

高分辨率血管壁成像评估颅内动脉瘤稳定性的研究进展

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摘要

与传统血管成像技术(CTA、MRA及DSA)相比, 高分辨血管壁成像技术不仅可以提供动脉瘤不同时期的形态学特征, 更可以清晰的显示血管壁的结构, 钆对比剂注射后还可以反映出血管壁的炎性改变, 通过评估动脉瘤壁强化, 从而评估颅内动脉瘤的稳定性。本文对HR-VWI在评估颅内动脉瘤稳定性的研究进展进行综述。

关键词

高分辨率血管壁成像, 颅内动脉瘤, 动脉瘤稳定性, 动脉瘤壁强化

Research Progress in Evaluating the Stability of Intracranial Aneurysms with High Resolution Vascular Wall Imaging

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Abstract

Compared with traditional angiography techniques (CTA, MRA and DSA), high-resolution vascular wall imaging can not only provide the morphological characteristics of aneurysms at different periods, but also clearly display the structure of the vascular wall. After injection of gadolinium con-

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trast agent, it can also reflect the inflammatory changes of the vascular wall, and evaluate the stability of intracranial aneurysms by evaluating the strengthening of the aneurysm wall. This article reviews the research progress of HR-VWI in evaluating the stability of intracranial aneurysms.

Keywords

High Resolution Vascular Wall Imaging, Intracranial Aneurysms, Aneurysm Stability, Aneurysm Wall Enhancement

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1. 引言

未破裂的颅内动脉瘤(Unruptured intracranial aneurysms, UIAs)的发病率很高,全球3%~5%的成年人可能患有动脉瘤[1]。但是动脉瘤性蛛网膜下腔出血(Aneurysmal subarachnoid hemorrhage, aSAH)的发病率却很低(每年每10万人中只有3~50例)[2][3],这表明大多数未破裂动脉瘤是没有症状表现的。动脉瘤破裂发生的危险因素很多,包括动脉瘤特异性(大小、形态和位置)和患者特异性(年龄、种族、性别、aSAH病史和高血压)因素;其中一些包含在破裂预测模型中,例如PHASES评分[4],但是,它们的临床应用并不广泛;尽管大多数未破裂动脉瘤都很小(破裂风险最低)[5],但是大多数破裂的动脉瘤也很小,这一观察结果被称为“动脉瘤悖论”,强调了动脉瘤不稳定性生物标志物的必要性,特别是在评估常见的、小的未破裂动脉瘤时。由于非侵入式神经血管成像技术的广泛应用,偶然发现动脉瘤的检出率增加,这表现更加明显[6]。

目前,评估颅内动脉的传统成像技术有磁共振血管造影(Magnetic resonance angiography, MRA)、计算机断层扫描血管成像(Computed tomography angiography, CTA)和数字减影血管造影(Digital subtraction angiography, DSA),这些成像技术倾向于显示血管腔的情况,缺乏对血管壁及灌注的评估。但是,管腔的改变例如狭窄和扩张一般是因为血管壁损伤引起的,因此这些传统的管腔成像技术在评估IA方面还是有一定的局限性。高分辨率磁共振血管壁成像(High-resolution magnetic resonance vessel wall imaging, HR-MR VWI)是一种能够提供动脉瘤壁特征信息的新兴技术模式[7],目前已应用于许多不同类型的颅内血管病,从动脉瘤到狭窄闭塞性血管病;HR-VWI能给我们提供管腔信息,使我们能直接可视化血管壁中的病理部位,从而使我们能够研究疾病机制;HR-MR VWI的成像原理是通过抑制血管内血流还有血管外脑脊液信号,利用高对比度分辨率和高空间分辨率,只显示血管壁的信号,使血管壁结构可视化成为可能[7]。

2. 动脉瘤壁强化

Matouk CC等人[8]首先提出使用HR-MR VWI来识别动脉瘤性SAH的破裂部位,他们发现与未破裂的IA相比,破裂的IA在所有病例中表现出厚壁强化。HR-MR VWI现在被提出用于根据动脉瘤壁强化(AWE)的存在来识别容易破裂的不稳定IA。Santarosa C等[7]提出已有定性和定量方法可用于评估AWE,最简单的方法是区分有或没有动脉瘤壁强化的IA;其他的定性方法是将AWE分为无强化/轻微强化/明显强化[9]、局灶性强化/环形强化[10][11]或薄壁强化/厚壁强化[10]。Nagahata等[9]将“明显的AWE”定义

为动脉瘤增强,与脉络丛或静脉丛的动脉瘤增强相同,“轻微的 AWE”定义为造影剂扫描前后壁信号强度增加;他们的结果显示,破裂动脉瘤组有 78.3%的动脉瘤出现了瘤壁强化,而未破裂组只有 4.8%的强化率,破裂组的动脉瘤瘤壁强化程度明显高于未破裂组的瘤壁强化。但是,瘤壁强化程度的高低与动脉瘤发生发展之间的关系还有待进一步验证。2018 年,Edjlali 等[10]提出了将 AWE 分为 4 级:0 级——无强化;1 级——局灶性厚壁强化(>1 mm);2 级——薄壁环形强化(≤ 1 mm);3 级——厚壁环形强化(>1 mm),他们发现环形强化的是大约 90%增大或破裂的动脉瘤,而稳定的动脉瘤只有 30%出现这一特征。AWE 评估的定量方法根据壁强化指数(WEI)的测量值,该指数定义是钆剂注射前后 IA 壁信号强度的变化,或动脉瘤与垂体柄强化比率的测量[7];结果表明,破裂动脉瘤组的动脉瘤壁强化指数显著高于未破裂组。这些研究都表明,IA 的瘤壁是否强化以及强化程度与动脉瘤是否稳定有关,然而 IA 的瘤壁发生的炎性改变又与动脉瘤的稳定性密切相关,因此我们认为或可将 AWE 作为血管壁炎性反应的标志。

2.1. 瘤壁强化与动脉瘤特征

多项研究提出 AWE 的存在与 IA 的解剖学特征相关,如大小、位置和形状。他们的研究结果[12] [13] [14]表明较大的 IA 中的 AWE 更高;但是,在较小的 IAs (尺寸 < 7 mm)中也会出现 AWE [14];高深度/颈宽长宽比被证明与较高的 AWE 相关[13] [15];较大的 AWE 值多见于位于大脑前动脉、后交通动脉、后循环动脉或大脑中动脉的 IAs [14]。在临床使用的评分(PHASES、UIAT 和 ELAPSS 评分)中,其中一些位置被认为具有破裂的高风险;不规则的 IA 形状可能会导致与内皮功能障碍相关的血流模式改变,进而导致通透性增加或造影剂停滞,尽管情况并不一定总是如此,但是 IA 不规则形状存在时,通常会观察到比较高的 AWE [15] [16] [17] [18] [19]。子囊的存在与异质性 AWE 有关,AWE 存在于动脉瘤的主囊中,但在子囊中通常不存在[16]。

有人认为 IA 的形成、重塑以及破裂与血流动力学力有关,Shimizu 等[20]在最近对大鼠进行的一项研究中证明,低壁剪切应力(WSS,即每单位面积流动的血液对动脉壁施加的切向力)和高振荡剪切指数(OSI,即 WSS 波动的大小与心动周期的函数)与动脉瘤生长区域共同定位,并且这些区域被巨噬细胞高度浸润;AWE 与低时间平均 WSS、低最大 OSI 和大的低剪切面积共定位[21] [22] [23],表明 AWE 与低 WSS 条件相关,但有必要进一步研究血流动力学与 AWE 之间的联系。一些研究调查了 AWE 是否与临床上用于评估特定 IA 破裂风险的评分相关,结果显示 AWE 与 PHASES 评分、UIAT 评分或 ELAPSS 评分呈正相关[12] [21],然而,也有研究[13]表明 UIAT 评分与 AWE 之间也不存在相关性。Hartman 等[24]描述,PHASES 评分 > 3 分的 IA 更常出现壁薄和 AWE。到目前为止,还没有证据表明 AWE 与吸烟状况、每日使用乙酰水杨酸或他汀类药物、高血压、性别、糖尿病或 IAs 家族史之间存在关联[13] [14] [18] [19]。

2.2. 瘤壁强化与动脉瘤的瘤壁组成

在发生动脉瘤性蛛网膜下腔出血的情况下,Matouk CC 等人[8]首先使用 AWE 来识别责任动脉瘤。事实上,几乎所有破裂的 IA 在成像中都会出现瘤壁的强化,在这类破裂的 IA 中,基于术中检查以及组织学检查,AWE 与炎症细胞浸润[9] [25]或者与动脉瘤的破裂部位存在止血血栓有关;更具体地说,有研究发现环形 AWE 与大量炎症反应和新生血管形成的关系更为密切,而局灶性 AWE 似乎更多的出现在新鲜腔内血栓滞留造影剂的情况下[26]。因为炎症也见于未破裂的 IA [27],并且容易导致 IA 不稳定,因此建议使用 AWE 的有/无来区分稳定和不稳定的未破裂 IA;AWE 与未破裂 IA 壁内中性粒细胞或巨噬细胞的存在呈正相关[17] [19] [28] [29]。在出现 AWE 但是没有髓过氧化物酶活性的动脉瘤中,存在病理性滋养血管[28];病理性的滋养血管十分脆弱,很容易出血破裂造成血液外渗,同时将造影剂以及一些炎性细胞运输到动脉瘤壁。病理性滋养血管通常在非病变颅内动脉中不存在,但它们可以在动脉粥样硬化性病

变和血管壁重塑的缺氧情况下出现; 因此, 在动脉瘤壁中发生动脉粥样硬化性病变和新生血管形成时, 就可以看到 AWE 的出现[17] [19] [29]。另外, 未破裂 IA 中的动脉粥样硬化斑块似乎与局灶性 AWE 比均匀性 AWE 更相关[17]。Ishii 等[30]通过比较未破裂 IA 管腔和载瘤动脉的脂蛋白(a)浓度, 发现较高的脂蛋白(a)浓度与未破裂 IA 的 AWE 增加有关, 血栓形成的动脉瘤壁的 AWE 也更高[15] [19]。Matsushige 等[16]报道, 分别在薄壁(20~50 μm)和厚壁(120~320 μm)中观察到局灶性和环形 AWE。总而言之, 对未破裂的 IA 进行的研究表明, AWE 可能是由于壁增厚伴炎性细胞浸润和滋养血管的存在、壁变薄伴内皮屏障完整性受损或壁内血肿。

2.3. 临床中瘤壁强化的应用

对于破裂的 IA, AWE 可用于识别多发性 IA 患者的责任动脉瘤。基于 AWE 的模式, 识别腔内血栓(局灶性 AWE), 提示 IA 破裂的部位, 有助于临床治疗[31]。目前, 在日常临床实践中使用 HR-MR VWI 检测和解释未破裂 IA 中的 AWE 尚未达成共识。然而, 无论使用何种方法对 AWE 的缺失/存在进行分类或对 AWE 进行分级, 不同的研究人员似乎都能够使用 HR-MR VWI 区分稳定和不稳定的 IA。最近一篇系统综述和荟萃分析文章[32]纳入了 6 项研究的 500 多例动脉瘤, 结果显示, AWE 筛查不稳定 IA 的敏感性较高(95%); 重要的是, 作者还表明, AWE 的缺失与 IA 稳定性密切相关(阴性预测值为 96%)。Gariel 等[33]在一项前瞻性队列研究中纳入了 2 例未破裂的小 IA, 随访了 25 年, 已经证明 AWE 增加是 IA 壁生长和不稳定性的标志。在两项回顾性纵向研究中[16] [34], 作者发现, 与稳定型 IA 相比, 有形态学改变的 IA 患者更常见 AWE。目前关于 HR-VWI 在颅内动脉瘤患者中的临床应用的证据有限, HR-VWI 尚未在任何临床研究中得到验证, 也可能不能一致地用于临床决策, 所以仍需要更长的纵向随访研究来确认 AWE 作为壁不稳定性的独立生物标志物的使用。

3. 小结

HR-VWI 对 IA 疾病来说是一个非常具有前途的工具, 目前的证据表明, HR-VWI 可能成为动脉瘤不稳定和破裂风险的一个重要的非侵入性生物标志物, 能更好地表征动脉瘤壁(不稳定性), 为颅内动脉瘤的治疗提供新的见解, 帮助临床医生决定观察或治疗未破裂的 IA。重要的是, 动脉瘤没有强化可能反映了稳定、未破裂的表型, 更大规模的多中心前瞻性研究将促进 HR-VWI 在常规临床实践中的广泛应用。

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