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 technology6,7; 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 studies 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).11

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 ≥4 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


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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，结果显示均为阴性，都未证实EVT优于静脉溶栓。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。

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；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，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。这种方法在临床已得到验证，在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。

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，但在过去2年，在血管造影室利用C型臂CT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。

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（大的和巨大的、梭形的或宽颈动脉瘤）。随着血流转向技术临床试验以及精确评价这项技术安全性和有效性的大宗病例报道出现，说明这项技术已发展到一个更为成熟的阶段。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。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栓塞装置与弹簧圈栓塞治疗的临床试验中，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栓塞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栓塞组（41%）。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，这原因部分是由于迟发性动脉瘤再破裂和同侧脑实质血肿。

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）。血流转向装置治疗的适应证也在扩大。血流阻断是一种新兴技术，将一个动脉瘤内装置放置在颈内动脉上，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，这种技术对宽颈分叉处动脉瘤具有很大的价值。

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。在人类动脉瘤破裂中尤为突出。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内，血栓不能机化，导致动脉瘤再通。动脉瘤壁退化和破裂。关于血栓形成不完全和随后瘤壁炎症性细胞浸润的类似结论在猪颈动脉瘤模型中也得到证实。最后，对动脉瘤病理生理的更深入了解可有助于建立识别有破裂风险的动脉瘤影像学方法或发现稳定动脉瘤的治疗药物。

过去的2年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。在诊断性神经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。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。今年报道了首例采用新的微血管造影透视技术做的动脉瘤栓塞术。上述这些灌注影像上的进展已经扩散到当今C型臂的功能研究上。
颅内外支架成形术治疗的动脉狭窄

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动脉狭窄患者卒中复发的疗效对比，最近又发表了关于两种治疗的远期疗效对比。27结论是，对颅内动脉高度狭窄的高危患者，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。41 作者还讨论了可能从支架成形术中潜在获益的患者亚组，这些患者动脉狭窄率高达 70%~99%，在积极内科治疗下仍有 ≥2 次的卒中发作，并且最近一次卒中发生在 > 7 天之前，与低灌注（如椎基底动脉供血不足）有关的症状性选择患者也可能会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颈动脉狭窄患者内膜剥脱术与血管成形术对比研究（EVA-3S）、支架保护下的血管成形术与颈动脉硬化症的益处（SPACE）和安全性，39 用 Onyx（Covidien eV3, Irvine, CA）栓塞治疗动静脉畸形（BRAVO）中，评价了应

结论是，对颅内动脉高度狭窄的高危患者，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。41 作者还讨论了可能从支架成形术中潜在获益的患者亚组，这些患者动脉狭窄率高达 70%~99%，在积极内科治疗下仍有 ≥2 次的卒中发作，并且最近一次卒中发生在 > 7 天之前，与低灌注（如椎基底动脉供血不足）有关的症状性选择患者也可能会看到支架成形术的益处。

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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，评价了应用 Onyx（Covidien eV3, Irvine, CA）栓塞治疗动静脉畸形的效果和安全性。32 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（A Randomised trial of Unruptured Brain Arteriovenous malformations, ARUBA）现在已经有了初步性结果。40 该试验比较了内科治疗与介入治疗对脑动静脉畸形的疗效，介入治疗包括外科手术、栓塞、立体定向射频治疗等。在纳入 223 例患者（预期为 800 例）后，由于主要终点事件发生率在内科治疗组为 10.1%，而介入治疗组为 3.7%，因此数据和安全委员会提前终止了该试验。卒中或死亡风险在内科治疗组更低（HR, 0.27; 95%CI, 0.4–0.54）。卒中例数在介入治疗组更高（45 vs 12: P < 0.0001），而且与卒中无关的神经功能缺陷在介入治疗组也更高（14 对 1: P < 0.0008）。该试验将继续观察这些差异在未来 5 年随访中是否会持续存在。

未破裂脑动静脉畸形随机试验的初步结果提示，未破裂脑动静脉畸形的内科治疗可能比介入治疗更安全。然而，由于样本量较小，需要进一步的研究来验证这一结论。此外，对于高风险患者，介入治疗可能仍然是必要的。

参考文献

急性期脳梗塞: 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、安全性に問題はなく、IMS IIIでは症状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更なる改善が望まれる。

脳動脈瘤: 塩栓再開通や塞栓術が困難な動脈瘤などで、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。脳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 10mm まで広範 (直径 4mm) な内頸動脈瘤に用いた PUFs 試験では、180 日後の完全閉塞率が 73.6% に達した。PED とコイル塞栓術の比較では、PED で完全閉塞が多かった (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。

顕著な用語文献


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