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Influence of Morbid Obesity on Parathyroidectomy Outcomes in Primary Hyperparathyroidism

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Abstract

Background—We sought to evaluate the influence of morbid obesity in patients undergoing parathyroidectomy for primary hyperparathyroidism (pHPT).

Methods—All patients with pHPT who underwent parathyroidectomy at a single institution between July 2002 and October 2008 were included. Body mass index (BMI), labs, operative findings, and outcomes were examined.

Results—Two hundred thirteen of the 776 patients identified (28%) were morbidly obese (BMI ≥ 35 kg/m²). When compared to non-morbidly obese patients, the morbidly obese patients were younger, had higher preoperative intact parathyroid hormone (iPTH) levels, heavier parathyroids, and required overnight stay more often ($p < 0.05$ for all). However, the rates of complications, eucalcemia, and recurrence were similar for all patients.

Conclusion—In this study, over a quarter of the patients who underwent parathyroidectomy for pHPT were morbidly obese and had significantly higher preoperative iPTH levels, heavier parathyroids, and longer hospital stay, but similar rates of complications and operative success.

Keywords

Morbid obesity; Primary hyperparathyroidism; Parathyroid hormone; Body mass index; Obesity

Obesity has become a global epidemic with over 300 million people who are clinically obese worldwide. In the United States (US) alone, the percent of obese patients increased almost 200% from 1986 to 2005 with the number of morbidly obese individuals increasing over 300% in the same time period. Currently, two-thirds of the US population is considered to be either overweight or obese. The National Institutes of Health (NIH) defines obesity as a body mass index (BMI) greater than or equal to 30 kg/m² and defines overweight as a BMI of 25 kg/m² or greater, but less than 30 kg/m². Meanwhile, individuals with a BMI greater than or equal to 35 kg/m² are considered to be morbidly obese.

When compared to non-obese people, obese patients are at increased risk of multiple health problems such as diabetes mellitus, hypertension, and osteoarthritis. Several recent reports have indicated that obese patients are at increased risk of morbidity and mortality following a

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variety of surgical procedures, especially major abdominal surgeries such as colectomy or pancreaticoduodenectomy (1–3). However, the effect of obesity on parathyroid surgery has yet to be fully elucidated (4). Therefore, the objective of this study was to evaluate the influence of morbid obesity in patients undergoing parathyroidectomy for primary hyperparathyroidism (pHPT).

Methods

We performed a retrospective review of a prospectively collected database to identify all patients with pHPT who underwent parathyroidectomy at the University of Wisconsin Hospitals & Clinics (Madison, WI) between July 2002 and October 2008. The following data were analyzed: patient demographics, laboratory values, operative details, and outcomes. All parathyroidectomies were performed by one of two surgeons (HC or RSS). Demographic and preoperative data that were included in this study consisted of age, gender, height, weight, serum calcium and intact parathyroid hormone (iPTH) levels, and ^{99m}Tc -sestamibi localization. As part of our preoperative work-up, patients routinely underwent parathyroid localization with ^{99m}Tc -sestamibi scintigraphy unless a simultaneous thyroid procedure was planned or other imaging was obtained prior to referral. A sestamibi scan was considered positive if parathyroid localization was interpreted by radiology. This localization was considered correct if the location of parathyroid on the scan correlated with intraoperative findings. BMI was calculated using the bodyweight (kg) divided by height squared (m^2). In accordance with the WHO and NIH, normal weight was defined as a BMI $<25 \text{ kg/m}^2$ but $\geq 18.5 \text{ kg/m}^2$, overweight as a BMI $\geq 25 \text{ kg/m}^2$ but $< 30 \text{ kg/m}^2$, obese as a BMI $\geq 30 \text{ kg/m}^2$ but $< 35 \text{ kg/m}^2$, and morbidly obese as a BMI $\geq 35 \text{ kg/m}^2$. Patients with a BMI $< 18.5 \text{ kg/m}^2$ were categorized as underweight.

Operative and outcomes variables that were examined included parathyroid gland weight, use of local anesthesia, hospital length of stay, complications, eucalcemia (cure), and recurrence. Parathyroid gland weight was measured in the operating room, and the weight of the heaviest gland recorded. When possible, parathyroidectomy was performed on an outpatient basis. Length of stay was recorded as the number of nights spent in the hospital (0, 1, 2, etc). Complications included transient or permanent hypocalcemia or hoarseness, wound infection, vascular injury, or any other event that required additional treatment or increased hospital stay. Eucalcemia was defined as a serum calcium level within the reference range ($8.5 - 10.2 \text{ mg/dl}$) at 6 months or greater following parathyroidectomy. Recurrence was considered to be a confirmed, elevated calcium level ($> 10.2 \text{ mg/dl}$) that occurred more than 6 months after surgery. This study was approved by the University of Wisconsin Human Subjects Institutional Review Board.

Data were recorded as mean $\pm$ SEM. Statistical analysis of the differences among groups was performed using univariate analysis of variance (ANOVA) or Chi-square with Bonferroni correction. For comparisons of morbidly obese patients versus non-morbidly obese patients, unpaired 2-sided t-tests were used for continuous variables, and Chi-square test was performed for categorical variables. Analyses were conducted utilizing SPSS software, version 10.0 (SPSS Inc, Chicago, IL). A *P* value of less than 0.05 was considered to be statistically significant.

Results

During the study period, 819 patients underwent parathyroidectomy for pHPT at the University of Wisconsin. Of these 819 patients, 776 (95%) had height and weight information collected at the time of surgery and were included in this study. The mean age of the patients was 61 ± 1 years and 76% (581 of 760) were female. In addition, the mean BMI was $31.7 \pm 0.3 \text{ kg/m}^2$.

Of the 776 patients, 11 (1.4%) were underweight, 158 (20.4%) were normal weight, 197 (25.4%) overweight, 197 (25.4%) were obese, and 213 (27.4%) were morbidly obese. The 11 underweight patients were analyzed with the normal weight patients, because no statistical differences existed between the two groups. Table 1 summarizes the preoperative characteristics of the patients by BMI category. Normal weight patients were more frequently female as compared to all other groups (Table 1). Additionally, morbidly obese patients were significantly younger than the normal and overweight patients and had higher preoperative serum iPTH levels when measured against their normal weight counterparts (Table 1).

Prior to parathyroidectomy, 634 of the 776 patients (82%) underwent preoperative localization with ^{99m}Tc -sestamibi. Other localization procedures, such as cervical ultrasound, were utilized, but were not included as part of this study. A positive "localizing" sestamibi scan was observed in 82% (139 of 169) of normal weight patients, 89% (168 of 188) of overweight patients, 84% (159 of 190) of obese patients, and 78% (159 of 203) of morbidly obese patients. The percent of sestamibi scans that correctly localized a parathyroid adenoma as determined by the surgeon's operative findings was similar among the four BMI categories (Table 1). The etiology of pHPT also was determined based on surgical findings as opposed to histology. Table 2 summarizes the etiology of pHPT by BMI category. No significant differences existed among the BMI groups with respect to the etiology of disease.

For the analysis of operative and outcome variables, morbidly obese patients were compared to all non-morbidly obese patients, since the purpose of this study was to examine the effects of morbid obesity on parathyroidectomy outcomes. In addition, when these same analyses were computed for all four BMI categories, the results were similar. For those data already presented, grouping of the patients into these two larger categories demonstrated that morbidly obese patients were younger than the non-morbidly obese patients as a whole (57 ± 1 vs 62 ± 1 yrs, $P < 0.001$) and had higher preoperative iPTH levels (142 ± 8 vs 121 ± 3 pg/ml, $P < 0.05$). When operative findings were examined, morbidly obese patients were found to have significantly heavier resected parathyroid gland weights (1060 ± 174 vs 665 ± 43 mg, $P < 0.05$). In contrast, the two groups had a similar proportion of ectopic parathyroids. Fifty of 213 morbidly obese patients (23%) and 134 of 563 non-morbidly obese patients (24%) had ectopic glands. All but two patients in this study (99.7%) had intraoperative PTH (ioPTH) testing, and 97.8% (759 of 776) of the parathyroidectomies were gamma probe guided. The ratio ex vivo to background gamma counts in the morbidly obese patients tended to be higher than those of the non-morbidly obese patients, though this difference was not statistically significant ($88 \pm 5\%$ vs $75 \pm 5\%$, respectively, $P = 0.08$). Parathyroidectomy was performed under local anesthesia in 6.1% (13 of 213) of morbidly obese patients and 18.3% (103 of 563) of non-morbidly obese patients ($P < 0.001$). In addition, 34% (71 of 213) of morbidly obese patients required an overnight stay compared to only 26% (145 of 563) of non-morbidly obese patients ($P < 0.05$). However, in comparing the morbidly obese patients to the non-morbidly obese, the postoperative serum calcium (9.8 ± 0.4 vs. 9.6 ± 0.1 mg/dl, $p=0.56$) and iPTH levels (47 ± 3 vs. 47 ± 1 pg/ml, $p=0.75$) of the patients were similar between the two groups.

When we examined additional outcomes, we found that the mean follow-up time for the morbidly and non-morbidly obese patients was virtually the same (15 ± 1 months for both, $P = 0.73$). The proportion of patients who experienced a complication also was comparable (2.3% vs 2.5%, respectively, $P = 0.57$). In the morbidly obese group, the complications included mediastinal air ($n=1$), carotid injury ($n=1$), transient hoarseness ($n=1$), and transient hypocalcemia ($n=2$). On the other hand, the non-morbidly obese patients had pneumonia ($n=1$), hematoma ($n=1$), cellulitis/abscess ($n=1$), thrombophlebitis ($n=1$), contamination ($n=1$), transient hoarseness ($n=4$), transient hypocalcemia ($n=3$), permanent hoarseness ($n=1$), and death ($n=1$). The one recorded mortality occurred within 30 days after surgery secondary to a ruptured abdominal aortic aneurysm and was considered to be unrelated to the

parathyroidectomy. With a minimum of 6 months follow-up after parathyroidectomy, eucalcemia (cure) was achieved in 99.5% (212 of 213) of morbidly obese patients and 98.8% (556 of 563) of non-morbidly obese patients ($P = 0.46$). The rates of recurrent pHPT (recurrent hypercalcemia > 6 months) also were similar between the two groups ($P = 0.53$). Two morbidly obese patients (0.9%) and 10 non-morbidly obese patients (1.8%) developed recurrent pHPT.

Discussion

With a worldwide epidemic of obesity, increasing numbers of obese patients are presenting for surgical evaluation and intervention. Multiple studies have documented the increased risk of surgical complications in obese patients for major abdominal and cardiac surgeries, while others have failed to show a difference for general elective cases (1–3,5–8). However, the role of obesity in parathyroid surgery has undergone little investigation (4). In this study, we sought to examine the impact of morbid obesity ($\text{BMI} \geq 35 \text{ kg/m}^2$) on parathyroidectomy outcomes in patients with primary hyperparathyroidism (pHPT). Our study indicates that morbid obesity does not influence the rates of complications, eucalcemia at 6 months (cure), or recurrence of pHPT. However, morbidly obese patients were younger and had higher preoperative iPTH levels with heavier parathyroid glands when compared to patients who were not morbidly obese ($\text{BMI} < 35$). In addition, local anesthesia and outpatient (“same-day”) surgery were performed less often in morbidly obese patients.

In our cohort of 776 patients, 27.4% were morbidly obese and an additional 25.4% each were either obese or overweight. Thus, more than three-quarters of the patients in this study were at least overweight. This proportion is higher than that observed in the US as a whole. Only two-thirds of the US population is considered to be at least overweight.. The larger proportion of patients in our study who were at a minimum overweight, likely reflects a higher prevalence of obesity in our region (9). Other investigations on the effects of BMI on surgical outcomes also have reported a lower rate of obese patients. In a study of 3,202 patients from a national surgical database who underwent colectomy for cancer, only 12.4% were morbidly obese and 19.0% were obese (1). Similarly, in a single institution study, only 27.5% of patients undergoing pancreaticoduodenectomy for pancreatic cancer were reported to be obese compared to 52.8% in our study population (2). While the decreased rates of obesity in these other studies could reflect regional variations in obesity prevalence, the lower proportion of obese patients also may be due to an increased rate of cancer cachexia in patients with colorectal or pancreatic carcinoma and underlying differences in disease pathophysiology. Several recent studies have documented an association between body mass and iPTH levels (10–15). In fact, research has shown that fat mass is an independent predictor of iPTH levels in postmenopausal women (15). Our data corroborate this significant positive correlation between iPTH and BMI (Pearson $r = 0.10$, $P = 0.005$). In addition, we show that morbidly obese patients have higher mean preoperative iPTH compared to non-morbidly obese patients.

This connection between iPTH and BMI has often been elucidated by comparing patients with pHPT to eucalcemic controls and demonstrating an increased mean weight and/or BMI in those with pHPT (11). However, reports of patients with morbid obesity also document higher rates of pHPT with as many as 39% of patients having pHPT at the time of bariatric surgery (12, 13). In contrast, the overall prevalence of pHPT in the general population is thought to be less than 2%. To the best of our knowledge, prior studies have not reported age differences in the development of pHPT in obese patients. Our finding that morbidly obese patients with pHPT were younger than non-morbidly obese patients may be explained by this relationship between BMI and iPTH levels such that an increased fat mass could lead to the earlier development of disease. Alternatively, the difference in mean age between the groups was only 5 years, and, thus, this finding may be an artifact of our data set.

In addition to higher iPTH levels prior to parathyroidectomy and presentation at younger age, on average morbidly obese patients in this study had heavier parathyroid glands compared to patients with a BMI less than 35. For all patients, parathyroid gland weight was associated with BMI as well as preoperative serum calcium and iPTH levels (Pearson $r = 0.10, 0.22,$ and $0.35,$ respectively, $P < 0.01$ for all). These data support the findings of Adam and colleagues who showed a similar relationship between BMI and resected adenoma weight that was independent of vitamin D status (10). One limitation of this study is that we did not examine vitamin D levels which, when deficient, may contribute to a state of secondary HPT in severely obese individuals. In a study examining factors related to parathyroid localization preoperatively, Berber et al reported that BMI, gland size, and gland volume were independent predictors of positive sestamibi and ultrasound localization in patients with pHPT (14). In their study, parathyroid gland size and volume were likely surrogate measures for gland weight. Our data would, therefore, suggest that the relationship between BMI and gland size or weight may not be independent. The underlying mechanism of this relationship between BMI and parathyroid weight is poorly understood, but does not appear to be related to fat infiltration of the gland (10).

Additional results of this study include that morbidly obese patients required an overnight stay more frequently than non-morbidly obese patients and underwent parathyroidectomy under local anesthesia less often. In a report of the differences observed in morbidly obese patients undergoing outpatient parathyroidectomies, Norman and Aronson similarly showed that morbidly obese patients spent a significantly longer time in the post-anesthesia care unit (PACU) compared to non-morbidly obese patients (4). These authors also demonstrated that morbidly obese patients required conversion to endotracheal intubation (from a laryngeal mask airway) with greater frequency (4). The definition of morbid obesity used in their study, however, was different. Patients were categorized as morbidly obese if they were more than 100 pounds over their ideal body weight and/or if their BMI was greater than 39. Nonetheless, the data from Norman's study support using a secure airway in morbidly obese patients undergoing parathyroid surgery to avoid potential complications related to airway management. Our finding that morbidly obese patients were less likely to have their procedure performed under local anesthesia (6% vs 18%) may be due to selection bias of the surgeon or anesthesiologist. In spite of this possibility, such bias is certainly justified on the basis of patient safety.

While investigations into the impact of obesity on outcomes of major surgeries have shown an increased risk of complications for certain procedures, our data do not demonstrate that morbidly obese patients undergoing parathyroidectomy have worse outcomes (1–3,5–7). The proportion of complications that occurred from parathyroidectomy was similar for all patients in this study and in line with previous reports (16,17). In addition, the rates of eucalcemia at 6 months and recurrence of hypercalcemia at any point thereafter were comparable between the groups with overall eucalcemia and recurrence rates of 99.0% and 1.6%, respectively. Norman and Aronson also reported that complication and cure rates for morbidly obese outpatient parathyroidectomy patients were no different than non-morbidly obese patient, though follow-up in their study was shorter with a minimum of only 6 weeks (4). Interestingly, their data did demonstrate that morbidly obese patients had larger incisions, increased operative time, and more frequently bilateral neck explorations due a higher false positive rate on sestamibi imaging (4). Similar to what we have reported here, their study also documented that the intraoperative gamma probe counts (parathyroid activity) were the same for all patients, including the morbidly obese.

In conclusion, this evaluation of the influence of morbid obesity on outcomes of parathyroidectomy for primary hyperparathyroidism (pHPT) provides evidence that the morbidity and prognosis is the same for all patients regardless of BMI. Preoperative

considerations for morbidly obese patients should include an increased probability of requiring an overnight stay and a decreased likelihood of having surgery under local anesthesia. By and large, patients with pHPT who present for parathyroidectomy should expect a safe and successful operation no matter what their bodyweight.

Summary

In this study, we evaluated the influence of morbid obesity on outcomes following parathyroidectomy in patients with primary hyperparathyroidism, and specifically examined differences in laboratory values, operative findings, complications, and surgical success.

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Table 1

Preoperative characteristics of the 776 patients by Body Mass Index (BMI) category

	Normal (BMI < 25) (n = 169)	Overweight (BMI 25 – 29) (n = 197)	Obese (BMI 30 – 34) (n = 197)	Morbidly Obese (BMI ≥ 35) (n = 213)
Gender, % Female	83 [*]	74	72	73
Age (yrs)	63 ± 1	63 ± 1	60 ± 1	57 ± 1 [†]
Serum calcium (mg/dl)	11.1 ± 0.1	11.2 ± 0.1	11.2 ± 0.1	11.2 ± 0.1
Serum iPTH (pg/ml)	116 ± 6	126 ± 6	119 ± 5	142 ± 8 [‡]
Correct MIBI localization, %	81	77	82	81

iPTH = intact parathyroid hormone level

^{*} $P < 0.05$ compared to all other groups using Chi square test with Bonferroni correction

[†] $P < 0.05$ compared to normal and overweight patients using ANOVA with Bonferroni correction

[‡] $P < 0.05$ compared to normal weight patients using ANOVA with Bonferroni correction

Table 2

Primary hyperparathyroidism etiology by Body Mass Index (BMI) category

	Normal (BMI < 25) (n = 169)	Overweight (BMI 25 – 29) (n = 197)	Obese (BMI 30 – 34) (n = 197)	Morbidly Obese (BMI ≥ 35) (n = 213)
Single Adenoma, (%)	123 (73)	160 (81)	159 (81)	162 (76)
Double Adenoma, (%)	20 (12)	15 (8)	18 (9)	15 (7)
Triple Adenoma, (%)	1 (<1)	1 (<1)	0	1 (<1)
Hyperplasia, (%)	25 (15)	21 (11)	20 (10)	30 (14)
Parathyroid cancer, (%)	0*	0	0	5 (2)