

## Original Research Article

# Effect of combined vitamin D and microwave ablation of parathyroid glands on blood pressure and cardiac function in maintenance-hemodialysis patients with uremic secondary hyperparathyroidism

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### Abstract

**Purpose:** To investigate the effect of microwave ablation of parathyroid glands in combination with active vitamin D on blood pressure and cardiac function in maintenance-hemodialysis patients with uremic secondary hyperparathyroidism.

**Methods:** One hundred and twenty maintenance-hemodialysis patients with uremic secondary hyperparathyroidism admitted to Meizhou People's Hospital were assigned to 2 groups (A and B) in the order of their admission. Each group had 60 patients. Both groups were treated with active vitamin D, while patients in group A were, in addition, subjected to microwave ablation of parathyroid glands. Blood pressure, and indices for cardiac function, thyroid function and anemia were determined.

**Results:** After treatment, the blood pressure of group A was significantly lower than that of group B ( $p < 0.05$ ). Moreover, after treatment, there were significant improvements in indices of cardiac function, thyroid function and anemia in group A patients, relative to group B patients.

**Conclusion:** Microwave ablation of parathyroid glands, when combined with active vitamin D, improves blood pressure, cardiac function and anemia status. Furthermore, the combined therapy enhances recovery of thyroid function in maintenance-hemodialysis patients with uremic secondary hyperparathyroidism. However, the combined therapy should be subjected to further clinical trials prior to application in clinical practice.

**Keywords:** Microwave ablation, Parathyroid glands, Active vitamin D, Hyperparathyroidism

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## INTRODUCTION

The number of people affected by chronic kidney disease has increased worldwide in recent years. Therefore, hemodialysis has become an important method for prolonging the lives of the

affected patients. However, long-term illness and continuous hemodialysis lead to many complications, an example of which is uremic secondary hyperparathyroidism [1-3]. Uremic secondary hyperparathyroidism not only causes skin pruritus, renal anemia and decreased quality

of sleep, but also accentuates cardiovascular calcification and increases mortality of patients. Therefore, there is need to carry out more studies on the treatment of uremic secondary hyperparathyroidism. Due to vitamin D deficiency in maintenance-hemodialysis patients, vitamin D drugs are often used in the treatment of uremic secondary hyperparathyroidism. However, these drugs are relatively expensive, and long-term medication leads to drug resistance, resulting in unsatisfactory long-term efficacy of active vitamin D when used alone [4-7]. As awareness of uremic secondary hyperparathyroidism continues to increase, the Kidney Disease Improving Global Outcomes (KDIGO) organization has proposed surgical treatment for uremic patients with secondary hyperparathyroidism. However, some uremic patients have poor cardiopulmonary function, and so cannot tolerate general anesthesia. Therefore, the application of conventional parathyroidectomy is limited.

At present, microwave ablation technology has made significant progress. The technology of microwave ablation involves using a microwave needle to puncture into the tumor tissues, resulting in tissue dehydration and necrosis due to frictional heating. Thus, it results in therapeutic effect [8-11]. The present research was carried out to study the influence of microwave ablation of parathyroid glands when used in combination with active vitamin D on blood pressure and cardiac function in 120 maintenance-hemodialysis patients with uremic secondary hyperparathyroidism.

## METHODS

### General profile of patients

The 120 selected maintenance-hemodialysis patients with uremic secondary hyperparathyroidism served as subjects in this study. The research subjects were assigned to 2 groups (A and B) according to their order of admission. There were 60 patients in each group. The research received approval from the ethical authority of *Meizhou People's Hospital* (approval no. 20181190), and was carried out in line with the guidelines of the Declaration of Helsinki [12]. The patients or their family members had a full understanding of the processes involved in the research process, and they submitted letters of consent with their signatures.

### Inclusion criteria

In this study, subjects who were diagnosed with uremic secondary hyperparathyroidism through

examination, with parathyroid hormone level above 800 ng/L, and patients who had received maintenance hemodialysis for more than 3 years [13].

### Exclusion criteria

The excluded patients were those with mental problems and those who had communication problems, those suffering illnesses in other organs, those with serious infections and low albumin levels [14], patients with inadequate dialysis, and patients with severe malnutrition.

### Treatments

All patients took active vitamin D daily according to the guidelines of *General Understanding on Reasonable Application of Active Vitamin D in Hyperparathyroidism Secondary to Chronic Kidney Disease* (revised edition) [15], and the treatment lasted for 3 months. In addition, patients in group A were subjected to microwave ablation of parathyroid glands, specifically as follows: an experienced doctor was selected to carry out the whole process of microwave ablation of parathyroid glands. First, the nodule location and echo features of the patient were examined using ultrasonic equipment (Germany Nicolet, TC8080). Then, a microwave equipment (Chengdu Jinjiang Microwave Electric Appliance Factory; National medical equipment health certificate no. 000263) was used for the follow-up operation. Under ultrasound guidance, the ablation needle was inserted into the hyperplastic parathyroid gland, and the instrument was switched on to trigger parathyroid ablation. After ablation, contrast-enhanced ultrasound was used to judge the ablation status of the lesions. After treatment, the ablation area was continuously pressed with the palm for 0.5 h, and the patient was monitored for 2 h.

### Evaluation of indices/parameters

#### Blood pressure

The patients were made to sit and rest for 10 min, with their feet naturally flat on the floor, and a standard mercury sphygmomanometer (Jiangsu Yuwell Medical Equipment & Supply Co. Ltd; Jiangsu Medical Products Administration, certificate no. 20152070945) was used to measure diastolic blood pressure and systolic blood pressure. The mean arterial pressure of the patients was computed as in Eq 1.

$$MAP = \frac{SBP + DBP \times 2}{3} \dots\dots\dots (1)$$

where *MAP* = mean arterial pressure, *SBP* = systolic blood pressure, *DBP* = diastolic blood pressure.

### Cardiac function indices

Color Doppler ultrasonography [GE Healthcare, Color ultrasonography Voluson P6, NMPA (I)20152062178] was used to examine the apical four-chamber section by setting the frequency of the three-dimensional probe at 2.0 - 3.8 mhz. Under the full volume mode, images of three consecutive stable cardiac cycles at the end-expiratory hold were collected, and the values of left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVDD) and interventricular septal thickness (IVST) were recorded and compared before and after treatment.

### Thyroid function indices

Following early morning fast, venous blood was taken from each subject. The serum levels of parathyroid hormone (PTH),  $Ca^{2+}$  and  $P^{3-}$  were measured with Sysmex CHEMIX-800 Automatic Biochemical Analyzer {NMPA (I)20112403311}, with matching agents. The PTH,  $Ca^{2+}$  and  $P^{3-}$  levels of the patients were compared before treatment, 1 month after treatment, 6 months after treatment and 1 year after treatment.

### Anemia indices

Venous blood was taken from each subject following a morning fast, and the Sysmex CHEMIX-800 automatic biochemical analyzer was used to determine the levels of hemoglobin (Hb), hematocrit (Hct) and erythropoietin (EPO). The Hb, Hct and EPO levels of the patients were compared before and after treatment.

### Statistical analysis

Data processing was done using SPSS 20.0, while graphs were prepared with GraphPad Prism 7. Data are presented as mean  $\pm$  SD. Statistical comparison was carried out with Chi square test and *t*-test. Values of  $p < 0.05$  were indicative of statistically significant differences.

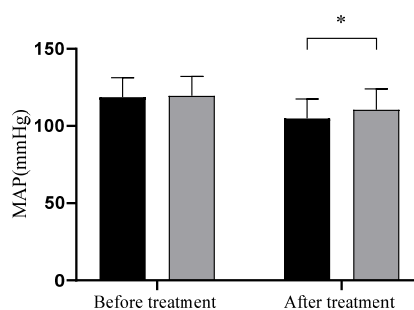
## RESULTS

### General patient data

Table 1 shows that general data were comparable in both groups.

### Blood pressure

Before treatment, the MAP was  $118.65 \pm 12.65$  mmHg in group A, and  $119.54 \pm 12.68$  mmHg in group B. After treatment, the MAP was ( $104.98 \pm 12.57$ ) mmHg in group A, and ( $110.58 \pm 13.52$ ) mmHg in group B. After treatment, the blood pressure of group A was significantly lower than that of group B ( $P < 0.05$ ), as shown in Figure 1.



**Figure 1:** Blood pressure values in the 2 groups ( $\bar{x} \pm s$ , mmHg). The black bars represent group A while gray bars represent group B; \*  $p < 0.05$

**Table 1:** General profile of patients

Item	Group A (n = 60)	Group B (n = 60)	$\chi^2/t$	P-value
Gender			0.034	0.853
Male	35	34		
Female	25	26		
Age (years)				
Range	32-74	33-74		
Mean	51.21±6.20	51.23±6.21	0.018	0.986
Hypertension	10	12	0.223	0.637
Diabetes mellitus	5	4	0.120	0.729
Cardiopulmonary disease	10	9	0.063	0.803
Thoracic deformity	3	3	< 0.001	< 0.001
Mean dialysis time (months)	87.65±30.12	88.65±31.56	0.178	0.859

**Table 2:** Comparison of cardiac function indices of patients in the two groups (mean ± SD)

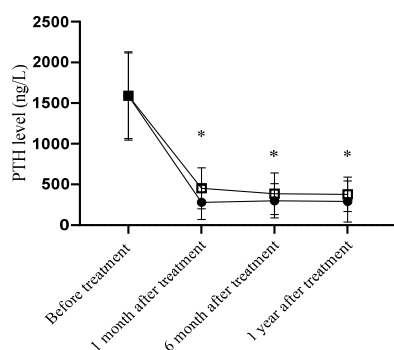
Item	LVEF (%)		LVDD (mm)		IVST (mm)	
	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy
A	46.12±7.59	56.12±7.58	57.56±5.45	50.65±5.54	16.59±2.57	12.11±2.10
B	46.52±7.54	51.11±5.68	57.98±5.26	53.11±5.68	16.98±2.54	15.21±2.65
t	0.290	4.097	0.430	2.402	0.836	7.102
P-value	0.773	< 0.001	0.668	0.018	0.405	< 0.001

**Cardiac function indices**

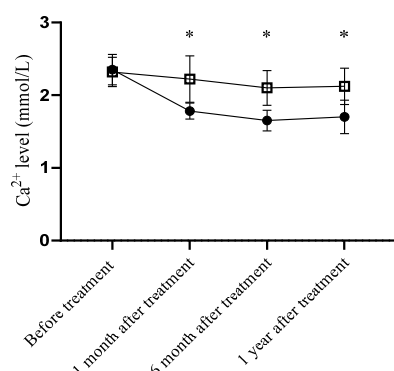
Table 2 indicates that after treatment, there were better cardiac function parameters in group A than in group B ( $p < 0.05$ ).

**Thyroid function indices**

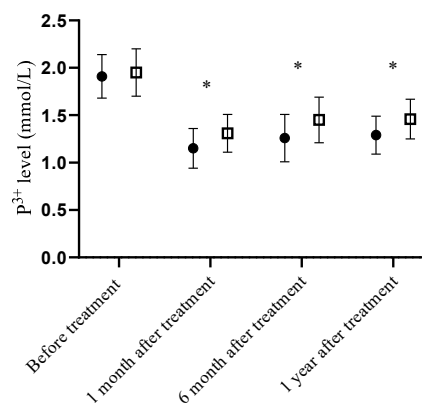
After treatment, the thyroid function indexes in group A were markedly improved, relative to group B, as presented in Figure 2, Figure 3 and Figure 4.



**Figure 2:** Comparison of PTH levels of patients (mean ± SD, ng/L). The dotted line represents group A, while the line with hollow squares represents group B. \* $P < 0.05$



**Figure 3:** Comparison of Ca<sup>2+</sup> levels of patients (mean ± SD, mmol/L). The line with dots represents group A while the line with hollow squares represents group B. \* $p < 0.05$



**Figure 4:** Comparison of P<sup>3+</sup> levels of patients ( $\bar{x} \pm s$ , mmol/L). The dots denote group A while the hollow squares denote group B

**Anemia indices**

As shown in Table 3, after treatment, the anemia indexes of group A were significantly better than those of group B ( $p < 0.05$ ).

**DISCUSSION**

Uremia occurs at the terminal stage of chronic kidney disease. Uremic patients often use maintenance hemodialysis to prolong their lives. However, long-term hemodialysis leads to complications such as uremic secondary hyperparathyroidism which adversely affects prognosis of uremia. In clinical practice, drug therapy is often used to treat uremic secondary hyperparathyroidism, but the patients are prone to developing drug resistance during the treatment. The Global Organization for Chronic kidney disease has recommended parathyroidectomy as a surgical treatment for chronic kidney disease, but some patients cannot be treated with this surgical treatment due to poor tolerance and other reasons. Therefore, it is extremely important to carry out more studies new and more effective treatment strategies [16-19]. In recent years, microwave ablation has been used in the treatment of many tumors. This treatment has remarkable advantages such as mini-incision and convenience.

**Table 3:** Comparison of anemia indexes of patients (mean  $\pm$  SD)

Group	Hb (g/L)		Hct (%)		EPO [U/(kg·week)]	
	Before therapy	Post-treatment	Pre-therapy	Post-therapy	Before treatment	After treatment
A	98.12 $\pm$ 12.65	130.98 $\pm$ 15.11	30.56 $\pm$ 5.24	38.98 $\pm$ 4.21	241.98 $\pm$ 60.65	110.98 $\pm$ 25.11
B	98.55 $\pm$ 12.54	124.51 $\pm$ 13.68	30.15 $\pm$ 5.26	32.15 $\pm$ 4.15	242.98 $\pm$ 62.15	130.65 $\pm$ 25.56
<i>t</i>	0.187	2.459	0.428	8.949	0.089	4.252
<i>P</i> -value	0.852	0.015	0.670	< 0.001	0.929	< 0.001

It is not clear whether microwave ablation can be used to treat uremic patients with secondary hyperparathyroidism. However, from a practical point of view, microwave ablation has a faster heating rate and wider ablation area than other ablation techniques.

Therefore, theoretically speaking, microwave ablation of parathyroid glands can be applied to uremic patients with secondary hyperparathyroidism who are unable to undergo surgical treatment. In the present research, subjects in group A who received combined therapy had markedly better thyroid function indexes after treatment than subjects in group B. This result showed that microwave ablation of parathyroid glands in combination with active vitamin D had produced superior therapeutic effect, relative to that of single drug therapy. Therefore, the combined treatment may be one of the treatment options for these patients.

Uremic patients usually have high blood pressure and need to take a lot of antihypertensive drugs during hemodialysis. However, for some patients, single drug therapy produces little effect, such that the patients still face the problem of high blood pressure. The PTH in uremic patients with secondary hyperparathyroidism increases the rate of secretion of aldosterone, thereby increasing sodium retention and pe-disposing the patients to risk of hypertension. Microwave ablation of parathyroid glands reduces the level of PTH and calcium in patients, thereby reducing the patient's blood pressure index [20-22].

Parathyroid hormone (PTH), a major index in the pathogenesis of uremic secondary hyperparathyroidism, not only affects the blood pressure level in patients, but also affects their renal anemia. The present research showed improved anemia indexes in group A after treatment, when compared with group B, indicating that with decrease PTH, there were significant improvements in Hb and HCT; EPO consumption was significantly reduced, and anemia status of patients was significantly improved. The decrease in Hb is closely related to vitamin D. Indeed, vitamin D supplementation increases Hb level of patients. Thus, the anemia status of both groups was significantly improved

after treatment. However, the relationship between vitamin D and anemia has not been elucidated, indicating the need for further investigations in this area [23, 24].

Uremic secondary hyperparathyroidism usually affects multiple organs in patients, and PTH has a significant negative impact on cardiac function in patients. Under the condition of persistent high PTH in patients, cardiac myocytes gradually become hypertrophic, and there are significant increases in insulin-like growth factor levels and significant increases in mitochondrial apoptosis. These changes indicate that uremic secondary hyperparathyroidism increases the possibility of cardiac death in patients, which is serious threat to their lives. After the combined treatment using microwave ablation of parathyroid glands and active vitamin D, there were improvements in cardiac function indexes of both groups, but the indexes were better in group A, indicating that microwave ablation of parathyroid glands was effective in improving patients' cardiac function. Therefore, this treatment method has high clinical value based on its potential to promote heart recovery in the patients.

In a previous study in which one group received combination of active vitamin d and microwave ablation of parathyroid glands, while the other group was given active vitamin D, the LVEF was markedly higher in the combined treatment group [25]. The results indicate that microwave ablation of parathyroid glands improved the patients' cardiac function, which is in agreement with the data obtained in the current investigation.

## CONCLUSION

The findings of this study show that the combined therapy of microwave ablation of parathyroid glands and active vitamin D improves blood pressure, cardiac function and anemia status, and enhances the recovery of thyroid function of maintenance-hemodialysis patients with uremic secondary hyperparathyroidism. However, the combined therapy should be subjected to further clinical trials prior to use in clinical practice.

## DECLARATIONS

### Acknowledgements

None provided.

### Funding

None provided.

### Ethical approval

None provided.

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Conflict of Interest

No conflict of interest associated with this work.

### Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. XZ and YL conceived and designed the study, and drafted the manuscript. LC, CD and JH collected, analyzed and interpreted the experimental data. AZ, BQ and JL revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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## REFERENCES

1. Fujioka A, Imanishi Y, Kobayashi I, Hirakawa T, Inoue A, Harada K, Taguchi M, Sugiura Y, Yamada H, Miyaoka D, et al. Effect of etelcalcetide on parathyroid hormone secretion by primary hyperparathyroidism patient-derived primary parathyroid cells. *J Bone Miner Metab* 2021; 39(3): 396-403.
2. Malberti F, Corradi B, Cosci P, Colecchia M, Leopardi O, Grossi L, Oldini C, Imbasciati E. Different effects of calcitriol and parathyroidectomy on the PTH-calcium curve in dialysis patients with severe hyperparathyroidism. *Nephrol Dial Transplant* 1996; 11(1): 81-87.
3. Halfen DP, Caragelasco DS, Nogueira JPS, Jeremias JT, Pedrinelli V, Oba PM, Ruberti B, Pontieri CFF, Kogika MM, Brunetto MA. Evaluation of Electrolyte Concentration and Pro-Inflammatory and Oxidative Status in Dogs with Advanced Chronic Kidney Disease under Dietary Treatment. *Toxins (Basel)* 2019; 12(1): 3.
4. Elbers LPB, Wijnberge M, Meijers JCM, Poland DCW, Brandjes DPM, Fliers E, Gerdes VEA. VEA Coagulation and fibrinolysis in hyperparathyroidism secondary to vitamin D deficiency. *Endocr Connect* 2018: 325-333.
5. Rao AR, Kumar P, Gunasekaran V, Dey AB. Reversible chorea secondary to uremia in an older adult. *Aging Med (Milton)* 2019; 2(2): 118-120.
6. Levy AR, Xing S, Brunelli SM, Cooper K, Finkelstein FO, Germain MJ, Kimel M, Platt RW, Belozeroff V. Symptoms of Secondary Hyperparathyroidism in Patients Receiving Maintenance Hemodialysis: A Prospective Cohort Study. *Am J Kidney Dis* 2020; 75(3): 373-383.
7. Steidl GK, Kuo JH. Surgical Management of Secondary Hyperparathyroidism. *Kidney Int Rep* 2020; 6(2): 254-264.
8. Massicotte-Azarniouch D, McLean L, Brown PA. Uremic leontiasis ossea due to secondary hyperparathyroidism complicated by vitamin C deficiency in a non-adherent chronic hemodialysis patient: A case report. *Clin Nephrol Case Stud* 2019; 7: 54-59.
9. Strambu V, Bratucu M, Garofil D, Paic V, Zurzu M, Tigora A, Popa F, Radu P, Costin P. The Value of Imaging of the Parathyroid Glands in Secondary Hyperparathyroidism. *Chirurgia (Bucur)* 2019; 114(5): 541-549.
10. Plasc W, Vogt L, Kruijff S. Advances in Diagnosis and Management of Secondary and Tertiary Hyperparathyroidism. *Advances in Treatment and Management in Surgical. Endocrinology* 2020: 85-99.
11. Mizobuchi M, Ogata H, Koiwa F. Secondary Hyperparathyroidism: Pathogenesis and Latest Treatment. *Ther Apher Dial* 2019; 23(4): 309-318.
12. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013 Nov 27;310(20):2191-4.
13. Sadowski SM, Pusztaszeri M, Brulhart-Meynet MC, Petrenko V, De Vito C, Sobel J, Delucinge-Vivier C, Kebebew E, Regazzi R, Philippe J, et al. Identification of Differential Transcriptional Patterns in Primary and Secondary Hyperparathyroidism. *J Clin Endocrinol Metab* 2018; 103(6): 2189-2198.
14. Patel R, Wiederkehr M. Acute neurological syndrome complicating secondary hyperparathyroidism. *Proc (Bayl Univ Med Cent)* 2018; 31(4): 534-536.

15. Lacitignola L, Luca P, Santovito R, Comite MSD, Crovace A. Nutritional secondary hyperparathyroidism in two ponies. *Open Vet J* 2018; 8(2): 149-153.
16. Tominaga Y. *Surgical Management of Secondary and Tertiary Hyperparathyroidism. Surgery of the Thyroid and Parathyroid Glands (Third Edition)* 2021.
17. Uludag M, Kartal K. The Impact of Surgical Strategy on the Consequences of Secondary Hyperparathyroidism. *Ann Surg* 2018; 268(6): e62-e63.
18. Dralle H. [Is autotransplantation with parathyroidectomy for secondary hyperparathyroidism outdated?]. *Chirurg* 2019; 90(Suppl 2): 109.
19. Imanishi Y. [Secondary osteoporosis. Secondary osteoporosis by primary hyperparathyroidism.]. *Clin Calcium* 2018; 28(12): 1627-1634.
20. Bayya N, Rowell C, Malek D, Andrews RH, Dobzyniak C. CT-guided cryoablation of mediastinal parathyroid adenoma: an alternative to surgery. *Radiol Case Rep* 2020; 15(11): 2418-2421.
21. Freedman J. Microwave ablation of hepatocellular carcinomas in octogenarians. *Hepatoma Res* 2020; 6(3).
22. Lachenmayer A, Tinguely P, Maurer MH, Frehner L, Knöpfli M, Peterhans M, Weber S, Dufour JF, Candinas D, Banz V. Stereotactic image-guided microwave ablation of hepatocellular carcinoma using a computer-assisted navigation system. *Liver Int* 2019; 39(10): 1975-1985.
23. Peissig K, Condie BG, Manley NR. Embryology of the Parathyroid Glands. *Endocrinol Metab Clin North Am* 2018; 47(4): 733-742.
24. Farina L, Marco AD, Bottiglieri A, et al. Microwave ablation antenna for functional adenomas in the adrenal gland. 2020.
25. Ierardi AM, Biondetti P, Coppola A, et al. Clinical effect of combined treatment of parathyroid microwave ablation and active vitamin D on maintenance hemodialysis patients with uremia secondary hyperparathyroidism. *Gland Surgery* 2018; 7(2): 59-66.