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Original Article

Impact of dexmedetomidine on secondary hyperparathyroidism recurrence in uremic patients who received parathyroidectomy with auto-transplantation: a retrospective propensity-matched study

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Abstract: Background: Recurrence of secondary hyperparathyroidism (SHPT) remains a big challenge in uremic patients who underwent total parathyroidectomy with auto-transplantation (tPTX-AT). However, the relationship between perioperative intervention and recurrence of SHPT remains unclear. Dexmedetomidine has been used safely and effectively in uremic patients' anesthesia. The aim of the study was to explore the effect of dexmedetomidine on the recurrence of SHPT and identify the possible mechanism of action. Methods: Records of patients who underwent tPTX-AT between 2017 and 2018 were retrospectively analyzed. The study consisted of patients who received dexmedetomidine intra-operatively and the control patients who did not receive dexmedetomidine. The primary endpoint was the difference in the recurrence of SHPT one year after the surgery between the two groups. The secondary endpoint was health-related quality of life scores. Analysis included propensity score matching and multivariable logistic regression. Results: Of 354 patients, 133 patients received dexmedetomidine intra-operatively, and the total recurrence rate of SHPT was 10.2%. After propensity score matching, we found that patients' age, dexmedetomidine infusion, comorbidity of diabetes, and preoperative serum phosphorus were independent factors for SHPT recurrence, and that patients who received dexmedetomidine had an estimated 3.80-fold decrease in the risk of SHPT recurrence (odds ratio, 0.263; 95% confidence interval, 0.081 to 0.854; *P*=0.026). Patients receiving intraoperative dexmedetomidine infusion exhibited a better quality of life in terms of physical functioning and general health, and less emotional role limitations compared with those in the control group. Conclusion: In uremic patients who received tPTX-AT, there was an association between dexmedetomidine use and decreased risk of SHPT recurrence one year after the surgery. Further studies are needed to accurately assess the effects and mechanism of action of dexmedetomidine on the prognosis of this population.

Keywords: Dexmedetomidine, secondary hyperparathyroidism, recurrence, end-stage renal disease, parathyroidectomy

Introduction

Secondary hyperparathyroidism (SHPT) is a common complication in uremic patients. It is characterized by markedly elevated intact parathyroid hormone (iPTH) concentrations due to persistent stimulation of the parathyroid tissue and resultant parathyroid hyperplasia in response to hypocalcemia [1]. Chronically elevated iPTH causes bone pain, fractures, cardiovascular disease, hematopoiesis, and immune dysfunction, all of which may influence the length and quality of life (QOL) of uremic patients [2].

Surgical total parathyroidectomy with auto-transplantation (tPTX-AT) significantly improves calcium and phosphorus metabolism, resulting in reduced mortality and morbidity rates. However, due to the pathological changes in the remaining tissue, including inflammation and perioperative stress, the incidence of SHPT recurrence may reach as high as 20% [3, 4]. Many cohort studies have demonstrated that

perioperative anesthetic and analgesic intervention play a critical role in the long-term prognosis of multiple disease [5, 6]. Therefore, the anesthetic impact on the recurrence of SHPT and quality of life in uremic patients after surgery needs to be identified.

Uremic patients undergoing maintenance hemodialysis develop both structural and functional cardiovascular abnormalities [7]. Dexmedetomidine (DEX), a highly selective alpha-2 adrenoceptor agonist, is increasingly used with the beneficial effects of analgesia, sympathetic tone inhibition, anti-inflammation and surgical stress inhibition [8-10]. DEX attenuates sympathetic hyperactivity by reducing circulating level of catecholamines and improving hemodynamic stability, which is beneficial to the uremic patients. DEX also exhibits potential renal protection in patients with renal disease [11]. In our previous study, we found that DEX could be safely used for anesthesia and analgesia in uremic patients [12]. However, there are no current studies focussing on the impact of DEX on the outcome in uremic patients after surgery. Therefore, we performed a single-centre retrospective study to evaluate the relationship between DEX use and SHPT recurrence in uremic patients undergoing tPTX-AT. Specifically, the primary aim was to test the hypothesis that infusion of DEX is associated with a lower incidence of SHPT recurrence one year after the surgery. Second, we aimed to test the hypothesis that DEX infusion elevated both the postoperative short-term outcome and long-term QOL in uremic patients.

Materials and methods

The study protocol (PJ-YX2019-049F2) was reviewed and approved by Ethics Committee for Clinical Trials of the Second Affiliated Hospital of Anhui Medical University, Anhui, China (Chairperson Prof. Chao Lu) on April 8, 2020, which waived the requirement for written informed consent because all data were de-identified and handled anonymously. The study was registered at the Chinese Clinical Trial Registry (ChiCTR-2000033811). All the work were done in accordance with the Ethical Principles for Medical Research Involving Human Subjects outlined in the Declaration of Helsinki.

Data were collected from the electronic medical records of all uremic patients who underwent tPTX-AT for SHPT by the same surgical team at the Second Affiliated Hospital of Anhui Medical University from January 2017 to August 2018. Patients were excluded if they met any of the following criteria: an American Society of Anesthesiologists (ASA) physical status of V, primary or tertiary hyperparathyroidism, a history of a previous thyroid operation, operation performed by any other surgeons, and incomplete records for anesthesia or surgery.

All patients received propofol-sufentanil-based general anesthesia and were transferred to the post-anesthesia care unit (PACU) after tracheal extubation in the operating room. DEX use was defined as a bolus infusion of 0.5 to 1 μg kg^{-1} for 10 min before induction followed by infusion of 0.3 to 0.5 μg kg^{-1} h^{-1} intra-operatively and ceased about 30 min before the end of the surgery. Patients were divided into two groups: those who received DEX (DEX group) and those who did not (control, CON group).

The patients' characteristics included age, sex, body mass index, comorbidities, physical ASA status, serum concentrations of calcium, phosphorus, iPTH, and alkaline phosphatase at baseline, dialysis modality, and the length of dialysis. Surgical information included the year of surgery, duration of anesthesia, consumption of sufentanil, time to extubation (defined as the interval between discontinuing the anesthetics to extubation), length of PACU stay, comorbidities in the PACU, length of hospitalization after surgery, and the concentrations of postoperative calcium, phosphorus, and iPTH at discharge. Patients were followed up for one year after the surgery. Follow-up assessments included the concentrations of iPTH and C-reactive protein (CRP), and a self-administered questionnaire on the health-related QOL, which was measured by a validated Chinese version of the 36-item Short Form Health Survey (SF-36) [13, 14] as a generic core. The SF-36 was developed to assess 8 different aspects of the physical and mental health status: physical functioning (10 items), physical role limitation (4 items), emotional role limitation (3 items), social functioning (2 items), mental health (5 items), bodily pain (2 items), vitality (4 items), and general health perception (5 items). Each component was analyzed individually as the average of a predefined sum of questions, ranging from 0 to 3 or from 0 to 5, depending on the number of possible answers. Each response was linearly transformed to 0 to 100, with higher scores indicating a better QOL.

Statistical analysis

In order to correct for selection bias and confounding factors, we used the propensity score matching method without replacement, which could balance the covariates between the two groups. The following covariates were matched at a 1:2 ratio with a 0.03 calliper by the nearest neighbour method: patient characteristics at baseline, preoperative comorbidities, ASA physical status, modality of dialysis, length of dialysis, year of surgery, and duration of anesthesia. To determine the balance between the two groups before and after propensity score matching, absolute standardized mean difference (ASD) was used; an ASD <0.1 for the covariates indicated that the two groups were sufficiently balanced.

Continuous variables were reported as mean ± standard deviation (SD) or median [interquartile range, IQR], and categorical variables were reported as number (percentage). Data with normal distribution were compared using independent-samples *t* test. For data that did not have normal distribution, the rank sum test was used. For categorical data, Pearson's χ^2 test was used. Potential confounders associated with recurrence after tPTX-AT, which were chosen on the basis of their clinical significance as reported in the literature, were analyzed using univariate and multivariable logistic regression. First, we performed a univariate analysis to identify potential risk factors for postoperative recurrence. Variables with *P*-values <0.5 were subjected to multivariable analysis, after which, the odds ratios (OR) and associated 95% confidence intervals (CI) were calculated. The multivariable logistic regression processes were additively adjusted for several potential confounding. The association between DEX administration and postoperative recurrence was also assessed by logistic regression analyses.

The study was powered to evaluate one primary outcome, the recurrence of SHPT one year after tPTX-AT in uremic patients. According to the previous study [3] and the historical medical data in our hospital, we hypothesized that uremic patients would have a 10% rate of recurrent SHPT. To detect a 4% (SD=3%) difference in the incidence of SHPT recurrence between patients received or did not receive DEX with a 0.05 chance of type I error and 80% power, 304 patients were required.

The package of the R program (version 2.15.X) was used as a propensity score matching tool; the analysis was performed with SPSS software version 22.0 (SPSS Inc., Chicago, IL). A *P*-value <0.05 was considered statistically significant.

Results

Patients

Among the 399 uremic patients who underwent tPTX-AT between January 2017 and August 2018, we excluded 18 with an ASA status of V, 2 with tertiary hyperparathyroidism, 9 with a history of previous thyroid operation, 13 with tPTX-AT by other surgeons, and 3 with incomplete or missing records for surgery. Finally, 354 patients were included in the analyses (**Figure 1**). One year after the surgery, recurrence occurred in 36 patients (10.2%) (**Table 1**).

Comparison of characteristics between patients who did and did not receive DEX

Table 1 shows the pre-propensity score matching (DEX group: n=133; CON group: n=221) and post-propensity score matching (DEX group: n=111; CON group: n=157) covariate comparisons. There were no significant differences between the two groups in terms of the characteristics of patients, dialysis, surgery and preoperative biochemical parameters. After propensity score matching, all covariates were well-balanced with an ASD <0.1. The postoperative recurrence rate was 4.5% in the DEX group, which was significantly lower than that in the CON group (13.6%, *P*=0.006), and the recurrence rate remained significantly lower in the DEX group after propensity score matching (4.5% *vs* 12.1%, *P*=0.032).

Association between DEX and postoperative recurrence of SHPT

The factors associated with recurrence of SHPT one year after tPTX-AT are presented in **Table 2**. After the univariate analysis, the covariates of patient characteristics at baseline and other relative parameters were adjusted in the multivariable analysis with propensity score matching, which showed that patients' age, DEX infusion, comorbidity of diabetes, and preoperative serum phosphorus were independent factors for SHPT recurrence, and that patients who received DEX had an estimated 3.80-fold de-

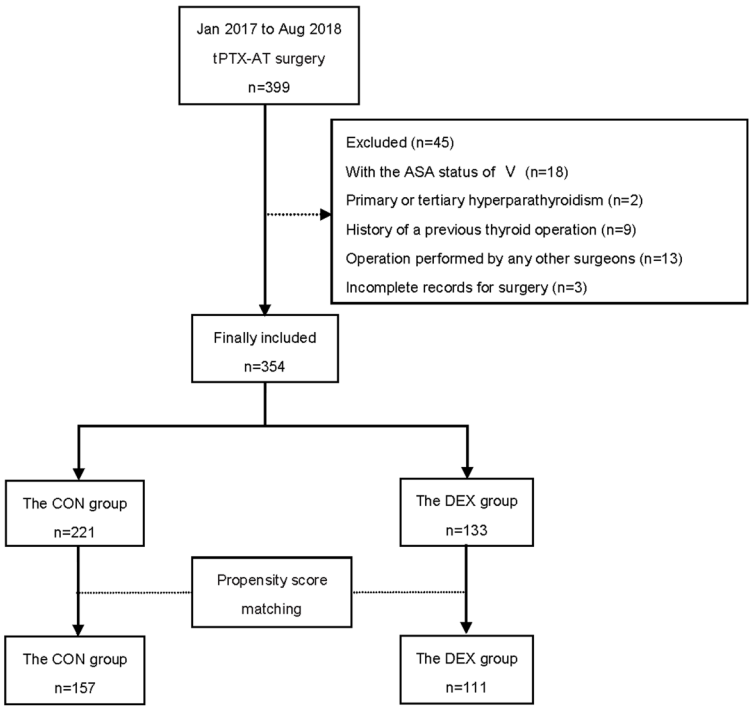

Figure 1. Flow chart of patient selection. tPTX-AT, parathyroidectomy with auto-transplantation; ASA, American Society of Anesthesiologists; DEX, dexmedetomidine; CON, control.

crease in the risk of SHPT recurrence (OR, 0.263; 95% CI, 0.081 to 0.854; *P*=0.026).

Comparison of outcomes between patients did and did not receive DEX

Patients who received DEX consumed less analgesics during the surgery. Specifically, sufentanil consumption in the DEX group was significantly decreased compared with that in the CON group (25.6 ± 7.1 μg *vs* 28.1 ± 4.9 μg, *P*=0.001). Meanwhile, DEX provided better pain control postoperatively. The number of patients with a pain numerical rating scale (0 to 10) ≥ 4 in the PACU of the DEX group was significantly lower than that of the CON group. However, DEX resulted in a lower heart rate postoperatively, which was treated with atropine accordingly, and no severe hemodynamic instability occurred. There were no significant differences between the two groups in terms of the risk of postoperative nausea and vomiting, hypertension, and hypotension after the surgery, nor in the length of hospital stay after surgery and hospitalization costs (**Table 3**). One year later, patients who received DEX exhibited a better QOL in terms of physical functioning, general health perception, and less emotional role limitation. However, there was no significant difference in the other items of the SF-36 assessment (**Figure 2**).

Part of the CPR concentration of patients was missing during the follow-up. The median [IQR] of CRP concentration was 80.4 [55.9 to 104.1] mg L^{-1} in DEX group (n=130, with 3 missing) and 89.5 [61.3 to 119.8] mg L^{-1} in CON group (n=65, with 156 missing). Patients in the DEX group exhibited a lower CRP concentration than those in the CON group one year after the surgery.

Discussion

In this analysis of consecutive patients with end-stage renal disease (ESRD) undergoing tPTX-AT at our institution, we found that patients who received intraoperative DEX infusion exhibited a lower risk of SHPT recurrence and higher health-related QOL one year after the surgery.

Parathyroidectomy with auto-transplantation involves the removal of all four parathyroid glands and the implantation of a section of one of the glands into a muscle, which leaves enough residual parathyroid tissue to support mineral homoeostasis. It has been reported that tPTX-AT has a high success rate and a slightly lower risk of hyperparathyroidism recurrence [15, 16]. During the data collection, we chose the patients who were operated by the same surgical team to exclude the influence of operative procedures on the results. The iPTH concentrations tested at discharge were all decreased to the normal level, which indicated a successful operation. However, because the pathogenic factors may persist and the residual parathyroid tissue may still show increased proliferation of parathyroid cells, SHPT recurrence remains a significant problem in the treatment of nephrogenic hyperparathyroidism.

Increased inflammation has been proposed to play an important role in the pathogenesis of

Table 1. Characteristics of patients, dialysis, surgery and preoperative biochemical parameters

Parameters	Before propensity score matching (n=354)			After 1:2 propensity score matching (n=268)		
	CON group n=221	DEX group n=133	ASD	CON group n=157	DEX group n=111	ASD
Recurrence	30 (13.6)	6 (4.5)	0.312	19 (12.1)	5 (4.5)	0.273
Age (years)	46.9 ± 9.6	48.1 ± 9.5	0.133	47.4 ± 9.6	47.3 ± 9.2	0.006
<40	45 (20.4)	25 (18.8)		29 (18.5)	23 (20.7)	
40 to 50	87 (39.4)	51 (38.3)		60 (38.2)	44 (39.6)	
50 to 60	71 (32.1)	40 (30.1)		55 (35.0)	32 (28.8)	
60 to 70	15 (6.8)	15 (11.3)		11 (7.0)	11 (9.9)	
≥ 70	3 (1.4)	2 (1.5)		2 (1.3)	1 (0.9)	
Female	92 (41.6)	52 (39.1)	0.052	66 (42.0)	44 (39.6)	0.028
BMI (kg m^{-2})	21.83 [19.72 to 24.43]	21.78 [19.82 to 24.22]	0.063	22.06 [19.88 to 24.74]	21.68 [19.59 to 24.09]	0.059
<18.5	33 (14.9)	15 (11.3)		21 (13.4)	13 (11.7)	
18.5 to 25	143 (64.7)	97 (72.9)		102 (65.0)	82 (73.9)	
25 to 30	41 (18.6)	18 (13.5)		32 (20.4)	14 (12.6)	
≥ 30	4 (1.8)	3 (2.3)		2 (1.3)	2 (1.8)	
Commoribidities						
Hypertension	186 (84.2)	114 (85.7)	0.044	135 (86.0)	94 (84.7)	0.026
Diabetes	6 (2.7)	3 (2.3)	0.031	5 (3.2)	3 (2.7)	0.030
Cardiopulmonary disease	13 (5.9)	5 (3.8)	0.111	6 (3.8)	5 (4.5)	0.047
ASA physical status						
III	203 (91.9)	127 (95.5)	0.174	152 (96.8)	105 (94.6)	0.086
IV	18 (8.1)	6 (4.5)		5 (3.2)	6 (5.4)	
Type of dialysis						
Hemodialysis	217 (98.2)	132 (99.2)	0.122	156 (99.4)	111 (100.0)	0.052
Peritoneal dialysis	4 (1.8)	1 (0.8)		1 (0.6)	0 (0)	
Dialysis duration (years)	7.7 ± 3.1	8.2 ± 3.0	0.170	7.9 ± 3.0	8.0 ± 2.7	0.007
Duration of anesthesia (min)	116.0 [92.5 to 152.0]	120.0 [89.0 to 152.5]	0.004	110.0 [90.0 to 147.5]	120.0 [89.0 to 155.0]	0.005
Year at surgery						
2017	113 (51.1)	74 (55.6)	0.090	80 (51.0)	60 (54.1)	0.027
2018	108 (48.9)	59 (44.4)		77 (49.0)	51 (45.9)	
Preoperative measures						
Serum Ca (mg dl^{-1})	2.36 ± 0.26	2.35 ± 0.25	0.020	2.37 ± 0.28	2.37 ± 0.22	0.014
Serum P (mg dl^{-1})	2.10 ± 0.54	2.09 ± 0.52	0.011	2.10 ± 0.54	2.10 ± 0.53	0.018
Serum iPTH (pg ml^{-1})	1768.0 [1219.0 to 2500.0]	1791.0 [1294.0 to 2500.0]	0.008	1790.0 [1218.0 to 2500.0]	1820.0 [1299.0 to 2500.0]	0.019
Serum ALP (U L^{-1})	462.0 [244.0 to 761.5]	414.0 [212.0 to 677.0]	0.233	463.0 [251.0 to 761.0]	414.0 [229.0 to 756.0]	0.042

Data are presented as the mean ± standard deviation or median [interquartile range] for continuous variables, and number (percentage) for categorical variables. Abbreviations: CON, control; DEX, dexmedetomidine; ASD, absolute standardized mean difference; BMI, body mass index; ASA, American Society of Anesthesiologist; Ca, calcium; P, phosphorus; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase.

Table 2. Association between dexmedetomidine and postoperative recurrence in patients with tPTX-AT surgery after multivariable logistic analyses with propensity score matching

Parameters		Univariate analysis			Multivariable analysis		
		OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age (years)	<40	1.000	ref				
	40 to 50	0.606	0.156 to 2.359	0.470	0.456	0.094 to 2.211	0.330
	50 to 60	1.050	0.292 to 3.775	0.940	0.998	0.219 to 4.555	0.998
	60 to 70	4.500	1.125 to 17.99	0.033	10.291	1.778 to 59.546	0.009
	≥ 70	24.000	1.768 to 325.783	0.017	161.745	3.123 to 8376.977	0.012
Female		0.850	0.358 to 2.017	0.712	0.560	0.187 to 1.672	0.298
BMI (kg m^{-2})	<18.5	1.000	ref		1.000	ref	
	18.5 to 25	0.618	0.190 to 2.004	0.422	0.374	0.089 to 1.569	0.179
	25 to 30	1.120	0.291 to 4.343	0.864	0.730	0.136 to 3.904	0.713
	≥ 30	N/A		0.999			
Comorbidities	Hypertension	0.615	0.215 to 1.758	0.364	0.556	0.163 to 1.892	0.347
	Diabetes	3.606	0.686 to 18.943	0.130	9.282	1.006 to 85.642	0.049
	Cardiopulmonary disease	2.374	0.482 to 11.678	0.288	0.309	0.017 to 5.698	0.430
ASA physical status	III	1.000	ref				
	IV	N/A		0.999			
Type of dialysis	Hemodialysis	1.000	ref				
	Peritoneal dialysis	N/A		1.000			
Dialysis duration (years)		1.063	0.923 to 1.224	0.398	1.175	0.975 to 1.417	0.090
Duration of anesthesia (min)		0.991	0.980 to 1.002	0.103	0.988	0.975 to 1.002	0.089
Year at surgery	2017	1.000	ref		1.000	ref	
	2018	0.630	0.266 to 1.495	0.295	0.812	0.266 to 2.478	0.714
Preoperative measures	Serum Ca (mg dl^{-1})	2.060	0.429 to 9.889	0.367	1.194	0.196 to 7.283	0.847
	Serum P (mg dl^{-1})	1.340	0.625 to 2.875	0.452	3.167	1.191 to 8.421	0.021
	Serum iPTH (pg ml^{-1})	1.000	1.000 to 1.001	0.418	1.000	0.999 to 1.001	0.930
	Serum ALP (U L^{-1})	1.000	0.999 to 1.001	0.984			
Intraoperative intervention	Dexmedetomidine infusion	0.343	0.124 to 0.947	0.039	0.263	0.081 to 0.854	0.026

Propensity score matching analyses were adjusted by factors in **Table 1**. Parameters of gender, BMI, and values with *P*-values <0.5 in univariate analysis were subjected to multivariable analyses. Abbreviations: tPTX-AT, parathyroidectomy with auto-transplantation; BMI, body mass index; ASA, American Society of Anesthesiologist; Ca, calcium; P, phosphorus; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase; OR, odds ratio; CI, confidence interval; ref, reference.

multiple diseases contributing to a low QOL in dialysis patients [17]. Compared with uremic patients without SHPT, patients with SHPT may have a higher prevalence of serum inflammatory cytokines, such as CRP, which is an acute phase protein, and is most often used as an inflammatory biomarker in nephrology [18]. Additionally, surgical trauma induces a variety of stress responses and further aggravates perioperative inflammation [9]. Therefore, controlling the inflammatory response perioperatively could help inhibit hyperfunction of parathyroid cells. Clinical studies have shown that DEX can attenuate perioperative stress and inflammation induced by surgical trauma and exhibit multifaceted protective effects when administered as an adjuvant [19]. It was reported that patients receiving DEX perioperatively had a significant decrease in CRP concentration 24 to 48 h after surgery compared with those who did not [20, 21]. In the current study, CRP concentrations were also collected from part of the patients. Patients in the DEX group exhibited lower CRP concentrations compared with those in the CON group postoperatively. This partly indicated an association of DEX with reduced inflammation, which may have resulted in a lower risk of SHPT recurrence. However, this anti-inflammatory mechanism should be explored further with a larger and integral sample size and prospective studies in the future.

We also found that infusion of DEX decreased opioid consumption intraoperatively and enhanced postoperative pain control for patients in the PACU. Previous studies have demonstrated that the opioid receptor antagonist, naloxone, had a suppressive effect on iPTH in patients with renal failure [22]. Therefore, we speculated that reduced opioid consumption may similarly lead to the inhibition of hyperfunction in parathyroid cells and decrease the risk of

Table 3. Postoperative parameters of patients who received dexmedetomidine and those who did not receive dexmedetomidine

Parameters	Before propensity score matching (n=354)			After 1:2 propensity score matchining (n=268)		
	CON group n=221	DEX group n=133	*P*-value	CON group n=157	DEX group n=111	*P*-value
Sufentanil consumption (μg)	27.9 ± 5.3	25.6 ± 7.1	0.001[a,d]	28.1 ± 4.9	25.6 ± 7.1	0.001[a,d]
Time to extubation (min)	5.0 [5.0 to 7.0]	5.0 [4.0 to 7.5]	0.337[b]	5.0 [4.5 to 7.0]	5.0 [4.0 to 8.0]	0.741[b]
Length of PACU stay (min)	50.0 [40.0 to 64.5]	48.0 [36.0 to 63.0]	0.216[b]	53.0 [41.0 to 65.0]	48.0 [38.0 to 63.0]	0.262[b]
VAS ≥ 4	35 (15.8)	11 (8.3)	0.067[c]	32 (20.4)	11 (9.9)	0.021[c,d]
Adverse events during PACU						
Hypertension	40 (18.1)	15 (11.3)	0.086[c]	31 (19.7)	15 (13.5)	0.183[c]
Hypotension	0 (0)	2 (1.5)	0.140[c]	0 (0)	2 (1.8)	0.171[c]
Bradycardia	14 (6.3)	19 (14.3)	0.013[c,d]	10 (6.4)	17 (15.3)	0.017[c,d]
Tachycardia	26 (11.8)	8 (6.0)	0.075[c]	21 (13.4)	6 (5.4)	0.033[c,d]
PONV	4 (1.8)	5 (3.8)	0.305[c]	3 (1.9)	5 (4.5)	0.282[c]
Postoperative measures at discharge						
Serum Ca (mg dl^{-1})	2.07 ± 0.3	2.08 ± 0.33	0.913[a]	2.08 ± 0.33	2.07 ± 0.32	0.751[a]
Serum P (mg dl^{-1})	1.98 ± 0.58	1.92 ± 0.50	0.350[a]	1.97 ± 0.56	1.91 ± 0.47	0.353[a]
Serum iPTH (pg ml^{-1})	3.0 [3.0 to 8.2]	3.0 [3.0 to 9.6]	0.930[b]	3.0 [3.0 to 10.0]	3.0 [3.0 to 6.0]	0.658[b]
Length of hospital stay after surgery (days)	5.7 ± 3.8	5.2 ± 2.6	0.170[a]	5.7 ± 4.0	5.3 ± 2.7	0.336[a]
Hospitalization cost (US dollars)	4038.6 ± 1213.4	4065.1 ± 1163.0	0.840[a]	4098.0 ± 1217.5	4067.9 ± 1163.2	0.839[a]

Data are presented as the mean ± standard deviation or median [interquartile range] for continuous variables, and number (percentage) for categorical variables. Abbreviations: CON, control; DEX, dexmedetomidine; PACU, post-anesthesia care unit; VAS, visual analog score; PONV, post-operative nausea and vomiting; Ca, calcium; P, phosphorus; iPTH, intact parathyroid hormone. [a]Independent-samples *t* test. [b]Rank sum test. [c]Pearson's χ^2 test. [d]$P<0.05$ versus control.

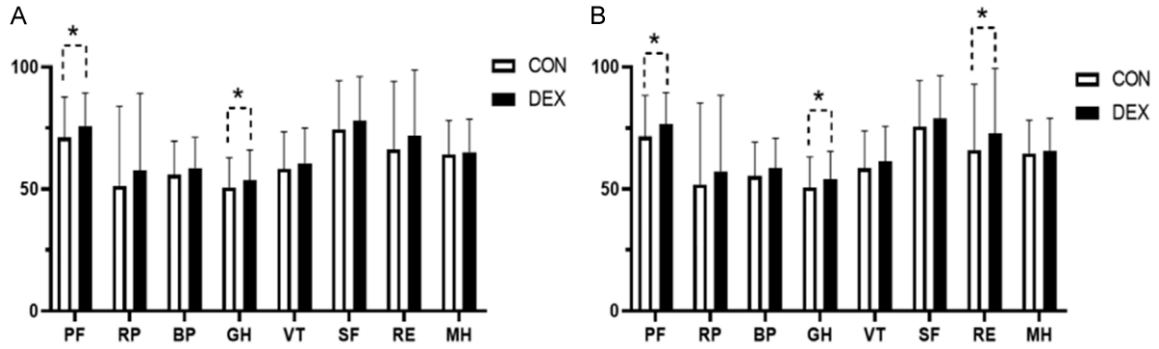

Figure 2. Scores of Short Form (SF)-36 items of patients one year after the surgery. A. Patients received dexmedetomidine exhibited a significantly higher score in terms of physical functioning (PF) and general health (GH) before propensity score matching (PF: 75.86 ± 13.52 vs 71.11 ± 16.56; GH: 53.74 ± 12.19 vs 50.71 ± 12.17). B. In addition to a significantly higher score in the PF and GH (PF:76.58 ± 12.90 vs 71.50 ± 16.79; GH:53.91 ± 11.48 vs 50.71 ± 12.17), patients who received dexmedetomidine also exhibited less emotional role limitation (RE) after propensity score matching (50.71 ± 12.17 vs 72.67 ± 12.17). Data were compared by independent-samples t test. **P*<0.05 compared between the two groups. CON, control group; DEX, dexmedetomidine group; PF, physical functioning; RP, physical role limitation, BP, bodily pain; GH, general health perception; VT, vitality; SF, social functioning; RE, emotional role limitation; MH, mental health.

SHPT recurrence. Meanwhile, with the development of opioid-sparing anesthesia, patients exhibit a better prognosis for multiple surgeries [23, 24]. As we know, patients with ESRD usually experience substantial physical, emotional, mental, and psychological impairments that are reflected in the decreased QOL [15, 25]. In the current study, DEX demonstrated a beneficial effect on the QOL in dialysis patients after tPTX-AT, and significant improvements were observed in physical functioning, general health, and role limitations due to the emotional problems, which may be an indirect result of the opioid-sparing effects of DEX.

In addition to DEX infusion, we found three independent risk factors associated with SHPT recurrence: higher age, comorbidity of diabetes mellitus, and high preoperative phosphorus concentrations. Elderly patients are more likely to represent an extreme model for arteriosclerosis, vascular calcification, and bone disorders with the progression of ESRD. Additionally, these pathological features are also relevant in other common chronic health abnormalities, such as diabetes mellitus and chronic inflammatory and electrolyte disturbances [26]. Thus, patients with higher age, comorbidity of diabetes mellitus, and high preoperative phosphorus concentrations may be vulnerable to SHPT recurrence.

There were some important limitations to this study. First, our study was limited by its relatively small sample size. Nevertheless, this is the largest study to assess the effect of DEX on SHPT recurrence after tPTX-AT. Second, as for any retrospective study, unknown confounding factors were a major limitation. Although our ASD analysis was based on preoperative baseline data, some other variables might have still differed between the patients who did and did not receive DEX. For instance, CRP data was incomplete, and we did not consider the consumption of anesthetics, hemodynamics, and the depth of anesthesia. However, we adjusted for the anesthetic time in the multivariable analysis of unmatched and matched patients. Third, this was a single-centre study, which may have compromised the generalizability of the findings, and the retrospective observational study design may have resulted in selection bias. Nevertheless, a large number of patients with SHPT visit our hospital; therefore, collecting data on the current cases of tPTX-AT for SHPT in a prospective registry would aid in future outcome analyses and high-quality research.

Conclusion

In conclusion, our clinical data suggest that intraoperative use of DEX is associated with a lower risk of SHPT recurrence one year after the surgery in uremic patients undergoing tPTX-AT, and that DEX use can improve the QOL in this population. We believe that the use of DEX as an adjuvant in general anesthesia contrib-

utes positively to the prognosis of uremic patients. Prospective randomized controlled trials are needed to accurately assess the effects of DEX on the prognosis of patients with ESRD undergoing tPTX-AT, and basic research should further elucidate the potential mediating mechanisms in this population.

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Disclosure of conflict of interest

None.

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