ENDOVASCULAR BARIATRIC SURGERY & BARIATRIC SURGERY

Cardio_Cast

Presented by:

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THIS EPISODE'S OVERVIEW

- Obesity Burden
- Bariatric surgery
- Endovscular Bariatric Surgery (EBS)
- EBS Procedure
- EBS Trials
- EBS Complication
- Bariatric Surgery and Cardiovascular Disease

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OBESITY BURDEN

- Nowadays, obesity represents one of the most unresolved global pandemics, posing a critical health issue in developed countries. According to the World Health Organization, its prevalence has tripled since 1975, reaching 13% of the world population in 2016.
- Obesity is defined as a body mass index (BMI) greater than 30 kg/m2 , while morbid obesity is defined as BMI > 40 kg/m2 .
- Numerous comorbidities such as major stroke, acute myocardial infarction, hypertension, type 2 diabetes, hyperlipidemia, obstructive sleep apnea, and all-cause mortality are strongly associated with this disease.
- As a result, approximately 2.8 million deaths per year may occur in adult populations affected by obesity.

Flegal, K.M.; Kit, B.K.; Orpana, H.; Graubard, B.I. Association of all-cause mortality with overweight and obesity using standard body mass index categories: A systematic review and meta-analysis. JAMA 2013, 309, 71–82. [CrossRef]

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- The cornerstone of obesity treatment is represented by behavioral modifications (i.e., diet and physical exercise), ideally in a highly motivated patient that should be followed by a multidisciplinary team of healthcare professionals. If successful, this strategy consents modest and durable weight loss reduction of 5% to 10%.
- The long-term efficacy of all behavioral therapies is limited. For those unable to reach these goals, few drugs (orlistat, lorcaserin, phentermine/topiramate, nartrexone/bupropion, semaglutide and liraglutide) are available as adjuvant therapy, but in general, are not free of side effects, usually dose-dependent, have limited adherence (frequently due to arbitrary withdrawal of the drug), and with suboptimal outcome in obtaining the goal of weight-reduction.
- Recently, non-surgical endoscopic bariatric therapies such as intragastric balloons, endoscopic gastric plication, and endoluminal duodenal-jejunal sleeve have been implemented in patients not willing to undergo conventional bariatric surgery. However, potentially severe compli cations have been reported with these techniques (gastric perforation, bowel obstruction, and gastrointestinal bleeding), and for these reasons they are currently performed only in highly experienced centers.

Jensen, M.D.; Ryan, D.H.; Apovian, C.M.; Ard, J.D.; Comuzzie, A.G.; Donato, K.A.; Hu, F.B.; Hubbard, V.S.; Jakicic, J.M.; Kushner, R.F.; et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society. Circulation 2014, 129, S102–S138.

BARIATRIC SURGERY

- Surgical approaches, mainly represented by Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy, and biliopancreatic division (Figure 1) are reserved to morbidly obese individuals or obese individuals with one or more obesity-related comorbidities (or even lower for uncontrolled diabetes) who have not been able to reach the aforementioned goals with behavioral modifications and drug therapy.

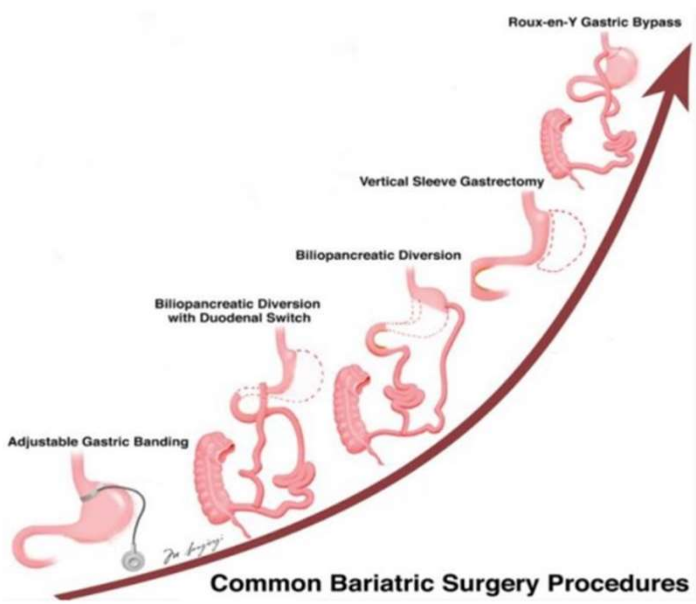

Figure 1. Overview of different bariatric surgery options. The most effective options in weight reduction are the Roux-en-Y gastric bypass and sleeve gastrectomy. Arrow indicates an increase in efficacy.

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Well-known short- and long-term complications, even if uncommon, including bleeding, infections, deep venous thrombosis, gastric dumping syndrome, and internal hernia have been reported with different surgical techniques.

Another frequent eventuality is post-bariatric surgery anemia: it is in most cases due to iron deficiency, along with vitamin B12 deficiency as a secondary cause. Iron deficiency is expressed by low serum ferritin and it occurs because of its lower absorption secondary to hypocloridria and the bypassing of the duodenum and proximal jejunum . In addition to anemia, vitamin B12 deficiency (resulting from inadequate secretion of intrinsic factor, limited gastric acidity and the bypassing of the duodenum) can lead to neurological disorders . In the absence of adequate vitamin B12 supplement, up to 30% of patients will be unable to maintain normal levels of plasma B12 at 1 year .

Bariatric surgery results in calcium/vitamin D malabsorption (results from bypassing the duodenum and proximal jejunum) with secondary hyperparathyroidism, changes in fat mass and alterations in fat- and gut-derived hormone; the final effect is an accelerated bone loss [4]. Patients affected by secondary hyperparathyroidism should obtain bone benefits from oral supplementation of vitamin D [ ]. In fact, the European Association for Endoscopic Surgery (EAES) Clinical practice guidelines on bariatric surgery strongly recommend vitamin D supplement post-surgery because the anticipated benefits outweigh the potential risks of vitamin therapy .

Poor protein digestion and absorption, secondary to altered biliary and pancreatic function, is involve in protein malnutrition and can be observed after bariatric surgery ; albumin levels can be considered as marker of protein deficiency .

Low serum levels of fat-soluble vitamins (vitamin A, K and E) usually occur after bariatric procedure [ ].

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PATHOPHYSIOLOGICAL BASIS FOR EBS

- Gastric fundus is mainly supplied by the left gastric artery (LGA) and sometimes by the gastroepiploic artery. The stomach has a neurohumoral role on hunger regulation through ghrelin: this is the rationale for gastric fundus embolization. Ghrelin is a ligand of the growth hormone secretagogue receptor (GHS-R) in neuropeptide Y (NPY) and agouti-related peptide (AgRP) in the arcuate nucleus of the hypothalamus with a downstream effect to inhibit the release of the α-melanocyte-stimulating hormone. Therefore, ghrelin acts to increase appetite and food intake, increasing weight gain.
- Practically, ghrelin plasma level rises sharply shortly before meals, which correlates with hunger sensation that occurs before consuming food. Conversely, ghrelin falls immediately after eating, which correlates with the sense of satiation after eating.
- In addition, ghrelin downregulates anorexigenic hormone receptors for PYY, GLP-1, and cholecystokinin and reduces the sensitivity of gastric distension by selectively inhibition of gastric subpopulation of mechanically sensitive vagal afferent nerves .

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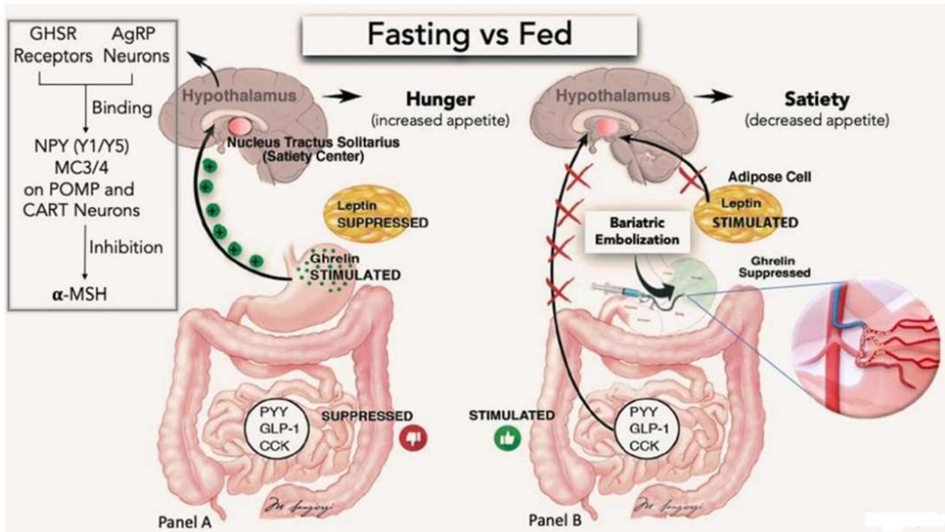

Figure 2. Hormonal changes and diagram of the ghrelin signal pathway. (**A**) The "hunger hormone" ghrelin is secreted by the gastric fundus, whereas peptide YY (PPY), cholecystokinin (CCK), and glucagon-like peptide (GLP-1) are secreted in the gut from L cells. Adipocytes produce leptin (LPT). In the fasting state, decreased food intake suppresses the release of PPY, GLP-1, CCK, and LPT, while stimulates ghrelin production from the stomach. Ghrelin binds in the hypothalamic arcuate nucleus to growth hormone secretagogue receptor (GHSR) in neuropeptide Y (NPY) and agouti-related peptide (AgRP) neu-rons. NPY and AgRP bind subsequently to NPY subtype 1 and 5 (NPH Y1/Y5) and melacortin-3 and-4 (MC3/4) receptors on proopiomelanocortin (POMP) and cocaine-amphetamine-regulated transcript neurons (CART), inhibiting the release of α- melanocyte-stimulating hormone (α-MSH). By inhibiting α-MSH, ghrelin acts to increase hunger and food intake. (**B**) BES procedure reducing ghrelin production in the stomach fundus area, mimics a fed state characterized by PYY, GLP-1, CCK, and LPT hormone increases. As a result, appetite decreases and an increase in the feeling of satiety occurs.

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EBS PROCEDURE

- The celiac trunk branches from the aorta at the level of the twelfth thoracic vertebra (T12). The LGA is the first and smaller branch of the celiac trunk, even if there are less common possibilities of independent origins from the aorta, splenic artery, common hepatic artery, gastroduodenal artery and superior mesenteric artery.
- It runs along the superior portion of the lesser gastric curvature and anastomoses with the right gastric artery that arises from the common hepatic artery. The left gastroepiploic artery (GEA) is the largest branch of the splenic artery and gives gastric branches to both surfaces of the stomach. It anastomoses with the right GEA that arises from the gastroduodenal artery.
- Normal anatomic variants are frequent and can be present in up to 30% of patients.
- Embolic material choice has been variable throughout trials with 300–500 μm and 500–700 μm microspheres and 300–500 μm or 500–700 μm polyvinyl alcohol (PVA) particles used. LGA embolization can also be performed with an occlusion balloon microcatheter (OBC) advanced into the target artery over a standard guidewire: a subsequent balloon inflation at the OBC tip can be used to prevent retrograde reflux, with tip pressure/resistance monitored to prevent overembolization and antegrade reflux. Embolization is taken to stasis, which was defined as the visual absence of the flow of contrast after five heartbeats; postembolization DSA is usually acquired to confirm the success of embolization .

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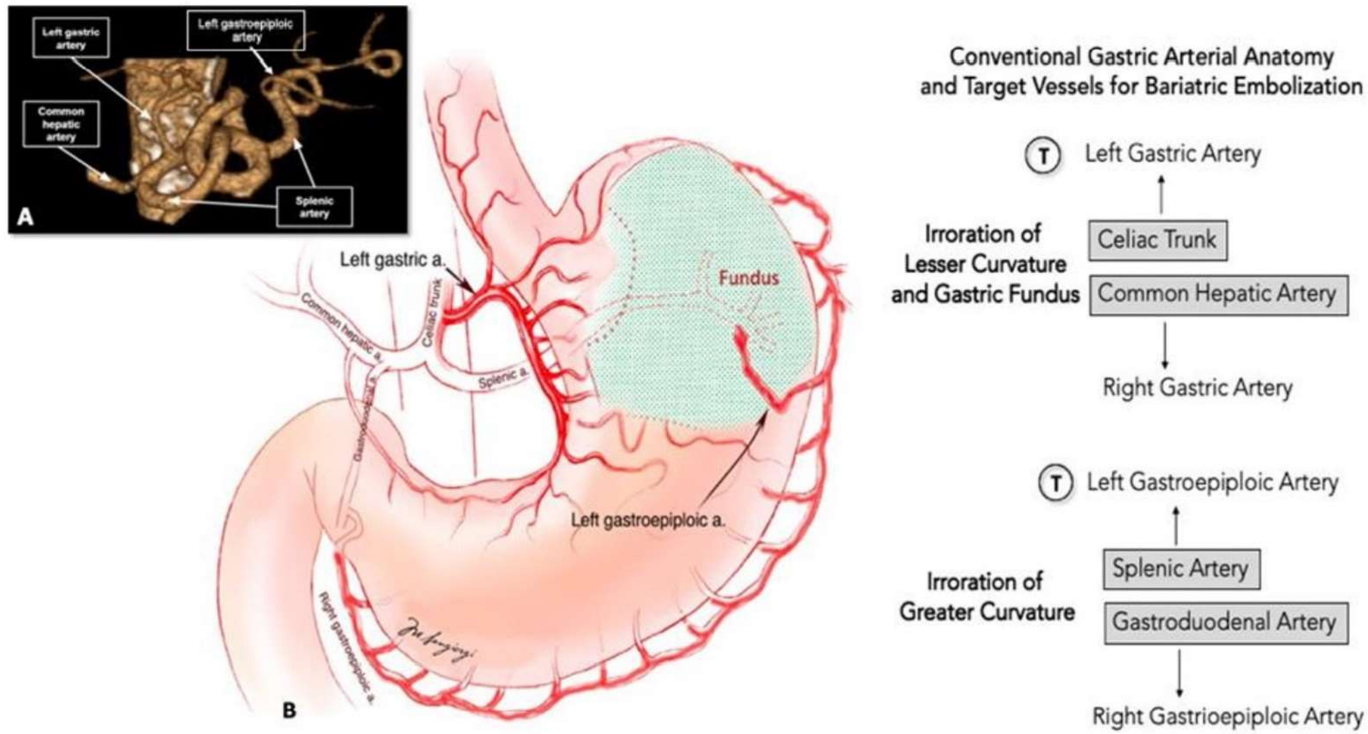

Figure 3. Voxel Gradient Angio-CT 3D reconstruction (**A**) and schematic drawn (**B**) of left gastric artery and left gastroepiploic artery normal anatomy. Most commonly the left gastric artery originates from the celiac trunk. Less frequently, the artery may arise directly from the aorta, splenic artery, common hepatic artery, and superior mesenteric artery. The superior part of the greater curvature of the stomach is supplied by the left gastroepiploic artery while the inferior part of the greater curvature by the right gastroepiploic artery. T indicates target for BES procedure.

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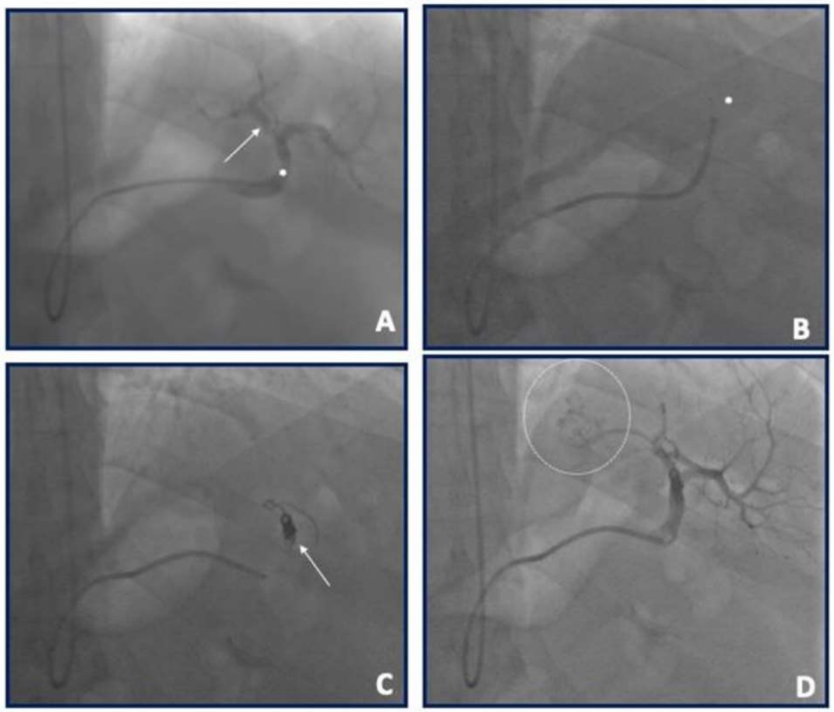

Figure 4. Case example of a left gastroepiploic artery (arrow) embolization in a 55 years old male with a BMI of 43.2. (**A**) Selective angiography by multipurpose 6F 125 cm into the splenic artery (asterisk). (**B**): A Rebar 0.27′ microcatheter (Medtronic, Santa Rosa, CA, USA—asterisk) was advanced into the multipurpose catheter selectively engaging the gastroepiploic artery. (**C**) Three contour spirals (Medtronic, Santa Rosa, CA, USA) of different size and length (4 × 40 mm; 4 × 40 mm; 5 × 30 mm) were subsequently released (arrow). (**D**) Final angiography with target fundus zone indicated by dashed circle.

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EBS HUMAN CLINICAL EVIDENCE

Table 2. Clinical Studies Evaluating BES procedure for Weight Reduction.

Author/Year/REF	Study Design	N of pts	Follow-UpLength	Total Weight Loss (%)	Embolic Material
Kipshidze 2015 [11]	Prospective	5	2 years	22 kg (17.1%)	300–500 µm BeadBlock embospheres
GET-LEAN 2016 [13]	Prospective	4	6 months	9.2 kg (8.5%)	300–500 µm BeadBlock embospheres
Bai 2018 [8]	Prospective	5	9 months	12.9 kg (12.6%)	500–710 µm PVA particles
Pirlet 2019 [12]	Prospective	7	12 months	13 kg (4.7%)	300–500 µm PVA particles
Elens 2019 [9]	Prospective	16	12 months	8 kg (10%)	500–700 µm Merit Medical embospheres
BEAT 2019 [29]	Prospective	20	12 months	7.6 kg (11.5%)	300–500 µm Merit Medical embospheres
Zaitun 2019 [30]	Prospective (pre-diabetic)	10	6 months	9 kg (8.9%)	300–500 µm Merit Medical embospheres
LOSEIT 2020 [31]	Randomized, sham-controlled	40	12 months	9.3 Kg (9.3%)	300–500 µm BeadBlock microspheres
BEATLES 2023 [32]On-going Trial	Randomized, sham-controlled	56	12 months	On-going trial	100–200 µm radiopaque microspheres

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COMPLICATIONS

- Most common complications in human studies were mild nausea, occasional vomiting, epigastric discomfort, and superfcial or very small gastric ulcers that did not demand any interventions and had gradually disappeared in a short time. In one patient, severe acute pancreatitis complicated by splenic infarction and late gastric perforation had developed, ending in an intensive care unit (ICU).
- Complications reported in animal studies were also considerable, with the largest proportion being mucosal ulcers, which could normally heal spontaneously, while three deaths had been comparably observed due to sepsis and tunneled central venous catheter infection. Moreover, approximately two thirds of the animals in one study presented gastric ulceration following bariatric LGA embolization.

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European Heart Journal (2022) **00**, 1–15
https://doi.org/10.1093/eurheartj/ehac071

META-ANALYSIS

Heart failure and cardiomyopathies

Bariatric surgery and cardiovascular disease: a systematic review and meta-analysis

Sophie L. van Veldhuisen [1,2], Thomas M. Gorter [3], Gijs van Woerden [3], Rudolf A. de Boer[3], Michiel Rienstra [3], Eric J. Hazebroek [1,4], and Dirk J. van Veldhuisen[3]*

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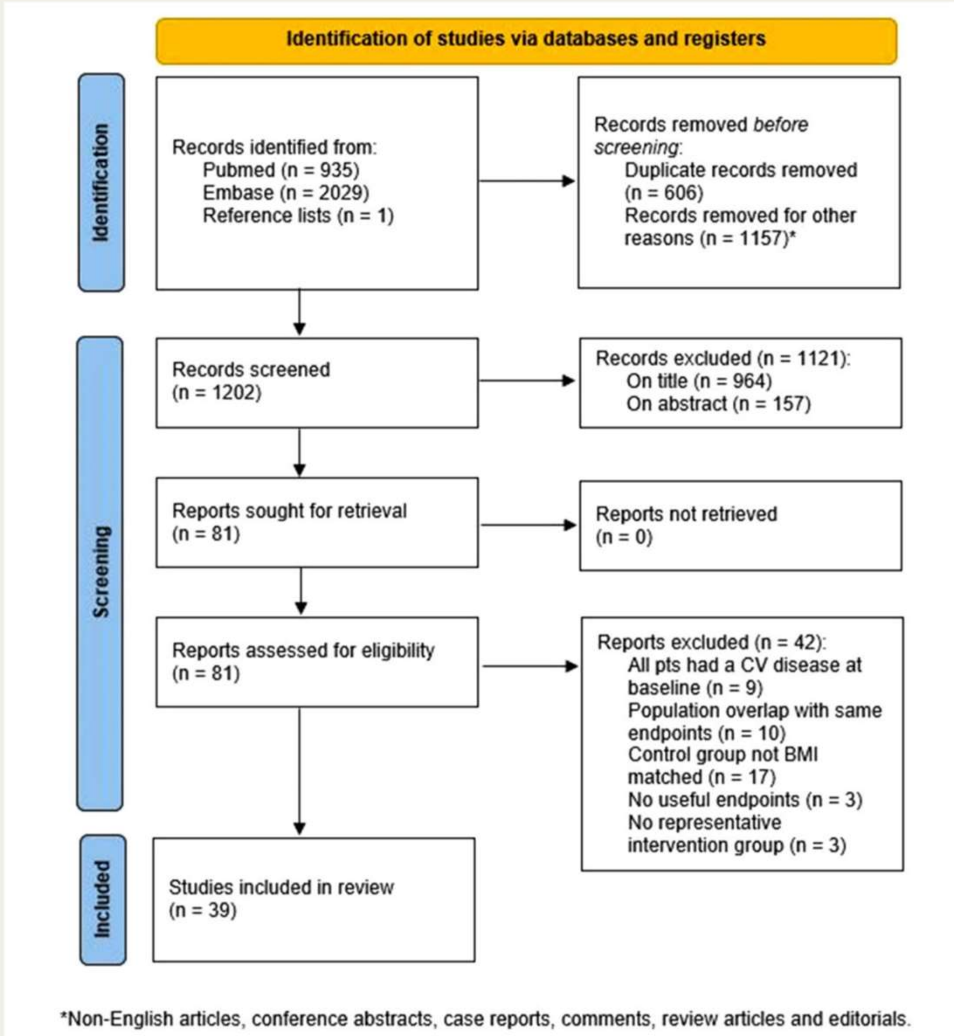

Figure 1 Flowchart of literature search according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. BMI, body mass index; CV, cardiovascular.

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.*[40]	RYGB (100%)	7925	39.5	45.3	NR	7925	39.3	46.7	NR	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.*[41]	RYGB or SG (% NR)	131	50.7	42.8	100%	579	52.0	40.6	100%	Retrospective cohort study	The Health Improvement Network (THIN) upon 2017	Age >18 years, insulin-treated DM2	DM1, or non-insulin-treated DM2	MI	Stroke, CAD, HF	10 years
Aminian *et al.*[42]	RYGB 63%, SG 32%, AGB 5%, duodenal switch 0.002%	2287	52.5	45.1	100%	11 435	54.8	42.6	100%	Retrospective cohort study	Cleveland Clinical Health System upon 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 <5 months, earlier gastric cancer surgery	6-Point-MACE[a]	All-cause mortality, CAD, HF, stroke, AF	3.9 years
Ardissino *et al.*[43]	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.*[44]	RYGB (80.2%), AGB (4.4%), SG (2.4%), other (13.2%)	1395	48.2	47.4	100%	62 322	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 GE surgery, peritoneal effusion/ascites	All-cause mortality	NA	2 years
Arterburn *et al.*[45]	RYGB (74%), SG (15%), AGB (10%), other (1%)	2500	52	47	NR	7462	53	46	NR	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.*[46]	RYGB (100%)	1724	45.0	46.5	NR	1724	45.1	46.6	NR	Retrospective cohort study	Geisinger Health Center 2002–12	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.*[47]	RYGB (52.2%), SG (13.8%), AGB (34%)	60 445	42.7	NR	72.7%	268 362	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.*[48]	AGB (100%)	821	38.2	48.6	NR	821	42.8	48.1	NR	Retrospective cohort study	University of Padova 1994–2001	BMI ≥40, age >18 years	BMI <40	All-cause mortality	NA	Surg: 5.6 years, Con: 7.2 years
Carlsson *et al.*[67]	Vertical banded gastroplasty (68%), AGB	2007	47.2	42.4	17.2%	2040	48.7	40.1	12.9%	Prospective matched cohort study	Swedish Obesity Subjects 1987–2001	Age 37–60 years, BMI men ≥34, women ≥38	Earlier gastric/duodenal surgery, ongoing	All-cause mortality	CV mortality	Surg: 24 years, Con: 22 years

Continued

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
	(19%), RYGB (13%)												malignancy, MI <6 months, drug/alcohol			
Ceriani *et al.*[60]	Biliopancreatic diversion/ biliointestinal bypass (100%)	472	43.1	47.3	23.5%	1405	43.5	46.8	27.4%	Retrospective cohort study	LAGB10 study group 1999–2008	BMI ≥40 or ≥35 with comorbidities	Not specified	All-cause mortality	CV mortality	12.1 years
Courcoulas *et al.*[49]	SG (45%), RYGB (55%)	31 158	44.6	43.6	26.1%	39 795	44.9	43.0	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.*[50]	ABG (47.1%), RYGB (36.6%), SG (15.8%), other (0.5%)	3882	45	44.7	34.0%	3882	45	42.1	33.4%	Retrospective cohort study	UK Clinical Practice Research Datalink upon 2014	>12 months prior registration in database	Reversal of bariatric surgery	MI	All-cause mortality, stroke	3.4 years
Doumouras *et al.*[51]	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.*[52]	RYGB (100%)	6132	48.5	42.0	95%	6132	50.5	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.*[53]	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.*[68]	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 procedures than RYGB	Incident AF	HF	4.5 years
Jamaly *et al.*[70]	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 Obesity 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.*[69]	Vertial 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

Continued

Table 1 ***Continued***

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							
	gastroplasty (68%), AGB (19%), RYGB (13%)									matched cohort study	Subjects 1987–2001	BMI men ≥34, women ≥38	months MI, earlier gastric surgery			
Lent *et al.*[54]	RYGB (100%)	625 1803	52.5 43.8	44.9 47.4	100% 0%	625 1803	52.5 43.9	44.9 47.3	100% 0%	Retrospective cohort study	Geisinger Health Center 2004–15	BMI ≥40 or ≥35 with comorbidities	Not specified	All-cause mortality	NA	5.8 years 6.7 years
Liakopoulos *et al.*[71]	RYGB (100%)	5321	49	42.0	100%	5321	47	41.0	100%	Prospective cohort study	National Diabetes Register and Scandinavian Obesity Surgery Registry 2007–15	Age 18–65 years, BMI >27.5, DM2, primary RYGB	Other procedures than RYGB	All-cause mortality	MI, HF, AF, stroke	4.5 years
Liakopoulos *et al.*[72]	RYGB (100%)	5321	49	42.0	100%	5321	47	41.0	100%	Prospective cohort study	National Diabetes Register and Scandinavian Obesity Surgery Registry 2007–15	Age 18–65 years, DM2, primary RYGB	Other procedures than RYGB	Incident HF	All-cause mortality	Surg: 4.7 years, Con: 4.6 years
Lundberg *et al.*[73]	RYGB (100%)	28 204	40.8	NR	14.7%	40 827	43.1	NR	16.2%	Prospective cohort study	Swedish National Patient Registry 2001–13	Age 20–65 years, BMI ≥35	Other bariatric surgery or died $<$2 years after obesity diagnosis	Incident MI	Stroke, mortality, CV mortality	Surg: 4.1 years, Con: 4.8 years
Lynch *et al.*[55]	RYGB or SG (% NR)	3572	42	47.1	23.3%	45 750	42	47.7	23.8%	Retrospective cohort study	Single Virginia Academic Hospital 1985–2015	Age >18 years	Banded gastroplasty pts, pre-existing AF	Incident AF	NA	Surg: 6.2 years, Con: 8.0 years
MacDonald *et al.*[56]	RYGB (100%)	154	41.9	50.6	100%	78	43.5	48.8	100%	Retrospective cohort study	Obesity Research Program 1979–94	Non-insulin dependent DM2	No non-insulin dependent DM2, no morbid obesity, age >64 years	All-cause mortality	NA	Surg: 9 years, Con: 6.2 years
Michaels *et al.*[57]	RYGB (78.9%), AGB (11.7%), SG (7.7%), other (1.7%)	3242	43	47.7	27.1%	3242	43	48.0	27.4%	Retrospective cohort study	Single Virginia Academic Hospital 1985–2015	Not specified other than BS	Not specified	Incident MI	NA	NR
Moussa *et al.*[74]	RYGB (38%), AGB (35%), SG (15%), other (1%), undefined (11%)	3701	36	40.5	25.0%	3701	36	40.3	23.9%	Prospective cohort study	UK Clinical Practice Research Datalink upon 2020	Not specified other than BS	BMI $<$35, MACE before index date, lost to follow-up $<$12 months after index date, missing data: age, BMI, sex	Combined MI/ stroke	All-cause mortality, MI, stroke, HF	140.7 months
Moussa *et al.*[75]	NR	4212	50	40.4	24.2%	4212	51	40.5	20.3%	Prospective cohort study	UK Clinical Practice Research Datalink upon 2021	Not specified other than BS	BMI $<$35, MACE before index date, lost to follow-up $<$12 months after index date,	Stroke	All-cause mortality, stroke	11.4 years

Continued

Table 1 *Continued*

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							
													missing data: age, BMI, sex			
Perry *et al.*[58]	Open RYGB (67%), (non-specified) laparoscopy procedure (28.5%), other (4.5%)	11 903	NR	NR	44.9%	NR	NR	NR	45.0%	Retrospective cohort study	Medicare claims 2022–2004	Not specified other than BS	Urgent BS code, active cancer, unstable angina, prior MI, inflammatory bowel disease	All-cause mortality	NA	2 years
Pontiroli *et al.*[59]	AGB (44.9%), biliopancreatic diversion/ biliointestinal bypass (55.1%)	857	42.6	44.7	19.0%	2086	43.2	44.1	24.5%	Retrospective cohort study	LAGB10 study group 1995–2008	BMI ≥40 or ≥35 with comorbidities	Not specified	All-cause mortality	NA	NR
Rassen *et al.*[61]	RYGB (50%), SG (44%), gastric resection (8%)	344	57.9	42.6	100%	551	59.0	42.1	100%	Retrospective cohort study	Electronic Health Records licenced from Optum 2007–18	Age 18–80 years, DM2, BMI ≥30	Solid organ transplant, severe HF, active cancer, ER admission 5 prior to index date, surgical procedures for GE cancer	6-Point-MACE[a]	All-cause mortality, CAD, CVA, HF, AF	2.5 years
Reges *et al.*[62]	AGB (55%), SG (40%)	8385	46	40.6	28.5%	25 155	46	40.5	28.5%	Retrospective cohort study	Clalit Health Service 2005–14	Age >24 years, membership Clalit health service	Missing BMI, BMI <30, pregnancy, severe comorbidities	All-cause mortality	NA	Surg: 4.3 years, Con: 4.0 years
Sampalis *et al.*[63]	RYGB (81.3%) vertical banded gastroplasty (18.7%)	1035	45	NR	0%	5746	47	NR	0%	Retrospective cohort study	McGill University Health Centre 1986–2002	Not specified other than BS	Cancer, haematological disease, CVD, digestive diseases, endocrinologic disease incl. diabetes, genitourinary, infectious, musculoskeletal, nervous system, psychiatric and mental, respiratory and skin diseases	Incident MI	NA	2.5 years
Singh *et al.*[64]	AGB, SG, RYGB, or duodenal switch (% NR)	5170	45.2	NR	22.7%	9995	45.3	NR	20.9%	Retrospective cohort study	The Health Improvement Network (THIN) 1990–2018	>1 year registered in general practice	BMI <30, age >75 years, gastric cancer, gastric balloon, endo-barrier, or revisional bariatric surgery	Stroke	All-cause mortality, CAD, HF, stroke, AF	3.9 years
Sjostrom *et al.*[76]	Vertical banded gastroplasty	2010	46.1	41.8	7.4%	2037	47.4	40.9	6.1%	Prospective	Swedish Obesity	Age 37–60 years,	Earlier gastric/duodenal surgery, ongoing	All-cause mortality	NA	14.7 years

Continued

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
	(68%), (A)GB (19%), RYGB (13%)									matched cohort study	Subjects 1987–2001	BMI men ≥34, women ≥38	malignancy, MI <6 months, drug/alcohol			
Sjostrom *et al.*[77]	Vertical banded gastroplasty (68%), (A)GB (19%), RYGB (13%)	2010	46.1	41.8	7.4%	2037	47.4	40.9	6.1%	Prospective matched cohort study	Swedish Obesity Subjects 1987–2001	Age 37–60 years, BMI men ≥34, women ≥38	Earlier gastric/duodenal surgery, ongoing malignancy, MI <6 months, drug/alcohol	CV mortality	MI, stroke	14.7 years
Sundstrom *et al.*[78]	RYGB 100%	25 804	41.3	41.5	15%	13 701	41.5	41.4	9.4%	Prospective cohort study	Scandinavian Obesity Surgery Registry 2007–12 and Itrim Health Database 2006–13	BMI 30–50, ≥18 years	Cross-over, HF at baseline, missing data on education or marital status	Incident HF	MACE	4.1 years
Thereaux *et al.*[65]	RYGB (55%) and SG (45%)	8966	40.4	NR	13%	8966	40.9	NR	13%	Retrospective matched cohort study	French National Health Insurance database 2009	Not specified other than BS	Cancer, pregnancy, chronic infectious disease, contra-indication for bariatric surgery, earlier bariatric surgery	All-cause mortality	NA	6.8 years
Wong *et al.*[66]	Sleeve gastroplasty (80.5%), RYGB (16.2%), revision procedure (3%)	303	51.4	37.4	100%	1399	51.0	36.6	100%	Retrospective matched cohort study	Hospital Authority data base Hong Kong adult diabetes population 2006–17	DM2	BMI <27.5, non-DM2, history of CVD, eGFR <30	All-cause mortality	CV disease, MI, stroke, HF	32 months

[a]First occurrence of all-cause mortality, coronary artery events (unstable angina, myocardial infarction, or coronary intervention/surgery), cerebrovascular events (ischaemic stroke, haemorrhagic stroke, or carotid intervention/surgery), heart failure, nephropathy, and atrial fibrillation.

(A)GB, adjustable gastric band; AF, atrial fibrillation; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index (in kg/m^2); BS, bariatric surgery; CAD, coronary artery disease; CKD, chronic kidney disease; CV, cardiovascular; DM1, Type 1 diabetes mellitus; DM2, Type 2 diabetes mellitus; eGFR estimated glomerular filtration rate (in mL/min/1.73 m^2); ER, emergency room; GE, gastroenterological; HbA1c, glycated haemoglobin; HF, heart failure; MACE, major adverse cardiovascular event; MI, myocardial infarction; NA, not applicable; NR, not reported; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

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: $Z = 9.41$ ($P < 0.00001$)

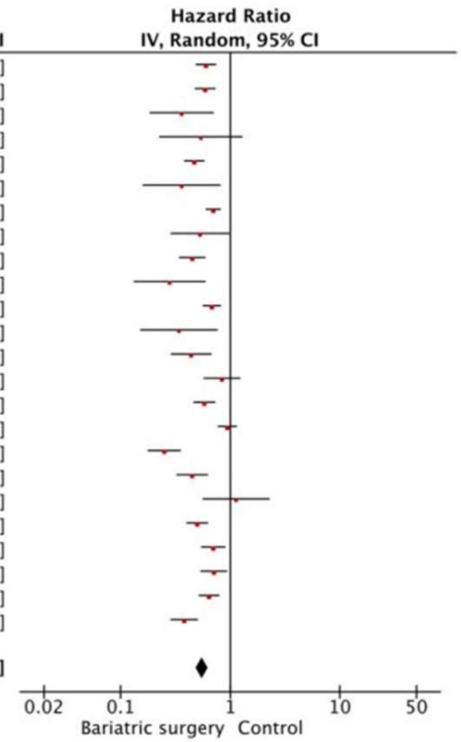

Figure 2 Forest plot of pooled hazard ratios of all-cause mortality. CI, confidence interval; DM2, Type 2 diabetes mellitus; RYGB, Roux-en-Y gastric bypass; SE, standard error; SG, sleeve gastrectomy.

Cardio_Cast

EFFECT ON ALL-CAUSE AND CARDIOVASCULAR MORTALITY

- The meta-analysis showed that patients who had undergone surgery had a pooled HR of all-cause mortality of 0.55 (95% CI 0.49–0.62, P , 0.001, I 2= 78%) compared with obese subjects in the control group. Three of these studies only reported adjusted HRs for separate subgroups [i.e. diabetic vs. non-diabetic, or Roux-en-Y gastric bypass (RYGB) vs. sleeve gastrectomy] and are thus mentioned twice in the forest plot.49,54,65 Seven studies investigated CV mortality, with incidences of 0.2–8.3% in bariatric patients and 0.5–12.9% in controls.
- The results in the meta-analysis showed that bariatric surgery also reduced CV mortality (HR 0.59, 95% CI 0.47–0.73, P , 0.001, I 2= 71%;

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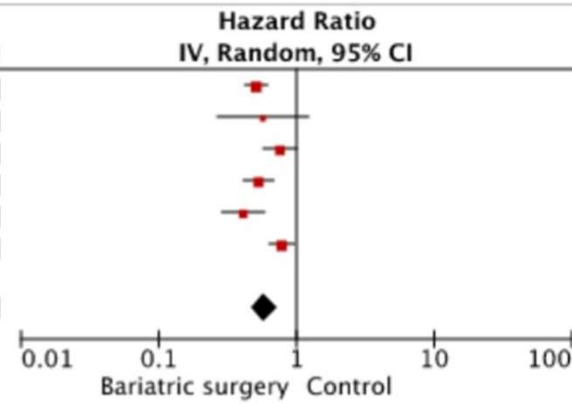
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Adams 2007	−0.67334455	0.09438776	21.5%	0.51 [0.42, 0.61]
Courcoulas 2021 (RYGB)	−0.56211892	0.3877551	6.0%	0.57 [0.27, 1.22]
Courcoulas 2021 (SG)	−0.27443685	0.14285714	17.8%	0.76 [0.57, 1.01]
Doumouras 2020	−0.63487827	0.12755102	19.0%	0.53 [0.41, 0.68]
Eliasson 2015	−0.89159812	0.18112245	15.0%	0.41 [0.29, 0.58]
Lundberg 2021	−0.24846136	0.10459184	20.8%	0.78 [0.64, 0.96]
Total (95% CI)			**100.0%**	**0.59 [0.47, 0.73]**

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 17.36$, $df = 5$ ($P = 0.004$); $I^2 = 71\%$
Test for overall effect: $Z = 4.92$ ($P < 0.00001$)



CI confidence interval; HR hazard ratio, RYGB Roux-en-Y gastric bypass, SG sleeve gastrectomy

EFFECT ON ATRIAL FIBRILLATION

- the incidence of AF (see Supplementary material online, Table S1), which ranged from 0.8–12.4% in patients after bariatric surgery to 1.3–16.8% in control subjects. Five of these studies were suitable for the meta-analysis, which accumulated to 24 015 patients following bariatric surgery and 80 394 controls.The overall effect in the meta-analysis was a non-significant reduction after bariatric surgery vs. controls with regard to the incidence of AF (HR 0.82, 95% CI 0.64–1.06, P = 0.12, I 2= 76%).

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EFFECT ON HEART FAILURE

- A total of 12 studies examined the effect of bariatric surgery on the incidence of HF (see Supplementary material online, Table S1). Incidence rates that were reported ranged from 0.4 to 9.9% in patients following bariatric surgery, as compared with 0.7–15.7% in controls.
- For the meta-analysis, eight studies fulfilled criteria and thus a total of 26 002 bariatric patients and 40 657 controls were examined. The pooled HR for incident HF following bariatric surgery vs. control subjects was 0.50 (95% CI 0.38–0.66, P , 0.001, I 2= 71%, Figure 3B).

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EFFECT ON MYOCARDIAL INFARCTION

- Nine studies reported on incident myocardial infarction after bar iatric surgery and controls, and six on incident coronary artery dis ease. Incidence of coronary artery disease following bariatric surgery ranged from 1.5 to 13.7% vs. 2.7 to 44.7% in controls (see Supplementary material online, Table S1), but these were not analysed further. Myocardial infarction after bariatric surgery occurred in 0.1–9.9% of patients, compared with 0.5–10.0% in controls.
- For the meta-analysis of incident myocardial infarction after bariatric surgery, seven of the nine studies were suitable, involving 101 536 patients following bariatric surgery and 322 551 controls. Bariatric surgery was associated with a lower incidence of myocardial infarction when compared with controls (HR 0.58, 95% CI 0.43–0.76, P , 0.001, I 2 = 82%, Figure 3C)

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EFFECT ON STROKE

- The incidence of stroke was investigated in 14 studies, and its inci dence was much lower than other CV events (Table 1). Incidence of stroke ranged from 0.5 to 6.1% in bariatric patients, and 0.5 to 6.9% in controls. Nine studies were suitable for meta-analysis, involving 86 601 bariatric patients, and 318 599 controls. The pooanalysis showed that bariatric surgery reduced the incidence of (all) strokes (HR 0.64, 95% CI 0.53–0.77, P , 0.001, I 2 = 80%).

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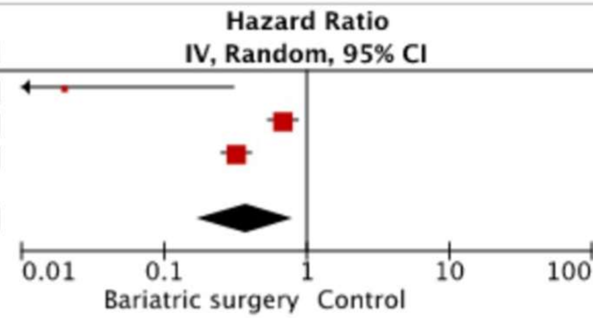
Figure S4. Forest plot of pooled HR of ischemic stroke

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Ardissino 2020	−3.912023	1.39028316	7.0%	0.02 [0.00, 0.31]
Lundberg 2021	−0.38566248	0.12244898	46.5%	0.68 [0.53, 0.86]
Moussa 2021	−1.13943428	0.12244898	46.5%	0.32 [0.25, 0.41]
Total (95% CI)			**100.0%**	**0.37 [0.17, 0.82]**

Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 24.06$, $df = 2$ ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: $Z = 2.47$ ($P = 0.01$)



CI confidence interval; HR hazard ratio

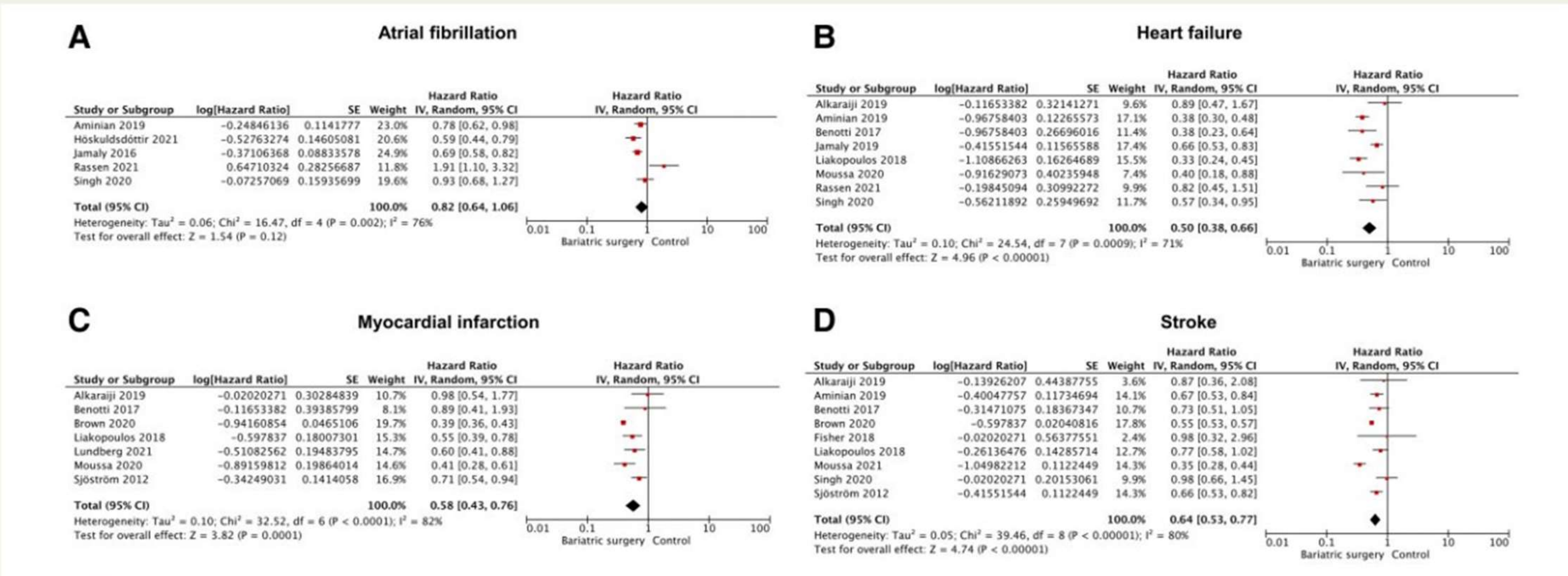
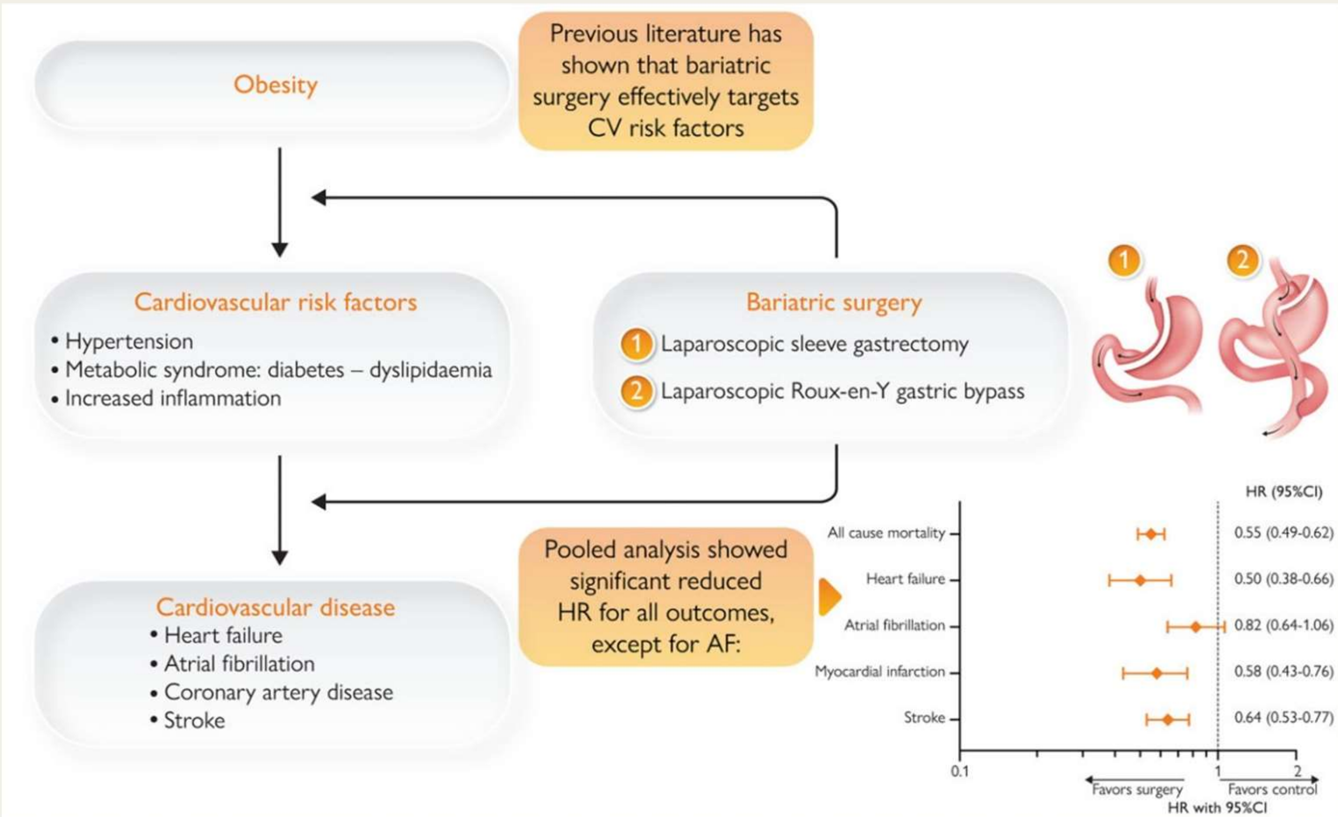


Figure 3 Forest plot of pooled hazard ratios of atrial fibrillation, heart failure, myocardial infarction, and stroke. CI, confidence interval; SE, standard error.

Take-home message

- This current systematic review and meta-analysis of cohort studies illustrates that all-cause and CV mortality, as well as the incidence of CV diseases, are reduced by bariatric surgery. Bariatric surgery should therefore be considered in these patients.



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