Objective: To examine the role of intraoperative rapid parathyroid hormone (PTH) monitoring in the surgical management of hyperparathyroidism.

Design: Thirty-eight–month retrospective review.

Setting: Tertiary care academic medical center.

Patients: One hundred consecutive patients undergoing surgery for primary hyperparathyroidism.

Intervention: All patients underwent preoperative technetium Tc 99m sestamibi scan localization and intraoperative blood PTH monitoring by means of a rapid (12-minute) immunochemiluminometric assay.

Main Outcome Measures: The influence of intraoperative PTH levels on extent of surgical dissection and achievement of postoperative normocalcemia.

Results: Intraoperative PTH levels dropped an average of 64%, 75%, and 83% at 5, 10, and 20 minutes, respectively, after excision of all hyperfunctioning parathyroid tissue. A PTH decrease of 46% or more at 10 minutes and 59% or more at 20 minutes after excision of hyperfunctioning tissue was predictive of postoperative normocalcemia. In 79 patients (79%), the sestamibi scan provided accurate preoperative localization; all but 1 of these patients were treated successfully, most often with a limited, gland-specific dissection. In 24 patients with inaccurate, negative, or misleading preoperative sestamibi scans, 23 (96%) were treated successfully with the use of the intraoperative PTH assay.

Conclusions: The rapid intraoperative PTH assay accurately predicts postoperative success in patients with primary hyperparathyroidism. The rapid PTH assay allows for greater confidence in performing limited dissections in well-localized uniglandular disease. In cases of inaccurate preoperative localization, the rapid PTH assay directly affects surgical decision making and provides greater confidence in determining when surgical success has been achieved.

PATIENTS AND METHODS

The study population consisted of consecutive patients undergoing surgery for primary hyperparathyroidism within the Department of Otolaryngology at Mount Sinai Hospital, New York, NY, from November 5, 1997, through January 31, 2001. All operations were performed by either of 2 of us (E.M.G. and M.L.U.) after patients gave informed consent for parathyroidectomy. Patient charts and detailed operative reports were reviewed retrospectively, and the following information was obtained for each patient: age at the time of surgery; sex; preoperative total serum calcium, intact serum PTH, and serum creatinine levels; total number of parathyroid glands removed; type of anesthesia (general vs regional); operative time from initial incision to final closure; length of hospital stay; and presence of coexisting thyroid gland disease. Patients with evidence of renal failure were excluded.

All patients underwent preoperative localization with 99mTc sestamibi nuclear imaging at Mount Sinai Hospital (Vision software; SMV America, Twinsburg, Ohio). Two scintillation images of the neck and upper mediastinum (1 at 15 minutes and 1 at 2 hours after injection of the radiotracer) were obtained with the patient supine and the neck extended. The recorded dose of radiotracer administered per patient ranged from 20 to 26 mCi (740-962 MBq). Initial uptake in the thyroid gland (seen at 15 minutes) was expected to decrease over time, whereas a parathyroid adenoma, if present, was expected to maintain uptake during the 2-hour time span.21 Recently, in our institution, traditional sestamibi parathyroid scintigraphic examinations have been routinely supplemented with images obtained by single-photon emission computed tomography, a technique that reportedly may identify smaller (<500 mg) parathyroid adenomas with improved accuracy.22 From a surgical perspective, we have yet to notice a distinct advantage in parathyroid adenoma detection with the use of single-photon emission computed tomography with sestamibi, but as more data are generated, this issue will deserve further study.

Blood was drawn for the rapid intraoperative PTH assay through a radial arterial line at the following times: “postinduction” (immediately after induction of general anesthesia, or immediately after completion of a regional nerve block for cases performed with the patient under local anesthesia); “postisolation” (immediately after dissection, but just before removal, of suspected hyperfunctioning parathyroid tissue); and 5, 10, and 20 minutes after excision of suspected hyperfunctioning tissue. It is generally accepted, on the basis of work by Irvin et al,8 that a drop in rapid PTH levels of more than 50% from baseline levels at 10 minutes after excision of hyperfunctioning tissue is predictive of postoperative normocalcemia. However, we decided to send 3 separate peripheral-blood samples for rapid PTH assessment at 5, 10, and 20 minutes after excision in every patient, to make sure our experience was consistent with that of the literature, and also simply to document and study longitudinally the fluctuations and variations in PTH levels that might occur during the early postexcision period.

The percentage decrease in rapid PTH levels after excision of hyperfunctioning tissue was determined by comparing each postexcision rapid PTH level to the highest preexcision level (either the postinduction or the postisolation level, whichever was higher). This technique has been previously described.4 Intraoperatively, the following general principles applied. In cases in which the preoperative sestamibi scan appeared to clearly identify a single hyperfunctioning gland, unilateral exploration with single-gland excision was performed. If rapid PTH levels dropped by 50% or more from either the postinduction or postisolation levels at 10 or 20 minutes after excision of suspected hyperfunctioning tissue, the operation was terminated. The decision to use the 50% decrease in PTH levels as an indicator of surgical success was based on data from Irvin et al.8 If rapid PTH levels failed to drop to 50% or less of baseline by 20 minutes after excision of suspected hyperfunctioning tissue, further exploration was performed.

In cases of inadequate preoperative sestamibi localization, bilateral neck explorations were planned. Rapid PTH levels were drawn at 5, 10, and 20 minutes after excision of suspected hyperfunctioning tissue. The operation was terminated if rapid PTH levels dropped by 50% or more8; otherwise, further exploration was pursued.

Postoperatively, blood samples for both total and ionized calcium levels were drawn every 6 hours until the patient was discharged from the hospital. This relatively frequent calcium monitoring regimen was followed to ensure that normocalcemia (and not substantial hypocalcemia) occurred in the early postoperative period, thus helping to determine the feasibility of early (possibly even same-day) hospital discharge after surgery. Patient discharge was based on the demonstration of a plateau in serial total and ionized calcium levels within the reference range after surgery. For the standard hospital assays used in our institution, the reference range of total serum calcium level is 8.5 to 11.0 mg/dL (2.1-2.8 mmol/L), while the reference range of ionized calcium is 4.36 to 5.00 mg/dL (1.14-1.29 mmol/L). A telephone survey was performed a minimum of 6 months (range, 6-33 months) after surgery in which patients were asked to recall the last time their serum calcium level was checked, and whether they were told the calcium level was normal or abnormal.

Rapid intraoperative PTH levels were determined by means of a commercially available ICMA kit (QuickIntraOperative Intact PTH Kit; Nichols Institute Diagnostics, San Juan Capistrano, Calif). The assay was performed by a technician stationed in a small anteroom directly adjacent to the operating room. The overall turnaround time from the moment the blood sample was drawn to the moment the rapid PTH level was reported to the surgeon was approximately 12 minutes. For the first 61 patients in the study, a 3-mL portion of each intraoperative blood sample was sent to the central hospital laboratory for analysis with the routine hospital PTH assay (an ICMA that requires 2 hours of incubation). The PTH results from the standard hospital assay correlated well with results from the rapid intraoperative assay (Pearson correlation coefficient r = 0.83; P <.01; based on 316 paired samples).

PTH immunochemiluminometric assay (ICMA) combined with preoperative localization by sestamibi scanning in a series of patients with primary hyperparathyroidism treated with targeted surgical exploration. The purposes of the study were to determine the ability of the rapid PTH assay to predict surgical success and to assess the influence of the assay on intraoperative decision making and surgical strategy.
One hundred consecutive patients who underwent operative management of primary hyperparathyroidism were studied. Average patient age at the time of surgery was 58 years (range, 30-91 years). There were 69 women and 31 men. Both the average preoperative serum calcium level (11.4 mg/dL [2.9 mmol/L]; range, 10.4-14.8 mg/dL [2.6-3.7 mmol/L]) and the average preoperative intact serum PTH level (179 pg/mL; range, 65-800 pg/mL) were elevated above the reference range for the assays used in all cases. The average preoperative serum creatinine (0.9 mg/dL [80 mmol/L]; range, 0.4-1.6 mg/dL [35-141 mmol/L]) and albumin (4.3 g/dL; range, 3.6-4.8 g/dL) levels were considered to be within the reference range for the assays used in all cases.

Of the 100 patients in the study, 89 had a single benign hyperfunctioning gland, 8 had 2 distinct parathyroid adenomas, 1 had multiple-gland hyperplasia, 1 had parathyroid carcinoma, and in 1 patient hyperfunctioning tissue was not found despite extensive exploration.

There was no mortality in this series. There were no cases of recurrent laryngeal nerve paralysis. One patient required a prolonged (20-day) postoperative stay because of persistent hypocalcemia after 4-gland parathyroidectomy with brachioradialis autotransplantation for multiglandular hyperplasia.

All 100 patients underwent preoperative localization with 99mTc sestamibi scanning. The scan accurately localized hyperfunctioning tissue to the correct side of the neck in 79% of the cases (79 true-positive scans). There were 20 false-negative scans (20% false-negative rate). There was 1 true-negative scan, in which rapid PTH levels remained elevated and hypercalcemia persisted postoperatively. There were 3 false-positive results. In 2 cases, a false-positive result occurred with a contralateral true-positive result in the same patient, leading to an unnecessary contralateral neck exploration in which no gross parathyroid or thyroid gland disease was found. The other false-positive result was due to a lymph node with metastatic papillary carcinoma; in the same patient, there was a false-negative result on the contralateral side, where a parathyroid adenoma was found. In 1 case, a false-negative result occurred with a contralateral true-positive result in a patient with 1 parathyroid adenoma on each side of the neck. Overall, there were 24 patients with inaccurate, negative, or misleading preoperative localization, of whom 23 (96%) were treated successfully with the use of the intraoperative PTH assay.

Of the 100 patients who underwent parathyroid surgery, 20 had coexistent thyroid gland disease requiring thyroid surgery. Of these, 5 patients had total thyroidectomy (2 patients with papillary carcinoma, 2 with multinodular goiter, and 1 with Hurthle cell adenoma), and 15 patients had thyroid lobectomy (8 patients with follicular adenoma, 6 with multinodular goiter, and 1 with papillary thyroid carcinoma).

The average length of hospital stay was 1.7 days (range, 0-20 days). Sixty-five patients (65%) were discharged home on the first postoperative day. Thirty-seven operations (37%) were performed with the patient under regional block anesthesia with intravenous sedation, and 7 (19%) of these patients were ambulatory. The remaining 63 operations were performed with the patient under general anesthesia, of whom 4 (6%) were ambulatory.

Excluding the 1 patient in whom abnormal parathyroid tissue was not found, intraoperative rapid PTH levels dropped an average of 64%, 75%, and 83% at 5, 10, and 20 minutes, respectively, after excision of all hyperfunctioning parathyroid tissue (Figure 1). A rapid PTH decrease of 46% or more at 10 minutes, and 59% or more at 20 minutes, after excision of suspected hyperfunctioning tissue was predictive of postoperative normocalcemia. In 99 of 100 patients, normocalcemia was demonstrated at the time of hospital discharge (average total serum calcium level, 8.7 mg/dL [2.2 mmol/L]; range, 7.4-10.3 mg/dL [1.9-2.6 mmol/L]; average ionized calcium level, 4.68 mg/dL [1.17 mmol/L]; range, 3.92-5.16 mg/dL [0.98-1.29 mmol/L]). In the 1 patient whose PTH levels did not decrease intraoperatively, hypercalcemia persisted during the immediate postoperative period. Selective venous sampling performed on the first postoperative day suggested the presence of a hyperfunctioning gland in the mediastinum; however, the patient refused any further surgical intervention and remained hypercalcemic after 9 months of postoperative follow-up.

Sixty-four patients were available for long-term follow-up by telephone survey. The most recent serum calcium levels had been drawn between 6 and 33 months after surgery (average, 14 months). Only 2 (3%) of 64 patients had experienced recurrent hyperparathyroidism. The first patient had undergone excision of a 0.1-g solitary left inferior parathyroid adenoma in November 1997 that had been well localized on preoperative sestamibi scan. Rapid PTH levels dropped by 75% and 78% at 5 and 10 minutes, respectively, after adenoma excision. Postoperative normocalcemia persisted for 2 years, at which time hyperparathyroidism recurred. A sestamibi scan at that time localized the abnormality to the left side of the neck, while an ultrasound scan of the neck was negative. Extensive exploration of the left side of the neck, including retroesophageal exploration and partial thymic excision, failed to show any parathyroid tissue. The right side of the neck was then explored, where an
enlarged inferior parathyroid gland was found. A superior right parathyroid gland could not be identified despite extensive exploration. After removal of the right inferior parathyroid gland, rapid PTH levels decreased by 95%. A small portion of the excised gland was used for brachioradialis autotransplantation. At 3 months’ follow-up, the patient remained normocalcemic. Because of the 2-year period of postoperative normocalcemia after the first operation, the rapid PTH assay was still considered to be accurate (true positive) in this case, and this case was not considered a surgical failure.

In the second case of recurrence, removal of a solitary left inferior parathyroid adenoma from a patient in September 1999 resulted in a drop in rapid PTH levels of 42%, 55%, and 64% at 5, 10, and 20 minutes, respectively, after excision. Preoperative sestamibi scanning had shown 2 foci of increased uptake, 1 on each side of the neck. Although a bilateral exploration had been performed, the only parathyroid adenoma identified was on the left side (weight, 0.23 g). More extensive exploration was not undertaken because of the marked decrease in rapid PTH levels after adenoma excision. The patient was normocalcemic on hospital discharge on the first postoperative day; however, within 1 week of surgery, hypercalcemia had recurred. At 8 months postoperatively, hyperparathyroidism with hypercalcemia persisted; the patient refused further workup and recently became unavailable for follow-up despite repeated attempts to maintain contact.

This case represents the only false-positive rapid PTH assay result in our series and is considered a surgical failure (1 of 2 in this series). We believe that the right-sided sestamibi localization represented a false-positive result and that any additional adenoma would likely reside in an ectopic location. Further workup, could it be obtained, would include repeated sestamibi and ultrasound. If these were negative, either selective venous PTH sampling or magnetic resonance imaging would be considered. In our department, we generally prefer ultrasound over magnetic resonance imaging to correlate with sestamibi results, as it is believed that ultrasound and magnetic resonance imaging have traditionally yielded similarly accurate results in our institution, with ultrasound representing the less expensive option.

Overall, our surgical success rate was 97% in patients with at least 6 months of follow-up.

The following represents a breakdown of the cases in our series based on degree of complexity, to determine the way in which the rapid PTH assay affected intraoperative decision making.

**ROUTINE CASES**

There were 67 cases of uncomplicated, primary hyperparathyroidism resulting from a single parathyroid adenoma with a true-positive sestamibi scan with a single positive site of uptake. None of these patients had a history of endocrine-related surgery. All patients had a marked drop in rapid PTH levels intraoperatively (average decrease of 64% [range, −18% to −96%] at 5 minutes, 75% [range, −46% to −94%] at 10 minutes, and 84% [range, −59% to −98%] at 20 minutes after excision), and all patients were normocalcemic on discharge from the hospital. Among these 67 cases, 60 (90%) were able to undergo unilateral exploration. Visualization of a second ipsilateral parathyroid gland was often not attempted. Seven patients underwent bilateral neck explorations because of bilateral or contralateral thyroid gland disease (6 patients) and temporary luminometer malfunction (1 patient). Excluding the 7 patients who underwent bilateral neck explorations, 6 who underwent attempts at endoscopic parathyroidectomy (as part of another simultaneous study protocol), and 5 who underwent unilateral exploration with thyroid lobectomy and parathyroidectomy, the average operative time in the remaining 49 patients who underwent limited, single-gland dissections was 54 minutes (range, 8–84 minutes). On long-term follow-up, 2 cases of recurrent hyperparathyroidism were identified (both were described in the “Results” section).

**CASES WITH A NEGATIVE PREOPERATIVE SESTAMIBI SCAN**

There were 17 patients with primary hyperparathyroidism with a negative preoperative sestamibi scan. One patient in this group had undergone a previous subtotal thyroidectomy, while the other 16 patients had no history of previous endocrine-related surgery. In 9 of these patients, an attempt was made to localize the side of the hyperfunctioning tissue by measuring rapid PTH levels from bilateral percutaneous internal jugular venous samples taken before skin incision, with the patient under anesthesia (Table). This technique provided accurate localization in only 3 of 9 patients; unilateral exploration with adenoma excision was performed in these 3 patients, followed in each instance by an appropriate decrease in rapid PTH levels. In 5 of 9 patients, right and left jugular venous samples were roughly equivalent to one another, despite the later discovery of unilateral parathyroid disease on surgical exploration. In one case, despite rapid PTH levels that were markedly higher in the left jugular venous sample than the right, hyperfunctioning parathyroid tissue could not be found despite extensive exploration. Rapid PTH levels remained elevated throughout the procedure, and postoperative hypercalcemia persisted. In another patient, a single adenoma was fortuitously encountered at the on-
set of neck exploration with a drop in rapid PTH levels, thus obviating the need for a contralateral exploration. In 2 patients, resection of an enlarged parathyroid gland resulted in a drop in rapid PTH levels of only 30% and 49%, respectively, from baseline at 20 minutes after excision; contralateral neck exploration subsequently disclosed another enlarged parathyroid gland, after excision of which rapid PTH levels dropped to 78% and 88%, respectively, of baseline at 20 minutes. These 2 patients were normocalcemic on hospital discharge; long-term follow-up is not yet available. Overall, 16 of 17 patients with negative preoperative sestamibi localization had successful resection of hyperfunctioning tissue (14 solitary parathyroid adenomas and 2 cases of double adenoma), with 4 unilateral and 12 bilateral explorations.

REVISION SURGERY FOR RECURRENT HYPERPARATHYROIDISM

Nine patients underwent revision surgery for previous failed parathyroid surgery. All 9 patients underwent preoperative sestamibi scanning. In 5 cases, the combination of successful preoperative sestamibi localization with marked postexcision decreases in intraoperative rapid PTH levels led to a limited, unilateral neck exploration, thus avoiding the need for extensive exploration in a previously operated-on field.

One patient had undergone previous bilateral neck exploration for primary hyperparathyroidism at another hospital; no adenoma had been found, and hypercalcemia persisted postoperatively. During the revision surgery in the present study, despite a sestamibi scan showing uptake in the right lower part of the neck, extensive bilateral exploration (including median sternotomy and mediastinal dissection) failed to reveal an enlarged parathyroid gland, as evidenced by a failure of rapid PTH levels to drop despite multiple biopsies. Finally, an intrathyroidic parathyroid adenoma was found, and rapid PTH levels decreased markedly after excision.

In another patient with recurrent hyperparathyroidism after excision of a single adenoma, preoperative sestamibi localized hyperfunctioning tissue to both sides of the neck. A parathyroid adenoma was successfully removed on one side of the neck, with an appropriate drop in rapid PTH levels. However, an unnecessary contralateral neck exploration was undertaken as a result of the false-positive sestamibi scan result.

One patient had undergone 2 previous neck explorations at another institution with removal of 1 right-sided parathyroid adenoma, 1 left-sided parathyroid adenoma, and a left intrathyroidal parathyroid cyst, with persistent hyperparathyroidism postoperatively. Sestamibi scanning localized the abnormality to the left superior mediastinum, where a parathyroid adenoma was found and excised. However, rapid PTH levels failed to decrease. After bilateral neck explorations with no parathyroid tissue identified, attention was returned to the mediastinum, where another left retroesophageal adenoma was identified. Rapid PTH levels decreased markedly after excision.

In another patient with persistent hyperparathyroidism after bilateral neck explorations at another institution, preoperative sestamibi scanning failed to localize the abnormality, and preoperative venous sampling demonstrated substantial elevation of PTH levels in the innominate vein. After bilateral neck exploration failed to show parathyroid tissue, a median sternotomy was performed. A 2.45-g parathyroid adenoma was identified within the left side of the thymus just below the level of the innominate vein. After excision, rapid PTH levels decreased appropriately.

MULTIPLE ADENOMAS

Six patients with primary hyperparathyroidism and no previous endocrine-related surgery were found to have 2 distinct adenomas. In each case, 1 adenoma was located on the right and 1 on the left side of the neck. Preoperative sestamibi scanning successfully localized both the right and left parathyroid adenomas in 3 of the 6 patients. In 2 patients, sestamibi scanning failed to localize the abnormality to either side of the neck, and in 1 patient, a true-positive sestamibi scan on one side of the neck was coupled with a false-negative result in the contralateral side. In each case, rapid PTH levels decreased in a sequential manner after excision of each of the adenomas (after first gland excision: average decrease, 55%; range, 30%-85%; after second gland excision: average decrease, 82%; range, 63%-93%). Of note, if a preoperative sestamibi scan had not been routinely performed, the second adenoma might not have been removed in 2 of these 6 patients, since in these cases the rapid PTH levels dropped by more than 50% after resection of the first adenoma, and the contralateral side was explored only because of bilateral sestamibi localization. The average weight of the first adenoma was 0.28 g (range, 0.06 to 0.70 g); the average weight of the second gland was 0.14 g (range, 0.06 to 0.28 g).

MULTIPLE-GLAND HYPERPLASIA

One patient with primary hyperparathyroidism demonstrated multiple-gland hyperplasia. The rapid PTH levels tended to decrease in a delayed, sequential manner after excision of each of the hyperplastic glands (Figure 2). The PTH levels did not decrease to less than 50% of baseline until 20 minutes after excision of the third
hyperplastic parathyroid gland. A 4-gland parathyroidectomy was performed, with an overall decrease in rapid PTH level of 81% from preexcision to final postexcision levels. A portion of 1 parathyroid gland was used for brachytherapy implantation. Postoperatively, the patient experienced persistent, profound hypocalcemia requiring nearly 3 weeks of in-hospital management with both oral and intravenous calcium supplementation. After 9 months of follow-up, hyperparathyroidism has not recurred, but the patient still requires daily oral calcium and vitamin D supplements.

MISCELLANEOUS

One patient with papillary thyroid carcinoma proved by fine needle aspiration biopsy and concomitant hyperparathyroidism demonstrated sestamibi localization to the left lower pole. In the operating room, a left paratracheal mass was excised and found to be a lymph node with metastatic papillary carcinoma on frozen-section analysis. Rapid PTH levels did not fall after removal of the mass. On the right side, a large superior parathyroid adenoma was seen and excised, after which the rapid PTH levels fell significantly. A total thyroidectomy was also performed.

The earliest clinical report of a rapid intraoperative PTH assay was described by Nussbaum et al in 1988. This 2-site immunoradiometric assay (IRMA) used radiolabeled anti-PTH antibody, with radioactivity quantified in a gamma counter. Total incubation time was shortened to just 15 minutes by raising the incubation temperature. While accurate in predicting successful surgical removal of hyperfunctioning parathyroid tissue, IRMA has been shown to have the following drawbacks: (1) limited assay shelf-life because of the short half-life of the radioisotopes and (2) cumbersome radiation-related waste removal and safety precautions, which hinder unit portability.

A more recent technique for rapid PTH measurement is the ICMA. This is a 2-site antibody assay similar to IRMA, but antibodies are labeled with a nonradioactive agent (acridinium ester). Trigger chemicals cause the acridinium ester to emit light, which is then measured in a luminometer. The nonradioactive ICMA kit can be safely placed on a cart outside the operating room, eliminating transport time and allowing immediate reporting of results to the surgeon.

Rapid PTH assays using ICMA have reported incubation times as short as 7 minutes, with the results being available to the surgeon within as little as 10 minutes of the sample being taken. It is generally believed, on the basis of work by Irvin et al, that a drop in rapid PTH levels of greater than 50% at 10 minutes after excision of hyperfunctioning tissue is predictive of postoperative normocalcemia in a variety of patients with hyperparathyroidism. Patients with no drop in intraoperative PTH levels have generally remained hypercalcemic immediately after surgery. Several so-called false-negative results have been reported in situations in which a delayed (up to 30 minutes) drop in PTH levels occurred. In addition, rapid PTH levels may initially rise within the first few minutes after excision of a hyperfunctioning gland, possibly because of manipulation of parathyroid tissue with augmented systemic release of PTH into the bloodstream before excision.

In patients with hyperparathyroidism from a variety of causes (most commonly primary hyperparathyroidism), sestamibi scanning has been reported to accurately localize the hyperfunctioning tissue in 75% to 94% of patients. In the present study, sestamibi accurately localized the hyperfunctioning tissue in 79% of patients. Among 24 patients in the present study with inaccurate, negative, or misleading preoperative localization, 9 patients (38%) demonstrated disease that might have affected the accuracy of the sestamibi scan, including 6 patients with concomitant thyroid disease, 2 patients with a history of parathyroid surgery, and 1 patient with multiglandular hyperplasia.

Some proponents of rapid intraoperative PTH monitoring have found the assay particularly useful in reoperative parathyroidectomy. Combined use of the rapid PTH assay with preoperative sestamibi localization may prevent dissection of previously operated-on tissue, with its attendant risks, in patients undergoing cervical or mediastinal reoperation. The present study, with 9 cases of reoperative parathyroidectomy, supports these contentions. In addition, one recent study has reported an improved operative success rate for reoperative parathyroidectomy with the use of the rapid PTH assay when compared with an earlier, pre–rapid PTH assay cohort of patients previously operated on.

The ability of the rapid PTH assay to detect the presence of multiglandular parathyroid hyperplasia is unclear. Some studies have suggested that intraoperative PTH levels will typically fall in a sequential manner as each of the hyperfunctioning glands is removed. This concept is supported by the 1 patient with multiglandular disease in the present study (Figure 2). However, others have demonstrated substantial (ie, >50%) decreases in intraoperative PTH levels after excision of the first gland in cases of multiglandular disease, “false-positive” PTH assay results represent a potential cause of operative failure should only 1 gland be removed. To avoid missed multiglandular disease, several strategies have been proposed. One study has recommended terminating parathyroid surgery only when postexcision PTH values (1) drop to 50% or less of baseline and (2) decrease below the upper limit of normal for the assay. Others have suggested changing the degree of decline in PTH level for prediction of operative success to more than 60% from baseline at 15 minutes after excision, or to more than 70% from baseline at 20 minutes after excision. One study has claimed that reevaluation of rapid PTH levels at 60 to 120 minutes after excision of a hyperfunctioning gland (after an initial decline) may indicate the presence of multiple-gland disease, although waiting up to 2 hours after gland excision to test rapid PTH assay results may be impractical in most centers.

It has been argued that the combination of intraoperative rapid PTH monitoring with preoperative sestamibi localization, by allowing targeted surgery in patients with hyperparathyroidism, (1) promotes the use
of local anesthesia \(^{13,17}\) (2) increases the rate of unilateral exploration.\(^{10}\) (3) may decrease the length of postoperative stay.\(^{8,10,17}\) (4) may decrease operative time,\(^{8,12}\) (5) may decrease operative failure rate to as little as 1.5%,\(^{10,16}\) and (6) may have positive economic implications because of shorter operative times\(^{8,12}\) and the avoidance of an overnight hospital stay.\(^{8,17}\) However, not all authors have demonstrated an economic benefit to use of the rapid PTH assay.\(^{10}\) In addition, a recent study demonstrated the feasibility of local anesthesia and same-day hospital discharge with bilateral neck exploration for parathyroidectomy without use of the rapid PTH assay or routine sestamibi localization.\(^{24}\)

In the present study, we cannot claim that overall operative time or hospital costs are now less than before the rapid PTH assay was used in our institution, as pre-assay data were not examined. In addition, only 11% of patients in our study were discharged home the same day as the surgery. We agree with Sofferman et al.,\(^{13}\) who believe that the true advantage of the intraoperative PTH assay is not in a possible reduction in surgical time, but rather in a confirmation that the hyperparathyroid state has been corrected while the patient is still on the operating room table. Persistently elevated rapid PTH levels alert the surgeon to inadequate excision of parathyroid tissue and the need for further exploration.\(^{9}\)

The use of the intraoperative PTH assay has not often been reported in patients with parathyroid carcinoma.\(^{3,4}\) In the present study, the 1 patient with parathyroid carcinoma demonstrated a decrease of 60% and 68% in rapid PTH levels 5 and 10 minutes, respectively, after excision of the involved gland. A month later, the patient underwent ipsilateral thyroid lobectomy to ensure adequate tumor margins. At 4 months after the original surgery, the patient remained normocalcemic and free of disease.

In the present study, percutaneous rapid PTH sampling from the internal jugular vein in the setting of negative preoperative localization studies (in patients with no previous parathyroid surgery) demonstrated poor sensitivity for identifying in which side of the neck an adenoma resided. These results are in contrast to those of Irvin et al.,\(^{14}\) who demonstrated successful lateralization in 9 of 10 patients with the use of a similar technique. Intraoperative direct sampling of blood for rapid PTH analysis from the superior, middle, and inferior thyroid veins bilaterally during surgery, as reported by Saharay et al.,\(^{25}\) may represent a more sensitive localization technique.

**CONCLUSIONS**

Intraoperative monitoring of PTH levels in patients with primary hyperparathyroidism using a rapid PTH assay successfully predicts early postoperative normocalcemia. The rapid PTH assay allows for greater confidence in performing limited dissections in unilobar disease that has been well localized with preoperative \(^{99m}\) Tc sestamibi imaging. In cases of inaccurate preoperative localization, the rapid PTH assay directly affects surgical decision making and provides greater confidence in determining when surgical success has been achieved.