·综述·

颅内动脉瘤介入围术期血栓的研究进展

石光玉[1)] 任登鹏[2)]

1)长治医学院研究生处,山西 长治 046000 2)山西医科大学附属运城市中心医院,山西 运城 044000

通信作者:任登鹏

【摘要】 颅内动脉瘤是先天遗传或后天获得性因素作用下,动脉壁内弹力层破坏导致颅内动脉壁向外病理性膨出形成的瘤样结构。颅内动脉瘤的治疗主要包括显微外科夹闭和血管内介入栓塞术。随着介入医学技术不断发展,颅内动脉瘤血管内介入为主流治疗方法,相较显微外科夹闭,适应范围广、创伤小、恢复迅速,但仍然存在围术期血栓的可能。本文就颅内动脉瘤介入围术期血栓形成机制、预防和无创监测做综述

【关键词】 颅内动脉瘤;介入;围术期;血栓形成

【中图分类号】 R739.41 【文献标识码】 A 【文章编号】 1673-5110(2022)08-1041-06

Advances in perioperative thrombosis in intracranial aneurysm intervention

SHI Guangyu[1)], REN Dengpeng[2)]

1) Graduate Office, Changzhi Medical College, Changzhi 046000, China; 2) Affiliated Yuncheng Central Hospital, Shanxi Medical University, Yuncheng 044000, China

Corresponding author: REN Dengpeng

【Abstract】 Intracranial aneurysms are tumor-like structures formed when the elastic layer within the arterial wall is disrupted by congenital genetic or acquired factors, resulting in pathological outward expansion of the intracranial arterial wall. The treatment of intracranial aneurysms mainly includes microsurgical clipping and endovascular interventional embolization. With the continuous development of interventional medicine technology, endovascular intervention for intracranial aneurysm is the mainstream treatment method, which is more adaptable, less traumatic and faster recovery than microsurgical clipping, but the possibility of perioperative thrombosis still exists. In this paper, we review the mechanism of perioperative thrombosis, prevention and noninvasive monitoring of intracranial aneurysm interventions

【Key words】 Intracranial aneurysm;Intervention;Perioperative period;Thrombosis

目前颅内动脉瘤已成为常见脑血管病,针对破裂和未破裂颅内动脉瘤的治疗主要包括显微外科夹闭和血管内介入栓塞,相较前者血管内介入栓塞创伤小、恢复快、住院时间短、临床适应症广。近年来血管内介入治疗不断发展,随着介入技术和材料的不断更新以及介入病例增多,其临床显现的问题日益显著,目前在临床上颅内动脉瘤介入围术期并发血栓形成逐渐增多,严重影响了患者的预后。本文就颅内动脉瘤介入围术期血栓形成机制、预防和无创监测做综述,为临床诊治提供基础

1 颅内动脉瘤简述

颅内动脉瘤是由遗传性或获得性因素导致动脉壁内弹力膜在局部血流动力学和血管内皮损伤因素作用下被破坏,动脉壁向外病理性膨出形成的瘤样结构[1],按形态分囊状动脉瘤、梭形动脉瘤及夹层动

DOI:10.12083/SYSJ.220672

本文引用信息:石光玉,任登鹏.颅内动脉瘤介入围术期血栓的研究进展[J].中国实用神经疾病杂志,2022,25(8):1041-1046. DOI:10.12083/SYSJ.220672

Reference information: SHI Guangyu,REN Dengpeng.Advances in perioperative thrombosis in intracranial aneurysm intervention[J]. Chinese Journal of Ptactical Nervous Diseases,2022,25(8):1041-1046. DOI:10.12083/SYSJ.220672

脉瘤[2]，用力大小便、咳嗽、情绪激动、性交、剧烈运动等因素可诱发其破裂出血，引起不同程度蛛网膜下腔出血，占到非创伤性蛛网膜下腔出血的80%～85%[3]，临床表现为剧烈头痛、恶心呕吐及其他神经系统症状[4-5]。血管内介入治疗颅内动脉瘤已成为一种公认的治疗方法，其经历了载瘤动脉和动脉瘤闭塞阶段、动脉瘤瘤腔栓塞阶段以及载瘤动脉重建阶段[6]。血管内介入进展迅速，然而其带来的围术期并发症却极为重要的影响了患者预后，相较显微外科夹闭，血管内介入治疗极大的避免了脑脊液漏、颅内感染的风险，同时其致死致残率明显下降，住院周期显著缩短[7]。国际蛛网膜下腔动脉瘤试验表明，对同时符合手术夹闭和血管内介入的破裂颅内动脉瘤，血管内介入临床效果更好[8]。然而尽管有充足的术前准备，但是介入围术期仍会存在颅内动脉并发症、颅外动脉并发症、导管相关并发症及穿刺部位并发症等[9]。临床研究表明在微小颅内动脉瘤破裂后行介入治疗安全可靠[10]，此外支架辅助弹簧圈介入主要用于治疗宽颈或复杂动脉瘤，虽然提高了栓塞率，但是围术期的并发症依然存在[11]，如急性支架内血栓形成[12-13]、动脉瘤破裂出血[14]、血管痉挛[15]、支架移位[16]、载瘤动脉闭塞[17]、弹簧圈脱落[18]等，特别是支架辅助弹簧圈栓塞术中血栓形成或血栓栓塞的发生率为2%～15%[19]。

2 颅内动脉瘤介入围术期血栓形成机制

2.1 介入血流动力学影响因素 目前已有关于颅内动脉瘤介入围术期动脉瘤瘤腔内及载瘤动脉局部血流动力学研究，利用有限元建模的计算流体力学分析是评估脑动脉瘤局部血流动力学变化的有效工具。下列血流动力学相关参数：壁面剪应力（wall shear stress，WSS）、振荡切变指数（oscillatory shear index，OSI）、WSS梯度（WSS gradient，WSSG）、相对停留时间（relative residence time，RRT）和流速（flow velocity，FV）可以评估支架放置后动脉瘤瘤腔和局部血流动力学变化。支架置入后的血流动力学变化包括WSS和FV的降低以及OSI、WSSG和RRT的上升，导致血流停滞和紊乱，促进血栓形成[20]。一项利用计算流体力学和建立动脉瘤模型的研究表明，动脉瘤的形态以及动脉瘤相对于载瘤血管的位置和方向均是影响动脉瘤瘤腔内血流动力学的因素[21]。有研究利用有限元及计算流体力学分析方法，建立基本侧壁和分叉型动脉瘤模型后模拟弹簧圈介入栓塞，表明弹簧圈的刚度和长度会影响弹簧圈在瘤腔内的分布及局部血流动力学[22]。在一项颈内动脉动脉瘤血流导向支架Pipeline置入的回顾性研究中[23]，利用定量磁共振血管成像技术（quantitative magnetic resonance angiography，QMRA）计算及统计分析研究队列中搏动指数、阻力指数、Lindegaard比率和WSS等参数，明确了血流导向支架置入后同侧载瘤动脉流速下降和远端颅内动脉的血流紊乱。NARATA等[24]在血流导向支架治疗颅内分叉型动脉瘤的研究中表明，分叉后子血管的直径比和分叉不对称程度是影响局部血流动力学的因素之一。KONO等[25]在基底动脉瘤内和附近的血流动力学的研究表明，支架结构及放置会影响流入瘤腔和远端动脉的血流动力学。GAO等[26]在一项关于支架辅助介入治疗分叉动脉瘤的回顾性研究表明，血管分叉处的这种角度重塑可能会导致血管分隔处血流动力学的改变，以及影响远端血管的血流动力学。上述研究结果表明，在血管内介入治疗围术期，动脉瘤的形态及其与载瘤动脉的位置关系，弹簧圈的材质，支架结构及支架置入操作，分叉型动脉瘤分叉后血管形态以及支架置入后局部血管重塑均是影响介入局部血流动力学的因素之一，可以利用有限元建模和计算力流体力学的方法分析相关参数去进一步明确介入围术期血流动力学改变及其对血栓形成的影响，也需要更进一步的多中心队列研究为临床决策做参考。

2.2 血栓形成其他相关因素 目前研究表明，多种因素共同影响了介入围术期支架内血栓形成，不同类型支架均可能发生支架内血栓，编织型支架比激光切割支架发生更早[12]。据血栓发生时间分为急性期（术后24 h内），亚急性期（术后1～30 d内）及晚期（术后30 d）[27]。荷兰一项多中心研究表明恶性肿瘤是支架内血栓的独立危险因素[28]，随访研究表明肾功能衰竭伴有微血管和代谢异常，可能容易形成血栓[29]，瑞士和荷兰两机构队列研究表明患有糖尿病是早期支架内血栓的独立危险因素[30]，一项国际多中心、观察性、病例对照的回顾性研究表明吸烟引起血小板反应性增高导致支架内血栓形成[31]。有病例报告表明携带CYP2C19等位基因个体可能导致氯吡格雷药效受到抑制，导致急性支架内血栓形成[32]。血管内皮功能障碍、氯吡格雷代谢不良、病变相关因素（如病变时间长、血管分叉处病变[28]）等均是血栓危险因素，血液为非牛顿流体，血液粘度增加时WSS的增加会损害血管内皮，因其与内皮细胞形态和一氧化氮的产生有关，血液高凝状态导致血栓形成[33]。抗血小板药物的选择及应用不规范，支架相关因素

如重叠支架，多个支架、支架过长[34]、支架对位不全等[35]，是血栓形成危险因素。介入手术时间过长导致血管内皮损伤暴露内皮下胶原，血小板聚集形成新鲜血小板血栓[36]，此外减少手术操作时间可以降低栓塞术后血栓栓塞的风险[37]，支架、导管和导丝作为外源性异物可以激活凝血系统引起血小板聚集形成血栓，支架植入后的内皮损伤、对金属支架过敏等可能是引起支架内狭窄的因素[38]。上述研究表明患有基础疾病、吸烟、血液高凝状态、血管内皮功能障碍、抗血小板药物选择不规范及药物代谢不良、介入支架及手术时间、介入术中内皮损伤等均是支架内血栓形成的影响因素，临床工作中应该根据患者情况个体化治疗，降低颅内动脉瘤介入围术期血栓形成风险。

3 颅内动脉瘤介入围术期血栓预防

3.1 抗血小板药物预防 为预防血管内介入治疗围术期血栓形成，尤其是支架内血栓形成，抗血小板药物治疗是有效方法，有回顾性研究表明使用抗血小板药物可以降低缺血性并发症同时不增加出血风险[39]，德菲尔共识提到倾向于围术期双重抗血小板方案，联合使用阿司匹林和糖蛋白Ⅱb/Ⅲa抑制剂，以降低缺血事件发生风险[40]。临床中阿司匹林抵抗少见，而氯吡格雷药效个体异质性较大[41-42]，阿司匹林是不可逆环氧合酶抑制剂，半衰期15～20 min，药效持续一个血小板生命周期（7～10 d），只有新生血小板才能抵消其血小板抑制[43]，氯吡格雷是不可逆腺嘌呤能受体拮抗剂，其母体及活性代谢物半衰期分别为6 h和30 min，口服氯吡格雷大约15%从肠道吸收生成活性代谢产物，其与P2Y12受体结合后血小板功能在7～10 d内被阻断[44]。目前常规双重抗血小板方案如下：未破裂颅内动脉瘤介入术前3～5 d给予阿司匹林100 mg和氯吡格雷75 mg每天1次，破裂颅内动脉瘤介入术前至少2 h给予一次负荷量阿司匹林300 mg和氯吡格雷300 mg[45]。此外替罗非班是可逆性非肽类糖蛋白受体Ⅱb/Ⅲa拮抗剂，为起效快、失活快、高度选择性的抗血小板药物，通过断裂血小板间硫酸氢键导致富含血小板的血凝块或血栓溶解，且不增加出血风险，为血管内介入围术期抗血小板治疗提供了新的选择，替罗非班联合双重抗血小板治疗可以改善支架辅助栓塞术后血栓栓塞患者的神经功能和预后[46]，术中预防性应用替罗非班可以降低缺血事件发生[47]。此外GP Ⅱb/Ⅲa抑制剂替罗非班和阿昔单抗在颅内动脉瘤血管内治疗后急性血栓形成事件中也有重要作用[48]。

3.2 应用抗血栓涂层支架 颅内动脉瘤介入术中置入支架具有血栓形成特性，与血液接触时会在一定程度上通过接触激活凝血途径形成白色血栓，而动脉血液的高切变率血流动力学促进了血栓形成过程[49]。支架涂层的目的是使材料更亲水并阻止血小板在其表面聚集，加速内皮细胞的覆盖，有助于预防围术期支架内血栓形成。相关研究表明支架表面涂层钝化、电抛光及褪火处理后不能显著降低血栓形成[50]，诸多研究表明比伐卢定、多巴胺固定化肝素、载肝素氧化石墨烯以及联合使用6-硫酸软骨素和肝素等已被证明可以减少支架表面血小板黏附性，白蛋白用作表面涂层也可以改善支架的血液相容性[51]，而聚氨酯涂层确实可以降低支架的血栓形成能力。聚苯-F是一种高纯亲水性高分子聚合物，用于支架金属表面涂层材料可以加速内皮化和降低局部血栓形成[52]。存在于红细胞膜上的磷酸胆碱（phosphorylcholine，PC）被认为可降低支架血栓形成能力，以此开发的PC涂层用于第三代Pipeline栓塞装置（pipeline embolisation device，PED），可以降低蛋白质吸附和凝血酶形成预防支架内血栓形成[53]，MARTINEZ-GALDAMEZ等[54]在一项使用PED Shield的多中心前瞻性研究中证实了其应用的安全性。一种尚在研究中的纳米基质涂层，可以持续释放一氧化氮招募内皮细胞覆盖[55]，且本身结合的内皮细胞黏附配体可以促进内皮细胞的保留和迁移[56]。新型聚合物支架涂层（聚双三氟乙氧基磷腈）（poly bis trifluoroethoxy phosphazene，PTFEP）在抗血栓形成和生物相容性都具有较好的表现[52]。上述关于支架涂层的相关研究表明，在介入手术中因为支架本身具有血栓形成特性，造成了围术期支架内血栓形成并发症，抗血小板黏附和促进内皮化的支架表面涂层也在不断优化，也有研究证实了其使用的安全性和有效性，是未来支架发展的一个方向。

4 颅内动脉瘤介入围术期血栓监测

4.1 应用血栓弹力图监测介入围术期血栓形成 抗血小板药物药效个体差异大，尤其是氯吡格雷，在颅内动脉瘤介入围术期应用抗血小板药物时需要监测血小板功能，便于及时调整药物剂量减少缺血并发症。血栓弹力图血小板图（thrombelastography platelet mapping，TEG-PM）临床上常用于血小板功能检测，其根据血凝块形成、强度和降解的整体评估来定量分析血小板功能，首先用高岭土和氯化钙测定

凝血酶最大止血活性，其次使用花生四烯酸（arachidonic acid，AA）或二磷酸腺苷（adenosine diphosphate，ADP）激活血小板，分别测量上述途径的凝血程度，通过与单纯凝血酶凝血程度的对比计算出抑制率[57]。AA抑制率（AA inhibition rate，AAi）和ADP抑制率（ADP inhibition rate，ADPi）与ADP途径血凝块最大强度（maximal amplitude of ADP，MA-ADP）分别提示阿司匹林及氯吡格雷对于血小板聚集功能抑制程度[58]。此外ADPi与MA-ADP指标变化反映氯吡格雷疗效，能够提示颅内动脉瘤术后发生缺血并发症发生风险[59]。MA-ADP被发现与血栓栓塞的发生显著相关，可作为支架辅助弹簧圈治疗的颅内动脉瘤患者的预后指标[60]。血栓弹力图血小板图在临床上用于血小板功能测定，研究显示TEG-PM指标改变与颅内动脉瘤介入术后出血或缺血并发症相关，其指标变化有助于发现介入术后患者并发出血或缺血风险，进而确定个体化抗血小板方案，回顾性临床研究表明颅内小动脉瘤行介入治疗中TEG检查对于抗凝药物的监测及预测并发症有重要临床意义[61]。因此，围术期支架局部血栓形成是多方面共同影响的，提高其预防及监测的标准或许更有利于降低患者的神经功能缺损率，改善预后。

4.2 应用经颅多普勒超声监测介入围术期血栓形成 数字减影血管造影（digital subtraction angiography，DSA）被认为是监测狭窄的金标准，但有创检查存在并发症[62]，不适用于颅内动脉瘤围术期动态监测，无创检查磁共振血管造影（magnetic reconance angiorgraphy，MRA）和CT血管造影（CT angiography，CTA）用于脑血管病围术期监测及随访，两者分别受到流动伪影和金属伪影的限制，难以准确评价围术期支架内狭窄及血栓形成[63]。经颅多普勒超声是以颅骨相对薄弱的颞部、眶部、枕部作为检测声窗评估颅底动脉血流动力学的无创监测方法，其指标包括收缩期和舒张期血流速度，平均血流速度、血管搏动指数及血流频谱变化等[64]，可以用来监测支架辅助弹簧圈介入围术期动脉血流微栓子信号，以及监测介入术中及术后早期有无急性支架内狭窄或血栓形成[65]，有研究表明经颅多普勒超声监测微栓子信号可以早期预测颅内动脉瘤介入术后的血栓形成[66]。还需注意的是超声检查医师操作时要根据血管的走形调整探头角度并保持探头的稳定，以免产生伪影影响结果判断[67-68]。据此经颅多普勒超声可以无创监测颅内动脉瘤支架辅助介入围术期相关的缺血并发症，包括急性支架内血栓形成，空气栓塞，微血栓形成等，可以及早发现并干预介入围术期血栓并发症，改善围术期并发症血栓患者预后。

血管内介入围术期血栓形成目前已经成为临床的重点诊治问题，在颅内动脉瘤介入治疗迅速发展的同时，介入围术期血栓形成的病例报告也日益增多，明确围术期血栓形成的机制，以进一步预防血栓形成，同时利用血栓弹力图血小板图和经颅多普勒超声联合监测等方法显得尤为重要，其应该具有广泛的临床应用前景及临床参考价值。

5 参考文献

[1] ETMINAN N, DRFLER A, STEINMETZ H. Unruptured Intracranial Aneurysms-Pathogenesis and Individualized Management[J]. Dtsch Arztebl Int, 2020, 117(14): 235-243. DOI:10.3238/arztebl.2020.0235.

[2] 张鸿祺，杨新健，屈延等. 中国颅内未破裂动脉瘤诊疗指南2021[J]. 中国脑血管病杂志，2021，18(9)：31. DOI：10.3969/j.issn.1672-5921.2021.09.008.

[3] Brown R, Broderick J. Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening[J]. Lancet Neurol, 2014, 13(4): 393-404. DOI: 10.1016/s1474-4422(14)70015-8.

[4] ETMINAN N, RINKEL G J. Unruptured intracranial aneurysms: development, rupture and preventive management[J]. Nat Rev Neurol, 2016, 13(2): 126-126. DOI: 10.1038/nrneurol. 2016. 150.

[5] ZAHRAH T, TERESA M, EMMA M, et al. Predictors of Poor Quality of Life 1 Year After Subarachnoid Hemorrhage[J]. Neurosurgery, 2016(2): 256-264. DOI: 10.1227/NEU.0000000000001042.

[6] LEE K, ZHANG J, NGUYEN V, et al. The evolution of intracranial aneurysm treatment techniques and future directions[J]. Neurosurg Rev, 2022, 45(1): 1-25. DOI: 10.1007/s10143-021-01543-z.

[7] HUANG X, YAN G, QIN Z, et al. To clip or to coil for unruptured intracranial aneurysm?: A protocol of randomized controlled trial[J]. Medicine (Baltimore), 2021, 100(11): e24692. DOI: 10.1097/MD.0000000000024692.

[8] ZHANG X, LI L, HONG B, et al. A Systematic Review and Meta-analysis on Economic Comparison between Endovascular Coiling versus Neurosurgical Clipping for Ruptured Intracranial Aneurysms[J]. World Neurosurg, 2018, 113: 269-275. DOI: 10.1016/j.wneu.2018.02.078.

[9] IHN Y, SHIN S, BAIK S, et al. Complications of endovascular treatment for intracranial aneurysms: Management and prevention[J]. Interv Neuroradiol, 2018, 24(3): 237-245. DOI: 10.1177/1591019918758493.

[10] 许华，宋国红. 介入栓塞治疗颅内破裂微小动脉瘤临床分析[J]. 中国实用神经疾病杂志，2019，22(22)：2510-2514. DOI：10.12083/SYSJ.2019.22.409

[11] PIOTIN M, BLANC R, SPELLE L, et al. Stent-assisted coiling of intracranial aneurysms: clinical and angiographic results in 216 consecutive aneurysms[J]. Stroke, 2010, 41(1): 110-115. DOI: 10.1161/strokeaha.109.558114.

[12] NII K, INOUE R, MORINAGA Y, et al. Evaluation of Acute In-stent Thrombosis during Stent-assisted Coil Embolization of Unruptured Intracranial Aneurysms[J]. Neurol Med Chir (Tokyo), 2018, 58(10): 435-441. DOI: 10.2176/nmc.oa.2018-0131.

[13] LI G, LIU T, WANG N, et al. Treatment of acute thrombosis during stent-assisted coil embolization of ruptured proximal posterior inferior cerebellar artery aneurysm[J]. Brain Circ, 2020,6(2):130-132. DOI:10.4103/bc.bc_51_19.

[14] PARK Y K, YI H J, CHOI K S, et al. Intraprocedural rupture during endovascular treatment of intracranial aneurysm:Clinical results and literature review[J]. World Neurosurg, 2018, 114: e605-e615. DOI:10.1016/j.wneu.2018.03.040.

[15] STAPLETON C J, WALCOTT B P, BUTLER W E, et al. Neurological outcomes following intraprocedural rerupture during coil embolization of ruptured intracranial aneurysms[J]. J Neurosurg, 2015, 122(1): 128-135. DOI: 10.3171/2014.9.JNS14616.

[16] LUO C B, TENG M H, CHANG F C, et al. Stent-assisted coil embolization of intracranial aneurysms: A single center experience[J]. J Chin Med Assoc, 2012, 75(7): 322-328. DOI:10.1016/j.jcma.2012.05.003.

[17] POTTS M B, SHAPIRO M, ZUMOFEN D W, et al. Parent vessel occlusion after Pipeline embolization of cerebral aneurysms of the anterior circulation[J]. J Neurosurg, 2017, 127(6):1-9. DOI:10.3171/2016.9.JNS152638.

[18] HOU K, LI G, GUO Y, et al. Endovascular treatment for aneurysms at the A1 segment of the anterior cerebral artery: current difficulties and solutions[J]. Acta Neurol Belg, 2021, 121(1):55-69. DOI:10.1007/s13760-020-01526-9.

[19] BRINJIKJI W, MORALES-VALERO S F, MURAD M H, et al. Rescue Treatment of Thromboembolic Complications during Endovascular Treatment of Cerebral Aneurysms: A Meta-Analysis[J]. AJNR Am J Neuroradiol, 2015, 36(1): 121-125. DOI:10.3174/ajnr.A4066.

[20] TANEMURA H, ISHIDA F, MIURA Y, et al. Changes in hemodynamics after placing intracranial stents[J]. Neurol Med Chir (Tokyo),2013,53(3):171-8. DOI:10.2176/nmc.53.171.

[21] LARRABIDE I, GEERS A, MORALES H, et al. Effect of aneurysm and ICA morphology on hemodynamics before and after flow diverter treatment[J]. J Neurointerv Surg,2015,7(4): 272-280. DOI:10.1136/neurintsurg-2014-011171.

[22] FUJIMURA S, TAKAO H, SUZUKI T, et al. Hemodynamics and coil distribution with changing coil stiffness and length in intracranial aneurysms[J]. J Neurointerv Surg, 2018, 10(8): 797-801. DOI:10.1136/neurintsurg-2017-013457.

[23] SHAKUR S, ALETICH V, AMIN-HANJANI S, et al. Quantitative assessment of parent vessel and distal intracranial hemodynamics following pipeline flow diversion[J]. Interv Neuroradiol,2017, 23(1):34-40. DOI:10.1177/15910199 16668842.

[24] NARATA A, DE MOURA F, LARRABIDE I, et al. The Role of Hemodynamics in Intracranial Bifurcation Arteries after Aneurysm Treatment with Flow-Diverter Stents[J]. AJNR Am J Neuroradiol,2018,39(2):323-330. DOI:10.3174/ajnr.A5471.

[25] KONO K, TERADA T. Hemodynamics of 8 different configurations of stenting for bifurcation aneurysms[J]. AJNR Am J Neuroradiol, 2013, 34(10): 1980-1986. DOI: 10.3174/ajnr.A3479.

[26] GAO B, BAHAROGLU M, COHEN A, et al. Stent-assisted coiling of intracranial bifurcation aneurysms leads to immediate and delayed intracranial vascular angle remodeling[J]. AJNR Am J Neuroradiol, 2012, 33(4): 649-654. DOI: 10.3174/ajnr.A2841.

[27] CUTLIP D, WINDECKER S, MEHRAN R, et al. Clinical end points in coronary stent trials:a case for standardized definitions[J]. Circulation, 2007, 115(17): 2344-2351. DOI: 10.1161/circulationaha.106.685313.

[28] VAN WERKUM J, HEESTERMANS A, ZOMER A, et al. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry[J]. J Am Coll Cardiol, 2009, 53(16): 1399-1409. DOI:10.1016/j.jacc.2008.12.055.

[29] IAKOVOU I, SCHMIDT T, BONIZZONI E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents[J]. JAMA, 2005, 293(17): 2126-2130. DOI:10.1001/jama.293.17.2126.

[30] WENAWESER P, DAEMEN J, ZWAHLEN M, et al. Incidence and correlates of drug-eluting stent thrombosis in routine clinical practice. 4-year results from a large 2-institutional cohort study[J]. J Am Coll Cardiol, 2008, 52(14): 1134-1140. DOI:10.1016/j.jacc.2008.07.006.

[31] WAKSMAN R, KIRTANE A, TORGUSON R, et al. Correlates and outcomes of late and very late drug-eluting stent thrombosis: results from DESERT (International Drug-Eluting Stent Event Registry of Thrombosis)[J]. JACC Cardiovasc Interv, 2014, 7(10):1093-1102. DOI:10.1016/j.jcin.2014.04.017.

[32] DING L, GU Z, WANG R, et al. Acute stent thrombosis after stent-assisted coiling in an intracranial aneurysm patient carrying two reduced-function CYP2C19 alleles: A case report[J]. Medicine (Baltimore), 2017, 96(47): e8920. DOI: 10.1097/md.0000000000008920.

[33] HONG H, SONG J, YEOM E. Variations in pulsatile flow around stenosed microchannel depending on viscosity[J]. PLoS One, 2019, 14(1): e0210993. DOI: 10.1371/journal.pone.0210993.

[34] COOK S, WENAWESER P, TOGNI M, et al. Incomplete stent apposition and very late stent thrombosis after drug-eluting stent implantation[J]. Circulation, 2007, 115(18):2426-2434. DOI: 10.1161/circulationaha.106.658237.

[35] YI L, ZHAO W, KRINGS T, et al. High-Flow Extracranial-to-Intracranial Bypass for Treatment of Thrombotic Parent Vessel Occlusion After Stent-Assisted Aneurysm Coiling as a Potential Rescue Therapy[J]. World Neurosurg, 2019, 127: 326-329. DOI:10.1016/j.wneu.2019.03.039.

[36] TAN L A, KEIGHER K M, MUNICH S A, et al. Thromboembolic complications with Pipeline Embolization Device placement: impact of procedure time, number of stents and pre-procedure P2Y12 reaction unit (PRU) value[J]. J Neurointerv Surg, 2015, 7(3): 217-221. DOI: 10.1136/neurintsurg-2014-011111.

[37] LEE S H, JANG M U, KANG J, et al. Impact of Reducing the Procedure Time on Thromboembolism After Coil Embolization of Cerebral Aneurysms[J]. Front Neurol, 2018, 9:1125. DOI: 10.3389/fneur.2018.01125.

[38] KIM S, KIM Y, KO J. Long Term Outcome of In-Stent Stenosis after Stent Assisted Coil Embolization for Cerebral Aneurysm[J]. J Korean Neurosurg Soc, 2019, 62(5):536-544. DOI:10.3340/jkns.2019.0087.

[39] YAMADA N K, CROSS D T, PILGRAM T K, et al. Effect of Antiplatelet Therapy on Thromboembolic Complications of Elective Coil Embolization of Cerebral Aneurysms[J]. AJNR Am J Neuroradiol, 2007, 28(9): 1778-1782. DOI: 10.3174/ajnr.A0641.

[40] OSPEL J, BROUWER P, DORN F, et al. Antiplatelet Management for Stent-Assisted Coiling and Flow Diversion of Ruptured Intracranial Aneurysms: A DELPHI Consensus Statement[J]. AJNR Am J Neuroradiol, 2020, 41(10): 1856-1862. DOI:10.3174/ajnr.A6814.

[41] FIFI J T, BROCKINGTON C, NARANG J, et al. Clopidogrel resistance is associated with thromboembolic complications in patients undergoing neurovascular stenting[J]. AJNR Am J Neuroradiol, 2013, 34(4):716-720. DOI:10.3174/ajnr.A3405.

[42] YI H J, HWANG G, LEE B H. Variability of Platelet Reactivity on Antiplatelet Therapy in Neurointervention Procedure[J]. J

Korean Neurosurg Soc, 2019, 62(1): 3-9. DOI: 10.3340/jkns.2018.0151.

[43] SANTOS-GALLEGO C G, BADIMON J. Overview of Aspirin and Platelet Biology[J]. Am J Cardiol, 2021, 144: S2-S9. DOI: 10.1016/j.amjcard.2020.12.018.

[44] SCHILLING U, DINGEMANSE J, UFER M. Pharmacokinetics and Pharmacodynamics of Approved and Investigational P2Y12 Receptor Antagonists[J]. Clin Pharmacokinet, 2020, 59(5): 545-566. DOI: 10.1007/s40262-020-00864-4.

[45] YANG H, LI Y, JIANG Y. Insufficient platelet inhibition and thromboembolic complications in patients with intracranial aneurysms after stent placement[J]. J Neurosurg, 2016, 125(2): 247-253. DOI: 10.3171/2015.6.JNS1511.

[46] 林宏卫, 姜浩, 余国锋, 等. 两种抗血小板方案治疗支架辅助栓塞术后出现血栓栓塞的颅内动脉瘤患者的疗效比较[J]. 中华危重症医学杂志: 电子版, 2021, 14(01): 56-59. DOI: 10.3877/cma.j.issn.1674-6880.2021.01.011.

[47] 吴桥伟, 李立, 邵秋季, 等. 替罗非班在血流导向装置治疗颅内未破裂动脉瘤术中的预防性应用研究[J]. 中华神经外科杂志, 2021, 37(4): 342-347. DOI: 10.3760/cma.j.cn112050-20200615-00350.

[48] DELVOYE F, LOYAU S, LABREUCHE J, et al. Intravenous abciximab as a rescue therapy for immediate reocclusion after successful mechanical thrombectomy in acute ischemic stroke patients[J]. Platelets, 2022, 33(2): 285-290. DOI: 10.1080/09537104.2021.1894326.

[49] CASA L, KU D. Thrombus Formation at High Shear Rates[J]. Annu Rev Biomed Eng, 2017, 19: 415-433. DOI: 10.1146/annurev-bioeng-071516-044539.

[50] TEPE G, SCHMEHL J, WENDEL H, et al. Reduced thrombogenicity of nitinol stents-in vitro evaluation of different surface modifications and coatings[J]. Biomaterials, 2006, 27(4): 643-650. DOI: 10.1016/j.biomaterials.2005.06.004.

[51] KRAJEWSKI S, NEUMANN B, KURZ J, et al. Preclinical evaluation of the thrombogenicity and endothelialization of bare metal and surface-coated neurovascular stents[J]. AJNR Am J Neuroradiol, 2015, 36(1): 133-139. DOI: 10.3174/ajnr.A4109.

[52] RICHTER G, STAMPFL U, STAMPFL S, et al. A new polymer concept for coating of vascular stents using PTFEP (poly(bis(trifluoroethoxy) phosphazene) to reduce thrombogenicity and late in-stent stenosis[J]. Invest Radiol, 2005, 40(4): 210-218. DOI: 10.1097/01.rli.0000156195.74967.47.

[53] MARTÍNEZ-GALDÁMEZ M, LAMIN S M, LAGIOS K G, et al. Periprocedural outcomes and early safety with the use of the Pipeline Flex Embolization Device with Shield Technology for unruptured intracranial aneurysms: preliminary results from a prospective clinical study[J]. J Neurointerv Surg, 2017, 9(8): 772-776. DOI: 10.1136/neurintsurg-2016-012896.

[54] MARTÍNEZ-GALDÁMEZ M, LAMIN S M, LAGIOS K G, et al. Treatment of intracranial aneurysms using the pipeline flex embolization device with shield technology: angiographic and safety outcomes at 1-year follow-up[J]. J Neurointerv Surg, 2019, 11(4): 396-399. DOI: 10.1136/neurintsurg-2018-014204.

[55] ANDUKURI A, MINOR W P, KUSHWAHA M, et al. Effect of endothelium mimicking self-assembled nanomatrices on cell adhesion and spreading of human endothelial cells and smooth muscle cells[J]. Nanomedicine, 2010, 6(2): 289-297. DOI: 10.1016/j.nano.2009.09.004.

[56] ANDUKURI A, SOHN Y, ANAKWENZE C, et al. Enhanced human endothelial progenitor cell adhesion and differentiation by a bioinspired multifunctional nanomatrix[J]. Tissue Eng Part C Methods, 2013, 19(5): 375-385. DOI: 10.1089/ten.TEC.2012.0312.

[57] LE QUELLEC S, BORDET J C, NEGRIER C, et al. Comparison of current platelet functional tests for the assessment of aspirin and clopidogrel response[J]. Thromb Haemost, 2016, 116(10): 638-650. DOI: 10.1160/TH15-11-0870.

[58] COLLYER T C, GRAY D J, SANDHU R, et al. Assessment of platelet inhibition secondary to clopidogrel and aspirin therapy in preoperative acute surgical patients measured by Thrombelastography Platelet Mapping[J]. Br J Anaesth, 2009, 102(4): 492-498. DOI: 10.1093/bja/aep039.

[59] GE H, YANG H, REN H, et al. Association of thrombelastographic parameters with complications in patients with intracranial aneurysm after stent placement[J]. World Neurosurg, 2019, 127: e30-e38. DOI: 10.1016/j.wneu.2019.02.007.

[60] YANG H, LI Y, JIANG Y, et al. Thromboelastography for monitoring platelet function in unruptured intracranial aneurysm patients undergoing stent placement[J]. Interv Neuroradiol, 2015, 21(1): 61-68. DOI: 10.15274/inr-2014-10094.

[61] 茹睿, 崔萍, 宗余余, 等. 血栓弹力图在小型颅内动脉瘤术后患者中的应用价值[J]. 中国实用神经疾病杂志, 2021, 24(20): 1802-1809. DOI: 10.12083/SYSJ.2021.09.016

[62] KWON M A, HONG C K, JOO J Y, et al. Headache After Cerebral Angiography: Frequency, Predisposing Factors, and Predictors of Recovery[J]. J Neuroimaging, 2016, 26(1): 89-94. DOI: 10.1111/jon.12290.

[63] GOLSHANI B, LAZZARO M A, RASLAU F, et al. Surveillance imaging after intracranial stent implantation: non-invasive imaging compared with digital subtraction angiography[J]. J Neurointerv Surg, 2013, 5(4): 361-365. DOI: 10.1136/neurintsurg-2012-010341.

[64] 华扬, 高山, 吴钢, 等. 经颅多普勒超声操作规范及诊断标准指南[J]. 中华医学超声杂志(电子版), 2008, 5(2): 2-6. DOI: 10.3969/j.issn.1672-6448.2008.02.002.

[65] MCDOUGALL C M, KHAN K, SAQQUR M, et al. Ultrasound for the evaluation of stenosis after flow diversion[J]. J Neurointerv Surg, 2018, 10(3): 297-300. DOI: 10.1136/neurintsurg-2017-013049.

[66] CHO J H, KANG D H, KIM Y W, et al. Microembolic signal monitoring and the prediction of thromboembolic events following coil embolization of unruptured intracranial aneurysms: diffusion-weighted imaging correlation[J]. Neuroradiology, 2015, 57(2): 189-196. DOI: 10.1007/s00234-014-1451-y.

[67] 邹成功, 冯浩, 陈兵, 等. 颅内动脉瘤夹闭术中动脉瘤破裂的影响因素及血流动力学参数的预测价值[J]. 中国实用神经疾病杂志, 2022, 25(4): 421-425. DOI: 10.12083/SYSJ.220125.

[68] KUSSMAN B D, IMADUDDIN S M, GHAREDAGHI M H, et al. Cerebral Emboli Monitoring Using Transcranial Doppler Ultrasonography in Adults and Children: A Review of the Current Technology and Clinical Applications in the Perioperative and Intensive Care Setting[J]. Anesth Analg, 2021, 133(2): 379-392. DOI: 10.1213/ANE.0000000000005417.