 2 years after surgery. We did not perform a formal comparison between open surgery and L-RPLND, but the oncological outcomes provided appear valid even without a direct comparative analysis, which may lead to few biases derived from surgeon choice.

Conclusions

L-RPLND is a safe and effective option. Currently, our series is the largest reported in Mexico and supports the evidence that the laparoscopic technique could be considered the standard for management of the retroperitoneum in patients with testicular germ cell cancer. It should be noted that retroperitoneal surgery remains a meticulous procedure regardless of the approach and should be reserved for high-volume centers with surgeons experienced in the management of the retroperitoneum and specifically in testicular cancer.

Funding

The authors declare that they received no funding for this study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data. Because of the nature of the study, individual informed consent was not necessary. The relevant ethical recommendations were followed.

Declaration on the use of artificial intelligence. The authors declare that no type of generative artificial intelligence was used for the writing or creation of content in this manuscript.

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