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SYSTEMATIC REVIEW/META-ANALYSIS

Middle meningeal artery embolization for non-acute subdural hematoma: a meta-analysis of large randomized controlled trials

Huanwen Chen, Matthew K McIntyre, Peter Kan, Dheeraj Gandhi, and Marco Colasurdo

ABSTRACT

BACKGROUND: Middle meningeal artery embolization (MMAE) has emerged as a novel treatment for non-acute subdural hematoma (SDH), particularly for reducing the risk of SDH recurrence. Recently, five randomized controlled trials (RCT) of MMAE as an adjunct to conventional management (surgical or observant) have concluded their investigation and reported their outcomes.

PURPOSE: To synthesize trial results to provide more definitive guidance on the role of MMAE in the management of non-acute SDH.

DATA SOURCES: MEDLINE database from inception up to November 23, 2024. English-language clinical articles reporting large randomized controlled trials (n=100 or more) investigating the efficacy and safety of MMAE for non-acute subdural hematoma patients were identified.

STUDY SELECTION: Five trials were identified – EMBOLISE, STEM, MAGIC-MT, EMPROTECT, and MEMBRANE.

DATA ANALYSIS: The primary efficacy endpoint was SDH treatment failure (broadly defined as SDH recurrence or requirement of surgical rescue) within 3 to 6 months. Safety endpoints include death and stroke.

DATA SYNTHESIS: There was significant heterogeneity in terms of patient populations as well as reported outcomes. Overall, MMAE was associated with significantly lower odds of SDH treatment failure (OR 0.51 [95%CI 0.39 to 0.67], p<0.001), with minimal inter-study heterogeneity. Compared to conventional management, MMAE was not significantly associated with different odds of death (OR 1.03 [95%CI 0.36 to 2.99], p=0.95) or stroke (OR 1.10 [95%CI 0.36 to 3.39], p=0.86).

LIMITATIONS: Our meta-analysis is limited by selection bias and high heterogeneity in study design and reported outcomes.

CONCLUSIONS: This study provides high-level evidence that, for patients with non-acute SDH, MMAE is safe and effective an adjunct to conventional management for preventing treatment failure.

ABBREVIATIONS: SDH = subdural hematoma; MMAE = middle meningeal artery embolization; RCT = randomized controlled trial.

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INTRODUCTION

Non-acute subdural hematoma (SDH) is a common pathology that is expected to surpass intracranial tumors as the most common cranial neurosurgical disease by 2030(1,2). Patients often present with headaches, seizures, or focal neurological deficits, and non-acute SDH is a major cause of morbidity and mortality(1). Conventionally, non-acute SDHs are managed with surgical drainage(3). Some patients, particularly those with smaller, less symptomatic hematomas or those who are not good surgical candidates, are managed expectantly(4). While many non-acute SDHs will resolve with conventional management, a substantial portion of patients will experience disease recurrence requiring surgical rescue, thus posing a unique clinical challenge(3).

Recently, middle meningeal artery embolization (MMAE) has emerged as a novel treatment for non-acute SDHs, and an expanding body of literature has suggested that MMAE as an adjunct to conventional management may be effective in reducing SDH recurrence(5–9). As such, multiple large randomized controlled trials (RCTs) were launched to formally assess MMAE's efficacy and safety(1). Recently, five trials have concluded their investigation and reported their outcomes – EMBOLISE(10), STEM(11), MAGIC-MT(12), EMPROTECT(13), and MEMBRANE(14). In this study, we seek to synthesize trial results to provide more definitive guidance on the role of MMAE in the management of non-acute SDH.

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MATERIALS AND METHODS

This study complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines(15). As meta-analysis of published data, this study did not involve human subjects; thus, ethics approval or informed consent was not required.

We searched the MEDLINE database from inception up to November 23, 2024 for English-language clinical articles reporting large randomized controlled trials investigating the efficacy and safety of MMAE for non-acute subdural hematoma patients. Studies were identified by the search terms "randomized," "middle meningeal artery," and "subdural" used in combination. Retrospective studies and non-randomized prospective studies were excluded. Trial protocols, review articles, meta-analyses, and non-research articles were excluded. Given the low rates of surgical recurrence reported in the literature, comparisons of small cohorts are likely to lack statistical power; thus, only studies with at least 100 participants were included. Eligible studies identified via other sources, such as conference proceedings, were also included. The Cochrane Handbook for Systematic Reviews of Interventions(16) highly recommend the inclusion of gray literature (available but unpublished data), specifically conference abstracts, to limit publication biases. Titles and abstracts of search results were screened independently by two investigators for eligibility. Risk of bias was assessed using the Rob-2 tool(17). Disagreements were resolved by consensus.

The following data were then extracted: trial name, patient inclusion/exclusion criteria, primary outcome, number of patients, patient demographics, presenting symptoms, laterality of SDH, SDH volume, SDH thickness, midline shift, and percentage of missing data were extracted. Outcomes of interest SDH recurrence, surgical rescue, patient death, and ischemic stroke.

For meta-analyses, effect sizes (odds ratios) of MMAE on SDH treatment failure (as defined by each study) for the intention-to-treat cohorts were pooled using random-effects models. For studies that do not report odds ratios, calculations were made using raw counts data. For trials that report zero counts, Yates' continuity correction was made to calculate odds ratios. Safety endpoints include death and stroke. Subgroup analyses were performed to assess the odds of the primary endpoint in surgical and non-surgical SDH patients. Estimates from individual studies and pooled estimates were presented using forest plots. Heterogeneity between studies was quantified using Cochran's Q and I-squared values. Egger's tests were used to assess publication bias. P-values less than 0.05 were considered statistically significant for overall effect estimates and Egger's tests, and p-values less than 0.10 were considered statistically significant for tests of homogeneity. Statistical analyses were conducted via SPSS (version 29.0).

RESULTS

Study and patient characteristics

Fifty-four results were identified during literature search; seven randomized controlled trials of MMAE as an adjunct to conventional management remained after abstract and title screening. Two of the seven studies had total recruitment of less than 100 patients were excluded, leaving five studies – EMBOLISE(10), STEM(11), MAGIC-MT(12), EMPROTECT(13,18), and MEMBRANE (14)(Figure S1). A summary of study protocols is detailed in Table 1, and patient characteristics are detailed in Table 2. Patient characteristics for EMPROTECT and MEMBRANE are not available at this time as while the primary outcomes were presented (at ESMINT 2024 and SVIN 2024, respectively(13,14)), final publication is pending. The final analysis of EMPROTECT included 319 patients, while MEMBRANE included 376.

Overall, the primary outcome for each trial varied (Table 1). Other notable design differences include type of SDHs – EMBOLISE and MAGIC-MT included patients with subacute and chronic SDH patients, while STEM, EMPROTECT, and MEMBRANE only included chronic SDH patients. However, as the definition of SDH chronicity is not well established; some trials formally used percentage of iso- hypo-intensity on CT imaging for patient selection (EMBOLISE, STEM, and MEMBRANE), while others did not (MAGIC-MT and EMPROTECT). Thus, whether these discrepancies in non-acute SDH classifications reflected meaningful differences in patient characteristics is unclear. Length of follow-up also varied across trials – EMBOLISE and MAGIC-MT followed patients for 90 days, while STEM, EMPROTECT, and MEMBRANE followed patients for 180 days. Another key difference was the number of patients who received surgical drainage, which ranged from approximately 60% in the STEM trial to 100% in the EMBOLISE and EMPROTECT trials due to protocol differences (Tables 1 and 2). There was also significant variability in number of patients with missing primary endpoint data requiring data imputation, ranging from 0% in MAGIC-MT to approximately 20% in STEM (which the study investigators attribute to the COVID-19 pandemic). The number of patients who did not receive the randomized treatment was higher in the MMAE arm for EMBOLISE, STEM, and MAGIC-MT, likely due to the discovery of dangerous anastomoses in which case MMAE cannot be safely performed per protocol with liquid embolic agents.

There was also some heterogeneity in how each trial dealt with treatment crossovers and patient death prior to occurrence of the primary endpoint. EMBOLISE continued to follow patients who were not treated with the randomized assignment for their intention-to-treat analysis, however, patients who did not have available 90-day follow-up due to withdrawal from the study, loss-to-follow-up, or death had their outcomes imputed randomly. STEM did not follow patients who did not receive assigned treatments, and randomly imputed primary endpoint data for those without evaluable 180-day outcomes due to non-neurological death, withdrawal, or lost to follow-up. MAGIC-MT had no withdrawals or lost to follow-up in their intention-to-treat cohorts, and continued to follow patients who did not receive the assigned treatments. Furthermore, MAGIC-MT considered death prior to recurrence as no recurrence; as such, there was no missing data that required imputation. Per the published protocol, EMPROTECT considered all-cause death as treatment failure during missing data imputation. Exact details regarding the handling of missing data in EMPROTECT and MEMBRANE are not available currently.

For risks of bias, EMBOLISE, MAGIC-MT, and STEM were deemed to have low risks in the "randomization process" and "selection of reported results" domains, and some concerns in the "deviations from the intended treatment" and "measurement of the outcome" domains (due to treatment crossovers, withdrawals, and open-label nature of the studies). For the "missing data" domain, there were some concerns for the EMBOLISE and STEM trials, and low concern for the MAGIC-MT study. Overall, all three trials had some concerns of bias, possibly favoring MMAE. Risk of bias assessment was partially performed for the EMPROTECT and MEMBRANE trials based available information on the trial protocols, and they were deemed to have at least some concerns of bias, possibly favoring MMAE, due to the open-label nature of the studies.

Table 1: Study Characteristics.

Characteristic	**EMBOLISE**	**STEM**	**MAGIC-MT**	**EMPROTECT**	**MEMBRANE**
Study design	Open Label RCT	Open Label RCT	Open Label RCT	Open Label RCT	Open Label RCT
Location	USA	USA	China	France	United States and China
Treatment arms					
Control	Burr-hole or craniotomy	CM (burr-hole, SEPS, or expectant management)	CM (burr-hole or expectant management)	Burr-hole only	CM (surgical evacuation or expectant management)
Experimental	MMAE + Surgery	MMAE + CM	MMAE + CM	MMAE + Surgery	MMAE + CM
Embolic Agent	Onyx (liquid non-adhesive)	SQUID (liquid non-adhesive)	Onyx (liquid non-adhesive)	EmboSpheres (particles) or proximal coiling	TRUFILL n-BCA (liquid adhesive)
Timing of MMAE relative to surgery	Before or after	Before	Before	After	Before or after
Inclusion criteria					
Age (years)	18-90	≥30	≥18	≥18	18-90
Chronicity	Subacute or chronic	Chronic	Subacute or chronic	Chronic	Chronic
Hematoma size	>15mm or midline shift >5mm	>10mm	Mass-effect	Not specified	Not specified
Pre-randomization mRS	0-3	0-1	0-2	0-3	0-3
Other inclusion criteria	Focal motor deficit attributable to the SDH, or a neurologic symptoms beyond headache, imbalance, and confusion;	Presence of neurological symptoms	Presence of neurological symptoms with mass-effect	Presenting as a recurrent SDH, or at high risk of recurrence following burr-hole surgery	-
Exclusion criteria	Life expectancy <1 year, Markwalder Granding Score >3	Undergone craniotomy, urgent emergent procedure, life expectancy <1 year, others	Bilateral SDH with unknown symptom source, serious or fatal co-existing condition or life, expectancy <1 year, emergency evacuation, craniotomy	Beyond 7 days after index surgery, life expectancy <6 months, renal failure, received twist-drill craniostomy or craniotomy	Prior treatment of target SDH, severe impairment in wakefulness, life expectancy <1 year
Primary endpoint	Hematoma recurrence or progression that led to repeat surgery	Recurrent or residual cSDH >10mm; reoperation or surgical rescue, major disabiling stroke, MI, neurological death	Symptomatic recurrence or progression of subdural hematoma	Symptomatic recurrence with cSDH >5mm or requiring hospitalization, residual cSDH >10mm, re-operation	Recurrent or residual cSDH >10mm; reoperation or surgical rescue,
Follow-up duration	90 days	180 days	90 days	180 days	180 days

Abbreviations: CM = conventional management, SEPS = subdural evacuating system, mRS = modified Rankin Scale, cSDH = chronic SDH.

PRISMA checklist (Online supplement)

Table 2: Patient population.

	EMBOLISE		**STEM**		**MAGIC-MT**	
Characteristic - mean (SD), median (IQR), or % (n)	*Control (N=203)*	*MMAE (N=197)*	*Control (N=161)*	*MMAE (N=149)*	*Control (N=362)*	*MMAE (N=360)*

Age	71 (11)	73 (11)	73 (11)	73 (10)	70 (61-75)	69 (60-74)
Male sex	73.4% (149)	72.6% (143)	74% (119)	65% (97)	84.0% (304)	81.1% (292)
Surgical drainage	100.0% (203)	100.0% (197)	60.9% (98)	61.1% (91)	78.5% (284)	78.1% (281)
Symptoms						
Headache	71.9% (146)	68.5% (135)	59% (95)	65% (97)	54.4% (197)	57.2% (206)
Gait instability	67.5% (137)	71.1% (140)	47% (75)	46% (68)	36.5% (132)	37.2% (134)
Limb weakness or hemiparesis	57.6% (117)	58.4% (115)	-	-	48.6% (176)	53.3% (192)
Cognitive impairment	45.3% (92)	45.2% (89)	28% (45)	28% (42)	8.3% (30)	10.3% (37)
Speech Disturbance	-	-	24% (39)	17% (26)	8.8% (32)	10.8% (39)
Focal neurological deficit	42.4% (86)	34.5% (68)	-	-	-	-
Antiplatelet or Anticoagulant use	38.9% (79)	38.1% (75)	42% (67)	38% (56)	6.9% (25)	7.8% (28)
SDH characteristics						
Bilateral hematoma	18.2% (37)	21.3% (42)	23% (37)	17% (26)	0.0% (0)	0.0% (0)
Volume (cc)	236 (118)	223 (110)	-	-	119 (88-142)	117 (93-144)
Thickness (mm)	21 (6)	22 (6)	18 (6)	18 (6)	22 (19-27)	23 (19-27)
Midline shift (mm)	8.6 (4.1)	7.9 (3.6)	5.6 (3.5)	5.8 (3.7)	10.8 (6.9-13.2)	10.5 (7.3-13.6)
Data completeness						
Did not receive randomized treatment	0.5% (1)	6.1% (12)	1.2% (2)	3.1% (5)	0.8% (3)	1.9% (7)
Withdrew/lost to followup	6.4% (13)	7.6% (15)	16.1% (26)	8.1% (13)	0.0% (0)	0.0% (0)
Died prior to primary endpoint	2.0% (4)	4.5% (9)	2.5% (4)	6.8% (11)	2.2% (8)	0.6% (2)
Missing primary endpoint requiring imputation	8.4% (17)	12.2% (24)	19.8% (32)	19.5% (29)	0.0% (0)	0.0% (0)

Efficacy outcomes

Overall, STEM, EMBOLISE, and MEMBRANE met primary efficacy outcomes, while MAGIC-MT and EMPROTECT did not. To synthesize outcomes, we compiled the odds of SDH treatment failure from each study, using estimates calculated after imputation of missing values per each trial's respective protocols. Overall, MMAE was associated with significantly lower odds of treatment failure (OR 0.51 [95%CI 0.39 to 0.67], p<0.001, Figure 1), and the prediction interval also reflected significant treatment benefit (OR 0.33 to 0.79, Figure 1). There was a low level of inter-study heterogeneity (I-squared=0%, Q-statistic=3.35, p=0.50, Figure 1), suggesting that despite significant variability in trial protocols, follow-up duration, and outcome measures, the effect sizes of MMAE on preventing SDH treatment failure consistent across the meta-analyzed trials. Egger's test did not reveal significant publication bias (p=0.30).

Next, we explored the effect of MMAE on surgical and non-surgical SDH patients. Here, we found that MMAE as an adjunct to surgical drainage was superior to surgery alone (OR for 3-6 month treatment failure 0.63 [95%CI 0.44 to 0.89], p=0.008, Figure S2A), again with a low level of inter-study heterogeneity (I-squared=0%, Q-statistic=2.98, p=0.40; Figure S2A). Egger's test did not reveal significant publication bias (p=0.51). For non-surgical SDH patients, standalone MMAE was significantly associated with lower odds of treatment failure (OR 0.25 [95%CI 0.13 to 0.48], p<0.001; Figure S2B), also with a low level of inter-study heterogeneity (I-squared=0%, Q-statistic=0.85, p=0.36; Figure S2B). Prediction interval and Egger's test were not assessed as only two studies reported the effect of MMAE for non-surgical SDH patients. Of note, while MEMBRANE included both surgical and non-surgical patients, the effect of MMAE on each subgroup has not been publicized at this time and thus were not incorporated in this study.

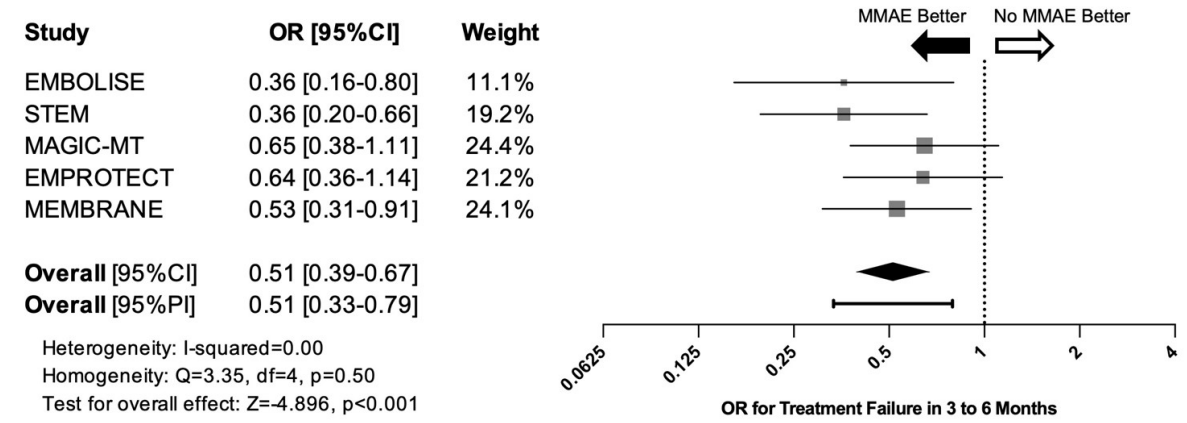

FIG 1. Forest plot of the effect of middle meningeal artery embolization (MMAE) on rates of subdural hematoma (SDH) treatment failure within 3 to 6 months, compared to conventional management. SDH recurrence, residual SDH, and requirement of surgical rescue were considered treatment failures for EMBOLISE, STEM, EMPROTECT, and MEMBRANE. MAGIC-MT only considered SDH recurrence and surgical rescue in defining treatment failure, while STEM additionally considered disabling stroke, myocardial infarction, and neurological death. Abbreviations: CI – confidence interval, PI – prediction interval.

Safety outcomes

For safety outcomes, we assessed the impact of MMAE on risk of all-cause mortality and stroke. For mortality, MMAE was not associated with significantly different odds compared to no MMAE (OR 1.03 [95%CI 0.36 to 2.99], p=0.95; Figure 2), however, there was significant inter-study heterogeneity (I-squared=62%, Q-statistic=4.85, p=0.089; Figure 2), where MAGIC-MT reported a numerically lower mortality risk associated with MMAE, while EMBOLISE and STEM reported the opposite (Figure 2). There were no significant differences in stroke risk between MMAE vs. no MMAE (OR 1.19 [95%CI 0.50 to 2.81], p=0.69, Figure 2), with minimal levels of inter-study heterogeneity (I-squared=0%, Q-statistic=0.63, p=0.73; Figure 2). Egger's tests did not reveal significant publication biases for death or stroke outcomes (p=0.29 and 0.52, respectively). At the time of this publication, EMPROTECT has not published death or stroke events, and MEMBRANE has not published death events.

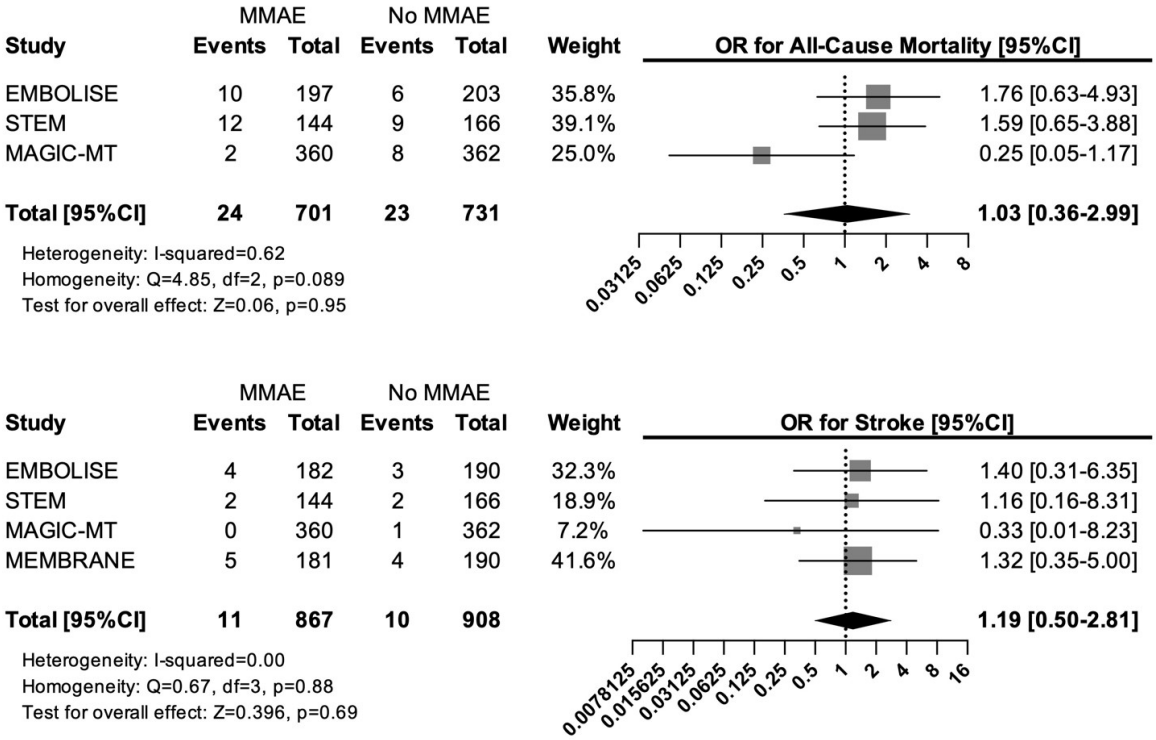

FIG 2. Forest plots of MMAE's impact on all-cause mortality and stroke within 3 to 6 months, compared to conventional management. For the stroke outcome, STEM reported major disabling stroke, whereas EMBOLISE, MAGIC-MT, and MEMBRANE reported all ischemic stroke. Given that the MMAE arm of MAGIC-MT had no stroke events, odds ratio was calculated with continuity correction. At the time of this publication, EMPROTECT has not published death or stroke events, and MEMBRANE has not published death events.

DISCUSSION

In this systematic review and meta-analysis of large randomized controlled trials of MMAE as an adjunct to conventional management of non-acute SDH patients, we found that MMAE is effective in preventing SDH recurrence for both surgical and non-surgical patients, while it was not significantly associated with higher odds of all-cause mortality or ischemic stroke.

While our meta-analysis found that MMAE is overall effective in reducing the risk of treatment failure with conventional management alone, it is important to recognize that only three of five trials (EMBOLISE(10), STEM(11), and MEMBRANE) met their primary endpoint. Thus, there appears to be substantial variability in MMAE treatment effectiveness across individual patients. This phenomenon likely stems from the highly heterogeneous nature of SDH pathology. For instance, SDH can present with various morphologies, which may portend significant differences in recurrence risk(19,20). None of the included trials stratified or selected patients based on radiographic predictors of SDH recurrence. Underlying risk factors such as coagulopathy, thrombocytopenia, and antithrombotic medication use may also influence SDH recurrence risk and MMAE efficacy(1,8,21); here, only EMPROTECT incorporated these factors into the trial design. Finally, while MMAE appeared to be effective, the absolute rate of recurrence without MMAE, especially among surgically evacuated patients, was lower than previously believed (6.7% in MAGIC-MT and 11.1% in EMBOLISE by 90 days)(3), and such low event rates present challenges on the accuracy of effect estimates despite a large number of enrolled patients. Interestingly, despite these challenges, the pooled estimates across the five meta-analyzed trials point to a convincing efficacy of MMAE. Thus, we believe our results provide high-level evidence that MMAE is a generally effective treatment for all non-acute SDH patients, likely regardless of their baseline risk of recurrence.

It is also important to note that while the five included trials diverged substantially on trial design (which has raised concerns in the past(22)), the effect size of MMAE appeared to be consistent with minimal levels of inter-study heterogeneity detected during meta-analysis. This observation provides key insights. First, MMAE is likely effective in preventing treatment failure in both surgical and non-surgical patients, an inference supported by our subgroup analyses. Second, the embolic agent (liquid non-adhesive, liquid adhesive, or particles) does not appear to overtly make a difference. Third, the safety data reported are consistent and reassuring. One of the most dreaded complications for MMAE is the inadvertent embolization of intracranial and/or extra-cranial vascular anastomoses (e.g. ophthalmic artery or petrosal branch of MMA). Prior reports have suggested a stroke risk of approximately 1% with MMAE(8), which was consistent with findings in this study (1.3%, 11 of 867 patients). Interestingly, stroke risk was similar in the control arm, suggesting that MMAE did not significantly increase stroke risk. One possible explanation of a lack of increased stroke risks in these trials is that these patients were likely carefully selected and are at very low risk of peri-procedural stroke. Future prospective studies are needed to confirm the safety of MMAE in a real-world setting. Of note, while MMAE did not significantly impact all-cause mortality risk across EMBOLISE, STEM, and MAGIC-MT, there was significant inter-study heterogeneity. Chronic SDH is known to be associated with increased mortality risk that can persist for decades, and the underlying pathophysiology of this phenomenon is not well understood(23,24). Future studies are needed to better explore the impact of MMAE on long-term patient mortality.

Our study has several limitations. First, while our study found that MMAE is effective for non-surgical patients, these data were derived from minority subgroups of two trials (STEM and MAGIC-MT) that did not specifically power enrollment for this patient population. Furthermore, both STEM and MAGIC-MT required large SDHs for enrollment, so it is likely that medically managed patients were poor surgical candidates that may have otherwise benefited from surgery, as opposed to those with smaller hematomas and milder symptoms. Future dedicated studies and reports (e.g. the non-surgical arms of EMBOLISE [NCT04402632] and MEMBRANE [NCT04816591]) are needed to confirm the safety and efficacy for standalone MMAE compared to observation, particularly for patients with smaller and clinically milder SDHs. Second, while MMAE performed well both with and without concomitant surgery, these trials did not compare standalone MMAE versus MMAE combined with surgery. While standalone MMAE has been suggested as a potentially safe and efficacious alternative to MMAE combined with surgery(6,25), the current data do not support standalone MMAE by patients who would otherwise be surgical candidates(1), and future trials are needed to further explore whether surgery can be replaced by MMAE in select patients. Finally, our meta-analysis included results from the EMPROTECT and MEMBRANE studies, these data were presented but not yet published at the time of writing this manuscript (13,14); thus, we were unable to fully evaluate trial data and protocols, and it is possible that there may be inaccuracies. However, the Cochrane Handbook for Systematic Reviews of Interventions(16) highly recommends the inclusion of gray literature (available but unpublished data), specifically conference abstracts, to limit publication biases. Nevertheless, we will actively monitor the literature for the eventual publication of these trials, and if the eventually published results significantly alter the conclusions of the present manuscript, we will submit a corrigendum to this manuscript as appropriate.

CONCLUSIONS

This study provides high level evidence that, among patients with non-acute SDH, MMAE is an effective adjunct to conventional management to prevent SDH treatment failure.

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REFERENCES

1. Kan P, Fiorella D, Dabus G, et al. ARISE I Consensus Statement on the Management of Chronic Subdural Hematoma. Stroke. 2024;55(5):1438–1448. doi: 10.1161/STROKEAHA.123.044129.
2. Balser D, Farooq S, Mehmood T, Reyes M, Samadani U. Actual and projected incidence rates for chronic subdural hematomas in United States Veterans Administration and civilian populations. J Neurosurg. 2015;123(5):1209–1215. doi: 10.3171/2014.9.JNS141550.
3. Ducruet AF, Grobelny BT, Zacharia BE, et al. The surgical management of chronic subdural hematoma. Neurosurg Rev. 2012;35(2):155–

169. doi: 10.1007/s10143-011-0349-y.

4. Bender MB, Christoff N. Nonsurgical Treatment of Subdural Hematomas. Arch Neurol. 1974;31(2):73–79. doi: 10.1001/archneur.1974.00490380021001.
5. Ironside N, Nguyen C, Do Q, et al. Middle meningeal artery embolization for chronic subdural hematoma: a systematic review and meta-analysis. J Neurointerv Surg. 2021;13(10):951–957. doi: 10.1136/neurintsurg-2021-017352.
6. Chen H, Colasurdo M, Kan PT. Middle meningeal artery embolization as standalone treatment versus combined with surgical evacuation for chronic subdural hematomas: systematic review and meta-analysis. J Neurosurg. 2023;1–7. doi: 10.3171/2023.7.JNS231262.
7. Jumah F, Osama M, Islim AI, et al. Efficacy and safety of middle meningeal artery embolization in the management of refractory or chronic subdural hematomas: a systematic review and meta-analysis. Acta Neurochir (Wien). 2020;162(3):499–507. doi: 10.1007/s00701-019-04161-3.
8. Salem MM, Kuybu O, Nguyen Hoang A, et al. Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: Predictors of Clinical and Radiographic Failure from 636 Embolizations. Radiology. 2023;307(4). doi: 10.1148/radiol.222045.
9. Kan P, Maragkos GA, Srivatsan A, et al. Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: A Multi-Center Experience of 154 Consecutive Embolizations. Neurosurgery. 2021;88(2):268–277. doi: 10.1093/neuros/nyaa379.
10. Davies JM, Knopman J, Mokin M, et al. Adjunctive Middle Meningeal Artery Embolization for Subdural Hematoma. New England Journal of Medicine. 2024;391(20):1890–1900. doi: 10.1056/NEJMoa2313472.
11. Fiorella D, Monteith SJ, Hanel R, et al. Embolization of the Middle Meningeal Artery for Chronic Subdural Hematoma. New England Journal of Medicine. 2024; doi: 10.1056/NEJMoa2409845.
12. Liu J, Ni W, Zuo Q, et al. Middle Meningeal Artery Embolization for Nonacute Subdural Hematoma. New England Journal of Medicine. 2024;391(20):1901–1912. doi: 10.1056/NEJMoa2401201.
13. Shotar E. The EMPROTECT randomized controlled trial, results and reflections on chronic subdural hematoma. European Society of Minimally Invasive Neurological Therapy Conference. 2024.
14. Rai A. Middle Meningeal Artery Embolization Treatment Of Subdural Hematomas With TRUFILL n-BCA: MEMBRANE Trial Primary Results. Society of Vascular and Interventional Neurology Conference. 2024.
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;n71. doi: 10.1136/bmj.n71.
16. Higgins JPT, Thomas J, Chandler J, et al., editors. Cochrane Handbook for Systematic Reviews of Interventions. Wiley; 2019. doi: 10.1002/9781119536604.
17. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;l4898. doi: 10.1136/bmj.l4898.
18. Shotar E, Mathon B, Rouchaud A, et al. Embolization of the middle meningeal artery for the prevention of chronic subdural hematoma recurrence in high-risk patients: a randomized controlled trial—the EMPROTECT study protocol. J Neurointerv Surg. 2024;jnis-2023-021249. doi: 10.1136/jnis-2023-021249.
19. Nakaguchi H, Tanishima T, Yoshimasu N. Factors in the natural history of chronic subdural hematomas that influence their postoperative recurrence. J Neurosurg. 2001;95(2):256–262. doi: 10.3171/jns.2001.95.2.0256.
20. Chen H, Colasurdo M, Malhotra A, Gandhi D, Bodanapally UK. Advances in chronic subdural hematoma and membrane imaging. Front Neurol. 2024;15. doi: 10.3389/fneur.2024.1366238.
21. Lee S, Srivatsan A, Srinivasan VM, et al. Middle meningeal artery embolization for chronic subdural hematoma in cancer patients with refractory thrombocytopenia. J Neurosurg. 2022;136(5):1273–1277. doi: 10.3171/2021.5.JNS21109.
22. Adusumilli G, Ghozy S, Kallmes KM, et al. Common data elements reported on middle meningeal artery embolization in chronic subdural hematoma: an interactive systematic review of recent trials. J Neurointerv Surg. 2022;14(10):1027–1032. doi: 10.1136/neurintsurg-2021-018430.
23. Rauhala M, Helén P, Seppä K, et al. Long-term excess mortality after chronic subdural hematoma. Acta Neurochir (Wien). 2020;162(6):1467–1478. doi: 10.1007/s00701-020-04278-w.
24. Miranda LB, Braxton E, Hobbs J, Quigley MR. Chronic subdural hematoma in the elderly: not a benign disease. J Neurosurg. 2011;114(1):72–76. doi: 10.3171/2010.8.JNS10298.
25. Chen H, Salem MM, Colasurdo M, et al. Standalone middle meningeal artery embolization versus middle meningeal artery embolization with concurrent surgical evacuation for chronic subdural hematomas: a multicenter propensity score matched analysis of clinical and radiographic outcomes. J Neurointerv Surg. 2023;jnis-2023-020907. doi: 10.1136/jnis-2023-020907.

Figure S1: PRISMA flow diagram

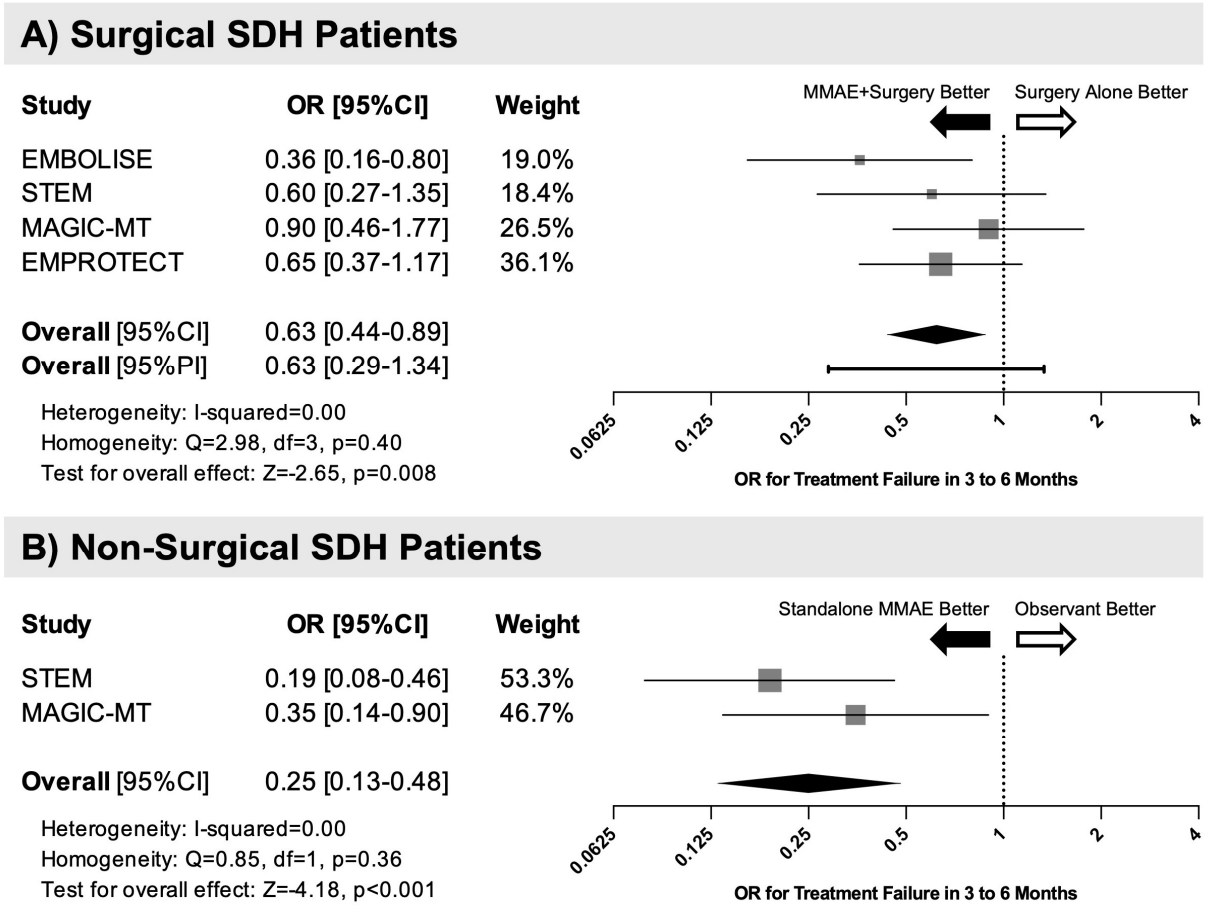

Figure S2: Forest plots of MMAE's effect on rates of subdural hematoma (SH) treatment failure within 3 to 6 months, compared to surgery (Panel A) or observant management (Panel B). SDH recurrence, residual SDH, and requirement of surgical rescue were considered treatment failure for EMBOLISE, STEM, and EMPROTECT. MAGIC-MT only considered SDH recurrence and surgical rescue in defining

treatment failure, while STEM additionally considered disabling stroke, myocardial infarction, and neurological death. Subgroup analyses for MEMBRANE have not been presented or published as the time of the present study. Abbreviations: CI - confidence interval, PI - prediction interval.