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Original Article

Total parathyroidectomy with autotransplantation vs. subtotal parathyroidectomy for secondary hyperparathyroidism: lower recurrence rates but comparable cardiovascular outcomes

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Abstract: Objective: This study aimed to compare the long-term efficacy and cardiovascular outcomes of total parathyroidectomy with autotransplantation (TPTX+AT) versus subtotal parathyroidectomy (SPTX) in maintenance hemodialysis (MHD) patients with refractory secondary hyperparathyroidism (SHPT). Methods: This retrospective cohort study enrolled MHD patients with SHPT who underwent parathyroidectomy between January 2020 and December 2022, with follow-up through December 2025. Patients were divided into TPTX+AT and SPTX groups. Serum intact parathyroid hormone (iPTH), corrected calcium, phosphorus, alkaline phosphatase, and 25-hydroxyvitamin D were measured preoperatively, on postoperative day 1, and at 3, 6, 12, and 36 months. Operative time, hospital stay, early complications, and long-term outcomes including SHPT recurrence, mortality, cardiovascular events, and permanent hypoparathyroidism were recorded. Results: Of 217 patients, 113 underwent TPTX+AT and 104 underwent SPTX. Operative time was longer with TPTX+AT (129.42 ± 34.74 min vs. 114.49 ± 29.71 min, $P < 0.001$). At 36 months, iPTH levels were significantly lower in the TPTX+AT group (209.74 ± 103.51 pg/mL vs. 464.53 ± 184.60 pg/mL, $P < 0.001$). SHPT recurrence was lower with TPTX+AT (14.16% vs. 36.54%, $P < 0.001$), while permanent hypoparathyroidism occurred only in the TPTX+AT group (5.31% vs. 0%, $P = 0.049$). All-cause mortality (13.27% vs. 13.46%), cardiovascular mortality (7.08% vs. 6.73%), and cardiovascular events (19.47% vs. 16.35%) were similar between groups (all $P > 0.05$). Conclusion: TPTX+AT achieves more durable biochemical control and lower SHPT recurrence but carries a definite risk of permanent hypoparathyroidism, with equivalent survival and cardiovascular outcomes, underscoring the need for individualized surgical selection.

Keywords: Secondary hyperparathyroidism, total parathyroidectomy with autotransplantation, subtotal parathyroidectomy, maintenance hemodialysis, cardiovascular events, recurrence

Introduction

Secondary hyperparathyroidism (SHPT) represents a prevalent and debilitating complication in patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis, with reported prevalence rates ranging from 27% to 41% and approaching 100% in those dialyzed for over a decade [1]. This disorder, characterized by excessive parathyroid hormone (PTH) secretion, is a central component of chronic kidney disease-mineral and bone disorder and is intrinsically linked to significant patient morbidity [2]. The clinical burden of SHPT remains substantial, as evidenced by contemporary data indicating its presence in nearly one-fifth of the hemodialysis population, with higher prevalence observed among males and individuals with longer dialysis vintage [3]. The pathophysiology of SHPT in the uremic milieu is driven by a complex interplay of hyperphosphatemia, hypocalcemia, and reduced renal synthesis of 1,25-dihydroxyvitamin D, which collectively stimulates parathyroid gland hyperplasia and autonomous PTH secretion. This progressive parathyroid hyperplasia, initially polyclonal and later monoclonal, underpins the refractoriness to medical therapy that ultima-

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tely necessitates surgical intervention in a substantial proportion of patients.

The clinical significance of SHPT extends beyond the skeletal system, as elevated PTH acts as a potent uremic toxin with a profound impact on cardiovascular health, with cardiovascular disease being the leading cause of mortality in the ESRD population [4, 5]. This hormone promotes vascular smooth muscle cell transdifferentiation, arterial stiffening, and endothelial dysfunction, thereby fostering vascular calcification and increased cardiac afterload [6-8]. These pathological alterations directly contribute to the development of left ventricular hypertrophy and other cardiovascular pathologies [4, 5, 8]. Critically, epidemiological studies consistently identify severely elevated PTH levels, particularly above 600 pg/mL, as an independent risk factor for all-cause and cardiovascular mortality in dialysis patients [9, 10]. This firmly establishes SHPT not merely as a biochemical derangement but as a key modifiable driver of fatal cardiovascular events in this vulnerable cohort. Moreover, the cardiovascular burden of SHPT is compounded by the high prevalence of traditional risk factors in the dialysis population, including hypertension, diabetes mellitus, and dyslipidemia, which synergistically amplify the adverse vascular effects of PTH excess.

For patients with severe SHPT refractory to medical management with vitamin D analogues and calcimimetics, parathyroidectomy (PTX) remains the definitive intervention [2, 11, 12]. The current surgical paradigm comprises two principal techniques: total parathyroidectomy with autotransplantation (TPTX+AT) and subtotal parathyroidectomy (SPTX). Each approach carries distinct theoretical advantages and trade-offs. TPTX+AT, by excising all cervical parathyroid tissue and transplanting a fragment, aims to minimize the risk of persistent or recurrent disease, though it may predispose patients to a higher incidence of transient hypocalcemia and carries a risk of graft-dependent recurrence [13, 14]. The AT technique, typically performed in the forearm musculature contralateral to the hemodialysis access site, offers the additional advantage of permitting localized reoperation under local anesthesia should graft-dependent recurrence occur, thereby avoiding the hazards of repeat neck exploration. Conversely, SPTX, which preserves a vascularized parathyroid remnant in situ, may maintain a more physiological PTH secretion pattern but is associated with a higher documented rate of disease recurrence originating from the remnant [13, 15]. The remnant is continuously exposed to the uremic proliferative stimuli of hyperphosphatemia, hypocalcemia, and calcitriol deficiency, which predispose to progressive hyperplasia and late recurrence.

The critical unresolved question pertains to the long-term consequences of these divergent surgical strategies on hard clinical endpoints, particularly cardiovascular outcomes. While both procedures effectively lower PTH levels, their comparative efficacy in mitigating the elevated cardiovascular risk inherent to SHPT over extended follow-up is poorly characterized and existing evidence is contradictory. Some data suggest SPTX may confer a cardiovascular advantage, possibly due to the avoidance of excessively low PTH levels [16], whereas other studies report no significant difference in mortality between the two techniques [17]. This equipoise highlights a significant evidence gap and raises the possibility that the superior biochemical control offered by TPTX+AT may not translate into superior cardiovascular outcomes. The clinical significance of this question is underscored by the fact that cardiovascular disease accounts for approximately 40-50% of all deaths in the dialysis population, and any surgical strategy that could differentially modify this risk would have substantial public health implications. Furthermore, the trade-off between disease recurrence and permanent hypoparathyroidism-two outcomes with opposing implications for bone health and quality of life-has not been adequately quantified in contemporary cohorts with standardized follow-up protocols.

The novel elements of this investigation encompass: a thorough longitudinal biochemical evaluation extending over 36 months, documenting the progression of PTH alongside bone turnover markers at various predetermined intervals; stringent and adjudicated recording of cardiovascular incidents and mortality as co-primary endpoints; adjustments for significant confounders through multivariable analysis, factoring in indicators of disease severity as well as preoperative therapeutic

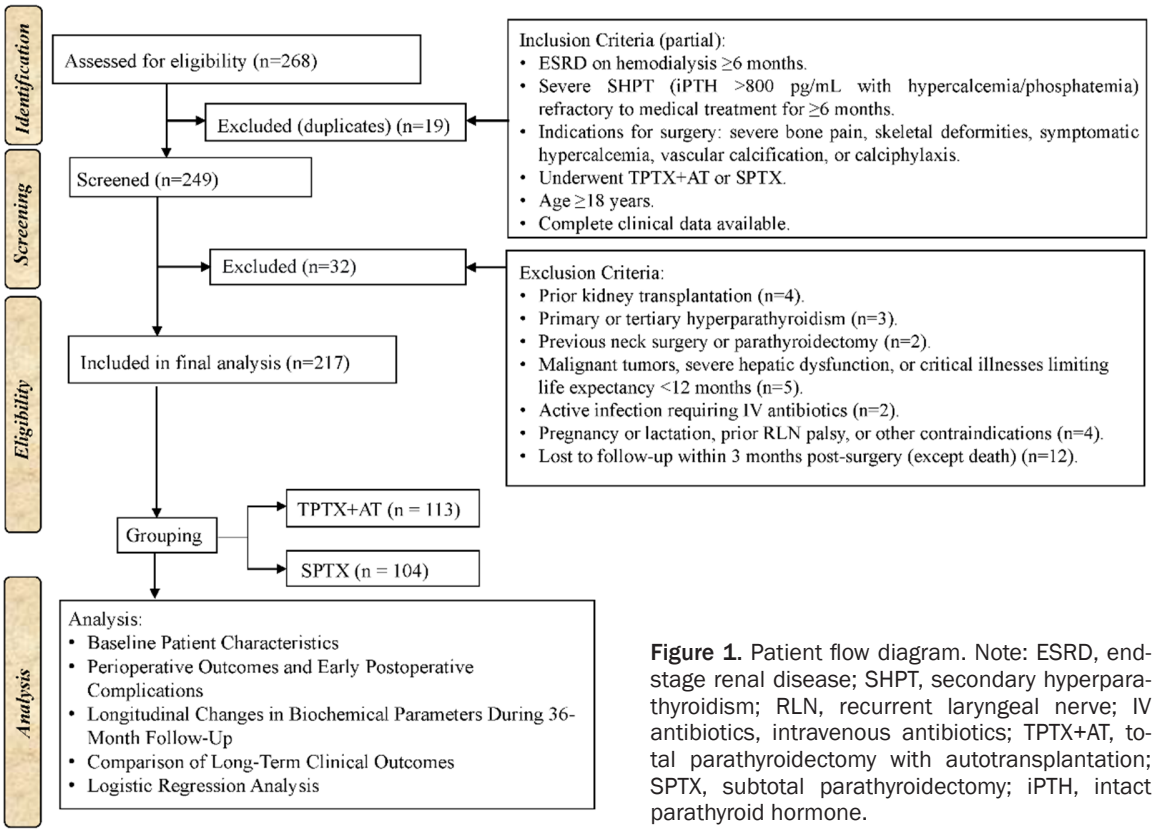

Figure 1. Patient flow diagram. Note: ESRD, end-stage renal disease; SHPT, secondary hyperparathyroidism; RLN, recurrent laryngeal nerve; IV antibiotics, intravenous antibiotics; TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; iPTH, intact parathyroid hormone.

regimens; and an in-depth delineation of the balance between recurrence and permanent hypoparathyroidism within a modern patient group. Consequently, the study was designed to evaluate and compare the 36-month long-term efficacy of TPTX+AT versus SPTX, as well as their effects on cardiovascular outcomes in maintenance hemodialysis patients with refractory SHPT, aiming to provide evidence to inform individualized surgical decision-making.

Methods

Study design and ethical approval

This retrospective cohort study included data from 217 patients admitted to The First People's Hospital of Yunnan Province between January 2020 and December 2022 with SHPT on maintenance hemodialysis and undergoing PTX, with follow-up lasting for 36 months and a cut-off date of December 2025. Clinical, laboratory, and follow-up data were systematically extracted from the electronic medical records using standardized data collection forms. The flow diagram is presented as **Figure 1**.

This study adhered to the ethical principles outlined in the Declaration of Helsinki. Due to its retrospective nature, the requirement for informed consent was waived by the Institutional Review Board and the Independent Ethics Committee of The First People's Hospital of Yunnan Province. All patient data were fully anonymized and de-identified before being extracted from the electronic health record system for research purposes, ensuring strict confidentiality and compliance with patient privacy regulations.

Case selection

Patients were eligible for inclusion if they met all the following criteria: (1) a confirmed diagnosis of ESRD and maintenance hemodialysis for at least 6 months [18]; (2) a biochemical diagnosis of severe SHPT refractory to medical management, defined as serum intact parathyroid hormone (iPTH) levels persistently > 800 pg/mL with concurrent hypercalcemia or hyperphosphatemia despite optimal medical therapy, including phosphate binders, active vitamin D analogues, and/or cinacalcet, for a minimum

of 6 months [19]; (3) clinical indications for surgical intervention, including severe bone pain, skeletal deformities, symptomatic hypercalcemia, progressive vascular calcification, or calciphylaxis; (4) surgical intervention with either TPTX+AT or SPTX as the initial procedure; (5) age of 18 years or older at the time of surgery; (6) adequate functional status with an Eastern Cooperative Oncology Group performance status of 0-2; and (7) the availability of complete clinical and laboratory data in the electronic health records system.

Patients were excluded from the analysis for any of the following reasons: (1) a history of kidney transplantation prior to PTX; (2) a confirmed diagnosis of primary hyperparathyroidism (e.g., parathyroid adenoma with suppressed PTH in other glands, hypercalcemia with inappropriately normal or elevated PTH, and normal renal function prior to ESRD) or tertiary hyperparathyroidism (autonomous hyperfunctioning parathyroid tissue after successful renal transplantation with normalization of renal function); (3) a history of prior neck surgery or PTX; (4) concomitant diagnosis of malignant tumors (active or within the past 5 years), severe hepatic dysfunction, decompensated heart failure, or any other critical illness that, in the judgment of the investigators, would confound the long-term outcomes or substantially limit life expectancy to less than 12 months; (5) active infection requiring intravenous antibiotic therapy at the time of surgery; (6) pregnancy or lactation; (7) known allergy to perioperative medications, or documented recurrent laryngeal nerve (RLN) palsy from prior neck/thyroid surgery; (8) any other contraindications determined by the attending surgeon to preclude safe surgery; or (9) loss to follow-up within the first 3 months post-surgery for reasons other than death.

Grouping criteria and clinical management protocols

The cohort of 217 eligible patients was divided into two groups based on the type of surgical procedure performed: 113 underwent TPTX+AT and 104 underwent SPTX. The selection of the surgical approach was non-randomized and was determined by the attending surgeon's clinical judgment based on a comprehensive preoperative evaluation that included disease severity, parathyroid gland morphology on cervical ultrasound and/or 99mTc-sestamibi scintigraphy, patient age, comorbidity burden, and individual risk-benefit considerations. As this was an observational retrospective cohort study, there was no randomization of treatment allocation, and the decision-making process reflected standard clinical practice in a real-world setting. Both surgical procedures were performed by a team of experienced endocrine surgeons (each with more than 10 years of experience in parathyroid surgery) to ensure technical standardization and minimize operator-dependent variability.

All operations were performed under general anesthesia with the patient in a supine position and the neck hyperextended. A standard transverse cervical collar incision was made to provide adequate exposure of the thyroid gland and all four parathyroid glands. In the TPTX+AT group, TPTX was initially performed. After meticulous identification and mobilization of all parathyroid glands, each gland was dissected and removed, with careful attention to preserving the RLNs and the superior laryngeal nerves. The inferior thyroid arteries were ligated close to the gland capsule to devascularize remaining microscopic rests. A bilateral cervical thymectomy was routinely performed to clear any potential supernumerary or ectopic glands within the thymic tongue. Following the complete removal of parathyroid tissue, a small, macroscopic portion of the most normal-appearing gland, free of obvious nodular hyperplasia, was selected for AT. This tissue was immediately placed in sterile, ice-cold normal saline and minced into fragments approximately 1 mm^3 in size. A total of 15-20 of fragments were implanted into a muscle pocket created in the brachioradialis muscle of the forearm contralateral to the functional dialysis arteriovenous fistula. In the SPTX group, SPTX was performed. The surgical principle was the removal of three and a half glands. After identifying all four glands, the smallest and most normal-appearing gland was identified as the remnant. The vascular pedicle to this gland was meticulously preserved to ensure a robust blood supply. The remaining three glands were completely removed, and a subtotal resection of the designated remnant gland was performed, leaving a well-vascularized fragment

estimated to be 50-60 mg, roughly equivalent to the size of two normal glands. The remnant was marked with a metal clip to facilitate future identification. The wound was closed in layers over a closed-suction drain after confirming meticulous hemostasis in both groups.

Data extraction and outcome measures

Data extraction was performed systematically from the electronic medical records using standardized data collection forms. Two trained research assistants independently extracted all baseline, perioperative, biochemical, and long-term outcome data, with any discrepancies resolved by consensus with a third senior investigator. The primary outcome measures of this study were SHPT recurrence, all-cause mortality, and cardiovascular mortality. Secondary outcome measures included cardiovascular events, reoperation for recurrence, persistent SHPT, fracture events, permanent hypoparathyroidism, and longitudinal changes in serum corrected calcium, phosphorus, alkaline phosphatase, and 25-hydroxyvitamin D measured at baseline, postoperative day 1, and at 3, 6, 12, and 36 months.

Baseline and general data: The baseline data collected focused on parameters known to influence the course of SHPT and surgical outcomes as presented in the study results. Preoperative demographic and clinical characteristics included sex, age, and body mass index. The dialysis vintage, defined as the total duration of hemodialysis before PTX, was recorded in years. The primary cause of ESRD was categorized into chronic glomerulonephritis, diabetic nephropathy, hypertensive nephropathy, polycystic kidney disease, and other causes. Clinically significant comorbidities were documented based on physician-confirmed diagnoses, including hypertension, diabetes mellitus, coronary artery disease, and a history of cerebral infarction. The preoperative pharmacological management of SHPT was also recorded, specifically noting the use of cinacalcet, active vitamin D analogues, and phosphate binders.

Perioperative parameters: The surgical data collected included operative time (measured from the initial skin incision to the completion of wound closure) and the number of parathyroid glands identified and confirmed by histopathology. The length of postoperative hospital stay was defined as the number of days from the date of surgery to discharge. Early postoperative complications occurring during the initial hospitalization were documented, including the incidence of RLN injury, cervical hematoma requiring intervention, and wound infection.

Longitudinal biochemical evaluation: Peripheral venous blood samples were collected from all patients at baseline (within one week prior to surgery), on postoperative day 1, and at 3, 6, 12, and 36 months after PTX. For follow-up time points, blood samples were drawn immediately before the initiation of a mid-week hemodialysis session. All blood samples were allowed to clot at room temperature for 30 minutes before being centrifuged at 3000 rpm for 10 minutes. The resulting serum was aliquoted into cryovials and stored at -80°C for batched analysis. Serum concentrations of iPTH and 25-hydroxyvitamin D were measured using electrochemiluminescence immunoassays on a Roche cobas e 801 immunoassay analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The iPTH assay employed the Elecsys PTH (1-84) kit (Roche Diagnostics GmbH; catalog no. 08928380190), which specifically detects the biologically active intact molecule. The 25-hydroxyvitamin D assay utilized the Elecsys Vitamin D total III kit (Roche Diagnostics GmbH; catalog no. 05894913190), which measures both 25-hydroxyvitamin D2 and D3 with equal affinity. Serum levels of corrected calcium, phosphorus, and alkaline phosphatase were determined using spectrophotometric assays on a Roche cobas c 702 clinical chemistry analyzer (Roche Diagnostics GmbH, Mannheim, Germany) with dedicated original Roche reagents.

Long-term clinical outcome assessment: The primary long-term clinical outcomes were assessed during a 36-month follow-up period. The primary endpoint was SHPT recurrence, specifically defined as a sustained elevation of serum iPTH levels above 500 pg/mL more than 6 months after surgery, in accordance with an adapted version of Kidney Disease Outcomes Quality Initiative guidelines for postoperative monitoring, which clearly demarcated the condition from persistent disease [20]. All-cause mortality and cardiovascular mortali-

ty were recorded as definitive endpoints. Cardiovascular events were defined as a composite of non-fatal myocardial infarction, hospitalization for acute decompensated heart failure, and acute stroke, with all events confirmed by review of discharge summaries and relevant diagnostic codes. Reoperation for SHPT recurrence, the development of persistent SHPT, fracture events, and the occurrence of permanent hypoparathyroidism were also documented. Permanent hypoparathyroidism was defined as persistent serum iPTH levels below 15 pg/mL accompanied by a need for ongoing calcium and calcitriol supplementation for a period beyond 12 months [21].

Follow up

Postoperative follow-up extended from the date of surgery to the prespecified study cutoff date of December 2025, ensuring a minimum potential follow-up of 36 months for all surviving patients. Follow-up data were systematically collected through outpatient dialysis unit visits and the hospital's integrated electronic health record system. For patients who received care at external facilities, relevant medical records were obtained through standardized health information exchange requests. Additionally, trained research nurses contacted patients or their designated family members via telephone at 3 to 12-month intervals to ascertain survival status, dialysis modality, and the occurrence of any interval clinical events. All reported cardiovascular events, reoperations, fractures, and deaths were rigorously verified against hospital discharge summaries, outpatient visit documentation, or death certificates. Patients who received a renal transplant during follow-up were censored at the date of transplantation for biochemical and recurrence analyses.

Statistical method

All statistical analyses were conducted using IBM SPSS Statistics, Version 29.0 (IBM Corp., Armonk, NY, USA). The normality of continuous data distributions was assessed using the Shapiro-Wilk test. Continuous variables that conformed to a normal distribution were presented as mean ± standard deviation, and comparisons between the TPTX+AT and SPTX groups were made using the independent samples t-test. Non-normally distributed continuous variables were expressed as median and interquartile range and analyzed using the Mann-Whitney U test. Categorical variables were presented as frequencies with corresponding percentages and compared using the Chi-square test or, when appropriate for small expected cell counts, Fisher's exact test. For longitudinal changes in biochemical parameters within each surgical group over the six time points (baseline, postoperative day 1, and at 3, 6, 12, and 36 months), a repeated-measures analysis of variance was performed. When the assumption of sphericity was violated, the Greenhouse-Geisser correction was applied. Pairwise comparisons between time points were adjusted using the Bonferroni method to control for multiple comparisons. To identify independent risk factors for SHPT recurrence, a multivariable logistic regression model was constructed. Variables with a *P*-value < 0.10 in univariable analysis, along with those considered clinically significant, were entered into the model using a backward stepwise elimination procedure. Given the total number of recurrence events (n = 54) and the events-per-variable principle requiring at least 10 events per predictor variable, a maximum of 5 variables could be included in the multivariable model to avoid overfitting. The final model included surgical procedure (TPTX+AT vs. SPTX), baseline iPTH (per 100 pg/mL), dialysis vintage (per year), and baseline alkaline phosphatase (ALP) (per 10 U/L), which were the only variables that met the threshold for entry ($P < 0.10$) in univariable analysis. Variable assignments were as follows: surgical procedure (TPTX+AT = 1, SPTX = 0, with SPTX as reference); all continuous variables retained in the final multivariate model (dialysis vintage, baseline iPTH, and baseline ALP) were entered as continuous measures with the specified unit increments; sex (male = 1, female = 0, with female as reference); diabetes mellitus (presence = 1, absence = 0); cinacalcet use (yes = 1, no = 0). The strength of these associations was reported as odds ratios with corresponding 95% confidence intervals. All tests performed were two-tailed, and a *P*-value of less than 0.05 was considered indicative of a statistically significant difference for all comparisons.

Table 1. Baseline demographic and clinical characteristics

Parameter	TPTX+AT (n = 113)	SPTX (n = 104)	t/χ^2	*P* value
Sex, n (%)			0.004	0.952
Male	68 (60.18%)	63 (60.58%)		
Female	45 (39.82%)	41 (39.42%)		
Age, years	51.83 ± 11.78	51.09 ± 10.66	0.485	0.628
BMI, kg/m^2	22.49 ± 3.19	22.57 ± 3.35	0.195	0.846
Dialysis vintage, years	7.17 ± 2.51	7.22 ± 2.40	0.126	0.900
Primary cause of ESRD, n (%)			0.656	0.957
Chronic glomerulonephritis	42 (37.17%)	37 (35.58%)		
Diabetic nephropathy	31 (27.43%)	28 (26.92%)		
Hypertensive nephropathy	27 (23.89%)	27 (25.96%)		
Polycystic kidney disease	8 (7.08%)	9 (8.65%)		
Other	5 (4.42%)	3 (2.88%)		
Comorbidities, n (%)				
Hypertension	98 (86.73%)	92 (88.46%)	0.150	0.699
Diabetes mellitus	39 (34.51%)	33 (31.73%)	0.189	0.664
Coronary artery disease	25 (22.12%)	22 (21.15%)	0.030	0.862
History of cerebral infarction	13 (11.50%)	12 (11.54%)	0.000	0.994
Preoperative medication use, n (%)				
Cinacalcet	68 (60.18%)	63 (60.58%)	0.004	0.952
Active vitamin D analogues	97 (85.84%)	90 (86.54%)	0.022	0.882
Phosphate binders	104 (92.04%)	96 (92.31%)	0.006	0.941

Note: TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; BMI, body mass index; ESRD, end-stage renal disease.

Results

Baseline patient characteristics

A total of 217 patients were included in the final analysis, with 113 undergoing TPTX+AT and 104 undergoing SPTX. The baseline demographic and clinical profiles of the two cohorts were well balanced, with no statistically significant differences detected across any measured parameter (all $P > 0.05$) (**Table 1**). The mean age was approximately 51 years with a male predominance of roughly 60%, and the average dialysis vintage was just over 7 years. Chronic glomerulonephritis represented the leading cause of ESRD, followed by diabetic nephropathy and hypertensive nephropathy. The burden of major comorbidities, including hypertension (affecting over 86% of patients in both groups), diabetes mellitus, and coronary artery disease, was similarly distributed. Notably, preoperative medical management for SHPT was intense and comparable in both groups, with over 85% of patients receiving active vitamin D analogues and approximately 60% being treated with cinacalcet. Collectively, these data confirm that the two surgical groups were highly comparable at baseline, supporting the validity of subsequent outcome comparisons.

Perioperative outcomes and early postoperative complications

The intraoperative details and immediate postoperative safety profiles are summarized in **Table 2**. The mean operative time was significantly longer for the TPTX+AT procedure compared with SPTX (129.42 ± 34.74 vs. 114.49 ± 29.71 minutes, $P < 0.001$), reflecting the additional steps required for AT and bilateral cervical thymectomy. Despite this difference, the length of postoperative hospital stay was similar between the two groups (8.82 ± 2.93 vs. 8.24 ± 2.48 days, $P = 0.122$). Early surgical morbidity was low overall, and no significant difference was observed in the incidence of RLN injury, cervical hematoma requiring intervention, or wound infection (all $P > 0.05$). In summary, although TPTX+AT required a longer

Table 2. Intraoperative details and early postoperative complications by surgical procedure

Parameter	TPTX+AT (n = 113)	SPTX (n = 104)	t/χ^2	*P* value
Operative time, min	129.42 ± 34.74	114.49 ± 29.71	3.389	< 0.001
Length of hospital stay, days	8.82 ± 2.93	8.24 ± 2.48	1.552	0.122
Recurrent laryngeal nerve injury, n (%)	1 (0.88%)	2 (1.92%)	0.005	0.942
Cervical hematoma, n (%)	2 (1.77%)	1 (0.96%)	0.000	1.000
Wound infection, n (%)	1 (0.88%)	0 (0.00%)	None	1.000*

Note: TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SD, standard deviation. *Fisher's exact test.

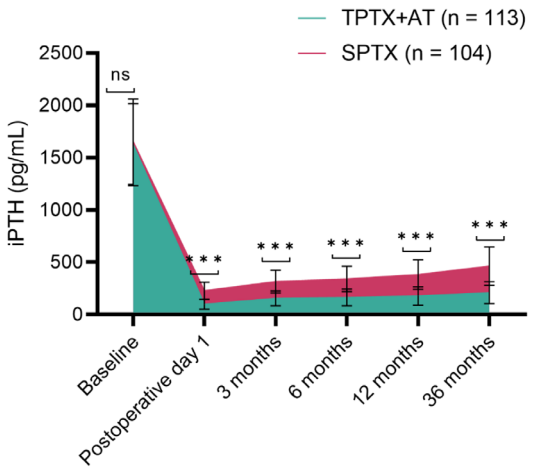

Figure 2. Longitudinal changes in serum intact parathyroid hormone levels from baseline to 36 months after parathyroidectomy (mean ± SD, pg/mL). Note: iPTH, intact parathyroid hormone; TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SD, standard deviation. ***$P < 0.001$.

operative time, it did not translate into a prolonged hospital stay or a higher rate of early postoperative adverse events.

Longitudinal changes in biochemical parameters during 36-month follow-up

The trajectory of serum iPTH over the 36-month follow-up period is depicted in **Figure 2**. Both surgical interventions produced a dramatic reduction in iPTH levels immediately following surgery, but the magnitude and durability of the suppression diverged markedly. At baseline, mean iPTH levels were similarly elevated (1624.13 ± 392.74 pg/mL for TPTX+AT vs. 1653.27 ± 408.62 pg/mL for SPTX, $P = 0.593$). On postoperative day 1, the iPTH concentration in the TPTX+AT group plummeted to 99.36 ± 48.27 pg/mL, which was significantly lower than the 228.71 ± 82.65 pg/mL observed in the SPTX group ($P < 0.001$). This pronounced separation persisted throughout the entire study; at 12 months, the respective values were 178.69 ± 87.42 and 382.91 ± 142.67 pg/mL, and by 36 months, they drifted to 209.74 ± 103.51 and 464.53 ± 184.60 pg/mL ($P < 0.001$ for all time points). The iPTH levels in the TPTX+AT group remained within a controlled, lower range, whereas the SPTX group demonstrated a progressive and substantial rise, approaching the threshold for recurrence. These findings underscore the superior and sustained biochemical control of SHPT afforded by TPTX+AT.

Postoperative changes in divalent ion homeostasis are illustrated in **Tables 3** and **4**. Serum corrected calcium levels, which were comparable preoperatively ($P = 0.201$), fell more precipitously in the TPTX+AT cohort immediately after surgery (1.74 ± 0.26 vs. 1.91 ± 0.29 mmol/L, $P < 0.001$) and remained marginally lower at the 3-month evaluation (2.13 ± 0.31 vs. 2.27 ± 0.30 mmol/L, $P = 0.001$) (**Table 3**). This early difference resolved by 6 months, and calcium levels from that point through to month 36 were virtually identical between the groups (all $P > 0.05$). The profile for serum phosphorus was notably consistent between the two procedures (**Table 4**); following a modest decline from baseline, levels stabilized without any significant between-group divergence at any postoperative time point, including the final measurement at 36 months (1.62 ± 0.39 vs. 1.68 ± 0.41 mmol/L, $P = 0.263$). This pattern indicates a temporary accentuation of postoperative hypocalcemia with TPTX+AT that normalized over time, while phosphorus control was equivalent.

The longitudinal evolution of ALP (a marker of high-turnover bone disease) and 25-hydroxyvitamin D status is presented in **Tables 5** and **6**.

Table 3. Longitudinal changes in serum corrected calcium levels from baseline to 36 months after parathyroidectomy (mean ± SD, mmol/L)

Parameter	Time Point	TPTX+AT (n = 113)	SPTX (n = 104)	t	*P* value
Corrected calcium	Baseline	2.57 ± 0.21	2.53 ± 0.23	1.282	0.201
	Postoperative day 1	1.74 ± 0.26	1.91 ± 0.29	4.571	< 0.001
	3 months	2.13 ± 0.31	2.27 ± 0.30	3.249	0.001
	6 months	2.32 ± 0.27	2.38 ± 0.31	1.668	0.097
	12 months	2.33 ± 0.25	2.37 ± 0.28	1.198	0.232
	36 months	2.35 ± 0.26	2.36 ± 0.27	0.432	0.666
F		78.43	52.67		
P value		< 0.001	< 0.001		

Note: TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SD, standard deviation.

Table 4. Longitudinal changes in phosphorus levels from baseline to 36 months after parathyroidectomy (mean ± SD, mmol/L)

Parameter	Time Point	TPTX+AT (n = 113)	SPTX (n = 104)	t	*P* value
Serum phosphorus	Baseline	2.32 ± 0.49	2.29 ± 0.52	0.405	0.686
	Postoperative day 1	1.83 ± 0.55	1.94 ± 0.57	1.401	0.163
	3 months	1.77 ± 0.43	1.81 ± 0.46	0.678	0.498
	6 months	1.67 ± 0.42	1.73 ± 0.44	1.134	0.258
	12 months	1.63 ± 0.37	1.68 ± 0.42	0.922	0.358
	36 months	1.62 ± 0.39	1.68 ± 0.41	1.122	0.263
F		32.15	28.94		
P value		< 0.001	< 0.001		

Note: TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SD, standard deviation.

Table 5. Longitudinal changes in serum alkaline phosphatase levels from baseline to 36 months after parathyroidectomy (mean ± SD)

Parameter	Time Point	TPTX+AT (n = 113)	SPTX (n = 104)	t	*P* value
ALP (U/L)	Baseline	382.64 ± 109.31	396.28 ± 118.47	0.882	0.379
	Postoperative day 1	387.92 ± 111.69	392.18 ± 115.37	0.276	0.783
	3 months	311.24 ± 99.27	344.62 ± 106.83	2.386	0.018
	6 months	248.36 ± 86.91	279.41 ± 93.78	2.531	0.012
	12 months	197.82 ± 74.53	242.16 ± 81.27	4.255	< 0.001
	36 months	186.47 ± 71.62	234.82 ± 83.49	4.589	< 0.001
F		86.24	43.17		
P value		< 0.001	< 0.001		

Note: ALP, alkaline phosphatase; TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SD, standard deviation.

Starting from a comparable preoperative elevation ($P = 0.379$), ALP levels declined more robustly in the TPTX+AT group (**Table 5**). A significant difference emerged as early as 3 months (311.24 ± 99.27 vs. 344.62 ± 106.83 U/L, $P = 0.018$), widened progressively, and was maintained at 36 months (186.47 ± 71.62 vs. 234.82 ± 83.49 U/L, $P < 0.001$).

Conversely, serum levels of 25-hydroxyvitamin D steadily and smoothly improved in both treatment arms to a similar extent from a baseline of approximately 17-18 ng/mL to over 27 ng/mL, with no statistically significant differences recorded at any follow-up visit (all $P > 0.05$) (**Table 6**). The combination of a more precipitous drop in iPTH and a significantly greater

Table 6. Longitudinal changes in serum 25-hydroxyvitamin D levels from baseline to 36 months after parathyroidectomy (mean ± SD)

Parameter	Time Point	TPTX+AT (n = 113)	SPTX (n = 104)	t	*P* value
25(OH)D (ng/mL)	Baseline	17.36 ± 6.48	18.09 ± 7.02	0.798	0.426
	Postoperative day 1	16.92 ± 6.14	17.63 ± 6.71	0.816	0.415
	3 months	21.42 ± 7.82	22.61 ± 8.24	1.091	0.276
	6 months	24.88 ± 8.29	25.39 ± 8.92	0.438	0.662
	12 months	27.39 ± 9.06	28.19 ± 9.39	0.637	0.525
	36 months	27.64 ± 9.12	28.33 ± 9.61	0.544	0.587
F		23.56	20.18		
P value		< 0.001	< 0.001		

Note: 25(OH)D, 25-hydroxyvitamin D; TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SD, standard deviation.

Table 7. Comparison of long-term clinical outcomes between the two surgical groups during the 36-month follow-up period [n (%)]

Parameters	TPTX+AT (n = 113)	SPTX (n = 104)	χ^2	*P* value
All-cause mortality, n (%)	15 (13.27%)	14 (13.46%)	0.002	0.968
Cardiovascular mortality, n (%)	8 (7.08%)	7 (6.73%)	0.010	0.919
Cardiovascular events, n (%)	22 (19.47%)	17 (16.35%)	0.358	0.549
Myocardial infarction	4 (3.54%)	3 (2.88%)		
Heart failure	12 (10.62%)	9 (8.65%)		
Stroke	6 (5.31%)	5 (4.81%)		
Recurrence of SHPT, n (%)	16 (14.16%)	38 (36.54%)	14.510	< 0.001
Reoperation for recurrence, n (%)	7 (6.19%)	3 (2.88%)	0.702	0.402
Persistent SHPT, n (%)	1 (0.88%)	3 (2.88%)	0.347	0.556
Permanent hypoparathyroidism, n (%)	6 (5.31%)	0 (0.00%)	3.876	0.049
Fracture events, n (%)	4 (3.54%)	6 (5.77%)	0.210	0.647
Renal transplantation, n (%)	2 (1.77%)	3 (2.88%)	0.009	0.925

Note: TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; SHPT, secondary hyperparathyroidism.

reduction in ALP in the TPTX+AT cohort points to a more complete resolution of the hyperparathyroid bone phenotype.

Comparison of long-term clinical outcomes

The hard clinical endpoints assessed during the 36-month observation period are reported in **Table 7**. The overall survival experience was similar, with all-cause mortality rates of 13.27% in the TPTX+AT group and 13.46% in the SPTX group ($P = 0.968$). Cardiovascular mortality (7.08% vs. 6.73%, $P = 0.919$) and the composite rate of incident cardiovascular events, which occurred in 19.47% and 16.35% of patients, respectively ($P = 0.549$), were also not significantly influenced by the choice of surgical technique. The most striking contrast was observed in the rate of SHPT recurrence, which was substantially lower following TPTX+AT (14.16%) compared with SPTX (36.54%, $P < 0.001$). A trade-off for this enhanced efficacy was the development of permanent hypoparathyroidism, which was documented exclusively in the TPTX+AT cohort (5.31% vs. 0.00%, $P = 0.049$). Other outcomes, including the need for reoperation due to recurrence, rates of persistent disease, fracture events, and the proportion of patients receiving a renal transplant, were broadly similar between the groups (all $P > 0.05$). Therefore, the selection of TPTX+AT was associated with a profoundly lower risk of recurrence but at the cost of a small yet measurable increase in permanent hypoparathyroidism, while mortality and cardiovascular event profiles remained unaffected.

Table 8. Univariate and multivariate logistic regression analysis for SHPT recurrence

Variables	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Surgical procedure				
TPTX+AT vs. SPTX	0.312 (0.163-0.598)	< 0.001	0.294 (0.147-0.586)	< 0.001
Age (per year)	0.992 (0.968-1.016)	0.493	\	\
Sex (Male vs. Female)	1.138 (0.622-2.084)	0.674	\	\
Diabetes mellitus (Yes vs. No)	1.421 (0.763-2.648)	0.268	\	\
Preoperative Cinacalcet use (Yes vs. No)	0.973 (0.527-1.797)	0.931	\	\
Baseline iPTH (per 100 pg/mL)	1.247 (1.128-1.379)	< 0.001	1.239 (1.102-1.393)	< 0.001
Dialysis vintage (per year)	1.183 (1.058-1.322)	0.003	1.192 (1.047-1.356)	0.008
Baseline ALP (per 10 U/L)	1.041 (1.021-1.062)	< 0.001	1.039 (1.016-1.063)	0.001

Note: OR, odds ratio; CI, confidence interval; TPTX+AT, total parathyroidectomy with autotransplantation; SPTX, subtotal parathyroidectomy; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase. Variable assignments: surgical procedure (TPTX+AT = 1, SPTX = 0, reference); sex (male = 1, female = 0, reference); diabetes mellitus (yes = 1, no = 0, reference); cinacalcet use (yes = 1, no = 0, reference); age, dialysis vintage, baseline iPTH, and baseline ALP entered as continuous variables with the specified unit increments. Variables not entering the final model (age, sex, diabetes, cinacalcet) had $P > 0.10$ in univariable analysis and were excluded to maintain an adequate events-per-variable ratio.

Logistic regression analysis

To delineate the independent predictors of SHPT recurrence, a multivariable logistic regression model was constructed, the results of which are detailed in **Table 8**. In univariate analysis, the TPTX+AT procedure emerged as a significant protective factor (OR 0.312, 95% CI 0.163-0.598, $P < 0.001$), whereas higher preoperative values of iPTH (per 100 pg/mL: OR 1.247, $P < 0.001$), longer dialysis vintage (per year: OR 1.183, $P = 0.003$), and elevated baseline ALP (per 10 U/L: OR 1.041, $P < 0.001$) were all associated with an increased risk of recurrence. After adjustment in the multivariate model, all four variables retained their independent prognostic significance. The protective effect of TPTX+AT over SPTX remained robust (adjusted OR 0.294, 95% CI 0.147-0.586, $P < 0.001$). Concurrently, the risk of recurrence was independently driven by a higher baseline iPTH concentration (OR 1.239, $P < 0.001$), a more extensive dialysis history (OR 1.192, $P = 0.008$), and a greater preoperative ALP level (OR 1.039, $P = 0.001$). Patient factors including age, sex, the presence of diabetes mellitus, and the use of cinacalcet did not enter the final model. In conclusion, the type of surgical procedure stands as a critical modifiable determinant of long-term disease control, with TPTX+AT offering a distinct protective advantage against recurrence independent of disease severity markers.

Discussion

This study compared the long-term biochemical and clinical outcomes of TPTX+AT versus SPTX in maintenance hemodialysis patients with refractory SHPT. Over a 36-month follow-up, several important differences emerged between the two procedures, particularly in operative time, PTH trajectories, bone turnover marker evolution, and the trade-off between disease recurrence and permanent hypoparathyroidism. These findings help clarify the distinct therapeutic profiles of each surgical strategy.

The TPTX+AT procedure required a longer operative duration, a finding consistent with earlier reports by Zhu et al. [17]. This prolongation is understandable given the additional steps of bilateral cervical thymectomy and the meticulous preparation and intramuscular implantation of parathyroid tissue fragments [17, 22]. Despite the extended time in the operating room, the postoperative hospital stay and the incidence of early surgical complications such as RLN injury, cervical hematoma, and wound infection were similar between the groups. Thus, the greater technical complexity of TPTX+AT did not translate into a higher perioperative morbidity burden.

The most pronounced divergence was observed in the biochemical control of SHPT. Immediately after surgery, circulating iPTH levels

fell substantially in both groups, yet the degree of suppression was far more profound following TPTX+AT. This difference widened over the 36-month observation period, with iPTH concentrations in the SPTX cohort exhibiting a progressive rise that approached the threshold for disease recurrence, whereas levels in the TPTX+AT group remained stably controlled. The gradual rebound in the SPTX group is biologically plausible, as the remnant parathyroid tissue left in situ continues to be exposed to the uremic milieu's proliferative stimuli, including hyperphosphatemia, hypocalcemia, and deficient calcitriol, which drive hyperplasia and progressive PTH oversecretion [16, 23]. In contrast, TPTX+AT removes all cervical parathyroid tissue, relying on a small autograft whose limited mass is less prone to runaway growth [24, 25]. The early postoperative period was also characterized by a more pronounced decline in serum corrected calcium after TPTX+AT, a pattern that reflects so-called hungry bone syndrome as mineral is avidly deposited into bone following the abrupt drop in PTH [26, 27]. Notably, this calcium differential resolved by the sixth month, indicating that the transient accentuation of hypocalcemia is a manageable, self-limited phenomenon.

The musculoskeletal impact of the two operations was reflected by the behavior of ALP, a surrogate for high-turnover bone disease [28, 29]. ALP levels fell to a greater extent in the TPTX+AT group, and the separation between the two surgical arms persisted at every follow-up visit, mirroring the sustained PTH difference. This suggests that the more complete and durable biochemical control afforded by TPTX+AT is accompanied by a more thorough resolution of the osteomalacic and osteitic components of renal osteodystrophy. Meanwhile, 25-hydroxyvitamin D concentrations improved equally in both groups, likely as a result of consistent postoperative supplementation protocols, indicating that the differential bone biomarker response was not confounded by vitamin D availability.

The central clinical divergence lay in the recurrence of SHPT. The recurrence rate was substantially lower in the TPTX+AT group. This advantage was confirmed by multivariable analysis, where TPTX+AT emerged as an independent protective factor against recurrence, while higher preoperative iPTH, longer dialysis vintage, and elevated baseline ALP were identified as independent drivers of treatment failure. These risk factors likely denote a greater parathyroid cell mass and a more intense proliferative drive, conditions under which a cervical remnant is especially vulnerable to re-expansion [26, 30]. The lower recurrence rate after TPTX+AT is therefore consistent with the principle of eliminating all orthotopic parathyroid tissue, leaving only a forearm autograft that, if hyperfunctioning later, can be partially resected under local anesthesia without a repeat neck exploration [31].

However, this superior recurrence control comes at a price. Permanent hypoparathyroidism, defined by persistently low iPTH requiring ongoing calcium and calcitriol supplementation beyond one year, occurred exclusively in the TPTX+AT group. Although the absolute proportion of affected patients was modest, this complication represents a clinically relevant failure of the autograft to provide sufficient parathyroid function. The resulting long-term dependence on supplementation exposes patients to risks of adynamic bone disease, hypercalciuria, and vascular calcification if monitoring is inadequate. This trade-off is well documented in the surgical literature by Black et al. [14], and it reinforces the notion that neither technique is universally superior.

From a clinical value perspective, these results highlight that the choice of PTX procedure should be individualized. For patients with severely elevated preoperative iPTH, extensive dialysis vintage, and pronounced skeletal involvement, TPTX+AT offers a substantially lower risk of recurrence and a more definitive correction of high-turnover bone disease. At the same time, the potential for permanent hypoparathyroidism mandates a postoperative surveillance protocol that includes regular iPTH monitoring and cautious titration of calcium and vitamin D therapy. The ability to avoid neck reoperation by addressing forearm autograft recurrence further adds to the practical advantages of TPTX+AT in carefully selected individuals. Conversely, in patients for whom even a small risk of permanent hypoparathyroidism is deemed unacceptable, SPTX may remain a suitable option, albeit with the understanding that recurrence surveillance must be rigorous.

Several limitations of this study should be acknowledged. Its retrospective, single-center, non-randomized design introduces inherent selection bias, as the surgical approach was based on surgeon preference. The sample size, while moderate, provides limited statistical power for detecting differences in infrequent events such as permanent hypoparathyroidism or mortality, and the 36-month follow-up may not capture later recurrences from the SPTX remnant or the TPTX+AT autograft. Outcome definitions, including the iPTH threshold for recurrence, were based on adapted guidelines and may influence the comparative estimates. Future prospective, multicenter randomized trials with extended follow-up are needed to conclusively delineate the long-term balance between recurrence prevention, bone health, cardiovascular outcomes, and patient quality of life. Integrating serial bone biopsy data and cost-effectiveness analyses would further refine the evidence base guiding the surgical management of refractory SHPT.

Conclusion

In conclusion, in maintenance hemodialysis patients with medically refractory SHPT, TPTX+AT provides more durable biochemical control and a lower risk of recurrence than SPTX, but it introduces a modest risk of permanent hypoparathyroidism. The two procedures yield comparable mortality and cardiovascular event rates over 36 months. These findings underscore a central therapeutic trade-off between lower disease recurrence and the risk of permanent hypoparathyroidism, reinforcing the need for individualized surgical decision-making. Vigilant, lifelong surveillance remains essential regardless of the chosen technique. Prospective randomized studies are required to validate long-term benefits and to refine patient selection and postoperative management protocols.

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