

Professor Li Yingang's Experience in Treating Alcohol-induced Osteonecrosis of the Femoral Head with Modified Yanghe Decoction

Hongwei Wang^{1,a}, Yingang Li^{2,b,*}

¹Shaanxi University of Chinese Medicine, Xiayang, Shaanxi, 712046, China

²Affiliated Hospital of Shaanxi University of Chinese Medicine, Xiayang, Shaanxi, 712000, China

^a809202458@qq.com, ^bliyingang9633@163.com

*Corresponding author

Abstract: This paper introduces Professor Li Yingang's experience in treating alcohol-induced osteonecrosis of the femoral head with modified Yanghe Decoction. Professor Li Yingang believes that the pathogenesis of alcohol-induced osteonecrosis of the femoral head is mainly for phlegm, blood stasis, and kidney deficiency. Among these three reasons, phlegm and blood stasis are more important. Modified Yanghe Decoction is based on Yanghe Decoction. It adds drugs such as leech, rhizoma drynariae and radix dipsaci, which could nourish Yin, tonify blood and reduce phlegm. There is abundant evidence that the clinical curative effect of Modified Yanghe Decoction is distinct.

Keywords: Li Yingang; modified Yanghe Decoction; osteonecrosis of the femoral head; alcohol-induced osteonecrosis of the femoral head

1. Introduction

Osteonecrosis of the femoral head is one of the most orthopedic common refractory diseases, which is due to the interruption of blood supply of the femoral head or damage, leading to bone cells and bone marrow cell death and imperfect repair. It can cause femoral head structure change, the collapse of the femoral head, joint pain, and joint dysfunction [1], as shown in Figure 1 and Figure 2. According to Chinese first large-scale non-traumatic osteonecrosis, the cumulative death toll of traumatic ischemic necrosis patients has reached 8.12 million. The prevalence of men (1.02%) than women (0.51%). The prevalence of northern residents (0.85%) than of southern residents (0.61%). The prevalence of for urban dwellers than for rural residents. Overall age for Chinese patients with osteonecrosis of the femoral head aged (46.45±13.8), males (45.44±12.83) [2]. Epidemiological survey alcohol-induced osteonecrosis of the femoral head accounted for about 37% of all patients, patients with 86% being male; Compared with other types of osteonecrosis of the femoral head patients, patients with alcohol-induced osteonecrosis of the femoral head are younger, whose incidence of the contralateral progress may be faster, higher and may result in poor prognosis [3,4]. Accumulating evidence has revealed that alcohol consumption and risk of osteonecrosis of the femoral head into nonlinear positive correlation [5,6]. For early femoral head necrosis, modern medicine treatment usually adopts drugs such as oral alendronate [7], as well as hip replacement therapy. However the treatment cost is high, and the service life of artificial joint is also a problem [8]. Many investigation data demonstrated that traditional Chinese medicine has a satisfactory curative effect in delaying osteonecrosis of the femoral head progress and improving clinical symptoms.

Li Yingang is a supervisor postgraduate. He is a professor at the Shaanxi University of Chinese Medicine. And he is working in Shaanxi University of Traditional Chinese Medicine hospital. He engaged in clinical, teaching, and scientific research with more than 40 years of traumatology, and orthopedics disease of TCM and has higher academic attainments. His scholarly, experienced, and tireless, are good at using the party for various orthopedic diseases of traditional Chinese medicine. The author is very lucky to be able to study with Professor Li Yingang's interpretation of the properties of modified Yanghe Decoction syndromes and found the clinical drug curative effect is distinct. The author applied Professor Li Yingang's application of modified Yanghe Decoction in the treatment of alcohol-induced osteonecrosis of the femoral head necrosis of experience summed up as follows.

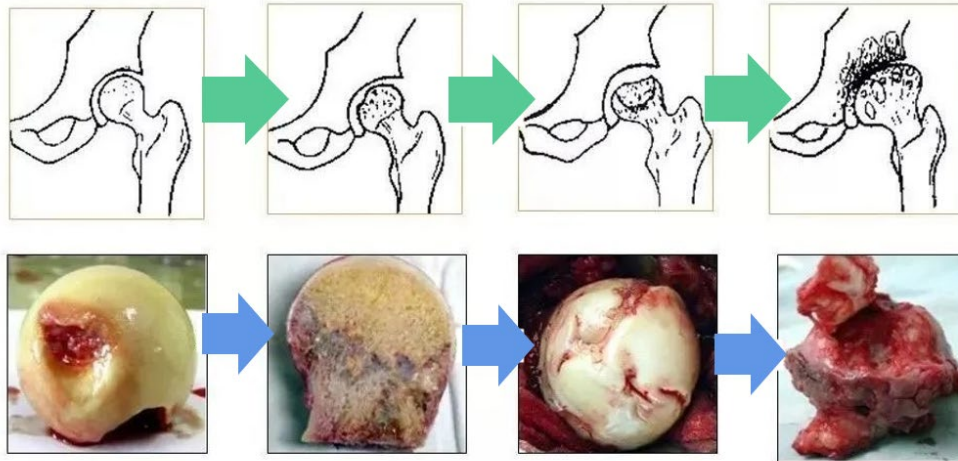


Figure 1: Pathological changes of osteonecrosis of the femoral head

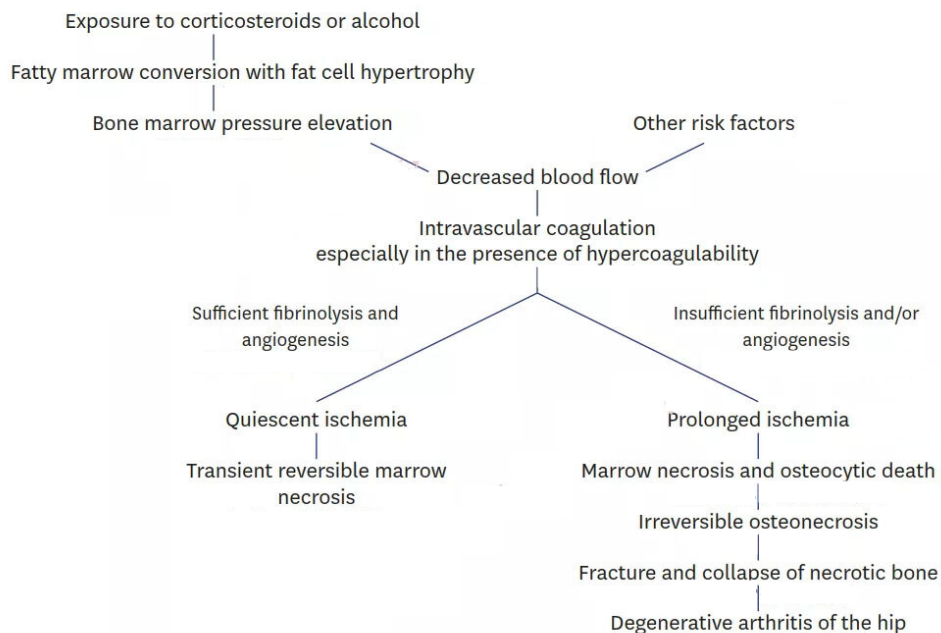


Figure 2: Pathogenesis of non-traumatic osteonecrosis of the femoral head

2. Summary of Yanghe Decoction

Yanghe Decoction was first recorded in the Life-saving Manual of Diagnosis and Treatment of External Diseases [9]. Yanghe Decoction's treatment of very extensive at present, the tumor, orthopedics, gynecology, and peripheral vascular disease have a good therapeutic effect. In Yanghe Decoction treating mastitis, breast cancer, and ankylosing spondylitis, joint pharmacological research, using modern science and technology methods has made great progress. It enriches the scientific connotation and pharmacological activity of the Yanghe Decoction and expands the research field of the Yanghe Decoction. Yanghe Decoction consists of rehmannia glutinosa, ephedra, antler glue, white mustard seed, ginger cinnamon, liquorice, etc. The Main effect is to nourish Yin blood and phlegm flux hysteresis. Modern professor of prescriptions of Chinese materia medica Chen Chaozu has in-depth research on Yanghe Decoction. He advocated drug hierarchical analysis, separately from marrow to blood and into muscle, cou justified, to fur and table is made by thorough analysis. Chen Chaozu thinks cultivated land can nourish Yin blood and fill in the pure pulp. Antler glue can fill JingXie and kidney Yang. Cultivated land and antler glue cooperate to make their efficacy, and Yin and Yang cooperation can make the effect of filling JingXie increased. The pharmacological levels in the bone marrow. Cinnamon has the function

of filling the kidney Yang, the pharmacological effects on veins. Ginger can tonify the spleen and nourish the muscles, to dispel cold evil invasion of muscle levels. White mustard can remove the lining membrane outside of phlegm and XuanTongCouLi. Ephedra can XuanTongMaoQiao. Used together like this can make bones, blood, muscle, CouLi, and MaoQiao unobstructed. Through these levels of nourishment and XuanTong makes a balance of Yin and Yang, Qi and blood, and semen run unobstructed. Clinical studies^[10] have shown that the use of Yanghe Decoction has a good clinical effect on early osteonecrosis of the femoral head.

3. The modern medicine understanding of alcohol-induced osteonecrosis of the femoral head

Ethanol is considered to be the main cause of alcohol-induced osteonecrosis of the femoral head^[11]. 25% ~ 45% of the patients with alcoholic avascular necrosis are associated with heavy drinking for a long time^[12]. It may need to rule out other related diseases before diagnosis. Diagnostic requirements are as follows^[13]: a: history of more than 6 months of alcohol; b: ethanol intake > 320 g per week; c: in addition to ethanol, exclude other risk factors. Osteonecrosis of the femoral head staging classification: for osteonecrosis of the femoral head pathophysiological progress a lot of staging methods. Association Research Circulation Osseous(ARCO) is recommended to use the 2019 newly released osteonecrosis staging system. The stage is shown in Table 1. Formed in 2019, ARCO is a revised "flow chart of osteonecrosis of the femoral head diagnosis" as the standard form of diagnosis. The stage is shown in Figure 3. Association for the study of the bone turnover stage is the most commonly used. Alcohol-induced osteonecrosis of the femoral head of the pain is mostly located around the hip. The hip and groin area may be accompanied by limited rotation around the knee and hip pain inside and outside. Patients often have a long history of alcoholism. Alcohol-induced osteonecrosis of the femoral head of the X-ray film in the early phase of bone sclerosis. Cystic change and "new moon", collapsed after femoral head loss of spherical shape, advanced degenerative arthritis lesions. Alcohol-induced osteonecrosis of the femoral head of the CT manifestations of normal alcoholic osteonecrosis femoral head is divergent bone transection, called "mount signs", ischemic necrosis of femoral head, trabecular bone damage, fracture, disappearance in the trabecular bone. CT characteristic of ischemic necrosis of femoral head "asterism" disappear. On the other hand, also can be observed within the femoral head cystic change. Characterized by low-density shadow, visible with high-density sclerosis, around late subchondral bone destruction, femoral head. Femoral head collapse deformation joint space narrowing. Alcohol-induced osteonecrosis of the femoral head of the MRI has high sensitivity, shown in T1 weighted image (T1WIS) cartilage under a linear low signal indicator is limited. Or in T2 weighted image (T2WIS) is shown as a "double-line sign"^[14]. Conforming to standard a, b, and c can clear alcohol-induced osteonecrosis of the femoral head diagnosis.

Table 1: ARCO is revised 2019 - stage osteonecrosis of the femoral head

Stage	Imaging findings	Detailed description
I	Normal X-ray	The dead zone around the strip lesions osteonecrosis of the femoral head of Abnormal MRI low signal intensity
	Abnormal MRI	Bone scan revealed osteonecrosis of the femoral head hot region exists between the cold area X-ray of normal osteonecrosis of the femoral head tips
II	Normal X-ray	(1) X-ray or CT scan, femoral head focal bone sclerosis, osteoporosis or cystic change osteonecrosis of the femoral head
	Abnormal MRI	Did not see the subchondral fracture, or femoral head necrosis part fracture flat signs of osteonecrosis of the femoral head
III	X-ray or CT tip	Subchondral fracture, fracture of necrosis and/or X-ray, a CT scan in the visible change osteonecrosis of the femoral head flat
	Subchondral fracture	—3A: the collapse of the femoral head≤2mm —3B: the collapse of the femoral head>2mm
IV	X-ray tip: hip arthritis	X-ray visible hip osteoarthritis with joint space narrowing, change, and destruction of osteonecrosis of the femoral head acetabulum

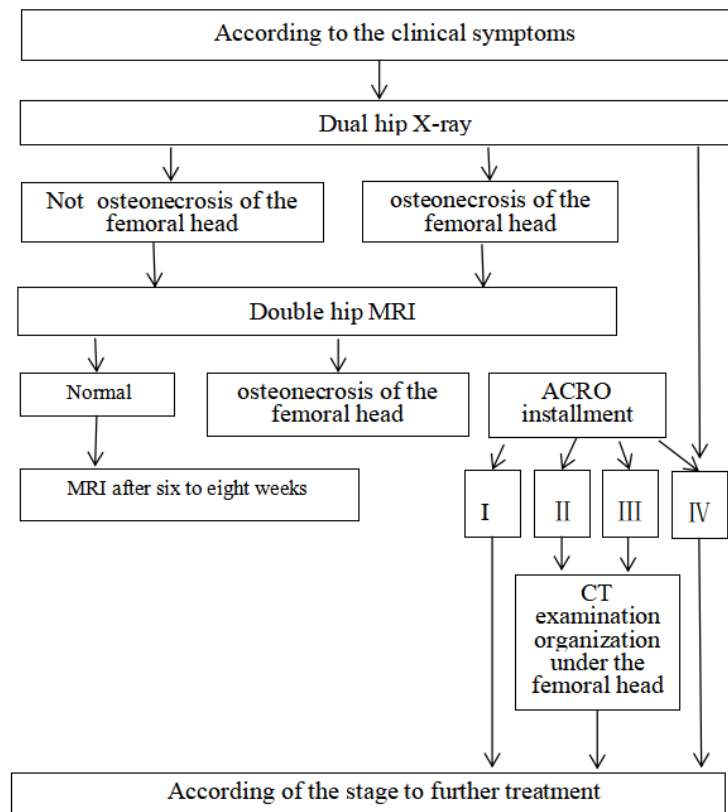


Figure 3: Osteonecrosis of the femoral head diagnosis process

4. Traditional medicine knowledge of alcohol-induced osteonecrosis of the femoral head

Traditional Chinese medicine to osteonecrosis of the femoral head of belonging to the "bone erosion" category. The pathogenesis of non-traumatic osteonecrosis of the femoral head, and traumatic osteonecrosis of the femoral head is blood stasis and kidney empty. Bone trauma can cause bone displacement to raise, kidney deficiency, vein stasis, and blood resistance; Patients with clinical manifestations of the main difficulties, hip restricted movement, and pain. Traditional Chinese medicine studies found that the kidney essence can be set, the Tibetan essence can be raw pulp, and the pulp can raise bone. If renal insufficiency, bone cannot be nourished which will lead to femoral head necrosis. Blood stasis resistance meridians lead to can't generate new blood, bone cannot be nourished, resulting in osteonecrosis of the femoral head. Professor Li Yingang thinks Yanghe Decoction in the treatment of alcohol-induced osteonecrosis of the femoral head is based on its pathogenesis. Zhang's medical said: "Alcohol is toxic and hot. " Roche will be about the medical mirror records: "Drink can consume spirit and blood. It can hurt a stomach, and let a person easy to anger. Drinking too much can make phlegmy, leading to the occurrence of many diseases. " Alcohol enters the body after the influence of Qi and blood, meridians and viscera function, the function of the liver, spleen, kidney disorders. Excessive drinking will consume the liver Yin blood, Liver Yin blood insufficient can cause kidney essence loss. Liver Yin blood and kidney essence insufficient can lead to kidney Yin deficiency, resulting in bone loss nourish, it damages the bones and muscles, resulting in osteonecrosis of the femoral head. Blood is burning into blood stasis, which can cause the meridians can't be smooth. Blood can't nourish the viscera and bone, resulting in bones and muscles loss of nourishment, and bone marrow along with; If the blood stasis lasts for a long time, it can change to heat. Heat can result in spleen deficiency and excessive phlegm-dampness. Humid and phlegm enter the bone, resulting in bone atrophy. A variety of pathogenic factors together eventually led to the alcohol-induced osteonecrosis of the femoral head.

5. Characteristics of interpretation and clinical features of modified Yanghe Decoction

Professor Li Yingang for the treatment of alcohol-induced osteonecrosis of the femoral head principle is to nourish Yin blood and phlegm stagnation. His own is based on Yanghe Decoction with leeches,

rhizoma drynariae, and radix dipsaci. Gentleman medicine chooses rehmannia glutinosa and antler glue. They can nourish Yin, blood, liver, and kidney, and fill lean pulp. Using the two drugs can make up for congenital inadequacy and nourish the bones. Leeches can break blood stasis. The three medicine cooperate to use can enhance efficacy. Official medicine chooses cinnamon, it can fill the kidney Yang, the pharmacological effects on veins; White mustard can alleviate the pain; Rhizoma drynariae and radix dipsaci can benefit the liver and kidney, strong bones and muscles; Rhizoma zedoariae can break blood stasis. Adjuvant medicine chooses ephedra, it can XuanTongMaoQiao. Licorice Licorice can detoxify, and cooperating with other drugs used together can make it effective. Process of clinical, Professor Li Yingang thinks the pathogenesis of alcohol-induced osteonecrosis of the femoral head is mainly for the "deficiency, phlegm, blood stasis", to the "phlegm and blood stasis". The Liver, spleen, and kidney are deficient, Qi and blood loss of nourishment. So using rehmannia glutinosa, antler glue, rhizoma drynariae to benefit the liver and kidney, blood tonic in essence. Alcohol damaged the spleen and stomach, making the phlegm and wet, with leeches to break blood stasis, alleviate the pain.

6. Typical medical record

Shen is a male. He is 35 years old. He visit on August 5, 2018. The chief complaint: "Right hip joint pain right 3 years increase two months". Patients in 2015 due to tiredness after feeling right hip pain. The local hospital diagnosis was "synovitis of the hip". It has given "diclofenac sodium", and "hot compress", such as treatment. After treatment the patient's pain relief. 2 months after the patient's symptoms became severe. His tongue was yellow. The patient's body before the pain was very healthy. But he has a long history of heavy drinking. His college of physical summed up as follows. He had tenderness at the midpoint of his bilateral groin, and the right side was more severe. He had percussion pain in the longitudinal axis of his right lower limb. He tested positive for the word "4" on his right. His modern medical diagnosis was bilateral alcohol-induced osteonecrosis of the femoral head (ARCO II period). His TCM diagnosis was bone erosion (phlegm and blood stasis resistance card). Professor Li Yingang adopted modified Yanghe Decoction to treat his illness. The specific prescription was as follows: rehmannia glutinosa 15 g, antler glue 6 g, scalding leech 6 g, white mustard 3 g, licorice 3 g, hot rhizoma drynariae 6 g, radix dipsaci 10 g, ginger charcoal 6 g, cinnamon 3 g, ephedra 6 g. The above drugs are 7 doses in total, 1 dose per day, boiled in 400ml of water, and taken warm in the morning and evening. At the same time, the patient was informed not to drink alcohol.

Two diagnoses were on September 5, 2018. Patients after taking Chinese traditional medicine, his bilateral hip pain relief, and activity were slightly better, but the pain and tired after walking for a long time, the tongue veins with former, did not see any adverse reaction, treat the effect at first, so continue with the original 10 doses.

Three diagnoses were on December 15, 2018. His bilateral hip pain got better earlier, walking for a long time, and did not see the pain significantly increase, but recently he felt difficulty breathing. His tongue is red, and yellow with a greasy coating on his tongue. Therefore, based on the original party and cortex phellodendri 6 g, cogongrass rhizome 30 g, 10 g dried tangerine or orange peel. A total of 7 doses, 1 dose per day, decocted in 400ml of water and taken warm in the morning and evening.

Four diagnoses were on February 1, 2019 patients with bilateral hip not seen obvious pain of private prosecution had no other discomfort, review the hip joint MRI in bilateral avascular necrosis femoral bone, compared with the original nuclear magnetic resonance hip lesions. Continue to be the original 15 doses.

6 months after the return visit, the patient has no special discomfort, bilateral hip pain does not appear, and activities are obstacles.

Comments: patients with alcohol-induced osteonecrosis of the femoral head, belong to the category of "bone erosion" in traditional Chinese medicine. Li Yingang thinks alcohol is invaded. Alcohol in the body inside is easy to cause damage and loss of human body blood, resulting in meridians. The meridians' long block will make the loss of nourishing kidney essence and bone, eventually leading to "bone erosion". Because of this, the winding resistance of phlegm and blood stasis, liver and kidney deficiency is the pathogenesis of the disease, local context femoral head block, loss of the essence, Qi, blood, moisten and lack of hemorrhagic necrosis occurs. In this case, promoting blood circulation to remove blood stasis, tonic kidney, strengthen the pain under the principle of bones, and filling lean pulp formula is given priority with Yanghe Decoction. The effect of warming Yang and promoting blood circulation to remove blood stasis runs through the whole process of treatment. Yanghe Decoction emphatically fills JingXie and lean pulp with rehmannia glutinosa. Antler glue can fill the liver and kidney, and benefit

intensive blood marrow, strong bones, and muscles. Scalding leech can promote blood circulation to remove blood stasis. Three drugs are used to make enhanced efficacy. Radix dipsaci and hot bone that is broken can benefit the liver and kidney. Cannon ginger charcoal and cinnamon can enter the blood and makes the blood flow. White mustard makes effect to inside and outside of the body, and it can phlegm. Use a small amount of ephedra to XuanTongMaoQiao. Licorice to reconcile the medicine to make medicine. 2 diagnoses, the patient had pain symptoms, no other discomfort, so the original was unchanged, usage to day 1 agent; 3 diagnoses, the patient's pain symptoms improved further, but his symptoms for the mouth and tongue-long sores. His tongue is red, and yellow with a greasy coating on his tongue. Because early antler glue and cinnamon lead to too much Yang in. This time adds cortex phellodendri and cogongrass rhizome, to let them heat-clearing and detoxify; 4 diagnoses, symptoms improved significantly, and review of the hip joint nuclear magnetic resonance in the femoral head necrosis area was relatively small. Yanghe Decoction has the remedial effect, therefore, the original unchanged, consolidating treatment.

7. Discussions

Osteonecrosis of the femoral head is a kind of hidden, trabecular bone and bone marrow necrosis a pathological characteristic of refractory orthopedic disease. It has good hair in young and middle-aged, with a large number of glucocorticoids for a long time. Long-time drinking and blood supply of femoral head trauma lead to damage or disruption^[15]. The way of modern medicine in the treatment of early osteonecrosis of the femoral head is taking anticoagulant drugs^[16], the late is hip replacement surgery. Osteonecrosis of the femoral head is a "bone erosion" category of traditional Chinese medicine. Traditional Chinese medicine thinks that internal causes of osteonecrosis of the femoral head are Qi, liver, and kidney deficiency. Traditional Chinese medicine thinks that external causes of osteonecrosis of the femoral head are phlegm and blood stasis resistance. The cause of osteonecrosis of the femoral head early is trauma. Common symptoms are hip pain, the feeling of pain like a needle. The patient looked bleak, the tongue is purple and its surface has spots. An image of the symptoms of qi and blood stasis. In the middle of the femoral head necrosis, the bone under the femoral head can appear cystic change, serious when there will be empty. Common symptoms are not flexible lower limb flexion and extension, it belongs to "bone impotent". In the late osteonecrosis of the femoral head, the femoral head will collapse. The common symptoms are activity limitations of lower limbs. When the condition is serious, the patient's lower limbs will atrophy, it belongs to "bone erosion". Of alcohol-induced osteonecrosis of the femoral head, the Master Lei's Discourse on Drug Processing load:" the wine which all the small places in our body can arrive, So it can access all the meridians of the body. Its curative effect is very good and can dispel wet and hot. But if drinking too much can produce fire, it can make Lung meridian sustained impact, resulting in a cough. The spleen because it led to a decrease in function. The stomach because it leads to vomiting. The heart because it causes people to become groggy. The liver because it causes people to become irritable. This bravery because it leads to forgetting fear "^[17]. In the treatment of Prescriptions of traditional Chinese medicine, the effect is remarkable. Yanghe Decoction is shown by research^[18] that may signal a pathway. Yanghe Decoction regulates immuno-inflammatory reaction, bone metabolism and blood circulation supply in the process of osteonecrosis of the femoral head through HIF-1 signal pathway, TNF signal pathway and PI3K-Akt signal pathway. Thus, it achieves the effect of interventional treatment for osteonecrosis of the femoral head. Professor Li Yingang thinks the pathogenesis of alcohol-induced osteonecrosis of the femoral head is mainly for the "deficiency, phlegm, blood stasis", to the "phlegm and blood stasis", based on Yanghe Decoction add leech, rhizoma drynariae, radix dipsaci, such as drugs to nourish Yin blood and phlegm flux hysteresis. The clinical curative effect is distinct.

References

- [1] Sun Wei, Li Zirong. Interpretation of the 2019 revised version of Association Research Circulation Osseous staging system of osteonecrosis of the femoral head [J]. Chinese Journal of Orthopaedics, 2020, 40(13):889-892.
- [2] Zhao DW, Yu M, Hu K, et al. Prevalence of Nontraumatic Osteonecrosis of the Femoral Head and its Associated Risk Factors in the Chinese Population: Result from a Nationally Representative Survey [J]. Chin Med J(Engl), 2015, 128(21):2843-2850.
- [3] Tan B, Li W, Zeng P, et al. Epidemiological study based on China osteonecrosis of the femoral head database [J]. Orthop Surg, 2021, 13(1): 153-160.
- [4] Tsai SW, Wu PK, Chen CF, et al. Etiologies and outcome of osteonecrosis of the femoral head:

- Etiology and outcome study in a Taiwan population [J]. Chin Med Assoc, 2016, 79(1): 39-45.*
- [5] Yoon BH, Kim TY, Shin IS, et al. Alcohol intake and the risk of osteonecrosis of the femoral head in Japanese populations: a dose-response meta-analysis of case-control studies [J]. *Clin Rheumatol*, 2017, 36(11): 2517-2524.
- [6] Maurel DB, Boisseau N, Benhamou CL, et al. Alcohol and bone: review of dose effects and mechanisms [J]. *Osteoporos Int*, 2012, 23(1): 1-16.
- [7] Chen Wei, Qing Liming, Wu Panfeng, et al. Progress of pathogenesis and genetics of alcohol-induced osteonecrosis of the femoral head [J]. *Chinese Journal of Reparative and Reconstructive Surgery*, 2022, 36(11):1420-1427.
- [8] Huang Yunying, Shi Weifa, Yin Dong, et al. Influence of perioperative insulation intervention on tranexamic acid hemostasis in patients with total hip replacement [J]. *Chinese Nursing Research*. 2018, 32(22):3617-3620.
- [9] Tao Fenfen. *A Study of Formula Syndrome and Application Rule of Yanghe Decoction [D]. Hubei University of Traditional Chinese Medicine, 2020.*
- [10] Liu Xiao, Jiang Wenrong. Modified Yanghe Decoction treatment of ischemic necrosis of femoral head and 54 cases analysis [J]. *Journal of Practical Traditional Chinese Internal Medicine*, 2004(01): 36-37.
- [11] Guo Y, Cao Y, Gong S, et al. Correlation analysis between CAR-MEN variants and alcohol-induced osteonecrosis of the femoral head in the Chinese population [J]. *BMC Musculoskelet Disord*, 2020, 21(1):547.
- [12] Liu F, Wang W, Yang L, et al. An epidemiological study of etiology and clinical characteristics in patients with nontraumatic osteonecrosis of the femoral head [J]. *J Res Med Sci*, 2017, 22:15.
- [13] Yoon BH, Jones LC, Chen CH, et al. Etiologic Classification Criteria of ARCO on Femoral Head Osteonecrosis Part 2: Alcohol-As-sociated Osteonecrosis [J]. *J Arthroplasty*, 2019, 34(1):169-174.
- [14] Yan Ran, Zhang Xuezhe. Preliminary clinical application of magnetic resonance perfusion imaging of avascular necrosis of femoral head [J]. *National Medical Journal of China*. 2008, 88(16):1107-1110.
- [15] Mongt Ma, Salem HS, PiuZZi NS, et al. Nontraumatic Osteonecrosis of the Femoral Head: Where Do We Stand Today: A 5-Year Update [J]. *Bone Joint Surg Am*. 2020; 102(12):1084-1099.
- [16] Zhang Qiankun, et al. Role of coagulopathy in glucocorticoid-in-duced osteonecrosis of the femoral head [J]. *J Int Med Res*, 2018, 46(6):2141-2148.
- [17] Zhang Heyong, Liu Zheng, Yang Shengwen. *The Traditional Chinese Medicine Effective Treatments for the Treatment of Femoral Head Necrosis [J]. Guide of China Medicine*, 2017, 15(30):3-4.
- [18] Sun Shihui, Xu Heng, Zhang Jinmin, et al. Applying network pharmacology and molecular docking in exploring the core mechanism of Yanghe Decoction in the treatment of femoral head necrosis [J]. *Medical Research and Education*, 2020, 37(05):36-49.