

绝经后妇女血脂水平与骨密度的关系

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【摘要】 目的 明确绝经后妇女血脂水平与骨密度有否联系。**方法** 测定 85 例绝经后妇女的甘油三酯和胆固醇水平, 双能 X 线法测定腰椎 L₂₋₄ 和股骨颈的骨密度(BMD)。**结果** 与未绝经妇女相比, 绝经后妇女甘油三酯($t = 3.74, P = 0.000$)和胆固醇($t = 3.75, P = 0.000$)水平均显著升高; 而 BMD 腰椎 L₂₋₄($t = 2.43, P = 0.017$)和股骨颈($t = 3.32, P = 0.002$)均显著降低; 绝经后妇女甘油三酯水平与股骨颈的 BMD 经 BMI 校正后有显著负相关, 偏相关系数 $r = -0.324, P = 0.003$; 而与腰椎 L₂₋₄ BMD 无相关。胆固醇水平则与股骨颈及腰椎 L₂₋₄ 的 BMD 均无相关性。**结论** 绝经后妇女甘油三酯水平的升高可能是绝经后骨量减少及骨质疏松发生的因素之一。

【关键词】 甘油三酯; 骨密度; 绝经; 骨质疏松

Relationship of serum lipid level and bone mineral density in postmenopausal women LI Wangen, CHEN Shu, WU Zhaozhong et al. Department of Endocrinology, 2nd Affiliated Hospital, Guangzhou Medical College, Guangzhou 510260 China

【Abstract】 Objective To investigate the relation between serum lipid level and bone mineral density (BMD) in postmenopausal women. **Methods** Eighty-five screened postmenopausal women were included. The period of menopause was from 1 to 10 years. Lumbar spine and femoral neck BMD were assessed by dual-energy X-ray absorptiometry technique with a Lunar densitometer. **Results** Both triglyceride (TG) and cholesterol (Chol) level were significantly increased compared to premenopausal women (1.50 ± 0.60 vs 0.92 ± 0.35 for TG, $t = 3.74, P = 0.000$; 5.77 ± 1.01 vs 5.07 ± 0.87 for Chol, $t = 3.75, P = 0.000$). Nevertheless, both lumbar spine and femoral neck BMD were significantly decreased compared to premenopausal women (0.972 ± 0.169 vs 1.056 ± 0.171 for lumbar spine, $t = 2.43, P = 0.017$; 0.829 ± 0.105 vs 0.930 ± 0.177 for femoral neck, $t = 3.32, P = 0.002$). The level of TG was inversely correlated with BMD of femoral neck after adjusted for BMI for its known effect on BMD. The partial relation coefficient was -0.342 at femur neck, The P-value was 0.003 . No association was found between the level of Chol and BMD in both lumbar spine and femoral neck. **Conclusion** The increased TG may be involved in the pathogenesis of postmenopausal osteopenia and osteoporosis.

【Key words】 Triglyceride; Bone mineral density; Postmenopausal; Osteoporosis

绝经后骨质疏松主要与雌激素的急剧减少有关, 但是其具体机理至今并不十分清楚。许多治疗骨质疏松的药物如雌激素和选择性雌激素受体调节剂有降低血脂的作用^[1], 而多年前就已经发现贝特类降脂药可以通过降低甘油三酯而预防糖皮质激素引起的股骨头坏死^[2], 而且骨质疏松经常伴有动脉粥样硬化^[3], 后者与脂代谢的关系则早已经得到公认。据此, 我们推测绝经后妇女的脂代谢与骨代谢

之间存在一定的内在联系。为此进行了本研究。

材料和方法

1. 研究对象与方法

广州某单位的正常绝经后妇女 85 例, 年龄 $46 \sim 63(54.4 \pm 4.1)$ 岁, 绝经年限 $1 \sim 10(5.0 \pm 3.7)$ 年, 有高血压病者 10 例, 冠心病者 3 例, 高甘油三酯血症者 30 例, 高胆固醇血症者 25 例, 混合性高脂血症者 15 例。过夜禁食, 测量身高、体重, 计算体重指数 ($BMI = \text{体重}/\text{身高}^2$), BMI 为 $16.8 \sim 30.4(23.5 \pm 3.2)$ kg/m^2 ; 抽静脉血, 用常规酶法测定甘油三酯、胆固醇水平。用美国 Lunar 公司的 DPX-L 骨密度分析仪测定腰椎 L₂₋₄ 和左侧股骨颈的骨密度(BMD)。每日测

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量前进行仪器质量控制,仪器的精确度为腰椎 0.005 g/cm^2 ,股骨 0.015 g/cm^2 ,准确度 $> 98\%$ 。

另外选取同一单位的 40 岁以上未绝经妇女 80 例作为对照,年龄 $40 \sim 52 (45.3 \pm 3.8)$ 岁,有高血压病者 4 例,高甘油三酯血症者 11 例,高胆固醇血症者 5 例,混合性高脂血症者 4 例,BMI 为 $15.2 \sim 27.1 (21.5 \pm 3.4) \text{ kg/m}^2$ 。

2. 研究人群的排除标准

血 $\text{Ca}^{2+} > 2.75 \text{ mmol/L}$,慢性肝炎、肾炎、糖尿病,应用雌激素、维生素 D、钙剂、调脂药或糖皮质激素超过 3 个月。

3. 统计学处理

用 SPSS11.0 统计软件分析数据,用 t 检验、直线相关、偏相关进行相应分析。

结 果

1. 绝经前、后妇女血脂水平的变化(表 1)。

绝经后妇女的甘油三酯和胆固醇水平均较绝经前升高,差异有显著性。

表 1 绝经前、后妇女血脂水平的对比(mmol/L)

项目	受检者(人)	甘油三酯	胆固醇
绝经前	80	0.92 ± 0.35	5.07 ± 0.87
绝经后	85	$1.50 \pm 0.60^*$	$5.77 \pm 1.01^{**}$

注:与绝经前比较 * $t = 3.74$ $P = 0.000$; ** $t = 3.75$ $P = 0.000$

2. 绝经前、后妇女腰椎 L_{2-4} 和股骨颈 BMD 的变化(表 2)。

绝经后妇女腰椎 L_{2-4} 和股骨颈 BMD 均较绝经前降低,差异有显著性。

表 2 绝经前、后妇女 BMD 的对比(g/cm^2)

项目	受检者(人)	腰椎 L_{2-4} BMD	股骨颈 BMD
绝经前	80	1.056 ± 0.171	0.930 ± 0.177
绝经后	85	$0.972 \pm 0.169^*$	$0.829 \pm 0.105^{**}$

注:与绝经前比较 * $t = 2.43$ $P = 0.017$; ** $t = 3.32$ $P = 0.002$

3. 绝经后妇女血脂水平与 BMD 的相关性分析(见表 3)。

由于 BMI 与 BMD 有相关性,而甘油三酯及胆固醇升高又经常与肥胖共存,所以用反映肥胖的 BMI 校正 BMD 求出偏相关系数。甘油三酯与股骨颈 BMD 经 BMI 校正后有显著的负相关,而与腰椎 L_{2-4} BMD 无相关;胆固醇与腰椎 L_{2-4} 及股骨颈 BMD 经 BMI 校正后均无相关性。

表 3 绝经后妇女血脂与 BMD 的相关系数/偏相关系数

项目		腰椎 L_{2-4} BMD	股骨颈 BMD
甘油三酯	r	$-0.120/-0.167$	$-0.191/-0.342$
	P	$0.276/0.134$	$0.082/0.003$
胆固醇	r	$-0.037/-0.041$	$-0.035/-0.036$
	P	$0.735/0.715$	$0.750/0.748$

注:/后的数值为经过 BMI 校正的偏相关系数, $n = 85$

讨 论

绝经后骨质疏松主要与雌激素水平急剧降低有关,继发钙调节激素、局部细胞因子和钙代谢的一系列紊乱。其中缺钙会加重骨的丢失,补钙可以矫正骨的高转换状态,主要是通过成骨细胞和破骨细胞上的钙感受受体和影响钙调节激素的分泌^[4]。

血脂水平与骨质疏松的直接关系尚不明确,但是其对骨代谢的影响却早已从多个角度得到证实。例如,长期应用糖皮质激素可以引起股骨头坏死,其原因与糖皮质激素引起血脂升高,进而引起脂肪栓塞及脂滴(甘油三酯)沉积到骨细胞,最后导致骨细胞(Osteocyte)的坏死及凋亡有关^[5],脂滴还可以沉积到成骨细胞的前体细胞影响其功能^[6]。上述不良影响可以被贝特类或他汀类降脂药物所预防^[2,7]。骨细胞虽然无直接的成骨和破骨作用,但是其对骨髓细胞及成骨细胞之间的信号传导至关重要。它感知机体对骨量的需要和微损伤的修复,同时还感受血液循环中激素的变化^[8]。上世纪 60 年代 Jones 就提出,骨细胞的功能障碍时,微损伤的信息不能传递给破骨细胞和成骨细胞,长期的结果就是骨小梁的变薄^[9]。甘油三酯对骨代谢的影响还可以从细胞分化的角度去认识。在成骨细胞的培养体系中加入脂肪酸,成骨细胞可以分化成脂肪细胞样细胞,而且骨髓细胞向成骨细胞的分化减少^[10]。

本研究发现,甘油三酯与股骨颈 BMD 呈负相关,但是与腰椎 L_{2-4} BMD 无相关,推测有以下原因:(1)两部位的解剖特点不同,因此血运情况不同^[11];(2)两部位的细胞特性不同^[12],因此可能对甘油三酯的反应不同。甘油三酯与骨密度的负相关关系还可以从多个研究得到间接的佐证:甘油三酯是动脉粥样硬化的独立危险因素,而动脉粥样硬化经常与骨质疏松并存^[3]。

我们的研究结合前人的研究结果提示:绝经后妇女血甘油三酯水平的升高可能是导致绝经后骨量

(下转第 212 页)

($R = 0.673$, $\text{Rad}^2 = 0.434$, $P = 0.000$) 的关键相关因素, 决定了 44% 腰椎骨矿量的变化。身高和体重即对青少年 AS 早期骨矿含量和骨密度有着极其重要的正相关意义。进而提示, 如果能在积极治疗 AS 的同时, 正确开展康复训练及促进青少年成长发育, 将有利于发挥身高和体重对骨矿含量和骨密度的正相关作用, 对于维持和增加骨量和骨密度、改善骨强度、降低 AS 相关性骨质疏松及骨折危险性都大有裨益。

参 考 文 献

- 1 Saggese G, Baroncelli GI, Bertelloni S. Osteoporosis in children and adolescents: diagnosis, risk factors, and prevention. *J Pediatr Endocrinol Metab*. 2001, 14: 833-859.
- 2 Baroncelli GI, Federico G, Bertelloni S, et al. Bone quality assessment by quantitative ultrasound of proximal phalanges of the hand in healthy subjects aged 3-21 years. *Pediatr Res*, 2001, 49: 713-718.
- 3 Maillefert JF, Aho LS, El Maghraoui A, et al. Changes in bone density in patients with ankylosing spondylitis: a two-year follow-up study. *Osteoporos Int*, 2001, 12: 605-609.
- 4 Capaci K, Heggeler S, Argin M, et al. Bone mineral density in mild and advanced ankylosing spondylitis. *Yonsei Med J*, 2003, 44: 379-384.
- 5 Gratacos J, Collado A, Pons F, et al. Significant loss of bone mass in patients with early, active ankylosing spondylitis: a followup study. *Arthritis Rheum*, 1999, 42: 2319-2324.
- 6 Goethe HS, Steven MM, van der Linden SM, et al. Evaluation of diagnostic criteria for ankylosing spondylitis: a comparison of the Rome, New York and modified New York criteria in patients with a positive clinical history screening test for ankylosing spondylitis. *Br J Rheumatol*, 1985, 24: 242-249.
- 7 Shih HC, Liu SC, Chang CP, et al. Positive association of ankylosing spondylitis with homozygous HLA-B2704, but protection with B2705 in Taiwan Chinese. *Kaohsiung J Med Sci*, 2001, 17: 509-516.
- 8 Duftner C, Goldberger C, Falkenbach A, et al. Prevalence, clinical relevance and characterization of circulating cytotoxic CD4⁺ CD28⁻ T cells in ankylosing spondylitis. *Arthritis Res Ther*, 2003, 5: R292-300.
- 9 Hitchon PW, From AM, Brenton MD, et al. Fractures of the thoracolumbar spine complicating ankylosing spondylitis. *J Neurosurg*, 2002, 97 (2 Suppl): 218-222.
- 10 Chen IH, Chien JT, Yu TC. Transpedicular wedge osteotomy for correction of thoracolumbar kyphosis in ankylosing spondylitis, experience with 78 patients. *Spine*, 2001, 26: E354-360.
- 11 Mehdian SM, Freeman BJ, Licina P. Cervical osteotomy for ankylosing spondylitis: an innovative variation on an existing technique. *Eur Spine J*, 1999, 8: 505-509.
- 12 Yilmaz N, Ozaslan J. Biochemical bone turnover markers in patients with ankylosing spondylitis. *Clin Rheumatol*, 2000, 19: 92-98.
- 13 Sampaio-Barros PD, Costallat LT, Bertolo MB, et al. Methotrexate in the treatment of ankylosing spondylitis. *Scand J Rheumatol*, 2000, 29: 160-162.
- 14 Toussiot E, Ricard-Bhim S, Dumoulin G, et al. Relationship between urinary pyridinium cross-links, disease activity and disease subsets of ankylosing spondylitis. *Rheumatology Oxford*, 1999, 38: 21-27.
- 15 Dos Santos FP, Constantin A, Laroche M, et al. Whole body and regional bone mineral density in ankylosing spondylitis. *J Rheumatol*, 2001, 28: 547-549.

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(上接第 194 页)

减少及骨质疏松发生的因素之一。

参 考 文 献

- 1 杨欣, 郑淑蓉. 选择性雌激素受体调节剂雷洛昔芬的临床研究进展. *中华妇产科杂志*, 2003, 38: 254-256.
- 2 Wang CJ, Moga DB, Richermer WG, et al. Cortisone induced bone changes and its response to lipid clearing agents. *Clin Orthop*, 1978, 130: 81-85.
- 3 Vonder Recke P, Hansoin MA, Haasger C. The association between low bone mass at the menopause and cardiovascular mortality. *Am J Med*, 1999, 106: 273-278.
- 4 Weinstein RS, Nicolas RW, Kirchner JR, et al. Anatomic juxtaposition of apoptotic osteocytes and avascular necrosis in femurs from patients with glucocorticoid excess. *Bone*, 1998, 23: S461.
- 5 朱汉民. 钙与骨质疏松症. *中国骨质疏松杂志*, 2001, 7: 262-266.
- 6 Enlow DH, Conclin JL, Bang Seong. Observation on the occurrence and the distribution of lipids in compact bone. *Clin Orthop*, 1965, 38: 157-169.
- 7 Pritchett JW. Statin therapy decreases the risk of osteonecrosis in patients receiving steroids. *Clin Orthop*, 2001, 386: 173-178.
- 8 Tomkinson A, Reeve J, Shaw RW, et al. The death of osteocytes via apoptosis accompanies estrogen withdrawal in human bone. *J Clin Endocrinol Metab*, 1997, 82: 3128-3135.
- 9 Jones. Alcoholism, hypercortisolemia, fat embolism and osseous avascular necrosis. In: Idiopathic ischemic necrosis of the femoral head in adults. Stuttgart, Germany, Thieme Publ, 1971. 112.
- 10 Daisiro Jr DD, Vogel RL, Jonson TE, et al. High fatty acid content in rabbit serum is responsible for the differentiation of osteoblasts into adipocyte-like cells. *J Bone Miner Res*, 1998, 13: 96-106.
- 11 Fisher DE. The role of fat embolism in the etiology of corticosteroid-induced avascular necrosis. *Clin Ortho*, 1978, 130: 68-79.
- 12 Ernst M, Heath JK, Rodon GA. Estrogen effects on proliferation messenger ribonucleic acid for collagen and insulin-like growth factor-1, and parathyroid hormone stimulated adenylate cyclase activity in osteoblastic cells from calvariae and long bones. *Endocrinology*, 1989, 125: 825-833.

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