Peer Review File

Article information: https://dx.doi.org/10.21037/gs-23-218

Reviewer A

A bibliometric study on postoperative management of thyroid cancer is oresented in this manuscript. Current hotspots of research are identified, as follow up, recurrent laryngeal nerve, and medullary thyroid carcinoma and future research trending areas are suggested, which is well within the scope of bibliometric research
Only one database (though large) was searched in this study and there likely is no representation of grey literature, conference proceedings and postgraduate thesis, which are sometimes sentinels of the forefront of research topics that may become mainstream in the near future. This is however also discussed in the limitations section.
Discussion is mostly balanced and informative, maybe a bit too lengthy.
English may in need of a grammar review ("management of thyroid cancer is important to optimize the clinical and quality of life of patients", "we suggest
that countries to jointly conduct high-quality multicenter-related studies", etc)

Response to Reviewer A
We gratefully thank you for the precious time the reviewer spent making constructive remarks. We feel sorry for the inconvenience brought to the reviewer. We have corrected the grammatical errors and realized the problem of unclear structure and too-long sentences in the discussion. We have made a lot of revisions. Because of your suggestions, the quality of our manuscript has been further improved. Below the comments of the reviewer are response point by point, and the revisions are indicated.

Reviewer B

Xi Yang, Yiming Wang, Yunpeng Luo, Teng Guio and Guangde Zhang performed a bibliometric analysis of research hotspots in postoperative management of thyroid cancer during the last 20 years. They identified the nations and institutions delivering the most cited literature, the journals publishing the most relevant evidence and described the most promising subjects for future research in postoperative management of thyroid cancer.

These issues are interesting to me as an academic thyroid surgeon. Unfortunately, the paper was difficult for me to read: many sentences are repeatedly used and redundant,

some are incomplete and most of them are too long. I miss a clear structure in the discussion. It lists plenty of study results instead of focusing on explaining the results of the bibliometric analysis.

I wish the author explained some bibliometric concepts they use (for example “centrality”) in the methods and concentrate in the discussion on why they think their analysis delivered those results. I also had the impression there is a lot of switching from pre to post to intraoperative management. They are certainly strongly related but the switching was too abrupt to me and confused me sometimes.

Response to Reviewer B

We gratefully thank the reviewer for their time spent making their constructive remarks and useful suggestions, which have significantly raised the quality of the manuscript and enabled us to improve it.

We apologize for not clearly explaining the results of the analysis. We have explained some of the concepts in the methods section and also rewritten the discussion section as you suggested. We have tried to make the structure as clear as possible. Please review the revised manuscript. Below the comments of the reviewer are response point by point, and the revisions are indicated.

Here some more comments.

Abstract

1) What do you mean by “to optimize the clinical and quality of life of patients”? “The clinical outcome and quality of life of patients”? I would erase the first part of the background and only leave: “This study aims to use bibliometric methods to uncover research hotspots and explore future directions in the field of postoperative management of thyroid cancer”.

Reply 1: Thank you for your rigorous consideration. I apologize for the ambiguity due to my poor English writing skill. I meant to write "The clinical outcome and quality of life of patients". We agree that the first part of the background needs to be erased, and we have modified our text as advised (see Page 2, line 19-20).

Changes in the text:

Objective: This study aims to use bibliometric methods to uncover research hotspots and explore future directions in the field of postoperative management of thyroid cancer.

2) “We comprehensively searched the Science Citation Index Expanded (SCI-E)

database of the Web of Science Core Collection (WOSCC) for literature published from 2003 to 2022 on the postoperative management of thyroid cancer, and used CiteSpace 6.1.R6 and Microsoft Office Excel to evaluate and visualize the search results, using R Studio generates a network of spatial geographic distribution maps and cooperative contacts" Please consider rephrasing. This is a very long sentence and I am not sure I understand what you mean. "We comprehensively searched the Science Citation Index Expanded (SCI-E) database of the Web of Science Core Collection (WOSCC) for literature published from 2003 to 2022 on the postoperative management of thyroid cancer, and used CiteSpace 6.1.R6 and Microsoft Office Excel to evaluate and visualize the search results. Uusing R Studio we generated a network of spatial geographic distribution maps and cooperative contacts"?

Reply 2: Thank you for your comment. We are very sorry for the long sentence that makes it hard to get to the point. I reconsidered the phrasing to clearly express what I mean (see Page 2, line 22-26).
Changes in the text:
Methods: We comprehensively searched the Science Citation Index Expanded (SCI-E) database of the Web of Science Core Collection (WOSCC) for literature published from 2003 to 2022 on the postoperative management of thyroid cancer. Using CiteSpace 6.1.R6 and Microsoft Office Excel, we evaluated and visualized the search results. Using R Studio, we generated a network of spatial geographic distribution maps and cooperative contacts.

3) Is it correct to write t "centrality (n=282, Centrality=0.28)" once small and once with capital letter?

Reply 3: Thank you so much for your careful check. I have changed all the "centrality" of the article to lower case. The following are some of the changes (see Page 2, line 29-33).
Changes in the text:
The United States has the largest number of publications and the highest centrality (n=282, centrality=0.28) and is in the lead. Johns Hopkins University showed significant centrality (centrality=0.15) and is the academic center of the field. THYROID was the journal with the highest number of citations (n=826), and the AMERICAN JOURNAL OF SURGICAL PATHOLOGY was the journal with the highest centrality (centrality=0.08).

4) I am not sure that "recurrent laryngeal nerve" is an issue in postoperative management. Most literature on "recurrent laryngeal nerve" includes intraoperative

aspects. Do you mean treatment of “recurrent laryngeal nerve palsy”?

Reply 4: Thank you for your comment. The recurrent laryngeal nerve is indeed an issue in intraoperative management. Although I searched for literature related to postoperative management of thyroid cancer, the laryngeal nerve was the keyword that appeared more frequently in the results of analyzing the data. Here I just want to list the final results of the bibliometric analysis in the "Results" and then link them together in the "Discussion". This includes your reference to recurrent laryngeal nerve palsy.

5) “microcarcinoma and differentiated thyroid cancer”: microcarcinoma is mostly papillary thyroid cancer (=differentiated thyroid cancer). I am not sure these two should be mentioned separately (s. also Highlight Box).

Reply 5: Thank you so much for your comment. I understand that it is inappropriate to refer to the two separately. I was trying to present the final analysis one by one and tell the reader that "microcarcinoma" and "differentiated thyroid cancer" are both current burst words. I apologize for overlooking the relationship between the two. We have modified our text as advised (see Page 3, line 42-44).
Changes in the text:
Future research is likely to revolve around guidelines and consensus on the management of thyroid cancer, active surveillance, and microcarcinoma in differentiated thyroid cancer.

Highlight Box

1) Consider erasing “The global incidence of thyroid cancer has continued to increase. Thyroid surgery is one of the main treatments for thyroid cancer and postoperative management of thyroid cancer is important to optimize the clinical and quality of life of patients.” Under "what is known" I would expect a sentence like “during the last 20 years several Guidelines for the treatment of thyroid cancer were published” and/or “literature on thyroid cancer has a volume of XXX articles/year, with XX journals publishing relevant literature on this subject”

Reply 6: We gratefully appreciate your valuable suggestion and we have modified our text as advised (see Page 4, line 51).
Changes in the text:
During the last 20 years, the volume of literature on postoperative management of thyroid cancer has been 1,040 articles, with 64 countries and 1,400 journals publishing relevant literature on this subject, as well as several guidelines for the treatment of

thyroid cancer.

2) Consider rephrasing “We look forward to the emergence of new relevant guidelines based on current evidence-based medical evidence to guide more optimal management.” “Evidence-based medical evidence” is a tautology. Perhaps “there is a need for international guidelines on postoperative management of patients with thyroid cancer”?

Reply 7: Thank you very much for your advice. We have considered your suggestion and modified the sentence (see Page 4, line 51).
Changes in the text:
To have better outreach in postoperative thyroid cancer management research, we suggest that countries jointly conduct high-quality multicenter-related studies and promote the globalization of postoperative thyroid cancer management research. There is a need for international guidelines on postoperative management of patients with thyroid cancer to guide more optimal management.

Introduction

Line 61: here I would expect you mention that the increase is due to low-stage-carcinomas including pT1a and b PTCs as opposed to a stable incidence of more aggressive carcinomas like medullary or anaplastic thyroid cancer. This explains why mortality is not increasing and why low morbidity and less aggressive strategies are required.

Reply 8: Thank you very much for your constructive advice. We have considered your suggestion and mentioned relevant content. I apologize that I did not search the literature on the increased incidence of pT1a and b PTCs, so I modified the wording (see Page 5, line 57-59).
Changes in the text:
The increase is primarily due to the increased detection of indolent papillary thyroid cancer (PTC) rather than the rare but highly aggressive follicular, medullary, and anaplastic thyroid cancer.

Line 62-63:” advances in surgical techniques have minimized the occurrence of postoperative complications in patients, patients are still at risk of developing postoperative complications.” Maybe “although technical devices like intraoperative neuromonitoring of the recurrent laryngeal nerve, ICG and autofluorescence of the parathyroid glands have been introduced, in XX% of cases permanent recurrent laryngeal nerve palsies and in XX% permanent hypoparathyroidism are still reported”?

Reply 9: We gratefully appreciate your valuable suggestion. We apologize that our search of the literature has not been comprehensive enough and that we have not kept up with the research frontiers, and we have re-written this part according to the Reviewer's suggestion (see Page 5, line 59-63).
Changes in the text:
Thyroid surgery is one of the main treatments for thyroid cancer, and although technical devices like intraoperative neuromonitoring of the recurrent laryngeal nerve, Intraoperative Indocyanine Green (ICG) and autofluorescence of the parathyroid glands have been introduced, in 0.3%-3% of cases permanent recurrent laryngeal nerve palsies and in 1%-4% permanent hypoparathyroidism are still reported.

63-67 sentence is too long "… and … and". I would rephrase.

Reply 10: We are very sorry for our redundant writing. This sentence is to further explain that "patients are still at risk of developing postoperative complications", so I cited a study. Unfortunately, I did not summarize this study well. I've revised the previous sentence as you suggested, and the previous sentence already expresses what I originally meant. So, I have deleted this sentence.

72-73 "optimizing the clinical and quality of life outcomes of patients (5-7)." The clinical what? clinical outcome? management?

Reply 11: Thank you for your rigorous consideration. I am sorry for the ambiguity due to my poor English writing skill. I have modified our text as advised (see Page 5, line 68-69).
Changes in the text:
Postoperative management of thyroid cancer, including …, is an important part of the individualized treatment plan and is significant for optimizing the clinical outcome and quality of life of patients.

121: can the author explain in the methods concepts like "centrality" and "keyword bursts"?

Reply 12: We are very sorry that we neglect to explain the concepts of "centrality" and "keyword bursts". We have added relevant content and made changes based on previous content (see Page 6, line 94-97).
Changes in the text:
Betweenness centrality measures the number of times a node lies on the shortest path

between other nodes. Nodes with high betweenness centrality generally are considered potential pivotal points. Keyword bursts indicate a specific duration of abrupt change in keyword frequency and burst detection algorithms for keywords identify emerging research frontiers

125-6 “indicating the importance of this institution for postoperative management of thyroid cancer.” I believe results should only be listed and not discussed in the "results".

Reply 13: We are very sorry for our irregularity in discussing the results in "results". We have made corrections according to your comment (see Page 8, line 123-126).

Changes in the text：

According to Figure 5 and Table 2, the institution with the highest number of publications is Memorial Sloan Kettering Cancer Center (n=52), located in the USA. The two institutions with the best centrality are Johns Hopkins University and Yonsei University, with Johns Hopkins University in the USA, having the best centrality (centrality=0.15). The network of national and institutional collaborations shows that the USA is the academic core of the field.

Discussion

186-9 “The literature related to the postoperative management of thyroid cancer and its citations has generally shown an increasing trend over the past 20 years, indicating a gradual academic focus on this area of research in the postoperative management of thyroid cancer and the possibility of more research in the future”. It should be "had" instead of "has". “Related to the postoperative management of thyroid cancer… in the postoperative management of thyroid cancer” is redundant.

Reply 14: Thank you so much for your careful check. We are very sorry for our incorrect writing and we have modified our text as advised (see Page 10, line 32-34).
Changes in the text:
The number of publications related to postoperative management of thyroid cancer and its citations have generally shown an increasing trend over the past 20 years, indicating a gradual academic focus on this area and the possibility of more research in the future.

216-8: What do you mean with "We look forward to the emergence of new relevant guidelines based on current evidence-based medical evidence to guide more optimal postoperative management of thyroid cancer"? ATA-Guidelines need an Update?

Reply 15: We apologize for not making our point clear. What we are trying to convey here, as modified in the Highlight Box section, is the need for updated international guidelines to guide more optimal management. We have modified this sentence (see Page 12, line 212-214).
Changes in the text:
We look forward to the guideline updates, and there is a need for international guidelines on postoperative management of patients with thyroid cancer to guide more optimal management.

220-7 I believe the authors mean that the research with the keyword "postoperative" delivered studies including pre- and intraoperative issues, thus showing how pre- and intra-operative management influence postoperative treatment. Is this correct?

Reply 16: Thank you for your comment. We apologize that we did not express this paragraph clearly and briefly. We mean that preoperative and intraoperative management influence postoperative treatment. We have revised this paragraph (see Page 12, line 216-221).
Changes in the text:
Our analysis of keyword co-occurrence and clustering, and literature co-citation timeline graphs reveal that the research hotspots of postoperative management of thyroid cancer in the past 20 years can be summarized into four aspects: pathological classification, surgical strategy, postoperative complications, and postoperative follow-up. These four aspects include preoperative and intraoperative issues, thus showing that preoperative and intraoperative management influence postoperative treatment.

240: “Due to the lack of relevant studies,” and/or the rarity. Most PTC are classical and follicular variant.

Reply 17: We gratefully appreciate your valuable suggestion. It really should be described in more detail here, and the lack of relevant studies is mainly due to its rarity. I have made extensive changes to the discussion section and removed this sentence. Please review the revised discussion.

What do you mean by “the predictive value” of PTC? Do you mean the outcome? The prognosis?

Reply 18: We feel sorry for the inconvenience brought to the reviewer. Here I mean prognosis. I apologize for using inappropriate words. I have made extensive changes to the discussion section and removed this sentence. Please review the revised discussion.

242: I was surprised that suddenly MTC was the subject here. You were talking about DTC.

Reply 19: We apologize for the abrupt and illogical turn here. I have restructured the discussion. Please review the revised discussion.

244-7: “Postoperative management of MTC unlike well-differentiated differentiated thyroid cancer, in which serum calcitonin and carcinoembryonic antigen (CEA) levels are critical for postoperative monitoring of MTC, guidelines recommend treatment with kinase inhibitors for patients with unresectable recurrent or persistent MTC (21, 24, 25)”. This sentence is not clear. A verb is lacking. MTC is repeated three times. Please rephrase.

Reply 20: We feel sorry for the inconvenience brought to the reviewer. We have made corrections according to the reviewer’s comments (see Page 13-14, line 253-259).
Changes in the text:
Medullary thyroid carcinoma (MTC) is a rare and aggressive neuroendocrine carcinoma that accounts for approximately 1-2% of all thyroid cancers but 15% of thyroid cancer-related deaths and has a poor prognosis (37, 38). Early surgery with complete tumor resection has the potential to cure MTC, and postoperative monitoring of serum calcitonin and carcinoembryonic antigen (CEA) levels is essential (39). Nevertheless, management of advanced, progressive MTC remains challenging and is currently dominated by targeted therapies with tyrosine kinase inhibitors (TKIs) (40, 41), whereas resistance and adverse effects of TKIs still require further studies to improve the prognosis (42, 43).

257-8 “both of these the cost-effectiveness …” I was expecting the end of the sentence after “and both of these” but a new sentence with capital letter is starting…

Reply 21: We are very sorry for our incorrect writing. I have made extensive changes to the discussion section and removed this sentence. Please review the revised discussion.

260-3 “some studies”: 28-31 should be quoted beside “some studies” in order to understand you mean them.

Reply 22: It is true as the reviewer suggested that 28-31 should be quoted beside “some studies”. I apologize for the irregular quotes. I deleted that part when I revised the

discussion section. Please review the revised discussion.

265-6 “Third, the controversy about endoscopic thyroidectomy and open thyroidectomy (OT).” I miss a verb.

Reply 23: We are very sorry for our incorrect writing. As previously mentioned, I've modified the discussion and this sentence has been removed.

277-8” laryngeal retro-lateral nerve”: “laryngeal recurrent nerve”?

Reply 24: Thank you so much for your careful check. We apologize for our irregular writing and we have modified our text (see Page 13, line 242-243).
Changes in the text:
Return laryngeal nerve (RLN) injury is a common complication after thyroidectomy (28, 29).

284 “who undergo central neck clearance or have larger tumors” there is also literature describing no increased risk if central lymphadenectomy is performed by a high-volume-surgeon.

Reply 25: Thank you for your rigorous consideration. We don't read enough literature, leading to some incomplete view and we have re-written this part according to the reviewer’s suggestion (see Page 13, line 244-248).
Changes in the text:
Risk factors for postoperative RLN injury correlate with reoperation, type of surgery, malignancy, and tumor size, and some studies have shown a higher risk of vocal cord dyskinesia in patients who undergo central neck dissection or have larger tumors (4, 5). There is also literature describing no increased risk if central neck dissection is performed by high-volume surgeons (31).

288-9 “and reduces the risk of RLN injury (41, 42). However, some studies have shown that IONM failed to significantly reduce the incidence of RLN injury”. These sentences are confusing. Consider rephrasing.

Reply 26: Thank you for your comment. We feel sorry for the inconvenience brought to the reviewer. We have considered rephrasing as advised (see Page 13, line 249-252).
Changes in the text:
The IONM uses vocal cord electromyography to monitor the electrophysiologic activity of the RLN, which can help identify anatomical changes in the RLN during

thyroidectomy (32, 33). However, several studies have shown (34-36) that IONM fails to significantly reduce the incidence of intraoperative RLN injury compared to conventional RLN visualization.

290 I am not sure I would call “hypothyroidism” a complication of thyroid surgery. It is rather a consequence, if the remaining tissue is not enough. Or do you mean insufficient thyroxin-therapy for patients who should have suppressed TSH for carcinoma?

Reply 27: We apologize that hypothyroidism should not have been categorized here as part of the postoperative complications. At the time, we were just trying to analyze all the results, and the categorization was not rigorous. We have revised the discussion section as advised. This section has been deleted. Please review the revised discussion.

297-300. “Furthermore, the 2015 American Thyroid Association guidelines recommend that TSH levels should be maintained at 0.5-2 mIU/L in patients with low-risk DTC after undergoing thyroidectomy, and although most patients do not develop hypothyroidism after surgery, many patients with TSH levels >2 mIU/L and within the normal reference range still require thyroid hormone supplementation therapy (27, 54)”. I am not sure what this sentence means.

Reply 28: We apologize for not making the point clearly. We would like to express that although many patients do not develop hypothyroidism after surgery, the guidelines recommend that TSH levels should be maintained at 0.5-2 mIU/L. Many patients with TSH levels above the guideline recommendation (2 mIU/L), but within the normal range, also require thyroid hormone supplementation. Regarding this section, we have removed it. Please review the revised discussion.

300 “Chyle” with capital letter. New sentence.

Reply 29: Thank you so much for your careful check. We are very sorry for our incorrect writing. Regarding this sentence, we have removed it. Please review the revised discussion.

316-22 this sentence is also too long.

Reply 30: Thank you for your advice. We apologize for the lack of concise sentences. We have modified our text as advised (see Page 12-13, line 231-237).
Changes in the text:

However, the optimal threshold regarding postoperative serum Tg levels to predict disease recurrence was not determined. A 2020 cohort study showed that early postoperative Tg <2 ng/mL could be used as a threshold to guide adjuvant therapy and determine the frequency of long-term monitoring (24). Other studies have shown that even with Tg <1ng/mL, 131I radioiodine whole-body imaging (131I-WBS) still detects functional remnants of thyroid tissue, suggesting the possibility of tumor recurrence, and that Tg may not be able to identify tumor metastases of smaller size (25, 26).

The discussion is too long in my opinion. I don´t think you need to describe the results of the publications on a certain issue in detail but you should mention, why you think that some subjects have gained attention and why some subject will probably be important for furture research. In this present form this paper (and particularly the discussion) is difficult to read. Most stentences are too long, several sentences are incomplete, some redundant. A thorough language revision should be performed and the discussion must be better structured on the results you are presenting:

-The United States has the largest number of publications and the highest centrality (n=282, Centrality=0.28)

-THYROID and the AMERICAN JOURNAL OF SURGICAL PATHOLOGY are the most cited journals.

- Keyword-based clustering revealed the prominence of clusters such as follow up, recurrent laryngeal nerve (palsy ?!), and medullary thyroid carcinoma (why is that? Were there any changes? is the high mortality the reason?)

- Keyword burst detection showed that papillary had the highest burst intensity – why? because it is the most common? because of the low malignancy of most tumors, requiring less aggressive treatment?

- why will active surveillance be a hot spot of research in the future? (For example, almost no similar management for other carcinomas, reluctance to accept it in Europe, geographic differences, reports on metastatic nicrocarcinomas and no currently available biomarkers, etc…)

Please shorten the discussion and introduce more structure.

Reply 31: We gratefully thank you for the precious time the reviewer spent making constructive remarks. Our discussion section is indeed too long. We should mention

why some subjects have gained attention and why some subjects are hot spots for future research. Thank you for pointing out this problem in the manuscript. We have rewritten this part according to the reviewer's suggestion. We have shortened the discussion as much as possible and introduced more structure. Please review our revised discussion.