

Peer Review File

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**Reviewer A**

This is a retrospective study which compared the outcomes of isolated coronary artery bypass grafting (CABG) performed by a single consultant versus trainees. The authors specifically focused on the intraoperative findings of transit time flow measurement (TTFM). TTFM for both arterial and venous grafts were similar between two groups, and there was no difference in postoperative complications and mortality either. Patients with arterial grafts with pulsatility index (PI) <3 were less likely to require an intra-aortic balloon pumping or prolonged ventilation. This is an interesting paper which compared the TTFM findings in CABG between a consultant and trainees. I read this article with a great interest. These are my questions and comments.

1. How did you distribute the patients between a consultant and trainees? What was the criteria that trainees could operate?

*Reply: Only cases with good anastomotic target are operated by trainees. A trainee who is in 3<sup>rd</sup> year of training and above can operate.*

*Changes in the text: We have added a statement in Methods (see page 6, line 108-110)*

2. A prolonged mechanical ventilation is usually defined as cumulative duration of 24 hours or more, not 5 days.

*Reply: NAMDR defines prolonged mechanical ventilation (PMV) as >21 days. We take 5 days as the cut-off as we usually decide for tracheostomy if patient needs to be ventilated for >5 days.*

3. How many patients received graft revision intraoperatively, depending on TTFM? What was the threshold of graft revision?

*Reply: Graft revision would be performed if PI >5 AND flow <15ml/min.*

*Changes in the text: We have added a statement in Methods (see page 6, line 121-124)*

4. The higher ratio of IABP was due to insufficient flow of LIMA? Didn't you revise LIMA graft when PI was high?

*Reply: Yes. Revision was performed if PI >5 AND flow <15ml/min. There are cases where PI is still high despite revision and it is due to poor distal run-offs.*

5. How do you explain that high PI was associated with prolonged mechanical ventilation?

*Reply: High PI is associated with graft failure and low cardiac output syndrome, thus patient usually require prolonged mechanical ventilation*

*Changes in the text: We have added a statement in Discussion (see page 11, line 226-230)*

## Reviewer B

Tan and co-authors present their single institutional experience of 155 patients who underwent CABG surgery Jan/2017 to Sept 2020. All patients underwent transit time flow measurement. They compared patients who underwent operation by an experienced consultant (trained) surgeon (n=84) vs. trainees under the surgeon's supervision (n=74). The compared outcomes between patients who had grafts with pulsatility indices < 3 vs. >3. Patients in the group who had surgery by the consultant were more often diabetic and had lower ejection fraction. The operative times by the consultant were shorter. Patients whose graft PI values were <3 has slightly worse outcomes; however, No difference were seen between the two groups with regard to mortality or other postop outcomes.

### Comments:

This investigation attempts to address multiple study questions: 1) what is the correlation between the PI value and outcome, 2) do patients who have their operation by supervised trainees have worse outcomes than those who have their operation by a consultant (trained) surgeon, and 3) should TTFM values of < 3 be interpreted differently for arterial grafts vs. ven grafts? . Limitations of the study include the small number of patients studied, limited data presented on the TTFM values, and what appears to be rather short follow-up and only two deaths - the main outcome measure. The comparable outcomes between the consultant and trainee groups was anticipated given patient selection bias with residents performing less complicated patients. Ultimately, it may be preferable for the authors to decide what study question they can best answer with the data they have and focus on that one question.

What was the total number of patients who underwent cardiac surgery during the study period, the number of patients excluded, and the reasons for the exclusion. Presumably, most excluded patients had either valve or some combined procedures.  
*Reply: Yes, the cases excluded are isolated valve cases or combined valve + CABG cases (mentioned in Methods, page 5, line 103-104)*

Based on line 117-118 it seems that there only one staff surgeon at this facility who performed all the CABG operations. Is this correct?  
*Reply: There are 3 surgeons at our facility but only the cases operated by 1 of the surgeons are included into this study to eliminate the bias between surgeons. (mentioned in Methods, page 6, line 107-108)*

The percentages presented in Table 2 are based on patients. It would make more sense to base the percentages on grafts - since (presumably) the same patient might have a combination "good" (PI < 3 or flow > 15ml/min) and "not so good" (PI> 3 or flow < 15 ml/min ) grafts.

*Reply: That is the reason we divide into arterial and venous grafts as TTFM may be*

*optimal in 1 but suboptimal in the other.*

How did the investigators interpret patients with inconsistent PI/flow values (e.g., low PI values but low flow or good flow but high PI values)?

*Reply: The decision to revise depends on how high is the PI or how low is the flow and the angiogram findings. If the targets are good based on angiogram, the threshold to revise will be low.*

*Changes in the text: We have added a statement in Methods (see page 6, line 121-124)*

The investigators should consider reporting the average number of grafts per surgery/patient. Were all grafts assessed for each patient?

*Reply: Yes, TTFM was performed for all grafts for each patient.*

*Changes in the text: We have modified our text in Methods (see page 6, line 118-120)*

This is a minor point given only two patients died - are the mortality rates (1.2 vs. 1.4%) based 30 day mortality or 30 day/in house mortality? Please include the mean follow-up times for the two cohorts and/or indicate completeness of follow-up.

*Reply: It is in-house mortality.*

*Changes in the text: We have modified our text in Methods (see page 6, line 126)*

## **Reviewer C**

I am pleased to review this interesting manuscript “Transit Time Flow Measurement and Outcome in Coronary Artery Bypass Grafting for Surgeon and Trainee” for Journal of Thoracic Disease.

The authors compared the intra- and postoperative outcomes, including TTFM, of isolated CABG performed by a single consultant versus trainees. They also investigated the relationship between the pulsatility index (PI) and postoperative outcomes.

Although the manuscript is well written, there are some concerns for it to appear in Journal of Thoracic Disease.

### **Major Concerns**

1. In Abstract, the authors describe that trainees can achieve good results in isolated CABG with appropriate case selection. However, this message can not be resulted from Methods and Results in Abstract. They should be consistent.

*Reply: Only cases with good anastomotic target are operated by trainees.*

*Changes in the text: We have added a statement in Methods (see page 6, line 108-110)*

2. The authors investigated the relationship between the PI and postoperative outcomes, as shown in Tables 4 and 5. Why they selected PI as an index of TTFM to investigate the relationship with the postoperative outcomes. Why neither mean flow

(Qm) nor diastolic filling?

*Reply: PI is used as a high PI is associated with early graft failure, as reported by Di Giammarco et al. (reference number 11, mentioned in Methods, page 7, line 140-141)*

3. In Patients and Methods, the authors should present the patient selection policy of the main surgeon, a consultant or trainees.

*Reply: Only cases with good anastomotic target are operated by trainees.*

*Changes in the text: We have added a statement in Methods (see page 6, line 108-110)*

4. In Patients and Methods, the authors should present the intraoperative timing and hemodynamic conditions of TTFM. They should also present how to respond when the TTFM showed the anastomosis error. Did they perform re-anastomosis under re-clamp of aorta or under off-pump or?

*Reply: The decision to revise depends on how high is the PI or how low is the flow and the angiogram findings. If the targets are good based on angiogram, the threshold to revise will be low.*

*Changes in the text: We have added a statement in Methods (see page 6, line 121-124)*

5. In Results, the authors should present the bypass numbers, bypass materials, bypass types, sequential bypass number, and so on, to increase the understanding of the readers.

*Reply: We do not have the data on the bypass types*

6. In Results, the authors should present the reasons of mortality (in-hospital death), because we infrequently experience in-hospital death in non-emergency isolated CABG.

*Reply: Both patients died due to hospital acquired pneumonia*

7. The authors showed major two results.

A= TTFM for both arterial and venous grafts were similar and no significant differences in postoperative complications and mortality were detected between the two groups.

B= Patients with arterial grafts with  $PI < 3$  were less likely to require an intra-aortic balloon pump or be ventilated for a prolonged period. No significant differences in postoperative outcomes and mortality were detected between venous grafts with  $PI < 3$  and  $PI > 3$ .

The authors should explain the interpretation of the both results A and B. They should be consistent, again.

*Reply:*

*A: TTFM for both arterial and venous grafts are similar between consultant and trainee group. The comparison is made between consultant and trainee group, not between arterial and venous grafts.*

*B: Patients with arterial graft with  $PI < 3$  are more likely to require IABP and ventilation for a prolonged period whereas there is no significant differences in post-operative outcome between venous graft with  $PI < 3$  and  $PI > 3$ .*

### Minor Concerns

The authors used  $PI = 3.0$ , not  $5.0$  as a threshold of TTFM. As they described in Discussion,  $PI = 5.0$  is popular, as most readers consider. We need more explanation.

*Reply: A PI of 3 was used as the cut-off because a  $PI > 3$  is predictive of early graft failure as reported by a study by Di Giammarco et al. (reference number 11, mentioned in Methods, page 7, line 140-141)*

### Reviewer D

Thank you for giving me the opportunity to review your manuscript. I would like to make the following suggestions that I believe will help you to develop your manuscript further.

- The analysis should be consistent (consultant -v- trainee or arterial-v-venous)

*Reply: The first analysis is the comparison of intra- and post-operative outcome between consultant and trainee- table 2 & 3. The second analysis is the comparison of post-operative outcome between  $PI < 3$  and  $PI > 3$  for both arterial and venous grafts- table 4 & 5. The results are consistent.*

- The analysis should include: clear definitions of perioperative MI, functional status, Euroscore (or other scoring system), revision rates

*Reply: Perioperative MI is defined as persistent ST changes which develops in perioperative period. We do not have the data on the intraoperative graft revision. Changes in the text: We have added a statement in Methods (see page 6, line 128-129)*

- Some of your reported outcomes are exceptional low (like postoperative AFib) ...this is intriguing by itself and you may wish to write a paper on how you managed to achieve this

*Reply: Yes, we have a very low incidence of postoperative AF which may be due to our vigilance is avoiding hypoxia and optimizing electrolytes.*

- Vein low less than 30ml for veins is very low and definitely less than 20ml, why did you use  $>15$ mls in your analysis?

*Reply: Again, we cited the study by Di Giammarco et al which also stated that mean flow values of 15 mL/min or less are independent variables for higher incidence of graft failure. (reference number 11)*

- Limitations section: small number of patients over  $>3.5$  years

*Reply: The total cases in our facility is divided among 3 consultants and the cases included in this study were operated by only one of the consultants to eliminate the confounders.*

- Each group has less than 100 patients so I would suggest to use median and range for descriptive statistics

*Reply: Mean is used as the data is normally distributed.*

- I am not sure that your analysis does support your conclusions.

*Reply: Yes, it does. As mentioned, there are 2 major analysis. The first analysis is the comparison of intra- and post-operative outcome between consultant and trainee- table 2 & 3. The second analysis is the comparison of post-operative outcome between  $PI < 3$  and  $PI > 3$  for both arterial and venous grafts- table 4 & 5. The results are consistent.*

### **Reviewer E**

The authors present the retrospective single-centre study findings where they compared the outcomes of patients with isolated CABG based on the operator experience (consultant vs trainees). TTFM was used in all cases to detect intraoperative graft failure. The authors found that TTFM for both arterial and venous grafts were similar, and no significant differences in postoperative complications and mortality were detected between the patients operated by the consultant and patients operated by trainees.

Main issues:

- please state clearly if these were only in-hospital outcomes that were analysed

*Reply: Yes, only in-hospital outcome were analysed.*

*Changes in the text: We have modified our text in Methods (see page 6, line 126)*

- did the postoperative length of stay differ between the two groups?

*Reply: We did not include this in the study.*

- no mortality scoring system (EuroSCORE II or STS) is presented

*Reply: Only cases with good anastomotic target are operated by trainees.*

*Distribution of cases between consultant and trainee is based on this.*

*Changes in the text: We have added a statement in Methods (see page 6, line 108-110)*

- no mention of the urgency and critical perioperative state

*Reply: All cases were elective cases.*

*Changes in the text: We have modified our text in Methods (see page 5, line 103-104)*

- have authors considered performing a ROC curve with a composite end-point to determine the best cut-off point for PI in the present cohort?

*Reply: No. PI of 3 was determined to be the cut-off based on the study conducted by Di Giammarco et al which stated that  $PI > 3$  is predictive of early graft failure.*

*(reference number 11)*

- I am not sure how the authors compared the outcomes of venous grafts if there were patients where two or more venous grafts in a single patient might have showed different results. The outcomes of venous grafts are confounded by the parameters of arterial grafts and vice versa. The clinical outcomes are on the patient level, whereas



PI is on a single graft level, so technically, only graft patency/failure should be assessed in this type of analysis. The authors state: suboptimal PI for arterial grafts leads to worse outcomes, whereas suboptimal PI for venous grafts does not affect the outcome. This statement does not hold up to scientific scrutiny, and the conclusion should be tuned down.

*Reply: Suboptimal PI for arterial graft leads to poorer outcome is logical as most arterial grafts are to the left anterior descending artery and left circumflex artery, whereas most venous grafts are to the left circumflex artery and right coronary system.*

*Changes in the text: We have modified our text in Discussion (see page 11, line 226-230)*

- how many trainees were the operators in the "trainee group"? Were they first operators in all analysed cases in trainee group?

*Reply: Yes, the trainees are first operators.*

- please describe in more detail how the TTF measurements were performed

*Reply: Arterial grafts are assessed using 2mm probe whereas venous grafts are assessed using 4mm probe. TTFM is measured after protamine administration is completed.*

*Changes in the text: We have added a statement in Methods (see page 6, line 118-120)*

- in the abstract, if odds ratios are provided, please also include confidence intervals. Where values are compared in the text, please state the p-value.

*Reply: Amendment done.*

*Changes in the text: We have removed the odds ratio in Abstract and added P-value and CI in Results (see page 8, line 152, 155 & 163)*

- I am concerned that the multivariable regression models were done incorrectly. The PI should be included in the model as a covariate, and it should be adjusted for other baseline and perhaps some intraoperative variables. Please do not adjust for mortality or outcomes that are likely directly linked to graft failure.

*Reply: It is a univariate logistic regression.*

*Changes in the text: We have modified the statement in Methods (see page 7, line 138)*

- as the authors mentioned, small sample, single-centre set-up and presumably only in-hospital follow-up significantly limit the generalizability of the findings

*Reply: Yes, further study which involves multiple centres with larger sample size is needed.*

Strengths:

- authors should be commended on the clear and concise structure of the manuscript and well-organised tables.

- originality of a research topic is relatively high. The manuscript may serve as a proof of concept study.

**Reviewer F**

Nice descriptive piece. I have no major comments