



Real-World Safety Profile of Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: a Multinational Multicenter Study

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Abstract

Background Middle meningeal artery embolization (MMAE) has emerged as a treatment for chronic subdural hematoma (cSDH), but comprehensive real-world safety data remain limited.

Methods We performed a multicenter retrospective analysis of 1781 consecutive patients undergoing MMAE for cSDH (2019–2025). The primary outcome was any procedure-related complication within 30 days. Inverse probability of treatment weighting (IPTW) assessed the association between technical success and complications, adjusting for demographic, clinical, and procedural confounders.

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Results Mean age was 72.8 ± 12.4 years; 68.1% were male. The 30-day complication rate was 5.1% (91/1781; 95% CI, 4.1–6.2). In-hospital mortality was 2.9% (47/1625). Technical success was achieved in 97.5% (1505/1543). Among documented complications, thromboembolic events were most common (37.2%; 32/86), followed by hemorrhagic complications (23.8%; 20/84) and access-site hematoma (10.4%; 8/77). Among patients with classifiable symptom status, 80.6% of complications were symptomatic, yielding an overall symptomatic complication rate of 3.0%. Neurological deterioration occurred in 27.1% (248/915). Among 1552 patients with documented surgical approach, complication rates were similar between surgery plus embolization (4.9%; 34/690) and embolization alone (5.2%; 45/860; OR, 0.94; 95% CI, 0.59–1.48; $p=0.79$). After IPTW adjustment, technical success was associated with an 86% reduction in complication odds (OR, 0.14; 95% CI, 0.05–0.40; $p<0.001$).

Conclusions In this large multicenter cohort, MMAE was associated with a 5.1% complication rate. Technical success was the strongest protective factor. Embolization with or without surgery showed equivalent safety profiles.

Keywords Middle meningeal artery embolization · Chronic subdural hematoma · Safety · Complications

Introduction

Chronic subdural hematoma (cSDH) is a frequent neurosurgical condition that disproportionately affects older adults and is increasingly encountered in patients receiving antiplatelet or anticoagulant therapy [1]. Population-based studies report an annual incidence spanning approximately 1.7–20.6 per 100,000 persons, and the burden is expected to rise further with population aging and expanding antithrombotic use [1].

Traditional management has relied on surgical evacuation (typically burr-hole drainage, twist-drill craniotomy, or craniotomy), yet postoperative recurrence remains clinically significant, with rates commonly reported in the 10–30% range across series and reviews [2]. Middle meningeal artery embolization (MMAE) aims to target the underlying disease process by theoretically stopping neoangiogenesis that leads to an inflammatory, angiogenic neomembrane with fragile new blood vessels partially supplied by the middle meningeal circulation [3]. This is achieved by reducing membrane perfusion, which limits ongoing exudation and microhemorrhages that contribute to persistence and recurrence.

Several randomized, prospective trials have provided efficacy signals suggesting that MMAE, used either as an adjunctive therapy or, in selected patients, as stand-alone therapy, can reduce recurrence/progression endpoints compared with standard management alone [4–7]. However, detailed real-world safety data remains relatively less developed. Previous systematic reviews and meta-analyses have generally shown low overall complication rates (e.g., approximately 2.3% in large pooled groups), but these estimates are limited by variable definitions, diverse indications, and small sample sizes within key groups and subgroups [8, 9]. Therefore, we performed a multicenter analysis of 1781 consecutive patients treated with MMAE to establish a detailed, contemporary real-world safety profile and identify patient- and procedure-level risk factors for complications.

Methods

Study Design and Patients

We performed a retrospective analysis of consecutive adult patients who underwent MMAE for cSDH at participating centers between January 2019 and June 2025. Patients were identified through institutional procedural databases using Current Procedural Terminology codes for cerebral endovascular procedures. We included all patients who underwent MMAE, either as monotherapy or in combination with surgical evacuation. Patients with incomplete outcome data were excluded from the primary analysis. The study was approved by the institutional review boards at participating centers with a waiver of informed consent given the retrospective nature of the analysis.

Procedures

MMAE was performed using standard endovascular techniques. Femoral arterial access was obtained, and diagnostic angiography was performed to identify the MMA and assess for dangerous anastomoses with ophthalmic or other critical vessels. Embolization was performed with liquid embolic agents or particles at the discretion of the operating physician. Technical success was defined on purely angiographic criteria as complete or near-complete occlusion of the target middle meningeal artery branches with appropriate deposition of the embolic material. Procedural complications were captured separately and were not included in this definition.

For patients undergoing combined treatment, surgical evacuation was performed either before or after embolization according to local institutional protocols. Surgical techniques included burr-hole drainage, twist-drill craniotomy, or craniotomy.

Outcomes

The primary outcome was any procedure-related complication within 30 days of embolization, defined as an adverse event judged by the local site investigator to be directly attributable to the procedure or its sequelae. Prespecified categories were thromboembolic event or stroke (clinical or imaging-confirmed ischemic event), hemorrhagic complication (any intracranial or extracranial procedure-related hemorrhage, including subdural, intraparenchymal, subarachnoid, contrast extravasation, and arterial dissection), access-site complication (hematoma, pseudoaneurysm, thrombosis, or limb ischemia), cranial nerve injury, unintended embolization of dangerous extracranial-intracranial collaterals, and other procedural complications (including vasospasm and contrast-related events). Each event was classified by the local site investigator as symptomatic (producing new clinical signs or symptoms attributable to the procedure), asymptomatic (detected on imaging or angiography without clinical manifestation), or indeterminate (insufficient documentation to confidently classify symptom status). Timing was recorded as intraoperative or postoperative, and permanence as transient (resolved before discharge or within 30 days) or permanent (present at discharge or last available follow-up). All events were captured on a common structured case-report form. Independent central adjudication was not performed.

Secondary outcomes included in-hospital mortality, 90-day mortality, new or worsening neurological deterioration, recurrence requiring intervention, need for rescue surgery, hospital readmission, and repeat embolization.

Data Collection

Baseline demographic, clinical, and procedural characteristics were abstracted from medical records. Demographic variables included age, sex, and body mass index. Clinical variables included admission neurological status (Glasgow Coma Scale score), medical comorbidities, medication use (particularly antithrombotic agents), and laboratory values (platelet count and hemoglobin level). Procedural variables included bilateral disease, prior subdural hematoma, concurrent surgical decompression, identification of dangerous collateral vessels, and surgical approach (embolization alone vs. surgery plus embolization).

Statistical Analysis

Continuous variables are presented as means with standard deviations or medians with interquartile ranges, as appropriate. Categorical variables are presented as frequencies with percentages. Complication rates with 95% confidence intervals were calculated using the Wilson score method.

To evaluate the association between technical success and complications while accounting for confounding, we used inverse probability of treatment weighting (IPTW). This method creates a pseudo-population in which the distribution of measured confounders is independent of the treatment (technical success), thereby balancing baseline characteristics between groups.

We first estimated each patient's propensity score, the probability of achieving technical success given their baseline characteristics, using multivariable logistic regression. The propensity score model included age, sex, admission Glasgow Coma Scale score, platelet count, hemoglobin level, prior subdural hematoma, bilateral disease, concurrent surgical decompression, presence of dangerous collateral vessels, antithrombotic therapy status, and surgical approach (embolization alone vs. surgery plus embolization). To enhance model stability and prevent overfitting, we standardized continuous variables and applied L2 regularization with a penalty parameter of 0.5.

From the propensity scores, we calculated stabilized inverse probability weights. For patients with technical success, the weight was the marginal probability of success divided by the propensity score. For patients with technical failure, the weight was the marginal probability of failure divided by one minus the propensity score. Stabilized weights prevent extreme values and preserve the original sample size. We further trimmed weights at the 1st and 99th percentiles to enhance stability.

We assessed covariate balance in the weighted pseudo-population using standardized mean differences, with values less than 0.1 indicating adequate balance. After confirming balance, we estimated the effect of technical success on complications using weighted logistic regression in the pseudo-population.

To address potential circularity in the technical-success indicator, technical success was defined on angiographic criteria alone for all primary analyses. A prespecified sensitivity analysis using a strict composite definition (angiographic success and absence of procedural complications) was performed and is reported in the Supplementary Appendix (eSection 1 and eTable 2) to demonstrate the magnitude of bias introduced by such a composite.

To evaluate whether the safety profile differed by embolic-agent class, we stratified 30-day procedure-related complications by primary embolic material into four prespecified classes: liquid embolic agents alone (Onyx, n-BCA, Squid, Phil, or combinations of liquid agents), particles alone (PVA), coils alone, and combinations of agents across classes. Crude complication rates with Wilson 95% confidence intervals were compared using the chi-square test, and a prespecified pairwise comparison between liquid embolic agents and particles was made using logistic regression. Embolic-agent class was additionally

Table 1 Baseline Characteristics of Patients.

Characteristic	Patients (N= 1781)
Age—yr	
Mean ± SD	72.8 ± 12.4
Male sex—no. (%)	1212 (68.1)
Admission Glasgow Coma Scale score—mean ± SD†	14.3 ± 1.5
Bilateral disease—no. (%)	613 (34.4)
Prior subdural hematoma—no. (%)	488 (27.4)
Concurrent surgical decompression—no. (%)	433 (24.3)
Antithrombotic therapy—no. (%)‡	879 (49.4)
Antiplatelet agent	591 (33.2)
Anticoagulant	423 (23.8)
Surgical approach—no. (%)§	
Surgery plus embolization	692 (44.6)
Embolization alone	860 (55.4)
Technical success—no. (%)¶	1505 (97.5)

† Scores on the Glasgow Coma Scale range from 3 to 15, with lower scores indicating worse neurological status

‡ Percentages may not total 100 because some patients received both antiplatelet and anticoagulant therapy

§ Percentages are based on 1552 patients with documented surgical approach

¶ Percentage is based on 1543 patients with documented technical success status

included as a covariate in a sensitivity IPTW analysis for the primary endpoint.

For comparisons between embolization alone and surgery plus embolization, we used chi-square tests for categorical variables and t-tests for continuous variables. Odds ratios (OR) with 95% confidence intervals (CI) were calculated using logistic regression. All statistical tests were two-

sided, and *p* values of less than 0.05 were considered to indicate statistical significance. The IPTW analysis of technical success and 30-day procedure-related complications was the prespecified primary inferential analysis. All other analyses were exploratory, including secondary outcomes, complication-subtype comparisons, the comparison of stand-alone embolization versus surgery plus embolization, embolic-agent stratified comparisons, and subgroup analyses. No adjustments were made for multiple comparisons; reported *p* values for these analyses should therefore be interpreted as descriptive, and the corresponding findings as hypothesis-generating rather than confirmatory.

Results

Patient Characteristics

Among 1781 patients who underwent MMAE, the mean age was 72.8 years (standard deviation, 12.4), and 1212 patients (68.1%) were male (Table 1). The mean admission Glasgow Coma Scale score was 14.3. Bilateral subdural hematomas were present in 613 patients (34.4%). Prior subdural hematoma occurred in 488 patients (27.4%). Concurrent surgical decompression was performed in 433 patients (24.3%).

Antithrombotic therapy was used by 879 patients (49.4%), including antiplatelet agents in 591 patients (33.2%) and anticoagulants in 423 patients (23.8%). Among 1552 patients with documented surgical approach, 692 (44.6%) underwent surgery plus embolization and 860 (55.4%) underwent embolization alone.

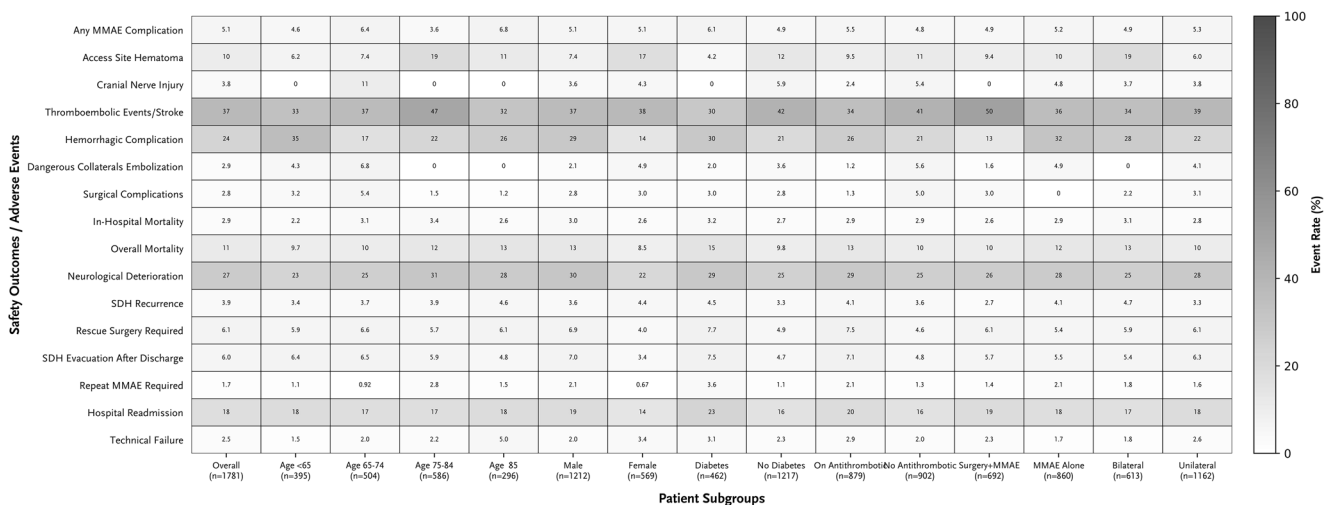


Fig. 1 Complications and Adverse Events by Patient Subgroup. The heatmap shows the percentage of patients with complications and adverse events, stratified by clinical subgroups. Color intensity indicates event frequency, with darker shading representing higher rates. Sample sizes for each subgroup are shown in parentheses

Primary Outcome

The overall complication rate was 5.1% (91 of 1781 patients; 95% CI, 4.1 to 6.2). Among patients with documented specific complications, thromboembolic events or stroke occurred in 37.2% (32 of 86 patients), hemorrhagic complications in 23.8% (20 of 84), access-site hematoma in 10.4% (8 of 77), cranial nerve injury in 3.8% (3 of 79), unintended embolization of dangerous collateral vessels in 2.9% (4 of 137), and surgical complications in 2.8% (11 of 390) (eTable 1). Denominators vary by complication type because they reflect the number of patients with a documented assessment for each category; patients with multiple complication types are counted under each applicable category, whereas eTable 1 classifies each patient by the primary complication. Among 67 patients with determinable symptom status, 54 (80.6%) had symptomatic complications and 13 (19.4%) had asymptomatic complications, corresponding to overall rates of 3.0% and 0.7%, respectively; the remaining 24 complications were classified as indeterminate due to insufficient documentation. Thromboembolic events were uniformly symptomatic, whereas access-site complications and procedural findings such as vasospasm and contrast extravasation were predominantly asymptomatic.

Complication rates varied across patient subgroups, as shown in Fig. 1. Hemorrhagic complications showed a mixed symptomatic profile: intracranial hemorrhages (subdural, intraparenchymal, and subarachnoid) were uniformly symptomatic (16 of 16), while contrast extravasation and MMA dissection were asymptomatic (2 of 2). Dangerous collaterals embolization events were angiographically asymptomatic at the component level in all 4 documented cases, although 3 of the 4 patients had concurrent symptomatic complications (thromboembolic events or other).

Secondary Outcomes

In-hospital mortality occurred in 2.9% of patients (47 of 1625). Neurological deterioration, defined as any new or worsening neurological deficit observed during the index admission, occurred in 27.1% of evaluable patients (248 of 915). Among the 144 events with both pre-morbid and discharge mRS available, 91 (63.2%) were mild (change

in mRS ≤ 1 from pre-morbid baseline, patient alive at discharge) and 53 (36.8%) were moderate-to-severe (change in mRS ≥ 2 or in-hospital death). Among the 115 surviving patients with both pre-morbid mRS and last-follow-up mRS available, 44 (38.3%) had transient deterioration (mRS returned to \leq pre-morbid baseline at last follow-up) and 71 (61.7%) had persistent deterioration (mRS remained $>$ pre-morbid baseline). Validated standardized instruments (NIHSS, full mRS schedule, validated delirium screens) were not uniformly applied across sites. Rescue surgery was required in 6.1% (95 of 1569), hospital readmission occurred in 17.7% (242 of 1370), and repeat embolization was performed in 1.7% (26 of 1563).

Technical success, defined on angiographic criteria alone, was achieved in 1505 of 1543 procedures (97.5%). Among 1505 patients with technical success, 79 (5.2%) experienced a 30-day procedure-related complication; among 37 patients with technical failure, 9 (24.3%) experienced a complication, confirming that the technical-success variable and the complication outcome were not deterministically linked.

After inverse probability of treatment weighting to adjust for baseline characteristics, all measured confounders achieved adequate balance between the technical success and failure groups (standardized mean differences < 0.1). In the weighted analysis, technical success remained strongly associated with reduced complications (adjusted OR, 0.14; 95% CI, 0.05 to 0.40; $p < 0.001$), representing an 86% reduction in the odds of complications (Table 2).

Risk Factors for Complications

In univariable analysis, several baseline characteristics were associated with complications (Fig. 2). Advanced age (≥ 75 years), male sex, bilateral disease, concurrent decompression, and antithrombotic therapy showed varying associations with complication risk. Technical success was the strongest protective factor.

Comparison of Embolization Alone Versus Surgery Plus Embolization

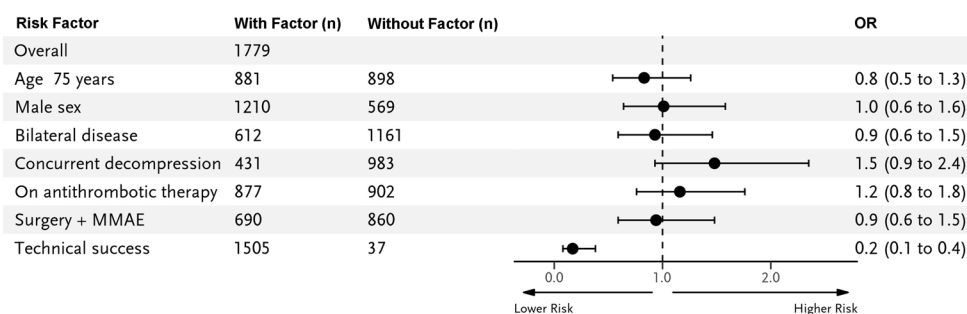
Among 1552 patients with documented surgical approach, complication rates were similar between surgery plus embolization (34 of 690 patients, 4.9%) and embolization alone (45 of 860 patients, 5.2%) (OR, 0.94; 95% CI, 0.59 to 1.48; $p = 0.79$) (Table 3). All secondary outcomes showed no significant differences between the two approaches. In-hospital mortality occurred in 2.6% of patients (18 of 680) with surgery plus embolization versus 2.9% (24 of 840) with embolization alone ($p = 0.80$). Neurological deterioration occurred in 26.0% (89 of 342) versus 27.9% (124 of 444) ($p = 0.55$). Rescue surgery was required in 6.1%

Table 2 Association between Technical Success and Complications.

Model	Odds Ratio	95% CI	P Value
Unadjusted	0.17	0.08–0.38	< 0.001
IPTW-adjusted	0.14	0.05–0.40	< 0.001

IPTW denotes inverse probability of treatment weighting. The IPTW model adjusted for age, sex, admission Glasgow Coma Scale score, platelet count, hemoglobin level, prior subdural hematoma, bilateral disease, concurrent surgical decompression, dangerous collateral vessels, antithrombotic therapy, and surgical approach

Fig. 2 Risk Factors for Complications. The forest plot shows odds ratios with 95% confidence intervals from univariable logistic regression



(40 of 656) versus 5.4% (44 of 808) ($p=0.59$). Hospital readmission occurred in 18.7% (110 of 589) versus 17.7% (120 of 678) ($p=0.65$). Technical success rates were similarly high: 97.7% (594 of 608) versus 98.3% (696 of 708) ($p=0.43$) (Fig. 3).

Detailed analysis of specific complication types revealed no significant differences between surgery plus embolization and embolization alone (Table 4). Among patients with documented specific complications, thromboembolic events or stroke occurred in 50.0% (16 of 32) of the surgery plus embolization group versus 35.7% (15 of 42) of the embolization alone group ($p=0.32$). Hemorrhagic complications occurred in 12.9% (4 of 31) versus 31.7% (13 of 41) ($p=0.09$). Access-site hematoma occurred in 9.4% (3 of 32) versus 10.0% (4 of 40) ($p>0.99$). Cranial nerve injury occurred in 0.0% (0 of 32) versus 4.8% (2 of 42) ($p=0.50$).

Subgroup Analysis

Complication rates were generally consistent across patient subgroups (Fig. 4). Age-stratified analysis showed rates of 4.6% in patients younger than 65 years, 6.4% in those 65 to 74 years, 3.6% in those 75 to 84 years, and 6.8% in those 85 years or older. Complication rates were identical in male and female patients (5.1% in each group). Among patients receiving antithrombotic therapy, the complication rate was 5.5% compared with 4.8% in those not receiving such therapy.

Embolitic-Agent Class and Complications

Among 1760 patients with documented primary embolic material, the agent was particles alone (PVA) in 808 (45.9%), a liquid embolic alone (Onyx, n-BCA, Squid, Phil, or a liquid-liquid combination) in 641 (36.4%), a combination of agents across classes in 267 (15.2%), and coils alone in 44 (2.5%). Thirty-day procedure-related complication rates were 4.71% (38/807; 95% CI, 3.45 to 6.40) with particles, 6.08% (39/641; 95% CI, 4.48 to 8.21) with liquid embolic agents, 6.82% (3/44; 95% CI, 2.35 to 18.23) with coils, and 3.37% (9/267; 95% CI, 1.78 to 6.28) with combination therapy. Within the liquid-embolic class, complication rates were 7.92% (27/341; 95% CI, 5.50 to 11.27) with Onyx, 5.00% (8/160; 95% CI, 2.56 to 9.56) with n-BCA, and 4.30% (4/93; 95% CI, 1.69 to 10.54) with Squid. In a logistic-regression comparison restricted to particles versus liquid, the odds ratio was 0.76 (95% CI, 0.48 to 1.21; $p=0.25$) for particles relative to liquid; the overall comparison across the four prespecified classes was non-significant (chi-square $p=0.32$). Inclusion of embolitic-agent class as an additional covariate in the propensity-score model did not materially change the estimated effect of technical success on complications (adjusted OR, 0.11; 95% CI, 0.03 to 0.37; $p<0.001$; Supplementary Appendix, eSection 2 and eTables 3–5).

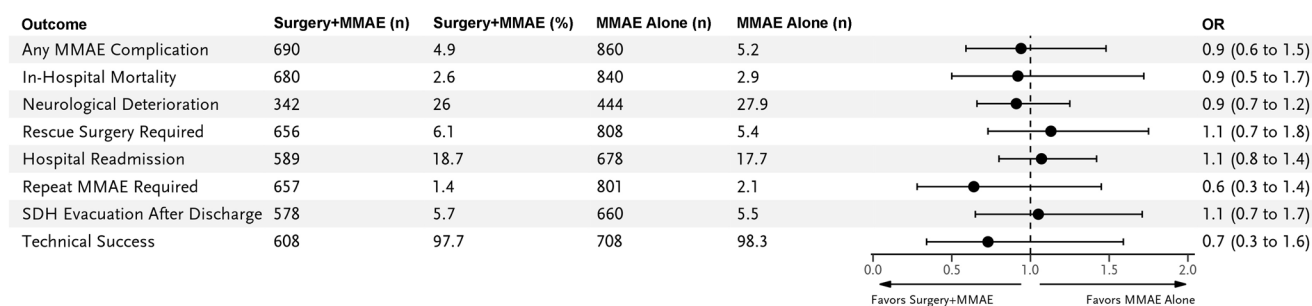


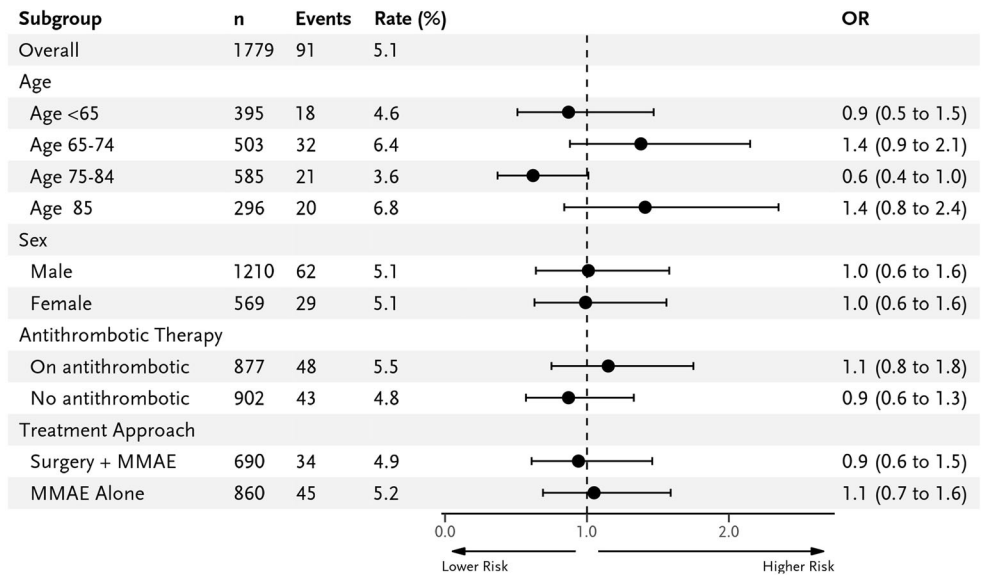
Fig. 3 Safety Outcomes: Embolization Alone versus Surgery Plus Embolization. The forest plot compares safety outcomes between surgery plus embolization and embolization alone

Table 3 Comparison of Embolization Alone versus Surgery Plus Embolization.

Outcome	Surgery Plus Embolization No./total no. (%)	Embolization Alone No./total no. (%)	Odds Ratio (95% CI)	P Value
Any complication	34/690 (4.9)	45/860 (5.2)	0.94 (0.59–1.48)	0.79
In-hospital mortality	18/680 (2.6)	24/840 (2.9)	0.92 (0.50–1.72)	0.80
Neurological deterioration	89/342 (26.0)	124/444 (27.9)	0.91 (0.66–1.25)	0.55
Rescue surgery	40/656 (6.1)	44/808 (5.4)	1.13 (0.73–1.75)	0.59
Hospital readmission	110/589 (18.7)	120/678 (17.7)	1.07 (0.80–1.42)	0.65
Repeat embolization	9/657 (1.4)	17/801 (2.1)	0.64 (0.28–1.45)	0.28
Evacuation after discharge	33/578 (5.7)	36/660 (5.5)	1.05 (0.65–1.71)	0.85
Technical success	594/608 (97.7)	696/708 (98.3)	0.73 (0.34–1.59)	0.43

Odds ratios compare surgery plus embolization with embolization alone (reference). All comparisons were exploratory and were not adjusted for multiple comparisons

Fig. 4 Subgroup Analysis of Complication Rates. The forest plot shows complication rates and odds ratios with 95% confidence intervals across patient subgroups



Discussion

In this multicenter retrospective analysis of 1781 consecutive patients undergoing MMAE for cSDH, the 30-day procedure-related complication rate was 5.1% (95% CI, 4.1–6.2%). Technical success, achieved in 97.5% of procedures, was independently associated with an 86% reduction in the odds of complications after IPTW adjustment (adjusted OR, 0.14; 95% CI, 0.05–0.40; $p < 0.001$). Complication rates were equivalent between stand-alone embolization and embolization combined with surgical evacuation (5.2% vs. 4.9%; OR, 0.94; 95% CI, 0.59–1.48; $p = 0.79$), with no significant differences in any secondary outcome. These findings advance the safety evidence base for MMAE in three ways: by establishing a real-world complication benchmark from a large, consecutive cohort; by validating technical success as a modifiable quality target linked to patient safety; and by demonstrating comparable short-term safety across treatment strategies.

The strong association between technical success and lower complication risk is most plausibly driven by operator- and technique-level factors. Achieving complete or near-complete distal occlusion of the target middle meningeal artery branches depends on operator experience, careful selection of the embolic agent and microcatheter, controlled penetration of the embolic material into the distal dural network, and systematic angiographic identification and avoidance of dangerous extracranial-intracranial anastomoses (including the meningo-ophthalmic, petrous, and accessory meningeal pathways). Higher procedure volume and team experience are likely to underpin the high technical-success rate (97.5%) observed across the participating centers. These technique- and experience-level determinants align with the membrane-mediated, neoangiogenic biology of chronic subdural hematoma, in which only complete devascularization of the membrane network meaningfully attenuates ongoing microhemorrhage and exudation. The actionable lever in clinical practice, however,

Table 4 Detailed Complications: Surgery Plus Embolization versus Embolization Alone.

Complication	Total	Surgery Plus Emboliza- tion	Embolization Alone	Odds Ratio (95% CI)	P Value
	No./total no. (%)	No./total no. (%)	No./total no. (%)		
Access-site hematoma	7/72 (9.7)	3/32 (9.4)	4/40 (10.0)	0.93 (0.19–4.50)	>0.99
Cranial nerve injury	2/74 (2.7)	0/32 (0.0)	2/42 (4.8)	NA	0.50
Thromboembolic events or stroke	31/74 (41.9)	16/32 (50.0)	15/42 (35.7)	1.80 (0.71–4.60)	0.32
Hemorrhagic complication	17/72 (23.6)	4/31 (12.9)	13/41 (31.7)	0.32 (0.09–1.10)	0.09
Dangerous collaterals emboliza- tion	4/125 (3.2)	1/64 (1.6)	3/61 (4.9)	0.31 (0.03–3.03)	0.36
Surgical complications	11/385 (2.9)	11/366 (3.0)	NA	NA	>0.99
Intraoperative timing	21/59 (35.6)	7/25 (28.0)	14/34 (41.2)	0.56 (0.18–1.68)	0.44
Permanent complication	19/61 (31.1)	7/28 (25.0)	12/33 (36.4)	0.58 (0.19–1.77)	0.50

Percentages are of patients with a documented value for the corresponding complication. NA denotes not applicable: surgical complications cannot occur in the embolization-alone group, and odds ratios were not estimable when a group contained zero events. All comparisons were exploratory and were not adjusted for multiple comparisons

is procedural quality. Taken together, technical success should be regarded not as a passive procedural endpoint but as a quality metric that is sensitive to operator training, case selection, and adherence to defined embolization technique, and therefore amenable to standardization and benchmarking as MMAE adoption expands.

The finding of comparable safety between stand-alone and combined MMAE strategies addresses a clinically important gap. Among 1552 patients with documented surgical approach, 860 (55.4%) underwent embolization alone and 692 (44.6%) underwent surgery plus embolization, with no significant differences in complication rates, in-hospital mortality (2.9% vs. 2.6%; $p=0.80$), neurological deterioration (27.9% vs. 26.0%; $p=0.55$), rescue surgery (5.4% vs. 6.1%; $p=0.59$), readmission (17.7% vs. 18.7%; $p=0.65$), or technical success (98.3% vs. 97.7%; $p=0.43$). While prior studies have evaluated MMAE both as monotherapy and as a surgical adjunct, direct safety comparisons in large multicenter cohorts have been limited [20–22]. Our data suggest that the choice between stand-alone and combined strategies should be guided by symptom burden, hematoma size, and mass effect, urgency of decompression, and institutional expertise rather than by differential short-term safety concerns [23, 24].

The granular characterization of specific complications provides actionable information for patient selection and informed consent. Thromboembolic events or stroke constituted the most common complication subtype (37.2% of specified complications; 32 of 86 patients), followed by hemorrhagic complications (23.8%; 20 of 84). These two categories together accounted for over 60% of adverse events and underscore the need for meticulous catheter technique, vigilance for routes of unintended intracranial or ophthalmic embolization, and careful peri-procedural antithrombotic management, particularly given that 49.4%

of this cohort was on antithrombotic therapy at baseline (33.2% antiplatelet agents, 23.8% anticoagulants) [25–27]. Evidence-based antiplatelet and anticoagulant pathways specific to MMAE remain underdeveloped and represent an important area for future investigation [28–30]. Access-site hematoma (10.4%; 8 of 77) and cranial nerve injury (3.8%; 3 of 79) were less frequent, and unintended embolization of dangerous collateral vessels occurred in 2.9% (4 of 137) of evaluable patients. Although uncommon, catastrophic nontarget embolization remains a central concern given the anatomic proximity of extracranial-intracranial anastomoses and cranial nerve vascular supply to the MMA territory [31]. When stratified by treatment approach, thromboembolic events were numerically more frequent in the combined group (50.0% vs. 35.7%; $p=0.32$), while hemorrhagic complications trended higher in the stand-alone group (31.7% vs. 12.9%; $p=0.09$), although neither difference reached statistical significance. These patterns warrant further exploration in larger, prospectively adjudicated datasets. More broadly, these data support the adoption of standardized complication reporting that explicitly characterizes severity, permanence, and timing to improve cross-study comparability and align safety reporting with patient-centered outcomes. Notably, among 67 patients with determinable symptom status, only 80.6% of documented complications were symptomatic, yielding an effective symptomatic complication rate of 3.0% (54 of 1781). Asymptomatic events, predominantly access-site findings, vasospasm, contrast extravasation, and incidental nontarget embolization detected on angiography, accounted for the remainder and, while clinically silent in the short term, warrant documentation because they may inform procedural technique refinement and long-term surveillance.

The 27.1% rate of neurological deterioration captures a broad composite ranging from transient confusion to per-

sistent focal deficits in an elderly cohort (mean age 72.8 years) and reflects both procedure-related events and the natural history of chronic subdural hematoma. When stratified, the majority of evaluable events were mild (63.2%) and a substantial fraction were transient with full return to pre-morbid baseline at last follow-up (38.3% of survivors), tempering the implication of the headline rate. This rate did not differ significantly between stand-alone MMAE and combined treatment (27.9% vs. 26.0%; $p=0.55$), suggesting that surgical evacuation did not confer additional neurological risk in this comparison. Future MMAE registries and trials should prespecify objective neurological outcome instruments (such as the NIHSS at admission, discharge, and 30 days; the modified Rankin Scale at 30 and 90 days; and validated delirium screens) with independent adjudication, so that procedure-related neurological injury can be distinguished cleanly from disease- and age-related trajectories. Subgroup analyses demonstrated generally consistent complication rates across demographic and clinical strata. Complication rates were identical between males and females (5.1% each) and showed no clear age gradient, ranging from 4.6% in patients younger than 65 years to 6.8% in those 85 years or older. Patients receiving antithrombotic therapy had a numerically higher complication rate (5.5% vs. 4.8%) that did not reach statistical significance, though the clinical relevance of antithrombotic management in this population remains an important consideration given the high baseline prevalence of these medications. The consistency of complication rates across subgroups supports the generalizability of the overall safety profile, although formal interaction analyses in larger datasets are needed to detect potentially meaningful effect modification.

Prior randomized and registry data suggest that liquid embolic agents may achieve more durable hematoma resolution in cSDH than particles. In our cohort, however, 30-day procedure-related complication rates did not differ significantly across embolic-agent classes (chi-square $p=0.32$), and the numerical point estimate for the prespecified liquid-versus-particles comparison ran in the opposite direction from what an efficacy-driven hypothesis would predict (particles 4.71% vs. liquid 6.08%; OR for particles, 0.76; 95% CI, 0.48 to 1.21; $p=0.25$). Within the liquid class, crude rates were lowest for Squid (4.30%) and highest for Onyx (7.92%). These comparisons are exploratory, unadjusted for confounding by indication, and underpowered for definitive inference at this event rate; embolic selection in this cohort was at operator discretion and likely correlated with case complexity, vascular anatomy, and site-level preferences that themselves influence complication risk. Taken together, the efficacy advantage of liquid embolics reported in the cSDH literature does not appear to extend to a measurable short-term safety advantage in this

cohort, and prospective head-to-head reporting of agent-stratified safety endpoints remains needed.

Limitations

This study has several limitations. The retrospective design introduces potential selection bias and precludes causal inference. Although IPTW was used to adjust for measured confounders including age, sex, GCS score, platelet count, hemoglobin level, prior subdural hematoma, bilateral disease, concurrent surgical decompression, dangerous collateral vessels, antithrombotic therapy, and surgical approach, unmeasured confounding remains possible, including operator experience, anatomic complexity, embolic agent selection, and center-specific peri-procedural protocols. Technical failure was uncommon (2.5%), and estimates of its association with complications may be unstable due to event sparsity in this subgroup. Adverse event attribution relied on retrospective documentation and likely varied across centers, introducing potential classification heterogeneity. Adverse-event ascertainment and classification relied on local site investigators using a common structured case-report form rather than independent central adjudication. This may have introduced between-site variability in detection thresholds and category assignment, and accounts for the proportion of events classified as indeterminate when the source documentation did not allow confident assignment of symptom status. Future prospective registries should incorporate independent adjudication and image-based event verification. Because secondary, subgroup, and complication-subtype analyses were not adjusted for multiple comparisons, the probability of one or more chance findings (type I error) is elevated. These analyses should be interpreted as exploratory and require confirmation in independent cohorts. Outcome data were not uniformly available for all secondary endpoints, with evaluable denominators ranging from 915 (neurological deterioration) to 1625 (in-hospital mortality), reflecting incomplete capture inherent to multicenter retrospective designs. Longer-term outcomes beyond 90 days were not systematically collected, and heterogeneity in embolic agents and technical strategies across sites may influence adverse event profiles in ways not fully captured. Future studies should prioritize prospective data collection with standardized outcome definitions, extended follow-up incorporating functional status and quality-of-life measures, and detailed reporting of angiographic anatomy and embolization strategy to enable meaningful subgroup safety analyses.

Conclusion

In this multicenter cohort of 1781 patients undergoing MMAE for cSDH, the 30-day procedure-related complication rate was 5.1%, with 3.0% being symptomatic. In-hospital mortality was 2.9%, and neurological deterioration occurred in 27.1% of evaluable patients, reflecting a composite measure that encompasses both procedure-related events and the natural history of this disease in an elderly population. Technical success was achieved in 97.5% of procedures and was independently associated with an 86% reduction in complication odds, supporting its role as a key quality metric. Complications were predominantly thromboembolic (37.2% of documented complications) and hemorrhagic (23.8%), highlighting the importance of meticulous technique, anatomic vigilance, and optimized peri-procedural antithrombotic management. Safety profiles were comparable between stand-alone embolization and combined surgical-embolization strategies, enabling individualized treatment selection based on clinical factors without differential short-term risk. Prospective multicenter studies with standardized definitions, independent event adjudication, and long-term follow-up are needed to refine risk stratification and evaluate how procedural and pharmacological variables influence safety outcomes.

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Data Availability The datasets generated and/or analyzed during the current study are not publicly available due to institutional data-sharing agreements and privacy restrictions but are available from the corresponding author on reasonable request and with permission of the participating institutions.

Declarations

Competing interests The following authors have declared conflicts of interest: • Matthew Alexander, MD: Medtronic, J&J Cerenovus, Route 92 Medical, Certus Critical Care, Piraeus Medical, Stryker, Galaxy Therapeutics. • Dominik F. Vollherbst, MD: Medtronic • Markus A. Möhlenbruch, MD: Johnson & Johnson, Balt, Siemens, Medtronic, TerumoNeuro, Stryker • Clemens M. Schirmer, MD: Medtronic, Stryker, Viz.ai, Balt, Microvention, Werfen, NTI, Reist, Penumbra, Cerenovus, Route 92, MIVI, NICO, NIH/NINDS • Fabio Settecase, MD, MSc: Stryker, Route 92 Medical, Medtronic, Microvention; Site-PI EMBOLISE trial • Stavropoula Tjoumakaris, MD: MicroVention, Medtronic (Consultant, Research grant) • Pascal Jabbour, MD:

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