Primary hyperparathyroidism with normal baseline intraoperative parathyroid hormone: A challenging population

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Background. *Patients with primary hyperparathyroidism and baseline intraoperative parathyroid hormone levels in the normal range are challenging. This study compares the predictive value of a commonly used intraoperative parathyroid hormone algorithm, a software model for cure prediction, and surgeon judgment in this population.*

Methods. *This was a retrospective review of consecutive patients who underwent parathyroidectomy for primary hyperparathyroidism at a single institution from March 2013 to October 2014.*

Results. *Of 541 operative patients, 114 (21.1%) had a mean normal baseline intraoperative parathyroid hormone of ≤69 pg/mL (median 59.0 ± 10.3; range 26–69). Of the 114 patients, 93 (81.6%) were women, median age was 61 years (range 18–88). Overall, 107/108 (99.1%) patients were cured; 47 (41.2%) patients had single adenomas, 16 (14%) had double adenomas, and 51 (44.7%) had multigland hyperplasia. Using the 50% decline algorithm, a correct prediction was made in 86 (75.4%) patients. Using the computer software, a correct prediction was made in 88 (77.2%) patients. Surgeon judgment, however, was 99.1% accurate.*

Conclusion. *Patients with normal baseline intraoperative parathyroid hormone have a high incidence of multigland disease (58.8%), greater than reported previously. Current software modeling and the 50% decline algorithm are insufficient to predict cure in this population; intraoperative parathyroid hormone interpretation combined with operative findings and surgical judgment yield optimal outcomes. (Surgery 2016;■:■-■.)*

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Primary hyperparathyroidism (PHPT) is a disorder caused by hyperfunctioning parathyroid glands. Operative resection of abnormal glands is the only option for cure.[1] A single, enlarged parathyroid gland (single adenoma) is the cause of PHPT in 85–90% of cases, and unilateral neck exploration with resection of the single, enlarged gland offers cure.[2,3] In the remaining 10–15% of patients, however, >1 gland is involved (double adenoma or multigland hyperplasia),[4] and bilateral neck exploration is needed to evaluate all of the parathyroid glands.[5] Employing an intraoperative parathyroid hormone (IOPTH) assay is a useful adjunct to indicate when adequate hyperfunctioning parathyroid tissue has been resected and biochemical cure has been achieved.[6]

One of the approaches used most widely for IOPTH monitoring during parathyroidectomy is the Miami criterion, which defines biochemical cure as ≥50% decline of PTH level from the initial baseline.[7] Wang et al[8] found the dual criteria of ≥50% decline in IOPTH from baseline with the PTH level falling into the normal range observed in normal individuals[9,10] to be taught most commonly in endocrine surgery fellowship programs.

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The value of IOPTH monitoring has been evaluated and deemed useful, even in patients with mild PHPT.[11] It allows for higher cure rates, decreased operative time, reduced morbidity and lower costs.[6,12] Patients with initial baseline IOPTH levels already in the normal range, however, pose a particular challenge. For these patients, the approach of a 50% decline of PTH level from the initial baseline may not be meaningful, and determination of biochemical cure may be compromised intraoperatively.

Our team has developed cure predictability software based on sophisticated, mathematical modeling with the ultimate goal of refining intraoperative PTH analysis.[13] The cure predictability software model was generated using detailed IOPTH data from a single, experienced, parathyroid surgeon (R.U.), with correlation to postoperative cure. The model has been validated retrospectively on 100 consecutive patients by the initial surgeon and has demonstrated an 83% improvement over the more commonly utilized Miami criterion.[13] The model, however, has not yet been validated for patients with biochemically confirmed PHPT who have an initial baseline PTH level within the normal range at the time of operation.

The aim of this study was to determine the characteristics of PHPT patients with a baseline IOPTH in the normal range, as their underlying pathophysiology may be different from PHPT patients with a baseline IOPTH above the normal range. We also sought to compare the predictive value of the 50% decline algorithm, the software model for cure prediction, and surgical judgment based on the operative findings.

METHODS

A retrospective review was performed of consecutive patients who underwent parathyroidectomy for PHPT at our institution from January 1, 2013, to September 30, 2014. The IOPTH levels from each patient who had an initial baseline PTH level within the normal range were analyzed using the 50% decline algorithm or the software model for cure prediction. For the latter, the IOPTH levels were entered retrospectively into the cure predictability computer software, generating a percent chance of cure. A stated percent chance of cure of ≥95% was considered indicative of intraoperative biochemical cure from the computer model, whereas a predictive percent chance of cure <95% was considered failure to achieve intraoperative biochemical cure.

The presence or absence of intraoperative biochemical cure predicted by the 50% decline algorithm and that generated by the computer software were compared to surgeon judgment and to actual biochemical cure of each patient, determined by postoperative calcium and PTH levels. Surgical judgment was defined by interpretation of the operative findings and the IOPTH response after parathyroid resection by the surgeon. Preemptive rules were not imposed on the surgeons. The surgeons used their interpretation of the decline in IOPTH after each parathyroid gland resection, as well as their judgment of the patient demographics, preoperative imaging, and size and appearance of the gland(s), to determine whether to continue on to a 4-gland exploration, regardless of whether a 50% decline in IOPTH was observed.

A correct prediction by each of the methods analyzed was defined as indicating no additional disease in a patient who was determined subsequently to have biochemical cure (ie, who was eucalcemic at ≥6-months postoperatively) or by indicating additional disease in a patient who was found subsequently to have further parathyroid pathology during operation or was not cured. Indication of no additional disease was defined by ≥95% stated chance of cure by the computer software method, ≥50% decline in IOPTH from baseline by the 50% decline algorithm, and by termination of the operation with a view to having cured the patient according to surgeon judgment.

Only patients with PHPT and a baseline IOPTH level in the normal range (ie, ≤69 pg/mL) were included for this study. Our protocol requires repeating the baseline IOPTH measurement if the first baseline level returns within the normal range. The initial baseline level is taken from an antecubital or dorsal hand vein while the patient is in the preoperative room. Our turnover time is 12 minutes from drawing of blood to obtaining the result. We routinely obtain a second baseline level if the first PTH is ≤69 pg/mL. We consider the mean of the 2 baseline samples as our initial baseline.

Only those patients in whom the mean of the 2 baseline IOPTH levels was ≤69 pg/mL were included in this study. Those with baseline IOPTH levels suspected to be in the normal range because of sample dilution were excluded. Confirmation of operative findings was made using operative reports, contemporaneous operative illustrations, and pathology reports of the weight and cellularity of resected parathyroid glands. The authors obtained Human Investigations Committee (Institutional Review Board) approval for this study and complied with all Health Insurance Portability and Accountability Act regulations; patient consent was waived as this was a retrospective study.