The indications for microsurgery in cerebrovascular pathology have been placed under increased scrutiny, given the continuous refinement of endovascular techniques. Several recent randomized studies and subgroup analyses of concluded studies have been particularly illuminating in this sense and will be the primary focus of this brief review.

Extracranial Carotid Stenosis
The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) has shown that the risk of perioperative stroke is slightly higher after carotid artery stenting (CAS) than after carotid endarterectomy (CEA), whereas the reverse is true for the risk of periprocedural myocardial infarction. Over the past year, the CREST investigators have also reported the results of some prespecified and some ad hoc subgroup analyses. Earlier trials of CAS versus CEA had suggested higher risk of restenosis after endovascular treatment of carotid stenosis compared with CEA. However, in CREST after 2 years, the incidence of restenosis >70% or occlusion was similar in the CAS (6%) and the CEA (6.3%) groups, suggesting that restenosis may not be a major concern if endovascular treatment is contemplated. Smoking increased the risk of restenosis in patients undergoing CEA but not after stenting. Subgroup analysis by age confirmed that increasing age is associated with a higher risk of periprocedural stroke after CAS but did not affect the risk profile in patients undergoing CEA. In the CREST group, there were only minor differences in healthcare costs and quality-adjusted life expectancy between CAS and CEA, which contradicted early studies that had suggested higher costs associated with CAS.

Symptomatic Intracranial Stenosis/Occlusion
The past 2 decades had witnessed a trend toward more aggressive invasive treatment of patients with symptomatic intracranial stenosis. However, completion of the Carotid Occlusion Surgery Study (COSS) and the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMPPRIS) has shown that neither surgical bypass nor angioplasty and stenting are better than maximal medical therapy in preventing future ipsilateral ischemic events in patients with symptomatic internal carotid artery occlusion and intracranial stenosis, respectively. In both studies, the lack of a positive effect after invasive therapy was related to both a higher (than expected) periprocedural complication rate than anticipated with invasive treatment and a lower incidence of end point events in patients treated with maximal medical therapy, including statins and antihypertensives. Predictably, publication of these trials has also triggered wide criticism of the studies’ methodology, inclusion criteria, and center selection. Nevertheless, these studies have had an impact in reducing the number of interventions done for symptomatic intracranial stenosis in North America.

Intracranial Aneurysms
The debate regarding the safest and most effective therapeutic strategy in patients with intracranial aneurysms has continued with refinements of endovascular techniques. The International Subarachnoid Aneurysm Trial (ISAT) study, completed in 2002, changed the practice for many patients with ruptured aneurysms. However, several issues remained unanswered by that landmark trial. A possible recruitment bias among ISAT patients was raised by some critics, given that 9559 patients were screened and only 2143 included. The Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms (CLARITY) registry was initiated to address this criticism and to address the applicability of the ISAT results to multiple endovascular centers. Among this registry, 405 consecutive patients with subarachnoid hemorrhage were treated with coil embolization at 19 French centers. Six-month mortality and morbidity were similar to ISAT, with 23.3% of all patients scoring ≥3 on the modified Rankin Scale at 3 to 6 months, despite 30% of patients being admitted in grade IV/V. Further concerns were raised regarding the applicability of ISAT results to North American centers with reputedly more subspecialized cerebrovascular surgeons. In response to the above concerns, surgeons at the Barrow Neurological Institute in Phoenix, Arizona, launched the Barrow Ruptured Aneurysm Trial (BRAT) in 2002. The results of this landmark study were recently published. The BRAT investigators assigned every patient with subarachnoid hemorrhage to either endovascular therapy or surgical clipping in an alternating fashion to more accurately model clinical realities. As a consequence of this design, a large number of patients allocated to endovascular treatment crossed over to surgical treatment because patients could be enrolled regardless of whether the aneurysm was
amenable to both treatment modalities. Therefore, aneurysms that could not be safely treated with coiling for technical reasons (ie, very small aneurysms) or clinical considerations (ie, aneurysms associated with intraparenchymal hematomas necessitating surgical evacuation) were still assigned to embolization. Despite a high rate of crossover, the BRAT study confirmed previous ISAT conclusions: outcomes at 1 year were better after coil embolization than after surgical clipping. The proportion of patients experiencing a poor outcome (defined by a modified Rankin score >2) was 33.7% in the surgical group versus 23.2% ($P=0.02$, intention-to-treat analysis) in the endovascular group. As-treated analysis yielded similar results, with 33.9% patients in the surgical group and 20.4% in the endovascular group experiencing a poor outcome at 1 year ($P=0.01$). Overall, the BRAT study confirmed the ISAT conclusions, while at the same time stressing that surgery continues to be a valid and important option for selected patients with ruptured intracranial aneurysms. Several considerations that include patient-related, aneurysm-related factors and local logistics and practice patterns have a very important role in deciding the best therapeutic strategy in a patient with a ruptured intracranial aneurysm.

Arteriovenous Malformations

The optimal management strategy in patients with intracranial parenchymal arteriovenous malformations continues to be controversial. An update of the Finnish database suggested a non-negligible risk of bleeding in patients with untreated high-grade AVMs. However, patients considered in that study spanned a very long time interval, presented mostly with hemorrhage, and often harbored AVMs considered not amenable to invasive treatment because of the risks involved. The ongoing A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) study compares outcomes of intervention versus best conservative therapy for unruptured AVMs considered amenable to invasive treatment. In a recent update, 193 of 389 eligible among 1294 screened patients were randomized by March 2012. Results of this study are eagerly awaited but should be interpreted with the caveat that important methodological flaws may be present. Josephson et al investigated the risk of seizures after either invasive treatment or conservative management of AVMs. No significant difference in the 5-year risk of unprovoked seizure was observed between the invasive treatment group and the conservatively managed group, irrespective of AVM obliteration status. For patients with an AVM who presented with seizures but no hemorrhage, no difference in seizure recurrence was observed during follow-up between patients treated invasively (39 patients) and those treated medically (21 patients).

Disclosures

G. Lanzino is a consultant for ev3/Covidien. The other authors have no conflicts to report.

References


KEY WORDS: arteriovenous malformations, carotid stenosis, cerebrovascular surgery, extra-intracranial bypass, intracranial stenosis, intracranial aneurysms
脳血管外科の進歩
Advances in Stroke: Vascular Neurosurgery

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脳血管疾患に対する血管内治療の進歩に伴い、従来からのマイクロサージェリーの治療適応が見直されつつある。以下、両治療法を比較した無作為化試験及びそのサブグループ解析について、疾患別にまとめる。

# 頭蓋外頸動脈狭窄症

CREST 試験では、頸動脈内膜剥離術（CEA）群と比較し、ステント留置術（CAS）群で周術期脳卒中がわずかに多く、逆に心筋梗塞は少なかった。以前の研究では、CAS 群で再狭窄率が高かったが、CREST サブ解析では 2 年以内の再狭窄/閉塞率には差がなく、CAS の適応検討時に再狭窄は大きな問題とならないことが示唆された1。両群とも、女性、糖尿病、脂質異常症が再狭窄の独立した危険因子であったが、喫煙による再狭窄リスクは CEA でのみ有意であった。CAS 群での周術期脳卒中は加齢により増加したが、CEA 群では関連しなかった。医療費、質調整余命に著明な群間差はなかった。

# 症候性頭蓋内動脈狭窄・閉塞症

過去 20 年間ほどの、症候性頭蓋内動脈狭窄・閉塞例に対して侵襲的な治療法が選択される傾向にあった。しかしながら、COSS 試験2 及び SAMMPRIS 試験3で、バイパス術、血管形成術+ステント留置術の虚血イベント発症抑制効果は、最良の内科治療に及ばなかった。侵襲的治療の周術期合併症発症率は予想以上に高く、逆に内科治療のイベント発症率は低かった。これらの結果、北米での侵襲的治療実施数は減少している。

# 頭蓋内脳動脈瘤

2002 年の ISAT 研究は、その後の破裂脳動脈瘤治療に多大な影響を与えたが、選択バイアス等の問題点も指摘された。こうした問題を検討するために行われた CLARITY 登録研究では、コイル塞栓術を行ったケモ薬下出血連続例の半年後の死亡率・障害残存率は ISAT 研究と同程度で、3 〜 6 カ月後の modified Rankin Scale（mRS）≧ 3 は 23.3% であった。北米の脳血管外科専門施設で実施された BRAT 研究でも、1 年後再発はクリッピング術群と比較しコイル塞栓術群で良好で（mRS ≧ 2 の 33.9% 対 20.4%）、ISAT の結果に一致した。しかし、症例によってはクリッピング術の方が適している場合があることも強調された。患者の状態、動脈瘤自体の情報、医療提供者側の条件等を総合的に勘案した治療法選択が重要であろう。

# 脳動静脈奇形

ARUBA 試験は、未破裂脳動静脈奇形に対する血管内治療と最良の内科治療との比較試験である5。2012 年 3 月までに 193 例が無作為割り付けられ、その結果が待たれる。ただし、方法論上の問題点も指摘されており、結果の解釈には注意が必要である。Josephson らの研究では、侵襲的治療群と内科治療群で 5 年以内の痙攣発症率に差はなく、痙攣再発のない有出血の脳動静脈奇形症例でも、痙攣再発率に群間差がなかった。

(文責：石上 晃子*、峰松 一夫)

# 代表的な引用文献


* 国立循環器病研究センター脳血管内科