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膝关节周围截骨的生物力学机制与临床研究进展

魏子程, 吴江栋, 王亦仓, 廖家伯, 江 旭, 王 燎, 谢 凯, 严孟宁
(上海交通大学医学院附属第九人民医院 骨科,上海市骨科内植物重点实验室, 上海 200011)

摘要:膝骨关节炎(osteoarthritis,OA)是导致关节功能障碍的主要原因之一。膝关节周围截骨因能延缓膝 OA 进展、改善关节功能而备受关注。膝关节力线异常是膝 OA 发生发展的关键生物力学因素,其精准控制是膝关节周围截骨术的核心目标。本文系统综述了膝关节周围截骨术相关的生物力学研究进展,重点围绕力线的精准化与个性化矫正展开:梳理了力线分型体系与测量技术的发展,分析了异常力学负荷诱发膝 OA 的生物力学机制,探讨了膝关节周围截骨术的力线目标与临床应用进展,以期为临床膝关节周围截骨治疗膝 OA 提供新的视角与思路。

关键词: 膝关节周围截骨; 下肢力线; 生物力学机制; 精准化治疗; 膝骨关节炎
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Biomechanical Mechanism and Clinical Research Progress of Knee Osteotomy

WEI Zicheng, WU Jiangdong, WANG Yicang, LIAO Jiabo, JIANG Xu, WANG Liao, XIE Kai, YAN Mengning
(*Shanghai Key Laboratory of Orthopaedic Implants, Department of Orthopaedic Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200011, China*)

Abstract: Knee osteoarthritis (OA) is a primary cause of joint dysfunction. Knee osteotomy has garnered significant attention due to its potential to delay the progression of knee OA and enhance joint function. As a pivotal biomechanical factor in the onset and progression of OA, the accurate correction of abnormal knee alignment is the central objective of knee osteotomy. This article systematically reviews the biomechanical research progress related to knee osteotomy, with a focus on the precision and personalized correction of force line. The development of new classification system and measurement technology of force line is summarized, the biomechanical mechanism of knee OA induced by abnormal mechanical load is analyzed, and the goal of force line and clinical application progress of knee osteotomy is discusses, so as to provide a new perspective and idea for the clinical treatment of knee OA with knee osteotomy.

Key words: knee osteotomy; lower limb alignment; biomechanical mechanism; precise treatment; knee osteoarthritis

膝关节作为人体最大的承重关节,其生物力学环境的稳定对维持正常运动功能至关重要。下肢力线的异常,尤其是膝关节内翻或外翻畸形,不仅改变了关节负荷的分布,还通过复杂的力学生物学

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通信作者:严孟宁,教授,主任医师,E-mail: yanmengning@163.com

机制诱发软骨下骨重塑、关节软骨退变及半月板损伤,最终导致膝关节骨关节炎(osteoarthritis,OA)的发生与进展。近年来,随着影像学技术的发展和个体化医疗理念的深入,传统基于"中立位"力线的评估模式正逐步被更具个性化的分类体系所取代。与此同时,膝关节周围截骨术作为一种保留自身关节、纠正力线异常的有效手段,在延缓膝 OA 进程、改善患者生活质量方面展现出重要价值。本文围绕膝关节力线的分类与测量、力学生物学机制及其在截骨术中的应用,系统综述当前研究进展,旨在为临床精准治疗提供理论依据和技术支持。

1 膝关节力线分型与测量

1.1 膝关节力线分型

下肢力线是指从髋关节延伸至踝关节的力传导路径。通常情况下,该力线可依据解剖轴或机械轴进行描述,并通过站立位下肢全长 X 线片进行精准测量[1]。临床上常用于判断膝关节力学传导的指标包括髋-膝-踝角(hip-knee-ankle,HKA)、负重力线(weight-bearing line, WBL)、机械股骨远端外侧角(mechanical lateral distal femoral angle, mLDFA)、机械胫骨近端内侧角(mechanical medial proximal tibia angle, mMPTA)、关节线会聚角(joint line convergence angle,JLCA)和关节线方向(joint line orientation, JLO)等[2]。

虽然目前已建立了基于下肢力线的膝关节人群标准(内翻、中立、外翻)[3],但不同个体之间仍存在力线差异[4]。Bellemans 等[5]提出了膝关节固有内翻概念,并指出非所有个体的膝关节都拥有"中立位力线"的特性。

为了更好地对个体下肢力线进行分型,Lin 等[6]基于胫骨和股骨对线的不匹配开发了一个新的分类系统,该分类方法提供了比传统分类更为详细的下肢对线的术前规划指导。此外,Hirschmann 等[7]提出了功能性膝关节表型(functional knee phenotypes),以及 MacDessi 等[4]提出了膝关节冠状位对线(coronal plane alignment of the knee,CPAK)分型系统(见表 1)。在 CPAK 分型系统中,最常见类别依次为Ⅱ、Ⅰ、Ⅴ型,也同样支持膝关节固有内翻的新认知。这些新分类提供了更细致的个体膝关节力线定义,使"力线个性化"理念得到了进一步完善。

表 1 CPAK 分型

Tab. 1 CPAK classification

CPAK 分型	aHKA/(°)	JLO	特点
Ⅰ型	<-2	<177	内翻 aHKA 及顶点远端 JLO
Ⅱ型	0±2	<177	中立 aHKA 及顶点远端 JLO
Ⅲ型	>2	<177	外翻 aHKA 及顶点远端 JLO
Ⅳ型	<-2	180±3	内翻 aHKA 及中立 JLO
Ⅴ型	0±2	180±3	中立 aHKA 及中立 JLO
Ⅵ型	>2	180±3	外翻 aHKA 及中立 JLO
Ⅶ型	<-2	>183	内翻 aHKA 及顶点近端 JLO
Ⅷ型	0±2	>183	中立 aHKA 及顶点近端 JLO
Ⅸ型	>2	>183	外翻 aHKA 及顶点近端 JLO

注:CPAK 为膝关节冠状位对线;aHKA 为算数髋膝踝角;JLO 为关节倾斜度。CPAK 法定义 aHKA=MPTA-LDFA,中立 aHKA 为 0°±2°,aHKA>2°为外翻,aHKA<2°为内翻;定义 JLO =MPTA+LDFA,夹角和若为 180°±3°则关节线为中立位,若<177°则顶点位于在关节线远端,反之则在关节线近端。其中,MPTA 为胫骨近端内侧角,LDFA 为股骨远端外侧角。

1.2 膝关节力线测量

膝关节力线的评估离不开影像学技术支持下的力线测量。传统的二维站立位全长 X 线片是评估下肢力线的基石,也是临床最常用的测量方法,但其局限性无法避免[8]。轻微的体位变化,均可能引发测量参数的显著偏差,严重影响测量的可重复性与准确性[9]。因而,越来越多研究聚焦于基于计算机断层(computed tomography, CT)/磁共振成像(magnetic resonance imaging, MRI)的三维重建的力线测量技术。

三维测量技术根本性地消除了投影误差和体位依赖。近年来,一系列研究证实了三维测量相较于二维测量有着更高的准确性和可重复性[10]。但是,三维测量技术的使用也带来了新的挑战,即方法学的异质性。不同研究在定义关节中心、力线参数及建立坐标系时,所采用的软件、算法及原则均存在差异,例如,有的采用解剖标志点法,有的则通过拟合平面来定义关节线[11-12]或使用不同的参考系定义力线参数等[13-14]。这导致不同研究的测量结果缺乏可比性,难以建立统一的测量标准和"正常值"范围。

针对这一问题,Veerman 等[10,15]提出了首个标准化 3 D 下肢对线分析的结构化框架共识,并提出了 3 项原则:① 全面利用数据原则;②坐标系分层原则;③ 标准化前提原则。这些原则共同为三维测量提供了标准化框架,但仍需进一步的临床验证。

1.3　人工智能辅助膝关节力线测量

精准测量是膝关节力线评估的基础。目前,膝关节力线参数主要由医生进行手工测量。但手工测量费时、费力,且测量的变异度较大,在大样本研究显示传统的手工或半自动的测量难以保证测量的准确性和可靠性[16]。

针对手工测量的弊端,人工智能(artificial intelligence,AI)为精准力线测量提供了新的方法。最新的 Meta 分析指出,AI 在下肢力线参数的二维测量中与人类专家高度一致(ICC≥0.90),表现出高可靠性和准确性,并且可在几秒内完成测量[17]。此外,AI 在不同人群(儿童、成人、有无植入物)中均表现稳定,不受植入物或病理条件影响[18]。这些研究凸显了 AI 辅助精准测量在临床应用中的能力。

相比二维,基于三维影像(如 CT、MRI)的下肢力线 AI 测量研究仍处于早期阶段。究其原因可能是三维 AI 测量面临着三维数据量大、标注复杂、计算成本高,且缺乏大规模标注数据集等挑战。

2　膝关节力线的力学生物学研究

正常情况下,下肢力学轴线穿过膝关节中心,使负荷得以均匀分布在关节面上。当力线发生内翻或外翻时,膝关节负荷分布发生显著改变,导致应力集中和组织适应性反应,最终引发膝关节退行性病变。这种异常力学环境通过复杂的力学生物学机制影响关节各个组成部分,包括软骨下骨、关节软骨和半月板等,造成组织结构破坏和功能丧失。

2.1　软骨下骨

在异常膝关节力学环境下,随着膝关节力线偏差和 OA 严重程度的增加,患侧胫骨平台软骨下骨小梁(subchondral trabecular bone, STB)骨体积、骨小梁数量和骨小梁厚度增加,骨小梁分离度降低。HKA 角是影响 STB 重塑和微观结构的最显著因素,表明力线异常是驱动软骨下骨改变的核心力学生物学诱因[19]。

异常力学刺激通过多个关键信号通路的复杂调控影响软骨下骨中骨细胞代谢和成骨破骨细胞平衡,进而造成软骨下骨结构异常。Wnt/β-catenin 通路作为重要的合成代谢途径,适度激活可促进成骨分化并抑制破骨形成,但异常力学负荷下的过度激活可上调炎症因子水平,导致软骨下骨代谢异常[20-21]。TGF-β/BMP 信号通路通过 Smad 蛋白磷酸化传递机械应力,调节间充质干细胞的成骨与破骨活性,其异常激活与骨重塑密切相关[20,22-25]。Hippo 通路的核心分子 YAP/TAZ 对外界机械刺激高度敏感,异常力学负荷可诱导其核转位,调控下游成骨相关基因表达和趋化因子分泌,打破骨细胞稳态[26-28]。此外,SDF-1/CXCR4 轴在力学刺激下参与成骨分化、血管生成及干细胞迁移的调节[29-30],RANTES-CCRs-Akt2 轴则介导机械负荷相关的免疫细胞募集和破骨细胞活化[31-33]。

在异常力学下,这些通路相互交织,使得异常受力侧软骨下骨呈现高转换骨重塑表型[34],打破了骨稳态,形成了"骨磨损"结构[35-36],进一步加重异常力学环境,形成恶性循环,造成关节损伤(见图 1)。

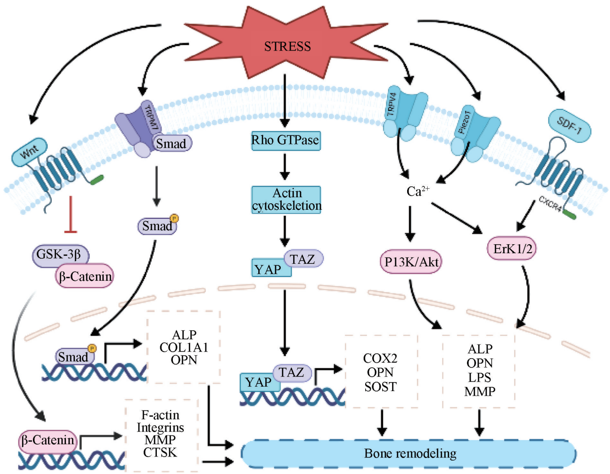

图 1　异常力学环境诱导软骨下骨骨重塑的机制

Fig. 1　Mechanism of subchondral bone remodeling induced by abnormal mechanical environment

2.2　软骨

在健康软骨中,机械负荷通过 TRPV4 通道介导的适度 Ca^{2+} 内流和整合素 $\alpha_5\beta_1$ 激活的 IL-4 信号来维持合成代谢与抗炎平衡,同时初级纤毛协调 TRPV4 与 Hedgehog 等通路感知环境变化,维持正常软骨代谢平衡[37-38]。而在 OA 状态下,炎症环境(如 IL-1β)上调 PIEZO1 通道导致 Ca^{2+} 超载和细胞死亡[39-43],整合素转而结合细胞外基质(extracellular matrix, ECM)降解碎片,从而触发 NF-κB 介导的炎症与分解代谢,初级纤毛在 IL-1β

作用下长度增加并加剧炎症反应，同时 Wnt/β-catenin 经典通路过度激活，驱动了软骨细胞肥大化和基质降解[44-46]，这些调控共同促进了软骨损伤（见图 2）。

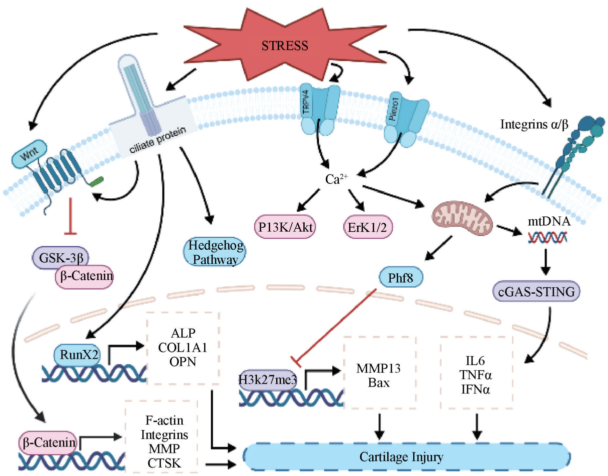

图 2　异常力学环境诱导软骨损伤的机制

Fig. 2　Mechanism of cartilage injury induced by abnormal mechanical environment

近年来研究表明，异常机械应力可通过机械敏感离子通道（如 Piezo1）和细胞器功能调控（如线粒体）在软骨退变中发挥关键作用。软骨细胞，作为机械敏感细胞，适当的动态压缩（如 0.1～1 Hz）可促进胶原和蛋白聚糖合成，而静态载荷或过度动态压缩则导致 ECM 降解或分解代谢增强。最新研究发现，在异常力学刺激下，软骨细胞通过机械敏感离子通道 Piezo1 触发 Ca^{2+} 内流并造成线粒体钙超载，钙超载迅速降低线粒体膜电位、诱导线粒体通透性转换孔开放，一方面导致腺苷三磷酸（adenosine triphosphate，ATP）合成减少、活性氧激增和线粒体分裂/融合失衡，组蛋白去甲基化酶 Phf8 的核转位上调，催化 H3K27me3 去甲基化，解除对基质降解酶 MMP13 及凋亡基因 Bax 的转录抑制[47]；另一方面促使线粒体 DNA 外泄至胞质，启动 STING-TBK1-IRF3 先天免疫轴，放大 IL-6、TNF-α、IFN-α 等炎症级联反应，最终协同加速软骨细胞外基质降解和细胞凋亡，驱动骨关节炎进展[48]。

2.3　半月板

异常力学负荷下，半月板的改变与软骨类似，均涉机械敏感离子通道 Piezo1、ECM、炎症介质等相关分子和 AMPK、PPAR 和 PI3K 等信号通路的改变。

最新的研究通过大鼠内侧半月板撕裂（medial meniscal tear，MMT）模型，分析了骨关节炎发展过程中不同时间节点关节组织（软骨、半月板和滑膜）的转录组学变化。研究发现，在所有时间节点，半月板中 ECM 成分及基质降解酶成分的表达增加，这些分子与 OA 的发生和进展相关。此外，研究确定了半月板中脂多糖失调、炎症介质 CCL2 和 CCL7 增加[49]。信号通路方面，半月板中 AMPK 和 PPAR 信号通路下调，ECM-受体相互作用、黏着斑、PI3K-Akt 和 HIF-1 信号通路上调。在机械刺激相关表达中，研究发现半月板中 Piezo1 和 Trpv4 的表达持续增加[49]。异常负荷影响 Piezo1，并通过 PI3K/AKT/mTORC1 通路促进半月板细胞外基质降解，从而驱动 OA 进展[40]。

3　膝关节周围截骨的生物力学考量与研究进展

膝关节周围截骨是改变下肢异常生物力学的常用方法，包括胫骨近端截骨术（high tibial osteotomy，HTO）和股骨远端截骨术（distal femur osteotomy，DFO）。两者主要目标都是在严重干骺端畸形的情况下减少膝关节内侧或外侧骨间室压力，从而延缓骨关节炎的进展[50-51]。

3.1　下肢力线矫正导致的膝关节组织学变化

基于绵羊动物模型的实验，有学者对比研究了内翻矫正（4.5°内翻）、标准矫正（4.5°外翻）和外翻矫正（9.5°外翻）HTO 术后膝关节组织学变化[52-53]。结果显示，在半月板和关节软骨方面，HTO 术后 6 个月均未观察到宏观和微观结构的显著变化；在软骨下骨方面，无负荷对照组和过度矫正组的软骨下骨的“骨面积/骨体积”存在显著差异，过度矫正组骨的面体比增大，其余无明显差异[54]。该研究揭示了膝关节力线矫正的生物安全性。

Reinhard 等[55]研究发现，过度负荷会导致软骨与软骨下骨的损伤，且软骨损伤先于软骨下骨。过度负荷会显著改变软骨下骨的微观结构，导致骨量减少。降低异常力学负荷抑制早期软骨退变，避免膝关节软骨下骨骨小梁的改变，防止原本正常的骨软骨关系受到影响。

同样，Oláh 等[56]通过临床病例研究与绵羊模型研究发现，降低应力负荷可使关节软骨和软骨下

骨恢复正常的组织学表型,表明降低应力负荷对骨软骨单元具有保护作用。这项研究为下肢力线矫正减轻 OA 进展提供了直接的组织学证据。

从组织学变化来看,下肢力线的矫正可以通过解除关节间室的压力负荷,减轻患者疼痛,部分恢复关节软骨和软骨下骨的生理功能,抑制骨关节炎的进展。

3.2 膝关节周围截骨术的最佳力线考量

对于 HTO 术而言,目前采用的术后力线范围大多基于早期的小样本回顾性临床研究。Hernigou 等[57]发现患者术后 HKA 角外翻 3°~6°的临床效果较好;Miniaci 等[58]和 Dugdale 等[59]建议目标 WBL 百分比为 60% ~70% 和 62% ~66%;Fujisawa 等[60]发现当 WBL 通过胫骨外侧平台的 30% ~40% 时膝关节内侧腔室的软骨不再退变,并认为 62.5% 的 WBL 百分比是最佳位置(Fujisawa 点)[61]。随着研究的深入,最近的共识建议采取个性化手术方案,将 WBL 百分比目标范围设定在 50% ~68% 之间,根据患者的具体情况来确定不同的矫正目标(见表 2),并避免术后膝关节关节线的过度倾斜(术后 JLO≤5°和 MPTA<94°)[62-65]。

表 2 HTO 术后胫骨平台 WBL 百分比的矫正目标

Tab. 2 Correction goals for the percentage of WBL in the tibial plateau after HTO

内翻畸形及以下情况	WBL 百分比的目标位置/%
① 内侧负荷过大但无相应的软骨损伤 ② 没有骨关节炎的手术操作	50~55
① 内侧关节腔骨关节炎 I 级或 II 级 ② 进行软骨重建术(OATS,ACT) ③ 半月板修复/移植 ④ 慢性外侧/后外侧不稳定	55~60
① 内侧关节腔骨关节炎 III 级或 IV 级	60~65

注:0% 表示胫骨平台内侧边缘,100% 表示胫骨平台外侧边缘。

在 DFO 术中,因为中性对线时内侧间室已经承受了 3/4 的负荷[3],目前建议矫正中性对线或是轻度内翻(0°~2°),不建议过度矫正[66],以免加速内侧的间室 OA 的过程。此外,早期的一项步态分析研究表明,在采用中性对线策略进行 DFO 后,患者在运动学和动力学方面表现出与健康对照组相似的特征[67]。最近的研究表明,DFO 术矫正至轻度内翻位(下肢力线通过距离为 48.6%)更有利于降低外侧间室关节接触力和软骨高应力[68]。

3.3 下肢力线的精确调控

良好的下肢力线矫正不仅仅要求个体化的力线规划,更需要术中的精准实施。为了实现下肢力线的精准矫正,近年来,越来越多的辅助手段被应用于膝关节周围截骨术,包括 3 D 打印个性化截骨导板、手术导航系统和手术机器人等。

传统的膝关节周围截骨术依赖术者经验判断截骨角度,易导致 HKA 矫正偏差。3 D 打印个性化截骨导板可以精准规划截骨位置与角度,具备良好的精准度[69]。本课题组前期基于二维/三维影像配准技术开发了新型 3 D 打印个性化截骨导板[70],可有效提高截骨的准确度。手术导航系统通过结合计算机视觉、空间定位和实时图像处理技术,实现精准入路与手术,提高截骨手术精确度,降低下肢力线不良率[71-73]。手术机器人大多在全膝关节置换术中使用,在膝关节周围截骨术中的使用较少。在膝关节周围截骨术失败的患者中,使用手术机器人进行全膝关节置换术可以提供更为精确的力线矫正,并降低肢体长度差异[74]。

4 总结与展望

本文系统梳理了膝关节力线评估与干预的最新进展。从二维 X 线测量到三维重建与 AI 辅助测量,再到新的分型体系的构建,膝关节力线的评估正朝着更精准、高效与个性化的方向发展。在病理机制层面,异常力线通过影响软骨下骨重塑、软骨及半月板代谢,驱动膝 OA 的发生发展。膝关节周围截骨术通过纠正异常负荷分布,可在组织学层面逆转早期 OA 进展,保护骨软骨单元结构完整性。同时,辅助手术技术的应用保证了手术中力线的精准控制。

未来,在膝关节周围截骨术术后最佳力线的选择上,随着大型动物试验、有限元分析、步态模拟与长期随访数据的补充与完善,有望构建个体化力线优化模型,实现真正意义上的"一人一策"精准矫形。

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