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REVIEW ARTICLE

Laparoscopic vs. robotic rectal cancer surgery and the effect on conversion rates: a meta-analysis of randomized controlled trials and propensity-score-matched studies

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Abstract

Background The usage of robotic surgery in rectal cancer is increasing, but there is an ongoing debate as to whether it provides any benefit. The aim of the present study was to determine if robotic surgery results in less conversion to an open operation than laparoscopic rectal cancer surgery.

Methods A meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP Journal Club and Database of Abstracts of Review of Effectiveness. Included were randomized controlled trials (RCTs) and propensity-score-matched (PSM) studies comparing a robotic vs. laparoscopic approach to rectal cancer surgery. The primary endpoint was conversion to open. All statistical analyses and data synthesis were conducted using STATA/IC version 14·2, Windows 64 bit (StataCorp LP, College Station, TX, USA)

Results Six hundred and twenty-one studies were identified through electronic database search. After application of selection criteria as per PRISMA and MOOSE criteria, six RCTs and five PSM articles were analyzed. From the six RCTs, 512 robotic and 519 laparoscopic cases were evaluated. There was a significantly lower rate of conversion for the robotic surgery arm (4.1% vs. 8.1%, OR 0.28; 95% CI 0.00–0.57). Of the five PSM studies, 2097 robotic and 3053 laparoscopic cases were evaluated. There was a significantly lower conversion to open rate found in the robotic surgery cohort (7.4% vs. 15.6%; OR 0.39; 95% CI 0.30–0.47). Pooled RCT and PSM data demonstrated significantly lower conversion rates for robotic surgery (6.7% vs. 14.5%; OR 0.38; 95% CI 0.30–0.46).

Conclusions Robotic surgery for rectal cancer is associated with reduced conversion to open surgery compared to a laparoscopic approach.

Keywords Robotic surgical procedures · Laparoscopic surgery · RECTUM/surg · Rectal cancer · Conversion to open surgery · Meta-analysis

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Introduction

Colorectal cancer (CRC) remains one of the most common cancers in the Western world [1, 2] and approximately 30% of CRCs are found in the rectum. While open surgery has been the traditional approach for rectal cancer, over the past two decades, there has been a trend towards performing rectal cancer surgery with minimally invasive techniques. However, high-quality evidence from the literature surrounding laparoscopic surgery has reported a wide range of results [3, 4]. Importantly, the recent ALaCaRT study failed to demonstrate that a laparoscopic technique was non-inferior to open surgery for rectal cancer in terms of a composite of oncological factors associated with adequate surgical resection [3].

From a technical viewpoint, laparoscopic surgery within the narrow confines of the pelvis is challenging, as there are limited space, limited maneuverability of instruments, fulcrum effects, and the influence of tremor. This may contribute not only to failure to proceed safely with laparoscopic techniques and conversion to open, but may compromise the total mesorectal excision (TME) plane. Robotic surgery offers improved ergonomics, three-dimensional vision, instrumentation with improved articulation, rotation, and dexterity, and a stable camera platform controlled by the surgeon with reduced tremor [5, 6] providing a technical advantage over the rigid instrumentation, two-dimensional vision and assistant-controlled cameras in traditional laparoscopic surgery, with its advantage particularly in the narrow pelvis. However, actual evidence of benefit of robotic approach over laparoscopic surgery for rectal cancer has to date been limited.

The main advantage of robotic rectal surgery reported by several cohort studies is reduced conversion to open rates compared to laparoscopic surgery [7], but the much anticipated Robotic vs. Laparoscopic Resection for Rectal Cancer (ROLARR) trial recently reported no significant difference in conversion to open rates overall between robotic and laparoscopic techniques [6]. This casts some doubt on the role of robotic surgery for rectal cancer. However, when evaluating the data carefully, it is important to note that in the ROLARR study, on subgroup analysis, there was a significant difference in conversion rates based on robotic surgeon caseload/experience.

Critics of robotic surgery argue that capital and maintenance costs [8, 9] as well as the steep learning curve associated with robotic technology outweigh potential modest benefits [10]. Existing meta-analyses comparing robotic and laparoscopic surgery for rectal cancer have either included lower quality observational evidence or had limited statistical power when only RCTs have been included, [11–13], such that the outcomes reported by been read with a 'pinch of salt'. With the inclusion of results from the ROLARR RCT and the inclusion of results from recent PSMs, the aim of the present study was to perform an updated meta-analysis of sufficient size with high-quality data from RCTs and PSMs only with appropriate statistical power to detect differences between the two groups.

We chose the primary outcome measure as rate of conversion to open surgery. First, conversion to open is a good measure of the technical aspect of minimally invasive surgery. Second, conversion to open is an outcome measure that has been consistently reported by majority of cohort studies and randomized evidence regarding robotic surgery. Third, conversion to open is a complication that has been shown to be associated with disease recurrence, morbidity, and mortality [14–16] and has both short- and long-term clinical importance in rectal cancer surgery. Our secondary outcome measure was to identify other independent risk factors for conversion to open including body mass index (BMI) and gender.

Materials and methods

Literature search strategy

The present systematic review and meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [17] and recommended guidelines [18]. Electronic searches were performed using Ovid Medline, PubMed, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club and Database of Abstracts of Review of Effectiveness (DARE) from their dates of inception to November 2017. To achieve maximum sensitivity of the search strategy and identify all studies, we combined the terms: "robotic", "laparoscopic", "Da Vinci", "robot", "conversion", "rectal", "cancer", and "tumor", as either keywords or MeSH terms. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. All identified articles were systematically assessed using the inclusion and exclusion criteria.

Selection criteria

Eligible randomized controlled trials (RCTs) and propensity-score-matched studies (PSM) for the present systematic review and meta-analysis included those in which patient cohorts with surgery for rectal cancer with either robotic or laparoscopic technique. The PSM statistical method aims to minimize bias in observational studies by matching the individual's measured covariates between two treatment groups, so that differences in the measured outcome can be more

directly attributed to the treatment rather than the individual's observed covariates [19]. Propensity-score matching is considered to significantly strengthen observational studies [19, 20]. Given the limited number of RCTs and sample sizes available on this topic, we decided to evaluate both RCT and PSM studies in this analysis.

Studies that did not report on conversion to open as a complication or endpoint were excluded from this systematic review. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for quantitative assessment at each time interval. Only publications involving human subjects and in the English language were included. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded. Review articles were omitted because of potential publication bias and duplication of results.

Data extraction and critical appraisal

All data were extracted from article texts, tables, and figures. Two investigators independently reviewed each retrieved article (K.P., J.T.). Discussion and consensus resolved discrepancies between the two reviewers. Because quality scoring is controversial in meta-analyses of observational studies, two reviewers (K.P., J.T.) independently appraised each article included in our analysis according to a critical review checklist of the Dutch Cochrane Centre proposed by MOOSE (refer to Supplementary Table 1) [21]. The key points of this checklist include: (I) clear definition of study population; (II) clear definition of outcomes and outcome assessment; (III) independent assessment of outcome parameters; (IV) sufficient duration of follow-up; (V) no selective loss during follow-up; and (VI) important confounders and prognostic factors identified. The Cochrane Risk of Bias tool was also used for assessment of bias associated with the RCTs (Supplementary Fig. 1). Outcomes from both the RCTs and PSMs were assessed using the GRADE approach (Supplementary Table 2). Discussion and consensus resolved discrepancies between the two reviewers.

Statistical analysis

The odds ratio (OR) was used as a summary statistic. In the present study, both fixed- and random-effects models were tested. In the fixed-effects model, it was assumed that treatment effect in each study was the same, whereas in a random-effects model, it was assumed that there were variations between studies. For assessment of independent risk factors for conversion to open complication, pooled multivariate-adjusted OR was used as a summary statistic. Pooled estimates and the corresponding 95% CI were determined using inverse variance fixed-effects model and the DerSimonian and Laird random-effects models. χ^2 tests were used to study heterogeneity between trials. I^2 statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values greater than 50% considered as substantial heterogeneity. I^2 can be calculated as: $I^2 = 100\% \times (Q - df)/Q$, with Q defined as Cochrane's heterogeneity statistics and df defined as degree of freedom. Both a random-effects model and a fixed-effects model have been provided. As the I^2 value was $< 50\%$, results from the fixed-effects model have been reported in the results. Specific analyses considering confounding factors were not possible, because raw data were not available. All p values were twosided. All statistical analyses and data synthesis were conducted using Revman 5.3 (K.P., J.T.) and STATA/IC version 14·2, Windows 64 bit (StataCorp LP, College Station, TX, USA) (H.R.K., J.T.).

Results

Study search

A total of 621 references were identified through electronic database search. After exclusion of duplicate or irrelevant references, 602 potential articles were retrieved. After detailed evaluation of these articles, 25 articles remained for assessment. After application of selection criteria, 6 RCTs [5, 6, 22–25] and 5 PSM articles [26–31] were selected for analysis. Figure 1 shows the PRISMA flow diagram. The study characteristics are summarized in Table 1. The majority of patients were male between the ages of 55–65 years. In the majority of studies, rectal cancer was defined as cancer within 15 cm from the anal verge, although several studies reported outcomes in a more stringent subset of rectal tumors within 5 cm from anal verge [24, 28]. The proportion of stage 2 cancers was 22.2–31% of robotic cases and 21.6–28.5% of laparoscopic cases. The proportion of stage 3 cancers was 24.1–50% of robotic cases, compared to 32.7–50% of laparoscopic cases. Assessment of quality of studies by meta-analyses of observational studies in epidemiology (MOOSE) criteria is presented in Supplementary Table 1.

Primary outcome measure: conversion to open rate in robotic vs. laparoscopic rectal cancer surgery

Six included RCTs reported conversion to open rates, including 512 robotic cases and 519 laparoscopic cases. There was a significantly lower rate of conversion for the robotic surgery arm compared to the laparoscopic surgery arm (4.1% vs. 8.1%, OR 0.28; 95% CI 0.00–0.57). There was no significant heterogeneity noted ($I^2 = 0.5\%$, $p = 0.403$).

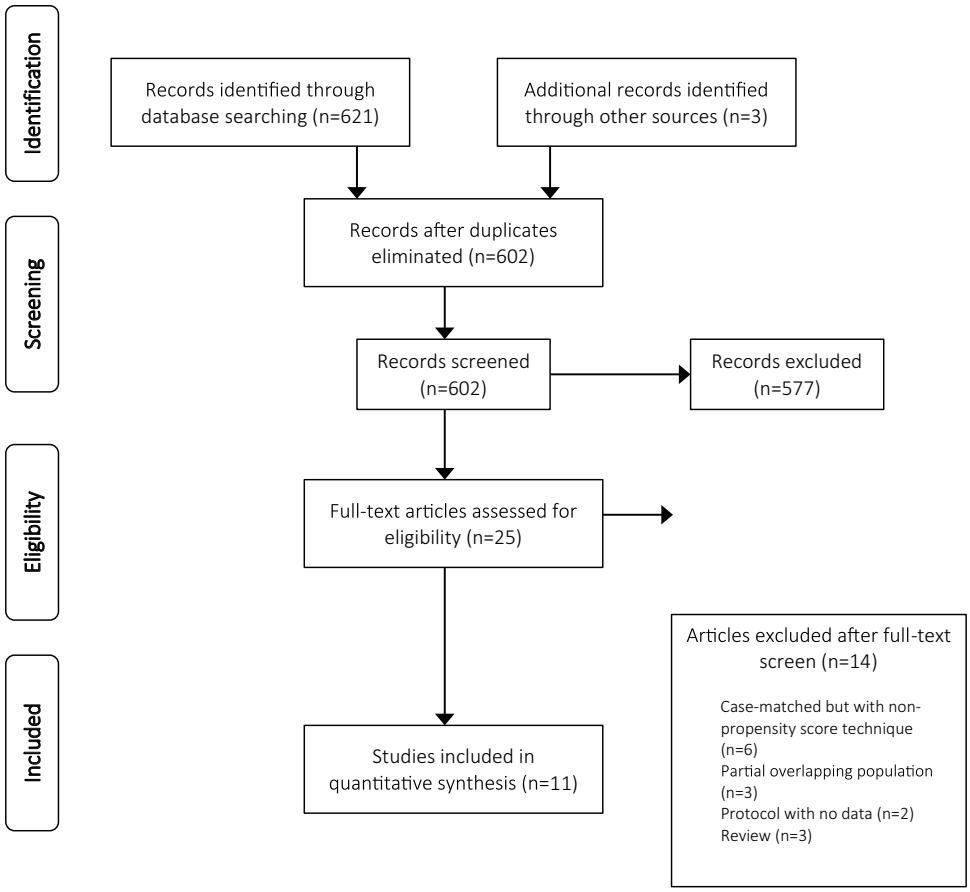

Fig. 1 PRISMA flowchart demonstrating search strategy for the present systematic review and meta-analysis

Five included PSM studies reported results from 2097 robotic and 3053 laparoscopic cases. There was a significantly lower conversion to open rate found in the robotic surgery cohort compared to laparoscopic surgery for rectal cancer (7.4% vs. 15.6%; OR 0.39; 95% CI 0.30–0.47). There was no significant heterogeneity noted ($I^2 = 4.3\%$, $p = 0.382$).

Pooled RCT and PSM data demonstrated significantly lower conversion rates for robotic surgery compared to laparoscopic surgery for rectal cancer (6.7% vs. 14.5%; OR 0.38; 95% CI 0.30–0.46) with no significant heterogeneity ($I^2 = 0\%$, $p = 0.464$) (see Figs. 2, 3).

Although absolute conversion to open rates were higher for PSM studies compared to RCT data, this difference was not significant (test for subgroup differences $p = 0.472$).

Two studies provided multivariate-adjusted data—Ackerman et al. [26] and Jayne et al. [6]. On pooling results from these studies, robotic vs. laparoscopic surgery was associated with a lower rate of conversion to open (OR 0.36; 95% CI 0.15–0.90), but with significant heterogeneity ($I^2 = 84\%$, $p = 0.01$).

Conversion to open in male subgroup in robotic vs. laparoscopic rectal cancer surgery

In RCTs, when considering males only, a robotic approach was associated with significantly lower conversion rates compared to laparoscopic approach (8.6% vs. 16.8%; OR 0.46; 95% CI 0.24–0.89; $p = 0.02$), with no significant heterogeneity ($I^2 = 0\%$, $p = 0.02$).

Only 1 PSM study reported outcomes in a male subgroup, with a significantly lower conversion rate seen in the robotic subgroup (OR 0.34, 95% CI 0.22–0.50).

The total pooled OR of conversion to open was lower for robotics compared to the laparoscopic approach in males (OR 0.36; 95% CI 0.26–0.52) (Online Appendix 1).

Secondary outcome: identifying other risk factors for conversion to open

Multivariate-adjusted OR were pooled for from Jayne et al. [6] and Ackerman et al. [26] Pooled adjusted odds found no difference in females vs. males in terms of conversion to open complication (OR 1.20; 95% CI 0.34–4.19), with

Table 1 Study characteristics and patient demographics

First author	Year	Study type	Study size	*n* (RS)/*n* (LS)	Males (%)		Age (years)		Rectal cancer definition (cm from verge)	TNM stage (II: III) (%)		Neoadjuvant therapy (%)		AR (%)		LAR (%)		APR (%)	
					RS	LS	RS	LS		RS	LS	RS	LS	RS	LS	RS	LS	RS	LS
Baik	2008	RCT	36	18/18	77.8	77.8	57.3	62	0–15	22.2/50	22.2/50	–	–	–	–	–	–	–	–
Jayne (ROLARR)	2017	RCT	471	237/234	67.9	67.9	64.4	65.5	0–15	–	–	46.8	46.2	11.9	8.3	64.4	71.7	22	19.6
Jimenez	2011	RCT	56	28/28	42.9	60.7	68	65.5	Sigmoid, rectal	–	–	–	–	–	–	–	–	–	–
Kim MJ	2017	RCT	139	66/73	77.3	71.2	60.4	59.7	0–9	–	–			–	–	98.5	95.9	1.5	2.7
Patriti	2009	RCT	66	29/37	62.1	67.6	68	69	0–15	31.0/24.1	21.6/27.0	24.1	5.4	–	–	–	–	17.2	5.4
Wei	2017	RCT	406	135/131	–	–	–	–	0–5	–	–	–	–	–	–	–	–	100	100
Ackerman	2017	PSM	1066	533/533	56.8	58.3	–	–	–	–	–	–	–	–	–	–	–	–	–
Cho	2015	PSM	556	278/278	65.5	66.2	57.4	58.3	0–15	–	–	32.7	28.4	–	–	80.9	84.5	19.1	15.5
Kim J	2016	PSM	448	224/224	64.7	63	59.2	63.9	0–15	26.3/33.5	24.1/33.5	22.3	22.3	0.9	3.1	75.4	75	5.4	6.3
Park	2015	PSM	212	106/106	70.8	67	59.6	61.7	0–4	–	–	64.2	56.6	–	–	–	–	–	–
Speicher	2015	PSM	2868	956/1912	58.8	58.1	59	61	–	–	–	52.1	31.4	–	–	100	100	–	–

RS robotic surgery, *LS* laparoscopic surgery, *AR* anterior resection, *LAR* low anterior resection, *APR* abdominoperineal resection, *RCT* randomized controlled trial, *PSM* propensity-score-matched study, – not reported

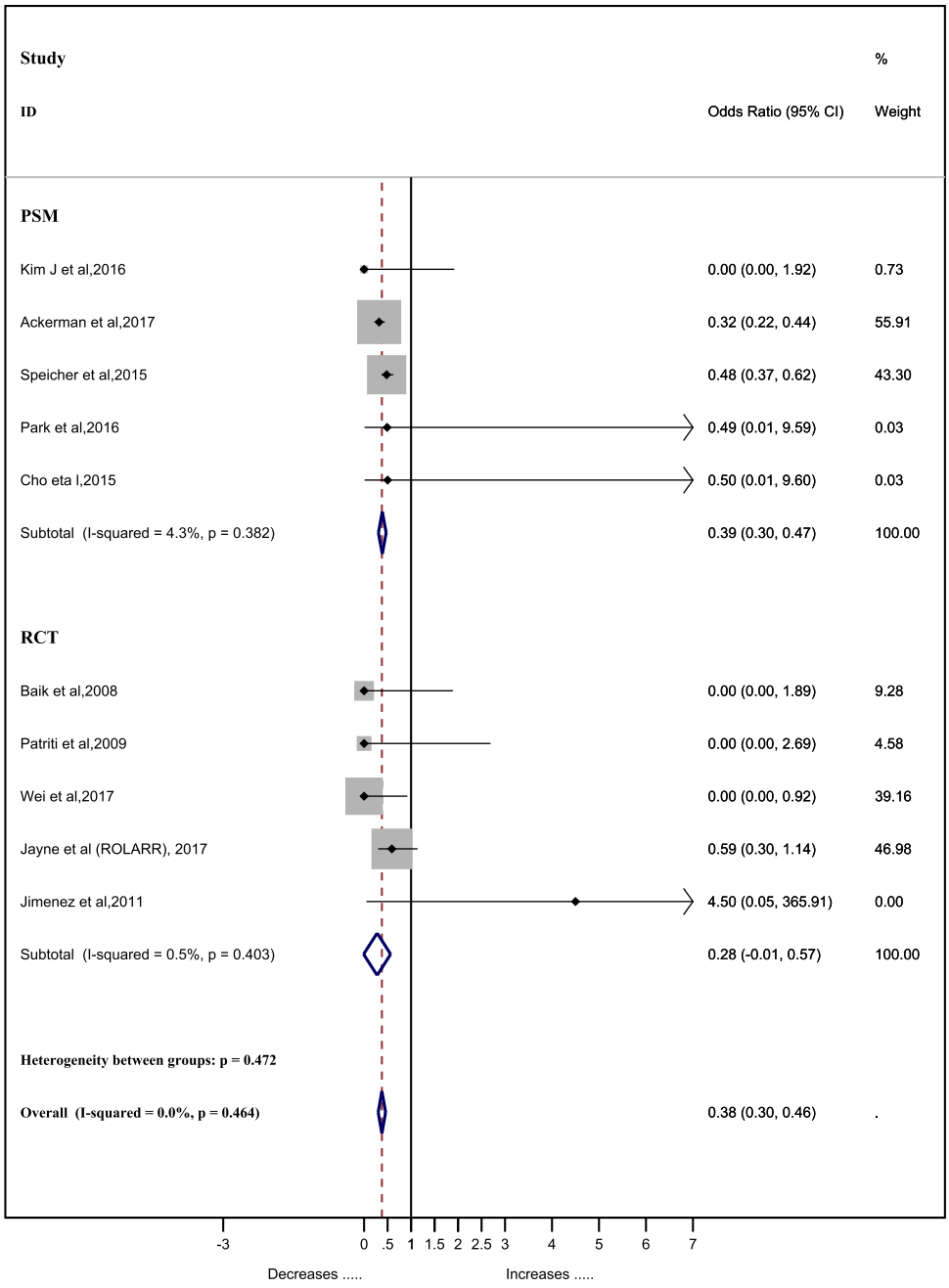

Fig. 2 Meta-analysis forest plot of conversion to open surgery rates, sub-grouped into randomized and propensity-score-matched studies (fixed-effects model)

significant heterogeneity ($I^2 = 88\%$, $p = 0.004$). Pooled adjusted odds also found no difference in overweight vs. normal BMI cases in terms to conversion to open (OR 1.01; 95% CI 0.36–2.87), with significant heterogeneity ($I^2 = 77\%$; $p = 0.04$). Obese BMI was found to be a risk factor for conversion to open surgery after pooled adjusted odds (OR 2.76; 95% CI 1.12–6.82), with significant heterogeneity ($I^2 = 74\%$, $p = 0.03$) (Online Appendix 1).

Several risk factors for conversion to open were reported by only 1 study, and these could not be pooled in a meta-analysis. The study by Ackerman et al. reported on conversion rates by colorectal vs. non-colorectal surgeons and small vs. large bed-size hospitals [26]. Jayne et al. compared conversion rate in abdominoperineal resection (APR) vs. low anterior resection, reporting a lower OR for APR [6]. In the same study, neoadjuvant chemotherapy/radiotherapy vs. no neoadjuvant therapy and high vs.. low anterior resection procedures were not risk factors for conversion.

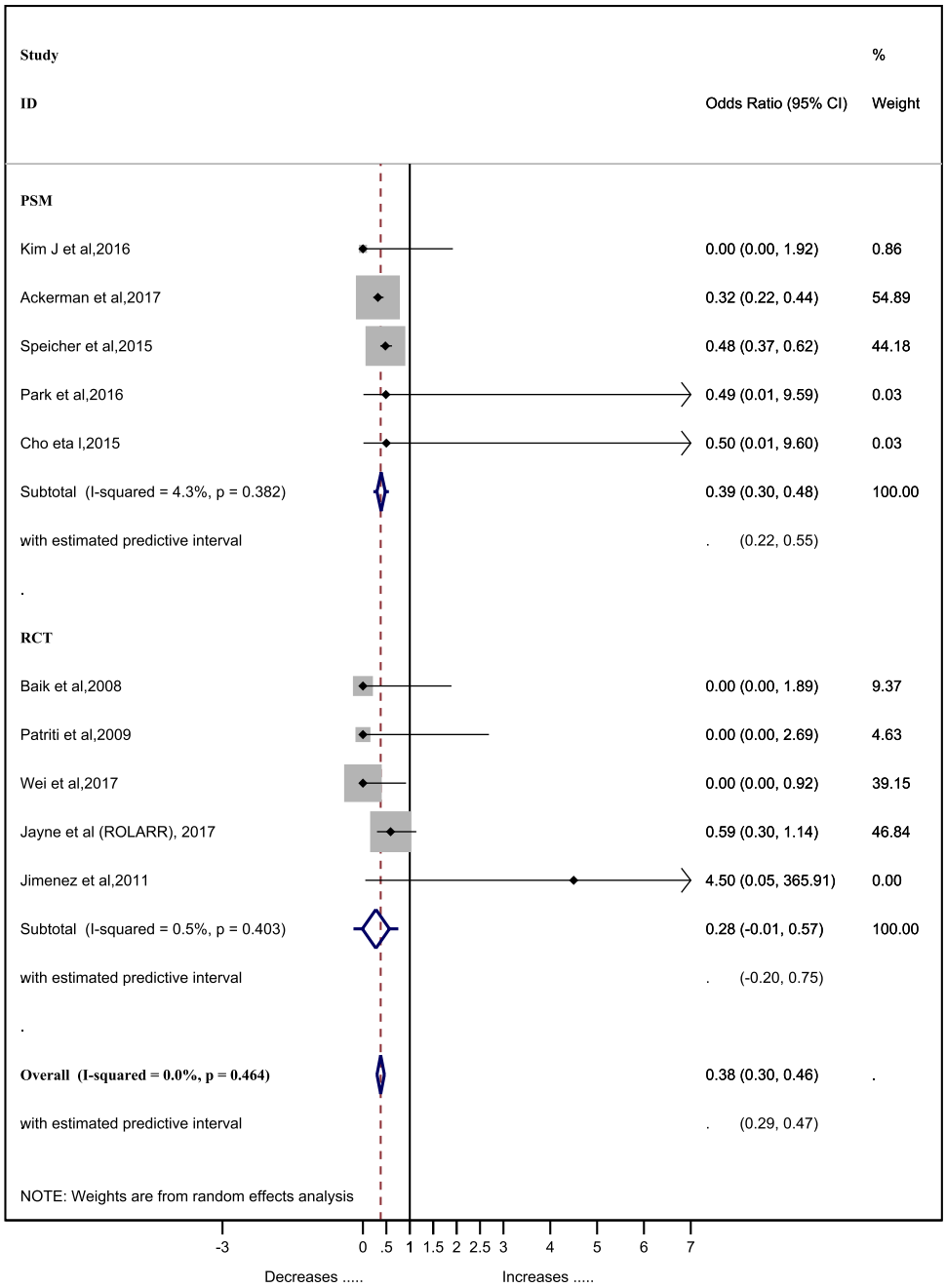

Fig. 3 Meta-analysis forest plot of conversion to open surgery rates, sub-grouped into randomized and propensity-score-matched studies (random-effects model)

Discussion

In this study, evaluating RCT and PSM evidence only, we demonstrated that robotic surgery was associated with a statistically significant lower conversion to open rate. This result was consistent when analysing RCT data and PSM data separately as well as on pooling RCT and PSM data. Pooled analysis of adjusted OR demonstrated that laparoscopic technique (when compared to robotic technique) and obese BMI (when compared to normal BMI range) were both independently associated with increased risk of conversion.

In the present study, the pooled conversion rate for robotic surgery was 6.7% compared to 14.5% for laparoscopic surgery for rectal cancer. Our pooled conversion for robotic surgery was lower than that reported by the ROLARR randomized study [6] which was 8.1%. Perhaps, this may be attributed to the fact that the ROLARR study involved participating surgeons with a wide range of expertise/caseload in robotic surgery for rectal cancer. Subgroup analysis of the ROLARR study demonstrated that surgeons with more than 100 prior robotic operations consistently had lower odds of conversion with robotic surgery when compared to laparoscopic surgery (OR 0.304, 95% 0.094–0.988). There was no

significant difference in conversion rate between robotic and laparoscopic surgery in surgeons with fewer than 100 robotic cases. Therefore, this suggests that the results of robotic rectal cancer are influenced by the learning curve effect and prior robotic and laparoscopic experience, although it has also been shown that previous laparoscopic experience is not essential for robotic surgery [32]. The wide range in robotic experience of surgeons performing procedures in the ROLARR study may explain why the lower conversion rate reported in the robotic cohort was not statistically significant. Our pooled conversion rate in laparoscopic rectal surgery (14.5%) was higher than that of the ROLARR study (10.1%) [6] and ALaCaRT (9%) [3] but comparable to that of major laparoscopic rectal cancer trials including COLOR II (16%) [33] and ACOSOG Z6051 (11%) [4]. Rates in ROLARR and ALaCaRT trials may be influenced by larger number of high-volume academic centres with more specialized surgeons participating in the studies.

This meta-analysis demonstrated several independent predictors of increased conversion to open surgery, including laparoscopic surgery (when compared to robotic), obese BMI (compared to normal BMI range), but conversion rate was not influenced by gender or overweight BMI (when compared to normal BMI range).

The benefit of lower conversion to open rates for robotic rectal cancer surgery, particularly in males (who are more likely to have a narrow pelvis), has been previously reported [6, 13]. Our subgroup analysis in males similarly showed a lower conversion rate in the robotic group when compared to the open group. However, our overall analysis including both males and females, also demonstrated lower conversion to open rates and we were unable to definitively show a statistically significant difference with gender in terms of conversion to open rates stratified by robotic vs. laparoscopic technique.

The PSM study by Ackerman et al [26] demonstrated that surgeon and hospital factors were independently associated with conversion to open rates, with higher conversion rates independent of robotic/laparoscopic technique when rectal surgery was performed by non-colorectal surgeons in hospitals with smaller number of beds. While outcome based on colorectal vs. non-colorectal surgeon was not evaluated in ROLARR [6], it did demonstrate that robotic caseload and the learning curve were a significant factor in conversion to open rates.

As discussed previously, conversion to open is a complication which not only increases the risk of 30-day morbidity and mortality, but may also be associated with long-term consequences. Several studies have shown that conversion to open may be associated with disease recurrence, morbidity, and mortality [14–16]. Clancy et al [14] performed a meta-analysis of 15 studies and 5293 patients. Of 4391 patients with laparoscopic resection, 902 were converted to open. Cases with conversion were associated with higher 30-day mortality, higher long-term recurrence, and higher overall mortality. In this study, male gender, rectal location of tumor, T3/4 tumor, node-positive disease, and higher BMI were risk factors for conversion to open.

Patient selection is an important consideration when comparing outcomes of robotic and laparoscopic surgery. Although it was not possible to account for case complexity from the studies evaluated in this meta-analysis, the technical advantage conferred by robotic technology would logically be most beneficial for difficult cases. A study by Ahmed et al. [34] showed that the greatest benefit for robotic surgery was in high-risk patients with obese BMI, male gender, pre-operative chemoradiotherapy, tumors <8 cm from anal verge and a history of the previous abdominal surgery and robotic surgery may also be associated with improved quality of life [35]. The study concluded that robotic surgery was associated with improved sphincter preservation rates, lower conversion, blood loss and shorter length of stay when compared to laparoscopic surgery in high-risk patients.

Strengths and limitations

Although we limited our analyses to higher quality evidence with RCTs and PSM studies, the majority of included RCTs were small. Furthermore, although PSMs adjust for confounding factors, PSMs only adjust for covariates selected by authors of the study, with inter-study variability. The majority of RCTs lacked blinding to treatment allocation. Confounding factors including grade of technical difficulty, hospital volume, and surgeon experience with robotic technique are difficult to adjust for in small RCTs.

Conclusions

Robotic-assisted minimally invasive rectal surgery may be associated with a reduction in conversion to open rates compared to laparoscopic surgery.

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Author contributions Conception and design: KP and JWTT conceived the study and contributed equally, and all authors substantially contributed to the design of the study. Analysis and interpretation of the data: KP, JWTT, and HRK were involved in the analyses and substantially contributed to interpretation of the data. Drafting of the article: KP and JWTT contributed to the first draft of the manuscript. All authors provided substantial contribution to the critical revisions of the manuscript. Collection and assembly of data: KP and JWTT were responsible for the data, and KP, JWTT, and HRK performed the data analysis with the other authors assisting in the interpretation. All authors take responsibility for the integrity of the data and the accuracy of the data

analysis. All of the authors were significantly involved in this work and provided final approval of the submitted manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The authors have complied with appropriate ethical standards in preparation and publication of this manuscript.

Informed consent For this type of study, formal consent is not required.

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