Impact of Obesity on Outcomes in Breast Reconstruction: A Systematic Review and Meta-Analysis

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Abstract

Background Increased rates of both breast cancer and obesity have resulted in more obese women seeking breast reconstruction. Studies demonstrate that these women are at increased risk for perioperative complications. A systematic review was conducted to assess the outcomes in obese women who underwent breast reconstruction following mastectomy.
Methods Cochrane, PUBMED, and EMBASE electronic databases were screened and data were extracted from included studies. The clinical outcomes assessed were surgical complications, medical complications, length of postoperative hospital stay, reoperation rate, and patient satisfaction.
Results Out of 33 studies met the inclusion criteria for the review and 29 provided enough data to be included in the meta-analysis (71,368 patients, 20,061 of whom were obese). Obese women (body mass index > 30 kg/m^2) were 2.29 times more likely to experience surgical complications (95% confidence interval (CI) 2.19–2.39; $p < 0.00001$), 2.89 times more likely to have medical complications (95% CI 2.50–3.35; $p < 0.00001$), and had a 1.91 times higher risk of reoperation (95% CI 1.75–2.07; $p < 0.00001$). The most common complication, wound dehiscence, was 2.51 times more likely in obese women (95% CI 1.80–3.52; $p < 0.00001$). Sensitivity analysis confirmed that obese women were more likely to experience surgical complications (risk ratio 2.36, 95% CI 2.22–2.52; $p < 0.00001$).
Conclusions This study provides evidence that obesity increases the risk of complications in both implant-based and autologous reconstruction. Additional prospective and observational studies are needed to determine if the weight reduction prior to reconstruction reduces the perioperative risks associated with obesity.

Keywords
- plastic surgery
- breast reconstruction
- obesity
- breast surgery complication
- breast cancer

Obesity has reached global epidemic proportions and is imposing a significant public health concern. The most recent data by the World Health Organization (WHO), which defines obesity as having a body mass index (BMI) of ≥30 kg/m^2, states that 13% of the world's adult population is obese.[1]

Obesity rates are even higher in women with 40% of the global female population being overweight and 15% obese.[1] Additionally, breast cancer is on the rise, accounting for ~30% of all newly reported cancer cases in women.[2,3] Consequently, it is likely that the proportion of women seeking

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breast reconstruction in the obese population will increase,[4] and it is imperative to evaluate the efficacy of available reconstructive techniques in these patients, as well as the rates of complications associated with these procedures.

It is well known that obese women have an increased risk for perioperative complications in various surgical procedures, including breast reconstruction.[5] The higher risk of medical complications in these patients creates unique challenges to health care systems.[6] Research suggests that obese women are also more likely to experience complications in both autologous and prosthetic breast reconstruction, with obese women demonstrating complication rates of 25% in comparison to 14% in nonobese individuals.[7]

Although it is believed that a high BMI ($>$30 kg/m^2) increases the risk of complications in breast reconstruction, a detailed comparison of the risks associated with the available reconstructive options has been elusive. Improved understanding of the effects of weight on surgical outcomes will enable health care professionals to identify the best strategy for each individual patient to minimize adverse effects. This review seeks to analyze and summarize the literature to provide a better understanding of the risks associated with breast reconstruction in obese women.

Patients and Methods

Selection Criteria

This review was conducted in line with the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0.[8] A protocol was published a priori[9] and the review was registered on the Research Registry UIN: reviewregistry191 (http://www.researchregistry.com). Cochrane, PUBMED, and EMBASE electronic databases were screened from their inception to 1 June 2016 using the keywords: obesity, weight, BMI, breast reconstruction, breast autologous tissue flap, breast free flap, transverse rectus abdominis myocutaneous (TRAM) flap, free muscle-sparing TRAM flap, pedicled TRAM flap, deep inferior epigastric perforators (DIEP) flap, latissimus dorsi myocutaneous (LDM) flap, superficial inferior epigastric artery flap (SIEA), breast tissue expander, and breast implant. The search format was tailored to the syntax of each database.

The inclusion criteria were cohort studies, case series, randomized controlled trials, and case–control studies reporting on breast reconstruction outcomes in obese women (BMI $>$ 30 kg/m^2) who underwent mastectomy for the treatment of breast cancer. The following surgical interventions were considered: prosthetic implants, including acellular dermal matrix use and tissue expander, and autologous reconstruction, including LDM flaps, pedicled, free and muscle sparing TRAM flaps, SIEA flaps, and DIEP flaps. These interventions were selected on the basis of the fact that they are the most commonly used reconstructive techniques, allowing us to set some limits to our search strategy. Given the inclusion of generic terms like breast reconstruction, we feel that the search strategy would be comprehensive. The inclusion and exclusion criteria are listed in ►**Table 1**.

The article selection process was a two-stage process completed by two reviewers (AP and BAS). Data were extracted into Microsoft Excel 2011 (Microsoft, Redmond, WA). First, the citation, title, and abstracts of studies from the search were independently screened to identify potentially relevant studies. The full manuscripts of articles that passed through this stage were then assessed for eligibility. Any inconsistency between the two reviewers was resolved by a third reviewer who was consulted to achieve consensus (DPO).

Quality Assessment

The grading of recommendation assessment, development, and evaluation (GRADE) guidelines were used to assess the methodological quality of the studies.[10]

Statistical Analysis

This meta-analysis was performed using RevMan (Review manager V5.2.6) in line with the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines.[11] The risk ratio (RR) were calculated using the fixed-effects model and heterogeneity was quantified using the I^2 and χ^2 statistics with the corresponding p-values.

Subgroup Analysis

Surgical complications were subdivided into wound infection and dehiscence, hematoma, seroma, fat necrosis, partial and total flap failure, and hernia occurrence. Additional analyses were performed to investigate the difference between surgical complication occurrence in implant versus autologous reconstruction and the difference between the nonobese population, and obesity Class I (30–34.9 kg/m^2), II (35–39.9 kg/m^2), and III ($>$40 kg/m^2) as defined by WHO.[12]

Sensitivity Analysis

A sensitivity analysis was performed to assess whether the outcomes were altered when the analysis was restricted to higher quality studies.

Results

Primary Studies Included in the Literature Review

A search of PUBMED yielded 102 articles and Embase yielded another 146 potentially relevant publications. No additional articles were identified from the Cochrane database (►**Fig. 1**). Of the 248 studies identified, 125 were excluded on the basis of their title, and 79 were based on their abstract. Full manuscripts were evaluated for 44 publications but only 33 fulfilled the entry criteria.[7,13–44] Eleven papers were excluded because: (a) they did not provide appropriate numerical data necessary for statistical analysis[45–50] and (b) they used the same patient population in different studies.[51–55] In cases utilizing the same population with an overlapping study period, only the study with the largest number of patients was included.

Main Study Characteristics and Methodological Quality Assessment

Of the 33 included studies only three were prospective (►**Table 2**). All studies were case series and had a level of

Table 1 Inclusion and exclusion criteria

Inclusion criteria
Cohort studies, case series, randomized controlled trials, and case–control studies
Prospective and retrospective studies
Patients who underwent breast reconstruction following a mastectomy for the treatment of breast cancer
Female patients of any age
Patients that underwent prosthetic implant (saline or silicone) or autologous tissue flap (TRAM flap, pedicled TRAM flap, free muscle-sparing TRAM flap, LDM flap, DIEP flap, SIEA flap) breast reconstruction
At least one primary outcome reported
Exclusion criteria
Unpublished trials and reports, case reports, duplicate studies, cost-effectiveness studies, and studies that do not provide the original data such systematic reviews, meta-analyses, editorials, discussions, commentaries and letters
Non–English language studies
Studies conducted on cadavers or animals
Studies conducted on male or transgender patients
Studies with no data on complications
Studies that used combined techniques
Studies that do not indicate a reason for the procedure
Patients who underwent breast reconstruction for aesthetic purposes or for traumatic breast defects
Studies that did not specify the number of patients

Abbreviations: DIEP, deep inferior epigastric perforators; LDM, latissimus dorsi myocutaneous; SIEA, superficial inferior epigastric artery flap; TRAM, transverse rectus abdominis myocutaneous.

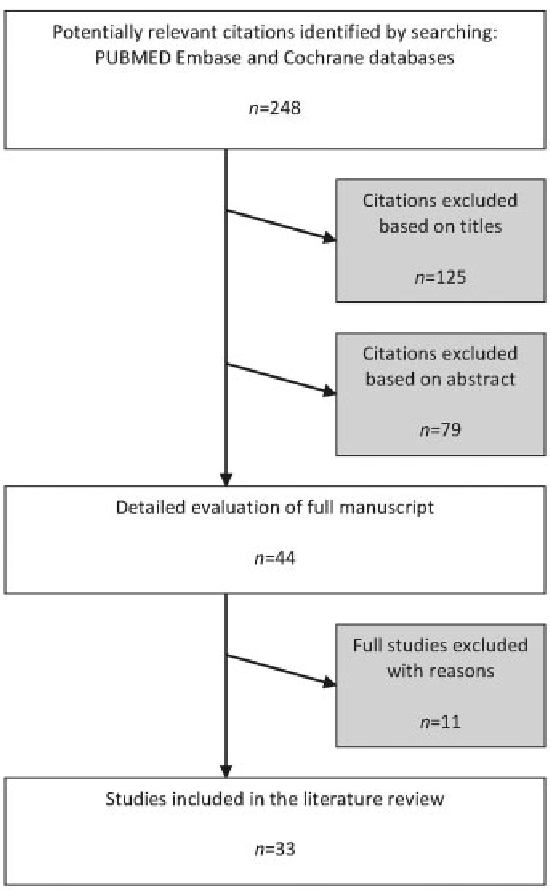


Fig. 1 The selection process of the studies included in the literature review.

evidence (LoE) of 4 as defined by the Oxford Centre for Evidence-Based Medicine.[56] No randomized controlled trials were found. Eighteen studies were specifically designed to investigate the effect BMI has on breast reconstruction,[7,13,15–19,23,25,26,30–33,38,42–44] whereas 15 studies investigated general risk factors, one of which was obesity.[14,20–22,24,27–29,34–37,39–41] Numerical data for meta-analysis could be extracted from 29 papers, six of which investigated prosthetic reconstruction,[7,13,14,22,27,28] 22 investigated autologous reconstruction,[15,18–21,23,25,26,29–37,39–43] and five looked at both.[16,17,24,38,44] Two studies presented data only from obese patients, comparing morbidly with non-morbidly obese patients, but were included in our meta-analysis as the prevalence of complications in these studies was not significantly different from that in other studies.[30,31] Fourteen of 29 studies were of low or very low quality on the GRADE scale. Fifteen studies that were comparative were deemed moderate quality.[13,15,17,18,23,25,26,30–34,36,39,42]

Definitions of Outcome Measures

Surgical Complications

This outcome was reported in 30 studies.[7,13–20,22–37,39–43] Wound infection was investigated in 25 studies,[7,13,15–18,20,22–33,35,39–43] wound dehiscence in 12,[13,16–18,20,22,24,27,28,30,32,36] abdominal hernia in 14,[15,18,23,29–31,34,36,37,39–43] hematoma in 17,[7,13,15,17,18,22,26,29,30,32,33,35,39–43] seroma in 18,[7,13,15,17,18,22,23,25,26 29–35,41,42] flap failure in 23,[7,15–20,22–26,29–35,40–43] and fat necrosis in 17 studies.[15,17,18,23,25,26,29–32,35,37,39–43]

Table 2 Studies included in the literature review

Study	Year	Country[a]	Type of study	Reconstructive technique	No. of patients	Outcomes
Huo et al	2016	USA	Retrospective	Autologous	549	Surgical
Sinha et al	2016	Australia	Retrospective	DIEP, msTRAM, SIEA	29	Surgical, medical, reoperation, satisfaction
Alipour et al	2015	Iran	Retrospective	TRAM	14	Surgical, reoperation
Massenburg et al	2015	USA	Retrospective	Pedicled and free TRAM, LD	2,433	Surgical, medical
Mennie et al	2015	UK	Retrospective	Pedicled and free TRAM, DIEP	208	Reoperation
Selber et al	2015	USA	Retrospective	ADM	94	Surgical
Fischer et al	2014	USA	Retrospective	TRAM, DIEP, SIEA	272	Surgical, medical, length of stay
Fischer et al	2014	USA	Retrospective	Implant, TE, pedicled and free TRAM, LD	4,321	Surgical, medical, reoperation
Nelson et al	2014	USA	Prospective	Autologous	57	Surgical, medical, reoperation
Nguyen et al	2014	USA	Retrospective	TE, implant	175	Surgical, reoperation
Ozturk et al	2014	USA	Retrospective	TRAM	63	Surgical, medical, reoperation
Wink et al	2014	USA	Retrospective	Implant	374	Surgical, medical, reoperation
Fischer et al	2013	USA	Retrospective	Implant	3,741	Surgical, medical, reoperation
Fischer et al	2013	USA	Retrospective	TE	2,390	Surgical, reoperation
Hanwright et al	2013	USA	Retrospective	TE, pedicled and free TRAM, LD flap	3,636	Surgical, medical, reoperation
Ireton et al	2013	USA	Retrospective	Pedicled TRAM	21	Surgical
Garvey et al	2012	USA	Retrospective	Implant, TE, msTRAM, DIEP, SIEA	700	Surgical, reoperation
Momeni et al	2012	USA	Retrospective	DIEP, msTRAM, SIEA	28	Surgical, medical, length of stay
Ochoa et al	2012	USA	Retrospective	DIEP	258	Surgical
Yezhelyev et al	2012	USA	Retrospective	LDF	103	Surgical
Seidenstuecker et al	2011	Germany	Prospective	DIEP, msTRAM	79	Surgical
Appleton et al	2010	Canada	Retrospective	DIEP	39	Surgical, medical
Rossetto et al	2010	Brazil	Retrospective	TRAM	39	Surgical
Wan et al	2010	USA	Retrospective	DIEP, msTRAM	103	Surgical
Atisha et al	2007	USA	Retrospective	Implant, TE, pedicled and free TRAM	47	Satisfaction
Greco et al	2007	USA	Retrospective	Autologous	62	Surgical, reoperation
McCarthy et al	2007	USA	Retrospective	Implant, TE	110	Surgical
Mehrara et al	2006	USA	Retrospective	Free TRAM	85	Surgical, medical, reoperation
Selber et al	2006	USA	Retrospective	Free TRAM	80	Surgical
Spear et al	2005	USA	Retrospective	TRAM	30	Surgical, medical
Moran et al	2001	USA	Retrospective	TRAM	114	Surgical, medical
Kulkarni et al	2001	USA	Retrospective	Implant, autologous	53	Satisfaction
Chang et al	2000	USA	Prospective	Free TRAM	64	Surgical

Abbreviations: ADM, acellular dermal matrix; DIEP, deep inferior epigastric artery perforator; LD, Latissimus Dorsi; MS, muscle-sparing; SIEA, superficial inferior epigastric artery; TE, tissue expander; TRAM, transverse rectus abdominis myocutaneous.
[a]Institution of lead author.

Medical Complications

Medical complications were reported in 14 studies.[16,18,20,23–28,31,35,40,42,43] Ten studies included deep venous thrombosis (DVT) in their definition[16,18,20,23,24,26,27,40,42,43] and seven studies included pulmonary embolism (PE).[16,18,20,23,24,27,42] Four studies included any National Surgical Quality Improvement Program-defined endpoints such as PE, myocardial infarction, pneumonia, urinary tract infection, sepsis, stroke, and coma in their definition.[16,20,24,27]

Length of Postoperative Hospital Stay

This was reported in four studies which defined the length of stay in days.[23,26,31,43] All four studies were limited to autologous reconstruction.

Reoperation

This was reported in 12 studies.[13,16,18,21,24–28,30,39,40] Reoperation was defined in numerous ways, for example, two studies defined it as unplanned return to the operating room within 30 days.[24,27] One study provided four reasons for reoperation: tissue expander explantation, tissue expander exchange, conversion to autologous reconstruction, and ultimate failure of reconstruction.[13] Another focused on hernia repair.[21] For the purpose of this study, any reason for return to the operating room was classified as reoperation.

Patient Satisfaction

Patient satisfaction was reported in three studies[18,38,44] and two of these assessed it using the BREAST-Q, a module measuring postreconstruction satisfaction on six subscales: (1) satisfaction with breasts; (2) psychosocial well-being; (3) sexual well-being; (4) physical well-being with respect to chest/abdomen donor site; (5) satisfaction with outcome; and (6) satisfaction with information provision.[18,44] The third study used a module, which assessed (1) general satisfaction with the treatment process including information provision, decision making and surgery and (2) aesthetic satisfaction in terms of breast contour and softness.[38]

Results for the Overall Meta-Analysis

The 29 studies that were analyzed involved 71,368 patients, including 20,061 obese patients. ►**Tables 3**, **4**, and **5** summarize the results of the primary outcomes of interest. Overall, obese women were more likely to experience surgical (RR 2.29, 95% CI 2.19–2.39; $p < 0.00001$) and medical complications (RR 2.89, 95% CI 2.50–3.35; $p < 0.00001$) and had a higher chance of returning to the operating room (RR 1.91, 95% CI 1.75–2.07; $p < 0.00001$).

Subgroup Analysis

►**Table 6** shows the subgroup analysis for surgical complications. Obese women were more likely to experience fat necrosis (RR 1.65, 95% CI 1.31–2.07; $p < 0.0001$), seroma (RR 1.96, 95% CI 1.57–2.45; $p < 0.00001$), partial flap failure (RR 1.60, 95% CI 1.06–2.41; $p = 0.03$), total flap failure (RR 1.97, 95% CI 1.34–2.91; $p = 0.0006$), wound dehiscence (RR 2.51, 95% CI 1.80–3.52; $p < 0.00001$), wound infection (RR 2.34, 95% CI 2.03–2.69; $p < 0.00001$), and hernia (RR 1.67, 95% CI 1.15–2.43; $p = 0.007$). No significant difference was found for the occurrence of hematoma.

Subgroup analysis for type of reconstruction (►**Tables 7** and **8**) showed that obese women were more likely to experience surgical complications during both implant (RR 2.64, 95% CI 2.25–3.09; $p < 0.00001$) and autologous reconstruction (RR 2.59, 95% CI 2.27–2.55; $p < 0.00001$).

Subgroup analysis for surgical complications in the different classes of obesity was based on four studies, two of which looked at flap complications[23,32] and two at implant failure.[27,28] Class II obese patients (RR 1.84, 95% CI 1.56–2.17; $p < 0.00001$) were more likely to develop surgical complications than Class I (RR 1.32, 95% CI 1.15–1.50; $p < 0.0001$) or III patients (RR 1.66, 95% CI 1.36–2.03; $p < 0.00001$) undergoing reconstruction (►**Table 9**). Class III patients were more likely to develop complications than Class I patients. Three of the four studies included in this subgroup analysis showed these results.[27,28,32]

Subgroup analysis for medical complications was not possible as the majority of papers gave the overall number of medical complications, without distinguishing the specific complication.[18,24,25,31] As only two papers provided numbers for specific medical complications the data were deemed inadequate for subgroup analysis.[16,23]

Sensitivity Analysis

When performing the meta-analysis with just the comparative studies, again the group of obese women was more likely to experience surgical complications (RR 2.36, 95% CI 2.22–2.52; $p < 0.00001$) and the RR was comparable to the analysis with all studies (►**Table 10**). A summary of the RRs of all outcomes is presented in ►**Table 11**.

Discussion

Main Findings

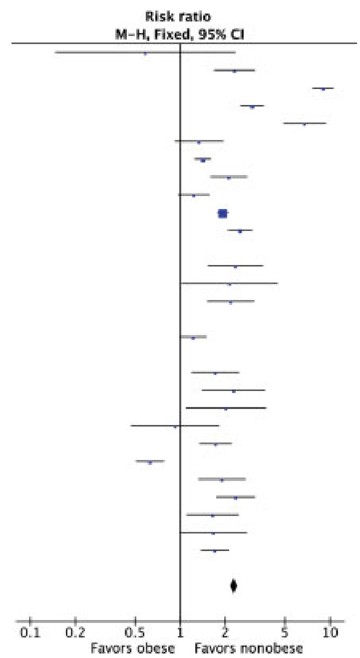
Surgical Complications

Consistent with this meta-analysis, there is a well-documented correlation between obesity and the development of both surgical and medical complications in the perioperative period. Obesity increases the risk for complications by influencing the normal physiology through various mechanisms. For example, animal studies have shown that the skin of obese mice is mechanically weaker and unable to generate as much hydrothermal isometric force as the skin of lean mice, believed to be due to a mismatch between the increase in skin surface area and collagen deposition.[57] In addition, decreased collagen deposition results in impaired wound healing in obese mice.[58] Overall, obese animal models display impaired myofibroblast activity and collagen maturation, processes which are both necessary for proper healing of surgical wounds.[59]

In addition, obesity is associated with a chronic, low-grade systemic inflammation referred to as metainflammation. This type of inflammation displays minimal increase in circulating proinflammatory factors and lacks the typical clinical signs of

Table 3 Forest plot for surgical complications (SC) in obese versus nonobese women

Study	Obese		Nonobese		Weight	RR
	SC	Total	SC	Total	%	M-H Fixed, 95% CI
Alipour et al (2016)	2	14	11	45	0.3	0.58 [0.15, 2.33]
Sinha et al (2016)	26	29	28	72	1.0	2.31 [1.68, 3.16]
Huo et al (2016)	523	549	135	1,274	4.8	8.99 [7.66, 10.56]
Massenburg et al (2015)	298	2,433	179	4,422	7.5	3.03 [2.53, 3.62]
Wink et al (2014)	97	374	47	1,229	1.3	6.78 [4.88, 9.42]
Fischer et al (2014a)	178	272	249	540	9.9	1.42 [1.25, 1.61]
Ozturk et al (2014)	47	63	42	119	1.7	2.11 [1.59, 2.80]
Nguyen et al (2014)	36	175	58	376	2.2	1.33 [0.92, 1.94]
Nelson et al (2014)	39	57	61	110	2.5	1.23 [0.97, 1.57]
Fischer et al (2014b)	792	4,321	1,116	11,742	35.6	1.93 [1.77, 2.10]
Fischer et al (2013b)	38	2,390	47	6,915	1.4	2.34 [1.53, 3.58]
Ireton et al (2013)	13	21	0	0		Not estimable
Fischer et al (2013a)	51	3,741	68	10,844	2.1	2.17 [1.52, 3.12]
Cleveland et al (2013)	14	272	13	540	0.5	2.14 [1.02, 4.48]
Hanwright et al (2013)	211	3,636	216	9,350	7.2	2.51 [2.09, 3.02]
Garvey et al (2012)	391	700	0	0		Not estimable
Momeni et al (2012)	9	28	0	0		Not estimable
Yezhelyev et al (2012)	65	103	90	174	4.0	1.22 [0.99, 1.50]
Ochoa et al (2012)	47	165	42	253	2.0	1.72 [1.19, 2.48]
Seidenstuecker et al (2011)	18	79	48	479	0.8	2.27 [1.40, 3.70]
Appleton et al (2010)	32	39	50	105	1.6	1.72 [1.34, 2.21]
Rossetto et al (2010)	8	39	37	167	0.8	0.93 [0.47, 1.83]
Wan et al (2010)	15	103	22	306	0.7	2.03 [1.09, 3.75]
Greco et al (2007)	36	62	109	118	4.5	0.63 [0.51, 0.78]
McCarthy et al (2007)	28	108	106	776	1.5	1.90 [1.32, 2.73]
Selber et al (2006)	38	80	85	420	1.6	2.35 [1.74, 3.16]
Spear et al (2005)	16	30	55	170	1.0	1.65 [1.11, 2.46]
Moran et al (2001)	32	114	18	107	1.1	1.67 [1.00, 2.79]
Chang et al (2000)	40	64	240	654	2.5	1.70 [1.37, 2.11]
Total (95% CI)		20,061		51,307	100.0	2.29 [2.19, 2.39]
Total SC	3,140		3172			



Abbreviations: CI, confidence interval; RR, risk ratio.
Heterogeneity $Chi^2 = 637.13$, df = 25 ($p < 0.00001$); $I^2 = 96\%$.
Test for overall effect: $Z = 35.94$ ($p < 0.00001$).

inflammation and may play a part in decreased flap survival.[60] Furthermore, the high mass of adipose tissue surrounding the perforating vessels in certain types of autologous reconstructions may compromise the patency of their lumen, consequently resulting in a decreased blood supply to the flap.[61] In addition, flap loss may be related to the increase in arterial thrombosis and secondarily to increased pedicle tension.[23] Overall, tissue flaps in obese patients are heavier and larger, and a limited vascular supply is may not able to adequately perfuse the greater volume of tissue.[15]

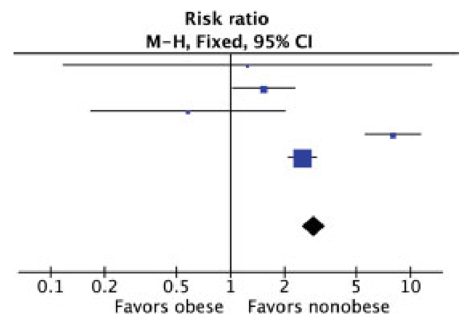
The increased occurrence of infection and necrosis is believed to be due to poor perfusion of the edges of the reconstruction furthest from the vascular inflow leading to relative hypoxia of these tissues.[62] Seroma formation is believed to be due to dead space formation in poorly perfused adipose tissue.[63] Furthermore, given that obesity is associated with increased intraabdominal pressure, it is believed this is what weakens the abdominal wall contributing to the increased risk of hernia occurrence.[64] Furthermore, hypoxia impairs collagen synthesis resulting in deficient healing. Research has also suggested that obesity may cause hernia occurrence by increasing the likelihood of wound infection.[65] A deficiency of macronutrients and micronutrients has also been suggested as a possible cause of inadequate wound healing in obese individuals.[62]

Medical Complications

The higher occurrence of medical complications seen in this meta-analysis is not surprising, as obese patients often have multiple medical comorbidities, which increase the risk for postoperative medical complications such as DVT and PE.

Table 4 Forest plot for medical complications (MC) in obese versus nonobese women

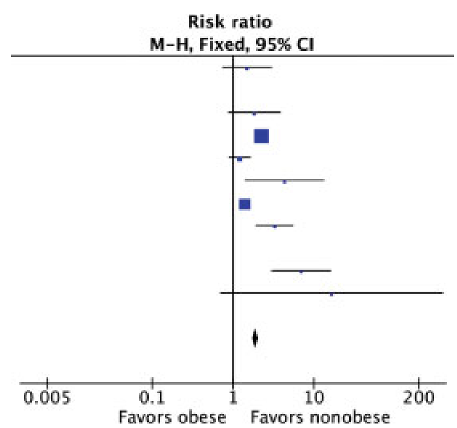
Study	Obese		Nonobese		Weight	RR
	MC	Total	MC	Total	%	M-H Fixed, 95% CI
Sinha et al (2016)	1	29	2	72	0.6	1.24 [0.12, 13.17]
Fischer et al (2014a)	37	272	48	540	17.7	1.53 [1.02, 2.29]
Nelson et al (2014)	3	57	10	110	3.7	0.58 [0.17, 2.02]
Fischer et al (2014b)	115	4,321	39	11,742	11.5	8.01 [5.58, 11.50]
Hanwright et al (2013)	211	3,636	216	9,350	66.4	2.51 [2.09, 3.02]
Momeni et al (2012)	1	28	0	0		Not estimable
Total (95% CI)		8,343		21,814	100.0	2.89 [2.50, 3.35]
Total MC	368		315			



Abbreviations: CI, confidence interval; RR, risk ratio.
Heterogeneity $Chi^2 = 49.16$, $df = 4$ ($p < 0.00001$); $I^2 = 92\%$.
Test for overall effect: $Z = 14.27$ ($p < 0.00001$).

Table 5 Forest plot for reoperation rates (reop) in obese versus nonobese women

Study	Obese		Nonobese		Weight	RR
	Reop	Total	Reop	Total	%	M-H Fixed, 95% CI
Sinha et al (2016)	9	29	15	72	1.3	1.49 [0.74, 3.02]
Alipour et al (2016)	0	14	0	45		Not estimable
Mennie et al (2015)	7	208	142	7,721	1.1	1.83 [0.87, 3.86]
Fischer et al (2014b)	519	4,321	628	11,742	50.7	2.25 [2.01, 2.51]
Nguyen et al (2014)	46	175	82	376	7.8	1.21 [0.88, 1.65]
Nelson et al (2014)	9	57	4	110	0.4	4.34 [1.40, 13.49]
Cleveland et al (2013)	33	272	20	540	2.0	3.28 [1.92, 5.60]
Hanwright et al (2013)	232	3,636	428	9,350	36.0	1.39 [1.19, 1.63]
Garvey et al (2012)	16	700	0	0		Not estimable
Greco et al (2007)	22	62	6	118	0.6	6.98 [2.99, 16.31]
Moran et al (2001)	1	30	0	170	0.0	16.55 [0.69, 397.00]
Total (95% CI)		9,504		30,244	100.0	1.91 [1.75, 2.07]
Total reop	894		1,325			



Abbreviations: CI, confidence interval; RR, risk ratio.
Heterogeneity $Chi^2 = 49.44$, $df = 8$ ($p < 0.00001$); $I^2 = 84\%$.
Test for overall effect: $Z = 15.24$ ($p < 0.00001$).

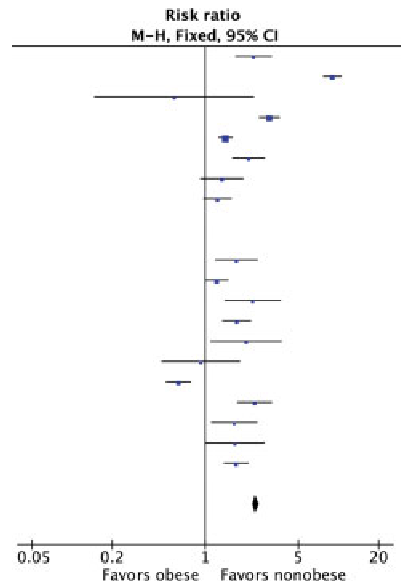
Table 6 Subgroup analysis of surgical complications in obese versus nonobese women

Surgical complication	Studies	Patients		RR (95% CI)	*p*-Value	Heterogeneity *p*-Value
		Obese	Nonobese			
Fat necrosis	9	1,430	2,227	1.65 [1.31–2.07]	<0.0001	0.07
Hematoma	9	771	2,356	1.05 [0.72–1.52]	0.82	0.006
Hernia	10	1,383	2,620	1.67 [1.15–2.43]	0.007	0.36
Partial flap failure	7	1,237	2,034	1.60 [1.06–2.41]	0.03	0.68
Seroma	10	816	2,717	1.96 [1.57–2.45]	<0.00001	0.002
Total flap failure	7	640	2,210	1.97 [1.34–2.91]	0.0006	0.21
Wound dehiscence	4	4,540	9,798	2.51 [1.80–3.52]	<0.00001	0.0007
Wound infection	13	533	11,216	2.34 [2.03–2.69]	<0.00001	0.0001

Abbreviations: CI, confidence interval; RR, risk ratio.

Table 7 Forest plot for surgical complications (SC) in autologous reconstruction

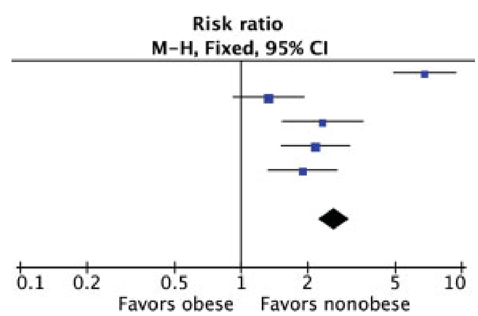
Study	Obese		Nonobese		Weight	RR
	SC	Total	SC	Total	%	M-H Fixed, 95% CI
Sinha et al (2016)	26	29	28	72	1.9	2.31 [1.68, 3.16]
Huo et al (2016)	523	549	135	1,274	9.6	8.99 [7.66, 10.56]
Alipour et al (2016)	2	14	11	45	0.6	0.58 [0.15, 2.33]
Massenburg et al (2015)	298	2,433	179	4,422	14.9	3.03 [2.53, 3.62]
Fischer et al (2014a)	178	272	249	540	19.6	1.42 [1.25, 1.61]
Nguyen et al (2014)	36	175	58	376	4.3	1.33 [0.92, 1.94]
Ozturk et al (2014)	47	63	42	119	3.4	2.11 [1.59, 2.80]
Nelson et al (2014)	39	57	61	110	4.9	1.23 [0.97, 1.57]
Ireton et al (2013)	13	21	0	0		Not estimable
Momeni et al (2012)	9	28	0	0		Not estimable
Ochoa et al (2012)	47	165	42	253	3.9	1.72 [1.19, 2.48]
Yezhelyev et al (2012)	65	103	90	174	4.0	1.22 [0.99, 1.50]
Seidenstuecker et al (2011)	18	79	48	479	1.6	2.27 [1.40, 3.70]
Appleton et al (2010)	32	39	50	105	3.2	1.72 [1.34, 2.21]
Wan et al (2010)	15	103	22	306	1.3	2.03 [1.09, 3.75]
Rossetto et al (2010)	8	39	37	167	1.6	0.93 [0.47, 1.83]
Greco et al (2007)	36	62	109	118	8.8	0.63 [0.51, 0.78]
Selber et al (2006)	38	80	85	420	3.2	2.35 [1.74, 3.16]
Spear et al (2005)	16	30	55	170	1.9	1.65 [1.11, 2.46]
Moran et al (2001)	32	114	18	107	2.2	1.67 [1.00, 2.79]
Chang et al (2000)	40	64	240	654	5.0	1.70 [1.37, 2.11]
Total (95% CI)		4,519		9,911	100.0	2.41 [2.27, 2.55]
Total SC	1,518		1,559			



Abbreviations: CI, confidence interval; RR, risk ratio.
Heterogeneity Chi^2 =598.15, df = 18 ($p < 0.00001$); $I^2 = 97\%$.
Test for overall effect: $Z = 29.70$ ($p < 0.00001$).

Table 8 Forest plot for surgical complications (SC) in implant reconstruction

Study	Obese		Nonobese		Weight	RR
	SC	Total	SC	Total	%	M-H Fixed, 95% CI
Wink et al (2014)	97	374	47	1,229	15.3	6.78 [4.88, 9.42]
Nguyen et al (2014)	36	175	58	376	25.6	1.33 [0.92, 1.94]
Fischer et al (2013b)	38	2,390	47	6,915	16.8	2.34 [1.53, 3.58]
Fischer et al (2013a)	51	3,741	68	10,844	24.3	2.17 [1.52, 3.12]
McCarthy et al (2007)	28	108	106	776	18.0	1.90 [1.32, 2.73]
Total (95% CI)		6,788		20,140	100.0	2.64 [2.25, 3.09]
Total SC	250		326			



Abbreviations: CI, confidence interval; RR, risk ratio.
Heterogeneity Chi^2 =48.97, df = 4 ($p < 0.00001$); $I^2 = 92\%$.
Test for overall effect: $Z = 12.01$ ($p < 0.00001$).

Despite a higher occurrence of DVT and PE being mentioned in the reviewed articles, numerical data were not sufficient to be used in the meta-analysis. It is recommended that obese patients with multiple comorbid conditions should be monitored closely for postoperative medical complications and should receive appropriate mechanical and pharmacological venous thromboembolic prophylaxis with weight-adjusted dosages calculated for the latter.[45] One study found that

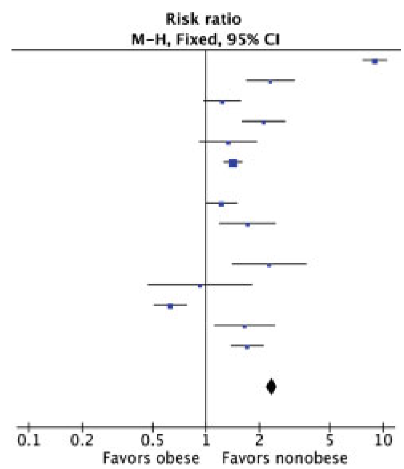
Table 9 Subgroup analysis of surgical complications in nonobese women versus Class I, Class II, and Class III obese women

Obesity class	Patients		RR (95% CI)	*p*-Value	Heterogeneity *p*-Value
	Obese	Nonobese			
Class I (30–34.9 kg/m^2)	2,899	13,533	1.32 [1.15–1.50]	$<$0.0001	0.68
Class II (35–39.9 kg/m^2)	1,181	13,533	1.84 [1.56–2.17]	$<$0.00001	0.02
Class III ($>$40 kg/m^2)	837	13,533	1.66 [1.36–2.03]	$<$0.00001	0.25

Abbreviations: CI, confidence interval; RR, risk ratio.

Table 10 Forest plot for sensitivity analysis of surgical complications (SC)

Study	Obese		Nonobese		Weight	RR
	SC	Total	SC	Total	%	M-H Fixed, 95% CI
Huo et al (2016)	523	549	135	1274	12.8	8.99 [7.66, 10.56]
Sinha et al (2016)	26	29	28	72	2.5	2.31 [1.68, 3.16]
Nelson et al (2014)	39	57	61	110	6.6	1.23 [0.97, 1.57]
Ozturk et al (2014)	47	63	42	119	4.6	2.11 [1.59, 2.80]
Nguyen et al (2014)	36	175	58	376	5.8	1.33 [0.92, 1.94]
Fischer et al (2014a)	178	272	249	540	26.3	1.42 [1.25, 1.61]
Garvey et al (2012)	391	700	0	0		Not estimable
Yezhelyev et al (2012)	65	103	90	174	10.6	1.22 [0.99, 1.50]
Ochoa et al (2012)	47	165	42	253	5.2	1.72 [1.19, 2.48]
Momeni et al (2012)	9	28	0	0		Not estimable
Seidenstuecker et al (2011)	18	79	48	479	2.1	2.27 [1.40, 3.70]
Rossetto et al (2010)	8	39	37	167	2.2	0.93 [0.47, 1.83]
Greco et al (2007)	36	62	109	118	11.8	0.63 [0.51, 0.78]
Spear et al (2005)	16	30	55	170	2.6	1.65 [1.11, 2.46]
Chang et al (2000)	40	64	240	654	6.8	1.70 [1.37, 2.11]
Total (95% CI)		2,415		4,506	100.0	2.36 [2.22, 2.52]
Total SC	1,479		1,194			



Abbreviations: CI, confidence interval; RR, risk ratio.
Heterogeneity Chi^2 =569.76, df = 12 ($p < 0.00001$); $I^2 = 98\%$.
Test for overall effect: $Z = 26.63$ ($p < 0.00001$).

medical complications were more likely to occur in patients undergoing pedicled TRAM reconstruction than latissimus and free flap reconstruction, suggesting that this increased risk may be due to either a selection bias, as patients prone to thrombotic events were more likely to undergo pedicled flap reconstruction, or due to the fact that perioperative anticoagulants are more routinely used in patients undergoing free tissue transfer.[16]

Length of Postoperative Hospital Stay

Despite the increase in postoperative complications, the mean length of postoperative hospital stay for obese women was comparable with studies of nonobese patients. The length of stay in the obese population varied from 4.2[23] to 7 days,[43] lengths of stay which are comparable with studies in nonobese populations.[35,40]

Reoperation

Overall, the rate of reoperation was higher in the obese population. This is not surprising given the increased occurrence of surgical complications in obese patients. One study differentiated between reconstruction types, reporting that free flap patients had the highest rate of reoperation, followed by TRAM flaps, tissue expander and, last latissimus flaps.[16]

Patient Satisfaction

Despite a higher occurrence of complications, obese women achieved equivalent postoperative satisfaction scores to the comparison group,[18] and reported similar satisfaction levels in terms of decision-making prior to surgery and also surgical outcome.[44] A significant decrease in aesthetic satisfaction was seen in obese women undergoing expander and implant reconstructions, reported to be due to the challenge in achieving symmetry to a native large volume contralateral breasts.[38]

Implications for Clinical Practice

To minimize the occurrence of the complications mentioned in this meta-analysis and provide better care for obese women, we recommend that clinicians counsel patients with a BMI $>$ 30 regarding the high risk of complications and to

Table 11 Summary of RRs for the primary outcomes in obese versus nonobese women

Outcome	Studies	Patients		RR (95% CI)	*p*-value	Heterogeneity *p*-Value
		Obese	Nonobese			
Surgical complications	29	20,061	51,307	2.29 [2.19–2.39]	<0.00001	<0.00001
Fat necrosis	9	1,430	2,227	1.65 [1.31–2.07]	<0.0001	0.07
Hematoma	9	771	2,356	1.05 [0.72–1.52]	0.82	0.006
Hernia	10	1,383	2,620	1.67 [1.15–2.43]	0.007	0.36
Partial flap failure	7	1,237	2,034	1.60 [1.06–2.41]	0.03	0.68
Seroma	10	816	2,717	1.96 [1.57–2.45]	<0.00001	0.002
Total flap failure	7	640	2,210	1.97 [1.34–2.91]	0.0006	0.21
Wound dehiscence	4	4,540	9,798	2.51 [1.80–3.52]	<0.00001	0.0007
Wound infection	13	533	11,216	2.34 [2.03–2.69]	<0.00001	0.0001
Autologous reconstruction	21	4,519	9,911	2.59 [2.44–2.75]	<0.00001	<0.00001
Implant reconstruction	5	6,788	20,140	2.64 [2.25–3.09]	<0.00001	<0.00001
Medical complications	6	8,343	21,814	2.80 [2.41–3.26]	<0.00001	<0.00001
Reoperation	11	9,504	30,244	1.91 [1.75–2.07]	<0.00001	<0.00001

Abbreviations: CI, confidence interval; RR, risk ratio.

consider weight loss with delayed reconstruction as an option. The literature regarding breast reconstruction following weight loss is not robust, requiring surgeons to utilize good clinical judgment in making individual patient recommendations in the setting of oncologic considerations. It should be emphasized that obesity should not be considered a contraindication for reconstructive breast surgery. Previous research suggests that the preoperative weight loss not only facilitates reconstruction and enhances outcomes[26] but also improves postreconstructive satisfaction in obese women.[66] Research has shown that the dilated perforators seen in obesity exist even after weight reduction and can consequently be harvested during surgery to supply a less bulky and robust flap.[67,68] It has also been suggested that the decreased fat in the flap leads to lower risk of fat necrosis[69] and the decreased density of the flaps seen in weight loss patients allows for easier perforator dissection and flap mobilization.[26]

Strengths and Limitations

The strengths of this systematic review and meta-analysis are that it is noncommercial, with strict inclusion and exclusion criteria; it assessed the methodological quality of the studies using the GRADE criteria, and performed a sensitivity analysis to provide more robust conclusions. A study protocol was published a priori following peer-review and we have reported in line with the PRISMA criteria.[9,70] At the time of writing, this review was the largest and most comprehensive review of the effect of obesity on breast reconstruction, analyzing the most recent studies including two from 2016.

There are several limitations to our work. Most importantly, only nonrandomized studies, which carry inherent biases such as selection bias, met the inclusion criteria. All studies were case series with an LoE of 4 and approximately half of the studies were of low or very low quality. This may weaken the strength of this review. It should be noted that the majority of discussions around case series revolve around their relevance to a potential cause–effect relationship.[71] By respecting the limitations of these studies and accepting them for what they are, we can learn a great deal from such evidence.[72] Our search criteria excluded unpublished data and abstracts and this could add to publication bias.

Unfortunately, only eight papers offered data on implant reconstruction, but these did not, however, distinguish between the different kind of implants. This would be a great future research question. This review did not provide a distinction between immediate and delayed reconstruction as the included papers either analyzed immediate and delayed reconstruction as a single group or did not clearly state whether reconstruction was immediate or delayed. Finally, autologous reconstruction, which includes TRAM, LDM, DIEP, and SIEA flaps, was analyzed as a single group as data for each flap individually were limited. These techniques have varying characteristics and consequently there is heterogeneity in the effect of obesity on each type, resulting in biased observations.

Assessing if different implants have a different relationship to obesity would be a useful research question to address. The impact of breast size would also be interesting to assess. Obesity has known hormonal and nutritional dimensions and given the strength of the effect shown in our meta-analysis, obesity is likely an independent risk factor. However, despite studies not controlling for breast size, breast size itself may be a confounder in this analysis and certainly could be another independent risk factor. Future studies could provide an answer for this question.

Implications for Future Research

This review and meta-analysis highlight the need for carefully assessing obese patients prior to reconstructive breast surgery but also highlight the need for further research. The majority of papers in this review investigated the group of obese women as a whole. The subgroup analysis of the different classes of obesity found that the Class II patients had higher surgical complication rates than the Class III patients. Current research on the reasons behind this is lacking and future research would ideally classify obesity into the different WHO classes, providing more specific information on the 30 to 35, 35 to 40, and > 40 BMI groups, helping to clarify the reasons and allowing for more tailored risk profiling. BMI was categorized into distinct group ranges but it is likely to be a continuous variable as far as risk is concerned. Ultimately identification of a "threshold" level of obesity would be ideal and this could be the subject of future research.

Furthermore, this review found that obese women were more likely to experience surgical complications during both implant and autologous reconstruction in comparison to nonobese women. Direct comparison of the two types of procedures was not possible in this review as the numerical data was limited. Future studies specifically aimed at comparing implant and autologous reconstruction are necessary to provide a more accurate comparison of the two procedures.

As previously mentioned, all the studies in this review were case series, which are known to suffer from methodological and reporting issues.[73] Issues with the reporting of surgical case series were highlighted in a systematic review of autologous fat grafting for breast reconstruction where the majority of studies failed to provide information about patient demographics and prior treatment.[74]

In the drive to improve the quality of research in clinical practice, various reporting guidelines for different study types have been developed, such as for case reports[75] and systematic reviews.[70] Examples include the CONSORT statement[76,77] and the STROBE guidelines.[78] Case series should be reported in line with recently published expert consensus guidelines such as the PROCESS guidelines.[79] There are a variety of outcome measures reported in case series and an agreement on a core set of outcome measures to report would help future researchers aggregate studies.

The lack of high-quality research underscores the need for authors to adhere to stringent reporting guidelines. All research should be registered before recruiting patients.[80] With the launch of the Research Registry, surgeons are encouraged to prospectively register their research and to submit a protocol, which will undergo peer review allowing them to enhance their work.[74]

Conclusion

According to this meta-analysis, obese women were more likely to experience surgical and medical complications and had a higher chance of returning to the operating room. Given the high rates of complications in patients undergoing breast reconstruction with a BMI over 30, careful counseling about the risks and possible delay in reconstruction until weight loss has occurred should be considered.

Conflict of Interest

None of the authors have any conflicts of interest, relevant to this article, to declare.

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