Prevention of Postoperative Complications by Prepectoral versus Subpectoral Breast Reconstruction: A Systematic Review and Meta-Analysis

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Background: Implant-based breast reconstruction has evolved over time. However, the effects of prepectoral breast reconstruction (PBR) compared with those of subpectoral breast reconstruction (SBR) have not been clearly defined. Therefore, this study aimed to compare the occurrence of surgical complications between PBR and SBR to determine the procedure that is effective and relatively safe.

Methods: The PubMed, Cochrane Library, and EMBASE databases were searched for studies published until April of 2021 comparing PBR and SBR following mastectomy. Two authors independently assessed the risk of bias. General information on the studies and surgical outcomes were extracted. Among 857 studies, 34 and 29 were included in the systematic review and meta-analysis, respectively. Subgroup analysis was performed to clearly compare the results of patients who underwent postmastectomy radiation therapy.

Results: Pooled results showed that prevention of capsular contracture (OR, 0.57; 95% CI, 0.41 to 0.79) and infection control (OR, 0.73; 95% CI, 0.58 to 0.92) were better with PBR than with SBR. Rates of hematoma, implant loss, seroma, skin-flap necrosis, and wound dehiscence were not significantly different between PBR and SBR. PBR considerably improved postoperative pain, BREAST-Q score, and upper arm function compared with SBR. Among postmastectomy radiation therapy patients, the incidence rates of capsular contracture were significantly lower in the PBR group than in the SBR group (OR, 0.14; 95% CI, 0.05 to 0.35).

Conclusions: The results showed that PBR had fewer postoperative complications than SBR. The authors' meta-analysis suggests that PBR could be used as an alternative technique for breast reconstruction in appropriate patients. *(Plast. Reconstr. Surg.* 153: 10e, 2024.)

Implants are most commonly used in breast reconstruction following mastectomy.[1] The availability of novel surgical techniques (skin-sparing mastectomy and nipple-sparing mastectomy), acellular dermal matrix (ADM), and perfusion imaging technology have substantially improved the clinical outcomes of this approach.[1,2]

Implant-based breast reconstruction was first introduced in the 1960s, and implants were placed subcutaneously, inferior to the mastectomy flap and superior to the pectoralis muscle. Although this approach was straightforward and preserved muscular integrity, the lack of overlying tissue support resulted in numerous complications, including flap necrosis, capsular contracture, implant exposure, and reconstruction failure.[3,4] Thus, the submuscular approach, in which the implant

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is placed inferior to the pectoralis and serratus anterior, replaced subcutaneous reconstruction and became the mainstay of breast reconstruction for decades.[3,4] However, submuscular placement of the implant may lead to significant morbidity because of the mobilization of the pectoralis major muscle and lateral deviation of the breast mound with poor inframammary fold definition. This has a significant negative effect on patients' quality of life.[5–7] The introduction of ADM permitted the use of new protocols for breast reconstruction. Implant coverage with ADM and prepectoral breast reconstruction (PBR) have shortened the duration of surgery and improved outcomes, thus solving the problems associated with subpectoral breast reconstruction (SBR).[5,8,9]

The use of PBR has recently been reinstated for implant-supplemented reconstruction because of technological advancements, necessitating the comparison of PBR and SBR results. However, existing comparative studies have small sample sizes. Moreover, a meta-analysis of the radiation effect with PBR seems necessary based on the evidence that the occurrence of capsular contracture is closely related to muscle fibrosis.[10–12] Although some meta-analyses have compared the difference between the occurrence of complications after PBR and SBR, no study has performed a meta-analysis considering the effect of postmastectomy radiation therapy (PMRT). Thus, this study aimed to conduct a large-scale systematic review and meta-analysis of the outcomes (complication and cosmetic outcomes) of PBR in comparison with those of SBR in patients who underwent PMRT.

PATIENTS AND METHODS

Literature Search

PubMed, the Cochrane Central Register of Controlled Trials, and Embase databases were searched for published studies up to April of 2021 by using various combinations of keywords as follows: ((((Mastectomies [Title/Abstract] OR Mastectomy [Title/Abstract] OR Mastectomy, skin sparing [Title/Abstract] OR Mastectomy, Nipple sparing [Title/Abstract] OR ((("Mastectomy"[Mesh]) OR "Mastectomy, Simple" [Mesh]) OR ("Mastectomy, Segmental" [Mesh] OR "Mastectomy Modified Radical" [Mesh] OR "Mastectomy, Extended Radical" [Mesh] OR "Mastectomy, Subcutaneous" [Mesh] OR "Mastectomy, Radical" [Mesh] OR "Prophylactic Mastectomy" [Mesh]))) AND ((Breast reconstruction [Title/Abstract] OR Breast reconstructions [Title/Abstract] OR Prepectoral [Title/Abstract] OR Subcutaneous [Title/Abstract] OR Subpectoral [Title/Abstract] OR Implant [Title/Abstract] OR Prosthesis [Title/Abstract] OR Prosthetic [Title/Abstract] OR ("Tissue Expansion Devices" [Mesh]))) AND ((Radiation [Title/Abstract] OR Radiotherapy [Title/Abstract] OR Radiation Therapy [Title/Abstract] OR (("Radiation" [Mesh] OR "Radiotherapy" [Mesh])). No publication date limitation or language restrictions were imposed. Further search conditions restricted studies to those conducted on humans.

Inclusion and Exclusion Criteria

Studies on patients who underwent mastectomy (prophylactic and/or therapeutic), followed by interventions including PBR and SBR, irrespective of the type of prosthesis, and studies that compared prepectoral and subpectoral tissue expanders (TEs) or implant-based breast reconstruction were included. The outcomes included the overall postoperative complications (ie, implant loss, seroma, wound-skin infection, nipple or skin-flap necrosis, hematoma, reoperation, wound dehiscence, and capsular contracture), patient-reported outcomes (eg, BREAST-Q scores), postoperative pain, and upper extremity function. The retrieved studies were screened by two reviewers, and inconsistencies were resolved by a third reviewer. Clinical trials that did not compare PBR with SBR, reviews, letters to the editor, abstracts or conference proceedings, duplicate publications, and studies not published in English were excluded.

Study Selection

The abstracts and titles of all selected studies were reviewed independently by two authors. Unrelated articles were excluded. On reviewing full texts of the remaining studies, those that met the inclusion criteria were selected, and the data of updated publications involving the same patient cohort were extracted synthetically.

Data Extraction

Relevant information and data were extracted from the selected studies, including the first author's name, year of publication, country where the study was conducted, study design (prospective or retrospective), participants' general characteristics, prosthesis used for reconstruction, mastectomy type, implant placement plane, follow-up duration, and complications.

Quality Assessment

The risk of bias in the included studies was assessed using the methodological index for nonrandomized studies (MINORS).[13] Two authors independently assessed the following parameters: clear statement of the aim, inclusion of consecutive patients, prospective collection of data, endpoints appropriate to the study aim, unbiased assessment of the study endpoint, follow-up period appropriate to the study aim, loss to follow-up rate less than 5%, prospective calculation of the study size and adequate control group, contemporary groups, baseline equivalence of groups, and whether the statistical analyses were adequate for each study. Disagreements, if any, were resolved by discussion between two authors and consultation with the third author. The items were scored as 0 (not reported), 1 (reported but inadequate), and 2 (reported and adequate). The ideal global score was 24 for comparative studies. The risk of bias was classified as low (≥75%), moderate (60 to 74%), or high (<60%) based on the MINORS criteria score.[14]

Statistical Analysis

The quantitative analysis consisted of two parts. The overall risks of each complication, including seroma, hematoma, skin-flap necrosis, implant loss, capsular contracture, wound dehiscence, and infection, were estimated and compared between the PBR and SBR groups. Subgroup analysis was conducted to determine whether the frequency of complications between the two groups changed depending on PMRT.

Statistical analysis was performed using STATA/MP v16 (StataCorp, College Station, TX). To estimate the weighted pooled odds ratios with 95% confidence intervals, the Mantel-Haenszel and restricted maximum likelihood methods were used in fixed-effects and random-effects models, respectively. The complication rates of seroma, hematoma, skin-flap necrosis, implant loss, capsular contracture, wound dehiscence, and infection between two groups were examined using chi-square test and presented using a forest plot. The level of statistical significance was set at $P < 0.05$.

Heterogeneity was evaluated using chi-square–based Q test and I^2 test. A fixed-effects model was used if significant heterogeneity was not detected ($P \geq 0.05$; $I^2 \leq 50\%$). If heterogeneity existed ($P < 0.05$; $I^2 > 50\%$), sensitivity analysis would be performed to identify the source of heterogeneity. If heterogeneity could not be eliminated, a random-effects model was used. Funnel plots and Egger linear regression test were used to evaluate potential publication bias; a value of $P < 0.05$ was considered statistically significant.

RESULTS

Literature Retrieval Results

A total of 857 articles were initially extracted from the databases (Fig. 1). Based on the elimination of duplicate publications, application of selection criteria, and availability of complete text, 34 studies were included in the systematic review. Of these, 29 studies containing numerical data on at least one of the outcomes (including seroma, hematoma, skin-flap necrosis, implant loss, capsular contracture, wound dehiscence, and infection) were included in the meta-analysis.

Study Characteristics

The 34 included studies were published between 2014 and 2021, of which 20 were conducted in the United States,[1–4,9,11,12,15–26] 10 in Europe,[6,27–35] two in Canada,[10,36] one in Australia,[7] and one in the Republic of Korea[37] (Table 1). Regarding the study type, 26 studies followed a retrospective design and five had a prospective design. A total of 7641 breasts from 4725 patients were included, of which PBR was performed in 3759 breasts (49.2%). The average ages were 49.18 and 48.91 years in the PBR and SBR groups, respectively. All studies except two used ADM to support the breast implants, one study did not use coverage materials,[6] and one study did not describe this item.[35] Seven studies used an ADM sling in some patients.[12,17,20,22,23,26,30] Among the included studies, six used PMRT after PBR and SBR.[1,11,12,17,23,24]

Methodologic Quality Assessment

Risk-of-bias assessment was performed in 34 studies (Table 2). All the included studies clearly described their research aim. Most studies ($n = 33$) adequately described the inclusion of consecutive patients, whereas only one study did not clearly report this item.[5] The protocols used for data collection were clearly reported in six studies.[21,23,24,27,29,30] The criteria for the evaluation of the main outcomes were clearly reported in most studies ($n = 31$); however, three studies did not describe their evaluation criteria adequately.[3,16,34] Blind evaluation was performed in only two
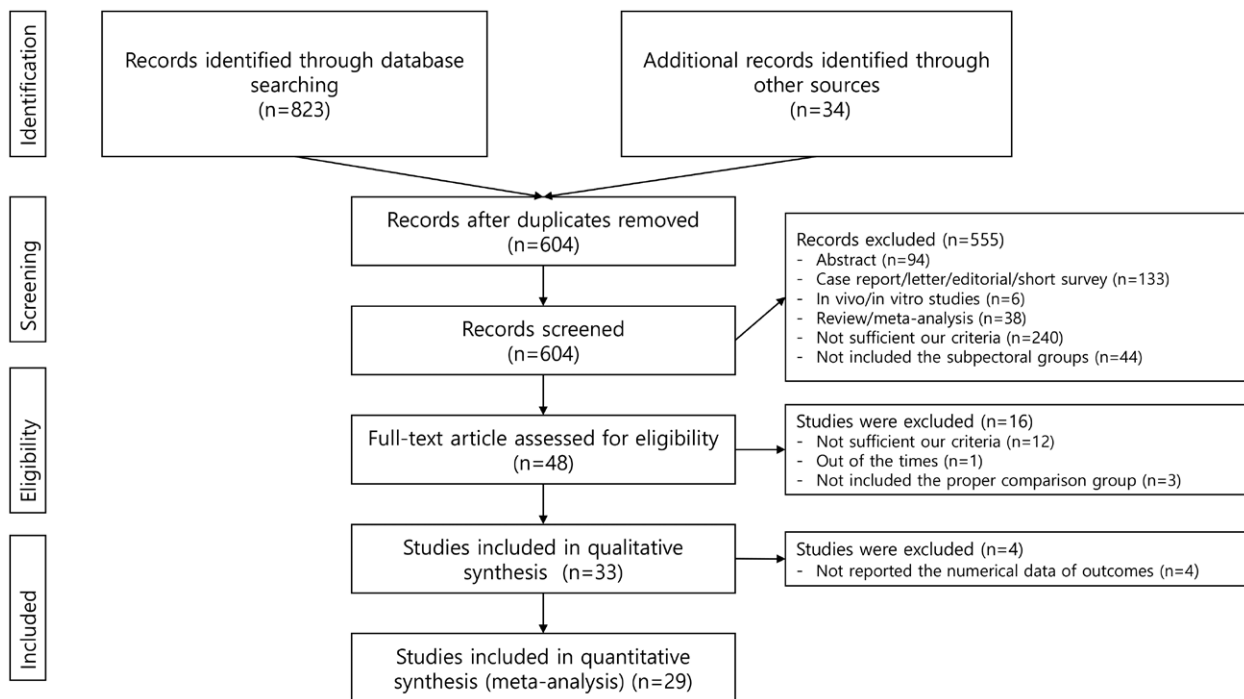
Fig. 1. Study selection process.

studies.[12,15] Most studies clearly reported a follow-up period of sufficient duration ($n = 29$). The loss to follow-up rate was less than 5% ($n = 33$), and the study sample size was prospectively calculated ($n = 32$) in most studies. Based on the MINORS scale, 29 studies were judged to have a low risk of bias, whereas five studies were judged to possess moderate quality.[2,3,16,21,34]

Quantitative Analysis

Overall Studies

Eleven studies that included 1276 breasts in the PBR group and 1428 breasts in the SBR group described capsular contracture.[10–12,15,20,22,31,33,35–37] The rates of capsular contracture were significantly lower in the PBR group than in the SBR group (OR, 0.57; 95% CI, 0.41 to 0.79) (Fig. 2, *above*), with high heterogeneity ($P = 0.025$; $I^2 = 52.37\%$). To reduce the heterogeneity, sensitivity analysis was subsequently conducted. After excluding the study by Ribuffo et al.,[33] the results were the same with the overall pooled data (OR, 0.37; 95% CI, 0.25 to 0.56) (Fig. 2, *center*), and heterogeneity was eliminated ($P = 0.476$; $I^2 = 0.00\%$). Small-study bias was not detected in the data from 10 studies reporting capsular contracture (Egger test, $t = -1.69$; $P = 0.128$) (Fig. 2, *below*).

For the quantitative analysis, infection rates were available from 28 of the 34 trials.[1–4,7,9–12,15–17,19–22,24–29,31,33–37] PBR significantly decreased the occurrence of infection compared with SBR (OR, 0.73; 95% CI, 0.58 to 0.92) (Fig. 3, *above*), with low heterogeneity ($P = 0.353$; $I^2 = 7.40\%$). No publication bias was detected in the pooled results of infection rates (Egger test, $t = 0.97$; $P = 0.340$) (Fig. 3, *below*).

The rates of hematoma, implant loss, seroma, skin-flap necrosis, and wound dehiscence were not significantly different between PBR and SBR (Table 3). There was no evidence of publication bias in the pooled results of these outcomes.

PMRT

Data ($n = 3$) from five studies were included in the quantitative analysis.[11,12,24] The pooled total number included 79 breasts in the PBR group and 60 breasts in the SBR group. In the study by Sobti et al.,[12] two reviewers assessed the incidence of capsular contracture in PBR and SBR patients; thus, for quantitative analysis, we used the average of the two values. The incidence rates of capsular contracture were significantly lower in the PBR group than those in the SBR group (OR, 0.14; 95% CI, 0.05 to 0.35), with low heterogeneity ($P = 0.765$; $I^2 = 0.00\%$) (Fig. 4, *above*). The results of the sensitivity analysis did not change significantly.

Table 1. General Characteristics of Included Studies

Authors, Year	Country	Publication Type	Study Type	Prosthesis	No. of Breasts		Mean Age (yr)		Coverage		Surgery	Follow-Up Duration (mo)		Outcomes[a]
					Prepectoral	Subpectoral	Prepectoral	Subpectoral	Prepectoral	Subpectoral		Prepectoral	Subpectoral	
Antony et al., 2019	United States	Journal	Retrospective	Implant	47	57	47.8	50.2	ADM	PMM + ADM	SSM, NSM, MRM (only in PBR group)	16.5	30.4	1
Avila et al., 2020	United States	Journal	Retrospective	Implant, TE-implant	203	202	46.5	45.9	ADM	PMM + ADM	NSM	No comments	No comments	1
Baker et al., 2018	United Kingdom	Journal	Prospective	Implant	43	19	47.5	48	ADM	PMM + ADM	No comments	3	3	1, 3
Banuelos et al., 2019	United States	Journal	Retrospective	TE-implant	189	147	54	54	ADM (93.7%)	PMM + ADM (93.2%)	SSM, NSM	17	18.1	1
Bozzuto et al., 2021	United States	Journal	Retrospective	Implant, TE-implant	132	128	49	49	ADM	PMM + ADM	NSM	No comments	No comments	2, 4 (length of stay)
Braun et al., 2020	United States	Journal	Retrospective	Implant, TE-implant	209	79	45	46	ADM	PMM + ADM	NSM	3	3	1
Caputo et al., 2020	Italy	Journal	Retrospective	Implant	54	67	53	53	ADM	PMM + ADM	SSM, NSM, MRM	6	6	1, 2, 3, 4 (rehabilitation)
Casella et al., 2014	Italy	Journal	Prospective	Implant	39	34	47	51	TCPM	PMM + TCPM	SSM, NSM	13	13	1
Cattelani et al., 2018	Italy	Journal	Prospective	Implant (PBR)/implant, TE-implant (SBR)	46	53	52.9	52.3	ADM	No	SSM, NSM	12	12	3, 4 (upper limb functionality, cost evaluation)
Chandarana et al., 2018	United Kingdom	Journal	Retrospective	Implant	71	83	51	50	ADM	PMM + ADM	No comments	11.8	11.8	1
Darrach et al., 2021	United States	Journal	Retrospective	TE-implant	212	134	48.37	48.87	ADM	PMM + ADM	NSM	3	3	2
Dyrberg et al., 2019	Denmark	Journal	Prospective	Implant	18[b]	19[b]	44	45	ADM	ADM	No comments	9	22.8	4 (breast animation deformity)
Franceschini et al., 2021	Switzerland	Journal	Retrospective	Implant	109	146	47	44	No	No	NSM	15.9	20	1, 2, 3, 4 (economic analysis)
Gabriel et al., 2020	Canada	Journal	Retrospective	TE-implant	129	128	49	53	ADM	PMM + ADM	SSM, NSM, unknown	22.7	24.1	1
Kraenzlin et al., 2021	United States	Journal	Retrospective	TE-implant	308	184	48.8	49.4	ADM	PMM + ADM	NSM	No comments	No comments	1, 4 (operative time, operating room charges)
Manrique et al., 2020	United States	Journal	Retrospective	Implant	55	69	54	47	ADM	PMM + ADM	SSM, NSM	20.3	21	1, 3
Manrique et al., 2019	United States	Journal	Retrospective	TE-implant	187	124	35.3	34.2	ADM (99.5%)	PMM + ADM (95.2%)	SSM, NSM	17.9	17.5	1
Mirhaidari et al., 2020	United States	Journal	Prospective	Implant	112	112	54	48	ADM	PMM + ADM	SSM, NSM	3–24	24–36	1

(Continued)

Table 1. Continued

Authors, Year	Country	Publication Type	Study Type	Prosthesis	No. of Breasts		Mean Age (yr)		Coverage		Surgery	Follow-Up Duration (mo)		Outcomes[a]
					Prepectoral	Subpectoral	Prepectoral	Subpectoral	Prepectoral	Subpectoral		Prepectoral	Subpectoral	
Momeni et al., 2019	United States	Journal	Retrospective	TE-implant	69	69	51.3	50.9	ADM	PMM + ADM	No comments	5.6	6.7	1, 4 (differences in the duration of antibiotic use, before 1 day/subpec 1 wk)
Nahabedian and Cociovo, 2017	United States	Journal	Retrospective	Implant, TE-implant	62	83	50.4	49.2	ADM	PMM + ADM	SSM, NSM	8.7	10.3	1
Nealon et al., 2020	United States	Journal	Retrospective	Implant	183	238	52.7	50.7	ADM (74.6%)	PMM + ADM (73.2%)	SSM, NSM	19.8	29	1
Ng et al., 2021	Australia	Journal	Retrospective	Implant	50	59	50.6	48.5	TCPM	PMM + TCPM	NSM	21	26.5	1, 3
Ribuffo et al., 2021	Italy	Journal	Retrospective	Implant	207	509	55.72	56.2	ADM	PMM + ADM	SSM, NSM	24	24	1
Sbitany et al., 2019	United States	Journal	Prospective	TE-implant	175	236	46.6	46.8	ADM	PMM + ADM (80%)	SSM, NSM	9	19.8	1
Sbitany et al., 2017	United States	Journal	Prospective	TE-implant	84	186	44.8	48.2	ADM	PMM + ADM	NSM	11.1	12.5	1
Schaeffer et al., 2019	United States	Journal	Prospective	TE-implant	45	90	50	50	ADM	PMM + ADM	No comments	No comments	No comments	1, 4 (functional recovery and time to drain removal)
Sinnott et al., 2018	United States	Journal	Retrospective	Implant, TE-implant	426	163	52.4	46.9	ADM	PMM + ADM	No comments	19	31.9	1
Sobti et al., 2020	United States	Journal	Retrospective	Implant	32	49	52.3	49.7	ADM (85%)	PMM + ADM (77.8%)	SSM, NSM	22.9	27	1
Suh et al., 2021	United Kingdom	Journal	Retrospective	TE-implant	27	62	47.4	47.9	ADM	PMM + ADM	No comments	No comments	No comments	1, 4 (postoperative drainage)
Thangarajah et al., 2019	Germany	Journal	Retrospective	Implant	34	29	49.9	49.3	No comments	No comments	SSM, NSM	18	18	1, 3
Viezel-Mathieu et al., 2020	Canada	Journal	Retrospective	Implant (PBR)/implant, TE-implant (SBR)	60	56	46.5	50.9	ADM	PMM + ADM	SSM, NSM	5.5	21.1	1, 4 (follow-up visits, cost comparison)
Wormer et al., 2019	United States	Journal	Retrospective	TE-implant	60	124	48.2	49.9	ADM	PMM + ADM	NSM	5.9	7.2	1, 4 (tissue expansion)
Yang et al., 2019	Republic of Korea	Journal	Retrospective	Implant, TE-implant	32	47	48.91	46.4	ADM	PMM + ADM	TM	11.9	13.9	1, 2
Zhu et al., 2016	United States	Journal	Retrospective	TE-implant	50	108	50.48	52.69	ADM (30%)	PMM + ADM (46.3%)	SSM, NSM	17.3	17.3	1, 2, 4 (expansion process)

SSM, skin-sparing mastectomy; NSM, nipple-sparing mastectomy; MRM, modified radical mastectomy; TM, total mastectomy; PMM, pectoralis major muscle; TCPM, titanium-coated polypropylene mesh.
[a]1, postoperative complication; 2, postoperative pain; 3, BREAST-Q; 4: others.
[b]No. of patients.

Table 2. Risk-of-Bias Assessment for Included Studies Based on MINORS Score[a]

Authors, Year	A Clearly Stated Aim	Inclusion of Consecutive Patient	Prospective Collection of Data	Endpoints Appropriate to the Aim of Study	Unbiased Assessment of the Study Endpoint	Follow-Up Period Appropriate to the Aim of Study	Loss to Follow-Up < 5%	Prospective Calculation of the Study Size	An Adequate Control Group	Contemporary Groups	Baseline Equivalence of Groups	Adequate Statistical Analyses	Total	Risk of Bias
Antony et al., 2019	2	2	1	2	2	2	1	0	2	2	2	2	20/24	Low (83%)
Avila et al., 2020	2	2	1	0	0	1	2	0	2	2	2	2	16/24	Moderate (67%)
Baker et al., 2018	2	2	2	2	1	0	2	1	0	2	2	2	18/24	Low (75%)
Bannuelos et al., 2019	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Bozzuto et al., 2021	2	1	1	2	0	2	2	1	2	1	2	2	18/24	Low (75%)
Braun et al., 2020	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Caputo et al., 2020	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Casella et al., 2014	2	2	2	2	0	2	2	1	2	2	2	2	21/24	Low (88%)
Cattelani et al., 2018	2	2	2	2	1	2	2	1	2	2	0	2	20/24	Low (83%)
Chandarana et al., 2018	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Darrach et al., 2021	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Dyrberg et al., 2019	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Franceschini et al., 2021	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Gabriel et al., 2020	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Kraenzlin et al., 2021	2	2	1	0	0	0	2	1	2	2	2	2	16/24	Moderate (67%)
Manrique et al., 2019	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Manrique et al., 2020	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Mirhaidari et al., 2020	2	2	2	2	0	1	2	1	2	1	2	2	19/24	Moderate (79%)
Momeni et al., 2019	2	2	1	2	0	2	2	1	2	1	2	2	19/24	Moderate (79%)
Nahabedian and Cocilovo, 2017	2	2	0	2	1	2	2	1	2	2	0	2	18/24	Low (75%)

(Continued)

Table 2. Continued

Authors, Year	A Clearly Stated Aim	Inclusion of Consecutive Patient	Prospective Collection of Data	Endpoints Appropriate to the Aim of Study	Unbiased Assessment of the Study Endpoint	Follow-Up Period Appropriate to the Aim of Study	Loss to Follow-Up < 5%	Prospective Calculation of the Study Size	An Adequate Control Group	Contemporary Groups	Baseline Equivalence of Groups	Adequate Statistical Analyses	Total	Risk of Bias
Nealon et al., 2020	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Ng et al., 2021	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Ribuffo et al., 2021	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Sbitany et al., 2017	2	2	2	2	1	2	2	1	2	2	0	2	20/24	Low (83%)
Sbitany et al., 2019	2	2	2	2	0	2	2	1	2	2	2	2	21/24	Low (88%)
Schaeffer et al., 2019	2	2	0	2	1	2	2	1	2	2	2	0	18/24	Low (75%)
Sinnott et al., 2018	2	2	0	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Sobti et al., 2020	2	2	1	2	2	2	2	1	2	2	2	2	22/24	Low (92%)
Suh et al., 2021	2	2	1	0	0	1	2	1	2	2	2	2	17/24	Moderate (71%)
Thangarajah et al., 2019	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Viezel-Mathieu et al., 2020	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Wormer et al., 2019	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Yang et al., 2019	2	2	1	2	0	2	2	1	2	2	2	2	20/24	Low (83%)
Zhu et al., 2016	2	2	0	2	1	2	2	1	2	2	2	2	20/24	Low (83%)

[a]0, not reported; 1, reported but inadequate; 2, reported and adequate.

Study	Prepectoral Yes	Prepectoral No	Subpectoral Yes	Subpectoral No	Odds Ratio with 95% CI	Weight (%)
Antony et al, 2019	0	47	1	56	0.40 [0.02, 9.96]	1.42
Chandarana et al, 2018	1	70	5	78	0.22 [0.03, 1.95]	4.79
Gabriel et al, 2020	1	128	9	119	0.10 [0.01, 0.83]	9.45
Manrique et al, 2020	6	49	7	62	1.08 [0.34, 3.44]	5.83
Nealon et al, 2020	2	181	12	226	0.21 [0.05, 0.94]	10.87
Ribuffo et al, 2021	18	189	29	480	1.58 [0.86, 2.91]	16.13
Sinnott et al, 2018	22	404	16	147	0.50 [0.26, 0.98]	23.13
Sobti et al, 2020	12	20	28	21	0.45 [0.18, 1.12]	14.57
Thangarajah et al, 2019	1	33	5	24	0.15 [0.02, 1.33]	5.52
Viezel-Mathieu et al, 2020	0	60	6	50	0.06 [0.00, 1.17]	7.02
Yang et al, 2019	0	32	1	46	0.48 [0.02, 12.08]	1.27
Overall					0.57 [0.41, 0.79]	

Heterogeneity: $I^2 = 52.37\%$, $H^2 = 2.10$
Test of $\theta_i = \theta_j$: $Q(10) = 21.00$, $p = 0.02$
Test of $\theta = 0$: $z = -3.33$, $p = 0.00$

1/256 1/32 1/4 2

Study	Prepectoral Yes	Prepectoral No	Subpectoral Yes	Subpectoral No	Odds Ratio with 95% CI	Weight (%)
Antony et al, 2019	0	47	1	56	0.40 [0.02, 9.96]	1.69
Chandarana et al, 2018	1	70	5	78	0.22 [0.03, 1.95]	5.71
Gabriel et al, 2020	1	128	9	119	0.10 [0.01, 0.83]	11.26
Manrique et al, 2020	6	49	7	62	1.08 [0.34, 3.44]	6.95
Nealon et al, 2020	2	181	12	226	0.21 [0.05, 0.94]	12.96
Sinnott et al, 2018	22	404	16	147	0.50 [0.26, 0.98]	27.58
Sobti et al, 2020	12	20	28	21	0.45 [0.18, 1.12]	17.37
Thangarajah et al, 2019	1	33	5	24	0.15 [0.02, 1.33]	6.58
Viezel-Mathieu et al, 2020	0	60	6	50	0.06 [0.00, 1.17]	8.37
Yang et al, 2019	0	32	1	46	0.48 [0.02, 12.08]	1.51
Overall					0.37 [0.25, 0.56]	

Heterogeneity: $I^2 = 0.00\%$, $H^2 = 1.00$
Test of $\theta_i = \theta_j$: $Q(9) = 8.59$, $p = 0.48$
Test of $\theta = 0$: $z = -4.78$, $p = 0.00$
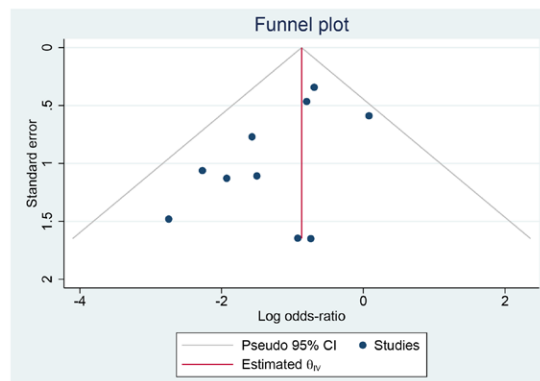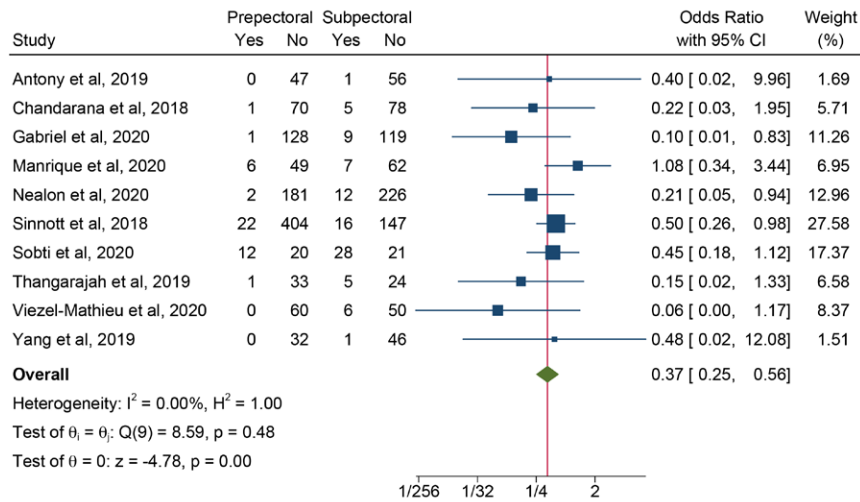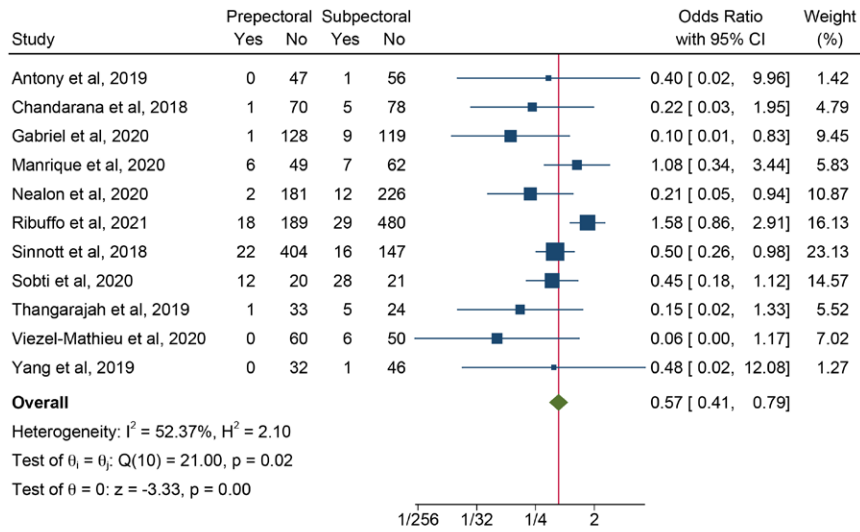
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Fig. 2. Forest plots and funnel plot for the comparison of capsular contracture between the PBP and SBR groups. Weights in forest plots are from fixed-effects analysis. (*Above*) The rates of capsular contracture were significantly lower in the PBR group than in the SBR group (OR, 0.57; 95% CI, 0.41 to 0.79), with high heterogeneity ($P = 0.025$; $I^2 = 52.37\%$). (*Center*) To reduce the heterogeneity, the results were the same with the overall pooled data (OR, 0.37; 95% CI, 0.25 to 0.56) after excluding data from one study (Ribuffo D, Berna G, De Vita R, et al. Dual-plane retro-pectoral versus pre-pectoral DTI breast reconstruction: an Italian multicenter experience. *Aesthetic Plast Surg*. 2021;45:51–60). (*Below*) Funnel plot of published studies reporting capsular contracture after excluding one study (Ribuffo et al., 2021).
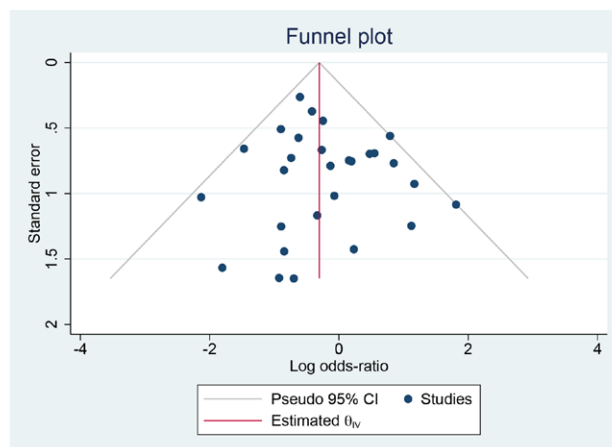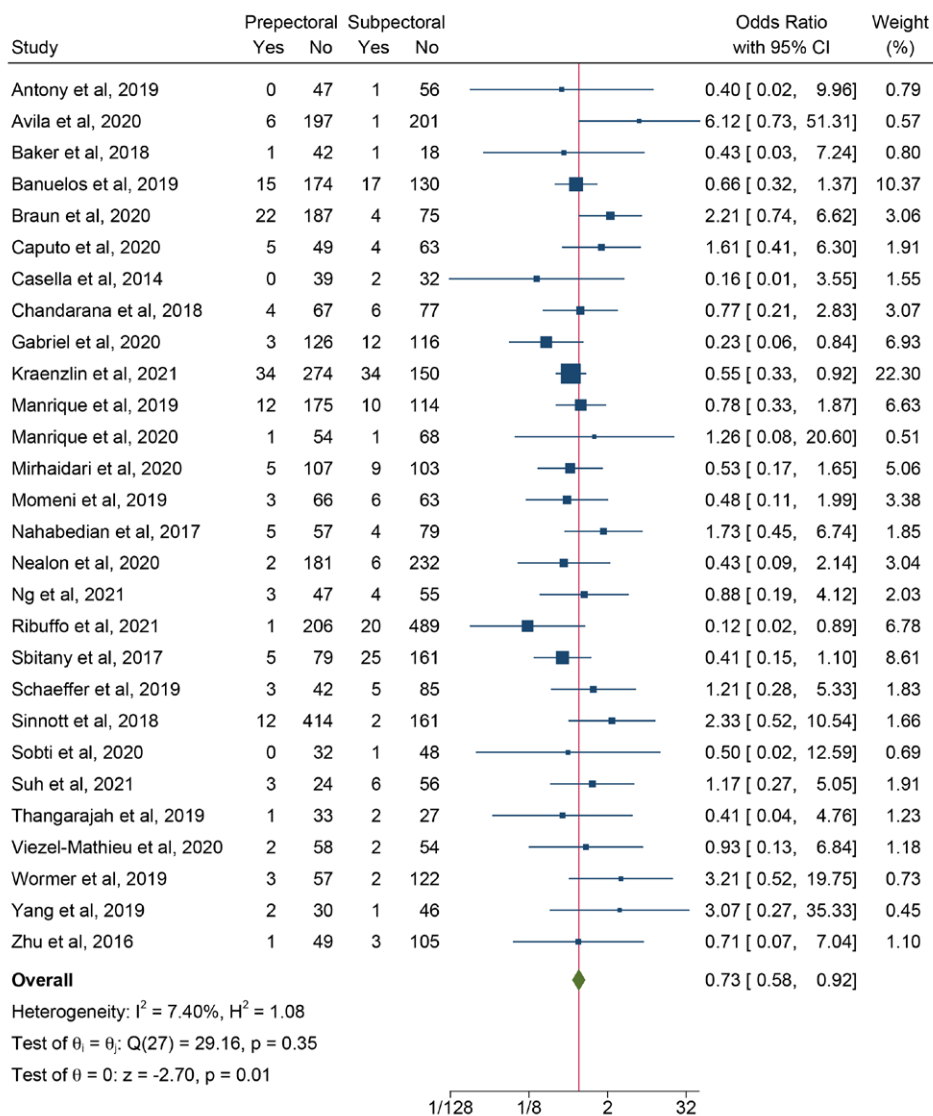
Study	Prepectoral Yes	No	Subpectoral Yes	No		Odds Ratio with 95% CI	Weight (%)
Antony et al, 2019	0	47	1	56		0.40 [0.02, 9.96]	0.79
Avila et al, 2020	6	197	1	201		6.12 [0.73, 51.31]	0.57
Baker et al, 2018	1	42	1	18		0.43 [0.03, 7.24]	0.80
Banuelos et al, 2019	15	174	17	130		0.66 [0.32, 1.37]	10.37
Braun et al, 2020	22	187	4	75		2.21 [0.74, 6.62]	3.06
Caputo et al, 2020	5	49	4	63		1.61 [0.41, 6.30]	1.91
Casella et al, 2014	0	39	2	32		0.16 [0.01, 3.55]	1.55
Chandarana et al, 2018	4	67	6	77		0.77 [0.21, 2.83]	3.07
Gabriel et al, 2020	3	126	12	116		0.23 [0.06, 0.84]	6.93
Kraenzlin et al, 2021	34	274	34	150		0.55 [0.33, 0.92]	22.30
Manrique et al, 2019	12	175	10	114		0.78 [0.33, 1.87]	6.63
Manrique et al, 2020	1	54	1	68		1.26 [0.08, 20.60]	0.51
Mirhaidari et al, 2020	5	107	9	103		0.53 [0.17, 1.65]	5.06
Momeni et al, 2019	3	66	6	63		0.48 [0.11, 1.99]	3.38
Nahabedian et al, 2017	5	57	4	79		1.73 [0.45, 6.74]	1.85
Nealon et al, 2020	2	181	6	232		0.43 [0.09, 2.14]	3.04
Ng et al, 2021	3	47	4	55		0.88 [0.19, 4.12]	2.03
Ribuffo et al, 2021	1	206	20	489		0.12 [0.02, 0.89]	6.78
Sbitany et al, 2017	5	79	25	161		0.41 [0.15, 1.10]	8.61
Schaeffer et al, 2019	3	42	5	85		1.21 [0.28, 5.33]	1.83
Sinnott et al, 2018	12	414	2	161		2.33 [0.52, 10.54]	1.66
Sobti et al, 2020	0	32	1	48		0.50 [0.02, 12.59]	0.69
Suh et al, 2021	3	24	6	56		1.17 [0.27, 5.05]	1.91
Thangarajah et al, 2019	1	33	2	27		0.41 [0.04, 4.76]	1.23
Viezel-Mathieu et al, 2020	2	58	2	54		0.93 [0.13, 6.84]	1.18
Wormer et al, 2019	3	57	2	122		3.21 [0.52, 19.75]	0.73
Yang et al, 2019	2	30	1	46		3.07 [0.27, 35.33]	0.45
Zhu et al, 2016	1	49	3	105		0.71 [0.07, 7.04]	1.10
Overall						0.73 [0.58, 0.92]	

Heterogeneity: $I^2 = 7.40\%$, $H^2 = 1.08$

Test of $\theta_i = \theta_j$: $Q(27) = 29.16$, $p = 0.35$

Test of $\theta = 0$: $z = -2.70$, $p = 0.01$

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Fig. 3. Forest plot and funnel plot for the comparison of infection between the PBR and SBR groups. Weights in forest plot are from fixed-effects analysis. (*Above*) the rates of infection were significantly lower in the PBR group than in the SBR group (OR, 0.73; 95% CI, 0.58 to 0.92), with low heterogeneity ($P = 0.353$; $I^2 = 7.40\%$). (*Below*) Funnel plot of published studies reporting infection.

Table 3. Summary of the Results from Meta-Analysis on Postoperative Complications between PBR and SBR Patients Using a Fixed-Effect Model

Outcome measures	Studies (No.)	Total (No.)		Event (No.)		Control (No.)		OR (95% CI)	Heterogeneity (%)[a]
		Prepectoral	Subpectoral	Prepectoral	Subpectoral	Prepectoral	Subpectoral		
Hematoma	20	2434	2476	46	82	2388	2394	0.73 (0.51–1.04)	2.38
Implant loss	22	2490	2650	98	111	2392	2539	0.83 (0.62–1.10)	0.00
Seroma	25	2956	3009	184	209	2772	2800	1.01 (0.83–1.23)	39.08
Skin flap necrosis	25	2755	2454	194	180	2561	2274	0.88 (0.72–1.07)	15.57
Wound dehiscence	13	2102	1826	53	71	2049	1755	0.74 (0.53–1.05)	0.00

[a]F.

Small-sample bias was not detected in the results of the analysis for capsular contracture (Egger test, $t = -0.69$; $P = 0.614$) (Fig. 4, *below*).

No significant differences were noted between the two treatments with respect to postoperative complications (including hematoma, implant loss, infection, seroma, skin-flap necrosis, and wound dehiscence) in patients who received PMRT (Table 4). No publication bias was detected in the results.

Qualitative Analysis

We only described outcome indicators that were described in at least two or more studies. Therefore, indicators presented only in one study, such as reoperation for aesthetic or functional concerns,[15] atopic reaction versus prosthesis,[29] economic analysis,[6] red breast syndrome,[1] local recurrence and metastatic disease,[11] and tissue expansion,[25] were not described.

Postoperative Pain

Nine studies[4–6,18,26–28,30,37] reported pain as an outcome measure. The PBR group demonstrated better pain outcomes than the SBR group in all included data sets, with eight of the nine studies demonstrating a significant difference, irrespective of the type of pain scale used for the assessment.[4–6,18,26,28,30,37] Only one study reported similar postoperative pain between PBR and SBR.[27]

Patient-Reported Outcomes (BREAST-Q)

Seven studies[6,7,20,27,28,30,35] assessed the quality of life of the patients. Most of these studies used the BREAST-Q questionnaire, but one study used its own questionnaire known as the "QOL assessment PRO survey replies."[6] The results of the studies that used the BREAST-Q questionnaire to validate the quality of outcomes showed that the quality-of-life scores were higher in the PBR group than in the SBR group.[6,7,20,27,28,30,35] Moreover, Franceschini et al., who devised their own questionnaire, showed that the prepectoral group scored significantly better than the subpectoral group in terms of "aesthetic satisfaction," "skin sensibility," "chronic pain in pectoral region," and "impaired arm motility."[6]

Upper Arm Function

Upper extremity motor function was evaluated to determine the outcomes of breast reconstruction in three studies.[4,28,30] Compared with SBR, PBR demonstrated a significantly positive effect on upper arm function.
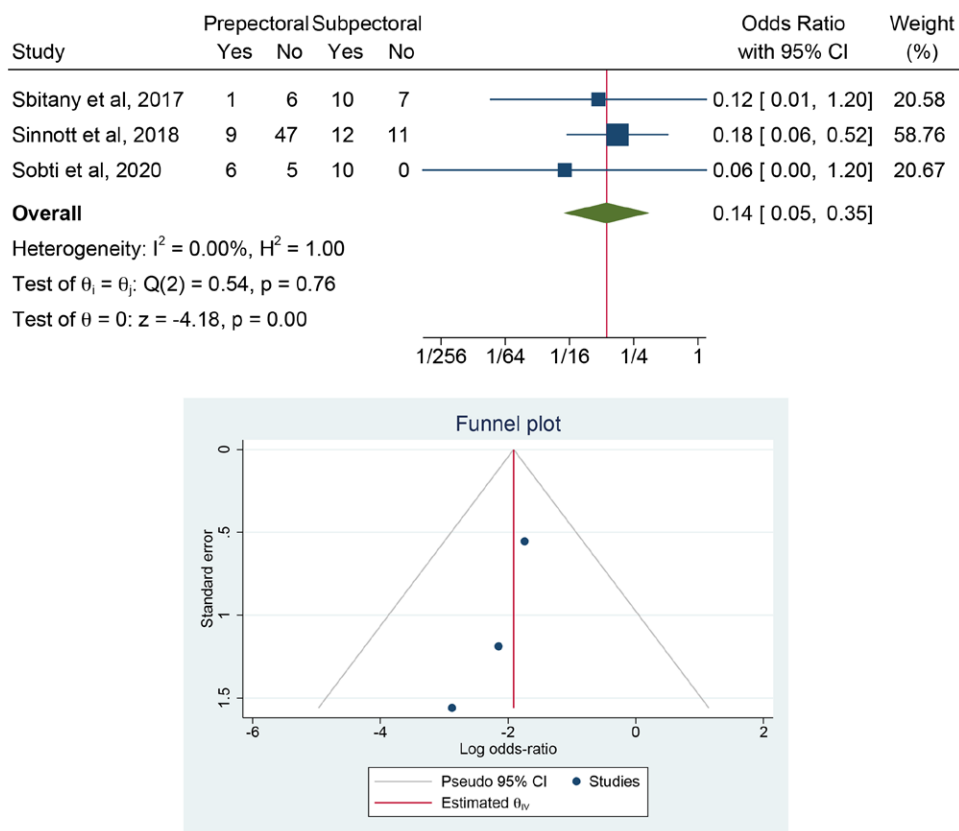
Fig. 4. Forest plot and funnel plot for the comparison of capsular contracture between the PBR and SPR groups with postmastectomy radiation therapy. Weights in forest plot are from fixed-effects analysis. (*Above*) The rates of capsular contracture were significantly lower in the PBR group than in the SBR group (OR, 0.14; 95% CI, 0.05 to 0.35), with high heterogeneity ($P = 0.765$; $I^2 = 0.22\%$). (*Below*) Funnel plot of published studies reporting capsular contracture.

Table 4. Summary of the Results from Meta-Analysis on Postoperative Complications between PBR and SBR Patients with Radiation Therapy Using a Fixed-Effect Model

Outcome Measures	Studies (No.)	Total (No.)		Event (No.)		Control (No.)		OR (95% CI)	Heterogeneity (%)[a]
		PBR	SPR	PBR	SBR	PBR	SBR		
Hematoma	3	112	75	3	1	109	74	1.69 (0.34–8.48)	0.00
Implant loss	5	131	99	14	19	117	80	0.74 (0.29–1.91)[b]	51.76[b]
Infection	4	119	92	20	22	99	70	0.97 (0.58–1.62)	0.00
Seroma	5	131	99	6	5	125	94	1.18 (0.40–3.53)	0.00
Skin flap necrosis	4	119	92	8	6	111	86	1.32 (0.54–3.22)	17.65
Wound dehiscence	3	112	75	6	6	106	69	0.92 (0.32–2.63)	0.00

[a]I^2.
[b]A random effect model was applied.

DISCUSSION

This study evaluated and compared the complications and patient-reported outcomes of PBR and SBR on a large scale. No significant differences were found between the two groups with respect to the specific complication rates, including seroma, hematoma, skin-flap necrosis, implant loss, and wound dehiscence. The rate of capsular contracture and infection was significantly lower in the PBR group than in the SBR group, with high heterogeneity. Furthermore, results of the comparative analyses of pain, BREAST-Q, and upper arm function confirmed that the PBR group showed considerably better progress than the SBR group.

One new development in implant-based breast reconstruction is complete prepectoral coverage of the implant using ADM, which eliminates the

need to elevate the pectoralis major from the chest wall to cover the superior pole of the implant.[27] With the widespread use of ADM, prepectoral prosthetic breast reconstruction has emerged as an alternative to the subpectoral approach. Prepectoral reconstruction avoids the disruption of the pectoralis major insertion and function, and achieves adequate implant coverage with the ADM, resulting in decreased rates of animation deformity and reduced postoperative pain and duration of postoperative recovery.[5] In our meta-analysis, except for two studies by Franceschini et al. and Nealon et al., ADM was used for implant coverage in the majority of the PBR group.[6,22] Moreover, the introduction of fluorescence imaging technologies has facilitated immediate evaluation of the vascularity of the residual mastectomy skin flap, which provides information to plastic surgeons that can significantly reduce potential wound-healing issues.[8]

In our meta-analysis, the postoperative complication rates in the PBR group were comparable with those in the SBR group, and the PBR group demonstrated better performance in reducing capsular contracture. Capsular contracture is a common adverse outcome following implant-based reconstruction and a reason for reoperation.[12,22] We found that the rate of capsular contracture was lower in the PBR group than in the SBR group for patients who underwent implant-based breast reconstruction.[10–12,15,22,35–38] This may be attributed to the partial coverage of the prosthesis with the ADM in the subpectoral approach, as opposed to the complete anterior coverage with the matrix in the prepectoral approach.[10,31,36,37] ADM mitigates the risk of capsular contracture by inhibiting inflammatory and profibrotic signaling, resulting in thinner capsules.[10] Moreover, it is reasonable to suspect that interference by the overlying muscle tissue may contribute to capsular contracture in SBR.[10,12,36]

PMRT is a risk factor of complications of breast reconstruction, particularly capsular contracture.[11,12] PMRT has been shown to increase the risk of complications in prosthetic reconstruction and negatively affect cosmetic outcomes, which is largely attributable to microvascular damage and fibrosis of the breast soft-tissue envelope.[39]

Radiation causes soft-tissue fibrosis. In patients with subpectoral implant-based breast reconstruction, the contracture affects the skin, capsule, and muscle. It has been suggested that fibrosis of the contractile muscle tissue could predispose patients after subpectoral reconstruction to breast contracture and implant deformation. Evidence supporting muscle fibrosis as the main contributor to contracture can be found in a recent investigation reporting favorable breast contracture rates following PBR when compared with submuscular placement in two-stage reconstruction. Implant placement in the prepectoral plane avoids the surgical manipulation of the muscle, and the implant is not at risk for deformation from muscle fibrosis and contracture following PMRT.[12] Sinnott et al. indicated that patients undergoing SBR who underwent PMRT had a three times greater capsular contracture rate with more severe contractures (Baker grade III or IV) than patients receiving PMRT who underwent PBR, and PBR was associated with a lower rate of capsular contracture regardless of the timing of breast irradiation.[11]

Postoperative infections are a significant issue that occur after breast reconstruction, with an incidence ranging from 0 to 9% in direct-to-implant reconstruction, as reported by a very recent literature review.[29] Several studies, such as those conducted by Nahabedian and Cocilovo, have shown higher rates of infection in the prepectoral group than in the subpectoral group. The topic of concern in prepectoral reconstruction with ADM was infection. The higher rate of infection in the prepectoral cohort was attributed to the fact that all cases with delayed healing gradually developed an infection that ultimately required explantation.[1] Subpectoral prosthesis placement has traditionally been the favored approach, as it was believed that the muscle allowed additional coverage of the underlying implant and helped reduce the risk of infection. However, several issues associated with the original iteration of prepectoral implant placement have been addressed by total coverage of the implant with a matrix, such as the synthetic titanium-coated polypropylene mesh (TiLOOP Bra) or ADM, as it prevents direct exposure of the implant to the mastectomy skin flap.[7,33] Our meta-analysis and review showed significantly lower rates of infection in the PBR group than in the SBR group.

Momeni et al. compared the infection rates between the prepectoral and subpectoral groups that received different antibiotic protocols. Immediate prepectoral TE insertion with anterior ADM coverage and antibiotic prophylaxis for less than 24 hours is safe and compares favorably with subpectoral TE placement with an inferior ADM sling and prolonged course of antibiotics. Patients who underwent the subpectoral approach received antibiotic prophylaxis for at least 1 week. The postoperative infection rate showed no significant difference. Concerns related to a more

tenuous soft-tissue coverage of the expander seem unfounded in the context of postoperative infection rate.[2]

Our study has some limitations. The designs of the primary studies were heterogeneous, rendering impactful pooled analysis difficult, as is the case for any meta-analysis. The articles included in our research were mainly retrospectively researched, and the PBR or SBR could not be applied randomly. Although this study did not choose only retrospective studies, it is considered that most studies were retrospective in nature. Prospective and randomized controlled research will be needed to find the answer to the appropriate reconstructive option. Moreover, some studies have placed emphasis on certain patient populations, such as those treated with PMRT or patients with obesity.[10,23] These studies focusing on specific clinical contexts could have disproportionately skewed the collated data, but the total sample population size was sufficiently large to minimize these effects. However, further randomized controlled trials with larger sample sizes are necessary to compare the clinical outcomes between PBR and SBR in postmastectomy patients.

CONCLUSIONS

We found that PBR is as safe as SBR after mastectomy. PBR is more beneficial to the patient in terms of reduced postoperative complications. This update on recently accumulated data demonstrates the resurgence of the PBR approach and its importance when discussing reconstruction options. Our meta-analysis suggests that PBR could be used as an alternative technique for breast reconstruction in the appropriate patient population. Comprehensive patient selection and skin perfusion assessment should be conducted before PBR to reduce the complication rates.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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