

# Treating Precursor of Stroke from the Syndrome of Liver Heat and Blood Stasis

Gaofeng Wang<sup>1</sup>, Yifan Yang<sup>2</sup>, Jie Rong<sup>2</sup>, Ruihua Yuan<sup>1</sup>, Yongmei Yan<sup>1,\*</sup>

<sup>1</sup>Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

<sup>2</sup>Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China

\*Correspondence Author

**Abstract:** *The theory of liver heat and blood stasis is one of the characteristic theories in traditional Chinese medicine (TCM) for understanding, preventing, and treating stroke. This article starts from the physiological and pathological relationships between the liver and the kidney and the connection between the liver, kidney, and brain in TCM, elaborates on how the syndrome of liver heat and blood stasis affects the precursor of stroke, and presents relevant modern clinical application studies.*

**Keywords:** Precursor of stroke, Liver heat and blood stasis, Clinical research.

## 1. Introduction

Stroke, ranking first among the four intractable diseases in TCM, has an extremely high incidence rate both in China and worldwide. It has numerous sequelae, a high recurrence rate, and is difficult to fully recover. According to the latest Global Burden of Disease report, stroke has become the third leading cause of death and disability globally [1]. The precursor of stroke is different from stroke itself. Stroke, as one of the most common neurological diseases, has an acute onset, a short optimal treatment time window, and a high risk of developing into a complete stroke. Therefore, it is of great significance to detect and seek medical treatment in a timely manner when there are precursors of stroke before its onset to prevent the aggravation of the condition. Emphasizing "preventive treatment of disease" and focusing on prevention is of great practical importance.

## 2. The Understanding of Stroke Precursor in Modern Medicine

The precursor of stroke, also known as "minor stroke", refers to the symptoms and signs that appear before a stroke. It is equivalent to transient ischemic attack (TIA) in modern medicine. TIA is an ischemic encephalopathy caused by focal ischemia of the brain and retina, resulting in transient neurological dysfunction, and it is a high-risk factor for cerebral infarction. Patients with stroke precursors usually have short-duration symptoms that mostly recover spontaneously without leaving residual damage symptoms, and many imaging examinations do not show obvious responsible lesions [2]. Modern scholars believe that TIA occurs when multiple risk factors such as atherosclerotic plaques, abnormal hemorheology, and changes in vascular dynamics act on the carotid artery system or the vertebrobasilar artery system [2]. The main manifestations of stroke precursors include transient dizziness, headache, limb numbness, weakness, slow movement, slurred speech, sudden fainting or falling, changes in mental state, and involuntary limb twitching. Liu Wansu believed that people who suffer from stroke usually have precursor symptoms. If a person feels numbness in the thumb and index finger, or has difficulty moving the hands and feet, or experiences involuntary muscle twitching, there is a high risk of a severe

stroke within three years [3]. This article focuses on explaining the mechanism of the "liver heat and blood stasis" syndrome in the occurrence and development of stroke and introducing relevant clinical studies.

## 3. The Mechanism and Significance of Stroke Precursor from the Perspective of Traditional Chinese Medicine

The record in "Suwen-Tiaojing Lun" that "muscle tremors are called slight wind" may be the earliest description of stroke precursor syndrome. Stroke precursor syndrome is a mild form of stroke and has the same etiology as stroke. It is the basis and premise of stroke. Its essence lies in the disorder of qi movement and the unsmooth blood circulation in the body under the influence of various factors, and even the formation of blood stasis. Therefore, the basic principles of treatment in clinical practice are to regulate qi movement and promote blood circulation to remove blood stasis [4]. The common syndromes of stroke precursors are as follows: patients over middle age experience dizziness, blurred vision, hemilateral numbness, transient slurred speech, transient limb weakness, constipation or unsmooth defecation. The tongue is usually light purple or dark purple, with ecchymoses and petechiae under the tongue, and the pulse is wiry and slippery (firm) or fine and unsmooth (slow) [5]. Modern research has also confirmed the close relationship between emotional disorders and stroke. A controlled study by Feng Yufang et al. showed that the mental health status of stroke patients before the onset was poor, and their scores of negative emotions such as depression, anxiety, and somatization were significantly higher than those of the normal group, suggesting that negative emotions may be a risk factor for stroke [6]. Through the analysis of the symptom combination patterns of stroke precursor syndrome, the combination of "irritability/agitation/restlessness - transient symptoms" has the highest frequency, and the syndrome factor belongs to "fire (heat) - wind"; "dry mouth and bitter taste - irritability/agitation/restlessness" and "foul breath - dry mouth and bitter taste" are all fire (heat) syndromes in terms of pathogenesis [7]. In patients with stroke precursors, liver heat can lead to the upward flaring of liver fire and disturb the mind. Because the fire pathogen has the characteristic of flaring upward, the disturbance of the mind by liver heat can

cause restlessness and irritability. Long-term liver heat will consume liver yin, resulting in liver yin deficiency. The liver is yin in nature and yang in function. The deficiency of liver yin will lead to the abnormal function of liver qi in dredging and regulating, which will then cause emotional depression. It is often accompanied by symptoms such as dull pain in the costal region, dizziness, dry eyes, and blurred vision. These physical discomforts will further aggravate the emotional depression, forming a vicious cycle.

#### **4. Liver Heat and Blood Stasis is the Core Pathogenesis of Stroke Precursor**

The syndrome of liver heat and blood stasis was proposed by Zhang Xuewen, a master of traditional Chinese medicine, when treating stroke precursors [8]. Master Zhang pointed out that although the etiology and pathogenesis of stroke are relatively complex, the blood stasis factor is the key link. The cerebral collaterals are the pathways for qi, blood, and body fluids to nourish the brain marrow. The obstruction of the cerebral collaterals by blood stasis will affect the clear yang of the brain, resulting in the failure of qi, blood, and body fluids to nourish the brain marrow and the loss of nourishment of the spirit, which is similar to ischemic stroke in modern medicine. If the blood stasis is severe and the collaterals are broken and bleeding occurs, it is similar to hemorrhagic stroke. Pathological changes such as cerebral vasospasm, cerebral infarction, cerebral thrombosis, cerebral embolism, and cerebral hemorrhage all fall within the scope of blood stasis in TCM. Therefore, blood stasis runs through the entire process of stroke. As for liver heat, it is mainly due to the fact that stroke patients usually have a preference for greasy and rich foods and a sedentary lifestyle, which leads to the failure of the spleen in transportation and transformation, the generation of phlegm-dampness, and the unsmooth blood vessels. Over time, phlegm turbidity and blood stasis combine to cause problems, further hindering the movement of pectoral qi and making it difficult for essence and blood to be replenished. This leads to the aggravation of liver-kidney yin deficiency, the failure of water to nourish wood, and then the hyperactivity of liver yang and heart fire, or the generation of wind causing dizziness and numbness of the limbs, which is the origin of liver heat. In general, the syndrome of liver heat and blood stasis is the main cause of stroke precursor syndrome. The liver heat syndrome mainly includes liver qi depression transforming into heat, liver yang hyperactivity, and liver-kidney yin deficiency. Blood stasis refers to the state of blood stasis in the blood vessels. Modern medicine believes that the pathological basis of the stroke precursor stage is atherosclerosis. The formation of microthrombi, changes in hemodynamics and blood components, and cerebral vasospasm can all affect the blood flow in the blood vessels, which is highly consistent with the characteristics of blood stasis syndrome in TCM, that is, the sluggish blood flow in the blood vessels or the accumulation of blood outside the blood vessels in the body [10].

In TCM theory, the liver stores blood, dominates tendons, and has the function of regulating the blood circulation of the whole body. It also dominates the dredging and regulating of qi and is the pivot of the qi movement of the whole body. Stroke patients often have factors such as high life pressure, excessive work, and irregular daily life, which lead to

emotional distress, disrupt qi movement, and cause the dysfunction of the qi and blood of the zang-fu organs. The abnormal function of liver qi in dredging and regulating leads to qi stagnation, which transforms into heat, resulting in the hyperactivity of liver yang and the damage of liver yin. Long-term illness will affect the kidney, leading to kidney yin deficiency, forming liver-kidney yin deficiency, and the sluggish blood flow will cause blood stasis. Or the liver qi transversely invades the spleen, causing the spleen to fail in transportation and transformation and the generation of phlegm turbidity. The liver-kidney yin deficiency can also generate internal heat or the transformation of phlegm-qi stagnation into fire. Or the sudden rise of liver yang can trigger the heart fire, the hyperactivity of liver yang can cause yang transforming into wind, and finally form the syndrome of liver heat and blood stasis. Most stroke patients are middle-aged and elderly. After middle age, the healthy qi gradually becomes deficient. The internal damage and accumulated deficiency often lead to liver-kidney deficiency. The kidney stores the essence of the five zang-organs and six fu-organs and is the root of the yin and yang of the human body. Kidney deficiency will affect the production and operation of qi and blood. The deficiency of primordial qi will lead to the inability to promote blood circulation and cause blood stasis.

TCM believes that the liver and the kidney have a close relationship. Zhang Lu in the Qing Dynasty clearly stated in "Zhang Shi Yi Tong · Zhu Xue Men" that "qi that is not consumed is transformed into essence in the kidney, and essence that is not leaked is transformed into clear blood in the liver" and "the monarch fire is unique and is the heart. There are two ministerial fires, which are the kidney and the liver... Therefore, it is known that when qi is excessive, it becomes fire, and the meaning of the homology of liver and kidney is more clearly understood" [11,12]. "The Inner Canon of Huangdi" records that "in the north, cold is generated, cold generates water, water generates saltiness, saltiness generates the kidney, the kidney generates bone marrow, and bone marrow generates the liver", which reflects the close physiological relationship between the liver and the kidney. That is, the kidney stores essence, dominates bone and generates marrow, and the marrow generates liver blood. The kidney nourishes the liver through the marrow. The liver and the kidney have the same origin in essence and blood, so they are called "homologous of liver and kidney" (homology of liver and kidney). The liver and the kidney not only have a close physiological connection but also affect each other pathologically. For example, "Ling Shu · Ben Shen" states that "the liver stores blood, blood houses the soul, liver qi deficiency leads to fear" and "if fear persists, it will damage essence, and essence damage will lead to bone soreness, weakness, and cold limbs" [13]. Modern animal experiments have shown that by establishing a rat model of liver-kidney essence and blood deficiency and treating it with Zuogui Pill, which has the functions of tonifying the kidney and filling essence and nourishing the liver and enriching blood, the damage to the hypothalamus was protected to a certain extent, the liver regeneration and hematopoietic function were enhanced, and anemia was improved, verifying the mechanism of "homology of liver and kidney" and "generation of essence and blood" [14]. The liver and the kidney are connected with the brain through "marrow". Zhang

Jingyue explained that "among all the bones with marrow, the brain has the largest amount of marrow, so the brain is the sea of marrow". Because "the kidney generates bone marrow" and "the brain is the confluence of marrow", the brain and marrow have the same origin and are both generated by kidney essence. The kidney nourishes the liver through the marrow and is regulated by the brain [15,16]. Zhao Xianke mentioned in "Yi Guan" that there is a small orifice on the left side of the body. The true yin and true water qi in it ascend through the paravertebral region to the brain and become the sea of marrow, secreting body fluids to nourish the whole body, which reflects the TCM theory of "the connection between the liver, kidney, and brain" [17]. The liver and the kidney have the same origin. Kidney yin nourishes liver yin to maintain the balance of liver yang. If kidney yin is deficient and cannot restrain liver yang, water fails to nourish wood, liver yang will become hyperactive, and even liver wind may be generated internally (wind stirring due to yin deficiency). Patients may experience symptoms such as soreness and weakness of the lower back and knees, dizziness, tinnitus, finger tremors, headache, and limb tremors. The disharmony of the zang-fu organs and the deficiency of ying and wei can lead to stroke [18].

## 5. Clinical Application

The theory of liver heat and blood stasis is one of the characteristic theories in TCM for treating stroke precursors and plays an important role in clinical practice. Based on the pathogenesis of liver heat and blood stasis, Master Zhang pointed out that clearing the liver and promoting blood circulation is the key to symptomatic treatment and created the Nao Qing Tong Decoction. In a clinical controlled study, the western medicine group was given Aspirin Enteric-coated Tablets (Bayer Healthcare Co., Ltd., National Drug Approval Number J20080078, Specification: 100 mg/tablet) 100 mg + Clopidogrel (Lepu Medical, National Drug Approval Number B190917A2, Specification: 75 mg/tablet) 75 mg + Atorvastatin 20 mg [Qilu Pharmaceutical (Hainan) Co., Ltd., National Drug Approval Number H20193144, Specification: 20 mg/tablet] orally, once a day. The Nao Qing Tong Decoction group took the Nao Qing Tong Decoction on the basis of the western medicine group. The composition of the Nao Qing Tong Decoction includes Radix Salviae Miltiorrhizae 15 g, Semen Cassiae 20 g, Hirudo 6 g, Rhizoma Chuanxiong 10 g, Radix Paeoniae Rubra 12 g, Rhizoma Pinelliae Preparatum 12 g, Fructus Crataegi 15 g, Massa Medicata Fermentata 30 g, Flos Chrysanthemi Indici 15 g, Herba Siegesbeckiae 30 g, Rhizoma Acori Tatarinowii 8 g, and Radix Glycyrrhizae 6 g. It was decocted and taken in divided doses, once a day. The course of treatment for both groups was 2 weeks. The results showed that in the Nao Qing Tong Decoction group, 6 cases were cured, 16 cases had marked effects, 6 cases were effective, and 2 cases were ineffective, with a total effective rate of 93.33% (28/30); in the western medicine group, 2 cases were cured, 10 cases had marked effects, 8 cases were effective, and 10 cases were ineffective, with a total effective rate of 66.67% (20/30). There was a significant difference in the total effective rate between the two groups ( $P < 0.05$ ) [19].

The syndrome of liver heat and blood stasis is not only reflected in stroke precursors but also in stroke sequelae,

especially post-stroke depression. In TCM, the presence of blood stasis is usually related to the disorder of qi movement. Qi and blood are the concrete manifestations of yin and yang. The harmony of qi and blood ensures the balance of yin and yang in the body and the absence of diseases. "Suwen·Tiaojing Lun" states that "what a person has are only blood and qi". Qi can promote blood circulation, and blood can carry qi. Qi deficiency leads to sluggish blood flow, and blood deficiency leads to weak qi. The liver dominates the dredging and regulating of qi and is closely related to the normal operation of qi and blood. It also regulates emotions. Patients with post-stroke depression are usually in a state of emotional dissatisfaction, which will inevitably affect the physiological function of the liver in dredging and regulating qi. The abnormal function of liver qi in dredging and regulating leads to qi stagnation, which damages yin and yang and causes blood stasis due to the stagnation of qi and blood. Or the long-term qi stagnation transforms into fire, burning the yin fluid, making the blood vessels astringent and the blood flow unsmooth, resulting in blood stasis. Or patients are usually emotionally depressed for a long time and easily become angry, leading to the hyperactivity of liver fire, the sudden rise of liver yang, the retrograde flow of qi, and the disorder of blood flow, resulting in blood stasis. Or the elderly have liver-kidney deficiency, the kidney yin is insufficient to restrain the liver yang, the liver yang is hyperactive, and the blood flow is disordered, resulting in blood stasis [20]. After a stroke, the liver qi is in disorder, qi and blood are disharmonious, and emotions are not smooth. The pathogenesis is the combination of qi stagnation, internal heat generation, and the residual heat of liver yang hyperactivity, resulting in the syndrome of liver heat and blood stasis and depression. In clinical practice, the treatment method of clearing the liver, extinguishing wind, promoting blood circulation, and regulating qi has achieved remarkable effects in treating post-stroke depression with the syndrome of liver heat and blood stasis [21].

## 6. Conclusion

Stroke remains a major global health problem, especially prominent in China. It has an acute onset, a short treatment window, and is prone to leave various sequelae. Analyzing the pathogenesis evolution of liver heat and blood stasis in stroke precursors from the perspective of TCM theory is of great significance for the development of TCM theory and clinical treatment. Through the analysis of the pathogenesis of stroke precursors, the exploration of syndrome patterns, and the summary of treatment methods, it is clear that "liver heat and blood stasis" is the core pathogenesis of stroke precursors and runs through the entire process of stroke. Conducting research on stroke precursors based on this can contribute to the innovation of TCM theory and provide effective TCM treatment strategies for the prevention of stroke.

## Fund Project

2024 Central Public Health Development Project: Construction Project of Real World Clinical Research Center for Traditional Chinese Medicine. Project leader: Yuan Ruihua, Shaanxi University of Chinese Medicine.

## References

- [1] Abdelwahab A, Abedi A, Aboagye R G, Ahmad D, Alam K, Alemayohu M A, et al. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet (British Edition)* 2024;403(10440):2100 - 2132.
- [2] Mayer L, Ferrari J, Krebs S, Boehme C, Toell T, Matošević B, et al. ABCD3 - I score and the risk of early or 3 - month stroke recurrence in tissue - and time - based definitions of TIA and minor stroke. *Journal of Neurology* 2024;265(0340 - 5354):530 - 534.
- [3] Liu Wansu. *Suwen Bingji Qiyi Baoming Ji*. Publishing House of Ancient Chinese Medical Books; 1998.
- [4] Zhang Xuewen, Tao Genyu, Li Jun, Kuang Shixiang. Research on the onset law of stroke precursor syndrome. *Journal of Emergency in Traditional Chinese Medicine (China)* 1993(01):7 - 15.
- [5] Zhang Xuewen, Li Jun, Tao Genyu. Theoretical, clinical and experimental research on stroke precursor syndrome and Qingnao Tongluo Tablets [C]. Chengdu, Sichuan, China: 1996.
- [6] Feng Yufang, Duan Ni, Liu Caixing, Feng Laihui. Influence of mental health status on the onset of stroke. *Acta Academiae Medicinae Qingdao Universitatis (China)* 2012;48(06):505 - 506.
- [7] Wang Yizhan, Fan Jiping, Xie Yingzhen, Chen Tingting. Research on syndrome rules of stroke precursor syndrome based on data mining. *Jilin Journal of Traditional Chinese Medicine (China)* 2017;37(02):136 - 140.
- [8] Sun Jingbo, Fu Wenbin, Hua Rong, Li Jun. Experience of Professor Zhang Xuewen in treating stroke precursor syndrome from liver heat and blood stasis. *Journal of Emergency in Traditional Chinese Medicine (China)* 2005(02):155.
- [9] Wen Ya. Experience summary of Professor Zhang Xuewen in treating liver heat and blood stasis syndrome of stroke precursor. *Clinical Journal of Traditional Chinese Medicine (China)* 2013;5(15):67 - 68.
- [10] Zhou Haizhe, Zhao Huan, Yan Yafeng. Analysis of the thought of Professor Zhang Xuewen in treating stroke precursor from heat stasis. *China Journal of Traditional Chinese Medicine and Pharmacy* 2022;37(07):3928 - 3931.
- [11] Zhang Lu. *Zhang Shi Yi Tong*. People's Medical Publishing House; 2023.
- [12] Luo Yun. Brief introduction to the origin and development of the theory of homology of liver and kidney. *Journal of Traditional Chinese Medical Literature (China)* 2012(01):16 - 18.
- [13] Li Ping. Brief discussion on the scientific connotation of the theory of homology of liver and kidney [C]. Shenzhen: 2014.
- [14] Li Hanmin, Zhang Liutong, Qiu Xingfan, Mei Jiajun, Wang Ping. Mechanism study of Zuogui Pill in improving liver - kidney essence and blood deficiency syndrome of MSG - liver regeneration - rats. *Journal of Hubei College of Traditional Chinese Medicine (China)* 2001;3(4):30 - 33.
- [15] Li Xiaoqian, He Jiancheng. Tracing the origin of the theory of homology of liver and kidney. *Western Journal of Traditional Chinese Medicine (China)* 2019;32(09):45 - 49.
- [16] Zhang Jingyue. *Lei Jing*. China Medical Science and Technology Press; 2011.
- [17] Sun Jianhong, Xu Chuanlian. Discussion on the relationship between the theory of "homology of liver and kidney from the brain" and the pathogenesis of stroke. *Journal of Emergency in Traditional Chinese Medicine (China)* 2008(04):485 - 486.
- [18] Li Hanmin, Zhang Liutong, Qiu Xingfan. Research on the essence of liver and kidney and the theory of "homology of liver and kidney from the brain". *Journal of Traditional Chinese Medicine (China)* 2000(02):69 - 71.
- [19] Fan Xiaohui, Liu Hua, Qing Hui, Fan Junming. Discussion on stroke from the theory of homology of liver and kidney. *Traditional Chinese Medicine Research (China)* 2016;29(03):5 - 7.
- [20] Zhao Huan, Zhou Haizhe, Pang Le. Clinical observation of Nao Qing Tong Decoction in treating liver heat and blood stasis type stroke precursor. *Western Journal of Traditional Chinese Medicine (China)* 2023;36(02):83 - 86.
- [21] Zhang Ziteng, Wang Dou, Feng Yalong, Yan Yongmei. Experience highlights of Yan Yongmei in treating post - stroke depression from liver heat and blood stasis. *Jiangsu Journal of Traditional Chinese Medicine (China)* 2022;54(05):44 - 47.
- [22] Li Jiankun, Xiao Chunfeng, Zhao Yaohui, Li Yuhong, Xiao Xu, Cui Wujun, et al. Efficacy of Qinggan Huayu Yin plus or minus combined with conventional western medicine in treating patients with liver heat and blood stasis type post - stroke depression and its influence on serum neurotransmitter levels. *Sichuan Journal of Traditional Chinese Medicine (China)* 2023;41(11):164 - 167.