

Stroke severity predicts transportation time and time until recanalization therapy in acute strokes

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Abstract

Background Ischemic stroke has rising prevalence in aging populations. Treatment depends on quick symptom recognition, transport to a hospital with a dedicated stroke care, imaging, and initiation of treatment, if indicated. The aim of this study is to show that transport, imaging, and treatment times depend on the severeness of the stroke, with more severe strokes being favored. Methods Statistical analysis was performed with data from a registry for quality assurance in stroke care in Hesse, Germany. Data was analyzed regarding ICD-10, and patients with I63 were further investigated. Patients with NIHSS ≥ 4 were included and subdivided into $4 \leq \text{NIHSS} \leq 11$ (moderate stroke) and $\text{NIHSS} \geq 12$ (severe stroke). Transport to hospital, time to image, and time to treatment were analyzed. Results Patients with severe strokes reach the hospital faster and in higher numbers in comparison to moderate strokes. If appropriate therapy is applied, in-hospital treatment regarding imaging is similar in both groups. Thrombolysis or endovascular treatment is initiated faster for severe strokes. Conclusion More public awareness of strokes is needed, specifically for moderate strokes to reach faster transport times to hospital as well as modern treatment options up to 24 hours for eligible patients. Individual standards need to be applied in each stroke treating hospital to guarantee the same fast treatment times for moderate and severe strokes.

Background

Ischemic stroke shows rising prevalence in an aging population, specifically in the Western world. Approximately one out of four will suffer a stroke during their lifetime, and 10% of the world's population die as a result of stroke (1). In Germany, 60,000 people die from the results of a stroke per year (2).

The treatment of ischemic stroke is an evolving field with new treatment options showing up every year. Treatment by systemic thrombolysis has been established in 1995 (3). Since then the time window for treatment was extended to 4.5 hours and more patient groups could be included for treatment (4) as well as individual treatment options of up to 6 hours (5). Endovascular approaches have been evolving since 2006 (6) and have found breakthrough methods since 2012 (7). Today, two treatment arms are established with systemic thrombolysis and endovascular treatment (8).

The American Heart Association (AHA) follows up on these researches and randomized trials with stent retriever and aspiration devices, and implanted the results into the latest version of their guidelines in February 2018. Prior updates were made in 2015. Real-life populations often do not match study populations, as patient characteristics often vary in age, sex, ethnicity, and background diseases, thus limiting the direct transfer of study outcomes and conclusions to the general public. Real-life observations are necessary to further establish treatments.

Most German hospitals offer standard procedures and quick response teams for acute stroke treatment. However, strokes are often not seen in time due to delays in pre-hospital management, wrong triaging or

wrong decisions in general emergency departments, and the neurologist not being the first responder. The stroke's severity, as well as the quick reactions of pre- and in-hospital teams, predefine the outcome.

Our aim was to show that stroke severity influences the treatment time and that severe strokes receive faster response in transport to hospital, imaging, and treatment.

Methods

Retrospective data from the Geschäftsstelle Qualitätssicherung Hessen database, – a state-wide prospective stroke registry in the State of Hesse, Germany, was used for this study. The acquisition of this data was regulated in Volume V of the Social Insurance Code (§112 SGB V and §136 SGB V). All facilities treating patients with stroke have mandatory to document within seven days. Patients' data were registered anonymously; therefore, no ethical board approval was necessary.

Data from 2010 to 2016 was screened for stroke patients and then further analyzed by ICD-10. The additional analysis allowed sorting for ischemic stroke (I63), transient ischemic attack (G45), subarachnoid bleeding (I60), intracerebral bleeding (I61), and cerebral vascular accident not further classified (I64). All patients identified with I63 were further sorted by NIHSS (9). In Hesse, a state in Germany with 6.2 million inhabitants, 164,209 patients were identified with stroke in the study's timeframe; 101,231 patients could be classified with ischemic stroke and 52,667 qualified with a NIHSS ≥ 4 . These patients were subdivided into $4 \leq \text{NIHSS} \leq 11$ (moderate stroke) and $\text{NIHSS} \geq 12$ (severe stroke). NIHSS below four was excluded as minor stroke. The cutoff was taken, as a NIHSS of at least four mandatory qualifies for systemic thrombolysis treatment by Germany and the AHA's guidelines.

Both groups were then analyzed for time of symptom onset and transport to hospital (symptom to door), first image in hospital (door to CT/MRI), and initiation of recanalization treatment (door to needle time, or door to groin time). Statistical analysis included onset of symptoms until admission to hospital, time to imaging, time to treatment, and mRS outcome at day of dismissal. Analysis was performed by SPSS with a chi-squared test.

Results

In total, 101,231 patients were eligible for the analysis, and 36,378 patients with a NIHSS between 4 and 11, as well as 16,324 patients with NIHSS of 12 or above, qualified for further statistical analysis (Graph 1). We excluded 111,542 patients due to NIHSS < 4 , TIA, intracranial bleeding, or strokes that were not clearly defined. In the moderate stroke group, 6,829 patients (18.8%) received recanalization treatment, either by systemic thrombolysis or mechanical thrombectomy. In comparison, 4,875 patients (29.9%) with severe strokes received treatment.

Of the patients with severe strokes, 38.7% reached the hospital within 2 hours after symptom onset and 14.7% arrived within the first hour. For the moderate group, 24.4% reached the hospital in the same time window with only 8.4% in the first hour. In both groups, 10.6% reached the hospital after 4 hours and up to 6 hours by the very limit of treatment options (Figure 2).

Regarding the door-to-image time, the time frames for both stroke grades were quite similar, with 95% of the moderate group and 93% of the severe group receiving imaging during the first hour after arrival if treatment was applied (Figure 4). Patients who did not receive treatment showed a delay in imaging time; this was seen more in the moderate stroke group. Only 47.8% of the moderate group and 53.6% of the severe group received imaging during the first 30 minutes in comparison to around 83% in the treatment groups. A further in-hospital delay can be seen, as more than 10% only received CT or MRI after 3–6 hours (Figure 3).

The door-to-needle/groin time differs between both groups. For the severe stroke group, 85.5% of patients received treatment in less than an hour while, 41% received treatment even in less than 30 minutes. In comparison, 61.5% of patients in the moderate stroke group were treated in the first hour after arrival, while 29.8% were treated in the first 30 minutes (Figure 5).

Discussion

About 270,000 people suffer from stroke in Germany every year (10). In Hesse, the annual incidence of stroke is 21,055 and only 27.1% of all patients eligible by NIHSS receive treatment. This real-world analysis of stroke treatment from 2010 to 2016 shows significantly faster transport and treatment times for severe strokes. Patients with NIHSS of at least 12 reach the hospital faster and in a higher percentage.

Both, fast recognition by ambulance teams and public awareness of stroke play an important role for fast transport times to the hospital. Patients with hemiplegia or aphasia are recognized faster than patients with hemianopsia, ataxia, or light hemiparalysis. After arrival at the hospital, patients are supervised by the medical team and an in-house analysis is possible.

More than 80% of patients in both stroke groups received imaging in the first 30 minutes after hospital admittance, if either systemic thrombolysis or mechanical thrombectomy was initiated. For patients that did not qualify for treatment, a delay in imaging can be seen. Only 48% of the moderate group and 54% of the severe group received imaging in the first 30 minutes. There might be different explanations. A stroke with a lower NIHSS that does not qualify for treatment might be delayed by the emergency department's triaging system. A severe stroke might reach faster imaging times because further treatment options, such as thrombectomy, need to be considered and are only ruled out after (i) regular CT that already shows an evolved stroke, or (ii) a CT-perfusion study that shows no meaningful penumbra.

In cases where patients were eligible for and received treatment, fast imaging responses were seen in both groups. Treatment is faster initiated with a severe stroke (Figure 5). On the one hand, the decision to use systemic thrombolysis as treatment is clearer for a severe stroke with hemiparalysis and cortical

signs; on the other hand, a faster response for moderate strokes would have been expected. Severe strokes might not always qualify for thrombolysis due to anticoagulation, falls caused by acute hemiparalysis, or other factors. In these cases, thrombectomy is the only option.

Mobilizing the thrombectomy team as well as the sedation and intubation of the patient are time-consuming; therefore, delays are expected, specifically with a slightly higher rate of ipsilateral carotid occlusion (0.7% vs. 2.0%). The early initiation of thrombolysis for eligible patients with severe strokes and less hesitation seem to be the major point for faster treatment times. The number of intubated patients is significantly higher with severe stroke cases, resembling the higher rates of mechanical thrombectomy. This correlates with the higher number of ICU admittances. Both stroke categories show a clear benefit of treatment with better outcome measured by mRS. Earlier studies in Germany (11, 12), Spain (13) and Japan (14) showed no in-hospital difference regarding daytime and weekday of stroke admission. A small study in Nashville, USA compared transportation times for myocardial infarction and showed no significant differences between weekdays and weekends (15). No sufficient data exist to date in Germany regarding prehospital transport for specific times and days of the week.

This study shows two major differences in stroke treatment. Patients with severe strokes reach the hospital faster, and a higher percentage arrives at the hospital in a time window that allows treatment. Further public awareness is necessary to improve these numbers, specifically, with new established treatments since 2012 with mechanical thrombectomy (16) and the 2017 published DAWN Trial (17) that shows a benefit for patients even in an extended time window up to 24 hours if diffusion or perfusion weighted imaging shows a meaningful penumbra. In light of these options, also time after 4 hours matters and awareness need to be risen that also after 4.5 hours treatment options exist, specifically for severe strokes with proximal large vessel occlusions. The in-hospital imaging treatment is very similar if treatment is initiated. Hesitation with age and risk factors might still play an important role and need to be investigated individually in each hospital treating stroke patients. This study shows that specifically patients with more risk factors are excluded from recanalization treatment that they might benefit from.

Conclusions

The stroke treatment system is biased both pre- and in-hospital. Patients with severe strokes reach the hospital in shorter time and their treatment is initiated faster. Raising the same awareness on all patient groups could lead to a better outcome for patients with a moderate stroke. Since endovascular treatment options exist, certain patient groups can benefit up to 24 hours after symptom onset. More public awareness campaigns need to be initiated to give patients the optimal treatment options. Time after 4 hours matters!

Another focus needs to be put on in-hospital treatment in each stroke treating facility individually, to reach the same results for all patients that are eligible for treatment.

Abbreviations

AF	atrial fibrillation
AHA	American Heart Association
CT	computed tomography scan
CVA	cerebrovascular accident
DM	Diabetes mellitus
EVT	endovascular treatment
ICD	International Statistical Classification of Diseases and Related Health Problems
MRI	magnetic resonance imaging
mRS	modified Ranking Scale
PAF	paroxysmal atrial fibrillation
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NIHSS	National Institutes of Health Stroke Scale
SGB	Sozialgesetzbuch
TIA	transitoric ischaemic attack
rtPA	recombinant tissue Plasminogen Activator

Declarations

The study was approved by the Geschäftsstelle Qualitätssicherung Hessen and is approved and regulated in Volume V of the Social Insurance Code (§112 SGB V and §136 SGB V). The consent for publication was given as well. No further consent is necessary as no personal data is used. The data and material are available at the Geschäftsstelle Qualitätssicherung Hessen. None of the authors has competing interests or received any kind of funding. S. Mausbach designed the study and wrote the paper. M. Stein provided the statistical analyzes. Juenemann helped with correciton of the paper and decisions regarding the figures. T. Braun did corrections of the paper. M. Kaps provided corrections and statistical input. No other acknowledgements are necessary or available.

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Tables

Due to technical limitations, Table 1 have been placed in the Supplementary Files section.

Figures

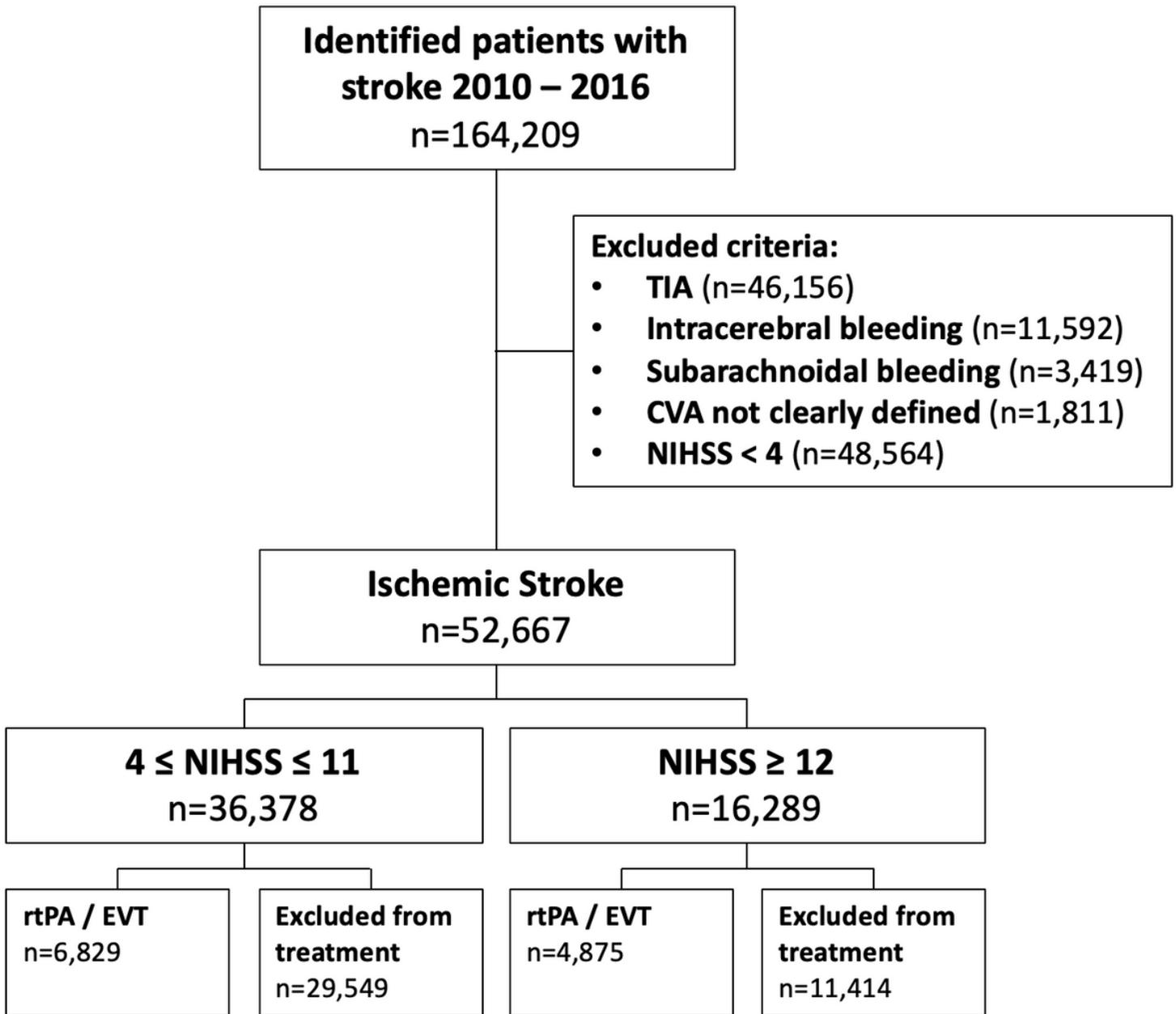


Figure 1

Figure 1: Classifying patients by ICD coding. Patients with ischemic stroke were further randomized by stroke severeness and analyzed by whether or not they received recanalization treatment (systemic thrombolysis or mechanical thrombectomy).

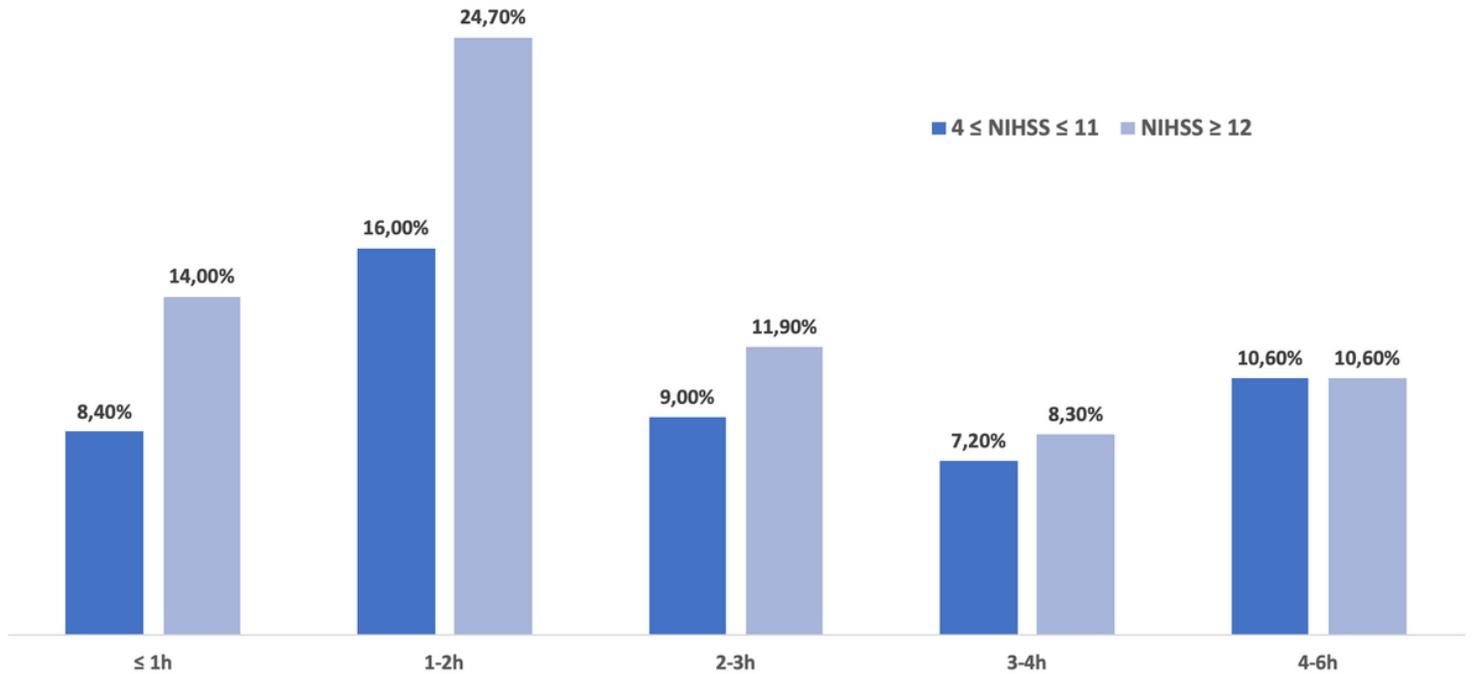


Figure 2

Comparison of symptom onset to arrival time to hospital. A higher percentage of severe strokes reached the hospital in the first 2 hours. This trend continues until 4 hours when patients are still eligible for thrombolysis treatment; afterwards, it evens out. Not shown: 40% of patients with moderate strokes reached the hospital after 6 hours, with 15.5% only after 24 hours. In comparison, 30.5% of patients with severe strokes did not arrive in a treatment window, with 8.5% arriving only after 24 hours.

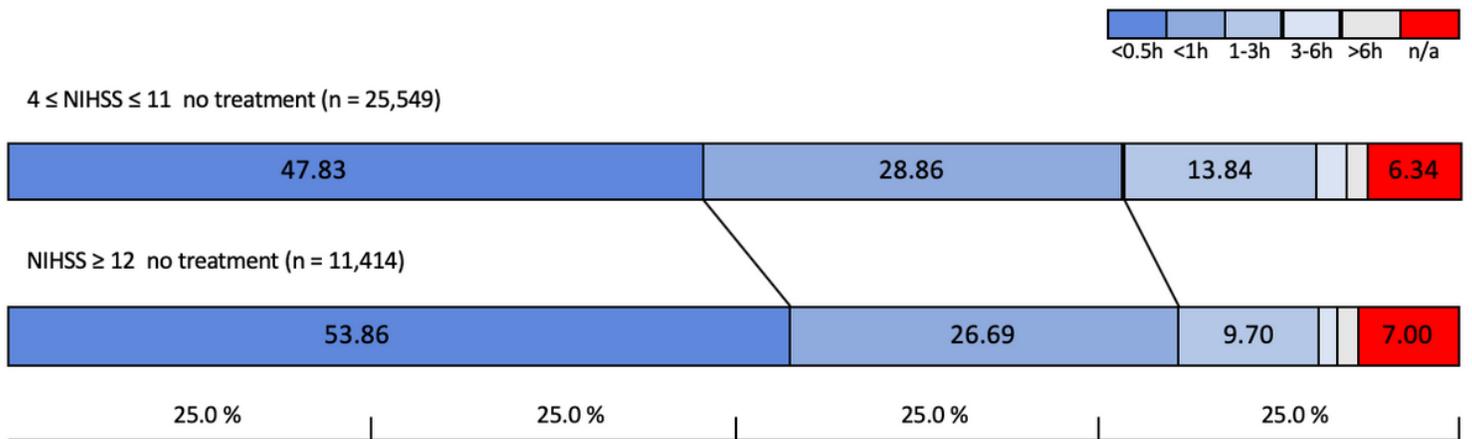


Figure 3

Comparison of time from hospital arrival to first imaging, either CT or MRI (door-to-image), for patients with moderate and severe strokes that did not receive treatment. Less patients with moderate strokes (76.7%) received imaging in the first hour than patients with severe strokes (80.6%).

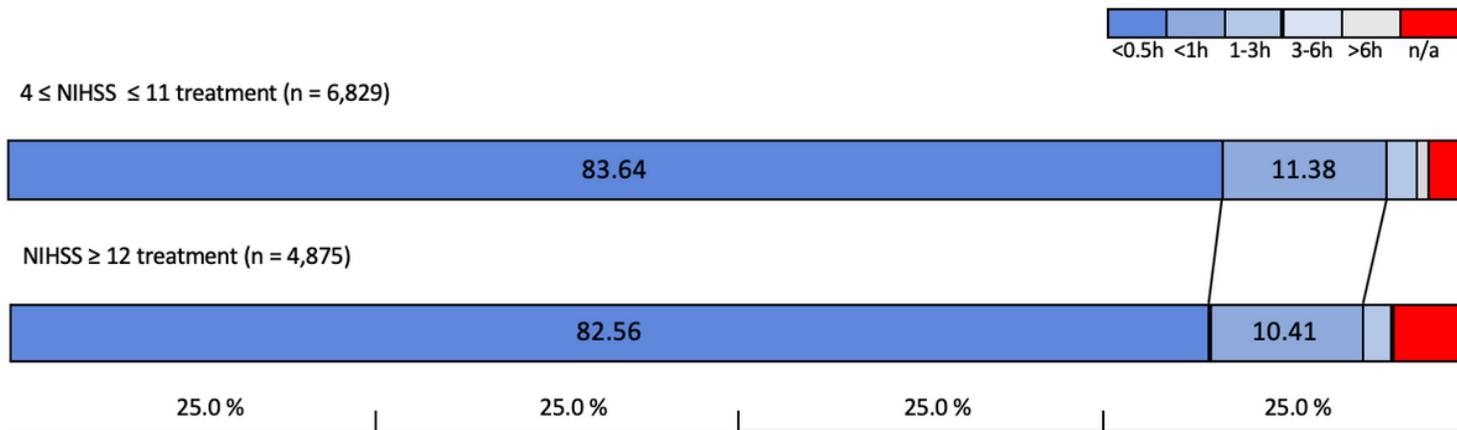


Figure 4

Comparison of time from hospital arrival to first imaging, either CT or MRI (door-to-image), for patients with moderate or severe stroke that received treatment. More patients with moderate strokes received imaging in the first hour after arrival (95%) than those who received it in the first 30 minutes (83.6%). These results were similar to the severe stroke patients, with 93% receiving imaging in the first hour total and 82.6% in the first 30 minutes.

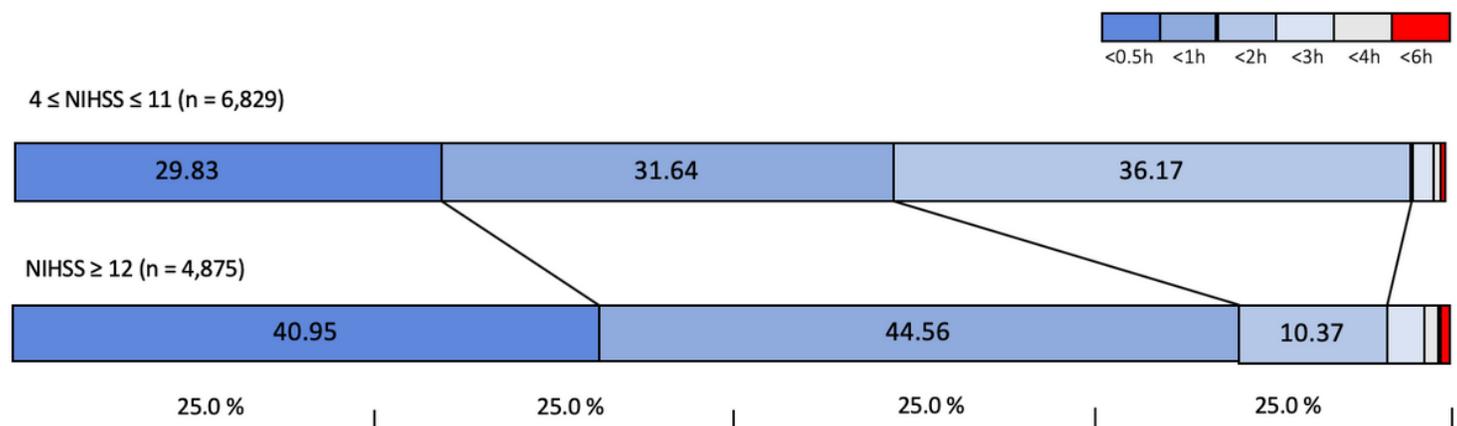


Figure 5

Comparison of treatment initiation from arrival to hospital (door-to-needle/groin). A total of 85.5% of patients with severe strokes received recanalization treatment (systemic thrombolysis or mechanical thrombectomy) during the first hour, whereas 41% received treatment during the first 30 minutes. With a moderate stroke, 61.5% received treatment in the first hour, whereas 29.8% received treatment during the first 30 minutes.

Supplementary Files

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- [supplement1.png](#)