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Choosing Meaningful Endpoints in Thrombectomy Trials: A Practical Review of Outcome Scales After Endovascular Thrombectomy

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Abstract

Background— Endovascular thrombectomy (EVT) has expanded treatment for acute ischemic stroke. Outcome scales capturing disability, neurological deficit, imaging, safety, and patient-centered recovery are critical for interpreting trials.

Objectives— To summarize clinical, patient-reported, imaging, and safety scales relevant to EVT trials and provide a practical framework for trialists selecting primary, secondary, exploratory, and safety endpoints.

Methods— We conducted a narrative synthesis of landmark EVT trials, contemporary guidelines, common stroke outcome measures, and clinimetric studies. Scales were included if they had been used in EVT trials, were widely used in acute stroke research, or were clinically relevant to EVT populations.

Results— The modified Rankin Scale (mRS), particularly the blinded 90-day ordinal mRS, remains the standard primary endpoint for most definitive EVT trials. Its limitations include interrater variability, ceiling and floor effects, and limited sensitivity to cognition, fatigue, aphasia, depression, return to work, and other patient-valued outcomes. Common secondary clinical outcomes include dichotomized mRS cut points, utility-weighted mRS, return-to-baseline mRS, National Institutes of Health Stroke Scale, Barthel Index, Functional Independence Measure, mortality, and discharge destination. Patient-reported, imaging, and safety measures should be selected as targeted complementary endpoints according to the population, intervention, and hypothesized mechanism.

Conclusions— No single scale adequately captures recovery after EVT. A well-designed protocol should prespecify a clinically meaningful primary endpoint, usually the 90-day ordinal mRS, together with a focused set of early neurological, safety, supportive imaging, and selected patient-reported outcomes tailored to the target population and anticipated treatment effect.

Keywords— acute ischemic stroke; endovascular thrombectomy; outcome assessment; modified Rankin Scale; NIH Stroke Scale; quality of life; patient-reported outcomes; clinical trials.

INTRODUCTION

Endovascular thrombectomy (EVT) is standard treatment for selected patients with acute ischemic stroke caused by large-vessel occlusion and is increasingly studied in late-window, large-core, posterior-circulation, low National Institutes of Health Stroke Scale (NIHSS) score, premorbid-disability, and pediatric populations.[1,2] EVT trial interpretation depends heavily on outcome measurement. Technical success may not produce meaningful recovery, while a favorable global disability score may overlook aphasia, cognition, fatigue, depression, gait instability, or return to valued activities.

Landmark EVT trials established the modified Rankin Scale (mRS) at 90 days as the central endpoint. Early positive trials included Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the

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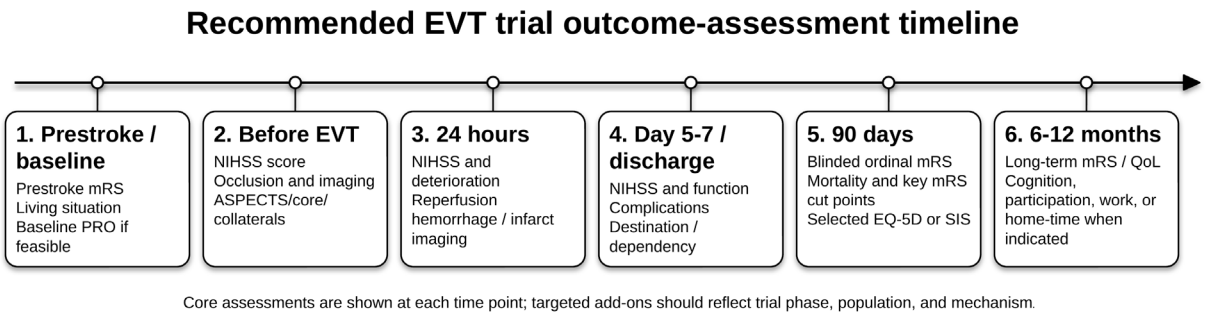


FIGURE 1: Recommended outcome-assessment timeline for EVT trials. The blinded 90-day ordinal mRS is the default primary endpoint for most definitive trials; other core and targeted assessments should be selected according to trial phase, population, and mechanism.
Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; EQ-5D, EuroQol 5-Dimension; EVT, endovascular thrombectomy; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PRO, patient-reported outcome; QoL, quality of life; SIS, Stroke Impact Scale.

Netherlands (MR CLEAN), Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing Computed Tomography (CT) to Recanalization Times (ESCAPE), Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial (EXTEND-IA), Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME), and Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours (REVASCAT); their patient-level synthesis by the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials collaboration paired mRS with neurological, imaging, and safety outcomes.[3–8] Diffusion-Weighted Imaging or Computed Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake-Up and Late-Presenting Strokes Undergoing Neurointervention With Trevo (DAWN) and Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE 3) expanded eligibility using clinical-imaging mismatch and perfusion selection. Large-core trials including Recovery by Endovascular Salvage for Cerebral Ultra-Acute Embolism–Japan Large Ischemic Core Trial (RESCUE-Japan LIMIT), A Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT2), Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients With a Large Infarct Core (ANGEL-ASPECT), Efficacy and Safety of Thrombectomy in Stroke With Extended Lesion and Extended Time Window (TENSION), Large Stroke Therapy Evaluation (LASTE), and Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke (TESLA) demonstrated the need for meaningful endpoints when baseline infarct burden is large.[9–16] The neutral medium-vessel occlusion trials, Endovascular Therapy Plus Best Medical Treatment Versus Best Medical Treatment Alone for Medium Vessel Occlusion Stroke (DISTAL) and Endovascular Treatment to Improve Outcomes for Medium Vessel Occlusions (ESCAPE-MeVO), similarly show that technical success or favorable early signals may not yield measurable 90-day disability benefit.[17,18]

This review summarizes trial-relevant outcome measures for patients undergoing EVT and aims to help investigators build a coherent endpoint framework linking treatment mechanism, clinically meaningful recovery, and safety.

METHODS

This narrative review drew on landmark randomized EVT trials, contemporary acute ischemic stroke guidelines, outcome-methodology publications, and clinimetric studies. We included measures used in EVT trials or broader acute stroke research; measures relevant to EVT populations, imaging-defined injury, or reperfusion safety; and measures capturing domains poorly represented by global disability scales.

Measures were organized into six categories: global disability and function; neurological impairment; activities of daily living (ADL) and rehabilitation; patient-reported quality of life and participation; domain-specific recovery; and imaging and safety. The tables serve as an endpoint-selection guide rather than a formal evidence ranking.

Table 1 maps primary-endpoint use across landmark and contemporary randomized EVT trials. mRS formulations dominate primary efficacy assessment; NIHSS score-based early improvement, imaging, quality-of-life, ADL, and hemorrhage measures are usually coprimary, secondary, selection, mechanistic, or safety endpoints. Basilar-artery and medium-vessel occlusion trials are included because they used different mRS formulations.[17–22]

Conceptual approach to outcome selection in thrombectomy trials

Outcome measures should answer three questions: Did the patient survive and recover meaningfully? Did neurological impairment improve early? Did imaging findings, hemorrhage, edema, procedural complications, or other adverse events explain benefit or harm?

These questions require a limited core battery. Most definitive trials should include prestroke mRS, baseline NIHSS and imaging severity, 24-hour neurological and hemorrhage assessments, discharge or day 5-7 function, and blinded 90-day ordinal mRS. Targeted patient-reported, domain-specific, imaging, or longer-term measures should be added only when justified by the population, intervention, or mechanism (Figure 1).

TABLE 1: Primary-endpoint use of reviewed scales in landmark and contemporary EVT randomized trials.

Scale or endpoint formulation	EVT trials using the scale as a primary or coprimary endpoint	Endpoint form and interpretation
Modified Rankin Scale (mRS), ordinal/ global disability	MR CLEAN;[3] ESCAPE;[4] SWIFT PRIME;[6] REVASCAT;[7] DEFUSE 3;[10] SELECT2;[12] ANGEL-ASPECT;[13] TENSION;[14] LASTE;[15] DISTAL.[17]	Usually assessed at 90 days as the full 0-6 mRS distribution, shift, or score; the dominant primary efficacy endpoint in EVT RCTs.
Dichotomized mRS 0-1, excellent functional outcome	ESCAPE-MeVO.[18]	Used when excellent recovery is clinically plausible or expected, such as medium-vessel or mild-deficit populations.
Dichotomized mRS 0-2, functional independence	SWIFT PRIME[6] (primary success criterion); DAWN[9] (coprimary).	Intuitive responder endpoint; frequently secondary in ordinal-mRS trials and useful for communicating independence.
Dichotomized mRS 0-3, favorable functional outcome or independent ambulation	RESCUE-Japan LIMIT;[11] BEST;[19] BASICS;[20] ATTENTION;[21] BAOCHE.[22]	Common in large-core or basilar-artery occlusion trials in which mRS 0-2 may be too restrictive to capture meaningful benefit.
Utility-weighted mRS	DAWN;[9] TESLA.[16]	Preference-weighted disability outcome used as a primary or coprimary endpoint in selected late-window or large-core designs.
NIHSS-based early neurological improvement	EXTEND-IA[5] (coprimary).	NIHSS component defined as major improvement or near-complete neurological recovery by day 3; 24-hour reperfusion was the paired coprimary imaging endpoint.
NIHSS alone or ordinal 24-hour NIHSS	No pivotal EVT efficacy RCT in this review used NIHSS alone as the sole primary endpoint.	Promising early response or surrogate measure; best suited to early efficacy, deterioration, and safety interpretation.
Barthel Index, FIM, and other ADL/ dependency scales	No landmark EVT efficacy RCT in this review used these as the primary endpoint.	Typically secondary, rehabilitation, discharge, or care-burden measures.
EQ-5D, Stroke Impact Scale, SS-QOL, PROMIS, Neuro-QoL	No landmark EVT efficacy RCT in this review used these patient-reported scales as the primary endpoint.	Important secondary or long-term endpoints for health utility, QALY, participation, and patient-centered recovery.
Domain-specific scales: MoCA, PHQ-9, aphasia, motor, balance, gait, fatigue	No pivotal EVT efficacy RCT in this review used these as primary endpoints.	Best suited to substudies, rehabilitation trials, and recovery studies targeting specific deficits.
ASPECTS, pc-ASPECTS, infarct-core volume, final infarct volume, infarct growth, collateral and thrombus-burden scores	No reviewed pivotal EVT RCT used these imaging scales as the primary clinical efficacy endpoint.	Primarily selection, stratification, prognostic, or mechanistic measures; should be paired with clinical endpoints.
Hemorrhage classifications, sICH definitions, and mortality	Frequently used as primary or key safety endpoints; examples include BASICS, BAOCHE, TESLA, and LASTE.[15,16,20,22]	Safety endpoints should be prespecified separately from the primary efficacy endpoint.

Abbreviations: ADL, activities of daily living; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; EQ-5D, EuroQol 5-Dimension; EVT, endovascular thrombectomy; FIM, Functional Independence Measure; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin Scale; Neuro-QoL, Quality of Life in Neurological Disorders; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior-circulation Alberta Stroke Program Early Computed Tomography Score; PHQ-9, Patient Health Questionnaire-9; PROMIS, Patient-Reported Outcomes Measurement Information System; QALY, quality-adjusted life-year; RCT, randomized controlled trial; sICH, symptomatic intracranial hemorrhage; SS-QOL, Stroke-Specific Quality of Life Scale.

Acronyms: ANGEL-ASPECT, Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients With a Large Infarct Core; ATTENTION, Endovascular Treatment for Acute Basilar-Artery Occlusion; BAOCHE, Basilar Artery Occlusion Chinese Endovascular Trial; BASICS, Basilar Artery International Cooperation Study; BEST, Endovascular Treatment Versus Standard Medical Treatment for Vertebrobasilar Artery Occlusion; DAWN, Diffusion-Weighted Imaging or Computed Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake-Up and Late-Presenting Strokes Undergoing Neurointervention With Trevo; DEFUSE 3, Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3; DISTAL, Endovascular Therapy Plus Best Medical Treatment Versus Best Medical Treatment Alone for Medium Vessel Occlusion Stroke; ESCAPE, Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing Computed Tomography to Recanalization Times; ESCAPE-MeVO, Endovascular Treatment to Improve Outcomes for Medium Vessel Occlusions; EXTEND-IA, Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial; LASTE, Large Stroke Therapy Evaluation; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; RESCUE-Japan LIMIT, Recovery by Endovascular Salvage for Cerebral Ultra-Acute Embolism–Japan Large Ischemic Core Trial; REVASCAT, Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours; SELECT2, A Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke; SWIFT PRIME, Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment; TENSION, Efficacy and Safety of Thrombectomy in Stroke With Extended Lesion and Extended Time Window; TESLA, Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke. The table summarizes the landmark and contemporary randomized EVT trials emphasized in this review and is not intended to replace a trial-registry search for device-performance or workflow trials.

Global disability and functional-outcome scales

The mRS is the most widely used global disability scale in acute ischemic stroke trials and is scored from 0 (no symptoms) to 6 (death).[23] Structured interviews improve reliability and are recommended, particularly in multicenter trials and blinded endpoint assessment.[24]

For most definitive EVT trials, the strongest default primary endpoint is blinded 90-day ordinal mRS. Ordinal analysis preserves all seven categories, whereas dichotomized endpoints are clinically intuitive but lose information.[25] mRS 0-2 indicates functional independence, mRS 0-1 indicates an excellent outcome, and mRS 5-6 indicates severe disability or death. In large-core, posterior-circulation, elderly, or premorbid-disability populations, mRS 0-3, return to baseline, or sliding dichotomy may better reflect benefit.

Utility-weighted mRS assigns preference-based values to mRS states, retaining the familiar scale while incorporating patient utility.[26] Because weights vary across studies and value sets, they and the analytic assumptions should be prespecified.

Other global scales, including the Oxford Handicap Scale, Glasgow Outcome Scale, and Extended Glasgow Outcome Scale, are less common in modern EVT trials. They may be useful for cross-condition comparisons, severe brain-injury contexts, or pragmatic registries, but they are not substitutes for mRS in pivotal EVT studies.

Neurological impairment scales

The NIHSS score is the core acute neurological impairment measure, quantifying consciousness, gaze, visual fields, facial and limb strength, ataxia, sensation, language, dysarthria, and neglect.[27] EVT trials use it for baseline severity, eligibility, stratification, early response, deterioration, and safety classification.

NIHSS score is valuable after EVT because effects may appear within hours. Early neurological improvement is often defined as an 8- to 10-point decrease or NIHSS score 0-1 or 0-2; deterioration is commonly defined as a 4-point increase and often informs symptomatic intracranial hemorrhage (sICH) definitions. Definitions vary and should be prespecified.

NIHSS score does not replace mRS as a definitive outcome. Low scores may coexist with disabling aphasia, hemianopia, neglect, gait instability, cognitive impairment, or fatigue, and posterior-circulation disability may be underrepresented. Early NIHSS score may nevertheless serve as a phase II endpoint. Modified NIHSS score, Scandinavian Stroke Scale, Canadian Neurological Scale, European Stroke Scale, Orgogozo Scale, pediatric NIHSS, and Glasgow Coma Scale may suit specific settings but are rarely primary EVT outcomes.

Activities of daily living, rehabilitation, and dependency scales

The Barthel Index is a 10-item ADL scale that measures independence in feeding, transfers, grooming, toileting, bathing, mobility, stairs, dressing, bowel control, and bladder control. It is simple, familiar, and useful for describing care needs, but it has ceiling effects in mild stroke and floor effects in severe stroke.

The Functional Independence Measure (FIM) is a broader 18-item rehabilitation measure spanning motor and cognitive domains. It provides granular information about assistance needs but is longer and less practical for hyperacute, multinational EVT trials. Other ADL or mobility measures, including the Katz ADL, Lawton instrumental ADL scale, Functional Ambulation Categories, Rivermead Mobility Index, and Rivermead Motor Assessment, can help characterize recovery trajectories, especially when rehabilitation or discharge planning is a major focus.

Discharge destination, need for institutional care, home-time, and caregiver burden are not scales in the narrow psychometric sense, but they are frequently paired with ADL measures because they translate disability into health-system and family consequences. These endpoints are especially relevant for pragmatic EVT, rehabilitation, or health-economic studies. The clinical, disability, neurological, ADL, and dependency measures discussed above are summarized in Table 2.

Patient-reported outcomes and health-related quality of life

Patient-reported outcomes address the major limitation of clinician-rated scales: patients with the same mRS score may differ substantially in pain, fatigue, mood, social participation, communication, cognition, and perceived recovery. The EuroQol 5-Dimension (EQ-5D) is the most common generic health-utility instrument in stroke research and is useful for cost-effectiveness analyses and quality-adjusted life-year estimates.

Stroke-specific patient-reported instruments include the Stroke Impact Scale (SIS) and the Stroke-Specific Quality of Life Scale (SS-QOL). The SIS measures strength, hand function, mobility, communication, emotion, cognition, and participation, whereas SS-QOL additionally covers energy, family and social roles, self-care, vision, and work or productivity.[28]

Selection should be purpose-driven. EQ-5D suits health-utility or cost-effectiveness analyses; SIS or SS-QOL suits multidomain stroke-specific recovery. The Patient-Reported Outcomes Measurement Information System and Quality of Life in Neurological Disorders offer item-bank and short-form measures across physical, mental, and social domains and are useful for digital or standardized neurological follow-up. The 36-Item Short Form Survey and 12-Item Short Form Survey enable cross-condition comparisons but may be less sensitive to stroke-specific recovery domains than SIS or SS-QOL.

TABLE 2: Patient-centered clinical, disability, and neurological outcome scales used or applicable in EVT trials.

Scale	Construct and scoring	Typical EVT trial role	Strengths	Limitations
Modified Rankin Scale (mRS)	Global disability, 0 to 6, with 6 indicating death.	Primary 90-day outcome; prestroke baseline; long-term follow-up.	Simple, familiar, accepted by trialists and regulators; spans complete disability spectrum.	Coarse; interrater variability; limited sensitivity to cognition, mood, fatigue, participation, and quality of life.
Ordinal mRS shift	Analysis of all mRS categories.	Preferred primary analysis in many definitive EVT trials.	Preserves information and increases statistical efficiency.	Requires prespecified ordinal model and proportional-odds considerations.
Dichotomized mRS	Common cut points include 0-1, 0-2, 0-3, 5-6, or return to baseline.	Secondary endpoint; sometimes primary in specific populations.	Clinically intuitive and easy to communicate.	Discards information; thresholds may be inappropriate for large-core or premorbid-disability populations.
Utility-weighted mRS	mRS categories transformed to health-utility values.	Patient-centered and health-economic analyses; selected trial designs.	Adds preference weighting while preserving familiar scale.	Utility weights vary by study and value set; assumptions must be prespecified.
Sliding dichotomy / responder analysis	Good outcome threshold varies by baseline severity or prestroke disability.	Heterogeneous severity or premorbid-disability trials.	More individualized than fixed mRS cut points.	More complex; thresholds require prespecification and justification.
NIHSS	Neurological impairment, 0 to 42; higher is worse.	Baseline severity; eligibility; early response; deterioration; sICH definitions.	Sensitive to early treatment effect; widely validated.	Not a direct measure of independence; underweights some posterior-circulation deficits.
Early neurological improvement	NIHSS improvement threshold, often >=8-10 points, or NIHSS 0-1/0-2.	Secondary early efficacy endpoint at 24 hours or day 5-7.	Captures rapid early treatment response.	Definitions vary; can be confounded by baseline severity.
Early neurological deterioration	Often NIHSS worsening >=4 points.	Safety endpoint; sICH component.	Clinically important and feasible.	Attribution to hemorrhage, edema, reocclusion, or medical complications can be difficult.
Barthel Index	Basic ADL scale, commonly 0 to 100; higher indicates greater independence.	Secondary functional and care-dependency outcome.	Simple and interpretable.	Ceiling effects in mild stroke; floor effects in severe stroke.
Functional Independence Measure (FIM)	18 motor and cognitive items, total 18 to 126.	Rehabilitation, discharge, and care-burden studies.	More granular than Barthel Index.	Longer; training/licensing considerations; less practical for hyperacute trials.
Other functional scales	Oxford Handicap Scale, Glasgow Outcome Scale, Extended Glasgow Outcome Scale, Katz ADL, Lawton IADL, Rivermead Mobility Index, Functional Ambulation Categories.	Historical studies, rehabilitation studies, pragmatic registries, special populations.	May capture specific care needs or mobility domains.	Less standardized than mRS/NIHSS in pivotal adult EVT trials.
Patient-reported quality-of-life instruments	EQ-5D, Stroke Impact Scale, Stroke-Specific Quality of Life Scale, PROMIS, Neuro-QoL, SF-36, and SF-12.	Secondary and long-term outcomes; health utility, quality-adjusted life-year, participation, and patient-centered recovery.	Captures recovery domains not reflected by mRS or NIHSS.	May be limited by aphasia, cognition, proxy response, language availability, and follow-up burden.
Domain-specific recovery instruments	MoCA, PHQ-9, aphasia, motor, balance, gait, fatigue, and participation measures.	Cognitive substudies, rehabilitation trials, recovery trials, and low-NIHSS or posterior-circulation studies.	Captures specific deficits that may persist despite favorable global disability scores.	Requires trained assessors and may not be feasible as a primary endpoint in pivotal EVT trials.

Abbreviations: ADL, activities of daily living; EQ-5D, EuroQol 5-Dimension; EVT, endovascular thrombectomy; FIM, Functional Independence Measure; IADL, instrumental activities of daily living; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin Scale; Neuro-QoL, Quality of Life in Neurological Disorders; NIHSS, National Institutes of Health Stroke Scale; PHQ-9, Patient Health Questionnaire-9; PROMIS, Patient-Reported Outcomes Measurement Information System; SF-12, 12-Item Short Form Survey; SF-36, 36-Item Short Form Survey; sICH, symptomatic intracranial hemorrhage; SS-QOL, Stroke-Specific Quality of Life Scale. The table summarizes representative clinical and patient-centered outcome measures relevant to EVT trials.

Cognition, mood, aphasia, fatigue, motor recovery, and mobility

Cognitive impairment, depression, anxiety, fatigue, aphasia, and mobility limitations can profoundly affect recovery after EVT even when mRS is favorable. The Montreal Cognitive Assessment is a widely used cognitive screening instrument and has been evaluated in stroke populations. More detailed neuropsychological batteries are preferable when cognition is a prespecified recovery domain, but they are harder to implement in global acute EVT trials.

Post-stroke depression and anxiety should be considered when quality of life or long-term recovery is important. The Patient Health Questionnaire-9 is a pragmatic depression screening tool after stroke, and the American Heart Association/American Stroke Association scientific statement on post-stroke depression highlights the clinical importance of screening and management. Other measures include the Patient Health Questionnaire-2, Hospital Anxiety and Depression Scale, Beck Depression Inventory, Geriatric Depression Scale, and Center for Epidemiologic Studies Depression Scale.

Language, motor, and mobility instruments are most relevant for recovery, neuroprotection, and rehabilitation substudies. The Western Aphasia Battery, Fugl-Meyer Assessment, Action Research Arm Test, Motricity Index, Motor Assessment Scale, Berg Balance Scale, Timed Up and Go, 10-meter walk test, 6-minute walk test, and Functional Ambulation Categories can characterize domain-specific recovery. These instruments are rarely appropriate as primary endpoints for pivotal thrombectomy device trials, but they are valuable when domain-specific recovery is central to the hypothesis.

Imaging selection and imaging outcome scales

Imaging scales are used for trial eligibility, stratification, mechanistic interpretation, and safety assessment. The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) is a 10-point noncontrast CT score for early ischemic change in the anterior circulation and remains one of the most important imaging measures in EVT trials.[29] Lower ASPECTS indicates larger established ischemic injury and is particularly important in large-core trial design.

Posterior-circulation EVT requires different imaging measures. The posterior-circulation ASPECTS (pc-ASPECTS) adapts the ASPECTS concept to basilar and posterior-circulation ischemia and is useful for posterior-circulation prognosis and trial interpretation.

Collateral scores quantify alternative blood supply and influence infarct growth, EVT benefit, and prognosis. Single-phase and multiphase computed tomography angiography collateral scores provide noninvasive assessment, while clot-burden scores quantify thrombus extent. Additional posterior-circulation tools include the Basilar Artery on Computed Tomography Angiography Prognostic Score (BATMAN), which incorporates thrombus burden and collateral quality.

Quantitative imaging endpoints include infarct-core volume, penumbral volume, mismatch ratio, final infarct volume, infarct growth, edema or mass effect, and hemorrhagic transformation. These endpoints are essential in mechanistic, neuroprotection, imaging-selection, and large-core trials, but they require standardized acquisition, central reading, and prespecified thresholds. Imaging may be primary or coprimary in early-phase or device-feasibility studies; in definitive efficacy trials, it should support rather than replace a patient-centered clinical primary endpoint.

Hemorrhage and safety outcome scales

EVT safety assessment requires both radiographic and clinical measures. European Cooperative Acute Stroke Study (ECASS) hemorrhagic transformation categories distinguish hemorrhagic infarction types 1 and 2 from parenchymal hematoma types 1 and 2. The Heidelberg Bleeding Classification was developed to harmonize bleeding-event definitions after ischemic stroke and reperfusion therapy, including thrombolysis and thrombectomy.[30]

sICH is not a single scale. It is a family of definitions combining radiographic hemorrhage with neurological deterioration, timing, and attribution. Common definitions include the National Institute of Neurological Disorders and Stroke, ECASS II/III, Safe Implementation of Thrombolysis in Stroke-Monitoring Study, and Heidelberg definitions.[30] Because reported sICH rates can vary by definition, EVT trials should prespecify a primary sICH definition and, when feasible, report additional definitions to support comparison across studies.

Other essential safety outcomes include all-cause mortality, stroke-related mortality, neurological deterioration, malignant edema, decompressive hemicraniectomy, recurrent ischemic stroke, embolization to a new territory, arterial perforation, dissection, vasospasm requiring treatment, access-site complications, contrast reactions, and serious adverse events. Safety outcomes should be adjudicated by blinded committees whenever feasible. Imaging and safety scales relevant to thrombectomy trials are summarized in Table 3.

Outcome-scale choices for special EVT populations

Large-core trials illustrate why endpoint choice matters. With extensive baseline infarction, mRS 0-2 may be too strict; ordinal mRS, mRS 0-3, return to baseline, mortality, institutionalization, quality of life, and caregiver burden may better capture benefit.[11–16] In elderly or frail populations, prestroke function, residence, cognition, quality of life, and caregiver burden are important secondary descriptors.

Low-NIHSS score large-vessel occlusion EVT trials require caution because deficits may be mild or fluctuating. mRS 0-2 may be insensitive when many untreated patients do well; worsening, rescue thrombectomy, return to baseline, cognition, language, vision, hand function, and patient-reported outcomes may be more informative.

TABLE 3: Imaging and safety scales used in EVT trials.

Category	Scale or definition	Construct	Typical EVT use	Key cautions
Baseline ischemic extent	ASPECTS, pc-ASPECTS.	Early ischemic changes on CT or CTA source images.	Eligibility, stratification, prognosis, large-core and posterior-circulation trials.	Reader training and modality differences affect reliability.
Quantitative tissue injury	Core volume, final infarct volume, infarct growth, edema/mass effect.	Tissue injury and treatment mechanism.	Neuroprotection, large-core, imaging-selection, and mechanistic trials.	Requires standardized imaging protocol and central analysis.
Collateral status	Menon multiphase CTA score, Tan, Miteff, Maas/rLMC, collateral ASPECTS.	Alternative blood supply and collateral timing on noninvasive imaging.	Eligibility, effect modification, prognosis.	Phase timing, acquisition protocol, and interrater variability matter.
Thrombus burden	Clot burden score, thrombus length, BATMAN score.	Occlusion extent and posterior-circulation burden/collaterals.	Baseline severity, prognosis, device-strategy substudies.	Mostly prognostic or stratification measures rather than patient-centered endpoints.
Radiographic hemorrhage	ECASS HI1, HI2, PH1, PH2; Heidelberg Bleeding Classification.	Hemorrhagic transformation and post-treatment bleeding.	Safety imaging endpoint.	Timing, imaging modality, and attribution rules must be specified.
Symptomatic hemorrhage	NINDS, ECASS II/III, SITS-MOST, Heidelberg sICH definitions.	Hemorrhage plus clinical deterioration.	Primary or key safety endpoint.	Rates differ by definition; prespecify primary definition and report alternatives when feasible.
Procedural safety	Perforation, dissection, embolization to new territory, vasospasm requiring treatment, access-site complication.	Procedure-related adverse events.	Device and strategy trials.	Requires standardized event definitions and blinded adjudication when possible.

Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; BATMAN, Basilar Artery on Computed Tomography Angiography Prognostic Score; CT, computed tomography; CTA, computed tomography angiography; ECASS, European Cooperative Acute Stroke Study; EVT, endovascular thrombectomy; HI1/HI2, hemorrhagic infarction types 1 and 2; NINDS, National Institute of Neurological Disorders and Stroke; pc-ASPECTS, posterior-circulation Alberta Stroke Program Early CT Score; PH1/PH2, parenchymal hematoma types 1 and 2; rLMC, regional leptomeningeal collateral score; sICH, symptomatic intracranial hemorrhage; SITS-MOST, Safe Implementation of Thrombolysis in Stroke-Monitoring Study.

TABLE 4: Practical endpoint-selection framework by EVT trial population or research question.

Trial population or question	Preferred primary endpoint	Core secondary clinical endpoints	Key imaging and safety endpoints	Additional recommended domains
Conventional adult anterior-circulation LVO	Blinded 90-day ordinal mRS.	mRS 0-2, mRS 0-1, mortality, NIHSS at 24 hours and day 5-7, EQ-5D.	sICH, hemorrhage classification, infarct volume, infarct growth, edema, procedural complications.	Barthel Index or FIM, discharge destination, home-time.
Large-core anterior-circulation stroke	Ordinal mRS; consider mRS 0-3 or UW-mRS as key secondary/coprimary.	Mortality, severe disability/death, return to baseline, institutionalization, quality of life.	ASPECTS/core volume, final infarct volume, infarct growth, edema, ICH.	Caregiver burden, home-time, decompressive hemicraniectomy.
Late-window or imaging-selected EVT	Ordinal 90-day mRS.	mRS 0-2, NIHSS response, EQ-5D.	Core-penumbra mismatch, infarct growth, collaterals, sICH.	Longer-term mRS and quality of life.
Posterior-circulation or basilar occlusion	Ordinal mRS; consider mRS 0-3 depending on severity.	Mortality, GCS, NIHSS, swallowing, ventilation/tracheostomy, gait/balance.	pc-ASPECTS, BATMAN, ICH, edema.	Dysphagia, diplopia/vision, gait, cognition, quality of life.
Low-NIHSS LVO	Ordinal mRS or utility/sliding endpoint tailored to baseline severity.	Worsening, rescue EVT, return to baseline, NIHSS item-level deficits.	Occlusion persistence on follow-up imaging, infarct growth, sICH.	Language, vision, hand function, cognition, patient-reported outcomes.
Premorbid disability or frailty	Ordinal mRS adjusted for prestroke status or return to baseline.	Living situation, mortality, severe disability, EQ-5D/proxy QoL.	ICH, infarct growth, edema, complications.	Caregiver burden, institutionalization, home-time.
Pediatric EVT	Age-appropriate functional outcome; mRS or pediatric functional scales as appropriate.	Pediatric NIHSS score, neurological recovery, mortality, school/participation outcomes.	ICH, infarct volume, edema, complications.	Pediatric quality of life, cognition, language, family impact.

Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; BATMAN, Basilar Artery on Computed Tomography Angiography Prognostic Score; EQ-5D, EuroQol 5-Dimension; EVT, endovascular thrombectomy; FIM, Functional Independence Measure; GCS, Glasgow Coma Scale; LVO, large-vessel occlusion; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior-circulation Alberta Stroke Program Early CT Score; QoL, quality of life; sICH, symptomatic intracranial hemorrhage; UW-mRS, utility-weighted modified Rankin Scale.

Posterior-circulation EVT trials should not rely solely on anterior-circulation scales. NIHSS score can underrepresent diplopia, dysphagia, truncal ataxia, vertigo, and fluctuating consciousness. Useful additions include the Glasgow Coma Scale, pc-ASPECTS, BATMAN, swallowing outcomes, gait and balance measures, ventilator dependence, tracheostomy, and mRS. Basilar-artery occlusion trials commonly use mRS 0-3 as a favorable-outcome threshold.[19–22]

Trials enrolling patients with prestroke disability should measure prestroke mRS and consider return-to-baseline, ordinal shift adjusted for baseline status, living situation, quality of life, and caregiver outcomes. Pediatric EVT research should use age-appropriate neurological, functional, and quality-of-life measures and should align with pediatric stroke guidance where available.[1]

Practical recommendations for EVT trial outcome batteries

For a conventional adult anterior-circulation large-vessel occlusion EVT trial, the recommended primary endpoint is blinded 90-day ordinal mRS. Key secondary clinical endpoints should include mRS 0-2, mRS 0-1, mRS 0-3 when appropriate, mortality, return to baseline, 24-hour and day 5-7 NIHSS, early neurological improvement, early neurological deterioration, discharge destination, and at least one quality-of-life measure such as EQ-5D.

Key imaging and safety endpoints should include ASPECTS or pc-ASPECTS, infarct-core and final infarct volumes when available, infarct growth, collateral status, edema or mass effect, hemorrhage classification, procedural complications, and mortality. Key safety endpoints should include sICH, any intracranial hemorrhage, parenchymal hematoma, neurological deterioration, malignant edema, recurrent stroke, serious adverse events, and death.

Endpoint definitions and roles should be prespecified in the protocol and statistical analysis plan. Reports should identify assessors and blinding, assessment windows, handling of death, missing data, intercurrent events, and prestroke disability, patient and proxy-response rules, and central imaging adjudication. Each endpoint should have a clear clinical, mechanistic, or safety purpose to limit follow-up burden and multiplicity. Suggested outcome batteries by thrombectomy trial population or research question are summarized in Table 4.

Statistical considerations

The statistical approach should be prespecified and aligned with the anticipated treatment effect. Ordinal analysis of the 90-day mRS retains information across the full disability distribution, whereas dichotomized analyses provide clinically intuitive secondary outcomes. When a proportional-odds model is used, the proportional-odds assumption should be assessed. Sliding dichotomy and utility-weighted mRS are alternative approaches for selected populations, provided thresholds or weights are defined in advance.[25,26]

Death should remain the worst mRS category rather than being treated as missing data. Reasons for missing 90-day outcomes should be documented, and their handling should be prespecified and examined in sensitivity analyses. Secondary endpoints should be ordered hierarchically or addressed using an appropriate multiplicity strategy; otherwise, they should be labeled exploratory.

Limitations of current outcome scales

The mRS is robust, familiar, and efficient, but it is coarse, susceptible to interrater variability, and vulnerable to ceiling and floor effects. Structured interviews and centralized blinded adjudication improve reliability but do not capture cognition, fatigue, aphasia, depression, return to work, participation, or patient preference.[24,25]

NIHSS is sensitive to early treatment effects but is not a measure of independence or quality of life. It is also anatomically biased toward certain anterior-circulation deficits and may underrepresent posterior-circulation disability. Barthel Index and FIM describe assistance needs but have their own feasibility and ceiling or floor limitations. Patient-reported outcomes add important information but can be limited by aphasia, cognition, proxy response, language availability, and follow-up burden.

Imaging scales are necessary mechanistic endpoints but remain surrogates. Favorable imaging findings do not guarantee good clinical outcome, and poor outcome may reflect established infarction, poor collaterals, hemorrhage, edema, comorbidity, age, frailty, or postprocedural care. Conversely, a clinical endpoint alone cannot determine whether an imaging-selection strategy, workflow intervention, adjunctive therapy, or recovery intervention succeeded mechanistically.

Future directions

Future EVT trials are likely to use richer endpoint frameworks, including hierarchical composite outcomes, win-ratio designs, utility-weighted disability, home-time, patient-reported digital follow-up, automated imaging measures, and domain-specific recovery batteries triggered by stroke location. These innovations should complement, not prematurely replace, the 90-day mRS unless they are validated, interpretable, and acceptable to patients, regulators, clinicians, and trialists.

Greater harmonization of mRS terminology, sICH definitions, imaging adjudication, and patient-reported outcomes would improve trial comparability and evidence synthesis.

CONCLUSION

Outcome measurement in thrombectomy trials must connect clinical recovery, tissue response, and safety. The blinded 90-day ordinal mRS remains the most defensible primary endpoint for most definitive adult EVT trials, but it cannot capture every dimension of recovery. A modern EVT trial should combine mRS with NIHSS, ADL or dependency measures, patient-reported quality-of-life instruments, imaging severity and infarct-growth measures, and standardized hemorrhage and safety outcomes. The optimal endpoint battery depends on the treatment question, stroke territory, baseline infarct burden, prestroke function, expected mechanism, and

recovery domains most meaningful to patients.

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