DOI: 10.53469/jcmp.2025.07(12).02

Exploring Acupuncture-Mediated Gut Microbiota Regulation for Post-PCI Depression in Coronary Heart Disease Based on the "Heart Corresponding to the Small Intestine" Theory

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Abstract: ***The incidence of depression significantly elevates in coronary heart disease (CHD) patients after percutaneous coronary intervention (PCI), a condition pathologically linked to disruptions in the gut microbiota-mediated "gut-heart-brain axis. This phenomenon has emerged as a critical risk factor impeding postoperative recovery. Grounded in the core principle of visceral synergy from the traditional Chinese medicine (TCM) theory of "heart-small intestine interconnection, this study integrates evidence from both Chinese and Western medical research to systematically investigate the mechanisms underlying acupuncture's regulation of gut microbiota and its therapeutic value for dual-heart diseases. This synergistic "treating heart via regulating intestine" effect provides a modern microbiological interpretation of visceral theory within the microbiota-gut-brain framework and establishes the scientific basis for acupuncture in managing post-PCI depression. Our findings offer theoretical support for integrated Chinese-Western treatment strategies and highlight acupuncture's unique advantage in multi-target modulation.***

Keywords: Heart-small intestine interconnection, Acupuncture, Gut microbiota, Post-PCI depression.

1. Introduction

Coronary atherosclerotic heart disease (CHD) refers to a heart disorder caused by atherosclerosis of the coronary arteries, a condition that leads to luminal stenosis or occlusion and subsequent myocardial ischemia, hypoxia, or necrosis [1]. Epidemiological surveys have shown that the incidence of CHD has been increasing annually and is trending toward affecting younger populations [2]. Percutaneous coronary intervention (PCI) is currently the primary treatment for CHD and is characterized by advantages including favorable efficacy, minimal invasiveness, and low risk [3]. However, following PCI, patients are more susceptible to developing emotional disorders after exposure to dual physical and mental stress; the interaction between physical and psychological factors contributes to the development of psychosomatic heart disease [4]. Studies have indicated that post-PCI depression in patients with CHD has become one of the key factors that induce the recurrence of adverse cardiovascular events [5]. In recent years, research has revealed that gut microbiota are closely associated with the occurrence, development, and prognosis of psychosomatic heart disease [6-7]. Gut microbiota and their metabolites not only exert an ameliorative effect on cardiovascular diseases but also participate in the regulation of the nervous system, contribute to the formation of the intestinal biological barrier, and exert a positive regulatory effect on mood.

2. Gut Microbiota and Psychosomatic Heart Disease

2.1 Gut Microbiota and Cardiovascular Diseases

The gut microbiota is composed of trillions of microorganisms, which coordinate and maintain the balance between the human body and its external environment. Changes in the composition of the gut microbiota have been shown to be strongly associated with cardiovascular diseases by Lin et al. [8]. Abnormal lipid metabolism is the most critical risk factor for atherosclerosis; alterations in the gut microbiota structure have been reported to affect cholesterol metabolism and promote the formation of intravascular atherosclerotic plaques, thereby laying the groundwork for the occurrence of cardiovascular events [9]. Short-chain fatty acids (SCFAs) are one of the major metabolites of the gut microbiota, and they are produced by gut microbiota through the fermentation of complex polysaccharides [10]. SCFAs can influence the permeability of the blood-brain barrier and neuroinflammatory responses by increasing the synthesis of neurotransmitters (e.g., serotonin) and improving neuronal homeostasis and function. Since the inhibition of inflammatory responses is regarded as an important strategy for treating myocardial ischemia and hypoxia, the prevention and treatment of cardiovascular diseases can be achieved by regulating SCFA levels [11]. Animal experiments conducted by Wu et al. have further confirmed that SCFAs can effectively repair post-infarction myocardial tissue and improve disease conditions, which provides a new target for the treatment and prognosis of patients after percutaneous coronary intervention (PCI) [12]. Trimethylamine N-oxide (TMAO) is an intestinal microbiota-derived metabolite that is synthesized in the host's liver. The production of its precursor, trimethylamine (TMA), is dependent on the involvement of gut microbiota [13]. Significant characteristic changes in the gut microbiota of rats with acute coronary syndrome (ACS) have been verified by Zhang N et al. [14]; elevated plasma TMAO levels can independently predict the risk of major adverse cardiac events, and the prognostic evaluation of related cardiovascular diseases also relies on changes in this index [15].

2.2 Gut Microbiota and Psychological/Psychiatric

Disorders

Modern medical studies have demonstrated that gut microbiota participate in the regulation of nervous system function through three pathways (immune, neuronal, and endocrine), thereby affecting patients' cognition, mood, and behavior [16]. This mechanism is collectively termed the "Gut-Heart-Brain Axis" multisystem interaction network, which exhibits interactive and interdependent relationships [17]. A similar phenomenon is prevalent in rodents; relevant laboratory data have confirmed that anxiety-like behaviors in mice can be induced by pathogenic bacteria in the body. These behaviors are mediated by the activation of the stress system via vagal afferent pathways, and this effect is bidirectional—psychological factors also affect intestinal motility and permeability and exert an impact on the function of the immune system [18]. Liu QF et al. have found that mice subjected to chronic restraint stress (CRS) exhibit reduced gut microbiota diversity, depressive behaviors, and elevated serum corticosterone levels [19]. After probiotic administration, corticosterone levels have been shown to decrease, and depressive-like behaviors have been significantly alleviated.

3. TCM Basis of the "Heart Corresponding to the Small Intestine" Theory

The theory of "heart corresponding to the small intestine" can be traced back to Huangdi Neijing (Inner Canon of the Yellow Emperor). As recorded in Lingshu·Benzang (Miraculous Pivot·Visceral Fundamental): "The heart corresponds to the small intestine, and the small intestine corresponds to the vessels" [20], which is consistent with the concept of the "Gut-Heart-Brain Axis" in modern medicine.

3.1 Physiological Synergy Between the Heart and Small Intestine

As recorded in Suwen·Linglan Midian Lun (Plain Questions·Treatise on the Spiritual Orchid Chamber): "The small intestine receives and stores cereal food, transforms it into clear juice, and transports it upward to the heart for blood formation" [21]. As summarized in Yijing Yunzhong (A Guide to Medical Classics): "The small intestine supplies the heart for blood formation; therefore, it is the fu-organ of the heart and the source of nutrients for the heart" [22]. Hence, a clear heart spirit is maintained by unobstructed intestines, smooth vessels, and unimpeded circulation of qi and blood.

3.2 Pathological Interaction Between the Heart and Small Intestine

Zhubing Yuanhou Lun (Treatise on the Causes and Manifestations of Diseases) records: "If there is heat accumulation in the heart, it will transmit to the small intestine, resulting in hematuria" [23]. Pathologically, the heart and small intestine restrict and affect each other. Hyperactivity of heart fire can transmit to the small intestine, leading to symptoms such as oliguria, dysuria, and even hematuria. Conversely, intestinal heat can also ascend to the heart along the meridians, which is clinically manifested as oral ulcers, palpitations, and insomnia. The upward flow of pathological fluid to the heart induces chest pain, while the failure of fluid to descend into the bladder causes lower limb edema. Therefore, the heart and small intestine are closely connected in terms of pathology.

3.3 Meridian Connection Between the Heart and Small Intestine

A comparison of the meridian courses of the heart and small intestine reveals significant overlaps. In addition to the regular meridians, the collateral of the Heart Meridian (Tongli Point, HT5) connects to the Small Intestine Meridian, and the collateral of the Small Intestine Meridian (Zhizheng Point, SI7) connects to the Heart Meridian. This forms a direct qi-blood exchange between the internally-externally related meridians, maintains the yin-yang balance of the two meridians, and embodies the meridian synergy mechanism of "integration and divergence of the internal-externally related meridian branches" [24].

3.4 Clinical Therapeutic Coordination Between the Heart and Small Intestine

As stated in Zhenjiu Dacheng (Compendium of Acupuncture and Moxibustion): "Diseases of the heart must be treated with points of the small intestine" [25]. That is, on the basis of internal regulation with Chinese herbs, external treatment with acupuncture at small intestine-related points is supplemented to stimulate the whole-body meridians, harmonize yin, yang, qi, and blood, and unblock the zang-fu organs and vessels, thereby nourishing the heart spirit. Points on the Heart Meridian of Hand-Shaoyin, such as Shenmen (HT7) and Shaochong (HT9), can be used to treat hematochezia and pus in the stool, while Shaofu (HT8) can treat dysuria and enuresis. Bianque Xinshu (Bianque's Heart Book): "Chest pain radiating to both hypochondria... moxibustion at Zuominguan (a historical point) for 200 moxa cones and at Guanyuan for 300 moxa cones" [26], which is used for the treatment of cardiovascular diseases. "In the syndrome differentiation and treatment starting from the small intestine, the regulation of intestinal qi and blood should be implemented throughout the entire treatment process.

4. Mechanisms and Advantages of Acupuncture Therapy

As a treasure of TCM, acupuncture therapy can dredge meridians, strengthen the body's resistance to pathogens. It is characterized by a short onset time and a wide range of indications [27]. Precise acupoint stimulation has been shown to exhibit unique advantages in reducing myocardial damage, regulating gene expression, and relieving neuralgia [28]. On the other hand, the combination of acupuncture points can act on neural pathways and regulate the release of central neurotransmitters, thereby restoring the normal homeostasis of the nervous system [29]. Based on the gut-brain axis, it regulates neuroendocrinology, corrects inflammatory responses, and alleviates oxidative stress damage, ultimately achieving the goal of stabilizing mood [30].

4.1 Acupuncture-Mediated Regulation of Gut Microbiota

Studies have shown that acupuncture therapy can effectively regulate the structure and abundance of intestinal

microorganisms, increase their diversity, and improve the proportion of beneficial microbiota [31,32]. For example, the metabolic state of gut microbiota can be adjusted, the uniformity of gut microbiota can be improved, and inflammatory responses can be reduced by acupuncture at "Zusanli (ST36)" and "Yanglingquan (GB34)"; these effects collectively improve motor function and alleviate comorbid anxiety in a mouse model of Parkinson's disease [33]. Depressive-like behaviors in rats with post-stroke depression (PSD) have been improved by Xu H et al. through stimulation of the "Siguan Points" (Hegu, LI4; Taichong, LR3) [34]. The mechanism of this improvement is related to the regulation of fecal SCFA content and the influence on the release of colonic serum 5-hydroxytryptamine (5-HT). Furthermore, clinical observational studies have pointed out that the 24-item Hamilton Depression Rating Scale (HAMD-24) scores of adolescents with depression can be significantly reduced by acupuncture, and depressive symptoms can be improved; this mechanism may be achieved by altering the structure of gut microbiota [35].

4.2 Acupuncture for Treating Psychosomatic Heart Disease

In terms of cardiovascular disease treatment, studies have indicated that acupuncture therapy exerts a cardioprotective effect through multiple pathways, including improving myocardial microcirculation, inhibiting inflammatory responses, and suppressing myocardial cell apoptosis and autophagy, thereby treating CHD [36]. In terms of clinical efficacy, acupuncture combined with conventional drug therapy has been proven to be more effective than drug therapy alone; it can significantly reduce the frequency of stable angina pectoris (SAP) attacks, improve electrocardiographic manifestations of myocardial ischemia, and decrease the dosage of nitroglycerin [37].

In terms of psychiatric disease treatment, Studies by Liang E et al. have pointed out that depressive-like behaviors in mice can be significantly improved by acupuncture at "Baihui (GV20)" and "Yintang (EX-HN3)" on the Governor Vessel [38]. The mechanism of this effect is related to the regulation of toll-like receptor 4/nuclear factor-kappa B (TLR4/NF-κB) signaling pathway-mediated microglial activation, thereby affecting the release of inflammatory factors. Liu L et al. conducted a study on 72 patients with post-stroke depression; statistical analysis has shown that the clinical symptoms of post-stroke depression can be treated by acupuncture through regulating serum 5-HT levels and mediating the "brain-gut axis" pathway [39].

4.3 Acupuncture for Post-PCI Depression in CHD Based on Gut Microbiota Theory

The occurrence of depressive symptoms in CHD patients after PCI is not only induced by surgical trauma and psychological stress but may also be associated with gut microbiota dysbiosis, which affects neurotransmitters and triggers inflammatory responses through the "brain-heart-gut axis" [40]. In patients with post-PCI depression, the number of butyrate-producing bacteria in the gut microbiota is reduced, and the level of serum lipopolysaccharides (LPS) is elevated. This elevation activates the hypothalamic-pituitary-adrenal (HPA) axis to exacerbate depression [41]; Clinical studies have shown that anxiety and depression in patients after interventional therapy can be improved by acupuncture, with no major adverse events occurring during the treatment process, indicating high safety [42]. One of the main acupoints selected in this study, "Baihui (GV20)", has been proven to exert a benign regulatory effect on the nervous, endocrine, and immune systems [43]. Meanwhile, Yu LY conducted a study on 80 patients with hypertension; by performing penetration acupuncture at "Baihui (GV20)" during the Chenshi period (7:00–9:00 a. m.), it was found that the levels of Bacteroides, Bifidobacterium, and Lactobacillus in the observation group were higher than those in the control group, indicating that the balance of intestinal microecology in patients can be significantly improved by acupuncture at "Baihui (GV20)" [44]. "Zusanli (ST36)" is the he-sea point of the Stomach Meridian of Foot-Yangming, and its regulatory effect on the gastrointestinal system is self-evident; it is commonly used in the clinical treatment of digestive diseases. On the other hand, Zhenjiu Dacheng (Compendium of Acupuncture and Moxibustion) states that it "treats fatigue due to overstrain, deficiency and exhaustion from seven injuries" and regards it as a key point for tonifying deficiency [45]. Laboratory studies have pointed out that an antidepressant effect is exerted by acupuncture at Zusanli (ST36), and this effect is achieved by influencing the composition of gut microbiota and metabolic functions such as retinol, ubiquitin, N-glycan, and steroid metabolism [46].

5. Conclusion

Acupuncture can exert a positive regulatory effect on the human body and maintain the balance of the intestinal flora environment. Acupuncture-based regulation of intestinal flora may become a new intervention strategy for depression after CHD PCI, but it still requires more clinical evidence support. Current studies are mostly animal experiments or small-sample clinical observations, lacking large-scale "flora-acupuncture" intervention studies targeting the population with depression after PCI. There is an urgent need to identify key flora targets and optimize acupuncture protocols (such as acupoint combinations and stimulation parameters). Meanwhile, in view of the specific conditions of different patients, individualized treatment plans are also required. By combining the advantages of traditional Chinese and Western medicine, better therapeutic effects can be achieved. In the future, with in-depth research and clinical practice on TCM characteristic therapies, it is believed that more progress and breakthroughs will be made, providing more options and hope for the treatment of psychosomatic heart diseases.

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