

Answer to reviewers

Dear Editor,

**Journal title:** World Journal of Cardiology      **Manuscript NO:** 40509

**Title:** Incidental congenital coronary artery vascular fistulas in adults: Evaluation with adenosine-13N-ammonia PET-CT.

Changes are indicated in the text and highlighted with yellow color.

**Reviewer #1:** Manuscript Number: 02446706 Incidental congenital coronary artery vascular fistulas in adults: Evaluation with adenosine-13N-ammonia PET-CT by Salah A.M. Said et al. This present manuscript is very interesting, and it is well written. However, some specific point should be considered. “Major comments Author should describe a **flowchart** of the present study. The **symptoms and physical findings** should be shown in Table. Minor comments Table 1, author should show all abbreviations, e.g. **CAFs**”

**Rebuttal:** Thank you for your kind comments.

Flowchart: Is added as a figure (Figure 1) to the manuscript. Patients were collected from the catheterization laboratories of three different Dutch non-academic centers: Amsterdam-Patients 4 and 8; Hengelo-patients 1, 3, 5, 6, 7 and 9 and Almelo-patients 2, 10, and 11. Symptoms and physical findings: Are shown in modified Table 1. Redundant “Old” Table 1 has been deleted. Table 1: CAFs: has been changed to → coronary artery fistulas.

**Reviewer #2:** In this study Salah Said et al report of the value of adenosine-<sup>13</sup>N-ammonia PET-CT in patients with coronary artery fistulas for the detection of reversible ischemia, which is currently used to guide interventional and surgical closure options. The study is relatively well written and presented.

**Rebuttal:** Thank you for taking the time to review our paper and offer constructive feedback.

“However, the novelty of this case series needs to be addressed in comparison to earlier reports”: There are few reports about the application of adenosine-<sup>13</sup>N-ammonia PET-CT in patients with congenital coronary artery fistulas or coronary-pulmonary artery fistulas. Adenosine <sup>13</sup>N-ammonia PET-CT scanning is routinely applied to assess the functional status and quantify flow in patients with CAD, which could also be used in subjects with congenital coronary artery anomalies of origin and termination. Quantification of myocardial perfusion facilitates the detection and localization of perfusion abnormalities. In the same patient with CAF, PET-CT was reported to show greater areas of ischemic change than <sup>99m</sup>Tc-sestamibi scintigraphy. In a comparative study by Kong *et al.*, adenosine stress <sup>13</sup>N-ammonia PET-CT imaging was shown to have higher diagnostic sensitivity (91% versus 65%) and specificity (89% versus 82%) compared with SPECT using Tc-99m sestamibi, providing better assessment of myocardial perfusion. A future prospective study involving the application of PET-CT in patients with congenital CAFs is needed.

“In addition, the authors need to show anatomical and also the corresponding functional images in their figures”: Functional images are added to the manuscript (Figures 2 and 11).

Some typos and errors need to be addressed. Are corrected.

**Reviewer #3:** coronary artery fistulas are an unexpected finding during coronary angiography often the difficulty is to decide, what the importance of the fistula is , do the complaints of the patient come from the fistula and what is the prognosis of the patient , is it hampered by the fistula? the authors describe 11 patients of whom they performed stress adenosine 13N-ammonia PET-CT in 5 patients the article is **difficult to read, difficult to understand** small retrospective study not all patients underwent imaging\ what is reason for this selection you cannot make the conclusion based on this small retrospective study it would be nice to know what were the reasons for treatment, on what reason was this decided it seems obvious that the larger are treated, sometimes decisions are made on technical reasons, feasible for closure of not so the main question is of course the selection of patients : which were treated, on what reason, which were undergoing additional imaging and the reason for that this is still unclear to me after reading this article.

**Rebuttal:** Thank you for taking the time to review our paper and offer constructive feedback. The manuscript has been adapted, restructured and formatted to increase the readability without difficulties.

“what is reason for this selection imaging”: patients were collected from different hospitals with various diagnostic facilities. High awareness of recognition of the CAFs on the catheterization laboratory with great affinity and commitment to analyze and assess the significance of these anomalies. Furthermore, to investigate the usefulness of PET-CT as a guide to the process of clinical decision-making.

“Conclusion”: We fully agree that conclusion based on this limited number of patients cannot be made. Conclusion has been mitigated. PET-CT may be helpful, in selected patients, in assessing the functional status of congenital CAFs regarding clinical decision-making. Further studies of large number of patients is warranted.

“The reasons for treatment”: Small fistula were left without percutaneous or surgical intervention. Surgical ligation of the fistula was performed in combination

with CABG in patient #2. Percutaneous closure of the fistulous tract (LCx→PA) and PCI of the LAD was undertaken due to chest pain and dyspnea on exertion in patient # 3. PCI of OM branch of the LCx and coiling of the fistula (LAD→PA) in patient # 5 who suffered from non-sustained ventricular tachycardia. Secondary to angina pectoris, transcutaneous obliteration of the fistula took place in patient # 10. In four patients (patients # 4, 7, 8 and 11), PET-CT showed no flow restrictions indicating conservative medical management and obviating the need for fistula closure.

**Reviewer #4:** Dear the authors of the above-mentioned manuscript Thank you for doing this good work in describing this rare condition and the added value of Adenosine 13N-ammonia PET-CT in decision making I have no concerns about this manuscript.

**Authors' reply:** Thank you for your kind comments.

**Reviewer #5:** Congenital coronary artery fistulas are rare anomalies. As coronary angiography and multidetector computed tomography have become more accessible, they have been increasingly used in the investigation of chest pain and heart failure. Coronary artery fistulas are often an incidental finding, which raises the question of how patients with this condition should be managed. Intervention with either transcatheter closure or surgical closure is often technically possible. In this article, the Authors review the published literature on the natural history and treatment outcomes in individuals with coronary artery fistulas. In addition, there are few data about the use of adenosine- N-ammonia PET-CT in patients with congenital coronary artery fistulas or coronary-pulmonary artery fistulas. The only limitations are that the study is retrospective and includes a limited number of patients, as pointed out by the authors themselves. However, the data are

interesting and well described. I have no specific comments.

**Authors' reply:** Thank you for your kind comments.

**Reviewer #6:** Dear author thanking you for your interest in coronary artery fistula. In the current shape your does not deserve publication standard Major Weaknesses Remedial measure

**Rebuttal:** Thank you for taking the time to review our paper and offer constructive feedback.

“1. Not focused Just provide the details of five cases”: details of five cases are given in Table 1 and Table 2 (patients 3, 4, 7, 8 and 11), and separately in Table 3.

“2. Figures are not informative Please those or provide informative images”: Are added to the manuscript.

“3. Tables are redundant Format those adequately and provide data only for 5 cases”. Table 1 has been restructured. Redundancy has been deleted. In Table 3 detailed data of five patients who underwent PET-CT are described.

“4. Text burden is high as a series of five cases and retrospective nature of study, be precise, reduce references”: This is an observational study. Due to answering comments of other reviewers it is not possible to reduce the text or references.

With kind regards,

Salah AM Said, MD, PhD, FESC