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Code Stroke in Acute Ischemic Stroke: A Narrative Review of 2021–2026 Evidence

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Abstract
Code stroke is a coordinated pathway linking symptom recognition, prehospital response, imaging, treatment decisions, and reperfusion in acute ischemic stroke. This narrative review synthesizes selected evidence published from 2021 to October 2026 on pathway components, reperfusion therapies, and implementation in Indonesia. A targeted web-based search of general search engines, publisher websites, and preprint repositories identified 30 relevant sources; the review was not designed as a PRISMA-based systematic review. Evidence from a prospective controlled study suggests that mobile stroke units can shorten onset-to-thrombolysis time and improve 90-day functional outcomes. Randomized trials support tenecteplase as non-inferior to alteplase in eligible patients, while SELECT2 supports thrombectomy in selected patients with large ischemic-core infarction. Indonesian studies report improvements in door-to-CT time following workflow refinement, but also describe late hospital arrival, low EMS use, and possible delays after imaging. The evidence is limited by heterogeneous study designs, the predominance of single-center Indonesian studies, and scarce standardized 90-day outcome data. The review proposes a three-segment evaluation framework—symptom-to-door, door-to-decision, and decision-to-reperfusion—to guide balanced monitoring and future multicenter evaluation.

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INTRODUCTION

Stroke remains a major cause of death and long-term disability worldwide. Global estimates indicate more than 11 million new strokes annually, with the overall burden increasing since 1990 (Feigin et al., 2022; GBD 2021 Stroke Risk Factor Collaborators, 2024). Ischemic stroke accounts for approximately two thirds of incident strokes and is particularly time-sensitive because the benefit of reperfusion treatment declines as treatment is delayed. Intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT) therefore depend on coordinated recognition, imaging, decision-making, and treatment processes (Prabhakaran et al., 2026).

A code stroke pathway is an organized alert and response system that activates relevant clinical personnel, diagnostic imaging, laboratory processes, and treatment decisions in parallel when acute stroke is suspected. It should be understood as a continuum extending from symptom recognition and emergency medical services (EMS) activation to hospital treatment and, where indicated, interhospital transfer. Consequently, its performance cannot be assessed solely through emergency-department (ED) time targets; delays before arrival and after the initial imaging assessment may also determine whether patients receive reperfusion treatment within an appropriate window (Astasio-Picado et al., 2023).

Evidence published since 2021 has implications for the organization of this continuum. The BEST-MSU study reported faster thrombolysis and better 90-day functional outcomes with mobile stroke units (MSUs) than with conventional EMS care, although its prospective alternating-week design was not a conventional individually randomized trial (Grotta et al., 2021). The AcT and TRACE-2 trials found tenecteplase non-inferior to alteplase for eligible patients with acute

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ischemic stroke (Menon et al., 2022; Wang et al., 2023). SELECT2 demonstrated a favorable shift in disability outcomes with EVT among selected patients with large ischemic-core infarction (Sarraj et al., 2023). The 2026 American Heart Association/American Stroke Association (AHA/ASA) guideline incorporates evidence on thrombolytic choice, prehospital triage, MSUs, and EVT eligibility; these recommendations apply to defined patient groups and should not be interpreted as universal eligibility for every patient with a large infarct or posterior-circulation stroke (Prabhakaran et al., 2026).

In Indonesia, delays occur both before and after hospital arrival. A study in Yogyakarta reported that 64.6% of patients arrived more than 4.5 hours after symptom onset and that only 1.7% received IV thrombolysis (Yang & Hartanto, 2024). Another tertiary-center study reported an overall thrombolysis rate of 6.90%, with late or unknown onset and patient or family refusal among the reported reasons treatment was withheld (Situmeang et al., 2023). Conversely, workflow refinement and moving CT access closer to the ED were associated with shorter door-to-CT time at an Indonesian national referral hospital (Rasyid et al., 2022). These findings point to a gap between improving an in-hospital process and demonstrating better patient-centered outcomes. They also suggest that the Indonesian pathway requires evaluation across the prehospital, intrahospital, and post-decision phases.

This narrative review addresses three questions: (1) what evidence published from 2021 to 2026 supports the main components of code stroke; (2) how changes in IV thrombolysis and EVT influence pathway design; and (3) what can be concluded, and what remains uncertain, from published Indonesian studies? The review synthesizes findings by phase of care, compares the designs and limitations of the available evidence, and proposes a three-segment framework with operational indicators for future evaluation.

RESEARCH METHOD

This article is a targeted narrative review of literature published from January 2021 to October 2026. It is not a systematic review and does not claim compliance with PRISMA. The search was conducted in October 2026 using general web search engines, journal and publisher websites, and preprint repositories. Search phrases combined the following terms: “code stroke”; “acute ischemic stroke”; “door-to-needle”; “door-to-CT”; “door-to-decision”; “prehospital notification”; “mobile stroke unit”; “tenecteplase”; “large-core thrombectomy”; and “Indonesia”. Indonesian-focused combinations included “code stroke Indonesia”, “stroke thrombolysis Indonesia”, and “prehospital delay Indonesia”. Reference lists of relevant articles and guidelines were also checked to identify additional eligible publications. The final manuscript includes 30 sources selected for direct relevance to code stroke organization, time metrics, reperfusion treatment, or Indonesian implementation.

Sources were eligible when they were published in 2021–2026 and reported clinical guidelines, randomized or non-randomized trials, observational studies, systematic or narrative reviews, or Indonesian implementation data relevant to the review questions. Preprints and conference abstracts were retained only when they contributed data not otherwise identified; their publication status is stated in the text and their findings are treated as preliminary. Sources were excluded when they did not address acute ischemic stroke pathways or did not provide information relevant to the review questions. For each included source, the review recorded its design, setting and sample (when reported), care phase, principal time or clinical outcomes, and major interpretive limitations. Evidence was then grouped into prehospital care, intrahospital workflow, reperfusion treatment, and Indonesian implementation. Study design was used as a qualitative indicator of evidential strength; no pooled effect estimate or formal certainty grading was attempted.

Several methodological constraints limit reproducibility and completeness. The search did not use a predefined database protocol in PubMed, Scopus, or Embase; complete search strings, search-result counts, and a study-selection log were not retained. Screening and data extraction were conducted by one reviewer, and no formal risk-of-bias tool was applied. Accordingly, the 30-

source set should be regarded as a purposive evidence sample rather than an exhaustive census of the literature. The review is intended to provide a critical narrative synthesis, not to estimate a definitive pooled treatment effect. Future updates should use database-specific searches, independent screening, documented exclusion reasons, and formal appraisal of study quality.

RESULT AND DISCUSSION

Result

The review included 30 sources: clinical guidelines, clinical trials, reviews, observational studies, Indonesian studies, one international preprint, and one conference abstract. The evidence varies substantially in design and directness. Randomized trials provide the strongest comparative evidence for reperfusion treatment; large registry and quality-improvement studies are informative about system performance but remain susceptible to confounding; single-center retrospective studies describe local barriers but have limited generalizability. Preprints and conference abstracts provide preliminary signals and should not carry the same evidential weight as peer-reviewed full articles. Table 1 summarizes selected international evidence by pathway component, while Table 2 summarizes the Indonesian studies identified.

Table 1. Evidence map by code stroke component, 2021–2026

Component	Study	Design and sample	Direction of main finding
Prehospital	Dylla et al. (2024)	Observational; GWTG-Stroke registry and EMS records, patients 2018–2020	EMS documentation and pre-notification associated with shorter door-to-CT
Prehospital	Grotta et al. (2021)	Prospective controlled, alternating weeks; 1,515 patients	Faster treatment and better outcomes with mobile stroke units
Prehospital	Chen et al. (2022)	Systematic review of mobile stroke units	Shorter time to therapy
Prehospital	Lodhi et al. (2025)	Conference abstract; before–after; 456 patients	DTN and mRS improved (indicative)
Intrahospital	Xian et al. (2022)	National initiative evaluation; 154,221 patients, 913 hospitals	DTN fell stepwise
Intrahospital	Ganti et al. (2023)	Prospective single-hospital registry	Longer DTN on night shift; shorter with a dedicated stroke team
Intrahospital	Buleu et al. (2024)	Single center; 258 patients	Longer door-to-CT and door-to-ED-physician times associated with longer DTN
Intrahospital	Alzahrani et al. (2023)	Retrospective single center; 69 patients	DTN decreased; clinical outcomes did not differ
Reperfusion	Menon et al. (2022)	Randomized non-inferiority trial; 1,600 patients	Tenecteplase non-inferior to alteplase
Reperfusion	Wang et al. (2023)	Randomized non-inferiority trial; 1,430 patients	Tenecteplase non-inferior to alteplase
Reperfusion	Sarraj et al. (2023)	Randomized trial; 352 patients with large core infarct	Better functional outcome with thrombectomy

Prehospital phase. Dylla et al. (2024) linked Get With The Guidelines–Stroke registry data with prehospital records for patients admitted in 2018–2020. Documentation of last-known-well time, blood-glucose measurement, EMS pre-notification, and greater adherence to prehospital recommendations were associated with shorter door-to-CT time. Because this was an observational analysis, the associations do not establish that any single prehospital action independently caused the shorter interval. In the BEST-MSU prospective, multicenter, controlled study, 1,515 patients were enrolled and 1,047 were eligible for tissue plasminogen activator (t-PA); median onset-to-treatment time was 72 minutes with MSU care and 108 minutes with conventional EMS care. Among eligible patients, 97.1% versus 79.5% received t-PA, and 55.0% versus 44.4% achieved an mRS score of 0–1 at 90 days (Grotta et al., 2021). A systematic review also reported

shorter time to therapy with MSUs, although estimates across included studies may reflect differences in setting and study design (Chen et al., 2022). Lodhi et al. (2025) reported improvements after direct prehospital notification to the stroke team, but this evidence is a conference abstract and should be interpreted as preliminary.

Intrahospital phase. In a national quality-improvement analysis involving 154,221 patients at 913 hospitals, median door-to-needle (DTN) time decreased from 78 minutes before the Target: Stroke intervention to 66 minutes in Phase I and 50 minutes in Phase II; the proportion treated within 60 minutes increased from 26.4% to 68.6% (Xian et al., 2022). These results support the value of coordinated quality-improvement bundles, although the before-and-after design cannot isolate the contribution of each intervention. Smaller studies identify operational bottlenecks. Buleu et al. (2024) found that longer door-to-CT and door-to-ED-physician intervals were associated with longer DTN, with additional delays during night shifts. Ganti et al. (2023) reported median DTN of 37 minutes during day shifts and 59 minutes during night shifts; the presence of a dedicated stroke team was associated with shorter DTN. Alzahrani et al. (2023) reported a 44% reduction in DTN after implementation of a stroke code during Hajj, but did not find a significant difference in clinical outcomes. These studies suggest that staffing, team readiness, and imaging access are relevant process determinants, while evidence that isolated workflow changes improve long-term function remains less consistent.

Tenecteplase. In the AcT pragmatic, multicenter randomized non-inferiority trial, 1,600 patients were assigned to tenecteplase or alteplase. The proportion achieving an mRS score of 0–1 at 90 days was 36.9% and 34.8%, respectively, and symptomatic intracranial hemorrhage rates were similar; tenecteplase met the prespecified non-inferiority criterion (Menon et al., 2022). In TRACE-2, involving 1,430 participants in China, 62% of the tenecteplase group and 58% of the alteplase group achieved mRS 0–1 at 90 days (RR 1.07, 95% CI 0.98–1.16); symptomatic intracranial hemorrhage occurred in approximately 2% of each group. Ninety-day mortality was numerically 7% versus 5%, but the confidence interval around the relative risk included no difference (Wang et al., 2023). The 2026 AHA/ASA guideline recommends either tenecteplase (0.25 mg/kg, maximum 25 mg) or alteplase (0.9 mg/kg) for eligible adults treated within 4.5 hours. Tenecteplase is administered as a single bolus, which may simplify workflow and transfer logistics; this is an operational advantage inferred from its mode of administration, rather than a primary outcome tested by the AcT or TRACE-2 trials (Prabhakaran et al., 2026).

Thrombectomy for large-core infarcts. SELECT2 randomized 352 patients with large ischemic strokes to EVT or medical care and was stopped early for efficacy. EVT improved the overall distribution of disability at 90 days (generalized OR 1.51, 95% CI 1.20–1.89); functional independence was achieved by 20% versus 7% (Sarraj et al., 2023). These results support EVT in selected patients rather than indiscriminate treatment of all large-core infarcts. The 2026 AHA/ASA guideline recommends EVT for defined groups with anterior-circulation large-vessel occlusion, including selected patients with ASPECTS 3–5 in specified time windows, and provides separate criteria for basilar-artery occlusion. Eligibility depends on vessel location, time from onset, imaging, age, baseline function, and clinical severity. The guideline also states that IV thrombolysis may be reasonable in selected patients 4.5–9 hours from last-known-well or after wake-up stroke when automated perfusion imaging demonstrates salvageable tissue (Prabhakaran et al., 2026). These eligibility criteria should be represented accurately in local protocols and referral algorithms.

Evidence from Indonesia. The Indonesian studies identified in this review are heterogeneous in setting, design, and outcome measurement; most are single-center studies from tertiary hospitals. At RSCM Jakarta, a study of 310 patients found that median door-to-CT time declined from 57 minutes in November 2016–April 2017 to 19.5 minutes in November 2018–April 2019. At the end of the study period, 43.23% achieved door-to-CT within 25 minutes. CT location outside the ED was associated with delay (unadjusted OR 12.6, 95% CI 6.8–23.35); the article also reports a larger adjusted association in its multivariable analysis (Rasyid et al., 2022). The improvement followed a package of workflow refinement, team training, a dedicated hotline,

patient prioritization, a stroke kit, and relocation of CT closer to the ED. Because these changes were implemented as a bundle, the independent effect of CT relocation cannot be isolated.

Table 2. Studies of code stroke and treatment delay in ischemic stroke from Indonesia

Study	Site and period	Design and sample	Main focus
Rasyid et al. (2022)	RSCM Jakarta, 2016–2019	Cross-sectional, code stroke registry; 310 patients	Door-to-CT and its determinants
Hidayat et al. (2025)	Universitas Indonesia Hospital, Depok, 2021–2023	Retrospective single center; 182 patients	MRI versus CT, thrombolysis eligibility
Situmeang et al. (2023)	Siloam Hospitals Lippo Village, 2019–2020	Retrospective single center; 145 patients	Reasons thrombolysis was withheld
Yang & Hartanto (2024)	Bethesda Hospital Yogyakarta, 2023	Cross-sectional in a prospective cohort; 175 patients	Delayed arrival
Permana et al. (2026), preprint	RSCM and RSPON Jakarta, 2017–2025	Two-center retrospective descriptive; 259 patients	Thrombectomy time metrics

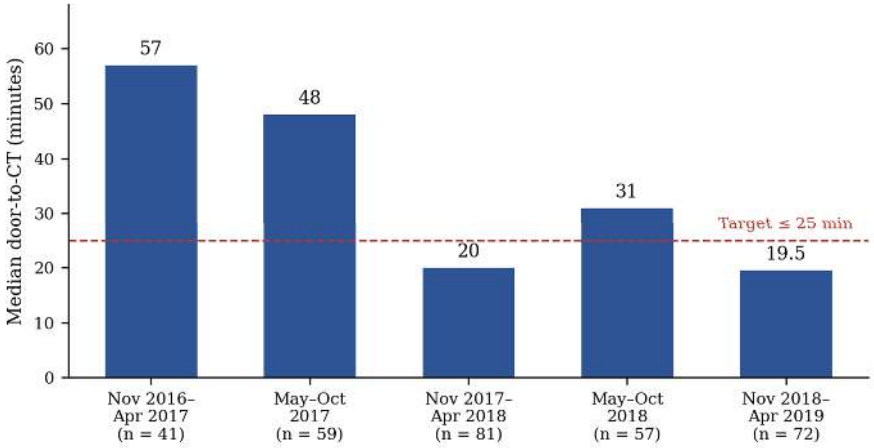


Figure 1. Median door-to-CT of code stroke patients at RSCM Jakarta by six-month period. Source: adapted from Rasyid et al. (2022).

Hidayat et al. (2025) compared a rapid MRI protocol with CT in 182 patients at a single Indonesian hospital. Thrombolysis eligibility was similar between groups, while a higher proportion of eligible patients in the MRI group received thrombolysis. The retrospective design and unequal group sizes mean that selection and workflow differences may partly explain this association; the findings should not be interpreted as evidence that MRI is generally preferable to CT for all code-stroke presentations. Situmeang et al. (2023) reported an overall thrombolysis rate of 6.90% at a tertiary hospital; late arrival or unknown onset was common, and patient or family refusal was a reported reason for withholding treatment among eligible patients. In Yogyakarta, only a minority of patients contacted EMS, while many arrived by private vehicle; delayed symptom recognition and waiting for spontaneous improvement were common explanations for late presentation (Yang & Hartanto, 2024). A two-center Indonesian preprint reported median door-to-CT of 9 minutes, door-to-decision of 101 minutes, and door-to-groin puncture of 272 minutes (Permana et al., 2026). As a preprint, these findings require peer-reviewed confirmation, but they highlight the need to measure delays after imaging as well as before it.

Discussion

The evidence indicates that code-stroke performance is shaped by the entire chain of care. The strongest prehospital evidence supports rapid recognition, accurate documentation, EMS

coordination, and early notification, but the type of evidence differs across interventions. Dylla et al. (2024) report observational associations, whereas BEST-MSU provides prospective controlled comparative evidence for MSUs (Grotta et al., 2021). The direct-notification findings from Lodhi et al. (2025) remain preliminary because they are available as a conference abstract. In Indonesia, low EMS use and delayed symptom recognition may limit the reach of pre-notification systems. Therefore, prehospital interventions should be adapted to local access patterns and include public symptom awareness, clear emergency activation routes, and structured referral communication rather than relying exclusively on ambulance-based alerts.

MSUs have the most direct evidence for accelerating prehospital treatment, but their staffing, imaging, laboratory, and operating costs may make them difficult to implement in resource-constrained settings. The available Indonesian literature identified in this review does not establish the cost-effectiveness or operational feasibility of MSUs in the national context. A pragmatic sequence for many hospitals may therefore be to strengthen existing EMS communication, establish direct notification to the stroke team, use rapid transport and direct-to-CT processes, and formalize referral arrangements. This is a context-sensitive implementation proposal, not a proven substitute for MSUs; it requires local evaluation of feasibility, treatment times, and outcomes.

Intrahospital quality-improvement studies consistently report shorter DTN or door-to-CT intervals after coordinated interventions (Xian et al., 2022; Alzahrani et al., 2023; Rasyid et al., 2022). However, process improvement should not be equated automatically with improved functional outcome. The Makkah study did not detect a significant clinical-outcome difference, and the Indonesian studies summarized here provide limited standardized 90-day modified Rankin Scale (mRS) data. Cross-study comparisons are also constrained by different definitions, patient populations, baseline severity, and measurement periods. The contrast between night-shift delays in some international studies and the absence of a significant association between admission outside working hours and door-to-CT in the RSCM study may reflect differences in infrastructure, staffing models, or the specific time interval measured; it does not establish that shift effects are absent in Indonesia.

Time metrics should be interpreted as a linked set rather than as interchangeable measures. Door-to-CT measures access to initial imaging; DTN measures time to IV thrombolysis among treated patients; door-to-decision captures the interval to a documented treatment or transfer decision; and door-to-groin puncture captures an important part of the EVT pathway. Each metric has a different denominator and may be affected by patient eligibility and case mix. A very short door-to-CT time does not guarantee rapid reperfusion if decision-making, consent, team activation, transfer, or catheter-laboratory access remains delayed. The Indonesian preprint by Permana et al. (2026) illustrates this possible pattern, but its estimates require confirmation. MRI-based pathways should likewise be evaluated against treatment delay and clinical eligibility, not only diagnostic yield (Hidayat et al., 2025).

The expansion of reperfusion options changes the organizational demands placed on code-stroke systems. Tenecteplase may simplify drug administration because it is delivered as a single bolus, but hospitals still need standardized eligibility checks, dosing safeguards, monitoring, and transfer protocols. EVT for selected patients with large-core infarction and extended time windows increases the importance of early vascular imaging when indicated, rapid specialist consultation, and explicit transfer pathways. The 2026 guideline emphasizes that eligible patients should receive IV thrombolysis without avoidable delay for additional advanced imaging and that destination decisions should reflect local stroke-system capability and the reliability of interhospital transfer (Prabhakaran et al., 2026). Hospitals without EVT capability should define who initiates referral, which imaging is required before transfer, how images are shared, and how transport is activated.

A conceptual contribution of this review is a three-segment evaluation framework that extends code stroke assessment beyond the ED. The framework links each segment to accountable

actors, measurable process indicators, and a patient-centered outcome. Segment 1, symptom-to-door, covers public recognition, emergency activation, EMS or referral access, and pre-arrival notification. Segment 2, door-to-decision, covers triage, imaging, clinical assessment, eligibility determination, and documented treatment or transfer decisions. Segment 3, decision-to-reperfusion, covers drug administration or transfer, receiving-center acceptance, EVT-team activation, and reperfusion. The framework is a synthesis-derived proposal and has not yet been prospectively validated.

Table 3. Proposed three-segment code-stroke evaluation framework

Segment	Core indicators	Primary accountable actors	Outcome / audit question
1. Symptom-to-door	Symptom-to-call; call-to-dispatch; dispatch-to-door; arrival mode; EMS use; pre-notification rate; proportion with documented last-known-well time	Public health services, EMS, referring facilities, community and family	How quickly are suspected stroke patients recognized and brought to an appropriate facility?
2. Door-to-decision	Door-to-triage; door-to-CT; door-to-imaging interpretation; door-to-needle among eligible treated patients; door-to-decision; proportion with documented eligibility and treatment decision	ED team, stroke team, radiology, laboratory, pharmacy	How quickly and safely is diagnosis translated into a documented treatment or transfer decision?
3. Decision-to-reperfusion	Decision-to-needle; decision-to-transfer; door-in-door-out; receiving-center acceptance time; door-to-groin puncture; reperfusion status	Stroke team, transfer coordinator, EMS, receiving EVT center, neurointerventional team	How efficiently does the system deliver definitive reperfusion after the decision?

Note. The proposed indicators should be reported with explicit definitions, denominators, missing-data rates, and stratification by shift, referral status, hospital capability, and treatment eligibility. The framework is conceptual and has not yet been validated.

Practice and research implications. Hospitals should monitor a balanced dashboard rather than a single time target. At minimum, audits should record symptom-onset/last-known-well time, arrival mode, arrival-to-triage, door-to-CT, door-to-needle among eligible treated patients, door-to-decision, decision-to-transfer, door-in-door-out, door-to-groin puncture, reperfusion status where available, and 90-day mRS. Results should be stratified by shift, hospital type, referral status, and treatment eligibility. For research, prospective multicenter studies should include district and non-university hospitals, use standardized definitions, report denominators and missing data, and link process metrics with 90-day functional outcomes. Implementation and economic evaluations are also needed before recommending resource-intensive models such as MSUs.

Limitations. This review has important limitations. The search was targeted and web-based rather than a comprehensive database search; search-result counts and a reproducible screening log were not retained. Single-reviewer selection and the absence of formal risk-of-bias assessment may have introduced selection and interpretation bias. The evidence base also includes a conference abstract and preprint, which have not undergone the same peer-review process as full journal articles. Indonesian studies are concentrated in tertiary centers, often use retrospective single-center designs, and rarely report standardized 90-day functional outcomes. Definitions and start/stop points for time metrics vary, limiting direct comparison. Finally, the proposed three-segment framework is conceptual and requires validation in prospective multicenter research.

CONCLUSION

Evidence published from 2021 to 2026 supports viewing code stroke as a continuum from symptom recognition to reperfusion, rather than as an ED alert alone. MSUs can accelerate prehospital treatment in settings where they are feasible; coordinated hospital quality-improvement programs can shorten imaging and thrombolysis intervals; tenecteplase is an evidence-supported

alternative to alteplase for eligible patients within 4.5 hours; and EVT benefits selected patients with large ischemic-core infarction. In Indonesia, available studies show that workflow refinement can improve door-to-CT performance, while late arrival, low EMS use, post-imaging decision delays, and limited 90-day outcome data remain important gaps. This review proposes a three-segment framework—symptom-to-door, door-to-decision, and decision-to-reperfusion—with linked indicators and accountability. Its validity and practical value should be tested in prospective multicenter Indonesian studies that include district hospitals and measure standardized 90-day functional outcomes.

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