

# *Advances in the Pathogenesis of Knee Osteoarthritis and the Application of Chinese and Western Medicine Treatment*

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**Abstract:** Osteoarthritis of the knee is a common chronic joint disease in clinical practice. The disease is common in middle-aged and elderly people, and patients are often accompanied by pain and discomfort, activity limitation, and in severe cases, even deformity of the knee joint, which seriously reduces the quality of life of patients and causes great pain to them. In recent years, the incidence of osteoarthritis of the knee has increased with the improvement of living conditions and lifestyle changes, and the increase in life expectancy. This paper reviews the clinical research progress of Chinese and Western medicine treatment of knee osteoarthritis at this stage.

## **1. Introduction**

Knee osteoarthritis (KOA) is a chronic joint disease characterized by degenerative changes of knee cartilage with or without osteophytes that seriously affects the quality of life, which is prevalent in middle-aged and elderly people [1], mainly in the age of 40 years and above [2-4]. Domestic treatment of KOA chooses mostly combined Chinese and Western medicine treatment, which has the advantages of reliable efficacy and less adverse effects [5], and with the in-depth research, there are new advances in both treatment and pathogenesis. This paper conducts a review as follows:

## **2. Pathogenesis**

### **2.1 Chinese medical etiology and pathogenesis**

Chinese medicine nowadays believes that this disease occurs mostly due to physical weakness, deficiency of liver and kidney, and wind, cold, and dampness evil taking advantage of the deficiency to enter the bones, resulting in the blockage of qi and blood by evil, congestion of the meridians, coagulation and astringency, and pain if not passed [6]. Modern physicians have broadened their understanding of the treatment of paralysis based on the summary and application of the experience of ancient physicians. Blood stasis can lead to intraosseous hypertension, and intraosseous hypertension can cause stagnation of the veins and channels in the bone, and changes in the direction of blood flow and hemodynamic changes, which eventually lead to more difficulties in the supply of

oxygen and blood to the bone tissues, and therefore the production of knee osteoarthritis pain is considered to be closely related to intraosseous stasis and increased intraosseous pressure, and stasis paralysis is the cause of the disease [7-8]. The theory of "deficiency of evil and stasis" [9] suggests that deficiency of positive energy, phlegm and stagnation of Qi, and invasion of evil are the causes of the disease, and that no evil is paralysis, no deficiency is paralysis, and no stasis is paralysis. Zhao Yong et al [10] treated the pain of knee osteoarthritis from the meridian tendon theory. These "knots" and "aggregates" are important causes of joint pain. The kidney is the master of bone and marrow production. According to "The First Recipe of the Surgical Collection", sufficient kidney energy is essential for bone development.

## 2.2 Western medical pathogenesis

The pathogenesis of KOA is a consequence of a multifactorial trigger, involving multiple mechanisms and acting synergistically, and is regulated by various signaling pathways, which involve inflammatory factors such as interleukin-1 $\beta$  (IL-1 $\beta$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) [11], growth factors, vascular factors (VEGF), proteases, free radicals, hormones, etc. These cytokines are widely present in various tissues and play an important regulatory role by stimulating the synthesis of OA articular cartilage matrix at the molecular level [12]. Meanwhile, inflammatory factors are divided into pro-inflammatory and anti-inflammatory factors, which are involved in metabolism while maintaining the homeostasis of the internal environment of the knee joint and have a significant impact on the development of KOA. [13] The release of pro-inflammatory cytokines such as IL-1 $\beta$ , IL-6, IL-8, and TNF- $\alpha$  is regulated by the MAPK signaling pathway, which promotes extracellular matrix (ECM) degradation and inhibits extracellular matrix synthesis, triggering articular cartilage degeneration and destruction [14]. It has been shown that the NF- $\kappa$ B signaling pathway is inactivated and undergoes abnormal activation upon stimulation by lipopolysaccharide and other stimuli, resulting in loss of Agg, a protein glycan that acts as a basal extracellular aggregate, and Col II, a type II collagen, leading to chondrocyte damage [15].

## 3. Treatment method

### 3.1 Basic treatment

Basic therapy, including health education, appropriate exercise and movement methods, physical therapy (e.g., transcutaneous electrical nerve stimulation, hydrotherapy [16], etc.), and mobility assistance, is a safe, simple, effective, and inexpensive treatment [17], and is most effective for patients with early KOA who have mild pain symptoms, no significant limitation in knee range of motion, and a single symptom. The simplicity of basic therapy is reflected in the fact that only changes in daily life and work patterns are required. Basic therapy not only relieves signs and symptoms, improves or even restores knee function, but also prevents the aggravation of KOA. However, the effectiveness of the treatment depends largely on the patient's compliance.

### 3.2 Drug treatment

#### 3.2.1 Herbal treatment

Yuan Chengfa et al [18] applied tonifying kidney and activating blood soup orally for 4 weeks to treat KOA with kidney deficiency and blood stasis, and the serum tumor necrosis factor TNF- $\alpha$  and BMP-2 values of the patients were significantly higher than those of the control group after treatment, indicating that tonifying kidney and activating blood soup could play an analgesic role. Xin Rongchao

et al [19] selected hot compressing powder combined with orthopedic manipulation from Chang'an Zhu's bone injury for 4 weeks, and the results showed that hot compressing powder combined with manipulation significantly reduced serum levels of IL-1 $\beta$  and TNF- $\alpha$  in the treated group and relieved joint pain. Wang Tao et al [20] applied the self-researched formula "Jianbu Tongluo Fumigation" to reduce the serum TNF- $\alpha$  and IL-1 values and increase the expression of TGF- $\beta$  after 6 weeks of fumigation on the basis of basic treatment, which promoted the repair and stability of joint cartilage.

### **3.2.2 Oral treatment with Western medicine**

Oral western drugs include analgesics, NSAIDs and chondroprotective drugs [21], among which analgesics such as acetaminophen and aspirin, are mostly chosen for rapid pain relief, not for delaying disease progression and long-term treatment. Selective oxidase-2 inhibitors have less gastrointestinal reactions, but have an increased risk of cardiovascular disease [22]. Commonly used chondroprotective agents include glucosamine sulfate, chondroitin sulfate, and diacetin, of which glucosamine sulfate has been shown to prevent structural changes in joints. When using oral medications, care should be taken to back up the gastric mucosa and cardiovascular medications and to regularly check liver and kidney function.

### **3.2.3 Joint cavity drug injection**

Joint cavity injections, including autologous platelet-rich plasma, medical ozone and sodium vitrate, are widely used in clinical practice. Studies have demonstrated [24] that sodium vitrate can enhance the viscosity and lubrication of joint fluid, enter the cartilage matrix and bind to glycoproteins, and promote cartilage healing and stability. Activated PRP plasma can release a variety of growth factors for necrosis removal, differentiation, and proliferation, and is mostly used for early KOA treatment [25].

## **3.3 Acupuncture and Tuina treatment**

Acupuncture treatment can promote local blood circulation, promote the metabolism of synovial fluid, help absorb inflammation, restore normal joint anatomy, and promote cartilage regeneration to a certain extent, thus relieving the symptoms of painful joints and improving joint flexion and extension mobility [26-27]. Acupuncture treatment can eliminate joint swelling, but it does not improve joint mobility significantly. Tui-na can improve joint mobility, but is not suitable for people with swollen joints [29].

## **3.4 Physiotherapy**

Ultrasound therapy is widely used in orthopedics, mainly based on its thermal effect, which results in increased capillary permeability, increased tissue metabolic level, and increased pain domain [30], but there is no optimal ultrasound treatment protocol yet, and the main controversy is over ultrasound mode, intensity, and duration of action. Extracorporeal shock wave (EWST) is used to relieve headache and improve joint function by directly acting on peripheral sensory nerve endings and increasing the pain threshold [31].

## **3.5 Surgical treatment**

The most commonly chosen clinical procedure is total knee arthroplasty, in addition to the minimally invasive concept of articular cartilage repair, arthroscopic debridement for cases of osteoarthritis with meniscal tears, free bodies resulting in interlocking and limited flexion and

extension activities [32]; unicondylar and total condylar arthroplasty, and proximal tibial osteotomy have been widely used in patients with KOA with internal and external rotational deformity [33]; and fibular osteotomy [34] is mainly used to treat KOA with early limited medial compartment with reduced medial gap and mild inversion deformity.

### 3.6 Other therapies

KOA treatments also include soft tissue engineering techniques, bone marrow mesenchymal stem cell transplantation, growth factor therapy, and exosome therapy of mesenchymal stem cell origin.

## 4. Summary

The etiology of KOA in Chinese medicine is the deficiency of liver and kidney, "wind, cold and damp" and other external evil invasion, and there are different opinions according to the different schools of understanding of the disease. In addition to degenerative lesions, Western medicine also fully recognizes the role of inflammatory factors, cellular metabolism and growth factors, and hormones in the disease. Depending on the course of the disease and the degree of pain, and the impact on life, drug therapy and surgical treatment have also been proposed. With the progress of research, the efficacy of combining multiple treatment options and giving full play to the advantages of comprehensive treatment will become better and better.

## References

- [1] Zhou Q, Wang YR, Zhou ZD, et al. Comparison of different molecular weights of sodium hyaluronate in the treatment of osteoarthritis of the knee[J]. *Journal of Shanghai Second Medical University*, 2000(04):361-363.
- [2] Li N. H. Epidemiological characteristics of osteoarthritis in the middle-aged and elderly population[J]. *China Clinical Rehabilitation*, 2005(38):133-135.
- [3] Liu Juncheng, Tan Chunlin, Ai Min et al. Progress in the literature and treatment of osteoarthritis of the knee[J]. *Guangming TCM*, 2023, 38(06):1197-1200.
- [4] Wang B, Xing D, Dong S J, Thea Ruxiu, Zhang C Q, Lin Jian H, Wei S C. Systematic evaluation of the epidemiology and disease burden of knee osteoarthritis in China[J]. *Chinese Journal of Evidence-Based Medicine*, 2018, 18(02):134-142.
- [5] Wang T, Wang G, Wang J, et al. Clinical observation of Chinese medicine fumigation combined with western medicine in the treatment of cold-damp paralysis and obstruction type knee osteoarthritis[J]. *Chinese Journal of Osteoporosis*, 2017, 23(04):506-510.
- [6] Li X. T. Clinical research progress of Chinese medicine in the treatment of osteoarthritis of the knee[J]. *Chinese healing medicine*, 2022, 31(12):1266-1269. DOI:10. 13517/j. cnki. ccm. 2022. 12. 009.
- [7] Zheng Weipeng, Wei Hewei, Huang Ziji, Luo Yuming. Current status and prospects of research on the treatment of osteoarthritis of the knee from stasis[J]. *New Chinese Medicine*, 2013, 45(11):122-124. DOI: 10. 13457/ j. cnki. jncm. 2013. 11. 013.
- [8] Cheng Fei, Yuan Puwei, Liu Deyu. Liu Deyu's treatment of knee osteoarthritis from deficiency and stasis theory[J]. *Journal of Changchun University of Traditional Chinese Medicine*, 2018, 34(01):61-63. DOI: 10. 13463/ j. cnki. cczyy. 2018. 01. 020.
- [9] Jing W, Fusheng X, Li L, et al. Advances in the treatment of knee osteoarthritis with integrated traditional Chinese and western medicine[J]. *China Medical Herald*, 2018.
- [10] Zhao Y, Qin W K, Gu L J, Cui X R, Qiu X D. Clinical thinking on the treatment of osteoarthritis pain in the knee from the meridian theory[J]. *Chinese Journal of Traditional Chinese Medicine Information*, 2012, 19(03):92-93.
- [11] Sun J M, Sun L Z, Liu J, et al. Serum Interleukin-15 Levels Are Associated with Severity of Pain in Patients with Knee Osteoarthritis[J]. *Disease Markers*, 2013, 35:203-206. DOI:10.1155/2013/176278.
- [12] Wang J. Expression and significance of IL-17, IL-19 and IGF-1 in synovial tissue of degenerative knee osteoarthritis [D]. *Qingdao University*, 2015.
- [13] He X, Wang L. Research progress of inflammatory factors and signaling pathways in knee osteoarthritis[J]. *Hebei Medicine*, 2023, 45(05):756-760.
- [14] Huang Q. E., Lai J. H., Wen L. C., et al. Advances in the study of inflammatory cytokines in osteoarthritis of the

- knee [J]. *Rheumatology and Arthritis*, 2016, 5(11):74-76+80.
- [15] Yunwei Guo, Xiaoying Zhang, Zhiyun Zhao, Hongyun Lu, Bilun Ke, Xin Ye, Bin Wu, Jianping Ye. *NF-κB/ HDAC1/ SREBP1c pathway mediates the inflammation signal in progression of hepatic steatosis*[J]. *Acta Pharmaceutica Sinica B*, 2020, 10(05):825-836.
- [16] Mattos F, Leite N, Pitta A, Bento PC. *Effects of aquatic exercise on muscle strength and functional performance of individuals with osteoarthritis. A systematic review. rev Bras Reumatol Engl Ed.* 2016 Nov-Dec;56(6):530-542. english, Portuguese. doi: 10. 1016/j. rbre. 2016. 09. 003. epub 2016 Oct 4. PMID: 27914601.
- [17] Thorstensson CA, Garellick G, Rystedt H, Dahlberg LE. *Better Management of Patients with Osteoarthritis: Development and Nationwide Implementation of an Evidence-Based Supported Osteoarthritis Self-Management Programme.* *Musculoskeletal Care.* 2015 Jun;13(2):67-75. doi. 10. 1002/msc. 1085. epub 2014 Oct 24. pmid: 25345913.
- [18] Yuan Chengfa, Han Song, Yu Pengfei et al. *Clinical efficacy of adding flavors to tonify the kidney and invigorate blood in the treatment of osteoarthritis of the knee with kidney deficiency and blood stasis*[J]. *Chinese Journal of Traditional Chinese Medicine and Orthopedics*, 2022, 30(09):36-42.
- [19] Xin Rongchao, Dang JJ, Zheng Y et al. *Clinical value of the "Chang'an Zhu's orthopedic injury school special treatment plan for knee osteoarthritis"*[J]. *Clinical Medicine Research and Practice*, 2021, 6(09):124-126. DOI: 10. 19347/j. cnki. 2096-1413. 202109043.
- [20] Wang T, Wang G, Wang J, et al. *Clinical observation of Chinese medicine fumigation combined with western medicine in the treatment of cold-damp paralysis and obstruction type knee osteoarthritis*[J]. *Chinese Journal of Osteoporosis*, 2017, 23(04):506-510.
- [21] Lin Chengyu, Chen Haipeng, Chen Kai. *Advances in non-surgical treatment of knee osteoarthritis* [J]. *Rheumatology and Arthritis*, 2018, 7(06):71-75.
- [22] Jiang S. Y., Wei N., Fu F. M. *Advances in anti-inflammatory research of dual-action inhibitors of cyclooxygenase-2/5-lipoxygenase* [J]. *Journal of Kunming University of Science and Technology (Natural Science Edition)*, 2017, 42(04): 73-78. DOI:10. 16112/j. cnki. 53-1223/n. 2017. 04. 012.
- [23] Zhang Zhiyi, Duan Xinwang, Gou Jieruo, Huang Cibo, Jiang Lindi, Lin Jin, Liu Xiangyuan, Li Zeguanguang, Ma Li, Qi Wencheng, Qian Xian, Wang Jibo, Wang Meimei, Wu Lijun, Wu Husheng, Xiao Weiguo, Zheng Yi, Zhang Zhuoli, Olivier Bruyère, Jean-Yves Reginster, Cyrus Cooper. *European Osteoporosis and Osteoarthritis A joint statement by the Society for Clinical and Economic Sciences (ESCEO) and Chinese experts in the field of osteoarthritis:ESCEO rules for the treatment of knee osteoarthritis should be equally applicable to Chinese patients*[J]. *Chinese Journal of Practical Internal Medicine*, 2016, 36(09):762-772.
- [24] Miao Guiqiang, Tan Wencheng, Wu Hao et al. *Long-term efficacy of sodium vitrate in the treatment of moderate knee osteoarthritis* [J]. *Journal of Jinan University (Natural Science and Medicine)*, 2011, 32(02):218-220.
- [25] Chen Y, Wang D, Sun WY, et al. *Efficacy of autologous platelet-rich plasma (PRP) in the treatment of osteoarthritis of the knee joint* [J]. *Guizhou Medicine*, 2019, 43(05):731-732.
- [26] Mai J. *A brief description of the mechanism and therapeutic principles of tui na manipulation* [C]// *Compilation of papers from the 14th Tui Na Academic Exchange Conference of the Tui Na Branch of the Chinese Society of Traditional Chinese Medicine*, 2013:237-238.
- [27] Zhuang Hong. *Clinical efficacy evaluation of Sun's nine-step Tuina method for the treatment of knee osteoarthritis* [D]. *Beijing University of Traditional Chinese Medicine*, 2014
- [28] Yang L, Lu Y. *Research progress of acupuncture in the treatment of osteoarthritis of the knee joint* [J]. *Xinjiang Traditional Chinese Medicine*, 2017, 35(01):91-94.
- [29] Zhou JH, Wu YJ, Xie YY, Zhang JunF, Huang ChengFei, Sun YJ. *Effectiveness and mechanism of application of acupuncture in the treatment of knee osteoarthritis* [J]. *Chinese Tissue Engineering Research*, 2013, 17(28):5255-5260.
- [30] Yang Y, Zeng Chao, Deng Zhenhan et al. *A meta-analysis of ultrasound therapy for osteoarthritis pain in the knee* [J]. *Chinese Tissue Engineering Research*, 2014, 18(33):5396-5401.
- [31] Zhao Z, Shi Z, Yan J, et al. *Effectiveness of extracorporeal shock wave treatment for early to mid-stage knee osteoarthritis* [J]. *Chinese Rehabilitation Theory and Practice*, 2014, 20(01):76-78.
- [32] LU Jingwei, XU Zhihong, CHEN Dongyang, SHI Dongquan, JIANG Qing. *Clinical efficacy analysis of arthroscopic treatment of knee osteoarthritis with meniscal tears and free bodies* [J]. *Chinese Journal of Bone and Joint Surgery*, 2015, 8(02): 112-115.
- [33] Luo W, Ma XL, Huang JIM. *Research progress of high tibial osteotomy* [J]. *Chinese Journal of Orthopaedic Surgery*, 2018, 26(19):1786-1789.
- [34] Liu HJ, Pei HP, Bai Y. *Short-term efficacy of proximal fibular osteotomy for osteoarthritis of the knee with internal derangement of the knee* [J]. *Rheumatism and Arthritis*, 2016, 5(01):35-36+63.