Research Progress on the Association between Depression and Coronary Heart Disease and Diabetes

Yong Tan[1,a], Bairong Wang[1,b], Danyang Hao[1,c], Xuebin Chen[2,d,*]

[1]Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712046, China
[2]Department of Cardiology, Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712000, China
[a]18591737307@163.com, [b]1063959162@qq.com, [c]1229543267@qq.com, [d]381104432@qq.com
*Corresponding author

Abstract: *As one of the important mental diseases, depression is closely related to coronary heart disease and diabetes. Depression belongs to the category of "depression" and "insomnia" in traditional Chinese medicine, among which coronary heart disease and diabetes are manifested in traditional Chinese medicine as depression caused by heartache, depression caused by thirst, disease depression, etc. Related studies have shown that MAPK signaling pathway, NF-κB signaling pathway, inflammatory response, HPA axis dysfunction, neurotrophic reduction, oxidative stress, insulin resistance, intestinal flora dysbiosis, behavioral abnormalities play important roles in the comorbidity pathological mechanism. This article summarizes relevant literature in recent years, exploring the etiology of traditional Chinese medicine and the pathogenesis of Western medicine, in order to provide reference for its clinical treatment.*

Keywords: *Depression; coronary heart disease; diabetes; traditional Chinese and Western medicine; research progress*

1. Introduction

Depression is a kind of mental disorder characterized by significant and lasting depression, mental retardation, decreased volitional activity, and cognitive impairment [1]. The World Health Organization (WHO) reported in 2018 that the number of patients with depression in the world has exceeded 300million, and China has now reached more than 54million [2]. Depression is closely related to the incidence and prognosis of coronary heart disease and diabetes mellitus. Studies have shown that the prevalence of depression is 51% among hospitalized patients with coronary heart disease in China [3]; The incidence of depression in diabetic patients is 2-4 times that of normal people [4]. At present, depression is often complicated with coronary heart disease and diabetes mellitus. However, due to insufficient cognition and low recognition rate, there are adverse reactions such as incomplete treatment, poor compliance and high recurrence rate. Depression belongs to the category of "depression syndrome" and "insomnia" in traditional Chinese medicine, coronary heart disease belongs to the category of "chest arthralgia" in traditional Chinese medicine, diabetes belongs to the category of "diabetes". Traditional Chinese medicine treatment of chest arthralgia and diabetes combined with depression syndrome is based on syndrome differentiation and treatment, emphasizing the overall concept of "form and spirit integration", which coincides with the current bio psycho social medical model. By summarizing the relevant literature in recent years, this paper intends to explore the comorbid mechanism of depression, coronary heart disease and diabetes, in order to provide reference for its clinical treatment.

2. Theoretical traceability

There is no disease name of "depression" in traditional Chinese medicine, which belongs to the categories of "depression syndrome", "insomnia", "epilepsy syndrome", "visceral irritability" and so on. Zhudanxi founded the "Qi, blood, phlegm, fire, dampness, food" six depression, of which Qi is the main, and Qi is the stagnation powder. "Ye Xuan Yi Heng" said that "the six depressions in Danxi are expressed in terms of etiology" [5], emphasizing the pathogenicity of depression, that is, under the invasion of factors such as cold and heat, disordered diet, excessive labor and so on, the fire of the five internal organs of the human body is aroused with the five Chi, resulting in six depressions, and then "when there is

depression, how many diseases occur. Therefore, many diseases of the human body are caused by depression". At the beginning of depression syndrome, the majority of cases were positive, and the common pathologies were qi stagnation, blood stasis, fire, phlegm, dampness, and food accumulation; If it does not heal for a long time, or if it is lost or mistakenly treated, it will change from excess to deficiency, from Qi into blood, and eventually become a disease of asthenia and fatigue, involving his internal organs. From the perspective of pathogenesis development, ye Tianshi's clinical guidelines medical records said: "depression leads to qi stagnation, and if the qi stagnation lasts for a long time, it will turn into heat, and if the body fluid is consumed but does not flow, the rise and fall of the machine is lost, the initial injury of Qi is divided, the blood is prolonged for a long time, and it extends to depression, fatigue and depression". The medical records contained therein are all depression of emotions, and the treatment principles involve soothing the liver and regulating qi, relieving pain and depression, calming the liver and calming the wind, clearing the heart and purging fire, strengthening the spleen and stomach, activating blood circulation and unblocking collaterals, resolving phlegm and drinking, supplementing qi and nourishing yin. Depression for a long time can lead to other diseases. For example, according to the Encyclopedia of ancient and modern medicine: depression syndrome gate, "depression is seven emotions that are not comfortable, so it becomes depression. It is not only a long period of depression, but also a variety of diseases. "; In addition, due to other diseases, Qi and blood are not adjusted, and visceral Qi is deficient, resulting in dissipation of heart and blood, loss of mental health, and anxiety and depression. According to Jingyue Quanshu, "anyone who has disorder of Qi and blood and causes disease can be called depression syndrome". It is believed that dysregulation of Qi and blood is the main cause of depression syndrome, and depression syndrome is divided into two types: "depression due to disease" and "disease due to depression". In addition, according to the theory of "deficiency of Qi and stagnation" proposed by academician wangyongyan, Professor Guo Rongjuan [6] believes that the internal cause of depression is "deficiency of vitality"; Emotional failure is caused by negative life events as the external cause of the disease. The interaction between vulva and internal causes leads to the imbalance of body and mind, which exceeds the body's self-healing ability, and finally causes a series of diseases with the evolution of the pathogenesis of "qi depression first, phlegm resistance gradually, blood stasis". And the interaction between deficiency Qi and stagnation finally forms a vicious cycle, and the interaction between diseases promotes the spiral aggravation of the disease. As it is said in "the source and flow of miscellaneous diseases: the source and flow of all kinds of depression": "all kinds of evils and diseases of visceral Qi also originate from deep thinking and weak visceral Qi, so the disease of six kinds of depression arises".

3. Etiology and pathogenesis

3.1. Heartache due to depression

Coronary heart disease belongs to the category of "chest arthralgia" in traditional Chinese medicine. Abnormal emotions can hurt the mind, blood and Qi are not harmonious, and all kinds of diseases are born. "Lingshu · evil guest chapter" says that "the heart hides the God, which is the master of the five Zang and six Fu organs, and the spirit is also given up". "God hides in the heart, and the heart governs seven emotions". "Lingshu · oral questions" said: "sorrow makes the heart beat, and the heart shakes all the viscera. ". Melancholy hurts the spleen, the spleen loses its health and circulation, the body fluid is disordered, the fluid accumulation is phlegm, or the blood circulation is blocked due to liver depression and qi stagnation, qi stagnation turns into fire, burning the fluid into phlegm, and the venation is unfavorable, which eventually leads to blood stasis, heart obstruction, and chest obstruction. As stated in the "rhinoceros candle of the origin of miscellaneous diseases": "in a word, the cause of seven emotions is heartache, and the disorder of seven emotions can lead to the depletion of Qi and blood, the blockage of heart obstruction, and heartache". The normal operation of the heart blood depends on the normal operation of the Qi machine. When the spleen is depressed, the biochemical source of Qi and blood in spleen deficiency is insufficient, and the blood circulation is unable to be promoted, the heart blockage caused by qi deficiency and blood stasis can lead to "chest pain and heartache". According to Chen wuze's "three causes and one extreme disease syndrome formula · internal causes and treatment of heartache", the true heartache is caused by uneven internal Qi, joy, anger and worry, which is the internal cause ", affirming that mental factors are the internal cause of chest pain. Qinjingming also said in the "treatment of symptoms due to pulse": "the cause of heart obstruction, or anxiety, mental injury. ". To sum up, abnormal emotions or internal injuries of seven emotions can lead to the loss of Qi and blood in the body, the dysfunction of viscera, and ultimately lead to heart and pulse obstruction, which is one of the important factors that lead to chest obstruction.

3.2. Diabetes due to depression

Diabetes belongs to the category of "diabetes mellitus" in traditional Chinese medicine, and yin deficiency, dryness and heat are its pathological basis. Many doctors recognize that the onset of diabetes mellitus is closely related to the "liver". The liver governs the drainage, regulates the Qi of the whole body, and emotional stimulation will first attack the liver. And emotional disorder is the main cause of diabetes mellitus. For example, the "clinical guidelines medical records" says: "depression of mood and spontaneous combustion of internal fire are major diseases of diabetes mellitus", emphasizing that depression can cause diabetes mellitus. "Su Ling Wei Yun. Diabetes mellitus" mentioned: "the disease of diabetes is solely responsible for the liver and not the lung. " the liver is mainly used for discharging Qi. The excess of Qi is fire, and the liver is hidden fire. Therefore, the liver Qi is stagnant, which is easy to ignite from the fire, and the internal fire ignites spontaneously. The upper part burns the lung yin, goes against the stomach, and causes water without wood, thus causing diabetes. As the "five changes in Lingshu" said, "the liver is fragile, the disease is good, and it is easy to be injured. ". Professor Chen Jiaxu [7] believes that the "liver spleen system" of traditional Chinese medicine is related to the imbalance of glucose metabolism in depression, and the release of Qi from the liver affects the operation of blood and body fluid, the movement of spleen and stomach, and the change of mood; The spleen is the biochemical source of Qi and blood. Only when the function of transportation is healthy and the central soil is irrigated around, can the body's refined substance glucose be transported to all tissues and organs of the body to play a role. In the pathological state, the liver wood loses its reach and the spleen soil loses its health. If they affect each other, the wood is depressed and the soil is blocked; The pathogenesis of depression syndrome is emotional disorder caused by liver loss and catharsis, while the transport capacity of glucose, a fine substance, is decreased due to the loss of healthy movement of spleen, resulting in abnormal glucose tolerance.

3.3. Depression due to illness

According to Jing Yue Quan Shu, depression syndrome, "all diseases have depression due to the depression of five Qi, which is also due to disease". The disease pathogen invades the human body, causing the imbalance of yin and Yang of Qi and blood, the retention of Qi and failure, the accumulation of Qi in the body, the stagnation of liver qi and stagnation of Qi, and due to a long illness and weakness, combined with emotional stimulation, the stagnation of liver Qi and spleen, diet gradually reduced, biochemical lack of source, over time, the deficiency of Qi and blood, the loss of nourishment of heart and spleen, or the dark consumption of blood, yin deficiency and fire hyperactivity, heart disease and kidney, resulting in the deficiency of Yin of heart and kidney, the loss of nourishment of mind and spirit, and ultimately the occurrence and development of depression syndrome. Yuan Peng [8] and others analyzed coronary heart disease complicated with diabetes from the perspective of "blood pulse heart spirit". They believed that the comorbidity of heart and spirit was always carried out in the evolution of coronary heart disease complicated with diabetes. After a long time of thirst depletion, the blood vessels lost harmony, the heart was out of care, and the function of heart and blood vessels was disordered, which led to the loss of care, unwilling to give up to the heart, confusion, weakening of spirit, consciousness, and thinking activities. The loss of clarity of mind would damage the heart, and the loss of blood vessel support would also damage the spirit, Clinical patients often have chest pain, pain without a definite place, mental depression, emotional anxiety and other symptoms. Depression leads to the imbalance of Qi and ultimately aggravates the harm of coronary heart disease combined with diabetes. Professor gaoyanbin pointed out from the perspective of collateral disease that diabetes mellitus complicated with depression has two characteristics of "form disease" and "spirit disease", and "collateral disease" is the pathological basis of "form" and "spirit"; In the early stage of diabetes, depression can be induced by emotional disorders and stagnation of collaterals and Qi; In the middle and late stages of diabetes, due to the loss of viscera, long-term illness and collaterals, or emotional failure, pathological changes such as collateral qi stagnation, collateral stasis, collateral Qi deficiency and stagnation, and collateral vessel failure can occur, on the contrary, depression will appear or aggravate [9]. The Confucian School of marriage said: "those who quench thirst... Consume their spirit, go against their standards, and become dry, hot and gloomy". Due to the deficiency of yin and Yang in Zang Fu organs caused by chronic illness of "Xiaoke", the long-term illness enters the collaterals, and the accumulation of pathological products such as phlegm, turbidity, blood stasis and toxin, thus causing the emotional state to be dominated by deficiency, Qi deficiency and essence deficiency, showing depression such as mental depression and body function decline, while the accumulation of pathological products such as blood stasis and phlegm turbidity can lead to the complications of chest pain and other diseases, further damage the mind and spirit, and aggravate the depression syndrome.

4. Mechanism research

4.1. Signal pathway

4.1.1. MAPK signaling pathway

Mitogen activated protein kinase (MAPK) cascade signaling pathway is an important signaling system that mediates cellular responses, regulating complex cellular events such as cell proliferation, differentiation, apoptosis, etc; MAPK pathway activated by stress and other risk factors is closely related to the occurrence of depression. P38 pathway, a member of MAPK subfamily, is a classic inflammatory pathway. C-Jun N-terminal kinase (JNK) pathway can participate in apoptosis after activation. JNK is a stress activated serine threonine protein kinase of MAPK signaling pathway, and both can promote the occurrence of depression; Depression involves inflammatory factors such as tumor necrosis factor (TNF-α, Interleukin (IL)-1β, Interleukin (IL)-6, etc.), oxidative stress, neuroexcitotoxicity, glucocorticoids, and psychological stress events can regulate the activity of JNK. JNK is likely to be an important effector molecule for these upstream signals to regulate depressive behavior. various chronic stressors lead to decreased p-ERK and increased P-P38MAPK in the prefrontal cortex and hippocampus of experimental rodents. Studies have found that endoplasmic reticulum membrane protein complex 10 (emc10) can stimulate the growth of endothelial cells in cardiac explants of infarcted mice through p38 mapk-mk2 signaling pathway and promote tissue repair after myocardial infarction [10]. Estrogen can protect vascular endothelium and prevent coronary restenosis by promoting p42/44 and p38 MAPK phosphorylation, migration and proliferation. Diabetes can lead to vascular dysfunction through a variety of mechanisms. P38 MAPK may be a new target of vascular cells. Diabetes can activate p38 MAPK through dependent or independent protein kinase C (PKC) pathway, thereby mediating the occurrence and development of vascular complications. The activation of p38 MAPK in the liver of obese and diabetic mice can reduce endoplasmic reticulum stress, increase glucose tolerance and reduce blood glucose levels, while specific activators of p38 MAPK may help rebuild ER homeostasis and treat type 2 diabetes in obesity [11].

4.1.2. NF-κB signaling pathway

Nuclear transcription factor κB (NF-κB) Signaling pathways are important regulators of many physiological and pathophysiological processes, including innate immune response, inflammatory response, proliferation, tumor and apoptosis. Astrocyte dysfunction and inflammation are related to the pathogenesis of major depressive disorder. Relevant studies have confirmed that [12] astrocyte midbrain protein deficiency leads to NF-κB activation promotes IL-1 βThe production of NF-κB increases, resulting in depression like behavior, in which NF-κB inhibitors or IL-1β Receptor antagonists restored depression like behavior in brain protein deficient mice. NF-κThe activation of B is also one of the important mechanisms for the occurrence and development of atherosclerosis. Studies have shown that [13] rats with depression can activate the inflammatory factor NF-κThe expression of B promotes the occurrence and development of coronary heart disease, and antidepressant treatment can reduce the level of inflammatory biomarker high-sensitivity C-reactive protein (hsCRP) in peripheral blood and vascular tissue. After coronary expansion, lipid-lowering, antiplatelet aggregation and other drug treatments, NF-κ The level of B activity was significantly lower than that before treatment, indicating that NF-κB activity level has a certain value in the treatment of coronary heart disease [14]. Inflammatory molecules and their NF-κB is thought to play an important role in diabetes induced cardiac dysfunction. Experimental studies showed that [15] NF on diabetic mice-κB blockade directly alleviates oxidative stress and improves mitochondrial structural integrity by downregulating increased oxygen free radicals, thereby increasing ATP synthesis, thereby restoring cardiac function in type II diabetes. These findings suggest that NF-κB may be an important molecule causing end organ damage in type II diabetes.

4.2. Inflammatory response

The inflammatory response and the occurrence of mental diseases such as depression have a two-way impact. When the body is under stress, it can cause the activation of the central and peripheral immune system. The immune cells of the central nervous system, including glial cells, neurons and astrocytes, produce cytokines, and the secretion of IL-6, TNF, IL-1B, interferon (IFN) and IL-10 increases. The excessive activation of inflammatory cytokines will disturb a variety of neuronal functions, Including damage to neurotransmitter signaling, synthesis, and reuptake and release of neurotransmitters [16]. This in turn affects neural circuit functions, including those related to emotion and cognition, and early inflammation leads to the dysregulation of microglial phagocytosis, thereby promoting the development of depression like symptoms in adolescence [17]. Proinflammatory cytokines play an important role in the

pathogenesis of depression. It has been confirmed that proinflammatory cytokines mainly cause depression by affecting monoamine neurotransmitters, hypothalamic pituitary adrenal axis (HPA) and reducing brain-derived neurotrophic factor (BDNF) [18]. In the event of infection, cancer or autoimmune disease, the production of proinflammatory cytokines by immune cells acting on the brain may also lead to the deterioration of the disease and the development of individual depressive symptoms [19]. At present, the elevated level of proinflammatory cytokines has also become one of the markers to judge the onset of depression. Some studies have found that in patients who experienced acute coronary events, the level of soluble intercellular adhesion molecule-1 (sICAM-1), a marker of endothelial activation, was significantly higher in patients with depression than in patients without depression. This relationship was particularly evident in those who experienced first-time depression. Because taking statins was associated with the reduction of C-reactive protein, in patients who did not take statins. The level of C-reactive protein in depressed patients was twice that in non depressed patients. This study showed that depression was associated with higher levels of inflammatory markers in patients recovering from acute coronary syndrome [20]. Inflammatory factors also mediate the occurrence of diabetes mellitus complicated with depression. Diabetic patients often have chronic inflammation, that is, show inflammatory factors such as TNF-α, Increased levels of IL factors [21].

4.3. HPA axis malfunction

The HPA axis is associated with the pathophysiology of anxiety and depression as well as cognitive function. This axis consists of a stimulus forward and feedback inhibitory loop, involving the brain, pituitary gland and adrenal gland, regulating the production of mineralocorticoids and glucocorticoids. Some studies have found that [22] hpa axis genetic variation and activity are important predictors of cognition in the whole depressed subjects and healthy control group samples. Among them, the genetic variability of the gene encoding glucocorticoid is associated with attention and working memory, while the genetic variability of the gene encoding mineralocorticoid is associated with verbal memory. Psychosocial stress is one of the risk factors of coronary heart disease. In healthy elderly subjects without a history of coronary heart disease or objective signs, increased cortisol reactivity is associated with coronary artery calcification. These findings support the hypothesis that hyperresponsiveness of the HPA axis is one of the mechanisms by which psychosocial stress may affect the risk of coronary heart disease [23]. In addition, HPA axis hyperactivity causes sustained elevation of atch and GCS, which can lead to glucose metabolism disorders and insulin resistance, and further accelerate the subsequent development of diabetes [24]. And there is increasing evidence that depression and type 2 diabetes have a common biological origin, including the dysregulation of hypothalamic pituitary adrenal axis [25].

4.4. Neurotrophic reduction

BDNF plays an important role in the development, response and neuronal differentiation of the central nervous system. A large meta-analysis [26] found that the serum BDNF concentration of patients with depression was abnormally low and normalized by antidepressant treatment. These findings are thought to reflect the peripheral manifestations of the neurotrophin hypothesis, which states that depression is secondary to changes in BDNF expression in the brain. The antidepressant ketamine can increase the expression of nrbp1, BDNF and phosphorylated cAMP response element binding protein (p-CREB) /creb in primary microglia culture through the activation of extracellular signal regulated kinase (ERK) [27]. BDNF is also expressed in several non neuronal tissues, and it can play an important role in other processes, such as angiogenesis. Platelets are the main source of peripheral BDNF. In the hippocampus of adult mice receiving peripheral BDNF, BDNF levels and the expression of pCREB and perk were elevated. These results suggest that peripheral / serum BDNF may not only serve as a biomarker of depression, but also have functional effects on molecular signaling substrates, neurogenesis and behavior [28]. Studies have shown that compared with healthy individuals, the serum level of BDNF in patients with coronary heart disease decreased significantly, and compared with patients with coronary heart disease without depression, patients with depression in coronary heart disease still had a similar trend. Multiple logistic regression analysis and the negative correlation between BDNF and PHQ-9 score further highlighted its key role in the development of depression in patients with coronary heart disease [29]. In addition, individuals with diabetes mellitus complicated with depression often show reduced levels of BDNF, and the lower the expression level of BDNF, the higher the degree of depression. However, whether the relationship between BDNF and depression may be mainly mediated by the relationship between depression and platelet activation is still controversial, and more research is needed to evaluate the complexity of the relationship between BDNF and platelet reactivity and its possible impact on the peripheral levels of some diseases (such as depression) [30].

4.5. Oxidative stress

Oxidative stress is the result of the imbalance between the generation of reactive oxygen species (ROS) and the antioxidant defense system. ROS plays an important role in vascular intimal thickening, vascular remodeling, arterial vascular injury, and myocardial ischemia / reperfusion injury. The accumulation of ROS eventually leads to cardiomyocyte damage and cardiovascular events [24]; However, the glucose metabolism in diabetic patients is disordered. Excessive glucose or fatty acid oxidation can lead to excessive ROS generation, which leads to the imbalance of peroxidation products and antioxidant defense system in the body, exacerbates tissue oxidative damage, and then causes pancreatic islets in diabetic patients βCells are dysfunctional and disrupt insulin signaling [31]. In addition, when oxidative stress occurs in patients with diabetes mellitus complicated with coronary heart disease, it is easy to cause no imbalance, and then lead to vascular endothelial damage, accelerating disease progression. In addition, the patient's body's antioxidant capacity is decreased, causing damage to arterial vascular endothelial cells, rapid proliferation of smooth muscle cells, increasing blood lipids and decreasing blood flow velocity, further promoting the occurrence of coronary heart disease [32]. At the same time, excessive oxygen free radicals in the body can promote individuals to produce depression like behavior by damaging DNA and RNA of cells, activating inflammatory factors, inducing apoptosis and other pathways [33].

4.6. Insulin resistance

Insulin resistance refers to the need to maintain normal glucose tolerance with a higher than normal blood insulin release level, indicating that the ability of body tissues to process glucose with insulin is reduced. Now research has proved that it is related to abdominal obesity, lipid metabolism disorder, hypertension and abnormal glucose tolerance. The modern "common soil" theory [34] believes that "insulin resistance" is the initiating factor, and hyperinsulinemia is the common soil of coronary heart disease and type 2 diabetes mellitus. Its pathological mechanism is mainly related to the disorder of glucose and lipid metabolism of cardiomyocytes under high glucose environment, and the electrophysiological abnormalities of cardiomyocytes caused by changes in energy metabolism. Hrnciar [35] found that 74.3% of patients with macrovascular lesions of coronary artery disease had insulin resistance. In addition, adipocytes in patients with type 2 diabetes also show insulin resistance, with continuous fat dissolution, elevated free fatty acids and transported to the liver, resulting in increased liver derived very low-density lipoprotein cholesterol, which eventually leads to the aggravation of atherosclerosis [36]. Insulin resistance can also increase the risk of depression, and some scholars believe that [37] brain insulin signaling disorder will affect brain circuits related to emotion, causing depression and other psychiatric diseases.

4.7. Dysbiosis of intestinal flora

Gut microbiota is the general name of all microorganisms parasitic in the human gut, which is essential to maintain the health of the body. Dysbiosis of gut microbiota can change the host gut microbiota interaction and the host immune system. Studies have found that changes in gut microbiota may lead to depression. There are significant differences in gut microbiota between patients with depression and healthy people, and the diversity and abundance of gut microbiota in patients with depression are significantly decreased compared with healthy people [38]. Intestinal flora may induce depression by mediating inflammation, activating HPA axis and regulating neurotransmitters. In the metagenomic association analysis of gut microbiota and type 2 diabetes, it was found that Dysbiosis of gut microbiota was prevalent in pre diabetes and type 2 diabetes patients [39]. At the same time, changes in intestinal flora can control brain insulin signaling and metabolite levels, which will lead to changes in neurobehavior and thus induce the onset of depression [40]. Dysbiosis of intestinal flora can directly induce atherosclerosis, but also indirectly lead to coronary artery disease by inducing hypertension, lipid metabolism disorders, obesity and other risk factors of coronary heart disease [41]. However, due to the complexity of gut microbiota, what role does gut microbiota play in depression, coronary heart disease and diabetic comorbidity need further exploration.

4.8. Behavioral abnormalities

Patients with depression often lose interest in the things around them and are lazy to talk and move less. This behavioral abnormality may promote the development of coronary heart disease and diabetes. In the evaluation of depressive symptoms and long-term follow-up of 5888 elderly people, it was found

that physical activity and depressive symptoms were both independent predictors of cardiovascular disease mortality, and there was a strong correlation between the two [42]. Patients with coronary heart disease complicated with depression have poor compliance and cannot effectively follow the doctor's advice to take drugs. In addition, such patients are more likely to smoke and drink alcohol. The above behavioral abnormalities increase the possibility of coronary heart disease. In addition, diabetic complications are positively correlated with patients' anxiety and depression. When diabetic patients are complicated with depression, patients are usually accompanied by poor blood glucose monitoring, cognitive dysfunction, low mood, reduced activity, etc, and psychosocial support can help relieve the psychological pressure of diabetic patients and reduce the occurrence of negative emotions such as depression [43].

5. Summary and Outlook

In conclusion, depression, as one of the important mental diseases, is closely related to coronary heart disease and diabetes. Depression, coronary heart disease and diabetes mellitus are manifested in heartache due to depression, diabetes due to depression, depression due to disease, etc. relevant studies have shown that MAPK signaling pathway, NF- κ B signaling pathway, inflammatory response, HPA axis dysfunction, neurotrophic reduction, oxidative stress, insulin resistance, intestinal flora imbalance, and behavioral abnormalities play important roles in the pathological mechanism of its comorbidity. The above mechanisms complement each other and cross link with each other, forming a complex causal network. At present, through research, it is found that intervention in depression can improve the symptoms and prognosis of patients with coronary heart disease and diabetes, which may be closely related to the reduction of stressors. Stress induced by stress can lead to the activation of a series of enzymatic cascade signaling pathways, resulting in the pathological manifestations of depression, coronary heart disease and diabetes, Therefore, it is expected to provide broad prospects for its treatment to find and intervene the common signaling pathway mechanism among the three.

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