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Association between clinical variables and mortality after parathyroidectomy in maintenance hemodialysis patients

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All-cause mortality;
Hemodialysis;
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Abstract

BACKGROUND: We investigated factors associated with all-cause mortality and cardiovascular disease (CVD)-associated mortality after parathyroidectomy (PTX) in patients on maintenance hemodialysis (HD).

METHODS: Our study population consisted of 161 consecutive HD patients who underwent PTX before 2009 and 354 consecutive HD patients without PTX as controls from those visiting the Kaohsiung Chang Gung Memorial Hospital, Taiwan between 2009 and 2013. All-cause and CVD mortality with clinical variables were compared in PTX and non-PTX HD patients.

RESULTS: PTX patients had significantly lower all-cause and CVD mortality than controls. Multivariate logistic regression analyses showed PTX patients had a lower odds ratio for all-cause mortality than those without (odds ratio = .35, 95% confidence interval = .16 to .74). Association analysis based on clinical variables revealed patients with higher hemoglobin, albumin, creatinine, and HD adequacy index-Kt/V levels had significantly decreased risk of all-cause mortality.

CONCLUSIONS: PTX in HD patients reduces the risk of death.

Secondary hyperparathyroidism (SHPT) is commonly observed in patients with chronic kidney disease (CKD). SHPT may be associated with a number of unfavorable outcomes, including uremic bone disease, vascular calcification, and death.[1–3] Despite the advances in the medical management of SHPT, parathyroidectomy (PTX) is necessary in some patients undergoing dialysis. The incidence of PTX is 8.09 to 14.2 cases per 1,000 patient-years.[4–7] A longer duration of renal replacement therapy (>10 years) has been reported to increase the incidence of PTX to 30 cases per 1,000 patient-years.[4] The benefits of PTX in dialysis patients include increased erythropoietin response to anemia treatment, improved left ventricular function, alleviation of skin itching, reduced bone pain and general weakness, improved cognitive function, improved spermatogenesis, less frequent

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sleep disturbances, and improved quality of life.[8–12] PTX is reportedly associated with a risk of mortality at different intervals after surgery. An analysis of Medicare patients in the United States revealed that PTX was associated with higher mortality rates in the first 3 to 6 months after surgery, followed by lower risks thereafter.[7] In one observational, matched-cohort study using data from the United States Renal Database System, the 30-day postoperative mortality rate after PTX was found to be 3.1%; moreover, the long-term relative risk of mortality was 10% to 15% lower for PTX patients than for patients who did not undergo the surgery.[13] In addition, demographic variables may affect the risks associated with PTX. The main variables appear to include age, duration of dialysis, bone metabolism, and hemoglobin (Hb) level.[5,14] Although certain studies have examined the association between PTX and mortality; only a few studies have examined the long-term effects of PTX on clinical variables and their association with mortality.[5,7,13,14] In the present study, our aim was to investigate the influence of PTX on clinical variables and to determine the factors associated with the mortality rate after PTX, through a 5-year cohort data analysis.

Methods

Data sources

We enrolled patients (n = 909) who attended regular outpatient hemodialysis (HD) sessions, 3 times a week, at the Kaohsiung Chang Gung Memorial Hospital in Taiwan. The patients were tracked from January 1, 2009 to December 31, 2013. The exclusion criteria were (1) patients who had initiated regular HD after January 1, 2009; (2) patients who were older than 90 years; (3) patients who received PTX after January 1, 2009; (4) patients transferred to other medical facilities; and (5) patients whose information was incomplete and/or those who were lost to follow-up during the study period. A total of 515 patients were eligible for inclusion in the survival analysis. Laboratory blood values were usually measured on a monthly basis, except for ferritin levels, which were measured every 3 months, as well as intact parathyroid hormone (iPTH) levels, urea reduction ratio (URR), and Kt/V[7] that were measured every 6 months. The cardiothoracic ratio (CT ratio) was assessed once a year. A 5-year average value was calculated for each blood analysis variable. Ten blood analysis variables were considered as continuous variables (Hb, albumin, blood urea nitrogen [BUN], creatinine [Cr], potassium, corrected serum calcium [Ca], and phosphate [P] levels), whereas the remaining variables (URR, iPTH levels, ferritin levels, Kt/V, and CT ratio) were considered categorical variables. URR was categorized as either less than 65% or $\geq$65%, whereas the CT ratio was categorized as either less than 50% or $\geq$50%. Ca levels were calculated using the following equation: measured total Ca (mg/dL) + .8 (4.0-serum albumin [g/dL]). Adequacy indices of HD were measured as URR and Kt/V urea. The URR was calculated using the following equation: (predialysis BUN–postdialysis BUN/predialysis BUN) $\times$ 100%. Kt/V urea was calculated using the following equation: Kt/V urea = $-$Ln (R$-$.008 $\times$ t) + (4$-$[3.5 $\times$ R]) $\times$ UF/W, where R is the ratio of postdialysis and predialysis serum urea nitrogen, t (in hours) is the duration of dialysis, UF (L) is the ultrafiltrate amount, and W (kg) is the postdialysis body weight. All blood samples were measured using commercial kits and an autoanalyzer (Hitachi 7600-210, Hitachi Ltd., Tokyo, Japan). Albumin levels were measured using the bromocresol green method. For the measurement of the CT ratio, chest radiography was performed after HD. Cardiac size was measured by dropping parallel lines at the most lateral points of each side of the heart and measuring the distance between them. The thoracic width was measured by dropping parallel lines down the inner aspect of the widest points of the rib cage and measuring the distance between the lines. The CT ratio is defined as cardiac size and/or thoracic width.

The indications for PTX were uncontrolled pruritus, generalized bone pain, resistance to medical treatment, and high iPTH levels (>1,000 pg/mL). Preoperative examinations included a thallium heart scan and a computed tomographic scan, if necessary. The PTX procedure included a total PTX and autotransplantation of 140 mg of hyperplastic tissue of the parathyroid gland into the subcutaneous forearm tissue.[15]

The protocol for this study was approved by the Committee on Human Research at the Kaohsiung Chang Gung Memorial Hospital (101-1595B), and the study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Baseline characteristics were calculated using descriptive statistics (means $\pm$ standard deviation) and percentages. Differences between the groups were estimated using the chi-square, Fisher's exact, and independent 2-sample *t*-tests. The effects of PTX on clinical variables were tested by multivariate linear regression, after adjusting for age, gender, diabetes mellitus, and duration of HD. Multivariate logistic regression analyses were used to derive adjusted odds ratios (ORs) for combinations of risk factors of all-cause mortality and cardiovascular disease (CVD) mortality. The 95% confidence interval (95% CI) and a *P* value were used to determine statistical significance. A *P* value less than .05 was considered statistically significant. All statistical analyses were conducted using STATA (version 11.1).

Results

The baseline characteristics of the study participants are presented in Table 1. A total of 161 PTX patients with 14.51 years mean HD duration and 354 controls with