

Peer Review File

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Reviewer A

Comments 1: More attention should be paid to improving the perioperation outcomes of radial artery grafts. This statement requires elaboration. We may assume that the surgical teams always try to optimize perioperative outcomes including early graft patency. The authors should specify how outcomes may be further improved, and in which way their research may facilitate that. Possibly, the manuscript is more important for guiding graft selection.

Reply 1: For RA grafts selection, we think some new techniques such as quantitative flow ration (QFR) may be more accurate than visual angiographic assessment in evaluating the appropriate target vessel. Appropriate antispasm treatment without low blood pressure is also important in the early stage post-operation. We also observed that the RA grafts patency rate at one-week post-operation maybe associated with the peak value of neutrophil count in the first 3 days post-operation, while we have not found the postulated mechanism behind the phenomenon.

Changes in the text: line 221, Appropriate antispasm treatment without low blood pressure maybe important in the early stage post-operation. For RA grafts target selection, we think some new techniques such as quantitative flow ration (QFR) may be more accurate than visual angiographic assessment in evaluating the appropriate target vessel.

Comments 2: Cohort selection should be better explained.

Reply 2: In the text, we stated that “This is an observational cohort study. From August 2019 to June 2021, there were altogether 118 coronary artery disease patients undergone urgent or elective CABG with RA grafts at Ruijin Hospital. All 80 (80/118, 67.8%) patients had 1 week coronary computed tomography angiography (CCTA) were included in this study”.

I am sorry we make a confused description. From August 2019 to June 2021, 118 patients undergone urgent or elective CABG with RA grafts at Ruijin Hospital. 18 patients refused to participate in the ASRAB or ROMA clinical trial. Of the remaining 100 patients, 80 patients accepted both RA graft and SV grafts. So this study only included 80 patients. We added a flowchart.

Changes in the text: line 80, 18 patients refused to participate in the clinical trials. Of the remaining 100 patients, 80 patients accepted both RA graft and SV grafts.

Comments 3: The targets for saphenous vein grafts should be described, as are those for radial artery grafts (line 154). Pertaining to this, one would like a discussion regarding the potential influence of target vessel properties upon graft patency. Were the radial artery targets generally larger and/or more stenotic than those of vein grafts? Many surgeons would assume radial artery superiority and select the more important targets for radial artery rather than saphenous vein grafting. If so, how would that be

interpreted?

Reply 3: Yes, we select more important targets for radial artery rather than saphenous vein grafting. 71 RA were anastomosed to LAD or LCX system. On the contrary, 10 SVG were anastomosed to DIA or LCX system, and 70 SVG were anastomosed to RCA system. There may be bias and we will add this as an limitation in the manuscript.

Changes in the text: line 241, there may be bias that we select more important targets for radial artery rather than saphenous vein grafts. 71 RA were anastomosed to LAD or LCX system. On the contrary, only 10 SVG were anastomosed to DIA or LCX system.

Comments 4: One would like to see an elaboration on the suggestion that “Much higher blood pressure may be reasonable in CAD patients treated with CABG and RA grafts” (line 213). Exactly what do the authors recommend – do their findings have bearings on graft type selection for various patient categories, on blood pressure therapy and/or intervention thresholds? The category Hypertension should be defined in the legends to tables 1 and 5.

Reply 4: We observed that patients with hypertension had an high patency rate of RA grafts 1 week post-operation. This maybe by chance. But our suggestion is that appropriate antispasm treatment should avoid low blood pressure.

Changes in the text: We deleted the sentence about hypertension maybe an protective factor, and add that, line 220, We analysed the data and found that hypertension is likely have some association with RA grafts failure within 1 week postoperation. Appropriate antispasm treatment without low blood pressure maybe important in the early stage post-operation.

Comments 5: It is not immediately clear why patency data are presented in a 2 x 2 table (Table 4). Further to this point, was there a correlation between radial artery and saphenous vein graft failure? Did failure of one type of graft represent a risk factor for occlusion of another, or did they appear to be independent processes?

Reply 5: We presented the patency data in a 2 x 2 table, because we performed self-paired comparison of the RA grafts patency and the SV grafts patency with McNemar’s test in each patient. In this way, we aim to compare the patency rate of different grafts in the same patient in order to exclude some interference factor.

Changes in the text: No change.

Comments 6: The works by Dreifaldt and collaborators should be considered among the references.

Reply 6: No-touch SV was a breakthrough in CABG. I was shocked by the excellent outcome of 8 year follow up. We will added the works among the references.

Changes in the text: line 224, At the same time, we should also keep attention on no-touch SV, Dreifaldt and collaborators reported excellent outcome of 8-years follow up. To find the appropriate secondary graft is always important for each coronary artery disease patient (28).

Comments 7: The concept patent should be defined in the abstract.

Reply 7: Thanks for the suggestion. We will add the definition in the abstract.

Changes in the text: We added definition of RA graft grade in the abstract. The follow up CCTA were completed about 1 year postoperation in out-patient clinic. We graded the grafts into 4 classes, A (excellent), B (graft diameter < 50% of target coronary artery), O (occluded), and S(string sign). Both S and O were defined as graft failure.

Comments 8: A randomized trial is mentioned in the methods section (line 77). This should be further explained, e.g. by a reference.

Reply 8: Thanks for suggestion. The randomized trials are ROMA and ASRAB. We will add references in the text.

Changes in the text: We added the references 7 and 8.

Comments 9: Were the number of anastomoses is reported, it might be specified that numbers reflect distal anastomoses (line 151).

Replay 9: Thanks a lot for pointing this that may cause misunderstanding.

Changes in the text: line 162, The mean number of distal anastomoses per patient was 3.82 ± 0.72 , with an average of 2.15 ± 0.48 arterial distal anastomoses and 1.68 ± 0.65 venous distal anastomoses per patient.

Reviewer B

Comments 1: The main criticism I would make is the lack of significant clinical data... The authors present a difference in patency between the grafts. They present the venous graft as superior to the arterial graft at one week.

It is difficult to draw any conclusions on how to choose the graft with these results.

It would be interesting to add the data on myocardial infarction and acute heart failure. Or at least the average troponin level. These data should be compared in the "permeable graft" and "non-permeable graft" groups.

This is all the more important as the analysis of graft patency using CT scans lacks sensitivity/specificity... And a "non-permeable" arterial graft at one week is probably not equivalent to a "non-permeable" venous graft at one week (the mechanism is not the same).

Therefore, it would be necessary to add significant clinical data and discuss the results a little more on this point. One cannot conclude that the vein graft is "superior" at one week. One can only conclude that its patency is better at one week...

Reply 1: Thanks for your helpful comments, clinical outcome is the most important than graft patency. According to your advice, we compared the highest troponin level post-operation in the "permeable graft" and "non-permeable graft" groups. In table 2, we showed the peak value of CK-MB, CTnI and myoglobin within 3 days post-operation. The echocardiography data before discharge were also shown in table 2. There were no statistical differences between the 2 groups for the tests. In fact, we collected some post-operation laboratory tests and examinations data, but failed to

find the association between them and 1 week RA graft failure. This needs further study.

Changes in the text: No change.

Comments 2: 41, conclusion, key finding, results: Please note that it is not possible to conclude that there is "similarity" between SVG and RA graft patency at one year. This is a retrospective study and only an "absence of significant difference" can be demonstrated. With greater power, a difference could be demonstrated... You should therefore change this to "did not show any significant difference" (to remain factual).

The way you turn this sentence is much better: "We speculated the crossing point of RA grafts and SV grafts patent rate were at about 1 year after CABG and the advantage of RA grafts compared with SV grafts may arise since 1 year after CABG." (195).

Reply 2: We will change the presentation according to your kind guidance. Thanks very much.

Changes in the text: Abstract line 48, the patent rate of the 2 kind of grafts did not show any significant difference at 1 year.

Key findings, The RA grafts patent rate was lower than SV grafts patent rate at 1 week post-operation, the patent rate of the 2 kinds of grafts did not show any significant difference at 1 year post-operation.

Conclusion line 249, the patent rate of the 2 kind of grafts did not show any significant difference (80% vs 81.3%, $P=1.00$).

Comments 3: 179: "The hypertension might be an independent protective factor for RA grafts failure within 1 week postoperation ($P=0.01$, OR 180 0.055-0.672, Table 5)"

The wording of the sentence should be put in the context of the discussion ("might"). Here you have to report the results: "There is a significant difference between..."

Reply 2: We will change the presentation according to your kindly guidance. Thanks very much. In fact, our suggestion is that appropriate antispasm treatment should avoid low blood pressure.

Changes in the text: We delete the sentence "The hypertension might be an independent protective factor for RA grafts failure within 1 week postoperation ($P=0.01$, OR 180 0.055-0.672, Table 5)". And we added that, line 221, appropriate antispasm treatment without low blood pressure maybe important in the early-stage post-operation.

Comments 4: 213/229: Intuitively one should say that hypertensive patients are often more at risk of being "spastic" than others... Here you report the opposite. It would be interesting to discuss this fact.

Furthermore, you draw the conclusion that a certain hypertension should be respected in these patients. This is a retrospective study with a small number of patients. It is therefore difficult to draw this conclusion. Especially as the treatments for spasm of the radial arterial graft are precisely anti-hypertensive treatments... This makes it

paradoxical or difficult to respect hypertension in these patients.

On the other hand, this paradox should be emphasized in the discussion...

Preoperative antihypertensive medication would have been studied too for the risk of reduced patency.

Reply 4: We just observed that hypertension was more common in RA patent patients. And our advice was that appropriate antispasm treatment should avoid low blood pressure. We did not express that clearly. We will revise the manuscript.

Changes in the text: We delete the sentence "The hypertension might be an independent protective factor for RA grafts failure within 1 week postoperation (P=0.01, OR 180 0.055-0.672, Table 5)". And we added that, line 221, appropriate antispasm treatment without low blood pressure maybe important in the early-stage post-operation.

Comments 5: Other risk factors: do you have data on patency according to the type of anastomosis (on the aorta, Y?). 210: perhaps cite some of the risk factors found in these references... This increases the pedagogical interest of the publication.

Reply 5: There were 11 RA Y grafts in this group of patients. 1 RA proximal site anastomosed to the LIMA and 10 RA proximal site anastomosed to the saphenous vein. The other 69 RA grafts proximal site anastomosed to the ascending aorta. There were 3 RA Y grafts failure at 1 week post-operation, 1 occlusion and 2 string signs. At 1 year, the 2 string sign grafts became excellent patent but the occlusion 1 was still occlusion. We did not find significant difference between the 2 kinds of proximal anastomosis.

Changes in the text: We added 2 references (17, 18) compared the outcome of different types of proximal anastomosis.

Comments 6: On which criteria did you do an angio CT scan at 1 week? At one year? Why did patients who had a CT scan at one week always have one at one year? The indication for a CT scan should be better detailed in this section.

Reply 6: From August 2019 to June 2021, 118 patients underwent urgent or elective CABG with RA grafts at Ruijin Hospital. 18 patients refused to participate in the ASRAB or ROMA clinical trial. Of the remaining 100 patients, 80 patients accepted both RA graft and SV grafts. So this study only included 80 patients. So all patients included in this study participated in the clinical trials. We tested the 1 week CCTA and 1 year CCTA for all of those patients.

Changes in the text: No change.

Comments 7: 219: You are discussing the possibility of performing a CT scan on all patients who are going to receive a radial graft... On the basis of the data from this study, it is really difficult to make this proposal: a CT scan is not ideal for assessing patency and we need to know whether there is any "clinical" interest beyond the images (as mentioned above). We'd like to see a more nuanced proposal... Maybe only in patient who have increased troponin.

Reply 7: It was a pity that we did not find any association of RA graft failure with

laboratory index or physical examination except for peak value of neutrophil count, but we have not found the postulated mechanism behind this phenomenon. I think patient who have increased troponin again after 48 hours post-operation should go to coronary angiography

Changes in the text: No change.

Comments 8: Can you describe a little more about how you removed the saphenous veins (Or, endoscopy, electric cautery...). And maybe explain how you choose your graft?

Reply 8: We harvested saphenous vein of the thigh with a traditional open incision. The SV was removed by scissors without peripheral adipose. In our center, LIMA to LAD was always the priority. In young patients with severe stenosis (75% stenosis for LCX, and 90% stenosis for RCA), RA was often used as the second artery graft.

We try to use multiple artery CABG in patients younger than 60 years old. If the stenosis is more than 80% in LCX or 90% in RCA with good run-off, RA is preferred. In patients without diabetes, we would try BIMA.

Changes in the text: Line 100, we give a simple description about how we remove the SV.

Comments 9: 55: The fifth reference is not very appropriate. It does not "prove" that patency is always associated with more adverse events. Particularly in the case of radial grafts. You should change it to something more precise. Or you could qualify your statement with "it is likely that ...".

Reply 9: The most recent article by Mario Gaudino also showed that graft failure remains common among patients undergoing CABG and is strongly associated with adverse cardiac events. So it is likely that occlusion is always associated with adverse events.

Change in the text: Add a new reference 5.

Reviewer C

Thanks very much for the advice. They were precious to lead our next study on RA graft.

Comments 1: I do not get the exclusion criteria about porcelain aorta

Reply 1: We always try to anastomoses RA on ascending aorta. It is difficult to do more anastomosis on a porcelain aorta and this manipulation may increase the risk of cerebral infarction. So we excluded patients with porcelain aorta.

Change in the text: No change.

Comments 2: You should explain better the resuscitation process that allow the improvement in radial arteries.

Reply 2: We completed CCTA in 2 time points post-operation. So it is hard to explain the resuscitation process of RA grafts. Thanks very much for this comment and it will

lead my next study on RA graft.

Change in the text: No change.

Reviewer D

Thanks very much for the comments. They are wonderful recommendations to improve the manuscript and my clinical skills.

Comments 1: The abstract includes words such as graded A, S, and O for which no definitions are provided, making them difficult to understand.

Reply 1: We will add definition of grade A, S, O in the abstract.

Change in the text: We revised abstract. The follow-up CCTA was completed about 1 year postoperation in out-patient clinic. We graded the grafts into 4 classes, A (excellent), B (graft diameter < 50% of target coronary artery), O (occluded), and S(string sign). Both S and O were defined as graft failure.

Comments 2: Page 4, line 69. Only 67.8% of all cases had a CT scan performed, which already has a selection bias. Therefore, the study may not be an accurate graft patency rate.

Reply 2: From August 2019 to June 2021, 118 patients underwent urgent or elective CABG with RA grafts at Ruijin Hospital. 18 patients refused to participate in the ASRAB or ROMA clinical trial. Of the remaining 100 patients, 80 patients accepted both RA graft and SV grafts. So this study only included 80 patients. Small simple size is a limitation.

Change in the text: No Change.

Comments 3: Page 4, line 78; please provide the Ethics Committee approval number.

Reply 3: (2019) 临伦审第 (42) 号

Change in the text: No Change.

Comments 4: Page 7, line 161. The early patency rate of the radial artery is 76%, a rather low patency rate, which may not be an acceptable outcome for surgical invasiveness in the era of minimally invasive PCI. The authors need to consider improvements in their own surgery in accordance with the guidelines and statements regarding CABG using the radial artery graft.

Reply 4: The RA grafts patency is excellent in your center. We believe RA grafts was preferred as a secondary grafts if used properly. In this study, we give much rigid judgment of RA grafts. Only excellent patent with smooth wall in CCTA was realized grade A. Any focal non-permeable was judged as occlusion of the whole grafts. String sign was defined as slim graft trunk diameter of less than 1.5mm. Some Occlusion or String Sign maybe judged as patent in previous studies. I have a request, please teach me some tips in using RA grafts, and I will appreciate them and improve myself. Thanks very much. It is my honor if you give me some technique guidance. My e-mail: liuyun3@mail3.sysu.edu.cn

Change in the text: No Change.