

Is the use of dual antiplatelet therapy following urgent and emergency coronary artery bypass surgery associated with increased risk of cardiac tamponade?

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1st Editorial

23-Jan-2021

Ref.: Ms. No. JCTRes-D-20-00085

The use of dual antiplatelet therapy following urgent and emergency coronary artery bypass surgery: Impact on risk of cardiac tamponade

Journal of Clinical and Translational Research

Dear Mr Hussain,

In the absence of the second reviewer's response, I perused over your paper again to ensure that no additional issues could be identified. The comments I had prepared for you were already relayed to you on December 28th, so I presume you have a revision ready.

For your guidance, my comments are appended below once again.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Feb 22, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #2: Dear authors, thank you for submitting your work to the Journal of Clinical and Translational Research. As we wait for the second reviewer, who received an extra week for the review as discussed with Dr. Hussain by email, I have performed a review of your manuscript that you may start to process in the interim. Dr. Hussain wanted to get a verdict on the paper asap so that he could decide whether the manuscript should be submitted elsewhere. I promised him to look at the manuscript while the second reviewer is hopefully appraising the paper to inform you about the acceptability of your work. In general, the manuscript is important for patients suffering from cardiac tamponade and cardiologists taking care of these patients. The manuscript is generally well-written and the analyses were performed properly. So your manuscript will be published in JCTR after implementing the following revisions and pending the possible comments of the other reviewer. Please answer my comments in a point-by-point manner and use track changes in the main text so that I can quickly validate your modifications.

1. The title should reflect the main conclusion of the work. For example: "Dual antiplatelet therapy in urgent or emergency CABG patients is not associated with an increased risk of cardiac tamponade, length of hospital stay, and mortality."

2. Although the manuscript is well-written, I kindly ask you to proofread the manuscript. A few examples in the abstract:

- Data is plural, not singular.

- ...whereas tamponade patients experienced a significantly longer hospitalisation... -> please remove the article ("a") before hospitalisation.

- "The 30-days and 1-year mortality was similar in both groups and were 0.8% and 1.6% respectively." should read "The 30-days and 1-year mortality were similar in both groups and were 0.8% and 1.6%, respectively."

- The phrase "...DAPT in urgent or emergency CABG patients is not associated with an increased risk of cardiac tamponade, length of hospital stay or mortality." should read "...DAPT in urgent or emergency CABG patients is not associated with an increased risk of cardiac tamponade, length of hospital stay, and mortality." Please use the Oxford comma throughout the text.

- Please use spaces before and after =/>/

3. Please use non-redundant keywords relative to title and abstract to increase retrievability of your article.

4. Please denote the primary outcome in the CURE and PLATO trials for readers not familiar with these trials. You may state these in parentheses. Also indicate which P2Y12 inhibitors were used when referencing a trial on antiplatelet therapy (i.e., clopidogrel, prasugrel, or

- ticagrelor). Finally, indicate which antifibrinolytics were used when referencing these. This also applies to the described study cohort.
5. Page 4, lines 8-13: specify to which group the outcome variable values belong and better indicate that the reduction in listed parameters pertain to the antiplatelet drugs compared to the aspirin only group. The sentence does not read very well.
 6. Please include the IRB protocol number and study approval date.
 7. Please write the figure designation and figure legend in plain text under the respective figure; do not embed the text in the figure.
 8. Group designations should be consistent throughout the text: either write out in full or abbreviated, but not mixed styles (see e.g., Figure 1, x-axis).
 9. Page 7, lines 49-51 should read ..., and the median age (range) in DAPT...
 10. Table 1 should also indicate that certain values in parentheses represent the range.
 11. Why was no statistical analysis performed on the cardiovascular risk factors and medical history variables? Hypertension may have an impact on the incidence of cardiac tamponade [Am J Cardiol 2012 Oct 1;110(7):1066-9], which was (significantly?) more prominent in the AMT group. This could have favorably skewed the results in favor of the DAPT cohort in terms of tamponade incidence. The same may apply to the hypercholesterolemia (https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0066-782X2001000500005).
 12. Please double-check the calculated values in the tables. For example, in the DAPT group, 16 patients presented with congestive heart failure, which you indicate is 69.6%. This seems incorrect. Similarly, 10 patients had a TIA/CVA, which is attributed to 81.3%. This too seems off. Make sure you recalculate all percentages.
 13. The mortality values in Table 2 are identical between the 2 groups. Please ensure all data have been correctly stated in all tables.
 14. Ensure that value notation is consistent throughout the text and tables; use a decimal value in both groups or in neither group for the same outcome parameter.
 15. In table 3, de unit "mls" should be rephrased to "mL".
 16. The authors should indicate what the p-values refer to in Table 3; the N or the Value columns.
 17. Table 3 is missing a footnote that explains what the superscripted symbols in the p-value column mean.
 18. The authors should also determine which risk factors are at play in CABG patients who experienced bleeding or tamponade after surgery. Are the risk factors the same for AMT versus DAPT?
 19. The authors should specify which concentrations of aspirin and antiplatelet agents were used. Is there a correlation between dosage and bleeding/tamponade?

Thank you for addressing these comments and good luck with preparing a revision.

Michal Heger
Editor-in-chief

Authors' response

1. The title should reflect the main conclusion of the work. For example: "Dual antiplatelet therapy in urgent or emergency CABG patients is not associated with an increased risk of cardiac tamponade, length of hospital stay, and mortality."

Ans: Agreed, title modified – page 1; line number 1-4

>> A conclusive title does not end with a question mark. Please revise according to my recommendation.

2. Although the manuscript is well-written, I kindly **ask you to proofread the manuscript**. A few examples in the abstract:

- Data is plural, not singular.

Ans: Manuscript revised as suggested.

>> Interesting to read “manuscript revised as suggested” only to encounter this:



119 IL, US). The collected data was a mixture of continuous and categorical variables. If
120 continuous (age, length of hospital stays), evaluation of normality, equality of variance,

6

121 outliers and missing data was performed. Continuous data is expressed as mean and
122 standard deviation (SD) or median with interquartile range (Q1 - Q3), if normally or
123 non-normally distributed, respectively. Descriptive analysis was undertaken for nominal
124 and ordinal data (number of coronary arteries affected, rates of cardiac tamponade,
125 incidence of mortality), which is expressed as numbers and percentages. Independent-
126 sample t-test was used for continuous variables, when homogeneity was assumed with
127 equal variances under Levene's test. Where Levene's was violated, variance was not
128 assumed. Independent-samples Mann-Whitney U test was performed for non-normally
129 distributed data. Pearson Chi-square test was undertaken to detect any statistical
130 significance amongst categorical data. Two-tailed statistical significance was identified for
131 $p < 0.05$.

132

133 Results

Please go through paper again and eliminate grammar and spelling errors. We cannot publish a manuscript that contains obvious linguistic mistakes. Above is just one example page, but the paper is still replete with errors and inconsistencies.

3. Please use non-redundant keywords relative to title and abstract to increase retrievability of your article.

Ans: Done – page 3, line 52

>> All listed keywords appear in title. The keywords should be non-redundant relative to the title. Please modify.

6. Please include the IRB protocol number and study approval date.

>> Remark ignored. Please implement.

7. Please write the figure designation and figure legend in plain text under the respective figure; do not embed the text in the figure.

Ans: revised figure attached.

>> The revised figure was not attached. Please send.

8. Group designations should be consistent throughout the text: either write out in full or abbreviated, but not mixed styles (see e.g., Figure 1, x-axis).

Ans: revised

>> Cannot check because you did not attach the figure.

9. Page 7, lines 49-51 should read ..., and the median age (range) in DAPT...

Ans: Please see page 7, line 145

>> Please specify in the text that the values in parentheses represent the range of the data. You don't have to do this every time, only at first mention, so that all readers know what you are reporting.

10. Table 1 should also indicate that certain values in parentheses represent the range.

Ans: Page 16, line 294

>> Again, this is not clear. In Table 2 you list "Time to reoperation in patients with tamponade (minutes)" and then report the values as "533 (471-942)," where the values in parentheses are minutes as by your definition. The units are minutes, but the values in parentheses are the range. Please correct properly (e.g., by using brackets to indicate the unit and parentheses to indicate the range).

11. Why was no statistical analysis performed on the cardiovascular risk factors and medical history variables? Hypertension may have an impact on the incidence of cardiac tamponade [Am J Cardiol 2012 Oct 1;110(7):1066-9], which was (significantly?) more prominent in the AMT group. This could have favorably skewed the results in favor of the DAPT cohort in

terms of tamponade incidence. The same may apply to the hypercholesterolemia (https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0066-782X2001000500005).

Ans: To analyse the effect of other risk factors we need to perform the propensity matching to identify two similar groups which is difficult as total number of patients are not enough and also its beyond the scope of this paper. But it's a very good suggestion and we will keep this is mind for future projects.

>> The significance of this discussion point should be added to the section entitled "Limitations of the study." Also indicate in the text why the analysis was not performed, as you have done here.

14. Ensure that value notation is consistent throughout the text and tables; use a decimal value in both groups or in neither group for the same outcome parameter.

Ans: checked and corrected

>> Again, this is a false response. See below and please carry this request out conscientiously.

293 Table 3: Blood products

	Aspirin monotherapy		DAPT		p value
	N	Value	N	Value	
Haemoglobin before procedure					
Tamponade	10	136.5 (133.3-139.3)	7	135 (121.8-147)	0.051 [#]
No tamponade	112	139.5 (126.3-149)	114	113 (96-134)	0.390 [#]
Lowest haemoglobin					

16. The authors should indicate what the p-values refer to in Table 3; the N or the Value columns.

Ans: Done

>> "p-values refers to the value columns" is not appropriate phrasing. Please replace by "the p-values refer to comparison between outcome parameter values"

17. Table 3 is missing a footnote that explains what the superscripted symbols in the p-value column mean.

Ans: Done

>> Please rephrase to "Independent Student's t-test"

18. The authors should also determine which risk factors are at play in CABG patients who experienced bleeding or tamponade after surgery. Are the risk factors the same for AMT versus DAPT?

Ans: this is the data from same centre that means likely both groups have same risks factors.

>> This is an uncorroborated inference simply because locality of incidence does not determine the risk factor. Risk factors are more likely co-morbidities, medical history, and habits such as smoking, etc. But I am fine with letting this one slip.

19. The authors should specify which concentrations of aspirin and antiplatelet agents were used. Is there a correlation between dosage and bleeding/tamponade?

Ans: Standard concentration of medicine used for both groups.

>> Great, please specify this in the text.

2nd Editorial decision
24-Jan-2021

Ref.: Ms. No. JCTRes-D-20-00085R1

Is the use of dual antiplatelet therapy following urgent and emergency coronary artery bypass surgery associated with increased risk of cardiac tamponade?

Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Feb 23, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

See attached document

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

Authors' response

1. The title should reflect the main conclusion of the work. For example: “Dual antiplatelet therapy in urgent or emergency CABG patients is not associated with an increased risk of cardiac tamponade, length of hospital stay, and mortality.”

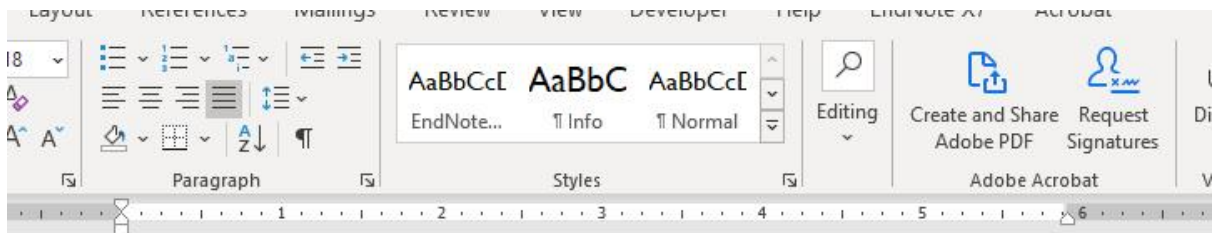
Ans: Title Changed

2. Although the manuscript is well-written, I kindly **ask you to proofread the manuscript**. A few examples in the abstract:

- Data is plural, not singular.


Ans: Manuscript revised as suggested.

>> Interesting to read “manuscript revised as suggested” only to encounter this:



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120 continuous (age, length of hospital stays), evaluation of normality, equality of variance,

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121 outliers and missing data was performed. Continuous data is expressed as mean and
122 standard deviation (SD) or median with interquartile range (Q1 - Q3), if normally or
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130 significance amongst categorical data. Two-tailed statistical significance was identified for
131 $p < 0.05$.

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133 Results

Please go through paper again and eliminate grammar and spelling errors. We cannot publish a manuscript that contains obvious linguistic mistakes. Above is just one example page, but the paper is still replete with errors and inconsistencies.

3. Please use non-redundant keywords relative to title and abstract to increase retrievability of your article.

Ans: Done – page 3, line 52

6. Please include the IRB protocol number and study approval date.

Ans: Done – page 6, line 99-100

7. Please write the figure designation and figure legend in plain text under the respective figure; do not embed the text in the figure.

Ans: revised figure attached. (was submitted earlier as a separate document but attached in this document)

8. Group designations should be consistent throughout the text: either write out in full or abbreviated, but not mixed styles (see e.g., Figure 1, x-axis).

Ans: revised – figure attached – page 14

9. Page 7, lines 49-51 should read ..., and the median age (range) in DAPT...

Ans: Please see page 7, line 137

10. Table 1 should also indicate that certain values in parentheses represent the range.

Ans: corrected

11. Why was no statistical analysis performed on the cardiovascular risk factors and medical history variables? Hypertension may have an impact on the incidence of cardiac tamponade [Am J Cardiol 2012 Oct 1;110(7):1066-9], which was (significantly?) more prominent in the AMT group. This could have favorably skewed the results in favor of the DAPT cohort in terms of tamponade incidence. The same may apply to the hypercholesterolemia (https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0066-782X2001000500005).

Ans: done – page 10-11 – line 205-208

14. Ensure that value notation is consistent throughout the text and tables; use a decimal value in both groups or in neither group for the same outcome parameter.

Ans: checked and corrected

16. The authors should indicate what the p-values refer to in Table 3; the N or the Value columns.

Ans: Done

”

17. Table 3 is missing a footnote that explains what the superscripted symbols in the p-value column mean.

Ans: Done

18. The authors should also determine which risk factors are at play in CABG patients who experienced bleeding or tamponade after surgery. Are the risk factors the same for AMT versus DAPT?

Ans: this is the data from same centre that means likely both groups have same risks factors.

>> This is an uncorroborated inference simply because locality of incidence does not determine the risk factor. Risk factors are more likely co-morbidities, medical history, and habits such as smoking, etc. But I am fine with letting this one slip.

19. The authors should specify which concentrations of aspirin and antiplatelet agents were used. Is there a correlation between dosage and bleeding/tamponade?

Ans: Standard concentration of medicine used for both groups. Page 6, line 117.

>> Great, please specify this in the text.

3rd Editorial decision
28-Jan-2021

Ref.: Ms. No. JCTRes-D-20-00085R2
Dual antiplatelet therapy in urgent or emergency CABG patients is not associated with an increased risk of cardiac tamponade, length of hospital stay, and mortality
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Journal of Clinical and Translational Research
Peer review process file 07.202102.003



Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: