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Pathogenesis and Treatment of Coronary Heart Disease Based on Metabolic Abnormalities from the Perspective of "Damp-Turbidity and Phlegm-Rheum Type of Diseases"

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Abstract: This paper explores the pathogenesis and treatment of coronary heart disease (CHD) from the perspective of metabolic abnormalities, guided by the Traditional Chinese Medicine (TCM) theory of "Damp-turbidity and Phlegm-rheum Type of Diseases." It examines the intrinsic connection between metabolic abnormalities and these syndromes, as well as their close link to the development of CHD. Metabolic disorders are the physiological foundation for the occurrence and progression of CHD and represent the microscopic essence of pathological products such as dampness and phlegm. Therefore, addressing metabolic imbalances is essential in the treatment process. At the onset of the disease, therapies should focus on eliminating dampness, invigorating the spleen, regulating qi, and promoting blood circulation to improve sugar and lipid metabolism. When dampness lingers for a long time, treatments should aim to transform dampness, clear turbidity, regulate qi, and activate blood circulation to protect vascular endothelial damage. As the disease progresses, treatment should aim at resolving phlegm, removing blood stasis and coordinating the internal organs to restore the damaged heart function. In severe cases, treatment should focus on warming Yang, transforming water and tonifying qi to prevent the occurrence of complications such as heart failure.

1. Introduction

Coronary heart disease (CHD) is a common cardiovascular disease, characterized by functional changes such as atherosclerosis or spasm of the coronary arteries, which lead to narrowing or obstruction of the coronary arteries, resulting in myocardial ischemia, hypoxia or necrosis. The main manifestations are chest tightness and chest pain, and it is one of the most common cardiovascular diseases in clinical practice [1]. In China, the incidence of coronary heart disease is increasing every year. This disease poses a significant threat to human health and poses major challenges to clinical

prevention and treatment [2-3]. Metabolic disorders, including abnormal metabolism of substances such as water, electrolytes and lipids, are an important mechanism for the occurrence of coronary heart disease [4-5]. These metabolic markers provide a theoretical basis for the diagnosis of coronary heart disease and offer new perspectives for its syndrome differentiation, quantification and clinical management.

In traditional Chinese medicine, coronary heart disease is classified into "chest obstruction" and "heart pain". The "Essential Prescriptions from the Golden Cabinet" concisely describes its pathogenesis as "deficiency of Yang and tightness of Yin" [6]. "Yang deficiency" refers to the deficiency of the five internal organs, while "Yin tightness" represents the pathological excess of dampness, turbidity, phlegm, fluid and blood stasis. Dampness, turbidity, phlegm and fluid retention are all related pathological conditions caused by abnormal transformation of body fluids. Professor Zhang Boli, a renowned master of traditional Chinese medicine, integrated these four symptoms into a unified conceptual framework, calling it " damp-turbidity and phlegm-rheum type of diseases "[7]. Dampness is described as the evaporation of water, turbidity as the stagnation of nutrients, phlegm as long-term dampness, and fluid retention as the accumulation of water. These pathological factors are both by-products of the disease and pathogenic factors, and they are the core pathological basis for the deterioration of coronary heart disease.

From a metabolic perspective, analyzing the unique metabolites involved in the development of coronary heart disease at both the global and micro levels can clarify the underlying mechanisms of dampness, turbidity, phlegm and fluid retention. This method provides a new approach for the diagnosis and treatment of coronary heart disease in traditional Chinese medicine. This article aims to explore the pathogenesis of coronary heart disease from the perspective of metabolic disorders and discuss the treatment methods of coronary heart disease in combination with the theory of " damp-turbidity and phlegm-rheum type of diseases ". It aims to enrich the scientific connotation of this theory in the treatment of coronary heart disease and provide theoretical support for future clinical practice and new drug development.

2. Exploring the Driving Mechanisms of Metabolic Disorders in the Onset and Progression of CHD

Metabolic disorders play a crucial role in the occurrence and development of coronary heart disease (CHD). Metabolic syndrome is characterized by a series of metabolic abnormalities. Generally, it is a factor that leads to the onset of coronary heart disease. The key to this syndrome is insulin resistance, or IR, which is the fundamental cause of the disease [8]. Insulin resistance causes pancreatic β-cells to secrete a large amount of insulin as compensation, thus resulting in hyperinsulinemia. In an environment where blood sugar is constantly high, the production of advanced glycation end products, or AGEs, will significantly increase. These AGEs can alter the proteins and lipids in the endothelium of blood vessels, destroying the integrity of the vascular wall structure and function. This kind of damage will accelerate endothelial injury and the development of atherosclerosis [9]. Studies have shown that among patients with coronary heart disease who do not have diabetes, those with insulin resistance have a significantly higher incidence rate [10]. Stern's [11] "common soil hypothesis" emphasizes that insulin resistance and the subsequent metabolic disorders it causes, such as abnormal glucose and lipid metabolism, oxidative stress, and chronic inflammation, constitute the common pathological basis of cardiovascular diseases. This hypothesis provides crucial theoretical support for us to understand the core mechanism of coronary heart disease related to metabolism.

Coronary atherosclerosis is the main pathological feature of coronary heart disease. Lipid metabolism disorder is the main cause of coronary heart disease [12]. Low-density lipoprotein, also

known as LDL, undergoes oxidation and then deposits in the endothelium, which triggers the infiltration of monocytes and the formation of foam cells, and this is the most initial event in the development of atherosclerotic plaques [13]. Additionally, elevated levels of triglycerides (TG) confer a high susceptibility to atherosclerosis. Excessive intake of saturated and trans fatty acids leads to increased serum TG levels. The conversion of TG-rich lipoproteins into excessive LDL particles, combined with reduced activity of LDL receptors, impairs the normal clearance pathways for glycosylated and oxidized LDL [14]. High levels of TG also destabilize high-density lipoprotein (HDL) particles, weakening their anti-atherosclerotic properties and consequently increasing the risk of CHD [15].

3. The Guiding Significance of the "Damp-turbidity and Phlegm-rheum Type of Diseases" Theory in the Pathogenesis of CHD

The basic pathogenesis of CHD is described as "deficient yang and excessive yin," which means insufficient heart yang in the upper burner and excessive yin cold in the lower burner. The spleen's yang deficiency is primarily responsible for this condition, as it fails to transform water and grain into essence, instead generating dampness. Professor Zhang Boli has emphasized that "dampness is the source of all diseases; if internal dampness is not eliminated, numerous diseases will arise." Dampness is a major factor in the progression of CHD, as it obstructs the heart vessels and impairs the smooth flow of qi and blood. Therefore, he advocates the principle of "focusing on dampness as the root, and always considering dampness in heart diseases" [16-17]. When dampness lingers for a long time, it gradually disrupts the balance of body fluid metabolism, creating conditions for the development of CHD and laying the foundation for the subsequent transformation into turbidity, phlegm, and fluid retention.

Turbidity originates from the thick and dense part of the essence derived from water and grain. When the spleen and stomach fail to transform and transport properly, the essence does not undergo normal metabolism and accumulates in the middle burner, forming turbidity. Turbidity is characterized by its sticky, obstructive, and filthy nature. Academician Zhang Boli has pointed out that turbidity is an important cause of many common cardiovascular and cerebrovascular diseases [7]. Over time, accumulated turbidity can penetrate into the blood vessels, meridians, and viscera. When blood vessels are affected, the endothelium is damaged, and turbidity can also lead to abnormal blood lipids [18]. This accelerates the progression of atherosclerosis and is a crucial link in the development of CHD.Phlegm is formed from the long-standing dampness in the body, which accumulates and transforms into a more adhesive substance. Phlegm is characterized by its stubborn and variable nature, easily obstructing the flow of qi and impeding the circulation of blood and qi. Phlegm often combines with blood stasis to form nests of pathology [7]. The presence of phlegm makes CHD more persistent and difficult to cure.Fluid retention results from the failure of qi to warm and transform body fluids due to qi deficiency. Fluid retention, characterized by its heavy and downward tendency, is a yin pathogenic factor that can further suppress yang qi, leading to increased yin cold and further depletion of yang qi, worsening the condition. In CHD, fluid retention can cause severe symptoms such as palpitations, coughing, wheezing, and edema. For example, when heart yang is insufficient and fluid retention affects the heart, palpitations may occur [19]. The presence of fluid retention indicates a more complex and severe condition, often seen in cases of heart and kidney yang deficiency in CHD, with outcomes frequently manifesting as critical heart failure.

4. Analysis of the Intrinsic Correlations between Metabolic Disorders and "Dampness, Turbidity, Phlegm, and Fluid Retention"

In clinical practice, TCM syndrome differentiation can be somewhat limited due to subjective

factors and the scope of differentiation. In recent years, metabolomics research has offered a microscopic perspective for syndrome differentiation. It can qualitatively and quantitatively analyze endogenous small-molecule metabolites in CHD to identify specific biomarkers. This not only enhances the accuracy of clinical diagnosis but also improves the scientific and objective nature of the TCM syndrome differentiation system, providing a basis for the early diagnosis and intervention of CHD [20-21]. From a metabolic standpoint, the formation and evolution of dampness, turbidity, phlegm, and fluid retention are all closely related to metabolic disorders. Their pathological characteristics exhibit specific differences and dynamic correlations at the metabolic level, collectively forming the core network of metabolic imbalance in CHD. Dampness, essentially a disorder of water metabolism, involves abnormalities in the excretion of water, electrolytes, and small-molecule metabolites (such as urea and creatinine) [22-23]. Dampness can disrupt the homeostasis of glucose and lipid metabolism, leading to increased levels of pyruvate and lactate in the blood and enhanced oxidation of LDL. This suggests that dampness triggers early metabolic imbalances by inhibiting mitochondrial energy metabolism and lipid clearance pathways [24]. Turbidity often coexists with phlegm and is highly correlated with lipid peroxidation and endothelial dysfunction. In metabolomics studies, turbidity may lead to increased levels of lipid metabolites such as LDL and TG in the blood [25]. Phlegm, a product of the coagulation of dampness and turbidity, often involves widespread disorders in the metabolism of sugars, lipids, proteins, and energy [26]. Phlegm can obstruct the flow of qi and blood, leading to dysfunction of the viscera and significantly increased levels of cholesterol, triglycerides, and blood glucose in the blood. In metabolomics studies, this state of phlegm and blood stasis may be manifested as increased levels of coagulation-related protein metabolites such as fibrinogen in the blood [27]. The metabolic characteristics of fluid retention often reflect the collapse of the heart and kidney energy metabolism system. In the terminal stage of CHD, patients commonly exhibit a decreased myocardial ATP/ADP ratio and significantly elevated levels of serum cystatin C [28-29]. These changes all indicate that fluid retention has a serious impact on the body's metabolism and is related to the severity of the disease.

5. Treating CHD Based on Metabolic Disorders and the Theory of "Damp-turbidity and Phlegm-rheum Type of Diseases "

5.1 Initial Dampness Invasion, Qi and Blood Stagnation—Eliminating Dampness, Regulating the Spleen, and Promoting Qi and Blood Flow to Restore Qi and Blood Circulation

At the onset of CHD, the flow of qi and blood becomes obstructed, and the metabolism of body fluids is disrupted, leading to the pervasive presence of dampness in the triple burner. Patients may experience disturbances in water and electrolyte metabolism at this stage. The treatment strategy focuses on eliminating dampness, regulating the spleen, and promoting qi and blood flow to adjust metabolic pathways. Medicinal herbs such as Atractylodes (Cangzhu), Magnolia Bark (Houpo), and Tangerine Peel (Chenpi) are commonly used to dry dampness and strengthen the spleen.Additionally, herbs like Atractylodes (Muxiang) and Amomum (Sharen) are employed to regulate qi and promote blood circulation. Finally, a small amount of blood-activating herbs such as Salvia (Danshen) and Paeonia (Chishao) can be added to address the root cause of heart vessel blockage. Atractylodes (Cangzhu) regulates cholesterol levels and accelerates lipid excretion, thereby significantly improving lipid metabolism [30]. Magnolia Bark (Houpo) contains honokiol, which can significantly inhibit the mRNA expression of pro-inflammatory cytokines and inducible nitric oxide synthase, regulating gastrointestinal function to regulate the body's water and salt metabolism [31]. Amomum (Sharen) can repair pancreatic β-cells and increase insulin sensitivity [32]. Atractylodes (Muxiang) ethanol extract can improve endothelial cell damage caused by high glucose [33]. The combined use of these herbs can improve CHD conditions caused by insulin resistance.

5.2 Dampness and Turbidity Entanglement, Qi Stagnation and Blood Stasis—Transforming Dampness, Clearing Turbidity, and Promoting Qi and Blood Flow to Unblock the Meridians

When dampness lingers for a long time, the stagnation of nutrient essence leads to turbidity, and dampness and turbidity often coexist with phlegm. At this stage, patients with persistent high blood sugar and lipids experience exacerbated vascular endothelial damage. The treatment emphasizes transforming dampness, clearing turbidity, and promoting qi and blood flow to regulate lipid metabolism.Herbs such as Lotus Leaf (He Ye) and Alisma (Zexie) are selected for their dampness-transforming and turbidity-clearing properties to expel phlegm and blood stasis from the body. Combined with Bupleurum (Chaihu) and Aurantium (Zhike) for promoting qi flow, and Prunus persica (Taoren) and Carthamus (Honghua) for activating blood circulation, these herbs help to relieve qi stagnation and blood stasis. Modern pharmacological studies have shown that nuciferine in Lotus Leaf can reduce the levels of TG and cholesterol in the blood, regulate lipid metabolism [34]. Alisma alcohol extract (Zexie) has anti-inflammatory and lipid-regulating effects [35]. Bupleurum saponin D in Bupleurum (Chaihu) can inhibit the production of reactive oxygen species and the activation of the NLRP3 inflammasome, significantly improving insulin resistance and glucose and lipid metabolism disorders [36]. Aurantium (Zhike) can regulate lipids and improve lipid metabolism disorders [37]. Prunus persica (Taoren) and Carthamus (Honghua) can improve free radical metabolism disorders, reduce enzyme leakage, and alleviate lipid peroxidation damage, thereby protecting ischemic myocardium [38].

5.3 Phlegm and Blood Stasis Interconnection, Viscera Malnourishment—Phlegm-Dispelling, Blood-Stasis-Removing, and Viscera-Regulating to Stabilize the Internal Organs

When dampness persists in the body for a long time, it transforms into phlegm, which easily combines with blood stasis to form nests of pathology. At this stage, the disorder of glucose and lipid metabolism becomes more severe, and cardiac function is significantly impaired. The treatment focuses on dispelling phlegm, removing blood stasis, and regulating the viscera to strictly control blood glucose and lipids, improve metabolic disorders. Pinellia (Banxia) and Trichosanthes (Gualou) are the first choices for phlegm-dispelling herbs to eliminate phlegm and turbidity from the body. Hirudo (Shuizhi) and Curcuma zedoaria (Sanleng) are used as blood-stasis-removing herbs to break and expel blood stasis, thereby improving the state of phlegm and stasis interconnection. Pharmacological studies have shown that the active ingredients in Pinellia (Banxia) can reduce lipid levels, prevent myocardial infarction, and stabilize atherosclerotic plaques by influencing the metabolism of inflammatory factors and reducing inflammatory reactions, thereby protecting the vascular endothelium [39]. Trichosanthes (Gualou) extract also has the effects of regulating glucose and lipid metabolism, dilating coronary arteries, and improving myocardial ischemia [40]. Hirudin in Hirudo (Shuizhi) and curcumenol in Curcuma zedoaria (Sanleng) can improve lipid metabolism and inhibit inflammatory reactions to prevent atherosclerosis [41-42]. The combined use of these herbs can regulate qi and blood, improve blood circulation, prevent and alleviate myocardial ischemia, and effectively treat CHD.

5.4 Fluid Retention Rampage, Declining Yang Qi—Yang-Warming, Fluid-Transforming, and Fundamental-Strengthening to Rescue Severe Conditions

In the terminal stage of the disease, the condition is critical, with deficient yang qi and impaired warming and transformation of body fluids, leading to the accumulation of fluid retention. Patients' physical functions are extremely fragile, and all metabolisms are severely disordered. The treatment primarily focuses on warming yang, transforming fluid retention, and strengthening the body's

fundamental energy, while closely monitoring the condition to prevent severe complications such as heart failure. Ginseng (Renshen) and Astragalus (Huangqi) are selected to tonify the heart and kidneys and invigorate yang qi. Poria (Fuling) and Atractylodes (Baizhu) are used to promote diuresis and eliminate fluid retention. Additionally, Dioscorea (Shanyao) and Rehmannia (Shudihuang) are included to nourish yin and assist in tonifying yang qi. Studies have shown that ginsenosides in Ginseng (Renshen) can regulate the metabolism of renin and angiotensin II, promote the expression of vascular endothelial growth factor and its receptors, and regulate the renin-angiotensin-aldosterone system, thereby improving myocardial contractility and relaxation [43]. Astragalus polysaccharides in Astragalus(Huangqi) can regulate the levels of proteins related to myocardial fatty acid metabolism, improve fatty acid metabolism disorders and fatty toxicity [44]. Poria cocos polysaccharides have a diuretic effect, and Atractylodes (Baizhu) macrocephala can promote fluid metabolism [45-46]. The combined use of these herbs can eliminate fluid retention and reduce the burden on the heart.

6. Conclusion

In conclusion, the onset of coronary heart disease is closely related to metabolic disorders in the body. The theory of "dampness-turbidity-phlegm-fluid stagnation syndrome" provides a unique perspective for understanding its etiology, pathogenesis and treatment. Metabolic disorders play a key role in the pathogenesis of coronary heart disease. The theory of " damp-turbidity and phlegm-rheum type of diseases " clarifies the pathological evolution of coronary heart disease. Dampness, turbidity, phlegm, fluid stagnation - each of which gradually builds upon the other and interacts with it - as well as blood stasis, run through the entire course of the disease. From a metabolic perspective, each pathogenic factor has its unique metabolites and influencing pathways, disrupting metabolic balance and jointly exacerbating the condition. In the initial stage, the focus of treatment is to eliminate dampness, regulate the spleen, and promote the flow of qi and blood to regulate metabolism. During the stage where dampness and turbidity are intertwined, the therapeutic objective is to eliminate dampness and clear turbidity, promote the circulation of qi and blood, and improve lipid metabolism and vascular function. When phlegm and blood stasis are interconnected, the goal of treatment is to dissolve phlegm, remove blood stasis, and regulate the overall condition of the internal organs to manage metabolism and repair heart function. In the final stage, warming Yang, altering fluid retention, and enhancing the body's basic energy are the priorities for addressing metabolic disorders and complications. Combining the theory of " damp-turbidity and phlegm-rheum type of diseases " with the study of metabolic disorders has enriched the theoretical framework of coronary heart disease in traditional Chinese medicine. It provides a scientific basis for precise clinical diagnosis and treatment as well as for the development of new drugs. This approach holds promise for forging new pathways in the integrated traditional Chinese and Western medicine treatment of CHD, thereby enhancing the prevention and treatment of this condition.

Contributors

Zhang Zhengwei (first author) conceived the theoretical framework, established the overall structure. Jia Fuyun conducted the initial literature review, screening, and synthesis of relevant theoretical sources. Ma Yinan coordinated resources, securing access to theoretical databases and academic materials. Cui Hanwen verified the theoretical derivations and refined the applied logic of the analysis. Zhao Xinwei assisted with theoretical investigation and validated specific theoretical hypotheses. Xu Qiang (corresponding author) critically reviewed and polished the manuscript for theoretical rigor and narrative coherence, and oversaw academic communication and publication processes.

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