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Original Investigation

Estimated GFR Before and After Bariatric Surgery in CKD

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Background: Several reviews have recently detailed the beneficial effects of weight loss surgery for kidney function. However, these studies have a number of limitations, including small sample size, few done in chronic kidney disease (CKD) stages 3 and 4, and many not including the main bariatric surgery procedures used in the United States today.

Study Design: This was an observational retrospective cohort study comparing propensity score–matched bariatric surgery patients and nonsurgery control patients who were referred for, but did not have, surgery. Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy were also compared using propensity matching.

Setting & Participants: Patients (714 surgery patients; 714 controls) were from a large integrated health care system, a mean of 58 ± 8 (SD) years old, and mostly women (77%) and non-Hispanic whites (56%) and had diabetes mellitus (66%) and/or hypertension (91%).

Predictor: Predictors at the time of surgery or referral to surgery were age, sex, race/ethnicity, weight, and presence of diabetes and/or hypertension.

Outcomes: The primary outcome for this study was change in estimated glomerular filtration rate (eGFR) from serum creatinine level over a median 3-year follow-up period.

Measurements: Serum creatinine was used to calculate eGFR using the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation.

Results: Surgery patients had 9.84 (95% CI, 8.05-11.62) mL/min/1.73 m^2 greater eGFRs than controls at a median 3 years' follow-up and RYGB patients had 6.60 (95% CI, 3.42-9.78) mL/min/1.73 m^2 greater eGFRs than sleeve gastrectomy patients during the same period.

Limitations: This study is limited by its nonrandomized observational study design, estimation of GFR, and large changes in muscle mass, which may affect serum creatinine level independent of changes in kidney function.

Conclusions: Bariatric surgery, especially the RYGB procedure, results in significant improvements for up to 3 years in eGFRs for patients with CKD stages 3 and 4.

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INDEX WORDS: Estimated glomerular filtration rate (eGFR); bariatric surgery; chronic kidney disease (CKD); obesity; eGFR trajectory; CKD stages 3-4; sleeve gastrectomy (SG); Roux-en-Y gastric bypass (RYGB); renal function; CKD progression.

Obesity-related mortality has surpassed that from tobacco, accounting for 6 million deaths annually.[1,2] It is estimated that part of the cost of severe obesity and its impact on life expectancy is due to severe illnesses (eg, chronic kidney disease [CKD], including end-stage renal disease [ESRD]). Patients with body mass index ≥ 40 kg/m^2 are more than 7 times more likely to develop ESRD than patients who are of normal weight.[3] In 2010, total Medicare expenditures for ESRD increased 8% to $32.9 billion.[4]

There is evidence that weight loss may prevent the progression of earlier stages of CKD to ESRD in some individuals.[5-7] Unfortunately, even with intensive multicomponent lifestyle interventions, only 50% of studies show a 5% weight loss (considered clinically meaningful) and most participants gain back at least half this lost weight over 18 to 30 months.[8] These outcomes have resulted in the development of surgical treatments, referred to as bariatric surgery, for severe obesity. A recent meta-analysis found that bariatric surgery resulted in significantly greater weight loss and higher rates of type 2 diabetes remission when compared with conventional weight loss methods.[9]

There has been growing interest in the effects of bariatric surgery on kidney function. Several reviews have recently been published[10-15] detailing the beneficial effects that weight loss surgery has on kidney function. However, there are a number of limitations in the literature to date. Most studies have 200 to 300 patients who are primarily non-Hispanic white, with only bypass and band operations, limited follow-up,

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and in primarily research academic medical settings. Three large population-based studies have been published: Swedish Obese Subjects (SOS),[16] patients from an existing statewide claims database,[17] and a recent study from an integrated health care system in the United States.[18] None of these studies included sleeve gastrectomy (SG), the most common procedure performed in the United States.[19] In addition, Johnson et al[17] studied only patients with type 2 diabetes for the development of microvascular complications (of which CKD was one), and Chang et al[18] studied all bariatric patients regardless of stage of kidney disease. No research has been published to date focusing solely on the impact of current United States bariatric procedures on advanced kidney disease.

To address these limitations, we conducted a large observational retrospective cohort study in a real-world clinical setting of 3-year outcomes for a diverse group of severely obese patients with CKD stages 3 and 4. Our primary hypothesis was that bariatric surgery would be associated with significant improvements in kidney function (operationalized by increased estimated glomerular filtration rate [eGFR]) when compared to nonsurgery controls. In addition, based on our previous work with metabolic syndrome and bariatric surgery,[20] we hypothesized that Roux-en-Y gastric bypass (RYGB) would be associated with significantly greater increases in eGFR than SG.

METHODS

Setting

Kaiser Permanente Southern California (KPSC) has 14 hospitals and nearly 200 other medical offices with a partnership of more than 5,700 physicians delivering care to more than 4 million members. Details of the bariatric surgery program at KPSC have been published elsewhere.[21] Briefly, more than 3,000 weight loss procedures are performed annually by 23 surgeons in 9 hospital facilities. Data about bariatric surgery patients at KPSC are maintained in a registry that contains electronic information from a number of sources (described in Measures section). Bariatric surgery patients at KPSC are similar to patients reported in national published findings from a variety of settings, with the exception that there is a much higher proportion of ethnic/racial minorities (55%) than in other published work.[22,23] All procedures were approved by the Institutional Review Board for Human Subjects at KPSC (study #10548). A waiver of consent was approved due to the minimal risk of the study.

Participants

Bariatric Surgery Patients

Bariatric surgery patients were eligible for the study if they had: (1) an RYGB or SG procedure from January 1, 2008, through December 31, 2012, without a history of a previous procedure or subsequent revisions of their initial procedure throughout the follow-up period (up to May 30, 2015); (2) body mass index $\geq$ 30 kg/m^2 at the time of surgery; and (3) eGFR of 11 to 59 mL/min/1.73 m^2 in the 12 months before the date of surgery (the eGFR value closest before the date of surgery meeting this criterion was used for baseline). We chose only RYGB and SG procedures because there were too few of the other primary procedures to study in the KPSC registry (ie, banding). We also chose not to study patients with eGFRs $<$ 11 mL/min/1.73 m^2 due to the risk for imminent dialysis, complicating any analysis of the effects of surgery on eGFR. Very few patients with this severity of CKD receive surgery at KPSC.

Of these surgery patients (n = 736), we eliminated those who were pregnant at the time of surgery and those who did not have serum creatinine measurements after 90 days following surgery when follow-up began (n = 22). The follow-up period did not begin until 90 days after surgery to avoid the direct effect of the surgical procedure on kidney and metabolic function. No patients were lost in the propensity matching (explained in the analysis section), so we had 714 surgery patients for the final analytic sample. The selection process for patients is shown in Fig 1.

Nonsurgery Control Patients

Initially, nonsurgery controls were selected based on the following criteria: (1) they had been referred for surgery January 1, 2008 to December 31, 2012, without a history of a bariatric procedure and did not go on to have a bariatric procedure at any time during the follow-up period (ending May 30, 2015); (2) had body mass index $\geq$ 30 kg/m^2 at the time of referral; and (3) had eGFR of 11 to 59 mL/min/1.73 m^2 in the 12 months before their referral date (the eGFR value closest in time before the referral date meeting this criterion was used for baseline).

From these control patients (n = 1,473), we eliminated those who were pregnant at the time of referral and those who did not have serum creatinine measurements after 90 days following their referral date when follow-up began (n = 62). After propensity matching, we had 714 nonsurgery control patients for the analyses. The selection process for patients is shown in Fig 1.

Measurements

All data for the study were abstracted from electronic medical records and outside claims processing databases. Data were collected from patients and entered into the electronic medical record by clinical staff as part of routine care. Date of birth, sex, and race/ethnicity were self-reported by patients. In general, height was self-reported by patients and weight and blood pressure were measured by clinical staff. Height and weight were used to calculate body mass index. Comprehensive prescription data were available for each drug sold at system pharmacies, as well as outpatient and inpatient laboratory results. Diagnoses were available for all types of health care use, including outpatient, inpatient, and emergency.

Analyses

Outcome Definition

Serum creatinine level was used to calculate eGFR. There are several equations that estimate GFR and can be applied retrospectively to readily obtainable data.[24] Although the most commonly used one is the NKF-KDOQI (National Kidney Foundation–Kidney Disease Outcomes Quality Initiative)–recommended 4-variable MDRD (Modification of Diet in Renal Disease) Study equation,[24-26] there are a number of limitations with its development, including that it does not predict with accuracy when eGFR is 60 to 90 mL/min/1.73 m^2.[25,27-31]

An alternative to the 4-variable MDRD Study equation is the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation.[32,33] A recent study by Friedman et al,[34] specifically testing GFR estimating equations for bariatric surgery patients, found that the most accurate estimates of GFR were obtained by using the CKD-EPI creatinine–cystatin C equation. However, if cystatin C level was not available (as was the case for our study), the CKD-EPI creatinine equation performed adequately. Friedman et al[34]