MEDICAL SCIENCE

Robotic mastectomy versus open mastectomy in patients with or at high risk of breast cancer: A systematic review and meta-analysis

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ABSTRACT

Objective: This study aimed to compare the efficacy and safety of robotic versus open technique in patients undergoing mastectomy for breast cancer treatment or risk-reduction. *Methods:* The literature search included English-published studies from inception to the 3rd of February 2023. The search included MEDLINE/PubMed, Cochrane Library, the Web of Science and Scopus, using the terms "robotic mastectomy" AND "open mastectomy". We calculated the odds ratio (OR) with 95% confidence intervals (CI) for categorical outcomes and standardized mean difference (SMD) for numerical outcomes. *Results:* Five studies were included. Robotic mastectomy was significantly associated with longer operative time (SMD=0.92 (95% CI: 0.34, 1.50), p-value=0.002) and hospital stay (SMD=0.53 (95% CI: 0.03, 1.02), p-value=0.04), but lower rates of overall complications (OR=0.56 (95% CI: 0.42, 0.75), p-value<0.001) and nipple-areola complex necrosis (OR=0.45 (95% CI: 0.24, 0.87), p-value=0.02). There was no significant difference between robotic and open mastectomy in terms of the involvement of surgical margin or locoregional recurrence of breast cancer. *Conclusions:* Robotic mastectomy can be considered a safe procedure. It may possibly reduce the probability of postoperative complications. The better aesthetic results accomplished with robotic mastectomy enhances the patient satisfaction. Yet, robotic mastectomy can lengthen the total operative time and increase the duration of hospital stay. The included studies showed several limitations, so there is a need to conduct large size, randomised, clinical trials with adequate follow-up before

recommending the routine use of the robotic technique for mastectomy.

Keywords: Breast cancer, conventional mastectomy, robotic surgery

1. INTRODUCTION

Globally, breast cancer occupies the first rank among cancers, accounting for 30% of all newly diagnosed cancer cases in women. In addition, breast cancer is responsible for approximately 15% of cancer-related deaths in women worldwide, representing the second cancer-specific cause of death (Siegel et al., 2019). Hereditary factors increase the risk of breast cancer and were identified in 5–10% of breast cancer cases. The most common genes associated with breast cancer are BRCA1 and BRCA2, which account for approximately 16% of the familial risk of breast cancer (Ford et al., 1998; Tung et al., 2015).

The gold standard treatment for the primary tumour is surgical resection. The choice of the type of surgery depends on the tumour stage and molecular characteristics. The most common procedures include mastectomy as well as breast-conserving surgery. Breast reconstruction may be performed concomitantly with mastectomy (Hartmann-Johnsen et al., 2015; Van-Maaren et al., 2016; Bhojwani et al., 2022). Patients with a high risk of hereditary breast cancer are candidates for bilateral prophylactic mastectomy (Casella et al., 2018).

Recently, many case series and clinical trials assessed robotic-assisted surgery in the performance of mastectomy and immediate breast reconstruction (IBR). The use of robotic surgery provides many benefits compared to open surgery, such as improving the visualization of tissue planes and reaching some tissues that are difficult to expose (Toesca et al., 2017; Lai et al., 2019; Park et al., 2019). Moreover, robotic mastectomy produces better cosmetic results, resulting only in small scars in the axillary region (Toesca et al., 2017; Lai et al., 2020). Previous studies concluded that robotic mastectomy is feasible and safe (Toesca et al., 2017; Houvenaeghel et al., 2019; Lai et al., 2019; Park et al., 2019).

However, there is currently no evidence that robotic mastectomy is superior to traditional open mastectomy, particularly in the terms of surgical complications and oncological outcomes. The Food and Drug Administration (FDA) stated that caution should be employed considering the use of robotic-assisted surgery for mastectomy (The US Food and Drug administration, 2021). Although several studies reported on the use of robotic mastectomy, their results were limited by their small sample size and the lack of a control group of traditional mastectomy (Park et al., 2019; Toesca et al., 2019; Lai et al., 2020; Ryu et al., 2022). Therefore, the present meta-analysis aims to compare the robotic and traditional mastectomies regarding their efficacy and safety in patients scheduled for mastectomy as a treatment for breast cancer or for risk-reduction.

2. MATERIALS AND METHODS

Methodology

The conduction of this meta-analysis complied with the principles of the Cochrane Handbook for Systematic Reviews of Interventions, version 6. The reporting of the methods and results followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009).

The research questions

Is robotic mastectomy (for breast cancer or risk-reduction) superior to open mastectomy in terms of efficacy and safety in patients with or at high risk of breast cancer?

Research aims and objectives

This meta-analysis aimed to compare the efficacy and safety of robotic mastectomy to open mastectomy in patients undergoing surgery for breast cancer or risk reduction, with the following objectives: a) To compare the efficacy (margin positivity and recurrence) of robotic mastectomy and open mastectomy and b) to compare the safety of robotic mastectomy and open mastectomy (intra- and postoperative complications, blood loss and conversion to open surgery).

Eligibility criteria for the studies

Types of studies

This meta-analysis included observational (cohort or case-control) studies and clinical trials. The search was limited to studies English-published studies from inception to the 3rd of February 2023.

Participants

Studies were included if patients were patients for whom mastectomy was indicated for treating breast cancer or for risk reduction.

Interventions

Eligible studies included a direct comparison between robotic and open mastectomy.

Exclusion criteria

We excluded conference abstracts, duplicate reports, case reports, review articles, commentaries, editorials and clinical guidelines. In addition, studies on cadavers and "single arm" studies were excluded.

Search strategy

Electronic searches

The search was conducted in the electronic databases of MEDLINE/PubMed, Cochrane Library, Web of Science and Scopus. The search was limited to English-published studies from inception till the 3rd of February 2023. The search was conducted during the period from the 30th of January 2023 to the 3rd of February 2023. The search terms included "robotic mastectomy" AND "open mastectomy".

Other resources

The reference lists of retrieved articles by electronic underwent scanning to identify other relevant studies that might have been missed by electronic search.

Selection of studies

The search process and screening were conducted. Then the full text of potentially relevant records was obtained and revised to assess fulfilment of the eligibility criteria for this meta-analysis. The search results, the screening of the titles and abstracts and the assessment of the full-text articles were checked.

Data extraction

Data abstraction from the eligible studies was performed using a standardised data sheet. The following data were extracted: (a) The study characteristics (the country, study design, time span of the study, the sample size for each arm, the study-specific eligibility criteria and the duration of follow-up); (b) patients' characteristics (age, body mass index); (c) the tumour details: Stage, size, grade, neoadjuvant and adjuvant therapy; (d) the surgical details dissection of axillary lymph nodes, operative duration and breast reconstruction and (d) the outcomes: Conversion to open surgery, blood loss, intraoperative complications, margin positivity, postoperative complications, hospital stay, reoperation and cancer recurrence. The extracted data were checked for consistency and clarity.

Measured outcomes

Primary outcomes

They included conversion to open mastectomy, blood loss, margin positivity and perioperative complications.

Secondary outcomes

Secondary outcomes included hospital stay, the rate of reoperation and cancer recurrence.

Assessment of the risk of bias in included studies

For assessing the risk of bias (ROB) in the included studies, we used the National Institute for Health and Care Excellence (NICE) checklist for cohort studies and clinical trials (NICE, 2016).

Data synthesis

Review Manager (Rev Man Version 5.4. The Cochrane Collaboration, 2020) was used for computing the standardized metrics, pooling the findings of the studies and creating forest plots. A narrative synthesis table Grimshaw et al., (2003) was created to report-for each outcome-the number of studies showing a positive direction of effect and the number of studies with statistically significant effects. Categorical dichotomous outcomes (e.g., margin positivity and recurrence) were expressed as odds ratio (OR) with 95% confidence intervals (CI). An OR > 1 indicated a higher risk in the robotic mastectomy group, while an OR< 1 indicated a higher risk in the open mastectomy group. Numerical outcomes (e.g., duration of surgery and hospital stay) were summarized using the standardized mean difference (SMD) by subtracting the mean for the open group from the mean for the robotic group and then dividing the result by the pooled standard deviation. A positive SMD indicated an increase in the outcome in the robotic group relative to the open mastectomy group, while a negative SMD value indicated the reverse. Significant heterogeneity across the studies was determined at a Cochrane Chi-square test with a p-value<0.1 and an I2 index ≥ 50%. The fixed-effect model was used for the pooling of data if heterogeneity was non-significant, while the random-effects model was used if heterogeneity was significant. A p-value<0.05 was selected for interpreting the comparisons between the robotic and open groups. The effect size was classified as follows: a) for ORs: Large ≥ 4.3; medium ≥ 2.5, small ≥ 1.5, negligible < 1.5; b) for SMDs: large ≥ 0.8; medium ≥ 0.5, small ≥ 0.2, negligible < 0.2 (Cohen, 1988).

3. RESULTS

Results of literature search and study selection

Figure 1 summarizes the results of the literature search and the processes of titles and abstracts screening as well as a review of full-text articles and the final selection of studies to be included in this meta-analysis. The conduction of the literature search yielded 180 records. Seventy-eight records were duplicates and removed. Then the remaining 102 records underwent screening of the titles and abstracts. At this step, 91 records were excluded because of the publication type (n = 36), non-relevance (n = 33), the lack of comparators (single-arm studies, n = 19) and conduction on cadavers (n = 3).

Next, we obtained the full texts of the remaining 11 records and assessed them for eligibility to be included in this meta-analysis. We excluded six records as two studies included both robotic and endoscopic mastectomies in the arm, one study lacked a comparator, one study was conducted on axillary lymph nodes but not the breast and one study compared endoscopic mastectomies to open surgery. The citation search indicated eight potentially relevant articles that were all excluded for the lack of a comparator (n = 2) and being duplicates (n = 6). Finally, five studies were eligible and included (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021; Park et al., 2022; Toesca et al., 2022).

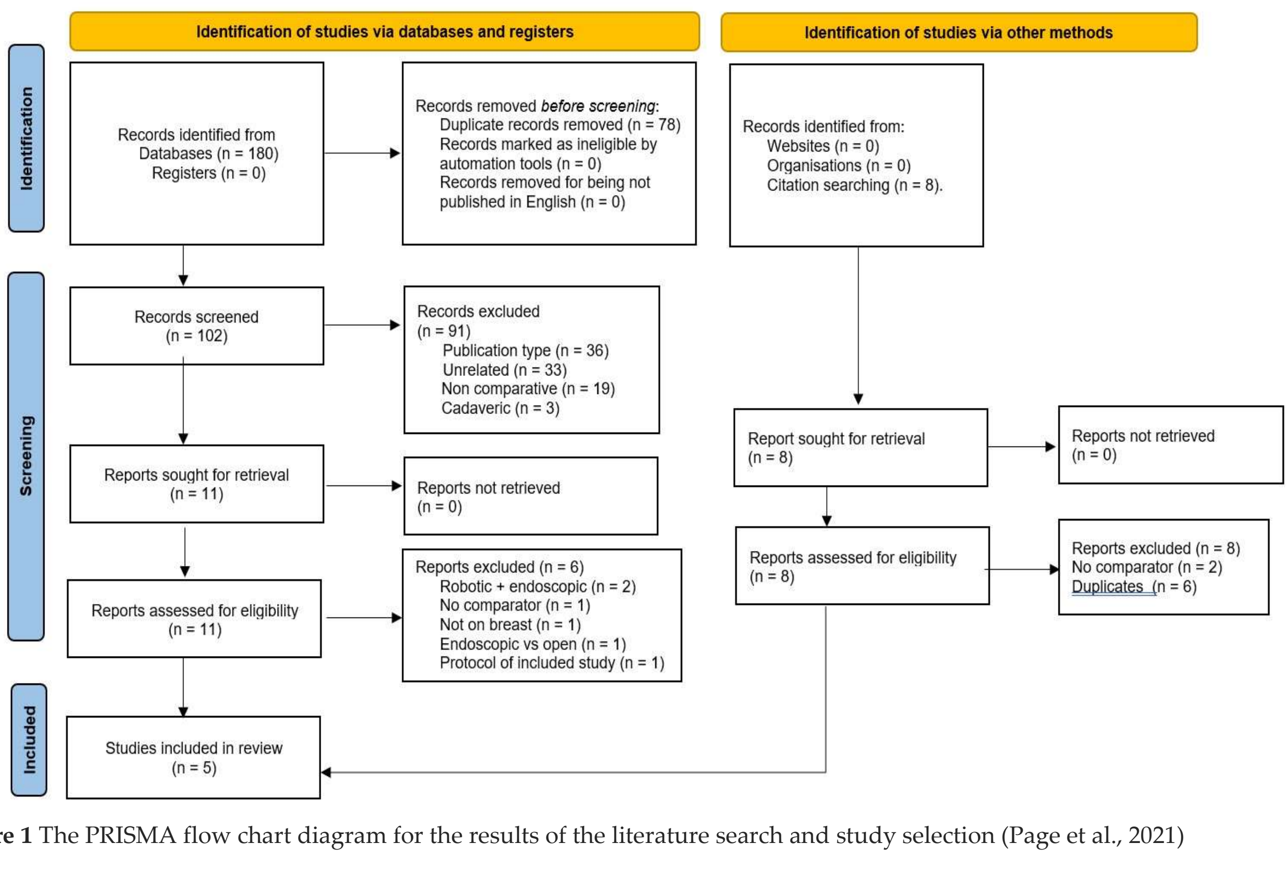

Figure 1 The PRISMA flow chart diagram for the results of the literature search and study selection (Page et al., 2021)

Basic characteristics and assessment of the risk of bias of the included studies

The basic characteristics of the included studies

Tables 1, 2 provide a summary of the basic characteristics of the five included studies. The design was a prospective cohort in one study (Houvenaeghel et al., 2020) and a retrospective cohort in two studies (Lai et al., 2020; Moon et al., 2021). One study pooled data from retrospective and prospective studies (Park et al., 2022) and one study was a randomized controlled trial (Toesca et al., 2022). The studies were conducted in France (Houvenaeghel et al., 2020), Taiwan (Lai et al., 2020), Korea (Moon et al., 2021) and Italy (Toesca et al., 2022). The study by Park et al., (2022) was an international study that included four centres in Taiwan, Korea and Italy. Mastectomy was indicated in the included patients as a treatment of breast cancer only in three studies (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021) and for both breast cancer treatment of and risk reduction in two studies (Park et al., 2022; Toesca et al., 2022).

Table 1 Characteristics of the included studies (n = 5)

Study	Study design	Country	Time span	Sample size Robotic: Open	Indication of mastectomy	Follow-up (months)
Houvenaeghel et al., (2020)	Prospective cohort	France	Mar 2016 – Jun 2019	46:59	Primary BC or local recurrence	NR
Lai et al., (2020)	Retrospective cohort	Taiwan-single centre	Jul 2011 - Sep 2019	54:62	Primary BC	Robotic: 14.6 ±8.8 Open: 47.3 ±19.6
Moon et al., (2021)	Retrospective cohort	Korea	Jan 2018 - Jun 2020	40:41	BC	NR
Park et al., (2022)	Pooled data from retrospective & prospective studies	International-multicentre	Jun 2014 – Mar 2020	292:463	BC & risk reduction	Median: 18
Toesca et al., (2022)	Phase III, open-label, RCT	Italy-single centre	Mar 2017 - Dec 2018	40:40	Operable primary BC & risk reduction	Median (range) = 28.6 (3.7-43.3)

NR: Not recorded; RCT: A randomized controlled trial

The eligibility criteria differed among the included studies and even in some studies were not clearly stated (Houvenaeghel et al., 2020; Moon et al., 2021; Park et al., 2022). The duration of follow-up also widely varied among the studies, with a median follow-up of 18 months in one study (Park et al., 2022) up to a mean of 47.3 months for the open surgery group in another study (Lai et al., 2020). Four studies included nipple-sparing mastectomies only (Lai et al., 2020; Moon et al., 2021; Park et al., 2022; Toesca et al., 2022), while the study of Houvenaeghel et al., (2020) included skin-sparing mastectomies only. In all studies, immediate breast reconstruction was performed using autologous flaps (Houvenaeghel et al., 2020; Park et al., 2022) or implants and prostheses (Lai et al., 2020; Moon et al., 2021; Park et al., 2022; Toesca et al., 2022).

Table 2 Interventions performed in the included studies (n = 5)

Study	Mastectomy	Reconstruction n/N	Sentinel LNs n/N	Axillary lymphadenectomy n/N
Houvenaeghel et al., (2020)	SSM	IBR with latissimus dorsi flap	Robotic: 20/46 Open: 13/59	Robotic: 13/46 Open: 17/59
Lai et al., (2020)	NSM	Immediate gel implant	Robotic: 51/54 Open: 49/62	Robotic: 13/54 Open: 18/62
Moon et al., (2021)	NSM	Immediate pre-pectoral prosthesis	Robotic: 40/40 Open: 41/41	Robotic: 3/40 Open: 5/41

Park et al., (2022)	NSM	IBR with Implant: Robotic: 276/292 Open: 375/463 Autologous: Robotic: 16/292 Open: 88/463	NR	NR
Toesca et al., (2022)	NSM	Implant: Robotic: 35/40 Open: 29/40 Tissue expander: Robotic: 5/40 Open: 11/40	Robotic: 34/40 Open: 35/40	Robotic: 34/40 Open: 35/40

IBR: Immediate breast reconstruction; n: number undergoing the procedure; N: Total number in each group; NR: Not recorded; NSM: Nipple-sparing mastectomy; SSM: Skin-sparing mastectomy

Summary of the included studies

Houvenaeghel et al., (2020) conducted a single-centre, prospective, cohort study on patients with primary breast cancer or local recurrence during the period from March 2016 to June 2019. The studied sample consisted of 46 patients in the robotic mastectomy group and 59 in the open mastectomy group. Both groups underwent a skin-sparing mastectomy and immediate breast reconstruction with latissimus dorsi-myocutaneous flap. The duration of follow-up was not reported. They found that the robotic group had a significantly longer mean operative time (290.5 min versus 259.7 min, p=0.016). The rate of complications was non-significantly lower in the robotic group compared to the open surgery group (45.7 vs. 62.7, p=0.061), but adjusting for confounders in the multivariate analysis showed a significantly lower rate of complications with the robotic technique (OR = 0.37, 95% CI: 0.142-0.966, p=0.042).

Lai et al., (2020) carried out a single-centre, retrospective cohort study on patients with operable primary breast cancer during the period from July 2011 to September 2019. The robotic and open surgery cohorts consisted of 54 and 62 patients, respectively. Both groups underwent nipple-sparing mastectomy and reconstruction using direct-to-cohesive gel implants by the same surgeon. They excluded patients who had a history of breast-conserving surgery or radiation to the chest wall. They also excluded patients who underwent another concomitant operation, prophylactic mastectomy or endoscopic mastectomy as well as patients without breast reconstructions or in whom reconstructions other than direct to cohesive gel implant were used. The mean follow-up duration was significantly shorter in the robotic group (14.6 ±8.8 vs. 47.3 ±19.6, p<0.01). They found that the robotic mastectomy was associated with significantly higher overall satisfaction (92% excellent and 8% good vs. 75.6% excellent and 24.4% good, p=0.046). However, there were no significant differences between the two groups regarding the amount of blood loss, the risk of nipple necrosis and the overall complication rate. The robotic groups showed a significantly longer operative time and higher overall medical cost (10,877±796 versus 5,702±661 US Dollars, P < 0.01) compared to the conventional mastectomy group.

Moon et al., (2021) carried out a retrospective, cohort study during the period from January 2018 to June 2020 on breast cancer patients. The eligibility criteria were not clearly reported. Their robotic and open surgery cohorts comprised 40 and 41 patients, respectively. All patients underwent nipple-sparing mastectomy with immediate pre-pectoral prosthesis. They reported that the robotic group had a significantly longer mean operative time compared to the open surgery group (279±63 vs. 207±46, p<0.001) as well as a longer hospital stay (9.2±2.7 vs. 7.1±2.0 days, p<0.001). There were no significant between-group differences in blood loss, postoperative wound-related complications and nipple necrosis.

Park et al., (2022) carried out a pooled data analysis of retrospective and prospective studies. Mastectomy was indicated in the studied patients as a treatment for breast cancer or for risk reduction. They excluded patients who had the nipple and areola resected no reconstruction, previous operation history or stage IV cancer. All patients underwent a nipple-sparing mastectomy and immediate reconstruction using either implants or autologous flaps during the period from June 2014 to March 2020. The robotic and open surgery groups consisted of 292 and 463 patients, respectively. As the two groups were not comparable at the baseline, they performed a propensity score matching. They reported significantly lower rates of postoperative complications and nipple necrosis in the robotic group compared to the CNSM group. Meanwhile, there was no significant difference regarding the rates of recurrence between the two groups.

Toesca et al., (2022) conducted a phase III, open label, randomized controlled trial on patients treated with mastectomy for operable breast cancer or risk reduction. All patients underwent nipple-sparing mastectomy with concurrent reconstruction using breast implant and tissue expander during the period from March 2017 to December 2018. The studied sample consisted of 40 patients for each group. They excluded patients with any of the following: Preoperative evidence of axillary nodes metastasis, inflammatory breast cancer, evidence of tumour involvement in the skin or nipple-areola complex, Paget's disease, mesenchymal, inflammatory or recurrent breast cancer, history of previous thoracic radiation therapy, pregnancy, ASA score >2, uncontrolled diabetes mellitus, heavy smokers (>20 cigarettes/day), large breast volume (greater than cup D breast) or previous surgery in the ipsilateral breast. They reported that the operation in the robotic group had a significantly longer duration. The rate or type of complications did not significantly differ between the two groups. Patients in the robotic group showed significantly higher satisfaction with breasts and psychosocial, physical and sexual well-being compared to those who underwent the open procedure.

The assessment of the risk of bias in the included studies

Table 3 demonstrates the assessment of the ROB using the NICE checklists for cohort studies and clinical trials. The NICE checklists assess four principal domains of bias: Selection, performance, attrition and detection.

Table 3 The risk of bias assessment for the included studies based on the NICE tools for clinical trials and cohort studies

	Houvenaeghel et al., (2020)	Lai et al., (2020)	Moon et al., (2021)	Park et al., (2022)	Toesca et al., (2022)*
A1	Yes	Yes	Yes	Yes	Yes*
A2	Yes	No	No	Yes	Yes*
A3	No	Yes	No	No	Yes
selection bias	Uncertain	Uncertain	High	Low	Low
B1	Yes	Yes	Yes	Yes	Yes
B2	Uncertain	No	No	Uncertain	No
B3	Uncertain	Uncertain	Uncertain	Uncertain	No
Performance bias	Uncertain	High	High	Uncertain	High
C1	Uncertain	No	Uncertain	Yes	Yes
C2a	None	None	None	None	None
C2b	Yes	Yes	Yes	Yes	Yes
C3a	None	None	None	None	None
C3b	Yes	Yes	Yes	Yes	Yes
Attrition bias	Low	High	Low	Low	Low
D1	Uncertain	Yes	Uncertain	Yes	Yes
D2	Yes	Yes	Yes	Yes	Yes
D3	Yes	Yes	Yes	Yes	Yes
D4	Uncertain	No	Uncertain	Uncertain	No
D5	Uncertain	No	Uncertain	Uncertain	No
Detection bias	Uncertain	High	Uncertain	Uncertain	High

As regards the selection bias, it did not seem that potential confounders had affected the way of choosing the technique of surgery. In two cohort studies, attempts were made to balance the compared groups for potential confounders using multivariate regression (Houvenaeghel et al., 2020) and propensity score matching (Park et al., 2022). Moreover, the groups were not comparable at baseline in three cohort studies (Houvenaeghel et al., 2020; Moon et al., 2021; Park et al., 2022), but the study by Park et al., (2022) achieved a balance between the two groups by propensity score matching. The clinical trial by Toesca et al., (2022) reported the process of randomization and allocation to groups, with low ROB. The overall risk of selection bias was high in one study (Moon et al., 2021), while the risk was unclear in two studies (Houvenaeghel et al., 2020; Lai et al., 2020) and low in the other two studies (Park et al., 2022; Toesca et al., 2022).

As for the assessment of the performance bias, all the included studies reported equal care for the two groups. None of the studies reported blinding of the patients or carers. The overall risk of performance bias was unclear in two studies (Houvenaeghel et al., 2020; Park et al., 2022) and high in the other three studies (Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022).

Regarding the attrition bias, the follow-up duration was not reported in two studies (Houvenaeghel et al., 2020; Moon et al., 2021) and was reported to be longer in the open mastectomy group in one study (Lai et al., 2020). All patients completed the treatment in all studies. The overall risk for attrition bias was low for all the studies except the study by Lai et al., (2020) due to the shorter follow-up in the robotic group.

As for the detection bias, the length of follow-up was considered adequate for outcome assessment in three studies (Lai et al., 2020; Park et al., 2022; Toesca et al., 2022), but uncertain for the other two studies as they did not report the duration (Houvenaeghel et al., 2020; Moon et al., 2021). The studies used appropriate methods for outcome assessment. Blinding of the investigators to the used surgical technique or other confounding factors was not reported by any of the studies. The overall risk of detection bias was uncertain in three studies (Houvenaeghel et al., 2020; Moon et al., 2021; Park et al., 2022) and high in the other two studies (Lai et al., 2020; Toesca et al., 2022).

Results of meta-analysis

Conversion to open surgery

Three studies commented on the outcome of conversion to open surgery, reporting that none of the patients in the robotic group required conversion (Lai et al., 2020; Park et al., 2022; Toesca et al., 2022).

Operative time

Four studies compared the operative time between the two groups (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022). All four studies reported a significantly longer total duration of operation in the robotic group relative to the open surgery group. The studies did not report the duration of each stage of surgery (i.e., durations of docking, mastectomy and reconstruction), so we were unable to assess whether the prolongation was mainly due to the added docking time or to the other stages. There was marked heterogeneity among the studies ($Chi^2 = 21.51$, p-value = 0.0001, $I^2 = 86\%$), so pooling was performed using the random effects model. The pooled effect estimate (SMD (95% CI)) was 0.92 (0.34, 1.50), p-value = 0.002, indicating a large, significant increase in the operative time in the robotic group compared to the open surgery group (Table 4) (Figure 2).

Table 4 Summary of the main results of narrative synthesis and meta-analysis

Outcomes	Studies with a positive direction of effect	Studies with statistically significant effects	Studies (Participants) number for meta-analysis	Effect Estimate SMD/OR (95% CI), Model, P	Interpreting effect size c	Heterogeneity
Total operative time	0/4 a	4/4 (-)	4 (382)	SMD = 0.92 (0.34, 1.50), Random, P = 0.002*	Large	$Chi^2 = 21.51$ (P = 0.0001); $I^2 = 86\%$
Estimated blood loss	0/3 a	0/3	2 (196)	SMD = -0.58 (-1.58, 0.43), Random, P = 0.26	Medium	$Chi^2 = 11.78$ (P = 0.0006); $I^2 = 92\%$
Positive surgical margin	0 /2 a	0/2	2 (196)	OR = 3.50 (0.14, 87.83), Fixed, P = 0.45	Medium	Not applicable
Nipple-areola complex necrosis	4/4 a	1/4 +	4 (778)	OR = 0.45 (0.24, 0.87), Fixed, P = 0.02*	Small b	$Chi^2 = 4.53$ (P = 0.21); $I^2 = 34\%$
Overall wound-related complications	5 /5 a	2/5 (+)	5 (883)	OR = 0.56 (0.42, 0.75), Fixed, P<0.001*	Small b	$Chi^2 = 2.01$ (P = 0.73); $I^2 = 0\%$
Seroma	4/4 a	0/4	4 (382)	OR = 0.59 (0.32, 1.09), Fixed, P = 0.09	Small b	$Chi^2 = 0.46$ (P = 0.93); $I^2 = 0\%$
Haematoma	2/3 a	0/3	3 (277)	OR = 0.50 (0.17, 1.48), Fixed, P = 0.21	Small b	$Chi^2 = 0.71$ (P = 0.70); $I^2 = 0\%$
Skin flap ischaemia/necrosis	3/3 a	0 /3	3 (277)	OR = 0.41 (0.18, 0.94), Fixed, P = 0.04*	Small b	$Chi^2 = 1.95$ (P = 0.38); $I^2 = 0\%$
Infection	0/2 a	0/2	2 (161)	OR = 1.02 (0.28, 3.66), Fixed, P =0.98	Negligible	$Chi^2 = 0.00$ (P = 0.98); $I^2 = 0\%$
Delayed wound healing/dehiscence	2/3 a	0 /3	3 (277)	OR = 0.66 (0.24, 1.81), Fixed, P = 0.42	Small b	$Chi^2 = 1.72$ (P = 0.42); $I^2 = 0\%$
Implant loss	1/2 a	0/2	2 (196)	OR = 1.06 (0.18, 6.32), Fixed, P = 0.95	Negligible	$Chi^2 = 0.68$ (P = 0.41); $I^2 = 0\%$
Length of hospital stay	0/4 a	2/4 (-)	4 (382)	SMD = 0.53 (0.03, 1.02), Random, P = 0.04*	Medium	$Chi^2 = 16.73$ (P = 0.0008); $I^2 = 82\%$

Recurrence	2/3 a	0/3	3 (659)	OR = 0.17 (0.02, 1.34), Fixed, P = 0.09	Large b	Chi² = 0.45 (P = 0.50); I² = 0%

a: indicate the decreased value of the outcome in the robotic group; b: the inverted odds ratio was used to classify the effect size; the (+) sign indicates a better effect in the robotic group and the (-) sign indicates the reverse; c: The effect size was classified according to the rule of thumb by Cohen (1988) (For ORs: Large ≥ 4.3; medium ≥ 2.5, small ≥ 1.5, negligible < 1.5 to 1 but OR less than 1 were interpreted after reversing them 1/OR; for SMDs: large ≥ 0.8; medium ≥ 0.5, small ≥ 0.2, negligible < 0.2); OR: odds ratio; SMD: Standardized mean difference.

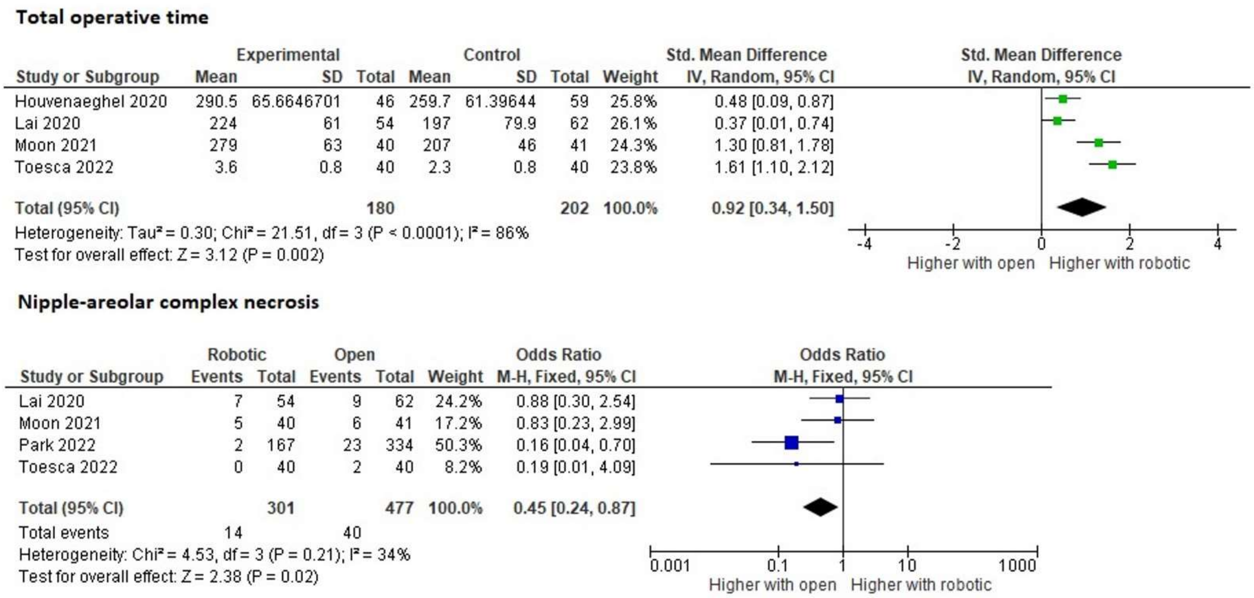

Figure 2 Forest plot showing pooling of the studies' findings regarding the total operative time and necrosis of the nipple-areolar complex

Blood loss

Three studies compared the amount of blood loss between the included groups (Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022). Two studies reported the outcome as a continuous variable and the comparison showed a non-significantly less blood loss in the robotic group in two studies (Lai et al., 2020; Toesca et al., 2022). The third study reported blood loss as a categorical variable (i.e., ≤100 mL and >100 mL), showing a non-significant association of robotic surgery with higher blood loss (Moon et al., 2021). Pooling of data was performed for the first two studies (Lai et al., 2020; Toesca et al., 2022). There was marked heterogeneity among the studies (Chi² = 11.78, p-value = 0.0006, I² = 92%), so pooling was performed using the random effects model. The pooled effect estimate (SMD (95% CI)) was -0.58 (-1.58, 0.43), p-value = 0.26, indicating a medium, non-significant decrease in the blood loss in the robotic group compared to the open surgery group (Table 4).

Positive surgical margin (PSM)

Two studies commented on the involvement of surgical margins in the two groups (Lai et al., 2020; Toesca et al., 2022). One study reported one case only in the robotic group (Lai et al., 2020), while no cases were reported in the open group in either study. Heterogeneity testing was non-applicable. The effect estimate depended on the results of one study only (Lai et al., 2020), which was (OR (95% CI)) 3.50 (0.14, 87.83), p-value = 0.45, indicating a medium, non-significant increase in the rate of PSM in the robotic group (Table 4).

Nipple-areolar complex necrosis

Four studies compared the rate of nipple-areola complex ischaemia/necrosis between the two surgical techniques (Lai et al., 2020; Moon et al., 2021; Park et al., 2022; Toesca et al., 2022). All studies reported a lower rate in the robotic group, reaching statistical significance in one study only (Park et al., 2022). Heterogeneity was not significant among the studies (Chi² = 4.53, p-value = 0.21, I² = 34%), so pooling was performed using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.45 (0.24, 0.87), p-value=0.02, indicating a small, significant reduction in the rate of nipple-areola complex ischaemia/necrosis in the robotic group compared to the open surgery group (Table 4) (Figure 2).

Overall wound-related complications

All studies compared the rate of overall, wound-related complications between the two surgical techniques (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021; Park et al., 2022; Toesca et al., 2022). All studies reported a lower rate in the robotic group relative to the open surgery group, reaching statistical significance in two studies only (Moon et al., 2021; Park et al., 2022). Heterogeneity was not significant among the studies (Chi² = 2.01, p-value = 0.73, I² = 0%), so pooling was performed using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.56 (0.42, 0.75), p-value<0.001, indicating a small, significant decline in the overall complication rates in the robotic group relative to the open surgery group (Table 4) (Figure 3).

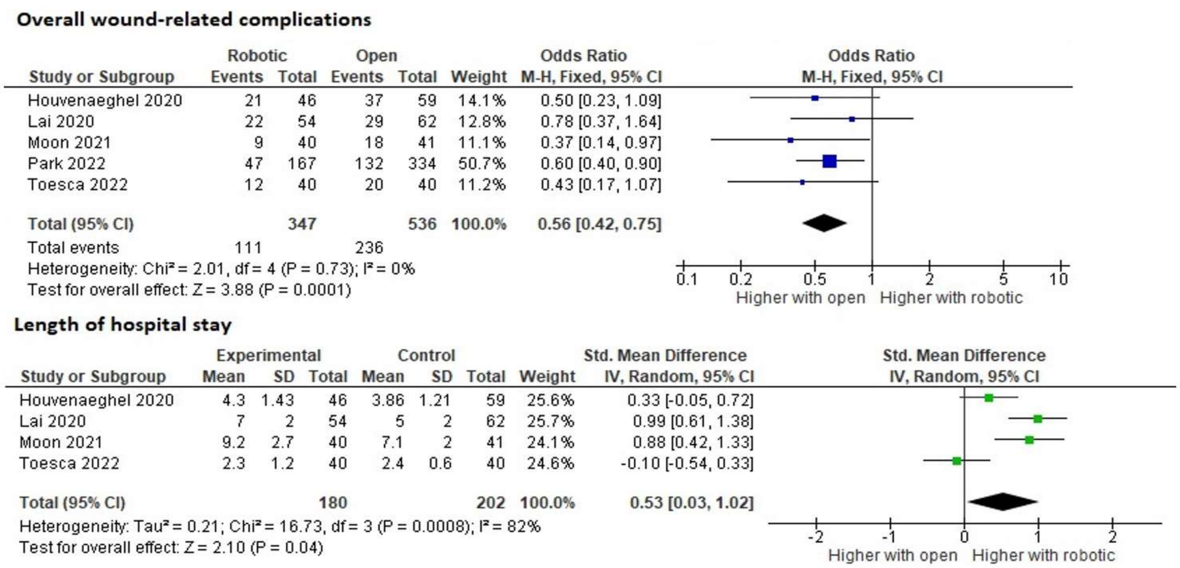

Figure 3 Forest plot showing pooling of the studies' findings regarding the rate of overall wound-related complications and the length of hospital stay

Seroma

Four studies compared the rate of seroma formation between the two surgical techniques (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022). Three studies reported a non-significantly lower rate in the robotic group relative to the open surgery group (Houvenaeghel et al., 2020; Lai et al., 2020; Toesca et al., 2022), while the fourth study reported a non-significantly higher rate in the robotic group (Moon et al., 2021). Heterogeneity was not significant among the studies (Chi² = 0.46, p-value = 0.93, I² = 0%), so pooling was performed using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.59 (0.32, 1.09), p-value=0.09, indicating a small, non-significant (marginal significance that may change in multivariate analysis) reduction in the seroma formation rate in the robotic group relative to the group of open surgery (Table 4).

Haematoma

Three studies assessed the rates of haematoma formation (Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022), with two studies reporting a non-significantly lower rate in the robotic group (Moon et al., 2021; Toesca et al., 2022), while the other study reported a non-significantly higher rate in the robotic group (Lai et al., 2020). Heterogeneity was not significant among the studies (Chi² = 0.71, p-value = 0.70, I² = 0%), so we pooled the data using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.50 (0.17, 1.48), p-value=0.21, indicating a small, non-significant decline in the rate of haematoma formation in the robotic group compared to the open surgery group (Table 4).

Skin flap ischaemia/necrosis

Three studies assessed the rates of skin flap ischaemia/necrosis (Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022), reporting a non-significantly lower rate in the robotic group. Heterogeneity was not significant among the studies (Chi² = 1.95, p-value = 0.38, I² = 0%), so we pooled the data using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.41 (0.18, 0.94), p-value=0.04, indicating a small, significant decline in the rate of skin flap ischaemia/necrosis in the robotic group (Table 4).

Infection

Two studies assessed the rates of infection (Moon et al., 2021; Toesca et al., 2022), reporting a non-significant increase in the robotic group in one study (Moon et al., 2021), while the other study showed similar rates in the two groups (Toesca et al., 2022). There was no heterogeneity between the studies ($Chi^2 = 0.00$, p-value = 0.98, $I^2 = 0\%$), so we pooled the data using the fixed-effect model. The pooled effect estimate (OR (95% CI)) 1.02 (0.28, 3.66), p-value=0.98, indicating a negligible, non-significant increase in the rate of infection in the robotic group, so the rates are practically comparable in both groups based on these two studies (Table 4).

Delayed wound healing/dehiscence

Three studies assessed the rates of Delayed wound healing/dehiscence b (Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022), reporting a non-significant decreases rate in the robotic group in two studies (Moon et al., 2021; Toesca et al., 2022), while the other study showed a non-significantly higher rate in the robotic group (Lai et al., 2020). There was no heterogeneity between the studies (Chi^2 1.72, p-value = 0.42, $I^2 = 0\%$), so we pooled the data using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.66 (0.24, 1.81), p-value=0.42, indicating a small, non-significant reduction in the rate of delayed wound healing/dehiscence in the robotic group (Table 4).

Implant loss

Two studies assessed the rates of implant loss (Lai et al., 2020; Toesca et al., 2022), with one study reporting a non-significantly lower rate in the robotic group (Lai et al., 2020), while the other study showed a slightly higher rate in the robotic group (Toesca et al., 2022). Heterogeneity was not significant among the studies ($Chi^2 = 0.68$, p-value = 0.41, $I^2 = 0\%$), so pooling was performed using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 1.06 (0.18, 6.32), p-value=0.95, indicating a negligible, non-significant increase in the rate of implant loss in the robotic group relative to the group of open surgery (Table 4).

Length of hospital stay

Four studies compared the operative time between the two groups (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022). Three studies reported a longer postoperative hospital stay in the robotic group relative to the open surgery group (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021), with the difference reaching a statistically significant difference in the two studies (Lai et al., 2020; Moon et al., 2021). The fourth study found that the length of postoperative stay was comparable in the two groups (Toesca et al., 2022). There was marked heterogeneity among the studies ($Chi^2 = 16.73$, p-value = 0.0008, $I^2 = 82\%$), so pooling was performed using the random effects model. The pooled effect estimate (SMD (95% CI)) was 0.53 (0.03, 1.02), p-value = 0.04, indicating a medium, significant prolongation in the hospital stay after robotic mastectomy compared to the open mastectomy group (Table 4) (Figure 3).

Locoregional recurrence

Three studies assessed the rates of locoregional recurrence of breast cancer after undergoing mastectomy (Lai et al., 2020; Park et al., 2022; Toesca et al., 2022). Two studies reported that all recurrences were in the group of open surgery, but the association did not reach statistical significance (Lai et al., 2020; Park et al., 2022). The third study reported that no recurrence was recorded in either group (Toesca et al., 2022). Among the included studies, we found no heterogeneity ($Chi^2 = 0.45$ ($P = 0.50$); $I^2 = 0\%$), so we pooled the data using the fixed-effect model. The pooled effect estimate (OR (95% CI)) was 0.17 (0.02, 1.34), p-value=0.09, indicating a large, non-significant decline in the rate of locoregional recurrence in the robotic group (Table 4).

4. DISCUSSION

Summary of the main findings

Robotic surgery possesses several advantages over open surgery. One advantage is better visualization of tissue planes as the robotic system has a three-dimensional high-resolution Camera. In addition, the flexible, rotating arms of the robotic systems allow surgeons to perform procedures in narrow fields, so they can access tissues that are difficult to reach. Furthermore, studies reported better cosmetic results and patients' satisfaction after robotic mastectomy, as the technique requires small inconspicuous incisions that are commonly placed in the axillary region or the lateral chest wall (Toesca et al., 2017; Lai et al., 2019; Park et al., 2019; Lai et al., 2020). Several single-arm studies showed the feasibility and safety of robotic mastectomy in patients who have breast cancer or for those who are at high risk of developing breast cancer (Toesca et al., 2017; Houvenaeghel et al., 2019; Lai et al., 2019; Park et al., 2019). Meanwhile, only a few studies compared robotic mastectomy to open surgery.

The FDA recommended the employment of caution regarding the use of robotic-assisted surgery for mastectomy (The US Food and Drug administration, 2021), owing to the lack of current evidence about its safety and efficacy relative to the traditional open mastectomy. Therefore, this meta-analysis was conducted to compare the robotic and traditional mastectomies regarding their efficacy and safety in patients scheduled for mastectomy as a treatment for breast cancer or for risk-reduction.

The literature search yielded five eligible studies for inclusion in this meta-analysis (Houvenaeghel et al., 2020; Lai et al., 2020; Moon et al., 2021; Park et al., 2022; Toesca et al., 2022). We compared the durations of operative time and hospital stay as well as the surgical and oncological safety between robotic mastectomy and open mastectomy groups. Surgical safety included conversion to open technique, blood loss amount and postoperative complications. Oncological safety was assessed by comparing the rates of PSM and locoregional recurrence of breast cancer.

The total operative time was significantly prolonged in the robotic mastectomy group (SMD = 0.92 (95% CI: 0.34, 1.50), p-value = 0.002), compared to the open surgery group. As the studies included did not report separately the duration of each stage of surgery, we were unable to attribute the prolongation to the added docking time or the performance of mastectomy and reconstruction stages through the small incision. However, studies assessing the learning curve of robotic mastectomy showed a decrease in the operative time after passing the initial phase of the learning curve. Lai et al., (2019) reported that the mean operative time of robotic mastectomy with nipple-sparing and immediate reconstruction of the breast was 287 ±77 mins in the initial learning phase and was significantly reduced to 236 ±31 mins (p-value = 0.02).

As for surgical safety, the results of this meta-analysis showed that robotic mastectomy is a safe procedure, with none of the patients requiring conversion to open mastectomy. Moreover, blood loss tended to be less with robotic surgery, though the difference was not statistically significant (SMD = -0.58 (95% CI: -1.58, 0.43), p-value = 0.26). We found also that robotic surgery was significantly associated with a reduced rate of ischaemia/necrosis of the nipple/areola complex (OR = 0.45 (95% CI: 0.24, 0.87), p-value = 0.02). This is presumable due to the placement of incisions in the lateral chest wall or axillary region, thus avoiding incisions over the breast skin flap or near the areola that could interfere with the blood supply (Toesca et al., 2017; Sarfati et al., 2018; Lai et al., 2019). This explains also why the robotic technique is mainly used for nipple-sparing mastectomy rather than skin-sparing mastectomy.

As regards the lower overall rate of wound-related complications in robotic surgery (OR = 0.56 (95% CI: 0.42, 0.75), p-value<0.001), this could be explained by the better visualization as well as the higher mobility of robotic arms that enables a more meticulous and efficient dissection of the tissue planes.

Studying individual wound-related complications showed a significant decline in the rates of skin flap ischaemia/necrosis (OR = 0.41 (95% CI: 0.18, 0.94), p-value = 0.04), which could also be attributed to the lesser disruption of vascular supply with the incisions used in robotic surgery. There was a tendency towards lower rates of seroma formation in the robotic group, but the analysis showed marginal statistical significance (OR = 0.59 (95% CI: 0.32, 1.09), p-value = 0.09). However, adjusting for potential confounders could have ascertained whether robotic surgery actually reduces the rate of seroma, but none of the studies conducted multivariate analysis for assessing the impact of potential confounding factors on individual types of complications. Our findings are in partial agreement with those reported by a recent meta-analysis that compared postoperative complications between robotic and open nipple-sparing mastectomies (Filipe et al., 2022), finding that robotic surgery was non-significantly coupled with a decreased overall postoperative complication rate (3.9% vs. 7%, p-value=0.07) and necrosis (4.3% vs. 7.4%, p-value=0.230). However, they reported a slightly higher rate of postoperative haematoma (4.3% vs. 2.0%, p-value=0.059), seroma (3.0% vs. 2.0%, p-value=0.421) and infection (8.3% vs. 4.0%, p-value=0.054) with robotic mastectomy than with open mastectomy. These differences could be partly explained by Filipe et al., (2022) that the recent meta-analysis was based principally on single-arm studies and included a higher number of studies on conventional mastectomy (with larger sample sizes) compared to the studies on robotic surgery.

As regards the oncological safety of robotic surgery, all locoregional recurrence cases were reported in the open mastectomy group, with no cases recorded after robotic mastectomy, but the result was marginally non-significant (OR = 0.17 (95% CI: 0.02, 1.34), p-value = 0.09). As we mentioned in discussing postoperative complications, adjusting for potential confounders could have elucidated the impact of robotic surgery on cancer recurrence, but none of the studies performed multivariate analysis. The study by Park et al., (2022) was the only one to perform propensity score matching.

The number of studies available for assessing surgical margin involvement was small (two studies only). Overall, there was only one case with PSM in the robotic mastectomy group, while no cases were recorded in the group undergoing open surgery. Future studies should include PSM as one of the main outcomes to assess the oncological safety of robotic mastectomy.

The hospital stay duration was found to be significantly longer in robotic mastectomy (SMD = 0.53 (95% CI: 0.03, 1.02), p-value = 0.04). One study explained the longer hospital stay by the need of patients undergoing robotic surgery to stay two more days in the hospital to receive claims from private insurance policies (Lai et al., 2020).

Overall completeness, applicability and quality of the evidence

This meta-analysis summarized the current evidence on the surgical and oncological safety of robotic mastectomy compared to the traditional open mastectomy. The results show favourable outcomes of robotic mastectomy, except for the prolonged operative time and hospital stay duration. The findings of the present meta-analysis are limited by the ROB of the included studies.

A high risk of selection bias was observed in one study (Moon et al., 2021), while the risk was unclear in another two studies (Houvenaeghel et al., 2020; Lai et al., 2020) and low in the remaining two (Park et al., 2022; Toesca et al., 2022). The risk stems principally from the impact of potential confounding factors on the choice of surgical procedure, particularly as most studies were retrospective cohorts and the two groups differed from each other at baseline. In addition, most studies did not attempt to adjust for these potential confounding factors, except for two studies that carried out multivariate analysis (Houvenaeghel et al., 2020) and propensity score matching (Park et al., 2022).

Another limitation was the non-blinding of participants or outcome assessors, which was due in most cases to the retrospective nature of the study design. As a result, the performance ROB was high in three studies (Lai et al., 2020; Moon et al., 2021; Toesca et al., 2022) and uncertain in the remaining two studies (Houvenaeghel et al., 2020; Park et al., 2022).

Three studies reported a relatively short mean or median duration of follow-up. A longer duration of follow-up after mastectomy is particularly essential to report on oncological outcomes such as recurrence and disease-free survival. Moreover, two studies did not report the duration of follow-up (Houvenaeghel et al., 2020; Moon et al., 2021). The study by Lai et al., (2020) reported a significantly longer duration of follow-up in the group having open surgery.

Based on these limitations in the currently available studies, we recommend the conduction of randomized controlled trials or high-quality prospective cohort studies with adequate duration of follow-up after mastectomy with special emphasis on assessing the oncological safety after robotic mastectomy. Also, future studies should adjust for potential confounders or differences in baseline characteristics. Subgroup analyses could be helpful after categorizing the patients based on tumour grading and stage as well as the body mass index, mastectomy weight and the procedures of breast reconstruction. We were unable to perform subgroup analyses in the present meta-analysis due to the low number of eligible studies and all studies did not report separately the outcomes for subgroups of patients.

A main concern in the routine use of robotic surgery is the cost-benefit value. Lai et al., (2020) reported that the overall medical cost of robotic mastectomy with nipple-sparing and immediate surgical reconstruction of the breast was significantly higher than that of open mastectomy, reaching up to double the cost of the conventional technique (10,877 ±796 vs. 5702 ±661 US Dollars, $P<0.01$). In the future, technological advances may increase the number of available robotic systems and reduce the cost of robotic surgeries.

5. CONCLUSIONS

Conclusions, implications for practice, policy and future research

The results of this meta-analysis showed favourable short-term surgical outcomes of robotic mastectomy, suggesting that robotic mastectomy is considered safe technique that potentially reduces the likelihood of postoperative complications. Robotic mastectomy also showed a higher rate of patient satisfaction due to better aesthetic results. However, robotic mastectomy seems to prolong the total operative time and duration of hospital stay, which theoretically exposes the patients to risks of prolonged anaesthesia and nosocomial infection as well as increasing health expenditure. Conclusions regarding the oncological safety of robotic surgery could not be reliably drawn due to the small number of studies that assessed oncological outcomes. Even the studies that reported on oncological outcomes had a relatively short duration of follow-up, so the actual rate of recurrence after robotic mastectomy could not be reliably ascertained. The included studies showed several limitations, so there is a need to conduct large-size randomised clinical trials with adequate follow-up to assess particularly the oncological outcomes before recommending the routine use of the robotic technique for mastectomy.

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Author Contributions

All authors contributed to the study conception and design. Literature search and data collection were performed by Ibtisam Shary J Hazazi, Nourah Eid A Alatwi, Nouf Ali S Alatawi, Bandar Sulaiman Alatawi and Yasir Mousa Alhusayni. Data extraction and risk of bias assessment were performed by Ibrahim Altedlawi Albalawi, Ibtisam Shary J Hazazi, Nadia Abdualla Alomrani, Rawan Hamoud M Alatawi, Maha Faisal M Aljohani and Hadeel Abdullah D Alosaimi. The first draft of the manuscript was written by Mazen Hamoud A Alatawi, Saleh Sulieman N Alatawi, Rafeef fahad Aljuhani, Raghad Dhafer E Alamri and Rahf Mohammed Alqarni. The final draft of the manuscript was written by Ibrahim Altedlawi Albalawi and Ibtisam Shary J Hazazi.

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Informed consent

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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