

# Outcome of Parathyroidectomy for Renal Hyperparathyroidism: A Single Center Experience

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**Background:** Renal hyperparathyroidism (HPTH) is a common complication of chronic kidney disease and is known to cause significant morbidity in these patients. There has been substantial debate on the best possible treatment of this condition. Surgical treatment is now considered to be of vital importance as its efficacy is well documented. The present study reported the outcome of parathyroidectomy in King Chulalongkorn Memorial Hospital, a university hospital in Bangkok, Thailand.

**Objective:** To determine surgical outcomes, including success rate and perioperative complications of parathyroidectomy in patients with renal HPTH.

**Materials and Methods:** The data was collected by retrospective review of patients' records between June 2014 and May 2019. One hundred ten patients were enrolled. Their demographic data, laboratory results, and outcomes were collected and categorized.

**Results:** Among 110 patients, men accounted for 48.6%. The mean age was 49.5 years (SD 13.3). The most frequent operation was total parathyroidectomy with autotransplantation (TPTX+AT). All four glands were identified and excised in 84.5% of all patients. The mean preoperative serum intact parathyroid hormone (iPTH) level was 1,938 pg per dL with a range of 171 to 5,000 pg per dL. Postoperative hypocalcemia requiring intravenous calcium supplement was present in 70%. Postoperative cardiovascular complication occurrences were 16.4%, with one mortality due to myocardial infarction. In addition, one patient suffered unilateral recurrent laryngeal nerve injury, while two had stroke. The overall success rate of treatment was 81.1%, with 7.3% and 8.2% of patients that had persistently high PTH and recurrence of HPTH, respectively.

**Conclusion:** Parathyroidectomy is an essential choice of treatment in patients with renal HPTH. Further validation of correlations with other factors is now being processed, and more data are needed.

**Keywords:** Secondary hyperparathyroidism; Tertiary hyperparathyroidism; Chronic kidney disease mineral bone disease; Parathyroidectomy

Received 26 July 2021 | Revised 21 November 2021 | Accepted 29 December 2021

**J Med Assoc Thai 2022; 105(1):40-5**

**Website:** <http://www.jmatonline.com>

Renal hyperparathyroidism, a secondary and tertiary hyperparathyroidism in chronic kidney disease, is a common complication of chronic kidney disease (CKD), occurring secondarily after long-standing exposure to metabolic disturbances, including hyperphosphatemia, abnormal calcium

absorption, and vitamin D deficiency. Diffuse hyperplasia of parathyroid glands, which causes secondary hyperparathyroidism is changeable after kidney transplantation, but the autonomy of the glands in tertiary hyperparathyroidism is immutable. Hyperparathyroidism also significantly affects the patients' quality of life, morbidity with osteopenia, osteoporosis, nephrocalcinosis, and calciphylaxis, and links to increased mortality<sup>(1)</sup>. Current treatment options consist of both medical and surgical. There are several classes of medications prescribed for the patients, such as vitamin D, phosphate binders, and calcimimetic agents such as Cinacalcet and Etelcalcetide. Still, all pharmacological options are not equivalent to surgical treatment in reducing serum parathyroid hormone (PTH). These days, there is no randomized controlled trial to compare long-term outcomes, including the risk of death, major cardiovascular events, and risk of fractures, of these

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## How to cite this article:

Samorn P, Supsupan W, Pak-art R, Sriussadaporn S, Sriussadaporn S, Kritayakirana K, et al. Outcome of Parathyroidectomy for Renal Hyperparathyroidism: A Single Center Experience. *J Med Assoc Thai* 2022;105:40-5.

**DOI:** 10.35755/jmedassocthai.2022.01.13231

medical treatments in patients with CKD<sup>(2)</sup>.

In contrast, some prospective trials have shown that parathyroidectomy may improve survival and reduce cardiovascular events and fractures<sup>(3)</sup>. Though, to this date, there has been no clear consensus on which option should be selected in a particular group of patients. Furthermore, there are surgery variations for this condition such as subtotal parathyroidectomy (SPTX) and total parathyroidectomy (TPTX) with or without autotransplantation (AT). The lack of randomized controlled trials and small sample size studies has hindered the development of a proper guideline. The present study reported the outcome of parathyroidectomy in a university hospital.

## Materials and Methods

The authors conducted the present study in King Chulalongkorn Memorial Hospital, Bangkok, Thailand. The patients' medical data was collected through a retrospective review of the records between June 2014 and May 2019. One hundred ten patients were enrolled. Their demographic data, laboratory results, and outcomes were collected and categorized. Eleven patients were excluded due to incomplete data.

Surgical indications included patients with persistently high parathyroid levels despite adequate medical treatment or those with persistent symptoms, such as bone pain, joint pain, or muscle weakness.

Three experienced surgeons performed the surgeries. The surgeons preferred complete four-gland exploration parathyroidectomy with or without AT. Unless the surgeons could identify all four parathyroid glands at the expected locations, cervical thymectomy was not routine. Parathyroid cryopreservation was not readily available at the authors' center.

The authors monitored the serum calcium every six hours for 48 hours postoperatively, then twice daily until stable. If the blood calcium level dropped below 7.2 mg/dL, intravenous infusion of 10% calcium gluconate with 93 mg of elemental calcium in 10mL solution, at 1 to 2 mg of elemental calcium per kilogram body weight per hour would be given to keep serum calcium level more than 8.0 mg/dL. All patients who had hypocalcemia would receive three to six grams of oral calcium carbonate and one gram of oral calcitriol per day.

The patients were arranged to follow up at one month postoperatively for informing the pathological reports, then every six months for two years, and finally annually. The authors requested the blood test for intact parathyroid hormone (iPTH) level, calcium level, phosphate level, and vitamin D level. If it were

inconvenient for the patients to test these in the present study hospital, they could bring their results from their primary healthcare facility.

There is no clear definition of persistent hyperparathyroidism and recurrent hyperparathyroidism<sup>(2-5)</sup>. Therefore, the authors defined persistent hyperparathyroidism as serum iPTH level three times above the normal upper limit or greater than 200 pg/mL on postoperative day 1, and recurrent hyperparathyroidism as serum iPTH level three times the normal upper limit of greater than 200 pg/mL at six months postoperatively.

The Institutional Review Board, Faculty of Medicine, Chulalongkorn University, approved the present study (IRB 339/63) and was conducted in compliance with the Declaration of Helsinki principles.

## Statistical analysis

Data were analyzed using the IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA). Numerical results were presented as mean  $\pm$  standard deviation (SD) or median (range) dependent on their distribution.

## Results

Among 110 patients, men accounted for 48.2% of the group. The mean age was 49.5 $\pm$ 13.3 years. Hypertension was the most common comorbidity at 69.1%. Before the surgery, every patient received renal replacement therapy, and eight had already undergone kidney transplantation. In addition, ten patients had been prescribed Cinacalcet. Approximately three-fourths of the patients were noted to be without bothersome symptoms before the operation, while 21.8% complained of bone or joint pain (Table 1).

Preoperative calcium and phosphate levels are shown in Table 2. The mean preoperative iPTH level was 1,938 pg/mL, ranging from 171 to 5,000 pg/mL.

The most frequent operation was total parathyroidectomy with autotransplantation (TPTX+AT). All four glands were identified and excised in 84.5% of all patients. Nine patients received cervical thymectomy. Up to one-third of all patients were discovered to have supernumerary glands during the operation. In addition, the surgeons could identify bilateral recurrent laryngeal nerves in 95.5% (Table 3-5).

Postoperative hypocalcemia requiring intravenous calcium supplement occurred in 66.3%, and no patients that underwent SPTX suffered from this complication. Postoperative cardiovascular

**Table 1.** Details of demographic data of all patients who received parathyroidectomy

Demographics data (n=110)	Value
Sex: male; n (%)	53 (48.2)
Age (year); mean±SD	49.5±13.3
Underlying diseases; n (%)	
Hypertension	76 (69.1)
Diabetes	20 (18.2)
Dyslipidemia	26 (23.6)
SLE	8 (7.3)
Coronary artery disease	5 (4.5)
Peripheral arterial disease	5 (4.5)
Cerebrovascular disease	4 (3.6)
Other	17 (15.5)
Calciophylaxis; n (%)	3 (2.7)
Bone pain; n (%)	24 (21.8)
Calcified valvular disease; n (%)	7 (6.4)
Previous cinacalcet use; n (%)	10 (9.1)
Renal replacement options; n (%)	
Hemodialysis	100 (90.9)
Peritoneal dialysis	2 (1.8)
Renal transplantation	8 (7.3)
Duration of dialysis (year); median (range)	6 (1 to 26)
Duration of hyperparathyroidism (month); median (range)	7.5 (0.5 to 120)

SD=standard deviation; SLE=systemic lupus erythematosus

**Table 2.** Preoperative laboratory results of patients undergone parathyroidectomy

Preoperative parameters	Median (range)
Predialysis creatinine (mg/dL)	6.70 (0.76 to 17.14)
Serum calcium (mg/dL)	10.0 (6.4 to 11.9)
Serum phosphate (mg/dL)	4.9 (1.6 to 9.4)
Serum ALP (IU/L)	408 (40 to 1,772)
Serum iPTH (pg/mL)	1,938 (171 to 5,000)

ALP=alkaline phosphatase; iPTH=intact parathyroid hormone

complications were as follows, postoperative arrhythmia 6.4%, congestive heart failure 4.5%, postoperative myocardial infarction 5.5%, and stroke 1.8%. One patient suffered unilateral recurrent laryngeal nerve injury. None of our patients suffered surgical site infections. The overall success rate of the treatment was 84.5%, with eight and nine patients that had persistently high PTH and recurrence of hyperparathyroidism, respectively.

## Discussion

Renal hyperparathyroidism is related to increased mortality and morbidity in patients with chronic kidney diseases. Managing renal hyperparathyroidism requires multidisciplinary cooperation. Initially,

**Table 3.** Operative details including type of operation and operative findings

Detail of operations (n=110)	Value
Operation; n (%)	
TPTX	10 (9.1)
TPTX+AT	95 (86.4)
SPTX	5 (4.5)
Location of autotransplantation; n (%)	
Chest wall	60 (63.2)
Biceps	35 (36.8)
Four-gland identified; n (%)	93 (84.5)
Cervical thymectomy; n (%)	9 (8.1)
Supernumerary gland; n (%)	
Right	19 (17.3)
Left	22 (20.0)
Ectopic parathyroid tissue; n (%)	
Thymic	5 (4.5)
Thyroid	1 (0.9)
Identified both RLN; n (%)	105 (95.5)
Operative time (minute); median (range)	90 (45 to 130)

TPTX=total parathyroidectomy; AT=autotransplantation; SPTX=subtotal parathyroidectomy; RLN=recurrent laryngeal nerve

**Table 4.** Postoperative short-term outcomes

Outcomes (n=110)	Value
Length of stay; mean [range]	5 [4-5]
Readmission; n (%)	2 (1.9)
30-day mortality; n (%)	1 (0.9)
Normalized iPTH; n (%)	93 (84.5)
Persistent hyperparathyroidism; n (%)	8 (7.3)
TPTX+AT (percent of the group)	7 (7.4)
SPTX (percent of group)	1 (20.0)
Recurrent hyperparathyroidism; n (%)	9 (8.2)
TPTX+AT (percent of the group)	8 (8.4)
TPTX (percent of group)	1 (10.0)

iPTH=intact parathyroid hormone; TPTX=total parathyroidectomy; AT=autotransplantation; SPTX=subtotal parathyroidectomy

nephrologists would prescribe phosphate binder and vitamin D for these patients. Normalized serum vitamin D levels, particularly in patients with vitamin D deficiency, may reduce serum PTH and reduce bone turnover. Using phosphate binders in patients with early secondary hyperparathyroidism may slow the progression of the disease. Unfortunately, these treatment options are scarce for reducing serum PTH, calcium, and phosphate in most patients. In recent times, calcimimetic agents, including Cinacalcet and Etelcalcetide, act at the calcium-sensing receptor, resulting in effective reduction of serum PTH, calcium, and phosphate compared to the prior

**Table 5.** In-hospital postoperative complications

Complications (n=110)	Value
Recurrent laryngeal nerve injury; n (%)	8 (7.3)
Transient	7 (6.4)
Permanent	1 (0.9)
Postoperative bleeding; n (%)	8 (7.3)
Hypocalcemia requiring IVCa2; n (%)	73 (66.3)
TPTX+AT (percent of the group)	66 (69.5)
TPTX (percent of the group)	7 (70.0)
SPTX (percent of the group)	0 (0.0)
IVCa2* use (days); median (range)	2 (0 to 34)
Cardiovascular events; n (%)	20 (18.2)
Arrhythmia	7 (6.4)
Congestive heart failure	5 (4.5)
Acute myocardial infarction	6 (5.5)
Stroke	2 (1.8)
Surgical site infection; n (%)	0 (0.0)

IVCa2\*=intravenous calcium supplement; TPTX=total parathyroidectomy; AT=autotransplantation; SPTX=subtotal parathyroidectomy

medications. Cinacalcet is an oral calcimimetic drug that has long-term use, and many articles show its efficacy for reducing serum PTH. Regrettably, there is no significant outcome for death and morbidity prevention<sup>(2)</sup>.

Furthermore, its gastrointestinal effects, such as vomiting and diarrhea, make it less tolerable. Etelcalcetide, given intravenously, is a new calcimimetic agent hoped to reduce the gastrointestinal side effect of Cinacalcet, but from recent data, it is not<sup>(6)</sup>. Moreover, the National Health Security Office (NHSO) does not pay for calcimimetic agents. The medications cost at least 6,600 Baht (200 United States Dollars) a month, which is unaffordable for some patients.

Despite novel medical agents, many still require surgical treatment. Current data suggests that surgical treatment was superior to medication alone in controlling the iPTH level, decreasing complications related to hyperparathyroidism, alleviating abnormal calcium metabolism, and reducing the overall mortality rate<sup>(5)</sup>.

There are several different surgical strategies, which are TPTX with or without synchronous AT and SPTX, but still, there is no clear consensus. Recent evidence suggested that TPTX might be superior to SPTX with regard to success rate, but it leads to more hypocalcemia<sup>(7-9)</sup>.

A debating issue about the surgical approach is cervical thymectomy. Since most patients who had persistent and recurrent disease retained the

supernumerary gland, which most found in the thymic tissue, some groups advocated routine cervical thymectomy along with parathyroidectomy. However, the authors performed cervical thymectomy when found less than four parathyroid glands in the typical locations, as data from only a few studies showed different success between these approaches.

The present study center mainly adopted the TPTX with AT approach for the dialysis patients because the authors believe that the systemic calcium metabolism disturbance was an ongoing process unless renal transplantation was performed. Subtotal parathyroidectomies were done in post-kidney transplantation patients.

As stated above, the present research group consisted of equally male and female. The group's mean age was 49.5 years, which is comparable to the previous studies<sup>(9,10)</sup>. The present study encountered supernumerary parathyroid in about one-fifth of the patients. This finding coincided with the earlier reports<sup>(3)</sup>. However, there was less ectopic parathyroid gland than other studies, which reported up to 14% to 45% intrathymic lesion and 17% thyrothymic lesion. This finding may be because of selective cervical thymectomy, as previously described. The present study preoperative iPTH level was comparable to the previous studies, though, because of technical issues, the maximal level possible from the present study laboratory result was at 5,000 pg/mL.

Both persistent and recurrent hyperparathyroidism in the present study center stood at 7.3% and 8.2%, respectively, which coincide with the previously reported 10% to 30%<sup>(4,12)</sup>, despite a higher initial iPTH level. Previous studies suggested that preoperative vitamin D level, iPTH level, alkaline phosphatase (ALP) level, and calcimimetics use could relate to postoperative outcome. The authors found no significant correlation among any preoperative factors on the treatment outcome in both recurrent and persistent group.

Postoperative hypocalcemia requiring intravenous calcium is a common complication after parathyroidectomy, which may occur up to 85%. Risk factors are low preoperative vitamin D level, high preoperative ALP level at more than 200 IU/L, and perioperative hypomagnesemia<sup>(3)</sup>. Some studies suggested that the type of operation may affect postoperative hypocalcemia such as TPTX was greater than TPTX+AT, which was greater than SPTX<sup>(9-11)</sup>, but the present study data show no difference between TPTX and TPTX+AT. Although there was no hypocalcemia in the SPTX group, it

could not compare to other groups because all the patients had undergone kidney transplantation, and their preoperative iPTH levels were lower.

The reported rate of complication in our center is comparable to others<sup>(6)</sup>. One mortality is a 56-year-old female with known calciophylaxis, valvular heart disease, and coronary artery disease. She had a postoperative myocardial infarction and succumbed to severe arrhythmia and cardiogenic shock afterward. The two readmissions were due to delayed surgical site hematoma that required neck re-exploration, and symptomatic hypocalcemia after discharge. Surgical wound infection did not occur in any of the present study patients.

An experienced laryngologist performed a fiberoptic video laryngoscopy two weeks after the initial operation to access those who had postoperative hoarseness of voice. Six of eight patients had recurrent laryngeal nerve injury, but only one of them suffered persistent unilateral vocal cord paralysis, though, she did not need any airway management.

The main limitation of the present study is the nature of the retrospective study. The present study center is a university hospital, so most patients were transferred from primary and secondary care units. Therefore, some necessary preoperative data were missing, such as vitamin D level, which is associated with iPTH level. Some patients requested to receive intravenous calcium infusion in facilities close to their residences, so the authors could not collect the amount of the treatment given to these patients. In addition, long-term follow-up was not readily available as most patients preferred to follow up at their primary care hospitals. The contact data provided were outdated, therefore, the authors did not report the follow-up data in the present study.

## Conclusion

Parathyroidectomy is a crucial choice of treatment in patients with renal hyperparathyroidism. The short-term outcome is decent in normalizing PTH, which may improve quality of life and survival. Further validation of correlations with other factors is now being processed, and more data is needed.

## What is already known on this topic?

Hyperparathyroidism is a common problem among patients with chronic kidney disease, and parathyroidectomy is an effective treatment.

## What this study adds?

Outcomes of parathyroidectomy in Thai patients

with renal hyperparathyroidism were comparable with other studies.

## Conflicts of interest

The authors declare no conflict of interest.

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