Author’s response to reviews

Title: Patient experience of the informed consent process during acute myocardial infarction: a sub-study of the VALIDATE-SWEDEHEART trial

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To the Editor-in-Chief
Trials

Dear Krishna Vairamani

Dear Reviewers,

Thank you again for considering the Manuscript TRLS-D-19-00945 "Patient experience of the informed consent process during acute myocardial infarction: a study of the VALIDATE-SWEDEHEART trial" for publication and for the thorough expert review. The valuable comments and suggestions have significantly improved the manuscript. Please find our answers as follows:
The authors have responded to the reviewers' comments and the revised manuscript is much improved. However, some areas require further revision and there are still some areas where a revision of English language usage is needed.

In general, the authors need to clearer about the limits to the study and how the findings relate to consent models used previous trials such as HEAT PPCI, and more careful when referring to research governance (clinical trials legislation and ethical requirements). This is a difficult and complex area, particularly given the different jurisdictions referred to, but an important one and so care must be taken when making claims about the study findings.

Specific comments:

Introduction

P. 4 line 23 'The use of the word 'motivated' should be amended e.g permitted or justified

Answer: Thanks for comment; justified inserted.

P.4 line 33 citation missing (et. al)

Answer: Thanks! Rewritten.

P.5 line 20 (and also P. 11 line 45) the phrase 'ethical committee' is usually referred to as an ethics committee or a research ethics committee

Answer: Thanks for valuable comment, changed to “ethics committee”.

P.5 line 23 'In accordance to the study protocol' should be 'in accordance with'

Answer: Changed as suggested.

P.5 line 25 It is important to add that in HEAT PPCI, when approached to provide consent after randomisation, they are being asked to provide informed consent to remain in the study. This is not equivalent to prospective consent to participate.

Answer: Correct, thanks! Changed to: “When asked for provide IC to remain in the study the day after randomization, only four out of 1829 patients refused consent”.

Methods
P.6 line 54 Thank you for clarifying in your comment to the reviewers that participants were consecutively enrolled in the sub-study. However, this detail should be included in the manuscript.

Answer: Consecutive enrolment included.

P.7 lines 23-24 requires rewording of 'Ages in subgroups, NSTEMI or STEMI and male versus female were categorized.'

Answer: Thanks for comment. The subgroups are specified in the next sentence, removed here.

Discussion

P. 11 line 16 the terms 'delayed consent' and 'deferred consent' are used inconsistently

Answer: Thanks for valuable comment. We have change delayed to deferred.

P. 11 line 24 The authors state that 'Thus, our findings do not support the use of delayed consent in patients with AMI who are capable of answering at the time of the IC process.' However, the question asked in the study (Would it have been better if you were included in the study without being informed until later?) does not explore deferred consent. Deferred consent (as used in HEAT PPCI for example) is used where obtaining patient consent is not feasible and there is also insufficient time to seek informed consent from the patient's representative). The question asked in this study does not appear to include any explanation as to why the patient would be included without being informed and what other ethical oversight/safeguards would be in place (trial presents minimal risk, risk of delaying treatment to obtain consent etc) and so cannot be said to 'investigate deferred consent'. The authors do not make clear that the essential elements of informed consent (being informed about the nature of the trial and the risks and benefits, retaining and understanding the information, coming to a reasoned decision, communicating that decision etc) are more than just being capable of 'answering' or recalling being in the study.

Answer: Thanks for important Q.

This study was not designed to investigate deferred consent in its full meaning. We merely aimed to explore the AMI- patients’ views of being informed and asked and in what time it would be preferable.

The conditions in Validate are similar of Heat PPCI. Similar medical condition, same medical products and similar emergency setting. Therefore we can conclude that most of these patients; involved in the same emergency settings as the patients in HEAT PPCI; did not want to be asked after randomization. Fully written IC was taken in Validate after the randomization as in the
HEAT PPCI. The difference was that patients were briefly told about the study, had a chance to decline and gave their verbal IC prior to randomization.

Well knowing that the IC process is complex and not only recalling being asked to participate in a study, the existing evidence indicates that AMI patients want to be involved in early stages of study-inclusion which is consistent with our results. However, this comment is certainly well-justified and in order to make it clearer the last meaning is rewritten to: Thus, our findings do not support the use of deferred consent without patient involvement pre-randomization.

A sentence under Ethical considerations is added as well: In this sub-study including patients with similar conditions as in HEAT-PPCI; we conclude that patients want to be involved in the IC process in early stages. A dialogue between the physician and the patient is essential. Despite the emergency setting patients can receive brief trial information and an opportunity to decline participation. Fully written IC is not feasible for many reasons in the emergency setting. This sub-study evaluates the verbal consent which many patients found sufficient.

P. 12 'assent' is not equivalent to informed consent and when referring to the Declaration of Helsinki, paragraph 29 (which refers to non-emergency situations) should also include the provisions in the following paragraph 30 which does refer to emergency situations and does not include the requirement for 'assent'. The 'd' in Declaration should be capitalised.

Answer: This sentence is removed.

p. 12 line 26 The phrase 'Most of the STEMI patients are awake' requires rewording. Are the authors referring to patients being conscious, or having decision-making capacity? The difference between patient populations in terms of the likelihood of having capacity to provide informed consent is the crucial criteria for the use of a deferred consent model. Are there differences between the patients and the urgency of the treatment in HEAT PPCI and the VALIDATE-SWEDEHEART trial that would justify (or not) the use of deferred consent?

Answer: This sentence is rewritten. According to the differences between the two trials-please see above q.

Thank you once again for your valuable remarks and for considering this manuscript for publication in Trials.

Best regards

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