

Peer Review File

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Reviewer A

The authors reported the multi-center registry data of 370 patients who underwent rapid aortic valve replacement (RD-AVR) deployment in 8 Spanish centers between 2012 and 2021. They compared patients performing combined surgery with RDAVR (n=128, 35%) and isolated RDAVR (n=242, 68%) without any adjustment or matching. Based on their observations, the authors suggest the Edwards Intuity valve system is safe and effective even in complex aortic valve disease with additional cardiac procedures.

Although this is a well-organized study of the multi-center registry experience, I have some comments and questions for the authors.

Line 68: Three-year survival of each population will be more informative for the readers.

Reply: Information included as recommended.

Line 74: "combinedsurgeries" There are many errors of this type in this manuscript.

Reply: Information included as recommended. Line 68

Line 105: "90" There are many errors of this type in this manuscript. It must be a mistake in changing the journal format from initial submission to the JTD, but this is a severe misbehavior to the reviewer.

Reply: Corrected (Also review for similar mistakes as described and corrected Line 133)

Line 165, 168 & 170: Please unify the style of presentation. "45±18 min and 63±25 min", "3.32±4.7 vs 4.24 ± 7.09 days"

Reply: Corrected

195: The authors mentioned, "Previous studies have linked the longer duration of myocardial ischemia and CPB times with higher perioperative mortality and morbidity 11,12." Following this statement, your interpretation of why the combined group showed similar outcomes despite statistically significantly longer CPB and ACC time is warranted.

Reply: We include a short statement to avoid confusion, the similar outcomes despite CPB and ACC time is one of the reasons why we consider Intuity prosthesis as safe in combined procedures.

212~220: It is hard to understand why the authors include this paragraph. Because fewer than ten patients underwent combined mitral valve surgery, this paragraph can send very little information to the reader.

Reply: We have included this statement because it has been prominently described in the cited literature to consider the mitro-aortic annular distance when implanting an Intuity valve.

241: "Hospital mortality was 3.7%, which is slightly higher than that calculated by the

preoperative Euroscore II (3.5%)": As we all know, the raw dataset of the Euroscore II system was collected from consecutive patients operated over 12 weeks (3 May–25 July 2010), and the improvement in recent surgical outcomes has been demonstrated to be uniform across all surgical disciplines. In this notion, the authors need to explain the reason for unfavorable early morality even with newly developed inventions such as RDAVR.

Reply: Mortality rate accuracy is almost the same as Euroscore II (3,7 Vs 3,5) the difference can be explained by standard deviation.

262: The reason the follow-up data was unavailable in all patients, including echocardiographic examinations, must be explained. Because this registry was supported by a research grant provided by Edwards Lifesciences. In Table 4, the echo data of the combined group is less than 50% of enrollment, and it is difficult to understand in a manufacture-supported manuscript.

Reply: We corrected and explain this statement. Study grant is limited and did not cover echocardiographic examinations in every center, so follow-up data collection can be variable between centers, and some of them were not available during the development of this article.

Table 1: Please compare the combined and isolated RDAVR.

Reply: Corrected. We have made it again and show the comparison suggested.

Tables 3 & 4. RVA vs. AVR: please unify.

Reply: Corrected.

Figure 2: Please explain the meaning of (17).

Reply: Corrected. Number in () is number of events.

Finally, if the authors want to conclude that "Rapid Deployment Aortic Valve Replacement could become a useful tool for combined and complex surgeries," the comparison between combined AVR with conventional stented valves and combined RDAVR seems to be more appropriate. A simplistic comparison of early outcomes and mid-term survival without adjustment undermines the authors' suggestions.

Reply: We totally agree with the fact that a comparison against conventional stented valves could be interesting. Our group is working in that issue for future publications. However, in this multicenter registry is quite difficult to do asked comparison, because the registry did not collect stented valve "patients" from every center participating in the study, and doing it with other population would suppose an important bias. Furthermore, as we concern, literature in the bibliography shows the benefits between stented and rapid development prostheses so we conclude our statement in order to those references.

Reviewer B

The Authors Victor Bautista-Hernandez et al. are to be congratulated for their work: Outcomes of Rapid Deployment Aortic Valve Replacement in Combined Surgery. Results from the RADAR Registry. The authors compared the outcomes of INTUITY valve as single AVR

procedure with those of INTUITY implantation in combined procedures. The paper is very well written. However, I have some concerns.

- First of all, INTUITY is not recently introduced, but more than a decade. So the evidence has grown, even in the setting of combined procedures.
- Only 370 patients included during a period of almost 9 years from 9 centers is a very small sample size. However the most point concerning me is that in the setting of combined surgery there are very few patients who underwent mitral procedures, and no one in a multiple valve setting is included. Exactly, this kind of operations can be challenging procedurally after or during INTUITY implantation, as well as about clinical outcomes. For instance: The fact that pacemaker rate in your study is similar in the both groups doesn't surprise me, as the most cases in the combined group are CABG or ascending procedures. Which may not be a case in mitral or multiple valve surgeries.
- Therefore, I think that this work doesn't add sufficiently to the literature and is not representative for combined procedures.
- The tables are not uniformly presented. Table 1 and 2 without grouping in the single and combined procedures.
- Further, the hemodynamic performance presentation is not valid as there has been no adjustment for the valve sizes.

Reply: Thanks for the suggestions and feedback. We have made many changes in the text to improve our article following recommendations.

Hemodynamic performance has been adjusted by size. However, we did not consider including it in the article because will suppose an important bias and confuse the reader. Smaller prostheses sizes always represent higher gradients and more mismatch cases than bigger sizes.

Combined mitro-aortic surgery supposes over 30% more risk of postoperative pacemaker rate. Despite in combined group there are many CABG cases (we agree that this fact must be considered) equal pacemaker rate between groups is an important achievement.

Changes in the Text:

Table 1 and 2: Corrected. We have made them again to present them uniformly.

Reviewer C

1. The article needs extensive English editing

Reply: Article has been re-arranged by a native speaker.

2. The structure of this article needs to be re-arranged

Reply: Structure and general description have been edited.

3. The follow-up duration was too short to validate efficacy or hemodynamic outcome of rapid development aortic valve prosthesis

- clinical outcomes mainly including perioperative outcomes is insufficient to show what authors tried to assert

Reply: To show Intuity valve safety we consider that postoperative outcomes and long-term survival are the most important factors to consider. However, future analysis with other clinical outcomes will be made.

4. A detailed description of echocardiographic examination protocol is required.

Reply: We cited full RADAR registry protocol with every echocardiographic detail in bibliography. It has been already published.

5. Were baseline characteristics adjusted while comparing the clinical outcomes between the isolated RVA and combined RVA group?

- baseline profile of each group, other than that of whole study cohort, should be provided and adjusted to demonstrate "comparable" outcomes.

Reply: We have corrected and made a new table 1 following the suggestion.

6. Statistical evidence (ex. p-value) should be provided in outcome comparison

- no evidence indicated in ICU & hospital stay

Reply: We have added statistical evidence to both parameters. (Line 166-167)

Reviewer D

This is undoubtedly an interesting, well-written paper, whose aim is to report mid-term outcomes of patients undergone RD-AVR combined with other surgical procedure.

Despite the well-known study limitations, data are well-described. Can you better underline the way data have been collected? Does a software exist?

In literature other papers focus on these topic (can you cite them? For example, Iacovelli et al doi DOI: 10.1016/j.hjc.2022.07.006

Minor issues:

In line 74, split two words combined and surgeries.

Reply: Thank you for the kind comments and the review of our article. We have made some changes according to your suggestions.

Changes in Text:

We have cited the first published RADAR protocol, in which is explained the data collection.

We have added the suggested bibliography and cited it in discussion.

Line 74: Corrected.

Reviewer E

In the manuscript entitled "Outcomes of Rapid Deployment Aortic Valve Replacement in Combined Surgery" Miguel Gonzalez-Barbeito et al. reported outcomes of rapid deployment aortic valve replacement in combined surgery.

This is a multicentric study conducted in 8 Centers in Spain. Data comes from a Registry that included 370 patients underwent RD valves implantation between 2012 and 2021. Among them 128 patients underwent concomitant surgery and were retrospectively analyzed.

In 54% of cases the concomitant surgery was CABG. Only 8 pts had concomitant mitral and aortic valve replacement.

Results are acceptable, with the ICU stay quite long (more than 3 days in isolated and 4 days in concomitant cases) and a fairly high mortality rate, mainly in isolated AVR.

They conclude that the Edwards Intuity valve is safe and effective even in complex aortic valve disease with additional cardiac procedures, where surgical times are expected to be prolonged. The manuscript is simple and the analysis quite superficial, but timely quite relevant in this confusing TAVR era, where the role of surgical AVR is debated, but, according the latest guidelines, concomitant AVR is still in favor of surgery.

I have several comments, questions, critiques, and suggestions to the authors as follows.

1) What was the indication to implant a RD valve? What the decision-making process to implant the Intuity rather than a stented or a Sutureless valve?

Reply: In Spain, and therefore in this registry, there is no indication to implant an RD valve over a sutureless one. Every surgeon decides which prosthesis is used. The purpose of this registry is to evaluate the safety of Intuity valve in a real-world setting scenario.

2) In essence, they compare two groups, isolated and concomitant AVR. Therefore, Table 1 should not present the entire cohort. In my opinion, demographic and risk factors data for isolated AVR and concomitant/combined with other procedures have to be presented separately.

Reply: Table 1: Corrected, made a new table considering recommendations.

3) Moreover, preoperative population data are scarce. An additional table showing preoperative echocardiographics data should be presented.

Reply: Preoperative echocardiographic data is limited to diagnosis. we have detailly explained this data in protocol which has been previously published and cited in bibliography.

4) If the intent of the manuscript is to show safety of RD Intuity valve in concomitant cases, why present data for isolated AVR?

Reply: The objective of presenting isolated AVR data is to show there is no differences in the groups outcomes despite combined surgery is more complex and challenging.

5) Concomitant procedures are very heterogeneous. AVR + CABG is different form AVR + MVR.

Reply: We described it as subgroups in tables.

6) The authors showed a quite long ICU stay, more than 3 days in isolated and more than 4 days in concomitant patients. Please, explain it. Moreover, no data was given on the ventilator times

and on ventilator time < 6 hours (an STS reported outcome). I believe a third table showing all postoperative outcomes should be added, and should include data about ventilation time, ICU stay, in-hospital stay, blood transfusion, new onset atrial fibrillation, post-op PM implantation, etc.

Reply: We correct it and comment it in results. Following cited and published protocol blood-transfusion and ventilation time are not collectable data, others postoperative parameters required are included and shown on Table 3.

Reviewer F

In their manuscript entitled “Outcomes of Rapid Deployment Aortic Valve Replacement in Combined Surgery”, the authors reported mid-term outcomes focusing on patients who had aortic valve replacement (AVR) using rapid deployment (RD) valves combined with other surgical procedures. The authors concluded that their study results support the safety and efficacy of the RD-AVR even in complex aortic valve disease with additional cardiac procedures.

The authors enrolled 370 RD-AVR patients from 8 centers during 10 years of periods and compared results in 35% of patients with combined procedures with those in 65% of patients without.

However, only 8 patients among the study patients underwent concomitant mitral valve replacement. As the authors discussed, mitro-aortic surgery using the RD valve possess a certain challenge and results of RD-AVR with the other combined procedures do not give any information to the readers of the Journal. In addition, there are too many typographical errors that interrupt the flow of the text.

Reply F: Thank you for the review of our article and comments. This article is focus on the safety use of Intuity valve in all kinds of combined surgery, and it is based in a wide open national Registry.

Changes in the text: We have corrected all typographical errors, also, we have edited the article by a native speaker.

Reviewer G

Thank you for inviting me to review this interesting paper.

The authors present their registry results after Rapid deployment aortic valve replacement in isolated and combined aortic valve surgery.

The Paper is well written and the results are discussed adequately.

However, some minor issues should be corrected.

1) The manuscript needs language editing by a native speaker

Reply: We have edited the language by a native expert.

2) Some abbreviations are not clear. For example, please provide a complete list of abbreviations.

Reply: We have corrected all abbreviations, unify them if needed, and provided a list in corresponding tables.

3) Table 4 shows a typing error – himodynamic behaviour. Please correct.

Reply: Corrected.

4) Congratulations! The pacemaker rates are rather low compared to other studies. Could you please describe the strategy to achieve these results more detailed?

Reply: We describe key factors to avoid high pacemaker rate between Line 212-220