推拿治疗膝骨关节炎疼痛机制研究进展*

周小元[1]，周运峰[2]，许辉[1,2]

1. 河南中医药大学第三附属医院，河南 郑州 450008；2. 河南中医药大学，河南 郑州 450046

摘要：外周伤害性刺激和中枢神经系统对疼痛信号的传导和调控是膝骨关节炎（knee osteoarthritis，KOA）疼痛的关键病理机制，而推拿可显著缓解 KOA 患者的膝关节疼痛，其机制与减少外周伤害性刺激、调控脑中枢密切相关。目前，推拿治疗 KOA 疼痛的现代科学机制有待明确，需进一步加强系统性、多层面的机制研究；脊髓中枢在 KOA 疼痛信号的传导及调控中具有重要作用，需从分子生物学、神经功能影像学层面进一步研究；KOA 推拿干预方案在实验动物上可操作性较差，或可将神经功能影像学相关技术作为推拿干预 KOA 疼痛活体、可视、无创伤性研究的新工具。未来可追踪 KOA 疼痛病理生理研究最新进展，采用新技术手段，开展推拿治疗 KOA 疼痛从外周到中枢多层次、多维度的高质量研究，更加全面具体地阐述其作用机理。

关键词：膝骨关节炎；疼痛；推拿；脑中枢；脊髓中枢
DOI：10.16368/j.issn.1674－8999.2023.09.307
中图分类号：R274.9　　**文献标志码**：A　　**文章编号**：1674－8999(2023)09－1895－07

Research Progress on Pain Mechanism of Tuina in Treatment of Knee Osteoarthritis

ZHOU Xiaoyuan[1]，ZHOU Yunfeng[2]，XU Hui[1,2]

1. The Third Affiliated Hospital to Henan University of Chinese Medicine，Zhengzhou Henan China 450008；
2. Henan University of Chinese Medicine，Zhengzhou Henan China 450046

Abstract：Peripheral nociceptive stimuli and the conduction and regulation of pain signals by the central nervous system are the key pathological mechanisms of knee osteoarthritis (KOA) pain，and Tuina can significantly relieve knee pain in patients with knee osteoarthritis，and its mechanism is closely related to reducing peripheral nociceptive stimuli and regulating brain center. At present，the modern scientific mechanism of Tuina in treating KOA pain needs to be clarified，and systematic and multi－level mechanism research needs to be further strengthened；Spinal cord center plays an important role in the transmission and regulation of KOA pain signal，which needs further study from the aspects of molecular biology and neurofunctional imaging. The intervention scheme of KOA Tuina is not feasible in experimental animals，or the related technology of neurofunctional imaging can be used as a new tool for the in vivo，visual and non－invasive study of Tuina intervention in KOA pain. In the future，we can trace the latest progress in the pathophysiology of KOA pain，adopt new technical means，carry out high－quality research on massage treatment of KOA pain from the outside to the center，and explain its mechanism more comprehensively and concretely.

Key words：knee osteoarthritis；pain；Tuina；brain center；spinal cord center；research progress

膝骨关节炎（knee osteoarthritis，KOA）作为临床常见的慢性退行性关节疾病[1－5]，主要临床症状为疼痛，同时是功能性致残的主要疾患之一[6－10]。KOA 患者初期自觉运动时疼痛，晚期自觉持续性静息痛或夜间痛。KOA 疼痛严重影响患者生活质量，甚至间接增加心血管事件的发生率及全因病死率[11－13]。目前，全球 KOA 患病率约为 4.2%～15.5%[14]，我国成年人 KOA 发病率约为 15%[15]。

KOA 疼痛的发生机制较为复杂，不仅和膝关节

*基金项目：河南省高层次人才特殊支持计划中原千人计划项目－中原名医（ZYQR201912120）；2022 年度中原英才计划（育才系列）项目——中原青年拔尖人才项目；河南省科技攻关项目（222102310214）；河南省中医药科学研究专项项目（2022ZY1108）；2023 年度河南省中医学“双一流”创建科学研究专项项目（HSRP－DFCTCM－2023－7－09）

外周损伤有关，还涉及遗传、环境、心理等因素[16]。目前，普遍认为外周伤害性刺激和脑中枢重塑均与 KOA 疼痛的形成密切相关。KOA 疼痛的治疗呈现阶梯化，最终目的是缓解疼痛，延缓病情进展，改善生活质量。推拿是治疗 KOA 常用的物理疗法，可有效缓解疼痛[17-24]。推拿干预 KOA 疼痛的机制除了和改善外周伤害性刺激有关外，关键还在于重塑异常的脑中枢功能和结构。本文就 KOA 疼痛机制研究进展和推拿治疗 KOA 疼痛的作用机理进行梳理，以期为推拿缓解 KOA 疼痛的机制研究提供思路和方法。

1　KOA 疼痛机制研究进展

1.1　外周伤害性刺激　关节软骨覆盖于膝关节表面，主要由软骨细胞和细胞外基质构成，营养软骨所需物质主要来自于关节液渗透，关节滑液由高分子糖胺聚糖、透明质酸等成分组成，软骨代谢异常、生物力学改变、外部创伤等多种因素均可导致软骨发生进行性破坏、流失。同时，软骨细胞外基质合成和分解代谢异常也是 KOA 病理生理改变的主要特征[25-30]。KOA 所引起的关节软骨退变始于浅表层，随着病变范围的扩大和深度的增加，最终会累及软骨下骨[31-35]。

KOA 患者软骨修复过程中，因破骨细胞活性增强导致软骨下骨到关节软骨间形成可供血管生长通道，受损软骨细胞所产生的促血管生成因子可刺激新生血管通过生长通道侵袭关节软骨，同时刺激、引导神经生长，使神经支配的关节软骨范围增大[36]；软骨修复过程中软骨细胞会表现出高合成活性，释放基质降解酶和炎症介质，诱导痛觉敏化，促进炎症介质释放自循环，刺激软骨感觉神经、膝关节周围组织发生炎症反应，从而产生外周伤害性刺激，导致 KOA 患者膝关节局部疼痛。同时，膝关节软骨退变和修复会导致滑膜发生增生、纤维化以及基质血管化[37-39]，增生滑膜会进一步释放炎症介质、降解酶，加重外周伤害性刺激[40]。

1.2　中枢神经系统因素

1.2.1　对脊髓中枢疼痛信号传导通路因素　KOA 局部炎症介质的释放导致膝关节周围的有髓鞘 Aβ、Aδ 纤维、无髓鞘 C 纤维接受一定量的物理、化学刺激[41]，这些外周伤害性刺激会转化成疼痛信号传至脊髓后角浅层，从而接受脊髓中枢疼痛调控。脊髓中枢参与疼痛调控的重要过程，包括接收 KOA 外周疼痛信号自初级感觉神经元纤维末梢传入，通过脊髓的痛觉二级神经元，将这些疼痛信息整合和传导，并继续传递疼痛信息上行至脑中枢。同时，脊髓中枢也是疼痛下行调控的效应部位，脊髓背角的抑制性、兴奋性中间神经元接受这些脑中枢疼痛调控信号后，可以进一步抑制或者增强疼痛信号传递。

1.2.2　对脑中枢疼痛信号传导通路因素　既往研究认为，关节软骨破坏、滑膜炎性反应等外周因素是 KOA 疼痛的关键环节[42-46]。但许多研究发现，X 线片的影像学严重程度以及滑膜的炎性反应程度和临床症状的严重程度并不呈正相关，说明外周机制不能完全解释 KOA 疼痛机制[41,47-48]。同时，KOA 患者存在非受累部位疼痛敏感性升高的现象，推测脑中枢对长期疼痛传入信号的“异常加工”可能是 KOA 疼痛的关键因素[48-49]。膝关节疼痛信号的持续传入会导致中枢各级痛觉投射神经元均处于高敏状态，并在上传过程中被不断放大，导致痛觉感受不断加强，加剧 KOA 疼痛，并诱发脑中枢功能和结构重塑。

研究发现，长期的外周伤害性刺激和脑中枢疼痛调控环路异常可使 KOA 患者各级痛觉投射神经元均处于高敏状态[49-50]。同时，基于功能磁共振成像（functional MRI，fMRI）技术的研究发现，KOA 疼痛通过改变不同脑区间信息流动、整合而对脑中枢功能和结构产生影响[51-53]。因此，基于 fMRI 技术对 KOA 疼痛脑功能重塑机制的进一步明确有利于深入研究脑中枢病理机制，并为治疗的多样性和疗效评价提供依据。

2　推拿治疗 KOA 疼痛研究进展

KOA 属中医“膝痹”的范畴。KOA 病机内责之于脏腑气血失和，外责之于风寒湿气侵袭[54-58]。《济生方·痹》载：“皆因体虚，腠理空疏，受风寒湿气而成痹也。”KOA 疼痛为“膝痹”的典型临床表现，如《景岳全书》记载：“盖痹者，闭也，以气血为邪所闭，不得通行而病也。”KOA 疼痛的病机总的可归纳为：①脏腑气血失和，导致筋骨失去濡养，因虚所致，不荣作痛；②风寒湿邪侵袭人体，留滞经脉、肌肉、骨骼，导致气血瘀滞，痰湿夹杂，因实所致，不通作痛。推拿作为传统中医药疗法的重要组成部分，具有普适性强和易于操作的特点，治疗 KOA 具有安全、有效、无创痛等优势，在临床应用中得到了广泛推广[59]。

2.1　减少外周伤害性刺激　推拿可以改善软骨细胞外基质合成和分解代谢，如增加Ⅱ型胶原蛋白表

达量,修复软骨细胞损伤状态,从而减少外周伤害性刺激,缓解 KOA 疼痛。同时,推拿可以促进血液循环,降低外周血清及膝关节局部组织炎性因子过度表达,改善膝关节内环境,消除外周疼痛信号输入。基于生物力学研究表明,推拿可以改善 KOA 患者膝关节周围肌肉组织力学特性,提高肌力,恢复膝关节动、静力性稳定[60]。

杨松滨等[61]研究发现,推拿缓解 KOA 疼痛的作用机制可能是抑制软骨丝裂原活化蛋白激酶(mitogen - activated protein kinase,MAPK)信号转导通路,延缓 KOA 软骨退变程度,影响炎症介质、细胞因子表达。马铭华等[62]发现推拿干预 KOA 模型兔 3 周后,推拿组相较于模型组,股直肌 FDD(软组织产生形变)值和 S(下压能量)值均升高,股二头肌 FDD 值和 S 值均降低,软骨组织 Mankin′s 评分降低,说明推拿可以增加膝关节周围肌力,改善组织张力,提高关节活动功能。

2.2　调控脑中枢　推拿治病的起效机制除了和局部生物力学有关外,关键还在于对脑中枢的调控,如推拿对穴位 - 脑、脑肠轴、骨骼肌 - 脑等均具有广泛的调整作用[63]。推拿可通过作用于 KOA 患者膝关节及其周围结构,减少外周伤害性刺激传入脑中枢,从而重塑异常的脑中枢功能和结构。推拿通过手法作用于 Aβ 神经纤维,能有效减少外周伤害性刺激的传递[64]。同时,推拿有利于提高机械感受器兴奋性,使手法的机械刺激与外周伤害性刺激竞争信号上传途径,在一定程度上起到抑制作用[65]。

基于功能分离的局部脑功能活动研究表明,推拿可通过调控丘脑、扣带回、辅助运动区等与疼痛密切相关的功能区域缓解疼痛[66-67]。基于功能整合局部脑区与远隔脑区之间的相互作用研究表明,推拿在缓解疼痛的过程中可以通过多靶点效应作用于多个脑区,同时调整关键节点以调节脑网络信息处理能力[68-69]。卿伦学[70]借助 fMRI 技术进行研究发现推拿手法治疗 KOA 疼痛的瞬时效应主要是镇痛,而长期累积效应则主要是对偏向于情绪以及认知功能的调整。郭光昕[71]采用多模态 MRI 技术证实推拿对 KOA 患者的中枢镇痛效应可能是通过丘脑、中央后回等不同脑区的协同调控实现的。

3　结语

目前,KOA 疼痛的发生机制复杂,尚未完全阐释,其疼痛机制可能是外周伤害性刺激和中枢神经系统的共同作用。大量的随机对照试验结果已经证实推拿治疗 KOA 疼痛的临床疗效,但其现代科学机制仍需进一步明确:(1)从推拿治疗 KOA 疼痛的膝关节局部因素研究可以看出,各环节相互交叉,需进一步进行多系统、多层面的深入研究;(2)脊髓中枢在 KOA 疼痛信号的传导及调控中具有重要作用,可从分子生物学、神经功能影像学视角加强相关研究,如多种针对脊髓中枢的定量成像方法、fMRI 技术,可对脊髓中枢感觉进行有效评估,在推拿干预 KOA 疼痛的基础研究中具有较大潜力;(3)目前,KOA 推拿干预方案由多种推拿手法组成,这就导致在动物实验上可操作性较差,神经功能影像学相关技术的发展为推拿干预 KOA 疼痛的活体、可视、无创伤性研究提供了新的工具,如基于 fMRI 技术可明确推拿干预 KOA 患者前后脑中枢功能和结构的变化,从而揭示脑中枢疼痛信号关键节点及脑网络在推拿干预 KOA 疼痛具体脑中枢中的作用机制。

未来可追踪 KOA 疼痛病理生理研究最新进展,采用新的技术手段,开展推拿治疗 KOA 疼痛从外周到中枢多层次、多维度的高质量研究,更加全面、具体阐述作用机理。

参考文献:

[1]CHEN L Z,YAO F,WANG T,et al. Horizontal fissuring at the osteochondral interface:a novel and unique pathological feature in patients with obesity - related osteoarthritis[J]. Ann Rheum Dis,2020,79(6):811 - 818.

[2]中华医学会骨科学分会关节外科学组,中国医师协会骨科医师分会骨关节炎学组,国家老年疾病临床医学研究中心(湘雅医院),等. 中国骨关节炎诊疗指南(2021 年版)[J]. 中华骨科杂志,2021,41(18):1291 - 1314.
Joint Surgery Group of Orthopaedic Branch of Chinese Medical Association,Osteoarthritis Group of Orthopaedic Branch of Chinese Medical Doctor Association,National Clinical Medical Research Center for Geriatric Diseases (Xiangya Hospital),et al. Chinese guideline for diagnosis and treatment of osteoarthritis (2021 edition)[J]. Chin J Orthop,2021,41(18):1291 - 1314.

[3]许学猛,刘文刚,许树柴,等. 膝骨关节炎(膝痹)中西医结合临床实践指南[J]. 实用医学杂志,2021,37(22):2827 - 2833.
XU X M,LIU W G,XU S C,et al. Clinical practice guidelines for knee osteoarthritis in integrated traditional Chinese and western medicine[J]. J Pract Med,2021,37(22):2827 - 2833.

[4]陈卫衡. 膝骨关节炎中医诊疗指南(2020 年版)[J]. 中医正骨,2020,32(10):1 - 14.

CHEN W H. Guidelines for TCM diagnosis and treatment of knee osteoarthritis(2020 edition)[J]. J Tradit Chin Orthop Traumatol,2020,32(10):1 - 14.

[5]王尚全,朱立国,展嘉文,等. 中医康复临床实践指南·膝骨关节炎[J]. 康复学报,2020,30(3):177 - 182.
WANG S Q,ZHU L G,ZHAN J W,et al. Clinical practice guidelines in traditional Chinese medicine rehabilitation - knee osteoarthritis[J]. Rehabil Med,2020,30(3):177 - 182.

[6]中国中西医结合学会骨伤科专业委员会. 膝骨关节炎中西医结合诊疗指南[J]. 中华医学杂志,2018,98(45):3653 - 3658.
Professional Committee of Orthopaedics,Chinese Society of Integrated Traditional Chinese and Western Medicine. Guidelines for Diagnosis and Treatment of Knee Osteoarthritis with Integrative Medicine[J]. Chinese Medical Journal,2018,98(45):3653 - 3658.

[7]刘军,黄和涛,潘建科,等. 膝骨关节炎中西医结合阶梯诊疗的发展现状及展望[J]. 广东医学,2019,40(9):1189 - 1192.
LIU J,HUANG H T,PAN J K,et al. The status quo and prospection of integrative therapy of western medicine and traditional Chinese medicine in the step - wise treatment of osteoarthritis at knee[J]. Guangdong Med J,2019,40(9):1189 - 1192.

[8]SHAO Z C,LIANG Z P,HU P,et al. A nomogram based on radiological features of MRI for predicting the risk of severe pain in patients with osteoarthritis of the knee[J]. Front Surg,2023,10:1030164.

[9]TASLAKIAN B,MILLER L E,MABUD T S,et al. Genicular artery embolization for treatment of knee osteoarthritis pain:systematic review and meta - analysis[J]. Osteoarthr Cartil Open,2023,5(2):100342.

[10]SWANSON J L. Genicular nerve radiofrequency ablation:an option for knee osteoarthritis pain[J]. JAAPA,2023,36(3):32 - 36.

[11]LIU Q,NIU J,HUANG J,et al. Knee osteoarthritis and all - cause mortality:the Wuchuan osteoarthritis study[J]. Osteoarthritis Cartilage,2015,23(7):1154 - 1157.

[12]WANG Y L,NGUYEN U D T,LANE N E,et al. Knee osteoarthritis,potential mediators,and risk of all - cause mortality:data from the osteoarthritis initiative[J]. Arthritis Care Res,2021,73(4):566 - 573.

[13]PARK D,PARK Y M,KO S H,et al. Association of general and central obesity,and their changes with risk of knee osteoarthritis:a nationwide population - based cohort study[J]. Sci Rep,2023,13(1):3796.

[14]HUANG D,LIU Y Q,LIANG L S,et al. The diagnosis and therapy of degenerative knee joint disease:expert consensus from the Chinese pain medicine panel[J]. Pain Res Manag,2018,2018:2010129.

[15]廖德发. 我国骨性关节炎流行病学调查现状[J]. 微创医学,2017,12(4):521 - 524.
LIAO D F. Epidemiological investigation of osteoarthritis in China[J]. J Minim Invasive Med,2017,12(4):521 - 524.

[16]徐波,邢润麟,茆军,等. 骨关节炎疼痛相关危险因素研究进展[J]. 中国现代医学杂志,2021,31(23):45 - 48.
XU B,XING R L,MAO J,et al. Research progress on pain related risk factors of osteoarthritis[J]. China J Mod Med,2021,31(23):45 - 48.

[17]张帆,周胜利,周奕璇. 膝骨关节炎中医外治研究进展[J]. 陕西中医,2022,43(6):814 - 817.
ZHANG F,ZHOU S L,ZHOU Y X. Research progress on external treatment of knee osteoarthritis with traditional Chinese medicine[J]. Shaanxi J Tradit Chin Med,2022,43(6):814 - 817.

[18]许辉,肖涟波,康冰心,等. 推拿手法治疗膝骨性关节炎临床疗效及安全性 Meta 分析[J]. 陕西中医,2019,40(12):1807 - 1813.
XU H,XIAO L B,KANG B X,et al. Clinical efficacy and safety of Chinese Tuina in treating knee osteoarthritis Meta - analysis[J]. Shaanxi J Tradit Chin Med,2019,40(12):1807 - 1813.

[19]XU H,ZHAO C,GUO G X,et al. The effectiveness of Tuina in relieving pain,negative emotions,and disability in knee osteoarthritis:a randomized controlled trial[J]. Pain Med,2023,24(3):244 - 257.

[20]宋石龙,薛明新,陶琦,等. 中医正骨推拿治疗早中期膝骨性关节炎随机对照研究[J/OL]. 中国中西医结合杂志,2023:1 - 6.(2023 - 02 - 24). https://kns.cnki.net/kcms/detail/11.2787.r.20230222.1547.006.html.
SONG S L,XUE M X,TAO Q,et al. Treatment of early - mid - stage knee osteoarthritis by Chinese medicine bone setting Tuina:a randomized controlled trial[J/OL]. Chin J Integr Tradit West Med,2023:1 - 6.(2023 - 02 - 24). https://kns.cnki.net/kcms/detail/11.2787.r.20230222.1547.006.html.

[21]浦媛,陈志,张树昆. 三步推拿点穴手法对膝关节炎患者疗效及炎性因子变化的前瞻性研究[J]. 光明中医,2023,38(3):509 - 511.
PU Y,CHEN Z,ZHANG S K. Prospective study on the curative effect of three - step massage and acupoint manipulation on patients with knee arthritis and the changes of inflammatory factors[J]. Guangming J Chin Med,2023,38(3):509 - 511.

[22]张涛,闫慧新,安云,等. 推拿治疗膝骨关节炎的诊疗思路与验案举隅[J]. 中华中医药杂志,2023,38(2):649 - 652.
ZHANG T,YAN H X,AN Y,et al. Treatment thoughts and cases study on knee osteoarthritis with tuina[J]. China J Tradit Chin Med Pharm,2023,38(2):649 - 652.

[23]黎璇,孙元丽,马杏娟. 推拿结合等速肌力训练治疗膝关节骨性关节炎对膝关节功能及疼痛的影响[J]. 实用中医药杂志,2022,38(12):2184 - 2186.
LI X,SUN Y L,MA X J. Effect of massage combined with isokinetic muscle strength training on knee joint function and pain in patients with knee osteoarthritis[J]. J Pract Tradit Chin Med,2022,38(12):2184 - 2186.

[24]李超,张贤,邵家豪,等. "腰 - 髋 - 膝 - 踝"整体性推拿手法治疗膝骨关节炎的可行性[J]. 中医正骨,2022,34(2):57 - 59.
LI C,ZHANG X,SHAO J H,et al. Feasibility of lumbar - hip - knee - ankle holistic massage in treatment of knee osteoarthritis[J]. J Tradit Chin Orthop Traumatol,2022,34(2):57 - 59.

[25]韦冰,李学飞,吴连国. 软骨下骨病变在骨关节炎发病进程中的作用[J]. 浙江中西医结合杂志,2023,33(1):91 - 94.
WEI B,LI X F,WU L G. The role of subchondral bone lesions in the pathogenesis of osteoarthritis[J]. Zhejiang J Integr Tradit Chin West Med,2023,33(1):91 - 94.

[26]王岩,王启印,王茂源. 线粒体自噬在骨关节炎软骨退行性变中的作用[J/OL]. 生理科学进展. (2023 - 03 - 16). https://doi. org/10. 20059/j. cnki. pps.
WANG Y,WANG Q Y,WANG M Y. The role of mitochondrial autophagy in cartilage degeneration of Osteoarthritis[J/OL]. Progress in physiological science. (2023 - 03 - 16). https://doi. org/10. 20059/j. cnki. pps.

[27]卢晓君,熊波涵,杨腾云,等. 骨关节炎软骨细胞的新型程序性死亡[J]. 中国组织工程研究,2023,27(28):4571 - 4576.
LU X J,XIONG B H,YANG T Y,et al. Novel programmed cell death of chondrocytes in osteoarthritis[J]. Chin J Tissue Eng Res,2023,27(28):4571 - 4576.

[28]桂超,保国锋,崔志明. 软骨细胞铁死亡在骨关节炎中的研究进展[J]. 江苏医药,2022,48(10):1070 - 1073.
GUI C,BAO G F,CUI Z M. Research progress of iron death of chondrocytes in osteoarthritis[J]. Jiangsu Med J,2022,48(10):1070 - 1073.

[29]方雨婷,柳直,姚五平,等. Wnt 信号通路在膝关节骨关节炎软骨退变的作用[J]. 中国骨与关节杂志,2022,11(10):782 - 785.
FANG Y T,LIU Z,YAO W P,et al. The role of the Wnt signaling pathway in osteoarthritis of the knee joint in cartilage degeneration[J]. Chin J Bone Jt,2022,11(10):782 - 785.

[30]陈财,曾平,刘金富. 介导软骨细胞相关机制调控骨性关节炎的长链非编码 RNA[J]. 中国组织工程研究,2023,27(29):4729 - 4735.
CHEN C,ZENG P,LIU J F. Long non - coding RNAs regulate osteoarthritis by mediating chondrocyte - related mechanisms[J]. Chin J Tissue Eng Res,2023,27(29):4729 - 4735.

[31]胡永召,阮志华,韩柄秋,等. 膝骨关节炎的软骨下骨改变[J]. 风湿病与关节炎,2022,11(8):42 - 46.
HU Y Z,RUAN Z H,HAN B Q,et al. Subchondral bone changes in knee osteoarthritis[J]. Rheum Arthritis,2022,11(8):42 - 46.

[32]周荣,廖文洁. 软骨下骨在骨关节炎中的病理改变及其机制研究[J]. 系统医学,2021,6(24):190 - 193.
ZHOU R,LIAO W J. Pathological changes of subchondral bone in osteoarthritis and its mechanism[J]. Syst Med,2021,6(24):190 - 193.

[33]李婧瑜,苏盈盈,白丁. 骨关节炎早期模型小鼠软骨下骨的形态学特征[J]. 中国组织工程研究,2022,26(11):1692 - 1698.
LI J Y,SU Y Y,BAI D. Morphological characteristics of subchondral bone in a mouse model of early osteoarthritis[J]. Chin J Tissue Eng Res,2022,26(11):1692 - 1698.

[34]杨明义,苏亚妮,马尧,等. 以软骨下骨硬化为靶点的骨关节炎治疗研究进展[J]. 中华关节外科杂志(电子版),2021,15(2):209 - 213.
YANG M Y,SU Y N,MA Y,et al. Research progress in treatment of osteoarthritis targeting subchondral bone sclerosis[J]. Chin J Jt Surg Electron Ed,2021,15(2):209 - 213.

[35]郭洁梅,陈鹏,肖艳,等. 软骨下骨重塑与骨关节炎综述[J]. 福建中医药,2021,52(1):54 - 57.
GUO J M,CHEN P,XIAO Y,et al. Summary of subchondral bone remodeling and osteoarthritis[J]. Fujian J Tradit Chin Med,2021,52(1):54 - 57.

[36]MAPP P I,WALSH D A. Mechanisms and targets of angiogenesis and nerve growth in osteoarthritis[J]. Nat Rev Rheumatol,2012,8(7):390 - 398.

[37]MATHIESSEN A,CONAGHAN P G. Synovitis in osteoarthritis:current understanding with therapeutic implications[J]. Arthritis Res Ther,2017,19(1):18.

[38]郭凤英,张晨,李燕,等. 关节软骨 Osterix 蛋白表达强度对膝关节骨性关节炎形态学变化的影响[J]. 陕西医学杂志,2021,50(3):366 - 369.
GUO F Y,ZHANG C,LI Y,et al. Effect of the expression

intensity of Osterix protein in articular cartilage on the morphological changes of knee osteoarthritis[J]. Shaanxi Med J,2021,50(3):366 - 369.

[39]周安远,梁朝鑫,杨斯淇,等. 富血小板血浆和弗林蛋白酶激动剂对大鼠膝骨关节炎的缓解作用实验研究[J]. 陕西医学杂志,2022,51(9):1043 - 1048,1054.
ZHOU A Y,LIANG C X,YANG S Q,et al. Remission effect of knee osteoarthritis in rats by platelet - rich plasma and furin agonists[J]. Shaanxi Med J,2022,51(9):1043 - 1048,1054.

[40]SCANZELLO C R,GOLDRING S R. The role of synovitis in osteoarthritis pathogenesis[J]. Bone,2012,51(2):249 - 257.

[41]FELSON D T. The sources of pain in knee osteoarthritis[J]. Curr Opin Rheumatol,2005,17(5):624 - 628.

[42]卢亮宇,王予彬. 膝骨关节炎疼痛机制及治疗研究现状[J]. 中国运动医学杂志,2007,26(4):512 - 516.
LU L Y,WANG Y B. Research status of pain mechanism and treatment of knee osteoarthritis[J]. Chin J Phys Med,2007,26(4):512 - 516.

[43]武新峰,史晓飞. 骨关节炎中的"滑膜炎"[J]. 中华临床免疫和变态反应杂志,2022,16(6):657 - 658.
WU X F,SHI X F. "Synovitis" in osteoarthritis[J]. Chin J Allergy Clin Immunol,2022,16(6):657 - 658.

[44]宋永嘉,张增乔,翟天军,等. 铁死亡在膝骨关节炎性滑膜炎中的作用机制[J]. 生命的化学,2022,42(10):1807 - 1812.
SONG Y J,ZHANG Z Q,ZHAI T J,et al. Mechanism of ferroptosis in knee osteoarthritis synovitis[J]. Chem Life,2022,42(10):1807 - 1812.

[45]黎柏军,郑洁,杨锋,等. 骨关节炎滑膜病变机制研究进展[J]. 中国骨与关节杂志,2022,11(10):777 - 782.
LI B J,ZHENG J,YANG F,et al. Research progress on the pathological mechanism of osteoarthritis synovium[J]. Chin J Bone Jt,2022,11(10):777 - 782.

[46]于洋. 滑膜细胞与骨关节炎疾病的相关性研究[J]. 医学信息,2022,35(20):170 - 172.
YU Y. Study on the correlation between synovial cells and osteoarthritis disease[J]. J Med Inf,2022,35(20):170 - 172.

[47]HANNAN M T,FELSON D T,PINCUS T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee[J]. J Rheumatol,2000,27(6):1513 - 1517.

[48]BEDSON J,CROFT P R. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature[J]. BMC Musculoskelet Disord,2008,9:116.

[49]ARENDT - NIELSEN L,NIE H L,LAURSEN M B,et al. Sensitization in patients with painful knee osteoarthritis[J]. Pain,2010,149(3):573 - 581.

[50]SUOKAS A K,WALSH D A,MCWILLIAMS D F,et al. Quantitative sensory testing in painful osteoarthritis: a systematic review and meta - analysis[J]. Osteoarthritis Cartilage,2012,20(10):1075 - 1085.

[51]PUJOL J,MARTINEZ - VILAVELLA G,LLORENTE - ONAINDIA J,et al. Brain imaging of pain sensitization in patients with knee osteoarthritis[J]. Pain,2017,158(9):1831 - 1838.

[52]LIAO X,MAO C P,WANG Y,et al. Brain gray matter alterations in Chinese patients with chronic knee osteoarthritis pain based on voxel - based morphometry[J]. Medicine,2018,97(12):e0145.

[53]KANG B X,MA J,SHEN J,et al. Altered brain activity in end - stage knee osteoarthritis revealed by resting - state functional magnetic resonance imaging[J]. Brain Behav,2022,12(1):e2479.

[54]施珊妮,黄泽灵,桂苗,等. 从"痹阻"与"脾虚"探讨膝骨关节炎的中医病机[J]. 中医正骨,2021,33(10):56 - 58.
SHI S N,HUANG Z L,GUI M,et al. Investigation on TCM Pathogenesis of knee osteoarthritis based on "wind - cold - damp blockade" and "spleen - deficiency"[J]. J Tradit Chin Orthop Traumatol,2021,33(10):56 - 58.

[55]杨威,郭斯印,易志勇,等. 由筋痹论膝骨关节炎病机[J]. 风湿病与关节炎,2021,10(6):53 - 56.
YANG W,GUO S Y,YI Z Y,et al. On the pathogenesis of knee osteoarthritis based on tendon Bi[J]. Rheum Arthritis,2021,10(6):53 - 56.

[56]谭旭仪,邝高艳,卢敏. 膝骨关节炎的"虚、瘀、毒"病机特点探析[J]. 中国实验方剂学杂志,2018,24(24):201 - 206.
TAN X Y,KUANG G Y,LU M. Pathogenesis characteristics of "deficiency,stagnation and toxin" in knee osteoarthritis[J]. Chin J Exp Tradit Med Formulae,2018,24(24):201 - 206.

[57]李西海,刘献祥. 骨关节炎的核心病机:本痿标痹[J]. 中医杂志,2014,55(14):1248 - 1249,1252.
LI X H,LIU X X. The core pathogenesis of osteoarthritis—deficiency in essence and biarthralgia in standard[J]. J Tradit Chin Med,2014,55(14):1248 - 1249,1252.

[58]丁琼浩,敖亮,潘正刚,等. 膝骨性关节炎的病因病机及用药分析[J]. 中医临床研究,2014,6(7):14 - 17.
DING Q H,AO L,PAN Z G,et al. Pathogenesis and medication analysis of Knee Osteoarthritis[J]. Clin J Chin Med,2014,6(7):14 - 17.

[59]许辉,康冰心,孙松涛,等. 膝关节骨性关节炎的中医临床研究进展[J]. 中医学报,2019,34(10):2124 - 2129.
XU H,KANG B X,SUN S T,et al. Clinical research progress of traditional Chinese medicine treatment of knee osteoarthritis[J]. Acta Chin Med,2019,34(10):2124 - 2129.

[60]邵盛,龚利,孙武权,等. 基于经筋理论的膝骨性关节炎下肢生物力学研究进展[J]. 中华中医药杂志,2021,36(11):6589 - 6591.
SHAO S,GONG L,SUN W Q,et al. Research progress on biomechanics of lower extremity in knee osteoarthritis based on meridian sinew theory[J]. China J Tradit Chin Med Pharm,2021,36(11):6589 - 6591.

[61]杨松滨,刘益杰,冯伟,等. 中医手法对兔膝骨关节炎软骨退变及 MAPK 信号转导通路的影响[J]. 上海中医药杂志,2018,52(6):72 - 77.
YANG S B,LIU Y J,FENG W,et al. Effects of Chinese medical manipulation on articular cartilage degeneration and MAPK signal transduction pathway in rabbits with knee osteoarthritis[J]. Shanghai J Tradit Chin Med,2018,52(6):72 - 77.

[62]马铭华,王一洲,赵强. 伸筋易骨法调节兔膝关节周围软组织张力影响软骨形态的研究[J]. 天津中医药,2020,37(9):1067 - 1070.
MA M H,WANG Y Z,ZHAO Q. Study on the effect of Shenjin Yigu method on cartilage morphology by adjusting the tension of soft tissue around knee joint in rabbit[J]. Tianjin J Tradit Chin Med,2020,37(9):1067 - 1070.

[63]李远明,范志勇,查和萍,等. 借助脑功能磁共振技术从中医整体恒动观入手探讨推拿脑激活的中枢响应机制[J]. 针灸临床杂志,2017,33(8):60 - 63.
LI Y M,FAN Z Y,ZHA H P,et al. Central response mechanism of brain activation by Tuina under holism and perpetual motion of TCM concept with brain MRI techinique[J]. J Clin Acupunct Moxibustion,2017,33(8):60 - 63.

[64]TAGHIPOUR M,GHAFFARPASAND F. Antinocioceptive effects of spinal cord stimulation by activation of periaqueductal gray matter and rostral ventromedial medulla: a mechanism beyond the gate control theory[J]. Neuromodulation,2018,21(5):520 - 521.

[65]王冰倩,陈水金,林志刚,等. 推拿对缓解疼痛的作用机制的研究进展[J]. 按摩与康复医学,2020,11(24):6 - 10.
WANG B Q,CHEN S J,LIN Z G,et al. Research progress on the mechanism of massage in relieving pain[J]. Chin Manip Rehabil Med,2020,11(24):6 - 10.

[66]谭文莉,王炜,姜宏宁,等. 推拿治疗慢性下腰痛的即时脑效应研究[J]. 中国中医骨伤科杂志,2019,27(1):11 - 16.
TAN W L,WANG W,JIANG H N,et al. Brain immediate analgesia mechanism of Tuina in low back pain[J]. Chin J Tradit Med Traumatol Orthop,2019,27(1):11 - 16.

[67]王昊,左伟斌,张慧,等. 推拿对慢性神经根型颈椎病疼痛相关脑区的影响[J]. 中国中医基础医学杂志,2017,23(6):854 - 857,860.
WANG H,ZUO W B,ZHANG H,et al. Effects of Tuina on pain - related brain area of chronic cervical spondylotic radiculopathy[J]. Chin J Basic Med Tradit Chin Med,2017,23(6):854 - 857,860.

[68]杨玉婵,谭文莉,王炜,等. 慢性腰痛推拿治疗前后默认脑网络功能连接变化研究[J]. 中国医学计算机成像杂志,2020,26(2):101 - 108.
YANG Y C,TAN W L,WANG W,et al. Study on the changes of default mode brain network function before and after Tuina treatment of chronic low back pain[J]. Chin Comput Med Imag,2020,26(2):101 - 108.

[69]张华,王昊,李多多,等. 中医推拿对颈椎病慢性疼痛患者静息态脑功能默认网络的影响[J]. 北京中医药大学学报,2014,37(12):845 - 850.
ZHANG H,WANG H,LI D D,et al. Effects of traditional Chinese tuina on Default Mode Network(DMN) of patients with chronic cervical radicular pain[J]. J Beijing Univ Tradit Chin Med,2014,37(12):845 - 850.

[70]卿伦学. 推拿治疗慢性膝骨关节炎疼痛的 fMRI 和股直肌超声造影研究[D]. 北京:北京中医药大学,2019.
QING L X. Study on massage treatment of chronic knee osteoarthritis pain by fMRI and contrast - enhanced ultrasound of rectus femoris[D]. Beijing:Beijing University of Chinese Medicine,2019.

[71]郭光昕. 推拿干预膝骨关节炎 MRI 多模态技术的中枢镇痛机制研究[D]. 上海:上海中医药大学,2020.
GUO G X. Central analgesic mechanism of Tuina for knee osteoarthritis based MRI multimodal technique[D]. Shanghai:Shanghai University of Traditional Chinese Medicine,2020.

收稿日期:2023 - 04 - 19

作者简介:周小元(1988 -),女,河南商丘人,大学本科,研究方向:骨关节疾病的护理。

通信作者:许辉(1990 -),男,河南周口人,主治医师,讲师,研究方向:推拿治疗膝骨关节炎的基础及临床研究。E - mail:15036065036@163.com

编辑:吴楠