

We thank the Reviewers very much for their reasonable and constructive comments that helped us improve the appearance of the manuscript, support our findings on a firmer basis and convey the message of this review more accurately.

## **Reviewer # 03722832**

### **SPECIFIC RESPONSES**

**1.The PRISMA checklist has not been followed to write this review 2.The author has not defined variant ,aberrant and anomalies of coronary 3.Table.1 has no contribution 4.The most of the images provided the author has been published several times ,please be selective 5.Clinical translation of this review is poor because the author has failed to mention the clinical importance**

**Reply/Actions:** We thank the Reviewer for these comments.

1. Our paper is mostly a descriptive, narrative review dealing with diverse coronary anatomical entities and their diagnostic workup and methods of treatment. Original research studies with adequate samples are not available in this field and have not been included. The PRISMA checklist applies to systematic reviews and metaanalyses of original research studies, which is not the case for our narrative review.
2. We agree that regarding coronary anatomy, the distinction between variants and aberrations/anomalies is sometimes vague. However, early in our manuscript we clearly define this difference, based on the most widely accepted definition. In particular, in the last paragraph of our introduction we state that: "Anatomical features of the coronary arteries should be considered variants rather than congenital anomalies, when they are prevalent in more than 1% of general population."
3. We share the Reviewer's concern about the utility of Table 1. Although most information contained in the Table is discussed in the text, we feel that Table 1 would enable the reader to quickly summarize the major variants/aberrations/anomalies, and we have therefore kept this table in this revised paper. However, we will be happy to remove it, should the Reviewer/Editor prefer.
4. Please be informed that 11 out of the 16 figures that appear in the paper come from our personal dataset and have never published before. Three figures (figs 6, 11 and 16) also come from our personal dataset and have been published only once (this is acknowledged in the manuscript, and respective citations were made). Only 2 figures (figs 9 and 10) have been reproduced from the literature and may have been published several times before (this is acknowledged in the manuscript, and respective citations were made).
5. We thank the Reviewer for this comment. After considering this comment and the relevant comments of the other Reviewers, we have made every effort to emphasize the clinical implications of the coronary variants/anomalies we describe in this revised manuscript. In the initial submission we had included the clinical implications of major anomalies like ectopic coronary arteries from contralateral sinus, ALCAPA, etc. In this revised paper, the discussion about clinical implications has been enriched, and several additional paragraphs have been included (such as the last paragraph in 'Coronary artery variants', and a new paragraph in 'Myocardial bridging: anomaly or variant?'). Furthermore, to address a comment from another Reviewer, we have added a paragraph dealing with the risk stratification and possible need for treatment in cases of co-existence of hypertrophic cardiomyopathy with myocardial bridging.

## **Reviewer # 03476635**

### **SPECIFIC RESPONSES**

**To: Editorial Board World Journal of Cardiology Title: "Overview of coronary artery variants, aberrations and anomalies"** Dear Editor, I read this manuscript and I think that: - I really appreciate the work from Kastellanos et al. I would like the authors pointed out some aspects about the therapies related to such anomalies and the clinical consequences of such anomalies. Therefore, I suggest to: **A. Include a paragraph dealing with the clinical aspects related to the presence of coronary artery variants. B. Include a paragraph dealing with pharmacological and surgical aspects related to the treatment of such anomalies. C. Considering the role of antiplatelets agents and secondary prevention treatments in such a context.** - The authors could provide a table gathering the main finding from literature, even considering case reports. - I really appreciate all of the figures. I think that they effectively complete the entire work and give it appreciable visibility.

**Replies/Actions:** We thank the Reviewer for the above comments.

**A and B.** Contrary to coronary artery anomalies, most coronary artery variants are benign and do not really need further work-up, follow-up or treatment. There may be, however, some implications during percutaneous interventions, and all these have now been made clear in the revised manuscript (last paragraph of part 3 of our review entitled 'Coronary Artery Variants'). The potential clinical implications of the co-existence of hypertrophic cardiomyopathy and myocardial bridging is also discussed in the revised paper (last paragraph of part 4 of our review entitled 'Myocardial bridging: anomaly or variant?'). Regarding coronary anomalies it must be stressed that follow-up and treatment options cannot be presented within a single paragraph since in reality they are a wildly diverse group of different entities some of which are completely benign with no clinical significance whereas others are strongly associated with high risk of ischaemia and sudden death. That is why we have opted to present clinical significance, prognosis, follow-up and treatment within the individual segment of our text that refers to each particular anomaly. For instance, we have gone into great detail regarding diagnostic investigation and possible treatment choices in the segments related to ectopic coronaries originating from the contralateral sinus of Valsalva and ALCAPA, which are both related to very high risk for sudden death.

**C.** We have not really been able to find any significant clinical data pertaining to the role of antiplatelets and pharmacological treatment in coronary anomalies. The very nature of these anomalies probably severely limits the efficacy of secondary prevention.

## **Reviewer # 01204088**

### **SPECIFIC RESPONSES**

**Kastellanos et al. reviewed coronary artery variants, aberrations and anomalies. This review is informative, and I only have a brief comment. Page 8. 4. Myocardial Bridging: Anomaly or Variant? Please mention about myocardial bridging in hypertrophic cardiomyopathy. And description about the difference between myocardial bridging and coronary artery squeezing or coronary spasm will be appreciated.**

**Reply/Actions:** We thank the Reviewer for the above comments. We have amended the section regarding myocardial bridging according to his suggestions and we now mention the clinical importance of myocardial bridging in the context of HCM. We have also inserted a short comment about the difference between myocardial bridging and coronary spasm.

## **Reviewer # 02634762**

### **SPECIFIC RESPONSES**

The authors wrote a review about normal and anomalous coronary anomaly. Although similar review was written by Angelini, the strength of this review has much more CAG pictures than the former article. Please see the comments. 1. Most of the figures are CAG. It would be better if the authors use VR images from CCTA because three-dimensional images from CT would allow to more easily understand the anatomy. 2. Did the authors experience ischemia due to malignant type of coronary anomaly? If so, please show some evidence such as SPECT or FFR, etc. 3. Please refer to Lipton's classification when describing single coronary artery. 4. Please refer to the article by Spindola-Franco when describing split LAD or dual LAD. 5. Do the authors have a color figure for Fig 9?

**Reply/Actions:** We thank the Reviewer for the above comments.

1. In this revised manuscript, we have enriched our figures by adding a CT coronary angiogram image of a LAD originating from the right coronary cusp, from our personal database (figure 7 in the revised paper).
2. Unfortunately we do not have any SPECT or FFR images in our personal database.
3. We have amended our text accordingly and now mention Lipton's classification of single coronary arteries.
4. Reference to the article by Spindola-Franco about split LAD has been added (reference 67 in the revised paper).
5. We have provided a color version of Figure 9.