REVIEW ARTICLE

Clinical Research

Robotic assisted simple prostatectomy versus other treatment modalities for large benign prostatic hyperplasia: a systematic review and meta-analysis of over 6500 cases

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BACKGROUND: Current guidelines recommend simple prostatectomy or endoscopic enucleation of the prostate (EEP) as treatment of choice for bladder prostatic obstruction (BPO) caused by large prostate glands. We aimed to provide a wide-ranging analysis of the currently available evidence, comparing safety and effectiveness of robot-assisted simple prostatectomy (RASP) versus open simple prostatectomy (OSP), laparoscopic simple prostatectomy (LSP), and laser EEP.
METHODS: A systematic search was performed across MEDLINE, EMBASE, and Web of Science databases for retrospective and prospective studies comparing RASP to OSP or LSP or laser EEP (HoLEP/ThuLEP). Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) recommendations were followed to design the search strategies, selection criteria, and evidence report. A meta-analysis evaluated perioperative safety and effectiveness outcomes. The weighted mean difference and risk ratio were used to compare continuous and dichotomous variables, respectively. Quality was assessed using the Newcastle-Ottawa scale and the Cochrane Collaboration's tool for RCT article assessing risk of bias.
RESULTS: 15 studies, including 6659 patients, were selected for meta-analysis: 13 observational studies, 1 non-randomized prospective study, and 1 randomized controlled trial. RASP was associated with statistically significant longer operative time (OT) and lower postoperative complication rate, length of stay (LOS), estimated blood loss (EBL), and transfusion rate (TR) compared to OSP. LSP showed longer LOS and lower postoperative SHIM score, with no difference in OT, EBL, and complications. Compared to laser EEP, RASP presented longer LOS and catheterization time and higher TR. ThuLEP presented shorter OT than RASP. No difference were found in functional outcomes between groups both subjectively (IPSS, QoL) and objectively (Qmax, PVR).
CONCLUSION: RASP has become a size-independent treatment for the management of BPO caused by a large prostate gland. It can duplicate the functional outcomes of OSP while offering a better safety profile. When compared to LSP, the latter still stands as a valid lower-cost option, but it requires solid laparoscopic skill sets and therefore it is unlikely to spread on larger scale. When compared to laser EEP, RASP offers a shorter learning curve, but it still suffers from longer catheterization time and LOS.

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INTRODUCTION

Current guidelines recommend simple prostatectomy (SP) or endoscopic enucleation of the prostate (EEP) as treatment of choice for bladder prostatic obstruction (BPO) caused by large (>80–100 ml) prostate glands [1–4]. Nowadays, minimally invasive surgery (MIS) and EEP offer alternatives to open simple prostatectomy (OSP), which has been considered the gold standard for a century [5, 6]. Indeed, laparoscopic simple prostatectomy (LSP) and robot-assisted simple prostatectomy (RASP), as well as laser technologies, have been widely

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implemented [7]. As a result, retrospective studies have shown a shift in favor of these novel minimally invasive approaches considering their lower perioperative morbidity [8–14].

Among MIS, some unquestionable benefits of robot-assisted surgery, such as three-dimensional vision, degrees of freedom, and tremor suppression have facilitated the adoption of the robotic approach over laparoscopy [15–17]. This might not necessarily translate into a clear advantage in the case of the SP procedure as the above mentioned benefits might be nullified by potential disadvantages (lack of tactile feedback, longer set-up times, higher overall costs) [18–20].

When considering EEP, different energy sources can be used. Holmium (HoLEP) and Thulium-YAG-Lasers (ThuLEP) are currently the ones most employed. Compared to OP, an increasing body of evidence favors HoLEP and ThuVEP in BPH treatment [21–24]. Nevertheless, despite its proven excellent "size-independent" outcomes, EEP presents a steep learning curve [25, 26].

To date, only one randomized controlled trial evaluating the comparative effectiveness of RASP, LSP, and HoLEP has been reported [27] and the evidence is primarily based on retrospective comparative studies. We aimed to provide a wide-ranging analysis of the current available evidence, comparing the outcomes of RASP versus those of OP, LSP, and laser EEP for the treatment of for bladder prostatic obstruction caused by large prostate glands.

METHODS

Search strategy

A systematic review of the literature was performed in April 2022 using the MEDLINE, EMBASE, and Web of Science databases. Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) recommendations were followed to design the search strategies, selection criteria, and evidence report. The International Prospective Register of Systematic Review (PROSPERO) protocol number is CRD42022344556. Patient-related and intervention search terms were combined to build the following search string: ((open OR Laparoscopy* OR robot*) AND (simple OR benign) AND prostatectomy) OR ((Endoscopic OR laser OR fiber) AND enucleation (prostate OR prostatic OR hyperplasia OR BPH)). Search results were filtered by language (English only), species (human), publication type (article).

Study eligibility was defined using the PICOS (patient, intervention, comparator, outcome, study type) approach. Inclusion criteria were: (P) studies focused on adults (>18 years of age) with a diagnosis of BPH; (I) undergoing RASP; (C) in which OSP or LSP or laser EEP (ThuVEP or HoLEP) was performed as a comparator; (O) evaluating one or more of the following outcomes: perioperative outcomes [operative time (OT), estimated blood loss (EBL), transfusion rate (TR), complication rate, length of hospital stay (LOS)], functional outcomes [ΔPVR, ΔIPSS, time of catheterization, transient incontinence, quality of life (QoL)]; (S) retrospective or prospective comparative studies, with a minimum cohort size of ten patients.

Exclusion criteria were: (1) non-comparative studies; (2) SP on animal or cadaveric models; (5) studies reporting fewer than ten cases; and (6) non-original studies including editorial comments, meeting abstracts, case reports, or letters to the editor or any form of gray literature because of the general lack of details or peer review.

Two independent authors (S.D.P. and F.C.) performed title and abstract screening and full-text review. The reviewers independently carried out data extraction, collecting the following baseline patient characteristics: number, age, body mass index (BMI), and American Society of Anesthesiologists (ASA) score; Sexual Health Inventory For Men (SHIM) [28], baseline adenoma volume, baseline prostate volume, baseline Qmax, baseline PVR, baseline IPSS, baseline QoL; perioperative safety outcomes: overall complications (defined as Clavien-Dindo grade ≥1), major complications (Clavien-Dindo ≥3) [29]; perioperative effectiveness: OT, EBL, TR, LOS, catheterization time; functional outcomes: postoperative Qmax, postoperative SHIM, postoperative PVR, postoperative QoL, postoperative IPSS, ΔQmax defined as the increase in Qmax (postoperative – baseline), ΔSHIM defined as the reduction in SHIM (baseline – postoperative), ΔPVR defined as reduction in PVR (baseline – postoperative), ΔQoL (postoperative – baseline), ΔIPSS (baseline – postoperative).

Quality assessment

The quality of the studies included was determined using the Newcastle-Ottawa scale for nonrandomized controlled trials [30]. A total score of 5 or less was considered low quality, 6–7 was considered intermediate quality, and 8–9 was considered high quality. The quality of RCT article and the risk of bias evaluation was assessed according to The Cochrane Collaboration's tool for assessing risk of bias [31]. The items under consideration were selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), reporting bias, and other sources of bias.

Statistical analysis

Pooled effect of continuous outcomes was calculated using mean and standard deviation (SD) when reported. In case of studies reporting only median and interquartile range (IQR) results were converted to means and SDs through validated methods: the method described by Wan et al. [32] was used for normally distributed data; the method of Box-Cox and Quantile Estimation described by McGarth et al. [33] was used for non-normally distributed data.

The inverse variance method was used to calculate pooled weighted mean difference (WMD) and 95% confidence intervals (CI) of continuous pooled results. The Mantel–Haenszel method was used to calculate Relative risk (RR) and 95% CI for binary outcomes. A random-effects model was used through all the analyses.

Each outcome was evaluated in three separate comparison groups, namely RASP versus OSP. RASP versus LSP and RASP versus laser EEP. Subgroup analysis was performed to evaluate the difference in estimates between different laser treatments, ie ThuLEP and HoLEP.

To account for differences in baseline measurements, the pooled effects of differences between treatments in IPSS, SHIM, QoL, PVR, and Qmax were assessed either as difference in final values and as difference in changes from baseline; in case of primary studies reporting only baseline and final scores, the mean value of the change-from-baseline score was calculated as the difference between preoperative and postoperative sample means and the variance as the sum of individual variances.

Comparison of baseline data including demographic characteristics, symptom scores, and prostate volumes was also performed. Statistical heterogeneity was assessed with the I^2 statistic; heterogeneity was considered low, moderate, and high for I^2 values less than 25%, 50%, and 75%, respectively [34]. Results were displayed using forest plots, reporting effect sizes as mean difference and 95% CI. We avoided assessing publication bias because of the inconsistency of the test results when applied to a limited number of studies [35]. Cochrane Collaboration Review Manager software (RevMan v.5.4 - Cochrane Collaboration, Oxford, UK) was used for statistical analysis. For all analyses, statistical significance threshold was set to $p = 0.05$.

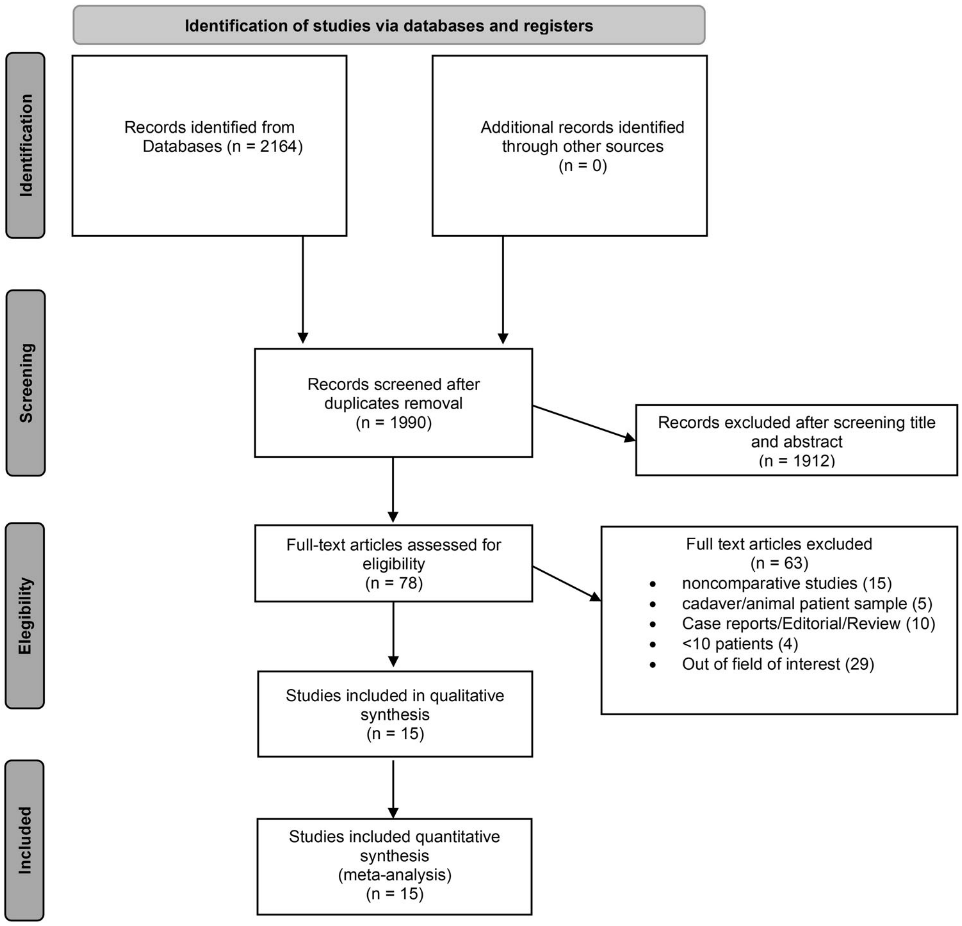


Fig. 1 PRISMA flowchart. PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow chart depicting included studies for the meta-analysis and studies selection process.

RESULTS

Literature search

The PRISMA flow chart of the study selection process is shown in Fig. 1. Initial search identified 1011 studies. Of these, 44 were excluded for duplication. After applying selection criteria, other 952 records were excluded. A total of 15 studies, including 6659 patients, were selected for meta-analysis. Included studies comprised 13 observational studies, 1 non-randomized prospective study, and 1 randomized controlled trial. 7 studies comparing RASP with OSP, 5 studies comparing RASP with LSP and 5 studies comparing RASP with laser EEP were found. All the studies included were of high quality (NOS score 8; Supplementary Table 1).

Baseline characteristics

Table 1 shows the demographic characteristics, symptom scores and prostate volumes of the patients included in each comparison arm. No statistically significant differences were found between RASP and OSP. Significantly higher prostate volumes ($p = 0.007$) and IPSS scores ($p = 0.05$) were found for RASP group compared to laser EEP group. RASP showed significantly higher Qmax ($p = 0.01$), larger adenoma volume ($p = 0.007$), and lower QoL ($p < 0.001$) than LSP. No difference was found in age, baseline BMI, baseline SHIM score, preoperative urinary retention rate and baseline PVR between groups (Table 2).

RASP vs OSP

Seven studies, including 3783 patients, compared RASP to OSP (Figs. 2–4) [8–12, 36, 37].

RASP was associated with statistically significant longer OT (WMD 46.78 min; CI 30.14, 63.42; $p < 0.001$) but shorter LOS (WMD −2.64 days; CI −3.49, −1.79; $p < 0.001$); No statistical differences between the two treatment groups were found in time of catheterization ($p = 0.3$).

RASP group showed statistically significant lower EBL (WMD −359 ml; CI −639, −79; $p = 0.01$) and TR (RR 0.26; CI 0.19, 0.36; $p < 0.001$).

Pooled analysis showed a significantly lower overall post-operative complication rate for RASP (RR 0.49, CI 0.26, 0.91, $p = 0.02$); however, no significant differences between treatments was found in major complications ($p = 0.4$) and transient incontinence ($p = 0.8$).

There were no statistically significant differences between RASP and OSP regarding postoperative IPSS score ($p = 0.7$) and post-operative reduction in IPSS (ΔIPSS) ($p = 0.12$), postoperative QoL ($p = 0.9$) and reduction in QoL (ΔQoL) ($p = 0.3$), postoperative Qmax ($p = 0.9$) and ΔQmax) ($p = 0.8$), postoperative PVR ($p = 0.9$) and reduction in PVR (ΔPVR) ($p = 0.5$).

Moderate to high heterogeneity between studies was found in most analyses. Low I^2 values were found in EBL (0%), major complications (0%), IPSS (0%), QoL and TR (0%).

RASP vs LSP

A total of 5 studies, including 2045 patients compared RASP to LSP (Figs. 5–7) [17, 27–30].

RASP showed a significantly shorter LOS (WMD −1.44 days; CI −2.48, −0.40; $p < 0.01$) compared to LSP. No statistically significant differences were found in OT ($p = 0.11$), intraoperative complications ($p = 0.9$),

Table 1. Main baseline patient characteristics for the studies included.

Studies	*Design*	*Intervention*	*n. patients*	*Age (years)*	*BMI*	*Prostate volume*	*Adenoma volume*	*IPSS*	*Qmax*	*PVR*	*Preoperative retention*	*SHIM*	*QoL*
Pavan	RS	RASP	130	67.8 (7.49)	26 (2.99)	119.5 (29.9)	79.9 (10.1)	23 (5.99)	9.35 (3.75)	NA	21 (16.3)	17.29 (7.49)	5.65 (0.75)
		LSP	189	67.8 (7.77)	26.8 (2.98)	109.5 (29.5)	70.3 (1.84)	17 (5.97)	6.75 (3.73)	NA	24 (12.7)	19.6 (7.47)	5 (1.49)
Autorino	RS	RASP	487	67.8 (7.73)	27.1 (2.97)	112.1 (40.1)	80.7 (23.79)	22.6 (6.69)	8 (4.46)	NA	102 (20.9)	15 (8.92)	4 (1.49)
		LSP	843	66.05 (6.68)	25.3 (2.23)	90 (9.2)	59.25 (15.6)	25.4 (8.9)	5.35 (0.74)	NA	70 (8.3)	17.95 (11.13)	5 (1.48)
Martin Garzon	NPS	RASP	154	67 (7.2)	26.7 (4.1)	77.9 (35.5)	NA	21.8 (5.45)	11.45 (11.2)	NA	NA	18.4 (2.8)	3.8 (1.4)
		LSP	82	66.7 (7.7)	27.4 (3.6)	80.6 (30.5)	NA	19.5 (7.5)	11.4 (14.3)	NA	NA	17 (4.3)	3.2 (1.2)
Fuschi	RCT	RASP	32	69.35 (6.19)	20.3 (3.09)	149.44 (35.15)	129.37 (26.58)	24.3 (1.87)	7.24 (2.31)	126.06	7 (21.8)	NA	3.83 (0.73)
		LPS	36	64.27 (7.21)	21.82 (2.98)	143.84 (31.32)	134 (28.9)	23.42 (2.8)	7.11 (1.77)	132.35	9 (25)	NA	3.85 (0.48)
		HoLEP	42	68.21 (6.09)	23.48 (3.34)	142.21 (30.14)	128 (27.9)	24.15 (3)	7.05 (1.88)	130.13	11 (23.8)	NA	3.89 (0.83)
Amenta	RS	RASP	25	69.9 (18.1)	27.8 (14.1)	159.7 (118.7)	NA	27.5 (7.86)	NA	NA	NA	NA	NA
		LSP	25	72 (11)	25.5 (7.1)	151 (86.5)	NA	29.1 (9.43)	NA	NA	NA	NA	NA
Zhang	RS	RASP	32	71 (8)	NA	NA	96 (54)	NA	NA	NA	11	NA	NA
		HoLEP	600	71 (8)	NA	NA	110 (47)	NA	NA	NA	140	NA	NA
Umari	RS	RASP	81	70.4 (7.55)	27.3 (5.28)	144.4 (59.6)	NA	24.3 (6.04)	8 (4.53)	75.8 (43.8)	28	NA	NA
		HoLEP	45	73.3 (9.19)	26.3 (3.83)	131 (28.33)	NA	19.9 (6.89)	8.75 (2)	107.44 (98.8)	23	NA	NA
Hou CP	RS	RASP	16	66.40 (6.42)	NA	116.37 (17.99)	72.22 (15.89)	26.27 (5.1)	5.4 (1.8)	185.8 (131.58)	4	NA	NA
		ThuLEP	57	71.88 (8.51)	NA	89.83 (7.8)	41.41 (41.41)	25.05 (5.5)	6.68 (4.12)	155.27 (152.6)	17	NA	NA
Nestler	RS	RASP	35	70.1 (5.1)	NA	104.8 (41.7)	NA	22.6 (3.86)	NA	NA	NA	NA	5 (1.55)
		ThuLEP	35	70.3 (7.5)	NA	95.2 (37.1)	NA	20.3 (3.86)	NA	NA	NA	NA	4.05 (1.55)
		Open	35	70.3 (6.34)	NA	104.2 (37.1)	NA	23 (3.09)	NA	NA	NA	NA	5.35 (0.77)
Cho JM	RS	RASP	29	70.5 (7.9)	NA	NA	58.7 (27.6)	23.3 (7.2)	8.1 (5.9)	134.3 (128.5)	NA	NA	4.3 (1)
		OSP	23	70.7 (6)	NA	NA	72.5 (39.2)	15.7 (8.3)	9 (5)	137.9 (97)	NA	NA	3.4 (1.5)
Golomb	RS	RASP	21	69.7 (25.4)	27.1 (11.68)	152 (49.2)	133.9 (149.5)	NA	NA	NA	11	NA	NA
		OSP	8	68.6 (16.9)	28.8 (6.43)	229 (114.8)	149.4 (171.5)	NA	NA	NA	3	NA	NA
Bhanvadia	RS	RASP	704	67.8 (8)	NA	NA	NA	NA	NA	NA	NA	NA	NA
		OSP	2551	71 (8.2)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mourmouris	RS	RASP	26	66.73 (8.63)	26.74 (4.85)	NA	115.33 (38.49)	22.87 (4.3)	10.11 (2.66)	178.5 (190.5)	6	NA	NA
		OSP	15	70.46 (4.76)	23.53 (9.76)	NA	101.86 (32.49)	23.54 (5.3)	9.10 (3.11)	246.5 (252.23)	7	NA	NA
Dotzauer	RS	RASP	103	71 (7.3)	27.3 (3.2)	NA	NA	17.3 (7.4)	6.1 (3.8)	185 (183)	55	NA	NA
		OSP	31	72 (6.9)	27.8 (4.7)	NA	NA	17 (6.6)	16.4 (16.8)	180 (178)	17	NA	NA
Sorokin	RS	RASP	63	68.8 (8.22)	28.5 (4.4)	136.2 (46.6)	NA	18.4 (8.1)	10.1 (6.8)	167 (111.5)	19	NA	3.9
		OSP	103	68.7 (8.42)	28.8 (4)	147.3 (50.1)	NA	18.2 (6.5)	8.9 (5)	153 (148)	29	NA	3.9

RASP robot-assisted simple prostatectomy, *OSP* open simple prostatectomy, *LPS* laparoscopic simple prostatectomy, *BMI* body mass index, *IPSS* International Prostate Symptom Score, *Qmax* maximum flow rate, *PVR* post-void residual volume, *SHIM* Sexual Health Inventory For Men, *QoL* quality of life, *RS* retrospective study, *RCT* randomized controlled trial, *NPS* nonrandomized prospective study.

Table 2. Comparison of baseline characteristics.

Baseline characteristic	*RASP vs OSP*	*p value*	*RASP vs LSP*	*p value*	*RASP vs Laser*	*p value*
Age (years) WMD (95% CI)	−0.79 (−2.31 to 0.73)	0.31	0.93 (−0.36, 2.23)	0.16	−1.93 (−4.30 to 0.44)	0.11
BMI WMD (95% CI)	−0.27 (−1.30 to 0.76)	0.61	−0.09 (−1.83 to 1.64)	0.92	1 (−0.6 to 2.60)	0.22
Prostate volume WMD (95% CI)	−9.53 (−29.03 to 9.96)	0.34	4.05 (−7.13 to 15.24)	0.48	16.68 (4.48–28.87)	0.007
Adenoma volume WMD (95% CI)	−1.52 (−23.35 to 20.31)	0.89	13.35 (3.62–23.08)	0.007	9.25 (−34.62 to 53.12)	0.68
IPSS WMD (95% CI)	0.90 (−1.16 to 2.97)	0.39	1.08 (−2.48 to 4.64)	0.55	1.88 (−0.01 to 3.78)	0.05
Qmax WMD (95% CI)	−1.02 (−3.91 to 1.88)	0.49	1.68 (0.38 to 2.99)	0.01	−1.3 (−2.69 to 0.09)	0.07
PVR WMD (95% CI)	5.09 (−24.46 to 34.64)	0.74	NA	NA	−10.15 (−67.56 to 47.27)	0.73
Preoperative retention RR (95%)	0.87 (0.67–1.14)	0.32	1.54 (0.81–2.92)	0.19	0.95 (0.54–1.65)	0.85
SHIM WMD (95% CI)	NA	NA	−1.26 (−4.24 to 1.72)	0.41	NA	NA
QoL WMD (95% CI)	0.09 (−0.27 to 0.45)	0.62	−30 (−0.42 to −0.18)	<0.00001	−0.10 (−0.43 to 0.23)	<0.0001

RASP robot-assisted simple prostatectomy, *OSP* open simple prostatectomy, *LPS* laparoscopic simple prostatectomy, *BMI* body mass index, *IPSS* International Prostate Symptom Score, *Qmax* maximum flow rate, *PVR* post-void residual volume, *SHIM* Sexual Health Inventory For Men, *QoL* quality of life WMD, weighted mean difference, *CI* confidence interval, *OR* odds ratio.

overall postoperative complications ($p = 0.08$), major complications ($p = 0.9$), EBL ($p = 0.5$) and time of catheterization ($p = 0.2$).

Compared to LSP, RASP showed a significantly higher postoperative IPSS (WMD 1.92, CI −0.42, 3.42; $p = 0.01$) but IPSS changes from baseline were not significantly different ($p = 0.7$). RASP was associated with a significantly higher postoperative Qmax (WMD 2.47 ml/sec; CI 0.73, 4.21; $p < 0.01$) and ΔQmax (WMD 1.14 ml/sec; CI 0.42, 1.87; $p < 0.01$), lower postoperative SHIM score (WMD −2.60 points; CI −4.98, −0.23; $p = 0.04$) but higher ΔSHIM (WMD 1.37 points; CI 0.48, 2.26; $p < 0.01$).

There were no statistically significant differences between the two groups regarding postoperative QoL ($p = 0.7$), ΔQoL($p = 0.4$).

Medium heterogeneity was found in the assessment of intraoperative complications (I^2 32%), postoperative complications (I^2 66%) and postoperative QoL (I^2 40%). High heterogeneity between studies was found in all other analyses.

RASP vs laser EEP

Three studies, including 868 patients, compared RASP to HoLEP [38, 39] and 2 studies, including 178 patients, compared RASP to ThuLEP [36, 40] (Figs. 8–10).

Overall, longer LOS was found for RASP (WMD 1.71 days; CI 1.04, 2.39; $p < 0.001$), but this difference reached statistical significance only when comparing RASP with HoLEP ($p < 0.001$).

Significantly longer OT was found only when comparing RASP to ThuLEP (WMD 85 min; CI 61, 110; $p < 0.001$).

No significant differences in postoperative complications were found comparing RASP with laser EEP ($p = 0.2$) and comparing RASP with HoLEP ($p = 0.5$). However, one study reported a significantly higher rate of overall complications for RASP compared with ThuLEP (RR 9; CI 1.2, 67.31; $p = 0.03$) without differences in major complication rates ($p = 0.3$).

RASP showed a higher TR (RR 5.26; CI 1.92, 14.41; $p = 0.001$), and this difference remained significant in the subgroup analysis for HoLEP and ThuLEP ($p = 0.01$ and $p = 0.04$, respectively).

Significantly shorter time of catheterization was found for laser in both combined (WMD 3.54 days; CI 1.65, 5.43; $p < 0.001$) and subgroup analysis for HoLEP ($p = 0.02$) and ThuLEP ($p = 0.01$).

No differences were found in postoperative IPSS ($p = 0.55$) and ΔIPSS ($p = 0.3$), but data were only available for comparison between RASP and HoLEP. Also, there was no significant difference in postoperative PVR ($p = 0.8$), ΔPVR ($p = 0.3$) and postoperative urinary incontinence ($p = 0.7$).

Low heterogeneity between studies was found in major complication rates and TR (I^2 0%). All other comparisons were hampered by moderate to high heterogeneity.

DISCUSSION

To the best of our knowledge, herein we report the first and largest comparative outcomes analysis of RASP versus other treatment modalities for large benign prostatic hyperplasia, including 15 studies and over 6.500 patients. Some key findings from this analysis are worth in-depth discussion.

RASP vs OSP

The prolonged OT for RASP versus OSP might be related to the learning curve and/or unstandardized intraoperative protocols, especially considering initial-experience studies and/or smaller cohorts [41]. For instance, Sorokin at al., performing RASP, described a cystoscopy-guided technique during apical dissection to avoid sphincteric injury in their early experience. Soon this step was no longer performed with OT decreasing [11]. Johnson and colleagues also described a reduction in OT for RASP of approximately two minutes case-by-case, which represents the gaining surgeon experience [42]. The exclusion of studies with <10 patients significantly limited the effect size and the

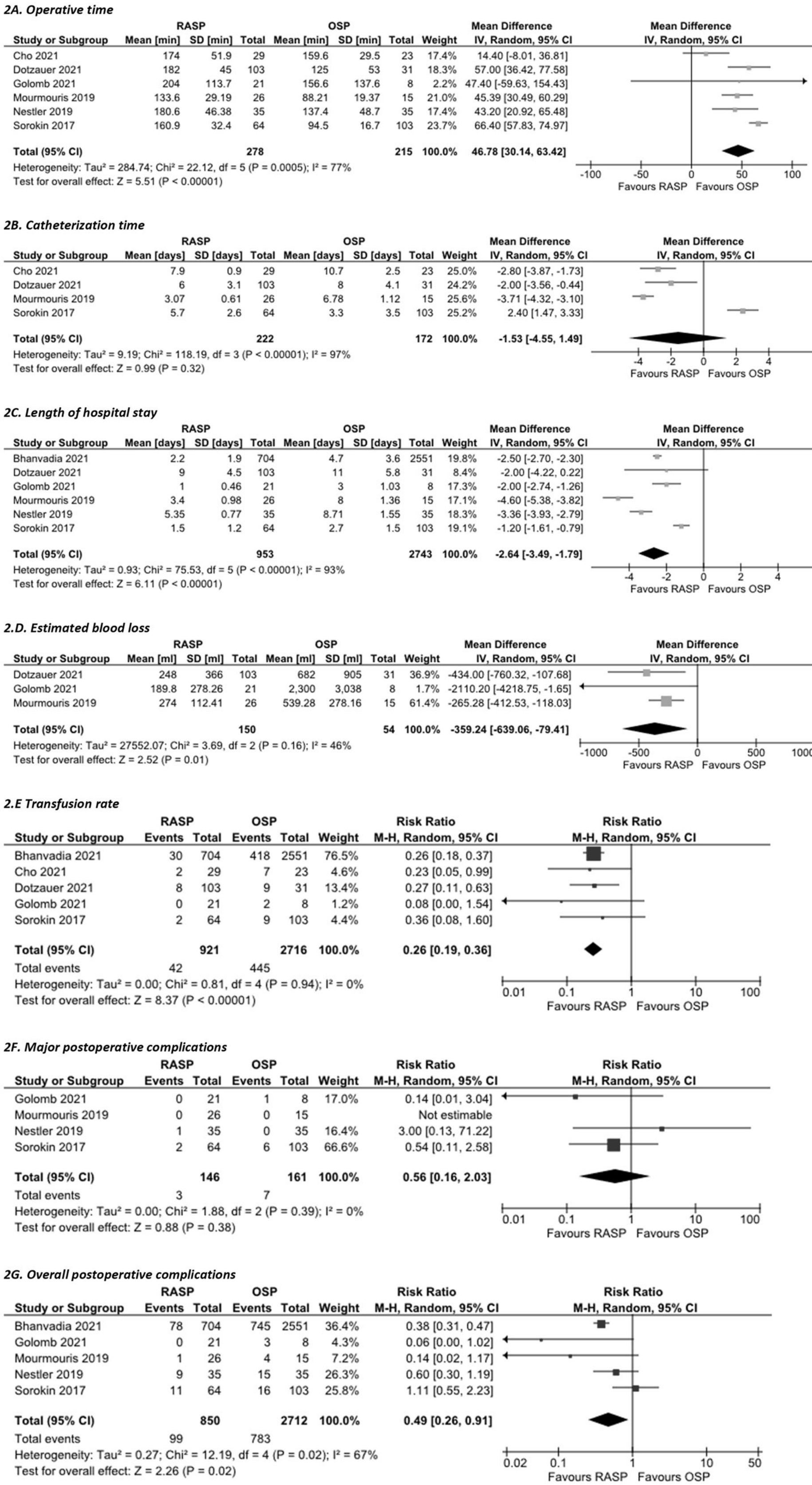


Fig. 2 Forest plots of perioperative outcomes and postoperative complications for robot-assisted simple prostatectomy (RASP) versus open simple prostatectomy (OSP). **A** Operative time. **B** Catheterization time. **C** Length of hospital stay. **D** Estimated blood loss. **E** Transfusion rate. **F** Major postoperative complications. **G** Overall postoperative complications.

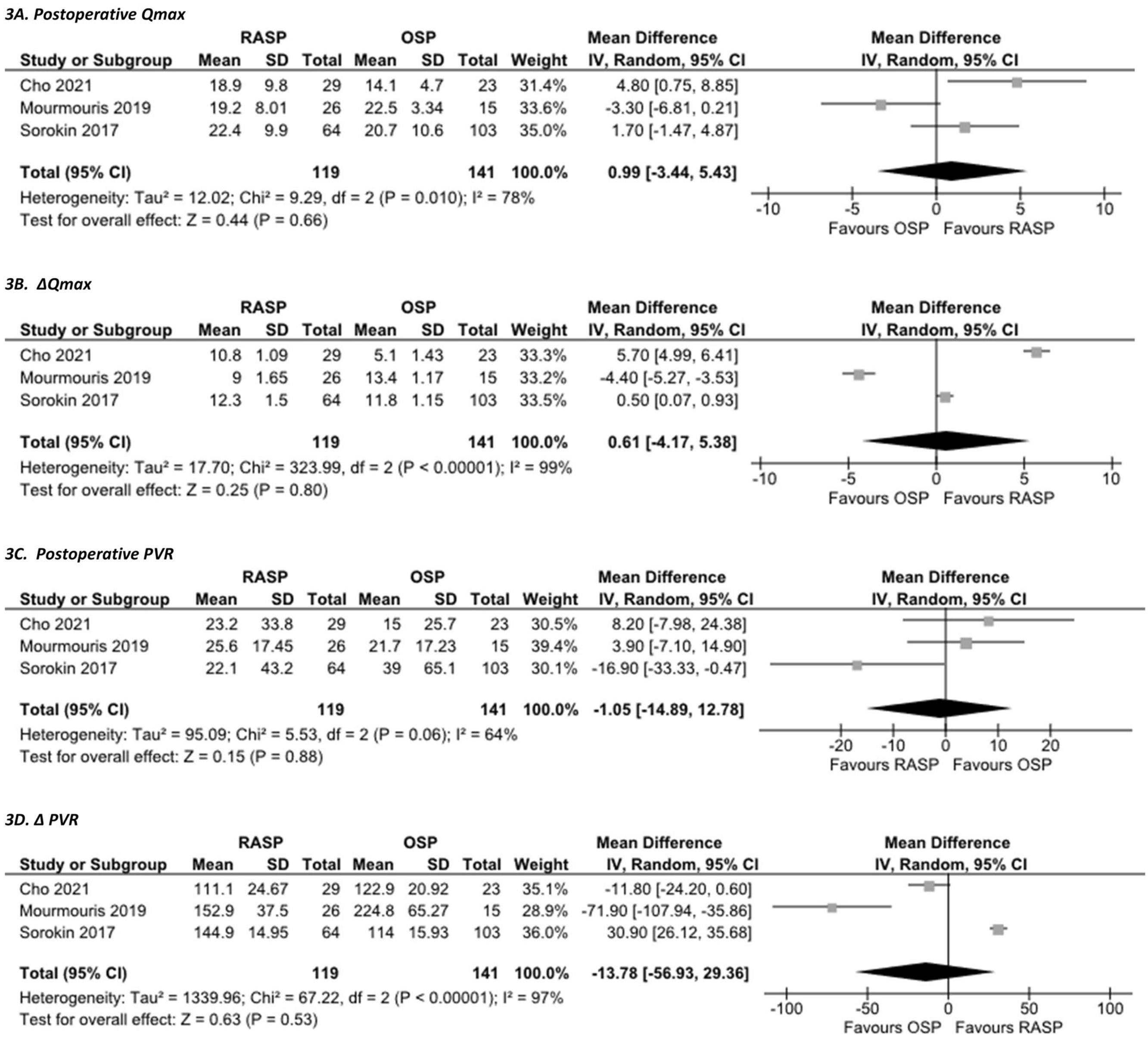


Fig. 3 Forest plots of urodynamic outcomes for robot-assisted simple prostatectomy (RASP) versus open simple prostatectomy (OSP). **A** Postoperative Qmax. **B** ΔQmax. **C** Postoperative PVR. **D** Δ PVR. Qmax maximum flow rate, PVR post-void residual volume.

significance of the difference between RASP and OSP in OT (WMD 46.78 min; $p < 0.00001$). However, as for other urologic procedures, most of the supplementary time reported for RASP could be due to port placement and docking (and undocking) [43, 44].

LOS was significantly lower for RASP than OSP (WMD −2.68 days). Even if LOS is mostly influenced by hospital protocols and surgeon confidence/experience, the robotic approach clearly offers advantages such as faster bowel recovery and lower postoperative pain, which translates into shorter hospital stay [45].

Three studies compared EBL between RASP and OSP [8, 10, 37], with a significantly lower EBL for RASP (MWD −359.24 ml). Correspondingly, the TR was higher for OSP in four of five studies pooled [8–12]. Only Sorokin and colleagues reported no significant difference in TR in their cohort [11]. Patient's comorbidities, indications to surgery and surgeon's preferences might explain these differences.

Complications rate is a key-index to evaluate surgery safety. Our meta-analysis showed a significantly lower overall postoperative complication rate for RASP vs OSP (RR 0.49, CI 0.26, 0.91, $p = 0.02$) while no significant differences between treatments was found in major complications ($p = 0.4$). Thus, the difference in complication rate is mainly explained by rates of low-grade complications.

As expected, no relevant differences in functional outcome both subjective (postoperative IPSS, ΔIPSS, postoperative QoL, ΔQoL) and objective (postoperative Qmax, ΔQmax, postoperative PVR, ΔPVR) were found.

RASP Vs LSP

Both MIS techniques seem to be equivalent considering OT, catheterization time, EBL, RT, overall and major complications. Five comparative studies, including 2045 patients, were pooled. Despite both techniques are minimally invasive, RASP provided a shorter LOS (MWD −1.44 d). This could be explained by three-dimensional vision and greeter degrees of freedom that allow avoiding unnecessary maneuvers on the gastrointestinal tract with faster recovery. However, as mentioned, differences in LoS could be related to different non-medical factors.

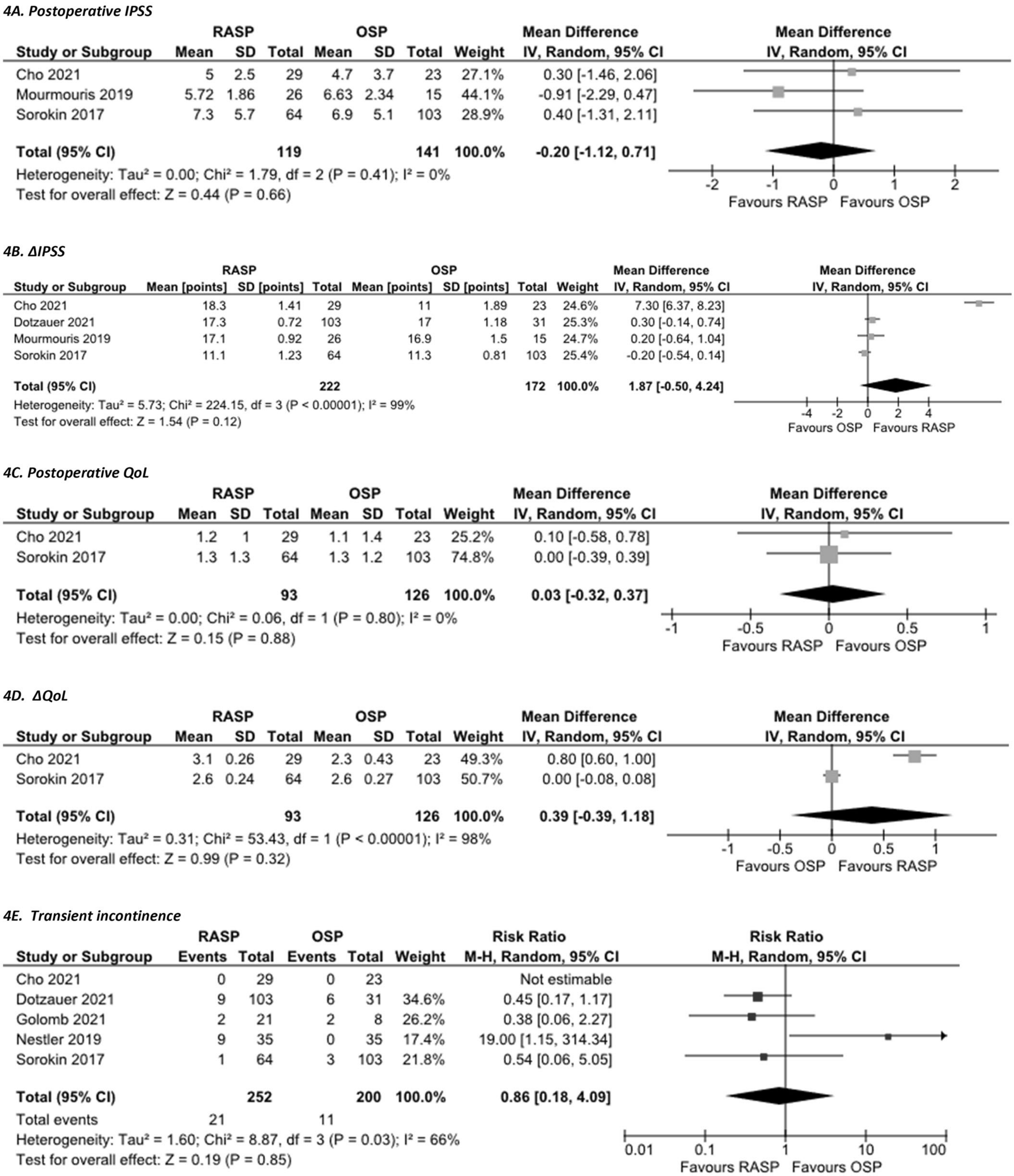
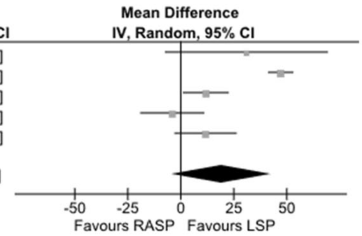


Fig. 4 Forest plots of functional outcomes for robot-assisted simple prostatectomy (RASP) versus open simple prostatectomy (OSP). **A** Postoperative IPSS. **B** ΔIPSS. **C** Postoperative QoL. **D** ΔQoL. **E** Transient incontinence. IPSS International Prostate Symptom Score, QoL quality of life.

5A. Operative time

Study or Subgroup	RASP Mean [min]	RASP SD [min]	RASP Total	LSP Mean [min]	LSP SD [min]	LSP Total	Weight	Mean Difference IV, Random, 95% CI
Amenta 2022	158.7	92	25	127.7	31.4	25	14.1%	31.00 [-7.11, 69.11]
Autorino 2015	144.3	59.5	487	97.2	26	843	22.4%	47.10 [41.53, 52.67]
Fuschi 2021	138.5	22.5	32	126.6	21	36	21.7%	11.90 [1.52, 22.28]
Martin Garzon 2016	157.2	58.4	154	161.2	53.2	82	20.8%	-4.00 [-18.75, 10.75]
Pavan 2016	142.2	61.4	130	130.5	67.2	189	20.9%	11.70 [-2.55, 25.95]
Total (95% CI)			**828**			**1175**	**100.0%**	**19.14 [-4.12, 42.39]**

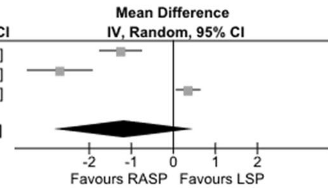
Heterogeneity: Tau² = 619.76; Chi² = 73.22, df = 4 (P < 0.00001); I² = 95%
Test for overall effect: Z = 1.61 (P = 0.11)



5B. Catheterization time

Study or Subgroup	RASP Mean [days]	RASP SD [days]	RASP Total	LSP Mean [days]	LSP SD [days]	LSP Total	Weight	Mean Difference IV, Random, 95% CI
Fuschi 2021	4.14	0.81	32	5.39	1.22	36	33.5%	-1.25 [-1.74, -0.76]
Martin Garzon 2016	9.2	3.2	154	11.9	2.6	82	32.2%	-2.70 [-3.46, -1.94]
Pavan 2016	5	1.46	130	4.65	0.75	189	34.2%	0.35 [0.08, 0.62]
Total (95% CI)			**316**			**307**	**100.0%**	**-1.17 [-2.84, 0.50]**

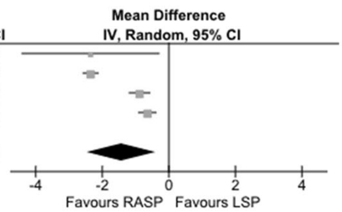
Heterogeneity: Tau² = 2.11; Chi² = 75.02, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.37 (P = 0.17)



5C. Length of hospital stay

Study or Subgroup	RASP Mean [days]	RASP SD [days]	RASP Total	LSP Mean [days]	LSP SD [days]	LSP Total	Weight	Mean Difference IV, Random, 95% CI
Amenta 2022	4.36	2.26	25	6.71	4.7	25	13.7%	-2.35 [-4.39, -0.31]
Autorino 2015	2.35	2.23	487	4.7	1.48	843	28.9%	-2.35 [-2.57, -2.13]
Fuschi 2021	3.84	0.53	32	4.72	0.71	36	28.6%	-0.88 [-1.18, -0.58]
Pavan 2016	5.36	0.75	130	6	1.49	189	28.8%	-0.64 [-0.89, -0.39]
Total (95% CI)			**674**			**1093**	**100.0%**	**-1.44 [-2.48, -0.40]**

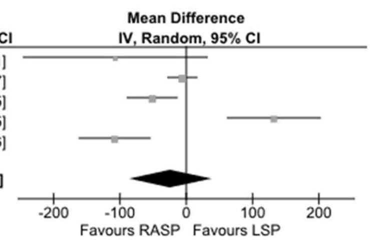
Heterogeneity: Tau² = 0.96; Chi² = 118.96, df = 3 (P < 0.00001); I² = 97%
Test for overall effect: Z = 2.71 (P = 0.007)



5D. Estimated blood loss

Study or Subgroup	RASP Mean [ml]	RASP SD [ml]	RASP Total	LSP Mean [ml]	LSP SD [ml]	LSP Total	Weight	Mean Difference IV, Random, 95% CI
Amenta 2022	150	157	25	257	314	25	11.4%	-107.00 [-244.61, 30.61]
Autorino 2015	235	223	487	241	111	846	24.6%	-6.00 [-27.17, 15.17]
Fuschi 2021	219	67	32	270	88	36	23.3%	-51.00 [-87.95, -14.05]
Martin Garzon 2016	463	278	154	331	251	82	19.2%	132.00 [62.15, 201.85]
Pavan 2016	227	242	130	335	224	189	21.5%	-108.00 [-160.44, -55.56]
Total (95% CI)			**828**			**1178**	**100.0%**	**-23.33 [-85.93, 39.27]**

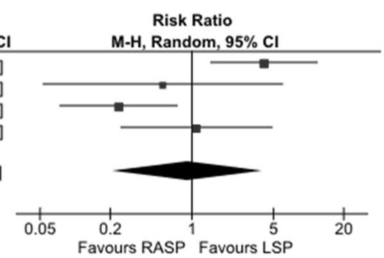
Heterogeneity: Tau² = 4029.21; Chi² = 34.92, df = 4 (P < 0.00001); I² = 89%
Test for overall effect: Z = 0.73 (P = 0.47)



5E. Major postoperative complications

Study or Subgroup	RASP Events	RASP Total	LSP Events	LSP Total	Weight	Risk Ratio M-H, Random, 95% CI
Autorino 2015	12	487	5	843	28.8%	4.15 [1.47, 11.72]
Fuschi 2021	1	32	2	36	18.2%	0.56 [0.05, 5.91]
Martin Garzon 2016	4	154	9	82	27.9%	0.24 [0.08, 0.75]
Pavan 2016	3	130	4	189	25.1%	1.09 [0.25, 4.79]
Total (95% CI)		**803**		**1150**	**100.0%**	**0.93 [0.21, 4.08]**
Total events	20		20			

Heterogeneity: Tau² = 1.71; Chi² = 13.51, df = 3 (P = 0.004); I² = 78%
Test for overall effect: Z = 0.10 (P = 0.92)



5F. Overall postoperative complications

Study or Subgroup	RASP Events	RASP Total	LSP Events	LSP Total	Weight	Risk Ratio M-H, Random, 95% CI
Amenta 2022	4	25	2	25	9.0%	2.00 [0.40, 9.95]
Autorino 2015	81	487	60	843	30.6%	2.34 [1.71, 3.20]
Fuschi 2021	5	32	7	36	15.6%	0.80 [0.28, 2.28]
Martin Garzon 2016	19	154	12	82	22.8%	0.84 [0.43, 1.65]
Pavan 2016	22	130	10	189	21.9%	3.20 [1.57, 6.53]
Total (95% CI)		**828**		**1175**	**100.0%**	**1.66 [0.94, 2.91]**
Total events	131		91			

Heterogeneity: Tau² = 0.24; Chi² = 11.88, df = 4 (P = 0.02); I² = 66%
Test for overall effect: Z = 1.75 (P = 0.08)

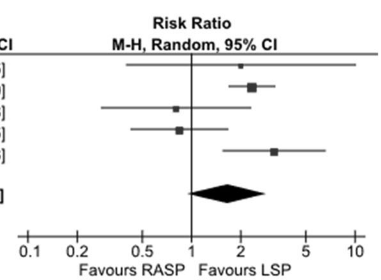


Fig. 5 Forest plots perioperative outcomes and postoperative complications for robot-assisted simple prostatectomy (RASP) versus laparoscopic simple prostatectomy (LSP). **A** Operative time. **B** Catheterization time. **C** Length of hospital stay. **D** Estimated blood loss. **E** Major postoperative complications. **F** Overall postoperative complications.

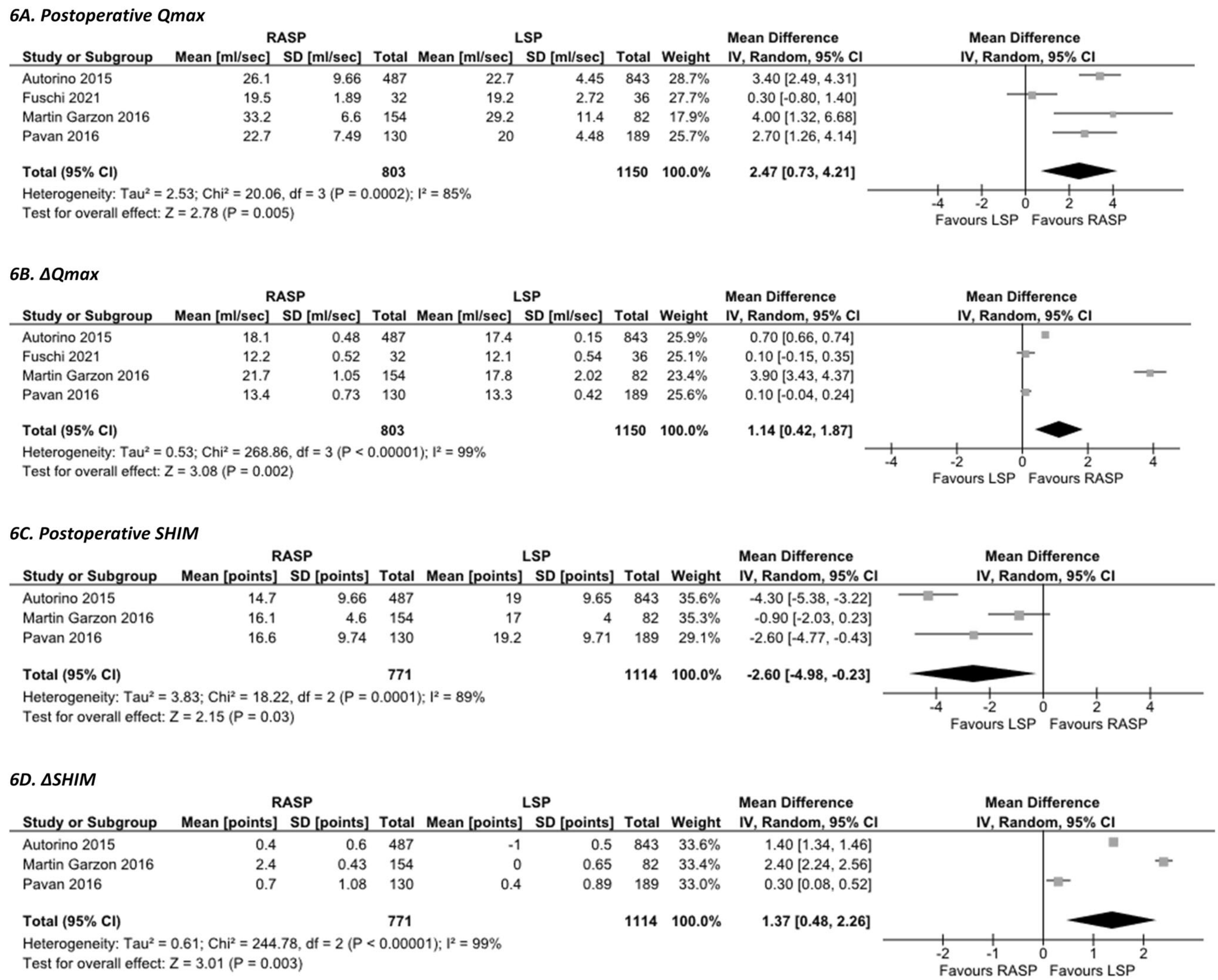


Fig. 6 Forest plots of urodynamic and sexual outcomes for robot-assisted simple prostatectomy (RASP) versus laparoscopic simple prostatectomy (LSP). A Postoperative Qmax. **B** ΔQmax. **C** Postoperative SHIM. **D** ΔSHIM. Qmax maximum flow rate, SHIM Sexual Health Inventory for Men.

Analysis of pooled data from four studies [27, 46–48], showed a significantly higher postoperative Qmax (WMD 2.47 ml/sec; CI 0.73, 4.21; $p < 0.01$) and ΔQmax (WMD 1.14 ml/sec; CI 0.42, 1.87; $p < 0.01$) for RASP. However, this finding must be interpreted with caution considering higher baseline Qmax for RASP ($p = 0.01$), which might account for a selection bias. Lucca et al. in their meta-analysis reported similar improvements in Qmax and IPSS comparing minimally invasive SP and OSP [22]. Same findings were described by Li and colleagues. They found no significant difference in postoperative Qmax, IPSS, QoL and PVR between RASP, LSP, and OSP [21]. Similar to our results, Li et al. also found no significant differences in terms of ΔIPSS [27, 46–49]. Pooled analysis of three studies [46–48], showed slight significant advantage for LSP in postoperative SHIM score (WMD −2.60 points; $p = 0.04$) and ΔSHIM (WMD 1.37 points; $p < 0.01$). This can be interpreted as a minimal impact of the minimally invasive SP procedure on sexual health function, as previously described [50, 51].

RASP vs laser EEP

ThuLEP showed a significantly shorter OT than RASP (WMD 85 min; $p < 0.00001$), while HoLEP did not reach statistical significance ($p = 0.2$). Pooled analysis for OT was still statistically significant (MWD 69 min; $p = 0.02$). It is worth mentioning that EEP was faster in all studies except the study by Umari et al. [39]. They found an identical OT of 105 min for both RASP and HoLEP, which is faster compared to all other studies. However, considering the unbalanced size of the treatment arms (RASP = 81, HoLEP = 45), this might account for a greater experience in robotic surgery than in EEP. In this regard, Johnson et al. and Brunckhorst at al [26, 42]. conducted studies to estimate the learning curve for RASP and HoLEP, respectively. They reported that 10–12 cases for RASP (for a surgeon with already robotic skills) and 40–60 for HoLEP may be required to become skillful. The authors concluded that the learning curve factor might favor RASP over EEP [52].

As expected, laser EEP showed lower LOS (WMD 1.71 days; $p < 0.00001$), and catheterization time (WMD 3.54; $p = 0.0002$). While this might be partially influenced by non-clinical factors such as discharge protocols, it is undeniable that while RASP procedure requires opening of the bladder wall with subsequent need for prolonged catheterization time, this is not the case for EEP. Agarwalk et al. reported a mean LOS of 2 days for HoLEP, while Lwin and colleagues demonstrated its feasibility as an in office procedure [53–55]. Noteworthy, with the introduction of the

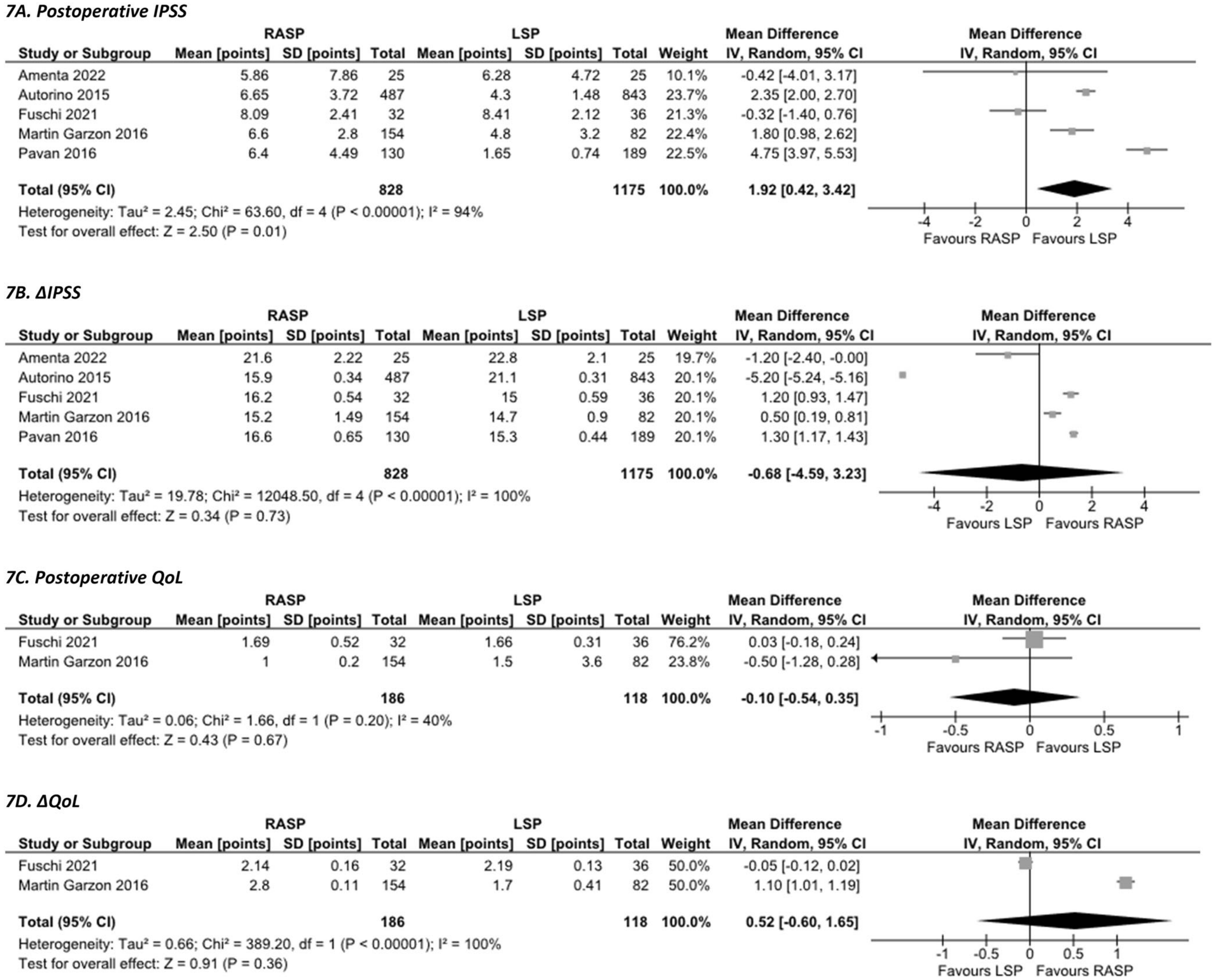


Fig. 7 Forest plots of functional outcomes for robot-assisted simple prostatectomy (RASP) versus laparoscopic simple prostatectomy (LSP). **A** Postoperative IPSS. **B** ΔIPSS. **C** Postoperative QoL. **D** ΔQoL. IPSS International Prostate Symptom Score, QoL quality of life.

single port platform, same-day discharge might also become feasible with RASP [56]. The relative risk of receiving blood transfusions was five times higher with RASP (RR 5.26, $p = 0.001$). This is consistent with current evidence, but such as the unequal size of treatment arms (RASP = 32; HoLEP = 600) reported by Zhang et al., could skew the comparison [38]. This is to emphasize how the surgeon and his experience have the greatest impact on outcome and complications, even more in complex procedures as RASP, LSP and EEP [52, 57].

The quantitative analysis demonstrated that the surgical procedures had similar postoperative IPSS, ΔIPSS, postoperative PVR, and ΔPVR. This is consistent with a previously meta-analysis by Kowalewski et al. [58], and is not surprising, as both interventions carry out a similar enucleation of the prostatic adenoma.

Overall and major postoperative complication rates were not different in the combined analysis when comparing RASP with EEP. Only Nestler et al. [36] reported a significantly higher rate of major complications for RASP compared to ThuLEP. In a recent comparative analysis between ThuLEP and LSP, ThuLEP resulted in a less invasive approach considering the lower postoperative Hb drop, catheterization time, and complications rate [59].

Regarding urinary incontinence, since Umari et al., Fuschi et al., and Nestler et al. did not provide specific description as this being transient or permanent, and lack of standardized definition of continence outcomes remains an issue. For the purpose of quantitative analysis, we assumed urinary incontinence to be transient [27, 36, 39, 60]. While our analysis did not detect differences when comparing RASP with EEP, it is worth looking at a recent report from one of the leading institutions that pioneered this procedure. Fallara et al. reported 10 years of outcomes for 125 patients who underwent HoLEP [61]. Of these, 26% were symptomatic at long-term follow-up, 5.7% reported urinary incontinence, and 4.7% underwent repeat surgery. These are clinically relevant findings that warrant consideration. Concerns about degree and duration of postoperative urinary incontinence may be one of the reasons EEP procedures failed to gain rapid diffusion as one would have been expected.

We could not analyze the range of indications, owing the comparative nature of included studies. RASP allows to tackle cases where concomitant bladder diverticula are present. Also, while laser EEP is proposed as size independent treatment, RASP has been used for "giant" glands [4].

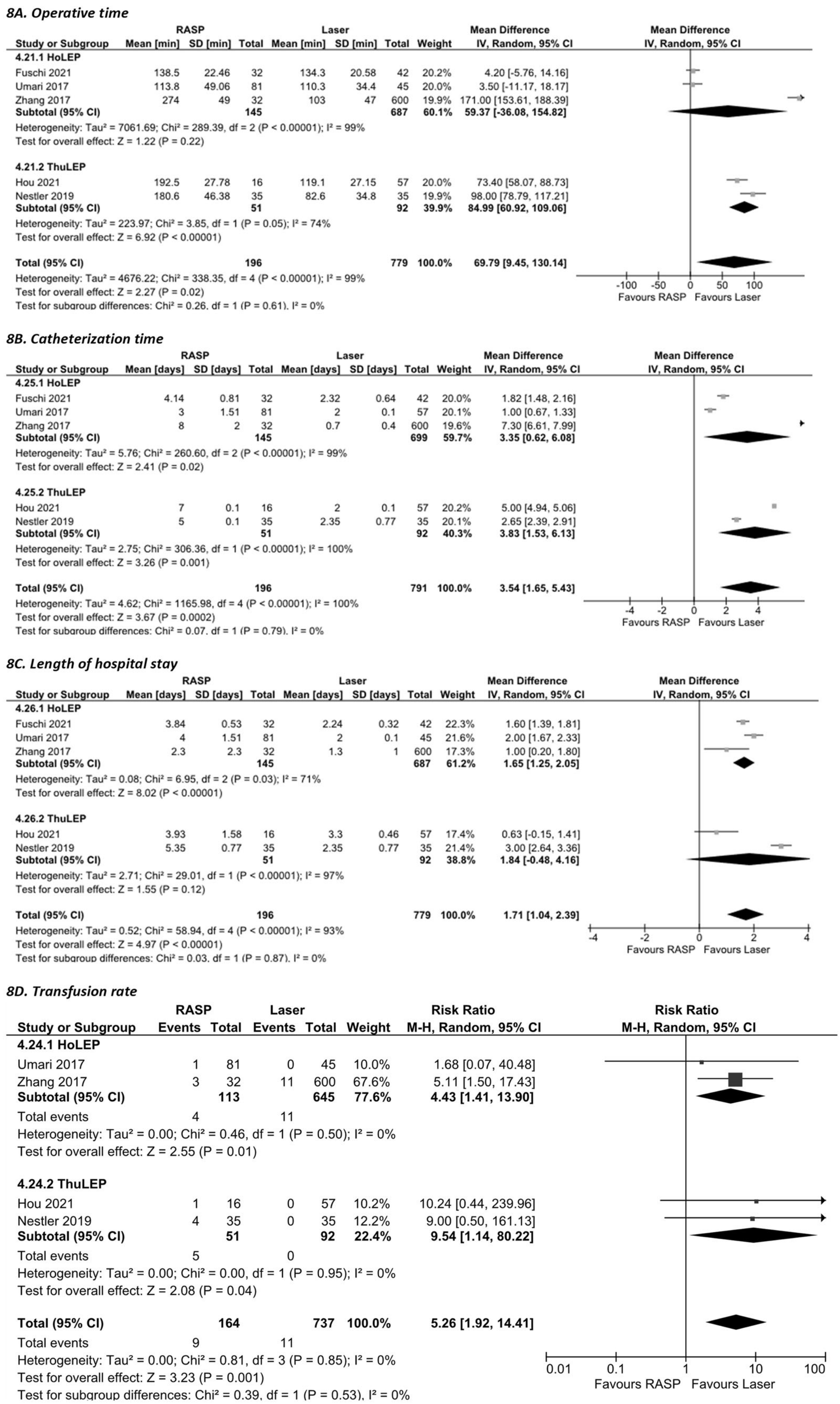


Fig. 8 Forest plots of perioperative outcomes for robot-assisted simple prostatectomy (RASP) versus endoscopic enucleation of the prostate (EEP). **A** Operative time. **B** Catheterization time. **C** Length of hospital stay. **D** Transfusion rate.

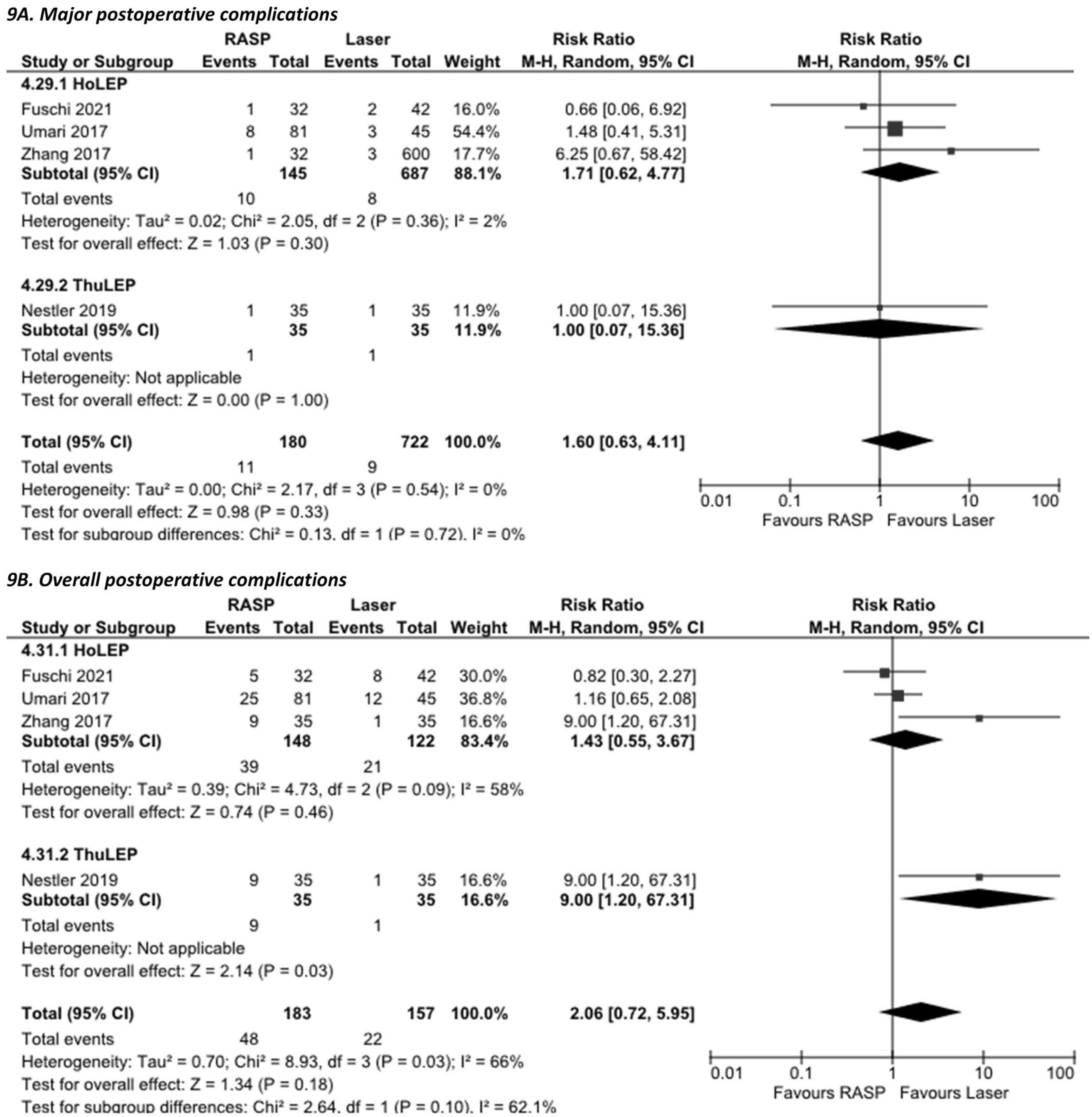


Fig. 9 Forest plots of postoperative complications for robot-assisted simple prostatectomy (RASP) versus endoscopic enucleation of the prostate (EEP). A Major postoperative complications. **B** Overall postoperative complications.

Differences in the occurrence of bladder neck contracture and urethral stenosis is worth of being further investigated, but lack of long-term data, especially for RASP procedure, represents a limiting factor in this regard [62].

Limitations

The present study is not devoid of limitations. Only one randomized controlled trial [27] and one prospective, non-randomized study [48] were included. A selection bias cannot be ruled out given the retrospective design of most studies. Moreover, some studies collected small number of patients and none of them reported surgeon experience. Overall, the studies were short of important functional outcomes, resulting in the inability to provide all outcomes for each comparison arms, which may limit the strength of our evidence.

CONCLUSIONS

RASP has become a well-established size independent treatment option for the management of BPO caused by a large prostate gland. It can duplicate the functional outcomes of OSP while offering a better safety profile, including lower EBL and lower complication rates. When compared to LSP, the latter still stands as a valid lower cost option, but it requires solid laparoscopic skill sets and therefore it is unlikely to spread on larger scale. When compared to laser EEP, RASP offers a shorter learning curve, but it still suffers from longer catheterization time and LOS.

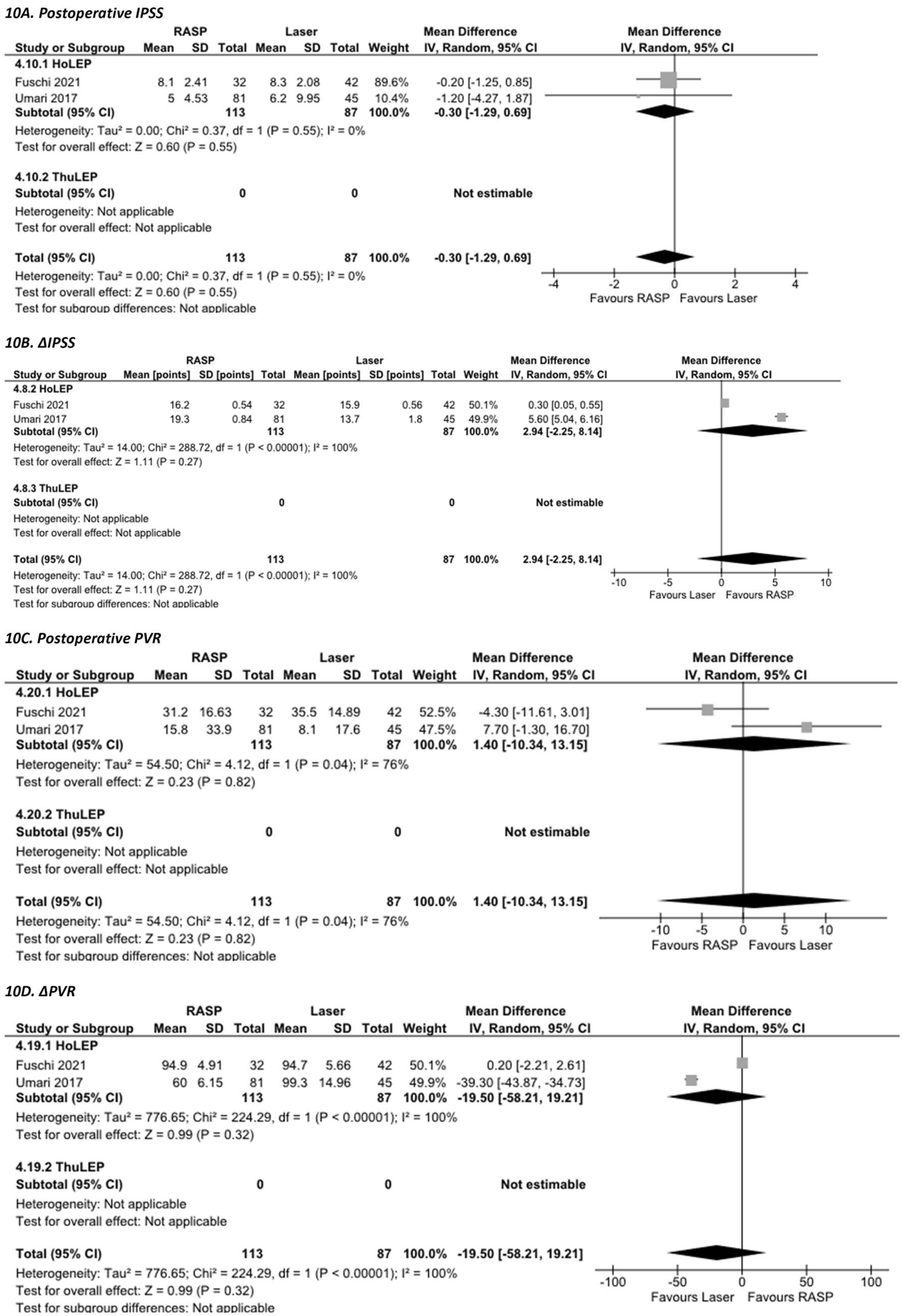


Fig. 10 Forest plots of urodynamic and functional outcomes for robot-assisted simple prostatectomy (RASP) versus endoscopic enucleation of the prostate (EEP). A Postoperative IPSS. **B** ΔIPSS. **C** Postoperative PVR. **D** ΔPVR. IPSS International Prostate Symptom Score, Qmax maximum flow rate, PVR post-void residual volume.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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AUTHOR CONTRIBUTIONS

Conceptualization: SDP, FC, RA; Methodology: SDP, FC, RA; Data acquisition: SDP; Analysis: SDP, FC; Writing—original draft preparation: SDP, FC, RA; Writing—review and editing: SDP, FC, RC; Supervision: FDG, BIC, CM, MDS, RD, EEC, CDN, GEC, LC, FP, VM, CI; Project administration: SDP, FC, RA. All authors have read and agreed to the published version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

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