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Hans汉斯

血管内超声在颈动脉支架置入术中应用的研究进展

袁杰宏

山东大学，山东省立医院神经内科，山东 济南

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摘 要

血管内超声(intravascular ultrasound, IVUS)是一种基于导管的超声装置，能清晰显示血管的横断面，准确测量管腔数据，其衍生的虚拟组织学(virtual histology, VH)技术可以识别动脉粥样硬化斑块的组成并进行组织学分型。传统的依靠狭窄程度评价病变的技术在颈动脉支架置入术(carotid artery stenting, CAS)中存在局限性，而IVUS可以优化支架的选择和评估置入效果，从而改善治疗结果。IVUS在CAS术后并发症的预测方面也表现出良好的应用价值。本文通过对IVUS辅助CAS的研究进行回顾，综合分析IVUS在CAS中的应用。

关键词

血管内超声，颈动脉支架置入术，颈动脉粥样硬化斑块，综述

Research Progress on the Application of Intravascular Ultrasound in Carotid Stenting

Jiehong Yuan

Department of Neurology, Shandong Provincial Hospital, Shandong University, Jinan Shandong

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Abstract

Intravascular ultrasound (IVUS) is a catheter-assisted ultrasound device that is able to provide cross-section images of vessel, accurate measurement of lumen. The derived virtual histology (VH) technique is capable of evaluating tissue properties and different components can be visualized as different colors. Traditional technology that depends on stenosis degree to evaluate lesions has

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limitations in carotid artery stenting (CAS), while IVUS can optimize the selection of stents and evaluate the effect of stent implantation, improving the treatment outcome. IVUS is also valuable in predicting postoperative complications of CAS. This review is aimed to describe the progress on the application of IVUS in CAS.

Keywords

Intravascular Ultrasound, Carotid Artery Stenting, Carotid Atherosclerotic Plaque, Review

1. 引言

在全球范围内，脑卒中是第二大死亡原因，具有高发病率、高复发率、高致残率、高死亡率的特点，带来了较高的经济负担[1]。其中，颈动脉斑块的脱落和颈动脉狭窄是引起缺血性卒中的重要原因[2] [3]。颈动脉支架置入术(carotid artery stenting, CAS)是临床上对中重度颈动脉狭窄患者的治疗方式之一。颈动脉斑块形态在决定 CAS 的预后中起着重要作用，常规的脑血管造影(digital subtraction angiography, DSA)存在着局限性，血管内超声(intravascular ultrasound, IVUS)及其扩展的虚拟组织学血管内超声(virtual histology intravascular ultrasound, VH-IVUS)技术可实时评估斑块特征并指导决策[4] [5]。

2. IVUS 的基本原理

2.1. IVUS

IVUS 的基本原理是将植入微型换能器的超声导管通过有创的介入技术置于目标动脉管腔内，利用换能器发射超声波，采集进入不同组织界面而产生的反射回波，再应用图像处理系统重建超声图像，可以在超声导管沿血管腔回撤的过程中采集并记录管腔形态和斑块的横截面图像[6]。图像的分辨率与超声换能器的频率直接相关，随着频率增加，轴向分辨率增加，但穿透深度下降，常规应用的频率为 20~40 MHz，其纵向分辨率 60~200 μm，横向分辨率 110~400 μm [7]。IVUS 应用超声原理成像，因此具有不受血流影响的优点，且有利于显示深部结构，结合图像处理系统，可较为准确地测量血管腔和斑块的大小，为血管腔内情况提供定量的数据作为参考[8]。

2.2. VH-IVUS

VH-IVUS 是在 IVUS 基础上进行的后处理技术，通过对反向散射的回声频谱信号进行分析，识别动脉粥样硬化斑块不同成分的回声频率，从而模拟斑块的组织学构成并使用不同颜色进行编码：纤维组织定义为绿色，主要由致密的胶原纤维组成；纤维脂肪组织定义为黄色，主要由包含脂质的松散胶原纤维组成；坏死核心组织定义为红色，主要包含死亡的泡沫细胞以及胆固醇结晶等；致密钙化组织定义为白色，主要为沉积的钙化晶体[9] [10]。既往研究已经证明 VH-IVUS 与传统的体外组织病理学结果有良好的一致性[9] [10]。

3. 在颈动脉支架置入术中的应用

3.1. 颈动脉粥样硬化斑块的分型与评估

动脉粥样硬化是一种脂蛋白驱动的疾病，在炎症细胞募集、泡沫细胞形成、细胞凋亡和坏死、纤维化和钙化等过程共同作用下形成斑块，斑块的破裂和血栓的形成是导致缺血性卒中的重要原因[11]。IVUS 衍生的 VH-IVUS 技术为颈动脉粥样硬化斑块的虚拟组织学评估提供了基础。Diethrich 等[12]在颈动脉粥样硬化斑块的 VH-IVUS 评估研究中引入组织学分型[13]，通过结合组织学切片分析证实 VH 技术具有较高的诊断准确率：薄帽纤维粥样斑块(Thin-cap fibroatheroma, TCFA) 99.4%、钙化的薄帽纤维粥样斑块(Calcified thin-cap fibroatheroma, CaTCFA) 96.1%、纤维斑块 85.9%、纤维钙化斑块 85.5%、病理性内膜增厚 83.4%。Fuchs 等[14]的研究发现组织学结果与 VH-IVUS 分类的一致性为 86.1%。González 等[15]将连续出现 3 帧图像为 TCFA 或 CaTCFA 特征的斑块定义为易损斑块，分析了 36 例接受 CAS 的患者，发现有症状患者易损斑块发生率明显高于无症状患者(52.6% vs 31.8%, $p < 0.022$)，进一步验证了伴坏死核心向管腔融合的 TCFA 以及伴钙化融合区域的 CaTCFA 具有较高的不稳定性。IVUS 可以作为一种额外的手段用于斑块稳定性的评估。

3.2. 指导支架的选择

IVUS 可以提供三维可视化的血管横截面图像，可精确显示管腔和管壁，多项研究报道了 IVUS 用于测量血管直径、评估病变程度，指导支架尺寸和种类的选择。Clark 等[16]对 98 例 CAS 患者的报道发现 IVUS 指导下选择的支架直径较 DSA 指导下的选择更大。Joan 等[17]报道了 18 例 IVUS 辅助的经股颈内动脉支架置入术，发现 IVUS 测量的颈内动脉平均直径较 DSA 估计值大 1.64 ± 0.22 mm，其中 5 例患者的支架尺寸从最初的 6~8 mm 更改为 8~10 mm。Bandyk 等[18]回顾性分析了 220 例 CAS 手术，IVUS 辅助下最终支架和球囊直径的选择较 DSA 显示的更大。IVUS 可以作为 DSA 的补充，为支架型号的选择提供依据。

3.3. 支架置入效果的评估

冠状动脉的经验支持支架扩张不足和显著残余狭窄与支架血栓形成有关[19] [20]，支架置入效果的评估具有重要意义，但常规的 DSA 可能难以识别。Chiocchi 等[21]对 60 例患者进行了颈动脉支架置入后的 IVUS 评估，发现 2 例患者存在造影未显示的支架贴壁不良，予以后扩张治疗。Clark 等[16]和 Irshad 等[22]的研究通过 IVUS 检测到支架错位。支架置入后应用 IVUS 检测可以及时发现支架贴壁不良、扩张不充分、支架异位等情况，从而采取补救措施改善治疗效果。目前在颈动脉支架置入术中 IVUS 的评价标准仍借用了冠状动脉的经验，包括：(1) 支架完全贴壁；(2) 支架内最小横截面积 ≥ 平均参考血管横截面积的 90%；(3) 偏心指数(每一帧图像测得最小支架直径/最大支架直径的平均值) ≥ 0.7；(4) 支架完全覆盖病变[23] [24]。

3.4. 支架术后并发症的预测

3.4.1. 卒中/短暂性脑缺血发作(Transient Ischemic Attack, TIA)

在描述 IVUS 辅助下 CAS 的研究中，术后卒中/TIA 的总患病率为 4% (95% CI 3%~5%) [25]，在描述 CAS 术后并发症的综述中，报道的缺血事件总发病率为 6% [26]。Musialek 等[27]在 222 例患者中前瞻性地评估了栓塞保护装置(embolic protection devices, EPD)辅助与无 EPD 辅助的 IVUS 在 CAS 中的安全性，没有发现 IVUS 相关的卒中或死亡事件，其他多项研究也报道了 IVUS 应用的安全性[16] [28]。但目前的研究结果显示 IVUS 在预测术后卒中/TIA 的应用价值有限。Clark 等[16]的研究在 98 例 CAS 患者中报道

了 4.7%的卒中发生率，并发现 IVUS 在动脉 3 或 4 个象限检测到浅表钙的患者与没有严重浅表钙的患者相比，卒中的发生率更高(31% vs 1%, $p < 0.001$)。TCFA 和 CaTCFA 被认为是易损斑块类型，可能导致术后栓塞[29]。然而 Sangiorgi 等的研究在 119 例 CAS 患者中报道了 3 例术后卒中/TIA，未发现术后并发症与 VH-IVUS 特征之间具有统计学关联[28]。目前认为这种结果可能与累积事件较少有关，需要更大规模的研究和更长期的随访[28]。

3.4.2. 无症状卒中/微栓塞/无症状脑缺血性病变(Silent New Ischemic Cerebral Lesions, sNICL)

无症状卒中/微栓塞/sNICL 均被定义为“CAS 术后颅脑磁共振弥散加权影像可发现的缺血性病变，但无明显中风或 TIA 的临床症状”[25] [30] [31]。目前的研究报道术后 sNICL 的发病率为 21%~85% [30]，且与认知功能受损有关[32] [33]。Timaran 等[34]和 Hitchner 等[35]应用 VH-IVUS 评估颈动脉粥样硬化斑块的组成成分，并未发现 VH 特征与 sNICL 的关联。Yamada 等[36]利用 VH-IVUS 对 45 例 CAS 患者进行了颈动脉斑块的分析，共 18 例患者出现术后同侧无症状缺血性病变(ipsilateral silent ischemic lesions, NISIL)，发现 NISIL 阳性组患者颈动脉最狭窄处相对纤维脂肪组织面积显著高于阴性组(32.7% ± 13.2% vs 18.3% ± 9.8%, $p < 0.001$)，且证实斑块最狭窄处的相对 FF 面积是 NISIL 的独立预测因子。

3.4.3. 斑块突出(Plaque Protrusion, PP)/支架内斑块突出(In-Stent Protrusion, ISP)

PP/ISP 被定义为在 CAS 过程中斑块突出到支架腔内，被认为与 CAS 术后栓塞并发症和急性支架内血栓形成有关[37] [38]。Shinozaki 等[39]评估了 77 例 CAS 手术，发现首次扩张后 IVUS 较 DSA 有更高的 PP 检出率(7.8% vs 2.6%)。Kotsugi 等[40]对 354 条颈动脉的研究得到了类似的结果，IVUS 对 PP 的检出率较 DSA 更高(7.6% vs 2.6%)，并验证了 PP 与缺血性并发症相关。Chiocchi 等[21]和 Okazaki 等[41]的研究也应用 IVUS 检出 PP/ISP，并采取抽吸或支架内置入支架的手段进行补救。检测 ISP 对预防术后并发症具有重要意义，也存在其他影像学手段进行检测[37] [42]，但暂无高质量的证据表示优于 IVUS。

3.4.4. 围手术期低血压

CAS 围手术期出现的血流动力学改变可能会增加缺血事件的发生率[43]，位于颈动脉窦的压力感受器在血压和心率的调节中起着重要作用[44]。只有一项研究报道了 VH-IVUS 用于预测 CAS 围手术期低血压，Tsurumi 等[45]在 45 例 CAS 患者中发现 VH-IVUS 上的纤维斑块是围手术期低血压的独立危险因素。

4. 小结与展望

IVUS 技术在 CAS 中可以提供更多的血管腔内信息，其衍生的 VH 技术可以直观地对评估颈动脉斑块的分型和组成，在指导支架置入和预测术后并发症等方面具有一定的价值。尽管在目前的研究中使用 IVUS 辅助 CAS 显示出积极的方向，但仍具有一些局限性。IVUS 会增加额外的手术费用，并且到目前为止，没有关于 IVUS 辅助 CAS 在住院时长、住院花费、再入院情况等成本效益方面的研究，无法证明常规应用 IVUS 的合理性。IVUS 可以提供更多的影像信息，但其直接改善手术结果的证据有限，仍需更大样本的临床研究提供高质量的数据。随着多模血管内影像的发展[46]，希望这些研究可以为更有意义和应用前景的诊断方法提供参考。

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