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. 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 259 patients undergoing TPTX+AT or SPTX between 2010 and 2021 in the Second Affiliated Hospital of Soochow University, and carried out follow-up. We compared the differences in symptoms, serological examinations, complications and mortalities between the two groups, and explored the risk factors of poor prognosis, death and recurrence.

Results: Of the 259 patients, 208 underwent TPTX+AT and 51 underwent SPTX. The postoperative day 1 serum intact PTH level was higher in TPTX+AT group than that in SPTX group ($P=.023$). The risk of all-cause mortality in TPTX+AT group was lower ($P=.018$), and recurrent PTX was more common in TPTX+AT group ($P=.011$). The risk of recurrence was similar. There was no significant difference in the incidence of most complications including hematoma, recurrent laryngeal nerve injury, wound infection, adverse cardiovascular outcomes, fracture and permanent hypoparathyroidism between two groups. Results from Cox regression showed the SPTX operation approach (HR 3.53, $P=0.021$) and older age (HR 1.06, $P=0.035$) were risk factors of all-cause mortality.

Conclusion: Due to the lower risk of death after TPTX+AT and the low renal transplantation rate, we prefer TPTX+AT to treat most Chinese population with secondary hyperparathyroidism.

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]. In more severe cases, pathological fractures, cardiovascular complications and death may occur [4, 5]. In addition, high levels of serum intact parathyroid hormone (iPTH), calcium and phosphorus are considered to be associated with an increased risk of death. All these can be improved by treating SHPT [6]. SHPT is mainly treated with pharmaceutical therapies and surgery, and microwave ablation also has a certain effect [7, 8]. The pharmaceutical therapies contain Vitamin D therapy, calcimimetics and phosphorus binders. Those who are unresponsive to drugs should consider parathyroidectomy (PTX) [1, 9]. With the use of cinacalcet and paricalcitol, more patients are able to control PTH levels. However, the rate of PTX did not therefore show a long-term decline accompanied with these therapeutic progress and parathyroidectomy is still an important treatment for SHPT [10]. About 38% of patients need PTX after 20 years' dialysis [11].

There are three main approaches of PTX, namely subtotal parathyroidectomy (SPTX), total parathyroidectomy with autotransplantation (TPTX + AT) and total parathyroidectomy (TPTX), of which

the former two are the most common [12–14]. Some scholars have also proposed other methods that are more conservative or more radical than these three traditional ones, depending on the goal of PTH control [15, 16]. Which way is the best is still in controversy [17, 18]. SPTX is more common in Europe and the United States, while TPTX + AT is conducted more frequently in Asian countries, which may be attributed to the difference of renal transplantation rate [1, 19].

A meta-analysis published in 2019 concluded that there is no significant difference in recurrence rate, complication rate and mortality between TPTX + AT and SPTX [18]. Polina V Zmijewski et al [20] found that TPTX + AT has the advantage of lower recurrence rate when compared with SPTX, but the incidence of long-term hypocalcemia was higher. The risk of permanent hypoparathyroidism after SPTX is relatively lower, while TPTX + AT has the advantage of avoiding another neck surgery [18]. Due to the differences in sample size, follow-up time and measurement, previous studies on these two surgical methods did not reach a consensus. The effects of postoperative level of PTH and calcium on cardiovascular complications and mortality need to be further evaluated. The aim of our study is therefore to compare the efficacy and safety of SPTX and TPTX + AT in short and long time from multiple perspectives.

Methods

Subjects

After the approval of the Review Board of the Second Affiliated Hospital of Soochow University, 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 on hemodialysis or peritoneal dialysis; diagnosed as SHPT by symptoms, signs, and serologic and imaging examination; operative approach was TPTX+AT or SPTX; all relating data were complete. We excluded those who had received renal transplantation before PTX. Finally, a total of 259 patients were included in this study. Before operation, all patients or their relatives signed informed consent forms to participate in the study. All procedures were in accordance with the relevant guidelines and regulations.

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 significant symptoms [1, 20, 21]. All patients were examined with parathyroid ultrasound and ^{99m}Tc-sestamibi radionuclide scan (Fig. 1). Serum iPTH, calcium and phosphorus were routinely evaluated before operation and in the early morning of the first day after operation. In TPTX+AT, all parathyroid glands were removed, and part of one approximately normal parathyroid was sliced into pieces at size of 1mm³, 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 and injected into deltoid muscle through syringe (Fig. 2). In SPTX, we retained about 50mg of the smallest parathyroid gland with all the remaining glands removed. Routine neck ultrasonography usually helps find thyroid lesions accidentally. Taking the complexity of reoperation

on neck into consideration, we aggressively performed unilateral or bilateral thyroidectomy for those who are at great risk of thyroid cancer, with lymph node dissection carried out when necessary.

After handling all parathyroid glands, intraoperative iPTH level and frozen pathological examination were used in most patients in order to improve the success rate of the operation. If the level of intraoperative iPTH failed to drop below 50% of the preoperative level, we would search for the residual parathyroid gland, then examine iPTH again.

All patients were treated with large doses of oral calcium, vitamin D3 or calcitriol, and intravenous calcium gluconate to prevent severe hypocalcemia, which was defined as serum calcium less than 1.6 mmol/L in any examination postoperatively. Serum calcium and phosphorus level were monitored every 6 hours within 24 hours after surgery. The frequency of monitoring and the dose of calcium supplement were adjusted according to the calcium level. When serum calcium rose to >1.9 mmol/L, 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 patients on peritoneal dialysis continued to dialysis on the night of surgery. Changes of patients' symptoms were evaluated within 7 days after operation. Perioperative complications, such as cervical hematoma, recurrent laryngeal nerve injury and infection, were recorded. Most patients were discharged after cervical drainage tube was removed and serum calcium reached a stable level. A few patients left hospital before that and immediately went to their dialysis center for further treatment.

Follow-up

All patients enrolled in the study were given a phone call for follow-up, which was conducted by the same doctor. The follow-up was accomplished with the assistance of patients and/or their close relatives who had a full comprehension of their own condition. We collected data of all-cause mortality, recurrence, reoperation, adverse cardiovascular outcomes, and the corresponding time. We also recorded other complications such as fracture and permanent hypoparathyroidism, the relapse of common symptoms, and indicators which can reflect the economic burden of patients, including long-term pharmaceutical therapies and renal transplantation. Since some patients' dialysis center were not in our hospital, results of their postoperative serological examination cannot be directly obtained. For those who lack objective data, we got the missing data from the call. In our study, adverse cardiovascular outcomes were defined as angina pectoris, myocardial infarction, stroke, aneurysm rupture, and limb ischemia. We defined persistent SHPT as elevated iPTH >300pg/ml in any monitoring within 7 days after operation, and recurrent SHPT as iPTH increased >300pg/ml again during follow-up after a successful decrease postoperatively. It should be noted that the definitions of persistent and recurrent disease vary between literatures [13, 20-24].

Statistical analysis

SPSS 23.0 and GraphPad Prism 5.01 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. Binary logistic regression analysis was used to look for risk factors for persistent SHPT. Kaplan-Meier method was utilized to show the incidence of all-cause death, recurrent SHPT, recurrent PTX (re-PTX) and adverse cardiovascular outcomes, and the differences between two groups were analyzed by stratified log-rank test. Risk factors for all-cause mortality and recurrent SHPT were evaluated by Cox-proportional hazard regression model. Covariates included gender, age, combined chronic diseases including hypertension, diabetes and coronary heart disease (others were not included because of the low quantity), level of preoperative serological examination, surgical method, number of parathyroid glands identified in operation and pathological results. P value was calculated by Wald test. Univariate Cox regression analysis was carried out for each covariate, then those with $P < .05$ were further enrolled into the multivariate analysis to determine the final risk factors. In all analyses, $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics of the SPTX and TPTX+AT groups

There was no statistical difference in gender, age, serum calcium and phosphorus level, common symptoms (orthopedic pain, pruritus, obvious fatigue) and combined chronic diseases (hypertension, diabetes, coronary heart disease, stroke) between the SPTX and TPTX+AT groups (all $P > .05$). Preoperative serum iPTH and ALP level was higher in SPTX group than that in TPTX+AT group ($P < .05$). Due to the change of the preference of our medical team, no patient underwent SPTX in this study ($P < .05$) (Table 1).

Table 1

Some baseline characteristics of patients undergoing parathyroidectomy

	TPTX+AT(n=208)	SPTX(n=51)	P value
Female sex	96 (46.2)	28 (54.9)	0.262
Age, y	50.3 (11.9)	49.0 (10.4)	0.479
Number of parathyroid glands found by ultrasound	3.04 (0.94)	3.43 (0.70)	0.006
Number of hyperfunctional parathyroid glands found by MIBI	3.14 (1.03)	2.67 (1.09)	0.004
Orthopedic pain			0.114
Severe	55 (26.4)	18 (35.3)	
Light	78 (37.5)	20 (39.2)	
Pruritus	148 (71.2)	34 (66.7)	0.530
Obvious fatigue	35 (16.8)	7 (13.7)	0.590
Hypertension	159 (76.4)	41 (80.4)	0.530
Diabetes	20 (9.6)	5 (9.8)	0.967
Coronary heart disease	14 (6.7)	2 (3.9)	0.673
Stroke	7 (3.4)	0 (0)	0.397
iPTH, pg/mL	1577.4 (1152.9-2177.8)	1835.5 (1275.4-2621.0)	0.023
Serum calcium, mmol/L	2.53 (0.23)	2.52 (0.23)	0.934
Serum phosphorus, mmol/L	2.29 (0.47)	2.31 (0.52)	0.838
ALP, U/L	254.5 (137.3-437.8)	488.0 (193.0-825.0)	<0.001
Year of parathyroidectomy			<0.001
≤2013	11 (5.3)	12 (23.5)	
2014-2017	72 (34.6)	39 (76.5)	
≥2018	125 (60.1)	0 (0)	

Values are numbers (percent), mean (standard deviation) or median (interquartile range).

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

Surgical results of the SPTX and TPTX+AT groups

The number of parathyroid glands identified during operation between the two groups had no statistical difference (P=.120). More patients in TPTX+AT group underwent thyroidectomy concurrently than SPTX group (P=.006). The operation time in TPTX+AT group was statistically longer than SPTX group (both P<.05). Additional thyroidectomy would increase operation time, as a result, when patients who underwent thyroidectomy were excluded, the difference in operation time became no longer statistically significant (TPTX+AT: 125.4±38.8min, SPTX: 117.0±27.4min, P=.096). There are more patients diagnosed as parathyroid adenoma in TPTX+AT group than SPTX group (P<.05).

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

On postoperative day 1 (POD1), the levels of serum iPTH, calcium and phosphorus decreased significantly compared with those before operation (all P<.05). The level of iPTH was significantly higher than that in TPTX+AT group (P=.023). The POD1 serum calcium level is higher in TPTX+AT group than that in SPTX group (P=.012), however, this difference was not statistically significant by 7 days after operation (P=.355). The results of laboratory examination on POD7 were lacked because they were discharged at that time. The rate of persistent SHPT in SPTX group is statistically higher than that in TPTX+AT group (P=.020). Further binary logistic regression analysis showed that high level of preoperative ALP (OR 1.002, 95% CI 1.000-1.004, P=.036) and small number of parathyroid glands identified during operation (OR 0.046, 95% CI 0.006-0.379, P=.004) were the risk factors for persistent disease. In terms of complications, severe hypocalcemia (TPTX+AT: 23.6%, SPTX: 19.6%, P=.547) was the most common. The incidence of cervical hematoma, wound infection and recurrent laryngeal nerve injury was very low, and there was no statistical difference between the two groups (all P>.05). No patient died during postoperative inpatient period. One patient who underwent TPTX+AT had blockage of lower limb dialysis fistula, resulting in local and systemic infection. The postoperative inpatient days was longer in SPTX group (P<.001) (Table 2). Common symptoms of most patients were improved after operation, and no statistical difference was found between the two groups (all P<.05) (Table 3).

Table 2

Perioperative information of patients undergoing parathyroidectomy

	TPTX+AT(n=208)	SPTX(n=51)	P value
Operation time, min	128.3 (38.8)	116.2 (27.0)	0.010
Number of parathyroid glands identified	3.93 (0.38)	3.80 (0.53)	0.120
Thyroidectomy performed concurrently	47 (22.6)	3 (5.9)	0.006
Pathological result			0.041
Hyperplasia	205 (98.6)	47 (92.2)	
Adenoma	3 (1.4)	4 (7.8)	
Diagnosed as thyroid carcinoma	14 (6.7)	0 (0)	0.119
POD1 iPTH, mmol/L	9.7 (5.4-24.2)	37.1 (7.0-121.8)	0.023
POD1 calcium, mmol/L	1.91 (0.28)	1.81 (0.23)	0.012
POD1 phosphorus, mmol/L	1.83 (0.53)	1.84 (0.53)	0.913
POD7 calcium, mmol/L (n=180)	1.86 (0.25)	1.90 (0.19)	0.355
POD7 phosphorus, mmol/L (n=180)	1.13 (0.38)	1.18 (0.53)	0.581
Persistent SHPT	4 (1.9)	5 (9.8)	0.020
Severe hypocalcemia	49 (23.6)	10 (19.6)	0.547
Hematoma	2 (1.0)	1 (2.0)	0.484
Recurrent laryngeal nerve injury	1 (0.5)	1 (2.0)	0.356
Wound infection	0 (0)	0 (0)	1.000
Postoperative inpatient days, d	7.32 (5.20)	10.29 (5.83)	<0.001

Values are numbers (percent) or mean (standard deviation).

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 in patients undergoing parathyroidectomy

			Postoperative			
Symptoms		Group	Preoperative	Completely improved	Partly improved	Barely changed
Orthopedic pain	Severe	TPTX+AT	55 (26.4)	43 (78.2)	8 (14.5)	4 (7.3)
		SPTX*	18 (35.3)	12 (66.7)	5 (27.8)	1 (5.6)
	Light	TPTX+AT	78 (37.5)	61 (78.2)	6 (7.7)	11 (14.1)
		SPTX*	20 (30.2)	14 (70.0)	2 (10.0)	4 (20.0)
Pruritus		TPTX+AT	148 (71.2)	85 (57.4)	31 (20.9)	32 (21.6)
		SPTX*	34 (66.7)	21 (61.8)	8 (23.5)	5 (14.7)
Obvious fatigue		TPTX+AT	35 (16.8)	13 (37.1)	10 (28.6)	12 (34.3)
		SPTX*	7 (13.7)	5 (71.4)	1 (14.3)	1 (14.3)

Values are numbers (percent).

*P>.05 compared with TPTX+AT group postoperatively

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

Follow-up results and long-term outcomes of the SPTX and TPTX+AT groups

After follow-up of all patients included in this study, we excluded 45 patients who were missed follow-up due to telephone change, inability to connect, reluctance to collaborate, and unclear memory. The remaining 204 patients included 165 in TPTX+AT group and 39 in SPTX group. The all-cause mortality in SPTX group is significantly higher than that in TPTX+AT group ($P<.001$). The causes of death included heart failure (4 cases), electrolyte disorder (4 cases), intracerebral hemorrhage (3 cases), malignant tumor (2 cases), myocardial infarction (1 case), infection (1 case) and accident (1 case). Recurrent SHPT happened in 29.7% of patients in SPTX group and 12.3% of patients in TPTX+AT group ($P=.013$). But conversely, re-PTX was less common in SPTX group (2.6%) than that in TPTX+AT group (9.1%), though not statistically significant ($P=.302$). There was no statistical difference between the two groups in complications like adverse cardiovascular outcomes, fracture, hypercalcemia, and permanent hypoparathyroidism. The two groups were similar in symptom deterioration, renal transplantation, and long-term pharmacal therapies (all $P>.05$) (Table 4, 5). Kaplan-Meier are shown in Fig. 3. Log rank test indicated TPTX+AT group has lower risk in all-cause death than SPTX group ($P=.018$), and re-PTX was more common in TPTX+AT group than that in SPTX group ($P=.011$). However, there was no statistical difference in recurrence and adverse cardiovascular outcomes between the two groups (both $P>.05$).

Table 4

Long-term outcomes of patients undergoing parathyroidectomy

	TPTX+AT(n=165)	SPTX(n=39)	P value
All-cause mortality	7 (4.2)	9 (23.1)	<0.001
Recurrent SHPT*	20 (12.3)	11 (29.7)	0.013
Re-PTX	15 (9.1)	1 (2.6)	0.302
Adverse cardiovascular outcomes	11 (6.7)	4 (10.3)	0.666
Fracture	3 (1.8)	2 (5.1)	0.244
Prevalent hypercalcemia	13 (7.9)	2 (5.1)	0.802
Permanent hypoparathyroidism	9 (5.5)	0 (0)	0.290
Orthopedic pain worsened	8 (4.8)	2 (5.1)	1.000
Pruritus worsened	7 (4.2)	0 (0)	0.412
Renal transplantation	2 (1.2)	1 (2.6)	0.473

*Persistent SHPT were excluded.

Values are numbers (percent).

TPTX+AT: total parathyroidectomy with autotransplantation; SPTX: subtotal parathyroidectomy; SHPT: secondary hyperparathyroidism; Re-PTX: recurrent parathyroidectomy.

Table 5

Long-term pharmaceutical therapies of patients undergoing parathyroidectomy

	TPTX+AT(n=165)	SPTX(n=39)	Pvalue
Cinacalcet	17 (10.3)	2 (5.1)	0.488
Calcium	60 (36.4)	10 (25.6)	0.205
Vitamin D	53 (32.1)	9 (23.1)	0.269
Calcitriol	46 (27.9)	6 (15.4)	0.107
Phosphorus binders	54 (32.7)	15 (38.5)	0.496

Risk factors for all-cause death and recurrent SHPT

Cox regression analysis was performed for all-cause death and recurrent SHPT, and the covariate stroke was not included for the number was too small. In individual variable Cox regression analysis, the SPTX operation approach, older age, lower level of preoperative serum phosphorus was found to be associated with all-cause death after operation (all $P<.05$). However, after multiple Cox regression analysis, only the

SPTX operation approach (HR 3.53, 95%CI 1.12-10.32, P=.021) and older age (HR 1.06, 95%CI 1.00-1.12, P=.035) were considered as risk factors for all-cause death (Table 6). No risk factor for recurrent SHPT was found in individual variable Cox regression analysis (all P>.05).

Table 6

Risk factors for all-cause death based on Cox regression analysis

Variables		Hazard Ratio	95% CI	Pvalue
<i>Step 1: Individual variable analysis</i>				
Operative approach	TPTX+AT	Comparison		
	SPTX	3.29	1.17-9.25	0.024
Age at operation		1.06	1.01-1.12	0.018
Hypertension	No	Comparison		
	Yes	3.67	0.48-27.77	0.209
Diabetes	No	Comparison		
	Yes	3.47	0.92-13.00	0.064
Coronary heart disease	No	Comparison		
	Yes	2.25	0.50-10.05	0.288
Preoperative iPTH		1.00	1.00-1.00	0.880
Preoperative serum calcium		1.39	0.15-12.82	0.772
Preoperative serum phosphorus		0.32	0.10-0.97	0.045
Preoperative ALP		1.00	1.00-1.00	0.060
Number of parathyroid glands identified		1.13	0.35-3.69	0.839
Pathological result	Hyperplasia	Comparison		
	Adenoma			
<i>Step 2: Multiple analysis</i>				
Operative approach	TPTX+AT	Comparison		
	SPTX	3.53	1.21-10.32	0.021
Age at operation		1.06	1.00-1.12	0.035
Preoperative serum phosphorus		0.60	0.21-1.70	0.338

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

Discussion

In this retrospective study of parathyroidectomy, we evaluated two surgical approaches from both short-term and long-term perspectives, and nearly 80% of patients completed follow-up. We found that although TPTX + AT seemed to be more effective in treating SHPT than SPTX within a short period after operation, there was no significant difference between these two surgical methods in the recurrence after a long time. The proportion of re-PTX was higher in patients after TPTX + AT than after SPTX. The incidence of complications in the two groups was similar. Nevertheless, the all-cause mortality of SPTX group was significantly higher than that of TPTX + AT group (23.1% and 4.2% respectively). Heart failure is the main cause of death in both groups.

TPTX + AT and SPTX are the two most common surgical treatments for SHPT, which can substantially improve patients' symptoms and reduce mortality [22]. Which is the best surgical method is still controversial. Moreover, PTX is not without risk [1]. Our results showed that these two surgical approaches are both of great benefit to SHPT patients. Most patients could completely or partially improve their postoperative symptoms, and could show a significant decrease in the level of serum iPTH, calcium and phosphorus. However, binary logistic regression analysis showed that the small number of parathyroid glands detected during operation was a risk factor for permanent SHPT, while the surgical method was not, suggesting that the occurrence of permanent SHPT may be attributed to the failure to detect all parathyroid glands during operation, rather than a specific surgical approach. Severe hypocalcemia was happened more commonly in TPTX + AT group than in SPTX group. Although the difference was not statistically significant, it indicated some potential risks may existed.

In this study, recurrent SHPT occurred in about 15% of the patients. We found that recurrent SHPT was not related to the surgical method. It should be noted that the rate of permanent hypoparathyroidism in TPTX + AT group was higher than that in SPTX group (5.5% vs 0%), although there was no statistical difference. These patients are being treated with calcium, vitamin D or calcitriol continuously. Some of them have had to be hospitalized for intravenous calcium supplement, which may increase the economic burden and nursing cost, but as far as we know, no serious event happened due to hypocalcemia. The KDIGO guideline also believes mild and asymptomatic hypocalcemia to be harmless [25]. Besides, only about 10% of patients need to take cinacalcet to inhibit the continuous increase of PTH after PTX, which means surgery can reduce the treatment cost of most patients.

The proportion of re-PTX was higher in TPTX + AT group than that in SPTX group, which probably be closely correlated with the mode of reoperation, in that most reoperation after TPTX + AT could be carried out inpatient or outpatient under local anesthesia. However, in patients undergoing SPTX, the degradation of systemic organ function led by ESRD may make them unable to tolerate another general anesthesia

operation a few years after the original operation. In addition, the acceptability of patients should be taken into account in the selection of surgical approach.

Elin Isaksson et al conducted a retrospective analysis of 824 patients in Sweden who underwent SPTX or TPTX (whether combined with AT was not distinguished), and concluded that SPTX had a lower risk of cardiovascular events but similar mortality when compared with TPTX + AT. They also suspected that the occurrence of cardiovascular events was associated with excessively low levels of iPTH after TPTX + AT [26]. Our study obtained different results. The incidence of adverse cardiovascular outcomes was lower in both groups, and there was no significant difference between the two groups, while the risk of death was significantly higher in the SPTX group. From these results, TPTX + AT seems to be a safer approach. However, the major cause of mortality of our patients is heart failure, which is also the main cause of death of ESRD. Since ESRD, and the combined hypertension or diabetes can also induce cardiovascular diseases by multiple mechanisms [27], the relationship between operative methods and death still needs further study. Meanwhile, considering that only few patients (3/204) underwent renal transplantation after PTX, which is much lower than that study (273/804), it could possibly be reasons for the different results.

We found that recurrent SHPT was not related to the surgical method. It should be noted that although the rate of permanent hypoparathyroidism in TPTX + AT group was higher than that in SPTX group (5.5% vs 0%), although there was no statistical difference. These patients are being treated with calcium, vitamin D or calcitriol continuously. Some of them have had to be hospitalized for intravenous calcium supplement, which may increase the economic burden and nursing cost, but as far as we know, no serious event happened due to hypocalcemia. The KDIGO guideline also believes mild and asymptomatic hypocalcemia to be harmless [25]. Besides, only about 10% of patients need to take cinacalcet to inhibit the continuous increase of PTH after PTX, which means surgery can reduce the treatment cost of most patients.

Generally speaking, three and a half parathyroid glands are resected in SPTX, and TPTX + AT removes all parathyroid glands and then takes part of the tissue for autologous transplantation [1, 24]. However, there are differences in detail. For instance, parathyroid autotransplantation can be occurred in sites like sternocleidomastoid muscle, subcutaneous abdominal adipose tissue, brachioradialis muscle, deltoid muscle and anterior tibial muscle [28–32]. In this study, the way of AT mainly depended on the preferences of surgeons, and was not distinguished.

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 [14, 17, 22]. Out of concern about the complications of TPTX alone, our center has not widely carried out this approach.

This study has some limitations. First, it is a retrospective study, lack of randomness. Second, there is imbalance in the follow-up time between the two groups. Though we have eliminated some of the effects through survival analysis, some information might still be missed. Third, the evaluation of patients'

subjective feelings was mainly obtained by oral way, and no specific scale was used, which could lead to a certain bias.

Conclusion

TPTX + AT and SPTX are both effective surgical approaches for the treatment of SHPT. Effectiveness and complication rates of them are similar. Considering the potential lower mortality risk of TPTX + AT and the quite low renal transplantation rate in Chinese population, we prefer TPTX + AT to treat SHPT patients in most Chinese population.

Abbreviations

SHPT: secondary hyperparathyroidism; ESRD: end-stage renal disease; PTH: parathyroid hormone; iPTH: intact parathyroid hormone; PTX: parathyroidectomy; TPTX+AT: total parathyroidectomy with autotransplantation; SPTX: subtotal parathyroidectomy; re-PTX: recurrent PTX; POD: postoperative day;

Declarations

Ethics approval and consent to participate

This study was approved by the Review Board of the Second Affiliated Hospital of Soochow University. All patients or their relatives signed informed consent forms to participate in the study. This study only collected the clinical data of patients and did not interfere with the treatment plan of patients. All patients' privacy has been well protected.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due the data collection process of this study took a large amount of time but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

ZJQ interpreted the patient data of perioperative period, and was a major contributor in writing the manuscript. WY carried out follow-up and interpreted the corresponding data, and was a contributor in writing the manuscript. HT was responsible for statistical analysis. JGQ and YZX participated in the design of the study, and YZX monitored its implement and revised the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 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 4cm found by ultrasound.

Figure 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).

Figure 3

Kaplan-Meier curves of patients undergoing parathyroidectomy.