

Peer Review File

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Reviewer A

The authors have created a well-thought-out manuscript with implications for all surgeons. Great work.

Response: Thanks for your recognition and encouragement.

Reviewer B

1. It would be more appropriate to further discuss your views and how your markers can be implemented in a routine clinical assessment. How would you select these patients and how would you re-address their treatment. What criteria would you use during their follow-up? How would you modify the TyG index and the TG/HDL-C ratio? Therefore, the discussion should be reviewed and focus more on your results and what your suggestions are in relation to the implementation of your findings in current clinical practice. Nevertheless, a certain degree of uncertainty remains.

Response: The reviewer raised very important issues. We have further discussed our views and how the markers can be implemented in a routine clinical assessment (see Page 13, line 329-351). Implementing the TyG index into routine clinical assessments requires more standardized protocols for measuring fasting triglyceride and glucose levels. Establishing threshold values indicating increased risk and developing guidelines for clinical decision-making based on these values would be essential. Large-scale prospective studies are needed to confirm its reliability and reproducibility across diverse patient populations. Patients with a higher TyG index than the threshold might be considered for more intensive monitoring post-TEVAR or could receive more aggressive management of cardiovascular risk factors, such as stricter blood pressure control and the utilization of antihypertensive drugs. Follow-up criteria for TBAD patients who have undergone TEVAR includes regular imaging studies, which are essential to evaluate the aortic repair site; regular clinical examinations to assess symptoms, including chest or back pain, signs of organ malperfusion; strict blood pressure control that is vital in preventing aortic expansion and reducing the risk of further dissection or rupture; periodic blood tests which can help assess renal function, monitor for end-organ damage, and evaluate metabolic parameters; medication adherence that ensure patients are compliant with prescribed medications, including antihypertensives, antiplatelet agents, or anticoagulants, if indicated.

Finally, TyG index and the TG/HDL-C ratio, representing the IR mechanism which is often neglected in the treatment of TBAD patients, may be used to improve the precision of traditional predication models. Combination indexes, such as TyG-platelets index, may also be made by integrating the TyG index and other traditional risk factors such as neutrophil-to-lymphocyte ratio, platelets, and D-dimer etc.

Due to the limitations of the current research, we have modified the theme of this article, which investigates the association of the TyG index and TG/HDL-c with the prognosis of all-cause mortality.

2. Page 2, line 24: it is more appropriate to say "...index is a reliable surrogate..."
Response: We have rectified that (see Page 2, line 32).
3. Page 2, line 26: it is more appropriate to say "...its association with..."
Response: We have rectified that (see Page 2, line 34).
4. Page 2, line 39: leave a space after full stop "...undergoing TEVAR. Special attention..."
Response: We have rectified that (see Page 2, line 50).
5. Page 3, line 54: it is more appropriate to say "...and postoperative monitoring."
Response: We have rectified that (see Page 3, line 66).
6. Page 5, line 79: it would be more appropriate to say "...with sparing of the ascending aorta."
Response: We have rectified that (see Page 5, line 91).
7. Page 5, line 80: it would be more appropriate to say "...is the highest in the 65 to 75 years age range..."
Response: We have rectified that (see Page 5, line 92).
8. Page 5, line 86: it would be more appropriate to say "...aortic dilatation..."
Response: We have rectified that (see Page 5, line 99).
9. Page 5, line 86: it would be more appropriate to say "...after TEVAR may undermine its advantage."
Response: We have rectified that (see Page 5, line 100).
10. Page 5, line 86-88: it is not clear what you are trying to say; it would be more appropriate to rephrase because it looks as if words are missing.
Response: We have rectified that (see Page 5, line 101).
11. Page 5, line 95: replace with "...in the tissues and..."
Response: We have rectified that (see Page 5, line 110).
12. Page 6, line 136: it would be more appropriate to say "...of patients requiring re-admission or reviewed in clinic."
Response: We have rectified that (see Page 7, line 159).
13. "Page 7, line 140-141: it would be more appropriate to say "Two clinicians experienced in the diagnosis and treatment of TBAD blindly evaluated the adverse events and patients' outcome."
Response: We have rectified that (see Page 7, line 165).
14. Page 10, line 256: it is more appropriate to say "It has been shown that..."
Response: We have rectified that (see Page 10, line 258).

15. Page 11, line 258-260: is it really necessary to say that this is the first study to investigate the association...? This sort of statements always sounds presumptuous and arrogant and do not add any value to the article. On the other hand, it would be more appropriate to say that the study has been designed specifically to analyse a potential relationship between TyG index and the long-term prognosis of TBAD patients undergoing TEVAR which may have a role to play in the management of the residual disease. Then, you can further develop your argument and your views on the subject.

Response: We have rectified that (see Page 10, line 260-263).

16. Page 11, line 265: it is more appropriate to say "Aortic dissection has been recognised as..."

Response: We have rectified that (see Page 11, line 268).

17. Page 11, line 266-267: it would be more appropriate to say "Local neutrophils recruitment and activation has been observed to trigger aortic rupture while disruption of IL-6 significantly decreases dilatation of the dissected aorta."

Response: We have rectified that (see Page 11, line 269-270).

Reviewer C

1. Line 106: long term outcomes in this manuscript are used referring to 1-year outcomes. However, 1-year time frame is usually indicated as short term or intermediate term. Therefore, the expression "long term" should be avoided to refer to 1-year. To avoid confusion, I recommend to replace any instance of "long term" with "1-year" in this manuscript.

Response: The reviewer raised a very important issue. We have replaced any instance of "long term" with "1-year".

2. Line 124 "limited surgery". The meaning of this expression is not clear. Do you refer to interventions that are not performed in urgent / emergency setting? please clarify and correct.

Response: We fully agree with the reviewer. We have clarified and corrected it (see Page 6, line 146-147).

3. Line 138 "long-term outcomes": see above.

Response: The reviewer raised a very important issue. We have corrected it.

4. Line 143-144 "According to TyG index levels, participants were categorized into three tertiles: Q1 (n =315, TyG index <8.44), Q2 (n =305, $8.44 \leq$ TyG index <8.93), and Q3 (n =315, TyG index \geq 8.93)" the use of "Q1, Q2, and Q3" could be misleading, as these labels are more conventionally used for quartiles, which divide the population into four equal parts. For tertiles, it's more appropriate to use terminology like "Tertile 1 (T1), Tertile 2 (T2), and Tertile 3 (T3)" or "Lower Tertile, Middle Tertile, and Upper Tertile." These labels clearly convey that the population is divided into three segments and avoid confusion with quartiles or other forms of segmentation. Please correct here and elsewhere in the text.

Response: Thank you for your kind reminder. We have modified our text as advised (see Page 7,

line 167-171).

5. Line 297, 299 “mellitus diabetes”: please correct into “diabetes mellitus

Response: We have modified our text as advised (see Page 12, line 304-305).

6. Line 521 (table 1) change “Diabetes mellites” into “Diabetes mellitus”

Response: We have modified our text as advised (see Page 21, line 558).

Reviewer D

Good idea. However, the paper presents many methodological biases.

In current form it adds nothing new to the knowledge of TBAD after TEVAR. It gives only another data to the population does not matter it has or not TABD.

Moreover, this presentation of data falsely suggests existing relationships between independent factors. It cannot be published in its current form.

I suggest a fundamental change in the methodology and removal of the bias associated with actual and recognized risk factors, and then extending the analysis to include the TyG index tested by the authors, the impact of which should be confirmed in a discriminatory analysis. I also suggest supplementing the statistics with an analysis of the determination of the criteria values for the 3 extracted groups, e.g. in the ROC analysis, because now it gives the impression of made-up values.

It is necessary to supplement table 1 with the actual radiologically significant factors influencing the risk of ARAEs and to analyze the possible impact of TyG in their context.

Please treat my comments as kind help in obtaining good quality work. Because the topic is worth publishing, but definitely not in such a poor form.

In detail

Title

The relationship indicated in the study generally applies to the population and is not related to whether the patient has undergone TEVAR or had TBAD. This is confirmed by supplementary tables 1-4. There is nothing at work that allows the paper to have the title it currently has. It should be changed from: “TyG-index predicts the prognosis in type B aortic dissection patients receiving TEVAR” On: “TyG-index predicts the prognosis in patients with type B aortic dissection receiving TEVAR.” Because this concerns patients with their medical burdens, not the disease itself or the treatment. Please change.

Response: We fully agree with the reviewer and have modified that (see Page 1, line 2-3).

Substantive comments on the methodology

1. In the assessment of selected ARAEs (aortic rupture, malperfusion, RTAD, aortic dilation, type I/III endoleak), there is no analysis of the impact of the actual anatomical factors causing them and those based on the assessment of FL outflow (e.g. Stanford Dissection Risk Calculator). See notes to table 1.

Response: The reviewer is definitely professional in that regard. However, due to the retrospective nature of this study and the relatively short revised time, data on entry tear > 1

cm, FL >22mm, high Fusifrm index, etc. may not all be available. We apologize for that and modify the theme of this article, which investigates the association of the TyG index and TG/HDL-c with the prognosis of all-cause mortality.

2. Incorrect or incorrectly defined landing zone (see line 121) Zone 1 is not a TBAD. TBAD is a one with entry in zone 3 or 4. Please clarify.

Response: We apologize for that error and have rectified that (see Page 6, line 143).

3. Undefined way of setting criteria values for TyG index. Line 143-145. How the authors set the criteria for TyG index? Please explain? ROC? Other methods? Moreover, it is not known whether the groups differing in the established TyG Index criterion >8.93 were homogeneous in terms of classic risk factors.

Response: The reviewer proposed an important question. We have revised the main conclusions. The participants were classified into five groups by the quintiles of TG/HDL-c ratio, [Q1 (n =186, TG/HDL-c ratio <1.44), Q2 (n =187, $1.44 \leq$ TG/HDL-c ratio <2.09), Q3 (n =188, $2.09 \leq$ TG/HDL-c ratio <2.97), Q4 (n =186, $2.97 \leq$ TG/HDL-c ratio <4.11), and Q5 (n =188, TG/HDL-c ratio \geq 4.11)], and the Q4 group was used as the reference group, (see Page 7, line 167-171).

4. Was discriminant analysis (Wilks Lambda) performed? To determine what independently influences ARAEs?

Response: The reviewer is definitely professional in that regard. We added the discriminant analysis (Wilks lambda), and the results are depicted in Supplementary Tables 3 and 4.

5. It is not specified in the limitations that the study was not originally planned for the TyG Index, but is a retrospective assessment of computer-collected data, including the TyG index?

Response: We appreciate the kind suggestion of the reviewer. We have added that in the limitation section (see Page 13-14, line 357-358).

Table1. Anatomical factors selected inappropriately. Please list and compare the classic recognized risk factors not only partial FL thrombosis. But also: Entry tear>1cm, FL >22mm, high Fusifrm index, Inner curve entry tear, aortic size>40mm, and Stanford Risk Calculator factors including number of patent intecostal arteries, out-flow entry in visceral and iliac arteris, angle dissection etc. What is in the table does not prove that the groups were similar. This is even contradicted, because the equal percentage of partial FL thrombosis proves that the patients differed in terms of outflow from FL. And this is the most important prognostic factor in TBAD. THIS is such a strong bias that it cannot be completely ignored. And please replace the length of dissection with the volume of perfused FL, because it is this volume that has a prognostic value (numerous studies!!!), not the length (it makes no sense at all). Although I understand that it was easy to measure so that's why it's in the table. Please complete otherwise the entire table 1 is useless.

Response: We fully agree with the reviewer and realize the importance of the anatomical factors for ARAEs. However, due to the retrospective nature of this study and the relatively short revised time, data on entry tear > 1 cm, FL >22mm, high Fusifrm index, etc. may not all be available. We apologize for that and modify the theme of this article, which investigates the

association of the TyG index and TG/HDL-c with the prognosis of all-cause mortality.

Table 2. The comparison of the TyG Index with complications such as malperfusion, RTAG and others makes no sense due to the lack of reference to the recognized factors causing them. Note that RTAD depends more on oversizing and the length of the landing zone (coverage distance from the entry) and the aortic angle at the landing zone rather than on TyG. The same applies to rupture and endoleaks, but also to malperfusion (here comes SINE and the length of coverage-which was not reported). What statistical basis are the authors' suggestions based on? Does anything support this claim? I didn't find anything like that in my work - please remove or modify it, specifying limits as suggested.

Response: We agree with the reviewer and have modified the table.

Table 3. The same applies to the cumulative risk of dilation, rupture, endoleaks and malperfusion during the one-year observation period!!!. Please remove or modify with reference to the actual risk factors for these complications and specify the limits of what the authors present in accordance with the above suggestion.

Response: We accepted the kind suggestions of the reviewer and made the modification (see Page 24, line 568).

Minor issue

Line 89-90. The cited paper (8-10) did not prove a relationship between the factors and the outcome after TEVAR. They only pointed to the possibility of some relations. Weak evidence. Please cancel or rephrase.

Response: We fully agree with the reviewer and rephrase that (see Page 5, line 104-105).

Line 121. Zone 1 is not a TBAD. TBAD is a one with entry in zone 3 or 4. Please clarify

Response: We agree with the reviewer and have corrected that (see Page 6, line 143).

Line 137-138. ARAE such as aortic rupture, malperfusion, RTAD, aortic dilation, type I/III endoleak are depend on technical failure only. No logical correlation witch metabolic disorders. Please clarify and comment

Response: We accept the suggestion of the reviewer and have rephrased that. We have modified the theme of this article, which investigates the association of the TG/HDL-c and TyG index with the prognosis of all-cause mortality.

Reviewer E

1. Line144: 935 patients are divided into TyG index values of 8.44~8.93, is this number common? Is there the evidence-based medicine for this number?

If the figures have the evidence of based medicine, please indicate the relevant literature.

Response: The reviewer raised a very important issue. We have revised the main conclusions. The participants were classified into five groups [Q1 (n =186, TG/HDL-c ratio <1.44), Q2 (n

=187, $1.44 \leq \text{TG/HDL-c ratio} < 2.09$), Q3 (n =188, $2.09 \leq \text{TG/HDL-c ratio} < 2.97$), Q4 (n =186, $2.97 \leq \text{TG/HDL-c ratio} < 4.11$), and Q5 (n =188, $\text{TG/HDL-c ratio} \geq 4.11$), by the quintiles of TG/HDL-c ratio, and the Q4 group was used as the reference group, (see Page 7, line 167-171).

2. Line 121~122: TBAD was classified as an aortic dissection with an entry tear in zone 1 or more distal aortic zone.

Does this mean that some of the type A aortic dissection are included in the treatment target?

Response: The reviewer raised a very important issue. This study focused on patients with type B aortic dissection receiving TEAVR and we have rectified that (see Page 6, line 143).

3. Line 123: AD was categorized as acute (1-14 days), subacute (15-90 days), and chronic (>90 days) according to SVS/STS recommendations.

In the first place, what are the indication criteria for the chronic phase of TEVAR? Also, in the evaluation of ARAEs, I understand that the timing of TEVAR is a factor that effects a major role in the development of RTAD.

Response: The reviewer raised a very important issue. Based on recommendations from the Society of Thoracic Surgeons/American Association Guide¹, indications for elective intervention in the chronic setting include aneurysmal dilatation (total ≥ 55 -60 mm), increasing rate of diameter (> 10 mm/y), and/or symptoms (pain, malperfusion). Acute redissection or rupture (ie, acute aortic syndrome) presentation should invoke intervention as appropriate for acute aortic dissection.

4. Line 178 Branch, adjunct, and hybrid technique,

It is stated that there is no difference in the content of the procedure, but is it your understanding that the rest of the cases are simple TEVAR?

Response: The reviewer is very professional and we apologize for the misunderstanding. It is not to suggest that the rest of the cases are simple TEVAR. There were also many other cases of chimney technique, in situ fenestration, and pre-fenestration techniques. However, they were not analyzed due to the relatively small number size and the missing data.

5. Table 1 shows the range of thrombosis in the false lumen, but is it possible that all 935 cases were treated in DeBakey IIIb aortic dissection in the first place? Since it contains ULP, I presume that DeBakey IIIa is also included, but at least there is no description of the indications for TEVAR in the chronic phase, which is very confusing.

Response: The reviewer is undeniably right on that and we apologize for the carelessness. DeBakey IIIa aortic dissection patients were also included in our study. The description of the indications for TEVAR in the chronic phase has been added (see Page 21, line 558, Table 1).

6. Line 182: There is no difference in the length of hospitalization, but there are many deaths in Q3 for 30-day mortality. Although it overlaps, the onset of the target is mixed, so it is difficult to understand whether it is aorta-related or associated with the procedure.

The mid-term results of TEVAR for TBAD differs not only in the therapeutic effect but also in aortic remodeling depending on the time of onset and the time of intervention of treatment.

The author's message is very impactful, but I get the impression that cardiovascular-related mortality is high when TyG index is high, regardless of the treatment target or TEVAR procedure.

Response: The reviewer is undeniably right on that and we apologize for the carelessness. DeBakey IIIa aortic dissection patients were also included in our study. The description of the indications for TEVAR in the chronic phase has been added.