Ultrasound-guided microwave ablation for secondary hyperparathyroidism: a systematic review and meta-analysis

Xiaofeng Zhoua, Yang Shenb, Ying Zhub, Qiang Lua, Weiyu Pua, Leiping Gab, Mingjia Gub and Chao Lib

aDepartment of Ultrasound, Changshu Hospital Affiliated to Nanjing University of Chinese Medicine, Changshu, China; bDepartment of Nephrology, Changshu Hospital Affiliated to Nanjing University of Chinese Medicine, Changshu, China

ABSTRACT

Objectives: Microwave ablation (MWA) is used for the treatment of severe secondary hyperparathyroidism (SHPT), but its efficacy and safety still remained unclear. This study aimed to investigate the efficacy and safety of ultrasound (US)-guided MWA in patients with SHPT.

Methods: The PubMed, Cochrane library, Embase, China national knowledge infrastructure (CNKI) and Wanfang databases were searched to identify published studies that evaluated the efficacy and safety of US-guided MWA in patients with SHPT. The primary outcomes were parathyroid hormone (PTH), serum calcium and phosphorus levels.

Results: A total of 26 studies with 932 patients were identified. The PTH levels showed significant reduction at 1 month [weighted mean difference (WMD) = 945.33, 95% CI: 797.15–1093.52] and 6 months (WMD = 1,151.91, 95% CI: 990.93–1312.89) after MWA of SHPT patients. The serum calcium (WMD = 0.39, 95% CI: 0.30–0.48) and phosphorus levels (WMD = 0.64, 95% CI: 0.43–0.85) showed significant reduction at 6 months after MWA of SHPT patients. The most common complications observed were hypocalcemia (35.2%) and transient hoarseness (9.2%). No other major complications or death occurred in our study patients.

Conclusion: These findings suggest MWA as a safe and effective minimally invasive technique for the management of SHPT. PTH, calcium, and phosphorus levels were significantly reduced at 1 and 6 months after MWA.

Abbreviations: MWA: Microwave ablation; SHPT: secondary hyperparathyroidism; PTH: parathyroid hormone; HPT: hyperparathyroidism; ESRD: end-stage renal disease; iPTH: intact parathyroid hormone; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analysis; CNKI: China national knowledge infrastructure; NOS: Newcastle-Ottawa Scale; ES: effect size; CIs: confidence intervals; ALP: Alkaline phosphatase; HIFU: high-intensity focused ultrasound

Introduction

Secondary hyperparathyroidism (SHPT) is a frequently encountered problem in patients with end-stage renal disease (ESRD) [1,2], and about one-third of the patients undergoing long-term dialysis are affected [3,4]. The patients with uncontrolled SHPT have increased risk of fractures and mortality [5,6]. Although disease development can be controlled clinically by using intravenous vitamin D analogs [7], orally active vitamin D sterols [8] and cinacalcet [9], parathyroidectomy in patients with severe SHPT is still considered necessary [10]. Surgical parathyroidectomy exposes patients to anesthesia risks and permanent parathyroid function reduction [11]. A minimally invasive alternative treatment with potential advantages of reduced risk, faster recovery, fewer side effects and lower costs when compared to traditional surgical treatment is warranted.

Recently, image-guided thermal ablation has been used for the treatment of hyperparathyroidism (HPT) [12,13]. As a method of ablation, ultrasound-guided percutaneous microwave ablation (MWA) has achieved good clinical results [14,15].

This technique has the advantages of least damage and effectively reduction of the levels of intact parathyroid hormone (iPTH), gradually becoming clinically acceptable. However, the results of existing studies on microwave ablation for SHPT are not completely consistent. Therefore, a systematic review and meta-analysis of published literature to evaluate the efficacy and safety of US-guided microwave ablation for SHPT was conducted. Although a previous meta-analysis has been constructed by Cao et al, the number of literatures included in the current study is more than triple that of it.
Materials and methods
The present meta-analysis study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [16].

Literature searches
The PubMed, EMBASE, Cochrane Library, China national knowledge infrastructure (CNKI) and Wanfang database were comprehensively searched from inception to March 2021 without any language restriction. The keywords used to search included “secondary hyperparathyroidism” plus “SHPT” and “microwave ablation” plus “MWA.” The reference lists of the relevant studies identified were manually scanned using these search terms.

Study selection
Relevant studies were included based on the following criteria: (1) observational cohorts including prospective and retrospective studies comparing pre-ablative and post-ablative clinical results; (2) patients with SHPT who underwent US-guided microwave ablation for therapy; (3) outcomes such as serum iPTH levels, serum calcium, serum phosphorus and complications; and (4) studies including a follow-up duration of at least 30 days. Studies were excluded if they met the following criteria: (1) studies published as case reports, conference abstracts, letters to editor, or reviews; (2) studies including patients with primary hyperparathyroidism; and (3) experimental studies of animal models or cell lines.

Data extraction and quality assessment
Data extraction was done using a standardized data collection form, which included author, year of publication, country, study design, number of patients, MWA power, number of lesion, age, gender, study duration, follow-up period and outcomes. The Newcastle-Ottawa Scale (NOS) [17] was used to evaluate the quality of included studies, in which studies with scores ≥ 6 represent high quality. Data extraction and quality assessment was independently done by two authors, and any disagreements between them were resolved by discussion.

Data synthesis and statistical analysis
Pooled estimates of proportions with corresponding 95% confidence intervals were calculated on the base of the Freeman Tukey double arcsine transformation [18,19]. Weighted mean difference (WMD) with 95% CIs were calculated as the difference between pre and post-treatment using random-effects model [20,21], in which $I^2 \geq 50\%$ or $p < 0.1$ represents notable heterogeneity. To detect robustness of the results, sensitivity analysis was conducted by sequential elimination of each study from the pool [21,22]. Potential publication bias was assessed using visual inspection of funnel plots, Begg’s and Egger’s tests [23,24]. Statistical analyses were performed using STATA software (version14, Statacorp, College Station, Texas, USA). $p < 0.05$ indicates statistically significant difference.

Results

Literature search and study characteristics
A total of 122 studies were screened, and 41 full-texts of these were assessed for eligibility. Finally, 26 studies [14,25–49] were included in the current systematic review. A flowchart depicting the study selection process was presented in Figure 1. The eligible articles were published between 2015 and 2021, and included a total sample size of 932. Among these studies, seven were prospective studies and 19 were retrospective studies. The mean age of participants ranged from 38.67 to 69.1. Both male and female patients were included in the studies. The main characteristics of the included studies are presented in Table 1. The quality of included studies was shown in Table 2. The quality assessment scores ranged from 7 to 8, with an average score of 7.5 points, which represent satisfactory quality of the studies.

Quantitative synthesis

Parathyroid hormone (PTH) levels
Data regarding PTH levels were reported in 23 studies. The results showed that the PTH levels were significantly reduced at week 1 (WMD = 901.1, 95% CI: 762.1 ~ 1,040.09, $p < 0.001, I^2 = 88.8\%$) (Figure 2(A)), 1 month (WMD = 945.33, 95% CI: 797.15 ~ 1,093.52, $p < 0.001, I^2 = 85\%$) (Figure 2(B)), 6 months (WMD = 1,151.91, 95% CI: 990.93 ~ 1,312.89, $p < 0.001, I^2 = 93.7\%$) (Figure 2(C)) and end of the follow-up period (WMD = 856.25, 95% CI: 680.8 ~ 1,031.71, $p < 0.001, I^2 = 89.7\%$) (Figure 2(D)) after microwave ablation of SHPT patients.

Calcium levels
Data regarding calcium levels were reported in 22 articles. The results revealed that the calcium levels were significantly reduced at week 1 (WMD = 0.36, 95% CI: 0.25 ~ 0.47, $p < 0.001, I^2 = 87.9\%$) (Figure 3(A)), 1 month (WMD = 0.40, 95% CI: 0.28 ~ 0.51, $p < 0.001, I^2 = 86.3\%$) (Figure 3(B)), 6 months (WMD = 0.39, 95% CI: 0.30 ~ 0.48, $p < 0.001, I^2 = 85.1\%$) (Figure 3(C)) and end of the follow-up period (WMD = 0.29, 95% CI: 0.23 ~ 0.36, $p = 0.001, I^2 = 67.5\%$) (Figure 3(D)) after microwave ablation of SHPT patients.

Phosphorus levels
Data regarding the phosphorus levels were reported in 19 articles. The results showed that the phosphorus levels were significantly reduced at week 1 (WMD = 0.42, 95% CI: 0.27 ~ 0.58, $p < 0.001, I^2 = 78.2\%$) (Figure 4(A)), 1 month (WMD = 0.52, 95% CI: 0.35 ~ 0.69, $p < 0.001, I^2 = 81.4\%$) (Figure 4(B)), 6 months (WMD = 0.64, 95% CI: 0.43 ~ 0.85, $p < 0.001, I^2 = 90.6\%$) (Figure 4(C)) and end of the follow-up period...
Figure 1. Flow diagram of study selection process.

Table 1. Characteristics of studies included in this meta-analysis.

| Author/ | Gender (Female %) | Mean age (Y) | Number of patients | MWA power (w) | Number of lesion | Conducted period | Follow-up | Study design |
|---------|-------------------|--------------|--------------------|--------------|-----------------|------------------|-----------|--------------|
| Luo/2015 [18] | China | 56.3% | 50.5 ± 10.7 | 16 | NA | 57 | NA | 6M | Retrospective |
| Diao/2016 [19] | China | 63.3% | 57.06 ± 9.14 | 30 | 25–35 | NA | 2009–2014 | 23M | Retrospective |
| Gao/2016 [20] | China | 50% | 56.6 ± 14.1 | 10 | NA | 32 | 2016 | 3M | Retrospective |
| Yu/2016 [21] | China | 72.7% | 51.3 ± 11 | 11 | 25 | 16 | 2014–2015 | 6.8M | Retrospective |
| Zhao/2016 [22] | China | 53.6% | 55.02 ± 10.01 | 56 | 30 | 138 | 2012–2013 | 6M | Prospective |
| Diao/2017 [23] | China | 61.5% | 55.1 ± 9.6 | 26 | 32.9 ± 5.13 | 60 | 2013–2014 | 16M | Prospective |
| Ding/2017 [24] | China | 64.5 | 53 ± 6.75 | 40 | 25–35 | NA | 2014–2015 | 6M | Retrospective |
| Liao/2017 [25] | China | 22.2% | 38.67 ± 8.32 | 18 | NA | 56 | 2015–2016 | 12M | Prospective |
| Liu/2017 [26] | China | 41.2 | 43.05 ± 7.71 | 34 | 25–35 | NA | 2014–2016 | 6M | Prospective |
| Zhuo/2017 [27] | China | 51% | 57.3 ± 12.9 | 51 | 25 | 96 | 2014–2015 | 11.1M | Prospective |
| Jiang/2019 [28] | China | 45.4% | 53.2 ± 14.2 | 33 | 25–35 | 115 | 2015–2017 | 24M | Retrospective |
| Li-a/2019 [29] | China | 33.3% | 49.7 ± 9.9 | 9 | 30 | 14 | 2016–2017 | 17.2M | Retrospective |
| Li-b/2019 [30] | China | 40% | 53.2 ± 10.3 | 20 | 30 | 22 | 2014–2016 | 15.3M | Retrospective |
| Zhuo/2019 [31] | China | 45.7% | 49.8 ± 12.9 | 35 | 25 | 63 | 2015–2017 | 15.9M | Prospective |
| Cao/2020 [32] | China | 49% | 50.8 ± 11.2 | 51 | NA | 83 | 2015–2018 | 6M | Retrospective |
| Fang/2020 [33] | China | 35.7% | 53.5 ± 12.44 | 14 | 30 | 42 | 2016–2018 | 6M | Retrospective |
| Kong/2020 [34] | China | 46.7% | 52.3 ± 8.74 | 60 | NA | 164 | 2017–2018 | 6M | Retrospective |
| Ma/2020 [35] | China | 56.3% | 55.38 ± 15.17 | 16 | 25–45 | 52 | 2014–2016 | 6M | Retrospective |
| Pan/2020 [36] | China | 35.7% | 52.46 ± 8.19 | 28 | 30–50 | NA | 2017–2019 | 6M | Retrospective |
| Song/2020 [37] | China | 58.6% | 69.1 ± 9.4 | 29 | 35 | NA | 2017–2019 | 6M | Retrospective |
| Xiao/2020 [38] | China | 48.8% | 49.5 ± 14.9 | 41 | 30 | NA | 2014–2019 | 6M | Retrospective |
| Wei/2020 [39] | China | 48.5 | 50.35 ± 13.12 | 171 | 30 | NA | 2018–2019 | 6M | Retrospective |
| Yu/2020 [40] | China | 40% | 48.9 ± 9.1 | 20 | 30 | 34 | 2016–2018 | 3M | Retrospective |
| Diao/2021 [41] | China | 51.1 | 53.3 ± 10.8 | 47 | 25–35 | 94 | 2010–2019 | 60M | Retrospective |
| Li/2021 [42] | China | 61.5 | 54.23 ± 10.96 | 13 | 25–35 | 26 | 2015 | 58M | Retrospective |
| Wang/2021 [43] | China | 37.7 | 50.1 ± 10.3 | 53 | 25–35 | NA | 2016–2020 | 41M | Retrospective |

Abbreviations: MWA: microwave ablation; Y: years; M: months; NA: not available.
Alkaline phosphatase (ALP) levels
Data regarding the ALP levels were reported in five articles. The ALP measurements obtained on day 1 after microwave ablation showed no significant differences (WMD = 17.67, 95% CI: -14.06 to 49.41, p = 0.999, I² = 0%) (Figure 5(A)) from those obtained before microwave ablation. However, the ALP levels were significantly reduced at the end of the follow-up period (WMD = 133.88, 95% CI: 9.93 to 257.82, p = 0.002, I² =77.2%) (Figure 5(B)) after microwave ablation of SHPT patients.

Adverse events
Hypocalcemia
Data regarding the incidence of hypocalcemia were reported in 13 articles. The incidence of hypocalcemia after microwave ablation of SHPT patients was shown to be 35.2% (136/386; ES = 0.35, 95% CI: 0.21 to 0.49, p < 0.001, I² =93.7%) (Figure 6(A)).

Table 2. Quality assessment of included studies by NOS.

| Author  | Year | Selection | Comparability | Outcome |
|---------|------|-----------|---------------|---------|
| Luo [18]| 2015| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Diao [19]| 2016| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Gao [20]| 2016| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Yu [21]| 2016| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Zhao [22]| 2016| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Diao [23]| 2017| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Ding [24]| 2017| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Liao [25]| 2017| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Liu [26]| 2017| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Zhao [27]| 2017| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Jiang [28]| 2019| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Li-a [29]| 2019| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Li-b [30]| 2019| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Zhuo [31]| 2019| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Cao [32]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Fang [33]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Kong [34]| 2021| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Ma [35]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Pan [36]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Song [37]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Xiao [38]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Yu [39]| 2020| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Wei [40]| 2021| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |
| Wang [41]| 2021| ★★★★☆☆☆ | ★★★★☆☆☆ | ★★★★☆☆☆ |

(WMD = 0.35, 95% CI: 0.20 to 0.49, p < 0.001, I² = 72.7%) (Figure 4(D)) after microwave ablation of SHPT patients.

Figure 2. Forest plots showing PTH levels in SHPT patients before and after MWA. A) Week 1; B) 1 month; C) at 6 months; and D) end of follow-up period.
Hoarseness
Data regarding the incidence of hoarseness were reported in 13 articles. The incidence of hoarseness after microwave ablation of SHPT patients was shown to be 9.2% (41/447; ES = 0.07, 95% CI: 0.04~0.11, p = 0.097, I² = 35.8%) (Figure 6(B)).

Nerve injury
Data regarding the incidence of nerve injury were reported in 7 articles. The incidence of nerve injury after microwave ablation of SHPT patients was found to be 7.2% (18/251; ES = 0.04, 95% CI: 0.02~0.07, p = 0.189, I² = 31.3%) (Figure 6(C)).

Hematoma
Data regarding the incidence of hematoma were reported in 7 articles. The results showed that the incidence of hematoma after microwave ablation of SHPT patients was 3.6% (8/222; ES = 0.03, 95% CI: 0.01~0.05, p = 0.913, I² = 0%) (Figure 6(D)).

Subcutaneous edema
Data on the incidence of subcutaneous edema were reported in 3 articles. The incidence of subcutaneous edema after microwave ablation of SHPT patients was shown to be 9.5% (13/137; ES = 0.09, 95% CI: 0.04~0.14, p = 0.79, I² = 0%) (Figure 6(E)).

Swallowing water
Data regarding the incidence of swallowing water has been reported in 4 articles. It was shown that the incidence of swallowing water after microwave ablation of SHPT patients was 10% (19/190; ES = 0.08, 95% CI: 0.04~0.12, p = 0.199, I² = 35.6%) (Figure 6(F)).

Sensitivity analysis
Sensitivity analyses were performed to examine the influence of exclusion of each study on the combined results, and assess the robustness of all results. Each study was excluded at a time, and the pooled results of the remaining studies showed no significant differences (Supplementary Figure 1).
Publication bias

The funnel plots for meta-analysis of US-guided microwave ablation for SHPT are shown in Supplementary Figure 2. The results of Begg’s and Egger’s tests (PTH levels: Begg’s test $p=0.276$, Egger’s test $p=0.637$; Calcium levels: Begg’s test $p=0.858$, Egger’s test $p=0.916$; Phosphorus levels: Begg’s test $p=0.251$, Egger’s test $p=0.355$) indicated no evidence of publication bias.
Discussion

Despite potential complications associated with parathyroidectomy, such as transient or permanent hypocalcemia and laryngeal nerve injury, SHPT patients still obtained many benefits from this surgery. These include improvements in serum phosphorus and calcium levels, bone density, survival and relief from symptoms. Therefore, the Kidney Disease Improving Global Outcomes (KDIGO) currently recommends parathyroidectomy for patients with severe SHPT who are ineffective to drug treatment [50]. However, parathyroidectomy is not suitable for all patients with severe SHPT due to various reasons, such as preoperative hypocalcemia, the elderly with multiple comorbidities. Therefore, treatment strategies remain challenging in these patients and for clinicians.

Several recent preliminary studies have confirmed that the destruction of parathyroid tissue in SHPT patients by

Figure 6. Forest plots showing complications in SHPT patients after MWA. A) Hypocalcemia; B) hoarseness; C) nerve injury; D) hematoma; E) subcutaneous edema; and F) swallowing water.
ultrasound-guided MWA is considered as a safe and effective approach [14,28,30]. In this study, the efficacy and safety of US-guided MWA of SHPT patients were evaluated by systematic review and meta-analysis. Eighteen studies consisting of 932 patients were included. Our meta-analysis results revealed that PTH, serum calcium and phosphorus levels were significantly reduced at week 1, 1 month, 6 months and end of the follow-up period after MWA of SHPT patients.

Different from the results of previous meta-analysis study [51], the current meta-analysis study has fully gathered the data from a wide range of results and provided more in-depth insights on important clinical results. Also, due to the inclusion of additional studies and larger amounts of pooling, the results are different from that of the previous meta-analysis. A previous meta-analysis conducted by Cao et al. [51] has been limited due to inclusion of only eight studies that compared pre-ablative and post-ablative clinical results. The present study included 18 additional eligible studies. In addition, the results of this meta-analysis are not exactly the same as those of Cao et al. on the primary outcomes assessed. Cao et al. found no significant differences in terms of calcium levels at 6 months after MWA of SHPT patients, which were inconsistent with that of the previous meta-analysis. However, the present results indicated that calcium levels were significantly reduced at 6 months after MWA in patients with SHPT. The difference in these results might again be due to the larger sample size of this study as compared to the previous studies.

The side effects and minor complications reported in the present study included subcutaneous edema (9.5%), swallowing water (10%), transient hoarseness (9.2%) and hypocalcemia (35.2%). In contrast, recurrent or persistent SHPT patients after percutaneous ethanol injection therapy (PET) experienced transient hoarseness (5–30.6%) and hypocalcemia (40.8%) [52,53], and transient hoarseness (16.7%) after laser ablation [54]. Minor complications or side effects after high-intensity focused ultrasound (HIFU) treatment of SHPT patients included mild subcutaneous edema (60%), prolonged vocal cord dysfunction (40%), difficulty in swallowing water (20%), and prolonged bitonal voice (20%) [55]. However, the main complications and mortality rates associated with surgery are 6–21.6% and 1.7% respectively. The major complications included permanent mono- or double-sided laryngeal nerve injury, permanent parathyroid dysfunction, wound infection, postoperative hemorrhage and pneumonia [56,57].

However, there are some limitations in this study that should be acknowledged. Firstly, the heterogeneity included in this study was significant and observed throughout the analysis. Despite the heterogeneity observed in the study, the results of sensitivity analysis were considered reliable and robust. Secondly, most of the samples included in this trial were small. Thirdly, although published bias and sensitivity analyses confirmed the credibility of our analysis, this meta-analysis still showed heterogeneity due to several factors such as patient characteristics, sample size and treatment procedures that were not included in our analysis. Finally, most of the articles included were retrospective studies, and not randomized controlled trials. This limitation leaves a large gap in the existing evidence, and so further analysis of randomized controlled trials should be conducted. These factors should be clarified in the future research.

In summary, this meta-analysis indicated that MWA significantly reduced PTH, serum calcium and phosphorus levels in SHPT patients without increasing overall complications. Therefore, MWA is considered as a minimally invasive technique that is safe and effective for the management of SHPT. In addition, large-scale studies, such as randomized controlled trials, should be designed in the future to obtain more results.

Disclosure statement
No potential conflict of interest was reported by the author(s).

Funding
The study was supported by the Science and Technology Bureau of Changshu City, Jiangsu Province in 2019(CS201911).

ORCID
Mingjia Gu http://orcid.org/0000-0001-9677-8279

References
[1] Tentori F, Wang M, Bieber BA, et al. Recent changes in therapeutic approaches and association with outcomes among patients with secondary hyperparathyroidism on chronic hemodialysis: the DOPPS study. CJASN. 2015;10(1):98–109.
[2] Druke TB. Cell biology of parathyroid gland hyperplasia in chronic renal failure. J Am Soc Nephrol. 2000;11(6):1141–1152.
[3] Hargrove GM, Pasieka JL, Hanley DA, et al. Short- and long-term outcome of total parathyroidectomy with immediate autografting versus subtotal parathyroidectomy in patients with end-stage renal disease. Am J Nephrol. 1999;19(5):559–564.
[4] Saunders RN, Karoo R, Metcalfe MS, et al. Four gland parathyroidectomy without reimplantation in patients with chronic renal failure. Postgrad Med J. 2005;81(954):255–258.
[5] Goldsmith D, Kothawala P, Chalian A, et al. Systematic review of the evidence underlying the association between mineral metabolism disturbances and risk of fracture and need for parathyroidectomy in CKD. Am J Kidney Dis. 2009;53(6):1002–1013.
[6] Floege J, Kim J, Ireland E, et al.; on behalf of the ARO Investigators. Serum iPTH, calcium and phosphate, and the risk of mortality in a European haemodialysis population. Nephrol Dial Transplant. 2011;26(6):1948–1955.
[7] Akizawa T, Akiba T, Hirakata H, et al. Comparison of paricalcitol with maxacalcitol injection in Japanese hemodialysis patients with secondary hyperparathyroidism. Ther Apher Dial. 2015;19(3):225–234.
[8] Komaba H, Moriwaki K, Goto S, et al. Cost-effectiveness of cinacalcet hydrochloride for hemodialysis patients with severe secondary hyperparathyroidism. Ther Apher Dial. 2015;19(3):225–234.
[9] Zhang Q, Li M, You L, et al. Effects and safety of calcimimetics in end stage renal disease patients with secondary hyperparathyroidism: a meta-analysis. PloS One. 2012;7(10):e48807.
[10] Raggi P, ADVANCE Study Group, Chertow GM, Torres PU, Csiky B, Naso A, Nossuli K; et al. The advance study: a randomized study to evaluate the effects of cinacalcet plus low-dose vitamin D on
vascular calcification in patients on hemodialysis. Nephrol Dial Transplant. 2011;26(4):1327–1339.

[11] Torres PU, Prie D, Beck L, et al. New therapies for uremic secondary hyperparathyroidism. J Ren Nutr. 2006;16(2):87–99.

[12] Xu SY, Wang Y, Xie Q, et al. Percutaneous sonography-guided radiofrequency ablation in the management of parathyroid adenoma. Singapore Med J. 2013;54(7):e137–e140.

[13] Kovatcheva R, Vlahov J, Stoinov J, et al. US-guided high-intensity focused ultrasound as a promising non-invasive method for treatment of primary hyperparathyroidism. Eur Radiol. 2014;24(9):2052–2058.

[14] Zhuo L, Peng LL, Zhang YM, et al. US-guided microwave ablation of hyperplastic parathyroid glands: safety and efficacy in patients with end-stage renal disease-a pilot study. Radiol. 2017;282(2):576–584.

[15] Liu F, Yu X, Liu Z, et al. Comparison of ultrasound-guided percutaneous microwave ablation and parathyroidectomy for primary hyperparathyroidism. Int J Hyperth. 2019;36(1):835–840.

[16] Moher D, PRISMA Group, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151(4):264–269.

[17] Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603–605.

[18] Miller JJ. The inverse of the Freeman-Tukey double arcsine transformation. Am Statist. 1978;32(4):138.

[19] Egger M, Smith GD, Schneider M, et al. Bias in meta-analysis. BMJ. 2003;327(7414):557–560.

[20] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. Eur J Epidemiol. 2010;25(9):603–605.

[21] Diao Z, Liu X, Qian L, et al. Efficacy and its predictor in microwave ablation for recurrent and persistent secondary hyperparathyroidism after parathyroidectomy: a retrospective pilot study. Int J Hyperth. 2016;32(2):180–186.

[22] Gao Z, Xiao L, Feng J, et al. Ultrasound-guided microwave thermal ablation for the treatment of severe secondary hyperparathyroidism in maintenance hemodialysis. CJITWN. 2016;17(12):1072–1073.

[23] Zhao J, Qian L, Zu Y, et al. Efficacy of ablation therapy for secondary hyperparathyroidism by ultrasound guided percutaneous thermoablation. Ultrasound Med Biol. 2016;42(5):1058–1065.

[24] Ding X, Chen Y, Wu Y, et al. Comparison of efficacy between microwave ablation and parathyroidectomy for secondary hyperparathyroidism. J Minim Invasive Med. 2017;12(3):334–337.

[25] Liu J. The effect of microwave ablation on secondary hyperparathyroidism. JCM. 2017;15(4):57–58.

[26] Liu X, An C, Yu M, et al. US-guided microwave ablation for secondary hyperparathyroidism in patients after renal transplantation: a pilot study. Int J Hyperth. 2019;36(1):322–327.

[27] Zhao J, Qian L, Zu Y, et al. Efficacy and safety of microwave ablation for severe secondary hyperparathyroidism in maintenance hemodialysis patients. Hemodial Int Symp Home Hemodial. 2019;23(2):247–253.

[28] Ma H, Ouyang C, Huang Y, et al. Comparison of microwave ablation treatments in patients with renal secondary and primary hyperparathyroidism. Ren Fail. 2020;42(1):66–76.

[29] Xiao R, Zhao Z, Wei Y, et al. Safety and efficacy of modified liquid isolation method in microwave ablation in treatment of secondary hyperparathyroidism. Chin J Interv Imaging Ther. 2020;17(3):137–140.

[30] Fang J, Zhao W, Li Q, et al. Ultrasound-guided microwave ablation for secondary hyperparathyroidism: the analysis of short-term efficacy. Chinese J Ultrasound Med. 2020;36(5):476–479.

[31] Song J. The study of clinical effects of microwave ablation in the treatment of secondary hyperparathyroidism. Master’s Thesis. 2019;1(1):1–43.

[32] Wei Y, Yu MA, Qian LX, et al. Hypocalcemia after ultrasound-guided microwave ablation and total parathyroidectomy for secondary hyperparathyroidism: a retrospective study. Int J Hyperth. 2020;37(1):819–825.

[33] Diao Z, Qian L, Teng C, et al. Microwave ablation versus parathyroidectomy for severe secondary hyperparathyroidism in patients on hemodialysis: a retrospective multicenter study. Int J Hyperth. 2021;38(1):213–219.

[34] Li D, Wang G, Chen X, et al. Long-term effect of microwave ablation on patients undergoing hemodialysis for moderate secondary hyperparathyroidism: a retrospective cohort study. J Ultrasound Med: Off J Am Ins Ultrasound Med. 2021. DOI:10.1002/jum.15638

[35] Wang K, Gao Z, Liu S, et al. Long-term outcomes of microwave ablation for secondary hyperparathyroidism in maintenance hemodialysis patients. Ther Apheresis and Dial: Off Peer-Rev J Int Soc Apheresis, Japanese Soc for Apheresis, Japanese Soc for Dial Ther. 2021. DOI:10.1111/1744-9987.13640

[36] Li X, Wei Y, Shao H, et al. Efficacy and safety of microwave ablation for ectopic secondary hyperparathyroidism: a feasibility study. Int J Hyperth. 2019;36(1):647–653.

[37] Yu M, Cao X, Peng L, et al. Ultrasound-guided microwave ablation of secondary hyperparathyroidism after renal transplantation. Chin J Interv Imaging Ther. 2020;17(3):133–136.
[50] KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl. 2009;(113): S1–S130.

[51] Cao XJ, Zhao ZL, Wei Y, et al. Efficacy and safety of microwave ablation treatment for secondary hyperparathyroidism: systematic review and meta-analysis. Int J Hyperth. 2020;37(1):316–323.

[52] Chen H, Lin C, Wu C, et al. Chemical ablation of recurrent and persistent secondary hyperparathyroidism after subtotal parathyroidectomy. Ann Surg. 2011;253(4):786–790.

[53] Ospina NS, Thompson GB, Lee RA, et al. Safety and efficacy of percutaneous parathyroid ethanol ablation in patients with recurrent primary hyperparathyroidism and multiple endocrine neoplasia type 1. J Clin Endocrinol & Metab. 2015;100(1).

[54] Andrioli M, Riganti F, Pacella CM, et al. Long-term effectiveness of ultrasound-guided laser ablation of hyperfunctioning parathyroid adenomas: present and future perspectives. AJR Am J Roentgenol. 2012;199(5):1164–1168.

[55] Kovatcheva R, Vlahov J, Stoinov J, et al. High-intensity focussed ultrasound (HIFU) treatment in uraemic secondary hyperparathyroidism. Nephrol Dial Transplant. 2012;27(1):76–80.

[56] Nawrot I, Chudziński W, Ciačka T, et al. Reoperations for persistent or recurrent primary hyperparathyroidism: results of a retrospective cohort study at a tertiary referral center. Med Sci Monit. 2014;20:1604–1612.

[57] Yue W, Chen L, Wang S, et al. Locoregional control of recurrent papillary thyroid carcinoma by ultrasound-guided percutaneous microwave ablation: a prospective study. Int J Hyperth. 2015; 31(4):403–408.