Advances in Clinical Medicine 临床医学进展, 2021, 11(7), 3191-3195
Published Online July 2021 in Hans. http://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2021.117463

Hans汉斯

2型糖尿病患者合并肌少症与骨质疏松关系的研究进展

李金霞[1]，杨历新[2]

[1]青海大学研究生院，青海 西宁
[2]青海省人民医院内分泌科，青海 西宁
Email: yanglx282@sina.com

收稿日期：2021年6月21日；录用日期：2021年7月11日；发布日期：2021年7月22日

摘 要

一直以来人们所熟知的糖尿病并发症是糖尿病视网膜病变、糖尿病肾病和神经病变等微血管并发症以及心血管疾病等大血管并发症。而随着世界人口老龄化趋势的加重，骨质疏松、肌少症作为老年人高发疾病，目前已有研究证实它们为糖尿病新型并发症。本文就糖尿病、肌少症与骨质疏松之间的相互关系、潜在的生物学机制加以综述，旨在提高人们对糖尿病、肌少症、骨质疏松三者的认识，并为它们的诊断、预防及综合治疗提供新思路。

关键词

糖尿病，肌少症，骨质疏松，关联性

Research Progress on the Relationship between Sarcopenia and Osteoporosis in Type 2 Diabetes Mellitus

Jinxia Li[1], Lixin Yang[2]

[1]Graduate School of Qinghai University, Xining Qinghai
[2]Department of Endocrinology, Qinghai Provincial People's Hospital, Xining Qinghai
Email: yanglx282@sina.com

Received: Jun. 21st, 2021; accepted: Jul. 11th, 2021; published: Jul. 22nd, 2021

文章引用: 李金霞, 杨历新. 2 型糖尿病患者合并肌少症与骨质疏松关系的研究进展[J]. 临床医学进展, 2021, 11(7): 3191-3195. DOI: 10.12677/acm.2021.117463

Abstract

The well-known complications of diabetes mellitus are microvascular complications such as diabetic retinopathy, diabetic nephropathy and neuropathy, and macrovascular complications such as cardiovascular disease. With the aggravation of the aging trend of the world population, osteoporosis and sarcopenia, as diseases with high incidence of the elderly, have been confirmed as new complications of diabetes mellitus. This article reviews the relationship between diabetes mellitus, sarcopenia and osteoporosis as well as the potential biological mechanism, aiming to improve people's understanding of diabetes mellitus, sarcopenia and osteoporosis, and to provide new ideas for their diagnosis, prevention and comprehensive treatment.

Keywords

Diabetes Mellitus, Sarcopenia, Osteoporosis, Correlation

Copyright © 2021 by author(s) and Hans Publishers Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/
Open Access

1. 引言

糖尿病以高血糖和糖尿病并发症为特点，严重影响患者的生活质量，给社会带来了重大的经济负担，骨质疏松及肌少症作为糖尿病的新型并发症，也成为了研究热点，但是否互为危险因素及机制目前仍缺乏有力证据。

2. 肌少症与 2 型糖尿病的关系

近来有研究证明 2 型糖尿病(type 2 diabetic mellitus, T2DM)患者骨骼肌减少症的患病率明显高于健康对照组[1] [2]，研究发现在多变量分析中，肌少症仍然与糖尿病(diabetes mellitus, DM)密切相关[3]，2 型糖尿病患者骨骼肌减少症和前骨骼肌减少症高患病率的潜在机制尚不清楚。有研究表明除了与衰老过程[4]所固有的肌肉力量丧失有关外，胰岛素抵抗和氧化应激是肌少症的病理生理基础组成部分[5] [6]。氧化应激被认为是肌少症的主要发病机制之一，这可能与糖尿病的特征性成分有关，如血管改变、慢性炎症、肌肉脂质浸润等，研究发现食用较少健康食品的患者出现较多的肌少症前症状，富含水果和蔬菜的饮食可以提供抗氧化剂，减少炎症状态造成的损害[7]，降低患肌少症的风险。其次不受控制的高血糖的代谢后果是分解代谢，伴随肌肉蛋白分解和能量使用不足，可能导致肌肉质量下降和肌肉功能降低[8]。另外骨骼肌不仅负责运动等生理功能，也是代谢活跃的组织[9]。人体的全身骨骼肌是负责胰岛素介导的葡萄糖处理的最大器官，骨骼肌的逐渐丧失可能导致胰岛素介导的葡萄糖处理的减少，并在肌少症中加重胰岛素抵抗，由于代谢异常和胰岛素抵抗，T2DM 患者是发生肌减少症的高风险人群[8] [10]。

此外，L. M. Pechmann [11]等人研究发现糖尿病患者中有白蛋白尿的患者发生骨骼肌减少症的几率约为不合并白蛋白尿患者的 2.8 倍。蛋白尿和肌少症之间的相互作用尚不完全清楚，可能的解释是胰岛素抵抗，它可以导致肾小球高滤过，内皮功能障碍，血管通透性增加，甚至在没有糖尿病的个体中出现蛋白尿，他们的研究提示白蛋白尿或许可以作为糖尿病患者发生肌少症的一个危险因素。

3. 骨密度与 2 型糖尿病的关系

骨病是糖尿病的严重并发症。有研究数据显示[12]，在调整了其他危险因素后，糖尿病患者发生骨质疏松性髋部骨折的风险几乎是非糖尿病患者的 2 倍。混杂因素如患者性别、年龄、体重指数、血糖状况、跌倒风险和糖尿病药物可能影响骨折风险。然而糖尿病患者的骨病诊断是一个挑战，因为目前的骨折预测方法，如骨密度 t 评分和骨折风险评估工具低估了 T1D 和 T2D 患者的骨折风险[13]。糖尿病持续时间和糖尿病控制状况与脆性骨折之间的关系仍在研究中，并显示了相互矛盾的结果，一项基于人群的研究表明，2 型糖尿病患者骨折的风险有两阶段模式，在诊断为 2 型糖尿病时，骨折风险实际上降低了，而在[14] 5 年后，骨折风险显著增加。研究人员推测，诊断时超重和肥胖与糖尿病相关并发症的影响可以解释观察到的双相骨折风险。较高的体重可以在一定程度上防止骨质流失。然而，这种关系并不是线性的。因此，当身体质量指数(BMI)值进入超重区，即大于 25 kg/m^2 时，就不会出现进一步的骨骼保护和额外的体重增加[15]。另一项大型研究表明骨小梁微结构的异常可能部分解释了 2 型糖尿病高骨密度患者骨折风险增加的悖论。骨小梁评分(TBS)是基于双能 X 线骨密度仪(DXA)图像[16]的像、分布广有关，而 TBS 值高与小梁结构好有关。TBS 已被证明可以预测骨质疏松性骨折，而不依赖于 BMD，它可能有潜力识别 DXA 扫描之间的差异，显示类似的 BMD 测量[16]。

越来越明显的是，糖尿病药物可以调节骨丢失和骨折的风险。应该谨慎选择药物，既不损害骨骼健康，同时又有助于优化血糖控制。研究证明噻唑二酮、罗格列酮、钠－葡萄糖共转运体 2 抑制剂，与骨折[17] [18]的风险增加有关，二甲双胍和磺脲类药物可能对骨折风险具有中性甚至轻微的保护性作用[19]。研究发现胰高血糖素样肽-1 (GLP-1)类似物利拉鲁肽和伊塞尼肽对骨折风险有所不同，发现利拉鲁肽显著降低骨折风险，而伊塞尼肽升高[20]。

糖尿病患者无疑增加了脆性骨折的风险。然而，如何正确评估糖尿病患者的骨折风险和管理骨质疏松症仍不清楚，也不存在有效的指南。目前，证据尚不成熟，无法作出明确的建议，现有的建议是基于专家共识。用于评估骨折风险和决定干预阈值的常规 BMD 和 FRAX 阈值仍然可以使用，尽管需要进行一些修改。在评估降糖药的风险效益比时，也应考虑其对骨骼脆性的影响。

4. 糖尿病、肌少症、骨质疏松三者的联系及潜在生物学机制

Hye-Sun Park [21]等人研究发现，肌肉质量、力量和体能与低骨量相关，肌肉内脂肪(肌肉持续受损的组织学标志)的积累可能在韩国绝经后妇女胰岛素抵抗的发展中起主要作用。他们研究发现在剔除年龄、体重等混杂因素后，肌肉面积、肌力与骨密度呈显著正相关，他们的研究结果表明，在胰岛素抵抗的发展过程中，持续损伤的肌肉伴随着脂肪浸润。推测细胞死亡过程是对肌肉废用或年龄相关性骨骼肌减少症的反应，当凋亡细胞积累和清除受损时，不适应性肌肉重塑发生，肌肉内脂肪浸润的同时释放炎症细胞因子和脂肪因子，可能导致胰岛素抵抗的发生。因此，这就产生了这样一种观点，即肌肉局部炎症的存在，紧接着脂肪的积累和脂肪因子和细胞因子失调的分泌，而不仅仅是肌肉质量或力量的减少，可能在胰岛素抵抗的发展中发挥更重要的作用。另外有研究显示，无论是男性还是女性，与非肌少症组相比，可能肌少症组的骨矿物质含量明显降低，提示肌少症糖尿病患者更容易发生骨质疏松症[22] [23]。一项国外研究表明瘦肉含量及握力与骨密度值呈正相关，四肢肌肉含量的增加可使骨量减少/骨质疏松症的发生风险下降，肌少症者较正常人罹患骨量减少或骨质疏松症的风险增加 1.8 倍[24]。这可能是由于骨骼和肌肉不仅通过相邻表面紧密相连，而且在化学和代谢上[25]也紧密相连。人们普遍认为，肌肉骨骼系统是一个完整的系统。肌生成抑制素是近年来备受关注的一种肌激素，主要由骨骼肌分泌的糖蛋白，是一种通过抑制成肌细胞和骨骼肌细胞增殖，抑制肌肉蛋白合成而负向影响肌肉增殖的调节因子[26]，肌肉

质量和骨量被认为随着肌生成抑制素表达水平的增加而减少。基于这些观察，肌生成抑制素被认为是参与骨骼肌相互作用[27]的预测候选调节因子。

5. 结论

临床上，糖尿病患者合并骨质疏松和肌少症与严重的身体残疾和负面健康结果相关，如摔倒、骨折、晚年生活独立性丧失和死亡率增加[28]，提示当肌少症与骨质疏松症同时发生时，迫切需要采取更多的预防和治疗措施。

参考文献

[1] Perkisas, S. and Vandewoude, M. (2016) Where Frailty Meets Diabetes. *Diabetes/Metabolism Research and Reviews*, **32**, 261-267. https://doi.org/10.1002/dmrr.2743

[2] Kim, T.N., Lee, E.J., Hong, J.W., *et al*. (2016) Relationship between Sarcopenia and Albuminuria: The 2011 Korea National Health and Nutrition Examination Survey. *Medicine*, **95**, e2500. https://doi.org/10.1097/MD.0000000000002500

[3] Souza, A.B.F., Nascimento, D.A.C., Rodrigues, I.J.M., *et al*. (2019) Association between Sarcopenia and Diabetes in Community Dwelling Elderly in the Amazon Region—Viver Mais Project. *Archives of Gerontology and Geriatrics*, **83**, 121-125. https://doi.org/10.1016/j.archger.2019.03.020

[4] Cruz-Jentoft, A.J., Baeyens, J.P., Bauer, J.M., *et al*. (2010) Sarcopenia: European Consensus on Definition and Diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age and Ageing*, **39**, 412-423. https://doi.org/10.1093/ageing/afq034

[5] Kim, T.N. and Choi, K.M. (2013) Sarcopenia: Definition, Epidemiology, and Pathophysiology. *Journal of Bone Metabolism*, **20**, 1-10. https://doi.org/10.11005/jbm.2013.20.1.1

[6] Morley, J.E., Malmstrom, T.K., Rodriguez-Mañas, L., *et al*. (2014) Frailty, Sarcopenia and Diabetes. *Journal of the American Medical Directors Association*, **15**, 853-859. https://doi.org/10.1016/j.jamda.2014.10.001

[7] Chan, R., Leung, J. and Woo, J. (2016) A Prospective Cohort Study to Examine the Association between Dietary Patterns and Sarcopenia in Chinese Community-Dwelling Older People in Hong Kong. *Journal of the American Medical Directors Association*, **17**, 336-342. https://doi.org/10.1016/j.jamda.2015.12.004

[8] Kim, T.N., Park, M.S., Yang, S.J., *et al*. (2010) Prevalence and Determinant Factors of Sarcopenia in Patients with Type 2 Diabetes: The Korean Sarcopenic Obesity Study (KSOS). *Diabetes Care*, **33**, 1497-1499. https://doi.org/10.2337/dc09-2310

[9] Argilés, J.M., Campos, N., Lopez-Pedrosa, J.M., *et al*. (2016) Skeletal Muscle Regulates Metabolism via Interorgan Crosstalk: Roles in Health and Disease. *Journal of the American Medical Directors Association*, **17**, 789-796. https://doi.org/10.1016/j.jamda.2016.04.019

[10] Kim, K.S., Park, K.S., Kim, M.J., *et al*. (2014) Type 2 Diabetes Is Associated with Low Muscle Mass in Older Adults. *Geriatrics & Gerontology International*, **14**, 115-121. https://doi.org/10.1111/ggi.12189

[11] Pechmann, L.M., Jonasson, T.H., Canossa, V.S., *et al*. (2020) Sarcopenia in Type 2 Diabetes Mellitus: A Cross-Sectional Observational Study. *International Journal of Endocrinology*, **2020**, Article ID: 7841390. https://doi.org/10.1155/2020/7841390

[12] Koh, W.P., Wang, R., Ang, L.W., *et al*. (2010) Diabetes and Risk of Hip Fracture in the Singapore Chinese Health Study. *Diabetes Care*, **33**, 1766-1770. https://doi.org/10.2337/dc10-0067

[13] Hygum, K., Starup-Linde, J. and Langdahl, B.L. (2019) Diabetes and Bone. *Osteoporosis and Sarcopenia*, **5**, 29-37. https://doi.org/10.1016/j.afos.2019.05.001

[14] Andersohn, F., Suissa, S. and Garbe, E. (2008) Re: Biphasic Fracture Risk in Diabetes: A Population-Based Study. *Bone*, **42**, 235, 236. https://doi.org/10.1016/j.bone.2007.09.003

[15] Cortet, B., Lucas, S., Legroux-Gerot, I., *et al*. (2019) Bone Disorders Associated with Diabetes Mellitus and Its Treatments. *Joint Bone Spine*, **86**, 315-320. https://doi.org/10.1016/j.jbspin.2018.08.002

[16] Martineau, P. and Leslie, W.D. (2017) Trabecular Bone Score (TBS): Method and Applications. *Bone*, **104**, 66-72. https://doi.org/10.1016/j.bone.2017.01.035

[17] Watts, N.B., Bilezikian, J.P., Usiskin, K., *et al*. (2016) Effects of Canagliflozin on Fracture Risk in Patients with Type 2 Diabetes Mellitus. *The Journal of Clinical Endocrinology and Metabolism*, **101**, 157-166. https://doi.org/10.1210/jc.2015-3167

[18] Napoli, N., Strotmeyer, E.S., Ensrud, K.E., *et al*. (2014) Fracture Risk in Diabetic Elderly Men: The MrOS Study. *Diabetologia*, **57**, 2057-2065. https://doi.org/10.1007/s00125-014-3289-6

[19] Chandran, M. (2017) Diabetes Drug Effects on the Skeleton. *Calcified Tissue International*, **100**, 133-149. https://doi.org/10.1007/s00223-016-0203-x

[20] Su, B., Sheng, H., Zhang, M., *et al*. (2015) Risk of Bone Fractures Associated with Glucagon-Like Peptide-1 Receptor Agonists' Treatment: A Meta-Analysis of Randomized Controlled Trials. *Endocrine*, **48**, 107-115. https://doi.org/10.1007/s12020-014-0361-4

[21] Park, H.S., Lim, J.S. and Lim, S.K. (2019) Determinants of Bone Mass and Insulin Resistance in Korean Postmenopausal Women: Muscle Area, Strength, or Composition? *Yonsei Medical Journal*, **60**, 742-750. https://doi.org/10.3349/ymj.2019.60.8.742

[22] He, Q., Wang, X., Yang, C., *et al*. (2020) Metabolic and Nutritional Characteristics in Middle-Aged and Elderly Sarcopenia Patients with Type 2 Diabetes. *Journal of Diabetes Research*, **2020**, Article ID: 6973469. https://doi.org/10.1155/2020/6973469

[23] Maratova, K., Soucek, O., Matyskova, J., *et al*. (2018) Muscle Functions and Bone Strength Are Impaired in Adolescents with Type 1 Diabetes. *Bone*, **106**, 22-27. https://doi.org/10.1530/boneabs.6.LB7

[24] He, H., Liu, Y., Tian, Q., *et al*. (2015) Relationship of Sarcopenia and Body Composition with Osteoporosis. *Osteoporosis International*, **27**, 473-482. https://doi.org/10.1007/s00198-015-3241-8

[25] Pereira, F.B., Leite, A.F. and de Paula, A.P. (2015) Relationship between Pre-Sarcopenia, Sarcopenia and Bone Mineral Density in Elderly Men. *Archives of Endocrinology and Metabolism*, **59**, 59-65. https://doi.org/10.1590/2359-3997000000011

[26] Elkina, Y., von Haehling, S., Anker, S.D., *et al*. (2011) The Role of Myostatin in Muscle Wasting: An Overview. *Journal of Cachexia*, *Sarcopenia and Muscle*, **2**, 143-151. https://doi.org/10.1007/s13539-011-0035-5

[27] Dankbar, B., Fennen, M., Brunert, D., *et al*. (2015) Myostatin Is a Direct Regulator of Osteoclast Differentiation and Its Inhibition Reduces Inflammatory Joint Destruction in Mice. *Nature Medicine*, **21**, 1085-1090. https://doi.org/10.1038/nm.3917

[28] Verschueren, S., Gielen, E., O'Neill, T.W., *et al*. (2013) Sarcopenia and Its Relationship with Bone Mineral Density in Middle-Aged and Elderly European Men. *Osteoporosis International*: *A Journal Established as Result of Cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, **24**, 87-98. https://doi.org/10.1007/s00198-012-2057-z