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Systematic Review and Meta-analysis of Studies Reporting Potency Rates After Robot-assisted Radical Prostatectomy

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Abstract

Background: Although the initial robot-assisted radical prostatectomy (RARP) series showed 12-mo potency rates ranging from 70% to 80%, the few available comparative studies did not permit any definitive conclusion about the superiority of this technique when compared with retropubic radical prostatectomy (RRP) and laparoscopic radical prostatectomy (LRP).

Objectives: The aims of this systematic review were (1) to evaluate the current prevalence and the potential risk factors of erectile dysfunction after RARP, (2) to identify surgical techniques able to improve the rate of potency recovery after RARP, and (3) to perform a cumulative analysis of all available studies comparing RARP versus RRP or LRP.

Evidence acquisition: A literature search was performed in August 2011 using the Medline, Embase, and Web of Science databases. Only comparative studies or clinical series including >100 cases reporting potency recovery outcomes were included in this review. Cumulative analysis was conducted using Review Manager v.4.2 software designed for composing Cochrane Reviews (Cochrane Collaboration, Oxford, UK).

Evidence synthesis: We analyzed 15 case series, 6 studies comparing different techniques in the context of RARP, 6 studies comparing RARP with RRP, and 4 studies comparing RARP with LRP. The 12- and 24-mo potency rates ranged from 54% to 90% and from 63% to 94%, respectively. Age, baseline potency status, comorbidities index, and extension of the nerve-sparing procedure represent the most relevant preoperative and intraoperative predictors of potency recovery after RARP. Available data seem to support the use of cautery-free dissection or the use of pinpointed low-energy cauterization. Cumulative analyses showed better 12-mo potency rates after RARP in comparison with RRP (odds ratio [OR]: 2.84; 95% confidence interval [CI]: 1.46–5.43; $p = 0.002$). Only a nonstatistically significant trend in favor of RARP was reported after comparison with LRP (OR: 1.89; $p = 0.21$).

Conclusions: The incidence of potency recovery after RARP is influenced by numerous factors. Data coming from the present systematic review support the use of a cautery-free technique. This update of previous systematic reviews of the literature showed, for the first time, a significant advantage in favor of RARP in comparison with RRP in terms of 12-mo potency rates.

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1. Introduction

International guidelines support opportunistic prostate-specific antigen (PSA) screening in well-informed patients and recommend a baseline PSA at 40 yr of age [1–3]. Although some relevant controversies continue about the real benefit of the screening program, the undisputable finding is that an increasing percentage of young men have an early prostate cancer diagnosis [4,5]. This, in turn, has led to an increase in the number of young candidates for radical prostatectomy with the expectation of curing cancer and minimizing the risk of urinary incontinence and erectile dysfunction.

Initially, Walsh's description of the anatomic nerve-sparing technique in 1982 was based on the concept that the neurovascular bundles (NVBs) are situated posterolaterally and symmetrically to the prostate in the space among the levator fascia, prostatic fascia, and Denonvilliers' fascia [6]. A comprehensive review of the literature including radical retropubic prostatectomy (RRP) series published between 1990 and 2005 showed a wide range of estimates after a minimum follow-up of 12 mo, with patients who received bilateral nerve-sparing RRP showing potency rates ranging from 31% to 86% [7]. Similar ranges of outcomes from 42% to 76% were reported after nerve-sparing laparoscopic radical prostatectomy (LRP) [8].

In the last decade, deeper insight into the distribution and course of the cavernous nerves showed that, especially in men with a small prostate, NVBs may have either an anterolateral position or, rarely, an asymmetric posterolateral position on one side while lateral on the other [9–11]. These new anatomic concepts supported the incision of the periprostatic fascia anteriorly and parallel to the NVBs to preserve cavernous nerves located at both the posterolateral and anterolateral surfaces of the prostate [9]. The multiple compartments that could be developed from the levator fascia to the prostate capsule by entering fascial planes during surgery explain the possibility of realizing a different extension of the nerve-sparing procedure according to cancer risk stratification and patient preoperative characteristics [12].

Although some surgeons demonstrated the feasibility of the anterior incision of the periprostatic fascia and the possibility of realizing an interfascial or intrafascial surgical plane in open surgery [13,14], it was hypothesized that the tridimensional magnification, scaling of movements, and 7 degrees of freedom associated with the robotic technology could significantly simplify and improve the results of nerve-sparing procedures [15,16]. Previously published surgical series showed 12-mo potency recovery after robot-assisted radical prostatectomy (RARP) in between 70% and 80% of cases [8]. Tewari et al. [17] supported these promising results, showing a significantly shorter time to reach erections in patients who underwent RARP compared with those receiving RRP. However, the very few available comparative studies did not permit any definitive conclusion about the superiority of RARP in comparison with RRP or LRP in terms of the recovery of potency.

The aims of this systematic review were to evaluate the current prevalence and the potential risk factors of erectile dysfunction after RARP, to identify surgical techniques able to improve potency recovery after RARP, and to perform a cumulative analysis of all available studies comparing RARP with RRP or LRP.

2. Evidence acquisition

To update the previous systematic review by two of the current authors [8,16], a literature search was performed in August 2011 using the Medline, Embase, and Web of Science databases. The Medline search included only a free-text protocol using the term *radical prostatectomy* across the title and abstract fields of the records. The following limits were used: humans; gender (male); and publications dating from January 1, 2008. The searches of the Embase and Web of Science databases used the same free-text protocol, keywords, and publication dates.

Two authors (G.N. and V.F.) reviewed the records separately to select RARP series and the studies comparing RARP with LRP or RRP, with any discrepancy resolved by open discussion. Other significant studies cited in the reference lists of the selected papers were also evaluated, as were studies published after the systematic search. All the noncomparative studies reporting the outcome of RALP on >100 cases were collected. In the present review, we included only studies reporting potency recovery outcome. Studies published only as abstracts and reports from meetings as well as population-based studies were not included in the review. From each comparative or noncomparative study, we extracted the number of analyzed patients; the study design; the potency definition; the data collection methods; and, when available, the 6-, 12-, 24-, and 36-mo potency rates. Some surgical aspects such as side (monolateral or bilateral), extension of the nerve-sparing procedure (intrafascial or interfascial), modalities to perform nerve-sparing dissection (athermal, monopolar, or bipolar), and pedicle control (clips or clipless techniques) were collected. Concerning postoperative care, we considered whether indications for penile rehabilitation were reported.

All of the data retrieved from the selected studies were recorded in an electronic database. Quality control of the electronic data recording was performed on a random sample of papers (accounting for about 15% of the papers).

All the papers were distinguished according to the 2011 level of evidence for therapy studies: systematic review of randomized trials or *n*-of-1 trials (level 1); randomized trials or observational studies with dramatic effect (level 2); nonrandomized controlled cohort/follow-up studies (level 3); case series, case-control studies, or historically controlled studies (level 4); and mechanism-based reasoning (level 5) [18].

The quality of data reporting concerning erectile function was assessed following the Mulhall criteria [19].

2.1. Statistical analysis

Cumulative analysis was conducted using the Review Manager v.4.2 software designed for composing Cochrane Reviews (Cochrane Collaboration, Oxford, UK). Statistical heterogeneity was tested using the χ^2 test. A p value <0.10 was used to indicate heterogeneity. In the case of lack of heterogeneity, fixed-effects models were used for the cumulative analysis. Random effects models were used in case of heterogeneity. The results were expressed as weighted means and standard deviations for continuous outcomes and as odds ratio (ORs) and 95% confidence intervals (CIs) for dichotomous variables. Due to the limitations of the Cochrane software, only studies presenting continuous data as means and standard deviations were included in the cumulative analysis. For all statistical analyses, a two-sided $p < 0.05$ was considered statistically significant.

3. Evidence synthesis

3.1. Quality of the studies and level of evidence

Figure 1 shows the flowchart of this systematic review of the literature. We selected 44 records reporting potency rates after RARP. Thirteen abstracts or meeting reports were excluded. The remaining studies included 15 case series (level 4), 6 studies comparing different techniques in the context of RARP (4 studies, level 3; 2 studies, level 4), 6 studies comparing RARP with RRP (3 studies, level 3; 3 studies, level 4), and 4 studies comparing RARP with LRP (1 study, level 2; 3 studies, level 4). One study comparing RARP and RRP [17] and one study comparing RARP and LRP [20] published before the search period were also included in the present analysis.

3.2. Incidence and predictors of potency recovery after robot-assisted radical prostatectomy

Table 1 summarizes the incidence of potency recovery reported in the surgical series published between 2008 and 2011. The mean values of the 3-, 6-, 12-, and 24-mo potency recovery rates are 50% (32–68%), 65% (50–86%), 70% (54–90%), and 79% (63–94%), respectively. Interestingly, selecting the series that fulfilled six or more Mulhall criteria, the mean 3-, 6-, 12-, and 24-mo potency rates were 48% (32–68%), 68% (50–86%), 76% (62–90%), and 82% (69–94%), respectively. Conversely, studies that reached fewer than six Mulhall criteria showed a mean value of 3-, 6-, 12-, and 24-mo potency rates of 56%, 62% (53–70%), 66% (62–83%), and 63%, respectively.

The observed wide variability can be due to different case mixes among studies such as patient age, preoperative potency status [28,29,32], comorbidity index [28], extension of the nerve-sparing procedure [29,32], and countertraction [32]. Novara et al. demonstrated that age >60 yr (OR: 2.828; 95% CI, 1.591–5.027), Charlson score $\geq$1 (OR: 2.992; 95% CI, 1.358–6.588), and baseline International Index of Erectile Function (IIEF)-5 score used as a continuous variable (OR: 0.843; 95% CI, 0.799–0.889) were

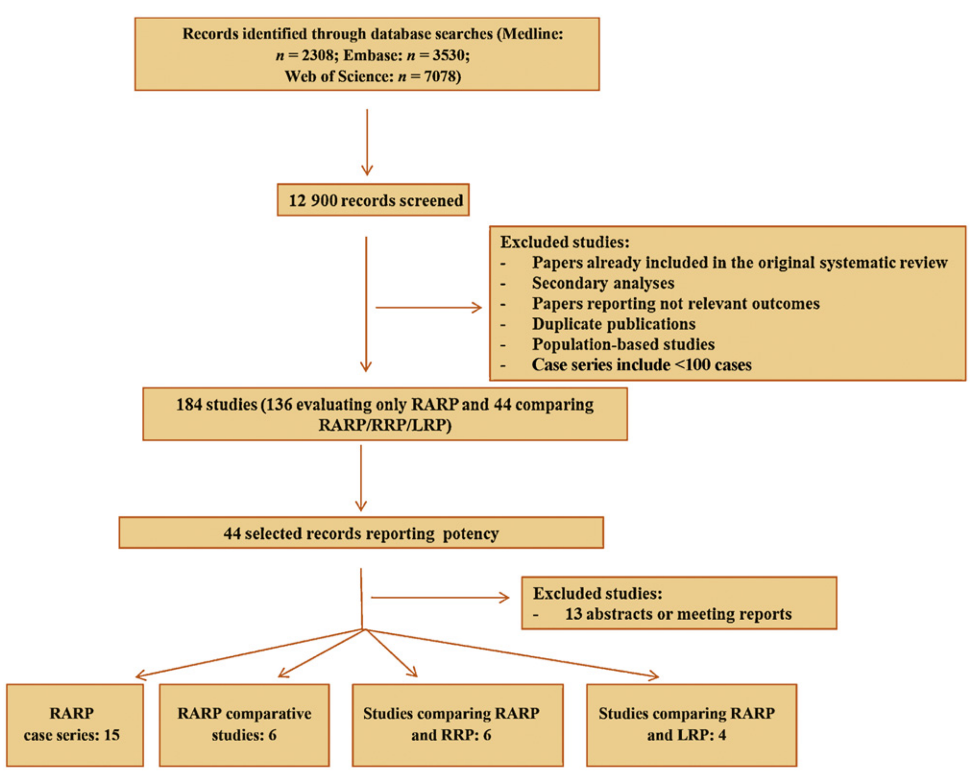

Fig. 1 – Flow chart of the systematic review. LRP = laparoscopic radical prostatectomy; RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

Table 1 – Potency rates reported in the robot-assisted radical prostatectomy series including >100 cases published between 2008 and 2011

First author	Cases, *n*	Patients characteristics	Surgical aspects (NVB dissection)	Study design	Potency definition	Data collection	3 mo, %	6 mo, %	12 mo, %	24–36 mo*, %	Mulhall criteria fulfilled
Park, 2008 [21]	58	Age: <65 yr Preoperatively potent	Unspecified NS	Retrospective analysis	ESI	Questionnaire	–	53	–	–	Unclear
Carlucci, 2009 [22]	700	Age: 40–78 yr Preoperatively potent	Interfascial bilateral NS Cautery-free/minimal use	Prospective case series	SHIM >21	Validated questionnaire	56	70	83	–	1
Murphy, 2009 [23]	232	Age: 43–75 yr Preoperatively potent	Unilateral NS (70) Bilateral NS (162) Interfascial cautery-free	Prospective case series	SHIM >21	Validated questionnaire	–	–	62	–	3
Rodriguez, 2009 [24]	58	Age: <65 yr Preoperatively potent	Monolateral (15) Bilateral (43) Interfascial/intrafascial Cautery-free NS	Prospective case series	ESI	Validated questionnaire	32	–	–	90	6
Shikanov, 2009 [25]	380	Age: 42–76 yr Preoperatively potent	Bilateral NS Interfascial Clipless (bipolar cautery)	Prospective case series	ESI	Validated questionnaire (interview)	44 (57)	50 (63)	62 (82)	69 (93)	7
Menon, 2009 [26]	85	Mean age: 55 yr (range: 42–72) Preoperatively potent	Bilateral NS Interfascial (Superveil) Clipless (monopolar cautery)	Prospective case series	ESI	–	–	–	–	94	7
Ploussard, 2010 [27]	189	Mean age: 63 yr (range: 47–75) Preoperatively potent (75%)	Monol (29) Bilateral (152) Intrafascial (73%) Extraperitoneal	Prospective case series	ESI	Validated questionnaire	19	24	39	–	4
Novara, 2010 [28]	208	Mean age: 61 yr Preoperatively potent (79%)	Bilateral NS Interfascial (60) Intrafascial (148) Clipless (monopolar cautery)	Prospective case series	SHIM >18	Validated questionnaire	–	–	62 (58) (63.5)	–	7
Shikanov, 2010 [29]	816	Age: 38–85 yr Preoperatively potent	Bilateral Interfascial NS Clipless (bipolar cautery)	Prospective case series	ESI	Validated questionnaire	–	–	75	–	7
Patel, 2011 [30]	332	Mean age: 58.7 yr Preoperatively potent	Bilateral NS Intrafascial (full) Athermal	Prospective case series	ESI	Validated questionnaire	68	86	90	–	7
Xylinas, in press [31]	433	Mean age: 62 yr (range: 43–79) Preoperatively potent	Monolateral (55) Bilateral NS (378) Extraperitoneal	Prospective case series	ESI	Validated questionnaire	–	–	54	63	4

ESI = erection sufficient for intercourse; NVB = neurovascular bundle; NS = nerve sparing; SHIM = Sexual Health Inventory for Men.
All studies are level 4 evidence.
* Same cohort at two different follow-up durations.

independent predictors of risk of postoperative erectile dysfunction. Therefore, the combination of these variables according to the Briganti risk group stratification allowed the authors to report 12-mo potency recovery of 81.9% in the low-risk group (patients age $\leq$60 yr with a baseline IIEF-6 >21 and a Charlson score $\leq$1), 56.7% in the intermediate-risk group (patients 66–69 yr of age, baseline IIEF-6 score ranging between 11 and 21, and Charlson score $\leq$1), and 28.6% in the high-risk group (age $\geq$70, baseline IIEF-6 score $\leq$10, and Charlson score $\leq$2) ($p < 0.001$) [28]. Similarly, Shikanov et al. reported in a large cohort of patients that age (OR: 0.92; $p < 0.0001$), baseline Sexual Health Inventory for Men (SHIM) score (OR: 1.1; $p < 0.0001$), and bilateral nerve sparing (OR: 2.92; $p < 0.0001$) were independently associated with achieving potency [29]. More recently, Kowalczyk et al. showed that only age (OR: 0.94; 95% CI, 0.89–0.98) and baseline sexual function (OR: 1.02; 95% CI, 1.00–1.03) predicted 12-mo postoperative potency rates after RARP. In this series, the monolateral or bilateral extension of the nerve-sparing procedure (OR: 2.07; 95% CI, 0.98–4.41) was not significant at multivariable analysis [32].

Looking at data reported in Table 1, the series including both the unilateral and bilateral nerve-sparing procedure showed 3-, 6-, 12-, and 24-mo potency recovery of 32%, 53%, 69% (62–90%), and 63%, respectively. Selecting clinical series for their analysis that included only the bilateral nerve-sparing procedure, potency rates were 56%, 69% (50–86%), 74% (62–90%), and 82% (69–94%), respectively.

Conflicting results were reported about body mass index (BMI). Wiltz et al. reported potency outcomes significantly lower for obese men at both 12 and 24 mo [33]. Conversely, two series recently failed to demonstrate significant differences in 12-mo potency rates after stratification according to the BMI values [34,35]. In 2009, Zorn et al. evaluated the potential impact of surgeon experience on potency recovery [36]. In this prospective case series, the authors reported overlapping results 3, 6, and 12 mo after the procedure in three different categories of patients represented by cases 1–300, cases 301–500, and cases 501–700 (Table 2).

3.3. *Surgical aspects influencing potency recovery after robot-assisted radical prostatectomy*

Six comparative studies evaluated the impact of different surgical aspects on postoperative erectile function recovery. Chung et al. recently compared 93 patients who received extraperitoneal RARP with a historical control group represented by 56 patients who had a transperitoneal RARP. All patients were preoperatively potent and received a bilateral nerve-sparing procedure. As reported in Table 3, the authors reported overlapping potency rates at 3, 6, and 12 mo after the surgical procedure (level 4) [37].

Some studies evaluated the difference between thermal and athermal dissection of the neurovascular bundles. In a 2008 prospective study, Ahlering et al. compared 38 patients receiving cautery nerve sparing with 50 receiving

Table 2 – Potency rates after robot-assisted radical prostatectomy stratified according to difficult cases (obese patients, large prostate) or surgeon experience (learning curve)

First author	Cases, n	Surgical technique	Study design	Potency definition	Data collection	3 mo, %	6 mo, %	12 mo, %	24–36 mo*, %	Mulhall criteria fulfilled
Wiltz, 2009 [33]	BMI <25 (155)	Monolateral (240)	Prospective case series	ESI	Validated questionnaire	48	58	68	80	7
	BMI 25–30 (312)	Bilateral (632)				44	52	60	79	
	BMI >30 (165)	Clipless (bipolar cautery) Interfascial				40	47	48	56	
Moskovic, 2010 [34]	BMI <25 (270)	Not reported	Prospective case series	SHIM >16	Validated questionnaire	70	74	86	–	3
	BMI 25–30 (600)					65	75	84		
	BMI >30 (242)					62	74	82		
Uffort, 2011 [35]	BMI <30 (69)	Bilateral NS	Prospective case series	SHIM >21	Validated questionnaire	6	10	20	–	8
	BMI >30 (54)					3	11	25		
Zorn, 2009 [36]	Case 1–300 (105)	Bilateral NS	Prospective case series	ESI	Validated questionnaire	41	47	61	–	5
	Case 301–500 (63)	Interfascial				43	51	63		
	Case 501–700 (62)	Clipless (bipolar cautery)				44	54	65		

BMI = body mass index; ESI = erection sufficient for intercourse; NS = nerve sparing; SHIM = Sexual Health Inventory for Men.
All studies are level 4 evidence.
* Same cohort at two different follow-up durations.

Table 3 – Prospective and retrospective studies comparing different robot-assisted radical prostatectomy surgical techniques

First author	Patient characteristics	Surgical technique	Study design	Potency definition	Data collection	3 mo, %	6 mo, %	12 mo, %	24–36 mo*, %	Mulhall criteria fulfilled
Chung, 2011 [37]	Mean age: 66 yr (transperitoneal), 65 yr (extraperitoneal) Preoperatively potent Bilateral NS	Extraperitoneal (93) Transperitoneal (56)	Historical control	SHIM >21	Validated questionnaire	36 39	51 48	55 52	–	3
Ahlering, 2008 [38]	Age: <65 yr Preoperatively potent Mono/bilateral NS	Cautery NS (38) Cautery-free NS (50)	Prospective comparative	ESI	Validated questionnaire	–	–	–	63 92	6
Shikanov, 2009 [39]	Mean age: 60 yr (extrafascial NS), 58 yr (interfascial NS) Preoperatively potent Bilateral NS	Extrafascial NS (110) Interfascial NS (703) Clipless (bipolar cautery)	Prospective comparative	ESI	Validated questionnaire	22 42	34 47	40 64	–	4
Finley, 2009 [40]	Mean age: 61 yr (cooling NS), 61 yr (standard NS) Preoperatively potent Bilateral NS: 78% (C), 67% (S)	Standard NS (157) Cooling NS (112)	Prospective comparative	ESI	Validated questionnaire	23 24	–	66 83	–	5
Samadi, 2010 [41]	Mean age: 59 yr Preoperatively potent Bilateral NS: 87% (cautery NS), 85% (athermal NS)	Antegrade cautery NS (590) Athermal NS (interm.) (170) Athermal NS (current) (421)	Prospective comparative	SHIM >15	Validated questionnaire	45 60 66	69 64 76	77 84 79	–	3
Kowalczyk, 2011 [32]	Mean age: 59 yr (NS no traction), 57 yr (NS with traction) Preoperatively potent Bilateral intrafascial	NS no traction (35) NS with traction (58)	Historical control	ESI	Validated questionnaire	–	45 28	50 54	–	7

ESI = erection sufficient for intercourse; NS = nerve sparing; SHIM = Sexual Health Inventory for Men.
* Same cohort at two different follow-up durations.

Table 4 – Studies comparing potency recovery after robot-assisted radical prostatectomy or retropubic radical prostatectomy

Level of evidence	First author	Cases, n	Patient characteristics (RARP)	Surgical aspects (RARP)	Study design	Potency definition	Data collection	12 mo, %	24 mo, %
3	Tewari, 2003 [17]	RRP (100) RARP (200)	–	–	Prospective comparison	Presence of erection	Interview	Median: 440 d Median: 180 d	
3	Ficarra, 2009 [42]	RRP (41) RARP (64)	Mean age: 61 yr Preoperatively potent Bilateral NS	Intrafascial Clipless (monopolar dissection)	Prospective comparison	SHIM >17	Validated questionnaire	49 81	–
3	Di Pierro, 2011 [43]	RRP (47) RARP (22)	Mean age: 62 yr Preoperatively potent Bilateral NS	Interfascial Athermal	Prospective comparison	ESI	Institutional questionnaire	26 55	–
3	Kim, 2011 [44]	RRP (122) RARP (373)	Mean age: 64 yr Preoperatively potent Mono/bilateral NS	Athermal dissection	Prospective comparison	ESI	Validated questionnaire	28 57	47 84
4	Krambeck, 2009 [45]	RRP (417) RARP (203)	Mean age: 61 yr Preoperatively potent Mono/bilateral NS	Interfascial Clipless (monopolar cautery)	Retrospective, contemporary series	ESI	Institutional questionnaire	63 70	–
4	Rocco, 2009 [46]	RRP (214) RARP (78)	Mean age: 63 yr Preoperatively potent	Athermal dissection	Historical control	ESI	Interview	41 61	–
4	Ou, 2009 [47]	RRP (2) RARP (16)	Mean age: 67 yr Preoperatively potent Mono/bilateral NS	Athermal dissection	Retrospective contemporary series	ESI	Unspecified	50 60	–

ESI = erection sufficient for intercourse; NS = nerve sparing; RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy; SHIM = Sexual Health Inventory for Men.

cautery-free cavernous nerve preservation. Selecting only patients <65 yr of age who were preoperatively potent, the authors reported significant advantages in favor of athermal dissection 24 mo after the procedures (level 3) [38]. In 2010, Samadi et al. compared 590 patients who received an antegrade cautery nerve-sparing procedure using the bipolar device with two other groups of patients who underwent athermal dissection using clips and a "curtain" technique. In this study, including preoperatively potent patients according to SHIM questionnaire with a mean age of 59 yr, the authors showed a statistically significant advantage only in favor of the athermal technique at 3-mo follow-up. Any difference disappeared after 6 or 12 mo postoperatively (level 3) [41].

Considering the data coming from the clinical series reported in Table 1, the mean potency rates at 3, 6, and 12 mo were 44%, 50%, and 66% (62–75%), respectively, in the four series using monopolar or bipolar dissection and 52%, 78% (70–86%), and 81% (62–90%), respectively, in the four studies using the athermal dissection. Interestingly, available data with longer follow-up showed a 24-mo mean potency rate as high as 82% (69–94%) in patients who received cautery nerve sparing.

Finley et al. evaluated the potential beneficial role of cold dissection of the cavernous nerves in a prospective study comparing 157 patients receiving the standard procedure with 112 patients in which cold irrigation and an endorectal cooling balloon cycled with 4 °C saline was performed. The authors reported statistically significantly better 12-mo potency rates in patients who received the hypothermic nerve-sparing dissection (level 3) [40].

Kowalczyk et al. investigated the potential role of countertraction during the nerve-sparing dissection in the context of a prospective study comparing 35 patients receiving RARP without countertraction and 58 patients receiving RARP with countertraction. This study showed a statistically significant advantage in favor of the cases without countertraction only at the 5-mo follow-up. No significant differences in terms of potency recovery were detected 12 mo after the procedure [32].

Only a single comparative study analyzed the impact of the extension of the nerve-sparing procedure. In 2009, Shikanov et al. compared 110 patients receiving an extrafascial nerve-sparing procedure with 703 who underwent intrafascial nerve-sparing RARP. The intrafascial nerve preservation was associated with dissection into the avascular plane between the prostatic fascia and Denonvilliers' fascia posteriorly and between the prostatic fascia and the anterior extension of Denonvilliers' fascia at the posterolateral aspect of the prostate. Conversely, the extrafascial technique should be more correctly considered as a partial nerve-sparing technique involving dissection lateral to the prostatic fascia and anterior extension of the Denonvilliers' fascia into the thickness of the NVB. Both bipolar cautery and suture ligation were used to control significant bleeding from transected NVB vessels. The authors showed statistically significant advantages in favor of the intrafascial technique at 3, 6, and 12 mo after the procedure [39].

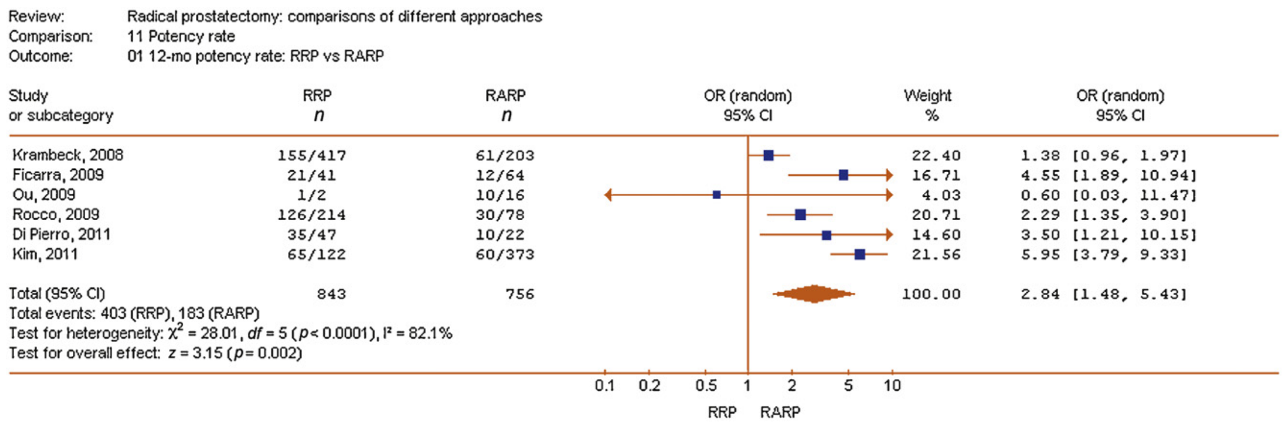

Fig. 2 – Cumulative analyses of 12-mo potency rates following robot-assisted radical prostatectomy or retropubic radical prostatectomy. CI = confidence interval; OR = odds ratio; RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

3.4. Cumulative analysis of studies comparing robot-assisted radical prostatectomy with radical retropubic prostatectomy or laparoscopic radical prostatectomy

Table 4 shows the characteristics of seven studies comparing RARP and RRP in terms of potency rates. Four were nonrandomized prospective comparative studies (level 3), and three were retrospective comparisons with contemporary series or a historical control (level 4). Only one of the previous studies was published before the period of this systematic review [17]. This study showed a significantly shorter median time to reach potency in patients who underwent RARP in comparison with those receiving RRP (180 d vs 440 d) (level 3) [17]. Unfortunately, this study did not report data in a format valid for inclusion in the cumulative analysis.

Six studies were included in the cumulative analysis evaluating the 12-mo potency recovery after RARP or RRP [42–47]. The prevalence of erectile dysfunction according to different definitions was 47.8% after RRP (403 of 843 cases) and 24.2% after RARP (183 of 756 cases). The cumulative analysis showed a statistically significant advantage in favor of RARP (OR: 2.84; 95% CI, 1.48–5.43; $p = 0.002$) (Fig. 2). The absolute risk reduction for erectile dysfunction was 23.6%. This result was also confirmed by data reported at a 24-mo follow-up by Kim et al. [44]. In this prospective comparative study, 24-mo potency rates were 47% after RRP and 84% after RARP (level 3) (OR: 6.01; 95% CI, 4.25–8.49; $p < 0.001$).

Table 5 reports the results of four studies comparing RARP and LRP. One study was a randomized controlled trial (RCT; level 2), and the remaining three were retrospective comparisons with contemporary series or a historical control (level 4). The available RCT showed a statistically significant advantage in favor of RARP in terms of 12-mo potency rates measured by the SHIM questionnaire. The 12-mo potency rates were 77% in the 52 cases treated with RARP and 32% in the 64 cases receiving LRP [48]. Four studies were included in the cumulative analysis evaluating potency rates after RARP or LRP [48–51]. The prevalence of erectile dysfunction was 55.6% after LRP (93 of 167 cases) and 39.8% after RARP (71 of 178 cases). The cumulative analysis showed a nonstatistically significant trend in favor of RARP (OR: 1.89; 95% CI, 0.70–5.05; $p = 0.21$) (Fig. 3).

Table 5 – Studies comparing potency recovery after robot-assisted radical prostatectomy or laparoscopic radical prostatectomy

Level of evidence	Authors	Cases, *n*	Patient characteristics (RARP)	Surgical aspects (RARP)	Study design	Potency definition	Data collection	12 mo, %
2	Asimakopoulos, 2011 [48]	LRP (64) RARP (52)	Mean age: 59 yr Preoperatively potent Bilateral NS	Athermal intrafascial dissection	RCT	ESI	Validated questionnaire	32 77
4	Park, 2011 [49]	LRP (62) RARP (44)	Mean age: 62.7 yr Preoperatively potent Mono/bilateral NS	Unclear	Retrospective, contemporary series	ESI	Interview	48 55
4	Cho, 2009 [50]	LRP (41) RARP (53)	Mean age: 66 yr Preoperatively potent Mono/bilateral NS	Unclear	Historical control	ESI	Interview	78 81
4	Hakimi, 2009 [51]	LRP (45) RARP (51)	Mean age: 59 yr Preoperatively potent Bilateral NS	Unclear	Historical control	ESI	Validated questionnaire	72 76

ESI = erection sufficient for intercourse; NS = nerve sparing; LRP = laparoscopic radical prostatectomy; RARP = robot-assisted radical prostatectomy; RCT = randomized controlled trial.

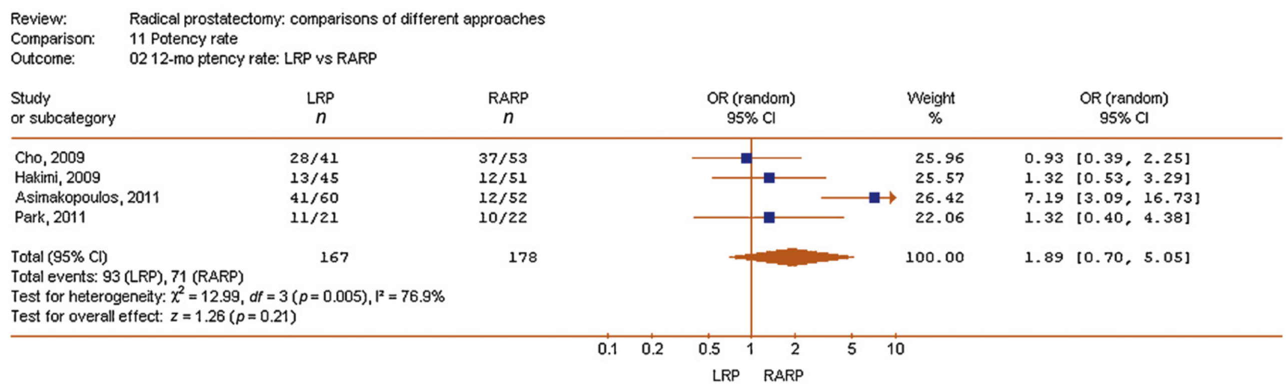

Fig. 3 – Cumulative analyses of 12-mo potency rates following robot-assisted radical prostatectomy or laparoscopic radical prostatectomy. CI = confidence interval; LRP = laparoscopic radical prostatectomy; OR = odds ratio; RARP = robot-assisted radical prostatectomy.

4. Discussion

Nerve-sparing RARP was associated with an incidence of 12- and 24-mo erectile dysfunction ranging from 10% to 46% and from 6% to 37%, respectively. These widely different rates of erectile dysfunction are attributable to several factors: (1) Different definitions and measures of erectile dysfunction have been used from study to study, (2) characteristics of the surgery and patient selection have varied across studies, and (3) postsurgical rehabilitation varies greatly from center to center. Our findings in this review are consistent with those reported in the previous systematic review, including data coming from relatively few referral centers [8,16]. Analysis of predictors showed that preoperative, intraoperative, and postoperative variables may play a role in influencing potency outcomes. This systematic review also confirmed that for patients who underwent RARP, relevant predictors of outcome are age at surgery, baseline erectile function, and presence of comorbidities. These data confirmed the classic suggestion that nerve-sparing procedures are better reserved for young, preoperatively potent patients without significant comorbidities.

Briganti et al, analyzing a series of patients who underwent bilateral nerve-sparing RRP, proposed a group stratification to predict potency recovery: Low-risk patients were $\leq$60 yr of age with a baseline IIEF-6 $>$ 21 and a Charlson score $\leq$1, intermediate-risk patients were 66–69 yr of age with a baseline IIEF-6 score ranging between 11 and 21 and a Charlson score $\leq$1, and high-risk patients were $\geq$70 yr of age with a baseline IIEF-6 score $\leq$10 and Charlson score $\leq$2 [52]. In the same year, Novara et al. performed the first external validation of this risk-group stratification in a series of consecutive patients who underwent nerve-sparing RARP [28]. The impact of patient age and baseline erectile function in candidates for nerve-sparing RARP was also confirmed by other authors [29,32]. No other preoperative factors seem to be significantly correlated with potency outcome.

The impact of monolateral or bilateral nerve sparing, different planes developed in the periprostatic tissue, and use of athermal or thermal dissection are the most discussed surgical issues. Similar to open surgery or traditional laparoscopy, the data of this systematic review reconfirmed that bilateral preservation of the cavernous nerve is associated with a lower risk of erectile dysfunction for RARP. The monolateral preservation of cavernous nerves should be taken into consideration, especially in patients with monolateral extraprostatic disease in which the partial preservation of bundles limited to the nonbearing tumor site may be indicated.

In recent years, deeper insights concerning the multilayer structure of the periprostatic fascia and the distribution and course of the cavernous nerves have supported the high incision of the levator ani fascia and the following development of intra- or interfascial surgical planes [53]. Data from this systematic review also showed wide variability in the choice between the interfascial or intrafascial dissection within the same surgical series. Therefore, no conclusion can be made about the comparison between the two different approaches. The only available comparative studies took into consideration the comparison between interfascial nerve sparing with the so-called extrafascial nerve-sparing technique. This last approach should be considered a minimally nerve-sparing procedure, considering that dissection with this technique is conducted laterally to the prostatic fascia and anteriorly to the extension of Denonvilliers' fascia into the thickness of the NVBs [39].

More recently, anatomic studies showed a better definition of the multiple compartments that could be developed from the levator fascia to the prostatic capsule by entering different fascial planes during surgery [12]. A new definition of the fascia approach and related surgical techniques should be formulated according to these new anatomic concepts to minimize the variability and subjectivity among surgeons regarding these facets of the procedure.

The classic nerve-sparing technique described by Walsh et al. was based on the idea that thermal dissection is harmful for the functional integrity of the cavernous nerves [6,54]. Although this concept was also supported by some experimental studies conducted on dogs [55], numerous laparoscopic and robotic surgeons used monopolar and bipolar energy for the NVB and reported good results [28,29]. Data coming from this systematic review showed significant advantages in terms of early potency recovery in favor of athermal dissection. However, conflicting results are available at longer follow-up in the comparative studies [38,41]. Taking into consideration all the potential methodological drawbacks, data coming from noncomparative studies showed better results in the series using athermal dissection. The good potency rates reported at 24-mo follow-up [25,26] and in the low-risk group according to the Briganti stratification [28] in the clipless series allow us to suppose that the potential damage produced by monopolar or bipolar dissection can be minimized with longer follow-up, particularly in younger patients. An unresolved critical issue relates to the level and the duration of energy used; these parameters are not reported in the description of the surgical technique.

Considering energy as a potential risk factor for nerve damage, Finley et al. evaluated the potential beneficial role of cold dissection of the cavernous nerves [40]. This technique is based on the use of cold irrigation and an endorectal cooling balloon cycled with 4 °C saline. The positive results reported by Finley et al. in terms of 12-mo potency rates should be reconfirmed by other authors, also taking into consideration the cost of the device.

Less relevant seems to be the effect of countertraction during cavernous nerve dissection. In their prospective comparative study, Kowalczyk et al. reported weak statistically significant advantages in favor of patients receiving a nerve-sparing technique without countertraction 5 mo after RARP. No significant differences were reported 12 mo after the procedure [32]. This study confirmed two aspects related to the nerve-sparing procedure: (1) the effect of mechanical trauma on the function of the cavernous nerves during the early follow-up and (2) the short time of this negative effect during the robotic procedure.

Concerning the methodological aspects, most of the evaluated studies used validated questionnaires to evaluate potency status during the follow-up. The impact of this methodological aspect was correctly evaluated by Shikanov et al. in 2009. Potency recovery rates at 3, 6, 12, and 24 mo were 44%, 50%, 62%, and 69%, respectively, using a validated questionnaire and 57%, 63%, 82%, and 93%, respectively, using the physician interview [25]. Heterogeneity was observed for the definition of potency. Most authors considered potent patients to be those with an erection sufficient for intercourse regardless of the use of phosphodiesterase type 5 inhibitors. Others used a more objective and reproducible definition represented by the SHIM score [22,23,28,34,35,37,41]. The SHIM cut-off value for *normal* is still an unresolved issue. Cut-off values ranging from 15 to 21 were reported [22,23,41]. The reported potency rate is strongly influenced by such parameters.

Until 2008, the promising potency outcomes of RARP were supported by only one prospective study comparing the robot-assisted approach with RRP. This study showed a statistically significant advantage in favor of RARP to reach potency recovery [17]. Similarly, only one study comparing RARP and LRP in terms of 3-mo potency rates showed better results for RARP (46% vs 36%) [20]. The current update of the previous systematic review allowed us to retrieve other studies comparing RARP and other surgical approaches. Although RCTs (level 2) were not available, this systematic review retrieved three new prospective studies comparing RARP and RRP (level 3) and another three studies using historical control series (level 4). Consequently, the present cumulative analysis of the literature showed, for the first time, significant advantages in terms of 12-mo potency recovery in favor of RARP as compared with RRP. Interestingly, 12-mo potency rates reported in the RARP arms of these comparative studies ranged from 55% to 81%, similar to those values reported in the noncomparative studies (ranging from 54% to 90%) (Tables 1 and 4). The only comparative study reporting potency outcomes at a longer follow-up confirmed a statistically significant advantage in favor of RARP [44].

Concerning the comparison between RARP and LRP, the present systematic review included one RCT (level 2) and three studies using historical control groups (level 4). The result of the RCT showed a significant advantage in favor of RARP in comparison with LRP [48]. However, our cumulative analysis was strongly influenced by the results of level 4 studies and showed only a nonstatistical trend in favor of RARP.

Some potential drawbacks must be taken into consideration. Similar to open and laparoscopic surgeons, robotic surgeons do not all have the same level of surgical ability, regardless of experience. Reaching an appropriate level of expertise could also require a different framework for each surgeon according to the different training programs. Therefore, other parameters that are difficult to extrapolate, such as looking at the available published data on surgeon and center volumes, could be considered potential drawbacks of this systematic review. Moreover, only few articles clearly reported information about the use of penile rehabilitation in the postoperative period. Therefore, it was not possible to have correct data stratification according to this important parameter.

From the methodological perspective, the most relevant limitations are represented by the quality of the available studies and by the definitions of potency. With the exception of a small RCT comparing RARP and LRP, all the other studies provided level 3 or 4 evidence. Concerning a definition of *potency*, most of the studies used the presence of an erection sufficient for intercourse as a definition of success. This definition is not very objective or reproducible. However, studies using the SHIM scores also suffered from a lack of standardization concerning the cut-off point. As recently proposed by Ficarra et al, a standardized classification distinguishing among patients with SHIM >17 without aids (P0), patients with SHIM >17 with phosphodiesterase type 5 inhibitors (P1), and patients with SHIM <17 and erections insufficient for intercourse (P2) should be strongly considered in future studies [56].

In this review we do not address outcomes related to sexual desire, ejaculatory dysfunction or retrograde ejaculation, or male infertility or sperm preservation. Moreover, data coming from population-based studies were not included in this systematic review because these studies were based on coding of erectile dysfunction and did not use standardized outcome definitions. Population-based studies also suffer from the lack of essential preoperative and intraoperative information, mainly concerning the nerve-sparing technique. In 2009, using a Surveillance Epidemiology and End Results registry cohort of patients who received radical prostatectomy (RP) between 2002 and 2005, Hu et al. reported a significantly higher prevalence of erectile dysfunction after minimally invasive RP (MIRP) in comparison with RRP; however, no differences were reported in the number of procedures performed to treat this complication [57]. In this population-based study, the comparison between the different approaches was significantly limited by the learning curve for MIRP. Recently, Barry et al. published a new population-based study analyzing 685 patients ($\geq$65 yr old) who were randomly selected by a nationwide sample of Medicare-age men who underwent RARP or RRP during 2008. A cross-sectional analysis performed 14 mo after surgery using a nonvalidated questionnaire showed similar results for the two techniques in terms of erectile function bother [58]. These conclusions are strongly limited by a number of significant limitations represented by patient age ($\geq$65 yr of age); impact of the learning curve for robotic surgeons; and absence of baseline functional, clinical, and bioptical data. Moreover, no information concerning the surgical technique was available, and only a nonvalidated questionnaire evaluating bother, rather than both function and bother, was administered [59]. In other words, data from this last-available population-based study are difficult to compare with data from comparative clinical studies.

5. Conclusions

Potency rates after RARP are influenced by numerous factors including baseline patient characteristics, nerve-sparing extension and techniques, definition of potency, and methods used to collect data. Our analysis showed a progressive increase in potency rates with follow-up after RP. Patient selection criteria and surgical techniques must be taken into consideration to attain excellent results after nerve-sparing RARP. Although the definition of *potency* remains a nonstandardized parameter, data from this systematic review highlighted a relevant improvement in the methodology used to evaluate potency recovery in the "robotic era," and well-conducted studies also seem to be associated with better results in terms of potency recovery. No definitive conclusions can be drawn concerning the use of energy during dissection of the cavernous nerves. Data coming from this systematic review support the cautery-free technique, but this aspect remains a relevant issue that needs further evaluation.

This update of previous systematic reviews of the literature showed, for the first time, that the cumulative analysis of available comparative studies demonstrates significant advantages in favor of RARP in comparison with RRP. Considering the limitations due to the limited number of patients included in the studies comparing RARP and LRP, a nonstatistically significant trend in favor of RARP was reported. These advantages are supported by the results of an RCT comparing the two laparoscopic techniques.

Author contributions: Vincenzo Ficarra had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Novara, Ficarra, Montorsi.
Acquisition of data: Novara.
Analysis and interpretation of data: Novara, Ficarra.
Drafting of the manuscript: Ficarra.
Critical revision of the manuscript for important intellectual content: Ficarra, Novara, Ahlering, Costello, Eastham, Graefen, Guazzoni, Menon, Mottrie, Patel, Van der Poel, Rosen, Tewari, Wilson, Zattoni, Montorsi.
Statistical analysis: Novara.
Obtaining funding: None.
Administrative, technical, or material support: Wilson, Rosen.
Supervision: Montorsi, Mottrie, Rosen, Wilson.
Other (specify): None.

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