

· 综述 ·

低蛋白血症和骨折、骨质疏松相关性研究

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摘要: 低蛋白血症是一种由多种原因引起的临床综合征,重度低蛋白血症因与病情严重程度及预后密切相关而被广泛研究。但低蛋白血症往往多为慢性过程,病因复杂,起病隐匿,易被临床医生忽视。近来,越来越多的学者指出低蛋白血症、骨折与骨质疏松之间具有相关性,对其发生机制也从多方面进行了研究。虽然目前对低蛋白血症、骨折与骨质疏松的研究不断深入,但对其认识依然欠缺。本文将通过对低蛋白血症、骨折与骨质疏松相关性研究进行综述,旨在为骨折预防及其危险因素的评估、骨质疏松的干预措施提供新的思路。

关键词: 低蛋白血症;骨质疏松;骨折

Research in the relationship between hypoproteinemia, fracture and osteoporosis

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Abstract: Hypoproteinemia is a kind of clinical syndrome aroused by various factors. Severe hypoproteinemia is widely researched as it is closely related to the severity and prognosis of the disease. However, hypoproteinemia generally assumes the chronic process. In addition, with complex etiological factors and insidious onset it is easy to be ignored by clinicians. Recently, an increasing number of scholars have pointed out that hypoproteinemia, fracture and osteoporosis are related, and thus the mechanism of its occurrence has been studied from many aspects. Although the research on hypoproteinemia, fracture and osteoporosis is deepening, our understanding is still lacking. This paper reviews the research on the relationship between hypoproteinemia, fracture and osteoporosis, and provides new ideas for the prevention of fracture, the evaluation of risk factors and the intervention measures of osteoporosis.

Key words: hypoalbuminemia; osteoporosis; fracture

低蛋白血症是指蛋白质严重缺乏所导致的营养不良综合征,具体指血清总蛋白低于 60 g/L 或者白蛋白低于 35 g/L^[1-2]。低蛋白血症是由多种相关因素综合所致的一种疾病。低蛋白血症常常与恶性肿瘤、肝病、肾病综合征和营养不良综合征等系统性疾病有关^[3-4]。因饮食习惯、人种、检测仪器及低蛋白血症诊断标准的差异等原因,低蛋白血症的流行病学资料并没有统一性的描述。Brown 等^[5]发现,在老年人群中适当增加蛋白质摄入可以预防骨折。近年来不断有新的研究发现,低蛋白血症与骨折之间

存在相关性,其可能机制一方面为低蛋白使骨骼肌强度下降,易引起摔倒,从而导致骨折^[39-44],另一方面为低蛋白状态影响骨代谢平衡,使骨脆性增加,从而发生骨折的几率增加^[45-48]。对低蛋白血症、骨折与骨质疏松之间的相关性研究不仅从临床而且从基础方面进行了多方面的实验,具有一定的基础。本文将对低蛋白血症、骨折与骨质疏松之间相关性的研究进展进行综述。

1 低蛋白血症与骨折的相关性研究

部分研究结果表明^[6-12]低蛋白血症使骨折术后相关并发症的风险上升。余江等^[13]的研究表明低蛋白血症与股骨近端骨折术后多种并发症存在关

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系。据文献统计,1/5 的老年髌部骨折患者存在营养不良^[14-15]。由于老年患者骨折后长期卧床,导致消化功能受影响,营养不良的相关性表现逐渐显现,最具有临床意义的还是低蛋白血症。Corti 等^[16-21]以社区为基础对大于 71 岁的 4 116 名老年人进行为期 1 年的随访,发现低白蛋白状态是老年人骨折后病死率的独立危险因素。Huang 等^[22]对骨折危险因素的研究中指出,低蛋白血症与髌部骨折风险成反比。表明低蛋白血症代表了生理上的一种危险状态,既增加了患者发生骨折的几率,又导致了不良后果的风险增加。Luk 等^[23]发现高蛋白水平与老年人骨折术后较短的平均住院日之间存在相关性,这可能意味着在较短的住院康复中,较高的白蛋白水平可以使患者在功能状态方面得到改善。随着低蛋白血症与骨折的研究进一步深化,学者们发现低蛋白血症、骨密度与骨质疏松之间也存在联系。于是不少研究认为低蛋白血症、骨密度与骨质疏松三者之间互为因果关系。Lingetsmo 等^[24]的一项研究表明,足够的蛋白质摄入量是降低脆性骨折发生率的一个重要因素,即蛋白质摄入量与骨密度及骨折有关。

2 低蛋白血症与骨质疏松相关性研究

随着社会的发展,人口老龄化的出现,随着年龄的增长,骨质疏松症发病率也随之上升,成为严重危害老年人身体健康的常见病。骨质疏松症不仅严重影响个人日常生活,还会给家庭和社会带来沉重的经济负担^[25-26]。

张智海等^[27]在分析国内 70 997 例 40 岁以上人群的骨质疏松患病率时发现,以 T 值 ≤ -2.5 为骨质疏松诊断标准,并结合中国第六次人口普查^[28]推算出中国大陆 40 岁以上人群骨质疏松症发病率为 19.74%,约 1.12 亿患病人群。人类从胎儿时期一直到生命结束,肌肉骨骼系统一直处于动态的平衡,在 25 岁前后人类骨总量及质量到达峰值,其后骨状态随着年龄增长逐渐下滑,在整个过程中,各种因素都会影响骨量,使其产生变化。近年来学者们进行了大量的研究,一些观点表明低蛋白血症与骨质疏松存在联系,但对其认识并不充分,需要更完善的证据支持。

Hannan 等^[29]进行了一项对 615 名年龄在 68~91 岁的老年人开展的为期 4 年的队列研究,其蛋白质的摄入在 14~175 g/d 之间,该结果表明低摄入量的蛋白质与股骨颈和腰椎骨量的减少具有统计学意

义($P < 0.05$)。Devine 等^[30]对平均年龄为 75 岁的 1 077 位绝经后女性进行为期 1 年的随访,发现饮食中不同的蛋白含量对骨质疏松的影响具有统计学意义($P < 0.05$)。Tucker 等^[31]对 855 名年龄为 69~97 岁的老年人中进行为期 4 年的队列研究,发现了与上述相同的结果。

但也有一些学者认为,低蛋白血症与骨质疏松之间并不存在联系,Sahni 等^[32]在对年龄为 26~86 岁的 497 位男性和 680 位女性平均 4.6 年的随访中,发现低蛋白饮食与骨质疏松之间的关系无统计学意义。Kerstetter 等^[33]和 Zou 等^[34]在长期的随访后,未发现低蛋白血症与骨质疏松之间存在统计学意义。

3 低蛋白血症与骨折、骨质疏松相关机制

3.1 低蛋白血症与跌倒、骨折相关性的研究

有研究结果^[35-37]表明,白蛋白浓度和骨骼肌强度下降在两年内有直接联系。然而肌肉质量和力量之间的关系不是线性的,它取决于肌肉的质量、肌肉脂肪的浸润和神经控制^[38-39]。白蛋白水平较低,肌肉质量减少和老年人肌肉力量减少存在相关性。低蛋白血症又限制了身体的活动和合成新白蛋白,导致肌肉萎缩和增加疾病的易感性,从而引起跌倒,甚至骨折的发生^[40]。低蛋白血症可能直接或者间接的影响骨骼状态,通过其对核因子- κ B 的作用使骨平衡发生转移,减少对矿物质在骨通道的转运,从而减少了钙盐的沉积,增加脆性骨折发生率^[41-44]。

3.2 低蛋白血症与骨密度、骨质疏松相关性的研究

3.2.1 激素调节理论:低蛋白饮食对生长因子的产生及其功能有一定影响,主要是通过下丘脑- GH-IGF 系统来影响骨的合成代谢,并且对肝脏产生 IGF-1 及血浆 IGF-1 水平都会产生影响。因而下丘脑激素调节轴对肝脏、软骨等 IGF-1 生成水平产生影响,所以对骨的合成代谢影响巨大。因此,低蛋白血症可影响体内骨代谢,体内长期的低蛋白水平则会导致骨质疏松的发生^[45-46]。

3.2.2 转录翻译调节:一方面,低蛋白血症可能导致 $\text{NF-}\gamma$ B 信号传导途径的各种有效成分合成受限,从而导致 $\text{NF-}\gamma$ B 信号传导通路受阻,最终造成激活破骨细胞,并且抑制了成骨细胞。另一方面,通过例如 $\text{NF-}\gamma$ B 受体激动剂配体、 $\text{TNF}\alpha$ 、淋巴毒素、细菌内毒素、Toll 样受体配体、 CD40 L 、 IL-1 或者氧自由基等炎性细胞因子而引起急性期反应,间接的与转录因子 $\text{NF-}\gamma$ B 结合^[47-49]。Sinaki^[50]认为低蛋

白血症使得固定化酶作用时间延长,从而导致骨质疏松的发生。

3.2.3 代谢在骨重建中的作用:有研究表明^[51-55],低蛋白血症会引起骨松质中白蛋白沉积减少,流出增多,降低了磷酸钙晶体对骨骼的亲合力,从而打破了甲状旁腺素与维生素 D 结合蛋白在体内的动态平衡。在女性中,使得雌激素对骨的敏感性降低。在成骨过程中,使得骨髓间质细胞优先向脂肪型转化,弱化了成骨蛋白对于提升破骨细胞活性,抑制成骨细胞活性的效应。

4 低蛋白血症、骨折、骨质疏松相关性研究的临床价值及实际意义

随着研究的深入,人们对于低蛋白血症所带来危害的认识也逐渐加深,其与多种疾病的发生、发展及转归均存在关联。由于低蛋白血症多为慢性过程,病因复杂,起病隐匿,故要提高对该种疾病的认识,并且对于疾病起因的各种因素要尽可能控制。其次,低蛋白血症与骨折、骨质疏松三者之间互为因果关系也逐渐确立,血清白蛋白检测可能成为老年人骨折风险预测的一种简单而有效的工具^[56]。可以通过对低蛋白血症发生的基础研究方面入手,为预防老年人骨质疏松骨折提供新思路。

5 低蛋白血症与骨折、骨质疏松相关性研究局限与展望

低蛋白血症的病因错综复杂^[3-4],因此在研究过程中要把低蛋白血症引起骨折、骨质疏松的原发病因考虑在内。目前,对于其之间关系的相关性研究仅局限于基础性的实验及回顾性的临床研究。对于病因及危险因素的流行病学及前瞻性临床研究还十分缺乏。因此,对低蛋白血症与骨折、骨质疏松之间因果关系的探讨还需要前瞻性流行病学方面的研究。

综上所述,已有相关研究证实低蛋白血症与骨折、骨质疏松三者之间具有相关性。但在我国仍缺乏对其预防、干预等临床措施,需要引起临床医师的重视。对于骨折及骨质疏松的预防、早期干预及风险评估都应予以密切关注。低蛋白血症与骨折、骨质疏松相关性的研究,可能为骨折的预防及危险因素评估、骨质疏松的干预措施提供新的思路。

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