

# Survival following parathyroidectomy among United States dialysis patients

**BRYAN KESTENBAUM, DENNIS L. ANDRESS, STEPHEN M. SCHWARTZ, DANIEL L. GILLEN, STEPHEN L. SELIGER, PARESH R. JADAV, DONALD J. SHERRARD, and CATHERINE STEHMAN-BREEN**

*Division of Nephrology, University of Washington, Veterans' Affairs Puget Sound Health Care System, Seattle, Washington; Department of Epidemiology, University of Washington, Cardiovascular Health Research Unit, Seattle, Washington; Fred Hutchinson Cancer Research Center, Program in Epidemiology, Seattle, Washington; Department of Health Studies, University of Chicago, Chicago, Illinois; Division of Nephrology, University of Washington, Seattle, Washington; and Amgen, Incorporated, Thousand Oaks, California*

## 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.

**Table 1.** Baseline characteristics of the individually matched patient cohort

	Parathyroidectomy (PTX) patients (N = 4558)	Matched control patients not undergoing PTX <sup>a</sup> (N = 4558)
Age years	47.6 (15.8)	47.6 (15.8)
Race		
White	2221 (48.7)	2221 (48.7)
Black	2212 (48.5)	2212 (48.5)
Other	125 (2.7)	125 (2.7)
Gender		
Male	1939 (42.5)	1939 (42.5)
Female	2619 (57.5)	2619 (57.5)
Cause of ESRD		
Hypertension	1611 (35.3)	1611 (35.3)
Diabetes	886 (19.4)	886 (19.4)
Glomerulonephritis	986 (21.6)	986 (21.6)
Polycystic disease	207 (4.5)	207 (4.5)
Other	868 (19.0)	868 (19.0)
Duration of dialysis years	3.4 (2.2)	3.3 (2.2)
Modality at PTX		
Hemodialysis	3769 (82.7)	3769 (82.7)
Peritoneal dialysis	789 (17.3)	789 (17.3)
Prior renal transplant	220 (4.8)	220 (4.8)

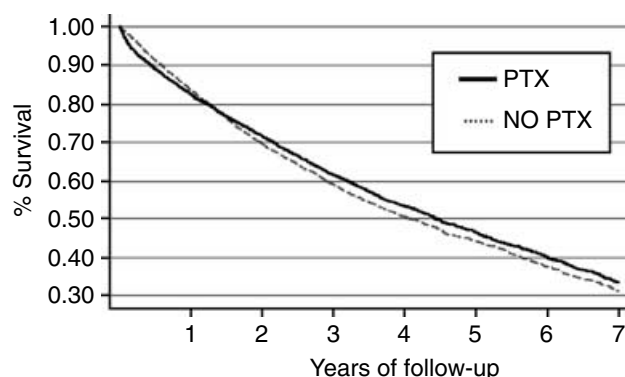
All values expressed as mean (SD) or N (%).

<sup>a</sup>Control patients individually matched to PTX patients by all characteristics listed in the Table, plus the date of initiation of renal replacement therapy and the date of prior renal transplantation, if applicable.

## RESULTS

Data were available for 769,179 ESRD patients initiating renal replacement therapy between January 1, 1988 and October 1, 1999. During the first 90 days of renal replacement therapy, 51,398 (6.7%) patients died, and 624 (0.1%) underwent PTX. These patients were excluded from analysis. Furthermore, 9826 (1.3%) patients younger than 18 years old, and 37,428 (4.9%) patients with incomplete data regarding modality or primary cause of ESRD were excluded. Finally, 199,887 (26.0%) patients were excluded because fee-for-service Medicare was not their primary payer 90 days after the initiation of dialysis. Following these exclusions, 470,016 patients were available for analysis. Patients whose primary payer was Medicare tended to be older than those with other insurance; however, other baseline characteristics were similar among patients covered by Medicare and patients excluded from study on the basis of other insurance coverage.

From the eligible patient pool, 4844 patients undergoing a first PTX while receiving hemodialysis or peritoneal dialysis were identified. A suitable matched control patient not undergoing PTX was found for 4558 (93.3%) of these patients. The remaining 286 unmatched PTX patients were excluded. Excluded, unmatched patients tended to be younger, and were more likely to be of race other than Caucasian or African American, to be receiving peritoneal dialysis rather than hemodialysis, and to have previously undergone renal transplantation. As a

**Fig. 1.** Kaplan-Meier estimates of cumulative survival among patients undergoing or not undergoing parathyroidectomy (PTX).

result, excluded, unmatched PTX patients had lower mortality rates than PTX who were matched.

The completed matched study cohort was relatively young (Table 1), with a high proportion of nondiabetic patients, as compared to the general United States dialysis population. The median hospital stay associated with PTX was 7 days (intraquartile range, 5–11 days). Among a subgroup of PTX patients and matched controls with a PTX date after January 1, 1994, mean injectable calcitriol use in the year prior to the PTX date was 4.63  $\mu\text{g}/\text{month}$  among PTX patients, and 4.15  $\mu\text{g}/\text{month}$  among matched controls (*P* value for comparison, 0.002).

Within the first 30 postoperative days there were 142 deaths among patients undergoing PTX (30-day postoperative mortality rate, 3.1%). In comparison, 1.2% (95% CI 0.9–1.6) of matched control patients not undergoing PTX died during the same 30-day period. Postoperative deaths among PTX patients were classified as cardiovascular (49.3%) and infectious (18.3%), with the remainder due to a variety of illnesses, or not classified.

Median follow-up times were 2.9 years (intraquartile range, 1.5–4.8 years) in the PTX group, and 2.7 years (intraquartile range, 1.4–4.4 years) in the matched control group. Survival was initially higher among patients not undergoing PTX, then became equal 587 days from the date of surgery (Fig. 1). After 587 days, a higher proportion of patients undergoing PTX remained alive throughout follow-up. 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 matched control group, a difference of 6.6 months.

As compared to matched controls, patients undergoing PTX experienced an early increase in mortality risk within 90 days of surgery, followed by a gradual decline in the relative risk of death (Table 2). Relative risks of death 0 to 30, and 30 to 90 days following PTX were 2.72 (95% CI 2.12–3.48) and 1.45 (95% CI 1.23–1.72), respectively, compared to matched control patients. Approximately 90 days after surgery, the instantaneous hazard (or risk) of

**Table 2.** Relative risk of mortality following parathyroidectomy by time interval from surgery

Time from PTX date	Mortality rate per 1000 person-years (number of deaths)		Adjusted RR <sup>a</sup> (95% CI)	P value
	PTX patients	Control patients		
0–30 days	385.8 (142)	148.0 (55)	2.72 (2.12, 3.48)	<0.001
30–90 days	257.7 (182)	179.5 (130)	1.45 (1.23, 1.72)	<0.001
90 days–1 year	159.5 (474)	184.3 (556)	0.90 (0.81, 0.99)	0.031
1 year–3 years	145.8 (884)	177.5 (1038)	0.85 (0.78, 0.92)	<0.001
>3 years	147.8 (753)	174.0 (757)	0.85 (0.75, 0.97)	0.014

<sup>a</sup>Control patients matched to PTX patients by age, race, gender, primary cause of ESRD, dialysis duration, dialysis modality at PTX, transplantation history, and the date of initiation of renal replacement therapy, and further adjusted for age, dialysis duration, and dialysis modality subsequent to PTX.

**Table 3.** Association between parathyroidectomy and 90-day mortality rate by patient subgroups

	Mortality rate per 1000 person-years 0–90 days following PTX (number of deaths)		Adjusted relative risk of mortality <sup>a</sup> (95% CI)
	PTX Patients	Control patients	
Overall	301.6 (324)	168.8 (185)	1.84 (1.52, 2.22)
Age			
<40 years	131.4 (52)	70.5 (28)	1.82 (1.14, 2.93)
40–60 years	280.9 (115)	157.7 (65)	1.91 (1.38, 2.65)
>60 years	583.0 (157)	321.1 (92)	1.85 (1.41, 2.42)
Race			
Caucasian	350.4 (182)	209.3 (111)	1.71 (1.34, 2.19)
African American	252.9 (133)	132.6 (71)	1.98 (1.47, 2.67)
Dialysis duration			
0–1 years	526.4 (76)	209.0 (37)	2.53 (1.57, 4.06)
1–3 years	288.6 (105)	151.7 (56)	1.85 (1.25, 2.74)
3 or more years	252.5 (143)	167.4 (92)	1.52 (1.15, 2.01)
Cause of ESRD			
Diabetes	604.5 (121)	285.5 (60)	2.12 (1.54, 2.93)
All other causes	232.2 (203)	141.1 (125)	1.71 (1.36, 2.16)
Dialysis modality			
Hemodialysis	303.3 (266)	170.1 (152)	1.85 (1.51, 2.27)
Peritoneal dialysis	329.7 (58)	205.7 (31)	1.77 (1.12, 2.80)

<sup>a</sup>Control patients matched to PTX patients by age, race, gender, primary cause of ESRD, dialysis duration, dialysis modality at PTX, transplantation history, and the date of initiation of renal replacement therapy, and further adjusted for age, dialysis duration, and dialysis modality subsequent to PTX.

death fell considerably among patients undergoing PTX. Relative mortality rates were approximately 10% lower among PTX patients between 90 days and 1 year following surgery, and were approximately 15% lower throughout the remainder of follow-up. Including baseline calcitriol dose in the multivariate models did not change mortality estimates for PTX.

To identify particular patient subgroups that might be at highest risk, or incur the greatest benefit from PTX, the relative mortality risk associated with PTX was analyzed among patient subgroups (Tables 3 and 4). Short- and long-term mortality rates were defined as 0 to 90 days, and greater than 90 days from the date of PTX, respectively. The short-term relative risk of death was higher

**Table 4.** Association between parathyroidectomy and long-term mortality rates by patient subgroups

	Mortality rate per 1000 person-years 90 days following PTX through follow-up (number of deaths)		Adjusted relative risk of mortality <sup>a</sup> (95% CI)
	PTX Patients	Control patients	
Overall	149.4 (2111)	177.9 (2351)	0.87 (0.80, 0.94)
Age			
<40 years	76.7 (466)	96.4 (539)	0.78 (0.66, 0.92)
40–60 years	163.7 (874)	187.0 (920)	0.88 (0.78, 1.00)
>60 years	283.6 (771)	329.9 (892)	0.89 (0.77, 1.03)
Race			
Caucasian	178.0 (1142)	201.5 (1214)	0.90 (0.80, 1.01)
African American	126.8 (931)	157.4 (1077)	0.84 (0.75, 0.94)
Dialysis duration			
0–1 years	182.9 (340)	193.1 (433)	1.07 (0.84, 1.36)
1–3 years	157.4 (773)	175.1 (805)	0.96 (0.81, 1.12)
3 or more years	135.6 (998)	174.6 (1113)	0.79 (0.70, 0.89)
Cause of ESRD			
Diabetes	261.3 (508)	283.8 (573)	0.96 (0.81, 1.14)
All other causes	131.5 (1603)	158.8 (1778)	0.84 (0.77, 0.92)
Dialysis modality			
Hemodialysis	154.0 (1465)	185.9 (1684)	0.87 (0.79, 0.95)
Peritoneal dialysis	163.8 (159)	205.8 (181)	0.86 (0.70, 1.05)

<sup>a</sup>Control patients matched to PTX patients by age, race, gender, primary cause of ESRD, dialysis duration, dialysis modality at PTX, transplantation history, and the date of initiation of renal replacement therapy, and further adjusted for age, dialysis duration, and dialysis modality subsequent to PTX.

among diabetic patients, African American patients, and patients who had received dialysis for less than 1 year (Table 3). Short-term relative mortality risks did not differ appreciably by age or dialysis modality, nor did they differ by gender, or whether a patient had previously undergone renal transplantation. After 90 days the relative risk of death associated with PTX was estimated to be 13% lower than that of matched control patients among the overall study cohort (Table 4). Relative risks of death tended to be lower among patients younger than 40 years of age, and those who had received dialysis for greater than 3 years. However, differences among subgroups in their response to PTX were not statistically distinguishable. The apparent lack of long-term benefit associated with PTX among diabetic patients was due to the fact that diabetics incurred a continually increased risk of death for up to 1 year following surgery. Among diabetic patients, the relative risk of death between 90 days and 1 year following PTX was 1.20 (95% CI 0.93–1.55), while the relative risk of death greater than 1 year following PTX was 0.79 (95% CI 0.63–1.00).

## DISCUSSION

In this observational study, we found PTX to be associated with lower long-term risks of mortality compared to matched control patients not undergoing PTX. These data suggest that control of SHPTH is likely to play an

important role in the long-term outcome of chronic dialysis patients.

Recent evidence has demonstrated important links between SHPTH and cardiovascular morbidity and mortality [12–15]. Excess circulating PTH concentrations lead to increased cellular calcium uptake and cardiac fibrosis experimentally [12, 13], and have been associated with an increased risk of aortic calcification clinically [3]. Phosphate directly alters the phenotype of smooth muscle cells *in vitro*, leading to the expression of bone matrix proteins [15]. The resulting medial vessel wall calcification leads to increased arterial stiffness, widened pulse pressures, aggravation of left ventricular hypertrophy, and inadequate tissue perfusion [16]. Excess serum levels of phosphate, the calcium-phosphate product, and PTH have been associated with an increased risk of all-cause [14] and cardiovascular-specific [2] mortality among ESRD patients. Given the link between SHPTH and cardiovascular disease, it would be expected that therapeutic measures to attenuate SHPTH would positively impact survival. PTX leads to immediate and dramatic reductions in circulating concentrations of PTH, calcium, and phosphate in more than 95% of patients undergoing surgery [17–19]. Although serologic data are not available for this population-based analysis, we hypothesize that long-term levels of PTH, calcium, and phosphate are, on average, lower among patients undergoing PTX compared to matched control patients not undergoing PTX.

A second mechanism by which PTX may lower long-term mortality is by reducing exposure to medical therapy prescribed to attenuate PTH and phosphate excess. Although PTX may result in an initial increase in calcium supplementation for postsurgical hypocalcemia [20], it would be expected that long-term exposure to calcium-containing binders might decrease following PTX. Higher doses of oral calcium binders have been associated with the extent of coronary artery calcification in a cohort of young ESRD patients [5].

Finally, it is possible that PTX contributes to lower long-term mortality rates by moderating hypertension. PTX has been observed to reduce blood pressure and improve anemia among patients with ESRD [7, 18]. In a series of 21 patients undergoing PTX, significant reductions in systolic and diastolic blood pressure of 9.4 mm Hg and 3.7 mm Hg were reported 18 months after surgery, respectively [7]. In another series of 45 ESRD patients undergoing PTX, mean reductions of 12.0 mm Hg and 6.2 mm Hg in systolic and diastolic blood pressure were reported 1 year following PTX, respectively [18]. These authors also found that mean hemoglobin levels increased significantly by 1.1 g/dL following PTX [18].

While long-term survival was found to be lower following PTX, we observed a 30-day postoperative mortality rate of 3.1%, which is comparable to other studies

of surgical mortality in the dialysis population. Single-center estimates of mortality following PTX are highly variable, but generally consistent with our findings [8, 10, 19, 21]. For example, a retrospective chart review from the University of Michigan reported 3 postoperative deaths among 80 ESRD patients undergoing PTX between 1969 and 1992 (postoperative mortality rate 3.8%) [8], and a case series of 20 consecutive patients undergoing PTX for renal hyperparathyroidism in Germany reported 1 death within 6 days of surgery [21]. In contrast, a series of 1053 patients undergoing PTXs from a single institution in Japan reported only 1 postoperative death [10]. Patient selection, regional differences in referral for PTX, and variability arising from small sample sizes likely account for the variation noted among previous case series.

Potential factors contributing to early mortality following PTX include the toxic effects of longstanding SHPTH, metabolic disturbances following PTX, general sensitivity of ESRD patients to surgical procedures, poor compliance among persons with longstanding SHPTH, and selection of a subgroup of patients who are at imminent risk of death. Typically, ESRD patients undergoing PTX have longstanding PTH and phosphate excess, chronic exposure to high doses of oral calcium binders and activated vitamin D, and, in some cases, hypercalcemia, all factors that may increase the risk of death. Given the link between these components of SHPTH and vascular calcification, it is possible that patients undergoing PTX have considerable vascular compromise at the time of surgery, placing them at high risk for postoperative complications. Furthermore, PTX results in the “hungry bone” syndrome [20], in which serum calcium levels fall precipitously, prompting large doses of administered calcium to maintain homeostasis. It is possible that electrolyte shifts that occur as a result of the hungry bone syndrome contribute to an increased risk of death following PTX. Dialysis patients with refractory SHPTH may be noncompliant with prescribed dietary recommendations and phosphate binders. As such, patients undergoing SHPTH may be generally less compliant with other important aspects of their medical care, placing them at high risk for postoperative complications. The fact that patients undergoing PTX tended to do relatively well in the long-term raises the issue of whether dietary compliance with phosphate may be less consequential once PTX is performed.

A generally poor response to surgery among ESRD patients and the potential selection of high-risk patients for PTX may also contribute to the substantial postoperative risk of death that we observed. ESRD patients are known to be at particularly high risk of mortality following surgical procedures. A recent study reported in-hospital mortality rates of 8.6% and 6.4% among ESRD patients undergoing coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, respectively

[22]. These postoperative mortality rates are markedly higher than those reported among the general population [23]. Further, ESRD patients undergoing a first cadaveric renal transplant experienced a 2.8-fold increased risk of death within the first 14 postoperative days compared to patients awaiting surgery on the transplant waiting list [24]. In addition to their overall sensitivity to surgical procedures, some ESRD patients may undergo PTX for the treatment of calciphylaxis [25], which carries a substantially elevated short-term risk of death [26]. Thus, it is possible that the high risk of postoperative mortality following PTX derives from a particularly high-risk subset of ESRD patients referred for PTX.

An important limitation of the present study is that differences in patient characteristics among subjects undergoing or not undergoing PTX may account for differences in mortality rates. Although control patients were specifically matched to PTX patients by multiple clinical factors, it is possible that patients undergoing PTX differed from non-PTX patients by characteristics that were not measured. ESRD patients who undergo elective surgery are likely to be generally healthier than those not undergoing surgery. Further, elevated levels of advanced glycation end products and hyperglycemia significantly blunt PTH secretion [27, 28], such that ESRD patients with a vigorous PTH response might be expected to have fewer cardiovascular risk factors. In this respect, the long-term decline in the relative risk of death may derive from presurgical health status, rather than from the potential benefit of attenuating SHPTH. Importantly, the present observational study does not intend to simulate a randomized trial comparing PTX to medical management, but instead focuses on long-term mortality rates following PTX, while selecting the most relevant control population to consider mortality rates in a relative context.

Other limitations of the present study include the lack of specific laboratory or medication data. Without serum PTH, phosphate, and calcium measurements, we cannot discern which component of SHPTH might be responsible for the observed survival data, or which levels of serum markers may be associated with the greatest risks and benefits of surgery. The restriction of the study cohort to those patient covered by Medicare, while necessary to perform analyses of USRDS data, reduces the generalizability of our results to those dialysis patients receiving Medicare. Because PTX was defined using the USRDS procedure data, no proper method of identifying non-Medicare patients who undergo PTX are available to study how the relative risk of death following PTX might vary by Medicare status. Other studies utilizing different data sources may be able to help answer these questions in the future.

The selection of ESRD patients on the date of PTX resulted in a cohort of relatively long-term survivors on renal replacement therapy. While the selection of long-term

survivors may limit the generalizability of our results, our findings are applicable to those ESRD patients considering PTX, who are often long-term survivors on dialysis. It is important to note that mortality risks that were analyzed greater than 3 years from the PTX date apply to patients receiving PTX relatively early in the study and, thus, under observation for greater than 3 years following PTX. Important strengths of the current study include the large sample of incident PTXs analyzed, providing adequate power to accurately estimate mortality risks over time, and the use of a national sample, which is not biased by practice patterns of a particular region or health care institution.

## CONCLUSION

PTX performed among dialysis patients is associated with an increased postoperative risk of death, followed by a gradual decline in the relative risk of mortality. Survival was initially lower among patients undergoing PTX until 587 days following surgery, at which time survival was higher in the PTX group. These data should be integrated into the clinical decision-making process of referring dialysis patients for surgery to correct SHPTH.

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Reprint requests to Bryan Kestenbaum, M.D., MS, Veterans' Affairs Puget Sound Health Care System, Division of Nephrology, Mail Stop 111A, 1660 South Columbian Way, Seattle, WA 98108.  
E-mail: brk@u.washington.edu

## REFERENCES

- SALEM MM: Hyperparathyroidism in the hemodialysis population: A survey of 612 patients. *Am J Kidney Dis* 29:862–865, 1997
- GANESH SK, STACK AG, LEVIN NW, et al: Association of elevated serum PO(4), Ca × PO(4) product, and parathyroid hormone with cardiac mortality risk in chronic hemodialysis patients. *J Am Soc Nephrol* 12:2131–2138, 2001
- RAGGI P, BOULAY A, CHASAN-TABER S, et al: Cardiac calcification in adult hemodialysis patients. A link between end-stage renal disease and cardiovascular disease? *J Am Coll Cardiol* 39:695–701, 2002
- SHERRARD DJ, HERCZ G, PEI Y, et al: The spectrum of bone disease in end-stage renal failure—An evolving disorder. *Kidney Int* 43:436–442, 1993
- GOODMAN WG, GOLDIN J, KUIZON BD, et al: Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *N Engl J Med* 342:1478–1483, 2000
- DE FRANCISCO AL, FRESNEDO GF, RODRIGO E, et al: Parathyroidectomy in dialysis patients. *Kidney Int (Suppl)*:161–166, 2002
- GOLDSMITH DJ, COVIC AA, VENNING MC, ACKRILL P: Blood pressure reduction after parathyroidectomy for secondary hyperparathyroidism: Further evidence implicating calcium homeostasis in blood pressure regulation. *Am J Kidney Dis* 27:819–825, 1996
- PUNCH JD, THOMPSON NW, MERION RM: Subtotal parathyroidectomy in dialysis-dependent and post-renal transplant patients. A 25-year single-center experience. *Arch Surg* 130:538–542, 1995

9. CHOU FF, HO JC, HUANG SC, SHEEN-CHEN SM: A study on pruritus after parathyroidectomy for secondary hyperparathyroidism. *J Am Coll Surg* 190:65–70, 2000
10. TOMINAGA Y, UCHIDA K, HABA T, et al: More than 1,000 cases of total parathyroidectomy with forearm autograft for renal hyperparathyroidism. *Am J Kidney Dis* 38:S168–171, 2001
11. SYSTEM URD: *Researcher's Guide to the USRDS Database*, Bethesda, The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1999
12. ZHANG YB, SMOGORZEWSKI M, NI Z, MASSRY SG: Altered cytosolic calcium homeostasis in rat cardiac myocytes in CRF. *Kidney Int* 45:1113–1119, 1994
13. AMANN K, RITZ E, WIEST G, et al: A role of parathyroid hormone for the activation of cardiac fibroblasts in uremia. *J Am Soc Nephrol* 4:1814–1819, 1994
14. BLOCK GA, HULBERT-SHEARON TE, LEVIN NW, PORT FK: Association of serum phosphorus and calcium  $\times$  phosphate product with mortality risk in chronic hemodialysis patients: A national study. *Am J Kidney Dis* 31:607–617, 1998
15. GIACHELLI CM, JONO S, SHIOI A, et al: Vascular calcification and inorganic phosphate. *Am J Kidney Dis* 38:S34–37, 2001
16. BLOCK G, PORT FK: Calcium phosphate metabolism and cardiovascular disease in patients with chronic kidney disease. *Semin Dial* 16:140–147, 2003
17. GAGNE ER, URENA P, LEITE-SILVA S, et al: Short- and long-term efficacy of total parathyroidectomy with immediate autografting compared with subtotal parathyroidectomy in hemodialysis patients. *J Am Soc Nephrol* 3:1008–1017, 1992
18. COEN G, CALABRIA S, BELLINGHERI G, et al: Parathyroidectomy in chronic renal failure: Short- and long-term results on parathyroid function, blood pressure and anemia. *Nephron* 88:149–155, 2001
19. JOFRE R, GOMEZ JM, MENARGUEZ J, et al: Parathyroidectomy: Whom and when? *Kidney Int (Suppl)*:97–100, 2003
20. HEADLEY CM: Hungry bone syndrome following parathyroidectomy. *Anna J* 25:283–289, 1998
21. STRACKE S, JEHLER PM, STURM D, et al: Clinical course after total parathyroidectomy without autotransplantation in patients with end-stage renal failure. *Am J Kidney Dis* 33:304–311, 1999
22. HERZOG CA, MA JZ, COLLINS AJ: Comparative survival of dialysis patients in the United States after coronary angioplasty, coronary artery stenting, and coronary artery bypass surgery and impact of diabetes. *Circulation* 106:2207–2211, 2002
23. MURPHY ML, HULTGREN HN, DETRE K, et al: Treatment of chronic stable angina. A preliminary report of survival data of the randomized Veterans Administration cooperative study. *N Engl J Med* 297:621–627, 1977
24. WOLFE RA, ASHBY VB, MILFORD EL, et al: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 341:1725–1730, 1999
25. GIROTTI JA, HARMON JW, RATNER LE, et al: Parathyroidectomy promotes wound healing and prolongs survival in patients with calciphylaxis from secondary hyperparathyroidism. *Surgery* 130:645–650, 2001
26. FINE A, ZACHARIAS J: Calciphylaxis is usually non-ulcerating: Risk factors, outcome and therapy. *Kidney Int* 61:2210–2217, 2002
27. SUGIMOTO T, RITTER C, MORRISSEY J, et al: Effects of high concentrations of glucose on PTH secretion in parathyroid cells. *Kidney Int* 37:1522–1527, 1990
28. YAMAMOTO T, OZONO K, MIYAUCHI A, et al: Role of advanced glycation end products in adynamic bone disease in patients with diabetic nephropathy. *Am J Kidney Dis* 38:S161–164, 2001