

冠状动脉 CT 血管造影评估冠状动脉功能性狭窄的研究进展

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【摘要】 冠状动脉 CT 血管造影可评估冠状动脉解剖学狭窄程度,但不能准确地判断冠状动脉狭窄是否引起功能性心肌缺血。血流储备分数是评估功能性狭窄的金标准,但有创且费用昂贵,限制了其临床应用。近年来,用于评价冠状动脉功能性狭窄的冠状动脉 CT 血管造影分析技术包括:冠状动脉 CT 血流储备分数、生物力学特征、基于管腔内密度衰减的参数、冠状动脉 CT 血管造影定量指标及泊肃叶冠状动脉指数等,这类技术无需额外的药物或图像采集即可实现解剖学狭窄程度与功能学缺血程度的一站式评估,对冠心病的诊断具有重要意义。现就这类技术在评估冠状动脉功能性狭窄方面的研究进展展开综述。

【关键词】 冠状动脉 CT 血管成像;血流储备分数;管腔内密度衰减梯度;定量

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Coronary Computed Tomography Angiography in Evaluation of Coronary Artery Functional Stenosis

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【Abstract】 Coronary computed tomography (CT) angiography can evaluate the degree of coronary artery anatomical stenosis, but it cannot accurately determine whether the stenosis causes functional myocardial ischemia. Fractional flow reserve is the gold standard for evaluating the functional stenosis, but it's invasive and expensive, which limits its clinical application. In recent years, coronary CT angiography analysis techniques used to evaluate coronary artery functional stenosis include coronary CT fractional flow reserve, biomechanical characteristics, parameters based on transluminal attenuation gradient, coronary CT angiography quantitative index and Poiseuille-based coronary angiographic index, etc. This kind of technology can achieve the one-stop evaluation of anatomical stenosis and functional ischemia without additional drugs or image acquisition, which is of great significance for the diagnosis of coronary heart disease. This article reviews the research progress of these techniques in the evaluation of coronary artery functional stenosis.

【Key words】 Coronary computed tomography angiography; Fractional flow reserve; Transluminal attenuation gradient; Quantification

有创冠状动脉造影是评价冠心病严重程度最常用的方法,在临床实践中被用作决定治疗策略的标准。然而,冠状动脉管腔狭窄程度与心肌缺血的严重程度并不一致,在中度狭窄的冠状动脉中这种不一致性为 37.8%^[1],故评价冠状动脉狭窄是否引起功能性缺血非常有必要。目前评估冠状动脉功能性狭窄的金标准是血流储备分数(fractional flow reserve, FFR),但其有创且费用昂贵,临床应用受限,因此研究人员致力于开发无创性评估冠状动脉功能性狭窄的检查方法。冠状动脉 CT 血管造影(coronary computed tomography angiography, CCTA)以其较高的阴性预测值在冠心病的筛查中得到广泛应用,但其

诊断缺血性病变的特异性较低。随着 CT 及计算流体力学(computational fluid dynamics, CFD)的飞速发展,用于评价冠状动脉功能性狭窄的技术日益进步。现介绍这类技术的最新进展及优缺点。

1 冠状动脉 CT 血流储备分数

冠状动脉 CT 血流储备分数(coronary CT fractional flow reserve, FFR_{CT})是一种以 CCTA 数据为基础,利用 CFD 原理,模拟计算出整个冠状动脉树任意一点 FFR 值的新型无创后处理技术。FFR_{CT}的计算主要分为以下三步:(1)识别斑块,提取管壁,构建冠状动脉三维解剖血管树模型;(2)定义入口、出口和边界条件,根

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据 Navier-Stokes 方程构建冠状动脉血流动力学模型；(3) 构建集总参数模型，联合解剖学模型模拟最大充血状态下的血流与血压。

早期研究表明，基于 3D 运算模型的 HeartFlow FFR_{CT} (美国, HeartFlow 公司) 在评估冠状动脉功能性狭窄方面具有较高的诊断价值，但 FFR_{CT} 的计算需将数据传送至超级计算机进行，运算量大，运算时间较长^[2]。近几年，研究人员试图基于不同的算法模型开发多种 FFR_{CT} 分析软件，研究的结果一致显示 FFR_{CT} 对功能性狭窄具有较高的预测价值^[3-5]。国内研究人员开发的一种新的基于 CFD 建模的现场 FFR 算法 (uCT-FFR) 来计算 FFR_{CT} 值，结果显示 uCT-FFR 诊断功能性狭窄的敏感度、特异度和准确度分别为 89%、91% 和 91%，其诊断效能优于 CCTA 和有创冠状动脉造影^[4]。最新研究表明，以 FFR ≤ 0.8 为参考标准，FFR_{CT} 诊断冠状动脉功能性狭窄的准确度 (87%) 略高于正电子发射计算机断层成像心肌灌注显像 (positron emission computed tomography myocardial perfusion imaging, PET MPI) (80%)，与单光子发射计算机断层成像心肌灌注显像 (single-photon emission computed tomography myocardial perfusion imaging, SPECT MPI) (82%) 相当。FFR_{CT} 的敏感度 (90%) 高于 PET MPI (81%) 和 SPECT MPI (42%)，特异度 (86%) 略高于 PET MPI (76%)，但低于 SPECT MPI (97%)^[6]。

FFR_{CT} 无需压力导丝及扩血管药物即可测得，具有无创、安全和经济等优点，但准确性受图像质量影响，对“灰区” (FFR 值在 0.75~0.8) 及高钙积分 (Agatston 钙化积分 ≥ 400) 病变的诊断效能欠佳，故临床应用价值还需进一步研究验证。此外，FFR_{CT} 在预测急性冠脉综合征^[7]、指导临床治疗决策及评估远期预后价值^[8-9] 等方面也具有较好的应用前景。

2 生物力学特征

壁面剪切应力 (wall shear stress, WSS) 及轴向斑块应力 (axial plaque stress, APS) 等生物力学因素在冠状动脉粥样硬化斑块的发生、进展及转化中具有重要作用。CT 技术与 CFD 的结合使得无创性评估生物力学特征成为可能。WSS 定义为血流与血管内皮摩擦产生的切线力，APS 指作用于狭窄病变的血流动力学应力的轴向分量。有研究显示，WSS 与冠状动脉功能性狭窄相关，但其并非功能性狭窄的独立预测因子^[10]。另有研究报道，FFR ≤ 0.8 组的 APS 明显高于 FFR > 0.8 组，但未对其诊断效能进行评估^[11]。WSS 与 APS 不仅可提供局部血流动力学信息，还可识别易损斑块及罪犯血管^[12]，但其评估冠状动脉功能性狭窄的准确性尚需大量研究证实。

3 基于管腔内密度衰减的参数

行 CCTA 检查时造影剂的变化可反映与血液流动相关的信息^[13]。基于此，研究者们提出一系列用来量化常规 CCTA 图像中造影剂变化的参数，包括管腔内密度衰减梯度 (transluminal attenuation gradient, TAG)、校正的冠状动脉腔内密度 (corrected coronary opacification, CCO)、校正的管腔内密度衰减梯度 (transluminal attenuation gradient-corrected coronary opacification, TAG-CCO)、腔内衰减血流编码 (transluminal attenuation flow encoding, TAFE) 及对比密度差 (contrast density difference, CDD) 等，笔者将分别介绍这些参数评估冠状动脉功能性狭窄的诊断价值。

3.1 TAG

TAG 定义为冠状动脉管腔内密度衰减与距冠状动脉开口长度之间的线性回归系数，反映造影剂通过血管腔的下降情况，有可能间接评估冠状动脉血流量。测量方法是从冠状动脉开口处起到管腔横截面积为 2 mm² 止，每隔 5 mm 在轴位图像显示的管腔中央放置大小为 1 mm² 的感兴趣区并测量平均 CT 值，建立管腔 CT 值与距冠状动脉开口长度之间的线性回归模型，此回归系数即为 TAG 值。有研究显示，以 FFR 为参考标准，TAG 诊断冠状动脉功能性狭窄的能力高于 CCTA 狭窄程度但不如 FFR_{CT}^[14]。另有研究报道，不管参考何种标准，TAG 均不能有效地识别冠状动脉功能性狭窄，且 TAG+CCTA 与单独 CCTA 的诊断价值相当^[15-16]。目前 TAG 能否准确地评估冠状动脉功能性狭窄尚存在争议，究其原因主要与 TAG 值变异性较大有关。TAG 值易受 CT 扫描机型、采集时相、造影剂、心输出量及图像质量等多种因素影响，降低了 TAG 对功能性狭窄的诊断效能^[17]。理论上讲，在一次心动周期中获取的 CT 图像是 TAG 应用的理想条件，因为单次扫描可避免扫描时相不均一对冠状动脉内造影剂的影响。Fujimoto 等^[18] 研究表明通过结合冠状动脉血流生理信息可提高 TAG 的准确性。

TAG 是最早提出的，应用最为广泛，不仅可提高 CCTA 对管腔狭窄程度诊断的准确性，还有可能使狭窄程度重新分级，尤其在钙化病变中具有重大价值^[19]。虽然评价功能性狭窄的诊断效能尚存在争议，但近年来的研究表明通过降低影响因素可提高 TAG 的准确性。此外，还有学者将 TAG 应用于心肌桥^[20]、动脉瘤^[21] 以及侧支循环^[22] 等的评估中，已取得较好成果。

3.2 CCO

CCO 为冠状动脉狭窄近端管腔内密度和同层面主动脉密度的比值与狭窄远端管腔内密度和同层面主

动脉密度的比值之差(即 $CCO = \text{狭窄近端管腔 CT 值} / \text{同层面主动脉 CT 值} - \text{狭窄远端管腔 CT 值} / \text{同层面主动脉 CT 值}$),理论上可避免图像采集时相及心输出量对管腔内密度值的影响。多项研究证实冠状动脉缺血性狭窄节段的 CCO 显著降低,其在预测血流动力学显著狭窄方面具有良好的诊断价值^[23-25]。报道显示 CCO 诊断功能性狭窄的能力不如 FFR_{CT} ,但高于 TAG 和 CCTA^[24]。此外,CCO 在评价支架内再狭窄^[26]、预测主要心脏不良事件^[27]及相对血流储备异常^[28]等方面也具有重要临床价值。

3.3 TAG-CCO

TAG-CCO 定义为冠状动脉和同层面主动脉管腔密度的比值与距冠状动脉开口长度之间的线性回归系数,是 Stuijzand 等^[23]为校正图像采集时相对 TAG 的影响而提出的,测量方法是在 TAG 的基础上加测同层面主动脉 CT 值。早期研究结果显示 TAG-CCO 诊断冠状动脉功能性狭窄的能力高于 CCTA^[23],但近几年研究表明 TAG-CCO 在识别功能性狭窄方面不能提供比单独 CCTA 更高的诊断价值^[15]。虽然 TAG-CCO 可避免图像采集时相对 TAG 的影响,但评估功能性狭窄的诊断效能仍存在争议。此外,还有学者将 TAG-CCO 应用于心肌桥^[29]和支架内再狭窄^[30]等的评估中,已取得较好成果。

3.4 TAFE

TAFE 是一种无创性测量冠状动脉血流量的新方法,由 4 个常规参数(包括 TAG、造影剂动脉输入时间间隔、平均横截面面积和血管长度)通过公式计算得出。Bae 等^[31]研究证实单位心肌血流量随狭窄程度的增加而持续下降,血流速度则通过微血管阻力和管腔的代偿性降低而保持不变。结果显示,由 TAFE 计算的狭窄和正常血管流量比与 CFD 模型计算的流量比具有很好的一致性,TAFE 测得的冠状动脉血流量与 CT 心肌灌注成像得出的血管特异性心肌血流量有很好的相关性。TAFE 无需复杂的计算即可提供全面的冠状动脉生理学信息,比 TAG 考虑的因素更多,其诊断冠状动脉功能性狭窄的效能应优于 TAG,但目前相关报道较少,仍需进一步研究证实。

3.5 CDD

CDD 定义为冠状动脉狭窄近段与狭窄处管腔对比密度的最大百分比差异(即 $CDD = \text{近段管腔 CT 值} / \text{横轴位面积} - \text{病变最狭窄处管腔 CT 值} / \text{横轴位面积}$),有可能反映狭窄前后冠状动脉血流量的变化,理论上可避免血管长度和管腔直径等因素对管腔内密度值的影响。有研究显示,CDD 与 FFR 呈负相关,其对冠状动脉功能性狭窄具有较高的预测价值^[32]。CDD

的测量方法较 TAG 更为简化,但同样受图像质量等因素影响,其诊断价值尚需大量研究证实。

4 CCTA 定量指标

随着 CT 采集技术和数据重建软件的发展,在后处理工作站上可快速地评估冠状动脉管腔狭窄程度、斑块特征及病变周围脂肪,研究结果显示,这些 CCTA 定量指标与血管特异性缺血密切相关。在狭窄定量指标方面,最小管腔面积和最大面积狭窄率是冠状动脉功能性狭窄的独立预测因子^[33]。在斑块特征方面,斑块长度、非钙化斑块体积、重构指数及餐巾环征能独立地预测功能性狭窄^[34]。另有研究报道,血管周围脂肪密度指数是功能性狭窄的独立预测因子^[35]。最新研究表明,将患者的临床资料及 CCTA 定量斑块特征通过机器学习进行客观组合可提高其对功能性狭窄的预测能力^[32]。在常规 CT 后处理工作站测得的 CCTA 定量指标可无创性地评估冠状动脉功能性狭窄,具有操作简单和可重复测量等优势,随着斑块定量分析技术的精准细化,CCTA 定量指标未来会有更好的应用前景。

5 泊肃叶冠状动脉指数

血液在心血管系统中的流动取决于泊肃叶和伯努利阐明的管内液体流动原理。据泊肃叶方程所述,通过狭窄管腔的流动阻力与半径的 4 次方成反比,与狭窄长度成正比,而泊肃叶冠状动脉指数具体指病变长度与最小管腔直径 4 次方的比值(ratio of lesion length to the forth power of minimal lumen diameter, LL/MLD^4)。研究结果显示, LL/MLD^4 是冠状动脉功能性狭窄的独立预测因子,当 $LL/MLD^4 > 3.54$ 时诊断功能性狭窄的敏感度为 92.3%,特异度为 86.1%^[36]。最新研究表明,以瞬时无波形比率为参考标准时, LL/MLD^4 可提高单独 CCTA 对血流动力学显著狭窄的检出率^[25]。另有研究报道, LL/MLD^4 识别功能性狭窄的能力高于 CCTA、TAG 及 CCO^[24]。 LL/MLD^4 本质上属于 CCTA 定量指标,测量方法简单,但目前相关研究较少,其准确性尚需大量研究证实。

6 小结与展望

目前的研究表明,这些方法对冠状动脉功能性狭窄的无创性评估可行。 FFR_{CT} 的诊断效能最高,现已取得较好的研究成果,有待在临床中进一步推广;WSS 与 APS 可反映斑块局部生物力学特征,其准确性仍需大量研究证实;TAG、CCO、TAG-CCO、TAFE 及 CDD 是基于管腔密度衰减的参数,无需复杂的计算即可测得,但影响因素较多,诊断价值有待提高;CCTA 定量指标在后处理工作站上即可测得,具有较好的应用前景; LL/MLD^4 的报道较少,其诊断效能尚需大量研究证实。

将来,随着 CT 技术的发展,这些方法会不断改进,有望成为指导临床治疗决策和评估预后的新手段。

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