JVIN | Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF ZEENAT QURESHI STROKE INSTITUTE

Middle Meningeal Artery Embolization for the Management of Chronic Subdural Hematoma: Updated Systematic Review and Meta-Analysis

Fawaz Al-Mufti, MD,[1,2,*] Vincent Dodson, BS,[3] Alejandro Enríquez-Marulanda, MD,[4] Kelvin Zheng, BA,[1] Christian Bowers, MD,[5] Namhee Kim, BA,[6] Michael Kim, MD,[1] Jared Pisapia, MD,[1] Chad Cole, MD,[5] Justin Santarelli, MD,[1] Chirag Gandhi, MD.[1]

[1]*Department of Neurosurgery, Westchester Medical Center, Valhalla, NY*

[2]*Department of Neurology, Westchester Medical Center, Valhalla, NY*

[3]*Department of Neurosurgery, Rutgers New Jersey Medical School, Newark, NJ*

[4]*Department of Neurosurgery, Boston Medical Center, Boston, MA*

[5]*Department of Neurosurgery, University of New Mexico, Albuquerque, NM*

[6]*Department of Neurosurgery, Weill Cornell Medical College, New York, NY*

Abstract

Background— Embolization of the middle meningeal artery (MMA) has emerged as a treatment strategy for chronic subdural hematoma (cSDH). We performed a systematic review and a meta-analysis of currently published literature on MMA embolization in patients with cSDH.

Methods— We searched Pubmed, Medline, and Cochrane databases for all studies that described the use of MMA embolization in patients with cSDH. We conducted a meta-analysis on the resulting studies and calculated event rates of treatment failure, procedural complications, and clinical and radiological improvements. From studies that compared MMA embolization with conventional treatment, we calculated the rates of treatment failure as an outcome of both methods using a fixed effects model.

Results— In this review, we included eleven studies with 212 total cases of cSDH treated with MMA embolization. While the average length of time to follow-up evaluation ranged widely between studies (1 month to 4 years), of the included patients in this review, 97.2% (95% confidence intervals [CI] 94.2 to 100) showed reduced cSDH size; 96.8% (95% CI 93.8 to 99.8) showed improvement on the modified Rankin Scale (mRS). Overall procedural complications were reported in 0.2% (95% CI -1.8 to 2.1) of patients. Three studies comparing MMA embolization and conventional treatment demonstrated that MMA embolization was associated with lower rates of treatment failure defined as cSDH recurrence or persistence of cSDH of a width of greater than 10mm (odds ratio [OR] 0.06 CI 95% 0.02 - 0.23, $P<0.01$; I^2:0.0%).

Conclusion— Our meta-analysis shows that MMA embolization is effective in reducing cSDH volume and was associated with lower rates of treatment failure when compared with conventional therapy. Randomized clinical trials examining MMA embolization as a potential standard therapy in patients with cSDH are required.

Keywords— Embolization, middle meningeal artery, chronic subdural hematoma, endovascular.

INTRODUCTION

Chronic subdural hematoma (cSDH) is a common neurosurgical diagnosis in adults (Figure 1). Currently, the two main options for treating cSDH are conservative management and surgical management. Conservative management typically employs serial imaging, antifibrinolytics, or statins.[1] Surgery consists of hematoma removal using burr hole drainage or craniotomy. Surgical evacuation is at times limited due to recurrence of cSDH and many cSDH patients have several medical comorbidities precluding general anesthesia.

Embolization of the middle meningeal artery (MMA) for treating cSDH is a new minimally invasive option that may reduce the need for surgical evacuation with craniotomy (Figure 2). By embolizing the branches of the middle meningeal

Vol.12, No. 1, pp. 42-49, Published March, 2021.

***Corresponding Author:** Fawaz Al-Mufti, M.D., Neuroendovascular Surgery and Neurocritical Care Attending, Westchester Medical Center at New York Medical College, 100 Woods Road, Macy Pavilion 1331, Valhalla, NY 10595, Cell: (508) 847 - 9277 Office: (914) 493-8795 Fax: (914) 493-2424, Email: fawaz.al-mufti@wmchealth.org.

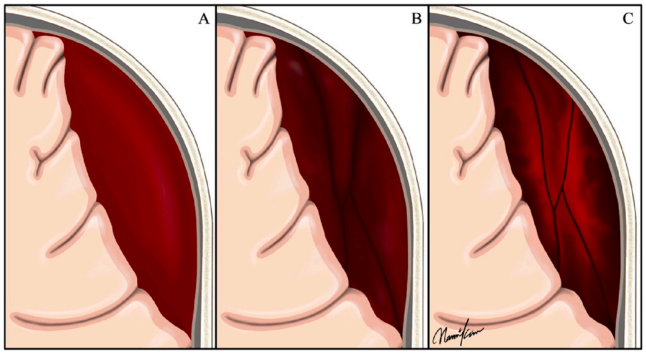

FIGURE 1: A representation of the pathogenesis of a chronic subdural hematoma. An acute subdural hematoma (A) liquefies and develops membranes, creating compartments within the chronic subdural hematoma (B). Microhemorrhages from these membranes lead to further enlargement of the chronic subdural hematoma (C).

artery which may contribute to neovascularization of cSDH, the rate of reabsorption of blood products becomes greater than the rate of their accumulation or rebleeding, leading to eventual resolution of cSDH. Most case series to date have reserved MMA embolization for cSDH patients who have failed surgical intervention.[2-7] The existing literature describing the natural history and outcomes for patients with cSDH who do not require surgical evacuation remains poorly defined. The role of MMA embolization in this subset of patients remains a point of debate in many institutions. Due to continued controversy, we performed a systematic review and meta-analysis of the current evidence for middle meningeal artery embolization for the management of cSDH.

METHODS

Literature search and study selection

A computerized literature search was done of Medline and Cochrane databases from inception to May 2019, with the following search terms: 'middle meningeal artery embolization', 'embolization', 'chronic subdural hematoma', 'outcome', 'endovascular treatment'. We also searched through the bibliography of the included studies to find additional studies that were not found in our initial literature search. Single case reports and duplicate publications were excluded. No other search restrictions were applied.

Two authors (VD and FAM) carried out the literature search and extracted data from relevant studies. The eligibility assessment of the articles was performed by the lead author (FAM).

Data Abstraction

From each included study, the following information was collected: type of study, age, sex, branches of MMA embolized, embolic materials used, previously failed surgical drainage before MMA embolization, use of adjunctive surgical drainage of cSDH with MMA embolization, MMA embolization procedural complications, mean follow-up, radiological improvement of SDH on follow-up, clinical improvement on follow-up (defined as mRS scores 0-2 or a decrease in at least 1 point) and treatment failure on follow-up (defined as recurrence of cSDH requiring surgical drainage).

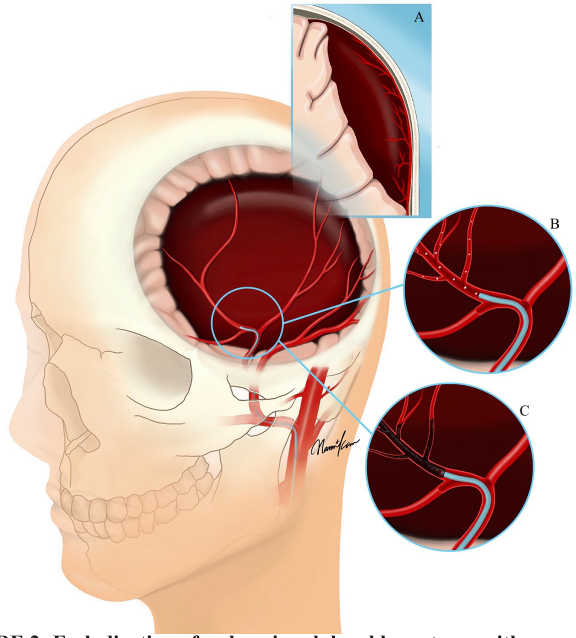

FIGURE 2: Embolization of a chronic subdural hematoma with neovascularization (A) of the subdural membranes. The microcatheter is within the anterior branch of the middle meningeal artery and there are two examples of embolization strategies: microparticles (B) and the Onyx liquid embolic system (C).

Statistical Analysis

The majority of included studies were single arm (non-comparative) with 3 studies that compared outcomes with MMA embolization with conventional management. Categorical variables were reported as proportions. Continuous variables were reported as mean ± standard deviation. For the non-comparative analysis, we estimated from each cohort the cumulative incidence (event rate) and 95% confidence intervals [CI] for each outcome. Event rates for each intervention were pooled across studies using meta-analysis with random effects model. For the comparative analysis, we used the studies by Ban et al.,[8] Kim et al.[9] and Matsumoto et al.[5] and compared the rates of treatment failure (recurrence of cSDH requiring surgical drainage) between MMA embolization and conventional management. Event rates for this comparative analysis were pooled across studies using meta-analysis with a fixed effects model as there was a low heterogeneity for treatment failure as an outcome among these specific studies. Heterogeneity of the treatment effect across studies was evaluated using the I^2 statistic, which was considered to indicate substantial heterogeneity if it was >50%. Publication bias was evaluated with a funnel plot for the comparative portion of the meta-analysis. Statistical significance was set to a p-value of less than 0.05. The meta-analysis was performed using STATA 14.0 software (StataCorp, Texas, USA).

RESULTS

Characteristics of Included Studies

The literature search yielded 45 articles, of which 34 were excluded because they were not relevant to our meta-analysis while the remaining 11 met our inclusion criteria (Table 1).[2-12] Six studies were single center case series, 4 were retrospec-

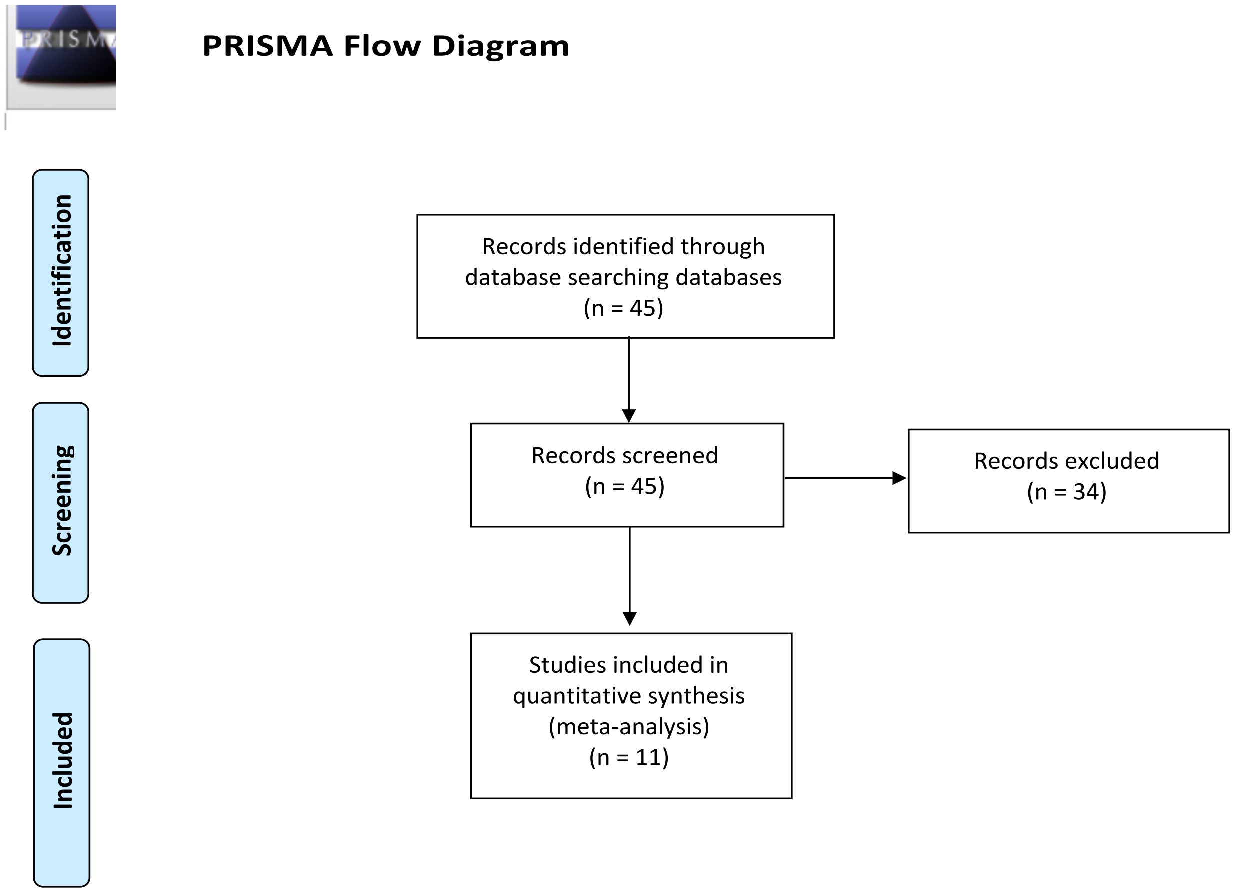

FIGURE 3: PRISMA flow diagram.

tive cohort studies and 1 was a prospective cohort study. Results of our PRISMA search are shown in Figure 3. A total of 212 chronic subdural hematomas treated with MMA embolization were included in this meta-analysis. Mean age (±standard deviation) of patients included was 72.5 (±5.2) years.

Non-comparative Analysis of Overall Outcomes

While time to follow-up varied from one month to four years, radiological evidence of cSDH size reduction was reported in 97.2% (95% CI 94.2 to 100) (Table 2). Clinical improvement rate was reported in 96.8% (95% CI 93.8 to 99.8) of treated patients. Treatment failure rate was 2.1% (95% CI -0.8 to 5.0). Procedural complications rate from MMA embolization was low and reported in 0.2% (95% CI -1.8 to 2.1) of treated patients.

Treatment failure comparative analysis

In three articles (Ban et al.,[8] Kim et al.[9] and Matsumoto et al.[5]) a total of 598 patients (96 who underwent MMA embolization and 502 who were treated with conventional treatment) were analyzed. MMA embolization had fewer treatment failures over three to six months compared with conventional treatment (odds ratio [OR] 0.06 95% CI 0.02 - 0.23, P<0.01; I^2:0.0%) (Figure 4). A funnel plot of the data showed a reasonable symmetric funnel shape, which may indicate that publication bias is unlikely (Figure 5).

DISCUSSION

MMA Embolization

Our updated meta-analysis shows that, across the included studies, most patients treated with MMA embolization demonstrated clinical and radiological improvement. In most cases, MMA embolization alone was sufficient to resolve the cSDH, with only 96 of the 201 embolized patients (47.8%) undergoing additional surgical procedures (i.e. burr hole drainage, craniotomy) after embolization. Furthermore, patients who underwent embolization had low rates of treatment failure, with only 7 (3.5%) developing recurrence of cSDH. When compared with conventional treatment options, MMA embolization was associated with lower rates of treatment failure. These studies also reported low rates of procedural complications demonstrating that this procedure can be performed with low rates of complications.

Only three studies compared patients undergoing MMA embolization with a control group of patients receiving conventional treatment. The smallest case series (n = 14) compared rates of cSDH recurrence among patients divided into three treatment groups: MMA embolization immediately followed by burr-hole irrigation and drainage, burr-hole irrigation and drainage alone, and craniotomy.[5] While two patients in the irrigation alone group experienced cSDH recurrence and none in the MMA embolization group, the difference in outcome was not statistically significant.[5] A retrospective cohort study (n = 43) compared patients who received MMA emboliza-

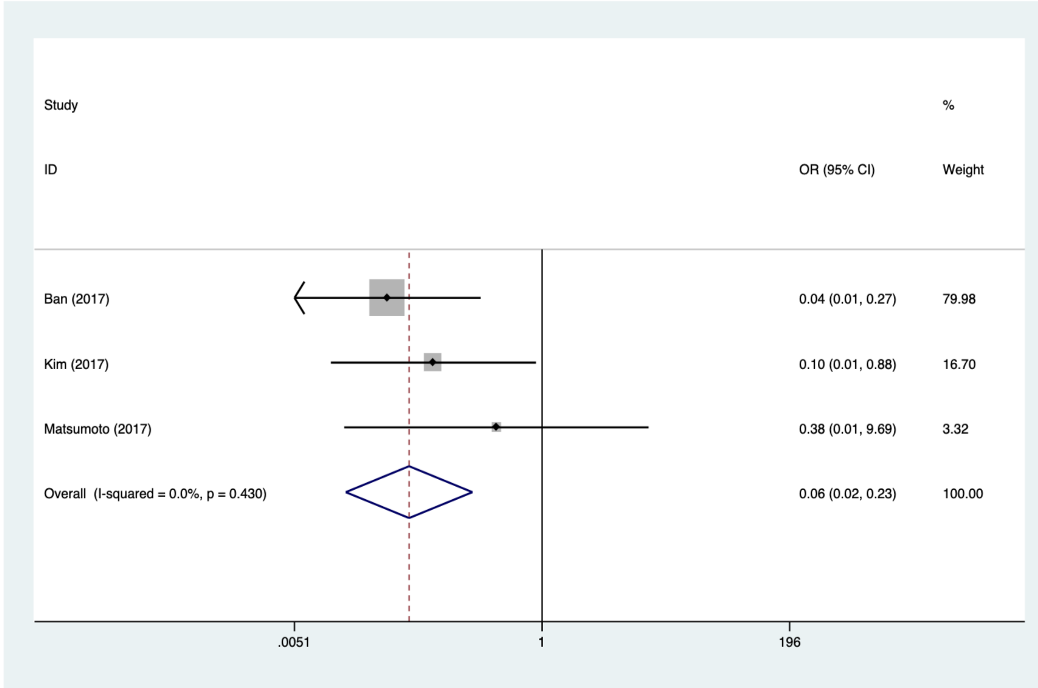

FIGURE 4: Forest plot of the three comparative studies demonstrating that MMA embolization had fewer treatment failures compared to the conventional treatment (odds ratio 0.06 95% confidence interval 0.02 - 0.23, P<0.01; I^2:0.0%).

tion after burr-hole drainage with patients who underwent craniotomy.[9] The authors found that the timespan for restoring brain symmetry as demonstrated by CT was significantly faster in the embolized group, and there were lower rates of cSDH recurrence in the MMA embolization group. However, there was no significant difference in clinical outcome between the two groups, as measured by patient functionality; in both groups, an mRS of 0-2 was demonstrated in 85-87% of the patients.[9] The largest study found that patients who underwent MMA embolization alone (n=72) experienced significantly lower rates of treatment failure (as defined by incomplete hematoma resolution) than patients who received conventional treatment (n=469), including surgical and conservative management.[8]

While these data suggest that MMA embolization is safer than conventional therapy, determining the patient selection criteria for MMA embolization is less clear. Overall, most of the included studies on MMA embolization were conducted in patients who developed recurrent cSDH after one or multiple surgical evacuations (Table 1). In the three controlled studies mentioned above, MMA embolization was performed in patients who failed conventional therapy initially, as demonstrated by recurrent SDH after burr hole surgery and/or craniotomy, and in high-risk surgical candidates such as those with chronic antiplatelet drug use or old age.[5,8,9] Further studies need to be conducted to investigate whether the benefits of embolization differ between patients refractory to conventional treatment and patients who are embolized initially.

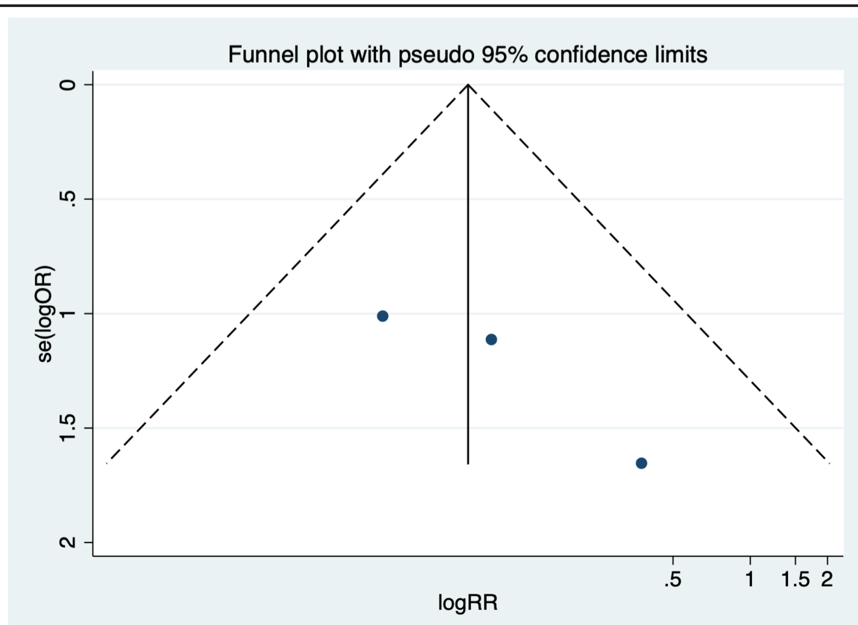

FIGURE 5: Funnel plot of the three comparative studies demonstrating a reasonable symmetric funnel shape, which may indicate that publication bias is unlikely.

TABLE 1: Characteristics of Included Studies in Meta-Analysis.

Study No	Author, journal, year	Type of study	Number of patients/ cSDH	Mean age (Years)	Sex (men/ women)	Branches of MMA embolized	Embolic materials used	MMA emboli-zation for upfront, previously untreated cSDH	Adjunctive surgical drainage in addition to MMA embolization	Previous failed surgical drainage before MMA emboliza-tion	Mean follow-up (Months)	Radiological improvement of SDH	Clinical improve-ment?	MMA embolization procedural complica-tions	cSDH recurrences
1	Ban et al., 2017	Pro-spective cohort study	72	69.3 (± 10.47)	48/24	Anterior and posterior divi-sions of MMA	PVA	27/72	45/72	0/72	6 months per protocol. But not reported specifically	98.6%	98.6%	0%	1.4%
2	Chihara et al., 2014	Case series	3	67 (± 9.84)	3/0	Not reported	PVA, coils	0/3	1/3	3/3	1 case was followed for 48 months, other two cases f/u was 6 months	66.7%	66.7%	0%	33.3%
3	Hashimo-to et al., 2013	Case series	5	71.4 (± 12.7)	3/2	Anterior and posterior divi-sions of MMA	4 cases NBCA, 1 case PVA	0/5	3/5	5/5	Reported f/u in two cases which was 3 and 4 months. No data for rest	100%	100%	0%	0%
4	Hirai et al., 2004	Case series	2	72 (± 12.7)	2/0	Not reported	PVA, platinum coils	0/2	0/2	2/2	9 months in one case. In the other case not specified	50%	100%	0%	0%
5	Kim et al., 2017	Retro-spective cohort study	20	73.6 (± 7.14)	14/6	Anterior and posterior divi-sions of MMA	PVA	0/20	0/20	20/20	3 months per protocol. But not reported specifically	95.0%	85.0%	10%	5%
6	Link et al., 2018	Retro-spective cohort study	49 patients / 60 cSDH	69 (±13)	39/12	Not reported	PVA	42/60	10/60	8/60	More than 6 weeks per protocol in only 45 cSDH. But not reported specifically	69% of patients achieved>50% reduction of SDH size	91%	0%	8.9%

TABLE 1: Characteristics of Included Studies in Meta-Analysis.

Study No	Author, journal, year	Type of study	Number of patients/ cSDH	Mean age (Years)	Sex (men/ women)	Branches of MMA embolized	Embolic materials used	MMA emboli-zation for upfront, previously untreated cSDH	Adjunctive surgical drainage in addition to MMA embolization	Previous failed surgical drainage before MMA emboliza-tion	Mean follow-up (Months)	Radiological improvement of SDH	Clinical improve-ment?	MMA embolization procedural complica-tions	cSDH recurrences
7	Matsu-moto et al., 2018	Case series	4	65 (± 16.9)	4/0	Anterior and posterior divisions of MMA	NBCA	0/4	4/4	4/4	3 months minimum per protocol. 1 year follow-up reported for 2 patients	100%	100%	0%	0%
8	Mino et al., 2010	Case series	4	73 (± 5.9)	4/0	Not reported	gelatin sponge and Guglielmi detachable coils	0/4	2/4	4/4	6 months per protocol. But not reported specifically	100%	100%	0%	0%
9	Nakaga-wa et al., 2019	Retro-spective cohort study	20	78.3 (± 11.4)	14/6	Anterior and posterior divi-sions of MMA and recurrent meningeal artery	NBCA	0/20	20/20	20/20	Up to 24 weeks post-embolization per protocol. But not reported specifically	100%	100%	0%	0%
10	Okuma et al., 2019	Retro-spective cohort study	17	76.5 (± 12.5)	12/5	Anterior and posterior divisions of MMA	NBCA and Em-bosphere	2/17	15/17	15/17	26.3 months (±17.4)	100%	70.6%	0%	0%
11	Tempaku et al., 2015	Case series	5	83 (± 7.07)	4/1	Anterior and posterior divisions of MMA	PVA	0/5	4/5	5/5	4.4 months (±5.97)	100%	100%	0%	0%

Abbreviations used:

cSDH	chronic subdural hematoma	MMA	middle meningeal artery
PVA	polyvinyl alcohol	NBCA	n-butyl cyanoacrylate

TABLE 2: Meta-analysis of non-comparative data for overall outcomes.

Outcome	All cSDH (%) (95% CI)	I^2
Radiological improvement	97.2 (94.2 to 100)	54.9%
Clinical improvement	96.7 (93.7 to 99.8)	41.8%
Treatment failure	2.1 (-0.8 to 5.0)	0.0%
Procedural complications	0.2 (-1.8 to 2.1)	0.0%

Abbreviations used:

cSDH chronic subdural hematoma

However, some case reports have described the use of MMA embolization as the sole therapy. Entezami et al.[13] describe an elderly patient with worsening headaches who was subsequently found to have a cSDH.

Given that the patient had relatively mild symptoms and required several anticoagulation medications, the decision was made to bypass surgery and proceed directly with MMA embolization. The patient subsequently demonstrated resolution of headaches and resolution of cSDH as demonstrated by follow-up CT three months later.[13]

Variations among MMA embolization protocols may influence clinical and radiological outcomes. Across the included studies, the most common embolic materials used were polyvinyl alcohol (PVA) particles and N-butyl-2-cyanoacrylate (NBCA). While all of these materials can be associated with the same outcome, some authors, for various reasons, reported a preference for a specific material.[12] Two studies recommended the use of low concentration NBCA as the ideal agent for embolizing peripheral branches of the MMA.[3,14] In contrast, Chihara et al.[2] specifically used PVA particles to avoid embolizing through a dangerous anastomosis and fibered coils to prevent recanalization. In addition, while many reports described embolizing both the anterior and posterior dural branches of the MMA, some publications did not state which branches were targeted (Table 1). Further studies will need to identify differences in technique, materials, and treatment protocols for MMA embolization.

The findings of this review corroborate prior studies that explore MMA embolization in patients with cSDH. Previous reviews reported MMA embolization as having lower rates of cSDH recurrence compared with conventional treatments.[15,16] A review by Waqas et al.[16] noted that no procedural complications were reported across 182 total patients who received MMA embolization.

LIMITATIONS

Certain limitations of this study need to be recognized. The majority of the included studies were non-randomized, single center, retrospective, self-adjudicated case series. These studies did not allow for a significant distinction between patients who received MMA embolization alone or after surgical interventions failed. There were only three studies that compared this intervention with conventional treatment options. In addition, the potential variation in MMA embolization protocols and conventional treatments of cSDH among the studies could contribute to different clinical outcomes. Many of these protocol variations reflect differences based on treating physicians' preferences.

CONCLUSION

Our review supports further evaluation of MMA embolization in treating patients with cSDH. Our results suggest that MMA embolization is associated with radiological and clinical improvement in patients with cSDH, along with low rates of complications. An adequately powered, multicenter, prospective randomized controlled trial examining the safety and effectiveness of MMA embolization as monotherapy and as an adjunct to surgery is required.

REFERENCES

1. Soleman J, Nocera F, Mariani L. The conservative and pharmacological management of chronic subdural haematoma. Swiss Med Wkly 2017;147:w14398.
2. Chihara H, Imamura H, Ogura T, et al. Recurrence of a Refractory Chronic Subdural Hematoma after Middle Meningeal Artery Embolization That Required Craniotomy. NMC Case Rep J 2014;1(1):1–5.
3. Hashimoto T, Ohashi T, Watanabe D, et al. Usefulness of embolization of the middle meningeal artery for refractory chronic subdural hematomas. Surg Neurol Int 2013;4:104.
4. Hirai S, Ono J, Odaki M, et al. Embolization of the Middle Meningeal Artery for Refractory Chronic Subdural Haematoma. Usefulness for Patients under Anticoagulant Therapy. Interv Neuroradiol 2004;10 Suppl 2:101–4.
5. Matsumoto H, Hanayama H, Okada T, et al. Which surgical procedure is effective for refractory chronic subdural hematoma? Analysis of our surgical procedures and literature review. J Clin Neurosci 2018;49:40–7.
6. Mino M, Nishimura S, Hori E, et al. Efficacy of middle meningeal artery embolization in the treatment of refractory chronic subdural hematoma. Surg Neurol Int 2010;1:78.
7. Tempaku A, Yamauchi S, Ikeda H, et al. Usefulness of interventional embolization of the middle meningeal artery for recurrent chronic subdural hematoma: Five cases and a review of the literature. Interv Neuroradiol 2015;21(3):366–71.
8. Ban SP, Hwang G, Byoun HS, et al. Middle Meningeal Artery Embolization for Chronic Subdural Hematoma. Radiology 2018;286(3):992–9.
9. Kim E. Embolization Therapy for Refractory Hemorrhage in Patients with Chronic Subdural Hematomas. World Neurosurg 2017;101:520–7.
10. Link TW, Boddu S, Paine SM, et al. Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: A Series of 60 Cases. Neurosurgery 2019;85(6):801–7.
11. Nakagawa I, Park HS, Kotsugi M, et al. Enhanced Hematoma Membrane on DynaCT Images During Middle Meningeal Artery Embolization for Persistently Recurrent Chronic Subdural Hematoma. World Neurosurg 2019;126:e473–9.
12. Okuma Y, Hirotsune N, Sato Y, et al. Midterm Follow-Up of Patients with Middle Meningeal Artery Embolization in Intractable Chronic Subdural Hematoma. World Neurosurg 2019;126:e671–8.
13. Entezami P, Nourollahzadeh E, Dalfino J. Embolization of Middle Meningeal Artery for the Treatment of Headaches Induced by Chronic Subdural Hematoma: A Case Report. Headache 2019;59(4):615–8.

14. Ishihara H, Ishihara S, Kohyama S, et al. Experience in endovascular treatment of recurrent chronic subdural hematoma. Interv Neuroradiol 2007;13 Suppl 1:141–4.

15. Srivatsan A, Mohanty A, Nascimento FA, et al. Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: Meta-Analysis and Systematic Review. World Neurosurg 2019;122:613–9.

16. Waqas M, Vakhari K, Weimer PV, et al. Safety and effectiveness of embolization for chronic subdural hematoma: systematic review and case series. World neurosurgery. 2019;126:228-236.