

Effect of Parathyroidectomy on Quality of Life Among Patients Undergoing Dialysis

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Purpose: There is a limited evidence of durable effect of parathyroidectomy (PTX) on the quality of life (QoL) in dialysis populations. We aimed to investigate this concern by comparing the QoL scores in the pre- and post-PTX periods in a cohort of dialysis patients.

Patients and Methods: A total of 212 dialysis patients were enrolled in a hospital-facilitated dialysis center in China between July 1, 2016 and June 30, 2021. The mean age was 46.4 years; the male:female ratio was 96:116; hemodialysis 191, peritoneal dialysis 21. Informative data relating to demographics and dialysis were recorded for comparison. QoL was measured using the Chinese version of the Kidney Disease Quality of Life-36 (KDQOL-36™) and compared subscale scores between the pre-and post-PTX period. Appropriate statistical methods and Pearson's correlation test were used for statistical analysis.

Results: Nutritional markers, including hemoglobin and albumin, significantly increased post-PTX than pre-PTX. KDQOL-36 domain scale scores, including Symptoms and Problems of Kidney Disease, Burden of Kidney Disease, Effects of Kidney Disease (EKD), Physical Component Summary (PCS) score, and Mental Component Summary score, significantly increased post-PTX than pre-PTX. All patients were further stratified into three groups based on the PTX duration—0–2 years, >2–<5 years, and ≥5 years—and all KDQOL-36 domain scale scores increased in individual PTX durations. The PTX duration showed a significant negative correlation between PCS subscale scores and a positive correlation between EKD subscale scores.

Conclusion: PTX could improve QoL in dialysis patients with medically refractory secondary hyperparathyroidism. The durable effects should be studied using a larger sample.

Keywords: dialysis, Kidney Disease Quality of Life-36, parathyroidectomy

Introduction

Elevated circulating parathyroid hormone (PTH) concentrations commonly appear in chronic kidney disease (CKD), and secondary hyperparathyroidism (HPT) is used to describe this complication. Insights into the complex pathogenesis of increased PTH in CKD have improved in the past decades.^{1,2} Given this achievement, it is well recognized that PTH can elicit untoward biological effects, such as mineral bone disease, soft tissue and vascular calcification, cardiac and skeletal myopathy, unfavorable anemia, cognitive impairment, and sleep disturbance.^{1,3–8} Clinical observational studies have also demonstrated increased mortality risk in CKD with elevated PTH concentrations.^{9–12}

Recently, quality of life (QoL) has been emphasized in CKD, especially in dialysis patient care. Symptoms in CKD itself and CKD treatment influence QoL in the CKD population.¹³ Clinical manifestations of secondary HPT confer QoL to somatic complaints or psychological disturbances. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend that parathyroidectomy (PTX) is indicated in patients with high PTH concentrations (>800 pg/mL) and patients refractory to medical treatment.¹ It is reasonable to assume that PTX relieves and/or alleviates clinical complaints in CKD patients with secondary HPT. Thus, PTX has a positive effect on QoL in patients with CKD undergoing dialysis.

Importantly, several clinical observational studies have demonstrated the role of the intrinsic value of PTX in QoL improvement in end-stage renal disease-related HPT.^{4,14–18}

Patient-reported outcome measurements are often used to assess and monitor the QoL of patients with disease. In dialysis patients, the Kidney Disease Quality of Life 36-item short form survey (KDQOL-36) is one of the most widely used tools to measure QoL in patients with end-stage renal disease.¹⁹ The measurements include both generic and disease-specific components for QoL assessment. It offers an instrument to detect treatment effects and is responsive to changes in specific conditions for end-stage renal disease.

Herein, we investigated a longitudinal PTX effect on QoL in a cohort of dialysis patients. Our study aimed to compare psychometric and somatic components between the pre- and post-PTX periods in dialysis patients using the KDQOL-36™.

Patients and Methods

Data Sources

We screened dialysis patients who had received PTX between July 1, 2016 and June 30, 2021 at the Dalian University Affiliated Xinhua Hospital, China. The inclusion criteria were (1) adult dialysis patients (≥ 20 years); (2) attended regular outpatient hemodialysis (HD) sessions thrice a week and peritoneal dialysis (PD). The exclusion criteria were as follows: (1) patients who had initiated regular HD or PD after July 1, 2016; (2) patients who were older than 90 years; (3) patients transferred to other medical facilities; and (4) patients whose information was incomplete and/or those who were lost to follow-up during the study period. A total of 420 patients were screened for inclusion in the study. Among them, we defined individuals who underwent PTX, and 212 patients who underwent PTX were included in the final study analysis (Figure 1).

The protocol of management hyperparathyroidism in dialysis patients was follow-up KDIGO chronic kidney disease-mineral bone disease (CKD-MBD) clinical practice guideline.²⁰ The indications for parathyroidectomy were uncontrolled pruritus, generalized bone pain, resistance to medical treatment, and high intact PTH levels (>1000 pg/mL). The

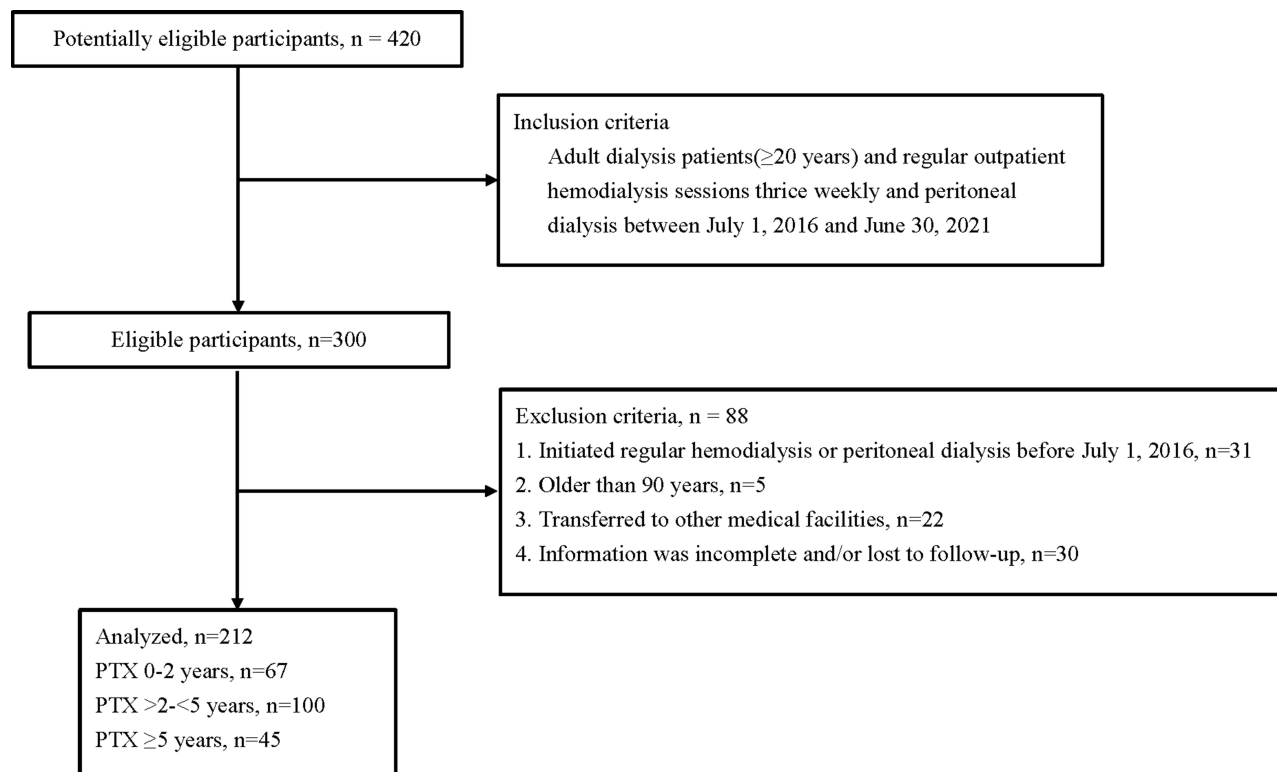


Figure 1 Participant deposition.

parathyroidectomy procedure included a total parathyroidectomy and auto-transplantation of 140 mg of hyperplastic tissue of the parathyroid gland into the subcutaneous forearm tissue.

Laboratory Measurement

Laboratory blood values were usually measured monthly, except for intact PTH levels, which were measured every 3 months, and urea clearance determined by kinetic modeling (Kt/V urea) (Daugirdas method),²¹ which was measured every 6 months. Baseline parameters were defined as the last blood test pre-PTX and the mean of the three consecutive monthly tests prior to censoring (July 1, 2021) for follow-up data. All blood samples were measured using commercial kits and an autoanalyzer (ADVIA1800, Siemens Healthcare Diagnostic Inc., NY, USA), and intact PTH levels were measured using chemiluminescence immunoassay (ADVIA Centaur 240, Siemens Healthcare Diagnostic Inc., NY, USA). Albumin levels were measured using the bromocresol green method. The indications for PTX were uncontrolled pruritus, generalized bone pain, resistance to medical treatment, and high intact PTH concentrations (>1000 pg/mL). The PTX procedure included total PTX and autotransplantation of 140 mg of hyperplastic tissue of the parathyroid gland into the subcutaneous forearm tissue.

Survey Instrument for QoL

The psychometric measurement used in this study was the KDQOL-36™ version 1.3. The KDQOL-36™ is available in English and translated into Mandarin Chinese by the KDQOL-SF™ group and RAND (The KDQOL Working Group. https://www.rand.org/health-care/surveys_tools/kdqol.html). The KDQOL-36™ comprises generic and disease-specific domains. The disease-specific domains comprise three scales: Symptoms and Problems of Kidney Disease (SPKD) (12 items), Burden of Kidney Disease (BKD) (4 items), and Effects of Kidney Disease (EKD) (8 items). The generic core is the 12-item Short Form Health Survey (SF-12). The results of the SF-12 instrument are summarized as the Physical Component Summary (PCS) score and Mental Component Summary (MCS) score. Scoring of the subscales was available from the free scoring guide (https://www.rand.org/health-care/surveys_tools/kdqol.html). PCS and MCS scores were determined using a T-score metric. SPKD, BKD, and EKD scores ranged from 0 to 100, with higher scores indicating better QoL. The pre-PTX measurement was performed 1 month prior to the PTX. The cross-sectional post-PTX measurement was initiated from June 1, 2021 to June 31, 2021.

Compliance with Ethical Standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted [Institutional Review Board (IRB) approval number 1.0, 2021.8.11 in Dalian University Affiliated Xinhua Hospital, China] and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Statistical Analysis

Baseline characteristics were calculated using descriptive statistics (mean ± standard deviation) and percentages. Differences between the groups were estimated using the chi-square test and independent two-sample *t*-test. The correlation between the KDQOL-36 components and clinical variables was estimated using the Pearson correlation test. Statistical significance was set at $P < 0.05$. All statistical analyses were conducted using the Statistical Package for Social Sciences (version 25.0).

Results

Characteristics of the Participants

The cohort comprised 212 patients, with a mean age of 46.4 years, and the male:female ratio was 96:116. Among them, 191 patients received HD and 21 patients received PD. Regarding comorbidities, 69.8% (n=148) had hypertension, 26.4% (n=56) had diabetes, and 10.8% (n=23) had coronary artery disease (Table 1).

Table 1 Baseline Characteristics (N=212)

Variables	n (%)
Sex (M/F)	96/116
Age (year)	46.4±11.3
Dialysis vintage (year)	10.0±4.0
Hemodialysis	191 (90.0)
Peritoneal dialysis	21 (10.0)
Diabetes	56 (26.4)
Hypertension	148 (69.8)
Coronary cardiac disease	23 (10.8)
Chronic hepatitis, B/C	11/15 (12.3)

Comparison of the Laboratory Parameters in the Pre- and Post-PTX Periods

Nutritional markers, albumin, significantly increased post PTX than pre PTX. CKD-mineral bone disease parameters, including calcium, phosphate, alkaline phosphatase, and intact PTH, significantly decreased post PTX than pre PTX (Table 2).

Comparison of KDQOL-36 Domain Scale Scores in the Pre- and Post-PTX Periods

In the analysis of all patients, the KDQOL-36 domain scale scores (PCS, MCS, BKD, SPKD, and EKD) significantly increased in the post-PTX period compared with the pre-PTX period (Table 3). We further stratified the patients into three groups based on the duration of PTX: 0–2 years, >2–<5 years, and ≥5 years. All KDQOL-36 domain scale scores increased with the duration of PTX treatment (Table 4).

Table 2 Distribution of Laboratory Parameters Pre- and Post-Parathyroidectomy (PTX) Periods (n=212)

Parameters	Pre-PTX	Post-PTX	P
Hemoglobin (g/L)	116.39±19.49	112.64±15.41	0.027
Albumin (g/L)	41.55±3.23	44.62±3.30	<0.001
Urea nitrogen (umol/L)	26.57±6.22	19.84±5.93	<0.001
Creatinine (umol/L)	924.17±362.39	819.21±166.42	<0.001
Uric acid (umol/L)	463.35±70.27	383.73±98.92	<0.001
Calcium (mmol/L)	2.64±1.42	2.10±0.40	<0.001
Phosphate (mmol/L)	2.13±0.54	1.82±0.50	<0.001
Potassium (mmol/L)	4.99±2.53	4.95±0.77	0.082
ALP (u/L)*	322 (135–781)	268 (108–422)	<0.001
iPTH (pg/mL)*	1812 (1171.25–2640.73)	13.9 (5.00–119.70)	<0.001
Kt/V	1.19±0.13	1.25±0.10	<0.001

Notes: Data are expressed as mean±SD, *expressed as median (interquartile range).

Abbreviations: iPTH, intact parathyroid hormone; ALP, alkaline phosphatase.

Table 3 KDQOL-36 Domain Scale Scores, Pre-and Post-PTX Periods

	Pre-PTX	Post-PTX	p
PCS	34.28±4.84	46.01±6.19	<0.001
MCS	47.08±6.75	51.99±5.22	<0.001
BKD	11.54±10.41	21.72±13.84	<0.001
SPKD	69.17±14.92	87.27±12.5	<0.001
EKD	70.43±12.64	76.01±13.37	<0.001

Abbreviations: BKD, burden of kidney disease; EKD, effects of kidney disease; MCS, mental component summary; PCS, physical component summary; PTH, parathyroid hormone; SPKD, symptoms and problems of kidney disease.

Table 4 KDQOL-36 Domain Scale Scores in Stratified PTX Duration

	PCS		MCS		BKD		SPKD		EKD	
	Pre-PTX	Post-PTX	Pre-PTX	Post-PTX	Pre-PTX	Post-PTX	Pre-PTX	Post-PTX	Pre-PTX	Post-PTX
PTX 0-2 years, n=67	35.02±5.6	44.78±5.66**	45.66±7.74	51.62±5.34**	10.94±11.51	21.88±13.9**	73.26±12.81	85.94±8.89**	73.96±12.59	79.08±13.89**
PTX >2-<5 years, n=100	34.35±4.61	46.95±5.92**	46.77±7.23	51.71±5.16**	11.63±9.91	20.14±13.03**	69.68±13.36	83.92±9.12**	70.66±13.11	77.08±13.03**
PTX ≥5 years, n=45	33.55±4.3	44.34±6.58**	49.43±5.31	54.17±3.39**	12.04±9.79	23.15±14.59*	64.58±10.93	81.94±7.6**	66.67±12.23	71.88±13.2*

Note: * $P < 0.01$, ** $P < 0.001$.

SPKD Scores in the Pre- and Post-PTX Periods

All individual patient-reported symptom scores, such as anorexia, dizziness, shortness of breath, pruritus, dry skin, cramps, chest pain, and bone pain, decreased in the post-PTX period compared with those in the pre-PTX period. The markedly decreased scores in the post-PTX period were found in the case of pruritus, dry skin, cramps, and bone pain (Figure 2).

Pearson's Correlation Analysis on the Study Parameters

PTX duration showed a significant negative correlation between PCS subscale scores ($P=0.001$) and a positive correlation between EKD subscale scores ($P=0.004$). Moreover, the SPKD subscale scores showed a significant negative correlation between age ($P=0.004$) and a positive correlation between calcium ($P=0.021$) (Table 5).

Discussion

It is well recognized that secondary HPT confers adverse health outcomes in CKD.²² PTX is an option for CKD patients with medically refractory secondary HPT, illustrating favorable long-term outcomes in observational cohort studies.^{11,23} Considering the improvement in clinical symptoms caused by PTX, it is reasonable to assume QoL improvement after PTX in patients with CKD. Commonly, the QoL assessment tool in CKD comprise general health scales and kidney-

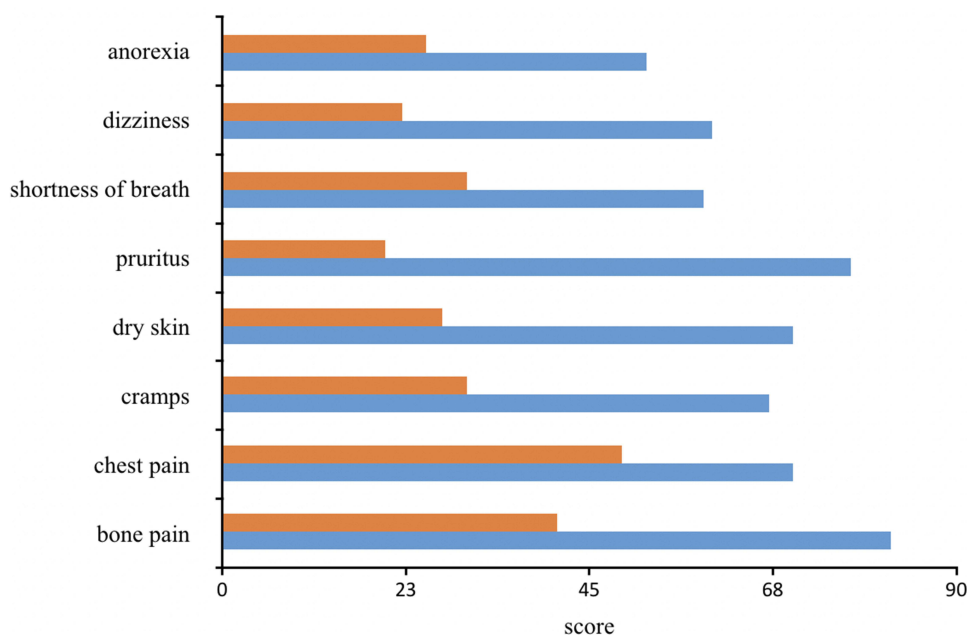


Figure 2 Distribution of Symptoms and Problems of Kidney Disease scale scores in the pre- and post-PTX periods. Data are expressed as mean values. $P < 0.001$.

Note: post-PTX. pre-PTX.

Table 5 Pearson's Correlation Analysis Between Studies Variables

	PCS		MCS		BKD		SPKD		EKD	
	r	P	r	P	r	P	r	P	r	P
Age	0.041	0.388	-0.043	0.365	0.022	0.639	-0.137	0.004	-0.056	0.242
Dialysis vintage	0.025	0.617	0.034	0.483	0	0.998	-0.08	0.103	-0.058	0.24
Hemoglobin	-0.032	0.503	0.021	0.653	-0.006	0.898	0.021	0.666	0.085	0.077
Albumin	0.044	0.358	0.067	0.161	0.032	0.504	0.02	0.674	-0.004	0.928
Calcium	-0.052	0.276	0.03	0.528	-0.001	0.977	0.109	0.021	0.088	0.063
Phosphate	-0.01	0.838	-0.027	0.561	0.01	0.828	-0.056	0.237	-0.002	0.958
Duration PTX	-0.180	0.001	-0.027	0.6	0.085	0.079	-0.07	0.17	0.146	0.004
iPTH	-0.109	0.021	-0.01	0.83	-0.01	0.826	-0.041	0.383	0.021	0.654

target scales. Given the nature of patient-reported forms in the tool, individuals vary in their ability to respond to the questionnaires, contributing to further intraindividual variability. Hence, the literature reports varied results. Considering the durable effects of PTX on QoL in dialysis patients, we conducted this study. Our study highlights that PTX could improve QoL components in dialysis patients.

In the present study, we used KDQOL-36TM to measure QoL in dialysis patients during the pre- and post-PTX periods. The Chinese version of the KDQOL-36TM has been demonstrated to be valid and reliable in dialysis populations who speak Mandarin.^{24–26} The drawback of the Chinese version of KDQOL-36 is the lack of a T-score metric in PCS and MCS subscale scores. Alternatively, we used reference values of the T-score metric in the Asian dialysis population reported in the US study.^{19,27} Our results showed that PCS and MCS subscale scores in our cohort exceeded the mean values reported in the Asian-US population. This implies that PTX may have a role in relieving physical and mental complex symptoms in the patients included in our study. Regarding symptom relief, pruritus, dry skin, cramps, and bone pain were especially marked in the post-PTX period. PTH is a uremic toxin that contributes to complex calcium-phosphate balance and multiorgan involvement.²⁸ Thus, decreased PTH concentrations could potentially explain the improvement in PTH-related clinical symptoms. Symptom burden and high level of disability are common in dialysis patients, and the executive summary of the KDIGO Controversies Conference on Support Care in CKD emphasizes difficulties in developing a treatment regimen for symptom management in CKD.²⁹ Although our results need to be further validated by screening tools, we expect PTX to be a potential management regimen for medically refractory secondary HPT in dialysis patients.

Previous studies investigated the effect of PTX on QoL between 6 and 12 months.^{4,14,15,17} The reason is to minimize interventional bias and patient expectations of the PTX effect. Briefly, these studies demonstrated that PTX had a beneficial effect on clinical outcomes and improvement in QoL scales. In the present study, we found that improvement in QoL scale scores showed a consistent pattern in the stratified PTX duration. On further analysis, our cohort showed increased serum albumin concentrations after PTX. Given the myriad of symptoms related to PTH, we suppose that improved QoL scales, particularly in the physical health domain, may be linked to beneficial effects on clinical parameters after PTX, such as nutrition, and calcium-phosphate homeostasis. Indeed, we cannot refute the contribution of other clinical factors in QoL improvement in our post-PTX cohort, such as dialysis adequacy, category of hemodialyzer and clearance of various unmeasured uremic toxins. A further comprehensive and informative evaluation in QoL improvement in post-PTX dialysis patients warrants to be continued. However, PTX duration showed a significant negative correlation between PCS subscale scores and a positive correlation between EKD subscale scores. These results may be biased owing to the small sample size. Nonetheless, a long-term effect on QoL after PTX is certainly affected by various uremic complications and the quality of health care providers.

Although the present study provided promising evidence of the PTX effect on QoL in dialysis patients, there were some limitations to the methods used. First, the questionnaires for QoL evaluation were conducted at various time points post-PTX in an individual patient. The results may confer a heterogeneous distribution of the KDQOL-36TM subscale scores. Although we have tried to analyze the KDQOL-36TM subscale scores using stratification of different years post-

PTX in the entire cohort, we admit that this stratified method cannot intrinsically realize the longitudinal effects of PTX on QoL in individual dialysis patients. Second, the PCS and MCS were scored on a T-score metric using a free scoring guide on a website (https://www.rand.org/health-care/surveys_tools/kdqol.html). To the best of our knowledge, there is still a lack of T-score metrics for PCS and MCS in Chinese dialysis patients. Therefore, we used reference values of the T-score metric in the Asian dialysis population reported in a United States study.¹⁹ Hence, the validity and reliability of PCS and MCS measurements in Chinese dialysis patients need to be further investigated. We admit that this approach may result in bias in subscale scores for PCS and MCS. This approach also makes it difficult to compare the effects of PTX on PCS and MCS in various dialysis populations worldwide. However, the present study investigated a cohort dialysis population in a single dialysis center within a limited period. Hence, the trajectory of PCS and MCS scale scores was not easily influenced by a non-generalized health care protocol and various environmental habits in the dialysis population. We believe that trend changes in the components of KDQOL-36™ between pre- and post-PTX periods are still reliable in the present study. Third, this study used a patient-reported QoL questionnaire survey. It is reasonable to assume that several patient perspectives could influence responses to questionnaires. Consequently, interpretation bias is unavoidable. Finally, our study included a relatively small number of dialysis patients in a hospital-facilitated dialysis center. The results could be influenced by patient characteristics, quality of health care providers, and heterogeneous habitual factors. Therefore, a detailed conclusion of the effects of PTX on QoL in dialysis patients may not be extrapolated to other dialysis populations.

Conclusion

PTX could improve QoL in dialysis patients with medically refractory secondary HPT. The long-term effects merit to be studied using a large sample.

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Disclosure

All the authors have declared no competing interest in this work.

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