Peer Review File

Article Information: http://dx.doi.org/10.21037/apm-20-591

Review Comments:

English language: A more comprehensive and clear formulation is advisable. There are also some grammatical errors. The consultation of a native English speaker or a professional language editing service is highly recommended. For example, in the Introduction section, on page 3, lines 47-48 the text might be reformulated such as: "… patients aged ≥75 years might account for up to 1/3 of the acute coronary syndrome population", in order to be more understandable.

Reply: Thank you very much for your comments. We have modified our language.

Methods:

Please define the study design: was it a prospective or a retrospective analysis of clinical data?

Reply: Thank you very much for your comments. We have added in the methods part "This is a prospective study."

Some information regarding the study population (number of included patients, gender proportions) should be presented in the Results section.

Reply: Thank you very much for your comments. We have described in the results section as "A total of 360 STEMI patients undergoing PCI in the Department of Cardiology of Anhui Provincial Hospital from January 2013 to April 2018 were consecutively recruited. Among them, there were 215 male and 145 females. According to the ACEF score upon admission, all patients were assigned into the low-to-intermediate risk group (n=80) and high-risk group (n=280). In the low-to-intermediate risk group, there were 53 male and 27 females, aged (78.76±3.36) years on average. In

the high-risk group, 162 patients were male and 118 females with a mean age of (80.95±459) years old."

Inclusion and exclusion criteria: some readers might not be familiar with the 2010 Chinese guidelines on acute myocardial infarction. As the guidelines on the Fourth universal definition of myocardial infarction were more recently issued (2018), it would be useful to briefly present the inclusion criteria in the Methods section.

Reply: Thank you very much for your comments. We have corrected our inclusion criteria and cited Fourth universal definition of myocardial infarction (2018).

Coronary angiography and PCI: for the same reason as above, it would be useful to summarize the technical details of coronary angiography and PCI: the time window in which an invasive strategy was adopted; the angiographic equipment used; the arterial approach chosen: femoral vs. radial; "ad-hoc" vs. postponed PCI strategies adopted – the authors stated in the Introduction section that "how to choose a reasonable revascularization strategy for the elderly patients (aged>75 years) with acute STEMI is still controversial" (p. p3, lines 54-56); the type of implanted stents (bare metal vs. drug eluting); ancillary procedures used (e.g. criteria for thrombus aspiration or intra-aortic balloon pump usage) . Please specify the timing of "complete revascularization", i.e. during the index intervention, the same hospitalization, the first month or the first year after the index event? Were there patients revascularized surgically (by coronary artery by-pass grafting) after the index event?

Reply: Thank you very much for your comments. We have added the description in the methods part as "As recommend by *Guidelines on the Diagnosis and Treatment of STEMI in China (2010)*, PCI should be directly performed in patients with STEMI (including positive and posterior myocardial infarction) or with new or possible new left bundle branch block. The patients who were more than 75 years old, had cardiogenic shock less than 36 hours of onset, were suitable for vascular reconstruction and could be performed within 18 hours after the onset of shock, if the patient's previous cardiac function is good, suitable for vascular reconstruction and agreed to

interventional treatment, direct PCI can be considered. If the patient is 12-24 hours after onset and has the one of the following conditions or more, direct PCI is feasible: ① severe heart failure; ② hemodynamic or ECG instability; ③ evidence of persistent ischemia. The arterial approach included radial, femoral and brachial arteries. Direct PCI is not recommended for STEMI patients with stable hemodynamics and electrocardiographic stability and without obvious ischemic symptoms for more than 12 hours. All patients enrolled in this study underwent primary PCI treatment. Thrombus aspiration was not routinely performed during the operation, but thrombus aspiration was performed in patients with heavy thrombus load. Intra-aortic balloon pump (IABP) is used in patients with STEMI complicated with hypotension, low cardiac output and ineffective drug therapy. In this study, drug-eluting stents were used in emergency PCI operations. Complete revascularization was defined when no visually estimated stenosis ≥70% for the left main and no stenosis ≥50% for other major arteries and/or their major branches at discharge. 30.0% of STEMI patients underwent complete revascularization during hospitalization, while 8 patients (2.2%) had persistent ischemia after PCI due to cardiogenic shock or infarction related artery. During hospitalization, complete revascularization was performed by PCI again. Since all the patients in this study were STEMI patients aged 75 years and above, emergency CABG (coronary arty bypass grafting) had not been carried out in our hospital when we choose the emergency reperfusion strategy."

Clinical endpoints: in the abstract the Authors state that the "primary endpoint event was cardiac death at postoperative 1 month and 1 year" (p. 2, lines 26-27). However, in the Methods section of the full text they present as primary and secondary endpoints a combination of major adverse cardiac events (MACEs). Which is the correct definition of the used clinical endpoints?

Reply: Thank you very much for your comments. The correct definition of the used primary endpoint was cardiac death at postoperative 1 month and 1 year.

Statistical analysis: While ANOVA analysis is usually used to compare three or more groups, the differences between two groups of continuous data are usually determined with the help of a t-test or a rank sum test. Which one was used in this analysis? In the other hand, usually only one of the crosstab analyses is used for the categorical data, i.e. the chi-square or the Fisher's exact test. Which of them was done in this study? The authors used ROC-curve analysis "to evaluate the ACEF scoring system to predict the postoperative 30-d and 1-year mortality rate" (p6, lines 130-131). What about the use of ROC-curve analysis to determine the predictive ability of ACEF score for the primary and secondary endpoints determined previously in the Methods section, i.e. the MACE rate at 1 month and 1-year post-intervention?

Reply: Thank you very much for your comments. We have corrected our statistical analysis as "SPSS 20.0 statistical software was used for data analysis (SPSS Inc., Chicago, IL, U.S.). The normally distributed measurement data were expressed as mean ± standard deviation (SD). Student t test was employed for comparison between two groups. The counting data were expressed as the percentage (%) and *chi*-square test were adopted. The ROC curve was delineated to evaluate the ACEF scoring system to predict the postoperative 30-d and 1-year mortality rate. Cox regression model using univariate analysis was carried out. A *P* value of less than 0.05 was considered as statistical significance." The primary endpoint was corrected as cardiac death at postoperative 1 month and 1 year.

Results:

The authors state that the patients were divided in tertiles according to the ACEF score. However, they present in the Results section only two patient groups: a low-to-intermediate- and a high-risk group. Please present the results according to the predefined methodology.

Reply: Thank you very much for your comments. As number of patients included in this study is limited, there were only 80 cases of low-risk and medium-risk patients together, and 280 cases of high-risk group. If they were divided into three groups, it

could not meet the statistical requirements. Moreover, the purpose of this paper is to illustrate the predictive value of ACEF for high-risk group.

Some of the presented data in the Results section were not pre-defined in the Methods: what was the definition of anemia and cardiogenic shock? How was measured the left ventricular ejection fraction? What formula was used to calculate the glomerular filtration rate? Please present these definitions in the Methods section.

Reply: Thank you very much for your comments. We have added the description as "Anemia was defined as hemoglobin less than 12 g/dL for men or less than 11 g/dL for women. Cardiogenic shock refers to the clinical syndrome of insufficient perfusion of tissues and organs due to the obvious decrease of cardiac output. The main manifestations include: (1) persistent hypotension (systolic blood pressure < 90mmHg for more than 30 min); (2) there were signs of organ perfusion injury (at least one item): mental state change, skin dampness and coldness, oliguria and elevated serum lactic acid level. The glomerular filtration rate (EGFR) was estimated by the modified dietary adjustment formula for Chinese people: EGFR (ml/min/1.73m^2) = 175 × (sCr) - 1.234 × (age) - 0.179 for adult males and 175 × (sCr) - 1.234 × (age) - 0.179 ×0.79 for females. Left ventricular ejection fraction was calculated as: M-mode echocardiography was performed at the mitral valve apex level on the long axis view of left heart, and ED and ES were measured respectively. EDV and ESV were obtained by the software of the instrument, and EF = (EDV-ESV) / EDV × 100%."

ROC-curve analysis: please present the 95% confidence interval near the area under the curve values. It would be useful to present the threshold values of ACEF score best discriminating the occurrence of primary and secondary endpoints.

Reply: Thank you very much for your comments. We have described in our results as "As demonstrated in **Figure 1**, the area under the ROC curve of the ACEF scoring system in predicting cardiac death at 1 month after PCI was calculated as 0.809. In addition, the sensitivity of the ACEF scoring system in predicting cardiac death at 1 month after PCI was 86.3% and the specificity of the ACEF scoring system in

predicting cardiac death at 1 month after PCI was assessed as 75.4%. Moreover, the area under the ROC curve of the ACEF scoring system in predicting cardiac death at 1 year after PCI was calculated as 0.763. In addition, the sensitivity of the ACEF scoring system in predicting cardiac death at 1 year after PCI was 81.9% and the specificity of the ACEF scoring system in predicting cardiac death at 1 year after PCI was assessed as 70.7%, as illustrated in **Figure 2**."

Please explain the abbreviations used in the Tables. Please review the results presented in the tables, as the p values are presented in different rows than the compared parameters (e.g. eGFR in Table 1, IRA and arterial puncture route in Table 2).

Reply: Thank you very much for your comments. We have modified our tables.

Discussion:

Regarding the information on page 8, line 176. Percutaneous coronary intervention (PCI) is an interventional cardiology procedure. What are the surgical indications for PCI?

Reply: Thank you very much for your comments. We have described as "As recommend by *Guidelines on the Diagnosis and Treatment of STEMI in China (2010)*, PCI should be directly performed in patients with STEMI (including positive and posterior myocardial infarction) or with new or possible new left bundle branch block. The patients who were more than 75 years old, had cardiogenic shock less than 36 hours of onset, were suitable for vascular reconstruction and could be performed within 18 hours after the onset of shock, if the patient's previous cardiac function is good, suitable for vascular reconstruction and agreed to interventional treatment, direct PCI can be considered. If the patient is 12-24 hours after onset and has the one of the following conditions or more, direct PCI is feasible: ① severe heart failure; ② hemodynamic or ECG instability; ③ evidence of persistent ischemia."

Not all abbreviations are explained in the text (e.g. SYNTAX on page 9, line 185).

Reply: Thank you very much for your comments. We have corrected it.

The SYNTAX score is not a surgical risk model (page 9, lines 185-189). Please be more specific when referring to surgical or any other type of risk models.

Reply: Thank you very much for your comments. We have corrected it.

Page 9, line 197: "After 1-year follow-up, ACEF score was considerably improved." How did this follow-up period improve the ACEF score?

Reply: Thank you very much for your comments. We have deleted this sentence.

The presented sensitivity and specificity values are not consistent with an "excellent predictive value" (page 10, line 210). Please reformulate.

Reply: Thank you very much for your comments. We have corrected it as "and have predictive value, which was consistent with previous findings."

On page 10, lines 213-214: "First, the prognostic significance of age, a key factor, is not reflected." – this is not understandable, please reformulate. The main reason for the low predictive ability of the ACEF score in reference number 14 is probably the low patient number (only 104 patients included).

Reply: Thank you very much for your comments. We have corrected it as "First, the prognostic value of age was not observed".

Please include the paragraph of study limitations in the Discussion section. If this analysis was a retrospective one, please specify this here.

Reply: Thank you very much for your comments. We have added the limitation as "There were still some limitations in this study. The sample size is relatively small, the follow-up time is 1 year, and all patients are recruited from a single center. It is necessary to further expand the sample size, prolong the follow-up duration to further consolidate the preliminary conclusion."

Conclusion: please do not repeat the results here.

Reply: Thank you very much for your comments. We have corrected our conclusion.