Revised: 11 March 2021

DOI: 10.1002/emp2.12441

#### **ORIGINAL RESEARCH**

#### Neurology



JACEP OPEN

### Potential accuracy of prehospital NIHSS-based triage for selection of candidates for acute endovascular stroke therapy

# Lauren E. Klingman MD<sup>4</sup>

<sup>1</sup> Department of Neurology, Kaiser Permanente, Northern California, Walnut Creek California USA

<sup>2</sup> Division of Research, Kaiser Permanente, Northern California, Oakland, California, USA

<sup>3</sup> Department of Emergency Medicine, Kaiser Permanente, Northern California, Roseville, California, USA

<sup>4</sup> Stanford University, Stanford, California, USA

#### Correspondence

Mai N. Nguyen-Huynh, MD, MAS, Department of Neurology, Kaiser Permanente, Walnut Creek, CA, USA. Email: mai.n.nguyen-huynh@kp.org

Meetings: Presented in part at the International Stroke Conference, Los Angeles, CA, January 26, 2018

Funding and support: By JACEP Open policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Jeffrey G. Klingman MD<sup>1</sup> | Janet G. Alexander MSPH<sup>2</sup> | David R. Vinson MD<sup>2,3</sup> Mai N. Nguyen-Huynh MD, MAS<sup>1,2</sup>

#### Abstract

Objective: Whether patients with acute stroke and large vessel occlusion (LVO) benefit from prehospital identification and diversion by emergency medical services (EMS) to an endovascular stroke therapy (EST)-capable center is controversial. We sought to estimate the accuracy of field-based identification of potential EST candidates in a hypothetical best-of-all-worlds situation.

Methods: In Kaiser Permanente Northern California, all acute stroke patients arriving at its 21 stroke centers between 7:00 am and midnight from January 2016 to December 2019 were evaluated by teleneurologists on arrival. Initial National Institutes of Health Stroke Scale (NIHSS) score, presence of LVO, and referral for EST were obtained from standardized teleneurology notes. Factors associated with LVO were evaluated using generalized estimating equations accounting for clustering by facility.

Results: Among 13,377 patients brought in by EMS with potential stroke, 7168 (53.6%) were not candidates for acute stroke interventions. Of the remaining 6089 cases, 2,573 (42.3%) had an NIHSS score >10, the cutoff with a higher association for LVO. Only 703 patients (27.3% with NIHSS score > 10) were ultimately diagnosed with LVO and referred for EST. Across all NIHSS scores, only 884 (6.6%) suspected acute stroke patients had LVO and EST referral.

Conclusions: Even if field-based tools were as accurate as NIHSS scoring and predictions by stroke neurologists, only about 1 in 4 acute stroke patients diverted to ESTcapable centers would benefit by receiving EST. Depending on geography and stroke center performance on door-to-needle time, many systems may be better served by focusing on expediting evaluation, treatment with intravenous thrombolysis, and transfer to EST-capable centers.

#### **KEYWORDS**

clinical decision rules, emergency medical services, ischemic stroke, stroke scale, thrombectomy, thrombolytic therapy

Supervising Editor: Bernard P. Chang, MD, PhD.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2021 The Authors. JACEP Open published by Wiley Periodicals LLC on behalf of American College of Emergency Physicians

#### 1 | INTRODUCTION

#### 1.1 Background

Both thrombolytic treatment and endovascular stroke therapy (EST) are highly effective therapies in acute stroke.<sup>1–6</sup> Number needed to treat (NNT) for thrombolytic treatment is 4 and NNT for endovascular treatment in patients without advanced imaging preselection is 7.<sup>7,8</sup> Both therapies are also highly time dependent with much better outcomes for both faster thrombolytic as well as faster endovascular therapy.<sup>7,8</sup> In patients with large vessel occlusion (LVO), EST plus intravenous thrombolysis are much more effective than thrombolysis alone in improving functional outcomes for patients with acute strokes and LVOs.<sup>7,9–12</sup> Consequently, identification of an accurate prehospital triage system to send patients with possible LVO to appropriate EST-capable centers has been a priority.

In this effort, at least 19 stroke scales have been developed. The National Institutes of Health Stroke Scale (NIHSS) is the most complete and detailed of these scales but has been thought too cumbersome for use by EMS in the field. Thus, LVO prediction scales have been developed as subsets of the full NIHSS and several of these have been evaluated in prehospital settings, but none are both highly sensitive and specific in accurately identifying patients with LVO.<sup>13-18</sup> Furthermore, whether field-based diversion based on such clinical scales improves outcomes is uncertain, as study results have been mixed.<sup>19-23</sup> Field-based triage and diversion comes at the risk of increasing treatment time for stroke patients qualifying for intravenous thrombolytic therapy if a closer hospital capable of treating the patient with thrombolytics is bypassed in favor of a more distant one with EST capabilities or in favor of an EST-capable center whose door-to-treatment time is slower than the primary hospital.

#### 1.2 | Importance

To maximize benefits of both forms of treatment (intravenous thrombolysis and EST) in a population of patients with acute strokes, it is important to understand the relative frequency of these treatments in the group, as well as the potential for accurate identification of patients likely to undergo EST. Modeling studies for field-based diversion suggest that the optimal decision depends upon the frequency of LVO in the population, travel time between centers, and performance of primary stroke centers (PSCs) and comprehensive stroke centers (CSCs) regarding time to treatment.<sup>24–26</sup>

#### 1.3 | Purpose/goals of this investigation

There were 3 primary goals of this study: (1) to investigate the current accuracy of emergency medical services (EMS) identification of acute strokes in a large population of suspected stroke patients brought to Kaiser Permanente Northern California (KPNC) hospitals; (2) to model

#### **The Bottom Line**

The initial out-of hospital evaluation of stroke is critical in determining preliminary stroke risk suspicion and possible transport to centers capable of advanced stroke interventions. This study in a single health system of 21 hospitals looked at 13,377 patients brought in by emergency medical services with potential stroke. Teleneurology evaluations on arrival found that 7168 (53.6%) were not candidates for acute stroke interventions. Of the remaining 6089 cases only 703 patients (27.3% with National Institutes of Health Stroke Scale score > 10) were ultimately diagnosed with large vessel occlusion and referred for endovascular stroke therapy.

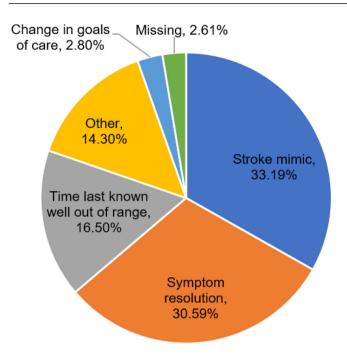
the best possible ability of EMS to accurately predict patients who were candidates for EST if they were to use the most complete current stroke scale in widespread use (NIHSS) with an accuracy equaling that of experienced stroke neurologists; and (3) to evaluate whether, based on the frequency of acute stroke treatments in this population, fieldbased clinical evaluation could be accurate enough to identify a subset of stroke patients who would benefit from diversion past a closer hospital without harming patients who would be better served by transport to a closer hospital.

#### 2 | METHODS

#### 2.1 | Study design and setting

KPNC provides care at 21 community hospitals serving a population of > 4.5 million members. There are  $\approx$  1.3 million emergency department visits and 3500 ischemic stroke discharges per year. Patients are demographically similar to the overall population of Northern California.<sup>27</sup> There are 13 separate EMS agencies operating in our catchment area, using at least 3 different prehospital stroke identification scales. Each EMS agency has its own administration and medical director and policies. Most agencies use the Cincinnati Prehospital Stroke Scale (CPSS).<sup>28</sup> One county uses a Gaze-Face-Arm-Speech-Time test (G-FAST) score of 4 or more to divert patients from the field to the nearest thrombectomy capable center.

All possible acute stroke patients presenting to KPNC hospitals were evaluated by a telestroke neurologist. All 21 KPNC hospitals are Joint Commission Stroke certified—19 as PSCs and 2 as CSCs. EST is provided at the 2 KPNC CSCs as well as at 7 local non-Kaiser Permanente (KP) community CSCs. We tracked all EST cases, including transfers to KP and non-KP facilities. Any KP-insured patients (members) presenting primarily to non-KP facilities were excluded from this study. KP facilities serve non-members as well as KP members, and non-members are included in the study population.



**FIGURE 1** Reason for stroke alert cancellation among 7168 patients determined not to qualify for acute interventions

In KPNC, all patients identified by EMS as having potential acute strokes are evaluated immediately upon arrival by a teleneurologist via remote video consultation without any nurse or ED physician prescreening. Details of the KPNC Stroke EXPRESS (EXpediting the PRocess of Evaluating and Stopping Stroke) program have previously been described.<sup>29</sup> Standardized information is recorded for all patients seen by the teleneurologists. For patients that the neurologist determined were not candidates for acute interventions with either thrombolysis or EST, the reasons of ineligibility are also recorded in the notes. This EXPRESS database provides a comprehensive view of the entire population of patients brought in as suspected strokes.

Reasons for ineligibility include stroke mimics, time last known well (TLKW) being outside of the appropriate treatment window, nondisabling/minor stroke where risk of treatment exceeds potential benefit, resolution of stroke symptoms by time of ED arrival/evaluation, and contraindications to thrombolysis/EST treatment (Figure 1).

#### 2.2 | Intervention and measurement

All patients being brought in by EMS for suspected acute stroke ("stroke alert") are evaluated on arrival in the ambulance bay by telestroke neurologists in conjunction with local ED teams. Assessment, treatment, and clinical notes are all standardized as is the acute stroke treatment protocol. Patients with acute stroke who were potential candidates for acute interventions proceeded with their stroke alerts. They have a more detailed standardized note that includes TLKW, ED arrival time, arrival mode, initial NIHSS score, whether computed tomography (CT) head scan showed intracranial hemorrhage, whether CT angiography was performed, whether the patient was treated with alteplase, location of LVO, and whether and where the patient was transferred for EST when indicated. These notes are standardized with desired key data elements that can be retrieved electronically along with the entire note contents.<sup>30</sup>

#### 2.3 Data sources and subjects

Patients were included in the study if they presented to any KPNC hospital with EMS-identified stroke symptoms between 7:00 am and midnight. Excluded patients were "walk-in," onset in ED, and inpatient strokes as the goal of the study was to evaluate EMS potential accuracy. Data were extracted from the electronic medical record for all stroke alerts brought in to KPNC hospitals between 7:00 am to midnight from January 1, 2016 to December 31, 2019. From January 1, 2016 to March 30, 2018, arrivals beyond 6 hours of EMS reported TLKW were generally not evaluated by the telestroke service since before 2018 evidence of benefit and criteria for EST of patients beyond 6 hours had not yet been established. Teleneurology services during this time were limited from 7:00 am to midnight. Teleneurology services were expanded after April 1, 2018 to include patients seen 24/7 as well as extended window cases (from 6 to 24 hours from TLKW). In order to keep the study population consistent across the entire study period, we limited our study cohort to cases brought in by EMS between 7:00 am and midnight, and with reported TLKW within 6 hours of ED arrival, that is, excluding extended window cases whose workups were different. Extended window cases are even more complex for EMS to screen as selection for EST in this group includes not just the presence of stroke symptoms and TLKW but also assessment of baseline Rankin score and presence of NIHSS >5. This additional screening is not currently being performed by EMS in any of the counties where KPNC cares for patients. Inpatient and non-EMS arrival stroke alerts were not included in the analysis because the goal of the study was to identify potential EMS accuracy and inpatient and walk-in strokes are not evaluated by EMS.

Permission to publish fully anonymized, aggregate data from this quality initiative, with waiver of the need for institutional review board evaluation and waiver of individual patient consent, was granted by the KPNC Research Determination Officer. The research was conducted in accordance with the principles of the Declaration of Helsinki. We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting of observational studies.<sup>31</sup>

#### 2.4 | Statistical analysis

Patient characteristics between those with and without an LVO were initially compared using chi-square tests for categorical variables and the Kruskal-Wallis test for continuous variables. The associations among patient and stroke characteristics and LVO were evaluated using generalized estimating equations to account for clustering by facility. Odds ratios (ORs) were adjusted for age, gender, initial NIHSS



#### TABLE 1 Presence of LVO among 6209 acute stroke patients evaluated January 1, 2016 to December 31, 2019

	LVO (N = 1314)	NO LVO (N = 4895)	Relative risk or mean difference	95% confidence interval	Р
Age, years, mean (SD)	74.7 (14.3)	71.0 (15.1)	3.7	(2.8, 4.6)	< 0.001
Gender, no. (%)					
Female	685 (21.5%)	2495 (78.5%)	1.0383	(0.90, 1.20)	0.612
Male	629 (20.8%)	2399 (79.2%)	-	-	-
Race, no. (%)					
Asian	239 (24.2%)	747 (75.8%)	1.15	(1.02, 1.28)	0.020
Black	153 (18.0%)	697 (82.0%)	0.85	(0.75, 0.97)	0.013
Hispanic	169 (20.4%)	658 (79.6%)	0.97	(0.84, 1.11)	0.616
Other	77 (21.7%)	278 (78.3%)	1.03	(0.88, 1.19)	0.744
White	676 (21.2%)	2515 (78.8%)	_	_	_
Health plan member, No. (%)					
Member	960 (20.8%)	3665 (79.2%)	0.93	(0.83, 1.03)	0.169
Non-member	354 (22.3%)	1230 (77.7%)	-	-	_
NIHSS score, median (IQR)	16 (10.0-23.0)	7 (3.0-14.0)	-9.00	(-10.05, -7.95)	_

Abbreviations: IQR, interquartile range; LVO, large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale. For each of the proportions, the 95% confidence interval reflects the within-hospital correlations.

score, and facility. A receiver-operating characteristic (ROC) curve was used to determine the optimal cutpoint to predict presence of LVO based on initial NIHSS scores. All hypothesis tests are 2-sided. A *P* value <0.05 was considered statistically significant. All analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

#### 3 | RESULTS

#### 3.1 | Accuracy of EMS diagnosis of acute stroke

Of 13,377 stroke alert patients brought by EMS to KPNC EDs during the study period, 6209 (46.4%) were identified by the telestroke neurologists as having a potential acute stroke within 6 hours of TLKW. One hundred twenty cases (out of 6209 acute stroke cases; 1.9%) did not have initial NIHSS recorded and were excluded from the study population.

The remaining 7168 stroke alerts (53.6%) were cancelled because they did not meet criteria for acute stroke interventions with either intravenous alteplase or EST after initial evaluation by teleneurologists. Cancellations were done when there was not an acute stroke present, or patients did not qualify for an acute stroke treatment— EST or intravenous thrombolytics. The most common reasons for cancelling a stroke alert included stroke mimics (n = 2379; 33.2%), TLKW determined to be >6 hours upon further investigation (n = 1183; 16.5%), and symptom resolution or absence of disabling stroke symptoms (n = 2193; 30.6%) (Figure 1). Common reasons for stroke mimics included sepsis, delirium, metabolic abnormalities, transient global amnesia, syncope, and Bell's palsy.

### 3.2 Characteristics of patients with LVO compared to non-LVO

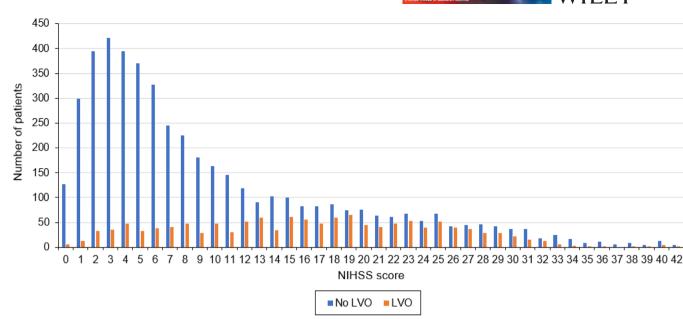
An LVO was found in 1314 (21.2%) of the acute stroke patients. Stroke patients with LVO were significantly more likely to be older, Asian, and have a higher initial NIHSS score (Table 1).

## 3.3 | NIHSS score of stroke patients and prediction of LVO

NIHSS score was available for 6089 (98.1%) out of 6209 patients with acute stroke. Scores ranged from 0 to 42 (Figure 2). The median NIHSS score for patients with LVO was 16.0 compared to 7.0 for those without LVO. We found that NIHSS scores >10 were significantly associated with presence of LVO with an adjusted OR of 4.82 (95% confidence interval [CI], 4.20–5.53). These results persisted using an NIHSS score cutoff of >5 (OR = 4.80, 95% CI [4.03 to 5.72]) and cutoff of >9 (OR = 4.99, 95% CI [4.03 to 5.76]). Based on the ROC curves, the best cutoff for maximal performance appears to be NIHSS score >10 (Figure 3). Using a cutoff of 10 in our population produced an accuracy of 0.67 (95% confidence interval 0.66 to 0.68).

#### 3.4 **Population overview of all patients**

Figure 4 summarizes the findings of all 13,377 patients brought in by EMS as stroke alerts. There were 6209 (46.4%) stroke alerts who met criteria for acute interventions, and 6089 had NIHSS score data available. Out of 6089 qualifying cases, 2573 (42.3%) patients had more severe strokes that were more likely to harbor an LVO



**FIGURE 2** Distribution of NIHSS score for LVO versus non-LVO among 6209 acute stroke patients with NIHSS score. LVO, large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale

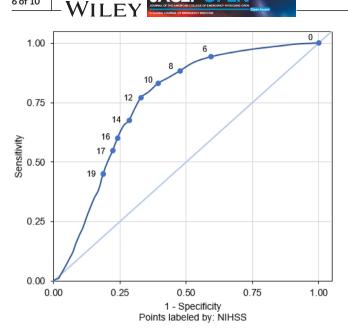
(NIHSS score >10). Among these, 2573 patients, 1103 (42.9%) were treated with intravenous alteplase, and 703 (27.3%) had LVO and were referred for EST. LVOs and referral for EST were found across the whole spectrum of NIHSS scores. Thus, although higher NIHSS scores correlated with greater likelihood of LVO and EST, it is not unusual for patients with much lower scores to also have LVOs and require transfer for EST. In our population, 20% of patients referred for EST had NIHSS scores below 11 and disabling stroke with LVO was seen in patients with NIHSS as low as 0.

#### 4 | LIMITATIONS

Our study has limitations. This is a retrospective analysis of data collected prospectively from a multicenter quality initiative; therefore, we cannot comment on how feasible it would be to have EMS actually perform NIHSS on all patients with potential acute stroke. Because of variability of clinical prehospital stroke scales used currently by EMS, we are unable to determine to what extent use of scales more predictive of LVO may have also improved EMS accuracy for diagnosis of acute stroke. NIHSS data were missing in 120 patients (1.9%) and these patients were excluded from the study population.

Because the majority of the study was conducted before the window for EST was expanded beyond 6 hours, the majority of patients presenting from 6 to 24 hours were not evaluated by teleneurology before 2018 and thus we cannot evaluate possible EMS accuracy in screening this population for LVOs. However, as the criteria for treatment in this population are considerably more restrictive than in the <6 hours acute stroke population, it is even less likely that EMS accuracy would be improved in this group. We did not collect information from EMS regarding whether a standardized stroke score was used on a given patient, the results of the stroke score, the score used, or whether a standard stroke score was proposed by various EMS agencies or the accuracy of EMS performance with the various scores. All information was obtained from the teleneurology examination and medical record after arrival at the KPNC facility, because the primary goal of the study was to evaluate the best possible performance of EMS personnel if they were to be as accurate as stroke neurologists in estimation of patients eligible for EST treatment using the full NIHSS. In 1 county out of 13 in the KPNC catchment area, patients were selected for transport to the closest CSC based on clinical findings (a high Balance, Eyes, Face, Arm and Speech Test [BEFAST] score) and it is possible that this diversion slightly skewed the data in this region in that patients with more likely LVO were thus excluded from the study population in this county. However, the small numbers likely did not materially affect the results. In the other counties, there was either no field-based diversion by EMS for stroke patients or patients with any suspected stroke were diverted to the closest certified PSC, which in many cases is a KPNC hospital. EMS agencies in different states, countries, and regions have very different protocols and the populations served have different demographics and it is possible that the applicability in our population may therefore be somewhat different than in other areas. However, the population of the region includes nearly 12 million ethnically and socially diverse patients, 4.5+ million of whom are KP members. This study did not evaluate actual transport times for patients evaluated in a PSC and then transferred for EST or patients taken directly to a center for EST. Thrombectomy indications changed substantially during the study period and therefore potential impact of EMS accuracy in the 6-24 hours since last known well period was not evaluated.

Strengths of the study include a large racially and demographically diverse patient population, involvement of numerous EMS agencies



NIHSS Score	Estimated Probability	Sensitivity	1 - Specificity
0	0.05	1	1
1	0.06	1.00	0.97
2	0.06	1.00	0.92
3	0.07	0.99	0.84
4	0.07	0.97	0.75
5	0.08	0.96	0.67
6	0.09	0.94	0.59
7	0.09	0.92	0.53
8	0.10	0.88	0.48
9	0.11	0.85	0.43
10	0.11	0.83	0.39
11	0.12	0.80	0.36
12	0.13	0.77	0.33
13	0.14	0.72	0.31
14	0.15	0.68	0.28
15	0.16	0.65	0.26

FIGURE 3 Receiver operating characteristic curve for predicting large vessel occlusion using NIHSS score (area under curve = 0.7677). NIHSS, National Institutes of Health Stroke Scale

and community hospitals, capture of data on all EMS-suspected strokes without prescreening by physicians or nurses, and complete capture of the entire study population regarding treatment with thrombolysis and thrombectomy.

#### 5 DISCUSSION

#### 5.1 EMS stroke identification and frequency of thrombolysis and EST treatments

In our study, we found only 46.4% of patients brought in by EMS for suspected acute stroke within 6 hours of symptom onset were candidates for any acute intervention. We found that inaccurate identification of TLKW and stroke mimics accounted for nearly half of the cases

that were brought in by EMS who did not meet criteria for acute treatment.

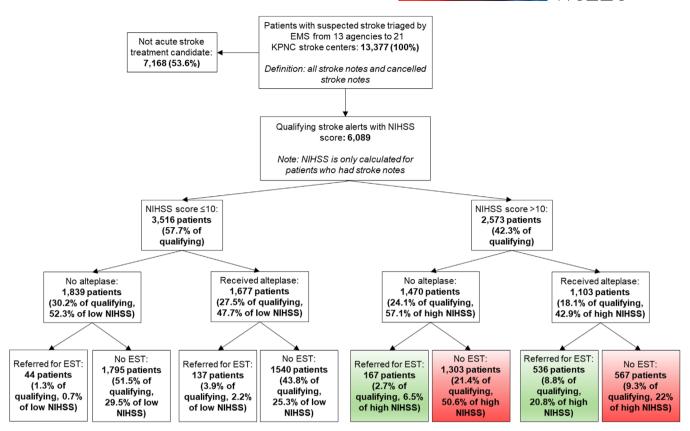
In most of our EMS regions, the primary scale used to identify acute strokes was the CPSS.<sup>28</sup> More specific LVO scales may increase accuracy of stroke diagnosis to an unknown extent but would not be expected to improve other items such as inaccuracy of TLKW. More accurate tools for stroke diagnosis might also come at the cost of missing patents who might qualify for acute stroke interventions. Although there are undoubtedly benefits to a high index of suspicion for patients with suspected acute stroke being brought immediately to the ED for evaluation, it also means that if a system is developed to have EMS make accurate destination decisions based on expected acute stroke interventions (EST or thrombolytic therapy), tools must improve the accuracy of prediction of the need for acute stroke treatment and accuracy of prediction of other clinical features such as TLKW.

#### 5.2 What if EMS personnel were as accurate as stroke neurologists?

When performed by experienced clinicians, accuracy of various scales designed to predict LVO varies considerably and is dependent on selected cutoff values. As expected, increased accuracy comes at the price of reduced sensitivity. At "optimal" cutoff values, accuracy of various scales (NIHSS, Face-Arm-Speech-Time test, G-FAST, Cincinnati Stroke Triage Assessment Tool, 3-Item Stroke Scale, Prehospital Acute Stroke Severity, Rapid Arterial Occlusion Evaluation) is reported to range from 51% to 70%, with negative predictive value ranging from 87% to 92% and positive predictive value from 31% to 42%.<sup>32</sup>

To evaluate the second goal, we evaluated the performance of stroke neurologists in their ability to accurately predict patients needing EST. Stroke neurologists in this study used the full NIHSS to predict potential presence of LVO and promptly initiated transfer protocols (eg., requesting critical care transport even before CT angiography). We found that in our population of EMS-identified suspected strokes, teleneurologist evaluation, and NIHSS scoring, an NIHSS of 10 was the optimal cut point based on the ROC curve, with a sensitivity of 83%. With this cutoff value, 17% of LVOs were missed. In previously reported studies, an NIHSS score of 8 or greater score accurately predicted presence of LVO 55% of the time.<sup>32-34</sup> In a metanalysis of multiple studies looking at NIHSS score as a predictor of LVO, a score of 11 or above was shown to be the best cutoff for LVO prediction.

The ultimate goal of prediction of likelihood of LVO based on clinical exam is whether patients ultimately undergo EST. This decision can be based on a variety of clinical features including several that are not addressed by the stroke scale alone, including (1) whether the patient actually has a stroke, as even high NIHSS scores are not always diagnostic of strokes. Patients may have high NIHSS scores from toxic metabolic conditions such as sepsis, intoxications, or delirium; (2) TLKW (accuracy of establishing this measure is not a function of the stroke scale and we found a third of EMS personnel's TLKW was inaccurate; (3) accuracy in performance of the scale; and (4) accuracy of the scale itself. In our population, EMS diagnosis of acute stroke was only



FIGURF 4 Population overview of suspected stroke patients delivered to Kaiser Permanente Northern California (KPNC) emergency departments by 13 emergency medical services (EMS) agencies. Red shade depicts patients with "potential harm"; if diversion was in place for NIHSS > 10, patients who would be diverted past local primary stroke centers to comprehensive stroke centers but not ultimately receiving EST. Green shading depicts patients who would potentially "benefit" from diversion. EST, endovascular stroke therapy; NIHSS, National Institutes of Health Stroke Scale

46.4% accurate. Given the inaccuracy of predicting an acute stroke, the ability to predict an LVO becomes less relevant.

#### 5.3 Would field-based triage and diversion of stroke patients make sense based on the accuracy of EST prediction and the frequency of acute stroke treatments in the population?

Patients with strokes <4.5 hours from TLKW benefit from prompt intravenous thrombolysis. The robustness of the data supporting the clinical efficacy of timely thrombolytics for acute ischemic stroke has long been called into question, more commonly in the emergency medicine community.<sup>35,36</sup> Despite this controversy, the practice is endorsed by both the American Heart Association/American Stroke Association (Class I, Level A)<sup>37</sup> and the American College of Emergency Physicians (Level B recommendation).<sup>38</sup> Patients with LVO benefit from prompt EST.<sup>37,39,40</sup> However, whether patients with acute stroke and LVO actually benefit from prehospital identification and diversion by EMS is controversial.<sup>41</sup> A recent metanalysis found improved outcomes in 8 studies of 2068 patients treated directly at the CSC rather than a "drip and ship" model with treatment with intravenous

thrombolysis initially at a PSC. However, the authors acknowledged significant limitations of the studies, including selection bias and retrospective data collection.<sup>42</sup> Furthermore, these studies focused solely on patients who ended up undergoing EST and did not address outcomes of patients without LVO who were treated only with intravenous thrombolytics. The model also lacked consideration for inaccuracy in field-based diagnosis of LVO. Because of lack of evidence for benefits of field-based diversion, current American Heart Association guidelines state the following: "When several IV alteplase-capable hospital options exist within a defined geographic region, the benefits of bypassing the closest to bring the patient to one that offers a higher level of stroke care, including mechanical thrombectomy, is uncertain. Further research is needed."37,43

Minutes matter in the treatment of acute stroke, with worse outcomes reported for every 15-minute delay in thrombolytic treatment<sup>44</sup> and any field-based bypass/diversion scheme that increases time to thrombolytic treatment risks worse outcomes for patients who are candidates for intravenous thrombolytic treatment but not candidates for EST. Other potential harms include overwhelming CSCs with patients who ultimately will not need EST, reduced volumes of acute stroke treatment at PSCs leading to reduced quality of treatment of acute stroke, and potentially poorer treatment by an outside facility

having limited access to full medical history compared with "home" facilities.

In our large population of patients brought in by EMS and evaluated by teleneurologists without any prescreening by ED nurses or physicians, we found that only 6.6% of patients ultimately were referred for EST but 20.8% received intravenous thrombolysis. Given that the goal of field-based prehospital triaging protocols is to select patients for EST, the fact that ultimately 72.7% of patients with NIHSS score >10 ended up not needing EST reduces the possible benefits of fieldbased diversion, especially because many more of these patients were treated with intravenous alteplase than with EST. Even in the largest strokes (NIHSS 11 or greater), more patients were treated with intravenous alteplase (43.0%) than EST (20.8%).

Our results suggest a possible alternative to field-based prehospital triaging schemes and suggest that a plan that would benefit the greatest number of patients could focus on expedited and efficient acute treatment and transfer protocols. There are proven methods to minimize door-to-treatment times for intravenous thrombolytic to 30 minutes or less as well as obtaining rapid CT angiogram identification of LVOs that can be implemented in community hospitals.<sup>29,45–48</sup> Expedited transfer protocols can considerably reduce transfer times between hospitals.<sup>49,50</sup> Early ordering of transportation for transfers, remote reviewing of neuroimaging studies by neurointerventionalists, and early activation of the EST team at the accepting facility could minimize treatment delays at the accepting hospital. Such approaches maximize the ability of all patients to receive timely intravenous thrombolysis.

Furthermore, about half of all acute stroke patients do not come in by EMS and 20% of patients brought in by EMS with acute strokes who were referred for EST had NIHSS scores  $<11.^{51}$  These patients still need screening for and identification of LVO and rapid transfer for EST, if indicated. Focus on rapid intravenous thrombolytic treatment and expedited transfer could also benefit these patients, who would not benefit from field-based diversion schemes.

If PSC performance is poor, interfacility transfer times are long or there are abundant CSC resources in a community, field-based diversion strategies may be a better solution for some patients. However, such schemes should be evaluated taking into account the potential accuracy of field-based identification of EST candidates as well as the frequency of EST versus thrombolytic treatment.

#### 6 CONCLUSION

In summary, in a community population of patients identified by EMS as having potential acute strokes, only a small percentage of patients harbor an LVO requiring EST (6.6%). Even in patients identified by experienced stroke neurologists as having acute strokes with NIHSS score >10, only about 1 in 4 ended up referred for EST. Many more of even these patients with severe strokes were more likely to receive intravenous thrombolysis than undergo EST. Any study evaluating the effectiveness of prehospital triaging for potential LVO must also measure treatment times and outcomes for patients with strokes that are

treated with intravenous thrombolysis but do not have LVO given that one of the primary potential harms is delay in intravenous thrombolysis in those without LVO.

#### ACKNOWLEDGMENTS

We would like to thank the Stroke FORCE (Fast Operating Remote Cerebrovascular Experts) team for their dedication to stroke care and research. MNN-H and DRV received support from The Permanente Medical Group's Delivery Science and Applied Research Program.

#### CONFLICTS OF INTEREST

None.

#### AUTHOR CONTRIBUTIONS

JGK and MNN-H conceived and designed the study. JGK and MNN-H supervised the conduct of the study and data collection. JGA managed the data, including quality control, provided statistical advice on study design, and analyzed the data. JGK and MNN-H drafted the article, and all authors contributed substantially to its revision. JGK takes responsibility for the paper as a whole.

#### REFERENCES

- Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. JAMA. 2016;316(12):1279-1288.
- Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet.* 2004;363(9411):768-774.
- Wardlaw JM, Murray V, Berge E, et al. Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. *Lancet*. 2012;379(9834):2364-2372.
- Lees KR, Bluhmki E, von Kummer R, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet*. 2010;375(9727):1695-1703.
- National Institute of Neurological D, Stroke rt PASSG. Tissue plasminogen activator for Acute Ischemic Stroke. N Engl J Med. 1995;333(24):1581-1587.
- Yang P, Zhang Y, Zhang L, et al. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. N Engl J Med. 2020;382(21):1981-1993.
- Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2015;372(1):11-20.
- Saver JL. Number needed to treat estimates incorporating effects over the entire range of clinical outcomes: novel derivation method and application to thrombolytic therapy for acute stroke. *Arch Neurol.* 2004;61(7):1066-1070.
- Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015;372(11):1009-1018.
- Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372(11):1019-1030.
- Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med. 2015;372(24):2296-2306.
- Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med. 2015;372(24):2285-2295.

- Hastrup S, Damgaard D, Johnsen SP, Andersen G. Prehospital acute stroke severity scale to predict large artery occlusion: design and comparison with other scales. *Stroke.* 2016;47(7):1772-1776.
- Lima FO, Silva GS, Furie KL, et al. Field assessment stroke triage for emergency destination: a simple and accurate prehospital scale to detect large vessel occlusion strokes. *Stroke*. 2016;47(8): 1997-2002.
- Noorian AR, Sanossian N, Shkirkova K, et al. Los Angeles motor scale to identify large vessel occlusion: prehospital validation and comparison with other screens. *Stroke.* 2018;49(3):565-572.
- Perez de la Ossa N, Carrera D, Gorchs M, et al. Design and validation of a prehospital stroke scale to predict large arterial occlusion: the rapid arterial occlusion evaluation scale. *Stroke*. 2014;45(1):87-91.
- Richards CT, Huebinger R, Tataris KL, et al. Cincinnati prehospital stroke scale can identify large vessel occlusion stroke. *Prehosp Emerg Care*. 2018;22(3):312-318.
- Smith EE, Kent DM, Bulsara KR, et al. Accuracy of prediction instruments for diagnosing large vessel occlusion in individuals with suspected stroke: a systematic review for the 2018 guidelines for the early management of patients with Acute Ischemic Stroke. *Stroke*. 2018;49(3):e111-e122.
- Froehler MT, Saver JL, Zaidat OO, 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*. 2017;136(24):2311-2321.
- Gerschenfeld G, Muresan IP, Blanc R, et al. Two paradigms for endovascular thrombectomy after intravenous thrombolysis for Acute Ischemic Stroke. JAMA Neurol. 2017;74(5):549-556.
- Schlemm L, Endres M, Scheitz JF, Ernst M, Nolte CH, Schlemm E. Comparative Evaluation of 10 prehospital triage strategy paradigms for patients with suspected Acute Ischemic Stroke. J Am Heart Assoc. 2019;8(12):e012665.
- Venema E, Groot AE, Lingsma HF, et al. Effect of interhospital transfer on endovascular treatment for Acute Ischemic Stroke. *Stroke*. 2019;50(4):923-930.
- Deguchi I, Mizuno S, Kohyama S, Tanahashi N, Takao M. Drip-and-Ship thrombolytic therapy for Acute Ischemic Stroke. J Stroke Cerebrovasc Dis. 2018;27(1):61-67.
- 24. Venema E, Lingsma HF, Chalos V, et al. Personalized prehospital triage in Acute Ischemic Stroke. *Stroke*. 2019;50(2):313-320.
- Milne MS, Holodinsky JK, Hill MD, et al. Drip 'n ship versus mothership for endovascular treatment: modeling the best transportation options for optimal outcomes. *Stroke.* 2017;48(3): 791-794.
- Holodinsky JK, Williamson TS, Demchuk AM, et al. Modeling stroke patient transport for all patients with suspected large-vessel occlusion. JAMA Neurol. 2018;75(12):1477-1486.
- Marras C, Van den Eeden SK, Fross RD, et al. Minimum incidence of primary cervical dystonia in a multiethnic health care population. *Neurology*. 2007;69(7):676-680.
- Glober NK, Sporer KA, Guluma KZ, et al. Acute stroke: current evidence-based recommendations for prehospital care. West J Emerg Med. 2016;17(2):104-128.
- Nguyen-Huynh MN, Klingman JG, Avins AL, et al. Novel telestroke program improves thrombolysis for acute stroke across 21 hospitals of an integrated healthcare system. *Stroke*. 2018;49(1):133-139.
- Flint AC, Melles RB, Klingman JG, Chan SL, Rao VA, Avins AL. Automated extraction of structured data from text notes in the electronic medical record. J Gen Intern Med. 2020. https://doi.org/10.1007/ s11606-020-06110-8.
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet.* 2007;370(9596):1453-1457.

### 

- , 9 of 10
- Scheitz JF, Abdul-Rahim AH, MacIsaac RL, et al. Clinical selection strategies to identify ischemic stroke patients with large anterior vessel occlusion: results from SITS-ISTR (Safe Implementation of Thrombolysis in Stroke International Stroke Thrombolysis Registry). *Stroke*. 2017;48(2):290-297.
- Antipova D, Eadie L, Macaden A, Wilson P. Diagnostic accuracy of clinical tools for assessment of acute stroke: a systematic review. BMC Emerg Med. 2019;19(1):49.
- Heldner MR, Hsieh K, Broeg-Morvay A, et al. Clinical prediction of large vessel occlusion in anterior circulation stroke: mission impossible? J Neurol. 2016;263(8):1633-1640.
- Dewar B, Shamy M. TPA for acute ischemic stroke and its controversies: a review. *Neurohospitalist*. 2020;10(1):5-10.
- Brown DL, Barsan WG, Lisabeth LD, Gallery ME, Morgenstern LB. Survey of emergency physicians about recombinant tissue plasminogen activator for acute ischemic stroke. *Ann Emerg Med.* 2005;46(1):56-60.
- 37. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke.* 2018;49(3):e46-e110.
- Brown MD, Burton JH, Nazarian DJ, Promes SB. Clinical policy: use of intravenous tissue plasminogen activator for the management of acute ischemic stroke in the emergency department. *Ann Emerg Med.* 2015;66(3):322-333.
- English JD, Yavagal DR, Gupta R, et al. Mechanical thrombectomyready comprehensive stroke center requirements and endovascular stroke systems of care: recommendations from the Endovascular Stroke Standards Committee of the Society of Vascular and Interventional Neurology (SVIN). *Interv Neurol.* 2016;4(3-4):138-150.
- 40. Holodinsky JK, Patel AB, Thornton J, et al. Drip and ship versus direct to endovascular thrombectomy: the impact of treatment times on transport decision-making. *Eur Stroke J.* 2018;3(2):126-135.
- Southerland AM, Johnston KC, Molina CA, Selim MH, Kamal N, Goyal M. Suspected large vessel occlusion: should emergency medical services transport to the nearest primary stroke center or bypass to a comprehensive stroke center with endovascular capabilities? *Stroke*. 2016;47(7):1965-1967.
- 42. Ismail M, Armoiry X, Tau N, et al. Mothership versus drip and ship for thrombectomy in patients who had an acute stroke: a systematic review and meta-analysis. *J Neurointerv Surg.* 2019;11(1):14-19.
- McCoy CE, Langdorf MI, Lotfipour S. American Heart Association/American Stroke Association deletes sections from 2018 stroke guidelines. West J Emerg Med. 2018;19(6):947-951.
- Saver JL, Fonarow GC, Smith EE, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. JAMA. 2013;309(23):2480-2488.
- Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology*. 2012;79(4):306-313.
- Meretoja A, Weir L, Ugalde M, et al. Helsinki model cut stroke thrombolysis delays to 25 minutes in Melbourne in only 4 months. *Neurology*. 2013;81(12):1071-1076.
- 47. Kircher C, Kreitzer N, Adeoye O. Pre and intrahospital workflow for acute stroke treatment. *Curr Opin Neurol*. 2016;29(1):14-19.
- Huang Q, Zhang JZ, Xu WD, Wu J. Generalization of the right acute stroke promotive strategies in reducing delays of intravenous thrombolysis for acute ischemic stroke: a meta-analysis. *Medicine (Baltimore)*. 2018;97(25):e11205.
- de Villiers JS, Anderson T, McMeekin JD, et al. Expedited transfer for primary percutaneous coronary intervention: a program evaluation. CMAJ. 2007;176(13):1833-1838.
- Harrington DT, Connolly M, Biffl WL, Majercik SD, Cioffi WG. Transfer times to definitive care facilities are too long: a consequence of an immature trauma system. *Ann Surg.* 2005;241(6):961-966.discussion 966–968.

10 of 10



 Mohammad YM. Mode of arrival to the emergency department of stroke patients in the United States. *J Vasc Interv Neurol*. 2008;1(3):83-86.

#### AUTHOR BIOGRAPHY



Mai N. Nguyen-Huynh, MD MAS, is a board certified vascular neurologist and a research scientist at the Kaiser Permanente Northern California Division of Research. How to cite this article: Klingman JG, Alexander JG, Vinson DR, Klingman LE, Nguyen-Huynh MN. Potential accuracy of prehospital NIHSS-based triage for selection of candidates for acute endovascular stroke therapy. *JACEP Open*. 2021;2:e12441. https://doi.org/10.1002/emp2.12441