Peer Review File

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Reviewer A

Comment 1: In the abstract line 16 the measure unit for the follow-up in missing. It should be year.

Reply 1: I appreciate your alerting us to this oversight. We added the absent unit.

Change 1: '. Long-term median follow-up 5.58 (3.27 - 8.48) years was available for 1089 patients (94.7%).'

Comment 2: I gently request the authors to comment about the learning curve on these procedure as they are a single center. Are all those cases performed by a single surgeon? Have the firsts CR cases being performed using more SVG and subsequently radial artery?

Reply 2: Every attending surgeon at our institution possesses the necessary expertise to execute OPCAB. We perform sequential bypasses with the bilateral internal thoracic arteries the majority of the time. When progressing, the initial step is to execute MIDCAB, followed by MICS CABG. The cases in the study were performed by five surgeons. The number of planned coronary bypasses, the comorbidities of the patient, and the coronary anatomy are factors in determining which surgeon will perform the procedure and its anticipated difficulty.

The selection between the saphenous vein and radial artery was determined by patient-specific factors rather than surgical or surgical expertise of the operating surgeon. In the event that the radial artery could not be utilised (due to atherosclerosis, dissection of the artery, Allen Test revealed pathology on both sides, and/or the radial artery was utilised for the coronary angiogram prior to surgery), the saphenous vein was employed.

Change 2: We added this explanation to the ‘Surgical Technique’ section of the paper.

‘A 6- to 7-cm left antero-lateral thoracotomy was performed through the bed of the fifth intercostal space. The LITA conduit was mobilised to revascularize the LAD in all cases. A T-graft construct was created to deliver blood flow to the lateral and/or posterior myocardial walls, with either the radial artery or saphenous vein used as bypass grafts and connected to the LITA. All operations were carried out on a beating heart using the off-pump approach. The operational specifics have been presented previously (7).

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Comment 3: I gently request the authors to address the % of LIMA to SVG Y anastomosed used for CR group and comment the discussion session on how this might have been an impact of not showing a statistical survival advantage. I mean that maybe the statistical significance has not been reached because during the first few years the CR have been carried out using more vein grafts with a paradoxically loss of the advantage on IR with only arterial graft (in particular single LIMA-LAD).

Reply 3: As previously stated, the selection of the bypass graft material did not have a temporal relationship; instead, there were patient-specific factors that impacted this determination. Furthermore, the percentage of patients who received a saphenous vein graft was relatively low, 3.2% in total, with 2.7% in Group I and 3.3% in Group C. I completely concur with the point you made; it could have provided us with a plausible explanation for why our study population did not exhibit a statistically significant difference in survival; however, this was not the case.

Change 3: We included this clarification in the paper's 'Discussion' section.

An inquiry was made regarding whether the selection of conduit and the improvement of the surgical procedure throughout the duration of the trial, particularly whether there was a higher utilisation of saphenous vein grafts compared to radial artery grafts at the beginning, could have influenced the survival outcomes. In our study group, we discovered that the choice of bypass graft material was not influenced by time, but rather by individual patient variables. In addition, the proportion of patients who underwent a saphenous vein graft was rather small, totaling 3.2%, with 2.7% in Group I and 3.3% in Group C. Thus, this discovery further supports the concept that bypass grafting of the LAD with the left internal thoracic artery may counterbalance the long-term prognostic effects of CAD.

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Reviewer B

I would want to begin by thanking you for taking the time to review our work and for your valuable comments in making our manuscript clearer to the readers.

Comment 1: Abstract

- Line 19-22. It should be specified that the reported survival rates were unadjusted.

Reply 1: I appreciate your alerting us to this oversight. We added the absent unit.

Change 1: The 1-, 3-, 5-, 8-, and 10-year unadjusted survival rates were 94%, 84%, 75%, 62%, and 51% for Group I, and 97%, 94%, 88%, 77%, and 72% for Group C, respectively (long-rank test p-value < 0.001), favouring complete revascularization. Following risk adjustment the long-rank test p-value for survival was 0.226.

Comment 2: Surgical technique

- Line 106. Why could the 57 patients not undergo PCI? Radiation exposure? Kidney disease? Clarifications are warranted regarding these patients.
- Line 108. Why were the 85 procedures not performed? It should be specified.

Reply 2: Thank you for highlighting the absence of clarity in these patients.

To answer your initial query, the referring interventional cardiologist determined that these patients' significantly calcified coronaries and complicated anatomy made them unsuitable for PCI. Additionally, the mean age of these patients was 79.7 years, and 29.8% of them experienced an acute myocardial infarction within three weeks prior to surgery. Also, 43.9% presented with chronic kidney disease.

In relation to your second inquiry, the reason why 85 patients did not undergo the intended PCI procedure can be attributed to one of two factors. Firstly, some patients did not experience angina symptoms after surgery, leading to the postponement of the procedure. Secondly, the procedure was conducted not only through a coronary angiogram but also involved subsequent hemodynamic measurements. As a result, it was determined that the remaining stenosis was not significant and did not require PCI or stent implantation.

Change 2: We added these clarifications to the ‘surgical technique’ chapter.

‘There were several reasons for incomplete revascularization.
In 57 cases, the heart team decided to perform incomplete revascularization (single LITA-LAD bypass) due to the patients' severe infirmity and multiple diseases. The mean age of these patients was 79.7 years, and 29.8% of them experienced an acute myocardial infarction within three weeks prior to surgery. Furthermore, 43.9% presented with chronic kidney disease. The referring interventional cardiologist determined that these patients' significantly calcified coronaries and complicated anatomy made them unsuitable for PCI.

In 85 cases, hybrid procedures were scheduled, but the intended PCI procedure was never performed. The reason can be attributed to one of two factors. Firstly, some patients did not experience angina symptoms after surgery, leading to the postponement of the procedure. Secondly, the procedure was conducted not only through a coronary angiogram, but also involved subsequent hemodynamic measurements. As a result, it was determined that the remaining stenosis was not significant and did not require PCI or stent implantation.

In 43 cases, the intended surgical operation could not be completed because the operating surgeon assessed that the patients' coronaries were too small and excessively atherosclerotic to be revascularized.'

Comment 3: Statistical analysis
- What is the extent of missing data? If excessive information is missing it could lead to over/under expression of the results.
- For the regression models used, was any form of collinearity detected? Some preoperative variables were somehow similar like creatinine, GFR, renal replacement therapy that could overfit the model.

Reply 3: Thank you for this important observation. The lack of data on survival or MACCE for the sixty cases that were lost to follow-up was treated as absent value. All the other variable sets that were gathered were full except for this information.
As for your second question, there was not collinearity detected.

Change 3: We added this explanation to the 'statistical analysis' chapter.

'A bootstrap-type method was employed to calculate the PS-adjusted p-value in the analysis of MACCE-free survival curves. In this method, the treatment variable was sampled based on the propensity score (PS) of each individual case. The lack of data on survival or MACCE for the sixty cases that were lost to follow-up was treated as absent value. All the other variable sets that were gathered were full except for this information.'

Comment 4: Results
- Line 176. Minor difference in % regarding the type of surgery is reported compared to Table 2. Please revise.
- The Authors should briefly describe the different preoperative outcome between group I and C regarding conversion rates and reoperations.

Reply 4: Thank you again for your valuable input. We adjusted the percentages in the text and provided brief summaries of the information you mentioned.

Change 4: ‘The rate of conversion to either sternotomy or sternotomy with CPB was extremely low. However, all five patients who required conversion belonged to Group C.’

‘50 patients had a myocardial infarction, accounting for 4.4%, whereas 134 patients, or 11.7%, required a PCI procedure. It is worth noting that none of the seven patients who underwent redo bypass surgery were designated from Group I.’

Comment 5:

Discussion

- Line 218-226. I suggest moving this limitation section at the end of the discussion paragraph, just before the conclusions.

Reply 5: Thank you for this suggestion. We moved the limitation section at the end of the discussion chapter.

Comment 6:

Language

- Sex and gender should not be used interchangeably, as they have a different meaning. I suggest using the word “sex”.

Reply 6: Again, I appreciate you bringing up a very valid point. The term "gender" was substituted with "sex."