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The cardioprotective effect of *Shengmai Zhenwu* decoction on patients with chronic heart failure based on the levels of soluble interleukin 1 receptor-like 1

Lei Zhang [a,1], Bing-Bing Ning [a,1], Si-Jia Ma [a], Lu-Ling Wang [a], Jing Wang [a], Dan Zhu [a], Wen Zhu [a], Feng-Qun Xie [a], Jie Cheng [a], Qi-Mao Feng [b,*]

[a] *Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Shang hai, 200071, China*
[b] *Department of Xin-Bing, Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Shang hai, 200071, China*

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ABSTRACT

Objective: The purpose of this study was to evaluate the protective effect of *Shengmai Zhenwu* decoction on patients with chronic heart failure (CHF) based on the levels of soluble interleukin 1 receptor-like 1 (ST2).

Methods: We included a total of 80 outpatients and inpatients with CHF who were undergoing treatment at the Shanghai Municipal Hospital of Traditional Chinese Medicine between March 2020 and March 2022. We randomly divided them into the observation group ($n = 40$) and the control group ($n = 40$). Patients in the control group received treatments as per conventional Western medicine, while those in the observation group were treated with the *Shengmai Zhenwu* decoction in conjunction with Western medicine for eight consecutive weeks. We then compared the pre- and post-treatment levels of ST2 and N-terminal pro-brain natriuretic peptide (NT-proBNP) of the patients in the two groups.

Results: There were no significant differences in the pre-treatment levels of ST2 and NT-proBNP indexes between the two groups ($P > 0.05$), while the post-treatment comparison between the two groups in terms of ST2 and NT-proBNP levels suggested that the effect in the observation group was better, with statistical significance ($P < 0.05$).

Conclusion: Shengmai Zhenwu decoction was beneficial in patients with CHF, suggesting that it could be a promising and effective method for the treatment of CHF.

1. Introduction

Chronic heart failure (CHF) is a clinical syndrome caused by abnormal cardiac structure and/or dysfunction. It is the major cause of fatal outcomes in the advanced stages of a number of cardiovascular illnesses. CHF has become the leading cardiovascular disease in modern times due to the increase in the aging population and the growing incidence of chronic diseases [1]. Recent research has shown

* Corresponding author. Department of Xin-Bing, Shanghai municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, No.274 of Middle Zhi-Jiang Road, Jing An District, Shang hai, 200071, China.
E-mail address: fengqimaofqm8@126.com (Q.-M. Feng).
[1] These authors contributed equally to this article.

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that the occurrence and progression of heart failure are associated with various changes in hemodynamic and neurohumoral factors. N-terminal pro-brain natriuretic peptide (NT-proBNP), a representative factor, has been extensively used [2], and soluble interleukin 1 receptor-like 1 (ST2), a new type of biomarker, has also been recommended in recent years. This biomarker, which belongs to the interleukin 1 receptor family, is involved in relieving the fibrosis and hypertrophy of mechanically stressed tissues. As a result, the change in ST2 levels is a reliable predictor of changes in heart functioning and fatal outcomes.

Shengmai Zhenwu decoction (consisting of *Ginseng Radix et Rhizoma*, *Aconiti Lateralis Radix Praeparaia*, *Ophiopogonis Radix*, *Atractylodis Macrocephalae Rhizoma*, *Poria* and *Polyporus*, *Schisandrae Chinensis Fructus, Paeoniae Radix Alba*, *Epimedii Folium*, *Cervi Cornu* and *Psoraleae Fructus*, *Crataegi Fructus, and Salviae Miltiorrhizae Radix et Rhizoma*) is a traditional Chinese medicine prescription based on conventional Western medicine. It is used to alleviate the clinical symptoms and improve myocardial function in patients with CHF with phlegm stagnation derived from the same fountainhead. In order to clarify the efficacy of this treatment, we used the NT-proBNP and ST2 levels to evaluate the condition and prognosis of heart failure and to explore its cardioprotective effect in such patients.

2. Materials and methods

2.1. Study population

We recruited a total of 80 outpatients and inpatients with CHF who were treated at the Shanghai Municipal Hospital of Traditional Chinese Medicine between March 2020 and March 2022. We divided these patients into the control group ($n = 40$) and the observation group ($n = 40$) using a random number table. The observation group consisted of 18 men and 22 women, with an age range of 54–79 years (average = 73.6 ± 5.6 years), while there were 19 men and 21 women in the control group, with an age range of 55–79 years (average = 71.9 ± 6.9 years). Both groups were comparable with regard to patients' gender, age, and history of underlying diseases, and the differences were not statistically significant.

2.2. Diagnostic criteria

2.2.1. Diagnostic criteria in western medicine

The Western medicine diagnostic criteria were based on the Framingham Criteria for Congestive Heart Failure [3], as shown in Table 1.

2.2.2. Cardiac function classification standards

The cardiac function classification standards that we used in this study were as per the New York Heart Association Classification of Cardiac Function [3], as shown in Table 2.

2.2.3. Traditional Chinese medicine syndrome differentiation criteria

We developed the traditional Chinese medicine syndrome differentiation criteria after a thorough review of the relevant content in the "*Guiding Principles for Clinical Research on New Drugs of Traditional Chinese Medicine*" [4] and the "*Diagnostics of Traditional Chinese Medicine*". The primary symptoms were shortness of breath, fatigue, and chest tightness (pain), while the secondary symptoms were weakness of the limbs, a floating pulse, coughing with viscous sputum, indigestion and loss of appetite, and nausea. For a diagnosis, the patient must have at least two primary symptoms and at least two secondary symptoms, combined with specific tongue characteristics (dark red tongue with petechia or bruise, or thick greasy or cloudy tongue coating) and pulse conditions (thin and weak pulse, sunken and astringent pulse, or wiry and rolling pulse).

2.2.4. Standards for the traditional Chinese medicine syndrome score

The traditional Chinese medicine (TCM) syndrome scoring was mainly based on the TCM diagnostic efficacy criteria and medication specifications for heart diseases published in 2002 [5]. We used a semi-quantitative grading scoring method based on clinical experience that consisted of four grades for the primary symptoms, with 0, 2, 4, and 6 points corresponding to no symptoms, mild,

Table 1
Framingham's diagnostic criteria for heart failure (1971).

Main criteria	Secondary criteria
Paroxysmal nocturnal dyspnea or orthopnoea	Ankle edema
Jugular vein distention	Nighttime cough
Lung rale	Dyspnea after activity
Cardiac dilatation	Hepatomegaly
Acute pulmonary edema	Pleural effusion
Third heart sound gallop	Vital capacity reduced to 1/3 of the maximum
Elevation in venous pressure >1.57kpa (16 cm H2O)	Tachycardia (≥120 bpm)
Cycle time >25s	Primary or secondary criteria
Hepatic-jugular reflux sign (+)	Weight loss >4.5 kg within 5 days after treatment

* Diagnosis of heart failure: There are two main items or one main item plus two secondary items.

Table 2
NYHA cardiac function classification criteria.

NYHA I	Activity not restricted Daily physical activity will not cause obvious shortness of breath, fatigue, palpitations, which is usually called the satisfactory functional compensation period;
NYHA II	Activity slightly limited. There is no discomfort at rest, but daily activities will cause obvious shortness of breath, fatigue, palpitations, which is also known as grade I or mild heart failure;
NYHA III	Activity significantly limited. There are no symptoms at rest, but mild daily activities will cause significant shortness of breath, fatigue, palpitation, which is also known as grade II or moderate heart failure;
NYHA IV	Symptoms even appear at rest and get worse after light physical activity. Any physical activity will cause discomfort, which is also known as grade III or severe heart failure.

moderate, and severe symptoms, respectively, and 0, 1, 2, and 3 points for secondary symptoms, corresponding to no symptoms, mild, moderate, and severe symptoms, respectively. We performed a statistical analysis of the scores pre- and post-treatment to evaluate the improvements in TCM symptoms and signs following treatment.

A marked response was defined as a reduction in the TCM syndrome score by >70% following treatment; a moderate response denoted that the score was reduced by >30% following treatment; and no response denoted that the score was reduced by < 30% following treatment.

2.3. Inclusion criteria

The inclusion criteria were as follows: i) patients diagnosed with heart failure at the Cardiology Ward and Outpatient Department of the Shanghai Municipal Hospital of Traditional Chinese Medicine between March 2020 and March 2022; ii) patients who were in clinical stage C of heart failure; and iii) patients with intermingled phlegm and blood stasis, which were diagnosed using four diagnostic methods—TCM inspection, olfaction, interrogation, and palpation, and TCM syndrome differentiation [6].

2.4. Exclusion criteria

The exclusion criteria were as follows: i) patients with acute coronary syndrome; ii) patients with acute left and right heart failure; and iii) patients with tumors and complications due to multiple organ failure.

2.5. Rejection and dropout criteria

These criteria included: i) patients who were not cooperative in the randomization and who exhibited poor compliance; ii) patients who did not take the medicine as prescribed or voluntarily discontinued the medication; iii) patients who took drugs that affected the relevant indexes of the study; and iv) patients who did not provide the relevant test indexes required as per the study schedule.

2.6. Treatment methods

The enrolled patients were divided into the observation group and the control group in a ratio of 1:1 as per random grouping principles. Patients in the control group received the following conventional Western medicine treatments: angiotensin II receptor antagonist/ACE inhibitor, β-blocker, aldosterone antagonist, diuretic, and digoxin, administered according to the guidelines. The medications were not adjusted when the patient's condition stabilized.

Patients in the observation group were administered *Shengmai Zhenwu* decoction (9 g of *Ginseng Radix et Rhizoma,* 12 g of *Ophiopogonis Radix,* 9 g of *Schisandrae Chinensis Fructus,* 12 g of *Aconiti Lateralis Radix Praeparaia,* 15 g of *Atractylodis Macrocephalae Rhizoma,* 15 g of *Root of Paeoniae Radix Alba,* 15 g of *Poria,* 15 g of *Polyporus,* 15 g of *Epimedii Folium,* 9 g of *Cervi Cornu,* 9 g of *Psoraleae Fructus,* 15 g of *Crataegi Fructus,* and 18 g of *Salviae Miltiorrhizae Radix et Rhizoma*) on the basis of conventional Western medicine treatments. The above traditional prescription was provided in granules by Jiangsu Tianjiang Pharmaceutical Co., Ltd. and was taken with 100 mL of warm water after the morning and evening meals for eight weeks.

2.7. Outcome measures: ST2 and NT-proBNP levels

A sample of 4 mL of fasting blood was collected from the patients through the median cubital vein in the morning, before and after treatment. The ST2 serum was detected via a latex immunoturbidimetric method using a kit manufactured by ATPO Bio-Tech (Tianjin) Co., Ltd. The procedures were carried out strictly in accordance with the instructions specified in the kit. Two mL of the collected venous blood was injected into the ethylenediamine tetraacetic acid anticoagulant tube, shaken, and centrifuged at 3000 r/min for 10 min within 2 h of being stored at room temperature. The plasma collected was immediately used for the detection of NT-proBNP plasma. The instrument used for testing was the Elecsys 2010 NT-probNP automatic analyzer, manufactured by Roche Diagnostics, Germany. We compared both groups for changes in serum ST2 and NT-proBNP plasma levels before and after treatment.

2.8. Statistical analysis

We used SPSS 26.0 statistical software for processing the experimental data. We used the χ^2 test for analyzing enumeration data, and measurement data were expressed in terms of ($\bar{x} \pm s$). We used the Student's t-test for inter-group comparisons pre- and post-treatment. A *P*-value of <0.05 indicated that the difference was statistically significant.

3. Results

3.1. Evaluation of efficacy

3.1.1. Comparison of traditional Chinese medicine syndrome efficacy between the two groups

The overall response rate was 95% (38/40 cases) in the observation group and 77.5% (31/40 cases) in the control group. The difference was statistically significant ($P < 0.05$), as shown in Table 3.

3.1.2. Comparison of pre-and post-treatment levels of soluble interleukin 1 receptor-like 1 between the two groups

There were no statistically significant differences in the ST2 level between the two groups pre-treatment ($P > 0.05$), but the post-treatment effect was better in the observation group, with a statistically significant difference ($P < 0.05$), as shown in Table 4.

3.1.3. Comparison of pre-and post-treatment levels of N-terminal pro-brain natriuretic peptide between the two groups

The pre-treatment levels of NT-proBNP between the two groups were not statistically significant ($P > 0.05$), but the post-treatment effect was better in the observation group, with the difference statistically significant ($P < 0.05$), as shown in Table 5.

3.2. Safety evaluation

During the clinical trial, the patients in the two groups underwent routine blood, urine, stool, liver, kidney, and other safety index investigations pre- and post-treatment. Neither group experienced any treatment-related adverse effects, and there was no statistically significant difference between the two groups before and after treatment ($P > 0.05$) in this aspect. There were no serious adverse events during treatment. All the patients completed the entire course of treatment.

4. Discussion

A variety of cardiac diseases can result in heart failure, a complex clinical syndrome. From a hemodynamic perspective, weakened myocardial contractility leads to decreased cardiac output, blood stasis in the venous system, increased end-diastolic pressure, excessive preload, peripheral vasoconstriction, and increased peripheral resistance, resulting in excessive cardiac load [7]. Conventional Western medicine treatments include angiotensin II receptor antagonists/ACE inhibitors, β-blockers, aldosterone antagonists, diuretics, and digoxin. However, patients can suffer from impaired liver and kidney functions and severe side effects due to the long-term use of these medications. TCM has been shown to improve myocardial metabolism and protect liver and kidney function with minimal side effects and a good prognosis [8–10].

The index that we used in this study, ST2, is a member of the interleukin (IL-1) receptor family and is a new cardiac marker that can be easily detected regardless of age, race, or renal function. Furthermore, elevation in ST2 levels is closely associated with the prognosis of chronic heart failure [11]. Therefore, ST2 is a suitable adjunct to the widely used NT-proBNP in the diagnosis and assessment of patients with heart failure.

The clinical symptoms of heart failure in TCM include chest obstruction, palpitation, and precordial pain with cold limbs. The *Synopsis of Golden Chamber* mentions the following: "Thorax cavity, heart yang … where there is obstruction, there will be phlegm obstruction." Heart failure is a syndrome caused by exhausted heart Qi due to prolonged illness and decline in heart Yang, which causes failure in the promotion of blood circulation and blood stasis, resulting in phlegm, water, and dampness retention. The formation of blood stasis and water dampness further impairs Yang Qi, forming a vicious cycle of excess syndrome caused by deficiency and more deficiency resulting from the excess syndrome [7].

In the present study, we assessed the efficacy and possible mechanism of action of *Shengmai Zhenwu* decoction based on measuring the levels of ST2 and NT-proBNP in the plasma of patients with heart failure. The principal drugs of *Shengmai Zhenwu* decoction include *Ginseng Radix et Rhizoma,* with a sweet-warm property that reinforces vital energy, and *Aconiti Lateralis Radix Praeparaia,* with a pungent and hot property, used to tonify the kidney and strengthen yang as well as supply the fire of the vital gate. When combined into a formula, these two Chinese herbs play an important role in transforming the Yang Qi by nourishing and warming the kidney

Table 3
Comparison between observation group and control group in terms of overall response rate.

Group	n	Marked response	Moderate response	No response	Overall response rate
Observation group	40	23	15	2	95.0%*
Control group	40	17	14	9	77.5%

Notes: Compared with the control group, $^*P < 0.05$.

Table 4
Comparison of ST2 level between observation group and control group ($n = 40$, $\bar{x} \pm SD$).

Group	Before treatment	After treatment	*P1*	*P2*	*P3*
Observation group	57.40 ± 31.82	40.06 ± 18.23	0.000	0.880	0.007*
Control group	58.62 ± 39.87	30.63 ± 11.75	0.000		

Note: '*P*1' represented the comparison of ST2 level between before and after treatment in the same group, and '*P*2' and '*P*3' represented the comparison of ST2 level among observation group and control group before and after treatment, respectively. *$P < 0.05$ *vs*. control group after treatment.

Table 5
Comparison of NT-proBNP levels between observation group and control group ($n = 40$, $\bar{x} \pm SD$).

Group	Before treatment	After treatment	*P1*	*P2*	*P3*
observation group	8502.05 ± 5222.44	4450.50 ± 2173.97	0.000	0.847	0.041*
control group	8733.58 ± 5475.75	3468.38 ± 2047.26	0.000		

Note: '*P*1' represented the comparison of NT-proBNP levels between before and after treatment in the same group, and '*P*2' and '*P*3' represented the comparison of NT-proBNP levels among observation group and control group before and after treatment, respectively. *$P < 0.05$ *vs*. control group after treatment.

yang and reinforcing vital energy.

Additionally, the ministerial drugs of *Shengmai Zhenwu* decoction consist of *Ophiopogonis Radix*, *Atractylodis Macrocephalae Rhizoma*, *Poria,* and *Polyporus*. These herbs have significant effects on nourishing yin to moisten dryness (*Ophiopogonis Radix*), strengthening the spleen, and replenishing Qi, as well as eliminating dampness and promoting urination (three other ministerial drugs) in treating the disease. *Schisandrae Chinensis Fructus* and *Paeoniae Radix Alba* were the assistant drugs in the *Shengmai Zhenwu* formula. *Schisandrae Chinensis Fructus* has effects on astringing lung Qi, enhancing Qi, and nourishing fluid, as well as reinforcing the kidney and nourishing blood, while *Paeoniae Radix Alba* plays an important role in astringing yin and activating tendons, promoting the circulation of qi to induce diuresis, and nourishing the liver to relieve pain. Additionally, the effects of reinforcing the kidney to strengthen yang in the *Shengmai Zhenwu* formula could be attributed to the combination of *Epimedii Folium*, *Cervi Cornu,* and *Psoraleae Fructus. Crataegi Fructus and Salviae Miltiorrhizae Radix et Rhizoma* had beneficial effects on removing blood stasis and promoting blood circulation.

This suggests that the *Shengmai Zhenwu* formula had protective effects, specifically for the heart, lungs, spleen, and kidney. This Chinese medicine formula is particularly used for warming and nourishing the nature, nourishing the nurture, eliminating phlegm, promoting urination, and activating blood circulation, and the decoction had significant effects through tonifying Qi and warming Yang, nourishing yin, and promoting diuresis, thereby promoting coronary circulation.

Recent pharmacological research on the effects of *Ginseng Radix et Rhizoma* extract on experimental animals has shown that it has an anti-shock effect, which is related to significantly increased cardiac output and coronary blood flow. In addition, when heart failure was induced in animal models, *Ginseng Radix et Rhizoma* extract had a stronger cardiotonic effect. *Aconiti Lateralis Radix Praeparaia,* another principal drug of the *Shengmai Zhenwu* formula, contains several chemical components, such as higenamine and coryneine chloride, which exert a cardiotonic effect mainly by increasing the heart rate and enhancing the contractility of cardiac muscle cells. In addition, there is evidence to show that *Aconiti Lateralis Radix Praeparaia* could dilate the coronary arteries, resist myocardial ischemia and had anti-inflammatory effects, which plays an important role in inhibiting capillary exudation and reducing swelling [12].

Overall, our findings in this study demonstrated that *Shengmai Zhenwu* decoction had a significant impact on the prognosis of heart failure, mainly manifested as reducing the infiltration of inflammatory cells and significantly protecting the myocardium [13]. We found that *Shengmai Zhenwu* decoction improved CHF by reducing the ST2 and NT-proBNP levels in the plasma.

The patients in this study had CHF with phlegm stagnation derived from the same fountainhead, as per TCM theory. Prior to treatment, the ST2 and NT-proBNP levels of the patients in the two groups were higher than the reference range. Post-treatment, the ST2 and NT-proBNP levels of patients in the observation group were reduced, the overall clinical response rate was significantly higher, and the curative efficacy was significantly better when compared with the control group. There has been notable progress in modern pharmacological research on the *Shengmai Zhenwu* decoction, one of Zhang Zhongjing's characteristic prescriptions for the treatment of chest congestion. These research developments can provide new ideas for the treatment of patients with CHF in the future.

There are several limitations to this study. First, while we compared the plasma levels of ST2 and NT-proBNP between the two groups during the treatment, we did not follow up with the patients regularly, due to which we could not ascertain the prognosis of the patients in the two groups. Second, the content of pharmacological studies on *Shengmai Zhenwu* decoctions is relatively diverse, with most addressing the pharmacological effects of a single ingredient and only a few addressing the pharmacological effects of combination medications. This does not do justice to the overall concept of TCM and merits further research and discovery.

In conclusion, in this study, we found that a combination of conventional western medicine and *Shengmai Zhenwu* decoction treatments could prevent cardiac damage in patients with CHF by regulating the levels of both ST2 and NT-proBNP. Therefore, it is an effective treatment for patients with CHF.

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Ethics approval and consent to participate

I confirm that I have read the Editorial Policy pages. This study was conducted with approval from the Ethics Committee of Shanghai municipal Hospital of Traditional Chinese Medicine (2020SHL-KYYS-94). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Availability of data and materials

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Author contribution statement

Qi-Mao Feng: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.
Lei Zhang: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.
Bing-Bing Ning: Conceived and designed the experiments; Performed the experiments.
Si-Jia Ma: Performed the experiments; Contributed reagents, materials, analysis tools or data.
Feng-Qun Xie, Wen Zhu: Performed the experiments; Wrote the paper.
Lu-Ling Wang: Analyzed and interpreted the data.
Jie Cheng: Analyzed and interpreted the data; Wrote the paper.
Dan Zhu, Jing Wang: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Chinese Society of Cardiology, Editorial Board of Chinese Journal of Cardiology. [Guidelines for the diagnosis and treatment of chronic heart failure], Chin. J. Cardiol. 12 (35) (2007) 1–29.
[2] Chinese expert consensus on biomarkers for heart failure, Chin. J. Lab. Med. 43 (Issue 2) (2020), 130-14.
[3] The Main Translation of Chen HZ,Braunwald Cardiology, seventh ed., People's Health Press, Beijing, 2007, p. 513.
[4] [Guiding principles for clinical research of new Traditional Chinese medicine drugs: trial implementation], in: X.Y. Zheng, chief (Eds.), Beijing, China Medical Science and Technology Press vol. 4, 2002, pp. 78–80.

[5] S.G. Shen, C.D. Wang, X.J. Yan, chief (Eds.), Efficacy Standard and Medication Standard for Heart Disease Diagnosis of Traditional Chinese Medicine, Beijing Press, Beijing, 2001.
[6] Chinese Society of Cardiology, Editorial board of Chinese Journal of Cardiology. Chinese guidelines for diagnosis and treatment of heart failure 2014, Chin. J. Cardiol. 42 (2) (2014) 98–122, e.
[7] X.M. Wang, Z.Q. Pan, Y.B. Yang, [The theory of "phlegm and blood stasis" is used for clinical observation to treat refractory heart failure], China Pract. Med. 5 (31) (2010) 505–507.
[8] Chinese Association of Integrated Traditional and Western Medicine cardiovascular disease committee, Expert consensus on the diagnosis and treatment of chronic heart failure with integrated Chinese and Western medicine, Prevent. Treat. Cardio-Cerebrovasc. Dis. 16 (5) (2016) 340–347.
[9] S.Y. Wan, J.G. Hu, Y. Zhang, B.Y. Yu, J.P. Kou, F. Li, Recent advances of traditional Chinese medicine in the regulation of myocardial mitochondrial function, World J. Tradit. Chin. Med. 8 (2022) 50–58.
[10] L. Peng, L. Ma, Q.Q. Jiang, X. Tian, M.Y. Shao, C.X. Li, et al., The mechanism of Panax notoginseng in the treatment of heart failure based on biological analysis, World J. Tradit. Chin. Med. 8 (2022) 530–538.
[11] R.V. Shah, J.L. Januzzi Jr., ST2: a novel remodeling biomarker in acute and chronic heart failure, Curr. Heart Fail. Rep. 7 (1) (2010 Mar) 9–14, https://doi.org/10.1007/s11897-010-0005-9. PMID: 20425491.
[12] Y. Li, T.J. Zhang, S.X. Liu, C.Q. Chen, Research progress of chemical constituents and pharmacology of ginseng, Chin. Herb. Med. 40 (1) (2009).
[13] L. Zhang, H.L. Li, Research progress of treatment for thoracic obstruction with gualou xiebai Banxia decoction, J. Emerg. Tradit. Chin. Med. 28 (9) (2019) 1689–1692.