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Parathyroidectomy decreases neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios

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ABSTRACT

Background: Systemic inflammation has been implicated in complications and heightened mortality of patients with secondary hyperparathyroidism. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are widely available surrogate markers of inflammation. This study sought to delineate the changes in NLR and PLR after parathyroidectomy.

Methods: A total of 213 patients undergoing initial parathyroidectomy from 2010 to 2015 for secondary hyperparathyroidism were identified from a prospectively maintained clinical database. Among 183 patients free of persistent or recurrent disease, follow-up NLR and PLR were available for analysis in 85 patients.

Results: In the whole study population, the baseline NLR was positively correlated with male sex, total white blood cell count, height, serum phosphorus, and calcium–phosphorus product levels. The baseline PLR was positively correlated with platelet count, serum phosphorus, and calcium–phosphorus product levels and negatively associated with patient age. Postoperative parathyroid hormone levels were positively correlated with NLR and PLR at follow-up. For patients who had successful parathyroidectomy, there was a decrease in NLR ($P = 0.0006$), PLR ($P = 0.0003$), and platelet count ($P = 0.033$), whereas hemoglobin significantly increased ($P = 0.0002$) after surgery. Those with persistent or recurrent hyperparathyroidism had no change in NLR, PLR, hemoglobin, total white blood cell, or platelet count.

Conclusions: Successful parathyroidectomy is associated with a decrease in NLR and PLR. The modulatory effects of parathyroidectomy on systemic inflammation may partially explain the benefits of surgery in secondary hyperparathyroidism.

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Introduction

Secondary hyperparathyroidism is a common complication of chronic kidney disease. Hyperplasia of parathyroid glands accompanied by an elevation in serum parathyroid hormone (PTH) levels results in untoward disturbances in mineral metabolism.[1] Severe hyperparathyroidism is associated with a higher risk of all-cause and cardiovascular mortality.[2,3] Studies have shown that parathyroidectomy effectively reduces long-term mortality risk in dialysis patients with uncontrolled hyperparathyroidism.[4,5] Despite the advancement in the medical treatment of hyperparathyroidism, particularly the advent of calcimimetic agents, rates of parathyroidectomy for secondary hyperparathyroidism have not declined in recent years.[6]

Systemic proinflammatory activity progressively increases with the deterioration of renal function.[7] Cohort studies consistently demonstrate that inflammatory markers, including C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor-α, are independent predictors of mortality in patients with chronic kidney disease.[8-10] Recently, we found that PTH levels were positively correlated with inflammatory markers in the general population.[11] These findings indicate that hyperparathyroidism may directly or indirectly, as a consequence of abnormal calcium and phosphate metabolism, augment systemic inflammation and related complications.

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are inexpensive, widely available parameters that could serve as potential surrogate markers of systemic inflammation.[12,13] Both NLR and PLR have been shown to be closely related to IL-6, tumor necrosis factor-α, and CRP levels in dialysis patients.[14,15] In addition, high NLR and/or PLR are associated with mortality in these populations.[16,17] It is therefore intriguing to investigate the relationship between NLR, PLR, and biochemical abnormalities in secondary hyperparathyroidism. Furthermore, whether parathyroidectomy alters these inflammatory markers is of utmost interest in this context.

The aim of this study was to delineate the postoperative changes in NLR and PLR in a large cohort of patients undergoing parathyroidectomy for secondary hyperparathyroidism. We also attempted to identify potential factors which would predict corresponding changes in these markers.

Material and methods

Study cohort

After institutional review board approval, a retrospective review of our prospectively maintained database was performed. Data were reviewed for all patients undergoing initial parathyroidectomy for secondary hyperparathyroidism from 2010 to 2015. We excluded patients aged < 20 y, patients who had prior parathyroidectomy, and those with functional kidney allografts. All patients were receiving renal replacement therapy and demonstrated biochemical criteria of secondary hyperparathyroidism.[18] The indication for parathyroidectomy was severe hyperparathyroidism associated with hypercalcemia and/or hyperphosphatemia that was refractory to phosphate binders, calcitriol, and/or calcimimetic agents.[19]

Data collection

Hemoglobin, total white blood cell, and platelet counts were routinely obtained on the day before surgery. NLR and PLR were calculated as the ratio of neutrophil count to lymphocyte count and as the ratio of platelet count to lymphocyte count, respectively.[20] Follow-up NLR and PLR were obtained from the latest laboratory data, if available, at least 1 y after parathyroidectomy. Albumin-corrected total calcium, phosphate, total alkaline phosphatase, and intact PTH (1-84) levels were determined preoperatively and regularly monitored during follow-up. Perioperative serum aluminum levels were analyzed as previously described.[19] Bone mineral density at the lumbar spine and hip was measured using dual-energy X-ray absorptiometry.

Subjective symptoms were evaluated by the Taiwan Chinese version of the parathyroidectomy assessment of symptoms questionnaire.[21] All patients underwent bilateral cervical exploration followed by subtotal parathyroidectomy or total parathyroidectomy with or without autotransplantation.[22] We aimed at a target PTH range of 150-300 pg/mL, as per the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines.[1] After parathyroidectomy, persistent disease was defined as any measurement of a PTH level $>$300 pg/mL within the postoperative 6 mo. Recurrence was defined as any measurement of a PTH level $>$300 pg/mL beyond 6 mo after surgery.

Statistical analyses

The statistical analyses were performed using STATA, version 14.0 (StataCorp, College Station, TX). Categorical variables were described as proportions, and continuous variables were expressed as medians with interquartile ranges (IQRs). Considering the skewed distribution of most measures, comparisons of continuous variables between paired and unpaired groups were made using the Wilcoxon signed-rank test and Mann–Whitney U test, respectively. Associations were assessed using the nonparametric Spearman rank correlation.[23] Quantile regression, which has no distribution assumption, was used to evaluate the predictive effect of independent variables on the changes in the dependent variable of interest (the NLR decrement). Quantile regression is more robust to extreme values and outliers and, therefore, a useful tool to reveal complex relationships between continuous variables.[24] All tests were two-sided, with $P < 0.05$ considered statistically significant.

Results

During the study period, 236 consecutive patients who underwent parathyroidectomy for secondary hyperparathyroidism fulfilled the inclusion criteria. As depicted in Figure 1, a total of 23 (10%) patients were excluded because the