

## Peer Review File

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### Reviewer A

Good audit of hypopara post thyroidectomy for benign and malignant causes. I agree about the discussion regarding central neck dissection and autotransplantation but I am curious to know why the authors demonstrate malignancy to be associated with greater hypopara rates.

Is the procedure done differently in known cancers? Total thyroidectomy without CND for malignancy is identical to the procedure for benign disease. Are the authors performing blunt dissection intraop to assess for nodes? Does the T stage of the cancer correlate to hypopara rates? Some discussion of this is useful.

Also, a significant percentage of patients would have had RAI - is there a difference in para recovery rates for RAI vs non-RAI patients at 6 months?

### Reply

- In regards to the association between malignancy and hypoparathyroidism rates we have expanded the discussion in our paper. There are some posited reasons in the literature likely secondary to adhesion formation and devascularization of parathyroids driven by the malignant disease. It appears that size/mass effect alone does not seem to be the primary mechanism for why the two variables are correlated.
- The surgeons at these institutes would not perform thyroidectomy differently for routine and malignant cases unless a central neck dissection was performed. Occasionally surgeons would perform blunt dissections for intraoperative nodal assessment but if suspicious nodes were found, a formal central neck dissection would be performed and the patient would be classified as such in our data set. T staging was available for 82 of the 143 patients who underwent an operation for malignant disease. A logistic regression analysis suggests that it is not a significant factor in determining post operative hypoparathyroidism outcomes nor accidental parathyroidectomy and we have added this to our tables. Interesting thyroid weight alone was not a significant factor in the occurrence of both variables once again suggesting that the link between malignancy and post operative hypoparathyroidism is not driven by gland size alone.
- Radioactive iodine does present another factor that can potentially contribute to rates of post operative hypoparathyroidism. This data however was not collected in this study and likely poses a clinical question that justifies its own independent study. We are only aware of one study by Abudwaili et al which has looked at this area and does suggest that there is a further delay in returning to normal parathyroid gland function in a thyroidectomy that is followed with adjuvant radioactive iodine treatment (1). Changes in Text
- Line 181 - Although the surgical operation is technically the same for benign and malignant thyroid surgery, malignant disease is often associated with perithyroidal inflammation making identification of parathyroid glands challenging (3,16). Inspection or dissection looking for clinically suspicious central compartment lymph nodes may compromise the blood supply to parathyroid glands and influence the hypoparathyroidism rate and local invasion by malignant lesions can create adhesions with nearby tissue increasing the risk of inadvertent resection (3). While not conclusive, the lack of significance of thyroid weight and T-staging for both accidental parathyroidectomy and temporary hypoparathyroidism suggest that the mechanism by which malignancy is associated with both factors is not mass effect alone.

### Reviewer B

This is a review of a large database to determine the factors contributing to transient and permanent hyperparathyroidism after thyroid surgery.

There is a significant amount of literature already published on this subject but it adds to the available Australian literature.

The findings are in line with other published series.

### Reviewer C

Abstract:

- Methods: "A retrospective analysis of 295 patients who underwent total thyroidectomy was performed."  
Rewrite to be more specific – where and when

- Results: Please include OR and CI for all p values quoted within abstract. Where possible also use whole numbers along with %.

- The version I read did not have keywords attached: please ensure keywords are MESH and/or Emtree terms to improve searchability.

Reply:

Methods: The requested line has been modified to be more specific referencing the number of Australian hospitals and the duration

Results: OR and CI have been included for all p values

Keywords: Keywords have been added to the title page

Changes in Text

Methods: Line 20: A retrospective analysis of 295 patients from three Australian tertiary referral hospitals from 2010 to 2020 who underwent total thyroidectomy was performed.

Results: Line 29: All missing confidence intervals and odds ratios were included with said p-values

Keywords Line 51: Thyroidectomy, hypoparathyroidism, accidental parathyroidectomy

Main body:

- Results:

As within the abstract always include OR and CI when stating p values – this is inconsistent within the text

Reply: OR and CI have been included for all p-values that were missing them.

Changes in text - Line 131: p values onwards had OR and CI supplemented.

- Tables 1: expand table titles to ensure all can be read without the body of the text eg "Demographic Profile of Patients Undergoing Total Thyroidectomy"

- Ensure consistency across all tables eg only one table is annotated with p-value referencing Fisher exact test. Which tables used Fisher exact and which are Chi square tests, annotate appropriately.

- In table 1 there are 144 malignant cases - this number is not the same in tables 2 and 3. In table 3 I expect this is because of incomplete biochemistry ( as per text), please add this as footnote to this table) Similarly in table 4 the total numbers differ due to the 8 patients, please add a footnote to the table description. Table 2: malignant yes and no both state 152 ( 52%) - please correct and ensure Or and CI are based on the correct figures.

- Table 4 title improve: Risk Factors for Permanent Hypoparathyroidism in Patients Undergoing Total Thyroidectomy

- Tables 5 and 6 include the statistical method( eg logistic regression) for predictive probabilities within an annotated footnote.

- Improved title for 5: Predicted Probability of Accidental Parathyroidectomy in Patients Undergoing Total Thyroidectomy Based on Risk Factors

And the column for probability: Predicted Probability of Accidental Parathyroidectomy

- Improved title for 6: Predicted Probability of Temporary Hypoparathyroidism in patients Undergoing Total thyroidectomy Based on Risk and the column for predicted probability : Predicted Probability of Temporary Hypoparathyroidism

Reply: The Improved titles for tables 1, 5 and 6 have been included into the text. A footnote has been added to the relevant tables explaining the discrepancy in malignant cases. Table 1 the number of malignant cases has been corrected, this was a transcription error and none of the subsequent statistics have had to be changed. Tables have all been annotated as requested.

Changes in text: See tables 1-6