

Parathyroidectomy in Dialysis Patients: What is the Risk?

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ABSTRACT

Aim: Patients with chronic kidney disease (CKD) on dialysis commonly develop hyperparathyroidism (HPT), but are often not referred for surgical evaluation because of the belief that the cardiopulmonary risks of a parathyroidectomy are prohibitively high. Previous studies have not adequately determined the surgical risks of parathyroidectomy in this population.

Materials and methods: We used the American College of Surgeons National Surgical Quality Improvement Program database from 2005 to 2013 to evaluate risk of complications for dialysis vs nondialysis patients undergoing parathyroidectomy using univariate and multivariate logistic regressions. We also compared outcomes between dialysis patients undergoing parathyroidectomy and arteriovenous fistula (AVF) creation to understand the relative risk between these procedures.

Results: A total of 28,438 patients underwent parathyroidectomy; 1,833 (6.5%) were on dialysis. Among patients undergoing parathyroidectomy, unadjusted mortality and complication rates were higher for patients on dialysis compared to those not on dialysis (1.4% vs 0.1%, $p < 0.001$; 7.9% vs 1.4%, $p < 0.001$). Multivariate analysis found increased odds of mortality, all complications, and cardiopulmonary complications among patients on dialysis compared to those not on dialysis [odds ratio (OR) 5.28, $p = 0.004$; 2.10, $p < 0.001$; 5.14, $p < 0.001$]. When compared to patients undergoing parathyroidectomy, dialysis patients undergoing AVF had no difference in odds of death ($p = 0.392$) or cardiopulmonary complications ($p = 0.138$), but did have an increased risk of any complication (OR 1.66, $p = 0.035$).

Conclusion: Dialysis patients undergoing parathyroidectomy have an increased risk of cardiopulmonary complications and mortality compared to patients not on dialysis; however, these risks are similar to patients undergoing AVF creation. The risks of parathyroidectomy in dialysis patients are likely similar to other commonly performed procedures for dialysis patients.

Clinical significance: The risk of mortality and complications should be discussed during informed consent with dialysis patients undergoing parathyroidectomy. These findings can also assist in preoperative risk assessments.

Keywords: Dialysis, Hyperparathyroidism, National surgical quality improvement program, Parathyroidectomy, Secondary hyperparathyroidism, Surgical outcomes.

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INTRODUCTION

Chronic kidney disease (CKD) affects approximately 25% of the US population, including 400,000 patients who are dialysis-dependent.¹ Renal hyperparathyroidism (rHPT) is a common complication of CKD characterized by derangements in the homeostasis of calcium, phosphate, and vitamin D leading to parathyroid hyperplasia.^{2,3} Renal hyperparathyroidism is classically broken into two types based on the patient's serum calcium level. Secondary hyperparathyroidism (2° HPT) is the elevation of parathyroid hormone (PTH) in response to hypocalcemia induced by phosphate retention and reduced calcitriol synthesis.⁴ Tertiary hyperparathyroidism (3° HPT) is seen in patients with longstanding 2° HPT who develop autonomous PTH secretion, often associated with hypercalcemia. The derangements in calcium and phosphate that result from rHPT likely accelerate coronary artery calcification.⁵ Cardiovascular disease in dialysis patients is common and previous reports have suggested that patients with end-stage renal disease (ESRD) have an increased risk of postoperative complications following elective surgery.⁶

Over the last two decades, improvement in medical management with vitamin D analogs, phosphate binders, and calcimimetic drugs, such as cinacalcet, has expanded treatment options for patients with rHPT, but parathyroidectomy remains an important option for many patients.⁷ Numerous studies have highlighted the survival benefit of parathyroidectomy in the treatment of rHPT, including significant reductions in the incidence of major cardiovascular events and all-cause mortality.⁸⁻¹⁰ Parathyroidectomy has also been shown to be more cost-effective than cinacalcet in patients fit for surgery or who will undergo transplantation.^{11,12}

Unfortunately, many patients with rHPT are never referred for surgical consultation because of concern for excessive operative risk. Most of this is driven by fear of cardiopulmonary complications from general anesthesia. Although it is assumed that the surgical risks of dialysis patients are increased when compared to

non-CKD patients undergoing a parathyroidectomy, large studies quantifying these perioperative risks are lacking. Furthermore, a better understanding of the relative risks of parathyroidectomy in dialysis patients when compared to other procedures, such as arteriovenous fistula (AVF) creation, is needed to help surgeons counsel patients prior to surgery.

The purpose of this study is to quantify the risks of cardiopulmonary complications and death in dialysis patients undergoing parathyroidectomy. This study also compares the risks of parathyroidectomy to AVF creation in dialysis patients to help surgeons and nephrologists understand the relative risk of the two procedures.

MATERIALS AND METHODS

We used the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database from 2005 to 2013. This nationally validated program measures over 135 variables on each patient, including 30-day postoperative outcomes. The 2005 to 2006 database included information from 121 hospitals, while data from 2013 included information from 435 hospitals.¹³ This dataset was chosen for its breadth of preoperative and postoperative variables collected for each patient.

In our first analysis, we compared outcomes between patients on dialysis to patients not on dialysis among all patients undergoing parathyroidectomy. Outcomes were 30-day mortality or 30-day morbidity (or complication). A patient was determined to have a cardiopulmonary complication if they had at least one of the following: pneumonia, unplanned intubation, pulmonary embolism, ventilator >48 hours, cardiac arrest requiring cardiopulmonary resuscitation, or myocardial infarction. All complications included cardiopulmonary complications and the following: Superficial surgical site infection (SSI), deep incisional SSI, organ space SSI, wound disruption, progressive renal insufficiency, acute renal failure, urinary tract infection, stroke/cerebrovascular accident with neurological deficit, coma>24 hours, peripheral nerve injury, bleeding requiring transfusions, graft, prosthesis or flap failure, deep vein thrombosis or thrombophlebitis, sepsis, or septic shock.

Multivariate logistic regressions always included age, race, sex, functional status, and American Society of Anesthesiologists (ASA) physical classification system. Functional status is defined as independent, partially dependent, and totally dependent. The ASA classification is defined as: (1) Normal healthy patient, (2) mild systemic disease, (3) severe systemic disease, (4) severe systemic disease that is constant threat to life, and (5) moribund, not expected to survive without the

operation. Other variables were included if they had p-values <0.05 on univariate logistic regression for both mortality and morbidity.

We performed a second analysis comparing mortality and morbidity of patients on dialysis who underwent parathyroidectomy to patients who underwent AVF creation. This analysis was limited to 2007 to 2008, since these were the only available years AVF creation were included in the database. We also limited AVF creation to those who underwent general anesthesia, for a more accurate comparison. Multivariate logistic regressions included age, race, sex, functional status, and ASA classification, and additional variables that were significant on univariate analysis for each outcome.

Summary statistics compared means using Student’s t-test and proportions using Pearson’s chi-squared test. Univariate and multivariate logistic regressions were performed for each outcome of interest. Statistical significance was defined as p < 0.05. Statistical analysis was performed using STATA 64-bit Special Edition, version 11.2 (Stata Corp, College Station, Texas).

RESULTS

Risk of Parathyroidectomy in Dialysis Patients vs Nondialysis Patients

A total of 28,438 patients underwent parathyroidectomy in this database, including 1,833 (6.5%) patients on dialysis, and 26,605 patients not on dialysis. Patients on dialysis were, on average, younger (49 vs 61 years old), more likely to be African American (55.0 vs 12.2%), less likely to be female (49.3 vs 77.0%), had a higher mean ASA classification (1.9 vs 1.3), and a longer mean length of stay (5.8 vs 0.9 days; Table 1). Patients on dialysis had higher rates of unadjusted mortality (1.4 vs 0.1%), overall

Table 1: Patient population among all patients undergoing parathyroidectomy, comparing patients on dialysis to patients not on dialysis

	Dialysis (n = 1,833, 6.5%)	Nondialysis (n = 26,605, 93.5%)	p-value
Age – mean years	48.5	60.5	<0.001
Race – n (%)			<0.001
White	562 (32.7)	19,707 (81.4)	
African American	946 (55.0)	2,946 (12.2)	
Other	212 (12.3)	1,571 (6.5)	
Female – n (%)	902 (49.3)	20,455 (77.0)	<0.001
ASA* classification – mean	1.9	1.3	<0.001
Length of stay – mean days	5.8	0.9	<0.001
Died – n (%)	26 (1.4)	26 (0.1)	<0.001
Complications – n (%)			
All complications	144 (7.9)	370 (1.4)	<0.001
Cardiopulmonary	74 (4.0)	121 (0.5)	<0.001



Table 2: Multivariate logistic regression predicting mortality among all patients undergoing parathyroidectomy

	Odds ratio (95% CI)	p-value
Dialysis	5.28 (1.70–16.42)	0.004
Female	0.92 (0.40–2.09)	0.838
Race		
White (reference)	1	
African American	0.69 (0.25–1.90)	0.468
Other	1.36 (0.36–5.20)	0.651
Age	1.05 (1.02–1.09)	0.002
Functional status		
Independent (reference)	1	
Partially dependent	2.73 (1.20–7.31)	0.046
Totally dependent	5.49 (0.85–35.48)	0.073
ASA class 2 (vs 1)	3.38 (1.03–11.12)	0.045
Chronic obstructive pulmonary disease (COPD)	2.35 (0.80–6.95)	0.121
Congestive heart failure (CHF)	6.75 (1.83–24.94)	0.004
Previous percutaneous coronary intervention	1.87 (0.72–3.87)	0.198
Hypertension	0.34 (0.15–0.79)	0.013
Peripheral vascular disease requiring previous revascularization procedure	2.59 (0.68–9.90)	0.164
Diabetes	1.81 (0.82–4.00)	0.145
Cerebrovascular accident	1.92 (0.52–7.12)	0.322
Bleeding disorder	5.76 (2.41–13.76)	<0.001
Dyspnea (chronic)	2.29 (1.00–5.26)	0.051
Creatinine >1.3	1.06 (0.35–3.18)	0.923
BUN >22	1.05 (0.42–2.64)	0.920
Hematocrit <30	4.85 (1.64–14.35)	0.004
INR >1.3	1.24 (0.56–2.77)	0.597

Table 3: Multivariate logistic regression predicting any complication among all patients undergoing parathyroidectomy

	Odds ratio (95% CI)	p-value
Dialysis	2.10 (1.42–3.10)	<0.001
Female	1.09 (0.84–1.41)	0.525
Race		
White (reference)	1	
African American	1.08 (0.80–1.46)	0.619
Other	1.04 (0.66–1.64)	0.871
Age	1.00 (0.99–1.01)	0.616
Functional status		
Independent (reference)	1	
Partially dependent	3.20 (2.11–4.84)	<0.001
Totally dependent	9.35 (4.05–21.57)	<0.001
ASA class 2 (vs 1)	2.02 (1.52–2.69)	<0.001
Chronic obstructive pulmonary disease (COPD)	1.51 (0.91–2.48)	0.108
Congestive heart failure (CHF)	3.27 (1.55–6.87)	0.002
Previous percutaneous coronary intervention	1.43 (0.94–2.17)	0.092
Hypertension	0.94 (0.72–1.23)	0.648
Peripheral vascular disease requiring previous revascularization procedure	1.70 (0.88–3.28)	0.112
Diabetes	1.25 (0.94–1.65)	0.128
Cerebrovascular accident	1.33 (0.76–2.33)	0.316
Bleeding disorder	1.27 (0.78–2.08)	0.338
Dyspnea (chronic)	1.21 (0.88–1.68)	0.243
Creatinine >1.3	1.18 (0.84–1.67)	0.340
BUN >22	1.09 (0.80–1.48)	0.598
Hematocrit <30	2.65 (1.71–4.10)	<0.001
INR >1.3	0.98 (0.76–1.25)	0.858

morbidity (7.9 vs 1.4%), and cardiopulmonary complications (4.0 vs 0.5%).

On multivariate logistic regression predicting mortality for patients undergoing parathyroidectomy, being on dialysis was associated with an increased odds of death (OR 5.28, $p = 0.004$; Table 2). Older age, dependent functional status, ASA classification 2 (vs 1), congested heart failure (CHF), hypertension, bleeding disorder, and anemia (hematocrit <30) were also associated with higher odds ratios of mortality.

On multivariate logistic regression for predicting morbidity, patients on dialysis were independently associated with an increased risk of having a complication (OR 2.10, $p < 0.001$; Table 3). Dependent functional status, ASA classification 2 vs 1, CHF, and anemia (hematocrit <30) were also associated with an increased risk of having a complication. When examining cardiopulmonary complications, patients on dialysis had a significantly increased risk (OR 5.14, $p < 0.001$; Table 4). Age, functional status, ASA classification, CHF, and dyspnea were also important predictors of a cardiopulmonary complication.

Risk of Parathyroidectomy vs Arteriovenous Fistula among Dialysis Patients

In our second analysis among patients on dialysis, 455 patients (30.3%) underwent parathyroidectomy and 1,048 patients (69.7%) underwent AVF creation in NSQIP from 2007 to 2008 (Table 5). Of a total of 1,843 patients from 2007 to 2008 undergoing AVF, 1,048 (56.9%) received general anesthesia. Only patients who underwent general anesthesia would be included to offer a more accurate comparison of the intraoperative risk between patients undergoing parathyroidectomy and AVF creation.

Patients undergoing parathyroidectomy were, on average, younger (48 vs 60 years), more likely to be African American (56.9 vs 34.3%), and had a longer mean length of stay (5.8 vs 2.9 days). There was no difference in sex or ASA classification. There was also no difference in unadjusted mortality or complication rate.

On multivariate logistic regression predicting mortality, there was no difference in the odds ratio of mortality comparing patients undergoing AVF vs parathyroidectomy (Table 6). The only variable predictive of mortality was dyspnea (OR 3.61, $p = 0.027$).

Table 4: Multivariate logistic regression predicting cardiopulmonary complications among all patients undergoing parathyroidectomy

	Odds ratio (95% CI)	p-value
Dialysis	5.14 (2.77–9.55)	<0.001
Female	1.38 (0.90–2.13)	0.140
Race		
White (reference)		
African American	1.22 (0.77–1.93)	0.394
Other	0.86 (0.38–1.92)	0.711
Age	1.02 (1.00–1.03)	0.025
Functional status		
Independent (reference)		
Partially dependent	1.85 (0.95–3.60)	0.070
Totally dependent	9.73 (3.34–28.3)	<0.001
ASA class 2 (vs 1)	2.94 (1.77–4.87)	<0.001
Chronic obstructive pulmonary disease (COPD)	1.71 (0.86–3.38)	0.124
Congestive heart failure (CHF)	3.72 (1.37–10.09)	0.010
Previous percutaneous coronary intervention	1.31 (0.69–2.49)	0.413
Hypertension	0.72 (0.47–1.10)	0.134
Peripheral vascular disease requiring previous revascularization procedure	1.18 (0.40–3.46)	0.760
Diabetes	1.09 (0.69–1.70)	0.719
Cerebrovascular accident	1.88 (0.90–3.90)	0.091
Bleeding disorder	1.22 (0.58–2.54)	0.603
Dyspnea (chronic)	1.89 (1.21–2.96)	0.005
Creatinine >1.3	0.94 (0.52–1.69)	0.824
BUN >22	0.91 (0.56–1.46)	0.684
Hematocrit <30	1.90 (0.72–3.83)	0.075
INR >1.3	1.06 (0.72–1.57)	0.774

Table 5: Patient population among all patients on dialysis, comparing patients undergoing parathyroidectomy to AVF creation

	Parathyroidectomy (n = 455, 30.3%)	AVF creation (n = 1,048, 69.7%)	p-value
Age – mean years	47.6	59.8	<0.001
Race – n (%)			<0.001
White	148 (33.9)	485 (50.6)	
African American	248 (56.9)	329 (34.3)	
Other	40 (9.2)	145 (15.1)	
Female – n (%)	226 (49.7)	496 (47.3)	0.404
ASA* classification – mean	1.9	2.0	0.074
Length of stay – mean days	5.8	2.9	<0.001
Died – n (%)	3 (0.7)	11 (1.1)	0.469
Complications – n (%)			
All complications	32 (7.0)	103 (9.8)	0.082
Cardiopulmonary	13 (2.9)	20 (1.9)	0.249

On multivariate logistic regression predicting complications, patients undergoing AVF had a higher risk of a complication (OR 1.66, p = 0.035; Table 7). Patients who were not white or African American had a decreased risk of a complication (OR 0.51, p = 0.042), whereas

Table 6: Multivariate logistic regression predicting mortality among all patients on dialysis, comparing patients undergoing parathyroidectomy to AVF creation

	Odds ratio (95% CI)	p-value
AVF (vs parathyroidectomy)	0.50 (0.11–2.42)	0.392
Female	1.51 (0.48–4.70)	0.480
Race		
White (reference)	1	
African American	0.75 (0.18–3.13)	0.691
Other	1.26 (0.24–6.52)	0.784
Age	1.05 (1.00–1.11)	0.066
Functional status		
Independent (reference)	1	
Partially dependent	3.06 (0.96–9.72)	0.058
Totally dependent	N/A	N/A
ASA classification	0.23 (0.02–2.31)	0.213
Previous percutaneous coronary intervention	2.24 (0.67–7.48)	0.189
Previous cardiac surgery	2.34 (0.69–7.93)	0.171
Diabetes	3.50 (0.99–12.41)	0.052
Bleeding disorder	2.53 (0.75–8.57)	0.136
Dyspnea (chronic)	3.61 (1.16–11.28)	0.027

Table 7: Multivariate logistic regression predicting complications among all patients on dialysis, comparing patients undergoing parathyroidectomy to AVF creation

	Odds ratio (95% CI)	p-value
AVF (vs parathyroidectomy)	1.66 (1.04–2.66)	0.035
Female	1.01 (0.69–1.48)	0.947
Race		
White (reference)	1	
African American	0.77 (0.51–1.17)	0.215
Other	0.51 (0.27–0.97)	0.042
Age	0.99 (0.98–1.00)	0.128
Functional status		
Independent (reference)	1	
Partially dependent	1.90 (1.11–3.24)	0.019
Totally dependent	3.18 (0.96–10.58)	0.059
ASA classification	1.23 (0.43–3.57)	0.698
Peripheral vascular disease requiring previous revascularization procedure	1.46 (0.80–2.67)	0.223
Current smoker within one year	0.59 (0.34–1.04)	0.067
Major operation within 30 days	2.91 (1.20–7.02)	0.018

patients who were partially or totally dependent and had an operation within 30 days were at a higher risk of a complication. There was no difference in odds ratio of cardiopulmonary complications between patients undergoing AVF vs parathyroidectomy (Table 8). The only variable that was significant in increasing the risk of cardiopulmonary complications among dialysis patients was fully dependent functional status (OR 5.91, p = 0.032).

DISCUSSION

Among patients undergoing parathyroidectomy, patients on dialysis have a much higher risk of 30-day mortality

Table 8: Multivariate logistic regression predicting cardiopulmonary complications among all patients on dialysis, comparing patients undergoing parathyroidectomy to AVF creation

	Odds ratio (95% CI)	p-value
AVF (vs parathyroidectomy)	0.54 (0.23–1.22)	0.138
Female	0.76 (0.36–1.59)	0.460
Race		
White (reference)		
African American	0.53 (0.23–1.24)	0.143
Other	0.74 (0.24–2.25)	0.591
Age	1.00 (0.97–1.03)	0.938
Functional status		
Independent (reference)		
Partially dependent	1.79 (0.65–4.97)	0.260
Totally dependent	5.91 (1.16–30.03)	0.032
ASA classification	N/A	N/A
Peripheral vascular disease requiring previous revascularization procedure	1.70 (0.46–5.10)	0.346
Current smoker within one year	0.47 (0.14–1.59)	0.224
Major operation within 30 days	2.61 (0.62–11.03)	0.193

and morbidity compared to patients not on dialysis, but had a similar risk of mortality and cardiopulmonary complications when compared to patients undergoing AVF creation. The risk of poor outcomes after parathyroidectomy is largely due to cardiopulmonary complications, for which all patients on dialysis are at greater risk.

This research has important implications. First, it quantifies the increased risk of mortality in dialysis patients undergoing a parathyroidectomy for rHPT. We found an unadjusted risk of death of 1.4%. Dialysis patients can also expect a longer length of stay (6 days vs 1 day) when compared to nondialysis patients. This is important information to discuss with patients when deciding whether to pursue surgery.

We also found that parathyroidectomy in dialysis patients does not have an increased risk of death when compared to AVF creation, which many of these patients have already undergone. These are two completely different operations with different indications, but these results can be used to better describe the risk of an operation in a context that the patient can understand, leading to more informed consent. Our finding that dialysis patients undergoing parathyroidectomy do not have an increased risk of mortality or cardiopulmonary complications compared to AVF creation is not surprising. This is likely because dialysis patients have baseline level of risk with general anesthesia, and regardless of the operation performed, it may be difficult to achieve outcomes superior to this risk level. Our study also highlights the importance of optimizing functional status and comorbidities, such as CHF and anemia prior to parathyroidectomy in an attempt to reduce postoperative complications.

Our rates of mortality and morbidity are similar to those published in the literature. In a study of 4,435 hemodialysis patients undergoing parathyroidectomy in the US, 2% of patients died during the hospitalization or within 30-days after discharge.¹⁴ Postoperative readmissions were also higher compared to the year prior to surgery, and were most often due to cardiac causes. In an observational matched cohort study of over 4,500 dialysis patients from 1988 to 1999, Kestenbaum et al described a 30-day parathyroidectomy postoperative mortality rate of 3.1%.⁹ However, they also demonstrated an average increase of 6 months of median survival in patients who underwent parathyroidectomy, with death rates 10 to 15% lower than those not undergoing surgery.

LIMITATIONS

We acknowledge several limitations. First, this study is limited to 30-day outcomes and does not consider long-term risk to patients. Multiple other studies in the literature describe improved survival in patients with rHPT undergoing parathyroidectomy compared to medical management.^{9-11,15-19} Second, we chose to focus on cardiovascular complications in this study. National Surgical Quality Improvement Program is not well suited to describe procedure-specific complications, such as hypocalcemia and injury to the recurrent laryngeal nerve. Third, even though statistically significant, our confidence intervals were wide in our multivariate logistic regressions. This is likely due to a small incidence of outcomes, especially mortality, and the disproportionate size of our two comparison groups. Fourth, AVF was not included in the database after 2008, although this should not dramatically impact our results.

CONCLUSION AND CLINICAL SIGNIFICANCE

In conclusion, we found an increased mortality and morbidity from parathyroidectomy in dialysis patients compared to patients not on dialysis, but a similar risk profile to patients undergoing AVF creation. These findings can assist in preoperative risk assessments and should be used in informed consent.

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