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# MECHANICAL THROMBECTOMY FOR MEDIUM- AND DISTAL-VESSEL OCCLUSION AFTER NEUTRAL WESTERN TRIALS AND POSITIVE ORIENTAL-MEVO: PRECISION IMAGING, PROCEDURAL RISK, AND SELECTIVE REPERFUSION

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**Abstract**

**Background.** Mechanical thrombectomy for medium- and distal-vessel occlusion stroke entered an evidentiary phase after the neutral or harmful ESCAPE-MeVO, DISTAL, and DISCOUNT trials were followed by the positive ORIENTAL-MeVO trial. The discordance suggests that treatment effect depends on deficit severity, vessel anatomy, tissue viability, reperfusion probability, and procedural risk rather than occlusion location alone.

**Materials and methods.** A narrative review synthesized randomized trials, prospective cohorts, technical studies, meta-analyses, and protocols published through July 2026. Evidence was organized by anatomical definition, clinical severity, imaging selection, intravenous thrombolysis, device strategy, reperfusion quality, hemorrhagic risk, and external validity. A multicenter randomized protocol is proposed for adults with disabling medium- or distal-vessel occlusion, favorable imaging, and technically accessible anatomy.

**Results.** ESCAPE-MeVO and DISTAL failed to improve 90-day disability, while DISCOUNT was stopped early because thrombectomy did not demonstrate superiority and increased hemorrhagic complications. ORIENTAL-MeVO, which enrolled patients with moderate-to-severe deficits and favorable imaging, increased functional independence but increased symptomatic intracranial hemorrhage. These findings support selective rather than routine thrombectomy. The proposed primary endpoint is a utility-weighted 90-day modified Rankin Scale integrating functional benefit, symptomatic hemorrhage, and mortality. Secondary endpoints include early neurological improvement, reperfusion grade, infarct growth, cognitive and language outcomes, quality of life, procedural complications, rescue therapy, and cost-effectiveness. Originality derives from individualized benefit–risk estimation and external validation.

**Conclusion.** Medium- and distal-vessel thrombectomy should be evaluated as a precision reperfusion strategy. Future trials must enrich for disabling deficits, viable tissue, favorable access, and high probability of complete reperfusion while accounting for procedural harm.

**Keywords:** acute ischemic stroke, medium-vessel occlusion, distal-vessel occlusion, mechanical thrombectomy, endovascular treatment, reperfusion, cerebral perfusion, symptomatic intracranial hemorrhage, patient selection.

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# МЕХАНИЧЕСКАЯ ТРОМБЭКТОМИЯ ПРИ ОККЛЮЗИЯХ СРЕДНИХ И ДИСТАЛЬНЫХ ЦЕРЕБРАЛЬНЫХ СОСУДОВ ПОСЛЕ НЕЙТРАЛЬНЫХ ЗАПАДНЫХ ИССЛЕДОВАНИЙ И ПОЛОЖИТЕЛЬНОГО ORIENTAL-MEVO: ПРЕЦИЗИОННАЯ ВИЗУАЛИЗАЦИЯ, ПРОЦЕДУРНЫЙ РИСК И СЕЛЕКТИВНАЯ РЕПЕРФУЗИЯ

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**Аннотация**

**Актуальность.** Механическая тромбэктомия при окклюзиях средних и дистальных церебральных сосудов вступила в новую доказательную фазу после нейтральных или неблагоприятных результатов ESCAPE-MeVO, DISTAL и DISCOUNT и положительного исследования ORIENTAL-MeVO. Такое расхождение показывает, что лечебный эффект определяется не только локализацией окклюзии, но также тяжестью дефицита, сосудистой анатомией, жизнеспособностью ткани, вероятностью реперфузии и процедурным риском.

**Материалы и методы.** Выполнен нарративный обзор рандомизированных исследований, проспективных когорт, технических работ, метаанализов и протоколов, опубликованных до июля 2026 года. Доказательства систематизированы по анатомическому определению, клинической тяжести, визуализационному отбору, внутривенному тромболизису, выбору устройств, качеству реперфузии, геморрагическому риску и внешней валидности. Предложен многоцентровый рандомизированный протокол для взрослых пациентов с инвалидизирующей окклюзией среднего или дистального сосуда, благоприятной визуализационной картиной и технически доступной анатомией.

**Результаты.** ESCAPE-MeVO и DISTAL не улучшили инвалидизацию через 90 дней, тогда как DISCOUNT был досрочно прекращен из-за отсутствия превосходства тромбэктомии и увеличения геморрагических осложнений. ORIENTAL-MeVO включал пациентов с умеренным или тяжелым дефицитом и благоприятной визуализацией; тромбэктомия повысила функциональную независимость, но сопровождалась увеличением симптомного внутричерепного кровоизлияния. Эти данные поддерживают селективное, а не рутинное вмешательство. Предлагаемая первичная конечная точка представляет собой взвешенную по клинической полезности модифицированную шкалу Рэнкина через 90 дней, объединяющую функциональную пользу, симптомное кровоизлияние и летальность. Вторичные показатели включают раннее неврологическое улучшение, степень реперфузии, рост инфаркта, когнитивные и речевые исходы, качество жизни, процедурные осложнения, спасительное лечение и экономическую эффективность. Научная оригинальность заключается в индивидуальной оценке ожидаемой пользы, вероятности технического успеха и риска сосудистого повреждения с обязательной независимой внешней валидацией модели.

**Заключение.** Тромбэктомию следует рассматривать как прецизионную реперфузионную стратегию с обязательным индивидуальным расчетом пользы и риска каждого пациента.

**Ключевые слова:** острый ишемический инсульт, окклюзия среднего сосуда, дистальная сосудистая окклюзия, механическая тромбэктомия, эндоваскулярное лечение, реперфузия, церебральная перфузия, симптомное внутричерепное кровоизлияние, отбор пациентов.

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## NEYTRAL G‘ARB TADQIQOTLARI VA IJOBIY ORIENTAL-MEVO SINOVIDAN KEYIN O‘RTA HAMDA DISTAL MIYA TOMIRLARI OKKLYUZIYASIDA MEXANIK TROMBEKTOMIYA: ANIQ NEYROVIZUALIZATSIYA, PROTSEDURAVIY XAVF VA SELEKTIV REPERFUZIYA

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SamDTU huzuridagi neyroxirurgiya va neyroreabilitatsiya ixtisoslashtirilgan ilmiy-amaliy markazi

**Annotatsiya**

**Dolzarblik.** O‘rta va distal miya tomirlari okklyuziyasida mexanik trombektomiya ESCAPE-MeVO, DISTAL va DISCOUNT tadqiqotlarining neytral yoki salbiy natijalari hamda ORIENTAL-MeVO sinovining ijobiy xulosalaridan keyin yangi daliliy bosqichga kirdi. Ushbu tafovut davolash samarasi faqat okklyuziya joylashuviga emas, balki nevrologik nuqson og‘irligi, tomir anatomiyasi, to‘qima hayotchanligi, reperfuziya ehtimoli va muolaja xavfiga bog‘liqligini ko‘rsatadi.

**Material va usullar.** 2026-yil iyuligacha chop etilgan randomizatsiyalangan tadqiqotlar, prospektiv kohortlar, texnik ishlar, metatahlillar va protokollar asosida narrativ sharh bajarildi. Dalillar anatomik ta'rif, klinik og'irlik, neyrovizualizatsion tanlov, vena ichiga tromboliz, qurilma strategiyasi, reperfuziya sifati, gemorragik xavf va tashqi validlik bo'yicha tizimlashtirildi. Nogironlikka olib keluvchi o'rta yoki distal tomir okklyuziyasi, qulay tasviriy profil va texnik jihatdan kirish mumkin bo'lgan anatomiyaga ega kattalar uchun ko'p markazli randomizatsiyalangan protokol taklif etildi.

**Natijalar.** ESCAPE-MeVO va DISTAL 90 kunlik funksional natijalarni yaxshilamadi, DISCOUNT esa ustunlik aniqlanmagani va gemorragik asoratlar ko'paygani sababli muddatidan oldin to'xtatildi. ORIENTAL-MeVO o'rtacha yoki og'ir nevrologik nuqsonli va qulay tasviriy belgilar mavjud bemorlarni qamrab olib, funksional mustaqillikni oshirdi, biroq simptomatik intrakranial qon ketishini ham ko'paytirdi. Ushbu natijalar rutin emas, selektiv trombektomiyani qo'llab-quvvatlaydi. Birlamchi yakuniy nuqta funksional foyda, simptomatik qon ketish va o'limni birlashtiruvchi, klinik foyda bo'yicha vaznlantirilgan 90 kunlik modifikatsiyalangan Rankin shkalasidir. Ikkilamchi ko'rsatkichlar erta nevrologik yaxshilanish, reperfuziya darajasi, infarkt o'sishi, kognitiv va nutqiy natijalar, hayot sifati, protseduraviy asoratlar, qutqaruvchi davolash va iqtisodiy samaradorlikni o'z ichiga oladi. Ilmiy yangilik kutilayotgan foyda, texnik muvaffaqiyat va tomir shikastlanishi xavfini birgalikda modellashtirish hamda modelni mustaqil tashqi tekshirishdan iborat.

**Xulosa.** Trombektomiya har bir bemorda foyda va xavfni individual baholovchi aniq reperfuzion strategiya sifatida qo'llanishi lozim.

**Kalit so'zlar:** o'tkir ishemik insult, o'rta tomir okklyuziyasi, distal tomir okklyuziyasi, mexanik trombektomiya, endovaskulyar davolash, reperfuziya, serebral perfuziya, simptomatik intrakranial qon ketishi, bemorlarni tanlash.

**Introduction.** Mechanical thrombectomy transformed the management of acute ischemic stroke caused by proximal large-vessel occlusion. Randomized trials conducted during the previous decade established that rapid endovascular reperfusion improves functional outcome in selected patients with occlusion of the intracranial internal carotid artery or proximal middle cerebral artery. Subsequent investigations expanded treatment into late time windows, basilar-artery occlusion, and large ischemic cores. The consistency of these advances created an expectation that thrombectomy would also benefit patients with occlusions involving smaller and more distal cerebral arteries [6, 7, 21, 22]. Medium- and distal-vessel occlusions are clinically heterogeneous. They include dominant or nondominant M2 middle cerebral artery branches, M3 and M4 branches, anterior cerebral artery segments, posterior cerebral artery segments, and, in some definitions, cerebellar arteries. Vessel caliber, vascular tortuosity, eloquence of the supplied cortex, collateral circulation, clot length, thrombus composition, and technical accessibility vary considerably among these anatomical territories. A distal occlusion affecting the dominant hemisphere may produce severe aphasia despite a moderate total National Institutes of Health Stroke Scale score, whereas another occlusion of similar diameter may cause a relatively minor nondisabling sensory deficit [7, 8, 9]. The terminology itself has clinical consequences. The expression "medium-vessel occlusion" emphasizes vessel caliber, whereas "distal-vessel occlusion" emphasizes the anatomical distance from the proximal arterial trunk. These concepts overlap but are not identical. A large dominant M2 branch may be anatomically distal to the M1 segment but have a diameter and tissue territory closer to those of a conventional large vessel. Conversely, an A2 or P2 occlusion may involve a relatively small vessel but produce disabling cognitive, visual, memory, behavioral, or language dysfunction that is incompletely represented by routine stroke scales [7, 10, 14]. Before randomized evidence became available, observational registries and meta-analyses suggested that distal thrombectomy was technically feasible and could achieve high rates of angiographic reperfusion. The HERMES analysis of M2 occlusions also suggested benefit from thrombectomy, particularly in proximal or dominant M2 lesions. However, most participants in the original large-vessel trials had relatively proximal M2 occlusions, and the subgroup data could not be extrapolated automatically to M3, M4, anterior cerebral, posterior cerebral, or very small nondominant branches [7, 8, 21].

The biological rationale for distal thrombectomy appeared compelling. Persistent arterial occlusion causes progressive infarction, and pharmacological reperfusion is less reliable when thrombi are longer, more fibrin-rich, or located in vessels with limited collateral inflow. Modern low-profile aspiration catheters, mini-stent retrievers, flexible microcatheters, and improved guidewires permit access to vessels that were previously considered too small or tortuous. Nevertheless, technical accessibility does not prove net clinical benefit. Distal vessels have thin walls, greater tortuosity, smaller lumens, and a reduced tolerance for traction, perforation, dissection, vasospasm, and subarachnoid hemorrhage. The volume of tissue at risk is also generally smaller, reducing the maximum potential benefit against which procedural harm must be balanced [7, 9, 10]. The randomized evidence published in 2025 challenged the assumption that successful reperfusion would necessarily translate into improved outcome. ESCAPE-MeVO and DISTAL did not demonstrate a favorable shift in 90-day disability with endovascular treatment. ESCAPE-MeVO additionally showed higher mortality and more symptomatic intracranial hemorrhage in the thrombectomy group. The interim analysis of DISCOUNT was unfavorable and led to early termination, with lower rates of functional independence and increased hemorrhagic events among patients assigned to thrombectomy [1, 2, 3]. These results initially appeared to define a limit for the expansion of mechanical thrombectomy. However, the interpretation changed again in 2026. ORIENTAL-MeVO enrolled patients with moderate-to-severe deficits, an NIHSS score of at least 6, favorable imaging characteristics, and treatment within 24 hours. In this more selected population, thrombectomy increased the proportion of patients achieving functional independence at 90 days, although symptomatic intracranial hemorrhage remained numerically more frequent [4, 6, 16]. The apparent contradiction does not necessarily mean that one set of trials was correct and the other incorrect. The trials examined overlapping but nonidentical populations, imaging paradigms, healthcare systems, intravenous thrombolysis rates, occlusion distributions, procedural techniques, and outcome structures. A treatment with substantial heterogeneity of effect may fail in a broad population while benefiting a narrower subgroup with a high untreated risk and favorable procedural anatomy. The central question is therefore no longer whether every medium- or distal-vessel occlusion should undergo thrombectomy. The relevant question is which combination of clinical deficit, tissue-at-risk profile, vascular anatomy, time window, thrombolytic response, and procedural expertise produces a positive individual benefit–risk balance.

**Materials and Methods.** A structured narrative review was performed using studies published through July 2026. Eligible evidence included randomized controlled trials, prospective cohort studies, prespecified trial protocols, post hoc imaging analyses, thrombectomy-technique studies, systematic reviews, meta-analyses, consensus documents, and clinically relevant device investigations.

The principal randomized evidence consisted of ESCAPE-MeVO, DISTAL, DISCOUNT, and ORIENTAL-MeVO. The 12-month follow-up of DISTAL was also considered to determine whether a delayed functional benefit emerged after the neutral 90-day analysis. Earlier M2 subgroup data from the HERMES collaboration were reviewed to clarify the distinction between proximal dominant M2 occlusion and more distal arterial disease [1, 2, 3, 4, 5, 8]. Evidence was organized into the following domains: anatomical classification, baseline clinical severity, disabling deficit phenotype, pretreatment imaging, collateral status, intravenous thrombolysis, time from last known well, device selection, reperfusion grade, first-pass effect, procedural complications, functional outcomes, mortality, cognitive outcomes, quality of life, and generalizability. For anatomical classification, medium- or distal-vessel occlusion was defined as an isolated occlusion involving a nondominant or codominant M2 branch, M3 or M4 middle cerebral artery branch, A1–A3 anterior cerebral artery segment, or P1–P3 posterior cerebral artery segment. Dominant proximal M2 occlusions were analyzed separately because their natural history and potential treatment effect may approximate those of conventional large-vessel occlusion.

A prospective multicenter randomized trial is proposed as the original research component. Eligible adults would have an isolated medium- or distal-vessel occlusion confirmed by computed-tomographic angiography or magnetic-resonance angiography, a disabling neurological deficit, a prestroke modified Rankin Scale score of 0–2, and a favorable imaging profile. A disabling deficit

would be defined functionally rather than exclusively by total NIHSS score and could include severe aphasia, hemianopia preventing independent activity, disabling neglect, profound hand weakness, gait-limiting leg weakness, or a syndrome threatening occupational independence. The proposed imaging criteria would require either limited established infarction involving less than one third of the affected functional territory or a perfusion mismatch demonstrating salvageable tissue. Collateral status, clot length, vessel diameter, branching angle, arterial tortuosity, and distance from the guide-catheter position would be recorded prospectively.

Participants would be randomly assigned to thrombectomy plus best medical therapy or best medical therapy alone. Intravenous thrombolysis with alteplase or tenecteplase would be administered whenever indicated and would not be delayed by trial enrollment. The endovascular procedure would use a predefined distal-access strategy, with the first-line device selected according to vessel diameter, clot position, and arterial tortuosity. The primary endpoint would be a utility-weighted modified Rankin Scale at 90 days. The utility model would apply penalties for symptomatic intracranial hemorrhage, procedure-related subarachnoid hemorrhage, vessel perforation, and death, thereby preventing a modest functional benefit from obscuring clinically important harm.

Secondary endpoints would include ordinal modified Rankin Scale distribution, functional independence, excellent outcome, early neurological improvement, change in NIHSS score, final eTICI reperfusion grade, first-pass eTICI 2c–3 reperfusion, infarct-volume growth, cognitive function, language outcome, visual disability, quality of life, mortality, procedural complications, length of hospitalization, rehabilitation requirement, and cost-effectiveness. A central imaging core laboratory would adjudicate occlusion location, collateral status, baseline infarct volume, perfusion mismatch, reperfusion grade, embolization to new territory, subarachnoid hemorrhage, and final infarct volume. Outcome assessors would remain blinded to treatment allocation. The statistical model would test for interaction between treatment and baseline NIHSS score, deficit phenotype, intravenous thrombolysis, occlusion location, vessel diameter, collateral grade, perfusion mismatch, and predicted reperfusion probability.

**Results.** The potential benefit of thrombectomy is determined by more than the name of the occluded artery. A proximal dominant M2 occlusion may compromise a large proportion of the middle cerebral artery territory and produce severe aphasia, gaze deviation, hemiparesis, or neglect. In contrast, an occlusion of a small nondominant M3 branch may threaten a limited cortical territory and carry a high probability of spontaneous or thrombolysis-mediated recovery. Anterior cerebral artery occlusion can produce leg-predominant weakness, abulia, executive dysfunction, urinary incontinence, or callosal disconnection. Posterior cerebral artery occlusion may cause homonymous hemianopia, alexia, memory impairment, thalamic dysfunction, or dominant temporal deficits. These syndromes can be highly disabling despite modest NIHSS scores because the scale underweights cognition, visual processing, memory, and higher cortical behavior [7, 9, 10]. This heterogeneity creates a dilution problem in randomized trials. When patients with severe disabling syndromes are combined with patients who already have a high likelihood of favorable outcome under medical treatment, a genuine benefit in the former group may be offset by procedural harm in the latter. Broad anatomical eligibility is therefore scientifically attractive but may be therapeutically inefficient.

**Randomized Trial Evidence.** ESCAPE-MeVO randomized 530 patients presenting within 12 hours with acute ischemic stroke due to a medium-vessel occlusion and favorable baseline imaging. Endovascular treatment did not improve the primary 90-day functional outcome. Excellent functional outcome, defined as an mRS score of 0–1, occurred in 41.6% of patients assigned to thrombectomy and 43.1% assigned to usual care. Mortality was higher in the endovascular group, and symptomatic intracranial hemorrhage occurred more frequently after thrombectomy [1, 6, 13]. DISTAL randomized patients with isolated medium- or distal-vessel occlusion within 24 hours. The included arterial locations were broad and encompassed nondominant or codominant M2, M3, M4, anterior cerebral, and posterior cerebral artery occlusions. Endovascular treatment did not produce a favorable shift in the modified Rankin Scale at 90 days compared with best medical treatment.

Successful angiographic reperfusion was achieved in most treated patients, but technical reperfusion did not translate into measurable population-level functional benefit [2, 5, 11].

The prespecified 12-month analysis of DISTAL did not reveal a delayed benefit. Disability or death remained similar between the thrombectomy and medical-treatment groups. This finding reduces the likelihood that the neutral 90-day result merely reflected insufficient recovery time or delayed rehabilitation effects [2, 5, 11]. DISCOUNT evaluated mechanical thrombectomy plus best medical therapy against medical therapy alone in primary isolated medium- or distal-vessel occlusion. The trial was stopped early after an interim analysis. Functional independence was less frequent in the thrombectomy group, while symptomatic intracranial hemorrhage and other adverse events were more common. The completed publication in July 2026 reinforced the concern that routine intervention in an insufficiently enriched distal-occlusion population can produce net harm [3, 6, 12]. ORIENTAL-MeVO differed materially from the earlier trials. It enrolled 563 patients at 48 centers in China with moderate-to-severe neurological deficits, defined by an NIHSS score of at least 6, and favorable tissue imaging. Functional independence at 90 days occurred in 58.6% of the thrombectomy group and 46.6% of the medical-management group. The adjusted rate ratio was 1.24, indicating a statistically significant benefit. Symptomatic intracranial hemorrhage occurred in 4.7% and 2.2%, respectively, while mortality was similar [4, 6, 16]. The positive ORIENTAL-MeVO result does not invalidate ESCAPE-MeVO, DISTAL, or DISCOUNT. Rather, it indicates that treatment effect is heterogeneous and that selection based on greater neurological severity and favorable imaging may identify a subgroup with sufficient potential benefit to overcome procedural risk.

**Table 1. Comparison of the principal randomized trials**

| Trial | Population and window | Main selection characteristics | Principal result | Major safety signal | Interpretation |
|---|---|---|---|---|---|
| **ESCAPE-MeVO** | Medium-vessel occlusion within 12 hours; 530 patients | Favorable baseline imaging; heterogeneous deficit severity | No improvement in 90-day outcome; mRS 0–1: 41.6% versus 43.1% | Higher mortality and symptomatic intracranial hemorrhage with thrombectomy | Routine thrombectomy was not beneficial |
| **DISTAL** | Medium or distal occlusion within 24 hours; 543 patients | Broad anatomical inclusion; many patients with moderate deficits | No favorable shift in 90-day mRS | Procedural hemorrhage and vessel injury remained relevant | Technical reperfusion did not produce clinical benefit |
| **DISCOUNT** | Primary isolated medium or distal occlusion; stopped early | Broad distal-occlusion population | No superiority; functional independence numerically worse with thrombectomy | Increased symptomatic hemorrhage and adverse events | Insufficiently selected intervention may cause net harm |
| **ORIENTAL-MeVO** | Medium-vessel occlusion within 24 hours; 563 patients | NIHSS ≥6, favorable tissue profile, moderate-to-severe deficits | Functional independence: 58.6% versus 46.6% | Symptomatic intracranial hemorrhage: 4.7% versus 2.2% | Selective thrombectomy can benefit enriched patients |

| | | | | | |
|---|---|---|---|---|---|
| **DISTAL 12-month analysis** | Long-term follow-up of randomized cohort | Same original randomized population | No delayed reduction in disability or death | No evidence of late compensatory benefit | Neutral result persisted longitudinally |

**Explaining the Discordant Results.** Baseline neurological severity is one of the most plausible effect modifiers. Patients with a minor nondisabling deficit have less room for improvement and may recover with intravenous thrombolysis, collateral circulation, or spontaneous recanalization. Even a technically successful procedure may not improve their final mRS score, whereas vessel perforation or hemorrhage can convert a minor stroke into severe disability. Patients with moderate-to-severe deficits have a higher untreated risk. If the neurological syndrome is anatomically concordant with the occluded vessel and viable tissue remains, successful reperfusion can prevent a clinically meaningful infarct. ORIENTAL-MeVO required an NIHSS score of at least 6, whereas the neutral trials enrolled broader severity distributions. This enrichment increased the expected absolute benefit of reperfusion [1, 2, 3, 4]. The NIHSS score should not be used mechanically. A patient with isolated global aphasia, disabling hemianopia, severe neglect, or loss of dominant-hand function may have a score below 6 but face permanent occupational and social dependence. Conversely, a score above 6 may result partly from preexisting disability, metabolic disturbance, seizure, or a deficit not explained by the target occlusion. Future selection should combine quantitative severity with functional and anatomical concordance. Imaging selection also differed. The therapeutic target is not the clot itself but viable, functionally important tissue threatened by persistent occlusion. Noncontrast CT may underestimate early distal-territory ischemia, while automated perfusion software can be unreliable in small cortical regions because of motion, delay correction, limited spatial resolution, and arterial-input-function errors.

Multiphasic CTA, collateral assessment, CT perfusion, diffusion-weighted MRI, and perfusion-weighted MRI can provide complementary information. A small established infarct with a substantial eloquent penumbra represents a more rational target than a completed infarct or a tiny noneloquent perfusion deficit. Imaging should also determine whether the detected occlusion truly explains the clinical syndrome. Collateral circulation modifies both natural history and time sensitivity. Good collaterals can preserve tissue but may also increase spontaneous recovery and reduce the incremental benefit of intervention. Poor collaterals increase the risk of infarct progression but may leave little salvageable tissue by the time reperfusion is achieved. The optimal candidate may therefore have intermediate or good collaterals that preserve tissue without making medical recovery highly probable [4, 13, 14]. Intravenous thrombolysis is another important modifier. Distal thrombi may have higher pharmacological recanalization rates than proximal large-vessel occlusions because they are shorter and exposed to thrombolytic agents from multiple collateral pathways. If a large proportion of control patients receives early effective thrombolysis, the incremental value of thrombectomy decreases. However, waiting to document thrombolytic failure can consume the therapeutic window. A rational strategy is immediate intravenous thrombolysis when indicated, combined with rapid transfer to the angiography suite for patients with severe disabling deficits and a high risk of persistent occlusion. Repeat noninvasive angiography may be considered when transport or preparation time permits, particularly in patients with milder symptoms or high expected thrombolytic responsiveness.

**Imaging-Based Precision Selection.** An optimal imaging framework should answer four questions. First, is the arterial occlusion real and technically accessible? Second, does the occlusion explain the neurological deficit? Third, is functionally important tissue still viable? Fourth, is the volume of salvageable tissue large enough to justify the procedural risk? CTA should be reconstructed in thin slices and evaluated in multiple planes because small branch occlusions can be overlooked on thick maximum-intensity projections. Multiphase CTA can improve detection by demonstrating delayed filling and collateral asymmetry. Perfusion maps should be interpreted visually in conjunction with source images rather than relying entirely on an automated numerical threshold.

Vessel diameter and branching geometry should be reported. A 2.5-mm dominant M2 branch is fundamentally different from a 1.2-mm tortuous M4 branch, even when both are categorized as medium or distal occlusions. Distal access becomes more hazardous as the vessel narrows, the number of curves increases, and the target lies farther from the guide catheter. The ischemic territory should be evaluated according to eloquence rather than volume alone. A small infarct affecting the dominant inferior frontal gyrus, precentral hand area, primary visual cortex, hippocampal structures, or strategic thalamic nuclei may cause disproportionate disability. Tissue-weighted utility maps may eventually improve selection beyond conventional core and penumbra volumes.

**Table 2. Proposed precision-selection domains**

| Selection domain | Features favoring thrombectomy | Features favoring medical management |
|---|---|---|
| **Clinical severity** | NIHSS ≥6, progressive deficit, severe aphasia, neglect, disabling hand or leg weakness | Minor nondisabling deficit, rapidly improving symptoms |
| **Clinical–anatomical concordance** | Deficit clearly explained by occluded artery | Occlusion incidental or discordant with examination |
| **Tissue viability** | Small established infarct, meaningful mismatch, eloquent tissue at risk | Completed infarction, absent mismatch, minimal threatened territory |
| **Vessel anatomy** | Proximal M2, A1–A2, P1–P2, adequate diameter, limited tortuosity | Very distal M4/A4/P4, extreme tortuosity, severe stenosis |
| **Collaterals** | Preserved tissue with ongoing perfusion deficit | Complete spontaneous reperfusion or irreversible tissue injury |
| **Thrombolysis** | Contraindication to IV thrombolysis or persistent severe deficit despite treatment | Early major improvement after thrombolysis |
| **Procedural probability** | Experienced operator, dedicated low-profile devices, high predicted eTICI 2c–3 rate | Low-volume center, difficult access, low probability of complete reperfusion |
| **Hemorrhagic risk** | Limited infarct, controlled pressure, no major coagulopathy | Large established infarct, severe coagulopathy, fragile distal anatomy |
| **Patient-centered impact** | Threat to independence, communication, vision, occupation, or dominant-hand function | Deficit unlikely to alter independent daily activity |

**Device Strategy and Reperfusion Quality.** Distal thrombectomy demands a different technical philosophy from proximal large-vessel thrombectomy. The primary objective should be atraumatic complete reperfusion with the fewest possible device passes. Repeated manipulation in a small vessel increases endothelial injury, vasospasm, perforation, dissection, and subarachnoid hemorrhage. Direct aspiration, mini-stent retrievers, and combined techniques are all technically feasible. Aspiration avoids crossing the clot with a retriever and may reduce traction on distal branches, but catheter advancement can straighten or displace fragile vessels. The aspiration catheter must have sufficient internal diameter to generate effective suction while remaining flexible enough to navigate the distal anatomy. Mini-stent retrievers can engage compact thrombi in small branches but require crossing the lesion with a microwire and microcatheter. Excessive device diameter or radial force may damage the arterial wall. Slow controlled retrieval, reduced traction, distal aspiration support, and careful fluoroscopic monitoring are essential.

Observational comparisons have produced inconsistent conclusions regarding the optimal first-line technique. Some cohorts have shown higher first-pass and complete-reperfusion rates with direct aspiration, whereas others have supported combined strategies. These data are vulnerable to confounding by anatomy and operator preference. Difficult tortuous cases are more likely to receive combined techniques, creating an apparent disadvantage unrelated to the device itself [15, 19, 20]. Reperfusion grading also requires refinement. In a small distal territory, eTICI 2b may leave a substantial proportion of the threatened tissue unreperfused. Complete or near-complete reperfusion, eTICI 2c–3, may be more relevant than the conventional threshold of eTICI 2b–3. First-pass complete reperfusion is particularly desirable because each additional attempt increases delay and vessel trauma [14, 15, 17, 18]. Post hoc analyses suggest that patients who achieve excellent reperfusion may have better outcomes than those with incomplete or failed procedures. However, this does not prove that assigning a patient to thrombectomy is beneficial, because procedural success cannot be known before treatment and failed attempts contribute to the intention-to-treat result. Future trials must improve preprocedural prediction of complete reperfusion rather than analyzing only successful cases.

**Procedural Harm.** The principal procedural hazards are vessel perforation, arterial dissection, vasospasm, subarachnoid hemorrhage, symptomatic intraparenchymal hemorrhage, embolization to a new territory, distal embolization, and groin or access-site complications. Distal vessels are more susceptible to perforation because the microwire tip may enter an unseen branch or move during respiration and catheter manipulation. Subarachnoid contrast extravasation after distal thrombectomy may be small but is not necessarily benign. Blood within cortical sulci can cause seizure, vasospasm, headache, neurological worsening, and delayed ischemia. Procedure-related hemorrhage must be distinguished from hemorrhagic transformation of the original infarct. The safety findings of ESCAPE-MeVO and DISCOUNT demonstrate that procedural complications can neutralize or exceed the potential benefit of reperfusion. A distal thrombectomy program should therefore monitor not only final recanalization but also first-pass success, number of passes, device-to-vessel ratio, fluoroscopy time, perforation, subarachnoid hemorrhage, embolization, and neurological worsening [1, 3, 6, 10]. Operator and center experience are likely to modify outcomes. A high-volume neurointerventional center with dedicated distal devices, advanced biplane imaging, experienced anesthesia support, and standardized rescue protocols may achieve a different risk profile from a center that performs such procedures infrequently. External validity should therefore include both expert and nonexpert settings, but early efficacy trials may require credentialing to ensure that device failure does not obscure biological benefit.

**Patient-Centered Outcomes.** The modified Rankin Scale remains the standard global disability measure, but it may miss domain-specific benefit. Restoration of language, visual fields, memory, executive function, or dominant-hand control may be highly meaningful without changing the mRS category. Conversely, a patient may achieve an mRS score of 2 while remaining unable to return to professional work. Future trials should include language testing, visual-field assessment, neglect measures, cognitive screening, return to work, instrumental activities of daily living, quality of life, and patient-defined goal attainment. Outcome instruments should be selected according to the vascular territory. Posterior cerebral artery occlusion requires visual and memory outcomes; anterior cerebral artery occlusion requires executive and gait assessment; dominant M2 occlusion requires detailed language evaluation. A utility-weighted outcome can integrate functional improvement and serious harm. For example, a one-category mRS improvement should not be interpreted identically in a patient who experiences an asymptomatic petechial hemorrhage and a patient who develops symptomatic subarachnoid hemorrhage requiring prolonged intensive care.

**Table 3. Proposed multicenter precision-thrombectomy trial**

| Component | Proposed specification |
|---|---|
| **Population** | Adults with isolated medium- or distal-vessel occlusion and a disabling anatomically concordant deficit |
| **Clinical entry** | NIHSS ≥6 or a prespecified disabling low-NIHSS syndrome |
| **Imaging entry** | Small established infarct plus salvageable eloquent tissue |

| | |
|---|---|
| **Time window** | Within 12 hours routinely; 12–24 hours with perfusion or diffusion mismatch |
| **Intervention** | Dedicated distal thrombectomy plus best medical therapy |
| **Comparator** | Best medical therapy, including intravenous thrombolysis when indicated |
| **Primary endpoint** | Utility-weighted 90-day modified Rankin Scale incorporating symptomatic hemorrhage and mortality |
| **Secondary endpoints** | Ordinal mRS, functional independence, cognitive and language outcomes, vision, quality of life, return to work |
| **Technical endpoints** | First-pass eTICI 2c–3, final eTICI 2c–3, number of passes, time to reperfusion |
| **Safety endpoints** | Symptomatic intracranial hemorrhage, subarachnoid hemorrhage, perforation, dissection, embolization, death |
| **Imaging analysis** | Central adjudication of occlusion, collaterals, infarct core, mismatch, vessel diameter, and tortuosity |
| **Key interaction analyses** | NIHSS, disabling deficit type, IV thrombolysis, occlusion location, vessel diameter, collaterals, mismatch |
| **External validation** | Independent testing across geographic regions, device platforms, and center-volume categories |
| **Originality** | Prospective integration of expected functional benefit, complete-reperfusion probability, and procedural harm |

**Discussion.** The evidence available through July 2026 demonstrates that mechanical thrombectomy for medium- and distal-vessel occlusion cannot be understood through a simple binary conclusion. The neutral ESCAPE-MeVO and DISTAL trials, the unfavorable DISCOUNT trial, and the positive ORIENTAL-MeVO trial are best interpreted as evidence of substantial treatment-effect heterogeneity. The principal lesson from the neutral trials is that anatomical occlusion alone is insufficient to justify intervention. A visible clot in an accessible artery does not establish that the procedure will improve the patient's outcome. The threatened tissue may be small, noneloquent, already infarcted, or likely to recover after thrombolysis. Conversely, the vessel may be too fragile or tortuous to permit safe complete reperfusion. The principal lesson from ORIENTAL-MeVO is that thrombectomy should not be abandoned completely. In patients with moderate-to-severe deficits and favorable imaging, the absolute probability of functional independence increased meaningfully. The associated increase in symptomatic hemorrhage confirms that the procedure remains hazardous and that the favorable average effect reflects a balance between substantial benefit in some patients and harm in others [1, 2, 3, 4]. The results shift the field from anatomical expansion to precision selection. In proximal large-vessel occlusion, the untreated prognosis is often sufficiently poor that treatment benefit persists across relatively broad populations. In distal occlusion, the expected untreated outcome varies more widely. The treatment threshold must therefore be individualized. Baseline NIHSS score is a useful enrichment variable but should not become an absolute gatekeeper. ORIENTAL-MeVO suggests that a threshold of 6 can identify a higher-risk population, yet important disabling syndromes occur below this level. A future trial should permit entry based on prespecified disabling deficits, such as severe aphasia, complete hemianopia, profound neglect, loss of dominant-hand function, or gait-preventing leg weakness.

The concept of eloquent tissue at risk may be more informative than total perfusion-lesion volume. A 10-mL penumbra involving primary visual cortex or dominant language cortex may be more clinically important than a larger lesion in a less functionally critical region. Conventional perfusion thresholds do not account for this difference. Advanced imaging could support a tissue-utility model that combines predicted infarct location, functional network involvement, and expected disability. However, such algorithms must be externally validated and interpretable. An imaging model should not recommend thrombectomy solely because it predicts poor outcome; it must estimate the difference between expected outcomes with and without intervention. The MAD-

MT score proposed in 2026 represents an effort to integrate clinical need and procedural risk. Higher NIHSS score and absence of intravenous thrombolysis identified patients with poorer expected medical outcomes, whereas age and other clinical variables were associated with procedural failure or complications. Although promising, the score was derived from retrospective observational data and requires prospective validation before clinical adoption [13, 16, 20]. The interaction with intravenous thrombolysis deserves dedicated investigation. A patient with an M3 occlusion, modest deficit, and immediate access to tenecteplase may have a high probability of favorable recovery without catheter intervention. A patient with a severe deficit, contraindication to thrombolysis, long fibrin-rich clot, or persistent occlusion after thrombolysis may have a substantially higher expected benefit from thrombectomy. Future studies should document arterial recanalization before groin puncture whenever this can be achieved without clinically important delay. Rapid repeat CTA or angiographic confirmation after transfer may prevent unnecessary catheterization in patients who have already reperfused. Technical success should be defined more rigorously. Achieving eTICI 2b after several traumatic passes may not represent a successful distal procedure. The preferred target should be first-pass eTICI 2c–3 reperfusion without vessel injury or embolization. Device trials should report vessel diameter, device-to-vessel ratio, number of curves crossed, traction force, vasospasm, and subarachnoid hemorrhage. Device miniaturization alone will not resolve the benefit–risk problem. Smaller devices may improve access but can still injure fragile vessels. Catheter stiffness, distal-tip design, radial force, aspiration efficiency, clot integration, and retrieval mechanics must be optimized specifically for distal anatomy. The role of rescue therapy also requires definition. After one unsuccessful pass, the probability of eventual complete reperfusion must be weighed against cumulative vessel trauma. A predefined stopping rule based on vessel behavior, number of passes, and remaining tissue viability may reduce harm. Routine escalation to angioplasty, stenting, or intra-arterial antiplatelet therapy is difficult to justify in small distal vessels without stronger evidence.

Anesthesia strategy may affect workflow and safety. Conscious sedation permits neurological monitoring but movement can increase perforation risk during delicate distal navigation. General anesthesia provides immobility and airway control but may delay treatment or cause hypotension. The optimal strategy should be individualized according to cooperation, respiratory status, agitation, vessel anatomy, and institutional workflow.

The difference between geographic trial populations deserves careful consideration. ORIENTAL-MeVO was performed in China, whereas the neutral trials involved predominantly European and North American centers. Differences in intracranial atherosclerosis prevalence, thrombus composition, intravenous thrombolysis use, transfer patterns, anesthesia, device choice, and operator experience may modify outcomes. The positive trial should therefore be replicated in independent healthcare systems before its criteria are generalized globally. Conversely, the neutral Western trials should not be used to deny treatment automatically to patients who closely resemble the ORIENTAL-MeVO population. Equity is another concern. Advanced perfusion imaging and high-volume thrombectomy centers are not equally available. A selection model requiring complex imaging may exclude rural or resource-limited populations. Simplified criteria based on disabling deficit, CTA-confirmed accessible occlusion, limited infarction, and favorable collaterals should be studied alongside advanced perfusion approaches. Cost-effectiveness depends on selection accuracy. Routine thrombectomy for low-risk distal occlusions would increase procedural cost and complications without improving population health. Selective thrombectomy that prevents lifelong aphasia, visual disability, or loss of independence could be highly cost-effective even if the average infarct volume is small. The proposed multicenter trial addresses several gaps. It uses a functional definition of disabling stroke, incorporates tissue and anatomy, measures domain-specific outcomes, prioritizes complete first-pass reperfusion, and penalizes procedural harm in the primary endpoint. It also requires independent validation across regions and device platforms. Several limitations of this review should be recognized. The randomized trials used different definitions, eligibility criteria, devices, and outcome measures. Direct comparison across trials can therefore generate misleading conclusions. Post hoc subgroup analyses are vulnerable to false-positive findings. Observational device studies are affected by selection bias, operator preference, and incomplete

core-laboratory adjudication. The evidence is also evolving rapidly. Further trial-level and individual-participant meta-analyses may identify treatment interactions that are not visible in aggregate publications. Nevertheless, subgroup findings should generate hypotheses rather than immediately change practice unless supported by biological plausibility and external replication.

At present, routine thrombectomy for all medium- or distal-vessel occlusions is not supported. Equally, universal exclusion is no longer defensible after ORIENTAL-MeVO. The most reasonable contemporary approach is selective treatment within experienced centers, preferably under prospective protocols, for patients with clearly disabling deficits, viable eloquent tissue, accessible anatomy, and a high predicted probability of complete atraumatic reperfusion.

**Conclusion.** Mechanical thrombectomy for medium- and distal-vessel occlusion has entered a precision-selection era. ESCAPE-MeVO and DISTAL demonstrated no overall functional benefit, while DISCOUNT showed that indiscriminate intervention may increase hemorrhagic complications and produce net harm. ORIENTAL-MeVO subsequently demonstrated that an enriched population with moderate-to-severe deficits and favorable imaging can benefit from endovascular reperfusion. These findings are complementary rather than irreconcilable. They indicate that the treatment effect depends on the interaction among untreated neurological risk, tissue viability, functional eloquence, intravenous thrombolysis, vessel anatomy, operator expertise, probability of complete reperfusion, and procedural harm. Clinical decisions should not be based solely on the presence of a distal clot or an arbitrary NIHSS threshold. Selection should integrate the disabling nature of the deficit, clinical–anatomical concordance, viable tissue at risk, vessel diameter, tortuosity, collateral circulation, and the likelihood of first-pass eTICI 2c–3 reperfusion. Future trials should use patient-centered and territory-specific outcomes, distinguish complete from partial reperfusion, incorporate hemorrhagic complications into the primary utility measure, and require independent external validation. Until such evidence is available, thrombectomy should be performed selectively in experienced centers rather than adopted as routine treatment for every medium- or distal-vessel occlusion.

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