

综述

磁共振及超声瞬时弹性成像对代谢相关脂肪性肝病定量评估的研究进展*

王妙艳¹ 朱立红² 华晨辰¹
钱超越¹ 章乐² 蒋昊翔^{1,*}

1.江南大学附属儿童医院影像科
(江苏 无锡 214000)
2.江南大学附属儿童医院中心实验室
(江苏 无锡 214000)

【摘要】代谢相关脂肪性肝病(MAFLD)会导致脂肪性肝炎、肝硬化及肝细胞性癌。肝穿刺是诊断MAFLD的金标准。然而,有创检查不能广泛应用于临床实践中,无创诊断MAFLD是未来发展趋势。目前主要的检查方法有超声瞬时弹性成像、磁共振质子密度脂肪分数、磁共振波谱成像、磁共振弹性成像等。因此,本文就MRI及超声瞬时弹性成像技术在MAFLD定量评估中的研究进展进行综述,旨在为临床精准诊疗提供影像标记物。

【关键词】代谢相关脂肪性肝病; 磁共振; 瞬时弹性成像; 肝纤维化
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Research Progress of Magnetic Resonance and Ultrasound Transient Elastography in the Quantitative Assessment of Metabolic-Related Fatty Liver Disease*

WANG Miao-yan¹, ZHU Li-hong², HUA Chen-chen¹, QIAN Chao-yue¹, ZHANG Le², JIANG Hao-xiang^{1,*}.

1.Department of Radiology, Affiliated Children's Hospital of Jiangnan University, Wuxi 214000, Jiangsu Province, China
2.Central Laboratory, Affiliated Children's Hospital of Jiangnan University, Wuxi 214000, Jiangsu Province, China

ABSTRACT
Metabolism-associated fatty liver disease (MAFLD) can lead to steatohepatitis, cirrhosis, and hepatocellular carcinoma. Liver biopsy is the gold standard for diagnosing MAFLD. However, invasive examinations cannot be widely used in clinical practice, and non-invasive diagnosis of MAFLD is the future development trend. At present, the main inspection methods include ultrasonic transient elastography, magnetic resonance proton density fat fraction, magnetic resonance spectroscopy, and magnetic resonance elastography. Therefore, this article reviews the research progress of MRI and ultrasound transient elastography in the quantitative assessment of MAFLD, aiming to provide imaging markers for precise clinical diagnosis and treatment.
Keywords: Metabolic Cassociated Fatty Liver Diseases; Magnetic Resonance; Transient Elastography; Liver Fibrosis

代谢相关脂肪性肝病(metabolic associated fatty liver diseases, MAFLD)是指肝组织学、影像学或检验学提示肝脏脂肪变,同时合并超重、2型糖尿病或代谢功能障碍^[1]。MAFLD全球患病率约25%,2型糖尿病及肥胖者患病率高达80%~95%^[2-3]。肝组织活检是诊断MAFLD的金标准,但属于有创性操作^[4]。联合影像及临床指标无创诊断MAFLD是未来发展趋势。本文就MRI及超声瞬时弹性成像(transient elastography, TE)在MAFLD定量评估中的研究进展进行综述,旨在为临床精准诊疗提供影像标记物。

1 MAFLD脂肪定量分析

MAFLD肝脂肪变性与糖尿病及心血管等疾病密切相关,后期可进展为肝炎、肝硬化,甚至肝癌^[5]。研究表明,肝脂肪变性是代谢性疾病的早期敏感指标^[6]。脂肪定量分析对早期识别肝脂肪变性及代谢性疾病有重要临床意义。诊疗指南建议MAFLD患者可采用基于TE的受控衰减参数(controlled attenuation parameter, CAP)、磁共振波谱(magnetic resonance spectroscopy, MRS)和MRI质子密度脂肪分数(proton density fat fraction, PDFF)定量检测肝脂肪含量^[7]。

1.1 TE-CAP 超声检查是一种低成本、广泛使用的脂肪变性评估技术。然而,它只能定性诊断,不能进行定量评估,并且对体重指数(BMI)>40kg/m²和肝脂肪含量20%患者敏感度降低^[8]。TE技术便捷无创伤、可以定量检测肝组织,检测范围较肝穿刺广泛^[9-10]。CAP以TE技术为基础,随着脂肪含量增多,CAP指数增加,从而定量评估肝脂肪含量。CAP用于肝脂肪变性分级(steatosis grades, SG)的最佳阈值为SG1≥238dB/m(≥10%)、SG2≥259dB/m(≥33%)、SG3≥292dB/m(≥67%)^[10],在诊断轻-中-重度肝脂肪变性时AUC值分别为0.96、0.82和0.70^[11]。因此TE-CAP可以较好预测肝脂肪变性^[12]。目前,国内以FibroScan设备应用较多。然而,该检查设备需放置于患者肋间隙,且对肝脏需达到一定检测深度,故不适合用于肥胖、肋间隙狭窄和腹水患者^[13]。

1.2 MRI技术 传统的MRI技术通过分辨肝组织信号有无升高判断是否存在肝脂肪变性,但无法定量评估肝脂肪含量^[14]。PDFF是一种基于MRI的肝脂肪变性生物标志物,定义为MR脂肪与MR脂肪和水质子之和的比例^[15]。目前主要有MRS和化学位移成像的PDFF技术,两者均基于水分子和脂肪组织中氢质子进动频率存在差异的原理,通过选择不同的水-脂分离技术定量评估肝脂肪含量^[16]。

1.2.1 MRS MRS可以无创、定量检测肝脂肪变性。由于脂肪组织和水分子共振频率不同,在MRS谱线上位于不同位置,MRS通过谱线分析计算出脂肪含量比例。有研究认为肝脏第V段的脂肪含量较其他段更能反应整体脂肪含量,故放置体素位置应尽量采用肝脏第V段^[17]。以肝穿刺结果作为参考标准,MRS评估肝脂肪变性敏感度为72.7%~88.5%,特异性为92.0%~95.7%^[18]。然而,MRS谱线分辨率不高,手动放置体素位置会产生采样误差,且只能检测单个脂肪峰,结果可能会高估实际肝脏脂肪含量^[19-20]。

1.2.2 MRI-PDFF 基于化学位移的MRI-PDFF是应用MRI特定序列测量脂肪含量的技术。通过调整参数降低T1、T2及T2*等因素的影响,从而检测肝组织的质子密度,只需屏气十几秒就可定量评估全肝脂肪含量。临床上广泛应用的序列主要包括Siemens的Liver

【第一作者】王妙艳,女,执业医师,主要研究方向:肝脏影像学。E-mail: wyflipped@gmail.com
【通讯作者】蒋昊翔,男,副主任医师,主要研究方向:腹部影像学。E-mail: wyszhl@126.com

Lab、GE的IDEAL-IQ序列及Philips的mDixon序列。目前,肝脏放置感兴趣区(region of interest, ROI)获取PDFF方法尚无统一标准,一般建议避开大血管、肝脏边缘、裂隙和胆囊窝,在肝脏第V段或肝脏多段放置多个ROI。有学者提出在不均匀性脂肪肝中使用全肝分割法可以更加准确的量化肝脂肪含量。全肝分割法虽包含了血管、胆管,但对检测结果无明显影响^[21]。MRI-PDFF诊断轻度脂肪肝的敏感度为90%,特异性为93%;诊断中度脂肪肝的敏感度为79%,特异性为84%;诊断重度脂肪肝的敏感度为74%,特异性为81%^[22]。有学者表明,无论以肝穿刺组织学结果还是以MRS作为参考标准,MRI-PDFF对肝脏脂肪变性的评估均具有很高的准确性^[23]。与肝穿刺相比,MRI-PDFF不仅无创伤,还可动态检测脂肪肝进展,对全肝脂肪含量进行测定,减少抽样误差。与MRS相比,MRI-PDFF操作简单,可重复性较高^[21]。并且,MRI-PDFF在评估脂肪变性方面比TE-CAP更准确,在诊断S1-3脂肪变性时,敏感度和特异性均高于TE-CAP^[24]。

2 MAFLD纤维化评估

肝纤维化是指在肝脏慢性炎症和肝细胞损伤时,通过在细胞外基质生成胶原纤维进行修复,然而胶原纤维的过度沉积会导致肝脏正常结构改变及肝功能损伤^[25]。MAFLD包括多种组织学特征,从简单的脂肪变性到伴有小叶炎症和肝细胞气球样变的脂肪变性,都可伴有不同程度的纤维化。研究表明单纯性脂肪变性合并丙氨酸氨基转移酶的患者中17%出现重度纤维化,强调早期检测肝脏纤维化的必要性^[26]。早期肝纤维化是可逆的,准确、及时的诊断对各种慢性肝病及相关并发症的治疗和预后改善有重要意义。肝穿刺是诊断肝纤维化及评估其严重程度的金标准,然而创伤性检查可能导致出血、疼痛、感染等并发症,且患者接受度低、费用较高、不适合连续监测等均限制了肝穿刺的普遍应用^[27]。无创检测肝脏纤维化依从性及重复性高,目前主要包括TE、磁共振弹性成像(magnetic resonance elastography, MRE)及基于扩散加权的弹性成像(diffusion weighted Magnetic resonance elastography, DW-MRE),给肝纤维化早筛提供了更多的选择。

2.1 TE TE作为一种重要的无创定量诊断技术,通过瞬时的振动产生剪切波,根据剪切波速度得到肝脏硬度值(liver stiffness measurement, LSM),从而判断肝纤维化程度。根据LSM可将肝纤维化程度分为5个等级:从F0~F5依次为无肝纤维化、轻度肝纤维化、中度肝纤维化、重度肝纤维化及肝硬化。不同肝脏疾病的LSM诊断阈值不同:LSM=15.0kPa考虑肝硬化;LSM=11.0kPa考虑进展期肝纤维化;LSM<10.0kPa排除肝硬化;LSM<8.0kPa排除进展期肝纤维化;LSM处于8.0~11.0kPa建议患者进一步肝穿刺明确纤维化程度^[28]。临床实践中可能导致LSM升高的因素包括:高体重指数(body mass index, BMI)、肝脏炎症活动度、肝静脉淤血、肝外胆汁淤积和进食^[29]。为避免上述因素可能导致的假阳性,患者应尽量在空腹或餐后3h且血清胆红素<51mol/L情况下进行检测。TE技术无创伤、快速、价格低廉、便携,最重要的是可以同时评估肝脏脂肪变性和纤维化。有学者指出:TE分辨肝纤维化(F2期)的灵敏度为95% (95%CI: 74%~99%),特异性为90% (95%CI: 81%~95%),AUC为0.96 (95%CI: 0.94~0.98)^[30]。然而,TE不能反映所测肝组织的实际位置,单靠TE无法评估肝纤维化的范围以及肝实质中是否存在肿块^[31]。

2.2 MRE MRE是目前最准确的肝纤维化检测及分期的无创技术^[32]。通常在普通MR设备上增加驱动设备,低频的机械振动在肝脏中产生剪切波,使肝组织内质点发生空间位移,根据质点位移幅度计算肝脏中剪切波的传播速度^[33]。采用的序列主要有梯度回波序列及自旋平面回波序列^[34]。最后,通过反演算法处理MR图像创建波图像和描绘组织硬度的定量弹性图像^[32]。研究表明MRE对于≥F2的肝纤维化,灵敏度为79%~94%,特异性为81%~95%,纤维化程度越重,灵敏度和特异性越高^[35]。与TE技术相比,MRE对肥胖和腹水患者的纤维化诊断表现更好,能够检测全肝的纤维化情况,并且能准确诊断肝脏轻度纤维化,诊断性能优于TE。然而,MRE在临床应用上仍有一定的局限性。由于需要额外的驱动设置、特定MRI序列和专业技术人员,普及度仍待提高。另外,

大量腹水、铁沉积、高BMI及患者无法屏气都可能影响MRE评估纤维化的结果^[36]。

2.3 DW-MRE DW-MRE是一种MRI功能成像新技术。DW-MRE根据组织间水分子扩散运动受限制方向和程度的差异得出图像对比度^[37],用表观扩散系数(apparent diffusion coefficient, ADC)值进行定量测量并转换为组织弹性值。肝纤维化程度越重,水分子扩散运动受限加重,血流灌注减少,ADC值降低,表明肝纤维化程度与ADC值呈负相关^[38]。不同分期的肝纤维化ADC值有显著差异,DW-MRE可早期诊断肝纤维化并协助分期^[39]。研究认为使用750s/mm²以上b值检测肝纤维化可以减少微灌注对ADC值的影响^[40],多b值设定为200和1500s/mm²可以更好地反映组织微观结构和生理状态^[41]。以往研究显示:DW-MRE与MRE评估肝纤维化分期具有高度一致性,在区分不显著纤维化(F0-F1)和显著纤维化(F2-F4)的一致性为85%^[42]。DW-MRE无需机械振动装置,可以在不到2分钟的时间内实现多个部分的高空间分辨率图像。然而,DW-MRE空间分辨率有限,图像质量也可能受到炎症、肝硬化、腹水等影响。并且,使用的MRI设备、设定的b值不同,是否采用屏气或呼吸技术都影响到最终的测量结果^[37]。

3 总结和展望

综上所述,MRI和超声TE技术作为无创评估脂肪含量、肝纤维化的检测手段,正逐渐应用于MAFLD临床诊断中。最新研究致力于开发一种自动化检测并评估的算法,不仅可以节约人工选择ROI的时间,还可以进一步减少人为误差,增加MRI技术的诊断准确性^[43]。未来超声TE及多参数MRI联合应用有望辅助MAFLD早期诊断,在指导临床个体化精准治疗中发挥关键作用。

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