Peer Review File

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Reviewer A

Thank you for submitting this article on the affect of hypertension on the risk of post operative heamatoma.

Revision/Review of article

1. 'Neck dissection is an increasingly used technique'

a. Suggest reworking this opening statement. Neck dissection is rarely a treatment in and of itself. Usually, it is used as a component of curative surgical treatment

Reply 1: Opening line reworded

Changes in text 1: Neck dissection is a well-established technique used alongside primary resection for the curative treatment of head and neck cancers.

2.Introduction

a. While some people include level 7 in lymph nodes, it is generally accepted that there are 6 cervical levels (the 7th is in the superior mediastinum which is outside of the territory of the cervical neck)

Reply 2: Amended to state six levels

Changes in text 2: The lymph nodes of the neck are subdivided into six levels.

3. 'Neck dissections are described based on what levels are resected and what other non-lymphatic structures are resected concurrently'

a. Suggest re-wording. We usually talk about neck dissection definition in the context of what structures can be persevered rather than resected

Reply 3: Text changed to represent this

Changes in text 3: Neck dissections are described by which levels of lymph nodes are resected and which non-lymphatic structures are preserved.

4. There is considerable variation in the literature on the rate of post-operative haematoma following neck dissection. Only one study has looked specifically at haematoma following neck dissection for head and neck cancers

a. This seems like a contradictory statement; initially saying there is variation but then saying there is only one published study. Thyroids are head and neck cancers. There are limited other reasons that a neck dissection would

be performed, outside of the context of treatment for head and neck cancer (be that epithelial malignancy or thyroid malignancy)

Reply 4: Only one study has looked solely at epithelial cancers (the majority of resections at our institution), I have clarified this in text.

Changes in text 4: Only one study has looked specifically at haematoma following neck dissection for epithelial head and neck cancers (1).

5. Post-operative hypertension is a well-recognised complication of lateral neck dissection. What data is there to support this statement?

Reply 5: References 14, 15 and 16 are case series that have reported on hypertension following neck dissection. Our paper shows that 14% of patients had a systolic BP of greater than 180 following neck dissection.

6. Given that the data only spans 8 months, would it be possible to collect the data over a longer period of time.

Reply 6: The sample size calculation at the end shows that it would take over 6 years of recruitment to have a study powered appropriately to detect a 50% reduction in haematoma formation if post-operative hypertension is a causative factor in haematoma formation. It is possible that a lack-of-effect study could be undertaken but this may not be of much clinical relevance.

Reviewer B

Great to see a prospective cohort used for this study:

1. Abstract:
   - Neck disssection is a well-established technique for curative managemnt in H&N. The opening line is incorrect.
   - Primary outcome should be simply "haematoma formation" not risk of

Reply 1: both changes made

Changes in text 1: Neck dissection is a well established technique used alongside primary resection for the curative treatment of head and neck cancers.

Our primary outcome was haematoma formation in those with post-operative hypertension (defined as a systolic blood pressure of greater than 180 at any time) compared to those without.

2. Introduction: neck dissection can involve other structures (alluded to at end of paragraph) so the 1st sentence is incorrect. Better phrase "Neck dissection is the surgical removal of lymph nodes, with or without other non-lymphatic structures, from the neck ..."

Reply 2: reworded

Changes in text 2: Neck dissection is the surgical removal of lymph nodes, with or without other non-lymphatic structures, from the neck. This may be performed either simultaneously or as a staged procedure after surgical excision of malignancies from the head or neck.

3. Method: the outcome is haematoma formation, not "risk of"

Reply 3: Reworded

Changes in text 3: This study is a prospective cohort study of all patients undergoing neck dissection at our institution. Our primary outcome was haematoma formation in those with post-operative hypertension compared to those without. Our secondary outcome was haematoma formation in those with pre-existing hypertension.

4. Need a reference for the AHA definition of hypertension

Reply 4: Added reference 20 (Whelton), which is the 2017 AHA guidelines for hypertension

5. Questions needing clarification:
    - were the patients who had a pre-operative HPT completely separate to those with post-op HPT? If not what was the overlap? ie did pre-op HPT diagnosis increase risk of post-op HPT

Reply: The phi-coefficient between diagnosed HT and post-op HT was 0.11 showing weak association.

    - anticoagulation use: was there a higher usage in pts with a pre-op diagnsosis of HPT? This is mentioned in discussion, however the recommended times for pre-op ceasation do not always enable normal clotting/ haemostasis at time of surgery. It would be of value to note the difference in percentage of those with pre-op HPT on anticoaagulants vs those with no pre-op HPT on anticoagulants: this may be the significant finding rather than the pre-op HPT itself

Reply: We did not collect data on pre-operative anticoagulant or antiplatelet use and this is a significant limitation of our study.

    - what is the impact on management with the finding that post-op HPT is not a significant risk factor for haematoma formation?

Reply: Our initial reason for planning this study was to provide evidence to support the creation of a hypertension management protocol in our institution for patients following neck dissection. The results of this study have meant that we are no longer pursuing this as an area of active research and that further studies looking at perioperative management of antihypertensive drugs or interventions targeted at only people with pre-existing hypertension may be more worthy areas of further research.

Editorial Comments

Title

1. The title could easily be misinterpreted to mean that this article is about the incidence of perioperative hypertension and haematoma. We recommend authors change the title to “Association between perioperative hypertension and haematoma formation in neck dissection for head and neck cancers” (just for your information).

Reply 1: Title amended as above

Abstract

2. Please briefly supplement measurement methods of parameters (such as the definition of hypertension and methods of measuring haematoma), and statistical methods in the Abstract-Methods.

Reply 2: Definition on hypertension added to abstract “the AHA definition of a hypertensive crisis”and statistical methods briefly mentioned “Risk ratios and Fisher’s exact test were used to calculate significance.”

3. “The relative risk of haematoma formation was 6.47 (95% CI 0.85 to 52.71, p=0.0397) in those with known pre-operative hypertension”, the 95% CI was wide (0.85 to 52.71) despite the p-value being significant. The authors should inform the readers to interpret the results with caution.

Reply 3: Statement added to results “However, due to the small sample size of our study and resulting wide confidence intervals, these results should be interpreted with caution.”

Introduction

4. Please describe the possible adverse outcomes of postoperative hematoma.

Reply 4: Statement added outlining some possible outcomes “Postoperative haematoma can cause damage to surrounding structures including neural damage, oedema, compressive effects on the airway and threaten the viability of grafted flaps requiring operative intervention.”

Methods

5. “The study was approved by institutional ethics committee of SLHD HREC (2019/ETH07164).” Please give the full name of the institution rather than an abbreviation.

Reply 5: Full name given “Sydney Local Health District Human Research Ethics Committee”

6. “Because of the retrospective nature of the research, the requirement for informed consent was waived.” and “This study is a prospective cohort study of … .”
Please clarify the type of this study. If the study is prospective, the informed consent of the patients must be obtained.

Reply 6: Our ethics approval allowed for collection of de-identified observational data to be collected from the notes of each patient upon discharge from hospital into a database. However, as it is observational data that we examined, this study is closer in nature to a retrospective cohort studuy and the text has been amended to reflect this.

7. “This study is a prospective cohort study of all patients undergoing neck dissection at our institution.”

Whether there is a more specific criteria for the inclusion and the exclusion of the patient such as the age of the patient, the previous history of surgery, and the medical history of the patient.

Reply 7: There were no exclusion criteria for our study, all patients undergoing a neck dissection were included.

8. “Data was also collected on whether there was a surgical review for haematoma and whether there was return to theatre within the first 24 hours and the indication for return to theatre.”
What are the indications for returning to the theatre, how did the researchers measure the hematoma, and were the measurers informed of the purpose of the study?

Reply 8: As data was collected from patient records, haematoma diagnosis was defined as when the treating surgical team included the word “haematoma” in their notes. The indication for returning to theatre was extracted from operation reports and if “evacuation of haematoma” was written then this was recorded as such. Return to theatre for other indications was not included in our database.

9. In the response letter, the authors declared that “The phi-coefficient between diagnosed HT and post-op HT was 0.11 showing weak association”. Please give the citation to back up the claim and this statement should be reported in the main text. The reader may be likely to have the same query as the reviewer.

Reply 9: Added in results “Seventeen patients had hypertension (SBP>180) in the 24 hours post-operatively. However, there was only a weak association between those experience post-operative hypertension and those patients who had a pre-existing diagnosis of hypertension (phi-coefficient 0.11).”

10. Please add a description of the qualitative data in the Methods section. Please report whether the P value was a one-sided or two-sided test. Also, please report if there are missing data.

Reply 10: Two sided p-values are given “A two-sided mid-p value of less than 0.05 was deemed statistically significant”. There was no missing data for our analysed outcomes as reported in the first paragraph of the results section.

Results
11. “127 patients underwent neck dissection at our institution between August 2021 and March 2022.” The study time span and patient numbers were not consistent with the Abstract. Please check it and be consistent.

Reply 11: Numbers have been corrected as follows “127 patients underwent neck dissection at our institution between August 2021 and April 2022”

12. If the research population has clear inclusion and exclusion criteria, we recommend authors use a flow chart to present a specific process for including participants, from the initial selection of potentially eligible patients to the final inclusion of patients, with reasons for any exclusion. For your information, here is an example of our sister journal (See Figure 1): https://qims.amegroups.com/article/view/92472/html.

Reply 12: All records of patients undergoing neck dissection were included

13. “The average age was 64.9 and 71.6% were male.” The percentage of males in Table 1 is 72.4%.

Reply 13: Corrected to reflect table 1

14. Additionally, there are other data errors in the table. The total number of people who took antihypertensive drugs on the day of surgery, yes or no, was 59 in Table 1 (rather than 127). Also, the total number of “Intravenous anaesthetic agents” was 125. In Table 2, the total number of “Primary” and “Revision” in Haematoma is 9 (rather than 8).

Reply 14: Valued have been corrected in table

15. Please add a column to Table 2 regarding the relative risk with 95% CI of hematoma formation.

Reply 15: Addition column added to table 2.

Discussion

16. The authors should analyze possible reasons for the occurrence of postoperative hematoma in the Discussion.

Reply 16: This was included in our initial manuscript but as we did not collect data for several confounders, it was recommended we omit this from the manuscript.

17. The author mentioned “Another interesting finding was that none of the patients who received a dexmedetomidine infusion developed a haematoma” in the discussion, please compare the published similar studies to analyze the possible reasons.

Reply 17: The sample size of 6 is too small to make any particular claims, I have included some results from the literature in the following paragraph.

18. In addition, for the occurrence of postoperative hematoma, on the basis of the rich clinical experiences of the author, does the author suggest any treatment or prevention?

Reply 18: Additional paragraph added to discussion discussing dexmedetomidine and our clinical experience.

Conclusion

19. You need to provide a separate paragraph to present the Conclusion, including the research significance, generalisability, and future prospects of this study.