·综述·

脑小血管病影像学评分方法

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【摘要】 脑小血管病的发病机制尚不明确，目前无有效治疗方法。MRI是其重要的影像学诊断方法，本文对脑小血管病影像学标志物及其评分方法和标准进行详细阐述，探讨脑小血管病的诊断依据及分级方法，为疾病的诊断与治疗提供理论依据。

【关键词】 大脑小血管疾病； 磁共振成像； 综述

Imaging scoring methods for cerebral small vessel disease

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【Abstract】 The pathogenesis of cerebral small vessel disease (CSVD) is not yet clear, and there is no effective treatment method at present. MRI is an important imaging in diagnosing. In this paper, the imaging markers and scoring methods and criteria of CSVD are elaborated, and the diagnosing and grading methods of CSVD are discussed, to provide theoretical basis for diagnosis and treatment of the disease.

【Key words】 Cerebral small vessel diseases; Magnetic resonance imaging; Review

This study was supported by the National Natural Science Foundation of China (No. 81971620).

Conflicts of interest: none declared

脑小血管病(CSVD)因主要发生于颅内小血管，如小动脉、小静脉，甚至毛细血管而得名，是脑血管和脑实质结构变化引起的不同临床表现和影像学特征病变的总称[1]。随着人口老龄化加剧，脑小血管病发病率呈不断升高趋势，中老年人群发病率>70%[2]。本文基于脑小血管病影像学检查方法探讨其评分标准，为临床诊断提供新的思路，有助于疾病早期精准诊断、病情进展评估和预测，进而改善患者预后。

一、影像学诊断

MRI是诊断脑小血管病的重要影像学方法，主要包括腔隙性梗死(LACI)、脑白质高信号(WMH)、脑微出血(CMBs)和扩大的血管周围间隙(EPVS)，亦有研究将脑萎缩作为脑小血管病的影像学标志物[3]。(1)腔隙性梗死：系指直径3～15 mm的梗死灶，亦包括脑梗死后残留的小腔隙即“空洞”[4]。其病因和发病机制尚不明确，目前认为脂质透明变性是其主要机制，此外还包括分支动脉粥样硬化以及颈动脉、主动脉或心脏等栓子致远端小血管病变。腔隙性梗死的早期机制主要是血管内皮功能障碍和血脑屏障破坏[5]。吸烟是首次发生腔隙性梗死的独立危险因素，此类患者亦同时存在脑微出血、重度脑白质高信号和中至重度扩大的血管周围间隙等，这些脑小血管病影像学改变阻碍腔隙性梗死患者早期神经功能恢复[6-7]。(2)脑白质高信号：系指脑室周围和脑深部白质高信号，常见于老年人，约94%的80岁以上人群存在脑白质高信号[8]。研究显示，脑小血管病患者右侧白质微结构改变较左侧显著，推测这种不对称性可能是发生神经功能障碍的主要原因之一[9]。此外，脑白质高信号还可以作为诊断短暂性脑缺血发作(TIA)的影像学标志物，脑白质高信号体积截断值为7.8 ml可区分短暂性脑缺血发作高危人群[10]；脑白质高信号程度还与脑卒中患者短期神经功能预后密切相关，程度越轻微、神经功能预后越佳[11]。(3)脑微出血：系由血管周围局灶性沉积的含铁血黄素形成，表现为小的低信号灶，直径上限5～10 mm，呈强度极低的圆形或椭圆

doi:10.3969/j.issn.1672-6731.2023.07.012

基金项目：国家自然科学基金资助项目(项目编号：81971620)

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形区域，与周围脑组织界限清晰[3]。根据病变部位分为脑叶微出血和脑深部微出血，其对周围脑组织可产生多维影响，不仅反映出脑出血的易发状态，即较高的脑微出血灶数目提示弥漫性血管损伤和神经变性，且更易发生无症状性脑梗死[12-13]。(4)扩大的血管周围间隙：血管周围间隙[PVS，亦称Virchow-Robin间隙(VRS)]是脑实质内围绕在小动脉、小静脉和毛细血管周围的充满液体腔隙，最常见于基底节区和半卵圆中心，表现为与脑脊液信号一致、直径＜3 mm的管状结构，根据其内是否存在液体提示其清晰性[3,14]。血管周围间隙扩大表明血管周围存在细胞碎片及其他代谢产物，可引起脑血管反应性(CVR)损害、血脑屏障破坏、血管周围炎症反应，使代谢产生的蛋白质自间质间隙清除障碍，导致毒素积聚、脑组织缺氧和损伤[15]。尽管已对脑小血管病的影像学标志物进行分类，但是上述影像学改变并非独立存在。腔隙性梗死与脑白质高信号分布之间存在特殊关联性，约50%的腔隙性梗死位于脑白质高信号边缘，脑室周围和脑深部白质高信号均为脑白质高信号边缘局灶性梗死的预测因素[16-17]；腔隙性梗死与脑白质高信号的不对称性相关，急性和陈旧性无症状性腔隙性梗死灶数目较多的大脑半球脑白质高信号更严重[18]。多数脑深部白质高信号与脑深部扩大的血管周围间隙直接相连，二者体积也具有一致性[19]。脑微出血与脑白质高信号体积和严重程度呈正相关[20-21]。

脑小血管病的某些影像学标志物并不稳定，随时间进展可逐渐明显，亦可自发性退化，例如，脑白质高信号体积可随年龄增长而增大或缩小[22]。因此，不仅需要及时有效的检查，而且需要跟踪随访和客观有效的影像学评分进行动态评估，为脑小血管病的诊断与治疗提供可靠依据。

二、影像学评分方法

脑小血管病的影像学评分方法主要分为两大类，一类是对特定的影像学表现进行深入研究和独立评分；另一类是对各种影像学表现进行整体评价和综合评分。独立评分是综合评分的基础，综合评分则是在独立评分基础上的发展。

1.脑白质高信号评分方法 Fazekas评分是目前普遍采用的脑白质高信号评分方法，包括脑室周围白质高信号和脑深部白质高信号两部分。脑室周围白质高信号的评分标准为：0分，无脑室周围白质高信号；1分，脑室周围白质可见帽状或线状改变；2分，脑室周围白质可见光滑的“晕”；3分，不规则的脑室周围白质高信号延伸至脑深部[23]。脑深部白质高信号的评分标准为：0分，无脑深部白质高信号；1分，脑深部白质点状高信号；2分，脑深部白质高信号开始融合；3分，脑深部白质高信号广泛融合[23]。二者评分之和即Fazekas评分，总评分6分。脑卒中急性期或无法行MRI检查时，Fazekas评分亦可用于CT检查，这也是判断脑卒中患者小血管病变的简便方法[24]。

2.扩大的血管周围间隙评分方法 目前应用最多的扩大的血管周围间隙评分方法为五分类法[25]，并且仍在不断完善中。有研究在五分类法的基础上补充部分标准，除对基底节区和半卵圆中心扩大的血管周围间隙进行分级外，还对中脑扩大的血管周围间隙进行简略分级：单侧基底节区和半卵圆中心扩大的血管周围间隙，0级为无病灶、1级为1～10个病灶、2级为11～20个病灶、3级为21～40个病灶、4级为＞40个病灶，若双侧病变不对称，则采用病变更严重一侧进行分级；中脑扩大的血管周围间隙仅分0级(病灶不可见)和1级(病灶可见)[26]。

3.脑白质高信号和扩大的血管周围间隙综合评分方法 脑白质高信号和扩大的血管周围间隙是颅内小血管重要的直接或间接生物学标志物，二者相互影响，具有空间相关性[27]，因此对二者进行综合评分以评价其联合效应。评分标准包括基底节区扩大的血管周围间隙3级(3分)、半卵圆中心扩大的血管周围间隙3级(3分)、中脑扩大的血管周围间隙(1分)，以及脑室周围Fazekas评分3分、皮质下Fazekas评分3分，总评分13分[28]。该综合评分主要用于预测认知功能障碍，痴呆和轻度认知损害(MCI)患者综合评分均较高[28]。

4.脑微出血解剖评分方法 脑微出血解剖评分量表包括以下两项内容：(1)脑微出血分为“确定的(definite)”和“可能的(possible)”两种类型，确定的脑微出血定义为脑实质内界限清晰的、直径为2～10 mm、环形或圆形低信号病变，T_2*-梯度回波序列(T_2*-GRE)显示边界清晰；可能的脑微出血界限不甚清晰，或不呈现严格意义上的环形或圆形低信号病变。(2)根据发生部位分为脑深部微出血、脑叶微出血和幕下微出血，脑深部包括基底节区、丘脑、内囊、外囊、胼胝体、脑室周围(毗邻脑室)和深部(脑室旁10 mm内)白质；脑叶指额叶、颞叶、顶叶、枕叶和岛叶；幕下包括脑干和小脑[29]。分别计数双侧脑

深部、脑叶和幕下确定的和可能的微出血灶数目，确定的和可能的微出血灶数目之和为总脑微出血灶数目，用以评估脑微出血严重程度，0级，无病灶；1级，1～4个病灶；2级，5～9个病灶；3级，≥10个病灶[29-30]。值得注意的是，该评分方法应对上述部位进行连续层面扫描以追踪病变，排除血管干扰，同时还应排除可能符合该标准的类似物低信号[31]。

5.脑淀粉样血管病评分方法　脑淀粉样血管病（CAA）作为脑小血管病的一种，MRI表现为多发性严重脑微出血、皮质浅表铁质沉着症（cSS）、半卵圆中心扩大的血管周围间隙和脑白质高信号[32]，对上述影像学标志物进行评分，用于评价脑淀粉样血管病相关小血管病变总负担。评分标准为[33-34]：（1）根据脑微出血解剖评分方法，2～4个脑叶微出血灶计1分、≥5个脑叶微出血灶计2分。（2）皮质浅表铁质沉着系大脑皮质表面慢性出血的线样残留物，MRI呈低信号脑回样特征且不与脑出血相邻，局限分布（分布范围≤3个脑沟）计1分、弥漫分布（分布范围＞3个脑沟）计2分。（3）半卵圆中心中至重度扩大的血管周围间隙（3～4级），计1分。（4）早期融合性（即皮质与脑室之间区域）脑深部白质高信号（Fazekas评分≥2分）或不规则脑室周围白质高信号延伸至脑深部（Fazekas评分3分），计1分。总评分为6分。该评分可以作为脑淀粉样血管病患者小血管病变严重程度的预测指标，与脑卒中、痴呆风险和病死率呈正相关，评分越高，脑卒中、痴呆风险和病死率越高[32,35]。

6.微血管功能障碍评分方法　微血管功能障碍（MVD）评分分为MRI表现和脑外测量两部分，包括4项脑小血管病影像学特征（腔隙性梗死、脑白质高信号、脑微出血和扩大的血管周围间隙）评分、4项微血管功能障碍血浆生物学标志物[可溶性细胞间黏附分子-1（sICAM-1）、可溶性血管细胞黏附分子-1（sVCAM-1）、可溶性E-选择素和血管性血友病因子（vWF）]测量值、尿白蛋白排泄率、闪烁光诱导下视网膜小动脉和小静脉扩张率（即闪烁光刺激下小动脉和小静脉直径变化）、热诱导下皮肤充血扩张率（即热刺激下手腕皮肤血流量变化）共12项指标，将上述测值转化为Z评分，再相加获得微血管功能障碍评分[36]。研究显示，微血管功能障碍评分脑外测量部分代表颅外血管床微血管功能，其功能障碍程度与脑白质高信号体积呈正相关[37]。因此认为，微血管功能障碍评分可用于评价认知功能障碍或即将出现的认知功能障碍等[38]。

7.脑小血管病总积分　脑小血管病总积分系指每项影像学标志物（腔隙性梗死、脑白质高信号、脑微出血和扩大的血管周围间隙）评分的总和，可以更好地反映颅内小血管病变对大脑的总体影响，有助于快速量化脑小血管病相关出血性转化或认知功能障碍风险[39-40]。脑小血管病总积分可对脑小血管病的MRI总负荷进行分级，共4分，存在以下每种情况计1分，即存在至少1个腔隙性梗死灶；存在任意部位脑微出血；存在扩大的血管周围间隙：基底节区中至重度扩大的血管周围间隙（2～4级）；存在脑白质高信号：早期融合性脑深部白质高信号（Fazekas评分2或3分）或不规则的脑室周围白质高信号延伸至脑深部（Fazekas评分3分）[41]。还有一种简化的脑小血管病评分方法仅对MRI特征进行评分，存在腔隙性梗死、脑白质高信号或脑微出血各计1分，总评分3分，同时根据腔隙性梗死灶数目和脑白质高信号严重程度进行分级，该简化评分有助于预测痴呆[42]。近年来，随着人工智能（AI）技术的革新，可通过计算机对脑小血管病的MRI表现进行全脑自动分割和评估，进而量化血管性认知损害相关综合影像学特征，有望成为未来理想的脑小血管病评估替代标志物[43]。

综上所述，脑小血管病的确切发病机制并未阐明，目前尚无有效治疗方法。因此针对其影像学标志物的综合评分即显得尤为重要，不仅为风险分层提供可能，而且是疾病早期诊断与治疗的重要方法。随着人工智能及其他影像学技术的发展，对脑小血管病的评估必将会向着更加智能化和全面化方向发展。

利益冲突　无

参　考　文　献

[1] Zhang XQ, Yang YX, Zhang C, Leng XY, Chen SD, Ou YN, Kuo K, Cheng X, Han X, Cui M, Tan L, Feng L, Suckling J, Dong Q, Yu JT. Validation of external and internal exposome of the findings associated to cerebral small vessel disease: a Mendelian randomization study[J]. J Cereb Blood Flow Metab, 2022, 42:1078-1090.

[2] Wang YL, Chen WQ, Ye JY, Zhou MY, Jiang LL, Liu D, Qiu BS, Gao Y, Zhao YL, Wang Z, Li PF. Cerebral small vessel disease: looking back on 2022[J]. Zhongguo Zu Zhong Za Zhi, 2023, 18:17-41.[王伊龙, 陈玮琪, 叶瑾怡, 周梦圆, 江凌玲, 刘东, 邱宝山, 高颖, 赵一龙, 王赞, 李鹏飞. 脑小血管病：回眸2022[J]. 中国卒中杂志, 2023, 18:17-41.]

[3] Chinese Consensus on Diagnosis and Therapy Cerebral Small Vessel Disease Writing Group, Chinese Society of Research Hospitals Cerebral Small Vascular Disease Professional

Committee. Chinese consensus on diagnosis and therapy cerebral small vessel disease 2021[J]. Zhongguo Zu Zhong Za Zhi, 2021, 16:716-726.[中国研究型医院学会脑小血管病专业委员会《中国脑小血管病诊治专家共识》编写组. 中国脑小血管病诊治专家共识2021[J]. 中国卒中杂志, 2021, 16:716-726.]

[4] Wang L, Ke J, Hu X, Zhu M, Yu Y. Preliminary findings on the potential use of magnetic resonance elastography to diagnose lacunar infarction[J]. Neuropsychiatr Dis Treat, 2022, 18:1583-1591.

[5] Jiang S, Wu S, Zhang S, Wu B. Advances in understanding the pathogenesis of lacunar stroke: from pathology and pathophysiology to neuroimaging[J]. Cerebrovasc Dis, 2021, 50:588-596.

[6] Gómez-Choco M, Mengual JJ, Rodríguez-Antigüedad J, Paré-Curell M, Purroy F, Palomeras E, Fuentes B, Ustrell X, Tembl J, Rodríguez-Yañez M, Castellanos M, Martí-Fabregas J, Serena J. Pre-existing cerebral small vessel disease limits early recovery in patients with acute lacunar infarct[J]. J Stroke Cerebrovasc Dis, 2019, 28:104312.

[7] Tang R, Liu Z. Relevance of cerebral small vessel disease load scores in first-ever lacunar infarction[J]. Clin Neurol Neurosurg, 2021, 200:106368.

[8] Wang T, Jin A, Fu Y, Zhang Z, Li S, Wang D, Wang Y. Heterogeneity of white matter hyperintensities in cognitively impaired patients with cerebral small vessel disease[J]. Front Immunol, 2021, 12:803504.

[9] Zhou H, Tang Y, Yuan Z. White matter asymmetries in patients with cerebral small vessel disease[J]. J Integr Neurosci, 2018, 17:159-167.

[10] Nagy M, Azeem MU, Soliman Y, Nawab SA, Jun-O'Connell AH, Goddeau RP Jr, Moonis M, Silver B, Henninger N. Pre-existing white matter hyperintensity lesion burden and diagnostic certainty of transient ischemic attack[J]. J Stroke Cerebrovasc Dis, 2019, 28:944-953.

[11] Mossa-Basha M, Zhu C. White matter hyperintensities and their relationship to outcomes after stroke intervention[J]. Radiology, 2022, 304:153-154.

[12] Deng R, Qin W, Li X, Li X. High prevalence of cerebral microbleeds in young ischemic stroke patients[J]. Curr Neurovasc Res, 2022.[Epub ahead of print]

[13] Akoudad S, Wolters FJ, Viswanathan A, de Bruijn RF, van der Lugt A, Hofman A, Koudstaal PJ, Ikram MA, Vernooij MW. Association of cerebral microbleeds with cognitive decline and dementia[J]. JAMA Neurol, 2016, 73:934-943.

[14] Barisano G, Lynch KM, Sibilia F, Lan H, Shih NC, Sepehrband F, Choupan J. Imaging perivascular space structure and function using brain MRI[J]. Neuroimage, 2022, 257:119329.

[15] Browm R, Benveniste H, Black SE, Charpak S, Dichgans M, Joutel A, Nenergaard M, Smith KJ, Zlokovic BV, Wardlaw JM. Understanding the role of the perivascular space in cerebral small vessel disease[J]. Cardiovasc Res, 2018, 114:1462-1473.

[16] Yi F, Cai M, Jacob MA, Marques J, Norris DG, Duering M, Tuladhar AM, de Leeuw FE. Spatial relation between white matter hyperintensities and incident lacunes of presumed vascular origin: a 14-year follow-up study[J]. Stroke, 2022, 53:3688-3695.

[17] Loos CMJ, Makin SDJ, Staals J, Dennis MS, van Oostenbrugge RJ, Wardlaw JM. Long-term morphological changes of symptomatic lacunar infarcts and surrounding white matter on structural magnetic resonance imaging[J]. Stroke, 2018, 49:1183-1188.

[18] Ryu WS, Schellingerhout D, Ahn HS, Park SH, Hong KS, Jeong SW, Park MS, Choi KH, Kim JT, Kim BJ, Han MK, Lee J, Cha JK, Kim DH, Nah HW, Lee SJ, Cho YJ, Lee BC, Yu KH, Oh MS, Park JM, Kang K, Lee KB, Park TH, Park SS, Smith EE, Lee J, Bae HJ, Kim DE. Hemispheric asymmetry of white matter hyperintensity in association with lacunar infarction[J]. J Am Heart Assoc, 2018, 7:e010653.

[19] Huang P, Zhang R, Jiaerken Y, Wang S, Yu W, Hong H, Lian C, Li K, Zeng Q, Luo X, Yu X, Xu X, Wu X, Zhang M. Deep white matter hyperintensity is associated with the dilation of perivascular space[J]. J Cereb Blood Flow Metab, 2021, 41:2370-2380.

[20] Balestrieri A, Lucatelli P, Suri HS, Montisci R, Suri JS, Wintermark M, Serra A, Cheng X, Jinliang C, Sanfilippo R, Saba L. Volume of white matter hyperintensities, and cerebral micro-bleeds[J]. J Stroke Cerebrovasc Dis, 2021, 30:105905.

[21] Zhou YN, Gao HY, Zhao FF, Liang YC, Gao Y, Liu XH, Wang T, Wang ZG, Wu QJ. The study on analysis of risk factors for severity of white matter lesions and its correlation with cerebral microbleeds in the elderly with lacunar infarction[J]. Medicine (Baltimore), 2020, 99:e18865.

[22] Duering M, Biessels GJ, Brodtmann A, Chen C, Cordonnier C, de Leeuw FE, Debette S, Frayne R, Jouvent E, Rost NS, Ter Telgte A, Al-Shahi Salman R, Backes WH, Bae HJ, Brown R, Chabriat H, De Luca A, deCarli C, Dewenter A, Doubal FN, Ewers M, Field TS, Ganesh A, Greenberg S, Helmer KG, Hilal S, Jochems ACC, Jokinen H, Kuijf H, Lam BYK, Lebenberg J, MacIntosh BJ, Maillard P, Mok VCT, Pantoni L, Rudilosso S, Satizabal CL, Schirmer MD, Schmidt R, Smith C, Staals J, Thrippleton MJ, van Veluw SJ, Vemuri P, Wang Y, Werring D, Zedde M, Akinyemi RO, Del Brutto OH, Markus HS, Zhu YC, Smith EE, Dichgans M, Wardlaw JM. Neuroimaging standards for research into small vessel disease: advances since 2013[J]. Lancet Neurol, 2023, 22:602-618.

[23] Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR signal abnormalities at 1.5T in Alzheimer's dementia and normal aging[J]. AJR Am J Roentgenol, 1987, 149:351-356.

[24] Rudilosso S, San Román L, Blasco J, Hernández-Pérez M, Urra X, Chamorro Á. Evaluation of white matter hypodensities on computed tomography in stroke patients using the Fazekas score[J]. Clin Imaging, 2017, 46:24-27.

[25] Maclullich AM, Wardlaw JM, Ferguson KJ, Starr JM, Seckl JR, Deary IJ. Enlarged perivascular spaces are associated with cognitive function in healthy elderly men[J]. J Neurol Neurosurg Psychiatry, 2004, 75:1519-1523.

[26] Potter GM, Chappell FM, Morris Z, Wardlaw JM. Cerebral perivascular spaces visible on magnetic resonance imaging: development of a qualitative rating scale and its observer reliability[J]. Cerebrovasc Dis, 2015, 39:224-231.

[27] Huo Y, Wang Y, Guo C, Liu Q, Shan L, Liu M, Wu H, Li G, Lv H, Lu L, Zhou Y, Feng J, Han Y. Deep white matter hyperintensity is spatially correlated to MRI-visible perivascular spaces in cerebral small vessel disease on 7 Tesla MRI[J]. Stroke Vasc Neurol, 2022, 8:144-150.

[28] Zdanovskis N, Platkājis A, Kostiks A, Šneidere K, Stepens A, Naglis R, Karelis G. Combined score of perivascular space dilatation and white matter hyperintensities in patients with normal cognition, mild cognitive impairment, and dementia[J]. Medicina (Kaunas), 2022, 58:887.

[29] Gregoire SM, Chaudhary UJ, Brown MM, Yousry TA, Kallis C, Jäger HR, Werring DJ. The Microbleed Anatomical Rating Scale (MARS): reliability of a tool to map brain microbleeds[J]. Neurology, 2009, 73:1759-1766.

[30] Yang Q, Yang Y, Li C, Li J, Liu X, Wang A, Zhao J, Wang M,

Zeng X, Fan D. Quantitative assessment and correlation analysis of cerebral microbleed distribution and leukoaraiosis in stroke outpatients[J]. Neurol Res, 2015, 37:403-409.

[31] Nagaraja N, Farooqui A, Bin Zahid A, Kaur S. Factors associated with the presence of cerebral microbleeds and its influence on outcomes of stroke not treated with alteplase[J]. Clin Neurol Neurosurg, 2021, 207:106798.

[32] Yilmaz P, Ikram MA, Ikram MK, Niessen WJ, Viswanathan A, Charidimou A, Vernooij MW. Application of an imaging-based sum score for cerebral amyloid angiopathy to the general population: risk of major neurological diseases and mortality[J]. Front Neurol, 2019, 10:1276.

[33] Schwarz G, Banerjee G, Hostettler IC, Ambler G, Seiffge DJ, Brookes TS, Wilson D, Cohen H, Yousry T, Salman RA, Lip GYH, Brown MM, Muir KW, Houlden H, Jäger R, Werring DJ, Staals J; CROMIS-2 Investigators. Magnetic resonance imaging-based scores of small vessel diseases: associations with intracerebral haemorrhage location[J]. J Neurol Sci, 2022, 434: 120165.

[34] Charidimou A, Martinez-Ramirez S, Reijmer YD, Oliveira-Filho J, Lauer A, Roongpiboonsopit D, Frosch M, Vashkevich A, Ayres A, Rosand J, Gurol ME, Greenberg SM, Viswanathan A. Total magnetic resonance imaging burden of small vessel disease in cerebral amyloid angiopathy: an imaging-pathologic study of concept validation[J]. JAMA Neurol, 2016, 73:994-1001.

[35] Ii Y, Ishikawa H, Shindo A, Matsuyama H, Matsuura K, Matsuda K, Yoshimaru K, Saton M, Kogue R, Umino M, Maeda M, Tomimoto H. Association between cortical microinfarcts and total small vessel disease burden in cerebral amyloid angiopathy on 3-Tesla magnetic resonance imaging[J]. Eur J Neurol, 2021, 28:794-799.

[36] Rensma SP, van Sloten TT, Houben AJHM, Köhler S, van Boxtel MPJ, Berendschot TTJM, Jansen JFA, Verhey FRJ, Kroon AA, Koster A, Backes WH, Schaper N, Dinant GJ, Schalkwijk CG, Henry RMA, Wolfs EML, van Heumen MJA, Schram MT, Stehouwer CDA. Microvascular dysfunction is associated with worse cognitive performance: the Maastricht Study[J]. Hypertension, 2020, 75:237-245.

[37] van Dinther M, Schram MT, Jansen JFA, Backes WH, Houben AJHM, Berendschot TTJM, Schalkwijk CG, Stehouwer CDA, van Oostenbrugge RJ, Staals J. Extracerebral microvascular dysfunction is related to brain MRI markers of cerebral small vessel disease: the Maastricht Study[J]. Geroscience, 2022, 44: 147-157.

[38] Rensma SP, Stehouwer CDA, Van Boxtel MPJ, Houben AJHM, Berendschot TTJM, Jansen JFA, Schalkwijk CG, Verhey FRJ, Kroon AA, Henry RMA, Backes WH, Dagnelie PC, van Dongen MCJM, Eussen SJPM, Bosma H, Köhler S, Reesink KD, Schram MT, van Sloten TT. Associations of arterial stiffness with cognitive performance, and the role of microvascular dysfunction: the Maastricht Study[J]. Hypertension, 2020, 75: 1607-1614.

[39] Zhou YY, Deng XL. The correlation between the burden of cerebral small vessel disease and the hemorrhagic transformation in patients with acute cerebral infarction[J]. Shen Jing Sun Shang Yu Gong Neng Chong Jian, 2022, 17:813-816.[周俞余, 邓晓玲. 脑小血管病总体负荷与急性脑梗死患者溶栓后出血转化的相关性研究[J]. 神经损伤与功能重建, 2022, 17:813-816.]

[40] Yuan XQ, Feng HT, Chen YK, Huang LL. Correlation analysis of total cerebrovascular disease burden and cognitive impairment in patients with acute basal ganglia infarction[J]. Zhongguo Shen Jing Jing Shen Ji Bing Za Zhi, 2022, 48:65-71. [袁锡球, 冯辉庭, 陈仰昆, 黄龙龙. 急性基底节区梗死的脑小血管病总负荷与认知功能损害相关性分析[J]. 中国神经精神疾病杂志, 2022, 48:65-71.]

[41] Staals J, Makin SD, Doubal FN, Dennis MS, Wardlaw JM. Stroke subtype, vascular risk factors, and total MRI brain small-vessel disease burden[J]. Neurology, 2014, 83:1228-1234.

[42] Amin Al Olama A, Wason JMS, Tuladhar AM, van Leijsen EMC, Koini M, Hofer E, Morris RG, Schmidt R, de Leeuw FE, Markus HS. Simple MRI score aids prediction of dementia in cerebral small vessel disease[J]. Neurology, 2020, 94:e1294-e1302.

[43] Jokinen H, Koikkalainen J, Laakso HM, Melkas S, Nieminen T, Brander A, Korvenoja A, Rueckert D, Barkhof F, Scheltens P, Schmidt R, Fazekas F, Madureira S, Verdelho A, Wallin A, Wahlund LO, Waldemar G, Chabriat H, Hennerici M, O'Brien J, Inzitari D, Lötjönen J, Pantoni L, Erkinjuntti T. Global burden of small vessel disease-related brain changes on MRI predicts cognitive and functional decline[J]. Stroke, 2020, 51: 170-178.

（收稿日期:2023-05-08）
（本文编辑:彭一帆）