



Safe Method for the Treatment of Primary Hyperparathyroidism in Geriatric Patients: Minimally Invasive Parathyroidectomy

Geriatrik Hastalarda Primer Hiperparatiroidi Tedavisinde Güvenli Yöntem: Minimal Invazif Paratiroidektomi

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ABSTRACT

Aim: Primary hyperparathyroidism is the most important cause of clinically hypercalcemia. Parathyroid adenomas are the most common endocrinology disorder in primary hyperparathyroidism. In this study, we aimed to evaluate the reliability of this surgery in patients older than 65 years by examining the data of patients who underwent parathyroidectomy for parathyroid adenoma.

Material and Method: Patients were divided into two groups as those aged 65 years and over and adults. Age, gender, comorbidities, ASA score, preoperative and postoperative laboratory findings, imaging methods and operative times were reviewed. A p value of <0.05 was used for significance.

Results: Ninety patients with parathyroid adenoma were included in the study. Female gender was dominant in both groups. The mean age was 52.15 ± 8.87 in Group 1 and 71.39 ± 5.76 in Group 2. When the associated co-morbidity was evaluated, no statistical difference was found between the two groups for diabetes mellitus and hypertension diseases. When the patients with nephrolithiasis were evaluated, there were 21/64 (32%) kidney stones in group 1 and 6/26 (23%) kidney stones in group 2 and there was no statistical difference in both groups. Although the ASA score was higher in the geriatric group, there was no difference between the duration of surgery and length of hospital stay. There were no postoperative complications and morbidity.

Conclusion: Adenoma surgery is an effective treatment method for primary hyperparathyroidism. Additional diseases and geriatric age period patients do not lead to an increase in surgical efficacy and complication rates. The surgeon procedure time was not prolonged despite the significant difference in ASA score in geriatric patients. Minimally invasive parathyroidectomy is a safe surgical procedure in geriatric patients. Our study as far as we know is the first in our literature about minimal invasive parathyroidectomy on geriatric patients.

Key words: minimally invasive parathyroidectomy; geriatric patient; primary hyperparathyroidism surgery

ÖZET

Amaç: Primer hiperparatiroidi klinik olarak saptanan hiperkalseminin en önemli sebebidir. Paratiroid adenomlar primer hiperparatiroidi tablosunda en sık rastalanan endokrinoloji bozukluğudur. Bu çalışmada paratiroid adenom nedeni ile paratiroidektomi yapılan hastaların verileri incelenerek minimal invazif paratiroid cerrahisinin 65 yaş üzeri hastalarda güvenilirliğinin değerlendirilmesi amaçlandı.

Materyal ve Metot: Hastalar 65 yaş üzeri olanlar ve erişkin yaş grubu olarak iki gruba ayrıldı. Yaş, cinsiyet, ek hastalıklar ASA skoru, preoperatif ve postoperatif laboratuvar bulguları, görüntüleme yöntemleri ve ameliyat süreleri gözden geçirildi. p değerinin anlamlılığı için <0,05 değeri kullanıldı.

Bulgular: Paratiroid adenomlu 90 hasta çalışmaya dahil edildi. Her iki grupta kadın cinsiyeti baskındı. Grup 1'de yaş ortalaması 52,15±8,87, Grup 2'de 71,39±5,76 idi. Ek hastalıklar değerlendirildiğinde, diabetes mellitus ve hipertansiyon hastalıkları açısından iki grup arasında istatistiksel fark bulunmadı. Nefrolityasizi olan hastalar değerlendirildiğinde grup 1'de 21/64 (%32) böbrek taşı ve grup 2'de 6/26 (%23) böbrek taşı vardı ve her iki grupta da istatistiksel fark yoktu. Geriatrik grupta ASA skoru daha yüksek olmasına rağmen ameliyat süresi ve hastanede kalış süreleri arasında fark yoktu. Ameliyat sonrası komplikasyon ve morbidite yoktu.

Sonuç: Adenom cerrahisi primer hiperparatiroidizm tedavisinde etkili tedavi metodudur. Ek hastalıklar ve geriatrik yaş grubu hastalar; cerrahinin etkinliğinde ve komplikasyon oranlarında artışa sebep olmamaktadır. Cerrahi işlem süresi geriatrik hasta grubunda ASA skorundaki anlamlı farklılığa rağmen uzamamıştır. Minimal invazif paratiroidektomi geriatrik hasta grubunda güvenle uygulanabilecek cerrahi yöntemdir. Çalışmamız literatürde ülkemizden geriatrik hastalarda minimal invaziv paratiroidektomi ile ilgili bildiğimiz ilk çalışmadır.

Anahtar kelimeler: minimal invaziv paratiroidektomi; geriatrik hasta; primer hiperparatiroidizm cerrahisi

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Introduction

The expected human life expectancy has increased due to developing technology including new treatment opportunities and screening modalities¹. Therefore, with the increasing elderly population, the number of elderly patients undergoing surgery are increasing day to day. The patients over 65 years old are named as geriatric patients².

Elderly patients in need of surgery represent a significant proportion of the general surgical population. Information collected from the American National Institute of Health (NIH) Survey reported that, 65 years and older patients accounted for 35.3% of all inpatient procedures and 32.2% of all outpatient procedures. Although the mortality risk is higher, there is a relative lack of scientific literature examining perioperative health care models in elderly patients (≥ 75 years)^{1,2}.

In the geriatric patients, endocrine disorders occur with atypical, nonspecific symptoms and are often not recognized earlier. The incidence of endocrine diseases, particularly diabetes mellitus (DM), hypothyroidism and hyperparathyroidism, increases with age; the latter two are more common in women².

Primary hyperparathyroidism (PHP) is the third most common endocrine disease among all endocrine diseases. 10% of cases are part of autosomal dominant hereditary diseases³.

PHP is the most important and common cause of hypercalcemia in geriatric patients⁴. The incidence increased from 10 in 100,000 people under the age of 40, to 40 in 100,000 among those up to the age of 65⁵.

The aim of this study is to determine the differences between geriatric patients and age under 65 years patients undergoing minimal invasive parathyroid surgery for PHP.

Material and Method

A retrospective study is designed to evaluate the outcomes after parathyroid surgery in geriatric patients. The study protocol was approved by the hospital administration. Informed consent was obtained from all patients and personal identification information of patients are not shared this study.

Demographic, clinical and laboratory data of patients who underwent parathyroid surgery for PHP between January 2014 and June 2019 at Kutahya

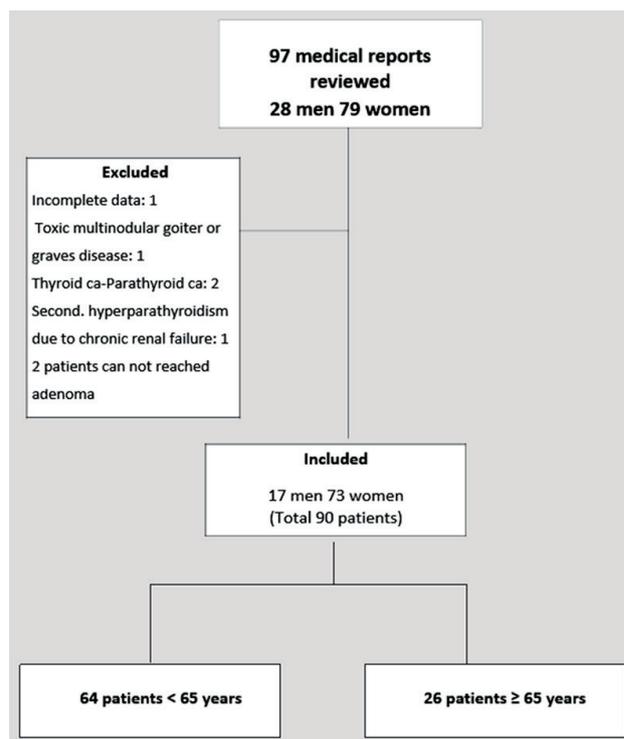


Figure 1. Group design in the study.

Health Sciences University Evliya Celebi Training and Research Hospital were retrospectively analyzed. 90 patients were included in the study. Patients with secondary hyperparathyroidism due to chronic renal failure, patients with toxic multinodular goiter or graves disease, incomplete data were excluded (7 patients). Two groups were designed to assess the role of age on parathyroid adenoma surgery. Patients were divided into two groups due to their age. First group patients were < 65 years and second group is geriatric group whose age were ≥ 65 years (Figure 1). Demographic parameters and their relations, with imaging and laboratory findings were compared between study groups (Table 1). Age, gender and related diseases (diabetes mellitus, hypertension) were recorded for analysis. Body mass index were excluded from the analysis due to incomplete records or inappropriate measurements. All related demographic and clinical information was retrieved and analyzed.

All patients were referred from an experienced endocrinologist. Preoperative blood tests, ultrasonography, 90 mTc-MIBI scintigraphy and washout examination were observed routinely before surgery. All of the patients who underwent surgery had single parathyroid adenoma. Parathyroid adenomas were

Table 1. Variables of the study

Variables	<65 years n: 64	>65 years n: 26	p value
Sex (F/M)	54/10	19/7	0,001
Age			
years (mean ± SD)	52,15±8,87	71,39±5,76	0,0412
Diabetes Mellitus	18/64 %28,12	13/26 %50	0,062
Hypertension	25/64 %39	7/26 %26,9	0,076
Nephrolithiasis	21/64 %32	6/26 %23	0,089
90 mTc-MIBI scintigraphy	52/64 %81	20/26 %76,9	0,072
USG	61/64 %95	24/26 %92	0,083
Washout examination	53/64 %83	21/26 %81	0,065
ASA Score	1–0,5 (1–2)	2–1 (2–3)	0,000
Operative time	75–20 (45–120)	75–28,75 (50–120)	0,074
Length of hospital stay	1–3 (1,2)	1–4 (1,4)	0,064

verified via gamma-probe and removed by dissection to the unilateral marked area in accordance with the principles of minimally invasive surgery. Vessel and tissue sealer ultrasonic dissector were used as an energy device in all operations. Postoperative bleeding status, nerve injury, seroma and wound infection data were obtained from all patients' medical records. Sucker drainage tube (hemovac) was placed at the operation site and removed at postoperative first 24th hour. Preoperative and postoperative calcium levels were calculated as corrected calcium levels with albumin levels. Surgical intervention failed in two patients. A 84-year-old female patient had an adenoma in the mediastinum; adenoma was not detected in the mediastinal exploration with sternotomy. A 72-year-old male patient with adenoma was not detected although all surgical thyroid lobes were evaluated. In these patients, PTH and calcium levels remained elevated during follow-up. One year later, the patient (72-year-old male) reevaluated with neck and thorax CT, adenoma was detected under the clavicle on the left side, the patient was reoperated and the adenoma under the left clavicle was excised.

In the postoperative period, biochemical hypocalcemia was defined as a total calcium level below 8,5 mg/dL and the level above 11 mg/dL was hypercalcemia.²⁵OHD, parathormone and thyroid stimulating hormone (TSH) chemilumination levels were determined by immunoassay measurement method (Beckman Coulter DXI-800, Beckman Coulter, Inc. Fullerton, CA 92835 USA). Alkaline phosphatase

(ALP), calcium, phosphorus levels were measured by Beckman Coulter AU 2700, Beckman Coulter, Inc., Brea, CA 92821 USA. The complete blood counts were determined with laserbased impedance using an automated blood cell counter (Mindray BC-6800, Nanshan, Shenzhen, PR China).

The statistical analysis of the data was performed using the "SPSS 18.0 (IBM statistics for Window version 18, IBM Corporation Newyork, USA). All data were summarized by supporting tables and graphs. During the evaluation, descriptive statistical methods (mean, standard deviation, median, interquartile range, minimum and maximum value) were used. T test was used in the same sample group of the quantitative data in the appropriate distribution of adult and geriatric groups in the appropriate distribution. Datas in groups not showing the appropriate distribution Wilcoxon Signed Rank test was used. The results were statistically with a confidence interval of 95%. Besides, the results of p value <0.05 were accepted as significant.

Results

The demographic and clinical profiles of patients in group 1 and group 2 were presented in Table 1. There were 54 female, 10 male patients in group 1 and 19 female and 7 male patients in group 2 ($p>0.001$). Mean age was 52 years (26–64) in group 1 and 71 years in group 2 ($p=0.0412$). (Table 1) There is no significant difference between groups including sex. There is a meaningful difference due to age between study groups.

When chronic diseases were evaluated; diabetes mellitus was present in 18 patients (28%) in group 1 and 13 patients (50%) in group 2 ($p=0.062$). Hypertension was present in 25 patients (38%) in group 1 and 7 patients (26.9%) in group 2 ($p=0.076$). In the preoperative period, nephrolithiasis was detected in 21 patients (32%) in group 1 and in 6 patients (23%) in group 2 ($p=0.089$). ASA score was significantly higher in group 2 ($p<0.001$). (Table 1)

In group 1, USG was 95% successful in detecting adenomas (61/64), and 92% in group 2 (20/26) ($p=0.083$). Ultrasound guided wash out was performed in all patients; 11 patients in group 1 were negative with wash out, in geriatric patients, 5 were negative. In 90 mTc-MIBI scintigraphy, 52 patients (81%) in group 1 and 20 patients (76.9%) in group 2 had positive results ($p=0.072$). (Table 1)

Preoperative corrected mean total calcium levels in group 1; 11.7 (10.1–14.2) mg/dl and 11.6 (10–13.3) mg/dl in group 2 ($p=0.0612$). Postoperative 10th minute mean total calcium measurement levels in group 1 was 8.78 (7.8–10.1) mg/dl and 8.6 (7.9–9.8) mg/dl in group 2 ($p=0.380$). Postoperative 1st Day mean corrected total calcium levels in group 1 was 9 (8.30–10.5) mg/dl and 8.9 (7.9–9.8) mg/dl in group 2 ($p<0.001$). Postoperative 1st Month mean corrected total calcium levels in group 1 was 9.53 (8.75–10.3) mg/dl and 9.54 (9–10.4) mg/dl in group 2 ($p=0.100$). (Table 2)

Preoperative mean PTH levels in group 1 were 202 (77–910) pg/dl, 229 (111–690) pg/dl in group 2 ($p=0.0761$). Postoperative 10. minute mean PTH levels in group 1 were 20 (0.01–200) mg/dl, 5 (3–29) pg/dl in group 2 ($p<0.001$). Postoperative 1st Month control mean PTH levels were in group 54 (10–190) pg/dl, 49 (10–90) pg/dl in group 2 ($p=0.010$) (Table 2).

When the operation time between the two groups was evaluated; there was no significant difference between geriatric and adult groups.

Discussion

Parathormone is the most important regulator of calcium level. Hypercalcemia, hypophosphatemia and severe osteoporosis may present with excessive secretion of parathormone. Besides, hyperparathyroidism is one of the leading endocrine diseases. It's classified as primary, secondary and tertiary in 3 groups. The most common parathyroid disease is PHP. PHP is also seen in multiple endocrine neoplasia (MEN) syndrome type I and rarely in IIA⁶. All patients included in our study had PHP and no MEN syndrome was detected.

The causes of PHP are parathyroid adenomas (80–90%), parathyroid hyperplasia (10–20%) and parathyroid malignancy (1%)⁷. The rate of ectopic localization among all parathyroid adenomas is 15–20%⁸. 5% of these ectopic adenomas are localized in the mediastinum, and these ectopic adenomas are usually located in the thymus⁹. In our study, surgery was unsuccessful in 2 patients, the first one had a mediastinal parathyroid adenoma in a 84-year-old woman and the other patient had adenoma in the subclavian area. Second patient's adenoma was removed at reoperation 1 year after the

Table 2. Biochemical variables of the study

Variables	<65 years n: 64	>65 years n: 26	p value
TSH. uIU/mL (mean ± SD)	1,98±1,24	1,75±1,09	0,104
Free T4. ng/dl (mean ± SD)	0,90±0,22	0,89±0,12	0,126
WBC. 10 ³ /mm ³ (mean ± SD)	7,8±2,76	7,19±1,44	0,473
Hemoglobine. g/dl (mean ± SD)	13,28±1,61	12,96±2,02	0,502
Hematocrit. % (mean ± SD)	40,486±4,35	39,693±5,76	0,413
Platelet. 10 ³ /mm ³ (mean ± SD)	273,4±78,17	230,78±62,13	0,937
25- Hidroksivitamine D (preop). ng/ml [median– IQR (min-max)]	10,9 –16 (4–76)	18,8–16 (4–71)	0,000
Preoperative Ca ⁺² . mg/dl (mean ± SD)	11,7±0,9	11,6±1,22	0,0612
Postoperative Ca ⁺² . 10. Minute mg/dl (mean ± SD)	8,78±0,96	8,66±1,09	0,380
Postoperative Ca ⁺² 1 st day. mg/dl (mean ± SD)	9±1,45	8,9±0,94	0,000
Postoperative Ca ⁺² 1 st month. mg/dl (mean ± SD)	9,53±0,87	9,54±0,54	0,100
Preoperative phosphorus. mg/dl (mean ± SD)	2,35±0,62	2,32±0,54	0,049
Postoperative phosphorus 1 st month. mg/dl (mean ± SD)	3,27±0,64	3,49±0,60	0,481
Parathormone preoperative pg/ml [median– IQR (min-max)]	202–228,5 (77–910)	229–326 (111–690)	0,0761
Parathormone postoperative 10th Minute pg/ml [median– IQR (min-max)]	20–14 (0,10–200)	5–8,5 (0,01–29)	0,001
Parathormone postoperative 1 st month pg/ml [median– IQR (min-max)]	54–49 (0,01–309)	49–48 (10–90)	0,010
Alkaline phosphatase preoperative. U/L [median– IQR (min-max)]	104–78 (37–728)	113–49 (43–139)	0,400
Alkaline phosphatase postoperative. U/L [median– IQR (min-max)]	93–65 (32–261)	85–51,25 (43–139)	0,920

first surgery. Our unsuccessful intervention rate is lower than 3% in PHP surgery and this correlated with literature^{8,9}.

PHP is seen in nearly 3% of postmenopausal women and 2% in elderly population. Parathyroidectomy provides curative treatment in 95% of patients with PHP. There is a consensus indicating that all PHP patients under the age of 50 should be treated with or without symptoms. There are also studies on the safety of parathyroidectomy in patients over 75 years of age⁴. In our study, the mean age was 71 in geriatric group and the age range was 65–90 years. Safe minimally invasive parathyroidectomy was performed in our all patients.

In PHP patients, high levels of hypercalcemia and low to normal levels of phosphorus are detected. In patients with moderate to mild hyperparathyroidism, calcium levels may be normal in some measurements. In the elderly patient group, serum calcium levels should be calculated considering albumin level. In the elderly patient group, despite high calcium levels, suppressed PTH levels should suggest malignant diseases¹⁰.

Hyperparathyroidism in the elderly patient population may present with different symptoms and signs than the young and middle aged patients. The clinical picture is generally includes fatigue, reduced intellectual capacity, emotional instability, loss of appetite and constipation and nephrolithiasis. Postmortem autopsy studies show a high rate of parathyroid adenoma in the geriatric group. Female gender is dominant. In our study, the female patient group was dominant in both groups. Kidney Stones develop in 10–25% of patients¹¹. In our study nephrolithiasis was present in 23% of elderly patients and there was no statistical difference between groups.

Geriatric patients are affected by the common burden of metabolic and cardiovascular comorbid diseases. However, the use of new surgical and anesthesia techniques reduces the duration of surgery and the incidence of some complications¹².

Operative risk increases due to co-morbid diseases in elderly patients with hyperparathyroidism. In geriatric group our patients' American Society of Anesthesiologists Score (ASA) were higher because of this. Surgical success rate has increased with shorter operation time and less complicated surgical models with minimally invasive approach targeting the location of adenoma¹³. In all patients multidisciplinary approach was preferred. In all patients; washout examination,

USG and 90 mTc-MIBI scintigraphy scans were performed routinely. There is no statistical difference between our groups for successful adenoma localisation. Frozen section pathologic evaluation was not preferred for any cases during surgery. Washout examination increases the localisation of suspected adenomas rate in the sestamibi scan negative patients^{14,15}. Therefore, we performed washout examination routinely. Further we used gama probe routinely instead of frozen section pathology examination. The localization of the adenoma was determined with the help of peroperative gamma probe. In this method, Tc-99 m MIBI was given intravenously to the patient preoperatively and surgery was started 30 minutes later.

The success rate of detection and removal of adenoma was found to be high with MIP (minimal invasive parathyroidectomy) using gamma probe. In addition, the radioactive material given for gamma probe was considered to be within the safe range when the level of absorbance in normal tissues was evaluated; compared to many other radiological examinations, it is considered to be at very low levels¹⁶.

In a study of 3388 patients with primary hyperparathyroidism, 964 (28%) patients underwent parathyroidectomy. It has been reported that comorbid causes are not statistically significant in the discontinuation of surgical treatment, and that withdrawal from surgery is not beneficial in the evaluation of life expectancy in elderly patients with primary hyperparathyroidism¹⁷. In some studies, only 10–20% of all patients with PHP undergo surgery^{18,19}. In our study group, the rate of geriatric patients was 40%. In contrast to the general population of our country, this ratio was accepted as normal due to the fact that we are in a region where the elderly population is higher. Young patients with PHP have significantly higher serum calcium levels than older patients. However, young patients are less likely to localize abnormal parathyroid glands on 90 mTc-MIBI scintigraphy or ultrasound. Although younger patients have a higher rate of hyperplasia than elderly patients, adenoma is still the most common cause²⁰. In our study, preoperative calcium and phosphorus values were significantly different in group 1. Although early postoperative calcium values differed, no difference was detected in both groups at first month control.

There is no globally accepted approach for PHP. Clinicians evaluate and determine their medical approaches in terms of cost, experience and suitability. In the United Kingdom, 90% of surgeons performed

preoperative USG and 90 mTc-MIBI scintigraphy; 30% had SPECT examination; it has been reported. 31% of surgeons performed frozen section and only 41% of surgeons performed intraoperative PTH (IOPTH) evaluation²¹.

It has been reported that intraoperative quick PTH follow-up increases the success rate in minimally invasive parathyroidectomy with intraoperative PTH (IOPTH) focusing and may be preoperative supportive in the detection of double adenomas¹⁴. However, IOPTH measurements were not performed in our clinic. Because we routinely used preoperative wash-out examination, USG and 90 mTc-MIBI scintigraphy scans. In addition to this gamma probe verification of suspected adenomas were used. Our success rate is higher as is the literature. Thus, we did not need to use IOPTH. Besides, we also correlate our results with 10th minute and 24th hour measurements. We claim that routine quick IOPTH may not be used in PHP surgery routinely.

If the blood PTH level decreases by 50% after the operation, it is decided that the adenoma is removed successfully^{8,16}. In our study, parathormone levels decreased significantly in the early postoperative period compared to the preoperative levels, especially in the group ≥ 65 years, statistically significantly lower than the other group PTH levels in both early postoperative and postoperative 1st month.

Since the beginning of the 21st century, minimally invasive techniques have been developed for unilateral exploration²¹. With minimally invasive surgery, more successful cosmetic results, lower pain, lower hospital stay were determined⁵. We performed minimally invasive surgery for all patients. In our study, the duration of discharge time from the hospital was found to be close in both groups without any statistical difference.

It was reported that the complication rate of conventional parathyroidectomy (3%) was higher than that of minimally invasive parathyroidectomy (1.2%) and the rate of unilateral nerve injury was close in both methods²².

Although minimally invasive parathyroidectomy has lower complication rates, shortened hospital stay, and a significant reduction in hospital bills. However, a study reported that only 3% of United Kingdom (UK) surgeons performed minimally invasive parathyroidectomy²³. We did not encounter with nerve injury or permanent hypocalcemia both in geriatric and adult

groups. Our mean discharge time from hospital is very low. To perform minimally invasive parathyroidectomy the surgery team should be experienced. Otherwise like in UK surgeons the rate of this surgery would be lower than 5%.

There are some studies reporting that; advanced surgical techniques even in geriatric patients could be safely preferable via outpatient clinic under local anesthesia²⁴. Although our patients are older we did not use local anesthesia surgery.

Limitations of our study are having a low volume of patient groups, lack of routine using of quick PTH assays and to be planned as a retrospective study.

As a result, minimally invasive parathyroid surgery can be safely performed in geriatric patients. In addition, to avoid from the complications of hypercalcemia due to delayed surgery, can be preventable by minimally invasive parathyroid surgery. Exact localisation of adenoma can be detected preoperatively with multidisciplinary approach including washout examination, USG and 90 mTc-MIBI scintigraphy scans even without IOPTH measurements. Furthermore, to reveal certain results, we need high volume prospective studies for minimally invasive parathyroid surgery. Our study is the first in our literature about minimal invasive parathyroid surgery on geriatric patients.

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