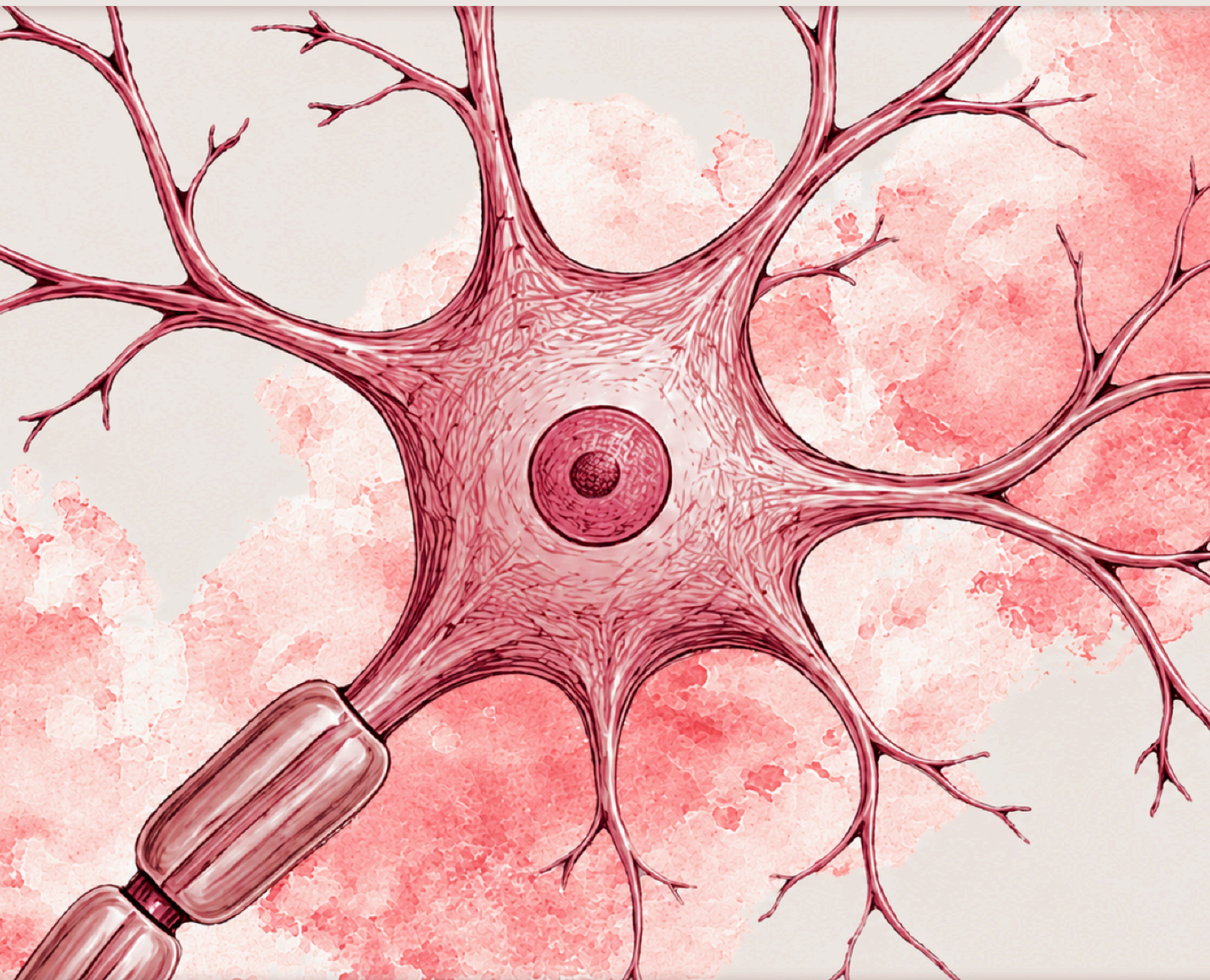


The 8th CUNEUS x Acta Neurologica Indonesia

SUPPLEMENTARY ABSTRACTS



***"Advances in Neurology and Neurosurgery:
Bridging Evidence and Clinical Practice"***

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REVIEW ARTICLE

**STRONGER PLATELET INHIBITION, UNCERTAIN CLINICAL GAIN:
PRASUGREL VERSUS CLOPIDOGREL AFTER ISCHEMIC STROKE—A
SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Clopidogrel responsiveness may be attenuated by CYP2C19 loss-of-function variants, particularly prevalent in East Asian populations. Prasugrel provides faster and more consistent P2Y₁₂ inhibition; however, whether this pharmacodynamic superiority translates into better post-stroke outcomes without excess bleeding remains uncertain. We compared the pharmacodynamic efficacy, clinical effectiveness, and safety of prasugrel versus clopidogrel after non-cardioembolic ischemic stroke or high-risk transient ischemic attack.

Methods: PubMed, Cochrane Library, Epistemonikos, ScienceDirect, Wiley Online Library, Google Scholar, Europe PMC, Semantic Scholar, and Scopus were systematically searched in accordance with PRISMA 2020. Five reports representing four independent randomized cohorts and up to 4,596 participants were included. Random-effects models generated mean differences (MDs) for P2Y₁₂ reaction units (PRU), odds ratios (ORs) for high platelet reactivity, and risk ratios (RRs) for clinical outcomes. Hartung–Knapp inference was applied to sparse clinical outcomes. Heterogeneity was quantified using I^2 , and risk of bias was assessed using Cochrane RoB 2. (PROSPERO ID: CRD420261468102).

Results: Prasugrel significantly reduced PRU (MD -41.54 ; 95% CI -50.21 to -32.88 ; $I^2=35.8\%$) and high platelet reactivity (OR 0.28 ; 95% CI 0.24 – 0.33 ; $I^2=0\%$). Yet this pharmacodynamic advantage did not translate into significant reductions in recurrent ischemic stroke (RR 1.01 ; 95% CI 0.42 – 2.43) or composite ischemic events (RR 1.00 ; 95% CI 0.40 – 2.51). There were no significant differences in life-threatening, major, or clinically relevant bleeding (RR 1.05 ; 95% CI 0.86 – 1.29) or bleeding leading to treatment discontinuation (RR 0.95 ; 95% CI 0.45 – 2.01). Clinical-outcome heterogeneity was low to moderate ($I^2=0\%$ – 47.4%). Risk of bias was low in three pivotal double-blind trials, with some concerns for open-label and post-hoc evidence.

Conclusion: Low-dose prasugrel achieves substantially stronger platelet inhibition than clopidogrel, but current randomized evidence does not demonstrate corresponding clinical benefit or harm. This pharmacodynamic–clinical disconnect highlights the need for adequately powered, multinational trials focused on patient-important outcomes.

Keywords: ischemic stroke; prasugrel; clopidogrel; platelet reactivity; secondary prevention

REVIEW ARTICLE

PROTEIN BIOMARKERS FOR MONITORING DISEASE PROGRESSION AND THERAPEUTIC RESPONSE IN DUCHENNE MUSCULAR DYSTROPHY: A SYSTEMATIC REVIEW

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Background: Duchenne muscular dystrophy (DMD) is a progressive X-linked neuromuscular disorder caused by mutations in the DMD gene, resulting in dystrophin deficiency and progressive muscle degeneration. Objective biomarkers are needed to complement conventional functional assessments for monitoring disease progression and therapeutic response. This systematic review evaluated current evidence on protein biomarkers in DMD.

Methods: A systematic literature search was conducted across PubMed, Google Scholar, ScienceDirect, Europe PMC, and EBSCO following PRISMA guidelines. Eligible studies included randomized and non-randomized clinical trials, cohort, case-control, and cross-sectional studies involving genetically confirmed DMD patients that evaluated circulating or tissue-based protein biomarkers. Data extracted included study characteristics, biomarker type, treatment exposure, disease stage, follow-up, functional outcomes, and principal findings. Risk of bias was assessed using RoB 2, ROBINS-I, and the Newcastle–Ottawa Scale according to study design.

Results: From 552 records identified, 13 studies met the inclusion criteria. Protein biomarkers were assessed using immunoassays, SomaScan aptamer technology, and mass spectrometry-based proteomics. Eteplirsen consistently increased dystrophin expression and exon-skipping efficiency while slowing functional decline. Proteomic studies identified biomarkers related to muscle integrity, extracellular matrix remodeling, inflammation, complement activation, and cardiac injury. Longitudinal protein profiles correlated with functional outcomes, including the North Star Ambulatory Assessment (NSAA), 6-minute walk test (6MWT), rise from supine velocity (RSV), and 10-meter run/walk velocity (10mRWV). Cardiac troponin I and skeletal muscle troponins also showed promise for monitoring cardiomyopathy and muscle injury.

Conclusion: Protein biomarkers demonstrate substantial potential for monitoring disease progression and therapeutic response in DMD. Longitudinal proteomic profiling supports the development of multimarker panels for objective disease monitoring. However, heterogeneity in study design, biomarker platforms, and outcome measures highlights the need for standardized methodologies and large prospective validation studies before routine clinical implementation.

Keywords: Duchenne muscular dystrophy; Protein biomarkers; Disease progression; Therapeutic response; Proteomics; Systematic review

RESEARCH ARTICLE

**NEUROPROTECTIVE EFFECT OF BLACK GARLIC EXTRACT ON
ALCOHOL-INDUCED OLFACTORY BULB NEURODEGENERATION IN A
BINGE DRINKING RAT MODEL: AN EXPERIMENTAL STUDY**

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Background: Binge drinking is commonly defined as consuming ≥ 60 g of ethanol on a single occasion at least once within the previous 30 days. Excessive alcohol consumption induces neurodegeneration in multiple regions of the central nervous system, including the olfactory bulb. Black garlic is rich in antioxidant compounds that may provide neuroprotective effects. This study investigated whether black garlic administration could reduce alcohol-induced olfactory bulb neurodegeneration in a binge drinking rat model.

Methods: This experimental study employed a posttest-only control group design using 30 male Sprague-Dawley rats (*Rattus norvegicus*), randomly allocated into three groups ($n = 10/\text{group}$). Animals received the assigned interventions for four consecutive days. The alcohol group received alcohol according to the binge drinking protocol, while the treatment group received both alcohol and black garlic extract (800 mg/kg body weight). Histopathological damage was quantified as the percentage of neurodegenerative cells observed in five microscopic fields. Data were analyzed using the Shapiro-Wilk test for normality, Levene's test for homogeneity of variances, the Kruskal-Wallis test, and post hoc Mann-Whitney U tests.

Results: The percentage of neurodegenerative cells was $0.73 \pm 0.12\%$ in the control group, $5.68 \pm 0.37\%$ in the alcohol-only group, and $2.83 \pm 0.31\%$ in the black garlic-treated group. Black garlic administration significantly reduced alcohol-induced neurodegeneration compared with the alcohol-only group (Mann-Whitney, $p < 0.001$).

Conclusion: Black garlic extract significantly reduced alcohol-induced olfactory bulb neurodegeneration in male Sprague-Dawley rats subjected to a binge drinking model.

Keywords: Black Garlic, Olfactory Bulb, Binge Drinking, Histopathology, Neuroprotection, Ethanol

REVIEW ARTICLE

POTENTIAL PROTECTIVE EFFECT OF FUCOXANTHIN ON MENINGIOMA: A GEO2R-BASED BIOINFORMATICS AND NETWORK PHARMACOLOGY ANALYSIS

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Background: Meningioma is one of the most common primary tumors of the central nervous system, and effective non-surgical treatment options targeting its molecular drivers remain limited. Fucoxanthin, a carotenoid derived from brown marine algae, has been reported to slow cancer growth, but the genes through which it could counteract meningioma-associated dysregulation have not been characterized.

Methods: Differentially expressed genes (DEGs) between meningioma and normal meningeal tissue were obtained from the GSE43290 dataset (47 meningioma vs. 4 normal meningeal samples, GPL96 platform) using GEO2R (adj. $p < 0.05$, $|\log_{2}FC| > 1$). These DEGs were compared against fucoxanthin-responsive genes reported in an independent glioblastoma cell line study (U87MG cells; PMID 32946518) using Venny 2.1.0 to identify genes with an inverse expression relationship. Gene Ontology (GO) Molecular Function and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment (Enrichr), protein-protein interaction (PPI) network construction (STRING, medium confidence score ≥ 0.400), and hub gene identification (CytoHubba, Maximal Clique Centrality [MCC] method) were performed on the resulting overlap.

Results: The comparison identified 65 genes upregulated in meningioma and downregulated by fucoxanthin, and 2 genes (WIPI1, ABLIM1) downregulated in meningioma and upregulated by fucoxanthin; the larger 65-gene set was used for downstream analysis. This set was enriched in single-stranded DNA helicase activity, DNA-binding transcription activator activity, and sequence-specific DNA binding, and in KEGG pathways including IGSF CAM signaling and HIF-1 signaling. The PPI network contained 65 nodes and 780 edges, and CCL2, SOX9, PLAU, ITGA5, and SPARC were identified as the top hub genes. None of these hub genes overlapped with hub genes reported by three other independent meningioma bioinformatics studies, although shared functional themes (transcription factors, adhesion/ECM genes, hypoxia-associated genes) were observed.

Conclusion: SPARC, PLAU, and TGM2 are the genes with prior direct experimental support in meningioma. Together with CCL2 and SOX9, are candidate genes through which fucoxanthin may counteract meningioma-associated gene dysregulation. Given the small control-group size of GSE43290 and the use of a non-meningioma cell line for the fucoxanthin gene list, these findings should be regarded as hypothesis-generating and require experimental validation.

Keywords: meningioma; fucoxanthin; GEO2R; bioinformatics; hub genes; protein-protein interaction network; network pharmacology

REVIEW ARTICLE

EFFICACY AND SAFETY OF EPIDURAL SPINAL CORD STIMULATION AS NEUROMODULATION FOR RECOVERY AFTER SPINAL CORD INJURY: A SYSTEMATIC REVIEW

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Background: Spinal cord injury (SCI) can cause permanent motor, sensory, and autonomic dysfunction, with limited neurological recovery in chronic stages. Epidural spinal cord stimulation (eSCS) has emerged as a neuromodulatory approach that enhances the excitability of residual spinal networks and facilitates neurological recovery. However, evidence regarding its efficacy and safety remains heterogeneous. This systematic review evaluates the efficacy and safety of eSCS for neurological recovery after SCI.

Methods: A systematic literature search was conducted across PubMed, Scopus, Cochrane Library, EBSCOhost, ProQuest, and Google Scholar following PRISMA guidelines. Eligible studies included clinical studies involving patients with complete or incomplete SCI who underwent eSCS implantation and reported neurological, functional, and safety outcomes. Data extracted included study and patient characteristics, stimulation protocols, functional outcomes, and adverse events. Risk of bias was assessed using appropriate tools according to study design.

Results: From 2,188 records identified, 13 studies met the inclusion criteria. eSCS was associated with improvements in motor and functional recovery, including voluntary lower-extremity activation, standing, stepping, walking, gait performance, and postural control. Improvements were also reported in sensory function, spasticity, and autonomic outcomes, including cardiovascular, urinary, and bowel function. Sustained improvements in motor scores, Barthel Index, and WISCI II were observed following prolonged eSCS combined with rehabilitation, while immediate neuromuscular facilitation was demonstrated during stimulation. Safety was generally favorable, with most adverse events being transient or manageable. However, some device- and procedure-related complications, including infection, lead migration, and battery failure, were reported.

Conclusion: eSCS was associated with improvements across motor, functional, sensory, and autonomic outcomes after SCI, with a generally favorable safety profile. These findings support eSCS as a promising neuromodulatory approach for enhancing neurological recovery after SCI. Further research should optimize stimulation protocols and establish long-term clinical outcomes.

Keywords: spinal cord injury, epidural spinal cord stimulation, neuromodulation, neurological recovery

REVIEW ARTICLE

PERFECT TARGET, IMPERFECT OUTCOMES? AN UPDATED META ANALYSIS REVIEWING EFFICACY AND SAFETY OF α -SYNUCLEIN MONOCLONAL ANTIBODIES IN EARLY PARKINSON'S DISEASE

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Background: α -Synuclein aggregation plays a central role in Parkinson's Disease (PD) pathogenesis with α -synuclein monoclonal antibodies offering potential disease-modifying effects compared to conventional treatment. However, recent phase 2 trials and previous meta-analysis have yielded inconsistent results regarding their clinical efficacy. This study aimed to evaluate the efficacy and safety of α -synuclein monoclonal antibodies in patients with early-stage PD.

Methods: Pubmed, Scopus, Proquest, and ScienceDirect were searched up to 13th August 2026. Randomised controlled trials (RCTs) evaluating α -synuclein monoclonal antibodies on early PD patients and reporting Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and/or Dopamine Transporter Single Photon Emission Computed Tomography (DaT-SPECT) were included. Risk of bias was assessed using the Cochrane Risk of Bias 2.0. Effect estimates were pooled using a random effects model in Review Manager 5.4.

Results: Pooled results from four RCTs (N = 1401) showed that α -synuclein monoclonal antibodies did not significantly improve MDS-UPDRS total score (MD = -0.62, 95% CI: -1.76 to 0.51, p = 0.28) as well as Part I-III subscales. Subgroup analysis based on drug dose showed no significant dose-response benefit. Similarly, objective neuroimaging analysis via DaT-SPECT of the ipsilateral putamen showed no significant difference to placebo (MD = -0.01, 95% CI: -0.04 to 0.02, p = 0.41). α -Synuclein was associated with a small but statistically significant increase in the risk of general adverse events (RR = 1.05, 95% CI: 1.01 to 1.09, p = 0.02). However, the risk of serious adverse events did not significantly differ between groups.

Conclusion: While α -synuclein monoclonal antibodies were generally well tolerated, it failed to significantly alter disease progression across clinical and neuroimaging outcomes. These findings further highlight the need for standardized trials with broader demographic representation and further verification of underlying α -synuclein pathology in PD.

Keywords: α -synuclein immunotherapy, parkinson's disease

REVIEW ARTICLE

MECHANISMS UNDERLYING THE PROGRESSION-FREE SURVIVAL AND OVERALL SURVIVAL DISCREPANCY OF BEVACIZUMAB IN GLIOBLASTOMA: A SYSTEMATIC REVIEW

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Background: Glioblastoma (GBM) remains the most aggressive primary brain tumor in adults despite maximal resection, radiotherapy, and temozolomide. Bevacizumab reliably extends progression-free survival (PFS) and reduces radiographic progression, yet consistently fails to improve overall survival (OS), exposing a critical disconnect between these endpoints. This systematic review evaluates the efficacy and safety of bevacizumab in newly diagnosed and recurrent GBM based on available randomized controlled trial evidence.

Methods: A systematic search of PubMed, Wiley, and medRxiv (January 2010 to June 2026) identified RCTs evaluating bevacizumab in GBM. Outcomes included PFS, OS, radiographic response, and complications. Study selection followed PRISMA 2020 guidelines, and risk of bias was assessed using the Cochrane RoB 2 tool.

Results: Five RCTs (n=2,422 patients) were included. The PFS-without-OS pattern was consistent across all trials. AVAglio and RTOG 0825, both large phase III RCTs in newly diagnosed GBM, demonstrated significant PFS benefit (HR 0.64, $P<0.001$; and HR 0.79, $P=0.007$) with no OS improvement. RTOG 0825 additionally showed greater neurocognitive decline and worse quality of life in the bevacizumab arm. In recurrent GBM, BELOB's promising combination signal (bevacizumab plus lomustine; 9-month OS 59%) did not replicate in the definitive EORTC 26101 phase III trial, where OS remained unchanged despite PFS improvement (4.2 vs 1.5 months; HR 0.95, $P=0.65$). Adverse events including hypertension and fatigue were higher in bevacizumab-containing arms.

Conclusion: Bevacizumab consistently improves PFS but not OS. Biomarker-driven patient selection and combination strategies are needed to convert imaging gains into meaningful survival benefits.

Keywords: Glioblastoma, Bevacizumab, VEGF Inhibition, Progression-Free Survival, Overall Survival.

REVIEW ARTICLE

RETINAL STRUCTURAL AND MICROVASCULAR BIOMARKERS ACROSS DEMENTIA SUBTYPES ASSESSED BY OPTICAL COHERENCE TOMOGRAPHY AND OCT ANGIOGRAPHY

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Background: The retina, as an accessible extension of the central nervous system, may provide non-invasive biomarkers of neurodegeneration. Optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) have been increasingly used to assess retinal structural and microvascular changes in Alzheimer's disease (AD) and related dementias, but findings remain inconsistent. This study systematically reviewed and quantitatively synthesized retinal OCT and OCTA biomarkers across dementia subtypes.

Methods: PubMed, Scopus, and Cochrane Library were searched according to PRISMA 2020 guidelines. Eligible case-control, cross-sectional, and cohort studies included adults (≥ 18 years) with clinically or biomarker-confirmed AD, mild cognitive impairment (MCI), frontotemporal dementia, dementia with Lewy bodies, or vascular dementia, compared with cognitively healthy controls. Risk of bias was assessed using an adapted QUADAS-2 framework, and certainty of evidence was evaluated using GRADE. Random-effects models (Hedges' g) pooled superficial capillary plexus (SCP) vessel density across comparable studies.

Results: Of 1,009 records identified, 15 studies met the inclusion criteria, with five studies ($n = 309$ eyes/participants) included in the meta-analysis. SCP vessel density was significantly reduced in dementia compared with controls (Hedges' $g = -0.83$; 95% CI, -1.06 to -0.59 ; $I^2 = 0\%$). Individual studies also reported reduced deep capillary plexus density, choroidal thinning, ganglion cell-inner plexiform layer and retinal nerve fiber layer thinning, and enlarged foveal avascular zone. Combined OCT and OCTA models demonstrated higher diagnostic accuracy (AUC 0.90–1.00) than either modality alone. Heterogeneity in imaging devices, scan protocols, dementia subtypes, and unit-of-analysis methods limited comparability.

Conclusions: Reduced SCP vessel density is the most consistent retinal microvascular finding across dementia subtypes. Combined OCT and OCTA biomarkers may improve diagnostic performance, although standardized imaging protocols and longitudinal biomarker-confirmed studies are needed before clinical implementation.

Keywords: Alzheimer's disease; dementia; optical coherence tomography; optical coherence tomography angiography; retinal biomarkers.

REVIEW ARTICLE

CROSS-COHORT TRANSCRIPTOMICS REVEALS CELL-INFORMED IMMUNE-VASCULAR REMODELING IN INTRACRANIAL ANEURYSM RUPTURE

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Background: Intracranial aneurysm rupture causes aneurysmal subarachnoid hemorrhage with substantial morbidity and mortality, yet rupture-risk assessment remains dominated by clinical and morphological parameters. Because wall instability is biologically driven, transcriptomic profiling may reveal molecular signatures that better reflect rupture-prone aneurysm phenotypes. This study aimed to identify reproducible, cell-informed immune-vascular signatures distinguishing ruptured from unruptured human intracranial aneurysm walls.

Methods: GSE13353 and GSE54083 were evaluated as discovery and replication microarray cohorts, while GSE122897 provided independent RNA-sequencing corroboration. Differential-expression findings were synthesized across cohorts at the gene and pathway levels, emphasizing directional consistency and recurrent biological functions. Functional interpretation incorporated GO, KEGG, and Reactome annotations, published STRING protein-protein interaction evidence, and immune-vascular cell signatures informed by recent human single-cell aneurysm-wall studies.

Results: GSE13353 reported 1,426 differentially expressed genes in ruptured aneurysm walls, including 686 upregulated and 740 downregulated genes. GSE54083 reported 1,047 early rupture-associated genes, comprising 430 upregulated and 617 downregulated genes. GSE122897 independently identified 1,489 rupture-associated genes and corroborated immune-response and lysosomal pathway dysregulation. Across cohorts, convergent biological programs involved leukocyte chemotaxis, immune activation, phagocytosis-lysosome signaling, extracellular-matrix remodeling, and impaired vascular-wall homeostasis. Published cross-dataset analyses identified rupture-associated expression changes in JUN, PPBP, THBS1, APP, GSK3B, and ERBB2. Cell-informed interpretation linked these patterns to macrophage/monocyte and neutrophil inflammatory states alongside reduced vascular smooth-muscle homeostasis.

Conclusion: Intracranial aneurysm rupture is characterized by a reproducible immune-vascular transcriptomic phenotype involving inflammatory activation, phagolysosomal signaling, and structural wall destabilization. This cell-informed cross-cohort framework provides a biologically interpretable foundation for future biomarker validation and molecular rupture-risk stratification in cerebrovascular neurosurgery.

Keywords: Intracranial aneurysm; Aneurysm rupture; Transcriptomics; Immune inflammation; Bioinformatics.

REVIEW ARTICLE

NEUROFILAMENT LIGHT CHAIN AS A PREDICTOR OF DISEASE SEVERITY IN PATIENTS WITH SUBARACHNOID HEMORRHAGE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Subarachnoid hemorrhage (SAH), particularly aneurysmal SAH (aSAH), is a life-threatening stroke associated with high mortality and long-term neurological disability. Prognostic assessment mainly relies on clinical and radiological grading systems, which may be limited by interobserver variability and reduced reliability in sedated or unconscious patients. Neurofilament light chain (NfL), a marker of axonal injury measurable in cerebrospinal fluid and blood using highly sensitive assays, has emerged as a potential prognostic biomarker. Although elevated NfL levels have been associated with greater disease severity and poor outcomes after SAH, evidence remains inconsistent. This systematic review and meta-analysis evaluated the association between NfL levels, disease severity, and functional outcomes in patients with SAH.

Methods: A literature search was performed on PubMed, Scopus, Wiley, ProQuest, Cochrane, Springer, Sage, and ScienceDirect. Study quality was assessed using the modified Newcastle Ottawa Scale. The outcome of the study is the level difference of NfL between severe and non severe SAH patients. Random-effects models were applied. Meta-regressions were performed to explore heterogeneity. Publication bias was assessed using funnel plot and Egger's test. A leave-one-out sensitivity analysis was performed to assess the influence of individual studies on the overall effect size.

Results: The pooled analysis demonstrated a significant effect size for NfL as a predictor of SAH severity (SMD = 0.90; 95% CI: 0.59–1.22; $p < 0.001$) with moderate heterogeneity ($I^2 = 56.37\%$). Leave-one-out sensitivity analyses confirmed the robustness of the findings (g range: 0.77–0.95; all $p < 0.001$), and funnel plot symmetry indicated no publication bias. While the intervention shows consistent clinical benefit across studies, the observed heterogeneity suggests that treatment effects may vary by patient or contextual factors, warranting further investigation.

Conclusion: Elevated NfL levels are significantly associated with greater disease severity and worse functional outcomes in patients with SAH, suggesting that NfL may serve as a promising prognostic biomarker. Future studies should focus on mitigating study heterogeneity to optimize personalized clinical application.

Keywords: Neurofilament Light Chain, Subarachnoid Hemorrhage, Biomarker, Disease Severity, Functional Outcome

REVIEW ARTICLE

ORDER, SESSION COORDINATION, AND TIMING OF ADJUNCTIVE MIDDLE MENINGEAL ARTERY EMBOLIZATION RELATIVE TO SURGICAL EVACUATION FOR CHRONIC SUBDURAL HEMATOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Chronic subdural hematoma (cSDH) frequently requires surgical evacuation, but recurrence remains a clinical concern. Although adjunctive middle meningeal artery embolization (MMAE) may reduce recurrence, its optimal order, session coordination, and timing relative to surgery remain uncertain. This review evaluated whether these strategies influence reoperation and hospital length of stay (LOS).

Methods: This PROSPERO-registered systematic review and meta-analysis (CRD420261462200) followed PRISMA. PubMed, ScienceDirect, the Cochrane Library, ProQuest, and Web of Science were searched through July 27, 2026, for comparative studies of adults receiving adjunctive MMAE and surgical evacuation for cSDH. Risk of bias was assessed using ROBINS-I. Comparisons were single-session versus staged, preoperative versus postoperative, and early versus delayed MMAE. Random-effects models pooled odds ratios (ORs) for reoperation and mean differences (MDs) for LOS with 95% confidence intervals (CIs). LOS synthesis was exploratory and based on median-to-mean conversion.

Results: Nine studies were included, of which five contributed to quantitative synthesis. Single-session MMAE showed a nonsignificant trend toward fewer reoperations than staged treatment (245 observations; 17 events; OR=0.49; 95% CI, 0.16–1.48; $p=0.206$; $I^2=0\%$). Preoperative versus postoperative MMAE showed no significant difference (479 observations; 50 events; OR=0.75; 95% CI, 0.14–4.12; $p=0.739$; $I^2=78.6\%$). Early versus delayed MMAE was likewise not associated with reoperation (415 observations; 31 events; OR=0.87; 95% CI, 0.42–1.81; $p=0.706$; $I^2=0\%$). Exploratory analysis suggested shorter LOS with single-session treatment, although the difference was not statistically significant (247 observations; MD=-1.58 days; 95% CI, -3.20 to 0.03; $p=0.055$; $I^2=51.8\%$).

Conclusion: Current evidence does not support a definitive MMAE sequencing strategy for reducing reoperation after surgical evacuation. Single-session treatment may improve hospital efficiency, but this estimate remains uncertain. Sequencing decisions should therefore remain individualized pending larger prospective studies using standardized timing definitions.

Keywords: Chronic Subdural Hematoma; Middle Meningeal Artery Embolization; Surgical Evacuation; Embolization; Treatment Outcome; Reoperation

REVIEW ARTICLE

**COMPARATIVE SAFETY OF TENECTEPLASE VERSUS ALTEPLASE FOR
INTRAVENOUS THROMBOLYSIS IN DIRECT ORAL
ANTICOAGULANT-PRETREATED ACUTE ISCHEMIC STROKE: A
SYSTEMATIC REVIEW**

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Background: Direct oral anticoagulants (DOACs) are the mainstay of stroke prevention in atrial fibrillation, and real-world data suggest intravenous thrombolysis (IVT) can be given with acceptable safety to selected patients who have recently taken one. Tenecteplase is rapidly replacing alteplase in routine care, yet how the two agents compare in DOAC-pretreated patients remains unsettled. This review compared the safety and functional outcomes of the two agents for IVT in DOAC-pretreated adults with acute ischemic stroke (AIS).

Methods: PubMed, Scopus, ScienceDirect, and Google Scholar were searched to 2 July 2026 without date or language limits. Eligible studies directly compared tenecteplase with alteplase in DOAC-pretreated AIS. Risk of bias was assessed with ROBINS-I and certainty of evidence with GRADE. Critical outcomes were symptomatic intracranial haemorrhage (sICH), any ICH or major bleeding, all-cause mortality, and functional outcome (modified Rankin Scale).

Results: Two non-randomized studies including 3,350 patients qualified: a propensity-matched multinational cohort (1,634 vs 1,634) and a single-centre registry (42 vs 40); they disagreed. The matched cohort linked tenecteplase to a higher early risk of intracranial haemorrhage (day 0-1 hazard ratio [HR] 3.26, 2.33-4.58), subarachnoid haemorrhage (HR 2.84, 1.66-4.76), and 24-hour mortality (HR 2.01, 1.19-3.39), confined to the first day; the registry found no difference but was underpowered. Both were at serious risk of bias, so results were synthesized narratively.

Conclusion: Current evidence comparing tenecteplase and alteplase in DOAC-pretreated AIS is confined to two small, discordant observational studies at serious risk of bias, leaving certainty very low across every outcome. The early haemorrhagic and mortality signal with tenecteplase arose in only one cohort, was not reproduced, and is best read as hypothesis-generating rather than causal. Until adequately powered, ideally randomized, trials are available, neither agent can be declared safer, and the choice should rest on individual risk assessment and existing guideline frameworks.

Keywords: tenecteplase; alteplase; direct oral anticoagulants; intravenous thrombolysis; acute ischemic stroke.

REVIEW ARTICLE

COMPARATIVE EFFICACY AND SAFETY OF TENECTEPLASE VERSUS ALTEPLASE IN ACUTE ISCHEMIC STROKE: A SYSTEMATIC REVIEW

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Background: Intravenous thrombolysis (IVT) is a cornerstone of acute ischemic stroke (AIS) management. Alteplase (ALT) 0.9 mg/kg is the conventional agent, whereas tenecteplase (TNK) 0.25 mg/kg offers greater fibrin specificity, a longer half-life, and single-bolus administration. This systematic review compared TNK with ALT in adults with AIS within 4.5 hours of symptom onset.

Methods: This systematic review followed PRISMA 2020. PubMed, Embase, Web of Science, and Cochrane Library were searched for phase III randomized controlled trials published during 2020–2026. Eligible studies included adults with AIS within 4.5 hours of symptom onset treated with TNK 0.25 mg/kg or ALT 0.9 mg/kg. Outcomes included excellent functional outcome (mRS 0–1) at approximately 90 days, symptomatic intracranial hemorrhage (sICH), and mortality. Studies evaluating other TNK doses or non-randomized designs were excluded. Risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool.

Results: Five multicenter phase III randomized controlled trials comprising 6,895 participants across their respective primary analysis populations met the eligibility criteria. TNK demonstrated non-inferior functional outcomes compared with ALT across the major trials. Non-inferiority was demonstrated for excellent functional outcome in three trials and for ordinal mRS in another, while one trial demonstrated non-inferiority in the per-protocol but not intention-to-treat analysis. sICH rates were broadly comparable between TNK and ALT, ranging from 1.2%–3.4% and 1.2%–3.2%, respectively. Mortality showed no consistent difference between treatment groups.

Conclusion: TNK 0.25 mg/kg demonstrates non-inferior efficacy and a broadly comparable safety profile to ALT 0.9 mg/kg for IVT in eligible patients with AIS. Its single-bolus administration provides a practical advantage and supports TNK as an evidence-based alternative to ALT.

Keywords: Acute Ischemic Stroke; Tenecteplase; Alteplase; Intravenous Thrombolysis; Symptomatic Intracranial Hemorrhage; Modified Rankin Scale

REVIEW ARTICLE

EFFICACY AND SAFETY OF ADJUNCTIVE MIDDLE MENINGEAL ARTERY EMBOLIZATION AFTER SURGICAL EVACUATION FOR CHRONIC SUBDURAL HEMATOMA: A SYSTEMATIC REVIEW

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Background: Chronic subdural hematoma (cSDH) remains a major clinical challenge, particularly in older adults, due to frequent recurrence after surgical evacuation. Increasing evidence suggests that cSDH is sustained by a vascularized inflammatory neomembrane supplied by distal branches of the middle meningeal artery (MMA), providing the rationale for middle meningeal artery embolization (MMAE). This systematic review evaluated the efficacy and safety of adjunctive MMAE following surgical evacuation using evidence from randomized controlled trials (RCTs).

Methods: PubMed, Wiley, ScienceDirect, and medRxiv were systematically searched for RCTs comparing adjunctive MMAE plus surgical evacuation versus surgery alone in adults with cSDH, with the search period limited to January 2010 to June 2026. Outcomes included symptomatic recurrence, reoperation, and treatment-related complications (follow-up ranged from 90 days to 12 months across trials). Study selection followed PRISMA guidelines, and risk of bias was assessed using the Cochrane RoB 2 tool.

Results: Six RCTs involving 1,743 patients were included. Four trials using liquid embolic agents (Onyx or Squid) demonstrated consistent clinical benefit. EMBOLISE reported lower reoperation rates with MMAE (4.1% vs 11.3%; $P=0.008$), while EMMA-Can showed significantly reduced symptomatic recurrence (4.3% vs 28%; $P<0.001$). Although MAGIC-MT did not meet its primary endpoint for recurrence (6.7% vs 9.9%; $P=0.10$), it reported a favorable safety profile with fewer serious adverse events in the MMAE group. A smaller trial by Lam et al. showed a similar trend but was underpowered. In contrast, EMPROTECT, which used particulate microspheres, did not demonstrate a significant benefit (14.8% vs 21.0%; $P=0.13$). Complication rates were low and comparable across studies.

Conclusion: Adjunctive MMAE with liquid embolic agents appears to reduce recurrence after surgical evacuation of cSDH without increasing complications. While randomized evidence favors liquid agents, the effectiveness of particulate embolization remains uncertain. Further studies with standardized core outcome sets, extended follow-up, and direct head-to-head agent comparisons are needed before MMAE can be established as standard of care.

Keywords: Chronic subdural hematoma, Middle meningeal artery embolization, Adjunctive therapy, Reoperation, Randomized controlled trial

REVIEW ARTICLE

EFFECTS OF ANTI-AMYLOID MONOCLONAL ANTIBODY THERAPY ON NEUROINFLAMMATORY BIOMARKERS IN ALZHEIMER'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Alzheimer's disease (AD) pathogenesis involves not only amyloid- β accumulation but also active neuroinflammatory processes driven by astrocytic and microglial activation reflected by biomarkers such as plasma GFAP, sTREM2 levels, and YKL-40. Although anti-amyloid monoclonal antibody therapies have demonstrated amyloid clearance and clinical benefit, their effects on neuroinflammatory biomarkers remain insufficiently understood.

Methods: The meta-analysis followed the PRISMA guidelines, with database searches conducted in PubMed, Scopus, EBSCOHost, and Wiley up to July 2026. Eligible studies compared anti-amyloid monoclonal antibody therapy against placebo, control, or baseline in AD patients, reporting change in plasma GFAP and/or CSF sTREM2 and YKL-40 levels. Quantitative synthesis was performed for plasma GFAP in Review Manager 5.4.1 using the inverse-variance random-effects model, pooling mean differences (MD) with standard errors derived from each study.

Results: A total of 10 studies comprising 4474 participants were included. Pooled analysis of placebo-controlled trials demonstrated a significant reduction in plasma GFAP levels on the log-transformed scale (MD=-0.10 [95% CI, -0.11 to -0.08], $p<0.0001$; $I^2=38\%$), whereas reduction on the raw scale was statistically insignificant (MD=-0.04 ng/mL [95% CI, -0.09 to 0.01], $p=0.14$, $I^2=50\%$). Pre-post single-arm analyses showed a significant reduction in plasma GFAP on the raw scale (MD=-28.28 pg/mL [95% CI, -45.54 to -11.02], $p=0.001$; $I^2=44\%$), while the log-transformed estimate showed insignificant reduction (MD=-0.16 [95% CI, -0.36 to 0.05], $p=0.13$; $I^2=69\%$). Qualitative analysis of CSF YKL-40 and sTREM2 levels showed inconsistent effects.

Discussion: Anti-amyloid therapy may differentially modulate astrocytic and microglial pathways, with microglial response potentially varying by disease etiology. The limited availability of studies reporting sTREM2 and YKL-40 prevented a quantitative meta-analysis of these biomarkers. Limited sample sizes and treatment variations may explain the marginal findings and moderate heterogeneity.

Conclusion: Anti-amyloid monoclonal antibody therapy is associated with a consistent reduction in plasma GFAP, but its effects on sTREM2 and YKL-40 remain inconclusive.

Keywords: Alzheimer's Disease, Anti-Amyloid Monoclonal Antibody, Neuroinflammation, GFAP, sTREM2, YKL-40

RESEARCH ARTICLE

ROBOTIC-ASSISTED FRAMELESS NAVIGATION VERSUS FRAME-BASED STEREOTACTIC SURGERY FOR INTRACEREBRAL HEMORRHAGE: A RETROSPECTIVE COMPARATIVE STUDY

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Background: Intracerebral hemorrhage (ICH) remains a leading cause of stroke-related morbidity and mortality. Minimally invasive stereotactic hematoma evacuation is increasingly used in patients with ICH. Robotic-assisted frameless navigation may simplify surgical planning and avoid the need for rigid frame fixation; however, direct comparisons with conventional frame-based stereotactic surgery remain limited. This study compared the perioperative efficacy, safety, and short-term clinical outcomes of these two approaches in patients with basal ganglia ICH.

Methods: We retrospectively reviewed 38 patients with basal ganglia ICH who underwent robotic-assisted frameless stereotactic hematoma evacuation using the RM-50 system (robotic group, n=20; Group B) or conventional frame-based stereotactic surgery (frame-based group, n=18; Group A). At our institution, the surgical approach was selected according to clinical stability, hematoma characteristics, and patient or family preference. Baseline characteristics, hematoma evacuation rate, length of hospital stay, hospitalization cost, discharge modified Rankin Scale (mRS) score, and postoperative complications were compared between the groups. Continuous variables with skewed distributions were summarized as median (range) and compared using appropriate nonparametric tests; categorical variables were compared using Fisher's exact test.

Results: The robotic group had a significantly higher preoperative mRS score than the frame-based group (4.90 ± 0.31 vs. 4.06 ± 0.42 , $P < 0.001$), indicating an imbalance in baseline neurological status. The hematoma evacuation rate did not differ significantly between the frame-based and robotic groups (82.7% [range 17.3–98.9%] vs. 76.7% [range 47.4–98.8%], $P = 0.915$). No statistically significant differences were observed in length of hospital stay, overall postoperative complication rate (55.6% vs. 75.0%, $P = 0.307$), hospitalization cost ($P = 0.171$), or discharge mRS score (3.94 ± 0.73 vs. 4.30 ± 0.57 , $P = 0.105$).

Conclusion: Robotic-assisted frameless navigation and conventional frame-based stereotactic surgery achieved similar hematoma evacuation rates and showed no statistically significant differences in short-term safety or clinical outcomes in this small retrospective cohort. Because treatment selection was nonrandomized and baseline neurological status differed between the groups, larger prospective studies with adjustment for confounding factors are required to determine whether robotic-assisted surgery provides clinical advantages.

Keywords: Intracerebral hemorrhage; Robotic-assisted surgery; Frameless stereotactic navigation; Frame-based stereotactic surgery; Hematoma evacuation; Modified Rankin Scale

REVIEW ARTICLE

**CAUSES, PREDICTORS, AND INDICATIONS FOR REOPERATION
FOLLOWING PRIMARY CRANIOSYNOSTOSIS SURGERY: A SYSTEMATIC
REVIEW**

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Background: Reoperation after craniosynostosis repair is clinically consequential, yet reported rates are difficult to interpret because planned staged procedures, acute returns to the operating room, and corrective revisions are frequently combined. This review synthesized the causes, predictors, and indications for unplanned reoperation after primary craniosynostosis surgery.

Methods: PubMed and Scopus were searched from inception for studies reporting reoperation, revision, repeat surgery, or secondary corrective procedures after craniosynostosis repair. Planned staged procedures were excluded when distinguishable. Evidence was stratified into acute return to the operating room, major long-term revision, revision for delayed intracranial hypertension, and secondary open surgery after minimally invasive repair.

Results: Twenty-seven studies met eligibility criteria, including seven retained for restricted extraction. Reoperation rates varied by definition: approximately 2.4% for 30-day return to the operating room, 2.4–11.8% for major long-term revision in general cohorts, and 14.3–45.5% in syndromic or complex populations. Broad definitions incorporating skull-defect repair, minor contouring, wound treatment, or hardware removal yielded rates up to 26.8%. Principal indications were recurrent intracranial hypertension, resynostosis or secondary suture fusion, progressive deformity, inadequate primary correction, persistent calvarial defects, and infection. Risk signals included syndromic or multisuture disease, coronal or complex involvement, nonoptimal operative timing, secondary synostosis, Chiari malformation, and FGFR3 P250R or TWIST1-associated disease. Pooling was limited by heterogeneous definitions, follow-up, planned-treatment contamination, and overlapping database cohorts.

Conclusion: Reoperation is not a single outcome. Standardized reporting must separate acute complications, major functional revision, aesthetic correction, and planned staged surgery. Long-term surveillance should prioritize syndromic, multisuture, genetically confirmed, and secondary-synostosis phenotypes.

Keywords: Craniosynostosis, reoperation, revision surgery, intracranial hypertension, resynostosis

REVIEW ARTICLE

EFFICACY AND SAFETY OF TAVAPADON IN EARLY-STAGE PARKINSON'S DISEASE: A SYSTEMATIC REVIEW

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Background: Existing dopamine agonists preferentially target D2/D3 receptors and associated with impulse control disorders, somnolence, and hallucinations. Tavapadon, an oral, once-daily, selective D1/D5 receptor partial agonist, may improve motor symptoms while reducing these adverse effects. This systematic review evaluated its efficacy and safety in early-stage PD.

Methods: Literature was searched across PubMed, Scopus, Embase, ScienceDirect, and Cochrane CENTRAL for randomised, placebo-controlled trials of tavapadon monotherapy in early-stage PD, following PRISMA 2020 guidelines. Two reviewers independently screened and filtered three literatures (adults with early-stage, treatment-naïve or minimally treated PD; tavapadon vs placebo; motor/functional and safety outcomes) for a combined N=890. Risk of bias was assessed using the Cochrane RoB 2 tool across five domains. Owing to heterogeneity in dosing strategies and assessment timepoints, findings were synthesized narratively.

Results: All three trials reported statistically significant, clinically meaningful improvement in MDS-UPDRS scores with tavapadon versus placebo, with treatment differences ranging from -4.8 to -12.1 points (all $p \leq 0.041$). Patient Global Impression of Change responder rates were consistently higher with tavapadon (44–50%) than with placebo (12–25%). Adverse events occurred more often with tavapadon (76–79%) than placebo (55–57%), mainly nausea, headache, and dizziness. Discontinuation due to adverse events was higher with tavapadon (24–38%) than placebo (4–15%). Impulse control disorders ($\leq 1.3\%$) and somnolence ($\leq 3.4\%$) were uncommon and comparable to placebo. All trials were rated “Some Concerns” overall, due to differential dropout and industry funding/analysis involvement, while other domains were low risk.

Conclusion: Tavapadon consistently improved motor and functional outcomes and showed low rates of impulse control disorders and somnolence. However, gastrointestinal and dizziness-related adverse effects contributed to substantial discontinuation. These findings are consistent but longer-term, and head-to-head trials are needed before firm clinical positioning.

Keywords: early-stage Parkinson disease, Tavapadon, D1/D5 dopamine agonist, MDS-UPDRS, systematic review, randomized controlled trial, safety and tolerability

RESEARCH ARTICLE

DIAGNOSTIC CHALLENGE OF CYTOMEGALOVIRUS ENCEPHALITIS WITH NEGATIVE CEREBROSPINAL FLUID PCR AND CONCURRENT RETROAURICULAR ABSCESS IN AN IMMUNOCOMPROMISED ADULT: CASE REPORT

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Background: CMV encephalitis is a life-threatening central nervous system infection in immunocompromised adults. Diagnosis is particularly challenging because cerebrospinal fluid (CSF) CMV polymerase chain reaction (PCR), although considered the diagnostic reference test, may yield false-negative results.

Case Presentation: A 56-year-old male with diabetes mellitus and hypertension presented with reduced consciousness (GCS 14), nausea, vomiting, left retroauricular abscess (3×4 cm, 3 weeks duration), and recurrent influenza-like illness. Admission labs revealed severe hyponatremia (Na = 105.9 mEq/L), hypokalemia (K = 1.73 mEq/L), leukocytosis (WBC = $15.72 \times 10^3/\mu\text{L}$), transaminitis (SGOT/SGPT elevated), and elevated creatinine (1.35 → 10.9 mg/dL). Head CT scan revealed an abscess (2.4×5.3×5 cm) with left mastoid erosion and a fistulating tract. Metabolic problems were corrected and adequate antibiotics for abscess were given. The course was complicated by generalized seizures and hemodynamic collapse requiring intubation and vasopressors. MRI (day 3) demonstrated left parietoccipital and thalamic T2/FLAIR hyperintensities without contrast enhancement, consistent with encephalitis, alongside mild communicating hydrocephalus. CSF CMV PCR was negative. On day 8, serum CMV IgG showed positive results with negative IgM, while IgG and IgM for alternative viral etiologies were negative. Intravenous antiviral Gancyclovir was initiated, with subsequent clinical recovery (GCS 15, extubated day 10). Repeated head MRI (day 54) confirmed complete resolution of encephalitis and reduction of retroauricular infiltrate.

Discussion: Uncontrolled diabetes permitted CMV reactivation from its latent reservoir, amplified by abscess-driven systemic inflammatory cytokine activation. Posterior cortical diffusion restriction is documented in metabolically immunocompromised hosts. Positive IgG with negative IgM and MRI resolution on antiviral therapy confirm reactivation etiology.

Conclusion: Negative CSF PCR must not exclude CMV encephalitis. Integrated diagnosis incorporating clinical presentation, neuroimaging, serology, and therapeutic response is essential.

Keywords: Cytomegalovirus encephalitis; cerebrospinal fluid PCR; false-negative PCR; retroauricular abscess; viral reactivation; immunocompromised host.

REVIEW ARTICLE

SINGLE VERSUS BILATERAL EXTERNAL VENTRICULAR DRAINAGE IN ADULTS WITH SEVERE INTRAVENTRICULAR HEMORRHAGE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Severe intraventricular hemorrhage (IVH) frequently causes acute hydrocephalus, intracranial hypertension, and poor neurological outcomes. Although bilateral external ventricular drainage (EVD) may facilitate evacuation of extensive ventricular clot, its clinical advantages over single EVD remain uncertain. Therefore, this study compared the efficacy and safety of bilateral (dual) versus single (unilateral) EVD in adults with severe IVH.

Methods: A systematic review and meta-analysis was conducted by searching PubMed, the Cochrane Library, and ScienceDirect from inception through July 2026. Comparative studies evaluating bilateral versus single EVD in adults with severe IVH were included. Outcomes comprised EVD duration, ventriculostomy-related infection, and intraventricular hemorrhage clearance. Mean differences (MD) and risk differences (RD) were pooled using random-effects models.

Results: Five studies involving 232 patients met the inclusion criteria. Four studies comprising 148 patients reported EVD duration. Bilateral EVD did not significantly reduce drain duration compared with single EVD (MD 0.89 days; 95% CI -0.15 to 1.93; $p=0.09$; $I^2=45\%$). Four studies involving 172 patients reported ventriculostomy-related infection, showing no significant difference between groups (RD 0.09; 95% CI -0.08 to 0.27; $p=0.31$; $I^2=77\%$). Meta-analysis of clot clearance was not feasible because of heterogeneous outcome definitions, measurement units, and assessment time points. Three studies reported greater or faster clot reduction with bilateral EVD, whereas one found comparable clearance. These findings suggest that although bilateral EVD may improve radiographic clot evacuation in selected patients with extensive or compartmentalized hemorrhage, this potential benefit does not translate into shorter drainage duration, while its effect on infection risk remains uncertain.

Conclusion: Current evidence does not support the routine use of bilateral EVD in adults with severe IVH. Bilateral EVD should be reserved for selected anatomical or mechanical indications until higher-quality comparative studies become available.

Keywords: Intraventricular hemorrhage; External ventricular drainage; Ventriculostomy; Hydrocephalus; Meta-analysis

REVIEW ARTICLE

DIAGNOSTIC PERFORMANCE OF THE KAPPA FREE LIGHT-CHAIN INDEX IN MULTIPLE SCLEROSIS: UPDATED META-ANALYSIS ACROSS EARLY DISEASE AND NEUROLOGICAL DIFFERENTIAL DIAGNOSES

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Background: Cerebrospinal fluid kappa free light chains (κ -FLC) have emerged as a quantitative marker of intrathecal immunoglobulin synthesis for multiple sclerosis (MS). However, the available evidence remains heterogeneous across diagnostic thresholds, study populations, and neurological comparator groups, while the role of κ -FLC in early disease and differential diagnosis remains incompletely defined.

Methods: This systematic review and meta-analysis was conducted in accordance with PRISMA-DTA and PRISMA 2020 recommendations. Eligible studies evaluated cerebrospinal fluid κ -FLC in patients with MS, clinically isolated syndrome (CIS), or relevant neurological controls. Random-effects models were used for quantitative synthesis. Diagnostic performance was assessed using pooled sensitivity, specificity, diagnostic odds ratios (DORs), and the Reitsma bivariate model. CIS-to-MS conversion, continuous κ -FLC differences, and single-arm proportions were analyzed separately.

Results: Thirty-two datasets contributed to the primary diagnostic analysis of the κ -FLC index. Pooled sensitivity was 0.888 (95% CI 0.860–0.911), specificity 0.874 (0.844–0.898), and DOR 64.60 (42.90–97.28). The Reitsma model yielded a summary AUC of 0.937. Oligoclonal bands showed similar sensitivity (0.890) but descriptively higher specificity (0.916) and AUC (0.953). κ -FLC index values were significantly higher in MS than in non-inflammatory neurological diseases (SMD 1.24), NMOSD (0.69), and MOGAD (0.96). Among OCB-negative MS patients, pooled κ -FLC positivity was 34.0%. κ -FLC-based reflex strategies could potentially avoid 68.6% of OCB examinations. The pooled HR for CIS-to-MS conversion was 2.70 (95% CI 0.24–29.89) and was not statistically significant.

Conclusion: The κ -FLC index demonstrates high diagnostic performance for MS and may provide complementary value in OCB-negative disease and selected neurological differential diagnoses. Substantial heterogeneity across several analyses highlights the need for more standardized diagnostic thresholds and comparator definitions in future studies.

Keywords: multiple sclerosis, kappa free light chain, cerebrospinal fluid, diagnostic performance, oligoclonal bands

RESEARCH ARTICLE

MOVEMENT DISORDER FOLLOWING BASAL GANGLIA INFARCTION IN A PATIENT WITH TYPE 2 DIABETES

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Background: Choreiform movement disorders are a rare presentation of infarcted stroke which occur only in 1–4% of cases caused by ganglia dysfunction particularly the putamen and caudate nucleus. Clinically, it resembles diabetic striatopathy (DS) a neuro-metabolic disorder triggered by severe hyperglycemia. Recent literature highlights a frequent clinical overlap or coexistence between DS and acute ischemic stroke which makes it challenging to differentiate both of them.

Case: We present a male patient with hemiballismus-hemichorea secondary to basal ganglia infarction with a history of Insulin Dependent-type 2 Diabetes as a comorbid. He's presented with 7-days of acute-onset left sided hemiballismus-hemichorea. Laboratory tests revealed fasting blood glucose of 133 mg/dL and HbA1c of 10%. A non-contrast CT-Scan revealed a basal ganglia infarctions especially in the bilateral side of the putamen correlating with his movement disorder. The patient was managed with insulin, gabapentin, cilostazol, phenytoin, and citicolin and showed progressive clinical recovery and was discharged with scheduled follow-up at the outpatient clinic.

Discussion: This case shows a rare presentation of basal ganglia infarction as hemiballismus-hemichorea which is challenging in a diabetic patient. The putaminal lesion disrupted the indirect motor pathway, reducing inhibitory control and triggering involuntary choreiform movements that mimics diabetic striatopathy making neuroimaging essential for accurate diagnosis. Coexisting diabetes may have increased the ischemic injury. Management required stroke prevention, glycemic control, and symptomatic treatment, leading to meaningful clinical improvement.

Conclusion: Hemiballismus-Hemichorea is a rare manifestation of ischemic stroke particularly in diabetic patients where diabetic striopathy could be another diagnostic option. Comprehensive history, appropriate laboratory evaluation including blood glucose, and neuroimaging with CT Scan are essential to establish the correct diagnosis allowing timely treatment and ultimately leading to a better prognosis while reducing the risk of adverse outcomes.

Keywords: Ischaemic Stroke, Hemichorea, Diabetes, Hemiballismus

REVIEW ARTICLE

SAFETY AND EFFICACY OF GREATER OCCIPITAL NERVE BLOCK IN CHRONIC MIGRAINE: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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Background: Chronic migraine (CM) is a major global health burden, particularly among women of reproductive age, and effective preventive treatments remain limited. Greater occipital nerve block (GONB) has emerged as a minimally invasive option based on the convergence of occipital nerve afferents with the trigeminocervical complex.

Objective: To systematically review recent randomized controlled trial (RCT) evidence on the efficacy and safety of GONB for chronic migraine.

Methods: Double-blind, placebo-controlled RCTs published within the last five years were reviewed. Eligible studies included adults with CM diagnosed according to International Classification of Headache Disorders criteria and compared GONB using local anesthetics, with or without corticosteroids, against placebo. Primary outcomes were headache frequency, intensity, duration, and adverse events.

Results: A recent meta-analysis of five RCTs ($n = 268$) showed that GONB significantly reduced headache intensity at one month (SMD -0.65) and two months (SMD -0.63), as well as headache frequency at one month (SMD -0.76) and two months (SMD -0.58), without increasing adverse events (OR 1.38, 95% CI 0.60–3.18). A 2025 systematic review of ultrasound-guided GONB (six studies, four RCTs; $n = 344$) similarly demonstrated significant reductions in pain intensity, monthly headache days, and analgesic use, with dizziness as the most common adverse event and serious complications being rare. These findings are consistent with earlier evidence showing reduced headache days despite no significant effect on acute medication use.

Conclusion: Recent RCT evidence supports GONB as an effective and well-tolerated preventive treatment for chronic migraine. Nevertheless, heterogeneity in anesthetic agents, injection techniques, and follow-up duration highlights the need for larger, multicenter RCTs using standardized protocols.

Keywords: Greater occipital nerve block; chronic migraine; randomized controlled trial; systematic review; local anesthetics.

RESEARCH ARTICLE

THE SPECTRUM OF GRADE III DIFFUSE AXONAL INJURY AND SECONDARY ORGANIC MENTAL DISORDER IN A PEDIATRIC PATIENT: A CASE REPORT

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Introduction: Diffuse axonal injury (DAI) is a severe form of traumatic brain injury, and neuropsychiatric complications may follow during recovery. However, the progression from pediatric grade III DAI to secondary organic mental disorder complicated by persistent agitation and tracheostomy self-removal has rarely been reported. We describe this rare clinical course and its multidisciplinary management.

Case Presentation: A 12-year-old boy presented with prolonged loss of consciousness following a motorcycle accident. The patient was diagnosed with severe traumatic brain injury with grade III diffuse axonal injury based on clinical and computed tomography findings and underwent subdural drainage and tracheostomy. During neurological recovery, the patient developed progressive agitation and was diagnosed with organic mental disorder following psychiatric consultation. Despite psychiatric treatment, severe agitation led to accidental self-removal of the tracheostomy tube, requiring repeat tracheostomy. Following a gradual improvement in behavioural symptoms, the patient was discharged with psychiatric medication, home tracheostomy care, and scheduled neurosurgical and psychiatric follow-up.

Discussion: Neuropsychiatric complications following pediatric grade III diffuse axonal injury remain underrecognized despite their potential impact on recovery. In this case, persistent agitation progressed to organic mental disorder, culminating in accidental self-removal of the tracheostomy tube, requiring repeat tracheostomy. This uncommon clinical course emphasises the importance of early psychiatric assessment and close collaboration between neurosurgical and psychiatric teams during neurological recovery.

Conclusion: This case demonstrates that the clinical spectrum of pediatric grade III diffuse axonal injury extends beyond severe neurological impairment to include neuropsychiatric complications. Early recognition of persistent behavioural changes and timely psychiatric evaluation may help prevent serious complications, including tracheostomy self-removal.

Keywords: Grade III diffuse axonal injury; Pediatric; Organic mental disorder; Agitation; Tracheostomy.

RESEARCH ARTICLE

TRIGEMINAL SCHWANNOMA: FEATURES OF DIAGNOSIS AND TREATMENT. A CASE REPORT

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Introduction: Trigeminal schwannoma is a rare benign intracranial tumour arising from Schwann cells of the trigeminal nerve. Owing to its slow growth and variable clinical manifestations, diagnosis is frequently delayed and may mimic other posterior fossa or cerebellopontine angle lesions. We report a petroclival trigeminal schwannoma presenting with atypical neurological symptoms, highlighting the diagnostic challenges and surgical management.

Case Presentation: A 56-year-old woman presented with a 5-year history of recurrent spinning dizziness accompanied by progressive hearing loss, ringing in the left ear, double vision, and gait disturbance. Initial neurological assessment suggested central vertigo secondary to suspected vertebrobasilar insufficiency. Cerebral computed tomography angiography demonstrated a left cerebellopontine angle mass initially suspected to be a meningioma. Contrast-enhanced magnetic resonance imaging subsequently identified a 3.59 × 3.32 × 3.80 cm petroclival mass arising from the left trigeminal nerve with active obstructive hydrocephalus, consistent with trigeminal schwannoma. The patient underwent tumour excision via a combined petrosal approach, and histopathological examination confirmed schwannoma. At follow-up, spinning dizziness, double vision, hearing loss, gait disturbance, and urinary symptoms improved markedly, although left peripheral facial nerve palsy persisted.

Discussion: Clinical manifestations of trigeminal schwannoma vary according to tumour size and extension and may occur without classic trigeminal symptoms. In this case, the absence of facial pain or sensory disturbance together with predominant vestibular and brainstem-related symptoms initially suggested an alternative diagnosis. Magnetic resonance imaging established the diagnosis, while combined petrosal tumour excision achieved favourable neurological recovery despite persistent facial nerve dysfunction.

Conclusion: This case demonstrates that a trigeminal schwannoma should be considered in patients with chronic progressive central vertigo and multiple cranial nerve deficits, even in the absence of typical trigeminal symptoms. Early recognition, appropriate magnetic resonance imaging, and timely microsurgical management are essential for achieving favourable neurological outcomes.

Keywords: Trigeminal schwannoma; Diagnostic challenge; Combined petrosal approach;

RESEARCH ARTICLE

BEYOND TYPICAL INTRACEREBRAL HEMORRHAGE: A CASE REPORT OF SIMULTANEOUS MULTIPLE INTRACEREBRAL HEMORRHAGES (SMICH)

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Background: Simultaneous Multiple Intracerebral Hemorrhages (SMICH) is an uncommon subtype of spontaneous intracerebral hemorrhage characterized by the presence of two or more acute hematomas occurring simultaneously in anatomically distinct brain regions. Representing only approximately 3.6–5.9% of all intracerebral hemorrhage cases, SMICH is associated with substantial morbidity and mortality. Early diagnosis, prompt blood pressure control, and comprehensive etiological evaluation are essential to optimize patient outcomes.

Methods: We report a descriptive case of a 52-year-old woman presenting with acute left-sided weakness, severe headache, paresthesia, and repeated projectile vomiting following a fall without direct head trauma. Clinical evaluation included neurological examination, National Institutes of Health Stroke Scale (NIHSS) assessment, routine laboratory investigations, chest radiography, and non-contrast computed tomography (CT) of the brain. Diagnostic findings were interpreted alongside current evidence regarding the pathophysiology, risk factors, diagnostic approach, and management of SMICH.

Results: On admission, the patient had a blood pressure of 180/100 mmHg, Glasgow Coma Scale score of 15, and an NIHSS score of 7, indicating moderate stroke severity. Neurological examination demonstrated left-sided motor weakness and hypoesthesia involving all branches of the trigeminal nerve. Brain CT revealed multiple acute intracerebral hemorrhages in the right basal ganglia with surrounding vasogenic edema, intraventricular hemorrhage involving both lateral ventricles, the third and fourth ventricles, and approximately 0.5 cm midline shift, confirming the diagnosis of SMICH. Clinical findings suggested uncontrolled hypertension as the most likely underlying etiology. The patient was managed with intensive blood pressure control, supportive therapy, close neurological monitoring, and multidisciplinary stroke care.

Conclusion: SMICH is a rare but life-threatening neurological emergency requiring rapid neuroimaging for diagnosis and immediate blood pressure optimization. Early identification of underlying etiologies, particularly hypertensive arteriopathy and cerebral amyloid angiopathy, combined with multidisciplinary management, is crucial to reduce neurological deterioration and improve functional outcomes.

REVIEW ARTICLE

CGRP-TARGETED THERAPIES FOR CHRONIC MIGRAINE PREVENTION : A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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Background: Chronic Migraine (CM) can be debilitating for many patients, with negative effects on physical, social, and occupational functioning, and a reduced health-related quality of life. The development of calcitonin gene-related peptide (CGRP)-targeting drugs has ushered in a new era for migraine therapy. The first class of treatment approved was monoclonal antibodies targeting CGRP or the CGRP-receptor (CGRP-mAbs) and a new generation of CGRP receptor antagonists (gepants) have been shown to be effective for the preventive treatment of migraine.

Methods: A systematic review were conducted following PRISMA guidelines. Comprehensive searches of PubMed, ScienceDirect, and Europe PMC were performed. Review included randomized controlled trials. Primary outcome was reduction in Monthly Migraine Days (MMD).

Results: A total of 13 randomized controlled trials involving approximately 9,000 participants with chronic migraine were included. CGRP-targeted therapies evaluated included fremanezumab, erenumab, galcanezumab, eptinezumab, and atogepant. Across studies, these therapies consistently demonstrated greater reductions in monthly migraine days and higher $\geq 50\%$ responder rates compared with placebo. Adverse events were generally mild to moderate, and serious adverse events and treatment discontinuations were uncommon. One eptinezumab trial conducted in patients with chronic migraine and medication-overuse headache did not achieve statistical significance for its primary endpoint.

Conclusion: CGRP-targeted therapies provide effective and well-tolerated preventive treatment for chronic migraine. The available evidence demonstrates consistent benefits in reducing migraine burden and improving patient-reported outcomes, supporting their role as an important therapeutic option in chronic migraine management.

Keywords: CGRP; Chronic Migraine; Migraine Prevention; Systematic Review

REVIEW ARTICLE

TARGETING DOPAMINE RESTORATION IN AADC DEFICIENCY: A SYSTEMATIC REVIEW OF INTRAPUTAMINAL AND MIDBRAIN AAV2 GENE THERAPY

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Background: Aromatic L-amino acid decarboxylase deficiency (AADCd) causes profound monoamine depletion, severe motor disability, oculogyric crises, and autonomic dysfunction. AAV2-mediated DDC gene therapy has been delivered to the putamen or midbrain dopaminergic nuclei, but comparative response patterns remain uncertain.

Methods: We systematically reviewed human studies of stereotactic AAV2-DDC/AADC gene therapy targeting the bilateral putamen or substantia nigra pars compacta/ventral tegmental area. Eligible reports included clinical trials, cohorts, long-term extensions, institutional series, and nonduplicative case reports. Full-text screening, patient-cohort mapping, and outcome extraction covered motor milestones, validated motor scores, oculogyric crises, biochemical and imaging responses, durability, and safety. Overlapping publications were retained only for unique outcomes.

Results: Twenty-one reports were included, comprising primary cohorts and companion procedural, imaging, biomarker, anesthetic, psychiatric, and safety reports. Intraputamenal therapy showed sustained gains in PDMS-2, AIMS, cognition, language, motor milestones, cerebrospinal-fluid homovanillic acid, and striatal fluorodopa uptake, with follow-up beyond 5 years. Midbrain delivery produced rapid oculogyric-crisis resolution, improved GMFM-88 scores, head control, sitting, supported walking, increased cerebrospinal-fluid homovanillic acid, and enhanced midbrain and striatal fluorodopa uptake. Transient dyskinesia was the most consistent treatment-emergent event. Neurosurgical complications were uncommon and usually self-limited. A secondary target-stratified analysis suggested a larger homovanillic-acid increase after midbrain delivery, but biomarker change did not significantly correlate with clinical improvement.

Conclusion: Both anatomical strategies produce clinically meaningful and durable neurological benefit. Current evidence is insufficient to establish target superiority because comparisons are indirect, nonrandomized, heterogeneous, and affected by overlapping cohorts.

Keywords: AADC deficiency; AAV2; eladocogene exuparvovec; gene therapy; putamen; substantia nigra.

REVIEW ARTICLE

MIDDLE MENINGEAL ARTERY EMBOLIZATION FOR SUBACUTE AND CHRONIC SUBDURAL HEMATOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED TRIALS

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Background: Middle meningeal artery embolization (MMAE) has emerged as a promising adjunctive and stand-alone treatment for symptomatic subacute and chronic subdural hematoma (SDH). However, evidence regarding its efficacy and safety compared with standard treatment remains limited. This systematic review and meta-analysis aimed to evaluate the efficacy and safety of MMAE compared to standard treatment in patients with symptomatic subacute and chronic SDH.

Methods: Following the PRISMA 2020 guidelines, four electronic databases were systematically searched from inception to July 18, 2026, for randomized controlled trials comparing MMAE with standard treatment in symptomatic subacute or chronic SDH. Risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool. The primary outcome was treatment failure. Secondary outcomes included all-cause mortality, stroke, and serious adverse events (SAEs). Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using fixed- or random-effects models according to statistical heterogeneity (I^2).

Results: Six randomized controlled trials involving 1,759 patients were included. Compared with standard treatment, MMAE significantly reduced treatment failure (RR 0.50, 95% CI 0.38–0.65; $I^2=0\%$) and serious adverse events (RR 0.83, 95% CI 0.70–0.98; $I^2=28\%$). No significant differences were observed in all-cause mortality (RR 0.66, 95% CI 0.28–1.57; $I^2=56\%$) or stroke (RR 1.19, 95% CI 0.40–3.49; $I^2=0\%$).

Conclusion: MMAE significantly reduced treatment failure and serious adverse events compared with standard treatment in patients with symptomatic subacute and chronic SDH, with no significant differences in all-cause mortality or stroke. These findings support MMAE as an effective and safe treatment strategy for symptomatic subacute and chronic SDH.

Keywords: Middle meningeal artery embolization; Chronic subdural hematoma; Nonacute subdural hematoma; Randomized controlled trials; Meta-analysis.

REVIEW ARTICLE

FLOW DIVERSION VERSUS COILING WITH OR WITHOUT STENTING FOR UNRUPTURED WIDE-NECK INTRACRANIAL ANEURYSMS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Conventional coiling of wide-neck intracranial aneurysms often leads to high recurrence rates. Flow diversion (FD) has emerged as an alternative for parent artery reconstruction, yet its comparative effectiveness and safety against coiling with or without stenting remain subjects of ongoing debate.

Methods: We conducted a systematic review and meta-analysis, including randomized controlled trials and propensity score-matched cohorts, were conducted following PRISMA guidelines. PubMed, Cochrane CENTRAL, and ScienceDirect databases were searched systematically until July 2026. Evaluated outcomes included long-term complete occlusion, immediate occlusion, retreatment, functional independence (mRS 0–2), and procedure-related complications.

Results: Results demonstrated that FD achieved significantly higher long-term complete occlusion rates than coiling (OR: 3.17; 95% CI: 1.90–5.30). Conversely, coiling was significantly more effective at achieving immediate complete occlusion following the procedure (OR: 0.11; 95% CI: 0.03–0.42). FD consistently lowered the risk of retreatment by 87% compared to the coiling group (OR: 0.13; 95% CI: 0.07–0.26). Subgroup analysis confirmed that the superior occlusion provided by FD was most prominent in aneurysms measuring ≥ 10 mm (OR: 6.09). No significant differences were observed between FD and coiling regarding functional independence (OR: 1.07), ischemic events (OR: 0.64), or hemorrhagic events (OR: 1.45).

Conclusion: FD provides superior long-term occlusion efficacy and a significant reduction in retreatment rates with a safety profile comparable to coiling, particularly for larger aneurysms. However, coiling remains more effective for achieving immediate post-procedural aneurysm exclusion.

Keywords: flow diversion, coiling, wide-neck aneurysm, unruptured

REVIEW ARTICLE

EXERCISE INTERVENTIONS ON ALZHEIMER'S DISEASE PLASMA BIOMARKERS IN HEALTHY AND COGNITIVELY IMPAIRED ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Alzheimer's Disease (AD) is increasingly diagnosed and monitored using blood-based biomarkers as a less invasive assessment. Physical exercise has been proposed as a promising modifiable factor influencing neurodegeneration, but its impact on the biomarkers remains unclear across cognitively healthy adults and those with mild cognitive impairment (MCI) or diagnosed with AD.

Methods: Randomized clinical trials (RCT) was searched through Pubmed and Cochrane. 10 RCTs were identified and assessed for bias using Cochrane RoB 2. Meta-analysis was done using Revman 5.4 software in which pooled A β 40, p-tau181, A β 42, BDNF, and A β 42/40 ratio were calculated.

Results: Pooled results indicated a null effect between exercise and AD plasma biomarkers. In healthy adults, pooled A β 40 (MD:0.16,95%CI:-3.60–3.91;p=0.93), A β 42 (MD:-0.06,95%CI:-0.34–0.23;p=0.71), A β 42/40 ratio (MD:0.00,95%CI:0.00–0.00;p=0.26), and p-tau181 results (MD:-0.00,95%CI:-0.19–0.19;p=0.99) lead to a null effect with low heterogeneity (I²=0–2%). This was similar in cognitively impaired adults. Pooled A β 42/40 ratio (MD:-0.00,95%CI:-0.00–0.00;p=0.32) with no heterogeneity (I²=0%), p-tau181 (MD:0.05,95%CI:-0.42–0.52;p=0.84) with moderate heterogeneity (I²=36%), and BDNF (MD:0.05,95%CI:-0.29–0.38;p=0.79) with low heterogeneity (I²=11%). Thus, no consistent evidence was found for exercise effect on AD plasma biomarkers in both healthy and cognitively impaired adults.

Conclusion: Due to the limited number of trials, results in pooled AD plasma biomarkers were statistically non-significant. Therefore, larger studies are needed to further assess the effect of exercise interventions on AD plasma biomarkers in healthy and cognitively impaired adults.

Keywords: Exercise, Alzheimer's Disease, plasma biomarkers, healthy adults, cognitively impaired adults

REVIEW ARTICLE

PROGNOSTIC VALUE OF THE BULBOCAVERNOSUS REFLEX IN CONUS MEDULLARIS AND CAUDA EQUINA LESIONS: A SYSTEMATIC REVIEW

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Background: Electrodiagnostic testing of the bulbocavernosus reflex (BCR) is well established for diagnosing conus medullaris and cauda equina lesions, but its prognostic value for functional recovery has not been systematically synthesized across etiologies.

Methods: A systematic review was conducted following a predefined protocol. Studies were eligible if BCR was assessed at a baseline or intraoperative timepoint distinct from outcome assessment, with the prognostic relationship explicitly reported and verified by full-text review. Screening was performed independently by two reviewers, and risk of bias was assessed using the QUIPS tool.

Results: Seven studies (combined N = 1,155) met eligibility criteria, spanning compressive cauda equina syndrome (n=1, N=40), traumatic spinal cord injury (n=1, N=769), neoplastic conus and cauda equina tumors (n=2, N=168), and congenital tethered cord (n=3, N=178). Prognostic performance varied markedly by etiology. In traumatic spinal cord injury, BCR status showed no association with neurological recovery at 6 months. In neoplastic tumors, intraoperative BCR amplitude reduction strongly predicted postoperative voiding dysfunction (AUC 0.976–0.996). In congenital tethered cord, BCR loss predicted worsened voiding function in non-lipomyelomeningocele patients (OR 11.04) but not in lipomyelomeningocele patients, with sensitivity across three pediatric studies ranging from 14.8% to 100%. A single study in classic compressive cauda equina syndrome reported perfect concordance between BCR status and 1-year bladder recovery, though based on a small sample. Risk-of-bias assessment identified recurring concerns in confounding adjustment and statistical precision.

Conclusion: The prognostic value of the bulbocavernosus reflex is etiology-dependent rather than uniform, strongest in neoplastic and non-lipomyelomeningocele congenital lesions, and absent in acute traumatic spinal cord injury.

Keywords: Bulbocavernosus reflex, Cauda equina syndrome, Conus medullaris, Prognosis, Electrodiagnosis

RESEARCH ARTICLE

**TRANSANAL VENTRICULOPERITONEAL SHUNT MIGRATION AFTER
TRANSANAL ENDORECTAL PULL-THROUGH IN AN INFANT WITH
HYDROCEPHALUS AND HIRSCHSPRUNG DISEASE**

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Background: Ventriculoperitoneal (VP) shunt migration with transanal extrusion is a rare but potentially life-threatening complication that may result in shunt failure, meningitis, ventriculitis, and recurrent hydrocephalus. Its occurrence after transanal endorectal pull-through (TAERPT) is exceedingly uncommon. We report a rare case of distal VP shunt migration with transanal extrusion following TAERPT in an infant with hydrocephalus and Hirschsprung disease.

Case Illustrations: A premature female infant born at 31 weeks and 5 days of gestation with a birth weight of 1,250 g developed non-communicating hydrocephalus secondary to aqueductal stenosis, presenting with seizures, macrocephaly, and sunset phenomenon. A VP shunt was inserted with neurological improvement. She was subsequently diagnosed with short-segment Hirschsprung disease and underwent TAERPT. On postoperative day 1, approximately 10 cm of the distal VP shunt catheter protruded through the anus with stool. Cerebrospinal fluid outflow during shunt chamber compression confirmed catheter continuity. Despite the absence of fever, peritonitis, neurological deterioration, or signs of raised intracranial pressure, abdominal radiography demonstrated distal catheter migration. Emergency shunt exploration revealed turbid cerebrospinal fluid, prompting complete shunt removal and culture sampling. No bowel perforation, anastomotic leak, abscess, or peritoneal contamination was identified. The patient remained neurologically stable without immediate shunt replacement.

Discussion: Catheter migration was likely multifactorial, with prematurity, low birth weight, malnutrition, and prior TAERPT as contributing factors. Postoperative changes in bowel motility and increased intra-abdominal pressure may have facilitated migration. Management is guided by clinical status. Clinically stable patients without peritonitis or central nervous system infection may undergo shunt removal without laparotomy.

Conclusion: Transanal extrusion of a distal VP shunt catheter after TAERPT is an exceptionally rare neurosurgical complication. Early recognition, multidisciplinary management, prompt shunt removal, and neurological surveillance are essential to prevent ascending infection and neurological morbidity.

Keywords: Hydrocephalus, ventriculoperitoneal shunt, transanal migration, hirschsprung disease

REVIEW ARTICLE

NEUROPHYSIOLOGICAL AND FUNCTIONAL BRAIN ALTERATIONS ASSOCIATED WITH SHORT-FORM VIDEO EXPOSURE: A SYSTEMATIC REVIEW OF FMRI, EEG, AND fNIRS EVIDENCE

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Background: Short-form video platforms increasingly dominate digital consumption, raising concerns about neurophysiological impacts. Using multimodal neuroimaging such as functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and functional near-infrared spectroscopy (fNIRS), this study comprehensively examines the neurophysiological effects of short-form video exposure on brain dynamics.

Methods: This study was conducted as a systematic review. Literature searches were performed in PubMed, ScienceDirect, Scopus, and Google Scholar. There are 12 eligible experimental and observational studies including young adults with short video exposure and reported outcomes such as fMRI, fNIRS, or EEG. Quality appraisal was conducted using the JBI Appraisal Tool.

Results: Multimodal evidence from EEG, fNIRS, and fMRI indicates that short-form video (SFV) exposure strongly engages the dopaminergic reward system, with personalized content enhancing VTA-DMN connectivity and reinforcing compulsive engagement. This reward activation is accompanied by reduced top-down control and altered resting-state activity, including deactivation of the dACC and dlPFC, changes in EEG microstates, increased amygdala and insula activity, reduced dlPFC activity, and disrupted DMN-CEN connectivity. These changes are associated with functional impairments in attention and executive control, reflected by altered P300, N200, theta-alpha activity, reduced prefrontal responses during risk decisions, impaired hippocampal-prefrontal connectivity, altered time perception, habit formation, and precuneus-related dissociation. Chronic SFV use is also associated with increased gray matter volume in the OFC and cerebellum and altered glutamatergic and GABAergic gene expression, suggesting persistent structural changes linked to SFV addiction.

Conclusion: SFV addiction may represent a progressive neurobiological cascade involving disrupted reward processing, impaired executive control, persistent baseline dysregulation, and structural remodeling, sharing neuroadaptive features with substance addiction.

Keywords: short-form video, neuroimaging, neurophysiology, brain dynamics, cognitive function