

Peer Review File

Article information: <https://dx.doi.org/10.21037/aot-22-17>

Reviewer A Comments:

The topic selected by the authors is interesting and the initial history of thyroid surgery and hypothyroidism is well-written and captivating. The review of hypothyroidism treatment and quality of life has many interesting observations and conclusions, but is more disjointed.

The study's conclusions do not clearly address its aim. From the article:

“The aim of this study is to

- 1) review the evidence-based management of thyroid hormone supplementation in the post-surgical setting,
- 2) and to better understand quality of life considerations in the post-thyroidectomy population.”

Focus in the review (aim 1) part of the text could be better or the aim redefined (see below).

These are the conclusion I can find in the text regarding aim 2:

1. Regular assessment of quality of life may guide providers toward new treatment methods and optimize patient experience in the setting of post operative hypothyroidism.
2. A more conservative treatment strategy for low-risk DTC reduces the impact on quality of life.
3. One way to increase quality of life could be incorporating multiple clinical factors in the algorithm for initial LT4 dose after total or completion thyroidectomy.

Are there any more conclusion that you would like to highlight, that I have missed? Could any of these conclusions be added to the end conclusion?

Overall, the article appears disjointed and might benefit from a more cohesive thread, both in terms of contents and language.

Comment 1: Line 60: Post-operative hypothyroidism is, as seen later in the text, largely dependent on type of surgery and not lack of good surgical technique. In some cases, as also discussed in the text, it is possible to choose surgical method, but many times the diagnosis dictates the choice of method. The sentence would benefit from a reformulation taking this in consideration.

Reply 1: This is precisely the point of this sentence, “Yet, despite scrupulous and multiply reiterated surgical technique, the reality of post-thyroidectomy hypothyroidism persists”, namely that we can do everything right surgically after total thyroidectomy but our patients will naturally be hypothyroid as a result of removing the gland.

Changes to Text: Added statement “we can do everything right and patients will inevitably become hypothyroid after removal of the thyroid gland” if felt that is necessary to clarify the meaning of the

prior text.

Comment 2: Line 74-75: You include publications with adult patients but exclude those that exclusively reviewed pediatric data. Does that mean that you did include articles that featured children in the population?

Reply 2: Articles that exclusively dealt with pediatric patients were excluded. Articles may have included some pediatric data in addition to that for adults.

Changes in text: Comment about possibility of some pediatric patients being included was added to the methods section (Line 76).

Comment 3: Line 79: How many articles were found using reference lists? Was it a substantial or insignificant contribution?

Reply 3: 1-3 articles were found using reference list. While each article reviewed offered important contributions, this was not a significant proportion of the articles reviewed for the purposes of this manuscript.

Changes in text: Numerical designations added to Literature Search Chart.

Comment 4: Discussion IV: This part could be shortened, since it seemingly deviates somewhat from the subject.

Reply 4: Per reviewer recommendation, this section was truncated (reassigned to section 3.4 per editor template review).

Changes in text: Information on LT4 absorption and dosing adjustments in various conditions were removed to make section more concise (see deleted material in tracked changes, ~Lines 166-167)

Comment 5: Line 137: Is focus on primary hypothyroidism or should it be “primary hypothyroidism, especially iatrogenic post-operative hypothyroidism” or something that more precisely describes your field of interest?

Reply 5: Yes, thank you I agree with this comment, Line 138 edited accordingly.

Changes in Text: Line 138 updated.

Comment 6: Line 190: Discussion V: Here is a shift in focus towards DTC which prevails in to next parts of the discussion. Should this be a focus for the whole article?

Reply 6: There seem to be important discussions here related to HT as well, so do not want to limit it completely. Attempt made to hone in on these complex treatment areas and, perhaps most importantly, note that further study to pinpoint QoL around management of DTC will be crucial.

Comment 7: Line 288-314: This concerns low-risk DTC. The conclusion that a more conservative treatment strategy for low-risk DTC reduces the impact on quality of life is not transferable to other indications for thyroid surgery. Maybe this (DTC) should be in the aim and title of the study?

Reply 7: See comment immediately above. Thank you for this suggestion and if the reviewers feel I should revamp the paper to focus only on DTC this can be considered.

Comment 8: Line 328-333: This is interesting! One way to increase quality of life could be incorporating multiple clinical factors in the algorithm for initial LT4 dose after total or completion

thyroidectomy. Example of such factors? Could this be included in the conclusion?

Reply 8: Thank you. This review does not feel robust enough to support creation of particular algorithm for LT4 dosing after surgery. If reviewers feel this is needed further research into this area could be considered.

Comment 9: Abbreviations should be explained the first time they are used. Here are several iterations of the same explanation for an abbreviation and also example of an abbreviation used before it is defined. Also, use the same terminology through the whole text. Go through the text and check this! There might be more, that I have missed. Examples:

Line 198: small, non aggressive differentiated thyroid cancers (DTC),

Line 288: differentiated thyroid cancer (DTC)

Line 133: antithyroid peroxidase (TPO) antibodies,

Line 218: thyroid peroxidase (TPO)

Line 245: QoL metrics

Line 257: quality of life (QoL)

Line 133: chronic lymphocytic thyroiditis (Hashimoto' s)

Line 266: Hashimoto' s thyroiditis (HT)

Reply 9: Thank you, these abbreviations should be all better organized. (See corresponding lines).

Reviewer B Comments:

I found this to be a well-researched and written manuscript, and have only a few suggestions for the authors to consider:

Comment 1. The quoted section from the ATA Guidelines (lines 151-155), having been directly quoted, may be indented in the same way Horsley' s statements (lines 100-106) were. This will distinguish that section from the rest of the text.

Reply 1: Thank you, this formatting was updated per reviewer recommendation.

Changes in Text: Reformatting lines 152-155.

Comment 2. It would be useful to include “primary hypothyroidism” in the abstract because it is emphasised later in the text that the review only focuses on primary hypothyroidism.

Reply 2: Thank you, this was added to the abstract.

Changes in Text: “Primary” hypothyroidism added to Key Content and Findings section of abstract per reviewer recommendation.

Comment 3. Another suggestion would be to include a table for the QoL findings from the papers to summarise the characteristics of the literature (aside from author/year details, the type of condition e.g. DTC, type of tool used to measure QoL e.g. SF-36 and summarised results). A table could make the similarities and contrasts clearer than is already described in the text (lines 254-314).

Reply 3: This chart is included in Figure 1. Thank you for the suggestion.