Lauren Garbutt

Project Title: Timing of intraoperative baseline parathormone estimation at the time of parathyroidectomy.

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Summary:
The objectives of this study were two-fold, firstly to determine the best tool to confirm completion of resection of all hypercellular parathyroid tissue. Secondly, to assess the optimal time for drawing baseline parathyroid hormone (PTH) sample on the day of surgery. 190 consecutive patients who underwent parathyroidectomy for sporadic primary hyperparathyroidism at a single tertiary care center between January 1, 2008 and May 31, 2012 were included in this largely retrospective study. Conventionally, a single baseline intraoperative PTH (ioPTH) measurement is collected; however, in a subset of these patients, we opted to collect two baseline samples in order to strengthen the data and create matched pairs. As part of the prospective arm of this study, 30 patients had both pre- and post-induction ioPTH levels measured; their mean PTH level pre-induction was 202 ng/L and mean PTH level post-induction was 292 ng/L. A paired-samples t-test demonstrated a statistically significant difference between the two means (p-value = 0.045). Mean percent change in ioPTH level from baseline to post-excision sample was also evaluated. Mean percent change in PTH from pre-induction to post-excision was 59.4% and from post-induction to post-excision was 68.0%. A paired-samples t-test demonstrated a statistically significant difference between the two means (p-value = 0.032). The clinical implication of these results is rooted in surgical decision-making. In 4 of the 30 cases, the Miami criterion was satisfied only with the post-induction measurement as baseline; if the pre-induction PTH measurement had served as a baseline, surgery would've continued needlessly.

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Introduction:

The parathyroid glands are typically situated on the posterolateral aspect of the thyroid gland; the superior glands are located in relation to the superior poles of the thyroid gland, while the inferior glands are commonly found in relation to the inferior poles. During the fifth week of gestation, the parathyroid glands develop from the third and fourth branchial pouches. The inferior glands are derived from the third pouches and descend in the neck with the thymus, while the superior glands are derived from the fourth pouches and remain in place. This requires that the inferior glands migrate past the superior glands and travel a greater distance. Knowledge of this embryologic migration is imperative when searching for ectopic glands intraoperatively. Aberrantly located glands are common in clinical practice as they occur in approximately 15-20% of patients. In addition to variation in location, there also exists a variation in number of parathyroid glands. While the majority of humans have four parathyroid glands, approximately 2 to 5% have an additional gland and a similar percentage have fewer than four glands (1).

Though the parathyroid glands were the last major organ to be recognized by humans, their importance in no way correlates with their late discovery. Their role in maintaining life is absolutely critical because the parathyroid glands synthesize and release parathyroid hormone (PTH), the key regulator of serum calcium. The level of free, or ionized, calcium in the bloodstream must be maintained in a tight physiological range and if that homeostasis fails, debilitating signs and symptoms can result. Absence of parathyroid glands results in hypocalcemia and subsequent tetany and death; over activity can cause a life-threatening hypercalcemic crisis. Decreased levels of calcium signal the release of PTH from chief cells, which through multiple facets, aims to correct serum calcium levels. PTH does this by increasing resorption of calcium from bone, increasing conversion of vitamin D into its active form in the kidney, increasing calcium reabsorption in the distal convoluted tubules and decreasing phosphate reabsorption in the proximal convoluted tubules (2).

Hyperparathyroidism (HPT) indicates an over activity of the parathyroid glands; primary HPT specifies that the over activity is inherent in the parathyroid gland. Primary HPT, due to parathyroid adenoma, is the most common of the parathyroid disorders. Nowadays, most patients with primary HPT are asymptomatic and identified incidentally on routine bloodwork. Classically, patients presented with a constellation of signs and symptoms loosely described as “stones, bones, abdominal groans, psychic moans, and fatigue overtones”. Patients often experienced a dramatic decrease in quality of life as they suffered from renal calculi, osteoporotic fracture, abdominal pain, depression, fatigue, and/or polyuria just to name a few. Nephrolithiasis, bone disease, and neuromuscular symptoms all respond very well post-operatively (1), and it is noted that many “asymptomatic” patients actually have neurocognitive symptoms that may be unmasked after successful surgery (3).

It is well established that nearly all patients who are symptomatic should undergo surgery. What to do for patients with asymptomatic primary HPT is not nearly as straightforward; however, in the National Institutes of Health Consensus Conference in

1990 and the reconvening workshop in 2009, asymptomatic patients who were deemed candidates for surgery had the following features: a serum calcium level greater than 0.25 mmol/liter above the upper limits of normal, a history of kidney stones or fractures, a creatinine clearance that was below 30% of age- and sex-matched controls, 24-h urine calcium level greater than 0.1 mmol/kg/day, and the presence of osteoporosis by T-score (3).

Since its inception, minimally-invasive parathyroidectomy (MIP) with adjunctive intraoperative parathyroid hormone (ioPTH) monitoring has become the treatment of choice for sporadic primary hyperparathyroidism (4). The use of ioPTH monitoring produces results similar to bilateral cervical exploration and does so with a smaller incision, faster recovery, shorter operative time and shorter hospital stay (5-8). IoPTH monitoring allows for a focused dissection by confirming the completeness of resection of hypercellular parathyroid tissue. Incomplete resection of parathyroid adenoma results in persistently high PTH levels, which requires a revision surgery (9). The Miami criterion, a drop of 50% or more from the highest of either preoperative baseline or pre-excision level compared with a 10 minutes post-excision level, is most commonly used to assist in surgical decision-making as it has the highest accuracy in intraoperative prediction of cure (10). It is undoubtedly the most examined and validated criterion, predicting postoperative calcium levels in the normal or low range with accuracy of 97-98% (11-15). In spite of this, there is a lack of consensus between head and neck surgeons regarding the appropriate timing of the baseline ioPTH sample(s) (16). This becomes even more significant when noting recent research documenting that airway manipulation associated with general endotracheal anesthesia increases circulating catecholamine levels which in turn influence ioPTH measurements (17). An objective of this study was to assess the optimal time for drawing a baseline ioPTH sample. Is the post-induction ioPTH level consistently higher than the pre-induction level? Does the collection of a sample before or after anesthesia alter surgical decision-making?

An early comprehensive review on ioPTH monitoring suggests that the baseline PTH must be drawn before any manipulation of the parathyroid glands, preferably just after induction of anesthesia, in order to prevent any factitious changes in the baseline level (18). A recent comprehensive review on ioPTH monitoring, published in 2011, addresses that many surgeons collect only preincision levels, at variable times, while others take pre-excision levels only. These differences impact the uniformity of ioPTH monitoring. Carneiro-Pla suggests collecting samples in the operating room before the skin incision is made (preincision), when all blood supply to the suspicious gland is ligated (pre-excision), 5 minutes, 10 minutes, and occasionally 20 minutes after excision of the suspected abnormal gland (16).

The cost of the rapid PTH assay depends on the particular test used and the length of turnaround time. However, based on a computer-generated model, the rapid PTH assay decreases costs by $2000.00 USD (US dollars) per patient, and the use of preoperative localization decreases costs by $3000.00 USD per patient. Limited parathyroid surgery using any localizing strategy is cost-effective; the cost benefit was primarily achieved by reduced operative charges and immediate hospital discharge rather than a lower need for re-exploration for persistent HPT (19).

The objectives of this study were two-fold, firstly to determine the best tool to confirm completion of resection of all hypercellular parathyroid tissue. Secondly, to assess the optimal time for drawing baseline parathyroid hormone (PTH) sample on the day of surgery. We arrived at these objectives in part by the emergence of two intriguing scenarios: 47-year-old patient A.K. who underwent parathyroidectomy in which frozen section results were conclusive for parathyroid tissue and no ioPTH monitoring was utilized and 48-year-old patient X.F. who underwent parathyroidectomy in which ioPTH level pre-induction was 99 ng/L and PTH level shortly after induction was 195 ng/L. We will return to these cases in the discussion.

Materials and Methods:

We conducted a largely retrospective chart review of all consecutive 208 parathyroidectomies at St. Boniface General Hospital (SBGH) during the time period January 1, 2008 to May 31, 2012. This was performed with the approval of the University of Manitoba Research Ethics Board and the SBGH Research Review Committee. A list of parathyroid procedures performed was obtained from SBGH operative records. Data was collected from patient medical charts from SBGH in addition to the electronic patient record systems for SBGH and CancerCare. This data was entered into a template that we created specifically for this study and then into SPSS Statistics 17.0 to create a database.

IoPTH assays were analyzed with the Intact-PTH-Elecsys-Immunoassay (Roche Cobas e601). The assay is affected by hemolysis $\geq$1.5 g/L and any sample that showed visible signs of hemolysis was not analyzed. The pre-induction ioPTH level was obtained in the preoperative holding area. After the induction of general anesthesia, a post-induction ioPTH level was obtained from an arterial or intravenous line in the patient's upper limb; ioPTH was drawn routinely at 10-minutes post-excision. The Miami criterion was used to assist in intraoperative decision making.

Conventionally, a single baseline ioPTH measurement is collected; however, in a subset of these patients, we opted to collect two baseline samples in order to strengthen the data and create matched pairs. As part of the prospective arm of this study, 30 patients had both pre- and post-induction ioPTH levels measured. To ensure accuracy, surgeons recorded the type of ioPTH sample measured (pre-induction versus post-induction) and this was compared with the anesthetists' intraoperative notes to identify the time of induction and confirm the designation of the ioPTH sample.

Our goal was to determine the best timing of the baseline ioPTH sample. Of all consecutive 208 parathyroidectomies, we included those that were for sporadic primary HPT and from that group, we determined how many surgeries utilized ioPTH monitoring. All 161 parathyroidectomies with ioPTH monitoring (pre-induction N = 63, post-induction N = 98) were analyzed via a combination of one-sample t-tests and paired-samples t-tests to assess differences in the means between groups. In the unpaired samples, we focused on percent change ((1 – (post-excision PTH / pre-incision PTH)) * 100) for the reason that comparing mean PTH levels in 2 different groups of patients is not meaningful; in the paired samples, both percent change and mean PTH levels were utilized.

Results:

Of 208 parathyroidectomies, we excluded 13 cases that were not for sporadic primary HPT (12 for secondary or tertiary HPT and 1 parotid gland procedure which was wrongly coded). Of the remaining 195 parathyroidectomies, we identified 5 patients that had undergone 2 parathyroid procedures, 4 owing to a failed first surgery and 1 due to recurrent HPT. Therefore, our study group comprised of 195 parathyroidectomies in 190 patients.

81% female and 19% male, the average age of our patients was 60.0 years (SD = 13.4 years). The majority of our patients had multiple signs and symptoms; only 12% had no symptoms referable to primary HPT in their history. The most common presenting signs and symptoms were nephrolithiasis (39%), bone and joint aches and pains (35%), fatigue (31%), and osteoporosis (25%). At the time of diagnosis, 30% of patients were positive for a single drug or compound that impacted either serum calcium levels or the evaluation of bone density while 7% were taking more than one substance that was considered impactful. In the total patient population, the substances are listed in order of frequency: bisphosphonates (16%), vitamin D (13%), daily multivitamin (9%), thiazide diuretics (8%), estrogens (6%), daily calcium supplement (4%), lithium (1.5%), and other (1%).

A preoperative sestamibi scan localized an adenoma, at minimum to one side of the neck, in 167 (86%) evaluations. 21 (11%) were non-localizing scans, 2 (1%) localized two adenomas and 5 (3%) preoperative evaluations did not include a sestamibi scan. Preoperative ultrasound was localizing in 83 (43%) evaluations, non-localizing in 20 (10%), and not performed in 92 (47%). All parathyroidectomies, except for one, utilized at least one form of preoperative localization. Both studies were performed in 99 (51%) and of those, 80 (81%) were concordant (at minimum to one side of the neck). In the remaining 19 (19%), use of both ultrasound and sestamibi scan proved invaluable because only one study was localizing.

Frozen section was performed in 175 (90%) parathyroidectomies, revealing parathyroid tissue conclusively in 170 (97%) and inconclusively in 5 (3%). The average turnaround time for frozen section results was 20.2 minutes ± 6.4 minutes. The average turnaround time for the post-excision ioPTH sample was 36.2 minutes ± 15.4 minutes. The average weight of an excised hypercellular gland was 1.3 grams ± 1.8 grams. Healthy parathyroid glands weigh 30 to 40 milligrams on average (1); the hypercellular glands we excised were on average 30x larger. Based on the pathology report and clinical correlation, 93% of our cases were due to single adenoma, 5% double adenoma, 1% multigland hyperplasia, and 0.5% parathyroid cyst.

Of 195 parathyroidectomies, 63 had both pre-induction and post-excision values, and 98 had both post-induction and post-excision values. One-sample t-tests, reported in Table 1, were conducted to evaluate the impact of baseline ioPTH sample timing on percent change in PTH.

Tables 2a and 2b show the results of the paired-samples t-tests, also referred to as repeated measures. A paired-samples t-test was conducted to evaluate the impact of general endotracheal anesthesia on PTH levels. There was a statistically significant increase in PTH level from pre-induction to post-induction ($p = 0.045$). The eta squared statistic (0.13) indicated a moderate effect size. A second paired-samples t-test was conducted to evaluate the impact of baseline sample timing on percent change in PTH. There was a statistically significant increase in percent change from pre-induction to post-induction ($p = 0.032$). The eta squared statistic (0.15) indicated a large effect size. Figures 1 and 2 portray these findings in graphical form.

Discussion:

Hypercalcemia has an incidence of approximately 0.5% in the general population and although the differential diagnosis is extensive, primary HPT is the most common cause of hypercalcemia in non-hospitalized patients (1). Primary HPT is of great medical importance as it is common, easily diagnosed, and treatable. “Classic” primary HPT is the elevation of both calcium and PTH above normal serum levels whereas “mild” primary HPT is the elevation of either calcium or PTH above normal or else an asymptomatic patient with mild elevations in both values (2). The disease occurs at all ages but most commonly in the seventh decade and in women (74%) (20). As for etiology, single adenomas accounts for 80-85%, double adenomas 2-3%, multigland disease 12-15% and rarely, carcinoma or cyst. In our study, single adenomas and double adenomas were detected at higher rates and multigland hyperplasia at a lower rate; this is likely due to patterns of practice in a public-funded healthcare system.

In the United States, approximately 80% of patients with primary HPT have no signs or symptoms that are referable to their disease (21); nephrolithiasis typically occurs in 4 to 15% of cases (22). We reported 12% of our patients were asymptomatic and 39% had at least one episode of kidney stones. A difference in practice may account for the disparity. As of 2005, the American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons advocate that, “operative management should be considered and recommended for all asymptomatic patients with primary HPT who have a reasonable life expectancy and suitable operative and anesthesia risk factors” (23). We, as part of a public-funded health care system, follow NIH criteria very strictly.

As part of the initial work-up for primary HPT, all medications, vitamins, and supplements need to be elucidated. Elevated calcium and PTH levels can occur with lithium or thiazide use (24). Hypercalcemia induced by thiazide diuretic therapy unmasks other disorders in an individual that predispose hypercalcemia, including vitamin D usage and primary HPT. Excessive use of calcium carbonate antacids or other calcium sources, can cause hypercalcemia (25). While intravenous forms of bisphosphonates are known to decrease serum calcium, oral forms increase bone mineral density without altering serum calcium. Estrogen also increases bone mineral density without altering serum calcium (26).

Preoperative imaging studies are not necessary to make the diagnosis of primary HPT but should be performed to help plan the operation. Noninvasive localization studies including ultrasound and sestamibi scans are often employed, especially in anticipation of focused explorations (3). In patients undergoing initial surgery for primary HPT with preoperative, localizing sestamibi scans and concordant ultrasound, 97% had successful excision with removal of the localized gland (27). Operative success is >99% when intraoperative PTH (ioPTH) monitoring is used in addition to preoperative localization (16). Recall that in our study, both ultrasound and sestamibi scans were performed in 99 (51%) preoperative evaluations and of those, 80 (81%) were concordant (at minimum to one side of the neck) and 19 (19%) were non-concordant. In all cases where imaging studies were non-concordant, one imaging study was non-localizing while the other study was localizing. Thus, we found that preoperative localizing studies are not always concordant but use of both imaging modalities can be extremely helpful in localizing an adenoma when one study is non-localizing. The importance of ioPTH monitoring combined with preoperative imaging studies is emphasized by the 9 out of 99 cases (9%) where both studies were non-localizing. These studies were "concordant" in the sense that they both failed to yield localization of an adenoma however, ioPTH monitoring was used in all of these cases and operative success was 100%. Our results are similar to the literature which indicates that both ultrasound and sestamibi scans are negative in 10-20% of cases (28). In the 6 patients who underwent a revision parathyroidectomy following a failed first surgery, each patient had at least one localizing imaging study prior to the first surgery.

The turnaround time of the post-excision ioPTH sample determines the duration of the parathyroidectomy procedure. The faster the post-excision results are received, the more efficient an operating room can run. A longer turnaround time equates to a longer time spent under general anesthesia for a patient. It is imperative that the results of the post-excision sample are received as quickly as the PTH assay will allow. In our study, frozen section turnaround time was faster than post-excision PTH turnaround time. However, as rapid as results may be, frozen section cannot confirm completion of resection of all hypercellular parathyroid tissue. The fact that 90% of our parathyroidectomies utilized frozen section only demonstrates the existence of a diversity between our knowledge and our current practice.

Standardization of ioPTH monitoring protocol is such a significant and relevant topic in primary HPT because surgery is the only effective treatment for the disease. Traditionally, surgeons opted for bilateral neck exploration where they would identify all glands and excise based on size. Today, this has largely been replaced by minimally-invasive parathyroidectomy where surgeons opt for uniglandular exploration based on preoperative localization and success is gauged with ioPTH monitoring via the Miami criterion. Currently, >90% of high-volume parathyroid surgeons use ioPTH monitoring to guide parathyroidectomy in patients with sporadic primary HPT (16).

In our study, we evaluated all operative failures and any contributing mechanisms; specifically, we examined frozen section and ioPTH monitoring. IoPTH monitoring is unique from frozen section in that it can detect residual hyperfunctioning parathyroid tissue (12, 13). Frozen section can tell us that the tissue removed is indeed parathyroid tissue however, it cannot provide information regarding the presence of additional hyperfunctioning tissue (18). We have included two index cases that each highlight a specific problem and an area where we lacked knowledge. None of these index cases are unusual situations. They highlight the importance of ioPTH monitoring, the dynamics of ioPTH, and the external factors that influence those dynamics.

Index case 1: 47-year-old patient A.K. underwent parathyroidectomy in which frozen section results were conclusive for parathyroid tissue and no ioPTH monitoring was utilized. Post-operatively, pathology indicated that the specimen removed consisted of thyroid tissue and normocellular parathyroid tissue. In the revision surgery, both ioPTH monitoring and frozen section were utilized. Miami criterion was satisfied, frozen section results were conclusive for hypercellular parathyroid tissue, and the corrected calcium (C.Ca) fell to a normal level within 24 hours after surgery. A.K.'s post-operative course has remained completely uneventful. This case highlights the inherent limitations of frozen section and the ability of ioPTH monitoring to alert a surgeon to the presence of additional hypercellular parathyroid tissue.

Index Case 2: 48-year-old patient X.F. underwent parathyroidectomy in which ioPTH level pre-induction was 99 ng/L and PTH level shortly after induction was 195 ng/L. After suspicious gland removal, a 10-minutes post-excision PTH level came back at 63 ng/L. A ≥ 50% drop in PTH from baseline to post-excision sample was evident for the post-induction sample but not for the pre-induction sample. Surgery was concluded, C.Ca fell into the normal range and was still normal at 8-months post-operatively.

In this case, only the post-induction PTH level was helpful in determining successful excision of a single parathyroid adenoma. In total, 13% (4 out of 30) of the paired samples cases met the Miami criterion with the post-induction sample only. In all 4 cases, surgery was considered successful after a ≥ 50% drop in PTH from post-induction, or highest baseline measurement, to 10-minutes post-excision and in all 4 cases, the C.Ca level normalized post-operatively. If a pre-induction sample had been collected as the sole baseline measurement, surgical decision-making would have stemmed from a failure to meet the Miami criterion and additional PTH measurements and possibly additional neck exploration would have been necessary. When we began our study, the baseline PTH sample was conventionally collected before the induction of anesthesia. However, it has been shown that catecholamines increase PTH levels in humans (29) and that all anesthetic techniques increase ioPTH levels by increasing circulating catecholamines (17).

Based on the literature, we expected that the percent change from baseline to 10-minutes post-excision would be higher for the post-induction sample. However, when we analyzed all 161 parathyroidectomies with ioPTH monitoring (pre-induction N = 63, post-induction N = 98) via one-sample t-tests, we did not see statistically significant results (reflected in the overlapping confidence intervals). This was not unexpected for the reason that comparing mean PTH levels in 2 different groups of patients is not meaningful. As a result, we prospectively created matched pairs. Tables 3 and 4 show our findings: mean PTH level was higher post-induction versus pre-induction, to a statistically significant degree, and mean percent change from post-induction to post-excision was higher than from pre-induction to post-excision, to a statistically significant degree. These results were consistent with what we expected and are so vital because the Miami criterion, and thus surgical decision-making, operates on the principle of percent change.

In total we had 6 patients who underwent a revision parathyroidectomy following a failed first surgery: 5 patients who had two surgeries at SBGH during the span of our study and 1 patient who underwent their first surgery at a different hospital. We defined persistent HPT or operative failure as a patient with hypercalcemia and elevated PTH levels that remain elevated post-operatively and do not normalize by 6 months post-op. In the 6 cases of operative failure, 4 utilized frozen section without ioPTH monitoring, with results as follows: 2 cases where normocellular parathyroid tissue was removed, 1 case where frozen section results were inconclusive and revealed thyroid tissue on permanent section, and a final case where only one of two adenomas was excised. In the other 2 cases of operative failure, both frozen section and ioPTH monitoring were utilized: frozen section results were conclusive for parathyroid tissue in both cases however, ioPTH monitoring was utilized incorrectly. A single adenoma was removed in each case but Miami Criterion was not satisfied and after revision surgeries, the diagnosis of double adenoma was confirmed for both patients. The inherent limitations of frozen section are apparent here.

In the final weeks of our study, we identified an especially intriguing case: 56-year-old patient F.Y. underwent parathyroidectomy in which ioPTH level pre-induction was 216 ng/L and PTH level shortly after induction was 211 ng/L. After suspicious gland removal, a 10-minutes post-excision PTH level came back at 281 ng/L. Miami Criterion was not satisfied with either baseline ioPTH sample and the surgeon followed with a negative four-gland exploration. A 50-minutes post-excision PTH level was reported at 123 ng/L and a 95-minutes post-excision value came back at 106 ng/L. Surgery was concluded. A 6-weeks post-operative C.Ca level was normal and post-operative course has remained uneventful.

In this case, neither the pre-induction nor the post-induction PTH level was helpful in determining successful excision of a single parathyroid adenoma. It is quite possible that intra-operative gland manipulation led to a substantial increase in PTH that went unnoticed. We hypothesize that a sample collected just before excision of the suspicious gland would have been significantly elevated. If this were the case, the pre-excision sample could have shortened the operation considerably. This hypothesis is bolstered by a recent review on ioPTH monitoring which specifies that the pre-excision sample is more helpful if there is gland manipulation leading to a significant increase in PTH levels (16).

In our prospective study, we now collected PTH samples just prior to gland excision. We compared this result with the 10-minutes post-excision PTH level. In 5 of 7 cases, both the pre-induction and the pre-excision sample satisfied the Miami Criterion. In one case, only the pre-excision sample satisfied the Miami Criterion: PTH levels climbed by 1194 ng/L in 67 minutes, likely due in small part to the induction process and in large part to intraoperative gland manipulation. In the remaining case, serum PTH actually increased from pre-induction to post-excision but fell 45% from pre-excision to post-excision; this is also likely due to induction and intraoperative gland manipulation. We concluded that due to the dynamics of ioPTH, if there is gland manipulation leading to a spike in PTH levels, the pre-excision sample becomes vital for optimal surgical decision-making.

In conclusion, this study found that ioPTH monitoring is superior to frozen section in confirmation of resection of all hypercellular parathyroid tissue. We also found that the optimal time for drawing a baseline PTH sample on the day of surgery is after induction of general anesthesia but a single sample may not be sufficient. Due to the relatively short half-life of PTH, its levels in the serum are labile and surgeons need to understand ioPTH dynamics to make optimal for optimal surgical decision-making. We found a statistically significant increase in percent change from baseline ioPTH to post-excision ioPTH when the post-induction sample was used as a baseline. We hypothesize that this is related catecholamine release as a result of airway manipulation during intubation. We also found that PTH levels drawn immediately before adenoma excision may spike significantly and we hypothesize that gland manipulation may be the etiology. Thus, collection of two baseline ioPTH samples (shortly after induction and immediately before excision) may be the most optimal timing. More research is warranted based on this study's findings to evaluate the accuracy of ioPTH monitoring when both post-induction and pre-excision ioPTH samples are collected.

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Table 1. One-Sample Test: Comparing Percent Change in ioPTH level from Baseline to Post-excision.

	N	Mean ± Std. Deviation (95% Confidence Interval)	p-value (2-tailed)
Percent (%) Change in PTH Pre-induction to Post-excision	63	65.0 ± 25.5 (58.6-71.4)	.000
% Change in PTH Post-induction to Post-excision	98	67.7 ± 36.5 (60.4-75.0)	.000

N = Sample size, Std. = Standard, PTH = Parathyroid hormone. Units are percentages.

Table 2a. Paired Samples Test: Comparing Mean Levels in ioPTH level from Baseline to Post-excision.

	N	Mean ± Std. Deviation	Paired Differences p-value (2-tailed)
Level of PTH Pre-induction	30	202.4 ± 166.0	.045
Level of PTH Post-induction	30	292.0 ± 313.7	

N = Sample size, Std. = Standard, PTH = Parathyroid hormone. Units are ng/L.

Table 2b. Paired Samples Test: Comparing Mean Percent Change in ioPTH level from Baseline to Post-excision.

	N	Mean ± Std. Deviation	Paired Differences p-value (2-tailed)
Percent (%) Change in PTH Pre-induction to Post-excision	30	59.4 ± 32.2	.032
% Change in PTH Post-induction to Post-excision	30	68.0 ± 27.2	

N = Sample size, Std. = Standard, PTH = Parathyroid hormone. Units are percentages.

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Figure 1. Comparing ioPTH Levels (in ng/L) in Paired Samples (N = 30).

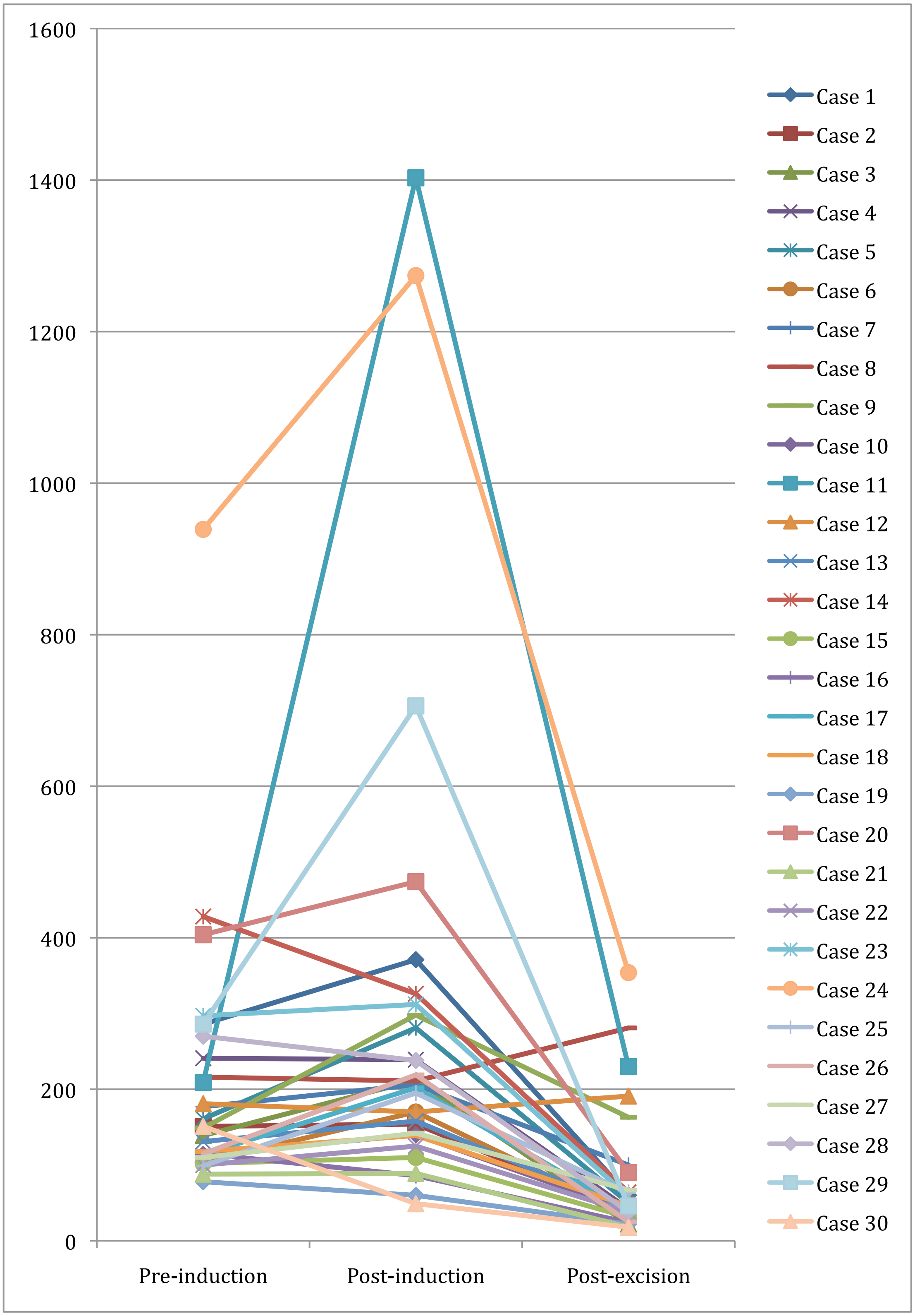

Figure 2. Comparing Percent Change in ioPTH Levels in Paired Samples (N = 30).