Systematic Review
Sample Work

A systematic review of bariatric surgery and the effects of cardiovascular disease

Abstract

Obesity is a global health issue that causes considerable morbidity and mortality, frequently as a result of cardiovascular (CV) illnesses. While bariatric surgery is widely used to treat obesity and lower CV risk factors, its effect on CV disease is unknown. In compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, we conducted a systematic review and meta-analysis to assess the effect of bariatric surgery on CV outcomes.

Methods and results

Until August 2021, PubMed and Embase were searched for material comparing bariatric surgery patients to non-surgical controls. All-cause and CV mortality, atrial fibrillation (A.F.), heart failure (H.F.), myocardial infarction (MI), and stroke were the outcomes of interest. We included 39 research, all of which were prospective or retrospective cohort studies; however, no randomized controlled trials were available. Bariatric surgery was related to a reduction in all-cause mortality [pooled hazard ratio (H.R.) of 0.55; 95% CI 0.49-0.62, P, 0.001 vs. controls] and CV mortality (HR 0.59, 95% CI 0.47-0.73, P, 0.001). Furthermore, bariatric surgery was linked with a lower incidence of H.F. (HR 0.50, 95% CI 0.38-0.66, P, 0.001), myocardial infarction (HR 0.58, 95% CI 0.43-0.76, P, 0.001), and stroke (HR 0.58, 95% CI 0.43-0.76, P, 0.001).

Conclusion:

According to the current systematic review and meta-analysis, bariatric surgery is related to decreased all-cause and Cardiovascular mortality, as well as a lower incidence of numerous CV illnesses in obese individuals. In certain cases, bariatric surgery should be explored.

Keywords:

Cardiovascular disease, Obesity, Heart failure, Atrial fibrillation, Myocardial infarction, Bariatric surgery, Metabolic surgery, Outcome, Ischaemic stroke

INTRODUCTION

Obesity is fast becoming one of the most serious healthcare issues in the Western world, with major morbidity and death.1-4 Obesity was linked to four million deaths per year in 2016.5 In the United States, the prevalence of obesity [measured as a BMI of 30 kg/m2] was 40% in adults in 2015-16,6 and is expected to grow to nearly 50% by 2030.7 Obesity is linked with increased adipose tissue, often known as adiposopathy,8, which may be harmful to the cardiovascular (CV) system via numerous processes (Structured Graphical Abstract). For starters, CV illness can be caused by the systemic effects of adipose tissue as a result of the development of risk factors. Second, adipose tissue may operate directly or regionally on the heart and blood vessels via epicardial and perivascular actions.8,9 Third, adipose tissue accumulation may produce (organ) compression, leading to hypertension, renal dysfunction,10 and obstructive sleep apnea.11 Hypertension is the most frequent CV risk factor related to obesity, followed by diabetes. Their incidence rises with the degree of obesity and is found in 30-40% of individuals.12

Obesity is also connected with dyslipidaemia and increased inflammation (20-40%). Obesity has been associated with cardiovascular diseases such as atrial fibrillation (A.F.), heart failure (H.F.), coronary artery disease/myocardial infarction, and stroke. The chance of getting these cardiovascular diseases is at least 1.5-2.0, but it climbs to 6.0 in severe obesity, defined as a BMI of 40 kg/m2. 13-15 Obesity is a well-known risk factor for stroke,16-18 and has been associated with an increased incidence of aortic valve stenosis, although there is much less evidence on this topic.19

However, because the H.R. for that specific outcome parameter could only be extracted once for each research population, no overlap in H.R. of the same outcome within the same study population was possible. The H.R. with the longest follow-up length was chosen for each endpoint.

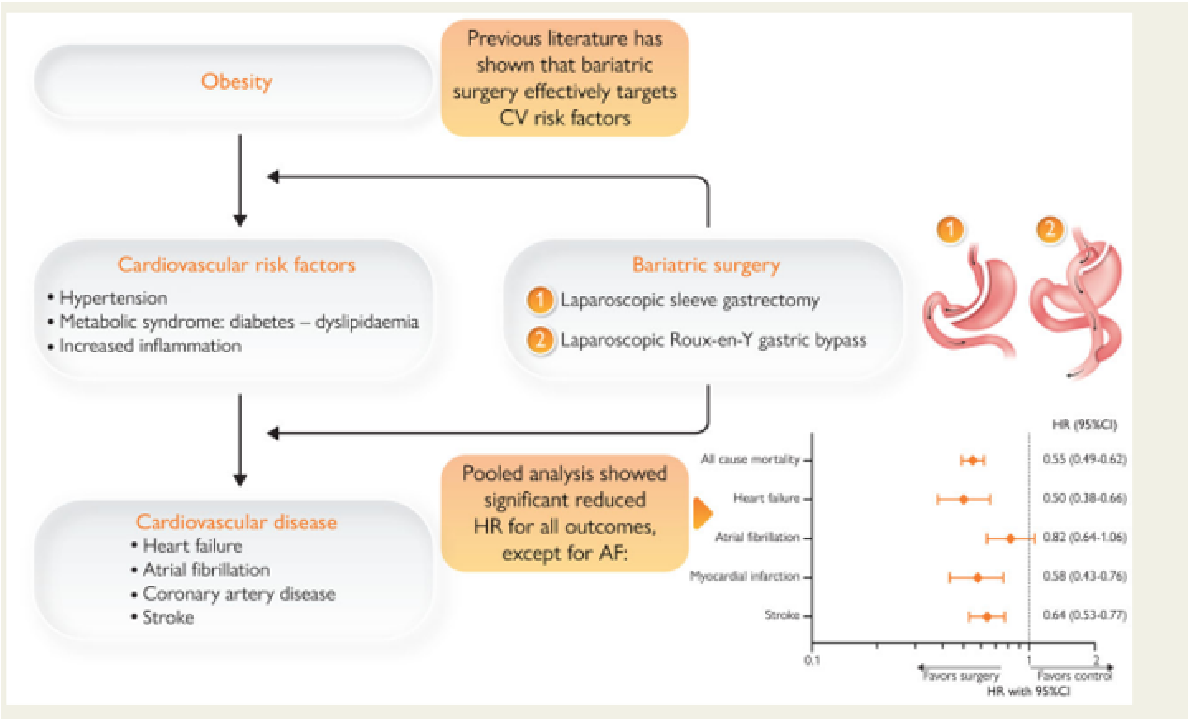


Figure: Schematic diagram of bariatric surgery (Sophie L van Veldhuisen et al 2022)

Methods

The 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was used to conduct this systematic review and meta-analysis—34 Figure S1 in the Supplementary material online details the PRISMA 2020 item checklist. We searched the Pubmed and Embase databases from conception to August 28, 2021. The PICO approach was used in the search strategy: patients of interest were obese adults (over the age of 18), The intervention was bariatric surgery, the controls were obese patients who did not have bariatric surgery, and the outcomes were all-cause mortality, CV mortality, and the incidence of CV disease, which was defined as incident A.F., incident H.F., incident myocardial infarction, incident stroke, and incident aortic stenosis—S2 Graph. The protocol for this systematic review and meta-analysis was submitted to PROSPERO (identification number: CRD42021277135). Our search was limited to studies conducted in adults, published in peer-reviewed journals and written in English.

Study selection

The study intended to compare the results of obese individuals who had weight-loss surgical intervention to those of a control group who did not. Randomized controlled trials, prospective or retrospective longitudinal cohort studies, and case-control studies were all included in the search. All non-surgical obesity treatment approaches were included in the control group. Studies were omitted if patients were not matched for age, gender, and BMI if outcome characteristics of relevance were not provided, or if they were not typical of the overall population of obese patients. Because the third criterion did not apply to Type 2 diabetes, research involving just Type 2 diabetes patients could be included. After removing duplicates and non-English papers, all records were checked independently by two observers, and studies were rejected based on title, abstract, and keywords.

Data extraction

The following information was extracted: (i) study characteristics (i.e. publication year, type of bariatric surgery, number of patients, mean age and BMI, and the percentage of patients diagnosed with Type 2 diabetes in both groups, study design, study cohort and recruitment period, major inclusion and exclusion criteria, primary and secondary outcome parameters, and follow-up period); (ii) event rate per outcome parameter for each group; and (iii) unadjusted and adjusted H.R.s with

Quality assessment

The Newcastle-Ottawa Quality Assessment Scale for Cohort Studies was used by two independent reviewers (S.L.v.V. and G.v.W.) to assess the likelihood of bias in each research. To be considered adequate, the period of follow-up was set at a minimum of 5 years. Both observers' agreement on the quality evaluation was evaluated, and disagreement was settled by consensus. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework was used to assess the quality of evidence for each outcome parameter.35 Two reviewers (S.L.v.V. and T.M.G.) independently evaluated all research results, and disagreements were handled by consensus.

Statistical analyses

The study analyzed the association between bariatric surgery and cardiovascular disease outcomes, using random effect models and adjusted H.R.s. Pooled H.R.s were calculated using inverse-variance weighted averaging and depicted in forest plots. The Hartung-Knapp–Sidik–Jonkman correction method was applied for analyses involving 20 studies. A sensitivity analysis was performed, focusing on prospective and retrospective studies. Heterogeneity among effect sizes was assessed using the Q-statistic and magnitude of heterogeneity with I2. Publication bias was tested using funnel plot asymmetry and Egger's regression test if a minimum of 10 studies was included. Inter-rater agreement for the quality assessment was tested using Cohen's kappa coefficient. Statistical analyses were performed using RevMan 5.4 and SPSS (Version 26).

Results

Search results

A systematic review of 2965 articles was conducted to identify 39 studies that examined the effect of bariatric surgery on mortality or cardiovascular disease. The review identified observational cohort studies, mostly retrospective, but also prospectively defined cohort studies. The quality assessment of these studies was ' very low' quality, with 19 studies rated as 'good' quality, one as 'fair' quality, and 19 as 'poor' quality. The inter-rater agreement was good/excellent, with Cohen's kappa being substantial. The heterogeneity among effect sizes was high for all outcome parameters, and publication bias could only be assessed for all-cause mortality. The study's quality assessment showed good/excellent inter-rater agreement, but the quality of evidence for all outcome parameters was very low quality.

The impact on overall and cardiovascular mortality

A meta-analysis of 28 studies found that bariatric surgery significantly reduced all-cause mortality (H.R.) compared to obese controls. The study included 133,524 patients after bariatric surgery and 263,478 obese controls. The meta-analysis showed that patients who underwent surgery had a pooled H.R. of 0.55 compared to obese subjects in the control group. Seven studies investigated CV mortality, with incidences of 0.2-8.3% in bariatric patients and 0.5-12.9% in controls. The meta-analysis also showed that bariatric surgery reduced CV mortality (HR 0.59, 95% CI 0.47–0.73, P 0.001, I 2= 71%).

The influence on atrial fibrillation

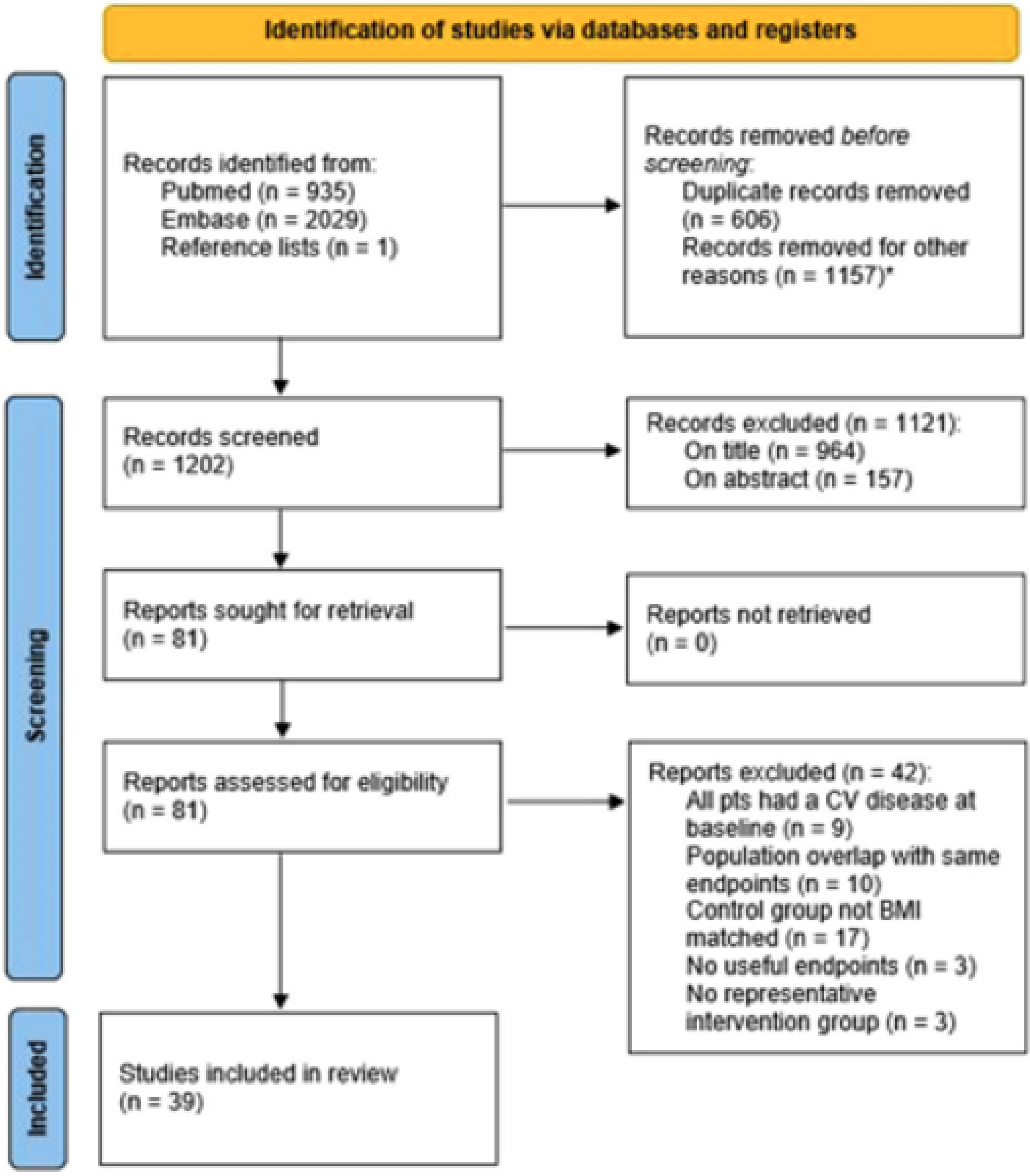
A total of seven studies looked at the influence of bariatric surgery on the incidence of A.F., which varied from 0.8-12.4% in patients following bariatric surgery to 1.3-16.8% in control participants (see Supplementary material online, Table S1). Five of these studies were appropriate for the meta-analysis, totaling 24 015 patients after bariatric surgery and 80 394 controls (Figure 3A). The overall impact in the meta-analysis was a non-significant decrease in the incidence of A.F. following bariatric surgery vs. controls (HR 0.82, 95% CI 0.64-1.06, P = 0.12, I 2=76%).

Effect on heart failure

A meta-analysis of 12 studies found that bariatric surgery can reduce the incidence of heart failure (H.F.) by 0.4 to 9.9% compared to 0.7 to 15.7% in controls. Eight studies, including 26002 bariatric patients and 40,657 controls, found a pooled H.R. of 0.50 for incident H.F. compared to control subjects. However, one large study, Sundstrom et al. 78, found a 46% reduction in H.F. incidence after four years of surgery, but the overall incidence was low, possibly due to less stringent event registration.

Effect on Myocardial Infarction

Nine studies found a lower incidence of myocardial infarction after bariatric surgery compared to controls, with a range of 1.5 to 13.7%. However, myocardial infarction occurred in 0.1-9.9% of patients, compared to 0.5-10% in controls. A meta-analysis of 101 536 patients and 322 551 controls found that bariatric surgery was associated with a lower incidence of myocardial infarction.



*Non-English articles, conference abstracts, case reports, comments, review articles and editorials.

Figure 1: Flowchart of literature search according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. BMI, body mass index; CV, cardiovascular.

Table 1 Key characteristics of included studies

First author/pub year	Intervention group					Control group				Study design	Cohort	Major inclusion criteria	Major exclusion criteria	Primary outcome	Secondary outcome	Follow-up period
	Surgery type	N	Age	BMI	% DM2	N	Age	BMI	% DM2							
Adams et al.	RYGB (100%)	7925	39.5	45.3	N.R.	7925	39.3	46.7	N.R.	Retrospective cohort study	Single Utah surgical practice 1984–2002	Not specified other than BS	Not specified	All-cause mortality	CV mortality	7.1 years
Alkharaiji et al.	RYGB or SG (% NR)	131	50.7	42.8	100%	579	52.8	40.6	100%	Retrospective cohort study	The Health Improvement Network (THIN) up to 2017	Age >18 years, insulin-treated DM2	DM1, or non-insulin-treated DM2	MI	Stroke, CAD, HF	10 years
Aminian et al.	RYGB 63%, SG 32%, AGB 0.5%, duodenal switch 0.02%	2287	52.5	45.1	100%	11435	54.8	42.6	100%	Retrospective cohort study	Cleveland Clinic Health System up to 2018	Age 18–80, BMI ≥30, HbA1c ≥6.5%, or ≥1 diabetic drug	Solid organ transplant, severe HF, active cancer, gastric cancer <1 year, ER admission <3 months, earlier gastric cancer surgery	6-Point MACE[a]	All-cause mortality, CAD, HF, stroke, AF	3.9 years
Ardissino et al.	NR	593	49.6	45.5	100%	593	49.5	45.1	100%	Retrospective cohort study	UK Clinical Practice Research Datalink	Age >18 years, BMI ≥30, DM2	CKD ≥III, missing data: age, sex, BMI, DM2	ASCVD	All-cause mortality, CAD, stroke	42.7 months
Arterburn et al.	RYGB (80.2%), AGB (4.4%), SG (2.4%), other (13.2%)	1395	48.2	47.4	100%	62322	49.1	42.6	100%	Retrospective cohort study	US health plan and care delivery systems 2005–08	Uncontrolled or medication controlled DM2, BMI ≥35, age 18–80	Gestational diabetes, pregnancy, history of malignancy, prior GI surgery, peritoneal or fluid ascites	All-cause mortality	NA	2 years
Arterburn et al.	RYGB (74%), SG (15%), AGB (10%), other (1%)	2500	52	47	N.R.	7462	53	46	N.R.	Retrospective cohort study	VA Surgical Quality Improvement Program data 2000–11	BMI ≥35	Missing BMI, BMI <35, no BS code, cancer, Crohn's disease, renal failure, pregnancy	All-cause mortality	NA	Max 14 years
Benotti et al.	RYGB (100%)	1724	45.8	46.5	N.R.	1724	45.1	46.6	N.R.	Retrospective cohort study	Geisinger Health Center 2002–13	Age 20–80 years, BMI >35, no pre-existing CVD (ICD9 410–449)	Missing data to calculate Framingham Risk Score	Combined MI HF stroke	Stroke, MI, HF	6.3 years
Brown et al.	RYGB (52.2%), SG (13.8%), AGB (3.4%)	68445	42.7	NR	73.7%	268362	43.3	NR	72.7%	Retrospective cohort study	Statewide Planning and Research Cooperative System database 2006–12	Age ≥18 years	In-hospital death in earliest records, duplicate records, missing data sex	CV event	Stroke, MI	NR
Busetto et al.	AGB (100%)	821	38.2	48.6	N.R.	821	42.8	48.1	N.R.	Retrospective cohort study	University of Padova 1994–2001	BMI ≥40, age >18 years	BMI <40	All-cause mortality	NA	Surg: 5.6 years, Con: 7.3 years
Carlsson et al.	Vertical banded gastroplasty (68%), AGB ...	2007	47.2	42.4	17.2%	2040	48.7	40.1	12.9%	Prospective matched cohort study	Swedish Obese Subjects 1987–2001	Age 37–60 years, BMI men ≥34, women ≥38	Earlier gastric surgery, ongoing [illegible]	All-cause mortality	CV mortality	Surg: 24 years, Con: 22 years

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Table 1 Continued

First author/pub year	Intervention group: Surgery type	N	Age	BMI	% DM2	Control group: N	Age	BMI	% DM2	Study design	Cohort	Major inclusion criteria	Major exclusion criteria	Primary outcome	Secondary outcome	Follow-up period
	(1.9%), RYGB (1.3%)												malignancy, MI < 6 months, drug/alcohol			
Cotoni et al.	Biliopancreatic diversion/ biliointestinal bypass (18.8%)	472	43.1	47.3	23.5%	1405	43.5	46.8	27.4%	Retrospective cohort study	LAGBIB study group 1999–2008	BMI ≥40 or ≥35 with comorbidities	Not specified	All-cause mortality	CV mortality	12.1 years
Courcoulas et al.	SG (45%), RYGB (55%)	31 158	44.6	43.6	26.1%	29 795	44.9	43.8	25.9%	Retrospective matched cohort study	Kaiser Permanente regions Washington and California 2005–15	Age 19–79 years, BMI ≥35	<1 year of enrolment, pregnancy, cancer	All-cause mortality	CV mortality	Up to 5 years
Douglas et al.	AGB (47.1%), RYGB (36.6%), SG (15.8%), other (0.5%)	3882	45	44.7	34.8%	3882	45	42.1	33.4%	Retrospective cohort study	UK Clinical Practice Research Datalink up to 2014	>12 months prior registration in database	Reversal of bariatric surgery	MI	All-cause mortality, stroke	3.4 years
Doumouras et al.	RYGB (87%), SG (13%)	13 679	45.2	47.2	26.7%	13 679	45.5	46.7	26.7%	Retrospective cohort study	Ontario Bariatric Network 2010–16	Not specified other than BS	Non-Ontario pts, age >70 years, BMI < 35, cancer, substance abuse, palliative care, pregnancy, organ transplantation, liver/heart disease	All-cause mortality	CV mortality	Surg: 4.9 years, Con: 4.8 years
Eliasson et al.	RYGB (100%)	6132	48.5	42.0	95%	6132	58.5	41.4	92%	Retrospective cohort study	National Diabetes Register and Scandinavian Obesity Surgery Registry 2007–14	Complete socioeconomic data	Not specified	All-cause mortality	MI, CV mortality	3.5 years
Fisher et al.	RYGB (76%), SG (17%), AGB (7%)	5301	49.5	44.7	100%	14 934	50.2	43.8	100%	Retrospective cohort study	US health plan and care delivery systems 2005–11	Age 19–79 years, BMI ≥35, DM2	<1 year of enrolment, cancer, pregnancy, gestational diabetes, CAD, or cerebrovascular disease, missing BMI	Macrovascular disease	All-cause mortality, CAD, stroke	Surg: 4.7 years, Con: 4.6 years
Höskuldsdóttir et al.	RYGB (100%)	5321	49	42.0	100%	5321	47	41.0	100%	Prospective cohort study	National Diabetes Register and Scandinavian Obesity Surgery Registry 2007–13	Age 18–65 years, BMI > 27.5, DM2	Other procedure than RYGB	Incident AF	HF	4.5 years
Jamaly et al.	Vertical banded gastroplasty (68%), AGB (19%), RYGB (13%)	2000	47.2	42.4	17.2%	2021	48.6	40.1	12.7%	Prospective matched cohort study	Swedish Obese Subjects 1987–2001	Age 37–60 years, BMI men ≥34, women ≥38	Earlier gastric/duodenal surgery, ongoing malignancy, MI < 6 months, drug/alcohol abuse	Incident AF	NA	19 years
Jamaly et al.	Vertical banded	2003	47.2	42.4	17.2%	2030	48.7	40.1	12.7%	Prospective	Swedish Obesity	Age 37–60 years,	Diagnosis of HF, < 6	Incident HF	NA	22 years

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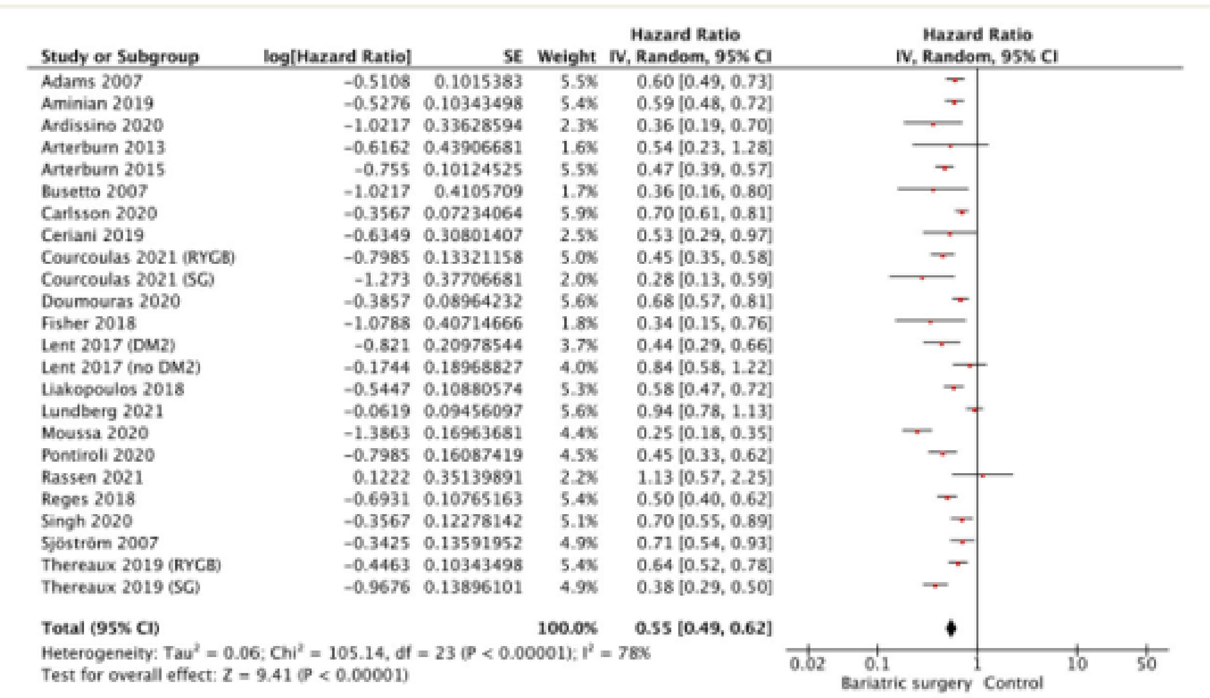

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Adams 2007	-0.5108	0.1015383	5.5%	0.60 [0.49, 0.73]
Aminian 2019	-0.5276	0.10343498	5.4%	0.59 [0.48, 0.72]
Ardissino 2020	-1.0217	0.33628594	2.3%	0.36 [0.19, 0.70]
Arterburn 2013	-0.6162	0.43906681	1.6%	0.54 [0.23, 1.28]
Arterburn 2015	-0.755	0.10124525	5.5%	0.47 [0.39, 0.57]
Busetto 2007	-1.0217	0.4105709	1.7%	0.36 [0.16, 0.80]
Carlsson 2020	-0.3567	0.07234064	5.9%	0.70 [0.61, 0.81]
Ceriani 2019	-0.6349	0.30801407	2.5%	0.53 [0.29, 0.97]
Courcoulas 2021 (RYGB)	-0.7985	0.13321158	5.0%	0.45 [0.35, 0.58]
Courcoulas 2021 (SG)	-1.273	0.37706681	2.0%	0.28 [0.13, 0.59]
Doumouras 2020	-0.3857	0.08964232	5.6%	0.68 [0.57, 0.81]
Fisher 2018	-1.0788	0.40714666	1.8%	0.34 [0.15, 0.76]
Lent 2017 (DM2)	-0.821	0.20978544	3.7%	0.44 [0.29, 0.66]
Lent 2017 (no DM2)	-0.1744	0.18968827	4.0%	0.84 [0.58, 1.22]
Liakopoulos 2018	-0.5447	0.10880574	5.3%	0.58 [0.47, 0.72]
Lundberg 2021	-0.0619	0.09456097	5.6%	0.94 [0.78, 1.13]
Moussa 2020	-1.3863	0.16963681	4.4%	0.25 [0.18, 0.35]
Pontiroli 2020	-0.7985	0.16087419	4.5%	0.45 [0.33, 0.62]
Rassen 2021	0.1222	0.35139891	2.2%	1.13 [0.57, 2.25]
Reges 2018	-0.6931	0.10765163	5.4%	0.50 [0.40, 0.62]
Singh 2020	-0.3567	0.12278142	5.1%	0.70 [0.55, 0.89]
Sjöström 2007	-0.3425	0.13591952	4.9%	0.71 [0.54, 0.93]
Thereaux 2019 (RYGB)	-0.4463	0.10343498	5.4%	0.64 [0.52, 0.78]
Thereaux 2019 (SG)	-0.9676	0.13896101	4.9%	0.38 [0.29, 0.50]
Total (95% CI)			**100.0%**	**0.55 [0.49, 0.62]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 105.14$, df = 23 (P < 0.00001); $I^2 = 78\%$
Test for overall effect: Z = 9.41 (P < 0.00001)

[Figure 2](#)Forest plot of pooled hazard ratios of all-cause mortality. CI, confidence interval; DM2, Type 2 diabetes mellitus; RYGB, Roux-en-Y gastric bypass; SE, standard error; SG, sleeve gastrectomy

Sensitivity analysis

Following bariatric surgery, outcomes for all-cause mortality (HR 0.50, 95% CI 0.43-0.59, P, 0.001, I 2 = 80%), CV mortality (HR 0.59, 95% CI 0.47-0.73, P = 0.002, I 2 = 63%), H.F. (HR 0.51, 95% CI 0.33-0.77, P = 0.001, I 2 = 56%), all types of stroke (HR 0.55, 95% CI 0.34-0. The results of this sensitivity analysis for A.F. and myocardial infarction (a single study on A.F.: HR 0.69, 95% CI 0.58-0.82, P = 0.001, and several studies on myocardial infarction: HR 0.61, 95% CI 0.39-0.94, P = 0.02, I 2 = 67%) were similar.

Discussion

Bariatric surgery is now the only therapy option that delivers significant and long-term weight loss in people with obesity, who have a significantly higher risk of CV disease. Although no randomized outcome trials are available, the current systematic review and meta-analysis of 39 controlled cohort studies demonstrates that bariatric surgery is strongly related to a reduction in not just mortality but also the incidence of CV disease. Nonetheless, the current systematic review and meta-analysis results clearly imply that bariatric surgery lowers the incidence of CV disease and death during follow-up (Structured Graphical Abstract).

The authors used this strategy to include nine studies and discovered that the favourable effect of surgery on outcome was mostly evident in individuals over the median age (about 40). However, it should be emphasized that the median follow-up time in their meta-analysis was 8.7 years, which may have been very short, especially in younger patients, because CV disease (and related death) frequently comes later, even in obese people. Cardoso et al. 33's 2017 evaluation omits current research owing to publication dates, and it only incorporates eight studies for its outcome analysis. Furthermore, that study only looked at short-term follow-up and had relatively few outcomes.

Limitations

The systematic review and meta-analysis of bariatric surgery data has limitations. The data is primarily from nonrandomized, prospective studies, and some studies only included patients with Type 2 diabetes. Recent studies with new drugs like glucagon-like peptide 1 agonist sodium–glucose cotransporter two inhibitors have shown promising results in patients with diabetes and obesity. However, no large studies are currently available on the additive effect of bariatric surgery in this population. The study only examined the effect of combined surgical techniques and did not investigate potential differences between techniques.

Additionally, the study did not specifically analyze H.R. of coronary artery disease in addition to myocardial infarction due to the scarce data on coronary artery disease. Future studies could provide valuable information on coronary artery disease following bariatric surgery. The analysis should be interpreted with caution, as some sensitivity analyses involved single studies analysis.

Conclusions

In summary, the results of this systematic review and meta-analysis of 39 studies suggest that bariatric surgery reduces mortality and incidence of CV disease in patients with obesity compared with non-surgical treatment. Bariatric surgery should, therefore be considered in these patients.

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