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Is intraoperative parathyroid hormone testing in patients with renal insufficiency undergoing parathyroidectomy for primary hyperparathyroidism accurate?



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Abstract

BACKGROUND: Our aim was to determine whether chronic renal insufficiency (CRI) impacted intraoperative parathyroid hormone (ioPTH) monitoring during parathyroidectomy. We hypothesized that ioPTH monitoring in patients with CRI would show slower decline, but would still accurately predict cure.

METHODS: A retrospective review was conducted of patients with primary hyperparathyroidism who underwent curative single adenoma parathyroidectomy. The percentage of patients reaching 50% decline of ioPTH was compared between groups stratified by renal function.

RESULTS: Between 2000 and 2013, 950 patients met inclusion criteria. At 5 minutes, 66% of patients with CRI met curative criteria versus 77% of normal renal function patients ($P = .001$). At 10 minutes, 89% vs 92% met criteria ($P = .073$), and by 15 minutes, the gap narrowed to 95% vs 97% ($P = .142$), respectively.

CONCLUSIONS: Despite CRI patients with primary hyperparathyroidism having slower ioPTH decline after curative parathyroidectomy, 95% met ioPTH criteria by 15 minutes. Standard ioPTH criteria can be used with CRI patients.

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Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia in the general population. It is often identified via routine laboratory testing, and only 20% of patients now present with any of the classic symptoms of kidney stones or severe bone disease behind the popular rhyme taught to medical students of “bones, stones, abdominal groans, psychic moans.”¹ The term asymptomatic hyperparathyroidism erroneously refers to the

remainder of patients with PHPT without the classic symptoms. Other symptoms attributable to hyperparathyroidism include sleep disturbances, cardiovascular disease, neurocognitive symptoms, fatigue, muscle weakness, and peptic ulcer disease.² Surgery not only remains the sole definitive treatment, but is cost effective, even in asymptomatic patients.³

The transition from open 4-gland exploration to minimally invasive parathyroidectomy has occurred following advances in imaging localization using ultrasound and 99m-technetium sestamibi radionuclide scans, and the widespread use of intraoperative parathyroid hormone (ioPTH) monitoring to predict successful resection of hyperfunctioning parathyroid tissue.⁴ Multiple criteria for ioPTH have been proposed to determine when intraoperative cure is achieved.⁵ Although it makes clinical sense that patient factors unrelated to PHPT, such as renal function or body habitus, may play a role in the kinetics of hormone clearance, few studies have examined the effect of patient preoperative characteristics on the accuracy of ioPTH monitoring to determine cure.^{6,7}

The main factor that determines the decline of serum ioPTH concentration is hormone clearance, and many providers erroneously believe that renal excretion is the main clearance mechanism for PTH. In fact, the kidneys account for only 20% to 30% of hormone clearance, with around 60% of clearance occurring in the liver, and the remainder rendered inactive in the periphery by oxidation of the active hormone.⁸ Not surprisingly then, mixed findings are reported on the predictive effect of renal function on ioPTH kinetics.^{6,7} If patients with normal renal function (NRF) clear PTH more rapidly than patients with chronic renal insufficiency (CRI), then there is a potential to reduce operative time and cost by requiring fewer ioPTH measurements. Furthermore, if surgeons believe that ioPTH is less accurate in patients with CRI, they may be inclined to put less trust in the ioPTH measurements, leading to longer operative times and potentially unnecessary dissections. We hypothesized that ioPTH monitoring in patients with CRI would show slightly slower decline, but would still accurately predict cure.

Patients and Methods

After approval from an Institutional Review Board, prospectively collected database of consecutive parathyroidectomies was queried to identify patients with the following: (1) a diagnosis of PHPT; (2) a curative single gland resection between November 2000 and October 2013, defined as normocalcemia (<10.2 mg/dL) at 6 months following surgery; (3) preoperative renal function assessment; and (4) age greater than 18. All parathyroidectomies were performed at an academic hospital by high-volume endocrine surgeons. Patients with multigland disease, autotransplantation of any parathyroid tissue, parathyroid carcinoma, reoperative parathyroid surgery,

5-minute ioPTH greater than baseline, multiple missing data points, follow-up less than 6 months, and disease persistence or recurrence at any time were excluded. The Cockcroft–Gault equation with appropriate weight adjustment was used to classify patients as having NRF when creatinine clearance was greater than or equal to 60 mL/min, or CRI when creatinine clearance was less than 60 mL/min.⁹

Intraoperative PTH levels were obtained after induction of anesthesia (baseline) and at 5, 10, and 15 minutes postexcision, or until 2 sequential measurements showed falling PTH levels with at least one being less than 50% of the baseline level.¹⁰ Additional levels were drawn at the surgeon's discretion.

The ioPTH values for each patient were fit via linear regression, and slope of the fit line was determined. Values greater than 2 standard deviations from the mean slope in the NRF or CRI groups were excluded from analysis. Statistical analysis was carried out using chi-square or Student *t*-tests where appropriate. The software used included Microsoft Excel and IBM SPSS Statistics for Windows Version 21.0 (Armonk, NY). A *P* value of less than .05 was considered statistically significant. Data were expressed as mean \pm standard error of the mean for continuous variables and percentage of total for categorical variables.

Results

Preoperative characteristics

A total of 950 patients met study criteria, of which 65% ($n = 621$) had NRF and 35% ($n = 329$) had renal insufficiency based on creatinine clearance. The patients with NRF had a mean creatinine clearance of $88.1 \pm .9$ mL/min (range 60 to 272 mL/min) and the patients with CRI had mean creatinine clearance of $46 \pm .6$ mL/min (range 21 to 59 mL/min) ($P < .001$). Patients with CRI were older ($72 \pm .6$ vs $56 \pm .4$ years, $P < .001$), more often female (90% vs 74%, $P < .001$), and had significantly higher 25-hydroxy vitamin D levels (34 vs 29 ng/mL, $P < .001$). No statistically significant difference was seen for preoperative serum calcium (11.1 vs 11.0 mg/dL), PTH (131 vs 122 pg/mL), and phosphate levels (2.9 mg/dL for both) (Table 1).

Intraoperative findings

Initially, NRF and CRI patients had similar ioPTH absolute fall rates between 0 to 5 minutes (21.2 vs 20.8 pg/min, $P = .867$) and 5 to 10 minutes (3.2 vs 3.4 pg/min, $P = .511$) following adenoma resection. Only between 10 to 15 minutes did CRI fall rates exceed those in the NRF group (2.0 vs 1.4 pg/min, $P = .028$). Although the mean slope of the linear regression fit to CRI ioPTH values was steeper, this was not significant (-7.8 vs -7.4 , $P = .392$). This trend was not explained by

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