

# Effect of Known Atrial Fibrillation and Anticoagulation Status on the Prehospital Identification of Large Vessel Occlusion

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*Introduction:* The Cincinnati Prehospital Stroke Severity scale (C-STAT), Los Angeles Motor Scale (LAMS), Rapid Arterial Occlusion Evaluation (RACE) score, and Field Assessment Stroke Triage for Emergency Destination (FAST-ED) scales were designed to aid emergency responder identification of patients with stroke related to large vessel occlusion (LVO). We hypothesized that the addition of a known history of atrial fibrillation (AF) without anticoagulation to currently used scales would improve LVO detection. *Methods:* Medical records of patients admitted to a Comprehensive Stroke Center with acute ischemic stroke in 2014-2015 were reviewed. LVO identification using the C-STAT, LAMS, RACE, and FAST-ED scores and the AF variable were compared using univariable analyses. The areas under the receiver operating curves (AUCs) were then compared for each score, the AF variable, and each score with the addition of the AF variable. *Results:* The sample included 233 patients without and 188 patients with an LVO. A history of known AF, history of AF with no anticoagulation, and the C-STAT, LAMS, RACE, and FAST-ED scores were each associated with LVO in univariable analyses. The AUCs for C-STAT, LAMS, RACE, and FAST-ED were similar. The addition of the known AF and no anticoagulation variable did not appreciably change these AUCs. *Conclusion:* Although known AF with no anticoagulation was associated with LVO in patients with acute ischemic stroke, this historic feature did not improve the accuracy of existing LVO detection scales.

**Key Words:** Stroke—atrial fibrillation—vessel occlusion—anticoagulants

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## Introduction

American Heart Association/American Stroke Association guidelines recommend that all patients with possible ischemic stroke within 24 hours of symptom onset be evaluated to identify those with a large vessel occlusion (LVO) who may benefit from mechanical thrombectomy.<sup>1</sup> This procedure is optimally provided at appropriately staffed and equipped hospitals, such as those identified by the Joint Commission as a Comprehensive Stroke Center (CSC) or a Thrombectomy capable Stroke Center. Direct transportation of patients with stroke caused by LVO to a CSC or Thrombectomy capable Stroke Center can reduce treatment delays and improve the probability of effective reperfusion.<sup>2</sup> However, for those without LVO, bypassing an otherwise appropriate hospital would delay their treatment with recombinant intravenous tissue plasminogen activator and could waste resources at thrombectomy-capable centers.

The Cincinnati Stroke Assessment Tool (C-STAT),<sup>3</sup> Los Angeles Motor Scale (LAMS),<sup>4</sup> Rapid Arterial Occlusion Evaluation (RACE),<sup>5</sup> and Field Assessment Stroke Triage for Emergency Destination (FAST-ED)<sup>6</sup> were developed to help emergency medical responders identify stroke patients more likely to have an LVO in the prehospital setting. Their sensitivities and specificities range from 47% to 73% and from 78% to 90%, respectively. A meta-analysis concluded: "No scale predicted LVO with both high sensitivity and high specificity."<sup>7</sup>

The currently available LVO identification scales rely on physical examination findings. Certain historical elements are also associated with LVO and might improve the predictive capacity of these tools.<sup>8</sup> Because LVO can be caused by cardiogenic embolism associated with atrial fibrillation (AF), we tested the hypothesis that a history of known AF, particularly among patients who were not receiving an anticoagulant (AC), would help identify those more likely to have an LVO, and that these historic features would improve the accuracy of LVO detection using the available scales. We also directly compared the accuracies of the common currently used LVO detection scores.

## Methods

We conducted a retrospective analysis of the medical records of all patients admitted to the University of Kentucky Medical Center in Lexington, Kentucky, United States, and diagnosed with an acute ischemic stroke between January 2014 and June 2015. Patency of a relevant proximal vessel was determined by initial computed tomography/magnetic resonance angiography or carotid

and transcranial Duplex ultrasound performed during the hospitalization. All patients who had an occlusion of the common carotid, internal carotid, middle cerebral (M1, M2, M3 segments), anterior cerebral (A1 segment), posterior cerebral artery (P1 segment), or vertebrobasilar system proximal to the area of ischemic injury (i.e., LVO) were included. Controls were patients without an LVO who were randomly selected from a cohort of 1275 patients discharged with a diagnosis of acute ischemic stroke over the same time period. This cohort was enriched by 25% oversampling; no cases were systematically excluded. Patients with intracranial hemorrhage and stroke mimics were excluded. The etiology of the stroke was determined based on the ASCOD (A: atherosclerosis; S: small-vessel disease; C: cardiac pathology; O: other cause, and D: dissection) system and patients with all etiologies were included.<sup>9</sup> A history of previously known AF documented at the time of initial encounter in the emergency department and whether the patient was or was not receiving an AC was recorded from chart review. Patients diagnosed with AF for the first time after hospital arrival were not considered as having known AF.

Scores on the C-STAT, LAMS, RACE, and FAST-ED scales were determined for each patient using elements of the initial National Institutes of Health Stroke Scale (NIHSS) score documented at the time of presentation to the emergency department or transfer from a primary stroke center. The area under the receiver operator curve (AUC) for each LVO scale was calculated. For every case or control, the AUC for each LVO scale was compared individually with the known AF and no AC variable and within models based on the addition of the known AF

**Table 1.** Univariable associations with vessel occlusion

Variable	No LVO (n = 233)	With LVO (n = 188)	P value
Mean age	64.93 (.98)	66.92 (1.07)	<i>P</i> = .1715
Known AF	43 (18.5%)	68 (36.2%)	<i>P</i> ≤ .0001
Known antiplatelet use	101 (43.3%)	86 (45.7%)	<i>P</i> = .6227
Known anticoagulant use	30 (12.9%)	19 (10.2%)	<i>P</i> = .3890
Known AF + no AC	25 (11.3%)	50 (27.0%)	<i>P</i> ≤ .0001
Known AF + yes AC or no known AF + no AC	196 (88.7%)	135 (73.0%)	
Mean NIHSS score	6.48 ± .43	14.21 ± .60	<i>P</i> ≤ .0001
Mean RACE score	2.10 ± .15	5.12 ± .22	<i>P</i> ≤ .0001
Mean C-STAT score	0.90 ± .07	2.21 ± .10	<i>P</i> ≤ .0001
Mean LAMS score	1.66 ± .11	3.29 ± .13	<i>P</i> ≤ .0001
Mean FAST-ED score	1.88 ± .12	4.55 ± .18	<i>P</i> ≤ .0001
Sex (female)	108 (46.4%)	96 (51.1%)	<i>P</i> = .3362
Sex (male)	125 (53.6%)	92 (48.9%)	
History of hypertension	195 (83.7%)	156 (83.0%)	<i>P</i> = .8453
History of hyperlipidemia	105 (45.1%)	81 (43.1%)	<i>P</i> = .6843
History of diabetes mellitus	87 (37.3%)	74 (39.4%)	<i>P</i> = .6712
History of stroke/TIA	42 (18.0%)	28 (14.9%)	<i>P</i> = .3908
History of smoking	64 (27.5%)	45 (23.9%)	<i>P</i> = .4108

*t* tests were used to determine the significance of the differences between groups for continuous variables and chi-square tests were used to compare differences in frequencies.

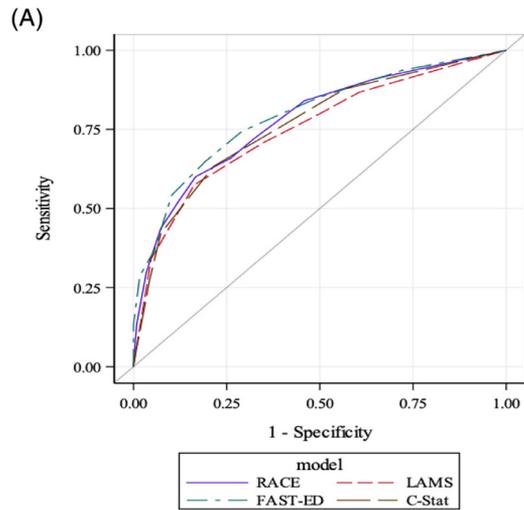
and no AC variable. All analyses were completed in SAS 9.4 (SAS Institute Inc., Cary, NC).

This research protocol was approved by the University of Kentucky institutional review board. The need for informed consent was waived due to retrospective study design. The data that support the findings of this study are available from the corresponding author upon reasonable request.

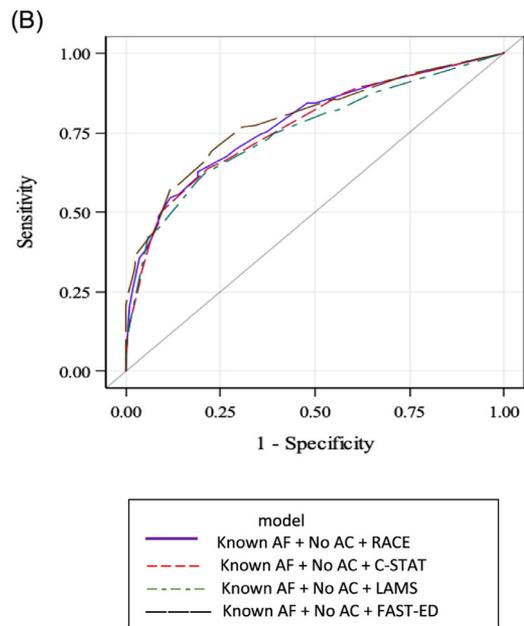
**Results**

The study cohort included 188 patients with a radiographically demonstrated, clinically relevant LVO and 233 without an occlusion. The NIHSS at admission and

the C-STAT, LAMS, RACE, and FAST-ED scores were all higher in those with an LVO. A history of AF, including those who were not anticoagulated, was also more frequent in those who had an LVO (Table 1; AF with no anticoagulation, AUC = .579; 95% CI .540-.617). There was no difference among the LVO detection scales for the identification of a large-artery occlusion when compared with each other (Fig 1A). After the addition of a history of AF with no AC use to the current validated scales, FAST-ED had the highest AUC which was significantly different than the modified LAMS model but similar to RACE and CSTAT models (Fig 1B). The addition of a history of AF with no AC use was associated with LVO independent of the LAMS, but not C-STAT, RACE or FAST-ED scores

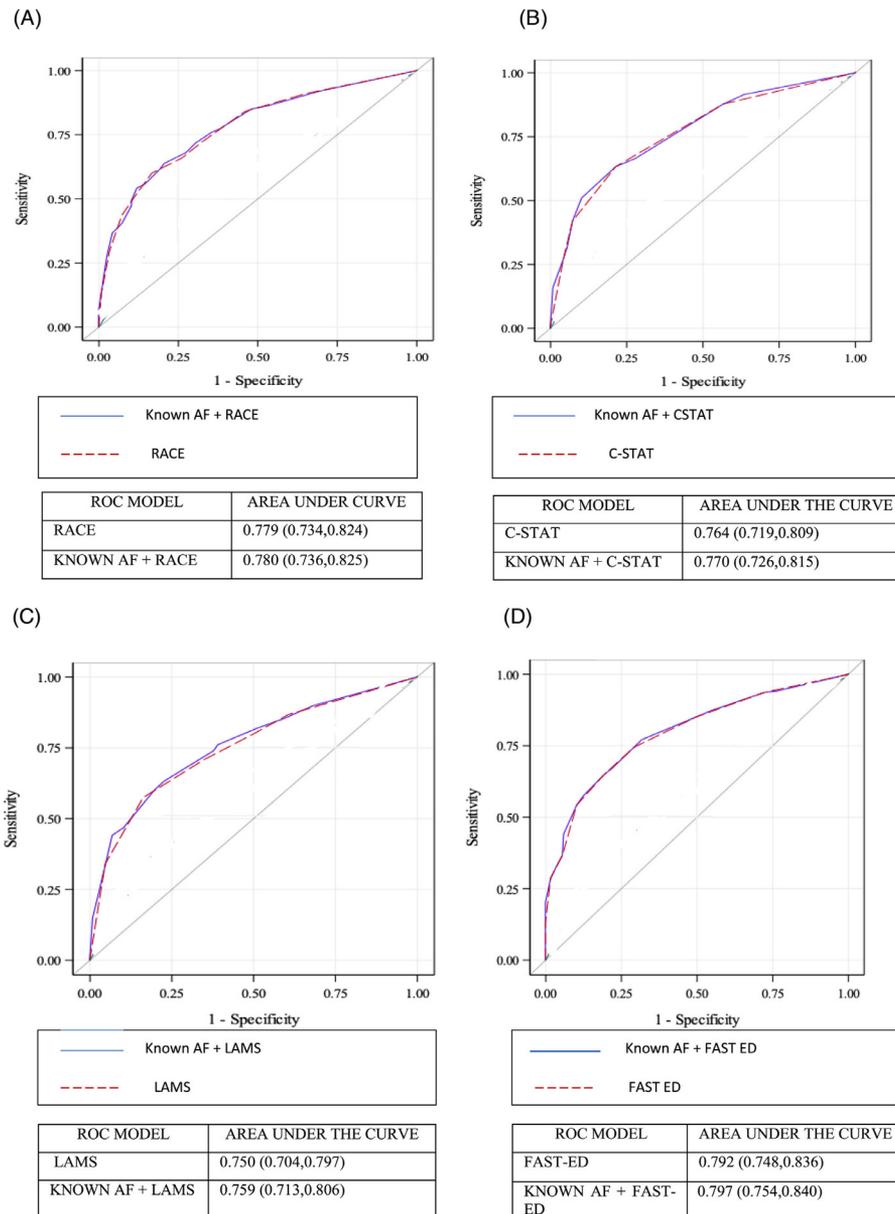


ROC CURVE	AUC (95% Confidence Interval)	CHI-SQUARE TEST STATISTIC (degrees of freedom), p-value
RACE	0.779 (0.734,0.823)	$X^2(1)=84.8, p<0.0001$
C-Stat	0.764 (0.719,0.808)	$X^2(1)=75.8, p<0.0001$
LAMS	0.750 (0.704,0.797)	$X^2(1)=77.7, p<0.0001$
FAST_ED	0.794 (0.751,0.837)	$X^2(1)=90.3, p<0.0001$



ROC CURVE	AUC (95% Confidence Interval)	CHI-SQUARE TEST STATISTIC (degrees of freedom), p-value
Known AF + no AC + RACE	0.779 (0.733,0.824)	$X^2(1)=1.624, p=0.2026$
Known AF + no AC + C-STAT	0.769 (0.724,0.814)	$X^2(1)=3.114, p=0.0776$
Known AF + no AC + LAMS	0.754 (0.706,0.801)	$X^2(1)=7.566, p=0.0059$
Known AF + no AC + FAST-ED	0.792 (0.747,0.836)	

**Figure 1.** (A) Comparison of RACE, C-STAT, LAMS and FAST-ED scores with each other validating the finding that all scales perform similarly. (B) Comparison of RACE, C-STAT, LAMS and FAST ED scores after addition of known AF + no AC variable. Because the FAST-ED model had the largest AUC, it was used as the reference model. The FAST-ED model was significantly different than the LAMS model, but not significantly different than the RACE and C-STAT model.



**Figure 2.** Receiver operating curves for LVO detection scales. The AUC for each LVO identification instrument (RACE (A), C-STAT (B), LAMS (C) and FAST-ED (D)) alone and with the addition of the known AF variable are shown. LVO prediction instrument alone and in combination of known AF variable had comparable AUCs to each other with no significant difference. Abbreviations: AF, atrial fibrillation; AUC, area under the curve; LVO, large vessel occlusion; no AC, no anticoagulation. See the text for definition of scale acronyms.

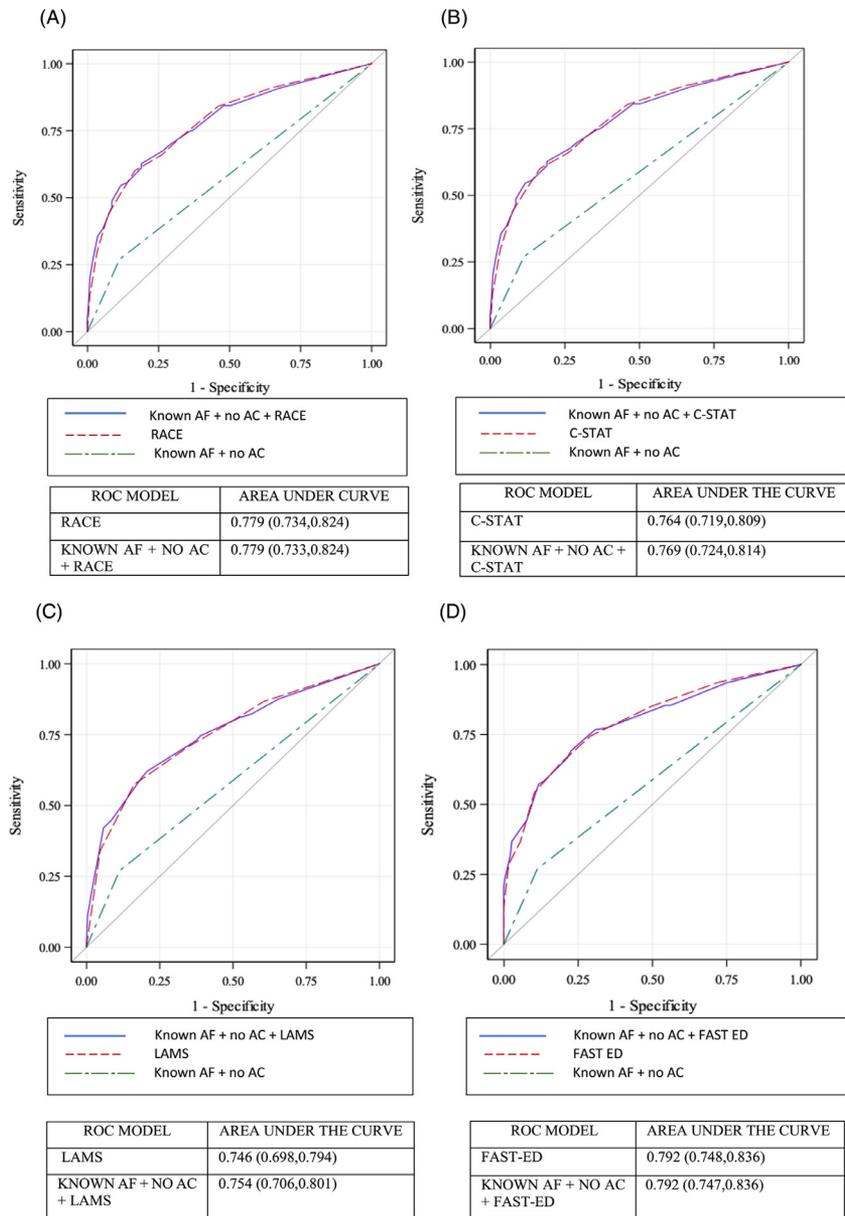
(data not shown). The addition of known AF alone or known AF with no anticoagulation did not improve the AUC for any of the scales (Figs 2 and 3).

## Discussion

We found that having a known history of AF at the time of stroke, including those who were not anticoagulated, was more common in patients with an LVO. This element of medical history, which could be obtained in the field by emergency medical responders, may be helpful as an aid in triage decisions, but did not add to the accuracy of

several of the currently used predictive scales (i.e., C-STAT, LAMS, RACE, and FAST-ED). Each of these scales similarly helped identify patients more likely to have an LVO.

C-STAT, LAMS, RACE, and FAST-ED were chosen for our study because they are among the most commonly used LVO prediction instruments and each has been at least partially validated.<sup>7</sup> FAST-ED has similar discrimination capacity for LVO compared to the more complex NIHSS score and greater discrimination compared with RACE.<sup>6</sup> RACE gives greater weight to motor symptoms than FAST-ED and does not include assessment of



**Figure 3.** Receiver operating curves for LVO detection scales. The AUC for each LVO identification instrument (RACE (A), C-STAT (B), LAMS (C) and FAST-ED (D)) alone and with the addition of the known AF with no AC variable (AF with no anticoagulation, AUC = 0.579; 95% CI .540 -.617) are shown. Both LVO prediction instrument alone and in combination of known AF with no AC variable were superior to known AF with no AC variable alone but had comparable AUCs to each other with no significant difference. Abbreviations: AF, atrial fibrillation; AUC, area under the curve; LVO, large vessel occlusion; no AC, no anticoagulation. See the text for definition of scale acronyms.

expressive aphasia. The C-STAT and LAMS scales are the simplest and most easily implemented, but do not assess cortical signs such as aphasia or neglect, which are commonly present in patients with a carotid-distribution LVO.<sup>4-6,10</sup> An NIHSS score greater than or equal to 10 points also identified those more likely to have an LVO but is difficult to perform reliably in the field by emergency responders.<sup>11</sup> Although the scales have different components, none has proven superior for the detection of an LVO and none had high sensitivity or specificity.<sup>6</sup>

Our study has several limitations. We conducted a retrospective analysis of patients admitted to a single CSC and the results may not be generalizable to other settings. Our data, including calculation of various prehospital LVO scores, were based on information available in the medical record at the time of emergency department presentation. Prospective validation of this work should be performed in the field, as physical findings may fluctuate between initial assessment on scene and after presentation to the emergency department. We were not able to assess

all potential predictors of LVO, such as having systolic blood pressure less than or equal to 170 mm Hg.<sup>8</sup> We systematically excluded stroke mimics, anticipating that this potential bias would be apportioned equally between our case and control populations.

We found that history of known AF, regardless of anticoagulation status, was associated with a higher likelihood of an LVO in patients with acute ischemic stroke. Although this did not improve the accuracy of existing LVO detection scales, quickly obtaining this information may help further inform triage and transport decisions. Additional prospective studies are needed to validate this observation and the potential impact of history of AF with no anticoagulation use on current EMS scoring systems.

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### Statement of Ethics

This research protocol was approved by the University of Kentucky institutional review board.

### Conflicts of Interest

None.

### Author Contributions

Parneet Grewal: Study design, acquisition of data, interpretation of data, manuscript writing and approval of final manuscript.

Sourabh Lahoti: Study design, interpretation of data, manuscript writing and approval of final manuscript.

Sushanth Aroor: Study design, acquisition of data, interpretation of data and approval of final manuscript.

Kaitlin Snyder: Acquisition of data and approval of final manuscript.

Luther C. Pettigrew: Study design, interpretation of the data and critical revision of the manuscript for intellectual content.

Larry B. Goldstein: Study design, interpretation of the data and critical revision of the manuscript for intellectual content.

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