Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2025; 42(1): 63-68
doi: 10.52142/omujecm.42.1.13

Statistical evaluation of the effects of stroke risk factors on NIHHS AND MRS

Gizem Gül KOÇ [1], Menşure Zühal BARAK[2,*], Pınar Bengi BOZ[3]

[1]Industrial Engineering Department, Alparslan Türkeş Science and Technology University, Adana, Türkiye
[2]Bussiness Department, Alparslan Türkeş Science and Technology University, Adana, Türkiye
[3]Neurology Department, Adana City Training And Research Hospital, Adana Faculty of Medicine, Health Sciences University, Adana, Türkiye

Received: 20.01.2025 • **Accepted/Published Online:** 25.03.2025 • **Final Version:** 28.03.2025

Abstract

Stroke is the second leading cause of death and the third leading cause of disability worldwide. Ischemic strokes, which result from disrupted cerebral blood flow, make up approximately 80–85% of all stroke cases. Key risk factors for stroke include hypertension, diabetes mellitus, heart disease, hyperlipidemia, smoking, and lifestyle factors. This study investigated the impact of stroke risk factors and lesion localization on stroke severity, as measured by the NIHSS scale, and patient independence at discharge, as evaluated by the Modified Rankin Scale (MRS). The analysis included 159 patients, comprising 82 women (51.6%) and 77 men (48.4%), with a mean age of 68.1±14.2 years, 93.1% of whom were over 45 years old. Stroke types were distributed as follows: 41.5% anterior circulation, 37.1% posterior circulation, and 21.4% lacunar strokes. The factors affecting the difference between NIHSS values (Delta NIHSS) at admission and discharge were analyzed by univariate and multivariate analysis methods. According to the results of univariate analysis, the presence of hypertension, myocardial infarction, coronary artery and carotid disease, previous insulin use, intravenous-tPA (iv-tPA), intra-arterial-tPA (ia-tPA) and thrombectomy treatments, age, NLR, mean blood pressure and exit MRS values were significantly associated with Delta NIHSS ($p<0.05$). Multivariate analysis revealed a positive correlation between Delta (Δ) NIHSS value and CAD and iv-tPA values and a negative correlation with exit MRS value ($p=0.021$; $p=0.012$ and $p<0.001$ respectively). Our model provides consistent results for the relationship between NIHSS and MRS scores and positive and negative functional outcomes.

Keywords: stroke, NIHSS score, Shapiro-Wilk test, Mann-Whitney U test, Spearman Rho test, regression analysis

1. Introduction

Globally, stroke ranks as the third most common cause of morbidity, and the second most common cause of death (1,2) The prevalence of stroke is 0.2% globally (3) Stroke also significantly affects expenses for healthcare in addition. (4) About 80% to 85% of all strokes are ischemic strokes, which are characterized by the disturbance of cerebral blood flow. (5) Stroke is a preventable neurological condition, and physicians have been working on modifiable risk factors for years. The main risk factors for stroke are hypertension, diabetes mellitus, heart disease, hyperlipidemia, smoking, and lifestyle. In addition to these factors that determine the prognosis, the treatment methods used, the presence, and degree of carotid stenosis, the localization of the stroke in the brain, and the neutrophil/lymphocyte ratio also contribute to the process. The National Institutes of Health Stroke Scale (NIHSS) is often used to measure stroke severity in emergency or neurology departments. This scale was first designed in 2001 by Neurologist Dr. Lyden et al. to assess the results of Recombinant Tissue Plasminogen Activator (rt-PA) administration in acute stroke. (6). NIHSS is a widely used tool for assessing stroke severity, comprising 11 categories with a total score range from 0 to 42. It evaluates various aspects of brain function, including vision, sensation, motor abilities, consciousness, speech, and language. A score of 42 represents the most severe and catastrophic stroke. The scoring system categorizes strokes as follows: 0 indicates no stroke, 1–4 corresponds to a minor, 5–15 to a moderate, 15–20 to a moderate-to-severe, and 21–42 to a severe stroke (6). Various outcomes scales assess stroke outcomes. One of the most commonly used outcome scales is the Modified Rankin Scale (MRS), which was developed to assess independence specifically. The MRS also evaluates whether the patient can perform all of the activities that he/she could do before the stroke (7). The levels of the scale are defined as follows: 0 - No

*Correspondence: mzbarak@atu.edu.tr

symptoms; 1 - Symptoms are present but do not cause significant impairment; the individual can carry out regular tasks and activities. 2: Mild impairment; cannot perform all previous activities, but can do his/her work without assistance; 3: Moderate impairment; needs some assistance, and can perform activities; 2: Mild disability; cannot fulfill all previous activities, Able to perform their tasks independently without requiring help. Level 3: Moderate disability, where some assistance might be needed, but the individual is still capable of walking unassisted. Level 4: Moderately severe disability, where walking without assistance is not possible, and the individual cannot manage their own needs without help. Level 5: Severe disability, characterized by being bedridden, incontinent, and dependent on continuous care. (8). In this study, the relationship between stroke risk factors and stroke lesion localization detected in patients admitted to neurology services with a stroke clinic, and the NIHSS scale, and MRS at discharge were examined.

2. Method

Adana City Training and Research Hospital Scientific Ethics Committee (312/9) permission was obtained for the cross-sectional study on stroke. This study comprised 159 individuals who were monitored in the neurology clinic after being diagnosed with ischemic stroke. Patients were classified as having posterior-anterior or lacunar infarcts based on their clinical findings, following the categorization outlined by Blanford et al. in 1991 (9). For each case, data on the NIHSS, MRS, carotid Doppler ultrasonography, laboratory results, comorbid conditions, and demographic details were collected. The MRS, which ranges from 0 to 6, is used to assess the level of dependency and disability in stroke patients during their daily activities.

A negative functional outcome was linked to MRS≥ 3, while a favorable functional outcome was linked to MRS <3. The study assessed some variables, such as demographics, the presence of comorbid conditions like diabetes mellitus (DM) and hypertension (HT), atrial fibrillation (AF), heart valve disease, history of stroke, heart failure, serum lipid and cholesterol levels and coronary artery disease (CAD). The study also evaluated the impact of medications, including antihypertensives, acetylsalicylic acid, clopidogrel, antilipidemic agents, and insulin, alongside treatments administered during hospitalization, such as intravenous (IV) and intra-arterial (IA) thrombolytics (tissue plasminogen activator, TPA) and thrombectomy. Furthermore, it analyzed parameters such as the neutrophil-to-lymphocyte ratio (NLR), admission glucose, fibrinogen, and creatinine levels, as well as neurological NIHSS scores at admission and discharge (or mortality) and the MRS (Table 1).

2.1. Statistical Evaluation

The data in the study were analyzed using SPSS version 27.0 (Statistical Package for the Social Sciences). Categorical variables were presented as frequencies and percentages, whereas continuous variables were summarized using the mean and standard deviation, along with the median, minimum, and maximum values when applicable. To ascertain whether the parameters were normally distributed, the Shapiro-Wilk test was employed. For non-normally distributed parameters, the Shapiro-Wilk Test determines whether a collection of data fits a normal distribution. It is particularly useful for small samples. The assumption of normal distribution is rejected and if the p-value is less than 0.05, it is accepted that the data are not normally distributed (10).

The Mann-Whitney U test was employed for pairwise group analysis. This nonparametric test is designed to compare two independent groups that do not follow a normal distribution. It evaluates whether there is a significant difference in the ranks between the two groups. Serving as a nonparametric alternative to the independent t-test, it is particularly suitable for data that does not meet the assumption of normality (11).

Spearman's rho correlation test was used to determine the relationship between continuous measures. The Spearman's Rho Correlation Test quantifies the degree and direction of a monotonic relationship—one that is rigorously non-linear—between two variables but if the data are ordinal or not normally distributed. A significant positive or negative association is indicated by a number around +1 or -1, whilst no relationship is indicated by a value near 0 (12).

Multivariate linear regression analysis was employed to investigate the factors influencing changes (Δ) in NIHSS scores. For all statistical tests, a significance level of $p<0.05$ was used. This analytical technique extends the principles of linear regression by modeling the relationships between multiple dependent variables and one or more independent variables. It is especially beneficial in situations where the response variables are correlated, providing a more detailed understanding of the data structure compared to univariate regression, which is limited to analyzing a single response variable (13).

The link between a dependent variable (outcome) and several independent variables (predictors) is modeled using multivariate linear regression. In this instance, the variables influencing the shift in the NIHSS score are investigated. Understanding how the predictor variables—such as age, therapy, etc.—affect the result while accounting for the impact of other variables is the goal.

Scientific Significance (p-value < 0.05). In these tests, a p-value below 0.05 is accepted as statistically significant. In other words, the observed outcome is unlikely to have happened by accident, and the null hypothesis—that is, the idea that there is no difference between the two groups is firmly rejected.

Table 1. Clinical and Demographic Characteristics on Admission to Hospital

	Numbers (n)	Percent (%)
Posterior infarct	59	37,1
Anterior infarct	66	41,5
Laküner infarct	34	21,4
Age		
≥ 45	11	6,9
<45	148	93,1
Gender		
Female	82	51,6
Male	77	48,4
Hypertension	121	76,1
Diabetes Mellitus type 2	59	37,1
Insulin Use	25	15,7
Atrial fibrilation	28	17,6
Valve disease	36	22,6
Heart failure	20	12,6
Myocardial infarction	18	11,3
Bypass	14	8,8
Cigarette	53	33,3
Alcohol	11	6,9
Coronary artery disease	44	27,7
Previous CVD	26	16,4
iv-tPA	11	6,9
ia-tPA	7	4,4
Thrombectomy	6	3,8
Hemorrhagic infarct	10	6,3
Substance use	2	1,3
Carotid artery stenosis		
<%50	98	61,6
>%50	61	38,4
Vertebral artery stenosis	19	11,9
Use of antilipidemic drugs	10	6,3
Acetyl salicylic acid-clopidogrel use	49	30,8
Use of antihypertensive drugs	83	52,2
NOACs use	6	3,8
Coumadin use	12	7,5
	Avarage±Sd	**Med**
Age	68,1±14,2	70
EF	53,9±8,9	55
HDL	37,2±11,8	36
LDL	118,8±38,5	117,2
Triglyceride	163,7±89,4	142
Fibrinogen	382,2±96,7	374
N/L	5,52±4,5	4,24
N/Platelet	0,034±0,02	0,03
Glucose level	177±104,5	138
Average blood pressure	108,1±22,9	103,4
INR	1,14±0,21	1,10
Creatine Level	1,03±0,7	0,89
NIHSS at hospital admission NIHSS	10,4±4,7	10
NIHSS on discharge from hospital	8,06±6,3	8
Delta(∆) NIHSS	2,35±3,7	2
Output mRS	3,21±1,9	3

N:neutrophil L: lymphocyte NOAC: New Oral Anti Coagulant INR: International Normalized Ratio EF: ejection fraction HDL: high-density lipoprotein LDL: low-density lipoprotein

3. Results

The study included 77 (48.4%) male and 82 (51.6%) female patients. The patients' average age was 68.1±14.2 years, and 93.1% of them were older than 45. Of the patients, 34 (21.4%) experienced a lacunar stroke, 59% (37.1%) experienced a posterior circulation stroke, and 66 (41.5%) experienced an anterior circulation stroke. Previous studies suggest that higher NLR and NPR levels recorded at initial admission in acute ischemic stroke cases are closely linked to worse functional outcomes and higher mortality rates, highlighting their significance as prognostic biomarkers. This research utilized both univariate and multivariate analyses to determine the factors influencing changes in patients' NIHSS scores between admission and discharge (∆ NIHSS).

When factors affecting (Δ) NIHSS are examined in univariate analysis; The presence of hypertension, myocardial infarction, coronary artery, and carotid disease, previous insulin use, iv-tPA, ia-tPA, and thrombectomy treatments, age, NLR, mean blood pressure and output MRS were associated (p<0.05) (Table 2).

Table 2. Factors affecting delta(Δ)NIHSS; univariate and multivariate analyses

	Univariate	Multivariate			
			%95 CI		
	p	β	Lowest	Highest	p
Posterior infarct	0,195				
Anterior infarct	0,471				
Laküner infarct	0,447				
Gender					
Female	0,058				
Male					
Hypertension	**0,022***	-0,681	-1,817	0,456	0,238
Diabetes Mellitus type 2	0,598				
Insulin use	**0,032***	-0,287	-1,539	0,966	0,652
AF	0,103				
Valve disease	0,308				
Heart failure	0,851				
MI	**0,009****	-1,053	-2,745	0,639	0,221
Bypass	0,656				
Cigarette	0,961				
Alcohol	0,072				
CAD	**0,049***	1,429	0,221	2,636	**0,021***
Previous CVD	0,395				
iv-tPA	**<0,001****	2,925	0,644	5,205	**0,012***
iatPA	**0,004****	1,768	-4,003	7,538	0,546
Thrombectomy	**0,016***	-0,273	-6,035	5,489	0,925
Hemorrhagic infarct	0,201				
Substance use	0,859				
Carotid artery stenosis					
<%50	**0,040***	-0,160	-1,150	0,829	0,749
>%50					
Vertebral artery stenosis	0,059				
Use of antilipidemic drug	0,109				
Use of Asa -clopidogrel	0,930				
Use of antihypertensive drugs	0,293				
NOACs usage	0,409				
Warfarine usage	0,159				
Age	**0,003****	-0,026	-0,061	0,010	0,153
EF	0,287				
HDL	0,157				
LDL	0,269				
Triglyceride	0,731				
Fibrinogen	0,486				
N/L	**0,006****	-0,070	-0,171	0,031	0,174
N/Platelet	0,063				
Glucose level	0,886				
Average Blood Pressure	**0,009****	-0,010	-0,030	0,011	0,354
INR	0,919				
Creatinine level	0,349				
Output mRS	**<0,001****	-1,091	-1,344	-0,838	**<0,001****

*p<0,05, *p<0,01, Delta(Δ)NIHSS: Difference between Input NIHSS and Output NIHSS
AF: atrial fibrillation MI: myocardial infarction CAD: coronary artery disease CVD:cerebrovascular disease NOACs: New oral anticoagulants asa: acetyl salicylic acid INR: International Normalized Ratio EF: ejection fraction HDL: high-density lipoprotein LDL: low-density lipoprotein N:neutrophil L: lymphocyte

A negative Delta (Δ)NIHSS value indicates that the NIHSS value increased at the end of the treatment, whereas a positive (Δ) NIHSS value indicates that the NIHSS value decreased at the end of the treatment.

When the factors affecting (Δ) NIHSS were analyzed in the univariate analysis, it was found that there was a significant relationship between HT, Insulin use, MI, CAD, iv-tPA, iatPA, Thrombectomy, Core disease, Age, N/L, Mean BP and Outcome MRS values (p<0.05). The model outlined in Table 2 incorporates the parameters identified as significant during the univariate analysis into the subsequent multivariate analysis. Multivariate analysis revealed a positive correlation between (Δ) NIHSS value and CAD and iv-tPA values and a negative correlation with Out MRS value (p=0.021; p=0.012 and p<0.001 respectively).

A multivariate analysis model was developed by incorporating the parameters identified as significant through the univariate analysis. As a result of multivariate analysis, it was determined that (Δ) NIHSS value had a positive relationship with coronary artery disease and the use of iv-tPA in treatment, and a negative relationship with the output MRS value (p=0.021; p=0.012; p<0.001, respectively), (Table 2). Accordingly, while a positive functional result (high (Δ) NIHSS) was detected in those with a history of concomitant coronary artery disease and those receiving IV-TPA treatment, a negative functional result (negative) was detected in those with high MRS or low (Δ) NIHSS. Our model provides consistent results for the relationship between NIHSS and MRS scores and positive and negative functional outcomes.

4. Discussion

According to data from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) spanning 1990 to 2019, stroke ranks as the second leading cause of death worldwide (14). Similarly, World Health Organization statistics for 2021 identify stroke as the leading cause of death after ischemic heart disease and COVID-19 (13). The organization's database reports that approximately 15 million people globally suffer a stroke each year, with one-third dying from it and another third experiencing long-term disabilities. This imposes significant social, psychological, and economic challenges on societies (15). GBD stroke project data predicts that between 2020 and 2050, stroke-related mortality and disability, as well as the economic burden on societies, will approximately double (16,17). Many risk factors cause stroke and most of these are modifiable causes such as hypertension, hyperlipidemia, and high blood sugar (18,19). Therefore, preventive medicine remains the most important pillar of treatment. Governments need to know the common stroke risk factors in their communities and why these risk factors are not being rehabilitated, inform physicians and citizens, and put forward feasible health programs. Another important issue is that physicians should know the main factor or factors that cause stroke in their patients as well as the other players that contribute to the disease. Because main and secondary factors will affect the prognosis. The incidence of stroke tends to increase especially in individuals younger than 55 years of age, which we will define as young stroke (16,17). In addition, the prevalence of metabolic syndrome and its components such as high blood pressure, overweight, and diabetes are increasing. Many different components such as processed food consumption, environmental factors, increased stress factors in living conditions, and epigenetic causes play a role in this. In our study, hypertension, diabetes, and cardiac pathologies were identified as the most important risk factors. In addition, it was determined that the neutrophil/lymphocyte ratio, which was calculated by considering the hemogram data of the patient during hospitalization, could be used as a prognostic indicator in our study as in many studies (20). When we looked at the treatment modalities applied after stroke, it was noteworthy that intravenous thrombolytic therapy and thrombectomy positively affected the prognosis and thus MRS. This once again highlights the importance of time of onset, patient assessment, and access to neuroimaging modalities in ischemic stroke. The data from our study are important to inform adequate healthcare planning, resource allocation, and prioritization for stroke, and to assess the success or failure of measures to reduce the burden of stroke. In medicine, many disease-specific scales have been developed to assess the severity of the disease and the current condition of the patient. NIHSS and MRS scales are only two of them (21,22). In our study, we statistically evaluated the effect of stroke risk factors and lesion localizations caused by stroke on the NIHSS scale and tried to reveal the effectiveness of medical treatments applied to the patient at the discharge stage with the MRS scale in addition to vascular risk factors. The information obtained guided the toolbar, which is being developed by us to determine the prognosis in stroke cases. In addition, it has contributed to the creation of mathematical models by setting targets that will reveal the strengths and weaknesses of the treatments applied in comorbid conditions accompanying stroke. In conclusion, the importance of early diagnosis and personalized treatment of stroke is undeniable. In solving this problem, health and engineering sciences should produce more joint projects and offer different perspectives on the subject.

Conflict of interest

The authors declare that there are no conflicts of interest related to this manuscript. No financial relationships, personal connections, or any other affiliations that could be perceived as influencing the objectivity or integrity of this research exist. All authors have contributed to the study’s design, data collection, analysis, and writing, and the results presented are solely based on the scientific data without any external bias. The authors further confirm that there are no competing interests that could have influenced the results or interpretation of the findings.

Funding

None the declare.

Acknowledgments

None the declare.

Ethical statement

Adana City Training and Research Hospital Scientific Ethics Committee (312/9) permission was obtained for the cross-sectional study on stroke.

Authors’ contributions

Concept: G.G.K., M.Z.B., P.B.B., Design: G.G.K., M.Z.B., P.B.B., Data Collection or Processing: P.B.B., Analysis or Interpretation: G.G.K., M.Z.B., Literature Search: G.G.K., M.Z.B., P.B.B., Writing: G.G.K., M.Z.B., P.B.B.

References

1. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, et al. Guidelines for The Primary Prevention of

Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2011; 42: 517–84.

2. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, et. al. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2015; 46: 3020–35.

3. Chang KC, Tseng MC, Weng HH, Lin YH, Liou CW, Tan TY. Prediction of Length of Stay of First-Ever Ischemic Stroke. Stroke. 2002; 33(11): 2670-74.

4. İldes S, Kavalcı C, Celik K, Tekten BÖ, Kavalcı G. Cost Analysis Of Stroke Cases Admitted To Our Emergency Department In Türkiye. Наука И Здравоохранение, 2023; 25(2): 35-40.

5. Special report from the National Institute of Neurological Disorders and Stroke. Classification of cerebrovascular diseases III. Stroke. 1990; 21(4): 637-76.

6. Lyden PD, Lu M, Levine SR, Brott TG, Broderick J. NINDS rtPA Stroke Study Group. A modified National Institutes of Health Stroke Scale for Use In Stroke Clinical Trials: Preliminary Reliability And Validity. Stroke. 2001; 32(6): 1310-7.

7. Sulter G, Steen C, De Keyser J. Use of the Barthel index and modified Rankin scale in acute stroke trials. Stroke. 1999; 30: 1538-41.

8. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver Agreement for The Assessment Of Handicap In Stroke Patients. Stroke. 1988; 19: 604-7.

9. Blanford, JH, Bernhofer Ch, Gay LW. Energy Flux Mechanisms Over A Pecan Orchard Oasis. Proc. 20th Conf. On Agricultural Forest Meteorology, Salt Lake City, Utah. Amer. Meteorol. Soc., Boston, MA, 1991: p. 116-119.

10. Razali NM, Yap BW. Power Comparisons of Shapiro-Wilk, Kolmogorov-Smirnov, Lilliefors and Anderson-Darling Tests." Journal of Statistical Modeling and Analytics 2.1, (2011): 21-33.

11. MacFarland TW, Yates JM. Mann–Whitney U Test. Introduction to Nonparametric Statistics for The Biological Sciences Using R. Springer International Publishing, 2016: p. 103-132.

12. Pratamaa D, Mulawardi M, Patrianef D. Correlation of Ankle-Brachial Index and Ultrasound Findings on Dorsalis Pedis Artery and Posterior Tibial Artery in Patients with Diabetic Foot Ulcer. Vascular, 10 (2020): 3.

13. Huang, Yuqin, et al. "Assessing the scale effect of urban vertical patterns on urban waterlogging: An empirical study in Shenzhen." Environmental Impact Assessment Review 106 (2024): 107486.

14. GBD 2019 Stroke Collaborators. Global, Regional, And National Burden Of Stroke And Its Risk Factors, 1990–2019: A Systematic Analysis For The Global Burden Of Disease Study 2019. Lancet Neurol. 2021; 20: 795-820.

15. World Health Organization, The top 10 causes of death [Internet]. 2025 [updated 2024 Aug 7; cited 2025 Jan 12]. Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

16. Feigin VL, Owolabi MO. Pragmatic solutions to reduce the global burden of stroke: a World Stroke Organization–Lancet Neurology Commission. Lancet Neurol. 2023; 22:1160-1206.

17. GBD 2021 Stroke Risk Factor Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2021: A Systematic Analysis for The Global Burden of Disease Study 2021. The Lancet Neurology. 2024; 10: 1973-1003.

18. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, Regional, And National Burden And Trend Of Diabetes In 195 Countries And Territories: An Analysis From 1990 To 2025. Sci Rep. 2020; 10, 14790.

19. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: update from the GBD 2019 Study. J Am Coll Cardiol. 2020; 76: 2982-3021.

20. Ying Y, Yu F, Luo Y, Feng X, Di D, Wei M, et al. Neutrophil-to-Lymphocyte Ratio as a Predictive Biomarker for Stroke Severity and Short-Term Prognosis in Acute Ischemic Stroke With Intracranial Atherosclerotic Stenosis. Front Neurol. 2021; 12: 705949.

21. Cummock JS, Wong KK, Volpi JJ, Wong ST. Reliability of the National Institutes of Health (NIH) Stroke Scale Between Emergency Room and Neurology Physicians for Initial Stroke Severity Scoring. Cureus. 2023; 14; e37595.

22. Yoshimura S, Sakai N, Yamagami H, Uchida K, Beppu M, Toyoda K, et al. Endovascular Therapy for Acute Stroke with a Large Ischemic Region. N Engl J Med. 2022; 386: 1303-13.