



Comparison of retropubic, laparoscopic and robotic radical prostatectomy: who is the winner?

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Abstract

Purpose This study is a systematic analysis of the evidence regarding oncological, perioperative and postoperative outcomes and the cost of open retropubic radical prostatectomy (ORP), laparoscopic radical prostatectomy (LRP) and robotic-assisted laparoscopic radical prostatectomy (RALP).

Methods Summary data was abstracted from 104 original research articles representing 227,400 patients. PubMed/Medline, Scopus, Google Scholar, EMBASE and the Cochrane Library were reviewed in December 2016. A total of 104 publications were selected for inclusion. The primary outcomes were positive surgical margin (PSM) and major complication rate according to Clavien classifications. Secondary outcomes were operative time, length of hospital stay, estimated blood loss, transfusions, conversions, rate of post-operative erectile dysfunction and incontinence and total cost of procedure.

Results ORP had a significantly higher rate than RALP for PSM (OR: 1.18; 95% CI 1.05–1.32; $p = 0.004$), but the rate of PSM was not significantly different between ORP versus LRP (OR: 1.37; 95% CI 0.88–2.14; $p = 0.17$) and RALP versus LRP (OR: 0.83; 95% CI 0.40–1.72; $p = 0.62$). The major Clavien complication rate was significantly different between ORP and RALP (OR: 2.14; 95% CI 1.24–3.68; $p = 0.006$). Estimated blood loss, transfusions and length of hospital stay were low for RALP, moderate for LRP and high for ORP. The rate of erectile dysfunction (OR: 2.58; 95% CI 1.77–3.75; $p < 0.001$) and incontinence (OR: 3.57; 95% CI 2.28–5.58; $p < 0.001$) were significantly lower after RALP than LRP and equivalent for other comparisons. Total cost was highest for RALP, followed by LRP and ORP.

Conclusions For PSM and peri- and post-operative complications, RALP showed better results than ORP and LRP. In the context of the biases between the studies, one should interpret the results with caution.

Keywords Robotics · Laparoscopy · Retropubic · Prostatectomy · Complications · Prostate cancer · Margins

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Introduction

Prostate cancer is the second leading cancer-related cause of death: [1]. For decades, open radical prostatectomy (ORP) has been the reference standard for treatment of localized prostate cancer [2]. More recently, surgical approaches to prostate cancer treatment have been replaced by minimally invasive techniques such as laparoscopic radical prostatectomy (LRP) and robotic-assisted laparoscopic radical prostatectomy (RALP) [3]. Minimally invasive approaches report improved post-operative outcomes with shorter recovery times and hospital stays and provide equivalent functional results [2, 4, 5].

Thus far, no difference in oncological outcomes has been demonstrated between RALP and ORP. Recent meta-analysis concluded that the positive surgical margin (PSM)

was similar, regardless of technique [6]. There is an ongoing debate concerning real improvements for minimally invasive surgeries over the open approach because of the additional costs linked with the generalization of these procedures [7]. The present study conducted a systematic literature review to determine the current position of open, laparoscopic and robotic radical prostatectomy.

Methods and materials

A systematic literature review was performed in December 2016 in multiple databases. The study design, search strategy, data abstraction and excluded studies were determined using Preferred Reporting Items for Systematic Reviews and Meta-analyses criteria (www.prisma-statement.org) (Table 1; Fig. 1). The items retrieved were restricted to publications in English.

Original research articles reporting on primary treatment of localized prostate cancer were included. The reference lists of prostatectomy review/meta-analysis articles that included articles not already in our database was also reviewed [8–11]. Conference abstracts were not included because they lacked detail and had not undergone rigorous peer review. The level of evidence of the studies included was rated according to criteria by the Center for Evidence-Based Medicine (<http://www.cebm.net>).

To assess the methodological quality of the studies included, they were initially reviewed by two independent reviewers using total quality assessment (QAS) (Table 1S). Although the QASs were reported for each study, they were not used to weigh the studies in the meta-analysis.

The same authors independently extracted the data, which were later jointly reviewed to reach agreement that the data was accurate. If disagreement existed, it was resolved by consensus or consultation with the senior authors. The data collected from all manuscripts regarding treatment groups included the radical prostatectomy surgical approach (retropubic open, laparoscopic, robotic), type of publication (retrospective, non-randomized trial or randomized trial), publication year (2002–2016; Fig. 1S), duration of follow-up, patient characteristics (number, age, preoperative Gleason score ≥ 8 and clinical stage; Table 2S), primary PSM rates, total intra- and perioperative major Clavien complication rates [12] and secondary outcomes (mean operative time, length of hospital stay, estimated blood loss, blood transfusions, rate of post-operative erectile dysfunction (definition: capability to achieve a spontaneous erection and/or maintain an erection adequate for intercourse after at least 12 month follow-up) and incontinence, conversion to ORP and total cost of procedure; Table 2S).

Statistical methods

Review Manager version 5.2 (downloaded from <http://community.cochrane.org/tools/review-production-tool/revman-5>) was used to analyze the selected studies. Continuous data for each arm of a particular study were expressed as mean and standard deviation (SD). Dichotomous data was expressed as proportions or risks and the treatment effect was reported as odds ratios (OR) with a 95% confidence interval (95% CI). To use all data, if only median and range were reported in an article, the median was substituted for the mean when the sample size was greater than 25. For range/4 [for moderately sized samples ($15 < n \leq 70$)] or range/6 [for large samples ($n > 70$)], SD was reported as in Hozo et al. [13].

Heterogeneity between studies was assessed using the Chi squared test and I^2 statistic. A p value of < 0.1 and an I^2 value $> 50\%$ were considered suggestive of statistical heterogeneity, prompting a random-effects modeling estimate. A non-significant Chi squared test result ($p \geq 0.1$ and $I^2 \leq 50\%$) suggested that there was no evidence of heterogeneity and a random-effect model was used. Funnel plots were constructed for the outcomes to assess publication bias, which is defined as the tendency not to publish studies with a negative result. The more asymmetric the funnel plot was, the higher the potential bias was. Statistical significance was set at $p < 0.05$.

Results

This systematic review and meta-analysis included 227,400 patients, 86,568 undergoing ORP, 22,177 undergoing LRP and 118,655 undergoing RALP. There were differences in the number of publications over time ($p < 0.0001$). In particular, a statistically significantly greater proportion of ORP versus LRP studies appeared in early publications (2002–2009; Fig. 1S).

Of the preoperative data, there were significant differences in preoperative clinical stages between studies (ORP: T1 61.1%; T2 34.3%; T3 4.5%, LRP: T1 57.4%; T2 38.7%; T3 3.7% and RALP: T1 71.3%; T2 26.5%; T3 2.1%, $p < 0.0001$). There were also significant differences in the percentage of high-grade disease found in preoperative biopsies (Gleason score > 7) in the different surgical approaches (ORP: 13.1%; LRP: 6.4%; RALP: 8.3%; $p < 0.001$).

In regard to stage by stage comparison of preoperative data, we sub-grouped the clinical stages into two groups as followed: Stage I and II (in which the tumor is limited into the prostate); and stage III and IV (in which the tumor

Table 1 Study design

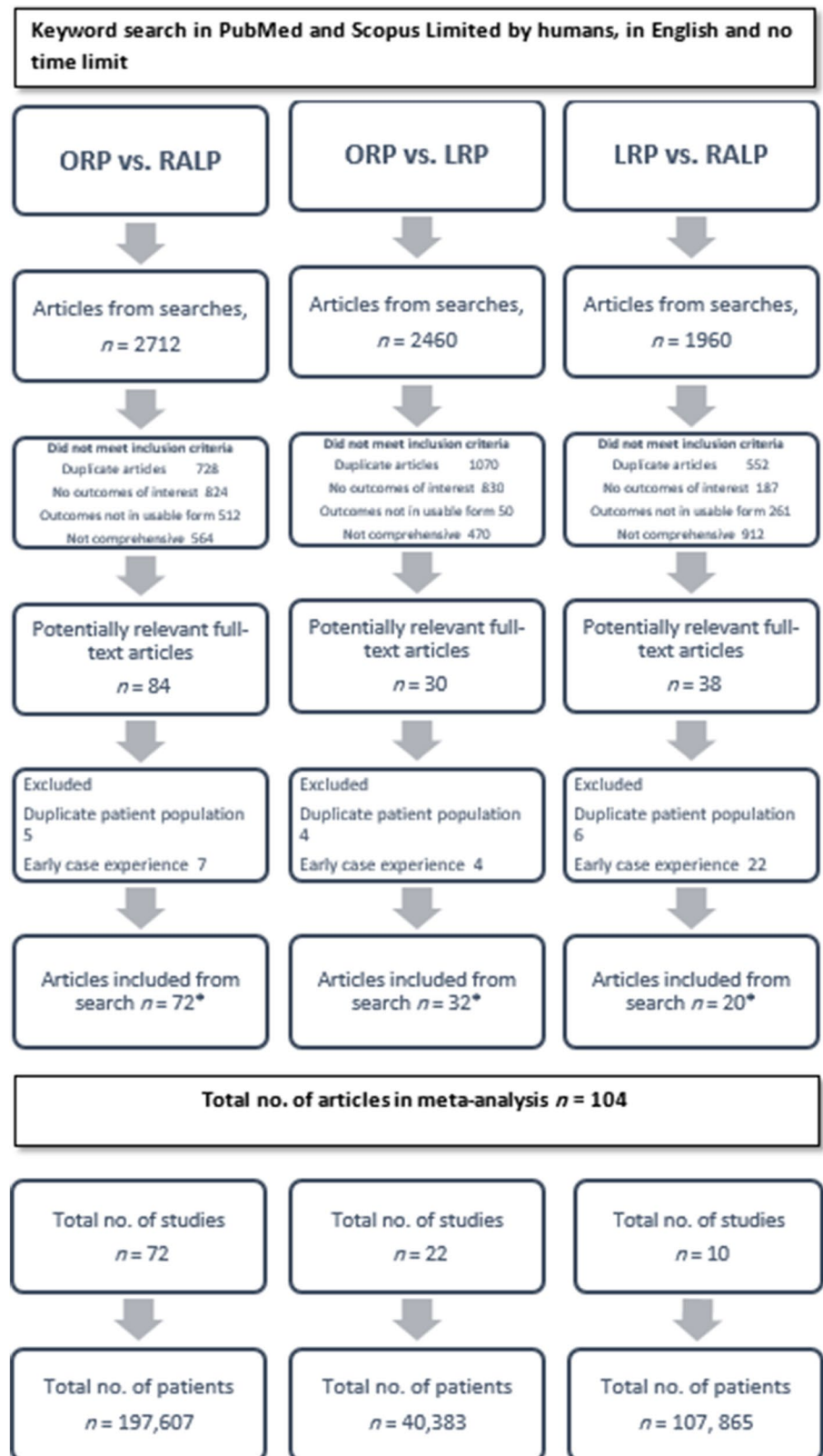
Patients	Patients underwent ORP, LRP, or RALP for the primary treatment of localized prostate cancer
Literature search	Keyword search in PubMed, Google scholar and Scopus
Databases	Pubmed, Ovid, MEDLINE, EMBASE, the Cochrane Controlled Trials Register, HealthSTAR, CINAHL, Google, and Google Scholar
Limits	Only comprehensive articles without time limit Humans In english Reported complications as Clavien classification
Keywords	Retropubic radical prostatectomy Open prostatectomy RRP, ORP Laparoscopic assisted radical prostatectomy Laparoscopic radical prostatectomy LRP Endoscopic extraperitoneal radical prostatectomy EERPE Robotic assisted radical prostatectomy Robotic assisted laparoscopic prostatectomy RALP
Eligibility criteria	Article in Full-text (no abstracts) Unique publication (no duplicate articles) Reported each of the interested outcomes (surgical margins, mean operative time, Mean hospital stay, Mean estimated blood loss, Transfusion rate, Erectile dysfunction rate, major Clavien complication rate, incontinency rate, conversion to open and cost) Original report as determined from reading the abstract or if necessary the full text Outcome reported in a usable form (each surgical approach was reported as a separate cohort, no additional confounding treatments, no missing or unreliable data; could not have >10% difference in values between text and tables Reported on surgical approaches of interest (no perineal prostatectomy)
Exclusion criteria	Duplicate patient population, where some or all of the same patients were included in a different study reporting on the same parameters (prevents double counting) Early case experience (prevents bias toward approaches with more experienced surgeons)
Data abstraction	Articles needed to report which contain each of outcome of interest to be included in the analysis. Data were abstracted by two individuals into a custom database table including list of variables. 50% of articles were abstracted by one reviewer and other 50% with other one. The data for 50% of the articles was double-entered by a second individual, and any discrepancies were resolved through repeated review and discussion prior to data analysis. All primary outcomes were then double-checked and any discrepancies resolved Variables in four types were abstracted from each study: those necessary to determine inclusion and exclusion criteria, surgical approach, baseline patient characteristics, and clinical outcomes In order to use all data as possible, if only median and range were reported in an article, we substituted the median for the mean (if sample size was greater than 25), and the Range/4 (for moderately sized samples (15 <n ≤ 70)) or Range/6 (for large samples (n > 70)) for the standard deviation All studies were reviewed by two independent reviewers using the total quality assessments (QASs) (Table 2) to assess the methodological quality of the studies that were included. Although the QASs were reported for each study, they were not used to weight the studies in the meta-analysis.
Primary outcomes	Positive surgical margins Total intraoperative and total perioperative major complication rates according to Clavien classification (grade ≥ III)
Secondary outcomes	Operative time Length of hospital stay Estimated blood loss Blood transfusion rates Conversion to open rate Erectile dysfunction rate Incontinency rate cost
Controls for differences in complication reporting	Calculated complication rate based on Clavien classification criteria rather than using author-provided complication rates
Controls for Publication bias	Performed a funnel plot analysis

HIFU high-intensity focused ultrasound, *PSM* positive surgical margin, *ORP* open retropubic radical prostatectomy, *RALP* robot-assisted laparoscopic prostatectomy, *LRP* laparoscopic radical prostatectomy, *RRP* retropubic radical prostatectomy

invades to adjusted organs). The results showed significant difference between ORP and RALP in frequencies of Stage I and II ($p < 0.001$) and Stage III and IV ($p < 0.001$) between the studies (Fig. 10S). Nevertheless, no significant

differences were found between ORP and LRP (stage I and II: $p = 0.64$ and stage III and IV: $p = 0.33$) and RALP and LRP (stage I and II: $p = 0.34$ and stage III and IV: $p = 0.30$) due to rates of tumor stages.

Fig. 1 Flowchart outlining the literature search and article evaluation process. * Included the studies which compared each three surgical methods (ORP vs. LRP vs. RALP)



Open versus robotic-assisted laparoscopic radical prostatectomy

There were significant heterogeneities between studies in PSM ($I^2 = 78\%$; $p < 0.001$), rate of major post-operative Clavien complications ($I^2 = 78\%$; $p < 0.001$), operative time ($I^2: 100\%$, $p < 0.001$), length of hospital stay ($I^2 = 100\%$; $p < 0.001$), estimated blood loss ($I^2 = 99\%$; $p < 0.001$), blood transfusion rate ($I^2 = 90\%$; $p < 0.001$), rate of erectile dysfunction ($I^2 = 84\%$; $p < 0.001$) and incontinence ($I^2 = 61\%$; $p = 0.002$), total cost of procedure ($I^2 = 100\%$; $p < 0.001$). Therefore, random effects were used to analyze these outcomes.

Positive surgical margins were significantly higher in ORP than RALP (OR: 1.18; 95% CI 1.05–1.32; $p = 0.004$; Fig. 2). Higher significant rate of major post-operative Clavien complications was detected for ORP than RALP (OR: 2.14; 95% CI 1.24–3.68; $p = 0.006$; Fig. 2S).

In order to compare mean operative time, higher significant operative time was found for RALP than ORP (mean difference: -44.41 min; 95% CI -64.79 to -24.02 ; $p < 0.001$; Fig. 3S).

In order to comparison of ORP with RALP, there were longer hospital stays (mean difference: 1.20 day; 95% CI 0.66–1.75; $p < 0.001$; Fig. 4S), higher blood loss (mean difference: 473.46 ml; 95% CI 424.67–522.24; $p < 0.001$; Fig. 5S), higher rate of blood transfusion (OR: 6.18; 95% CI 4.37–8.74; $p < 0.001$; Fig. 6S) and lower total cost of procedure (mean difference: $-\$4727.36$; 95% CI -6487.89 to -2926.83 ; $p < 0.001$; Fig. 9S) for ORP over RALP.

There was no significant difference between approaches in regard to rates of erectile dysfunction (OR: 1.12; 95% CI 0.75–1.66; $p = 0.57$; Fig. 7S) and incontinence (OR: 1.20; 95% CI 0.87–1.64; $p = 0.26$; Fig. 8S).

Considering of design weight in final analysis

The Yaxley study [14] is the only randomized controlled trial comparing open and robotic prostatectomy. This is a well-conducted study which is weighted only 1.6% in the review. We re-analyzed the outcomes due to giving more design weight (approximately 3.8%) to this study. There was a significant difference in order to PSM between ORP and RALP (OR: 1.07; 95% CI 0.85–1.12; $p = 0.02$). Higher significant rate of major post-operative Clavien complications (OR: 1.84; 95% CI -1.34 to 2.54; $p = 0.003$) for ORP than RALP, longer mean operative time for RALP than ORP (mean difference: -42.01 min; 95% CI -54.16 to -22.12 ; $p < 0.001$), longer hospital stays (mean difference: 1.30 day; 95% CI 0.71–1.72; $p < 0.001$); higher blood loss (mean difference: 443.16 ml; 95% CI 404.01–515.34; $p < 0.001$) and higher rate of blood transfusion (OR: 5.28; 95% CI 3.91–8.93; $p < 0.001$) for ORP than RALP.

Open versus laparoscopic radical prostatectomy

Table 2 shows the rate of heterogeneity and meta-analysis of the data. LRP was associated with a longer operative time and hospital stay, lower blood loss and higher rates of blood transfusion. PSM, rate of major complications and post-operative rates of erectile dysfunction and incontinence were comparable between approaches. LRP had a higher total cost than ORP.

Laparoscopic versus robotic-assisted laparoscopic radical prostatectomy

LRP is associated with longer hospital stays, greater blood loss, total cost and post-operative rate of erectile dysfunction and incontinence (Table 2). PSM, rate of major complication, operative time and need for blood transfusions was comparable between approaches. Table 3 lists the results of the meta-analysis of open, robotic and laparoscopic radical prostatectomy over time. The rates of PSM, major complications, erectile dysfunction and incontinence over time are shown in Fig. 3.

Discussion

This study is the largest compilation of comprehensive studies on radical prostatectomy patients to date. It is a systematic review and meta-analysis of this large body of literature. Due to the lack of randomized clinical trials (only one RCT exist [14]), differences in patient characteristics between the surgical cohorts could explain differences in outcomes between treatment groups. These differences cannot be fully corrected by statistical methods. Additionally, unknown differences in the attributes of the patients and physicians and/or the treatments administered could contribute to the highly heterogeneous outcomes between studies. Caution is advised when interpreting the findings of this meta-analysis within the context of the considerations just described. The large number of patients included in the meta-analysis means that the statistically significant results may not necessarily be clinically meaningful.

Traditionally, open radical prostatectomy was the treatment of choice for localized prostate cancer. Over the last two decades, surgical approaches have tended toward endoscopic and minimally invasive surgery such as LRP or RALP. The efficacy and safety of LRP has been questioned because of concerns about its technical difficulty, risk of complications and undefined benefits over open surgery. Previous studies have shown the rate of PSM to be 10–23% for ORP and 9–26% for LRP [14–21]. The results of the current study agree with these results and show no significant difference between ORP and LRP for PSM. Nevertheless,

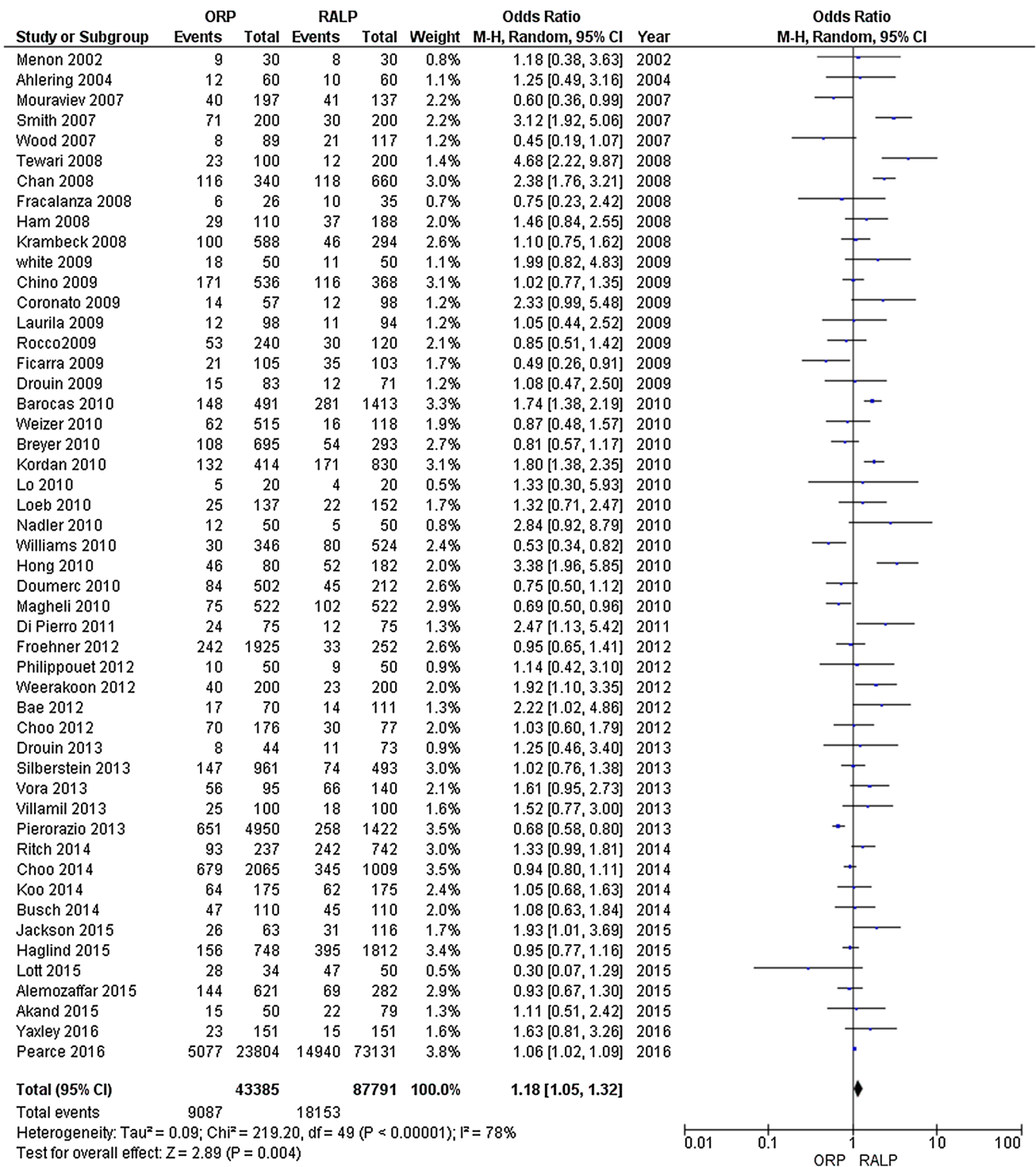


Fig. 2 Forest plot of included studies which comparing positive surgical margin in open versus robotic-assisted laparoscopic radical prostatectomy

ORP has been associated with higher rates of transfusion and longer catheterization and hospital stays. These results have been confirmed by the results of the current study and of other studies [5, 15, 16, 22, 23].

Rassweiler et al. [5] reported a higher incidence of rectal injury in LRP over ORP (1.8 and 3.2%, respectively) and urinary leakage (0.5 and 2.3%, respectively). An increase in lymphoceles (6.9 and 0%, respectively), wound infection

Table 2 heterogeneity and meta-analysis the outcomes

Outcome	Heterogeneity		Meta-analysis (fixed or random effect)		
	I^2 (%)	<i>P</i> value	OR/mean difference	CI 95%	<i>P</i> value
ORP vs. LRP					
PSM	94	< 0.001	1.37	0.88 to 2.14	0.17**
Major Clavien complication	76	< 0.001	1.73	0.82 to 3.64	0.15**
Operative time (min)	99	< 0.001	– 65.16	– 85.25 to – 45.06	< 0.001**
Length of hospital stay (day)	100	< 0.001	1.82	1.04 to 2.60	< 0.001**
Estimated blood loss (ml)	99	< 0.001	529.39	348.26 to 710.52	< 0.001**
Transfusion	90	< 0.001	5.67	03.42 to 9.38	< 0.001**
Erectile dysfunction	27	0.24	1.25	0.97 to 1.60	0.09*
Incontinency	77	< 0.001	1.04	0.71 to 1.51	0.85**
Total cost (\$)	100	< 0.001	– 1996.13	– 3571.62 to – 420.65	0.01**
LRP vs. RALP					
PSM	96	< 0.001	0.83	0.40 to 1.72	0.62**
Major Clavien complication	70	0.002	1.2	0.52 to 3.02	0.61**
Operative time (min)	96	< 0.001	12.92	0.17 to 25.67	0.05**
Length of hospital stay (day)	96	< 0.001	0.64	0.19 to 1.09	0.006**
Estimated blood loss (ml)	93	< 0.001	136.89	55.47 to 218.32	0.001**
Transfusion	69	< 0.001	1.32	0.68 to 2.56	0.69**
Erectile dysfunction	0	0.84	2.58	1.77 to 3.75	< 0.001*
Incontinency	0	0.43	3.57	2.28 to 5.58	< 0.001*
Convert to open	16	0.31	7.42	6.49 to 8.48	< 0.001*
Total cost (\$)	100	< 0.001	– 1290.70	– 1732.67 to 848.73	< 0.001**

ORP open radical prostatectomy, LRP laparoscopic radical prostatectomy, RALP robotic-assisted laparoscopic radical prostatectomy, CI confidence interval, PSM positive surgical margin

*Fixed effect analysis; **Random effect analysis

(2.3 and 0.5%, respectively), embolism/pneumonia (2.3 and 0.5%, respectively) and anastomotic strictures (15.9 and 6.4%, respectively) for ORP over LRP. Roumeguere et al. [24] postulated that this difference held true only for minor complications and both approaches experienced similar major complications (5% for ORP and 2.4% for LRP). Recent studies have shown the complication rate to be similar between these surgical methods [18]. This may be the result of the increase in experience and standardization of the approaches.

The previous studies for cohort design indicated several biases related to design. Guazzoni et al. [16] randomized 120, consecutive, age-matched patients into ORP ($n = 60$) and LRP ($n = 60$) groups. They showed the operating time was significantly shorter and blood loss and use of analgesia were significantly higher for the ORP group over the LRP group. The overall percentage of post-operative complications and positive margins were comparable. The current results were in agreement with this study.

Post-operative continence and potency are very important aspects, especially for the patient. Comparative studies reported the rate of post-operative continence to be 47–91% in ORP compared to 40–97% in LRP [5, 15, 18,

22, 25]. The potency rate was estimated to be 44–72.4% after ORP and 41–58% after LRP [15, 18].

The cost difference between studies was evaluated by Al-Shaji et al. [26]. They found that LRP costs are slightly lower than those for ORP. This may be because the longer operative time and disposable instrument expenses are offset by the shorter hospital stay, fewer blood transfusions and lower analgesic requirements for the LRP group. A recent study reported a higher total cost for LRP than ORP [27], possibly because of differences in hospital protocol.

Previous studies showed few advantages for LRP over ORP. The factors limiting the performance of LRP are the lack of 3D visualization and loss of freedom of motion using the robot in the laparoscopic approach. Menon et al. [28] showed that RALP is a longer procedure than ORP; however, blood loss is minimal and patients feel less pain and can be discharged from the hospital sooner. These results have been confirmed by other studies [29–36]. Wood et al. [30] found no difference between ORP and RALP for median time to normal activity, 100% activity, and time to driving. The results of the current study are in agreement with their findings.

Table 3 Comparison of Open vs. Robotic vs. Laparoscopic radical prostatectomy in order to time distribution

	2000–2005	2006–2009	2010–2013	2014–2016
ORP vs. RALP				
Mean operative time (min)	– 82.76 [– 213.09, 47.57], 0.21	– 51.18 [– 71.44, – 30.93], < 0.001	– 36.10 [– 78.75, 6.55], 0.1	– 41.33 [– 82.98, 0.31], 0.05
Mean hospital stay (days)	0.97 [0.58, 1.36], < 0.001	0.77 [– 0.26, 1.81], 0.14	1.86 [0.92, 2.80], < 0.001	1.22 [0.09, 2.35], 0.03
Mean estimated blood loss (ml)	466.60 [147.91, 785.30], 0.004	505.05 [357.76, 652.33], < 0.001	567.19 [385.17, 749.21], < 0.001	425.56 [174.45, 676.68], 0.0009
Transfusion rate	25.59 [0.42, 1541.77], 0.12	6.86 [2.93, 16.06], < 0.001	4.15 [2.41, 7.15], < 0.001	11.84 [10.68, 13.12], < 0.001
Erectile dysfunction rate	–	1.69 [0.96, 2.95], 0.07	1.30 [0.81, 2.10], 0.28	0.54 [0.21, 1.40], 0.21
Incontinuity rate	–	1.93 [0.87, 4.28], 0.11	1.11 [0.53, 2.32], 0.78	0.85 [0.71, 1.00], 0.05
Major Clavien complication rate	–	0.55 [0.14, 2.14], 0.39	1.73 [1.01, 2.95], 0.05	5.94 [2.42, 14.58], < 0.001
Positive surgical margin	1.22 [0.60, 2.50], 0.59	1.26 [0.90, 1.75], 0.17	1.22 [0.97, 1.53], 0.08	1.04 [0.95, 1.14], 0.36
ORP vs. RLP				
Mean operative time (min)	– 95.74 [– 125.49, – 66.00], < 0.001	– 53.38 [– 79.62, – 27.15], < 0.001	– 49.43 [– 61.50, – 37.35], < 0.001	–
Mean hospital stay (days)	2.40 [– 0.36, 5.17], 0.09	1.29 [1.15, 1.44], < 0.001	1.48 [0.11, 2.85], 0.03	1.74 [0.14, 3.33], 0.03
Mean estimated blood loss (ml)	538.63 [– 59.97, 11.37.23], 0.08	579.52 [306.28, 852.76], < 0.001	396.66 [– 2.92, 796.23], 0.05	–
Transfusion rate	3.94 [0.98, 15.82], 0.05	5.23 [1.92, 14.27], 0.001	13.19 [4.31, 40.40], < 0.001	5.37 [2.26, 12.77], 0.0001
Erectile dysfunction rate	1.13 [0.70, 1.84], 0.62	1.00 [0.68, 1.46], 0.99	–	–
Incontinuity rate	1.20 [0.81, 1.76], 0.36	1.05 [0.46, 2.38], 0.91	–	–
Major Clavien complication rate	1.65 [0.50, 5.44], 0.41	1.16 [0.36, 3.68], 0.81	–	3.19 [0.40, 25.62], 0.27
Positive surgical margin	1.26 [0.98, 1.62], 0.07	1.34 [0.83, 2.16], 0.24	2.35 [0.67, 8.25], 0.18	0.94 [0.72, 1.23], 0.66
RLP vs. RALP				
Mean operative time (min)	– 11.34 [– 21.12, – 1.56], 0.02	43.99 [19.67, 68.31], 0.0004	19.63 [– 64.41, 103.67], 0.65	1.00 [0.88, 1.11], < 0.0001
Mean hospital stay (days)	–	1.10 [0.15, 2.06], 0.02	0.47 [– 0.09, 1.03], 0.10	0.72 [– 0.28, 1.72], 0.16
Mean estimated blood loss (ml)	23.03 [– 202.15, 248.21], 0.84	246.27 [28.24, 464.31], 0.03	327.93 [– 222.15, 878.01], 0.24	–
Transfusion rate	0.57 [0.07, 4.73], 0.60	1.18 [0.45, 3.12], 0.74	1.18 [0.13, 10.98], 0.89	2.24 [0.80, 6.26], 0.13
Erectile dysfunction rate	–	–	2.79 [1.79, 4.33], < 0.001	–
Incontinuity rate	–	–	4.61 [2.62, 8.13], < 0.001	–
Major Clavien complication rate	–	1.12 [0.41, 3.08], 0.82	0.28 [0.01, 7.12], 0.44	2.36 [0.80, 6.95], 0.12
Positive surgical margin	0.96 [0.50, 1.81], 0.89	1.14 [0.61, 2.12], 0.69	0.58 [0.17, 1.96], 0.38	1.08 [0.84, 1.38], 0.55

Results are presented as Mean [confidence interval], *P* value

ORP open retropubic radical prostatectomy, RALP robot-assisted laparoscopic prostatectomy, LRP laparoscopic radical prostatectomy

The PSM has been shown to be 9–39% in RALP and was comparable between groups in most studies [19, 28, 32, 35, 37–43]. Yaxley et al. [14] conducted a randomized clinical trial with 326 patients who were randomly divided into ORP ($n = 151$) and RALP ($n = 157$) groups. Equivalence testing of PSM between groups [15 (10%) in ORP and 23 (15%) in RALP] showed similarity between the two techniques.

In the current study, a comparison of ORP and RALP for PSM showed significant differences, with higher rates for ORP. This result contrasts with that of Tewari et al. [44], who

showed that, after propensity adjustment, the only significant differences were lower PSM rates for RALP compared with LRP. This difference may result from the high sample size of studies published after 2013 included in the meta-analysis [14, 45]. The current results are not in agreement with one randomized trial which compared ORP with RALP and showed no significant difference in PSM [14]. This may be because methods of detecting PSM vary depending on the pathologist's experience and, in some cases, interpretation can be difficult and result in over-diagnosis [46]. It is also

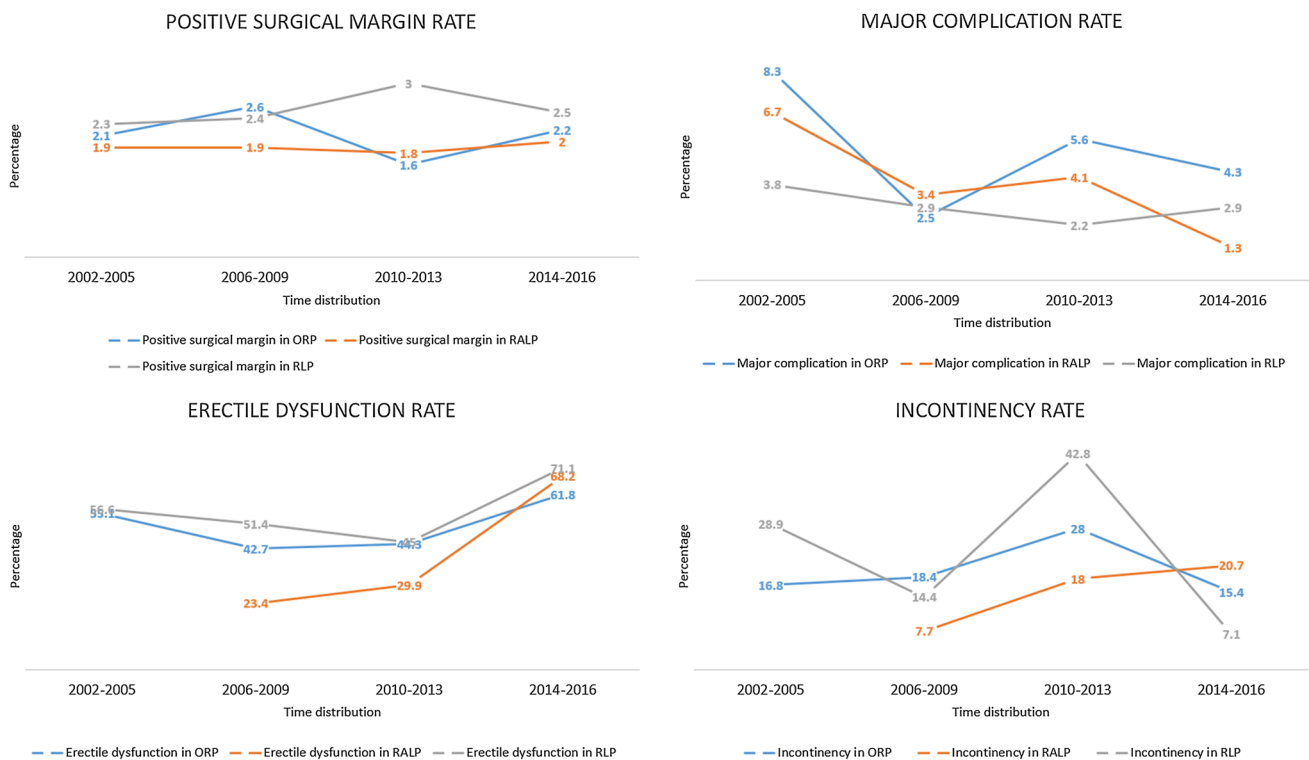


Fig. 3 The incidences of positive surgical margin, Major complication rate, erectile dysfunction and incontinency rate in order to time span of study publication

accepted that patients with extracapsular extension (pT3) have an increased risk of PSM; however, in RCT, the overall PSM for pT3 tumors was 10%, although the small sample size meant they could not be further analyzed.

Studies show that overall post-operative complications were similar between RALP and ORP [19, 28, 32, 37–42]. Krambeck et al. [31] postulated that wound herniation was more common after RALP (1.0% for RALP and none for ORP) and development of bladder neck contracture was more common after ORP. A recent study [47] showed that major complications (Clavien grade III–IV) were less common in the RALP group than in the ORP group (3.4 and 7.6%, respectively). These complications could lead to readmission. The results of the current study were similar and found that major complication rates were significantly higher in ORP over RALP.

Yaxley et al. [14] conducted a randomized clinical trial and showed that urinary function and sexual function scores did not differ significantly between the two methods. The rate of post-operative continence was estimated to be 76–95% [31, 32, 34, 39, 40, 42, 48, 49]. Son et al. [49] showed that of the factors affecting cessation of pad use, only operating method, age and membranous urethral length were significant. The current study found no significant differences in incontinence rates between ORP and RALP. This may be because of differences in patient age between studies,

different urethral length retained and the type of questionnaire used to evaluate the post-operative contingencies.

The overall rate of post-operative potency in RALP was reported to be 31–70% [32, 34, 35, 39, 42, 43, 48]. In the results of an inter-subgroup analysis [42], recovery of potency was more rapid in patients who underwent RALP for a small-volume prostate than for those who underwent ORP for a small-volume prostate (3 months: 24 vs. 0%; 6 months: 36 vs. 10%). Patients who underwent RALP for a large-volume prostate were less likely to recover continence than those patients who underwent ORP for a large-volume prostate (97 vs. 88%).

RALP is associated with substantially higher operative and total hospital charges in addition to capital expenses incurred by the hospital in acquiring and maintaining the robotic system. The operative charges decreased substantially (27%) once the learning curve had been overcome [50]. In another single-institution analysis, the total actual costs associated with RALP were significantly greater than those for ORP and could be attributed to the robotic equipment and supplies [51].

LRP and RALP are the members of the same family. Studies have demonstrated that extra peritoneal LRP is non-significantly better than RALP in the hands of a skilled laparoscopic urological surgeon with respect to operative time, operative blood loss, hospital stay and length of bladder

catheterization [52, 53]. Nevertheless, Hakimi et al. [54] showed significant differences in LRP compared to RALP with regard to operative time, intraoperative blood loss, and length of stay. This can be explained by differences in surgeon experience and limitations in the studies. Porpiglia et al. [55] randomized 120 patients into LRP ($n = 60$) and RALP ($n = 60$) groups and showed no differences in terms of perioperative and pathologic results, complication rate, or PSM measurements. The current study found that RALP was associated with lower estimated blood loss and length of hospital stay. This difference may stem from different levels of surgical experience over time. Most studies which compared LRP and RALP found more experience with LRP and less experience with RALP, but that over time, the outcomes were better with RALP. The current study found that over time (Fig. 3), major complication rates decreased with RALP but were steady between 2006 and 2009 and 2014 and 2016.

The continence rate was found to be higher for RALP group at every time point. Continence after 3 months was 80% in the RALP group and 61.6% in the LRP group. After 1 year, the continence rate was 95.0 and 83.3%, respectively. Among preoperative potent patients treated with nerve-sparing techniques, the rate of erection recovery was 80.0 and 54.2%, respectively.

Overall PSM was estimated to be 13–77% [52, 53, 55–57] and was comparable between approaches [52, 58, 59]. The current results were in agreement with these studies; however, in a non-randomized study, Magheli et al. [56] found a higher overall PSM rate for the RALP group compared to the LRP group. There was no difference with respect to biochemical recurrence-free survival between groups.

The rates of post-operative continence and potency were comparable between approaches at 82–95% for continence and 56–80% for potency in LRP [53–55]; however, analysis showed that incontinence and erectile dysfunction was significantly lower in RALP compared with RLP. These differences could result from factors affecting post-operative continence and potency and the assessment tools used.

After analysis using preoperative data, it is clear that significant differences existed between studies in the preoperative clinical stages. Pathology has changed, evolved over time and this may favor the results of more recent studies, which indicates possible bias in comparison of PSM between studies.

As for PSM, different major Clavien complication rates were found only with comparison of ORP and RALP and not for other comparisons. The complications included in this meta-analysis were abstracted from articles that reported them using a standardized method such as the Clavien classification system [12]; therefore, it is not possible that differential reporting of complications affected the findings. It could also be the reason for the difference in findings

compared to other recent meta-analyses [38]. With the increased use of robots in urological surgery, surgeon experience has increased and the expected lower rate of complications in recent studies could weigh the current meta-analysis.

Studies were analyzed for timespan distribution of publications with regard to comparison of the outcomes of the three surgical approaches. The analysis showed that earlier studies favored ORP and more recent studies favored RALP. This could be because of greater surgeon experience with ORP than LRP in earlier studies and, more recently, with RALP.

Centralization of the care of prostate cancer has resulted in better outcomes. This is often not captured in the studies, therefore, the incidence of complications, PSM, continence and erectile dysfunction for different procedures were assessed with regard to the timespan of the publication. Nevertheless, the graphs showed no predictable trend and the incidence of the outcomes did not follow the same pattern. This could result from the use of different questionnaires to evaluate erectile dysfunction and incontinence and the factors that affected the PSM report.

This meta-analysis had the largest sample size of comprehensive studies that compared the three surgical methods for radical prostatectomy in many outcomes. Nevertheless, there were some limitations. The study only included retroperic OP and not studies which evaluated perineal OP. Only English literature was included and only included extraperitoneal LRP studies were examined. Studies which did not determine the mean and SD were estimated from the median and range, which may have slightly differed from the real numbers. The included studies reported different definitions for erectile dysfunction, incontinence and operative time. Therefore, we just analyzed the report of the authors for these outcomes and determining standard definitions for future study are warranted.

Conclusion

Our study showed RALP showed obviously better results than ORP and LRP for PSM and peri- and post-operative complications. Nevertheless, LRP and ORP had comparable outcomes.

In the context of the considerations just described, one should interpret this meta-analysis with caution. The quality of the results of systematic reviews and meta-analyses depend on the quality of the studies included. Sylvester et al. [60] described the ways to resolve discrepancies when findings from RCTs and meta-analyses disagree and showed a correlation between methodological quality and discrepancies in the results of large and small studies included in a meta-analysis. As the quality of the studies included in the current analysis were evaluated by questionnaire, it showed

that some studies were not of good quality and also most of the outcomes were not evaluated clinically stage by stage for these three approaches. Therefore, a well-powered study with a good volume of candidate articles is suggested to better evaluate the outcomes of the three surgical approaches especially with the help of International Prostate Cancer Outcomes Registry such as Prostate Cancer Outcomes Registry-Australia and New Zealand (PCOR-ANZ) [61]. Also, to avoid the heterogeneity of future studies to be compared, a standardized international protocol for this type of research could be drafted (by CROES for example) to facilitate the comparison of future similar studies.

Author contributions AB: Protocol/project development; data collection or management. JJR: protocol/project development; data collection or management. ST: protocol/project development; data collection or management, manuscript writing/editing. HHW: manuscript writing/editing, data analysis. MPL: manuscript writing/editing, data analysis. HS: protocol/project development; data collection or management, manuscript writing/editing.

Compliance with ethical standards

Conflict of interest No conflict of interest existed.

Research involving human participants and/or animals The data was gathered as systematic review and no human/animal was involved.

Informed consent The data was gathered as systematic review and no human/animal was involved.

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