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Large-core ischemic stroke: Who really benefits from thrombectomy?

Ictus isquémico large-core: ¿a quién sí beneficia la trombectomía?

Angie Valeria Hernández Bernal[1], Aldemar Cedeño Bernal[2], Natalia Gallego Valencia[3], Juan Felipe Chaustre Soledad[4], Judit Mauri Juliachs[5]

[1]Departamento de Medicina, Fundación Universitaria en Ciencias de la Salud, Bogotá, Colombia. https://orcid.org/0009-0009-7030-6412

[2]Departamento de Medicina, Universidad de Manizales, Manizales, Colombia. https://orcid.org/0009-0009-3709-194X

[3]Departamento de Medicina, Universidad de Antioquia, Medellín, Colombia. https://orcid.org/0009-0008-2739-5635

[4]Departamento de Medicina, Universidad del Rosario, Bogotá, Colombia. https://orcid.org/0000-0002-2777-8539

[5]Centre d'Atenció Primària La Pau-Institut Català de la Salut, Barcelona, Espanya. https://orcid.org/0009-0004-9440-1397

Corresponding author: Judit Mauri Juliachs. Centre d'Atenció Primària La Pau-Institut Català de la Salut, Barcelona, Espanya. Email: juditmauri.bcn.ics@gencat.com

Correspondence

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The question is no longer whether endovascular thrombectomy (EVT) can benefit some patients with large-core ischemic stroke. The more difficult (and now clinically decisive) question is which patients derive a benefit large enough to justify the procedural burden, the hemorrhagic risk, and the use of highly time-sensitive stroke resources.

The recent meta-analysis by Lin et al. [1], synthesizing six randomized trials and 1,870 patients with anterior-circulation large-vessel occlusion and moderate-to-large ischemic cores, provides the most comprehensive summary to date. EVT combined with medical care improved functional independence at 90 days, shifted ordinal disability outcomes toward less severe states, and reduced the proportion of patients with very poor outcomes (modified Rankin Scale 5-6), while mortality remained unchanged and symptomatic intracranial hemorrhage was numerically higher [1].

Beyond statistical significance, however, the magnitude of benefit warrants explicit clinical interpretation. In absolute terms, the proportion of patients achieving functional independence remains modest, and the primary effect is better understood as a shift in the overall disability distribution rather than a consistent return to independence. This distinction is not merely semantic: it reflects a scenario in which EVT increases the likelihood of avoiding the most severe outcomes (e.g., modified Rankin Scale 5-6) and promotes transitions toward intermediate functional states, rather than reliably restoring baseline function. From a decision-making perspective, this translates into a probabilistic gain in disability reduction, which may be meaningful for some patients but insufficient for others depending on premorbid status, goals of care, and tolerance for severe residual disability.

This distinction carries direct clinical implications. Large-core stroke does not represent a uniform biological entity. Patients grouped under this label differ in infarct topography, collateral robustness, age, premorbid reserve, reperfusion success, and the extent to which the core truly reflects irreversible tissue loss. The field has therefore moved beyond a binary treatment-versus-no-treatment paradigm. What emerges instead is a model of selective benefit: EVT shifts outcome distributions in a favorable direction, but the absolute clinical gain depends on who is treated, how they are selected, and how effectively reperfusion is achieved [2,3].

The subgroup most consistently associated with benefit includes patients who retain a plausible trajectory toward disability reduction despite a large baseline lesion. Typically, this encompasses anterior-circulation occlusions in individuals with limited premorbid disability and imaging profiles that do not suggest completed hemispheric infarction or major mass effect. The 2025 American Heart Association science advisory and the 2026 AHA/ASA guideline reflect this conceptual transition, as large infarct is no longer considered an automatic exclusion for EVT [4,5]. Nevertheless, expansion of eligibility should not be conflated with therapeutic indiscrimination.

A second clinically relevant scenario involves patients in whom imaging may overestimate irreversibility. Core definitions varied substantially across trials included in the meta-analysis, ranging from

computerized tomography perfusion thresholds to ASPECTS-based selection and magnetic resonance imaging criteria. Lin et al. [1] acknowledge that pooled estimates include both true large cores and larger moderate infarcts. This heterogeneity likely explains the apparent tension between a favorable ordinal shift and relatively modest rates of full independence.

A similar pattern can be observed in the TESLA trial, which relied on noncontrast computerized tomography in patients with ASPECTS 2-5 within 24 hours and did not demonstrate definitive functional benefit, although confidence intervals remained compatible with clinically meaningful effects [3]. Imaging strategy, therefore, is not a technical detail (it is intrinsically linked to the observed treatment effect).

Notably, available data also challenge a strictly penumbral interpretation of benefit. In exploratory analyses of the SELECT2 trial, EVT improved outcomes across a broad spectrum of core volumes and penumbral profiles, without clear evidence that mismatch status modified treatment effect [2]. Yet outcomes worsened progressively as core volume increased, reinforcing that benefit is not binary but gradient-based: it persists across profiles, but prognosis deteriorates as baseline injury expands.

From a clinical standpoint, these data can be translated into a pragmatic decision framework that helps bridge trial evidence with bedside judgment. EVT is more likely to provide meaningful benefit in patients with preserved premorbid function, limited signs of established mass effect, and a realistic probability of achieving timely and effective reperfusion. The expected gain is not necessarily full independence, but a clinically relevant reduction in disability that may preserve autonomy in key domains.

By contrast, caution is warranted when large core volume coexists with extensive edema, poor collateral circulation, advanced frailty, or a low likelihood of successful reperfusion. In such scenarios, the probability that EVT will translate into meaningful functional improvement decreases substantially, and the risk of survival with severe disability becomes more prominent. Framing the decision in these terms allows clinicians to move beyond eligibility criteria and toward individualized, probability-based reasoning aligned with patient-centered goals of care.

Age adds further complexity. Older patients, particularly those over 80 years, exhibit worse absolute outcomes following EVT for large infarcts, including higher mortality and lower rates of independent ambulation. However, current evidence suggests that age alone does not negate the relative benefit associated with successful reperfusion and should not serve as an isolated exclusion criterion [6]. Rather, it must be interpreted alongside premorbid function, frailty, and overall clinical context.

Accordingly, patients who truly benefit from thrombectomy in large-core stroke are not defined by a single imaging threshold such as ASPECTS 0-5 or a fixed core volume. They are those in whom three conditions converge: a plausible opportunity for tissue and network salvage, a realistic probability that reperfusion will translate into reduced dependency rather than survival with severe disability, and a premorbid context in which that reduction in disability is clinically meaningful.

Despite recent advances, a critical and still insufficiently formalized knowledge gap remains. Current evidence does not provide sufficiently granular, patient-level predictive tools to guide individualized decision-making in large-core stroke. Trial populations remain heterogeneous, definitions of large core vary, and imaging strategies are not standardized, limiting the ability to translate group-level effects into reliable predictions for individual patients. As a result, clinical decisions continue to rely heavily on expert judgment rather than on validated, individualized risk–benefit models.

The next step is unlikely to be another binary trial, but rather a more refined approach. Future research should prioritize integrative models that combine core burden, markers of edema and mass effect, collateral status, age, prestroke disability, and reperfusion quality. Large-core stroke should be approached as a probabilistic decision problem rather than a categorical imaging definition.

EVT has moved beyond a rigid indication paradigm into a domain defined by conditional and context-dependent benefit. In large-core stroke, the question is no longer whether the intervention works, but whether it meaningfully alters the trajectory of disability for a given patient. This distinction reframes EVT not as a categorical indication, but as a probabilistic clinical decision shaped by biology, timing, and individual context. Without this shift in perspective, there is a real risk of replacing historical therapeutic nihilism with a different form of imprecision, one driven not by omission, but by indiscriminate application.

These considerations extend beyond immediate clinical decision-making. The complexity and evolving nature of the evidence surrounding EVT in large-core stroke underscore the need to strengthen training in research methodology and critical appraisal across all levels of medical education [7,8]. From students to specialists, the ability to interpret heterogeneous but high-quality evidence is now foundational. Without this competency, there is a risk of both overextending indications and withholding beneficial therapies.

In a context where decisions must often be made under time pressure and uncertainty, cultivating a scientifically literate and critically engaged workforce is essential to ensure that advances in evidence translate into judicious, patient-centered care.

Conflicts of interest

The authors declare no conflict of interest.

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Data, Materials, and Code Availability

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