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Erectile dysfunction in patients with prostate cancer who have undergone surgery: Systematic review of literature

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A B S T R A C T

Objective: To assess erectile dysfunction in patients with prostate cancer undergoing surgery by radical prostatectomy, laparoscopic prostatectomy or robotic prostatectomy.
Material and methods: Systematic review of literature based on a search strategy (2000-10) in MedLine, Embase, Cochrane Library, CRD, ECRI, and Hayes. Mesh terms used were "Prostatectomy", "Prostatic Neoplasm", "Transuretral Resection Prostate", "Impotence" and as free terms "erectile dysfunction" and "prostatectomy". Studies included patients with prostate cancer who underwent radical prostatectomy with open surgery (retropubic), laparoscopic or robotic surgery.
Results: Ten observational studies with moderate quality and 29 case series with low quality were selected. Observational studies showed lower percentages of erectile dysfunction after intervention in the patients who underwent robotic surgery (3-51%). Radical surgery (36-91%) and laparoscopic surgery showed higher values of impotence. In the studies that compared surgery versus radiotherapy, the results were better for radiotherapy (3-72% erectile dysfunction). In the case series, lower percentages of erectile dysfunction were shown in patients who underwent robotic surgery (22%), the following was for laparoscopic surgery (40%) and open radical prostatectomy (41.4%).
Conclusions: This result should be considered with caution because of the low methodological quality of the studies included. However, the different surgical techniques assessed showed similar effects in the two types of studies included and we found that robotic surgery presented lower percentages of sexual impotence.

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Disfunción eréctil en pacientes intervenidos de cáncer de próstata. Revisión sistemática de la literatura médica

Palabras clave:
Prostatectomía
Disfunción eréctil
Cirugía robótica
Cáncer de próstata

R E S U M E N

Objetivo: Evaluar la aparición de la disfunción eréctil en pacientes con cáncer de próstata sometidos a prostatectomía radical (PR) retropúbica, prostatectomía laparoscópica y/o prostatectomía robótica.

Material y métodos: Revisión sistemática de la literatura médica mediante búsqueda bibliográfica (2000-2010) en MedLine, Embase, Cochrane Library, Center for Review Dissemination, ECRI y Hayes. Los términos Mesh fueron «Prostatectomy», «Prostatic neoplasm», «Transuretral resection prostate», «Impotence» y los términos libres fueron «erectile dysfunction» y «prostatectomy». Los estudios incluían pacientes con cáncer de próstata intervenidos para la extirpación de la glándula mediante cirugía abierta (retropúbica), laparoscópica o robótica.

Resultados: Se seleccionaron diez estudios observacionales de calidad moderada y 29 series de casos de baja calidad. Los estudios observacionales presentaban los menores porcentajes de disfunción eréctil en pacientes intervenidos mediante cirugía robótica (3-51%). La PR retropúbica (36-91%) y la laparoscópica registraban cifras superiores de aparición de impotencia. Los estudios que comparaban intervenciones, cirugía y radioterapia obtenían con las radiaciones menores índices de disfunción sexual (3-72%). En las series de casos, los menores porcentajes de disfunción eréctil acontecieron en pacientes con cirugía robótica (22%), seguido de cirugía laparoscópica (40%) y de PR retropúbica (41,4%).

Conclusiones: Los resultados, aunque deben interpretarse con cautela dada la limitada calidad de los estudios, presentan efectos similares en la evaluación de las diferentes técnicas quirúrgicas, observándose que la cirugía robótica registra los menores porcentajes en relación con la aparición de impotencia sexual.

Introduction

Prostate adenocarcinoma is the leading cancer in males and the second leading cause of death after lung cancer.[1] In Spain, prostate adenocarcinoma was the third leading cause of death from cancer in 2005, causing 5,511 deaths (3.2% less than in 2004), after lung cancer (causing 16,628 deaths) and colorectal cancer (causing 5,565 deaths).[2]

Advances in urological surgery, particularly those related to radical prostatectomy (RP), are mainly aimed at minimizing invasiveness to decrease damage that could affect the quality of life and return to social and occupational life of patients. Thus, a number of changes have been made in conventional RP to preserve lateral prostatic neurovascular bundles and to assess the criteria for indicating ilio-obturator lymphadenectomy based on predictive nomograms[3,4] because damage to neurovascular bundles and tissues during lymphadenectomy appears to be involved in the occurrence of these side effects affecting the quality of life of patients undergoing prostatectomy.

Laparoscopic RP has advantages such as a shorter hospital stay, less postoperative pain and blood loss, and a fast return to social and occupational activities. The precision of the procedure allows for oncological results similar to those of conventional surgery.[5] Laparoscopic RP has, however, some disadvantages as compared to open surgery, such as its longer learning curve and operating time, and technical difficulties associated to limitation in the degrees of mobility of surgical instruments.

The aim of robotic surgery was to try and control the disease while minimizing the potential side effects and the disadvantages of the conventional open and laparoscopic surgical procedures.[6,7] Robotic surgery adds to the advantages of conventional laparoscopy shorter learning curves and operating times, an improved mobility, and instrument articulation and stereoscopic vision.[8]

Several side effects occur after these procedures. Among those affecting patient quality of life, special mention should be made of urinary incontinence and loss of sexual potency or erectile dysfunction. This is why research is also being done on the prostatic resection procedures associated to higher rates of preservation of sexual potency in cancer patients.[9]

The primary objective of this review was to assess the prevalence rates of erectile dysfunction occurrence in prostate cancer patients as a consequence of retropubic, laparoscopic, and robotic RP.

Materials and methods

A systematic literature search (January 2000-January 2010) was made in the MedLine, Embase, Cochrane Library, Center

for Review Dissemination, ECRI, and Hayes databases, and in the databases of the agencies for healthcare technology evaluation. A manual search was also made in journals specialized in cancer, prostate, and urology. The search strategy consisted of use and combination of the mesh descriptors «*prostatectomy*», «*prostatic neoplasm*», «*transuretral resection prostate*», and «*impotence*», and the free search terms «*erectile dysfunction*» and «*prostatectomy*». The search was aimed at primary studies. There was no language restriction.

Articles selected should have as their defined study population patients with prostate cancer undergoing surgery for radical resection of the prostate gland using open (retropubic), laparoscopic, or robotic surgery. If the study compared different therapies, the comparative procedure (surgical or even radiotherapy) should be detailed. Outcome measures considered would include postoperative sexual potency, degree of impotence, and erectile dysfunction, as assessed by an objective test or a clinical questionnaire.

The quality of observational studies was measured using the STROBE checklist.[10] For case series, heterogeneity in various aspects, selection criteria and follow-up of patients, description of baseline status of patients, procedure performed, questionnaire definition of sexual dysfunction, and type of questionnaire used were assessed.

Because of heterogeneity of studies in terms of both the procedures compared and the designs used and results achieved, a meta-analysis for a quantitative synthesis could not be designed. A qualitative synthesis of the most relevant results was made, using the critical assessment of study quality in order to qualify the conclusions.

Results

The systematic search for original articles yielded 626 references. Thirty-nine studies meeting the predefined criteria were finally included after reading the full texts (fig. 1). These were 29 case series and 10 observational studies.

Methodological quality of selected studies

The observational studies analyzed[11-20] were of a moderate quality due to patient selection bias. All studies reported the setting, recruitment dates, patient eligibility criteria, and quantitative variables used, but none mentioned the method used for sample size estimation and only four[11-14] reported the measures taken to avoid potential bias. Results given were not homogeneous, no adjustment for confounding variables was made in description of results, and three studies[15-17] provided no subgroup analyses. A study[12] did not specify its objective, and the number of participants was not clear in another study.[18] The external validity to be able to extrapolate the results to other studies was discussed in three studies only.[12,16,17]

Case series[21-49] were of a poor quality and highly heterogeneous. Selection criteria were not clearly stated. Sample size was small in several studies,[22,24,27,31,35,36,39,41,46] even lower than 50 patients. Follow-up after surgery was less than 12 months in six studies.[22,27,29,31,40,46] The surgical procedure was assessed in different ways. While some used pre- and post-surgical scores, others assessed the occurrence of impotence using questionnaires that were not always validated. Baseline patient status was not reported in several studies.[21,22,33,37,39,44,45]

Descriptive analysis of studies included

Ten observational studies[11-20] of a total of 8,135 males aged 55-74 years were included prostate-specific antigen levels (when recorded) ranged from 2.15 and 20.2 ng/mL (table 1).

Four of the studies selected[11,13,15,16] used unvalidated questionnaires to assess erectile dysfunction. Authors used such questionnaires to measure the ability to maintain an erection sufficient for a complete satisfactory sexual relation (or penetration or intercourse). Five studies[12,14,17,19] used validated questionnaires (three of them used the IIEF) to assess the sexual potency of the patient using a scoring system. A single study[20] did not detail the assessment system. When studies were categorized based on the procedure performed, five[11-14,20] were found to compare retropubic RP to radiotherapy, two[15,16] assessed retropubic versus perineal open surgery, another two[17,19] assessed robotic surgery, and a single study[18] compared radical retropubic surgery to laparoscopic surgery.

The 29 case series examined in our study included 7,581 adult males, of whom 5,665 patients underwent radical retropubic surgery in 24 studies. The two studies where laparoscopic surgery was performed[45,46] enrolled 127 patients, while the three studies with robotic surgery[47-49] included 1,789 subjects. Mean age range was 55-80 years. Prostate-specific antigen levels ranged from 0.3 and 20 ng/mL. Dysfunction was assessed using unvalidated medical questionnaires in nine studies,[26,29,30,34,35,38,39,43,47] and the assessment system used was not reported in five studies[33,40,44-46] (table 2).

Summary of the main results

Observational studies comparing retropubic versus perineal RP[15,16] reported better results after the first procedure (incidence rate of impotence ranging from 88.3% and 91.1%) as compared to the second (91.8%-93.3%). The only study assessing retropubic RP as compared to laparoscopic surgery[18] using questionnaire scores yielded better results with RP (score decrease, 8.5 vs 9.5). A study assessed robotic versus retropubic RP,[19] and reported erectile dysfunction rates of 3% and 26% respectively. Another study[17] assessed the dysfunction occurring after robotic surgery depending on the body mass index (BMI) of patients. The lowest impotence rates (31.5%) were seen in patients with BMI <25, and the highest rate (51.6%) was found in patients with BMI >30. In the five studies[11-14,20] comparing retropubic RP versus radiotherapy, more favorable results were seen in patients undergoing radiotherapy (3%-72.5%), in four of them as compared to RP (36%75%). Of these four studies, two[11,13] assessed dysfunction 24 months after the procedure. A single study[14] reported better results with retropubic RP (table 1).

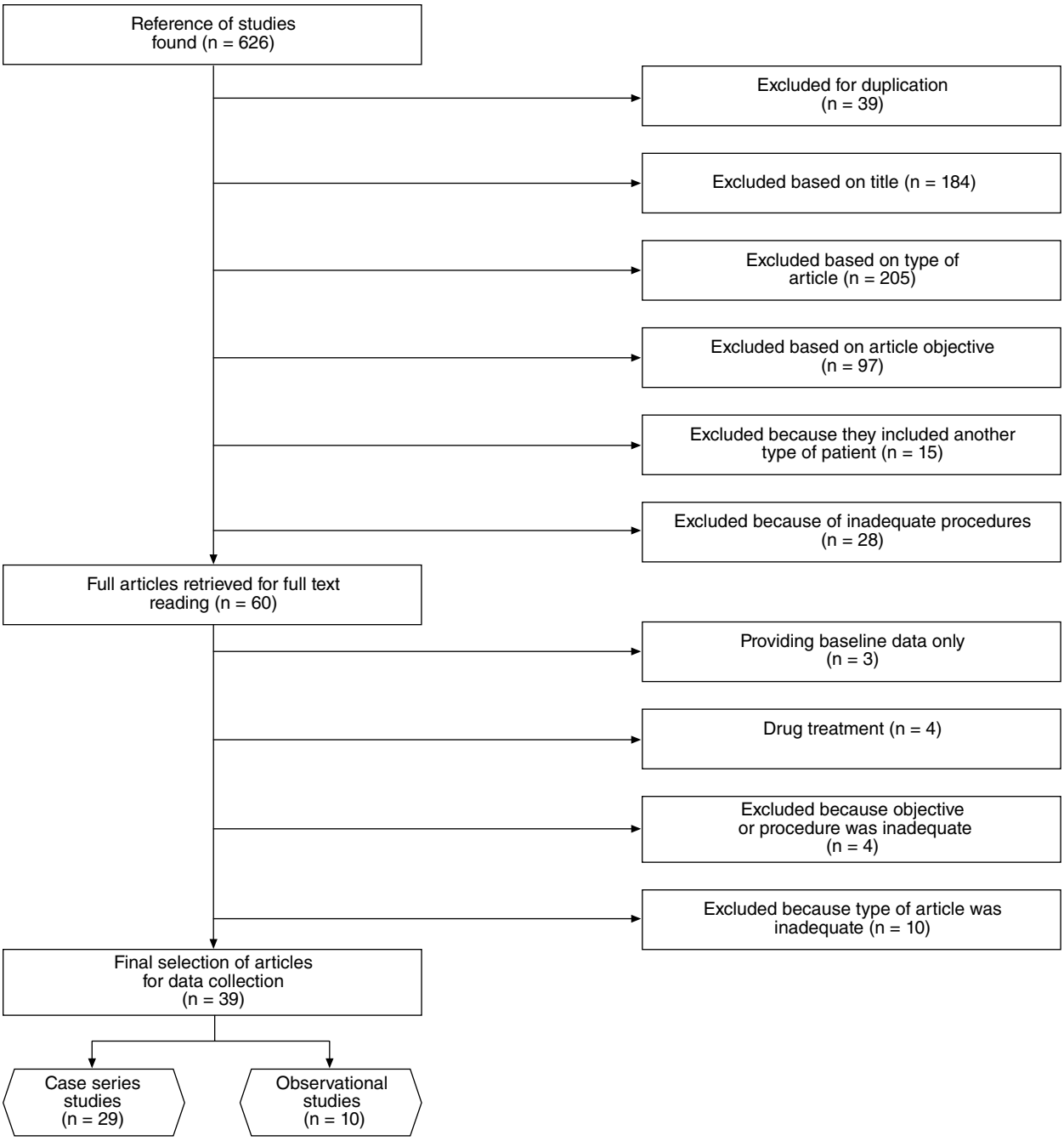

Figure 1 – Flow chart: overall scheme of study selection.

Results of the case series evaluating retropubic RP were reported in three different ways. Thus, three studies[28,32,41] assessed erectile dysfunction based on score in a questionnaire. A decrease in score by at least 20 points (21-41.7) was seen 12 months after the procedure. In 16 studies, impotence rate ranged from 10%-97.6%. If case series with an assessment period of 12 months are only considered, the rates ranged from 41.4% and 97.6%. Finally, in four studies[24,33,34,38] impotence was stratified as partial (13.6%-45.7%) and total (23.9%-73.6%). Laparoscopic surgery was assessed in two studies[45,46] in which erectile dysfunction rates of 40% and 43% respectively were reported. The assessment period was different from 12 months in both studies. One of them[45] provided no data about the baseline patient status. In the three studies[47,48,49] assessing robotic surgery, prevalence rates of impotence ranged from 22% and 30% (table 2).

Discussion

This review summarizes and evaluates the results of 10 observational studies and 29 case series. The main result

Table 1 – Main characteristics and results of the 10 observational studies analyzed

Study		Descriptive characteristics						Results		
Author	Year	Comparative procedure	Number of patients	Mean age	PSA (ng/mL)	Definition of impotence	Type of questionnaire	Baseline impotence (%)	Postoperative impotence (%)	Occurrence of impotence (%)
Lance[15]	2001	Retropubic RP	1,382	63.7	6.93	Erectile capacity	Not validated	NA	91.1	91.1
		Perineal RP	316	62.2	6.93			NA	91.8	91.8
May[16]	2008	Retropubic RP	1,184	63.6	13.6	Erectile capacity	Not validated	NA	88.3	88.3
		Perineal RP	120	64.1	10.3			NA	93.3	93.3
Hara[18]	2003	RP	57	66.5	NA	Score	IIEF5	Score: 11.5	Score: 3	Decrease by 8.5
		Laparoscopy	54	68.2				Score: 12	Score: 2.5	Decrease by 9.5
Menon[19]	2005	Da Vinci robot	35	57.4	4.9	Score 21	SHIM	0	3	3
		Retropubic RP	23	60.5	5.8			0	26	26
Wiltz[17]	2009	Robot. 3 groups by BMI	BMI <25: 216	60.3	6.4	Erection quality	UCLA	0	31.5	31.5
			BMI 25-30: 464	59.7			SF36v2. IPSS	0	40.4	40.4
			BMI >30: 265	59.4			SHIM+21	0	51.6	51.6
Van der Poel[20]	2008	RP	32	61.9	4.9	NA	NA	45	81	36
		Radiotherapy	41	62.7	2.15			58	61	3
Potosky[11]	2000	RP	1,591	55-74	NA	Score	Not validated	21	82.1	61.1
		Radiotherapy	435					38	50.3 (2 years)	12.3
Gugliotta[12]	2008	RP	100	60	4-12	Score	IIED	NA	75	75
		Radiotherapy	40	70	5-10			NA	72.5	72.5
Potosky[13]	2004	RP	961	55-74	<20. 92%	Erectile capacity	Not validated	21	82.1	61.1
		Radiotherapy	373		<20. 88%			38	50.3 (2 years)	12.3
Ponholzer[14]	2006	RP	364	65.5	10.5	Score<21	IIEF5	NA	93	93
		Radiotherapy	82	70.3	20.2			NA	100	100

BMI: body mass index; NA: not available; RP: radical prostatectomy; PSA: prostate-specific antigen.

Table 2 – Main characteristics and results of case series analyzed

Study		Descriptive characteristics							Results		
Author	Year	Patients	Number of patients	Mean age	PSA (ng/mL)	Definition of impotence	Questionnaire	Follow-up	Baseline impotence (%)	Postoperative impotence (%)	Occurrence of impotence (%)
Mols[21]	2009	257	257	72	NA	Score	Dutch Sac	10 years	NA	74	74
Kelovic[22]	2009	33	33	67	NA	Score > 10	IIEF	0.5 years	NA	78.43	78.43
Marien[23]	2008	1,110	610	57.2	5.95	Score 0-100	UCLA PCI	2 years	0	48 (2 years)	48
Joffe[24]	2007	22	22	62	NA	Score 0-30	IIEF	1.9 years	0	72 T; 13.6 P	72 T; 13.6 P
Wille[25]	2007	403	327	66.3	7.9	Score 17	IIEF5	2.2 years	32	94	62
Juan Escudero[26]	2006	168	168	63	12.47	Erection	Not validated	2.2 years	0	97.6	97.6
Bellina[27]	2005	21	21	65	5.5	Score>21	IIEF5	0.75 years	0	10	10 (9m)
Haffner[28]	2005	342	163	58.2	5.6	Score 0-100	UCLA PCI	2 years	71.7 score	47.6 score	–24.1 score
Masterson[29]	2005	100	59	NA	NA	Erection	Not validated	NA	0	90	90 (5 years)
Penson[30]	2005	1,288	1,213	<65 (56%)	NA	Erection	Not validated	5 years	17	81	64
Trincheri[31]	2005	30	16	66.6	NA	Score 6-25	IIEF5	0.4 years	13	100	87
Yang[32]	2005	266	187	59	NA	Score	EPIC	5.3 years	Score 52.8	Score 11.1	–41.7 score
Chiva Robles[33]	2004	127	97	60.7	9.45	NA	NA	3.3 years	NA	76.3 T; 15.5 P	76.3 T; 15.5 P
Deliveliotis[34]	2004	441	142	55-80	<10	Erection	Not validated	2 years	5 T; 29.7 P	75.2 T; 19.5 P	75.2 T; 19.5 P
Reis[35]	2004	34	33	62.3	<10 (50%)	Score	Not validated	1 year	0	84.80	84.80
Lee[36]	2003	44	18	68.7	14	NA	IIEF6	1.5 years	0	77.8	77.8 (11.6m)
Salomon[37]	2003	146	146	64.1	10.6	Score	ICS-male	1 year	NA	41.4	41.4
Van der Aa[38]	2003	55	46	59.9	8.2	Erection	Not validated	1.5 years	0	23.9 T; 45.7 P	23.9 T; 45.7 P
Fischetti[39]	2001	38	38	62.4	NA	Erection	Not validated	2.6 years	NA	47	47
Kawanishi[40]	2001	123	21	65	NA	NA	NA	6 weeks	0	57	57
Kim[41]	2001	23	23	58	<0.3	Score	IIEF	1 year	Score 29	Score 8	–21 score
Madalinska[42]	2001	119	102	62.7	NA	Score 0-100	SF36. UCLA. HIS	1 year	11.2	82.3	71.1
Siegel[43]	2001	419	392	<70 (62%)	NA	Erection	Not validated	1 year	22.7	90.1	67.4
Cal[44]	2000	56	56	64.9	16.1	NA	NA	2.5 years	NA	53.57	53.57 (30m)
Eden[45]	2006	100	100	62.3	<20	NA	NA	3 years	NA	40 (3 years)	40 (3 years)
Cecchini[46]	2003	27	7	59.9	6.15	NA	NA	0.5 years	0	43.0	43 (6m)
Boorjian[47]	2008	447	268	61	4.9	Erection	Not validated	1 year	0	26.8	26.8
Patel[48]	2007	200	200	63.2	6.9	Score>21	SHIM	1 year	0	22	22
Menon[49]	2007	1,142	1,142	60.2	NA	Score >21	SHIM	5.5 years	0	30	30

NA: not available; P: partial; T: total.

analyzed was the prevalence of erectile dysfunction after prostatectomy using different procedures in patients with prostate cancer.[5,50] Heterogeneous results were reported for the different procedures analyzed.

Overall, observational studies reported the lowest rates of postoperative erectile dysfunction in patients undergoing robotic surgery (3%-51%) as compared to other surgical procedures. Higher impotence rates were reported for both retropubic (36%-91%) and laparoscopic surgery. In studies comparing surgery to radiotherapy, lower but highly variable sexual dysfunction rates (3%-72%) were reported after use of radiation. However, no studies comparing robotic surgery to radiotherapy were found.

In studies of case series, the lowest erectile dysfunction rates 12 months after surgery were reported in patients undergoing robotic surgery (22%), while higher rates were found for laparoscopic (40%) and retropubic surgery (41.4%).

Although study methods, comparative groups, outcome measures, and quality were different in both types of study analyzed, evaluation of the different surgical procedures provided similar results, i.e. robotic surgery was associated to lower sexual impotence rates. These results are similar to those reported by other authors.[50-52] Therefore, based on the results analyzed, implementation of robotic surgery in clinical practice could improve the results in terms of erectile dysfunction in patients undergoing surgery for prostate cancer.

This systematic review had a number of limitations, such as the very high number of documents answering the initial research question of the review and the generally low quality of the reports. In addition, since studies were identified through literature searches in scientific publications, a publication bias cannot be ruled out. In studies evaluating a given healthcare technology, this publication bias usually tends to substitute the results by the effects of the intervention performed.

No randomized clinical trials, the top quality studies, or other high quality studies providing clear scientific evidence for the procedures assessed were found. In both observational studies and case series, the main bias seen was heterogeneity between the studies, mainly in terms of patient selection, procedures performed, and comparators of observational studies, which were not always similar. Results should therefore be interpreted with caution because of the limited strength of the scientific evidence from analyzed articles.[51]

Overall, our study demonstrates the need for results based on quality studies with an adequate number of patients undergoing these procedures, particularly robotic surgery, because few studies addressing this new technology are available.[50,52] A homogeneous patient selection is also important to be able to adequately summarize results. An adequate patient description at study start or baseline should be given, including stratification by age and tumor stage, and specific and validated questionnaires should be used to be able to define and categorize erectile dysfunction in a comprehensive and generalizable way.

It would be advisable to conduct quality studies comparing treatment with radiotherapy and robotic surgery in order to be able to determine whether this new technology also achieves better results than drug treatments.

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