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Kidney Disease Improving Global Outcomes guidelines and parathyroidectomy for renal hyperparathyroidism

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ABSTRACT

Background: Patients with end-stage renal disease develop hypocalcemia, resulting in secondary hyperparathyroidism (SHPT). No clear criterions exist to aid in surgical decision making for SHPT. The 2009 Kidney Disease Improving Global Outcomes (KDIGO) guidelines provide target ranges for serum calcium, phosphate, and parathyroid hormone (PTH) levels in patients with end-stage renal disease. Parathyroidectomy can help achieve these targets. The study purpose was to examine how parathyroidectomy for SHPT impacts KDIGO targets during immediate and long-term follow-up and to evaluate KDIGO categorization with receipt of additional surgical intervention.

Methods: A retrospective review of a prospective parathyroidectomy database was performed. Included patients had SHPT, were on dialysis, and underwent parathyroidectomy. Calcium, phosphate, and PTH values were classified as below, within, or above KDIGO targets.

Results: Between 2000 and 2013, 36 patients with SHPT met criteria. Subtotal parathyroidectomy was performed in 89%, total parathyroidectomy in 11%. Follow-up time was 54 ± 7 mo. Eight patients (22%) required additional surgery. Twenty-eight patients (76%) were alive at the last follow-up. At the last-follow up, patients had phosphate (46%), and PTH (17%) above KDIGO ranges. Factors associated with reoperation were assessed. Patient PTH within or above target immediately postoperative had a higher rate of reoperation ($P < 0.01$). At the last follow-up, higher phosphate ($P = 0.054$) and PTH ($P < 0.001$) were associated with higher reoperation rates, but calcium ($P = 0.33$) was not.

Conclusions: PTH and phosphate levels above KDIGO indices were associated with additional surgical intervention. Many patients had laboratory indices above range at the last follow up, suggesting more patients had persistent or recurrent disease than those who underwent reoperation. Patients may benefit from more aggressive medical and/or surgical management.

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1. Introduction

Secondary hyperparathyroidism (SHPT) makes up a small fraction of patients undergoing parathyroidectomy [1,2]. Underlying renal disease leads to calcium excretion and loss, inability to activate vitamin D, and hyperphosphatemia. This ultimately results in hypocalcemia, and ongoing parathyroid gland stimulation [1,3,4]. Parathyroidectomy under these circumstances can provide significant reductions in serum parathyroid hormone (PTH) and to a lesser degree phosphate, but can exacerbate issues with hypocalcemia [5,6]. Often, patients with SHPT are only referred for surgical management after they are felt to be refractory to medical management. Nephrologists make this determination and historically only considered referral when PTH was >800 pg/mL despite medical treatment, although upper limits of normal vary [7–9]. Elevated calcium phosphate product (>55–70) was another historic indication for parathyroidectomy, while the development of calciphylaxis or severe renal osteodystrophy are still considered indications for surgery [8,10–12]. Indications for reoperation are equally ambiguous. At present, there are no standardized criterions for parathyroidectomy indications, nor is success, persistence, or recurrence after parathyroidectomy for SHPT well defined [8,9,11,13–17].

In efforts to better standardize the management of mineral and bone disorders (MBD) in patients with chronic kidney disease (CKD), the Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines were developed [5]. These guidelines established definitions for both MBD and renal osteodystrophy and provided evidence-based recommendations regarding diagnosis, management, and treatment of abnormal biochemistries, vascular calcification, and bone disorders. Achievement of these parameters benefits not just bone health but results in decreased cardiovascular morbidity and decreased mortality in hemodialysis patients [18]. Target ranges were provided for serum calcium, phosphate, and PTH, which prompted intervention when targets were not attained [5]. Specifically, when PTH are unable to be maintained within two to nine times the upper limits of the assay with maximum medical therapy, parathyroidectomy is recommended [5]. These recommendations were subsequently supported by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) for use in the United States and replaced older guidelines, which had previously been developed by the National Kidney Foundation KDOQI in 2003 [6,19].

The aim of this study was to describe the natural history of SHPT after parathyroidectomy with respect to alteration of the biochemical parameters set forth in the KDIGO guidelines. The hypothesis was that the KDIGO guidelines for CKD and MBD can be used to determine which patients require initial surgical referral for SHPT and may be used to assess need for further medical and/or surgical intervention after parathyroidectomy.

2. Materials and methods

With institutional review board approval, we conducted a retrospective review of a prospective parathyroidectomy database at a large tertiary referral center with both endocrine surgery and renal transplant services. All patients with SHPT due to end-stage renal disease (ESRD) and on dialysis, who underwent parathyroidectomy, were identified. Patients with SHPT due to gastrointestinal malabsorption were excluded. A minimum of 6 mo follow-up after surgery was required for inclusion. Patients with a failed previous transplantation were still considered to have SHPT. Decision to operate was based on preoperative laboratory values and clinical symptomatology (severity of bone disease, calciphylaxis, and so forth) [5,11,12]. Serum calcium, phosphate, and PTH were noted preoperative, at the time of postoperative visit (1–2 wk), and 6 mo and last available laboratory data within the electronic medical record (EMR). EMR was accessed to determine the need for subsequent surgery or clinical concern for disease recurrence or persistence based on physician notes.

Operative procedures were defined as a subtotal parathyroidectomy with a cervical remnant, a total parathyroidectomy with autotransplant to the forearm, or a minimally invasive parathyroidectomy ± autotransplant in cases of revision surgery [11,20]. Additionally, operative reports were reviewed to determine if a cervical thymectomy was performed as unilateral, bilateral, or not at all. Patients were classified as no further surgery or additional parathyroidectomy. Renal transplantation after parathyroidectomy was noted. Patients were classified as either having a successful renal transplant at time of the last follow-up or no transplant and/or a failed transplant. Survival after parathyroidectomy was noted. As the EMR received information from the social security registry regarding mortality; to the best of our ability, we assume those patients not otherwise designated as expired are still alive, even if no recent follow-up laboratory data are available.

KDIGO target values based on the 2009 guidelines on CKD and MBD were used to classify patients as normal, above, or below target for serum calcium, phosphate, and PTH [5]. As per these guidelines, calcium is to be maintained within the normal range (8.4–10.2 mg/dL), as is phosphate (2.5–4.6 mg/dL). PTH is to be maintained between two to nine times the upper limit of normal (130–600 pg/mL). These definitions were applied to all time points.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 22 (IBM Corporation, Armonk, NY). Categorical variables were compared using χ^2 and Fisher exact test. Independent *t*-test and one-way analysis of variance were used for continuous variables. A Kaplan–Meier analysis was performed to calculate estimated all-cause survival after parathyroidectomy. A *P* value of <0.05 was determined to be significant. Data are expressed as mean ± standard error of the mean for continuous variables and as number and percentage of total for categorical variables, unless otherwise specified.

3. Results

Between 2000 and 2013, 44 patients with SHPT were identified, and 36 patients met inclusion criteria (Table 1). Mean patient age was 44 ± 2.1 y. Fifteen patients were female (42%).