Peer Review File

Article information: http://dx.doi.org/10.21037/gs-20-468.

Reviewer A

In this retrospective study clinical outcomes of TORT (n=248; between 2008-2016) and BABA-RT (n=316; from 2012 onwards) performed by a single suregon were compared. Authors found that TORT had not only advantages in better cosmetic outcomes with minimized postoperative scars, but also showed comparable, or even superior, surgical outcomes with shorter operation time than the former BABA-RT procedure.

Novelty of this study is that it compared a large number of patients operated on by a single surgeon with two different remote access robotic approaches to the thyroid (as previous contribution on the same topic was based on 90 patients only). The study is properly reported. The outcomes are of interest in the field. However, there are few point which need to be addressed in a reised manuscript.

Major issue:

1. It is not fair to state in the conclusion that TORT had shorter operation time than the BABA-RT procedure taking into consideration that the former one consisted of unilateral thyroid lobectomy in 93.5% of operations and in the the latter one the extent of surgery was total thyroidectomy performed in 64.2% of operations. I would suggest to show in Table 3 operation time for TORT vs. BABA-RT separately for lobectomy vs. total thyroidectomy with respect to the surgical approach used. Please revise this part of your conclusion. Discuss your previous contribution (J Surg Oncol 2018 Sep;118(3):381-387) on the same topic in which there was no difference in operation time between these two approaches.

2. There was not difference in tumor size between TORT vs. BABA-RT groups (0.96 ± 0.95 vs. 0.86 ± 0.91 ; p=0.209) and I wonder why two-thirds of patients had total thyroidectomy in the latter group vs. 5.6% in the former group taking into consideration that it was reserved for: tumors > 4 cm, extrathyroidal extension, clinically apparent lymph nodes or distant metastases. In all other cases, lobectomy \pm CND was performed. 3. It looks that authors have abandoned performing BABA-RT since 2017 and TORT is the preferred surgical approach in all eligible patients for remote access thyroid

surgery. Please comment in the discussion if this is a surgical bias or choice supported by superior cosmetic outcomes of TORT (or maybe a better patients acceptance of the method).

Other issues are relatively minor:

4. Almost one-third of your patients has thyroiditis hhich per se is considered an exclusion criterion for minimally invasive thyroid surgery. Please clarify if it was pathological finding or positive anti-TPO and corresponding preoperative ultrasonographic characteristics.

5. Please clarify in the methods section if prevalence of nerve events was calculated per nerves at risk.

6. Please indicate in how many patients CND was unilateral vs. bilateral (separately for TORT vs. BABA-RT).

7. Use of English should be improve through the entire manuscript.

Reply: Thanks for your good point. The difference between lobectomy and total thyroidectomy has changed according to the trend of the times, and this paper wants to argue that TORT is not bad compared to the previous BABA surgery method, and since statistics have already been completed, the results cannot be turned back now. Regarding your point of view, I will write it down as a limitation in this paper. Also, This operation—lobectomy and unilateral prophylactic central neck node dissection—is not a standard operation in the United States. The 2015 ATA guidelines recommend either a lobectomy or active surveillance for micropapillary thyroid cancer. For 1–4-cm papillary cancer, lobectomy or total thyroidectomy is recommended, but prophylactic central neck dissection is discouraged. However, central neck compartment dissection is not technically difficult in TORT as mentioned earlier, and it is difficult to perform reoperation in the case of a later central lymph node recurrence; therefore, we performed prophylactic ipsilateral central neck compartment dissection initially.

Reviewer B

The retrospective nature of the study makes an objective comparison between the two

techniques impossible. Even if the surgeon is only one, 10 years has a significant influence on the learning curve and therefore the comparison is not reliable again. The groups are not homogeneous and therefore not comparable: lobectomies cannot be mixed with total thyroidectomies, benign vs malignant, as the lymphadenectomies of the central compartment cannot be compared with the unilateral paratracheal ones (in addition the mean number of lymph nodes removed is below the standard and in most cases was not indicated following recent guidelines

Reply: It shouldn't be compared with a doctor's 10-year learning curve, it was when I performed 300 cases of thyroidectomy with each method.

Reviewer C

This is a fairly large series of one surgeon's experience by two different procedures for thyroidectomy. The manuscript requires extensive language corrections, the lack of which makes this manuscript difficult to interpret. There are several issues which probably should be expanded to make the manuscript more appealing to readers. The rationale for two different approaches and the selection of patients needs to be described. The authors have described TORT. They have also described about the axillary port. This needs to be expanded since majority of the transoral procedures in the recent literature are without axillary port. The rationale for extent of surgery needs to be explained in the manuscript as to extent of thyroidectomy and extent of neck dissection. It remains unclear in this manuscript as to the message of the manuscript. This should be expanded more in the discussion, which is very superficial and does not convey the message of this manuscript. The indications for the two procedures and the selection is separate and I'm not sure the comparison of the two procedures is scientific. However, since this is an experience of one surgeon, it would be appropriate to reconsider for publication.

Reply: Thanks for the good advice. When writing the next paper, I will refer to your advice and write it.

Reviewer D

This paper reports a retrospective study that compares the surgical outcomes of transoral robotic thyroidectomy (TORT) and Bilateral Axillo-Breast Approach Robotic Thyroidectomy (BABA-RT) performed by a single surgeon at a single centre in South Korea.

The authors should be commended for undertaking this study. While this is not the first paper in the literature to compare outcomes between TORT and BABA-RT, this paper reports the largest number of patients in the two groups to date, allowing for a better powered study to compare the postoperative outcomes between them. Therefore, there is certainly sufficient merit for this paper to be published.

However, there are several important points that need to be addressed before this paper is suitable for publication. Please refer to the list below.

In addition, the manuscript requires extensive English language editing – I have highlighted these areas of deficiency and suggested amendments.

1. Page 3, line 3: "The use of robotic systems for thyroidectomy has increase as it enables for more diverse approaches than the conventional open methods". The English grammar is wrong. The sentence should be rewritten as "The use of robotic systems for thyroidectomy has increased as it enables more diverse approaches than the conventional open method".

2. Page 3, line 8: "This study was designed as a retrospectively". The sentence structure is wrong. It should be rewritten as "This study was designed as a retrospective study".

3. Page 3, line 10: Suggest to rewrite "Total thyroidectomy + Central node dissection (CND)" as "Total thyroidectomy with central node dissection (CND)..."

4. Page 3, line 11: "... had an extrathyroidal extension..." should be written as "... had extrathyroidal extension...". Remove the word "an".

5. Page 3, line 15: Please refer to point number 29.

6. Page 3, line 25: "the former BABA-RT procedure" should be written as "the BABA-RT procedure"

7. Page 5, line 4: "Endoscopic surgery was the first attempt by Gagner and then, Hushcher et al. for the surgical treatment of thyroid and parathyroid glands" should be written as "Endoscopic techniques for the surgical treatment of parathyroid and thyroid glands were first reported by Gagner (1) and Huscher et al. (2) respectively."

8. Page 5, line 15: "This technique of natural orifice transluminal endoscopic surgery applied to the thyroidectomy through an intraoral approach has been started in pigs, bodies, and since 2008 in humans (4 - 6)" should be rewritten as "This technique of natural orifice transluminal endoscopic surgery applied to thyroidectomy through an intraoral approach has been performed in a porcine model and human cadavers (4 - 6), and since 2009, in patients (7)". Reference number 7 [Wilhelm T, Metzig A. Endoscopic minimally invasive thyroidectomy (eMIT): a prospective proof-of-concept study in humans. World J Surg (2010)] should be cited here since it is the first paper that reports using endoscopic minimally invasive thyroidectomy in patients, with the first successful demonstration in humans done in 2009 (and not 2008).

9. Page 5, line 17: "There are two methods of transoral natural orifice transluminal endoscopic thyroidectomy". Can the authors please provide the reference for this statement?

10. Page 5, line 19: "The trans-sublingual method is not well used because of the relatively large number of complications...". Can the authors please provide the reference for this statement?

11. Page 5, line 22: "since it has become popular" should be rewritten as "since then, it has become popular".

12. Page 5, line 23: "and one additional axillar port on the right axilla" should be

rewritten as "and one additional axillary port in the right axilla".

13. Page 5, line 24: "The use of robotic systems for thyroidectomy has increase as it enables for more diverse approaches than the conventional open methods" should be rewritten as "The use of robotic systems for thyroidectomy has increased as it enables more diverse approaches than the conventional open method".

14. Page 5, line 26: "However, we have reported the feasibility of TORT in our previous study (12), but we could not demonstrate the advantages of TORT compared to BABA-robotic thyroidectomy (RT)" should be rewritten as "We have reported the feasibility of TORT in our previous study (12), but our study did not compare the clinical outcomes of TORT with BABA-robotic thyroidectomy (RT)".

15. Page 7, line 4: The authors should provide any institutional review board approval reference number if available.

16. Page 7, line 5: "TORT is on place since 2012" should be rewritten as "TORT is in place since 2012"

17. Page 7, line 8: "According to ATA guidelines,...". Can the authors please write the full name as American Thyroid Association (instead of abbreviating it as ATA) and state the year of the guidelines (e.g. 2015) and provide reference to the publication? Additionally, the following sentence "total thyroidectomy + central node dissection (CND) was performed only if tumors were > 4 cm and had an extrathyroidal extension..." should be rewritten as "total thyroidectomy with central node dissection (CND) was performed only if tumors were > 4 cm and had extrathyroidal extension..."

18. Page 7, line 9: Regarding extrathyroidal extension (ETE), the authors need to state whether they are referring to microscopic ETE or gross ETE, or if they do not make any distinction between the two. This is important since the latest AJCC/UICC TNM 8th Edition Guidelines makes a distinction between the two, and only gross ETE (but not microscopic ETE) upstages a tumour to a T3 disease.

19. Page 7, line 14: Could the authors please add the word ''indirect" to "laryngoscopy" to be more specific?

20. Page 7, line 15: Could the authors please explain what they mean by 'breast subcutaneous insufficiency'? Such a term is not commonly used.

21. Page 7, line 19: Could the authors please provide a reference to the authors' previous publication where the surgical technique was described in more detail? Could the authors also specify in more detail the exact location of the trocars on the lower lip? This point is important since positioning of the trocars previously have been shown to affect the rate of mental nerve injury.

22. Page 7, line 21: "and to drain post-surgery insert" should be rewritten as "and to insert drain post-surgery".

23. Page 7, line 21: "Epinephrine dilution (1:200.000) was injected.." Can the authors clarify what they mean by the dilution? Epinephrine (1:200, 000) mixed with lidocaine HCl 0.5%? Mixed with saline? Besides that, 1:200.000 should be written as 1:200,000.

Reply: This is to minimize bleeding during surgery.

24. Page 7, line 22: "The upper and lower margins of the flap were the thyroid cartilage, the sternal notch, and the medial border of the sternocleidomastoid muscle". This sentence does not make sense. Perhaps the authors meant "The upper and lower margins of the flap were the thyroid cartilage and sternal notch, with the lateral margins being the medial border of the sternocleidomastoid muscle of either side"?

25. Sample size & power calculation: Was any power calculation done to determine the sample size needed to detect a clinically significant mean difference of their endpoints between the two groups of the study?

Reply: The number of patients is for the total patient group who underwent surgery on the thyroid gland with robots.

26. Page 9, line 4: the authors mention that there are no differences between the mean age, BMI and sex distribution. However, for the sex distribution, the p value stated is 0.009 (see line 7). The next sentence in line 7 mentions that "There was a difference in gender between the two groups.....". Can the authors please explain this discrepancy?

27. Page 9, line 8: Can the authors please explain what do they mean by "There was a difference in gender between the two groups, which is probably thought to have a cosmetic importance in men recently." This sentence structure does not make sense. Do they mean "There was a difference in gender between the two groups. This is probably thought to be due to men in our population placing a greater emphasis in cosmetic importance in recent times, causing them to opt for TORT." Is this merely a speculation or a valid reason? – the authors need to state which is the case, and if this is a valid reason, the authors ought to provide a reference.

28. Page 9, line 12: Can the authors please explain why the fact that most thyroid surgeries are done by a robot at their hospital means that the ratio of benign tumors in the TORT group is higher? Is there a selection bias? And aren't both groups different forms of robotic surgery anyway?

Reply: As the rate of open surgery has decreased and almost all thyroid surgery is performed with TORT robotic surgery, it is thought that the rate of benignity of TORT has increased.

29. Page 9, line 13: The authors state that the postoperative stay was shorter in the TORT group compared with the BABA-RT group, yet the mean difference is only 0.6 day, which is about 14 hours. While this may be statistically significant, is this clinically significant? The authors should mention this in their Discussion.

30. Page 9, line 13: The authors state that the number of retrieved lymph node was higher in the TORT groups with a p value of 0.01. Yet the spread of values of both groups, as defined by the standard deviation, show a large overlap (4.9 ± 4.4 vs 4.2 ± 4.9). Could the authors please justify this and confirm that the p value is indeed 0.01? Additionally, even if there was true statistical significance, would a difference of 4.9

versus 4.2 lymph nodes be clinically significant? The N stage in the TNM staging for thyroid cancers does not depend on the number of harvested lymph nodes. The authors should mention this in their Discussion.

31. Page 9, line 18: Regarding postoperative time, the authors acknowledge that the greater number of lobectomies done in TORT may contribute to the shorter operative time. As such, it is unfair and inappropriate to pool together the operative times from total thyroidectomy, lobectomy and bilateral subtotal thyroidectomy in comparing TORT vs BABA-RT. Perhaps the authors should also consider separate comparisons of the operative times of the three different types of thyroidectomies (total thyroidectomy, bilateral subtotal thyroidectomy and lobectomy) in TORT vs BABA-RT. It may be likely that when such like-for-like comparisons are made, the respective operative times may not actually be shorter. This is an important issue that the authors should address.

Reply: This was done for all patients, and if the number of total thyroidectomy through TORT increases in the future, we will divide it into groups and compare them.

32. Page 9, line 20: Could the authors explain why there was a recent trend toward lobectomy in their cases? Is this because their practice changed with change in the ATA guidelines? If that is the case, the authors should justify how they decide on patients for total thyroidectomy vs lobectomy before the introduction of the new guideline and how their decision-making changed after introduction of the guideline. The authors should mention this in their Discussion.

33. Page 9, line 24: It would be useful if the authors elaborate when did the bleeding occur (which postoperative day), where the source of bleeding was, and how the postoperative bleeding was addressed? Did they have to create a new collar incision in the anterior neck (as in conventional open thyroidectomy) to stop the bleeding?

34. Page 9, line 24: regarding chyle leak, it would be useful if the authors elaborate when was the chyle leak detected. Did they attempt conservative medical management of chyle leak first (as is usually the case) or did they proceed straight to surgery? How did they surgically address the chyle leak? Did they have to create a new collar incision

in the anterior neck as well?

Reply: When chyle leakage, we solved it again with a robotic surgery, and bleeding can be solved with laparoscopy. In the case of seroma complication, continuous drain (hemovac) was applied.

35. Page 9, line 28: regarding postoperative seroma, how did the authors manage this complication in the 7 cases? Were they conservatively managed or surgically/percutaneously drained?

36. Page 10, line 7: Could the authors please elaborate more the initial learning curve period of TORT – in the authors' experience, how many cases must a surgeon perform before he or she achieves proficiency in performing TORT? Since the single surgeon first performed BABA-RT in 2008 before starting to perform TORT in 2012, will his experience with BABA-RT give him a better head-start with learning TORT? Therefore, will the surgical outcomes reported in this study be directly comparable with a hypothetical situation where another surgeon with no experience of BABA-RT starts out to learn TORT? The authors should consider addressing this question in the Discussion. I acknowledge that the authors did mention that as experience increased with the number of cases, this could cause bias; however, more needs to be mentioned regarding this issue, as I have elaborated in this paragraph.

Reply: This paper is the main paper on the prognosis for TORT and BABA surgery. I will write the pointed out by referring to the next paper.

37. Page 11, line 3: Can the authors explain what they mean by 'total surgical outcome'? And how can this be equivalent between TORT and BABA-RT when they state that the TORT group have better outcomes for retrieved lymph nodes in papillary thyroid cancer, decreased postoperative pain, hospital stay, etc.?

38. Page 11, line 6: "postoperative complications in seroma" should be rewritten as "postoperative complications of seroma".

39. Page 11, line 9: "smaller flap range" should be reworded as "smaller flap dissection area"

40. Page 11, line 13: "This causes many surgeons to try trans-oral surgery...". Suggest to reword this to "Many surgeons have attempted trans-oral surgery..."

41. Page 11, line 23: "There was a statistically significant difference in the total number of thyroidectomies between both groups" is erroneous as the authors are actually referring to total thyroidectomies and not total number of thyroidectomies. Therefore, it should be rewritten as "There was a statistically significant difference in the number of total thyroidectomies between both groups

42. Page 11, line 24: Please state which guideline for thyroid surgery the authors are referring to.

43. Page 11, line 25: "Another difference was the number of retrieved LNs. There was a relatively high difference in TORT, since this procedure is performed in a head-to-food operative position meaning that the operation is more delicate due to a more comfortable posture and view." This sentence is rather confusing and vague. What do the authors mean by a 'delicate operation' and how does a comfortable posture and view in TORT cause the operation to be 'more delicate'? Additionally, how does the operative position of the procedure and the 'delicateness' influence the number of retrieved lymph nodes? The authors need to clarify this.

44. Page 11, line 29: "relative small selective bias..." should be reworded as "relatively small selection bias..."

45. Page 12, line 4: Could the authors please state how long was the follow-up period for TORT and BABA-RT was in this study?

Reply: This paper did not investigate recurrence, so we did not investigate statistically.

46. Page 12, line 5: Could the authors please state which different time periods are

associated with the change in operation method?

47. Page 12, line 6: "It cannot be seen as completely randomized study, but it can be free from the selection bias, because the data were collected consecutively and we used whole data without omission." Suggest to rewrite the sentence as "It is not a randomized study, but it is free from selection bias because the data were collected consecutively and we used whole data without omission."

48. Page 12, line 10: '...BABA-RT. TORT not...". The punctuation mark should be a comma between BABA-RT and TORT, not a full stop.

49. Page 12, line 12: please remove the word 'former'.

Reviewer E

There are a number of issues with this paper which would need to be addressed if it were to be published.

1. The statement in abstract and background "robotic systems for thyroidectomy enables more diverse approaches than conventional open methods" seems to be used a justification for using this approach. I think there needs to be more discussion of why a procedure which takes 3.5-4 hours is being done to avoid a neck scar, when in the UK at least, satisfaction with cosmesis from open methods is very high, particularly in the long-term.

I realise there may be cultural reasons why neck scars are considered so problematic in Korea, but this needs to be discussed, as these robotic thyroidectomies are more time consuming, involve more extensive tissue dissection, as access to thyroid is remote, are more painful therefore and expensive, and also introduce complications such as mental nerve injury that we do not have with open methods.

2. The statement that TORT has better cosmetic outcomes in the abstract and discussion is not backed up by any evidence from the results. In fact there has been no evaluation of cosmetic or quality of life outcomes in this study despite the fact that were a number of reported complications in the TORT group that could have affected cosmetic outcome (dimpling skin flap, chin flap perforation) and quality of life (mental nerve injury). Note also the incidence of mental nerve injury is high 3.6%. This is not mentioned in the results text though appears in the table. Needs further discussion as this is a potential cause for medicolegal issues particularly as this complication does not occur in open thyroidectomy or BABA-RT.

3. The reason for the shorter operating time in TORT is likely to be due to a significantly higher proportion of lobectomies in the TORT group (93.5% v 35.1% in the BABA-RT group). This is not apparent from the abstract. Likewise the incidence of RLN palsies needs to be quoted per nerve at risk and the incidence of hypoparathyroidism is heavily influenced by the extent of surgery, and is in fact negligible after first-time thyroid lobectomy. So in fact the difference in the outcomes of operating time, RLN palsy and hypoparathyroidism between TORT and BABA-RT found in this study are likely to be due to the higher proportion of lobectomies in the TORT group rather than any difference from operative approach.

4. Its not clear how many lymph node dissections were undertaken.

5. The mean tumor size was 0.8-0.9 cm. Hence these are mostly PTMC. Discussion has to made therefore regarding the need for surgery in such small cancers particularly as there is growing recognition that the prognosis of these tumours is excellent and trials of observation without operative intervention are now occurring.

6. There are a number of typos and grammatical errors.

7. Apologies for rejecting this paper but I don't think it comes near to the standard needed for publication, though there are good numbers in the study and the outcomes are from a relatively new approach to thyroidectomy.

8. The reasons why patients were chosen for each approach are not clearly described also.

Reply: Thanks for your advice. The difference between lobectomy and total has changed according to the trend of the times, and what we would like to argue through this paper is that TORT is not bad compared to the previous BABA surgery method.

The authors have completed a promising review of more than 500 patients over the last decade. The strengths of this work include that all cases were completed by a single surgeon who utilized different techniques at different time points.

In its current form, the article will require significant edits for grammar and syntax, as well as readability.

A few additional points

1- between 2008-2020, there were significant changes in ATA guidelines. The authors state that they followed the most recent (2015) ATA guidelines, but that does not seem intuitive for those earliest cases before current ATA guidelines were in force. In earlier guidelines, total thyroidectomy had been recommended more liberally.

2- operative times should be compared lobe:lobe and total:total instead of in aggregate3- please clarify why the difference in rates of malignancy differ between the 2 cohorts4-please explain "chin dimpling," and whether or not this was permanent. A photo or figure may help

5- the list of citations is somewhat limited with regards to the available literature on this topic

In conclusion, interesting work, but needs significant editing for style, grammar, and syntax before this paper is ready for publication.

Reply: Thanks for the good advice. When writing the next paper, I will refer to your advice and write it.

Reviewer G

This is a well-written paper. I have a few questions to ask:

How did the surgeon chose TORT or BABA to perform? Was it based on patients' perference?

Authors concluded that TORT have several advantages compared with BABA, including complications. However, the extent of surgery have significant difference since different time period. To fix this issue, authors could compared those patients who underwent lobectomy and total thyroidectomy by TORT and BABA, respectively. OR added this limitation to the discussion section.

Reply: It was not a method of selecting surgery depending on the patient. In the early days of robotic surgery, the operation was performed through BABA surgery, and after that, as the transoral surgery method that did not leave a wound was developed, TORT surgery was performed later. The difference between lobectomy and total has changed according to the trend of the times, and what we want to argue through this paper is that TORT is not bad compared to the previous BABA surgery method. The point you pointed out is that we will intervene additionally as a limitation.