

Research Progress of CT and MRI in Noninvasive Assessment of Cardiac Adipose Tissue*

综述

CT及MRI无创评估心脏脂肪组织的研究进展*

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【摘要】近年来研究表明,心脏脂肪组织含量与多种心血管疾病存在密切关联,是心血管疾病潜在的治疗靶点。影像学是检测和评估心脏脂肪最主要手段,无创、安全并且可以定性定量评估心脏脂肪的基本结构、病理生理功能。本文就计算机断层扫描(computed tomography, CT)和磁共振成像(magnetic resonance imaging, MRI)两种可以定量评估脂肪含量的方法,在评估心脏脂肪临床及科研应用、研究进展作一综述。

【关键词】心脏脂肪;心外膜脂肪;心包脂肪;
冠周脂肪;影像学技术

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ABSTRACT

Recent studies have shown that heart adipose tissue content is closely related to a variety of cardiovascular diseases, and it is a potential therapeutic target for cardiovascular diseases. Imaging is the most important method to detect and evaluate cardiac fat, which is non-invasive, safe, and can qualitatively and quantitatively evaluate the basic structure and pathophysiological function of cardiac fat. This article reviews the clinical and scientific application and research progress of computed tomography (CT) and magnetic resonance imaging (MRI) in the evaluation of cardiac fat content.

Keywords: Heart Fat; Epicardial Adipose Tissue; Pericardial Fat; Pericoronary Fat; Imaging Techniques

目前,心血管疾病(cardiovascular disease, CVD)是我国各年龄段致残和致死的主要原因之一。CVD的风险因素主要包括遗传、高血压、高血脂、高血糖、肥胖等。其中,肥胖不仅可以诱导CVD发生,还会加速CVD的进展,因此评估脂肪组织含量及分布在CVD患者治疗和生活习惯干预中具有重要价值。但是研究表明,并非全身各部位所有的脂肪组织沉积都是CVD的风险因素,其中心脏脂肪的沉积与CVD的风险增加尤为相关^[1-4]。

心脏脂肪组织是心脏周围及心肌内的脂肪库,主要包括心外膜脂肪(epicardial adipose tissue, EAT)、心包脂肪(pericardial adipose tissue, PAT)和冠状动脉周围脂肪(PCAT)。目前大多数研究通过MRI、CT及人工智能等成像技术或图像分析手段,定性定量的评估心脏脂肪的沉积情况,进而分析患者心功能改变、评估患者CVD风险或预测患者预后^[5]。因此本文对近些年使用不同技术手段测量心脏脂肪的方法及其优缺点进行综述,为CVD的治疗及风险评估提供证据。

1 磁共振评估心脏脂肪组织

相比于超声心动图更容易受声窗影响,磁共振检查可以更加准确的将心外膜脂肪与其他心脏脂肪区分开。虽然价格较高、检查时间长,但是磁共振成像一直以来仍然被认为是测量心外膜脂肪体积(epicardial adipose tissue volume, EATV)的“金标准”^[6-7]。此外,随着高场强磁共振机的应用和序列的更新迭代,磁共振成像在心包脂肪及冠状动脉周围脂肪的应用也在逐渐增加,以下对相关成像序列和及其临床应用情况进行综述。

1.1 黑血序列 黑血序列也被称为黑血快速自旋回波T1序列,通过两次反转脉冲抑制血液信号,保留周围背景组织信号,让血液信号压低呈现黑色得名。Bizino等^[8]使用3.0 T磁共振机和此序列,对EAT和心旁脂肪(paracardiac adipose tissue, PAT)的体积测量,定量分析利拉鲁肽在体内不同部位及不同脂肪含量时的影响。Arnold等^[9]通过黑血序列成像量化EAT体积指数、LV心肌脂肪含量和细胞外体积,发现EAT容积指数增加与心肌脂肪堆积增加、间质性心肌纤维化关系密切。黑血序列在临幊上应用较多,便于采集数据,但扫描时间长,需要患者依从度高,可以保持憋气状态,在这种限制下扫描图像质量很容易受心律、呼吸等影响,易出现运动伪影。

1.2 DIXON序列 DIXON序列是利用水、脂内部质子之间的化学位移,将脂肪和水成分分离成像,从而可重建纯水相、脂相和脂肪分数图等,一次扫描可得到多重组织成分显像,是评价心外膜脂肪的良好序列^[10]。Rami Homsi等^[11]使用1.5T磁共振机及此序列对高血压患者主动脉硬化、心肌梗塞等与心外膜、心旁脂肪体积之间的关系进行分析,在场强较低的情况下,仍然对脂肪体积进行了精确定量,发现心肌梗死与心外膜脂肪含量较高之间存在显著关联。Iulia Skoda等^[12]使用晚期钆增强结合DIXON序列的LGE-Dixon序列,同时可视化和分析左心房纤维化和EAT,且使得扫描时间与单独DIXON序列基本一致。综合来看本序列及联合其他序列共同成像的技术目前较新,成像难度较大,需要专门的序列开发,且会增加整体成像时间,其临幊应用目前尚较少,多为与人工智能相结合进行组学分析或者深度学习分析^[12,14]。

1.3 SSFP序列 SSFP序列全称平衡稳态自由进动心功能电影序列(steady-state free precession, SSFP),其图像取决于T2/T1,血液、脂肪和液体组织由于有着较大的T2/T1值,在Balance SSFP上表现为高信号,俗称“三亮”序列。Hang Zhou等^[15]通过此序列不仅测量了EAT,还分析了心包脂肪组织和心旁脂肪组织,最终发现EAT的含量与心脏舒张功能相关,其积累可能是透析患者心脏舒张功能障碍的独立危险因素。Rado

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等^[16]选择四腔心切面作为基线，测量最大收缩期及舒张期的EAT量，发现收缩末期测量结果的一致性高于舒张末期，造成这一现象可能由于在收缩末期EAT的边界显示更加清晰，使得组织对比度更高。Leo等^[17]放弃了定量分析EAT，转而通过此序列分析EAT的生物学特性，研究发现当EAT含量较高时，其具有侵入性。并且可以深入心脏周围的细小间隙并且影响解剖结构。虽然SSFP序列组织对比度高，但是也有一定的缺点，由于本序列组织对比度由T2/T1体现，病理状态下的组织水肿、脓性渗出、心包积液等可能干扰EAT等脂肪区域的边界划分，需结合其他序列进行界限分割才可以继续分析。

1.4 T1 Mapping T1 Mapping是通过特定序列在受试者心脏短轴位不同时间进行数据采集，经图像后处理，计算心肌平扫T1值及细胞外间质容积分数(extracellular volume, ECV)。Requena-Ibáñez JA等^[18]研究恩格列净对射血分数降低的非糖尿病心力衰竭患者影响，使用本序列分析间质性心肌纤维化，较为直接的评估了治疗结果。Wu CK等^[19]同样在研究心衰患者群体时，使用T1-Mapping分析发现EAT 体积与ECV 高度相关，与传统心衰危险因素和左心室质量或体积无关。Nezafat M等^[20]使用T1-Mapping的STONE序列与DIXON序列结合，同时量化心外膜脂肪含量和心肌 T1弛豫时间，评估心肌病变情况及心脏周围脂肪。结合上面提到大量EAT可对心脏产生侵袭性，未来此种序列的临床应用有希望对EAT的心肌侵袭作出预测。

2 计算机断层扫描评估心脏脂肪

与前两种成像技术相比，CT具有较高的空间分辨率、便捷的三维重建以及可重复性，因此CT扫描目前是心脏脂肪评估的应用较多的方法，优于其他成像方式。更有意义的是，CCTA不仅可以分析EAT及PAT，可以同时对冠状动脉及周围的PCAT进行成像，而不增加额外扫描时间，从而深入了解血管壁的炎性改变与血管周围脂肪之间的关系，对心脏整体的解剖结构乃至心功能作出分析评估^[21]。尽管现在磁共振多模态成像也可以对PCAT进行分析，但是还在处于起步阶段，主流分析手段仍然是基于CCTA图像^[22]。可以发现，使用CT成像技术对心脏脂肪评估具有普适性及准确性。

2.1 CT评估心外膜脂肪 结合前述，心外膜脂肪含量与心脏功能及多种疾病发生发展关系密切，脂肪CT上具有良好的密度对比，因此CT可以更方便的研究脂肪与多种心血管病变等之间的关系^[23]。Kataoka T等^[24]通过CT分析EAT在血管内皮功能中发挥的关键作用，探究其与冠状动脉痉挛之间的关系，发现EAT 与冠状动脉痉挛之间强相关，而与腹部脂肪却没有关系。Lee KC等^[25]使用优化后的OSEM算法，提高了低剂量CT图像的重建质量，并用于心外膜脂肪体积的定量测量。同样发现EAT是冠心病的独立危险因素，与冠脉病变数量、Gensini评分呈正相关，对冠心病未来情况的预测具有重要价值。同样，在心脏功能更脆弱的新冠患者群体中，Abrishami A等^[26]测量EAT 体积与患者其他炎症生物标志物，发现之间存在显著关联，并且与其他患者相比。Slipczuk L等^[27]同样应用胸部扫描结果分析，发现钙化评分 ≥ 4 和EAT $\geq 98 \text{ ml}$ 是新冠患者死亡率的独立预测因子，当指标超过截断值，死亡率分别增加63% ($P=0.003$) 和43% ($P=0.032$)。一次扫描，即可获得多组结果，对临床工作具有显著意义。

2.2 CT评估心包脂肪 相比于EAT的研究数量，PAT明显要少一些。尽管有大量研究确定了EAT 与 CAD 严重程度或心功能之间的相关性，但也有一些研究^[28]未发现它们之间存在任何关联，或疾病严重程度与EAT关联较少，这时就需要考虑其他心脏脂肪产生的影响。Panda S等^[29]对比了正常人和不同严重程度CAD患者之间心脏脂肪的差异，发现CAD和显着CAD组患者的EAT体积、PAT体积、血糖和脂质标志物分别更高，与没有DM的患者相比，DM患者的PAT体积显着增加，并且即使PAT体积较小，左前降支也可能存在CAD。Liu J等^[30]同样将目光放在了PAT的评估，发现EAT及PAT体积可能是冠状动脉钙化评分 (CCS) $\geq 100 \text{ AU}$ 的临床预测因子，尤其是在超重和肥胖个体中，这一手段也可以进一步应用于冠脉急性事件发生概率的预测中。

2.3 CT评估冠状动脉周围脂肪 PCAT作为冠状动脉周围的脂肪沉积物，也是心脏脂肪组织库的一部分，它在动脉粥样硬化发展过程中具有不同的病理生理学特征和作用^[31-33]。同时，数年前研究发现作为衡量心脏炎症指标之一的EAT 体积有一些局限性，比如肥胖和糖尿病的全身性影响；患者使用药物出现的相互作用、副作用；乃至季节变化都会影响EAT的基本状态^[34]，这些系统性影响可能会导致人群之间的差异，或反映机体暂时的变化，无法准确评估冠状动脉炎症。由此PCAT评估开始起步，在近3年中它仍是一个相对较新的概念，并且在各种疾病及患者心功能的预测中体现出了十分优秀的临床应用。Ichikawa K等^[35]在接受冠状动脉CTA的T2DM患者中，证明了评估 LAD-PCAT 衰减可以帮助医生识别高危T2DM患者。类似分析PCAT衰减的研究在近3年的高水平研究中逐渐增多，因此出现了描述PCAT衰减的定量值——脂肪衰减指数 (FAI)，由此对冠状动脉炎性情况进行描述和量化^[36-37]。FAI是一种基于CCTA的冠状动脉炎症生物标志物，在心脏风险及心功能改变的预测方面提供了许多证据，比如可检测更多永久性不良纤维化和血管PVAT重塑，进一步扩大了PVAT表型的价值。You D等^[38]通过收集临床疑似冠状动脉疾病的CCTA检查数据，提取FAI值后，分析其与Gensini评分、左心室功能参数的相关性，结果发现在疑似冠脉疾病患者队列中，高血压、血脂异常、吸烟饮酒史等冠心病危险因素与PCAT均无显著相关性，但LAD-FAI 与多个左室功能参数呈正相关，这也说明FAI作为预测心功能和心肌缺血情况等方面指标，具有简单便捷、高效能的特点，为FAI未来的研究提供了全新的思路^[39-42]。

3 人工智能分析评估心脏脂肪

尽管我们现在有诸多检测手段用于评估心脏脂肪情况，对心脏脂肪组织库进行非侵入性量化，但是执行量化时，手动分割仍然是当今首选的方法^[43]。这种方法需要放射科医生对相关解剖结构进行逐步手动分割，依赖于操作且耗时，不适合常规临床实践。因此近3年，基于人工智能自动分割心脏脂肪，或分析其肉眼无法识别的影响特征作为疾病的诊断预测手段的研究逐渐增多。

人工智能 (AI) 解决方案，临幊上包括机器学习和深度学习，可以在CT和MRI的结果图上快速、自动以及准确的测量及分析^[44-46]。机器学习是指构建基于计算机的算法，无需明确编程即可执行任务，并且可以通过从工程特征中学习分类模式来执行分类或回归任务^[47]。它是影像组学中特征选择和高级模型构建的主要工具，影像组学同样是一个新兴领域，主要工作重点是广泛挖掘从医学图像中提取的高通量特征特点以支持临幊决策或进行建模预测，经常与机器学习同时进行研究^[48]。深度学习则是直接从图像中获取特征和模式进行模型构建与验证，其中卷积神经网络 (CNN) 是最流行的深度学习架构之一，它利用有效减少参数数量的卷积运算，因此需要更少的临幊数据^[49-50]。Commandeur F等^[51]将临床参数与冠状动脉钙化评分 (CAC) 和EAT自动量化相结合，以预测心肌梗死 (MI) 的长期风险和无症状患者的心源性死亡。证明机器学习方法显着改善了心源性死亡的预测效能。Oikonomou EK等^[52]则将关注点放在了PCAT上面，常规CCTA分析PCAT会将更多注意力放在血管周围炎症上，但炎症并不是动脉粥样硬化形成的唯一过程，研究希望通过影像组学特征分析，将脂肪组织不良纤维化和冠周脂肪微血管重塑的影响加入风险预测中，希望可以进一步改善急性心血管事件风险预测。最终发现冠周脂肪的纹理特征可以作为一全新的成像生物标志物 (FRP) 显着改善急性心血管事件预测效能。Lin A等^[53]也把目光放在了PCAT的影像组学特征上，研究其是否可以区分MI患者与稳定或无冠状动脉疾病 (CAD) 患者。发现在 1,103 个计算的影像组学参数中，20.3% 在 MI 患者和对照组之间存在显着差异，这一模型在准确识别 MI 患者方面优于视觉评估 PCAT 衰减的模型。

4 总结与展望

综上所述，心脏脂肪沉积与多种心血管疾病的发生发展、心功能的改变、急性心血管事件的发生均具有重要意义。相比于其他检查手段，MRI、CT的普适性和分辨率使其成为评估心脏脂肪

沉积的首选影像学方法，为正确认识心脏脂肪沉积与诸多心脏病理变化之间的关系提供了可能。除了人工评估心脏脂肪组织外，影像组学与深度学习作为近三年来蓬勃发展的领域。通过这些手段对FAI值进行定量分析和建模，用于诊断和预测心血管疾病的风险及心功能改变的情况，拓展了心血管影像方面的研究。

此外，目前通过CT分析EAT与PAT等心脏脂肪研究趋于饱和，而分析PACT却亟待投入更多精力进行探索。基于大队列患者PCAT的FAI值分析较少，与之相关联的临床研究更少。为了验证FAI值作为成像生物标志物的临床价值，需要进行更多的多中心研究，使其在影像学无创性评估心脏脂肪中具有更高价值。我们也希望未来可以将多参数多模态心脏脂肪影像数据应用于临床，为临床诊治提供更多有价值的信息。

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