Interventional procedure overview of middle meningeal artery embolisation for chronic subdural haematomas

Contents

Table 1 Abbreviations

Abbreviation	Definition
CI	Confidence interval
CSDH	Chronic subdural haematoma
DAVF	Dural arteriovenous fistula
HCO	Health care organisation
HR	Hazard ratio
MMA	Middle meningeal artery
MMAE	Middle meningeal artery embolisation
mRS	Modified Rankin Scale
NASH	Non-acute subdural haematoma
NBCA	n-butyl-2-cyanoacrylate
NIS	National inpatient sample
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
OR	Odds ratio
PVA	Polyvinyl alcohol
RCT	Randomised controlled trial
SD	Standard deviation
SDH	Subdural haematoma
SEM	Standard error of the mean
SEPS	Subdural evacuating port system

Indications and current treatment

CSDH is characterised by a pathological collection of blood in the subdural space, and usually has an insidious onset and progression. It may begin forming several days or weeks after bleeding initially starts. Bleeding is usually caused by a head injury, which may be minor in nature.

People who are asymptomatic or have minor symptoms with smaller haematomas are usually offered conventional treatment with careful monitoring and medical management. In contrast, people who have more severe symptoms and larger haematomas, and who have acceptable surgical risks, are generally offered burr hole surgery or a craniotomy.

What the procedure involves

This procedure is done using general or local anaesthesia, under fluoroscopic guidance. A catheter is inserted into the common femoral or radial artery, and a microcatheter is then guided into the MMA. Angiography is used to select MMA branches for embolisation and to detect collateral vessels.

If there are no significant collateral vessels, target branches are embolised. If there are significant collateral vessels, MMA embolisation may not be offered after the initial angiography. In the case of offering this procedure, the collateral vessels are either occluded using coils before embolisation, or the microcatheter is advanced more distally to avoid them. Once there is no flow in the MMA target branches on angiography, the catheters are removed.

This procedure aims to eliminate the blood supply from the MMA to the membrane around the haematoma, to allow the eventual spontaneous resolution of the haematoma, and to reduce the risk of recurrence.

Outcome measures

The main outcomes included haematoma resolution, reduction in size of haematoma, CSDH recurrence and surgical rescue, functional outcomes (mRS), length of hospital stay, mortality and (in-hospital) complications. Some measures are defined in the following paragraphs.

Complete resolution or near-complete resolution of haematoma was defined as a lesion measuring less than 5 mm on axial head CT after MMAE.

CSDH recurrence was defined as an increase of haematoma width on follow-up imaging compared with the immediate postoperative imaging.

Surgical rescue was defined as the need for surgical evacuation for recurrent or persistent CSDH after MMAE.

Functional outcome: mRS was used to assess the degree of disability or dependence in the daily activities. The scale ranges from 0 (no symptoms) to 6 (dead). A favourable outcome was defined as mRS score of 0 to 2.

In-hospital complications were defined as any adverse event related to the endovascular procedure, including new neurological deficit or radiological evidence of acute ischaemic or haemorrhagic changes on postembolisation imaging.

Evidence summary

Population and studies description

This interventional procedure overview is based on approximately 66,088 patients with CSDHs from 4 systematic reviews and meta-analyses (Haldrup 2020; Ironside 2021; Abdollahifard 2022; Ku 2023), 3 cohort studies (Dicpinigaitis 2021; Nia 2022; Scoville 2022), 2 case series (Catapano 2021; Khorasanizadeh 2022) and 2 case reports (Piergallini 2019; Wilseck 2022). Of these 66,554 patients, only 2,028 patients had MMAEs, with most patients having primary MMAEs, followed by rescue MMAEs and then prophylactic MMAEs when reported.

This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 9 studies as the main evidence in table 2 and table 3, and lists other 78 relevant studies in table 5.

Of the 11 studies included in the main evidence, 6 primary studies were done in the US, 3 systematic reviews and meta-analyses included studies which were done in various countries, 2 articles did not report the countries (Haldrup 2020; Piergallini 2019). Six articles reported the outcomes based on number of patients (Haldrup 2020; Abdollahifard 2022; Ku 2023; Dicpinigaitis 2021; Nia 2022; Scoville 2022), 4 articles presented the outcomes using number of treated CSDHs (Catapano 2021; Khorasanizadeh 2022; Piergallini 2019; Wilseck 2022), and 1 systematic review by Ironside (2021) mainly considered number of patients (only 1 included study reported the outcome data using number of cases of CSDHs). Patients were recruited from 2012 to 2021. Five primary studies had follow-up durations of 3 to 6 months, 4 systematic reviews included studies with follow-up periods ranging from 6 weeks to 5 years, and 1 study (Dicpinigaitis 2021) did not report the follow-up duration.

Four systematic reviews and meta-analyses were included. The systematic review and meta-analysis by Ironside (2021) compared MMAE with conventional management (surgical drainage or observation). The Haldrup (2020) systematic review and meta-analysis investigated the effect of MMAE for primary and recurrent CSDH. The Abdollahifard (2022) article evaluated the efficacy and safety of MMAE using particle embolic agents to treat CSDH, and the Ku (2023) paper assessed outcomes after MMAE by different techniques, including in comparison with traditional surgical methods.

Two cohort studies compared MMAE with surgery (Nia 2022; Dicpingigaitis 2021) and 1 cohort study (Scoville 2022) compared outcomes after particle or liquid MMAE. Two case reports were included because of unique safety outcomes identified (Piergallini 2019; Wilseck 2022). Table 2 presents study details.

Figure 1 Flow chart of study selection

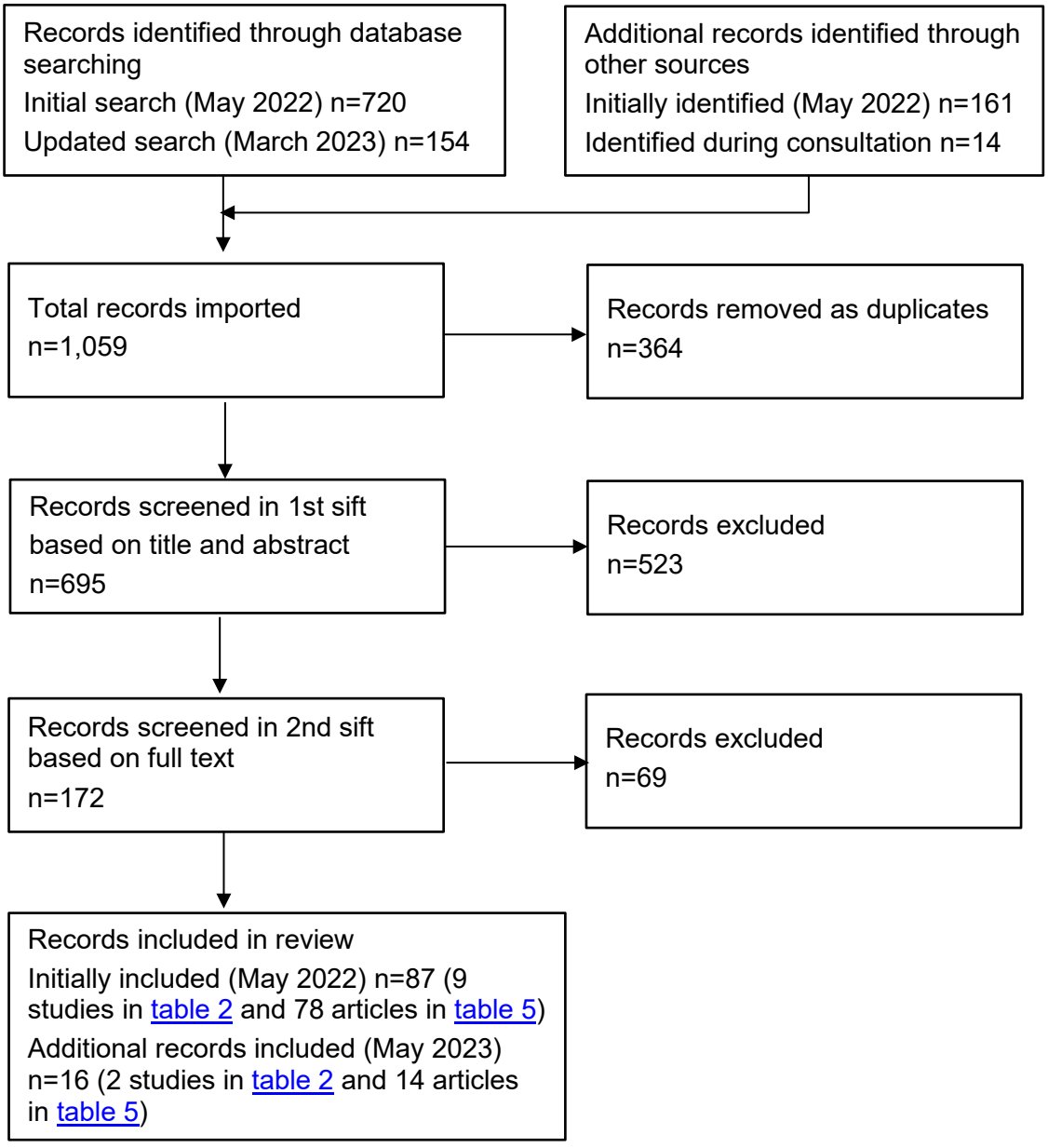

Table 2 Study details

Study no.	First author, date country	Patients (male: female)	Age (mean, years)	Study design	Inclusion criteria	Intervention	Follow up
1	Ironside 2021 Japan (n=8), USA (n=7), Korea (n=2), France (n=2), and China (n=1).	1,386 (20 studies: 5 double-arm studies and 15 single-arm studies) (MMAE: 74% male)	MMAE:72.7	Systematic review and meta-analysis	Studies with 3 or more patients having MMAE for CSDH; postembolisation outcomes data describing CSDH recurrence being reported; and English language.	MMAE using particles, liquid, coils, microspheres, or Onyx (n=688 patients with 714 MMAEs) • Upfront MMAE: 28.4% • Prophylactic MMAE: 23.2% • Rescue MMAE: 47.8% Conventional management (n=698); observation with serial neuroimaging or surgical drainage	Mean 1.5 to 26.3 months
2	Haldrup 2020 Not reported for individual studies	191 (18 single-arm studies)	45 to 91 years (apart from 1 case report of patient being 13 years old)	Systematic review and meta-analysis	Not reported	MMAE using PVA, NBCA or coils for: • Primary CSDH: n=119 • Recurrent CSDH after burr hole craniostomy: n=72	6 weeks to 5 years
3	Abdollahifard 2022 US (n=5), Israel (n=2), South Korea	1,234 (11 studies; sex, not reported)	MMAE: 74.2 Conventional management: 73.1	Systematic review and meta-analysis	Studies that evaluated the effect of MMAE with the use of particle embolic agents for the treatment of	MMAE using particles: • MMAE alone • adjunct MMAE Conventional management	Mean 124 days

Study no.	First author, date country	Patients (male: female)	Age (mean, years)	Study design	Inclusion criteria	Intervention	Follow up
	(n=2), France (n=1), and Germany (n=1)				CSDH and reported clinical outcomes either in comparison with conventional treatment or as sole intervention.		
4	Ku 2023 US (n=11), Japan (n=5), Korea (n=2), France (n=2), Germany (n=1), and China (n=1)	1,755 (22 studies; sex, not reported)	Not reported	Systematic review and meta-analysis	Studies that were randomised or had an observational prospective or retrospective study design and reported outcomes following MMAE in patient CSDH.	MMAE using PVA, n-BCA, Onyx, or PVA with or without coils: • MMAE alone • adjunct MMAE	Mean 2 to 26.3 months (19 studies)
5	Nia (2022) US (31 HCOs)	4,274 (2,966: 1,326)	Primary MMAE: 72.0; Adjunct MMAE: 67.9;Rescue MMAE: 69.8; Primary surgery; 62.4.	Cohort study (TriNetX Analytics Network - national registry)	A confirmed diagnosis of nontraumatic CSDH and nontraumatic SDH in patients who had embolisation or surgical procedures for evacuation of haematoma within 1 month of the CSDH diagnosis.	MMAE: • Primary MMAE: n=209 (4.9%) • Adjunct MMAE: n=15 (0.03%) • Rescue MMAE: n=18 (0.42%) Primary surgery: n=4,050 (94.8%)	6 months

Study no.	First author, date country	Patients (male: female)	Age (mean, years)	Study design	Inclusion criteria	Intervention	Follow up
6	Scoville 2022 US (15 academic centres)	208 (155:53)	Mean 61.8 to 73.5 years	Cohort study	Presence of NASH and treatment with MMAE.	MMAE using particles or liquid embolisates: • Upfront MMAE: n=133 • Rescue MMAE: n=59 • Prophylactic MMAE: n=16	90 days
7	Dicpinigaitis (2021) US (NIS)	60,045 (42,115:17, 930)	62.1	Cohort study	Adult patients with primary admission diagnoses of non-traumatic SDH; treatment modalities including craniotomy, burr hole craniostomy, and MMAE.	MMAE for CSDH: n=390 (0.6%) • MMAE with prior evacuation by craniotomy or burr hole craniostomy: n=75 Craniotomy or burr hole craniostomy: n=59,655 (99.4%)	Not reported
8	Catapano (2021) US	66 (84 treated CSDHs) (51:15)	70	Case series	Not reported	MMAE using liquid (Onyx), particles, coils or NBCA: • MMAE combined with surgery: n=31 (37%) • MMAE alone: n=53 (63%)	180 days
9	Khorasanizadeh (2022) US	78 (94 hemispheres treated CSDHs)	72	Case series	Diagnosis of CSDH and treatment by MMAE	MMAE: • Upfront MMAE: n=72 (76.6%) • prophylactic MMAE: n=14 (14.9%)	Mean 113.9 days

Study no.	First author, date country	Patients (male: female)	Age (mean, years)	Study design	Inclusion criteria	Intervention	Follow up
						• rescue MMAE: n=8 (8.5%)	
10	Piergallini (2019) Not reported	2 (3 treated CSDHs) (0:2)	82	Case report	Not reported	Prophylactic MMAE using PVA at 2 and 4 days after burr hole surgery	3 months
11	Wilseck (2022) US	1 (male) (bilateral acute on CSDH)	62	Case report	Not reported	Upfront MMAE: bilateral embolisation.	90 days

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Ironside (2021)	MMAE compared with conventional management (n=698): • **Rate of CSDH recurrent**: 4.8% (95% CI 3.2 to 6.5%) compared with 21.5% (95% CI 0.6 to 42.4%) • **Surgical rescue**: 4.4% (95% CI 2.8 to 5.9%) compared with 16.4% (95% CI 5.95 to 27.0%) • **mRS score of 0 to 2 at last follow up**: 72.8% (95% CI 46.3 to 99.2%) compared with 92.3% (95% CI 10.8% to 100%) 5 double-arm studies (n=902): MMAE (n=204) compared with conventional management (n=698)	MMAE compared with conventional management: • **In-hospital complications**: 1.7% (95% CI 0.8 to 2.6%) compared with 4.9% (95% CI 2.8 to 7.1%) 5 double-arm studies (n=902): MMAE (n=204) compared with conventional management (n=698) • **In-hospital complications**: OR=0.78, 95% CI 0.34 to 1.76, p=0.55, I^2=0%

First author, date	Efficacy outcomes	Safety outcomes
	• **CSDH recurrence**: OR 0.15, 95% CI 0.03 to 0.75, p=0.02, I^2=38% (n=639; 4 studies) • **Surgical rescue**: OR 0.21, 95% CI 0.07 to 0.58, p=0.003, I^2=19% (902; 5 studies) Subgroup analysis of upfront (n=43; 4 studies) compared with postoperative MMAE (n=256; 15 studies): • Rate of CSDH recurrence: 0% compared with 3.9% (95% CI 1.4 to 6.4%) • Surgical rescue: 0% compared with 2.9% (95 CI 0.8 to 5.0%)	Subgroup analysis of upfront (n=43) compared with postoperative MMAE (n=256): • **In-hospital complications**: 0% compared with 2.8% (95% CI 0.7 to 4.8%)
Haldrup 2020	**Recurrence rate**: • Primary CSDH (n=119): 4% (n=5), 95% CI 1.4 to 11.4%, I^2=6% • Recurrent CSDH (n=72): 2.4% (n=2), 95% CI 0.5 to 11.0%, I^2=6% **OR for recurrence** - primary compared with recurrent CSDH: 1.7 (95% CI 0.3 to 11.1), p>0.05	No complications were described (not defined in 6 studies and 0 complication in 12 studies)

Abdollahifard 2022	MMAE using particles as a single proportion:
	• **Overall procedural success rate**: 100% (95% CI 19% to 100%; I^2=0%)
	  ○ Adjusted rate: 97% (95% CI 96% to 98%)
	• **Rate of reduction in haematoma size**: 85% (95% CI 66% to 94%)
	• **Rate of haematoma resolution**: 66% (95% CI 39% to 86%)
	• **Recurrence rate**: 5% (95% CI 3% to 8%; I^2=0%)
	• **Reoperation rate**: 5% (3% to 9%; I^2=0%)
	MMAE compared with conventional management:
		MMAE using particles:
		• **Periprocedural complication rate**: 4% (95% CI 2% to 9%)
		• **Mortality rate**: 1% (95% CI 0% to 3%; I^2=0%)
		  ○ Adjusted rate: 3% (95% CI 0.2% to 4%)
		MMAE compared with conventional management:
		• **Mortality**: RR 0.17 (95% CI 0.01 to 2.01; I^2=0%; 5 studies)

First author, date	Efficacy outcomes	Safety outcomes
	• **Recurrence**: RR 0.10 (95% CI 0.04 to 0.27; I^2=0%; 6 studies) • **Reoperation**: RR 0.25 (95% CI 0.13 to 0.49; I^2=37%; 6 studies) Reduction in size or resolution of haematoma: • MMAE: 91% (95% CI 40% to 99%; I^2=82%; 5 studies) Conventional treatment: 63% (95% CI 39% to 81%; I^2=93%; 5 studies)	**Periprocedural complication:** 0.34 (95% CI 0.16 to 0. 2; I^2=0%; 6 studies)
Ku 2023	Single-arm overall outcomes including both MMAE alone and adjunct to surgery: • **Intraprocedural complete embolisation of the MMA**: 96% (397/421; 95% CI 93.4% to 98.7%) • **Recurrence rate** after MMAE (both primary and adjunct treatment): 4.1% (50/898; 95% 2.8% to 5.4%) On person-time analysis, the rate of SDH recurrence over time was 0.6% (95% CI 0.3% to 1%) per month • **Reoperation rate** for recurrent or residual haematomas: 4.2% (50/888; 95% CI 2.9% to 5.5%) • **Rate of good radiological outcome** (>50% haematoma resolution, <10mm residual haematoma width, or improvement on the last CT scans): 83.1% (382/518; 95% CI 74.6% to 91.5%; I^2=85.03%) • **Rate of good clinical outcome** (MR spectroscopy 0 to 2, Glasgow outcome score 4 to 5, Glasgow outcome scale-extended 5 to 8, and improvement in neurological or functional status or neurological deficit at the last follow up): 73.3% (292/372; 95% CI 60% to 86.6%; I^2=92.37%) • **Mean reduction in haematoma volume**: 54.2 mL (95% CI 46.3 to 62)	Single-arm overall outcomes including both MMAE alone and adjunct to surgery: **Postoperative complications**: 2.6% (36/890; 95% CI 2.9% to 5.5%) • groin complications: n=2 (1 groin haematoma, 1 femoral artery occlusion) • procedural complications: n=3 (rupture of the MMA, 1 transient bradycardia during embolisation) • postprocedural infarcts: n=4 (clinical or radiologic) • medical complications: n=10 (urinary tract infection, pneumonia, deep vein thrombosis, pulmonary embolism) • seizures or new neurological deficits or unspecified complications: n=15 MMAE alone compared with adjunct to surgery:

First author, date	Efficacy outcomes	Safety outcomes
	• **Mean reduction in haematoma width**: 9.9 mm (95% CI 7.5 to 12.2; I^2=93.99%) MMAE alone compared with adjunct to surgery: • **Recurrence rate:** 6.3% (95% CI 3.3% to 9.3%) compared with 5.3% (95% CI 2.7% to 7.9%), p=0.976, I^2=0% Person-time analysis: 1.7% (95% CI 0.7% to 2.6%) per month compared with 0.3% (95% CI 0% to 0.6%) per month, p=0.035, I^2=11.91% Pair-wise meta-analysis: OR 0.36, 95% CI 0.12 to 1.09, p=0.071, I^2=41.63%; 5 studies • **Reoperation rate**: 5.4% (95% CI 2.6% to 8.2%) compared with 4.6% (95% CI 2% to 7.2%), p=0.912, I^2=0% Pair-wise meta-analysis: OR 0.48, 95% CI 0.23 to 0.99, p=0.047, I^2=37.49%; 8 studies • **Rate of good radiological outcome:** 94.1% (95% CI 84.8% to 100%) compared with 92.1% (95% CI 85.8% to 98.5%), p=0.187, I^2=0% Pair-wise meta-analysis: OR 1.72, 95% CI 0.16 to 18.7, p=0.657, I^2=94.51%; 3 studies • **Rate of good clinical outcome**: 81.2% (95% CI 66.7% to 95.6%) compared with 75.3% (95% CI 36% to 100%), p=0.569, I^2=71.81% Pair-wise meta-analysis: OR 0.88, 95% CI 0.31 to 2.49, p=0.308, I^2=51.01%; 3 studies Embolisation comparing agent choice:	**Postoperative complications:** 2.2% (8/243; 95% CI 0.6% to 4%) compared with 5.5% (22/280; 95% CI 1.5% to 9.5%), p=0.025, I^2=43.18% Pair-wise meta-analysis: OR 0.81, 95% CI 0.49 to 1.33, p=0.407, I^2=0%; 7 studies Embolisation comparing agent choice: **Complication rate**: PVA, 5.6% (95% CI 1.1% to 10.1%); n-BCA, 3% (95% CI 0% to 6.9%); Onyx, 2% (95% CI 0% to 6.4%); PVA with or without coils, 1.4% (95% CI 0% to 3.7%).

First author, date	Efficacy outcomes	Safety outcomes
	• **Recurrent rate**: PVA, 4.7% (95% CI 1.5% to 8%); n-BCA, 3.5% (95% CI 0% to 8.1%), PVA with or without coils, 2.2% (95% CI 0% to 5.1%); Onyx, 2% (95% CI 0% to 6.4%) • **Reoperation rate**: PVA, 4.2% (95% CI 1.2% to 7.3%); PVA with or without coils, 4.1% (95% CI 1% to 7.3%); n-BCA, 3.7% (95% CI 0% to 8.2%); Onyx, 2% (95% CI 0% to 6.4%) • **Rate of good radiological outcome:** Onyx, 82% (95% CI 57% to 100%); PVA with or without coils, 84.4% (95% CI 63.9% to 100%) **Rate of good clinical outcome:** PVA with or without coils, 85.2% (95% CI 68.1% to 100%); n-BCS, 78.5% (95% CI 55.9% to 100%); Onyx, 75.7% (95% CI 63.8% to 87.5%)	
Nia (2022)	**Hospital stay** (mean, 95% CI): • Primary MMAE: 7.74 days (95% CI 6.04 to 9.44) • Primary surgery: 30.20 days (95% CI 26.38 to 34.02) • P value: <0.0001 **6-month survival ratio:** the difference is 1.25% for the primary MMAE compared with primary surgery (p=0.35) **Treatment failure or need for surgical rescue**: • Primary MMAE compared with primary surgery: OR 0.47, 95% CI 0.25 to 0.90, p=0.02 (4.8% absolute risk difference in favour of primary MMAE) • Primary MMAE, adjunct MMAE and rescue MMAE: no statistically significant difference between groups (p>0.05).	Occurrence of headaches or facial weakness, or mortality between primary MMAE and primary surgery: all p>0.05
Scoville 2022	**50% reduction in maximal haematoma thickness at 90 days** - particles compared with liquid embolisates:	**Complications** - particles compared with liquid embolisates:

First author, date	Efficacy outcomes	Safety outcomes

	• Upfront MMAE: 61.8% (63/102) compared with 61.3% (19/31), p=0.962
	• Rescue MMAE: 61.0% (25/41) compared with 55.6% (10/18), p=0.696
	• Prophylactic MMAE: 72.7% (8/11) compared with 20% (1/5), p=0.106
	Time to reach 50% reduction in haematoma size - particles compared with liquid embolisates:
	• Upfront MMAE: HR 1.31, 95% CI 0.78 to 2.18, p=0.310
	• Rescue MMAE: HR 1.09, 95% CI 0.52 to 2.27, p=0.82
	• Prophylactic MMAE: HR 1.5, 95% CI 0.14 to 16.54, p=0.74
	Retreatments within 90 days - particles compared with liquid embolisates:
	• Upfront MMAE: 8.0% (8/100) compared with 0% (0/31), p=0.197
	• Rescue MMAE: 2.4% (1/41) compared with 5.6% (1/18), p=0.521
	• Prophylactic MMAE: 0% (0/11) compared with 0% (0/5), p=1.00
		• Upfront MMAE: 11.6% (11/102) compared with 3.2% (1/31), p=0.465
		• Rescue MMAE: 7.3% (3/41) compared with 0% (0/18), p=0.549
		• Prophylactic MMAE: 0% (0/11) compared with 0% (0/5), p=1.00
		Detailed complications:
		• **Neurological complications**: n=9
		  ○ Stroke: n=5 (because of subdural compression, increased lethargy, increased balance difficulties, intermittent aphasia, and numbness)
		  ○ Worsening headaches: n=2
		  ○ New-onset seizures: n=2
		• **Technical complications**: n=4
		  ○ MMA rupture: n=1 (the patient died from unrelated causes)
		  ○ External carotid artery spasm: n=1
		  ○ Postprocedural facial droop from Onyx infiltrating the meningeal branches of the skull base and resulting in facial nerve damage: n=1
		  ○ Uncategorised technical complication: n=1

First author, date	Efficacy outcomes	Safety outcomes
		• **Postsurgical infections that needed surgical treatment**, n=2
Dicpinigaitis (2021)	Clinical outcome comparison – MMAE compared with surgical evacuation by craniotomy or burr hole craniostomy: • **Routine discharge**: 39.7% (155/390) compared with 38.8% (23,175/59,655), p=0.858 • **Hospital length of stay** (mean [SEM], days): 13.0 (2.0) compared with 8.3 (0.1), p=0.023 Propensity score-adjusted comparison – MMAE compared with surgical evacuation by craniotomy or burr hole craniostomy: • **Routine discharge**: 39.7% (159/390) compared with 29.5% (390), p=0.141 • **Hospital length of stay** (mean [SEM], days): 13.0 (1.8) compared with 7.4 (0.8); p=0.006	Intracranial complications: MMAE compared with surgical evacuation by craniotomy or burr hole craniostomy • **Peri or postoperative haemorrhagic or ischaemic complications**: 0% (0/390) compared with 0.6% (335/59,655), p=0.591 • **Facial drop**: less than 3% in MMAE • **Visual deficit/blindness**: 0% (0/390) compared with 0.2% (140/59,655), p=0.703 **In-hospital mortality**: less than 3% in MMAE
Catapano (2021)	**CSDH size** (mean [SD], mm): • Baseline: 16.9 (4.8); 30 days: 8.8 (4.3); 90 days: 3.4 (3.0); 180 days: 1.0 (1.7) • All p<0.001 compared with baseline. **Complete or near-complete resolution**: • 30 days: 18% (15/84); 90 days: 63% (45/72); 180 days: 92% (67/73), p<0.001 compared with 30 and 90 days postembolisation. **Surgical rescue** within 30 days after MMAE: 4% (3/84) In the multivariable analysis, only distal embolysate penetration (into the vertex) was independently associated with rapid clearance (OR 3.9, 95% CI 1.4 to 11.1; p=0.01) and resolution of CSDHs at 90 days (OR 5.0, 95% CI 1.7 to 14.6; p=0.003).	Complication: **cerebrovascular accident**, 1% (1/84) likely caused by instability of the access catheter (via a transfemoral route).

First author, date	Efficacy outcomes	Safety outcomes
Khorasaniza deh (2022)	**Haematoma axial thickness** (mean, mm): • All patients: Baseline, 16.0; last follow up: 5.7; mean reduction, 59.2% • Coils only (n=12 CSDHs) compared with coils and particles (n=82 CSDHs): mean reduction, 59.5% (55.4%) compared with 59.1% (63.8%), p=0.96 **Haematoma volume** (mean [SD], ml): • All patients, Baseline, 92.3; last follow up: 29.6 ml; mean reduction, 71.4% • Coils only compared with coils and particles: mean reduction, 68.3% (35.8%) compared with 71.8% (43.7%), p=0.8 **Haematoma axial thickness decreased by at least 50%:** coils only, 83.3% (n=10) compared with 72.0% (n=59), p=0.4 **Haematoma volume decreased by at least 50%:** • All patients, 79.8% • Coils only compared with coils and particles: 81.8% (n=9) compared with 76.3% (n=58), p=0.68 **Rescue surgery:** • All patients: 8.5% (n=8, including 6 surgical evacuation by craniotomy and 2 by burr-hole surgery, after a mean 33.1 days after MMAE) • Coils only compared with coils and particles: 8.3% (n=1) compared with 8.5% (n=7), p=0.98 **mRS stabilisation or improvement:** • All patients: 83.0% • Coils only compared with coils and particles: 91.7% (n=11) compared with 81.7% (n=67), p=0.39	Procedure-related complications: n=2 • **Left-eye pain, vision loss, and dilated nonreactive pupil** (MRI or MRA showed left central retinal artery occlusion and evidence of optic nerve infarction), n=1 • **Global aphasia and right hemiplegia** (CT angiogram showed occlusion of the anterior division of the left middle cerebral artery), n=1 The patient had emergent thrombectomy of the left M_2 clot with successful recanalisation and neurological recovery.

First author, date	Efficacy outcomes	Safety outcomes
Piergallini (2019)	**Discharge:** 1 week after MMA **CT and angio-CT scans at 3 months:** no recurrence of the SDH or fistula and no signs of intracranial bleeding.	**DAVF** after MMAE: n=2 Both patients remained completely asymptomatic after the development of the fistula, which was occluded by coiling the MMA at the level of the point of shunt.
Wilseck (2022)	**Discharge:** 1 day after MMAE Sequential imaging showed decreasing density and size of the treated subdural collections leading to less mass effect and midline shift. There was no evidence of subsequent acute bleed. The patient's headache improved, and the patient remains neurologically intact.	**Iatrogenic MMA pseudoaneurysm** related to use of a dual-lumen balloon catheter: n=1 This event was successfully treated with ethylene vinyl alcohol embolisation.

Procedure technique

The embolisation procedure was not thoroughly described in all studies, but in general, the procedures were done under general or local anaesthesia with light or no sedation. Endovascular access to the MMA was through the radial or femoral artery, and a microcatheter was advanced under roadmap guidance. Target branches were embolised using liquid embolics, particles, coils, or a combination. Particles and liquid embolics were used more often than coils, while coils were likely to be used in combination with particles. If dangerous anastomoses including ophthalmic collaterals were seen, coils were used exclusively.

MMAE was used to treat primary or recurrent CSDHs, and when combining with surgical evacuation, MMAE was also applied to prevent the recurrence of CSDHs. Therefore, MMAE has been done in 3 treatment stages:

- upfront or primary embolisation in patients with a previously untreated CSDH so embolisation was used as the first treatment without concomitant surgical intervention.
- prophylactic or adjunct embolisation after surgical evacuation without evidence of interval postoperative CSDH recurrence (surgery and embolisation usually within 7 days).
- rescue embolisation for recurrent CSDH after previous surgical evacuation (more than 7 days after primary surgery).

Of the 9 studies, 3 studies presented the outcome data for different treatment purposes separately (Ironside 2021; Haldrup 2020; Nia 2022), 1 study focused on different embolic agents in each treatment stage (Scoville 2022), and 3 studies (Dicpinigaitis 2021; Catapano 2021; Khorasanizadeh 2022) reported the outcomes of MMAE used in different treatment stages as a whole. Where

possible, the outcomes for MMAE used in specific treatment stage will be described separately.

Efficacy

Haematoma resolution

Data on resolution of haematoma was described in 2 studies. Abdollahifard (2022) reported that the pooled rate of haematoma resolution was 66% (95% CI 39% to 86%). Based on follow-up imaging, the rate of reduction in size or resolution of haematoma was 91% (95% CI 40% to 99%; I^2=82%; 5 studies) after MMAE and 63% (95% CI 39% to 81%; I^2=93%; 5 studies) after conventional management. Catapano (2021) found that the rate of complete or near-complete resolution was in 18% (15/84) of treated CSDHs at 30 days, 63% (45/72) at 90 days and 92% (67/73) at 180 days after MMAE. This study also found that there were statistically significantly more instances of complete or near-complete resolution at 180 days compared with at 90 and 30 days after MMAE.

Haematoma reduction

Data on haematoma size before and after MMAE was presented in 5 studies. Abdollahifard (2022) found a pooled rate of 85% (95% CI 66% to 94%) for reduction in size**.** Ku (2023) reported that the rate of good radiological outcome (>50% haematoma resolution, <10 mm residual haematoma width, or improvement on the last CT scans) was 83% (95% CI 74.6% to 91.5%; I^2=85.03%). When considering MMAE used alone or as an adjunct to surgery, the rate of good radiological outcome was 94% (95% CI 84.8% to 100%) compared with 92% (95% CI 85.8% to 98.5%, p=0.187), respectively.

Catapano (2021) reported that the mean CSDH size statistically significantly reduced from 16.9 mm (SD 4.8) at baseline to 8.8 mm (SD 4.3) at 30 days, 3.4 mm (SD 3.0) at 90 days, and 1.0 mm (SD 1.7) at 180 days after MMAE. Khorasanizadeh (2022) found that the mean haematoma axial thickness and

volume reduced from 16.0 mm and 92.3 ml to 5.7 mm (mean reduction 59.2%) and 29.6 ml (mean reduction 71.4%) at a mean of 114 days after MMAE. The authors did not find statistically significant differences between MMAE using coil only and MMAE using coils and particles in haematoma axial thickness reduction by at least 50% (83% compared with 72%) or in haematoma volume reduction by at least 50% (82% compared with 76%). Similarly, Scoville (2022) reported that the proportions of patients who had a 50% hematoma thickness reduction were not statistically significantly different between particles and liquid embolisates at 90 days after upfront MMAE (62% compared with 61%), rescue MMAE (61% compared with 56%) or prophylactic MMAE (73% compared with 20%).

Haematoma recurrence and surgical rescue

Data for haematoma recurrence and surgical rescue was described in 8 studies. When comparing MMAE with standard management, Ironside (2021) reported that the pooled recurrence rate of CSDH recurrence from 20 studies was 5% (95% CI 3.2 to 6.5%) in the MMAE group and 22% (95% CI 0.6 to 42.4%) in the conventional management group. MMAE was associated with a lower rate of CSDH recurrence compared with conventional management (OR 0.15, 95% CI 0.03 to 0.75, p=0.02, I^2=38%; n=639, 4 studies). In terms of surgical rescue, the authors found that the pooled rate was 4% (95% CI 2.8 to 5.9%) in the MMAE group and 16% (95% CI 5.95 to 27.0%) in the conventional management group. MMAE was also associated with a lower rate of surgical rescue than conventional management (OR 0.21, 95% CI 0.07 to 0.58, p=0.03, I^2=19%; n=902, 5 studies). Abdollahifard (2022) reported a pooled recurrence rate of 5% (95% CI 3% to 8%) and a need for reoperation rate of 5% (3% to 9%) after MMAE (both MMAE alone and adjunct MMAE). Ku (2023) found that the rate of subdural haematoma recurrence was 4% (95% CI 2.8% to 5.4%) after MMAE (both primary and adjunct treatment). The authors also described that the rate of reoperation for recurrent or residual haematomas was 4% (95% CI 2.9% to 5.5%). Nia (2022)

reported a lower rate of treatment failure or need for surgical rescue after primary MMAE than primary surgery (OR 0.47, 95% CI 0.25 to 0.90, p=0.02).

In 2 case series, the rate of surgical rescue was from 4% (3/84) within the 30 days after MMAE (Catapano 2021) to 8.5% (8/94) after a mean follow up of 33.1 days (Khorasanizadeh 2022).

When considering MMAE used in different treatment stages, Ironside (2021) described that the recurrent rate was 0% after upfront MMAE (n=43, 4 studies) and 4% (95% CI 1.4 to 6.4%) after postoperative, adjunct MMAE (n=256, 15 studies). The authors also reported that the rate of surgical rescue was 0% after upfront MMAE and 3% (95% CI 0.8 to 5.0%) after postoperative MMAE. Haldrup (2020) found that the recurrence rate for patients having primary MMAE was 4% (95% CI 1.4 to 11.4%, I^2=6%) and for patients having rescue MMAE it was 2% (95% CI 0.5 to 11.0%, I^2=6%), with the OR being 1.7 (95% CI 0.3 to 11.1, p>0.05). Abdollahifard (2022) described that, when comparing MMAE with conventional management, the risk ratio (RR) was 0.10 (95% CI 0.04 to 0.27; I^2=0%; 6 studies) for recurrence and 0.25 (95% CI 0.13 to 0.49; I^2=37%; 6 studies) for reoperation. Ku (2023) found that the recurrence rate was 6% (95% CI 3.3% to 9.3%) after MMAE alone compared with 5% (95% CI 2.7% to 7.9%) after adjunct MMAE (p=0.976, I2=0%). The authors also reported that the reoperation rate was 5% (95% CI 2.6% to 8.2%) compared with 5% (95% CI 2% to 7.2%, p=0.912). Nia (2022) did not report any statistically significant difference in treatment failure or need for surgical rescue between primary, adjunct and rescue MMAEs.

Taking into consideration different embolisates, Scoville (2022) reported that surgical retreatments within 90 days were not statistically significantly different between MMAE using particles and MMAE using liquid embolics in the upfront MMAE (8% [8/100] compared with 0% [0/31]), rescue MMAE (2% [1/41] compared with 6% [1/18]), and prophylactic MMAE (0% [0/11] compared with 0%

[0/5]) groups. Khorasanizadeh (2022) found that the rates of rescue surgery were similar between MMAE using coil only (8%, 1/12) and MMAE using coils and particles (9%, 7/82) groups. Ku (2023) described that the lowest rates of subdural haematoma radiological recurrence and reoperation were seen in patients having MMAE using Onyx, whereas good overall clinical outcome happened most commonly with combined PVA and coils.

Functional outcomes and survival

mRS scores before and after MMAE were reported in 2 studies. Ironside (2021) stated that an mRS score of 0 to 2 at the last follow up was observed in 73% (95% CI 46.3 to 99.2%) of patients who had MMAE and 92% (95% CI 10.8% to 100%) of patients who had conservative management. Khorasanizadeh (2022) described that mRS remained stable or improved in 83% of patients at a mean of 114 days after MMAE compared with baseline scores.

The 6-month survival ratio was reported in the study by Nia (2022). The authors found that the survival ratio was estimated to be 1.25% higher in patients who had primary MMAE compared with patients who had primary surgery, but the effect was not statistically significant.

Good clinical outcome (MR spectroscopy 0 to 2, Glasgow outcome score 4 to 5, Glasgow outcome scale-extended 5 to 8, and improvement in neurological or functional status or neurological deficit at the last follow up) was observed in the study by Ku (2023). The authors found that the rate of good clinical outcomes was 73% (95% CI 60% to 86.6%; I2=92.37%). When considering MMAE used alone or as an adjunct to surgery, the rate was 81% (95% CI 66.7% to 95.6%) compared with 75% (95% CI 36% to 100%, p=0.569, I^2=71.81%).

Length of hospital stay

The length of stay in hospital after MMAE compared with surgical evacuation was assessed in 2 studies. Nia (2022) reported that the mean length of hospital stay

was statistically significantly shorter in patients who had primary MMAE (7.74 days) than in those who had primary surgery (30.20 days). Dicpinigaitis (2021) found that the mean length of hospital stay was statistically significantly longer after MMAE (13.0 days) than after surgical evacuation (8.3 days). This statistically significant finding was also supported by a propensity score-adjusted comparison (13.0 days compared with 7.4 days).

Safety

Overall complications and mortality

The rates of complications were reported in 5 studies. Ironside (2021) found the pooled rate of in-hospital complications was 2% (95% CI 0.8 to 2.6%) after MMAE compared with 5% (95% CI 2.8 to 7.1%) after conventional management. The meta-analysis of 5 double-arm studies showed a lower rate of in-hospital complications after MMAE than conventional management, but the effect was not statistically significant (OR 0.78, 95% CI 0.34 to 1.76, I^2=0%; n=902). Haldrup (2020) reported no complications during or after the embolisation procedure (0 complications in 12 studies and not defined in 6 studies). Abdollahifard (2022) described that the periprocedural complication rate was 4% (95% CI 2% to 9%) after MMAE. When comparing MMAE with conventional management, the analysis showed that RR was 0.34 (95% CI 0.16 to 0.27; I^2=0%; 6 studies) for periprocedural complications. Ku (2023) reported that the overall rate of postoperative complications was 3% (95% CI 2.9% to 5.5%) after MMAE alone and as an adjunct to surgery. These complications included groin complications (n=2), procedural complications (n=3), postprocedural infarcts (n=4), medical complications (n=10), and seizures or new neurological deficits or unspecified complications (n=15). When comparing MMAE alone with MMAE as an adjunct to surgery, the postoperative complication rate was 2% (95% CI 0.6% to 4%) compared with 6% (95% CI 1.5% to 9.5%; p=0.025, I^2=43.18%).

Taking into consideration different embolisates, Ku (2023) reported that the postoperative completion rate was 6% (95% CI 1.1% to 10.1%) for PVA, 3% (95% CI 0% to 6.9%) for NBCA, 2% for Onyx, and 1% for PVA with or without coils. Scoville (2022) considered complications between particles and liquid embolisates, and found no statistically significant differences after upfront (12% compared with 3%), rescue (7% compared with 0%) and prophylactic (0% compared with 0%) MMAEs.

Mortality outcomes were described in 3 studies. Abdollahifard (2022) reported that the pooled mortality rate was 1% (95% CI 0% to 3%) after MMAE. When comparing MMAE with conventional management, the RR was 0.17 (95% CI 0.01 to 2.01; I^2=0%; 5 studies) for mortality. Dicpinigaitis (2021) reported that in-hospital mortality was less than 3% in patients who had MMAE. Nia (2022) did not find any statistically significant difference in mortality between the primary MMAE cohort and the primary surgery cohort within 6 months postoperatively.

Neurological complications

Data for neurological complications was reported in 4 studies. Dicpinigaitis (2021) found that the rate of haemorrhagic or ischaemic complications was 0% (0/390) after MMAE compared with less than 1% (335/59,655) after surgical evacuation. Scoville (2022) reported neurological complications within the 90 days after MMAE in 9 patients (9/208), including stroke (n=5), worsening headaches (n=2) and new-onset seizures (n=2). Khorasanizadeh (2022) reported global aphasia and right hemiplegia in 1 patient. Nia (2022) did not find any statistically significant difference in the occurrence of headaches between primary MMAE and primary surgery.

Facial droop

Facial droop or weakness was reported in 3 studies. Dicpinigaitis (2021) reported that, of the 390 patients, facial droop was seen in less than 3% of patients after

MMAE. Scoville (2022) described 1 case (1/208) of facial droop from Onyx infiltrating the meningeal branches of the skull base and resulting in facial nerve damage. Nia (2022) did not find any statistically significant difference in the occurrence of facial weakness between primary MMAE and primary surgery.

Visual loss

Dicpinigaitis (2021) reported the rate of visual deficit or blindness was 0% (0/390) after MMAE compared with less than 1% (140/59,655) after surgical evacuation. Khorasanizadeh (2022) reported 1 patient (1/78) developed left eye pain, vision loss and dilated nonreactive pupil while recovering from the procedure in the postanaesthetic care unit.

Other procedural complications

Scoville (2022) reported MMA rupture (n=1), external carotid artery spasm (n=1), and uncategorised technical complication (n=1) within 90 days after MMAE. Catapano (2021) found a cerebrovascular accidence (n=1), which was likely caused by instability of the access catheter via a transfemoral route.

Piergallini (2019) presented 2 cases of immediate development of a DAVF after prophylactic MMAE using microparticles. Wilseck (2022) reported a case of development of an iatrogenic MMA pseudoaneurysm during endovascular embolisation using a dual-lumen balloon catheter used for injection of a liquid embolic agent.

Infections

Postsurgical infections that necessitated surgical treatments were found in 2 patients after MMAE (Scoville 2022).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. They were asked if they knew of

any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly happen, even if they have never happened (theoretical).

They listed the following anecdotal and theoretical adverse events not reported in the literature: cerebral infarction, access site bleeding/complications, contrast reactions, radiation related risk, complications of general anaesthesia in a frail and elderly population.

Four professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

In the main evidence, 11 articles were included but there was no data relevant to the UK context. The 7 primary studies were retrospective and observational in design. The 3 cohort studies used real-world data from multiple sites or a national sample, which might increase the generalisability and external validity of the results. But there was missing data (such as radiographic data and neurological assessment outcomes) and lack of procedural details and standardised treatment protocols.

Potential conflicts of interest were declared by the authors of 3 papers (Abdollahifard 2022; Catapano 2021; Scoville 2022) and 1 study reported that the data access was supported by NIH grant TR001439 and Clinical and Translational Science Award (UL1).

Patient selection for MMAE was heterogeneous and varied between studies (such as age, severity of the condition with or without midline shift, comorbidity, previous trauma, preoperative anticoagulant or antiplatelet use, unilateral or

bilateral haematomas). Many studies did not report long-term outcomes. The definitions of prophylactic and rescue MMAE might have been inconsistent across different studies. There was variation in treatment regimens in both MMAE and conventional management, and different embolisation agents were used across studies. It was noted that a major disadvantage of liquid embolics is their possible penetration into meningeal arteries in the skull base, which can lead to permanent cranial nerve damage resulting in facial droop and blindness. To avoid such complications, the anatomical anastomoses between the extracranial and intracranial arteries should be avoided (Scoville 2022). It might be worth noting that not all embolic materials are CE marked for the procedure and indication, although some are not excluded for use.

Evidence showed reduction in haematoma, and when comparing with standard management, there were significantly lower rates of CSDHs recurrence and surgical rescue. Although Nia (2022) found the 6-month survival ratio was estimated to be 1.25% higher after primary MAAE than after primary surgery, the difference was not statistically significant. Using different embolic materials did not lead to statistically significant differences in haematoma reduction, surgical rescue or overall complications. There was a lack of data in haematoma resolution, functional outcomes and quality of life. When comparing MMAE used at different stages, the outcomes in haematoma recurrence and surgical rescue were mixed. It would be beneficial for further studies to be done to elucidate the appropriate patient selection for primary MMAE, recurrent MMAE or in MMAE in combination with surgical intervention.

To date, there is only a pilot randomised study. There is no data from full-scale RCTs comparing MMAE with standard treatment and a lack of long-term outcomes to determine the efficacy of this endovascular approach as an upfront, adjunct or rescue treatment for CSDH. However, numerous clinical trials are underway, including RCTs (NCT04742920, NCT04372147, NCT04511572,

NCT04402632, NCT04272996, NCT04270955, NCT05327933, NCT05267184, NCT05220826, NCT04410146, NCT04750200, NCT04095819, NCT05374681, NCT04816591), non-randomised controlled trials (NCT04065113, NCT04500795), and single-arm trials (NCT04923984, NCT04574843). These RCTs and non-randomised controlled trials compare MMAE with standard (surgical or conservative) management with sample sizes ranging from 40 to 600 patients. These ongoing trials are located in Canada, China, France, Germany, Netherlands, Spain, Sweden and US. These trials would add further data to the existing literature.

Professional societies

- British Society of Neuroradiologists (BSNR)
- Association of British Neurologists
- Society of British Neurological Surgeons (SBNS)
    - British Neurotrauma Group
- United Kingdom Neurointerventional group (UKNG).

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Ironside N, Nguyen C, Do Q et al. (2021) Middle meningeal artery embolization for chronic subdural hematoma: a systematic review and meta-analysis. Journal of neurointerventional surgery 13(10): 951-7
2. Haldrup M, Ketharanathan B, Debrabant B et al. (2020) Embolization of the middle meningeal artery in patients with chronic subdural hematoma - a systematic review and meta-analysis. Acta Neurochir 162: 777-84

3. Abdollahifard S, Farrokhi A, Yousefi O et al. (2022) Particle embolic agents for embolization of middle meningeal artery in the treatment of chronic subdural hematoma: A systematic review and meta-analysis. Interventional Neuroradiology
4. Ku JC, Dmytriw AA, Essibayi MA et al. (2023) Embolic agent choice in middle meningeal artery embolization as primary or adjunct treatment for chronic subdural hematoma: a systematic review and meta-analysis. AJNR. American journal of neuroradiology
5. Nia AM, Srinivasan VM, Siddiq F et al. (2022) Trends and outcomes of primary, rescue, and adjunct middle meningeal artery embolization for chronic subdural hematomas. World neurosurgery 164: e568-e573
6. Scoville JP, Joyce E, Tonetti DA et al. (2022) Radiographic and clinical outcomes with particle or liquid embolic agents for middle meningeal artery embolization of nonacute subdural hematomas. Interventional Neuroradiology
7. Dicpinigaitis AJ, Al-Mufti F, Cooper JB et al. (2021) Nationwide trends in middle meningeal artery embolization for treatment of chronic subdural hematoma: A population-based analysis of utilization and short-term outcomes. Journal of clinical neuroscience: official journal of the Neurosurgical Society of Australasia 94: 70-75
8. Catapano JS, Ducruet AF, Srinivasan VM et al. (2021) Radiographic clearance of chronic subdural hematomas after middle meningeal artery embolization. Journal of neurointerventional surgery
9. Khorasanizadeh M, Shutran M, Garcia A et al. (2022) Middle meningeal artery embolization with isolated use of coils for treatment of chronic subdural hematomas: a case series. World Neurosurgery
10. Piergallini L, Dargazanli C, Derraz I et al. (2019) Immediate development of dural arteriovenous fistula after middle meningeal artery embolization: first angiographic demonstration. World neurosurgery 128: 606-610e1
11. Wilseck ZM, Khan AA, Chaudhary N et al. (2022) Iatrogenic pseudoaneurysm of the middle meningeal artery during embolization of bilateral chronic subdural hematomas. Interventional Neuroradiology

Methods

NICE identified studies and reviews relevant to middle meningeal artery embolisation for CSDH from the medical literature. The following databases were searched between the date they started to 9 March 2023: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries

and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients: adult patients with CSDH.
- Intervention or test: MMAE as upfront/primary, prophylactic/adjunct, or rescue treatment.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	10/03/2023	1946 to March 09, 2023
MEDLINE In-Process (Ovid)	10/03/2023	1946 to March 09, 2023
MEDLINE Epubs ahead of print (Ovid)	10/03/2023	March 09, 2023

EMBASE (Ovid)	10/03/2023	1974 to March 09, 2023
EMBASE Conference (Ovid)	10/03/2023	1974 to March 09, 2023
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	10/03/2023	Issue 3 of 12, March 2023
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	10/03/2023	Issue 2 of 12, February 2023
International HTA database (INAHTA)	10/03/2023	-

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

1 Meningeal Arteries/
2 (middle adj4 meningeal adj4 arter*).tw.
3 MMA.tw.
4 or/1-3
5 Embolization, Therapeutic/
6 Endovascular Procedures/
7 (Emboli* or endovascular).tw.
8 or/5-7
9 4 and 8
10 exp Intracranial Hemorrhages/
11 ((Intracranial or subdural or brain or Posterior Fossa) adj4 (h?ematoma* or h?emorrhag*)).tw.
12 craniocerebral trauma/ or head injuries, closed/ or head injuries, penetrating/
13 ((head or skull or cranio*) adj4 (injur* or trauma)).tw.
14 CSDH.tw.
15 or/10-14
16 9 and 15
17 (ONYX* adj4 ((liquid adj4 embolic adj4 system) or LES or Medtronic)).tw.
18 15 and 17

19 16 or 18
20 Animals/ not Humans/
21 19 not 20

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Al-Mufti F, Kaur G, Amuluru K et al. (2021) Middle meningeal artery embolization using combined particle embolization and n-BCA with the dextrose 5% in water push technique for chronic subdural hematomas: a prospective safety and feasibility study. AJNR. American journal of neuroradiology 42(5): 916-920	Case series n=12 follow up: 3 months	Embolisation of the MMA using diluted n-BCA and ethiodized oil (1:6) is safe and feasible from a technical standpoint. The use of a dextrose 5% bolus improves distal penetration of the glue.	Small sample
Badger CA, Shaikh HA and Jankowitz BT (2020) Treatment of chronic subdural hematomas utilizing middle meningeal artery embolization. Journal of Radiology Nursing 39(4): 298-301	Case report n=1	Current evidence suggests that embolisation of the MMA is a safe and effective method for treatment of chronic subdural haematomas. It can be utilised as an additional intervention to surgical evacuation or as a primary treatment method. After the intervention, nursing care for the patient should focus on	Single case report

		detailed neurological assessments with special attention to the unique potential risk to this procedure.	
Ban SP, Hwang G, Byoun HS et al. (2018) Middle meningeal artery embolization for chronic subdural hematoma. Radiology 286(3): 992-9	Non-randomised comparative study n=541 (MMAE, n=72; historic control group, n=469) follow up: 6 months	MMAE has a positive therapeutic effect on CSDH and is more effective than conventional treatment.	This study was included in Ironside (2021)
Barros G, Meyer RM, Bass DI et al. (2022) Clinical utility of routine postprocedural computed tomography of the head following elective neuroendovascular interventions. World neurosurgery 167: e1426-31	Case series (retrospective) n=354 MMAE, n=20	In a large cohort of patients having elective neuroendovascular intervention, no patients were identified for whom routine postprocedural CT of the head (CTH) alone meaningfully altered their clinical care. Routine CTH is not necessary after uncomplicated elective neuroendovascular interventions performed with careful postprocedural neurological assessment.	Small sample and outcomes for MMAEs not reported separately.
Bounajem MT, Campbell RA, Denorme F et al. (2021) Paradigms in chronic subdural hematoma pathophysiology: Current treatments and new directions. The journal of trauma and acute	Review	Targeted approaches, such as MMAE and anti-inflammatory therapies, have become increasingly common and require further prospective analysis to aid in the determination of their efficacy.	Review article

care surgery 91(6): e134-e141			
Carpenter A, Rock M, Dowlati E et al. (2022) Middle meningeal artery embolization with subdural evacuating port system for primary management of chronic subdural hematomas. Neurosurgical review 45(1): 439-49	Non-randomised comparative study n=250 (surgery, n=185; SEPS, n=19; surgery plus MMAE, n=23; MMAE and SEPS placement, n=23)	Patients treated with MMA/SEPS were more likely to be older, be on anticoagulation, have significant comorbidities, have shorter length of stay, and less likely to have symptomatic recurrence compared to SEPS only cohort. Thus, MMAE/SEPS appears to be a safe and equally effective minimally invasive treatment for CSDH patients with significant comorbidities who are poor surgical candidates.	Number of patients having MMAE (plus surgery or SEPS placement) was small.
Catapano JS, Ducruet AF, Nguyen CL et al. (2021) A propensity-adjusted comparison of middle meningeal artery embolization versus conventional therapy for chronic subdural hematomas. Journal of Neurosurgery 135(4): 1208-13	Non-randomised comparative study n=231 (MMAE, n=35, conservative or surgical treatment, n=196)	This propensity-adjusted analysis suggests that MMAE for CSDH is associated with a greater extent of haematoma volume reduction with fewer treatment failures than conventional therapy.	Small sample (35 patients having MMAE)
Catapano JS, Koester SW, Srinivasan VM et al. (2021) Total 1-year hospital cost of middle meningeal artery embolization compared to surgery for chronic	Non-randomised comparative study n=170 (MMAE, n=48; surgery, n=122)	MMAE is associated with decreased total hospital cost compared with surgery for CSDH. This lower cost is directly related to the decreased need for additional treatment interventions.	This study focused on hospital cost with limited efficacy and safety data being reported.

subdural hematomas: a propensity-adjusted analysis. Journal of neurointerventional surgery			
Catapano JS, Nguyen CL, Wakim AA et al. (2020) Middle meningeal artery embolization for chronic subdural hematoma. Frontiers in Neurology 11: 557233	Review	MMAE for CSDH represents an emerging treatment modality, with a rapidly increasing number of studies analysing this innovative and largely successful technique. However, many questions remain, including appropriate patient selection, efficacy as a stand-alone procedure, optimal embolisation techniques, and timing of embolisation with regard to surgical intervention in symptomatic patients. Furthermore, most literature on MMAE for CSDH reports cases studies and small case series, whereas several RCTs have shown efficacy with surgical interventions. Hence, many RCTs using MMAE as a treatment for CSDH are underway. These studies will ultimately provide insight on the safety, efficacy, and use of this novel technique in the treatment of CSDH.	Review article
Catapano JS, Ducruet AF, Nguyen CL et al. (2021) Middle	Case series n=35	MMAE of CSDH appears to be both safe and efficacious. Furthermore,	This study was included in Ironside (2021).

meningeal artery embolization for chronic subdural hematoma: an institutional technical analysis. Journal of neurointerventional surgery 13(7): 657-60	follow up: mean 120 days	embolization of both the anterior and posterior MMA branches may be associated with increased odds of complete resolution.	
Catapano JS, Scherschinski L, Rumalla K et al. (2022) Emergency department visits for chronic subdural hematomas within 30 days after surgical evacuation with and without middle meningeal artery embolization. American Journal of Neuroradiology 43(8): 1148-51	Non-randomised comparative study n=137 (surgery and MMAE, n=28; surgery only, n=109)	Surgical evacuation combined with middle meningeal artery embolisation in patients with chronic subdural hematoma is associated with fewer 30-day emergency department visits compared with surgery alone.	Small sample (the number of patients who had surgery and MMAE was 28).
Court J, Touchette CJ, Iorio-Morin C et al. (2019) Embolization of the middle meningeal artery in chronic subdural hematoma - A systematic review. Clinical neurology and neurosurgery 186: 105464	Systematic review n=18 studies (190 patients)	MMAE is a feasible technique for CSDH, but the current body of evidence does not yet support its use as a standard treatment. Further studies with a higher level of evidence are necessary before MMAE can be formally recommended.	Of the 18 studies, 13 studies were included in Ironside (2021) or Haldrup (2020), and 5 studies with small samples (a total of 15 patients).
Cutler C, Azab M, Lucke-Wold B et al. (2022) Endoscope-assisted evacuation of nonacute subdural hematoma: a technical case series and systematic review.	Case series n=9 MMAE, n=2 Systematic review of 14 studies (MMAE, 1 study)	Endoscopic visualisation can be a useful adjunct in the modern treatment of NASH. Reduced risk of recurrence was seen compared with those of historical surgical drainage methods including burr holes (20-30%). The	Small sample

World neurosurgery 168: e636-44		inclusion of endoscopic visualization in the modern era with MMAE may potentially combine methods that can dramatically reduce the recurrence of nonacute subdural haematoma.	
Di Cristofori A, Remida P, Patassini M et al. (2022) Middle meningeal artery embolization for chronic subdural hematomas. A systematic review of the literature focused on indications, technical aspects, and future possible perspectives. Surgical Neurology International 13: a4	Systematic review n=35 studies	The global impression deriving from the data available, and the literature is that MMAE is a safe procedure with very low complications and with a low failure rate, both when associated with surgery or in case of a standalone treatment.	Of the 35 studies, 25 studies were included in Ironside (2021), Haldrup (2020) and Piergallini (2019), 10 small scale studies had a total of 57 patients). No meta-analysis was conducted.
Dian J, Linton J and Shankar JJ (2021) Risk of recurrence of subdural hematoma after EMMA vs surgical drainage - Systematic review and meta-analysis. Interventional neuroradiology: journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences 27(4): 577-83	Systematic review and meta-analysis n=4 studies	Based on limited data, MMAE reduces the risk of recurrence by 20% compared to surgical treatment for CSDH.	All 4 studies were included in Ironside (2021)
Dofuku S, Sato D, Nakamura R et al. (2023) Sequential	Case series (retrospective)	As a minimally invasive treatment for recurrent CSDH, sequential	Small sample

middle meningeal artery embolization after burr hole surgery for recurrent chronic subdural hematoma. Neurologia medico-chirurgica 63(1): 17-22	n=9 Follow up: 9 to 185 days	MMAE using NBCA performed within 2 weeks after burr hole surgery may be a safe and effective option to prevent recurrence, although further studies with larger sample sizes and long-term follow-up periods are needed.	
Dowlati E, Chesney K, Carpenter AB et al. (2021) Awake transradial middle meningeal artery embolization and twist drill craniostomy for chronic subdural hematomas in the elderly: case series and technical note. Journal of neurosurgical sciences	Case series n=20 follow up: mean 3.6 months	In select elderly patients with high perioperative risk factors, primary treatment of CSDH using awake transradial MMAE and subdural evaluation port system placement is a minimally invasive, feasible, and safe option. Further comparative studies are warranted to evaluate efficacy of the treatment.	Small sample.
Entezami P, Field NC and Dalfino JC (2021) Outpatient management of chronic expanding subdural hematomas with endovascular embolization to minimize inpatient admissions during the COVID-19 viral pandemic. Interventional neuroradiology: journal of peritherapeutic neuroradiology, surgical procedures and related	Case series n=5	MMAE as a primary treatment for chronic expanding SDH in the outpatient setting is safe. Giving the current viral pandemic, outpatient management of elderly patients is an attractive option, providing neurosurgeons the ability to procedurally manage patients with progressive haemorrhage while minimising or eliminating the length of inpatient admission.	Small sample

neurosciences 27(5): 716-21			
Entezami P, Nourollahzadeh E and Dalfino J (2019) Embolization of middle meningeal artery for the treatment of headaches induced by chronic subdural hematoma: A Case Report. Headache 59(4): 615-618	Case report n=1 follow up: 3 months	As embolisation techniques improve, its utility continues to increase. Authors believe that using MMAE as the first-line treatment in difficult CSDH cases (elderly patients, those needing anticoagulation resumption, etc) or in patients who are only mildly symptomatic with minimal mass effect from the subdural hematoma is a powerful new adjunct to the management of CSDH.	Single case report
Entezami P, Boulos A, Paul A et al. (2019) Contrast enhancement of chronic subdural hematomas after embolization of the middle meningeal artery. Interventional neuroradiology: journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences 25(5): 596-600	Case report n=2	Embolisation of the MMA may be a useful adjunct in the management of CSDHs, although further investigation is needed. Minimally invasive angiographic embolisation procedures may be an attractive option in patients who are poor candidates for more invasive surgery. Contrast staining of the haematoma following embolisation may suggest sufficient penetration into the fragile neovasculature that accounts for the persistent nature of CSDHs. More cases and dedicated outcomes research is needed to evaluate	Small sample

		better this radiographic feature postembolisation, and determine its utility in predicting outcomes following MMAE for CSDHs.	
Feghali J, Yang WYand Huang J (2020) Updates in chronic subdural hematoma: epidemiology, etiology, pathogenesis, treatment, and outcome. World neurosurgery 141: 339-345	Review	MMAE represents one of the latest additions to the therapeutic arsenal of cerebrovascular specialists in treating CSDH and is being critically evaluated in numerous ongoing clinical trials.	Review article
Ferber A, Zhou Y and Greenwald B (2023) Persistent facial nerve palsy after middle meningeal artery embolization for subdural hematoma: a case report. Brain Injury	Case report n=1 Follow up: 83 days	CSDH is increasingly more common and is on trajectory to become the most prevalent cranial neurosurgical condition. MMA embolisation is described as a safe and minimally invasive procedure; however, as a relatively new procedure further research is needed to elucidate associated complications.	Small sample
Fiorella D and Arthur AS (2019) Middle meningeal artery embolization for the management of chronic subdural hematoma. Journal of neurointerventional surgery 11(9): 912-5	Review	Based on the existing literature, it is difficult to ascertain a sense of the natural history of the group of CSDH patients who do not need emergency surgery. Superimposed on this background of uncertainty is the new minimally invasive technique of MMAE. While the existing	Review article

		studies suggest a robust treatment effect, they are relatively small and also not prospective or randomized. As such, an adequately sized, multicentre, prospective RCT of MMAE both as sole therapy and as a surgical adjunct is needed. Such a trial will be critical in defining the safety and effectiveness (or lack thereof) of MMAE. Moreover, the data on conventional management will also be important in defining both the natural history and surgical outcomes for this disease state.	
Fuentes AM, Khalid SI and Mehta AI (2023) Predictors of subsequent intervention after middle meningeal artery embolization for treatment of subdural hematoma: a nationwide analysis. Neurosurgery 92(1): 144-9	Case series (retrospective) n=322 Follow up: 5 years	Although previous literature has shown MMA embolisation to be safe and successful in preventing recurrent SDH, patients undergoing this procedure still carry a risk of future interventions. Patients taking factor Xa inhibitors are at especially high risk of subsequent intervention after MMA embolisation	Studies with larger samples or better designs are included in the main evidence.
Gomez-Paz S, Akamatsu Y, Salem MM et al. (2021) Upfront middle meningeal artery embolization for treatment of chronic	Case series n=23 follow up: 90 days	Upfront MMAE for CSDH with a thickness up to 25 mm provides adequate symptom relief, stabilisation and/or progressive resorption of the CSDH	Small sample

subdural hematomas in patients with or without midline shift. Interventional neuroradiology: journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences 27(4): 571-6		during follow up in carefully selected asymptomatic or mildly symptomatic patients even in the presence of a midline shift greater than 5 mm.	
Hashimoto T, Ohashi T, Watanabe D et al. (2013) Usefulness of embolization of the middle meningeal artery for refractory chronic subdural hematomas. Surgical Neurology International 4:104	Case series n=3	Embolisation of the MMA is effective for refractory CSDH or CSDH patients with a risk of recurrence, and is considered an effective therapeutic method to stop hematoma enlargement and promote resolution.	Small sample
Henry J, Amoo M, Kissner M et al. (2022) Management of chronic subdural hematoma: a systematic review and component network meta-analysis of 455 studies with 103 645 cases. Neurosurgery 91(6): 842-855	Systematic review and component network meta-analysis	Recurrence after evacuation occurs in approximately 10% of CSDHs, and the various surgical interventions are approximately equivalent. Corticosteroids are associated with reduced recurrence but also increased morbidity. Drains reduce the risk of recurrence, but the position of drain (subdural vs subgaleal) did not influence recurrence. MMA embolisation is a promising treatment warranting further	Most studies are included in the systematic reviews in the main evidence.

		evaluation in randomised trials.	
Hirai S, Ono J, Odaki M et al. (2004) Embolization of the middle meningeal artery for refractory chronic subdural haematoma. Usefulness for patients under anticoagulant therapy. Interventional Neuroradiology 10(suppl2): 101-4	Case series n=2	Endovascular embolisation of the MMA was done in 2 patients with refractory CSDH after repeated burr hole and irrigation surgeries. The embolisation prevented expansion of the CSDH in both patients, and the haematoma disappeared completely in one case. The expansion of CSDH is considered to result from repeated bleeding from the macrocapillaries on the haematoma capsule. Embolisation of the MMA appears to be useful to eliminate the blood supply to this structure.	Small sample
Housley SB, Monteiro A, Khawar WI et al. (2022) 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. Journal of NeuroInterventional Surgery: jnis-2022	Non-randomised comparative study (retrospective) n=92 (MMAE, n=44; surgical evacuation, n=48) follow up: within 60 weeks	In comparable CSDH patients, surgical evacuation resulted in better volumetric outcomes in immediate postoperative and early follow-up periods, as expected. However, this difference was not significant at more distant follow-up intervals. Furthermore, surgical patients experienced a significantly higher rate of recurrence.	Studies with larger samples are included in the key evidence.
Imai R, Akiyama T, Mizutani K et al.	Case report	Under the circumstances where	Single case report

(2022) A case of refractory chronic subdural hematoma and internal carotid artery stenosis sequentially treated with surgical drainage, middle meningeal artery embolization, and carotid artery stenting. Surgical Neurology International 13	n=1	CSDH is present but antiplatelet therapy is inevitable, MMAE could be a reasonable treatment option to avoid additional surgical procedures. Furthermore, early intervention should be considered even for asymptomatic carotid stenosis in terms of shortening the administration period of antiplatelet agents.	
Ishihara H, Ishihara S, Kohyama S et al. (2007) Experience in endovascular treatment of recurrent chronic subdural hematoma. Interventional Neuroradiology 13(suppl1): 141-4	Case series n=7 follow up: up to 15 months	Seven cases of intractable CSDH were treated by MMAE and no recurrence took place in all cases for up to 15 months. Endovascular treatment may be a good alternative modality for recurrent CSDH.	Small sample
Joyce E, Bounajem MT, Scoville J et al. (2020) Middle meningeal artery embolization treatment of nonacute subdural hematomas in the elderly: a multiinstitutional experience of 151 cases. Neurosurgical focus 49(4): e5	Non-randomised comparative study n=121 (age 65 to 79 years, n=70; age 80 years and above, n=51) follow up: 90 days	MMAE can be used safely and effectively as an alternative or adjunctive minimally invasive treatment for nonacute subdural haematomas in elderly and advanced elderly patients.	This study was included in Ironside (2021).
Jumah F, Osama M, Islim AI et al. (2020) Efficacy and safety of middle meningeal artery embolization in the management of	Systematic review and meta-analysis n=11 studies (3 cohort studies	Although MMAE appears to be a promising treatment for refractory or CSDH, drawing definitive conclusions remains limited by paucity of	Of the 11 studies, 8 studies (3 cohort studies and 5 case series) were included in Ironside (2021) and 3 studies had

refractory or chronic subdural hematomas: a systematic review and meta-analysis. Acta neurochirurgica 162(3): 499-507	and 8 case series)	data and small sample sizes. Multicentre, randomised, prospective trials are needed to compare embolisation to conventional treatments like watchful waiting, medical management, or surgical evacuation. More extensive research on MMAE could begin a new era in the minimally invasive management of CSDH.	small sample (<10 patients in each study).
Kan P, Maragkos GA, Srivatsan A et al. (2020) Middle meningeal artery embolisation for chronic subdural hematoma: a multi-center experience of 154 consecutive embolisations. Neurosurgery 88: 268-77	Case series n=138 follow up: mean 95 days	MMAE may provide a safe and efficacious minimally invasive alternative to conventional surgical techniques.	This study was included in Ironside (2021).
Kanazawa T, Miwa, Tomoru A, Takenori et al. (2019) A case of aggressive recurrent intracranial subdural hematoma associated with angiosarcoma originating from the skull. World neurosurgery 126: 120-123	Case report n=1 follow up: 16 days after the first surgery	In addition to cancers metastatic to the skull or dura mater, angiosarcoma should be included in the differential diagnosis for patients with repeated SDH and bone defect. An effective treatment for angiosarcoma with SDH that shows an unfavourable prognosis has not been established; however, an early diagnosis might be useful for a novel treatment.	Single case report

Kim E (2017) Embolization therapy for refractory hemorrhage in patients with chronic subdural hematomas. World neurosurgery 101: 520-527	Non-randomised comparative study n=43 follow up: 3 months	This pilot study indicated that perioperative MMAE could be offered as the least invasive and most effectual means of treatment for resistant patients of CSDHs with 1 or more recurrences.	Small sample
Kocharian G, Zappi KB, Carnevale J et al. (2022) Recent advances and future directions in middle meningeal artery embolization for chronic subdural hematomas. Current pain and headache reports 26(8): 657-65	Review	In reviewing the literature on MMAE, there are numerous retrospective studies and systematic reviews demonstrating its safety and efficacy, and some prospective dual-arm studies that present novel information. The numerous clinical trials that are currently underway should help to further establish MMAE as standard of care in the management of CSDH.	Review article
Komiyama M, Yasui T, Tamura K et al. (1994) Chronic subdural hematoma associated with middle meningeal arteriovenous fistula treated by a combination of embolization and burr hole drainage. Surgical neurology 42(4): 316-9	Case report n=1 follow up: 2 months	A rare case of CSDH associated with a middle meningeal arteriovenous fistula was treated by a combination of embolisation and burr hole drainage. The patient was discharged without any neurological deficit about 2 months later.	Single case report
Kosaka T, Ikeda N, Furuse M et al. (2020) Refractory chronic subdural hematoma	Case report n=1	Embolisation of the MMA has few surgical risks and could be a treatment option for refractory CSDH	Single case report

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 neurosurgery 133: 256-259	follow up: 1 month	associated with dural metastasis because it might prolong the therapeutic time window until radical therapies are administered.	
Krothapalli N, Fayad M, Patel S et al. (2022) Use of reverse angle guide catheter with trans-radial approach in patients undergoing middle meningeal artery embolization. Frontiers in Neurology 13: 990722	Non-randomised comparative study (retrospective) n=71 (trans-femoral access, n=65; trans-radial access, n=11)	Trans-radial approach using 6F-SIM2 guide catheter coupled with 5F Sofia intermediate catheter is safe and effective. It provides an alternative approach to access distal branches of bilateral anterior circulation in elderly patients with difficult anatomy having MMA embolisation.	Studies with larger samples are included in the key evidence.
Krothapalli N, Patel S, Fayad M et al. (2023) Outcomes of particle versus liquid embolic materials used in middle meningeal artery embolization for the treatment of chronic subdural hematoma. World neurosurgery	Non-randomised comparative study (retrospective) n=116 (liquid embolic material, n=48; particle, n=68)	This study shows that liquid embolic and particle embolisation are equally safe and effective among patients having MMA embolisation for management of CSDH.	Studies with larger samples are included in the key evidence.
Larson A, Savastano L, Rammos S et al. (2020) Middle meningeal artery embolixation for chronic subdural hematoma: rationale,	Review	As with any currently investigated and proposed procedure that has the potential to incur additional cost and/or risk, it will be of pivotal importance to properly select patients who could significantly	Review article

technique, and results. Contemporary Neurosurgery 42		benefit from embolisation at minimal risk. Although demographics and clinical features are expected to play a predominant role in patient selection, imaging features on standard axial and perfusion studies, such as the presence of hyperdense, densely septated pseudomembranes, or ones with increased blood flow or metabolic activity, are expected to steer rigorous selection of patients for embolization either as an exclusive or adjunctive CSDH treatment option in the future.	
Lee S, Srivatsan A, Srinivasan VM et al. (2021) Middle meningeal artery embolization for chronic subdural hematoma in cancer patients with refractory thrombocytopenia. Journal of neurosurgery: 1-5	Case series n=22 follow up: up to 453 days	Transfemoral or transradial MMAE is a potential therapeutic option for thrombocytopenic cancer patients with SDH. However, treatment benefit may be marginal for patients with high disease burden and limited life expectancy. A prospective trial is warranted to address these questions.	Small sample
Li G, Zhang Y, Zhao J et al. (2019) Isolated subdural hematoma secondary to Dural arteriovenous fistula: a case	Case report n=1 follow up: 1 month	Isolated SDH is a rare complication of DAVF. In this report, a rare case of CSDH secondary to an intracranial DAVF was presented. The so-	Single case report

report and literature review. BMC neurology 19(1): 43		called benign type of DAVF without cortical venous drainage does not always warrant a benign process and might be complicated with SDH. Careful preoperative investigation is needed for relatively young patients presenting with idiopathic or atypical SDH.	
Link TW, Boddu S, Marcus J et al. (2018) Middle meningeal artery embolization as treatment for chronic subdural hematoma: a case series. Operative neurosurgery (Hagerstown, Md.) 14(5): 556-62	Case series n=6 follow up: 3 to 31 weeks	In this case series of 6 patients harbouring 7 recurrent, chronic SDHs, 6 of the 7 were successfully treated with MMAE and able to avoid surgery for reevacuation, suggesting that this minimally invasive technique may represent an effective alternative to surgery.	Small sample
Majidi S, Matsoukas S, De Leacy RA et al. (2022) Middle meningeal artery embolization for chronic subdural hematoma using N-Butyl cyanoacrylate with d5w push technique. Neurosurgery 90(5): 533-7	Case series n=61 follow up: 6 months	MMAE using diluted n-BCA with concomitant D5W injection is associated with a high degree of distal penetration and complete branch occlusion and minimal risk of cranial nerve palsy or other thromboembolic complications.	Studies with larger samples or better designs are included in the main evidence.
Mandai S, Sakurai M and Matsumoto Y (2000) Middle meningeal artery embolization for refractory chronic subdural hematoma. Case	Case report n=1	Embolisation therapy for CSDH is a possible new treatment. Although a single case does not establish a management regimen, authors believe that this represents a	Single case report

report. Journal of neurosurgery 93(4): 686-8		significant fronted with this challenging clinical situation.	
Matsumoto H, Hanayama H, Okada T et al. (2018) Which surgical procedure is effective for refractory chronic subdural hematoma? Analysis of our surgical procedures and literature review. Journal of clinical neuroscience: official journal of the Neurosurgical Society of Australasia 49: 40-7	Case series n=14 (irrigation, n=8; MMAE and irrigation, n=4; craniotomy, n=2)	When selecting a surgical procedure for refractory CSDH, assessing whether CSDH is organised is crucial. Because embolisation of the MMA was effective for refractory CSDH, the surgical procedure may be considered as one of the treatment options for refractory CSDH without organised hematoma. On the other hand, for refractory cases of organized CSDH, hematoma evacuation with craniotomy or endoscope rather than embolization of the MMA may be suitable, as previous reports have recommended.	Small sample
Mewada T, Ohshima T, Yamamoto T et al. (2016) Usefulness of embolization for iatrogenic dural arteriovenous fistula associated with recurrent chronic subdural hematoma: a case report and literature review. World neurosurgery 92: 584e7-584e10	Case report n=1	Refractory chronic subdural hematoma with reaccumulation within a short interval should be subjected to digital subtraction angiography of the MMA. Embolisation of ipsilateral MMA is safe, effective, and a useful option for the treatment of iatrogenic DAVF and resolution of hematoma	Single case report
Mino M, Nishimura S, Hori E et al. (2010) Efficacy of middle meningeal	Case series n=4	MMAE can be an effective adjuvant procedure in preventing	Small sample

artery embolisation in the treatment of refractory chronic subdural hematoma. Surgical Neurology International 1:78	follow up: more than 6 months	the recurrence of CSDH.	
Muhl-Benninghaus R (2022) Middle meningeal artery embolization for treatment of chronic subdural hematoma. Radiologie (Heidelberg, Germany) 62(suppl1): 17-21	Case report n=2 Follow up: 3 months	Embolisation of the middle meningeal artery appears to be a promising treatment for patients with CSDH, both before and after surgical excision.	Small sample
Mohamed S, Villabona A, Kennion O et al. (2022) Middle meningeal artery embolisation for chronic subdural haematomas: the first prospective UK study. British Journal of Neurosurgery	Case series n=15 follow up: 3 months	For select patients, MMAE is a safe alternative treatment option for chronic subdural haematoma. As more experience is gained, the procedure could be done under local anaesthetic.	Small sample
Moshayedi P and Liebeskind DS (2020) Middle meningeal artery embolization in chronic subdural hematoma: implications of pathophysiology in trial design. Frontiers in Neurology 11: 923	Review	Frequent multimodal imaging and CSDH sampling would enable us to understand mechanisms of MMAE in CSDH treatment and therefore improve our ability to offer MMAE to the eligible population.	Review article
Mureb MC, Kondziolka D, Shapiro M et al. (2020) DynaCT enhancement of subdural	Case series n=8	The data lend support to the theory of contiguous vascular networks between the MMA and SDH membranes. Targeting	Small sample

membranes after middle meningeal artery embolization: insights into pathophysiology. World neurosurgery 139: e265-e270	follow up: mean 89 days	these leaky vascular networks might remove the source of haematoma accumulation. These data add to the pathophysiological understanding of the disease and suggests potential insights into the mechanism of action of MMAE.	
Nakagawa I, Park HS, Kotsugi M et al. (2019) Enhanced hematoma membrane on DynaCT images during middle meningeal artery embolization for persistently recurrent chronic subdural hematoma. World neurosurgery 126: e473-e479	Case series n=20	Repeatedly recurrent CSDH can be safely treated and cured by MMAE. Hematoma membrane enhancement pattern using DynaCT images can predict repeated recurrences CSDH.	Small sample
Neth BJ, Ighodaro ET, Brinjikji W et al. (2021) Management of chronic subdural hematoma in patients requiring therapeutic anticoagulation. Neurologist: a214	Case series n=2	The cases provide anecdotal evidence of a challenging clinical scenario where there is a necessary indication for therapeutic anticoagulation and comorbid SDH. Endovascular MMAE may be an effective adjunct therapy for clinical scenarios in patients with SDH and an urgent indication for anticoagulation. Longer follow-up, prospective series, and future RCTs are needed to objectively assess outcomes in this	Small sample

		clinically challenging patient population.	
Ng S, Derraz I, Boetto J et al. (2020) Middle meningeal artery embolization as an adjuvant treatment to surgery for symptomatic chronic subdural hematoma: a pilot study assessing hematoma volume resorption. Journal of neurointerventional surgery 12(7): 695-9	Pilot study (randomised) n=41 (surgery, n=22; surgery and MMAE, n=19) follow up: 3 months	The addition of MMAE to surgery led to an increase in CSDH resorption at 3 months. One recurrence of CSDH was reported in each group, and there were no treatment-related complications.	This study was included in Ironside (2021).
Okuma Y, Hirotsune N, Sotome Y et al. (2022) Middle meningeal artery embolization for chronic subdural hematoma with cerebrospinal fluid hypovolemia: A report of 2 cases. Neuro-Chirurgie 68(1): 123-8	Case series n=2	MMAE might be considered as a preferred therapeutic option for CSDHs with cerebrospinal fluid hypovolemia syndromes in order to buy time before the epidural blood patch starts working.	Small sample
Okuma Y, Hirotsune N, Sato Y et al. (2019) Midterm follow-up of patients with middle meningeal artery embolization in intractable chronic subdural hematoma. World neurosurgery 126: e671-e678	Case series n=17 follow up: mean 26.3 months	Despite the known unfavourable outcomes of patients with intractable CSDHs, MMAE was not associated with recurrent CSDH or rehospitalisation in the current case series. MMAE should be considered a preferred therapeutic option for intractable CSDHs.	Small sample

Onyinzo, Christina, Berlis, Ansgar, Abel, Maria et al. (2022) Efficacy and mid-term outcome of middle meningeal artery embolization with or without burr hole evacuation for chronic subdural hematoma compared with burr hole evacuation alone. Journal of neurointerventional surgery 14(3): 297-300	Non-randomised comparative study n=132 (burr hole irrigation and MMAE, n=31; burr hole irrigation, n=82; MMAE, n=19) follow up: mean 3.2 months	MMAE is a safe and efficacious minimal invasive adjuvant and/or alternative procedure for the treatment of CSDH with a reduced recurrence rate.	Small sample for patients who had MMAE.
Petrov AE, Rozhchenko LV, Ivanov AA et al. (2021) The first experience of endovascular treatment of chronic subdural hematomas with non-adhesive embolization materials of various viscosities: Squid 12 and 18. Zhurnal voprosy neirokhirurgii imeni N. N. Burdenko 85(5): 80-7	Case report n=1	The technique protected by the RF patent confirmed an effectiveness of liquid non-adhesive embolisation agents of various viscosities for the treatment of chronic subdural hematomas. Endovascular embolisation ensures delivering the embolizing material directly into the newly formed vessels supplying hematoma capsule. Reflux of embolisation agent into dangerous anastomoses should be avoided in this case.	Single case report
Petrov A, Ivanov A, Rozhchenko L et al. (2021) Endovascular treatment of chronic subdural hematomas through	Case series n=10 follow up: 6 months	A distal catheterization of the MMA for the endovascular embolisation of CSDH with Squid allowed for the devascularization of the MMA and the dependent vessels of	Small sample

embolization: A pilot study with a non-adhesive liquid embolic agent of minimal viscosity (squid). Journal of Clinical Medicine 10(19): 4436		the hematoma capsule. This procedure resulted in a partial or complete resolution of the CSDH. Procedural complications were not encountered.	
Rajah GB, Waqas M, Dossani RH et al. (2020) Transradial middle meningeal artery embolization for chronic subdural hematoma using Onyx: case series. Journal of neurointerventional surgery 12(12): 1214-8	Case series n=46 follow up: mean 8 weeks	Transradial Onyx MMAE under conscious sedation is safe and effective for CSDH treatment. TRA may be especially useful in elderly patients with numerous comorbidities.	This study was included in Ironside (2021).
Raviskanthan S, Mortensen PW, Zhang YJ et al. (2021) Bilateral abducens nerve palsies after middle meningeal artery embolization for chronic subdural hematoma. Journal of neuro-ophthalmology: the official journal of the North American Neuro-Ophthalmology Society	Case report n=1 follow up: 2 months	There are many potential mechanisms for abducens nerve palsy in the setting of SDH, including traumatic, ischemic, and nonlocalising, increased or decreased intracranial pressure. There was no imaging evidence for direct mass effect, tractional irritation on the abducens nerves, or typical imaging features of altered intracranial pressure or large vessel or brainstem stroke. No systemic hypotension occurred. The possible role of indirect ischemia after embolisation of the middle meningeal artery cannot be completely excluded.	Single case report

Rennert, Janine, Seiz, Marcel, Nimsky, Christopher et al. (2008) Endovascular treatment of traumatic high flow dural arterio-venous fistula involving the middle meningeal artery and facial veins. Rontgenpraxis; Zeitschrift fur radiologische Technik 56(5): 164-8	Case report n=1	This case illustrates possible ‘‘dangerous’’ collateral circulation to the ophthalmic artery–a feature that should be kept in mind during endovascular treatment of this entity.	Single case report
Rutledge C, Baranoski JF, Catapano JS et al. (2021) Republished: Resolution of an enlarging subdural haematoma after contralateral middle meningeal artery embolisation. Journal of NeuroInterventional Surgery	Case report n=1 follow up: 3 months	There are cross-midline collaterals and anastomoses between MMA branches. Distal penetration of embolic material may increase the efficacy of MMAE by occluding these collaterals and anastomoses. There may be a role for contralateral embolisation in cases where the ipsilateral proximal MMA is not navigable or is surgically truncated.	Single case report
Samarage HM, Harary M, Morales J et al. (2022) Epidural empyema following nBCA embolization of the middle meningeal artery for the treatment of a chronic subdural hematoma. British	Case report n=1 Follow up: 8 weeks	MMA embolisation is an increasingly popular and effective endovascular treatment modality for CSDHs. However, the population for which this treatment is undertaken may have underlying comorbidities and risk factors that may make	Small sample

Journal of Neurosurgery		them prone to developing rare intracranial infections. When using permanent embolic material that is likely to remain in a devascularised tissue compartment, the possibility that the material may act as a nidus for infection should be borne in mind.	
Sato M, Mochizuki Y, Fukuchi M et al. (2022) Middle meningeal artery embolization before craniotomy for infected organizing chronic subdural hematoma: A case report and review of the literature. Surgical Neurology International 13: 186	Case report n=1 follow up: 6 months	Craniotomy is effective for the treatment of infected organising SDH, and MMAE is useful to reduce the risk of bleeding complications in the perioperative period and may also reduce the recurrence of CSDH.	Single case report
Samarage HM, Kim WJ, Zarrin D et al. (2022) The "bright falx" sign-midline embolic penetration is associated with faster resolution of chronic subdural hematoma after middle meningeal artery embolization: a case series. Neurosurgery 91(3): 389-398	Case series n=37 follow up: 6 months	Distal penetration of embolic material, particularly n-butyl cyanoacrylate, into the falx may lead to more rapid improvement of CSDH.	Small sample
Sarma P, Garg M, Prem P et al. (2022) Embolization of the middle meningeal artery for the	Case series n=5	In carefully selected patients based on clinical profile and angiographic findings, MMAE can be an	Small sample

treatment of chronic subdural hematoma: a path less travelled so far. Journal of Neurosciences in Rural Practice 13(3): 471-5	follow up: 6 months	effective modality for the treatment in CSDH.	
Sattur MG and Spiotta AM (2020) Anomalous "middle" meningeal artery from basilar artery and implications for neuroendovascular surgery: case report and review of literature. World neurosurgery 133: 84-9	Case report n=1 follow up: 5 weeks	The embryologic origin of the entity is briefly discussed, along with suggestions for managing such an anomaly during endovascular embolisation.	Single case report
Scerrati A, Visani J, Ricciardi L et al. (2020) To drill or not to drill, that is the question: nonsurgical treatment of chronic subdural hematoma in the elderly. A systematic review. Neurosurgical focus 49(4): e7	Systematic review n=29 studies (pharmacological treatment, n=15 studies; MMAE, n=14 studies)	The results showed that surgery still represents the mainstay in cases of symptomatic patients with large CSDHs; however, adjuvant and alternative therapies can be effective and safe in a carefully selected population. Their inclusion in new guidelines is advisable.	No meta-analysis was conducted and limited outcomes for MMAE were reported.
Schwarz J, Carnevale JA, Goldberg JL et al. (2021) Perioperative prophylactic middle meningeal artery embolization for chronic subdural hematoma: a series of 44 cases. Journal of	Case series n=44 follow up: mean 321 days	Perioperative prophylactic MMAE in the setting of surgical evacuation, via either craniotomy or SEPS, may help to lower the recurrence rate of CSDH.	Small sample

Neurosurgery 135(6): 1627-35			
Seok JH, Kim JH, Kwon TH et al. (2022) Middle meningeal artery embolization for chronic subdural hematoma in elderly patients at high risk of surgical treatment. Journal of cerebrovascular and endovascular neurosurgery, 25(1): 28-35	Case series (retrospective) n=9 Follow up: mean 160 days	MMAE for CSDH in selected high-risk elderly patients and relapsed patients might be effective. Despite the small cohort, our findings showed a high rate of complete resolution with no complications. Further prospective randomised trials are warranted to evaluate its usefulness as a primary treatment option for CSDH.	Small sample
Shotar E, Meyblum L, Premat K et al. (2020) Middle meningeal artery embolization reduces the post-operative recurrence rate of at-risk chronic subdural hematoma. Journal of neurointerventional surgery 12(12): 1209-13	Non-randomised comparative study n=263 (MMAE, n=89; conventional management, n=174)	Postsurgical embolisation of the MMA may reduce the recurrence rate of CSDHs with a risk factor of recurrence.	This study was included in Ironside (2021)
Shotar E, Barberis E, Chougar L et al. (2022) Long-term middle meningeal artery caliber reduction following trisacryl gelatine microsphere embolisation for the treatment of chronic subdural hematoma. Clinical Neuroradioly	Case series n=30	Long-term follow-up MRI demonstrated a significant impact of TAGM embolisation on MMA proximal caliber as well as on the visibility of the two main MMA branches. All comparisons indicated that there was a probable lasting impact of embolisation on the patency of distal branches.	Small sample

Shotar E, Premat K, Barberis E et al. (2021) Dural arteriovenous fistula formation following bilateral middle meningeal artery embolization for the treatment of a chronic subdural hematoma: a case report. Acta neurochirurgica 163(4): 1069-73	Case report n=1 follow up: 3 months	The case highlights the possible role of local tissue hypoxia as a significant component of DAVF pathogenesis. Moreover, it has potential implications for MMAE as a management strategy for CSDH.	Single case report
Shotar E, Premat K, Lenck S et al. (2022) Angiographic anatomy of the middle meningeal artery in relation to chronic subdural hematoma embolization. Clinical neuroradiology 32(1): 57-67	Case series n=122	In the majority of CSDH patients both anterior and posterior branches of the MMA should be targeted to achieve extensive convexity devascularisation. Frequent anatomical variations of the MMA with respect to emergence of the posterior branch and MMA orbital branches are expected to impact CSDH embolisation strategy.	This study describes MMA angiographic anatomy in relation to CSDH embolisation.
Srivatsan A, Mohanty A, Nascimento FA et al. (2019) Middle meningeal artery embolization for chronic subdural hematoma: meta-analysis and systematic review. World neurosurgery 122: 613-619	Systematic review and meta-analysis n=9 studies (3 double-arm studies and 6 case series)	MMAE is a promising treatment for CSDH. Future randomised clinical trials are needed.	Three double-arm studies in the meta-analysis were included in Ironside (2021). Of the 6 case series, 4 were also included in Ironside (2021) and 2 case series had a total of 9 patients.
Stanishevskiy AV, Babichev KN, Vinogradov EV et al. (2021) Middle meningeal artery	Case series n=32 (MMAE alone, n=22; MMAE followed	MMAE in patients with CSDH is a justified, highly effective and relatively safe approach. This method	Small sample

embolization for chronic subdural haematoma. Case series and literature review. Zhurnal voprosy neirokhirurgii imeni N. N. Burdenko 85(5): 71-9	by debridement through a milling hole, n=10) follow up: 1 to 5 months	is characterised by lower risk of recurrence compared to surgical and conservative treatments and can be considered as an alternative to traditional treatment options.	
Tabibian BE; Liptrap E and Jones J (2021) Incidentally discovered dural arteriovenous fistula during middle meningeal artery embolization for the treatment of chronic subdural hematoma. Surgical Neurology International 12: 438	Case series n=3	As MMAE for CSDH becomes more frequent, so may the incidental diagnosis of DAVF. Awareness of this potential association is critical to diagnosing DAVF with angiography and altering treatment strategies as needed.	Small sample
Tanoue, Shunsuke, Ono, Kenichiro, Toyooka, Terushige et al. (2023) The Short-Term Outcome of Middle Meningeal Artery Embolization for Chronic Subdural Hematoma with Mild Symptom: Case Series. World neurosurgery 171: e120-e125	Case series (retrospective) n=15 Follow up: 28 days	MMAE alone provides relatively early improvement in cases of mildly symptomatic CSDH and may be a potential alternative to surgical evacuation or medical therapy.	Small sample
Tavakkoli A, Montejo JD, Calnan DR et al. (2022) Intra-operative emergence of occult dural arteriovenous fistula after middle meningeal artery	Case report n=1	This is the first case of intraoperative emergence of occult MMA-DAVF with intracranial drainage during MMAE for chronic subdural hematoma treatment. This observation	Single case report

embolization for chronic subdural hematoma: Case report and literature review. Radiology Case Reports 17(5): 1470-4		supports monitoring for and embolising spontaneous MMA-DAVF following MMAE.	
Tempaku A, Yamauchi S, Ikeda H et al. (2015) Usefulness of interventional embolization of the middle meningeal artery for recurrent chronic subdural hematoma: Five cases and a review of the literature. Interventional neuroradiology: journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences 21(3): 366-71	Case series n=5 follow up: 4 to 60 weeks	No more recurrence of CSDH was observed in any of the patients. During the follow-up period, no patients suffered from any side effects or complications from the interventional treatment. MMAE with careful attention paid to the procedure might be a treatment for recurrent CSDH.	Small sample
Tiwari A, Dmytriw AA, Bo R et al. (2021) Recurrence and coniglobus volumetric resolution of subacute and chronic subdural hematoma post-middle meningeal artery embolization. Diagnostics 11(2): 257	Case series n=10 follow up: 91+ days	MMAE contributed to a marked reduction in SDH volume postoperatively and can be used as a curative therapy for primary or recurrent CSDH.	Small sample
Vilanilam GK, Pokhylevych H, Kamran M et al. (2023) Ischemia of the parotid gland and adjacent	Case report n=1 Follow up: 3 months	This study presented the case of ipsilateral parotid gland, temporalis muscle, adjacent superior aspect of masseter	Small sample

muscles of mastication following middle meningeal artery embolization. Neuroradiology Journal		muscle, and pterygoid muscle ischaemia secondary to non-target particle embolisation following MMA embolisation in CSDH. Knowledge of normal and variant origin of the MMA and various anastomoses of the MMA with branches of the ICA, ECA, and vertebrobasilar system is crucial to avoid complications during MMA embolisation.	
Wang HL, Wang C and Li ZF (2020) Recurrent bilateral chronic subdural hematoma after interventional embolization combined with drilling and drainage treatment. The Journal of craniofacial surgery 31(2): e171-e173	Case series n=2	For unilateral CSDH, MMAE combined with drilling could be an effective strategy for treating CSDH. However, for patients with bilateral CSDH, because the recurrence mechanism of bilateral CSDH rebleeding on the contralateral side may be more similar to that of the initial occurrence mechanism of unilateral CSDH, a more effective method is needed to treat it.	Small sample
Waqas M, Vakhari K, Weimer PV et al. (2019) Safety and effectiveness of embolization for chronic subdural hematoma: systematic review and case series. World neurosurgery 126: 228-36	Systematic review and case series n=15 studies n=8 patients	MMAE of CSDH is safe and effective for CSDH treatment based on a documented recurrence rate of 3.6% and lack of reported complications.	Of the 15 studies, 12 studies were included in Ironside (2021) and Haldrup (2020), and 3 studies had a total of 12 patients. The case series had a small sample.
Wei Q, Fan G, Wang Q et al.	Case series	Bilateral MMAE combined with bilateral	Small sample

(2021) Middle meningeal artery embolization for the treatment of bilateral chronic subdural hematoma. Frontiers in Neurology 12: 651362	n=10 follow up: 4 months	burr-hole drainage is an available treatment for patients with bilateral CSDH and may have the potential for preventing recurrence.	
Wong GK, Cheung EY, Ng RY et al. (in press) Middle meningeal embolization for chronic subdural hematoma: a case series of 7 patients and review of time course of resolution. Brain Hemorrhages	Case series n=7 follow up: 6 months	MMAE is safe and feasible within the framework of surgery to cure and prevent recurrence.	Small sample
Yajima H, Kanaya H, Ogino M et al. (2020) Middle meningeal artery embolization for chronic subdural hematoma with high risk of recurrence: A single institution experience. Clinical neurology and neurosurgery 197: 106097	Case series n=18 follow up: 2 to 53 months	MMAE is effective and safe in preventing recurrence of CSDH with high risk of recurrence and could be a standard treatment for such cases.	Small sample
Yu J, Guo Y, Xu B et al. (2016) Clinical importance of the middle meningeal artery: A review of the literature. International journal of medical sciences 13(10): 790-9	Review	For recurrent CDSHs, after burr hole irrigation and drainage have failed, MMAE may be attempted. The vessels in the outer membrane of the CSDH cross the dura mater to connect to the MMA. This becomes the basis for performing MMAE.	Review article

		However, MMAE was only effective when diffuse dilatation of the MMA and the abnormal vascular networks could be observed. When embolising the MMA, caution should be exercised to prevent aberrant flow into the dangerous anastomosis, which can cause complications.	