

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-22-846>

Reviewer A

The authors presented their experience regarding the CABG in patients with ischemic cardiomyopathy. A total of 57 patients were analyzed. The authors reported that six months after surgery, 64.9% had improved cardiac function. The findings of regression analysis are logical and confirm the effect of CABG and limitations.

Reply: Thank you very much for taking time out of your busy schedule to review our manuscript. I sincerely thank you for your affirmation of this study, and thank you very much for giving us valuable opinions and giving us the opportunity to improve. We have carefully read your comments and discussed with other authors. Now we will reply to your comments point-by-point, and have made corresponding corrections in accordance with the requirements, which have been marked in yellow font. Due to the limitation of our ability, we are not satisfied with the explanation of some problems. We sincerely hope that you can understand and correct us!

Minor points:

1) CMR-LGE is contraindicated in patients with renal dysfunction, but is this not added to the exclusion criteria in this report?

Reply: We have modified our text as advised (see Page 6, line 118).

Changes in the text: We added this phrase to the methods section: Preoperative complications such as a malignant tumor and chronic renal failure.

2) I would like to know more details about CABG. For example, operative time, percentage of arterial grafts, whether bilateral ITAs were used, percentage of grafts evaluated and patency rate, etc.

Reply: We have modified our text as advised (see Page 11 and Page 23, line 228-234 and line 489).

Changes in the text: We added this phrase to the results section:

Comparison of surgical data between the two groups

Bilateral internal mammary artery bypass was not used in either group. There were no significant differences between the two groups in the use of cardiopulmonary bypass, left internal mammary artery utilization rate, number of bypass, operation time, and blood product dosage ($P > 0.05$). Although the intensive care unit stay time, ventilator use time and postoperative hospital stay in the unimproved group were higher than those in the improved group, the differences were not statistically significant ($P > 0.05$) (Table 2).

3) What is the basis for the 5% cutoff value for improvement in cardiac function?

Reply: According to previous literature reports (1), improvement in cardiac ejection fraction $\geq 5\%$ following revascularization was considered clinically significant. So we have modified our text as advised (see Page 9, line 195-196).

Changes in the text: We added this phrase to the methods section: After six months, improvement in cardiac function was defined as $\Delta\text{LVEF} \geq 5\%$ on transthoracic echocardiographic.

Reference

1.Schinkel AF, Poldermans D, Rizzello V, et al. Why do patients with ischemic cardiomyopathy and a substantial amount of viable myocardium not always recover in function after revascularization? J Thorac Cardiovasc Surg 2004; 127: 385-90.

Reviewer B

The manuscript entitled "Myocardial scar is associated with improved cardiac function after coronary artery bypass grafting in patients with ischemic cardiomyopathy" by Wei Fu et al. presents an analysis of observational data collected retrospectively from late gadolinium enhancement cardiac magnetic resonance imaging (CMR-LGE) before coronary artery bypass grafting (CAGB) surgery and associated data, including echocardiography, occurrence of major adverse cardiovascular and cerebrovascular events (MACCE), collected retrospectively from a single institution's clinical database. There are severe major concerns with the data and with the manuscript presentation.

Reply: Thank you very much for taking time out of your busy schedule to review our manuscript. I sincerely thank you for your affirmation of this study, and thank you very much for giving us valuable opinions and giving us the opportunity to improve. We have carefully read your comments and discussed with other authors. Now we will reply to your comments point-by-point, and have made corresponding corrections in accordance with the requirements, which have been marked in yellow font. Due to the limitation of our ability, we are not satisfied with the explanation of some problems. We sincerely hope that you can understand and correct us!

TITLE

1- Considering the authors' data being retrospective and observational, the wording of and conclusion presented in the title is too strong. The study design (retrospective, observational) must be written in the title, and a descriptive title should be formulated e.g. "Retrospective, observational analysis of cardiac function associated with global preoperative myocardial scar in patients with ischemic cardiomyopathy after coronary artery bypass grafting"

Reply: We have modified our text as advised (see Page 1, line 1-3)

Changes in the text: We have changed the title: Retrospective, observational analysis of cardiac function associated with global preoperative myocardial scar in patients with ischemic cardiomyopathy after coronary artery bypass grafting.

ABSTRACT

2-The description of the study objective must present the aim according to the retrospective and observational data the authors have used. Thus, the objective must be defined as e.g. "By using the hospital database of accumulated patient data in a retrospective manner, the goal of this study was to..."

Reply: We have modified our text as advised (see Page 3, line 46-47)

Changes in the text: We have changed the abstract: By using the hospital database of accumulated patient data in a retrospective manner, the goal of this study was to...

3-The total amount of all patients' data in the database as well as the time interval of the patients' surgeries were carried out must be clearly presented.

Reply: We have modified our text as advised (see Page 3, line 51-53)

Changes in the text: We have changed the abstract: A total of 57 patients diagnosed with ICM who underwent isolated CABG at Beijing Anzhen Hospital between September 2017 and September 2019 were enrolled in this retrospective study.

4-The heterogeneity of the patients' disease must be presented in the abstract. Thus, include a description and number of patients by disease complexity e.g. using SYNTAX score. Present the SYNTAX scores for the "improved" and "unimproved" groups.

Reply: We have modified our text as advised (see Page 3, line 59-60)

Changes in the text: We have changed the abstract: The two groups had no statistical difference in the SYNTAX score (47 ± 7.6 vs 42.8 ± 8.3 , $P=0.603$).

5-The selection criteria for the 57 patients and the overall number of CMR-LGEs available from CABG patients with ischemic cardiomyopathy. What percentage does the selected 57 patients data represent overall?

Reply: We have modified our text as advised (see Page 5-6 and Page 28, line 103-126 and line 543)

Changes in the text: We have changed the methods: Between September 2017 and September 2021, 129 patients diagnosed with ICM and received preoperative CMR-LGE at Beijing Anzhen Hospital. Among 129 patients, 6 received drug treatment, 33 underwent mitral valve surgery, 4 underwent tricuspid valve surgery, 19 underwent aneurysm resection, and 67 patients received CABG surgery alone. Of the 67 patients, two died of postoperative low cardiac output syndrome, two failed to follow up six months after surgery, three had bypass grafts failure 6 months postoperatively, and three patients could not accurately assess preoperative myocardial scar. As a result, 57 patients who met the criteria were included in this study (Figure 1).

6-The sentence "The factors contributing to these patients' unimproved were investigated." is nonsensical. Do the authors mean unimproved cardiac function?

Reply: We have modified our text as advised (see Page 3, line 56-57)

Changes in the text: We have changed the abstract: The factors contributing to these patients' unimproved cardiac function were investigated.

7-The definition of functional improvement must be clearly stated.

Reply: We have modified our text as advised (see Page 3, line 54-56)

Changes in the text: We have changed the abstract: These patients were divided into two groups based on postoperative echocardiography results at six months: improved cardiac function (Δ left ventricular ejection fraction greater than or equal to 5%) and

unimproved.

8-The authors present myocardial scar data from both the improved and unimproved groups however no postoperative scar evaluation was carried out. Changes in myocardial scar can't thus be presented. The authors should only use a definition such as "preoperative myocardial scar quantified by CMR-LGE" and when describing its association with postoperative cardiac parameters, should use wording such as "postoperative cardiac function evaluated by echocardiography".

Reply: We have modified our text as advised (see Page 3, line 53-57)

Changes in the text: We have changed the abstract: All of these patients had a preoperative CMR-LGE examination. These patients were divided into two groups based on postoperative echocardiography results at six months: improved cardiac function (Δ left ventricular ejection fraction greater than or equal to 5%) and unimproved. The factors contributing to these patients' unimproved cardiac function were investigated.

9-Clearly state which parameters are compared.

Reply: We have modified our text as advised (see Page 3, line 59-62)

Changes in the text: We have changed the abstract: The two groups had no statistical difference in the SYNTAX score (47 ± 7.6 vs 42.8 ± 8.3 , $P=0.603$), but compared to the improved group, preoperative myocardial scar was significantly enlarged in the unimproved group ($41.9\% \pm 6.4\%$ vs. $27.8\% \pm 8.5\%$, $P < 0.001$).

10-"Myocardial scar" -> Preoperative myocardial scar, "improvement after CABG"-> "change in cardiac function evaluated by echocardiography after CABG"

Reply: We have modified our text as advised (see Page 3, line 62-64)

Changes in the text: We have changed the abstract: In regression analysis, only preoperative myocardial scar (OR:1.44, 95%CI:1.13-1.83, $P=0.003$) was associated with no change in cardiac function evaluated by echocardiography after CABG.

11-It should be clearly stated what parameter the cutoff represents. Assuming the authors mean "preoperative scar size cutoff"?

Reply: We had hoped to use receiver operating characteristic curves to detect the cut-off value of preoperative myocardial scar to assist in predicting unimproved cardiac function after CABG, but it was inaccurate because just tweating endocardial and epicardial contours a little bit on CMR-LGE changes LGE%, coupled with the small sample size.

So we have modified our text as advised (see Page 4, line 69-71)

Changes in the text: We have changed the abstract: In ICM patients, a greater amount of preoperative myocardial scar was associated with unimproved cardiac function after CABG. Measuring preoperative myocardial scar may aid clinicians in identifying patients who would benefit from CABG.

12-The authors incorrectly present a definitive conclusion from the retrospective and

observational data. The conclusion must reflect the authors' data. Thus, a careful rewording of the conclusions in a descriptive manner is needed.

Reply: We have modified our text as advised (see Page 4, line 69-71)

Changes in the text: We have changed the abstract: In ICM patients, a greater amount of preoperative myocardial scar was associated with unimproved cardiac function after CABG. Measuring preoperative myocardial scar may aid clinicians in identifying patients who would benefit from CABG.

METHODS

13-The authors describe continuous enrolment to the study. This can't have occurred as the study is retrospective. Thus, the description of the study must be rewritten to clearly reflect how the study was actually carried out. In the authors case, the patients can be selected from a pool of data according to specific criteria, but not enrolled.

Reply: We have modified our text as advised (see Page 5, line 103-106)

Changes in the text: We have changed the methods: Between September 2017 and September 2021, 129 patients diagnosed with ICM and received preoperative CMR-LGE at Beijing Anzhen Hospital. According to the inclusion and exclusion criteria, 57 patients were finally analyzed.

14-As the data was retrospectively collected, the text must be written in a relevant grammatical tense, such as "the patients had undergone both preoperative CMR-LGE and their cardiac function had been evaluated by echocardiography six months postoperatively".

Reply: We have modified our text as advised (see Page 5, line 109-111)

Changes in the text: We have changed the methods: The patients had undergone both preoperative CMR-LGE and their cardiac function had been evaluated by echocardiography six months postoperatively.

15-The selection criteria for these patients must be clearly presented, preferably in a table format. Also a flow-chart detailing the total pool of patients in the database as well as the exclusion of patients from the current study must be shown. A flowchart figure is preferred.

Reply: We have modified our text as advised (see Page 6 and Page 28, line 120-126 and line 543)

Changes in the text: We have changed the methods: Among 129 patients, 6 received drug treatment, 33 underwent mitral valve surgery, 4 underwent tricuspid valve surgery, 19 underwent aneurysm resection, and 67 patients received CABG surgery alone. Of the 67 patients, two died of postoperative low cardiac output syndrome, two failed to follow up six months after surgery, three had bypass grafts failure 6 months postoperatively, and three patients could not accurately assess preoperative myocardial scar. As a result, 57 patients who met the criteria were included in this study (Figure 1).

16-It is not clear if the authors performed some of their data collection for this study only, or were some parts of the data collection only specifically designed for this study. Data collected from the database and specific data collected only for this study separately must be clearly

and separately described.

Reply: We have modified our text as advised (see Page 5, line 103-106)

Changes in the text: We have changed the methods: Between September 2017 and September 2021, 129 patients diagnosed with ICM and received preoperative CMR-LGE at Beijing Anzhen Hospital. According to the inclusion and exclusion criteria, 57 patients were finally analyzed.

RESULTS

17-Table 1 shows the preoperative baseline data for the Improved (n=37) and Unimproved groups. There were significant differences in several left ventricular functional parameters such as the LVEDD and LVESD. Were the groups different in terms of ventricle wall thickness and hypertrophy?

Reply: We have modified our text as advised (see Page 22-23, line 466)

Changes in the text: We have changed the Table 1.

18-What were the numbers of anastomoses made at surgery for the groups?

Reply: We have modified our text as advised (see Page 24, line 489)

Changes in the text: We have changed the Table 2.

19-The description of disease severity and complexity is missing. This is a crucial determinant, and should be described using e.g. the SYNTAX score. Were the groups different according to disease complexity? Patients with severe disease and ischemia (putatively also with more hibernating myocardium as well as more global preoperative scar) and numerous anastomoses can be envisioned to profit more from the CABG surgery, also on functional level.

Reply: We have modified our text as advised (see Page 22-23, line 466)

Changes in the text: We have changed the Table 1.

20-The authors do not present medical therapy data. This is one of the key culprits as drug therapy, different selection of treatments postoperatively and changes in drug treatment significantly affect the cardiac function. The authors should present the preoperative medications as well as the postoperative medications, compare medications between groups. Also the medication changes during the six months time before functional assessment need to be documented and compared between groups.

Reply: According to the 2021: The AATS Expert Consensus Document: Coronary artery bypass grafting in patients with ischemic cardiomyopathy and heart failure (1), Patients who are maintained on optimal medical therapy have the best long-term outcomes.

So we have modified our text as advised (see Page 9, line 183-188)

Changes in the text: We have changed the methods: All patients received guideline-directed medical therapy after CABG (1), including: renin-angiotensin system inhibitors, such as an angiotensin-converting enzyme inhibitor, angiotensin type II receptor blocker, or an angiotensin receptor neprilysin inhibitor; a beta-blocker; and a mineralocorticoid receptor antagonist, such as spironolactone, while taking long-term antiplatelet drugs.

Reference

(1)Bakaeen FG, Gaudino M, Whitman G, et al. 2021: the American Association for Thoracic Surgery expert consensus document: coronary artery bypass grafting in patients with ischemic cardiomyopathy and heart failure. J Thorac Cardiovasc Surg 2021;162: 829- 50.

21-In Table 1, the authors present myocardial scar mean percentage for the improved group as 27.8% and for the unimproved group as 41.9%. This fully contradicts the authors conclusion as the improved group had less myocardial scar while the unimproved group had 41.9% scar. A clear difference of 1.5-fold favouring functional improvement when myocardial preoperative scar is smaller.

Reply: We have modified our text as advised (see Page 4, line 69-71)

Changes in the text: We have changed the conclusion: In ICM patients, a greater amount of preoperative myocardial scar was associated with unimproved cardiac function after CABG. Measuring preoperative myocardial scar may aid clinicians in identifying patients who would benefit from CABG.

22-Table 2 has a Chinese symbol, this should be removed from English text.

Reply: We have modified our text as advised (see Page 25, line 503)

Changes in the text: We have changed the Table 3 (The original Table 2 becomes Table 3 due to the addition of a table 2).

23-NYHA classes at baseline and follow-up must both be presented. Changes in NYHA class are the ones important, not merely the NYHA classes at follow-up as these do only characterise the cohorts but do not demonstrate what happened to the patients after surgery.

Reply: We have modified our text as advised (see Page 22-23, line 466)

Changes in the text: We have changed the Table 1.

DISCUSSION

24-As the result and analyses of the manuscript are flawed (see data in Table 1 and the comment #21), the conclusion of the manuscript is not relevant.

Reply: We have modified our text as advised.

Changes in the text: We have changed the discussion.

Reviewer C

Important question asked by the authors to assess if presence of scar and how much scar on MRI predicts better outcome after CABG.

Reply: Thank you very much for taking time out of your busy schedule to review our manuscript. I sincerely thank you for your affirmation of this study, and thank you very much for giving us valuable opinions and giving us the opportunity to improve. We have carefully read your comments and discussed with other authors. Now we will reply to your comments point-by-point, and have made corresponding corrections in accordance with the requirements, which have been marked in yellow font. Due to the limitation of our ability, we are not satisfied with the explanation of some problems. We sincerely hope that you can understand and correct us!

The manuscript needs to be reviewed in details. There are quite a few typographical errors like : "The degree of myocardial scar in the 193 unimproved group was significantly higher than that in the improved group (27.8% ± 8.5% vs. 41.9 ± 6.4, P < 0.001) (Table 1)". no.s are reversed and no % given...

Reply: We have modified our text as advised (see Page 11, line 225-227)

Changes in the text: We have changed the results: The degree of myocardial scar in the unimproved group was significantly higher than that in the improved group (41.9%±6.4% vs. 27.8%±8.5%, P < 0.001) (Table 1).

In the abstract results section: "Myocardial scar was significantly increased in the improved 35 group compared to the unimproved (27.8%±8.5% vs. 41.9%±6.4%, P < 0.001)." numbers are reversed and needs to be corrected

Reply: We have modified our text as advised (see Page 3, line 60-62)

Changes in the text: We have changed the abstract: but compared to the improved group, preoperative myocardial scar was significantly enlarged in the unimproved group (41.9%±6.4% vs. 27.8%±8.5%, P < 0.001).

Another point:

based on 57 patients authors are suggesting 36.8% as cut off for LGE for clinical improvement and LVEF improvement. It is a very bold statement. Just tweaking contours a little bit on MRI changes LGE%, I would suggest more of a range compared to one specific no.

Reply: We have modified our text as advised (see Page 4, line 69-71)

Changes in the text: We have changed the conclusion: In ICM patients, a greater amount of preoperative myocardial scar was associated with unimproved cardiac function after CABG. Measuring preoperative myocardial scar may aid clinicians in identifying patients who would benefit from CABG.

Another point:

cut off of improvement in LVEF >5% is also prone to interobserver and measurement variability. I would use a little higher cut off as a predictor of LV function improvement after CABG.

Reply: According to previous literature reports (1), improvement in cardiac ejection fraction $\geq 5\%$ following revascularization was considered clinically significant. So improvement in cardiac function was defined as $\Delta\text{LVEF} \geq 5\%$.

Reference

1. Schinkel AF, Poldermans D, Rizzello V, et al. Why do patients with ischemic cardiomyopathy and a substantial amount of viable myocardium not always recover in function after revascularization? J Thorac Cardiovasc Surg 2004; 127: 385-90.