

## ROLE OF PREOPERATIVE ENDOVASCULAR EMBOLIZATION PRIOR TO MICROSURGICAL RESECTION IN ADULT UNRUPTURED SPETZLER–MARTIN GRADE II–III INTRACRANIAL ARTERIOVENOUS MALFORMATIONS: A NARRATIVE REVIEW

Agung Bagus Sista Satyarsa,<sup>1</sup> Made Gemma Daniswara Maliawan,<sup>1</sup> I Wayan Nirvana,<sup>1</sup>  
I Putu Ananta Wijaya Sabudi,<sup>2</sup>

1. Division of Neurosurgery, Department of Surgery, Faculty of Medicine, Udayana  
University, Ngoerah Hospital, Denpasar, Indonesia

2. Department of Neurosurgery, Klungkung Regional Hospital, Bali, Indonesia

[abssatyarsa@student.unud.ac.id](mailto:abssatyarsa@student.unud.ac.id)

### Abstract

**Background:** Unruptured Spetzler–Martin (SM) grade II–III brain arteriovenous malformations (bAVMs) sit at the inflection point of management decisions: they are common enough to be encountered in everyday neurosurgical practice, yet diverse enough that the optimal treatment combination remains contested. Microsurgical resection is the only modality reliably producing immediate and complete obliteration, but adjunctive preoperative endovascular embolization (PE) has become routine in many centers, even though high-level evidence of clinical benefit is lacking. **Objective:** To synthesize contemporary literature on the indications, techniques, efficacy, and complications of PE prior to microsurgical resection in adult unruptured SM grade II–III bAVMs, with particular attention to the heterogeneity within the SM grade III category and to embolic-agent–related considerations. **Findings:** PE reliably reduces nidus blood flow and intraoperative blood loss but has not been shown in pooled analyses to improve obliteration rates or functional outcomes in unselected low- to intermediate-grade lesions. In SM grade II AVMs, surgery alone produces excellent results in most series and PE is generally unnecessary except for targeted vascular features. In SM grade III AVMs—a heterogeneous category better stratified by Lawton’s modification and by the Lawton–Young supplementary score—PE appears most useful for large lesions, deep perforator supply, and surgically inaccessible feeders. Onyx and other ethylene-vinyl alcohol copolymers have largely supplanted N-butyl cyanoacrylate (NBCA) for preoperative use in many centers, although evidence of clinical superiority is mixed. Embolization-related morbidity (transient or permanent neurological deficit in roughly 6–11%, hemorrhagic complication 2–6%) must be weighed against an annual rupture risk in unruptured AVMs that recent MARS data place around 1.4% per year. **Conclusion:** PE before microsurgery in unruptured SM grade II–III AVMs should be individualized rather than routine. It is most defensible for SM grade III lesions with high-flow, deep, or inaccessible feeders and least defensible for compact SM grade II lesions with superficial feeders. Decisions must be made in experienced multidisciplinary centers, recognizing that the cumulative morbidity of multi-modality treatment can equal or exceed that of well-selected surgery alone.

**Keywords:** arteriovenous malformation; preoperative embolization; microsurgery; Spetzler–Martin grade; Onyx; unruptured brain AVM.

## 1. Introduction

Brain arteriovenous malformations (bAVMs) are congenital cerebrovascular lesions characterized by an abnormal tangle of vessels (the nidus) in which arterial blood passes directly into draining veins without an intervening capillary bed. Although uncommon (population prevalence approximately 10–18 per 100,000), they account for a disproportionate share of intracranial hemorrhage in young adults and carry meaningful lifetime morbidity. Hemorrhage is the most consequential presentation and confers an approximately 42% risk of combined morbidity and mortality when it occurs. In unruptured AVMs, annual hemorrhage rates have classically been quoted at 2–4% per year, although the recent multicenter MARS cohort of more than 3,000 patients found a lower contemporary rate of approximately 1.4 per 100 person-years, with increasing age, associated arterial aneurysms, and deep or cerebellar location as independent predictors.

The Spetzler–Martin (SM) grading scale, introduced in 1986, remains the most widely used predictor of microsurgical morbidity, assigning points for nidus size, venous drainage pattern, and eloquence of adjacent brain. SM grades I and II are considered low-risk surgical lesions; SM grade III occupies an acknowledged "gray zone" of intermediate risk; and grades IV and V are typically managed conservatively or with multimodality strategies. SM grade III lesions are heterogeneous, prompting Lawton's 2003 subclassification (III–, III, III+, III\*) and the 2010 Lawton–Young supplementary grading scale, which incorporates patient age, hemorrhagic presentation, and nidal diffuseness.

Since publication of A Randomized Trial of Unruptured Brain AVMs (ARUBA) in 2014, the indication for treating unruptured AVMs has been heavily debated. ARUBA reported a higher rate of stroke or death with intervention than with medical management at short- to intermediate-term follow-up. However, the trial has been widely criticized for substantial selection bias, short follow-up relative to the lifetime risk of hemorrhage, underrepresentation of microsurgery (only 15.8% of intervention-arm patients), and inclusion of high-grade AVMs that most neurosurgeons would not have offered surgery. Several post-ARUBA single-center microsurgical series have reported markedly better outcomes than ARUBA, particularly in SM grade I–II lesions, reigniting interest in surgical cure for carefully selected unruptured patients.

Preoperative endovascular embolization (PE) has become a routine adjunct in many AVM programs. Proposed benefits include reduction of nidal flow and intraoperative bleeding, targeted occlusion of deep or inaccessible feeders, devascularization of intranidal aneurysms or high-risk angioarchitectural features, and—in staged regimens—reduction of normal perfusion pressure breakthrough phenomena. The risks, however, are not trivial:

embolization carries its own ischemic, hemorrhagic, and procedural complication profile, and accumulating evidence suggests that for many low-grade lesions PE does not improve, and may not even meaningfully facilitate, the surgical procedure.

This narrative review focuses specifically on adult patients with unruptured SM grade II and III bAVMs, the population in which the trade-off between presumed surgical facilitation and added procedural morbidity is most clinically relevant. We summarize the current evidence for PE prior to microsurgery in this subset, discuss embolic agents and technique, examine subgroup data from the literature, and propose a practical framework for case selection.

## **2. Methods**

This narrative review was based on a focused search of PubMed, Web of Science, and the Cochrane Library for English-language publications from 2000 to 2026, using combinations of the terms "arteriovenous malformation," "Spetzler–Martin," "preoperative embolization," "microsurgery," "Onyx," "NBCA," "unruptured," and "ARUBA." Primary clinical studies, systematic reviews, meta-analyses, and authoritative narrative reviews were prioritized. Pediatric series, studies limited to ruptured AVMs without separable unruptured-cohort data, and studies of curative-intent embolization or radiosurgery without microsurgical resection were excluded from the central synthesis but are cited where they inform comparative context. Because this is a narrative rather than systematic review, no formal quality assessment or quantitative pooling was undertaken; emphasis was placed on the highest-quality and most recent evidence applicable to adult unruptured SM grade II–III lesions.

## **3. Classification and Natural History of Unruptured SM Grade II–III AVMs**

### **3.1 The Spetzler–Martin grading scale and its refinements**

The five-point SM scale assigns 1–3 points for nidus size (<3 cm, 3–6 cm, >6 cm), 0–1 point for venous drainage (superficial only vs. any deep), and 0–1 point for eloquence of adjacent brain. The summed score corresponds to surgical risk strata that have remained remarkably durable across decades. Spetzler and Ponce later collapsed these into three classes (A: SM I–II; B: SM III; C: SM IV–V) for treatment counseling.

SM grade III, however, is internally heterogeneous. Lawton's 2003 modification subdivided it into four subtypes based on the underlying S/V/E combinations: III– (S1V1E1, small/eloquent/deep), III (S2V1E0, medium/deep/non-eloquent), III+ (S2V0E1, medium/eloquent/superficial), and III\* (S3V0E0, large/non-eloquent/superficial). In Lawton's original cohort, III– lesions had a permanent morbidity rate comparable to SM grade I–II AVMs, whereas III+ lesions had outcomes approaching those of high-grade AVMs. This stratification has been validated in subsequent independent series and is particularly relevant when deciding whether PE is justified, because the dominant risk factors differ substantially between subtypes.

The 2010 Lawton–Young supplementary scale (Supp-SM) added points for patient age (<20, 20–40, >40), hemorrhagic presentation (no/yes), and nidus compactness (compact/diffuse),

yielding a 0–10 composite score. Multiple validation cohorts have confirmed that the Supp-SM score offers superior predictive accuracy compared with SM grade alone, particularly in the intermediate-risk band where PE decisions are most contested.

### 3.2 Natural history of unruptured AVMs

Decisions to treat unruptured AVMs at all rest on the lifetime risk of hemorrhage compared with treatment morbidity. Older series reported annual hemorrhage rates of 2–4%, with previous hemorrhage the strongest and most reproducible risk factor. Additional contributors include exclusively deep venous drainage, deep or infratentorial location, associated intranidal or feeding-artery aneurysms, and increasing age. More contemporary data—most notably the multicenter MARS study (n = 3,030; 11,339 person-years)—suggest a contemporary annual first-hemorrhage rate of approximately 1.4 per 100 person-years for truly unruptured lesions, with the same risk factors emerging on multivariable analysis.

These contemporary risk estimates are highly relevant when justifying PE: a procedure with a 5–10% permanent morbidity rate is more difficult to defend against a 1% annual rupture risk than against a 4% annual rupture risk, particularly in older patients whose remaining life-years are fewer.

### 3.3 The ARUBA controversy

ARUBA randomized 226 patients with unruptured AVMs to intervention or conservative management and reported significantly fewer strokes/deaths in the medical arm at a mean follow-up of 33 months. Criticisms include: (1) only 13% of screened patients were randomized, suggesting selection bias toward lesions that interventionists were already uncertain about treating; (2) microsurgery, the modality with the highest single-procedure obliteration rate, was offered to only 15.8% of intervention-arm patients despite 68% of those patients having SM grade I–II lesions; (3) follow-up duration was insufficient to capture the lifetime hemorrhage risk these treatments aim to eliminate; (4) substantial portion of "interventional" treatments were embolization or radiosurgery, which carry a high rate of incomplete obliteration and continued bleeding risk during the latency period. Post-ARUBA microsurgical series in ARUBA-eligible patients have consistently reported lower stroke/death rates and high obliteration rates (typically 92–99%), supporting the position that experienced surgical management of low- and intermediate-grade unruptured AVMs may still be justified despite the trial's headline conclusions.

## 4. Rationale for Preoperative Embolization

The conceptual basis for PE prior to microsurgery of SM grade II–III AVMs includes:

- Reduction of nidus blood flow, thereby decreasing intraoperative blood loss, shortening dissection time, and improving the surgeon's view of the operative field.
- Selective devascularization of deep or surgically inaccessible feeders (e.g., lenticulostriate, anterior choroidal, or thalamoperforator branches) that are best occluded endovascularly before they are encountered late in the dissection.

- Targeted occlusion of high-risk angioarchitectural features such as intranidal aneurysms, flow-related arterial aneurysms, and venous outflow stenoses that may bleed during surgical manipulation.
- Reduction of the nidal volume in large lesions, theoretically mitigating the risk of normal perfusion pressure breakthrough (NPPB) postoperatively, though this concept remains debated.
- Conversion of higher-risk lesions to a more manageable surgical profile, particularly in SM grade III AVMs at the upper end of the surgical risk spectrum.

These rationales are anatomical and intuitive rather than evidence-based in the strict sense. They have driven the routine adoption of PE in many programs, but as the following sections show, controlled comparative data have generally failed to confirm consistent clinical benefit, particularly in low-grade lesions where surgery alone is already effective.

### 5. Evidence in Unruptured SM Grade II AVMs

In SM grade I–II AVMs, microsurgery alone produces excellent results. Large series report complete obliteration rates of 94–99% and permanent neurological morbidity of 1.8–4.5% in unruptured cohorts. In one consecutive 288-patient series, unruptured SM grade I–II AVMs had only a 1.8% permanent significant deficit rate; another microsurgical series of 232 low-grade AVMs reported 78% mRS 0–1 outcomes overall, with 91% of unruptured patients achieving a good functional outcome. In post-ARUBA microsurgical cohorts, ARUBA-eligible patients—predominantly SM grade I–II—have shown complete obliteration in 94–99%, with permanent disabling deficits in approximately 4.5%.

In the same 232-patient low-grade cohort, 43% underwent PE preoperatively, with unruptured AVMs embolized more often than ruptured ones. The authors concluded that surgery should remain the gold standard for most low-grade AVMs but advocated only "conservative" PE used selectively as an adjunct, not routinely. A 2024 cohort study from NHS Lothian (Scotland) examining 2004–2022 AVM resections used Spetzler–Martin–adjusted analysis to test whether PE increased the rate of complete first-resection AVM removal. After adjustment, no significant increase in complete-resection rate was demonstrated, mirroring the conclusions of a 2022 meta-analysis of 36 studies and 2,108 patients in which PE achieved a mean nidal obliteration of approximately 80% on pre-resection angiography but did not produce a statistically significant difference in clinical outcomes between embolized and non-embolized patients.

The implication for SM grade II AVMs is that routine PE is difficult to justify on grounds of either obliteration efficacy or functional outcome. Selective PE may still be appropriate for: (1) demonstrable deep feeders that will be encountered late in the surgical corridor, (2) intranidal aneurysms with high bleeding risk during manipulation, (3) high-flow shunts where ipsilateral edema or NPPB is a concern, or (4) lesions in motor or language eloquent cortex where flow reduction may permit a less aggressive dissection. For compact, superficial SM



grade II AVMs supplied by accessible cortical feeders, the literature supports primary microsurgery without PE.

## **6. Evidence in Unruptured SM Grade III AVMs**

### **6.1 The most actively studied subgroup**

Because SM grade III AVMs straddle the operability threshold, this is the group in which PE has been most actively studied and in which the most plausible benefit may exist. A multicenter propensity-adjusted analysis specifically of SM grade III AVMs reported that non-embolization was independently associated with an increased risk of poor neurological outcome after microsurgical resection. The authors advocated for liberal use of PE in SM grade III lesions selected on the basis of large size, surgical inaccessibility of feeding arteries, and high flow, even in the context of increasing surgical experience.

A single-center series of 27 SM grade III AVMs embolized with Onyx before resection reported a mean embolization-related obliteration of 28.8%, embolization morbidity of 3.7%, and surgical obliteration of 92.6%, with mRS 0–2 outcomes in 70.4%. The authors noted that Onyx embolization made the nidus easier to identify and excise, facilitated hemostasis, and was particularly useful for small or racemose niduses where intraoperative recognition can be difficult.

A two-center 250-patient German series (1989–2023) of multi-stage PE plus microsurgery for SM grade III–V AVMs achieved >80% devascularization in 68.4% of cases, with an 82.3% complete-resection rate; permanent disabling deficit occurred in 13.2% and combined death or dependency (mRS  $\geq 3$ ) in 18.8%. Importantly, the degree of devascularization was not independently associated with the investigated outcomes, suggesting that the act of embolization itself, rather than the quantity of nidus occluded, may be the surgically relevant factor.

### **6.2 Subtyping matters**

The heterogeneity of SM grade III lesions means that group-level conclusions can be misleading. Series stratifying by Lawton's subtypes have shown that III– (S1V1E1) lesions behave surgically like SM grade I–II AVMs, while III+ (S2VoE1) lesions behave like high-grade AVMs. In a 55-patient subtype-stratified series, incomplete resection rates were 5.6% for III–, 12.5% for III, and 15.0% for III+. The rationale for PE differs accordingly:

- Grade III– (small, eloquent, deep): the deep feeders are the principal surgical concern. Targeted PE of accessible deep feeders may be highly valuable; however, many III– lesions are sufficiently compact that surgery alone is feasible.
- Grade III (medium, deep, non-eloquent): a classical PE indication because of medium size with deep drainage. The German multistage series and most U.S. multicenter data support PE here when deep feeders are inaccessible to early surgical control.

- Grade III+ (medium, eloquent, superficial): the eloquence is the dominant risk; PE addresses flow but not the eloquent cortex. Many authors consider these lesions better suited to radiosurgery or conservative management than to surgery, with or without PE.
- Grade III\* (large, non-eloquent, superficial): essentially theoretical in most series;

staged PE plus surgery is reasonable in the rare clinical case.

## 7. Embolic Agents and Technical Considerations

### 7.1 Available agents

Liquid embolic agents dominate contemporary AVM PE. The principal agents are:

- N-butyl cyanoacrylate (NBCA): an adhesive cyanoacrylate-based glue with rapid polymerization upon contact with ionic blood. Historically the agent of choice in many centers, NBCA is associated with shorter procedure and fluoroscopy times than Onyx. A 2014 meta-analysis suggested lower permanent complication rates with NBCA than with Onyx (poor neurological outcome 5.2% vs. higher with Onyx in pooled data), though this finding is heavily confounded by indication and operator learning curves.
- Onyx (ethylene-vinyl alcohol copolymer in DMSO with suspended tantalum): a non-adhesive, lava-like cohesive precipitate enabling the "plug-and-push" technique with prolonged controlled injection. Onyx has become the dominant agent for both preoperative and curative embolization in many centers since its 2005 FDA approval. A meta-analysis of 103 studies showed higher complete nidus obliteration rates with EVOH-based agents than with NBCA (30.5% vs. lower for NBCA). For preoperative use specifically, a Japanese 38-patient comparative cohort found significantly lower intraoperative blood loss with Onyx (mean 130 mL) than with NBCA/coils (mean 449 mL;  $p = 0.0008$ ), with comparable surgical complication rates.
- Squid (Balt): an EVOH-based agent similar to Onyx but with smaller tantalum grains, providing more homogeneous radiopacity and a longer injection window.
- PHIL (precipitating hydrophobic injectable liquid): a non-adhesive iodinated copolymer with covalently bound radiopacifier, eliminating the radiopacity drift seen with tantalum-suspended agents.
- Coils and particles: largely supplanted for nidus embolization but still useful for high-flow fistulous components and feeding-artery aneurysms.

| Agent       | Chemistry              | Strengths                                                                 | Limitations / Considerations                                                                       |
|-------------|------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| NBCA (glue) | Adhesive cyanoacrylate | Rapid polymerization; shorter procedure and fluoroscopy times; lower cost | Operator-dependent; risk of microcatheter retention; non-cohesive; older comparative meta-analyses |

| Agent | Chemistry                                       | Strengths                                                                                                         | Limitations / Considerations                                                                                                                                      |
|-------|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|       |                                                 |                                                                                                                   | suggest lower permanent morbidity                                                                                                                                 |
| Onyx  | EVOH copolymer in DMSO + tantalum               | Cohesive, lava-like injection; "plug-and-push" enables long, controlled embolization; high obliteration potential | Long fluoroscopy times; DMSO angiotoxicity; intraoperative high-pressure casting can cause hemorrhage; recanalization in approximately 14% of pathology specimens |
| Squid | EVOH copolymer + smaller tantalum grains        | More homogeneous radiopacity; longer injection window; lower viscosity options                                    | Limited comparative outcome data versus Onyx; case-series level evidence                                                                                          |
| PHIL  | Iodinated copolymer with covalent radiopacifier | Stable radiopacity over time; no tantalum sedimentation; non-adhesive                                             | Limited comparative outcome data; mainly small case series                                                                                                        |

*Table 1. Principal liquid embolic agents used for preoperative embolization of brain AVMs.*

## 7.2 Procedural strategy: staging and timing

PE for surgical adjuvancy is generally performed in 1–3 sessions, with mean session counts in large series ranging from 1.1 to 1.6 for SM grade III lesions and substantially more for higher-grade multimodal regimens. The interval between final embolization and surgery is typically 1–7 days—short enough to avoid recanalization (observed pathologically in approximately 14% of Onyx-embolized vessels) but long enough to permit any postembolization edema or transient ischemic phenomena to declare themselves. Same-day surgery after embolization is feasible in dedicated hybrid operating rooms and may reduce the window for postembolization hemorrhage in high-risk lesions.

Target selection within the nidus is fundamental: ideal embolization targets are deep, surgically inaccessible feeders; feeders supplying the deep portion of the nidus that will be encountered late in dissection; and high-flow feeders contributing disproportionately to nidal flow. Conversely, embolization of superficial feeders that the surgeon would readily clip is wasteful at best and may increase the embolic burden delivered to the patient without surgical benefit.

## 7.3 Complications of preoperative embolization

Embolization-specific complications are a substantial part of the multimodal risk profile and must not be subsumed under the global "interventional" outcome rates. Reported rates vary widely depending on series composition:



- Total embolization-related complications: approximately 29% in a pooled systematic review of 588 patients across 8 studies (95% CI 19.6–40.2).
- Permanent neurological deficits attributable to embolization: approximately 6% (95% CI 3.9–8.5) overall, with mortality approximately 0.4%.
- Postembolization hemorrhage: 2–6%, with mechanisms including high-pressure Onyx casting, venous outflow occlusion, and NPPB.
- Microcatheter retention: 1–3% with conventional microcatheters, reduced with detachable-tip designs.
- Ischemic complications: from non-target embolization of perforators or distal cortical branches.

Importantly, the same systematic review concluded that available comparative studies were of insufficient quality to recommend routine PE; the authors found no studies that directly compared surgical excision with and without PE in a randomized or rigorously matched fashion. This methodological gap is the central evidence problem in the field.

## **8. Weighing Benefits and Risks: A Synthesis**

Three observations summarize the contemporary evidence base:

- PE consistently and reliably reduces intraoperative blood loss and provides angiographic devascularization of 50–80% on average. These intraoperative benefits are real and have been documented in multiple comparative series.
- PE has not been shown, in pooled or propensity-adjusted analyses, to improve complete-resection rates or long-term functional outcomes in unselected SM grade I–III AVMs. The 2022 meta-analysis of 36 studies and 2,108 patients and the 2024 NHS Lothian cohort both reached this conclusion after appropriate adjustment.
- PE itself carries a 6% permanent neurological deficit rate and an approximately 0.4% mortality. When added to the surgical risk, the cumulative multimodal morbidity may equal or exceed the morbidity of single-modality treatment in selected lesions.

In SM grade II AVMs with accessible feeders and superficial drainage, the marginal benefit of PE is small and the added morbidity may not be justified. In SM grade III AVMs, particularly those of Lawton subtypes III and III\* (medium-large lesions with deep drainage or inaccessibility), PE is most clearly defensible. In Lawton III+ lesions (medium/eloquent/superficial), the dominant risk is eloquence rather than flow; PE addresses the wrong variable and these patients are often better managed with radiosurgery or observation. In Lawton III– lesions (small/eloquent/deep), the deep feeders may be highly targetable by PE, and selective embolization of these feeders is well supported.

Patient-level factors matter as much as lesion-level factors. Age, comorbidity, hemorrhagic risk factors (associated aneurysms, deep drainage), and the patient’s own risk tolerance all enter the calculus. A 30-year-old with an SM grade III lesion and a 1.4–2% annual hemorrhage

rate faces a markedly different lifetime cumulative risk than a 65-year-old with the same lesion, and the threshold for adding embolization morbidity should differ accordingly.

### **9. A Practical Decision Framework**

Based on the available evidence, the following framework may guide decision-making for adult unruptured SM grade II–III AVMs being considered for microsurgical resection:

- Step 1: Confirm a treatment indication. Apply the Supplemented Spetzler–Martin score, consider patient age and remaining life expectancy, and weigh the contemporary annual hemorrhage risk (approximately 1.4% per year overall, higher with deep drainage, associated aneurysm, or deep/cerebellar location) against the institution’s composite treatment morbidity.
- Step 2: Confirm that microsurgery is the optimal modality. For SM grade II and Lawton III– lesions, surgery is usually the preferred approach in centers with appropriate expertise. For Lawton III+ lesions, consider radiosurgery instead. For very high Supp-SM scores (>7), reconsider intervention altogether.
- Step 3: Determine whether PE is likely to add value. Indications favoring PE include deep or inaccessible feeders, intranidal aneurysms, high-flow fistulous components, large nidal volume, and angioarchitectural features that will be encountered late in the surgical corridor. Indications disfavoring PE include compact lesions, exclusively superficial accessible feeders, and SM grade II lesions without high-risk vascular features.
- Step 4: Plan the embolization with surgical endpoints in mind. Target deep and surgically inaccessible feeders. Avoid excessive embolization of superficial feeders that would be clipped easily intraoperatively. Limit the number of sessions to minimize cumulative procedural risk. Time the final embolization 1–7 days before surgery in most cases.
- Step 5: Monitor for postembolization complications—new neurological deficit, headache out of proportion to procedure, or imaging signs of hemorrhage or venous outflow compromise—and have a surgical pathway available for emergent resection if needed.
- Step 6: Document outcomes prospectively. The persistent lack of randomized data in this field means that center-level prospective data collection remains essential.

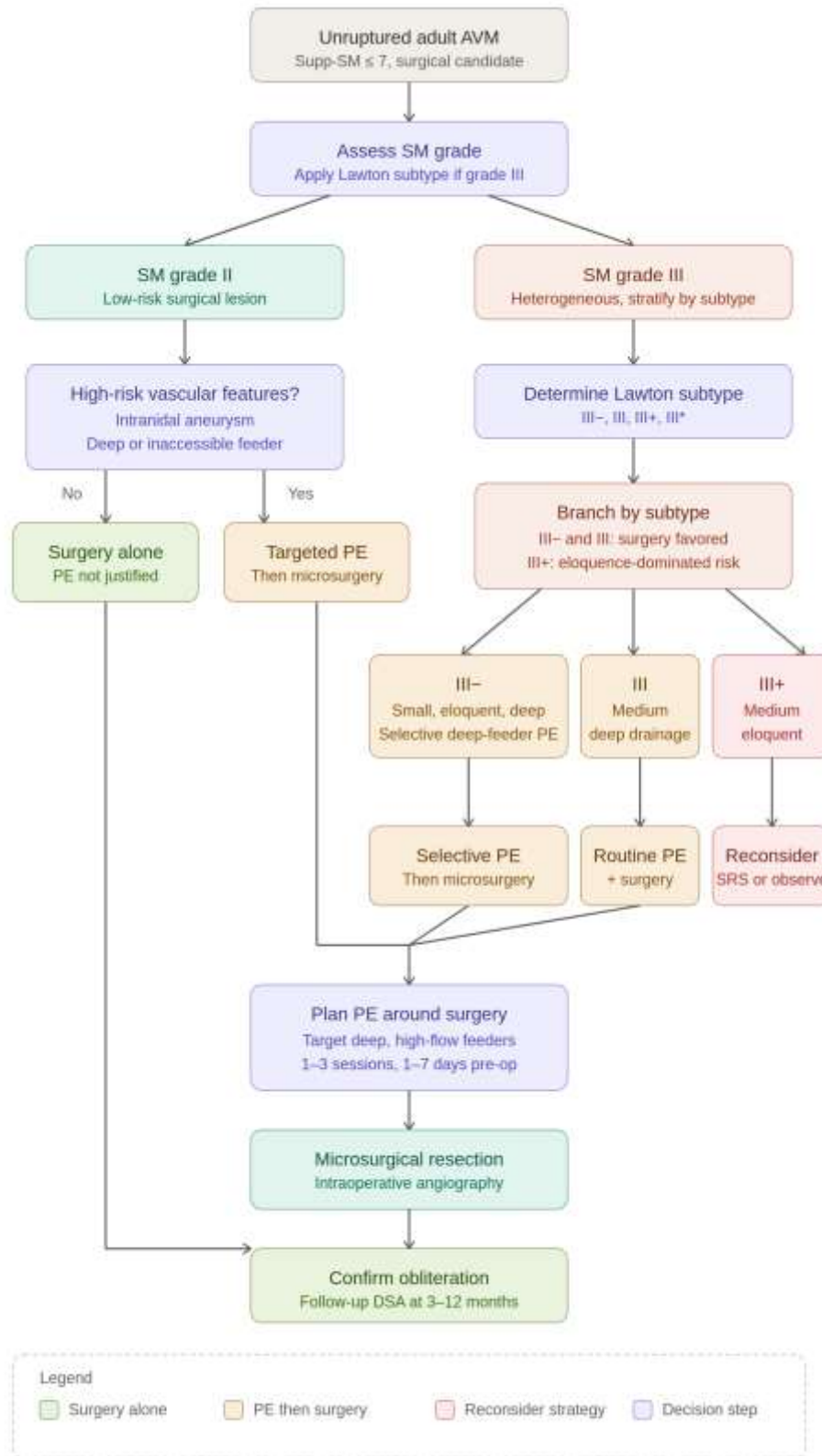


Figure 1. Role of Preoperative Endovascular Embolization Prior to Microsurgical Resection.

## 10. Limitations of the Current Evidence Base

Several limitations qualify all conclusions in this review. First, no randomized controlled trial directly compares microsurgery alone with microsurgery preceded by PE in SM grade II–III AVMs; all available data are observational and subject to indication bias, with sicker lesions preferentially receiving PE. Second, propensity adjustment can partially mitigate but not eliminate confounding by unmeasured variables such as angioarchitectural complexity that drove the decision to embolize in the first place. Third, embolic agents, microcatheter technology, and operator experience have evolved substantially over the past two decades, so older data may not reflect contemporary practice. Fourth, the heterogeneity of SM grade III lesions makes aggregated outcomes difficult to interpret without subtype stratification, which most series do not provide. Fifth, ARUBA and its critics have reframed the entire question of when to treat unruptured AVMs, and conclusions about PE necessarily depend on prior acceptance of treatment in this population—a position that itself remains contested. Finally, publication bias favoring positive case series may exaggerate the apparent safety of PE in expert centers.

## 11. Conclusions

Preoperative embolization of unruptured Spetzler–Martin grade II–III brain AVMs reliably reduces intraoperative blood loss and selectively devascularizes inaccessible feeders, but the contemporary evidence base does not support its routine use across all such lesions. For SM grade II AVMs with favorable angioarchitecture, microsurgery alone yields excellent results and PE adds procedural risk without convincing functional benefit. For SM grade III AVMs, the picture is more nuanced: PE is most defensible in lesions with deep, inaccessible, or high-flow feeders—particularly those of Lawton subtypes III and III\*—and least defensible in lesions whose dominant surgical risk is eloquence rather than flow. Embolization-related morbidity is non-trivial (approximately 6% permanent deficit, approximately 0.4% mortality) and must be added to, not absorbed into, the cumulative multimodal treatment risk. Decisions should be individualized in experienced multidisciplinary centers using both the original SM grade and the Lawton–Young supplementary score, and prospective registry-level data collection should be strengthened to inform the field while randomized trials remain infeasible.

In an era of increasingly nuanced understanding of natural-history risk—lower than historically quoted, especially for non-deep, non-aneurysm-bearing lesions—the threshold for adding embolization morbidity to surgical morbidity should be set thoughtfully and lesion-specifically rather than reflexively.

## References

1. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. *J Neurosurg.* 1986;65(4):476–483.
2. Lawton MT. Spetzler–Martin grade III arteriovenous malformations: surgical results and a modification of the grading scale. *Neurosurgery.* 2003;52(4):740–749.
3. Lawton MT, Kim H, McCulloch CE, Mikhak B, Young WL. A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. *Neurosurgery.* 2010;66(4):702–713.
4. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. *Lancet.* 2014;383(9917):614–621.
5. Kim H, Al-Shahi Salman R, McCulloch CE, et al. Risk of future hemorrhage from unruptured brain arteriovenous malformations: the Multicenter Arteriovenous Malformation Research Study (MARS). *JAMA Neurol.* 2025 (published online).
6. Lawton MT, Rutledge WC, Kim H, et al. Brain arteriovenous malformations. *Nat Rev Dis Primers.* 2015;1:15008.
7. Schramm J, Schaller K, Esche J, Boström A. Microsurgery for cerebral arteriovenous malformations: subgroup outcomes in a consecutive series of 288 cases. *J Neurosurg.* 2017;126(4):1056–1063.
8. Catapano JS, Frisoli FA, Nguyen CL, et al. Spetzler–Martin grade III arteriovenous malformations: a multicenter propensity-adjusted analysis of the effects of preoperative embolization. *Neurosurgery.* 2021;88(5):996–1002.
9. Potts MB, Lau D, Abula AA, Kim H, Young WL, Lawton MT; UCSF Brain AVM Study Project. Current surgical results with low-grade brain arteriovenous malformations. *J Neurosurg.* 2015;122(4):912–920.
10. Lawton MT; UCSF Brain AVM Study Project. Microsurgery for ARUBA trial–eligible unruptured brain arteriovenous malformations. *Stroke.* 2017;48(1):136–144.
11. Wong J, Slomovic A, Ibrahim G, Radovanovic I, Tymianski M. Microsurgery for ARUBA–eligible unruptured brain arteriovenous malformations. *Stroke.* 2017;48(1):136–144.
12. Goyal N, Hoit D, DiNitto J, et al. Surgical management outcomes of intracranial arteriovenous malformations after preoperative embolization: a systematic review and meta-analysis. *Neurosurg Rev.* 2023;46(1):1.
13. Featherstone WJ, Sebastian J, Salman RA-S, et al. Preoperative embolisation of brain arteriovenous malformations: a systematic review and meta-analysis. *Neurosurg Rev.* 2022;45(4):2509–2521.
14. Tian B, Featherstone WJ, Salman RA-S, et al. Influence of preoperative embolisation on resection of brain arteriovenous malformations: cohort study. *Acta Neurochir (Wien).* 2024;166(1):348.
15. Vollherbst DF, Chapot R, Bendszus M, Möhlenbruch MA. Glue, Onyx, Squid or PHIL? Liquid embolic agents for the embolization of cerebral arteriovenous malformations and dural arteriovenous fistulas. *Clin Neuroradiol.* 2022;32(1):25–38.
16. Izumo T, Okamura K, Takahira R, et al. Impact of pre-operative embolization with Onyx for brain arteriovenous malformation surgery. *Front Neurol.* 2022;13:875260.

17. Pierot L, Cognard C, Herbreteau D, et al. Endovascular treatment of brain arteriovenous malformations using a liquid embolic agent: results of a prospective, multicentre study (BRAVO). *Eur Radiol.* 2013;23(10):2838–2845.
18. Pasqualin A, Zampieri P, Nicolato A, Turazzi S, Bricolo A, Cevolani A. Onyx embolization before the surgical treatment of grade III Spetzler–Martin brain arteriovenous malformations: single-center experience and technical nuances. *World Neurosurg.* 2018;115:e408–e417.
19. Tonetti DA, Gross BA, Atcheson KM, Jankowitz BT, Kano H, Lunsford LD. The benefit of preoperative embolization in brain AVM resection: a single-center experience. *World Neurosurg.* 2019;126:e289–e296.
20. Rutledge WC, Ko NU, Lawton MT, Kim H. Hemorrhage rates and risk factors in the natural history course of brain arteriovenous malformations. *Transl Stroke Res.* 2014;5(5):538–542.
21. Spetzler RF, Ponce FA. A 3-tier classification of cerebral arteriovenous malformations. *J Neurosurg.* 2011;114(3):842–849.
22. Brown RD Jr, Wiebers DO, Forbes G, et al. The natural history of unruptured intracranial arteriovenous malformations. *J Neurosurg.* 1988;68(3):352–357.
23. Stapf C, Mast H, Sciacca RR, et al. Predictors of hemorrhage in patients with untreated brain arteriovenous malformation. *Neurology.* 2006;66(9):1350–1355.
24. Loh Y, Duckwiler GR; Onyx Trial Investigators. A prospective, multicenter, randomized trial of the Onyx liquid embolic system and N-butyl cyanoacrylate embolization of cerebral arteriovenous malformations. *J Neurosurg.* 2010;113(4):733–741.
25. Pellettieri L, Svendsen P, Wikholm G, Carlsson CA. Multidisciplinary therapy of arteriovenous malformations: a review of the literature and a comparison with surgical results. *Stroke.* 1985;16(2):216–219.
26. Yu S, Yan L, Yao Y, et al. Intra- and post-operative acute hemorrhagic complications of Onyx embolization of brain arteriovenous malformations: a single-center experience. *Front Neurol.* 2022;13:974954.
27. Goldberg J, Raabe A, Bervini D. Natural history and management options of unruptured brain arteriovenous malformations. *World Neurosurg.* 2020;139:601–611.