

Intraoperative PTH Monitoring in Normohormonal Primary Hyperparathyroidism

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INTRODUCTION

Normohormonal hyperparathyroidism (NHPHP) is a subset of primary hyperparathyroidism where patients present with normal PTH levels despite elevated serum calcium^{1,2,3}. This disease variant creates clinical challenges regarding intraoperative PTH (IOPTH) monitoring during parathyroidectomy. NHPHP patients are more likely to have multiglandular disease and smaller sized adenomas, making it more difficult to reliably localize the adenomas using pre-operative imaging². This more often leads to bilateral neck exploration to successfully identify and remove all hyperactive glands.

Furthermore, reliance on IOPTH decay proves challenging since preoperative IOPTH is already in the normal range of 14-72 pg/ml. Traditionally, intraoperative success has been defined as decline in IOPTH levels $\geq 50\%$ from the baseline pre-operative level. This study aimed to determine what percent reduction in post-excision IOPTH from baseline would yield a cure rate in NHPHP patients similar to that of classic primary hyperparathyroidism (PHP).

METHODS

This was a single institution retrospective cohort study of 497 patients that underwent parathyroidectomy for primary hyperparathyroidism between July 2013 and February 2020. Information collected via chart review included patient demographic information, symptoms, prior neck surgeries, pre-, intra-, and post-operative laboratory values, and pathology reports. NHPHP was subdivided into two treatment groups based on 1) diagnosis of NHPHP based on preoperative intact PTH in the normal range and 2) diagnosis of NHPHP based on pre-incision IOPTH in the normal range. The respective control groups were based on patients with classic PHP. Cure rates and percent decline in IOPTH from baseline were compared between groups. Cure was defined as intact PTH and calcium levels in the normal range ≥ 6 months after the time of surgery.

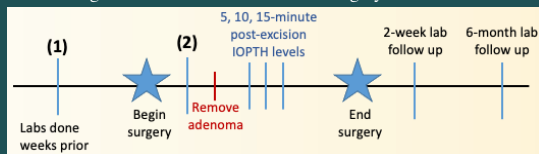


Figure 1: Timeline of typical parathyroidectomy patient.

Continuous variables in the data set were not normally distributed, thus, medians and their interquartile ranges were used. Two-sample Wilcoxon test and Chi-squared test were used to analyze the differences between the various groups.

RESULTS

Of the 497 patients, 496 were included in the study. There were 66 patients (13.3%) in the NHPHP group based on preoperative intact PTH (Group 1) and 430 patients in the control group based on patients who demonstrated classic PHP based on preoperative intact PTH. There were 28 patients (5.6%) in NHPHP group based on baseline IOPTH on the day of surgery (Group 2) and 467 patients in the control group based on patients who demonstrated classic PHP based on baseline IOPTH. Patient information regarding age, gender, BMI, and pre-operative laboratory values can be found in Tables 1 and 2.

| | Group 1: NH based on Pre-operative Intact PTH | | | | Group 1 Control (PHP) | | | |
|--------------------------|---|--------|-------------|--|-----------------------|--------|-------------|--|
| | N | Median | IQR | | N | Median | IQR | |
| Gender (Female) | 53 of 66 (80.3%) | | | | 333 of 430 (77.4%) | | | |
| Age (years) | 66 | 61.5 | 50.0 - 66.0 | | 430 | 61 | 52.0 - 70.0 | |
| BMI (kg/m ²) | 66 | 27.5 | 24.4 - 31.9 | | 429 | 30.6 | 26.0 - 34.9 | |

Table 1: Demographic data for the NHPHP group based on preoperative intact PTH compared to its control group.

| | Group 2: NH based on Pre-Incision IOPTH | | | | Group 2 Control (PHP) | | | |
|--------------------------|---|--------|-------------|--|-----------------------|--------|-------------|--|
| | N | Median | IQR | | N | Median | IQR | |
| Gender (Female) | 19 of 28 (67.9%) | | | | 366 of 467 (78.4%) | | | |
| Age (years) | 28 | 57.5 | 50.5 - 65.0 | | 467 | 61.0 | 52.0 - 70.0 | |
| BMI (kg/m ²) | 28 | 28.5 | 24.1 - 31.9 | | 466 | 30.4 | 25.8 - 34.8 | |

Table 2: Demographic data for the NHPHP group based on pre-incision IOPTH compared to its control group.

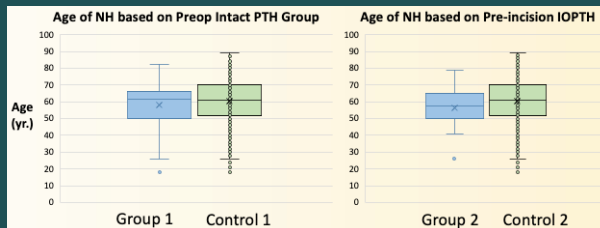


Figure 2: Box & Whisker plots of age distribution of Group 1 and 2 compared to their respective controls.

The cure rates in the NH groups were not significantly different from their classic counterparts. As shown in Table 3, the cure rate in Group 1 was 98.4% compared to 97.1% in the control group, $p = 1.000$. The cure rate in Group 2 was 100.0% compared to 97.1% in the control group, $p = 1.000$.

| | Group 1 | Control 1 | Group 2 | Control 2 |
|-----------|--------------|----------------|-------------|----------------|
| | % (R/N) | % (R/N) | % (R/N) | % (R/N) |
| Cure Rate | 98.4 (63/64) | 97.1 (405/417) | 100 (28/28) | 97.1 (439/452) |
| p-value | 1.000 | | 1.000 | |

Table 3: Cure rates in NH subgroups compared to their control groups.

Table 4 shows the median percent decline in post-excision IOPTH from baseline that achieved cure in Group 1 was 82.8% compared to its control at 87.3%, $p = 0.017$. In Group 2, the percent drop was 80.4% compared to its control at 87.1%, $p = 0.001$. These findings were statistically significant for both NHPHP subgroups compared to their respective controls.

| | Group 1: NH based on Pre-operative Intact PTH (n=63) | | Group 1 Control (n=405) | | Group 2: NH based on Pre-Incision IOPTH (n=28) | | Group 2 Control (n=451) | |
|-----------------|--|-------------|-------------------------|-------------|--|-------------|-------------------------|-------------|
| | Median | IQR | Median | IQR | Median | IQR | Median | IQR |
| % Drop in IOPTH | 82.8 | 75.8 - 89.3 | 87.3 | 80.7 - 90.8 | 80.4 | 75.0 - 83.5 | 87.1 | 79.9 - 90.8 |
| p-value | 0.017 | | | | 0.001 | | | |

Table 4: Percent drop in IOPTH in NH subgroups and their control groups.

CONCLUSIONS

The traditional $\geq 50\%$ decline in 15-minute post-excision IOPTH from baseline may still be adequate in achieving reasonable rate of cure in NHPHP patients. However, a $\geq 75\%$ decline provides a more stringent criterion for achieving high rates of cure in NHPHP parathyroidectomy patients for surgeons who prefer stricter criterion.

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