

Dear Professor,

We sincerely appreciate the opportunity you've given us to resubmit our revised manuscript. We have diligently addressed the revisions based on your valuable feedback, as outlined below. Furthermore, we have requested language polishing services to enhance the linguistic proficiency of the entire text.

1. First of all, the world journal of gastroenterology is not suitable to this article. The world journal of cardiology would be suitable for target readers, because the novel treatment such as Yangxinshi Tablet for chronic cardiac failure is being explored in the world.

R: Thank you for your reminder. Our manuscript has been transferred to the *World Journal of Clinical Cases*.

2. Please add the information about left ventricular function and type of chronic heart failure (HFrEF/HFpEF etc.) and baseline cardiac disease (ischemic/non ischemic) in each adopted study in Table 1. By this information readers will be able to know which patients were treated with Yangxinshi Tablet in the review and met-analysis.

R: We have added entries such as left ventricular function, type of CHF, and baseline cardiovascular disease in Table 1, providing readers with more comprehensive basic information.

[The modification is located in Table 1.](#)

3. To know the effects of Yangxinshi Tablet on cardiac failure, it would be crucial to consider the use of the guidelines-based treatment (β blocker, ACEI/ARB, MRA, SGLT2i, ARNI etc.) in all patients. Please show the prescription rate and adherence to the guidelines-based treatments in the adopted studies.

R: We have added the prescription rate and compliance with the guidelines for the included studies in "Basic characteristics of the included literature". The "2023

Focused Update of the 2021 European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure” was used to evaluate the standardization of basic treatments included in the study.

The revised content is as follows: Among the 20 clinical trials, 19 (95%) followed the 2023 Focused Update of the 2021 European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure, while one trial conducted by Fan et al. did not describe specific treatment plans.

4. The treatment strategy for HFrEF has been almost established. Meanwhile, the beneficial drugs for HFpEF is scarce besides SGLT2i and ARNI. Thus, readers may want to know the effects of Yangxinshi Tablet on HFpEF. Please show the data and or discuss about this theme.

R: Thank you for your professional guidance. We added "HFpEF subgroup analysis" in the results and a corresponding analysis in the discussion to independently analyzed the effectiveness of YXST in treating HFpEF.

The revised content is as follows:

Heart failure with preserved ejection fraction (HFpEF) subgroup analysis

An HFpEF subgroup analysis was employed to explore the clinical efficacy of YXST in the treatment of HFpEF. The results confirmed that, compared to the conventional drug group, the YXST combination group significantly improved the clinical effective rate by 19% (RR=1.19, 95%CI (1.06, 1.33), $P=0.003$), and increased the 6-MWT by 44.61 m (MD=44.61, 95%CI (17.58, 71.65), $P=0.001$). Additionally, the YXST combination group decreased the NT-proBNP by 0.73 ng·L⁻¹ (MD=-0.73, 95%CI (-0.95, -0.51), $P<0.00001$). As shown in Table 2.

HFpEF is the most common type of CHF, accounting for more than 50% of all cases^[42]. An observational study in a Western country demonstrated that the 1-year mortality rate of patients with HFpEF was 20%–29%, whereas the 5-year mortality rate was as high as 53%–74%^[43]. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) and angiotensin receptor/neprilysin inhibitors (ARNI) are commonly used for HFpEF and they effectively improve its prognosis^[18,44]. However, apart from SGLT2i and ARNI, few beneficial drugs are available for HFpEF. The current treatment regimens are still inadequate for the management of all patients with HFpEF^[45]. In this study, we

evaluated the clinical efficacy of YXST in treating HFpEF. The results of the HFpEF subgroup analysis demonstrated that YXST significantly increased the clinical effective rate by 19%, 6-MWT by 44.61 m, and decreased NT-proBNP by 0.73 ng·L in patients with HFpEF. This suggests that YXST can reduce clinical symptoms, enhance exercise tolerance, and improve the overall prognosis of patients with HFpEF. Therefore, we hypothesized that YXST has the potential to complement SGLT2i and ARNI in the treatment of HFpEF.

5. In Page 11 Lines 1-3 Left ventricular diastolic function can not be evaluated by LVEDD, LVESD, or LVEF. Thus, this description is incorrect.

R: We apologize for this basic mistake. We have adjusted the content of this sentence based on relevant professional knowledge.

The revised content is as follows: LVEF represents the ratio of stroke volume to the left ventricular end-diastolic volume. The parameter serves as an objective indicator of the severity of heart failure (HF). Mortality in patients with HF is closely correlated with the LVEF. Additionally, LVESD and LVEDD are indicative of the volume load on the left ventricle. Increases in LVEDD and LVESD signify cardiac dilation and compromised ventricular compliance. Both LVEF and LVEDD reflect the extent of left ventricular remodeling.

6. Page 4: Line 3 from the bottom: TCM Please show the full spelling at the first presentation for TCM.

R: We have added its full name "traditional Chinese medicine" when TCM first appeared.

The revised content is as follows: Traditional Chinese Medicine (TCM).

7. Page 4 Line 3 from the bottom to Page 5 Line 5 Please add the references for this sentence.

R: We have added references to this paragraph.

The added references are as follows:

[13][Zang Y, Wan J, Zhang Z, Huang S, Liu X, Zhang W. An updated role of astragaloside IV in heart failure. Biomed Pharmacother 2020; 126: 110012. \[PMID: 32213428 DOI: 10.1016/j.biopha.2020.110012\]](#)

[14][Liu H. Interpretation of Consensus of Experts on Clinical Application of Yangxinshi Tablets in Treatment of Coronary Heart Disease. World Chinese Medicine 2020; 15: 637-642. \[DOI: 10.3969/j.issn.1673-7202.2020.04.034\]](#)

8. Please add the Chinese name in Chinese letters for Yangxinshi Tablet, Qi, Yang.

R: We have added their Chinese names in the “Introduction”.

The revised content is as follows: [Yangxinshi Tablet \(养心氏片\), Qi \(气\), Yang \(阳\).](#)

9. Page 6 the boeeom line In each exercise→Please explain these words. I cannot understand them.

R: We apologize for the incorrect expression. We have changed "in each exercise" to "at each step".

The revised content is as follows: [At each step, the two researchers ensured that the results were consistent.](#)

10. Reference 「20」 Is the data incomplete?

R: We have supplemented the detailed information of reference [20]. As a Master's thesis, it does not have an issue or volume number. We sincerely request your understanding.

The revised reference is as follows: [Chen Q. Clinical study of Yangxinshi tablet treating chronic heart failure with Qi deficiency and blood stasis syndrome. *Anhui University of Chinese Medicine* 2019; 1-47.](#)

11. Please explain the missing data in male age in Table 1.

R: We have added a note in Table 1 stating that the missing data is due to the inclusion of studies that were not reported.

The revised content is as follows: “/” stated that this data was not reported in the included study.

We are immensely grateful for your guidance, which has significantly contributed to the refinement of our manuscript.

If you identify any further issues that require attention, please do not hesitate to inform us. Thank you.

Best regards,

Shenghua Lu