Response to reviewers

Reviewer #1:

Comment 1.This is a potential interesting paper flawed by many concerns. First, this is not cohort of special patient but a Practical Clinical Trial (please report clinicaltrials.gov registration number in the paper).

Our Response- We thank the reviewer for their kind comments. We wish to submit that as mentioned in the methods section, the study was a prospective registry of patients undergoing PCI at our centre. We did not randomize the patients into any group and patients were divided into the two groups based on their time of presentation /intervention.

Comment 2. Second, please explain the definition of patients representing the objects of acute myocardial infarction between the two groups, and which of the following types are respectively. (1) Direct PCI: refers to direct percutaneous coronary intervention without intravenous thrombolysis to the catheter room. (2) Immediate PCI: It means that the TIMI blood flow of the vessel has been re opened after thrombolysis ≥ 2 levels for immediate PCI treatment. Its purpose is to deal with residual stenosis and prevent ischemia and reinfarction. (3) Remedial PCI: refers to immediate PCI treatment when the blood vessels are not reopened after thrombolysis and TIMI blood flow is less than level 2, which aims to make up for the failure of thrombolysis and

save the myocardium. (4) Delayed PCI: In recent years, the literature has been less and less used. It refers to interventional therapy within 1-7 days after thrombolysis. Whether the thrombolysis is successful or not, the purpose is to deal with residual stenosis and prevent ischemia and reinfarction. Some literatures focus on 6-48 hours of this period. In fact, from clinical practice, most delayed PCI focuses on this period. (5) Selective PCI: PCI is performed at a selected time after myocardial infarction. For patients without symptoms or evidence of persistent ischemia, it is usually performed 1 week later. (6) Facilitating PCI: a new concept proposed in recent years, which refers to PCI after reduced thrombolysis or platelet IIb/IIIa receptor antagonist is used. The purpose is to achieve reperfusion as soon as possible, shorten the waiting time to the greatest extent, and reduce myocardial damage.

Our Response- We thank the reviewer for their detail analysis and description of PCI following ACS/STEMI. As per the definition described above, our patients would fit into categories no. 2 & 4 i.e. “Immediate PCI” & “Delayed PCI”. However, as per contemporary guidelines (ACC & ESC) there were three major groups of PCI i.e. Primary PCI (PCI < 24 hrs without antecedent fibrinolysis), pharmaco-invasive PCI (PCI 3-24 hrs after fibrinolysis) and delayed PCI (PCI > 24 hrs after symptom onset). Hence, we have adopted these terminologies in our manuscript.

However, in resource poor countries despite successful fibrinolysis, patients may not reach PCI capable centres within desirable time i.e. 3-24 hours due to various logistic , personal, religious, and systematic factors. At times, even if they present within 24 hours of fibrinolysis, due to lack of insurance coverage there may be a delays in PCI due to financial reasons. Hence, we utilized the term “Delayed Pharmacoinvasive” approach to denote these practical cohort of patients which we all encounter in routine clinical practice.

Comment 3.Third,the statistical methods are inadequate. (1) Prospective research should adopt Cox proportional hazard analyses, rather than logistic regression. Cumulative event rates were estimated with Kaplan-Meier survival curves, and probability values were calculated with the log-rank test. (2) For Practical Clinical Trial, the baseline comparison between the two groups should preferably adopt the propensity scoring method.

Our response -We thank the reviewer for their kind comments. We agree with the reviewer’s suggestion that since it was a prospective study it should have adopted cox proportional hazard analysis and event rates should have been estimated with KM curves, but could not be done due to small sample size. Use cox proportional hazard model has been shown have more statistical power than logistic regression model in some cross sectional studies.[***Van der Net et al. Cox proportional hazards models have more statistical power than logistic***

regression models in cross-sectional genetic association studies. Eur J Hum Genet 2008; 16:1111–1116*]** However, when the follow up is short and event rates are low (as in our study) both methods may be comparable.[Annesi et al. Efficiency of the logistic regression and cox proportional hazards models in longitudinal studies. Stat Med 1989;8(12):1515-21.***]** However , in line with reviewer's suggestions, we have added this as a limitation of the study.

Reviewer #2

Comment 1.This is a very well-written and interesting paper. It is educational and the findings are important and relevant.

Our Response- We thank the reviewer for their kind comments. Their appreciation is vindication of hard work devoured into the manuscript.

Comment 2.I have several observations and questions. If I read this correctly, it is neither randomized nor prospective. The patients were selected by features other than chance: 'various nonspecific reason….', so the data could have essentially been collected retrospectively and any group selection applied, right? I would make it very clear in the materials and methods section exactly how you obtained your two groups. It is easy. 'The groups were not randomized. Group 1 represented < 24 hrs and Group 2 represented the 24.1-

72 hrs' or something simple. 'results stated no statistically significant difference in the clinical outcome between two therapies within 30 days of the procedure.'

Our Response- We thank the reviewer for their kind comments. We regret for the error in communication and lack of clarity in methods. We have modified the methods section in the revised manuscript as per your suggestion.

Comment 3.Do you think you should state 'no statistically significant difference in the MEASURED clinical outcome'.

Our Response- We thank the reviewer for their kind comments. We regret for the error in communication and lack of clarity in conclusion. We have modified the conclusion section in the revised manuscript as per your suggestion.

Comment 4.How many of each group still smoked after their 'heart attack' scare? 50% in both groups were tobacco users before. Did waiting an extra day provide PTSD to incentivize that group to decrease tobacco?

Our Response- We thank the reviewer for their kind comments. We did not collect the data regarding patients “still smoked“ after MI but wish to submit that smoking cessation counselling was provided to all patients. Evaluation of PTSD while waiting for an extra day as an incentive for smoking cessation is an interesting thought which we have ignored, thanks again for the insight. However, most of the patients who underwent delayed PCI were primarily because they presented late to the centre or delayed due to financial reasons and rarely due to illness related factors like deranged renal function, sepsis, refractory shock, pneumonia etc. But we still have added this as a limitation.