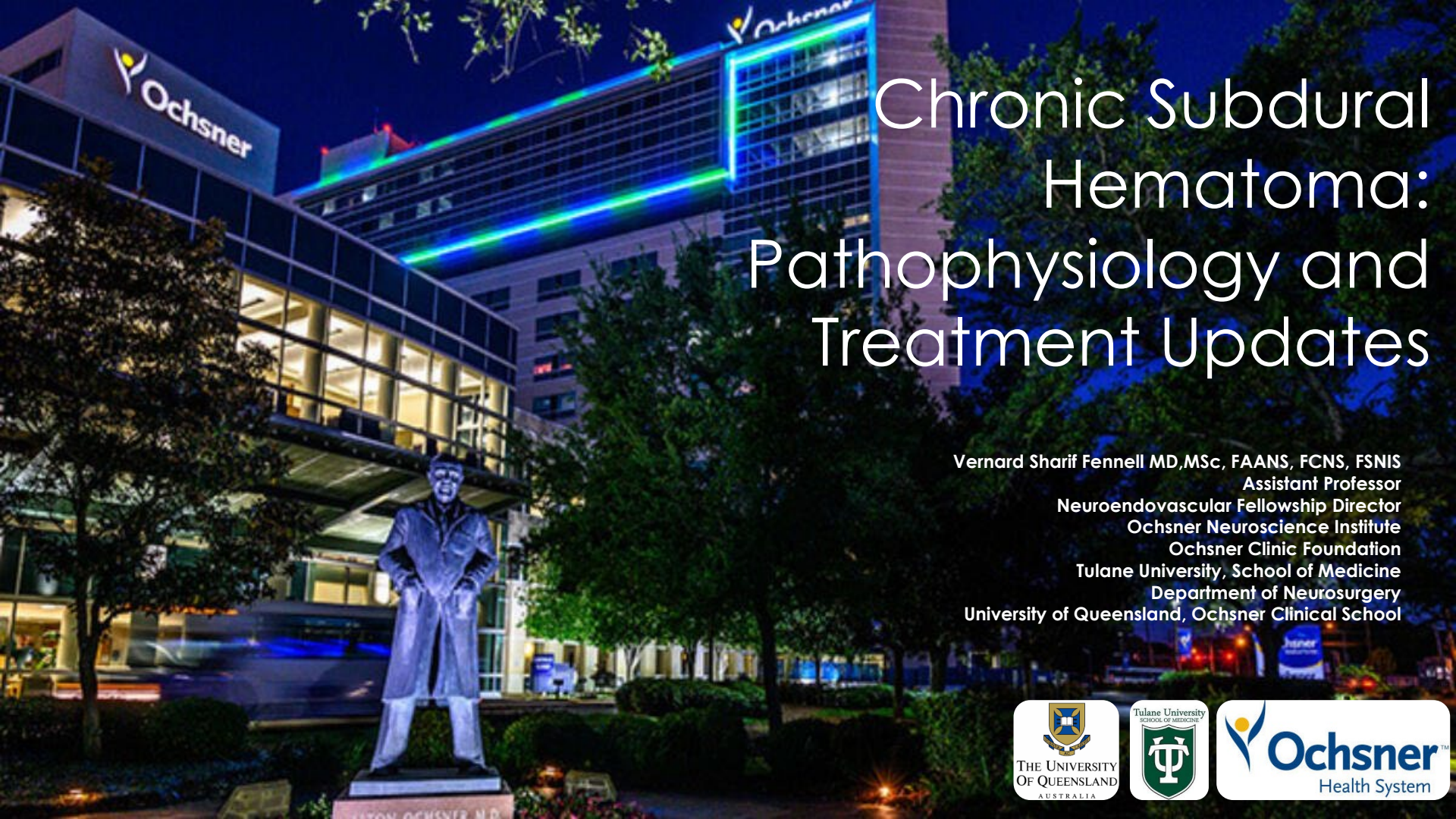

Chronic Subdural Hematoma: Pathophysiology and Treatment Updates

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Agenda: What We Will Cover Today

A journey from bench to bedside—from molecular pathophysiology to the latest randomized trial evidence on endovascular therapy

01

Epidemiology & Anatomy

Defining cSDH, at-risk populations, and the critical role of the dural border cell layer

02

Pathophysiology (4-Part Deep Dive)

Bridging vein rupture → membrane formation → inflammatory cascade → coagulation dysregulation

03

Clinical Diagnosis & Risk Stratification

CT/MRI grading, Markwalder Scale, recurrence predictors, anticoagulation considerations

04

Traditional vs. Endovascular Management

Burr hole craniotomy outcomes, MMA embolization rationale, technique, and landmark trial data

05

Emerging Therapies & Practice Recommendations

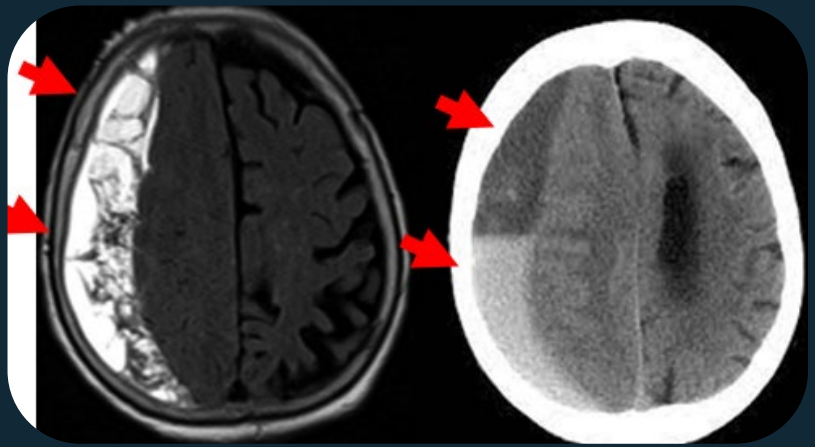
Dexamethasone, TXA, combined protocols, special populations, and future directions

Defining Chronic Subdural Hematoma

Epidemiology, Incidence, and At-Risk Populations

Chronic subdural hematoma (cSDH) is defined as a collection of blood and its degradation products in the subdural space, typically presenting 3 or more weeks after the initial hemorrhagic event. It represents one of the most common neurosurgical conditions encountered in clinical practice.

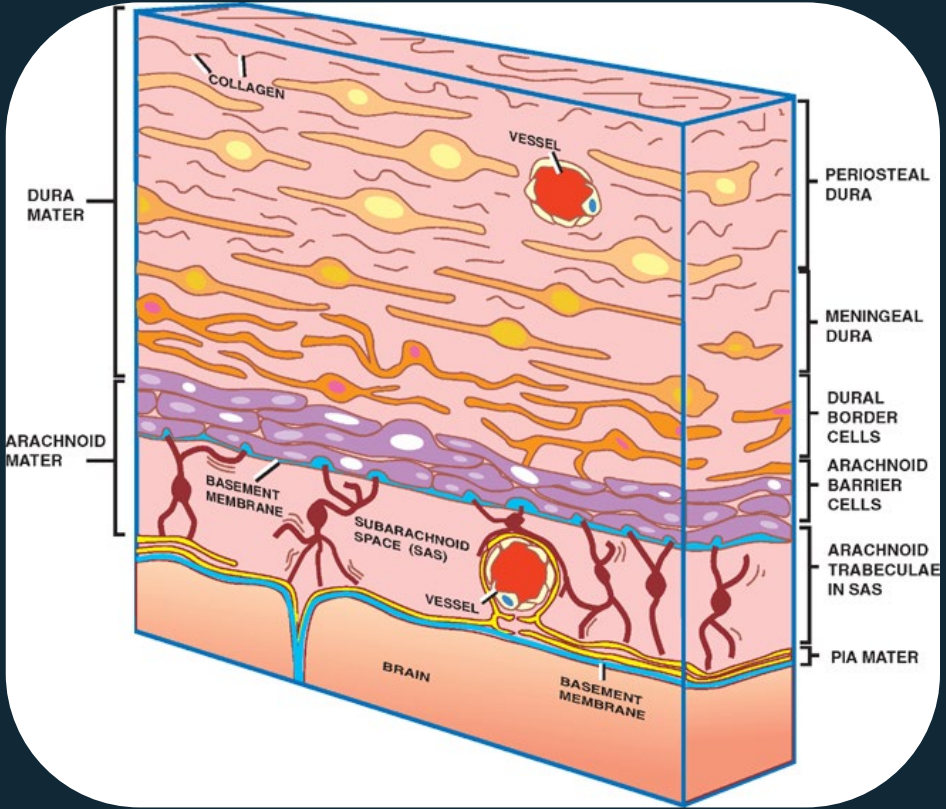
The annual incidence is approximately 1–5 per 100,000 in the general population, rising dramatically to 58 per 100,000 in adults over age 70. With global aging demographics, cSDH is projected to become the most common neurosurgical condition by 2030 *(Kalanithi et al., Neurosurgery 2013)*



High -Risk Populations

- Age >65 years (cerebral atrophy increases bridging vein tension)
- Chronic anticoagulation or antiplatelet therapy
- Alcoholism and hepatic coagulopathy
- History of falls or recurrent minor head trauma
- CSF shunted patients (low intracranial pressure)
- Hemodialysis-dependent patients

The Subdural Space: Anatomy and the Dural Border Cell Layer



Dura Mater (Outer)

Dense fibrous layer—anchored to inner skull table

Dural Border Cell Layer

Plane of cleavage—no tight junctions, fragile intercellular connections

Arachnoid Mater

Barrier layer with tight junctions—resists further inward hemorrhage spread

Subarachnoid Space

CSF-filled, contains bridging veins traversing to cortical surface

Pathophysiology Part 1

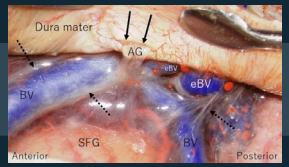
Initial Hemorrhage, Bridging Vein Rupture, and the Role of Trauma

1

Triggering Event

Rotational or translational head acceleration—often trivial or unrecalled. Stretches cortical bridging veins.

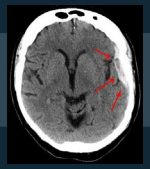
2



Bridging Vein Rupture

Low-pressure venous bleeding into the DBC layer. In atrophic brains, veins span a greater distance—dramatically increasing vulnerability.

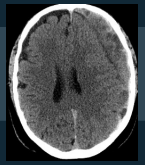
3



Acute Subdural Hematoma

Initial high-density clot on CT. If small and not surgically evacuated, the body initiates an inflammatory response—rather than resorption.

4



Chronic Transformation

Over 3–21 days, enzymatic lysis, hygroma formation, and membrane encapsulation transform the acute clot into the chronic hypodense collection.

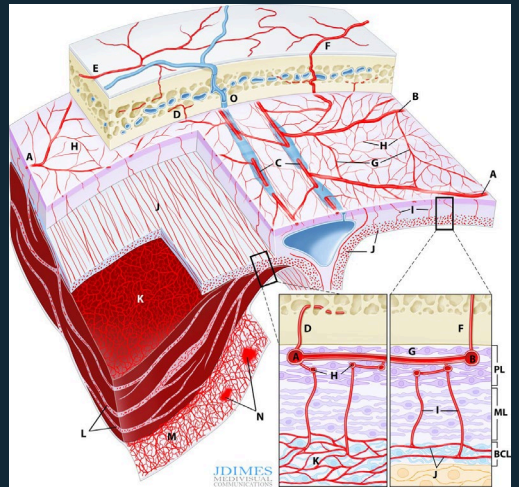
The transition from acute to chronic hematoma is governed not merely by time, but by a complex interplay of local coagulation failure, fibrinolysis, and nascent inflammatory signaling—setting the stage for the pathological cycle described in subsequent slides.

Pathophysiology Part 2

Outer Membrane Formation, Neovascularization, and the Cycle of Re-bleeding

Within days of the initial hemorrhage, dural fibroblasts proliferate and form a highly vascular outer membrane (neomembrane) derived from the inner dural layer. This membrane is histologically immature, characterized by sinusoidal capillaries with absent or deficient tight junctions, wide intercellular gaps, and fenestrated endothelium.

These pathological microvessels are structurally incompetent: they leak plasma proteins and red blood cells continuously into the hematoma cavity, perpetuating expansion. This was elegantly demonstrated by Ito et al. using radioisotope-labeled albumin studies (*J Neurosurg, 1976*), establishing that ongoing micro-hemorrhage—not osmotic gradient alone—drives hematoma growth.



Day 3 – 7

Dural fibroblast activation and outer membrane anlage formation begins

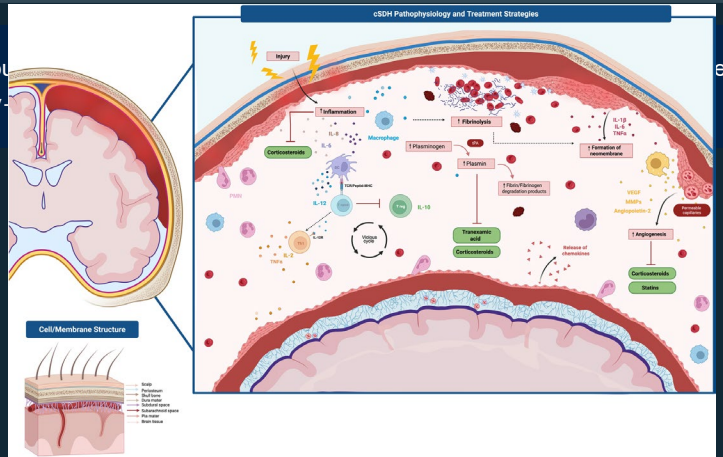
Day 7 – 14

Sinusoidal neovascularization from dural vessels—VEGF-driven, structurally incompetent capillaries

Day 14 – 21+

Established outer and inner membranes encapsulate the liquefied hematoma; recurrent microbleeds sustain and expand the collection

The ou… …eningeal artery…



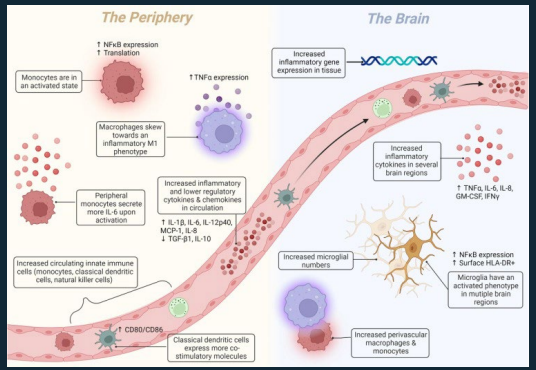
Pathophysiology Part 3

Inflammatory Cascade: Cytokines, VEGF, and Fibrinolytic Dysregulation

The cSDH microenvironment is a **biochemically hostile milieu** that actively resists resolution. Seminal work by Frati et al. *(Neurosurgery, 2004)* and Weigel et al. characterized the following key mediators:

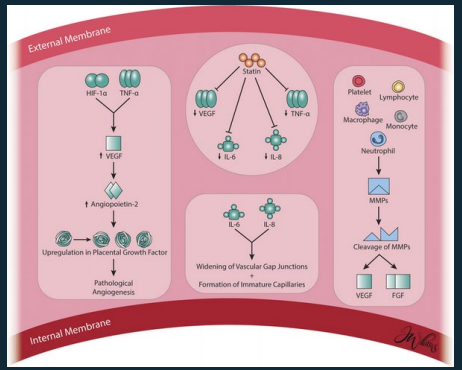
Pro-Inflammatory Cytokines

IL-6, IL-8, TNF-α, and IL-1β are markedly elevated in cSDH fluid vs. serum. IL-6 in particular drives ongoing vascular permeability and fibroblast proliferation within the outer membrane.



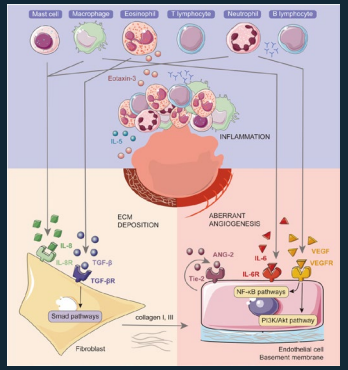
VEGF — The Key Angiogenic Driver

Vascular endothelial growth factor is significantly elevated in cSDH fluid. VEGF promotes the pathological neovascularization of the outer membrane—producing the leaky, incompetent vessels responsible for recurrent micro-hemorrhage *(Stanisic et al., Acta Neurochir, 2012)*



Fibrinolytic Dysregulation

Elevated tissue plasminogen activator (tPA) and reduced plasminogen activator inhibitor-1 (PAI-1) within the hematoma cavity create a hyperfibrinolytic state—preventing clot organization and resolution. D-dimer levels in cSDH fluid are 10–100× serum levels *(Fujisawa et al., Neurosurgery, 1995)*



Pathophysiology Part 4

Osmotic and Coagulation Theories: Evidence Review and Current Consensus

The Osmotic Gradient Theory

Gardner's classic hypothesis *(1932)* proposed that protein degradation products within the hematoma create an osmotic gradient, drawing fluid across the inner membrane by osmosis and driving progressive expansion. This theory gained wide acceptance for decades.

Current status: Largely refuted. Gardner et al. and subsequent investigators including Rabe et al. demonstrated that cSDH fluid osmolality is *not* consistently higher than serum, and that inner membrane permeability to proteins does not support net osmotic fluid influx as the primary mechanism *(J Neurosurg, 1981)*

Current Evidence Consensus

Primary Mechanism

Recurrent microhemorrhage from the pathological outer neomembrane vasculature is the **dominant driver** of cSDH expansion—confirmed by Ito et al. isotope studies and modern histopathological series

Contributing Factor

Local coagulopathy and hyperfibrinolysis prevent clot consolidation and maintain a liquid hematoma susceptible to continued expansion

Facilitating Factor

Impaired intracranial compliance in the atrophic brain prevents the tamponade effect that limits hematoma growth in younger patients

Clinical Presentation and Neuroimaging

CT, MRI Grading Systems, and the Markwalder Scale

Clinical Presentation

cSDH presents insidiously, often mimicking stroke, dementia, or depression. Cardinal symptoms include **progressive headache, cognitive decline, contralateral hemiparesis, and gait instability.** Acute-on-chronic presentations may include sudden neurological deterioration. Up to 30% present without any identified antecedent trauma

CT Characteristics by Age

Timing	CT Density	Appearance
Acute (0–3d)	Hyperdense	Bright white crescent
Subacute (3-21d)	Isodense	May be isoattenuating—subtle
Chronic (>21d)	Hypodense	Dark crescent, brain compression
Mixed density	Heterogeneous	Active re-bleeding on chronic

Markwalder Grading Scale

1	**Grade 0** No neurological deficits—incidental finding
2	**Grade 1** Alert, oriented—mild symptoms: headache, cognitive slowing
3	**Grade 2** Drowsy/disoriented—focal neurological deficit present
4	**Grade 3** Stuporous—severe focal deficits, response to stimuli preserved
5	**Grade 4** Comatose—absent motor response, decerebrate posturing

Risk Factors and Recurrence

Anticoagulation, Brain Atrophy, Bilateral cSDH, and Predictive Models

20%

Recurrence Rate

After standard burr hole drainage—overall surgical recurrence requiring reoperation

33%

Anticoagulated Patients

Recurrence rate in patients on therapeutic anticoagulation—nearly double the baseline risk

30%

Bilateral cSDH

Proportion of cSDH cases that are bilateral—associated with higher recurrence and morbidity

58x

Age >70 Risk

Per 100,000 incidence in patients over 70—vs. 1.5 per 100,000 in the general population

Independent predictors of recurrence include **hematoma volume >100 mL, bilateral presentation, brain atrophy index (Evans ratio >0.3), antiplatelet or anticoagulant use, a postoperative residual hematoma thickness >10 mm**. The Recurrence Risk Score proposed by Uno et al. (*J Neurosurg, 2015*) integrates these variables into a validated clinical tool. MMA embolization has been specifically studied as a recurrence-reduction strategy in this high-risk cohort.

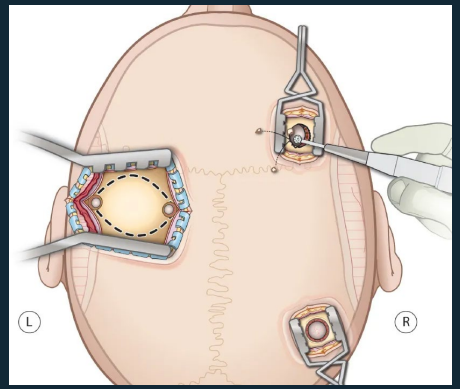
Traditional Surgical Management

Burr Hole Craniotomy, Twist Drill, and Craniotomy — Outcomes and Limitations

Surgical evacuation remains the **standard of care for symptomatic cSDH**. Three primary surgical modalities exist, with burr hole craniotomy representing the most widely performed approach globally.

Procedure	Indication	Recurrence	Mortality
Burr Hole (42 holes)	Standard cSDH, most cases	10–20%	0–8%
Twist Drill Craniostomy	High surgical risk, bedside use	18–28%	5–10%
Craniotomy	Recurrent, organized, calcified	5–12%	3–10%

Data synthesized from: Weigel et al. *Neurosurg Rev, 2003*; Ducruet et al. *Neurosurg Focus, 2013*; Santarius et al. *Lancet, 2009*



Key Limitations of Surgery

High Recurrence

Does not address the underlying pathological neomembrane—recurrence is inevitable if the biology is not corrected

Operative Risk

General anesthesia risk in elderly, frail, anticoagulated patients—pneumonia, DVT, delirium

Bilateral Cases

Bilateral craniotomies carry additive morbidity and do not address systemic recurrence drivers

Why Endovascular?

Rationale, the Problem of Recurrence, and the Middle Meningeal Artery

The middle meningeal artery (MMA) is the primary vascular supply to the **outer neomembrane** of cSDH. Embolization of the MMA eliminates the arterial supply to the pathological vascular network within this membrane, thereby:

- Interrupting the cycle of recurrent micro-hemorrhage
- Promoting membrane regression and hematoma resorption
- Reducing intracranial pressure without cranial surgery
- Preserving definitive surgical options if needed

This rationale was first proposed by Mandai et al. (*Neurosurg, 2000*) and validated in subsequent series prior to the modern RCT era.

The Core Insight Surgery drains the hematoma but leaves the bleeding source intact. MMA embolization eliminates the bleeding source—addressing the root pathophysiology rather than its consequence.

Procedure Characteristics

Minimally Invasive

Femoral or radial arterial access—no craniotomy required

Local Anesthesia

Typically performed under conscious sedation—ideal for frail elderly patients

Brief Procedure

30–90 minutes procedural time—same-day or next-day discharge feasible

The MMA Embolization Paradigm

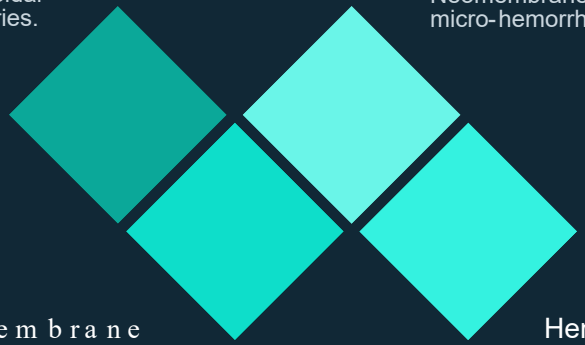
Mechanistic Basis and Preclinical Evidence Supporting Intervention

Embolization Occlusion

Embolic agents block pathological sinusoidal capillaries.

Ischemic Involution

Neomembrane ischemia halts micro-hemorrhage.



Neomembrane Perfusion

MMA branches supply the outer neomembrane.

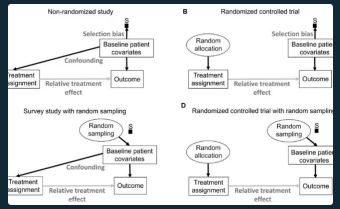
Hematoma Resorption

Fibrinolysis and macrophages clear the hematoma.

Histopathological studies of outer membranes retrieved at post-embolization surgery demonstrate **ischemic involution, reduced microvessel density, and decreased VEGF immunoreactivity** compared to non-embolized controls—confirming the mechanistic basis at the tissue level (*Link et al., J Neurointerv Surg, 2019*). Angiographic studies confirm complete or near-complete devascularization of the outer membrane blush in >90% of cases when distal MMA branches are targeted.

Key Clinical Evidence

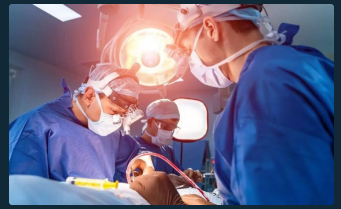
STEM Trial, EMBOLIZE Trial, and SELECT-2 Subgroup Analysis



STEM Trial (2021)

Stroke & J Neurointerv Surg, Catapano et al.

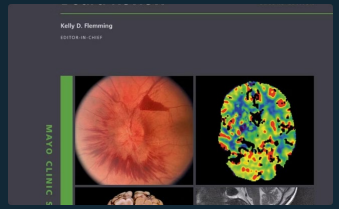
Prospective multicenter series MMA embolization as adjunct to surgery reduced recurrence from **27% to 3.6%** compared to surgery alone (p<0.001). 144 patients. First major prospective data establishing clinical benefit of adjunct embolization.



EMBOLIZE Trial (2023)

NEJM, Ban et al.

Phase II RCT. 400 patients randomized to MMA embolization ± standard care vs. standard care alone. Primary endpoint: hematoma failure (recurrence, progression, or lack of resolution at 90 days). **Embolization group: 10.6% vs. 26.4%** (RR 0.40; 95% CI 0.25–0.64; p<0.001). Landmark Level I evidence.



SELECT -2 Subgroup (2023)

NEJM, Bhogal et al. / Subgroup Analysis

Secondary analysis of cSDH patients within the SELECT-2 LVO stroke trial. Demonstrated favorable safety profile of endovascular access in cSDH comorbid patients. Supports procedural feasibility and tolerability in a high-acuity population with concurrent cerebrovascular disease.

ORIGINAL ARTICLE

Middle Meningeal Artery Embolization for Nonacute Subdural Hematoma

J. Liu, W. Ni, Q. Zuo, H. Yang, Y. Peng, Z. Lin, Zhenbao Li, J. Wang, Y. Zhen, J. Luo, Y. Lin, J. Chen, X. Hua, H. Lu, M. Zhong, M. Liu, J. Zhang, Y. Wang, J. Wan, Yi Li, T. Li, G. Mao, W. Zhao, L. Gao, C. Li, E Chen, X. Cheng, P. Zhang, Z. Wang, L. Chen, Yongxin Zhang, B. Tian, F. Shen, Y. Lei, Y. Wu, Yanjiang Li, G. Duan, L. Xu, N. Lv, J. Yu, X. Xu, Z. Du, H. Zhang, J. Hu, Zifu Li, Q. Yuan, Y. Zhou, G. Wu, L. Zhang, C. Gao, D. Dai, X. Wu, Yongwei Zhang, H. Jiang, R. Zhao, J. Su, Y. Xu, J.M. Ospel, C.B.L.M. Majoie, M. Goyal, Q. Li, P. Yang, Y. Gu, and Y. Mao, for the MAGIC-MT Investigators*

ABSTRACT

BACKGROUND

The effect of embolization of the middle meningeal artery in patients with subacute or chronic subdural hematoma is uncertain.

METHODS

We performed a multicenter, open-label, randomized trial in China, involving patients with symptomatic nonacute subdural hematoma with mass effect. Patients were assigned to undergo burr-hole drainage or receive nonsurgical treatment at the surgeon's discretion, and patients in each group were then randomly assigned, in a 1:1 ratio, to undergo middle meningeal artery embolization with liquid embolic material or to receive usual care. Patients whose condition warranted craniotomy were excluded. The primary outcome was symptomatic recurrence or progression of subdural hematoma within 90 days after randomization. Secondary outcomes included clinical and imaging outcomes. The main safety outcome was any serious adverse event (including death).

RESULTS

The analysis included 722 patients, of whom 360 were assigned to the embolization group and 362 to the usual-care group. Burr-hole drainage was performed in 78.3% of the enrolled patients; among the patients who underwent burr-hole drainage, the procedure occurred after embolization in 99.6%. Symptomatic recurrence or progression of subdural hematoma within 90 days occurred in 24 patients (6.7%) in the embolization group and in 36 (9.9%) in the usual-care group (between-group difference, −3.3 percentage points; 95% confidence interval, −7.4 to 0.8; P=0.10). The incidence of serious adverse events was lower in the embolization group than in the usual-care group (6.7% vs. 11.6%, P=0.02).

CONCLUSIONS

Among patients with symptomatic nonacute subdural hematoma (of whom 78% underwent burr-hole drainage), middle meningeal artery embolization resulted in a 90-day incidence of symptomatic recurrence or progression similar to that with usual care but was associated with a lower incidence of serious adverse events. (Funded by Shanghai Shenkang Hospital Development Center and others; MAGIC-MT ClinicalTrials.gov number, NCT04700345.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Y. Mao can be contacted at maoying@fudan.edu.cn or at the Department of Neurosurgery and National Center for Neurological Disorders, Huashan Hospital, Shanghai Medical College, Fudan University, 12 Middle Wulumuqi Rd., Shanghai 200040, China.

*A complete list of the MAGIC-MT Investigators and collaborators is provided in the Supplementary Appendix.

Drs. J. Liu, Ni, Zuo, H. Yang, and Peng and Drs. Q. Li, P. Yang, Gu, and Y. Mao contributed equally to this article.

N Engl J Med 2024;391:1901-12.
DOI: 10.1056/NEJMoa2401201

Key Clinical Evidence

MAGIC-MT Trial (Nov 2024)

Primary Endpoint:

MMA embolization (using Onyx) combined with standard care (surgery or conservative) resulted in significantly lower rates of symptomatic subdural hematoma recurrence or progression within 90 days compared to standard care alone (7.2% vs 12.2%, P=0.02).

Safety:

The incidence of serious adverse events (SAEs) was significantly lower in the embolization group (6.7%) than in the usual-care group (11.6%).
Mortality: The 90-day mortality was numerically lower in the embolization group (0.6%) compared to the standard care group (2.2%).

Subgroup Benefit:

The benefits were most pronounced in patients who did not undergo initial burr-hole drainage, those with a mid-line shift (MLS) of < 10mm, and smaller hematoma volumes.

Study Design:

This was a multi-center, prospective, randomized (1:1) controlled trial conducted in China, involving 360 patients in the embolization group and 362 in the usual-care group.

Embolization Technique

Access, Agent Selection (PVA, Onyx, n-BCA), and Procedural Pearls

Procedural Workflow

01

Arterial Access

Femoral (transfemoral) or radial (transradial) approach—radial increasingly preferred for elderly ambulatory patients

02

Diagnostic Angiography

4-vessel angiography to map MMA anatomy, identify dangerous anastomoses (orbital, lacrimal, petrosal), and confirm neomembrane blush

03

Microcatheter Navigation

Coaxial system: 6F guide → microcatheter into MMA via foramen spinosum. Target anterior and posterior MMA divisions.

04

Embolization

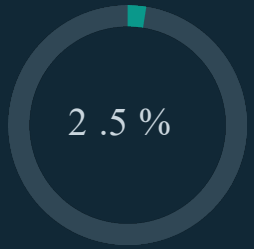
Deploy embolic agent to obliterate MMA and outer membrane vascularity—confirm devascularization on completion angiography

Embolic Agent Comparison

Agent	Type	Advantages	Limitations
PVA Particles (150–250 μm)	Particulate	Low cost, widely available, predictable distal penetration	Recanalization risk, less precise control
Onyx (EVOH)	Liquid cohesive	Excellent penetration, controlled injection, durable occlusion	Higher cost, DMSO toxicity, longer injection time
n-BCA (Glue)	Liquid adhesive	Rapid polymerization, permanent occlusion, widely available	Technique-demanding, catheter gluing risk
Coils ± Liquid	Mechanical + Liquid	Proximal control before liquid agent deployment	Incomplete distal occlusion if used alone

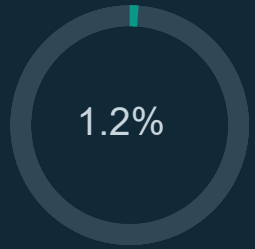
Safety Profile of MMA Embolization

Complication Rates, Cranial Nerve Risk, and Stroke — Literature Review



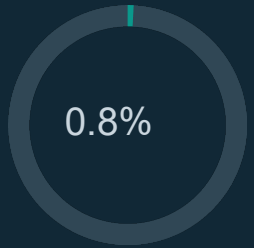
Overall Complication Rate

Pooled major complication rate across published series. EMBOLIZE trial reported comparable safety to standard care. *(Ban et al., NEJM 2023)*



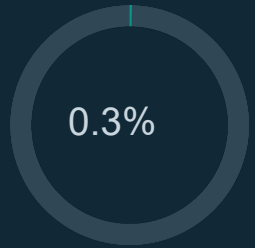
Thromboembolic Stroke

Ischemic stroke rate in published MMA embolization series — comparable to other neurointerventional procedures. *(Catapano et al., 2021)*



Cranial Nerve Palsy

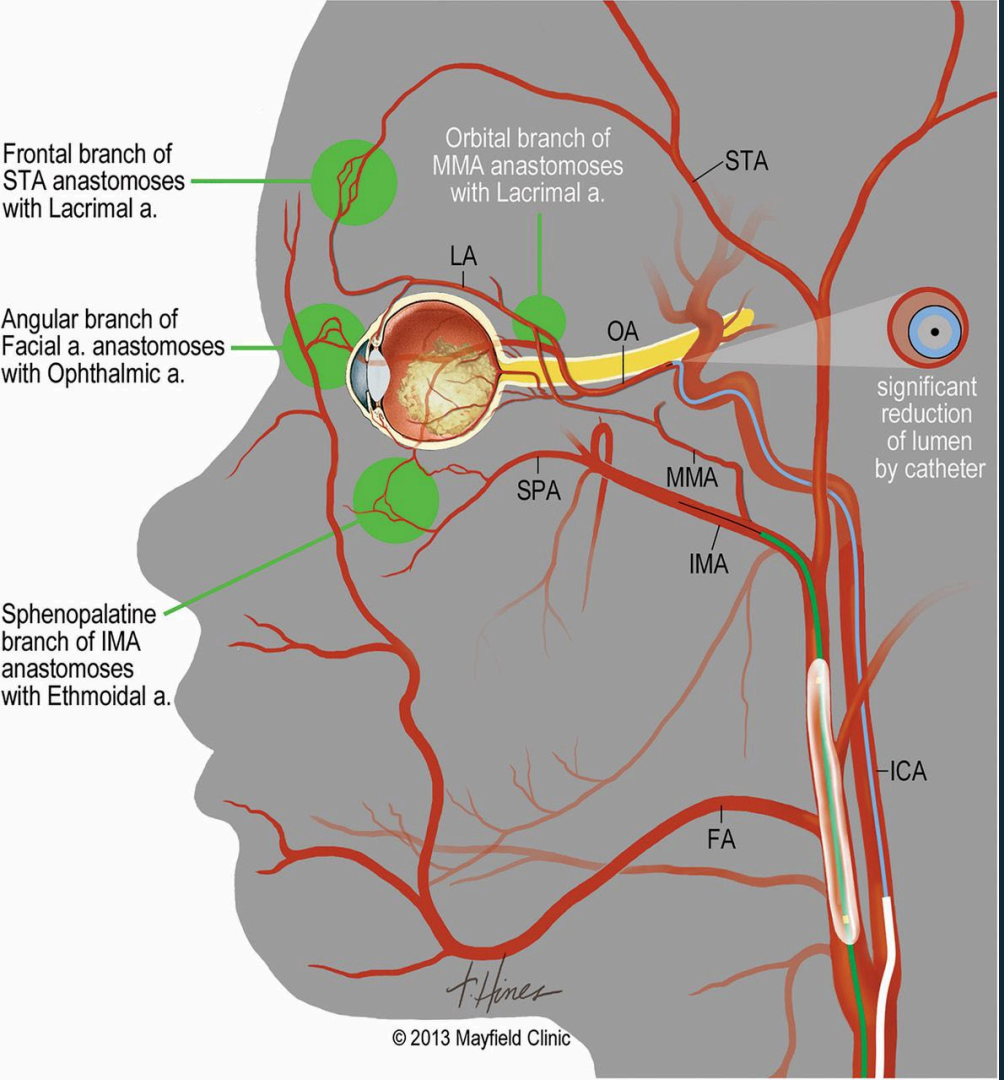
Risk of CN VII (facial) or CN V (trigeminal) injury via inadvertent petrous branch embolization. Typically transient and resolving. *(Link et al., 2019)*

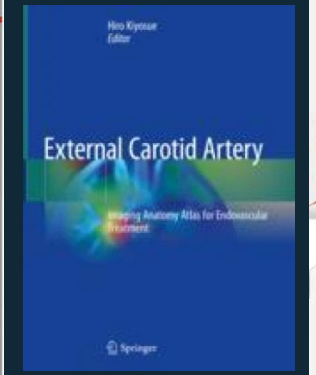


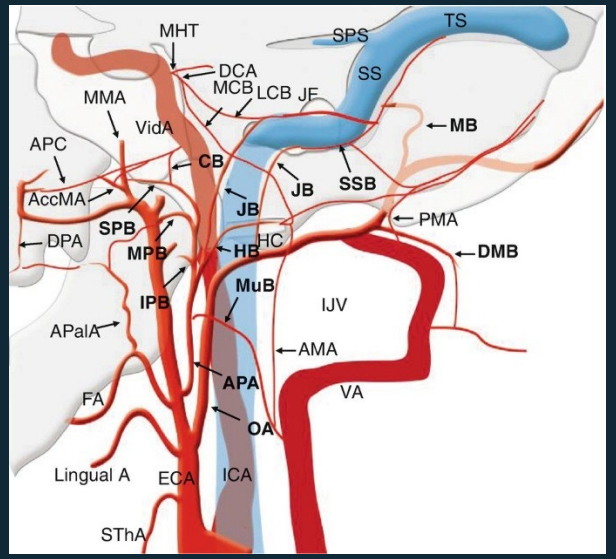
Visual Complication

Visual field defect or visual loss from dangerous ophthalmic anastomosis. Rare with careful pre-procedural angiographic mapping

The overall **safety profile of MMA embolization compares favorably** with burr hole surgery in equivalent patient populations. Meta-analysis by Ironside et al. *(J Neurosurg, 2021)* pooled 258 patients across 6 studies and reported a 98.1% technical success rate with major complication rates consistently below 3%. The procedure does not preclude subsequent surgery if needed.


Frontal branch of STA anastomoses with Lacrimal a.
Orbital branch of MMA anastomoses with Lacrimal a.
STA
LA
Angular branch of Facial a. anastomoses with Ophthalmic a.
OA
significant reduction of lumen by catheter
SPA
MMA
IMA
Sphenopalatine branch of IMA anastomoses with Ethmoidal a.
ICA
FA
© 2013 Mayfield Clinic


External Carotid Artery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LCB
JF
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VidA
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APC
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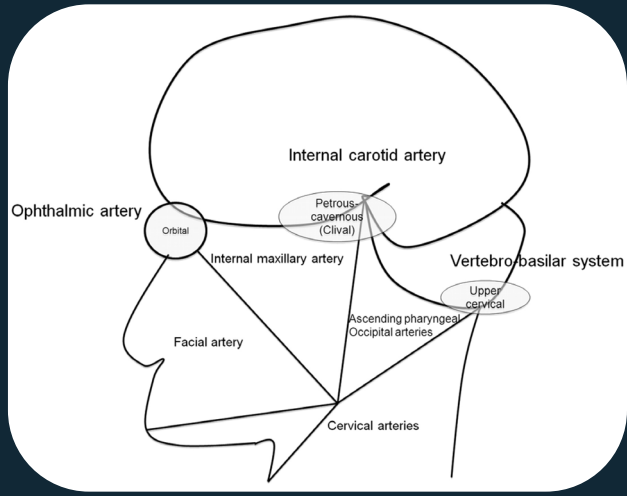
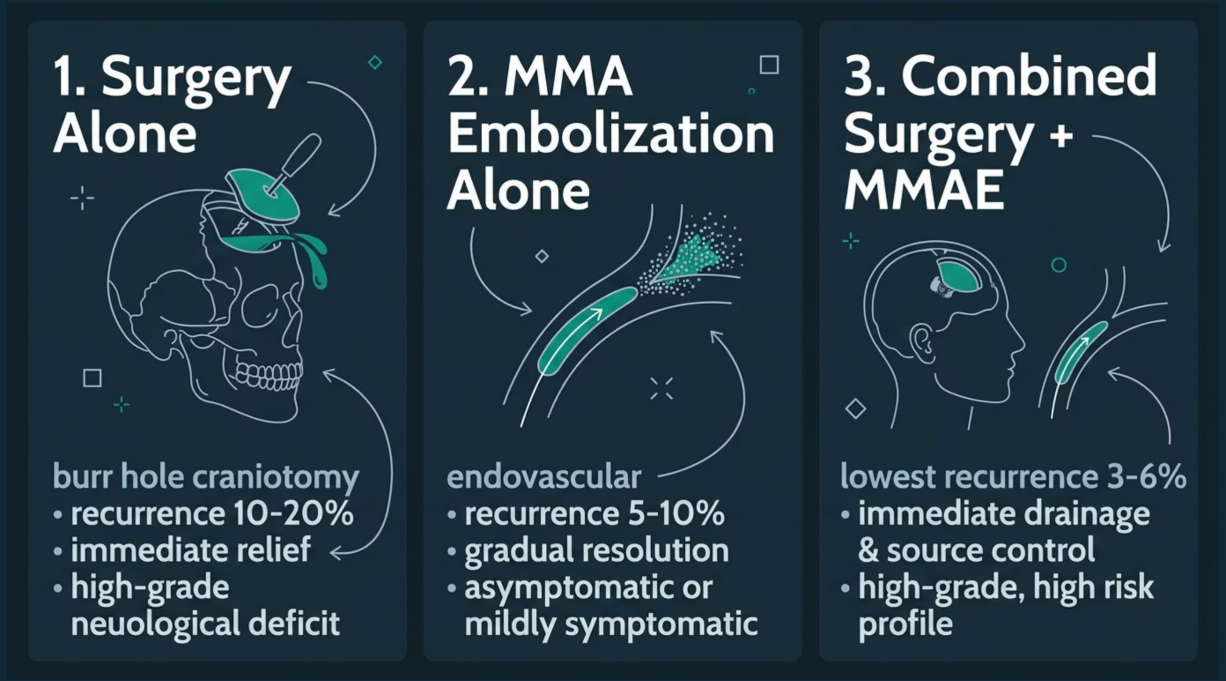
PMA
SPB
DPA
HC
MPB
HB
DMB
MuB
IPB
IJV
APalA
AMA
APA
VA
FA
OA
Lingual A
ECA
ICA
SThA


Internal carotid artery
Ophthalmic artery
Orbital
Petrous cavernous (Clival)
Internal maxillary artery
Vertebro-basilar system
Upper cervical
Ascending pharyngeal
Occipital arteries
Facial artery
Cervical arteries

MMA Embolization: Standalone vs. Adjunct Therapy

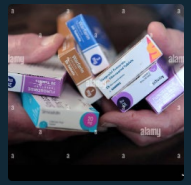
Comparative Outcomes and Patient Selection Criteria



Patient selection remains the most critical determinant of strategy. **Markwalder Grade 0-1 patients** may be managed with standalone MMA embolization with expectant radiographic follow-up. **Grade 2-3 patients** with significant mass effect typically require surgical evacuation, with MMA embolization as an adjunct to prevent recurrence. **Grade 4 patients** require emergent surgical decompression regardless of embolization status

Special Populations

Anticoagulated Patients, Elderly, Bilateral cSDH — Tailoring the Endovascular Approach

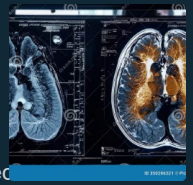


Anticoagulated Patients

Patients on **warfarin**, **DOACs**, or **antiplatelet** therapy represent the highest risk cSDH subgroup—surgical **recurrence** approaches **33%**. MMA embolization can be performed on **reduced anticoagulation** (hold DOAC for 24h) with minimal procedural thromboembolic risk. Post-procedure anticoagulation restart timing should be individualized based on thromboembolic indication urgency. EMBOLIZE trial included anticoagulated patients with comparable safety outcomes *(Ban et al., NEJM 2023)*

Frail Elderly Patients (Age >80)

General anesthesia carries significant **morbidity** in octogenarians: aspiration pneumonia, delirium, DVT, and prolonged hospital stay. MMA **embolization** under **local anesthesia and mild sedation** dramatically reduces this risk profile. **Transradial** access enables **same-day ambulation**. Evidence from retrospective series shows that even **Markwalder Grade 2–3 patients over 80** show favorable neurological outcomes with embolization ± conservative management *(Ironside et al., J Neurosurg 2021)*



Bilateral cSDH

Bilateral cSDH occurs in **30%** of cases and carries higher recurrence risk and morbidity from bilateral craniotomy. MMA embolization is particularly advantageous here: **both MMAs can be embolized in a single angiographic session**, eliminating the need for bilateral craniotomies. Outcomes in bilateral cases have been consistently favorable in reported series, with radiographic resolution achieved in >85% of cases at 90-day follow-up.

Emerging Evidence and Future Directions

Dexamethasone, TXA, Combined Endovascular-Medical Protocols

Dexamethasone in cSDH

The **DRESH trial** *(Hutchinson et al., NEJM 2020)* randomized 748 patients to dexamethasone vs. placebo without surgery. While dexamethasone reduced hematoma volume on imaging, it did not improve functional outcome at 6 months (mRS 0–2: 56% vs. 64% placebo, p=0.03 favoring placebo for favorable outcome). **Current recommendation: dexamethasone should NOT be routinely used as primary cSDH therapy**—its anti-inflammatory effects do not translate to meaningful clinical benefit and may increase infection and hyperglycemia risk.

Tranexamic Acid (TXA)

Given the hyperfibrinolytic microenvironment of cSDH, TXA has biological rationale. The **TRACS trial** *(Edlmann et al., Trials 2022)* is an ongoing phase II RCT evaluating oral TXA 1g TID for 4 weeks as adjunct therapy. Preliminary data suggests a signal toward reduced recurrence in anticoagulation-naïve patients. Results are awaited.

MAGIC -MT Trial (Nov 2024)

Phase III RCT comparing MMA embolization + standard care vs. standard care alone. Primary endpoint: treatment failure at 180 days. Results provide some of the highest-level evidence to date

Future Directions

→ **Biomarker -Guided Selection**

Serum and hematoma fluid VEGF, IL-6, and fibrinolytic markers as predictors of recurrence and endovascular response—personalized medicine approach under investigation

→ **Combined Endovascular -Medical Protocols**

MMA embolization + TXA combinations—early institutional series suggest additive benefit in recurrence reduction. Prospective validation needed

→ **Novel Embolic Agents**

Resorbable microspheres and anti-VEGF eluting particles under preclinical investigation—targeting the inflammatory biology directly at the neomembrane level

Key Takeaways and Clinical Practice Recommendations

Pathophysiology

cSDH is driven by recurrent micro-hemorrhage from a pathological, VEGF-driven neomembrane—not osmotic gradient. The outer membrane receives blood supply from the MMA.

Diagnosis

Use Markwalder grading to guide management intensity. MRI is superior to CT for isodense subacute collections. High-risk features: bilateral, large volume, anticoagulation, brain atrophy.

Evidence Base

EMBOLIZE (NEJM 2023): MMA embolization reduces hematoma failure from 26.4% to 10.6% (RR 0.40). Level I evidence supports adoption into clinical practice for appropriate candidates.

Patient Selection

MMA embolization standalone: Markwalder 0-1, high surgical risk, anticoagulated. Adjunct: Grade 2-3 with high recurrence risk. Emergency surgery: Grade 4. Bilateral: embolize both MMAs in one session.

Selected References

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2. Catapano JS et al. *Stroke*. 2021;52:2456–2462. (STEM Trial)
3. Hutchinson PJ et al. *N Engl J Med*. 2020;383:2616–2627. (DRESH Trial)
4. Ironside N et al. *J Neurosurg*. 2021;135:1685–1694.
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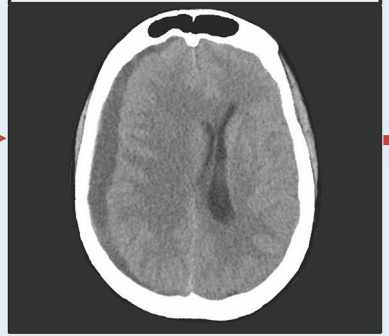
6. Frati A et al. *Neurosurgery*. 2004;54:1198–1207.
7. Stanisic M et al. *Acta Neurochir*. 2012;154:563–573.
8. Haines DE et al. *Neurosurgery*. 1993;32:111–120.
9. Ito H et al. *J Neurosurg*. 1976;44:693–697.
10. Mandai S et al. *J Neurosurg*. 2000;93:686 –688.

Thank You!!!

Incidence and Mortality of Chronic Subdural Hematomas: A Population-Based Study

There are ~1.3 millions individuals living in the 5-county region around Cincinnati, which is representative of the US in terms of age, race, and socioeconomic status.

353 of these individuals developed a chronic subdural hematoma in 2019 and 2020



Overall Incidence rate: 16.3 cases/100,000 persons/year

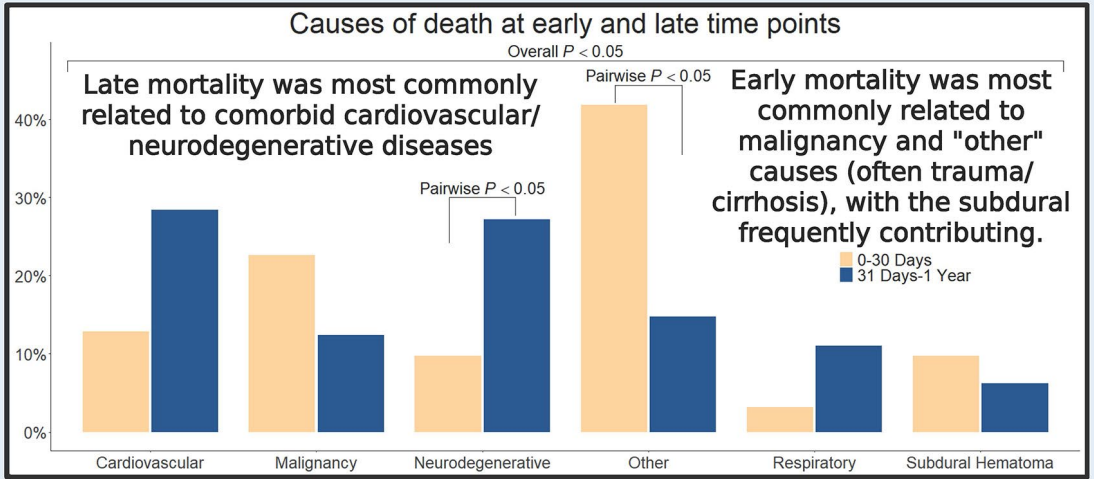
43,121 annual cases in the USA

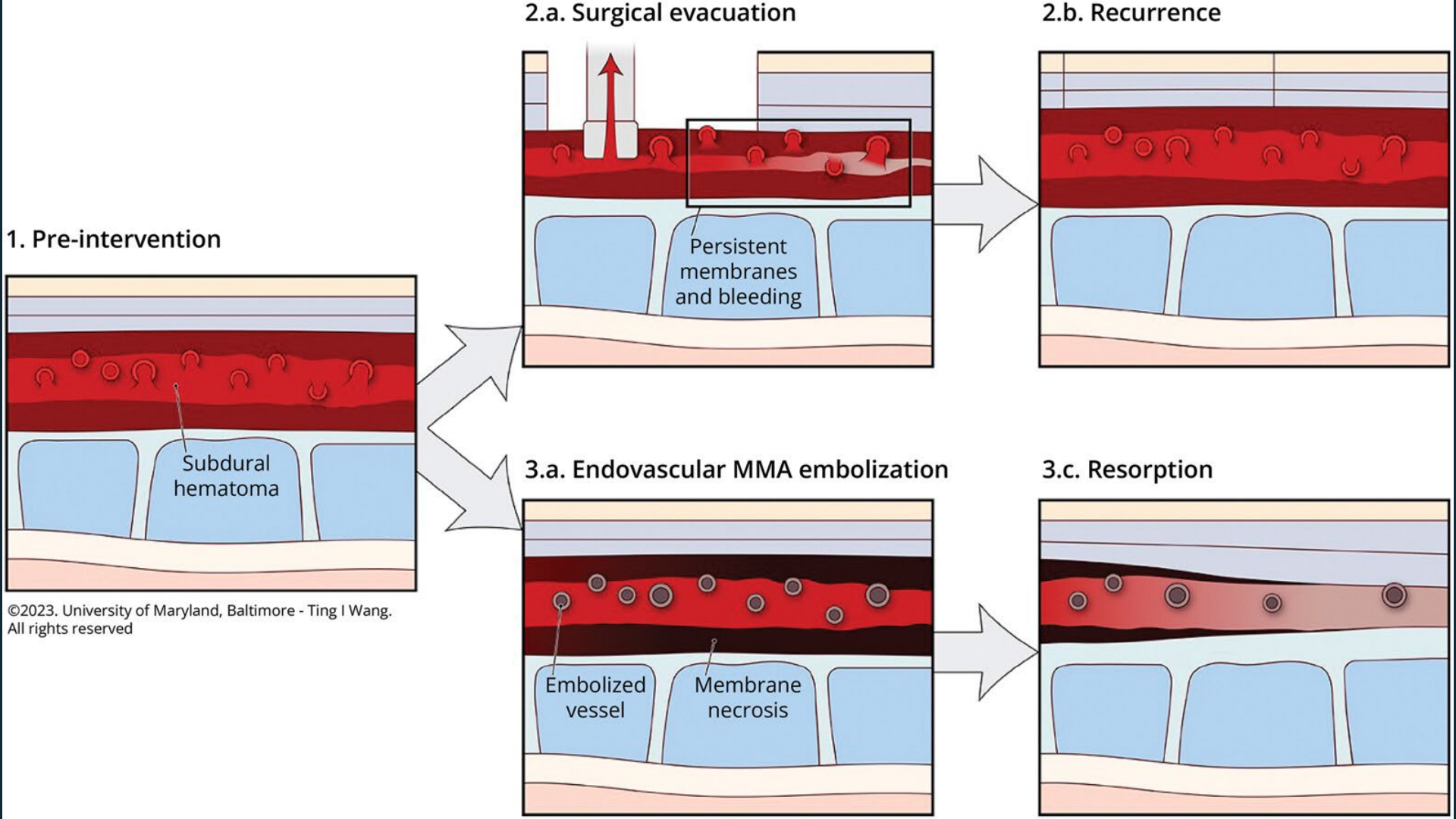
~2/3rd of patients have premorbid disability

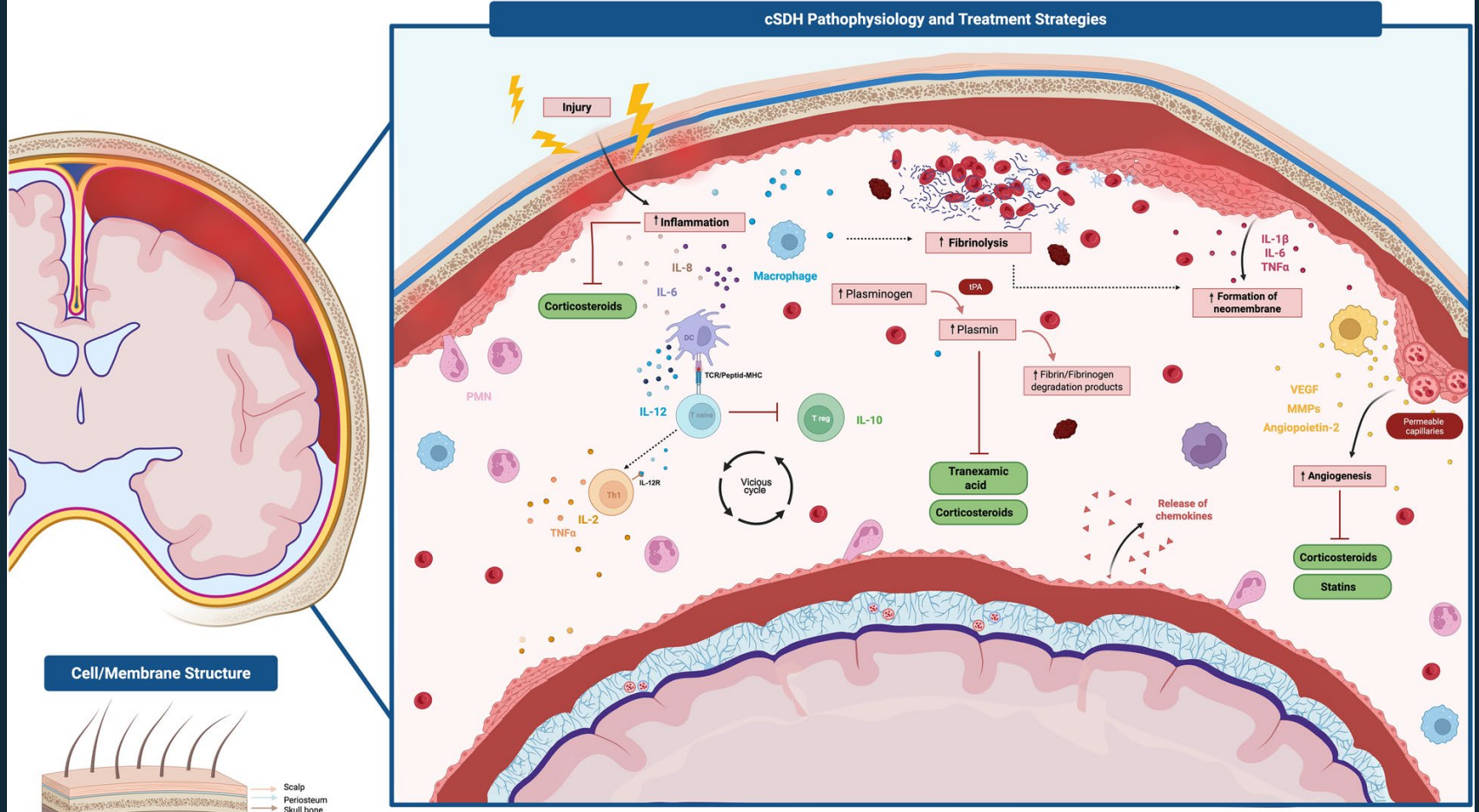
30-Day Mortality: 9.4%

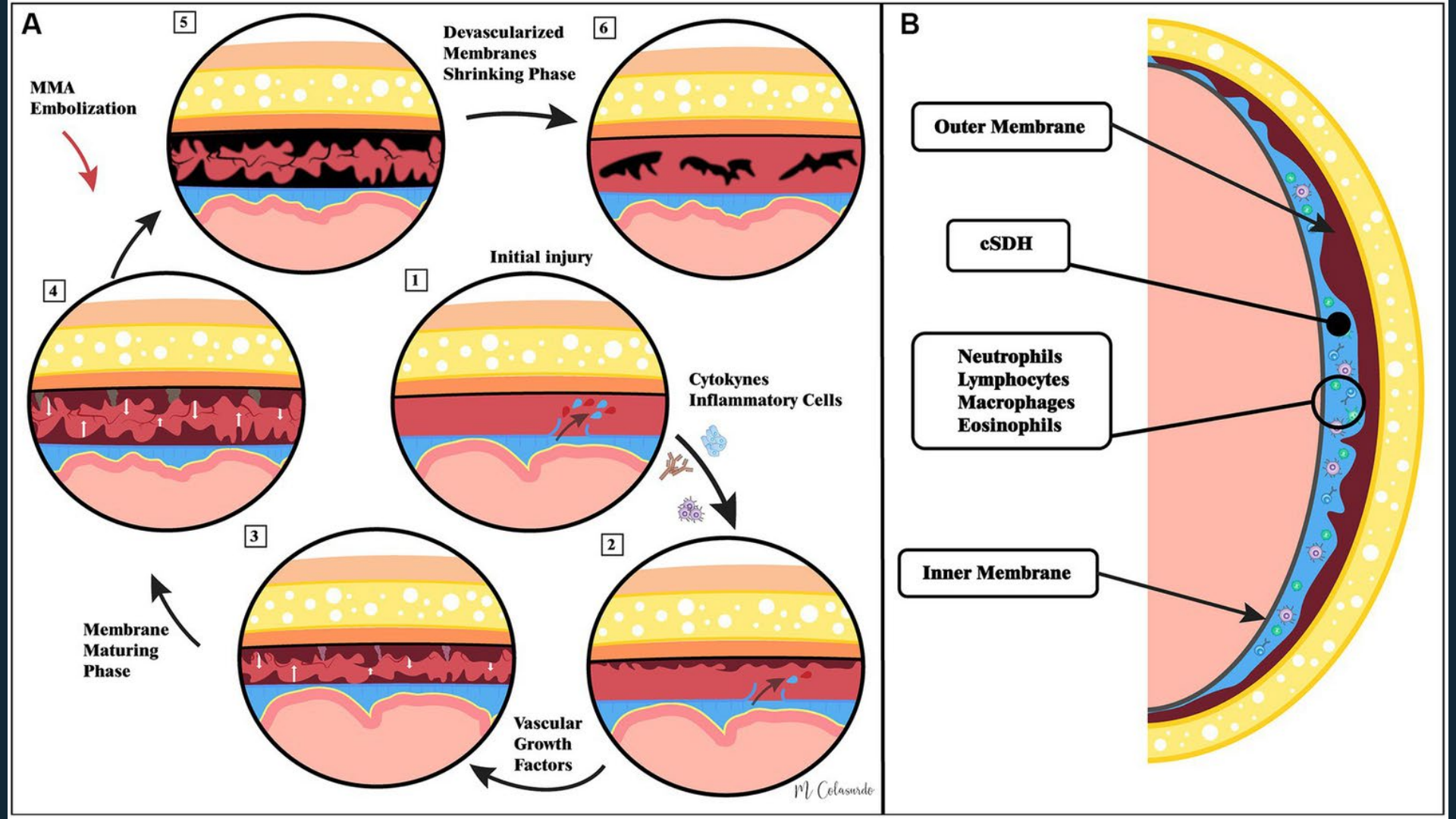
1-year Mortality: 32.9%

Causes of death at early and late time points






cSDH Pathophysiology and Treatment Strategies
Injury
↑ Inflammation
IL-8
IL-6
Macrophage
Corticosteroids
↑ Fibrinolysis
↑ Plasminogen
tPA
↑ Plasmin
↑ Fibrin/Fibrinogen degradation products
IL-1β
IL-6
TNFα
↑ Formation of neomembrane
DC
TCR/Peptid-MHC
PMN
IL-12
T naive
T reg
IL-10
Vicious cycle
Th1
IL-12R
IL-2
TNFα
Tranexamic acid
Corticosteroids
Release of chemokines
VEGF
MMPs
Angiopoietin-2
Permeable capillaries
↑ Angiogenesis
Corticosteroids
Statins
Cell/Membrane Structure
Scalp
Periosteum
Skull bone
Dura mater
Subdural space
Subarachnoid space
Pia mater
Brain tissue


A
5
Devascularized
Membranes
Shrinking Phase
6
MMA
Embolization
Initial injury
4
1
Cytokynes
Inflammatory Cells
3
2
Membrane
Maturing
Phase
Vascular
Growth
Factors
M Colasurdo
B
Outer Membrane
cSDH
Neutrophils
Lymphocytes
Macrophages
Eosinophils
Inner Membrane

Optimized Treatment Approaches for Chronic Subdural Hematoma

Chronic subdural hematoma (CSDH), or blood clotting between the brain surface and its outer covering, mostly affects older adults with underlying health conditions

However, limited data on CSDH multimodal treatment hampers informed decision-making in clinical settings

What factors influence treatment outcomes in patients with CSDH in the Chinese population?

Multicenter registry study of the CSDH (MRCSDH)

Patients from 59 hospitals in mainland China

Data collection (March 2022 – February 2024)

Treatment groups

- Observation
- Conservative management
- Surgical intervention
- Embolization
- Multimodal treatment

Measures analyzed:

- Hematoma resolution
- Recurrence rates
- Neurological status
- Complications

From March 2022 to August 2023

2,173 patients with CSDH enrolled

Male: **81.1%**

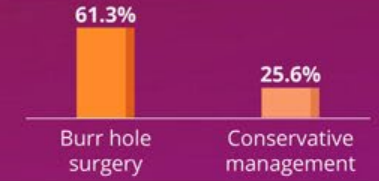
Patients with a history of trauma

Average age: **70.12 ± 14.53 years**

Prominent clinical symptom

Headache

Widely used treatment modalities



Clinical outcomes

Treatment

After 3 months

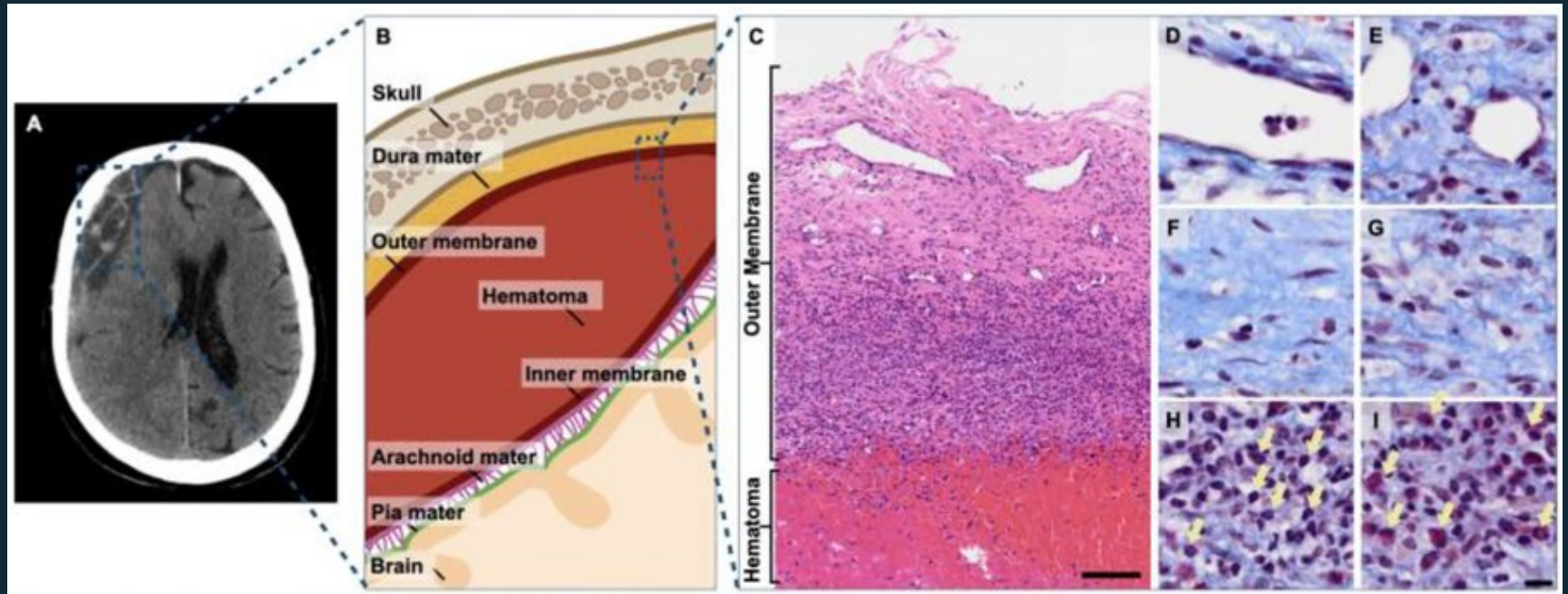
Follow-up

Patients who presented a positive clinical prognosis

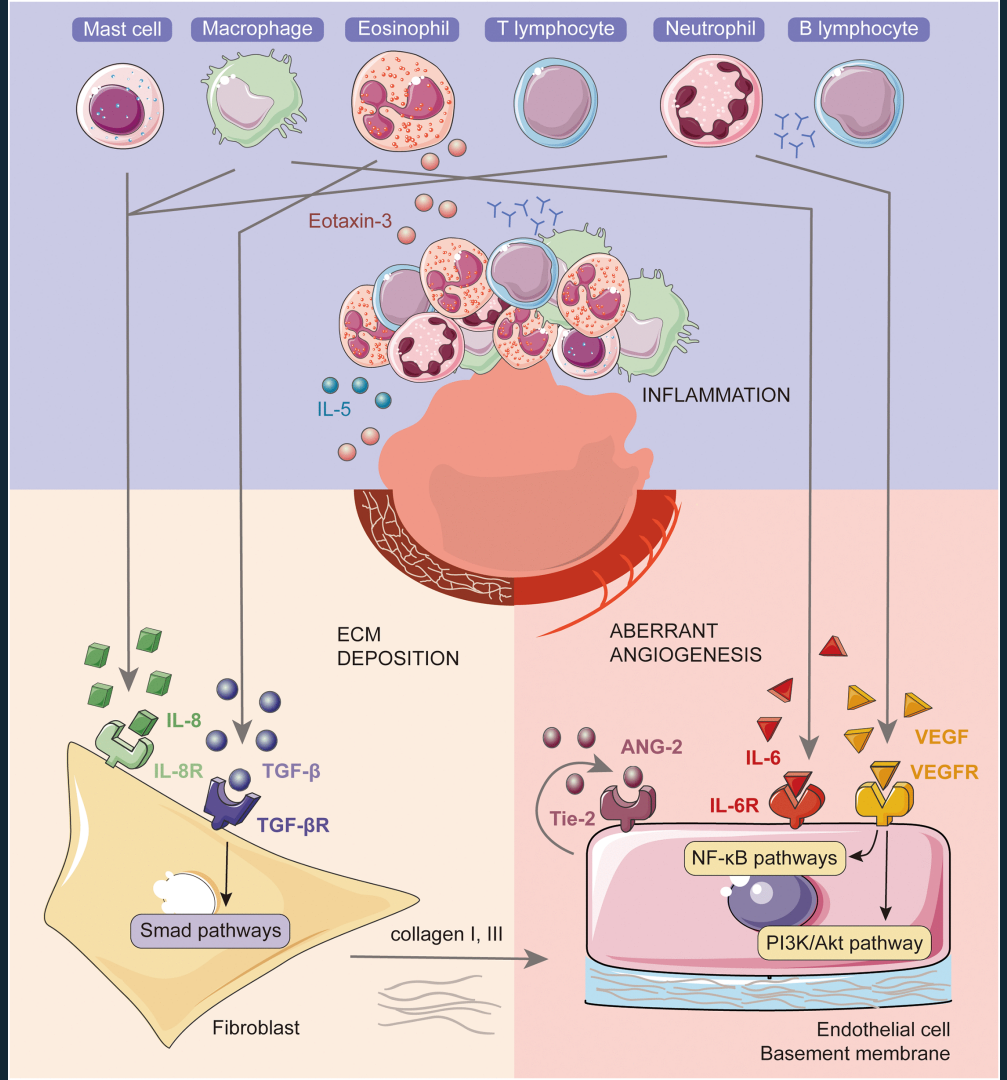
Recurrence rate

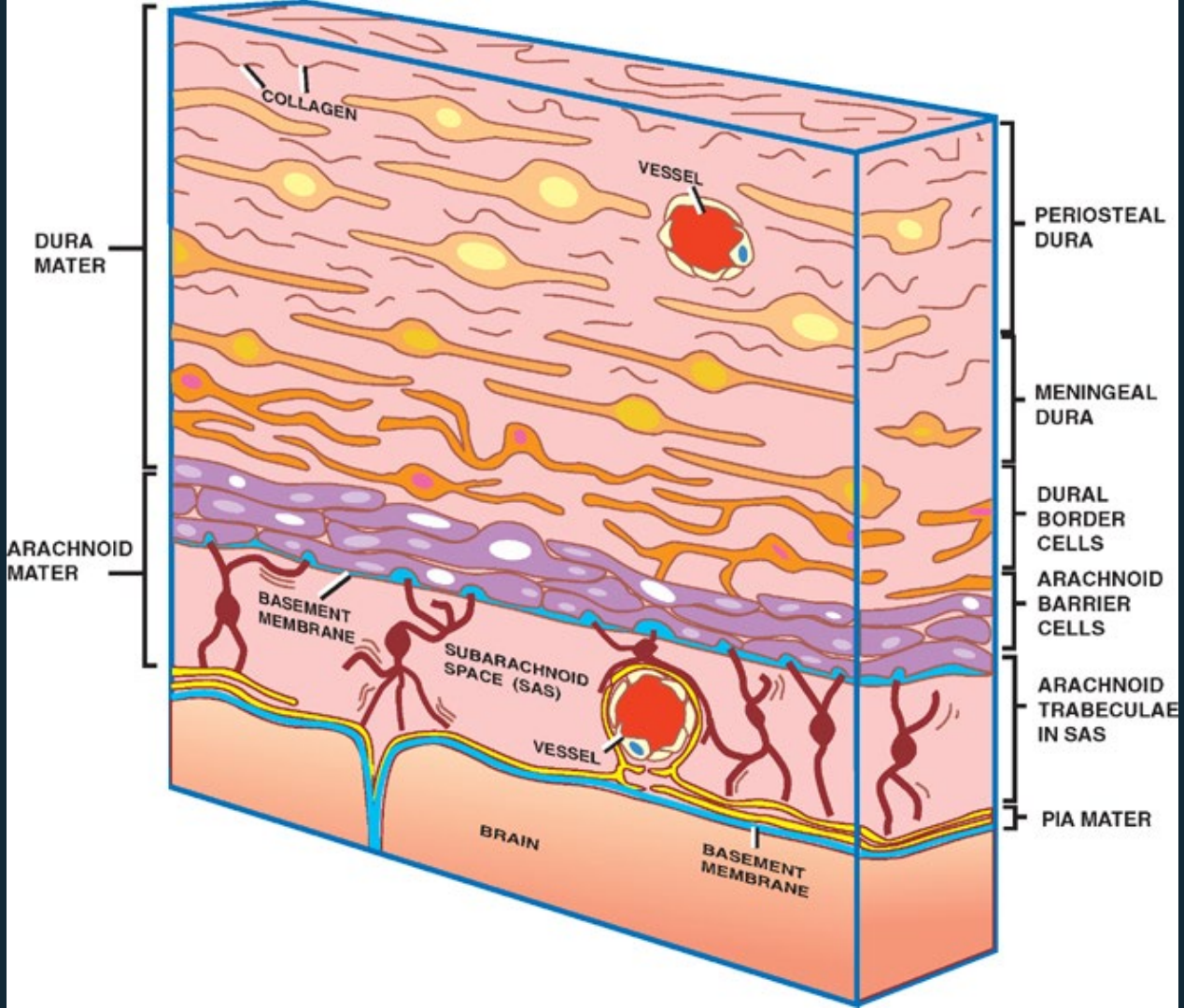
This MRCSDH study provides insights into factors like age, comorbidities, medication history, and treatments, which are vital for improving care and guidelines for patients with CSDH

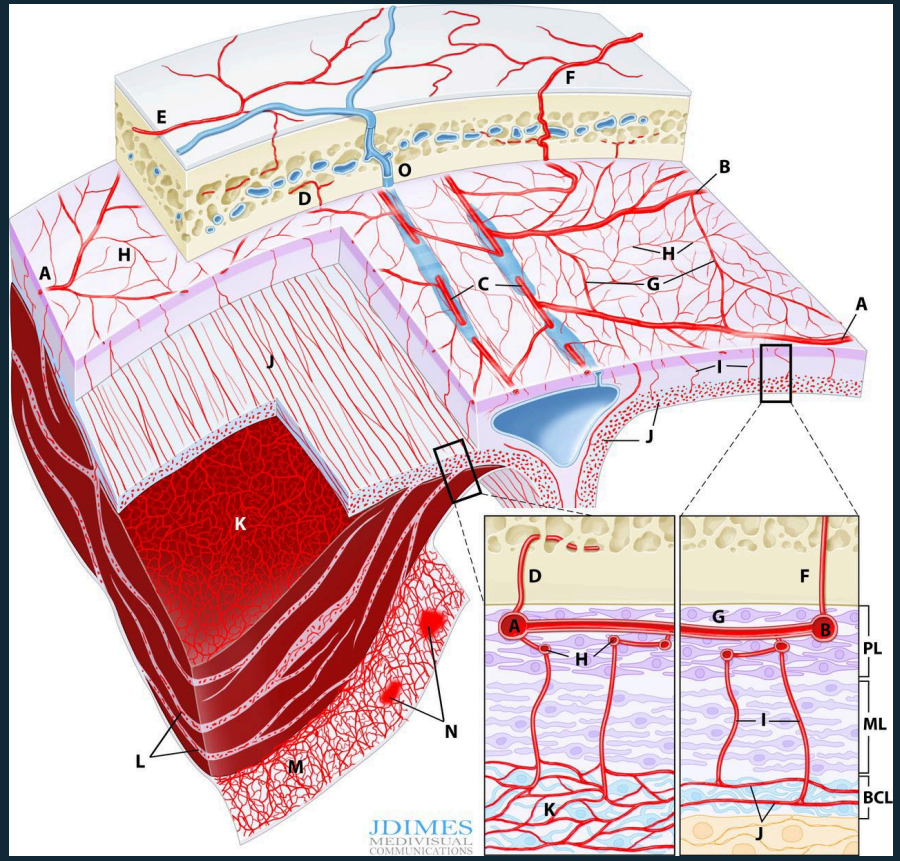
Multimodality Management for Chronic Subdural Hematoma in China: Protocol and Characteristics of an Ambidirectional, Nationwide, Multicenter Registry Study
Liu *et al.* (2024) | *Chinese Neurosurgical Journal* | DOI: 10.1186/s41016-024-00356-5



Chronic subdural hematoma (cSDH) A) A CT scan captures cSDH hematoma fluid density and membrane architecture. B) A diagram of cSDH anatomy highlights the hematoma encased by an outer and inner membrane. C) Hematoxylin & eosin staining of an outer membrane depicts a spatial organization of membrane architecture from dura-facing to hematoma-facing surfaces (scale bar 100μm). D-I) Masson's trichrome staining (scale bar 10μm) highlights specific cell types and structures across the OM: vasculature on dura-facing regions (D,E), woven collagen fibers and fibroblasts (F,G), and a high density of lymphocytes and neutrophils (H), and eosinophils (I) located near hematoma-facing regions (yellow arrows).


Mast cell
Macrophage
Eosinophil
T lymphocyte
Neutrophil
B lymphocyte
Eotaxin-3
IL-5
INFLAMMATION
ECM
DEPOSITION
ABERRANT
ANGIOGENESIS
IL-8
IL-8R
TGF-β
TGF-βR
Smad pathways
collagen I, III
Fibroblast
ANG-2
Tie-2
IL-6
IL-6R
VEGF
VEGFR
NF-κB pathways
PI3K/Akt pathway
Endothelial cell
Basement membrane


COLLAGEN
VESSEL
DURA MATER
PERIOSTEAL DURA
MENINGEAL DURA
DURAL BORDER CELLS
ARACHNOID MATER
ARACHNOID BARRIER CELLS
BASEMENT MEMBRANE
SUBARACHNOID SPACE (SAS)
ARACHNOID TRABECULAE IN SAS
VESSEL
PIA MATER
BRAIN
BASEMENT MEMBRANE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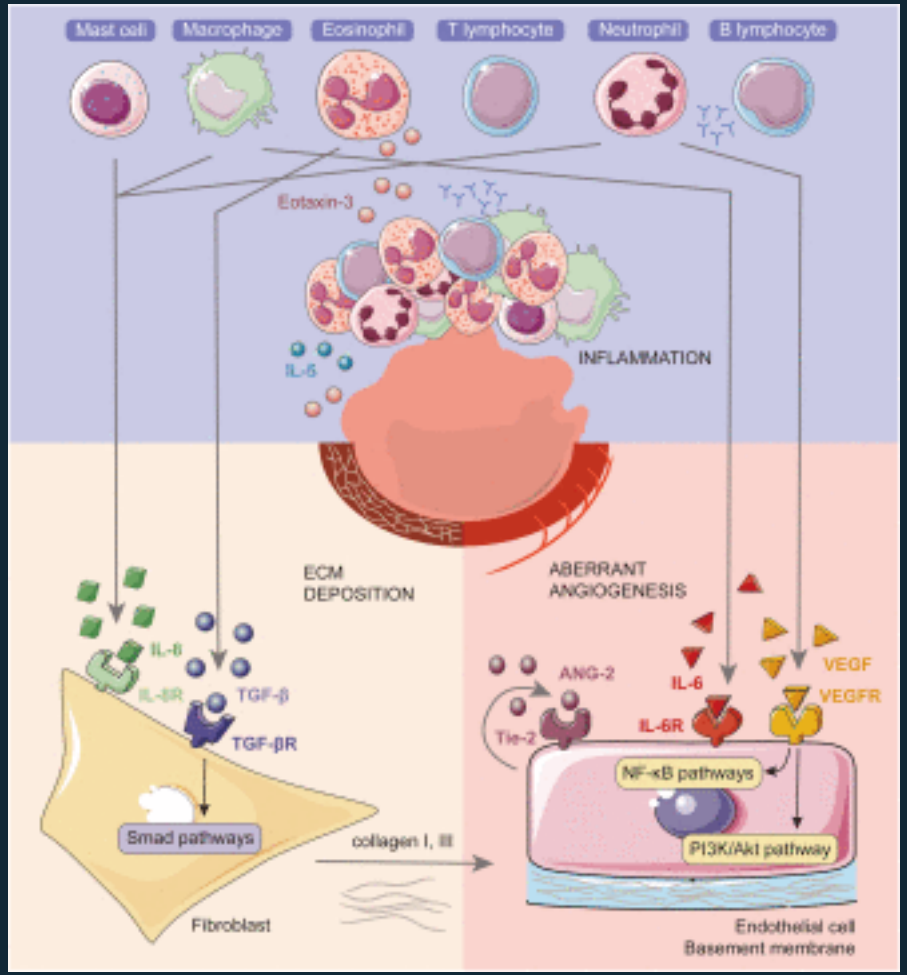
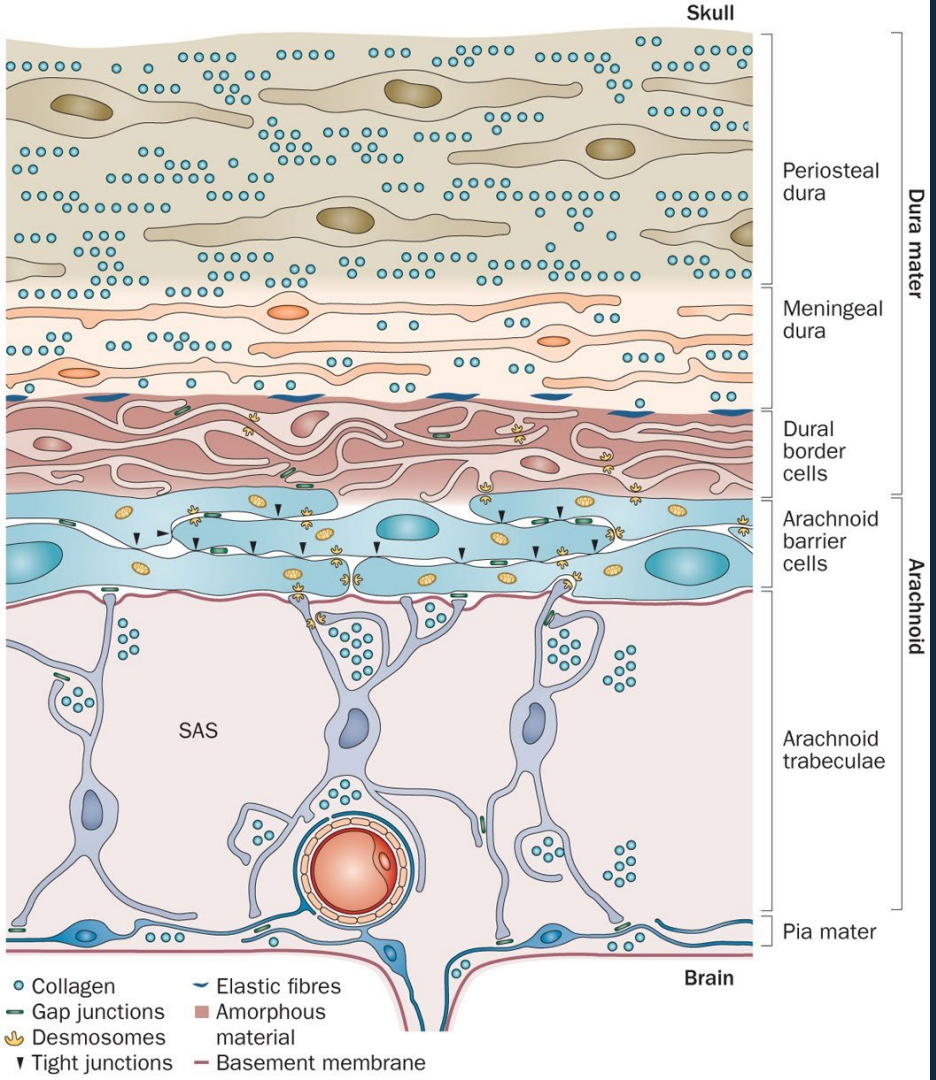

Mast cell
Macrophage
Eosinophil
T lymphocyte
Neutrophil
B lymphocyte
Eotaxin-3
IL-5
INFLAMMATION
ECM
DEPOSITION
ABERRANT
ANGIOGENESIS
IL-6
IL-6R
TGF-β
TGF-βR
Smad pathways
collagen I, III
Fibroblast
ANG-2
Tie-2
IL-6
IL-6R
VEGF
VEGFR
NF-κB pathways
PI3K/Akt pathway
Endothelial cell
Basement membrane


Skull
Periosteal dura
Meningeal dura
Dural border cells
Dura mater
Arachnoid barrier cells
Arachnoid
SAS
Arachnoid trabeculae
Pia mater
Brain
Collagen
Gap junctions
Desmosomes
Tight junctions
Elastic fibres
Amorphous material
Basement membrane

EMBOLISE: Embolization of the MMA with Onyx™ Liquid Embolic System in the Treatment of Subacute and Chronic Subdural Hematoma

RESULTS: In participants with symptomatic subacute or chronic subdural hematoma (SDH), the addition of middle meningeal artery (MMA) embolization with Onyx™ resulted in nearly a 3-fold reduction in hematoma recurrence/progression requiring re-operation compared to surgery alone.

PURPOSE: To assess both the safety and effectiveness of utilizing the Onyx™ Liquid Embolic System (LES) for embolization of the MMA in the treatment of symptomatic subacute or chronic SDH as an adjunct to conventional treatment.

TRIAL DESIGN: A multicenter, prospective, randomized, interventional controlled, open-label, adaptive trial (n=400).

	Onyx Embo +Surgery (Treatment) N=197	Surgery Only (Control) N=203	Relative Risk (95%CI)	P value
Primary Endpoint				
SDH recurrence/progression requiring surgical drainage through 90 days (ITT population)	4.1 % (1.8%, 7.8%)	11.3% (7.3%, 16.5%)	0.36 (0.11, 0.80)	0.0081
Secondary Endpoints				
Incidence of deterioration in neurologic function	11.9% (21/177) (7.5%, 17.6%)	9.8% (18/184) (5.9%, 15.0%)	2.08% (-4.76%, 8.92%)	0.0022

Key Takeaways: The use of MMA embolization is a promising additional approach to the surgical management of subacute or chronic SDH.