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Research article

# Efficacy and safety of total parathyroidectomy with autotransplantation vs. subtotal parathyroidectomy for secondary hyperparathyroidism: A retrospective study

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ABSTRACT

*Background:* No consensus has been reached on the best surgical approach for secondary hyperparathyroidism (SHPT). We evaluated the short-term and long-term efficacy and safety of total parathyroidectomy with autotransplantation (TPTX + AT) and subtotal parathyroidectomy (SPTX).
*Methods:* We retrospectively analyzed the data of 140 patients undergoing TPTX + AT and 64 undergoing SPTX between 2010 and 2021 in Second Affiliated Hospital of Soochow University, and carried out follow-up. We compared the differences in symptoms, serological examinations, complications and mortality between the two methods, and explored the independent risk factors of secondary hyperparathyroidism recurrence.
*Results:* In short time after surgery, serum intact parathyroid hormone and calcium level was lower in TPTX + AT group than that in SPTX group (both $P < 0.05$). Severe hypocalcemia was more common in TPTX group ($P = 0.003$). The recurrent rate was 17.1% for TPTX + AT and 34.4% for SPTX ($P = 0.006$). There was no statistical difference in all-cause mortality, cardiovascular events, cardiovascular mortality between the two methods. Higher preoperative serum phosphorus level (HR: 1.929 95% CI 1.045–3.563, $P = 0.011$) and the SPTX surgical method (HR: 2.309, 95% CI 1.276–4.176, $P = 0.006$) were found to be independent risk factors for SHPT recurrence.
*Conclusions:* Compared with SPTX, TPTX + AT is more effective in reducing the recurrent risk of SHPT without increasing the risk of all-cause mortality and cardiovascular events.

## 1. Introduction

Secondary hyperparathyroidism (SHPT) is a common complication of chronic renal failure. It exists in almost all patients with end-stage renal disease (ESRD), mainly caused by the metabolic disorder of calcium, phosphorus and vitamin D [1]. The most obvious feature of SHPT is the elevated level of parathyroid hormone (PTH). Patients suffer from symptoms of bone and joint pain, pruritus, fatigue, insomnia, constipation [2,3]. Complications related to SHPT include pathological fractures and cardiovascular events, which could lead to mortality [4,5]. High levels of serum intact parathyroid hormone (iPTH), calcium and phosphorus are considered to be

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associated with an increased risk of mortality. All these can be improved by treating SHPT [6]. SHPT is mainly treated with pharmaceutical therapies and surgery. The pharmaceutical therapies contain Vitamin D therapy, calcimimetics and phosphorus binders. Patients who are unresponsive to drugs should consider parathyroidectomy (PTX) [1,7]. With the use of cinacalcet, some SHPT patients are able to control PTH at a low level. However, the rate of PTX has not therefore decline remarkably in recent years and parathyroidectomy is still an important treatment for SHPT [8]. About 38% of patients need PTX after 20 years' dialysis [9].

There are three main approaches of PTX, including subtotal parathyroidectomy (SPTX), total parathyroidectomy with autotransplantation (TPTX + AT) and total parathyroidectomy, of which the former two are the most common [10–12]. Three and a half parathyroid glands are resected in SPTX, while all parathyroid glands are resected and part of the tissue is taken for autologous transplantation in TPTX + AT [1,13]. Which technique is the best is still in controversy. SPTX is more common in Europe and the United States, while TPTX + AT is performed more frequently in Asian countries, which may be attributed to the difference of renal transplantation rate [1,14].

It is necessary to retain certain parathyroid function while controlling PTH level. The risk of permanent hypoparathyroidism after SPTX is relatively lower, while TPTX + AT has the advantage of avoiding another neck surgery caused by recurrent SHPT [15]. Due to the differences in sample size, follow-up time and measurement, previous studies on these two surgical techniques did not reach a consensus. The effects of postoperative PTH and calcium level on cardiovascular complications and mortality need to be further evaluated. It is still unclear whether continuous low postoperative PTH level is harmful to prognosis. These questions prompted our study. The aim of this study is therefore to compare the short-term and long-term efficacy and safety of SPTX and TPTX + AT for SHPT patients, and to evaluate the prognosis of patients undergoing these two surgical techniques, such as mortality and recurrence.

## 2. Materials and methods

### 2.1. Subjects

After the approval of the Review Board of the Second Affiliated Hospital of Soochow University (JD-HG-W5-6G), we collected the data of patients diagnosed as SHPT and undergoing parathyroidectomy from January 1, 2010 to January 31, 2021. The inclusion criteria included: ESRD patients treated with hemodialysis or peritoneal dialysis; diagnosed as SHPT by symptoms, serologic testing and imaging examination; operative approach was TPTX + AT or SPTX; all relative data were complete. We excluded those who had received renal transplantation before PTX. Before operation, all patients or their relatives signed informed consent forms to participate in the study.

### 2.2. Perioperative procedure

Indications for PTX included persistently elevated iPTH level >800 pg/ml for more than 6 months that pharmaceutical therapies became ineffective, or there were clinical symptoms [1,16,17]. All patients were examined with 99mTc-sestamibi radionuclide scan (Fig. 1A) and parathyroid ultrasound (Fig. 1B). Serum iPTH, calcium and phosphorus were routinely measured before operation and in the morning of the first day after operation. In TPTX + AT, all parathyroid glands were removed (Fig. 2A and B), and part of one approximately normal parathyroid was sliced into pieces at size of 1 $mm^3$, then 12–20 pieces were evenly transplanted in brachioradialis muscle in which side dialysis fistula was not located. Or parathyroid tissue can be directly made into homogenate, mixed with 1 mL normal saline and injected into deltoid muscle through syringe. In SPTX, we retained about 50 mg of the smallest parathyroid gland along with its blood supply, with all the remaining glands removed. Selections of operation methods depended on the size of the smallest parathyroid gland. Patients were not suitable for taking SPTX if all of their parathyroid glands were found to exist obvious hyperplasia before or during operation. Also, if enough blood supply of the reserved parathyroid gland could not be guaranteed in SPTX, we would switch to perform TPTX + AT. Patients' potential needs for renal transplantation were also considered. Thymectomy was performed routinely in both groups. Routine neck ultrasonography usually helps find additional thyroid lesions accidently. For SHPT patients with concomitant thyroid cancer or thyroid nodules that were suspicious of malignancy (if they refused fine needle aspiration), we would perform thyroidectomy and parathyroidectomy together, taking the complexity of reoperation on neck into

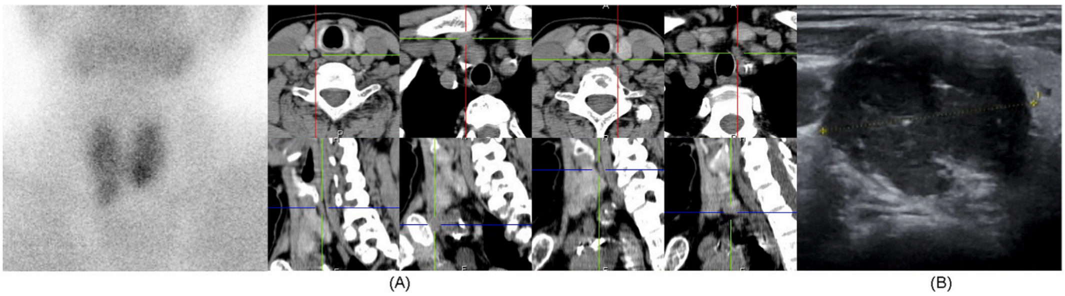


**Fig. 1.** Typical imaging appearances of SHPT. (A) Four hyperfunctional parathyroid glands (the center of the cross) found by radionuclide imaging. (B) A huge parathyroid gland with a maximum diameter of about 4 cm found by ultrasound.

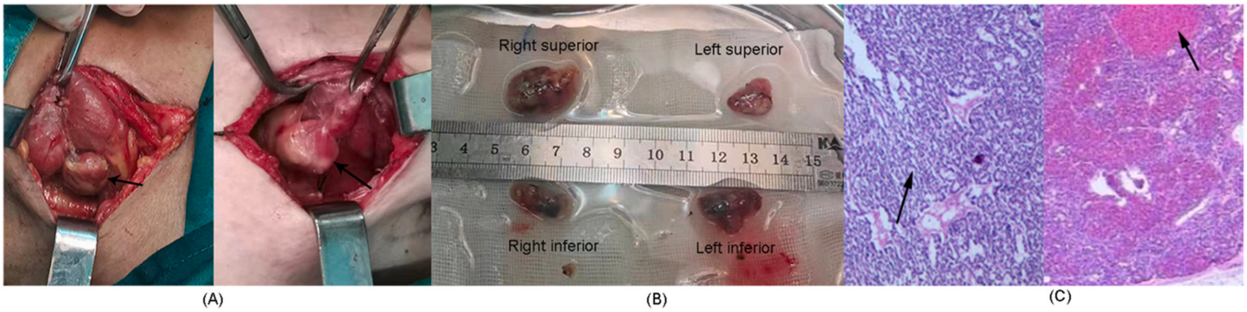


**Fig. 2.** Intraoperative findings and typical pathological appearances of SHPT. (A) Hyperplastic parathyroid glands found behind the thyroid (indicated by arrows). (B) Four completely resected parathyroid glands which were preserved in ice normal saline. (C) Microscopic appearances of parathyroid hyperplasia (left) and parathyroid adenoma (right). Typical areas are highlighted with arrows.

consideration. This would not affect the selection of surgical techniques of parathyroidectomy. Thyroid lobectomy or total thyroidectomy were performed based on the stage of thyroid lesions. Whether to perform prophylactic cervical neck dissection was determined by the results of perioperative imaging examination. Lateral lymph node dissection was not performed because no abnormal lymph node was found in any patient. Intraoperative iPTH monitoring and frozen section biopsy was performed in each patient. Intraoperative iPTH level was measured 10 min after resecting the last parathyroid gland. If there was a >75% drop compared with the preoperative level, we considered it a successful operation and would not carry out further exploration for the possible residual parathyroid glands for safety concern. This cut-off value is currently is currently inconclusive and is based on our experience. Intraoperative iPTH level was related to operation time. It took more time to resect parathyroid glands in complex cases, and the iPTH level would drop more significantly because of its short half-life period.

All patients were treated with large doses of oral calcium, calcitriol, and intravenous calcium gluconate to prevent severe hypocalcemia. Serum calcium and phosphorus levels were monitored every 6 h within 24 h after surgery. Postoperative serum iPTH and calcium levels were affected by calcium supplementation therapy. However, we used a unified standard for treatment and adjusted the dose of calcium supplementation in time according to calcium level. When serum calcium rose to >1.9 mmol/L and with no symptoms of hypocalcemia like numbness and limb cramp, intravenous calcium was stopped to given. Patients on hemodialysis underwent dialysis on the day before and after surgery, while those on peritoneal dialysis continued to dialysis on the night of the operation day. Postoperative complications, such as cervical hematoma, recurrent laryngeal nerve injury and infection, were recorded. Severe hypocalcemia was defined as serum calcium <1.6 mmol/L in any examination postoperatively. The identification of recurrent laryngeal nerve injury was initially based on the change of patient's voice. If hoarseness occurred, further direct laryngoscopy would be performed to check the motion of vocal cords. Patients were discharged after the serum calcium reached a stable level.

### *2.3. Follow-up*

We collected the pathological results (Fig. 2C) of each patient, including the parathyroid glands and thyroid glands that were removed. After discharge, patients were asked to recheck regularly in outpatient department. We looked up the relevant medical records up to January 2022. Patients treated in other institutions were asked them to provide relevant medical documents in order to minimize subjectivity and recall bias caused by self-report. Short follow-up of symptom resolution was carried out at about 1 month after operation. Numeric rating scale (NRS) was used to assess bone and joint pain before and after operation. Patients rated their pain on a scale from 0 to 10, with higher scores meaning more severe pain [18]. We also asked patients to use 'completely improved', 'partly improved' or 'barely changed' to describe the degree of pruritus and fatigue relief. In long-term follow-up, we recorded all-cause mortality, SHPT recurrence, reoperation, adverse cardiovascular events, and other complications such as fracture and permanent hypoparathyroidism. Renal transplantation was also recorded. We defined persistent SHPT as iPTH >300 pg/ml immediately after operation, and recurrent SHPT as iPTH >300 pg/ml at 6 months or more after surgery. It should be noted that the definitions of persistent and recurrent disease vary between literatures [11,13,16,17,19,20].

### *2.4. Statistical analysis*

SPSS 23.0 and GraphPad Prism 8 were used for statistical analysis. Continuous variables are shown with means and standard deviations if they approximately conform to normal distribution, otherwise they are displayed by medians and interquartile ranges. Categorical variables are presented in numbers and percentages. Independent samples *t*-test, chi-square test, Fisher's exact test and Wilcoxon signed rank test were used to compare differences between the two groups depending on the type of variables when appropriate. Kaplan-Meier curve was utilized to show the incidence of all-cause death, recurrent SHPT, recurrent PTX and cardiovascular events, and the differences between two groups were analyzed by stratified log-rank test. Independent risk factors for recurrent SHPT were evaluated by univariate and multivariate Cox proportional hazards regression model with forward LR model. P value was calculated by Wald test. In all analyses, $P < 0.05$ was considered statistically significant.

## 3. Results

### 3.1. Baseline characteristics of the SPTX and TPTX + AT groups

A total of 204 patients met the inclusion criteria, including 140 in TPTX + AT group and 64 in SPTX group. There was no statistical difference in gender, age, preoperative serum iPTH, calcium and phosphorus level, common symptoms (including bone and joint pain, pruritus and obvious fatigue) and combined chronic diseases (including hypertension, diabetes, coronary heart disease and stroke) between the SPTX and TPTX + AT groups (all $P > 0.05$). Mean follow-up time was 55.3 ± 24.7 months for TPTX + AT group and 60.8 ± 24.4 months for SPTX group ($P = 0.138$) (Table 1).

### 3.2. Surgical outcomes of the SPTX and TPTX + AT groups

The number of parathyroid glands identified in operation between the two groups was similar (TPTX + AT: 3.90 ± 0.39, SPTX: 3.91 ± 0.34, $P = 0.912$). The operation time in TPTX + AT group (128.6 ± 37.1 min) was statistically longer than SPTX group (115.6 ± 31.1 min) ($P = 0.010$). There was no statistical difference in the rate of thyroidectomy (TPTX + AT: 3.6%, SPTX: 6.3%) and central neck dissection (TPTX + AT: 3.6%, SPTX: 4.7%) (both $P > 0.05$). The most common pathological result was parathyroid hyperplasia, and none of the cases was diagnosed as parathyroid carcinoma. There were also 5 and 3 patients diagnosed as papillary thyroid carcinoma in TPTX + AT group and SPTX group, respectively.

### 3.3. Short-term efficacy and complications of the SPTX and TPTX + AT groups

On postoperative day (POD) 1, serum iPTH, calcium and phosphorus levels of patients decreased significantly compared with those before operation (all $P < 0.05$). The iPTH level was 9.5 (5.0–21.8) pg/mL in TPTX + AT group and 19.8 (5.9–74.8) pg/mL in SPTX group ($P = 0.007$). The POD1 serum calcium level is statistically lower in TPTX + AT group (1.71 ± 0.26 mmol/L) than that in SPTX group (1.91 ± 0.26 mmol/L) ($P < 0.001$). After calcium supplement therapy, serum calcium level in most patients rose to within a safe range. The POD7 calcium level was 1.87 ± 0.26 mmol/L in TPTX + AT group, also statistically lower than 1.97 ± 0.29 mmol/L in SPTX group ($P = 0.018$). Persistent SHPT occurred in 2 patients in TPTX + AT group (1.4%) and 2 patients in SPTX group (3.1%) ($P = 0.363$). There was more severe hypocalcemia in TPTX + AT group (50/140, 35.7%) than in SPTX group (10/64, 15.6%) ($P = 0.003$). Cervical hematoma, wound infection and recurrent laryngeal nerve injury were rare, and there was no statistical difference between the two groups (all $P > 0.05$). The length of stay was 10.91 ± 2.68 days for TPTX + AT group and 9.66 ± 2.50 days for SPTX group, with no statistical difference ($P = 0.396$) (Table 2). No patient died in postoperative inpatient period. One patient who underwent TPTX + AT had blockage of lower limb dialysis fistula, resulting in local and systemic infection. In short-term follow-up carried out at about one month after operation, most patients reported improvement in common symptoms. Postoperative NRS pain score (TPTX + AT: 1.32 ± 1.78, SPTX: 1.48 ± 2.11) decreased markedly when compared with preoperative level (TPTX + AT: 2.19 ± 1.90, SPTX: 2.47 ± 1.80) (Table 3).

### 3.4. Long-term follow-up and outcomes of the SPTX and TPTX + AT groups

There was no statistical difference in all-cause mortality between TPTX + AT (13/140, 9.3%) and SPTX (8/64, 12.5%) group ($P = 0.483$). The causes of mortality included heart failure, electrolyte disorder, intracerebral hemorrhage, malignant tumor, myocardial

**Table 1**
Some baseline characteristics of patients undergoing parathyroidectomy.

| | TPTX + AT (n = 140) | SPTX (n = 64) | P value |
|---|---|---|---|
| Female sex, n (%) | 66 (47.1) | 34 (53.1) | 0.428 |
| Age, y, Mean (SD) | 50.3 (11.9) | 49.0 (10.4) | 0.196 |
| NRS pain score | 2.19 (1.90) | 2.47 (1.80) | 0.328 |
| Pruritus, n (%) | 102 (72.9) | 47 (73.4) | 0.931 |
| Fatigue, n (%) | 80 (57.1) | 39 (60.9) | 0.610 |
| Hypertension, n (%) | 107 (76.4) | 55 (85.9) | 0.119 |
| Diabetes, n (%) | 14 (10.0) | 7 (10.9) | 0.838 |
| Coronary heart disease, n (%) | 10 (7.1) | 5 (7.8) | 1.000 |
| Stroke, n (%) | 6 (4.3) | 1 (1.6) | 0.564 |
| iPTH, pg/mL, Median (IQR) | 1604 (1273–2176) | 1713 (1064–2471) | 0.535 |
| Serum calcium, mmol/L, Mean (SD) | 2.55 (0.20) | 2.52 (0.27) | 0.289 |
| Serum phosphorus, mmol/L, Mean (SD) | 2.33 (0.48) | 2.25 (0.49) | 0.241 |
| ALP, U/L, Median (IQR) | 265 (143–408) | 298 (132–688) | 0.028 |
| Number of parathyroid glands found by ultrasound, Mean (SD) | 3.10 (0.94) | 3.14 (0.96) | 0.776 |
| Number of hyperfunctional parathyroid glands found by MIBI, Mean (SD) | 3.21 (1.03) | 2.81 (1.10) | 0.012 |
| Follow-up time, m, Mean (SD) | 55.3 (24.7) | 60.8 (24.4) | 0.138 |

TPTX + AT: total parathyroidectomy with autotransplantation; SPTX: subtotal parathyroidectomy; MIBI: $^{99m}$Tc-sestamibi radionuclide scan; SD: standard deviation; IQR: interquartile range; NRS: numeric rating scale; iPTH: intact parathyroid hormone; ALP: alkaline phosphatase.

**Table 2**
Perioperative outcomes of patients undergoing parathyroidectomy.

| | TPTX + AT (n = 140) | SPTX (n = 64) | P value |
|---|---|---|---|
| Operation time, min, Mean (SD) | 128.6 (37.1) | 115.6 (31.1) | 0.010 |
| Number of parathyroid glands found in operation, Mean (SD) | 3.90 (0.39) | 3.91 (0.34) | 0.912 |
| Thyroidectomy performed, n (%) | 5 (3.6) | 4 (6.3) | 0.619 |
| Central neck dissection performed, n (%) | 5 (3.6) | 3 (4.7) | 1.000 |
| Pathological result, n (%) | | | 0.790 |
| Parathyroid hyperplasia | 138 (98.6) | 62 (96.9) | |
| Parathyroid adenoma | 2 (1.4) | 2 (3.1) | |
| POD1 iPTH, pg/mL, Median (IQR) | 9.5 (5.0–21.8) | 19.8 (5.9–74.8) | 0.007 |
| POD1 calcium, mmol/L, Mean (SD) | 1.71 (0.26) | 1.91 (0.26) | <0.001 |
| POD1 phosphorus, mmol/L, Mean (SD) | 1.83 (0.54) | 1.92 (0.57) | 0.301 |
| POD7 calcium, mmol/L, Mean (SD) | 1.87 (0.26) | 1.97 (0.29) | 0.018 |
| POD7 phosphorus, mmol/L, Mean (SD) | 1.17 (0.33) | 1.18 (0.43) | 0.801 |
| Persistent SHPT, n (%) | 2 (1.4) | 2 (3.1) | 0.363 |
| Severe hypocalcemia, n (%) | 50 (35.7) | 10 (15.6) | 0.003 |
| Cervical hematoma, n (%) | 2 (1.4) | 1 (1.6) | 1.000 |
| Recurrent laryngeal nerve injury, n (%) | 1 (0.7) | 1 (1.6) | 0.530 |
| Wound infection, n (%) | 0 (0) | 0 (0) | 1.000 |
| Length of stay, d, Mean (SD) | 10.91 (2.68) | 9.66 (2.50) | 0.396 |

PTX: parathyroidectomy; TPTX + AT: total parathyroidectomy with autotransplantation; SPTX: subtotal parathyroidectomy; IQR:interquartile range; iPTH: intact parathyroid hormone; POD: postoperative day; SHPT: secondary hyperparathyroidism.

**Table 3**
Changes of common symptoms at one month after operation.

| Symptoms | Group | Preoperative | Postoperative | | |
|---|---|---|---|---|---|
| | | | Completely improved | Partly improved | Barely changed |
| Pruritus | TPTX + AT | 102 (72.9%) | 62 (60.8%) | 18 (17.6%) | 22 (21.6%) |
| | SPTX | 47 (73.4%) | 21 (44.7%) | 14 (29.8%) | 12 (25.5%) |
| Fatigue | TPTX + AT | 80 (57.1%) | 30 (37.5%) | 29 (36.3%) | 21 (26.2%) |
| | SPTX | 39 (60.9%) | 16 (41.0%) | 13 (33.3%) | 10 (25.7%) |
| NRS pain score | TPTX + AT | 2.19 ± 1.90 | 1.32 ± 1.78 | | |
| | SPTX | 2.47 ± 1.80 | 1.48 ± 2.11 | | |

TPTX + AT: total parathyroidectomy with autotransplantation; SPTX: subtotal parathyroidectomy.

infarction, infection and accident. The proportion of recurrent SHPT was higher in SPTX group (22/64, 34.4%) than in TPTX + AT group (24/140, 17.1%) ($P = 0.006$). Meanwhile, after SHPT recurrence, more patient chose recurrent PTX in TPTX + AT group (12/24, 50%) than in SPTX group (3/22, 13.6%) ($P = 0.009$). Recurrent PTX after TPTX + AT was to remove the autologous gland under local anesthesia, while a neck operation under general anesthesia was required after SPTX. Permanent hypoparathyroidism occurred only in TPTX + AT group (8/140, 5.7%). No statistical difference was found in cardiovascular events and fracture between the two groups (both $P > 0.05$). Renal transplantation was rare in both groups (Table 4). Kaplan-Meier curves for all-cause mortality (Fig. 3A), recurrent SHPT (Fig. 3B), recurrent PTX (in recurrent SHPT) (Fig. 3C) and cardiovascular events (Fig. 3D) are shown. Log-rank test indicated recurrent SHPT was statistically more common in SPTX group than in TPTX + AT group ($P = 0.016$). Recurrent PTX was more commonly performed after TPTX + AT than SPTX ($P = 0.029$). The risk for all-cause mortality and cardiovascular events were similar ($P = 0.091$ and 0.955, respectively). The occurrence rate of main outcomes in defined postoperative time is displayed in Table S1. We found that the 2-year, 3-year and 5-year recurrence rate of SPTX was higher compared with TPTX + AT (all $P < 0.05$).

**Table 4**
Long-term outcomes of patients undergoing parathyroidectomy.

| | TPTX + AT (n = 140) | SPTX (n = 64) | P value |
|---|---|---|---|
| All-cause mortality | 13 (9.3%) | 8 (12.5%) | 0.483 |
| Recurrent SHPT | 24 (17.1%) | 22 (34.4%) | 0.006 |
| Recurrent PTX (in recurrent SHPT) | 12 (50.0%) | 3 (13.6%) | 0.009 |
| Cardiovascular events | 13 (9.3%) | 7 (10.9%) | 0.713 |
| Cardiovascular mortality | 7 (5.0%) | 4 (6.3%) | 0.974 |
| Fracture | 2 (1.4%) | 3 (4.7%) | 0.363 |
| Permanent hypoparathyroidism | 8 (5.7%) | 0 (0) | 0.118 |
| Renal transplantation | 2 (1.4%) | 1 (1.6%) | 1.000 |

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

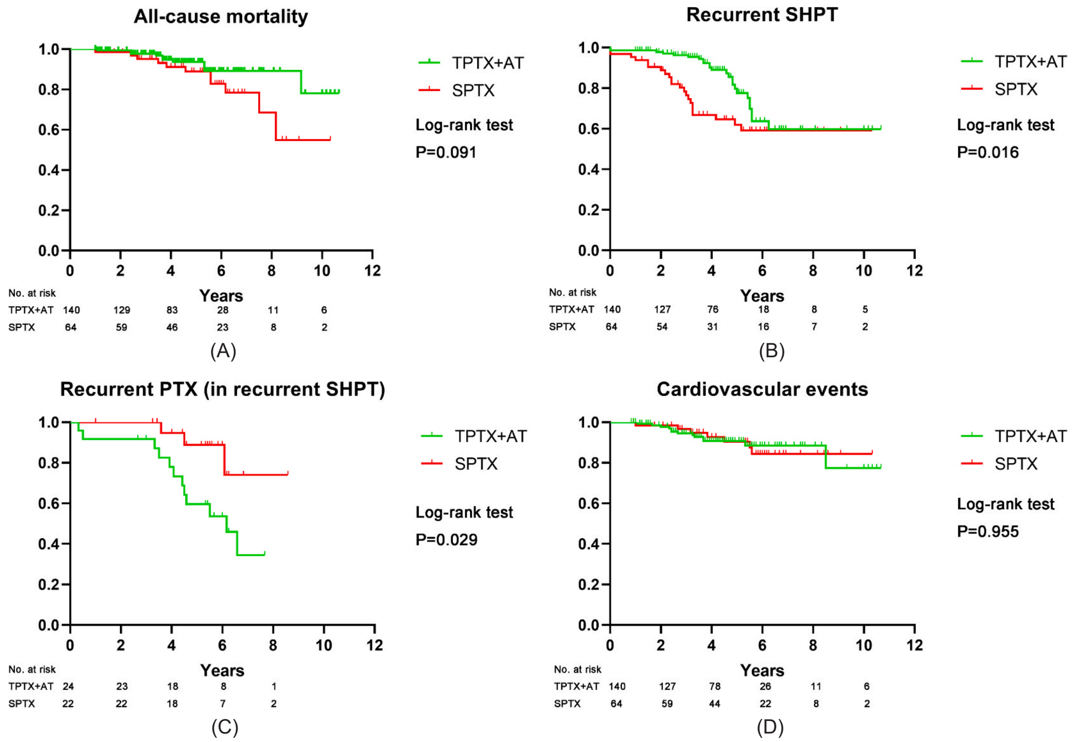


**Fig. 3.** Kaplan-Meier curves of patients undergoing parathyroidectomy. (A) All-cause mortality. (B) Recurrent SHPT. (C) Recurrent PTX (in recurrent SHPT). (D) Cardiovascular events.

### 3.5. *Independent risk factors for SHPT recurrence*

Univariate and multivariate Cox regression analysis with forward LR model was used to identify the independent risk factors for SHPT recurrence (Table 5). In univariate analysis, age at operation, preoperative serum phosphorus and surgical method were considered to be associated with SHPT recurrence (all $P < 0.05$). After multivariate analysis, higher preoperative serum phosphorus level (HR: 1.929 95% CI 1.045–3.563, $P = 0.011$) and the SPTX surgical method (HR: 2.309, 95%CI 1.276–4.176, $P = 0.006$) were found to be independent risk factors for SHPT recurrence.

## 4. Discussion

In this retrospective study of 204 SHPT patients undergoing parathyroidectomy, we compared the two surgical methods from both short-term and long-term perspectives. The average follow-up period is nearly 5 years. We found that TPTX + AT was more effective in

**Table 5**
Cox regression analysis for SHPT recurrence.

| Covariates | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | HR (95% CI) | P value | HR (95% CI) | P value |
| Sex (male vs. female) | 1.213 (0.677–2.174) | 0.516 | | |
| Age at operation | 0.969 (0.945–0.995) | 0.018 | | |
| Hypertension (yes vs. no) | 0.810 (0.400–1.641) | 0.559 | | |
| Diabetes (yes vs. no) | 0.272 (0.037–1.979) | 0.198 | | |
| Coronary heart disease (yes vs. no) | 0.385 (0.053–2.808) | 0.346 | | |
| Preoperative iPTH, pg/mL | 1.000 (1.000–1.000) | 0.676 | | |
| Preoperative serum calcium, mmol/L | 1.098 (0.295–4.082) | 0.889 | | |
| Preoperative serum phosphorus, mmol/L | 1.929 (1.045–3.563) | 0.036 | 2.227 (1.204–4.122) | 0.011 |
| Preoperative ALP, U/L | 1.000 (0.999–1.000) | 0.247 | | |
| Surgical method (SPTX vs. TPTX + AT) | 2.010 (1.122–3.600) | 0.019 | 2.309 (1.276–4.176) | 0.006 |
| Number of parathyroid glands identified | 1.078 (0.518–2.245) | 0.841 | | |
| Pathological result (adenoma vs. hyperplasia) | 0.528 (0.072–3.864) | 0.530 | | |

CI: confidence interval; TPTX + AT: total parathyroidectomy with autotransplantation; SPTX: subtotal parathyroidectomy; iPTH: intact parathyroid hormone; ALP: alkaline phosphatase.

reducing SHPT recurrence than SPTX. The risk of all-cause mortality and cardiovascular events had no statistical difference between the two surgical methods.

TPTX + AT and SPTX are the two most common surgical techniques for SHPT, which can substantially improve patients' symptoms and reduce mortality [19]. Our results showed that these two surgical approaches are both beneficial to SHPT patients. The level of serum iPTH, calcium and phosphorus decreased markedly. Common symptoms of most patients could also be completely or partially improved after operation. However, PTX is not without risk [1]. Severe hypocalcemia was the most frequently happened postoperative complication. Within a few days after surgery, the serum calcium level was statistically lower in patients undergoing TPTX + AT compared with SPTX. It usually caused numbness and sometimes cramp. Owing to the active postoperative interventions, no serious adverse event happened. In long-term follow-up, we found permanent hypoparathyroidism occurred only in patients undergoing TPTX + AT. Most of them were asymptomatic. The KDIGO guideline also agrees that mild and asymptomatic hypocalcemia to be harmless [21].

The selection of surgical methods partly reflects the goal of PTH control. The KDOQI guideline recommends to control post-operative iPTH level at 150–300 pg/ml, which is most beneficial to survival [19]. Hirotaka komaba et al. in Japan found that patients in the low-level group of postoperative iPTH (median 19 pg/ml) had the greatest survival advantage [22]. Elin Isaksson et al. in Sweden concluded that SPTX had a lower risk of cardiovascular events when compared with TPTX (whether or not combined with AT was not distinguished) and suspected that cardiovascular events were associated with the excessively low levels of iPTH after TPTX [23]. These different results illustrate the complexity of SHPT patients and also indicate that patients with low-level PTH after operation could get potential survival benefit through good management. Our study has strengthened this point. Considering the very low rate of renal transplantation after PTX in our cohort, we consider it appropriate to choose TPTX + AT to control PTH at a relatively low level to prevent SHPT recurrence. In addition, end-stage renal disease could induce cardiovascular diseases by multiple mechanisms [24]. The incidence of cardiovascular event and cardiovascular mortality had no statistical difference between the two surgical methods in this study.

The surgeon factor is also related to the decisions of surgical methods, which can also affects the surgical results. In this study, both surgical approaches were performed by experienced surgeons that had been engaged in our department for at least 10 years. They were able to perform both approaches skillfully and complied with standard techniques.

The proportion of recurrent PTX was higher in patients undergoing TPTX + AT than SPTX, which was closely correlated with the approach of reoperation. In our study, the autogenous implanting site of parathyroid glands in TPTX + AT enabled recurrent PTX to be carried out under local anesthesia. In patients undergoing SPTX, the degradation of basic conditions led by end-stage renal disease may make them unable to tolerate the reoperation under general anesthesia a few years after the original operation. Patients' acceptability of the two forms of reoperation also led to this difference.

Parathyroidectomy is applicable to most SHPT patients, but there are exceptions. Both surgical approaches have contraindications like bad physical condition and severe electrolyte disturbances. Beyond that, there are no more special contraindications for TPTX + AT. However, as to SPTX, it is necessary to ensure that the reserved parathyroid gland in situ is nearly normal, otherwise it will increase the recurrent risk. Also, the blood supply of the reserved parathyroid gland must be maintained to prevent necrosis.

In recent years, more scholars have recommended TPTX alone for patients who have no hope of renal transplantation, and confirmed its safety and effectiveness, while TPTX + AT is still more recommended [12,19,25]. Out of concern about the complications of TPTX alone, our center has not widely carried out this approach. Brachioradialis muscle is the most commonly used location for autotransplantation worldwide. In the past two decades, various autotransplantation techniques have been described. Parathyroid tissue can be transplanted into sternocleidomastoid muscle, subcutaneous abdominal adipose tissue, brachioradialis muscle, deltoid muscle and anterior tibial muscle, etc [26–30]. In our study, there were two techniques to autotransplant parathyroid tissue, namely implantation into brachioradialis muscle and intramuscular injection into deltoid muscle. We did not distinguish these two techniques because we believe that this would not have a significant impact on the operation time (generally less than 5 min) and patients' prognosis.

There are some limitations in our study. One is that this is a retrospective study and lacks randomization. Another is that, due to the defect of medical records, we could not compare the changes of pharmaceutical supplementation for SHPT before and after operation. The treatment of SHPT is lifelong, while most of the previous studies on these two surgical techniques focused on short-term outcomes and did not have a long follow-up period that over 1 year. Therefore future studies are needed to evaluate the long-term outcomes of the two surgical techniques through longer follow-up.

## 5. Conclusion

Compared with STPX, TPTX + AT is more effective in reducing the recurrent risk of SHPT. The occurrence of severe hypocalcemia is higher in TPTX + AT, while the risk of all-cause mortality and cardiovascular events were similar in both surgical methods.

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## Author contribution statement

Jiaqi Zhu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Yan Wu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Ting Huang: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Guoqin Jiang; Zhixue Yang: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

## Data availability statement

Data will be made available on request.

## Declaration of interest's statement

The authors declare no conflict of interest.

## Declaration of competing interest

The authors declare that they have no competing interests.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15752.

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