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·文献综述·

动脉钙化与下肢动脉硬化闭塞症的关联及临床研究进展

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摘　要　下肢动脉硬化闭塞症（ASO）是常见的外周动脉疾病，全球发病率逐年上升。动脉钙化作为ASO的重要病理改变，在其发病机制、诊断评估、治疗策略和预后判断中均具有重要意义。近年来，随着影像学和生物标志物检测技术的不断进步，动脉钙化的定量评估和临床研究不断深入，为个体化诊疗提供了新思路。本综述从动脉钙化的病理生理机制出发，系统梳理其检测方法、对腔内治疗的影响以及在预后评估中的应用进展，旨在为ASO患者的精准治疗提供理论依据和实践参考。

关键词　闭塞性动脉硬化；下肢；血管钙化；综述

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Association between arterial calcification and lower extremity atherosclerotic occlusive disease and its clinical research progress

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Abstract　Lower extremity atherosclerotic occlusive disease (ASO) is a common peripheral arterial disease with a steadily increasing global incidence. As a key pathological change in ASO, arterial calcification plays a crucial role in its pathogenesis, diagnostic evaluation, treatment strategies, and prognosis. In recent years, with the continuous advancement of imaging and biomarker detection technologies, quantitative assessment and clinical research on arterial calcification have deepened, providing new perspectives for individualized diagnosis and treatment. This review begins with the pathophysiological mechanisms of arterial calcification and systematically summarizes current detection methods, its impact on endovascular therapy, and recent progress in prognostic evaluation, aiming to provide theoretical support and practical reference for precision treatment of ASO patients.

Key words　Arteriosclerosis Obliterans; Lower Extremity; Vascular Calcification; Review

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下肢动脉硬化闭塞症（arteriosclerosis occlusion disorder，ASO）通常表现出间歇性跛行、小腿麻木、远端肢体疼痛、发凉等慢性缺血症状[1]，严重肢体缺血（critical limb ischemia，CLI）阶段会出现静息痛、溃疡、坏疽等，显著增加截肢和死亡风险，影响患者生活质量和生存率[2-3]。血管钙化是动脉粥样硬化的特征性表现，在过往的研究中血管钙化不仅与心血管事件高度相关，也是下肢ASO患者血管病变和治疗预后的重要影响因素[4]。本文针对动脉钙化机制、测量、腔内治疗中的应用作一综述。

1 动脉钙化的病理生理

动脉钙化是一种复杂的病理过程，表现为钙盐等矿物质在血管壁异常沉积，根据不同部位主要分为内膜钙化及中膜钙化。其中，内膜钙化与动脉粥样硬化斑块形成相关，往往伴随炎症反应、脂质沉积、细胞凋亡及坏死等病理过程[5-6]，微钙化的形成由巨噬细胞释放的促骨生长因子推动，通过平滑肌细胞释放的基质小体和凋亡小体所提供的钙沉积成核点，最终发展为大面积钙化病灶[7]。中膜钙化常发生于血管的中间薄层[8]，其机制包括平滑肌细胞的成骨性转分化、细胞外基质改变以及遗传和代谢因素，St Hilaire[9]指出，中膜钙化主要以血管硬化、弹性下降为特征，可引起血栓形成及血流阻塞，尤其在膝下动脉中显著，这是下肢血管病变的另一个重要因素。而针对中膜钙化的特异性诊断和治疗仍需进一步研究[10]。尽管不同类型动脉钙化在发生机制及解剖分布上存在差异，但动脉钙化本质上是全身性钙盐代谢紊乱驱动的系统性病理过程。研究[11]显示，下肢动脉钙化与冠状动脉钙化呈显著相关，二者在糖尿病等高风险人群中常同步发生。慢性高血糖状态会促进血管平滑肌细胞骨化转化、氧化应激水平升高，进而容易导致内膜与中膜的钙盐沉积加重[12-13]。

2 动脉钙化的临床检测方法

术前精确评估血管钙化对下肢ASO患者选择合适的手术方案至关重要，目前对于血管钙化的量化评估尚未建立全球范围内统一的标准或共识，这为临床实践带来了挑战。

2.1 X线平片

X线是最早用于检测动脉钙化的影像学工具，可显示动脉壁钙化的线性或环形结构，但其敏感度较低，难以精确评估钙化的范围和程度。基于腰椎侧位X线片可对L1~L4椎体区域进行Kauppila评分，其广泛应用于血透患者及普通人群的腹主动脉钙化定量评估[14-15]。有研究[16]表明，超声对早期和轻微钙化敏感度更高，而X线对严重钙化检测更具优势，两者在广泛钙化评估中具有较高的一致性。

2.2 多普勒超声

超声是一种经济、便捷的评估手段，其优势在于能够提供血管壁的结构和功能信息，包括血流速度和斑块特征。Maahs等[17]开发的超声股动脉钙化评分方法可中等程度地反映股动脉钙化程度（r=0.64），较高的超声钙化评分（>0.8）与外周动脉疾病患者的截肢和死亡风险显著相关（OR=3.4），这也提示基于超声的评分可能是一种有效预测下肢动脉疾病患者截肢或死亡风险的工具。近年来，血管内超声（intravascular ultrasound，IVUS）通过高分辨率成像，被更多地用于评估动脉钙化引起的血管壁和腔内结构变化[18]，为钙化检测提供了更多可能性。

2.3 多排螺旋CT

多排螺旋CT是动脉钙化评估的重要检查方式[19]。其高分辨率和定量分析能力能够准确检测动脉的钙化范围、密度和分布。Rimmerman等[20]采用CT对患者足部动脉的钙化负担进行了逐血管的定量分析，该研究强调了CT影像在量化远端血管钙化、优化风险分层中的潜力，并指出未来应结合CT定量成像和其他多模态影像技术以实现更全面的血管钙化评估。目前对于外周动脉钙化评分测量方法及标准尚未统一，Ichihashi等[21]采用外周动脉钙化评分系统（peripheral arterial calcium scoring system，PACSS）进行测量；Konijnd等[22]从钙化的严重程度，钙化环状态，钙化的厚度以及连续性进行评估；耿跃[23]改良既往方法，对膝下3支血管以小腿中点进行分段得到6段血管，再根据各血管段前壁和侧壁钙化斑块长度进行评分；Yan等[24]及Chowdhury等[25]则采用冠脉系统应用的Agaston评分方法计算下肢动脉钙化积分来研究不同部位下肢动脉钙化积分与心脏相关疾病病死率

及发病率的关系等。最近的研究[26]指出，不同的CT扫描仪和评分平台对下肢动脉钙化的量化结果也存在显著差异，标准化的评分方法对于提升钙化量化结果的可靠性和临床可用性是至关重要的。

2.4 磁共振血管成像（magnetic resonance angiography，MRA）

MRA作为一种非侵入性、综合影像工具，提供高分辨率的血管解剖信息，并通过多模态技术评估钙化斑块的性质、血管狭窄的程度，以及局部组织的灌注和代谢变化。Elsaid等[27]指出在钙化评估方面，增强MRA展示了在诊断和量化钙化负荷上的优势，而无对比剂的成像技术则为肾功能受损的患者提供了安全有效的替代方法。这些技术的结合使MRA成为患者个性化治疗的重要工具，有助于从宏观血管到微观组织层面，全面评估疾病的进展和治疗效果。

2.5 生物标志物

生物标志物在评估动脉钙化方面具有重要的应用潜力，可作为预测疾病进展和探索治疗靶点的工具。根据Golüke等[28]的综述，包括磷酸盐、成纤维细胞生长因子23、骨保护素、骨桥蛋白及基质Gla蛋白等标志物，与动脉钙化的发生和发展密切相关，反映了钙磷代谢及骨–血管交互作用的过程。目前相关研究多为横断面设计，缺乏因果关系验证，未来仍需更多纵向研究和机制性探索，以优化生物标志物在钙化评估和精准医疗中的应用。

3 动脉钙化与下肢ASO的关系

3.1 动脉钙化与疾病严重程度、疾病分级

动脉钙化与下肢ASO的严重程度密切相关，重度钙化会影响血管弹性和血流动力学，增加病变的复杂性，钙化模式和负荷可用于评估疾病复杂性及预测临床结局[29]。研究[30]显示钙化程度高的患者其血运重建的成功率较低，并发症发生风险较高，长期预后较差。Jeremias等[31]研究显示，髂动脉钙化评分的增高与疾病严重程度Rutherford分级5~6级密切相关，同时在TASC分级中与更复杂的C或D类病变显著相关。Azeez等[32]进一步发现，不同类型的血管钙化（结节型钙化和片状钙化）与下肢动脉疾病严重程度之间的关系不同，通过对股动脉斑块进行定量分析，发现结节型钙化与较轻的病情相关，而片状钙化与疾病严重程度无显著关联。Conte等[33]在GLASS分级系统中指出，解剖复杂性与干预结果密切相关，钙化程度和下肢动脉病变的分布共同影响患者的肢体保留率和伤口愈合率。此外，Morisaki等[34]也指出钙化程度越高，截肢和死亡的风险越大，介入治疗的效果也越差，钙化程度作为截肢风险增加的标志已被纳入全球肢体解剖分期系统。

3.2 动脉钙化对腔内治疗的影响

动脉钙化在下肢ASO的腔内治疗中扮演着复杂角色，钙化导致血管顺应性降低，直接影响了多种干预手段的技术成功率及临床效果[35-36]。腔内治疗是目前下肢ASO的主要手术治疗方式[37]，然而动脉钙化会导致血管壁弹性下降，顺应性降低，增加手术治疗的难度，现有术式多以压碎钙化斑块为主，本质上并没有将钙化斑块从血管中去除，导致管腔恢复不完全[38]。严重的钙化会引起支架植入困难，增加术后再狭窄和支架断裂的风险。一项随机对照试验中阶段性结局的分析[39]表明：在观察期内高钙化评分组截肢风险是低评分组的2.88倍，全因死亡风险高出5.16倍。Pan等[40]发起的多中心研究显示，在股腘动脉中–重度钙化患者中，药物洗脱球囊、定向斑块旋切术、Eluvia药物洗脱支架等新型腔内技术可有效提升通畅率与减少再干预，但治疗方案仍需根据病变特征和患者状况个体化制定。Kronlage等[41]同样表明，钙化斑块显著限制了药物涂层球囊（drug-coated balloon，DCB）中药物的吸收率和渗透深度，而通过切割或旋转斑块切除术预处理后，可有效清除钙化负荷，改善腔道扩张，显著增强DCB和药物洗脱支架在高度钙化动脉中的效果。Fujihara等[42]使用倾向评分匹配分析比较不同剂量DCB的疗效，结果显示，高剂量DCB在1年内的无再狭窄率（86.2% *vs.* 73.3%）和无再血运重建率（92.5% *vs.* 84.9%）均显著高于低剂量DCB组，通过进一步分析指出严重钙化[外周动脉钙化评分系统（peripheral arterial calcium scoring system，PACSS）4级]可能与低剂量DCB组疗效较差相关。另外，钙化还影响支架植入的效果，Bausback等[43]指出，高钙化会导致支架扩展不全、支架变形或断裂，从而增加术后再狭窄和急性闭塞的风险。在钙化病变中精准评估钙化类型及范围对于优化腔内治疗策略至关重要[44]。因此术前精准评估钙化程度非常关键，结合影像

学技术诊断和先进设备预处理，可改善腔内治疗的安全性和效果，然而针对动脉钙化的处理仍是腔内治疗中的挑战，需进一步优化治疗策略和评估标准。

3.3 动脉钙化对下肢ASO预后的预测价值

动脉钙化程度是评估术后并发症发生风险的重要预测因子[45-46]。Rocha-Singh等[47]提出了PACSS用于量化钙化的程度及其对治疗复杂性的影响，研究表明，高度钙化的患者会经历更高的再狭窄率和再干预率。Sundaram等[48]在对136条慢性足部伤口肢体的回顾性研究中发现，中膜动脉钙化评分不仅能显著预测1年大截肢风险还能独立预测伤口愈合延迟。Ferraresi等[49]提出了一种结合小动脉疾病和中层动脉钙化的新评分系统，用于预测慢性肢体威胁性缺血（chronic limb-threatening ischemia，CLTI）患者的临床结局，研究显示，该评分是主要不良肢体事件的独立预测因子，与伤口愈合率、肢体保留率和生存率显著相关，该评分系统在影像学上具有高度重现性（r=0.96）。另一项研究[50]开发的足部动脉中层钙化（pedal medial arterial calcification，pMAC）评分系统在预测CLTI患者大型截肢和再次血运重建需求中具有显著价值。最近的研究[51]发现，pMAC评分高的患者发生主要肢体不良事件的风险显著增加，其截肢率从低评分组的6.7%上升至高评分组的50%。国内通过回顾性研究[52]，参考Agaston积分算法，分析得出双下肢动脉钙化积分是ASO患者行球囊扩张成形术后复发的独立危险因素（敏感度87.1%，特异度58%）。Megale等[53]研究表明，术前增强CTA计算的手术肢体钙化评分（calcium score of the operated limb，CSOL）可预测CLI患者血运重建术后30 d和6个月内的死亡风险，且30 d预测模型具有高敏感度和特异度（AUC=0.89，敏感度100%，特异度82.6%），研究验证了CSOL作为术前风险评估标志物的可行性，为CLI患者的治疗决策提供了重要依据。基于钙化特征的预测模型正在帮助临床医师优化治疗策略，从而改善患者的长期结局，未来研究需进一步验证这些模型在不同患者群体中的适用性，并探索新的治疗手段以应对钙化对腔内治疗的挑战。

4 小结与展望

尽管目前已有许多关于动脉钙化与下肢ASO关系的研究，但仍然存在一些局限性。钙化定量的测量标准尚未统一，不同方法之间的结果可能存在差异，钙化评估的临床应用仍需更多的大规模临床试验支持，而钙化对治疗的影响也存在显著异质性，针对钙化治疗的干预手段有限，也制约了其进一步发展。推动个性化医疗发展，制定精准治疗方案，深入理解钙化在下肢ASO中的作用，将为新的治疗手段提供理论基础，期望在提高治疗效果和患者预后方面取得突破。

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