

# Survival following parathyroidectomy among United States dialysis patients

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## Survival following parathyroidectomy among United States dialysis patients.

**Background.** Secondary hyperparathyroidism (SHPTH) is highly prevalent among persons with end-stage renal disease (ESRD). SHPTH has been linked to uremic bone disease, vascular calcification, and a higher risk of death. Parathyroidectomy (PTX) can dramatically reduce parathyroid hormone (PTH) and phosphate levels; however, the relationship between PTX and survival is not known.

**Methods.** We conducted an observational matched cohort study utilizing data from the United States Renal Database System (USRDS) in which 4558 patients undergoing a first PTX while on hemodialysis or peritoneal dialysis were individually matched by age, race, gender, cause of ESRD, dialysis duration, prior transplantation status, and dialysis modality to 4558 control patients who did not undergo PTX. Patients were followed from the date of PTX until they died or were lost to follow-up.

**Results.** The 30-day postoperative mortality rate following PTX was 3.1%. Long-term relative risks of death among patients undergoing PTX were estimated to be 10% to 15% lower than those of matched control patients not undergoing surgery. Survival curves between the 2 groups crossed 587 days following PTX. Median survival was 53.4 months (95% CI: 51.2–56.4) in the PTX group, and 46.8 months (95% CI: 44.7–48.9) in the control group.

**Conclusion.** PTX was associated with higher short-term, and lower long-term, mortality rates among U.S. patients receiving chronic dialysis. Measures to attenuate SHPTH may play an important role in reducing mortality among patients with end-stage renal disease.

Secondary hyperparathyroidism (SHPTH) is present among the majority of patients with end-stage renal dis-

ease (ESRD) [1]. Excess circulating levels of parathyroid hormone (PTH), phosphate, and the calcium-phosphate product have been linked to uremic bone disease, vascular calcification, and death [2–4]. Standard medical therapy for SHPTH often includes high doses of oral calcium binders, which have recently been associated with the extent of vascular calcification [5]. Parathyroidectomy (PTX) can dramatically lower PTH and phosphate levels, but is typically reserved for patients with refractory secondary and tertiary hyperparathyroidism [6].

Case series have reported improvements in bone pain, pruritis, anemia, and hypertension following PTX for renal hyperparathyroidism; however, postoperative deaths are not uncommon [7–10]. Estimates of long-term mortality rates following PTX are not available due to the small number of patients and limited follow-up of single-center studies. Without such information, referral for PTX is based on a combination of patient symptoms, serum markers of SHPTH, lack of response to medical therapy, and the discretion of the practicing physician.

Given the link between SHPTH and adverse cardiovascular outcomes, we hypothesized that PTX would be associated with lower long-term mortality rates. We utilized data from the United States Renal Database System (USRDS) to estimate postoperative and long-term mortality rates following PTX. We compared short- and long-term mortality rates among patients undergoing PTX with a matched cohort of patients not undergoing PTX.

## METHODS

### Patient population

Data were utilized from the USRDS, which collects clinical, demographic, and dialysis information for all patients receiving chronic renal replacement therapy in the United States. Details of the USRDS are described elsewhere [11]. Patients were considered for the present

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analysis if they were at least 18 years old and had initiated renal replacement therapy between January 1, 1988 and October 1, 1999. Patients who died, were lost to follow-up, or underwent PTX during the first 90 days of renal replacement therapy were excluded. The exclusion of the first 90 days of dialysis time is due to potential delay of the Medicare eligibility application process, which can take up to 90 days. Because USRDS hospitalization data is obtained from Medicare inpatient claims, the study cohort was further restricted to patients with fee-for-service Medicare as their primary payer 90 days after the initiation of dialysis. Payer status was determined from the longitudinal *Payer History* file maintained by the USRDS.

### Determination of parathyroidectomy

Patients were considered to have undergone PTX if they received an International Classification of Diseases–Clinical Modification 9th Edition (ICD9-CM) hospital procedure code 06.81, “total parathyroidectomy,” or 06.89, “other parathyroidectomy.” The USRDS obtains hospital procedure codes through Medicare institutional inpatient claims sourced from the Centers for Medicare and Medicaid Services (CMS, formerly HCFA). Up to 10 procedure codes were analyzed per hospitalization. The first PTX occurring between the initiation of dialysis and December 31, 1999 was utilized for analysis.

### Selection of patient cohorts

From the eligible patient population, all dialysis patients undergoing a first PTX between January 1, 1988 and December 31, 1999 were selected. Because indications for PTX, as well as the response to PTX, may differ between dialysis and transplant patients, patients undergoing PTX with a functioning renal transplant were excluded from the present study.

For each eligible PTX patient, 1 control patient was selected on the basis of being alive on the PTX date, and individually matched by age (plus or minus 2 years), race (African American, Caucasian, other), gender, year of initiation of dialysis (plus or minus 1 year), primary cause of ESRD (diabetes, hypertension, glomerulonephritis, polycystic kidney disease, other), and modality at the time of PTX (hemodialysis, peritoneal dialysis). For PTX patients who had previously received a renal transplant, a similar control patient was found who had also received a renal transplant, and matched by the transplant date (plus or minus 1 year).

### Determination of risk time

For each matched patient pair consisting of 1 PTX patient and 1 control patient, the study start date was defined as the PTX date. Thus, each matched patient pair began accruing risk time on the date of PTX. Pa-

tients were considered at risk until the first occurrence of death, loss to follow-up, loss of Medicare coverage, or the study’s close on December 31, 2001. Transplantation after PTX was handled as a time-dependent covariate. Dates of death are obtained by the USRDS from CMS form #2746, which is completed by the primary nephrologist following the death of any dialysis patient. Patients were considered lost to follow-up by the USRDS if they received no dialysis billing claims for 1 consecutive year without a notification of death. For patients determined to be lost to follow-up, the last date of dialysis billing claims was considered the last date of follow-up. Survival, follow-up data, and insurance status were complete through December 31, 2001.

### Calcitriol data

Baseline injectable calcitriol use was examined by linking USRDS Medicare institutional claims files to the study cohort. For each calendar month, calcitriol dose was calculated by summing the number of injectable 1- $\mu$ g units billed during that month. Because claims for calcitriol were rare prior to 1993, we limited our subanalyses of calcitriol use to patient pairs with a PTX date after January 1, 1994.

### Statistical analysis

Mortality rates were calculated by dividing the number of deaths by the number of person-years at risk within each time period following PTX. Baseline calcitriol dosages were compared between PTX and non-PTX groups using the Student *t* test. Unadjusted Kaplan-Meier survival curves were constructed by PTX group. Survival analysis was used to estimate the relationship between PTX and the instantaneous relative hazard of mortality. Elapsed time from PTX was modeled as a categorical time-dependent covariate. Time intervals were chosen as 0 to 30 days, 30 to 90 days, 90 days to 1 year, 1 to 3 years, and greater than 3 years following PTX to convey short-term and long-term mortality risks.

Multivariate models were stratified by matched patient pair to most precisely control for confounding by the matching variables. In addition to matching, multivariate models were adjusted for age and dialysis duration to correct for slight differences in these continuous variables within each matched pair. Multivariate models were further adjusted for dialysis modality following PTX (hemodialysis, peritoneal dialysis, transplant), which was modeled as a time-dependent covariate. Scaled Schoenfeld residuals and graphical methods were examined to confirm that assumptions of the proportional hazards model were satisfied within each time interval.

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