Utilization of Ultrasound for Management of Surgical Intervention of Secondary Hyperparathyroidism and Prolonged Hypocalcemia Post-Parathyroidectomy

Ying Liu, MM^{a,1}, Yang Zhou, MD^{a,1}, Hong Zhou, BS^{a,*}, Yuanyuan Chen, MM^b, Jian Wu, MD^c, Juan Wang, BS^a, Bin Wang, MM^c, Changyu Chen, MM^a, Ming Ye, MM^a

^a Department of Ultrasound, The Third People's Hospital of Chengdu, The Affiliated Hospital of Southwest Jiaotong University and the Second Affiliated Clinical Hospital of Chongqing Medical University, Chengdu, China; ^b Department of Pathology, The Third People's Hospital of Chengdu, The Affiliated Hospital of Southwest Jiaotong University and the Second Affiliated Clinical Hospital of Chongqing Medical University, Chengdu, China; ^c Department of Thyroid and Breast Surgery, The Third People's Hospital of Chengdu, The Affiliated Hospital of Southwest Jiaotong University and the Second Affiliated Clinical Hospital of Chongqing Medical University, Chengdu, China
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Objective: To evaluate the application of ultrasound (US) for the surgical intervention in patients with moderate and severe secondary hyperparathyroidism (SHPT), and to identify the risk of prolonged hypocalcemia after parathyroidectomy (PTX).

Methods: A consecutive series of moderate and severe SHPT patients ($n = 64$) underwent ultrasound evaluation of parathyroid glands. Among the 64 patients who received 6-month medication therapies, ten patients with parathyroid hormone (PTH) 300~500 pg/mL were excluded from the study while 32 patients unresponsive to medication therapy (PTH > 500 pg/mL) received surgical interventions and 22 patients with PTH < 300 pg/mL received medication treatment alone. The correlations between the number, location, volume, sonographic features of parathyroid glands (PTGs), laboratory examinations, the duration of dialysis and the surgical necessity were analyzed. Total parathyroidectomy with synchronous auto-transplantation (PTX + AT) was performed in the surgical group. In both the surgical and medication group, patients with hyper-vascularity of the PTGs dominated ($\geq 50\%$) were classified as a hyper-vascular subgroup, and the others as a hypo-vascular subgroup. The differences of post-operative calcium (Ca^{2+}) levels and the incidence of prolonged hypocalcemia between hyper- and hypo-vascular subgroups were assessed.

Results: Sonographic evaluations revealed that the numbers of detectable PTGs were higher in the surgical group than that of the medication group ($p < 0.05$). The detection of supernumerary PTGs was higher in the surgical group than that in the medication group (13/121, 10.7% vs. 2/71, 2.8%, $p < 0.05$). Baseline PTH, >2 detectable PTGs, detection of supernumerary PTGs, patients with hyper-vascular, and the duration of dialysis were positively associated with the necessity of surgical intervention. For patients in the hyper-vascular subgroup, the serum Ca^{2+} level was lower than that in the hypo-vascularity subgroup ($p < 0.01$).

Conclusion: Ultrasonic features can provide useful information for management of surgical intervention of SHPT and prediction of the risk of prolonged hypocalcemia after PXT.

Key words: Secondary hyperparathyroidism; Ultrasound; Total parathyroidectomy; Auto transplantation; Hypocalcemia

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¹ Co-first author

* Corresponding author: Hong Zhou, Department of Ultrasound, The Third People's Hospital of Chengdu, The Affiliated Hospital of Southwest Jiaotong University and the Second Affiliated Clinical Hospital of Chongqing Medical University, Chengdu, China.
e-mail: 664121529@qq.com

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Secondary hyperparathyroidism (SHPT) is caused by the hyperplasia of the parathyroid glands (PTGs) in patients with chronic renal failure (CKD) [1,2]. Severe SHPT is associated with increased cardiovascular mortality [3]. Hyperplasia of PTGs is only reversible at early stage [4]. The response of SHPT patients to pharmacological therapy fell short of expectations in the past few decades. New pharmacological therapies (calcitriol, active vitamin D, and phosphate-binding drugs) significantly delay the surgery timeline for two years [5]. Nevertheless, surgical intervention, which is cost-saving, is still meaningful for the alleviation of symptoms in patients who fail to respond to medication therapy. Previous studies revealed that the sizes of PTGs and the level of parathyroid hormone (PTH) could predict the patients' response to drugs, however, such studies included patients with mildly increased PTH, which could be managed medically [6-8].

Meanwhile, the cut-off value of PTH for aggressive intervention has not yet been established. The acceptable PTH values in the JSDT guidelines is < 240 pg/mL, whereas those in the National Kidney Foundation Kidney Disease Outcomes Quality Initiative and the Kidney Disease Improving Global Outcomes guidelines are < 300 pg/mL and < 600 pg/mL, respectively [7-9]. In clinical practice, patients were categorized according to the PTH values: mild (< 500 pg/mL), moderate (500–800 pg/mL), and severe (> 800 pg/mL). Mild patients more likely respond to pharmacological therapies [9]. At present, there are no clinical guidelines advocating a timely parathyroidectomy for moderate and severe patients. Ultrasonography, as a useful tool to define the size, structure, vascularity of PTGs even the type of hyperplasia, is rarely utilized to help clinicians make clinical decisions, such as whether the surgical intervention should be considered [8, 10].

Hungry bone syndrome (HBS), mainly manifested as prolonged hypocalcemia (serum $\text{Ca}^{2+} < 2.1$ mmol/L, lasting more than 4 d), is a critical post-parathyroidectomy complication, with an incidence ranging from 27.8% to 72% [11]. It may cause laryngeal muscle spasm leading to asphyxia, cardiac dysfunction, or even cardiac arrest. The sudden decline of PTH leads to an enhanced bone uptake of Ca^{2+} , phosphate (P) and magnesium (Mg^{2+}) with unaffected osteoblast activity, which results in an increase in bone density. Several risk factors have been identified to indicate the development of HBS, including age, size of resected parathyroid glands, preoperative serum PTH and alkaline phosphatase (ALP) level [12]. However, there is a paucity of data concerning the preoperative sonographic assessment to predict the prolonged hypocalcemia or even HBS in patients with SHPT.

Therefore, the aim of this was to evaluate the application of ultrasound (US) for the surgical intervention in patients with of moderate and severe secondary hyperparathyroidism (SHPT), and to identify the risk of prolonged hypocalcemia after parathyroidectomy (PTX). We analyzed the association between the PTGs' sonographic patterns and the necessity of surgeries, and predicting the risk for prolonged hypocalcemia after PXT accordingly.

Materials and Methods

Study design and ethical approval

Between January 2018 and July 2019, a consecutive series of 64 patients on maintenance bicarbonate hemodialysis at the dialysis unit of the Third People's Hospital of Chengdu had PTH levels > 500 pg/mL at admission and enrolled in this study. To reduce the PTH level in 6 months, 52 participants received combined administration of elemental calcium (Ca^{2+}) 1000 mg to 1200 mg and vitamin D₃ 20 mg (800 IU) daily, while the other 12 patients were prescribed calcimimetics. According to consecutive laboratory testing and clinical features within the previous 6 months, ten patients whose PTH levels were between 300 pg/mL and 500 pg/mL after treatments were excluded as the dubious curative effect of medication. Among the other 54 patients, the surgical group consisted of 32 patients unresponsive to medication therapy (defined as PTH > 500 pg/mL independent of serum Ca^{2+} level) who received surgical intervention. Surgical exclusion criteria included heart failure, severe pulmonary hypertension, and coagulation disorders. The medication group consisted of the remaining 22 patients with progressive decline of PTH, defined as median PTH level < 300 pg/mL over three consecutive monthly measurements after the 6-months therapy [6], who had received pharmacological treatment.

At admission and 6 months after medication therapy, all patients received high-resolution US examination by two independent sonographers (both of which had more than 10 years experiences and performed a consistency test at the start of the study). An IU Elite scanner (Phillips Medical Systems, Bothell, WA, USA) equipped with an L12-5 transducer was used. The number, position, volume, sonographic structures and vascularity of detectable PTGs were recorded, including classical pairs of PTGs and all supernumerary PTGs. Standardized video documentation of ultrasonic scan from the bilateral lower jaw to the supraclavicular fossa was recorded, followed by standardized longitudinal and transverse views of each detectable PTG. In addition, the three dimensions of PTGs were measured. The PTG size was defined as the maximal longitudinal diameter (MLD),

and the volume of each PTG was estimated as $\pi/6 \times \text{width (mm)} \times \text{length (mm)} \times \text{depth (mm)}$ [13]. After that, the section with the most abundant blood flow of each PTG was recorded, while the vascularity was assessed and graded according to Doppler score Onoda [6]: (1) a few star or dot blood flow signals in surrounding glands presents Peripheral P1, (2) long streak signals surrounding more than 30% of PTG circumference presents Peripheral P2, (3) a few short or dot blood flow signals in the central region of glands presents Central C1, (4) long streak bloodstream in the inside of the

gland ($> 30\%$ of the surface) presents Central C2, and (5) no blood flow inside the gland presents Central C0. Since the central blood supply is more important than the peripheral flow, hypo-vascular PTGs were defined as scored P0/1/2, C0 while hyper-vascular PTGs as scored P0/1/2, C1 or P0/1/2, C2. Patients whose hypo-vascularity of the PTGs dominated ($\geq 50\%$) were categorized as the hypo-vascular subgroup (Fig. 1), while the others as the hyper-vascular subgroup (Fig. 2). Meanwhile, 32 patients in surgical group received preoperative ^{99m}Tc -MIBI SPECT/CT scans.

Figure 1 Sonographic images of PTGs in a 31 years old female patient in the hypo-vascular subgroup. There were five detectable PTGs, in which most of them (4/5) were hypo-vascular feature. (A). Longitudinal image of the gland in a right superior position (*), the gland was slightly heterogeneous, appearing to be partial hypoechoic and partial hyperechoic. The Doppler score Onoda was P1, C0; (B). Longitudinal image of the gland in the right inferior position (*), appearing to be hypoechoic with Doppler score Onoda P1, C0; (C). Longitudinal image of a supernumerary PTG in the right inferior position. This “newborn” echoic gland (*) was with Doppler score Onoda P1, C0; (D). Longitudinal image of a gland in a left superior position (*), appearing to be hypoechoic with the Doppler score Onoda P2, C0; (E). Longitudinal image of a gland in the left inferior position, appearing to be highly heterogeneous with partial hyperechoic (Δ) and partial hypoechoic. The Doppler score Onoda was P2, C2.

Total parathyroidectomy with synchronous auto-transplantation (PTX + AT) was performed with careful exploration and intraoperative pathology to ensure thorough removal of all PTGs [14, 15]. Pieces (10–20 mm³) minced from the most normal appearing gland were implanted into the forearm of each patient. All patients received a postoperative intravenous Ca²⁺ infusion at a rate of 2720 mg elemental Ca²⁺/day. If serum Ca²⁺ level was 2.1 mmol/L or lower, standard calcium dialysate was used. Additionally, an extra 10 mL of 10% calcium chloride solution (272 mg elemental Ca²⁺) was given with monitoring calcium ions [16]. Serum Ca²⁺ and PTH levels were monitored every 6 h immediately after the surgery for a week, then every two days for another one week, after which, the laboratory tests were ordered biweekly during the 6-month follow-up. This study was approved by the Ethics Committee of the Third People’s Hospital of

Chengdu (Sichuan, China), and all participants provided written informed consent.

Statistical analysis

The SPSS 22.0 software package (IBM, Armonk, NY, USA) was used for statistical analysis. Values were expressed as the mean $\pm$ SD. Continuous variables were compared between groups using the *t*-test. Chi square test was used to compare and analyze the frequencies. Multiple logistic regression analysis was used to analyze the association between sonographic features, laboratory examinations and the necessity of surgeries of SHPT. Statistical significance was considered as $p < 0.05$.

Results

Sonographic evaluations revealed that the numbers of detectable PTGs were higher in the surgical group than

that of the medication group ($p < 0.05$). In the surgical group, in addition to the classical pairs of superior and inferior PTGs, thirteen supernumerary PTGs were detected by US and confirmed by surgeries. In contrast, only two supernumerary PTGs located posterior to the thyroid gland were identified in the medication group. The detection of supernumerary PTGs was higher in the surgical group

than that in the medication group (13/121, 10.7% vs. 2/71, 2.8%, $p < 0.05$). Compared with the medication group, the surgical group had a higher proportion of hyper-vascular subgroup patients ($p < 0.05$) and a lower proportion of hypo-vascular subgroup patients ($p < 0.05$). All ultrasonic features of PTGs in both groups remained unchanged after 6 months (Table 1).

Figure 2 Sonographic images of PTGs of a 46 years old female patient in hyper-vascular subgroup. The total number of detectable PTGs was 5. Most of these PTGs (4/5) were hyper-vascular. (A) The longitudinal image showed the gland in right superior position (*), which was heterogeneously hyperechoic with the Doppler score Onoda was P1, C2; (B) The longitudinal image showed the gland in the right inferior position (*), which was medium heterogeneous, appearing to be partial hypoechoic and partial hyperechoic, The Doppler score Onoda was P2, C2; (C) The longitudinal image showed a supernumerary PTG gland (*) in the right inferior position, which shown to be homogeneous hypoechoic with Doppler score Onoda P2, C2; (D) The longitudinal image showed a gland (*) in the left superior position, which was slightly heterogeneous with Doppler score Onoda P1, C0; (E) The longitudinal image showed another gland (*) in the left inferior position, which was highly heterogeneous with annular calcification (white ★), cystic appearance (white circle) and Doppler score Onoda P1, C2.

Table 1 Patients with ultrasonic detective PTGs in surgical and medication group

Items	Numbers of patients	Numbers of PTGs in 4 classical positions	Numbers of supernumerary PTGs
Surgical Group	32	108	13
Patients with 1 US detectable PTG	1	1	0
Patients with 2 US detectable PTGs	4	8	0
Patients with 3 US detectable PTGs	5	14	1
Patients with 4 US detectable PTGs	16	61	3
Patients with 5 US detectable PTGs	3	12	3
Patients with 6 US detectable PTGs	3	12	6
Medication Group	22	69	2
Patients with 1 US detectable PTG	3	3	
Patients with 2 US detectable PTGs	10	20	0
Patients with 3 US detectable PTGs	4	11	1
Patients with 4 US detectable PTGs	5	19	1
Patients with 5 US detectable PTGs	0	0	0
Patients with 6 US detectable PTGs	0	0	0

Chi square test was used to compare and analyze the frequencies.

As shown in Table 2, serum P, calcium-phosphorus product, baseline PTH (PTH at admission), duration of dialysis, the number, the average MLD and volume of US detectable PTGs were increased in the surgical group versus the medication group (all $p < 0.05$, respectively). In contrast, the serum Ca^{2+} was lower in the surgical group compared to the medication group ($p < 0.01$). In the surgical group, 32 patients received PTX + AT due to poor response to pharmacological therapy after 6 months. A higher proportion of patients with > 2 detectable PTGs was observed in the surgical group compared to the medication group (84.4% vs. 40.9%, $p < 0.05$). Between

the two groups, there was no statistical significance found in the prevalence of PTGs with hyper-echogenicity, hypo-echogenicity, heterogeneity, calcification, or cystic degeneration, respectively. Multiple logistic regression analysis revealed that the baseline PTH (HR 95%CI 3.5, $p < 0.05$), > 2 detectable PTGs (HR 95%CI 1.8, $p < 0.05$), detection of supernumerary PTGs (HR 95%CI 1.2, $p < 0.05$), patients of the hyper-vascular subgroup (HR 95%CI 1.5, $p < 0.05$), and the duration of dialysis (HR 95%CI 2.40, $p < 0.05$) were correlated with the necessity of surgeries of SHPT (Fig. 3).

Figure 3 Multiple logistic regression analysis of the association between sonographic features, laboratory examinations and the necessity of surgeries.

In both groups, US detectable PTGs were more commonly seen in the left and right inferior regions than in the two superior regions, in spite of statistical insignificance ($p = 0.58$) (Fig. 4). The MLDs of PTGs in the four regions have no statistical difference either ($p = 0.20$).

Surgical pathologies confirmed 121 PTGs, of which ten glands (8.3%) were ectopic PTGs, including eight intra-thyroidal, one in carotid sheath, and one in submandibular region. Except for the one in submandibular region which was missed by US but detected by $^{99\text{m}}\text{Tm}$ -MIBI tomography, pre-operative US accurately distinguished 120 PTGs. On the other hand, six intra-thyroidal and 17 PTGs posterior to the thyroid gland were missed by $^{99\text{m}}\text{Tm}$ -MIBI tomography. Hence, the detection rate of US was better than that of $^{99\text{m}}\text{Tm}$ -MIBI tomography (99.1% vs. 81.0%, $p < 0.01$).

In the hyper-vascular subgroup, the average pre-operative PTH was significantly higher than that in the hypo-vascular subgroup (1219.5 ± 783.1 vs. 893.3 ± 652.2 pmol/L, $p < 0.05$), while the pre-operative Ca^{2+} was significantly lower (2.1 ± 0.2 vs. 2.4 ± 0.2 mmol/L, $p < 0.05$) in the hyper-vascular subgroup (Table 3). In correspondence with the result that the incidence of prolonged hypocalcemia was higher (15.9% vs. 3.8%, $p < 0.05$) in the hyper-vascular subgroup, the post-operative Ca^{2+} during the first 14 d after surgeries was also lower in the hyper-vascular subgroup (the average Ca^{2+} level, 2.0 ± 0.1 vs. 2.3 ± 0.1 mmol/L, $p < 0.01$) (Fig. 5). The median follow-up time was 10 months (7-15 months) and 14 months (11-18 months) for patients in the surgical group and the medication group, respectively. Post-operative PTH levels in the surgical group declined to the KDIGO target range (57-275 pg/mL, average value

104.9 ± 41.4 pg/mL) [9], significantly lower than that in the medication group (185–475 pg/mL, average 226.9 ± 143.4 pg/mL, $p < 0.05$). During the 7–18 months follow-

up period, one patient had mild bone pain, and one presented with itching in the medication group. Patients in neither group had severe clinical manifestations.

Figure 4 The distribution and maximal longitudinal diameters (MLDs) of US detectable parathyroid glands (PTGs) in surgical group and medication group.

Figure 5 The average serum calcium (Ca^{2+}) monitoring curves from post-operative day 1 to day 14 for patients in hyper-vascular and hypo-vascular groups. According to the pre-operative sonographies, there were: (i) 22 cases in hyper-vascular subgroup, shown in gray line, (ii) 10 cases in hypo-vascular subgroup, shown in black line. The average serum Ca levels of patients in hyper-vascular subgroup was significantly lower than that in hypo-vascular subgroup (2.0 ± 0.1 vs. 2.3 ± 0.1 , $p < 0.05$).

Discussion

Associated with complications such as renal stones, osteoporosis, muscle weakness, itching, growth retardation, bone pain and cardiovascular events, SHPT is to blame for the substantial morbidity and mortality rate of patients on chronic hemodialysis. Approximately 40%–80% of SHPT patients with conservative treatments failed to maintain a PTH level to < 300 pg/mL [6, 17].

For advanced SHPT, parathyroidectomy improves survival and cardiovascular outcomes [18, 19]. In this study, medications were effective for 34.4% (22/64) of SHPT patients, when 15.6% (10/64) of patients were excluded because of dubious curative effect of medication. The rest 50% refractory to medication therapy had received surgical intervention in this patient study group. Ultrasonography of PTGs could be used to detect patients who are unlikely to respond to further medical therapy. But surgical indications based on sonographic findings for intervention were not conclusive. Additionally, the baseline and “cut-off” PTH levels of SHPT varied widely in reported studies [7–10]. Since mild patients more likely respond to pharmacological therapies [9], the present study focused on moderate and severe SHPT patients.

Compared to the medication group, the surgical group had a lower level of serum Ca^{2+} but a higher level of serum P and calcium-phosphorus product. These findings were similar to previous studies [3, 5]. However, Ca^{2+} , P and calcium-phosphorus product had no correlation with the patient response to drug therapy, this might be ascribed to the adequate control of serum electrolyte during six months of medication treatment. On the other hand, the baseline PTH > 2 detectable PTGs, detection of supernumerary PTGs, patients of hyper-vascular subgroup, and the duration of dialysis were positively associated with the necessity of surgical intervention in SHPT treatment.

Table 2 Demographics and clinical features of patients in the surgical group and medication group

Items	Surgical group	Medication group	P
Age (years)	47.7 ± 12.8	46.8 ± 14.0	n.s
Patients	32	22	
Sex			
Male	20	7	n.s
Female	12	15	
Duration of dialysis (years) ^a	6.3 ± 2.6	5.4 ± 3.5	< 0.05
BUN (μg/L)	13.5 ± 7.4	16.4 ± 5.5	n.s.
Scr (mmol/L)	529.1 ± 423.2	557.5 ± 307.3	n.s
Ca ²⁺ (mmol/L) ^a	2.3 ± 0.5	2.5 ± 0.5	< 0.01
P (mmol/L) ^a	2.0 ± 0.3	1.7 ± 0.5	< 0.05
Baseline PTH (pg/mL) ^a	924.5±781.7	671.3 ± 509.6	< 0.05
Ca ²⁺ *P ^a	4.6 ± 2.2	3.1 ± 1.3	< 0.05
Supernumerary PTGs locating posterior of the thyroid gland (num, %) ^a	13 (10.7%)	2, 2.8%	< 0.05
Average volume of PTGs (cm ³) ^a	1.0 ± 0.6	0.9 ± 0.7	< 0.05
Total volume of PTGs (cm ³)	2.7 ± 1.9	2.3 ± 2.2	n.s
US detectable PTGs (num, %)	120	71	
Homogeneous PTGs (num, %)	32, 26.6%	13, 18.3%	n.s
Hyper-echoic PTGs (num, %)	4, 3.3%	6, 8.5%	
Hypo-echoic PTGs (num, %)	73, 60.8%	47, 66.2%	
PTGs with calcification (num, %)	7, 5.8%	3, 4.2%	
PTGs with cystic degeneration (num, %)	4, 3.4%	2, 2.8%	
Doppler score Onoda assement ^a			
Patients in hyper-vascular subgroup (num, %)	18, 56.3%	10, 45.4%	< 0.05
Patients in hypo-vascular subgroup (num, %)	14, 43.7%	12, 54.6%	

Scr, the serum creatinine; Ca²⁺, calcium; P, phosphorus; BUN, blood urea nitrogen; Ca*P, the calcium-phosphorus product; PTH, parathyroid hormone; Variables are expressed as mean ± SD. Continuous variables were compared between groups using the *t*-test. Chi square test was used to compare and analyze the frequencies. ^a, the symbols indicate the difference (*p* < 0.05) between subgroups with respect to the higher value.

Table 3 Comparison between hyper- and hypo-vascular PTGs in the surgical group

Surgical group (<i>n</i> = 32)	Numbers of excised PTGs	Average volume of excised PTGs of each patient (cm ³)	Average pre- operative PTH (pmol/L)	Average pre- operative Ca ²⁺ (mmol/L)	Patients with prolonged hypocalcemia (<i>n</i> = 15)	Average post- operative Ca ²⁺ in 14 days (mmol/L)
Hyper-vascular subgroup (<i>n</i> = 18)	69	3.7 ± 1.8	1219.5 ± 783.1 ^a	2.1 ± 0.5 ^a	11(15.9%) ^a	2.0 ± 0.7 ^a
Hypo-vascular subgroup (<i>n</i> = 14)	52	4.0 ± 2.1	893.3 ± 652.2 ^a	2.4 ± 0.4 ^a	2 (3.8%) ^a	2.3 ± 0.6 ^a

Ca, calcium; PTH, parathyroid hormone. Variables are expressed as mean ± SD. Continuous variables were compared between groups using the *t*-test. Chi square test was used to compare and analyze the frequencies. ^a, the symbols indicate the difference (*p* < 0.05) between subgroups with respect to the higher value.

Most current researches emphasized the laboratory measurements, but few explored the ultrasonic features of SHPT. In this study, it was first proposed that, US was effective and essential to detect the number and the vascularity of PTGs, it could help clinicians to determine surgical intervention for moderate and severe SHPT patients refractory to medical management.

In the surgical group, only 50% patients had 4 PTGs, much lower than that reported previously [20]. The detection of supernumerary PTGs was significantly higher in the surgical group than that in the medication group ($p < 0.05$). There was a medical hypothesis “seed, environment, and soil” proposing that, during embryonic development, multiple “micro-parathyroids” may become potential auxiliary sources secreting PTH. In patients undergoing dialysis, various physiological stimuli may result in the activation of micro-parathyroids, even the development of “newborn” supernumerary PTGs [21–23]. However, the “micro-parathyroids” might only be recognized by postoperative pathologies rather than the surgeons. Thus, some experts proposed a novel surgical strategy for SHPT, namely purge parathyroidectomy (PPTX), to remove all PTGs posterior to the thyroid gland and the potential supernumerary or ectopic parathyroid tissues, the thymus tongue, and the cervical fibro-fatty tissues through the routine curved neck incision [21]. Our opinion is that the US detection of supernumerary PTGs posterior to the thyroid gland might predict the necessity of surgical intervention.

Patients with SHPT were considered as not to have symmetric enlargement of the PTGs [24]. Instead, the MLD of PTGs presented in the four typical regions had no statistic difference in this study. For moderate and severe patients with $\text{PTH} > 500 \text{ pg/mL}$, volumetric changes of PTGs might be symmetric. Detectable PTGs in bilateral inferior positions were more common than that in superior positions. This could be attributed to the relative independent blood supply of inferior PTGs than that of superior ones, which made the glands easier to be traced and identified by US.

US findings appeared to be related to the serum Ca^{2+} level after operation within a short timeframe. Patients in the hyper-vascularity subgroup were more likely to have severe hypocalcemia despite receiving standard postoperative supportive treatment. Hyper-vascularity might implicate supplementing adequate nutrition to maintain the hyper-function of PTGs. Hence, serum Ca^{2+} , which was regulated by PTGs, would decrease sharply after removing the abundant blood supply to the PTGs. Previous studies only revealed age, preoperative PTH and Ca^{2+} level as risk factors of severe hypocalcemia after PXT. This study presented that patients with hyper-vascularity of the PTGs dominated

($\geq 50\%$) was correlated with increased risk of severe hypocalcemia after PXT. US might help screen high-risk patients of severe hypocalcemia, and implement preventative calcium dialysate and large doses of Ca^{2+} supplementation after surgeries.

There are some limitations of this study. Certainly, larger sample sizes and a longer follow-up period are required to fully determine the efficacy of US features to help the management of SHPT.

Conclusion

For moderate and severe SHPT patients, US features can provide useful information for surgical intervention of SHPT and predict the risk of prolonged hypocalcemia after PXT, which might optimize clinical managements, such as implementation of surgical intervention, supplementation of preventative Ca^{2+} dialysate and large doses of Ca^{2+} postoperatively.

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Conflict of Interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of the manuscript.

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