Endocrine Surgery Review

Effect of parathyroidectomy on quality of life and non-specific symptoms in normocalcaemic primary hyperparathyroidism

Bannani S, Christou N, Guerin C, Hamy A, Sebag F, Mathonnet M, et al. Effect of parathyroidectomy on quality of life and non-specific symptoms in normocalcaemic primary hyperparathyroidism. Br J Surg. 2018;105(3):223-9.

Reviewer:
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In Brief

Normocalcemic primary hyperparathyroidism (NcPHPT) is a clinical entity that has been increasingly recognized as a biochemical variant of PHPT where parathyroid hormone (PTH) levels are elevated but calcium levels remain normal. To establish this diagnosis, causes of secondary hyperparathyroidism (vitamin D deficiency, medications, malabsorption syndromes) must be ruled out (1). While some consider NcPHPT a milder form of PHPT, the pathophysiology and natural history of this clinical phenotype remains relatively unknown and has been highlighted as an important topic for future studies in the fourth international workshop guidelines for asymptomatic PHPT (2). Importantly, the best practice management of patients with NcPHPT and those with mild PHPT who do not meet surgical criteria is also uncertain. Although many patients with PHPT complain of non-specific symptoms such as abdominal pain, polyuria, fatigue and muscle aches, the presence of these non-specific symptoms has not been established as a criterion for undergoing surgery. It remains unknown if these symptoms improve after parathyroidectomy in patients with NcPHPT or mild PHPT.

In this study, Bannani and colleagues sought to understand: 1) if non-specific symptoms often identified in patients with classic PHPT are also present in those with NcPHPT, 2) if present, how they might affect quality of life (QoL) and 3) if parathyroidectomy could improve and ameliorate these symptoms and patient QoL. Over three years the authors prospectively enrolled 114 patients with mild PHPT and classified them as either NcPHPT (serum calcium at the upper limit of normal with elevated PTH) or mildly hypercalcemic (Hc-m-PHPT, serum calcium ranging from 10.4-11.4mg/dL with elevated PTH). All patients underwent a parathyroidectomy and were evaluated before surgery, and at 3, 6, and 12 months after parathyroidectomy. At each time point laboratory data was collected (total serum calcium, serum phosphate, creatinine, PTH, 25-OH vitamin D) and two self-administered questionnaires were performed. The first questionnaire, Short Form 36 questionnaire (SF-36-v2), assessed QoL using eight health concepts and obtained from this two summary outcomes: the physical component summary (PCS) and mental component summary (MCS). The second questionnaire assessed for twenty-five non-specific physical and neurocognitive symptoms associated with PHPT.

The authors found that at baseline the only significant preoperative difference between the NcPHPT and Hc-m-PHPT groups was the serum calcium level. There was no difference in MCS or PCS scores and no difference in the frequency of nonspecific symptoms.

Postoperatively the overall cure rate was 98.2% at 6 months and 25-OH vitamin D levels improved significantly for the Hc-m-PHPT group at 3 months but remained unchanged in the NcPHPT group. After surgery, the NcPHPT group had significant improvement in QoL in three of eight aspects of the SF-36-v2 at 3 months, one of eight at 6 months and three of eight at 1 year. However, after Bonferroni correction there was no significant improvement in any of the eight aspects at either 3 or 6 months and only the role (physical aspect) was improved at one year. After surgery, the Hc-m-PHPT showed significant improvement in almost all of the eight aspects at 3, 6 months and 1 year, even after Boferroni correction. Regarding non-specific symptoms, more patients in the Hc-m-PHPT improved than in the NcPHPT group.

Critique

This study from Bannani and colleagues investigates an important question regarding the effect of parathyroidectomy on quality of life and non-specific symptoms frequently reported by patients with PHPT. One of the strengths of the study lies in its study design and execution of a multicenter prospective trial using a validated QoL survey. The authors found that patients with NcPHPT and Hc-m-PHPT both reported non-specific complaints, such as bone and joint pain, muscle weakness and anxiety. This is data that has not been previously reported and adds valuable insight into a disease process that has only recently become increasingly studied. After parathyroidectomy, patients in both groups reported variable QoL and non-specific symptom improvement which is consistent with studies investigating hypercalcemic PHPT patients.

Little remains known about the benefits of parathyroidectomy for patients with Nc-PHPT. While well-established guidelines exist for the surgical management of typical hypercalcemic PHPT, there is currently a paucity of data available to help guide practitioners on when or whether parathyroidectomy is beneficial for patients with NcPHPT. Among the few studies that have investigated therapies for NcPHPT patients, Koumakis and colleagues have reported an improvement in bone mineral density for patients with NcPHPT after parathyroidectomy (3). This multicenter prospective trial by Bannani and colleagues significantly adds to the growing literature on the symptoms and treatment effect of surgery in NcPHPT patients.

However, there are limitations to this study, which include the lack of an untreated control group to better compare the effectiveness of surgery. Also, ionized calcium levels were intentionally excluded from the laboratory assessment. Current criteria for defining NcPHPT include ionized calcium as a metric to be evaluated as it can be elevated while total serum calcium levels remain normal. This inclusion of ionized calcium levels may have reclassified some patients as having mild rather than normocalcemic PHPT, thus altering the reported outcomes.

References:

1. Cusano NE, Silverberg SJ, Bilezikian JP. Normocalcemic primary hyperparathyroidism. J Clin Densitom. 2013;16(1):33-9.

2. Bilezikian JP, Brandi ML, Eastell R, Silverberg SJ, Udelsman R, Marcocci C, et al. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. J Clin Endocrinol Metab. 2014;99(10):3561-9.
3. Koumakis E, Souberbielle JC, Sarfati E, Meunier M, Maury E, Gallimard E, et al. Bone mineral density evolution after successful parathyroidectomy in patients with normocalcemic primary hyperparathyroidism. J Clin Endocrinol Metab. 2013;98(8):3213-20.

Additional High Yield Reading:

1. Pawlowska M, Cusano NE. An overview of normocalcemic primary hyperparathyroidism. Curr Opin Endocrinol Diabetes Obes. 2015;22(6):413-21.
2. Lowe H, McMahon DJ, Rubin MR, Bilezikian JP, Silverberg SJ. Normocalcemic primary hyperparathyroidism: further characterization of a new clinical phenotype. J Clin Endocrinol Metab. 2007;92(8):3001-5.
3. Caillard C, Sebag F, Mathonnet M, Gibelin H, Brunaud L, Loudot C, et al. Prospective evaluation of quality of life (SF-36v2) and nonspecific symptoms before and after cure of primary hyperparathyroidism (1-year follow-up). Surgery. 2007;141(2):153-9; discussion 9-60.