Advances in Clinical Medicine 临床医学进展, 2022, 12(5), 4122-4126
Published Online May 2022 in Hans. http://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2022.125597

Hans汉斯

血清25-(OH)D、FIB、MPV/PLT水平与慢性心力衰竭的相关性研究

胡菲菲，韩吉祥

青海大学附属医院，青海 西宁

收稿日期：2022年4月16日；录用日期：2022年5月11日；发布日期：2022年5月18日

摘　要

慢性心力衰竭(Chronic Heart Failure)是终末期心血管疾病。此外，CHF的病理生理机制极其复杂，包括血流动力学异常、神经内分泌激活、心肌损伤和心室重塑。心力衰竭的特征是由心脏结构或功能异常引起的一系列临床综合征，导致心室充盈和/或射血受损。

关键词

血清25-(OH)D，FIB，MPV/PLT，慢性心力衰竭

Correlation Studies of Serum 25-(OH)D, FIB, MPV/PLT Levels and Chronic Heart Failure

Feifei Hu, Jixiang Han

The Affiliated Hospital of Qinghai University, Xining Qinghai

Received: Apr. 16th, 2022; accepted: May 11th, 2022; published: May 18th, 2022

Abstract

Chronic heart failure (CHF) is an end-stage cardiovascular disease. Furthermore, the pathophysiology of CHF is extremely complex, including hemodynamic abnormalities, neuroendocrine activation, myocardial injury, and ventricular remodeling. Heart failure is characterized by a series of clinical syndromes caused by structural or functional abnormalities of the heart, resulting in impaired ventricular filling and/or ejection.

文章引用: 胡菲菲, 韩吉祥. 血清 25-(OH)D、FIB、MPV/PLT 水平与慢性心力衰竭的相关性研究[J]. 临床医学进展, 2022, 12(5): 4122-4126. DOI: 10.12677/acm.2022.125597

Keywords

Serum 25-(OH)D, FIB, MPV/PLT, Chronic Heart Failure

1. 引言

慢性心力衰竭(CHF)是一个影响全球 2300 多万人的主要公共卫生问题。最近的一项大型流行病学研究，包括来自德国的 300 万人，至少有两次记录在案的 HF 相关诊断，显示仅在德国，患病率为 3.96%，每 10 万人中有 655 例新病例有 HF 风险[1]。HF 是一种复杂的临床综合征，包括呼吸急促和外周水肿等非特异性症状，因此需要进一步的侵入性和非侵入性诊断工具[2]。目前的 HF 分类基于左心室射血分数(LVEF)分为 1) 射血分数保留的 HF，伴有 HF 的体征和症状，超声心动图显示舒张异常，2) HFpEF 临界或 HF 伴中程射血分数(HFmrEF)，EF 为 41%~49%和 3) HF 伴射血分数降低(HFrEF)，EF ≤ 40%。特别是对于 HFpEF，其发病机制，诊断和最佳治疗方法仍然存在相当大的不确定性[3] [4]。内皮功能障碍、炎症、心肌细胞功能障碍和心肌纤维化被认为是 CHF 发展的关键因素[5] [6] [7]。

近年来，CHF 的预后明显改善，5 年生存率从 43%提高到 52%。CHF 的主要治疗药物仍为 β 阻滞剂、血管紧张素转换酶抑制剂、血管紧张素受体阻滞剂和醛固酮受体拮抗剂[8]。虽然众所周知，这些药物可以降低心脏不良事件的发生率并改善心脏功能，但 HF 仍然是全球死亡的主要原因[9]。目前，有多种血清指标与老年心力衰竭患者的严重程度相关，但关于老年心力衰竭患者的诊断与预后预测仍然不够准确，因此，继续探索补充治疗方法从而能够为早期评估 CHF 患者的病情变化提供有效依据，从而为心衰程度评判和临床用药提供参考依据，进行早期干预，提高患者生存质量。本文简单总结了目前血清 25-(OH)D、FIB、MPV/PLT 水平与慢性心力衰竭的研究现状。

2. 维生素 D 与慢性心力衰竭

大约90%的慢性HF患者维生素D水平不足，即使在阳光明媚的气候下也是如此[10] [11]。血清25-(OH)D在慢性 HF 病理学中具有多效性作用[12]。在 HF 中，由于心肌细胞中 Ca^{2+}离子过载，心脏收缩和松弛受到影响。缺乏维生素 D 可能会干扰心肌细胞中 Ca^{2+}的功能，导致心肌细胞肥大、组织内炎症反应和纤维化[13] [14]。维生素 D 抑制心脏肾素－血管紧张素系统和利钠肽的激活，调节细胞外基质更新、钙通量和心肌收缩力，影响心肌细胞的分化和增殖，可介导维生素 D 的抗肥厚和抗高血压作用，防止心肌功能障碍。低维生素 D 水平可能激活肾素-血管紧张素系统[15]，引起炎症反应并导致内皮功能障碍[16] [17]。维生素 D 受体系统性敲除的小鼠随着心脏肾素－血管紧张素系统的激活增加而发展为心脏肥大和功能障碍，并且在维生素 D 缺乏的大鼠中，心脏肥大，心肌胶原蛋白含量增加和 QT 间期缩短也被证明[18] [19]。维生素 D 对心血管系统的影响还通过甲状旁腺激素水平升高来介导[20]。几项研究证实了甲状旁腺激素水平与年龄相关的升高[21]。

3. 纤维蛋白原与慢性心力衰竭

纤维蛋白原(Fibrinogen)主要由肝细胞合成，属于一种血浆糖蛋白，所分泌的分子量大约在 340 KDa，

而分子的长大约是 450A 的可溶性糖蛋白；纤维蛋白原是由两个相同的亚基来组成的，且每一个亚基都含有三条肽链，其内部则是由多个二硫键进行衔接，从而形成完善的二聚体结构。当纤维蛋白原经凝血酶裂解释放 FPA 与 FPB 片段之后，其就会形成纤维蛋白单体，这时的单体就会形成一个有组织结构的纤维蛋白多聚体 MPV，从而与其它的凝血因子形成稳定的交联纤维蛋白凝块，并促进血栓的形成[22]。其不仅能够介导血小板凝聚，而且还能参与凝血过程的后期阶段；其次，它在对抗炎症时也有着非常关键的作用，且两者通过互相影响还能有效降低心血管疾病的发生。有相关研究数据显示，FIB 可以通过与炎性细胞表面的 CD11b 相互作用，从而激活信号通道，这可以起到调节固有免疫细胞活化的作用，还能直接与粘附分子共同参与到炎症反应过程中。越来越多的证据表明，纤维蛋白原是心血管疾病的不良预后预测指标。纤维蛋白原可能通过血小板聚集、血浆粘度和纤维蛋白形成增加心血管风险[23]。慢性心衰患者纤维蛋白原水平升高[24] [25] [26]。

4. 平均血小板体积与血小板计数比值与慢性心力衰竭

平均血小板(Average Platelet)是反映血小板体积大小的指标，反映骨髓巨核细胞增生与代谢活性及血小板生成状况。血小板平均体积(MPV)可有效反映血小板活化功能，在正常情况下维持在稳定状态，但当其升高后可介导急性心肌梗死、脑梗死、心绞痛、心力衰竭等多种疾病的发生[27]。临床研究发现，MPV 升高可能与线粒体、血小板的 α-颗粒、致密体等多种细胞器增加相关，释放更多的血小板颗粒蛋白、血栓素 A2 以及 5-羟色胺等物质，增加单核细胞、内皮细胞黏附功能，诱导血小板聚集，最终促进血栓形成[28] [29]。目前已有研究表明，MPV 在心力衰竭发生后明显升高[30] [31]，而 MPV 升高与下列多种因素相关：① 心力衰竭发生会促使血栓素、二磷酸腺苷(ADP)、凝血酶、花生四烯酸等血小板激动剂含量增加；② 心力衰竭发生后机体处于缺氧、缺血状态，损伤血管内皮细胞，暴露管壁胶原纤维，诱导血小板聚集；③ 心力衰竭发生后会损伤心肌细胞，增加细胞中游离钙的含量。上述因素均会导致血小板聚集、黏附、释放等。经一系列的反应产生体积大、活性高的血小板。大体积血小板的代谢和功能比较活跃，对胶原黏附性强于体积小者，极易形成血栓。心力衰竭程度越重，血小板激活程度越明显。一方面可能促进血栓形成，另一方面也可通过炎症免疫系统，对心衰的发生发展和预后起关键作用[32] [33] [34]。血小板(Blood Platelet)是血液循环中最小的血细胞，没有细胞核，却有活跃的酶活性和重要的生理功能。血小板数量、大小或体积一方面反映骨髓巨核细胞的增生与代谢活性、新生血小板生成情况以及循环血中血小板的年龄。另一方面反映血小板的超微结构、酶活性及功能状况。血小板在血栓形成和心脑血管疾病的发病机制中发挥重要作用。研究认为，心力衰竭时患者体内存在持续的血小板激活，伴随着血栓形成和血栓栓塞的危险性增加。同时异常的血小板激活在某种程度上参与了心力衰竭并发症的病理生理过程[35] [36]。

综上所述，25-(OH)D、FBI、MPV/PLT 与慢性心力衰竭可能存在一定的相关性，因此探讨 25-(OH)D、FBI、MPV/PLT 指标水平与慢性心衰的相关性，从而可以为心衰患者的风险预测提供更多的指标，同时为心衰患者提供早期干预，减少心血管不良事件的发生率及提高生存质量。

参考文献

[1] Roger V.L. (2013) Epidemiology of Heart Failure. *Circulation Research*, **113**, 646-659. https://doi.org/10.1161/CIRCRESAHA.113.300268

[2] Störk, S., Handrock, R., Jacob, J., Walker, J., Calado, F., Lahoz, R., Hupfer, S. and Klebs, S. (2017) Epidemiology of Heart Failure in Germany: A Retrospective Database Study. *Clinical Research in Cardiology*, **106**, 913-922. https://doi.org/10.1007/s00392-017-1137-7

[3] Chung, I., Goyal, D., Macfadyen, R.J. and Lip, G.Y. (2008) The Effects of Maximal Treadmill Graded Exercise Testing on Haemorheological, Haemodynamic and Flow Cytometry Platelet Markers in Patients with Systolic or Diastolic

Heart Failure. *European Journal of Clinical Investigation*, **38**, 150-158. https://doi.org/10.1111/j.1365-2362.2008.01909.x

[4] Yancy, C.W., Jessup, M., Bozkurt, B., Butler, J., Casey Jr., D.E., Drazner, M.H., *et al*. (2013) 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*, **128**, e240-e327. https://doi.org/10.1161/CIR.0b013e31829e8776

[5] Lee, D.S., Gona, P., Vasan, R.S., Larson, M.G., Benjamin, E.J., Wang, T.J., Tu, J.V. and Levy, D. (2009) Relation of Disease Pathogenesis and Risk Factors to Heart Failure with Preserved or Reduced Ejection Fraction: Insights from the Framingham Heart Study of the National Heart, Lung, and Blood Institute. *Circulation*, **119**, 3070-3077. https://doi.org/10.1161/CIRCULATIONAHA.108.815944

[6] Andries, L.J., Kaluza, G., De Keulenaer, G.W., Mebazaa, A., Brutsaert, D.L. and Sys, S.U. (1996) Endocardial Endothelial Dysfunction and Heart Failure. *Journal of Cardiac Failure*, **2**, S195-S202. https://doi.org/10.1016/S1071-9164(96)80077-7

[7] Westermann, D., Lindner, D., Kasner, M., Zietsch, C., Savvatis, K., Escher, F., *et al*. (2011) Cardiac Inflammation Contributes to Changes in the Extracellular Matrix in Patients with Heart Failure and Normal Ejection Fraction. *Circulation*: *Heart Failure*, **4**, 44-52. https://doi.org/10.1161/CIRCHEARTFAILURE.109.931451

[8] Tsutsui, H., Isobe, M., Ito, H., Okumura, K., Ono, M., Kitakaze, M., *et al*. (2019) JCS 2017/JHFS 2017 Guideline on Diagnosis and Treatment of Acute and Chronic Heart Failure-Digest Version. *Circulation Journal*, **83**, 2084-2184. https://doi.org/10.1253/circj.CJ-19-0342

[9] Heidenreich, P.A., Albert, N.M., Allen, L.A., Bluemke, D.A., Butler, J., Fonarow, G.C., *et al*. (2013) Forecasting the Impact of Heart Failure in the United States: A Policy Statement from the American Heart Association. *Circulation*: *Heart Failure*, **6**, 606-619. https://doi.org/10.1161/HHF.0b013e318291329a

[10] Kim, D.H., Sabour, S., Sagar, U.N., Adams, S. and Whellan, D.J. (2008) Prevalence of Hypovitaminosis D in Cardiovascular Diseases (From the National Health and Nutrition Examination Survey 2001 to 2004). *American Journal of Cardiology*, **102**, 1540-1544. https://doi.org/10.1016/j.amjcard.2008.06.067

[11] Ameri, P., Ronco, D., Casu, M., Denegri, A., Bovio, M., Menoni, S., Ferone, D. and Murialdo G. (2010) High Prevalence of Vitamin D Deficiency and Its Association with Left Ventricular Dilation: An Echocardiography Study in Elderly Patients with Chronic Heart Failure. *Nutrition, Metabolism & Cardiovascular Diseases*, **20**, 633-640. https://doi.org/10.1016/j.numecd.2010.01.002

[12] Gardner, D.G., Chen, S. and Glenn, D.J. (2013) Vitamin D and the Heart. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, **305**, R969-R977. https://doi.org/10.1152/ajpregu.00322.2013

[13] Weishaar, R.E. and Simpson, R.U. (1987) Involvement of Vitamin D3 with Cardiovascular Function. II. Direct and Indirect Effects. *American Journal of Physiology*, **253**, E675-E683. https://doi.org/10.1152/ajpendo.1987.253.6.E675

[14] Chen, S., Law, C.S., Grigsby, C.L., Olsen, K., Hong, T.T., Zhang, Y., Yeghiazarians, Y. and Gardner, D.G. (2011) Cardiomyocyte-Specific Deletion of the Vitamin D Receptor Gene Results in Cardiac Hypertrophy. *Circulation*, **124**, 1838-1847. https://doi.org/10.1161/CIRCULATIONAHA.111.032680

[15] Vaidya, A. and Williams, J.S. (2012) The Relationship between Vitamin D and the Renin-Angiotensin System in the Pathophysiology of Hypertension, Kidney Disease, and Diabetes. *Metabolism*, **61**, 450-458. https://doi.org/10.1016/j.metabol.2011.09.007

[16] Zhang, Y., Leung, D.Y., Richers, B.N., Liu, Y., Remigio, L.K., Riches, D.W. and Goleva, E. (2012) Vitamin D Inhibits Monocyte/Macrophage Proinflammatory Cytokine Production by Targeting MAPK Phosphatase-1. *The Journal of Immunology*, **188**, 2127-2135. https://doi.org/10.4049/jimmunol.1102412

[17] Caprio, M., Mammi, C. and Rosano, G.M. (2012) Vitamin D: A Novel Player in Endothelial Function and Dysfunction. *Archives of Medical Science*, **8**, 4-5. https://doi.org/10.5114/aoms.2012.27271

[18] Pilz, S., März, W., Wellnitz, B., Seelhorst, U., Fahrleitner-Pammer, A., Dimai, H.P., Boehm, B.O. and Dobnig, H. (2008) Association of Vitamin D Deficiency with Heart Failure and Sudden Cardiac Death in a Large Cross-Sectional Study of Patients Referred for Coronary Angiography. *The Journal of Clinical Endocrinology & Metabolism*, **93**, 3927-3935. https://doi.org/10.1210/jc.2008-0784

[19] Pilz, S., Tomaschitz, A., Drechsler, C., Dekker, J.M. and März, W. (2010) Vitamin D Deficiency and Myocardial Diseases. *Molecular Nutrition & Food Research*, **54**, 1103-1113. https://doi.org/10.1002/mnfr.200900474

[20] Schluter, K.D. and Piper, H.M. (1998) Left Ventricular Hypertrophy and Parathyroid Hormone: A Causal Connection? *Cardiovascular Research*, **39**, 523-524. https://doi.org/10.1016/s0008-6363(98)00097-2

[21] Haden, S.T., Brown, E.M., Hurwitz, S., Scott, J. and El-Hajj Fuleihan, G. (2000) The Effects of Age and Gender on Parathyroid Hormone Dynamics. *Clinical Endocrinology*, **52**, 329-338. https://doi.org/10.1046/j.1365-2265.2000.00912.x

[22] DeBoer, R.A., Nayorm, M., de Filippi, C.R., Enserro, D., Bhambhani, V., Kizer, J.R., *et al.* (2018) Association of Cardiovascular Biomarkers with Incident Heart Failure with Preserved and Reduced Ejection Fraction. *JAMA Cardiology*, **3**, 215-224. https://doi.org/10.1001/jamacardio.2017.4987

[23] Jiang, P., Gao, Z., Zhao, W., Song, Y., Tang, X.-F., Xu, J.-J., Wang, H.-H., *et al*. (2019) Relationship between Fibrinogen Levels and Cardiovascular Events in Patients Receiving Percutaneous Coronary Intervention: A Large Single-Center Study. *Chinese Medical Journal*, **132**, 914-921. https://doi.org/10.1097/CM9.0000000000000181

[24] Mongirdiene, A., Kursvietiene, L. and Kasauskas, A. (2010) The Coagulation System Changes in Patients with Chronic Heart Failure. *Medicina*, **46**, 642-647. https://doi.org/10.3390/medicina46090091

[25] Witte, K.K., Ford, S.J., Preston, T., Parker, J.D. and Clark, A.L. (2008) Fibrinogen Synthesis Is Increased in Cachectic Patients with Chronic Heart Failure. *International Journal of Cardiology*, **129**, 363-367. https://doi.org/10.1016/j.ijcard.2007.07.119

[26] Zhao, T.J., Yang, Q.K., Tan, C.Y., Bi, L.D., Li, J. and Miao, Z.L. (2020) Prognostic Value of D-Dimer/Fibrinogen Ratio in the Adverse Outcomes of Patients Hospitalized for Heart Failure. *Biomarkers in Medicine*, **14**, 1733-1745. https://doi.org/10.2217/bmm-2020-0553

[27] 张洋, 于金星, 叶中倪, 李新强, 刘建茹, 王锡鸣, 李袁, 康金锁, 陈曦. MPV 与冠心病心力衰竭患者预后的相关性研究[J]. 标记免疫分析与临床, 2016, 23(4): 360-363.

[28] 刘建华, 顾蓉, 乔建忠, 王涟, 徐标. 心力衰竭患者 MPV 的水平及其与 BNP 的相关性研究[J]. 现代生物医学进展, 2016, 16(16): 3058-3061+3093.

[29] 陆云燕, 魏文娟. 平均血小板体积与慢性心力衰竭的相关性[J]. 心脑血管病防治, 2019, 19(6): 531-533.

[30] 李艳秋, 陈广生, 马德渊, 贾仲瑞. 平均血小板体积与血小板计数比值对急性 ST 段抬高性心肌梗死患者行 PCI 预后的预测价值[J]. 中国急救医学, 2019, 39(5): 412-415.

[31] Czerniuk, M.R., Bartoszewicz, Z., Dudzik-Niewiadomska, I., Pilecki, T., Górska, R. and Filipiak, K.J. (2019) Simple Platelet Markers: Mean Platelet Volume and Congestive Heart Failure Coexistent with Periodontal Disease. Pilot Studies. *Cardiology Journal*, **26**, 253-259. https://doi.org/10.5603/CJ.a2017.0085

[32] Moertl, D., Berger, R., Hammer, A., Hutuleac, R., Koppensteiner, R., Kopp, C.W., *et al*. (2011) Dose-Dependent Decrease of Platelet Activation and Tissue Factor by Omega-3 Polyunsaturated Fatty Acids in Patients with Advanced Chronic Heart Failure. *Thrombosis and Haemostasis*, **106**, 457-465.

[33] Pasic, J., Sullivan, M.D., Russo, J., Chandler, W.L. and Levy, W.C. (2004) Lack of Depression Effect on Platelet Activation in Patients with Heart Failure. *Psychiatry Research*, **129**, 289-292. https://doi.org/10.1016/j.psychres.2004.09.008

[34] Chung, I., Choudhury, A., Patel, J. and Lip, G.Y.H. (2008) Soluble CD40L, Platelet Surface CD40L and Total Platelet CD40L in Congestive Heart Failure: Relationship to Platelet Volume, Mass and Granularity. *Journal of Internal Medicine*, **263**, 313-321. https://doi.org/10.1111/j.1365-2796.2007.01891.x

[35] Chung, I., Choudhury, A. and Lip, G.Y. (2007) Platelet Activation in Acute, Decompensated Congestive Heart Failure. *Thrombosis Research*, **120**, 709-713. https://doi.org/10.1016/j.thromres.2007.01.003

[36] Kandis, H., Ozhan, H., Ordu, S., Erden, I., Caglar, O., Basar, C., *et al*. (2011) The Prognostic Value of Mean Platelet Volume in Decompensated Heart Failure. *Emergency Medicine Journal*, **28**, 575-578. https://doi.org/10.1136/emj.2009.088401