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The devil is in the details: Assessing treatment and outcomes of 6,795 patients undergoing remedial parathyroidectomy in the Collaborative Endocrine Surgery Quality Improvement Program[☆]

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ABSTRACT

Background: Multi-institutional data describing remedial parathyroidectomy compared with index parathyroidectomy are scarce.
Methods: Using data in the Collaborative Endocrine Surgery Quality Improvement Program (2014–2017), baseline characteristics and outcomes of patients undergoing remedial parathyroidectomy versus index parathyroidectomy were examined using bivariate and multivariate methods. Rates of hypercalcemia and hypocalcemia at $\geq$ 180 days were assessed.
Results: Among 6,795 patients, 367 (5.4%) underwent remedial parathyroidectomy. A single localization study was done in 24.8% versus 26.9% of remedial parathyroidectomy versus index parathyroidectomy ($P = .37$). Patients undergoing remedial parathyroidectomy had higher rates of preoperative laryngoscopy (45.5% versus 6.2%, $P < .001$), intraoperative nerve monitoring (57.5% versus 34.5%, $P < .001$), and < 50% drop in hyperparathyroidism than those undergoing index parathyroidectomy (9.6% versus 3.3%, $P < .001$). Among patients with $\geq$ 180 days follow-up, none of the remedial parathyroidectomy versus three index parathyroidectomy patients (0.3%) had vocal cord dysfunction. Hypercalcemia rates for remedial parathyroidectomy and index parathyroidectomy were 10.5% versus 5.0 ($P = .07$), and hypocalcemia rates were 10.5% versus 2.4% (P < .001). After multivariate adjustment, failure to cure was 4.0 times more likely in remedial parathyroidectomy than index parathyroidectomy ($P < .001$).
Conclusion: This is the first multi-institutional examination of remedial parathyroidectomy outcomes in the Collaborative Endocrine Surgery Quality Improvement Program. Nerve injury rates are low; high rates of hypercalcemia and hypocalcemia suggest potential opportunities to refine the preoperative and intra-operative management of patients undergoing remedial parathyroidectomy.

Introduction

Hyperparathyroidism (HPT) is a common endocrine disease.[1,2] A single benign parathyroid adenoma is the most common etiology; multigland disease can occur, as in cases of familial HPT syndromes and patients with underlying kidney disease. HPT is often a surgical disease that can be approached via focused or bilateral cervical exploration. The goal of parathyroidectomy is cure; operative failure remains the most common complication of parathyroidectomy.[2]

Index parathyroid operations are associated with cure rates that exceed 95% when performed by experienced surgeons.[1,3,4] Approximately 3%–10% of patients require remedial parathyroidectomy for persistent or recurrent HPT.[4,5] In the remedial setting, the recurrent laryngeal nerves and eutopic or ectopic parathyroid glands can be more difficult to identify secondary to scarring, distorted neck anatomy, and obliteration of normal planes. Existing data regarding remedial parathyroidectomy are derived largely from high-volume single institutions or surgeons. These clinical series have mostly reported success rates >90%,[6–8] and in some cases, similar success to those of index operations.[3,5,6,9] Multi-institutional level contemporary data that describe patient outcomes after remedial parathyroidectomy in the setting of improved preoperative imaging, intraoperative adjuncts, and focused exploration are scarce.

We used data from the Collaborative Endocrine Surgery Quality Improvement Program (CESQIP) to examine the characteristics and

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outcomes of patients undergoing remedial parathyroidectomy (R-PTx) compared with those undergoing index surgery (I-PTx). Considering that a significant proportion of institutions participating in CESQIP are well-established endocrine surgery centers,[10] the hypothesis of the study was that patients undergoing R-PTx would have similar rates of endocrine-related outcomes, such as recurrent laryngeal nerve injury and failure to achieve eucalcemia, compared with those undergoing I-PTx, with substantial use of preoperative imaging and intraoperative adjuncts.

Materials and Methods

Database

Data collected prospectively from 53 providers participating in CESQIP Participant User Files ([PUF] January 2014–June 2017) were used.[10] Formed in 2012 by leaders from the American Association of Endocrine Surgeons, CESQIP aims to improve endocrine surgery outcomes and optimize costs. The CESQIP-PUF is an endocrine surgery–specific dataset that contains more than 300 variables, including demographic, clinical, pathologic, imaging, surgical, and outcomes data for patients undergoing parathyroid, thyroid, adrenal, and operations for neuroendocrine tumors. The CESQIP-PUF does not identify hospitals, individual providers, or operative volume. Data are based on standardized definitions for pre-, intra-, and postoperative variables specific to endocrine surgery (see Supplementary Material). CESQIP has been approved by the Centers for Medicare and Medicaid Services as a Qualified Clinical Data Registry.

Patients

All parathyroidectomy cases were abstracted from the CESQIP-PUF file. Baseline characteristics included patient age, sex, race, and body mass index. Clinical characteristics included diagnosis, use of preoperative laryngoscopy, and documentation of preoperative vocal cord dysfunction. In CESQIP, diagnosis was provided as the following: "primary sporadic", "familial", or "secondary/tertiary" HPT. The use and type of preoperative localization studies (ultrasound [US] Sestamibi, computed tomography [CT], magnetic resonance imaging [MRI], and selective venous sampling [SVS]) were included. Results of imaging studies were provided as categoric entries in CESQIP, namely: negative, nonlocalizing, positive, localized single gland with low confidence, localized single gland with high confidence, and multigland disease. Utilization of intraoperative nerve monitoring and operation type (focused, bilateral, conversion from focused to bilateral approach, or other) were examined. In CESQIP-PUF, operation time was provided as categorical data (<1 hour, 1–2 hours, 2–3 hours, and >3 hours); preoperative calcium, postoperative calcium, and PTH levels were provided as categoric values (normal, low, high, and/or very high). In CESQIP, very high calcium denotes calcium >2mg/dl than upper normal limi, and very high PTH denotes PTH >1000 pg/ml. Utilization of intraoperative parathyroid hormone levels, concomitant thymectomy, number of glands removed, and performance of parathyroid autotransplantation were assessed. CESQIP only provides binary data with regard to whether a >50% drop in intraoperative PTH was achieved by the end of the procedure. Final pathology (parathyroid tissue not found, normal, solitary adenoma, atypical adenoma, multigland disease, and cancer) was noted.

Longitudinal follow-up data are predesignated in the database. Follow-up time was computed by subtracting date of operation from date of the most recent follow-up. Hypercalcemia and hypocalcemia rates ≥180 days after the operation were assessed. In its longitudinal outcomes data, CESQIP includes a distinct variable that captures "clinical concern for recurrent or persistent HPT." To enable robust, clinically meaningful analyses, failure to cure in this study was defined as presence of hypercalcemia or clinical concern for recurrent or persistent HPT at ≥180 days; all analyses were restricted to patients with primary sporadic or familial HPT because CESQIP combines secondary and tertiary HPT into a single diagnosis, which would lead to conflicting results. To eliminate duplication of outcomes for patients with multiple follow-up visits, only data from the first visit ≥180 days after the date of surgery were included in analyses of longitudinal outcomes. Subanalyses by diagnosis comparing R-PTx versus I-PTx was limited by sample size. Therefore, diagnosis was categorized into sporadic primary HPT and secondary, tertiary, and familial HPT.

Statistical analysis

Patient demographic, clinical, and pathologic characteristics along with information about outcomes were reported as *n* (%) for categorical variables and median (interquartile range [IQR]) for continuous variables. Differences between study groups were tested using the χ^2 test, Fisher exact test, or Student *t* test, as appropriate. Multivariate logistic regression was used to estimate the independent effect of R-PTx versus I-PTx on the likelihood of failure to cure among patients with sporadic or familial HPT because both these groups of patients have HPT associated with baseline hypercalcemia. A 2-sided P value $< .05$ was considered significant. Analyses were performed using SPSS v 19.0 (SPSS Inc, Chicago, IL), and SAS v 9.4 (SAS Institute Inc, Cary, NC). Data used in this study are deidentified, and the study was exempted by the Duke University Institutional Review Board (Durham, NC).

Results

Baseline characteristics

A total of 6,795 parathyroid surgeries were studied. Of these, 367 (5.4%) represented R-PTxs; 83.0%, 13.5%, and 3.5% had undergone 1, 2, and ≥3 prior parathyroid surgeries, respectively. The median patient age was 61 years. Most patients were female and nonblack by race (Table 1). Patients undergoing R-PTx were more likely to have a preoperative diagnosis of secondary, tertiary, or familial HPT than those undergoing I-PTx (19.0% versus 8.2%, respectively, $P < .001$). R-PTx patients had higher rates of preoperative laryngoscopy (45.5% versus 6.2%, $P < .001$); 2.5% of R-PTx patients versus 0.9% of I-PTx patients had evidence of vocal cord dysfunction in the preoperative setting. Rates of earlier neck irradiation were the same between study groups (1.9% versus 1.9%).

Imaging

A single localization study was done in 24.8% R-PTx vs 26.9% I-PTx ($P = .37$; Table 2). In comparing localization imaging modalities, CT was less likely to result in a negative or nonlocalizing study when compared with US and Sestambi. For I-PTx patients, CT results were negative or nonlocalizing in 11.5% vs 23.3% US and 25.6% Sestamibi ($P < .001$). CT results were negative/nonlocalizing in just 15.0% of cases vs 28.1% US and 20.3% Sestambi ($P < .001$) in the context of R-PTx.

Operative details

The majority of patients had a focused parathyroid surgery (Table 3). Transection of the recurrent laryngeal nerve was rare in both groups (0.8% of R-PTx [$N = 3$] vs 0.1% of I-PTx patients [$N = 6$], $P < .001$). More patients undergoing R-PTx failed to have >50% drop in intraoperative PTH when compared with I-PTx (9.6% vs 3.3%, $P < .001$). Concurrent thymectomy (15.3% versus 8.6%) and

Table 1
Baseline characteristics of patients undergoing parathyroidectomy, CESQIP (2014–2017)*.

	I-PTx (N = 6,428)	R-PTx (N = 367)	*P* value
Demographics			
Age (years); median (IQR)	61 (52–69)	61 (52–69)	.81
Race			.55
Non-Black	4,805 (74.8)	271 (73.8)	
Black	606 (9.4)	39 (10.6)	
Asian	85 (1.3)	8 (2.2)	
Hispanic	483 (7.5)	27 (7.4)	
Unknown	437 (6.8)	21 (5.7)	
Sex, female	4,838 (75.3)	279 (76.0)	.74
BMI > 40	600 (9.3)	42 (11.4)	.18
Preoperative			
Diagnosis			< .001
Sporadic primary hyperparathyroidism	5,860 (91.2)	294 (80.1)	
Secondary/tertiary hyperparathyroidism	423 (6.6)	44 (12.0)	
Familial hyperparathyroidism	97 (1.5)	25 (6.8)	
Preoperative laryngoscopy	401 (6.2)	167 (45.5)	< .001
Vocal cord dysfunction	25 (0.4)	9 (2.5)	.70
Vitamin D			.003
Low	2,467 (38.4)	109 (29.7)	
Normal	2,960 (46.0)	188 (51.2)	
Preoperative calcium			.02
Normal	722 (11.2)	58 (15.8)	
High	5,251 (81.7)	290 (79.0)	
Very high	331 (5.1)	14 (3.8)	
Preoperative PTH			0.002
Low	11 (0.2)	1 (0.3)	
Normal	682 (10.6)	42 (11.4)	
High	5,263 (81.9)	287 (78.2)	
Very high	325 (5.1)	36 (9.8)	

* Data are presented as *n* (%) unless otherwise specified. Percentages may not add up to 100 because of rounding or missing values. *IQR*, interquartile range; *BMI*, body mass index; *PTH*, parathyroid hormone.

Table 2
Preoperative localization studies for patients undergoing parathyroidectomy, CESQIP (2014–2017)*.

	I-PTx (N = 6,428)	R-PTx (N = 367)	*P* value
≥1 localization study	6,100 (94.9)	348 (94.8)	.94
Single localization study	1,729 (26.9)	91 (24.8)	.37
Localization study type			
Ultrasound	5,505 (85.6)	278 (75.7)	< .001
Sestamibi	4,161 (64.7)	256 (69.8)	.05
CT	1,238 (19.3)	147 (40.1)	< .001
MRI	17 (0.3)	4 (1.1)	.006
SVS	8 (0.1)	7 (1.9)	< .001
Localization grades			
Ultrasound			.19
Negative/not localized	1,281 (23.3)	78 (28.1)	
Positive/low confidence for single gland	1,077 (19.6)	59 (21.2)	
Localized single gland with high confidence	2,721 (49.4)	125 (45.0)	
Multigland disease	376 (6.8)	15 (5.4)	
Sestamibi			.26
Negative/not localized	1,066 (25.6)	52 (20.3)	
Positive/low confidence for single gland	798 (19.2)	56 (21.9)	
Localized single gland with high confidence	2,048 (49.2)	133 (52.0)	
Multigland disease	214 (5.1)	14 (5.5)	
CT			.46
Negative/not localized	142 (11.5)	22 (15.0)	
Positive/low confidence for single gland	175 (14.1)	24 (16.3)	
Localized single gland with high confidence	778 (62.8)	84 (57.1)	
Multigland disease	130 (10.5)	14 (9.5)	
Combination of localization studies			< .001
Ultrasound only	1,184 (18.4)	33 (9.0)	
Sestamibi only	456 (7.1)	30 (8.2)	
CT only	84 (1.3)	28 (7.6)	
Ultrasound and Sestamibi	3,199 (49.8)	132 (36.0)	
Ultrasound and CT	653 (10.2)	30 (8.2)	
Sestamibi and CT	43 (0.7)	12 (3.3)	
Ultrasound, Sestamibi, and CT	452 (7.0)	73 (19.9)	
Other	29 (0.5)	10 (2.7)	
None	327 (5.1)	19 (5.2)	

* Data are presented as *n* (%) unless otherwise specified. Percentages may not add up to 100 because of rounding or missing values. Localization grade percentages are out of total number of patients who underwent each type of localization study. *CT*, computed tomography; *MRI*, magnetic resonance imaging; *SVS*, selective venous sampling.

Table 3
Operative characteristics of patients undergoing parathyroidectomy, CESQIP (2014–2017)*.

	I-PTx (N = 6,428)	R-PTx (N = 367)	*P* value
Operative approach			<.001
Focused	3,592 (55.9)	221 (60.2)	
Bilateral	2,155 (33.5)	112 (30.5)	
Focused converted to bilateral	643 (10.0)	9 (2.5)	
Other approach for ectopic gland	23 (0.4)	24 (6.5)	
Intraoperative PTH used	5,903 (91.8)	331 (90.2)	.32
<50% drop in intraoperative PTH	188 (3.3)	31 (9.6)	<.001
Nerve monitor used	2,218 (34.5)	211 (57.5)	<.001
Concomitant thymectomy	555 (8.6)	56 (15.3)	<.001
Parathyroid autotransplantation	104 (1.6)	35 (9.5)	<.001
Number of glands removed			<.001
0	13 (0.2)	13 (3.5)	
1	4,059 (63.1)	249 (67.8)	
2	751 (11.7)	66 (18.0)	
3	561 (8.7)	16 (4.4)	
3.5	566 (8.8)	4 (1.1)	
4	127 (2.0)	2 (0.5)	
>4	31 (0.5)	3 (0.8)	
Level of surgical assistant			<.001
Cosurgeon	91 (1.4)	12 (3.3)	
Fellow	1,398 (21.7)	106 (28.9)	
Resident	4,144 (64.5)	230 (62.7)	
PA/SA	685 (10.7)	18 (4.9)	
Other	110 (1.7)	1 (0.3)	
Operation time (hours)			<.001
<1	2,811 (43.7)	121 (33.0)	
1–2	2,894 (45.0)	170 (46.3)	
2–3	601 (9.3)	58 (15.8)	
>3	122 (1.9)	18 (4.9)	
Final pathology			<.001
Normal	41 (0.6)	5 (1.4)	
Solitary adenoma	4180 (65.0)	194 (52.9)	
Atypical adenoma	182 (2.8)	21 (5.7)	
Multi-gland disease	1649 (25.7)	110 (30.0)	
Cancer	6 (0.1)	4 (1.1)	
Not found	41 (0.6)	5 (1.4)	

* Data are presented as *n* (%) unless otherwise specified. Percentages may not add up to 100 because of rounding or missing values. *PTH*, parathyroid hormone; *PA*, physician assistant; *SA*, surgeon assistant.

parathyroid auto-transplantation (9.5% versus 1.6%) were significantly more likely during R-PTx ($P < .001$ for both; Table 3).

Subanalyses by diagnosis

Among patients with a preoperative diagnosis of sporadic primary HPT, 4.8% represented R-PTxs; 9.4% of patients had secondary/tertiary, and 20.5% of patients with familial HPT had R-PTx. The utilization of preoperative imaging and operative approach differed significantly by preoperative diagnosis (Table 4).

Longitudinal outcomes

A total of 1,157 patients had ≥180 days of follow-up data, representing 17.0% of the study cohort (mean 255 days; range 180–886 days); 17.1% of I-PTx ($N = 1{,}100$) and 15.5% ($n = 57$) of all R-PTx patients had longitudinal data. Permanent vocal cord dysfunction was documented in 0% of R-PTx versus 0.3% of I-PTx patients. For sporadic primary HPT undergoing R-PTx versus I-PTx, 78.7% vs 93.6% were normocalcemic, 10.6% vs 1.7% were hypocalcemic, and 10.6% vs 4.7% were hypercalcemic. For secondary/tertiary or familial HPT having R-PTx, 80.0% vs 78.0% were normocalcemic, 10.0% vs 11.9% were hypocalcemic, and 10.0% vs 10.1% were hypercalcemic. Overall, R-PTx patients had higher rates of hypercalcemia, hypocalcemia, and failure to cure (Fig. 1). After multivariate adjustment, R-PTx was 4 times as likely to result in failure to cure as I-PTx (95% confidence interval: 1.8 –8.7, $P < .001$; Fig. 2).

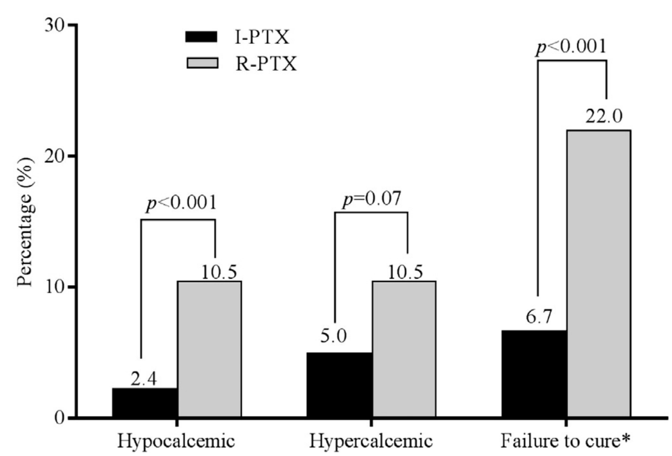

Fig. 1. Outcomes of R-PTx and I-PTx patients at ≥180 days after parathyroidectomy, CESQIP (2014–2017).
*All analyses of failure to cure were restricted to patients with primary sporadic or familial HPT.

Discussion

The surgical management of HPT has changed significantly during the past 2 decades with regard to imaging, intraoperative adjuncts, and operative approach. This is the largest comprehensive study examining the characteristics and outcomes of patients

Table 4
Subanalyses of patients undergoing parathyroidectomy by diagnosis, CESQIP (2014–2017)*.

	Sporadic primary HPT		*P* value	2^0, 3^0, or Familial HPT		*P* value
	I-PTx (N = 5,860)	R-PTx (N = 294)		I-PTx (N = 520)	R-PTx (N = 69)	
Single localization study	1,486 (25.4)	71 (24.1)	.66	224 (43.1)	19 (27.5)	.001
Combination of localization studies			<.001			<.001
Ultrasound only	999 (17.0)	26 (8.8)		169 (32.5)	7 (10.1)	
Sestamibi only	402 (6.9)	22 (7.5)		51 (9.8)	8 (11.6)	
CT only	80 (1.4)	23 (7.8)		4 (0.8)	4 (5.8)	
Ultrasound and Sestamibi	3,008 (51.3)	102 (34.7)		171 (32.9)	29 (42.0)	
Ultrasound and CT	637 (10.9)	28 (9.5)		13 (2.5)	2 (2.9)	
CT and Sestamibi	43 (0.7)	9 (3.1)		0 (0)	3 (4.3)	
Ultrasound, Sestamibi, and CT	442 (7.5)	64 (21.8)		7 (1.3)	8 (11.6)	
Other	28 (0.5)	8 (2.7)		1 (0.2)	2 (2.9)	
None	221 (3.8)	12 (4.1)		104 (20.0)	6 (8.7)	
Operative approach			<.001			<.001
Focused	3,502 (59.8)	177 (60.2)		55 (10.6)	40 (58.0)	
Bilateral	1,700 (29.0)	93 (31.6)		446 (85.8)	19 (27.5)	
Focused converted to bilateral	624 (10.6)	8 (2.7)		15 (2.9)	1 (1.4)	
Other approach for ectopic gland	21 (0.4)	15 (5.1)		2 (0.4)	9 (13.0)	
<50% drop in intraoperative PTH	178 (3.3)	25 (9.4)	<.001	10 (2.5)	6 (10.5)	.002
Nerve monitor used	2,001 (34.1)	174 (59.2)	<.001	203 (39.0)	37 (53.6)	.02
Concomitant thymectomy	398 (6.8)	41 (13.9)	<.001	153 (29.4)	14 (20.3)	.11
Parathyroid autotransplantation	54 (0.9)	16 (5.4)	<.001	50 (9.6)	18 (26.1)	<.001

* Data are presented as *n* (%) unless otherwise specified. Percentages may not add up to 100 because of rounding or missing values. *2^0*, secondary; *3^0*, tertiary.

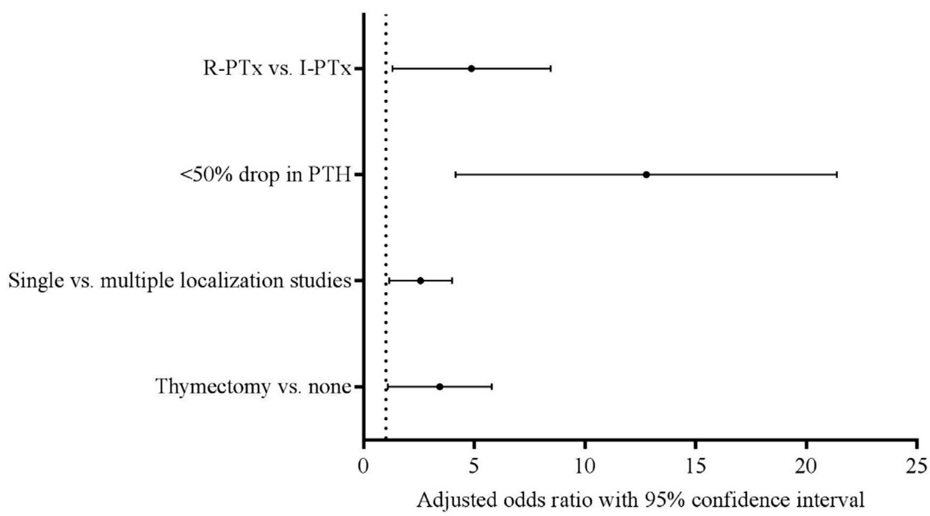

Fig. 2. Multivariate analysis of factors independently associated with failure to cure among patients with primary sporadic or familial HPT, CESQIP (2014–2017). Model adjusted for age, body mass index, diagnosis, R-PTX versus I-PTX, < 50% drop in intraoperative PTH or not, the use of single versus multiple localization studies, concomitant thymectomy, and performance of parathyroid autotransplantation. (*Dotted line* on the x-axis denotes 1.)

undergoing R-PTx, using contemporary, multi-institutional data. In CESQIP, 5.4% of patients undergoing parathyroidectomy had R-PTx. There was prominent variation in utilization of adjunctive studies, such as imaging, perioperative laryngoscopy, and intraoperative nerve monitoring in the remedial setting. Procedure-specific complications after R-PTx were higher than reported in existing literature; approximately 1 in 5 patients in CESQIP experienced either hypercalcemia or hypocalcemia ≥180 days after their operation.

In a study of reoperations for primary HPT, Shen et al[9] reported a 95% success rate with the aid of preoperative localization studies and a focused approach. Hessman et al[6] reported a 98% cure rate for 46 patients undergoing reoperation for nonmalignant HPT from the years 2000–2007. The authors emphasized the significance of consistently applying sensitive methods of preoperative imaging to enhance success rates of remedial surgery. R-PTx was often done via a focused approach in this study, underscoring the importance of preoperative localization to facilitate a successful operation. Several studies have shown CT to be more sensitive than Sestamibi and US for preoperative parathyroid localization for single adenomas and for multigland disease.[11–13] Mortenson et al[14] showed that sensitivity of CT for localization was 88% compared with 54% for Sestamibi, and that particular study recommended CT for preoperative localization of in the reoperative setting. Consistent with these studies, in CESQIP, CT had the highest rates of localizing a single gland with high confidence and showing evidence of multigland disease; however, Sestamibi and US were done more commonly, and CT was employed in just 40% of patients preparing for R-PTx. Our results echo those of a multi-institutional study,[11] which showed that CT has not been widely adopted for parathyroid localization and that there are variations in its role in the imaging algorithm according to local expertise and availability.

Previous studies have demonstrated the importance of a multimodal approach for parathyroid localization.[9,15] In an analysis involving 43 patients who underwent reoperative parathyroidectomy, Yen et al[16] proposed an algorithm for preoperative imaging involving US and Sestamibi for all patients and sequential CT, MRI, and

SVS until localization is achieved. Wang et al[17] showed that the combination of US, Sestamibi, and 4D-CT is the most cost-effective imaging approach for parathyroid localization. Our results revealed that almost a quarter (24.8%) of patients undergoing R-PTx underwent just one localization study. We found that patients undergoing a single preoperative localization study (compared with multiple studies) had approximately a 2.3-fold likelihood of failure to cure among patients with primary sporadic or familial HPT. Overall, our findings suggest that the use of preoperative localization studies before R-PTx is not optimized among CESQIP surgeons.

The hypocalcemia rate after R-PTx was as high as 21% in 1980 for patients with primary HPT and this decreased to 1%–2% by 1996.[9] Contemporary data on hypocalcemia rates in the remedial setting are scant. One study demonstrated a 13% rate of permanent hypocalcemia[18]; another study of 77 patients who underwent reoperative parathyroidectomy at a single institution reported an 8% rate of permanent hypocalcemia.[19] In CESQIP, 10.5% of patients undergoing R-PTx experienced hypocalcemia at ≥180 days, suggesting that the appropriate extent of gland resection may be an understated challenge in R-PTx, even among experienced surgeons.

Laryngeal nerve injury is one of the dreaded complications of R-PTx. In the preoperative setting, laryngoscopy was done in <50% of patients in CESQIP, which indicates poor adherence to current guidelines that recommend objective evaluation of vocal cord function before remedial surgery.[2] Intraoperatively, the use of nerve monitoring was higher in the remedial versus index setting. Still, more than 40% of R-PTx were done without nerve monitoring. We found that the incidence of nerve injury in patients undergoing R-PTx was very low (< 1%). The low nerve-injury rate in this study is consistent with published data from high-volume surgeons who have rates of approximately 1%.[4,6,7,9]

The meta-analysis of R-PTx for patients with secondary HPT found by Richards et al[20] found that autograft/remnant hyperplasia and the presence of supernumerary glands accounted for 86% of failed operations. The authors concluded that limitations in preoperative localization and inadequate exploration were among reasons for operative failures. Another study[9] showed that a parathyroid gland in an ectopic position and incomplete resection of multiple abnormal glands comprised 90% of the reasons for a failed parathyroid operation in patients undergoing reoperation for primary HPT. On the one hand, our study revealed low nerve-injury rates and a 93.6% success rate for patients undergoing I-PTx for sporadic primary HPT. On the other hand, the failure rate experienced by patients undergoing remedial surgery was 20%–22%, regardless of diagnosis (primary sporadic versus secondary, tertiary, or familial HPT). Overall, our study suggests that a failure to achieve eucalcemia after R-PTx in CESQIP is less about technical expertise and may be more related to suboptimal localization, exploration, and extent of gland resection.

In this study, a failure to cure among patients with primary sporadic or familial HPT was strongly associated with a <50% drop in intraoperative PTH. This is consistent with the results of several studies that have investigated the utility of intraoperative PTH monitoring in both I-PTx and R-PTx.[6,7,21] Subanalyses show higher rates of thymectomy in R-PTx for sporadic primary HPT, likely reflecting an attempt to eliminate a common location of missed ectopic glands; in contrast, thymectomy rates were lower in patients with secondary, tertiary, and familial HPT and undergoing R-PTx. In some studies, surgeons routinely perform concomitant thymectomy during initial operations for this patient subset; however optimal management remains a matter of debate.[22–24]

Limitations of this study include the fact that the CESQIP-PUF is deidentified; therefore, surgeon and hospital volume could not be analyzed. Reasons underlying the choice of imaging are not included. Details regarding previous operations, disease severity (including symptoms and numeric data for biochemical values with reference ranges), anesthesia type, location of missed or abnormal glands, and surgical approach are not included in the CESQIP-PUF. Gland size or volume and weight, and genetic information (particularly for those with familial forms of HPT) are not collected. Limited operative data and the relatively small sample size of patients undergoing R-PTx precluded further analysis on sensitivity of localization studies. Some results, such as the finding that 10.6% of patients undergoing initial surgery for secondary, tertiary, or familial HPT underwent a focused exploration, indicate variations in care and guidelines adherence; this could not be investigated further in CESQIP. Because CESQIP providers are more likely to perform high-volume parathyroid surgery, our results likely underestimate complication rates at a nationwide level because most parathyroid surgeries are performed by low-volume providers who tend to have higher complication rates.[25] The follow-up rate at ≥180 days in this study was low at <20%; this may allude to a high rate of patients being lost to follow-up and potentially inconsistent entry of longer term data. Loss of follow-up is an important surgical quality assessment parameter that will need to be further investigated. Coding accuracy between institutions participating in CESQIP will need to be validated as data abstraction guidelines are not yet standardized.

The CESQIP database is the first of its kind in the United States, providing multi-institutional and endocrine surgery–specific data that overcome significant data limitations of existing large databases, such as the American College of Surgeons National Surgical Quality Improvement Program and the Healthcare Cost and Utilization Project databases. This study revealed compromised outcomes for patients undergoing R-PTx regardless of their HPT diagnosis. Avenues for quality improvement and improved outcomes include optimizing preoperative imaging for patients undergoing R-PTx. Differences in patterns of care for parathyroidectomy patients at CESQIP centers highlighted in this study merit further investigation.

Disclosures

CESQIP and the hospitals participating in CESQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors. The conclusions, findings, and opinions expressed by the authors do not necessarily reflect the official position of the AAES or CESQIP. Use of CESQIP data does not imply endorsement by any of the groups named above.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.surg.2018.03.026.

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Discussion

Dr. Roger Tabah (Montreal, QC5, Canada): Certainly, one of the most challenging undertakings is a redo parathyroidectomy. I'll take all the help I can get preoperatively from the imaging studies and reviewing the operative note and the pathology from the original surgery.

The last factor is that there's a big difference in doing a redo parathyroidectomy on a patient that had been, say, operated on by my colleague, Dr Pasieka, versus the local community surgeon.

Dr Hadiza S. KazaurE: Thank you.

Dr. Poonghodi Karunakaran (Salem, India): Congratulations on your work. It is a well-established fact that index parathyroidectomy has better outcomes than remedial parathyroidectomy. Your study shows that subjects undergoing index parathyroidectomy had a focused approach and therefore should have had primary hyperparathyroidism as the etiology. I want to know the diagnosis in these index parathyroidectomy cases. On the other hand, you mentioned that remedial cases had secondary, tertiary, and familial hyperparathyroidism and could have undergone 3.5 gland parathyroidectomy. If so, can these two groups with different etiology and different type of surgical procedures be compared head-on?

Dr Hadiza S. Kazaure: That was one of the startling results that we saw. In the index patients undergoing parathyroidectomy for secondary, tertiary, or familial disease, about 10.6% had a focused approach. I think that's a bad setup to start and probably predisposes these patients toward remedial operation in their future. It's hard to tell why those cases were approached that way. That will need to be further investigated.

Dr. Sarah Oltmann (Dallas, TX): With regard to the remedial patients, in CESQIP we designate separate new records when we are documenting subsequent operations. Were you able to tell how many of the remedial operations were done by the same surgeon versus being able to tell how many of these complex patients they may have been inheriting from outside of their system? Your data clearly demonstrate the importance of a well-performed initial operation, and I'm curious to know how much of this could indicate that the initial operation was not done by the expert, but rather that the subsequent consequences were inherited by them.

Dr Hadiza S. Kazaure: CESQIP does not include that information about where these patients are coming from. The surgeon identifiers are removed prior to receiving the data file, so we have no way of tracing a specific surgeon. The identified patient information and surgeon information are not included in the data file that we receive.

Dr. Sally E. Carty (Pittsburgh, PA): I'm wondering if your failure rates may be artifactually high. In the reoperative setting, I follow the commonly used "Steve Libutti plan," which is to do one side and come back another day if disease persists. A staged operation is safer, so in reoperative bilateral disease, I just go in on the side where the imaging is most positive, and live to fight another day on the other side.

Dr Hadiza S. Kazaure: That's hard to tell from the database. We only have the number of operations the patients had, but it's hard to tell who is having a third operation compared to a second operation in a continuous manner because the patient's ID is taken out of the database.

Dr. Mahsa Javid (Charleston, SC): A quick question about the patients who did not have a 50% drop in PTH. Firstly, was this correlated with a failure to cure? Secondly, presumably, you have the preoperative PTH level for these patients. Were these high or were they in the normal range? If so, that may not correlate with having a 50% drop and a cure.

Dr Hadiza S. Kazaure: In CESQIP, that 50% drop is at the end of the case. We don't have the raw value of the PTH preop and postop and so forth, so we can't tell how much of a drop it was. But, in terms of the correlation between intraoperative PTH and failure to cure, yes, it was actually the strongest factor of an odds ratio of about 12 or so. There was a wide confidence interval because of the size of the sample, but it was the strongest predictor of failure to cure.

Dr. Jocob Moalem (Rochester, NY): I'm going to follow up that question. Are you sure that that's the end of the case? Because in a case where PTH doesn't drop and you initially started out with a focused parathyroidectomy, I would presume that that would prompt a four-gland exploration, and then perhaps the use of frozen section or other means of confirming that you have identified all four glands. In a situation like that, I would rarely use PTH again.

Dr Hadiza S. Kazaure: So, the definition of PTH drop was at the end of the case. So, it would be hard to know at what point some surgeons stopped checking the PTH levels. The database does not include that.