# Parathyroidectomy prior to kidney transplant decreases graft failure

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Background. Uncorrected uremic hyperparathyroidism is associated with delayed graft function after kidney transplantation. The current guidelines of the Kidney Disease Improving Global Outcomes recommend maintaining parathyroid hormone  $\leq 9x$  normal in patients pre-kidney transplantation. This study explores the effect of increased levels of serum parathyroid hormone and preoperative parathyroidectomy on outcomes after kidney transplantation.

Methods. A retrospective review was performed of adult patients who underwent kidney transplantation between January 1, 2005, and December 31, 2014, at a single institution. Biochemistries and outcomes were analyzed pre-kidney transplantation and at 30 days, 6 months, and 1 year post-kidney transplantation.

Results. A total of 913 patients underwent kidney transplantation from 2005–2014. Graft survival 1 year post-kidney transplantation was 97.8%. Overall, 462 (50.6%) patients had a pre-kidney transplantation diagnosis of uncorrected uremic hyperparathyroidism, which was associated with complications in the first year post-kidney transplantation (odds ratio 1.44; 95% confidence interval, 1.11-1.87); no statistical association with delayed graft function or graft failure was detected. Pre-kidney transplantation parathyroid hormone  $\geq 6x$  normal was associated with post-kidney transplantation graft failure (P < .05). A total of 57 (6.2%) patients underwent pre-kidney transplantation parathyroidectomy, which was associated with lesser risk of graft failure (odds ratio: 0.547; 95% confidence interval, 0.327-0.913), but no statistically significant association with delayed graft function or complications were detected.

**Conclusion.** Pre-kidney transplantation parathyroidectomy decreases post-kidney transplantation graft failure and may benefit patients whose serum parathyroid hormone levels decrease into the target range of current Kidney Disease Improving Global Outcomes guidelines. (Surgery 2016;■:■-■.)

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UREMIC HYPERPARATHYROIDISM (UHPT) is a disorder characterized by excess secretion of parathyroid hormone (PTH) in response to chronic hypocalcemia caused by inadequate hydroxylation of vitamin D to its active form. Patients with end-stage renal disease (ESRD) are particularly susceptible to this increase in PTH production, which can lead to

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the PTH secretion becoming uncoupled from calcium levels, resulting in abnormal growth of the parathyroid glands and continued inappropriate secretion of PTH.

Kidney transplantation (KTX) in this population has been associated with negative outcomes, including the presence of microvascular thrombosis in transplanted allografts and an increased incidence of delayed graft function (DGF).<sup>2-4</sup> In rarer circumstances, the rapid correction of the underlying renal disease that occurs with KTX can lead to hypercalcemia and hypophosphatemia, increasing the risk of calciphylaxis in the immediate postoperative period.<sup>2</sup>

Current management of patients with UHPT who are eligible for KTX includes pharmaceutical intervention with active forms of vitamin D and/or calcimimetic agents or parathyroidectomy if the patient fails to respond to medical management. There remains, however, a lack of consensus as to what plasma level of PTH is high enough to recommend parathyroidectomy prior to KTX. Clinical practice guidelines of the Current Kidney Disease: Improving Global Outcomes (KDIGO) highlight that the optimal level of PTH is unknown in patients with chronic kidney disease, although they recommend that the serum PTH level be maintained in the range of approximately 2 to 9 times the upper normal limit for the assay in patients on dialysis (chronic kidney disease stage 5D).

In spite of this attempt to provide target serum levels of PTH for patients with chronic renal disease, nearly a quarter of pretransplant patients experience PTH values that are greater than recommended levels, which is most often attributed to calcimimetic intolerance.<sup>2</sup> Given that no guideline exists to recommend parathyroidectomy based on specific PTH levels, many transplant centers recommend parathyroidectomy in patients who are candidates for KTX if a patient exhibits at least a moderate form of UHPT.<sup>5</sup>

In a study assessing the risk of death and graft failure, pretransplant PTH levels were a significant risk factor for graft failure but not for death. A multivariate analysis in the same study found an exponential association between the risk for graft failure and greater pretransplant PTH levels.<sup>2</sup> The critical gap that exits currently in the management of these patients is to understand which PTH level requires parathyroidectomy prior to KTX. This determination could provide a new management paradigm designed to improve post-transplant outcomes, which would translate directly into decreased morbidity of patients with ESRD.

This study explores the effect of increased serum levels of PTH and preoperative parathyroid-ectomy on outcomes after KTX with the specific goal of determining the PTH level that should initiate parathyroidectomy in patients waitlisted for KTX. We hypothesize that a greater preoperative PTH would be associated with worse outcomes after KTX and that pre-KTX parathyroidectomy would lead to improved outcomes after KTX.

#### **METHODS**

Institutional review board approval was obtained for this study. The database of the United Network for Organ Sharing was queried to identify adult patients who underwent KTX between January 1, 2005, and December 31, 2014, at a single, tertiary care institution. United Network for

Organ Sharing data included vital statistics and the status of the transplanted kidney. A retrospective review was performed of the institutional electronic medical record in order to obtain the remaining data.

Relevant biochemical values, including serum levels of calcium, intact PTH, phosphorus, and estimated glomerular filtration rate (eGFR), were analyzed prior to KTX and at the 30-day, 6-month, and 1-year periods after KTX. Predictor variables used to test relevance were age, sex, raceethnicity, diagnosis of UHPT, presence of pre-KTX diabetes, type of transplant (live donor versus deceased donor), and parathyroidectomy status. Outcomes included post-KTX calcium and PTH levels, eGFR at 1 year, DGF, graft failure, complications (including acute rejection and chronic nephropathy), and death. A stepwise backward elimination strategy was used to identify potentially significant covariates in the multivariate modeling. Statistical analysis was performed using SAS software (version 9.3; SAS Institute, Inc, Cary, NC).

Patients were considered to have a diagnosis of UHPT if they had the diagnosis code for UHPT listed in their medical records, were treated medically for UHPT (eg, with vitamin D analogues or calcimimetics), or underwent parathyroidectomy. Institutional protocol for parathyroidectomy in the setting of UHPT is a subtotal parathyroidectomy and transcervical thymectomy when possible, with the goal of leaving 20–30 mg parathyroid tissue in one location in the neck.

To determine optimal PTH levels, thresholds were established at 2–9 times the upper limit of the normal range of PTH. During the 10-year time period analyzed in this study, serum PTH levels were derived from multiple different laboratories, and upper limits of the normal range varied from 65–84 pg/mL depending on the laboratory; however, the value of 84 pg/mL was utilized in this study as the value for the upper limit of normal in order to establish PTH thresholds.

#### **RESULTS**

A total of 913 patients underwent KTX from 2005–2014. Most patients were white (59.4%) and male (65.2%), with a median age of 53 (range 18–83) years. Just over 40% had a pre-KTX diagnosis of diabetes. Demographic information is summarized in Table I.

Graft survival 1 year post-KTX was 97.8%. Post-operative complications included acute rejection in 102 (11.2%) patients, DGF requiring dialysis in 74 (8.1%), infection in 51 (5.6%), reoperation

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