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Practice Patterns, Equipoise, and Trial Priorities for Adjunct Intra-Arterial Thrombolysis After Mechanical Thrombectomy: A Physician Survey

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Abstract

Background— Adjunct intraarterial (IA) thrombolysis after mechanical thrombectomy may improve distal or microvascular reperfusion, but randomized trial results vary by agent, dose, vascular territory, and final reperfusion grade.

Objectives— To assess current practice patterns, safety thresholds, clinical equipoise, implementation barriers, and priorities for future trials of adjunct IA thrombolysis after mechanical thrombectomy.

Methods— We conducted a descriptive cross-sectional electronic survey in May 2026 among clinicians who personally performed thrombectomy or were involved in acute ischemic stroke care and thrombectomy decision-making. Thirty responses were analyzed overall and by self-reported annual thrombectomy volume. Outcomes included institutional and case-level use, agent and delivery practices, willingness to treat residual distal occlusion or no-reflow, acceptable symptomatic intracranial hemorrhage (sICH) risk, evidence interpretation, equipoise, trial preferences, and implementation readiness.

Results— Among 30 respondents, 25 (83.3%) practiced at comprehensive stroke centers. Although 26 (86.7%) reported at least occasional institutional use of adjunct IA thrombolysis, 25 (83.3%) estimated that adjunct IA thrombolysis was used in 10% or fewer thrombectomy cases, and only 1 (3.3%) reported routine institutional use. Alteplase was used by 21 of 28 respondents with agent data (75.0%). Residual distal branch occlusion was more accepted than no-reflow as an indication (70.0% vs 46.7%). Twenty-four respondents (80.0%) required an acceptable sICH rate below 5%, and 26 (86.7%) reported moderate or strong equipoise regarding adjunct IA thrombolysis after thrombectomy. Insufficient evidence and absent protocols were the leading institutional barriers to routine use. Routine use remained uncommon across thrombectomy-volume groups. Twenty-two respondents (73.3%) required a larger randomized trial to change practice, while 28 (93.3%) would implement treatment after demonstrated efficacy.

Conclusions— Among surveyed clinicians, adjunct IA thrombolysis was already used selectively but was not as standard practice. Persistent equipoise and conservative safety expectations support an enriched, stratified randomized trial with standardized angiographic definitions, dosing, safety monitoring, and parallel implementation planning.

Keywords— acute ischemic stroke, mechanical thrombectomy, intra-arterial thrombolysis, alteplase, tenecteplase, physician survey, clinical equipoise.

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INTRODUCTION

Endovascular thrombectomy is standard treatment for eligible patients with acute ischemic stroke caused by large-vessel occlusion and substantially improves functional outcomes.[1,2] Angiographic reperfusion, however, is an imperfect surrogate for tissue recovery. Functional outcomes differ across expanded Treatment in Cerebral Ischemia (eTICI) grades,[3,4] and impaired microvascular reperfusion may persist even after apparently complete macrovascular recanalization.[5–7] Residual distal emboli, microvascular thrombi, endothelial swelling, capillary obstruction, and impaired collateral washout may contribute to persistent tissue hypoperfusion. These mechanisms provide a biological rationale for local thrombolytic therapy after thrombectomy, either as rescue treatment for visible distal occlusion or as an adjunct intended to improve tissue-level reperfusion after successful recanalization.

The Chemical Optimization of Cerebral Embolectomy (CHOICE) trial suggested a higher likelihood of an excellent 90-day functional outcome with intra-arterial (IA) alteplase after successful thrombectomy.[8] Subsequent randomized trials have evaluated tenecteplase, urokinase, and alteplase across anterior- and posterior-circulation occlusion populations and different reperfusion thresholds, with heterogeneous efficacy and safety findings.[9–16] The studies also differed in prior intravenous thrombolysis use, treatment timing, dose, catheter position, and primary outcome definition. Pilot and observational data demonstrate additional variation in agent, dose, delivery location, and indication.[17,18] Contemporary systematic reviews therefore support possible benefit in selected populations while emphasizing uncertainty regarding the optimal biological target, drug regimen, angiographic threshold, imaging phenotype, and balance between functional benefit and hemorrhagic risk.[19–22] An earlier survey of neurointerventionalists, conducted before CHOICE and subsequent randomized trials, found frequent but nonstandardized use of IA thrombolysis.[23] To our knowledge, the present survey is the first to evaluate contemporary practice patterns after publication of multiple randomized IA thrombolysis trials. Clinical practice may evolve before definitive guideline adoption, particularly when an intervention can be delivered through an arterial catheter already in place. Selective off-label use may coexist with uncertainty regarding efficacy, safety, and patient selection. Understanding how clinicians interpret the emerging evidence, which scenarios they consider sufficiently uncertain for randomization, and what operational barriers would affect adoption is important for both trial design and implementation. We conducted a physician survey to describe current practice patterns, clinical decision-making, safety thresholds, residual equipoise, and priorities for future trials of adjunct IA thrombolysis after mechanical thrombectomy.

METHODS

Study Design and Reporting

We performed a descriptive cross-sectional survey of clinicians who personally performed thrombectomy or were involved in acute ischemic stroke care and mechanical thrombectomy decision-making. Reporting was guided by the Checklist for Reporting of Survey Studies and principles for web-based and clinician surveys.[24–27] The survey link was distributed by email to clinicians identified through the investigators' professional networks, and recipients could forward the invitation to eligible colleagues. Responses were collected electronically using Jotform (Jotform Inc, San Francisco, California, USA) during May 2026. The analytic dataset comprised 30 completed responses from a descriptive convenience sample. Because the eligible clinician denominator, unique exposure to reminders, and onward forwarding could not be verified, a conventional response rate was not calculated.

Participants and Survey Instrument

The questionnaire contained seven domains: respondent characteristics; familiarity with and interpretation of randomized trial evidence; current practice; decision-making for residual distal branch occlusion and no-reflow; equipoise and future trial design; implementation barriers; and open-ended comments (Supplementary Table 1). The instrument included single-response, multi-select, matrix, and free-text items and is reproduced in Supplementary Appendix 1. Annual thrombectomy volume was categorized using the observed survey response categories as low (0 or 25-50 cases/year), mid (50-100 cases/year), or high (>100 cases/year), reflecting cases personally performed or managed. The trial matrix was worded as familiarity on a 1-5 scale; it is therefore reported as familiarity rather than favorability (Supplementary Table 2). The instrument used eTICI terminology for the “already eTICI 3” avoidance item and modified Thrombolysis in Cerebral Infarction (mTICI) terminology for future-trial eligibility; those labels are retained as administered. Current-practice items asked about institutional frequency of use, the estimated proportion of thrombectomy cases receiving adjunct IA therapy, the agent and dose used, and catheter-delivery location. The use-frequency and case-proportion items were institution-level, whereas annual volume referred to cases personally performed or managed. Clinical-scenario items separately addressed residual distal branch occlusion and no-reflow without a visible residual occlusion, including the principal angiographic method used to assess no-reflow and the maximum acceptable symptomatic intracranial hemorrhage (sICH) rate. Future-trial items assessed eligible final reperfusion grade, target populations, primary endpoint, agent and dose, evidence required to change practice, willingness to implement after demonstrated efficacy, and preferred implementation leadership. Two open-ended prompts elicited respondents' current treatment philosophy and the questions they believed future trials should resolve.

Data Completeness and Response Handling

Each submitted record was treated as one clinician response. The analytic dataset retained 30 records, while item-specific denominators were used when a response was missing. Agent-use data were available for 28 respondents and the method of assessing no-reflow for 29; missing responses were not recoded as nonuse. For multi-select questions, each option was counted once per respondent, and the denominator remained the number of respondents eligible to answer the item. Site identifiers and invitation-level metadata were

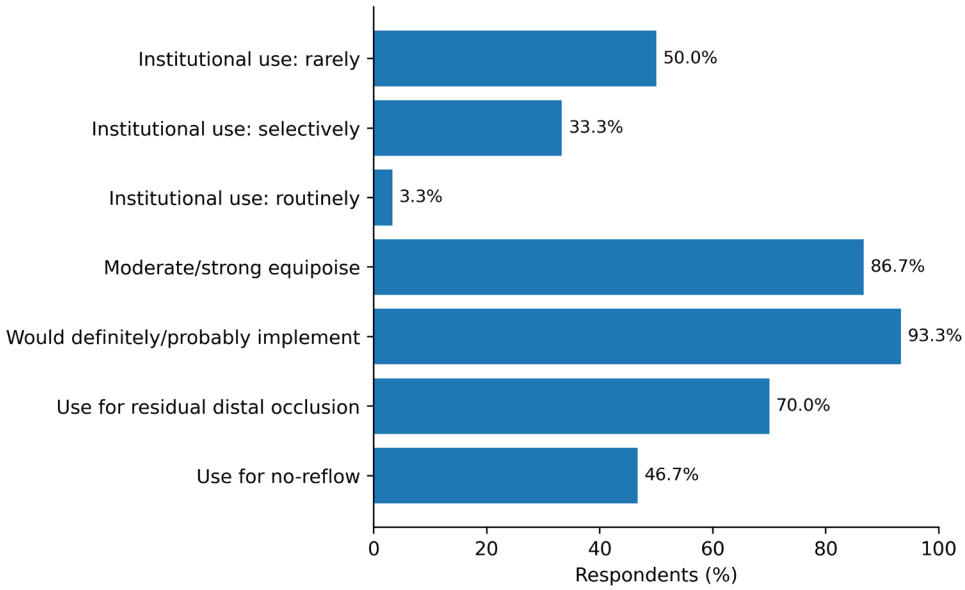


FIGURE 1: Current practice, clinical equipoise, and implementation readiness for adjunct intra-arterial thrombolysis after thrombectomy.
Note: Bars show the percentage of all respondents (N=30). Categories are not mutually exclusive across domains.
Abbreviations: IA, intra-arterial.

unavailable, preventing reduplication by institution and assessment of institutional clustering. Free-text responses were reviewed to contextualize the quantitative findings and were not treated as a qualitative dataset.

Outcomes

Prespecified descriptive outcomes included institutional use and estimated case-level use of adjunct IA thrombolysis; agent, dosing, and catheter-delivery practices; willingness to treat residual distal branch occlusion or no-reflow; methods used to assess no-reflow; patient and procedural factors discouraging use; acceptable sICH thresholds; interpretation of evidence; remaining equipoise; preferred trial populations, reperfusion grades, endpoints, and doses; institutional barriers; additional evidence required to change practice; and implementation willingness and leadership models. Current-use outcomes were distinguished from stated future preferences because reported practice reflects both evidence interpretation and local access, whereas trial-design responses reflect willingness to randomize under specified conditions. The analysis therefore did not combine these domains into a composite score or rank respondents according to overall enthusiasm for the intervention.

Statistical Analysis

Respondent-level data were audited before analysis. Categorical variables are presented as counts and percentages. Unless otherwise stated, the denominator was 30; item-specific missing responses are identified. Multi-select items could total more than 100%, and each option was counted once per respondent. Volume-stratified results are descriptive because of the small convenience sample: no hypothesis testing, weighting, imputation, or clustering adjustment was performed. Open-text responses were reviewed for recurring themes without formal qualitative coding. Trial-familiarity scores were summarized by mean and median by annual thrombectomy-volume group. Confidence intervals and P values were not calculated for subgroup comparisons because the sample was nonprobability based and the strata were small.

Results

Respondent Characteristics

Thirty clinicians completed the survey. Twelve (40.0%) were in the low-volume group, ten (33.3%) in the mid-volume group, and eight (26.7%) in the high-volume group. Vascular neurologists constituted 19 respondents (63.3%), neurointerventional surgeons 9 (30.0%), and other procedural specialists 2 (6.7%). Twenty-five respondents (83.3%) practiced at comprehensive stroke centers, and 13 (43.3%) personally performed thrombectomy (Table 1). Geographic location and unique institutional identifiers were not available.

Evidence Interpretation and Current Practice

Nearly half of respondents interpreted the evidence as showing some benefit (14/30, 46.7%), while one-third viewed the evidence as uncertain or mixed (10/30, 33.3%) and 3 (10.0%) viewed it as strongly supportive. Most respondents reported at least some institutional use of adjunct IA thrombolysis after thrombectomy (26/30, 86.7%), but reported use was predominantly rare (15/30, 50.0%) or selective (10/30, 33.3%); only one respondent (3.3%) reported routine use (Figure 1). In estimated case-level use, 13 (43.3%) reported that 1%-5% of thrombectomy cases receive IA therapy, 7 (23.3%) reported 6%-10%, 3 (10.0%) in 11%-25%, and 1 each (3.3%) in 26%-50% and >50%. Alteplase was the most common agent (21/28 nonmissing responses, 75.0%), followed by tenecteplase (7/28, 25.0%). Delivery through a microcatheter positioned in the distal territory (13/30, 43.3%) or into the residual occlusion (11/30, 36.7%) was most common responses (Table 2).

Self-reported familiarity was highest for the Intra-Arterial Tenecteplase for Acute Stroke After Successful Endovascular Therapy (ANGEL-TNK) trial (mean, 4.23; median, 4.5),

TABLE 1: Respondent and practice characteristics.

Characteristic	Category	n (%)
Annual thrombectomy volume	Low (0 or 25-50 cases/year)	12 (40.0)
	Mid (50-100 cases/year)	10 (33.3)
	High (>100 cases/year)	8 (26.7)
Primary specialty	Vascular neurology	19 (63.3)
	Neurointerventional surgery	9 (30.0)
	Other procedural specialty	2 (6.7)
Practice setting	Comprehensive stroke center	25 (83.3)
	Academic center	4 (13.3)
	Primary stroke center with transfer capability	1 (3.3)
Role in thrombectomy	Clinical care, nonprocedural	17 (56.7)
	Performs the procedure	13 (43.3)

Note: Percentages use N=30. Volume refers to cases personally performed or managed. The low-volume group comprised the observed survey categories 0 and 25-50 cases/year.

TABLE 2: Current practice, clinical scenarios, and safety thresholds.

Domain	Response distribution
Interpretation of evidence	Strongly supportive, 3 (10.0%); some benefit, 14 (46.7%);uncertain/ mixed, 10 (33.3%); little benefit/possible harm, 3 (10.0%)
Institutional use	Rarely, 15 (50.0%); selectively, 10 (33.3%); routinely, 1 (3.3%); never, 4 (13.3%)
Estimated cases receiving IA thrombolysis	0%, 5 (16.7%); 1%-5%, 13 (43.3%); 6%-10%, 7 (23.3%); 11%-25%, 3 (10.0%); 26%-50%, 1 (3.3%); >50%, 1 (3.3%)
Agent used (n=28)	Alteplase, 21 (75.0%); tenecteplase, 7 (25.0%)
Drug-delivery location	Distal-territory microcatheter, 13 (43.3%); residual occlusion, 11 (36.7%); distal to clot terminus, 5 (16.7%); perforator origins, 1 (3.3%)
Residual distal branch occlusion	Yes, 21 (70.0%); unsure, 8 (26.7%); no, 1 (3.3%)
No-reflow without visible occlusion	Yes, 14 (46.7%); unsure, 10 (33.3%); no, 6 (20.0%)
No-reflow assessment (n=29)	Delayed digital subtraction angiography washout, 20 (69.0%); parenchymal blush abnormality, 4 (13.8%); arterial-venous transit/venous delay, 4 (13.8%); does not assess, 1 (3.4%)
Acceptable sICH threshold	<2.5%, 12 (40.0%); <5%, 12 (40.0%); <7.5%, 3 (10.0%); <10%, 3 (10.0%)
Remaining equipoise regarding adjunct IA thrombolysis	Strong, 10 (33.3%); moderate, 16 (53.3%); mild, 2 (6.7%); none, 2 (6.7%)

Note: Percentages use N=30 unless an item-specific denominator is shown.
Abbreviations: IA, intra-arterial; sICH, symptomatic intracranial hemorrhage.

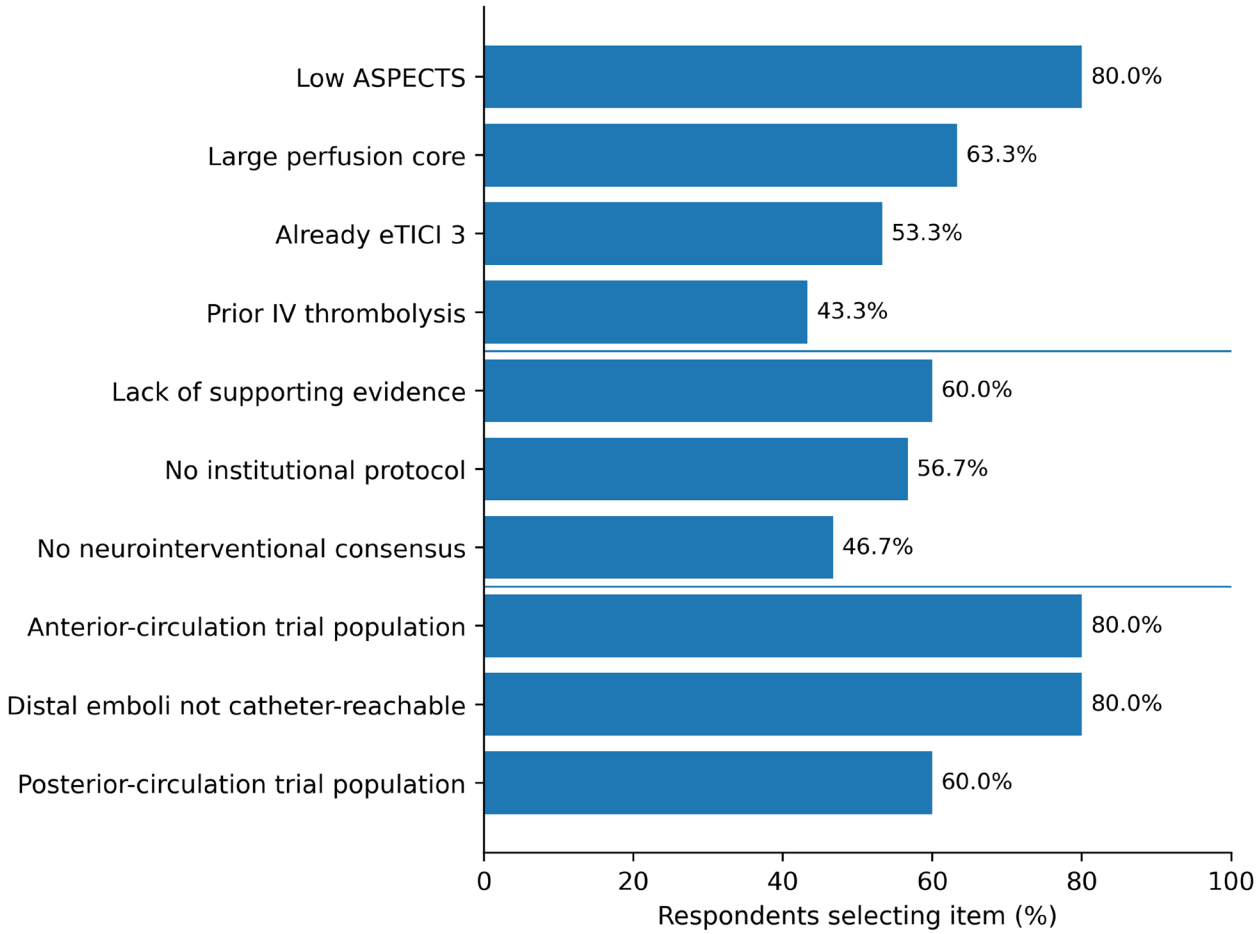


FIGURE 2: Leading barriers and future trial priorities.
Note: The upper four bars show patient/procedural deterrents, the middle three bars show institutional barriers, and the lower three bars show preferred future trial populations. Multi-select responses could exceed 100%.
Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; eTICI, expanded Treatment in Cerebral Ischemia; IV, intravenous.

CHOICE (mean, 4.20; median, 5.0), and the Chemical Optimization of Cerebral Embolectomy 2 (CHOICE-2) trial (mean, 4.10; median, 5.0). Familiarity was lower for the Adjunctive Intra-Arterial Urokinase After Near-Complete to Complete Reperfusion for Acute Ischemic Stroke (POST-UK) trial (mean, 3.07) and the Intra-Arterial Alteplase Thrombolysis After Successful Thrombectomy for Acute Ischemic Stroke in the Posterior Circulation (IAT-TOP) trial (mean, 3.03). High-volume respondents reported higher mean familiarity with several recent trials, including ANGEL-TNK, CHOICE, CHOICE-2, and the Adjunctive Intra-Arterial Tenecteplase Following Near-Complete to Complete Reperfusion for Large-Vessel Occlusion Stroke (POST-TNK) trial, but these small descriptive strata were not compared inferentially (Supplementary Table 2).

Clinical Scenarios, Safety Thresholds, and Equipoise

Twenty-one respondents (70.0%) would use IA thrombolysis for a residual distal branch occlusion; 8 (26.7%) were uncertain and 1 (3.3%) would not. For no-reflow without a visible residual occlusion, 14 (46.7%) would treat, 10 (33.3%) were uncertain, and 6 (20.0%) would not. Delayed contrast clearance or washout on digital subtraction angiography was the predominant assessment method (20/29 nonmissing responses, 69.0%). Twelve respondents each selected an acceptable sICH threshold below 2.5% or below 5%; thus, 24 (80.0%) required a threshold below 5%. Moderate or strong equipoise was reported by 26 respondents (86.7%), whereas 2 (6.7%) reported mild equipoise and 2 (6.7%) reported none (Figure 1 and Table 2). The remaining respondents primarily used parenchymal blush abnormalities (4/29, 13.8%) or delayed arterial-venous transit or venous-phase filling (4/29, 13.8%); 1 respondent (3.4%) reported not assessing no-reflow. This distribution indicates that clinicians relied on qualitative angiographic interpretation rather than quantitative transit-time mapping.

Practice patterns also varied descriptively by annual thrombectomy volume. Selective or routine institutional use was reported by 4 of 12 low-volume respondents (33.3%), 5 of 10 mid-volume respondents (50.0%), and 2 of 8 high-volume respondents (25.0%). Rare use was reported by 6 low-volume respondents (50.0%), 4 mid-volume respondents (40.0%), and 5 high-volume respondents (62.5%). Use for no-reflow was reported by 6 of 12 low-volume respondents (50.0%), 3 of 10 mid-volume respondents (30.0%), and 5 of 8 high-volume respondents (62.5%). These differences are hypothesis-generating and should not be interpreted as volume effects.

TABLE 3: Factors limiting or discouraging adjunct IA thrombolysis, overall and by annual thrombectomy volume.

Factor	Overall n (%)	Low n=12	Mid n=10	n=8
Patient/procedural factors				
Low ASPECTS	24 (80.0)	10 (83.3)	6 (60.0)	8 (100.0)
Large core on perfusion imaging	19 (63.3)	8 (66.7)	6 (60.0)	5 (62.5)
Already eTICI 3	16 (53.3)	3 (25.0)	8 (80.0)	5 (62.5)
Prior IV thrombolysis	13 (43.3)	3 (25.0)	5 (50.0)	5 (62.5)
High systolic blood pressure	12 (40.0)	4 (33.3)	4 (40.0)	4 (50.0)
Institutional factors				
Insufficient supporting evidence	18 (60.0)	9 (75.0)	5 (50.0)	4 (50.0)
No institutional protocol	17 (56.7)	9 (75.0)	5 (50.0)	3 (37.5)
No neurointerventional consensus	14 (46.7)	6 (50.0)	4 (40.0)	4 (50.0)
Medicolegal concern	9 (30.0)	3 (25.0)	4 (40.0)	2 (25.0)
Concern about workflow delay	5 (16.7)	1 (8.3)	2 (20.0)	2 (25.0)

Note: Multi-select responses could exceed 100%. Descriptive volume strata were not compared inferentially.
Abbreviations: ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; eTICI, expanded Treatment in Cerebral Ischemia; IA, intra-arterial; IV, intravenous.

TABLE 4: Future trial design and implementation preferences.

Domain	Most selected responses
Preferred trial populations	Anterior circulation, 24 (80.0%); distal emboli not reachable by catheter, 24 (80.0%); posterior circulation, 18 (60.0%); no prior IV thrombolysis, 14 (46.7%); no-reflow, 13 (43.3%)
Eligible final reperfusion grade	mTICI 2b-3, 7 (23.3%); mTICI 2b only, 7 (23.3%); mTICI 0-2a rescue, 6 (20.0%); mTICI 2c-3, 6 (20.0%); mTICI 2b-2c, 4 (13.3%)
Preferred primary endpoint	90-day mRS shift, 9 (30.0%); mRS 0-2, 6 (20.0%); mRS 0-1 plus EQ-5D index ≥0.8, 6 (20.0%); mRS 0-1, 5 (16.7%); utility-weighted mRS, 3 (10.0%); imaging biomarker, 1 (3.3%)
Agent/dose for further study	Tenecteplase 0.125 mg/kg, 10 (33.3%); alteplase 0.225 mg/kg, 7 (23.3%); tenecteplase 0.0625 mg/kg, 6 (20.0%); tenecteplase 0.0313 mg/kg, 6 (20.0%); unsure, 1 (3.3%)
Evidence required to change practice	Larger randomized trial showing benefit, 22 (73.3%); other safety, subgroup, imaging, or registry evidence, 8 (26.7%)
Implementation after demonstrated efficacy	Definitely, 20 (66.7%); probably, 8 (26.7%); uncertain, 2 (6.7%)

Note: Percentages use N=30.
Abbreviations: EQ-5D, EuroQol 5-Dimension; IV, intravenous; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction.

Factors Limiting Use

The most frequent patient or procedural deterrents were low Alberta Stroke Program Early Computed Tomography Score (ASPECTS) (24/30, 80.0%), large perfusion core (19/30, 63.3%), already achieving eTICI 3 reperfusion (16/30, 53.3%), prior intravenous thrombolysis (13/30, 43.3%), and high systolic blood pressure (12/30, 40.0%). The leading institutional barriers were insufficient supporting evidence (18/30, 60.0%), absence of a protocol (17/30, 56.7%), lack of neurointerventional consensus (14/30, 46.7%), medicolegal concern (9/30, 30.0%), and anticipated workflow delay (5/30, 16.7%) (Figure 2 and Table 3). Low-volume respondents more often selected lack of evidence and absence of a protocol (9/12, 75.0% for each), whereas mid-volume respondents more frequently identified eTICI 3 as a deterrent (8/10, 80.0%).

Future Trial and Implementation Priorities

The most frequently supported future trial populations were anterior-circulation stroke (24/30, 80.0%), distal emboli not reachable by catheter (24/30, 80.0%), posterior circulation stroke (18/30, 60.0%), patients without prior intravenous thrombolysis (14/30, 46.7%), and no-reflow (13/30, 43.3%) (Figure 2). Preferences for final angiographic grade were dispersed across mTICI 2b-3 (7/30, 23.3%), mTICI 2b only (7/30, 23.3%), mTICI 0-2a rescue (6/30, 20.0%), mTICI 2c-3 (6/30, 20.0%), and mTICI 2b-2c (4/30, 13.3%). The leading endpoint was 90-day modified Rankin Scale (mRS) shift analysis (9/30, 30.0%), followed by mRS 0-2 (6/30, 20.0%) and a composite of mRS 0-1 with EuroQol 5-Dimension index ≥0.8 (6/30, 20.0%). Tenecteplase 0.125 mg/kg was the most commonly selected dose for future study (10/30, 33.3%), although lower tenecteplase doses and alteplase 0.225 mg/kg also received substantial support (Table 4). Twenty-two respondents (73.3%) required a larger randomized trial showing benefit to change practice. If efficacy were established, 20 (66.7%) would definitely implement adjunct IA thrombolysis and 8 (26.7%) would probably implement it. Open-text responses repeatedly emphasized safety, dose and route, final reperfusion grade, infarct core, clot location, imaging adjudication, and the need for adequately powered subgroups. Alternative endpoint preferences included mRS 0-1 (5/30, 16.7%), utility-weighted mRS (3/30, 10.0%), and an imaging biomarker (1/30, 3.3%). Dose preferences were also distributed across alteplase 0.225 mg/kg (7/30, 23.3%), tenecteplase 0.0625 mg/kg (6/30, 20.0%), and tenecteplase 0.0313 mg/kg (6/30, 20.0%), with 1 respondent (3.3%) uncertain.

Implementation preferences were similarly oriented toward shared responsibility rather than isolated operator discretion. High-volume respondents most often favored a multidisciplinary implementation team with a designated coordinator (5/8, 62.5%). Across the open-text responses, clinicians repeatedly requested clearer definitions of the intended treatment target, standardized imaging and angiographic adjudication, agent- and dose-specific safety data, and adequately powered analyses by final reperfusion grade, infarct core, vascular territory, and prior intravenous thrombolysis.

Discussion

In this survey of predominantly vascular neurologists and neurointerventional specialists, adjunct IA thrombolysis was familiar and available at most institutions but was generally reserved for selected cases. The distinction between institutional exposure and case-level use is important: 86.7% reported at least occasional institutional use, whereas 83.3% estimated use in 10% or fewer thrombectomy cases and only one respondent reported routine institutional use. Residual distal branch occlusion was the most accepted indication, whereas no-reflow generated substantial uncertainty. In addition, 86.7% reported moderate or strong equipoise regarding adjunct IA thrombolysis after thrombectomy, and 93.3% would implement treatment if efficacy were demonstrated. Together, these findings show a mismatch between selective real-world use, persistent equipoise, conservative safety expectations, and limited protocolization. The results update a 2019 survey of neurointerventionalists, conducted before the current randomized evidence base, which similarly found that IA thrombolysis was used in practice without consensus regarding administration criteria.[23]

The survey results should be interpreted against a rapidly changing evidence base. Randomized trials have differed in agent, dose, vascular territory, prior intravenous thrombolysis, final angiographic reperfusion threshold, and outcome definition.[8–16] This heterogeneity helps explain why respondents simultaneously perceived a signal of benefit and requested a larger definitive trial. Recent meta-analyses have also differed according to included trials and dose assumptions.[19–22] The survey findings therefore favor a trial strategy that prespecifies clinically coherent strata rather than treating adjunct IA thrombolysis as a single uniform intervention.

These findings reflect cautious optimism: the intervention is biologically plausible and procedural access is already established at the end of thrombectomy, but the risk-benefit balance may depend strongly on residual thrombus burden, infarct core, blood pressure, prior intravenous thrombolysis, final reperfusion grade, and the presence of true no-reflow. The distinction between rescue treatment for a visible distal occlusion and adjunctive treatment after near-complete or complete reperfusion is therefore important because the two strategies target different biological problems and may have different efficacy and safety profiles. For no-reflow, delayed contrast washout was the predominant assessment method; but this qualitative judgment can vary with angiographic technique and hemodynamic conditions. Future trials should prespecify an operational definition, standardize angiographic acquisition and timing, and use blinded core-laboratory adjudication, with perfusion imaging incorporated where appropriate.[5–7]

Respondents identified patient-selection concerns as the most prominent reasons to avoid IA thrombolysis. Low ASPECTS and large perfusion core were especially common deterrents, indicating concern about hemorrhagic transformation when infarct burden is substantial. The fact that already achieving eTICI 3 was also commonly selected suggests that some

clinicians view adjunct IA thrombolysis primarily as a rescue or optimization strategy rather than as a universal post-reperfusion therapy. However, support was distributed across rescue and successful-reperfusion populations, from mTICI 0-2a through mTICI 2c-3, showing that no consensus exists regarding whether therapy should target incomplete macrovascular reperfusion, residual distal emboli, microvascular no-reflow, or all successfully reperfused patients. Notably, 24 of 30 respondents (80.0%) required an acceptable sICH rate below 5%, making hemorrhagic safety a central constraint for both trial design and implementation. This threshold, together with concern regarding prior intravenous thrombolysis, supports prespecified safety strata and strict monitoring rather than leaving these decisions entirely to operator judgment.

The volume-stratified findings were inconsistent and should remain descriptive. Although high-volume respondents reported greater familiarity with several recent trials and more frequent treatment of no-reflow, routine use was uncommon across all volume groups, and the small strata do not support inference about experience-related differences. Dose preferences were also distributed across multiple tenecteplase and alteplase regimens, underscoring unresolved pharmacologic uncertainty.

The survey also underscores the implementation work that would be required even after a positive trial. Lack of supporting evidence, absence of protocols, and lack of neurointerventional consensus were the most common institutional barriers. Because medicolegal concern was assessed separately, protocol absence cannot be assumed to reflect perceived procedural or legal risk, but it identifies a concrete implementation gap. Institutions considering adoption would need standardized eligibility criteria; agent and dose preparation workflows; pharmacy stocking; catheter position and delivery guidance; blood pressure and antithrombotic management; post-procedure imaging; hemorrhage surveillance; documentation of the treatment indication; and clear interdisciplinary ownership. The preference for multidisciplinary implementation teams suggests that adoption may require coordination among proceduralists, vascular neurologists, nursing, pharmacy, quality teams, and hospital leadership rather than a purely operator-driven protocol.

Future trials should not use a broad "give lytic after thrombectomy" model. An enriched design should prioritize residual distal emboli not reachable by catheter, incomplete reperfusion, and suspected no-reflow, with prespecified strata by final eTICI/mTICI grade, infarct core, prior intravenous thrombolysis, vascular territory, agent, dose, catheter position, and no-reflow definition. Although endpoint preferences were dispersed, 90-day ordinal mRS remains the most defensible primary clinical endpoint; mRS 0-1, EuroQol 5-Dimension, angiographic or perfusion biomarkers of reperfusion and no-reflow, and sICH should be prespecified secondary or exploratory outcomes. Because existing randomized trials have not consistently demonstrated benefit on ordinal mRS, sample-size assumptions should be conservative and tailored to the selected phenotype and regimen.[8–16] Blinded core-laboratory adjudication and strict safety monitoring are essential.

Limitations

This analysis has important limitations. The sample was small, descriptive, and nonprobability based. The eligible clinician denominator and response rate could not be established because invitation exposure and onward forwarding were not verifiable. Geographic distribution and unique institutional identifiers were unavailable, so respondents may not represent unique centers and institutional clustering could not be assessed. Annual thrombectomy volume was self-reported and referred to cases personally performed or managed rather than verified institutional volume. Institutional-use estimates likewise reflected respondents' reports rather than audited site-level data. The questionnaire was structured but not formally validated, and several items were conditional, multi-select, or open text. The trial matrix assessed familiarity rather than objective knowledge or appraisal of trial quality. Because respondents were predominantly vascular neurologists and comprehensive stroke center clinicians, and fewer than half personally performed thrombectomy, the findings may not generalize to proceduralists or other practice settings and this composition may have influenced views on equipoise, barriers, and trial priorities. Current practice and stated preferences may be affected by recall and social-desirability bias. Volunteer bias is also possible because clinicians interested in IA thrombolysis may have been more likely to participate. Descriptive volume-stratified differences were not tested and should not be interpreted as volume effects. Finally, the survey was conducted while major evidence was emerging, and opinions may change as newer trial results are disseminated. Open-text observations were not formally analyzed and should be considered illustrative rather than evidence of thematic saturation.

Conclusions

Among surveyed clinicians, adjunct IA thrombolysis after mechanical thrombectomy was not standard practice but was already used selectively, and substantial equipoise remained regarding when and how it should be used. The next randomized trial should not test a broad universal post-thrombectomy strategy; it should use enriched, prespecified cohorts for residual distal emboli, incomplete reperfusion, and no-reflow, with standardized dosing, angiographic definitions, and strict safety monitoring. Parallel implementation planning will be required if efficacy is demonstrated.

Declarations

Ethics approval and consent to participate: This voluntary survey involved healthcare professionals and did not include patient data or identifiable individual-level information. Completion and submission of the survey constituted consent to participate.

Consent for publication: Not applicable. The manuscript contains no identifiable individual-level information.

Availability of data and materials: The deidentified respondent-level data supporting the findings of this study

are available from the corresponding author upon reasonable request.

Competing interests: Thanh N. Nguyen reports serving as an Associate Editor for Stroke, serving on advisory boards for Bayer and Route 92, and consulting for Medtronic. All other authors declare no competing interests.

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Authors' contributions: AIQ conceived and designed the study and supervised the work. HR performed data curation and analysis and drafted the manuscript. RET contributed to the statistical methodology and interpretation. DEF, WRG, AEH, PL, DRM, TNN, LAR, and DFH contributed to interpretation of the findings and critically revised the manuscript. All authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

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REFERENCES

1. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387(10029):1723–31. doi: 10.1016/S0140-6736(16)00163-X.
2. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2019;50(12):e344–418. doi.org/10.1161/STR.0000000000000211.
3. Liebeskind DS, Bracard S, Guillemin F, et al. eTICI reperfusion: defining success in endovascular stroke therapy. J Neurointerv Surg 2019;11(5):433–8. doi: 10.1136/neurintsurg-2018-014127.
4. Dargazanli C, Consoli A, Barral M, et al. Impact of Modified TICI 3 versus Modified TICI 2b Reperfusion Score to Predict Good Outcome following Endovascular Therapy. AJNR Am J Neuroradiol 2017;38(1):90–6. doi: 10.3174/ajnr.A4968.
5. Ng FC, Churilov L, Yassi N, et al. Prevalence and Significance of Impaired Microvascular Tissue Reperfusion Despite Macrovascular Angiographic Reperfusion (No-Reflow). Neurology 2022;98(8):e790–801. doi: 10.1212/WNL.0000000000013210.
6. Ter Schiphorst A, Charron S, Hassen WB, et al. Tissue no-reflow despite full recanalization following thrombectomy for anterior circulation stroke with proximal occlusion: A clinical study. J Cereb Blood Flow Metab 2021;41(2):253–66. doi: 10.1177/0271678X20954929.
7. Jia M, Jin F, Li S, et al. No-reflow after stroke reperfusion therapy: An emerging phenomenon to be explored. CNS Neurosci Ther 2024;30(2):e14631. doi: 10.1111/cns.14631.
8. Renú A, Millán M, San Román L, et al. Effect of Intra-arterial Alteplase vs Placebo Following Successful Thrombectomy on Functional Outcomes in Patients With Large Vessel Occlusion Acute Ischemic Stroke: The CHOICE Randomized Clinical Trial. JAMA 2022;327(9):826–35. doi: 10.1001/jama.2022.1645.
9. Huang J, Yang J, Liu C, et al. Intra-Arterial Tenecteplase Following Endovascular Reperfusion for Large Vessel Occlusion Acute Ischemic Stroke. JAMA 2025;333(7):579–88. doi: 10.1001/jama.2024.23466.
10. Liu C, Guo C, Li F, et al. Intra-Arterial Urokinase After Endovascular Reperfusion for Acute Ischemic Stroke: The POST-UK Randomized Clinical Trial. JAMA 2025;333(7):589–98. doi: 10.1001/jama.2024.23480.
11. Hu W, Tao C, Wang L, et al. Intra-arterial tenecteplase after successful endovascular recanalisation in patients with acute posterior circulation arterial occlusion (ATTENTION-IA): multicentre randomised controlled trial. BMJ 2025;388:e080489. doi: 10.1136/bmj-2024-080489.
12. Hou X, Huang J, Wang L, et al. Intra-Arterial Tenecteplase After Successful Reperfusion in Large Vessel Occlusion Stroke: A Randomized Clinical Trial. JAMA Neurol 2025;82(9):895–904. doi: 10.1001/jamaneurol.2025.2036.
13. Miao Z, Luo G, Song L, et al. Intra-arterial Tenecteplase for Acute Stroke After Successful Endovascular Therapy: The ANGEL-TNK Randomized Clinical Trial. JAMA 2025;334(7):582–91. doi: 10.1001/jama.2025.10800.
14. Writing Committee for the PEARL Investigators, Yang X, He X, et al. Intra-Arterial Alteplase After Successful Endovascular Reperfusion in Acute Stroke: The PEARL Randomized Clinical Trial. JAMA 2025;334(19):1728–39. doi: 10.1001/jama.2025.16876.
15. Chen W, Yang B, Bai X, et al. Intra-arterial Alteplase Thrombolysis After Successful Thrombectomy for AIS in the Posterior Circulation: The IAT-TOP Randomized Clinical Trial. JAMA Neurol 2026;e261074. doi: 10.1001/jamaneurol.2026.1074.
16. Renú A, Fernández-Couto MD, de la Riva P, et al. Adjunctive Intra-Arterial Alteplase After Successful Thrombectomy for Acute Ischemic Stroke: The CHOICE-2 Randomized Clinical Trial. JAMA 2026;335(21):1859–69. doi: 10.1001/jama.2026.5164.
17. Zaidi SF, Castonguay AC, Zaidat OO, et al. Safety of Adjunctive Intraarterial Tenecteplase Following Mechanical Thrombectomy: The ALLY Pilot Trial. Stroke 2025;56(2):355–61. doi: 10.1161/STROKEAHA.124.048846.
18. Kaesmacher J, Abdullayev N, Maamari B, et al. Safety and Angiographic Efficacy of Intra-Arterial Fibrinolytics as Adjunct to Mechanical Thrombectomy: Results from the INFINITY Registry. J Stroke 2021;23(1):91–102. doi: 10.5853/jos.2020.01788.
19. Diprose WK, Wang MTM, Ghate K, et al. Adjunctive Intra-arterial Thrombolysis in Endovascular Thrombectomy: A Systematic Review and Meta-analysis. Neurology 2021;96(24):1135–43. doi: 10.1212/WNL.0000000000012112.
20. Al-Salihi MM, Al-Jebur MS, Saha R, et al. Adjunctive Intra-Arterial Thrombolysis Following Endovascular Thrombectomy in Acute Ischemic Stroke: A Meta-Analysis. J Neuroimaging 2025;35(3):e70054. doi: 10.1111/jon.70054.
21. Almekhlafi MA, Park H, Singh N, et al. Adjunctive Intraarterial Thrombolysis after Thrombectomy in Large Vessel Occlusion Stroke: A Meta-Analysis of RCTs. Can J Neurol Sci 2025;1–9. doi: 10.1017/cjn.2025.10354.
22. Frechiani LEC, Louzada HL. Dose-Specific Intra-Arterial Thrombolysis After Endovascular Thrombectomy for Large-Vessel Occlusion Stroke: A Network Meta-Analysis of Randomized Trials. Stroke: Vascular and Interventional Neurology 2026;6(3):e002292. doi.org/10.1161/SVIN.125.00229.
23. Castonguay AC, Jumaa MA, Zaidat OO, et al. Insights Into Intra-arterial Thrombolysis in the Modern Era of Mechanical Thrombectomy. Front Neurol 2019;10:1195. doi: 10.3389/fneur.2019.01195.
24. Sharma A, Minh Duc NT, Luu Lam Thang T, et al. A Consensus-Based Checklist for Reporting of Survey Studies (CROSS). J Gen Intern Med 2021;36(10):3179–87. doi: 10.1007/s11606-021-06737-1.
25. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res 2004;6(3):e34. doi:10.2196/jmir.2042.
26. Burns KEA, Duffett M, Kho ME, et al. A guide for the design and conduct of self-administered surveys of clinicians. CMAJ 2008;179(3):245–52. doi: 10.1503/cmaj.080372.
27. Kelley K, Clark B, Brown V, et al. Good practice in the conduct and reporting of survey research. Int J Qual Health Care 2003;15(3):261–6. doi: 10.1093/intqhc/mzg031.

SUPPLEMENTARY MATERIAL

Practice Patterns, Equipoise, and Trial Priorities for Adjunct Intra-Arterial Thrombolysis After Mechanical Thrombectomy: A Physician Survey

Supplementary Table 1: Survey domains and item content.

Section	Domain	Content
A	Respondent characteristics	Primary specialty; annual thrombectomy volume; practice setting; procedural role
B	Evidence awareness	Familiarity with nine trial programs; overall evidence interpretation
C	Current practice	Institutional use; case proportion; agent; dose; delivery location
D	Clinical scenarios	Residual distal branch occlusion; no-reflow; assessment method; avoidance factors; acceptable sICH threshold
E	Equipoise and trial design	Remaining equipoise; reperfusion grade; populations; endpoint; agent/dose
F	Implementation	Institutional barriers; evidence needed; implementation willingness; leadership model
G	Open text	Current philosophy and unanswered questions

Abbreviations: sICH indicates symptomatic intracranial hemorrhage.

Supplementary Table 2: Trial familiarity scores overall and by annual thrombectomy volume.

Trial	Overall mean	Overall median	Low mean	Mid mean	High mean
ANGEL-TNK	4.23	4.5	3.75	4.40	4.75
CHOICE	4.20	5.0	3.67	4.40	4.75
CHOICE-2	4.10	5.0	3.75	4.20	4.50
POST-TNK	3.80	4.0	3.33	3.70	4.63
PEARL	3.57	4.0	3.17	3.80	3.88
DATE	3.57	4.0	3.00	4.00	3.88
ATTENTION-IA	3.33	4.0	2.75	3.70	3.75
POST-UK	3.07	3.0	2.83	2.80	3.75
IAT-TOP	3.03	3.0	2.42	3.30	3.63

Note: The source instrument asked respondents to rate familiarity from 1 to 5. Higher values therefore indicate greater self-reported familiarity, not a more favorable interpretation of trial results. Overall N=30; low n=12, mid n=10, and high n=8. Trial acronyms are presented as published study names.

Supplementary Appendix 1. Survey Instrument

Section A. Respondent Characteristics

- Primary specialty: vascular neurology; neurointerventional surgery; interventional neuroradiology; neurosurgery; emergency medicine; other.
- Annual mechanical thrombectomy volume personally performed or managed: 0; 1-25; 25-50; 50-100; >100 cases/year.
- Practice setting: comprehensive stroke center; primary stroke center with transfer capability; academic center; private hospital; other.
- Role in mechanical thrombectomy: performs the procedure; clinical care, nonprocedural.

Section B. Awareness and Interpretation of Evidence

- Rate familiarity from 1 to 5 for CHOICE, PEARL, DATE, ANGEL-TNK, POST-TNK, POST-UK, ATTENTION-IA, IAT-TOP, and CHOICE-2.
- Overall interpretation: strongly supportive of benefit; some evidence of benefit; uncertain/mixed; little or no benefit; possible harm.

Section C. Current Practice Patterns

- Current institutional use: routinely; selectively; rarely; never.
- Approximate proportion of thrombectomy cases receiving adjunct IA therapy in typical practice or the past 12 months: 0%; 1%-5%; 6%-10%; 11%-25%; 26%-50%; >50%.
- Agent used: alteplase; tenecteplase; urokinase; other.
- Dosing strategy: alteplase 0.225 mg/kg; tenecteplase 0.0313, 0.0625, or 0.125 mg/kg; fixed-dose urokinase 100,000 IU; custom/center-specific dose.
- Delivery location: distal to clot terminus; into residual occlusion; at perforator origins; through a microcatheter in distal territory.

Section D. Decision-Making in Clinical Scenarios

- Would use adjunct IA thrombolysis for residual distal branch occlusion: yes; no; unsure.
- Would use adjunct IA thrombolysis for no-reflow without visible residual occlusion: yes; no; unsure.
- Primary no-reflow assessment: delayed digital subtraction angiography contrast clearance/washout; arterial-venous transit or venous-phase delay; parenchymal blush/capillary abnormality; quantitative transit-time maps; other.
- Factors discouraging use (multi-select): low Alberta Stroke Program Early CT Score (ASPECTS); large perfusion core; prior intravenous (IV) thrombolysis; high systolic blood pressure; high glucose; recent surgery; prolonged onset-to-puncture time; expanded Treatment in Cerebral Ischemia (eTICI) grade 3; off-hours constraints; unavailable drug; anticipated IV or oral antiplatelet therapy.
- Acceptable symptomatic intracranial hemorrhage (sICH) rate: <2.5%; <5%; <7.5%; <10%.

Section E. Equipoise and Future Trial Design

- Remaining equipoise: strong; moderate; mild; none because evidence is sufficient.
- Eligible final reperfusion grade: modified Thrombolysis in Cerebral Infarction (mTICI) 0-2a; 2b only; 2b-2c; 2b-3; 2c-3.
- Populations for future trials (multi-select): anterior circulation; posterior circulation; no-reflow; distal emboli not reachable by catheter; prior IV thrombolysis; no prior IV thrombolysis; early window; late window; no further trial needed.
- Preferred primary endpoint: modified Rankin Scale (mRS) 0-1; mRS 0-2; mRS shift; utility-weighted mRS; mRS 0-1 plus EuroQol 5-Dimension (EQ-5D) index ≥0.8; perfusion imaging biomarker; other.
- Agent/dose for further study: alteplase 0.225 mg/kg; fixed-dose urokinase; tenecteplase 0.0313, 0.0625, or 0.125 mg/kg; other.

Section F. Implementation

- Institutional barriers (multi-select): no protocol; drug not stocked; workflow delay; no neurointerventional consensus; reimbursement; medicolegal risk; insufficient evidence.
- Evidence needed to change practice: larger randomized trial; clear safety advantage; subgroup data by reperfusion grade; imaging biomarker evidence; real-world registry.
- Willingness to implement after demonstrated efficacy: definitely; probably; uncertain; probably not; definitely not.
- Preferred organization: nonprocedural champion; procedural champion; co-leadership; multidisciplinary team with coordinator; unclear pathway/other.

Section G. Open-Ended Items

- Current philosophy toward adjunct IA thrombolysis after thrombectomy.
- Specific unanswered questions future trials should address.