Peer Review File

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Reviewer A

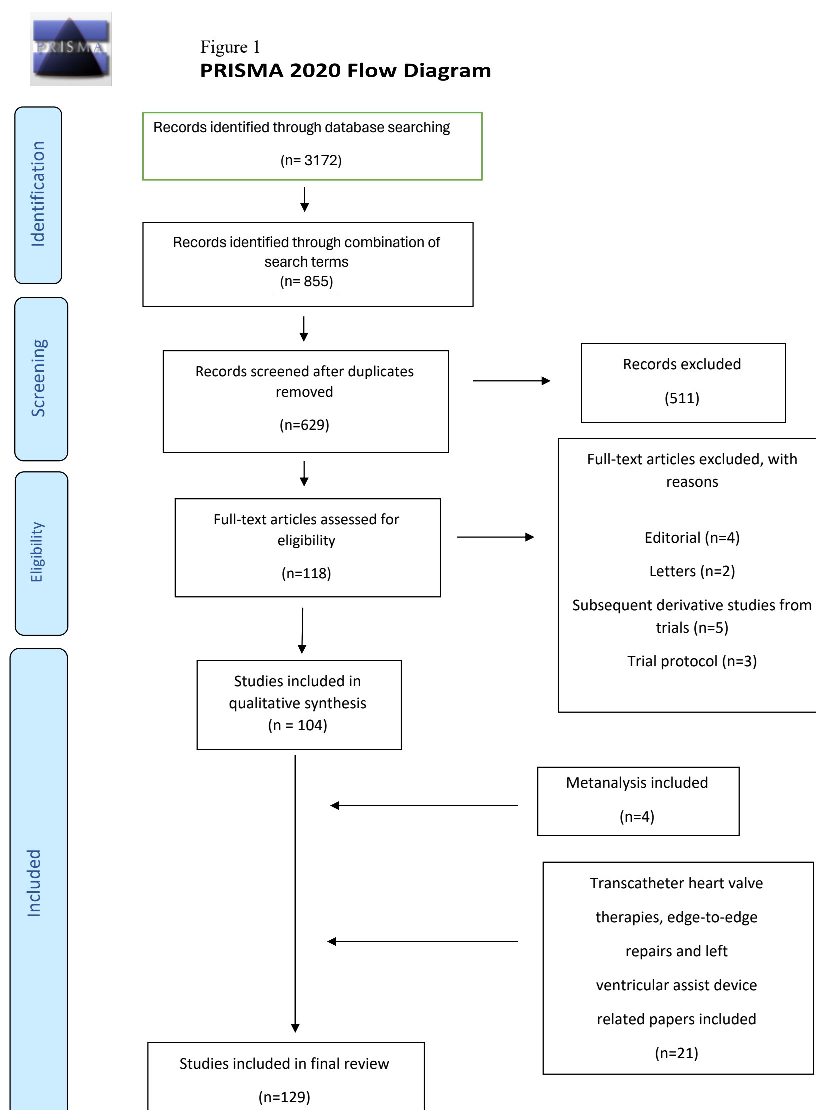
This is a paper that review the technical options of treatment in secondary ischemic MR (SIMR), an unclear topic. The authors performed an extensive review about techniques in a well written and structured paper.

I was pleased to receive your article as a reviewer, and I enjoyed reading about it, however I had some suggestions that I think could enhance your paper:

Reply. I thank the reviewer for the comments received. The following are my responses to the reviewer's suggestions. Reply are in bold black and comments are in bold red

Comment 1 The authors made a review in some databases, even when it is not a systematic review, more information about decision-making should be given. Even more, a PRISMA-like chart should be requested.

Reply 1 PRISMA has been added.



Comment 2 In line 76 the name of the trial should be given as it was written in following sections. Moreover, the authors should state in terms of what replacement was superior to repair. Reading this line, you could think that repair had higher mortality than replacement.
Reply 2. The text was revised and the modification is marked in red. More specific description of the Trial is given beginning on line 101.
Changes 2 in the text. PDF Line 75: However, a recent randomized trial from Cardiothoracic Surgical Trials Network (CTSN)…….. The American College of Cardiology/American Heart Association classifies the recommendation for surgical valve replacement as Class of Recommendation (COR) 2b and Level of Evidence (LOE) B-R. [2].

Comment 3 More information about this trial should be given because it is the main available evidence supporting replacement in secondary MR patients. For example: did they use chordal preservation? Was restrictive annuloplasty the main method of repair?
Reply 3 The author thanks the reviewer for the comment. A paragraph has been added reporting the results of this RCT
Changes 3 in the text. An explanatory paragraph was included and marked in red in the document word listed as "marked"

Comment 4. In lines 110-113: The authors referenced a review in which mortality after replacement was higher than in repair group. It requires a more extensive discussion in the discussion section in my opinion.
Reply 4 The author thanks the reviewer for the suggestion . An explanatory paragraph was included and marked in red in the manuscript listed as "marked"
Changes 4 in the text. Changes are marked in red in the word document listed as marked in the "Discussion" chapter,

Comment 5 I suggest to the authors to make a table reassuming treatment option with pros/cons or evidence behind each technique (meta-analysis, RCT, PSM, observational studies…). It would be useful to the readers.
Reply 5 The author thanks the reviewer for the suggestion.
Changes 5 in the text. A summary table has been added and included at the end of the chapter results

Comment 6. Section number 7 should be section number 5.2. because the authors are writing about repair techniques. It is applicable also for the section number 8, however section number 8.4. (LVAD) should be a different one because is not a repair technique
Reply 6. The author agrees with the reviewer's suggestion.
Changes 6. Chapters have been renumbered

Comment 7. Regarding LVAD use in SIMR, the risk of postoperative severe MR and management should be clarified. Is postoperative severe MR related with postoperative RV failure?

Reply 7. The author agrees with the reviewer's suggestion. An explanatory paragraph was included and marked in red in the manuscript listed as "marked" in the chapter discussion

Changes 7. Paragraph in the discussion

Comment 8. For many surgeons, replacement keeps as the standard treatment in SIMR. I suggest to the authors to perform a more extensive explanation about studies supporting replacement vs repair in the discussion section.

Reply 8. The author agrees with the reviewer's suggestion. An explanatory paragraph was included and marked in red in the manuscript listed as "marked" in the chapter discussion

Changes 8. Paragraph in the discussion

Comment 9 In conclusion, you wrote an excellent paper. However, resolution of the above issues would greatly improve the manuscript. I encourage you to carefully consider these points during the revision process. Once these issues are adequately addressed, I believe your work could make a valuable contribution to the literature.

Reply 9. The author thanks the reviewer for the Comment.

Reviewer B

The authors have carried out a comprehensive review on strategies for treatment of secondary MR. The review is thorough and adequate.

Reply . The author thanks the reviewer for the Comment.

Reviewer C

I would recomment clear definition of the aim of this study, clear delimitation adn description of the methodology, subsequent presentation of the "results" and dircussion of the "Results" whit final presentation of some sort of conclusions of this study.

The manuscript in its present form looks like the first raw form of a dissertation about secondary mitral valve regurgitation.

It does not look like a review, state-of-the art manuscript or meta-analysis.

The authors shoud decide which form a a scientific manuscript they want to aply to this publication and conform to it.

Some conclusions at the end of the manuscript are obligatory.

Reply. The author thanks the reviewer for the comment. This seminar offers a thorough review of all surgical procedures for SMR. The author has a significant body of literature available on PubMed, including randomized

and observational studies, meta-analyses, editorials, and correspondence, including biomechanical models. It is suggested that the reviewer consults this literature, although it may require a significant amount of time. The text has been improved.

Reviewer D

The authors provide a detailed review of current surgery for secondary ischemic mitral regurgitation. The authors conclude that there currently is no consensus on the optimal management strategy for patients with secondary IMR and that therefore, a multidisciplinary cardiac team should manage patients with secondary mitral regurgitation to ensure the best outcome by matching the ideal intervention with the patient.

This review may be the best yet in depth and being up to date. The review is well illustrated. There may be some sections where enthusiasm for certain procedures may need to be tempered, but the review is otherwise well supported by the references. This review reflects a lot of hard work digesting the literature. This should be useful to the surgical and cardiology community and should stimulate further investigation.

Suggestions:

1. Line 24. "valve sparing" should be "chord sparing"
2. Line 29. Most would argue that the role of MitraClip is not "shrouded in uncertainty" for IMR. As Grayburn showed in reference 102, the COAPT and MITRA-FR trials are consistent in showing potential benefit in patients with disproportionate IMR and less likely benefit in those with proportionate MR. A better statement might be "remains controversial" instead of "is shrouded in uncertainty"
3. Line 76. The word "shown" should more accurately be "suggested". This single CTSN trial has issues (like being reported as intention to treat where patients randomized to repair but treated with replacement were counted as severe postop MR even though none of the replacement patients actually had postop MR). The CTSN trial also looked at larger ventricles with lower ejection fraction than other studies like Reference 43. While this trial has changed practice in most cases, caution is need in extrapolating this small trial of a specific patient subset to all IMR patients. This is a standard limitation of randomized trials.
4. Line 200. "recurrence of MR" should be specified to "recurrence of moderate or more MR"
5. Line 241. "Studies" should be changed to "Some studies". Reference 43 and others do not support making RMA "unadvisable" in all circumstances.
6. Lines 328-329. The phrase "although the use of restrictive mitral annuloplasty in MV surgery may increase severe ischemic mitral regurgitation" should be omitted. While RMA may not eliminate severe MR, this reviewer has never seen nor read any report of RMA causing severe MR short of technical errors like ring dehiscence. If severe MR was present preop and after RMA, then it is hard to argue

that RMA caused something that was present before RMA.
7. Line 331. The words “due to” should be softened to “associated with”
8. Line 333. “the proven lack of benefit” should be changed to “the limited benefit”. Many studies have seen improved heart failure symptoms after RMA relative to preoperative symptoms.
9. Line 386. “statistically substantial difference” should be “trend”. P=0.153 is not convincing.
10. Line 388. “had” should be “tended to have”. P=0.136 is also unconvincing.
11. Line 399. “was consistently and independently linked with” should be “tended to have”. P=0.09 is not the most convincing.
12. Line 403. “a significant” should be “a trend toward”. P=0.428 is not convincing.
13. Line 413. IPMD was not defined.
14. Line 509. “There is a widespread consensus to complement” should be “Many favor complementing”. Those 5 references are not yet reflected in general practice.
15. Line 552. “it is recommended” should be changed to “some recommend”
16. Line 566. Reference 92 is missing.
17. Line 576. “Failure to repair” should be “Freedom from repair failure”
18. Fig 4. A line is missing from “LVEF>30% Low Operative Risk” to “Chordal Sparing MVR”
19. Line 862. “Segul” should be “Seagull”
20. Line 986. “Kron” should be “Kwon”

Reply . The author thanks the reviewer for the Comment.

Changes. Modifications are easily identifiable in the text as they are highlighted in red. Additionally, a comprehensive list of all changes can be found in the accompanying PDF document.