Author's response to reviews

Title: Distal end side-to-side anastomoses of sequential vein graft to small target coronary arteries improve intraoperative graft flow

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Version: 2
Date: April 26, 2014
Author's response to reviews: see over

Reviewer 1
Title: Distal end side-to-side anastomoses of sequential vein graft to small target coronary arteries improve graft patency

Version: 2

Date: 25 March 2014

Reviewer: Uzair Ansari

Reviewer’s report:

Minor essential revisions.

1. More figures and diagrams explaining the procedure.

To meet the reviewer’s request, we have included additional diagrams in the Figure 1A to illustrate the side-to-side anastomosis procedure. The diagram i displays the first step of the procedure, which is the side-to-side anastomosis of the graft to target coronary artery. The diagram ii shows that the distal end of graft is cut at 45-degree angle toward the anastomosis. The diagram iii illustrates that the 45-degree slope at the distal end of the graft is sealed with polypropylene 7-0 suture. We also updated the figure legend on page 18 line 4.

Discretionary revisions

1. If similar procedures have been attempted at other centers and where?

As far as we know, we are the only cardiac surgery center in China where this distal end side-to-side anastomosis has been attempted. We have not encountered any publications describing similar procedures.

2. Proposed follow up?

All the patients were followed-up 3 months after the operation. Electrocardiography and echocardiography performed during the follow-up examination showed that patients’ cardiac function had been improved. The results from 3-month follow-up examination were described in the RESULT section on page 9. Now, we are following-up these patients to further evaluate the mid-term and long-term patient outcomes of this procedure.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests
Reviewer 2

Title: Distal end side-to-side anastomoses of sequential vein graft to small target coronary arteries improve graft patency

Version: 2

Date: 26 February 2014

Reviewer: Soichiro Kitamura

Reviewer's report:

"Major Compulsory Revisions" Reviewer's report

1. The conclusion of this paper is based upon intraoperative flow measurement which can be influenced by many other factors undescribed or unmeasured in this study, such as aortic pressure, use of coronary dilators and heart rates. These factors vary among patients but not reported at all in this study.

We agree with the reviewer that heart rate and blood pressure can influence intraoperative graft flow. Thus, during the operation, we discontinued coronary dilators. Additionally, we measured intraoperative graft flow and PI when blood pressure became stable. We added these statements in the METHOD section on page 7 line 4.

2. The authors stated that they believed the reason for initial poor graft flow was not technical errors, instead was associated with unfavorable hemodynamic characteristics,..., but there was no evidence to show us readers. One may say that it was still due to technical errors (kinking, twisting, and/or anastomotic narrowing) because graft flow is determined by driving pressure, graft diameter and length (graft resistance) and distal coronary artery resistance, which would not change much by anastomotic technique, if stenosis is not made. Turbulent flow due to size mismatch between the graft and recipient coronary artery may influence early or late graft patency due to blood clotting but not absolute flow volume itself during operation. The authors must explain the reasons for graft flow volume difference for us either by citing the previous hemodynamic studies or your experimental studies. The cited papers 4, 5 did not mention the flow-volume difference between the 2 anastomotic techniques.

As the reviewer mentioned, driving pressure, graft diameter and length (graft resistance), and recipient coronary artery resistance determine graft flow. We also believe when the graft-host diameter ratio becomes very big, for instance, 4:1 in our patients, anastomotic geometry can affect graft flow significantly. Frauenfelder et al. reported that flow stagnation zones exist in end-to-side but not in side-to-side anastomosis. The stagnation zones and turbulent flow resulting from an end-to-side anastomosis might not cause immediate adverse effects on graft flow when graft-host diameter ratio is within the normal range. However, in an end-to-side anastomosis with oversize graft-host diameter ratio, those factors might become critical to determine graft flow. We are currently using computational simulation and animal model to investigate the hemodynamic
characteristics in anastomoses with different configuration and with oversize graft-host diameter ratio.

3. Also, the authors admitted that in this study, there was no control arm and they described that it would violate medical ethics to have a control group of patients. But it seems to me that the concept is more emotional than scientific because it is not scientifically determined that distal end to side anastomosis is inferior to distal side to side anastomosis in obtaining the higher flow when the distal coronary artery is small. I would like to expect your experimental studies.

We agree with the reviewer that it is still unknown whether distal end-to-side anastomosis is inferior to distal side-to-side anastomosis in terms of obtaining the higher flow when the distal coronary artery is small. As long as a distal end-to-side anastomosis can result in satisfactory intraoperative flow parameters, we believe it is fine to include a control group of distal end-to-side anastomosis. In this report, all the 14 patients had an oversize graft-host diameter ratio (approximately 4:1), and the distal end-to-side anastomosis produced unsatisfactory graft flow parameters in these patients. We had to revise the end-to-side anastomosis into side-to-side anastomosis for these patients.

Indeed, we are currently collaborating with experts in computational fluid dynamics to investigate the flow characteristics in graft and host vessel with various graft-host diameter ratios under different anastomotic geometry. We are currently also using animal model to compare the long term graft patency of distal side-to-side anastomosis versus end-to-side anastomosis for small host coronary artery with an oversize graft-host diameter ratio.

To address the reviewer’s concern, we have replaced the sentence “However, it violates medical ethics to leave unsatisfactory anastomoses uncorrected.“ with the following version: “However, in the present study, we had to revise the problematic distal end-to-side anastomoses, which produced unsatisfactory graft flow parameters, into the distal side-to-side anastomoses” on page 12 line 6.

4. Lastly, there are no graft patency reports at all in this paper, but the title of this paper is “--- improve GRAFT PATENCY”, which is apparently misleading.

To address the reviewer’s concern, we have replaced the title with the following new version: Distal end side-to-side anastomoses of sequential vein graft to small target coronary arteries improve intraoperative graft flow on page 1.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I declare that I have no competing interests.

Reviewer 3

Title: Distal end side-to-side anastomoses of sequential vein graft to small target
coronary arteries improve graft patency

Version: 2

Date: 14 March 2014

Reviewer: Michael Behnes

Reviewer's report:

Major compulsory revisions: None

Minor essential revisions and discretionary revisions:

1. Were the revisions from end-to-side to side-to-side anastomosis performed within one operating procedure in all of the 14 patients? Please clear this up.

Yes. The revision was performed under off-pump condition within one operating procedure in all of the 14 patients.

2. Measurements of CKMB levels as a biomarker of sufficient side-to-side anastomosis are questionable. CKMB levels are expected to decrease after successful cardiac surgery anyway, independently of the different techniques of distal anastomosis. There is no direct comparative group indicating CKMB levels in patients with end-to-side versus side-to-side anastomosis. Please add this to the study's limitation.

According to the reviewer's comments, reduced CK-MB levels after surgery is associated with a successful cardiac surgery. Our purpose to describe patient’s CK-MB levels in the result section on page 8, which was to show the absence of serious postoperative complication after the surgical procedure, is actually consistent with the reviewer’s opinion. We did not intend to use CK-MB levels as a biomarker of sufficient side-to-side anastomosis.

We agree with the reviewer that a direct comparison of CK-MB levels in patients with end-to-side versus side-to-side anastomosis is missing in our study due to the absence of a control group with end-to-side anastomosis. According to our experience, the average CK-MB levels on arrival to the surgical ICU and 48 hours post-operation in patients undergoing routine CABG in our department are not significantly different from the CK-MB levels described in this report, suggesting that the distal end side-to-side anastomosis procedure do not appear to cause more postoperative complications compared to standard CABG procedure.

To further clarify this concern, we have added the following statements in the DISCUSSION section on page 12 line 15:

“The CK-MB levels in our patients significantly dropped 48 hours after the operation, indicating the absence of serious complication associated with the surgical procedure. In this study, we were unable to directly compare CK-MB levels in patients with end-to-side anastomosis versus side-to-side anastomosis due to the absence of a control group with end-to-side anastomosis. However,
according to our experience, the average CK-MB levels on arrival to the surgical ICU and 48 hours post-operation in patients undergoing routine CABG in our department are not significantly different from the CK-MB levels described in this report, suggesting that the distal end side-to-side anastomosis procedure do not appear to cause more postoperative complications compared to standard CABG procedure.”

3. Please add some more literature specifically about distal anastomosis techniques, which might illustrate the problems within this specific setting. Please include these within introduction and discussion.

According to the reviewer’s suggestion, 3 additional references about distal anastomosis techniques have been added in the introduction (page 4 line 9) and discussion sections. Studies about the effects of oversize graft-host diameter ratio on anastomotic hemodynamics do not seem to be available.

4. Please summarize limiting parts of the study (as the authors describe them already within the discussion section) within a separate section “study limitations”. Thereby, discussion will be shortened and become easier to read (also see above).

A “study limitations” section has been added according to the reviewer’s suggestion on page 11.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I declare that I have no competing interests.