

Pentafecta evaluation in robot-assisted radical prostatectomy by risk group

Evaluación de pentafecta en prostatectomía radical asistida por robot por grupo de riesgo

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Abstract

Objetivo: Radical prostatectomy is a therapeutic option in organ-confined prostate cancer. As the development of robotic systems progresses, the approach with this technology has begun to impact the functional and oncological outcomes of urological patients. The objective is to report the rate of pentafecta in patients undergoing robot-assisted radical prostatectomy (RARP) stratified by risk groups. **Method:** Retrospective, observational, descriptive study from 2013 to 2020 that included 112 patients undergoing RARP. **Results:** A rate of pentafecta at 12 months of follow-up of 35.7% (n = 40) was obtained. In the subanalysis by risk groups, at 1-year follow-up, was obtained an index of 43% (n = 26), 26% (n = 9) and 22% (n = 4) in low-, intermediate-, and high-risk patients, respectively. **Conclusions:** Prostatectomy showed functional and oncological results similar to those reported in the literature with robotic approach, regardless of the risk group for prostate cancer.

Keywords: Prostate cancer. Robotic surgery. Urology.

Resumen

Objetivo: La prostatectomía radical es la alternativa terapéutica de elección en el cáncer de próstata confinado al órgano. Conforme avanza el desarrollo de los sistemas robóticos, el abordaje con esta tecnología ha comenzado a impactar en los desenlaces funcionales y oncológicos de los pacientes urológicos. El objetivo es reportar el índice de pentafecta en pacientes sometidos a prostatectomía radical asistida por robot (PRRA) estratificados por grupos de riesgo. **Método:** Estudio retrospectivo, observacional, descriptivo, de 2013 a 2020, que incluyó 112 pacientes sometidos a PRAR. **Resultados:** Se obtuvo un índice de pentafecta a 12 meses de seguimiento del 35.7% (n = 40). En el subanálisis por grupos de riesgo, al año de seguimiento, se obtuvieron unos índices del 43% (n = 26), el 26% (n = 9) y el 22% (n = 4) en los pacientes de bajo, intermedio y alto riesgo, respectivamente. **Conclusiones:** La prostatectomía demostró resultados funcionales y oncológicos similares a lo reportado en la literatura con abordaje robótico independientemente del grupo de riesgo del cáncer de próstata.

Palabras clave: Cáncer de Próstata. Cirugía robótica. Urología.

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Introduction

Prostate cancer is the second most common oncological disease among men older than 50 years and the sixth leading cause of mortality in this population group, becoming a serious problem of public health worldwide^{1,2}.

The clinical spectrum of the disease is diverse. In its initial stages, when the disease is confined to the prostate gland, there are multiple treatment modalities, with radical prostatectomy (surgical removal) offering the best rates of cancer-specific survival and disease-free survival³⁻⁵.

Radical prostatectomy as a therapeutic option for managing prostate cancer can be performed using open, laparoscopic, or robot-assisted approaches, being oncological outcomes very similar. However, there are significant differences in terms of functional outcomes and perioperative complications that favor robot-assisted surgery, making it a safer, more effective alternative with better satisfaction rates reflected in the patients' quality of life^{6,7}.

The introduction of robotic systems in the field of urology has allowed for the optimization of the management of patients with prostate cancer, thanks not only to the optical system that provides 3D vision and the ergonomics it provides to the surgeon but also to the freedom of movement that the identification and preservation of anatomical structures provides allowing nerve preservation and helping us preserve erectile function and urinary continence without sacrificing oncological control⁸.

The beginning of the 21st century started a technological revolution in our discipline, and robotic systems have continued to advance since their inception. However, their safety and efficacy profile still needs to be evaluated, which is why various groups have investigated parameters to achieve this.

Regarding prostate cancer and robot-assisted surgery, in 2003, Salomon et al.⁹ developed the first concept they called "trifecta," to evaluate the efficacy profile of robot-assisted radical prostatectomy (RARP), which included: 1) postoperative biochemical control, 2) urinary continence, and 3) preserved erectile function.

The trifecta concept has some limitations that do not allow for adequate evaluation of the overall results of RARP. For example, it does not consider perioperative complications, meaning that a patient could require a transfusion during RARP and still meet the operational definition.

Therefore, in 2011, Patel et al.¹⁰ redefined the objectives of RARP in prostate cancer and added the absence of perioperative complications and negative surgical margins to revolutionize the concepts of safety, efficacy, and oncological control. Since then, oncological, and functional outcomes of patients diagnosed with prostate cancer undergoing radical prostatectomy, regardless of the approach, are reported using the "pentafecta" concept, which includes the following:

- Perioperative complications: reported according to the standardized Clavien-Dindo classification system¹¹ as minor (grades I and II), or major (grades III, IV, and V) complications.
- Negative surgical margins: absence of neoplastic cells in the surgical bed. It is the most important independent predictor of biochemical and local recurrence, and metastasis. According to the scientific medical literature currently available, it is inversely proportional to the learning curve and the number of cases performed each year per hospital center.
- Urinary continence: defined as the ability to avoid involuntary urinary leaks after removal of the transurethral catheter. Evaluation can be subjective, based on the need to use protectors to remain dry, or with validated tools such as the International Consultation Questionnaire Urinary Incontinence Short Form (ICIQ-UISF).
- Erectile function: the ability to achieve and maintain an erection with erotic stimulation that allows for satisfactory sexual intercourse for the patient and his partner. It is evaluated using standardized questionnaires, such as the International Index of Erectile Function (IIEF-5), or the Sexual Health Inventory for Men (SHIM).
- Biochemical control: defined as an increased prostate-specific antigen (PSA) > 0.2 ng/mL in 2 consecutive measurements after RARP.

In the last decade, various groups have tried to demonstrate the safety and efficacy profile of RARP with various associated technique variants (anterior, posterior, lateral, nerve-sparing, etc.) based on the pentafecta concept, making robot-assisted surgery the best option to achieve oncological control and optimize the quality of life of patients with prostate cancer^{6,12-14}.

The population diagnosed with prostate cancer in Mexico differs from reality in other parts of the world. Although sometimes prostate cancer is found in the prostate gland, there is a high risk for regional or

systemic metastatic activity, as well as more aggressive cellular components¹⁵. Added to the limited accessibility to robot-assisted surgery systems, reports on functional and oncological outcomes are scarce and incomplete, which limits the acceptance of the utility of RARP among the urological community.

In the Mexican scientific medical literature, there are only 2 partial reports of pentapecta. In the first report, from a hospital in the south of Mexico City, a rate of complications of 29% has been reported, with rates of positive surgical margins and urinary continence (3 months) of 63% and 57%, respectively; biochemical control and erectile function post-RARP were not reported, making the overall evaluation of pentapecta virtually impossible¹⁵. The second report from a Mexican naval hospital reported rates of positive surgical margins, urinary incontinence, erectile dysfunction, and biochemical complications of 45.8%, 91%, 53%, and 14.6%, respectively; perioperative complications were not reported, also making the evaluation of pentapecta impossible¹⁶.

The objective of our research is to report the oncological and functional outcomes, and perioperative complications, of patients with organ-confined prostate cancer undergoing RARP stratified by risk groups.

Method

This was a retrospective, observational, descriptive study conducted from 2013 to 2020, using clinical data from the health records of patients diagnosed with clinically localized prostate cancer undergoing RARP. Inclusion criteria were a diagnosis of clinically localized prostate cancer, initial treatment with RARP, and a 12-month clinical and biochemical control. Exclusion criteria were metastatic prostate cancer, therapies prior to RARP, inability for intraoperative nerve preservation, and need for adjuvant treatment to RARP. A descriptive study was conducted, obtaining simple frequencies and measures of central tendency.

Results

A total of 112 patients undergoing RARP from 2013 through 2020 were included. Their mean age was 63 years, with an initial PSA of 13.3 ng/mL. A total of 93% (n = 104) were in clinical stage T1. The mean surgical time was 199 minutes, and the conversion rate was 0%. The mean intraoperative bleeding was 357 mL, and the blood transfusion rate was 6% (n = 7).

The rate of complications was 10.7%, all being Clavien-Dindo I-II (n = 12). Bilateral nerve preservation was performed in 70% of patients (n = 79) and unilateral nerve preservation in 19% (n = 22). The mean length of stay was 3.1 days, and the duration of transurethral catheterization, 5.6 days. All clinical and surgical characteristics are shown in table 1.

Pathology reports documented positive surgical margins in 22.3% (n = 25). Immediate biochemical control was achieved in 88.4% (n = 99); subsequently, 89.3% (n = 100) at 3 months, 90.2% (n = 101) at 6 months, and 80.4% (n = 90) at 12 months.

Continence rates were 96.4% (n = 108) immediately after transurethral catheter removal, 95.5% (n = 107) at 3 months, 98.2% (n = 110) at 6 months, and 99.1% (n = 111) at 12 months. Erectile function was present in 61.5% (n = 69) at 3, 6, and 12 months.

Overall, pentapecta rates in patients undergoing RARP were 39% (n = 44) at 3 and 6 months, and 35.7% (n = 40) at 12 months. Functional and oncological outcomes at 3, 6, and 12 months are shown in table 2.

In low-risk patients, unilateral nerve preservation was achieved in 18% (n = 11) and bilateral nerve preservation in 68% (n = 41); in intermediate-risk patients, unilateral nerve preservation was achieved in 24% (n = 8) and bilateral nerve preservation in 74% (n = 25); and in high-risk patients, unilateral nerve preservation was achieved in 28% (n = 5) and bilateral nerve preservation in 61% (n = 11).

Finally, in the subgroup analysis by risk groups, pentapecta was achieved in 43% (n = 26) of low-risk patients, 26% (n = 9) of intermediate-risk patients, and 22% (n = 4) of high-risk patients at the 12-month follow-up (Table 3).

Discussion

We presented the results of the first cohort of Mexican patients undergoing RARP for prostate cancer and the pentapecta rates achieved through this approach. At the 12-month follow-up, the rates of continence, erectile function, and biochemical control were 99.1%, 61.5%, and 80.4%, respectively. The complication-free rate was 89.3%, and the positive surgical margins-free rate was 77.7%. Our 12-month pentapecta rate was 35.7%.

Overall, our results are debatable compared to what has been previously reported in the scientific medical literature. We have sufficient follow-up to compare the outcomes of prostate cancer patients. Individually

Table 1. Clinical and procedural characteristics of patients undergoing robot-assisted radical prostatectomy for prostate cancer.

Age	63 years		
Initial PSA, mean	13.3 ng/mL		
Gleason score (biopsy), n (%)	ISUP 1 (G 6): 61 (54.4%)	ISUP 2-3 (G 7): 35 (31.2%)	ISUP 4-5 (G 8, 9, 10): 16 (14.4%)
Clinical state, n (%)	≤ T2: 109 (97.3%)	≥ T3: 3 (2.7%)	
Risk (D'Amico), n (%)	Low: 60 (53%)	Intermediate: 34 (30%)	High: 18 (16%)
Surgical time, mean	199 minutes		
Bleeding, mean	357 mL		
Blood transfusion, n (%)	7 (6%)		
Conversion to open surgery, n (%)	0 (0%)		
Complications (Clavien-Dindo), n (%)	I-II: 12 (10.7%)	III-IV: 0 (0%)	V: 0 (0%)
Positive surgical margins, n (%)	25 (22.3%)		
Pathological state, n (%)	pT2: 85 (75.8%)	pT3: 27 (24.1%)	pT4: 0 (0%)
Length of stay, mean	3.1 days		
Duración de sonda transuretral, media	5.6 days		

ISUP, International Society of Urological Pathology; PSA, prostate specific antigen.

Table 2. Functional and oncological outcomes in our series

	Immediate	3 months	6 months	12 months
Erectile function, n (%)	69 (61.5%)	69 (61.5%)	69 (61.5%)	69 (61.5%)
Continence, n (%)	108 (96.4%)	107 (95.5%)	110 (98.2%)	111 (99.1%)
Biochemical control (PSA), n (%)	99 (88.4%)	100 (89.3%)	101 (90.2%)	90 (80.4%)
Pentafecta, n (%)	47 (42%)	44 (39.3%)	44 (39.3%)	40 (35.7%)

PSA, prostate specific antigen.

Table 3. Pentafecta results by risk groups of prostate cancer

Low risk (n = 60)		Intermediate risk (n = 34)	High risk (n = 18)	Total (n = 112)
Pentafecta, n (%)	26 (43%)	9 (26%9)	4 (22%4)	39 (35%39)
Complications, n (%)	8 (13%)	4 (12%)	0 (0%)	12 (11%)
Negative surgical margins, n (%)	50 (83%)	22 (65%)	15 (83%)	87 (77.6%)
Biochemical control, n (%)	54 (90%)	25 (74%)	11 (61%)	90 (80.4%)
Erectile function, n (%)	42 (70%)	20 (59%)	7 (39%)	69 (61.5%)
Continence, n (%)	59 (98%)	34 (100%)	18 (100%)	111 (99%)

speaking, strictly regarding continence, our results are superior to those of the series by Patel et al.¹⁰ (96%), Ou et al.¹² (98%), and Ihsan-Tasci et al.⁶ (96%). Regarding the rates of complication and the oncological

outcomes reported (positive surgical margins and biochemical recurrence-free rates), our results are within the average of the series provided by Anastasis et al.⁹, and Gárate et al.¹³. However, in terms of erectile function,

Table 4. Pentafecta report of patients undergoing robot-assisted prostatectomy worldwide

Authors	n	Clinical state (%) (T1/T2)	Low/ Intermediate/ High risk (%)	Follow-up (months)	Continence (%)	Erectile function (%)	Biochemical relapse-free rate (%)	Complication-free rate (%)	Negative surgical margins (%)	Pentafecta (%)
Patel et al. ¹⁰	332	92.7/7.3	67.2/28.9/3.9	12	96.4	89.8	96.4	93.4	90.7	70.8
Anastasis et al. ⁹	136	-	-	12	90.4	66.2	95.6	85.3	84.6	45.6
Gárate et al. ¹³	100	-	54.3/31.3/14.3	12	87.5	59.5	87.5	81.1	79.2	-
Ou et al. ¹²	230	58.7/41.3	-	28	98.3	86.1	92.6	93.9	77	60.4
Ihsan-Tasci et al. ⁶	334	-	59/32.9/8.1	12	96.7	74.5	96.7	94	89.3	-
Soto et al. ¹⁶	48	12.5/70	52/29/19	6	91.3	53.5	85.4	67.9	54.2	-
Herrera et al. ¹⁵	35	-	12/16/4	12	100	57	94.3	79	78	-
Corona et al.	112	93/4/2	53/30/16	12	99.1	61.5	80.4	89.3	77.7	35.7

we presented worse results (61.5%) compared to those reported by Patel et al.¹⁰ (89%), Ou et al.¹² (86%), and Ihsan-Tasci et al.⁶ (74%). This can be explained by the proportion of patients in our series with some degree of pre-existing erectile dysfunction, pre-existing comorbidities (diabetes mellitus, hypertension, arteriosclerosis, etc.), elevated initial PSA levels, and unfavorable conditions (Gleason score, digital rectal examination, risk group, etc.).

Overall, the pentafecta rate presented in our series is lower than the most important international series reported (Patel et al.¹⁰, 70.8%), but it is the only series in Mexico presenting individual and combined functional and oncological outcomes, which is very relevant. Table 4 illustrates the main reports in the scientific medical literature currently available on pentafecta in RARP.

In our setting, there are reports of isolated functional and oncological outcomes in the last 5 years of patients undergoing RARP. Comparatively, our results are individually better (continence, erectile function, biochemical control, complications, and surgical margins) than those reported by Soto et al.¹⁶ and Herrera et al.¹⁵, and we are the only ones reporting the pentafecta rate.

Finally, our study has some important limitations. The first one being its retrospective design; secondly, the high prevalence of comorbidity in our series; and thirdly, the relatively short follow-up, which we propose to extend to confirm the oncological results and achieve a positive impact on disease-free survival and cancer-specific survival through adequate biochemical control. However, we perform an analysis by

risk groups, which is inversely proportional to a higher risk of positive surgical margins to achieve nerve preservation, which gives us in-depth information on each of these areas, exposing the risk of preservation despite the robotic haptic system. Additionally, we have an objective evaluation of functional outcomes, as it was performed using standardized surveys (SHIM for erectile function and the PAD test validated by Ahlering et al.¹⁷); strengths of our research that minimize the relativity of functional results.

Conclusions

Our study presents an overall pentafecta rate in patients undergoing RARP of 35.7%, a rate that can be optimized over time through better patient selection, disease identification at earlier stages, and exceptional technical development during nerve preservation.

Standardization of outcomes in the context of robotic surgery is crucial to consolidate this approach as the one of choice, as functional and oncological outcomes are promising in the short and medium term in expert hands.

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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 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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