

Peer review file

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Reviewer A

This is quite an interesting topic.

ESRD is unfortunately a growing clinical scenario; different studies showed an higher mortality compared with the general population. The AURORA trial identifies the predictors for mortality.

The structure of the manuscript is well done, with good statistical analysis and narrative discussion. The Authors follow the STROBE checklist.

The results are in keeping with those of previous studies (the incidence of IHD in ESRD is almost >50% in the overall cohort of ESRD patients, with the ARTS study showing CABG a decreased mortality rate compared to medical treatment and PCI).

Therefore, the manuscript confirms the already known outcomes as early or late mortality.

The findings of LIMA-LAD graft, as positive predictor, is quite interesting, with an hazard ratio of 0.42.

Few questions may rise:

Comment 1:

- Why the off pump surgery was performed only in 11 patients? Why, even in case of porcelain aorta, CPB was performed against off pump surgery?

Reply 1: On-pump beating surgery was the preferred technique in patients where there was sufficient plaque-free area to perform aortic cannulation safely but insufficient safe area for cross-clamping of the aorta. Off-pump surgery was reserved for patients without safe areas for both aortic cannulation and cross-clamping.

Change in the text: This has been added to the manuscript (page 6, lines 154 – 158).

Comment 2:- In the quoted: "Amongst the 9 patients who did not receive a LIMA-LAD graft, 5 patients (55.6%) underwent non-elective surgery. This group of patients had a higher mean EuroSCORE II compared to LIMA-LAD graft recipients", it is not clear the incidence of mortality for emergency surgery (37 total - 10 not survived) in relation to the use of LIMA-LAD graft and the Euroscore. How many of those patients underwent emergency surgery and only vein grafts? (should be a total of 9 patients - but are these elective cases or no?)

Reply 2: To improve on clarity, the statement "Amongst the 9 patients who did not receive a LIMA-LAD graft, 5 patients (55.6%) underwent non-elective surgery. This group of patients had a higher mean EuroSCORE II compared to LIMA-LAD graft recipients", page, lines? has been removed.

To address the reviewer's comments, the following paragraph has been added "Operative mortality occurred in 20 patients (13.4%) and was higher in patients undergoing non-elective (emergent and urgent) surgery (27% [10 of 37 patients] vs 8.9% [10 of 112 patients], $P=0.005$). Amongst the 37 patients who underwent non-elective surgery, patients suffering early mortality had a higher EuroSCORE II compared to those who survived (10.4 vs 5.2, $P=0.008$). Operative mortality was 40% (2 of 5 patients) in patients receiving only vein grafts (non-LIMA-LAD group) compared to 25% (8 of 32 patients) in LIMA-LAD graft recipients, ($P=0.482$)."

Changes in the text:

To improve on clarity, the statement "Amongst the 9 patients who did not receive a LIMA-LAD graft, 5 patients (55.6%) underwent non-elective surgery. This group of patients had a higher mean EuroSCORE II compared to LIMA-LAD graft recipients", page, lines? has been removed (page 7, lines 187 – 189).

To address the reviewer's comments, the following paragraph (page 6, line 167 to page 7, line 172) has been added "Operative mortality occurred in 20 patients (13.4%) and was higher in patients undergoing non-elective (emergent and urgent) surgery (27% [10

of 37 patients] vs 8.9% [10 of 112 patients], $P=0.005$). Amongst the 37 patients who underwent non-elective surgery, patients suffering early mortality had a higher EuroSCORE II compared to those who survived (10.4 vs 5.2, $P=0.008$). Operative mortality was 40% (2 of 5 patients) in patients receiving only vein grafts (non-LIMA-LAD group) compared to 25% (8 of 32 patients) in LIMA-LAD graft recipients, ($P=0.482$).”

Comment 3: Why the LIMA graft was not performed? (age, small target, emergency?)

Reply 3: Nine patients (6.0%) received a saphenous vein graft to the LAD. Within this group, the LIMA was not used in view of haemodynamic stability in 7 patients (77.8%), insufficient LIMA length in 1 patient (11.1%) and poor LIMA quality in 1 patient (11.1%).

Changes in the text. The following paragraph has been added to the text “Nine patients (6.0%) received a saphenous vein graft to the LAD. Within this group, the LIMA was not used in view of haemodynamic stability in 7 patients (77.8%), insufficient LIMA length in 1 patient (11.1%) and poor LIMA quality in 1 patient (11.1%).” (page 6, lines 159 - 161).

Comment 4: In the ESRD patients, the incidence of mediastinitis and sternal wound dehiscence is greater when compared with non ESRD. In the reported septic cases, is there any weight of this complication?

Reply 4: Thirty-two patients (21.4%) developed postoperative sepsis. The most common sources of sepsis were pneumonia in 21 patients (14.1%), intra-abdominal in 4 patients (2.7%), central venous catheter in 4 patients (2.7%), superficial sternal wound infection in 3 patients (2.0%), saphenous vein graft harvest site infection in 2 patients (1.3%) and urinary tract infection in 2 patients (1.3%). One patient (0.7%) developed deep sternal wound infection and mediastinitis.

Changes in the text: The following paragraph has been added to the text “The most common sources of sepsis were pneumonia in 21 patients (14.1%), intra-abdominal in 4 patients (2.7%), central venous catheter in 4 patients (2.7%), superficial sternal wound infection in 3 patients (2.0%), saphenous vein graft harvest site infection in 2 patients (1.3%) and urinary tract infection in 2 patients (1.3%). One patient (0.7%) developed deep sternal wound infection and mediastinitis.” (page 7, lines 183 - 187).

Comment 5: In the quoted "Low cardiac output syndrome occurred in 36 patients (24.2%). Seventeen patients (11.4%) required insertion of an intra-aortic balloon pump for haemodynamic support": it can be interesting to know how this was related to EF, euro score and mortality.

Reply 5: Postoperative low cardiac output syndrome was associated with lower preoperative LVEF (38.2% vs 44.5%, $P=0.009$), higher EuroSCORE II (6.3 vs 3.0, $P<0.001$) and higher inpatient mortality (52.8% [19 of 36 patients] vs 0.9% [1 of 113 patients], $P<0.001$), when compared to patients without this complication.

Changes in the text: The following paragraph has been added to the text “Postoperative low cardiac output syndrome was associated with lower preoperative LVEF (38.2% vs 44.5%, $P=0.009$), higher EuroSCORE II (6.3 vs 3.0, $P<0.001$) and higher inpatient mortality (52.8% [19 of 36 patients] vs 0.9% [1 of 113 patients], $P<0.001$), when compared to patients without this complication.” (page 7, lines 177 - 180).

Comment 6: I would suggest to change the conclusion "CABG is associated with high operative mortality and poor long-term survival in ESRD patients": this is true but should be referred as comparison with non surgical treatment.

Reply 6: We were unable to compare the results of our surgical cohort with patients who received non-surgical treatment (PCI or medical therapy) at our centre during the same period. This limitation is described in the manuscript (Page 11, lines 295 - 297).

Changes to the text: Nil.

- Overall, it is an interesting manuscript.

Reviewer B

This is a single center retrospective study. Despite of small number, they summarized their experience of CABG for ESRD patients pretty well.

Comment 1: There are several reports already published from other centers regarding the similar experiences, they better mention this is a center experience in Singapore in the title.

Reply 1: [The country of study has been added to the manuscript.](#)

Changes to the text: [The country of study has been added to the manuscript \(Page 4, Line 109\).](#)

Additionally, I have a couple of comments.

Comment 2: Although some cases were urgent or emergent, I'm curious their selection criteria for CABG in those patients.

Reply 2: [Thirty-seven patients \(24.8%\) underwent urgent \(29 patients \[19.4%\]\) or emergent surgery \(8 patients \[5.4%\]\). In the urgent surgery group, the indications for surgery were recurrent unstable angina in 24 patients \(82.8%\), critical left main artery stenosis in 3 patients \(10.3%\), and hypotension during dialysis in 2 patients \(6.9%\). In the emergent surgery group, surgery was indicted for critical left main artery stenosis with ongoing myocardial ischaemia in 6 patients \(75.0%\) and ongoing myocardial ischaemia with recurrent ventricular arrhythmias in in 2 patients \(25.0%\).](#)

Changes to the text: [The following paragraph has been added to the text “Thirty-seven patients \(24.8%\) underwent urgent \(29 patients \[19.4%\]\) or emergent surgery \(8 patients \[5.4%\]\). In the urgent surgery group, the indications for surgery were recurrent unstable angina in 24 patients \(82.8%\), critical left main artery stenosis in 3 patients \(10.3%\), and hypotension during dialysis in 2 patients \(6.9%\). In the emergent surgery group, surgery was indicted for critical left main artery stenosis with ongoing](#)

myocardial ischaemia in 6 patients (75.0%) and ongoing myocardial ischaemia with recurrent ventricular arrhythmias in in 2 patients (25.0%).” (page 6, lines 146 - 152).

Comment 3. If they have data of dialysis (HD/PD) duration (year) before surgery, please show them and add them in the analysis.

Reply 3: The duration of dialysis prior to CABG was not available for analysis.

Changes to the text: Nil.

Comment 4. For figure 1, I think they better add survival curves for only survivors and a comparable control which is the patients without CABG.

Reply 4: We were unable to compare the results of our surgical cohort with patients who received non-surgical treatment (PCI or medical therapy) at our centre during the same period. This limitation is described in the manuscript (Page 11, lines 295 - 297).

Changes to the text: Nil.

Reviewer C

Thank you for the opportunity to review this interesting study. This provides important data for medical professionals and patients faced with CABG in the setting of ESRD. My questions are as follows:

Comment 1. Pls clarify the method of dialysis for these patients. was it through a arteriovenous fistula on the right or left side? if on the left side, do the authors do a a pedicled or free LIMA graft over concern from steal from the fistula? I am not sure there is a data to support a "right" answer for this but it puts the presented data in perspective. What proportion were peritoneal or temporary dialysis catheter access patients?

Reply 1: An in-situ pedicled LIMA was grafted to the LAD routinely. The site of arteriovenous fistula was not recorded consistently and hence unavailable for further analysis. The authors agree that this important information would have been very useful, if available.

Changes in the text: The word “pedicled” has been added to the manuscript (page 6, lines 158).

Comment 2. Due to the low numbers of OPCAB patients, it is best not to comment on equivalence or superiority/inferiority of one over the other. Would just present the data without judgment of efficacy and state the limitations.

Reply 2: The authors agree with the reviewer’s comment.

Changes in the text: The original statement “In the present study, only 7.4% of our cohort underwent off-pump CABG, which did not appear to influence operative mortality or long-term survival” has been amended to “In the present study, only 7.4% of our cohort underwent off-pump CABG.” (page 11, lines 279 - 280).

Comment 3. Older age by definition is a predictor of death even in individuals without any major medical issues when examining survival for any disease. Can the authors pls split the study population into 2 groups according to either side of the median age and state the 1, 5, and 10 year survivals for each group. This quantification of differences in life expectancy post-CABG will be more useful information for the reader.

Reply 3: The authors agree with the reviewer that age is a predictor of death when examining survival for any disease. Multivariable analysis was performed and results showed that age was an independent predictor of poorer long-term survival in our study population. Splitting the study population into 2 groups by median age and describing 1, 5 and 10 year survivals may not account for other age-related confounding factors.

Changes in the text: Nil.

Comment 4. What were the causes of death? Was it avoidable in this ESRD population? What are the complications to anticipate?

Reply 4: Causes of death included multi-organ failure in 11 patients (55.0%), sepsis in 5 (25.0%) and mesenteric ischaemia in 4 patients, (20.0%) (page 7, lines 173 - 175). These deaths were unavoidable despite prompt diagnosis and treatment. Compared to patients without ESRD, thromboembolic complications (stroke, mesenteric ischaemia, limb ischaemia) and septic complications (superficial and deep sternal wound infection, pneumonia, mediastinitis) occur more frequently in patients with ESRD who undergo CABG.

Changes in the text: The following statement has been added to the text “No patients suffered stroke or limb ischaemia.” (page 7, line 175). The following paragraph has been added to the text “The most common sources of sepsis were pneumonia in 21 patients (14.1%), intra-abdominal in 4 patients (2.7%), central venous catheter in 4 patients (2.7%), superficial sternal wound infection in 3 patients (2.0%), saphenous vein graft harvest site infection in 2 patients (1.3%) and urinary tract infection in 2 patients (1.3%). One patient (0.7%) developed deep sternal wound infection and mediastinitis. No patients suffered stroke or limb ischaemia.” (page 7 lines 183 - 187).

Comment 5. It is much less common now to not do a LIMA-LAD even in patients who need to go on cardiopulmonary bypass emergently as the patient is usually stable on pump thus allowing time to take down the mammary which conservatively adds only 30-40min or so to the operation but has long term survival implications. I would encourage more LIMA-LAD than the stated rate. But I appreciate there were previous paradigms that called for vein to the LAD in more urgent situations. Just food for thought.

Reply 5: The authors agree with the reviewer’s valuable suggestion. We will explore this option and review our institutional practice. Harvesting the LIMA while on cardiopulmonary bypass was not practiced during the study period.

Changes to the text: Nil.

Comment 6. Many of these patients have aortic calcifications. Do the authors do a preop noncontrast or contrast chest CT to evaluate for cannulation and cross-clamp strategy purposes. Pls add this practice pattern to the paper.

Reply 6: Prior to surgery, a non-contrasted CT scan of the chest was performed routinely in all patients with ESRD planned for CABG, to assess the burden of calcific plaque in the aorta, in particular the ascending aorta. This information was useful to stratify the risk of thromboembolic complications and to plan the most appropriate surgical strategy.

Changes to the text: The following paragraph has been added to the text “Prior to surgery, a non-contrasted CT scan of the chest was performed routinely in all patients with ESRD planned for CABG, to assess the burden of calcific plaque in the aorta, in particular the ascending aorta. This information was useful to stratify the risk of thromboembolic complications and to plan the most appropriate surgical strategy.” (page 4, line 111 to page 5, line 115).

Thank you again for sharing this very interesting study. I applaud your group for your excellent efforts.