Resolution of Comorbidities and Impact on Longevity Following Bariatric and Metabolic Surgery

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KEYWORDS

• Obesity • Mortality • Bariatric surgery • Metabolic syndrome • Cancer mortality

KEY POINTS

- Overweight is a modifiable risk factor directly linked to 3 of the 5 leading causes of death. This effect is seen most notably at body mass indexes greater than 35 (class II and III).
- Multiple studies have been conducted demonstrating the reduction in mortality associated with bariatric surgery. Most studies have been conducted on young females; however, the results have been reproducible in older, male patients within the Veterans Affairs health system.
- Recent systematic reviews and meta-analyses have shown dramatic reduction in rates of cardiovascular events, myocardial infarction, and stroke in patients undergoing bariatric surgery. Lower levels of medication use associated with hypertension have also been found in bariatric surgical patients.
- The increase in incidence of type II diabetes is rising commensurate with the increase in obesity rates. Bariatric surgery has been shown in multiple studies to be superior to medical management for treatment and remission of diabetes.
- Several cancers have been identified that are associated with obesity. Data are accumulating demonstrating reduction.

IMPACT OF OBESITY ON MORTALITY

Obesity is a global epidemic with well-documented links to decreased life expectancy. Overweight and obesity are linked to more deaths worldwide than underweight. According to the most recent data from the World Health Organization, most of the world's population live in countries where overweight and obesity result in more deaths than being underweight.[1]

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Among the 5 leading causes of death in the United States, being overweight is a major modifiable risk factor for 3 (cardiovascular, cancer, stroke).[2] In a comprehensive, quantitative assessment of the mortality burden of key modifiable risk factors, Harvard researchers found that, in those younger than 70 years, overweight and obesity causes more deaths than did high blood pressure. This modifiable risk factor was second only to tobacco smoking.[3]

The risk of increased mortality due to excess weight seems to vary based on the severity of the disease. In a 2013 meta-analysis, there was a significant increase in mortality among higher grades of obesity. Grades 2 and 3 obesity (body mass index [BMI] >35) were found to have an adjusted hazard ratio [HR] of 1.34 compared with 0.97 and 0.94 in grade 1 obesity (BMI between 30 and 35) and overweight (BMI between 25 and 30), respectively. Further analysis revealed that the overweight group was associated with a significantly lower overall mortality relative to the normal weight category (BMI 20–25) with an overall summary HR of 0.94.[4] The cause for this decrease in HR in the overweight and grade 1 obese population is not clear. Possible explanations for this protective effect of overweight and mild obesity have included earlier presentation of heavier patients,[5] greater likelihood of receiving optimal medical treatment,[6–8] cardioprotective metabolic effects of increased body fat,[9,10] and benefits of higher metabolic reserves.[11]

The increase in rates of obesity over the past several decades in the United States are well understood. What is not frequently discussed though is that during the period between 1960 and 2006, the total US population has also increased. Therefore, the total number of Americans affected has also increased. Looking at the numbers of people affected, the overweight population has doubled, the obese population has increased 5-fold, and the population with extreme or morbid obesity has increased by a factor of nearly 12 (**Figs. 1** and **2**).[12,13]

Given the detrimental effect of grade II and III obesity on mortality, coupled with the significant change in absolute numbers of Americans involved, it is clear that this is a public health crisis. Bariatric surgery remains the most cost-effective treatment of

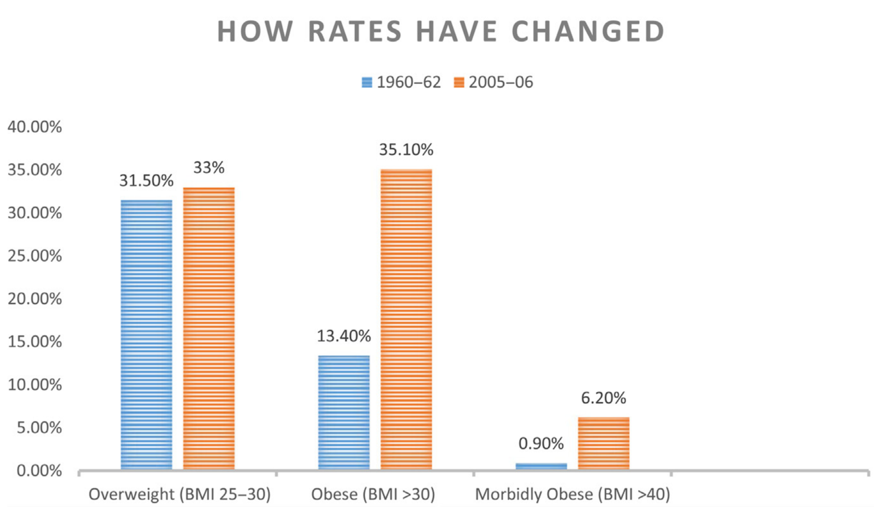

Fig. 1. Changes in the percentage of the US population who are overweight and obese over the last 4 decades. (*Data from* The Downey Obesity Report. Downey fact sheet 2 – quick facts. Available at: http://www.downeyobesityreport.com/2009/09/fact-sheet-2-quick-facts/.)

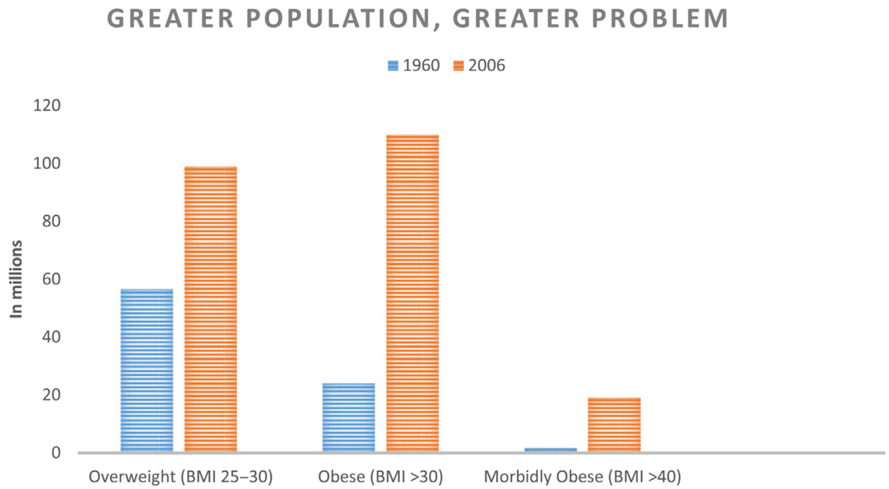

Fig. 2. The number of people with obesity and severe obesity as the population has grown over the last 4 decades. (*Data from* The Downey Obesity Report. Downey fact sheet 2 – quick facts. Available at: http://www.downeyobesityreport.com/2009/09/fact-sheet-2-quick-facts/.)

most patients with clinically severe obesity with a safety profile better than many commonly performed general surgery procedures.[14]

EFFECT OF BARIATRIC AND METABOLIC SURGERY ON ALL-CAUSE MORTALITY

There are almost 2 decades of published data regarding the impact that bariatric surgery has on reducing mortality. In 2015, Adams and colleagues[15] published a review of 28 articles, reporting on mortality rates at least 2 years after bariatric surgery. As expected, these studies have included a wide variety of methodological approaches.

In one of the earlier published studies, Flum and Dellinger[16] conducted a retrospective cohort study in 2004, using the Washington State Comprehensive Hospital Abstract Reporting System database and the Vital Statistics database. They demonstrated after 15 years of follow-up, 16.3% of nonoperated patients had died, compared with 11.8% of patients who had undergone a Roux-en-Y gastric bypass (RYGB). In this study, using Cox proportional hazards, when patient survival was compared starting at 1 year after hospitalization, the hazard for death was significantly less for operated patients than for those who did not have the procedure (HR, 0.67; 95% confidence interval [CI], 0.54–0.85) after adjusting for age, sex, and comorbidity index. In their study, 80.5% of the operated patients were female with a mean age (standard deviation [SD]) of 43.1 years (±10.1).[16]

During the same year, Christou and colleagues[17] conducted an observational 2-cohort study demonstrating a significant decrease in overall mortality in patients who had an RYGB compared with a well-matched cohort that did not undergo the surgery. During the 5-year follow-up period, the mortality rate in the bariatric surgery cohort was 0.68% compared with 6.17% for controls (relative risk [RR] 0.11; 95% CI 0.04–0.27). The mean age (SD) of the surgical group was 45.1 (±11.6) years. This finding was similar to the population in the Flum and Dellinger[16] study. The percentage of female patients was slightly lower, however, at 65.6%. In addition to the mortality results, Christou and colleagues[17] also found, on average, the total direct health care cost for the nonoperated control group was 45% higher compared with the bariatric surgery patients.

In 2007, 2 key studies were published that further demonstrated the association between decreased overall mortality in bariatric surgery patients. To date, the Swedish Obesity Subjects (SOS) study is the only prospective matched cohort study. This study involved 4047 obese subjects. The surgery group consisted of 2010 subjects who underwent gastric bypass (13%), vertical banded gastroplasty (68%), or adjustable gastric band (19%). During a 16-year follow-up period, subjects in the surgery group had a mortality HR of 0.76, as compared with the control group (95% CI, 0.59–0.99). After multivariate adjustments for baseline conditions, the risk reduction was almost 30%. During the follow-up period, 6.3% in the control group died, compared with 5.0% in the surgery group. The surgical population in this study was more than 70% female with a mean (SD) age of 46.1 ($\pm$5.8) years.[18]

The second key study published in 2007 by Adams and colleagues[19] evaluated the rates of death over a 7-year follow-up period between subjects who had undergone gastric bypass compared with severely obese control subjects from the general population in Utah. After covariate adjustment, the rate of death from any cause was 40% lower in the surgery group than in the control group (HR 0.60; 95% CI, 0.45–0.67); without covariate adjustment, the rate of death was 34% lower in the surgery group. The surgical arm was 86% female with an average age (SD) of 39.3 ($\pm$10.3) years. Interestingly, the researchers also reported deaths not caused by disease (including suicide, accidents not related to drugs, poisonings of undetermined intent, and other deaths) were 1.58 times as great in the surgery group as in the control group, though the overall number of these events was low (P = .04). The researchers suggested that further research is warranted to explore the optimal approach to evaluating candidates for surgery, including aggressive psychological evaluation before and after surgery.[19]

In comparison with the previous studies conducted in predominately younger, white, female populations, 2 studies have been published analyzing results in bariatric surgery patients within the Veterans Affairs (VA) medical centers. In 2011, Maciejewski and colleagues[20] evaluated the association of survival and bariatric surgery in a cohort of older, high-risk male patients. The mean age (SD) was 49.5 ($\pm$8.3) years in the surgical cohort, and 74% of the patients were male. In propensity score-adjusted analyses of 2 cohorts of 847 patients, bariatric surgery compared with usual care, was not associated with decreased mortality during a mean 6.7 years of follow-up (HR 0.83; 95% CI, 0.61–1.14). These findings were attributed to the possibility of higher perioperative mortality for RYGB in veteran cohorts. The 30-day mortality rates of 1.3% observed in this study was 4-fold higher than that reported in a multicenter Longitudinal Assessment of Bariatric Surgery study, which included a younger, predominantly female cohort.[21]

In a second study of VA bariatric centers published in 2015, Arterburn and colleagues[14] found contrasting results compared with the Maciejewski study after following patients for a longer time. They hypothesized that longer follow-up and a larger sample size of patients might yield findings similar to prior studies, given that it took 10 years to observe a significant relationship between bariatric surgery and survival in the SOS study.[18] In Arterburn and colleagues'[14] study, the mean age was 52 years with 74% male in the surgical group. Among the bariatric patients, 74% had RYGB, 15% had sleeve gastrectomy, 10% had adjustable gastric banding, and 1% had another procedure. The Kaplan-Meier estimated mortality rates were 2.4% at 1 year, 6.4% at 5 years, and 13.8% at 10 years for surgical patients; for matched controls, the estimated mortality rates were 1.7% at 1 year, 10.4% at 5 years, and 23.9% at 10 years. In multivariate-adjusted Cox regression, bariatric surgery was not associated with a difference in all-cause mortality in the first year of follow-up (HR 1.28, 95% CI, 0.98–1.68) but was associated with lower mortality after 1 to 5 years (HR 0.45, 95% CI, 0.36–0.56) and 5 or more years of follow-up (HR 0.47, 95% CI, 0.39–0.58).[14] By extending the follow-up period from 5 to 10 years, the findings were consistent with several observational studies that examined lower-risk, predominantly female cohorts.[16,18,19]

A 2015 study from New York by Telem and colleagues[22] reported on long-term mortality rates of patients undergoing surgery and, additionally, identified specific patient risk factors for long-term mortality. The New York State Planning and Research Cooperative System longitudinal administrative data were used to identify 7862 adult patients undergoing a primary bariatric surgery from 1999 to 2005. Of the surgical cohort, 7.5% underwent sleeve gastrectomy, 57.2% RYGB, 26.8% adjustable gastric band, and 8.5% had vertical banded gastroplasty. Patients who had bariatric procedures had significantly decreased long-term mortality compared with the general or obese populations. The estimated mortality rate from 1999 to 2010 for the general population as derived from the Centers for Disease Control and Prevention (CDC) Web site was 2.1% versus 1.5% for the bariatric surgery population ($P = .006$). Comparison of the actual predictions for the obese population during this time frame to the bariatric surgery population also demonstrates significant improvement in long-term mortality (2.3% vs 1.5%, $P = .0008$). This study is the first to demonstrate, regardless of procedure, the positive impact of surgery on long-term mortality as compared with both obese controls and the general population.[22]

Bariatric surgery is associated with improved long-term survival compared with matched cohorts. In the studies reviewed, the benefits can be seen as early as 2.5 years across several types of procedures and in both female and male cohorts. Importantly, there are no studies that demonstrate an increase in all-cause long-term mortality after bariatric surgery compared with obese controls (**Table 1**).

EFFECT OF BARIATRIC AND METABOLIC SURGERY ON WEIGHT-RELATED COMORBIDITIES AND DISEASE-SPECIFIC MORTALITY

Cardiovascular Disease

Myocardial infarction and stroke, either separately or in combination, were predefined secondary end points in the SOS trial.[23] In January 2012, Sjöström and colleagues[24] reported that bariatric surgery is associated with a reduced number of cardiovascular deaths and with a lower number of total first-time (fatal or nonfatal) cardiovascular events.

The same year, Vest and colleagues[25] published a systematic review that evaluated the impact of bariatric surgery on cardiovascular risk factors and on cardiac structure and function. Seventy-three cardiovascular risk factor studies involving 19,543 subjects were included (mean age 42 years, 76% female). Baseline prevalence of hypertension, diabetes, and hyperlipidemia were 44%, 24%, and 44%, respectively. The mean follow-up was 57.8 months. Postoperative resolution/improvement of hypertension occurred in 63% of patients, of diabetes in 73%, and hyperlipidemia in 65%. Echocardiographic data demonstrated statistically significant improvement in 713 patients that data were available.

A second systematic review and meta-analysis, published a year later by Gloy and colleagues[26] aimed to summarize the effects of bariatric surgery on cardiovascular risk factors and other end points in patients with a BMI of 30 or greater compared with patients who had nonsurgical treatment. The meta-analysis included 11 studies with 796 individuals. They were unable to show a significant difference between bariatric surgery and nonsurgical treatment for changes in blood pressure and levels

Table 1
Bariatric surgery studies evaluating long-term mortality

Author	Type	Start Year	Surgical n (M/F)	Control n	Follow-up, Years Surgery	Follow-up, Years Controls	Types of Surgery	Mortality Results	Comments
Christou et al,[17] 2004	Retrospective cohort	1986	1035 (356/679)	5746 (2068/3678)	2.5	2.5	RYGB	HR, 0.11 (95% CI, 0.04–0.27)	Control data extracted from hospital records (ICD codes); surgeries Canada
Flum & Dellinger,[16] 2004	Retrospective cohort	1987	233 (46/187)	11,132 (3975/7157)	10	10	RYGB	HR, 0.67 (95% CI, 0.54–0.85)	Control data extracted from hospital records (ICD codes); surgeries United States
Zhang[43]	Retrospective cohort	1986	18.972 (2526/16,446)	None	8.3	NA	Simple or complex	Death rate of 3.4%	Data extracted from 55 data sites (77 surgeons) using IBSR data collection system
Sjöström et al,[18] 2007	Prospective cohort	1990	2010 (590/1420)	2037 (590/1447)	10	10	VBG, band, RYGB	HR, 0.76 (95% CI, 0.59–0.99; *P* = .04)	Only prospective long-term mortality study; preclinical and postclinical data available; surgeries Sweden
Adams et al,[19] 2007	Retrospective cohort	1984	7925 (1268/6657)	7925 (1268/6657)	7.1	7.1	RYGB	HR, 0.60 (95% CI, 0.45–0.67; *P*<.001)	Control data extracted from driver's license applications; surgeries United States

Marsk[44]	Retrospective cohort	1980	12,379 (2756/9614)	None	10.9	NA	VBG, RYGB, jejunoileal bypass, other	Mortality rate 60 per 10,000 person-years; estimated mortality rate ratio 1.8 (95% CI, 1.5–2.1)	Longer-term mortality greater in men than women; surgeries Sweden
Perry[45]	Retrospective cohort	2001	11,903 (2665/9238)	190,488 (42,669/ 147,819)	2	2	RYGB, band, VBG	Mortality rate 4.5% vs 8.6% for surgical vs nonsurgical (*P*<.001) for <65 y; 8.0% vs 12.2% (*P*<.001) for surgery vs nonsurgery >65 y	Surgical and control groups were severely obese Medicare patients; surgeries United States
Maciejewski[20]	Retrospective cohort	2000	850 (628/222)	41,244 (37,840/3404)	6.7	6.7	None indicated	HR, 0.64 (95% CI 0.51–0.80) unmatched; HR, 0.83 (95% CI, 0.61–1.14, not significant) propensity matched	All subject data (surgical and nonsurgical) from VA medical centers; unmatched and propensity matched; propensity matched no significant mortality reduction; surgeries United States

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Table 1
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Author	Type	Start Year	Surgical n (M/F)	Control n	Follow-up, Years Surgery	Follow-up, Years Controls	Types of Surgery	Mortality Results	Comments
Telem et al,[22] 2015	Retrospective cohort	1999	7862 (sex not indicated)	General and estimated obese population	4–6	4–6	RYGB (57%), band (27%), VBG (9%), sleeve (8%)	Observed mortality rate of bariatric surgery 1.5% vs predicted general population (NY state) 2.1% (*P* = .005) Mortality rate of bariatric surgery 1.5% vs 2.3% estimated obese population (NY state) (*P* = .0008)	Bariatric surgeries in NY state; comparative data included actuarial projections for NY mortality rates (CDC) for obese population assumed one-third NY population obese; surgeries United States
Arterburn et al,[14] 2015	Retrospective cohort	2000	2500 (1850/650)	7462 (5542/1920)	6.9	6.6	RYGB, band, BD, sleeve, VBG	After 1–5 y surgery, HR, 0.45 (95% CI, 0.36–0.56) 5–14 y after surgery, HR, 0.47 (95% CI, 0.39–0.58)	Expanded follow-up of previous study (Maciejewski, 2011); 74% male surgical patients; data (surgical and nonsurgical) from VA medical centers; surgeries United States

Abbreviations: BD, biliopancreatic diversion; F, female; ICD, International Classification of Diseases; M, male; NA, not applicable.

Adapted from Adams TD, Mehta TS, Davidson LE, et al. All-cause and cause-specific mortality associated with bariatric surgery: a review. Curr Atheroscler Rep 2015;17:74; with permission.

of total or low-density lipoprotein cholesterol, although some studies in the analysis were able to demonstrate concomitant reductions in drug use for these conditions. They were, however, able to demonstrate higher rates of remission of type 2 diabetes and metabolic syndrome. One reported limitation of this meta-analysis was that they were not able to investigate the effect of bariatric surgery on cardiovascular morbidity and mortality.

In 2014, Kwok and colleagues[27] published a third systematic review and meta-analysis to evaluate the impact of bariatric surgery on long-term incident cardiovascular disease and mortality. Fourteen studies met their inclusion criteria with 195,408 participants. The bariatric surgery cohort consisted of 29,208 subjects compared with 166,200 nonsurgical controls, with an overall mean age of 48 years (70% female). At the time of publication, it was the first meta-analysis to demonstrate that bariatric surgery is associated with a reduced risk of myocardial infarction, stroke, and composite adverse cardiovascular events. The reduction in risk of these events was approximately 50% after surgery compared with nonoperated cohorts. In terms of absolute event rates, they found that there was a lower fraction of events in the surgery group for all outcomes (mortality 3.6% vs 11.4%, cardiovascular events 2.4% vs 4.0%, myocardial infarction 1.3% vs 2.5%, and stroke 0.8% vs 1.5%). These findings suggest that patients who are both candidates for bariatric surgery and are at high risk of cardiovascular events should undergo bariatric surgery.

Diabetes

According to the American Diabetes Association National Diabetes Statistics Report, released in 2014, 29.1 million Americans, 9.3% of the US population, have diabetes. More than 95% of these cases are type 2 diabetes. In 2012, 86 million Americans aged 20 years and older had prediabetes; this is up from 79 million in 2010. According to this report, diabetes remains the seventh leading cause of death in the United States and affects almost 37% of the population either as a definitive diagnosis or as prediabetes. Most patients with type 2 diabetes are obese or, if not obese by traditional BMI calculations, have increased body fat distributed in the abdominal region.[28]

Metabolic surgery has been recommended as an effective treatment option for obese patients with type 2 diabetes mellitus who do not achieve satisfactory control with only lifestyle changes.[29] According to the 2010 position statement from the Diabetes Surgery Summit, surgery should be accepted as an option in patients with diabetes and a BMI of 35 or greater and be considered as an option with a BMI of 30 to 35 when diabetes is poorly controlled, particularly in the presence of other major comorbidities.[30]

In 2012, Arterburn and colleagues[31] conducted a retrospective cohort study of adults with uncontrolled or medication-controlled type 2 diabetes who underwent gastric bypass. A total of 4434 adults underwent gastric bypass over a 13-year period and 68.2% (95% CI, 66% and 70%) experienced complete diabetes remission within 5 years after surgery. Among these, 35.1% (95% CI, 32% and 38%) redeveloped diabetes within 5 years. Significant predictors of complete remission and relapse were poor preoperative glycemic control, insulin use, and longer diabetes duration.

Mingrone and colleagues,[32] in 2012, reported results from one of 2 prospective, randomized trials comparing RYGB and biliopancreatic diversion (BPD) with medical therapy for the treatment of diabetes. In this trial, the primary end point was the rate of diabetes remission at 2 years (defined as a fasting glucose level <100 mg/dL and a glycated hemoglobin level of <6.5% in the absence of pharmacologic therapy). Sixty patients were randomized; at 2 years, diabetes remission had occurred in no patients in the medical-therapy group vs 75% in the gastric-bypass group and 95% in the biliopancreatic-diversion group (*P*<.001 for both comparisons). At the end of the study period, baseline glycated hemoglobin level (8.65 ±1.45%) had decreased in all groups, but patients in the two surgical groups had the greatest degree of improvement (average glycated hemoglobin levels, 7.69 ±0.57% in the medical-therapy group, 6.35 ±1.42% in the gastric bypass group, and 4.95 ±0.49% in the BPD group). Preoperative BMI and weight loss did not predict the improvement in hyperglycemia after these procedures.

The second prospective, randomized trial in 2012 by Schauer and colleagues[33] assessed outcomes of 150 obese patients with uncontrolled type 2 diabetes who were randomized to receive either intensive medical therapy alone or intensive medical therapy plus RYGB or sleeve gastrectomy. Their primary end point was a glycated hemoglobin level of 6.0% or less. Three-year outcomes were reported in 2014 demonstrating intensive medical therapy plus bariatric surgery resulted in glycemic control in significantly more patients than did medical therapy alone.

In an attempt to assess diabetic remission rates after bariatric surgery compared with usual care on a longer-term basis, Sjostrom and colleagues[34] provided an update in 2014 from the ongoing prospective SOS intervention study. In this observational study, the prevalence of diabetes remission after 2, 10, and 15 years was evaluated. The proportion in remission after 2 years was 72.3% in the surgery group and 16.4% in the control group. The difference at 2 years between the two groups remained significant after multivariate adjustments (odds ratio [OR], 40.5; 95% CI, 21.0–78.2; *P*<.001). The proportion of surgery patients in remission decreased to 38.1% and 30.4% after 10 and 15 years, respectively, but remained higher than in the controls (10 years: OR 5.3; 95% CI, 2.9–9.8, and 15 years: OR 6.3; 95% CI 2.1–18.9). In further analysis, the study showed that short diabetes duration at baseline was associated with higher diabetes remission rates in surgery patients after 2, 10, and 15 years of follow-up.[34]

The impact on glycemic control after bariatric surgery is well studied; however, the question whether this improves life expectancy is not well understood. A study published in 2015 by Schauer and colleagues[35] developed a Markov state transition model from data obtained from 3 large cohorts: (1) 159,000 severely obese diabetic patients (4185 had bariatric surgery) from 3 HMO Research Network sites; (2) 23,000 subjects from the Nationwide Inpatient Sample; and (3) 18,000 subjects from the National Health Interview Survey linked to the National Death Index. In their analysis, they found a 45-year-old woman with diabetes and a BMI of 45 gained an additional 6.7 years of life expectancy with bariatric surgery. Sensitivity analysis revealed that the gain in life expectancy decreased with increasing BMI, until a BMI of 62 is reached, at which point nonsurgical treatment was associated with greater life expectancy. Similar results were seen for both men and women in all age groups. However, only 2.7% of the surgical cases had a BMI of 60 or more. It is possible though that diabetic patients with a BMI more than 60 may reap benefits from surgery, such as improved quality of life and reduced burden of obesity-associated diseases, which were not modeled.[35]

Cancer

In 2015, the World Cancer Research Fund has estimated that up to one-third of the cancer cases that occur in economically developed countries like the United States are related to overweight or obesity, physical inactivity, and/or poor nutrition and, thus, could be prevented.[36] Being overweight or obese is clearly linked with an increased risk of many cancers, including cancers of the breast in postmenopausal women, colon and rectum, endometrium, esophagus, kidney, and pancreas. In addition, having too much visceral fat (that is, a larger waistline), regardless of body weight, is linked with an increased risk of colon and rectal cancer and is probably linked to a higher risk of cancers of the pancreas, endometrium, and breast cancer (in women past menopause).[37]

Bariatric surgery patients have lower cancer rates and lower cancer mortality when compared with obese patients who have not had this surgery.[38]

In addition to the decrease in all-cause mortality reported by Adams and colleagues[19] in the previous discussion, their study also reported on the rate of death from cancer. After all deaths from cancer that occurred within the first 5 years after baseline were excluded, the reduction in the rate of death from any cause in the surgery group was 36% ($P<.001$) and the reduction in the rate of death from cancer was 46% ($P<.05$). After matching the surgery and nonsurgery groups and excluding prevalent cancers at baseline, the reduction in the rate of death from any cause was 38% (HR 0.62, 95% CI, 0.51–0.74) and the reduction in the rate of death from cancer was 61% (HR 0.39, 95% CI, 0.24–0.64).[19]

In 2013, Sjöström[39] published a review of the key results from the SOS trial. Although cancer was not a predefined secondary end point of the trial, it was found to be the most common cause of death among the study participants. The number of first-time cancers after inclusion was lower in the surgery group than in the control group (HR 0.67, 95% CI 0.53–0.85). The effect was more significant in women, with no effect of surgery on cancer-related mortality seen in men.[39]

A review and meta-analysis by Tee and colleagues[40] evaluated the RR of cancer in obese patients undergoing bariatric surgery versus obese control subjects. Six observational studies, including 51,740 subjects, found the RR in obese patients after undergoing surgery was 0.55 (95% CI, 0.41–0.73). The effect of bariatric surgery on cancer risk was modified by sex ($P = .021$). The pooled RR in women was 0.68 (95% CI 0.60–0.77) and in men was 0.99 (95% CI 0.74–1.32), again demonstrating the effect of bariatric surgery on oncologic outcomes is protective in women but not in men.

A second systematic review and meta-analysis released in 2014 by Casagrande and colleagues[41] also demonstrated reduced cancer risk in obese patients treated with bariatric surgery. Four controlled studies were selected with 11,087 patients in the bariatric surgery group and 20,720 patients in the control group. In these studies, bariatric surgery was associated with a reduction in the risk of cancer (OR 0.42, 95% CI 0.24–0.73). After adjusting for heterogeneity, the association between bariatric surgery and low cancer risk was maintained. Data from the surgery group of controlled[4] and uncontrolled[9] studies displayed a cancer incidence density rate of 1.06 cases per 1000 person-years in a postoperative follow-up period of 2 to 23 years.[41]

Although there is a lack of randomized controlled trials, there is an association between bariatric surgery and risk reduction for cancer. This association seems to affect women in a greater way.

Obesity's link to cardiovascular disease, diabetes, and certain cancers is clear and well documented. Obesity is also associated with an increased risk of numerous other comorbidities. In general, the risk of a comorbidity increases as the degree of obesity increases. The risk of developing a comorbidity with increasing weight varies by sex, racial/ethnic group, and genetic factors.[42] The figures depict the body systems that are impacted with obesity (**Fig. 3**).

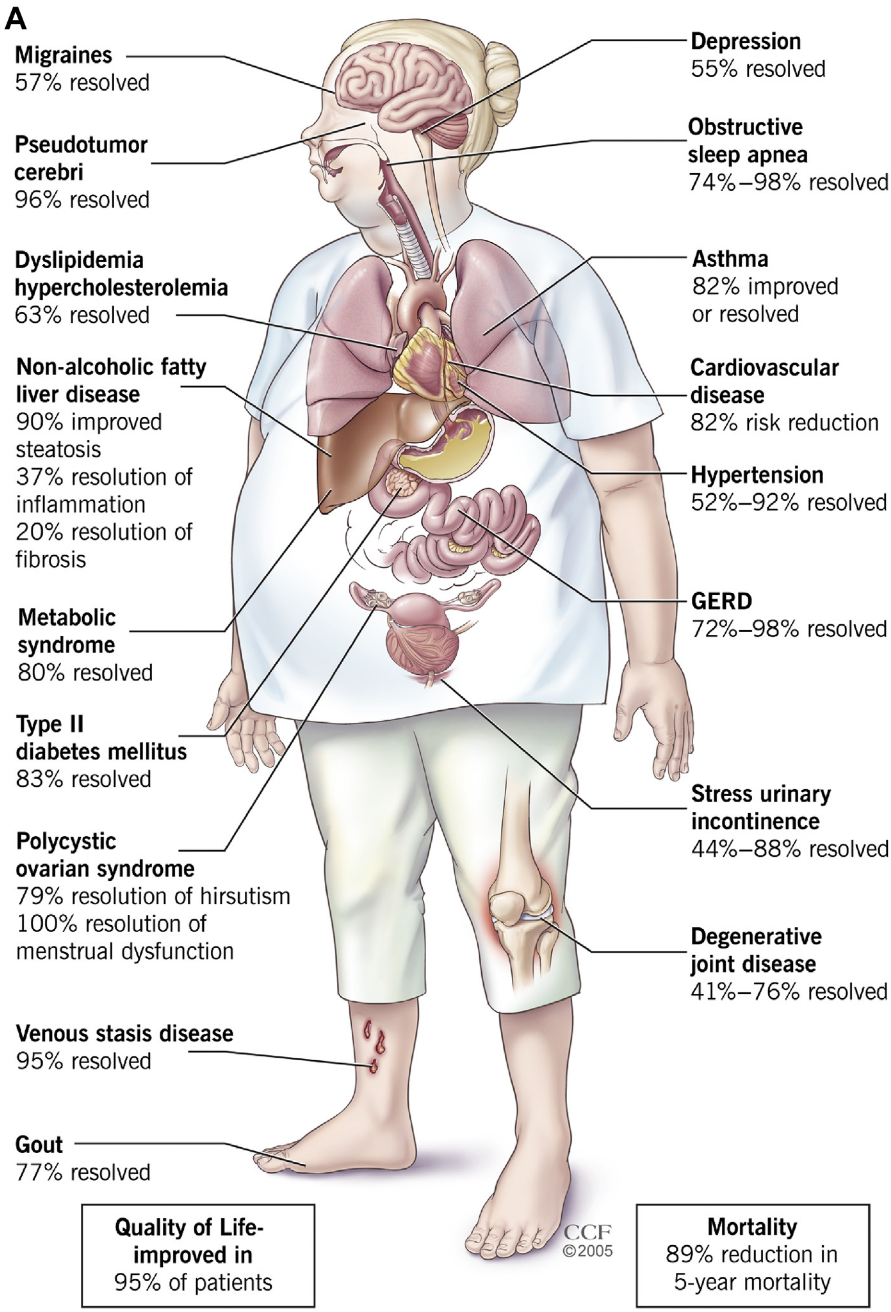

Fig. 3. (*A*) Body systems impacted by obesity in females. (*B*) Body systems impacted by obesity in males. (Copyright © The Cleveland Clinic Foundation 2014.)

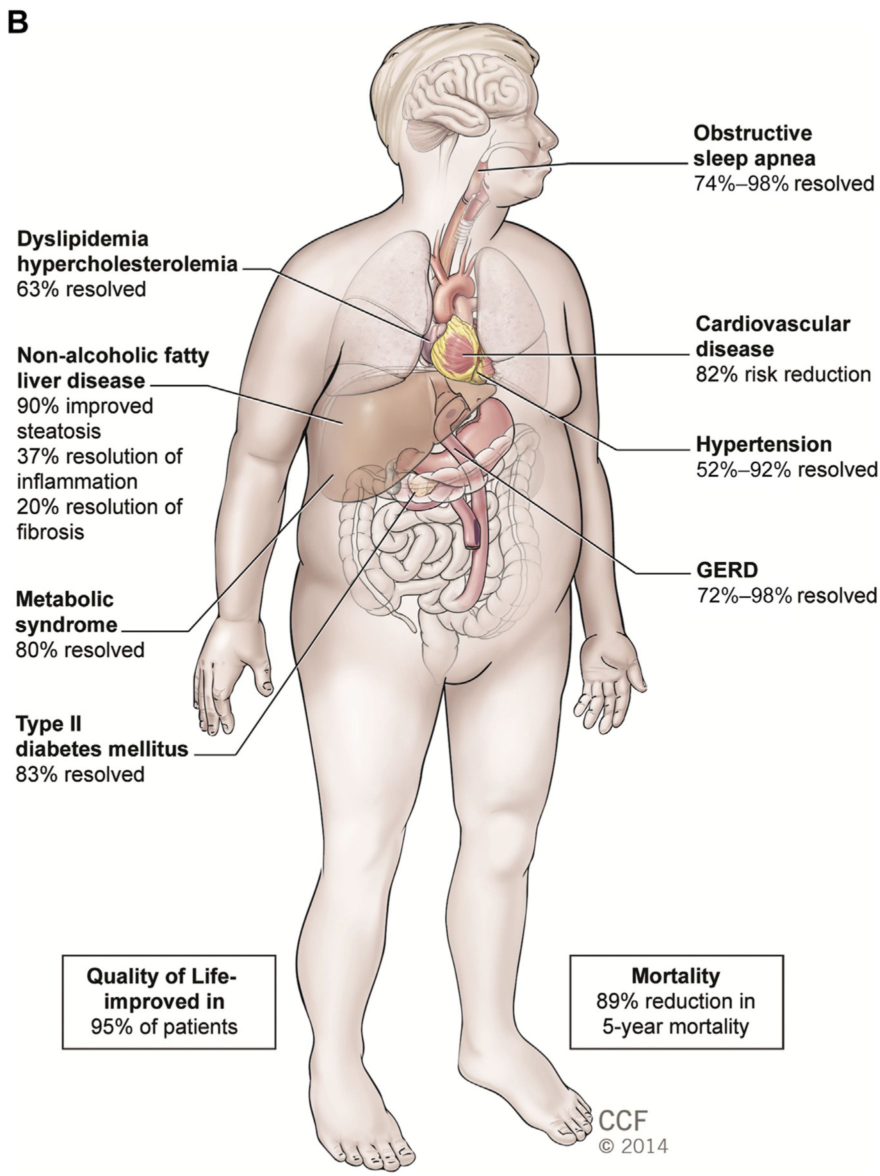

Fig. 3. (*continued*)

SUMMARY

Obesity and its impact on overall mortality is a significant public health burden in both the United States and world populations. Obesity has been identified as a leading modifiable risk factor for death attributed to cardiovascular disease, cancer, and stroke. Multiple studies have demonstrated the protective effect of bariatric surgery on reducing mortality. Studies have been primarily conducted in young women; however, the results were reproducible in older, obese men enrolled in VA medical centers.

In addition to increased mortality, obesity is linked to increased incidence of obesity-related comorbidities. Multiple studies have demonstrated improvement/resolution of weight-related comorbidities (ie, cardiovascular disease, diabetes, cancer, metabolic syndrome) after bariatric surgery. Some researchers have demonstrated a level of recalcitrance in remission of diabetes, particularly in patients with long-standing disease. More studies are needed to identify subgroups of patients that are at risk for nonresponsiveness to bariatric surgery. However, overall results are supportive of surgical cure of obesity as a treatment of weight-related comorbidities and mortality risk reduction.

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