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高分辨率磁共振血管壁成像在动脉粥样硬化性缺血性脑卒中诊治中研究进展

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摘　要

缺血性脑卒中(ischemic stroke, IS)具有高发病率、高致残率及高复发率特点，颅内动脉粥样硬化为其主要致病原因。高分辨率磁共振血管壁成像(high-resolution magnetic resonance vessel wall imaging, HRMR-VWI)是直接评估血管及斑块的血管壁成像技术，通过体外对血管壁的无创可视化，定量评估血管壁及动脉斑块的特征，为临床医生提供进一步的疾病信息。本文就高分辨率磁共振血管壁成像对动脉粥样硬化性缺血性脑卒中的临床应用进行综述。

关键词

缺血性脑卒中，动脉粥样硬化，高分辨率磁共振血管壁成像，不稳定斑块

Research Progress of High-Resolution Magnetic Resonance Vascular Wall Imaging in the Diagnosis and Treatment of Atherosclerotic Ischemic Stroke

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Abstract

Ischemic stroke (IS) is characterized by high incidence, high disability and high recurrence rate, and intracranial atherosclerosis is the main cause. High-resolution magnetic resonance vessel wall imaging (HRMR-VWI) is a vascular wall imaging technique that directly evaluates blood vessels and plaques, and quantitatively evaluates the characteristics of vascular walls and arterial plaques through non-invasive visualization of vascular walls *in vitro*, providing clinicians with further disease information. This article reviews the clinical application of high-resolution magnetic resonance vascular wall imaging in atherosclerotic ischemic stroke.

Keywords

Ischemic Stroke, Atherosclerosis, High-Resolution Magnetic Resonance Vascular Wall Imaging, Unstable Plaques

1. 引言

全球疾病负担研究显示，脑卒中已经成为近三十年(1990~2020)世界范围内导致健康损失的十大主要原因之一，其中有 62.4%为缺血性卒中[1]。颅内动脉粥样硬化疾病(Intracranial atherosclerosis disease, ICAD)是 IS 的主要原因[2]，动脉粥样硬化斑块的特点(如斑块负荷和稳定性)与 IS 的高发病率、高复发率有关。HRMR 能够直接观察活体动脉管腔、管壁以及管周情况，可以提供多维度的血管评估，包括管腔狭窄程度、管壁形态、斑块的形态和分布、斑块内出血、斑块的强化程度，其影像结果与病理学结果具有良好一致性，对动脉粥样硬化性 IS 的风险评估、诊断，治疗方式选择及预后判断具有重要的临床价值[3] [4] [5] [6] [7]。本文将 HRMR 在动脉粥样硬化性 IS 中的临床应用从 IS 的风险评估、病因及机制判定、治疗方案选择三个方面进行综述。

2. HRMR 在缺血性卒中风险评估中的应用

颅内动脉粥样硬化(Intracranial atherosclerosis, ICAS)在不同种族人群发生的比例不同。与颅外动脉粥样硬化相比，ICAS 在亚洲裔、西班牙裔和非裔美国人 IS 患者中的发生率更高，我国合并有颅内动脉粥样硬化狭窄的 IS 患者占 50%。传统的血管评估手段，如磁共振血管成像(Magnetic Resonance Angiography, MRA)、计算机断层扫描血管造影(computed tomographic angiography, CTA)、数字减影血管造影(digital subtraction angiography, DSA)能对血管狭窄程度进行评估，但不能评估斑块特点，而 HRMR 有助于评估包括管腔特点、斑块形状及分布、斑块成分等动脉斑块的特征，分析斑块特征与 IS 发生风险成为了近年来的研究热点[6] [7] [8]。

2.1. 管腔特点

通常认为动脉粥样硬化狭窄，是导致 IS 的主要因素之一，研究提出重度狭窄(≥70%)是 IS 的独立危险因素[9]，可导致一年内 5%~19%的复发[6]，斑块的大小直接影响了血管腔内直径，决定狭窄程度，HRMR

研究发现，除了管腔直径外，不同的血管重构模式也在 IS 进程中发挥了重要作用[8]，血管重构是动脉粥样硬化发生时血管做出的适应性改变，常规检查手段无法识别，但 HRMR 不仅可以直观地观察血管重构的状态，还可以通过测量狭窄处血管的面积与参考层面血管面积定量计算管腔的重构指数。根据重构指数分为正性重构(Positive remodeling, PR)和负性重构(negative remodeling, NR)，PR 的特点是血管向外扩张，代偿维持血管管腔大小的同时斑块破裂风险增高，从而导致 IS 发生，NR 的特点是血管向内收缩，可加重狭窄，但可使斑块相对稳定[10] [11]，因此，正性重构被认为是 IS 的风险因素，但相关研究样本量均较少，且目前尚无研究同时将狭窄程度与重构模式进行系统分层，以评估二者对于 IS 的独立风险，重构模式在 IS 发生机制中扮演的角色仍需进一步探索。

2.2. 斑块形状及分布

大量研究指出，斑块的形状和分布对 IS 风险评估有重要作用，斑块的规则性、弧形影响着血流对斑块表面的作用力和作用点，与斑块不稳定性相关；斑块的分布，决定了其与具体血管的相应关系，从一定程度上划定了梗死的可能性和发生区域。目前对斑块形状的研究多局限于偏心和同心角度，Xu 的研究证明，偏心斑块常表现为正性重构，同心性斑块表现出负性重构[12]，因此偏心性斑块更可能是 IS 的风险因素。Hyung-So 研究团队发现，同时存在同心斑块和偏心斑块预测未来狭窄加重的可能性很高[13]，但该团队只纳入了来自单一中心的少量患者，且并未将其与同心、偏心斑块独立比较。在对颈内动脉的研究中，可根据斑块形状预测斑块内出血风险，斑块弧形位于最大壁厚的上游者(Type I 型)比起下游者(Type III 型)更容易引起斑块内出血，颈动脉分叉处的上方也更容易引起斑块内出血[14]，斑块内出血与 IS 的关系将在后文阐述。斑块位置分布对 IS 发生部位、风险均有一定预测作用，例如，分布在基底动脉的斑块多与后循环 IS 相关，位于基底动脉后壁的斑块，IS 部位更常出现在桥脑，位于侧壁、前壁的斑块无明确指向性[14] [15]。在大脑中动脉中，位于上、后血管壁的斑块比位于前、下血管壁的斑块更容易诱发 IS [16]，可能是因为一些穿透性动脉起源于大脑中动脉的后壁，而这些斑块靠近穿透动脉的孔口[17]，阻塞穿透动脉[18]，但相关的病理结果较少，且目前 HRMR 并没有提供大脑中动脉斑块阻塞孔口的直接影像证据[19]。斑块位置分布与 IS 进展相关性的研究多以基底动脉及大脑中动脉为研究对象，而大脑前动脉及椎动脉相关研究较少。

2.3. 斑块成分

动脉粥样硬化斑块的脆弱性更多地取决于斑块组成成分[20]，这是近年来大多数学者的主要观点，与传统血管评估手段相比，HRMR 可通过 3D-TOF MRA 定位扫描重建和 3D T1WI、3D T2WI、CE-T1WI 等序列进行分析，多对比 HRMR 技术可以提供不同斑块成分的同时成像，更准确地表征斑块[23]。根据斑块成分与卒中的关联性，分为稳定和不稳定斑块。稳定斑块主要由纤维组成，不稳定斑块的典型特征是内含大的脂质核或斑块内出血[24] [25]，除此之外斑块强化也被视作不稳定信号。其中，斑块内出血被认为是初发 IS 最重要的危险因素，在 HRMR 影像上常表现为 TIWI 的高信号[26]，合并斑块内出血的动脉粥样硬化患者五年内 IS 发生率相比无此影像特征的患者高一倍[27]。钙化已被证明为 IS 的独立危险因素[28]，在所有序列上的斑块中都存在一个低信号区域被认为是钙化，Bos 的研究团队发现，斑块内出血伴有钙化对卒中的风险评估效果较斑块内出血单因素更为显著[27]，不足之处在于该实验对钙化未具体分型，钙化形态和斑块易损性之间的联系亟待阐明。T1 加权序列上的斑块增强信号与 IS 有极强相关性[29] [30]，有观点认为其与内部新生血管或炎症反应有关[31]。研究表明，症状性斑块常表现出增强，增强斑块所在动脉供应组织发生梗死的可能性是非增强斑块所在动脉供应组织的 10 倍[32]，且随着增强分级水平的增加，急性缺血事件的高风险存在剂量反应关系[33]，但大多数研究纳入患者合并中–重度的动脉狭

窄，Erling Wang 在利用统计方法消除动脉狭窄影响后得出结论：强化类似或大于垂体柄漏斗部的斑块与IS 的发生仍存在相关性[9]，认为斑块增强是 IS 的独立危险因素，但该研究纳入病例数较少，且缺乏相关的直接研究证据。尽管有研究显示斑块增强也可能预测未来的复发 IS [34] [35]，仍有必要进一步研究以更全面地阐明斑块增强、先前缺血性卒中和未来缺血性卒中风险之间的时间关系。

3. HRMR 在缺血性卒中病因及机制分型判定中的应用

在 IS 的临床诊疗中，病因及机制分型是充分理解 IS 病理生理过程不可或缺的环节，准确分类 IS 的病因及发病机制对于优化治疗和预后评估具有重要意义。然而，IS 的病因繁多，并含有血管夹层、血管炎、血液系统疾病等少见病因，很难用一种分型概括[36]。目前临床上普遍采用的分型是国际上 1993 年提出的 TOAST 标准(Trial of Org 10172 in Acute Stroke Treatment, TOAST)和 CISS 分型(Chinese ischemic stroke subclassification, CISS) [37]，相对于 TOAST 分型，CISS 分型对于动脉粥样硬化原因所致的 IS 更注重致病机制的分析，通过评估斑块的位置、易损性[38]、筛查危险因素，建立关系网络，显著减少不明型原因卒中，更适用于我国 IS 患者颅内动脉粥样硬化多发的实际情况。HRMR 可通过高分辨率血管成像，判断斑块形状及分布、管腔特点、斑块成分，对于 CISS 分型具有显著的临床应用价值。研究显示 HRMR 提高了识别颅内动脉粥样斑块敏感性及准确率[39]，通过对斑块的精准评估，① 在较多原本分型为穿支病变和一些不明原因型的病人中发现责任血管有动脉粥样硬化斑块[40]，更正了原有分型；② 发现了梗死区责任动脉近端载体动脉的动脉粥样硬化，为载体动脉阻塞穿支动脉的归类提供了解剖依据[41]；③ 高信号斑块和表面不规则斑块(>2 mm)多表明为动脉-动脉栓塞，可能与不规则斑块使表面血栓形成的风险增高有关[42] [43]。研究证实，在轻度至中度动脉狭窄的患者中载体动脉阻塞穿支动脉发生率更高，而动脉间栓塞、低灌注主要发生在严重动脉狭窄的患者[44]。除此之外，与常规检查手段相比，HRMR 可以显示管壁结构，为解剖走形变异和狭窄的鉴别提供了有力依据，同时也有助于对动脉狭窄原因如血管畸形、动脉炎、动脉夹层的鉴别，例如，烟雾病常在影像上表现为同心闭塞性病变，这些病变很少增强，这与病理学报告结果一致[4]。HRMR 对于动脉狭窄原因的鉴别，也有助于 TOAST 分型中大动脉粥样硬化、其他病因分型的准确评估。

4. HRMR 在缺血性脑卒中治疗中的应用

IS 是全球范围内导致死亡和残疾的主要原因[1]，积极干预斑块进展和预防卒中复发是当前药物治疗的主要目标。HRMR 可通过明确机制分型来制定进一步治疗方案，也可在治疗进程中通过监控斑块特点以评估疗效。

4.1. 制定治疗方案

HRMR 可通过明确致病机制对 IS 患者行针对性治疗：如动脉-动脉栓塞、低灌注的治疗重点分别为稳定斑块、稳定血压。近来有证据表明，可通过 HRMR 指导 IS 患者的强化降脂时间，斑块的易损性(增强强度)是重要影响因素：根据 T1 加权像，在相邻正常血管壁 < 强化程度 < 垂体漏斗时，是强化降脂治疗的最佳时期。对于强化程度 ≥ 垂体漏斗时，应更加注意抗炎反应来稳定斑块[33]，该研究有样本量和选择偏差，且需要减小正常减轻的斑块增强程度的影响。

目前已有大量研究利用其指导择期脑血管介入手术及术式选择，HRMR 可以充分识别斑块特征及血管壁条件，补充成像、评估手术风险、预测再通效果。首先，HRMR 对血管壁的成像、斑块特点的显示可以指导在 DSA 上不可见的闭塞段的球囊或支架大小的选择；其次，术前 HRMR 有助于评估手术风险[45]，狭窄动脉的重塑模式[46]、脂质核大小与介入手术围手术期并发症相关，NR 及大脂质核患者在介入治疗过程中可能有更大的损伤风险，因为在外力作用下的血管内治疗期间，斑块破裂的风险会增加[47]

[48]。除此之外，Chao 的团队提出，通过 HRMR 对血管壁进行成像，非增强 t1 空间 MRI 腔内信号短、无血管壁塌陷或可成为成功再通新增的预测因素[49]，该研究缺乏病理学依据，样本量有限。HRMR 对于急诊手术的指导相关研究较少，目前 Sami 提出取栓术后血管不稳定性增加，支架取栓相比抽吸取栓对血管损伤更大[50]。临床上运用 HRMR 对择期手术进行评估已初见成效，其在急诊手术的具体应用仍需进一步探索。

4.2. 评价治疗效果

目前评估 IS 患者治疗有效性多通过临床症状、功能指标的改善(如 mRS 评分，NIHSS 评分)，HRMR 可以直接观察血管壁和管腔，并对斑块进行定量和定性分析，从而提供更多的临床信息，为评估疗效作出了补充。近来大量研究指出[51] [52] [53]，可通过 HRMR 对斑块负荷进行计算，对 IS 后治疗进行客观、量化的疗效评估；现计算斑块负荷的主要方法有归一化壁指数(NWI)及墙体面积指数(WAI)两种，前者计算方法更为客观，被认为是目前评价斑块负荷的最佳指标之一。Zheng 利用 HRMR 随访脑梗死患者，得出 WAI 从 1.14 下降到 0.76，NWI 从 79.38 下降到 53.28%，量化说明药物干预下斑块负荷明显降低[54]。

脑血管介入术后患者 HRMR 的测量结果与 DSA 高度一致，与 DSA 对比，除了仍能在大多数支架被放置后提供准确的管腔信息外，还可以提供管壁图像，有助于进一步评估术后情况[55]。研究指出，血管内治疗是大多数 IS 后续复发的原因[56]，在血管内治疗后，再狭窄率高达 30%，IS 再发率高达 70% [57] [58]。数名学者通过 HRMR 评估发现，斑块负荷、重构指数与术后 IS 复发相关：Cao Y 指出，质核越大的斑块负担越大，血管内治疗后发生 IS 的风险就越高[47]；Ma 等人发现，基底动脉支架植入术后具有 NR 的患者与穿透性 IS 相关[59]。HRMR 对内科治疗的 IS 患者可量化评估疗效，对血管内治疗患者更倾向于关注血管及支架条件、不良事件发生风险，运用更加广泛。

5. 总结

HRMR 对血管及斑块的显影，对脑梗死的发作风险分层、机制分型、指导治疗、复发评估有一定作用。基于 HRMR 成像过程，会有血流伪影或内膜钙化阴影，需要考虑通过标准化报告系统和共识标准来提高 HRMRI 的准确性和可重复性[60]。目前对该领域的研究多为回顾性、小样本，因此，HRMR 评估动脉粥样硬化脑梗死研究领域的发展需要建立一个多机构网络，以促进协作、共享协议和数据。通过对 HRMR 的充分了解、利用，将提高药物使用效率，有助于评估手术治疗时机、术式，有效预防梗死发生、再发，降低脑梗死患者的致残率和致死率、复发率。

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