

·综述·

骨质疏松性髋部骨折研究进展

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摘要：骨质疏松性髋部骨折的防治日益受到重视，本文就近年来骨质疏松性髋部骨折的研究进展作一综述，主要包括流行病学、危险因素、风险评估、外科治疗以及药物治疗方面进展，特别是外科治疗中如何选择合理的内固定植入物以及抗骨质疏松药物对提高骨密度和降低髋部骨折风险的作用。

关键词：骨质疏松；髋部骨折；危险因素；外科治疗；药物治疗

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Abstract: More and more attention has been paid to the prevention and treatment of osteoporotic hip fractures. This paper reviews the research progress in osteoporotic hip fractures in recent years, mainly including the progress in epidemiology, risk factors, risk evaluation, surgical treatment, and drug therapy. In the surgical treatment, special attention should be paid to the selection of reasonable internal fixation, and the effect of anti-osteoporosis drug therapy on improving bone mineral density and reducing the risk of hip fractures.

Key words: Osteoporosis; Hip fracture; Risk factors; Surgical treatment; Drug therapy

骨质疏松性髋部骨折是一个严峻的公共健康问题，具有较高发病率、死亡率及致残率，手术风险大，若发生髋部骨折后的 1 年内，死于各种并发症者达 30%，致残率高达 50%^[1]。据报道 2050 年全世界的髋部骨折人数将达到 626 万，其中亚洲将占 50% 以上^[2]。近年来，我国髋部骨折的发病率有明显上升趋势，在 2002~2006 年髋部骨折率大约每年增长了 10%，增长为男性 129/10 万和女性 229/10 万^[3]。骨质疏松性髋部骨折的防治日益受到重视，取得了明显进展，对此综述如下。

1 危险因素

1.1 骨密度

双能 X 线(DXA)测定的骨密度是诊断骨质疏松的金标准，也是评估骨折风险的重要因素。脆性骨折患者存在骨质疏松或者骨量减少，同时骨密度随年龄增大而降低，65 岁以前股骨颈骨密度年降低

率为 0.64%，而 65 岁以后仅为 0.36%^[4]。骨密度与骨折风险密切相关，特别是股骨颈骨密度每减少一个 1SD，髋部骨折风险增加 2.6 倍。老年人从 50~80 岁髋部骨折风险增加 30 倍，而骨密度因素仅使髋部骨折风险增加 4 倍^[5]。Siris^[6]等报道许多骨折发生在骨密度值在骨质疏松阈值之上，尤其是骨量减少的绝经后妇女。显然，骨密度在临床评估骨折风险中存在一定的局限性，骨密度并不是预测髋部骨折风险唯一指标，髋部骨折风险与年龄、性别、维生素 D 水平及跌倒等其他因素均有关。

1.2 股骨近端几何结构

髋部为骨质疏松性骨折的常见部位，结构决定功能，几何结构特点与髋部骨折风险的关系日益受到重视。几何参数主要包括颈轴长、颈宽度以及颈干角等，随年龄及骨量的变化小而显得相对稳定。Bergot^[7]等认为较长的颈轴长与髋部骨折风险呈正相关。El-Kaissi^[8]等报告颈宽度每增加 1 个 SD，髋部骨折风险增加 1.7 倍。Alonso^[9]等报告颈干角每增加 1SD，女性髋部骨折危险性增加 3.48 倍。蔡思清^[10]等研究发现国人的颈干角大小与股骨颈骨折

危险性并无明显相关。几何参数与髋部骨折风险关系的研究也存在一些争议^[7-10],如果把颈宽度和颈轴长两者结合在一起作分析,能消除个体差异性,更准确体现出股骨近端几何结构特点,股骨颈颈轴长/颈宽度的比值与髋部骨折风险呈正相关^[11]。股骨颈皮质骨厚度随着年龄的增长而变薄,是重要的结构参数^[12]。股骨颈机械测试表明皮质骨在股骨头下区、中段、基底部、转子间区分别承受 30%、50%、96% 和 80% 的压力负荷^[13]。在股骨颈去松质骨的情况下,股骨颈强度仅小幅度下降,提示皮质骨在股骨颈强度中所起主要作用^[14]。Zebaze^[15]等报告绝经后松质骨快于皮质骨,但在 65~75 岁骨丢失最多是皮质骨,80 岁以后 90% 的骨量丢失来自皮质骨。

1.3 维生素 D 缺乏

血清 25(OH)D 反映维生素 D 的营养状态,血清 25(OH)D 的水平分为维生素 D 缺乏 (< 50 nmol/L)、维生素 D 不足 (50~75 nmol/L)、维生素 D 充足 (> 75 nmol/L)。据保守估计全世界约有 10 亿人维生素 D 缺乏或不足,广泛存在于老年人和绝经后妇女,甚至婴幼儿、青少年也是潜在的高危人群,即使在我国亚热带海滨城市人群也普遍存在^[16]。血清 25(OH)D 水平的降低与老年人握力的减退和四肢肌肉量的减少有关,为重要的跌倒风险因子,因此血清 25(OH)D 水平可以作为骨质疏松和骨折风险的判断指标^[17]。Bischoff^[18]等研究发现维生素 D 水平与骨密度密切相关,维生素 D 缺乏组和不足组的骨密度分别比正常下降了 7.3% 和 8.5%。Fisher^[19]等研究发现老年髋部骨折患者血清 25(OH)D < 80 nmol/L 的比例高达 97.1%,维生素缺乏达到 79.8%。

2 风险评估

骨质疏松预防的重点在于降低骨折风险,WHO 提出了骨折风险评估 (FRAX) 系统,用于评估未来 10 年发生髋部骨折及任何重要骨质疏松性骨折的发生风险,根据临床危险因素单独或与股骨颈骨密度进行评估,该系统适用于 40~90 岁的男女。在美国的治疗阈值是 10 年的髋部骨折风险高于 3% 或任何重要的骨质疏松骨折风险高于 20%,而一些欧洲国家的治疗阈值髋部骨折风险是 5~7%^[21-22]。FRAX 对评估 10 年骨折风险性的具有显著的优势,也存在以下不足:①采用的骨折危险因子种类有限;②未考虑量的因素,如使用糖皮质激素的剂量和病程,抽烟、~~吸烟的数据~~、持续时间等;③FRAX 只结合

股骨颈的骨密度,而对于股骨颈骨密度正常而腰椎骨密度减少的人来说可能计算有误差等。如果能将 FRAX、骨密度以及骨代谢指标等结合分析,可以明显提高骨折风险评估的准确性^[22-23]。

3 外科治疗

对全身情况相对稳定、可耐受手术的患者多主张积极早期手术治疗。Moran^[24]等发现髋部骨折患者伤后 4 天内手术并不会增加死亡率,但是若手术时间延迟超过 4 天,其在伤后 90 天、1 年内之死亡率分别增加了 2.24 倍和 2.5 倍。骨科医师在骨质疏松性髋部骨折的治疗原则基本达成共识,主要差别在于内固定植入物选择,但是目前对内固定植入物选择及其效果常常不能令人满意^[25]。

3.1 股骨粗隆间骨折

股骨粗隆间骨折手术方法主要是切开复位内固定术,髓外固定以动力髋螺钉 (DHS) 为代表,髓内固定以股骨近端髓内钉 (PFNA) 为首选。导致手术失败的主要原因是不稳定骨折和骨质疏松症,因此内固定器必须具备抗内翻支撑和防止近端骨折块旋转两种基本功能。DHS 作为治疗股骨粗隆间骨折的重要方式之一,但是 DHS 内固定失败率较高,1 年内再次手术率高达 14%^[26],主要原因有:①螺钉力臂较长,使应力集中在螺钉与套管交界处,易引起断钉、断板;②单螺钉固定,抗旋转能力差;③作为滑动固定系统用于骨质疏松患者时,因疏松的骨质不能对螺钉产生足够的锚合力;④对不稳定骨股粗隆间骨折,因其力学特性失败率很高。外侧壁作为 DHS 内固定的重要部位,与内固定失败率密切相关,外侧壁骨折患者中半年内再手术率高达 22%,是无外侧壁骨折者的 8 倍^[27]。目前 DHS 主要适用于 A1、A2.1 稳定型股骨粗隆间骨折,对不稳定型骨折及老年骨质疏松患者,应防止外侧壁骨折,可加用大粗隆稳定钢板等。PFNA 恰好能地克服了 DHS 的这些缺点,受外侧壁因素影响小,1 年内再次手术率仅为 4%,其设计是以击入螺旋刀片并对周围骨质进行加压夯实,尤其是在骨质疏松的情况下,具有更好的锚合力,避免了对股骨颈内骨质的切割和丢失,能很好地防止旋转和塌陷^[26,28]。PFNA 具有手术创伤小、保留原始骨折血肿、骨折愈合率高等优点,显然更适用于骨质疏松性股骨粗隆间骨折。

3.2 股骨颈骨折

髋关节置换术为治疗股骨颈骨折的首选方法之一。随着髋关节置换单数和随访时间的延长,相关

的并发症也明显增多。人工髋关节早期失败排前三位的原因分别是无菌性松动 51%，关节不稳定 18%，感染 11%^[29]。股骨假体初始不稳定及松动，常为股骨假体与髓腔不匹配所致，因此选择人工髋关节股骨假体时，必须考虑髓腔形状的影响。Noble^[30]等提出髓腔开放指数(CFI)用于描述髓腔形状，CFI 是小粗隆上方 20mm 髓腔内径和峡部髓腔内径的比值，按比值分三型：CFI < 3(烟囱型)，3 ≤ CFI < 4.7(正常型)，CFI ≥ 4.7(漏斗型)。正常型和漏斗型髓腔，适宜选择锥型圆柄，也可选择解剖柄、矩型柄。烟囱型髓腔，适宜选择骨水泥假体，也可选择远端粗大的柱形柄、远端宽大型的矩形柄。Kobayashi^[31]等随访 CFI 与假体寿命 16 年发现，CFI ≥ 3 组为 96.1%，而 CFI < 3 组的假体生存率仅为 81.6%。股骨颈骨折病人，CFI 平均值为 2.3，烟囱型髓腔占有较高比例，一般的非骨水泥近端固定型假体很难达到牢固的稳定，易出现假体松动，因此适宜选择骨水泥柄，若要选择非骨水泥假体，可根据股骨髓腔内侧径测量法及股骨峡部最小髓腔内径测量法，选择与髓腔匹配的组配式或生物型假体，可较好克服了非骨水泥假体与髓腔不匹配的问题^[31-33]。

4 药物治疗

外科治疗的同时不应忽视对全身性骨质疏松的药物治疗，这往往是骨科医师容易疏忽的。17% ~ 21% 的髋部骨折患者在 2 年内将再发骨折有效的抗骨质疏松治疗可减少再发骨折风险^[34]。

4.1 双膦酸盐

双膦酸盐是临幊上常用的抑制骨吸收药物，代表药物有阿仑膦酸盐、唑来膦酸盐等。但是骨折早期使用双膦酸盐，可能抑制骨吸收，延长骨折愈合的时间，一般术后 2 周开始使用^[35]。阿仑膦酸盐有对提高骨密度和降低髋部骨折风险的效用，阿仑膦酸盐(10mg/d)治疗组其骨密度持续增加，10 年时股骨颈、大转子、髋部分别增加了 5.4%、10.3% 和 6.7%^[36]。骨折干预治疗研究发现阿仑膦酸盐治疗 4 年后，髋部骨折风险降低 51%^[37]。唑来膦酸盐是首个静脉用药的双膦酸盐，HORIZON—PFT 研究发现接受唑来膦酸盐治疗组(5mg/年)，3 年时髋部骨密度、股骨颈骨密度分别增加了 6.02% 和 5.06%，髋部骨折相对风险降低 41%^[38]。相对于安慰剂组，唑来膦酸盐组骨小梁容量更高，骨小梁数目增加，断裂下降，交联强度有改善趋势^[39]。Lyles^[40]等对有髋部骨折史患者随访 5 年，唑来膦酸盐组再次

骨折率减少 35%，死亡率降低 28%。相对于口服双膦酸盐，静脉注射唑来膦酸盐的药物依从性更好，药物依从性好的人群髋部骨折风险下降更明显^[39]。

4.2 甲状旁腺激素(PTH)

PTH 是促进骨形成药物之一，代表性药物为 rhPTH(1-34)。小剂量 rhPTH(1-34) 具有促进骨形成的作用，提高髋部骨密度，降低骨折风险的作用。Neer^[41]等对 1637 例既往有椎体骨折史的绝经妇女随机分组给与 rhPTH(1-34) 20 μg/d 或 40 μg/d 或安慰剂，平均随访 21 个月，20 μg/d 和 40 μg/d 治疗组股骨颈骨密度分别上升了 3% 和 6%，全身骨密度分别上升了 2% 和 4%，非椎体骨折危险性下降至 53% 和 54%。rhPTH(1-34) 能显著增加了小梁骨数量和皮质骨的厚度^[42]，但是在大鼠研究实验^[43]中发现 rhPTH(1-34) 使骨肉瘤发生率增加，并且与给药剂量、治疗持续时间相关。临幊上对 rhPTH(1-34) 推荐剂量为 20 μg/d，使用时间一般不超过 2 年。

4.3 锶盐

锶盐具有抑制骨吸收和促进骨形成双重作用的药物。SOTI 和 TROPOS 等研究^[44-45]发现，经 3 年治疗，骨密度锶盐组股骨颈、髋部分别了增加 7.2% 和 8.6%，非椎体骨折风险降低 16%，其中髋部骨折高危病人髋部骨折风险降低 36%。并对再次接受为期 3 年的治疗者，骨密度持续增加，8 年时股骨颈、髋部骨密度分别增加了 10.3% 和 10.7%，治疗的 5 ~ 8 年与最初 3 年非椎体骨折风险分别为 12.0% 和 9.6%，提示长期使用雷奈酸锶治疗预防骨折也是安全和有效的^[46]。Arlot 等^[47]对随访 3 年的 49 例接受雷奈酸锶(2g/d)治疗绝经后骨质疏松症妇女进行骨活检，结果发现皮质骨厚度增加 18%，骨小梁数目增加 14%，骨小梁分离减少 16%。

4.4 维生素 D 及其类似物

维生素 D 及其类似物是防治骨质疏松的常用药物，国际骨质疏松基金会对人群维生素 D 水平总结分析^[48]，认为血清 25(OH)D 浓度 ≥ 60 nmol/L 才能有效预防跌倒，≥ 66 nmol/L 和 ≥ 75 nmol/L 才能分别有效预防非椎体骨折和髋部骨折。每补充 100 IU 普通维生素 D 大约提高血清 25(OH)D 浓度 2.5 nmol/L，显然传统的补充 200 ~ 400 IU/d 普通维生素 D 远远不够。每天补充 700 ~ 1000 IU 维生素 D 仅能使 50% 的人群达到 75 nmol/L 以上，补充 4000 IU 维生素 D 只能使 88% 的人群达到 75 nmol/L 以上^[49]。Bischoff^[50]等研究发现 700 ~ 1000 IU/d

的普通维生素 D 而获得的血清 25(OH)D 浓度 ≥ 60 nmol/L 使老年人的跌倒风险下降 19%, 髋部骨折危险降低 26%, 维生素 D 的剂量 < 700 IU/d 或血清 25(OH)D 浓度 < 60 nmol/L 不会降低老年人的跌倒风险和髋部骨折风险。因此, 至少需要补充 700~1000 IU/d 维生素 D, 血清 25(OH)D 达到 75 nmol/L 以上, 才能有效预防跌倒及降低髋部骨折风险。活性维生素 D 在防治骨质疏松方面比普通维生素 D 有较好的疗效, 高剂量普通维生素 D 组、活性维生素 D 治疗组分别使跌倒风险下降 19% 和 22%, 在骨折风险方面分别降低了 2% 和 10%^[50-51]。

综上所述, 骨质疏松性髋部骨折的防治日益受到重视, 需要外科和药物的综合治疗, 外科治疗重点如何选择合理的内固定植入物, 同时应重视抗骨质疏松药物的治疗, 特别是选择能明显提高骨密度和降低髋部骨折风险的药物, 使得该病得到充分有效预防和治疗。

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骨质疏松性髋部骨折研究进展

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