Acta Biomed 2023; Vol. 94, N. 2: e2023040 DOI: 10.23750/abm.v94i2.13998 

Original article

# Role of intraoperative parathyroid hormone in guiding parathyroidectomy

*Chirag Pereira*
Department of General Surgery, Royal Lancaster Infirmary, Lancaster, UK

**Abstract**. *Background and Aim:* The aim of the study was to determine the sensitivity, specificity and diagnostic accuracy of intra-operative parathyroid hormone (IOPTH) in patients undergoing surgery for primary hyperparathyroidism based on Miami criteria. *Methods:* A total of 107 medical records of patients who underwent surgery for primary hyperparathyroidism were reviewed from August 2018 to December 2021. Patients that underwent surgery for recurrent or persistent pHPT were excluded from the study and the following data was analysed: sex, age, pre-operative PTH and 10 minutes post excision PTH levels, type of surgery and histopathological features. *Results:* There was a greater number of women (79.5%) in the study with a mean age of 65.14 years. The mean preoperative PTH were 17.7 pmol/L while the mean intra-operative PTH following excision was 6.5 pmol/L. The sensitivity, specificity and diagnostic accuracy of intra-operative PTH were 86.14%, 100% and 86.9%, respectively. *Conclusion:* Intra-operative PTH is a valuable investigation that can guide successful parathyroidectomy. (www.actabiomedica.it)

**Key words**: parathyroidectomy, intra-operative PTH, primary hyperparathyroidism, Parathyroid hormone

## Introduction

Primary hyperparathyroidism (pHPT) is a disease caused due to the excessive production of the parathyroid hormone (PTH), which results in hypercalcemia and hypophosphatemia. The clinical manifestation of hypercalcemia is often described as "stones, bones, groans and psychic moans" (1). About 70-95% of pHPT cases result from a single parathyroid adenoma, 15% from glandular hyperplasia, 4% from double adenomas and rare cases due to carcinoma of the parathyroid gland (2).

The traditional surgical approach for the management of parathyroid disease involved bilateral neck dissection where all four parathyroid glands are visualized and the abnormal glands were excised. The use of intraoperative parathyroid hormone (IOPTH) monitoring along with ultrasound and sestamibi scan has made a minimally invasive approach to treating parathyroid adenomas possible (3). A minimally invasive approach is associated with less postoperative pain, shorter duration of surgery, short hospital stays and fewer complications (4). There are instances in which ultrasound and sestamibi fail to localize parathyroid adenomas. In these situations, IOPTH is recommended to monitor successful adenoma excision, where a minimally invasive approach is considered (5).

Nowadays, IOPTH monitoring is used in most centers where parathyroid surgery is conventionally being performed. The advantage of IOPTH is its ability to confirm the successful removal of the hyperactive parathyroid gland or guide in the bilateral neck exploration (6,7). According to Miami criteria, the successful excision of parathyroid is a fall in PTH levels of >50% at 10 minutes post excision from baseline. This has an accuracy of 97% (8,9). The failure of IOPTH in reducing is usually due to microadenomas or multiglandular disease.

The aim of our study was to determine the sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of IOPTH in guiding successful parathyroidectomy.

## Patients and methods

A total of 107 medical records of patients who underwent surgery for pHPT were reviewed from August 2018 to December 2021 at Royal Lancaster Infirmary, UK. Only patients with pHPT were included in this study, and patients who underwent surgery for recurrent or persistent pHPT were excluded from the study.

The following data was analysed: sex, age, preoperative and 10 minutes post excision PTH levels, preoperative localization, type of surgery and histopathological features. Preoperative localization was performed using neck ultrasound (USG), and localization was performed using a 99mTc-labelled sestamibi scan and 4D computed tomography (CT). None of the patients underwent pre-operative positron emission tomography for localization. When localization scans were concordant, a focused minimally invasive approach was used to identify the abnormal gland, and when scans were discordant, a standard bilateral neck exploration was performed. IOPTH levels were checked first after induction by anaesthesia. They were then checked again 10 minutes after the surgical excision of the parathyroid gland. A >50% drop in IOPTH levels at 10 minutes post excision was used to confirm the successful excision of the abnormal gland (Miami criteria). Frozen section histopathology was also performed to confirm the successful removal of the parathyroid gland when available. When the frozen section was unavailable, specimens were sent for formal histopathology. Since there was no direct patient interaction informed consent was not needed and waiver of consent was sought with ethical committee.

### *Statistical analysis*

All data was collected from an online database and inputted into Microsoft Excel. True positive (TP), false positives (FP), true negatives (TN) and false negatives (FP) were determined based on frozen section or formal histology. Formulas used to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy are as follows:

- Sensitivity = TP / (TP+FN)
- Specificity = TN / (TN+FP)
- Positive predictive value = TP / (TP+FP)
- Negative predictive value = TN / (FN+TN)
- Diagnostic Accuracy = (TP+NP) / (TN+FP+FN+TN)

## Results

The age of the patients ranged from 31 to 89 years with the average age being 65.14 ± 12.7 years. The majority of the patients were female and they amounted to 79.5% of the sample, while the males made up 20.5%. The female-to-male ratio was 3.8:1. Out of the total, 16.6 % of cases in this study had osteoporosis while 8.4% had nephrolithiasis, which was confirmed on bone scan and renal ultrasound, respectively. The average preoperative calcium level was 2.77 ± 0.13 mmol/L and ranged from 2.47 to 3.14 mmol/L. 86% of the patients had mild hypercalcemia (2.5-3mmol/L) while 14% had moderate hypercalcemia (3-3.5mmol/L) (Table 1).

USG neck was negative in 54 patients (50.4%) while sestamibi scan was negative in 43 patients (40.1%). Discordant USG and sestamibi scans were 23.3%. 4D CT was performed in 65.4% of cases and was negative in 3.7% of cases. 65 patients underwent minimally invasive focused parathyroidectomy while 35 patients underwent standard neck exploration. Among the 35 patients, 2 patients also had thyroid

**Table 1.** Patient demographic and clinical data.

| Characteristics | Value |
|---|---|
| Female / Males | (79.5%) / (20.5%) |
| Age | 65.14 ± 12.7 years |
| Preoperative Calcium | 2.77 ± 0.13 mmol/L |
| Preoperative PTH | 17.7 ± 8.1 pmol/L |
| 10-minute post-excision PTH | 6.5 ± 5.6 pmol/L |

**Table 2.** Intraoperative PTH results.

| | |
|---|---|
| True Positives | 87 (81.3%) |
| True Negatives | 14 (13.1%) |
| False Negatives | 6 (5.6%) |
| Sensitivity | 86.14% |
| Specificity | 100% |
| Positive Predictive Value | 100% |
| Negative Predictive Value | 30% |
| Diagnostic Accuracy | 86.9% |

lobectomy performed in the same sitting. Six patients had conversion from focused surgery to bilateral neck exploration and one patient had thoracoscopic video assisted surgery. Based on histopathology there were 67 (62.6%) cases of single parathyroid adenoma, three (2.8%) cases of double adenoma and 37 (34.5%) cases of hyperplasia.

IOPTH monitoring was performed in all cases. Mean pre-incision PTH was 17.7 ± 8.1 pmol/L and mean 10 minutes post excision PTH was 6.5 ± 5.6 pmol/L (Table 1). Ten-minute post excision PTH levels dropped to >50 % in 87 (81.3%) patients. True positive among these patients based on histopathology were 87 (81.3%), false negative 14 (13.1%) and true negative were 6 (5.6%). Intraoperative PTH monitoring had a diagnostic accuracy of 86.9% (Table 2).

## Discussion

pHPT is a disease that affects women more than men (10). In our study, 79.5% of females were affected with the disease, and the female-to-male ratio was 3.8:1. Naik et al. (3) found that 68.9% females in their study were affected by pHPT, with a female-to-male ratio of 2.2:1, which is comparable to our study. The usual age of presentation for pHPT ranges from 40 to 75 years (10), and it is uncommon to occur in younger patients. Younger patients are more likely to have genetic mutations such as RET, MEN1 or CASR (11). In our study, the age ranged from 31 to 89 years, with a mean age of 65.14 ± 12.7 years. This was similar to a study conducted by Dobrinja et al. (12) and Naik et al. (3).

The most common cause of pHPT is a single parathyroid adenoma, which accounts for nearly 85% of cases (13). Surgery has always been the definitive approach for the management of pHPT, under which, for many years, bilateral neck exploration had been the standard approach. This approach involved direct visualization and removal of abnormal parathyroid glands that were then confirmed on a frozen section. In our study discordant USG and sestamibi scans were 23.3%. The use of preoperative localization techniques has made the minimally focused approach to parathyroidectomy successful. When these localization techniques are concordant, they have a sensitivity as high as 94% (14,15); however, when they are discordant, the sensitivity can drop down to 77% (15). It is in these situations that IOPTH can be overtly useful.

There is still an ongoing debate regarding which is the most appropriate baseline to use for IOPTH monitoring. The Miami criteria require a drop of > 50% in baseline PTH after excision, which was employed in the current study. Other commonly used criteria include the Vienna and Rome criteria, which have a reported diagnostic accuracy of 92.3% and 83.8%, respectively (16). PTH has a half-life of < 5 minutes, and hence, serum concentration of PTH drops drastically following an excision of the abnormal parathyroid gland. Failure of PTH to drop after 10 minutes strongly indicates the presence of more than one abnormally functioning parathyroid gland (17,18). In the current study, a drop in PTH based on the Miami criteria was observed in 81.3% patients. This gave IOPTH monitoring a diagnostic accuracy of 86.9 %. In their study, Naik et al. (3) showed that IOPTH monitoring had a sensitivity of 91.2%, a specificity of 72.7% and a diagnostic accuracy of 86.7%, which is comparable to our study. Irvin et al. (9) in their study had a higher diagnostic accuracy of 97% which was higher than ours. This may be due to the fact that in addition to USG and sestamibi scan they also used differential jugular venous hormone sampling for parathyroid localization when carrying out a focused parathyroidectomy.

Studies have also shown that the use of IOPTH monitoring can reduce the overall operative time especially when a frozen section is unavailable (12,18).

Frozen section biopsy does play an important role in confirming the excision of the parathyroid gland. It, however, cannot confirm the presence of more than one abnormal gland. IOPTH's failure to drop after the excision of a suspicious gland strongly indicates the presence of more than one abnormal gland.

## Conclusions

IOPTH is a valuable investigation that can be used to confirm the successful excision of the abnormal parathyroid gland. It has a diagnostic accuracy of 86.9%, which can prove to be very useful to the surgeon while performing a minimally focused approach to parathyroidectomy.

**Conflict of Interest:** The author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

## References


1. Saleem M, Iftikhar H. Stones, Bones, Groans, and Psychic Moans: Primary Hyperparathyroidism Presenting as Surgical Emergency. Cureus. 2019;11(6):e4989.
2. Khan AA, Khatun Y, Walker A, Jimeno J, Hubbard JG. Role of intraoperative PTH monitoring and surgical approach in primary hyperparathyroidism. Ann Med Surg (Lond). 2015;4(3):301-305.
3. Naik AH, Wani MA, Wani KA, Laway BA, Malik AA, Shah ZA. Intraoperative Parathyroid Hormone Monitoring in Guiding Adequate Parathyroidectomy. Indian J Endocrinol Metab. 2018;22(3):410-416.
4. Thier M, Nordenström E, Bergenfelz A, Westerdahl J. Surgery for patients with primary hyperparathyroidism and negative sestamibi scintigraphy – A feasibility study. Langenbecks Arch Surg 2009;394:881-4.
5. Bergenfelz AO, Wallin G, Jansson S, et al. Results of surgery for sporadic primary hyperparathyroidism in patients with preoperatively negative sestamibi scintigraphy and ultrasound. Langenbecks Arch Surg 2011;396:83-90.
6. Cayo AK, Sippel RS, Schaefer S, Chen H. Utility of intraoperative PTH for primary hyperparathyroidism due to multigland disease. Ann Surg Oncol. 2009 Dec;16(12):3450-4.
7. Chen H, Pruhs Z, Starling JR, Mack E. Intraoperative parathyroid hormone testing improves cure rates in patients undergoing minimally invasive parathyroidectomy. Surgery. 2005 Oct;138(4):583-7; discussion 587-90.
8. Irvin GL 3rd, Carneiro DM, Solorzano CC. Progress in the operative management of sporadic primary hyperparathyroidism over 34 years. Ann Surg. 2004 May;239(5):704-11.
9. Irvin GL 3rd, Solorzano CC, Carneiro DM. Quick intraoperative parathyroid hormone assay: surgical adjunct to allow limited parathyroidectomy, improve success rate, and predict outcome. World J Surg. 2004 Dec;28(12): 1287-92.
10. Yu N, Donnan PT, Murphy MJ, Leese GP. Epidemiology of primary hyperparathyroidism in Tayside, Scotland, UK. Clin Endocrinol (Oxf). 2009 Oct;71(4):485-93.
11. Starker LF, Akerström T, Long WD, et al. Frequent germ-line mutations of the MEN1, CASR, and HRPT2/CDC73 genes in young patients with clinically non-familial primary hyperparathyroidism. Horm Cancer. 2012 Apr;3(1-2):44-51.
12. Dobrinja C, Santandrea G, Giacca M, et al. Effectiveness of Intraoperative Parathyroid Monitoring (ioPTH) in predicting a multiglandular or malignant parathyroid disease. Int J Surg. 2017;41 Suppl 1:S26-S33.
13. Duan K, Gomez Hernandez K, Mete O. Clinicopathological correlates of hyperparathyroidism. J Clin Pathol. 2015 Oct;68(10):771-87.
14. Lumachi F, Zucchetta P, Marzola MC, et al. Advantages of combined technetium-99m-sestamibi scintigraphy and high-resolution ultrasonography in parathyroid localization: comparative study in 91 patients with primary hyperparathyroidism. Eur J Endocrinol. 2000;143(6):755-760.
15. Paek SH, Kim SJ, Choi JY, Lee KE. Clinical usefulness of intraoperative parathyroid hormone monitoring for primary hyperparathyroidism. Ann Surg Treat Res. 2018;94(2):69-73.
16. Carneiro DM, Solorzano CC, Nader MC, Ramirez M, Irvin GL 3rd. Comparison of intraoperative iPTH assay (QPTH) criteria in guiding parathyroidectomy: which criterion is the most accurate? Surgery 2003;134:973-9.
17. Reiher AE, Schaefer S, Chen H, Sippel RS. Does the final intraoperative PTH level really have to fall into the normal range to signify cure? Ann Surg Oncol. 2012 Jun;19(6):1862-7.
18. Barczyński M, Gołkowski F, Nawrot I. The current status of intraoperative iPTH assay in surgery for primary hyperparathyroidism. Gland Surg. 2015;4(1):36-43


**Correspondence:**
Received: 28 November 2022
Accepted: 28 December 2022
Chirag Pereira, MBBS, MS, MRCS
Department of General Surgery,
Royal Lancaster Infirmary
Lancaster, LA14RP, UK
Phone: 07565590080
E-mail: chirag.pereira@mbht.nhs.uk