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Impact of Sleeve Gastrectomy on Hip Structural Analysis in Adolescents and Young Adults with Obesity

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Abstract

Background: Sleeve gastrectomy (SG), the most commonly performed metabolic and bariatric surgery (MBS), is associated with reductions in areal bone mineral density (aBMD) at multiple sites, and changes in bone structure at the distal radius and tibia without reductions in strength estimates at these peripheral sites. Data are lacking regarding effects on hip strength estimates.

Objective: To evaluate effects of SG on measures of hip structural analysis (HSA) in adolescents and young adults over 12 months using dual energy x-ray absorptiometry (DXA).

Settings: Translational and Clinical Research Center

Methods: We enrolled 48 youth 14–22 years old with moderate-to-severe obesity; 24 underwent SG and 24 controls were followed without surgery (18 females, 6 males in each group). Hip structure was assessed using DXA at baseline and 12 months. Analyses are adjusted for age, sex, race and the baseline bone measure.

Results: The SG group lost 25.9% body weight versus 0.3% in controls. Compared to controls, SG had reductions in narrow neck, intertrochanteric and femoral shaft BMD Z-scores ($p = 0.012$). Further, SG had greater reductions in narrow neck and intertrochanteric region (but not femoral

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shaft) cross-sectional area, cortical thickness, cross-sectional moment of inertia and section modulus, and increases in buckling ratio ($p = 0.039$). Differences were attenuated after adjusting for 12-month body mass index (BMI) change. At 12 months, differences were minimal after adjusting for age, sex, race and weight.

Conclusions: Over 12 months, SG had negative effects at the narrow neck and intertrochanteric regions of the hip, but not the femoral shaft. Reduced BMI may compensate for these deleterious effects on bone.

Keywords

Hip structural analysis; adolescents; metabolic and bariatric surgery; sleeve gastrectomy; bone strength; bone structure

1. Introduction

In adolescents and young adults with moderate to severe obesity in whom lifestyle and pharmacological interventions are not effective in achieving weight loss, metabolic and bariatric surgery (MBS) is a very effective strategy to achieve sustained weight loss^(1–4), with improvements reported in most metabolic parameters. As a consequence, a marked increase in MBS in adolescents has been reported in recent times in the United States^(5, 6), with almost a doubling in its reported utilization between 2012–2016. However, a known deleterious effect of MBS is its impact on bone health, as reported in studies of adults^(7–12) and adolescents^(13, 14) undergoing gastric bypass, and adults undergoing sleeve gastrectomy^(8, 15–17).

Some^(8, 10, 18), but not all^(16, 17, 19), studies in adults suggest that sleeve gastrectomy may have a lesser impact on bone than gastric bypass, attributed to less marked hormonal changes and less malabsorption following sleeve gastrectomy vs. gastric bypass procedures. This is particularly important given the increasing use of sleeve gastrectomy in individuals with moderate to severe obesity, especially in younger populations, in whom body mass index (BMI) reductions appear to be similar following sleeve gastrectomy as with gastric bypass⁽²⁰⁾, with a similar extent of skeletal unloading following surgery. We have recently reported significant reductions in areal bone mineral density (aBMD) measures at the hip (but not the spine) using dual energy x-ray absorptiometry (DXA) in adolescents and young adults following sleeve gastrectomy, mostly related to skeletal unloading from weight loss⁽²¹⁾. However, using high resolution peripheral quantitative computed tomography (HRpQCT) and microfinite element analysis, we found no change in total volumetric BMD (vBMD) or strength estimates at the distal radius and tibia over 12 months⁽²¹⁾, suggesting that at least in the short-term, sleeve gastrectomy may not increase fracture risk at these sites.

Importantly, our previous study did not examine proximal femur geometry or strength estimates, and this is relevant because studies in adults following MBS have reported reductions in vBMD of the hip assessed by quantitative computed tomography (QCT)⁽⁸⁾, and bone geometry is an additional important contributor to fracture risk⁽²²⁾. Given the significant morbidity associated with hip fractures, if this site is impacted deleteriously in

adolescents and young adults undergoing sleeve gastrectomy, this will need to be monitored and preventive strategies identified. QCT of the hip involves significant radiation exposure, limiting its use in youth. Hip structural analysis (HSA) is a validated DXA-based technique to assess proximal femoral geometry and could be employed for a preliminary understanding of the impact of skeletal unloading on the proximal femur following sleeve gastrectomy. Strong correlations have been reported between HSA and QCT of the hip for cross-sectional area, cross-sectional moment of inertia (CSMI) and section modulus ⁽²³⁾, and studies have demonstrated that HSA measures predict hip fractures ^(24–26).

In order to address these knowledge gaps, we examined HSA measures in youth aged 14–22 years old (a critical period of bone acquisition ⁽²⁷⁾) with moderate-to-severe obesity undergoing sleeve gastrectomy, as well as non-surgical controls of comparable body size matched for age and sex. Based on DXA data indicating a reduction in hip BMD following such surgery, we hypothesized that participants undergoing sleeve gastrectomy would demonstrate alterations in proximal femur geometry and strength estimates commensurate with the degree of skeletal unloading following weight loss.

2. Participants and Methods

2.1. Participant Selection:

We enrolled 75 adolescents and young adults aged 14–22 years old with moderate to severe obesity in an ongoing longitudinal study examining bone outcomes following sleeve gastrectomy versus routine care. Data at baseline and 12-months were available for 48 matched participants, 24 of whom underwent sleeve gastrectomy (18 female and 6 male) and 24 non-surgical controls (18 female and 6 male). Data for DXA measures of aBMD have been previously reported in a subset of this sample ⁽²¹⁾. Participants met BMI criteria for MBS, namely BMI of ≥ 35 kg/m² (Class II or moderate obesity) with one or more obesity related complications, or a BMI of ≥ 40 kg/m² (Class III or severe obesity). Exclusion criteria included conditions or medications that may affect bone metabolism (other than use of calcium and/or vitamin D supplementation or hormonal contraception) within eight weeks of the baseline visit. Use of estrogen-progesterone combination preparations was not an exclusion criterion for concern that the sample would not be representative of the general population of females with obesity in this age range, as many are on such medications for management of polycystic ovarian disease and/or for contraception. We did exclude participants on depot medroxyprogesterone injections, given their marked deleterious effects on bone health, but not those on the progestin releasing intrauterine device given limited systemic effects, or those with progestin implants given limited bone effects. We recruited participants from area hospitals and specialized weight regulation programs.

The Partners Institutional Review Board approved this Health Insurance Portability and Accountability Act compliant study. We obtained informed consent from participants 18 years and older, or parents of participants < 18 years. Informed assent was obtained from participants younger than 18 years.

2.2. Experimental Protocol:

Eligible participants were assessed at baseline and 12-month follow-up visits. The baseline visit occurred shortly before surgery in the sleeve gastrectomy (surgical) group. We measured height on a wall mounted stadiometer as the average of three measurements, and weight to the nearest 0.1 kg using an electronic scale. Body mass index (BMI) was calculated as weight in kg/(height in meters)². Standard deviation scores (SDS) or z-scores for anthropometric measurements were determined using CDC 2000 databases⁽²⁸⁾. Fasting blood samples were obtained for calcium, phosphate, and 25(OH) vitamin D (25OHD) levels and measured by a reference laboratory (LabCorp, Burlington, NC, USA). Hemoglobin A1C (HbA1C) was assayed in the Diabetes Core Laboratory. The Paffenbarger questionnaire was used to determine hours per week of moderate to vigorous physical activity^(29, 30). Diet and exercise counseling for controls was provided throughout the study by Translational and Clinical Research Center (TCRC) dietitians, specialized weight regulation programs, or their physicians. Calcium and vitamin D intake was assessed by TCRC dietitians using a calcium and vitamin D food frequency questionnaire⁽³¹⁾. Participants were offered at least 1200 mg elemental calcium and 800 IUs vitamin D daily to optimize calcium intake and absorption. Additional recommendations for vitamin D supplementation (based on 25OHD levels) were based on standard guidelines^(32, 33).

2.3. Dual Energy X-Ray Absorptiometry:

DXA (Hologic 4500 A, Waltham, MA) was used for hip structural analysis, as well as measures of fat and lean mass at the baseline visit and one-year post gastrectomy in the surgical group, and one year following the baseline visit in the non-surgical group by an International Society of Clinical Densitometry (ISCD) certified DXA technologist on a single instrument (coefficients of variation for areal BMD, fat and lean mass 0.8%, 2.1% and 1.0%, respectively; least significant change 0.024 g/cm² and 0.048 g/cm² for total hip and femoral neck respectively). All scans were analyzed using the same software.

HSA provides data for three proximal femoral sites (Figure 1) using averages from five parallel lines 1 pixel apart across the cross-section of these sites: (i) narrow neck (NN), the narrowest point of the femoral neck, (ii) the trochanteric region, along the bisector of the angle of the axes of the neck and femoral shaft, and (iii) the femoral shaft (FS), a site across the shaft at a distance of 1.5 cm minimum neck width distal to the intersection of the neck and shaft axes⁽³⁴⁾. The specific measures obtained using HSA include (i) subperiosteal (or outer) diameter, (ii) estimated endosteal (or inner) diameter, (iii) cross-sectional area, an index of resistance to axial forces (excludes soft spaces in marrow and pores), (iv) estimated cortical thickness, (v) cross-sectional moment of inertia, an estimate of resistance to bending forces in a cross-section, (vi) section modulus, an index of strength of bending (vii) buckling ratio, an index of susceptibility to local cortical buckling under compressive loads, (viii) neck shaft angle, and (ix) hip axis length, the distance in mm from the inferolateral aspect of the greater trochanter to the pelvic inner rim, measured along the long axis of the femoral neck⁽³⁴⁻³⁶⁾.

2.4. Statistical Analysis:

We present data as mean \pm SE or median (interquartile range) unless otherwise indicated. JMP Statistical Discovery Software (Version 14, SAS Institute, Carey, NC) was used for statistical analysis. The study was powered (based on preliminary data) at 97% and 90%, respectively, to detect a 3.5% difference between groups for changes in specific bone parameters over time at an alpha level of .05, based on an estimated standard deviation of change of 2.85%. We used the Student t-test or the Wilcoxon Rank Sum test to compare differences between surgical and non-surgical groups depending on the data distribution. Within group comparisons were performed using the paired t-test. We used multivariable analysis to determine differences between groups after controlling for possible covariates (age, sex, race and baseline bone measure \pm 12-month change in BMI). Pearson correlations were used to determine associations of covariates known to impact bone (i.e. change in BMI, lean mass, fat mass, 25OHD levels, HbA1C, and physical activity) (37–39) with HSA parameters. A p value of <0.05 was considered to be statistically significant.

3. Results

3.1. Baseline Characteristics:

The sleeve gastrectomy (surgical) and non-surgical groups did not differ for baseline characteristics except for weight, BMI and fat mass, which were higher in the surgical group. However, BMI standard deviation score (SDS) and percent fat mass did not differ across groups (Table 1). Also, the proportion of study participants with HbA1C levels in the normal ($<5.7\%$), prediabetes (5.7–6.4%) and diabetes ranges ($>6.5\%$) did not differ across groups (75.0, 20.8 and 4.2% respectively in the surgical group, and 58.3, 33.3 and 8.3% respectively in the non-surgical group, $p=0.492$). Race was self-reported by study participants and did not differ across groups (19 non-Black and 5 Black participants in each group).

3.2. Changes in Anthropometric Measures and Body Composition over 12 Months:

The surgical group had greater reductions in weight, BMI, BMI z-scores, fat and lean mass, and HbA1C over 12 months compared to the non-surgical group (Table 1). Total body weight loss was greater in the surgical [-25.9% (-29.2% , -22.6%)] vs. non-surgical group [-0.30% (-3.58% , 2.99%)] ($p<0.0001$). Percent excess BMI loss was also greater in the surgical ($-55.8\pm 4.4\%$) vs. non-surgical group ($-2.6\pm 4.5\%$) ($p<0.0001$). The surgical group had greater reductions in percent fat mass and greater increases in percent lean mass than the non-surgical group (Table 1).

3.3. Changes in Hip Structural Analysis Measures over 12 Months:

Table 2 shows baseline measures for study participants, the within group change over 12 months, and significances for differences between groups after adjusting for age, sex, race, baseline bone measure \pm 12-month BMI change. The surgical and non-surgical groups did not differ for baseline measures of HSA at any site. Similar to reductions in total hip aBMD following surgery, the surgical group had significant within group reductions from baseline in narrow neck and intertrochanteric region BMD and BMD Z-scores, cross-sectional area,

CSMI, average cortical thickness and section modulus, and differed significantly from the non-surgical group for these changes over 12 months after adjusting for baseline covariates (age, sex, race and baseline bone measure) (Table 2). The surgical group also had significant within group increases in buckling ratio at the intertrochanteric region, and differed significantly from non-surgical controls for changes in this measure over 12-months at both the narrow neck and inter-trochanteric region. Groups did not differ for changes over 12 months in any HSA measure at the femoral shaft except BMD Z-scores. Of note, there was a within group increase in hip axis length in the surgical group, with a between group difference when compared with non-surgical controls. Results did not change after also controlling for height.

Percent changes for HSA measures at the narrow neck and intertrochanteric region are shown in Figure 2 for the surgical and non-surgical groups. No differences were noted between groups at the femoral shaft (not shown).

Differences between groups for 12-month change and percent change in narrow neck BMD, average cortical thickness and buckling ratio remained significant even after controlling for 12-month change in BMI. However, all significant differences for 12-month change (and percent change) in HSA measures at the intertrochanteric region and femoral shaft, and for changes in hip axis length were lost after controlling for 12-month change in BMI. Study participants did not report any new fractures during the study duration.

3.4. Hip Structural Analysis Measures at 12 Months after Controlling for Body Weight:

We also examined differences in HSA measures between groups at 12 months after controlling for age, sex, race and weight at 12 months, and found no differences between the groups except for narrow neck subperiosteal width ($p=0.009$), endocortical diameter ($p=0.014$) and buckling ratio ($p=0.024$), all of which were higher in the surgical group.

3.5. Determinants of Changes in Hip Structural Analysis Parameters:

For all participants taken together, Table 3 shows associations of changes in BMI z-scores, lean mass, fat mass, 25OHD and physical activity levels with changes in bone parameters between surgical and non-surgical groups over time.

Narrow Neck: Changes in BMI z-scores, lean mass and fat mass were associated positively with changes in narrow neck BMD Z-scores, cross-sectional area, CSMI and section modulus. Further, a change in 25OHD levels correlated inversely with changes in narrow neck BMD, BMD Z-scores, CSMI, average cortical thickness and section modulus, and positively with changes in buckling ratio. Changes in physical activity were associated positively with increases in subperiosteal width and endocortical diameter.

Intertrochanteric Region: Changes in lean mass and fat mass correlated positively with changes in BMD, BMD Z-score, cross-sectional area, CSMI, average cortical thickness and section modulus at the intertrochanteric region. Changes in BMI, lean mass and fat mass were associated inversely with changes in the buckling ratio. No associations were noted for

changes in 25OHD levels of in physical activity levels with any measure at the intertrochanteric region.

Femoral Shaft: Changes in lean mass were positively associated with changes in femoral shaft BMD Z-scores, cross sectional area and CSMI; no other significant associations were noted.

Shaft Neck Angle and Hip Axis Length: Changes in BMI, lean mass and fat mass were associated inversely with changes in hip axis length, and changes in 25OHD correlated positively with changes in shaft neck angle.

4. Discussion

This is the first report of hip structural analysis following sleeve gastrectomy in adolescents and young adults, demonstrating changes at the narrow neck and intertrochanteric region, such as reductions in BMD Z-scores, cross-sectional area, CSMI and section modulus, and an increase in the buckling ratio following surgery. Most of these changes were attributable to 12-month reductions in BMI following surgery, as differences between groups were no longer significant after controlling for 12-month change in BMI. The femoral shaft, however, was spared for the most part.

HSA uses properties of DXA to derive geometrical parameters for the hip associated with bone strength⁽⁴⁰⁾. In a study of 7474 women with 635 incident hip fractures over 13 years, women with fracture had greater neck-shaft angles, subperiosteal and endosteal diameters, and buckling ratios, and lower areal hip BMD, cross-sectional area, cortical thickness, CSMI, and section modulus than those without fracture⁽²⁶⁾. Another large study of postmenopausal women also reported that buckling ratio was an independent predictor of fracture risk even after controlling for age, body size, clinical risk factors and areal BMD⁽³⁴⁾. Further, hip axis length has been implicated in fracture risk, particularly in younger women without osteoporosis, even after controlling for aBMD and Fracture Risk Assessment Tool (FRAX) measures⁽⁴¹⁾. HSA has been used in studies assessing the impact of exercise and mechanical loading on bone^(40, 42), and in large and longitudinal studies in children^(43, 44).

We found alterations in several HSA parameters at the narrow neck and intertrochanteric region in the surgical group over 12 months vs. the non-surgical group, including in specific parameters implicated in fracture risk in the studies described above in other populations. These include reductions in aBMD, cortical thickness, cross-sectional area, CSMI and section modulus, all of which have been implicated in fracture risk in studies of postmenopausal women⁽²⁶⁾, and increases in the buckling ratio (implicated in fracture risk in postmenopausal women⁽³⁴⁾) and hip axis length (implicated in fracture risk in younger women without osteoporosis⁽⁴¹⁾). However, periosteal width and endocortical diameter, associated with fracture risk in postmenopausal women⁽²⁶⁾, were spared at these sites in our participants, and the femoral shaft was mostly spared, with the only significant reduction being in aBMD. Similar to our data, a study examining hip structural analysis endpoints in patients enrolled in a multidisciplinary weight loss program involving nutritional and

exercise intervention reported a sparing of the femoral shaft, although in that study, the intertrochanteric region was also spared⁽⁴⁵⁾. The extent of weight loss was much less in this study, which did not involve MBS.

Overall, these data are concerning for a decrease in bone strength at the hip following sleeve gastrectomy, attributable to the reduction in BMI (and skeletal unloading) following surgery, or metabolic and hormonal changes^(12, 46) associated with weight reduction⁽⁹⁾, given that many differences in HSA parameters were no longer significant after adjusting for 12-month change in BMI. This is of potential concern because hip geometry parameters in childhood correlate with adult hip geometry⁽⁴⁷⁾; thus deficits incurred during adolescence and young adulthood may persist over the lifespan. However, we found that at 12-months, most HSA measures (other than narrow neck width and buckling ratio) did not differ between groups after adjusting for body weight at 12-months, suggesting that despite reductions in these HSA measures over time following surgery, fracture risk may not differ significantly from controls because of the concurrent reduction in body weight and therefore the force of a fall. Thus, changes in HSA measures may merely reflect an appropriate adaptation to skeletal unloading from reduced body weight.

Changes in BMI, lean mass and fat mass were positively associated with changes in HSA measures at the narrow neck and intertrochanteric region, consistent with the known impact of these measures on bone outcomes. Clinical protocols for vitamin D supplementation are now in place at centers performing MBS to maintain 25OHD levels in the normative range and reduce the impact on bone^(9, 46). Inverse associations of changes in 25OHD levels with changes in HSA measures in this study may reflect the impact of changes in fat mass following MBS on 25OHD levels. Specifically, reductions in fat mass following surgery (which reflect reductions in body weight), would be associated with increases in systemic 25OHD levels (as 25OHD is sequestered in adipose tissue). Thus, inverse associations of changes in 25OHD levels with HSA measures may merely reflect positive associations of changes in fat mass with changes in HSA measures. Regardless, we found no difference between surgical and non-surgical groups for changes in 25OHD levels over time. Changes in physical activity correlated only with changes in subperiosteal width and endocortical diameter at the narrow neck, and suggest that changes in weight and body composition may be greater drivers of change in bone outcomes following surgery than physical activity.

Study limitations include a relatively small number of participants and lack of data for fractures. Studies are necessary in a larger group of adolescents over a longer duration following sleeve gastrectomy as well as gastric bypass to assess the impact of these two surgical techniques on bone outcomes, particularly fracture risk. Of note, although HSA does not directly assess bone geometry but converts two dimensional data to make inferences about geometry using engineering models, HSA measures correlate strongly with volumetric measures obtained by quantitative computed tomography⁽²³²³⁾. A study limitation is the use of self-report data for assessment of exercise activity, calcium and vitamin D intake in study participants. It is reassuring though that these data did not differ across study groups; thus, errors from self-report are less likely to contribute to observed differences across groups. Finally, it will be important to determine how and whether changes in gut hormones, gonadal steroids, 1,25(OH)₂D or PTH impact bone outcomes. An

important strength is that this is the first detailed analysis of HSA endpoints in adolescents and young adults following sleeve gastrectomy.

Overall, our study indicates a deterioration in hip structural measures at the narrow neck and intertrochanteric region following sleeve gastrectomy in adolescents and young adults. However, reduced body mass may compensate for the observed deleterious effects on bone following metabolic and bariatric surgery.

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Abbreviations:

25OHD	
1,25(OH)₂D	1,25 dihydroxy vitamin D
BMD	Bone mineral density
aBMD	Areal bone mineral density
BMI	Body mass index
CSMI	Cross-sectional moment of inertia
DXA	Dual energy x-ray absorptiometry
FRAX	Fracture Risk Assessment Tool
HbA1C	Hemoglobin A1C
HRpQCT	High resolution peripheral quantitative computed tomography
HSA	Hip structural analysis
MBS	Metabolic and bariatric surgery
PTH	Parathyroid hormone
QCT	Quantitative computed tomography
SDS	Standard deviation score
vBMD	Volumetric bone mineral density

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Highlights:

- Sleeve gastrectomy (SG) in youth results in reduced hip bone density over 12 months
- Narrow neck and intertrochanteric region geometry and strength are impacted negatively
- These effects are attenuated after controlling for changes in body mass index
- After adjusting for weight, groups did not differ for bone measures at 12 months

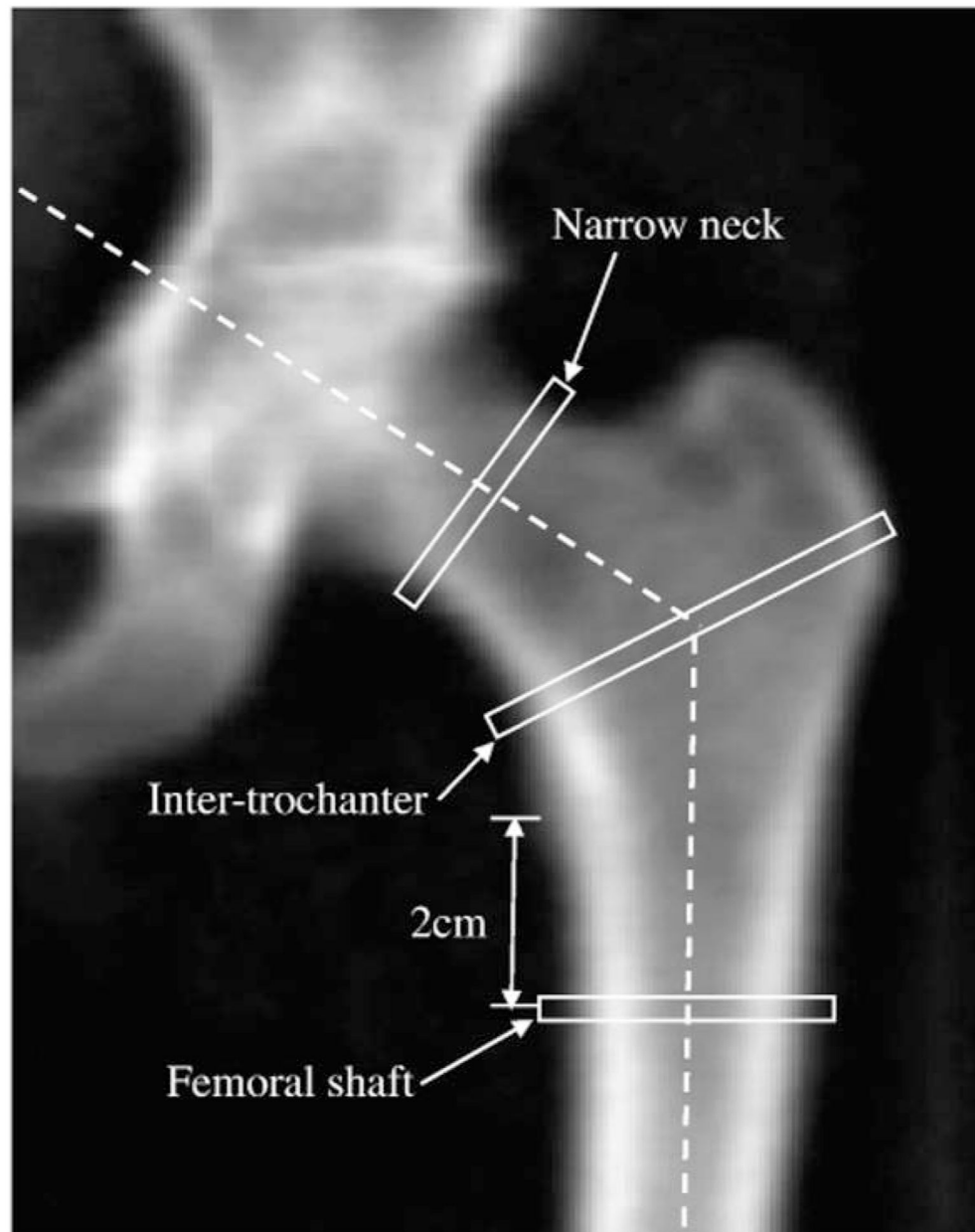


Figure 1: Hip image from Hologic DXA scanner showing locations of HSA narrow neck, intertrochanteric and femoral shaft regions of interest (ROI). From *Laskey MA, Price RI, Khoo BCC, Prentice A. Proximal femur structural geometry changes during and following lactation. Bone. 2011 Apr 1; 48(4): 755–759. Copyright Elsevier 2011.*

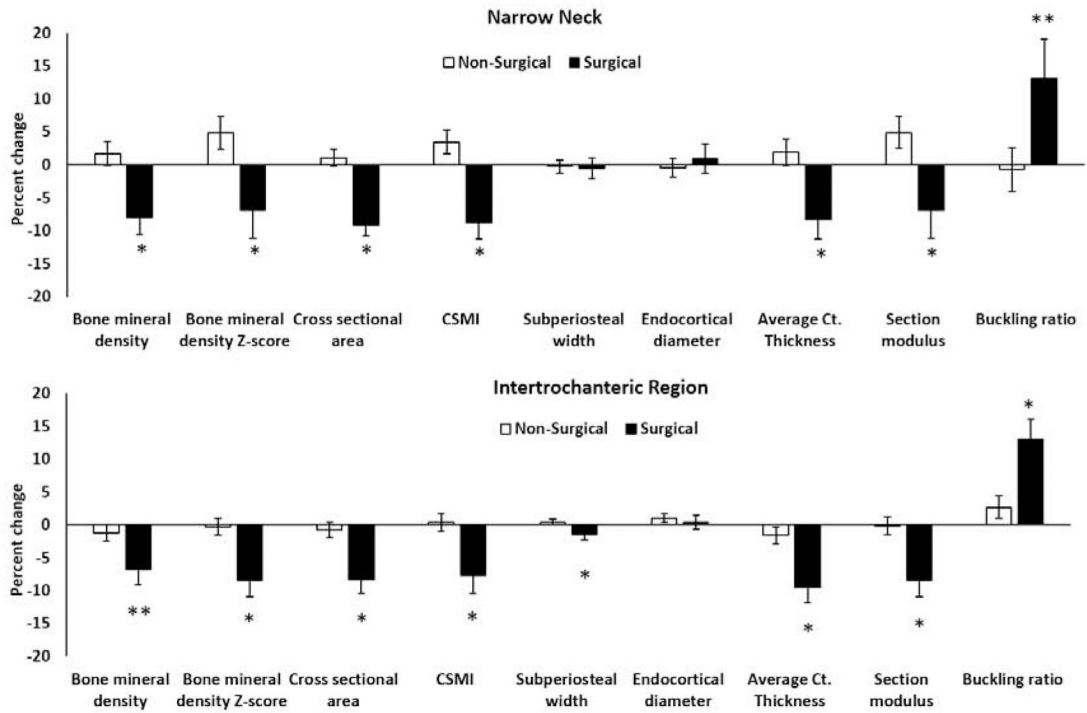


Figure 2: Percent change in hip structural analysis (HSA) measures at the narrow neck and intertrochanteric region in the surgical vs. non-surgical groups over 12 months. The groups differed for percent change in several measures at the narrow neck and intertrochanteric region. No differences were noted in percent changes in HSA measures at the femoral shaft (not shown). CSMI: cross sectional moment of inertia; Ct.: cortical; *P<0.05; **P<0.10 (both after controlling for age, sex and race).

TABLE 1: Clinical Characteristics and Body Composition Measures at Baseline and Changes over 12 Months in the Surgical and Non-Surgical Groups

Clinical Characteristics	Baseline Measure (Mean ± standard error of mean)		Within group change over 12-months [Mean (95% confidence interval)]		P-value comparing changes over 12 months in surgical vs. non-surgical groups
	Non-Surgical (n=24)	Surgical (n=24)	Non-Surgical (n=24)	Surgical (n=24)	
Age (years)	17.1 ± 0.5	17.8 ± 0.4	-	-	-
Height (cm)	167.1 ± 1.6	168.6 ± 1.8	-	-	-
Weight (kg)	120.7 ± 4.8	134.4 ± 3.7*	-1.0 (-5.0, 3.1)	-39.0 (-46.1, -32.0)	<0.0001
Body mass index (kg/m ²)	43.0 ± 1.2	47.4 ± 1.3*	-0.8 (-2.3, 0.8)	-13.7 (-16.1, -11.2)	<0.0001
Body mass index z-score	2.5 ± 0.1	2.6 ± 0.1	-0.1 (-0.2, -0.0)	-0.8 (-1.0, -0.5)	<0.0001
25-hydroxy vitamin D (ng/ml)	23.4 ± 1.5	23.9 ± 2.0	-1.5 (-4.8, 1.8)	5.5 (-1.0, 12.0)	0.054
Calcium (mg/dl)	9.3 ± 0.1	9.3 ± 0.1	-0.1 (-0.2, 0.1)	0.0 (-0.1, 0.2)	0.963
Phosphorus (mg/dl)	3.5 ± 0.1	3.5 ± 0.2	0.1 (-0.3, 0.4)	0.2 (-0.1, 0.5)	0.329
Hemoglobin A1c ** (%)	5.5 (5.2, 5.7)	5.6 (5.4, 5.8)	-0.7 (-1.8, 0.3)	-0.7 (-1.2, -0.2)	0.003
Moderate to vigorous physical activity (hours/week)	27.5 ± 4.9	29.6 ± 4.3	4.0 (-10.5, 18.4)	3.0 (-10.0, 16.1)	0.868
Dual Energy X-Ray Absorptiometry (DXA) Measures of Body Composition					
Lean Mass (kg)	64.5 ± 2.3	68.8 ± 1.9	1.5 (0.5, 2.5)	-9.2 (-12.3, -6.1)	<0.0001
Lean Mass (%)	53.3 ± 0.9	51.5 ± 1.0	1.4 (-0.3, 3.1)	7.6 (3.9, 11.3)	0.0002
Fat Mass (kg)	57.1 ± 2.8	65.5 ± 2.6*	-1.5 (-5.1, 2.2)	-23.1 (-31.4, -14.7)	<0.0001
Fat Mass (%)	46.7 ± 0.9	48.5 ± 1.0	-1.4 (-3.1, 0.3)	-7.6 (-11.3, -3.9)	0.0002

* p<0.05 for baseline differences between groups; significant changes from baseline, and significant differences between groups are bolded

** Baseline measure indicated as median (interquartile range)

TABLE 2: Hip Structural Analysis Parameters: Baseline Values and Changes over 12 Months in the Surgical and Non-Surgical Groups

	Baseline Measures (Mean ± standard error of mean)		Change over 12-months [Mean (95% confidence interval)]		P-value comparing changes over 12 months in surgical vs. non-surgical groups	
	Non-Surgical (n=24)	Surgical (n=24)	Non-Surgical (n=24)	Surgical (n=24)	Adjusted for age, sex, race and baseline	Adjusted for age, sex, race, baseline and change in BMI
Total hip BMD (g/cm ²)	1.17 ± 0.02	1.18 ± 0.03	0.00 (-0.01, 0.02)	-0.07 (-0.10, -0.04)	0.849	0.0003
Total hip BMD Z-score	1.78 ± 0.21	1.81 ± 0.27	-0.15 (-0.28, -0.03)	-0.88 (-1.21, -0.55)	0.931	<0.0001
Femoral neck BMD (g/cm ²)	1.07 ± 0.03	1.09 ± 0.02	0.00 (-0.02, 0.03)	-0.08 (-0.13, -0.04)	0.685	<0.0001
Femoral neck BMD Z-score	1.70 ± 0.23	1.88 ± 0.26	-0.104(-0.32, 0.11)	-1.00 (-1.36, -0.63)	0.605	<0.0001
NARROW NECK						
BMD (g/cm ²)	1.23 ± 0.04	1.22 ± 0.03	0.01 (-0.03, 0.06)	-0.10 (-0.16, -0.04)	0.003	0.031
BMD Z-score	0.06 ± 0.04	-0.16 ± 0.07	0.06 (-0.02, 0.14)	-0.16 (-0.32, -0.01)	0.012	0.174
Cross sectional area (cm ²)	3.98 ± 0.11	4.15 ± 0.10	0.03 (-0.07, 0.14)	-0.38 (-0.52, -0.24)	<0.0001	0.051
CSMI (cm ⁴)	3.17 ± 0.16	3.67 ± 0.22	0.11 (-0.01, 0.23)	-0.36 (-0.57, -0.15)	0.0005	0.304
Subperiosteal width (cm)	3.43 ± 0.08	3.60 ± 0.08	-0.02 (-0.09, 0.06)	-0.03 (-0.16, 0.10)	0.650	0.090
Endocortical diameter (cm)	2.95 ± 0.09	3.12 ± 0.08	-0.02 (-0.11, 0.07)	0.01 (-0.14, 0.16)	0.346	0.067
Average cortical thickness (cm)	0.24 ± 0.01	0.24 ± 0.01	0.00 (-0.01, 0.01)	-0.02 (-0.03, -0.01)	0.005	0.035
Section modulus (cm ³)	1.76 ± 0.09	1.92 ± 0.11	0.06 (-0.01, 0.14)	-0.16 (-0.32, -0.01)	0.011	0.176
Buckling ratio	7.99 ± 0.53	8.47 ± 0.47	-0.25 (-0.88, 0.38)	0.91 (-0.17, 1.98)	0.029	0.022
INTERTROCHANTERIC REGION						
BMD (g/cm ²)	1.22 ± 0.03	1.21 ± 0.04	-0.02 (-0.05, 0.02)	-0.09 (-0.16, -0.03)	0.026	0.481
BMD Z-score	-0.02 ± 0.07	-0.55 ± 0.16	-0.02 (-0.18, 0.13)	-0.55 (-0.88, -0.22)	0.011	0.375
Cross sectional area (cm ²)	6.44 ± 0.17	6.54 ± 0.24	-0.06 (-0.22, 0.09)	-0.60 (-0.94, -0.26)	0.003	0.313
CSMI (cm ⁴)	16.55 ± 0.75	17.83 ± 1.08	0.07 (-0.42, 0.56)	-1.60 (-2.78, -0.41)	0.039	0.445
Subperiosteal width (cm)	5.55 ± 0.09	5.68 ± 0.10	0.02 (-0.02, 0.07)	-0.08 (-0.18, 0.01)	0.063	0.385
Endocortical diameter (cm)	4.56 ± 0.10	4.69 ± 0.11	0.04 (-0.02, 0.10)	0.02 (-0.09, 0.13)	0.820	0.718

	Baseline Measures (Mean ± standard error of mean)		Change over 12-months [Mean (95% confidence interval)]		P-value comparing changes over 12 months in surgical vs. non-surgical groups	
	Non-Surgical (n=24)	Surgical (n=24)	Non-Surgical (n=24)	Surgical (n=24)	Adjusted for age, sex, race and baseline	Adjusted for age, sex, race, baseline and change in BMI
Average cortical thickness (cm)	0.50 ± 0.01	0.50 ± 0.02	-0.01 (-0.02, 0.01)	-0.05 (-0.08, -0.03)	0.004	0.295
Section modulus (cm ³)	5.48 ± 0.18	5.71 ± 0.27	-0.02 (-0.17, 0.14)	-0.55 (-0.88, -0.22)	0.011	0.366
Buckling ratio	6.17 ± 0.20	6.37 ± 0.25	0.15 (-0.05, 0.34)	0.80 (0.44, 1.16)	0.004	0.250
FEMORAL SHAFT						
BMD (g/cm ²)	1.70 ± 0.03	1.73 ± 0.04	0.01 (-0.03, 0.05)	-0.02 (-0.06, 0.02)	0.409	0.999
BMD Z-score	0.07 ± 0.04	-0.02 ± 0.06	0.07 (-0.02, 0.16)	-0.02 (-0.31, 0.09)	0.012	0.891
Cross sectional area (cm ²)	5.18 ± 0.13	5.31 ± 0.17	0.06 (-0.06, 0.18)	-0.05 (-0.20, 0.11)	0.625	0.603
CSMI (cm ⁴)	4.60 ± 0.27	4.83 ± 0.33	0.13 (-0.03, 0.28)	-0.02 (-0.26, 0.22)	0.602	0.733
Subperiosteal width (cm)	3.20 ± 0.06	3.23 ± 0.06	0.02 (-0.03, 0.07)	0.02 (-0.02, 0.06)	0.470	0.408
Endocortical diameter (cm)	1.89 ± 0.08	1.90 ± 0.07	0.02 (-0.07, 0.10)	0.05 (-0.00, 0.01)	0.353	0.676
Average Ct. Thickness (cm)	0.66 ± 0.02	0.67 ± 0.02	0.00 (-0.02, 0.02)	-0.02 (-0.03, 0.00)	0.375	0.970
Section modulus (cm ³)	2.77 ± 0.12	2.78 ± 0.18	0.07 (-0.02, 0.16)	0.08 (-0.16, 0.33)	0.693	0.123
Buckling ratio	2.58 ± 0.11	2.60 ± 0.13	-0.03 (-0.19, 0.14)	0.04 (-0.07, 0.15)	0.418	0.744
Shaft neck angle (degrees)	131.5 ± 0.8	130.5 ± 1.2	-1.0 (-3.1, 1.0)	0.1 (-2.2, 2.3)	0.668	0.610
Hip axis length (mm)	104.1 ± 1.4	104.9 ± 2.4	0.6 (-0.8, 2.0)	3.2 (1.4, 4.9)	0.006	0.543

BMD: bone mineral density; CSMI: cross-sectional moment of inertia; Ct.: cortical

Significant changes from baseline, and significant differences between groups are bolded.

Associations of Changes in Anthropometric Measures and Body Composition with Changes in Bone Parameters Over 12 Months

Table 3:

	BMI z-score		Lean Mass		Fat Mass		25OHD		Physical activity	
	r	p	r	p	r	p	r	p	r	p
HSA measures										
NARROW NECK										
Bone mineral density (g/cm ²)	0.298	0.059	0.309	0.032	0.246	0.092	-0.342	0.020	-0.214	0.157
Bone mineral density Z-score	0.384	0.013	0.335	0.020	0.294	0.043	-0.377	0.010	-0.132	0.389
Cross sectional area (cm ²)	0.491	0.001	0.600	< .0001	0.468	0.0008	-0.290	0.051	0.006	0.970
CSMI (cm ⁴)	0.540	0.0003	0.574	< .0001	0.460	0.001	-0.322	0.029	0.076	0.621
Subperiosteal width (cm)	0.114	0.480	0.236	0.106	0.179	0.224	0.221	0.140	0.348	0.019
Endocortical diameter (cm)	0.038	0.815	0.140	0.342	0.104	0.484	0.258	0.084	0.338	0.023
Average cortical thickness (cm)	0.285	0.071	0.292	0.044	0.234	0.110	-0.337	0.022	-0.221	0.146
Section modulus (cm ³)	0.388	0.012	0.336	0.020	0.294	0.042	-0.379	0.009	-0.131	0.393
Buckling ratio	-0.155	0.334	-0.121	0.412	-0.083	0.575	0.345	0.019	0.292	0.052
INTERTROCHANTERIC REGION										
Bone mineral density (g/cm ²)	0.228	0.152	0.524	0.0001	0.286	0.049	-0.050	0.741	0.096	0.532
Bone mineral density Z-score	0.214	0.179	0.630	< .0001	0.364	0.011	-0.102	0.500	0.046	0.762
Cross sectional area (cm ²)	0.244	0.125	0.639	< .0001	0.371	0.010	-0.105	0.490	0.082	0.594
CSMI (cm ⁴)	0.136	0.397	0.596	< .0001	0.321	0.026	-0.116	0.444	-0.022	0.884
Subperiosteal width (cm)	0.004	0.983	0.354	0.014	0.223	0.128	-0.182	0.227	-0.124	0.419
Endocortical diameter (cm)	-0.151	0.347	-0.003	0.987	0.008	0.960	-0.145	0.336	-0.155	0.308
Average cortical thickness (cm)	0.278	0.078	0.606	< .0001	0.365	0.011	-0.040	0.793	0.102	0.507
Section modulus (cm ³)	0.214	0.178	0.632	< .0001	0.367	0.010	-0.103	0.496	0.038	0.802
Buckling ratio	-0.366	0.019	-0.552	< .0001	-0.362	0.011	0.071	0.639	-0.109	0.477
FEMORAL SHAFT										
Bone mineral density (g/cm ²)	0.182	0.254	0.243	0.096	0.119	0.419	0.006	0.967	0.285	0.058
Bone mineral density Z-score	0.111	0.491	0.336	0.020	0.168	0.253	-0.056	0.714	0.144	0.345

	BMI z-score		Lean Mass		Fat Mass		25OHD		Physical activity	
	r	p	r	p	r	p	r	p	r	p
Cross sectional area (cm ²)	0.133	0.408	0.293	0.043	0.119	0.423	-0.075	0.621	0.215	0.156
CSMI (cm ⁴)	0.053	0.744	0.302	0.037	0.121	0.415	-0.127	0.400	0.074	0.628
Subperiosteal width (cm)	-0.077	0.632	0.097	0.510	-0.007	0.962	-0.140	0.354	-0.127	0.405
Endocortical diameter (cm)	-0.171	0.285	-0.079	0.596	-0.087	0.557	-0.106	0.482	-0.255	0.091
Average cortical thickness (cm)	0.195	0.221	0.228	0.119	0.133	0.369	0.021	0.889	0.283	0.059
Section modulus (cm ³)	0.107	0.506	0.097	0.511	0.080	0.588	-0.089	0.558	0.163	0.284
Buckling ratio	-0.162	0.312	-0.134	0.362	-0.058	0.695	-0.103	0.498	-0.255	0.091
Shaft neck angle (degrees)	-0.185	0.247	-0.130	0.380	-0.036	0.809	0.337	0.022	-0.092	0.546
Hip axis length (mm)	-0.431	0.005	-0.319	0.027	-0.414	0.004	0.206	0.169	-0.195	0.199

: Change; CSMI: cross sectional moment of inertia; BMD: bone mineral density; 25OHD: 25-hydroxy vitamin D. Significant p values are bolded