

# Fracture Risk After Roux-en-Y Gastric Bypass vs Adjustable Gastric Banding Among Medicare Beneficiaries

Elaine W. Yu, MD, MMSc; Seoyoung C. Kim, MD, ScD, MSCE; Daniel J. Sturgeon, MS; Katherine G. Lindeman, BA; Joel S. Weissman, PhD

**IMPORTANCE** Roux-en-Y gastric bypass (RYGB) is associated with significant bone loss and may increase fracture risk, whereas substantial bone loss and increased fracture risk have not been reported after adjustable gastric banding (AGB). Previous studies have had little representation of patients aged 65 years or older, and it is currently unknown how age modifies fracture risk.

**OBJECTIVE** To compare fracture risk after RYGB and AGB procedures in a large, nationally representative cohort enriched for older adults.

**DESIGN, SETTING, AND PARTICIPANTS** This population-based retrospective cohort analysis used Medicare claims data from January 1, 2006, to December 31, 2014, from 42 345 severely obese adults, of whom 29 624 received RYGB and 12 721 received AGB. Data analysis was performed from April 2017 to November 2018.

**MAIN OUTCOMES AND MEASURES** The primary outcome was incident nonvertebral (ie, wrist, humerus, pelvis, and hip) fractures after RYGB and AGB surgery defined using a combination of *International Classification of Diseases, Ninth Edition* and *Current Procedural Terminology 4* codes.

**RESULTS** Of 42 345 participants, 33 254 (78.5%) were women. With a mean (SD) age of 51 (12) years, recipients of RYGB were younger than AGB recipients (55 [12] years). Both groups had similar comorbidities, medication use, and health care utilization in the 365 days before surgery. Over a mean (SD) follow-up of 3.5 (2.1) years, 658 nonvertebral fractures were documented. The fracture incidence rate was 6.6 (95% CI, 6.0-7.2) after RYGB and 4.6 (95% CI, 3.9-5.3) after AGB, which translated to a hazard ratio (HR) of 1.73 (95% CI, 1.45-2.08) after multivariable adjustment. Site-specific analyses demonstrated an increased fracture risk at the hip (HR, 2.81; 95% CI, 1.82-4.49), wrist (HR, 1.70; 95% CI, 1.33-2.14), and pelvis (HR, 1.48; 95% CI, 1.08-2.07) among RYGB recipients. No significant interactions of fracture risk with age, sex, diabetes status, or race were found. In particular, adults 65 years and older showed similar patterns of fracture risk to younger adults. Sensitivity analyses using propensity score matching showed similar results (nonvertebral fracture: HR 1.75; 95% CI, 1.22-2.52).

**CONCLUSIONS AND RELEVANCE** This study of a large, US population-based cohort including a substantial population of older adults found a 73% increased risk of nonvertebral fracture after RYGB compared with AGB, including increased risk of hip, wrist, and pelvis fractures. Fracture risk was consistently increased among RYGB patients vs AGB across different subgroups, and to a similar degree among older and younger adults. Increased fracture risk appears to be an important unintended consequence of RYGB.

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**Author Affiliations:** Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (Yu, Lindeman); Division of Pharmacoepidemiology and Pharmacoeconomics; Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (Kim); Division of Rheumatology, Immunology and Allergy; Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (Kim); Center for Surgery and Public Health; Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (Sturgeon, Weissman).

**Corresponding Author:** Elaine W. Yu, MD, MMSc, Endocrine Unit, Massachusetts General Hospital, 50 Blossom St, Thier 1051, Boston, MA 02114 (ewyu@mgh.harvard.edu).

Use of bariatric surgery procedures has increased owing to the growing obesity crisis.<sup>1-3</sup> Numerous studies, including randomized clinical trials, have demonstrated that bariatric surgery is a superior and cost-effective treatment for severe obesity compared with lifestyle and medical treatments.<sup>4-7</sup> The Centers for Medicare & Medicaid Services has approved the use of bariatric surgery in adults with body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) greater than 35 and at least 1 obesity-related comorbidity.<sup>8</sup> Recent data, however, demonstrate that certain bariatric procedures are associated with development of metabolic bone disease.<sup>9,10</sup> In particular, Roux-en-Y gastric bypass (RYGB) is associated with high-turnover bone loss with significant, long-term declines in bone density and deterioration of microarchitecture.<sup>11-15</sup> In contrast, most studies have observed no increases in bone turnover markers and minimal bone loss after adjustable gastric banding (AGB), a purely restrictive bariatric procedure.<sup>16-18</sup> Adjustable gastric banding is a less-invasive procedure that typically involves less weight loss than RYGB.<sup>19</sup> Whereas studies consistently report that AGB and other restrictive procedures do not increase fracture risk,<sup>20-22</sup> there is more concern and less consensus about fracture risk after RYGB, with some studies finding no statistically significant association with fracture risk<sup>20,22,23</sup> and others associating RYGB with increased fracture risk.<sup>24-26</sup>

Current studies of fracture risk among patients who have undergone bariatric surgery have little representation of older adults. Nevertheless, these procedures are increasingly being offered to adults 60 years and older,<sup>27</sup> especially as complication rates from bariatric surgical procedures continue to decline.<sup>28</sup> One large study of 119 US academic medical centers documented that more than 10% of all bariatric procedures are performed in adults 60 years and older.<sup>29</sup> Older adults have higher baseline risks of osteoporosis and fracture and may have increased vulnerability to bone loss after bariatric surgery.<sup>12</sup> It is unknown whether older age modulates the association between bariatric surgery and fractures.

We sought to determine the magnitude of RYGB-associated fracture risk among a population enriched for older adults. We took advantage of the observation that AGB is associated with neutral bone outcomes to compare fracture risk between these 2 popular bariatric procedures and to minimize confounding by indication for bariatric surgery. We hypothesized that RYGB would increase the risk of fracture compared with AGB, and that older adults would have greater increases in fracture risk after RYGB.

## Methods

### Data Source

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. We performed a cohort study using longitudinal Medicare claims data for procedures performed from January 1, 2006, to December 31, 2014. Medicare, a federal health insurance program in the United States, provides coverage for

## Key Points

**Question** How does the fracture risk associated with Roux-en-Y gastric bypass compare with that of adjustable gastric banding among older adults?

**Findings** This cohort study analyzed claims data from 42 345 Medicare beneficiaries from 2006 to 2014 and found a 73% increased risk of nonvertebral fracture among adults who received Roux-en-Y gastric bypass compared with those who received adjustable gastric banding.

**Meaning** Although bariatric surgery is associated with health benefits, increased fracture risk is an important factor to consider for patients seeking Roux-en-Y gastric bypass.

legal residents 65 years and older, patients younger than 65 years of age with certain disabilities, and those with end-stage renal disease requiring dialysis or transplant. Qualifying disabilities include obesity-associated musculoskeletal, cardiovascular, and respiratory impairments that limit basic work-related activities.<sup>30</sup> We included claims from Part A (inpatient care), Part B (physician's services and outpatient care), and Part D (outpatient prescription drug coverage). The Partners Health Care Institutional Review Board approved the study protocol and informed consent was deemed to be unnecessary because the study data were deidentified.

### Study Cohort

Our study eligibility encompassed adults with severe obesity (BMI  $\geq 40$ ; *International Classification of Diseases, Ninth Revision [ICD-9] code 278.0*, also defined as "morbid obesity due to excess calories") who were undergoing either RYGB (*Current Procedural Terminology [CPT] codes 43644-45, 43846-47*) or AGB (*CPT code 43770*). Inclusion criteria were age 21 years and older at date of surgery and at least 1 severe obesity *ICD-9* code before surgery code. Exclusion criteria included less than 365 days of insurance eligibility in Part A, B, or D before index (surgery) date (which would preclude assessment of baseline covariates), cancer or chemotherapy, renal disease or transplant, other gastric surgery (*CPT codes 43842, 43775, 43845, 43633*), or residence in a long-term care facility in the 365 days before the index date. Beneficiaries with Medicare Advantage (Part C, administered by private health insurance companies) were not included in this cohort owing to lack of available claims data.

### Outcome Definition

The primary outcome of interest was incident nonvertebral fracture, defined using a combination of *ICD-9* and *CPT-4* codes (eTable 1 in the Supplement) to identify fractures of the humerus, wrist, hip, and pelvis. These claims-based algorithms have been shown to have high positive predictive value for these types of fracture.<sup>31,32</sup> Secondary analyses included evaluation of site-specific fracture risk. We did not assess vertebral fracture outcomes, owing to challenges in identifying incident cases of vertebral fractures accurately using claims data.<sup>33</sup>

Patients were followed up from the index date until the earliest occurrence of one of the following events: primary outcome (any nonvertebral fracture), admission to long-term care

facility, second bariatric surgery code occurring more than 90 days after index date, death, or end of the database.

### Covariates

We assessed potentially confounding covariates associated with type of surgery and fracture risk in the 365 days before surgery date. Covariates of interest included age, sex, year of surgery, geographical region, race, diabetes, bone-modifying comorbidities and medications, diagnosis of osteoporosis or use of antiosteoporotic medication, history of fall, bone mineral density testing, and markers of health care utilization intensity. In addition, we calculated a comorbidity score that combined more than 20 conditions in the Charlson and Elixhauser measures.<sup>34</sup>

### Statistical Analyses

We compared baseline characteristics of the 2 surgical groups using standardized differences (the absolute difference of the means divided by the within-group SDs), with an absolute standardized mean difference less than 0.1 considered as well balanced between the groups.<sup>35</sup> We calculated incidence rates (IRs) per 1000 person-years for any nonvertebral fracture and site-specific fractures of the hip, pelvis, wrist, and humerus in the 2 surgical groups. Fracture survival curves were estimated using the Kaplan-Meier method. We performed multivariable Cox regression analyses to estimate hazard ratios (HRs) for overall and site-specific fractures in the RYGB group, using the AGB group as the reference population. The proportional hazards assumption was tested by including an interaction term between surgery type and follow-up time, and was not violated in any of the models.

We further assessed interactions by age, sex, race, and diabetes status on fracture risk. To assess fracture risk within an older population, subgroup analyses for overall and site-specific fracture were performed in patients 65 years or older. Further sensitivity analyses were performed on a propensity-score (PS)-matched subset of the overall cohort.<sup>36</sup> Multivariable logistic regression estimated the PS for receiving RYGB vs AGB for each patient using the baseline covariates presented in Table 1. We used nearest neighbor matching within a caliper of 0.05 on the PS scale to pair RYGB and AGB recipients with a ratio of 1:1.<sup>37</sup> Cox proportional hazards models were then used to calculate HRs of fracture within this PS-matched cohort. A 2-sided  $P < .05$  was considered significant for all analyses. All analyses were performed using SAS version 9.4 statistical software (SAS Institute Inc).

## Results

### Cohort Selection and Characteristics

We identified 3 908 991 patients with severe obesity, of whom 151 979 had undergone bariatric surgery (Figure 1). After applying our eligibility criteria, our final cohort included 29 624 patients who received RYGB and 12 721 patients who received AGB. Most exclusions occurred owing to the lack of continuous enrollment in Medicare Part D. With a mean (SD) age of 51 (12) years, recipients of RYGB were younger than AGB recipi-

ents (55 [12] years). Both surgical groups showed similar female predominance (RYGB, 78.8%; AGB, 77.9%)

The baseline characteristics for patients receiving RYGB and AGB are given in Table 1. Patients who underwent RYGB were more likely to have fatty liver disease, but otherwise had similar rates of other comorbidities such as hypertension, diabetes, and chronic obstructive pulmonary disease compared with those with AGB. The combined comorbidity scores between RYGB and AGB recipients were similar, and both groups showed similar use of prescription medications, including proton pump inhibitors, oral glucocorticoids, thiazolidinediones, and insulin. Health care utilization also did not differ significantly between RYGB and AGB patients.

Mean (SD) follow-up was 3.3 (2.2) years in the RYGB group and 3.9 (2.1) in the AGB group. Within the AGB group, 600 patients (4.7%) were censored after the index date owing to receiving a second bariatric operation, as opposed to 149 (0.5%) within the RYGB group.

### Risk of Fracture

There were 658 total fracture events among both RYGB and AGB groups during the follow-up period (Table 2). The overall IR for any nonvertebral fracture was 6.6 per 1000 person-years (95% CI, 6.0-7.2) for RYGB recipients, compared with 4.6 per 1000 person-years (95% CI, 3.9-5.3) for AGB recipients. The increased risk of nonvertebral fracture among RYGB recipients compared with AGB recipients (Figure 2) persisted after multivariable adjustment, with an adjusted HR of 1.73 (95% CI, 1.45-2.08). Skeletal site-specific analyses demonstrated an increased risk of fracture at the hip (HR, 2.81; 95% CI, 1.82-4.49), wrist (HR, 1.70; 95% CI, 1.33-2.14), and pelvis (HR, 1.48; 95% CI, 1.08-2.07) (Table 3).

In subgroup analyses of patients 65 years and older, the IR for any nonvertebral fracture was 9.9 per 1000 person-years (95% CI, 7.6-11.7) among patients who underwent RYGB and 5.3 per 1000 person-years (95% CI, 3.6-6.7) among those who underwent AGB. Multivariable-adjusted HR within this older subgroup revealed that RYGB was associated with a similar increased risk of fractures as in the overall Medicare cohort. In particular, RYGB recipients 65 years and older had an increased risk of any nonvertebral fracture (HR, 1.75; 95% CI, 1.22-2.52), hip fracture (HR, 2.51; 95% CI, 1.25-5.93), and wrist fracture (HR, 1.65; 95% CI, 1.25-2.77) compared with AGB recipients 65 years and older.

We examined whether sex, age, diabetes, or race modified the association between RYGB and fracture risk. Although higher IRs of fracture in both RYGB and AGB groups were predictably seen among patients who were older, female, and of white race, we found no significant interactions of HR with sex, age, diabetes, or race (eFigure 1 in the Supplement).

We performed sensitivity analyses with a propensity score (PS)-matched cohort of 12 183 pairs of RYGB and AGB recipients to better balance for potential baseline differences. All baseline characteristics were similar between the 2 groups after PS matching (eTable 2 in the Supplement). Within this PS-matched cohort, we found that RYGB was associated with a greater risk of nonvertebral fracture (HR, 1.68; 95% CI, 1.38-2.05) vs AGB, to a similar degree as in the main Medicare

Table 1. Baseline Characteristics in 365 Days Before RYGB or AGB Surgery Within Main Medicare Cohort

Characteristic	RYGB (n = 29 624)	AGB (n = 12 721)	RYGB vs AGB, Standardized Difference of the Means <sup>a</sup>
Demographic characteristics			
Age, mean (SD), y	51 (12)	55 (12)	0.287
Female, No. (%)	23332 (78.8)	9915 (77.9)	-0.020
Geographic region, No. (%)			0.106
Midwest	8101 (27.3)	2988 (23.5)	NA
Northeast	5361 (18.1)	2195 (17.3)	NA
South	11 171 (37.7)	5361 (42.1)	NA
West	4964 (16.8)	2168 (17.0)	NA
Combined comorbidity score, <sup>b</sup> mean (SD)	1.1 (1.7)	0.9 (1.7)	-0.090
Comorbidities, No. (%)			
Hypertension	18 880 (63.7)	8027 (63.1)	0.013
Hyperlipidemia	14 700 (49.6)	6331 (49.8)	-0.003
Diabetes	6574 (22.2)	2767 (21.8)	0.011
COPD	9216 (31.1)	3678 (28.9)	0.048
Smoking	4536 (15.3)	1635 (12.9)	0.071
CHD	6698 (22.6)	3166 (24.9)	-0.054
Fatty liver	2890 (9.8)	861 (6.8)	0.109
Osteoporosis	730 (2.5)	415 (3.3)	-0.048
Medications, No. (%)			
Antihypertensives	11 107 (37.5)	5382 (42.3)	-0.098
NSAIDs	9640 (32.5)	4399 (34.6)	-0.043
SSRIs	8761 (29.6)	3867 (30.4)	-0.018
PPIs	8072 (27.2)	3529 (27.7)	-0.011
Benzodiazepines and other sleeping pills	4139 (14.0)	1837 (14.4)	-0.013
Statins	8788 (29.7)	4266 (33.5)	-0.083
Oral glucocorticoids	6625 (22.4)	3086 (24.3)	-0.045
β-Blockers	5173 (17.5)	2630 (20.7)	-0.082
Thyroid medications	3975 (13.4)	2003 (15.7)	-0.066
TZDs	10 606 (35.8)	5029 (39.5)	-0.077
Insulin	4352 (14.7)	1631 (12.8)	0.054
Osteoporosis medications	422 (1.4)	302 (2.4)	-0.070
Health care utilization, mean (SD)			
No. of physician visits	5.1 (7.8)	4.9 (7.3)	-0.027
No. of hospitalizations	0.14 (0.50)	0.16 (0.52)	0.033
No. of ED visits	0.8 (1.9)	0.7 (2.5)	-0.027
BMD ordered, No. (%)	1211 (4.1)	722 (5.7)	-0.074

Abbreviations: AGB, adjustable gastric banding; BMD, bone mineral density measurement; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; ED, emergency department; NA, not applicable; NSAIDs, nonsteroidal anti-inflammatory drugs; PPIs, proton pump inhibitors; RYGB, Roux-en-Y gastric bypass; SSRIs, selective serotonin reuptake inhibitors; TZDs, thiazolidinediones.

<sup>a</sup> The absolute difference of the means divided by the within-group SDs.

<sup>b</sup> Higher score indicates greater number of comorbidities.

cohort (eFigure 2 in the Supplement), including significantly increased risk fracture at the hip (HR, 2.51; 95% CI, 1.57-4.16) and wrist (HR, 1.66; 95%CI, 1.38-2.05) (eTable 3 in the Supplement).

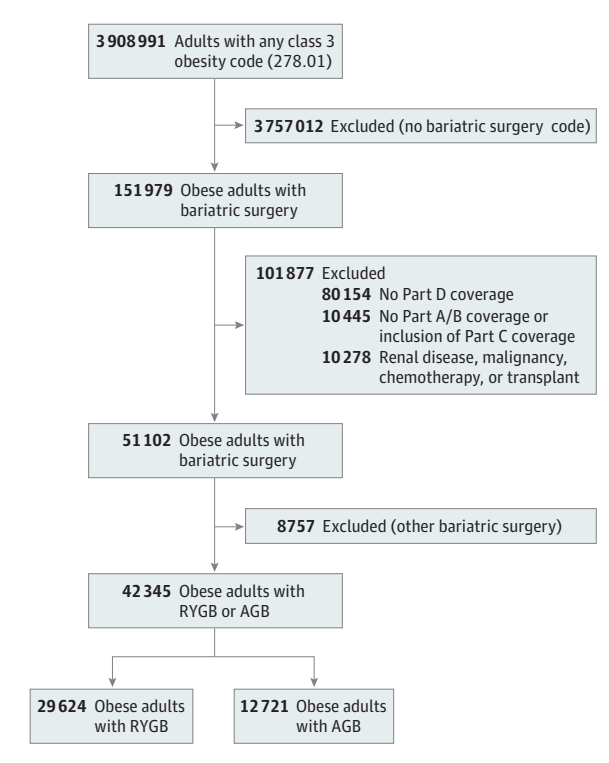
## Discussion

In this cohort analysis of 42 345 bariatric patients enrolled in Medicare, we found a 73% increased risk of nonvertebral fractures after RYGB vs AGB, especially at the hip and wrist. This increased risk was maintained in patients 65 years and older and included a 151% increased risk of hip fracture. Fracture risk was increased equally among RYGB recipients regardless of sex,

age, diabetes status, or race. Results from PS-matched analyses were also consistent.

This study provides clinically valuable information to the bariatric field by providing RYGB-specific analyses of fracture outcomes. Most previous studies involved mixed populations of bariatric surgery procedures.<sup>20,22,23</sup> It is critical to study the bariatric procedures separately given the known differential rates of bone loss and fractures.<sup>9,10</sup> Roux-en-Y gastric bypass is associated with high-turnover bone loss, with bone density and skeletal microarchitectural declines that persist for up to 5 years after surgery,<sup>11</sup> whereas significant changes in bone markers and bone density have not been reported after AGB.<sup>16-18</sup> Bariatric studies that have a predominance of AGB procedures have accordingly found no association with

Figure 1. Study Flow Diagram.



AGB indicates adjustable gastric banding and RYGB, Roux-en-Y gastric bypass.

fracture risk.<sup>22,23</sup> Furthermore, subset analyses focused on AGB and other restrictive bariatric procedures found no fracture signal.<sup>20-22</sup> Various studies have reported fractures rates within RYGB subsets, but earlier study populations included fewer than 1000 RYGB recipients.<sup>20-22,24</sup> Limited power may thus explain why many of these earlier studies were unable to detect statistically significant increases in fractures in RYGB subset analyses.<sup>20-22</sup> Two previous studies were powered to evaluate RYGB-specific fracture risk in large population data sets (albeit with younger patients), one from a US-based commercial database<sup>25</sup> and the other from a Swedish national database.<sup>26</sup> Their results show a magnitude and pattern of increased fracture risk that is similar to what we observed in the Medicare population. In particular, these studies support our finding of more hip and upper-extremity fractures after RYGB, although the Swedish study found a paradoxically reduced risk of lower-leg fracture.<sup>26</sup>

Our current study presents, to our knowledge, the first analysis to specifically assess fracture risk among RYGB recipients older than 65 years. A substantial limitation to all previous bariatric studies has been the focus on a predominantly young population, with mean ages ranging from 32 to 47 years.<sup>20-26</sup> For example, 6% and 3% of the earlier RYGB-specific cohorts were aged 60 years or older.<sup>25,26</sup> Yet older adults are seeking bariatric surgery with increasing frequency.<sup>27-29</sup> We had hypothesized that older adults would be more susceptible to fractures after RYGB given signals indicating that postmenopausal women have greater bone loss after RYGB surgery than younger women.<sup>12</sup> In our Medicare

cohort, which is enriched for older patients, we discovered that older age did not further magnify RYGB-associated fracture risk. Nevertheless, although the relative hazard of fracture was similar among younger and older RYGB recipients, the greater baseline rate of fractures among patients 65 years and older led to quantitatively more fractures among older patients who received RYGB. The large increase in hip fracture risk (HR, 2.51) is of particular concern among an older population that is more vulnerable to morbidity and mortality as a consequence of these fractures.<sup>38</sup>

The mechanism of increased fracture risk after RYGB is likely multifactorial. We determined that neither diabetes, nor sex, nor race modified the HR for fracture after RYGB, which suggests that these variables do not directly interact with the pathologic mechanism(s). Skeletal unloading from weight loss as well as surgically induced calcium malabsorption may play contributing roles. Roux-en-Y gastric bypass leads to greater weight loss than AGB,<sup>39</sup> but we were unable to directly assess the association between weight loss and fracture risk owing to lack of weight data in Medicare claims. However, multiple lines of evidence from clinical and animal studies suggest that weight loss and secondary hyperparathyroidism are not the primary drivers of high-turnover bone loss.<sup>11,40,41</sup> Many RYGB-associated alterations in gut hormones, metabolism, and the microbiome have the potential to directly alter bone physiology,<sup>42,43</sup> although to date none has been causally proven to instigate bone loss after RYGB. Several studies also suggested an increased risk of injurious falls after RYGB,<sup>26,44</sup> which suggests that nonskeletal factors may contribute to fracture incidence. Given the profusion of factors that may influence skeletal fragility, the appropriate management strategy to prevent RYGB-associated fractures is not clear. Guidelines for health management in patients who received bariatric surgery recommend lifelong calcium citrate and vitamin D supplementation.<sup>45</sup> Studies have demonstrated that lack of supplementation can substantially increase the risk of osteomalacia and hasten bone loss, but use of high-dose supplements cannot by itself prevent bone loss.<sup>46,47</sup> Exercise programs and protein supplementation to maintain lean mass may also be beneficial for skeletal health in the RYGB population.<sup>48</sup> Bone density screening for RYGB recipients is controversial, but guidelines do suggest assessment of bone density after surgery.<sup>45</sup> We previously documented that bone density scans are ordered in 11% of postoperative RYGB recipients.<sup>25</sup> In theory, careful use of antiresorptive osteoporosis agents could inhibit high bone turnover associated with RYGB, but no trials have been conducted to test the safety and efficacy of this therapeutic strategy.

### Strengths and Limitations

Strengths of the present study are the large size of this nationally representative cohort with analyses of RYGB-specific fracture outcomes. Unlike previous cohorts, this study is also enriched with older patients, which allowed us to perform age-stratified analyses. In addition, we used an active surgical comparator group as opposed to a nonsurgical control group, which reduced confounding by indication for bariatric surgery. Identifying an appropriately BMI-matched nonsurgical group is

Table 2. Incidence Rates and HRs for Fracture After RYGB and AGB Within the Main Medicare Cohort

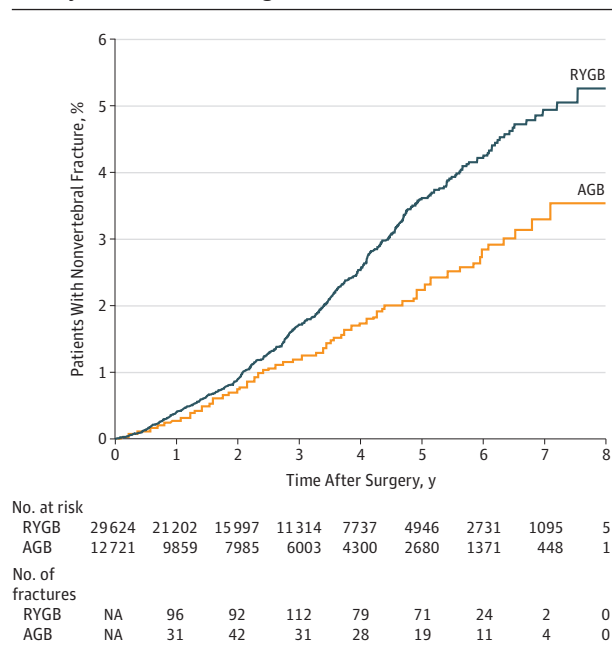
Outcome	No. of Events	Person-Years	Incidence Rate/1000 Person-Years (95% CI)	HR (95% CI)		
				Unadjusted	Age, Sex-Adjusted	Fully Adjusted <sup>a</sup>
Any fracture						
RYGB	491	74 243	6.6 (6.0-7.2)	1.48 (1.24-1.77)	1.68 (1.41-2.01)	1.73 (1.45-2.08)
AGB	167	36 592	4.6 (3.9-5.3)	1 [Reference]	1 [Reference]	1 [Reference]
Wrist fracture						
RYGB	270	74 243	3.6 (3.2-4.1)	1.43 (1.14-1.82)	1.61 (1.27-2.05)	1.70 (1.33-2.14)
AGB	95	36 592	2.6 (2.1-3.2)	1 [Reference]	1 [Reference]	1 [Reference]
Hip fracture						
RYGB	103	74 243	1.4 (1.1-1.7)	2.10 (1.38-3.31)	2.92 (1.91-4.65)	2.81 (1.82-4.49)
AGB	25	36 592	0.7 (0.4-1.0)	1 [Reference]	1 [Reference]	1 [Reference]
Humerus fracture						
RYGB	34	74 243	0.5 (0.3-0.6)	1.21 (0.66-2.33)	1.43 (0.77-2.77)	1.49 (0.80-2.92)
AGB	14	36 592	0.4 (0.2-0.6)	1 [Reference]	1 [Reference]	1 [Reference]
Pelvis fracture						
RYGB	166	74 243	2.2 (1.9-2.6)	1.30 (0.96-1.80)	1.37 (1.00-1.91)	1.48 (1.08-2.07)
AGB	62	36 592	1.7 (1.3-2.1)	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: AGB, adjustable gastric banding; HR, hazard ratio; RYGB, Roux-en-Y gastric bypass.

<sup>a</sup> Adjusted for age, race, region, sex, year, chronic obstructive pulmonary disease, fall, hypertension, proton pump inhibitors, smoking, stroke, coronary heart disease, heart failure, osteoporosis, chronic kidney disease, drug count,

anticonvulsants, diuretics, insulin, opioids, statins, antidiabetic medications, benzodiazepines, β-blockers, selective serotonin reuptake inhibitors, nonsteroidal anti-inflammatory drugs, oral glucocorticoids, bone mineral density testing, emergency department visits, outpatient visits, acute care hospitalizations, prior fracture, and reason for eligibility.

Figure 2. Nonvertebral Fracture After Roux-en-Y Gastric Bypass (RYGB) and Adjustable Gastric Banding (AGB)



Kaplan-Meier curves illustrate time to fracture and corresponding patient populations in which the fractures occurred.

uniquely difficult when using claims databases owing to selection bias in who receives a severe obesity diagnosis as well as inaccuracies in obesity coding of BMI categories.<sup>49,50</sup> Different classes of obesity have a complex association with skeletal

health and fractures,<sup>51</sup> but our use of an active surgical comparator group likely minimized baseline BMI differences between groups despite our inability to directly match for baseline weight. Finally, we used rigorous methodology that demonstrated the robustness of our findings across subgroups and within a PS-matched cohort.

Our study has limitations. First, we did not include vertebral fracture as an outcome owing to an inability to accurately classify incident vertebral fracture. Second, a large proportion of the cohort had disability as the reason for Medicare eligibility, which may limit the generalizability of the results. Nevertheless, it is possible that some of these younger patients qualified for disability based on obesity-related chronic conditions; furthermore, subset analysis within the group of adults who qualified for Medicare based on age verifies results similar to the overall cohort. Third, although we adjusted for many known factors that may confound the association between bariatric surgery and fractures, there may still be residual confounding. In particular, there may be confounding by indication, such that older and more frail patients preferentially receive AGB. Indeed, we found that the mean age of patients who received AGB was 4 years older than those who received RYGB. However, this confounding would bias results toward the null hypothesis, whereas we found that RYGB recipients had higher fracture risk in both unadjusted and adjusted analyses. Finally, although sleeve gastrectomy has recently eclipsed RYGB in popularity<sup>1</sup> and may also be associated with adverse skeletal effects,<sup>9,10,20,52</sup> it is a relatively new procedure and our database did not have sufficient numbers or length of follow-up to characterize fracture outcomes in this population.

Table 3. Incidence Rates and HRs for Fracture in a Cohort Aged 65 Years and Older

Outcome	No. of Events	Person-Years	Incidence Rate/1000 Person-Years (95% CI)	HR (95% CI)		
				Unadjusted	Age, Sex-Adjusted	Fully Adjusted HR <sup>a</sup>
Any fracture						
RYGB	88	9132	9.9 (7.6-11.7)	1.86 (1.32-2.66)	1.93 (1.37-2.77)	1.75 (1.22-2.52)
AGB	49	9302	5.3 (3.8-6.7)	1 [Reference]	1 [Reference]	1 [Reference]
Wrist fracture						
RYGB	42	9132	4.6 (3.2-6.0)	1.66 (1.02-2.74)	1.70 (1.04-2.81)	1.65 (1.25-2.77)
AGB	26	9302	2.8 (1.7-3.9)	1 [Reference]	1 [Reference]	1 [Reference]
Hip fracture						
RYGB	30	9132	3.3 (2.1-4.5)	2.91 (1.50-6.09)	3.22 (1.65-6.77)	2.51 (1.25-5.93)
AGB	Censored <sup>b</sup>	Censored <sup>b</sup>	1.2 (0.5-1.9)	1 [Reference]	1 [Reference]	1 [Reference]
Humerus fracture						
RYGB	Censored <sup>b</sup>	Censored <sup>b</sup>	0.44 (0.01-0.87)	0.55 (0.14-1.83)	0.60 (0.16-2.0)	0.40 (0.09-1.64)
AGB	Censored <sup>b</sup>	Censored <sup>b</sup>	0.75 (0.20-1.31)	1 [Reference]	1 [Reference]	1 [Reference]
Pelvis fracture						
RYGB	33	9302	3.6 (2.4-4.8)	1.67 (0.87-3.33)	1.64 (0.85-3.29)	1.75 (0.89-3.56)
AGB	17	9132	1.9 (1.0-2.7)	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: AGB, adjustable gastric banding; HR, hazard ratio; RYGB, Roux-en-Y gastric bypass.

<sup>a</sup> Adjusted for age, race, region, sex, year, chronic obstructive pulmonary disease, fall, hypertension, proton pump inhibitors, smoking, stroke, chronic heart disease, heart failure, osteoporosis, chronic kidney disease, drug count, anticonvulsants, diuretics, insulin, opioids, statins, antidiabetic medications,

benzodiazepines,  $\beta$ -blockers, selective serotonin reuptake inhibitors, nonsteroidal anti-inflammatory drugs, oral glucocorticoids, bone mineral density testing, emergency department visits, outpatient visits, acute care hospitalizations, previous fracture, and reason for eligibility.

<sup>b</sup> Censored because there were fewer than 11 events.

## Conclusions

In a large US population-based cohort of 42 345 severely obese patients, RYGB was associated with an increased risk of non-vertebral fractures, including hip, wrist, and pelvis fractures compared with AGB. Older adults in our analysis had similar RYGB-associated increases in fracture risk as younger adults.

Thus, although bariatric surgery is associated with myriad health benefits, increased fracture risk is an important factor to discuss with patients seeking RYGB, and aggressive management of bone health (eg, bone density scans, calcium and vitamin D supplementation and physical activity) is warranted. Additional trials are required to evaluate pharmacologic strategies that can mitigate fracture risk after RYGB, particularly among older patients and those with higher baseline fracture risk.

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