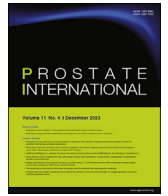




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Review Article

Single-port and multiport robot-assisted radical prostatectomy: A meta-analysis

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ABSTRACT

Objective: To compare the perioperative, oncological, and functional outcomes between single-port robot-assisted radical prostatectomy (SP-RARP) and multiport robot-assisted radical prostatectomy (MP-RARP) via a meta-analysis.

Methods: For relevant articles, three electronic databases, including PubMed, Scopus, and Web of Science, were searched from their inception until January 15, 2022. A meta-analysis has been reported in line with PRISMA 2020 and AMSTAR Guidelines. The risk ratio and weighted mean difference (MD) were applied for the comparison of dichotomous and continuous variables with 95% confidence intervals (CI).

Results: Of the 368 retrieved abstracts, 41 underwent full-text review, and seven studies were included in the final analysis, comprising a total cohort of 1,934 cases of RARP (355 SP-RARP cases and 1,579 MP-RARP cases). Compared to MP-RARP, the SP-RARP group had less postoperative pain score (MD = -0.7, 95% CI -1 to -0.4, $P < 0.001$), morphine milligram equivalents usage (MD = -3.8, 95% CI -7.5 to -0.1, $P = 0.04$), hospital stay (MD = -1, 95% CI -1.8 to -0.1, $P = 0.019$), and urinary catheterization time (MD = -1.1, 95% CI -1.9 to -0.3, $P = 0.008$). However, the SP-RARP group had a longer console time than the MP-RARP group (MD = 5.3, 95% CI 2.6 to 7.9, $P < 0.001$).

Conclusions: Our study demonstrated that early results were mostly equivalent with the single-port approach. This technology may help to reduce the hospital stay and postoperative pain for patients undergoing radical prostatectomy compared to MP-RARP, without compromising the functional and early oncological outcomes.

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Abbreviations: CI, Confidence Interval; CT, Computer Tomography; MP-RARP, Multiport Robot-assisted Radical Prostatectomy; MRI, Magnetic Resonance Imaging; NOS, Newcastle–Ottawa Scale; OR, Odds Ratio; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RARP, Robot-assisted Radical Prostatectomy; RR, Risk Ratio; SD, Standard Deviation; SP-RARP, Single-Port Robot-assisted Radical Prostatectomy.

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1. Introduction

For men, prostate cancer (PCa) is the most common non-cutaneous malignant disease, with 1.6 million new cases per year in the world¹. According to the American Cancer Society report, the estimated new PCa cases and deaths from PCa are 268,490 and 34,500, respectively, in the United States in 2022². Clinical management of PCa may vary significantly according to the age, tumor stage, risk stratification, hereditary predisposition, and patient's comorbidities^{3,4}. Hence, managing this heterogeneous disease requires a multidisciplinary approach, including surgical, medical,

and radiation oncology disciplines to apply the most appropriate treatment for these patients^{5,6}.

Radical prostatectomy remains the standard for curative treatment for localized PCa, while also demonstrating a survival benefit for patients with high risk PCa^{7–9}. In the United States, robotic surgery has replaced open surgery as the most common surgical approach for radical prostatectomy. Compared to open radical prostatectomy, the robot-assisted radical prostatectomy (RARP) offers comparable oncological outcomes with advantages of minimally invasive surgery, including less blood loss, shorter hospital stay, shorter convalescence period, fewer postoperative complications, and improved cosmetic outcomes^{10,11}. Furthermore, compared to the open approach, RARP may be associated with improvements in urinary continence and erectile function (EF) recovery after surgery^{12–14}.

In 2018, the Food and Drug Administration (FDA) approved the urologic surgical use of the da Vinci Single Port platform, which includes three articulating instruments and a flexible camera through a single cannula¹⁵. Since the approval of the FDA, several centers have reported their experience with single-port robotic radical prostatectomy (SP-RARP)^{16–21}. SP-RARP is associated with a higher cost for disposables as compared to MP-RARP²². However, the ability of the SP-RARP to deliver improved surgical outcomes and its cost-effectiveness are still debated^{23–25}. Until now, most of the SP-RARP studies are retrospective single-center designs and/or single surgeon resulting in unavoidable selection bias that can cause an appreciable imbalance in baseline factors between the groups that are also associated with the outcome. To overcome the shortcomings of individual retrospective studies, we compared the perioperative, oncological, and functional outcomes of SP-RARP to multiport robot-assisted radical prostatectomy (MP-RARP) via meta-analysis to help guide treatment comparisons.

2. Methods

2.1. Literature search

This study was conducted following the accepted methodology recommendations of PRISMA (preferred reporting items for systematic reviews and meta-analyses) and AMSTAR (assessing the methodological quality of systematic reviews) Guidelines for systematic reviews and meta-analyses (Supplemental Table 1)²⁶. Three electronic databases, the Scopus, Web of Science (ISI), and PubMed, were searched to identify relevant studies regarding perioperative outcomes between SP-RARP and MP-RARP from their inception until January 15, 2022. The following search terms were used: (“prostatic” “prostate cancer”) and (“robotic” “robot-assisted”) and (“single” “multi-port”). Additionally, we performed a manual search of references from articles included in Scopus, PubMed and Web of Science to avoid missing any relevant publications²⁷.

2.2. Selection criteria and abstract screening

The inclusion criteria were the relevant original articles reporting the perioperative, oncological, and functional outcomes between single-port robot-assisted radical prostatectomy (SP-RARP) and multiport robot-assisted radical prostatectomy (MP-RARP). There were no restrictions on study design, country, or language. While there have been significant improvements in robotic surgery over the past two decades, we elected not to have any restriction on the publication date to assess perioperative, oncological, and functional outcomes between SP-RARP and MP-RARP. We conducted a comprehensive literature search without

restrictions on study design, country, language, or publication date to avoid selection bias and erroneous conclusions. Articles were excluded if they met one of the following exclusion criteria: (1) Not relevant to the study topic, in vitro or animal study; (2) Cases report or series with less than five cases; (3) Review, book chapter, thesis; (4) Conference papers, editorials, letters, oral presentation, correspondence, communications, and posters; (5) Duplicated articles. Two independent groups of reviewers performed title and abstract screening to select relevant papers. Eligible publications were further screened for inclusion in the systematic review and meta-analysis. Any disagreement was resolved by discussion and consensus if necessary.

2.3. Full-text screening and data extraction

Regarding data extraction, we developed the extraction form using Microsoft Excel (Redmond WA, USA). Two groups of reviewers independently extracted data from the included studies using an Excel sheet. Two independent reviewers validated the data to ensure the accuracy of all extracted data. All disagreements and discrepancies were resolved by discussion and consensus. Articles published by the same research group were checked for potential overlapping data based on the period of case recruitment, the center where the cases were recruited, and confirmation from the study authors when necessary. For those studies that selected the patients from the same institutions or databases, we chose the studies with the highest number of patients for the primary analyses.

2.4. Quality assessment

The Newcastle–Ottawa Scale (NOS) was used to evaluate the quality of studies included in our meta-analyses in which stars were awarded for cohort or case-control studies (maximum nine stars) based on a developed checklist²⁸. Studies that were awarded at least six stars were considered moderate to high-quality studies, while those with a NOS value of less than six were regarded as low-quality studies²⁸.

2.5. Statistical analysis

Comprehensive Meta-analysis (Englewood NJ, USA) was used for statistical analyses. Among-study heterogeneity was assessed by the I^2 statistic, which shows the total variation across studies that is not a result of chance²⁹. An I^2 statistic ranging from 25%–49%, 50%–74%, and $\geq 75\%$ indicate a low, moderate, and high amount of heterogeneity, respectively³⁰. Sensitivity or subgroup analyses were performed to handle heterogeneity. We used risk ratios (RR) with 95% confidential intervals (CI) for categorical variables. The pooled results are presented as a forest plot using the random-effect models. Egger’s regression test and funnel plot were calculated to assess the presence of publication bias. A p -value of less than 0.05 was considered statistically significant.

3. Results

3.1. Search results and study characteristics

A total of 368 articles were identified from three electronic databases, including Scopus, PubMed and Web of Science. After screening those articles by title and abstract, 41 articles were selected for full-text assessment. Upon full-text review, 34 articles were excluded due to lack of proper information, study design, and duplication. In total, seven articles that met the inclusion

criteria were included in the final cohort analysis, comprising 1,934 cases of robot-assisted radical prostatectomy, including 355 cases of SP-RARP and 1,579 cases of MP-RARP^{17-19,23,25,31,32}. The evidence acquisition flow chart is shown in Fig. 1. The individual characteristics of all included studies are described in Table 1.

3.2. Perioperative outcomes among the patients who underwent RARP

A summary of this meta-analysis for the perioperative outcomes of two groups (SP-RARP and MP-RARP) is demonstrated in Table 2. Compared to MP-RARP, the SP-RARP group had a significantly lower postoperative pain score (MD = -0.7, 95% CI -1 to -0.4, $P < 0.001$), fewer morphine milligram equivalents usage (MD = -3.8, 95% CI -7.5 to -0.1, $P = 0.04$), shorter hospital stay (MD = -1, 95% CI -1.8 to -0.1, $P = 0.019$), and shorter urinary catheterization time (MD = -1.1, 95% CI -1.9 to -0.3, $P = 0.008$). However, the SP-RARP group had a longer console time compared to the MP-RARP group (MD = 5.3, 95% CI 2.6 to 7.9, $P < 0.001$). There were no significant differences in other outcomes between the two techniques, including the overall operation time, estimated blood loss, and postoperative complications (Fig. 2).

The heterogeneity of the outcomes, including operative time, estimated blood loss, postoperative pain score, hospital stay and pain free on postoperative day, was high. We used sensitivity analysis for assessment of heterogeneity (Supplemental Figure 4).

3.3. Oncological and functional outcomes among the patients who underwent RARP

A summary of this meta-analysis for the oncological and functional outcomes of two groups (SP-RARP and MP-RARP) is displayed in Table 2. There were no significant differences in other oncological and functional outcomes between the two techniques, including positive surgical margins, three-month continence, six-month continence, and three-month potency rates (Table 2).

The heterogeneity of the functional outcomes, including continence recovery in 3 months, were high. We used sensitivity analysis for assessment of the heterogeneity (Supplemental Figure 4).

3.4. Risk of bias assessment

The NOS tool was used to evaluate the study quality. Most of the included studies were retrospective studies. The number of stars awarded to each included study ranged from six to nine stars. Details of given stars within each NOS domain are shown in Supplemental Table 3.

3.5. Publication bias

We used Egger's regression test to assess the publication bias, and it did not suggest any evidence of bias. Moreover, the funnel plot showed no evidence of asymmetry, which was further confirmed by the Egger's regression test ($P = 0.378$) (Supplemental Figure 1).

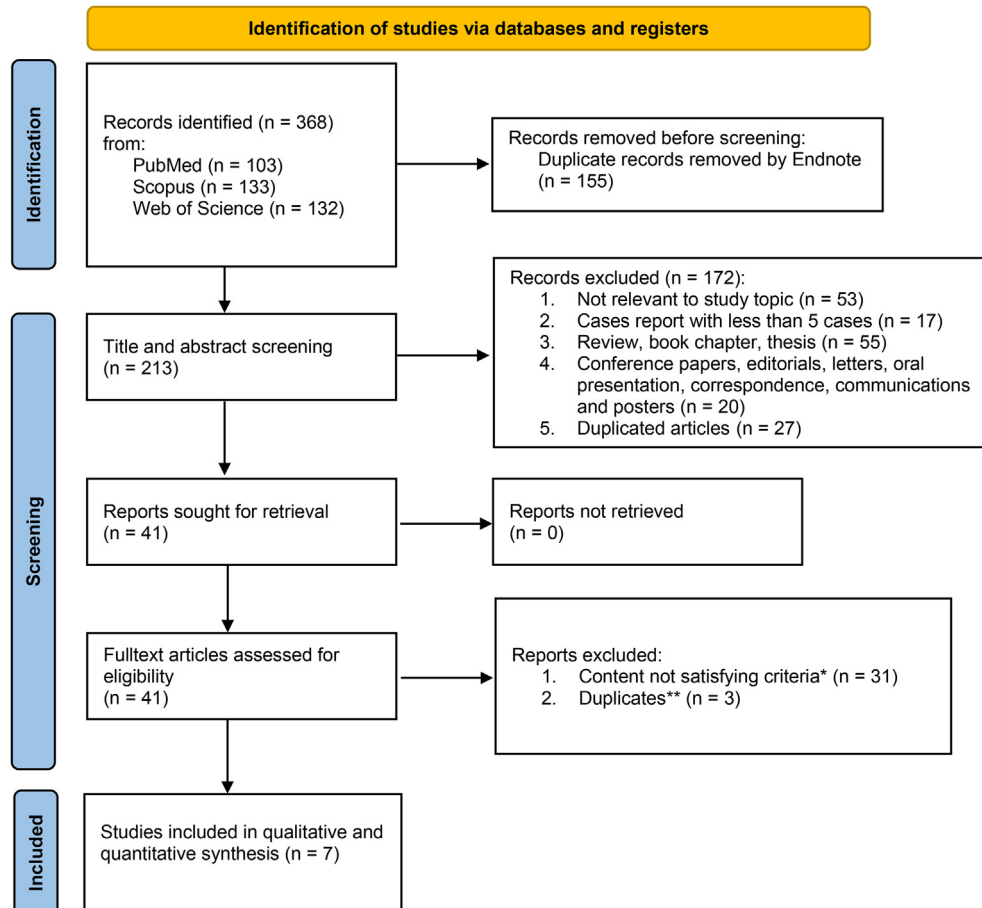


Figure 1. Evidence acquisition flow chart. *Records excluded due to single-arm study design or lack of information related with perioperative, functional, and oncological outcomes; **Includes no reliable or overlapped data.

Table 1
Characteristics of included studies

Study ID (Author/Year/ Country)	Period	Study design	No. of patients	No of cases		Surgical approach		Age (in years)		BMI		Previous abdominal surgery		PSA (ng/mL)		Prostate volume (mL)		Pathologic stage \geq T3a		Nerve-sparing	
				SP	MP	SP	MP	SP	MP	SP	MP	SP	MP	SP	MP	SP	MP	SP	MP	SP	MP
Saidian/2020/USA	2018–2019	Retrospective cohort	95	47	48	Transperitoneal	Transperitoneal	64.7	64.2	30.4	31.2	12/47	9/48	8.3	8.5	NA	NA	30/47	17/48	NA	NA
Huang/2021/USA	2017–2019	Retrospective cohort	402	26	376	Transperitoneal	Transperitoneal	63	61.9	28.5	27.9	NA	NA	6.87	6.04	NA	NA	12/26	158/376	NA	NA
Ju/2021/China	2019–2020	Prospective cohort	56	30	26	Retroperitoneal	Retroperitoneal	64.5	65.8	23.6	23.7	6/30	5/26	8.92	9.58	NA	NA	4/30	3/26	26/30	22/26
Lenfant/2020/USA	2019–2020	Prospective cohort	210	100	110	Transperitoneal	Retroperitoneal	64.7	64.2	28.6	29.3	26/100	31/110	6.56	6.92	53.5	44.1	51/100	61/110	85/100	89/110
Moschovas/2021/USA	2019–2020	Retrospective cohort (Propensity score matching)	946	71	875	Transperitoneal	Transperitoneal	63.3	63.6	25.3	28.3	NA	NA	5.88	6.82	49	52.6	17/71	4/71	NA	NA
Vigneswaran/2020/USA	2017–2019	Retrospective cohort	163	50	113	Transperitoneal and Retroperitoneal (10%)	Transperitoneal	63	62.3	28.9	28.3	11/50	30/113	9.32	9.33	53	45.7	20/50	50/113	32/50	71/113
Noh/2021/Korea	2019–2021	Retrospective cohort (Propensity score matching)	62	31	31	Transperitoneal	Transperitoneal	68.5	67	24.6	24.9	NA	NA	9.9	8.8	33.9	37	9/31	11/31	NA	NA

MP, Multiport; NA, Not available; SP, Single-port.

Table 2
Meta-analysis of the perioperative and postoperative outcomes between single-port and multiport robot-assisted radical prostatectomy

Outcomes	No. of studies	No. of patients		Heterogeneity		Overall effect		
		SP	MP	I ² (%)	P	MD/RR (95% CI)	P	
Perioperative outcomes	Operative time (in min)	7	355	775	80	< 0.001	5.2 (-1.4, 11.8)	0.124
	Console time (in min)	2	102	102	0	0.732	5.3 (2.6, 7.9)	< 0.001
	Estimated blood loss (in mL)	6	284	704	96	< 0.001	-20 (-50.8, 10.6)	0.201
	Pain score (n = 1–10)	4	158	504	82	0.001	-0.7 (-1,-0.4)	< 0.001
	Morphine Milligram Equivalents (in MME)	3	176	599	23	0.27	-3.8 (-7.5,-0.1)	0.04
	Hospital stay (in days)	4	227	297	98	< 0.001	-1 (-1.8, -0.1)	0.019
	Urinary catheterization time (in days)	3	197	271	61	0.072	-1.1 (-1.9,-0.3)	0.008
Postoperative outcomes	Postoperative complication	4	203	560	0	0.65	1.2 (0.8, 1.8)	0.317
	Minor post-operative complication (Clavien-Dindo I–II)	4	203	560	0	0.612	0.9 (0.6, 1.5)	0.927
	Major post-operative complication (Clavien-Dindo III–V)	3	173	534	0	0.572	2.5 (0.9, 6.7)	0.051
	Pain free on postoperative day #1	2	150	223	79	0.026	4.8 (1.2, 18.4)	0.019
	Positive surgical margins	7	353	775	0	0.788	0.8 (0.7, 1.1)	0.211
	Continence recovery in 3 months	6	305	381	88	< 0.001	1.3 (0.9, 2)	0.109
	Continence recovery in 6 months	2	131	141	29	0.234	1 (0.8, 1.2)	0.854
	Potency recovery in 3 months	4	179	176	0	0.763	0.8 (0.5, 1.1)	0.312

CI, Confidence Interval; MD, Mean Difference; MP, Multiport; RR, Risk Ratio; SP, Single-port.

4. Discussion

Published studies have demonstrated that the single-port robotic technique is a safe and feasible approach for performing radical prostatectomy. This is consistent with our reported findings^{15,23,25,33}. As compared to the widely accepted MP-RARP, our analysis found that the single-port approach has comparable outcomes, including operation time, estimated blood loss and postoperative complications. With regards to perioperative outcomes, SP-RARP was associated with a significant reduction in postoperative pain, postoperative morphine usage, length of hospital stay and indwelling urinary catheter duration.

These relative improvements in perioperative outcomes appear to be responsible for the greater likelihood of SP-RARP being performed as an outpatient procedure than standard MP-RARP^{18,19,34}. This higher rate of outpatient surgery in the SP-RARP group could have resulted from reducing opioid consumption following a reduction in postoperative pain in this patient group¹⁸. Therefore, the patients can be discharged earlier due to reduction in the side effects of opioids, such as nausea and vomiting, hypotension, constipation, and dependence^{35,36}. Shorter length of hospital stay has also been associated with decreased nosocomial infection rates and reduced hospitalization cost^{22,37,38}.

SP-RARP is reported to have better surgical scar cosmesis therefore a lesser perceived psychosocial impact on patients^{17,24}. This is important as it can affect the patient's decision for surgery^{17,24}. However, most studies which demonstrated a preference for single site robotic surgery predominantly studied patients undergoing reconstructive surgery for benign diseases^{15,39,40}. The impact of cosmetic advantages on older oncological patient population is not clear but may not be negligible^{39,40}.

The single-port technique is currently not widely applied due to concerns regarding the learning curve, technical difficulties, and cost-effectiveness¹⁵. Initial reports reported apparently higher rates of positive surgical margin during the early part of the learning curve of the SP-RARP technique^{15,41,42}. With experience, our analysis demonstrated comparable positive surgical margin rates between SP-RARP versus MP-RARP in mature series. Another concern of the single-port technique has been its oncological and functional outcomes^{18,32}. This meta-analysis showed no significant differences in oncological and functional outcomes of over 350 SP-RARP compared to MP-RARP. If a new technology is merely improving the

existing available technology without significantly improving patient outcomes, then this new technology implementation is unlikely to justify any additional cost^{15,43}.

This study has some limitations inherent to the meta-analysis study design. Included studies used heterogenous definitions of outcomes to assess postoperative urinary continence and erection function recovery. As a result, these functional outcomes could not be included for analysis because the relevant data was inadequate. It is known that the single-port surgical system was used first by very experienced surgeons already competent in MP-RARP. Hence, the results from this meta-analysis may not be extrapolated to novice practitioners of SP-RARP. Another limitation was the short-term follow-up period of currently published studies; thus, our meta-analysis did not compare long-term outcomes of biochemical recurrence, continence, and sexual function recovery. This may not be a major issue as early outcome data, as in our study, should be first verified before longer term data of new technologies can be compared. Lastly, the MP-RARP group used either da Vinci Si or Xi platforms in the included studies. Although a recent study from Lei *et al.* reported that the Xi system had apparently better perioperative outcomes, compared with the Si system⁴⁴, we considered them essentially equivalent as multiport surgical systems. Despite these limitations, this study represents the most comprehensive meta-analysis of this subject with a larger robotic prostatectomy population than previously published meta-analyses^{45,46}. Furthermore, we showed more analysis results regarding functional outcomes including three-month continence, six-month continence, and three-month potency rates. We believe this review is timely as it provides health systems and surgeons an insight to the potential advantages of the single port system before consideration of purchasing or adopting it.

5. Conclusions

Our study results demonstrated favorable postoperative results of the single-port approach as a minimally invasive choice for radical prostatectomy. This technology may help reduce the hospital stay and postoperative pain for patients undergoing radical prostatectomy compared to even a mature procedure such as MP-RARP, without compromising the functional outcomes and positive surgical margin rates. However, further well-designed studies and clinical trials are necessary to determine the role of single-port

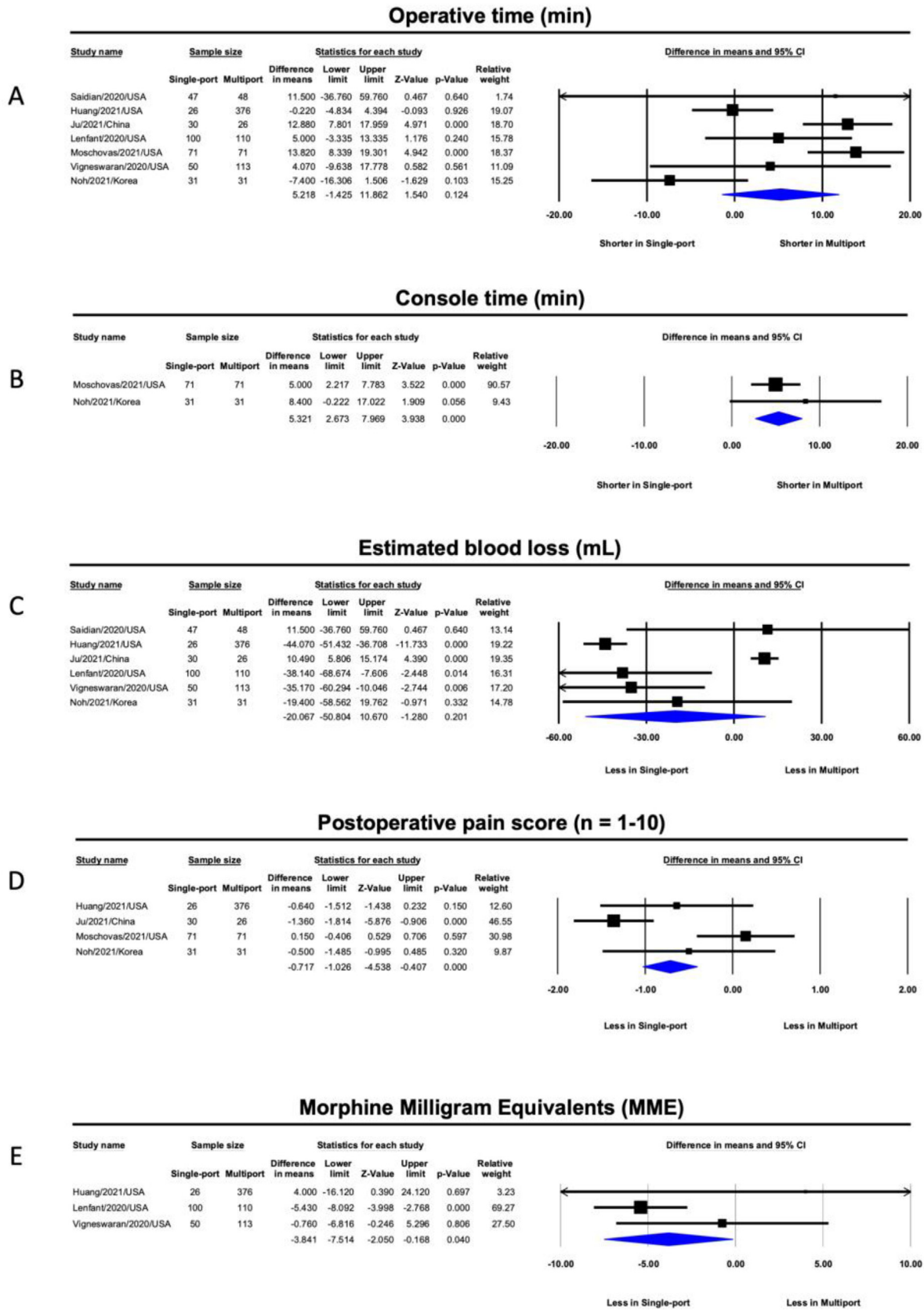


Figure 2. Forest plots for the meta-analysis comparing the outcomes between single-port and multiport robot-assisted radical prostatectomy: (A) operative time; (B) console time; (C) estimated blood loss; (D) postoperative pain score; (E) morphine milligram equivalents.

robot-assisted radical prostatectomy in regard to long-term oncological and functional outcomes.

Author's contribution

TT Nguyen: Project development, manuscript writing.
RW Dobbs: Data analysis, manuscript writing and editing.
HG Vuong: Project development, data analysis, manuscript writing.

K Quy: Data collection, data analysis.
HTT Ngo: Data collection, data analysis.
AT Mai: Data collection, data analysis.
M Tran: Data collection, data analysis.
MS Thai: Data analysis, manuscript writing and editing.
HY Tieng: Protocol development, manuscript writing and editing.
SY Choi: Manuscript writing and editing.
M Shahait: Manuscript writing and editing.
DI Lee: Project development, manuscript editing.

Ethical approval and consent to participate

Not applicable since this is a systematic review and meta-analysis.

Registration of research

Registry used: Prospero.
Unique Identifying number or registration ID: CRD42022331348.

Conflict of interest

The authors declare that they have no conflict of interest.

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Availability of supporting data

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

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pnrl.2023.04.002>.

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