

Clinical Research Advances in Traditional Chinese Medicine for Chronic Heart Failure Complicated with Depression

Qian Li¹, Guangping Zhang^{2,*}

¹Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

²Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, Shaanxi, China

*Correspondence Author

Abstract: *Chronic heart failure (CHF) is a common critical and severe condition in clinical practice, with high incidence and mortality rates. When the body develops CHF, as the disease progresses, patients will experience negative emotions such as anxiety and depression, which further aggravate the condition and seriously affect the prognosis. Currently, clinical practice mostly focuses on the treatment of CHF, often neglecting the diagnosis and treatment of anxiety and depression symptoms. This article explores the main treatment methods for CHF combined with anxiety and depression symptoms, the understanding of the etiology and pathogenesis of chronic heart failure combined with anxiety and depression by traditional Chinese medicine, summarizes the commonly used therapeutic methods and prescriptions as well as the unique traditional Chinese medicine therapies, in order to provide reference for clinical practice.*

Keywords: Chronic heart failure, Anxiety, Depression.

1. Introduction

Chronic heart failure (CHF) is a complex clinical syndrome triggered by structural and/or functional abnormalities of the heart secondary to diverse etiological factors. These abnormalities impair ventricular systolic and/or diastolic function, ultimately giving rise to a spectrum of characteristic clinical manifestations [1].

According to the China Cardiovascular Health and Disease Report 2024, the number of heart failure patients in China currently exceeds 10 million, with an in-hospital mortality rate of 2.6%, a non-rehabilitation discharge rate of 10.2%, and an 11% 30-day readmission rate. The incidence and mortality of this condition remain persistently high; its therapeutic challenges and poor prognosis not only severely compromise patients' quality of life but also pose a significant threat to human life and health [2]. Patients with chronic heart failure (CHF) frequently present comorbid anxiety and depression. Relevant research indicates that the prevalence of these psychological disorders exceeds 50%, which not only undermines patients' treatment adherence and rehabilitation progress but also exacerbates disease deterioration [3]. Moreover, anxiety and depression are identified as critical contributors to heart failure onset and readmission [4]. Beyond increasing patients' psychological burden, these conditions can impair cardiac function via neuroendocrine mechanisms, creating a vicious cycle [5]. In clinical practice, mental health disorders and cardiovascular diseases are often treated as separate entities. However, concurrent use of heart failure medications and psychotropic drugs frequently leads to multiple adverse reactions affecting systems such as the endocrine and digestive systems, thereby reducing the overall therapeutic efficacy [6]. In contrast, traditional Chinese medicine (TCM) demonstrates unique advantages in addressing "dual heart diseases" (cardiovascular and mental health comorbidities) through its characteristics of multi-component, multi-target, multi-pathway action, and holistic regulation.

2. Modern Medicine Explores the Pathogenesis of Chronic Heart Failure Combined with Depression

From a physiological perspective, the pathogenesis of CHF combined with anxiety and depression may be closely related to immune, neuro-humoral, and autonomic nerve mechanisms. Studies have found [7-8] that the immune process mediated by various inflammatory factors (C-reactive protein, interleukins, etc.) is one possible mechanism, but the specific mechanism remains unclear. From the neuro-humoral perspective, the bodies of patients with heart failure are prone to be in a state of insufficient perfusion and hypoxia. The hyper-hormonal level brought about by the hyperfunction of the hypothalamic-pituitary-adrenal cortex axis (HPA) [9] is also a possible inducing mechanism. Changes in the excitability of the sympathetic and parasympathetic nerves can easily lead to autonomic nerve dysfunction, thereby indirectly causing mental and psychological disorders.

3. Traditional Chinese Medicine's Understanding of Heart Failure Combined with Depression Syndrome

3.1 The Understanding of Heart Failure in Traditional Chinese Medicine

In traditional Chinese medicine, there is no specific term for heart failure. According to traditional Chinese theory, heart failure can be classified into a series of diseases such as "palpitation", "edema", "asthenia syndrome", "heart water", etc., and can also be classified as critical conditions such as "decompensation syndrome" and "death syndrome". The syndrome types of this disease have been elaborated in the "Neijing". The "Bie Lun" chapter of "Shangqing" records: "All five zang-fu organs have their respective combinations. If the disease persists and does not subside, it is attributed to the combination of the internal organs... If the pulse disorder

does not subside and is further affected by external pathogenic factors, it will be attributed to the heart... If the heart is diseased, the pulse will not be smooth, and the heart area will bulge suddenly, and there will be sudden shortness of breath and panting.” The “Jin Kui Yao Lue” states: “When water flows widely, it accumulates in the limbs... Coughing and shortness of breath, shortness of breath and inability to sleep, the appearance is like swelling... When water is in the heart, the heart area becomes firm and solid, shortness of breath, aversion to water, and unwillingness to drink... If a patient drinks a lot, they will suddenly have shortness of breath and fullness. When food intake is small and water intake is large, water accumulates in the heart area, and in severe cases, there will be palpitations, and in mild cases, there will be shortness of breath.” Song Zhaoji [10] claimed in “Shengji Zonglu” that “heart failure leads to forgetfulness” and first proposed the term “heart failure”. Professor Tang Fenying [11] proposed that chronic heart failure is related to pathological factors such as insufficient heart qi, insufficient heart yang, liver and kidney yin deficiency, and blood stasis and water retention. When heart yang qi is insufficient, its promoting effect will weaken, thereby causing blood to not run normally, and resulting in blood stasis. Zhang Gensheng [12] proposed that the etiology and pathogenesis of this disease is a mixture of deficiency and excess, with “deficiency” mainly being “heart-kidney yang deficiency” and “excess” mainly being “blood stasis” and “phlegm turbidity”. Cheng Xiaoyu et al. [13] proposed that the pathogenesis of this disease belongs to a mixture of deficiency and excess, with “excess” including cold congealing, qi stagnation, blood stasis, phlegm turbidity, etc., blocking the chest yang and heart meridians; “deficiency” is mostly due to insufficient heart, liver, spleen, and kidney, resulting in the failure of yang qi to extend and the loss of nourishment of the heart meridians.

Lei Zhongyi, a master of traditional Chinese medicine, believes that the most fundamental pathological change in heart failure is the deficiency of heart qi and heart yang. The deficiency of yang and the accumulation of water are the fundamental pathogenesis [14]. At the same time, Master Lei advocated that “phlegm and stasis” play a very crucial role in the pathogenesis of heart diseases. When qi is deficient and yang is weak, blood stasis and water retention are the basic pathogenesis of heart failure. Water pathogen can arise from the deficiency of heart yang qi, or from stasis. Its location is in the heart, and it is closely related to the lungs, spleen, liver, and kidneys. It is a syndrome of underlying deficiency and superficial excess. The underlying deficiency is the insufficiency of heart yang qi, and the superficial excess is blood stasis and water retention [15]. Thus, the occurrence of heart failure is caused by dysfunction of the five internal organs, external pathogenic factors, excessive fatigue, and emotional distress. The pathogenesis is characterized by deficiency of qi (yang) as the foundation and blood stasis and water retention as the manifestation.

3.2 The Understanding of Depression in Traditional Chinese Medicine

In traditional Chinese medicine, “depression” is classified under the category of emotional disorders. It is related to conditions such as “yuyi”, “zangcha”, “bulian disease”, and “binxiao” in traditional Chinese medicine. The research on

“yuyi” in traditional Chinese medicine has a long history, with numerous negative emotions such as “sadness”, “unhappiness”, and “worry” recorded in “The Yellow Emperor’s Inner Classic”. These are in line with modern mood depression. Moreover, emotional blockage is regarded as one of the main causes of “yuyi”. In “The Jingui Yaolue”, it is stated: “When one is happy, sad, or wants to cry, it resembles something created by a deity. One often stretches out their limbs repeatedly.” It also proposed two diseases: “zangcha” and “meikong qi”, and specially prescribed Ganmai Dazao Decoction and Banxia Houpu Decoction to treat these two diseases. “The Danxi Heart Method” established special treatment formulas such as “six depression decoction” and “Yuji Pill” based on the theory of six syndromes of qi, blood, fire, food, dampness, and phlegm, specifically creating formulas to treat depression. Ancient and modern physicians generally believe that stagnation of qi movement is the basic pathogenesis of this disease. The treatment mainly focuses on regulating qi and relieving depression in combination with psychological counseling. Gong Tingxian [16] believes that the mechanism of depression is the obstruction of qi movement, and qi stagnation is the source of all depression. Imbalance of emotions can cause poor blood circulation and dysfunction of the internal organs. Master Zhang Zhenguo, a renowned doctor [17], advocated the academic thought of “one body with two wings, regulating qi movement”, emphasizing promoting the rise and fall of qi through regulating the liver to facilitate smooth qi movement and using the spleen and kidney as the two wings to fundamentally unify the innate and acquired aspects. Thus, ensuring the smooth circulation of qi throughout the body to achieve emotional stability and sleep. Zhu Zhusheng [18] believes that qi stagnation is considered the basic pathological change of this disease. As the disease progresses, the syndrome gradually transforms from a real condition to a virtual condition, leading to deficiency of qi, blood, yin, and essence in the spleen, heart, liver, etc., resulting in a syndrome characterized by predominance of virtual conditions. In summary, the main pathogenesis of depression (yuyi) is emotional injury and qi stagnation, related to abnormal circulation of qi, blood, and body fluids, involving the functions of the five internal organs.

3.3 The Understanding of the Relationship Between Heart Failure and Depression in Traditional Chinese Medicine

According to traditional Chinese medicine theory, the causes of the dual-heart disease, such as chronic heart failure combined with depression, are complex and diverse. They mainly include factors like weak congenital constitution, seasonal changes, emotional fluctuations, and excessive fatigue. These factors do not exist independently but often interact with each other and influence one another, thereby causing the disease to worsen continuously. The “Huangdi Neijing” states: “The heart governs blood circulation and the spirit. The heart is the emotion of joy.” Therefore, it can be seen that the heart not only provides nutrients to the entire body through blood flow but also coordinates the physiological activities of various organs through people’s mental activities. The “Linghu Xi” says: “When one is sad, worried, or fearful, the heart beats, and the beating of the heart causes all the internal organs to shake.” The “Linghu Xi · Xieqi Hangfu Bingxing” states: “When one is sad, fearful,

or anxious, it harms the heart.” This further explains this point. Therefore, a good mental state is one of the necessary conditions for the normal physiological activities of all organs.

4. Treatment

4.1 Modern Medicine's Treatment of Biphasic Disorders

At present, for patients with CHF accompanied by anxiety and depression, heart failure treatment usually takes the dominant position. For anxiety and depression, there are both drug and non-drug treatments. The first-line treatment drugs are mainly selective serotonin reuptake inhibitors (SSRIs, such as sertraline, escitalopram), but they have no significant effect on the incidence of cardiovascular events and mortality [19-20]. Flupentixol-melitracen is a compound preparation of thioxanthine and tricyclic drugs, suitable for patients with mild to moderate anxiety and depression, and can improve clinical prognosis and quality of life. Benzodiazepine drugs (BDZ) are mainly used to relieve acute anxiety and insomnia, and there is evidence suggesting that proper use may reduce all-cause mortality and the risk of rehospitalization for heart failure [20]. Traditional tricyclic drugs are generally not used in patients with organic heart diseases due to cardiovascular side effects (QT interval prolongation, orthostatic hypotension). According to literature reports, the adverse reactions of antidepressants to the cardiovascular system mainly include changes in blood pressure, weight gain, metabolic disorders, ventricular arrhythmias and sudden cardiac death [21], all of which are related to the poor prognosis of CHF. At the same time, study [22] indicates that patients with heart failure who take antidepressants have an increased risk of all-cause death and cardiovascular death.

In terms of non-drug treatments, common methods include exercise rehabilitation, psychological intervention, and cognitive behavioral therapy (CBT). Studies have shown that cardiac rehabilitation can reduce the readmission rate of patients with CHF by more than 30% [23-24]. Psychological intervention can effectively improve the anxiety and depression of patients with chronic heart failure and alleviate their clinical symptoms [25]. CBT, as a practical form of psychological treatment, is recommended by domestic and international guidelines as a first-line treatment method [26-27]. These therapies can stimulate patients' ability to concentrate, thereby enhancing their control over their own emotions. At the same time, they can effectively improve their thinking ability and stress coping ability, thereby reducing the degree of emotional tension and depression faced by patients with cardiovascular diseases, and ultimately improving their overall quality of life.

4.2 The Treatment of Dual-cardiac Diseases in Traditional Chinese Medicine

4.2.1 Traditional Chinese medicine syndrome-based treatment

Research on the treatment of heart failure combined with anxiety and depression (dual heart disease) using traditional Chinese medicine has also been increasing. However, most scholars have used self-designed formulas for intervention.

For instance, Gu Yanfen et al [28]. found that the Yixin Jiuyu Decoction (*Salvia miltiorrhiza*, *Ligusticum chuanxiong*, *Pueraria lobata*, Xie Bai, Xiangjiang, Pearl Mother, *Rehmannia glutinosa*, *Farfarae Semen*, *Prunella vulgaris*, *Ginkgo biloba*, *Prunella vulgaris*, Yulan, Jujube, *Platycodon grandiflorum*, *Zingiber officinale*, *Cinnamomum cassia*, *Paeonia lactiflora*, Safflower, *Glycyrrhiza uralensis*) could increase the level of brain-derived neurotrophic factor (BDNF) and improve the left ventricular systolic function of patients. Sun Shuyun [29] treated patients with heart failure with preserved ejection fraction and anxiety on the basis of conventional Western medicine treatment with the Jiaoyin Yangxin Decoction (*Astragalus membranaceus*, Ginseng, *Chuanxiong*, Peony, *Poria cocos*, *Atractylodes macrocephala*, Chaihu, Danshen, Fried jujube kernels, Wuwei, *Schisandra chinensis*, Radix et Semen *Platycodi*, *Zingiber officinale*, *Platycodon grandiflorum*, *Zingiber officinale*, *Platycodon grandiflorum*, Red flower, *Glycyrrhiza uralensis*), and found that it could significantly improve clinical symptoms and TCM syndrome scores, relieve anxiety, and had good safety. Its mechanism of action may be related to the improvement of left ventricular diastolic function. Sun Youpeng et al. [30] treated patients with chronic heart failure and depression with the Kanyixiaoyao Decoction (Ginseng, Danggui, Bai Zhu, Fuling, Chaihu, Bai shao, *Chuanxiong*, Taohua, Huanglian, *Rehmannia glutinosa*, Shexiangpi, Yanzhi, Baihe, Huaer, Licorice) combined with Eszopiclone Oxalate Tablets. In addition to improving the patient's cardiac function and reducing the depression score, it could also reduce the levels of inflammatory factors such as hs-CRP, IL-6, and TNF- α . The Kanyi Huoxue Decoction is an experience formula for treating coronary heart disease summarized by the renowned TCM master Lei Zhongyi for many years. Animal experiments have shown that the Kanyi Huoxue Decoction has a myocardial protective effect and can regulate the levels of atrial natriuretic peptide, aldosterone, angiotensin II, and brain natriuretic peptide in the serum of heart failure model rats, thereby improving heart failure [31-32]. Clinical studies have found that the Kanyi Huoxue Decoction can effectively improve the quality of daily life of elderly patients with heart failure [33].

According to a meta-analysis [34], it was shown that the combined intervention of traditional Chinese medicine and anti-anxiety and anti-depression drugs could further improve the clinical symptom improvement rate, LVEF, NT-proBNP level, and reduce the HAMA score, HAMD score, and SDS score of patients with CHF and anxiety and depression. Moreover, the adverse reaction rate of the combined treatment with Chinese and Western medicines was lower than that of the group using Western medicine alone. And a study [35] indicated that adding traditional Chinese medicine to the conventional Western medicine group could reduce the adverse reactions caused by conventional anti-anxiety and anti-depression drugs. A related meta-analysis [36] showed that the combination of traditional Chinese medicine and conventional treatment could increase the effective rate of cardiac function and LVEF score, and reduce the HAMD and MLHFQ scale scores. It is a potential treatment strategy for improving the management of patients with CHF and depression. Given that the pathogenesis of heart failure and depression is similar, there is a broad research prospect for

traditional Chinese medicine in this field.

4.2.2 acupuncture therapy

Acupuncture therapy has been widely used in the treatment of bipolar disorders. Studies have shown [37] that acupuncture is a safe and effective treatment for CHF accompanied by anxiety and depression. Acupuncture can play a positive role in regulating the HPA axis, promoting the release of monoamine substances such as 5-HT and norepinephrine (NE), promoting the secretion of anti-inflammatory cytokines, protecting vascular endothelium, regulating autonomic nerve function, and improving sleep [38].

4.2.3 massage treatment

Acupoint massage is also commonly used in clinical practice. Massage can regulate the qi and blood of the internal organs, balance the yin and yang, and unblock the meridians. It can alleviate the physical symptoms of patients, improve their negative psychological states, and enhance their quality of life. Studies have found that applying massage stimulation to acupoints such as Baihui, Yinqiao, Yangshu, and Hegu, combined with the five-tone therapy, can effectively alleviate patients' anxiety, promote the recovery of their cardiac function, and improve the prognosis [39].

4.2.4 Acupoint application (ear points)

Ear acupressure beads are a simple, safe and effective traditional Chinese medicine therapy. When used alone or in combination with traditional Chinese medicine for the treatment of cardiovascular diseases, they can alleviate symptoms such as chest tightness and chest pain, and effectively improve the anxiety and depression of patients with coronary heart disease and heart failure [40].

4.2.5 Guidance and Five-Note Therapy

Years of clinical practice have proved that traditional Chinese health care therapies such as Baduanjin, Wuzhenyu, Tai Chi, the Twelve Exercises of Guidance, and the Five-Note Therapy can significantly improve patients' anxiety and depression, further alleviate their clinical symptoms, and thereby enhance their quality of life [41-43]. This provides doctors with another option to assist in treatment.

5. Discussion

Although there is still controversy regarding the long-term prognosis of CHF combined with anxiety and depression when treated with antidepressant drugs by modern medicine, its efficacy in alleviating patients' mood and improving somatic symptoms is definite. Both traditional Chinese medicine and Western medicine have their own advantages, and by complementing each other's strengths, they can make synergistic contributions in improving and stabilizing CHF combined with anxiety and depression. Currently, the research on the combination of traditional Chinese and Western medicine for CHF combined with anxiety and depression is in the development stage. There are more studies on the combined treatment of CHF and "manic depression" in both traditional Chinese and Western medicine, but there are

relatively fewer studies on the combined treatment of CHF combined with anxiety and depression. This lack of a unified understanding of the etiology and pathogenesis and the guidance of treatment methods and prescriptions, as well as the lack of statistical research on the syndrome types with sufficient sample sizes, and the clinical research on specific acupoints for syndrome selection based on traditional Chinese medicine characteristics, such as acupuncture, massage, and auricular point pressing pills, need to be further expanded and extended. Thus, it can be seen that the treatment of CHF combined with anxiety and depression with traditional Chinese medicine has a large research space and development potential. And we have reason to believe that the combined treatment of CHF combined with anxiety and depression with traditional Chinese and Western medicine will help to form a more standardized diagnosis and treatment system and more reasonable evaluation criteria for efficacy.

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