Decision Letter (JCQ-2025-0003)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0003

Body: 01-February-2025

Dear Dr Yu,

Manuscript ID JCQ-2025-0003 entitled "Transcatheter Therapy for Severe Symptomatic Tricuspid Regurgitation: A Systematic Review and Network Meta-Analysis of Randomized Trials" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
3. Click "Manuscripts with Decisions" on Author Dashboard page.
4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

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Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Professor Richard Isaacs
Editor in Chief, Journal of Clinical Question
jcqeic@gleampub.com

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]

Reviewer: 1

Comments to the Author
Dear Authors,
I have well - revised your manuscript entitied , " Transcatheter Therapy for Sever Symptomatic Tricuspid Regurgation: A Systematic Review and Network Meta-Analysis of Randomized Trials." and I'm sending you my greetings.
Your research gives useful information about how well and how safely transcatheter therapy works for tricuspid regurgitation which is an important medical issue
Therefore,here are my Minor comments regarding your manuscript .

1. Clarify Study Differences
The variability in NYHA improvement (I^2 = 86%) is quite high. It would be helpful to discuss potential reasons, such as differences in patient selection, procedural techniques, or device types.

2. Compare Device-Specific Outcomes
• If possible, consider a brief comparison of different transcatheter devices (TriClip, EVOQUE, Edwards) to determine if there are notable differences in effectiveness or safety.

3. Address Long-Term Durability
• Since the study focuses on 12-month outcomes, a discussion on the long-term durability and potential complications of transcatheter therapy would add value.

4.Explain Pacemaker Implantation Risk
• The increased need for pacemaker implantation is a significant finding. Elaborating on why this occurs and whether specific devices contribute more to conduction disturbances would strengthen the discussion.

5. Discuss Surgical Comparisons
• The study compares transcatheter therapy to medical treatment, but a brief mention of how it compares to surgical repair/replacement would provide useful clinical context.

6. Highlight Patient Selection Criteria
• A discussion on which patient populations are most likely to benefit from transcatheter therapy, versus those who might be better candidates for surgery, would enhance clinical applicability.

7. Interpret the Mortality Findings
• Despite symptomatic improvement, no significant mortality benefit was observed. Providing possible explanations for this outcome would add depth to the discussion.

8. Mention Additional Studies
• Given that only four RCTs were included, referencing any ongoing or recently published trials could provide a broader perspective.

9. Clarify Outcome Definitions
• Since different studies may define outcomes slightly differently, explaining how these variations were addressed in the analysis would improve transparency.

Reviewer: 2

Comments to the Author
This manuscript presents a well-structured and timely systematic review and network meta-analysis evaluating the efficacy and safety of transcatheter therapies in the management of severe symptomatic tricuspid regurgitation (TR). The study follows PRISMA guidelines, employs a comprehensive literature search strategy, and applies appropriate statistical methods. It addresses a clinically significant topic that is gaining increasing attention in cardiovascular medicine.

The manuscript can be further improved by addressing the following comments:

Comment 1: The current description of control groups—specifically the phrasing “transcatheter therapy plus medicine” versus “transcatheter therapy alone”—is unclear (lines 224–226). It is recommended to clarify the comparator arms for each included study and specify whether patients in the control groups received standard medical therapy alone or in combination with the intervention. Providing a summary table or explicitly referencing this distinction in the text would enhance clarity and transparency.

Comment 2: The phrase “larger sample size” in line 198 may overstate the scope of the evidence, given that only four randomized controlled trials were included. A more precise phrase, such as “recent randomized data” or “updated trial evidence,” would better reflect the actual scale of the analysis and maintain appropriate interpretive balance.

Comment 3: The discussion could be further strengthened by elaborating on the observed risk of permanent pacemaker implantation. For example, are certain devices (e.g., TriClip vs. EVOQUE) more likely to cause conduction disturbances? Would preprocedural electrophysiologic evaluation be beneficial in identifying high-risk patients? Addressing these questions would provide more nuanced guidance for clinical decision-making and patient selection.

Date Sent: 01-February-2025

Author's Response to Decision Letter for (JCQ-2025-0003)

Transcatheter Therapy for Severe Symptomatic Tricuspid Regurgitation: A Systematic Review and Network Meta-Analysis of Randomized Trials

Dear Reviewers,

We thank the reviewers for their thoughtful and constructive comments, which have significantly improved the quality and clarity of our manuscript. We have carefully addressed each point raised and have revised the manuscript accordingly. Our point-by-point responses to the reviewers' comments are provided below.
Reviewer: 1
Comment 1. The variability in NYHA improvement (I^2 = 86%) is quite high. It would be helpful to discuss potential reasons, such as differences in patient selection, procedural techniques, or device types.
Response: We appreciate the reviewer's insightful comment regarding the high heterogeneity observed in NYHA improvement (I^2 = 86%). First, the observed heterogeneity in certain outcomes, particularly NYHA improvement, may be attributed to differences in patient populations, procedural techniques, and device selection. Notably, two studies compared transcatheter therapy plus medication with medication alone, while the other two compared transcatheter therapy alone with medication alone, which may have influenced the pooled results. To further explore this, we conducted a sensitivity analysis, excluding one outlier study. This yielded an OR of 2.72 (95% CI: 1.56–4.87, $p < 0.001$; I^2 = 50%), indicating consistent findings with substantially reduced heterogeneity (Figure S2). We modified the manuscript in page 10 line 165-166 and page12-13 line210-213

Comment 2. If possible, consider a brief comparison of different transcatheter devices (TriClip, EVOQUE, SAPIEN XT) to determine if there are notable differences in effectiveness or safety.
Response: Thank you for this helpful suggestion. We have now briefly compared the transcatheter devices used across the included studies. EVOQUE, TriClip, and SAPIEN XT differ in mechanism and application for treating tricuspid regurgitation. EVOQUE is a transcatheter valve replacement system, offering anatomical correction by replacing the native valve. TriClip achieves functional improvement through leaflet approximation. SAPIEN XT, repurposed for caval valve implantation (CAVI), targets venous congestion rather than the tricuspid valve itself. While promising, these devices have not been directly compared, limiting conclusions about their relative efficacy and safety. This limitation has been noted in the revised Discussion section on page 13, lines 214 to 219.

Comment 3. Since the study focuses on 12-month outcomes, discussing the long-term durability and potential complications of transcatheter therapy would add value.
Response: Thank you for this valuable comment. As all included studies primarily reported 12-month outcomes, our analysis is limited to this time frame. However, we fully agree that long-term durability and potential complications are important considerations. Currently, data beyond one year remain scarce, and long-term risks such as device malposition, structural valve degeneration, and progression of right heart dysfunction warrant further investigation. We have now included a brief discussion of these points in the revised manuscript. In page 12 line 206-219

Comment 4. The increased need for pacemaker implantation is a significant finding. Elaborating on why this occurs and whether specific devices contribute more to conduction disturbances would strengthen the discussion.
Response: Thank you for highlighting this important point. We agree that the increased need for pacemaker implantation following transcatheter therapy is a clinically relevant finding. This may be explained by the anatomical proximity of the tricuspid valve apparatus to the atrioventricular node and conduction pathways, making them susceptible to mechanical compression or injury during device deployment, particularly with valve replacement systems such as EVOQUE. While limited data prevent definitive attribution to specific devices, observational trends suggest that transcatheter valve replacement may carry a higher risk of conduction disturbances compared to leaflet repair systems like TriClip. We have expanded the discussion to reflect these considerations and emphasize the need for future studies to report device-specific conduction outcomes. Page 13 line 217-219.

Comment 5. The study compares transcatheter therapy to medical treatment, but a brief mention of how it compares to surgical repair/replacement would provide useful clinical context.
Response: Thank you for these insightful suggestions. We agree that providing clinical context regarding surgical repair or replacement is valuable. Surgical treatment for tricuspid regurgitation has traditionally been reserved for patients undergoing left-sided valve surgery or those with severe symptoms refractory to medical therapy, due to its high operative risk and limited standalone outcomes. In contrast, transcatheter therapy offers a less invasive alternative, making it particularly suitable for high-risk or inoperable patients.Page 13, lines 224-229.

Comment 6: A discussion on which patient populations are most likely to benefit from transcatheter

therapy, versus those who might be better candidates for surgery, would enhance clinical applicability.
Response: We appreciate the reviwer's comment on this point. Regarding patient selection, current evidence suggests that individuals with severe symptomatic TR, preserved right ventricular function, and less advanced end-organ dysfunction may benefit most from transcatheter intervention. Conversely, patients with favorable surgical risk profiles, complex anatomical pathology, or concurrent cardiac conditions requiring open surgery may be better candidates for surgical repair or replacement. These points have now been briefly addressed in the revised Discussion section (page 13 line 226-233).

Comment 7. Despite symptomatic improvement, no significant mortality benefit was observed. Providing possible explanations for this outcome would add depth to the discussion.
Response: Thank you for this important observation. We acknowledge that although transcatheter therapy resulted in symptomatic improvement, no significant reduction in all-cause mortality was observed. This may be attributed to several factors. First, the included studies had relatively short follow-up durations (typically 12 months), which may be insufficient to capture long-term survival benefits. Second, many patients with severe TR present with advanced comorbidities and right heart dysfunction, which may limit the impact of isolated valve intervention on overall mortality. Lastly, while transcatheter therapy improves functional status and quality of life, its effect on disease progression and end-organ damage may require longer-term evaluation. We have expanded the Discussion to include these possible explanations. (page 12-13, lines 206-213)

Comment 8. Given that only four RCTs were included, referencing any ongoing or recently published trials could provide a broader perspective.
Response: Thank you for this constructive suggestion. We acknowledge that the number of included RCTs is limited. To provide a broader perspective, we have now referenced ongoing and recently registered trials evaluating transcatheter therapies for tricuspid regurgitation, such as the TRI-RECRUIT (NCT06862765) and CAPTURE (NCT06838611) studies. These trials are expected to provide important data on long-term outcomes, device-specific performance, and comparative effectiveness, thereby contributing to the evolving evidence base and informing future clinical practice.(Page 15, lines 219-223)

Comment 9. Since different studies may define outcomes slightly differently, explaining how these variations were addressed in the analysis would improve transparency.
Response: Thank you for this important observation. We acknowledge that clinical outcome definitions varied slightly across the included studies. To address this, we extracted outcome data based on each study's original definitions but conducted sensitivity analyses to assess the impact of this variability. When feasible, we also harmonized similar endpoints under broader outcome categories to ensure consistency in the synthesis. These approaches to enhancing transparency are described in the Methods section.(Page 9 lines 141-142)

Reviewer : 2
Comment 1: The current description of control groups—specifically the phrasing "transcatheter therapy plus medicine" versus "transcatheter therapy alone"—is unclear (lines 224–226). It is recommended to clarify the comparator arms for each included study and specify whether patients in the control groups received standard medical therapy alone or combined with the intervention. Providing a summary table or explicitly referencing this distinction in the text would enhance clarity and transparency.
Response: Thank you for this helpful suggestion. We have revised the text to clarify the comparator arms in each included study, explicitly distinguishing between transcatheter therapy combined with standard medical therapy and medical therapy alone. Additionally, Table 1 has been updated to detail treatment allocation and comparator definitions, enhancing clarity and transparency regarding study design and comparisons. (page 20, lines 368-360)

Comment 2: The phrase "larger sample size" in line 198 may overstate the scope of the evidence, given that only four randomized controlled trials were included. A more precise phrase, such as "recent randomized data" or "updated trial evidence," would better reflect the actual scale of the analysis and maintain appropriate interpretive balance.
Response: Thank you for pointing this out. Given the limited number of included RCTs, we agree that the phrase "larger sample size" may be misleading. We have revised the wording to "more recent and comprehensive patient-level data" to more accurately reflect the scope of the evidence and ensure appropriate interpretive balance. (page10, line 199)

Comment 3: The discussion could be further strengthened by elaborating on the observed risk of permanent pacemaker implantation. For example, are certain devices (e.g., TriClip vs. EVOQUE) more likely to cause conduction disturbances? Would preprocedural electrophysiologic evaluation be beneficial in identifying high-risk patients? Addressing these questions would provide more nuanced guidance for clinical decision-making and patient selection.
Response: Thank you for this insightful comment. Thank you for this insightful comment. As also noted by Reviewer 1, we have expanded the discussion to address the observed risk of permanent pacemaker implantation, highlighting that certain devices may exert greater mechanical impact on the cardiac conduction system. Although comparative data remain limited, this potential risk emphasizes the importance of individualized device selection. These additions have been incorporated into the discussion section to enhance clinical relevance. (page 13, lines 214-219)

We sincerely appreciate the reviewers' valuable insights and the opportunity to revise our manuscript. We believe the changes made in response to the comments have strengthened the scientific rigor and clinical relevance of our work. We hope the revised version meets the expectations of the reviewers and the editorial team.

Best Regards,
Zaiqiang Yu
Department of Thoracic and Cardiovascular Surgery, Hirosaki University
Email: yuzaiqiang@hirosaki-u.ac.jp
Tel: 0172-33-5111
Fax: 0172-37-8340

1. response letter.pdf PDF

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