

# Research progress of traditional Chinese and western medicine on myocardial dysfunction in sepsis

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**Abstract:** Sepsis is a dangerous disease with high mortality, which brings a huge economic burden to patients and society and has attracted more and more attention from the society. Sepsis is a systemic infectious disease. The dysregulated host immune response caused by infection is easy to cause multiple organ damage, and the heart is one of the most vulnerable organs, which leads to septic myocardial dysfunction. Therefore, the treatment of sepsis-induced myocardial dysfunction is a difficult and important point. In recent years, traditional Chinese medicine has shown great advantages in the treatment of this disease. Through the combination of disease differentiation and syndrome differentiation, the overall treatment rate can be significantly improved. Therefore, it is a bright prospect for the treatment of sepsis myocardial dysfunction with integrated traditional Chinese and western medicine. In recent years, the combination of traditional Chinese medicine and western medicine has made some progress in the treatment of sepsis, which has significantly reduced the mortality of sepsis.

**Keywords:** Integrated traditional Chinese and Western medicine; Sepsis; Myocardial dysfunction; Research progress

## 1. Introduction

Sepsis is a life-threatening organ dysfunction caused by infection. Sepsis can be diagnosed when there is infection in the body and the systemic sepsis related organ failure assessment (SOFA) score is  $\geq 2$  [1]. According to the latest epidemiological study of sepsis ICU in China, the 90-day mortality rate of sepsis ICU is 35.5%, which puts a huge burden on people [2]. The heart is one of the most vulnerable organs. According to clinical studies, about 50% of patients with sepsis will have varying degrees of myocardial dysfunction. Sepsis-induced myocardial dysfunction (SIMD) is a global but reversible biventricular dysfunction, and the mortality rate can be as high as 80% [2]. Therefore, it is of great significance to study myocardial dysfunction in sepsis. In the past, a large number of western medicine treatments were focused on myocardial dysfunction in sepsis. In recent years, traditional Chinese medicine treatment has its unique advantages and made certain progress. This article reviews the research progress of myocardial dysfunction in sepsis in recent years, in order to provide theoretical basis for clinical diagnosis and treatment.

## 2. Modern medical understanding of sepsis-induced myocardial dysfunction

Studies have shown that the plasma levels of troponin I and troponin T are increased in sepsis patients, which may be related to left ventricular systolic dysfunction and myocardial injury. The mechanism may be reversible myocardial membrane leakage or cytokine-mediated apoptosis. The latest clinical studies have found that serum BNP in patients with sepsis is significantly increased, and is positively correlated with the severity of the disease, which has a good predictive value for the prognosis of patients with sepsis [3]. The pathogenesis of sepsis is complex and diverse. At present, myocardial inhibitory factors have been identified (Figure 1), including cytokines, oxidative stress, changes in nitric oxide metabolism, myocardial cell apoptosis, and mitochondrial dysfunction [4].

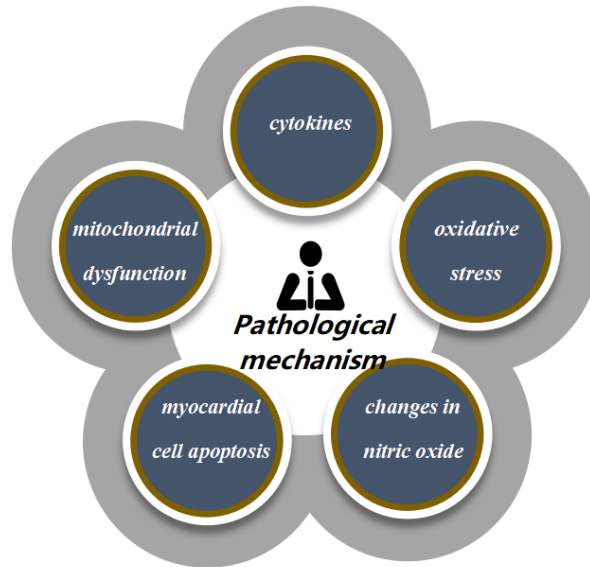


Figure 1: Pathological mechanism

### 3. Traditional Chinese medicine understanding of myocardial dysfunction in sepsis

There is no corresponding record of myocardial dysfunction in traditional Chinese medicine. According to the typical clinical manifestations and characteristics of sepsis, it can be classified into the categories of "chest obstruction", "edema", "syncope syndrome", and "desyndrome". As Yi Fa Yintong (Yintong) puts it: "Who is Yang syncope? Since the zhengqi has been deficient, Yin and cold everywhere, Yin and Yang are slightly, the meridians are blocked, and Yang qi cannot reach the limbs, so the limbs are cold, and the person's eyes are drowsiness and sleeping, less qi and lazy speech. . . ."; Modern doctors have made some progress in the study of sepsis. Professor Liu Qingquan, based on years of experience in the diagnosis and treatment of sepsis, combined with the six meridians and the dialectics method of defending qi, nutrition and blood, believes that the main cause of sepsis is "heat toxin", heat is Yang factor, easily damage body fluid, over time damage body fluid consumption, condensation to phlegm, due to toxicity, stasis and internal obstruction, phlegm and blood consumption injury affects the rise and decline of body qi, and finally consumes qi and blood. The decline of Yang qi forms the syndrome of deficiency of the essence and excess of the standard. Qi and blood failure of Zangfu organs is the intrinsic root cause, and the excessive heat and poison in the body is the main pathological factor. Professor Wang Jinda summarized sepsis as the result of the invasion of pathogenic toxin or various trauma, which leads to the conflict between pathogenic toxin and normal qi, the loss of damage caused by pathogenic toxin, the block of pathogenic toxin, and the formation of the situation of deficiency of positive toxin and excess of negative toxin. Zhang Yunsong pointed out that the basic pathogenesis of sepsis is the interaction of poison, stasis and deficiency, the internal accumulation of blood stasis and the internal accumulation of warm poison, which consumes the vital qi of the human body, and the deficiency of the vital qi cannot run, which in turn consumes the vital qi of the human body, forming a vicious cycle. Therefore, the loss of vital qi is the root cause, and then a variety of solid pathogens are generated and block the body. The concept of wholeness is the essence of traditional medicine in the treatment of diseases. The human body itself is an independent world. The internal viscera, qi and blood, meridians, external and limb skeleton can all affect each other, and the damage of each viscera can affect the heart. The heart contains the spirit, governs the spirit, is the official of the sovereign, is the major master of the five zangfu, and is the master of the life activities of the human body. Just as the "Inner Diameter" contains: "The heart is the master of the five zangfu", "the heart is the official of the sovereign, and the spirit is out of the Yan". In this connection, Huang Danhong proposed the research theory of "heart disease and four zang organs" and "diseases of the four zang organs and heart disease" [5].

### 4. Research on the dialectical classification of myocardial dysfunction in sepsis by TCM

In 1989, after years of experimental research and clinical verification, Professor Wang Jinda's team

established a new theoretical system of "combined treatment of bacteria and toxin" to treat this disease. In addition, the multiple organ dysfunction syndrome appeared in the process of the occurrence and development of this disease was standardized, and the corresponding TCM syndrome differentiation classification and treatment principles and methods were improved, and the "four syndromes and four methods" was gradually formed. The principle of syndrome differentiation and treatment of "four syndromes and four methods" aims to treat the symptoms of blood stasis, toxic heat, acute deficiency and qi obstruction by activating blood circulation to remove blood stasis, clearing heat and detoxification, strengthening the body and strengthening the root, and promoting the internal circulation to attack the lower organs [6].

## 5. Current status of treatment of myocardial dysfunction in sepsis

### 5.1. Western medicine treatment of septic dysfunction

There is a lack of high-quality clinical research evidence for the treatment of myocardial dysfunction in sepsis, but it is generally believed that the treatment of myocardial dysfunction in sepsis is the same as that in sepsis without cardiomyopathy. It includes both routine sepsis treatment and symptomatic treatment. The cornerstones of treatment of septic myocardial dysfunction are control of the underlying infectious process (antibiotic therapy, removal of the source of infection) and hemodynamic stabilization (fluids, vasopressors, and inotropic agents). Positive inotropic drugs can be selected when the hemodynamics is still unstable after conventional anti-infection treatment, early fluid infusion, and norepinephrine vasopressor [7]. In general, invasive cardiac output monitoring and echocardiography can be used for diagnosis and given to guide treatment.

Levosimendan (Figure 2) is a potent calcium sensitizer, which can effectively reduce peripheral vascular resistance and pulmonary artery pressure by opening ATP-sensitive potassium channels, and enhance calcium sensitivity of cardiac troponin C myofilaments. Positive inotropic support can effectively reduce cardiac oxygen demand, improve right ventricular and left ventricular function, and significantly increase LVEF and cardiac output, so as to improve cardiac function of patients. A recent clinical study showed that the risk of arrhythmia induced by levosimendan was significantly lower than that induced by dobutamine in the cardiotoxic treatment of septic myocardial dysfunction [8].



Figure 2: Levosimendan

In patients with further complicated shock, vascular arterial extracorporeal membrane oxygenation is generally considered to be a viable rescue option. A retrospective study showed a 75% survival rate with extracorporeal membrane oxygenation. Although more studies are needed to assess its full effectiveness and feasibility, this regimen is considered to be an appropriate treatment option in a subset of patients with septic shock and heart failure. Intraaortic balloon counterpulsation has been shown in clinical studies to be effective in critically ill patients because it reduces cardiac afterload and increases coronary blood flow [9]. Unfortunately, only a few cases can discuss the role of intra-aortic balloon counterpulsation in sepsis-induced myocardial dysfunction, limiting the evaluation of its true efficacy.

### 5.2. TCM treatment of septic myocardial dysfunction

Traditional Chinese medicine therapy for dysfunction dysfunction includes four methods including. (Figure 3)

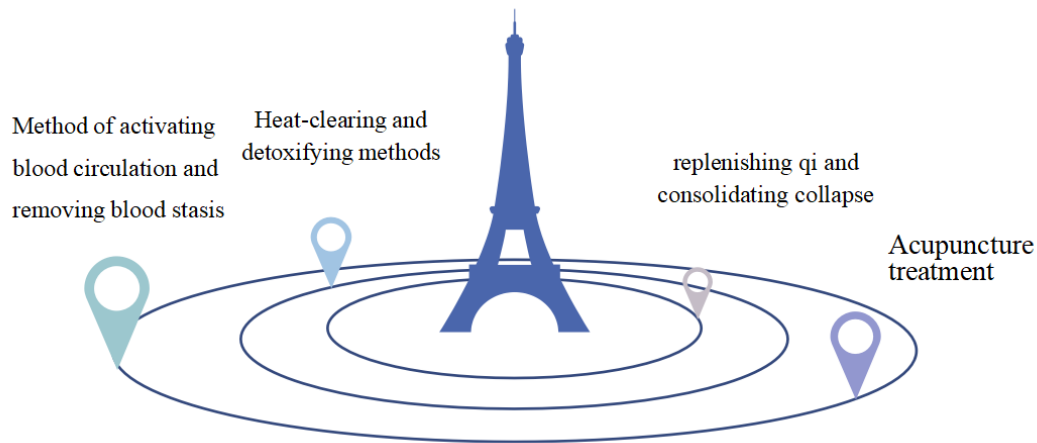


Figure 3: The four dialectical methods of traditional Chinese medicine

5.2.1. Heat-clearing and detoxifying methods

In the early stage of sepsis, hormone body deficiency, pathogen invasion, pathogen induction and infection, "toxin-heat syndrome" to "blood stasis syndrome" are the key stages of treatment, so the first treatment is to clear heat and detoxification. The clinical manifestations of toxin-heat syndrome are often high fever, fear of cold, red face and red eyes, irritability, even trance, excessive phlegm and salivation, thirst and drink, yellow tongue coating, flood or thin pulse and other symptoms. Huanglian-jiedu decoction, a classic prescription for clearing heat and detoxifying, is mainly used to reduce fire and detoxifying. Longmin treated with Huanglian-Jiedu decoction combined with conventional western medicine was found to significantly increase the level of SOD in the body, reduce the damage of myocardial function caused by oxidative stress in sepsis, and effectively prevent further deterioration of septic shock [10].

5.2.2. Method of activating blood circulation and removing blood stasis

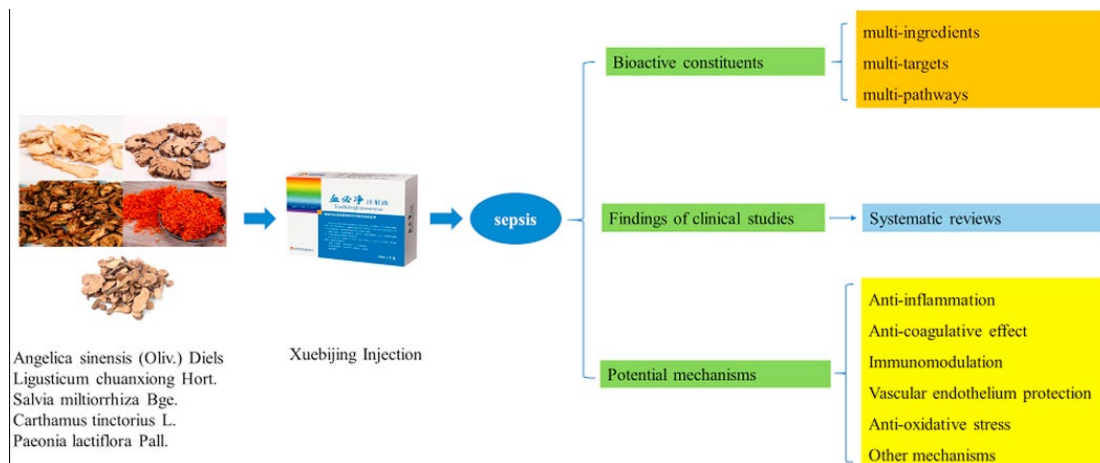


Figure 4: Xuebijing injection

Blood stasis syndrome is the most critical pathological development process in the treatment of sepsis. Clinically, patients often have dizziness and high fever, pain such as acupuncture, pain is fixed, the tongue is dark purple or ecchymosis, and the pulse is heavy and astringency. Xuebijing injection is commonly used in the treatment of blood stasis syndrome. Xuebijing injection (Figure 4) is a first-aid Chinese patent medicine developed by professor Wang Jinda on the basis of the famous Xuefuzhuyu Decoction of the Qing Dynasty. The prescription follows the principle of "treating bacteria, toxicity and inflammation at the same time". It has the effects of improving microcirculation, inhibiting inflammatory reaction, protecting organ function and regulating immunity. Han Ning combined Xuebijing injection with western medicine in clinical practice, and the results showed that the combined use of Xuebijing injection could significantly reduce the level of myocardial injury indicators [11]. Taohe-chengqi Decoction comes from the TCM classic Treatise on Febrile Diseases (Treatise on Febrile Diseases) written by Zhang Zhongjing in the Eastern Han Dynasty. It treats the

syndrome of lower jiao and blood storage caused by the mutual accumulation of pathogenic factors and blood stasis. Studies have shown that transcription factor AP-1 plays an important role in cardiovascular diseases. It can regulate the apoptosis, proliferation, anti-inflammation and anti-oxidation of cardiomyocytes, and participate in cell proliferation, differentiation and apoptosis, thus playing a key role [12].

### 5.2.3. Replenishing qi and consolidating collapse

If there is no timely treatment in the early stage of sepsis, the condition develops rapidly and develops into septic shock stage. At this time, the pathogenesis is that the pathogenic factors and essence have not been removed and the Zhengqi is deficient, which can be seen as Yang syndrome such as cold sweat, cold limbs, and hand enuresis, and Yin syndrome such as flushing face, thirst and food, red and dry tongue, and even Yin and Yang deficiency. As stated in Yifangtong: "A person who has been ill for a long time and has insufficient nourishment suddenly has a great discharge and gradually develops a great fever, which is the syndrome of Yang withdrawal. Those who are hot, Yang is exhausted on the top, and those who are discharged, Yin is removed on the bottom. "In the treatment of Yin and Yang deficiency, the method of strengthening and solid removal should be used to strengthen the body. By supporting the body's own positive qi, Yang qi is vigorous and smooth, and the positive qi is strong, the ability to remove pathogens is strong, it is easy to encourage pathogens to go out, restore the body balance, and avoid the development and invasion of poison and evil. It is described in Huangdi Neijing, "If the positive qi does not exist, the evil will be able to dry up; When the evil is gathered together, its qi will be deficient. "Shenfu injection and Astragalus injection are commonly used in the treatment of septic shock in recent years. Shenfu injection is a Chinese patent medicine preparation, composed of red ginseng and aconite, red ginseng taste sweet, slightly bitter, the two must be used, not only Zhenzhong Yang, but also help the heart Yang, the kidney Yang, a total of play back Yang save inverse, qi solid off the work. A recent meta-analysis showed that Shenfu injection can effectively reduce myocardial injury and improve cardiac CI and LVEF in patients with sepsis [13]. Astragalus injection is beneficial to nourishing qi, strengthening the body, eliminating factors, nourishing the heart, strengthening the spleen and dampness, etc. Astragalus is the long of tonic medicine, and can also improve heart damage while supplementing the body. Clinical studies have shown that the combination of astragalus injection in the clinical treatment of sepsis can significantly reduce the levels of IL-6, TNF- $\alpha$ , hs-CRP, BNP, cTnI, reduce myocardial injury, and improve hemodynamics [14].

### 5.2.4. Acupuncture treatment

Acupuncture (Figure 5) can dredging meridians, strengthening health and dispelling pathogenic factors, moving qi and blood, nourishing the whole body, and enhancing the role of healthy qi in the human body. In recent years, conventional treatment combined with acupuncture and moxibustion has made some progress. Recent studies have shown that electroacupuncture at "Zusanli", "Guanyuan" and other acupoints has obvious clinical effect on patients with sepsis, which can significantly reduce the APACHE-II score and blood lactic acid in patients with sepsis, and can effectively work together with drugs to treat septic myocardial dysfunction and protect the heart. Its mechanism of action may be involved in immune stimulation, so as to improve the low immune state of patients with sepsis and correct immune disorders [15].

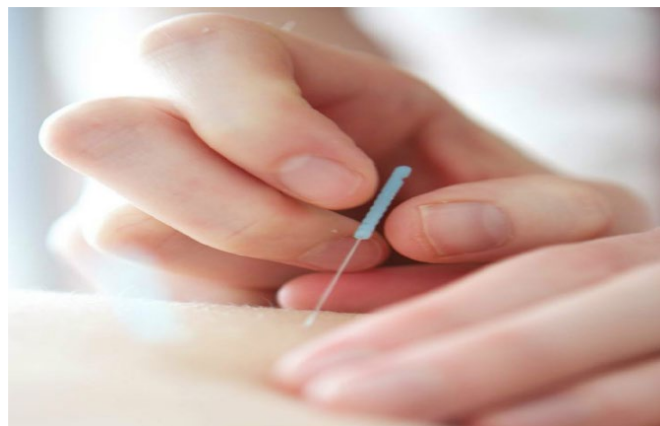


Figure 5: Acupuncture treatment

## 6. Outlook and Summary

So far, clinical studies have confirmed the pathological mechanism and diagnosis of sepsis-induced myocardial dysfunction to a certain extent. However, more research is needed in the management of the disease. However, there is still a need for more research on the management of the disease. Due to the multifactorial pathogenic factors and the uncertainty of the pathogenesis of the disease, there is no specific and targeted treatment plan or drug. It is still too early to establish a clear treatment for SIMD. It is believed that specific targeted therapeutic drugs can be developed in the near future, and Chinese medicine also plays an important role in the treatment of sepsis. In the future, we should give full play to the advantages of traditional Chinese medicine and western medicine, and strive to strengthen and overcome the difficulties in treatment.

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