

Clinical Practice Guidelines for the Pre-hospital Stage of Acute Stroke in Korea II : Transport Decisions for Patients with Acute Ischemic Stroke

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ABSTRACT

The mothership (MS) model, where patients are directly transferred to a thrombectomy-capable center, and the drip-and-ship (DS) model, where thrombolysis is initiated at the nearest primary stroke center before transfer for thrombectomy, are the primary transport modes for patients with stroke. We aimed to establish guidelines for selecting the appropriate transfer strategy based on emergent large vessel occlusion (LVO). We developed this guideline based on evidence from systematic reviews and meta-analyses via a *de novo* process. A systematic literature review was conducted across four databases (MEDLINE, Embase, Cochrane, and KoreaMed) to answer three Population, Intervention, Comparison, and Outcome questions comparing MS and DS models. The risk of bias was assessed using the Newcastle–Ottawa Scale. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagrams and meta-analyses were generated for functional outcomes, mortality, and successful recanalization. Twenty-six non-randomized controlled studies showed that the MS model improved good functional outcomes by approximately 14% compared with the DS model (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.00–1.30). Fifteen studies reported that mortality in the MS and DS models showed no significant differences (OR, 0.97; 95% CI, 0.84–1.11). Twenty-four studies revealed no significant difference in successful recanalization between the MS and DS models (OR, 0.87; 95% CI, 0.68–1.10). The MS model should be considered first to improve the functional outcome of patients with LVO. However, if thrombectomy cannot be performed immediately after thrombolysis, or if a thrombectomy-enabled hospital is not nearby, the DS model should be considered by stroke specialists depending on transportation time and regional factors. We suggest a mixed approach with the DS model based on specific circumstances or regions to ensure the optimum treatment of patients with acute ischemic stroke (AIS). Appropriate transport for patients with LVO improves the prognosis of AIS.

Key Words : Guidelines · Acute ischemic stroke · Large vessel occlusion · Mechanical thrombectomy · Intravenous thrombolysis · Transport.

INTRODUCTION

Concurrent acute ischemic stroke (AIS) and large vessel occlusion (LVO) require two major acute-phase treatments: intravenous thrombolysis (IVT) and mechanical thrombectomy (MT). There are two primary transport strategies for these recanalization therapies. First, the "mothership (MS)" model, where the patient is directly transferred to an IVT- and MT-enabled comprehensive stroke center (CSC). The other is the "drip-and-ship (DS)" model, where IVT is first administered at a nearby primary stroke center (PSC), and the patient is subsequently transferred to an MT-capable center. Studies have evaluated the clinical effectiveness of each model; however, the results varied depending on regional infrastructure, transport times, and institutional capacity. Korea has an efficient national health insurance system and an increasing number of certified endovascular neurosurgeons, neurointerventionists, and stroke centers. However, optimal emergency transport strategies for patients with AIS are inadequately standardized. Furthermore, disparities in geographical accessibility to thrombectomy-capable centers hinder the establishment of a nationwide unified protocol. This guideline aims to provide evidence-based recommendations for selecting the most appropriate hospital transfer strategy for patients with concurrent AIS and LVO. We aim to offer a practical framework adaptable to various clinical and geographic settings in Korea by systematically reviewing the current literature and incorporating expert consensus. We hope that this guideline will facilitate the development of a national protocol, which will be updated regularly to reflect emerging evidence and changes in healthcare delivery systems.

MATERIALS AND METHODS

Development of clinical practice guidelines

This guideline was developed using the methodology recommended by the relevant Korean medical society. Four key questions were established, and four recommendations were derived. For areas where recommendations could not be drawn from meta-analyses, a systematic review was conducted. Continuous revisions and further guideline development will be conducted subsequently with related society and experts. This guideline was approved by the Institutional Review Board (UC24ZISE0069), and the requirement for informed consent was waived. The participants and progress in developing this guideline are described in detail in Supplementary Material 1.

Rationale for developing guidelines

Emergency patient transfer has become a significant social concern in Korea, as highlighted by the ongoing media reports about emergency room crises. In addition, since February 2024, legislative conflicts have exacerbated the shortage of specialists, intensifying the crises in essential medical services. Thus, the challenge of transferring patients between hospitals has emerged as a major concern in Korea's healthcare system. Therefore, developing guidelines about decisions for patients with LVO is crucial to addressing this social challenge.

Selection of Key questions

The selection of key questions for the clinical practice guideline topic began with a survey among all members of the society. The survey was conducted before and after ASCENT between May and June 2024. Following the survey and the collection of topics by the working committee, two rounds of meetings were held among the development committee members to finalize the key questions. The key questions for each recommendation were formulated based on the Population, Intervention, Comparison, and Outcome (PICO) framework, and a systematic literature search was conducted. Our key questions are described below. In the hyperacute treatment of AIS, prompt and appropriate therapy is critical. For

patients eligible for IVT and MT, thrombolysis is required before thrombectomy. Deciding on the suitable approach is a daily challenge for emergency physicians. When determining the transport strategy to a stroke center for the initial reperfusion therapy, does a DS model approach—administering thrombolysis followed by a transfer to a thrombectomy-capable center—affect prognosis? Or is it preferable to transport the patient directly to a thrombectomy-capable center (MS model) to receive both treatments in one setting and potentially improve outcomes? This dilemma highlights the importance of choosing between the MS and DS models. The clinical question addressed in this guideline was structured according to the PICO format as follows: we included patients diagnosed with AIS requiring IVT and MT. The intervention group comprised patients managed using the MS model, and the comparison group consisted of patients treated with the DS model. The primary outcomes evaluated were good functional outcome, defined as a modified Rankin Scale (mRS) score of less than 3, all-cause mortality at 3 months, and successful recanalization (TICI 2b or higher). Furthermore, through systematic review, we assessed whether these outcomes varied according to transfer time and distance between the PSC and the thrombectomy-capable center (Supplementary Material 1). A summary of each key question and its corresponding recommendation is provided in Table 1.

Literature search and selection

The selection of relevant studies was conducted separately for each key question, with two, seven, or three development committee members assigned depending on the volume of the literature available for each topic. Duplicate exclusion and literature selection followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart (Fig. 1). The inclusion and exclusion criteria for each key question were formulated and applied based on the PICO framework.

Systematic review

For each subtopic selected by the Clinical Practice Guideline Executive Committee, at least two responsible reviewers were designated. Subsequently, a systematic review was conducted based on key questions, literature selection processes, supporting evidence, and meeting records. In Korea, where hospitals are predominantly located in urban centers, distinguishing between urban and rural settings is crucial when comparing the MS and DS models. A meta-analysis showed that available data were insufficient; therefore, we conducted a systematic review to examine the effects of transfer time and distance under the MS and DS paradigms.

Financial support and independence in clinical practice guideline development

The development of this guideline was funded by the Korean Neuroendovascular Society (KoNES) and the Korea Health Industry Development Institute, and no conflicts of interest were associated with this funding. The Clinical Practice Guideline Development Committee operated independently from KoNES, and during the guideline development process, the funding sources had no direct, indirect, or potential influence on the content of the guideline or the development process.

Publication and future updates of the clinical practice guideline

This clinical practice guideline will be published in medical journals affiliated with one of the Korean Neurosurgical Society. Additionally, it will be made publicly available on the society's official website, Instagram, and other online platforms, ensuring that physicians, healthcare professionals, and the general public can easily download and access the guidelines.

Furthermore, the guidelines will be registered on the official website of KoNES for promotional purposes. A summary booklet will also be produced and actively distributed at future academic conferences and events.

The KoNES Academic Committee and the Clinical Practice Guideline Committee will continue to monitor research findings in specific areas, including early diagnosis, the transfer of patients with emergency stroke, and treatment selection for subarachnoid hemorrhage. Additionally, they will track updates from international clinical guidelines. If new research accumulates, warranting additions or modifications to the recommendations, a Clinical Guideline Revision Committee under the society will be formed to revise the guideline every 5 years.

RESULTS

When considering IVT and MT, we identified 26 studies comparing the MS and the DS models, all of which were non-randomized studies (NRS). Among the studies, 26 evaluated functional outcomes at 3 months, 15 assessed mortality, and 24 compared successful recanalization. A good functional outcome was defined as a mRS score of less than 3, and successful recanalization was defined as a TICI grade of 2b or 3 on angiographic results after MT. In Korea, where hospitals are predominantly in urban centers, differentiating between urban and rural settings is crucial when comparing the MS and DS models. A preliminary meta-analysis revealed insufficient data; therefore, we conducted a systematic review to examine the effects of transfer time and distance under each model.

Functional outcomes

For patients with concurrent AIS and LVO requiring MT, transfer to a thrombectomy-capable center should be prioritized to improve post-treatment functional outcomes (level of evidence [LOE]: Moderate, grade of recommendation [GOR]: B).

Twenty-six studies^{1–12,14–18,20–22,24–29} compared the functional outcomes of the MS and DS models, with moderate heterogeneity observed. A follow-up at 3 months after AIS treatment showed that 1,863 of 3,803 patients (49.0%) in the MS model group achieved a good functional outcome, compared with 1,827 out of 4,186 patients (43.6%) in the DS model group. A meta-analysis of these 26 studies showed that the MS model improved good functional outcomes by approximately 14% compared with the effect of the DS model (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.00–1.30) (Fig. 2).

A good functional outcome is a primary endpoint in studies on MT. In AIS, the two major treatments should be delivered within a limited time, requiring the simultaneous efforts of a large medical team and sufficient healthcare resources. The MS model improves functional outcomes; therefore, providing both key treatments immediately after stroke in one comprehensive center improves outcomes. Additionally, receiving acute-phase care at hospitals with specialists and modern facilities improves outcomes. The MS model may be associated with adequate medical systems for immediate intervention, post-procedural patient care, and standardized clinical pathways. Therefore, patients should receive treatment at a CSC where IVT and MT are feasible to improve functional outcomes in cases of LVO-associated ischemic strokes.

However, treating LVO-induced AIS has a high risk of reperfusion injury and disability if recanalization is delayed. In addition to high recanalization rates and good post-procedural care, patients should receive IVT and MT sequentially within an optimal time window. If the time from symptom onset to recanalization exceeds a specific time limit, patients are less likely to achieve favorable outcomes, including those with good collateral circulation. Furthermore, in some cases, IVT alone may lead to successful recanalization. Therefore, the DS model should be considered first if MT cannot be performed immediately after thrombolysis or if thrombectomy-capable hospitals are not nearby.

For LVO-associated AIS, transporting the patient to the nearest MS hospital improves functional outcomes. However, the DS model should be considered if the transportation time is expected to be long or the distance is considerably long (LOE: Moderate, GOR: B).

Mortality

MS and DS models do not differ in terms of mortality for AIS with LVO. Consequently, the selection of the MS or DS Model should be based on local infrastructure, expertise, and specialist assessment, with emphasis on minimizing delays through a well-coordinated transport protocol (LOE: Moderate, GOR: C).

Fifteen studies reported mortality outcomes, and all were NRS with low heterogeneity. The follow-up was 3 months. Among 2,377 patients in the MS model group, 518 (21.8%) died. In the DS model group, 628 (21.7%) of 2,899 patients died. The MS model mortality was not significantly different from that of the DS model (OR, 0.97; 95% CI, 0.84–1.11) (LOE: Moderate) (Fig. 3). Previous studies on patients with stroke and LVO undertaking thrombectomy showed that mortality risk is influenced by initial patient condition and other factors, including age, time of treatment, and hospital infrastructure. Although previous major randomized control trials on MT revealed reduced mortality with aggressive treatment, mortality reductions between the MS and DS models were statistically insignificant. Therefore, in this study, there were no significant differences in mortality between the MS and DS models, consistent with the findings of previous thrombectomy studies (LOE: Moderate, GOR: C).

Recanalization rate

No significant differences in successful recanalization rates of reperfusion therapy were observed between the MS and DS Models. This guideline emphasizes the integration of thrombolysis and thrombectomy and recommends a good transport strategy to ensure that either procedure is performed promptly by stroke specialists (LOE: Low, GOR: C).

Twenty-four NRS with high heterogeneity reported recanalization rates. Among 3,123 and 3,515 patients in the MS and DS model groups, 2,486 (79.6%) and 2,889 (82.2%) achieved successful recanalization, respectively. A meta-analysis revealed no significant difference in successful recanalization between the MS and DS models (OR, 0.87; 95% CI, 0.68–1.10) (LOE: Low) (Fig. 4), possibly because both models recommended rapid and active treatments. MT was ultimately performed in all cases; therefore, the recanalization rates exhibited no differences. Thus, we concluded that there were no significant differences in the successful recanalization rate between the MS and DS models, consistent with the findings of previous studies (LOE: Low, GOR: C).

Distance and time

MS models are effective in urban areas or regions with many IVT- and MT-enabled hospitals—such as CSC or thrombectomy-capable centers. However, in rural areas with insufficient stroke centers and medical personnel or locations where the distance to a thrombectomy-capable center is significantly far, the DS model may be more effective, particularly when a PSC is nearby and can initiate thrombolysis before transfer. The appropriate model should be selected based on the transport time and distance to CSC or thrombectomy-capable centers that provide definitive treatment in each region (LOE: very low, GOR: C).

In patients with AIS, short transfer distances and reduced time to revascularization directly impact functional outcomes. Previous studies have revealed that long transfer distance is associated with poor functional outcomes and high mortality. Rinaldo et al. reported a significantly shorter time to revascularization under the MS model than under the DS model (277.4 vs. 420.4 min; $p \leq 0.0001$)²¹. Among the transferred patients, the long distance between the transferring and receiving hospitals was associated with a high mortality risk (unit OR, 1.26; 95% CI, 1.07–1.54; $p = 0.0061$). As long transfer distances were associated with high mortality, the MS model is more effective under such conditions. According to a multicenter observational study on Endovascular Treatment in Ischemic Stroke in

France, the MS model resulted in greater functional independence than that of the DS model among patients traveling over 20 km between the PSC and CSC (adjusted relative risk, 0.82; 95% CI, 0.71–0.94)²⁸. In the DS group with transfer distances under 20 km, outcomes did not differ significantly from those in the MS group, indicating that the MS model exhibited better outcomes as the transfer distance increased. Schlemm et al.²³ reported that long door-to-needle time (DNT) or door-out time at the PSC was associated with poor outcomes. Furthermore, if there were treatment delays (e.g., DNT and door-out time) at the PSC, better outcomes were observed when patients were directly transferred to a CSC²³. Previous studies have revealed that MT alone is not inferior to combined IVT and MT therapies. Based on these findings, recent guidelines (although limited) recommend direct transfer (MS model). Consequently, clinical practice is shifting toward the MS model to expedite MT, which may improve outcomes. Per previous studies, the MS model outperforms the DS model in time metrics, including DNT, onset-to-needle time (ONT), and onset-to-groin puncture time (OGT), resulting in reduced treatment time and improved functional outcomes. Therefore, physicians suggest that the choice of transfer model reduces the time to recanalization and improves patient prognosis. These studies share a common conclusion. For patients with LVO residing far from stroke centers or likely to experience a prolonged ONT, the MS model, which directs transportation to a thrombectomy-capable center, is recommended.

Other studies have reported contradictory results, exhibiting no significant differences in transport time or patient outcomes. The 2019 American Heart Association guideline suggests that the treatment of LVO-associated AIS is affected by door-in-door-out time, DNT, interhospital transport time, and various other factors, such as the allocation of medical resources¹⁹. Sallustio et al.²² compared cases with transport times to the CSC within 30 min versus >30 min, regardless of the transport method, and found no significant difference in 90-day functional outcomes and mortality or successful reperfusion rates²². Milne et al.¹³ revealed that the distance between medical institutions and the swiftness of treatment are critical in choosing between DS and MS models¹³. When the PSC is close to the CSC and intravenous alteplase can be administered within 30 min, the DS model may be effective.

If treatment is promptly administered in the DS model, outcomes may not significantly differ from those of the MS model. Simulation models have revealed no significant difference in prognoses between the two models when the transport time is <60 min¹³. Cabaraux conducted a single-center retrospective observational study by dividing 229 DS group patients into subgroups based on transport time to a CSC (within or >20 min) and comparing them with the MS model group patients and revealed no significant difference in functional outcomes between the models when the transport time was under 20 min⁴. Gerschenfeld et al. conducted a retrospective cohort study of 159 patients and found no significant differences in functional outcomes between the two models despite a treatment delay (approximately 50 min) in the DS group (MS, 240 min [interquartile range (IQR) 202–285] vs. DS, 297 min [IQR 255–357])⁹. In another retrospective cohort study, Adams et al. analyzed data from 214 patients and found no significant differences in functional outcomes despite a mean delay of 147 min in EVT for the DS model owing to transfer¹. These findings indicate that the DS model is not inferior to the MS model and, depending on the situation, can be an effective transport strategy. Thus, the optimal strategy may vary depending on the local medical infrastructure and transport time from the site of stroke onset.

These discrepancies among studies may be owing to the differences in regional and national settings where the models were studied. The DS model is used in rural areas without a nearby thrombectomy-capable center and 24-h on-site medical personnel, resulting in longer transport times. Delays in DNT, OGT, and onset-to-reperfusion time worsen outcomes. Therefore, we conclude that the MS model is effective in urban areas or regions with multiple hospitals where IVT and MT can be performed—such as CSC or thrombectomy-capable centers. However, in rural areas with insufficient stroke centers and medical personnel or locations where the distance to a thrombectomy-capable center is significantly far, the DS model may be more effective, particularly when a PSC is nearby and can initiate thrombolysis before transfer. The appropriate model should be selected based on the transport time and distance to CSC or thrombectomy-capable center capable of providing definitive treatment in each region (LOE: very low, GOR: C).

DISCUSSION

This clinical practice guideline primarily intends to guide paramedics responsible for emergency transport, emergency room medical staff, and specialists in emergency medicine, neurology, and neurosurgery who treat AIS. In cases of LVO-induced AIS, the rapid selection of an appropriate treatment hospital for timely intervention greatly improves functional outcomes. Through this guideline, we recommend transporting patients to the nearest hospital using the MS model when feasible. However, in instances where transport time to a thrombectomy-capable center is significantly prolonged or the distance is long, we suggest a mixed approach with the DS model based on the specific circumstances to ensure the optimal treatment of patients.

The KoNES has established certification systems for neuro-endovascular surgeons and stroke intervention-certified hospitals capable of performing thrombectomy (<https://www.konesonline.or.kr/certification/certiList.php>; Supplementary Material 1). As of November 29, 2024, there were 311 certified stroke interventionists and 106 certified institutions. In Korea, IVT and thrombectomy can be performed at centers certified by academic societies. When transferring emergency patients with LVO to certified centers, they should be transported to a nearby stroke intervention-certified hospital within an hour if acute severe cerebral infarction is suspected. KoNES plans to investigate and monitor the acute-phase major treatments and the current status of transferred patients and hospitals for patients with AIS and will actively introduce this guideline to its members. Although implementing the human network project in collaboration with the Ministry of Health and Welfare since 2024, KoNES will inform medical professionals and its members of the guidelines that actively incorporate the MS model or, depending on the state of the hospital or regional differences, allow for the application of the DS model, and will monitor their implementation. The final PICO was developed through a public hearing that included emergency medicine specialists and experts from relevant fields. The recommendation was formulated based on expert consensus, taking into

account the unique healthcare environment and characteristics of Korea. Because of the limited availability of data, a meta-analysis could not be conducted for this topic.

Through the guidelines developed in this study, we aim to support clinical decision-making in the early treatment of patients with AIS and restructure the patient transport system for those requiring urgent and critical care. Thus, we intend to redistribute medical resources more efficiently while improving the quality of stroke treatment, enhancing the health of patients and the general public.

CONCLUSION

IVT and MT, the primary treatments for LVO-induced AIS, are crucial. Thrombectomy requires consistently available infrastructure, personnel, and equipment, making the MS model challenging to implement without adequate resources. If a nearby facility can apply the MS model with minimal distance and transport time, immediate treatment implementation is recommended. However, if transport time is prolonged, the MS model may not be feasible. Similarly, if the thrombectomy-capable center is excessively distant or time-consuming to reach, the DS model should be prioritized. The appropriate model should be determined by a stroke specialist based on transport time and distance to thrombectomy-capable centers that provide definitive treatment in each region.

AUTHOR'S DECLARATION

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Informed consent

This type of study does not require informed consent.

Data sharing

None

Author contributions

Conceptualization : JSO; Data curation : JSO, YNJ; Formal analysis : JSO; Funding acquisition : JSO; Methodology : JSO; Project administration : JSO, JML, YNJ, JML, HSA, JJK, KMJ, GYY, JHK, DWS, HJL, JWJ, KCC, YSC, SJK, JKP, WSC, HK, YWK, SHS, SWL, JWL, TGK, SKH, SQP, SCK; Visualization : JSO; Writing - original draft : JSO, YNJ; Writing - review & editing : JSO, YNJ

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• Supplementary materials

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References

1. Adams KM, Burns PA, Hunter A, Rennie I, Flynn PA, Smyth G, et al. : Outcomes after thrombectomy in Belfast: mothership and drip-and-ship in the real world. **Cerebrovasc Dis** 47 : 231–237, 2019
2. Bourgeois-Beauvais Q, Sellin D, Arnaud I, Tuttle C, Landais A, Lannuzel A, et al. : Initiation of mechanical thrombectomy in an insular setting with helicopter transfer: a 2-year experience from the first, complete, tertiary stroke center in the Caribbean. **J Neurointerv Surg** 17 : 595–601, 2025
3. Brochado AP, Muras AC, Oyarzun-Irazu I, Rodriguez-Sainz A, Caballero-Romero I, Aguilera-Irazabal B, et al. : Drip and ship and mothership models of mechanical thrombectomy result in similar outcomes in acute ischemic stroke of the anterior circulation. **J Stroke Cerebrovasc Dis** 31 : 106733, 2022
4. Cabaraux P, Bellante F, Gaspard N, Dusart A : Comparison between “mothership” and “drip and ship” models in the management of acute ischemic strokes eligible for mechanical thrombectomy in the Charleroi area, Belgium. **J Stroke Cerebrovasc Dis** 33 : 108011, 2024
5. Černík D, Cihlár F, Neumann J, Doláková L, Šaňák D, Cihlár D, et al. : Transport strategy for ischaemic stroke patients with large vessel occlusion. **Neurol Neurochir Pol** 56 : 464–471, 2022
6. Feil K, Rémi J, Küpper C, Herzberg M, Dorn F, Kunz WG, et al. : Drip and ship for mechanical thrombectomy within the Neurovascular Network of Southwest Bavaria. **Neurology** 94 : e453–e463, 2020
7. Ferreira Cristina S, Fior A, Alves M, Papoila AL, Nunes AP : Functional outcome of endovascular treatment in patients with acute ischemic stroke with large vessel occlusion: mothership versus drip-and-ship model in a Portuguese urban region. **Cureus** 14 : e32659, 2022
8. Froehler MT, Saver JL, Zaidat OO, Jahan R, Aziz-Sultan MA, Klucznik RP, et al. : Interhospital transfer before thrombectomy is associated with delayed treatment and worse outcome in the

STRATIS registry (systematic evaluation of patients treated with neurothrombectomy devices for acute ischemic stroke). **Circulation** 136 : 2311–2321, 2017

9. Gerschenfeld G, Muresan I-P, Blanc R, Obadia M, Abrivard M, Piotin M, et al. : Two paradigms for endovascular thrombectomy after intravenous thrombolysis for acute ischemic stroke. **JAMA Neurol** 74 : 549–556, 2017

10. Hou J, Guo ZL, Huang ZC, Wang HS, You SJ, Xiao GD, et al. : Influences of different referral modes on clinical outcomes after endovascular therapy for acute ischemic stroke. **BMC Neurol** 22 : 228, 2022

11. Jiang F, Yin W, Jia J, Zhong H, Yang H, Huang J, et al. : Clinical outcomes after endovascular thrombectomy in different triage methods. **Heliyon** 9 : e19113, 2023.

12. Luchowski P, Wojczal J, Prus K, Szmygin M, Sojka M, Luchowska E, et al. : Direct admission vs. secondary transfer for mechanical thrombectomy: long-term clinical outcomes from a single Polish Comprehensive Stroke Centre. **Neurol Neurochir Pol** 55 : 494–498, 2021

13. Milne MSW, Holodinsky JK, Hill MD, Nygren A, Qiu C, Goyal M, et al. : Drip 'n ship versus mothership for endovascular treatment: modeling the best transportation options for optimal outcomes. **Stroke** 48 : 791–794, 2017

14. Morey JR, Oxley TJ, Wei D, Kellner CP, Dangayach NS, Stein L, et al. : Mobile interventional Stroke Team model improves early outcomes in large vessel occlusion stroke: the NYC MIST trial. **Stroke** 51 : 3495–3503, 2020

15. Paolucci M, Biguzzi S, Cordici F, Romoli M, Altini M, Agnoletti V, et al. : Drip-and-ship toward mothership model for mechanical thrombectomy during COVID-19 pandemic: a retrospective analysis. **Neurol Sci** 44 : 1–7, 2023

16. Park MS, Lee JS, Park TH, Cho YJ, Hong KS, Park JM, et al. : Characteristics of the drip-and-ship paradigm for patients with acute ischemic stroke in South Korea. **J Stroke Cerebrovasc Dis** 25 : 2678–2687, 2016
17. Park MS, Yoon W, Kim JT, Choi KH, Kang SH, Kim BC, et al. : Drip, ship, and on-demand endovascular therapy for acute ischemic stroke. **PLOS One** 11 : e0150668, 2016
18. Pfaff J, Pham M, Herweh C, Wolf M, Ringleb PA, Schönenberger S, et al. : Clinical outcome after mechanical thrombectomy in non-elderly patients with acute ischemic stroke in the anterior circulation: primary admission versus patients referred from remote hospitals. **Clin Neuroradiol** 27 : 185–192, 2017
19. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, 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** 50 : e344–e418, 2019
20. Prothmann S, Schwaiger BJ, Gersing AS, Reith W, Niederstadt T, Felber A, et al. : Acute Recanalization of thrombo-embolic ischemic Stroke with pREset (ARTESp): the impact of occlusion time on clinical outcome of directly admitted and transferred patients. **J Neurointerv Surg** 9 : 817–822, 2017
21. Rinaldo L, Brinjikji W, McCutcheon BA, Bydon M, Cloft H, Kallmes DF, et al. : Hospital transfer associated with increased mortality after endovascular revascularization for acute ischemic stroke. **J Neurointerv Surg** 9 : 1166–1172, 2017
22. Sallustio F, Mascolo AP, Marrama F, Lacidogna G, D’Agostino F, Rocco A, et al. : Comparison between different referral strategies for acute ischemic stroke patients in a hub-spoke emergency stroke network: a real-world experience in South-East Lazio. **Neurol Sci** 45 : 203–211, 2024

23. Schlemm E, Ebinger M, Nolte CH, Endres M, Schlemm L : Optimal transport destination for ischemic stroke patients with unknown vessel status: use of prehospital triage scores. **Stroke** 48 : 2184–2191, 2017
24. Seker F, Fiehler J, Möhlenbruch MA, Herweh C, Flottmann F, Ringleb PA, et al. : Clinical outcome after endovascular thrombectomy in 3 triage concepts: A prospective, observational study (NEUROSQUAD). **Stroke** 52 : e213–e216, 2021
25. Taschner CA, Trinks A, Bardutzky J, Brich J, Hartmann R, Urbach H, et al. : Drip-and-ship for thrombectomy treatment in patients with acute ischemic stroke leads to inferior clinical outcomes in a stroke network covering vast rural areas compared to direct admission to a comprehensive stroke center. **Front Neurol** 12 : 743151, 2021.
26. van Veenendaal P, Yan B, Churilov L, Dowling R, Bush S, Mitchell P, et al. : Endovascular clot retrieval by hub-and-spoke service delivery is feasible compared with direct-to-mothership. **Cerebrovasc Dis** 46 : 172–177, 2018
27. Weber R, Reimann G, Weimar C, Winkler A, Berger K, Nordmeyer H, et al. : Neurovascular net Ruhr. Outcome and periprocedural time management in referred versus directly admitted stroke patients treated with thrombectomy. **Ther Adv Neurol Disord** 9 : 79–84, 2016
28. Weisenburger-Lile D, Blanc R, Kyheng M, Desilles J-P, Labreuche J, Piotin M, et al. : Direct admission versus secondary transfer for acute stroke patients treated with intravenous thrombolysis and thrombectomy: insights from the endovascular treatment in ischemic stroke registry. **Cerebrovasc Dis** 47 : 112–120, 2019
29. Weiss D, Rubbert C, Kaschner M, Jander S, Gliem M, Lee JI, et al. : Mothership vs. drip-and-ship: evaluation of initial treatment strategies for acute ischemic stroke in a well-developed network of specialized hospitals. **Neurol Res** 45 : 449–455, 2023

Accepted article

Table 1. Summary of key questions and recommendations

Key question	Recommendation	GOR	LOE
In the hyperacute treatment of acute ischemic stroke (AIS) with large vessel occlusion (LVO), prompt and appropriate therapy is critical. For patients eligible for thrombolysis and thrombectomy, thrombolysis should precede thrombectomy. Selecting the appropriate transport strategy remains a daily challenge for emergency physicians. When determining transport to stroke centers for initial reperfusion, does a drip-and-ship (DS) model—administering thrombolysis followed by transfer to a thrombectomy-capable center—affect prognosis? Or is it preferable to transport the patient directly to a thrombectomy-capable center (mothership [MS] model) to receive both treatments in a single setting and potentially improve outcomes?			
Does the MS model improve functional outcomes compared with the effectiveness of the DS model?	The MS model improves patient prognosis compared with the effect of the DS model by enhancing good functional outcomes.	B	Moderate
Does the MS model reduce mortality compared with the efficiency of the DS model?	MS and DS models do not differ in terms of mortality for AIS with LVO.	C	Moderate
Does the MS model increase the recanalization rate compared with the effect under the DS model?	MS and DS models do not differ in terms of successful recanalization among treatment outcomes for AIS with LVO.	C	Low
Can the application of the MS and DS models vary depending on different regions and factors such as time and distance of	In urban areas or regions with multiple well-equipped hospitals—such as thrombectomy-capable or comprehensive stroke centers—the MS model is likely to be more effective.	C	Very Low

transfer to thrombectomy-capable hospitals?	However, in rural regions, areas with a shortage of stroke centers and medical personnel, or locations where the distance to a thrombectomy-capable center is significantly greater, the DS model may be more effective, particularly when a nearby primary stroke center (PSC) can initiate thrombolysis before transfer. The appropriate model should be selected based on the transport time and distance to PSCs and thrombectomy-capable centers, under the discretion of a stroke specialist.		
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GOR, grade of recommendation; LOE, level of evidence

FIGURE LEGENDS

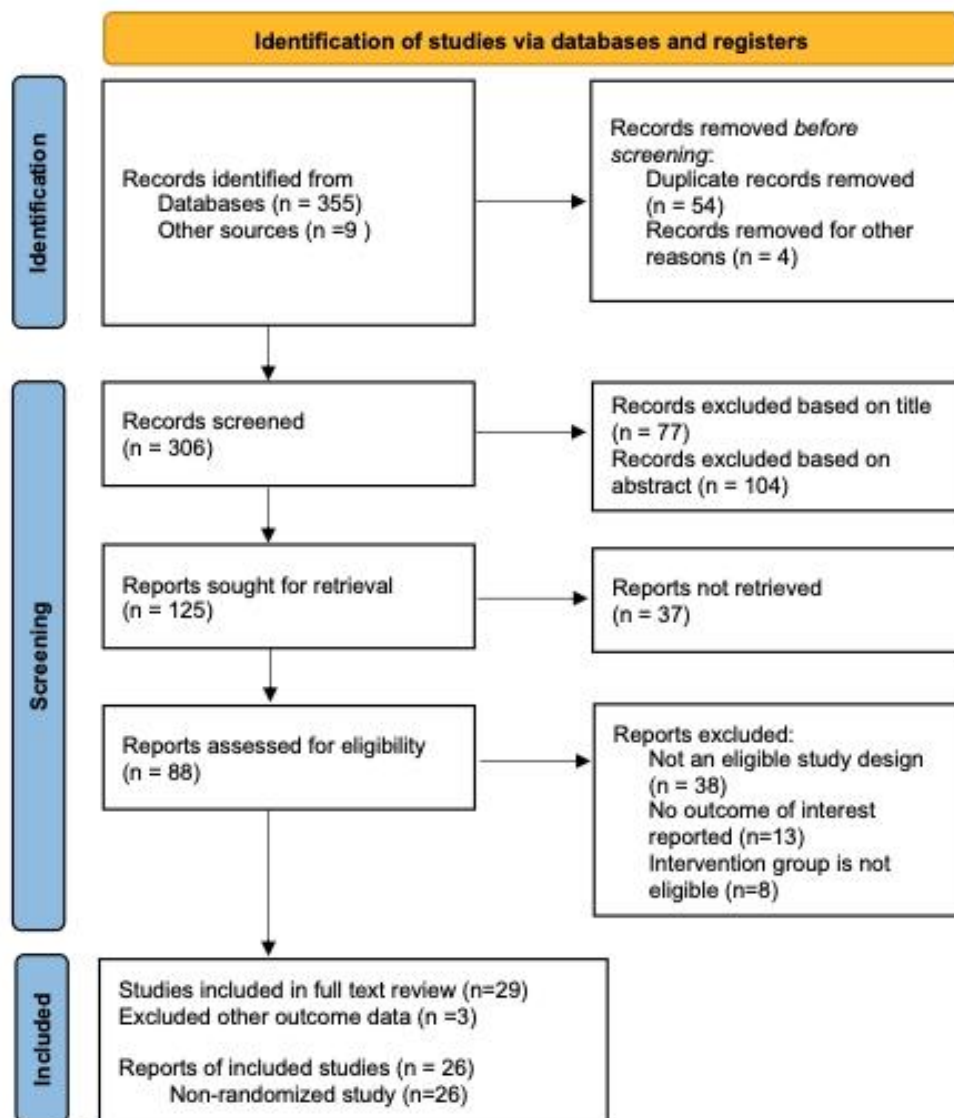


Fig. 1. PRISMA flow.

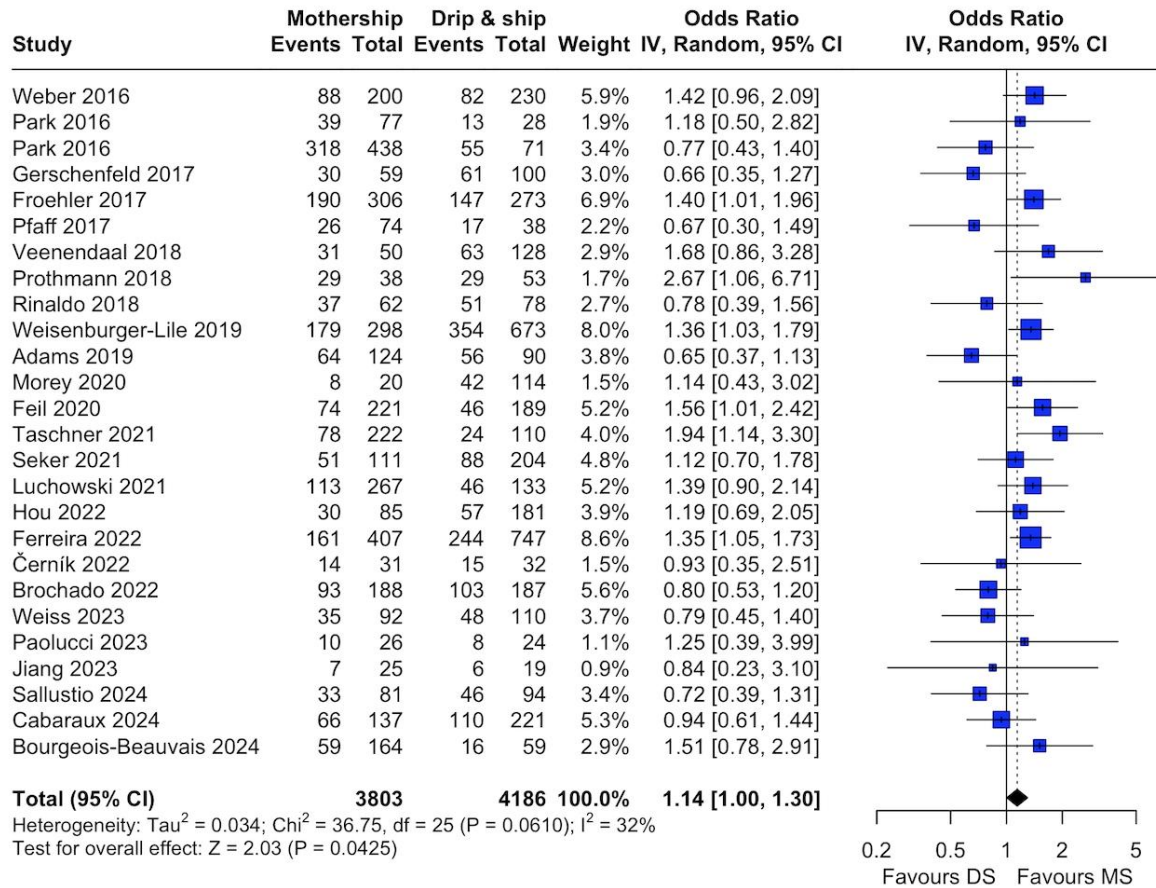


Fig. 2. Forest plot of functional outcome between mothership and drip-and-ship model.

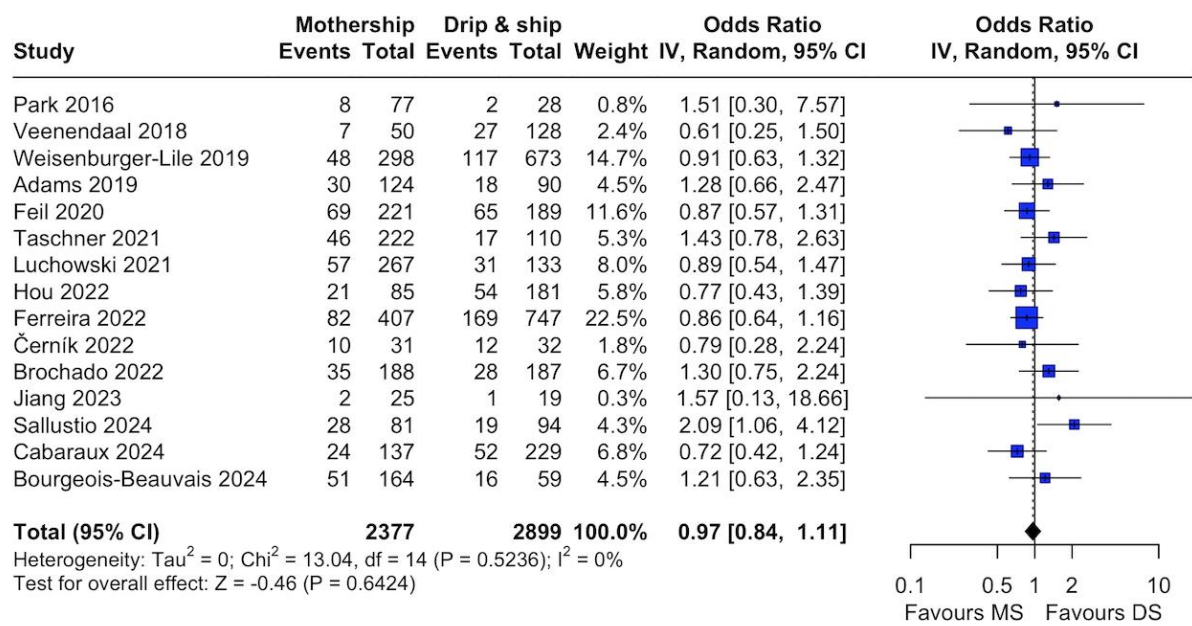


Fig. 3. Forest plot of mortality between mothership and drip-and-ship model.

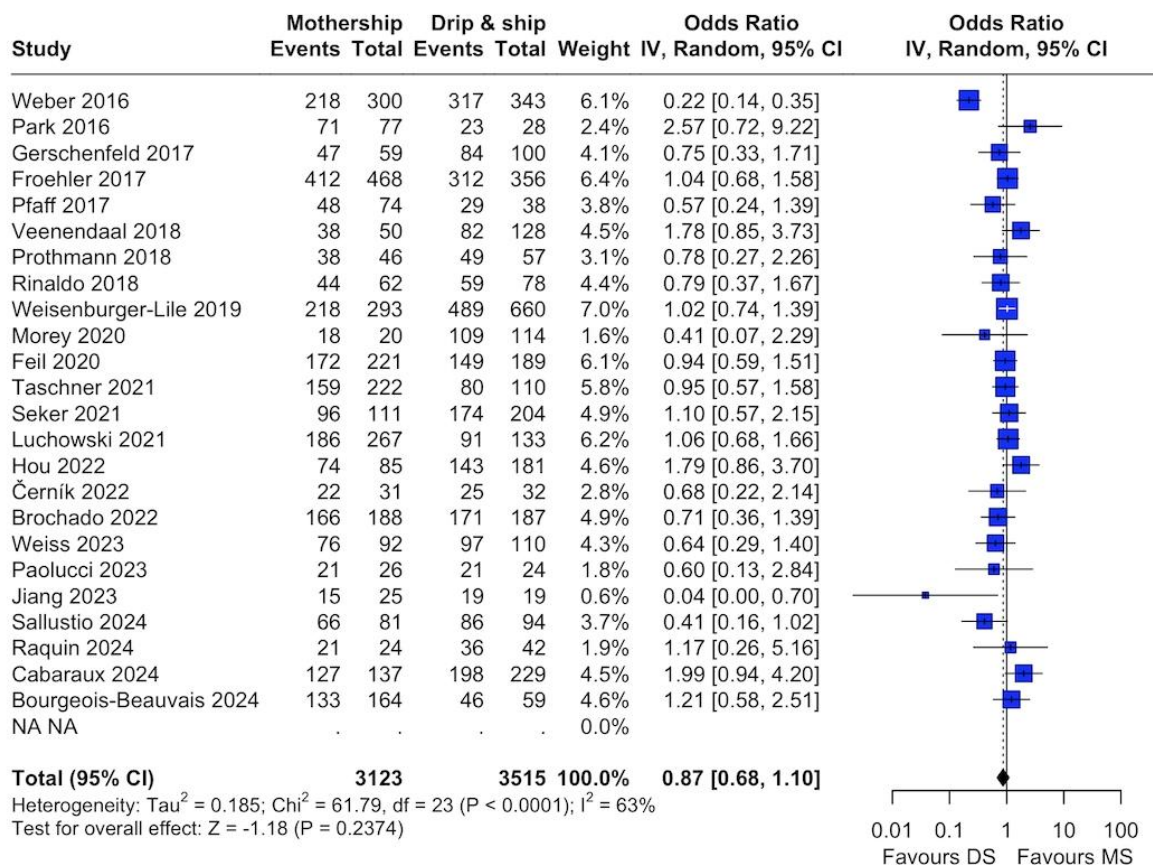


Fig. 4. Forest plot of successful recanalization between mothership and drip-and-ship model.

Supplementary Material 1.

Composition of the clinical practice guideline committee and multidisciplinary participation

The Clinical Practice Guideline Committee comprises the Executive, Working, and Internal and External Review Committees. The Executive Committee, led by the president and executives of the society, establishes the strategy and direction for the development of guidelines, reviews and approves the budget, coordinates with stakeholders, and ensures the independence of the developmental process.

The Working Committee is primarily composed of the president of the Korean Neuroendovascular Society (KoNES), the chair of the Clinical Practice Guideline Committee, and key executive board members. Additionally, representatives from the Korean Society of Emergency Medicine and the Korean Society of Cerebrovascular Surgeons were appointed to the committee. Neurologists and methodology experts also participated in this study, forming a multidisciplinary panel. The committee was structured as follows: Executive Committee (10 members), Guideline Development Working Committee (14 members), Advisory Committee (eight members), Conflict of Interest Committee (seven members), Administrative Support Team (two members), Internal Review Committee (two members), and External Review Committee (two members).

The establishment of the guideline was officially announced in January 2024 during the New Year Executive Meeting (Clinical Practice Guideline Director: Jae Sang Oh, President: Soon-Chan Kwon) of the KoNES. Thirteen meetings were held in 2024, followed by five additional conferences in 2025, including committee executive gatherings, public hearings, and internal/external surveys.

Clinical medical guideline development process

There have been attempts to develop stroke medical guidelines in Korea. Therefore, existing medical guidelines, domestic and international, were reviewed to define the scope and target population of the new guidelines. Based on this review, it was determined that stroke is a broad topic. Attempting to cover all aspects of stroke in the first edition of the guidelines might lead to an excessively extensive scope and potential overlap with existing international guidelines.

Stroke treatment is categorized into three phases: pre-hospital care, hospital treatment, and post-treatment management. Most of the previously established Korean guidelines have focused on hospital-based treatment, and many were created by modifying or adapting existing international guidelines.

Emergency patient transfer has become a significant social concern in Korea, as highlighted by ongoing media reports about emergency room crises. Furthermore, since February 2024, legislative conflicts have exacerbated the shortage of specialists, intensifying the crises in essential medical services. Thus, the challenge of transferring patients between hospitals has become critical in Korea's healthcare system. Therefore, this guideline about decisions for patients with large vessel occlusion will help mitigate this social challenge.

Selection of Key questions

The selection of key questions for the clinical practice guideline topic began with a survey conducted among all members of the society. The survey was collected before and after ASCENT between May and June 2024. Following the survey and the collection of topics by the working committee, two rounds of meetings were held among the development committee members to finalize the key questions.

Each development and working committee member underwent training on guideline development provided by the Korean Academy of Medical Sciences. Following the training, the key questions for

each recommendation were formulated based on the Population, Intervention, Comparison, and Outcome (PICO) framework, and a systematic literature search was conducted accordingly.

Literature search and selection

The literature search was conducted through discussions between methodology experts and the development committee members. An initial set of search terms was formulated, and a search strategy was established accordingly. Based on this strategy, searches were conducted across four major databases: MEDLINE (PubMed), Embase, Cochrane Library, and KoreaMed. The search was performed on November 11, 2024.

For all key questions, no restrictions were applied regarding publication year, language, or publication status. The retrieved records were compiled using EndNote, and duplicates were removed based on title, author name, publication year, and journal name. The final search strategy has been provided as a supplementary file.

MEDLINE

1. (((((((("Brain Infarction"[Mesh:NoExp]) OR "Brain Stem Infarctions"[Mesh]) OR "Cerebral Infarction"[Mesh:NoExp]) OR "Infarction, Anterior Cerebral Artery"[Mesh]) OR "Infarction, Middle Cerebral Artery"[Mesh]) OR "Infarction, Posterior Cerebral Artery"[Mesh]) OR "Ischemic Stroke"[Mesh]
2. ("Anterior Circulation"[TIAB] OR "Posterior Circulation"[TIAB] OR Brainstem[TIAB] OR Basilar[TIAB] OR Medullary[TIAB] OR cerebellar[TIAB] OR cerebellum[TIAB] OR Subcortical[TIAB] OR Cerebral[TIAB] OR brain[TIAB]) AND (infarction[TIAB] OR Infarct[TIAB] OR Infarcts[TIAB] OR infarctions[TIAB])
3. (Ischemic[TIAB] OR Ischemic[TIAB] OR Ischemia[TIAB] OR Embolism[TIAB] OR Embolic[TIAB] OR Cardio-embolic[TIAB] OR Thrombotic[TIAB]) AND ("Large Vessel

Occlusion"[TIAB] OR stroke[TIAB] OR strokes[TIAB])

4. 1-3/OR

5. "Mothership"[TIAB] OR "Drip and Ship"[TIAB] OR "Drip-and-Ship"[TIAB]

6. 4 AND 5

Embase

1. 'brain infarction'/de

2. 'brain stem infarctions'/exp

3. 'cerebral infarction'/de

4. 'infarction, anterior cerebral artery'/exp

5. 'infarction, middle cerebral artery'/exp

6. 'infarction, posterior cerebral artery'/exp

7. 'ischemic stroke'/exp

8. ('anterior circulation':ab,ti OR 'posterior circulation':ab,ti OR brainstem:ab,ti OR basilar:ab,ti OR medullary:ab,ti OR cerebellar:ab,ti OR cerebellum:ab,ti OR subcortical:ab,ti OR cerebral:ab,ti OR brain:ab,ti) AND (infarction:ab,ti OR infarct:ab,ti OR infarcts:ab,ti OR infarctions:ab,ti) 99565

9. (ischemic:ab,ti OR ischemic:ab,ti OR ischemia:ab,ti OR embolism:ab,ti OR embolic:ab,ti OR 'cardio embolic':ab,ti OR thrombotic:ab,ti) AND ('large vessel occlusion':ab,ti OR stroke:ab,ti OR strokes:ab,ti)

10. 1-9/OR

11. 'mothership':ab,ti OR 'drip and ship':ab,ti OR 'drip-and-ship':ab,ti

12. 10 AND 11

Cochrane

1. MeSH descriptor: [Brain Infarction] this term only

2. MeSH descriptor: [Brain Stem Infarctions] explode all trees

3. MeSH descriptor: [Cerebral Infarction] this term only

4. MeSH descriptor: [Infarction, Anterior Cerebral Artery] explode all trees
5. MeSH descriptor: [Infarction, Middle Cerebral Artery] explode all trees
6. MeSH descriptor: [Infarction, Posterior Cerebral Artery] explode all trees
7. MeSH descriptor: [Ischemic Stroke] explode all trees
8. ("Anterior Circulation" OR "Posterior Circulation" OR Brainstem OR Basilar OR Medullary OR cerebellar OR cerebellum OR Subcortical OR Cerebral OR brain) AND (infarction OR Infarct OR Infarcts OR infarctions):ti,ab,kw
9. (Ischemic OR Ischemic OR Ischemia OR Embolism OR Embolic OR Cardio-embolic OR Thrombotic) AND ("Large Vessel Occlusion" OR stroke OR strokes):ti,ab,kw
10. 1-9/OR
11. "Mothership" OR "Drip and Ship" OR "Drip-and-Ship":ti,ab,kw
12. 10 AND 11

KoreaMed

((((((("Brain Infarction"[MH]) OR "Brain Stem Infarctions"[MH]) OR "Cerebral Infarction"[MH]) OR "Infarction, Anterior Cerebral Artery"[MH]) OR "Infarction, Middle Cerebral Artery"[MH]) OR "Infarction, Posterior Cerebral Artery"[MH]) OR "Ischemic Stroke"[MH]) OR ("Anterior Circulation"[TIAB] OR "Posterior Circulation"[TIAB] OR Brainstem[TIAB] OR Basilar[TIAB] OR Medullary[TIAB] OR cerebellar[TIAB] OR cerebellum[TIAB] OR Subcortical[TIAB] OR Cerebral[TIAB] OR brain[TIAB]) AND (infarction[TIAB] OR Infarct[TIAB] OR Infarcts[TIAB] OR infarctions[TIAB]))) OR ((Ischemic[TIAB] OR Ischemic[TIAB] OR Ischemia[TIAB] OR Embolism[TIAB] OR Embolic[TIAB] OR Cardio-embolic[TIAB] OR Thrombotic[TIAB]) AND ("Large Vessel Occlusion"[TIAB] OR stroke[TIAB] OR strokes[TIAB]))) AND ("Mothership"[TIAB] OR "Drip and Ship"[TIAB] OR "Drip-and-Ship"[TIAB])

Quality assessment of the literature and meta-analysis

The quality assessment of primary studies was conducted based on their respective study designs. The evaluation was independently performed by two reviewers, and any discrepancies in the assessment results were resolved through consensus between at least two reviewers. To minimize inconsistencies in evaluations among committee members, individual meetings and workshop training sessions on literature assessment were conducted. The results of individual evidence-level assessments were provided within each key question section of the clinical recommendations. For quality assessment, the following tools were used: Non-randomized studies: Newcastle–Ottawa Scale. A meta-analysis was conducted if there was no substantial unexplained heterogeneity among the included studies and if at least two studies reported comparable outcomes. However, if the included studies had different study designs, their results were presented separately.

In cases where duplicate data were suspected, the most recently published study or that with the largest sample size was included in the final meta-analysis. A random-effects model was applied for the meta-analysis, and statistical heterogeneity was evaluated using I^2 statistics. The meta-analysis considered the benefits and harms associated with the intervention under investigation.

Systematic review

For each subtopic selected by the Clinical Practice Guideline Executive Committee, at least two responsible reviewers were designated. Subsequently, a systematic review was conducted based on key questions, literature selection processes, supporting evidence, and meeting records. In Korea, where hospitals are predominantly located in urban centers, distinguishing between urban and rural settings is crucial when comparing the MS and DS models. A meta-analysis showed that available data were insufficient; therefore, we conducted a systematic review to examine the effects of transfer time and distance under the MS and DS paradigms.

To ensure the objective validation of the drafted content, two reviewers independently evaluated each subtopic. Subsequently, the manuscript drafted by the Clinical Practice Guideline Development Committee was reviewed by two independent stroke emergency experts who had not been directly involved in the guideline development process. Comments and suggestions from internal and external reviews were discussed and incorporated through internal deliberation.

Derivation of recommendations, determination of recommendation strength, and evidence levels

Evaluation of recommendation strength and evidence level followed the criteria established by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). The final clinical recommendations were determined through a review process involving the internal and external committees.

The recommendation levels were classified into four grades based on the balance between benefits and harms associated with each intervention.

- A. Strong Recommendation: Applied when the desirable effects of an intervention clearly and substantially outweigh the undesirable effects. In such cases, most well-informed patients choose this intervention.
- B. Recommendation: Applied when the desirable effects of an intervention outweigh the undesirable effects; however, some well-informed patients consider alternative interventions.
- C. Conditional Use: Suggested when the decision to use an intervention depends on clinical circumstances or patient social values, recommending selective or conditional use.
- D. Not Recommended: Applied when the harms of an intervention outweigh its benefits, advising against its use.
- E. Not Recommended: Harm is considered to outweigh the benefit.

Quality of evidence

We applied the GRADE approach to rate the quality of evidence of each outcome and to determine the strength of each recommendation. The GRADE evidence level was determined through discussions among key question reviewers to ensure objectivity and consistency across all clinical recommendations. Subsequently, the entire process was disclosed during a public hearing for transparency. The evidence level was assigned separately for each outcome measure, and the final recommendation was based on the highest priority primary outcome within each clinical guideline.

The evidence levels were classified into four categories and summarized using GradePro: high, moderate, low, and very low. Evidence-level downgrading and upgrading were considered based on the following criteria:

For observational studies, evidence was upgraded if (1) a large effect size was observed, (2) a dose-response relationship was identified, and (3) confounding factors increased confidence in the estimated effect. Each key question reviewer summarized the evidence and its level, considering various factors, such as the strength and limitations of the available evidence, the balance of benefits and harms, patient values and preferences, potential barriers for physicians, financial implications, and feasibility in clinical settings. Based on these considerations, the initial draft of the clinical recommendations and recommendation grading was developed.

Supplementary Material 2.

Consensus and adoption of recommendations

The guideline recommendations were derived under two major topics, resulting in a total of two recommendations. The principle for determining recommendation grades within the internal committee required that at least 80% of committee members participate, and a minimum of 70% approval was needed for a decision to be considered a consensus. If the approval rate did not reach 70%, the committee engaged in further discussions to draft a revised proposal, followed by a second round of voting. Recommendations that failed to gain final approval in the first round were revised and subjected to a second vote. During the second voting round, the two revised recommendations reached a consensus, and ultimately, one final recommendation was adopted.

Internal and external reviews

For each recommendation, the designated reviewers selected by the Clinical Practice Guideline Executive Committee drafted manuscripts based on key questions, the recommendation development process, the supporting literature, and meeting records.

To ensure objective validation, the manuscripts prepared by the Clinical Practice Guideline Development Committee were reviewed by two independent stroke emergency experts who were not directly involved in the development process. Feedbacks from internal and external reviews were discussed and incorporated through an internal revision process.

For external expert review, on March 5, 2025, a draft of the clinical practice guideline recommendations was presented to a broad audience, including specialists in emergency medicine, neurosurgery, neurology, and radiology, as well as representatives from related academic societies and non-member

physicians, along with members of the patient and public people. The recommendations were fully disclosed, and an open public discussion was conducted to collect feedback.

All meetings were conducted online. Based on the feedback received, revised recommendations were formulated and underwent a second round of expert review before finalization.

Financial support and independence in clinical practice guideline development

This guideline was developed with funding from KoNES and the Korea Health Industry Development Institute (KHIDI); however, no conflicts of interest were associated with this funding. The Clinical Practice Guideline Development Committee operated independently from KoNES, and during the guideline development process, the funding sources had no direct, indirect, or potential influence on the content of the guideline or the development process.

To ensure transparency, all participating committee members underwent a conflict of interest (COI) disclosure process to confirm that no actual or potential conflicts of interest were present. The evaluation included: 1) Any advisory roles or honoraria received in the past 2 years related to topics covered in the guideline development, 2) Financial interests, such as stock holdings or shares, in institutions related to the guideline content, 3) Any official or unofficial positions held at organizations relevant to the guideline, 4) Intellectual property rights, including patents related to medications covered in the guideline.

Through this process, it was confirmed that no committee member had any actual or potential COI that could influence the development of this guideline.

Supplementary Table 1. Key clinical questions

Disease	Category	Clinical question
Acute ischemic stroke with large vessel occlusion	Prognosis	In patients with acute ischemic stroke accompanied by large vessel occlusion, which model provides more benefit to the patient — mothership (MS) or drip-and-ship (DS)?
		1. Does the MS model improve functional outcomes compared with the effect of the DS model? 2. Does the MS model reduce mortality compared with the impact of the DS model? 3. Does the MS model more effectively increase the angiographic recanalization rate than does the DS model? 4. Can the application of the MS and DS models vary depending on different regions and factors such as time and distance of transfer to thrombectomy-capable hospitals?

Supplementary Table 2. Level of evidence (LOE) definition

Grade	Meaning	Level of evidence (LOE) definition
A	High	1. Highly reliable evidence: At least one randomized controlled trial (RCT) with consistency 2. High-quality meta-analysis
B	Moderate	1. Reliable evidence: Well-designed controlled trials exist, but no RCTs 2. Moderate-quality meta-analysis
C	Low	1. Evidence is unclear. 2. Physiological or mechanistic studies in human participants
D	Very low	1. Insufficient evidence. 2. Consensus of expert opinion based on clinical experience

Supplementary Table 3. Grade of recommendation (GOR) definition

Grade	Meaning	Grade of recommendation (GOR) definition
A	Strongly Recommended	Clinical benefit significantly outweighs the harm.
B	Recommended	Clinical benefit is considered to outweigh the harm.
C	Consider as an Option	The balance between benefit and harm is unclear.
D	No Recommendation	Insufficient evidence to determine the balance of benefit and harm.
E	Not Recommended	Harm is considered to outweigh the benefit.

Supplementary Table 4. Certainty of evidence assessed using GRADE

Certainty assessment							№ of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mothers hip model	Drip & ship model	Relative (95% CI)	Absolute (95% CI)		
Functional outcome												
26	non-randomized studies	not critical	not critical	not critical ^a	not critical	all plausible residual confounding would reduce the demonstrated effect	3,690 cases, 4,299 controls		OR 1.14 (1.00–1.30)	-	⊕⊕⊕○ Moderate ^a	IMPORTANT
							-	40.0 %		32 more per 1,000 (from 0 fewer to 64 more)		

							-	30.0 %		28 more per 1,000 (from 0 fewer to 58 more)		
							-	30.0 %		28 more per 1,000 (from 0 fewer to 58 more)		
Mortality												

15	non-randomized studies	not critical	not critical	not critical ^a	not critical	all plausible residual confounding would suggest spurious effect, whereas no effect was observed	1,146 cases, 4,130 controls	OR 0.97 (0.84 – 1.11)	-	⊕⊕⊕ ○ Moderate ^a	NOT IMPORTANT	
Successful recanalization												
24	non-randomized studies	not critical	critical ^b	not critical ^a	not critical	all plausible residual confounding would reduce the demonstrated effect	5,375 cases, 1,263 controls	OR 0.87 (0.68 – 1.10)	-	⊕⊕○ ○ Low ^{a,b}	NOT IMPORTANT	

CI : confidence interval, OR : odds ratio. Explanations : a. Various models for stroke center and b. high heterogeneity

Supplementary Table 5. Institutions of thrombectomy-capable center

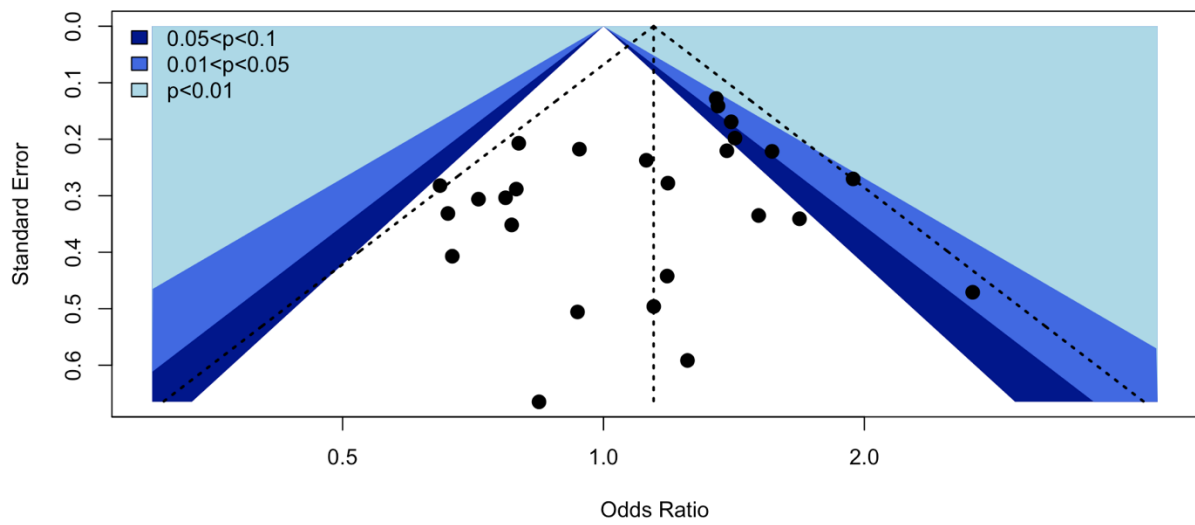
번호	지역	기관명
110	부산	부산부민병원
109	경기	시화병원
108	세종	세종충남대학교병원
107	전남	목포한국병원
106	경기	화흥병원
105	인천	인천사랑병원
104	경기	월스기념병원
103	부산	동남권원자력의학원
102	울산	울산중앙병원
101	경기	오산한국병원
100	인천	가톨릭관동대학교 국제성모병원
99	서울	서울의료원
98	서울	연세대학교 세브란스병원
97	충북	청주하나병원
96	경기	한림대학교 동탄성심병원
95	경기	의정부 을지대학교병원
94	대구	대구굿모닝병원
93	강원	울산대학교 강릉아산병원
92	경기	명지병원
91	서울	홍익병원
90	경남	창원한마음병원

89	충남	단국대학교병원
88	경기	한양대학교 구리병원
87	경기	참조은병원
86	경기	연세대학교 용인세브란스병원
85	경기	남양주현대병원
84	인천	나사렛국제병원
83	서울	한일병원
82	충북	청주성모병원
81	충북	청주한국병원
80	충북	건국대학교 충주병원
79	경남	양산부산대학교병원
78	부산	인제대학교 해운대백병원
77	광주	광주기독병원
76	울산	울산병원
75	경남	연세에스병원
74	경북	차의과학대학교 구미차병원
73	경기	인제대학교 일산백병원
72	서울	가톨릭대학교 은평성모병원
71	경남	창원경상국립대학교병원
70	경기	PMC 박병원
69	경북	포항성모병원
68	경기	김포우리병원
67	인천	인천세종병원

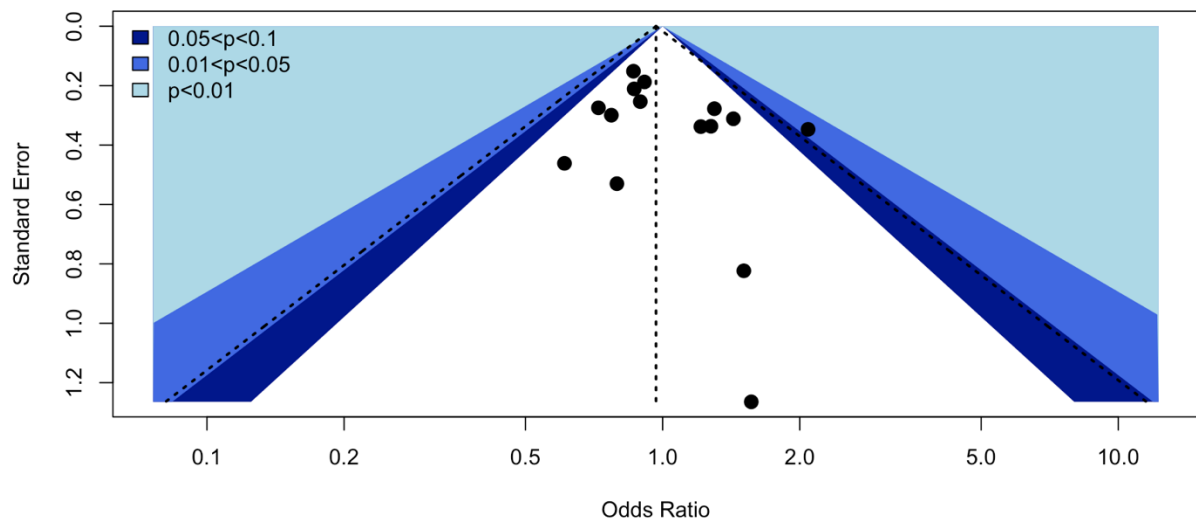
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65	서울	한림대학교 강남성심병원
64	경북	순천향대학교 구미병원
63	전북	원광대학교병원
62	부산	인제대학교 부산백병원
61	대전	유성선병원
60	강원	한림대학교 춘천성심병원
59	경기	뉴고려병원
57	울산	울산동강병원
56	전북	전북대학교병원
55	제주	제주한라병원
54	제주	제주대학교병원
53	전북	전주예수병원
52	전북	동군산병원
51	광주	조선대학교병원
50	경북	에스포항병원
49	경북	안동병원
48	경남	성균관대학교 삼성창원병원
47	경남	경상국립대학교병원
45	대구	영남대학교병원
44	대구	대구파티마병원
43	대구	대구가톨릭대학교병원
42	대구	계명대학교 동산병원

41	대구	경북대학교병원
40	울산	울산대학교병원
39	부산	부산대학교병원
38	부산	동의의료원
37	부산	동아대학교병원
36	부산	동래봉생병원
35	부산	김원묵기념 봉생병원
33	충북	효성병원
32	대전	충남대학교병원
31	대전	을지대학교병원
30	대전	건양대학교병원
29	대전	가톨릭대학교 대전성모병원
28	충남	순천향대학교 천안병원
27	강원	연세대학교 원주세브란스기독병원
26	강원	강원대학교병원
25	인천	인하대학교병원
24	경기	순천향대학교 부천병원
23	인천	가톨릭대학교 인천성모병원
22	경기	가톨릭대학교 부천성모병원
21	인천	가천대학교 길병원
20	경기	한림대학교 성심병원
19	경기	차의과학대학교 분당차병원
18	경기	아주대학교병원

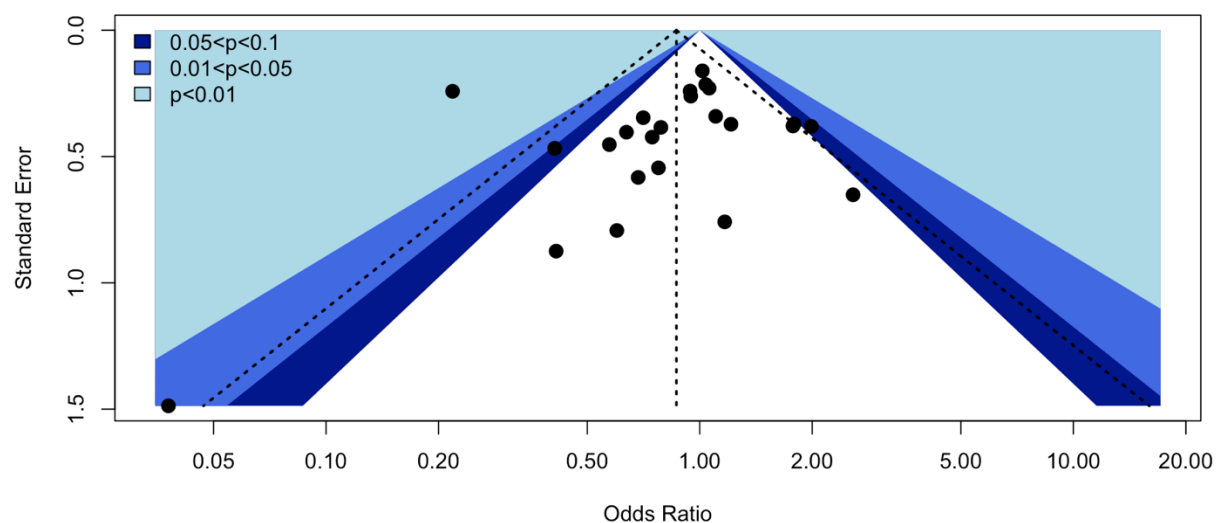
17	경기	분당제생병원
16	경기	분당서울대학교병원
15	경기	동국대학교 일산병원
14	경기	고려대학교 안산병원
13	경기	가톨릭대학교 의정부성모병원
12	경기	가톨릭대학교 성빈센트병원
11	서울	한양대학교병원
10	서울	한림대학교 강동성심병원
9	서울	노원을지대학교병원
8	서울	순천향대학교 서울병원
7	서울	서울특별시 보라매병원
6	서울	보훈공단 중앙보훈병원
5	서울	명지성모병원
4	서울	건국대학교병원
3	서울	강동경희대학교병원
1	서울	가톨릭대학교 서울성모병원



Supplementary Fig. 1. Funnel plot of a meta-analysis of functional outcome.



Supplementary Fig. 2. Funnel plot of a meta-analysis of mortality.



Supplementary Fig. 3. Funnel plot of a meta-analysis of successful recanalization.