Article

Rates and Outcomes of Parathyroidectomy for Secondary Hyperparathyroidism in the United States

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Abstract

Background and objectives Secondary hyperparathyroidism is common among patients with ESRD. Although medical therapy for secondary hyperparathyroidism has changed dramatically over the last decade, rates of parathyroidectomy for secondary hyperparathyroidism across the United States population are unknown. We examined temporal trends in rates of parathyroidectomy, in-hospital mortality, length of hospital stay, and costs of hospitalization.

Design, setting, participants, & measurements Using the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample, a representative national database on hospital stay regardless of age and payer in the United States, we identified parathyroidectomies for secondary hyperparathyroidism from 2002 to 2011. Data from the US Renal Data System reports were used to calculate the rate of parathyroidectomy.

Results We identified 32,971 parathyroidectomies for secondary hyperparathyroidism between 2002 and 2011. The overall rate of parathyroidectomy was approximately 5.4/1000 patients (95% confidence interval [95% CI], 5.0/1000 to 6.0/1000). The rate decreased from 2003 (7.9/1000 patients; 95% CI, 6.2/1000 to 9.6/1000), reached a nadir in 2005 (3.3/1000 patients; 95% CI, 2.6/1000 to 4.0/1000), increased again through 2006 (5.4/1000 patients; 95% CI, 4.4/1000 to 6.4/1000), and remained stable since that time. Rates of in-hospital mortality decreased from 1.7% (95% CI, 0.8% to 2.6%) in 2002 to 0.8% (95% CI, 0.1% to 1.6%) in 2011 (P for trend <0.001). In–hospital mortality rates were significantly higher in patients with heart failure (odds ratio [OR], 4.23; 95% CI, 2.59 to 6.91) and peripheral vascular disease (OR, 4.59; 95% CI, 2.75 to 7.65) and lower among patients with prior kidney transplantation (OR, 0.20; 95% CI, 0.06 to 0.65).

Conclusions Despite the use of multiple medical therapies, rates of parathyroidectomy of secondary hyperparathyroidism have not declined in recent years.

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Introduction

Secondary hyperparathyroidism (sHPT) is common among patients with ESRD. Excessive parathyroid hormone (PTH) can contribute to the development of bone pain, fracture, cardiomyopathy, vascular and cardiac valve calcification, calcific uremic arteriolopathy (calciphylaxis), and other adverse clinical effects among patients with ESRD (1–3). Left unchecked, severe sHPT can result in devastating bone deformities. Before the widespread use of calcium–based phosphate binders and 1,25-dihydroxy vitamin D (calcitriol), surgical (total with autotransplant or subtotal) parathyroidectomy was the primary means of management of severe sHPT.

In the 1990s, calcium–containing phosphate binders and calcitriol were increasingly used in the management of bone and mineral disorders in patients receiving dialysis in the United States, and the parathyroidectomy rate decreased from 11.6/1000 patient-years in 1992 to 6.8/1000 patient-years in 1998 (4,5). With concerns about hypercalcemia and its associated adverse effects, synthetic active vitamin D analogs and noncalcium–containing phosphate binders were developed, replacing calcitriol and calcium–containing phosphate binders in some patients. For instance, from 1998 to 2002, the use of calcitriol declined to <10% of patients receiving hemodialysis, whereas that of paricalcitol reached >60% (6). However, the parathyroidectomy rate, which implies patients with sHPT refractory to medical therapy, increased to 11.8/1000 patient-years in 2002 (5,6).

In 2004, cinacalcet was introduced in the United States, and prescription rates have increased over time: 10% in 2004, 32% in 2006, and 31% in 2010 (7,8). Although the use of calcitriol, active vitamin D analogs, and cinacalcet has been shown to reduce PTH and although cinacalcet reduced rates of parathyroidectomy in some clinical studies (9–11), little is known regarding effects of medical management on parathyroidectomy rates in clinical practice. Some reports showed that the laboratory changes observed in clinical practice were less dramatic than those in clinical trials (7), and parathyroidectomy rates decreased through 2004 and 2005 but increased again in 2006 (6).

Most previous reports of parathyroidectomy rates were derived from the older population of Medicare beneficiaries receiving dialysis (4–6), excluding many younger patients and those covered by other forms of health insurance. Although the vast majority of patients receiving dialysis in the United States are eligible for Medicare coverage (12), many other forms of health insurance provide payment for dialysis and hospital care (*e.g.*, employer group health insurance), particularly in the first 3 years of a person's dialysis experience. Restricting evaluation of a surgical therapy to older patients can be a serious limitation, because younger patients tend to receive surgical treatment more frequently than older patients (4,5,13). To overcome this limitation, we used the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS), which includes data on hospital stay, regardless of age and payer. In this study, we sought to determine rates of parathyroidectomy for sHPT and associated in–hospital mortality, length of hospital stay, and costs. We hypothesized that rates of parathyroidectomy would decline after introduction of the calcimimetic cinacalcet and steadily decline further with increased use of cinacalcet over time.

Materials and Methods

Data Source and Study Population

We performed this study using the NIS database, the largest publically available all–payer database of hospital inpatient stays in the United States. The NIS is an administrative dataset created by the Agency for Healthcare Research and Quality from data contributed by participating states (14). The NIS contains all discharge records for the sampled hospitals and includes data on about 8 million inpatient stays from about 1000 hospitals to approximate a 20% stratified sample of all United States hospitals, with the exception of Veterans Affairs hospitals, long–term nonacute care hospitals, and chemical dependence or alcohol treatment facilities. It includes information on all patients regardless of payer, including persons covered by Medicare, Medicaid, and private insurance and the uninsured. Numbers of annual discharges were weighted to generate national estimates for each year. Each hospitalization is treated as an individual entry in the database and coded with one principal diagnosis, up to 24 secondary diagnoses, and 15 procedural diagnoses associated with that stay.

We used the NIS data to identify admissions for parathyroidectomy for sHPT between January 1, 2002 and December 31, 2011. We included all admissions with a procedural diagnosis code for parathyroidectomy using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 06.81 and 06.89, which indicate that parathyroidectomy was performed during the hospitalization. Among all admissions for parathyroidectomy, we identified parathyroidectomy for sHPT using relevant ICD-9-CM diagnosis and procedure codes (Supplemental Table 1). Considering that surgical treatment would be suggested for patients with ESRD (and possibly, those with advanced CKD) who had refractory sHPT, we assumed that the patient underwent parathyroidectomy for sHPT if there were relevant diagnostic and procedural codes for renal failure, ESRD, dialysis, kidney transplantation, and renal hyperparathyroidism during the same hospitalization. We excluded patients who had ICD-9-CM codes indicating thyroid or parathyroid cancer (193 and 194.1, respectively), because parathyroidectomy could be performed in the setting of cancer, even if the patient did not have hyperparathyroidism.

Study Variables and Study Outcomes

We ascertained basic demographic variables and hospital information and identified the following comorbidities using ICD-9-CM codes: prior kidney transplantation, diabetes mellitus, hypertension, heart failure, cerebrovascular disease, peripheral vascular disease, fracture, and the development of sepsis during the admission (Supplemental Table 1). We also determined the number of days to parathyroidectomy and postparathyroidectomy length of stay. We focused our analysis on rates of parathyroidectomy over time and trends of clinical characteristics associated with parathyroidectomy. We calculated rates by categories of age (0–19, 20–44, 45–64, and ≥65 years old) and sex. Total hospital charges were converted to costs using cost-to-charge ratio files in the NIS database (15). Costs reflect the actual costs of production, whereas charges represent what the hospital billed for the patient. The cost-to-charge ratio files contain a hospital–wide cost-to-charge ratio for each hospital. We did not adjust for inflation. We further examined trends in in-hospital mortality, length of stay, costs, and determinants thereof.

Statistical Analyses

We estimated the total number of hospitalizations for parathyroidectomy for sHPT and summarized baseline characteristics by year (2002–2011). All estimates from the NIS sampling data were transformed into national estimates using survey procedures with appropriate weights and stratifications recommended by the NIS (14). Medians and interquartile ranges were used for continuous variables, and percentages were used for categorical variables. P value for linear trend across years was computed through logistic regressions using continuous year as the sole predictor. We examined trends in duration of hospitalization using log–transformed postparathyroidectomy lengths of stay because of the skewness of the data. We computed rates of parathyroidectomy for each year (with corresponding 95% confidence intervals [95% CIs]) by dividing the national estimates obtained from the NIS data by the total ESRD population (obtained from the US Renal Data System [USRDS] annual report) (12). Total ESRD population includes patients on dialysis and kidney transplant recipients. We performed subgroup analyses by age and sex in a similar fashion. We calculated in–hospital mortality rates among patients who underwent parathyroidectomy for sHPT using logistic regression with categorical calendar year as the predictor. Additional patient–level covariates were then entered into the model to determine the degree to which temporal trends might otherwise be explained. We created the cohort using the SAS software (SAS Institute Inc., Cary, NC) and conducted the analyses using SAS and StataMP, version 11 (StataCorp., College Station, TX).

Results

Population Characteristics

We estimated 33,814 hospitalizations including parathyroidectomy for sHPT from the NIS between 2002 and 2011. After excluding thyroid or parathyroid cancer, 32,971 parathyroidectomies for sHPT remained for the United States population (Figure 1). The proportions of all possible combinations of ESRD, CKD, and kidney transplantation hospitalizations during the study period are shown in Supplemental Figure 1. More than three fourths (76.4%) of patients had an ICD-9-CM code specific for ESRD, a diagnosis or procedure code for dialysis, or both; the remainder had other codes for renal failure or kidney transplantation. Table 1 describes baseline characteristics of the study population in each year. Nearly four in five patients (78.9%) undergoing parathyroidectomy for sHPT were <65 years old; the majority (54.0%) were women. Mean age, prevalence of diabetes mellitus, and hypertension increased over time.

Parathyroidectomy Rates

When considering prevalence counts available from the USRDS as the denominator of all patients receiving dialysis or all kidney transplant recipients in the United States, we estimated the overall rate of admission for parathyroidectomy at 5.4/1000 patients (95% CI, 5.0/1000 to 6.0/1000). Figure 2 shows estimated parathyroidectomy rates over time. The number of parathyroidectomy events and parathyroidectomy rates decreased from 2003 (4210 events; 95% CI, 3321 to 5099; 7.9/1000 patients; 95% CI, 6.2/1000 to 9.6/1000), reached the lowest in 2005 (1890 events; 95% CI, 1481 to 2298; 3.3/1000 patients; 95% CI, 2.6/1000 to 4.0/1000), increased through 2006 (3225 events; 95% CI, 2602 to 3848; 5.4/1000 patients; 95% CI, 4.4/1000 to 6.4/1000), and has been sustained since that time (in 2011; 3496 events; 95% CI, 2784 to 4207; 4.9/1000 patients; 95% CI, 3.9/1000 to 6.0/1000). Dividing the study timeframe in monthly intervals, we found that number of parathyroidectomies decreased from March of 2004 and reached the nadir in May of 2005 (Figure 3). We also determined unadjusted parathyroidectomy rates by age group and sex in each year (Supplemental Figure 2). Parathyroidectomy rates were highest for the age group of 20–44 years old. There was a dip in 2005 and a rise in 2006 for all age groups; the dip and rise pattern was most pronounced for the age group 20–44 years old. Although parathyroidectomy was more prevalent in women relative to men, similar trends over time were observed.

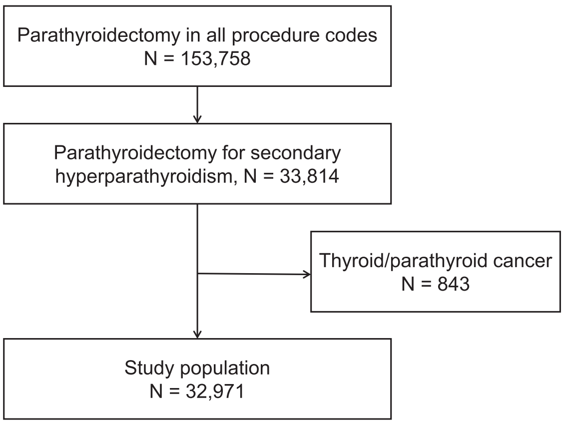

Figure 1. | Flow diagram of patients enrolled in the study.

Incidence and Risk Factors of In-Hospital Mortality

Unadjusted rates of in-hospital mortality decreased significantly from 1.7% (95% CI, 0.8% to 2.6%) in 2002 to 0.8% (95% CI, 0.1% to 1.6%) in 2011 (*P* for trend <0.001) (Figure 4). A similar decline was found when adjusting for age, sex, and comorbidities (*P* for trend <0.001) (Table 2). In–hospital mortality rates were significantly higher in patients with heart failure (odds ratio [OR], 4.23; 95% CI, 2.59 to 6.91) and peripheral vascular disease (OR, 4.59; 95% CI, 2.75 to 7.65) and lower among patients with prior kidney transplantation (OR, 0.20; 95% CI, 0.06 to 0.65). Sepsis was more prevalent in patients who died during hospitalization compared with those who survived (40.8% versus 2.2%; *P*<0.001). Parathyroidectomy was performed on hospital days 0–3 in 80.0%, 5.4%, 2.2%, and 1.5% of admissions, respectively; 6.3% of patients underwent parathyroidectomy after 7 days of admission. In-hospital mortality was 6.4% in patients who underwent parathyroidectomy after 7 days of admission, whereas mortality was 0.9% in patients who underwent parathyroidectomy within 7 days of admission (*P*<0.001).

Disposition, Length of Hospital Stay, and Hospital Costs

Overall, >80% of survivors discharged to home, and <10% of patients discharged to a health care facility (Supplemental Table 2). These proportions did not change materially over time. The median duration of the hospitalization after parathyroidectomy was 3 days (25th–75th percentiles = 2–6 days) (Supplemental Table 2). Lengths of stay after parathyroidectomy declined significantly over time, whereas the median hospital costs steadily increased between 2002 and 2011 ($7981 in 2002 versus $11,412 in 2011; *P* for trend <0.001) (Supplemental Figure 3). Owing to skewness of data, the mean value was approximately 1.5-fold higher than the median.

Discussion

Using a representative national cohort in the United States, we found that rates of parathyroidectomy for sHPT rose from 2002 to 2003, declined abruptly from 2004 to 2005, and increased again during 2006, remaining relatively stable thereafter. In contrast to the 1990s and early 2000s, during which time parathyroidectomy rates reached 10/1000 patient-years, we observed generally lower parathyroidectomy rates thereafter. However, rates did not materially change from 2006 to 2011. Notably, in–hospital mortality rates after parathyroidectomy for sHPT steadily declined between 2002 and 2011 and were <1% in several recent years. Among patients undergoing parathyroidectomy for sHPT, heart failure and peripheral vascular disease were independently associated with in-hospital mortality. Although lengths of hospital stay for patients undergoing parathyroidectomy have decreased, hospital costs for the parathyroidectomy have increased.

Table 1. Baseline characteristics of patients undergoing parathyroidectomy because of secondary hyperparathyroidism in the United States from 2002 to 2011

Variables	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	All	*P* Value
N	3737	4210	3287	1890	3225	3368	3564	2908	3288	3496	32,971	
Age, yr, median (IQR)	50 (40–60)	50 (40–60)	50 (40–59)	50 (37–61)	49 (39–61)	53 (41–63)	52 (41–63)	51 (40–62)	53 (41–65)	53 (42–66)	51 (40–62)	<0.001
Age, yr, %												
0–19	1.1	1.2	1.5	1.3	1.3	1.0	1.6	1.2	1.4	1.0	1.3	0.98
20–44	36.3	33.6	31.2	36.6	36.2	29.9	30.3	34.8	30.4	28.9	32.6	0.004
45–64	45.0	47.7	52.4	44.2	42.3	47.2	44.7	42.1	41.6	41.4	45.0	0.001
65+	17.5	17.5	14.9	17.9	20.2	22.0	23.3	21.9	26.6	28.6	21.1	<0.001
Men, %	45.3	48.2	45.5	49.3	45.5	49.9	43.3	42.8	46.6	46.1	46.0	0.31
Region, %												
Northeast	19.2	16.6	13.3	18.6	17.3	12.7	23.0	15.5	15.2	13.7	16.5	0.64
Midwest	22.2	21.4	26.6	21.4	19.6	24.3	18.7	20.2	21.6	23.6	22.0	0.85
South	37.1	41.6	38.4	39.9	41.3	41.2	35.8	44.9	46.9	46.6	41.3	0.21
West	21.4	20.4	21.7	20.1	21.9	21.8	22.5	19.3	16.3	16.1	20.2	0.24
Hospital status, %												
Rural	3.7	3.9	3.5	3.1	2.6	3.6	3.9	5.0	4.0	1.4	3.5	0.62
Urban nonteaching	27.2	27.1	26.4	35.3	27.4	35.3	28.1	29.1	29.6	32.0	29.4	0.37
Urban teaching	69.1	69.0	70.1	61.6	70.0	61.1	68.0	65.9	66.3	66.6	67.1	0.47
Payer, %												
Medicare	77.0	80.9	79.0	75.6	77.2	77.7	79.0	79.6	78.2	79.6	78.6	0.75
Medicaid	5.0	4.9	5.8	8.2	6.7	5.9	5.5	7.9	6.7	6.2	6.1	0.11
Private	17.0	13.0	13.4	15.7	14.4	13.4	13.6	10.8	13.2	12.5	13.7	0.04
Other	1.0	1.2	1.3	0.5	1.6	3.0	1.8	1.4	1.8	1.7	1.6	0.05
Comorbidities, %												
Diabetes	22.0	26.1	22.9	24.5	25.8	28.6	24.5	29.2	32.2	32.6	26.8	<0.001
Hypertension	79.2	85.2	85.8	84.6	85.6	87.4	90.2	87.7	91.6	91.2	86.8	<0.001
Heart failure	7.9	11.8	10.3	11.1	10.7	10.4	11.1	10.0	12.5	15.1	11.1	0.003
Cerebrovascular disease	1.6	1.0	1.4	1.2	1.3	1.2	1.5	1.2	1.3	1.9	1.4	0.72
Peripheral vascular disease	4.5	7.2	4.3	7.4	5.6	6.7	5.9	5.8	5.7	6.1	5.9	0.58
Prior fracture	2.2	1.6	2.4	1.0	2.3	1.7	1.3	2.0	1.0	1.4	1.7	0.11
Prior kidney transplant	20.5	16.1	24.8	20.7	13.6	14.6	16.2	18.3	16.4	16.0	17.6	0.09

P value for linear trend across years was computed through logistic regressions using continuous year as the sole predictor. IQR, interquartile range.

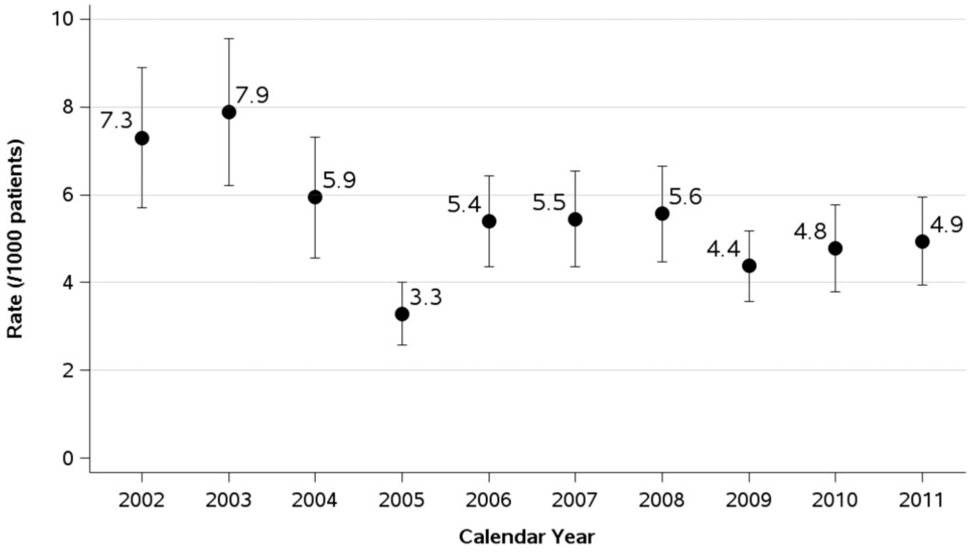

Figure 2. | **Temporal trends in parathyroidectomy rates and 95% confidence intervals for secondary hyperparathyroidism.**

In contrast to previous studies using the USRDS database that were restricted to patients with ESRD for whom Medicare was the primary payer, excluding younger patients and patients relatively new to dialysis (4–6), we used the NIS, allowing us to obtain rates among a broader spectrum of patients, irrespective of age or insurance coverage. We observed that the distribution of primary payer differed by patient's age. Medicare was the most common insurance type among all age groups. However, Medicare covered 92.4% of patients ≥65 years old and only 74.9% of patients <65 years old. Younger patients were more likely to have insurance other than Medicare and undergo parathyroidectomy (4,5,13).

The findings are in contrast with a Canadian study (16) and the international Dialysis Outcomes and Practice Patterns Study (DOPPS) (17). The Canadian study, although restricted to a single province (Quebec), showed a sustained reduction in parathyroidectomy rates after 2006. The DOPPS reported that prescriptions of active vitamin D analogs and cinacalcet increased and that parathyroidectomy rates decreased between 1996 and 2011. Because the DOPPS investigators divided the timeframe into 3-year increments (1996–2001, 2002–2004, 2005–2008, and 2009–2011), their analysis could not identify the sharp changes that occurred during 2004 and 2005; these individual years were diluted by inclusion within 3-year blocks before and after.

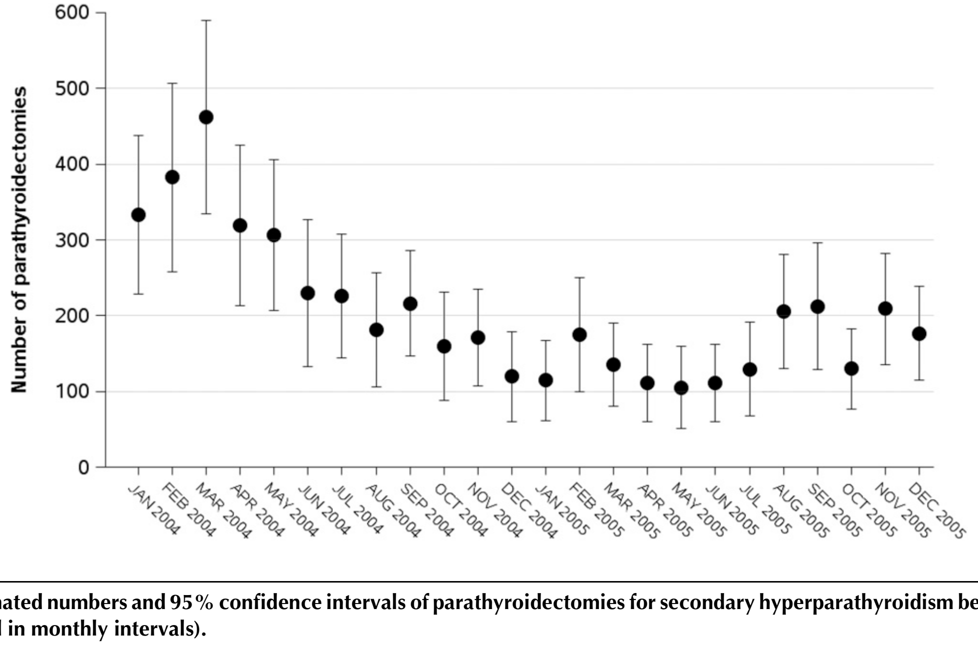

Figure 3. | **Estimated numbers and 95% confidence intervals of parathyroidectomies for secondary hyperparathyroidism between 2004 and 2005 (described in monthly intervals).**

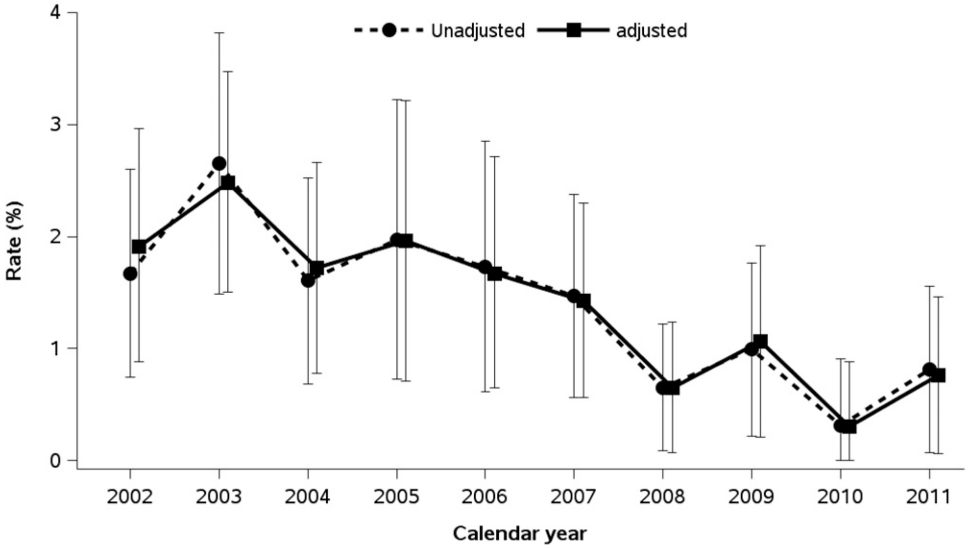

Figure 4. | **In–hospital mortality rates and 95% confidence intervals of parathyroidectomy for secondary hyperparathyroidism, 2002–2011.**

The most likely explanation for the abrupt decline in parathyroidectomy for sHPT in 2005 is the introduction of cinacalcet. We found that the number of parathyroidectomies began to decrease from March of 2004. Cinacalcet was approved by the US Food and Drug Administration in March of 2004 and launched commercially soon thereafter. During 2004 and 2005, clinicians might have deferred parathyroidectomy in some patients, anticipating improved control of sHPT. However, parathyroidectomy rates rose through 2006. In addition to the anticipated and/or actual effects of cinacalcet, parathyroidectomy rates might have been affected by the publication of clinical practice guidelines. There were no published guidelines addressing parathyroidectomy for sHPT before 2003. However, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Workgroup on bone and mineral disease in CKD recommended parathyroidectomy for patients with refractory hyperparathyroidism in guidelines published in October of 2003 (18). Guidelines put forth by the Kidney Disease Improving Global Outcomes Workgroup published in 2009 also stated that patients with refractory hyperparathyroidism should undergo parathyroidectomy (19). Adoption of these guidelines may have sustained parathyroidectomy rates through subsequent years.

Our examination of time trends in parathyroidectomy for patients with sHPT after introduction of cinacalcet contrasts sharply with results reported from the Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (EVOLVE) Trial (11). In the EVOLVE Trial, rates of parathyroidectomy (and of severe, unremitting hyperparathyroidism) were reduced by >50% with cinacalcet relative to placebo (used in combination with conventional therapy for sHPT), despite poor adherence to cinacalcet and the use of commercial cinacalcet in >20% of patients randomized to placebo. In fact, although parathyroidectomy rates dropped abruptly during late 2004 and early 2005, they increased and remained stable, despite more widespread use of cinacalcet in clinical practice. This discordance suggests that either the treatment benefit was overestimated in the randomized clinical trial or alternatively, cinacalcet use in clinical practice does not mirror the approach taken in the EVOLVE Trial. The latter is plausible in that the EVOLVE Trial protocol specified titration of cinacalcet to a maximum daily dose of 180 mg during the first 20 weeks of the trial. Observational studies in which the dose of cinacalcet was recorded suggests that relatively few patients are titrated to doses >60 or 90 mg daily (7,20,21). The relative frequency of gastrointestinal side effects seen with cinacalcet therapy—principally nausea and vomiting—may be limiting the observed benefit, at least vis-à-vis parathyroidectomy—a potential example of efficacy versus effectiveness. An intravenous calcimimetic agent currently under development may have a role as primary therapy

Table 2. Logistic regression analysis of factors associated with in-hospital mortality among patients undergoing parathyroidectomy

Variables	Odds Ratio (95% Confidence Interval)	*P* Value
Age (≤44 yr as reference), yr		
45–64	1.88 (1.07 to 3.30)	0.03
65+	1.65 (0.84 to 3.21)	0.14
Men	0.73 (0.47 to 1.13)	0.16
Diabetes	1.18 (0.73 to 1.90)	0.51
Hypertension	0.57 (0.34 to 0.95)	0.03
Heart failure	4.23 (2.59 to 6.91)	<0.001
Peripheral vascular disease	4.59 (2.75 to 7.65)	<0.001
Prior kidney transplantation	0.20 (0.06 to 0.65)	<0.01
Incident year (2002 as reference)	0.85 (0.79 to 0.92)	<0.001

Variables were calendar year (continuous), age group, sex, diabetes, hypertension, heart failure, peripheral vascular disease, and prior kidney transplantation.

for sHPT or in patients intolerant of or nonresponsive to oral or intravenous active vitamin D analogs and/or cinacalcet (22,23).

Although many studies have highlighted the risks associated with sHPT, relatively few published studies have reported risks associated with the parathyroidectomy procedure itself. Kestenbaum *et al.* (24) reported 30-day mortality of 3.1% using the USRDS data during the timeframe 1988–1999, whereas Ishani *et al.* (25) reported 30-day mortality of 2.0% and in-hospital mortality of 0.9% during the timeframe 2007–2009. Baseline clinical characteristics of patients undergoing parathyroidectomy were similar in both studies. In-hospital and short-term mortality of parathyroidectomy for sHPT has declined over time. Lower mortality rates in more recent years could reflect residual selection effects and/or advances in dialysis and related care. Moreover, Komaba *et al.* (26) studied the effect of parathyroidectomy on survival in patients with severe sHPT. They compared mortality among patients who underwent parathyroidectomy and propensity score–matched patients who did not undergo parathyroidectomy, despite severe sHPT, and suggested that parathyroidectomy reduced the risk for all-cause and cardiovascular mortality in patients with severe sHPT (26).

Strengths of this analysis include the large sample size, generalizability (results were derived from a database capturing a large fraction of all United States hospitals), inclusion of patients irrespective of age or insurance status, and the availability of multiple diagnosis and procedure codes to adjust for comorbid conditions and determine correlates of in-hospital mortality and lengths of stay. Important limitations include the lack of patient–specific follow-up information to determine longer-term associations of parathyroidectomy with mortality, cardiovascular events, fractures, and other complications and sustained biochemical control of sHPT. We could not distinguish patients by the severity of sHPT. In other words, there were no laboratory data (*e.g.*, PTH, calcium, and bone–specific alkaline phosphatase) available in the NIS that might be used to gauge the severity of sHPT. The identification of comorbid conditions was limited to codes provided during hospitalization; no outpatient codes or inpatient codes from other hospitalizations could be included. Moreover, we used the USRDS population as a denominator to estimate the rate of parathyroidectomy. Not all of patients with sHPT are included in the USRDS, and therefore, our estimates may not precisely correspond to parathyroidectomy rates derived from the USRDS itself. Finally, because the NIS tracks hospital admissions and not patients *per se*, we may have included in our analysis some patients who underwent repeat parathyroidectomy, although these patients likely represent a very small minority of patients overall.

In summary, using a nationally representative database, we examined rates of parathyroidectomy for sHPT over the last decade for which data were available. We found an abrupt decline in rates after introduction of the calcimimetic cinacalcet, with stabilization of rates from 2006 to 2011. In–hospital mortality rates declined steadily over that timeframe, suggesting either improved surgical and perioperative medical care or selection effects. sHPT remains an important complication associated with advanced CKD and especially, ESRD, despite the use of multiple medical therapies. In which clinical settings and at what stage of CKD, ESRD, or sHPT that parathyroidectomy is best applied remain unknown. As with any surgical procedure, anticipated benefits over the long-term need to be balanced with the short–term perioperative increase in risk. Although clinical practice guidelines have suggested parathyroidectomy in patients refractory to medical therapy (15,16), treatment strategies must be individualized.

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Disclosures

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References

1. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM: Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 15: 2208–2218, 2004
2. Floege J, Kim J, Ireland E, Chazot C, Drueke T, de Francisco A, Kronenberg F, Marcelli D, Passlick-Deetjen J, Schernthaner G, Fouqueray B, Wheeler DC; ARO Investigators: Serum iPTH, calcium and phosphate, and the risk of mortality in a European haemodialysis population. *Nephrol Dial Transplant* 26: 1948–1955, 2011
3. Ganesh SK, Stack AG, Levin NW, Hulbert-Shearon T, Port FK: Association of elevated serum PO(4), Ca x PO(4) product, and parathyroid hormone with cardiac mortality risk in chronic hemodialysis patients. *J Am Soc Nephrol* 12: 2131–2138, 2001
4. Kestenbaum B, Seliger SL, Gillen DL, Wasse H, Young B, Sherrard DJ, Weiss NS, Stehman-Breen CO: Parathyroidectomy rates among United States dialysis patients: 1990-1999. *Kidney Int* 65: 282–288, 2004
5. Foley RN, Li S, Liu J, Gilbertson DT, Chen SC, Collins AJ: The fall and rise of parathyroidectomy in U.S. hemodialysis patients, 1992 to 2002. *J Am Soc Nephrol* 16: 210–218, 2005
6. Li S, Chen YW, Peng Y, Foley RN, St Peter WL: Trends in parathyroidectomy rates in US hemodialysis patients from 1992 to 2007. *Am J Kidney Dis* 57: 602–611, 2011
7. St Peter WL, Li Q, Liu J, Persky M, Nieman K, Arko C, Block GA: Cinacalcet use patterns and effect on laboratory values and other medications in a large dialysis organization, 2004 through 2006. *Clin J Am Soc Nephrol* 4: 354–360, 2009
8. Yusuf AA, Howell BL, Powers CA, St Peter WL: Utilization and costs of medications associated with CKD mineral and bone disorder in dialysis patients enrolled in Medicare Part D. *Am J Kidney Dis* 64: 770–780, 2014
9. Cunningham J, Danese M, Olson K, Klassen P, Chertow GM: Effects of the calcimimetic cinacalcet HCl on cardiovascular disease, fracture, and health-related quality of life in secondary hyperparathyroidism. *Kidney Int* 68: 1793–1800, 2005
10. El-Shafey EM, Alsahow AE, Alsaran K, Sabry AA, Atia M: Cinacalcet hydrochloride therapy for secondary hyperparathyroidism in hemodialysis patients. *Ther Apher Dial* 15: 547–555, 2011
11. Chertow GM, Block GA, Correa-Rotter R, Drüeke TB, Floege J, Goodman WG, Herzog CA, Kubo Y, London GM, Mahaffey KW, Mix TC, Moe SM, Trotman ML, Wheeler DC, Parfrey PS; EVOLVE Trial Investigators: Effect of cinacalcet on cardiovascular disease in patients undergoing dialysis. *N Engl J Med* 367: 2482–2494, 2012
12. United States Renal Data System: *2014 Annual Data Report: An Overview of the Epidemiology of Kidney Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2014

13. Malberti F, Marcelli D, Conte F, Limido A, Spotti D, Locatelli F: Parathyroidectomy in patients on renal replacement therapy: An epidemiologic study. *J Am Soc Nephrol* 12: 1242–1248, 2001
14. Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project: Introduction to the HCUP Nationwide Inpatient Sample (NIS), 2011. Available at: https://www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2011.jsp. Accessed July 10, 2015
15. Healthcare Cost and Utilization Project (HCUP): Cost-to-Charge Ratio Files. Available at: http://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp. Accessed September 23, 2015
16. Lafrance JP, Cardinal H, Leblanc M, Madore F, Pichette V, Roy L, Le Lorier J: Effect of cinacalcet availability and formulary listing on parathyroidectomy rate trends. *BMC Nephrol* 14: 100, 2013
17. Tentori F, Wang M, Bieber BA, Karaboyas A, Li Y, Jacobson SH, Andreucci VE, Fukagawa M, Frimat L, Mendelssohn DC, Port FK, Pisoni RL, Robinson BM: Recent changes in therapeutic approaches and association with outcomes among patients with secondary hyperparathyroidism on chronic hemodialysis: The DOPPS study. *Clin J Am Soc Nephrol* 10: 98–109, 2015
18. National Kidney Foundation: K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis* 42[Suppl 3]: S1–S201, 2003
19. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group: KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl* 113: S1–S130, 2009
20. Kilpatrick RD, Newsome BB, Zaun D, Liu J, Solid CA, Nieman K, St Peter WL: Evaluating real-world use of cinacalcet and biochemical response to therapy in US hemodialysis patients. *Am J Nephrol* 37: 389–398, 2013
21. Ureña P, Jacobson SH, Zitt E, Vervloet M, Malberti F, Ashman N, Leavey S, Rix M, Os I, Saha H, Ryba M, Bencova V, Baños A, Zani V, Fouque D: Cinacalcet and achievement of the NKF/K-DOQI recommended target values for bone and mineral metabolism in real-world clinical practice–the ECHO observational study. *Nephrol Dial Transplant* 24: 2852–2859, 2009
22. Martin KJ, Pickthorn K, Huang S, Block GA, Vick A, Mount PF, Power DA, Bell G: AMG 416 (velcalcetide) is a novel peptide for the treatment of secondary hyperparathyroidism in a single-dose study in hemodialysis patients. *Kidney Int* 85: 191–197, 2014
23. Bell G, Huang S, Martin KJ, Block GA: A randomized, double-blind, phase 2 study evaluating the safety and efficacy of AMG 416 for the treatment of secondary hyperparathyroidism in hemodialysis patients. *Curr Med Res Opin* 31: 943–952, 2015
24. Kestenbaum B, Andress DL, Schwartz SM, Gillen DL, Seliger SL, Jadav PR, Sherrard DJ, Stehman-Breen C: Survival following parathyroidectomy among United States dialysis patients. *Kidney Int* 66: 2010–2016, 2004
25. Ishani A, Liu J, Wetmore JB, Lowe KA, Do T, Bradbury BD, Block GA, Collins AJ: Clinical outcomes after parathyroidectomy in a nationwide cohort of patients on hemodialysis. *Clin J Am Soc Nephrol* 10: 90–97, 2015
26. Komaba H, Taniguchi M, Wada A, Iseki K, Tsubakihara Y, Fukagawa M: Parathyroidectomy and survival among Japanese hemodialysis patients with secondary hyperparathyroidism. *Kidney Int* 88: 350–359, 2015

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