Peer Review File

Article information: https://dx.doi.org/10.21037/tp-23-369

Reviewer A

General comment
The authors investigated the morphology of aortic valve leaflets in children by echocardiographic measurement. They also analyzed the relationship between leaflet shape and the origin of coronary arteries. They concluded that the non-coronary has the largest size and the right and left cusps have similar areas but different shapes. They also concluded that in cases with a major source of blood supply from a right-coronary artery, the difference in shape between left and right coronary disappeared.

The reviewer thinks that this research is interesting and important to improve our understanding of the natural shape of the aortic valve. However, there are some concerns to be solved.

General answer.
Thank you so much for your very detailed and proactive comments, highly appreciated.

Specific comment

Major comment 1
The authors should describe the reliability of the echocardiographic measurements at the study center using inter- and intra-observer variability; ex. intraclass correlation coefficient.

Reply 1: We have calculated the inter-observer variability and added the results to the section "Agreement between measurements" and added an additional table with appropriate adjustment of the other table numbers. We did not perform repeated measurements by each observer during the initial measurements, so we are not able to calculate intra-observer variability without repeating our measurements. We have also commented on correlation in the section on limitations. We have added a statement in the statistical methods section to explain our calculations.

Changes in the text: Despite the need to remeasure, we had strong inter-observer correlation with intraclass correlation coefficients >0.95 for all length and inter-commissural distance measurements on transthoracic and transesophageal echocardiograms. These full results are presented in Table 2.
Line 291 "as confirmed by our calculated inter-rater intraclass correlation coefficients all being >0.95."
Line 178: "Intraclass correlation coefficient and its corresponding 95% CI were computed to examine the inter-reader agreement."

Major comment 2
The children in this study should have a variety of different physiques, and the size of the aortic valve leaflet naturally varies depending on their physique. However, to the best of my knowledge, there is no published normal value for aortic leaflet size in children. Considering this, in this study, is “mm” the most appropriate unit for expressing the size of the aortic valve cusps in children, or is a unit such as “mm/m2” more appropriate considering the children’s physique? Please discuss this point in the Discussion section.

Reply 2: We have added a comment on our reasoning for choosing to use absolute rather than adjusted measurements for the aortic valve in the section “implications and actions needed”

Changes in the text: We chose to use the absolute value of the leaflet length and inter-commissural distance rather than adjusting for body surface area as we were comparing the relative size of the leaflets in each patient. Further measurements repeated on many patients, could possibly allow for normative indexed values of leaflet size to be determined which method could be used for comparison to identify patients with abnormalities of the aortic valve size and shape and/or origin of the coronary arteries.

Minor comment 1
The reviewer may be misunderstanding, however, were there any cases where the diagnosis of coronary artery origin was different between TTE and TEE?

Reply 3: We have reviewed our data and identified 4 cases in which there was disagreement and commented on this in the section "comparison of measurements between TTE and TEE.”

Changes in the text: For the 85 patients whose TTE and TEE both commented on origin of the coronary arteries, only 4 (4.7%) showed a discrepancy between the origin of the coronary arteries. In all of these patients advanced imaging confirmed that the TEE correctly identified the origin of the coronary arteries in all cases.

Minor comment 2
From lines 426 to 452, the authors only describe the review of past literature about the flow mechanics of the aortic root, however, there is no mention of how those reviews relate to the results of the current study. Please add the relationship between the past literature and current result.

Reply 4: We have added a few additional sentences to the manuscript to further elucidate this relationship.

Changes in the text: line 336 added the phrase “resulting in the differences in leaflet size and shape our research demonstrated.”
Line 342 added “As previous reports have shown, there likely is a relationship between the hemodynamics and the structure of the leaflets; while our research was not intended to investigate this relationship, our results should prompt further studies to explore this

connection."
Line 350 added "Further research studies could evaluate how the asymmetry of the leaflets is related to movement patterns of the valve and define an optimum geometry to facilitate opening."

Reviewer B

Congrats to the authors for the huge job that they have done. The paper is well written and reads well. The results were clearly presented and the authors did a good job specifying all the limitation of the study.

Just some minor comments:
-Table 1: authors should remove SD deviation columns, placing the SD in the columns of the mean
-Table 2,3,4,5,6,7: authors should add SD and IQR.
-Table 2,3: authors should remove 95% IC column and show the data as table 4,5,6,7.

General answer.
Thank you so much for your generous comments, highly appreciated, and the precise suggestions related to missing important data.

Reply: the tables have been revised to include the missing data and re-formatted, following all the detailed suggestions received by the reviewer.

Reviewer C

This is an undoubtedly interesting, well written paper, aimed to evaluate the relationship between size and shape of aortic valves leaflets and origin of the coronary arteries.
Although the limits, highlighted by the authors, introduction, methods, results and discussion are well written and clear. Conclusion are appropriate. no other issues.

General answer.
Thank you so much for your positive and encouraging comments, and for the stimulating question.

Regards the content:
Why did not the authors use their findings in a prospective cohort to validate them?

Reply.
Because first we wanted to verify our hypothesis, as it was never tested previously. After the collection of all TTE and TEE echo registrations, performed as pre-operative investigations, we decided to first analyze the data available. Based on our findings, in the future a prospective

investigation would be more than justified.