



Contents lists available at ScienceDirect

## The American Journal of Surgery

journal homepage: [www.americanjournalofsurgery.com](http://www.americanjournalofsurgery.com)

## Subtotal vs. total parathyroidectomy with autotransplantation for patients with renal hyperparathyroidism have similar outcomes

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### ARTICLE INFO

#### Article history:

Received 14 February 2017

Received in revised form

14 June 2017

Accepted 2 July 2017

A portion of these data were presented at the 2016 Endocrine Society Annual Meeting in Boston, MA (4/3/16).

#### Keywords:

Parathyroidectomy  
Hyperparathyroidism  
Surgical outcomes

### ABSTRACT

**Background:** The optimal surgery for patients with renal hyperparathyroidism has been controversial, as either subtotal parathyroidectomy (subtotal PTX) or total parathyroidectomy with auto-transplantation (total PTX-AT) may be employed.

**Methods:** Adult patients having subtotal PTX or total PTX-AT for secondary hyperparathyroidism were identified from the American College of Surgeons National Surgical Quality Improvement Program, 2005–2013.

**Results:** Of 1130 patients, the majority ( $n = 765$ , 68%) underwent subtotal PTX. Total PTX-AT was associated with longer operative time (median 150 vs. 120 min,  $p < 0.001$ ). Rates of complications, reoperation, readmission, and 30-day mortality were not significantly different. After adjustment, the odds of having a complication [OR 0.97,  $p = 0.88$ ] and being readmitted within 30 days [OR 0.86  $p = 0.62$ ] were similar between the two procedures. Total PTX-AT was associated with prolonged hospital stay [Adjusted mean 5.0 vs. 4.1 days; (RR) 1.22,  $p < 0.001$ ] compared to subtotal PTX.

**Conclusions:** Subtotal PTX and total PTX-AT have similar rates of complications, readmission, and 30-day mortality, but subtotal PTX is less likely to have extended hospital stay. These findings have important cost implications for patients, payers, and hospitals.

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### 1. Introduction

Secondary hyperparathyroidism (SHPT) is a major cause of morbidity, including renal osteodystrophy, anemia, calciphylaxis, ectopic calcifications, and cardiovascular mortality, for patients with chronic kidney disease and end-stage renal disease (ESRD).<sup>1–4</sup> For patients with SHPT who fail medical therapy, including vitamin D analogues and calcimimetics, parathyroidectomy (PTX) is the treatment of choice. Surgery is associated with improved all-cause mortality and cardiovascular mortality for patients with ESRD.<sup>5–8</sup>

The two most common surgical approaches are subtotal PTX and total PTX with heterotopic autotransplantation (AT) - typically with tissue transplanted into the brachioradialis muscle of the non-dominant arm. However, the optimal operative management of SHPT has not reached consensus and remains controversial.<sup>9–12</sup>

With regard to surgical approach, the risk of disease recurrence vs. the morbidity of surgery and risk for hypoparathyroidism must be considered. Subtotal PTX typically involves resection of at least three glands and a less-than-total resection of the last in situ gland remnant with the intention of reducing the potential for significant post-operative hypocalcemia and permanent hypoparathyroidism. Total PTX-AT involves resection of all ( $\geq 4$ ) glands with concomitant AT of a small portion of a minced parathyroid gland into heterotopic tissue, aiming to avoid disease recurrence in the neck and thus alleviating the risks of re-operative neck surgery.<sup>13</sup> A study by

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Wetmore et al. determined that approximately 17% of patients were re-hospitalized for hypocalcemia within 90 days of any PTX procedure, and acknowledged that comparison of the specific surgical approaches with regard to postoperative morbidity would provide valuable insights.<sup>14</sup> The aim of our study was to evaluate, at a national level, short-term outcomes of adult patients with ESRD who undergo initial subtotal PTX vs. total PTX-AT.

## 2. Methods

### 2.1. Patient population

Data for this study were extracted from the American College of Surgeons – National Surgical Quality Improvement Program (ACS-NSQIP) Participant User Files (PUF) from 2005 to 2013. This database is a prospective, risk-adjusted, validated, national program maintained by the ACS that has demonstrated accuracy in recording postoperative complications. Information is collected for variables that include patient demographics, comorbidities, and morbidity and mortality outcomes up to 30 days postoperatively. This program is continuously audited, and each patient is followed until postoperative day 30 by trained and certified reviewers at each site. Specific data regarding candidacy for kidney transplant is not available nor is data available regarding intraoperative or postoperative biochemical data such as PTH level.

The PUFs were queried for all adult patients on dialysis with SHPT. These patients were identified using the International Classification of Disease, 9th edition. Patients who met inclusion criteria and underwent a PTX were then classified by surgical approach: subtotal PTX vs. total PTX-AT.

Definitions of the variables included in this database are described in the ACS-NSQIP user guide.<sup>15</sup> Demographic variables included patient gender, age at diagnosis, race, smoking status, diabetic status, and functional status prior to surgery. Clinical characteristics included surgeon specialty, American Society of Anesthesiologists (ASA) classification, operative time, overall time in the operating room, including time under anesthesia, and inpatient vs. outpatient surgery. Patient comorbidities were measured with the modified Charlson-Deyo score.<sup>16</sup> Outcomes measured included complications (primary), likelihood of receipt of subtotal PTX vs. total PTX-AT, hospital length of stay (LOS) in days, rates of 30-day readmission and 30-day mortality, and time to readmission within 30-days (secondary).

### 2.2. Statistical analysis

Baseline characteristics along with primary and secondary outcomes were compared between cohorts using the Chi-square or Fisher's exact test, as appropriate, and the Student's t-test for categorical and continuous variables, respectively. Multivariable logistic regression analyses were used to examine factors associated with receipt of subtotal PTX vs. total PTX-AT, incidence of any complication and 30-day readmission, and the estimated odds ratios (ORs), and 95% confidence intervals (CIs) are reported. These models were adjusted for the effects of demographic and clinical factors, including year of operation, gender, race, Charlson-Deyo score, diabetes status, and general, vascular, or ENT surgeon specialty. The association of LOS and surgery type was estimated with negative binomial regression; risk ratios (RRs), and 95% CIs are reported. The adjusted mean LOS was estimated from this model and is also reported with 95% CI for each procedure. Kaplan-Meier curves and log-rank tests were used to compare time to readmission within 30-days, and 7- and 10-day readmission rates and 95% CIs were estimated using the Kaplan-Meier method. A two-sided p-value of 0.05 was used to indicate statistical significance.

Only patients with available data were included in each model, and effective sample sizes are reported in the title of each table. All statistical analyses were performed using SPSS Version 22.0 (IBM Corp., Armonk, NY) or SAS, version 9.4 (SAS Institute, Cary, NC). This study was granted exempt status from the Duke University Institutional Review Board (IRB).

## 3. Results

A total of 1130 patients met study criteria and were included; 765 (67.7%) underwent subtotal PTX, and 365 (32.3%) underwent total PTX-AT. The two groups were similar with respect to age, gender, smoking status, comorbidities, independent preoperative functional status, and ASA class (all  $p > 0.05$ ) (Table 1). Those who received a total PTX-AT were more likely to be black (60.5 vs. 51.8% subtotal PTX,  $p = 0.01$ ), non-diabetic (84.9 vs. 77.8%, respectively,  $p = 0.007$ ), and have their operation done by a general surgeon (94.2 vs. 92.8%,  $p = 0.01$ ).

### 3.1. Impact of the extent of parathyroidectomy on complications, readmission, and LOS

Patients who received a total PTX-AT had a longer median operative time compared to patients who underwent subtotal PTX (150 vs. 120 min, respectively,  $p < 0.001$ ) and spent a greater amount of time in the operating room (204 vs. 170 min,  $p < 0.001$ ), but did not differ in time from admission to operation ( $p = 0.96$ ). On unadjusted analysis, there was no difference in inpatient status (91.8 total PTX-AT vs. 90.3% subtotal PTX), rates of cervical thyrectomy (2.8 vs. 4.4%), reoperation rate (5.8 vs. 4.1%), and 30-day mortality (0.8 vs. 1.2%, all  $p > 0.05$ ) (Table 1). There was also no difference in 7- (1.7 vs. 1%) or 10-day (3.3 vs. 3.3%) readmission rates (log-rank  $p = 0.99$ , data not shown).

On univariate analysis, the rate of occurrence of a complication was similar for PTX-AT vs. subtotal PTX (15.1% vs. 15.0%, respectively,  $p = 0.99$ ) (Table 1). After multivariable adjustment, complication rates remained similar between patients who underwent total PTX-AT and subtotal PTX (Odds Ratio [OR] = 0.97; 95% Confidence Interval (CI) 0.68–1.40,  $p = 0.88$ ). White race, female gender, and Charlson-Deyo score  $>2$  were associated with increased rates of complications (Table 2).

Multivariable logistic regression analysis with adjustment for patient demographic characteristics showed that there was no difference in 30-day readmissions between those patients who received total PTX-AT vs. subtotal PTX (OR = 0.86; 95% CI 0.47–1.56,  $p = 0.62$ ) (Table 3) Using negative binomial regression modeling, greater patient comorbidity as measured by Charlson-Deyo score  $>2$  (RR = 1.17; 95% CI 1.02–1.34,  $p = 0.03$ ) and total PTX-AT (RR = 1.22; 95% CI 1.10–1.34,  $p < 0.001$ ) were associated with increased likelihood of a longer hospital LOS (Table 4). After adjustment, patients who received total PTX-AT had longer hospital LOS on average compared to subtotal PTX (5.0 vs. 4.1 days,  $p < 0.001$ ).

In examining factors that may have influenced the choice of surgery, year of operation (OR = 1.10; 95% CI 1.03–1.16,  $p = 0.002$ ) and diabetes (insulin-treated: OR = 1.74; 95% CI 1.08–2.82, oral medication-treated: OR = 3.54; 95% CI 1.64–7.65,  $p = 0.002$ ) were associated with a higher likelihood of receipt of subtotal PTX, while black or unknown race (black: OR = 0.64; 95% CI 0.48–0.85, unknown: OR = 0.55; 95% CI 0.32–0.95,  $p = 0.01$ ) and treatment by a vascular surgeon (OR = 0.40; 95% CI 0.17–0.98,  $p = 0.04$ ) were associated with higher likelihood of receipt of total PTX-AT. Gender and Charlson-Deyo score were not associated with receipt of one procedure over the other ( $p$ 's  $> 0.05$ ) (Table 5).

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