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Restoring Point-of-Care Testing during Parathyroidectomy with a Newer Parathyroid Hormone Assay

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Abstract

Objective. Intraoperative parathyroid hormone (IOPTH) monitoring has emerged as a useful adjunct in parathyroidectomy. Originally performed within the operating room, removal of the Nichols assay from the market forced many surgeons to rely on testing done in central laboratories, reducing convenience and prolonging operative times. The authors hypothesized that PTH assessment with a newer point-of-care (POC) assay would reduce results reporting time compared with central-laboratory PTH assays.

Study Design. Cross-sectional study with planned data collection.

Setting. Academic medical center.

Subjects and Methods. Patients underwent parathyroidectomy for primary or recurrent hyperparathyroidism. Intraoperative monitoring of serum PTH levels was used to confirm biochemical cure following adenoma excision. Samples were run in duplicate using both a POC PTH assay (Future Diagnostics) located within the operating room and a laboratory-based assay (Turbo PTH). Samples were taken at incision and at 5-, 10-, and 15-minute intervals following removal of suspected parathyroid adenomas. Results reporting time was recorded and compared by nonparametric Wilcoxon rank sum test.

Results. Sixty-six serum samples were assayed. There was excellent correlation between POC and central-laboratory IOPTH results ($r = 0.880, P < .001$). The POC IOPTH results were available faster than corresponding central-laboratory results, with a mean of 14.4 minutes compared with 30.7 minutes, respectively ($P < .001$). All patients (100%) demonstrated a biochemical cure by the end of the procedure.

Conclusion. Use of a rapid POC IOPTH assay results in a significant decrease in the amount of time for laboratory results to be communicated to the surgical team. This reduces operative times for parathyroidectomy and improves patient care.

Keywords

parathyroidectomy, parathyroid hormone assay, point of care, minimally invasive parathyroidectomy, targeted parathyroid surgery

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Primary hyperparathyroidism is a relatively common medical problem, with a reported incidence of 4 to 112 per 100,000 person-years. In approximately 85% to 88% of cases, the condition is a single benign parathyroid adenoma. The remainder of cases result from diffuse hyperplasia of all parathyroid glands (–11%) or multiple adenomas (1% to 5.4% of cases).2–4 Asymptomatic hyperparathyroidism may be observed conservatively if well-defined criteria are satisfied. Nevertheless, surgical removal of hyperfunctioning parathyroid tissue has been proven to be the only definitive cure for primary hyperparathyroidism.5

While often straightforward, parathyroidectomy can present numerous challenges to the endocrine surgeon, including ectopic locations of parathyroid glands in the neck and mediastinum, occasional presence of supernumerary glands, and difficulty distinguishing hyperplastic and adenomatous parathyroid tissue by visual inspection or even frozen section.5,6 Recent advances include improved preoperative localization of abnormal parathyroid glands with ultrasonography and sestamibi scintigraphy, as well as intraoperative parathyroid hormone (PTH) testing that allows the confirmation of successful

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removal of hyperfunctioning parathyroid tissue during the primary surgery.5-10 These advances have facilitated the performance of targeted and minimally invasive parathyroidectomies, resulting in a reduction in surgical morbidity as well as decreased incidence of treatment failures.10-12

The Nichols Advantage kit was introduced in 1996 and was the first widely available rapid intraoperative PTH assay. It was generally performed within the operating room and was quickly embraced by most high-volume endocrine centers. Unfortunately, the assay was removed from the market by the Food and Drug Administration in 2005. This action forced many surgeons to use laboratory-based assays to obtain intraoperative PTH level information. Among the many disadvantages of this approach are the logistical challenges of rapid sample transport and the lengthier time to conduct the assay.

A newer version of a point-of-care (POC) intraoperative PTH assay has been introduced by a Dutch company (Future Diagnostics, Wijchen, the Netherlands), and because of the rapid assay time (as short as 8 minutes) combined with a small equipment footprint that fits on a moveable cart, the assay has emerged as an improved intraoperative tool. We hypothesized that this POC assay would allow restoration of the many advantages compared with the performance of the intraoperative PTH (IOPTH) assay within a central laboratory.

**Methods**

This was a systematic cohort study of prospectively collected data. Consecutive patients who underwent parathyroidectomy for parathyroid gland adenoma/hyperplasia by the senior author from May 2009 to June 2009 were included in this study. Permission to access protected health information and analyze these data was granted by the Institutional Review Board at Georgia Health Sciences University. All patients underwent minimally invasive parathyroidectomy for primary hyperparathyroidism, with 1 patient representing reoperative surgery for persistent hypercalcemia. All patients underwent preoperative 99mTc-sestamibi imaging and neck ultrasound in pursuit of parathyroid adenoma localization.

At the start of the surgical procedure, baseline blood samples were submitted to a POC rapid IOPTH assay (STAT Intra-operative Intact PTH Immunoassay System; Future Diagnostics) and simultaneously sent to the hospital’s central laboratory for PTH assay (Turbo PTH; Diagnostics Products Corporation, Los Angeles, California). Minimally invasive parathyroidectomy was performed as previously reported,9 beginning on the side indicated by preoperative imaging studies. Following excision of abnormal parathyroid tissue, serial blood samples were submitted for IOPTH assay (as above) at 5, 10, and 15 minutes postexcision. The time interval until each result was reported back to the surgical team was recorded. The procedure was terminated when a >50% drop in PTH compared to baseline was achieved with a final result in the reference range, indicating a biochemical cure.

PTH levels and elapsed time until results were reported to the surgical team and compared using the nonparametric Wilcoxon rank sum test. Correlation between the central-laboratory and the POC assay was explored using the Spearman correlation test. All statistical comparisons were performed using SPSS version 14.0 and were 2-tailed (where applicable).

**Results**

A consecutive series of 66 IOPTH assay events were included in this study. They were obtained during the surgical interventions of 8 patients (3 men and 5 women) who had a median age at the time of surgery of 52 years (range, 38-89 years). All patients underwent preoperative sestamibi scanning, which was localizing in 88% of patients, and preoperative ultrasound, which was localizing in 63% of patients.

**Time Intervals for Test Results**

There were 32 central-laboratory PTH assays and 34 POC assays performed. The POC PTH results were reported to the surgical team at a mean of 14.4 ± 2.8 minutes after the blood was drawn (range, 11-27 minutes). This was significantly faster than the corresponding central-laboratory results, which were reported to the surgical team in a mean 30.7 ± 4.5 minutes after blood draw (range, 25-42 minutes; $P < .001$). Paired time-to-results data were available for 30 assays. Using the POC IOPTH result to designate biochemical cure and proceed with termination of the surgical procedure therefore resulted in a mean time savings of 16.6 ± 4.5 minutes (range, 10-28 minutes) per patient in this paired data set. These results are summarized in Figure 1.

**Correlation of Central-Laboratory versus POC IOPTH Assay**

The mean baseline PTH using the central-laboratory assay was comparable (245.3 pg/mL) to the POC assay baseline PTH (233.9 pg/mL, $P = .38$ for difference) for patients for whom both assays were performed (7 of 8). This trend was confirmed when comparing all samples in which paired data were available (n = 30 events), with central-laboratory PTH (101.1 pg/mL) comparable to the POC assay PTH (98.3 pg/
mL, \( P = .27 \) for difference). There was excellent correlation between central-laboratory and POC IOPTH results \( (r = 0.880 \text{ by Spearman correlation, } P < .001) \). These results are summarized in Figure 2. Following initial excision, 5 of 8 patients demonstrated a sufficient drop in PTH level compared with baseline at 5 minutes, which increased to 7 of 8 patients by 10 minutes (following the last adenoma excision). Two patients had multigland disease (1 each with 4-gland hyperplasia and a double adenoma), and all patients demonstrated a biochemical cure by the termination of surgery.

**Discussion**

The application of intraoperative PTH assays as an adjunct to parathyroidectomy has facilitated targeted or minimally invasive parathyroid surgery. Multiple studies have validated the use of serial PTH levels during parathyroid surgery as a sensitive method of detecting residual hyperfunctional parathyroid tissue.\(^9,11-13\) A POC assay would appear to be the optimal model for acquisition of PTH levels in the operating room setting. Unfortunately, the prevalent assay (produced by the Nichols Institute) was removed from the market in 2005, forcing many institutions to rely instead on central laboratory–based methods, which are not only slower but also harbor inherent logistical challenges.

We describe POC PTH monitoring with a system that has its origins in the Netherlands (Future Diagnostics), although there may be other manufacturers of POC PTH testing. This system has enabled us to achieve an assay time reduction of more than 16 minutes. While the exact origin of this time savings was not analyzed on a case-by-case basis, it came from 3 principal sources: elimination of specimen transport time (approximately 5 minutes), reduced centrifugation time to 1 minute (compared with 5 minutes for central laboratory), and assay time of 8 minutes (compared with 16 minutes for central laboratory). Importantly, there was excellent correlation \( (r = 0.88) \) between the results obtained by the assays.

Because of the more rapid result reporting, the overall procedural cost may also be reduced. The POC assay costs approximately $37.50 per level acquired (reagent costs), compared with $3.61 for the central-laboratory PTH assay. Labor costs (salary and benefits) for the POC laboratory technician add an additional $28 per case (assuming 1 hour of technician time). There is an approximately $30,000 capital equipment investment required. However, operating room time is billed at $94 per minute at our institution. Therefore, a reduction in operating time of 16.6 minutes results in an overall savings that exceeds $1400 per patient. In complicated cases, in which multiple parathyroid tissue excisions are necessary, the time and cost savings are even greater. It must be acknowledged, however, that this analysis assumes operating rooms that are running at 100% efficiency, which is rarely the case. Our operating room utilization averages between 80% and 85%. As a result of implementing the POC assay, we routinely accomplish 4 parathyroidectomies per day (8 AM to 4 PM), compared with 3 per day previously. The benefit of a shorter procedural time for the patient remains the principal driver for adoption of this assay, but there may be institutional cost savings as well.

A final, unanticipated benefit realized during the implementation of this technology was the incorporation of the laboratory medical technologist into the surgical team. This resulted in improved job satisfaction and a sense of *esprit de corps* that is difficult to quantify but nonetheless important. It is likely that as technology for other assays (eg, molecular surgical margin analysis, etc) evolves, the role of intraoperative testing may expand and provide additional opportunities for assimilation of medical technologists into the surgical team.

**Conclusion**

The value of intraoperative PTH testing using a rapid PTH assay as an adjunct to parathyroidectomy is well established. Moving the administration of the PTH assay back into the operating room with a newer POC IOPTH test results in a significant reduction in the time required for laboratory results to be communicated to the surgical team, improving patient care and reducing overall costs. This assay should be considered by any moderate- to high-volume surgical center that pursues targeted parathyroidectomy.

**Author Contributions**

David J. Terris, corresponding author, conception, design, data acquisition, data analysis, writing; Paul M. Weinberger, conception, design, data acquisition, data analysis, writing; Tarik Farrag, data analysis, writing; Melanie Seybt, conception, editing; Joyce E. Oliver, conception, editing.

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