Balloon Angioplasty for Intracranial Atherosclerotic Disease Periprocedural Risks and Short-Term Outcomes in a Multicenter Study

Thanh N. Nguyen, MD; Osama O. Zaidat, MD; Rishi Gupta, MD; Raul G. Nogueira, MD; Nauman Tariq, MD; Junaid S. Kalia, MD; Alexander M. Norbash, MD; Adnan I. Qureshi, MD

Background and Purpose—Whether stenting is superior to angioplasty in the treatment of intracranial atherosclerotic disease is unknown. Dissections, vessel rupture, and lesion recoil observed with primary angioplasty using balloon catheters designed for coronary arteries have undermined the role of primary angioplasty as a preferred treatment for intracranial atherosclerotic disease. The goal of this study is to report the immediate and 3-month outcomes of treating patients with intracranial atherosclerotic disease with angioplasty balloon catheters in a multicenter study.

Methods—This is a retrospective review of 74 patients from 4 institutions treated with primary angioplasty for intracranial atherosclerotic disease over a 6-year time period. Technical success (residual stenosis ≤50%), periprocedural success (no vascular complication within 72 hours), and 3-month outcomes are reported.

Results—The mean degree of stenosis pretreatment was 79% ± 14% and reduced to 34% ± 18% after angioplasty. Technical success was achieved in 68 (92%; 95% CI, 83% to 97%) of the 74 patients. Periprocedural success was achieved in 65 (88%; 95% CI, 78% to 94%) of the 74 patients. There were 4 (5%; 95% CI, 1.5% to 13%) major procedure-related strokes, 2 of which resulted in death within 6 hours of the procedure. The 30-day stroke/death rate was 5% (4 of 74; CI, 1.5% to 13%). Three-month follow-up was available in 71 patients. In this interval, 2 patients had new stroke, 1 in the ipsilateral territory and the other in the contralateral territory. The 3-month stroke or death rate was 8.5% (6 of 71; CI, 3.1% to 17.5%); the retreatment rate was 2.8% (2 of 71; CI, 0.3% to 10%).

Conclusion—Balloon angioplasty is a relatively safe alternative treatment for intracranial atherosclerotic disease. Its role in the long-term secondary prevention of recurrent stroke as compared with intracranial stenting and medical therapy remains to be determined, preferably in a randomized study. (Stroke. 2011;42:107-111.)

Key Words: angioplasty and stenting • complications • intracranial disease • intracranial stenosis

Intracranial atherosclerotic disease (ICAD) remains an important cause for ischemic stroke, particularly in patients of black, Asian, or Hispanic origin as well as in diabetics. The annual risk of recurrent stroke is high despite medical therapy, estimated at 10% to 23% of patients with symptomatic stenosis. Endovascular therapy has emerged as an important alternative treatment for ICAD and a large randomized study is in progress to evaluate the safety and efficacy of angioplasty with stenting compared with intensive medical therapy alone. However, whether stenting is superior to angioplasty alone in the treatment of ICAD remains unknown.

A consensus conference on ICAD concluded that no clear data are available to support the effectiveness of primary angioplasty over stent placement for treatment of intracranial atherosclerotic stenosis. Both primary angioplasty alone and angioplasty with self-expanding stents have been evaluated in nonrandomized trials with high technical success and with recurrent ischemic events no worse than the natural history of lesions treated with medical management alone. The safety of balloon-expandable stents has been tested in 1 prospective nonrandomized trial and a monorail balloon-expandable stent has recently become available. Treatment paradigms are currently based on operator preference and experience. In most practices, reports of dissections, vessel rupture, lesion recoil, and restenosis observed with angioplasty using balloon catheters designed for use in coronary arteries have undermined the role of primary angioplasty as a preferred treatment for ICAD. On the other hand, obligate dual-antiplatelet agents, the challenge of navigating through tortuous carotid siphon anatomy, restenosis and cost are important limitations of intracranial stenting. The goal of this retrospective multicenter study is to report the immediate and 3-month outcomes of patients
with ICAD treated with primary angioplasty using angioplasty balloon catheters.

Methods
We conducted a retrospective review from prospectively collected databases of patients undergoing neurointerventional treatment at 4 stroke centers. An Excel spreadsheet (Microsoft) including nonidentifying demographic variables index events (transient ischemic attack, ischemic stroke), location and degree of stenosis, timing of the procedure, type of balloon used, periprocedural antiplatelet or antithrombotic therapy, procedural complications, clinical follow-up, and 3-month outcomes were recorded by each site. Institutional Review Board approval for the study was obtained from each institution as well as the coordinating institution. There was no financial nor industry support for the study. One author (O.O.Z.) has consulted for Boston Scientific.

Patient Selection
Patients with ICAD and treated with balloon angioplasty (Gateway or Maverick balloon catheters; Boston Scientific, Fremont Calif) between 2003 and 2009 were included in the study. A policy of optimizing medical therapy was agreed among investigators and modeled after the ICAD consensus conference guidelines. Most patients were treated with aspirin and/or clopidogrel, cholesterol-lowering agents (target <70 mg/dL), glucose-lowering agents for diabetes mellitus (target HbA1c <7%), and smoking cessation. With the emergence of the Warfarin–Aspirin Symptomatic Intracranial Disease (WASID) data, long-term blood pressure control was targeted to maintain a value <140/90 mm Hg. An intracranial lesion was defined as at the level or above the upper petrous carotid artery in the anterior circulation and above the C1 portion of the distal vertebral artery in the posterior circulation. All patients had measured baseline stenosis of ≥50% using WASID criteria, which measures the narrowest diameter of the stenosed artery as compared with the diameter of the most proximal, normal portion of the artery.

Patients were selected for endovascular intervention by the following criteria: ischemic events referable to the artery with the stenosis; ischemic symptoms despite antiplatelet therapy defined as regular use of ≥81 mg aspirin, 75 mg clopidogrel, or antiocoagulation, defined as intravenous heparin or oral warfarin. A stroke was defined as a clinical event with acute onset of neurological symptoms and accompanying radiographic demonstration of ischemia by CT or MRI.

Intracranial stent placement was attempted when considered feasible based on an assessment of vessel tortuosity, lesion length, and vessel size. In 1 center, before the availability of the Wingspan stent, angioplasty was preferred to avoid the technical difficulty of navigating nonintracranial stents. In general, primary angioplasty was preferred for patients with small vessels (<2 mm diameter), long lesions that would require multiple stents (>12 mm), tortuous proximal vessels (>2 acute curves requiring traversing, judged by experience or trial), limited vessel length available distal to the lesion to allow stable placement of microcatheter, lesions located in the anterior cerebral, posterior cerebral or M2 segment lesions, or if a guide catheter could not be placed in the distal vertebral artery or internal carotid artery.

Procedure
Participating neurointerventionalists were qualified for performing neurovascular procedures by criteria as outlined by the Society of Neurointerventional Surgery, Society of Vascular and Interventional Neurology, and American Academy of Neurology. General anesthesia was used in 62 of 74 (84%) patients. The procedural protocol was standard across the 4 centers and closely adhered. Patients were treated using femoral access and placement of a 6-Fr or 7-Fr guide catheter in the cervical carotid or vertebral artery. Intravenous heparin was given after groin puncture with the goal to maintain activated clotting time >250 seconds. After diagnostic angiography, a Gateway or Maverick balloon was advanced across the lesion over a 0.014-inch microwire either with direct access or after microcatheter exchange. The diameter of the balloon was undersized to 80% of the normal arterial diameter, and the shortest length was selected to cover the lesion. The balloon was inflated slowly under fluoroscopic roadmap guidance over several seconds to the nominal inflation pressures and kept inflated for approximately 15 to 30 seconds and then deflated. After the procedure, careful attention was paid to monitor and maintain the blood pressure <130/80 mm Hg in most scenarios to prevent reperfusion hemorrhage. Patients were discharged on antiplatelet therapy unless warfarin was required for a history of atrial fibrillation. Follow-up of patients was obtained within at least a 3-month interval.

Results
We evaluated 74 consecutive patients with ICAD (50% to 99%) treated between August 2003 and September 2009 at 4 centers. The mean age was 62 ± 14 years; 41 patients were men (55%). Patient race/ethnicities were as follows: white, 35 (47%); black, 24 (32%); Hispanic, 10 (14%); and other, 5 (7%). Stroke risk factors included hypertension in 61 patients (82%), diabetes mellitus in 31 (42%), hyperlipidemia in 55 (47%), atrial fibrillation in 10 (14%), and cigarette smoking in 21 (28%). Indications for angioplasty were stroke (n=43), transient ischemic attack (n=29), tinnitus (n=1), and pre-coronary artery bypass graft (n=1). Early angioplasty, defined as treatment within 7 days from the index event, was performed in 33 (45%) patients. Reasons for not treating early include concern for reperfusion hemorrhage with early intervention and moderate-sized strokes, need for optimizing the patient’s medical or neurological condition before intervention, lack of a recommendation for timing of intervention before WASID data, or physician preference.

The distribution of lesion location is described in the Table with 47 (64%) of stenoses in the anterior circulation. Balloon catheters used were Gateway (n=34) and Maverick (n=39). One patient was treated with both balloons. Another patient failed with navigation of a Gateway 1.5×9-mm balloon across an A2 stenosis due to vessel tortuosity and therefore a 1.5×6-mm Sprinter balloon (Medtronic, Minneapolis, Minn) was used, successfully reducing a 75% lesion to 25% residual stenosis. This patient was counted as a failure for balloon angioplasty success.

The average pretreatment stenosis was 78.7%±14.2% and reduced to 33.8%±17.9% after primary angioplasty. Technical success, defined as residual stenosis of ≤50%, was achieved in 68 of 74 (92%; 95% CI, 83% to 97%) patients. Procedure success, defined as balloon angioplasty success without stroke or death at discharge or within 72 hours postprocedure, was achieved in 65 of 74 (88%; 95% CI, 78% to 94%) patients.

There were 4 (5%; 95% CI, 1.5% to 13%) major procedure-related strokes, 2 of which resulted in death. One patient with a basilar artery stenosis of 50% treated with a Maverick balloon developed subarachnoid hemorrhage secondary to microcatheter perforation of the basilar artery and died within 6 hours of the procedure. A patient with 90% basilar artery stenosis developed bilateral posterior fossa ischemic stroke and died within 6 hours after angioplasty with the Maverick/Gateway balloons. The other procedure-related strokes occurred in a patient with 70% M2 segment stenosis...
and another patient with 90% vertebral artery stenosis. The 30-day stroke or death rate was 5% (4 of 74; 95% CI, 1.5% to 13%). Three-month follow-up was available in 71 patients. One patient was lost to follow-up because he returned to his home country 1 week after his procedure. According to the patient’s son, the patient was doing well but this could not be clinically verified. In the 3-month interval, 2 patients had new stroke, 1 related to recurrent stroke in the ipsilateral territory and was also retreated. The 3-month stroke and death rate was 8.5% (6 of 71; CI, 3.1% to 17.5%); the retreatment rate was 2.8% (2 of 71; CI, 0.3% to 10%).

### Discussion

After the Food and Drug Administration Human Device Exemption approval of the Wingspan stent, intracranial angioplasty followed by stenting became increasingly used for the treatment of symptomatic ICAD worldwide, especially in the United States. It is estimated that 10,000 patients have been treated worldwide. The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) study is currently evaluating in a large randomized trial whether intracranial angioplasty and stenting is superior to intensive medical therapy alone in the treatment of ICAD.

However, it is unknown whether stenting should be the primary endovascular modality of choice for intracranial atherosclerotic disease management. In the extracranial circulation (carotid and coronary), stent-assisted angioplasty has been shown to have superior safety and efficacy compared with balloon angioplasty alone. This has not been demonstrated in the intracranial circulation. The current SAMMPRIS trial has excluded balloon angioplasty alone as a treatment arm for symptomatic ICAD; their assessment that stenting is the better option over angioplasty alone in the treatment of ICAD has not been validated in prospective randomized trials.

Several problems emerged with data from 2 large Wingspan prospective registries. The National Institutes of Health multicenter Wingspan registry revealed a 5% rate of any stroke or death within 24 hours of the stenting procedure and 9% within 30 days. Another prospective Wingspan registry showed that in-stent restenosis, defined as stenosis of ≥50%, was found in 25% to 30% of patients treated with the Wingspan stent over a 6-month period. In half of the in-stent restenosis patients, lesions were more extensive than the original lesion treated in by length or stenosis severity. Treatment of in-stent restenosed lesions did not produce durable results.

In the present study, we evaluated the immediate procedural risks and 3-month outcome of patients with ICAD treated with the Gateway or Maverick balloon angioplasty catheters. In this series, there were several reasons why balloon angioplasty was favored over stenting. Wingspan may have failed or been judged difficult or too risky to navigate through tortuous carotid siphon anatomy. Stent placement involves leaving in situ a foreign body behind with unknown long-term consequences. Fear of restenosis with the Wingspan stent, particularly in young patients with lesions in the anterior circulation, was another concern. Obligate clopidogrel with stenting can increase hemorrhagic risk, particularly in patients who also require anticoagulation or present with larger strokes. Dual antiplatelet agents with aspirin and clopidogrel, as often used with stenting, can increase risk of life-threatening or major bleeding in patients with recent ischemic stroke or transient ischemic attack as demonstrated in the Management of Atherothrombosis With Clopidogrel in High-Risk Patients (MATCH) trial. Jailing important branch points, particularly at the middle cerebral artery bifurcation, was another concern. From an anatomic perspective, primary angioplasty was preferred for small vessels (<2 mm in diameter), long lesions (>12 mm), limited vessel length distal to the lesion to allow stable placement of microwire (basilar stenosis with hypoplastic or aplastic posterior cerebral arteries), and lesions in the anterior cerebral or posterior cerebral artery. Last, in this era of healthcare fiscal conservatism, cost may have been a consideration. The Wingspan stent is priced at approximately $6000 in the United States compared with $800 for a Gateway balloon catheter.

### Table. Patient and Lesion Characteristics

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>N=74, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years±SD</td>
<td>62±14</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>41 (55%)</td>
</tr>
<tr>
<td>Race, no. (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>35 (47)</td>
</tr>
<tr>
<td>Black</td>
<td>24 (32)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10 (14)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Risk factors, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>31 (42)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>61 (82)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>55 (74)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>10 (14)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>21 (28)</td>
</tr>
<tr>
<td>Lesion location</td>
<td></td>
</tr>
<tr>
<td>M1 segment</td>
<td>21</td>
</tr>
<tr>
<td>M2 segment</td>
<td>8</td>
</tr>
<tr>
<td>A1 segment</td>
<td>1</td>
</tr>
<tr>
<td>A2 segment</td>
<td>1</td>
</tr>
<tr>
<td>A3 segment</td>
<td>2</td>
</tr>
<tr>
<td>ICA ophthalmic segment</td>
<td>10</td>
</tr>
<tr>
<td>ICA below ophthalmic</td>
<td>4</td>
</tr>
<tr>
<td>Basilar</td>
<td>16</td>
</tr>
<tr>
<td>Vertebral, intracranial</td>
<td>8</td>
</tr>
<tr>
<td>PIKA</td>
<td>1</td>
</tr>
<tr>
<td>PCA</td>
<td>2</td>
</tr>
</tbody>
</table>

PCA indicates internal carotid artery; PIKA, posterior inferior cerebellar artery; PCA, posterior cerebral artery.
The Gateway balloon catheter, developed from the platform of the Maverick balloon catheter with additional hydrophilic coating to enhance intracranial navigability, is currently approved for ICAD with the Wingspan stent (Boston Scientific, personal communication). This additional property may enhance navigation through the tortuosity of the carotid siphon and intracranial arteries.

In this multicenter series, balloon angioplasty was associated with periprocedural stroke and death rate of 5% and technical success of 92%. It should be noted that 12 patients in this series achieved 50% residual stenosis, which was still improved compared with the preangioplasty degrees of stenosis. In patients with hemodynamic compromise as the mechanism of ischemia, a marginal 10% or 20% opening in an ICAD lesion may be conjectured as helpful because small increases of the vessel diameter can result in large increases in perfusion. These patients should demonstrate improved symptoms postprocedure and future prospective studies should evaluate for this hypothesis.

Previous reports of balloon angioplasty for ICAD have also demonstrated high technical and long-term success. Marks et al reported 23 patients who underwent Stealth (Boston Scientific) balloon angioplasty with high technical success. In 1 patient, the stenosis could not be crossed safely and in another, balloon dilatation resulted in vessel rupture, which was fatal. Over a mean follow-up of 35 months, the annual stroke rate was 3%. Wojak et al reported a series of 62 patients treated with angioplasty balloons marketed for coronary use, Stealth or Stratus (MicroInterventional Systems), and 22 patients who underwent stent placement either primarily or because of inadequate response to angioplasty. The total periprocedural stroke and death rate was 5% and the annual stroke rate was 2%.22

In studies comparing primary angioplasty versus intracranial stenting, a single-center study showed similar results of primary angioplasty (reserved for more complex lesions) versus stent placement for ICAD treatment in 44 patients.14 There was no difference in time to major stroke or death between the treatment groups, although the numbers in this study were too small to draw firm conclusions. In a subsequent multicenter review, outcomes were compared for 190 patients treated with 95 primary angioplasty procedures and 98 intracranial stents placements (total 193 procedures) at 3 major centers.23 Again, there was no difference in survival at 2 years (stroke or death) between the angioplasty- versus the stent-treated groups. A recent large meta-analysis demonstrated technical success in 80% of angioplasty-treated patients (n=1027) versus 95% (n=1291) in the stent-treated group.24 There were a total of 91 stroke and deaths reported in the angioplasty-treated group (9%) compared with 104 in the stent-treated group (8%) during a 1-month period. In these studies, because comparisons were not based on randomized design, a selection bias may have been present with triage between stenting and angioplasty modalities based on angiographic and clinical criteria. Although it is difficult to relate directly, the immediate and short-term outcome results achieved in our ICAD series of patients treated with primary angioplasty compare favorably with published data. The main difference is that our study is limited to inclusion of only patients treated with the Gateway or Maverick balloons.

There are several limitations to this study. Because it is a retrospective multicenter registry, reporting standards may not have been consistent across institutions and according to recommended guidelines.18 The absence of a valid comparison (ie, medical treatment or stenting arm) is another limitation. The neurologist performing the postprocedure neurological assessment may not have been operator-independent, which may bias our results in favor of angioplasty. Furthermore, we did not centralize angiographic imaging to measure stenosis by WASID criteria pre- and postangioplasty. Further study is in progress to evaluate long-term risk of stroke and restenosis after intracranial angioplasty in this patient population.

Conclusion

Compared with medical therapy and intracranial stenting, endovascular treatment of ICAD with balloon angioplasty is relatively safe with periprocedural morbidity and mortality estimated at 5% in this multicenter series. A randomized controlled study to evaluate among the 3 treatment modalities is needed to understand optimal treatment for patients with symptomatic ICAD.

Disclosures

O.O.Z. is a consultant and on the Advisory Board of Boston Scientific.

References


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*Stroke*. 2011;42:107-111; originally published online November 11, 2010;
doi: 10.1161/STROKEAHA.110.583245

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/42/1/107

Data Supplement (unedited) at:
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Revascularization for Intracranial Atherosclerotic Disease
Periprocedural Risks and Short-Term Outcomes in a Multicenter Study

Thanh N. Nguyen, MD; Osama O. Zaidat, MD; Rishi Gupta, MD; Raul G. Nogueira, MD; Nauman Tariq, MD; Junaid S. Kalia, MD; Alexander M. Norbash, MD; Adnan I. Qureshi, MD

Background and Objective: Balloon angioplasty is an established treatment for intracranial atherosclerotic disease (ICAD). However, it is not clear if line balloon angioplasty (BA) should be performed before stenting or if BA should be used alone. We sought to compare the periprocedural risk and short-term outcomes of balloon angioplasty with stenting versus balloon angioplasty alone in a retrospective multicenter study.

Methods: We performed a retrospective review of procedures performed at four centers from 2006 to 2010 on patients with ICAD. We compared the periprocedural risk and short-term outcomes of BA with stenting versus BA alone.

Results: In total, 74 procedures were performed on 73 patients. The mean follow-up was 3 months. The procedural success rate was 92% and the periprocedural complication rate was 5%. The 30-day mortality rate was 2.7%. The 3-month mortality rate was 8.5%.

Conclusion: Balloon angioplasty is a safe and effective treatment for ICAD. The long-term efficacy of balloon angioplasty alone versus stenting with balloon angioplasty is not yet known and requires further study.

Keywords: Intracranial atherosclerotic disease, balloon angioplasty, stenting, periprocedural risk, short-term outcomes.
置入术的重要缺陷。本多中心回顾性研究的目的是报道 ICAD 患者行球囊导管血管成形术术后即刻及 3 个月时的预后。

**方法**

我们回顾性分析了 4 个卒中中心前瞻性收集的进行神经介入治疗的患者数据。各中心采用 Excel 表 (Microsoft) 记录未明确流行病学特征、事件类型 (TIA, 缺血性卒中)、部位和狭窄程度、手术时间、球囊类型、围手术期抗血小板或抗栓治疗、手术并发症、临床随访和 3 个月的预后。各中心及合作机构的伦理委员会都批准了本项研究。本研究无经济支持或商业赞助。本文作者之一 (D.M.) 为波士顿科技公司 (Boston Scientific) 的顾问。

**患者选择**

纳入自 2003 年至 2009 年期间经球囊成形术治疗 (Gateway 或 Maverick 球囊导管; 波士顿科技公司, 弗里蒙特,加州) 的 ICAD 患者。研究者统一使用最优化的药物治疗方案，并根据 ICAD 共识会议指南 [3] 进行修订。多数患者予阿司匹林和 / 或氯吡格雷、降血脂 (目标值 <70 mg/dL)、降糖治疗 (目标 HbA1c<7%; 糖尿病患者) 和戒烟治疗。根据华法林 - 阿司匹林治疗症状性颅内血管病变 (WASID) 的数据, 长期血压控制目标值为 <140/90 mmHg [11]。

颅内病变定义为前循环的颈动脉岩段水平及以上及后循环的远端椎动脉 C1 段以上 [12]。所有患者按 WASID 标准 [13], 测量基线时血管最狭窄处直径与最近端正常的血管直径相比较, 若狭窄程度 ≥50% 定义为血管狭窄。

血管内介入治疗的患者的入选标准 : 责任狭窄动脉引起的缺血事件; 在常规抗血小板治疗如阿司匹林 81 mg, 氯吡格雷 75 mg, 或静脉肝素或口服华法林的抗凝治疗 [14] 时, 仍发生缺血症状。卒中定义为急性起病的神经系统症状, 并经头颅 CT 或 MRI 确诊的临床事件。

**结果**

我们评估了 2003 年 8 月至 2009 年 9 月期间 4 个中心的 74 例 ICAD(50%-99%) 患者, 平均年龄 62±14 岁, 男性 41 例 (55%)。患者人种 / 种族如下 : 白人 35 例 (47%), 黑人 24 例 (32%), 拉美裔 10 例 (14%), 其他 5 例 (7%)。卒中危险因素包括高血压 61 例 (82%), 糖尿病 31 例 (42%), 高血脂 55 例 (47%), 房颤 10 例 (14%), 吸烟 21 例 (28%)。血管成形术的适应症包括卒中 (n=39)、TIA(n=29)、耳鸣 (n=1) 及冠状动脉移植术前 (n=1)。早期血管成形术, 定义为卒中发病 7 天内的治疗, 完成 33 例 (45%)。未能早期治疗的原因包括 : 考虑到早期干预可能造成再灌注出血、中等体积的卒中, 需要神经介入前改善患者的临床和神经系统情况、在 WASID 资料 [16] 前缺乏干预时机的推荐和医师的偏好。

归类分析了病灶部位的分布, 47 例 (64%) 为前循环狭窄。球囊导管分别使用了 Gateway(n=34) 和 Maverick(n=39)。一名患者同时使用了两种球囊, 另一名患者由于血管迂曲, 使用 Gateway 的 1.5×9-mm 球囊无法通过 A2 段的狭窄, 所以改用了 Sprinter 的 1.5×6-mm 球囊 (美敦力, Minneapolis, 明尼苏达州), 成功将 75% 的狭窄缩小至 25%, 本例患者归入了 M2 段的病灶, 或导丝无法到达的椎动脉或颈内动脉远端的病灶 [14]。

**手术**

参与研究的神经介入医师均达到了神经介入手术委员会、血管和神经介入委员会及美国神经病学学会制订的从事神经血管手术的标准 [15]。74 例患者中 62 例予全身麻醉 (84%)。4 个中心都按照标准的操作流程进行手术并严格遵守。手术均从患者股动脉穿刺置入 6-Fr 或 7-Fr 导管至颈动脉或椎动脉, 从股静脉予肝素化使活化凝血时间 >250 秒。经诊断性动脉造影后, 将 Gateway 或 Maverick 球囊通过 0.014 英寸微丝直接或微导管置换后推进超过病灶。球囊的直径不足正常血管直径的 80%, 选择可覆盖病灶的最短长度。在透视路径图引导下, 球囊在数秒内缓慢膨胀, 直达到额定的压力或持续加压 15-30 秒, 然后放气。术后予监护仪严密监测, 多为防止再灌注性出血, 血压控制 <130/80 mmHg。除了既往有房颤史的患者需予华法林外, 其余患者予抗血小板治疗。至少 3 个月时随访一次。
球囊血管成形术失败者。治疗前平均狭窄程度为 78.7%±14.2%，血管成形术后降低至 33.8%±17.9%。手术成功定义为残留狭窄 ≤50%，74 例患者中 68 例达到了手术成功（92%；95% CI，83%-97%）。围手术期成功定义为球囊血管成形术后 72 小时内或住院期间无卒中和死亡，74 例中 65 例达到了围手术期成功（88%；95% CI，78%-94%）。

4 例发生了手术相关的卒中 (5%；95% CI，1.5%-13%)，其中 2 例患者死亡。另 1 例患者为基底动脉狭窄 50%，采用 Maverick 球囊治疗时微丝捅破了基底动脉，造成继发性蛛网膜下腔出血，术后 6 小时内死亡。又 1 例为基底动脉 90% 狭窄，Maverick/Gateway 球囊血管成形术后 6 小时内由于双侧后颅窝锁骨性卒中而死亡。其它围手术期相关的卒中中，1 例为 M2 段 70% 狭窄的患者，另 1 例为椎动脉 90% 狭窄的患者。30 天时卒中或死亡的发生率为 5% (74 例中 4 例；95% CI，1.5%-13%)。至 3 个月时，随访到 71 例患者，1 例患者在术后 1 周由于回国而失访，根据其儿子的描述，病人情况不错，但这不能作为临床依据。3 个月随访时，2 例患者新发卒中，1 例为同侧血管再发卒中，再治疗），另 1 例为对侧血管区域。3 个月随访时，1 例患者出现肢体强直的 TIA，也进行了再治疗。3 个月时卒中及死亡的发生率为 8.5%(71 例中 6 例；95% CI，3.1%-17.5%)，再治疗率 2.8%(71 例中 2 例；95% CI，0.3%-10%)。

### 讨论
自美国食品药品监督管理局人道主义器械豁免批准 Wingspan 支架的上市，全球范围内，颅内支架置入术也在血管成形术之后越来越多地用于治疗症状性 ICAD，尤其是在美国[17]。据估计，世界范围内已有 10000 个患者接受了 Wingspan 的治疗。支架置入和积极药物治疗颅内血管狭窄以预防复发性卒中的临床研究 (Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis, SAMMPRIS) 是目前正在进行的一项大型随机化研究，拟评估 ICAD 患者的颅内血管成形术和支架术是否优于单独药物治疗[2]。

然而，对于颅内动脉粥样硬化疾病的治疗而言，血管内治疗中是否应首选支架置入？颅外血管 (颈动脉及冠状动脉) 的研究已明确支架置入血管成形术在安全性及有效性上明显优于单纯的球囊血管成形术[18]。但这不一定适用于颅内血管。目前的 SAMMPRIS 研究没有设立单纯球囊血管成形术治疗症状性 ICAD 的一组，而他们认为的支架置入在 ICAD 治疗中优于单纯的血管成形术[2]，并没有在前瞻性随机研究中得到证实。

既往两项大型 Wingspan 前瞻性注册研究中发现了数个问题。美国 NIH 多中心 Wingspan 注册研究提出支架置入术 24 小时内卒中或死亡的发生率为 5%，30 天内为 9%[17,19]。另一项前瞻性 Wingspan 注册研究提出，25%-30% 环 Wingspan 支架治疗的患者随访 6 个月时发现支架内再狭窄，即定义为狭窄程度 ≥50%[18,17]。在半数支架内再狭窄的患者中，其病灶长度及狭窄程度均比治疗前原始的病灶更广泛[5]，而且再狭窄后的治疗也难以达到持久的效果[20]。

本研究中，我们评估了经 Gateway 或 Maverick 球囊血管成形术治疗的 ICAD 患者术后即刻及 3 个月随访时的情况。在本队列中，因为下述原因使我们更倾向于选择球囊血管成形术而非支架置入术：Wingspan 可能无法通过迂曲的颈动脉虹吸部，或被认为难度太大或太危险；支架置入意味着异物置入而其长期的后果未知；担忧 Wingspan 支架可能造成再狭窄，尤其是前循环存在狭窄的年轻患者[19]；支
架置入术后必须使用氯吡格雷可能增加出血风险，尤其对需要抗凝或较大面积卒中的患者来说风险更大；支架置入术后予阿司匹林和氯吡格雷双联抗血小板药物治疗，可增加近期卒中或 TIA 患者发生致命或大出血的风险。支架置入术后予阿司匹林和氯吡格雷双联抗血小板药物治疗，可增加近期卒中或 TIA 患者发生致命或大出血的风险，这在高风险患者氯吡格雷抗栓治疗研究 (the Management of Atherothrombosis With Clopidogrel in High-Risk Patients, MATCH) 中得到了证实[21]；堵塞脑血管的重要分支，尤其是大脑中动脉分支处也是支架置入术的顾虑之一。从解剖学看，血管成形术更适宜在小血管 (直径 <2 mm)、长病变 (>12 mm)、病灶远端可使微丝稳定置入的血管长度有限 (伴有大脑后动脉发育不全或未发育的基底动脉狭窄)，位于大脑前动脉和大脑后动脉的病灶[14]。最后，当前医疗财政紧缩，成本也是一个不得不考虑的问题，在美国 Wingspan 支架标价约 6000 美元，而相比之下，Gateway 的球囊导管价格仅 800 美元。

Gateway 球囊导管是从 Maverick 球囊导管发展演变而来的，增加了亲水涂层以提高其在颅内血管的通过率，目前已被批准与 Wingspan 支架 (波士顿科技公司，个人交流) 联合使用。附加的亲水涂层有利于其通过迂曲颈内动脉虹吸段及其它颅内血管。本多中心研究中球囊血管成形术围手术期卒中及死亡的发生率为 5%，手术成功率达 92%，其中值得一提的是 12 例患者的血管残余狭窄达 50%，但仍较血管成形术前的狭窄有明显改善。缺血机制影响下血流动力学代偿的患者，ICAD 病灶血流开放增加 10%-20%，其血管直径的轻度增加有助于很大程度上增加再灌注。这些病人的术后症状应得以改善，今后的前瞻性研究应对此假说进行验证。ICAD 患者球囊成形术治疗的既往报道显示其手术成功率高，远期预后好。Marks 等报道了 23 例执行 Stealth(波士顿科技公司) 球囊成形术患者的手术成功率高，1例患者由于血管过于狭窄而球囊无法安全通过，1例患者由于球囊扩张导致血管破裂而致命。平均随访 35 个月期间，年卒中发生率仅 3%[22]。Wojak 等报道了 62 例采用冠脉 Stealth 或 Stratus 球囊 (MicroInterventional Systems) 于血管成形术的患者，22 例首选支架置入术或因对血管成形术不理想而采用支架置入术。总体围手术期卒中及死亡的发生率为 5%，年卒中发生率为 2%[22]。

在比较血管成形术与颅内支架置入术的研究中，一项单中心的研究比较了 44 例 ICAD 患者进行血管成形术 (用于更复杂的病灶) 或支架置入术，得出了相似的结论[44]，治疗组间发生主要卒中和死亡的时间无明显差异，然而，该研究病例数较少无法得出明确的结论。随后的一项多中心分析，比较了 3 个主要中心的 190 例 ICAD 患者，95 例予球囊血管成形术，98 例予颅内支架置入术 (共计 193 例手术)[23]，两个治疗组间的 2 年生存率 (卒中或死亡) 无统计学差异。近期，有一项大型 Meta 分析显示血管成形术的手术成功率为 80% (n=1027)，而支架置入术的手术成功率达到 95% (n=1291)[24]。随访 1 个月，血管成形术组发生卒中或死亡 91 例 (9%)，而支架置入术组发生了 104 例 (8%)。该 Meta 分析纳入的研究并非随机化研究，故可能在选择支架置入术或血管成形术时因血管条件或临床标准而发生了选择偏移。尽管本研究结果与既往研究结果较难直接比较，但本研究显示的 ICAD 患者血管成形术组后即刻及短期预后与已报道的研究结果相当。本研究的主要不同在于仅纳入了使用 Gateway 或 Maverick 球囊治疗的患者。本研究也存在一些缺陷。由于本研究是一项回顾性的多中心注册研究，各中心根据指南推荐指南的标准可能略有不同[18]。此外，本研究还缺乏与药物或支架治疗的有效比较。神经科医师对术中神经功能评价的不独立，可能造成有利于血管成形术结果的偏移。此外，我们未将血管造影影像学中心化，未采用 WASID 标准分析患者术前和术后血管的狭窄程度。本研究还在进行中，以评价这批患者长期的卒中风险和颅内血管成形术后的再狭窄情况。

结论
本多中心研究显示，与药物治疗与颅内支架置入术相比，血管内球囊成形术治疗 ICAD 是相对安全的，其围手术期死亡率及致残率约 5%。需对这 3 种治疗方法进行随机对照研究，以明确症状性 ICAD 患者的最佳治疗选择。

参考文献
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