膝骨关节炎的临床分型初探

徐斌斌[1],王瑞[2],张晶晶[2]
（1. 余姚市中医医院,浙江　宁波　315400;
2. 浙江中医药大学第一临床医学院,浙江　杭州　310053）

摘　要　膝骨关节炎（knee osteoarthritis,KOA）是一种多因素导致的异质性疾病,临床上常采用 Kellgren－Lawrence 影像分级标准、Recht 分级标准、中医辨证分型标准等对 KOA 的类型进行划分,但此类划分标准多根据 KOA 患者的某一特征进行划分,不够细致和全面。我们在总结 KOA 相关研究的基础上,根据 KOA 的临床表现、病理特征及影响因素等,将 KOA 详细地划分为慢性疼痛型、骨代谢失衡型、炎症型、生物力学异常型、局部损伤型、代谢异常型、心理障碍型等类型。本文就该 KOA 临床分型进行初步探讨。

关键词　骨关节炎,膝;临床分型

膝骨关节炎（knee osteoarthritis,KOA）是一种多因素导致的异质性疾病,其典型临床表现为膝关节疼痛、肿胀、活动受限,病理表现以软骨破坏、软骨下骨硬化、骨赘形成为主要特征[1]。临床上常采用 Kellgren－Lawrence 影像分级标准[2]、Recht 分级标准[3]、中医辨证分型标准[1]等对 KOA 的类型进行划分,但此类划分标准多根据 KOA 患者的某一特征进行划分,虽然对于临床治疗 KOA 具有一定的指导意义,但不够细致和全面。我们在总结 KOA 相关研究的基础上,根据 KOA 的临床表现、病理特征及影响因素等,探讨 KOA 的临床分型及针对不同分型的治疗措施,以期为临床治疗 KOA 提供指导。

1　KOA 临床分型

1.1　慢性疼痛型　慢性疼痛型 KOA 患者多存在持续神经病理性疼痛、痛觉过敏或痛觉异常[4]。此类型患者根据疼痛与膝关节结构改变的关系可进一步分为早期疼痛（疼痛早于膝关节结构改变发生）、结构改变并发疼痛和晚期疼痛（疼痛晚于膝关节结构变化发生）[5]。Ohashi 等[6]研究发现,KOA 患者的滑膜液和滑膜组织中神经生长因子水平升高。神经生长因子与其受体结合后,能够激活感觉神经元,引起痛觉感受器的超敏性和高兴奋性[7]。此外,焦虑、抑郁等心理状态也会影响患者的疼痛敏感性,慢性疼痛型 KOA 常存在一定的心理障碍。因此,对于慢性疼痛型 KOA 患者,采用常规消炎镇痛联合疼痛教育与心理疏导进行治疗,其疗效可能优于运动疗法等传统治疗方法。

1.2　骨代谢失衡型　软骨丢失和骨赘形成是骨代谢失衡型 KOA 的主要病理特点,其与骨形成和骨吸收间的平衡密切相关。KOA 早期骨代谢以骨吸收为主,表现为软骨丢失;KOA 晚期骨代谢以骨形成为主,表现为骨赘形成。临床上针对骨代谢失衡型 KOA 患者,应重点关注其骨代谢变化,可以通过Ⅰ型胶原 C 末端肽、Ⅰ型胶原 N 末端肽、Ⅱ型胶原 C 端肽片段及 X 型胶原等分子标志物进行监测[8－9]。在治疗方面,对于以软骨丢失为主的患者,可通过关节腔注射玻璃酸钠、干细胞、富血小板血浆、外泌体等进行治疗,同时通过应用双膦酸盐类药物、组织蛋白酶 K 抑制剂、降钙素等抑制骨吸收;但对于异常骨形成导致的骨赘生成,尚缺少靶向性的治疗药物。

1.3　炎症型　炎症型 KOA 患者的主要特征是炎症因子的高表达。Rim 等[10]研究发现,白细胞介素（interleukin,IL）－1β、IL－6、IL－8 和肿瘤坏死因子－α 等促炎性细胞因子能够促进炎症反应和软骨降解,导致 KOA 不断进展。巨噬细胞存在于滑膜内,可分为 M1 巨噬细胞和 M2 巨噬细胞,其在 KOA 进展中发挥重要作用[11]。M1 巨噬细胞能够分泌大量的促炎性细胞因子,抑制软骨修复;M2 巨噬细胞则具有抗炎作用[12]。Dai 等[13]研究发现,巨噬细胞在鱿鱼Ⅱ型胶原蛋白的刺激下可向 M2 巨噬细胞活化,M2 巨噬细胞能够释放调节细胞因子,抑制炎症反应并促进组织愈合。Manferdini 等[14]研究发现,脂肪间充质干细胞能够将 M1 巨噬细胞转化为 M2 巨噬细胞。对于炎症

通讯作者:徐斌斌　E-mail:xubinbin89@163.com

型 KOA 患者,临床采用口服非甾体抗炎药、关节腔注射皮质类固醇类药物治疗,能够起到良好的抗炎镇痛作用。

1.4　生物力学异常型　生物力学异常型 KOA 的主要特点是膝关节部分间室负荷过载。膝关节结构异常、下肢力线不稳、股四头肌肌力减弱等都是导致膝关节生物力学异常的危险因素[15-17]。Sharma 等[15]研究表明,膝内翻会导致膝关节内侧间室退变,促进 KOA 进展。Wang 等[16]研究发现,膝外翻与膝关节外侧间室骨关节炎的影像学进展密切相关。Hsu 等[18]根据下肢力线将 KOA 患者分为了力线内翻型、力线对齐型和力线外翻型。对于生物力学异常型 KOA 患者,可以通过肌肉力量训练[19]、步态改良等方式调整下肢力线,进而减缓 KOA 进展;对于病情严重者,采用全膝关节置换术可取得良好的治疗效果。

1.5　局部损伤型　局部损伤型 KOA 的主要特征是膝关节存在半月板、软骨或韧带等局部组织损伤。前交叉韧带和半月板损伤会导致膝关节软骨的机械载荷分布不均,影响膝关节的稳定性[20]。Endo 等[21]研究发现,软骨、半月板损伤是继发 KOA 的重要影响因素。Snoeker 等[22]的研究结果表明,膝关节损伤的青年人未来发生 KOA 的风险约是未发生膝关节损伤者的 6 倍,而半月板撕裂、交叉韧带损伤和关节内骨折等因素可能导致 KOA 发生的风险升高。局部损伤型 KOA 患者存在局部组织微小病变,但由于没有典型的临床特征,临床上多通过长期随访才能确定患者属于该类型。

1.6　代谢异常型　代谢异常型 KOA 是指 KOA 合并代谢综合征。代谢综合征是指多种代谢成分异常聚集的病理状态导致的一组复杂的代谢紊乱综合征。Dubey 等[23]研究发现,高血糖能够通过影响软骨特异性蛋白表达来增强软骨基质的分解代谢。肥胖是导致 KOA 早期发生和发展的重要因素[24]。体质量过大导致膝关节负载增加,而过多脂肪组织导致机体产生的瘦素、内脏脂肪素、脂肪因子、炎症因子等物质参与 KOA 进展[25]。此外,膝关节髌上脂肪垫能够通过限制膝过伸、减少髌腱和胫骨摩擦的作用保护膝关节,而髌下脂肪垫异常可能导致膝关节疼痛和结构异常,而其产生的多种促炎性细胞因子能够促进 KOA 进展[26-27]。对于代谢异常型 KOA 患者,如合并肥胖,则需注意合理饮食和体育锻炼,通过减轻自身体重能够缓解 KOA 带来的不适症状;采用药物治疗则避免使用非甾体抗炎药和皮质类固醇,以免进一步影响患者自身的代谢功能;采用葡萄糖胺、软骨素等慢作用药物联合抗氧化药物,能够获得良好的治疗效果[28]。

1.7　心理障碍型　心理障碍型 KOA 指 KOA 患者合并焦虑、抑郁等心理问题。Rathbun 等[29]研究发现,KOA 患者抑郁程度与膝关节疼痛程度之间存在正相关。Johnson 等[30]研究发现,合并严重心理障碍的 KOA 患者,其临床症状与影像学表现之间存在显著差异。因此,临床上应注重对患者心理状态的识别和评估,尤其对于临床症状与影像学改变、病理改变严重不符的患者,应考虑其为心理障碍型 KOA[31]。对于心理障碍型 KOA,应针对患者特定的心理状态采取疼痛管理、心理治疗、抗抑郁药物治疗等多种个性化治疗方案[32]。

2　小　结

临床上提出了多种 KOA 的分级、分期及分型标准,但均不够细致、全面。我们在总结 KOA 相关研究的基础上,根据 KOA 的临床表现、病理特征以及影响因素等,将 KOA 详细地划分为慢性疼痛型、骨代谢失衡型、炎症型、生物力学异常型、局部损伤型、代谢异常型、心理障碍型等类型。这些分型并非独立存在,同一患者可能同时符合多种分型。该分型更能够体现患者的临床特征,有利于临床医师开展针对性治疗。但该分型是我们基于 KOA 的相关研究进行总结归纳而获得的,其准确性和合理性尚需进一步研究予以验证。

参考文献

[1]　中国中医药研究促进会骨伤科分会. 膝骨关节炎中医诊疗指南(2020 年版)[J]. 中医正骨,2020,32(10):1-14.

[2]　KELLGREN J H,LAWRENCE J S. Radiological assessment of osteoarthrosis[J]. Ann Rheum Dis,1957,16(4):494-502.

[3]　RECHT M P,KRAMER J,MARCELIS S,et al. Abnormalities of articular cartilage in the knee:analysis of available MR techniques[J]. Radiology,1993,187(2):473-478.

[4]　LLUCH E,NIJS J,COURTNEY C A,et al. Clinical descriptors for the recognition of central sensitization pain in patients with knee osteoarthritis[J]. Disabil Rehabil,2018,40(23):2836-2845.

[5] LI M,LAN L,LUO J,et al. Identifying the phenotypic and temporal heterogeneity of knee osteoarthritis:data from the osteoarthritis initiative[J/OL]. Front Public Health,2021,9 [2021 - 09 - 13]. https://www. ncbi. nlm. nih. gov/pmc/articles/PMC8416902/.

[6] OHASHI Y,UCHIDA K,FUKUSHIMA K,et al. NGF expression and elevation in hip osteoarthritis patients with pain and central sensitization[J/OL]. Biomed Res Int,2021 [2021 - 09 - 13]. https://www. ncbi. nlm. nih. gov/pmc/articles/PMC8476257/.

[7] HU W,CHEN Y,DOU C,et al. Microenvironment in subchondral bone:predominant regulator for the treatment of osteoarthritis[J]. Ann Rheum Dis,2020,80(4):413 - 422.

[8] FERNANDES T L,GOMOLL A H,LATTERMANN C,et al. Macrophage:a potential target on cartilage regeneration[J]. Front Immunol,2020,11:111.

[9] LV Z,YANG Y X,LI J,et al. Molecular classification of knee osteoarthritis[J/OL]. Front Cell Dev Biol,2021,9 [2021 - 09 - 13]. https://www. ncbi. nlm. nih. gov/pmc/articles/PMC8429960/.

[10] RIM Y A,NAM Y,JU J H. The role of chondrocyte hypertrophy and senescence in osteoarthritis initiation and progression[J]. Int J Mol Sci,2020,21(7):2358.

[11] MOBASHERI A,BATT M. An update on the pathophysiology of osteoarthritis[J]. Ann Phys Rehabil Med,2016,59(5/6):333 - 339.

[12] ZHANG H,CAI D,BAI X. Macrophages regulate the progression of osteoarthritis[J]. Osteoarthritis Cartilage,2020,28(5):555 - 561.

[13] DAI M,SUI B,XUE Y,et al. Cartilage repair in degenerative osteoarthritis mediated by squid type Ⅱ collagen via immunomodulating activation of M2 macrophages,inhibiting apoptosis and hypertrophy of chondrocytes[J]. Biomaterials,2018,180:91 - 103.

[14] MANFERDINI C,PAOLELLA F,GABUSI E,et al. Adipose stromal cells mediated switching of the pro - inflammatory profile of M1 - like macrophages is facilitated by PGE2:in vitro evaluation[J]. Osteoarthritis Cartilage,2017,25(7):1161 - 1171.

[15] SHARMA L,CHANG A H,JACKSON R D,et al. Varus thrust and incident and progressive knee osteoarthritis[J]. Arthritis Rheumatol,2017,69(11):2136 - 2143.

[16] WANG B,LIU Q,WISE B L,et al. Valgus malalignment and prevalence of lateral compartmental radiographic knee osteoarthritis (OA):the Wuchuan OA study[J]. Int J Rheum Dis,2018,21(7):1385 - 1390.

[17] BRISSON N M,STRATFORD P W,MALY M R. Relative and absolute test - retest reliabilities of biomechanical risk factors for knee osteoarthritis progression:benchmarks for meaningful change[J]. Osteoarthritis Cartilage,2018,26(2):220 - 226.

[18] HSU C E,HUANG J T,TONG K M,et al. Total knee arthroplasty according to the original knee phenotypes with kinematic alignment surgical technique - early clinical and functional outcomes[J]. BMC Musculoskelet Disord,2020,21(1):839.

[19] VERONESE N,STEFANAC S,KOYANAGI A,et al. Lower limb muscle strength and muscle mass are associated with incident symptomatic knee osteoarthritis:a longitudinal cohort study[J/OL]. Front Endocrinol (Lausanne),2021,12 [2021 - 09 - 13]. https://www. ncbi. nlm. nih. gov/pmc/articles/PMC8716541/.

[20] WANG L J,ZENG N,YAN Z P,et al. Post - traumatic osteoarthritis following ACL injury[J]. Arthritis Res Ther,2020,22(1):57.

[21] ENDO J,SASHO T,AKAGI R,et al. Comparative analysis of gene expression between cartilage and menisci in early - phase osteoarthritis of the knee - an animal model study[J]. J Knee Surg,2018,31(7):664 - 669.

[22] SNOEKER B,TURKIEWICZ A,MAGNUSSON K,et al. Risk of knee osteoarthritis after different types of knee injuries in young adults:a population - based cohort study[J]. Br J Sports Med,2020,54(12):725 - 730.

[23] DUBEY N K,NINGRUM D N A,DUBEY R,et al. Correlation between diabetes mellitus and knee osteoarthritis:a dry-to-wet lab approach[J]. Int J Mol Sci,2018,19(10):3021.

[24] LAMBOVA S N,BATSALOVA T,MOTEN D,et al. Serum leptin and resistin levels in knee osteoarthritis - clinical and radiologic links:towards precise definition of metabolic type knee osteoarthritis[J]. Biomedicines,2021,9(8):1019.

[25] GEORGIEV T,ANGELOV A K. Modifiable risk factors in knee osteoarthritis:treatment implications[J]. Rheumatol Int,2019,39(7):1145 - 1157.

[26] SCHWAIGER B J,MBAPTE WAMBA J,GERSING A S,et al. Hyperintense signal alteration in the suprapatellar fat pad on MRI is associated with degeneration of the patellofemoral joint over 48 months:data from the Osteoarthritis Initiative[J]. Skeletal Radiol,2018,47(3):329 - 339.

[27] ZHOU Z,TANG S,NIE X,et al. Osteoarthritic infrapatellar fat pad aggravates cartilage degradation via activation of p38MAPK and ERK1/2 pathways[J]. Inflamm Res,2021,

70(10/12):1129 - 1139.

[28] GAO Y H,ZHAO C W,LIU B,et al. An update on the association between metabolic syndrome and osteoarthritis and on the potential role of leptin in osteoarthritis[J/OL]. Cytokine,2020,129[2021 - 9 - 13]. https://www. sciencedirect. com/science/article/abs/pii/S1043466620300594?via%3Dihub.

[29] RATHBUN A M,STUART E A,SHARDELL M,et al. Dynamic effects of depressive symptoms on osteoarthritis knee pain[J]. Arthritis Care Res (Hoboken),2018,70(1):80 - 88.

[30] JOHNSON A J,LAFFITTE NODARSE C,PERAZA J A,et al. Psychological profiles in adults with knee OA - related pain:a replication study[J/OL]. Ther Adv Musculoskelet Dis,2021,13[2022 - 01 - 13]. https://www. ncbi. nlm. nih. gov/pmc/articles/PMC8664321/.

[31] BANNURU R R,OSANI M C,VAYSBROT E E,et al. OARSI guidelines for the non - surgical management of knee,hip,and polyarticular osteoarthritis[J]. Osteoarthritis Cartilage,2019,27(11):1578 - 1589.

[32] LENTZ T A,GEORGE S Z,MANICKAS - HILL O,et al. What general and pain - associated psychological distress phenotypes exist among patients with hip and knee osteoarthritis? [J]. Clin Orthop Relat Res,2020,478(12):2768 - 2783.

(收稿日期:2021-10-23　本文编辑:吕宁)

(上接第 56 页)

[47] WENDT M,NOVAK C B,ANASTAKIS D J. Prevalence of cold sensitivity in upper extremity nerve compression syndromes[J]. J Hand Surg Eur Vol,2018,43(3):282 - 285.

[48] TIMMERMANS E J,VAN DER PAS S,SCHAAP L A,et al. Self - perceived weather sensitivity and joint pain in older people with osteoarthritis in six European countries:results from the European Project on Osteoarthritis (EPOSA)[J]. BMC Musculoskelet Disord,2014,15:66.

[49] DE KONING E J,TIMMERMANS E J,VAN SCHOOR N M,et al. EPOSA Group. Within - Person pain variability and mental health in older adults with osteoarthritis:an analysis across 6 european cohorts[J]. J Pain,2018,19(6):690 - 698.

[50] SIVIERO P,VERONESE N,SMITH T,et al. EPOSA research group. association between osteoarthritis and social isolation:data from the EPOSA study[J]. J Am Geriatr Soc,2020,68(1):87 - 95.

[51] PEULTIER L,LION A,CHARY - VALCKENAERE I,et al. Influence of meteorological elements on balance control and pain in patients with symptomatic knee osteoarthritis[J]. Int J Biometeorol,2017,61(5):903 - 910.

[52] BONGERS J,VANDENNEUCKER H. The influence of weather conditions on osteoarthritis and joint pain after prosthetic surgery[J]. Acta Orthop Belg,2020,86(1):1 - 9.

[53] MCALINDON T,FORMICA M,SCHMID C H,et al. Changes in barometric pressure and ambient temperature influence osteoarthritis pain[J]. Am J Med,2007,120(5):429 - 434.

[54] AZZOUZI H,ICHCHOU L. Seasonal and weather effects on rheumatoid arthritis:myth or reality? [J/OL]. Pain Res Manag,2020[2021 - 12 - 04]. https://pubmed. ncbi. nlm. nih. gov/32963656/.

[55] SAVAGE E M,MCCORMICK D,MCDONALD S,et al. Does rheumatoid arthritis disease activity correlate with weather conditions? [J]. Rheumatol Int,2015,35(5):887 - 890.

[56] MOSS P,BENSON H A E,WILL R,et al. Patients with knee osteoarthritis who score highly on the paindetect questionnaire present with multimodality hyperalgesia,increased pain,and impaired physical function[J]. Clin J Pain,2018,34(1):15 - 21.

[57] WRIGHT A,BENSON H A E,WILL R,et al. Cold pain threshold identifies a subgroup of individuals with knee osteoarthritis that present with multimodality hyperalgesia and elevated pain levels[J]. Clin J Pain,2017,33(9):793 - 803.

[58] FERREIRA M L,ZHANG Y,METCALF B,et al. The influence of weather on the risk of pain exacerbation in patients with knee osteoarthritis - a case - crossover study[J]. Osteoarthritis Cartilage,2016,24(12):2042 - 2047.

[59] FU K,METCALF B,BENNELL K L,et al. Association of weather factors with the risk of pain exacerbations in people with hip osteoarthritis[J]. Scand J Rheumatol,2021,50(1):68 - 73.

[60] JENA A B,OLENSKI A R,MOLITOR D,et al. Association between rainfall and diagnoses of joint or back pain:retrospective claims analysis[J]. BMJ,2017,359:j5326.

[61] TIMMERMANS E V J,VAN DER PAS S,DENNISON E V M,et al. EPOSA research group. The influence of weather conditions on outdoor physical activity among older people with and without osteoarthritis in 6 european countries[J]. J Phys Act Health,2016,13(12):1385 - 1395.

(收稿日期:2022-01-14　本文编辑:时红磊)