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MLR、WLR和OSTA指数与2型糖尿病患者骨密度的研究进展

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摘　要

2型糖尿病性骨质疏松(Type 2 Diabetic Osteoporosis, T2DOP)是由2型糖尿病(Type 2 Diabetes Mellitus, T2DM)导致的以骨量减少、骨微结构受损、骨强度降低和骨折风险增加为特征的肌骨系统并发症，早期无症状且发病机制复杂，诊断方法有限，患者的致残率和死亡率高。当前对T2DOP的治疗主要采用抗糖尿病药物和抗骨质疏松药物。糖尿病患者任意部位骨折风险增加达32%，髋部骨折风险增加77%。即使部分2型糖尿病患者有较高的骨密度，仍具有较高的骨折风险，而骨折风险评分可能低估其骨折风险。糖尿病患者血糖控制差和病程延长是骨折的决定性因素，跌倒是外周骨折的主要危险因素，微血管病变加速骨量丢失。糖尿病影响所有类型骨细胞，降低骨转换率，降低骨强度。为此，本文总结相关文献内容，并介绍MLR、WLR和OSTA指数与2型糖尿病患者骨密度的研究进展为今后的研究提供参考。

关键词

2型糖尿病，骨密度，骨质疏松，单核细胞与淋巴细胞计数比，白细胞与淋巴细胞计数比，亚洲人骨质疏松自我筛选筛查工具(OSTA指数)

Research Progress on MLR, WLR and OSTA Indices and Bone Mineral Density in Patients with Type 2 Diabetes Mellitus

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Abstract

Type 2 diabetic osteoporosis is a musculoskeletal system complication caused by type 2 diabetes mellitus, characterized by decreased bone mass, impaired bone microstructure, decreased bone strength, and increased risk of fracture. It is asymptomatic in the early stage, with complex pathogenesis, limited diagnostic methods, and high morbidity and mortality. At present, T2DOP is mainly treated with anti-diabetic drugs and anti-osteoporosis drugs. Patients with diabetes had a 32 percent increased risk of fracture at any site and a 77 percent increased risk of hip fracture. Even if some people with type 2 diabetes have higher bone density, they still have a higher risk of fracture, and the fracture risk score may underestimate their fracture risk. Poor glycemic control and prolonged disease course in diabetic patients are the decisive factors for fracture, fall is the main risk factor for peripheral fracture, and microvascular disease accelerates bone mass loss. Diabetes affects all types of bone cells, reducing the rate of bone turnover and reducing bone strength. To this end, this paper summarizes the relevant literature and introduces the research progress of MLR, WLR and OSTA index and BMD in type 2 diabetes patients to provide reference for future research.

Keywords

Type 2 Diabetes Mellitus, Bone Mineral Density, Osteoporosis, Ratio of Monocyte to Lymphocyte Count, Ratio of White Blood Cell to Lymphocyte Count, Asian Osteoporosis Self-Screening Screening Tool (OSTA Index)

1. 引言

糖尿病(Diabetes Mellitus, DM)是高发病率、高致残率和致死率的严重公共卫生问题[1]，是一种由胰岛素分泌和活性的相对不足或绝对缺乏而引发糖、脂肪、蛋白质等营养成分代谢紊乱的疾病，是一种发病率和死亡率都很高的大流行性代谢性疾病[2]。随着人口老龄化和生活方式的改变，糖尿病的患病率持续上升。世界卫生组织(World Health Organization, WHO)于 2016 年报道称，全球糖尿病患病人数约为 4.22 亿，其中 2 型糖尿病(Type 2 Diabetes Mellitus, T2DM)占大多数，其发病率随着年龄增加而增加[3]。2045 年，数字将会达到 6.93 亿人，患病率上升到 9.9%。此外，国际糖尿病联盟还指出 DM 的高患病率具有重要的社会经济和发展意义，在中低收入国家更为显著[4]。

骨质疏松症(Osteoporosis, OP)是指各种原因导致骨量减少或骨组织显微结构受损，致使骨脆性增加，最终导致骨折易于发生的一种全身性代谢性骨病[5]。这一公认的定义是 1993 年国际共识提出的，它包含了该病的两个重要特征：对骨量和微结构的不良影响以及骨折的临床结果。随着人类平均寿命的延长和人口老龄化的发展，骨质疏松已成为影响全人类健康的重要问题，据估计，全球有超过 2 亿人患有 OP，发病率随着年龄的增长而增加，超过 70%的 80 岁以上的人受到影响，女性比男性更常见[6]。根据五大洲 86 项研究的骨质疏松症患病率报告，世界骨质疏松症的患病率为 18.3%。据报道，世界女性骨质疏松症患病率为 23.1%，而世界男性骨质疏松症患病率为 11.7%，非洲骨质疏松症的患病率最高为 39.5% [7]。2016 年，我国 60 岁以上老年人 OP 的总患病率为 36%，其中女性为 49%，男性为 23% [8]，截至 2010

年的数据显示超过 230 万例骨质疏松性骨折导致我国医疗保健系统支出约 649 亿。预计到 2035 年，与骨质疏松症相关的骨折的数量和支出将翻一番，到 2050 年，将增长到约 600 万例骨折，花费超过 254 亿美元[9]。

研究发现，在同龄、同性别人群中，T2DM 患者的骨质减少和 OP 的发生率均较高[10]。世界卫生组织提出，可将骨矿含量作为 OP 诊断的参考指标，而双能 X 线骨密度测量仪测得的骨密度值可在宏观上反映骨矿含量，是临床诊断 OP 的金标准[11]。但双能 X 线骨密度仪在诊断 OP 时也存在一定弊端，如适用人群局限、OP 早期易误诊漏诊、机体照射损伤等[12]。

2. 单核细胞计数与淋巴细胞计数(MLR)

MLR 是指单核细胞与淋巴细胞的比值，是国外学者提出的在肿瘤转归、心血管疾病和糖尿病视网膜病变等炎症相关疾病的预测和预后中发挥重要作用的新型炎症指标[13]。Grossman 等人发现血糖正常者的白细胞、粒细胞和单核细胞水平低于糖尿病患者[14]。MLR 水平可能比独立的单核细胞、淋巴细胞和白细胞水平更稳定，这是因为单核细胞和淋巴细胞水平之间的平衡，受各种生理和病理状态的影响较小。近些年有研究表明 MLR 比白细胞亚群更适合作为炎症标志物。此外，MLR 在部分免疫疾病中报道了其诊断价值，宣布它可能反映全身炎 症和免疫损伤的严重程度[15] [16]。免疫因素对骨质疏松症的进展有着重要影响，骨免疫学是一门新兴的交叉学科，为骨质疏松症的发病机制提供了新的方向[17]。许多炎性细胞因子、免疫细胞、信号因子参与了这个过程，其中淋巴细胞可以通过分泌各种细胞因子在骨形成及骨吸收上发挥重要作用[18] [19]。Li 等人提示淋巴细胞是骨转换的重要稳定器，也是峰值骨量的调节因子，他们发现，B 细胞占骨髓产生的护骨素(OPG)总量的 64%，B 细胞基因敲除的小鼠容易发生骨质疏松症[20]。Leena Sapral 等人研究调查发现调节性 B 淋巴细胞(Bregs)在调节破骨形成中发挥重要作用，Bregs 以剂量依赖性方式通过产生 IL-10 细胞因子，从而抑制 RANKL 诱导的破骨形成[21]。此外还有研究表明，单个 T 淋巴细胞亚群在激活后，通过产生可溶性因子以不同的方式影响成骨细胞成熟，在所有 T 细胞中，促炎 T 细胞，包括 T 辅助 17 细胞，对成骨刺激性最强[22]。Gao 等人在纳入的 316 名骨质疏松和 111 名健康对照受试者的研究表明，发现健康对照组患者 MLR 水平明显低于骨质疏松组，MLR 对骨质疏松症有较好的诊断价值[23]。随着对 MLR 的研究不断深入，相信它将在临床诊断和治疗中发挥越来越重要的作用。

3. 白细胞计数与淋巴细胞计数比值(WLR)

WLR：是白细胞与淋巴细胞平衡的标志，WLR 比值增高，可能是机体处于慢性炎症状态。国外有关于 WLR 的文献研究证明炎症因子是胰岛素抵抗的起始因素，并与胰岛素抵抗密切相关[24]。而 2 型糖尿病患者机体内胰岛素抵抗均可导致炎症反应并促进其进展[25]，2 型糖尿病患者血糖控制不良可影响到骨量和骨密度的变化，导致骨量和骨密度减低，进而引发骨质疏松症[26]。WBC：慢性炎症时白细胞数量增多，释放大量炎性介质，使机体处于慢性应激状态，从而引起胰岛素抵抗[27]。淋巴细胞：在其功能失调的淋巴细胞可启动炎症因子和趋化因子的级联反应，引起中性粒细胞和巨噬细胞的聚集，进而打破骨形成的动态平衡，诱导破骨细胞的吸收[28]。同样在细胞层次，骨质疏松组的淋巴细胞、淋巴细胞百分比均显著低于健康研究人群，这表明淋巴细胞与骨密度存在一定的相关性[29]。在一项实验研究中，由于适应性免疫系统的效应细胞和骨重塑的淋巴细胞的缺失，骨折愈合延迟[8]。然而，在最近的一些报告集中在免疫系统和骨组织之间的联系上，表明淋巴细胞可以调节骨重塑，这些发现导致了免疫系统细胞在骨健康[30]中发挥的关键作用，淋巴细胞在体内的最终作用可能是抑制破骨细胞的形成。至少在某些条件下[31]，淋巴细胞可能刺激成骨细胞分化，增强骨形成。正如关于骨再生[32]和异位骨化[33]的研究表明淋

巴细胞水平反映感染情况可通过体育锻炼增强体质，提高免疫力，达到降低各种感染的概率以减少骨质疏松症的发生[34]。但是目前 WLR 与 2 型糖尿病患者骨密度改变之间的机制尚未明确的阐述且研究甚少，但对淋巴细胞和白细胞的意义认识较为成熟。因此，研究并发现 WLR 与 2 型糖尿病患者与骨密度的关系显得至关重要。

4. OSTA ((体重 − 年龄)*0.2)指数

随着人们生活水平的提高和生活方式改变，2 型糖尿病(T2DM)的患病率也逐渐增高。骨质疏松则是 T2DM 常见并发症，可增加患者骨折风险，早期识别 T2DM 合并骨质疏松的相关影响因素对其临床诊疗及预防尤为重要。亚洲人骨质疏松自我筛查工具(OSTA)指数对骨质疏松评估有重要的应用价值[35]。DEXA 为骨质疏松诊断仪器，但由于其使用成本过高，无法满足临床广泛筛查需求，在基层医院也缺少使用条件。OSTA 指数则是一种计算骨质疏松情况的有效简便方法，在早期筛查及评估中简单易行[36]。张静等[37]研究表明，OSTA 指数与骨质疏松患者腰椎、股骨颈、大转子、全股骨等部位的 BMD 均呈正相关，但在预测 BMD 值的效能方面有待提高。

5. 总结

综上所述，2 型糖尿病患者与骨质疏松症都是全国范围内高发的慢性代谢性疾病，严重影响人们的生活质量，降低人们的生活水平，近年来越来越受到人们的广泛关注与重视，根据以上相关研究结果可见，以上 MLR、WLR 及 OSTA 指数与 2 型糖尿病患者骨质疏松之间可能存在一定的相关性。因此探讨 MLR、WLR 及 OSTA 指数与 2 型糖尿病患者骨质疏松的相关性，为早期防治 2 型糖尿病患者骨质疏松提供一定的理论依据，为 2 型糖尿病患者骨质疏松的病情评估及相关治疗疗效判断提供更有价值的方法和手段。从而进行早期干预，进而提高患者的生存质量。

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