Author’s response to reviews

Title: The efficacy and safety of Shenzhu Guanxin Recipe Granules for treatment of patients with coronary artery disease: protocol for a double-blind, randomized controlled trial

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Author’s response to reviews:

RE: TRLS-D-19-00162, entitled “The efficacy and safety of Shenzhu Guanxin Recipe Granules for treatment of patients with coronary artery disease: protocol for a double-blind, randomized controlled trial“

Dear Editor,

We would first like to thank you and the reviewers for your kind letter and professional advice concerning our article (Manuscript No. TRLS-D-19-00162). The following advice was valuable and helpful in improving our article. All authors have seriously discussed the review and opinions on the article and based on these reviews, we have modified our manuscript to meet the requirements of your journal. In this revised version of the manuscript, changes to our manuscript are presented in red text. Point-by-point responses to the reviewers are listed below.
Reviewer reports:

Thank you for the revision you have provided.

Below there is another reviewer comment that should be addressed before final acceptance. Some comments might not be implemented into your trial, since you have started your study. In case of not being able to add your protocol, you may discuss some points in "discussion" section.

Reviewer #2:

In the current manuscript, the authors have provided a protocol for a RCT to evaluate effect of a Chinese herbal medicine on patients with CAD.

The manuscript is well-written but followings should be addressed.

1- The authors should gather and provide other important baseline data such as EF which may affect the treatment protocols significantly.

2- Patients who have survival gains from revascularization should be excluded from the study including those with 2 or 3- vessel dx involving proximal LAD with either DM or low EF.

3- Patients whose symptom especially chest pain is not relived during the study should exit and undergo revascularization.

4- The authors should provide a description for any abbreviation used for the first time in the manuscript (for example SGR in the abstract).
The authors should gather and provide other important baseline data such as EF which may affect the treatment protocols significantly.

Response:

Thank you for your advice. Cardiac echocardiography can not only check the size and malformation of the heart, but also check the blood flow and blood flow of the heart, which is very important for the diagnosis and evaluation of patients with heart disease. Ejection fraction (EF) is an important indicator to evaluate the function of heart.

In fact, most of the patients in our study had already finished the cardiac echocardiography before being recruited into the trial, and only the patients with good heart function will be included in the study. But we did not treat the indicators including EF as one of the endpoint outcome indicators. In our study, we had included the SAQ score to evaluate the clinical condition of patients. Just as the points that reviewer had pointed out, we should consider to gather and provide other important baseline data such as EF which may affect the treatment protocols significantly.

However, since we have started your study and part of the patients had been recruited and completed the trial, consequently, this suggestion might not be implemented into our trial, but we will consider to perform the cardiac echocardiography before and after the trial in the rest of the patients, and explore whether Shenzhu Guanxin Recipe Granules (SGR) can influence the indicators including the EF significantly. And the points that the reviewer pointed out will be discussed as the limitations of our study.

The revised content will be included in the discussion part, which are presented on page 5, lines 14-28:

There are some limitations in this study. Firstly, although we recruited patients with PBSS due to qi deficiency, however, this Chinese medicine syndrome can dynamically change after the intervention. Secondly, the calculation of sample size was based on a pilot study and clinical observations, in which a larger sample size may result in different achievements. Third, even though several endpoints had been included in our trial to evaluate the efficacy of SGR on patients with CAD, and most of the patients in our study had already finished the cardiac echocardiography. However, the indicators of color Doppler echocardiography were not listed as endpoint indicators in our study. In order make the trial to be more rigorous and comprehensive, we should consider to gather and provide other important baseline data such as EF which may affect the treatment protocols significantly in our future studies.
2- Patients who have survival gains from revascularization should be excluded from the study including those with 2 or 3-vessel dx involving proximal LAD with either DM or low EF.

Thank you for your advice, because the defect of the defect of our experimental design, it is kind of you to remind us to exclude the patients who have survival gains from revascularization, including those with 2 or 3-vessel dx involving proximal LAD with either DM or low EF.

We had examined medical history the patients who had already been recruited, and no patients had the above medical history.

We will make the following changes in the manuscript, which are presented on page 3, lines 7-9:

The exclusion criteria were as follows: (1) patients were complicated with other serious diseases, including malignant tumor, severe infection, and other significant life-limiting comorbidities; (2) pregnant and lactating women and those allergic to TCM; (3) poor compliance, and failure to visit regularly; (4) Valvular heart disease; (5) patients with congenital metabolic abnormalities or immune diseases. (6) the patients who have survival gains from revascularization, including those with 2 or 3-vessel dx involving proximal left anterior descending branch (LAD) with either diabetes mellitus (DM) or low ejection fraction (EF).

3. Patients whose symptom especially chest pain is not relived during the study should exit and undergo revascularization.

Answer:

Thank you for your advice. The symptoms of chest pain were accessed by the Seattle Angina Questionnaire (SAQ). In our previous manuscript, we had explained that the patients develop another severe disease that needs to be treated during the study. It is kind of you to remind us to add the criteria: Patients whose symptom especially chest pain is not relived during the study should exit and undergo revascularization.

We had made the following corrections, which are presented on page 5, lines 16-17.

Dropout criteria

The included patients have the right to stop treatment and withdraw from the research project for any reason at any time, and the reason why they want to quit the research project will be recorded in their CRF. Participants who do not complete the research project with the following reasons should be considered as dropped out. (1) The patient chooses to quit the research project. (2) loss to follow-up. (3) Poor compliance. (4) The participant develops another severe disease that needs to be treated during the study. (5) Patients whose symptom especially chest pain is not relived during the study should exit and undergo revascularization.
4- The authors should provide a description for any abbreviation used for the first time in the manuscript (for example SGR in the abstract)

Answer

Thank you for your advice, we had carefully checked the manuscript, and provide a description for any abbreviation used for the first time in the manuscript including SGR in the abstract.