· 综述 ·

影响城乡骨密度差异的因素分析

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摘要: 城乡间骨密度(bone mass density,BMD)存在差异,但是对于差异高低的具体归属尚无定论,而且造成差异的众多因素互相交叉渗透,对于其中造成差异的生理学机制往往较少涉及,甚至有诸多矛盾之处。本综述力求归纳总结目前较成熟的研究结论,并以各自支持的观点分类列举,分为乡村 BMD 高于城市、城市 BMD 高于乡村及其他影响因素 3 部分,其中乡村 BMD 高于城市的理由包括:生活节奏、日照时间、睡眠时间、重体力活动 4 个方面;而城市 BMD 高于乡村的原因则包括:社会经济水平、教育水平、生育水平及初潮年龄及大气环境 4 个方面;其他不确定的影响因素主要涉及吸烟饮酒、膳食摄入和先天方面。在以城乡间各个因素具体差异数值支撑的同时,挖掘并整理了可能造成差异背后的生理病理学机制,以及相关临床试验及动物学实验的内容,综合国内外较为权威的结论进行综述。一方面在于整理目前最新的研究结果,为将来严格意义的城乡 BMD 水平临床研究提供一定借鉴;另一方面为深入探究导致二者差异的实验研究提供实践基础。

关键词: 骨质疏松;骨密度;城乡地区;影响因素

Analysis of the influential factors of BMD difference between rural and urban area

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Abstract: There is difference of the level of bone mineral density (BMD) between urban and rural areas. However, there is no conclusion where is the location of high or low BMD level. The influential factors intervene and twist with each other. The physiological mechanism has not been explored, and there have been some contrary conclusion . This review summarizes the mature research conclusion . The respective supporting points are arranged and divided into 3 parts, including higher BMD in rural over in urban, higher BMD in urban over in rural, and other factors. Among those, the reasons for higher BMD in rural than in urban include life rhythm, sunshine exposure, sleeping-time, and heavy physical activity. The reasons for higher BMD in urban than in rural include social economic level, education, disparities pregnancy time, menarche age, and environment. The uncertain reasons include smoking, drinking, dietary, and congenital factor. The summary is supported by concrete data and investigates the possible physical and pathologic mechanism causing the difference result . We aim at analyzing and concluding the latest research result to provide data for the further clinical research of BMD between urban and rural areas. On the other hand, we provide the fundamental physical mechanism for improving the relative trial research.

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骨质疏松症(osteoporosis,OP)是临床常见的老年退变性疾病,可以诱发关节、四肢骨折,严重的骨质疏松可以导致残疾降低患者生活水平,甚至死亡等严重后果[1]。骨密度(bone mass density,BMD)水平是反映骨质疏松情况的常用指标,临床中一般通过双能X线(dual energy X-ray absorptiometry,DXA)测量腰椎或髋关节股骨近端获得[2]。根据世界卫生组织规定,乡村一般是指以从事农业生产为主的农业人口居住的地区,在中国则普遍以户籍来确定。近年来很多文献报道BMD水平在城乡居民之间存在差异,乡村要显著高于城市,与此相对应的是城市老年人骨折水平高于乡村[3]。然而也有学者[4]认为城市BMD水平要显著高于乡村,尤其对于绝经妇女来说,这一差异更为明显。对于两者的争论目前还没有权威的定论[5],但是在临床中对于造成该差异的因素进行了广泛的探讨,主要包括城乡间高钙食物的摄入[6]、教育[7]、体力活动[8]、医疗水平[9]等差异。但是对于各因素对于城乡BMD差异具体归属及分析则涉及不多,因此有必要作一综述,为临床研究提供一些借鉴。

1 乡村BMD高于城市的原因

1.1 生活节奏

社会经济水平与多种急慢性疾病的发生均有密切关联[10]。城乡间社会经济水平差异明显。一般认为城市的社会经济水平要优于乡村,生活节奏也显著高于乡村,尤其对于中国等广大的发展中国家来说,由于人口资源间匹配的不均衡性,这一现象表现的更为明显[11]。Song及其研究团队[12]通过探究人群内分泌系统及与地区(城市/农村)相关性,发现某些"应激性"激素,例如糖皮质激素、甲状腺激素等在城市人群中较高,且与低水平BMD有显著相关性。Zhu等[13]认为下丘脑-垂体-肾上腺轴可能对于BMD和骨矿含量有重要影响,社会经济等压力可能通过刺激下丘脑-垂体-肾上腺轴产生过量糖皮质激素,抑制成骨促进破骨从而诱发BMD降低[14]。

1.2 日照时间

由于缺乏阳光照射,低水平血清1,25(OH)$_2$D导致的骨软化等骨代谢疾病在西欧比较常见,与此相对应在阳光充足的美国则该类疾病较少[15]。据统计,由于生活方式及居住条件的差异,乡村人群平均每日接受的太阳照射时间是城市人群的1.3倍[16]。1,25(OH)$_2$D是重要的钙调节物质,具有促进钙吸收,骨骼中矿物质沉积的作用[17]。皮肤中7脱氢胆固醇在光照作用下生成VitD3,之后在肝肾羟化酶的作用下生成具有活性的1,25(OH)$_2$D[18],Sato等[19]通过临床流行病学调查发现在一定程度内日照与BMD水平呈正相关,与骨折发生呈负相关。

1.3 睡眠时间

由于生活压力或娱乐方式的多样化导致熬夜或晚睡在城市生活中较为普遍[20]。Yang等[20]针对城乡睡眠时间的调查发现,乡村人口睡眠时间要显著高于城市人群(P<0.05,9.0 VS 11.3)。Fu等[21]对国人熬夜与BMD相关性进行研究发现熬夜与BMD水平具有显著关联,Pearson线性相关系数约为-0.43,尤其对于绝经期妇女来说两者负相关更为明显。Magali等[22]以白人为试验对象的相关研究也证实了熬夜与BMD呈现一定程度的负相关性。从生理学角度看来熬夜影响BMD的机制可能与减少快速动眼睡眠抑制人生长激素分泌有关[23]。

1.4 重度体力活动

对于社会个体来说城市化是一种由传统重体力活动向轻体力甚至以坐位为主要劳动形式转变的过程[24]。重体力活动而非一般的轻体力活动可以通过增加骨骼微动促进长骨关节端骨质沉积,从而增加BMD水平[25]。Kelly等[26]认为青少年时期的BMD蓄积高峰水平可以影响中老年期BMD水平,通过增加青少年时期的BMD水平可以降低老年后骨质疏松及骨质疏松性骨折的发生。对于女性来说成年后50%以上的BMD来源于青春期的积累[27]。重度体力活动一般指非机械性农业工作或使人出汗、心跳较基础心率增加20%及以上的活动[28]。

2 城市BMD水平高于乡村的原因

2.1 社会经济水平

一些研究[29]认为社会经济水平可以影响BMD或者骨质疏松症的发生,因此城市人口的BMD水平要高于乡村。可能与城市人口高钙食物、肉类等高级蛋白质的摄入增加有关,研究发现肉类和菌类食物中VitD$_2$含量较高[30]。VitD$_3$由人体皮肤内的7-脱氢胆固醇经紫外线照射生成,是人体内重要的内源性VitD组成部分,而食物中的VitD$_2$是重要的外源性VitD来源,Sgambat等[31]认为通过补充外源性

的 VitD 可以增加 BMD 水平,预防骨质疏松性骨折的发生。而 Aoe 等[32]则认为与钙质相比以牛奶为代表的高级蛋白质促进骨骼发育和增加骨基质的作用更为明显。也有一些学者[33]认为海苔等含氮端肽(N-terminal peptide)的食物可以升高 BMD 平升,海苔等食物中的氮端肽与甲状旁腺激素前体化学结构相类似,经代谢后就可生成小剂量外源性甲状旁腺激素从而促进钙的吸收及骨沉积。另一方面与乡村相比城市可以提供更高水平的医疗服务,同时城市人口也更加关注健康问题[34],有很多城乡骨密度差异的研究[35]最后发现高水平的医疗服务和对自身健康问题的关注往往是造成 BMD 水平差异的重要因素。

2.2 教育水平

研究发现多种急慢性疾病与受教育程度明确相关[36]。社会研究发现城乡之间的教育差异巨大,在发达国家城市本科教育是乡村的 3~4 倍,而对于发展中国家来说这种差异更为明显[37]。Brennan 等[38]通过临床流行病学调查发现绝经期妇女 BMD 水平和受教育程度有明显的正相关性,而与收入或者职业无关,同时对于男性来说这种相关性并不存在。

2.3 生育水平及初潮年龄

生育水平及初潮年龄可能影响女性 BMD 水平,Tsvetov 等[39]认为过多的生育次数和过长时间的哺乳可以降低绝经后妇女的 BMD 水平,同时发现生育次数和哺乳时间对 BMD 的影响各不相同,与生育次数相比哺乳时间对绝经期妇女 BMD 的影响时间更长,程度也更高,与哺乳时间较少的妇女相比哺乳时间较长的妇女绝经后 BMD 水平明显偏低。与城市相比乡村妇女的生育次数及哺乳时间往往较多(1.7 胎 vs 2.3 胎)和较长(0.7 年 vs 1.2 年)[40-41],尤其对于国内来说由于计划生育等人口政策的实施导致这一差异更为明显[30]。过去的研究认为初潮年龄主要通过卵泡促激素、黄体生成素[42]和雌激素[43]影响成骨破骨细胞分化参与骨的形成;最新研究[44]发现初潮年龄是影响绝经期妇女 BMD 水平独立而重要的因素之一,机制可能与较早初潮年龄可能导致围绝经期提早来临降低雌激素分泌相关。雌激素是 BMD 的保护性因子,可以通过促进成骨细胞活性及增加骨钙蛋白等抑制骨量丢失。相关研究[45]认为与城市女性相比乡村女性的初潮年龄要提早 1~2 岁。

2.4 大气环境

大气环境污染对于 BMD 水平影响的研究较少,一般认为与农村相比城市大气污染更为严重[46]。大气污染中汽车尾气约占到 70%,而二氧化氮(NO_2)是汽车尾气的重要组成部分[47]。一项研究[48]将小鼠暴露于高浓度的 NO_2 气体中,3 个月后发现小鼠 BMD 水平显著升高,而对小鼠血清学检查发现小鼠体内外源性促进骨形成物质-脱氧吡啶诺林显著增加。将大气污染或较高浓度 NO_2 作为解释城市 BMD 水平较高的原因显然过于草率,对于大气污染与 BMD 相关性尚需要进一步的研究。

3 其他可能影响 BMD 的因素

吸烟与饮酒对 BMD 具有影响[49],与非吸烟人群相比,吸烟人群血清 1,25$(OH)_2$D 的水平约较正常水平降低 4.2 ng/dL。Thuesen 等[50]通过临床调查发现非吸烟人群与吸烟人群罹患低水平血清 1,25$(OH)_2$D [1,25$(OH)_2$D < 10 ng/mL/(1,25$(OH)_2$D < 20 ng/mL)] 的优势比分别为 1.47 和 1.36。吸烟人群除了可能伴有不良的生活习惯例如缺乏锻炼、酗酒、挑食、户外日晒时间短外,也可能与烟草中的四氢萘醌特异性的损伤肝细胞酶 CYP27A1 导致 25(OH)D 生成减少有关[51]。

Kaats 等[52]认为平衡的膳食对于维持绝经期妇女 BMD 水平至关重要,而非肉食或奶制品为主的饮食,同时发现长期高钙饮食并不能增加绝经期妇女 BMD 水平,可能与长期高钙水平诱导钙离子受体凋亡有关。除以上因素外,先天因素例如血清中维生素 D 结合蛋白受体、组织维生素 D 受体的基因多态性[53]也对 BMD 有深刻的影响。

综上所述,对于城乡人群 BMD 水平孰高孰低目前尚无明确的结论,但对于造成城乡两者 BMD 差异因素进行了广泛的研究和探索,本文从城市 BMD 水平高于乡村/乡村 BMD 水平高于城市两个角度阐释了目前较为成熟的研究结论或实验结果,同时对可能影响 BMD 水平确并无明显城乡差异的因素进行了涉及(表 1),以求为将来严格意义的城乡 BMD 差异水平临床研究提供一定借鉴。

表1 影响城乡骨密度差异的因素总结

Table 1 The summary of factors contributing to the BMD difference between urban and rural area

因素	城市	乡村
生活节奏	-	+
日照时间	−	+
睡眠时间	−	+
重体力活动	−	+
社会经济水平(高钙优质蛋白食物,医疗保健)	+	−
教育水平	+−	−
生育水平及初潮年龄	+	−
大气环境	+/?	−/?
吸烟饮酒	?	?
平衡膳食	?	?
先天因素	?	?

注:"+"即正向影响,"−"即负向影响关,"?":影响未知。

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