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冠状动脉钙化积分在冠心病中的研究进展

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摘　要

冠状动脉粥样硬化的临床表现是冠状动脉疾病(CAD)，其症状从因冠状动脉血流储备减少而引起的劳力性胸痛到因通常为非阻塞性斑块破裂而引起的冠状动脉血流突然减少而引起的急性冠状动脉综合征。CAD是全世界发病率和死亡率的主要原因。因此，识别CAD无症状高危人群是指导一级预防决策的关键。冠状动脉钙(CAC)是冠状动脉粥样硬化的标志。它可以通过心脏计算机断层扫描检测到，并通过Agatston方法进行量化。CAC检查是一种廉价、快速、低辐射剂量的检查，无需注射造影剂。它提供了其他传统心血管风险标志物和已建立的评分系统的预后信息，特别是对于低风险亚群体，如妇女和年轻人，并指示实施一级预防的适当时机，包括乙酰水杨酸和他汀类药物。在这篇综述中，我们讨论了CAC评估的方法，CAC评分为零的意义，其转化为CAC > 0及其对心血管风险的影响，他汀类药物和蛋白酶转化酶/可欣9型抑制剂对CAC进展的影响，CAC结果的解释，以及无症状和有症状患者的CAC预后价值。

关键词

计算机断层扫描，冠状动脉钙化，冠状动脉疾病

Research Progress of Coronary Artery Calcification Score in Coronary Artery Disease

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Abstract

The clinical manifestation of coronary artery atherosclerosis is coronary artery disease (CAD)

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with symptoms ranging from exertional chest pain due to reduction of coronary flow reserve to acute coronary syndrome due to rupture of usually a nonobstructive plaque with abrupt coronary blood flow reduction. CAD is the leading cause of morbidity and mortality worldwide. Therefore, identifying asymptomatic people at risk of CAD is pivotal to guide decision-making for primary prevention. Coronary artery calcium (CAC) is a hallmark of coronary artery atherosclerosis. It can be detected using cardiac computed tomography and quantified by the Agatston method. CAC examination is a cheap, fast and low radiation dose test, without injecting a contrast agent. It provides prognostic information over other traditional cardiovascular risk markers and established scoring systems, especially for low-risk subgroups such as women and younger adults, and indicates the appropriate moment to implement primary prevention, including acetylsalicylic acid and statins. In this review, we discuss the methods of CAC evaluation, the meaning of a zero CAC score (CACS), its conversion to CACS > 0 and the impact of this fact on cardiovascular risk, the effect of statins and proprotein convertase subtilisin kexin type 9 inhibitor on CAC progression, interpretation of CACS results, and CACS prognostic value in both asymptomatic and symptomatic patients.

Keywords

Computed Tomography, Coronary Artery Calcium, Coronary Artery Disease

1. 引言

冠状动脉疾病(CAD)是冠状动脉粥样硬化的症状表现，是全球发病率和死亡率较高的疾病之一，超过70%的心源性猝死均是由CAD造成的[1]。冠状动脉粥样硬化的临床症状通常在40岁以后或更晚出现，但在此之前会出现冠状动脉钙化(CAC)，CAC对动脉粥样硬化具有高度特异性。冠状动脉CT检测冠状动脉壁的任何钙化都意味着动脉粥样硬化，目前研究表明，冠状动脉CT提供了比其他传统心血管风险标志物和已建立的评分系统更多的预后信息[2] [3] [4] [5]。例如：危险因素负荷为0且CAC为300的个体心血管事件发生风险比危险因素负荷 ≥ 3且CAC为0的个体高3.5倍，CAC积分 ≥ 300的低风险个体(弗洛明翰评分0%~6%)的冠心病事件总发生率为20.5/1000人年，而CAC积分为0的高危个体(弗洛明翰评分 ≥20%)的冠心病事件发生率为2.5每1000人年[2]。

在这篇综述中，我们讨论了CAC积分的评估方法，CAC积分为零的意义，其转化为CAC > 0，他汀类药物和蛋白酶转化酶枯草菌素/可欣9型抑制剂对CAC积分进展的影响，以及CAC积分在无CAD症状和有CAD症状患者预后中的价值。

2. CAC积分的评估

CAC积分可以用电子束计算机断层扫描和多层螺旋CT检测。CAC积分可以用三种方法进行半定量估计：质量当量评分、体积评分和最广泛使用的Agatston评分。所有这些评分之间的相关性都很强[6]。Agatston评分计算得出的CAC积分值是通过钙化斑块面积乘以密度评分。130~199 Hounsfield单位(HU)的密度分数为1；200~299 HU为2；对于300~399 HU为3；400 HU对应密度分数为4。例如：如果钙化斑点面积为6 mm²，衰减最大为400 HU，则分数为24。钙化缺失则被认为是检查结果为“阴性”或CAC积分为零。在CAC积分存在的情况下，将每个钙化斑块的评分加起来，得出总CAC积分。

3. CAC 积分为零

仅 CAC 积分可能无法评估斑块形成的早期阶段(“低衰减斑块”)，然而，CAC 积分为零实际上提示 CAD 发生概率较低[7]。当前一项 meta 分析显示，在无 CAC 积分的有症状患者中，冠状动脉 CT 血管造影(CCTA)提示阻塞性 CAD (定义为管腔狭窄 ≥ 50%)的发病率为 4.4% [8]。在大量的横断面研究和临床试验中已证明CAC积分为零的受试者心血管疾病发生风险较低[9]-[15]。在一项涉及19,898名无症状且CAC积分为零的患者的多中心试验中，10 年全因死亡率低于 1% [9]。在另一项多中心回顾性队列研究中，29,757 名 CAC 积分为零的无症状参与者，随访了 12 年，CAD 和心血管疾病(CVD)的死亡率分别为每 1000 人年 0.32 与 0.43 [11]。一项在有症状的受试者中也发现了类似的观察结果，例如，在多中心国际 CCTA 临床结果评估中：一项国际多中心(CONFIRM)注册研究，平均随访了 2.1 年，CAC 积分为零的有症状患者的死亡率为 0.4% [10]。在前瞻性多中心胸痛评估影像学研究(PROMISE)试验中也发现了类似的结果[12]。在一项动脉粥样硬化的多种族研究中，共招募了 6814 名无已知动脉粥样硬化性心血管疾病的成年人，平均随访 10.2 年后 CAC 为 0 的患者动脉粥样硬化性心血管疾病发病率(每 1000 人年)为 4.4 [14]。一项多种族的研究，纳入了 561 名符合他汀类药物治疗的患者，经过平均 12 年的随访，结果表明：在 CAC 为 0 的个体中，15 年动脉粥样硬化性心血管疾病事件发生率在有和没有动脉衰老的个体中都很低(4.3 vs 8.6 每 1000 人年) [15]。在另一项观察性队列研究中，纳入了 1978 例 CAC 积分为零且为稳定性胸痛或呼吸困难的患者，平均随访 5.2 ± 2.8 年，无因 CAD 死亡的患者[16]。

由于 45~84 岁 CAC 积分为零的患者 CAD 的发生风险非常低，因此，不建议在 3~5 年的时间内重新扫描，具体间隔时间取决于个人的风险状况评估[13]。根据 Lehmann 等人的研究，基线 CAC 积分为零(平均年龄：58.7 ± 7.5)，在随访 5 年后 CAC 积分依旧为零的受试者不需要再次行冠状动脉 CT 扫描[17]。

总体而言，无 CAD 症状和有 CAD 症状患者的死亡风险较低，根据美国心脏病学会基金会指南，CAC 积分为零的患者不需要服用他汀类药物来降低胆固醇水平，除非他们是吸烟、DM 或有 CAD 家族史的患者[18]。MESA 研究结果显示，在没有 DM 的受试者中，当 CAC 积分为零时，服用阿司匹林的净危害出现，当 CAC ≥ 100 时，服用阿司匹林的净获益出现[19]。

4. CAC 积分为零到 CAC > 0

CAC > 0 的风险随年龄呈非线性增加[20]。MESA 研究表明，新检出 CAC > 0 的概率每年平均为 6.6%，并随着年龄的增长而增加，年龄 < 50 岁的人群每年 CAC > 0 的发生率 < 5%，年龄 < 80 岁的人群每年 CAC > 0 的发生率为 12%。如果 CAC > 0 在年轻个体检出，比发生在老年人中检出有更多的临床意义。例如，在 32 岁至 46 岁的个体中，CAC ≥ 100 与早期死亡相关[21]。在有症状的年轻个体中，即使最低的 CAC 积分(1~10)也会显著增加 CAD 事件发生率[21] [22]。Lehmann 等人发现了潜在的心血管危险因素，包括年龄、高收缩压、低密度脂蛋白胆固醇升高和吸烟等[23]。Brodov 等人做了一项研究，发现胸主动脉钙化(TAC)水平越高的患者 CAC > 0 的风险越高。此外，在多变量分析中，TAC ≥ 100 是 CAC > 0 的独立预测因子。根据遗传风险评分的结果，有可能估计出进行第一次 CT 扫描的最佳时间来预测转换时间[24]。CAC 积分从零到 CAC > 0 的转换时刻是关键的，因为从那时起 CAC 积分只会呈指数增长。当 CAC ≥ 100 时，应开始给予预防性治疗，包括乙酰水杨酸和他汀类药物[19] [20]。在一级预防方面，对于冠状动脉危险因素较多或具有动脉粥样硬化遗传特征的相对年轻的个体，可考虑选择性使用 CAC 积分进行筛查。

5. CAC 积分的进展

如前所述，CAC 积分在连续几十年的生命中呈指数增长[20] [21]。较快 CAC 积分的进展与较差的临床结局相关[25]。然而，一项纳入 45 岁至 74 岁患者的大型前瞻性观察性研究表明，基于危险因素、基线

CAC积分或随访5年后的CAC积分，研究结果显示Berry、Hokanson、Slow vs expected、Rapid vs expected、Absolute、Root、Log、Log obs-log exp、Raggi、Percent算法预测CAD的风险比分别为1.1、1.14、0.7、0.97、1.11、1.08、0.96、1.05、1.12、0.89，但p值均小于0.05，因此，10种不同的CAC积分进展算法在预测CAD和CVD事件方面均无优势[17]。目前还没有已知的能够使CAC积分减小的药理学方法，甚至他汀类药物的使用也与钙化进展有关[26] [27] [28]。事实上，五项对照试验的meta分析显示，尽管给予他汀类药物治疗，CAC积分仍在持续进展[29]。尽管他汀类药物在治疗过程中加速了CAC积分的进展，但他汀类药物降低了动脉粥样硬化体积的百分比，降低了主要不良心血管事件的风险[26]。这种钙悖论很可能与斑块特征的变化(增加斑块钙含量)，导致斑块稳定有关。一项研究发现，通过在他汀类药物治疗中添加一种原蛋白转化酶枯草杆菌素/可欣9型抑制剂，可以减缓CAC积分的年进展[30]。CAC积分的年进展率通常为20%~25%，但进展速度取决于危险因素，尤其是DM [30] [31]。结合目前的CAC积分和年龄，可以估计出CAC积分从零到CAC > 0的年龄，这与动脉“年龄”的概念相关[32]。

6. CAC积分对无症状患者的预后价值

CAC积分已成为无症状患者最具预测性的单一心血管风险标记物，无论男性或女性，年轻(< 40岁)或年长(65岁) [33]。CAC积分能够将CAD中度风险的患者重新分类[2]。Silverman等人评估了CAC积分的分布与血运重建需求之间的相关性。研究表明，冠状动脉斑块负荷越大或病变血管数量越多，血运重建的可能性就越大。即使在调整了CAC积分后，病变血管的数量仍然是行血运重建(经皮冠状动脉介入治疗或冠状动脉旁路移植)的重要预测因素。在一项前瞻性多种族队列研究中，6814名年龄45~84岁无症状患者，随访中位时间为11.1年，发现CAC积分的分层与未来CVD事件风险呈正相关，与年龄、性别或种族/民族无关[34]。这些大型观察性研究表明，在无症状个体中，CAC积分的存在与未来CVD风险的增加显著相关。

7. CAC积分对有症状患者的预后价值

一项meta分析评估了来自19项观察性研究的34,041名稳定的、有症状的患者，结果显示CAC积分与主要不良心脏事件呈正相关[35]。Mortensen等人对23,759名有症状的患者进行了4.3年的随访，发现CAC积分越高，CVD事件的发生率越高[36]。另一项对3,691名有症状的年轻患者(18~45岁)中位随访时间为4.1年的研究显示，与CAC 1~10和CAC = 0相比，无论危险因素数量如何，具有3种以上危险因素和CAC > 10的患者心血管事件发生率最高[22]。综上所述，CAC积分为有症状的患者提供了更多的预后信息，以指导诊断和治疗方案的选择。

8. 总结

CAC积分是动脉粥样硬化的标志，可通过心脏CT量化。CAC积分已成为广泛应用的心血管风险分层工具。CAC积分为零与较低的心血管事件风险相关。CAC积分转化的时间对预后评估和他汀类药物治疗的开始至关重要，但很难捕捉。接受他汀类药物治疗的患者CAC积分进展较快，但这种钙悖论可能与斑块稳定有关。CAC积分扫描通常使用Agatston评分，对于患者来说，更容易理解的形式可能是将CAC积分表示为动脉“年龄”。我们目前有足够的科学证据在无症状和有症状的患者中使用CAC积分来预测心血管风险。

参考文献

[1] Taylor, A.J., Byers, J.P., Cheitlin, M.D. and Virmani, R. (1997) Anomalous Right or Left Coronary Artery from the Contralateral Coronary Sinus: “High-Risk” Abnormalities in the Initial Coronary Artery Course and Heterogeneous Clinical Outcomes. *American Heart Journal*, **133**, 428-435. https://doi.org/10.1016/S0002-8703(97)70184-4

[2] Sanz, J., Dellegrottaglie, S., Fuster, V. and Rajagopalan, S. (2006) Calcium Scoring and Contrast-Enhanced CT Angiography. *Current Molecular Medicine*, **6**, 525-539. https://doi.org/10.2174/156652406778018644

[3] Waxman, S., Ishibashi, F. and Muller, J.E. (2006) Detection and Treatment of Vulnerable Plaques and Vulnerable Patients: Novel Approaches to Prevention of Coronary Events. *Circulation*, **114**, 2390-2411. https://doi.org/10.1161/CIRCULATIONAHA.105.540013

[4] Sørensen, M.H., Gerke, O., Lambrechtsen, J., *et al*. (2012) Changes in Medical Treatment Six Months after Risk Stratification with Heartscore and Coronary Artery Calcification Scanning of Healthy Middle-Aged Subjects. *European Journal of Preventive Cardiology*, **19**, 1496-1502. https://doi.org/10.1177/1741826711428063

[5] Silverman, M.G., Blaha, M.J., Krumholz, H.M., *et al*. (2014) Impact of Coronary Artery Calcium on Coronary Heart Disease Events in Individuals at the Extremes of Traditional Risk Factor Burden: The Multi-Ethnic Study of Atherosclerosis. *European Heart Journal*, **35**, 2232-2241. https://doi.org/10.1093/eurheartj/eht508

[6] Głowacki, J., Krysiński, M., Czaja-Ziółkowska, M. and Wasilewski, J. (2020) Machine Learning-Based Algorithm Enables the Exclusion of Obstructive Coronary Artery Disease in the Patients Who Underwent Coronary Artery Calcium Scoring. *Academic Radiology*, **27**, 1416-1421. https://doi.org/10.1016/j.acra.2019.11.016

[7] Budoff, M.J., Achenbach, S., Blumenthal, R.S., *et al*. (2006) Assessment of Coronary Artery Disease by Cardiac Computed Tomography: A Scientific Statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation*, **114**, 1761-1791. https://doi.org/10.1161/CIRCULATIONAHA.106.178458

[8] Koopman, M.Y., Willemsen, R.T.A., Van der Harst, P., *et al*. (2022) The Diagnostic and Prognostic Value of Coronary Calcium Scoring in Stable Chest Pain Patients: A Narrative Review. *RöFo*, **194**, 257-265. https://doi.org/10.1055/a-1662-5711

[9] Blaha, M., Budoff, M.J., Shaw, L.J., *et al*. (2009) Absence of Coronary Artery Calcification and All-Cause Mortality. *JACC*: *Cardiovascular Imaging*, **2**, 692-700. https://doi.org/10.1016/j.jcmg.2009.03.009

[10] Villines, T.C., Hulten, E.A., Shaw, L.J., *et al*. (2011) Prevalence and Severity of Coronary Artery Disease and Adverse Events among Symptomatic Patients with Coronary Artery Calcification Scores of Zero Undergoing Coronary Computed Tomography Angiography: Results from the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) Registry. *Journal of the American College of Cardiology*, **58**, 2533-2540. https://doi.org/10.1016/j.jacc.2011.10.851

[11] Blaha, M.J., Cainzos-Achirica, M., Dardari, Z., *et al*. (2020) All-Cause and Cause-Specific Mortality in Individuals with Zero and Minimal Coronary Artery Calcium: A Long-Term, Competing Risk Analysis in the Coronary Artery Calcium Consortium. *Atherosclerosis*, **294**, 72-79. https://doi.org/10.1016/j.atherosclerosis.2019.11.008

[12] Budoff, M.J., Mayrhofer, T., Ferencik, M., *et al*. (2017) Prognostic Value of Coronary Artery Calcium in the PROMISE Study (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). *Circulation*, **136**, 1993-2005. https://doi.org/10.1161/CIRCULATIONAHA.117.030578

[13] Dzaye, O., Dardari, Z.A., Cainzos-Achirica, M., *et al*. (2021) Warranty Period of a Calcium Score of Zero: Comprehensive Analysis from MESA. *JACC*: *Cardiovascular Imaging*, **14**, 990-1002. https://doi.org/10.1016/j.jcmg.2020.06.048

[14] Patel, J., Al Rifai, M., Blaha, M.J., *et al*. (2015) Coronary Artery Calcium Improves Risk Assessment in Adults with a Family History of Premature Coronary Heart Disease: Results from Multiethnic Study of Atherosclerosis. *Circulation*: *Cardiovascular Imaging*, **8**, e003186. https://doi.org/10.1161/CIRCIMAGING.115.003186

[15] Razavi, A.C., Kelly, T.N., Budoff, M.J., *et al*. (2021) Atherosclerotic Cardiovascular Disease Events among Statin Eligible Individuals with and without Long-Term Healthy Arterial Aging. *Atherosclerosis*, **326**, 56-62. https://doi.org/10.1016/j.atherosclerosis.2021.03.018

[16] Mittal, T.K., Pottle, A., Nicol, E., *et al*. (2017) Prevalence of Obstructive Coronary Artery Disease and Prognosis in Patients with Stable Symptoms and a Zero-Coronary Calcium Score. *European Heart Journal-Cardiovascular Imaging*, **18**, 922-929. https://doi.org/10.1093/ehjci/jex037

[17] Lehmann, N., Erbel, R., Mahabadi, A.A., *et al*. (2018) Value of Progression of Coronary Artery Calcification for Risk Prediction of Coronary and Cardiovascular Events: Result of the HNR Study (Heinz Nixdorf Recall). *Circulation*, **137**, 665-679. https://doi.org/10.1161/CIRCULATIONAHA.116.027034

[18] Grundy, S.M., Stone, N.J., Bailey, A.L., *et al*. (2019) 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*, **139**, e1082-e1143. https://doi.org/10.1161/CIR.0000000000000698

[19] Miedema, M.D., Duprez, D.A., Misialek, J.R., *et al*. (2014) Use of Coronary Artery Calcium Testing to Guide Aspirin Utilization for Primary Prevention: Estimates from the Multi-Ethnic Study of Atherosclerosis. *Circulation*: *Cardi-*

ovascular Quality and Outcomes, **7**, 453-460. https://doi.org/10.1161/CIRCOUTCOMES.113.000690

[20] Blaha, M.J. (2021) Predicting Age of Conversion to CAC >0: A Role for Polygenic Risk Scores? *JACC*: *Cardiovascular Imaging*, **14**, 1407-1409. https://doi.org/10.1016/j.jcmg.2020.12.007

[21] Carr, J.J., Jacobs Jr., D.R., Terry, J.G., *et al*. (2017) Association of Coronary Artery Calcium in Adults Aged 32 to 46 Years with Incident Coronary Heart Disease and Death. *JAMA Cardiology*, **2**, 391-399. https://doi.org/10.1001/jamacardio.2016.5493

[22] Mortensen, M.B., Dzaye, O., Bødtker, H., *et al*. (2021) Interplay of Risk Factors and Coronary Artery Calcium for CHD Risk in Young Patients. *JACC*: *Cardiovascular Imaging*, **14**, 2387-2396. https://doi.org/10.1016/j.jcmg.2021.05.003

[23] Lehmann, N., Möhlenkamp, S., Mahabadi, A.A., *et al*. (2014) Effect of Smoking and Other Traditional Risk Factors on the Onset of Coronary Artery Calcification: Results of the Heinz Nixdorf Recall Study. *Atherosclerosis*, **232**, 339-345. https://doi.org/10.1016/j.atherosclerosis.2013.11.045

[24] Severance, L.M., Carter, H., Contijoch, F.J. and McVeigh, E.R. (2021) Targeted Coronary Artery Calcium Screening in High-Risk Younger Individuals Using Consumer Genetic Screening Results. *JACC*: *Cardiovascular Imaging*, **14**, 1398-1406. https://doi.org/10.1016/j.jcmg.2020.11.013

[25] Budoff, M.J., Hokanson, J.E., Nasir, K., *et al*. (2010) Progression of Coronary Artery Calcium Predicts All-Cause Mortality. *JACC*: *Cardiovascular Imaging*, **3**, 1229-1236. https://doi.org/10.1016/j.jcmg.2010.08.018

[26] Lee, S.-E., Chang, H.-J., Sung, J.M., *et al*. (2018) Effects of Statins on Coronary Atherosclerotic Plaques: The PARADIGM Study. *JACC*: *Cardiovascular Imaging*, **11**, 1475-1484. https://doi.org/10.1016/j.jcmg.2018.04.015

[27] Henein, M., Granåsen, G., Wiklund, U., *et al*. (2015) High Dose and Long-Term Statin Therapy Accelerate Coronary Artery Calcification. *International Journal of Cardiology*, **184**, 581-586. https://doi.org/10.1016/j.ijcard.2015.02.072

[28] Nakazato, R., Gransar, H., Berman, D.S., *et al*. (2012) Statins Use and Coronary Artery Plaque Composition: Results from the International Multicenter CONFIRM Registry. *Atherosclerosis*, **225**, 148-153. https://doi.org/10.1016/j.atherosclerosis.2012.08.002

[29] Henein, M.Y. and Owen, A. (2011) Statins Moderate Coronary Stenoses but Not Coronary Calcification: Results from Meta-Analyses. *International Journal of Cardiology*, **153**, 31-35. https://doi.org/10.1016/j.ijcard.2010.08.031

[30] Ikegami, Y., Inoue, I., Inoue, K., *et al*. (2018) The Annual Rate of Coronary Artery Calcification with Combination Therapy with a PCSK9 Inhibitor and a Statin Is Lower Than That with Statin Monotherapy. *NPJ Aging and Mechanisms of Disease*, **4**, Article No. 7. https://doi.org/10.1038/s41514-018-0026-2

[31] Raggi, P., Cooil, B., Ratti, C., Callister, T.Q. and Budoff, M. (2005) Progression of Coronary Artery Calcium and Occurrence of Myocardial Infarction in Patients with and without Diabetes Mellitus. *Hypertension*, **46**, 238-243. https://doi.org/10.1161/01.HYP.0000164575.16609.02

[32] Czaja-Ziółkowska, M., Głowacki, J., Krysiński, M., Gąsior, M. and Wasilewski, J. (2023) Relationship between Left Main Trifurcation Angulation, Calcium Score, and the Onset of Plaque Formation. *Kardiologia Polska*, **81**, 48-53. https://doi.org/10.33963/KP.a2022.0161

[33] Hecht, H.S. (2015) Coronary Artery Calcium Scanning: Past, Present, and Future. *JACC*: *Cardiovascular Imaging*, **8**, 579-596. https://doi.org/10.1016/j.jcmg.2015.02.006

[34] Budoff, M.J., Young, R., Burke, G., *et al*. (2018) Ten-Year Association of Coronary Artery Calcium with Atherosclerotic Cardiovascular Disease (ASCVD) Events: The Multi-Ethnic Study of Atherosclerosis (MESA). *European Heart Journal*, **39**, 2401-2408. https://doi.org/10.1093/eurheartj/ehy217

[35] Lo-Kioeng-Shioe, M.S., Rijlaarsdam-Hermsen, D., Van Domburg, R.T., *et al*. (2020) Prognostic Value of Coronary Artery Calcium Score in Symptomatic Individuals: A Meta-Analysis of 34,000 Subjects. *International Journal of Cardiology*, **299**, 56-62. https://doi.org/10.1016/j.ijcard.2019.06.003

[36] Mortensen, M.B., Dzaye, O., Steffensen, F.H., *et al*. (2020) Impact of Plaque Burden versus Stenosis on Ischemic Events in Patients with Coronary Atherosclerosis. *Journal of the American College of Cardiology*, **76**, 2803-2813. https://doi.org/10.1016/j.jacc.2020.10.021