

·讲座 Lecture·

急性缺血性脑卒中血管腔内治疗后对比剂外渗影像学研究现状

梁 高, 余 薇, 谢明国, 刘 敏, 刘姝芬, 侯中华, 张明星

【摘要】 对比剂外渗(CE)和出血性转化(HT)是急性缺血性脑卒中血管腔内治疗(EVT)后的常见并发症,两者有相似的影像学表现,不同的临床治疗方法和转归。早期鉴别诊断CE和HT,对临床治疗和预后至关重要。本文就临床CE影响因素,常规CT、双能CT(DECT)及MRI诊断EVT后CE研究现状作一综述,为预防CE和早期鉴别诊断提供帮助。

【关键词】 对比剂外渗;血管腔内治疗;出血性转化;研究现状

中图分类号:R816 文献标志码:A 文章编号:1008-794X(2023)-01-0098-04

Research status of contrast extravasation imaging in acute ischemic stroke after endovascular therapy LIANG Gao, YU Wei, XIE Mingguo, LIU Min, LIU Shufen, HOU Zhonghua, ZHANG Mingxin. Department of Radiology, Affiliated Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan Province 610075, China

Corresponding author: XIE Mingguo, E-mail: xmg6806@163.com

【Abstract】 Contrast extravasation (CE) and hemorrhagic transformation (HT) is a common occurrence after endovascular therapy (EVT) for acute ischemic stroke. CE and HT have similar imaging manifestations, but their clinical treatment methods and outcomes are different. Early differential diagnosis of CE and HT is essential for clinical treatment and prognosis. This paper aims to make a comprehensive review about the recent advances in CE, focusing on the CE influencing factors and the diagnosis of post-EVT CE by conventional CT, dual-energy CT (DECT) and MRI, so as to provide useful references for prevention of CE and early differential diagnosis.

【Key words】 contrast extravasation; endovascular therapy; hemorrhagic transformation; research status

急性大血管闭塞性脑卒中病情较危急,血管腔内治疗(endovascular therapy, EVT)是最新国内外指南均推荐的标准治疗方式,可降低患者病死率^[1]。EVT后出现脑实质及蛛网膜下腔的高密度影如对比剂外渗(contrast extravasation, CE)和出血性转化(hemorrhagic transformation, HT)并不少见。HT是急性缺血性脑卒中最为严重并发症之一,致残率较高达50%,甚至增加死亡风险^[2-3]。HT需立即停止抗凝,给予止血治疗,中和肝素和停用抗血小板药物。目前多数研究认为单纯CE与EVT后未见高密度影患者预后相近^[4-5],相关系统综述评价研究显示CE与EVT后院内病死率或90 d病死率无关联^[6]。

CE患者为预防血管再通后发生二次闭塞,无需停止抗凝、抗血小板治疗等,此类治疗可增加新出血和已存在实质内出血加重的风险。CE和HT在常规CT均表现为高密度影,很难鉴别,而临床及时鉴别对后续治疗和预后至关重要。本文就EVT后CE影像学研究现状作一综述,以期预防CE和早期鉴别诊断提供帮助。

1 CE原因

正常情况下,由于血脑屏障(blood-brain barrier, BBB)存在,对比剂不会进入脑实质及蛛网膜下腔。CE和HT是BBB通透性和完整性受到不

DOI:10.3969/j.issn.1008-794X.2023.01.023

作者单位: 610075 四川成都 成都中医药大学附属医院放射科(梁 高、余 薇、谢明国、刘姝芬、侯中华、张明星);成都华西海圻医药科技有限公司毒理部(刘 敏)

通信作者: 谢明国 E-mail: xmg6806@163.com

同程度损伤的结果。BBB 完整性依赖血管内皮细胞和基底膜,CE 引发损伤往往仅限于内皮细胞通透性屏障,而 HT 损伤通常延伸至基底膜层^[7-8]。综合相关文献,目前认为 CE 主要原因:远端毛细血管床灌注压增高导致渗出和 BBB 破坏,如缺血区过度再灌注损伤和对比剂注射导致局部血管压力骤然增高^[9]。缺血区侧支循环代偿差,对比剂排空缓慢^[10]。手术操作过程手术器材对血管壁损伤,导致 BBB 短期破坏^[11]。缺血时间增加也会加重血管壁损伤,多项研究显示 EVT 手术操作时间、血管再通时间及拉栓次数等增加均与 CE 发生相关^[12-15]。对比剂有一定的神经毒性,即使是渗透压与血浆相近的非离子型对比剂碘克沙醇,也会导致 BBB 损伤^[16]。

2 影像学检查

2.1 常规 CT

常规 CT 平扫适应证宽,有良好的密度和空间分辨率,是鉴别 EVT 后 CE 和 HT 最便捷的影像学检查方法。相关研究显示,31%~85%缺血性脑卒中患者 EVT 后常规 CT 检查出现高密度区,其中 16%~46%为 HT^[17-18]。参考相关研究,常规 CT 上 CE 主要分为 3 型:①对比剂滞留或代谢缓慢所致假外渗现象,表现为对称性高密度影,按血管分布多位于颅内较大血管、小脑幕、大脑镰及静脉窦,短期 4 h 内随访即可消失^[4,19-20];②脑缺血梗死区高密度影,可似蛛网膜下腔出血表现,但无明显占位效应,随访 24 h 高密度影明显吸收消失,最终快速完全吸收^[17,19,21];③4 h、24 h 随访颅内高密度影不减或减小不显著,且存在占位效应^[22]。研究显示常规 CT 诊断 CE 和 HT 的灵敏度和特异度不高^[17]。Payabvash 等^[23]研究常规 CT 对 CE 和 HT 的鉴别价值,发现术后即刻行常规 CT 示高密度灶 CT 值 <50 HU,可排除 HT。但该研究中患者接受多种 EVT,部分患者在血管内溶栓/取栓前接受静脉重组组织型纤溶酶原激活剂治疗,这可能带来异质性。也有学者研究认为 CT 值 50~90 HU 为 HT,>50 HU 不能排除 CE,>90 HU 多有 CE,而血肿一般不 >90 HU^[24]。但是上述研究的 CT 扫描时间为 EVT 术后即刻 24 h 内。此外,相关指南及研究有将 CT 高密度影大小、形态及占位效应进行分级,分级越高提示 HT 风险越大^[25]。有研究基于常规 CT 联合影像组学诊断区分机械取栓后 CE 和 HT,诊断准确率为 77.6%,灵敏度为 76.7%,特异度为 78.9%^[26]。

2.2 双能 CT

随着影像技术发展,双能 CT(dual-energy CT, DECT)逐渐应用于临床。利用双能物质分离技术,可鉴别具有不同衰减特性的物质。利用碘和血液在不同能级(通常为 80 kW 和 140 kW)衰减特性不同,可获得碘基图(iodine overlay map, IOM)和不含碘的虚拟平扫(virtual non-contrast, VNC)图像并鉴别 CE 和 HT,仅在 VNC 上显示高密度影为脑出血, IOM 上显示高密度影为 CE, VNC 和 IOM 均显示高密度影为 HT 伴 CE。一些研究表明,DECT 鉴别 EVT 后 CE 和脑出血有很高的灵敏度(99.1%~100%)和特异度(96.1%~98.2%)^[22,27-32]。Bonatti 等^[33]利用 DECT 研究碘 CE 定量预测机械取栓术后脑出血的价值,发现脑实质内碘浓度 >1.35 mg/mL 预测出血的灵敏度为 100%,认为 CE 是 BBB 破坏的标志,易导致 HT,碘浓度与 HT 严重程度呈正相关。然而 VNC 图像可能因碘去除不完全而出现假阳性结果,即碘浓度 >37 mg/dL 时存在饱和效应^[5]。钙化和金属伪影在 VNC 和 IOM 图像上均表现为高密度,这在一定程度上降低了 DECT 诊断出血的特异度^[25,27,34]。尽管 DECT 鉴别 CE 和 HT 有明显优势,但与传统单源 CT 检查相比费用昂贵,尚未在临床广泛应用。

2.3 MRI

目前国内外关于 MRI 诊断 CE 研究较少,但诊断 HT 研究较多。MRI 临床应用很大程度上受扫描速度及禁忌证的影响,对患者配合度要求高。Jenkins 等^[35]于 1992 年最先观察到碘对比剂对质子弛豫的影响。有研究指出,假体模型中碘对比剂引起的 T1WI 和 T2WI 图像特点与亚急性期(3~7 d) HT 表现相近^[36]。Hergan 等^[37]也得出一致结论,证实这种质子弛豫的影响与碘对比剂浓度有关。理论上含碘对比剂会使组织的 T1 和 T2 弛豫时间缩短,其作用机制包括顺磁性、束缚水效应和偶极-偶极相互作用^[36-38]。Morales 等^[38]研究显示,碘克沙醇和碘帕醇可缩短组织的 T1 和 T2 弛豫时间,且 T2 弛豫时间缩短所致 T2WI 图像上信号变化比 T1WI 变化更明显,但在血液降解的不同时期,降解产物组成是复杂的,可表现为顺磁性或抗磁性,这为 CE 伴 HT 诊断带来挑战。Nikoubashman 等^[39]通过动物实验研究不同稀释倍数下碘对比剂在场强 1.5T MR 的信号改变,提出碘对比剂稀释 10 倍以上时对组织 T1 和 T2 弛豫时间的影响可忽略,并认为碘对比剂注射至体内被大量血液稀释对 MR 信号影响可忽略。然而该研究是将对比剂直接注射至动物模型

或行体外实验,未能真实地模拟出 CE 状态。You 等^[40]应用 3.0T MR 对 EVT 后患者即刻行弥散加权成像(diffusion weighted imaging, DWI)及梯度回波(gradient recalled-echo, GRE)序列检查,结果显示 DWI 和 GRE 序列可早期有效鉴别 HT。马永青等^[41]研究磁敏感加权成像诊断微出血灶、评估脑梗死预后的价值,结果显示磁敏感序列对微出血灶的灵敏度优于 T2WI 序列,微出血灶数与 HT、脑梗死患者预后有关。

3 结语

EVT 后影像学早期鉴别患者 CE 和 HT 对诊疗和转归有着重要临床意义。开通绿色通道、选择合理的 EVT 治疗方式、提高 EVT 术者操作熟练度、减少对比剂用量,有助于减少 CE 和 HT 发生。CT 平扫用于早期鉴别有一定帮助,有待于进一步研究探索,CT 联合影像组学有待于深度研究。DECT 可明确诊断 CE 和 HT,但设备昂贵,普及率低,期待降低设备成本,提高普及率。MRI 可准确诊断 HT,但临床禁忌证多,期待新技术应用,减少禁忌证。

〔参考文献〕

- [1] Wollenweber FA, Tiedt S, Alegiani A, et al. Functional outcome following stroke thrombectomy in clinical practice [J]. *Stroke*, 2019, 50: 2500–2506.
- [2] Horsch AD, Bennink E, Van ST, et al. Computed tomography perfusion derived blood–brain barrier permeability does not yet improve prediction of hemorrhagic transformation [J]. *Cerebrovasc Dis*, 2018, 45: 26–32.
- [3] 刘钦晨,贾振宇,赵林波,等. 梗死核心容积预测急性前循环大血管闭塞患者机械取栓术后出血转化的价值[J]. *介入放射学杂志*, 2021, 30: 756–760.
- [4] Mokin M, Kan P, Kass-Hout T, et al. Intracerebral hemorrhage secondary to intravenous and endovascular intraarterial revascularization therapies in acute ischemic stroke: an update on risk factors, predictors, and management [J]. *Neurosurg Focus*, 2012, 32: E2.
- [5] Parrilla G, Garcia-Villalba B, Espinosa de Rueda M, et al. Hemorrhage/contrast staining areas after mechanical intra-arterial thrombectomy in acute ischemic stroke: imaging findings and clinical significance [J]. *AJNR Am J Neuroradiol*, 2012, 33: 1791–1796.
- [6] Xu T, Wang Y, Yuan J, et al. Contrast extravasation and outcome of endovascular therapy in acute ischaemic stroke: a systematic review and meta-analysis [J]. *BMJ Open*, 2021, 11: e044917.
- [7] Alvarez-Sabin J, Maisterra O, Santamarina E, et al. Factors influencing haemorrhagic transformation in ischaemic stroke [J]. *Lancet Neurol*, 2013, 12: 689–705.
- [8] Shi ZS, Duckwiler GR, Jahan R, et al. Early blood–brain barrier disruption after mechanical thrombectomy in acute ischemic stroke [J]. *J Neuroimaging*, 2018, 28: 283–288.
- [9] Sun Y, Su Y, Chen Z, et al. Contrast extravasation after endovascular treatment in posterior circulation stroke [J]. *World Neurosurg*, 2019, 130: e583–e587.
- [10] Molina CA, Alvarez-Sabin J. Recanalization and reperfusion therapies for acute ischemic stroke [J]. *Cerebrovasc Dis*, 2009, 27 (Suppl 1): 162–167.
- [11] Keulers A, Nikoubashman O, Mpotsaris A, et al. Preventing vessel perforations in endovascular thrombectomy: feasibility and safety of passing the clot with a microcatheter without microwire: the wireless microcatheter technique [J]. *J Neurointerv Surg*, 2019, 11: 653–658.
- [12] 杜川,程文,杨全龙,等. 急性大血管闭塞性卒中机械取栓术后对比剂外渗的影响因素研究[J]. *中华脑科疾病与康复杂志(电子版)*, 2020, 10: 106–109.
- [13] 王大巍,高阿芳,束汉生,等. 急性缺血性脑卒中机械取栓后造影剂渗出的临床研究[J]. *蚌埠医学院学报*, 2019, 44: 1170–1172.
- [14] 付睿,贺茂林,赵星辉,等. 急性缺血性卒中动脉溶栓后造影剂渗出的临床分析[J]. *中华临床医师杂志(电子版)*, 2013, 7: 2365–2369.
- [15] Liu K, Jiang L, Zhao Y, et al. Risk factors of contrast extravasation and subsequent hemorrhagic transformation after thrombectomy [J]. *J Int Med Res*, 2021, 49: 3000605211049074.
- [16] Yedavalli V, Sammet S. Contrast extravasation versus hemorrhage after thrombectomy in patients with acute stroke [J]. *J Neuroimaging*, 2017, 27: 570–576.
- [17] Kim JT, Heo SH, Cho BH, et al. Hyperdensity on non-contrast CT immediately after intra-arterial revascularization [J]. *J Neurol*, 2012, 259: 936–943.
- [18] Whitney E, Khan YR, Alastrá A, et al. Contrast extravasation post thrombectomy in patients with acute cerebral stroke: a review and recommendations for future studies [J]. *Cureus*, 2020, 12: e10616.
- [19] Jang YM, Lee DH, Kim HS, et al. The fate of high-density lesions on the non-contrast CT obtained immediately after intra-arterial thrombolysis in ischemic stroke patients [J]. *Korean J Radiol*, 2006, 7: 221–228.
- [20] Yoon W, Seo JJ, Kim JK, et al. Contrast enhancement and contrast extravasation on computed tomography after intra-arterial thrombolysis in patients with acute ischemic stroke [J]. *Stroke*, 2004, 35: 876–881.
- [21] Nakano S, Iseda T, Kawano H, et al. Parenchymal hyperdensity on computed tomography after intra-arterial reperfusion therapy for acute middle cerebral artery occlusion: incidence and clinical significance [J]. *Stroke*, 2001, 32: 2042–2048.
- [22] 刘美洲,刘辉佳,富彦,等. 双源双能量 CT 在鉴别急性缺血性脑梗死血运重建术后碘造影剂外渗和继发脑出血中的价值 [J]. *实用医学杂志*, 2017, 33: 2569–2572.
- [23] Payabvash S, Qureshi MH, Khan SM, et al. Differentiating

- intraparenchymal hemorrhage from contrast extravasation on post-procedural noncontrast CT scan in acute ischemic stroke patients undergoing endovascular treatment [J]. *Neuroradiology*, 2014, 56: 737-744.
- [24] Xu C, Zhou Y, Zhang R, et al. Metallic hyperdensity sign on noncontrast CT immediately after mechanical thrombectomy predicts parenchymal hemorrhage in patients with acute large-artery occlusion [J]. *AJNR Am J Neuroradiol*, 2019, 40: 661-667.
- [25] Chen S, Zhang J, Quan X, et al. Diagnostic accuracy of dual-energy computed tomography to differentiate intracerebral hemorrhage from contrast extravasation after endovascular thrombectomy for acute ischemic stroke: systematic review and meta-analysis [J]. *Eur Radiol*, 2022, 32: 432-441.
- [26] Chen X, Li Y, Zhou Y, et al. CT-based radiomics for differentiating intracranial contrast extravasation from intraparenchymal haemorrhage after mechanical thrombectomy [J]. *Eur Radiol*, 2022, 32: 4771-4779.
- [27] Gupta R, Phan CM, Leidecker C, et al. Evaluation of dual-energy CT for differentiating intracerebral hemorrhage from iodinated contrast material staining [J]. *Radiology*, 2010, 257: 205-211.
- [28] Zauwak Y, Sadeghi N, Sarbu N, et al. Differentiation between cerebral hemorrhage and contrast extravasation using dual energy computed tomography after intra-arterial neuro interventional procedures [J]. *J Belg Soc Radiol*, 2020, 104: 70.
- [29] Tijssen M, Hofman P, Stadler A, et al. The role of dual energy CT in differentiating between brain haemorrhage and contrast medium after mechanical revascularisation in acute ischaemic stroke [J]. *Eur Radiol*, 2014, 24: 834-840.
- [30] 陈国强, 刘国荣, 韩 洋, 等. 头颅双能量CT平扫在介入治疗后颅内出血诊断中的应用 [J]. *中华老年心脑血管病杂志*, 2018, 20: 576-579.
- [31] 朱凤英, 陈英敏, 马书敏, 等. 双能CT鉴别卒中取栓术后造影剂外渗与脑出血的价值 [J]. *中国实用神经疾病杂志*, 2019, 22: 1877-1884.
- [32] 郭 爽, 李 清, 吴 芳, 等. 双能CT在急性缺血性卒中血管内治疗术后早期脑出血与碘对比剂外渗鉴别诊断中的应用 [J]. *首都医科大学学报*, 2018, 39: 173-177.
- [33] Bonatti M, Lombardo F, Zamboni GA, et al. Iodine extravasation quantification on dual-energy CT of the brain performed after mechanical thrombectomy for acute ischemic stroke can predict hemorrhagic complications [J]. *AJNR Am J Neuroradiol*, 2018, 39: 441-447.
- [34] Phan CM, Yoo AJ, Hirsch JA, et al. Differentiation of hemorrhage from iodinated contrast in different intracranial compartments using dual-energy head CT [J]. *AJNR Am J Neuroradiol*, 2012, 33: 1088-1094.
- [35] Jenkins JR, Robinson JW, Sisk L, et al. Proton relaxation enhancement associated with iodinated contrast agents in MR imaging of the CNS [J]. *AJNR Am J Neuroradiol*, 1992, 13: 19-27.
- [36] Ganguly A, Gold GE, Butts PK, et al. Quantitative evaluation of the relaxivity effects of Iodine on GD-DTPA enhanced MR arthrography [J]. *J Magn Reson Imaging*, 2007, 25: 1219-1225.
- [37] Hergan K, Doring W, Langle M, et al. Effects of iodinated contrast agents in MR imaging [J]. *Eur J Radiol*, 1995, 21: 11-17.
- [38] Morales H, Lemen L, Samarasinghe R, et al. Effects of iodinated contrast on various magnetic resonance imaging sequences and field strength: implications for characterization of hemorrhagic transformation in acute stroke therapy [J]. *World J Radiol*, 2016, 8: 588-593.
- [39] Nikoubashman O, Jablawi F, Dekeyser S, et al. MRI appearance of intracerebral iodinated contrast agents: is it possible to distinguish extravasated contrast agent from hemorrhage? [J]. *AJNR Am J Neuroradiol*, 2016, 37: 1418-1421.
- [40] You SH, Kim B, Kim BK, et al. MR imaging for differentiating contrast staining from hemorrhagic transformation after endovascular thrombectomy in acute ischemic stroke: phantom and patient study [J]. *AJNR Am J Neuroradiol*, 2018, 39: 2313-2319.
- [41] 马永青, 尹 喜, 王成伟. 磁敏感加权血管成像对脑微出血的诊断及对急性脑梗死预后的评估 [J]. *中国医学影像学杂志*, 2019, 27: 584-588.

(收稿日期: 2021-11-13)

(本文编辑: 边 倩)