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**PRECISION MIDDLE MENINGEAL ARTERY EMBOLIZATION FOR CHRONIC  
SUBDURAL HEMATOMA: RANDOMIZED EVIDENCE, EMBOLIC-AGENT  
SELECTION, RECURRENCE PHENOTYPING, AND INTEGRATION WITH SURGICAL  
DRAINAGE**

**Abstract**

**Background.** Chronic subdural hematoma is one of the most common neurosurgical disorders in older adults and is increasingly encountered in patients receiving antiplatelet or anticoagulant therapy. Burr-hole evacuation with closed-system drainage remains the standard treatment for symptomatic lesions producing significant mass effect, but recurrence after apparently successful decompression remains a clinically important problem. Middle meningeal artery embolization has emerged as a pathophysiologically targeted treatment aimed at interrupting the vascular supply of the inflammatory neomembranes responsible for persistent exudation and recurrent bleeding.

**Materials and Methods.** A structured narrative review was performed using randomized controlled trials, prospective multicenter studies, large observational cohorts, surgical trials, and embolization studies available through August 2026. Particular attention was directed toward EMBOLISE, MAGIC-MT, STEM, EMPROTECT, and MEMBRANE; surgical drainage; recurrence-risk factors; liquid and particulate embolic agents; anatomical safety; radial versus femoral access; radiographic resorption; and patient selection for adjunctive or stand-alone embolization.

**Results.** Contemporary randomized evidence supports a clinically meaningful role for middle meningeal artery embolization, but treatment effects differ according to patient selection, embolic agent, timing, and definition of treatment failure. EMBOLISE demonstrated lower recurrence or progression requiring repeat surgery when embolization was added to surgical evacuation. STEM demonstrated a reduction in a broader composite treatment-failure endpoint across surgical and nonsurgical management pathways. MAGIC-MT showed a numerically lower rate of symptomatic recurrence or progression but did not demonstrate superiority for its primary 90-day endpoint. EMPROTECT, which used microparticle embolization after surgery in high-risk patients, did not achieve a statistically significant reduction in six-month recurrence. In contrast, the 2026 MEMBRANE randomized trial using n-butyl cyanoacrylate demonstrated a significant reduction in residual or recurrent hematoma or surgical failure at six months. These apparently discordant findings suggest that middle meningeal artery embolization should not be viewed as a single homogeneous procedure.

**Conclusion.** Middle meningeal artery embolization represents a major evolution in chronic subdural hematoma management, but it should complement rather than indiscriminately replace neurosurgical decompression. The most rational strategy is phenotype-specific: urgent surgery for clinically significant mass effect, adjunctive embolization for recurrence-prone disease, and selected stand-alone embolization for stable patients without an immediate decompressive requirement. Future research should focus on individualized recurrence prediction, embolic penetration, standardized radiographic endpoints, cost-effectiveness, and long-term functional outcomes.

**Keywords:** chronic subdural hematoma; middle meningeal artery embolization; MMAE; burr-hole drainage; recurrence; Onyx; Squid; n-butyl cyanoacrylate; particles; EMBOLISE; STEM; MAGIC-MT.

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## **ПРЕЦИЗИОННАЯ ЭМБОЛИЗАЦИЯ СРЕДНЕЙ МЕНИНГЕАЛЬНОЙ АРТЕРИИ ПРИ ХРОНИЧЕСКОЙ СУБДУРАЛЬНОЙ ГЕМАТОМЕ: РАНДОМИЗИРОВАННАЯ ДОКАЗАТЕЛЬНАЯ БАЗА, ВЫБОР ЭМБОЛИЗАТА, ФЕНОТИПИРОВАНИЕ РИСКА РЕЦИДИВА И ИНТЕГРАЦИЯ С ХИРУРГИЧЕСКИМ ДРЕНИРОВАНИЕМ**

### **Аннотация**

**Актуальность.** Хроническая субдуральная гематома является одной из наиболее распространенных нейрохирургических патологий у пациентов пожилого возраста. Традиционное хирургическое лечение посредством burr-hole эвакуации и закрытого дренирования эффективно устраняет масс-эффект, однако не воздействует непосредственно на сосудисто-воспалительный механизм, поддерживающий патологические субдуральные мембраны и рецидив заболевания. Эмболизация средней менингеальной артерии направлена на девакуляризацию этих мембран и стала одним из наиболее активно развивающихся направлений современной нейрохирургии.

**Материалы и методы.** Проведен структурированный нарративный обзор рандомизированных исследований, многоцентровых проспективных работ, крупных клинических серий и исследований хирургического лечения, доступных до августа 2026 года. Основное внимание уделено исследованиям EMBOLISE, MAGIC-MT, STEM, EMPROTECT и MEMBRANE, выбору эмболизирующего материала, хирургическому дренированию, факторам риска рецидива, сосудистому доступу и динамике резорбции гематомы.

**Результаты.** Современные рандомизированные исследования подтверждают потенциальную эффективность ММА-эмболизации, однако величина эффекта зависит от клинического сценария и используемой технологии. В EMBOLISE добавление эмболизации к хирургическому лечению уменьшало частоту рецидива или прогрессирования, требующего повторной операции. STEM продемонстрировал уменьшение комбинированной конечной точки неудачи лечения. MAGIC-MT не показал статистически значимого преимущества по первичной 90-дневной конечной точке. EMPROTECT с использованием микрочастиц также не достиг статистически значимого снижения шестимесячного рецидива, тогда как MEMBRANE с применением n-BCA продемонстрировал значимое уменьшение остаточной или рецидивной гематомы и необходимости повторного хирургического вмешательства.

**Заключение.** Эмболизация средней менингеальной артерии должна рассматриваться как патофизиологически обоснованный компонент персонализированного лечения хронической субдуральной гематомы. Оптимальная стратегия зависит от необходимости

срочной декомпрессии, риска рецидива, ангиоархитектуры, общего состояния пациента и возможности безопасного эндоваскулярного вмешательства.

**Ключевые слова:** хроническая субдуральная гематома; средняя менингеальная артерия; эмболизация; burr-hole; рецидив; Onyx; Squid; n-BCA; микрочастицы.

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**SURUNKALI SUBDURAL GEMATOMADA O'RTA MENINGEAL ARTERIYA  
PRETSIZION EMBOLIZATSIYASI: RANDOMIZATSIYALANGAN DALILLAR,  
EMBOlizAT TANLOVI, RETSIDIV XAVFINI FENOTIPLASH VA JARROHLIK  
DRENAJI BILAN INTEGRATSIYA**

**Annotatsiya**

**Dolzarblik.** Surunkali subdural gematoma keksa yoshdagi bemorlarda eng ko'p uchraydigan neyroxirurgik kasalliklardan biridir. Burr-hole orqali gematomani evakuatsiya qilish va yopiq drenaj miya kompressiyasini tez bartaraf etadi, biroq patologik subdural membranalaridagi yallig'lanish va neovaskulyarizatsiya mexanizmini to'liq yo'q qilmaydi. O'rta meningeal arteriya embolizatsiyasi ushbu membranalarining arterial ta'minotini kamaytirishga qaratilgan yangi patofiziologik davolash usulidir.

**Material va usullar.** 2026-yil avgustigacha mavjud bo'lgan randomizatsiyalangan klinik tadqiqotlar, prospektiv ko'p markazli ishlar, yirik kohortalar va jarrohlik tadqiqotlari strukturaviy narrativ tahlil qilindi. EMBOLISE, MAGIC-MT, STEM, EMPROTECT va MEMBRANE tadqiqotlari, embolizatsion materiallar, burr-hole drenaji, retsidiv xavfi va gematoma rezorbsiyasi asosiy tahlil yo'nalishlari bo'ldi.

**Natijalar.** Randomizatsiyalangan tadqiqotlar MMA embolizatsiyasining samaradorligini qo'llab-quvvatlaydi, biroq natijalar klinik fenotip va embolizatsiya usuliga bog'liq. EMBOLISE jarrohlik bilan birgalikdagi embolizatsiya qayta operatsiyani talab qiluvchi retsidivni kamaytirishini ko'rsatdi. STEM kombinatsiyalangan davolash muvaffaqiyatsizligi xavfini kamaytirdi. MAGIC-MT va EMPROTECT tadqiqotlarida asosiy yakuniy ko'rsatkich bo'yicha statistik ustunlik aniqlanmadi. 2026-yildagi MEMBRANE tadqiqotida n-BCA yordamidagi embolizatsiya gematoma qoldig'i yoki qayta to'planishi va takroriy jarrohlik ehtiyojini sezilarli kamaytirdi.

**Xulosa.** MMA embolizatsiyasi surunkali subdural gematomani davolashning muhim komponentiga aylanmoqda, biroq u barcha bemorlarda jarrohlik dekompressiyasining o'rnini bosmasligi kerak. Davolash bemorning klinik holati, massa-effekt, retsidiv xavfi va tomir anatomiyasiga qarab individual tanlanishi lozim.

**Kalit so'zlar:** surunkali subdural gematoma; o'rta meningeal arteriya; embolizatsiya; burr-hole drenaji; retsidiv; n-BCA; Onyx; Squid.

**Introduction.** Chronic subdural hematoma is increasingly recognized not as a static collection of old blood but as a dynamic inflammatory and angiogenic disease of the dural border-cell

compartment. Minor traumatic separation of the dural border-cell layer can initiate formation of a vascularized outer membrane, inflammatory-cell recruitment, fibrinolytic activation, increased vascular permeability, recurrent microhemorrhage, and progressive enlargement of the subdural collection. This biology helps explain why a hematoma can recur despite apparently complete mechanical evacuation. Traditional surgery immediately relieves intracranial mass effect but does not necessarily eliminate the biological substrate responsible for reaccumulation [1–4]. The clinical burden is rising because the population at greatest risk is also expanding. Chronic subdural hematoma occurs predominantly in older adults, many of whom have cerebral atrophy, recurrent falls, frailty, cardiovascular disease, antiplatelet exposure, or oral anticoagulation. Large prospective surgical cohorts have demonstrated that cSDH is not a benign neurosurgical condition; recurrence, medical complications, functional decline, and excess mortality remain important even when the initial operation is technically straightforward [2–4]. Increasing numbers of older patients receiving anticoagulation have further amplified the importance of developing strategies that reduce repeated surgery [3, 4]. The projected epidemiological burden has therefore stimulated interest in treatments directed at the underlying membrane vascularity rather than repeated evacuation alone [27–29]. Burr-hole craniostomy with postoperative closed-system drainage remains one of the most established treatments for symptomatic cSDH. The randomized trial by Santarius et al. demonstrated that placement of a subdural drain after burr-hole evacuation reduced recurrence and improved six-month survival compared with burr-hole evacuation without a drain [1]. Subsequent multicenter experience reinforced burr-hole drainage as a highly effective decompressive strategy, although recurrence remains clinically relevant [2, 3]. Comparisons between burr-hole, twist-drill, and minicraniotomy approaches have shown that more than one drainage strategy can be effective, with procedure selection influenced by hematoma organization, membranes, anesthesia risk, and local expertise [7].

Adjunctive pharmacological approaches have produced mixed results. The Dex-CSDH randomized trial demonstrated that dexamethasone reduced repeat operations but resulted in fewer favorable functional outcomes and more adverse events than placebo, substantially limiting its role as routine therapy [5]. Atorvastatin has demonstrated potential hematoma-volume reduction and neurological benefit in selected nonsurgical populations, but it has not replaced decompressive surgery in patients with clinically significant mass effect [6]. These studies illustrate a recurring principle in cSDH management: radiographic reduction or lower reoperation rates cannot be considered independently of global functional outcome and treatment toxicity [5, 6]. The biological rationale for middle meningeal artery embolization is fundamentally different. The external carotid circulation, particularly anterior and posterior branches of the middle meningeal artery, supplies the vascularized outer membrane of chronic subdural collections. Angiographically, this can manifest as diffuse dural hypervascularity and fine abnormal membrane vessels. Embolization reduces arterial perfusion to the membrane, promoting thrombosis and involution of pathological neovasculature while decreasing continued plasma exudation and recurrent microbleeding. Instead of immediately removing the hematoma, MMAE attempts to alter the biological conditions required for its persistence [8–12].

Early clinical studies were encouraging. Ban et al. reported favorable outcomes with MMA embolization used both as primary treatment and as prophylaxis after surgery [8]. Link and colleagues subsequently reported a 60-case experience demonstrating feasibility across upfront, recurrent, and

prophylactic treatment scenarios [9]. Ng et al. prospectively examined postoperative embolization and demonstrated accelerated hematoma-volume reduction after adjunctive MMAE [10]. Shotar et al. found a lower postoperative recurrence rate among selected high-risk patients treated with embolization [11], while Yajima and colleagues similarly explored preventive MMAE in recurrence-prone cSDH [12]. Collectively, these early studies established biological plausibility and clinical feasibility but were subject to selection bias and lacked the statistical power to establish routine treatment standards [8–12]. An important step toward precision patient selection came from the multicenter analysis by Salem et al., which included 636 MMA embolizations. Clinical failure occurred in a minority of patients, but baseline anticoagulation and an MMA diameter below 1.5 mm were associated with increased clinical failure. Smaller MMA diameter also predicted radiographic failure, whereas use of liquid embolic material was associated with a lower probability of failure in multivariable analysis [13]. These findings suggested that the procedure cannot be reduced to catheterization and vessel occlusion; target-vessel caliber, embolic penetration, baseline hematoma physiology, concurrent surgery, and anticoagulant exposure may modify response [13].

At the same time, observational comparisons have not consistently demonstrated superiority of one embolic agent. Particle embolization, ethylene-vinyl alcohol copolymers such as Onyx and Squid, and adhesive liquid agents such as n-butyl cyanoacrylate can all reduce MMA vascularity. Large observational cohorts have reported broadly comparable radiographic success and rescue-surgery rates across particles, Onyx, and n-BCA [14, 15]. This creates an important distinction between embolic material and embolic distribution: the therapeutic effect may depend less on the commercial agent itself than on distal penetration of the pathological membrane circulation while preserving safety around dangerous anastomoses [14, 15, 21]. The evidence base changed dramatically with publication of several randomized trials. EMBOLISE randomized patients who required surgical evacuation to surgery alone or surgery plus MMAE using Onyx. Recurrence or progression requiring repeat surgery occurred less frequently in the embolization group, establishing high-level evidence for adjunctive MMAE in surgically treated symptomatic subacute or chronic subdural hematoma [16]. The trial is particularly important because the comparison did not ask whether embolization can replace urgent decompression; it asked whether devascularizing the pathological membranes provides additional protection after decompression [16].

MAGIC-MT addressed a broader nonacute subdural population and included both surgical and nonsurgical pathways. Among 722 patients, symptomatic recurrence or progression by 90 days occurred numerically less frequently after MMAE, but the primary endpoint did not reach statistical superiority. The trial nevertheless reported a lower incidence of serious adverse events with embolization and provided important evidence that the magnitude of benefit may differ between surgical and nonsurgical strata [17]. The STEM trial similarly enrolled symptomatic cSDH patients for whom surgical or nonsurgical standard management had been determined before randomization. Adjunctive MMAE using Squid significantly reduced the composite primary efficacy outcome encompassing residual or recurrent cSDH, retreatment or rescue surgery, and major disabling vascular events at 180 days, without increasing the short-term incidence of disabling stroke or death [18]. The extended 180-day endpoint is clinically relevant because hematoma resolution and recurrence evolve over months rather than days [18]. The apparent uniformity of these positive signals was challenged

by EMPROTECT. This French randomized trial enrolled 342 surgically treated patients with recurrent cSDH or a first episode considered at high risk of recurrence. Embolization was performed using 300–500  $\mu\text{m}$  trisacryl gelatin microspheres. At six months, recurrence occurred in 14.8% of evaluable patients in the MMAE group and 21.0% in controls, but the difference was not statistically significant. Repeat surgery was also numerically less frequent without reaching statistical significance [19]. EMPROTECT is therefore scientifically important because it prevents the field from treating “MMAE” as a uniform intervention and raises questions about embolic penetration, power, endpoint definition, baseline risk, and material-specific biological effects [19].

The 2026 MEMBRANE randomized trial added another major data point. Three hundred seventy-six participants were randomized within predefined surgical and nonsurgical pathways to standard care with or without MMAE using n-BCA. The primary effectiveness endpoint, consisting of residual or reaccumulated hematoma greater than 10 mm at six months or need for surgical treatment, occurred in 11.6% of the MMAE group compared with 22.1% of controls. The odds of treatment failure were therefore significantly reduced, while good functional outcome was noninferior to standard care [20]. These findings strengthen the case for MMAE but also reinforce the need to understand why outcomes vary among different randomized trials [20].

**Materials and Methods.** A structured narrative review was performed using randomized controlled trials, prospective multicenter studies, observational cohorts, and major surgical studies published through August 2026. The evidence was organized into five domains: conventional neurosurgical management, randomized evidence for MMA embolization, anatomical and technical determinants of embolization, radiographic and clinical predictors of treatment response, and phenotype-specific integration of embolization with surgical drainage. Priority was given to EMBOLISE, MAGIC-MT, STEM, EMPROTECT, and MEMBRANE because these randomized trials provide the strongest contemporary evidence for MMAE. Earlier prospective and retrospective studies were used to interpret pathophysiological mechanisms, embolic material, anatomical technique, recurrence prediction, and treatment sequencing. The principal conceptual endpoint was precision control of recurrence biology, defined as prevention of clinically meaningful hematoma persistence or reaccumulation without delaying necessary decompression or exposing the patient to disproportionate endovascular risk. The review distinguished radiographic improvement from clinical success. Hematoma thickness, volume reduction, midline-shift resolution, reoperation, neurological deterioration, modified Rankin Scale outcome, mortality, and treatment-related complications were considered separately.

## **Results.**

**Surgical Decompression Remains Essential in the Mass-Effect Phenotype.** MMAE is a biological treatment whose effect develops over time. It does not immediately evacuate the subdural collection. Therefore, a patient with declining consciousness, progressive hemiparesis, severe headache associated with substantial mass effect, or clinically important midline shift may require immediate surgical decompression regardless of whether embolization is also planned. Burr-hole drainage rapidly reduces intracranial volume and restores cortical expansion. This immediate mechanical effect cannot be reproduced by embolization. The most rational use of MMAE in this

phenotype is therefore adjunctive: surgery treats the immediate mechanical problem, while embolization targets the membrane biology responsible for recurrence.

**Why Chronic Subdural Hematoma Recurs.** After drainage, the brain may not completely re-expand, particularly in older patients with substantial cerebral atrophy. A persistent subdural space remains. Residual vascularized membranes can continue to exude protein-rich fluid and undergo repeated microhemorrhage. Local fibrinolysis prevents stable clot organization. Anticoagulants, antiplatelet therapy, chronic kidney disease, liver dysfunction, and severe brain atrophy can further impair durable resolution. This explains why recurrence is not simply a consequence of technically inadequate surgery. A perfectly positioned drain can decompress the hematoma while leaving the entire inflammatory vascular membrane intact. MMAE addresses this residual mechanism.

**Randomized Trials Should Not Be Interpreted as One Identical Experiment.** The major contemporary trials differed in several clinically important ways. EMBOLISE exclusively tested embolization as an adjunct to surgery. MAGIC-MT included surgical and nonsurgical treatment pathways and evaluated a 90-day symptomatic recurrence/progression endpoint. STEM included both pathways but used a 180-day composite endpoint. EMPROTECT focused on surgically treated high-risk patients and used microparticles. MEMBRANE evaluated n-BCA in both surgical and nonsurgical cohorts with a six-month radiographic or surgical-failure endpoint. Consequently, apparently conflicting results can arise even when the biological effect of embolization is similar.

**Table 1. Major contemporary randomized trials of MMA embolization**

| Trial     | Population                                                | Embolitic strategy        | Approximate sample size | Principal follow-up | Main interpretation                                                           |
|-----------|-----------------------------------------------------------|---------------------------|-------------------------|---------------------|-------------------------------------------------------------------------------|
| EMBOLISE  | Symptomatic subacute/cSDH requiring surgery               | Onyx + surgery            | 400                     | 90 days             | Reduced recurrence/progression requiring repeat surgery                       |
| MAGIC-MT  | Symptomatic nonacute SDH; surgical or nonsurgical pathway | MMAE + usual care         | 722                     | 90 days             | Primary symptomatic recurrence/progression endpoint not significantly reduced |
| STEM      | Symptomatic cSDH; surgical or nonsurgical standard care   | Squid + standard care     | 310                     | 180 days            | Reduced composite treatment failure                                           |
| EMPROTECT | Postoperative high-recurrence-risk cSDH                   | 300–500 µm microparticles | 342                     | 6 months            | Numerically lower recurrence, not statistically significant                   |
| MEMBRANE  | Symptomatic cSDH; surgical                                | n-BCA + standard care     | 376                     | 6 months            | Reduced residual/recurrent                                                    |

|  |                                |  |  |  |                                 |
|--|--------------------------------|--|--|--|---------------------------------|
|  | and<br>nonsurgical<br>pathways |  |  |  | hematoma or surgical<br>failure |
|--|--------------------------------|--|--|--|---------------------------------|

**Adjunctive MMAE After Surgery.** The clearest current indication is a symptomatic cSDH that requires evacuation and has an appreciable probability of recurrence. Surgery provides immediate neurological decompression. MMAE is then performed either before or after evacuation, depending on workflow and patient stability. Postoperative embolization has a conceptual advantage because the urgent neurosurgical problem is treated first. Preoperative embolization may be reasonable in stable patients, but the procedure should never meaningfully delay required decompression. Patients with recurrent cSDH are especially attractive candidates because recurrence after technically adequate drainage demonstrates persistence of the biological substrate. Other potential high-risk features include bilateral hematomas, marked cerebral atrophy, anticoagulant use, large residual postoperative subdural space, mixed-density or separated hematoma architecture, and multiple previous evacuations. However, the relative predictive value of these variables requires further prospective validation.

**Stand-Alone MMAE.** Stand-alone embolization is conceptually different from adjunctive treatment. The patient must be sufficiently stable to tolerate gradual radiographic resolution. Suitable candidates may include patients with mild symptoms, limited or moderate mass effect, high surgical/anesthetic risk, recurrent disease without severe neurological compromise, or patients in whom avoiding repeated surgery is especially desirable. The primary danger is inappropriate delay of decompression. A large hematoma can continue to exert mass effect despite successful devascularization. Therefore, embolization should not be viewed as a minimally invasive substitute for surgery merely because it can be performed without craniotomy. Clinical physiology determines the appropriate treatment.

**Embolic Materials.** The ideal embolic agent should penetrate the distal MMA branches supplying the pathological membranes while avoiding reflux or passage into dangerous anastomoses. Particles produce distal occlusion but their final distribution is not directly visible after delivery. Nonadhesive liquid agents such as Onyx and Squid permit continuous fluoroscopic visualization and can produce extensive distal penetration. n-BCA polymerizes rapidly and can penetrate the target bed when appropriately diluted and delivered, but requires careful control because reflux and unintended embolization can occur. Observational comparisons have generally not demonstrated dramatic differences in major clinical outcomes among commonly used materials. However, randomized evidence is currently heavily weighted toward specific liquid agents, whereas EMPROTECT used microspheres and did not achieve its primary endpoint. This discrepancy is hypothesis-generating rather than proof of material superiority.

**Membrane Penetration May Matter More Than Proximal Arterial Occlusion.** A technically completed embolization can range from proximal truncal occlusion to extensive penetration into distal meningeal branches and the abnormal membrane vascular network. These are unlikely to be biologically equivalent. Recent imaging work has shown that visible membrane penetration of liquid embolic material is associated with faster hematoma resorption and greater radiographic response. This supports a mechanistic model in which the therapeutic target is not the MMA trunk itself but the pathological vascular interface between the dura and chronic subdural membrane. The procedural

endpoint should therefore increasingly shift from “MMA occluded” toward “pathological membrane supply adequately devascularized.”

**Dangerous Anastomoses.** The MMA has clinically important connections to the ophthalmic and cranial-nerve circulations. Orbital branches can communicate with lacrimal and ophthalmic circulation. Petrosal branches may contribute to facial nerve vascular supply. Unrecognized embolization through these pathways can produce visual loss or cranial neuropathy.

Superselective angiography is therefore essential before embolic delivery. The microcatheter should be positioned to achieve distal membrane penetration while avoiding dangerous arterial communications. This balance is particularly important with low-viscosity liquid agents.

**Radial Versus Femoral Access.** Both radial and femoral approaches can be used for MMAE. The transradial approach is attractive in elderly patients because it may facilitate early mobilization and reduce groin-related complications. Comparative studies show broadly similar technical and clinical outcomes between access strategies. The optimal route depends on arch anatomy, catheter stability, operator experience, target laterality, and whether bilateral embolization is planned. In patients at high risk of postoperative delirium or prolonged immobilization, radial access may offer practical workflow advantages.

**Bilateral Chronic Subdural Hematoma.** Bilateral cSDH represents a distinct anatomical phenotype. Even when one side is clinically dominant, both hemispheres may contain active membrane vascularity. Treatment of only one MMA can theoretically leave the contralateral pathological process untreated. Whether bilateral embolization should be routine for bilateral hematomas is not established. The decision should consider hematoma symmetry, interval growth, neurological dominance, procedural duration, contrast burden, and radiation exposure. Bilateral procedures also predictably increase fluoroscopy time and radiation dose.

**Radiographic Resolution Is Gradual.** One of the most important counseling points is that embolization does not cause immediate disappearance of the hematoma. The collection may remain visible for weeks or months. Progressive reduction in hematoma thickness and midline shift is expected as membrane exudation decreases and physiological resorption dominates. A residual hematoma on early follow-up CT should therefore not automatically be labeled treatment failure if the patient is clinically improving and the collection is stable or decreasing. Conversely, progressive neurological symptoms override radiographic expectations and may require rescue surgery.

**Table 2. Suggested interpretation of post-MMAE follow-up**

| Finding                                        | Suggested interpretation                  |
|------------------------------------------------|-------------------------------------------|
| Clinically improved + decreasing hematoma      | Expected response                         |
| Clinically stable + unchanged early CT         | Observation may remain reasonable         |
| Persistent but gradually decreasing collection | Normal delayed resorption phenotype       |
| Increasing thickness without symptoms          | Requires close reassessment               |
| Increasing midline shift                       | Possible treatment failure                |
| New neurological deficit                       | Urgent imaging and surgical evaluation    |
| Acute rebleeding                               | Rescue treatment according to mass effect |

|                                          |                                                               |
|------------------------------------------|---------------------------------------------------------------|
| Persistent large collection after months | Evaluate residual membrane activity and alternative diagnosis |
|------------------------------------------|---------------------------------------------------------------|

**Proposed Precision Treatment Model.** A precision model should separate patients according to the dominant therapeutic problem. The first phenotype is acute mechanical compression within chronic disease. These patients require surgery. MMAE is considered adjunctively if recurrence risk is meaningful. The second phenotype is recurrent biological disease after adequate surgery. These patients are among the strongest candidates for MMAE because repeated recurrence demonstrates persistent membrane pathology. The third phenotype is stable, minimally symptomatic cSDH without urgent decompressive requirement. Stand-alone MMAE may be considered when gradual resolution is acceptable. The fourth phenotype is high surgical-risk disease. Frailty, severe cardiopulmonary comorbidity, antithrombotic requirements, or repeated anesthesia exposure may shift the risk-benefit balance toward embolization. The fifth phenotype is organized or heavily septated cSDH with significant mass effect. These lesions may respond less predictably to embolization alone because mechanical organization and loculations can prevent adequate decompression even if membrane vascularity is reduced.

**Table 3. Phenotype-oriented strategy for chronic subdural hematoma**

| Clinical phenotype                             | Immediate problem                           | Preferred conceptual strategy               |
|------------------------------------------------|---------------------------------------------|---------------------------------------------|
| Progressive neurological deficit + mass effect | Mechanical compression                      | Burr-hole/minicraniotomy ± adjunctive MMAE  |
| First cSDH with high recurrence risk           | Compression + biological recurrence risk    | Surgery + consider MMAE                     |
| Recurrent after previous drainage              | Persistent membrane biology                 | Strong consideration of adjunctive MMAE     |
| Mild symptoms, no urgent mass effect           | Chronic membrane activity                   | Selected stand-alone MMAE                   |
| Frail/high anesthesia risk                     | Treatment morbidity                         | MMAE when delayed resorption is safe        |
| Organized/septated large hematoma              | Mechanical compartmentalization             | Surgical treatment often necessary          |
| Bilateral stable cSDH                          | Bilateral biological disease                | Individualized unilateral/bilateral MMAE    |
| Anticoagulation-dependent patient              | Recurrence and interruption-of-therapy risk | Consider MMAE within multidisciplinary plan |

**Discussion.** The publication of five major randomized studies has moved MMA embolization from an experimental neurointerventional concept into an evidence-based component of chronic subdural hematoma management. However, the most important lesson is not simply that “MMAE works.” The trials demonstrate that effectiveness depends on treatment context, follow-up interval, endpoint definition, embolic agent, and baseline probability of recurrence [16–20]. EMBOLISE, MAGIC-MT, STEM, EMPROTECT, and MEMBRANE should therefore be interpreted together but not treated as biologically identical experiments. EMBOLISE provides the strongest conceptual support for adjunctive embolization after surgical evacuation [16]. The recurrence or progression rate

requiring repeat surgery was approximately threefold lower with MMAE plus surgery than with surgery alone. The relevance of this endpoint is high because repeat operation exposes an elderly patient to another hospitalization, anesthesia, infection risk, immobilization, and interruption of anticoagulation. The result also supports the central pathophysiological hypothesis of MMAE: surgical evacuation treats intracranial volume, while arterial devascularization treats recurrence biology [1–4, 8–12, 16]. MAGIC-MT provides a useful counterbalance [17]. Although symptomatic recurrence or progression was numerically less frequent after embolization, the primary 90-day comparison was not statistically significant. This should not be interpreted as proof of inefficacy. The study population included both patients selected for burr-hole drainage and patients selected for nonsurgical management before randomization. An intervention that acts over months may also be incompletely characterized by a relatively early endpoint. At the same time, the neutral primary result cautions against assuming that every stable nonacute SDH derives a clinically important benefit from routine embolization [17]. STEM extended follow-up to 180 days and used a broader composite endpoint including recurrent or residual hematoma, retreatment, rescue surgery, and disabling vascular events [18]. Adjunctive MMAE reduced treatment failure without a short-term excess of disabling stroke or death. The trial is important because it reflects real-world pathways: some patients were treated surgically, whereas others were observed. Thus, references [16–18] collectively indicate that the treatment effect of MMAE is probably strongest when recurrence or progression is clinically meaningful and when follow-up extends sufficiently to capture the natural evolution of the hematoma. EMPROTECT is essential because it prevents confirmation bias [19]. A 14.8% recurrence rate after embolization compared with 21.0% after standard postoperative care represents a potentially clinically meaningful numerical difference, but the confidence interval crossed the null and the primary endpoint was not met. The trial enrolled high-risk surgical patients and used 300–500  $\mu\text{m}$  microspheres. Several interpretations are possible. The study may have been underpowered for the true effect size; the selected recurrence definition may have influenced statistical power; distal membrane penetration may have differed from liquid-agent trials; or the underlying treatment effect may simply be more modest in this phenotype. None of these explanations can be considered proven. The correct scientific conclusion is that microparticle postoperative MMAE was not shown to be superior under the EMPROTECT trial conditions [19].

MEMBRANE then provided positive randomized evidence using a different embolic platform [20]. Among 376 participants, the six-month composite of residual or recurrent hematoma greater than 10 mm or need for surgical treatment occurred in 11.6% with n-BCA plus standard care versus 22.1% with standard care alone. Importantly, the trial included both surgical and nonsurgical treatment pathways and demonstrated noninferiority with respect to functional outcome. This reinforces the therapeutic signal identified in EMBOLISE and STEM while simultaneously making the negative EMPROTECT findings more scientifically interesting [16, 18–20].

The embolic-agent question therefore remains unresolved. Observational multicenter analyses involving particles, Onyx, and n-BCA have not demonstrated major differences in surgical rescue, radiographic success, or major complications [14, 15]. Yet randomized liquid-agent trials have generally produced stronger positive signals than EMPROTECT. This discrepancy could reflect true material effects, but it could equally reflect trial design, operator technique, endpoint definitions,

patient selection, distal catheter position, or membrane penetration. Reference [13] found liquid agents associated with lower failure in multivariable analysis, whereas more direct material-comparison cohorts did not identify meaningful outcome differences [14, 15]. A randomized head-to-head embolic-agent trial would therefore be more informative than indirect comparison across independently designed studies. The concept of distal membrane penetration may ultimately be more important than the distinction between liquid and particulate agents. Ganga et al. demonstrated that angiographically visualized membrane penetration was associated with faster resorption, greater percentage reduction, and increased odds of complete resolution [21]. If confirmed prospectively, this could redefine the technical endpoint of MMAE. Rather than documenting proximal occlusion of the MMA, procedural quality would be graded according to the degree of pathological membrane devascularization [21]. This has direct implications for catheter position. Extremely proximal embolization may interrupt major MMA flow but fail to reach the fine distal vascular network sustaining the membrane. Conversely, overly aggressive distal delivery can increase the risk of embolization through orbital or cranial-nerve anastomoses. The optimal treatment is therefore not maximum embolic penetration but maximum safe pathological membrane penetration. Access strategy is less likely to influence biological efficacy but may alter the overall treatment burden. Transradial MMAE has demonstrated feasibility and safety [22]. Larger comparative studies suggest similar procedural and clinical outcomes with radial and femoral approaches [23]. In elderly patients, radial access may facilitate early mobilization and may reduce postprocedural immobilization-related discomfort or delirium [24]. These advantages are relevant because the typical cSDH population is substantially older and frailer than many conventional neurointerventional populations [22–24]. Outcome measurement also requires refinement. A hematoma that remains 8 mm thick at three months but has fallen from 24 mm, with complete symptom resolution and no repeat surgery, represents a very different biological outcome from a stable 8-mm collection that later re-expands. Santiago and colleagues demonstrated that cSDH resolution after MMAE can continue for many months, with substantial radiographic improvement often preceding complete disappearance [25]. Squid-treated cohorts similarly illustrate the delayed nature of the radiographic response [26]. Therefore, early complete disappearance of the hematoma should not be required to define successful embolization [25, 26].

The long-term epidemiological context further favors recurrence prevention. Brennan et al. demonstrated the substantial hospital burden associated with cSDH in a prospective UK cohort [2], while population-based analyses have documented both rising incidence and repeated-operation burden [3, 4, 27–29]. The clinical value of MMAE may therefore extend beyond an individual CT endpoint. Preventing repeat hospitalization could reduce functional decline, interruption of antithrombotic therapy, nosocomial complications, and cost. However, universal embolization is unlikely to be economically efficient if many low-risk patients would never recur after a single burr-hole operation [27–29]. Precision selection is therefore important both medically and economically. Conventional surgery must remain central to this treatment framework. The randomized drainage trial by Santarius [1], large surgical cohort studies [2, 3], repeated-operation data [4], and randomized comparisons of surgical approaches [7] demonstrate that effective neurosurgical drainage remains the fastest and most predictable method of treating clinically significant compression. The development

of MMAE should not reverse this principle. A severely symptomatic patient should not wait for biological hematoma resorption simply to avoid an operation. Similarly, medical therapies should be interpreted within the same risk-benefit framework. Dexamethasone reduced repeat procedures but worsened overall functional outcomes and increased adverse events [5]. Atorvastatin produced encouraging nonsurgical hematoma reduction in a randomized study [6]. These findings [5, 6] emphasize why cSDH trials must measure function and complications rather than radiographic recurrence alone. MMAE should be judged by the same standard. The strongest candidate for adjunctive MMAE may be the patient who demonstrates both a need for decompression and a high biological probability of recurrence. Potential features include recurrent disease, anticoagulation, marked atrophy, bilateral cSDH, persistent postoperative space, and complex internal hematoma architecture [3, 11–13]. However, existing prediction models remain insufficiently validated to select embolization automatically. Salem et al. identified anticoagulation and small MMA caliber as independent predictors of clinical failure after MMAE, demonstrating that the recurrence phenotype and the embolization-response phenotype are not necessarily identical [13]. A patient at high risk of recurrence may simultaneously be less likely to respond to embolization.

This distinction suggests that future prediction models should include two separate outputs. The first should estimate the probability of recurrence after standard surgical or conservative treatment. The second should estimate the probability of successful response to MMAE. Only patients with a sufficiently high first probability and a sufficiently favorable second probability would be expected to obtain the largest absolute benefit.

**Table 4. Proposed variables for a precision-MMAE prediction model**

| Domain        | Candidate variable                                                 |
|---------------|--------------------------------------------------------------------|
| Clinical      | Age, baseline mRS, frailty, recurrence history                     |
| Medication    | Anticoagulant and antiplatelet exposure                            |
| CT morphology | Thickness, midline shift, density, septations, bilateral disease   |
| Brain anatomy | Degree of cerebral atrophy and re-expansion potential              |
| Surgery       | First operation vs recurrent disease, postoperative residual space |
| MMA anatomy   | Diameter, anterior/posterior branch dominance                      |
| Angiography   | Degree of membrane blush and dangerous collaterals                 |
| Procedure     | Proximal vs distal catheter position                               |
| Embolization  | Material and penetration pattern                                   |
| Follow-up     | Rate of thickness and volume reduction                             |
| Outcome       | Rescue surgery, functional recovery, mortality                     |

A prospective study could use such a model to assign patients to surgery alone, surgery plus MMAE, or stand-alone MMAE. Randomizing all cSDH patients indiscriminately to embolization or no embolization may underestimate the value of the treatment in recurrence-prone phenotypes and over-treat low-risk individuals. Future trials should also standardize what constitutes recurrence. EMBOLISE focused on recurrence or progression leading to repeat surgery [16]. MAGIC-MT emphasized symptomatic progression or recurrence within 90 days [17]. STEM used a composite 180-day treatment-failure endpoint [18]. EMPROTECT incorporated clinical and radiographic recurrence at six months [19]. MEMBRANE included residual or reaccumulated hematoma greater than 10 mm

or a surgical procedure within six months [20]. These are not interchangeable outcomes. A future core outcome set should include clinically indicated rescue surgery, symptomatic progression, standardized CT volumetrics, mRS, cognition, mortality, antithrombotic resumption, hospitalization days, and quality of life. The timing of follow-up should extend beyond 90 days because embolization produces delayed biological involution.

The procedure itself can also be refined. Automated angiographic quantification could grade distal membrane penetration. Cone-beam CT could characterize embolic distribution. Radiomics may identify CT phenotypes associated with highly vascularized membranes. Artificial intelligence could integrate CT morphology, anticoagulation, frailty, and procedural variables to predict both recurrence and embolization response. Such tools would be particularly valuable if they reduce the current tendency to select treatment primarily on the basis of hematoma thickness. The central conceptual shift is therefore from drainage versus embolization to mechanical decompression plus biological disease control. These are not competing therapeutic principles. They treat different components of the same disorder.

**Conclusion.** Chronic subdural hematoma is a dynamic inflammatory and angiogenic disease rather than a purely mechanical accumulation of old blood. Surgical evacuation remains the most appropriate treatment for patients with clinically important neurological deterioration or significant mass effect because it provides immediate intracranial decompression. Middle meningeal artery embolization addresses a different component of the disease by reducing arterial supply to the pathological subdural membranes that sustain exudation and recurrent microhemorrhage. Contemporary randomized trials demonstrate an overall therapeutic signal in favor of MMAE, particularly as an adjunct to standard management, but trial results are not uniform. The benefit appears to depend on patient phenotype, timing, treatment pathway, embolic agent, technical penetration, follow-up duration, and definition of treatment failure. The strongest current clinical model is therefore not replacement of burr-hole surgery by embolization, but integration of the two treatments according to pathophysiology. Patients with urgent compression require decompression. Patients with recurrent or recurrence-prone disease may benefit from adjunctive MMAE. Selected stable patients without an immediate decompressive requirement may be candidates for stand-alone embolization. Future treatment should increasingly use individualized recurrence prediction, detailed MMA angiography, quantification of membrane penetration, standardized radiographic outcomes, and long-term functional endpoints. The evolution of MMA embolization therefore represents a broader transition in neurosurgery from treating the radiographic manifestation of chronic subdural hematoma toward treating the biological mechanism responsible for its persistence.

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