

HYPERCALCEMIA AFTER KIDNEY TRANSPLANTATION AS PREDICTOR FOR PATIENT AND GRAFT OUTCOMES

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BACKGROUND: Demand for kidney transplantation greatly exceeds the supply of transplantable organs. Patients on kidney transplant wait-lists typically wait 5-8 years on dialysis for transplants, and develop chronic uremic complications that can limit the health benefits of transplantation. The development of tertiary hyperparathyroidism and hypercalcemia in kidney transplant recipients is increasingly common in clinical transplant practice, but little is known about the natural history of this complication. The purpose of this study was to determine the incidence, risk factors and consequences of hypercalcemia in kidney transplant recipients.

METHODS: With the approval of our local hospital research ethics board, we conducted a retrospective study of n=1352 consecutive adult kidney-only transplant recipients in two of the largest Canadian transplant centers (Toronto General Hospital, and St. Paul's Hospital, Vancouver) between January 2000 and August 2007. Research datasets were constructed from electronic data banks common to both hospitals that contain all laboratory test results used to support clinical patient management as well as key outcomes including allograft and patient survival.

RESULTS: In the first post-transplant year, a striking 40% of patients developed at least one episode of hypercalcemia (defined as albumin-corrected serum calcium ≥ 2.6 mmol/l), and 12% of patients had mean serum calcium ≥ 2.6 mmol/l (post-transplant hypercalcemia). Post-transplant hypercalcemia resolved in 25%, 36%, and 54% of patients by 2, 3, 5 years post-transplant, respectively, with n=21 patients requiring surgical parathyroidectomy.

In a multivariate logistic regression model, the follow factors were associated with development of post-transplant hypercalcemia: older age (OR 1.89 (1.07-3.33), 1.75 (1.00-3.07), 2.14 (1.19-3.86) for patients aged 40-9, 50-9, ≥ 60 , respectively, compared to <40 years); high pre-transplant serum calcium (OR 5.77 (3.17-10.49) for >2.6 compared to ≤ 2.6 mmol/l); elevated pre-transplant parathyroid hormone (iPTH) (OR 4.11 (1.69-10.00), 11.18 (4.60-27.18) for iPTH 10.6-53, >53 , respectively, compared to <10.6 pmol/l); and pre-transplant dialysis duration > 5 years (OR 2.75 (1.29-5.86), compared to <1 year).

In repeated measures regression analysis, annualized decline in estimated glomerular filtration rate (eGFR) was -1.81 and +0.22 ml/min/1.73m² in post-transplant hypercalcemic and non-hypercalcemic patients, respectively ($p=ns$).

In Cox multivariate regression analysis, increased allograft failure was not associated with posttransplant hypercalcemia, but was associated with

elevated pre-transplant iPTH (HR 1.80 (1.05-3.61) for iPTH >53 compared to <10.6 pmol/l). Post-transplant iPTH values are not obtained in routine clinical practice and were not available for analysis.

CONCLUSIONS: We conclude that hypercalcemia is a common post-transplant complication that can be predicted by pre-transplant clinical and laboratory data. Derangements of bone mineral metabolism are associated with an increased risk of allograft failure and are not directly dependent on development of hypercalcemia. Prevention and treatment of hyperparathyroidism may be an important strategy to improve transplant outcomes and further studies are warranted.