Blister Aneurysms: Decision-Making When There’s No Perfect Answer

A review of current meta-analyses on the management of blister aneurysms.

BY PARAMPREET SINGH, MD; ARATI PATEL, BS; AND WILLIAM J. MACK, MD

Blister aneurysms (BAs) have been described as half-dome–shaped aneurysmal bulges, with a broad neck, located at nonbranching sites or sidewalls of intracranial arteries. BAs were first described by Sundt and Murphey in 1969, and in 1979, Ohara and colleagues described these lesions as bulges in sclerotic vessels, which were distinct from typical cerebrovascular berry aneurysms. In 1988, the Japanese term chimame (blood blister) was used for the first time to describe this specific aneurysm morphology. Initial descriptions of BAs were limited to those found in the internal carotid artery (ICA); however, more recently, authors have noted similar sidewall aneurysms in other intracranial vessels, including the circle of Willis. BAs are relatively rare, found in only 1% to 2% of all aneurysmal subarachnoid hemorrhages. BAs are reported in 0.6% to 1.7% of all ICA aneurysm cases treated operatively and in up to 6.6% of all ruptured ICA aneurysms. Given the overall rarity of this entity, differences in pathogenesis between the ICA BAs and those encountered elsewhere in the intracranial circulation are not known. Reports suggest that these aneurysms occur in younger populations, with a predisposition to occur on the right side and a predilection to affect women.

Angiographic and direct intraoperative observations reveal thin fibrous tissue covering the BA walls, with a gap in the actual vessel wall. This structure is suggestive of a pseudoaneurysm pathology, possibly arising from a dissection. However, histologic studies have shown no evidence of dissections associated with BAs, further confounding the etiology. Arteriosclerosis with subsequent ulceration and hypertension are the major proposed mechanisms of origin for BAs. A single case of Aspergillus mycotic BA has also been reported. Despite differences in understanding the etiology of BAs, there is consensus on the fragility of the aneurysm wall and the high rupture risk, which poses significant technical difficulty in open vascular or endovascular management of these aneurysms. A single-center study at our institution revealed an overall intraoperative rupture risk of approximately 28% in prediagnosed patients and approximately 57% in undiagnosed patients with BAs undergoing surgical treatment.

MANAGEMENT OF BLISTER ANEURYSMS

Early management approaches for BAs advocated wrapping the vessel with muscle and applying adhesive coating or clipping. Later, the use of Sundt encircling clips, clip wrapping with synthetic wrapping materials, or vessel sacrifice (aneurysm trapping) with or without bypass revascularization gained popularity. Endovascular therapy (EVT) including the use of coils and/or stents represent a promising alternative. Open surgical techniques provide durable results; however, the thin-walled anatomy of BAs poses a higher risk of intraoperative rupture. Endovascular options may be safer from the standpoint of intraoperative complications, but they necessitate the use of dual antiplatelet therapies, limiting their use in ruptured aneurysms. There are no randomized controlled studies available to help establish an optimal treatment strategy. Recently, four comparative meta-analyses were published reviewing numerous observational case series on the available treatment options for BAs.

Open Surgical Treatment

Open microsurgical treatments involve direct clipping, wrapping, trapping, and bypass, which can be
used alone or in combination. In a meta-analysis by Peschillo et al, 114 patients with ICA BAs undergoing open surgery were reviewed. Outcomes (modified Rankin Scale [mRS] 0–2) were better in groups undergoing trapping with a radial artery bypass (92.3%) followed by wrapping with clipping (82.9%) and clipping with an arteriotomy (68.4%) (P = .12). Nearly all patients (96.4%) achieved early complete occlusion of the aneurysm.27 A systematic review by Szücs et al analyzed 117 pooled patients undergoing microsurgery for BAs, including clipping and wrapping (32.5%), clipping (29%), and trapping with a bypass (30.8%). The highest morbidity and mortality (Glasgow Outcome Scale [GOS] 1–3) was noted in the clipping group (29%). The overall angiographic occlusion rate was 92.9%.29 Another meta-analysis by Shah et al reviewed 139 patients undergoing microsurgical interventions for ICA BAs. The majority of the surgical procedures included clipping (45%), trapping alone (17%), and trapping with bypass (17%). This meta-analysis did not report data from subgroup analyses on outcomes of individual surgical options.30

In a systematic review and case series by Gonzalez et al, 40 studies of surgical interventions for BAs were reviewed. Of the pooled patients, 80% underwent clipping, with a 30% perioperative complication rate (ie, rupture). In 21% of cases, a second treatment modality was required to secure the BA. Surgical trapping was the next most common technique (29.4%) for primary or rescue treatment. Regrowth and recurrent hemorrhage occurred in 5% and 30% patients, respectively. Rescue treatments included a second clipping attempt, arterial suturing, trapping with or without bypass, or bypass alone. Morbidity/mortality was highest in the clipping group (75% of overall surgical morbidity/mortality).17

Endovascular Treatments

With advancements in technique and the development of new devices, many new endovascular options have become available for treating BAs, including primary coiling, stent-assisted coiling/liquid embolization, and flow diversion. In the meta-analysis by Peschillo et al, 199 patients with BAs underwent endovascular treatment with embolization. Good outcomes (mRS 0–2) were noted in the primary stenting (86.4%), stent-assisted coiling (85.2%), and flow diversion (82.2%) groups. Complete early angiographic occlusion was noted in only 44.5% (41% near-complete occlusion) of patients.27 The review by Szücs et al evaluated 180 pooled patients undergoing EVT for BAs. Treatments included stent-assisted coiling (43.3%), flow diversion (31.1%), primary stenting (15.6%), and stent-assisted liquid embolization (1.1%). The stent-assisted coiling group had the poorest outcomes (GOS 1–3 in 24.4% of patients). Overall angiographic occlusion was 76.5% and highest in the flow diversion cohort (88.9%).29

The systematic review by Shah et al included 122 patients undergoing EVT for ICA BAs. Individual therapies included stent-assisted coiling (60%), primary coiling (17%), and flow diversion (17%). Subgroup outcome analyses (clinical/angiographic) for different therapies were not reported in this study.30 Gonzalez et al evaluated 87 patients in 26 different case series in which 34.5% of patients underwent stent-assisted coiling. Recanalization and recurrent bleeding occurred in 38% and 12.5% of patients, respectively. In 46% of patients, a rescue treatment with either flow diversion or surgical trapping was required. Multilayer conventional stenting was used in 20% of patients, and about 20% of the cases required rescue treatment with either flow diversion or parent artery occlusion with coiling.17

In a meta-analysis of 31 studies that included 258 patients who underwent EVT for BAs, 90.6% underwent reconstructive procedures and the remainder were deconstructive. Among the reconstructive group, therapies included stent-assisted coiling (44.1%), flow diversion (25.8%), primary stenting with single or multiple overlapping stents (18.7%), primary coiling with or without balloon assistance (6.25%), and stent-assisted liquid embolization (1.25%). Overall occlusion rates were 40.6% immediately following treatment and 72.8% on follow-up. The retreatment rate was 19.3%. The perioperative morbidity rate (eg, stroke, perioperative bleeding) was 13.4% and mortality was 7.3%. Good neurologic outcomes (mRS ≤ 2) were noted in 76.2% of all patients. Comparatively, deconstructive techniques had higher rates of immediate complete occlusion than reconstructive techniques (77.3% vs 33%; P = .0003), although there was a higher risk of perioperative stroke (29.1% vs 5%; P = .04). Long-term outcomes were similar in both groups. Within the reconstructive group, the flow diversion cohort had a better long-term complete occlusion rate than non–flow diverter groups (90.8% vs 69.7%; P = .005); other outcomes were similar in both cohorts.31

Microsurgery Versus Endovascular Interventions

Among the available comparative meta-analyses of observational case series, Peschillo et al noted that across all Hunt and Hess (HH) grades in their pool of 334 patients, treatments with microsurgery and EVT were associated with good outcomes (mRS, 0–2) in 67.4% and 78.9% of patients, respectively (P = .038). Final angiographic occlusion rates were significantly
higher in the surgical group than the EVT group (97.3% vs 76.9%; \( P < .001 \)). In terms of perioperative mortality and morbidity, patients who underwent EVT fared better than open surgical patients, with a combined morbidity of 7% and 20%, respectively. Similarly, mortality was higher in the surgical group in patients with HH grades < 4 (14.3% vs 4.6%; \( P = .009 \)). Interestingly, for those with HH grades > 3, mortality was higher in the EVT group (37% vs 9.1%; \( P = .043 \)), which could be related to complications associated with antiplatelet agents. The most concerning complications were rupture in the open surgical group (81.5%) and thromboembolism (33.3%) in the EVT group.\(^27\)

### TABLE 1. SUMMARY OF REVIEWS ON BLISTER ANEURYSM MANAGEMENT

<table>
<thead>
<tr>
<th>Author</th>
<th>Therapeutic Group</th>
<th>N</th>
<th>Clinical Outcome</th>
<th>Procedural Complications</th>
<th>Angiographic Occlusion</th>
<th>Retreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonzalez et al(^{27})</td>
<td>Microsurgery</td>
<td>268</td>
<td>18% morbidity; 14% mortality</td>
<td>32% perioperative</td>
<td>No data</td>
<td>22.3%</td>
</tr>
<tr>
<td></td>
<td>EVT</td>
<td>147</td>
<td>3.4% morbidity; 11.5% mortality</td>
<td>14.9% perioperative</td>
<td>No data</td>
<td>36.7%</td>
</tr>
<tr>
<td>Peschillo et al(^{27})</td>
<td>Microsurgery</td>
<td>114</td>
<td>mRS 0–2, 67.4% (( P = .034 ))</td>
<td>Surgery vs EVT: intraoperative, 24.1% vs 10.5% (( P &lt; .001 )); postoperative, 35.7% vs 21.1% (( P &lt; .001 ))</td>
<td>96.4% early; 97.3% follow-up</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>EVT</td>
<td>199</td>
<td>mRS 0–2, 78.9% (( P = .034 ))</td>
<td>Surgery vs EVT: intraoperative bleeding, 23% vs 3.4%; all complications, 11.2% vs 15.9%</td>
<td>44.5% early; 76.9% follow-up</td>
<td>No data</td>
</tr>
<tr>
<td>Szmuda et al(^{29})</td>
<td>Microsurgery</td>
<td>117</td>
<td>Morbidity and mortality (GOS 1–3): 29.2% for surgery vs 21.1% for EVT (( P = .14 ))</td>
<td>Surgery vs EVT: intraoperative bleeding, 23% vs 3.4%; all complications, 11.2% vs 15.9%</td>
<td>92.9%</td>
<td>8.5%</td>
</tr>
<tr>
<td></td>
<td>EVT</td>
<td>180</td>
<td>Morbidity and mortality (GOS 1–3): 29.2% for surgery vs 21.1% for EVT (( P = .14 ))</td>
<td>Surgery vs EVT: intraoperative bleeding, 23% vs 3.4%; all complications, 11.2% vs 15.9%</td>
<td>76.5%</td>
<td>18.4%</td>
</tr>
<tr>
<td>Shah et al(^{30})</td>
<td>Microsurgery</td>
<td>139</td>
<td>Unfavorable outcomes (across mRS, GOS): 27.8% for surgery vs 26.2% for EVT</td>
<td>14% perioperative; 45% postoperative</td>
<td>88.9% early; 88.4% follow-up</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>EVT</td>
<td>122</td>
<td>mRS ≤ 2, 76.2%</td>
<td>2.1% perioperative; 29% postoperative</td>
<td>63.9% early; 75.9% follow-up</td>
<td>No data</td>
</tr>
<tr>
<td>Rouchaud et al(^{31}) (EVT only)</td>
<td>Overall EVT group</td>
<td>265</td>
<td>mRS ≤ 2, 76.2%</td>
<td>Perioperative: 12.6% complications; 13.4% morbidity; 7.3% mortality</td>
<td>40.6% early; 72.8% follow-up</td>
<td>19.3%</td>
</tr>
<tr>
<td></td>
<td>Deconstructive therapy</td>
<td>25</td>
<td>mRS ≤ 2, 79.9%</td>
<td>Perioperative: 26.1% complications; 23.4% morbidity; 15.1% mortality</td>
<td>81%</td>
<td>19%</td>
</tr>
<tr>
<td></td>
<td>Reconstructive therapy</td>
<td>240</td>
<td>mRS ≤ 2, 76.2%</td>
<td>Perioperative: 10.1% complications; 6.7% morbidity; 10.5% mortality</td>
<td>73.6%</td>
<td>17.2%</td>
</tr>
<tr>
<td></td>
<td>FD (cohort analysis)</td>
<td>62/240</td>
<td>mRS ≤ 2, 86% for FD vs 75% for non-FD</td>
<td>Perioperative FD vs non-FD: 12.6 vs 13.2% morbidity; 8.7% vs 7.2% mortality</td>
<td>Follow-up occlusion: 90.8% for FD vs 69.7% for non-FD (( P = .005 ))</td>
<td>6.6% for FD vs 27.1% for non-FD</td>
</tr>
</tbody>
</table>

Abbreviations: EVT, endovascular therapy; FD, flow diversion; GOS, Glasgow Outcome Scale; mRS, modified Rankin Scale.
Gonzalez et al demonstrated overall morbidity/mortality rates of 38% for surgery and 15% for EVT ($P < .01$). However, nearly 50% of EVT patients required retreatment. Szmuda et al included 311 pooled patients undergoing surgical and endovascular interventions and found modest differences in morbidity favoring EVT, without significant differences in mortality between groups. With logistic regression, neither therapeutic approach predicted outcomes as well as the initial clinical status and presence or absence of procedural complications. Overall, outcomes were worse for primary clipping and stent-assisted coiling and best for trapping and flow diversion.

In a review of 24 studies on surgery and EVT, Shah et al found the overall negative outcomes among surgical and EVT cohorts were 27.8% and 26.2%, respectively (intraoperative complications, 14% vs 2.1%; postoperative complications, 45% vs 29%, respectively). Although these results heavily favored EVT, overall immediate (88.9% vs 63.9%) and follow-up (88.4% vs 75.9%) occlusion rates were substantially higher for the surgical group. In these reviews, the authors ultimately concluded that both surgical and endovascular options had merits; however, superiority of a specific therapy could not be established with the available data (Table 1).

**DISCUSSION**

BAs are rare, complex, and poorly understood cerebrovascular pathology. Given their fragile anatomy, treatment is technically difficult with high rates of intraoperative rupture and potential for morbidity and mortality. A search of the available literature on managing BAs did not find any randomized controlled studies. Major meta-analyses of observational case series had mixed results with no consensus on the superiority of microsurgery versus EVT. The conclusions suggested lesser complications and peri-procedural morbidity/mortality with EVT compared to microsurgery. Surgical options provided > 90% occlusion rates, whereas a significant number of incomplete occlusions and retreatments was noted with EVT. Gonzalez et al and Shah et al favored EVT both in terms of complication rates and overall outcomes. Szmuda et al observed similar trends in their systematic review. However, the authors challenged these results in their linear regression analysis, which failed to show that a specific treatment can successfully predict outcome.

In each review, the overall outcome was most dependent on initial HH or Fisher grades rather than a specific therapy. Further, these reviews analyzed observational case series at different institutions, each with individual protocols on first-line treatment based on the level of available expertise. This introduces an inherent selection bias. Further, as noted by Shah et al, authors often focus on publishing case series with favorable clinical and radiologic outcomes, which introduces a publication bias. Ultimately, the authors suggested a need for further (potentially randomized controlled) studies to better explore this subject. Until such studies are conducted, they advocated individualizing treatment based on the available institutional expertise.

Among the individual surgical options, trapping with bypass showed the best outcomes. Among EVT, reconstructive therapies with flow diversion have shown the most promise from a safety and outcomes standpoint. At our institution, the EVT paradigm for acutely ruptured BAs involves a first-line consideration of reconstructive therapy with flow-diverting stents, which not only preserves the vessel, but also prevents any direct manipulation of the aneurysm, which is the most common cause of rupture (during attempted coiling or microsurgery). The trade-off is instituting dual antiplatelet therapy in the setting of an acute hemorrhage and delayed occlusion of the aneurysm. Among the surgical options, vessel sacrifice with bypass revascularization is the therapy of choice at our institution. The advantages include instant occlusion of the aneurysm, avoidance of dual antiplatelet therapy, and a potential extra conduit in the setting of severe vasospasm. Challenges include poor-grade hemorrhages with significant swelling and vasospasm. Furthermore, graft spasm can often be very difficult to treat after bypass revascularization.

**CONCLUSION**

BAs are complex lesions that pose significant treatment challenges in the setting of subarachnoid hemorrhage. Evidence-based guidelines that advocate optimal management algorithms are lacking. Both endovascular and open surgical treatments have advantages and disadvantages in terms of morbidity, mortality, and complications. At our institution, we favor flow diversion or surgical trapping with bypass revascularization. Factors considered in choosing treatment paradigms include patient age, clinical grade, potential need for cerebrospinal fluid diversion, and likelihood of cerebral vasospasm. In the absence of robust data from randomized clinical trials, reliance on available institutional expertise can help guide treatment choices.


(Continued on page 90)