Incidence and Risk Factors of Persistent Hyperparathyroidism After Kidney Transplantation

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ABSTRACT

Persistent hyperparathyroidism after kidney transplantation is related to graft function, but pre-transplantation risk factors of persistent hyperparathyroidism have not been evaluated in detail. We enrolled 86 patients who had undergone kidney transplantation between 2008 and 2014. Nine patients showed persistent hyperparathyroidism characterized by the following: 1) serum parathyroid hormone levels >65 pg/mL and serum calcium levels >10.5 mg/dL at 1 year after kidney transplantation; 2) parathyroidectomy after kidney transplantation; and 3) reintroduction of cinacalcet after kidney transplantation. Compared with other patients, these 9 patients had significantly longer duration of dialysis therapy (186 ± 74 mo vs 57 ± 78 mo) and more frequent treatment with cinacalcet during dialysis (89% vs 12%). Multivariate analysis showed that dialysis vintage, calcium phosphate products, and cinacalcet use before kidney transplantation were independent risk factors of persistent hyperparathyroidism after kidney transplantation. A receiver operating characteristic curve showed 72 months as the cutoff value of dialysis vintage and 55 as the cutoff value of calcium phosphate products. In conclusion, dialysis vintage >6 years, calcium phosphate products >55 $(mg/dL)^2$, and cinacalcet use before kidney transplantation are strong predictors of persistent hyperparathyroidism. High-risk patients should be evaluated for parathyroid enlargement, and parathyroidectomy must be considered before kidney transplantation.

CHRONIC kidney disease mineral and bone disorder often persists after kidney transplantation and is related to graft function. Although high pre-transplantation levels of parathyroid hormone and phosphate are well known risk factors of persistent hyperparathyroidism [1,2], calcimimetics that modulate the calcium-sensing receptor have dramatically improved control of hyperparathyroidism during dialysis therapy [3]. In the cinacalcet era, it was difficult to predict the persistence of hyperparathyroidism only by checking serum levels of parathyroid hormone and phosphate before kidney transplantation [4]. The present study aimed to evaluate the risk factors of persistent hyperparathyroidism after kidney transplantation.

METHODS

All study patients had undergone kidney transplantation from 2008 to 2014. Patients with the following characteristics were excluded from the present study: 1) pediatric patients; 2) patients undergoing simultaneous pancreas and kidney transplantation; and 3) patients with primary nonfunction of the graft. In total, 86 patients (60 men and 26 women; overall age, 47 ± 13 years) were included in this study. We evaluated the relationship of persistent hyperparathyroidism with the use of clinical characteristics and laboratory parameters. Persistent hyperparathyroidism was defined as follows:

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1) serum parathyroid hormone levels >65 pg/mL and serum calcium levels >10.5 mg/dL at 1 year after kidney transplantation; 2) parathyroidectomy after kidney transplantation; and 3) reintroduction of cinacalcet after kidney transplantation. The study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983. All statistical tests were 2 sided, and $P < .05$ was considered to be statistically significant. Statistical analyses were performed with the use of JMP version 7.0 (SAS Institute, Cary, North Carolina).

RESULTS

Six of the 86 patients underwent parathyroidectomy or received cinacalcet prescription within 1 year after kidney transplantation; in addition, 3 patients exhibited high serum levels of calcium and parathyroid hormone at 1 year after kidney transplantation. Compared with other patients, these 9 patients with persistent hyperparathyroidism (HPT group) had significantly longer duration of dialysis therapy (186 ± 74 mo vs 57 ± 78 mo) and more frequent treatment with cinacalcet during dialysis (89% vs 12%; Fig 1). Although ultrasonography was performed in only 46% of patients, the prevalence of parathyroid enlargement was significantly higher in the HPT group. No significant differences were observed regarding age at transplantation, sex, diabetes, and serum levels of parathyroid hormone, alkaline phosphatase, phosphate, and calcium between the 2 groups (Table 1). Serum calcium phosphate products were higher, but not significantly, in the HPT group than in the control group. Moreover, multivariate analysis indicated that dialysis vintage, calcium phosphate products, and cinacalcet use before kidney transplantation were independent risk factors of persistent hyperparathyroidism (Table 2). A receiver operating characteristic curve showed 72 months as the cutoff value of dialysis vintage and 55 $(mg/dL)^2$ as the cutoff value of calcium phosphate products.

DISCUSSION

The results of our study suggested that dialysis vintage >6 years, calcium phosphate products >55 $(mg/dL)^2$, and cinacalcet use before kidney transplantation were strong predictors of persistent hyperparathyroidism. Although parathyroid enlargement may be a reliable predictor, it can not be relied on, because ultrasonography was underperformed before kidney transplantation.

Persistent hyperparathyroidism was associated with poor prognosis and graft loss [5]. In multivariate analyses, patients with parathyroid hormone levels above the normal limit (65 pg/mL) exhibited a significantly higher risk than those with normal/low levels of all-cause death

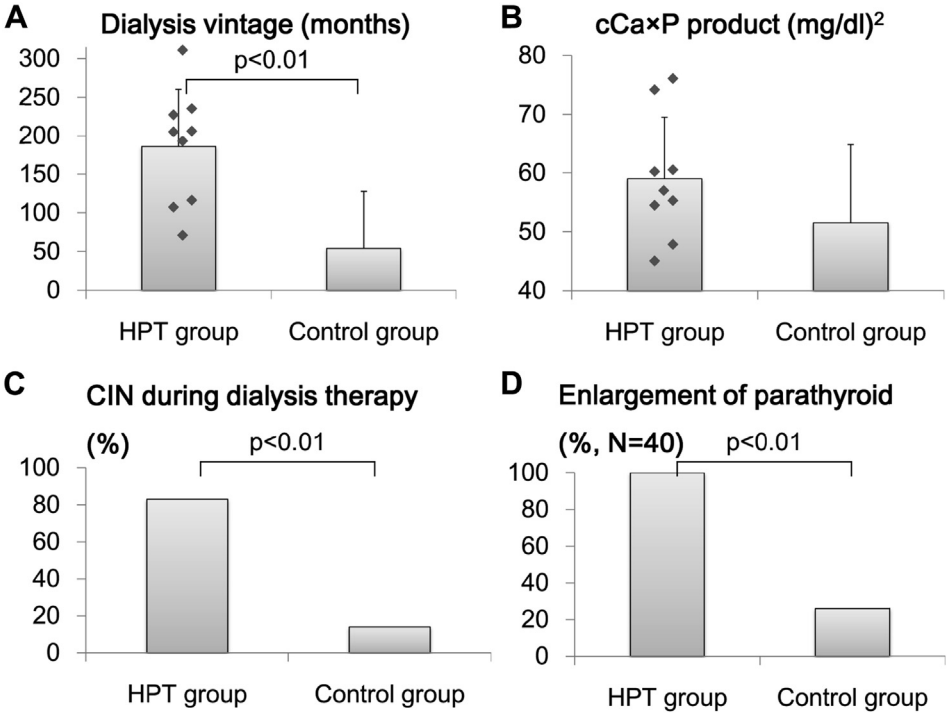

Fig 1. Clinical and biochemical characteristics of patients from both study groups. (**A**) Duration of dialysis vintage was significantly longer (186 ± 74 mo vs 57 ± 78 mo) in patients with persistent hyperparathyroidism (HPT group) than in the other patients (control group). (**B**) Serum calcium phosphate products were higher, but not significantly higher, in the HPT group than in the control group ($P = .12$). (**C**) Cinacalcet treatment during dialysis was more frequent (89% vs 12%) in the HPT group than in the control group. (**D**) Although ultrasonography was performed in only 46% patients, the prevalence of parathyroid enlargement was significantly higher in the HPT group.