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Original Article

Outcome of Parathyroidectomy for Renal Hyperparathyroidism : a Single-Center Experience

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Abstract

Objective: To evaluate and compare early and long-term outcomes and of total (TPTX) and partial parathyroidectomy (PPTX) operations in the management of patients with resistant renal hyperparathyroidism (rHPT) at Chonburi Hospital, Thailand.

Methods: A single center retrospective medical record review of parathyroidectomy, with or without autotransplantation (AT), from 1 January 2012 to 31 March 2021 was performed.

Results: A total of 110 patients were operated on for rHPT during the study period. The preoperative parathyroid hormone (PTH) levels were markedly high in both groups. Preoperative parathyroid localization was performed in less than 50% of cases. Eighty-four received TPTX, with or without AT, and 26 received PPTX. The average post-operative PTH levels at 24 hours, at 1, 3, 6 and 12 months after operation in TPTX group were significant lower compared with those of the PPTX group. Postoperative blood calcium levels (48 hours after operation) were found to be very low in both groups. Postoperative phosphate level (48 hours after operation) in the TPTX group returned to normal, while it remained elevated in PPTX group. Overall complications of either operation were very low. Eight patients in the PPTX group required reoperation for persistent hyperparathyroidism resistant to non-operative treatment. Five patients had successful primary operations. The remaining 18 PPTX cases continued medical treatment. Sixty patients received TPTX without AT and 24 patients received TPTX with AT. The blood PTH levels of those who had TPTX with AT tended to be higher than that of those who had TPTX without AT at 1, 3, 6 and 12 months after operation, but without statistical significance. Five of 24 patients (20%) who had TPTX with AT experienced recurrent HPT, while none of those who had TPTX without AT did. Two patients with recurrent HPT received autografectomy. Persistent hypoparathyroidism (PTH < 10 pg/mL) was found 10 patients (16%) who had TPTX without AT, but did not occur in any case of TPTX with AT, with a follow up of more than 12 months.

Conclusion: Total parathyroidectomy with or without autotransplantation is the operation of choice for rHPT. The experience of the surgeon is the most important factor for operative success.

Keywords: Secondary hyperparathyroidism, Renal hyperparathyroidism, Total parathyroidectomy, Partial parathyroidectomy, Autotransplantation, Outcome

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Introduction

End-stage renal disease (ESRD) is a common condition. Most patients with ESRD develop renal hyperparathyroidism (rHPT). Renal HPT results from long-term parathyroid hyperplasia, which can become functionally independent adenomas. Renal HPT can lead to high-turnover bone disease, interstitial and vascular calcifications and as well as cardiovascular diseases. The current treatment of rHPT is mainly medical, by using oral calcimimetic drugs.[1-3] However, some patients will develop resistance to medications.

Approximately 1 to 2% of patients with ESRD require parathyroidectomy. Surgical treatment is recommended for patients with parathyroid hormone (PTH) levels higher than 800 pg/mL, those with severe symptoms (bone pain, pruritus, calciphylaxis), serum calcium level over 11 mg/dL, and soft tissue calcification.[4,5] One study of rHPT showed significantly improvement in bone density after parathyroidectomy,[5] and a few studies showed benefit of surgery for patients with calciphylaxis.[3] In a study of patients with rPTH who underwent parathyroidectomy, the average hemoglobin level also increased from from 8.6 g/mL to 9.4 g/mL.[6]

Types of parathyroidectomy include: subtotal parathyroidectomy (removal of 3½ glands) with or without bilateral cervical thymectomy (BCT), total parathyroidectomy (TPTX) with or without autotransplantation (AT) at the nondominant forearm and with or without BCT.[7,8] There is no consensus on the best procedure. TPTX with AT by an experienced surgeon is an effective long-term treatment, which can stabilize PTH, calcium and phosphate levels. The incidence of recurrent hyperparathyroidism at the site of implantation is 7 to 9%. Autografectomy may be needed when the PTH level is greater than 800 pg/mL, with lack of response to medical therapy, and detectable hypertrophy of the implanted tissue.[5]

Preoperative sestamibi (MIBI) scanning of the parathyroid glands in rHPT varies greatly in sensitivity and specificity. A 2012 meta-analysis reported 58% sensitivity and 93% specificity. More recent studies have showed 43% to 88% sensitivity and 60 to 75% specificity.[9,10] Combined sestamibi/CT has greater sensitivity than sestamibi alone, but performs poorly in identifying ectopic glands.10 Many surgeons also use ultrasonography to help identify parathyroid glands in the neck, but its accuracy is extremely variable and likely user-dependent.[9-11]

Patients and Methods

A single-center medical record review of patients who underwent parathyroidectomy for rHPT with or without AT, from 1 January 2012 to 31 March 2021, was performed. All patients were operated on by the author. Patients who were candidates for kidney transplantation received TPTX with AT. Patients who required life-long dialysis received TPTX without AT. A total of 110 patients were included in the present study. Preoperative MIBI scan, computerized tomography (CT) or unltrasonography of the neck were not routinely performed. Data collected included preoperative and postoperative PTH, serum calcium, and phosphate levels, as well as operative complications.

Surgical indications for parathyroidectomy followed existing guidelines as well as expert opinions. These included severe hyperparathyroidism (HPT) refractory to medical treatment (e.g., PTH level greater than 800 pg/mL, hypercalcemia and hyperphosphatemia), intolerance to medical therapy, severe symptomatic HPT including intractable bone pain, pruritus, osteoporosis, calciphylaxis, erythropoietin-resistant anemia and dilated cardiomyopathy.[12-14]

Adequate hemodialysis was performed 24 hours before surgery. Intraoperative frozen section examination of the all parathyroid glands was performed in all cases. All patients received bilateral neck exploration and at least 4 parathyroid glands were removed. Intraoperative serum PTH level measurement was not performed due to lack of availability in this hospital setting. Parathyroid tissue which was normal in appearance was minced into smaller pieces 1 mm to 3 mm in size, and reimplanted intramuscularly into the non-dominated forearm (usually the brachioradialis muscle). Cryopreservation of parathyroid tissues was not performed.

PTH levels were obtained for all patients on the first postoperative day, and calcium and phosphate levels were checked 24, 48, and 72 hours after operation. Recurrent HPT was defined as a new onset of PTH level 9 times the upper limit of normal during follow-up, and permanent hypoparathyroidism was defined as postoperative PTH level less than 10 pg/mL for over 6 months. Indication for autografectomy was based on a PTH level greater than 800 pg/ml without responding to medical treatment, and hypertrophy of the implanted parathyroid tissue.

Data analysis was done using STATA version 15.0

(Stata Corp, College Station, TX, USA). Quantitative data were contrasted using unpaired t test, while Chi-square or Fisher's exact test was used for categorical data. A *p*-value of less than 0.05 was considered statistically significant.

Results

There were 110 patients who were operated on for rHPT during the years 2011 to 2021 in our hospital. TPTX was performed on 84 patients (4 glands were removed) and 26 patients underwent PPTX (less than 4 glands removed). In the PPTX group, 8 patients underwent re-exploration of the neck, and 5 were successful. The remaining (18 PPTX patients) received medical treatment (see Figure 1). Patients in both TPTX and PPTX groups were similar in terms of gender, age, preoperative PTH, calcium and phosphate levels (see Table 1). Preoperative PTH levels were markedly high in both groups. The average postoperative PTH level at 24 hours after operation was significantly lower in

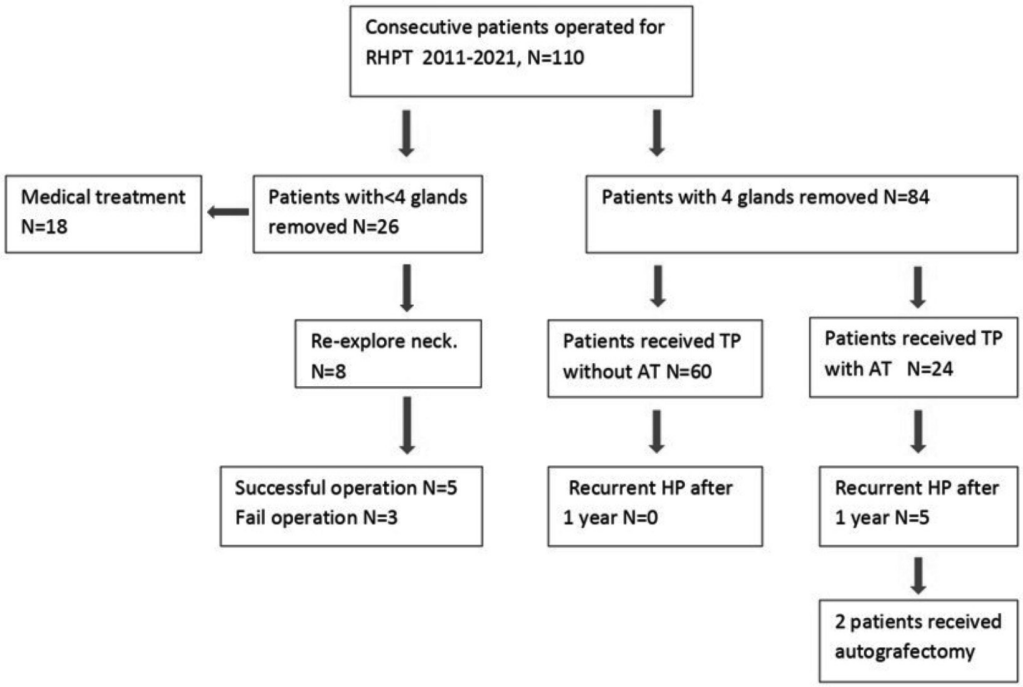

Figure 1 Chart of patient flow in the study; RHPT: renal hyperparathyroidism; TP: total parathyroidectomy; AT: autotransplantation; HP: hyperparathyroidism

Table 1 Comparing preoperative baseline characteristics of patients undergoing total parathyroidectomy (TPTX) and partial parathyroidectomy (PPTX).

	TPTX N = 84	PPTX N = 26	*p*-value
Men: no. (%)	34 (40)	12 (46)	0.608
Women: no. (%)	50 (60)	14 (54)	
Age (years): mean ± sd	50.7 ± 12.8	49 ± 14.3	0.566
Hemodialysis: no. (%)	79 (94)	26 (100)	0.337
Pre-PTH (pg/mL): mean ± sd	1527.1 ± 621.4	1593.9 ± 836.2	0.809
Pre-calcium (mg/dL): mean ± sd	9.7 ± 0.92	9.5 ± 0.46	0.289
Pre-phosphate (mg/dL): mean ± sd	6.5 ± 1.9	6.6 ± 1.9	0.815

Pre-PTH: preoperative parathyroid hormone level; Pre-calcium: preoperative calcium level; Pre-phosphate: preoperative phosphate level; no.: number; sd: standard deviation

Normal range of serum parathyroid hormone level is 16-65 pg/mL; calcium level is 8.6-10.2 mg/dL; phosphate level is 3.5-5.2 mg/dL.

the TPTX group. Average postoperative PTH levels at 1, 3, 6 and 12 months were also significantly lower in the TPTX group (see Table 2). Postoperative calcium levels at 48 hours were very low in both groups and some patients had symptoms of hypocalcemia which required intravenous infusion of calcium. Postoperative phosphate levels in the TPTX group returned to normal, but were more likely to remain high in the PPTX group. Very few operative complications occurred in either group (see Table 2).

Sixty patients underwent TPTX without AT and 24 patients underwent TPTX with AT. There were no significant differences in terms of gender, age, type of dialysis, preoperative PTH and postoperative PTH levels. The average PTH levels in the TPX with AT group were higher than those in the TPX without AT group at 1, 3, 6 and 12 months after operation, but these differences were not statically significant. Patients in the TPTX without AT group had no recurrence of HPT, whereas 5 of 24 patients (20%) in the TPX with AT group had recurrent HPT within 12 months of the operation. Two patients received autografectomy under local anesthesia. Persistent hypoparathyroidism was seen in 10 cases in the TPTX without AT group, but none in the TPTX with ATgroup within a follow up time of more than 12 months (see Tables 3 and 4).

Table 2 Comparing postoperative laboratory values between patients undergoing total parathyroidectomy (TPTX) and partial parathyroidectomy (PPTX).

	TPTX N = 84	PPTX N = 26	*p*-value
Post-PTH (24 hours)	40.9 ± 40.3	564.9 ± 439.3	< 0.001
1 month-PTH	104 ± 289.6	618 ± 707.7	< 0.001
3 months-PTH	122 ± 456.4	666 ± 919.1	< 0.001
6 months-PTH	104 ± 218.1	1010 ± 2653.3	0.002
12 months-PTH	219 ± 872.1	786 ± 1538.2	0.019
Post-calcium (48 hours)	6.7 ± 1.0	6.9 ± 1.3	0.410
Post-phosphate (48 hour)	3.5 ± 1.5	5.0 ± 2.2	< 0.001
Post-operative complications			
RLN injury: number	1	0	
Neck hematoma: number	1	0	
Intrahospital mortality: number	0	0	

Post-PTH (24 hours): parathyroid hormone level at 24 hours after operation; post-calcium (48 hours): calcium level at 48 hours after operation; RLN = recurrent laryngeal nerve; units for PTH levels are pg/dL; units for calcium and phosphate levels are mg/dL; all are displayed as mean ± standard deviation unless stated otherwise.

Table 3 Comparing preoperative baseline characteristics of patients undergoing total parathyroidectomy (TPTX) with and without autotransplantation (AT).

	TPTX without AT N = 60	TPTX with AT N = 24	*p*-value
Men: no. (%)	20	14	0.035
Women: no. (%)	40	10	
Age (years): mean ± sd	51.7 ± 13.4	48.3 ± 13.7	0.230
Hemodialysis: no. (%)	54	24	0.176
Pre-PTH (pg/dL): mean ± sd	1506.9 ± 652.8	1577.5 ± 544.8	0.641
Pre-calcium (mg/dL): mean ± sd	9.7 ± 0.77	9.5 ± 0.88	0.305
Pre-phosphate (mg/dL): mean ± sd	6.5 ± 2.2	6.6 ± 1.4	0.837

Pre-PTH: preoperative parathyroid hormone level; Pre-calcium: preoperative calcium level; Pre-phosphate: preoperative phosphate level; no.: number; sd: standard deviation

Normal range of serum parathyroid hormone level is 16-65 pg/mL; calcium level is 8.6-10.2 mg/dL; phosphate level is 3.5-5.2 mg/dL.

Table 4 Comparing laboratory values of patients undergoing total parathyroidectomy (TPTX) with and without autotransplantation (AT)

	TPTX without AT N = 60	TPTX with AT N = 24	*p*-value
Post-PTH (24hours)	43.1 ± 45.9	35.3 ± 21.8	0.429
1 month-PTH	54.9 ± 94.9	171.4 ± 341.1	0.017
3 months-PTH	63.7 ± 159.6	240.1 ± 692.6	0.065
6 months-PTH	78.4 ± 199.1	137.6 ± 214.1	0.232
12 months-PTH	167.0 ± 928.4	289.7 ± 773.5	0.569
Post-calcium (48 hour)	6.9 ± 1.0	6.4 ± 1.1	0.063
Post-phosphate (48 hour)	3.4 ± 1.6	3.9 ± 1.6	0.199
Recurrent HPT: number	0	5	
Persistent Hypo-PT: number	10	0	
Autografectomy: number	0	2	

Post-PTH (24 hours): parathyroid hormone level at 24 hours after operation; post-calcium (48 hours): calcium level at 48 hours after operation; HPT: hyperparathyroidism; Hypo-PT: hypoparathyroidism; units for PTH levels are pg/dL; units for calcium and phosphate levels are mg/dL; all are displayed as mean ± standard deviation unless stated otherwise

Preoperative parathyroid localization including MIBI scan, CT scan and ultrasonography of the neck was not routinely performed, and was used in less than half of patients. Most of these investigations were requested by the consultant nephrologist or endocrinologist. There were only 5 patients for whom imaging studies could detect 4 parathyroid glands. In no patient was any ectopic parathyroid gland detected (see Table 5).

Table 5 Preoperative parathyroid gland localization

Imaging procedure	All patients: Number	Identified 4 glands: Number	Identified < 4 glands: Number
Ultrasonography	26	3	23
CT scan	23	2	21
MIBI scan	1	0	1
None	60	-	-

Discussion

As mentioned previously, parathyroid surgery for rHPT includes PPTX with or without bilateral cervical thymectomy (BCT), TPTX with or without autotransplantation (AT) at the nondominant forearm and with or without BCT.[3,14,15] At Chonburi Hospital, TPTX with or without AT is routinely performed. BCT was done in cases of PPTX (less than 4 parathyroid glands removed). A previously reported randomized controlled trial showed that TPTX with AT significantly decreases the rate of HPT recurrence, normalizes the serum calcium, and improves clinical signs such as pruritus when compared with subtotal PTX.[16]

Several retrospective case series and cohort studies found that the rate of recurrent or persistent HPT and permanent hypoparathyroidism ranged between 0 to 12% and 2 to 17% for PPTX, respectively. For TPTX with AT, these rates varied between 0 to 10% and 0 to 85% respectively. The actual rates of persistent HPT (defined as occurring within 6 months of surgery) and recurrent HPT (occurring over 6 months after surgery) are very difficult to estimate as studies have used variable cutoffs in defining these conditions. These cutoffs are significantly more conservative than those of the Kidney Disease Improvng Global Outcomes (KDIGO) guideline that only requires the PTH level to be maintained under 9-fold the upper limit of normal (at Chonburi hospital, a 9-fold upper limit would be 614.7 pg/mL, since the upper

limit of normal is 68.3 pg/mL) and persistent postoperative hypoparathyroidism to have values of PTH levels less than 10 pg/mL after 6 months.[17,18] In the present study the rate of recurrent HPT was 20% (5 cases) in the TPTX with AT group, but there was no recurrence in the TPTX without AT group after 1 year follow up. However, there was a high incidence of hypoparathyroidism (16%). Therefore, patients who are candidates for kidney transplantation should be recommended TPTX with AT to avoid permanent hypoparathyroidism.

In a review of anatomic and functional studies, supernumerary parathyroid glands occur in up to 33% of patients, especially in men.[19] A study recommended more extensive operation including all 4 parathyroid gland removal, bilateral thymectomy and bilateral central neck dissection (level VI).[20] The results of this study showed the disease did not persist in 91% of patients and the operation had low complications. The present author would consider performing more extensive operations, especially including bilateral cervical thymectomy, for further improvement of results.

Postoperative hypocalcemia almost always occur after TPTX, but only some patients will have symptoms and signs of hypocalcemia. These patients would require calcium supplement by oral and intravenous route. Calcium level should normalize within 2 to 3 months after surgery. Phosphate levels usually return to normal within 24-72 hours.

Conclusion

From the present case series of rHPT at a single tertiary hospital, total parathyroidectomy with or without autotransplantation has remained the operation of choice. The operation is safe, with good results. Routine preoperative localization of the parathyroid glands does not appear necessary. An experienced surgeon is still the most important factor in a successful parathyroidectomy.

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บทคัดย่อ ผลการรักษาโรคพาราไทรอยด์ฮอร์โมนสูงจากภาวะไตวายระยะสุดท้ายด้วยการผ่าตัดต่อมพาราไทรอยด์ของโรงพยาบาลชลบุรี

เกรียงศักดิ์ ชัยนาภาพงษ์, พบ.
กลุ่มงานศัลยกรรม โรงพยาบาลชลบุรี จังหวัดชลบุรี

ความเป็นมา: ภาวะพาราไทรอยด์ฮอร์โมนสูงจะพบร่วมกับไตวายเรื้อรังระยะสุดท้าย การรักษาหลักคือการล้างไตและการให้ยาเพื่อลดระดับฮอร์โมน จะมีผู้ป่วยบางรายที่ล้มเหลวจากการให้ จำเป็นต้องผ่าตัดเอาต่อมพาราไทรอยด์ออกหมดเพื่อลดระดับฮอร์โมน

วัตถุประสงค์: เพื่อศึกษาผลการรักษาการผ่าตัดต่อมพาราไทรอยด์ ผู้ป่วยภาวะไตวายเรื้อรังระยะสุดท้ายของโรงพยาบาลชลบุรี

ผลการศึกษา: ผู้ป่วยพาราไทรอยด์ฮอร์โมนสูงจากไตวายทั้งหมด 110 คน ได้รับการผ่าตัดระหว่างปี 2011-2020 ผู้ป่วย 84 คนได้รับการผ่าตัดเอาต่อมพาราไทรอยด์ออกทั้งหมด (4 ต่อม) และ 26 คน ได้รับการผ่าตัดต่อมพาราไทรอยด์ออกบางส่วน (น้อยกว่า 4 ต่อม) ในกลุ่มนี้มี 8 คนได้รับการผ่าตัดซ้ำ และพบว่ามี 5 คนที่ผ่าตัดสำเร็จ ส่วนผู้ป่วยที่เหลือ (18 คน) ได้รับการรักษาแบบให้ยา กลุ่มที่ผ่าต่อมพาราไทรอยด์ออกทั้งหมดพบว่ามีระดับฮอร์โมนพาราไทรอยด์หลังผ่าตัดต่ำกว่าอย่างมีนัยสำคัญทางสถิติ ระดับแคลเซียมของทั้งสองกลุ่มต่ำมากหลังผ่าตัด 48 ชั่วโมง ส่วนระดับฟอสเฟตพบกลับมาเป็นปกติในกลุ่มที่ผ่าตัดต่อมพาราไทรอยด์ออกได้หมด พบภาวะแทรกซ้อนจากการผ่าตัดอยู่ในระดับต่ำ

ผู้ป่วย 60 คนได้รับการผ่าตัดต่อมพาราไทรอยด์ออกทั้งหมดและไม่ได้รับการฝังเนื้อเยื่อ และ 24 คนได้รับการผ่าตัดต่อมพาราไทรอยด์ออกทั้งหมดร่วมกับการฝังเนื้อเยื่อพาราไทรอยด์ที่แขน ระดับพาราไทรอยด์หลังผ่าตัดในกลุ่มที่ฝังเนื้อเยื่อที่แขน มีค่าเฉลี่ยสูงกว่ากลุ่มที่ไม่ฝังเนื้อเยื่อที่แขนที่ระยะเวลา 1, 3, 6 และ 12 เดือน แต่ไม่มีนัยยะสำคัญทางสถิติ และพบการกลับมาเป็นใหม่ของโรคพาราไทรอยด์ฮอร์โมนสูงในกลุ่มที่ฝังเนื้อเยื่อที่แขน 5 ราย (20%) และพบภาวะพาราไทรอยด์ฮอร์โมนต่ำ 16% (10 ราย) ในกลุ่มที่ไม่ได้ฝังเนื้อเยื่อที่แขนหลังจากติดตามอาการมากกว่า 12 เดือน

การหาตำแหน่งต่อมพาราไทรอยด์ก่อนการผ่าตัดพบว่ามีโอกาสพบทั้ง 4 ต่อมหรือต่อมที่อยู่ผิดที่ (ectopic) น้อยมาก

สรุปผลการศึกษา: การผ่าตัดต่อมพาราไทรอยด์ออกหมดร่วมกับการฝังและไม่ฝังเนื้อเยื่อที่แขนให้ผลการรักษาที่ดีในผู้ป่วยไตวายที่มีภาวะพาราไทรอยด์ฮอร์โมนสูง มีภาวะแทรกซ้อนต่ำ การหาตำแหน่งต่อมพาราไทรอยด์ก่อนการผ่าตัดไม่มีความจำเป็น