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颈动脉粥样硬化MRI的临床启示和发展方向

[摘要]粥样硬化被广泛公认为是一种多因素疾病，由各种复杂的因素导致，包括斑块成分、血流量和炎症。尽管在认识斑块生理、诊断和治疗上得到发展，粥样硬化仍然是死亡和残疾的主要原因之一，非常需要进一步的研究来发展和验证患者高危的可靠指标。颈动脉MRI是一个经过组织结构验证的无创性方法，可用来追踪疾病的发展及消退，并可定量评估体内斑块形态和组成的参数范围。颈动脉MRI可见的斑块内出血和富脂质坏死核是表示损害程度的最好指标，然而，MRI还可对颈动脉粥样硬化疾病的其他重要方面成像，包括炎症、新生血管、机械力，这些能够帮助我们更好的认识这种多因素疾病的病理生理学。

简介

目前，美国心脏协会估计美国每年新发或复发的脑卒中约为795000人。每年美国脑卒中的患病和长期残疾需要689亿美元直接或间接成本^[1]。多项随机前瞻性研究^[2-4]已经把颈动脉狭窄与症状性神经病学事件联系起来。然而，管腔狭窄可能不是疾病严重程度分类的最好标准，因为，在欧洲颈动脉手术试验中^[5]，3018名症状性颈动脉疾病研究对象中有43.8%狭窄率小于30%。此外，在北美症状性颈动脉内膜切除手术试验(NASCET)中^[2]，狭窄小于50%的患者5年内任何同侧脑卒中患病率为22.2%。相应地，在1996 - 2006年期间，应用狭窄严重性管理颈动脉粥样硬化疾病只减少了7%的脑卒中事件^[1]，8 - 83台颈动脉内膜切除术在术后2年内预防脑卒中再次复发是必要的^[6]。

适应性动脉重塑现象^[7]是一个以最初斑块向外扩张的负荷来保持管腔直径，已经逐渐转向探究代替的或互补的策略来改善颈动脉疾病血管壁进展。无创性颈动脉血管壁成像方法包括超声(平面^[8, 9]和三维^[10])、CT^[11]和MRI^[12]。相对于超声和CT，MRI的主要优点是可以获得并比较鲜血(如TOF)和黑血(如血流抑制的T1W)的多个不同造影加权来区分动脉壁内组织成分。应用多个高清造影加权评估体内颈动脉粥样硬化疾病被称为“颈动脉磁共振成像”。重要的是，组织学已经系统验证了颈动脉磁共振成像量化颈动脉主要成分病变:富脂质坏死核

(LRNC)、^[13-17]钙化、^[13, 14]斑块内出血(IPH)^[13,14,16,18-21]和表面破裂。^[17,22-24]此外，同一医师和不同医师^[14, 18, 20, 25, 26]及不同扫描^[25]间量化形态和成分测量的再现性也被广泛报道。尽管目前颈动脉磁共振成像致力于确定成像工具的研究，但是前瞻性研究的新数据显示即将迎来颈动脉核磁共振成像向临床实践的转化。

要点

- 颈动脉粥样硬化是一种斑块组成、炎症、新生血管和机械力等多因素作用疾病
- 颈动脉磁共振成像能够监测体内动脉粥样硬化疾病
- 颈IPH与加速斑块增长，管腔缩小，症状性事件的发展有关
- 富脂质坏死核是预测体内颈动脉表面破裂的最具代表性的指标
- 新兴颈动脉磁共振技术允许评估体内炎症、新生血管和机械力

颈动脉磁共振成像相关的硬件、序列设计和成像标准以前已总结过。^[31-34]在本篇综述中，我们越过技术开发和验证，来揭示体内核磁共振成像在粥样硬化性疾病方面的理解和潜在临床启示。首先，我们检查和揭示颈动脉MRI最关键的两个用以区分损害严重程度的可视化成分：IPH和LRNC的现有知识差异。然后，我们通过体内斑块成像可以评估炎症、新生血管和管壁机械力继续探索可能扩大当前体内MRI潜力的MRI新技术，并讨论扩展MRI研究来评估颈动脉疾病其他潜在的结果。这些发展方向可能会帮助我们更好地理解颈动脉粥样硬化性疾病的病理生理学。

疾病的当前测量值

颈动脉磁共振成像固有的三维数据采集为评估斑块形态和成分提供了很多参数，包括厚度、面积、体积和比例关系。后者类型参数的一个例子是管壁体积百分比(PWV=100%×管壁体积/总血管体积)，类似于Nissen等^[35]人描述的侵入性冠状动脉血管内超声研究的动脉粥样硬化体积百分比，是一种有效的、重现性^[27]高的非侵入性颈动脉斑块负荷的测量。目前，在所有颈动脉磁共振成像可识别和可测量的特点中，IPH和富脂质坏死核相关参数已经成为颈动脉粥样硬化疾病严

重程度最重要的指标。前瞻性研究已经将IPH和富脂质坏死核加速斑块的增长,^[36-38]症状性疾病^[39-41]或表面破裂的进展联系起来^[37]。于是,我们关注判断颈动脉IPH和富脂质坏死核并综述那些为检测、量化、临床转化提供了有力证据的研究。

IPH

1979年,Imparato等人确定了颈动脉内膜切除术的IPH标本和相应的神经活动存在联系^[42]。多个后续研究^[43,44]也支持这种相关性,但其他研究^[45]提供了相互矛盾的结果。系统综述1979年—2006年实施的31个以组织学为基础的研究,Gao等人报道IPH能够区分无症状组和症状组^[46]。然而,以适当的观点理解颈动脉IPH的临床意义的两点值得注意。首先,具有类似狭窄(> 70%)的症状性和无症状的病变没有证明IPH患病率有显著差异^[46]。这一观点与以前的研究相一致^[47],强烈表明IPH可能不是鉴别高度狭窄斑块病变的最优指标。第二,IPH似乎对于小于70%的狭窄有重要作用,但是区分IPH真正的临床意义需要比较这个群组中狭窄相似的有症状和无症状性斑块^[46]。目前无症状患者手术治疗标准为狭窄程度达70 - 80%^[48],颈动脉磁共振成像等替代方法评估体内狭窄小于70%病变的斑块成分对于解决一直以来组织学为基础的横断面研究结果的不一致是必要的。

颈动脉MRI成像依据出血退化为高铁血红蛋白来检测IPH,这就缩短周围质子纵向松弛时间(T1),伴随的颈动脉磁共振成像效果是一个T1加权序列高亮信号,如黑色血液T1加权快速旋转超声心动图,飞行时间(TOF;图1),磁化快速梯度回波序列(MP-RAGE)。组织学已经验证可在1.5T和3.0T检测出颈动脉粥样硬化病变IPH的各个序列^[4,18-21,49]。自然史的研究应用这些技术,在IPH加速斑块负荷增长和IPH与未来缺血性事件发展相关性方面已经取得了令人兴奋结果。

IPH加速颈动脉斑块增长

在一个为期18个月的前瞻性病例对照研究中,29名狭窄为50 - 79%无症状患者中有IPH的和没有IPH相比,Takaya等人发现了一个明显的变化:管壁体积(6.8% vs-0.15%,P = 0.009)和富脂质坏死核体积(28.4% vs-5.2%;P =0.001)^[36]。Underhill等人报道了狭窄为16-49%无症状的患者IPH的纵向效应^[38]。正如Takaya和他的同事的研究,与没有IPH的病灶相比,IPH明显地增加了血管壁体积(44.1±36.1 vs 0.8±34.5 mm³;P < 0.001)。重要的是,Underhill和他的同事们还发现IPH改变了重塑

模式^[38]。Glagov等人^[7]1987年的假说提出不伴有IPH的病灶会向外扩展以保护内腔,但是IPH病灶扩展与管腔缩小(每年-24.9±21.1mm³;P=0.002)有关^[38]。先前的以组织学为基础的研究表明随着颈动脉狭窄严重增加,IPH也会增加^[50,51]。然而,Underhill等^[38](图1)的发现为IPH可能是管腔闭塞的驱动力提供了前瞻性证据。

这些前瞻性研究^[36,38]除了提供IPH对斑块负荷的影响外,也为IPH的病理生理学提供了线索。Takaya等人指出,IPH 18个月后其大小和信号强度保持不变,并且一些实例证明也存在较新病灶的间歇出血^[36]。这一发现表明颈动脉斑块出血时间与脑出血不同或者红细胞持续向病灶处渗入,两者也可能同时发生。Underhill等人发现IPH降低了他汀类药物对颈动脉粥样硬化病变的积极作用^[38]。结合这些发现表明,IPH可能从根本上改变病变的生物学,因此,其他成功管理临床IPH的策略是必需的。

IPH和缺血性事件

2006年,Takaya等人狭窄率为50-79%先前无症状的患者伴有颈动脉磁共振成像检测到IPH,与那些没有颈动脉IPH患者相比,同侧脑卒中事件的危险度为5.2(P=0.005)^[39]。Altaf等人报道,对64名狭窄率为30-69%伴有IPH的症状性患者,在初次卒中发生后进行的为期平均28个月随访中,发生缺血性事件的危险度为9.8(P =0.03)^[41]。最近,Singh等对初始无症状狭窄为50 - 70%的男性进行为期平均25个月的随访,记录的6次脑血管事件中所有的患者都发生在首次检测到IPH(Hr = 3.6,P < 0.001)的动脉中^[40]。虽然这些研究^[39-41]有限的样本量妨碍多变量分析,但是他们共同为IPH在恶性病变中所起的关键性作用提供了有说服力的前瞻性证据。

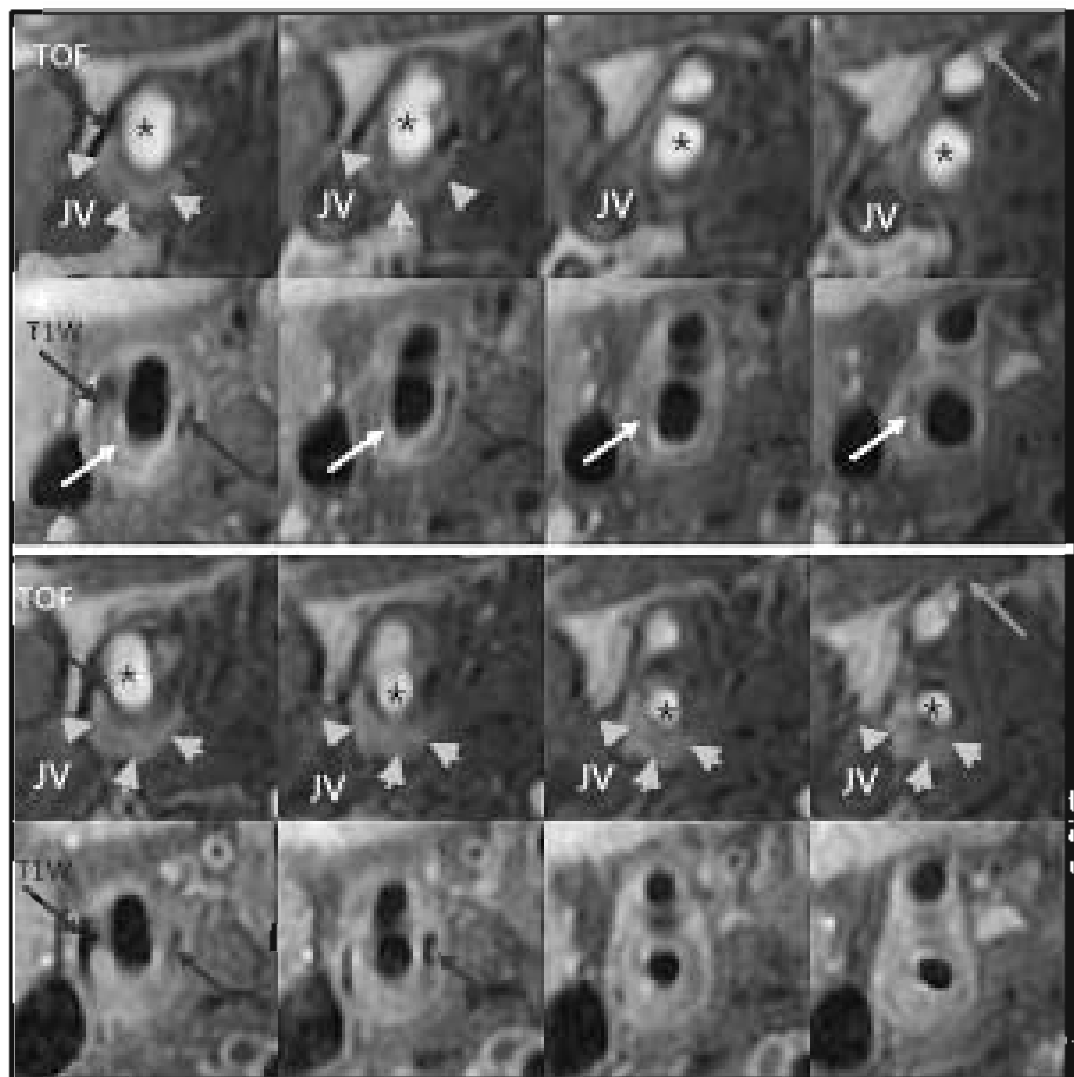


图1 IPH效果的体内证据。图像是颈动脉的病变通过TOF和T1W对比-增强序列的连续轴向横断面。上面的板块是基线扫描, 下面的板块是36个月跟踪匹配相对应的轴向截面。通过钙化(红色箭头), 分流(第2列), 外部颈动脉(蓝色箭头, 列4)远端的锁骨上动脉分支确定匹配位置。星号表示常见的颈动脉内腔。病变包含富脂质坏死核(白色箭头, CE-T1W低信号)和IPH(黄色箭头, TOF为高信号)。请注意列3和列4后续的IPH明显增加、管腔面积相应减少。缩写:IPH: 斑块内出血; JV: 颈静脉; T1W: T1-加权; TOF: 飞行时间。

IPH的临床意义

体内评估颈动脉粥样硬化性疾病揭示,IPH并不局限于不同程度狭窄的症状性患者和高度狭窄的无症状性患者。除了自然史研究报告无症状IPH患者狭窄<70%^[38],Saam等人报道狭窄≤50%有症状的患者颈动脉斑块伴IPH的出现率(大约9.7%)较高^[52]。在只有1-15%狭窄的动脉中,5.4%的病灶中出现IPH^[52]。最近Dong

等人扩展这些发现, 纳入了已知对侧颈动脉粥样硬化患者的磁共振造影没有狭窄的病变,报道的IPH出现率为8.7%^[53]。虽然每个研究的局限性使结果推广到一般人群存在困难,但这些报告的确强调了将狭窄严重程度作为疾病评估的原则标准具有局限性。因此,发现有亚临床影像的患者应根据传统的管腔造影考虑血管壁成像,但是适当的临床风险因素、神经系统事件史也应该考虑其中。此外,发现有IPH的患者,不论狭窄严重程度如何,应密切关注或采取更积极的治疗是很必要的。

药物治疗的影响

体内数据明确显示,降脂治疗能减少斑块负荷^[54]和富脂质坏死核的大小(下文讨论)^[28,55]。然而,到目前为止,提供IPH和降脂治疗相互作用的唯一信息来自Underhill和他的同事们的自然史研究^[38]。虽然他们报道的IPH似乎能抑制他汀类药物的治疗斑块发展的效果,但是药物治疗和剂量在研究样本队列中不是随机分配的和统一的^[38]。然而,他汀类药物以外的治疗药物(例如,抗高血压药或抗炎药)对于改善患者IPH的有效。

改善IPH的评估

在进行评估IPH治疗效果的临床试验前,发展其他成像工具来评估IPH是必要的。IPH通常视为一个二分变量(即存在或不存在)。然而,组织学研究证实IPH的大小^[56,57]、时间长短^[43,58]可能对评估疾病严重程度很重要。不幸的是,与富脂质坏死核(Pearson's $r = 0.87$)^[15]等其他参数相比,目前IPH量化值与组织学(Pearson's $r = 0.66$)^[13]相关性弱。此外,颈动脉磁共振成像和不同时间的IPH组织学检测之间的一致性是可变的,甚至经验丰富的评审员间组织学一致性Cohen's kappa值从0.4到0.7^[18]。因此,体内评估IPH时间和大小在前瞻性研究上的应用有限。准确量化IPH时间能力的进一步研究可能丰富我们对IPH和动脉粥样硬化性疾病间关系的理解。

富脂质坏死核

LRNC是一个脂质和坏死组织混合物组成的多细胞光滑纤维帽^[59]。LRNC的主要成分是胆固醇和胆固醇酯,它与周围的纤维组织相比有较短的横向弛豫时间(T2)^[12]。因此,最初发现的LRNC在体内T2W影像中表现为低信号^[12]。然而,在后续的工作中, T1W影像结合应用钆剂改善了LRNC的再现性^[26]和量化性^[15],并提高了鉴别LRNC中的纤维帽^[60]。IPH的量化评估有两个重要的临床意义: 识别

易表面破裂的病灶；直接评估动脉粥样硬化性疾病的降脂治疗效果。

预测表面破裂

表面破裂、溃疡或纤维帽破裂促进斑块内血栓碎片暴露到凝血因子中，而形成远端栓塞^[61]。组织学溃疡与术前经颅多普勒检查发现的脑部微栓塞存在相关性^[62]。横断面组织学研究发现有症状的患者比无症状患者溃疡患病率更高^[63,64]。类似的,体内颈动脉MRI横断面研究表明纤维帽破裂和症状性疾病存在相关^[65,65]。特别是,Takaya等人的前瞻性自然历史研究中,薄或破裂纤维帽的基线和后续发展的同侧颈动脉缺血性事件(Hr = 17.0,P < 0.001)有显著相关性^[39]。Takaya 等人^[39]将薄纤维帽与破裂纤维帽进行分组,这与来自组织学研究^[67,68]提出的假说即“薄纤维帽出现在纤维帽破裂之前”是一致的。Takaya等人^[39]的发现表明颈动脉磁共振检测到薄或破裂纤维帽的患者,都有可能进一步发生缺血性事件。

今年早期,Underhill等人的观察性前瞻性研究,研究对象为85位狭窄率为50-79%且在基线水平斑块表面没有破裂的患者,后接受颈动脉MRI连续造影增强,在随后的3年随访扫描中,LRNC的大小是发生新的表面破裂的最好的分类指标(曲线下面积(AUC)= 0.95) (图2),值得注意的是,IPH(AUC = 0.73)的出现也是一个新的表面破裂重要的但相对较弱的分类指标^[37]。这些发现不仅强调了定性评估LRNC的重要性,也强调全面理解斑块而不是集中在某一个特点如IPH来进行风险评估。此外,正如IPH, LRNC和表面破裂可发生在所有类别的狭窄上^[52,53],这进一步支持评估可疑颈动脉粥样硬化疾病的血管壁情况,而不是使用传统的方法测量狭窄率。

降脂治疗的影响

多项长期随机研究已经证明他汀类药物可以减少临床事件^[69-71]。此外,一些前瞻性调查也表明他汀类治疗能降低颈动脉斑块负荷^[54,72]。他汀类药物也证明能特异性降低LRNC的大小(图3)^[28]。2009年,Zhao等人报道了一项旨在验证脂质损耗假说的随机双盲试验的颈动脉MRI结果,该长达3年的试验随机将apoB \geq 120 mg/dl和脂质治疗史< 1年的55位冠状动脉或颈动脉疾病患者分配到阿托伐他汀(10-80毫克/天),阿托伐他汀(10-80毫克/天)加上烟酸控释片(ERN)(2克/天),或阿托伐他汀(10-80毫克/天)、烟酸控释片(ERN)(2克/天)和盐酸考来维仑(3.8克/天),并用安慰剂进行对照。对所有试验研究对象每年用造影增强颈动脉

磁共振成像以定量评估LRNC。33名伴有LRNC(均无IPH)的患者,LRNC第一年平均缩小了12mm³(P = 0.007),第二年13mm³(P=0.004),第三年1mm³(P=NS)^[55]。这些发现明确了降脂对于颈动脉粥样硬化斑块组成具有深刻的积极影响作用,这可以在治疗一年后,通过对相对较小人群进行造影增强MRI观察到。

LRNC减小可能不需要通过强化降脂治疗就可实现。在一项前瞻性临床试验中,瑞舒伐他汀无论使用高剂量(40毫克)还是低剂量(5毫克)对LRNC的作用是相似的^[28]。zhao等人的研究表明没有迹象显示不同的治疗方案(以上所述,各个LDL-胆固醇和HDL-胆固醇目标不同)表现不同,这进一步支持了以上的结论^[55]。

肾系统性纤维化

虽然利用造影增强MRI评估LRNC的效果是明显的,但钆造影剂和肾系统性纤维化(NSF)之间的关系是需要讨论的。NSF已成为肾功能不全的患者使用钆造影剂的相关临床综合征^[73,74]。尽管数据表明,钆造影剂的选择可能会影响NSF的风险^[75,76],由于大剂量、适应症外使用等混淆问题而致NSF的病因还不清楚。然而,当前指南表明可以通过限制正常肾功能(GFR > 60)的患者应用钆对比造影剂来最小化NSF的风险^[77]。肾功能代偿期使用NSF的风险小^[73,74]。然而,在美国食品药品监督管理局制定下一步指南前,肾功能不全患者LRNC的评估应限于不需要进行造影的T2W成像。

未来的发展方向

多重造影MRI通过直接观察体内斑块形态和成分,使我们能更好地理解颈动脉粥样硬化疾病。然而,粥样硬化是一种多因素疾病,不仅仅由狭窄、形态学和斑块成分等各种复杂的因素造成。组织学研究将炎症和新生血管作为动脉粥样硬化至关重要的因素,特别是关于IPH和表面破裂的病因^[78,79]。当前新兴^[78,79]技术不仅允许体内评价炎症和新生血管,另外扩展到影响疾病发展的机械力的诊断。

炎症

动脉粥样硬化越来越被认为是炎症性疾病。尤其是单核细胞/巨噬细胞的炎症标志物涉及各个方面的疾病,从开始^[80]、进展^[81,82]到纤维帽破裂^[83-85]。体内评估炎症有两种MRI策略:分子成像和动态成像。

“被动”和“积极”分子核磁共振技术用于标记单核细胞/巨噬细胞以评估动脉粥样硬化疾病。组织学研究表明,超小超顺磁氧化铁粒子(USPIOs)被动地聚集在

斑块巨噬细胞内^[86-88]，增加的USPIOs聚集与较高的狭窄^[89]程度和症状性动脉有关^[90]。2009年，Tang等人报道USPIOs确定的炎症患者经80毫克阿托伐他汀治疗6周后，炎症显著减少^[91]。活跃的分子成像已经以包装MRI造影剂为指定的脂质为基础的纳米颗粒^[92, 93]或高密度脂蛋白的前提。^[94-96]由于这些造影剂还处于开发阶段，所以研究在很大程度上局限于动物调查；然而，预试验表明造影剂在增强体内巨噬细胞聚集区域上有巨大的改进^[95]。当应用钆对比造影剂时，动态MRI通过短时间间隔(< 5分钟)连续扫描捕获灌注动力学。动态MRI的来源基于肿瘤学^[97]，但目前这项技术已经应用到颈动脉。体内动态MRI的动力学参数与组织学巨噬细胞含量^[98]和新生血管^[98, 99]一致。类似于USPIOs，评估降脂治疗对动态核磁共振参数的影响^[100]目前已成为持续性临床试验的一部分。

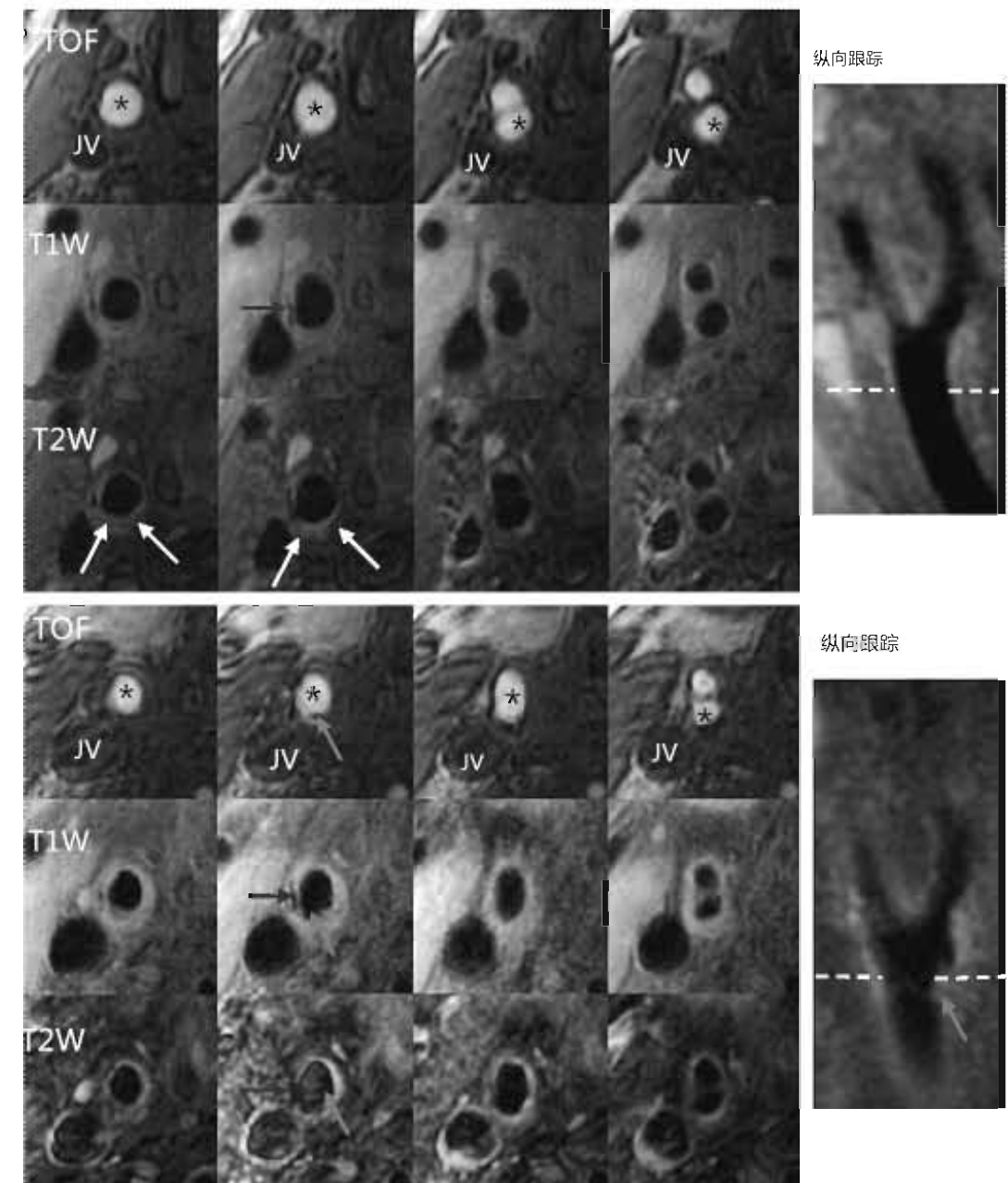


图2 右颈动脉表面破裂的发展。基线影像(顶端板块)显示在最小管腔狭窄处存在一个相对较小的病灶。然而,LRNC占据了大部分动脉壁。T2W影像中有一个可识别的组织条,把LRNC(白色箭头;T2低信号)与内腔分开,这与厚纤维帽的出现是一致的。在3年随访(底端板块)中,轴向图像和纵向监测图像(绿色箭头)都有一个可识别的表面破裂。纵向图像上的虚线代表列2轴向图像的成像位置。IPH没有出现在基线或随访中,但有斑块负荷增加和管腔面积减少的可视证据,特别是在列4。星号表示颈总动脉和颈内动脉内腔,红色箭头表示钙化。缩写:IPH:斑块内出血;JV:颈静脉;LRNC,富脂质坏死核;T1W:T1-加权;T2W:T2-加权;TOF:飞行时间。获得美国神经放射学会许可

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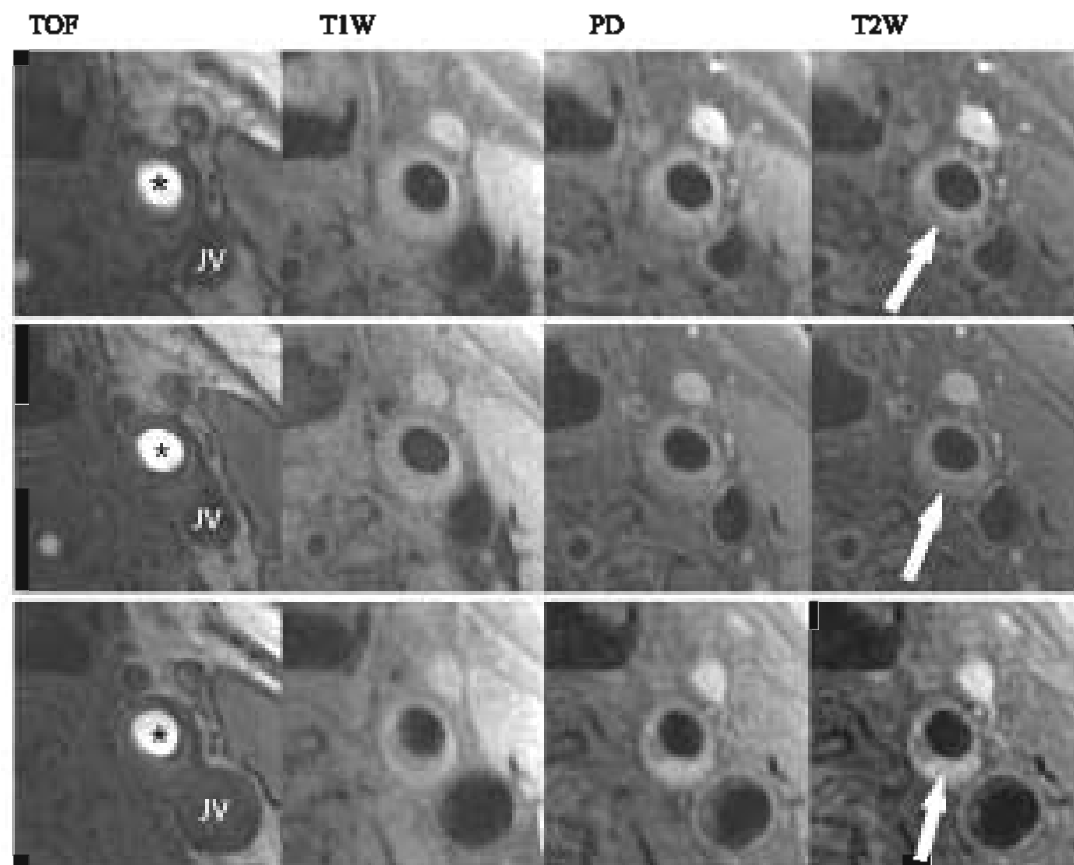


图3 LRNC对他汀类药物治疗的反应变化。多造影加权影像来自同一位患者左颈总动脉同一个位点的2次基线扫描和2年的随访扫描, 请注意, 基线扫描得到的T2W图像上的低信号可解释为LRNC (白色箭头), 经2年随访, 变成了高强度信号。这种变化表示LRNC被纤维组织取代。斑块负担没有出现大幅改变。星号表示常见颈动脉内腔。缩写:JV: 颈静脉;LRNC,富脂质坏死核;PD,质子密度;T1W: T1-加权; T2W: T2-加权;TOF: 飞行时间。

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新生血管

除了能提供炎症相应的数据,动态MRI已经用来进行营养血管成像^[101]。动脉粥样硬化斑块内形成的新血管关系到IPH病因^[79]。新生血管主要起源于血管滋养管^[102]。鉴于IPH在疾病进展中的影响,体内识别和监测新生血管不仅有机会提供IPH病因学的证据,也可能提高评估疾病严重程度的能力。

压力成像

本文前面部分主要集中于动脉壁的组织特点;然而,有很多核磁共振方法评估机械力和动脉粥样硬化疾病之间的关系。Steinman等人提出了一个结合计算流

体动力学模拟流型阶段对比MRI测量颈动脉黑色血液MRI流率的结构信息和管壁剪切力的方法^[103]。有限元分析用于动脉壁内结构压力的分析。Li等人使用依据体内颈动脉磁共振成像量化斑块成分的一个超弹性模型,来证明有症状的斑块压力比无症状的病人明显高于最大预测^[104]。Tang等人提出了一种固液体相结合的模式方法来评估动脉管壁压力与张力^[105]。这个模型用来证明颈动脉表面破裂点与较高的临界压力条件有关^[106]。虽然这些和其他方法^[107]大部分是实验性的,但他们强调了多种因素可导致动脉粥样硬化,且可以从颈动脉磁共振成像获得大量数据。

斑块特性和无症状性脑梗塞

评估颈动脉疾病和脑卒中^[9-41]之间关系的前瞻性研究集中在有症状的颈动脉疾病。然而,无症状性脑梗塞(SBI)在普通人群中很常见,SBI的患病率在高血压患者约为43%,无症状性颈动脉疾病患者多达22%。此外,所有年龄组人群SBI的发生率大约是脑卒中发病率的5倍^[108],SBI使后期脑卒中风险增加超过三倍^[109]。心血管健康研究的3324个无症状患者,28%的研究对象MRI基线表明有SBI^[110]。此外,5年MRI随访1433名没有梗塞基线研究对象,17.7%的对象出现有一个或多个梗塞,而其中只有11.4%是有症状的^[111]。SBI与颈动脉疾病的关系尚不清楚。一些研究如ACAS发现两者无相关性^[112],但是其他研究报道有显著相关性,特别是,Norris等人发现10%轻度狭窄(35-50%)、17%的中度狭窄(50 - 75%)和30%严重颈动脉狭窄(> 75%)的颈动脉狭窄患者有同侧SBI^[113]。虽然这些研究中不是所有事件都归因于颈动脉疾病,但这些发现表明颈动脉粥样硬化性疾病的影响因素包括IPH、表面破裂、炎症和机械力,进一步评估SBI的研究(横断面和前瞻性)将会更好的理解这些。

结论

相比其他成像方法,颈动脉MRI的进展能无创性评估动脉粥样硬化疾病的包括管腔狭窄的大范围参数。目前,IPH和富脂质坏死核——发生在各狭窄水平的斑块成分——已经被认定为临床疾病评估的关键因素。IPH与加速斑块增长,管腔狭窄,有症状事件的发生有关。LRNC是评估未来表面破裂最有力的体内预测指标,也已经被用于监测体内治疗效果。为了进一步理解这些特性及提高其临床重要性,进一步研究应该评估IPH治疗的反应并且结合大脑MRI来评估与颈动脉粥样硬化

相关疾病的SBI。持续发展的MRI新技术可评价炎症和机械力，能更好的理解病因和危险因素。此外，类似的评估大动脉和外周动脉MRI也是有可能的并且也许将补充颈动脉磁共振成像评估^[14]。全面的动脉粥样硬化性疾病影像可能揭开许多残留问题的答案，并进一步改善颈动脉粥样硬化的临床管理。

综述标准

在PubMed全面搜索时使用以下术语(各种组合): “carotid”, “MRI”, “atherosclerosis”, “hemorrhage”, “inflammation”, “stress”, and “prospective” 搜索仅限于英语语言研究。体内组织学验证的交叉-截面研究或特定颈动脉是优先选择，但是本次审查主要纳入标准是前瞻性、体内、颈动脉数据。

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