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Original Article Analysis of middle meningeal artery embolization for the treatment of chronic, acute on chronic, and subacute subdural hematomas

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ABSTRACT

Background: Chronic subdural hematoma (cSDH) is a common sequela of traumatic brain injury. Middle meningeal artery embolization (MMAE) has shown promising results as an emerging minimally invasive alternative treatment. The purpose of this study is to examine the safety and efficacy of MMAE performed in patients with cSDH, acute-on-chronic, and subacute SDH with a traumatic etiology.

Methods: This retrospective study included cases performed at a Level II Trauma Center between January 2019 and December 2020 for MMAE of cSDHs. Data collected included patient demographic characteristics and comorbidities, SDH characteristics, complications, and efficacy outcomes. The lesion measurements were collected before the procedure, 4–6 weeks and 3–6 months post-procedure.

Results: In our patient population, 78% (39) either had lesions improve or completely resolved. The sample included 50 patients with a mean age of 74 years old. Statistically significant reductions in lesion size were found from pre- to post-procedure in the left lesions, right lesions, and midline shifts. The left lesions decreased from 13.88 ± 5.70 mm to 3.19 ± 4.89 mm at 3–6 months with P < 0.001. The right lesions decreased from 13.74 ± 5.28 mm to 4.93 ± 7.46 mm at 3–6 months with P = 0.02. Midline shifts decreased from 3.78 ± 3.98 mm to 0.48 ± 1.31 mm at 3–6 months with P = 0.02. No complications were experienced for bleeding, hematoma, worsening SDH, pseudoaneurysm, or stroke.

Conclusion: Our pilot study from a single center utilizing MMAE demonstrates that MMAE is successful without increasing treatment-related complications not only for cSDH but also in acute-on-cSDH and SDH with a subacute component.

Keywords: Interventional radiology, Middle meningeal artery, Neurosurgery, Subdural hematoma, Trauma

INTRODUCTION

Chronic subdural hematoma (cSDH) is an increasingly common sequela of traumatic brain injury. It is estimated that by 2030, there will be 60,000 new cases of cSDH each year, largely due

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to an increase in the elderly population and widespread use of anticoagulation and antiplatelet medications. This includes those with a high risk of ground-level falls due to frailty and instability due to other chronic diseases.^[9]

Burr-hole irrigation surgery has traditionally been considered the gold standard treatment for cSDH requiring operative management.^[5,15,23] Although treatment outcomes are widely considered positive, recurrence rates following surgical treatment range from 5% to 33%.^[4,5,20,29] Higher risk for recurrence has been noted in elderly patients, those on anticoagulant and antiplatelet medications, and those with an underlying coagulopathy.^[5,9,17,29]

A cSDH is often precipitated by relatively mild head trauma, particularly in the elderly population. This results in an acute subdural hematoma (SDH), which may not be initially significant enough to cause neurologic deficit or hospitalization.^[2] Following the initial insult, growth and recurrence of cSDH are believed to develop over weeks to months due to neovascularization of the dural layer and subsequent microhemorrhages that ensue.^[9,21] The middle meningeal artery (MMA) is thought to contribute to the development of cSDH by feeding the hematoma capsule.^[15,24]

Over the past several years, MMA embolization (MMAE) has shown promising results as an emerging minimally invasive alternative treatment for patients with cSDH. ^[1,12,13,15,16,20,24,27,29] Eliminating the MMA blood flow through embolization is thought also to inhibit the blood supply to the hematoma.^[24] Mandai *et al.* provided the first published article in 2000 that described the successful use of a surgical procedure to embolize the MMA to treat a recurrent SDH.^[22] Published reports suggest that the annual use of MMAE has risen to 50% since the technique was first described.^[6,14]

Despite its increase in utilization, publications have been largely limited to analyses of the procedure in small studies, and case reports focusing on cSDH and typically on patients with a non-traumatic etiology. The purpose of this single-site study is to retrospectively examine the safety and efficacy of MMAE performed in patients with not only cSDH but also acute-on-chronic and subacute SDH with a traumatic etiology. Most of the study cohort sustained traumatic injuries, with falls being the predominant mechanism of injury. In a review of studies since 2000, this patient population is drastically understudied. This analysis sought to add to the existing literature, hoping to benefit trauma and neurosurgery patients with a potential change in trauma practice.

MATERIALS AND METHODS

The study protocol was reviewed and approved by the Institutional Review Board. This single-center retrospective observational study included patients who were above the age of 18 and admitted to this Level II trauma center, and underwent MMAE between January 2019 and December 2020. Electronic medical records were utilized to obtain data. The study sample criteria included patients with computed tomography (CT) images confirming cSDH, acute-on-cSDH, acute-on-subacute, or subacute SDH with mass effect or midline shift while maintaining a Glasgow Coma Scale (GCS) of >13. The presence of a cSDH membrane was not necessary for study inclusion due to the variability of its presence on a CT image. Rather, patients experiencing symptoms of inflammation and bleeding provided indications for the MMAE procedure. Patients were excluded if there was a need for urgent intervention or if no subacute or chronic subdural component was identified.

Data collected included demographic characteristics and comorbidities, SDH characteristics, procedural details, complications, follow-up neurological examinations, and safety and efficacy outcomes. MMAE was performed by our neurosurgeons utilizing particles alone, coils, or a combination. SDH characteristics were determined by reports of CT of the head (non-contrast) as interpreted by a fellowship-trained neuroradiologist. Patient charts and images were examined for up to 6 months post-procedure.

The size of the SDH by CT, as well as the patient's symptoms by the modified Rankin score (MRS) and GCS score as documented in clinical examination notes, were recorded at three-time points of interest: before the procedure, 4–6 weeks post-procedure, and 3–6 months post-procedure. Complications occurring during the admission and up to 6 months were also recorded and included bleeding requiring transfusion, hematoma at the vascular access site, worsening SDH, pseudoaneurysm/dissection of the vessel, stroke, contrast-induced kidney damage, and worsening neurological deficits despite treatment requiring additional intervention.

The primary outcome of interest was the successful treatment of the SDH, which was defined as the lesion being the same size, smaller, or if there was complete reabsorption by CT imaging by six months post procedure. The procedure was defined as a failure if the size of the SDH was larger or if the patient required surgical rescue due to an expanding hematoma. The key dependent variable was the size of the lesion/s (right, left, and midline).

Descriptive statistics, including means, standard deviations, and frequencies, were calculated for patient demographic characteristics and comorbidities, SDH characteristics, procedural details, complications, and safety and efficacy outcomes. In addition, a repeated measures analysis of variance (ANOVA) was conducted for each dependent variable (left lesion [mm], right lesion [mm], midline shift [mm], MRS, and GCS) with one within subjects' factor time (pre, 4–6 weeks, and 3–6 months). If the repeated measures ANOVA was significant at $\alpha < 0.05$, *post hoc* testing was conducted.

RESULTS

In our patient population, 78% (39) either had lesions improve or completely resolve. Figure 1 exhibits the pre- and post-embolization images of a study patient demonstrating the immediate effect of embolizing the MMA. In the postprocedure image, the MMA is successfully occluded after the placement of particles and coils. The full study sample included 50 patients with a mean age of 74 years old, the majority of whom were male 56% (28). The patients' descriptive statistics and frequencies are presented in Table 1. Of note, common medical comorbidities included hypertension at 88.0% (44), cardiovascular disease at 48% (24), diabetes at 38.0% (19), and head trauma at 18.0% (9). The use of antithrombotic therapies was prevalent, including 34.0% (17) patients on antiplatelet agents and 30.0% (15) patients on anticoagulant medications. The MMAE was performed with either particles alone 26% (13) or a combination of particles and coils 74% (37).

Supplemental Figure 1 shows the surgical case flow diagram by diagnoses and includes surgical progression and history. The majority of patients had acute-on-cSDH 76% (38), three had acute-on-subacute, three had subacute SDH, three had cSDH, and three had subacute-on-chronic. Importantly, the results of the MMAE were grossly similar for these different SDH characteristic groups with no major variance. Most patients, 56% (28), required only the MMAE procedure for SDH resolution, whereas 36% (18) patients had an additional procedure, such as a craniotomy or burr-hole surgery, and the MMAE. In addition, 8% (4) of patients underwent two additional procedures along with the MMAE procedure. Only two (4%) of the patients that had initial MMAE required additional subsequent evacuation of the SDH due to the progression of the lesion. For the rest of the patients who required multiple procedures, MMAE was the last procedure needed for the treatment of the lesion.

No complications were experienced by any of the patients for bleeding, hematoma, worsening SDH, pseudoaneurysm, stroke, or kidney damage. However, one patient did



Figure 1: Middle meningeal artery embolization pre- and post-procedure.

experience a complication of worsening neurologic deficit consistent with a worsening SDH. Three patients expired before the completion of the 6-month follow-up; however, all were unrelated to the MMAE or SDH. Two of these three patients, in fact, experienced a clinical improvement following the MMAE.

Among the 50 patients, 67 lesions were present, with 24 lesions under 10 mm, 31 between 10 and 20 mm, and then 12 over 20 mm. The largest hematoma was 27 mm in width, pre-procedure, in an acute-on-cSDH. The treatment team did not utilize a cutoff value for the hematoma size but was

Table 1: Demographics and characteristics.			
Characteristic	Value		
Age, Mean±SD	74.66±11.34		
Sex, Count (%)			
Male	28 (56.0)		
Female	22 (44.0)		
Diagnosis			
Acute on chronic	41 (82.0)		
Acute on subacute	3 (6.0)		
Subacute	3 (6.0)		
Chronic	3 (6.0)		
Lesion location			
Left	17 (34.0)		
Right	17 (34.0)		
Bilateral	16 (32.0)		
Comorbidities			
Diabetes	19 (38.0)		
Hypertension	44 (88.0)		
Cerebral atrophy	22 (44.0)		
Previous cerebrovascular accident	11 (22.0)		
Cardiovascular disease	24 (48.0)		
Antiplatelet medication	17 (34.0)		
Anticoagulant medication	15 (30.0)		
Previous head trauma	9 (18.0)		
Cancer	16 (32.0)		
Outcomes			
Symptomatic hematomas	0		
MMA embolization material			
Particles	13 (26.0)		
Coils	0		
Both	37 (74.0)		
Antiplatelet medication	15 (30.0)		
Anticoagulant medication	8 (16.0)		
Mortality	0		
Complications			
Bleeding	0		
Hematoma	0		
Worsening subdural hematoma	0		
Pseudoaneurysm	0		
Stroke	0		
Kidney damage	0		
Complications worsening neurological deficits	1 (2.0)		
SD: Standard deviation, MMA: Middle meningeal artery			

guided by clinical presentation. Subsequently, if the patient was clinically stable despite how large the hematoma was, MMAE was still offered. Again, if there was any evidence of clinical deterioration of the patient on presentation, they were automatically excluded from MMAE as sole treatment. SDH lesion descriptive statistics over time are shown in Table 2. Statistically significant reductions in lesion size from pre- to 3-6 months were found for the left lesion, right lesion, and midline shift. The left lesion experienced a decrease in size from pre-13.88 \pm 5.70 mm to 3.19 \pm 4.89 mm at the 3–6 months follow-up with P < 0.001. The right lesion also demonstrated a decrease in size from pre-13.74 \pm 5.28 mm to 4.93 \pm 7.46 mm at the 3-6 months follow-up with P = 0.02. Midline shift decreased from pre-3.78 \pm 3.98 mm to 0.48 \pm 1.31 mm at 3–6 months follow-up with P = 0.02. Furthermore, Figure 2 depicts the change in lesion size over time for left lesion, right lesion, and midline shift, respectively. The MRS and GCS mean scores did not change significantly over time.

Based on our statistical analysis, repeated measures ANOVA demonstrated change over time with a comparison of means.

The repeated measures ANOVA showed significant Cohen's d effect sizes for the left lesion size, right lesion size, and midline shift (P < 0.05). In addition, Cohen's d-effect sizes were small for the mean MRS and mean GCS (P > 0.05), showing no significant change over time. Specifically, for the left lesion, there was a significant decrease in size from pre to 4-6 weeks, pre to 3-6 months, and from 4-6 weeks to 3-6 months with medium to large effect sizes (d = 0.64, d = 2.01, and d = 1.08, respectively). For the right lesion, there was a significant decrease in size from pre to 3-6 months and from 4-6 weeks to 3–6 months with large effect sizes (d = 1.36 and d = 0.87, respectively) but not from pre to 4–6 weeks (P > 0.05). Finally, for the midline shift, there was a significant decrease in size from pre to 4-6 weeks, pre to 3-6 months, and from 4-6 weeks to 3-6 months with small to large effect sizes (d = 0.79, d = 1.11, and d = 0.40, respectively).

DISCUSSION

In this study of MMAE for the treatment of cSDH, acuteon-cSDH and subacute SDH, we found that the majority

Table 2: Subdural hematoma lesion descriptive statistics.				
Pre-procedure lesion size	<10 mm	10–20 mm	>20mm	
67 total lesions in 50 patients	24	31	12	
Mean lesion measurements over time	Pre Mean±SD	4-6 weeks Mean±SD	3-6 months Mean±SD	
Left lesion (mm)	13.88±5.70	9.79±7.03*	3.19±4.89* ^H	
Right lesion (mm)	13.74±5.28	10.93±6.19	4.93±7.46* ^I	
Midline shift (mm)	3.78 ± 3.98	1.22±2.26*	$0.48 \pm 1.31^{*1}$	
Modified Rankin score	3.82 ± 0.88	4.17±0.98	3.50 ± 1.0	
Glasgow coma score	14.74±0.66	14.95±0.23	15.00 ± 0.00	

*Significant difference between time point and pre, iSignificant difference between time point and mid, SD: Standard deviation



Figure 2: Lesion sizes over time, line graphs.

of the patients were successfully and safely treated. SDH is a common disease injury encountered by traumatologists and neurosurgeons. While acute SDHs generally entail observation versus evacuation based on clinical symptomatology, the presentation of acute-on-cSDH, subacute SDH, and cSDH can often be much more variable. This is most likely secondary to the overall pathophysiology of SDH as it progresses from an acute to a chronic lesion. The development of a cSDH begins as an acute SDH heals and causes dural border cells to separate, along with granulation tissue and macrophage to form.^[1,9,27] Increased injury inflammation can then advance clot hyperfibrinolysis and angiogenic factor release, which also produces capillary friability and neovascularization.^[8]

Various nonsurgical treatments have, therefore, been proposed to counteract this inflammatory pathophysiology. However, these treatments have not had widespread success, especially when compared to surgical evacuation.^[19,26] A potential explanation for this is that a SDH that has a chronic component has an outer membrane derived from the dura mater, which tends to have repeated bleeding. Hence, to address this issue, embolization of the MMA has been proposed as these arteries provide blood supply to the dura mater.^[13,17,20,28] Embolization impedes the blood supply to the meningeal arteries, fostering spontaneous hematoma resolution. Not only does the hematoma resolve sooner, but also studies have shown that MMAE decreases the likelihood of additional hematoma formation.[1,13,22,28] While MMAE was initially used in the setting of refractory cSDH status post-evacuation, studies have now also shown the benefits of this procedure as a primary treatment in the setting of new cSDH.^[1,11,20,29]

This study continues to show the benefits of MMAE both as a sole and adjuvant treatment option for cSDH. However, we have additionally demonstrated the safe and successful expanded application of this procedure for our patient population of acute-on-cSDH as well as a SDH with a subacute component. Our theory for the expanded application revolves around the outer membrane of a SDH that is generally derived from the dura mater. While this membrane is generally seen in cSDH, we theorize that some early formation or precursor of this membrane is also developing or developed in acute-on-cSDH and subacute SDH patients. In these SDH cases, a radiographic presence of the membrane is not always seen in CT imaging. Relying on established knowledge of physiology, we know that as a SDH ages and where persistent inflammation and bleeding exist, a SDH membrane will form. For our study, we focused on the overall aging of the SDH on imaging rather than the presence of the outer membrane. Hence, we felt that MMAE in the setting of these different SDH characteristics would also be beneficial.

While surgical evacuation remains the gold standard treatment for any aged SDH that is symptomatic, the literature and clinical practice for asymptomatic hematomas are more variable.^[3,7,10,20] Historically, these specific hematomas could have been monitored with the outcome being resolution over time versus potential expansion of the hematoma, which could then require surgical intervention, especially if symptomatic.^[3,18,25] With the increased application of MMAE, we now know that there is an additional treatment option for this specific patient population. Furthermore, this treatment option is not as invasive as surgical evacuation itself. MMAE allows us to consider other treatment options with fewer risks as compared to observation alone.^[15] This is especially important for those patients who need to be resumed on antiplatelet or anticoagulant agents soon after being diagnosed with these SDH. In our study, 64% of the patients were on some form of antiplatelet or anticoagulant agent when diagnosed with their SDH, with the majority needing it resumed as soon as possible due to their other medical comorbidities. For our patients that underwent MMAE, we, therefore, restarted antiplatelet agents on post-procedure day three and anticoagulation on post procedure day 7. Despite the early restart of these medications, our results show no increased complication rates (0% bleeding issues) or increased rates of reaccumulating SDH (0% vs. upward of 22% in the literature). While the goal of this study was to focus on the safety and efficacy of MMAE in SDH of varying characteristics, this study does show an increased utility of MMAE in SDH patients on antiplatelet or anticoagulant agents that need to be resumed sooner rather than later. This does, however, warrant a more thorough prospective evaluation.

Overall, our study results coincide with the literature in showing the safety and efficacy results of MMAE as a sole treatment intervention.^[11,21,27,29] Fifty-six per cent (28) of our SDH patients only underwent MMAE with good results. However, as also seen in the literature.^[13,15,22-24,28] MMAE has been very beneficial for residual SDH after evacuation, as 36% (18) of our patients underwent the procedure after surgical evacuation. Six per cent (3) of our patients required surgical evacuation following MMAE. Regardless of how MMAE was utilized as a treatment choice, 78% (39) of our patients had lesions that improved or completely resolved. This is in comparison to only 8% (4) of our patients having worsening lesions as seen on CT imaging. Importantly, 82% of our patients undergoing MMAE had an acute-on-cSDH, 6% had acute-on-subacute SDH, 6% had subacute SDH, and 6% had classic cSDH. Despite the variable presentations of the SDH appearance, we show that MMAE was certainly beneficial across the SDH appearance and aging spectrum. While we do not have a proven explanation for this finding, we again theorize that even with a SDH with an acute-onchronic or subacute component, the local inflammation

seen in cSDH outer membrane is possibly also seen in a less aged SDH but to a lesser degree. This still potentially allows for MMAE to be successful by inhibiting blood flow to pathologic structures supplied by the meningeal arteries. However, additional work and investigation are needed to prove this theory.

Our study is limited by a retrospective design, and our treatment arm was not directly compared with a control group, such as no treatment or surgical evacuation. Furthermore, our analysis was limited by some gaps in patient follow-up that prevented further CT imaging in some cases. The results overall demonstrate the need for a larger, multicenter, randomized study to support our findings.

CONCLUSION

Our study demonstrates that MMAE is safe and successful in treating cSDH in addition to acute-on-cSDH and SDH with a subacute component. Furthermore, this can be done without increasing treatment-related complications. As a potential added benefit, our study also demonstrates the safe and efficacious use of MMAE in patients on antiplatelet or anticoagulation agents that need to be resumed somewhat acutely after intervention on the SDH. While clinical judgment and equipoise should always be of paramount importance with this disease process, it is promising for us to demonstrate the potential expanded successful application of MMAE as this procedure continues to be more widely used and accepted in the fields of neurosurgery and trauma.

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Ethical approval

The research/study approved by the Institutional Review Board at Institutional Review Board at Kettering Health Network, number KHN #2021-27, dated January 14, 2021.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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*A total of 3 cases required surgical procedure following middle meningeal artery embolization (MMAE) with acute-on-chronic subdural hematoma. Supplemental Figure 1: Surgical case diagnosis and treatment course.