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颅内动脉并存粥样硬化斑块的研究进展



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【摘要】 颅内动脉并存粥样硬化斑块在亚洲人群中很常见。越来越多的研究发现, 与单一动脉粥样硬化斑块患者相比, 颅内动脉并存粥样硬化斑块患者发生脑血管事件的风险更高。本文简述了颅内动脉并存粥样硬化斑块的影像学诊断方法, 并回顾了颅内动脉并存粥样硬化斑块特征与脑血管疾病相关性的研究, 分析得出, 虽然斑块钙化、斑块大脂质坏死核心(LRNC)、斑块内出血(IPH)及斑块强化对脑血管疾病的影响尚存在争议, 但颅内动脉并存粥样硬化斑块患者远期预后差, 血管事件或死亡风险可能更高。因此, 重视颅内动脉并存粥样硬化斑块的评估, 可能为脑血管疾病防治提供新的见解。

【关键词】 斑块, 动脉粥样硬化; 颅内动脉硬化; 颅外动脉; 综述

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Research Progress of Coexisting Atherosclerotic Plaques in Both Intracranial and Extracranial Arteries XUE Lili¹, WANG Lingjie², SHI Caiyun², ZHANG Hua²

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【Abstract】 Coexisting atherosclerotic plaques in both intracranial and extracranial arteries is very common in Asian populations. Increasing evidences have shown that patients with coexisting atherosclerotic plaques in both intracranial and extracranial arteries have higher risk of cerebrovascular events compared with patients with single vascular atherosclerotic plaque. This study briefly describes the imaging diagnosis methods of coexisting atherosclerotic plaques in both intracranial and extracranial arteries, and reviews the studies on the correlation of coexisting atherosclerotic plaques in both intracranial and extracranial arteries characteristics with cerebrovascular disease, and points out that although the effect of plaque calcification, plaque lipid-rich necrotic core (LRNC), intraplaque hemorrhage (IPH) and plaque enhancement on cerebrovascular diseases is still controversial, patients with coexisting atherosclerotic plaques in both intracranial and extracranial arteries have poor long-term prognosis and higher risk of vascular events or death. Therefore, paying attention to the evaluation of coexisting atherosclerotic plaques in both intracranial and extracranial arteries may provide new insights for the prevention and treatment of cerebrovascular disease.

【Key words】 Plaque, atherosclerotic; Intracranial arteriosclerosis; Extracranial arteries; Review

动脉粥样硬化是脂质、炎性细胞及血管壁斑块中纤维成分逐渐积累的结果, 是大多数心脑血管疾病最主要的病因^[1]。动脉粥样硬化作为一种全身性疾病, 常累及多个血管床, 颅内动脉和颅外动脉同时存在粥样硬化斑块在亚洲人群中很常见, 其发生率为18.0%~77.6%^[2-7]。若闭塞血管近端管腔同时存在重度狭窄(70%~99%)或闭塞称为串联病变^[8], 其在前循环中表现为颈内动脉重度狭窄或闭塞合并同侧颈内动脉末端、大脑中动脉或大脑前动脉闭塞。颅内外动脉并存粥样硬化斑块的主要诊断依据是影像学检查评估管腔

狭窄程度和检出易损斑块。易损斑块指发展迅速和较易变成血栓的斑块, 此类斑块通常具有薄和/或破裂的纤维帽、大脂质坏死核心(lipid-rich necrotic core, LRNC)、斑块表面溃疡、血栓形成、斑块内出血(intraplaque hemorrhage, IPH)、炎性细胞浸润、新生血管形成等病理特点^[9]。越来越多的研究表明, 相对于单一病变, 颅内外动脉并存粥样硬化斑块会增加脑血管事件发生风险、造成更严重的损伤^[10-13], 尤其是合并颅内外动脉串联病变的急性缺血性脑卒中患者, 其静脉溶栓治疗血管再通率和早期功能改善率均较低^[14]。而了解颅内外动脉并存粥样硬化斑块的影像学特征及其与脑血管疾病的相关性, 对脑血管疾病防治具有重要意义, 因此, 本文对颅内外动脉并存粥样硬化斑块的研究进展进行综述。

1 颅内外动脉并存粥样硬化斑块的影像学诊断方法

影像学检查是颅内外动脉并存粥样硬化斑块最重要的诊断方法, 传统的影像学检查技术如经颅多普勒超声

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(transcranial Doppler, TCD)、计算机断层扫描血管成像(computed tomography angiography, CTA)、磁共振血管成像(magnetic resonance angiography, MRA)、数字减影血管造影(digital subtraction angiography, DSA)均可有效显示病变血管的狭窄程度^[15-17]。DSA是评价管腔狭窄程度的金标准,但由于其有创性及有造成脑栓塞的风险等,常不作为临床一线诊断方法。颈动脉管腔狭窄程度测量方法有北美症状性颈动脉内膜切除术(North American Symptomatic Carotid Endarterectomy Trial, NASCET)的方法、欧洲颈动脉手术试验(European Carotid Surgery Trial, ECST)的方法和颈总动脉(common carotid, CC)法^[18-20],目前比较公认的方法是华法林、阿司匹林治疗症状性颅内动脉狭窄的随机对照研究(the Warfarin-Aspirin Symptomatic Intracranial Disease Study, WASID)公布的方法^[21]。

头颈动脉管腔常存在正性重构的情况,而单纯评价管腔狭窄程度常低估动脉粥样硬化病变严重程度,因此,多项指南提示应关注斑块性质^[22-24]。高分辨率磁共振成像(high resolution magnetic resonance imaging, HRMRI)不仅可以清晰显示纤维帽、LRNC大小及IPH等斑块内成分,还可以识别斑块强化程度及管壁重构状态,与组织病理学检查结果高度一致,且可重复性操作,是目前比较适合用于检测斑块易损性特征的成像技术^[25-26]。虽然超声及CT成像技术也可以发现斑块易损性特征的部分信息,如超声及CTA可检测和量化斑块内新生血管数量^[27-28],但其评估价值不及HRMRI^[29-31]。近年来,分子影像学、血管内超声、光学相干断层扫描检查技术也被许多机构作为传统影像学检查的补充,其可以在分子水平检测动脉粥样硬化斑块发展情况以及不稳定斑块,发现斑块炎症、新生血管形成等重要血管壁信息^[32-34]。然而,动脉粥样硬化斑块是多个病理生理机制作用的结果,仅凭一种影像学检查或一种征象预测脑血管疾病风险并不可靠,多模态、多种影像学检查结合有助于脑血管疾病风险分层。

2 颅内动脉粥样硬化斑块特征与脑血管疾病的相关性

动脉粥样硬化斑块主要通过斑块造成管腔狭窄或阻塞及斑块破裂两种形式引起脑血管事件(一个或多个部位的缺血性卒中或短暂性脑缺血发作),通常表现为突发的、与动脉供血区相对应的局灶性神经系统症状^[15]。

2.1 斑块狭窄与脑血管疾病的相关性 既往有多项研究分析了颅内动脉粥样硬化斑块狭窄对脑血管疾病的影响,其中一项基于香港人群的研究显示,症状性颅内动脉粥样硬化狭窄患者5年累积死亡率、卒中复发率和不良结局发生率分别为31%、41%和51%^[4]。MAN等^[35]研究证实,伴有颅内动脉粥样硬化狭窄的缺血性卒中患者远期预后较差,发生血管事件或死亡的风险较高。HOSHINO等^[36]研究报道,有明显颅内动脉粥样硬化狭窄的患者合并颅外动脉粥样硬化狭窄时不良心血管事件发生风险从9.0%增加至23.4%。此外,还有研究发现,一些预后良好的脑血管疾病如短暂性脑缺血发作、短暂性脑缺血发作、磁共振弥散加权成像阴性的缺血性卒中患者,合并颅内动脉粥样硬化狭窄时,其卒中复发及复合血管事件发生风险更高^[37-38]。由此可见,颅内动脉粥样硬化

狭窄可能严重影响脑血管疾病的发生及患者预后。虽然已有研究提示,颅内动脉粥样硬化狭窄与颅外动脉粥样硬化狭窄间存在相关关系^[11, 39],但具体机制并不明确。

2.2 斑块钙化与脑血管疾病的相关性 作为系统性动脉粥样硬化性疾病的标志,斑块钙化与卒中密切相关^[40-41],尽管斑块钙化在斑块易损性中的作用是矛盾的,但越来越多的证据发现,斑块钙化的类型、数量和位置均与IPH密切相关^[42-43],斑块外周薄钙化可能是血管外膜慢性炎症的标志^[41],这表明斑块钙化在斑块易损性中起着重要的作用。一项基于中国动脉粥样硬化风险评估(CARE-II)数据的研究探讨了颅内动脉粥样硬化并存粥样硬化与同侧急性脑梗死的相关性,结果发现,颅内动脉粥样硬化合并斑块钙化与同侧急性脑梗死相关^[44]。国内外对于颅内动脉粥样硬化并存粥样硬化斑块钙化与脑血管疾病相关性的报道少,故斑块钙化对脑血管疾病的影响仍需要更多研究进一步证实。

2.3 斑块LRNC与脑血管疾病的相关性 LRNC是易损斑块的重要特征,既往研究表明,斑块LRNC与卒中风险增加有关,特别是当LRNC占比>40%(LRNC占比=LRNC面积/壁面积×100%)时,斑块更容易出现纤维帽破裂和IPH^[45-46]。LI等^[13]采用心血管磁共振对2周内前循环系统症状的患者进行颅内动脉成像,发现颅内动脉粥样硬化合并颈动脉粥样硬化斑块、颅内动脉粥样硬化合并颅外颈动脉粥样硬化斑块LRNC与血管事件相关。CARE-II研究表明,颅内动脉粥样硬化合并颈动脉粥样硬化斑块LRNC与同侧急性脑梗死相关^[44]。颅内动脉粥样硬化合并颈动脉粥样硬化斑块LRNC可能代表颅内动脉和颅外颈动脉均存在易损斑块。研究表明,颈动脉粥样硬化斑块LRNC与同侧脑缺血事件相关^[47],但LI等^[13]研究提出,这些并存粥样硬化斑块的颅内动脉不一定与脑血管疾病同侧,提示未来研究可能需要分析不同侧别颅内动脉粥样硬化斑块的特征及其与脑血管疾病的相关性。

2.4 IPH与脑血管疾病的相关性 IPH是易损斑块的关键特征之一,其具体的病理生理机制尚不明确,主要是粥样硬化斑块增大引起组织缺氧,刺激新生血管形成,而新生血管的渗漏可形成IPH^[48]。Meta分析结果显示,无论是否出现临床症状,IPH均与患者未来的卒中风险增加有关^[49]。然而,LI等^[13]研究结果并未发现颅内动脉粥样硬化合并颈动脉IPH与随后的血管事件相关。XU等^[12]在探讨颅内动脉粥样硬化斑块特征时并未发现易损斑块特征(斑块钙化、LRNC、IPH)与缺血性卒中中复发相关。

易损斑块特征与脑血管疾病相关性的研究结果存在差异,一方面可能因为研究的样本量小及研究人群的异质性,另一方面可能是颅内动脉粥样硬化斑块分布、易损性特征不同所致。既往研究报道,相较于颅外动脉,颅内动脉粥样硬化斑块发生率低、斑块LRNC少见,但IPH发生率高、血管狭窄程度更严重^[50],且IPH多见于后循环^[51],而目前已发表的研究多针对前循环血管。但颅内动脉粥样硬化斑块分布特点尚不清楚,易损斑块特征差异也缺乏研究证据。除此之外,动脉粥样硬化病变在不同侧别的颅内动脉

间复杂的关联也可能是影响研究结果的原因之一。有研究报道,在症状性脑血管疾病中,存在斑块易损性特征(IPH、薄和/或破裂的纤维帽等)的左侧颅外颈动脉粥样硬化斑块与同侧大脑中动脉斑块狭窄相关,但在右侧并未发现这种关联^[52],提示促进双侧颅内外动脉并存粥样硬化斑块进展的因素可能不同。由此可见,颅内外动脉并存粥样硬化斑块易损性特征对脑血管疾病风险的预测价值有待进一步明确。

2.5 斑块强化与脑血管疾病的相关性 多项研究报道,颅内外动脉并存粥样硬化斑块强化与脑血管事件相关^[53-56],有学者认为,斑块强化可能是血管内皮炎症反应的标志,而炎症引起的内皮屏障是斑块强化的主要原因^[57]。CUI等^[58]在调整了血管狭窄程度、IPH和传统动脉粥样硬化危险因素后发现,多区域颈动脉粥样硬化斑块强化程度对急性脑梗死的预测效能较单一区域颈动脉粥样硬化斑块好,但由于该研究为横断面研究,并不能明确斑块强化对未来脑血管疾病的预测价值。斑块强化程度在疾病不同时期的变化也存在争议,有学者认为,斑块强化程度可反映不稳定粥样硬化斑块的动态演变情况,急性脑卒中早期症状性粥样硬化斑块明显强化,但随着发病时间延长斑块强化程度减弱^[59-60];然而,也有研究者认为疾病后期粥样硬化斑块仍存在持续强化^[61]。多区域动脉粥样硬化斑块强化程度可能反映动脉粥样硬化新生血管形成情况或总的炎症负担。未来,通过分子影像学、血管内超声、光学相干断层扫描检查技术对粥样硬化斑块炎症的准确评估有望明确颅内外动脉并存粥样硬化斑块强化与脑血管疾病的相关性。

3 小结

综上所述,颅内外动脉并存粥样硬化斑块在亚洲人群中常见,诸多研究表明颅内外动脉并存粥样硬化斑块增加了动脉粥样硬化疾病负荷、脑血管疾病发生风险,虽然颅内外动脉并存粥样硬化斑块易损性特征与脑血管疾病的相关性尚存在争议,但积极推动多血管床斑块研究对心脑血管疾病防治具有重要意义。未来需要覆盖整个头颈部的快速、简便的成像技术来确定多血管床斑块及狭窄的存在、评估斑块易损性特征,多模态影像技术结合临床表现、分子生物学将有助于精准诊断和预测严重血管事件的发生。

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本文无利益冲突。

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