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Clinical outcomes of parathyroidectomy *versus* cinacalcet in the clinical management of secondary hyperparathyroidism

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Abstract. Parathyroidectomy (PTX) is the standard treatment for secondary hyperparathyroidism (SHPT); however, the administration of cinacalcet has gained prominence as a noninvasive treatment. We aimed to determine whether PTX or cinacalcet is more effective in preventing morbidity and mortality through reviewing follow-up data concerning surgical management of SHPT. We retrospectively analyzed and divided 209 patients with SHPT into two treatment groups: PTX (n = 78) and cinacalcet (n = 131) groups. We compared clinical features, the over-the-target range rate during pre- and post-intervention periods, new cardiovascular events, and all-cause mortality between both groups. Almost all biochemical parameters were well controlled in the post-intervention period, and were within the recommended target range for the PTX group but not for the cinacalcet group. A significant difference was observed in the over-the-target range rate during the post-intervention period between the groups. PTX and cinacalcet interventions significantly lowered the over-the-target range rates for serum intact parathyroid hormone (iPTH) (>300 pg/mL), corrected calcium (>10.5 mg/mL), serum phosphorus (>5.5 mg/dL), and calcium–phosphorus product (>55) in both groups (p = 0.001). PTX reduced the risk of new cardiovascular events by 86% compared to cinacalcet (p = 0.001); however, all-cause mortality did not differ significantly (14.1% *vs.* 7.6%, p = 0.132). For patients with SHPT, PTX helps prevent cardiovascular events through normalizing biochemical variables, according to recommended guidelines. PTX should be considered before cinacalcet treatment to prevent new cardiovascular events. Early PTX for appropriate patients can help prevent immediate postoperative complications and mortality.

Key words: Secondary hyperparathyroidism, Parathyroidectomy, Cinacalcet, Survival, Mineral and bone disorder

SECONDARY HYPERPARATHYROIDISM (SHPT) is a common complication among patients undergoing hemodialysis for end-stage renal disease (ESRD), affecting quality of life (QOL) and leading to mortality. Surgical parathyroidectomy (PTX) is necessary for patients resistant to medical therapy. Recent studies have shown that, with the emergence of cinacalcet, treatment has been managed without PTX [1-7]. Calcimimetics such as cinacalcet may allow nephrologists and/or endocrinologists to avoid invasive procedures and bridge the gap between renal transplantation and medical therapy. The Evaluation of Cinacalcet HCL Therapy to Lower Cardiovascular Events (EVOLVE) trial and the INDEPENDENT study both aimed to determine the benefits of cinacalcet, and the findings of these studies indicated that cinacalcet treatment was superior to other medical treatments [8-10]. Nevertheless, PTX continues to play an important role in the management of uncontrolled SHPT [11-13]. The prevalence rates for PTX have been reported to vary by country, ranging from 4% to 14.3% [14]. A recent multicenter study in Korea reported that the proportion of dialyzing patients with ESRD having biochemical parameters outside the recommended target range, according to clinical practice guidelines, was modest [15]. One study reported that PTX was not an optimal procedure to achieve adjustment for all biochemical parameters to within a normal range [16]. However, a recent study showed that a shorter dialysis period prior to PTX facilitated normalization of biochemical parameters to within the recommended target range postopera-

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tively [17]. Since the benefits of PTX are not clearly proven and early postoperative mortality rates are high, nephrologists have tended to prefer noninvasive medical treatments over PTX. However, if early PTX can reduce mortality and complications and improve QOL, early PTX should be considered for patients with biochemical parameters outside the recommended clinical guideline target range who may benefit from active surgical treatment.

We hypothesized that early PTX could reduce mortality and complications. This study aimed to determine whether PTX or cinacalcet was more effective in reducing mortality and cardiovascular events using follow-up data involving the surgical management of SHPT.

Materials and Methods

This study was approved by the Institutional Review Board of Yonsei University. The requirement for informed consent was waived because of the retrospective nature of the study.

We retrospectively analyzed 360 patients with SHPT at the Yonsei University Health System between 2006 and 2015. Of these, 151 patients were excluded. We excluded 60 patients with a short-term follow-up period of <6 months, and 91 patients were excluded due to missing data concerning biochemical parameters required for risk factor analysis. The remaining 209 patients were divided into two groups according to their treatment method, namely, those who had undergone PTX (n = 78) and those who had been treated with cinacalcet (n = 131). All pathology-based diagnoses were histopathologically confirmed postoperatively in the PTX group. We did not monitor parathyroid hormone (PTH) levels intraoperatively prior to May 2014. Instead, we assessed postoperative PTH levels within 2 hours postoperatively. The PTX group included patients who had undergone a subtotal PTX or a total PTX with autotransplantation of the parathyroid. We compared patient clinical signs and symptoms; and preoperative calcium, PTH, phosphorus, and calcium–phosphorus product levels; the over-the-target range rates in the pre- and post-intervention period; bone mineral density (BMD); bone markers such as osteocalcin and Collagen type 1 C-telopeptide (CTX), and alkaline phosphatase (ALP) levels; postoperative calcium and PTH levels; pathological diagnosis; multiplicity; and the results of a localization study.

We defined the over-the-target range for serum intact PTH (iPTH) (>300 pg/mL), corrected calcium (>10.5 mg/mL), serum phosphorus (>5.5 mg/dL), and calcium–phosphorus product (>55). Recurrence was defined as elevated calcium and PTH levels occurring >6 months postoperatively. Persistence was defined as elevated calcium and PTH levels within 6 months postoperatively.

Statistical analysis

Data are expressed as mean ± standard deviation. A Fisher's exact test or a Pearson's chi-squared test was used to compare the clinical findings in the cinacalcet and PTX groups. Logistic regression analysis was used to compare the clinicopathological findings in the cinacalcet and PTX groups. Univariate and multivariate analyses using Cox proportional hazards models were performed to identify risk factors for the occurrence of new cardiovascular events. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Survival outcomes were analyzed using the Kaplan–Meier method and log-rank tests. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS version 20.0 for Windows (Chicago, IL, USA).

Results

There were no differences in the type of dialysis and follow-up period after diagnosis between the PTX and cinacalcet groups. Patients were significantly older in the cinacalcet group than in the PTX group (48 *vs.* 53 years, p = 0.04). Patients in the cinacalcet group had more comorbidities, such as diabetes mellitus (DM), cerebrovascular disease (CBVD), dyslipidemia, but not more coronary artery occlusive disease (CAOD), arrhythmia, valvular heart disease, and hypertension. The dialysis period for patients was longer in the PTX group than in the cinacalcet group (180 *vs.* 154 months, p = 0.019). The largest parathyroid lesions, measured using ultrasonography, were greater in size in the PTX group than in the cinacalcet group (2.37 *vs.* 1.48 cm, p = 0.001) (Table 1).

The mean cinacalcet dose was 54.8 mg and the mean period of cinacalcet administration was 34.9 months. New cardiovascular events occurred more frequently in the cinacalcet group than in the PTX group (27.5% *vs.*. 15.4, respectively, p = 0.044). However, there was no significant difference between the two groups for all-cause mortality (14.1% *vs.* 7.6%, p = 0.132). Post-intervention hypocalcemia was common in the PTX group. The period of hypocalcemia (corrected calcium <7.5 mg/mL) post-intervention was longer in the PTX group (3.44 *vs.*. 0.14 months, p = 0.001). Unexpected adverse events with PTX are inevitable in some patients due to morbidity and surgical complications, such as postoperative bleeding, injury to the recurrent laryngeal nerve, persistent hyperparathyroidism due to missing a supernumerary parathyroid gland, and mortality due to

Table 1 Clinical parameters of the patient between parathyroidectomy and Cinacalcet groups

	Parathyroidectomy ($N = 78$)	Cinacalcet ($N = 131$)	p value
Age (years)	48.05 ± 11.74	53.11 ± 12.37	0.04*
Sex (female:male)	50:28	63:68	0.025*
Parathyroid size (cm)	2.37 ± 0.81	1.48 ± 0.41	0.001*
Dialysis type at the time of intervention (HD:PD)	50:28	74:57	0.278
Dialysis period (month)	180.7 ± 76.9	154.3 ± 78.3	0.019*
Follow up period after the diagnosis of HPT (month)	78.6 ± 51.1	73.8 ± 43.0	0.464
Period of follow up after intervention (month)	49.3 ± 36.1	38.1 ± 21.4	0.005*
Cormorbidity			
Hypertension	68 (87.2%)	123 (93.9%)	0.094
Diabetes mellitus	7 (9%)	26 (19.8%)	0.037*
CAOD	15 (19.2%)	22 (16.8%)	0.655
Arrthymia	18 (23.1%)	19 (14.5%)	0.116
Valvular heart disease	8 (10.3%)	20 (15.3%)	0.304
CBVD	3 (3.8%)	23 (17.7%)	0.003*
Dyslipidemia	19 (24.4%)	60 (45.8%)	0.002*

* $p < 0.05$

Table 2 Clinical outcome and complication of the patient between parathyroidectomy and Cinacalcet groups

	Parathyroidectomy ($N = 78$)	Cinacalcet ($N = 131$)	p value
New cardiovascular event requiring admission	12 (15.4%)	36 (27.5%)	0.044*
All cause mortality	11 (14.1%)	10 (7.6%)	0.132
Period of hypocalcemia after intervention (month)			
Corrected Calcium <7.5	3.44 ± 5.53	0.14 ± 0.59	0.001*
Dose of Cinacalcet (mg)		54.8 ± 29.3	
Period of Cinacalcet (month)		34.9 ± 21.4	
Type of parathyroidectomy			
Total PTX with autotransplantation	58		
Subtotal PTX	20		
Adverse event with parathyroidectomy	1 RLN injury → thyroplasty		
	1 postoperative bleeding → Reoperation		
	1 Dilated cardiomyopathy aggravation → mortality		
	2 persistent → miss a supernumerary parathyroid gland, 1 Reoperation		
Total cost	1,600$ for parathyroidectomy	1,800$/year (2 tablet/day) increase with time	

* $p < 0.05$

the aggravation of dilated cardiomyopathy (DCMP). More expense was incurred in the cinacalcet group, despite the short-term follow-up period post-intervention. However, the cost of treatment remained almost unchanged in the PTX group, if there was no recurrence of the parathyroid lesion (Table 2).

Biochemical parameters of the patients were analyzed between the PTX and cinacalcet groups through measuring serum iPTH, corrected calcium, serum phosphorus, calcium–phosphorus product, ALP levels, BMD, CTX, and osteocalcin. There were significant differences in all parameters during the first year following the post-intervention period. The post-intervention period was determined as 2–3 months post-PTX, and from the start of cinacalcet administration. Almost all biochemical parameters were well controlled in the post-intervention period and remained within the recommended target range in the PTX group, but not in cinacalcet group,

Table 3 Biochemical parameter of the patients between parathyroidectomy and Cinacalcet groups

	Parathyroidectomy (N = 78)	Cinacalcet (N = 131)	p value
Serum iPTH (pg/mL)			
Before intervention	1,249.5 ± 645.93	718.5 ± 351.7	0.001*
After intervention	108.2 ± 173.2	553.0 ± 308.9	0.001*
1 year after intervention	77.4 ± 96.3	519.1 ± 319.3	0.001*
Corrected calcium (mg/dL)			
Before intervention	10.62 ± 1.17	10.17 ± 0.87	0.002*
After intervention	7.97 ± 0.93	9.59 ± 0.94	0.001*
1 year after intervention	8.76 ± 1.03	9.69 ± 0.82	0.001*
Serum phosphorus (mg/dL)			
Before intervention	6.02 ± 1.42	6.17 ± 1.55	0.493
After intervention	4.80 ± 1.33	5.79 ± 1.36	0.001*
1 year after intervention	4.46 ± 1.29	5.52 ± 1.67	0.001*
Calcium-phosphorus product			
Before intervention	64.42 ± 16.83	62.29 ± 14.87	0.343
After intervention	38.57 ± 11.74	55.08 ± 13.64	0.001*
1 year after intervention	39.06 ± 12.40	53.52 ± 16.60	0.001*
Alkaline phosphatase (ref. 37–109)			
Before intervention	335.88 ± 543.58	103.59 ± 81.73	0.001*
6 month after intervention	150.24 ± 224.47	121.51 ± 140.52	0.281
1 year after intervention	65.37 ± 27.76	114.44 ± 103.42	0.042*
BMD			
Before intervention	–2.4 ± 1.2	–2.1 ± 1.1	0.271
1 year after intervention	–1.4 ± 1.2	–2.2 ± 1.2	0.007*
CTX (ref. <0.8)			
Before intervention	4.5 ± 1.6	3.4 ± 1.7	0.022*
1 year after intervention	1.4 ± 1.6	3.3 ± 1.7	0.001*
Osteocalcin (ref. 11–70)			
Before intervention	530 ± 454	406 ± 486	0.222
1 year after intervention	149 ± 211	514 ± 466	0.001*

Reference range of Serum iPTH (pg/mL, 15–65), Corrected calcium (mg/dL, 8.5–10.5), Serum phosphorus (mg/dL, 2.5–4.2), Calcium-phosphorus product (<55). * $p < 0.05$

which still presented with high levels of serum PTH, calcium–phosphorus product, and bone markers (Table 3).

Paired *t*-tests were performed to evaluate clinical outcomes in the post-intervention period using the over-the-target range rate, according to intervention type. When comparing the PTX group with the cinacalcet group in relation to a serum parathyroid hormone level rate of >300 pg/mL (8.8% *vs.* 75.3%, respectively, $p = 0.001$), a calcium–phosphorus product of >55 (9.0% *vs.* 42.3%, respectively, $p = 0.001$), a corrected calcium of >10.5 (5.0% *vs.* 16.8%, respectively, $p = 0.001$), and a phosphorus level of >5.5 (19.3% *vs.* 47.9%, respectively, $p = 0.001$), the percentages were significantly lower in the PTX group. Cardiovascular events were defined as coronary artery occlusive disease (CAOD), arrhythmia-induced heart failure, valvular heart disease, stroke, peripheral arterial occlusive disease (PAOD), sudden cardiac death, and heart failure due to other organ failure. The number of patients with cardiovascular events requiring admission was also significantly lower in the PTX group (15.4% *vs.* 27.5%, $p = 0.044$). Therefore, we consider that both treatment options were effective in controlling the aforementioned biochemical parameters (Table 4).

Factors related to new cardiovascular events in the post-intervention period were analyzed according to age, the dialysis period, comorbidity, type of intervention, and the over-the-target range rate (Table 5). In the univariate analysis, there was a significantly higher occurrence of new cardiovascular events in patients with comorbidities such as age, DM, CAOD, arrhythmia, valvular heart disease, CBVD, and dyslipidemia. In the multivariate analy-

Table 4 Clinical outcomes after intervention using the rate of over the target range according to intervention type

Variable	Parathyroidecotmy ($N = 78$)			Cinacalcet ($N = 131$)			*p*-value
	Before	1 year after	*p*-value	Before	1 year after	*p*-value	1 year after
Rate of over the target range(%)							
Serum iPTH >300 (pg/mL)	92.9 ± 18.9	8.8 ± 21.9	0.001*	81.8 ± 22.2	75.3 ± 25.5	0.014*	0.001*
Corrected serum calcium >10.5 (mg/dL)	46.4 ± 42.1	5.0 ± 13.1	0.001*	22.6 ± 31.4	16.8 ± 22.9	0.015*	0.001*
Serum phosphorus >5.5 (mg/dL)	58.5 ± 37.5	19.3 ± 25.5	0.001*	57.7 ± 31.2	47.9 ± 31.0	0.001*	0.001*
Calcium-Phosphorus product >55	62.1 ± 38.2	9.0 ± 16.8	0.001*	52.1 ± 31.3	42.3 ± 30.6	0.001*	0.001*

Over the target range of Serum iPTH >300 (pg/mL), Corrected serum calcium >10.5 (mg/dL), Serum phosphorus >5.5 (mg/dL), Calcium-phosphorus product >55. * $p < 0.05$

Table 5 Cox regression analysis for factors related to new cardiovascular event

Factor	Univariate analysis Hazard ratio (95% CI)	*p*-value	Multivariate analysis Hazard ratio (95% CI)	*p*-value
Age (year)	1.04 (1.01–1.08)	0.009*	1.04 (1.00 –1.08)	0.039*
Dialysis period(year)	0.98 (0.93–1.03)	0.441	1.01 (0.95 –1.07)	0.791
Hypertension	1.78 (0.43–7.37)	0.424		
Diabetes mellitus	1.98 (1.04–3.76)	0.037*	1.35 (0.64–2.85)	0.433
CAOD	2.21 (1.23–3.98)	0.008*	1.19 (0.58–2.44)	0.637
Arrthymia	2.02 (1.12–3.65)	0.002*	2.26 (1.14–4.47)	0.019*
Valvular heart disease	3.10 (1.60–6.01)	0.001*	2.36 (1.04–5.36)	0.009*
CBVD	2.77 (1.42–5.38)	0.003*	1.13 (0.48–2.64)	0.778
Dyslipidemia	2.25 (1.27–3.97)	0.005*	1.12 (0.58–2.16)	0.742
PTX (*vs.* cinacalcet)	0.16 (0.07–0.37)	0.001*	0.14 (0.05–0.39)	0.001*
Period of over the target range (year)				
Serum iPTH >300 (pg/mL)	1.08 (0.99–1.17)	0.057		
Corrected serum calcium >10.5 (mg/dL)	1.10 (0.95–1.28)	0.20		
Serum phosphorus >5.5 (mg/dL)	1.07 (0.98–1.18)	0.135		
Calcium-phosphorus product >55	1.11 (1.01–1.23)	0.04*	1.24 (1.08–1.43)	0.003*

CI, confidence interval. * $p < 0.05$

sis, patients with arrhythmia (HR, 2.26; 95% CI, 1.14–4.47) and valvular heart disease (HR, 2.36; 95% CI, 1.04–5.36) were at a significantly higher risk of cardiovascular events. A longer duration of calcium–phosphorus product >55 indicated a significantly higher risk of cardiovascular events compared to other biochemical variables (HR, 1.24; 95% CI, 1.08–1.43). As a prognostic factor, the type of intervention helped determine the likelihood of new cardiovascular events. The PTX group appeared to be at low risk for new cardiovascular events in both univariate (HR, 0.16; 95% CI, 0.07–0.37) and multivariate analyses (HR, 0.14; 95% CI, 0.05–0.39). These findings suggest that PTX reduced the risk of new cardiovascular events by 86% compared to cinacalcet.

Cardiovascular event-free survival significantly differed between the PTX and cinacalcet groups. The PTX group presented a longer period of cardiovascular event-free survival than the cinacalcet group ($p = 0.001$; Fig. 1). No significant difference was observed in the overall survival rate between the two groups ($p = 0.424$; Fig. 2).

Discussion

Many studies have been conducted to assess the clinical outcomes of the calcimimetic cinacalcet, but improvements in the mortality rate and in bone metabolism have not been consistently confirmed. However, medical treatment using cinacalcet has been reported to have significantly lowered calcium, phosphorus, calcium–phosphorus product, and PTH levels [1, 3, 5-7, 18]. The effectiveness of cinacalcet on bone metabolism was recently confirmed in the 2006–2011 BONAFIDE trial [19]. However, additional randomized controlled trials (RCTs) have been recommended to evaluate its bene-

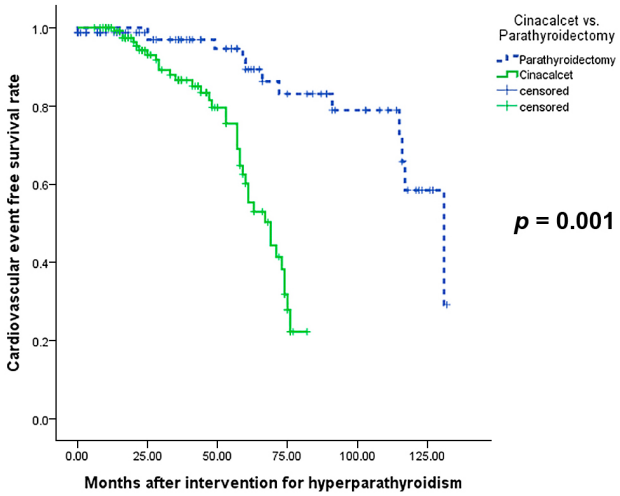

Fig. 1 Cardiovascular disease-specific event-free survival curves according to the treatment types of secondary hyperparathyroidism ($p = 0.001$).

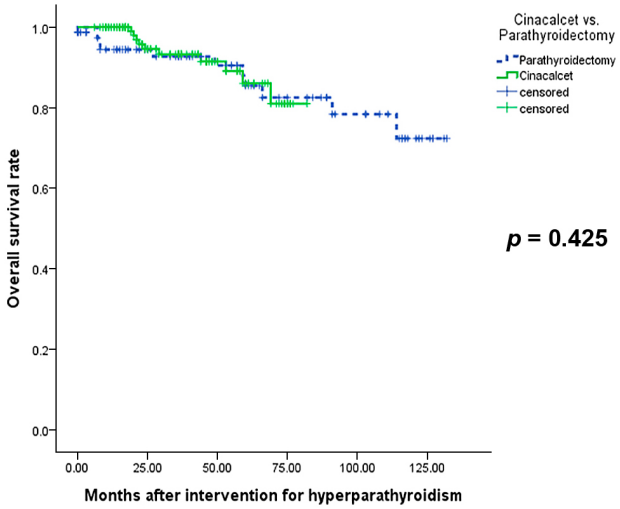

Fig. 2 Overall survival curves according to the treatment types of secondary hyperparathyroidism ($p = 0.425$).

fits compared to conventional treatments [7]. Several studies have shown that cinacalcet is effective in adjusting the target range of calcium, phosphorus, calcium–phosphorus product, and PTH [20]. Some studies have reported that mortality rates were related to increases in the levels of phosphorus and not those of calcium and PTH [21, 22]. It has been proposed in observational studies that adjusting mineral levels to within a target range would positively affect mortality rates, but no RCT has been conducted. However, more research is needed to confirm whether calcium, phosphorus, and PTH are potentially modifiable risk factors. In addition, there is increasing interest in the use of bone-derived biomarkers for predicting and monitoring vascular calcification [23]. Moreover, according to Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, mineral abnormality begins to appear when the glomerular filtration rate (GFR) is <60 mL/min at stage II of chronic kidney disease (CKD). In such cases, the PTH level is used as the earliest marker for predicting mineral abnormality. One study reported that mineral abnormality could be confirmed at an early stage of CKD (GFR <50) through observing increased levels of fibroblast growth factor 23 (FGF-23) and PTH. An increase in FGF-23 has been reported to be associated with mortality, progression of CKD, left ventricular hypertrophy (LVH), and cardiovascular events [24].

Phosphorus levels rise with the decline of the GFR and are the main target for correction during dialysis treatment. If SHPT occurs when phosphorus levels are affected due to the GFR, calcium levels are also affected, resulting in an increased calcium–phosphorus product, which can easily lead to sediment formation and calcification. Some authors have contended that previous relevant guidelines can be set aside and that target phosphorus levels should be set to within the normal range [25]. Therefore, physicians have tried to reduce phosphate imbalance and maintain PTH levels within the target range, to reduce CKD-accelerated cardiovascular calcification [18, 23, 26].

No significant reductions in disease mortality and major cardiovascular complications were demonstrated in the EVOLVE trial when validating the effects of cinacalcet treatment. Although gastrointestinal side-effects have frequently been reported, treatment with cinacalcet can maintain PTH levels to within the target range without the need for PTX, thus, reducing the frequency of PTX by >50% [10]. However, despite the reported advantages of cinacalcet, PTX remains the treatment of choice [2]. Early-stage PTX has been reported to reduce mortality [27]; however, because physicians prefer non-invasive procedures, PTX may be delayed in some cases. Bryan *et al.* reported a short-term mortality rate of 3% post-PTX and a low long-term mortality rate. Another Japanese study reported that only one of 1,053 patients had died due to PTX. The risk of calcification and cardiovascular complications, such as arterial stiffness, conduction delay, and LVH, are likely to increase with age. If patients are exposed to uncontrolled calcium and phosphorus levels over a long duration, the risk of complications is likely to increase.

In the recent INDEPENDENT study, the use of calcium-free phosphate binders and cinacalcet in open-label RCTs demonstrated significant improvement in overall survival and a 71% reduction in the risk of complications. According to previously reported data, cinacalcet did not significantly reduce the risk of com-

plications when used with vitamin D and calcium-containing phosphate binders [9].

Multicenter studies conducted in Korea in 2014 reported that many patients undergoing dialysis were being treated without appropriate control of phosphorus levels and calcium–phosphorus products. The percentages of patients with phosphorus and calcium–phosphorus product levels within the KDOQI guideline ranges, which are known to be associated with cardiovascular complications, were 51% and 70.7%, respectively. In addition, 26.5% of the patients were reported to have a PTH level >300 pg/mL. Therefore, a surgical approach should be considered to reduce complications and improve QOL, through adjusting the mineral levels to within a target range. Furthermore, it has been suggested that treatment for maintenance within the target range and normalization of bone metabolism should be considered [15]. Initial treatments have involved various medications in preference to invasive surgical management. As a result, some patients have experienced increased vascular comorbidity. In addition, cinacalcet has been reported to be less cost-effective compared to PTX when assessed over a 16-month period [28].

Parathyroid gland function usually recovers after kidney transplantation. Therefore, patients tend to undergo dialysis while awaiting kidney transplantation, thereby delaying PTX despite SHPT. However, one study reported that a secondary parathyroid nodule might progress to the nodular hyperplasia stage in the diffused hyperplasia stage, and progress further into the irreversible stage when the size of the nodule increases 500 mm^3 and is >1 cm [14].

Regardless of attempts to normalize parathyroid function, it has been well established that vascular calcification is irreversible. Therefore, efforts should be made to minimize vascular calcification in preparation for effective kidney transplantation [29].

Future research is required to improve QOL and reduce mortality through active surgical treatment for patients who are currently eligible for PTX surgery, according to KDOQI guidelines, at experienced centers. Surgical treatment for SHPT in CKD patients with ESRD who require dialysis has been considered helpful in reducing long-term vascular complications and mortality. Large-scale studies to confirm the effectiveness of such an approach are needed.

Although the perioperative mortality rate is high in patients who undergo secondary parathyroid surgery, long-term survival rates have been reported to vary postoperatively [30]. In addition to potentially serious complications, complications related to PTX may incline patients to opt for other treatment procedures.

In this study, we noted surgery-related complications. We identified one case of postoperative mortality due to aggravation of DCMP and one case of persistent hyperparathyroidism due to the presence of a supernumerary ectopic parathyroid gland. If the risk of persistent hyperparathyroidism is minimized through intraoperative PTH monitoring during surgery, surgeons can address the likelihood of short-term complications using appropriate procedures and achieve better long-term survival without cardiovascular complications.

The rate of new cardiovascular events was significantly lower in the PTX group than the cinacalcet group. The outcomes were more favorable for patients who had undergone PTX and who had a short period of uncontrolled calcium–phosphorus product levels than for patients in the cinacalcet group. PTX can prevent cardiovascular events through adjusting the biochemical levels to within the target range in patients with SHPT. PTX should be considered to help prevent new cardiovascular events in preference to cinacalcet treatment.

This study was limited due to its retrospective design and the possibility of selection bias. Comparing the baseline characteristics between the included and excluded patients in the analysis was not feasible. Several patients were lost to follow-up, or the patients consulted local clinics, or there was only a short-term follow-up because our hospital was a referral center. Evidence-based RCTs are needed to determine the effects of treatment between the two groups. Therefore, we intend to undertake a prospective cohort observational study in future.

Conflict of Interest Statement

All authors declare no conflicts of interest.

Author Contributions

W.W.K. generated population data and generated tables drafted and edited the manuscript. Y.R. and B.S.K provided oversight, and reviewed the manuscript. K.K. reviewed the manuscript. C.R.L., S.W.K., and J.L. reviewed the manuscript. K.H.N. reviewed the manuscript. J.J.J. and W.Y.C. provided oversight, formulated hypotheses, and reviewed the manuscript.

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