电子、语音版

·综述·

颅内动脉粥样硬化狭窄相关急性大血管闭塞早期血管内治疗的研究进展

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摘　要：早期血管内治疗已成为大血管闭塞(LVO)性缺血性脑卒中的标准再灌注治疗方法。而颅内动脉粥样硬化狭窄(ICAS)是亚洲人大血管闭塞性缺血性脑卒中的主要病因之一。对于此类病变，进行急诊机械取栓时容易发生早期再闭塞，相比较心源性栓塞常需要更多的补救措施、更长的手术时间，以实现血管再通。其最佳治疗策略尚没有大规模循证医学证据支持。因此术前尽早预判动脉粥样硬化性狭窄病变、制定合理、高效的血管内治疗策略至关重要。该文就近年来ICAS相关LVO的血管内治疗研究作一总结。
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关键词：颅内动脉粥样硬化性狭窄；大血管闭塞；缺血性脑卒中；血管内治疗

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Research advances in early endovascular treatment of large vessel occlusion due to intracranial atherosclerotic stenosis

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Abstract: Early endovascular treatment has become the standard reperfusion therapy for ischemic stroke due to large vessel occlusion (LVO), and intracranial atherosclerotic stenosis (ICAS) is one of the main causes of ischemic stroke due to LVO in Asian people. For such lesions, emergency mechanical thrombectomy may lead to early reocclusion, and compared with cardiogenic embolism, it often requires more rescue measures and a longer time of operation to achieve successful revascularization. There is still a lack of evidence-based medicine support for the optimal treatment strategy for ICAS-related LVO. Therefore, it is of great importance to early identify ICAS-related LVO and formulate reasonable and effective endovascular treatment strategy before surgery. This article reviews the recent studies on the endovascular treatment of ICAS-related LVO.
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Keywords: intracranial atherosclerotic stenosis; large vessel occlusion; ischemic stroke; endovascular treatment

颅内动脉粥样硬化性狭窄(intracranial atherosclerosis, ICAS)是亚洲人群缺血性脑卒中的主要病因之一[1-2]，源于ICAS的大血管闭塞(large vessel occlusion, LVO)也是亚洲人大动脉闭塞性急性缺血性脑卒中(acute ischemic stroke, AIS)的常见原因。血管内治疗(endovascular treatment, EVT)是目前LVO-AIS的一线治疗，快速再通是预后良好的关键。然而，欧美国家由于ICAS-LVO比例较低，目前临床上所运用的一线取栓装置，如可回收支架、抽吸导管等，均针对心源性栓塞设计的，运用于ICAS-LVO无法取得同等疗效[3-4]。ICAS-LVO患者的穿刺—再

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通时间、补救措施和再闭塞的发生率均远高于栓塞性病变,并通常需要永久性支架植入[5-6]。因此,快速、准确地识别ICAS-LVO,制定针对性的血管内治疗策略,一直是亚洲神经介入医师探究的话题。本文通过回顾ICAS相关LVO的血管内治疗相关文献,对其定义、早期判断、治疗现状及策略等方面进行阐述,以对临床实践提供借鉴。

1　ICAS-LVO的流行病学及定义

颅内动脉粥样硬化性狭窄在不同人种之间差异明显。在白种人中,ICAS仅占到所有卒中病因的9%[7]。而亚洲人常见,如韩国人中ICAS(≥50%)约占所有缺血性脑卒中的29.6%[8],中国人其比例高达46.6%[9]。因此亚洲人群ICAS-LVO发病更多见(表1)。

表1　符合EVT条件的ICAS-LVO发生率

作者	发表年份	国家	ICAS-LVO定义	前后循环	例数	发生率/%
Matias等[10]	2014	西班牙	TOAST分型	均有	88	17
Gascou等[11]	2014	法国、英国	颅内动脉狭窄	均有	144	5.5
Lee等[12]	2015	韩国	显著固定局灶性狭窄	均有	158	15.2
Yoon等[13]	2015	韩国	严重狭窄≥70%	均有	172	22.9
Hwang等[14]	2016	韩国、美国	靶血管狭窄≥50%	均有	163	25
Kim等[15]	2016	韩国	显著固定局灶性狭窄	后	51	37.3
Al Kasab等[16]	2017	美国	固定局灶狭窄≥70%	均有	435	8.3
Lee等[17]	2017	韩国	严重狭窄≥70%	后	62	24.1
Jia等[18]	2018	中国	固定局灶性狭窄	前	140	34.0
Kang等[19]	2018	韩国	严重狭窄≥70%	均有	955	14.6
Yi等[20]	2018	中国	显著固定局灶性狭窄	均有	61	36.1
Zhang等[21]	2019	中国	显著固定局灶性狭窄	后	133	71.4
Fan等[22]	2019	中国	靶血管狭窄>50%	后	67	52.5

但目前尚无公认的ICAS-LVO定义,报道的比例也受影响。Kasab等[16]和Kang等[19]将ICAS定义为闭塞部位严重狭窄(≥70%)。Lee等[12]和Kim等[14]将ICAS定义为“显著”的固定局灶性狭窄:①固定狭窄程度>70%;或②中度的固定狭窄(>50%)伴血流障碍或有再闭塞倾向。Yi等[20]在上述条件的基础上将狭窄程度定义在严重狭窄≥70%,中度狭窄≥50%。Jia等[18]将ICAS定义为固定局灶性狭窄,不考虑狭窄程度和血流状态。当原位狭窄难以与血管痉挛区别时,可于导管内动脉注射血管扩张剂,在3~5 min后再次造影确认。因此术中的标准极为重要,未来需要提出一个公认的统一标准供临床和科研使用。

2　ICAS-LVO的早期判断

明确ICAS是LVO的潜在机制是具有挑战性的,通常只有在最初的血运重建尝试之后才能做出诊断。但仍可根据病史、影像学特点作出预判(表2)。

2.1　临床特点

ICAS患者更年轻,男性多见,高血压、糖尿病、血脂异常和吸烟的患病率更高,但起病时症状相对较轻[23]。Li等[24]学者认为若发病前出现同侧反复波动的症状或与短暂性脑缺血发作相关的表现,应高度怀疑ICAS病变所致。

2.2　闭塞血管部位

ICAS-LVO在前循环多位于大脑中动脉M1近段,后循环多位于基底动脉近段或中段[15,25];栓塞性闭塞多位于血管分叉或转角处,如颈内动脉末端、大脑中动脉M1末端、基底动脉尖端。

2.3　影像学

Kim等[26]发现,CT平扫大脑中动脉高密度征多提示栓塞性病变。在后循环血管中,也可以观察到CT扫描中的高密度斑块来判断ICAS病变[27]。Chen等[28]发现,在动态CTA上观察到多层面血栓征(multisegment clot sign,MSC)也常提示心源性栓塞。另一些研究发现在MR-

表2　ICAS和栓塞性病变早期判断鉴别点

鉴别点	ICAS	栓塞性
发病平均年龄	较年轻(63.7岁)	较高龄(67.2岁)
性别	男性多见	/
危险因素	高血压、糖尿病、高脂血症、吸烟	心房颤动、近期心肌梗死、风湿性瓣膜病或扩张型心肌病
临床症状	反复波动或逐渐进展	瞬间达峰、病程单向(严重持续或戏剧性好转)
NIHSS	较低	较高
病变部位	大脑中动脉M1近段、基底动脉近段及中段	颈内动脉末端、大脑中动脉M1末端、基底动脉尖端
CT平扫	靶血管钙化高密度影	大脑中动脉高密度征
MR-GRE/SWI	/	磁敏感血管征
CTA	TTO、射流征	BSO、杯口征
动态CTA	/	多层面血栓征
DSA	TTO、射流征、首过效应、蜂腰征	BSO、杯口征
梗死区域	基底节或半卵圆中心	皮质为主
梗死面积	较小	较大
侧支循环	代偿≥50%闭塞区域	较差

注:NIHSS:美国国立卫生研究院卒中量表;TTO:主干型闭塞;BSO:分叉型闭塞;GRE:梯度回波序列;SWI:磁敏感序列

GRE/SWI中,由于血栓中的红细胞成分会引起铁磁场扭曲,出现超过血管管径的"开花"伪影,这种直径增大的磁敏感血管征(susceptibility vessel sign, SVS)多与栓塞有关[29-30]。ICAS-LVO导致的核心梗死在MR-DWI表现多累及大脑的深部,如基底节或半卵圆中心,敏感性和特异性分别为93.3%和87.5%[31]。但由于MR本身局限性,如扫描时间长、设备要求高,在急诊救治中并不能广泛应用。

血管造影可以提供更多血管管腔的信息。Baek等[32-35]将闭塞类型分为主干型闭塞(truncal-type occlusion, TTO)即血管闭塞未累及主要分支及远端血管分叉处,以及分叉型闭塞(branching-site occlusion, BSO)即累及了血管分叉处的闭塞。通过DSA及CTA的影像分析,提示了TTO病变诊断ICAS-LVO的价值。Yi等[20]发现微导管首过效应(first-pass effect),识别ICAS-LVO的敏感性、特异性和精确性分别为90.9%、87.2%、88.5%。笔者所在团队[36]认为ICAS-LVO在CTA/DSA上常表现为射流征(jet-like apperance),闭塞血管残端表现为逐渐变细,呈铅笔尖样或者细线样,在主要侧支发出后明显;如果在侧支发出前,由于血流动力不足,闭塞残端常常显示不清。

2.4　侧支循环

侧支循环也是辅助判断ICAS-LVO的手段。ICAS患者的侧支循环比其他卒中亚型的患者更好[37]。Suh等[38]发现ICAS-O患者的基线梗死核心体积明显小于心源性栓塞患者,可能与良好的侧支代偿有关。完整的软脑膜侧支代偿在一定程度上也可以简单地预测ICAS-LVO[39]。Rebello等[40]也发现,CTA显示侧支循环代偿区域≥50%闭塞区域,是ICAS-LVO的独立预测因素。

3　ICAS-LVO血管内治疗现状与策略

血管内治疗难以避免ICAS病变的再闭塞,可能与残留严重狭窄、不稳定斑块以及血管内皮损伤再发原位血栓有关[41]。在有关ICAS- LVO报道中,EVT期间的第一次再通后再闭塞的发生率从57.1%~77.3%[15,32,34,42]。对于这类患者的处理,常通过一系列的补救措施,如糖蛋白IIb/IIIa抑制剂使用(替罗非班)、球囊扩张或支架植入[43]。这也导致了手术时间的显著延长[16,21-22],反映了手术的操作难度及复杂性。在预后方面,临床结局并不一致。除一项研究外[15],良好预后的比率与再通成功率成正比。而在再通成功率类似的情况下,ICAS-LVO患者比栓塞性LVO患者有更好的预后[12,18,22]。Lee等[5]学者认为,ICAS-LVO相对较差的结果主要归因于较长的手术时间延长了发病—再通时间,延误了仍可挽救的组织窗。因此,制定高效的手术策略至关重要。

3.1　支架取栓

在ICAS-LVO中,为获得首次再通而进行支架取栓与栓塞性LVO同样有效[19,33]。支架的摆放有利于观察血管展开后形态,更容易揭示潜在的狭窄,并能暂时恢复血流。支架的取出有利于清除原位狭窄基础上的急性血栓,减少后续操作中可能的血栓逃逸。ICAS-LVO的血栓负荷量较少,临床上主张尽可能少的取栓(一次即可),尽快地进行球囊扩张成形。

3.2　抽吸取栓

尽管抽吸取栓对栓塞性LVO的疗效与机械取栓类似,但对ICAS-LVO的再通效果较差。Kang等[44]的分析显示,抽吸从穿刺到首次再通的时间更长(31 min vs 17 min),操作时长更长(75.5 min vs 39 min)。抽吸取栓需要将大口径导管尽可能接近病变段,而责任动脉往往是曲折并且逐渐变细至闭塞,无法紧密贴合造成无效抽吸。

3.3　直接血管成型

直接血管成型的方式也在急救中进行摸索。国内学者分别在前、后循环的被研究者中发现[45-47],直接血管成型组(球囊扩张/支架植入)能缩短手术时间,安全性与有效性不亚于机械取栓组。Kim等[48]发现,首次使用Solitaire取栓支架但不进行取栓而直接释放,也可能是一种合理的策略。直接血管成型的优势在于微导丝、微导管不用反复通过病变血管,节约了操作时间;但临床医师往往担心血栓逃逸,因此通过术中影像预判出极小负荷血栓或者无血栓,进而选择直接血管成型是值得探索的。

3.4　抗血小板药物

动脉内或静脉内注射替罗非班,已被报道为ICAS-LVO的合适补救方法。替罗非班是一种短效糖蛋白IIb/IIIa抑制剂,竞争性抑制纤维蛋白原介导的血小板聚集。Park等[3]学者在术中补救时运用动脉内注射替罗非班,首次0.3~0.5 mg,每隔10 min复查造影,如果再闭塞不能解决,再加用0.3~0.5 mg替罗非班,总量不超过1.5 mg。Yan等[49]学者认为,在术中使用小剂量替罗非班动脉推注+静脉维持与良好预后、低闭塞率相关;且认为无论残余狭窄程度如何,再通后至少20 min维持顺行血流,就不会进行血管内干预。笔者所在团队通常在术前判断为ICAS-LVO的即预先使用静脉替罗非班,并在其持续维持基础上进行血管内治疗,尽可能减少取栓后血管内膜损伤后导致的再闭塞。

3.5　组合方式

目前ICAS-LVO的传统EVT策略包含两点:①一线取栓技术快速实现靶血管的初次再通;②补救措施稳定ICAS病变以防止再闭塞。而Wu等[50]为此类病变提出了取栓支架+通过病变+抽吸+补救+微导丝+血管成型(Stent-Pass-Aspiration-resCuE-Micowire-Angioplasty, SPACE-MAN)取栓技术,该技术较经典的取栓技术明显缩短手术时间,在血管再通率、良好预后、死亡率方面无明显差异。刘沛等[51]介绍了阶梯式血管内治疗策略。对于微导管首过效应为阴性的患者,先进行机械取栓,若判断为ICAS-LVO且残余狭窄<70%,予替罗非班静脉维持;若残余狭

窄≥70%,直接行球囊扩张辅以替罗非班静脉维持。对于微导管首过效应为阳性的患者,直接予球囊扩张辅以替罗非班。所有患者均在观察前向血流20 min后待血流稳定则结束手术,若前向血流无法维持则进行支架成形术。

在ICAS-LVO病变的处理上,需要更好的工具以最大限度地减少操作步骤和血管损伤。带不透射线标记物的可拆卸取栓支架和带球囊的微导管,可能是未来的一个方向。可拆卸支架优势在于支架植入过程中提供更好的支架可视化,展现支架受压区域及贴壁情况。带球囊的微导管可带来极简的手术操作。

4　结语

目前ICAS-LVO的早期血管内治疗仍存在许多挑战。现有研究表明,ICAS-LVO比栓塞性闭塞有更多不同的神经影像学特征。而更多的操作措施、更高的再闭塞率及更长的手术时间会使此类患者错失救治机会。因此,尽早地判断、选择合适的EVT策略尤为重要。

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