

·综述·

腰椎骨小梁生物力学特性及其在骨质疏松骨折治疗中的应用

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【摘要】伴随中国社会的进步及人口老龄化加剧,骨质疏松性骨折快速增多。文章详细探讨了骨小梁生物力学及其在椎体骨质疏松骨折治疗中的应用。椎体是骨质疏松骨折最常见的部位,其主要由松质骨构成。文章首先介绍了椎体松质骨的宏观结构和生物力学特性。而后介绍了骨小梁的微结构参数对骨小梁的形态特征及力学性质的重要作用。重点介绍了常用于定量描述骨小梁微结构的三维形态学参数,及骨小梁异质性、在空间上的连接方向、年龄增长、性别对其力学性质的影响。继而介绍骨质疏松性腰椎压缩骨折的传统诊断及创新诊断方式。在治疗方面,文章概述了现如今应用于临床的多种治疗骨质疏松性骨折术式的优缺点,包括椎体成形术、椎体融合术和经皮椎弓根钉内固定术等。最后介绍了新兴技术3D打印在脊柱手术中的创新应用,如使用3D打印多孔金属内植物和仿生内固定物。未来将3D打印技术与传统治疗方法相结合,可以达到更好的治疗效果和提高生活质量。

【关键词】 骨小梁; 松质骨; 微结构; 骨质疏松骨折; 生物力学

Biomechanical characteristics of lumbar trabecular bone and its application in the treatment of osteoporotic fractures Li Yanlin^{1, 2, 3, 4}, Wang Haicheng^{2, 3, 4}, Quan Yuanyuan^{2, 3, 4, 5}, Zhang Yifan^{2, 3, 4}, Chen Wei^{2, 3, 4}.

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【Abstract】 With the progress of Chinese society and the intensification of population aging, osteoporotic fractures are rapidly increasing. The article discusses in detail the biomechanics of trabeculae and its application in the treatment of vertebral osteoporotic fractures. The vertebral body is the most common site of osteoporotic fractures, mainly composed of trabecular bone. The article first introduces the macroscopic structure and biomechanical properties of vertebral trabecular bone. Then, the important role of microstructure parameters of bone trabeculae in the morphological characteristics and mechanical properties of bone trabeculae was introduced. The focus is on the three-dimensional morphological parameters commonly used to quantitatively describe the microstructure of bone trabeculae, as well as the effects of bone trabecular heterogeneity, spatial connectivity direction, age growth, and gender on their mechanical properties. Subsequently, traditional and innovative diagnostic methods for osteoporotic lumbar vertebral compression fractures will be introduced. In terms of treatment, the article provides an overview of the advantages and disadvantages of various clinical treatments for osteoporotic fractures, including vertebroplasty, vertebral fusion, and percutaneous pedicle screw fixation. Finally, the innovative application of emerging technology 3D printing in spinal surgery was introduced, such as the use of 3D printing porous metal implants and biomimetic internal fixation devices. Combining 3D printing technology with traditional treatment methods can achieve better therapeutic effects and improve quality of life.

【Key word】 Bone trabeculae; Cancellous bone; Microstructure; Osteoporosis fractures; Biomechanics

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脊柱作为人体中最为重要的支撑骨骼,由于其本身特殊的解剖结构及生物力学性质,导致50岁以上人群脊柱骨折的发生率高达25%~50%^[1]。老年人骨骼易发生骨质疏松,在此基础上遭受轻微暴力就可能发生骨质疏松性椎体骨折(osteoporotic vertebral body compression fractures, OVCFs)。由于人口老龄化加剧,OVCFs已成为全球最主要的健康问题之一^[2-4]。OVCFs有多种并发症,如持续疼痛、后凸畸形、抑郁、体重减轻、生活质量下降等,甚至会导致死亡^[5]。OVCFs患者松质骨骨量减少,骨小梁的微结构遭到破坏,骨强度和骨质量均会降低。了解椎骨的微结构、及时对骨质疏松症做出诊断,可以大大延缓疾病的进展。并且早期重建压缩骨折的松质骨结构,恢复伤椎的力学结构,能够提高手术的成功率。因此,了解生理和病理情况下的椎体松质骨结构及生物力学功能格外重要,本文将对上述内容作重点介绍(见图1)。

一、椎体松质骨结构和生物力学



图1 腰椎骨小梁生物力学特性及其在骨质疏松骨折治疗中应用的图形目录

(一) 椎体松质骨宏观结构

临幊上常常通过评估骨强度来预测患者的骨折风险,骨的大小、形态、成分、结构特征等均会影响骨强度。其中,椎体形态和结构特性是影响骨强度的主要因素之一^[6]。正常椎体由骨小梁及皮质终板组成,脊柱所承受的外力经由椎间盘传导至椎体终板,最终到达骨小梁,并以骨小梁为中心向周围放射。骨骼为了适应人体机械功能,从纳米到宏观尺度有所不同^[7]。在宏观尺度,骨分为皮质骨和松质骨;在亚显微结构水平(1~10微米),骨由许多矿化的胶原纤维组成,这些纤维单向排列称为薄片^[8];在纳米结构水平(<100纳米),骨是类似于板状增强复合材料,由分布在有机胶原纤维和非胶原蛋白中的羟基磷灰石矿物晶体组成。

椎体骨小梁在横向及垂直方向形成立体的网状结构,同时表面覆盖整齐、紧密排列的胶原纤维丝以加固其结构,使椎体能够承受相当的负荷^[9],能够保护脊髓和马尾等神经结构^[10]。由于松质骨间隙较大,内部含有丰富的骨髓组织,且

在椎体骨小梁内没有血管,由周围骨髓扩散供应营养^[11],导致骨表面与骨体积的比率高。椎体是造血和矿物质储存的主要部位,这也意味着椎体内部的孔隙率更高,限制了它的强度和刚度^[12]。并且研究表明椎体皮质骨及松质骨可以承受的压缩负荷比例与年龄相关,40岁以前为45%和55%,40岁以后达到65%和35%^[13]。且由于随年龄增长松质骨质量下降,发生腰椎骨折的概率大大增加。

(二) 椎体骨小梁生物力学

椎体为适应机械外力以及承受特定类型载荷,演化出特殊的骨小梁微结构和力学性能^[12]。椎体内骨小梁的微结构差异对评估椎体的骨强度和骨质量具有重要意义,这与骨质疏松性椎体骨折的发病机制具有相关性。人类椎体骨小梁的骨密度和力学性能在结构上表现出很大的异质性,并与年龄和性别高度相关。

Gong等^[14]的研究表明,骨小梁的微结构参数对骨小梁的形态特征及力学性质起着重要作用。通过使用 μ CT和 μ MRI成像技术,用三维形态学参数定量描述骨小梁的微结构,如结构模型指数(structure model index, SMI)、骨小梁分离度(trabecular separation, Tb.Sp)、骨小梁数量(trabecular number, Tb.N)、骨小梁厚度(trabecular thickness, Tb.Th)、连接密度(connectivity density, Conn.D)等^[15-17]。与椎体周围区域相比,中央区的骨密度(bone mineral density, BMD)、骨体积分数(bone volume fraction, BV/TV)和Tb.Th较低,而Tb.N较高。与前部相比,后部具有较高的BMD、BV/TV、Tb.N和Conn.D,较低的Tb.Sp、各向异性程度(degree of anisotropy, DA)和SMI^[18-21]。Vom等^[20]在水平方向上将椎体均分为上、中、下三层,BV/TV在上层最低,Tb.Th在中层最高,Tb.N在中层最低,下层最高。

除了骨小梁微结构的三维形态参数,单个骨小梁的空间/方向异质性和面积/长度分布,也对骨小梁的力学性能有非常重要的作用^[22]。利用ITS技术将椎体骨小梁沿纵向(0°~30°),斜向(30°~60°)和横向(60°~90°)三个方向分为板状骨小梁和杆状骨小梁,发现大部分板状骨小梁沿着主应力的方向排列^[23]。一些基于椎体松质骨显微结构分析的研究表明,约70%的板状骨小梁与骨的主要负载方向(纵向)对齐,约70%的杆状骨小梁与横轴对齐连接纵向排布的板状骨小梁^[15, 24-25]。同时,椎体刚度与沿纵向的骨小梁骨量分数关系较大^[24]。最近的研究认为,板状骨小梁体积分数和杆状骨小梁长度是椎体弹性模量的两个显著预测因子,而只有与板状骨小梁相关的参数(板状骨小梁体积分数、连接密度、表面积和厚度)是屈服强度变化的显著预测因子^[26-27]。Liu等^[28]通过实验证明,在决定弹性模量和BV/TV方面,板状骨小梁比杆状骨小梁发挥更重要的作用,而杆状骨小梁则是在骨破坏时起到分散载荷和吸收能量的作用^[29]。

年龄和性别也是椎体骨小梁微结构的重要影响因素之一。Jiang等^[30]通过对第三腰椎椎体的研究发现,随着年龄的增长,BV/TV、BMD、Tb.Th、弹性模量和极限应力均显著降低,Tb.Sp增加,Tb.N随年龄增长而下降,男性下降19%,女性下降16%。从60岁到90岁,椎体松质骨的SMI增加了

20%左右^[31],随着SMI的增加,椎体前柱更容易出现楔形骨折^[32]。在这一年龄段男性和女性的BV/TV均下降22%~24%,呈现出相似的下降趋势^[33],而与年龄相关的BV/TV下降主要与Tb.Sp升高和Tb.N降低相关^[31~33]。但是女性垂直骨体积分数(BV.vert/TV)随年龄增长的下降速度明显快于男性。垂直骨小梁厚度和水平骨小梁厚度与年龄无关,而横向/纵向骨小梁厚度的比率随着年龄的增长而显著下降,提示横向骨小梁的变薄受年龄因素影响更大^[34]。并且与年龄相关的骨小梁丢失会使女性纵向骨小梁出现代偿性肥大,但在男性中不会出现此种情况^[35]。随着松质骨骨量的下降,Conn.D也会显著降低,男性和女性的Conn.D的年龄相关性变化几乎相同^[36]。

综上所述,椎体内骨小梁结构的异质性、在空间上的连接方向及年龄增长、性别等因素均会影响到椎体的骨强度。这提示我们在手术过程中应重点考虑这些因素,在选用椎体内植人物时,应注意最大限度地减少植人物对周围骨骼的破坏。

二、椎体骨质疏松性骨折

(一)骨质疏松症临床诊断

骨质疏松症是一种骨组织结构破坏、骨密度降低,骨折风险增加的进行性骨代谢性疾病^[37,38]。其临床诊断具有挑战性,需要使用综合成像方法进行详细评估^[39,40]。双能X线测得的骨密度值(T值)是诊断骨质疏松症的“金标准”,即当T≤-2.5 SD(SD为受试者骨密度的测量结果同健康年轻人数据之间的标准差)时确诊^[41~42]。但是,骨密度只占骨脆性变异的60%^[43],因为它不能描述骨材料成分和结构设计的差异(即骨质量)。骨质量主要包括骨结构、矿化程度、转化率、微损伤累积及修复、胶原矿物的基质特性等。骨微结构被认为是影响骨脆性的主要因素,可独立于骨密度而起作用,与骨强度改变密切相关^[44]。

骨小梁评分(TBS)是与骨微结构相关的纹理参数,其可以提供BMD测量中未捕获的骨骼信息。通过评估骨小梁的微结构纹理参数,有助于评估骨强度,从而有助于诊断骨质疏松和估计未来骨质疏松性骨折的风险。高TBS值与更好的骨骼结构相关(反映了更好的微观结构)^[45];低TBS值与较弱的骨骼结构相关,表明存在骨小梁微结构的退化^[46,47]。TBS与Tb.BV/TV、Tb.N及Conn.D和骨小梁硬度有很强的正相关;它与骨小梁间距和SMI呈负相关^[48,49]。Lee等^[50]通过实验证明,在骨质疏松症以及BMD正常的受试者中,TBS与椎体骨折显著相关。另有研究证明,腰椎低TBS值与既往骨折史有关,并且这种相关性与BMD无关^[51]。使用TBS对骨微结构进行额外评估,能够更好地识别有骨折风险的女性,尤其是那些BMD相对较高的女性。Hsu等^[52]通过研究发现,如果将BMD的改变和TBS的退化结合起来对骨质疏松症进行诊断,骨折的风险将增加5.0%。因此,TBS可以提供更多关于骨强度的信息,这些信息可以提高诊断骨质疏松症的准确性。

除了广泛使用的BMD测量、TBS测量等方法,还有其他方式可以辅助诊断骨质疏松症。骨应变指数(bone strain index, BSI)是最近提出的一种基于DXA的骨指数^[53],它是通过有限元分析,对从腰椎DXA扫描获得的图像建造的数学

模型中得到的椎体变形指数。BSI值代表整个椎骨的平均等效应变,BSI越高意味着骨折风险越高^[54]。BSI可以作为其他临床评估的辅助工具,识别具有骨折风险的患者,并且能更好地描述继发性骨质疏松症年轻患者的骨质量^[55~57]。骨髓脂肪组织(marrow adipose tissue, MAT)在骨髓中扮演着“空间填充物”的角色,它不同于其他脂肪库的性质和功能,对骨量和骨质量起着动态作用^[58,59]。使用磁共振技术可以对MAT进行量化,横断面研究表明MAT与骨量呈负相关,骨小梁与MAT的相关性比皮质骨更强^[60]。研究发现,在MAT较高的人群中,女性椎体的松质骨vBMD、椎体的抗压强度下降得更快^[61]。在临床中,根据不同患者的个人情况,综合合理地使用多种检测手段有助于骨质疏松症的早期诊断,以及尽早开展治疗。

(二)椎体骨质疏松骨折

腰椎以松质骨为主体,是人体关键的承重器官,也是骨质疏松症最先影响的部位之一^[62],而腰椎同样也是椎体中骨折发生率最高的节段。严重的骨质疏松会影响骨骼的形状,导致腰椎高度的改变,并使相邻椎骨的椎弓更近。根据脊柱三柱理论,腰椎在脊柱生物力学中起着缓冲和应力分散的作用^[63]。当腰椎发生骨质疏松时,腰椎承受传递力的方式也会发生变化^[40]。当破坏性载荷产生的有害应力过于集中在骨小梁的某一部位时,已经发生骨质疏松的骨小梁更容易发生断裂继而骨折。在承受轴向压缩或轴向压缩并前屈的胸腰椎中,当椎体屈服时,椎体内的应变达到最高,应力极限值出现在椎体终板或其附近^[64,65]。一些研究^[66,68]将生理载荷下大于5 000 με的松质骨判断为存在骨折风险,以此来计算存在骨折风险的松质骨体积占松质骨总体积的比例,以此来评估椎体的骨折风险。Homminga等^[67]按照上述规定发现,正常的椎体中存在骨折风险的松质骨体积占比为1.2%,低骨量椎体占比为2.6%,具有骨质疏松的椎体达16.1%。因此相对于健康椎体,骨质疏松性椎体更容易发生骨折。

(三)骨小梁微结构的改变

骨质疏松引起的椎体骨折是一种“骨小梁骨折”,通常发生在非创伤性负荷条件下^[68,69]。如前文所说,与椎体骨折风险有关的骨质量的一个广泛研究方向是骨小梁微结构。从生物力学的角度来看,骨小梁材料特性和微结构决定了骨小梁在载荷作用下的强度,是影响椎体脆性的一个重要因素^[70~72]。随着年龄的增长,椎体松质骨的减少主要是由于骨小梁穿孔而不是骨小梁的变薄^[31,36]。在一项针对中年男性骨小梁骨质减少的研究中,在没有骨折的椎体中,骨小梁的连接性和Tb.N更高^[72]。另有研究表明,椎体骨小梁结构的恶化会增加松质骨的各向异性,从而更容易发生骨折。横向的骨小梁优先变薄和穿孔,而垂直骨小梁保持其厚度。这样的结构很可能让椎体在正常的压缩载荷下更容易屈曲,使椎体承受超载或离轴载荷的能力降低^[73]。这种效应在低BV/TV骨中更为突出,因为单个骨小梁非常薄,而且缺乏水平支撑,伴随着骨量和BV/TV的降低,极大地降低了骨强度^[70]。

此外,板状骨小梁和杆状骨小梁的分布比例也会影响骨折的发生。早期的研究定性地表明,随着年龄的增长和骨质疏

松,骨小梁由板状向杆状急剧变化,导致机械能力下降^[74,75]。在纵向压缩载荷下,屈服可能发生在板状骨小梁和杆状骨小梁的交汇处,在骨重塑过程中,破骨细胞的再吸收可能会使应力集中于这些位置^[14]。当BV/TV一定时,松质骨的骨强度与板状骨小梁数量和体积分数呈正相关;与杆状骨小梁数量和骨体积分数呈负相关^[74]。Wehrli等^[75]首次证明骨质疏松症患者的骨小梁丢失主要表现为板状骨小梁板转变为杆状骨小梁,并最终导致骨小梁的断裂。其他文献也表明,除了骨小梁间距和微观结构各向异性的增加会导致不良的生物力学后果之外,板状骨小梁数量的减少会造成椎体强度的下降^[76-79]。

微损伤也被认为是发生骨质疏松骨折的一个重要因素^[80]。微损伤发生在日常生活活动中,可以通过重塑进行修复^[81]。然而,如果微损伤的累积超过了骨的修复能力,特别是在骨质疏松或老年人的骨中,会对骨的机械性能产生不利影响^[82,83]。微损伤与结构参数的相关性表明,微损伤在骨质疏松的骨中比在正常骨中更容易形成和扩散。较高的微裂纹密度与较低的体积分数、较薄的骨小梁和杆状骨小梁相关^[84]。当沿着主要的骨小梁方向加载样本时,尽管大部分产生屈服的组织在纵向板状骨小梁中,但杆状骨小梁的相对数量,特别是纵向杆,是决定整个结构对微损伤形成的敏感性的主要因素。无论从数量上还是从体积上看,纵向杆状骨小梁只占骨小梁的一小部分,但它是骨小梁结构易损性的一个主要因素^[25]。

三、临床治疗

(一)传统手术方式

为了脊柱外科的未来发展,生物力学首先应该解决手术疗效和稳定性之间的矛盾。目前临幊上常用的手术方式,包括椎体成形术、椎体融合术、经椎弓根内固定术和关节突切除术等,都会在不同程度上破坏脊柱的稳定性^[85,86]。

在采取有效治疗的同时最大程度地保留或修复脊柱原有的解剖结构和功能,是脊柱外科重要的研究内容。人体研究表明,椎体成形术可以恢复部分被压缩的骨质疏松椎体的生物力学完整性^[87]。骨水泥压缩能力强,剪切力和拉力弱,是治疗骨质疏松性椎体及干骺端“骨小梁骨折”的极佳辅助工具^[88,89]。如果早期实施,还可以预防神经损伤。有限元研究表明,适量的骨水泥注射能恢复或增加骨折椎体的刚度^[90]。然而,骨水泥在强化椎体刚度的同时改变了骨折节段的生物力学,改变了骨折椎体相邻节段的生物力学反应^[91]。根据不同作者报道,椎体成形术后相邻椎体新发椎体骨折的发生率为6.2%~51.9%^[92]。全程、规范抗骨质疏松治疗十分重要,可明显提高椎体强化术后患者临床效果,同时降低再骨折发生率^[93]。目前,抗骨质疏松症的药物按作用机制的不同分为骨吸收抑制剂、骨形成促进剂、解偶联剂、骨矿化促进剂等^[94-95]。

椎体融合术也是脊柱外科中常见的手术方式,但其在获得脊柱长期稳定的同时,损失了相应节段的活动性,并且会导致邻近椎体节段的应力增加^[96]。如今脊柱微创技术发展迅速,经皮椎弓根钉内固定技术也逐渐应用于临幊。但该术式术后有螺钉松动的风险^[97]。螺钉松动的生物力学机制包括应力遮挡、前柱支撑不足、置入物磨损碎屑的出现、内置物相关的感染等^[98]。

(二)3D打印技术

由于脊柱解剖结构的特殊性,同时周围毗邻脊髓、血管、神经等重要组织,手术风险较大、失败率较高,通过3D打印技术研发仿生内固定物较上述手术方式有一定的优势。近年来,用于脊柱手术的3D打印内植物主要包括螺钉插入导向系统、人工椎体、全椎间盘置换术、椎间融合器和教育教学等方面^[99,100]。

在脊柱外科手术中,常需要在椎弓根放置螺钉。但在较复杂的手术中,准确放置椎弓根螺钉仍较为困难,并且容易损伤到周围的血管和神经^[101]。3D打印导向模板的应用可以提高椎弓根螺钉插入手术的准确性(减少螺钉偏差)、效率(减少术中时间)和安全性(减少辐射)^[99]。椎间融合器是脊柱外科常用的植入物,主要用于将其放置在椎间隙中,实现相邻椎骨之间的融合^[102,103]。3D打印技术目前还常应用于制作椎间融合器,其具有可定制化、表面附着物修饰、可控的刚度及孔隙率的优点,可降低传统钛合金材料融合器、聚醚醚酮材料融合器的应力屏蔽效应,以此来改善生物活性及解决成骨能力差等问题,从而降低融合器塌陷、移位和脱出的风险^[104,105]。近来有报道称3D技术还可用于打印为髓核细胞生长提供支架的生物基质,为构造人工椎间盘提供了新思路^[106]。Sun等^[107]使用3D打印技术创建了由生物材料、生长因子和细胞组成的解剖椎间盘支架,将其皮下植入实验小鼠的背部,发现3个月后,椎间盘支架内生长了大量软骨细胞和软骨组织。Cui等^[108]使用3D生物打印技术将人软骨细胞与聚乙二醇二甲基丙烯酸酯甲酯结合显示,生物材料支架不仅提供了良好的机械稳定性,而且保持了人类软骨细胞的活力,有助于修复受损的软骨。

周围骨组织与置入物之间的固定骨长上与骨长入两种方式。3D打印技术在材料设计中的高精度和可控性使多孔钛合金具有更理想的骨诱导性能和足够的机械强度,而为成骨细胞的长入提供了更好的力学属性及生物相容性^[109]。Yang等^[110]使用3D打印技术,对实验绵羊进行了多孔钛合金自稳人工颈椎置换术,组织学观察表明,骨组织可以顺利地生长到人工椎体的孔隙中,并保持颈椎的稳定性^[111]。另外,通过3D打印技术制作的个性化人工椎体可以呈现复杂的几何形状,并与相邻椎体具有高度的生理贴合度。目前的个性化人工椎体多采用钛合金多孔结构,形态、尺寸及孔隙率更符合生理需求,使假体弹性模量与椎体相匹配,同时促进骨长入,从而实现良好的长期稳定性^[111-112]。根据本课题组在股骨近端骨折研究中发现,骨小梁结构通过钉孔生长重建可加强对内固定物的把持,使内固定更加牢固^[113-115]。研究显示,通过3D打印技术制备的孔隙在300~600 μm,孔隙率在70%~90%的置入物最有利于骨质的长入^[116]。

我们可以发现,目前临幊上使用的手术方式,并非十分完美的治疗手段。3D打印内置物在脊柱外科领域仍处于早期发展阶段。但其可以从置入物的宏观形状和微观结构实现仿生设计,在修复脊柱缺损解剖结构的同时复原原有结构和生物力学^[117-118]。3D打印技术的出现对骨重建及周围软组织修复均有一定启发作用,为脊柱疾病的治疗提供了新的思

路和机遇。

四、结语

在椎体骨折后，骨结构的破坏及肌肉的损伤等情况都会破坏人体原本的生物力学。依靠现有的技术手段，我们只能在体外进行单椎体或多椎体的生物力学实验。但是，我们无法还原带有人体内椎间盘、韧带、肌肉等附属结构的完整力学模型。因此，目前的研究结论均具有一定的局限性。我们仍需进一步发展技术，争取能够研究出在完整人体结构作用下的骨小梁生物力学。日后，我们的研究重点应旨在确定骨小梁微结构如何影响椎体的生物力学功能，结合有限元分析方法及3D打印技术制定出适合患者个人的仿生内固定装置，尽量在恢复伤椎形态的同时，复原椎体内部骨小梁的形态，从而更好地还原椎体原有的力学功能，提高手术成功率及患者的生存质量。

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