Answering reviewers

July 31, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: **3803**-Review.doc).

Title: Coronary-cameral fistulas in adults: acquired types: Review (second of two parts)

Author: Salah AM Said, Rikke HM Schiphorst, Richard Derksen and Lodewijk Wagenaar

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 3803

The manuscript has been improved according to the suggestions of reviewer. Changes are highlighted with yellow text marker for (Reviewer 1), blue text marker for (Reviewer 2), green for (reviewer 3) and violet for Reviewer 4.

A) Format of the paper and references has been updated. The total number of references in part I and part II is 138 which is divided into 60 references for part I and 78 for part II. The cover letter has been addressed to the acquired CCFs.

B) Revision has been made according to the suggestions of the reviewer and editor:

Reviewer 1: Thank you for your important suggestions:

(1) Page 2, key words: adults: Key words need better classification. What does "adults" mean as a keyword? adults has been removed: spontaneous resolution, and surgical treatment are added.

(2) Cover letter is related to another paper!: Cover letter has been changed to include the acquired CCFs (second of two parts)(part II).

(3) The authors should discuss further the relation of coronary cameral fistulas with myocardial ischemia. While some papers relate myocardial ischemia and myocardial infarction as causes of CCFs, coronary cameral fistula itself is one of the reasons of coronary steal that causes myocardial ischemia (see and include in the discussion: Cihan Sengul, Recep Ciftci, Furkan Ubeydullah Ertem, Cihan Cevik. Coronary Cameral Fistula: A Rare Cause of Coronary Ischemia. ACHAIKI IATRIKI 2012; 31:159-161). Page 12: We have updated our discussion with adding of the suggested reference which is dealing with congenital CCFs. "In contrast to congenital CCFs between the LAD and LV which may cause angina pectoris secondary to myocardial ischemia documented with myocardial perfusion test [58], acquired CCFs may develop and emerge secondary to MI or severe atherosclerotic lesions."

Reviewer 2: The authors deserve praise for producing an excellent review on acquired coronary-cameral fistulas. In the opinion of this reviewer the following minor changes will further enhance the quality of the manuscript. 1. Please rephrase the first sentence of the manuscript. 2. Please change the section Conclusions from

listed format to continuous text.

Thank you very much for your kind appraisal and important suggestions.

1) Please rephrase the first sentence of the manuscript: The first sentence has been rephrased to: Acquired coronary artery fistulas (CCFs) are infrequently detected during conventional coronary angiography (CAG).

2) Please change the section Conclusions from listed format to continuous text: The text of the section Discussion has been changed to continuous text.

Reviewer 3: Thank you, we appreciate your valuable comments and suggestions.

1. The authors could consider adding a flow chart of study selection, which detailed how you screen literatures. Better presented as PRISMA flow chart. The flow chart is added.

2. The authors should discuss the prognosis of these different types of CCF. The prognosis of different types is outlined in the discussion section.

3. In the discussion section, I suggest the author arrange the MS as Etiology and prevalence, mechanism, clinical manifestation, diagnosis, management and prognosis, making it easier to read. The discussion section has been rearranged according to etiology and prevalence, mechanism, clinical manifestation, diagnosis, management and prognosis.

4. I believe the readers will be interested in the following questions, which the authors should emphasize and put them into the conclusion. First, in what kinds of patients should we consider the potential diagnosis of CCF or we could just only find CCF accidentally. Second, in the patients with CCF, who should be treated (and what is preferred treatment, surgical or precutaneous), who should considered medical therapy only. This has been added in the discussion part.

5. No need to present data in the conclusion, should be concise. The data have been deleted from the conclusion section.

Reviewer 4 Thank you for your valuable comments and pivotal suggestions.

Title: Coronary-cameral fistulas in adults: acquired types. Review: (Second of two parts)(part II) Good analysis, very informative, but needs lot of changes as it is difficult to understand what authors want to say. Needs to rephrase and rearrange the entire article. 1. Introduction.....Need to 'define' CCF first –in each article and then tell about congenital or acquired ones. 2. There is confusion in using terms acquired accidental.....traumatic....accidental....iatrogenic..... 3. "Acquired CCFs are rare disorders which have been reported since 1935".....reference please. " They usually occur when the continuity or the vicinity of a coronary artery is lacerated subsequent to severe blunt or sharp chest trauma." ....here it is said that acquired CCF are only due to trauma ruling out other 2 types.....confusing!. 4. "Acquired types of CCFs may develop secondary to exogenous injuries [3] or endogenous trauma [4".....again confusion.....this should be 'aquired traumatic' type.....not general term 'aquired' CCF. 5. 'Furthermore, these acquired fistulas may be iatrogenic secondary to surgical intervention [5] or subsequent to accidental trauma caused by deceleration [6] or sharp chest injuries [7].'....please rephrase your sentences.....readers get confused what is what.....first classify as 'acquired traumatic' type and .... 'spontaneous' type... then in 'acquired traumatic' type divide into 'acquired traumatic accidental' and 'acquired traumatic iatrogenic types' 6. Methods..... 'Acquired traumatic (accidental or iatrogenic) coronary-cameral fistulas'.....please follow one classification. 7. where is C. should define spontaneous type also in the methods. 8. Results.....'Among the reviewed subjects with acquired fistulas, (7/243= 3%) were

traumatic accidental, (67/243= 27%) were traumatic iatrogenic of origin and in (12/243= 5%) spontaneous occurrence developed post-MI'. In the abstract it is 3%, 28% and 4%.....big difference.....Also, it is mentioned.....'among the reviewed subjects with acquired fistulas'.....i.e 84 patients.....but it is calculated for 243 patients.....243 is total CCF including congenital.....do you want to give percentage among all CCF or for only acquired type..... confusing..... 9. 'Acquired traumatic iatrogenic (67/243= 27%)'..... These CCFs involve complication of permanent pacing and implantable cardioverter-defibrillator (ICD) leads, trans-septal puncture, and electro-physiologic procedures (8/243= 3%).....very confusing ...from where did 8/243 come when already you mention in the heading 67/243.....please write up all the values of each etiology with percentages.....so that it is clear what you want to say..... 10. The data of 8 patients (5 male and 3 female) were analyzed...who are they post EP or pacing or pci.....??????? 11. Acquired traumatic iatrogenic:.....this heading is already there in previous paragraph and again this is repeated??????? and you say these occur due to surgical procedures(1%).....what about above procedures?????? then again from 1% prevalence has jumped to 2.1%!!!!!!! 12.]. In 2004, Barcelo et al. reported the percutaneous occlusion of an acquired iatrogenic CCF between LAD and RV [11].....results section is to mention your analysis and results...not to write about other studies or references..... 13. Discussion part need lot of rearranging and more headings and sub classifications. Otherwise it is very confusing to read and understand what authors really want to say. 14. Table 2.....percentages are from your study or other studies?? please give data of your study and not other references.

Thank you for your valuable comments and pivotal suggestions.

-but needs lot of changes as it is difficult to understand what authors want to say. Needs to rephrase and rearrange the entire article: The manuscript has been reorganized and rearranged to reach good readability.

-1. Introduction.....Need to 'define' CCF first –in each article and then tell about congenital or acquired ones: The definitions have been reshaped and rephrased.

-2. There is confusion in using terms acquired accidental.....traumatic....accidental....iatrogenic.....: The definitions have been reshaped to avoid any confusion.

3. "Acquired CCFs are rare disorders which have been reported since 1935".....reference please. " They usually occur when the continuity or the vicinity of a coronary artery is lacerated subsequent to severe blunt or sharp chest trauma." ....here it is said that acquired CCF are only due to trauma ruling out other 2 types.....confusing!.: Reference has been added [5] and the sentence has been adapted.

4. "Acquired types of CCFs may develop secondary to exogenous injuries [3] or endogenous trauma [4".....again confusion.....this should be 'acquired traumatic' type.....not general term 'acquired' CCF.: has been changed.

5. 'Furthermore, these acquired fistulas may be iatrogenic secondary to surgical intervention [5] or subsequent to accidental trauma caused by deceleration [6] or sharp chest injuries [7].'....please rephrase your sentences.....readers get confused what is what.....first classify as 'acquired traumatic' type and .... 'spontaneous' type... then in 'acquired traumatic' type divide into 'acquired traumatic accidental' and 'acquired traumatic iatrogenic types': has been rephrased.

6. Methods..... 'Acquired traumatic (accidental or iatrogenic) coronary-cameral fistulas'.....please follow one classification.: One classification is followed: Coronary-cameral fistulas: congenital or

acquired --> spontaneous or traumatic --> accidental or iatrogenic --> surgical procedures (septal myectomy and other cardiac surgical procedures) or non-surgical interventions (endomyocardial biopsy, electrophysiological procedures "pacing, ICD and RF cardio-ablation", percutaneous coronary interventions).

7. where is C. should define spontaneous type also in the methods.: Has been added. C- Spontaneous CCFs: These are coronary-cameral fistulas, spontaneously emerging, associated with severe atherosclerotic lesions [26] or develop following myocardial infarction [18, 4], resulting in direct communication between the culprit coronary artery and an adjacent cardiac chamber.

8. Results.....'Among the reviewed subjects with acquired fistulas, (7/243= 3%) were traumatic accidental, (67/243= 27%) were traumatic iatrogenic of origin and in (12/243= 5%) spontaneous occurrence developed post-MI'. In the abstract it is 3%, 28% and 4%.....big difference.....Also, it is mentioned.....'among the reviewed subjects with acquired fistulas'.....i.e 84 patients.....but it is calculated for 243 patients.....243 is total CCF including congenital.....do you want to give percentage among all CCF or for only acquired type..... confusing..... : The figures have been adjusted. From the world literature, 243 adult patients were selected with congenital (159/243= 65%) or acquired (84/243= 35%) CCFs. Among the reviewed subjects with acquired fistulas, (72/84= 85.7%) were traumatic iatrogenic or traumatic accidental in origin and in (12/84= 14.3%) were presented with spontaneous occurrence of fistulas developing post-MI.

9. 'Acquired traumatic iatrogenic (67/243= 27%)'..... These CCFs involve complication of permanent pacing and implantable cardioverter-defibrillator (ICD) leads, trans-septal puncture, and electro-physiologic procedures (8/243= 3%).....very confusing ...from where did 8/243 come when already you mention in the heading 67/243.....please write up all the values of each etiology with percentages.....so that it is clear what you want to say.....: Acquired coronary artery fistulas are subdivided into spontaneous (12/84= 14.3) and traumatic (72/84=85.7%). The traumatic fistulas encounter iatrogenic (65/72=90%) and accidental (7/72=10%) subtypes. The iatrogenic fistulas are secondary to non-surgical (n=40/65, 62%) interventions (endomyocardial biopsy, permanent pacing and implantable cardioverter-defibrillator (ICD) leads and radiofrequency cardio-ablation) and cardiac surgical (n=25/65, 38%) procedures(septal myectomy and other cardiac surgical procedures).

10. The data of 8 patients (5 male and 3 female) were analyzed...who are they post EP or pacing or pci.....???????: The figures have been specified as follow: Coronary-cameral fistulas: congenital (n=159) or acquired (n=84) --> spontaneous (n=12) or traumatic (n=72)--> accidental (n=7) or iatrogenic (n=65)--> surgical procedures (n=25)(septal myectomy (n=20) and other cardiac surgical procedures (n=5)) or non-surgical interventions (n=40) (endomyocardial biopsy (n=25), electrophysiological procedures and baro-traumas (n=15) "pacing, ICD and RF cardio-ablation" (n=8), percutaneous coronary interventions (n=7)).

11. Acquired traumatic iatrogenic:.....this heading is already there in previous paragraph and again this is repeated??????? and you say these occur due to surgical procedures(1%).....what about above procedures?????? then again from 1% prevalence has jumped to 2.1%!!!!!!!: The figures have been specified and subheadings have been imbedded for clarity.

12.]. In 2004, Barcelo et al. reported the percutaneous occlusion of an acquired iatrogenic CCF between LAD and RV [11].....results section is to mention your analysis and results...not to write about other studies or references.....: This part has been removed to the discussion section.

13. Discussion part need lot of rearranging and more headings and sub classifications. Otherwise it is very confusing to read and understand what authors really want to say.: The discussion part has been fully rearranged.

14. Table 2.....percentages are from your study or other studies?? please give data of your study and not other references.: Percentages from the current review are inserted.

C) References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

PhD, FESC, Department of Cardiology, Hospital Group Twente, 5 DL Hengelo, the Netherlands. samsaid@home.nl
5 286 Fax : + 31 74 2905 289