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Original Article

Timing of chronic subdural hematoma treatment affects middle meningeal artery embolization outcome

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ABSTRACT

Background: Chronic subdural hematoma (CSDH) is a condition that tends to recur frequently. Although middle meningeal artery embolization (MMAE) is an effective CSDH treatment, there is currently no consensus regarding the optimal timing for embolization.

Methods: In this single-center and retrospective study, we reviewed 72 cases with 1st-time recurrent CSDH from January 2018 to July 2023 and identified those treated with MMAE to examine its effect and the impact of differences in the timing of treatment.

Results: Of the 72 cases with CSDH recurrence for the 1st time (mean age: 80.4 ± 9.7 years; men: 62 [86.1%]; mean first recurrence interval: 33 ± 24 days), 27 (37.5%) experienced a second recurrence. The mean first recurrence interval was shorter in cases with a second recurrence compared to cured cases: 24.3 ± 18.6 versus 38.3 ± 25.6 days, respectively ($P = 0.005$). MMAE was performed in 17 (23.6%) cases (mean age: 82 ± 6.2 years; men: 14 [82.4%]). The mean time from initial surgical treatment to embolization was 52.4 ± 35.4 days, and the mean recurrence interval before MMAE was 24.9 ± 19.6 days. Six cases (35.3%) experienced post-embolization recurrence and required surgical treatment. The mean recurrence interval before MMAE was shorter in cases with recurrence after MMAE (15 ± 6.4 vs. 30 ± 22.1 days, $P = 0.023$). The time from initial surgical treatment to embolization was significantly shorter: 31.3 ± 12.8 versus 63.9 ± 38.9 days ($P = 0.039$).

Conclusion: Cases with a short first recurrence interval were more likely to experience a second recurrence. Repeated recurrences within a short time increased the likelihood of post-embolization recurrence. MMAE performed early following the initial surgical treatment increased the recurrence risk.

Keywords: Chronic subdural hematoma, Embolization, Endovascular therapy, Recurrence

INTRODUCTION

Chronic subdural hematoma (CSDH) is a prevalent neurosurgical condition characterized by symptoms resulting from the gradual accumulation of blood in the subdural space, which compresses the brain. There are two main forms of CSDH: traumatic and spontaneous. Traumatic CSDH is triggered by trauma that could sometimes be so minor that the individual is either unaware of its occurrence or may have forgotten it. CSDH that is not linked to any underlying trauma and without a known cause is referred to as spontaneous. Examples of spontaneous

CSDH include patients with increased bleeding tendency and those with cancer, but many aspects of the disease remain unknown. As the severity of symptoms increases, surgical intervention, such as burr-hole drainage of the hematoma, may be necessary; however, the likelihood of recurrence is high. CSDH often occurs in older adults, and it is anticipated that the number of cases will increase as the population ages.[1,18] Several studies have reported the outcomes and procedures of middle meningeal artery embolization (MMAE) in relation to traumatic and spontaneous CSDH (such as patients with bleeding tendencies, cancer, arachnoid cysts, and pediatric cases).[4,9,13,19] However, there are few reports on the treatment timing of CSDH and MMAE, including the recurrence intervals. The appropriate timing of MMAE treatment remains unclear.

In this single-center and retrospective study, we examined the recurrence interval and treatment course of cases with recurrent CSDH and discussed the postoperative course of MMAE and the timing of embolization.

MATERIALS AND METHODS

This study is a single-center and retrospective analysis of 72 lesions of 1st-time recurrent symptomatic CSDH that occurred between January 2018 and July 2023. We examined the case background, number of recurrences, recurrence interval (the period between surgical treatments), and treatment outcomes for each patient. Further, we retrospectively reviewed the chronological sequence from initial onset to cure, embolization method, and treatment outcomes of patients who underwent MMAE. The Institutional Ethics Review Board approved the study (approval number: 2023-013). The timing and methods of treatment at our center are as follows: symptomatic CSDH was initially treated using burr-hole evacuation or drainage. If the hematoma regrew and became symptomatic again, further surgical treatment was performed. Surgical treatment included mini craniotomy and endoscopic removal of the hematoma, particularly for organized hematomas or those that could not be removed through burr holes.

MMAE was usually performed at the second recurrence, making it the third surgical treatment. At other times, MMAE was performed when there was a high risk of recurrence or contralateral symptomatic disease at the time of embolization. The embolization material used was n-butyl-2-cyanoacrylate. Proximal and distal branch embolization was performed if dangerous anastomoses were absent and catheter guidance was possible; otherwise, proximal or distal branch embolization was performed.

Continuous variables are reported as means and standard deviations, whereas categorical variables are reported as numbers and frequencies (percentages). EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) was used for all statistical analyses. The Mann–Whitney U-test was used for continuous variables, and Pearson's Chi-square test was used for categorical variables. Statistical significance was set at $P < 0.05$.[7]

RESULTS

Seventy-two cases with a second recurrence were included in the study. No cases were excluded from the study. The mean age of participants was 80.4 ± 9.7 years; 62 (86.1%) were men, and 28 (38.9%) recurrences were right-sided. The mean first recurrence interval was 33 ± 24 days, and the mean of all recurrence intervals was 31.9 ± 26.3 days. Bleeding tendency (hematological disease or oral antithrombotic medication) was present in 25 cases (34.7%) [Table 1]. There was no difference in the recurrence interval between cases with and without bleeding tendency (34.4 ± 25.5 vs. 32.3 ± 23.4 days, respectively, $P = 0.70$.). The interval for first recurrence was compared between cases who experienced a second recurrence and those who did not [Table 2]; the mean interval was 24.3 ± 18.6 versus 38.3 ± 25.6 days ($P = 0.005$), indicating that cases with recurrence had a shorter interval for first recurrence [Figure 1].

MMAE was performed in 17 (23.6%) cases (mean age: 82 ± 6.2 years; men: 14 [82.4%]), and 8 (47.1%) were right-sided. The mean first recurrence interval was 22.1 ± 15.9 days, the mean time from initial surgical treatment to embolization was 52.4 ± 35.4 days, and the mean recurrence interval before embolization was 24.9 ± 19.6 days. Embolization was performed 2 days before and 6 days after surgical treatment, with a mean of 1.2 ± 2.3 days after surgery. Embolization was performed in 2 cases (11.8%) at the first recurrence, 13 (76.5%) at the second, 1 (5.9%) at the third, and 1 (5.9%) at the fourth recurrence (mean: 2.1 recurrences). Three cases had an increased bleeding tendency, two were receiving antithrombotic medication, and one had myelodysplastic syndrome [Table 3].

Table 1: Baseline characteristics of cases (*n*=72) with recurrent chronic subdural hematoma.

Age (years)	80.4±9.7
Men	62 (86.1%)
Right-sided	28 (38.9%)
Bleeding tendency	25 (34.7%)
The mean interval for the first recurrence (days)	33.0±24.0
The mean interval for all recurrences (days)	31.9±26.3
Number of recurrences mean	1.6±0.9
1	45 (62.5%)
2	16 (22.2%)
3	7 (9.7%)
4	3 (4.2%)
5	1 (1.4%)

Table 2: Comparison of recurrent and cured cases after the first recurrence.

	Recurrence (*n*=27)	Cure (*n*=45)	*P*-value
Age (years)	82.4±5.5	79.3±11.3	0.34
Men	24 (88.9%)	38 (84.4%)	0.6
Right-sided	15 (55.6%)	19 (42.2%)	0.45
Bleeding tendency	10 (37%)	15 (33%)	0.75
The mean interval for first recurrence (days)	24.3±18.6	38.3±25.6	0.005

Table 3: Baseline characteristics and treatment details of 17 cases who underwent middle meningeal artery embolization.

Age (years)	82±6.2
Men	14 (82.4%)
Right-sided	8 (47.1%)
Tendency to hemorrhage	3 (17.6%)
Time from initial surgical treatment to embolization (days)	52.4±35.4
The mean interval for first recurrence (days)	22.1±15.9
Recurrence interval before embolization (days)	24.9±19.6
From surgical treatment to embolization	1.2±2.3
Number of recurrences eligible for embolization, mean	2.1±0.6
1	2 (11.8%)
2	13 (76.5%)
3	1 (5.9%)
4	1 (5.9%)
Embolization with n-butyl-2-cyanoacrylate	17 (100%)
Number of embolized middle meningeal artery branches	
1	9 (52.9%)
2	8 (47.1%)
Complication	1 (5.9%)
Surgical treatment after embolization	6 (35.3%)
Recurrence interval after embolization (days)	24.7±18.9

All cases underwent successful embolization using n-butyl-2-cyanoacrylate (20–33%); nine cases underwent embolization of one branch of the MMA, eight underwent embolization of two branches, and one had a complicated middle meningeal arteriovenous shunt. After embolization, 6 cases (35.3%) became symptomatic and required surgical treatment [Table 3]. The progress of all cases, including the embolization date, is displayed in order based on the number of days from initial surgical treatment to embolization [Figure 2]. The mean recurrence interval after embolization was 24.7 ± 18.9 days.

In cases that required surgical treatment after embolization compared to those that were cured, the mean first recurrence interval was 13.8 ± 4.4 versus 26.6 ± 18.1 days, respectively (P = 0.63). The mean interval for all recurrences before MMAE was shorter in cases that required surgical treatment after MMAE compared to those not requiring surgery (15 ± 6.4 vs 30 ± 22.1 days, respectively; P = 0.023). The time from initial surgical treatment to embolization was also significantly shorter (31.3 ± 12.8 vs. 63.9 ± 38.9 days; P = 0.039; Table 4). There were no significant differences regarding age, presence of hemorrhagic predisposition, number of MMA branches embolized, number of recurrences before embolization, or number of days between embolization and surgical treatment. There was no difference in the recurrence interval before and after MMAE (24.9 ± 19.6 vs. 24.7 ± 18.9 days, respectively; P = 0.32).

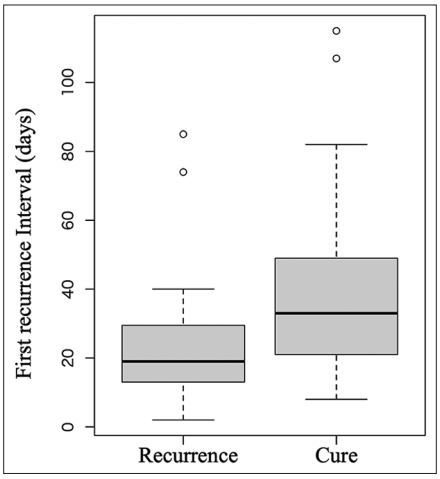

Figure 1: Box plots comparing the first recurrence interval of recurrent and cured cases after the first recurrence. The mean recurrence interval was shorter in cases with a second recurrence: 24.3 ± 18.6 versus 38.3 ± 25.6 days, respectively (P = 0.005).

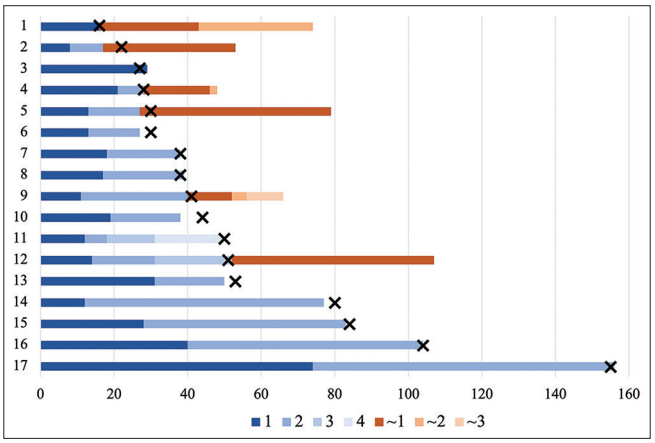

Figure 2: The treatment course progress of middle meningeal artery embolized cases, including the embolization date, in order of the number of days from initial surgical treatment to embolization. The blue bar indicates the recurrence interval of pre-middle meningeal artery embolization (MMAE). × indicates the timing of embolization. Red indicates the recurrence interval after MMAE.

Table 4: Comparison of recurrent and cured cases after middle meningeal artery embolization.

	Recurrence (*n*=6)	Cure (*n*=11)	*P*-value
Age (years)	82.8±5.1	81.5±6.9	0.84
Embolization of two middle meningeal artery branches	2	6	0.4
Bleeding tendency	1	2	0.62
Time from initial surgical treatment to embolization (days)	31.3±12.8	63.9±38.9	0.039
The mean interval for the first recurrence (days)	13.8±4.4	26.6±18.1	0.063
Recurrence interval before embolization (days)	15.0±6.4	30.0±22.1	0.023
Number of recurrences eligible for embolization	2.0±0.63	2.1±0.7	0.94
From surgical treatment to embolization	1.3±2.3	1.1±2.4	0.76

DISCUSSION

Older age, antithrombotic medications, pre-and post-operative hematoma status, and volume are known risk factors for CSDH recurrence. Although there are reports that drainage does not affect the time to recurrence,[11] there are few reports examining the recurrence interval. The median interval for all recurrences was 24 days (interquartile range: 14–36 days), this result is similar to the findings in the previous report.[11] In this study, the first recurrence was observed at a mean of 33 ± 24 days, and the second recurrence was less frequent in cases with a longer interval between the first and second recurrences.

Several studies have documented the efficacy of MMAE for CSDH. Although various reports have focused on whether embolization should be performed as a standalone treatment or in conjunction with surgical treatment, the type of embolization material to be used, the number of vessels to be embolized,[8] complications, and other factors, there is no clear consensus. In addition, no consensus has been reached on the timing of embolization. Regarding the timing of embolization, there are reports on treatment with embolization alone, failure at 1–3 recurrences, and embolization at 2–11 weeks after initial treatment.[3,5,6,10] In the present study, on average, 2.1 ± 0.6 times recurrences cases experienced MMAE 52.4 ± 35.4 days after the initial surgical treatment. Moreover, post-MMAE recurrence was more common in cases with a short time between the initial surgical treatment and MMAE and in cases with repeated recurrences during a short time interval.

CSDH formation involves the recruitment of inflammatory cells, angiogenesis of highly permeable and leaky capillaries, processes supporting membrane formation, and fibrinolysis, which promote further bleeding.[2] The etiology of CSDH involves inflammation, but inflammatory cytokines have been reported to decrease over time.[17] If the inflammation is still active, CSDH will recur whether MMAE or burr-hole evacuation. The treatment timing is also considered an important factor in CSDH treatment.

Embolization of the MMA is believed to be due to its hemostatic effect and inflammatory cascade arrest. MMA embolization alone reportedly reduces the hematoma after 3–12 weeks.[3] Even if the MMA is embolized early in CSDH development, the inflammatory cascade may cause further angiogenesis and bleeding, leading to recurrence. Even if the MMA is embolized, CSDH is not cured immediately. This report supports the finding that early MMAE was associated with a higher incidence of recurrence.

The potential for bleeding, including the use of antithrombotic therapy, is an important factor in the recurrence of CSDH. Although reports are indicating that antithrombotic therapy increases the likelihood of CSDH recurrence and the recurrence after MMAE, particularly in spontaneous cases,[14,15,19] our series did reveal any impact on recurrence. Nonetheless, antithrombotic therapy may have influenced the treatment course. For cases at high risk of recurrence, including those on antithrombotic therapy, MMAE is expected to reduce the number of recurrences and extend the recurrence interval.

The first recurrence interval was associated with the second recurrence of CSDH but not with the recurrence after MMAE. In cases with a short interval to the first recurrence, MMAE may reduce the number of recurrences and extend the recurrence interval. However, it should be noted that recurrence after MMAE may occur if the time between initial treatment and embolization is short.

A limitation of this study was the high recurrence rate after embolization. Previous meta-analyses have reported a 3–5% likelihood of surgical treatment following MMA treatment.[4,12,16] This could potentially be because the meta-analyses included embolization as the initial treatment, whereas this study included many cases with repeated short-term recurrences. Other possible reasons include bias regarding patient backgrounds and treatment modalities. Further, case accumulation is required due to our small sample size.

CONCLUSION

Cases with a short first recurrence interval were more likely to experience a second CSDH recurrence. Cases with repeated recurrences within a short time were more likely to experience recurrence after embolization. Cases in

which MMAE was performed early after the initial surgical treatment were prone to recurrence. The treatment timing is also an important factor impacting recurrence rates and should be carefully considered. Prospective studies and accumulating cases are required, with a special focus on the timeline, including recurrence interval and treatment timing.

Ethical approval

The research/study was approved by the Institutional Review Board at Daiyukai General Hospital, number 2023–013, dated September 06, 2023.

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.

REFERENCES

1. Adhiyaman V, Chattopadhyay I, Irshad F, Curran D, Abraham S. Increasing incidence of chronic subdural haematoma in the elderly. QJM 2017;110:375-8.
2. Edlmann E, Giorgi-Coll S, Whitfield PC, Carpenter KL, Hutchinson PJ. Pathophysiology of chronic subdural haematoma: Inflammation, angiogenesis and implications for pharmacotherapy. J Neuroinflammation 2017;14:108.
3. Housley SB, Monteiro A, Khawar WI, Donnelly BM, Lian MX, Fritz AG, *et al*. Volumetric resolution of chronic subdural hematomas treated with surgical evacuation versus middle meningeal artery embolization during immediate, early, and late follow up: Propensity-score matched cohorts. J Neurointerv Surg 2023;15:943-7.
4. Ironside N, Nguyen C, Do Q, Ugiliweneza B, Chen CJ, Sieg EP, *et al*. Middle meningeal artery embolization for chronic subdural hematoma: A systematic review and meta-analysis. J Neurointerv Surg 2021;13:951-7.
5. Izawa D, Matsumoto H, Nishiyama H, Toki N, Kawaguchi T, Yako R, *et al*. Efficacy of middle meningeal artery embolization for organized chronic subdural hematoma. J Neuroendovasc Ther 2019;13:321-8.
6. Kan P, Maragkos GA, Srivatsan A, Srinivasan V, Johnson J, Burkhardt JK, *et al*. Middle meningeal artery embolization for chronic subdural hematoma: A multi-center experience of 154 consecutive embolizations. Neurosurgery 2021;88:268-77.
7. Kanda Y. Investigation of the freely-available easy-to-use software "EZR" (Easy R) for medical statistics. Bone Marrow Transplant 2013;48:452-8.
8. Khorasanizadeh MH, Shutran M, Garcia A, Enriquez-Marulanda A, Moore J, Ogilvy CS, *et al*. Middle meningeal artery embolization for treatment of chronic subdural hematomas: Does selection of embolized branches affect outcomes? J Neurosurg 2022;138:1494-502.
9. Kosaka T, Ikeda N, Furuse M, Nonoguchi N, Hiramatsu R, Yagi R, *et al*. Refractory chronic subdural hematoma associated with Dural metastasis of lung adenocarcinoma treated with endovascular embolization for the middle meningeal artery: A case report and review of the literature. World Neurosurg 2020;133:256-9.
10. Link TW, Boddu S, Paine SM, Kamel H, Knopman J. Middle meningeal artery embolization for chronic subdural hematoma: A series of 60 cases. Neurosurgery 2019;85:801-7.
11. Lutz K, Kamenova M, Schaedelin S, Guzman R, Mariani L, Fandino J, *et al*. Time to and possible risk factors for recurrence after burr-hole drainage of chronic subdural hematoma: A subanalysis of the cSDH-drain randomized controlled trial. World Neurosurg 2019;132:e283-9.
12. Mowla A, Abdollahifard S, Farrokhi A, Yousefi O, Valibeygi A, Azami P. Middle meningeal artery embolization with liquid embolic agents for chronic subdural hematoma: A systematic review and meta-analysis. J Vasc Interv Radiol 2023;34:1493-500.e7.
13. Paro MR, Ollenschleger MD, Fayad MF, Bulsara KR, Stoltz P, Martin JE, *et al*. Middle meningeal artery embolization for primary treatment of a chronic subdural hematoma in a pediatric patient: A systematic review of the literature and case report. Oper Neurosurg 2023;24:3-10.
14. Poon MT, Al-Shahi Salman R. Association between antithrombotic drug use before chronic subdural haematoma and outcome after drainage: A systematic review and meta-analysis. Neurosurg Rev 2018;41:439-45.
15. Salem MM, Kuybu O, Hoang AN, Baig AA, Khorasanizadeh M, Baker C, *et al*. Middle meningeal artery embolization for chronic subdural hematoma: Predictors of clinical and radiographic failure from 636 embolizations. Radiology 2023;307:e222045.
16. Sattari SA, Yang W, Shahbandi A, Feghali J, Lee RP, Xu R, *et al*. Middle meningeal artery embolization versus conventional management for patients with chronic subdural hematoma: A systematic review and meta-analysis. Neurosurgery 2023;92:1142-54.
17. Stanisic M, Aasen AO, Pripp AH, Lindegaard KF, Ramm-Pettersen J, Lyngstadaas SP, *et al*. Local and systemic pro-inflammatory and anti-inflammatory cytokine patterns in patients with chronic subdural hematoma: A prospective study. Inflamm Res 2012;61:845-52.
18. Yang W, Huang J. Chronic subdural hematoma: Epidemiology

and natural history. Neurosurg Clin N Am 2017;28:205-10.
19. Zhang P, Li Y, Huang J, Zhang H. Chronic subdural haematoma in antithrombotic cohorts: Characteristics, surgical outcomes, and recurrence. Br J Neurosurg 2020;34:408-15.

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