

脑桥梗死的研究进展

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脑桥梗死是脑干梗死中最常见类型^[1],发病率也能占到全部脑梗死的 7%^[2]。脑桥的解剖结构较为复杂,因而脑桥梗死症状及体征复杂,临床上早期诊断存在困难。临床上,脑桥梗死除表现特殊的症状和体征外,也可有如基底节或放射冠梗死类似的特征^[3]。本研究对其国内外诊断和治疗进展进行综述。

1 脑桥的解剖结构及血供

脑桥解剖结构复杂,包括基底部及被盖部,其中有复杂的神经核团及神经纤维,例如皮质脊髓束、脊髓丘脑束和颅神经核(如面神经核、外展神经核等)、内侧纵束和网状结构^[4]。脑桥血供主要来自椎动脉和基底动脉,根据血液供应区域分为三部分:1)前内侧组,即由中央支和旁中央分支组成;2)前外侧组,即由短旋动脉组成;3)外侧组,即由长旋动脉组成。

2 脑桥梗死的危险因素

脑桥梗死的危险因素包括年龄、吸烟史、高血压病史、高脂血症史、糖尿病史、冠心病史、既往脑卒中或短暂性脑缺血发作史等^[5-7]。有研究表明,其中高血压病是最重要的危险因素,而糖尿病是一个独立的危险因素^[8]。糖尿病可引起植物神经功能紊乱,这使得椎-基底动脉系统的交感神经的血管舒缩调节减弱,尤其脑桥旁正中动脉^[9]。Zhang 等^[10]研究了基底动脉弯曲长度、血管危险因素和脑桥梗死之间的关系,提出患者的基底动脉弯曲且合并多种血管危险因素可增加脑桥梗死风险,并且认为弯曲长度>3.77 mm可作为独立预测因子来评估脑桥梗死风险。

3 脑桥梗死分型

目前,参照国内外比较常见的形态学分类方法,将其分为①大动脉闭塞性病变(large-arteryocclusive disease, LAOD);影像学检查确定与梗死部位对应的椎动脉或基底动脉狭窄>50%,行高分辨磁共振成像(high resolution Magnetic resonance imaging, HR-MRI)在梗死相应的椎基底动脉部位可见动脉粥样硬化斑块;②基底动脉分支病变(basilar artery branching disease, BABD);脑桥梗死病灶蔓延至脑

桥腹侧表面,并且没有潜在的心源性栓子或 LAOD。HR-MRI 显示基底动脉分支中存在粥样硬化斑块;③小动脉病变(small-artery disease, SAD);脑桥梗死病灶的直径<1.5 cm,并且病灶未蔓延至脑桥腹侧表面,没有潜在的心源性栓子或 LAOD。HR-MRI 的相应部位没有明显动脉粥样硬化斑块。其中, BABD 最常见,其次为 SAD, LAOD 最少见^[5,11-14]。BABD 的概念最初是由 Fisher 和 caplan 提出的^[15],它的发病机制可能是基底动脉主干斑块堵塞穿支动脉口,也可能是穿支动脉本身的动脉粥样硬化斑块引起的血管闭塞^[16]。然而,关于单纯脑桥梗死的 TOAST 分型研究很少,朱子龙等联合许多脑动脉检测方法,证明了 TOAST 分型在单纯脑桥梗死诊断与治疗中的适用性^[17]。

4 临床表现及经典的综合征

4.1 脑桥梗死的常见临床症状:头晕或眩晕、恶心、呕吐、头面部及肢体的麻木、肢体活动不灵、行走不稳、跌倒、视力障碍、言语吞咽障碍、意识障碍等。体征:眼球运动障碍、面瘫、肢体麻痹和共济失调、感觉异常、步态异常、构音障碍、Horner 综合征等。Tan 等^[18]报道 1 例迅速起病的单侧肌张力障碍为表现的脑桥梗死。Obaid 等^[19]报道 1 例脑桥背外侧梗死表现为对侧热性感觉障碍和孤立性同侧听力丧失。Hosaka 等^[20]报道 1 例脑桥梗死表现为对侧抽搐和共济失调性震颤。另外,还有仅表现为抑郁的脑桥梗死报道^[21]。

4.2 经典的脑桥综合征:Millard-Gubler 综合征、Foville 综合征、闭锁综合征、Ishizawa 等^[22]及 Debraj 等^[23]报道双侧脑桥前内侧区病变,有“心型”特征,表现为闭锁综合征,但 MRA 显示椎-基底动脉系统完整。还有一个半综合征,表现病灶同侧的眼球固定位,外展和内收受限,病灶对侧眼球不能内收,可以外展,外展时有水平眼震。然而,单纯的一个半综合征是相对少见的,常伴有其他神经系统症状如颅神经麻痹、偏瘫、单侧感觉障碍等。当合并面神经麻痹时可有中枢性面瘫表现或周围性面瘫表现,因为由于面神经是第七对颅神经,因此它被称为八个半综合征^[24-26]。如累及皮质脊髓束及内侧丘系通路,导致偏身浅感觉减退及偏侧瘫痪,表现为九个综合征^[27]。当与双侧周围性面瘫同时合并时被称作十五个半综合征,临床罕见^[28]。

5 影像学诊断

目前常用且有效的为 MRI 检查^[29],文献报导 MRI 的检出率可达 92%~100%^[30]。因此,当临床怀疑脑桥梗死时,

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MRI 应为首选项目, MRI 检查在脑桥梗死诊断中具有独特的优势^[31]。其中弥散加权成像(diffusion-Weighted imaging, DWI)对急性病变最有诊断价值^[32]。另外, 还需在磁共振平扫基础上完善 MRA 检查, 排查血管因素如血管病变、分布位置及侧支循环等, 为病因诊断治疗、预后的判断及复发的预防提供依据^[33]。有条件情况下可行 HR-MRI。有研究表明, 与 MRA 相比, HR-MRI 对颅内动脉狭窄情况的显示更加明显, 动脉粥样硬化斑块检出率更高, 还可更好地显示斑块特征(如斑块位置、成分、血管重构和穿支动脉口的关系等), 其敏感性和特异性较高^[34-35]。Cho 等^[36]利用 HR-MRI 研究 MR 未能检测到的基底动脉斑块对急性桥脑梗死患者功能预后的影响, 结果显示基底动脉血管斑块的存在与不良功能预后有着密切的关系。其中, “黑血”技术可以通过抑制流动伪影从而更清晰地显示出斑块^[37]。三维时间飞跃法磁共振血管成像(3D time-of-flight MR angiography, 3D tof MRA)可以三维角度显示斑块及其形态特征, 它在发现小的动脉硬化斑块方面具有优势, 并且扫描时间短, 可以显示多个血管壁, 为研究颅内分支动脉粥样硬化疾病的病因提供了依据^[38]。另外, 还有三维各向同性高分辨磁共振成像(3D High Isotropic Resolution MRI), Zhu 等提出与非孤立性脑桥梗死组相比, 孤立性脑桥梗死组在基底动脉上表现出更广泛的斑块^[39]。另外, 如患者不能完善磁共振检查, 可完善非创伤性血管成像技术(computed tomography angiography, CTA)检查, 有研究证实其可详细描述动脉狭窄程度、发育情况、斑块特征及血流状态等^[40], 其敏感性和特异性优于 MRA^[41], 可与数字减影血管造影(digital subtraction angiography, DSA)相媲美^[42]。

6 进展性脑桥梗死

进展性脑卒中目前尚缺乏明确定义^[43]。根据现有的研究分类, 包括以下两种: (1) 神经功能恶化(neurological deterioration, ND)是指入院后 7 d 内美国国立卫生研究院卒中量表(National Institute of Health Stroke Scale, NIHSS)评分最大值较初始值增加 ≥ 2 分^[44]; (2) 进展性运动功能缺损(progressive motor deficits, PMD)指入院后 7 d 内 NIHSS 评分中运动项目增加 ≥ 1 分^[45-46]。脑桥梗死在急性期病情进展较常见, 发生率 10%~60%^[47]。有研究表明, 脑桥梗死患者急性期神经功能恶化是由中枢神经系统自身因素和/或系统因素引起的^[48]。在血管因素方面, 一些研究认为 BABD 是急性孤立性脑桥梗死最为常见的病因, 并且与急性期的病情进展相关^[17, 49-50]。Zhao 等^[45]发现 PMD 组基底动脉狭窄和闭塞的比例(62.5%)明显高于非 PMD 组(27.1%), 认为基底动脉狭窄和闭塞是孤立性脑桥梗死出现 PMD 的独立危险因素。同时, 他们发现 PMD 组病灶累及脑桥基底表面情况明显比非 PMD 组多, 这也被认为是急性孤立性脑桥梗死发生 PMD 的独立危险因素, 上述结论与国内外的多项研究相符^[51-54]。Nam 等^[55]评估了严重白质病变作为孤立性脑桥梗死(Isolated pontine infarction, IPI)终点预测因子的可能, 他们发现严重的脑室周围和皮质下白质病变在恶化患者中更为常见, 提示严重的脑室周围和皮质下白质病变对 IPI 患者

的进展有一定的预测价值。作为缺血性脑卒中急性期的主要炎症反应物, C 反应蛋白(C-reactive protein, CRP)在评估动脉粥样硬化性脑梗死风险和预后方面具有较高敏感性^[56]。许多研究证实, 血浆 CRP 水平与以穿支动脉病变为发病机制的脑梗死的进展密切相关^[54, 57]。Chen 等^[58]研究发现急性进展性脑卒中的血浆纤维蛋白原(FIB)水平明显增高, 后又有研究发现血浆 CRP 和 FIB 的水平变化可能对我们早期识别和及时治疗进展性缺血性脑卒中中提供帮助^[59]。

7 治疗

7.1 药物治疗

7.1.1 常见的抗血小板聚集治疗药物有阿司匹林和氯吡格雷, 主要用于缺血性脑卒中的二级预防。在脑桥梗死中的用法和用量与前循环供血区梗死无明显差异。王拥军教授^[60]的 CHANCE 研究结果证实, 相对短期联合使用阿司匹林和氯吡格雷抗血小板聚集治疗可在 3 个月内降低再梗死的风险; 它不会增加出血风险, 并对目前的抗血小板聚集治疗实践产生重要影响。常见的抗凝药物有华法林、低分子肝素或其他新型抗凝药(如达比加群、利伐沙班等)。华法林—阿司匹林治疗有症状颅内病变研究(Warfarin—Aspirin Symptomatic Intracranial Disease, WASID)^[61]表明, 当严格的抗血小板聚集或抗凝治疗时, 椎-基底动脉系统狭窄血管供血区的梗死每年发生率分别为 10.7% 和 7.8%。Kang 等^[62]报道, 37 例急性后循环供血区梗死患者经肝素抗凝治疗, 其中 4 例出现小脑水肿, 总结显示急性后循环供血区梗死应用肝素抗凝治疗继发颅内出血的风险不高, 而且与患者血清胆固醇水平及脑白质缺血的程度等无相关性, 只与在 DWI 序列上计算出的梗死体积大小有关。然而, 目前对于急性脑梗死抗凝治疗效果的研究中许多临床试验(包括设计良好的随机、对照、双盲试验)的结论不一致。脑桥梗死急性期神经功能恶化常见, 直接影响患者预后, 而积极的抗凝或抗血小板聚集治疗还不能有效地阻止其进展^[63-64]。孙向军等^[65]研究提出, 阿司匹林联合依诺肝素钠治疗进展性穿支动脉病(包括脑桥旁正中动脉供血区和豆纹动脉), 可明显改善患者的早期神经功能恶化(early neurological deterioration, END), 提高其生活自理能力, 临床疗效优于阿司匹林和氯吡格雷双联抗血小板聚集治疗。

7.1.2 重组组织型纤溶酶原激活剂(recombinant tissue plasminogen activator, rt-PA)是目前治疗急性缺血性脑卒中最有效的治疗药物, 但目前静脉溶栓的主要困境是时间窗。2004 年包括 NINDS 及其他 4 项国际多中心、随机、双盲、安慰剂对照研究[欧洲急性卒中研究(the European Cooperative acute stroke study, ECASS-I 和 ECASS-II)、阿替普酶急性非介入溶栓治疗缺血性卒中研究(Alteplase thrombolysis for acute noninterventional therapy in ischemic stroke, ATLANTIS-A 和 ATLANTIS-B)]亚组的汇总分析为发病 3~4.5 h 内 rt-PA 静脉溶栓提供了初步依据(预后良好 OR = 1.40, 95% CI = 1.05~1.85)^[66]。随后的中国溶栓注册研究^[67]、国际溶栓注册研究^[68]和 2010 年的溶栓荟萃分析^[69]提供了在发病后 3~4.5 h 内 rt-PA 静脉溶栓获益的进一步

证据。然而,对于发病4.5~6 h的急性缺血性脑卒中患者,可能需要进一步的证据,证明其能从rt-PA静脉溶栓中获益^[70]。此外,在多模式影像技术的指导下进行3~9 h溶栓治疗的研究仍在进行中^[71]。关于后循环供血区梗死的溶栓治疗时间窗没有达成共识,也没有相对明确的规定。Montavont等^[72]研究18例后循环供血区梗死的患者在发病7 h内给予rt-PA静脉溶栓治疗,对患者进行长期随访3个月,结果其中大多数患者生活自理(mRS评分0~2分),因此他们认为对发病7 h内的后循环供血区梗死进行rt-PA静脉溶栓治疗是安全有效的。关于轻型脑卒中是否溶栓治疗仍存在争议,因此临床医师对一些接受过治疗但症状轻微的患者静脉溶栓更为谨慎^[73-75]。黄如月等^[76]研究提出脑桥梗死超急性期静脉溶栓可能有效且安全的,虽然溶栓后神经功能恶化或波动发生率较高,但短期预后仍然较好。

7.2 目前血管内治疗手段包括动脉溶栓、动脉取栓、血管形成术,后循环供血区梗死的时间窗可酌情延长到24 h^[77]。PROACT II研究和MELT研究为急性缺血性脑卒中动脉溶栓治疗提供了证据,但适宜使用机械取栓的情况下不应优先使用动脉溶栓治疗。针对适于静脉溶栓的患者,首先推荐静脉溶栓,然后可考虑桥接动脉取栓,不建议直接进行血管内治疗^[78]。血管形成术在椎-基底动脉病变的治疗上已经取得了较好的效果,包括经皮腔内血管成形术(percutaneous transluminal angioplasty, PTA)和(或)经皮腔内血管成形支架置入术(percutaneous transluminal angioplasty and stenting, PTAS)。缺血性脑卒中患者血管内治疗的脑动脉再通率高于静脉溶栓治疗。然而,上述两种治疗方法的临床效果须进一步的研究和比较。Cicone等最近的一项研究发现,急性缺血性脑卒中患者的血管内治疗并不优于rt-PA静脉溶栓治疗^[79]。

7.3 根据WHO提出的标准进行康复治疗,当患者生命体征稳定且神经系统功能不再恶化48 h后开始。Maulden等研究发现,急性脑卒中越早康复功能恢复越好^[80];Musicco等对比急性脑卒中后7 d内与15 d后开始康复的患者,发现前者远期预后明显好于后者^[81];Bernhardt等也研究建议早期康复^[82];国家“九五”攻关课题研究提出在急性脑卒中后2周内开始康复可获得良好效果^[83]。Patterson等报道1例位因脑桥梗塞而从闭锁综合征中恢复良好的患者,提出患者表现出良好的恢复可能是由于梗死部位水肿的消退和脑干可塑性被重症监护室的初步支持措施和早期的强化康复所增强,并认为早期和强化康复的患者^[84-86]的长期生存率 and 功能性结局有所改善。

8 预后及展望

Vemmos等^[87]提出孤立性脑桥梗死的临床症状一般轻微,且远期预后较好。脑桥梗死在临床上很常见,其表现复杂多变,目前借助MRI检查,临床诊断相对容易,仍有部分病例的病因诊断较为困难,治疗方面也正在进行许多新的尝试,我们相信伴随医学发展(包括病理学、影像学等),我们对脑桥梗死的认识和研究也将越来越深入。

参 考 文 献

- [1] Chen WH, Yi TY, Chen YE, et al. Assessment of bilateral cerebral peduncular infarction: Magnetic resonance imaging, clinical features, and prognosis[J]. J Neurol Sci, 2015, 357(1/2): 131-135.
- [2] Huang R, Zhang X, Chen W, et al. Stroke subtypes and topographic locations associated with neurological deterioration in acute isolated pontine infarction[J]. J Stroke Cerebrovasc Dis, 2016, 25(1): 206-213.
- [3] Kim JS, Lee JH, Im JH, et al. Syndromes of pontine base infarction-A clinical-radiological correlation study[J]. Stroke, 1995, 26(6): 950-955.
- [4] 方岩, 袁向东, 李家亮, 等. 临床脑血管疾病[M]. 石家庄: 河南医科大学出版社, 1998: 194.
- [5] Kobayashi J, Ohara T, Minematsu K, et al. Etiological mechanisms of isolated pontine infarcts based on arterial territory involvement[J]. J Neurol Sci, 2014, 339(1-2): 113-117.
- [6] Lv P, Jin H, Liu Y, et al. Comparison of risk factor between lacunar stroke and large artery atherosclerosis stroke: a cross-sectional study in China[J]. PLoS One, 2016, 11(3): e0149605.
- [7] Manukyan L, Boyajyan A, Arakelyan A, et al. Immunochemical composition of cryoglobulins generated in stroke[J]. J Clin Immunol, 2009, 29(3, SI): 274-281.
- [8] Olindo S, Khaddam S, Bocquet J, et al. Association between basilar artery hypoplasia and undetermined or lacunar posterior circulation ischemic stroke[J]. Stroke, 2010, 41(10): 2371-2374.
- [9] Ichikawa H, Mukai MHieda S, et al. Involvement of the basilar artery in diabetes mellitus: An MRI study of brainstem infarctions[J]. Eur Neurol, 2010, 64(4): 230.
- [10] Zhang DP, Zhang SL, Zhang JW, et al. Basilar artery bending length, vascular risk factors, and pontine infarction[J]. J Neurol Sci, 2014, 338(1/2): 142-147.
- [11] Erro ME, Gállego J, Herrera M, et al. Isolated pontine infarcts: etiopathogenic mechanisms[J]. Eur J Neurol, 2005, 12(12): 984-988.
- [12] Vemmos KN, Spengos K, Tsvigoulis G, et al. Aetiopathogenesis and long-term outcome of isolated pontine infarcts[J]. J Neurol, 2005, 252(2): 212-217.
- [13] Kumral E, Bayülkem G, Evyapan D. Clinical spectrum of pontine infarction[J]. J Neurol, 2002, 249(12): 1659-1670.
- [14] Lx1 Z, Yao M, Ni J, Zhu YC, Peng B, Cui LY. morphological classification of acute isolated pontine infarction and its clinical relevance[J]. Zhonghua Yi Xue Za Zhi, 2018, 98(45): 0376-2491.
- [15] Fisher CM, Caplan LR. Basilar artery branch occlusion: a cause of pontine infarction[J]. Neurology, 1971, 21(9): 900-905.
- [16] Yamamoto Y, Ohara T, Hamanaka M, et al. Characteristics of intracranial branch atheromatous disease and its association with progressive motor deficits[J]. J Neurol Sci, 2011, 304(1/2): 78-82.
- [17] 朱子龙, 任宁, 王世民, 等. 单纯脑桥梗死的 TOAST 分型特征分析[J]. 脑血管疾病临床与基础研究, 2013, 13(4): 308-312.
- [18] Tan EK, Chan LL, Auchus AP. Hemidystonia precipitated by acute pontine infarction[J]. J Neurol Sci, 2005, 234(1-2): 109-

- 111.
- [19] Obaid SI, Magro E, Seizeur R. A case of dorsolateral pontine infarct; Description of a new vascular alternating syndrome[J]. *Neurochirurgie*, 2016, 62(2): 100-104.
- [20] Hosaka A, Tsunoda R, Yamaguchi T, et al. Body lateropulsion and cerebellar tremor in a patient with pontine infarction[J]. *Internal Medicine*, 2017, 56(5): 563-565.
- [21] Kang HG, Cheong JS, An H. Acute pontine infarction presenting with depressive mood only[J]. *Geriatr Gerontol Int*, 2016, 16(9): 1085-1086.
- [22] Ishizawa K, Ninomiya M, Nakazato Y, et al. "Heart appearance" infarction of the pons: A case report[J]. *Case Rep Radiol*, 2012, 2012: 690903.
- [23] Sen D, Arora V, Adlakha S, et al. The 'heart appearance' sign in bilateral pontine infarction[J]. *Journal of Stroke & Cerebrovascular Diseases*, 2015, 24(1): E21-E24.
- [24] Eggenberger E. Eight-and-a-half syndrome; one-and-a-half syndrome plus cranial nerve VII palsy[J]. *J Neuroophthalmol*, 1998, 18(2): 114-116.
- [25] Bocos-Portillo J, Ruiz OJ, Gomez-Beldarrain M, et al. Eight-and-a-Half syndrome[J]. *JAMA Neurol* 830. doi: 10. 1001/jama-neurol. 2015. 72(7): 0255.
- [26] Kumar N, Raju CG, Kiran PR, et al. Eight-and-a-Half syndrome: a rare presentation of pontine infarction[J]. *Journal of Stroke & Cerebrovascular Diseases*, 2014, 23(8): E389-E391.
- [27] Maas RPPWM1, Verrips A2. Teaching video neuroImages: Nine syndrome in inferior paramedian pontine infarction; More than meets the eye[J]. *Neurology*, 2017, 89(8): 51-52.
- [28] FeiYan, ZhuBai, ChenWang, et al. ZhenZhongZhang, fifteen-and-a-half syndrome; a rare presentation of pontine infarction [Z]. *Clin Neurol Neurosurg*, 2018, 173: 150-153.
- [29] 林琅, 濮捷, 崔敏, 等. 磁共振检查对基底动脉血栓形成患者的诊断价值[J]. *卒中与神经疾病*, 2007, 14(3): 150-153.
- [30] Dieterich M, Brandt T. Vestibular system-Anatomy and functional magnetic resonance imaging[J]. *Neuroimaging Clin N Am*, 2001, 11(2): 263.
- [31] Klein IF, Lavallée PC, Mazighi M, et al. Basilar artery atherosclerotic plaques in paramedian and lacunar pontine infarctions: a high-resolution MRI study[J]. *Stroke*, 2010, 41(7): 1405-1409.
- [32] Wintermark M, Sanelli PC, Albers GW, et al. Imaging recommendations for acute stroke and transient ischemic attack patients[J]. *J Am Coll Radiol*, 2013, 10(11): 828-832.
- [33] Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/ American Stroke Association[J]. *Stroke*, 2013, 44(3): 870-947.
- [34] Xu WH, Li ML, Gao S, et al. In vivo high-resolution Mr imaging of symptomatic and asymptomatic middle cerebral artery atherosclerotic stenosis[J]. *Atherosclerosis*, 2010, 212(2): 507-511.
- [35] Ma N, Jiang WJ, Lou X, et al. Arterial remodeling of advanced basilar atherosclerosis: a 3-tesla MRI study[J]. *Neurology*, 2010, 75(3): 253-258.
- [36] Cho HJ, Kim KH, Kim EJ, et al. Clinical implications of basilar artery plaques in the pontine infarction with normal basilar angiogram: a High-Resolution magnetic resonance imaging study[J]. *J Stroke Cerebrovasc Dis* 10. 1016/j. jstrokecerebrovasdis. 2018. 27(12): 3591-3598.
- [37] 于瑾, 白晶, 吴士文, 等. 应用高分辨率磁共振成像评估脑动脉粥样硬化斑块的研究进展[J]. *中国康复理论与实践*, 2016, 22(2): 164-167.
- [38] Miyaji Y, Kawabata Y, Joki H, et al. High-resolution magnetic resonance imaging findings of basilar artery plaque in a patient with branch atheromatous disease: a case report[J]. *J Med Case Rep*, 2014, 8(1): 395.
- [39] Zhu XJ, Jiang WJ, Liu L, et al. Plaques of nonstenotic basilar arteries with isolated pontine infarction on three-dimensional high isotropic resolution magnetic resonance imaging[J]. *Chin Med J (Engl)*, 2015, 128(11): 1433-1437.
- [40] Gonzalez RG, Lev MH, Goldmacher GV, et al. Improved outcome prediction using CT angiography in addition to standard ischemic stroke assessment: results from the STOPStroke study[J]. *PLoS One*, 2012, 7(1): e30352.
- [41] Nonent M, Ben Salem D, Serfaty JM, et al. Overestimation of moderate carotid stenosis assessed by both Doppler US and contrast enhanced 3D-MR angiography in the CARMEDAS study[J]. *Journal of Neuroradiology*, 2011, 38(3): 148-155.
- [42] Anna MH, Janneke P, Joachim E, et al. Cost-effectiveness of CTA, MRA and DSA in patients with non-traumatic subarachnoid haemorrhage[J]. *Insights Imaging*, 2013, 4(4): 499-507.
- [43] Saia V, Pantoni L. Progressive stroke in pontine infarction[J]. *Acta Neurol Scand*, 2009, 120(4): 213-215.
- [44] Aoki J, Iguchi Y, Kimura K, et al. Diameter of the basilar artery May be associated with neurological deterioration in acute pontine infarction[J]. *Eur Neurol*, 2010, 63(4): 221-226.
- [45] 赵吴, 曹树刚, 吴倩, 等. 孤立性脑桥梗死后进展性运动功能缺损的预测因素: 回顾性病例系列研究[J]. *国际脑血管病杂志*, 2015(3): 1673-1675.
- [46] Lim SH, Choi H, Kim HT, et al. Basilar plaque on high-resolution MRI predicts progressive motor deficits after pontine infarction[J]. *Atherosclerosis*, 2015, 240(1): 278-283.
- [47] Gokcal E, Niftaliyev E, Baran G, et al. Progressive deficit in isolated pontine infarction: the association with etiological subtype, lesion topography and outcome[J]. *Acta Neurol Belg*, 2017, 117(3): 649-654.
- [48] Nakase T, Sasaki M, Ikeda Y, et al. Progressing small vessel pontine infarction includes different etiologies[J]. *Annals of clinical and translational neurology*, 2014, 1(2): 75-79.
- [49] Mehdiratta M, Caplan LR, Kumar S. Basilar artery branch disease imaged by magnetic resonance imaging[J]. *Arch Neural*, 2007, 64(11): 1666.
- [50] Kaps M, Klostermann W, Wessel K, et al. Basilar branch disease presenting with progressive pure motor stroke[J]. *Acta Neurol Scand*, 1997, 96(5): 324-327.
- [51] 陈珂楠, 郭舜源, 陈桂花, 等. 累及脑桥表面的孤立单侧脑桥梗死与进展性运动障碍的关系[J]. *中华神经科杂志*, 2013, 46(3): 172-175.
- [52] Toyoda K, Saku Y, Ibayashi S, et al. Pontine infarction extending to the basal surface[J]. *Stroke*, 1994, 25(11): 2171-2178.
- [53] 陈红兵, 王莹, 李玲, 等. 累及脑桥表面和脑桥内部的单侧孤立性脑桥梗死[J]. *中国神经精神疾病杂志*, 2011, 37(5): 280-284.

- [54] Duan SS, Li L. Carotid artery intima • media thickness associated with prognosis of intracranial branch atheromatous disease [J]. *Int J Neurosci*, 2017, 127(4): 367.
- [55] Nam KW, Lim JS, Kang DW, et al. Severe white matter hyperintensity is associated with early neurological deterioration in patients with isolated pontine infarction [J]. *Eur Neurol*, 2016, 76(3/4): 117-122.
- [56] Zhao L, Zhai Z, Hou W. Analysis of carotid color ultrasonography and high sensitive c-reactive protein in patients with atherosclerotic cerebral infarction [J]. *Pak J Med Sci*, 2016, 32(4): 931-934.
- [57] Men XJ, Zhang B. Homocysteine and C-reactive protein associated with progression and prognosis of intracranial branch atheromatous disease [J]. *PLoS One*, 2013, 8(9): e73030.
- [58] Chen YJ. Multiple factors involved in acute progressive cerebral infarction and extra-and intracranial arterial lesions [J]. *Exp Ther Med*, 2014, 7(6): 1495-1505.
- [59] Zang RS, Zhang HY. Serum C • reactive protein, fibrinogen and D-dimer in patients with progressive cerebral infarction [J]. *Transl Neurosci*, 2016, 7(1): 84-88.
- [60] Wang Y, Wang Y, Zhao X, et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack [J]. *N Engl J Med*, 2013, 369: 11-19.
- [61] The Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Study Group. Prognosis of Patients with symptomatic vertebral or basilar artery stenosis [J]. *Stroke*, 1998, 29(7): 1389-1392.
- [62] Kang K, Yoon BW. Symptomatic intracerebral hematomas in posterior circulation stroke patients anticoagulated with heparin [J]. *J Thromb Thrombolysis*, 2006, 21(3): 249-255.
- [63] Oh S, Bang OY, Chung CS, et al. Topographic location of acute pontine infarction is associated with the development of progressive motor deficits [J]. *Stroke*, 2012, 43(3): 708.
- [64] Huang R, Zhang X, Chen W, et al. Stroke subtypes and topographic locations associated with neurological deterioration in acute isolated pontine infarction [J]. *J stroke cerebrovasc Dis*. DOI: 10.1016/j.jstrokecerebrovasdis.2015.25(1): 206-213.
- [65] 孙向军, 寇桂娟, 张珊珊, 等. 不同治疗方案进展性分支动脉粥样硬化病的 1 临床疗效 [J]. *1 临床与病理杂志*, 2017, 37(6): 1194.
- [66] Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of Atlantis, ECASS, and NINDS rt-PA stroke trials [J]. *Lancet*, 2004, 363(9411): 768-774.
- [67] Liao XL, Wang YL, Wang CJ, et al. Thrombolysis with intravenous recombinant tissue plasminogen activator 3 to 4 [Z]. 2012; A62.
- [68] Schneider D, von Kummer R, Wahlgren N, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke [J]. *N Engl J Med*, 2008, 359(13): 1317-1329.
- [69] Ahmed N, Wahlgren N, Ground M, et al. Implementation and outcome of thrombolysis with alteplase 3-4.5h after an acute stroke: An updated analysis from SITS-ISTR [J]. *Lancet Neurol*, 2010, 9(9): 866-874.
- [70] 重组组织型纤溶酶原激活剂治疗缺血性卒中共识专家组. 重组组织型纤溶酶原激活剂治疗缺血性卒中中国专家共识 (2012 版) [J]. *中华内科杂志*, 2012, 51(12): 1006-1010.
- [71] Ma H, Parsons MW, Christensen S, et al. A multicentre, randomized, double-blinded, placebo-controlled phase III study to investigate EXtending the time for Thrombolysis in Emergency Neurological Deficits (EXTEND) [J]. *Int J Stroke*, 2012, 7(1): 74-80.
- [72] Montavoni A, Nighoghossian N, Derex L, et al. Intravenous r-TPA in vertebrobasilar acute infarcts [J]. *Neurology*, 2004, 62(10): 1854-1856.
- [73] Shi L, Zhang M, Liu H, et al. Safety and outcome of thrombolysis in mild stroke: a meta-analysis [J]. *Med Sci Monit*, 2014, 20: 2117-2124.
- [74] Group Collaborative IST-3, Sandercock P, Wardlaw JM, et al. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial [J]. *Lancet*, 2012, 379(12): 60765-60768.
- [75] Greisenegger S, Seyfang L, Kiechl S, et al. Thrombolysis in patients with mild stroke results from the Austrian stroke unit registry [J]. *Stroke*, 2014, 45(3): 765-769.
- [76] 黄如月, 邵蓓, 王鹏, 等. 孤立性脑桥梗死患者静脉溶栓的短期预后及安全性探讨 [J]. *中华老年心脑血管病杂志*, 2017, 19(4): 395-398.
- [77] 中华预防医学会卒中预防与控制专业委员会介入学组. 急性缺血性卒中血管内治疗中国专家共识 [J]. *中华医学杂志*, 2014, 94(27): 2097-2010.
- [78] 中华医学会神经病学分会. 中国急性缺血性脑卒中早期血管内介入诊疗指南 2018 [J]. *中华神经科杂志*, 2018, 51(9): 683-691.
- [79] Ciccone A, V. L., Synthesis E. I. Endovascular treatment for acute ischemic stroke [J]. *N Engl J Med*, 2013, 368(10): 904-913.
- [80] Maulden SA, Gassaway J, Horn SD, et al. Timing of initiation of rehabilitation after stroke [J]. *Arch Phys Med Rehabil*, 2005, 86(12 Suppl 2): S34-S40.
- [81] Musicco M, Emberti L, Nappi G, et al. Early and long-term outcome of rehabilitation in stroke patients: the role of patient characteristics, time of initiation, and duration of intervention [J]. *Arch Phys Med Rehabil*, 2003, 84(4): 551-558.
- [82] Bernhardt J, Dewey H, Thrift A, et al. A very early rehabilitation trial for stroke (AVERT): phase II safety and feasibility [J]. *Stroke*, 2008, 39(2): 390-396.
- [83] 九五. 攻关课题组. 急性脑卒中早期康复的研究 [J]. *中国康复医学杂志*, 2001, 16(5): 266-272.
- [84] Patterson JR, Grabis M. Locked-in syndrome: a review of 139 cases [J]. *Stroke*, 1986, 17(4): 758-764.
- [85] Casanova E, Lazzari RE, Lotta S, et al. Locked-in syndrome: Improvement in the prognosis after an early intensive multidisciplinary rehabilitation [J]. *Arch Phys Med Rehabil*, 2003, 84(6): 862-867.
- [86] Leemann B, Schneider A. Unusually favorable recovery from locked-in syndrome after basilar artery occlusion [J]. *Rev Med Suisse*, 2010, 6(241): 633-635.
- [87] Vemmos KN, Spengos K, Tsivgoulis G, et al. Aetiopathogenesis and long-term outcome of isolated pontine infarcts [J]. *J Neurol*, 2005, 252(2): 212-217.