Acute Stroke Treatment

The simultaneous publication of 3 randomized control trials comparing intravenous thrombolysis therapy to the endovascular treatment (EVT) of acute ischemic stroke might have lead to the erroneous conclusion that EVT has no place in the management of acute ischemic stroke.1-3 However, careful analysis of these studies shows that these reports have shortcomings because of changes in imaging and device technology and to study designs.4,5

These randomized control trials have demonstrated that the EVT is not deleterious for the patients and subgroup analyses in Interventional Management of Stroke III have shown that the EVT can provide some benefits for some patients. Dedicated research in the area of EVT of stroke continues to expand having the goal to optimize devices, techniques, and c-arm–based imaging. The new generation of stent-retrievers has shown great improvement during the earlier technology;6,7 however, further refinements are desired to select patients properly that will benefit from EVT, efficiently transfer those patients selected for EVT to the angiosuite, and to facilitate all aspects of the thrombectomy procedure to provide rapid and complete revascularization.

A potential factor that may contribute to poor clinical outcomes in mechanical thrombectomy is fragmentation of the clot leading to downstream emboli. This has been characterized in vitro, and reduction of distal emboli was achieved using a proximal balloon guide catheter with aspiration during stent-retriever EVT.8 This experimental approach has been validated by clinical data that show the use of the balloon guide catheter is an independent predictor of good functional outcome at 90 days.9

Although the role of perfusion computed tomography in triage of acute ischemic stroke is still debated,10 tremendous advances to perform perfusion imaging with c-arms in the angiosuite have been realized in the past 2 years. C-arm–based cerebral blood volume and cerebral perfusion assessments have evolved to clinical evaluation.11,12

Intracranial Aneurysm Treatment

Tremendous efforts have been made in the past years to develop new endovascular approaches that will overcome the limitations of the procedure, including aneurysm recanalization and difficulty to treat some complex aneurysms (large and giant, fusiform, or wide-neck aneurysms).13

Flow diversion has now entered in a more mature phase with the appearance of trials and large series evaluating precisely the safety and efficacy of this technique. Pipeline for Uncollapsible or Failed aneurysms (PUFs) trial included 108 patients with aneurysms arising from the internal carotid artery measuring ≥10 mm diameter and a neck ≥24 mm.14 Complete occlusion at day 180 without major stenosis or use of adjunctive coils was reached in 73.6% of the aneurysms. The primary safety end point (major ipsilateral stroke or neurological death) was reported in 5.6% of patients. A comparison of flow diversion (pipeline embolization device) and coiling in large unruptured intracranial saccular aneurysms showed that the rate of procedure-related complications did not differ between the pipeline embolization device (7.5%) and the coil group (7.5%) and that a significantly higher proportion of aneurysms treated with pipeline embolization device (86%) achieved complete occlusion compared with coiled aneurysms (41%).15

This high efficacy of flow diverters was confirmed in several multicenter or large single-center series also showing a slightly higher rate of complications or morbidity and mortality compared with PUFs trial.16-18 This safety issue is partially explained by 2 emerging complications, which are delayed ruptures and delayed ipsilateral parenchymal hematomas.19-21

New flow diverters are now available for aneurysm treatment, including Surpass (Stryker Neurovascular, Fremont, CA)22 and FRED (Microvention, Tustin, CA).23 Indications for flow diverter treatment are also expanding.24

Flow disruption is an emerging technique using an intra-aneurysmal device placed at the level of the neck to disrupt the intra-aneurysmal flow and subsequently create intra-aneurysmal thrombosis. Preliminary experience with the WEB shows the great value of this treatment in the management of wide-neck bifurcation aneurysms.25-27

Promising advances in the understanding of aneurysm wall biology are important to design future treatment strategies. Similar to vulnerable plaque, inflammation is central to a vascular remodeling process that may lead to rupture—essentially engendering the concept of a vulnerable aneurysm. The Helsinki group recently reported that oxidative stress may be the cause of programmed cell death that is
prominent in ruptured human aneurysms. Building on previous work identifying mural cell loss association with rupture, a rat model was developed using decellularized arterial graft as an aneurysm sac. Pathological analysis demonstrated that thrombus formation within the decellularized aneurysm could not organize thereby leading to recanalization, inflammation, wall degeneration, and rupture. Similar conclusions on the role of incomplete thrombosis and subsequent inflammatory cell infiltration into the aneurysm wall was confirmed in a swine venous pouch aneurysm model. Ultimately, thorough understanding of aneurysm pathophysiology may enable imaging approaches to identify those at risk of rupture or pharmacological treatment for stabilization.

Perhaps the most exciting advances in interventional neuroradiology during the past 2 years involve the imaging system used for EVT. Remarkable radiation dose reduction during diagnostic neuroangiography without sacrificing image quality will benefit patients and operators alike. The decades-long quest to measure blood during angiography may be finally realized with high-frame rate detectors and analysis based on the optical flow algorithm. The first case of deploying a novel microangiographic fluoroscope for aneurysm embolization was reported this year. These developments along with perfusion imaging described above have expanded the capabilities of today’s C-arm.

### Intracranial and Extracranial Stenting for Atherostenotic Disease

The most recent and final publication on Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) analyzes the long-term benefit of both therapies. The investigators concluded that for high-risk patients with recent stroke associated with a high-grade intracranial stenosis, aggressive medical management is beneficial over stenting using the Wingspan system, and the benefit persists for 3 years. The authors also discuss that the only subgroup that may potentially benefit from stenting include patients with 70% to 99% stenosis who present with ≥2 strokes despite aggressive medical management, and whose last stroke occurred >7 days ago. Selected patients with symptoms related to hypoperfusion (eg, vertebrobasilar insufficiency) may also see a benefit from stenting.

Multiple past randomized clinical trials on carotid artery stenting (CAS), including the European studies Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis (EVA-3S), Stent-Protected Angioplasty Versus Carotid Endarterectomy (SPACE), International Carotid Stenting Study (ICSS), and the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST), could not show a superiority of stenting over carotid artery surgery. A recently published retrospective survey of carotid artery stenting performed in 8092 patients in Japan during a period of 10 years reports acceptable low incidence of 30-day morbidity and mortality. The rate of major adverse events (stroke, myocardial infarction, or death) at 30 days was varied from 3.5% to 10.2% depending on the distal protection method. The data are excellent and comparable with CEA.

### Brain Arteriovenous Malformation

The efficacy and safety of Onyx (Covidien eV3, Irvine, CA) embolization in arteriovenous malformation treatment has been evaluated in a prospective, multicenter, consecutive study (Brain Arteriovenous Malformations Embolisation With Onyx [BRAVO]). The morbidity rate in BRAVO was 5.1%, whereas the mortality was 4.3%.

The long-awaited initial results from A Randomised trial of Unruptured Brain Arteriovenous malformations (ARUBA) are now available. Medical management for brain arteriovenous malformation was compared with interventional therapy, which included surgical resection, embolization, stereotactic radiotherapy, alone or a combination thereof. After enrollment of 223 patients (800 were expected), the data and safety committee stopped the trial as primary end point was reached by 10.1% in the medical arm as compared with 30.7% in the interventional therapy group. The risk of death or stroke was significantly lower in the medical management group (hazard ratio, 0.27; 95% confidence interval, 0.14–0.54). In the interventional therapy arm a higher number of strokes were encountered as compared with medical therapy arm (45 versus 12; P<0.0001) as well as neurological deficits unrelated to stroke (14 versus 1; P=0.0008). The trial will also investigate whether the differences will continue during a follow-up period of next 5 years.

Detailed information for the interventional arm on technical aspects and periprocedural complications has not yet been provided. Unlike BRAVO, the rate of stroke and death in patients that received interventional therapy is high, especially because 68% of patients allocated to interventional therapy presented with Spetzler–Martin grade I or II brain arteriovenous malformation. As the enrollment was nonblinded, brain arteriovenous malformation with anatomic risk factors for hemorrhage, for example, associated aneurysms, deep venous drainage, or venous outflow obstruction, may have been excluded from enrollment.

### Disclosures

Dr Wakhloo is consultant for Stryker Neurovascular, member of the Scientific Advisory for Philips Medical and has research support from Philips Medical. Dr Pierot is consultant for Codman, Covidien, Microvention, Penumbra, and Sequent. The other authors report no conflicts.

### References


**Key Words:** aneurysm ■ arteriovenous malformations ■ endovascular procedures
急性卒中治疗

同时发表的 3 项比较急性缺血性卒中静脉溶栓治疗与血管内治疗（EVT）的随机对照试验，结果研究均为阴性，都未证实 EVT 优于静脉溶栓 1-3。然而，对这些研究仔细分析发现，这些研究在影像技术、取栓装置和研究设计上存在着诸多缺陷 4,5。

这些随机对照试验已经证实 EVT 对患者不是有害的，在 IMS–III（Interventional Management of Stroke）研究中的亚组分析已经显示 EVT 能为一些患者提供获益。在卒中血管内治疗领域，以新一代取栓装置、介入操作技术和 C 型臂影像技术为目标的专项研究不断扩大。新一代支架取栓器 retrievers 已经显示了很大的技术改进 6,7；然而，还需在以下各个方面进一步改进：能获益于血管内治疗的患者筛选上、高效将患者转运到血管造影室，以及加快血管内治疗的各个环节上，从而提供快速和完全的血管再通。

在机械血栓清除术中，可能导致不良临床预后的一个潜在因素是血栓碎片引起下游栓塞。在应用支架 retriever 血管内治疗中，使用近端球囊和抽吸导管可减少远端栓塞 8。这种方法在临床上已得到验证，临床研究资料显示应用球囊导向导管是 90 天良好功能结局的独立预测因素 8。

虽然灌注 CT 在急性缺血性卒中诊断分类中的作用还存争议 10，在过去 2 年，在血管造影室利用 C 型臂灌注成像已经取得了巨大进展。带 C 型臂的脑血容量和脑灌注评估已经发展到临床评估阶段。11,12

颅内动脉瘤治疗

在过去几年间，新型血管内治疗方法取得了巨大进展，从而能够克服手术操作的一些局限性，包括动脉瘤血管再通和某些复杂动脉瘤治疗（大的和巨大的、梭形的或宽颈动脉瘤）。13

随着血流转向技术临床试验以及精确评价该技术的临床试验数量不断增加，PUFs（Pipeline for Uncoilable or Failed aneurysms，PUFs）试验纳入了 108 例直径≥10mm（国际颈动脉测量标准）和颈≥4mm 的动脉瘤患者。14 第 180 天随访，73.6% 的动脉瘤达到完全闭塞，且没有严重的动脉狭窄或应用辅助弹簧圈。主要安全终点事件（严重的同侧卒中或神经源性死亡）的发生率是 5.6%。一项比较血流转向 Pipeline 植入装置与弹簧圈填充治疗的颅内未破裂囊状动脉瘤研究中，结果表明操作相关的并发症在两组间无差异（7.5% vs. 7.5%），而且采用 Pipeline 植入装置治疗的动脉瘤达到完全闭塞的比例（86%）显著高于采用弹簧圈装置组（41%）。15 血流转向装置这种高疗效也在几项多中心或单中心大规模病例研究中得到证实，但并发症发生率和死亡率略高于 PUFs 试验。16-21 这一原因部分是由于迟发性动脉瘤再破裂和同侧脑实质血肿。18-21

现在已有新的血流转向装置用于动脉瘤治疗，包括 Surpass（Stryker Neurovascular, Fremont, CA）和 FRED（Microvention, Tustin, CA）。22 血流转向装置治疗的适应证也在扩大。23

血流阻断是一种新兴技术，将一个动脉瘤内装置放置在瘤颈位置，阻断动脉瘤内血流，随后制造一个瘤内栓塞。应用 WEB 的初步经验表明，这种治疗对宽颈分叉处动脉瘤具有很大的价值。20-22

关于动脉瘤壁生物学方面的巨大进展对设计未来治疗策略非常重要。类似易损斑块，炎症是血管重塑过程中可能导致动脉再破裂的中心环节 - 本质上也就是易损动脉瘤（vulnerable aneurysm）。Helsinki 研究组最近报道，氧化应激可能是细胞程序性死亡的原因，这在人类动脉瘤破裂中尤为突出。24,25 在既往研究中，为确定动脉瘤破裂是否与血管壁细胞缺失有关，人们利用去细胞化的动脉移植物作为瘤囊制作了一个大鼠模型。病理分析表明在去细胞化动脉瘤中的血栓不能机化，导致瘤内血流再通，炎症、血管壁退化和破裂。关于血栓形成不完全和后续瘤壁炎症和细胞浸润的类似结论在猪颈动脉囊状动脉瘤模型中也得到证实。26 最后，对动脉瘤病理生理的更深入理解可有助于建立识别有破裂风险的动脉瘤影像学方法 27 或发现稳定动脉瘤的治疗药物。23

过去的 2 年间介入神经放射学上最令人振奋的进展或许是用于 EVT 的影像学系统。在诊断性血管造影检查期间放射剂量的显著降低而不影响图像质量使患者和手术医师都受益。34 数十年来探求血管造影时能测定血流可能最终会通过高频探测器和光流算法分析实现。35 今年报道了首例采用新的微血管造影透视技术的动脉瘤栓塞术。36 上述这些灌注影像上的进展已经扩展到当今 C 型臂的功能研究上。
颅内外支架成形术治疗血管成形术

去年发表的 SAMMPRIS 研究是关于支架成形术与积极内科治疗用于预防颅内外动脉狭窄患者卒中复发的疗效对比，最近又发表的关于两种治疗的远期疗效对比，结果是，对于颅内外动脉狭窄的高危患者，积极内科治疗比使用 Wingspan 支架治疗更有益处，而且这一益处会持续 3 年。作者还讨论了可能从支架成形术中获益的患者亚组，这些患者动脉狭窄程度 70%~99%，在积极内科治疗下仍有 ≥2%的卒中发作，并且在最近一次卒中发生在 >7 天之前，有低血糖（如糖尿病或低血压）有关的症状性选择患者也可能看到支架成形术的益处。

过去多项关于颈动脉支架成形术 (CAS) 的随机临床试验，包括欧洲症状性严重颅内外动脉狭窄患者血管成形术与支架成形术对比研究 (EVA-3S)，支架保护下的血管成形术与颈动脉血管成形术 (SPACE)、国际颈动脉支架成形术研究 (ICSS) 和颈动脉血管重建血管成形术与支架成形术实验 (CREST)，都未能显示支架成形术优于血管成形术。最近一项关于 CAS 的 10 年回顾性调查报告，共 8092 例行 CAS 治疗的患者，显示了较低的 30 天并发症发生率和死亡率。38 这可能是因为 CAS 治疗的远期疗效对比，最近最后发表了 CAS 治疗的益处。

脑动静脉畸形 (AVM)

在前瞻性、多中心连续性 BRAVO 研究 (Brain Arteriovenous Malformations Embolisation With Onyx, BRAVO) 中，对应用 Onyx (Covidien eV3, Irvine, CA) 栓塞治疗动静脉畸形的疗效和安全性，结果显示并发症发生率是 5.1%，死亡率是 4.3%。

令人期待已久的未破裂脑动静脉畸形随机试验 (ARUBA) 现在已经完成了初步性结果。60 该研究比较了内科治疗与介入治疗对脑动脉畸形的疗效和安全性，结果显示并发症发生率是 5.1%，死亡率是 4.3%。

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急症期脳梗塞：静脈血栓溶解療法と血管内治療の無作為化比較試験（RCT）としてIMS III、SYNTHESIS expansion、MR RESCUEが実施されたが、いずれも血管内治療の優位性を示せなかった。しかし、安全性に関問題はなく、IMS IIIでは症例によっては有効性が示唆された1。新しいステント型血栓回収機器の性能は、上記3試験で使用された従来型デバイスを凌駕するが、迅速で完全な再開通を得るには、血管内治療の症例選択や、治療までの時間の短縮などに要する改善が望まれる。

脳動脈瘤：塞栓後再開通や塞栓術が困難な動脈瘤など、コイル塞栓術の弱点を克服する血管内治療戦略が検討されている。親血管への留置により動脈瘤の血栓化をもたらすflow diversion（分流）デバイスの研究が本格化してきた。Pipeline Embolization Device（PED）を直径3.0mmで応用（直径4mm）な内頸動脈瘤に用いたPUPs試験では、180日後の完全閉塞率が73.6%に達した2。PEDとコイル塞栓術の比較では、PEDで完全閉塞が多く（86% vs 41%）、合併症は同等であった（各7.5%）。動脈瘤内留置により血栓化を促すflow disruptionデバイスであるWEBの有効性も報告されている。

頭蓋内・頭蓋外動脈硬化性狭窄病変に対するステント留置術：SAMMPRISの最終報告では、症候性頭蓋内動脈狭窄に対するWingspanステント留置術に比べて内科的治療の優位性は3年後も持続していた3。狭帯率70%で内科的治療下に複数回再発し、最終発作より7日以上経過した症例ではステント留置術の有効性が期待できるかもしれません。過去のRCTでは、内膜剥離術（CEA）による頭動脈ステント留置術（CAS）の有効性は示されていないが、8,092例を後向きに集積したJapanese CAS Surveyでは、30日後の脳卒中/心筋梗塞/死亡は遠位段階防止法によれば10.2%から3.5%まで低率となり、少なくともCEAと同等の良好な結果であった4。

脳動脈脅帯形：前向多施設BRAVO試験では、液状塞栓物質であるOnyxによる血管内治療の症候性合併症5.1%、死亡4.3%と良好な成績であった。一方、未破壊脳動脈脅帯形に対する内科的治療と侵襲的治療（外科的切除/血管内治療/定位放射線治療またはそれらの併用）をRCTで比較したARUBA試験では、登録途中で症候性脳卒中/死亡が内科的治療群10.1%に対し侵襲的治療群で30.7%に生じたため、新規登録は中止となった5。ARUBAは非盲検試験のため出血リスクが高いため症例が除外された可能性がある。

（著者が早川・幹人・峰松・一夫）

資料文献

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