

## Peer Review File

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### Reviewer A

This paper reviews literature and adds a solid local experience in redo aortic root surgery to examine contemporary outcomes in this growing field. The vast majority of the literature-based data come from the STS database just published in 2023. They describe current spectrum of reasons for redo surgery and explore the risks unique to specific situations requiring reoperation. The Bologna experience clearly demonstrates the excellent outcomes that can be achieved in a center of excellence.

There is a striking difference in the incidence of endocarditis as the primary driver of reoperation between the Bologna experience and the STS database. (19% vs. 35 %) What are possible explanations for this difference?

The primary cause for redo root in Bologna in 36.9% of cases was progression of aortic root dilatation. Obviously, these patients did not have a full root replacement at the original operation. Was that because the primary surgery was for acute dissection? If isolated valve replacement was done in the setting of mild root dilatation, did you learn from this experience how much dilatation is too much to leave behind? Only 12 patients had redo root for prosthesis dysfunction – do you have an estimate of how many had redo AVR without root replacement during this period?

Next most common (25.9%) reason for redo root surgery was chronic or residual dissection after type A dissection repair. Were most of these the 84 patients that required arch replacement? If so, do you have a sense of which could have undergone arch replacement as part of their original operation? We are more likely to do that now than in the past. Have you also been more aggressive with the arch in recent years? What devices or techniques have made this safer and more reasonable to do?

Only 59 patients had a Bentall at their first operation but 162 got a Bentall at the redo operation. What percentage of the original Bentall cases got a new Bentall the second time? Was infection or pseudoaneurysm the problem?

Were all the prosthesis-sparing roots done in the setting of a previous mechanical AVR? The most frequent subsequent procedure was TEVAR. Does this suggest that we should use more frozen elephant trunks at the time of primary arch replacement?

Do you have any suggestions as to how we can prevent pseudoaneurysm formation? Does this represent suture line failure or lack of adequate debridement of infected tissue in endocarditis cases?

Do you have any experience with aortic homograft roots, stentless porcine roots (Freestyle), or Ross procedures (full root) that required redo surgery?

Redo “buttons” are challenging as you point out. Do you have any advice like avoiding felt and glue or making smaller buttons at the original surgery? Clearly, the patient who needs a new root placement after a previous root replacement is high on the list of challenging redo cardiac surgery.

This paper would benefit from a native English speaker review. For example:

line 77 - main criticalities.

line 148 - excellent organs protection.

line 145 - very demolitive “Commando”.

Thank you very much for your consideration and observations.

Regarding your first question, we think that the reason of the different percentage of endocarditis in our center in comparison with the STS database is not caused by a lower incidence of endocarditis, but to a larger proportion of patients with a progression of aortic root dilatation, since Bologna is considered a reference center for complex aortic procedures in our area to which patients who need redo aortic surgery are often referred. Furthermore, patients who are followed by our center for Marfan syndrome and other collagen diseases are treated here and often require more than one surgery. Lastly, our aortic disease outpatient clinic allows a strict follow up for patients operated for aortic surgery, which allows us to swiftly identify and treat patients who may need reoperations. For all these reasons, our population naturally tends to include many patients reoperated for root dilation. In this group, the primary surgery was usually an AVR or an ascending aorta replacement. All these patients did not have a type A aortic dissection, but the first diagnosis was usually a valvular disease or an ascending aorta aneurism.

At the moment we cannot give a precise estimate of how many redo AVRs were performed in the same time period, however we know from our internal database that, from the beginning of the 2000s to December 2022 approximately 50 patients underwent redo AVR with bioprosthesis without root replacement. Obviously, this number does not include mechanical redo AVRs, which we estimate could be at least as numerous as they are performed in young patients after failure of valve repair, endocarditis, or other causes.

Among the 104 patients who required arch replacement, 70 had a diagnosis of chronic or residual dissection after type A dissection repair. Most of the patients, however, underwent the first, emergent surgery in other centers closer to home, so it is difficult for us to say if arch replacement would have been more appropriate as part of their original operation. In our experience, in a patient with type A aortic dissection, if there is a tear in the arch we prefer to be more aggressive and usually we replace the arch. 71% of patients who underwent a Bentall as first operation got a new Bentall at redo.

The main indication was endocarditis (52%). A pseudoaneurysm was diagnosed in 22% of patients in the re-Bentall group.

Concerning the prosthesis-sparing roots operation, it is always performed in the setting of a previous mechanical AVR (if you are interested, the technique was described here Di Eusanio M, Berretta P, Cefarelli M, Di Bartolomeo R. Root graft substitution after aortic valve replacement: sparing the valve prosthesis is a valid option. *Eur J Cardiothorac Surg.* 2013 Sep;44(3):427-30).

As regards TEVAR at reoperation, though we perform FET in many cases and extend the arch replacement towards the descending aorta when needed, over the years we have come to realize that FET is not to be considered a one-step procedure and requires TEVAR extension often (you can learn more about our experience on the matter here Di Marco L, Nocera C, Snaidero S, Campanini F, Buia F, Lovato L, Murana G, Pacini D. Staging TEVAR after FET - an exception or the rule? *Indian J Thorac Cardiovasc Surg.* 2023 Dec;39(Suppl 2):224-232).

Periprosthetic pseudoaneurysm is a complication of Bentall procedure that is often associated with the use of glue, infection, or connective tissue diseases such as Marfan syndrome. Though we have no statistical data on this, we have learned empirically that the use of topical hemostatic agents such as BioGlue is associated with pseudoaneurysm formation. We recommend a limited use of glue and an adequate debridement of the infected tissue in endocarditis case.

We don't have any experience with aortic homograft roots, stentless porcine roots (Freestyle), or Ross procedures (full root) that required redo surgery.

Dissecting out the coronary buttons is one of the most critical parts of the procedure, and it is made more difficult by the presence of felt and biologic glue from the previous operation. However, most of the time we use a very thin felt strip on the coronary buttons in Bentall operations to reduce the risk of bleeding and complications such as coronary reimplantation pseudoaneurysms, which can have dramatic consequences.

An English language review was performed, several mistakes were corrected, and the form of some passages was changed, including the three examples you cited at line 77, 148 and 145.

**Changes in text:** corrections at lines 77, 148 and 145. General English language review

## **Reviewer B**

This is a review of an important issue, namely the problem of reoperation on the aortic root. The authors have analyzed the pertinent Literature and their personal experience. My only observation pertains to the article format. I would move most of the data concerning the surgical techniques (cannulation strategies, cerebral protection, etc) in the Methods section. Considering the experience of the center with aortic surgery and aortic reoperations, details of their strategies should be underlined. Moreover, since their experience and that of the other centers considered in this review span a long time interval, how the techniques have evolved with time and a possible progressive improvement of the results may be described and discussed.

Thank you very much for your consideration and observations. We have moved the surgical strategy portion of the paper to the methods section as you suggested. We hope that section could be interesting for readers since we share what we learned from experience in a high-volume center. The main change over the years regards the cannulation strategies and timing of CPB, which we tried to highlight more in the text. We also specified how CPB before sternotomy has become less frequent over the years and should not be performed routinely. We hope you find our changes appropriate.

**Changes** in text: the “surgical strategy” section has been moved the “methods” part of the paper. We tried to highlight the changes over time more in terms of cannulation and CPB start (lines 113-122).

## **Reviewer C**

The authors present in this study their single-center 36- years experience with 344 cases of re operative surgery of the aortic root and illustrate a review of the currently available literature concerning this interesting subject.

They conclude that re-do aortic root surgery it's becoming more and more frequent, and despite its complexity, experienced aortic surgery centers achieve good results with satisfactory survival and few further reoperations.

The topic is undoubtedly interesting, and the single-center long-term outcomes illustrated in the study are quite remarkable. The literature review is accurate and appropriate to the subject.

Nevertheless, this article need to be fully re-written for several drawbacks inherent to the structure of the manuscript. The study design itself is incorrect. Starting from the title. I would suggest an alternative title such as: RE-DO Aortic Root Surgery: Single-Center Long-time Outcomes and Review of the Literature.

My comments to the authors are summarized as follows:

- 1) The narration of the paper should respect the conventional structure of a scientific publication: The surgical technique should be described in the Methods section, while in this case is reported in the Comments. The Review of the literature should be illustrated in the Comments paragraph, while in this case it is reported in the Methods and Results .... And so on. The authors ended up doing a great confusion of concepts, descriptions and data, all mixed together, without a logical storytelling. Therefore, the reading results quite confusing and difficult to follow.
- 2) The Tables illustrating published studies must be condensed to a single line per author and study.
- 3) The causes of death after aortic root re-do surgery should be described. An additional KM for Long-term Cardiac Mortality would be appropriate. A Table illustrating the pre-operative and intra-operative characteristics of the patients along with a better presentation of the patient's population should be added. A statistical analysis of risk factors for bad outcomes would be welcome.
- 4) The English language and grammar need a major and complete revision.
- 5) Conclusions are not consistent with the title and with the objectives of the study, as, for instance, the Bologna Center experience and surgical outcomes reported by the authors are not mentioned at all in the same conclusions.
- 6) For the same reasons as stated in the previous comments, the abstract should be fully re-written as well.

In summary, in my opinion the contents of this article are interesting and noteworthy, but the manuscript and the tables need to be fully re-written, updated and revised, according to comments, in order to be re-evaluated for possible publication.

We are thankful for your interest in our paper and your insightful input. You had some very valuable observations which inspired us to make changes to the manuscript which we hope will make it clearer and more enjoyable for readers. First, we changed the title. We will now answer your comments point by point.

- 1) The surgical technique portion has now been moved to the methods section. As regards the review of literature, the JTD Author Guidelines for reviews recommend including information about the literature search and data appraisal criteria in the methods section. This kind of structure (with a portion of the methods and results sections dedicated to the literature review) can be found in numerous reviews published on the Journal, even by some of the authors who collaborated on this paper (for instance “Murana G, Costantino A, Campanini F, Fiaschini C, Buia F, Mariani C, Leone A, Di Marco L, Pacini D. Distal stent graft-induced new entry (dSINE) after frozen elephant trunk: a scoping review. *Cardiovasc Diagn Ther.* 2023 Apr 28;13(2):408-417. doi: 10.21037/cdt-22-234.

Epub 2023 Mar 30. PMID: 37583692; PMCID: PMC10423728.)

However, we hope the changes made to the surgical technique part makes the manuscript clearer and more enjoyable for readers.

- 2) We reduced the tables to two lines per study. We found it difficult to reduce it to one line while keeping them clear due to the abundance of parameters considered in the table. However, we agree that reducing it to two lines makes the tables much more legible (you might find the difference especially in tables 3 and 4). Thank you.
- 3) The causes of death at follow-up have been added (lines 173-175), along with a table describing the patients pre- and intra-operative characteristics. Regarding The KM for Long-term cardiac mortality, unfortunately at the follow-up we only have a percentage of death cause, thus we cannot appropriately describe cardiac mortality through a KM analysis. Though we agree a risk factor analysis would be interesting for us and the readers, we are unable to perform it in a statistically correct way at the moment.
- 4) We performed an extensive English language revision of the text, corrected several mistakes, and changed the form of many passages.
- 5) We changed the conclusions to clear that they are based on the data presented in our population.
- 6) We also changed the conclusions of the abstract to better reflect our results. We would like to thank you for this observation, since we feel it makes our abstract more coherent and informative for the reader.

We hope the changes made improve the manuscript's structure and make it more comprehensible. We look forward to your notes on the revised manuscript and thank you for your attention.

**Changes in text:** The title has been changed. The “surgical strategy” section has been moved the “methods” part of the paper. Both the tables format and several grammar mistakes have been revised. An additional KM and table were added. The paper and abstract conclusions have been changed.