

Research Progress of Integrated Chinese and Western Medicine in Chronic Heart Failure

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Abstract: *Chronic heart failure (CHF), as a complex syndrome caused by impaired myocardial structure and function resulting in decreased cardiac function, is a common manifestation of various heart diseases at their advanced stages. Its incidence has significantly increased with the aging of our population, and the annual mortality rate is as high as 40%. Although modern medicine has continuously made progress in exploring the pathogenesis of CHF and optimizing treatment plans, its incidence and mortality rate remain high. Moreover, the efficacy of conventional Western medicine treatment is limited and the targets are single, and long-term application may lead to drug resistance. In recent years, the application of traditional Chinese medicine in the clinical treatment of heart failure has become increasingly common. Based on modern pharmacological research, traditional Chinese medicine has the effects of increasing patients' exercise tolerance, improving cardiac function, diuresis, dilating blood vessels, regulating neuroendocrine function, inhibiting inflammatory cytokines, etc. Therefore, this article aims to comprehensively elaborate on the main treatment methods of both for heart failure, in order to provide evidence support for clinical researchers to conduct more in-depth studies on heart failure in the future.*

Keywords: Chronic heart failure, Research progress, Integrated Chinese and Western medicine.

1. Introduction

Chronic heart failure is a clinical syndrome caused by various etiological factors that lead to abnormal cardiac structure and/or function, resulting in dysfunction of ventricular contraction and/or relaxation. Its characteristic manifestations include dyspnea, fatigue, and fluid retention (such as pulmonary congestion, systemic congestion, and peripheral edema) [1]. Professional studies have shown that the incidence of cardiovascular diseases (CVD) in China is showing a continuous upward trend. It is estimated that the current number of patients with cardiovascular diseases in China is approximately 330 million, among which the number of patients with heart failure is as high as 8.9 million [2]. With the continuous advancement of medical technology and the deepening of clinical practice, the concept of integrated treatment of CHF by traditional Chinese and Western medicine has gradually gained wide recognition. Traditional Chinese medicine emphasizes the holistic concept and syndrome differentiation and treatment, aiming to improve the condition by balancing the body's yin and yang and regulating the functions of the internal organs; while Western medicine focuses on treating the causes, alleviating symptoms, and maintaining and supporting organ functions. The combination of the two can not only intervene in the essence of the disease but also relieve the clinical symptoms of patients, thereby improving the treatment effect and quality of life.

2. Modern Medical Understanding of Heart Failure

2.1 Etiology of Heart Failure

Heart failure is a series of clinical symptoms caused by the heart's inability to pump blood effectively. The causes are diverse and usually result from specific factors affecting the heart, such as congenital heart disease, different types of cardiomyopathy, myocarditis or cardiac toxicity. In contrast,

the mechanism of heart failure development in the elderly is not yet fully determined. In elderly patients, specific risk factors such as smoking, coronary heart disease, hypertension, diabetes, hyperlipidemia, coronary artery disease, obesity, etc. ... Any cause of myocardial damage will lead to heart failure and accelerate cardiovascular aging, having a significant impact on the heart [3].

2.2 Pathogenesis of Heart Failure

The pathophysiological process of heart failure is extremely complex, and modern medicine's understanding of it has always been in a state of continuous development and deepening. The basic mechanism of the occurrence and development of heart failure is myocardial remodeling [4].

This includes excessive activation of the sympathetic nervous system and the RAAS system, as well as abnormal immune regulation, inflammatory response, mitochondrial dysfunction, and oxidative stress [5]. The pathophysiological mechanism of heart failure is closely related to the excessive activation of the neuroendocrine system, mainly manifested as hyperactivity of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS), which subsequently leads to abnormal release of various bioactive substances, jointly causing myocardial tissue damage. As the myocardial damage continues to progress, the abnormalities in cardiac structure and function gradually worsen, and further stimulate the activation of the neuroendocrine system, ultimately forming a positive feedback loop that promotes the progression of heart failure [6]. RAAS plays a key role in regulating cardiovascular homeostasis, mainly mediated by angiotensin I, angiotensin-converting enzyme, and angiotensin II. Chronic activation of the sympathetic nervous system is the key initiating factor for RAAS activation, and in heart failure, the reduction of cardiac output reflexively activates RAAS, thereby mediating the side effects of angiotensin II. Angiotensin II binds to receptors, causing an increase in aldosterone secretion, leading to cell apoptosis and

interstitial fibrosis, promoting ventricular remodeling, and thereby accelerating the development of HF [7]. When RAAS is overactivated, the levels of renin and angiotensin II increase sharply, and subsequently stimulate the massive production of pro-inflammatory cytokines. The excessive expression of these pro-inflammatory cytokines can trigger a series of pathological changes such as left ventricular dysfunction, ventricular remodeling, and myocardial cell necrosis, further accelerating the deterioration process of heart failure. Pro-inflammatory factors such as interleukin-1 β , interleukin-6, and tumor necrosis factor- α play a key role in this process. The integrity of the mitochondrial membrane structure is crucial for maintaining normal energy metabolism. Damage to the mitochondrial membrane by oxygen free radicals significantly increases its permeability, disrupts mitochondrial membrane potential, and leads to ion imbalance. As the damage intensifies, mitochondria swell, their internal structure is destroyed, and even rupture occurs. If mitochondrial function is severely damaged, cells will be unable to obtain sufficient energy supply, thereby activating the apoptotic signaling pathway within the cell, ultimately causing cell death. Long-term myocardial cell death stimulates the activation and proliferation of fibroblasts, leading to excessive deposition of extracellular matrix components such as collagen, and thereby causing myocardial fibrosis and its development, further damaging the normal structure and function of the heart [8].

2.3 Pharmacological Treatment of Heart Failure

Currently, the latest guidelines for heart failure [9] emphasize that the "new quadruple" composed of ARNI/ACEI/ARB, SGLT2i, BB, and MRA drugs holds a cornerstone position in the treatment of HFrEF, and recommend adding the soluble guanylate cyclase receptor agonist vildagliptin as soon as possible on top of standard basic treatment. ARNI has the dual effects of ARB and neprilysin inhibitor, which can inhibit the activation of RAAS, inhibit ventricular remodeling, improve cardiac function, and reduce the risk of hospitalization due to heart failure and cardiovascular mortality. Its representative drug is sacubitril/valsartan. The 2021 US guidelines [10] first listed SGLT2i as the first-line medication for HFrEF treatment, and the new Chinese guidelines [11] recommend using SGLT2i for the treatment of HFrEF, HFmrEF (heart failure with reduced ejection fraction), and HFpEF patients, both as I, A recommendations, indicating that SGLT2i is applicable to all patients with heart failure like ARNI. Beta-blockers are represented by metoprolol and bisoprolol, and their mechanism of action is to block beta-adrenergic receptors, effectively inhibiting excessive activation of the sympathetic nervous system. The birth of vildagliptin is based on another pathway of cGMP, the NO-soluble guanylate cyclase (sGC)-cGMP pathway. Endothelial cells produce endogenous NO, which, after binding with sGC, can promote the generation of cGMP, subsequently activating PKG, phosphodiesterase inhibitors, and cyclic nucleotide gated ion channels, resulting in vasodilation, anti-inflammatory, increasing coronary and renal blood flow, inhibiting platelet aggregation, anti-vascular and cardiac remodeling, anti-fibrosis, and improving ventricular diastolic function [12]. Currently, the guidelines [13] recommend ivalopril for use in chronic heart failure patients who have used standard treatment but still have a resting heart rate of ≥ 70 beats per

minute or who cannot tolerate BB for various reasons.

3. TCM Understanding of Heart Failure

3.1 Etiology and Pathogenesis

The "Pulse Classic" records that "when the heart is weakened, it becomes dormant", and the "Holy Prescriptions for All Diseases" mentions that "when the heart is weakened, one becomes forgetful". However, this "heart weakness" is not a medical term or a modern medical explanation of heart failure. Both of their pathogenesis are the weakening of the heart function and the inability of qi and blood to circulate properly, resulting in clinical symptoms in traditional Chinese medicine. The symptoms described in ancient Chinese medical texts such as "heart water", "heart cough", "heart distension", "heart syndrome", "phlegm fluid", "edema", and "asthenic syndrome" are very similar to the clinical manifestations of heart failure. Zhang Zhongjing's "Essential Prescriptions from the Golden Chamber: Water-Related Diseases and Their Treatment" first proposed the term "heart water", which is considered to be the closest description to the clinical manifestations of heart failure. Its location is in the heart, and the pathogenesis is water retention, which is quite similar to the description of "congestive heart failure" in Western medicine [14]. In 1997, China published the "Clinical Diagnosis and Treatment Terminology of Traditional Chinese Medicine", which designated "heart failure" as the standard disease name. In 2012, in the "Twelfth Five-Year Plan" textbook "Internal Medicine of Traditional Chinese Medicine", "heart failure" was first mentioned as a disease. However, due to lacking the characteristics of traditional Chinese medicine, it is still referred to as "heart water" in clinical practice to this day.

The causes of heart failure are complex and mainly include exposure to external pathogenic factors, improper diet, emotional imbalance, internal injury from overwork, failure to properly treat the condition, and other factors. There are 7 main aspects: [15] Chen Xinyu believes that the key pathogenesis of heart failure lies in insufficient yang and excessive yin, with yin deficiency (including phlegm, water, and blood stasis) being the important factors for its development. Yang deficiency is the fundamental pathological factor throughout the course of heart failure, and it is mainly characterized by heart-kidney yang deficiency. It emphasizes the positive role of tonifying yang in the treatment of heart failure. [16] Hu Fang et al. believe that yang deficiency is the continuous pathological factor throughout heart failure, which is the fundamental cause of its occurrence and development. The yang deficiency is mainly characterized by heart-kidney yang deficiency, and they also emphasize the positive role of tonifying yang in the treatment of heart failure. [17] Dong Xiao et al. classified the causes of heart failure according to traditional medicine into diseases of the heart itself and diseases of other organs. The diseases of the heart itself mainly include constitution deficiency, invasion by six external pathogenic factors, internal emotional stress, improper diet, inappropriate medication, excessive work and rest, and depletion of qi, blood, and body fluids due to pregnancy and childbirth in women. Diseases of other organs are caused by long-term ineffective treatment of heart-pulmonary diseases, resulting in yin deficiency and

exhaustion, leading to the heart losing its nourishment and developing into heart failure. This is largely consistent with the causes of heart failure discussed in contemporary medicine.

4. TCM Treatment of Chronic Heart Failure

4.1 Internal TCM Therapy

Deficiency of qi and stasis of blood are the fundamental pathogenesis of chronic heart failure. In clinical practice, formulas that tonify qi and activate blood circulation are commonly used for treatment, such as the "Supplementing Yang and Restoring Five Viscera Decoction" where Astragalus is an essential qi-tonifying herb, allowing qi to be strengthened and blood to flow; Angelica sinensis tail tonifies blood and resolves stasis without harming the body's normal functions; Ligusticum chuanxiong, Red Peony Root, Peach Kernel, and Red Flower all activate blood circulation and resolve stasis without harming the body's normal functions; Earthworm helps to unblock meridians and relieve arthralgia. The "Bao Yuan Decoction" contains Ginseng, Astragalus, and Licorice to tonify the middle qi and restore the functions of the spleen and stomach, and is combined with Cinnamon to warm and nourish the lower jiao. The first choice of prescription for Yang deficiency and water retention is the "Zhen Wu Decoction", where Cinnamomum is the sovereign herb. It is used to warm the kidney and assist yang, to transform qi and promote water metabolism, and also to warm the spleen soil to promote the movement of water and dampness; Poria cocos promotes water metabolism and diuresis; Atractylodes macrocephala tonifies the spleen and dries dampness; Ginger not only helps Cinnamomum warm yang and dispel cold, but also combines with Poria cocos and Atractylodes to disperse water dampness; White Peony can promote urination to promote qi flow and can soften the liver and relieve urgency to stop pain. The sovereign herb of Liang Gui Zhu Gan Decoction, Poria cocos, has the function of tonifying the spleen and promoting diuresis and diuresis. Cinnamon twig warms yang and transforms qi, Atractylodes dries dampness and tonifies the spleen, and roasted Licorice harmonizes all the herbs. When these four herbs are combined, the middle qi becomes healthy, phlegm and water metabolism are transformed, and the body's fluids are distributed properly.

In the treatment of chronic heart failure, commonly used traditional Chinese medicine decoctions include Zhennwu Decoction, Wulinqi Powder, and Tuling Dazha Xialong Decoction, etc. These prescriptions can effectively alleviate the symptoms and improve the quality of life of patients with heart failure. Modern physicians have also demonstrated significant efficacy in treating heart failure with traditional formulas. Many renowned physicians have achieved remarkable results by formulating their own prescriptions based on their clinical experience. Wu Peiheng, as a representative physician of the Yang-preserving school, created the Daohuang Yangfu Decoction, which embodies the core treatment principle of "warming the yang and consolidating the foundation". This formula has shown good efficacy in the clinical treatment of CHF and has been applied in clinical practice by many physicians [18]. The "Shanghan Lun" records: "In case of feverish illness, with a thready and intermittent pulse, palpitations and restlessness, It is treated

with Zhi Gan Cao Decoction." The Zhi Gan Cao Decoction has the effects of invigorating qi and nourishing yin, and promoting yang and restoring pulse. This formula is a classic prescription for treating qi and yin deficiency syndromes. For patients with chronic heart failure, commonly used Chinese patent medicines include Qili Jiangxin Capsules, Shensong Yangxin Capsules, and Wenxin Granules. The pharmacological effects of Qili Jiangxin Capsules are systematic and complex. It not only enhances myocardial contractility and promotes urination, but also inhibits excessive activation of neuroendocrine systems and blocks the process of ventricular remodeling through multiple pathways, achieving multi-targeted coordinated treatment [19]. Shensong Yangxin Capsules can regulate the balance of the autonomic nervous system, optimize myocardial energy metabolism, and enhance myocardial contractility, thereby reducing the occurrence of malignant arrhythmias in patients with heart failure. Traditional Chinese medicine injection preparations directly inject the extracted components of traditional Chinese medicine into the body, featuring rapid onset and strong effect. During the acute exacerbation period of chronic heart failure, the use of traditional Chinese medicine injection preparations can quickly relieve symptoms and stabilize the condition. For example, Shentie Injection, Shuimai Injection, and Xinpianlong Injection, etc. These drugs can enhance myocardial contractility, improve cardiac pumping function, and reduce mortality rates.

4.2 External TCM Therapy

Acupuncture, by harmonizing the internal organs, unblocking the meridians, and combining with acupoint stimulation, can improve myocardial contraction and hemodynamic after ischemia, regulate the sympathetic nerve activity of the heart, alleviate myocardial ischemia, and promote myocardial remodeling. Moxibustion, through warm stimulation of specific acupoints on the body, activates the circulation of meridians and qi, regulates disordered physiological functions, and restores the body's balance. Chinese herbal acupoint application by applying the medicine to specific acupoints achieves therapeutic effects such as unblocking meridians, eliminating stasis, and harmonizing qi and blood, ultimately achieving the goal of improving clinical symptoms of CHF. Tai Chi can improve cardiac function, enhance myocardial contractility, and reduce myocardial oxygen consumption. Ba Duan Jin can promote the recovery of cardiac function in patients with chronic heart failure of coronary heart disease and enhance their exercise tolerance [20]. Auricular acupuncture therapy stimulates specific acupoints on the ear, corresponding to regulating the functions of the internal organs of the human body, achieving the effect of treating diseases, as it is inexpensive, safe, and easy to operate and is widely used.

5. Conclusion

The treatment paths for heart failure in Western medicine and Chinese medicine are distinct yet naturally complementary. Western medicine focuses on precisely targeting and blocking excessive activation of neuroendocrine systems, dominating in reversing remodeling and prolonging survival; while

Chinese medicine adopts an overall perspective to coordinate qi, blood, and yin-yang, offering unique advantages in alleviating shortness of breath and edema, improving exercise tolerance and quality of life, with fewer adverse drug effects. The combination of the two is not a simple addition but should be a deep integration in a phased and sequential manner within the framework of disease and syndrome correlation: in the acute decompensation stage, Western medicine takes the lead, supplemented by traditional Chinese medicine injections to stabilize hemodynamics; in the chronic stable stage, traditional Chinese medicine with functions of tonifying qi and warming yang, promoting blood circulation and eliminating water, plays a systemic regulatory role, which can enhance the tolerance to Western medicine, reduce resistance to diuretics and electrolyte disorders, and directly target residual symptoms and the root causes of qi deficiency and blood stasis.

First, the diagnosis and differentiation of traditional Chinese medicine faces an objective bottleneck and urgently needs to utilize metabolomics and proteomics to construct a spectrum of biomarkers related to syndromes, achieving "precise differentiation of syndromes" and enabling the selection of treatment methods and prescriptions to be based on evidence. Secondly, although studies such as QUEST have achieved methodological breakthroughs, more large-scale confirmatory trials with hard endpoints are still needed, and network pharmacology and multi-omics technologies should be utilized to deeply analyze the multi-component synergistic target network of compound formulations. Moreover, the digitalized collection and decision-making system assisted by artificial intelligence for the "four diagnostic methods" is expected to provide intelligent support for individualized treatment plans in the integration of traditional and Western medicine. In the future, a better direction is to promote the deep integration of traditional and Western medicine. Through rigorous research, it is necessary to clarify the optimal timing and method of the integration of traditional and Western medicine. Through strengthening research, optimizing treatment plans, promoting the integration of traditional and Western medicine and internationalization development, it is expected to provide more comprehensive and efficient treatment options for patients with CHF.

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