Systematic Review And Meta-Analysis

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Is obesity a predisposing factor for free flap failure and complications? Comparison between breast and nonbreast reconstruction

Systematic review and meta-analysis

Jin Yong Shin (MD), Si-Gyun Roh (MD)*, Nae-Ho Lee (MD, PhD), Kyung-Moo Yang (MD, PhD)

Abstract

Obesity is a risk factor for postoperative morbidity in breast reconstruction. Although existing studies about nonbreast reconstruction are limited, previous research has demonstrated that obesity is not an important factor in poor outcomes in nonbreast reconstruction. Our study evaluates the effects of obesity on postoperative morbidity in nonbreast reconstruction in comparison to breast reconstruction. A systematic literature review and meta-analysis was performed using Medline, EMBASE, and Cochrane databases. Obesity was extracted for predictor variables and partial, total loss of flap, and complication were extracted for outcome variables. Subgroup analyses were performed according to reconstruction site. The Newcastle-Ottawa scale (NOS) was used to assess the quality of the studies, and the Cochrane risk of bias tool was used. Publication bias was evaluated using funnel plots. The search strategy identified 944 publications. After screening, 19 articles were selected for review. Partial flap loss, total flap loss, and complications in breast reconstruction occurred significantly more often in obese patients in comparison to nonobese patients (OR = 2.479, $P = 0.021$ for partial loss, OR = 3.083, $P = 0.002$ for total loss, OR = 2.666, $P = 0.001$ for complications). In contrast, partial flap loss, total flap loss, and complications in nonbreast reconstruction were not significantly different in obese patients in comparison to nonobese patients (OR = 0.786, $P = 0.629$ for partial loss, OR = 0.960, $P = 0.961$ for total loss, and OR = 1.009, $P = 0.536$ for complications). In contrast to the relationship between obesity and poor outcomes in breast reconstruction, our study suggests the obesity is not a predisposing factor for poor outcomes in nonbreast reconstruction. Long-term studies are needed to confirm these findings.

Abbreviation: NOS = Newcastle-Ottawa scale.

Keywords: complications, free flap failure, nonbreast reconstruction, obesity, risk factor

1. Introduction

Free flaps are complex surgeries requiring a lot of experiences on the part of plastic surgeons. The objective of free flap surgeries is to cover various tissue defects owing to cancer or trauma, and this type of surgery has a profound impact on restoring function and improving the quality of life of patients.[1,2] Improvement in microsurgical techniques and technologies over the past several decades have found free flap surgery to be safe and effective.[3–5] Nevertheless, complications, including total flap failure, may occur and may have a significant impact on outcomes of treatment and costs. These complications are frequently attributed to surgical technique. However, several existing studies have investigated the extent to which patient factors may be associated with free flap failure.[6–8]

Among the possible factors potentially leading to postoperative complications, obesity has become a popular a topic of interest. In comparison to patients with normal weight status who undergo surgery, obesity in patients may lead to a sharp increase in morbidity due to perioperative risks, including cardiovascular disease,[9] respirator morbidities,[10] and increased susceptibility to wound infection[11,12] due to complex effects.[13,14] However, the implications of obesity for surgery remain unclear.

It is widely known in the field of plastic surgery that obesity has adverse effects on free flap surgeries when breast reconstruction is performed.[15–17] Although several studies have stated different results according to varying methods of muscle inclusion in reconstructive procedures,[18,19] the majority of existing research suggests that obesity is a critical risk factor for postoperative complications in breast reconstruction.[20,21] However, whether we can define obesity as a risk factor for postoperative complications in general free flap surgery remains controversial. Some past studies investigating risk factors for the reconstruction of sites other than breasts have determined that obesity is not an important predisposing factor for postoperative complications.[22–24]

Accordingly, we hypothesize that a systematic review of existing studies in conjunction with meta-analysis will provide a

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more comprehensive overview of the impact of obesity in free flap surgeries. Our study estimates the relationship between postoperative complications and obesity in patients undergoing free flap surgery. In addition, it analyzes postoperative morbidity in breast reconstruction and compares the findings with nonbreast reconstruction to determine whether obesity is a risk factor in nonbreast reconstruction.

2. Materials and methods

2.1. Literature search

A search for eligible articles using the PubMed, EMBASE, and Cochrane databases for all studies published prior to October 2015 was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) check list.[25] The purpose of the literature search was to identify various risk factors for free flap failure or complications. The search terms included "risk," "predisposing," "free flap," "free tissue transfer," "reconstruction," "obesity," "body mass index," "failure," and "complication." Only human studies were included, and relevant articles were also examined for references to additional eligible studies.

2.2. Selection criteria

The inclusion criteria were a full-length article that provided sufficient data to enable evaluation of obesity on free flap failure or complications, a brief description of the reconstruction site, prospective or retrospective trials, and a brief explanation of outcome variables (free flap failure or complications). Studies were excluded if they involved incomplete or interim data, they were written in languages other than English, there was no information regarding the effects of obesity on free flap failure or complications, the article described fewer than ten cases, and there were overlapping authors.

2.3. Selection of relevant studies

Two of the authors (JYS and SGR) independently evaluated the eligibility of all the studies yielded by the literature search according to the predetermined selection criteria. The abstracts of all the studies were reviewed to exclude articles according to our exclusion criteria. Full-text reviews were performed to determine whether the remaining studies satisfied the inclusion criteria. Disagreements between the 2 evaluators were resolved by a third author (NHL).

2.4. Data extraction

Two of the authors independently extracted the outcomes from included studies. The predictor variables were obesity of patients (BMI > 30) in need of free flap reconstruction procedures. The outcome variables were partial flap loss, total flap loss, and complications.

2.5. Assessment of methodological quality

The methodological quality of the studies was assessed using the Newcastle-Ottawa scale (NOS) for nonrandomized studies. The parameters of the NOS comprise 3 categories, including selection of the study population, comparability of the groups, and ascertainment of the exposure or outcomes. Each parameter consists of subcategorized questions based on selection, comparability, and exposure or outcomes.[26,27] If the methodology of a study rated the highest quality, then the study was awarded a maximum of 9 stars. Two of the authors independently evaluated the methodological quality of all the studies. Subgroup analyses were performed according to reconstruction sites noted in the studies.

2.6. Statistical evaluation

Comprehensive Meta-Analysis software version 3.3.070 from Biostat (Borenstein M., Hedges L., Higgins J., and Rothstein H., Englewood, NJ) was used for this meta-analysis. The Cochrane Review Manager (RevMan version 5.3: The Cochrane Collaboration, Oxford, England) was also utilized to graphically represent the selected literature. We calculated the rate of both free flap failure and complications according to obesity status. The heterogeneity of each study was assessed using the I^2 test, which measures the percentage of total variation across studies.[28] The heterogeneity measure, I^2, was calculated as follows: $I^2\ (\%) = 100 \times (Q - df)/Q$, where Q is Cochrane heterogeneity statistic and df is the number of degrees of freedom. The 95% confidence interval (CI) was then computed for each treatment option using both random and fixed effects models. These results were confirmed by I^2 tests. Significance was set at a value of P less than 0.05 in both models. We established forest plots to illustrate the effects of study size, and funnel plots to ascertain whether there was evidence of publication bias.

2.7. Ethical review

Institutional review board approval is not required for a meta-analysis.

3. Results

3.1. Identification of relevant studies

Figure 1 shows a flow diagram of how the eligible studies were investigated. Searches of the databases identified 944 publications that potentially met the study criteria. Duplicate records from 394 studies were excluded. The screening process, consisting of a review of titles and abstracts, excluded 263 studies that did not meet the inclusion criteria. A total of 287 articles were reviewed for eligibility by accessing the full text. The reasons for study exclusion during the final review were as follows: review articles (n = 6), incomplete data (n = 179), abstract only (n = 36), letter (n = 16), or case report (n = 31). The remaining 19 nonrandomized studies were included in the final analysis.

3.2. Characteristics of studies included in the final analysis

Among the 19 studies, we identified a total of 10,269 patients that underwent free flap reconstruction procedures. Enrolled studies were divided into studies about breast reconstruction and nonbreast reconstruction. Each outcome was analyzed. In the included studies, 4770 patients who underwent breast reconstruction and 1684 patients who underwent nonbreast reconstruction were investigated. The clinical data and pooled analysis of the enrolled studies are shown in Tables 1 and 2. Only studies written in English were selected. All studies reported partial flap loss, total flap loss, or complications. In nonrandomized studies, the mean value awarded for quality was 7.3 (Table 3).

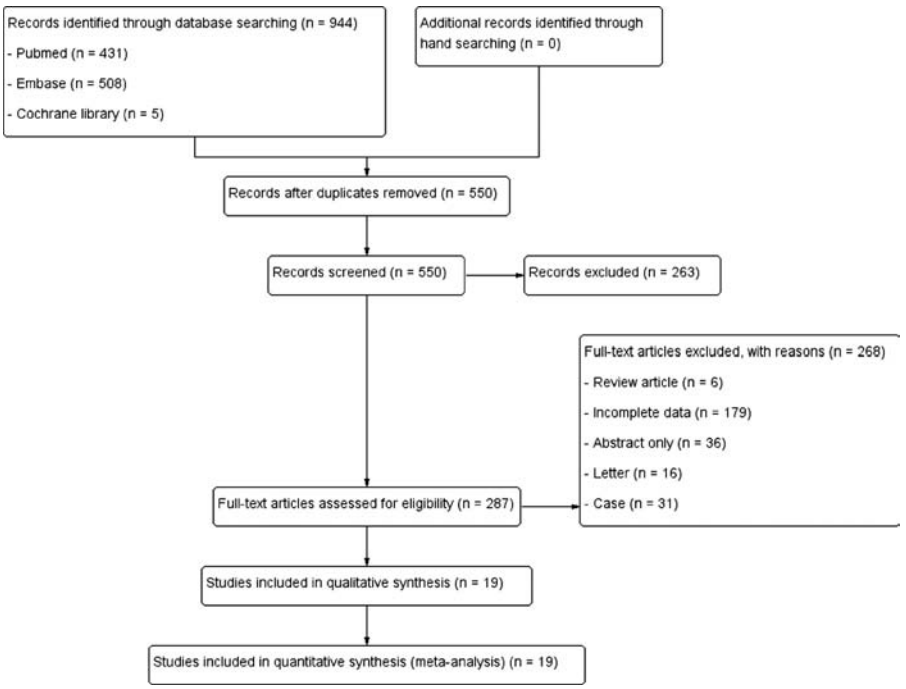


Figure 1. Flow diagram for the identification of relevant studies.

3.3. Overall impact of obesity in free flap procedures

The partial loss, total loss, and complication of free flap were occurred more frequently in obese patients compared than in nonobese patients. Total loss of free flaps and complications were significantly more common in obese patients (odds ratio = 1.910, $P = 0.017$ for flap loss, odds ratio = 2.024, $P = 0.004$ for complications) (Figs. 2–4).

3.4. Subgroup analysis

3.4.1. Impact of obesity in breast reconstruction. Partial loss, total loss and complications of free flaps in breast reconstruction occurred significantly more frequently in obese patients than in nonobese patients (OR = 2.479, $P = 0.021$ for partial loss, OR = 3.083, $P = 0.002$ for total loss, OR = 2.666, $P = 0.001$ for complications) (Figs. 5–7).

Table 1

Clinical data of included studies.

Refs.	Study design	Total no. of patients (or no. of flap)	Age (nonobese/obese)	BMI (nonobese/obese)	Reconstruction site	Location, language
Wong et al[29]	Prospective	639	Mean 51.7 ± 11.4	Mean 28.2 ± 6.2	All	United states (English)
Chang et al[1]	Retrospective	151	Mean 60.0 ± 14.5	Mean 27.6 ± 7.1	Head and neck	United states (English)
Ozturk et al[30]	Retrospective	264	Mean 49.6 ± 8.6	Mean 28.1 ± 2.5	Breast	United states (English)
Patel et al[22]	Prospective	796	Median 62.1 (14.3–100)	Median 24.3 (11.9–65.4)	Head and neck	Canada (English)
Fosnot et al[32]	Retrospective	1173	*	*	Breast	United states (English)
Offodile et al[31]	Retrospective	2008	Mean 54.9 ± 13.3	Median 26.9	All	United states (English)
de la Garza et al[23]	Retrospective	582	Mean 61.9/mean 59.3	*	Head and neck	United states (English)
Ochoa et al[19]	Retrospective	638	Mean 50.4 (27–74)	Mean 28.3 (17–42)	Breast	United states (English)
Jandali et al[33]	Retrospective	403	Mean 49.9/mean 48.5	Mean 27.6/mean 43.3	Breast	United states (English)
Yezhelyev et al[34]	Retrospective	277	Mean 51.1 ± 10.1	*	Breast	United states (English)
Chang et al[35]	Prospective	718	*	*	Breast	United states (English)
Cleveland et al[24]	Retrospective	119	Mean 43.4 ± 17.5/mean 51.8 ± 18.1	Mean 25.0 ± 2.9/ mean 35.1 ± 5.1	Lower extremity	United states (English)
Moran et al[36]	Retrospective	159	Mean 48	Mean 32	Breast	United states (English)
Mirzabeigi et al[37]	Retrospective	1051	Mean 50.6 ± 9.2	*	Breast	United states (English)
Garvey et al[38]	Retrospective	80	Mean 53.0/mean 56.7	*	Breast	United states (English)
Berrino et al[15]	Retrospective	117	*/Mean 51 (38–65)	*	Breast	Italy (English)
Seidenstuecker et al[39]	Prospective	558	*	*	Breast	Germany (English)
Selber et al[21]	Retrospective	500	*	*	Breast	United states (English)
Lim et al[40]	Retrospective	36	Mean 59.4	*	Head and neck	Republic of Korea (English)

* Data unextractable, unclear, or not available.

Table 2

Pooled analysis according to reconstruction site.

Refs.	Reconstruction site	Partial loss		Flap loss		Complication	
Ozturk et al[30]	Breast	Obese patients 7/95	Nonobese patients 5/169	Obese patients 1/95	Nonobese patients 2/169	Obese patients 49/95	Nonobese patients 46/169
		OR = 2.609		OR = 0.888		OR = 2.848	
Ochoa et al[19]	Breast	Obese patients *	Nonobese patients *	Obese patients 3/258	Nonobese patients 3/380	Obese patients 147/258	Nonobese patients 184/380
				OR = 1.478		OR = 1.411	
Yezhelyev et al[34]	Breast	Obese patients *	Nonobese patients *	Obese patients 3/103	Nonobese patients 0/174	Obese patients 65/103	Nonobese patients 90/174
				OR = 12.154		OR = 1.596	
Chang et al[35]	Breast	Obese patients 2/64	Nonobese patients 10/654	Obese patients 2/64	Nonobese patients 4/654	Obese patients 25/64	Nonobese patients 149/654
		OR = 2.077		OR = 5.242		OR = 2.173	
Garvey et al[38]	Breast	Obese patients *	Nonobese patients *	Obese patients 0/15	Nonobese patients 3/65	Obese patients 5/15	Nonobese patients 19/65
				OR = 0.576		OR = 1.211	
Seidenstuecker et al[39]	Breast	Obese patients 3/79	Nonobese patients 7/479	Obese patients 3/79	Nonobese patients 2/479	Obese patients 18/79	Nonobese patients 48/479
		OR = 2.662		OR = 9.414		OR = 2.650	
Selber et al[21]	Breast	Obese patients *	Nonobese patients *	Obese patients 4/80	Nonobese patients 7/420	Obese patients 38/80	Nonobese patients 82/420
				OR = 3.105		OR = 3.729	
Fosnot et al[32]	Breast	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *	Obese patients 388/1173	Nonobese patients 17/785
						OR = 22.329	
Jandali et al[33]	Breast	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *	Obese patients 5/142	Nonobese patients 9/261
						OR = 1.022	
Moran et al[36]	Breast	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *	Obese patients 14/42	Nonobese patients 17/127
						OR = 3.235	
Cleveland et al[24]	Lower leg	Obese patients 2/43	Nonobese patients 6/76	Obese patients 3/43	Nonobese patients 2/76	Obese patients 6/43	Nonobese patients 13/76
		OR = 0.569		OR = 2.775		OR = 0.786	
Chang et al[1]	Head and neck	Obese patients 4/45	Nonobese patients 10/106	Obese patients 13/45	Nonobese patients 47/106	Obese patients	Nonobese patients
		OR = 0.937		OR = 0.510			
Patel et al[22]	Head and neck	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *
						OR = 1.010	
de la Garza et al[23]	Head and neck	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *	Obese patients *	Nonobese patients *
						OR = 0.920	
Lim et al[40]	Head and neck	Obese patients *0	Nonobese patients *	Obese patients *	Nonobese patients *	Obese patients 2/7	Nonobese patients 8/29
						OR = 1.050	

* Data unextractable, unclear, or not available.

3.4.2. Impact of obesity in nonbreast reconstruction. Partial loss, total loss and complications in nonbreast reconstruction were not significantly different in obese patients in comparison to nonobese patients (OR = 0.786, $P = 0.629$ for partial loss, OR = 0.960, $P = 0.961$ for total loss, OR = 1.009, $P = 0.536$ for complications) (Figs. 8–10).

3.5. Publication bias

Funnel plots for the included studies are depicted in Figs. 11–13. These plots show low levels of asymmetry. Overall, there was no evidence of publication bias in this analysis.

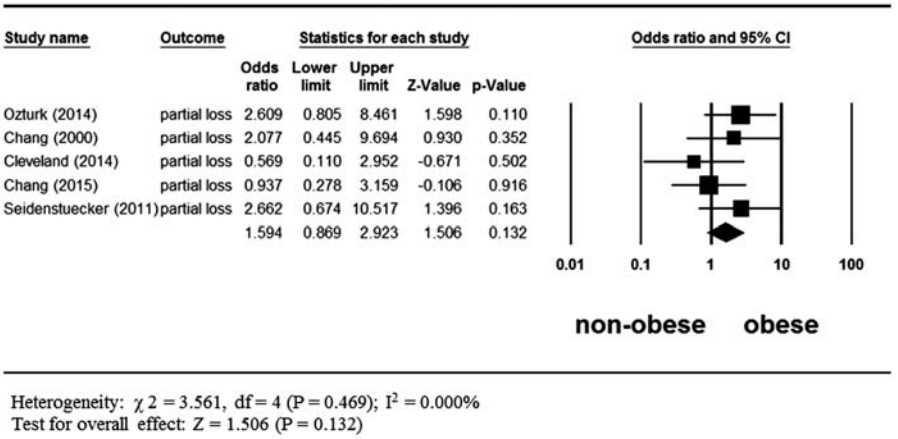
4. Discussion

This study identified the effect of obesity on the outcome of free flap surgeries from 19 studies,[1,15,19,21–24,29–40] which include a total of 10,269 patients. Obesity in overall free flap surgeries is identified as a meaningful risk factor for total flap loss and complications. However, these results reflect findings from a group of studies of which the majority are in breast reconstruction, so we performed subgroup analyses for only breast reconstruction patients and for patients who underwent procedures of reconstruction other than breast reconstruction.

Table 3

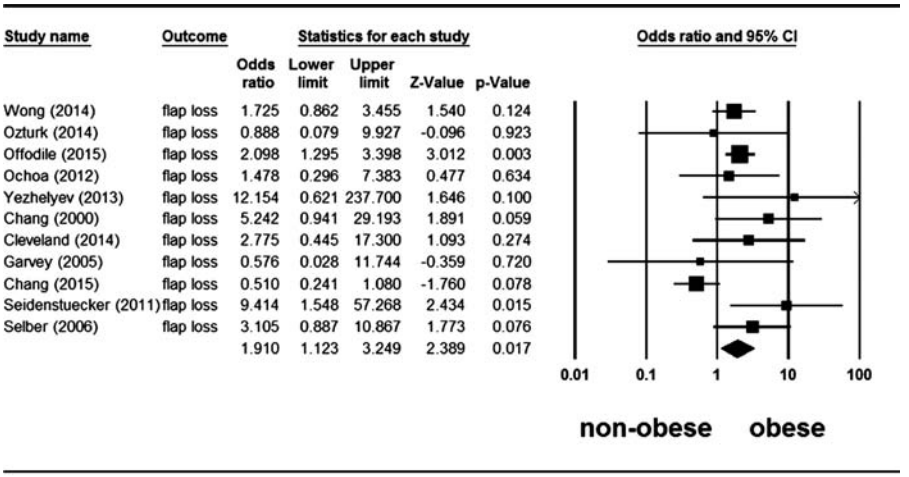
Methodological quality of included studies measured by Newcastle-Ottawa scale.

Refs.	Selection	Comparability	Exposure or outcome	Total
Wong et al[29]	☆	☆☆	☆☆☆	7
Chang et al[1]	☆	☆☆	☆☆☆	7
Ozturk et al[30]	☆	☆☆	☆☆	8
Patel et al[22]	☆	☆☆	☆☆☆	7
Fosnot et al[32]	☆	☆☆	☆☆☆	7
Offodile et al[31]	☆	☆☆	☆☆	8
de la Garza et al[23]	☆	☆☆	☆☆☆	7
Ochoa et al[9]	☆	☆☆	☆☆☆☆	9
Jandali et al[33]	☆	☆☆	☆☆	7
Yezhelyev et al[34]	☆	☆☆	☆☆	8
Chang et al[35]	☆	☆☆	☆☆	7
Cleveland et al[24]	☆	☆☆	☆☆	6
Moran et al[36]	☆	☆☆	☆☆	7
Mirzabeigi et al[37]	☆	☆☆	☆☆	8
Garvey et al[38]	☆	☆☆	☆☆	7
Berrino et al[15]	☆	☆☆	☆☆	7
Seidenstuecker et al[39]	☆	☆☆	☆☆	7
Selber et al[21]	☆	☆☆	☆☆	7
Lim et al[40]	☆	☆☆	☆☆	7



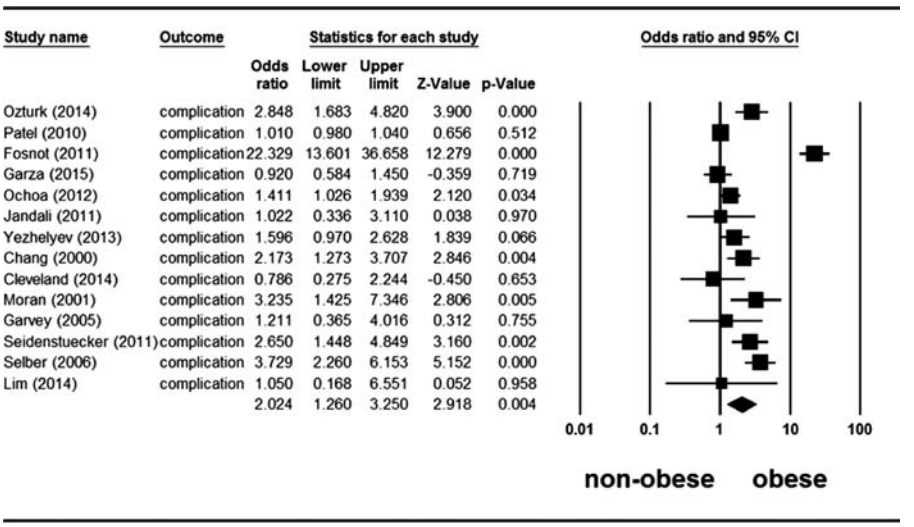
Heterogeneity: $\chi 2 = 3.561$, df = 4 (P = 0.469); $I^2 = 0.000\%$
Test for overall effect: Z = 1.506 (P = 0.132)

Figure 2. Forest plot comparing the incidence of partial flap loss between obese and nonobese patients in overall free flap surgeries.



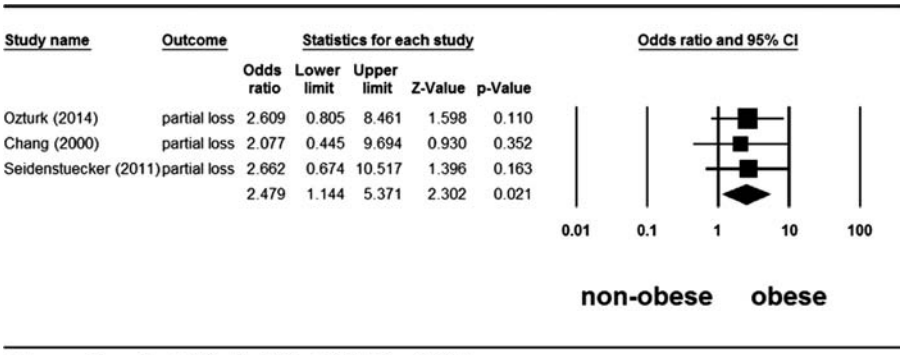
Heterogeneity: $\chi 2 = 19.376$, df = 10 (P = 0.036); $I^2 = 48.390\%$
Test for overall effect: Z = 2.389 (P = 0.017)

Figure 3. Forest plot comparing the incidence of total flap loss between obese and nonobese patients in overall free flap surgeries.



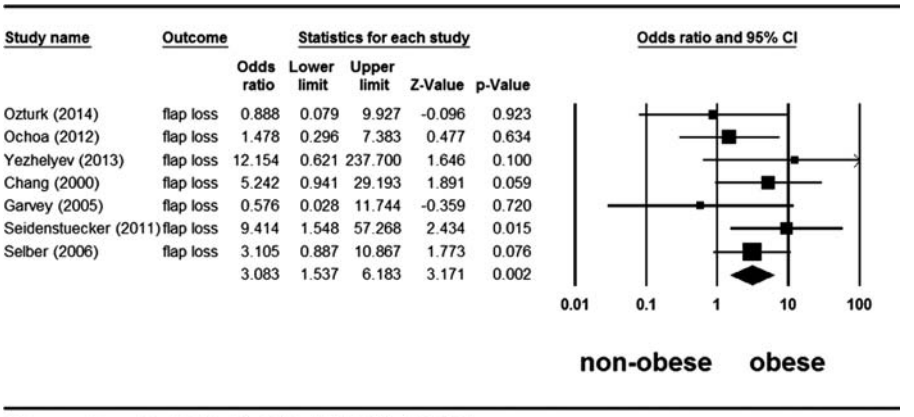
Heterogeneity: $\chi 2 = 220.636$, df = 13 (P = 0.000); $I^2 = 94.108\%$
Test for overall effect: Z = 2.918 (P = 0.004)

Figure 4. Forest plot comparing the incidence of complications between obese and nonobese patients in overall free flap surgeries.



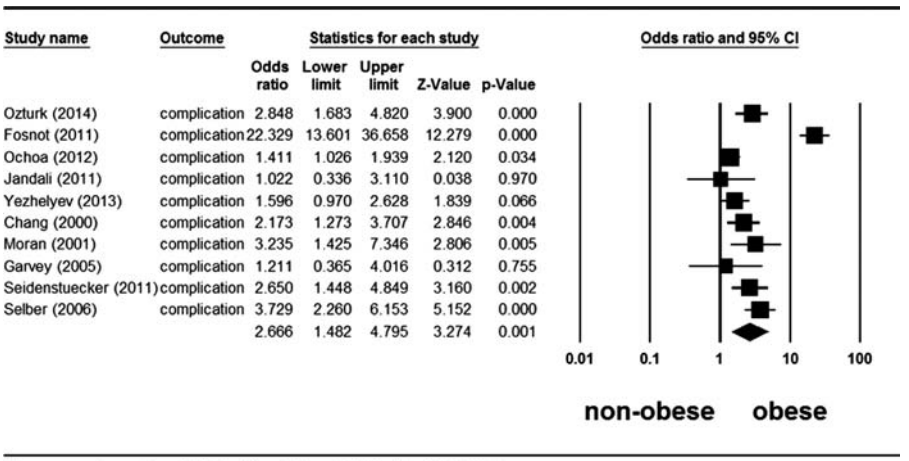
Heterogeneity: $\chi 2 = 0.068$, df = 2 (P = 0.967); $I^2 = 0.000\%$
Test for overall effect: Z = 2.302 (P = 0.021)

Figure 5. Forest plot comparing the incidence of partial flap loss between obese and nonobese patients in breast reconstruction.



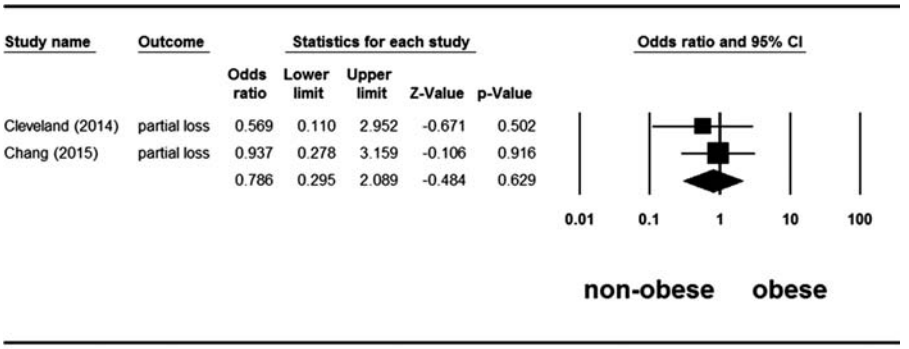
Heterogeneity: $\chi 2 = 5.666$, df = 6 (P = 0.462); $I^2 = 0.000\%$
Test for overall effect: Z = 3.171 (P = 0.002)

Figure 6. Forest plot comparing the incidence of total flap loss between obese and nonobese patients in breast reconstruction.



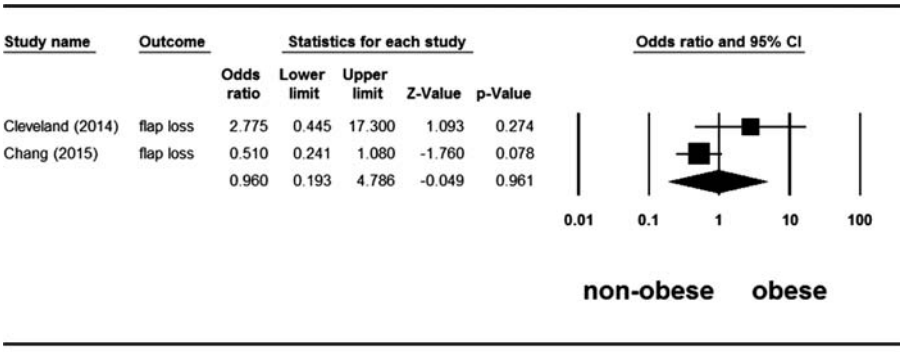
Heterogeneity: $\chi 2 = 97.123$, df = 9 (P = 0.000); $I^2 = 90.733\%$
Test for overall effect: Z = 3.274 (P = 0.001)

Figure 7. Forest plot comparing the incidence of complications between obese and nonobese patients in breast reconstruction.



Heterogeneity: $\chi 2 = 0.228$, df = 1 (P = 0.633); $I^2 = 0.000\%$
Test for overall effect: Z = -0.484 (P = 0.629)

Figure 8. Forest plot comparing the incidence of partial flap loss between obese and nonobese patients in nonbreast reconstruction.



Heterogeneity: $\chi 2 = 2.818$, df = 1 (P = 0.093); $I^2 = 64.519\%$
Test for overall effect: Z = -0.049 (P = 0.961)

Figure 9. Forest plot comparing the incidence of total flap loss between obese and nonobese patients in nonbreast reconstruction.

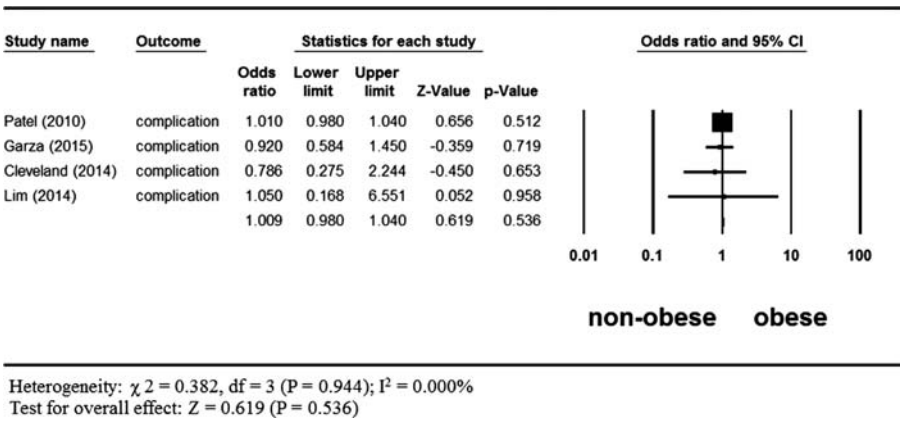


Figure 10. Forest plot comparing the incidence of complications between obese and nonobese patients in nonbreast reconstruction.

In terms of breast reconstruction only, obesity has an important role as a predisposing factor for partial loss of flaps, total loss of flaps, and complications. These results are consistent with the results of many previous studies[15,17,33,41] and the danger of obesity in this context has been widely discussed. Obese patients frequently have comorbidities such as diabetes, hyperlipidemia, hypertension, and cardiovascular disease.[42,43] These diseases potentially compromise microvascular hemodynamics, which could lead to flap loss and complications. Therefore, we are not able to conclude precisely which factor leads to eventual flap loss and complications. It is clear, however, that surgeons should take particular care with obese patients because of the high rate of flap loss and complications among obese patients. Fortunately, the majority of these complications in obese patients tend to be minor and not to require reoperation.[35,44] In addition, the outcomes of implant-based breast reconstruction in obese patients tend to be poor in comparison to the outcomes of breast reconstruction with free flap surgery.[45,46] Accordingly, free flap surgeries are mainly performed in obese patients in spite of the possible complications.

In the group of patients who underwent nonbreast reconstruction, reconstruction sites included the head, neck, and lower leg. Subgroup analysis was performed in 5 studies[1,22–24,40] representing a total of 1684 patients. This subgroup analysis showed no significant differences in partial loss of flaps, total loss of flaps, and complications between obese and nonobese patients. Several previous studies have asserted that the relationship between obesity and the outcomes of free flap surgeries in nonbreast reconstruction is not relevant, even though the mechanism of the association is unclear. In fact, previous studies acknowledge that a relatively lower body mass index or recent weight loss are independent risk factors for poor outcomes in

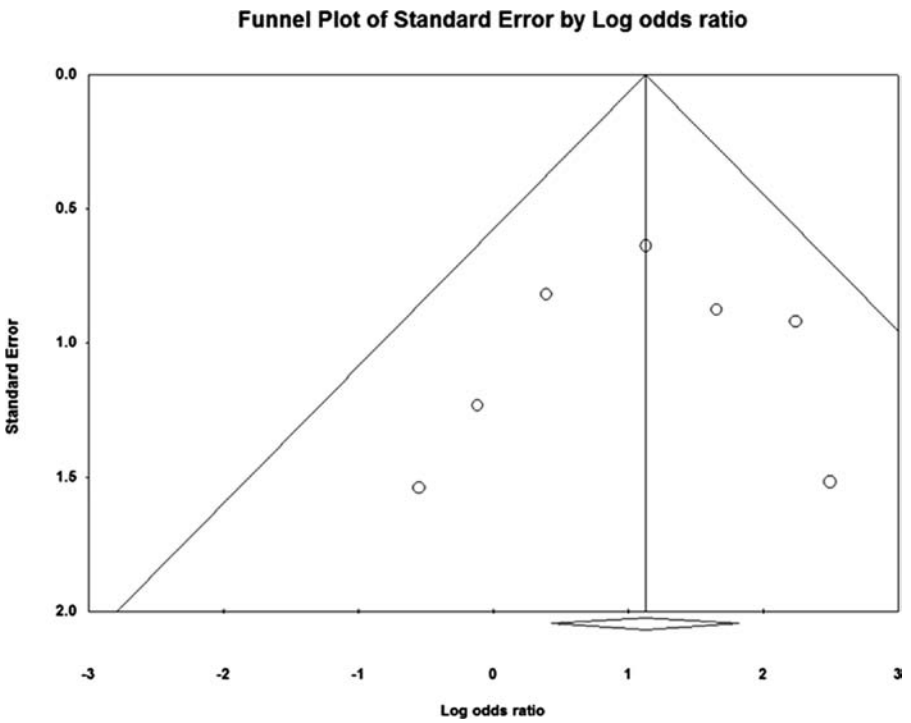


Figure 11. Funnel plot of direct-comparison meta-analysis for total flap loss in breast reconstruction.

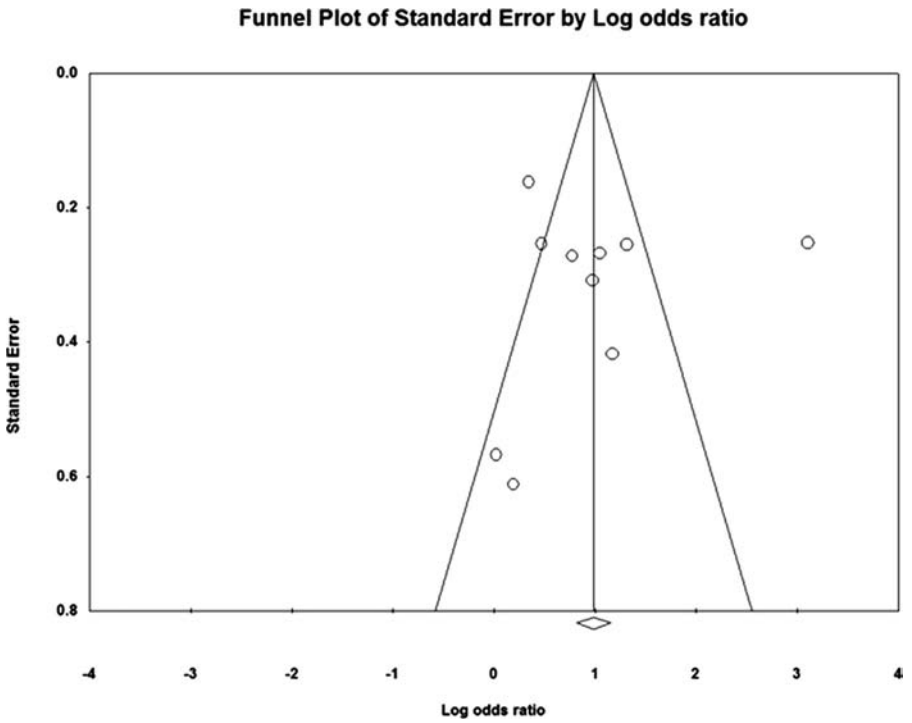


Figure 12. Funnel plot of direct-comparison meta-analysis for complications in breast reconstruction.

nonbreast reconstruction,[22] because these variables may be a reflection of poor nutritional status and general health status. In addition, being overweight has been associated with improved long-term survival and recurrence rates in patients with head and neck cancer.[47,48]

According to the results of our meta-analysis, whether or not obesity is a risk factor for free flaps changes according to the site of reconstruction. Our results that identified obesity as a risk factor in breast reconstruction provide necessity of knowing difference between breast and nonbreast reconstruction. Free flap

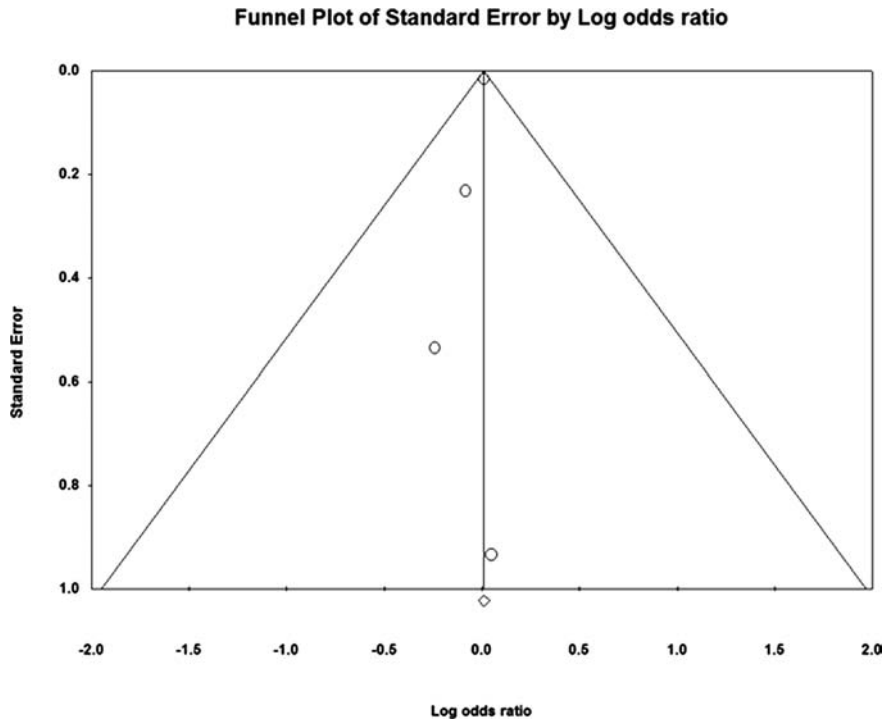


Figure 13. Funnel plot of direct-comparison meta-analysis for complications in nonbreast reconstruction.

in breast reconstruction was usually performed by abdomen-based autologous free flap compared with nonbreast reconstruction. Large and heavy abdominal flaps in obese patients attenuate the perforators, and thus, may eventually compromise blood supply to the flap.[49] Careful attention in insetting the flap may prevent potential stretching, together with recommended securing of the flap to the chest wall with sutures.[35] In addition, the larger donor site can be technically harder to dissect and prevent tension in harvest process. Furthermore, impaired wound healing owing to decreased myofibroblast activity may predispose obese patients to wound complications.[42]

This is the first meta-analysis relating to obesity as a predisposing factor for outcomes in breast and nonbreast reconstruction. The strength of this study is its rigorous search of recent literature. Subgroup analyses were performed to confirm the robustness of results. Despite the strengths, there are some limitations to the present study. Although all the included studies were high in quality according to their NOS scores, no studies were adequately powered by randomized controlled. Randomized studies on this topic, together with large-scale, well-organized, long-term follow-up studies are needed to confirm our findings. Also, there are fewer studies about nonbreast reconstruction than about breast reconstruction, which is a potential source of bias.

5. Conclusion

This study demonstrates that obesity is not a predisposing factor for poor outcomes in nonbreast reconstruction, unlike the association of obesity and poor outcomes in free flap breast reconstruction. Future large-scale and randomized studies with sufficient follow-up should be conducted to clarify this finding.

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