Middle Meningeal Artery Embolization (MMAE) Versus Surgical Evacuation for Recurrent and Refractory Chronic Subdural Hematoma: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Recurrent and refractory chronic subdural hematoma (cSDH) remains a significant neurosurgical challenge due to high recurrence rates and morbidity associated with repeated surgical interventions. Middle meningeal artery embolization (MMAE) has recently emerged as a minimally invasive alternative, but its efficacy compared to surgical evacuation in this specific subgroup has not been systematically evaluated.
Methodology: A systematic search of Pubmed was conducted to identify studies reporting outcomes of MMAE and surgical evacuation in recurrent or refractory cSDH cases. Pooled efficacy rates and complication rates were extracted and analyzed using fixed-effects meta-analysis. Statistical significance was assessed with a p-value threshold of 0.05.
Results: Sixteen studies were included in the meta-analysis. 181 patients underwent surgical evacuation while 97 patients underwent MMAE for recurrent and refractory cSDH. MMAE demonstrated significantly higher efficacy with a pooled success rate of 95% versus 84% for surgery (p=0.002, I2=0). Complication rates were lower in the MMAE group (6%) versus the surgical group (10%), though the difference was not statistically significant (p=0.06, I2=0).
Conclusions: MMAE shows promise as a highly effective and safe treatment modality for recurrent and refractory cSDH, potentially surpassing surgical evacuation in both efficacy and safety. Given these findings, MMAE should be strongly considered not only as a salvage therapy but also as a frontline treatment option in this challenging patient population. Further high-quality randomized controlled trials are warranted to confirm these results and refine patient selection criteria.

KEYWORDS

Middle meningeal artery embolization; recurrent; refractory; chronic subdural hematoma; surgery

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INTRODUCTION

Chronic subdural hematoma (cSDH) is a common neurosurgical condition, especially in the elderly, typically caused by minor head trauma and characterized by the slow accumulation of blood between the dura and arachnoid membranes (1). Surgical evacuation via burr-hole craniostomy is the standard treatment; however, recurrence occurs in up to 30% of cases, often requiring repeat interventions and prolonged care (2).

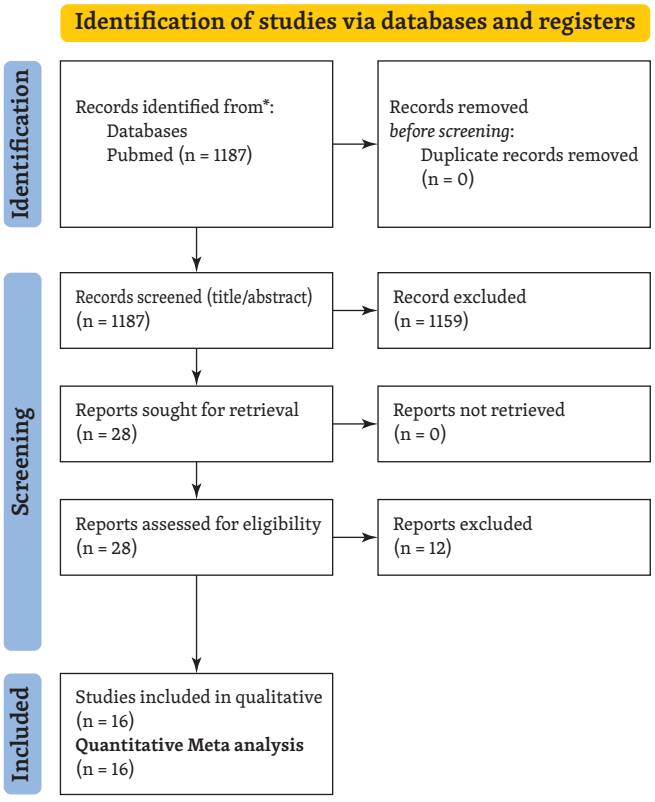
Middle meningeal artery embolization (MMAE) has recently emerged as a minimally invasive alternative or adjunct, aimed at occluding the vascular supply to the neo membranes that contribute to hematoma recurrence (3). Several studies have demonstrated promising outcomes with MMAE, particularly in reducing recurrence rates compared to surgical evacuation (4). While comparative studies and meta-analyses have examined MMAE versus surgery for cSDH in general (5), there is a lack of comprehensive reviews specifically focused on recurrent and refractory cases, a challenging subset with no clearly established management algorithm.

This systematic review and meta-analysis aims to bridge this gap by systematically evaluating the evidence comparing MMAE and surgical evacuation specifically in the context of recurrent and refractory chronic subdural hematomas, with a focus on clinical outcomes, recurrence, and safety profiles.

METHODS

LITERATURE SEARCH

We screened PubMed systematically as per the PRISMA guidelines (Fig. 1) from inception till May 1, 2025 for articles reporting the outcomes in patients undergoing surgery or MMAE for recurrent and refractory cSDH. Search strategy was generated using the terms similar to and including "MMAE", "surgery", "recurrent cSDH" and "refractory cSDH" along with boolean operators, AND, OR, NOT. The reference lists of the respective articles were also screened manually to prevent exclusion of any potential study.



INCLUSION AND EXCLUSION CRITERIA

We included the studies that were, 1) Reported in English language, 2) included patients with recurrent and refractory cSDH, 3) underwent surgery or MMAE, 4) had adequate outcomes data, success rate, and complications rate. Studies were excluded if they, 1) Were in a non-English language, 2) Had mixed data for recurrent and primary cSDH, 3) had inadequate outcomes data, 4) were reviews, case reports, editorials or commentaries. Two authors (BP, NP) independently reviewed the articles as per the inclusion and exclusion criteria and collected the required data for analysis. The senior author (IB) settled any disagreements.

In this review, 'recurrent' cSDH was defined as the re-accumulation of hematoma requiring intervention within 6 months of initial surgical evacuation. 'Refractory' cSDH was defined as persistent or re-accumulating hematoma that failed to resolve despite conservative treatment or more prior procedural interventions.

DATA COLLECTION

Following data points were extracted from each study included in this analysis:

- Patient's details (number of patients, age, gender)
- cSDH characteristics (volume)
- Type of therapy: Surgery or MMAE
- Follow up
- Outcomes – success rates and complication rates

QUALITY ASSESSMENT

Newcastle-Ottawa Quality Assessment Scale was utilized to assess the level of evidence of each study

STATISTICAL ANALYSIS

Meta-analysis was conducted using Jamovi software (version 2.3.1). DerSimonian and Laird models were generated to compare success rates and complication rates of surgery and MMAE.

RESULTS

Following PRISMA, 1187 studies were retrieved for title and abstract search. Twenty eight studies were selected for full article retrieval and finally, 16 studies met the inclusion and exclusion criteria. A total of 16 articles were included in this review. Nine studies reported the utilization of MMAE (Table 1), while seven studies involved invasive surgical procedures (Table 2).

Tab. 1 Summary of studies reported on MMAE for recurrent and refractory cSDH.

Author, year	Type of embolus	N	Age (years)	Gender	Volume (ml)/ thickness (mm)	Successful (%)	LOS (days, SD)	Complications	Quality of study
Liebert et al., 2023[6]	17 Onyx, 5 Squid & 1 PHIL	23	78.3	–	75.1 ml	20 (87)	5.45 (1.97)	2	7 Good
Dofuku et al., 2022[7]	NBCA	9	85	6M 3F	30 mm	9 (100)	–	0	8 Good
Tempaku et al., 2015[8]	PVA	5	83	4M 1F	–	5 (100)	–	0	7 Good
Link et al., 2018[9]	PVA	6	64.5	5M 1F	12.57 ml	6 (100)	–	0	8 Good
Nakagawa et al., 2019[10]	NBCA	20	78.3	14M 6F	–	20 (100)	–	0	7 Good
Mino et al., 2010[11]	Gelatin sponge & Guglielmi detachable coils	4	73	4M 0F	–	4 (100)	–	0	7 Good
Hashimoto et al., 2013[12]	5 NBCA, 1 PVA	5	71.4	3M 2F	–	5 (100)	–	0	7 Good
Kim, 2017[13]	PVA	20	73.65	14M 6F	19 mm	19 (95)	19.96 (13.44)	5	8 Good
Matsumoto et al., 2018[14]	NBCA	5	68.2	5M 0F	–	5 (100)	–	–	8 Good

n-butyl cyanoacrylate (NBCA), polyvinyl alcohol (PVA)

Tab. 2 Summary of studies reported on Surgical evacuation for recurrent and refractory cSDH.

Author, year	Modality	Demographics of patients	cSDH characteristics	Successful (%)	Complications	Quality
Liebert et al., 2023[6]	Surgery	27 hematomas 24 patients mean age:78.3 yrs	75.1ml volume, 2.67mm midline shift	19 (70.3)	2 patients developed a subdural empyema	7 Good
Kim 2017[13]	Surgery	24 hematomas 23 patients. Mean age: 65.65 yrs 16M, 7F	21mm thickness	16 (67.7) Hospital stay: 14.25 days	4	8 Good
Matsumoto et al., 2018[14]	Craniotomy	n=2 Mean age: 70yrs 2M	Refractory Organised: 2	2 (100)	0	8 Good
	Irrigation and drainage (I & D)	n=7 Mean age: 75yrs 6M, 1F	Refractory Organized: 0	7 (100) 1 patient underwent I & D 4 times	0	
Ichimura et al., 2020[15]	Neuroendoscope + small craniotomy	n=17 Mean age:83yrs 13M, 4F	Max diameter: 22.4 mm (range 15-37mm) Septations: 10	16 (94.1)	4 (postoperative seizures)	8 Good
Santarius et al., 2010[16]	Burr Hole without drain	n=36 Mean age:73 yrs 25M, 11F	-	24 (67)	6 1 subdural empyema, 3 pneumonia, 1 ASDH, 1 brain swelling.	8 Good
	Burr Hole with drain	n=14 Mean age:78 yrs 11M, 3F		12 (86)	2 1 ASDH, 1 subdural empyema	

Author, year	Modality	Demographics of patients	cSDH characteristics	Successful (%)	Complications	Quality
	Burr hole with subdural-to-peritoneal catheter	n=13 Mean age:79 yrs 9M, 4F		12 (92)	1 brain swelling	
Yamamoto et al., 2023[17]	Butterfly needle tap and suction	34 hematomas 26 patients Mean age: 78.8 yrs 19M, 7F	Midline shift: 7.5mm 42ml mean volume	21 (81)	2 headaches	8 Good
Sato et al., 2001[18]	Ommaya reservoir	23 hematomas, 16 patients Mean age: 74 yrs 13M, 3F	Mean volume: 100ml 11 unilateral 6 bilateral	13 (81.25) The hematoma size decreased to <3 mm at a median of 60 days after introduction of the reservoir	Occlusion of reservoir in 2 Minor bleeding in 2	8 Good

Ninety seven patients were treated with MMAE for their recurrent and refractory cSDH at a mean age of 75 years (SD: 6.7 years) with predominant male population (n=55, 74%). The most commonly used embolic agent was n-butyl cyanoacrylate (NBCA) (39 patients) followed by polyvinyl alcohol (PVA) (32 patients) and Onyx (17 patients).
Two hundred thirteen hematomas in 181 patients were treated with surgical evacuation. The mean age was 75.5 years (SD: 5 years) with 114 males (74%) and 40 females. There was no significant difference in the mean age (p=0.87) or gender wise distribution (p=0.96) between the MMAE and surgery cohorts.
There was a significant difference in the success (95% vs 84%, p=0.003, Welch's test, respectively) and complication rates (6% vs 10%, p=0.038, Mann Whitney test, respectively) between MMAE and surgical groups.
Fig. 2 depicts the longitudinal trends in the management options for recurrent and refractory cSDH.

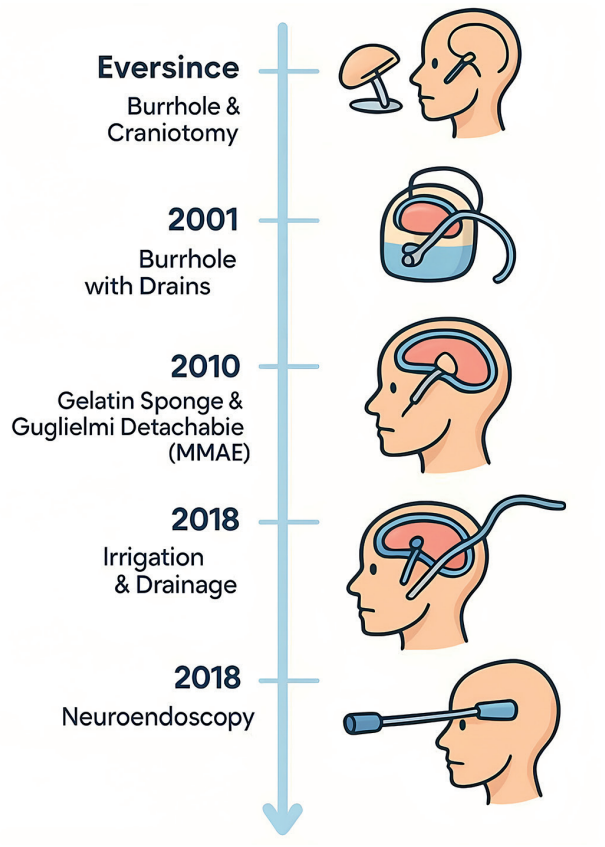


Fig. 2 Longitudinal trends in the management options for recurrent and refractory cSDH.

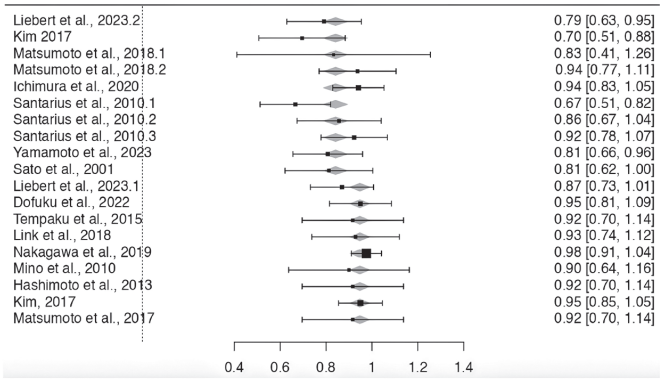


Fig. 3 Meta analysis of Success rates of MMAE and surgery for recurrent and refractory cSDH.

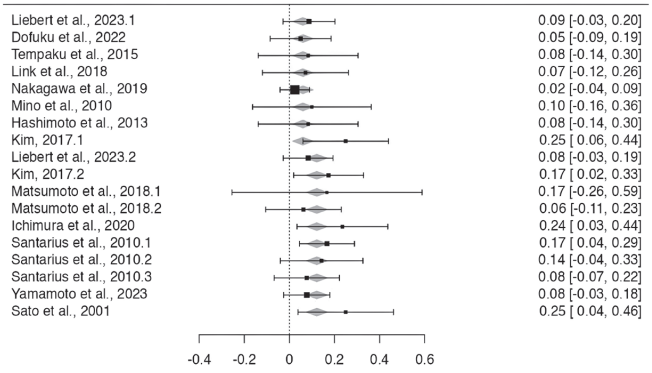


Fig. 4 Meta analysis of Complication rates of MMAE and surgery for recurrent and refractory cSDH.

META-ANALYSIS

The pooled success rate of MMAE was significantly higher than the surgery group (95% vs 84%, I^2=0%, p=0.002) (Fig. 3). However, there was no significant difference in the pooled complication rates of both groups (6% vs 10%, respectively I^2=0%, p=0.06) (Fig. 4).

DISCUSSION

This meta-analysis demonstrates that MMAE offers significantly higher efficacy than repeat surgical evacuation in the management of recurrent and refractory cSDH, with pooled success rates of 95% versus 84%, respectively

(p=0.002). To our knowledge, this is the first comprehensive meta-analysis specifically comparing MMAE and surgical evacuation in the challenging subgroup of recurrent and refractory cSDH patients, filling an important gap in the literature. These findings provide compelling evidence that MMAE is not only a viable alternative but may be a superior therapeutic option across a broad spectrum of patients. By targeting the vascular supply to the hematoma's outer membrane, MMAE addresses the pathophysiological driver of recurrence, chronic inflammation and fragile neovascularization; rather than merely removing the hematoma volume (18). This mechanistic advantage likely underpins the higher efficacy seen in this analysis and positions MMAE as a potentially transformative strategy in the treatment algorithm for recurrent cSDH.[5] Moreover, while the difference in complication rates between MMAE (6%) and surgical evacuation (10%) was not statistically significant (p=0.06), the trend favors MMAE in terms of safety. Reported complications with MMAE were infrequent, mostly minor, and often self-limiting, including groin hematomas and transient neurological symptoms. Surgical evacuation, in contrast, carried higher risks of infection, acute rebleeding, and postoperative seizures, particularly in older or medically fragile patients. Given its minimally invasive nature, superior efficacy and favorable safety and efficacy profile, MMAE shows promise not only as a salvage option but as a potential first-line treatment for recurrent – and possibly even primary – cases of cSDH in the future. Though the majority of the studies reported the use of MMAE in recurrent CSDH, the study by Hashimoto et al. implicated the utilization of MMAE in refractory cases (12). Similarly, only one study by Matsumoto et al. reported the surgical management of refractory cases (14). Therefore, there is a dearth of literature in the management of refractory cSDH and warrants more research.

MIDDLE MENINGEAL ARTERY EMBOLIZATION (MMAE)

MMAE has emerged as a successful and efficacious management option for recurrent and refractory cSDH with an estimated efficacy of 95% on this study. Of the nine studies included in this analysis, one study each reported a success rate of 87% and 95%, while the other seven had a success rate of 100%, establishing the superiority of MMAE to other techniques. Liebert et al (6) described that MMAE is suited for recurrent hematomas with a lower pre interventional volume and midline shift as well as mildly symptomatic cases.

In their comparative study between surgery and MMAE for recurrent cSDH, MMAE had significantly higher efficacy than surgery (87% vs 70.3%), shorter length of hospital stay and superior ability to detect treatment failure earlier. In another comparative study by Kim et al. (13) the second recurrence rates were significantly lower in the MMAE group as compared to the surgical group (3.8% vs 33.3%, p=0.024). Furthermore, MMAE significantly decreased the time required to restore the bihemispheric symmetry of the brain (34.65 vs. 98.29 days; $P < 0.001$). Owing to the lower rates of recurrence for MMAE, MMAE may be performed prophylactically in patients with the risk factors for recurrence after burr hole especially in elderly patients on anticoagulant therapy. Dofuku et al. (7) established a time frame appropriate for ensuring a good outcome. MMAE was performed within 2 weeks of the second burr hole surgery at a median duration of 10 days and gave a 100% success rate. They embolized both the anterior and posterior branches of MMA, irrespective of the dominant branch and found no recurrence or need of surgical rescue. However, the anatomical variations in the branches need to be kept in mind since that could give rise to complications, for instance, the anastomosis of the anterior branch with the ophthalmic artery, which can be catastrophic.

The most commonly used embolic agent was NBCA (39 patients) followed by PVA (32 patients) and Onyx (17 patients). NBCA is a liquid adhesive with a rapid onset of action, decreasing the operation time and facilitates performing the procedure under local anesthesia, which is desirable in elderly patients. NBCA and Onyx do not let the catheter tip adhere to the vessel wall, allowing for a long duration administration. Additionally, these can be easily visualised on CT, which is of importance since the agent has the tendency to penetrate the inner and outer membranes of the hematomas. PVA has an advantage of being cost effective and reaching a wider anatomical vasculature over NBCA and onyx which provides 'stump' embolization proximally, owing to the ability of the PVA particles to travel more distally within the MMA and restricting the formation of newer distal collaterals. The major disadvantage of onyx is that it is DMSO based with a higher risk of cranial nerve injury and toxicity.

The pooled complication rate for the MMAE cohort was 6% (n=7), however none of the patients had any permanent neurological deficits and recovered rapidly in the follow up period. MMAE is usually performed after gaining access to the MMA via the radial or femoral artery route. A novel route to perform MMAE through a puncture directly in superficial temporal artery in a patient with aortic dissection involving common carotid artery precluding the access through radial or femoral artery is described by Eccles et al. (19). This significantly reduces the operative time, however best performed at the hands of a trained personnel.

INSIGHTS FROM RECENT RANDOMIZED TRIALS

The landscape of cSDH management experienced a paradigm shift in 2024 with the publication of three landmark multicenter randomized controlled trials: MAGIC-MT, EMBOLISE, and STEM (29-31). While our meta-analysis highlights the efficacy of MMAE in the recurrent and refractory population, these recent trials provide robust, high-level evidence regarding its timing and application; specifically delineating its role as an adjunctive measure versus a standalone, first-line therapy.

As an adjunctive treatment to surgery, MMAE has definitively proven its value in preventing recurrence. Both the EMBOLISE and STEM trials evaluated MMAE performed concurrently with or shortly after surgical evacuation. In the EMBOLISE trial, patients who received adjunctive Onyx embolization after surgery had a significantly lower rate of

hematoma recurrence requiring reoperation compared to those who underwent surgery alone (4.1% vs. 11.3%). Similarly, the STEM trial demonstrated a significant reduction in treatment failure and recurrence when embolization was used alongside standard surgical care. By shutting down the fragile neovasculature of the dural membrane, adjunctive MMAE acts as a prophylactic mechanism, strongly supporting its routine use following initial evacuation to prevent patients from entering the refractory cycle.

Furthermore, recent data increasingly supports MMAE as a first-line, standalone treatment for appropriately selected patients, potentially bypassing the need for surgery altogether. In the MAGIC-MT trial, symptomatic patients randomized to receive standalone MMAE alongside conservative management showed significantly lower rates of subsequent surgical intervention and disease progression compared to those receiving conservative management alone. For patients with recurrent or refractory cSDH who have already failed standard surgical evacuation, these findings are particularly highly relevant. They suggest that standalone MMAE can successfully halt the inflammatory cycle of rebleeding without the morbidity of repeat open surgery. Consequently, rather than viewing MMAE solely as a salvage option after multiple surgical failures, the convergence of this recent RCT data suggests MMAE should be strongly considered as a primary, upfront intervention for early recurrences, or as a standalone first-line option for medically fragile patients with non-life-threatening hematoma volumes.

SURGICAL INTERVENTION

In the past decades, burr hole was the mainstay treatment for recurrent and refractory cases, due to the absence of any other efficacious alternatives. However, the success rates were moderate and recurrence rates were high, necessitating innovations in already existing modalities at the time, which included the use of Ommaya reservoirs and drains. Burr hole with external drain and subdural to peritoneal catheter had significantly higher success rates (86% vs 67%, 92% vs 67% respectively) and lower complication rates than burr hole alone for recurrent cSDH (16). Ommaya reservoirs placed between the scalp and the skull are proven to be instrumental in managing refractory cases complicated by severe diseases with a success rate of 81.25%. Matsumoto et al. (18) achieved a success rate of 100% for their patients with refractory cSDH undergoing craniotomy and I&D (14). They suggested MMAE to be suitable for refractory cases without organised hematomas, while for organized hematomas large craniotomy or mini craniotomy be performed as per the size and location of hematoma with a 100% success rate (14). The use of a rigid neuroendoscopy was implicated for the first time for recurrent cSDH by Ichimura et al. in 2020 in 17 patients (15). They performed a minicraniotomy at the same site as previous surgery followed by entry of the endoscope and the suction tube to evacuate the hematoma and remove the septations. Thereafter, the inner membrane was incised allowing for brain expansion. The endoscope facilitated the easy visualisation of the hematoma and the septations making the evacuation an unchallenging task. Only one patient underwent endoscopic evacuation twice owing to the regrowth of hematoma. Four patients had postoperative seizures which was easily managed with one time administration of antiepileptics in the hospital. Endoscopic evacuation not only managed but also reduced the recurrence of cSDH (15). In a study of 229 cases divided into two cohorts, endoscopic membranectomy and non endoscopic evacuation of cSD, the recurrence rate in the endoscopic group was 0% and significantly lower than the second cohort (20).

Yamamoto et al. introduced a novel and innovative technique, Butterfly needle tap and suction (BTS) for recurrent cSDH wherein hematoma was punctured percutaneously with a butterfly needle (NIPRO Safe Touch PSV, 23G × 3/4, 0.6 × 19 mm) at the site of previous burr hole connected to a 20 ml syringe and evacuated at a speed of 5 ml/min (17). The mean number of punctures was 2.2 and only 5 patients (19%) in their cohort needed a reoperation. BTS can be performed bedside, provided the hemorrhagic complications are prophylactically managed. This can be achieved by opening the dura in a cruciate manner and cauterising the critical vessels until occlusion, implicated in the burr hole during first surgery. Periprocedural headache was observed in 2 patients, which could be attributed to the temporary decrease in the intracranial pressure while aspirating the hematoma, giving rise to intracranial complications. Therefore, aspiration must be performed slowly at a speed of ≤ 5 ml/min (17).

In a refractory case with recurrence over 5 times, fibrin glue injection into the hematoma cavity after fifth surgery achieved full resolution of cSDH (21). 5 ml of 10,000 U Urokinase for two days directly injected into the hematoma cavity achieved a rapid and long term resolution of a bilateral refractory cSDH without any residual neurological deficits (22). Although the volume of hematoma was less than 50 ml in both these case reports, minimally invasive nature, zero complications and faster recovery makes fibrin glue and urokinase promising modalities.

ROLE OF MEDICATIONS

One study described the efficacy of pharmacological agents in the management of recurrent cSDH. Dexamethasone achieved a success rate of 71% and baseline functional rate of 87.5% in recurrent cSDH patients who took 4mg oral or systemic dexamethasone every 8 hours for 3 days.23 When compared with the cohort that underwent surgical evacuation of recurrent cSDH, there was no significant difference in the outcomes. Complication rate was 12.5%; complications were transient and easily managed within a month. A recent study on Japanese herbal medicines established their role in decreasing the recurrence of cSDH (24-28). The cohort of patients receiving the japanese herbal extracts had significantly lower recurrence rates than the control group undergoing surgery alone. The complication rates were 0%.

LIMITATIONS

The majority of the studies included for MMAE in the meta-analysis are from the developed world, limiting the understanding of its efficacy since the burden of

neurotrauma is highest in the developing world. Secondly, there is scarcity of studies in refractory cSDH and warrants more research to derive meaningful conclusions. Third, we could not assess other measures like operative time, blood loss and length of hospital stay in the meta analysis owing to the inadequacy of data. Fourth, there is a relative paucity of randomized controlled trials directly comparing MMAE and surgery, limiting the strength of causal inferences. Lastly, long-term functional outcomes and quality-of-life measures were inconsistently reported, restricting assessment of the broader clinical impact.

CONCLUSION

With the advancement in the understanding of recurrent cSDH, the shift of management has happened from surgical evacuation to MMAE. MMAE is a promising approach to manage recurrent and refractory cSDH cases with a pooled efficacy of 95% and minimal complications across all age groups. However, more complicated refractory cases might require surgical intervention and direct injections into the hematoma cavity.

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