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ORIGINAL RESEARCH

Potential Effects of Bariatric Surgery on the Incidence of Heart Failure and Atrial Fibrillation in Patients With Type 2 Diabetes Mellitus and Obesity and on Mortality in Patients With Preexisting Heart Failure: A Nationwide, Matched, Observational Cohort Study

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BACKGROUND: Obesity and diabetes mellitus are strongly associated with heart failure (HF) and atrial fibrillation (AF). The benefits of bariatric surgery on cardiovascular outcomes are known in people with or without diabetes mellitus. Surgical treatment of obesity might also reduce the incidence of HF and AF in individuals with obesity and type 2 diabetes mellitus (T2DM).

METHODS AND RESULTS: In this register-based nationwide cohort study we compared individuals with T2DM and obesity who underwent Roux-en-Y gastric bypass surgery with matched individuals not treated with surgery. The main outcome measures were hospitalization for HF and/or AF and mortality in patients with preexisting HF. We identified 5321 individuals with T2DM and obesity who had undergone Roux-en-Y gastric bypass surgery between January 2007 and December 2013 and 5321 matched controls. The individuals included were 18 to 65 years old and had a body mass index >27.5 kg/m^2. The follow-up time for hospitalization was until the end of 2015 (mean 4.5 years) and the end of 2016 for death. Our results show a 73% lower risk for HF (hazard ratio [HR], 0.27; CI, 0.19–0.38), 41% for AF (HR, 0.59; CI, 0.44–0.78), and 77% for concomitant AF and HF (HR, 0.23; CI, 0.12–0.46) in the surgically treated group. In patients with preexisting HF we observed significantly lower mortality in the group who underwent surgery (HR, 0.23; 95% CI, 0.12–0.43).

CONCLUSIONS: Bariatric surgery may reduce risk for HF and AF in patients with T2DM and obesity, speculatively via positive cardiovascular and renal effects. Obesity treatment with surgery may also be a valuable alternative in selected patients with T2DM and HF.

Key Words: atrial fibrillation ■ bariatric surgery ■ heart failure ■ obesity ■ type 2 diabetes mellitus

Heart failure (HF) and atrial fibrillation (AF) are common worldwide. The global burden of type 2 diabetes mellitus (T2DM) and obesity is also well known. Furthermore, diabetes mellitus and obesity increase risk for HF. The European Society of Cardiology divides causes of HF into 3 main categories based

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CLINICAL PERSPECTIVE

What Is New?

- In a population of more than 5000 individuals with type 2 diabetes mellitus and obesity we found that bariatric surgery was associated with a reduced risk for heart failure and atrial fibrillation and with reduced mortality in a subgroup with known heart failure.

What Are the Clinical Implications?

- Surgical treatment of obesity is an important treatment option for individuals with type 2 diabetes mellitus and obesity and might even be considered for selected individuals with known heart failure.

Nonstandard Abbreviations and Acronyms

NDR	National Diabetes Register
RYGB	roux-en-Y gastric bypass
SOReg	Scandinavian Obesity Surgery Registry
T2DM	type 2 diabetes mellitus

on etiology: diseased myocardium, abnormal loading conditions, and arrhythmias. According to these categories diabetes mellitus and obesity are classified as metabolic derangements that mainly cause diseased myocardium. However, diabetes mellitus and obesity can also be seen as mediating factors that lead to HF through other mechanisms such as ischemia as well as abnormal loading conditions caused by hypertension, renal failure, and volume overload.[1,2]

The prevalence of HF in patients with T2DM is up to 4 times higher than in the general population and studies have implied that HF in patients with diabetes mellitus is likely underdiagnosed.[3] Previous reports have in fact shown that even younger patients with good glycemic control have a 2-fold excess risk for hospitalization for HF as compared with their age-similar controls without diabetes mellitus and that obesity is a particularly strong risk factor for HF in young individuals.[4,5] The strong links between AF and obesity have recently been reviewed,[6] and apart from previous HF and ischemic heart disease, both obesity and diabetes mellitus as well as risk factors related to these conditions are strongly associated with AF.[6,7]

Weight loss and effective treatment of T2DM are cornerstones in the prevention of HF and AF in patients with concomitant obesity and T2DM.[6] Bariatric surgery is an accepted and effective method for weight reduction and treatment and prevention of T2DM. The benefits of bariatric surgery on cardiovascular and renal outcomes have previously been presented in people with or without diabetes mellitus.[8–10] It is therefore possible that surgical treatment of obesity can greatly reduce the incidence of HF and AF in obese individuals with T2DM.

Retrospective obeservational studies have indeed suggested positive effects of bariatric surgery in mixed populations (with small proportion of patients with diabetes mellitus) on incidence of HF, better in-hospital outcomes and reduction in in-hospital mortality rates in patients with HF on admission.[11–14] In the absence of prospective trial results, more knowledge on the effects of bariatric surgery on HF and AF, as well as mortality in individuals with HF, is crucial. In this register-based cohort study we therefore used nationwide data to study hospitalization for HF and/or AF in a large population of patients with T2DM and obesity who had undergone Roux-en-Y gastric bypass surgery (RYGB) in comparison with matched diabetes mellitus patients who had not received surgical treatment. We also examined mortality in a subgroup of patients with known HF.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Cohort

We conducted a cohort study January 31, 2007 through December 31, 2013 using nationwide register data from the NDR (National Diabetes Register)[15] and the SOReg (Scandinavian Obesity Surgery Registry).[16] This patient population and data originating from it have been presented earlier.[17]

Data Sources

To summarize; the patients' unique 10-digit personal identification number was used to link data for clinical characteristics and treatment from NDR with date and type of surgery from SOReg. Socioeconomic variables, information on hospital admissions, and dates and causes of death were gathered from Statistics Sweden, the Swedish Inpatient Registry, and the Cause of Death register respectively. All databases and registries mentioned have been described and validated.[18] The NDR was started in 1996 and contains information on diagnosis and clinical information on nearly all individuals with diabetes mellitus reported from healthcare professionals within outpatient clinics and primary care facilities in Sweden.

SOReg contains information on 98% of all bariatric surgery performed in the country including type of surgery as well as results and adverse effects up to 10 years postoperatively since 2007.

In this study we included all patients who were registered in SOReg after primary RYGB from January 31, 2007 until December 31, 2013 with T2DM and registration in NDR. We selected matched controls who were registered in NDR with T2DM and who had no history of bariatric surgery.[17] Controls did not undergo surgical treatment of obesity during the follow-up period.

Eligible patients were between the age of 18 and 65 with a body mass index (BMI) >27.5 kg/m^2. Fifty-one patients were excluded because of use of surgical methods other than primary RYGB. Follow-up time for end point events other than death was until the end of 2015 and for all-cause mortality until the end of 2016 owing to availability of data.

Outcomes

The *International Classification of Diseases, Tenth Revision* (*ICD-10*) diagnosis was used for definition of HF (I50.0–I50.9) and AF (I48.0–I48.9). As in earlier studies published with data from NDR and SOReg,[17] the epidemiological definition of T2DM was used in this study. This includes a diagnosis at the age of 40 or later with dietary treatment only or treatment with noninsulin hypoglycemic drugs, insulin, or a combination of the 2. The surgical treatment chosen was RYGB because this was the most common surgical treatment at the time. The procedure was described by Lönroth and colleagues in 1996.[19] The mortality outcome was defined as all-cause mortality. Causes of death were described according to *ICD-10* category (A-Y).

All patients have given consent to inclusion in the NDR. No individual consent is required for inclusion in this study, according to Swedish law. The study was approved by the Swedish Ethical Review Authority, DNR 56312.

Statistical Analysis

Matching was performed using time dependent propensity score matching[20] where the propensity score is estimated using a Cox proportional hazards regression with time updated covariates modeling the time to exposure using calendar time as underlying time scale. The propensity score is derived from the risk score at the time of intervention for each exposed individual and controls are matched using greedy 1-1 matching from the persons still at risk for exposure at that time. The index date for the surgical group was the date of surgery. The index date for the selected control was set to the date of selection as a control who then became a perfect match to the date of exposure for the corresponding case. The subsequent analysis was done using Cox proportional hazards regression that adjusts for age, duration of diabetes mellitus, BMI, sex, baseline levels of glycated hemoglobin (HbA1c), systolic and diastolic blood pressure, smoking, levels of physical activity, presence of micro- and macro albuminuria, glomerular filtration rate, levels of high- and low-density lipoprotein cholesterol, levels of triglycerides, treatment with blood pressure-lowering medication, education, income, and country of birth. A less adjusted model including only the exposure and age as independent variables was used in comparison.

The analysis of AF was based on individuals without preexisting AF at the index date and the analysis of HF is based on individuals without preexisting HF at the index date. Post index HF was not considered a censoring event for the analysis of AF and vice versa. Thus, individuals with pre (or post) index HF are considered to be at risk for AF. The individuals included in the study population that had preexisting HF were analyzed separately. The effect of RYGB on mortality in these individuals was visualized using a Kaplan-Meier estimator and compared between treatment groups using a fully adjusted Cox regression model first and then the model using the treatment group and age as the only independent variables.

Descriptive statistics are presented as means with SD for continuous variables or counts with percentages for categorical variables with standardized mean difference (SMD) as a measure of distance between the group means (difference in means divided by the SD). The cumulative incidence was estimated using Kaplan-Meier curves. Missing observations were imputed using multiple chained equations creating 10 imputed data sets, which were analyzed separately before weighing the results together using Rubins rules. The statistical analyses were done using R 4.0.2 employing the mice package for multiple imputation and the survival package for survival analysis.

RESULTS

A total of 5321 patients with registered T2DM diagnosis in NDR and RYGB surgery in SOReg were identified as well as 5321 matched controls from NDR. Baseline characteristics of both groups can be seen in Table 1. Both groups were composed of slightly more women. The mean age of the surgical group was 49 years compared with 47 years in the control group and the BMI was slightly higher in the RYGB group (42 versus 41 kg/m^2). Both groups had a mean diabetes mellitus duration of between 6 and 7 years and a mean HbA1c under 60 mmol/mol (7.6%). The mean follow-up time was 4.5 years for both groups.

Table 1. Baseline Characteristics

	Control	Roux-en-Y Gastric Bypass	*P* Value	Standardized Mean Difference
No.	5321	5321		
Female (%)	3395 (63.8)	3223 (60.6)	0.001	0.067
Age, y*	47.14 (11.49)	48.96 (9.50)	<0.001	0.173
Diabetes mellitus duration, y*	6.40 (6.35)	6.63 (6.23)	0.074	0.036
Body mass index, kg/m^2*	40.95 (7.30)	42.03 (5.65)	<0.001	0.165
HbA1c, mmol/mol*	58.52 (16.93)	59.93 (16.93)	<0.001	0.083
HbA1c (%)	7.5 (1.55)	7.6 (1.55)	<0.001	0.083
Systolic BP, mm Hg*	132.49 (15.60)	132.78 (14.51)	0.392	0.019
Diastolic BP, mm Hg*	80.01 (9.83)	80.30 (9.59)	0.183	0.030
Low-density lipoprotein cholesterol, mmol/L*	2.83 (0.92)	2.77 (0.92)	0.005	0.065
High-density lipoprotein cholesterol, mmol/L*	1.13 (0.32)	1.10 (0.32)	<0.001	0.089
Creatinine, mg/dL*	68.01 (25.40)	68.11 (27.65)	0.867	0.004
Estimated glomerular filtration rate, mL/min per 1.73 m^2*	98.29 (27.49)	97.24 (25.02)	0.075	0.040
Micro albuminuria	697 (19.5)	481 (19.3)	0.876	0.005
Macro albuminuria	298 (7.9)	199 (7.5)	0.600	0.015
Smoking	942 (19.7)	576 (15.9)	<0.001	0.100
Physical activity			0.049	0.077
Level 1 (never)	836 (20.8)	551 (21.0)		
Level 2 (once weekly)	627 (15.6)	477 (18.1)		
Level 3 (1–2 times/wk)	992 (24.7)	515 (19.6)		
Level 4 (3–5 times/wk)	805 (20.0)	515 (19.6)		
Level 5 (daily)	763 (19.7)	450 (17.1)		
Marital status			<0.001	0.197
Married	2227 (43.1)	2518 (48.3)		
Separated	881 (17.0)	1092 (20.9)		
Single	2064 (39.9)	1602 (30.7)		
Widowed	0 (0.0)	1 (0.0)		
Coronary heart disease	313 (5.9)	395 (7.4)	0.002	0.062
Stroke	103 (1.9)	109 (2.0)	0.729	0.008
Myocardial infarction	169 (3.2)	173 (3.3)	0.869	0.004
Cardiovascular disease	408 (7.7)	475 (8.9)	0.020	0.046
Atrial fibrillation	149 (2.8)	148 (2.8)	1.000	0.001
Heart failure	166 (3.1)	142 (2.7)	0.184	0.027
Valvular disease	27 (0.5)	24 (0.5)	0.779	0.008
Kidney failure	82 (1.5)	56 (1.1)	0.032	0.043
Psychiatric disease	529 (9.9)	520 (9.8)	0.795	0.006
Alcohol or drug abuse	122 (2.3)	94 (1.8)	0.063	0.037
Anticoagulation	170 (3.2)	153 (2.9)	0.366	0.019
Beta blockers	1522 (28.6)	1681 (31.6)	0.001	0.065
BP-lowering drugs	3034 (60.4)	2504 (66.2)	<0.001	0.121
Calcium channel blockers	1096 (20.6)	1326 (24.9)	<0.001	0.103
Digoxin	43 (0.8)	39 (0.7)	0.739	0.009
Dipeptidyl peptidase-4	239 (4.5)	257 (4.8)	0.434	0.016
Glitazones	150 (2.8)	190 (3.6)	0.032	0.043
GLP1-analogues	245 (4.6)	310 (5.8)	0.005	0.055
Insulin	1886 (35.4)	1967 (37.0)	0.107	0.032

(*Continued*)

Table 1. Continued

	Control	Roux-en-Y Gastric Bypass	*P* Value	Standardized Mean Difference
Lipid-lowering drugs	2414 (45.4)	2688 (50.5)	<0.001	0.103
Loop diuretics	834 (15.7)	935 (17.6)	0.009	0.051
Meglitinide	132 (2.5)	138 (2.6)	0.758	0.007
Metformin	3769 (70.8)	3947 (74.2)	<0.001	0.075
Nitrates	220 (4.1)	241 (4.5)	0.341	0.019
Other diuretics	744 (14.0)	821 (15.4)	0.038	0.041
Platelet inhibitors	1160 (21.8)	1284 (24.1)	0.005	0.055
Sodium glucose cotransporter 2 inhibitors	1 (0.0)	1 (0.0)	1.000	<0.001
Sulfonylureas	541 (10.2)	627 (11.8)	0.008	0.052

Data presented as n (%) or as * mean (SD). BP indicates blood pressure; and HbA1c, glycated hemoglobin.

There were minor differences between the groups with regard to marital status, usage of calcium channel blocker, and pharmaceutical treatment for hypertension and hyperlipidemia (SMD >0.1). The groups were well matched with respect to other cardiovascular risk factors. A history of cardiovascular disease was found in 8.9% of the surgical group and 7.7% of the control group. Around 3% in both groups had known preexisting HF and 2.8% in both groups a previous history of AF. History of psychiatric disorders and abuse of alcohol or drugs was similar between the groups (SMD <0.1). The groups were also well matched with regard to pharmaceutical treatment for heart disease and diabetes mellitus.

The subgroups with preexisting HF were not primarily matched because of the limited number of patients and thus differed with regard to most baseline characteristics other than smoking (Table 2). The surgical group had a longer reported duration of diabetes mellitus, worse glycemic control, and higher blood pressure. The lipid profile in the control group was better. The surgical group had more cardiovascular disease and AF but less valvular disease and kidney failure.

Follow-Up Data on Risk Factors and Mortality

One-year follow-up showed a mean reduction in BMI of 9.3 kg/mg^2 (23.7 kg weight reduction) in the surgically treated group compared with 1.8 kg/m^2 (2.7 kg weight reduction) in the control group. Reported HbA1c was 16.4 mmol/mol (1.4%) lower in the surgical group and 1.6 (0.1%) lower in the control group after 1 year. There was also a significant improvement of other cardiorenal variables in the surgical group compared with the control group (see Table 3).

In the subgroup with preexisting HF, the reduction of BMI was 10.1 kg/m^2 (25.8 kg in weight) and 1.4 kg/m^2 (3.3 kg in weight) in the surgical group and control group respectively. There was also a significantly greater improvement of HbA1c in the surgical group, 18.3 mmol/mol (1.6%) versus 1.4 mmol/mol (0.2%) for controls. Mean blood pressure, levels of high-density lipoprotein, and glomerular filtration rate were also significantly improved (see Table 4).

Nonadjusted analysis of the groups showed lower incidence rate for hospitalization for AF (4.32 versus 5.80) and HF (1.93 versus 6.37) in the RYGB groups compared with controls (Table 5). The incidence rate for hospitalization with diagnosis of both AF and HF was also lower in the surgical group (0.50 versus 1.91). After analysis using the fully adjusted Cox regression model described in the statistical analysis section, we observed a 41% lower risk (hazard ratio [HR], 0.59; 95% CI, 0.44–0.78) for hospitalization for AF (Figure [A]) and 73% lower risk for HF (HR, 0.27; 95% CI, 0.19–0.38, Figure [B]) in the RYGB group compared with controls (Table S1). There was a 77% lower risk for hospitalization with diagnoses of both AF and HF in the surgical group (HR, 0.23; 95% CI, 0.12–0.46, Figure [C]). A separate analysis of the subgroup that had preexisting HF showed a significant reduction in mortality in the population that underwent surgery (HR, 0.23; 95% CI, 0.12–0.43; Figure [D]). The less adjusted model showed almost identical results for both risk for hospitalization of AF and/or HF and for mortality in the subgroup with HF (Table S2).

The causes of death were divided by *ICD-10* category (A-Y). The most common cause of death in both categories was disease of the circulatory system (I00–199) with 31 events (18.7%) in the control group and 5 events (3.5%) deaths in the surgical group. Four individuals in the control group and 1 individual in the surgical group had HF (I50) as the registered primary cause of death (SMD=0.138). Apart from these, there was a great but similar variation and no discernible patterns in causes of death in both groups.

Table 2. Baseline Characteristics, Subpopulation With Preexisting Heart Failure

	Control	Roux-en-Y Gastric Bypass	*P* Value	Standardized Mean Difference
No.	166	142		
Female (%)	94 (56.6)	48 (33.8)	<0.001	0.471
Age, y*	57.46 (9.11)	54.67 (7.38)	0.004	0.336
Diabetes mellitus duration, y *	9.67 (7.44)	10.79 (8.92)	0.249	0.137
Body mass index, kg/m^2*	45.65 (8.12)	43.67 (6.63)	0.021	0.268
HbA1c, mmol/mol*	64.82 (17.22)	68.08 (19.97)	0.158	0.175
HbA1c (%)	8.1 (1.58)	8.4 (1.83)	0.158	0.175
Systolic BP, mm Hg*	126.97 (17.34)	130.04 (14.24)	0.145	0.194
Diastolic BP, mm Hg*	75.07 (10.24)	77.46 (8.93)	0.060	0.248
Low-density lipoprotein cholesterol, mmol/L*	2.54 (0.89)	2.35 (0.90)	0.138	0.206
High-density lipoprotein cholesterol, mmol/L*	1.07 (0.32)	0.95 (0.24)	0.003	0.415
Creatinine, mg/dL*	87.94 (51.33)	87.95 (36.91)	0.998	<0.001
Glomerular filtration rate, mL/min per 1.73 m^2*	77.75 (29.70)	81.83 (30.71)	0.294	0.135
Micro albuminuria	32 (28.3)	19 (30.2)	0.933	0.040
Macro albuminuria	28 (21.1)	17 (21.5)	1.000	0.011
Smoking	28 (19.4)	19 (18.8)	1.000	0.016
Physical activity			0.204	0.360
Level 1 (never)	54 (47.4)	26 (33.8)		
Level 2 (once weekly)	21 (18.4)	13 (16.9)		
Level 3 (1–2 times/wk)	17 (14.9)	13 (16.9)		
Level 4 (3–5 times/wk)	11 (9.6)	15 (19.5)		
Level 5 (daily)	11 (9.6)	10 (13.0)		
Marital status				
Married	66 (43.4)	64 (45.7)		
Separated	29 (19.1)	28 (20.0)		
Single	57 (37.5)	48 (34.3)	0.849	0.067
Coronary heart disease	53 (31.9)	54 (38.0)	0.317	0.128
Stroke	8 (4.8)	7 (4.9)	1.000	0.005
Myocardial infarction	29 (17.5)	30 (21.1)	0.504	0.093
Cardiovascular disease	58 (34.9)	58 (40.8)	0.343	0.122
Atrial fibrillation	46 (27.7)	42 (29.6)	0.814	0.041
Valvular disease	14 (8.4)	8 (5.6)	0.466	0.110
Kidney failure	21 (12.7)	13 (9.2)	0.427	0.112
Psychiatric disease	31 (18.7)	20 (14.1)	0.354	0.124
Alcohol- or drug abuse	10 (6.0)	4 (2.8)	0.283	0.157
Anticoagulation	43 (25.9)	40 (28.2)	0.751	0.051
Beta blockers	139 (83.7)	120 (84.5)	0.977	0.021
BP-lowering drugs	145 (89.5)	100 (92.6)	0.520	0.108
Calcium channel blockers	59 (35.5)	55 (38.7)	0.646	0.066
Digoxin	22 (13.3)	19 (13.4)	1.000	0.004
Dipeptidyl peptidase-4	14 (8.4)	7 (4.9)	0.322	0.141
Glitazones	3 (1.8)	3 (2.1)	1.000	0.022
GLP1-analogues	11 (6.6)	14 (9.9)	0.409	0.118
Insulin	94 (56.6)	93 (65.5)	0.141	0.183
Lipid-lowering drugs	103 (62.0)	107 (75.4)	0.017	0.290
Loop diuretics	125 (75.3)	110 (77.5)	0.756	0.051
Meglitinide	7 (4.2)	6 (4.2)	1.000	<0.001

(*Continued*)

Table 2. Continued

	Control	Roux-en-Y Gastric Bypass	*P* Value	Standardized Mean Difference
Metformin	106 (63.9)	99 (69.7)	0.334	0.125
Nitrates	40 (24.1)	27 (19.0)	0.348	0.124
Other diuretics	90 (54.2)	67 (47.2)	0.264	0.141
Platelet inhibitors	86 (51.8)	70 (49.3)	0.745	0.050
Sodium glucose cotransporter 2 inhibitors	0 (0.0)	1 (0.7)	0.938	0.119
Sulfonylureas	21 (12.7)	17 (12.0)	0.995	0.021

Data presented as n (%) or as *=mean (SD). BP indicates blood pressure; and HbA1c, glycolated hemoglobin.

DISCUSSION

In this large study we found that bariatric surgery might be associated with lower risk for HF and AF in individuals with T2DM and obesity. The results also provide novel but preliminary data to suggest that surgical treatment of obesity may be safe and reduce mortality in a selected population of patients with T2DM and obesity who have preexisting HF.

In Swedish public health care, the criteria for bariatric surgery are according to international guidelines: BMI >35 kg/m^2 with obesity-related comorbidities such as sleep apnea or T2DM or BMI >40 kg/m^2 without comorbidities. Contraindications include unstable psychiatric disease, substance abuse, age under 18 years, and cancer during the last 5 years.[21] Bariatric surgery should be considered as a treatment option in individuals with T2DM and obesity.[22] The potential benefits of RYGB on cardiovascular outcome and mortality in this group of patients are well described.[10] Surgical treatment of obesity is known to lead to diabetes mellitus remission for many patients and is the most effective strategy for weight loss.[23]

Although diabetes mellitus and obesity increase the risk for HF through effects on cardiovascular and renal risk factors, these diseases are also directly causal in the development of HF.[24] Diabetes mellitus leads to cardiac dysfunction that is not necessarily secondary to coronary artery or valvular heart disease[25] and the concept of diabetes mellitus cardiomyopathy has been discussed for many years. Diabetes mellitus and obesity lead to hyperinsulinemia that in turn theoretically leads to sodium retention in the kidneys, volume overload, and hypertension. These and other related perturbances in hemodynamic pathways increase cardiac workload.[2] Obesity affects cardiac structure and function and causes left ventricular hypertrophy, enlargement of the left atrium, and diastolic and systolic dysfunction.[26]

The pathogenesis of AF in patients with diabetes mellitus and obesity is also specific for these patients and is believed to be associated with oxidative stress, inflammation and fibrosis.[27,28] Aggressive treatment of obesity and diabetes mellitus has been shown to lead to significant improvement of long-term outcomes after ablation for AF likely associated with structural remodeling.[29] It is therefore likely that the weight loss and positive effects on glycemic control after surgery are particularly important with regard to the risk reduction observed in this patient group. Notably, in a recent mendelian randomization study, obesity has been linked causally to both incident HF and AF.[30]

The patient populations included in this study had similar risk profiles with regard to HF and AF at baseline. After 1 year there were significant improvements in weight and glycemic control as well as cardiovascular and renal variables in the surgical group compared with the control group, all of which can be expected to contribute to the risk reduction observed. In the subgroup with previously diagnosed HF, less than half of the population had known cardiovascular- or valvular disease and kidney failure was present in a small group, which indicated that diabetes mellitus and obesity might have been primary contributors to the etiology of HF in many of these patients and not only through mediating effects on other risk factors.

The great reduction in BMI and HbA1c may have affected mortality although positive effects on other cardiovascular and renal variables also contributed. However, a previous causal mediation analysis on patients with T2DM and obesity from NDR and SOReg have indicated that RYGB has positive effects on mortality risk (all cause and cardiovascular) mainly through weight reduction rather than changes in HbA1c, blood pressure, or blood lipids. The effect on myocardial infarction, however, could not be attributed to any of these covariates.[31] Changes in lifestyle, for example physical activity, dietary habits, and smoking cessation, might also be more common after surgery. However, there were no differences between the groups with regard to physical activity reported 1 year after surgery, accepting caveats in self-reporting of activity.

The positive effect of SGLT2 (sodium-glucose cotransporter-2) inhibitors and GLP-1 analogues on glycemic control, cardiovascular outcomes, and even weight is established.[32,33] It is likely that a larger population of the patients included would have been treated with these drugs if the study had been done today.

Table 3. Clinical Variables After 1 Year, Total Study Population

	Control	Roux-en-Y Gastric Bypass	*P* Value
No.	5321	5321	
Body mass index, kg/m^2*	39.04 (7.04)	32.60 (5.69)	<0.001
Compared with baseline	−1.79 (5.58)	−9.30 (4.45)	<0.001
Weight, kg*	112.86 (23.18)	96.67 (21.24)	<0.001
Compared with baseline	−2.73 (11.37)	−23.71 (14.89)	<0.001
HbA1c, mmol/mol*	56.97 (16.56)	44.34 (11.83)	<0.001
Compared with baseline	−1.64 (14.40)	−16.38 (15.23)	<0.001
HbA1c (%)*	7.4 (1.51)	6.2 (1.08)	<0.001
Compared with baseline	−0.1 (1.32)	−1.4 (1.39)	<0.001
Systolic BP, mm Hg*	131.55 (15.26)	126.60 (14.69)	<0.001
Compared with baseline	−0.86 (15.06)	−6.31 (15.69)	<0.001
Diastolic BP, mm Hg*	79.30 (9.67)	76.80 (9.10)	<0.001
Compared with baseline	−0.51 (9.74)	−3.41 (10.37)	<0.001
Low-density lipoprotein cholesterol, mmol/L*	2.66 (0.89)	2.44 (0.82)	<0.001
Compared with baseline	−0.13 (0.74)	−0.29 (0.89)	<0.001
High-density lipoprotein cholesterol, mmol/L*	1.16 (0.33)	1.23 (0.37)	<0.001
Compared with baseline	0.03 (0.22)	0.13 (0.33)	<0.001
Creatinine, mg/dL*	68.65 (27.79)	67.58 (30.14)	0.122
Compared with baseline	0.81 (13.92)	−0.87 (23.15)	<0.001
Glomerular filtration rate, mL/min per 1.73 m^2*	97.34 (27.72)	97.94 (24.08)	0.333
Compared with baseline	−1.11 (9.44)	0.27 (11.41)	<0.001
Micro albuminuria	632 (20.9)	413 (16.6)	<0.001
Macro albuminuria	226 (7.6)	166 (6.6)	<0.001
Physical activity			<0.001
Level 1 (never)	604 (18.8)	274 (11.0)	
Level 2 (once weekly)	478 (14.9)	246 (9.9)	
Level 3 (1–2 times/wk)	800 (24.9)	529 (21.3)	
Level 4 (3–5 times/wk)	696 (21.7)	670 (27.0)	
Level 5 (daily)	634 (19.7)	762 (30.7)	

Data presented as n (%) or as *=mean (SD). BP indicates blood pressure; HbA1c, glycolated hemoglobin.

Strengths of the Study

This study focuses on the treatment of HF, AF and obesity, all of which affect individuals worldwide in epidemic proportions. The study includes a large population of individuals with long-term follow-up. The surgical method studied is still the most common procedure used for the treatment of obesity in the country and a wide range of risk factors for HF and AF were included. The study gathered information from databases (NDR and SOReg) with nationwide coverage and therefore includes all possible candidates. The subpopulation of patients with a known diagnosis of HF studied also adds valuable information to the possible treatments of these patients.

Limitations of the Study

The study is a retrospective register-based study and the quality of the data therefore dependent on the reporting of healthcare professionals to the registries as well as the *ICD* codes assigned. The *ICD* classification of HF is crude and lacks subclassifications with regard to ejection fraction. There were minor differences between the groups at baseline with the surgical group being slightly older and with a higher BMI than the control population although these differences should be in favor of the control group with regard to risk for HF and AF. A slightly larger part of the surgical group was married or separated. More individuals in the control group were treated with blood pressure medication but a larger proportion of the surgical group received treatment with calcium channel blockers or lipid-lowering drugs. These differences in pharmaceutical treatment were not represented by significant differences in levels of blood pressure or blood lipids. In an attempt to minimize possible effects of differences between the groups as well as other unknown confounding factors, the groups were matched with regard to age, sex,

Table 4. Characteristics After 1 Year, Subgroup With Preexisting Heart Failure

	Control	Roux-en-Y Gastric Bypass	*P* Value
No.	166	142	
Body mass index, kg/m^2*	43.97 (8.19)	33.17 (5.36)	<0.001
Compared with baseline	−1.38 (3.32)	−10.08 (5.77)	<0.001
Weight, kg*	125.17 (25.93)	102.61 (23.35)	<0.001
Compared with baseline	−3.30 (7.98)	−25.79 (17.48)	<0.001
HbA1c, mmol/mol*	62.74 (17.00)	51.11 (11.89)	<0.001
Compared with baseline	−1.44 (14.62)	−18.26 (17.32)	<0.001
HbA1c (%)*	7.9 (1.56)	6.8 (1.09)	<0.001
Compared with baseline	−0.2 (1.34)	−1.6 (1.58)	<0.001
Systolic BP, mm Hg*	130.23 (17.37)	125.52 (14.87)	0.046
Compared with baseline	3.81 (14.78)	−7.14 (16.34)	<0.007
Diastolic BP, mm Hg*	75.62 (11.55)	72.91 (9.06)	0.076
Compared with baseline	0.21 (10.20)	−4.22 (10.33)	0.007
Low-density lipoprotein cholesterol, mmol/L*	2.49 (0.95)	2.16 (1.01)	0.031
Compared with baseline	−0.02 (0.84)	−0.23 (1.09)	0.200
High-density lipoprotein cholesterol, mmol/L*	1.12 (0.38)	1.08 (0.31)	0.520
Compared with baseline	0.04 (0.19)	0.13 (0.26)	0.015
Creatinine, mg/dL*	87.45 (31.10)	92.87 (83.92)	0.535
Compared with baseline	1.80 (16.93)	−3.44 (33.97)	0.188
Glomerular filtration rate, mL/min per 1.73 m^2*	74.91 (29.29)	85.45 (32.06)	0.016
Compared with baseline	−2.20 (13.02)	5.26 (19.80)	0.004
Micro albuminuria	76.57 (24.96)	85.15 (24.87)	0.017
Macro albuminuria	6 (17.4)	16 (23.5)	0.447
Physical activity			0.002
Level 1 (never)	36 (41.9)	12 (20.0)	
Level 2 (once weekly)	10 (11.6)	3 (5.0)	
Level 3 (1–2 times/wk)	22 (25.6)	15 (25.0)	
Level 4 (3–5 times/wk)	8 (9.3)	18 (30.0)	
Level 5 (daily)	10 (11.6)	12 (20.0)	

Data presented as n (%) or as *=mean (SD). BP indicates blood pressure; and HbA1C, glycolated hemoglobin.

BMI, and calendar time and then a Cox proportional hazards regression model that included all baseline characteristics was applied. Still, some individuals in the control group might have been ineligible for surgical treatment. In the subpopulation with preexisting HF there were differences between the groups at baseline. These individuals were not matched from the start and the groups were small. Great care should therefore be taken in the interpretation of the results regarding surgical treatment of obesity in patients with HF. The fact that one surgical method, RYGB, was included may also be seen as a limitation. Today, laparoscopic sleeve gastrectomy is also applied in Sweden in around 45% of the patients.

Table 5. Events and Event Rates During Follow-Up

Event	Control (n=5321)	RYGB (n=5321)	HR (95% CI)	*P* Value
AF*	138 (5.80)	104 (4.32)	0.59 [0.44–0.78]	<0.001
HF*	151 (6.37)	47 (1.93)	0.27 [0.19–0.38]	<0.001
AF and HF*	45 (1.91)	12 (0.5)	0.23 [0.12–0.46]	<0.001
HF mortality†	63 (98.10)	16 (23.66)	0.23 [0.12–0.43]	<0.001

Number of events during follow-up period reported with incidence rate per 1000 person-years. HR, comparing individuals treated with RYGB to controls, adjusted models. AF indicates atrial fibrillation; HF, heart failure; HR, hazard ratio; and RYGB, Roux-en-Y gastric bypass.

*Hospitalization for event.

†Mortality in subpopulation with preexisting heart failure.

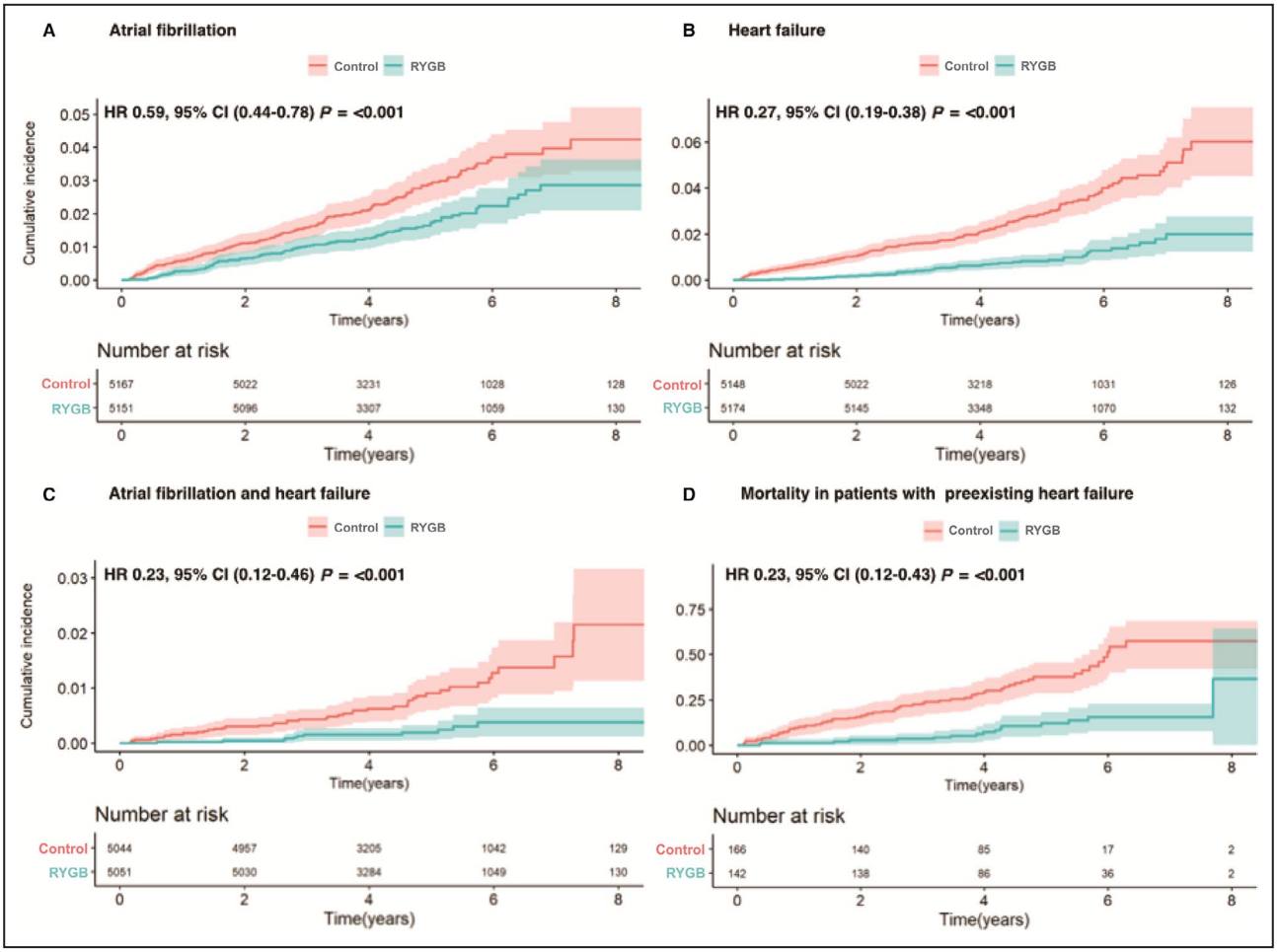

Figure. Cumulative incidence with number of subjects at risk and time in years.
Control group represented by red and surgical group by turquoise. **A**, Cumulative incidence of atrial fibrillation. **B**, Cumulative incidence of heart failure. **C**, Cumulative incidence of atrial fibrillation and heart failure. **D**, Cumulative incidence of mortality in subpopulation with preexisting heart failure. CI indicates cumulative incidence; HR, hazard ratio; and RYGB, Roux-en-Y gastric bypass surgery.

CONCLUSIONS

The results of our study further strengthen earlier recommendations that bariatric surgery should be considered as a treatment option for individuals with T2DM and obesity. Surgery might even be considered in certain subgroups with known HF, a provocative but important suggestion because of the existence and complexity of the obesity paradox in HF. Further studies are needed on effects of bariatric surgery on subtypes of HF as well as studies comparing surgical treatment with newer pharmaceutical treatment for T2DM.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Tables S1–S2

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SUPPLEMENTAL MATERIAL

Table S1. Hazards ratio, fully adjusted model.

Endpoint	HR (95% CI)	p-value
AF	0.59 (0.44, 0.78)	<0.001
HF	0.27 (0.19, 0.38)	<0.001
AF and HF	0.23 (0.12, 0.46)	<0.001
Mortality, pre-existing HF	0.23 (0.12,0.43)	<0.001

Cox-proportional hazards regression adjusted for age, diabetes duration, BMI, sex, HbA1c levels, systolic and diastolic blood pressure, smoking, levels of physical activity, presence of micro- and macro albuminuria, glomerular filtration rate, levels of high- and low-density lipoproteins, levels of triglycerides, treatment with blood pressure-lowering medication, education, income and country of birth

Table S2. Hazards ratio, less adjusted model.

Endpoint	HR (95% CI)	p-value
AF	0.59 (0.45, 0.78)	<0.001
HF	0.29 (0.21, 0.40)	<0.001
AF and HF	0.24 (0.12, 0.47)	<0.001
Mortality, pre-existing HF	0.27 (0.15, 0.47)	<0.001

Cox-proportional hazards regression adjusted for exposure and age