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超声评估颈动脉斑块易损性研究新进展

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摘　要

缺血性脑卒中很大程度威胁患者生命，其主要是颈动脉斑块不稳定，脱落所致，采取有效手段评估颈动脉斑块的易损性尤为关键。对于易损斑块的诊断，尚无统一标准，超声因其无创、价格低廉、可重复性高等优势已成为评估斑块稳定性重要手段。

关键词

缺血性脑卒中，斑块，超声

Advanced Research Progresses in Ultrasound Assessment of Carotid Plaque Vulnerability

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Abstract

Ischemic stroke, mainly caused by vulnerable carotid plaque prone to rupture, threatens the life of patients to a great extent. It is particularly important to take effective measures to assess the vulnerability of carotid plaque. There is no uniform standard for the diagnosis of vulnerable plaque and ultrasound has played an importance role in the assessment of plaque stability because its of advantages of non-invasive, low cost and high reptoducibility.

Keywords

Ischemic Stoke, Plaque, Ultrasound

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1. 引言

缺血性脑卒中极大地威胁人类生命健康，已成为中国第一大死因，全球第二大死因[1] [2]，大约18%~25%的缺血性脑卒中是由于颈动脉粥样斑块脱落所致的血栓栓塞引起，尤其是颈内动脉斑块[3]。既往学者发现缺血性脑卒中风险主要取决于颈动脉狭窄程度，然而，近期研究表明，易损斑块破裂出血是脑卒中的独立危险因素，评估斑块的构成及特征能更好地预测脑卒中的发生[4] [5]。超声能较好地识别颈动脉斑块，且操作简便、可重复性高、价格低廉，已被广泛用于颈动脉斑块易损性评估[6] [7]。本文就多种超声成像技术评估斑块稳定性进行综述。

2. 易损斑块的特征

易损斑块是指易破裂出血、易脱落并导致栓塞及一系列中枢系统症状的斑块，有其特定的形态及组成特征。易损斑块组织病理学表现为活动性炎性反应(大量巨噬细胞浸润)、纤维帽较薄、脂质核心体积占比较大(>40%)、斑块裂隙及斑块内新生血管[8]。超声通过声波在不同成分声阻抗不同评估斑块组成及易损性，斑块低回声或者混合回声、形态不规则、表面凹凸不平、斑块内出血、斑块纤维帽薄及斑块内新生血管均提示斑块易损[3]。然而，斑块内钙化对其稳定性影响是复杂的，研究[9]表明，微钙化及边缘钙化斑块不稳定，而致密结节状钙化斑块却很稳定。

3. 超声评估斑块易损性

3.1. 常规二维超声

常规二维超声可直观显示颈动脉斑块的表面特征及内部回声，并可测得斑块的大小、颈动脉狭窄程度、狭窄处的血流参数。斑块表面不光滑、形态不规则、内富含脂质及出血、回声为低回声、斑块厚度变厚、斑块面积明显变大及溃疡斑块均提示斑块易损。为了避免评判斑块回声及表面特征的主观性，有些学者采用灰阶中位数去量化斑块的回声，且研究[10]表明，灰阶中位数与斑块硬度呈负相关，灰阶中位数越小，斑块越硬，其构成纤维帽的胶原蛋白含量越高，斑块的稳定性越高。

二维超声识别易损斑块的特异性较高，但是仍有其局限性，对于中度及重度颈动脉狭窄患者，其诊断敏感性较低，且不能识别斑块内新生血管并区分富含脂质核心和斑块出血[11] [12]。二维图像仅仅显示斑块截断面，无法提供斑块的三维空间位置及体积信息。

3.2. 三维超声(Three-Dimensional Ultrasound, 3DUS)

相较于常规二维超声，3DUS 优势在于可显示颈动脉斑块的立体形态，测量斑块的体积，能更好地评估颈动脉狭窄程度，提高颈动脉易损斑块的检出率。由三维超声测得的斑块负荷(斑块总面积和最大厚度)及斑块体积变化，类似于冠状动脉评分，是预测心脑血管事件的主要因素之一[13]。三维超声可以更好地识别斑块形态特征及区分相邻斑块的溃疡，且表面不规则的斑块及溃疡斑块更易脱落，导致脑卒中。研究[14]表明，在狭窄率 > 60%的患者中，溃疡斑块 ≥ 3 个患者更易导致脑卒中(18% vs 1.7%)。相较于易损斑块患者，3DUS 测得稳定斑块患者斑块体积更大，回声更高，而易损斑块中体积 ≥ 5 mm^3 的患者有更高心血管事件的风险及死亡率[15] [16]。

常规 3DUS 局限性在于其仅仅提供斑块的表面特征，对斑块内部组成如新生血管，并不能加以区分。

此外，3DUS 测量体积精确度易受钙化斑声影的影响。

3.3. 超声造影(Contrast-Enhanceed Ultrasound, CEUS)

CEUS 检查利用超声造影剂(含六氟化硫的微气泡)在血液中产生的散射信号可明显提高时间和空间分辨力，能更清晰地反映粥样斑块所处位置与性质，敏感地呈现斑块动态增强形式，并准确识别斑块表面的溃疡及斑块内新生血管，更好地评估斑块易损性[17]。常规二维彩色多普勒对于严重颈动脉狭窄处低速血流显示不敏感，而 CEUS 可克服其不足，并清晰显示管腔及斑块的轮廓及性质。对比常规二维超声，CEUS 对溃疡斑块的诊断具有更高的准确度、灵敏度[18]。研究[19]表明，彩色多普勒对溃疡斑块的敏感度仅有 41.2%，而 CEUS 高达 94.1%，且 CEUS 结果与 CT 血管造影高度一致。斑块内新生血管的增强程度与组织学微血管密度呈现良好的相关性，CEUS 显示斑块内新生血管增强分级越高，组学学微血管密度越高，且超声造影结果与血清学标志物也呈高度相关，C 反应蛋白含量越高，其斑块内增强程度越高[20]。最近，有学者将 CEUS 联合三维血管分析，对颈动脉斑块进行评估，与 CTA (Computed Tomography Angiography, CTA)及组织学结果一致，其中 CTA 诊断为严重颈动脉狭窄患者，CEUS 诊断准确率为 94.5%，三维血管分析诊断准确率为 98.4%。组织病理学检查显示 71 个易损斑块，各检查诊断准确率分别为 CEUS 93.4%，三维血管分析 90.3%，CTA 92%。证实了两者联合可行性及实用性[21]。目前有关三维超声造影技术数据较少，有待进一步探究其临床价值。

CEUS 仍有其局限性，斑块内钙化对 CEUS 干扰无法避免。虽然超声造影剂经呼吸道即可代谢，但是极少数患者存在一些过敏反应，造影剂的使用扔存在禁忌症，如急性冠脉综合征和急性心衰。

3.4. 超微血流成像(Superb Micro-Vascular Imaging, SMI)

SMI 采取自适应算法，可去除组织运动的杂乱信号，将微小血管可视化，已经广泛用于甲状腺及乳腺肿块的良恶性评估，且收到良好社会评价[22]。SMI 相较于常规二维超声，能更好地滤过低速血流信号，优势明显。对于颈动脉斑块，SMI 可将斑块内新生血管可视化，有助于评估斑块易损性及预测患者脑血管意外风险。有 Meta 分析[23]表明，SMI 与 CEUS 对斑块内新生血管的检测结果高度一致(Kappa = 0.743, $P < 0.01$)。CEUS 和 SMI 对斑块新生血管评估中分级越高，术后组织中新生血管的密度越大，且都与斑块的厚度相关[24] [25]。SMI 价格低廉，方便快捷，无造影剂过敏且适用于急性冠脉综合征患者，因此，在评估颈动脉斑块内新生血管及易损性方面，SMI 有替代 CEUS 的潜力。但现阶段其应用较少，需要大量的临床数据来支撑，

3.5. 剪切波弹性成像(Shear Wave Elastography, SWE)

SWE 通过剪切波在不同硬度物质之中的传播速度不同，从而可反应组织的软硬度并测得其杨氏模量，评估其组成成分，进而评估斑块的易损性。斑块的平均杨氏模量值越小，则其内坏死脂质核心占比越多，斑块越易损，越容易脱落形成血栓；相反，其钙化及纤维组织含量就越高，斑块稳定性越好[26]。

有学者研究发现，在有颈动脉斑块患者中，无同侧脑缺血症状着及稳定斑块的杨氏模量值高于有症状着及不稳定斑块[27]。有学者联合 SMI 和 SWE 评估斑块的稳定性，对比患者症状、多种影像学结果及组织学病理结果，证明了超声检查优势，二维超声测得灰度中位值和 SWE 测得杨氏模量能较好地反应斑块软硬度，有症状患者比无症状患者杨氏模量值小；SMI 和 CEUS 可以识别斑块内新生血管，其分级越高，斑块越不稳定[28] [29]。

3.6. 斑点追踪成像(Speckle Tracking Imaging, STI)

STI 是用来评估组织硬度的一种新技术，通过追踪标记点在心动周期内的运动，将动脉的力学参数(应

变和应变率等)进行量化，在心血管方面的应用具有较高的价值[30]。研究表明，较低的颈动脉管壁应变提示较高的脑卒中风险。脑卒中组的应变明显低于对照组(5.6 ± 1.6 vs 4.2 ± 1.7，$P < 0.001$)，且应变与卒中独立相关，结合传统的颈动脉中内膜厚度能更好地预测脑卒中风险[31]。关于这项技术在颈动脉斑块研究较少，有待更多临床数据证实其实际价值。

3.7. 血管内超声(Intravascular Ultrasound, IVUS)

IVUS 通过探头发出声波信号在患者体内产生散射形成的图像，可以实时显示斑块的形态和性质，有较高的血管分辨力。IVUS 虚拟组织学成像(Virtual Histology-Intravascular Ultrasound, VH-IVUS)是基于 IVUS 的新技术，可实现血管三维可视化并分析不同斑块成分[11]。VH-IVUS 可将斑块分为坏死核心、纤维斑块、纤维脂质斑块和致密钙化斑块 4 种。研究表明，IVUS 显示斑块特征与内膜剥脱术后组织学结果高度相关[32]。但 IVUS 属于有创性检查，对于微钙化敏感性较差，且不能定量评估斑块的力学特征。

4. 小结

颈动脉斑块易损性评估对预测缺血性脑卒中有重大意义，不同超声检查技术对斑块评估各有其优势，如三维超声能立体显示斑块，CEUS 和 SMI 能显示斑块内新生血管，SWE 能量化斑块硬度以推测其构成，而多项超声技术联合能更好地评估斑块的易损性，如三维超声联合 CEUS。多种超声检查技术的联合应用对颈动脉斑块稳定性的评估意义重大，有助于预测缺血性脑卒中发生风险。

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