

Peer Review File

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Reviewer A

I read with great interest the retrospective study carried out by Yang and coworkers. The study analysis involved 1,276 patients previously undergoing CABG who subsequently underwent PCI on either native coronary arteries (1,072 patients, 84%) or graft (n = 204, 16%) predominantly saphenous vein grafts.

The main findings of the study are that patients undergoing graft PCI have an increased risk of peri-procedural complications (such as stroke), no-reflow, and non-fatal myocardial infarction during the medium-term follow-up. On the one hand, these results can intuitively be expected given that the procedure on a venous graft is generally more complex, therefore the study does not capture particular aspects of originality. However, in my opinion it turns out to be very interesting, since, as explained in the discussion, the authors state that it is a sample of patients that is very well represented in China. In the discussion and in the conclusions, the authors could underline that in fact it is not always possible to perform PCI on the native coronary artery. And probably the less optimal results observed in the PCI graft group in comparison with PCI patients on native coronary arteries derives precisely, regardless of the statistical evaluations, from a greater severity of coronary ischemic pathology (longer time between CABG and CI for example). The materials and methods, the results and the Tables/figures are well representative and clear to the readers, and the work is written in good English. Please check NSET in NSTEMI myocardial infarction.

Comment 1: In the discussion and in the conclusions, the authors could underline that in fact it is not always possible to perform PCI on the native coronary artery.

Reply 1: Thanks for the valuable advice. We added contents about “it is not always possible to perform PCI on the native coronary artery” in the Discussion.

Changes in the text: we have modified our text as advised (see Page 14, line 325-326)

Comment 2: Please check NSET in NSTEMI myocardial infarction.

Reply 2: Thanks for your suggestion. We have changed NSET-ACS into NSTEMI-ACS.

Changes in the text: we have modified our text as advised (see Page 9, line 200)

Reviewer B

I congratulate the authors for their work. The paper is well-written and the data are robust.

My concerns are as follows.

#1: Over 95% of PCI was performed in patients with acute coronary syndrome in this study. These PCI were performed emergently? urgently? or electively? The authors should describe the status of PCI.

Comment 1: Over 95% of PCI was performed in patients with acute coronary syndrome in this study. These PCI were performed emergently? urgently? or electively? The authors should describe the status of PCI.

Reply 1: Thanks for your suggestion. There were 1276 patients in total, 156 (12.2%) patients received emergency PCI and the rest with elective PCI.

Changes in the text: we have added related content in text and table 2 as advised (see Page 7, line 159-160 and Table 2)

#2: Outcomes in patients with chronic coronary syndrome (CCS) were similar to in patients with acute coronary syndrome patients? I think the number of CCS patients was major limitation of this study.

Comment 2: Outcomes in patients with chronic coronary syndrome (CCS) were similar to those with acute coronary syndrome patients? I think the number of CCS patients was major limitation of this study.

Reply 2: In our study, there are 1241 ACS patients, only 35 CCS patients, and we find that patients with CCS have similar outcomes with ACS patients. The main reason of the finding is the number of CCS patients, and one of the limitations of the study.

Changes in the text: we have modified our text as advised (see Page 19, line 435)

#3: Native coronary PCI was performed on a non-protected/new lesion coronary artery or previously protected coronary artery by CABG?

Comment 3: Native coronary PCI was performed on a non-protected/new lesion coronary artery or previously protected coronary artery by CABG?

Reply 3: Thanks for the valuable suggestion. It is a valuable question we think about all the time when writing. In our study, there were 1168 target native vessels performed PCI with protected coronary artery by CABG. We have illustrated in the Results.

Changes in the text: we have modified our text as advised (see Page 9-10, line 220-221)

#4: I confused the distribution of the target vessel in the bypass graft PCI group. Why was the amount of the target vessel smaller than the patients' number?

Comment 4: Why was the amount of the target vessel smaller than the patients' number?

Reply 4: In our study, there were 1276 patients in total, including 1072 patients in native group, and 204 patients in graft group. There were 1698 target vessels and 1744 lesions in the study.

#5: The reviewer would like more information on the bypass site of LIMA and SVG which performed PCI

Comment 5: The reviewer would like more information on the bypass site of LIMA and SVG which performed PCI?

Reply 5: Thanks for your suggestion. More information on the bypass site of LIMA and SVG was performed in the Table 2. Due to lots of patients with sequential graft, such as AO-SVG-D1-SVG-OM-SVG-PDA, OM and PDA are also considered as target vessels if PCI is performed at the site of AO-SVG-D1.

Changes in the text: we added related data in Table 2 (see Table 2).

Reviewer C

This is a large volume single-center study from China which studies. I congratulate on detailed study utilizing IPTW to balance the characteristics. Well-analyzed study but I would add some comments as follows.

1. In bypass graft group, all targets were SVG? Is there any information about which vessel was grafted (in terms of target, e.g. SVG-OM, SVG-PDA, etc), as you demonstrated target vessels on native PCI group?

Comment 1: In bypass graft group, all targets were SVG? Is there any information about which vessel was grafted (in terms of target, e.g. SVG-OM, SVG-PDA, etc), as you demonstrated target vessels on native PCI group?

Reply 1: Patients in graft group are received PCI of both a native coronary artery and/or a bypass graft. Bypass grafts including LIMA and SVG. Specific information about target graft was added in the Table 2.

Changes in the text: we added related data in Table 2 (see Table 2).

2. In terms of non-fatal MI, there is a difference between GRAFT-PCI and Native-PCI (Figure 2D, and 3D). This difference seems to become significant after 6-7 years although survival curve was quite similar up to 6 years. Why do authors think this happens? I though significant problem usually happens earlier.

Comment 2: In terms of non-fatal MI, there is a difference between GRAFT-PCI and Native-PCI (Figure 2D, and 3D). This difference seems to become significant after 6-7 yeas although survival curve was quite similar up to 6 years. Why do authors think this happens? I though significant problem usually happens earlier.

Reply 2: In our observational study, we found that patients in graft group had a significant higher incidence of non-fatal MI at long-time follow-up. In general, MI usually occurs earlier in ACS patients, but this result comes from a retrospectively study and all patients with a history of CABG, which might be the characteristic of the study. Progression of atherosclerosis in native coronary artery and bypass graft, which might be the major cause of the finding. More related studies needed to demonstrate the

convincing findings. We have explained possible reasons in the Discussion.
Changes in the text: we have modified our text in discussion as advised (see Page 18, line 409-411)

3. In line with a higher slow-flow rate in bypass graft group, why did event occur in the later period of follow-up rather than the early events such as peri-procedural MI, etc.

Comment 3: In line with a higher slow-flow rate in bypass graft group, why did event occur in the later period of follow-up rather than the early events such as peri-procedural MI, etc.

Reply 3: In this study, no-reflow/slow-flow, peri-procedural MI, and etc. were the procedural-related complications that were early rather than late events. All procedural-related complications including, in-hospital mortality, peri-procedural MI, peri-procedural stroke, perforation of target vessel, dissection of target vessel, intramural hematoma of target vessel, slow-flow/no-reflow, temporary pacing, cardiopulmonary resuscitation, equipment loss or entrapment, hemodynamic instability, and other complications. Detailed statistics are shown in Table 4.

4. Is that correct TIMI 3 flow was higher in bypass graft group given the higher rate of slow-flow in this group?

Comment 4: Is that correct TIMI 3 flow was higher in bypass graft group given the higher rate of slow-flow in this group?

Reply 4: As shown in Table3, there were 1399 (91.5%) and 202 (94.0%) lesions with TIMI 3 flow grade, 23 (1.5%) and 10 (4.7%) lesions with TIMI 1-2 flow grade, 107 (7.0%) and 3 (1.4%) lesions with TIMI 0 flow grade post-PCI (p for post-PCI TIMI flow grade <0.001). Besides, there was 1 (0.1%) and 3 (1.5%) patients with the procedural-related complication of slow-flow/no-reflow before IPTW (p=0.011), and the p<0.001 after IPTW. I think the major reason was the difference of the sample size between the two groups, and is one of the limitations of the study.

Changes in the text: we have modified our text in Limitations as advised (see Page 19, line 436)

5. I would like to clarify if Figure 4 is univariable analysis or multivariable Cox proportional hazard analysis. This needs to be clarified in the Table legend. If univariable, why not multivariable?

Comment 5: I would like to clarify if Figure 4 is univariable analysis or multivariable Cox proportional hazard analysis. This needs to be clarified in the Table legend. If univariable, why not multivariable?

Reply 5: Thanks for your reminding. Figure 4 is multivariable Cox proportional hazard analysis, and the adjustment model is the same as the IPTW model.

Changes in the text: we have modified our text as advised (see Page 9, line 206-209) and clarified in the Table legend.

6. “We are looking forward to the results of the PROCTOR randomized trial. More large-scale randomized trials are needed to provide more evidence for clinical practice.” Do authors really think this population need RCT? This type of intervention is case by case as some patients do not have alternative options (e.g. Grafts are the only source of blood supply). Thus, I would say “native coronary artery might be preferred to be selected for PCI in patients with prior CABG if feasible (when possible)“. As you demonstrated, a success rate of native PCI (+/- CTO) was lower which is another consideration or discussion authors can add.

Comment 6: Do authors really think this population need RCT? This type of intervention is case by case as some patients do not have alternative options (e.g. Grafts are the only source of blood supply). Thus, I would say “native coronary artery might be preferred to be selected for PCI in patients with prior CABG if feasible (when possible) “. As you demonstrated, a success rate of native PCI (+/- CTO) was lower which is another consideration or discussion authors can add.

Reply 6: It is a good question that you have asked, and worth discussing. Patients with prior CABG had complex lesions in native coronary artery and/or bypass graft. At most conditions, native coronary artery PCI was the preferred choice for such patients, as you have said that some patients do not have alternative options, grafts are the only source of blood supply. However, the RCT study results will be more convincing in some condition, such as both the native lesion and the venous graft lesion are suitable for PCI, and meet with other criteria are listed in the PROCTOR trial (NCT03805048). I am very interested in it.

I will further discuss the possible reasons for the lower success rate of native PCI in the Discussion.

Changes in the text: we added some content about “the success rate of native PCI was lower” in Discussion (see Page 15, line 329-340)

7. Another question is how much impact does “non-fatal MI” have? This is always the discussion when it comes to outcome of CABG vs PCI.

Comment 7: How much impact does “non-fatal MI” have? This is always the discussion when it comes to outcome of CABG vs PCI.

Reply 7: Our observational study found that patients in graft group have a higher incidence of non-fatal MI than those in native group regardless of IPTW adjustment (7.8% versus 3.8%, $p=0.018$ and 8.3% versus 3.9%, $p=0.030$, separately). Kaplan-Meier analysis revealed that patients in graft group showed higher incidence of non-fatal MI (Log-rank $p=0.017$). Besides, graft group was associated with a higher risk of non-fatal MI compared with native group (HR: 2.091, 95% CI: 1.069-4.089; $p=0.031$). Several previous studies reported that there was significant difference between patients with native coronary artery PCI and graft PCI in non-fatal MI, but other studies with different results. We thought the question worth further investigate.

Reviewer D

In their manuscript entitled “Comparison of Percutaneous Coronary Intervention of Native Coronary Artery Versus Bypass Graft in Patients with Prior Coronary Artery Bypass Grafting”, Dr. Yang and colleagues enrolled 1276 patients with prior coronary artery bypass grafting (CABG) who underwent percutaneous coronary intervention (PCI). The authors compared the clinical outcomes in 1072 patients with PCI to native coronary artery with those in 197 patients with PCI to bypass graft. They performed inverse probability of treatment weighting (IPTW) analysis to overcome the retrospective nature of their study. The authors included a large number of patients and performed comparative analyses. This study might give valuable information regarding results of native vessel vs graft PCI in patients with prior CABG.

I would like to recommend the authors to implement the following suggestions to strengthen their paper.

1. I would like to recommend the authors to consult a statistician to more clearly demonstrate statistical methods and results, and correct some statistical terms such as ‘free survival probability’ ‘survival free of non-fatal MI’.

Comment 1: Recommend the authors to consult a statistician to more clearly demonstrate statistical methods and results, and correct some statistical terms such as ‘free survival probability’ ‘survival free of non-fatal MI’

Reply 1: Thanks for your suggestion. I have consulted with statistician and made the changes as requested.

Changes in the text: we have modified our text as advised (see Page 9, line 203-206 and Page 12, line 278-284)

2. It might be better to shorten the ‘Discussion’ section.

Comment 2: It might be better to shorten the ‘Discussion’ section.

Reply 2: I will simplify the discussion based on the overall structure and content of the article

Changes in the text: we have modified our text in Discussion as advised

3. Tables 2 and 3 might be too complicated.

Comment 3: Tables 2 and 3 might be too complicated.

Reply 3: Thanks for your advice. The variables displayed were statistical differences or clinical importance. I will simplify the tables 2 and 3 as appropriate.

Changes in the text: we have simplified table 2 and 3 as advised (see Table 2 and 3)

4. In table 2, number of target vessels in the bypass graft group should be corrected.

Comment 4: In table 2, number of target vessels in the bypass graft group should be corrected.

Reply 4: In our study, there were 204 patients in graft group, 197 patients with SVG-PCI and 7 patients with LIMA-PCI. Take previous studies as reference, bypass graft group including patients with SVG-PCI and LIMA-PCI. In table 2, there was 204 patients in graft group, including 197 patients with SVG-PCI and 7 patients with LIMA-PCI. Do you mean to exclude patients with LIMA PCI.

5. The terms ‘prior CABG’ and ‘undergoing index PCI’ could be omitted after firstly describing that the authors enrolled patients with prior CABG undergoing index PCI.

Comment 5: The terms ‘prior CABG’ and ‘undergoing index PCI’ could be omitted after firstly describing that the authors enrolled patients with prior CABG undergoing index PCI.

Reply 5: I will omit the terms “prior CABG” and “undergoing index PCI” after firstly described.

Changes in the text: we have modified our text as advised in the manuscript.

6. It might be better to name the two groups rather than repetitively describing the patient’s as ‘patients undergoing bypass graft PCI’, ‘patients of bypass graft PCI’ and ‘those who received PCI of native coronary artery’.

Comment 6: It might be better to name the two groups rather than repetitively describing the patients such as ‘patients undergoing bypass graft PCI’, ‘patients of bypass graft PCI’ and ‘those who received PCI of native coronary artery’.

Reply 6: We have named the 2 groups according to the PCI target vessel, including native group and graft group. Besides, we have revised it in the manuscript.

Changes in the text: we have modified our text as advised in the manuscript.

7. What does it mean the word ‘CAPTAIN’ in figure 1?

Comment 7: What does it mean the word ‘CAPTAIN’ in figure 1?

Reply 7: The “CAPTAIN” is the protocol ID of the study when we registered in the ClinicalTrials, and all the letters comes from the name of the study of “CompARison of PCI in NaTive Arteries Versus ByPAss Grafts In PatieNts With Prior CABG”. This study has relatively large samples in the China, and we hoped that it can provide valuable clinical reference for prior CABG patients and supply reference value for the subsequent studies.