



Robotic-assisted versus open simple prostatectomy: Results from a systematic review and meta-analysis of comparative studies

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Purpose: To review safety and efficacy of robotic-assisted simple prostatectomy (RASP) compared to open simple prostatectomy (OP).

Materials and Methods: A comprehensive literature search was performed to assess the differences in perioperative course and functional outcomes in patients with benign prostatic hyperplasia and surgical indication. The incidences of complications were pooled using the Cochran–Mantel–Haenszel Method and expressed as odds ratio (OR), 95% confidence interval (CI), and p-values. Perioperative course and functional outcomes were pooled using the inverse variance of the mean difference (MD), 95% CI, and p-values. Analyses were two-tailed and the significance was set at $p < 0.05$.

Results: Eight studies were accepted. Meta-analysis showed significantly longer surgical time (MD, 43.72; 95% CI, 30.57–56.88; $p < 0.00001$) with a significantly lower estimated blood loss (MD, -563.20; 95% CI, -739.95 to -386.46; $p < 0.00001$) and shorter postoperative stay (MD, -2.85; 95% CI, -3.72 to -1.99; $p < 0.00001$) in RASP. Catheterization time did not differ (MD, 0.65; 95% CI, -2.17 to 3.48; $p = 0.65$). The risk of blood transfusion was significantly higher in OP (OR, 0.23; 95% CI, 0.17–0.33; $p < 0.00001$). The risk of re-catheterization (OR, 1.96; 95% CI, 0.32–11.93; $p = 0.47$), postoperative urinary infections (OR, 0.89; 95% CI, 0.23–3.51; $p = 0.87$) and 30-day readmission rate (OR, 0.96; 95% CI, 0.61–1.51; $p = 0.86$) did not differ. At 3-month follow-up, functional outcomes were similar.

Conclusions: RASP demonstrated a better perioperative outcome and equal early functional outcomes as compared to OP. These findings should be balanced against the longer operative time and higher cost of robotic surgery.

Keywords: Patient outcome assessment; Postoperative complications; Prostatectomy; Prostatic hyperplasia; Robotic surgical procedures

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INTRODUCTION

Open simple prostatectomy (OP) for benign prostatic hyperplasia (BPH) was first described by Fuller in 1885 and Freyer in 1900 [1]. Even after the introduction of monopolar transurethral resection of the prostate (TURP), OP remained the gold standard surgical therapy in prostate volume larger than 80 mL for more than 50 years [1]. Bipolar and laser energies have been introduced in the '90 to decrease early morbidity of traditional surgery (bleeding, catheterization time, and postoperative stay), challenging the role of monopolar TURP and OP as the reference standard. Holmium and Thulium laser enucleation of the prostate has been demonstrated to be size-independent, minimally invasive procedures and promising competitors of OP in patients with large volume prostates [2,3]. Meanwhile, the surgical armamentarium for the treatment of BPH has been implemented by the introduction of laparoscopic and robotic-assisted simple prostatectomy (RASP). As demonstrated in a large series with lower transfusion rate and shorter postoperative stay, RASP is a very attractive option especially in patients with concomitant bladder diverticula and stones [4]. In the present study, we aimed to review the safety and efficacy of RASP as compared to OP in patients with symptomatic BPH and surgical indications.

MATERIALS AND METHODS

1. Aim of the review and literature search

We aimed to perform a systematic review to assess the differences in the perioperative and postoperative period (surgical time, estimated blood, rate of complications), and functional outcomes after RASP versus OP for symptomatic BPH. Functional outcomes were measured by gathering the International Prostate Symptom Score (IPSS) score, maximum flow rate (Q_{max}), and post-voiding residual (PVR) during follow-up. This systematic review was performed according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method [5]. A comprehensive literature search was performed on April 10, 2021, using PubMed Central, Embase and Cochrane Central Controlled Register of Trials (CENTRAL). Medical Subject Heading (MeSH) terms and Boolean operators were used: “robotic” OR “open” AND “(prostatectomy) AND (benign prostatic hyperplasia OR BPH)”. No date limits were imposed. Non-English, animal, and pediatric studies were also excluded. There was no clinical justification for excluding non-English studies but this relied only on authors' language skills. Additional articles were sought from the reference

lists of the included articles. The study protocol was registered on OSF registries (registration DOI 10.17605/OSF.IO/A6C93). This study does not require ethical approval because it is a systematic review.

2. Selection criteria

The PICOS (Patient Intervention Comparison Outcome Study type) model was used to frame and answer the clinical question: (1) P: patients with BPH surgical indication; (2) Intervention: patients undergoing RASP; (3) Comparison: patients undergoing OP; (4) Outcome: perioperative and functional outcomes; and (5) Study type: randomized clinical trials, prospective, and retrospective studies. Only studies comparing both procedures were accepted. Patients were assigned in two groups according to the type of surgery (robotic vs. open). We gathered the following perioperative data: surgical time; estimated blood loss; blood transfusion; postoperative lower urinary tract infection; the number of days to trial off catheter and length of hospital stay after surgery and readmission within 30 days. We also sought the following outcomes: IPSS, Q_{max}, and PVR at the last follow-up visit.

3. Study screening and selection

All retrieved records were screened by two independent authors (DC and SS) through Covidence Systematic Review Management[®] (Veritas Health Innovation, Melbourne, Australia). Discrepancies were fixed by discussion. Studies were included based on PICOS eligibility criteria. Case reports, meeting abstracts, editorials, single series, and letters to editors were rejected. The full text of the screened papers was selected if found appropriate to the subject of this review. The search was further expanded by performing a manual search based on the references of the full-text relevant papers.

4. Statistical analysis

We aimed to perform a meta-analysis comparing the outcomes after BPH surgery among men undergoing RASP as compared to traditional OP. Meta-analysis was performed when two or more studies were reporting the same outcomes under the same definition. The incidences of complications were pooled using the Cochran–Mantel–Haenszel method with the random effect model and expressed as odds ratio (OR), 95% confidence interval (CI), and p-values. Unadjusted estimates were used. OR of less than one indicate a lower risk of complications in patients undergoing robotic-assisted surgery. Perioperative course and functional outcomes were pooled using the inverse variance of the mean difference

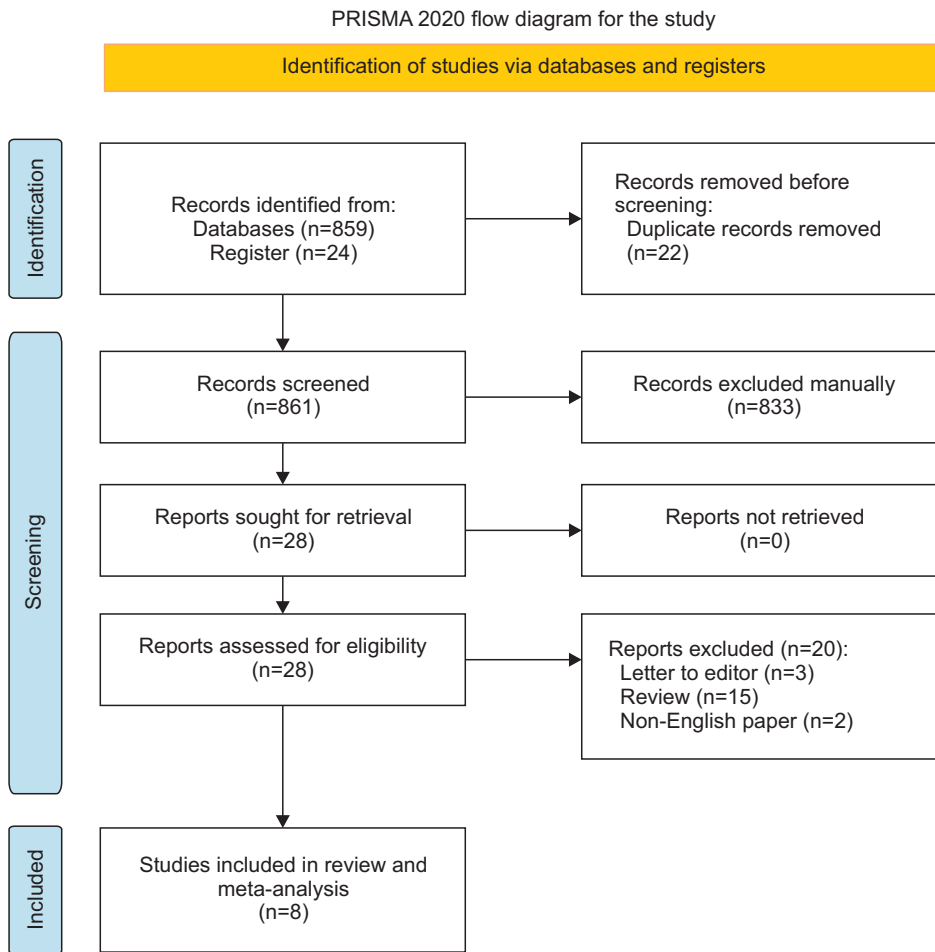


Fig. 1. PRISMA flow diagram of the study. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

(MD) with a fixed effect, 95% CI, and p-values. Analyses were two-tailed and the significance was set at $p < 0.05$ and a 95% CI. Study heterogeneity was assessed utilizing the I^2 value. Substantial heterogeneity was defined as an I^2 value $> 50\%$. Meta-analysis was performed using Review Manager (RevMan) 5.4 software by Cochrane Collaboration. The risk of bias was assessed using the Cochrane Risk of Bias tool, using ROBINS-I (Risk Of Bias in Non-Randomized Studies - of Interventions) for non-randomized studies [6].

RESULTS

The literature search retrieved 883 papers. After removing 22 duplicates, screening against title and abstract excluded 833 papers as the content was unrelated to this review. Full text of the remaining 28 papers was evaluated per eligibility and 20 studies were excluded (3 letters to editor, 15 reviews, 2 non-English papers). Finally, 8 studies were accepted and included in the quantitative analysis [7-14]. Seven studies were retrospective [7-11,13,14] and one was prospective [12]. All were non-randomized. Fig. 1 shows the PRISMA flow

diagram.

1. Study characteristics

There were 5,848 patients involved in 8 studies: 4,667 had OP and 1,181 had a RASP. However, two large studies were population-based cohort studies reporting mainly cost-analysis and postoperative complications [8,13]. Table 1 shows the characteristics of the studies included in this meta-analysis.

2. Quality assessment

Supplementary Fig. shows the details of quality assessment, as measured by the Cochrane Collaboration risk-of-bias tool. Five studies demonstrated a critical overall risk of bias and the remaining three had moderate risk of bias. The most common risk factors for quality assessment were the risk of bias in the selection of participants and confounding, followed by bias due to missing data as most of the studies are retrospective.

3. Perioperative course

Data from seven available studies (290 patients in the

Table 1. Characteristics of included studies comparing robotic vs. open simple prostatectomy

Reference	Robotic platform	Continent/country	Type of study	Type of robotic approach	Enrolled patients, robotic vs. open (total)	Prostate volume (mL), robotic vs. open	Age (y), robotic vs. open	Specimen weight (g), robotic vs. open	Length of follow-up (mo)
Mourmouris et al., 2019 [12]	Da Vinci Si	Europe	Prospective, non-randomized	Transperitoneal, transvesical	26 vs. 15 (41)	115.33±38.4 vs. 101.86±32.4	70.46±4.76 vs. 66.73±8.63	115.33±38.49 vs. 101.86±32.47	3
Sorokin et al., 2017 [14]	Da Vinci Si	USA	Retrospective	Transperitoneal, transvesical	64 vs. 103 (167)	136.2±46.6 vs. 147.3±50.1	68.8±8.0 vs. 68.7±7.5	81.3±36.0 vs. 103.8±49.1	3
Nestler et al., 2019 [11]	Da Vinci Si	Europe	Retrospective	Not reported	35 vs. 35 (70)	94.5 (82–136) vs. 95 (84–132)	70.9 (66.5–73.1) vs. 70.6 (66.5–73.1)	Not reported	3
Dotzauer et al., 2021 [9]	Da Vinci Xi	Europe	Retrospective	Transperitoneal, transvesical	103 vs. 31 (134)	127±32 vs. 119±25	71±7.39 vs. 72±6.9	Not reported	3
Bhanvadia et al., 2021 [8]	Da Vinci Xi	Europe	Retrospective	Not reported	704 vs. 2,551 (3,255)	Not reported	67.8±8.0 vs. 71.0±8.1	Not reported	Not reported
Hoy et al., 2015 [10]	Da Vinci Xi	USA	Retrospective	Transperitoneal with prostatic capsulotomy	4 vs. 28 (32)	239±49.8 vs. 180±54.7	69.3±2.9 vs. 75.18±6.4	123.6±40.8 vs. 122.9±53.6	3
Ravivarapu et al., 2021 [13]	Da Vinci Xi	USA	Retrospective	Not reported	216 vs. 1,881 (2,097)	Not reported	67.5±7.4 vs. 66.3±7.9	Not reported	Not reported
Cho et al., 2021 [7]	Not reported	Asia	Retrospective	Transperitoneal, transvesical	29 vs. 23 (52)	108.2±25.0 vs. 118.6±21.7	70.5±7.9 vs. 70.7±6.0	58.7±27.6 vs. 72.5±39.2	3

Values are presented as number only, mean±standard deviation, or median (interquartile range).

robotic vs. 258 in the open group) showed a significantly longer operative time in the robotic-assisted group (MD, 43.72; 95% CI, 30.57–56.88; p<0.00001) (Fig. 2A). Data on two studies of 166 patients (107 in the robotic group) showed a significantly lower estimated blood loss in the robotic group (MD, -563.20; 95% CI, -739.95 to -386.46; p<0.00001) (Fig. 2B). Data from six studies of 464 patients (257 in the robotic group) showed no difference in postoperative catheterization time (MD, 0.65; 95% CI, -2.17 to 3.48; p=0.65) (Fig. 2C).

Data from five studies of 3,699 patients (936 in the robotic group) showed a significantly shorter postoperative stay in the robotic group (MD, -2.85; 95% CI, -3.72 to -1.99; p<0.00001) (Fig. 3A). Study heterogeneity was not significant in estimated blood loss (I²=0%). Study heterogeneity was significant in surgical time (I²=83%), postoperative catheterization time (I²=97%), and length of stay (I²=94%).

4. Postoperative complications

Data from seven studies of 3,751 patients (965 in the robotic group) showed a significant risk of blood transfusion in the open group (OR, 0.23; 95% CI, 0.17–0.33; p<0.00001) (Fig. 3B). Study heterogeneity was not significant (I²=0%). Data from three studies including 245 patients (164 in the robotic group) showed no difference in the risk of re-catheterization between the two groups (OR, 1.96; 95% CI, 0.32–11.93; p=0.47) (Fig. 3C). Study heterogeneity was not significant (I²=28%). Data from three studies including 3,141 patients (836 in the robotic group) showed no difference in the risk of postoperative urinary infections (OR, 0.89; 95% CI, 0.23–3.51; p=0.87) (Fig. 4A). Study heterogeneity was not significant (I²=23%). Data from four studies of 2,333 (358 in the robotic group) showed no difference in the 30-day readmission rate between the two groups (OR, 0.96; 95% CI, 0.61–1.51; p=0.86) (Fig. 4B). Study heterogeneity was not significant (I²=0%).

5. Functional outcomes

Fig. 5 shows meta-analysis of functional outcomes. Data from three studies of 260 patients (119 in the robotic group) describing postoperative lower urinary tract symptoms and objective voiding parameters at 3 months showed no difference between the two groups in the mean IPSS score (MD, 0.43; 95% CI, -1.36 to 2.23; p=0.64), PVR (MD, -0.58; 95% CI, -13.54 to 12.39; p=0.93) and Qmax (MD, 0.97; 95% CI, -3.52 to 5.45; p=0.67). Study heterogeneity was substantial in all outcomes (I²=66%, 59%, and 79%, respectively).

DISCUSSION

OP has stood the test of time, remaining the surgical

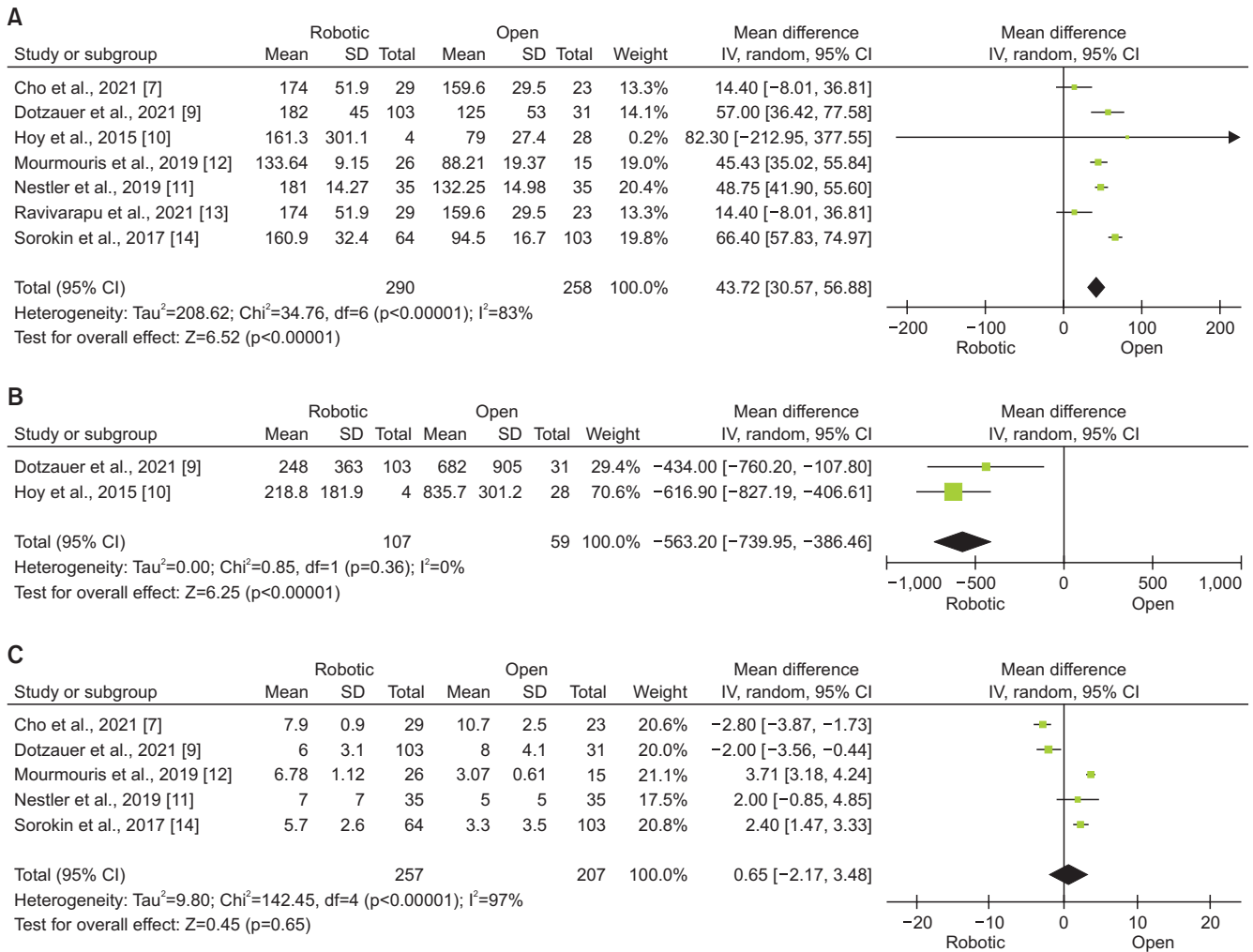


Fig. 2. Meta-analysis of (A) operative time (min), (B) blood loss (mL), and (C) postoperative catheterization time (d). SD, standard deviation; CI, confidence interval; df, degree of freedom.

standard for symptomatic BPH patients with large prostatic glands and concurrent bladder stones and/or diverticula. Since the introduction of the precursor of the modern resectoscope in 1932 by Stern and McCarthy [1], new minimally invasive transurethral procedures have been introduced to challenge the morbidity of OP, showing a better safety profile (lower transfusion rate, shorter catheter time, and hospital stay) and equivalent functional outcomes as compared to OP [3,15-17]. Indeed, the surgical management of BPH patients has been stratified according to prostate size with an increased range of options thanks to the emergence of minimally invasive surgical options. According to international guidelines, OP, holmium laser and bipolar enucleation of the prostate are considered current standard/first choice in men with a prostate volume larger than 80 mL [18]. Sotelo et al. [19] described in 2008 the first series of RASP using the 4-arm da Vinci[®] Surgical System (Intuitive, Sunnyvale, CA, USA) with a 6 port transperitoneal approach. They demonstrated

that the EndoWrist[®] (Intuitive, Sunnyvale, CA, USA) of the robotic instrument facilitated hemostatic figure-of-8 sutures to control the main prostatic vessels, resulting in less intraoperative blood loss [19]. Since then, several series have been published reporting promising results thanks to its ergonomic advantage over pure laparoscopy, and its shorter learning curve as compared to laparoscopic simple prostatectomy [20-22]. With the increasing number of robotic platforms installed worldwide and the growing robotic procedures in oncological urology, RASP could represent a logical next step also for the treatment of large benign prostatic enlargement. This assumption is mainly related to the fact OP is associated with relatively high morbidity. The results of our meta-analyses regarding the perioperative course confirmed the superiority of RASP in intraoperative blood loss and the need for blood transfusions that were significantly higher in the OP group. This is related to the robotic approach that allows a blunt dissection of the adenoma with reduced intra-

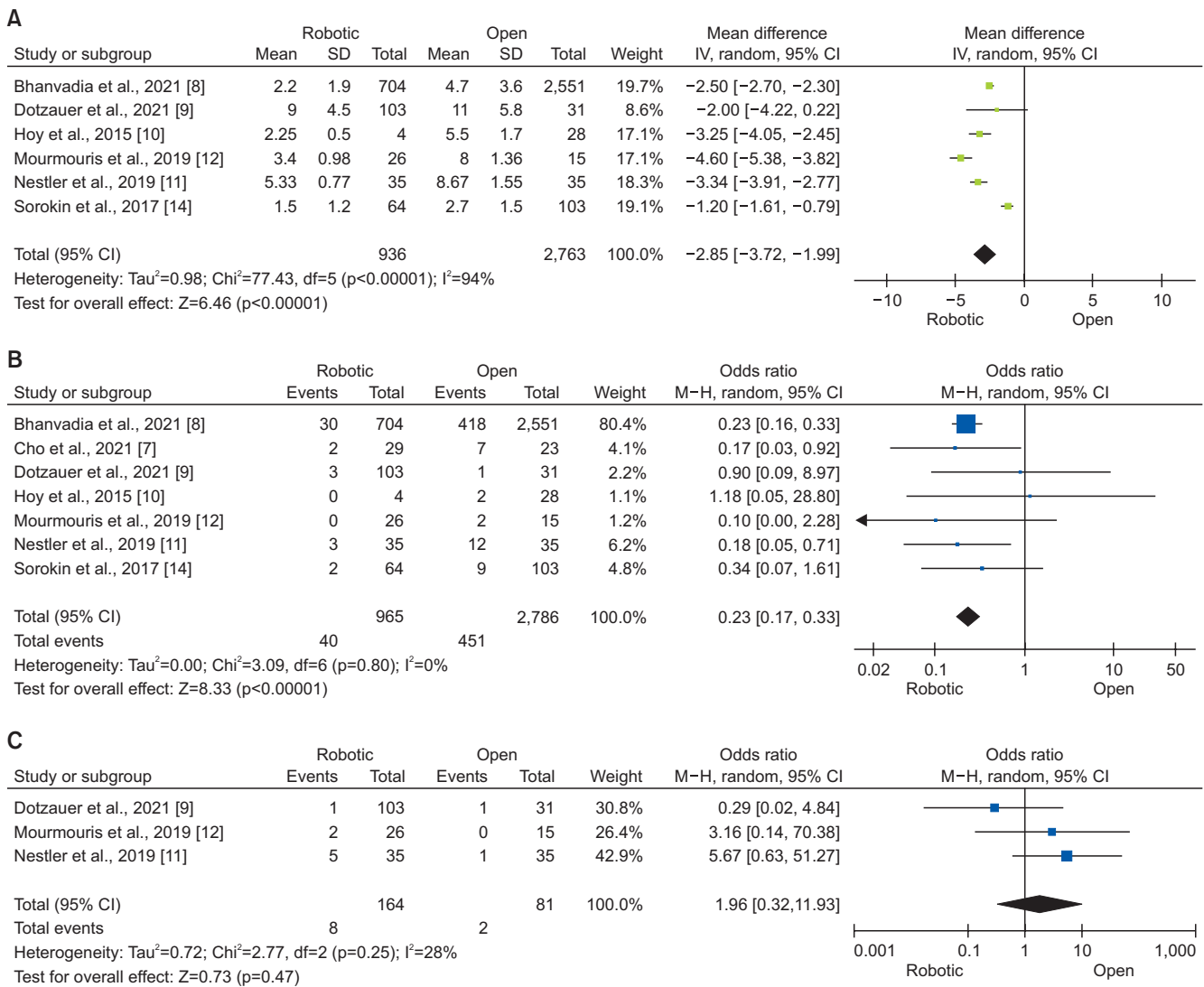


Fig. 3. Meta-analysis of (A) postoperative stay (d), (B) blood transfusion rate, and (C) postoperative catheterization rate. SD, standard deviation; CI, confidence interval; df, degree of freedom.

operative venous bleeding, thanks also to the carbon dioxide compression. Furthermore, the robotic approach facilitates precise hemostasis with both electro-cautery and suturing under an enhanced three-dimensional view by accurately identifying the exact site of bleeding and precise reconstruction of the prostatic bed [19,20]. Although the robotic approach was associated with a longer operative time, this may not be clinically significant. More importantly, the advantages of RASP in bleeding control converted into a shorter hospital stay. A similar rate of postoperative urinary tract infections, risk of re-catheterization and 30-day readmission rate strengthens the odds in favor of RASP over OP.

The advantages of RASP in terms of lower length of stay and need for blood transfusion should be balanced against cost. Cost-effectiveness analysis is a complex matter that is subject to several issues among different healthcare

systems. Bhanvadia et al. [8] reported the largest population-based analysis of the cost of 3,255 patients who underwent RASP (n=704) or OP (n=2,551). The authors showed that despite a lower rate of postoperative complications and shorter hospital stay, RASP was associated with a mean of US \$1,734 in additional total hospitalization costs compared to OP. They also found that increasing length of stay was associated with an additional cost of \$1,687 per day. Thus, the length of stay of RASP needs to be 3 to 4 days shorter than OP to offset the cost of robotic utilization, but the mean hospital stay of RASP was 2.2±1.9 days as compared to 4.7±3.6 days of OP. Our findings confirm that the MD in postoperative stay in favor of RASP was 2.5 days, thus lower than expected 3 to 4 days. Faster recovery may be enhanced with better postoperative pain control and early catheter removal. The single port robotic approach has been introduced

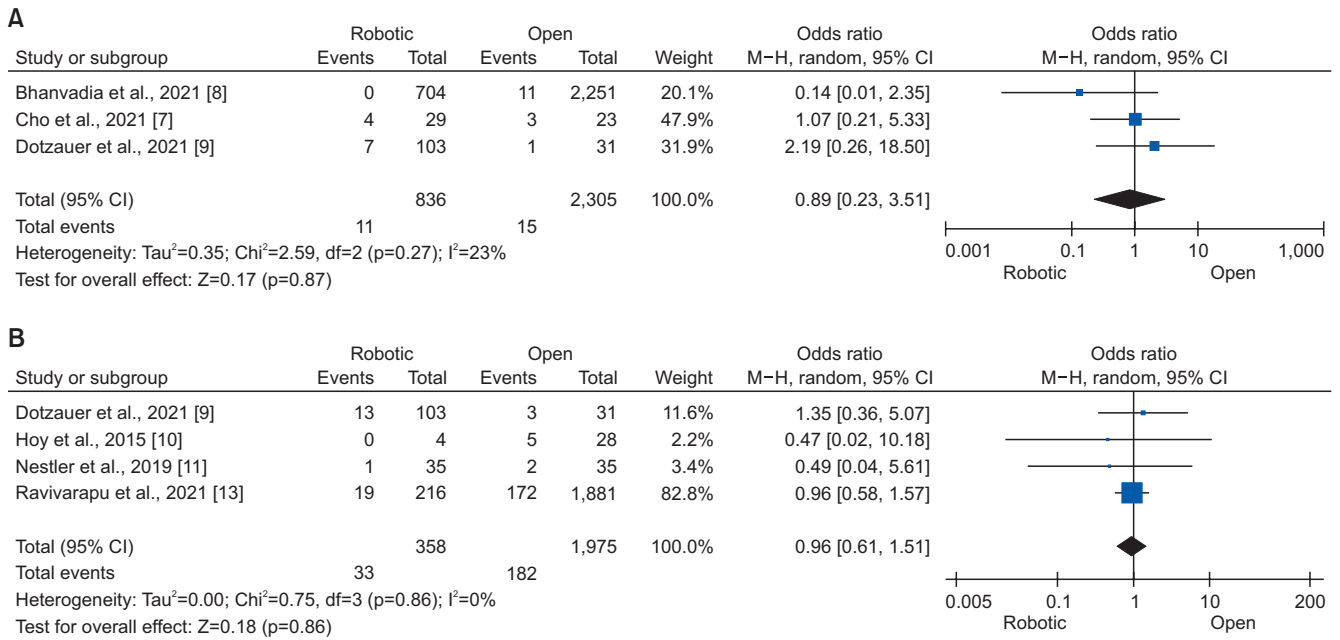


Fig. 4. Meta-analysis of (A) urinary tract infection and (B) 30-day readmission rate. SD, standard deviation; CI, confidence interval; df, degree of freedom.

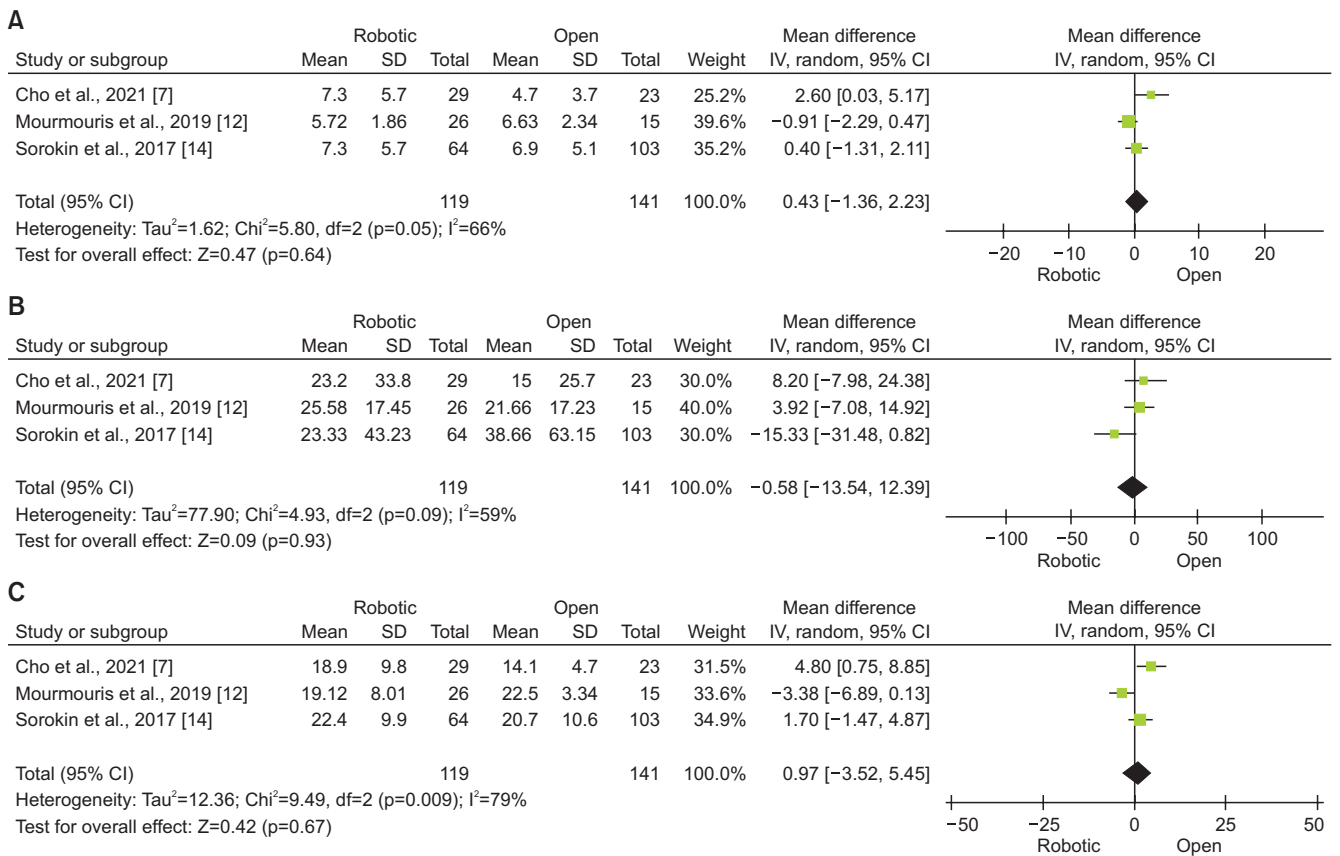


Fig. 5. Meta-analysis of 3-month functional outcomes. (A) IPSS. (B) Post-voiding urine residual (mL). (C) Maximum flow rate (mL/s). IPSS, International Prostate Symptom Score; SD, standard deviation; CI, confidence interval; df, degree of freedom.

to further decrease the morbidity of RASP and it might be the way to decrease the postoperative stay and consequently the total cost of RASP. Steinberg et al. [23] first described a series of 10 men undergoing single-port RASP. They found the procedure feasible, and no patients required conversion to a multi-port robotic platform or open approach. Furthermore, no procedure necessitated the placement of additional assistant ports. No complications occurred. Interestingly, the catheter was removed in the first postoperative day in 9 patients and 8 of them were able to void and were discharged home on the same day [23]. The same group compared two groups of patients undergoing single-port versus multiport RASP. The single-port procedure was associated with 50% decrease in the post-operative opioid use. Still, 44% of single-port RASP patients did not required any narcotics postoperatively as compared to 19% in the multiport group ($p=0.036$) [24]. Kaouk et al. [25] also published a series of 10 patients undergoing single port RASP. All procedures were completed without the need of additional port placement. Patients were discharged after a median stay of only 19 hours (interquartile range, 17–28 h) [25]. Therefore, additional cost-saving might be associated with faster convalescence and earlier return to work after single-port RASP. Further prospective and comparative studies are needed to prove this hypothesis.

Functional outcomes evaluation and comparison are of paramount importance after BPH surgery. In this systematic review we considered three pivotal outcomes: IPSS, PVR, and Qmax. We found no differences regarding early mean IPSS score, PVR, and Qmax. Long-term follow-up are indeed required, even if single case series of RASP with 12-month follow-up demonstrated durable functional outcomes [26].

Our work is not devoid of limitations. First of all, the absence of randomized controlled trials comparing these two surgical approaches. The second drawback is represented by the retrospective nature of the studies included, characterized by a limited number of patients evaluated and with selection bias due to the choice of the technique and a short follow-up time of only 3-month. Third, this review was limited to English-only studies and this might be a bias. However, it has recently been demonstrated that exclusion of non-English publications from systematic reviews had a minimal effect on overall conclusions [27,28]. Fourth, we used unadjusted estimates from non-randomized studies since we did not consider baseline differences and confounders. Finally, since RASP has been adopted since 2008, its application is limited mainly to referral robotic centers.

CONCLUSIONS

This systematic review pointed out that RASP had a better safety profile as compared to OP, with lower intra-operative blood loss and transfusion rate. Despite similar postoperative catheterization times, RASP demonstrated significantly shorter postoperative stay with comparable postoperative morbidity (catheterization, urinary infections, and readmission). In terms of early functional outcomes, both procedures showed comparable results. These findings should be taken with caution because critical overall risk of bias was found in five studies and the remaining three had a moderate risk of bias. Implementation of RASP in centers with established robotic programs will probably make this approach attractive. RASP is currently an investigational technique due to the lack of large sample size randomized controlled studies. Longer follow-up is mandatory to evaluate the long-term efficacy of this approach and the exact rate of reintervention.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Daniele Castellani and Simone Scarcella. Statistical analysis: Daniele Castellani. Data analysis and interpretation: Carlo Andrea Bravi, Vineet Gauhar, Jeremy Yuen-Chun Teoh, Pietro Piazza, Ruben De Groot, Geert De Naeyer, and Stefano Puliatti. Drafting of the manuscript: Daniele Castellani, Simone Scarcella, and Carlo Giulioni. Critical revision of the manuscript: Andrea Benedetto Galosi and Alexandre Mottrie. Supervision: Andrea Benedetto Galosi. Approval of the final manuscript: all authors.

SUPPLEMENTARY MATERIAL

Supplementary material can be found via <https://doi.org/10.4111/icu.20210297>.

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