Subtotal Parathyroidectomy vs Total Parathyroidectomy with Autotransplantation for Secondary Hyperparathyroidism in Dialysis Patients: Short- and Long-Term Outcomes

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BACKGROUND: Two operations are performed for management of secondary hyperparathyroidism, subtotal parathyroidectomy (SPTX) and total parathyroidectomy with autotransplantation (TPTX-AT). There is no consensus among endocrine surgeons about which operation is the preferred treatment. This study compares the short- and long-term outcomes of SPTX and TPTX-AT for dialysis patients with secondary hyperparathyroidism.

STUDY DESIGN: This is a retrospective review of 46 dialysis patients undergoing PTX from 2006 to 2017 at a 719-bed tertiary care hospital.

RESULTS: Calcium on postoperative day 1 was 7.7 ± 0.8 mg/dL for SPTX and 7.9 ± 1.3 mg/dL for TPTX-AT ($p = 0.49$). Parathyroid hormone values on postoperative day 1 were 32.6 ± 26.0 pg/mL for SPTX and 9.5 ± 4.2 pg/mL for TPTX-AT ($p \leq 0.05$). Hospital length of stay was 3.7 ± 1.9 days for SPTX and 4.4 ± 3.5 days for TPTX-AT ($p = 0.46$). The required doses of calcium and calcitriol at discharge did not differ significantly. Reoperation for recurrence or persistence of disease was required in 6 SPTX patients and 2 TPTX-AT patients ($p = 0.12$). Parathyroid hormone values <15 pg/mL at long-term follow-up occurred in 5.6% of SPTX patients and 26.7% of TPTX-AT patients ($p = 0.09$). Parathyroid hormone values >200 pg/mL at long-term follow-up occurred in 38.9% of SPTX patients vs 6.7% of the TPTX-AT patients ($p \leq 0.05$). Calcium supplementation at more than 6 months was required for 36.8% of SPTX and 71.4% of TPTX-AT patients ($p < 0.05$).

CONCLUSIONS: The long-term control of parathyroid hormone elevation and avoidance of recurrent disease is improved with TPTX-AT, but carries a higher risk of long-term hypocalcemia. (J Am Coll Surg 2019;228:831−838. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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Secondary hyperparathyroidism in renal failure patients is a complex disease characterized by increased parathyroid hormone (PTH) production in response to dysregulation of calcium, phosphorus, and vitamin D metabolism. In response to relative hypocalcemia and hyperphosphatemia, there is persistent stimulation of parathyroid tissue, usually leading to 4-gland hyperplasia. Ultimately, chronically elevated levels of PTH can lead to symptoms of bone pain, muscle weakness, neurologic dysfunction, depression, and osteoporosis (otherwise known as renal osteodystrophy in secondary hyperparathyroidism patients).

Medical management with phosphate binders, activated vitamin D (calcitriol), and calcimimetics (cinacalcet) can

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Abbreviations and Acronyms

IOPTH = intraoperative parathyroid hormone
POD = postoperative day
PTH = parathyroid hormone
SPTX = subtotal parathyroidectomy
TPTX-AT = total parathyroidectomy with autotransplantation

often be inadequate. Cinacalcet is a calcimimetic agent that sensitizes calcium receptors to extracellular calcium and lowers PTH levels through improvement of calcium and phosphorus homeostasis.[1] Activated vitamin D analogues, such as paricalcitol or calcitriol, are used frequently, although the value of these medications in the management of severe secondary hyperparathyroidism remains uncertain.[2,3]

Referral for surgical management for renal hyperparathyroidism is generally considered when PTH levels rise to >800 pg/mL, though there are no firmly established criteria for referral.[4] The surgical options include either subtotal parathyroidectomy (SPTX) or total parathyroidectomy with autotransplantation (TPTX-AT). Surgical intervention leads to marked improvement in postoperative PTH levels, as well as improved bone mineral density.[5] There is also recent literature showing improved renal transplant function and survival in patients who had severe secondary hyperparathyroidism addressed surgically before transplantation.[6]

Currently, there is no consensus among endocrine surgeons about which operation is superior. Questions still remain about rates of recurrence and reoperation in patients undergoing either of these 2 operations and the risks of potential long-term consequences, such as permanent hypoparathyroidism and hypocalcemia. These questions prompted the current study.

The main outcomes measures included immediate and long-term resolution of PTH elevations, duration of hospital stay, degree of postoperative hypocalcemia as judged by the patient's needs for calcium and calcitriol at time of discharge, and need for reoperation.

METHODS

After approval by the IRB, we performed a retrospective review of the endocrine surgery database at a 719-bed tertiary care referral hospital. We reviewed the records of 77 patients with renal disease who underwent PTX by a single endocrine surgeon between 2006 and 2017. The patients included in our study were all aged older than 18 years and carried a diagnosis of end-stage renal disease on hemodialysis or peritoneal dialysis at the time of operation. They all underwent SPTX or TPTX-AT at our institution by a single endocrine surgeon and carried a final diagnosis of secondary hyperparathyroidism with enlargement of multiple parathyroid glands. Each patient included in the study had at least 6 months of follow-up data. From our original list of 77 patients, 22 were excluded due to a final diagnosis of tertiary hyperparathyroidism. Four were excluded because they had renal insufficiency not requiring dialysis at the time of operation. Two were excluded because they lacked 6 months of follow-up data. Three were excluded because they had revision operations for recurrent or persistent disease at our institution, but their original operations took place at an outside hospital. This resulted in a final total of 46 patients, 23 who underwent SPTX and 23 who underwent TPTX-AT.

All subjects were referred by their nephrologists for secondary hyperparathyroidism refractory to medical management. The indications for operation were the presence of severe disease, defined as PTH levels approaching or higher than 1,000 pg/mL, and/or significant symptoms, usually manifesting as bone pain and fatigue.

Each patient in the study underwent either SPTX or TPTX-AT. Subtotal PTX was defined as removal of all parathyroid tissue except a well-vascularized 30- to 50-mg remnant of the most normal of the parathyroid glands. Total PTX-AT was defined as removal of all parathyroid tissue from the neck, followed by AT of 30 to 50 mg of minced parathyroid tissue from the most normal gland into 3 subcutaneous pockets on the upper chest. Thymectomies were performed as part of both operative approaches, as the thymus is a common place for supernumerary glands.

The type of operation performed was determined by the operating surgeon intraoperatively based on the sizes of the parathyroid glands and technical feasibility of leaving a 30- to 50-mg viable parathyroid remnant on a vascular pedicle. If at least 1 of the parathyroid glands had a region of fairly normal parenchyma that could be maintained on a healthy vascular pedicle, and it was in a location that could be readily approached should future operations be required, then SPTX was performed. However, if all 4 glands were markedly enlarged and nodular, TPTX-AT was done. It was more technically challenging to fashion a small, well-vascularized remnant from large, firm, nodular glands. Therefore, by removing the entirety of each gland, it was possible to be more precise with the amount of parathyroid tissue left in the patient. The aim of such decisions was always to decrease rates of disease recurrence due to remnant hypertrophy.

Intraoperative PTH (IOPTH) monitoring was used in all cases. However, due to the delayed PTH clearance

common in dialysis patients, these levels often remained above the upper limit of normal at the time an operation was concluded. Therefore, if all 4 parathyroid glands were clearly identified and bilateral thymectomies had been performed, the final IOPTH level was not always relied on to determine operative success. However, if the IOPTH failed to drop by at least 50%, this would always prompt a search for additional ectopic parathyroid tissue. Because of this relatively slower clearance of PTH, postoperative day (POD) 1 PTH levels were compared in this study, instead of final IOPTH levels.

Postoperatively, all patients were immediately begun on substantial doses of oral calcium and calcitriol to combat expected bone hunger. Calcium was given in the form of Tums (GlaxoSmithKline) beginning at 800 mg of elemental calcium (4 Tums) every 6 hours. Calcitriol was initiated at 0.5 μg twice daily. Both were titrated as necessary. If hypocalcemia was refractory to oral replacement with a serum calcium <7 mg/dL, IV calcium gluconate in doses of 1 to 5 g was administered. Due to deficiencies in the medical records, the exact amounts of IV calcium administered in the immediate postoperative period were not available. All hemodialysis patients were scheduled for dialysis on the morning after operation, and peritoneal dialysis patients had dialysate infused on the evening of operation. High calcium baths were used in both groups.

Analysis included PTH and calcium levels preoperatively, immediately postoperatively, and more than 6 months postoperatively. The hospital electronic medical record and dialysis center records were used to determine total parathyroid gland weight excised, hospital length of stay, doses of calcium and calcitriol at time of discharge, and most recent levels of calcium and PTH at 6 months or more after operation. Medication lists for each patient were also obtained to determine whether the patients were taking calcium, calcitriol, paricalcitol, or cinacalcet in the 6 months before operation, or more than 6 months after. In the calculations of the means of POD1 calcium, PTH, length of stay, discharge calcium, and calcitriol, we excluded the small number of patients who had persistence of disease, as their POD1 laboratory values and hospital courses differed greatly from the majority of patients whose original operations were successful.

The definitions of persistent and recurrent disease in renal failure patients with secondary hyperparathyroidism are not as well defined in the literature as they are for patients with primary hyperparathyroidism. For the purposes of this analysis, persistent disease was defined as failure of the POD1 PTH to fall to <150 pg/mL. Recurrent disease was defined as PTH elevation >200 pg/mL occurring 6 months or more after an initial successful PTX.

Data were analyzed using Excel for Windows and GraphPad Prism, version 7.03. Student's *t*-test was used to compare numerical data and chi-square analysis was used to compare categorical data. A p value <0.05 was considered significant. Data were expressed as mean ± SEM for all continuous variables.

RESULTS

Between 2006 and 2017, forty-six dialysis patients were treated surgically for severe secondary hyperparathyroidism. Twenty-three patients had SPTX and 23 had TPTX-AT. Patients in each group were demographically similar, without significant differences in sex, age, or weight of parathyroid glands removed. Mean age was 51.7 ± 15.1 years for SPTX and 48.4 ± 11.5 years for TPTX-AT ($p = 0.41$). Fifty-two percent of SPTX patients were female vs 48% of TPTX-AT patients ($p = 0.77$). Total weight of the parathyroid glands removed was 2.4 ± 1.7 g for SPTX and 4.4 ± 5.0 g for TPTX-AT ($p = 0.08$) (Table 1).

The preoperative medical management of the 2 groups was also similar. Mean preoperative calcium was 9.0 ± 0.9 mg/dL for the SPTX group and 9.3 ± 1.0 mg/dL for the TPTX-AT group ($p = 0.35$). The preoperative PTH was 1,599.7 ± 794.0 pg/mL in the SPTX group and 1,936.7 ± 1,076.1 pg/mL in the TPTX-AT group ($p = 0.23$). Preoperative medication lists were accessible for 18 of 23 SPTX patients and 22 of 23 TPTX-AT patients. Preoperatively, 57.9% of SPTX patients were on cinacalcet vs 77% of TPTX-AT patients ($p = 0.18$). Mean preoperative dose for SPTX patients was 71 ± 43 mg vs 73.8 ± 41.7 mg ($p = 0.87$). Of SPTX patients, 33.3% were on paricalcitol vs 22.7% of TPTX-AT patients ($p = 0.45$). Mean dose for SPTX patients was 3.75 ± 1.0 μg vs 4.2 ± 3.4 μg for TPTX-AT patients ($p = 0.8$). Only 22.2% of patients in the SPTX group were on preoperative calcium vs 9.1% of TPTX-AT patients ($p = 0.25$). Mean dose of elemental calcium for the SPTX group was 1.54 ± 3.7 g vs 1.2 ± 0 g in the TPTX-AT group ($p = 0.59$). Only 1 of 18 (5.7%) patients in

Table 1. Demographic Characteristics of Patients Undergoing Subtotal Parathyroidectomy or Total Parathyroidectomy with Autotransplantation

Characteristic	SPTX	TPTX-AT	p Value
Female, n/N	12/23	11/23	0.77
Male, n/N	11/23	12/23	0.77
Age at operation, y, mean ± SD	51.7 ± 15.1	48.4 ± 11.5	0.41
Gland weight, g, mean ± SD	2.4 ± 1.7	4.4 ± 5.0	0.08

SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

the SPTX group was taking calcitriol preoperatively vs 4 of 22 (18.2%) in the TPTX-AT group (p = 0.23) (Table 2).

On POD1, calcium values were not significantly different between the 2 groups, 7.7 ± 0.8 mg/dL in the SPTX group and 7.9 ± 1.3 mg/dL in the TPTX-AT group (p = 0.49). However, PTH levels on POD1 were significantly higher in patients who had SPTX, 32.6 ± 26.0 pg/mL vs 9.5 ± 4.2 pg/mL in TPTX-AT patients (p < 0.05). Hospital length of stay was not significantly different between groups, with 4.4 ± 3.5 days observed in the TPTX-AT group vs 3.7 ± 1.9 days for the SPTX group (p = 0.46). At discharge, the daily doses of elemental calcium were 3.1 ± 2.0 g in SPTX patients and 2.6 ± 1.1 g in TPTX-AT patients (p = 0.38). Discharge doses of calcitriol were 1.5 ± 0.9 μg/d in the SPTX group and 1.8 ± 1.0 μg/d in the TPTX-AT group (p = 0.30) (Table 3).

Most recent PTH levels at 6 months or more postoperatively were 238.7 ± 302.8 pg/mL for SPTX and 87.3 ± 98.7 pg/mL for TPTX-AT (p = 0.07). At 6 months or more postoperatively, the percentage of patients with a PTH level <15 pg/mL was higher in the TPTX-AT group, 26.7% vs 5.6%, although this was not statistically significant (p = 0.09). The percentage in the normal range (15 to 65 pg/mL) was similar, 22.2% for SPTX vs 26.7% for TPTX-AT (p = 0.77). The percentage of patients with mildly elevated PTH of 66 to 200 pg/mL was 33.3% in the SPTX group and 40% in the TPTX-AT group (p = 0.69). The percentage of patients with markedly elevated PTH (>200 pg/mL) at 6 months postoperatively was significantly higher in the SPTX group, 38.9% vs 6.7% (p < 0.05) (Table 4).

Most recent calcium levels at 6 months or more postoperatively were 8.7 ± 1.2 mg/dL for SPTX and 8.5 ± 1.2 mg/dL for TPTX-AT (p = 0.61). At 6 months or more postoperatively, the percentage of patients with a calcium level <7 mg/dL was approximately the same, with 9.5% in the SPTX group and 11.7% in the TPTX-AT group (p = 0.82). The percentage of patients with calcium levels between 7 and 8 mg/dL was 23.8% for SPTX and 18% for TPTX-AT (p = 0.64). The percentage of patients with calcium values between 8 and 10.5 mg/dL was 66.7% in the SPTX group and 70.5% in the TPTX-AT group (p = 0.80) (Table 5).

Surgical complications after operation were rare, with only 1 patient undergoing urgent reoperation for hematoma evacuation. The difference in rates of reoperation for recurrent or persistent disease, though not statistically significant, was 26% in the SPTX group vs 8.7% in the TPTX-AT group (p = 0.12).

Of the 23 patients who had TPTX-AT, 4 eventually underwent successful renal transplantation. Two of the patients in the SPTX group also eventually underwent successful renal transplantation. None of these patients experienced recurrence of disease or tertiary hyperparathyroidism.

There were 4 patients with persistent disease after the original operation, 3 in the SPTX group and 1 in the TPTX-AT group. The TPTX-AT patient had a fifth parathyroid gland subsequently identified beneath the left thyroid lobe on a follow-up sestamibi scan, which was resected for cure 7 months after his initial operation. Of the patients with persistent disease in the SPTX group, 1 was lost to follow-up. One patient had a fifth parathyroid found in the mediastinum on sestamibi and 4-dimensional CT imaging, which was resected by video-assisted thoracoscopy 6 months after the index operation. The third SPTX patient had a large remnant responsible for the operative failure. She returned to the operating room 24 months after the index operation for curative resection of the remnant with AT (Table 6).

There were 4 patients who returned to the operating room for recurrence of disease, 3 in the SPTX group and 1 in the TPTX-AT group. The 3 in the SPTX group were all eventually taken back to the operating room for PTH values >1,000 pg/mL. All 3 underwent resection of

Table 2. Preoperative Characteristics of Patients Undergoing Subtotal Parathyroidectomy or Total Parathyroidectomy with Autotransplantation

Characteristic	SPTX	TPTX-AT	p Value
Preoperative calcium, mg, mean ± SD	9.0 ± 0.9	9.3 ± 1.0	0.35
Preoperative PTH, mean ± SD	1,599.7 ± 794.0	1,936.7 ± 1,076.1	0.23
% on cinacalcet	57.9	77.3	0.18
% on paricalcitol	33.3	22.7	0.45
% on calcium	22.2	9.1	0.25
% on calcitriol	5.6	18.2	0.23
Dose of cinacalcet, mg, mean ± SD	71 ± 43	73.8 ± 41.7	0.87
Dose of paricalcitol, μg, mean ± SD	3.75 ± 1.0	4.2 ± 3.4	0.8
Dose of calcium, mg, mean ± SD	1.54 ± 3.7	1.2 ± 0	0.59

PTH, parathyroid hormone; SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

Table 3. Hospital Course of Patients Undergoing Subtotal Parathyroidectomy or Total Parathyroidectomy with Autotransplantation

Variable	SPTX, mean ± SD	TPTX-AT, mean ± SD	p Value
POD1 calcium, mg/dL	7.7 ± 0.8	7.9 ± 1.3	0.49
POD1 PTH, pg/mL	32.6 ± 26.0	9.5 ± 4.2	<0.05
Length of stay, d	3.7 ± 1.9	4.4 ± 3.5	0.46
Discharge calcium dose (grams of elemental calcium)	3.1 ± 1.9	2.6 ± 1.1	0.38
Discharge calcitriol, μg	1.5 ± 0.9	1.8 ± 1.0	0.30

POD, postoperative day; PTH, parathyroid hormone; SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

a hypertrophied remnant parathyroid gland, with autotransplantation of 30 mg of residual parathyroid tissue into the upper chest wall. Those operations were performed at 16, 61, and 70 months after the original SPTX. Recurrence developed in 1 patient in the TPTX-AT group after 54 months and resection of a portion of the previously autotransplanted tissue was performed.

The most recent pharmaceutical regimens were reviewed for all patients. Complete medication lists were available for 19 of 23 SPTX patients and 14 of 23 TPTX-AT patients. An incomplete list within a provider note was available for 1 additional TPTX-AT patient, stating that they were taking calcitriol at more than 6 months postoperatively. Calcium supplementation was prescribed in 36.8% of SPTX patients vs 71.4% of TPTX-AT patients ($p < 0.05$). Calcitriol was prescribed in 36.8% of SPTX patients and 66.7% of TPTX-AT patients ($p = 0.08$), and another activated vitamin D analog, paricalcitol, was prescribed in 21.1% of SPTX patients vs 35.7% of TPTX-AT patients ($p = 0.35$), demonstrating an overall trend for greater need of pharmacologic supplementation of calcium and vitamin D in the TPTX-AT group. At long-term follow-up, 10.5% of SPTX patients were on cinacalcet vs 0% of TPTX-AT patients ($p = 0.21$) (Table 7).

DISCUSSION

Although secondary hyperparathyroidism remains a disease that is primarily medically managed, approximately 15% of patients on dialysis for 10 years and 38% of patients on dialysis for 20 years undergo PTX.[6] Despite advances in medical management of chronic renal failure and secondary hyperparathyroidism, there has been no demonstrable change in the number of patients requiring surgical management.[7] For such patients, PTX has consistently been shown to improve quality of life.[8] In addition to treating symptoms of renal osteodystrophy, PTX has also been shown to reduce all-cause mortality.[9] There is also mounting evidence that PTX in patients with poorly controlled secondary hyperparathyroidism prolongs renal allograft survival.[10-12]

The goals of this study were 2-fold. First, we wanted to compare the relative level of difficulty in the initial postoperative management of hypocalcemia due to bone hunger. Second, we sought to determine what differences exist in the short- and long-term efficacy of the 2 operative approaches. To accomplish this, we compared 2 similar groups of dialysis patients who underwent either SPTX or TPTX-AT during the last 11 years.

We first examined the immediate perioperative period to see if one group was more difficult to manage with regard to maintaining adequate serum calcium. To answer that question, we examined calcium levels on POD1 and hospital length of stay. Surprisingly, although it was thought that POD1 calcium would have been significantly lower in the TPTX-AT group because of the expectedly lower PTH levels in these patients, there was no significant difference in POD1 calcium level. This most likely reflects a very aggressive postoperative replacement regimen of oral calcium and calcitriol in these patients. One of the details of postoperative management that was not possible to accurately define was the amount

Table 4. Parathyroid Hormone Levels at More than 6 after Operation

Variable	SPTX	TPTX-AT	p Value
PTH, pg/mL, mean ± SD	238.7 ± 302.8	87.3 ± 98.7	0.07
PTH <15 pg/mL, %	5.6	26.7	0.09
PTH 15–65 pg/mL, %	22.2	26.7	0.77
PTH 66–200 pg/mL, %	33.3	40	0.69
PTH >200 pg/mL, %	38.9	6.7	<0.05

PTH, parathyroid hormone; SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

Table 5. Calcium Levels at More than 6 Months after Operation

Variable	SPTX	TPTX-AT	p Value
Calcium, mg/dL, mean ± SD	8.7 ± 1.2	8.5 ± 1.2	0.61
<7 mg/dL, %	9.5	11.7	0.82
7–8 mg/dL, %	23.8	18	0.64
>8 mg/dL, %	66.7	70.5	0.80

SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

of IV calcium administered to each patient, so it is possible that more IV calcium was required in the TPTX-AT group.

We used the total doses of elemental calcium and calcitriol prescribed at discharge as surrogates to indicate degrees of bone hunger. Based on these values, there was no significant difference between the 2 groups. The length of stay was a direct reflection of the time needed to achieve calcium homeostasis, and no statistical difference was observed between the 2 groups.

Several studies have examined potential patient factors associated with development of post-PTX hungry bone syndrome in dialysis patients. A recent study by Ferreira and colleagues[13] looked at 45 patients who underwent TPTX-AT after calcitriol loading. Despite this intervention, 28% still developed severe prolonged hypocalcemia, and there was an association with higher preoperative PTH and longer times on renal replacement therapy. The studies by Ho and colleagues[14] and Latus and colleagues[15] both showed young age and lower preoperative calcium to be predictive of hungry bone syndrome. However, both preoperative PTH levels and preoperative vitamin D loading were not preventative. In our study, there was neither a significant difference in the preoperative levels of PTH nor vitamin D administration preoperatively.

To evaluate the long-term durability of each operation, we looked at mean PTH levels more than 6 months from the date of the original operation. We did not observe a statistical difference between the 2 groups. However, there were significantly more patients with very high PTH values (>200 pg/mL) in the SPTX group (38.9% vs 6.7%). A small number of patients in the SPTX group were also found to be back on cinacalcet for their recurrent PTH elevations. These numbers indicate that TPTX-AT will be more durable in the long-term and keep PTH levels from trending upward. There were also 3 patients undergoing repeat PTX for removal of hypertrophied parathyroid remnants in the SPTX group, vs only 1 in the TPTX-AT group. Based on this observation, it is likely that autotransplanted tissue is less apt to hypertrophy than a remnant in situ parathyroid gland in the face of ongoing dialysis.

Long term, nearly 27% of patients having TPTX-AT had PTH levels <15 pg/mL, and they were significantly more likely to be prescribed calcium supplementation (71.4% vs 36.8% in the SPTX group). Calcitriol and paricalcitol use at more than 6 months postoperatively did not significantly differ between the 2 groups. There is clearly a trend toward increased rates of long-term hypoparathyroidism in the TPTX-AT group. However, despite poor or absent graft function, these patients are generally well managed with a regimen of calcium and calcitriol, as evidenced by similar rates of normocalcemia at more than 6 months postoperatively between the 2 groups (66.7% in SPTX patients and 70.5% in TPTX-AT patients). Also, the infrequency of severe hypocalcemia <7 mg/dL at more than 6 months postoperatively (9.5% in the SPTX group and 11.7% in the TPTX-AT group) is another indicator of the relative ease of medically managing patients whose parathyroid hormone levels remain chronically low.

Recent meta-analyses have demonstrated the curative nature of both procedures, with similar rates of complications, readmission, and 30-day mortality. In 2006, Richards and colleagues[16] performed a meta-analysis of 53 studies to determine the most common causes of reoperation. They found that TPTX-AT patients have a higher rate of reoperation for recurrent disease. They also showed that initial inadequate cervical exploration resulting in persistent

Table 6. Recurrent and Persistent Disease

Operation	Recurrence vs persistence	Cause	Time between initial and repeat operation, mo
SPTX	Recurrence	Remnant hypertrophy	61
SPTX	Recurrence	Remnant hypertrophy	70
SPTX	Recurrence	Remnant hypertrophy	16
SPTX	Persistence	Fifth gland	6
SPTX	Persistence	Unknown, likely missed parathyroid	Did not return to OR, lost to follow-up
SPTX	Persistence	Remnant too large	24
TPTX-AT	Recurrence	Autotransplant hypertrophy	54
TPTX-AT	Persistence	Missed mediastinal fifth parathyroid	7

OR, operating room; SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

Table 7. Patients on Pharmacologic Supplementation More than 6 Months after Operation

Variable	SPTX	TPTX-AT	p Value
% on Cinacalcet	10.5	0	0.21
% on Paricalcitol	21	35.7	0.35
% on Calcitriol	36.8	66.7	0.08
% on Calcium	36.8	71.4	<0.05

SPTX, subtotal parathyroidectomy; TPTX-AT, total parathyroidectomy with autotransplantation.

disease occurred in 42% of SPTX patients and 34% of TPTX-AT patients. A recent study by Anderson and colleagues[17] reviewed American College of Surgeons NSQIP data from 2005 to 2013, and included 1,130 patients. Sixty-eight percent had SPTX and 32% TPTX-AT. The only significant finding was that patients undergoing TPTX-AT had a longer hospital stay. There were no differences in complication rates or 30-day readmission rates.[17] In 2017, Chen and colleagues[18] published a meta-analysis of 13 comparative studies, including 1,685 patients, and concluded there was no significant difference between the 2 operations with regard to initial success, perioperative drop in calcium and PTH levels, recurrence, reoperation rate, and long-term hypocalcemia.

Interestingly, a study published recently in *Surgery* looked at 824 patients who underwent SPTX or TPTX-AT and compared outcomes, finding no difference in mortality risk between the 2 procedures, but a higher risk of cardiovascular complications postoperatively for TPTX-AT patients vs SPTX patients. However, risk of recurrence was lower with TPTX-AT.[19]

Our study demonstrates that both procedures are initially effective at treating secondary hyperparathyroidism in dialysis patients. In the perioperative period, there were no significant differences noted in the degree of bone hunger between the 2 groups. Immediate postoperative calcium levels on aggressive replacement regimens of calcium and calcitriol were similar. Hospital length of stay was used as a surrogate for time to stabilize calcium levels postoperatively, and it was not significantly different between the 2 groups. The long-term control of PTH elevation and avoidance of recurrent disease was improved with TPTX-AT, but came at the expense of a higher risk of long-term hypoparathyroidism requiring calcium and calcitriol supplementation to maintain eucalcemia.

The limitations of this retrospective study include the small patient sample size and lack of randomization.

CONCLUSIONS

In the management of severe secondary hyperparathyroidism in dialysis patients, both SPTX and TPTX-AT are initially equally effective. Contrary to what one might expect based on the relative absence of PTH immediately postoperatively in the TPTX-AT group, these patients were not significantly more difficult to manage. The TPTX-AT patients also had better long-term control of PTH levels, and therefore less likelihood of recurrence requiring additional operations.

Author Contributions

Study conception and design: Zmijewski, Mazzaglia
Acquisition of data: Zmijewski, Staloff, Wozniak
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Invited Commentary

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Dr Zmijewski and colleagues provide an important and insightful study evaluating the optimal surgical remedy for uremic hyperparathyroidism (UHPT). Renal failure-induced vitamin D dysregulation and hyperphosphatemia causes hypocalcemia, ultimately driving parathyroid hyperplasia and the development of UHPT.[1] Uremic hyperparathyroidism causes a myriad of end-organ effects, including bone and cardiovascular complications. Furthermore, for patients undergoing renal transplantation, graft failure is higher in poorly controlled UHPT patients.[2] Therefore, proper management of UHPT is very important to improve patient outcomes before and after transplantation.

The definitive treatment for UHPT is subtotal parathyroidectomy, with preservation of a 30- to 50-g piece of remnant parathyroid tissue. The remnant tissue may either be preserved with its native blood supply in-situ (SPTX) or be autotransplanted (TPTX-AT) at a location that is readily accessible (ie forearm, chest wall, etc). This study is unique in that it compares the outcomes at a single institution of 1 high-volume endocrine surgeon between the 2 different procedures. Despite the limitations of a retrospective study, the treatment arms are well matched and provide adequate longitudinal follow-up data to draw several important conclusions.

Some results of this study are intuitive and align with most surgeons' general understanding of the clinical entity. For example, postoperative and 6-month parathyroid hormone (PTH) levels were lower in the TPTX-AT group. That said, the authors propose that TPTX-AT is a better operation overall. Despite the difference in 6-month PTH, both groups had similar serum calcium levels at 6 months. And while the TPXT-AT group required greater levels of vitamin D supplementation, the SPTX group had greater usage of cinacalet, a pharmacologic agent with an exorbitantly high cost. There is also a trend of increased frequency of persistent disease in the SPTX group requiring reoperation. This is very important because the potential complications of reoperation in the SPTX group are higher, including nerve injury and neck hematoma.

While not a main point of this study, the frequency of patients requiring reoperation is much lower in this study than in previously published studies.[3] These findings highlight the unfailing link between surgeon volume and outcome. Similar results have also been recently shown with patients undergoing thyroidectomy by high-volume endocrine surgeons at tertiary referral centers.[4]

The authors do not mention whether they used intraoperative PTH monitoring or nerve monitoring, which would be helpful to know when comparing their results with those from other institutions. That said, those are only minor weaknesses, given the recent proliferation of outcomes research using large administrative databases. In that context, studies like this demonstrate the ongoing value of single-surgeon retrospective reports. The authors present here an insightful study that evaluates the proper surgical approach for patients with untreated UHPT. Their findings are a significant addition to the growing body of evidence that TPTX-AT is the superior procedure.

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