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INVITED COMMENTARY

Is There an Optimal Time for Parathyroidectomy in Patients with Secondary Hyperparathyroidism?

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In contrast to primary hyperparathyroidism (HPT), secondary HPT is characterized by increased production of parathyroid hormone (PTH) as a response to external stimuli, as opposed to an intrinsic abnormality of the parathyroid gland(s). Most commonly this occurs as a result of chronic kidney disease, and medical management is guided by the severity of renal disease with the goal of minimizing cardiovascular and skeletal-related morbidity and mortality. In 1971, Richard Wilson and colleagues first reported experience with subtotal parathyroidectomy in patients with severe secondary hyperparathyroidism and renal failure, intended to delay progression of osteitis fibrosis cystica in patients. Since that time, parathyroidectomy has been shown to result in durable decreases in serum PTH, phosphorus, and calcium levels, with decreases in patient morbidity and mortality.

Sparked by identification of the calcium-sensing receptor (CaSR) in the 1990s, development of a new class of drugs, calcimimetics, which act on the CaSR to suppress PTH secretion, has led to improved control of biochemical and mineral metabolism parameters in patients with secondary HPT, leading to a reduction in rates of parathyroidectomy. However, more recent studies have suggested that there may yet be benefits to parathyroidectomy, with respect to a decrease in all-cause mortality, and in particular, that the timing of parathyroidectomy may affect post-transplant graft function [1, 2]. A consensus report of the European Society of Endocrine Surgeons in the surgical management of patients with secondary HPT due to chronic kidney disease found (Level 2B evidence, defined as individual cohort studies or low-quality randomized controlled studies) that very high and very low PTH levels might be associated with increased CVE patients, using these findings as a guide to recommend consideration of parathyroidectomy in this subset of patients. These guidelines did not address the role of parathyroidectomy in subsequent renal allograft function [3].

In this issue, Ivarsson et al. and van der Plas et al. studied the effects of parathyroidectomy on renal function after kidney transplantation and the incidence of cardiovascular events after parathyroidectomy in patients with secondary HPT, respectively [4, 5]. Utilizing data from four university hospitals over a 21-year period, van der Plas et al. compared renal function (as defined by glomerular filtration rate [GFR]) in patients, according to whether parathyroidectomy was performed before or after renal transplantation. Of the 185 patients (102 underwent parathyroidectomy first and 83 underwent renal transplantation first), there was no difference in GFR between the two groups, 5 years after transplantation, either before or after adjustment for age, sex, and type of parathyroidectomy (subtotal vs. total), or PTH levels.

Ivarsson et al. utilized the Swedish Renal Registry to perform a nested case–control study; 579 secondary HPT patients on dialysis or with a functioning allograft were matched with 1970 control patients with secondary HPT who had not undergone parathyroidectomy by age, sex, and underlying renal disease. The time to a cardiovascular or cerebrovascular event (CVE) was measured, and patients who had parathyroidectomy and were on dialysis were found to have a higher risk of a CVE than patients who had not yet had parathyroidectomy; in contrast, the risk of a CVE after parathyroidectomy was lower in patients with a functional renal allograft.

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The findings of these two studies contrast with findings of the previous studies, with respect to the effect on allograft function and the true risk of CVE events. This is likely secondary to many confounding factors and variables in the medical and surgical management of secondary HPT patients, including use of medications, indications for surgery, and extent of parathyroidectomy. These same variables in management make future large-scale prospective studies on the optimal timing of parathyroidectomy for secondary HPT patients challenging and underscore the importance of continued discussion of optimal management that includes a multidisciplinary team of endocrinologists, nephrologists, and parathyroid surgeons in the management of patients with secondary HPT.

References

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