

Immediate and Medium-Term Results of Intraoperative Parathyroid Hormone Monitoring During Video-Assisted Parathyroidectomy

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Hypothesis: Using an intraoperative parathyroid hormone (IOPTH) assay during video-assisted parathyroidectomy by lateral approach is useful in patients with sporadic primary hyperparathyroidism, and the medium-term results of surgery are excellent.

Design: Retrospective study of patients with sporadic primary hyperparathyroidism following video-assisted parathyroidectomy by lateral approach with IOPTH measurement.

Patients: Of 394 patients with sporadic primary hyperparathyroidism, 200 (67%) were eligible for video-assisted parathyroidectomy by lateral approach: patients in whom a single enlarged gland was clearly localized by ultrasonography, sestamibi scintigraphy, or both.

Main Outcome Measures: An IOPTH assay was used in 198 patients. Intraoperative parathyroid hormone was measured at induction, skin incision, ablation, and 5 and 15 minutes after ablation.

Results: The immediate results of the IOPTH assay were true positive in 187 cases (94.4%), true negative in 8 cases (4%), false negative in 2 cases (1%), and false positive in 1 case (0.5%). The overall accuracy of the IOPTH assay was 98.5%. All patients were normocalcemic postoperatively. The median follow-up was 20.5 months in 150 reviewed: 149 patients (99.4%) were normocalcemic, 17 patients (11.3%) had an elevated PTH level with normocalcemia, and 1 patient (0.6%) had recurrent primary hyperparathyroidism.

Conclusions: In our experience, IOPTH monitoring during video-assisted parathyroidectomy by lateral approach is useful in detecting multiple gland disease not suspected by preoperative localization studies. Overall, IOPTH monitoring predicts medium-term normocalcemia with a success rate of 98.5% in patients with sporadic primary hyperparathyroidism.

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THE PRINCIPLES OF PARATHYROID surgery have evolved since the development of preoperative localization studies such as sestamibi (MIBI) scintigraphy and the widespread use of intraoperative parathyroid hormone (IOPTH) monitoring. The first report of unilateral neck exploration for sporadic primary hyperparathyroidism (sPHPT) was by Tibblin et al¹ in 1982. Several techniques of parathyroidectomy have been described in the literature: unilateral neck explorations, radio-guided parathyroidectomy, and total endoscopic and video-assisted parathyroidectomy. These operations are performed under local or general anesthesia. Compared with bilateral neck exploration, they offer reduced surgical trauma, a better cosmetic result, perhaps a decreased operating time, and the possibility of same-day discharge. Conventional bilateral neck exploration remains, however, the

gold standard with which other techniques are compared, with a cure rate of more than 95% in experienced hands.

Since 1997, we have developed in our department the technique of video-assisted parathyroidectomy by lateral approach (VAPLA) for patients with sPHPT.² Intraoperative parathyroid hormone is widely used and has a key role in focused surgical approaches, including VAPLA, to assess the initial adequacy of surgery. The long-term results of newer surgical techniques using IOPTH are not known. The purpose of this study was to assess the accuracy of an IOPTH assay during VAPLA in patients with sPHPT and to assess the medium-term results of VAPLA.

METHODS

Between March 1998 and December 2001, 394 patients with sPHPT underwent surgery in our

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Table 1. Reasons for Conversion

Reason	No. of Patients
Adenoma not found	6
Atypical/large adenoma	4
Sestamibi scintigraphy false-positive result	9
Multiglandular disease*	1
IOPTH assay false-positive result	1
Gland effraction	1
IOPTH assay false-negative result	1
IOPTH assay true-negative result	8
Total	31

Abbreviation: IOPTH, intraoperative parathyroid hormone.

*Two abnormal glands seen during video-assisted parathyroidectomy by lateral approach.

Table 2. Intraoperative Parathyroid Hormone Results

Result	No. of Patients (%)
True positive	187 (94.44)
False positive	1 (0.50)
True negative	8 (4.04)
False negative	2 (1.01)

department. Of these patients, 200 were eligible for VAPLA based on the following criteria: no previous cervicotomy, no concomitant goiter, no family history of hyperparathyroidism, and a single enlarged gland clearly localized preoperatively by ultrasonography and/or MIBI scintigraphy. Video-assisted parathyroidectomy by lateral approach permitted a unilateral neck exploration under videoscapy, and the gland was removed directly through the 10-mm trocar site. The diagnosis was confirmed in all patients before surgical intervention with serum measurements of calcium (normal range, 9-10.5 mg/dL [2.20-2.60 mmol/L]), creatinine (normal range, 0.38-1.02 mg/dL [50-110 μ mol/L]), and parathyroid hormone (PTH) (normal range, 10-55 pg/mL).

During the operation, we utilized a commercially available IOPTH immunoassay (Nichols Institute Diagnostics, San Juan Capistrano, Calif) that uses 2 polyclonal antibodies directed against the intact PTH peptide. Parathyroid hormone levels were measured at baseline, at skin incision, at gland resection, and at 5 and 15 minutes following parathyroidectomy. A decrease in IOPTH of 50% from the highest preablation level signified a positive test result, and there was no further neck exploration. When the IOPTH decrease was less than 50%, the test result was negative, and we performed a bilateral neck exploration. Following parathyroidectomy, we measured the serum calcium and PTH levels on days 1 and 8 and again at months 1 and 4. All patients had their vocal cords inspected before and after intervention. The median follow-up in 150 patients reviewed was 20.4 months (range, 1.15-40.90 months).

RESULTS

Of 394 patients with sPHPT, 200 (50.7%) were eligible for VAPLA. The ratio of women to men in this group was 4:1 (160/40), and the median age was 61 years (range, 20-89 years). The median preoperative calcium level was 11.3 mg/dL (2.83 mmol/L) (range, 9.6-16.12 mg/dL [2.42-4.03 mmol/L]). The median preoperative PTH level was 125

pg/mL (range, 44-725 pg/mL). The median length of stay from the day of surgery to discharge from the hospital was 3 days (range, 1-13 days). There were 192 patients (95.5%) with uniglandular disease: 175 with adenoma, 14 with hyperplasia, 2 with carcinoma, and 1 with lipoadenoma. Eight patients (4.5%) had multiglandular disease: 6 with hyperplasia, 1 with double adenoma and 1 with association of an adenoma and hyperplasia. The average weight of the parathyroid gland was 600 mg (range, 75-7080 mg).

CONVERSION TO CERVICOTOMY

We performed 31 bilateral neck explorations (15.5%) (**Table 1**), 9 following an inappropriate PTH level decrease.

IOPTH RESULTS

Intraoperative parathyroid hormone level was measured in 198 patients (99%): 187 (94.4%) true positives, 8 (4%) true negatives, 1 (0.5%) false positive, and 2 (1%) false negatives (**Table 2**). Intraoperative parathyroid hormone specificity was 88.8%, sensitivity was 98.9%, and overall accuracy was 98.5%. In 2 patients, we did not perform IOPTH monitoring. Both of those patients had an early conversion to cervicotomy: one after a gland effraction and the other following a false-positive MIBI result.

FOLLOW-UP

There were a total of 8 complications (4%): 5 cases of transitory hypocalcemia, 1 definitive recurrent nerve palsy, 1 chest infection, and 1 cardiac arrhythmia. The median serum calcium level on day 1 was 9.12 mg/dL (2.28 mmol/L); on day 8, 9.32 mg/dL (2.33 mmol/L); and at month 1, 9.24 mg/dL (2.31 mmol/L).

The median follow-up in 150 patients reviewed was 20.4 months (range, 1.15-40.90 months). One hundred forty-eight patients were normocalcemic, and 2 patients had recurrent hypercalcemia. One patient had recurrent sPHPT 15 months after the resection of a solitary adenoma, and the other patient had persistent hypercalcemia (10.88 mg/dL [2.72 mmol/L]) associated with a low PTH level (15 pg/mL).

Eleven percent of the reviewed patients had a high PTH level with a normal serum calcium level. Persistent moderate increase in PTH levels without hypercalcemia following surgery have been well described³ and do not represent a major risk of recurrent disease.

COMMENT

The principles of parathyroid surgery have dramatically evolved since the development of minimally invasive surgery. These new techniques rely on preoperative localization studies and on IOPTH. The focused approach can only be proposed in selected patients: those in whom MIBI scintigraphy and ultrasonography show a single tumor. In our current experience, 57% of patients with sPHPT are suitable for a focused approach.

Although the sensitivity of MIBI scintigraphy varies between centers, the range in the literature is 54% to 82%.⁴⁻⁸ Miura et al⁹ showed that MIBI scintigraphy correctly detected the hypersecreting tissue in uniglandular disease in 88% of patients but only in 13% of patients with multiglandular disease. Failure of the focused or unilateral approach is due to unrecognized multiglandular disease at the preoperative investigation. The use of IOPTH can decrease this risk. Indeed, IOPTH has been successfully utilized by several authors.¹⁰⁻¹⁵ In our series, the IOPTH results correctly predicted cure in 98.5% of patients. In 7 of 8 patients with multiglandular disease, IOPTH correctly predicted the presence of remaining hypersecretory tissue. There was only 1 false-positive result with an IOPTH level decrease of 54%. In this case, we performed a bilateral exploration because the IOPTH level's decrease was borderline, and we found another enlarged gland that had the same size as the first resected gland. This approach can be criticized because of the lack of rigor, but it avoided a persistent PHPT.

There were 2 false-negative results from the IOPTH monitoring. These 2 patients had bilateral neck exploration, but no additional enlarged gland could be found. The explanation for these results may be a longer half-life of the PTH in these patients. Indeed, Libutti et al¹⁶ showed that the half-life of PTH could vary substantially from 0.42 to 3.81 minutes.

The overall accuracy of the IOPTH monitoring is 98.5%. The test reliably predicts the surgical outcome and may be especially useful when localization studies are less certain (ie, only 1 localization test result is positive). Miura et al⁹ showed that if both MIBI scintigraphy and ultrasonography identified the same single abnormality, a focused exploration had a 95% success rate even without IOPTH, and they believe that the less certain the localization studies, the more certain the need for IOPTH.

A new rapid IOPTH assay is now available. The results can be obtained in 8 rather than 15 minutes, and the results are equally accurate.^{11,13,17} Surgeons can have rapid feedback of hormone levels. This can be very useful not only after parathyroid resection to assess the adequacy of resection but also in differential venous sampling for the localization of an ectopic gland at open surgery.

In the reviewed group, 17 patients (11.3%) had a persistent increased PTH level and a normal calcium level. Other groups have reported an incidence of normocalcemic hyperparathormonemia of up to 31%.^{3,18,19} Several explanations have been proposed, and there is no evidence that these patients have a higher risk of recurrence.³

One patient had recurrent hypercalcemia (calcium level, 10.72 mg/dL [2.68 mmol/L]) with a high PTH level 15 months after VAPLA. It is difficult to say if this was an early recurrence or a persistence of sPHPT. Indeed, the PTH level after 6 months was normal. Recurrences after conventional parathyroidectomy for sPHPT typically appear after several years. The significance of this early recurrence is not clear. Perhaps this was due to a remaining enlarged nonsecretory parathyroid gland, which subsequently became secretory following the removal of an adenoma (ie, it acted as if suppressed). Carneiro et al¹² assume that 9% to 19% of cured patients have macroscopically enlarged glands that remain. We do not know how these enlarged

but nonhypersecretory parathyroid glands evolve after surgery and if they become autonomous later. It is therefore important to monitor these patients in the long term.

In conclusion, the use of VAPLA with IOPTH monitoring in the treatment of sPHPT produces results comparable with those of conventional cervicotomy. In our series, IOPTH monitoring maximized the success rate of primary intervention.

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