Prehospital triage of intracranial hemorrhage and anterior large-vessel occlusion ischemic stroke: value of the rapid arterial occlusion evaluation

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Stroke: Vascular and Interventional Neurology

ORIGINAL RESEARCH

Prehospital Triage of Intracranial Hemorrhage and Anterior Large-Vessel Occlusion Ischemic Stroke: Value of the Rapid Arterial Occlusion Evaluation

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BACKGROUND: The Rapid Arterial oCclusion Evaluation (RACE) score can identify patients with anterior circulation large-vessel occlusion (aLVO) ischemic stroke for transportation to a comprehensive stroke center for endovascular thrombectomy. However, patients with intracranial hemorrhage (ICH) may also benefit from direct transportation to a comprehensive stroke center for neurosurgical treatment. We aimed to assess if the RACE score can distinguish patients with ICH in addition to aLVO stroke from other patients with suspected stroke.

METHODS: We analyzed data from the LPSS (Leiden Prehospital Stroke Study), a multicenter, prospective, observational cohort study in 2 Dutch ambulance regions. Ambulance paramedics documented prehospital observations in all patients aged ≥18 years with suspected stroke. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of a positive RACE score (≥5 points) for a diagnosis of ICH or aLVO stroke, compared with patients with non-aLVO stroke, transient ischemic attack, or stroke mimic. In addition, we performed a multivariable logistic regression analysis and calculated adjusted odds ratios (ORs).

RESULTS: We included 2004 patients with a stroke code, of whom 149 had an ICH, 153 had an aLVO stroke, 687 had a non-aLVO stroke, 262 had a transient ischemic attack, and 753 had a stroke mimic. Patients with ICH and aLVO stroke more often had a positive RACE score than other patients with suspected stroke (46.2% and 58.0%, respectively, versus 6.4%; $P<0.01$). A positive RACE score had a sensitivity of 52.7%, a specificity of 93.6%, a positive predictive value of 55.4%, and a negative predictive value of 92.9% for a diagnosis of ICH or aLVO stroke. In multivariable analysis, a positive RACE score had the strongest association with ICH or aLVO stroke (adjusted OR, 10.11 [95% CI, 6.84–14.93]).

CONCLUSIONS: Our study shows that the RACE score can also identify patients with ICH in addition to aLVO stroke. This emphasizes the potential of the RACE score for improving prehospital triage and allocation of patients with stroke.

Key Words: endovascular thrombectomy ■ hemorrhagic stroke ■ intracerebral hemorrhage ■ intracranial hemorrhage ■ large-vessel occlusion ■ prehospital triage ■ stroke

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Stroke is a leading cause of death and disability worldwide.[1] Most of these are ischemic, and immediate treatment options, including intravenous thrombolysis and endovascular thrombectomy (EVT), are highly time sensitive.[2–4] Intravenous thrombolysis can be administered in all stroke centers, but is less effective in patients with an underlying anterior circulation large-vessel occlusion (aLVO).[5] In contrast, EVT is effective in these patients, but is restricted to comprehensive stroke centers (CSCs). Patients with aLVO who first present in a primary stroke center (PSC) therefore require subsequent transfer to a CSC, resulting in treatment delays and worse clinical outcomes.[6–8]

Treatment options for hemorrhagic stroke have been limited to date. However, it is becoming increasingly clear that fast initiation of treatment, including blood pressure management and reversal of coagulopathy, also improves outcomes in these patients.[9,10] Although the exact role of surgery is still unclear, a recent meta-analysis showed that it is more effective when performed shorter after onset.[11] Moreover, new techniques, such as minimally invasive surgery, are promising and demonstrated better results when performed earlier.[11–15] Similarly, timely neurosurgical interventions may be necessary in other types of intracranial hemorrhage (ICH) as well, including subarachnoid or traumatic hemorrhages.[9,10]

These neurosurgical interventions are also restricted to CSCs, which stresses the importance of prehospital recognition of patients with ICH alongside aLVO stroke for direct transportation to a CSC. Previous studies have shown that certain demographic characteristics and clinical observations (eg, advanced age, use of oral anticoagulation, decreased consciousness, vomiting, and elevated blood pressure) are associated with ICH.[16–22] However, sample sizes of these studies were generally small, and they often assessed only a few features. Furthermore, other studies demonstrated that it is difficult to specifically identify patients with ICH based solely on clinical assessment, and that current triage scores are insufficient.[22–26] Concerning the triage of patients with aLVO, studies comparing several clinical scales demonstrated that the Rapid Arterial oCclusion Evaluation (RACE) score performs relatively well.[27–29] However, it is yet unclear if the RACE score can also be used for recognition of patients with ICH. Therefore, we aim to (1) assess the utility of the RACE score for prehospital identification of patients with ICH in addition to aLVO stroke and (2) compare the RACE with other demographic characteristics and clinical observations that have been shown to distinguish patients with ICH or aLVO stroke from patients with non-aLVO ischemic stroke, transient ischemic attack, or stroke mimic.

Nonstandard Abbreviations and Acronyms

aLVO	anterior circulation large-vessel occlusion
CSC	comprehensive stroke center
EVT	endovascular thrombectomy
ICH	intracranial hemorrhage
LPSS	Leiden Prehospital Stroke Study
PSC	primary stroke center
RACE	Rapid Arterial oCclusion Evaluation

CLINICAL PERSPECTIVE

What Is New?

- With ongoing studies investigating promising new treatment options for intracranial hemorrhage, recognition of these patients by paramedics in the prehospital setting is of increasing importance to aid in their allocation and subsequently expedite their treatment, similar to patients with an anterior circulation large-vessel occlusion ischemic stroke eligible for endovascular thrombectomy.
- This study shows that the Rapid Arterial oCclusion Evaluation scale can also identify patients with intracranial hemorrhage in addition to patients with anterior circulation large-vessel occlusion ischemic stroke, and that an increase of ≥2 points in Rapid Arterial oCclusion Evaluation score has the strongest association with presence of intracranial hemorrhage or anterior circulation large-vessel occlusion compared with other demographic and clinical characteristics that have previously been demonstrated to be associated with such strokes.

What Are the Clinical Implications?

- This further emphasizes the importance of implementation of the Rapid Arterial oCclusion Evaluation for improving prehospital triage and subsequently expediting treatment and improving outcomes for patients with intracranial hemorrhage as well as for patients with anterior circulation large-vessel occlusion stroke.

METHODS

Study Population and Data Collection

We used data from the LPSS (Leiden Prehospital Stroke Study), a large prospective, multicenter, observational cohort study in 2 emergency medical services (EMS) regions in the Netherlands. These regions encompass 4 PSCs and 3 CSCs, serving ≈2 million inhabitants.[27] The study included all patients aged ≥18 years for whom an EMS-initiated acute stroke code was activated between July 2018 and October 2019. EMS paramedics were registered nurses with specialized training in ambulance care, who activated a stroke code based on a positive face–arm–speech time test or other (focal) neurologic symptoms at the discretion of the individual paramedics. Policy was to transport patients to the nearest hospital (PSC or CSC) if onset was <6 hours before presentation, and to the nearest CSC if onset was between 6 and 24 hours. Paramedics routinely documented patient characteristics and clinical observations in electronic transport records, including blood pressure, glucose level, assessment of consciousness with the alert/verbal/pain/unresponsive score and Glasgow Coma Scale, pupillary assessment, and presence of nausea/vomiting. For the LPSS, for each patient, paramedics filled in an additional web-based application containing 10 to 13 structured clinical items derived from the National Institutes of Health Stroke Scale either on site or during transportation.[30] This enabled the prehospital reconstruction of several aLVO scales, including the RACE. The RACE encompasses 6 clinical observations (facial palsy, arm and leg motor deficits, gaze deviation, and either agnosia or aphasia), resulting in a score of 0 to 9 points. A RACE score of ≥5 points was considered positive.[29] Corresponding electronic patient records from the hospitals were used to extract medical history, medication use, admission National Institutes of Health Stroke Scale score, data on neuroimaging, including location of ICH and aLVO, final diagnosis after 3 months, and functional outcome after 3 months using the modified Rankin Scale.[31] ICHs were categorized on the basis of the underlying cause and location as either primary hemorrhages, including deep, lobar, or posterior fossa intraparenchymal hemorrhages, subarachnoid hemorrhages, or intraventricular hemorrhages; or as secondary traumatic hemorrhages. aLVO was defined as an occlusion of the internal carotid artery, M1 or M2 part of the middle cerebral artery, or A1 or A2 part of the anterior cerebral artery. Patients with missing transport records, unused web-based applications, or missing hospital records were excluded. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting this observational study (Table S1).[32] In compliance with Dutch law, individual patient data cannot be made available since participants were not informed during the opt-out procedure about the public sharing of their data in de-identified form. Syntax and output files of the statistical analyses can be made available from the corresponding author upon reasonable request.

Statistical Analysis

Patients were categorized into 3 groups based on their final diagnosis: (1) ICH; (2) aLVO stroke; or (3) other (non-aLVO stroke, transient ischemic attack, or stroke mimic). Independent *t*-tests and χ^2 tests were used to compare baseline characteristics between the 3 groups. For our first aim, we calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value of a positive RACE score for a diagnosis of ICH or aLVO stroke. To explore how use of the RACE for direct transportation to a CSC might influence patient allocation, we provided a hypothetical example in our cohort. In this example, patients with a positive RACE score who first presented to a PSC were redirected to a CSC, and we evaluated the change in patient flow for the different groups (ICH, aLVO stroke, or other). For our second aim, we conducted multivariable logistic regression analyses to investigate associations of other demographic characteristics and prehospital EMS observations with a diagnosis of ICH or aLVO stroke, and to compare these with the RACE score. These characteristics and observations were selected on the basis of previous literature, and included age, sex, history of atrial fibrillation, use of oral anticoagulation, mean arterial blood pressure, glucose level, consciousness, as measured with the alert/verbal/pain/unresponsive score and Glasgow Coma Scale, pupillary assessment, and presence of nausea/vomiting.[16–22,33] We calculated adjusted odds ratios (ORs) with 95% CIs to determine associations with a final diagnosis of ICH or aLVO stroke, with the RACE score as (1) a dichotomized variable (positive ≥5 points or negative <5 points) and (2) a categorical variable, ranging from 0 to 9 points. A 2-sided $P \leq 0.05$ was considered statistically significant.

Missing Data

For patients in whom ≥1 items of the RACE were untestable or missing, we assessed if the cutoff of ≥5 was already reached with the points scored in documented items (positive), or if the score would still be <5 even when assigning maximal scores to missing items (negative). Patients in whom it could not be determined if the RACE was positive or negative were excluded from analysis of sensitivity, specificity, PPV, and negative predictive value of the RACE, and

from the hypothetical example in our cohort. In case a history of atrial fibrillation or use of oral anticoagulation was not documented by EMS personnel, this was extracted from hospital records. For multivariable analyses, missing data, including RACE scores, were filled using multiple imputation by chained equations with 5 imputations.[34] Variables used during multiple imputation by chained equations constituted all variables used in the multivariable analyses and the final diagnosis. We used Rubin's rules to pool outcomes of the multivariable analyses from the 5 imputations.

Outcomes

Primary outcomes were the sensitivity, specificity, PPV, and negative predictive value of the RACE score for ICH or aLVO stroke. Secondary outcome was the adjusted OR of the RACE compared with other characteristics and observations in multivariable analysis.

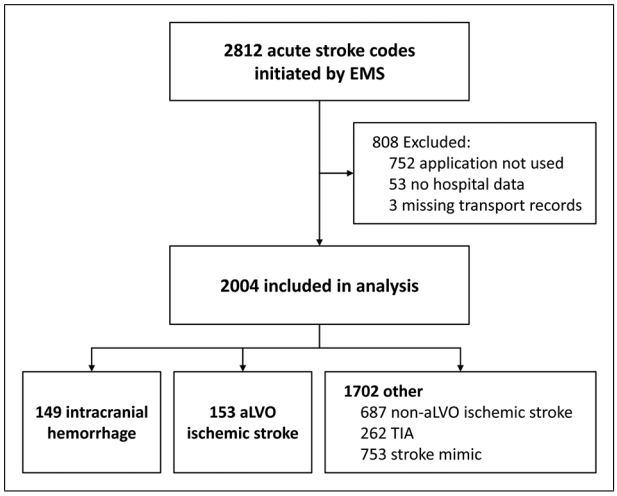

FIGURE 1. Flowchart of included patients. aLVO indicates anterior circulation large-vessel occlusion; EMS, emergency medical services; and TIA, transient ischemic attack.

RESULTS

Of 2812 acute stroke codes activated, 808 (28.7%) were excluded because no web-based application was used by EMS (n=752), or hospital records (n=53) or transport records (n=3) were missing. In a previous analysis, patients in whom the application was not used had similar baseline characteristics, incidence of aLVO, and stroke severity, but slightly more often had an ICH (12.0% versus 7.4%) or stroke mimic (44.6% versus 37.5%) compared with included patients.[27]

Of the 2004 included patients with a stroke code, 149 (7.4%) had an ICH, 153 (7.6%) had an aLVO stroke, and 1702 (84.9%) had other diagnoses (687 had a non-aLVO stroke, 262 had a transient ischemic attack, and 753 had a stroke mimic) (Figure 1). In total, 780 (38.9%) first presented to a PSC and 1224 (61.1%) first presented to a CSC. Of the 149 patients with ICH, 130 (87.2%) had a primary hemorrhage, of which 116 were intraparenchymal, 13 were subarachnoid, and 1 was intraventricular, and 19 had a secondary traumatic hemorrhage. Thirty-eight (25.5%) presented to a PSC and 111 (74.5%) presented to a CSC. Of the 153 patients with an aLVO stroke, 31 (20.3%) were first transported to a PSC, and 98 (64.1%) underwent EVT. Of these EVT-treated patients, 25 initially presented to a PSC and subsequently transferred to a CSC (Table 1).

Atrial fibrillation was more common in patients with ICH (21.8%) and aLVO stroke (18.8%) compared with other patients (12.6%; $P<0.01$ and $P=0.03$, respectively). Furthermore, patients with ICH more often had a history of previous intracranial hemorrhage (9.5% versus 1.3% and 3.9%, respectively; both $P<0.01$) and used oral anticoagulation (27.6% versus 14.6% and 16.4%, respectively; both $P<0.01$) than patients with aLVO stroke or other diagnoses (Tables 1 and S2). Concerning EMS observations, patients with ICH had higher blood pressure (median, 178/98 versus 155/90 and 159/90 mmHg, respectively; both $P<0.01$), and more often had an abnormal pupillary assessment (8.1% versus 3.9% and 1.6%, respectively; $P=0.13$ and <0.01) and nausea/vomiting (65.0% versus 41.2% and 52.3%, respectively; $P=0.03$ and 0.06) than patients with aLVO stroke or other diagnoses. Also, patients with ICH and, to a lesser extent, aLVO stroke more often had decreased consciousness, scoring a verbal/pain/unresponsive on the alert/verbal/pain/unresponsive score (38.3% versus 23.5% versus 11.2%; $P<0.01$ for all differences) and fewer points on the Glasgow Coma Scale (<15 points: 43.9% and 32.0% versus 18.8%; both $P<0.01$) than patients with other diagnoses (Tables 1 and S2). Statistical analysis of differences between the 3 groups can be found in Table S2, and further specification of characteristics of patients with non-aLVO stroke, transient ischemic attack, or stroke mimic can be found in Table S3.

It was possible to determine a positive or negative RACE score in 1565 (78.1%) patients. Patients with ICH or aLVO stroke more often had a positive RACE score than patients with other diagnoses (46.2% and 58.0% versus 6.4%; both $P<0.01$) (Tables 1 and S2). When combining the groups of patients with ICH and aLVO stroke, a positive RACE score had a sensitivity of 52.7%, a specificity of 93.6%, a PPV of 55.4%, and a negative predictive value of 92.9% (Table 2). Hypothetically, if the RACE would have been applied to our cohort, 9 of the 38 patients with ICH and 17 of the 31 patients with aLVO stroke (15 treated with EVT) who first

TABLE 1. Characteristics of Patients With ICH, aLVO Stroke, or Other Diagnoses

Variable	Total (n=2004)	ICH (n=149)	aLVO stroke (n=153)	Other (n=1702)*
Demographic characteristics				
Age, mean (SD), y	71.1 (14.9)	73.7 (13.2)	72.7 (13.0)	70.7 (15.1)
Sex, male	1020/2004 (50.9)	82/149 (55.0)	90/153 (58.8)	848/1702 (49.8)
Presentation				
PSC	780/2004 (38.9)	38/149 (25.5)	31/153 (20.3)	711/1702 (41.8)
CSC	1224/2004 (61.1)	111/149 (74.5)	122/153 (79.7)	991/1702 (58.2)
Premorbid mRS score ≤2	1566/1833 (85.4)	119/149 (79.9)	123/135 (91.1)	1324/1549 (85.5)
Wake-up/unknown time of symptom onset	326/1604 (20.3)	16/102 (15.7)	46/149 (30.9)	264/1353 (19.5)
Onset-to-EMS arrival time, median (IQR), min	93 (32–276)	91 (20–332)	92 (17–305)	93 (34–273)
Onset-to-door time, median (IQR), min	119 (61–300)	118 (51–352)	115 (45–324)	119 (64–300)
Medical history and medication				
Atrial fibrillation	272/1982 (13.7)	32/147 (21.8)	28/149 (18.8)	212/1686 (12.6)
ICH	83/1995 (4.2)	14/147 (9.5)	2/148 (1.3)	67/1698 (3.9)
Ischemic stroke or TIA	670/1984 (33.8)	36/146 (24.7)	32/150 (21.3)	602/1688 (35.7)
Diabetes	420/1983 (21.2)	23/147 (15.6)	36/150 (24.0)	361/1686 (21.4)
Epilepsy	106/2004 (5.3)	4/149 (2.7)	4/153 (2.6)	98/1702 (5.8)
Use of oral anticoagulation	336/1964 (17.1)	40/145 (27.6)	22/151 (14.6)	274/1668 (16.4)
Use of antiplatelet medication	689/1974 (34.9)	42/145 (29.0)	49/151 (32.5)	598/1678 (35.6)
EMS observations				
Blood pressure, median (IQR), mm Hg				
Systolic	160 (141–182)	178 (155–197)	155 (138–178)	159 (141–181)
Diastolic	90 (80–102)	98 (86–110)	90 (80–101)	90 (80–101)
Glucose level, median (IQR), mmol/L	6.5 (5.5–7.8)	6.9 (5.7–8.4)	6.6 (5.5–8.0)	6.4 (5.5–7.8)
Abnormal AVPU score (verbal/pain/unresponsive)	283/2004 (14.1)	57/149 (38.3)	36/153 (23.5)	190/1702 (11.2)
Abnormal Glasgow Coma Scale score (<15 points)	433/1995 (21.7)	65/148 (43.9)	49/153 (32.0)	319/1694 (18.8)
Eyes: not open spontaneously (<4)	169 (8.5)	42 (28.4)	21 (13.7)	106 (6.3)
Motor: does not execute commands (<6)	192 (9.6)	44 (29.7)	30 (19.6)	118 (7.0)
Verbal: not oriented (<5)	394 (19.7)	59 (39.9)	48 (31.4)	287 (16.9)
Abnormal pupillary assessment (anisocoria or not reactive to light)	46/2004 (2.3)	12/149 (8.1)	6/153 (3.9)	28/1702 (1.6)
Nausea/vomiting	370/700 (52.9)	39/60 (65.0)	14/34 (41.2)	317/606 (52.3)
RACE score positive (≥5 points)	195/1565 (12.5)	43/93 (46.2)	65/112 (58.0)	87/1360 (6.4)
In-hospital NIHSS score, median (IQR)	2 (0–5)	11 (4–18)	11 (5–17)	1 (0–4)
Imaging findings, treatment, and outcome				
Primary ICH		130 (87.2)		
Intraparenchymal		116 (77.9)		
Deep		65 (43.6)		
Lobar		42 (28.2)		
Posterior fossa (brainstem/cerebellum)		9 (6.0)		
Subarachnoid		13 (8.7)		
Intraventricular		1 (0.7)		
Traumatic ICH		19 (12.8)		
Isolated subdural hematoma		13 (8.7)		
Combined†		6 (4.0)		
Large-vessel occlusion	173 (8.6)		153	20
Anterior circulation	153 (7.6)		153	
Internal carotid artery			16 (10.5)	
Middle cerebral artery M1			75 (49.0)	
Middle cerebral artery M2			58 (37.9)	
Anterior cerebral artery			4 (2.6)	

(*Continued*)

TABLE 1. (Continued)

Variable	Total (n=2004)	ICH (n=149)	aLVO stroke (n=153)	Other (n=1702)*
Posterior circulation	19 (0.9)			19 (95.0)
Multiple occlusions‡	1 (0.1)			1 (0.5)
IVT	314 (15.7)		63/153 (41.2)	251/1702 (14.7)
EVT	98 (4.9)		98/153 (64.1)	
Transfer from PSC to CSC for EVT			25/98 (25.5)	
mRS score ≤2 after 3 mo	470/787 (59.7)	27/103 (26.2)	45/112 (40.2)	398/572 (69.6)

Data are given as number/total (percentage), number (percentage), or number unless otherwise specified. aLVO indicates anterior circulation large-vessel occlusion; AVPU, alert/verbal/pain/unresponsive; CSC, comprehensive stroke center; EMS, emergency medical services; EVT, endovascular thrombectomy; ICH, intracranial hemorrhage; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PSC, primary stroke center; RACE, Rapid Arterial oCclusion Evaluation; and TIA, transient ischemic attack.

*Other diagnoses include non-aLVO stroke, TIA, and stroke mimic.

†Combined: hemorrhage on multiple locations (eg, epidural, subdural, subarachnoid, and/or intraparenchymal).

‡One patient had multiple occlusions in the anterior as well as posterior circulation.

TABLE 2. Sensitivity, Specificity, PPV, and NPV of a Positive RACE Score (≥5 Points) for a Diagnosis of ICH or aLVO Stroke

Variable	Sensitivity, %	Specificity, %	PPV, %	NPV, %
ICH vs all other diagnoses (aLVO stroke, non-aLVO stroke, TIA, and stroke mimic)	46.2	89.7	22.1	96.4
ICH vs non-aLVO stroke, TIA, and stroke mimic (without aLVO stroke)	46.2	93.6	33.1	96.2
aLVO stroke vs all other diagnoses (ICH, non-aLVO stroke, TIA, and stroke mimic)	58.0	91.1	33.3	96.6
aLVO stroke vs non-aLVO stroke, TIA, and stroke mimic (without ICH)	58.0	93.6	42.8	96.4
ICH and aLVO stroke vs non-aLVO stroke, TIA, and stroke mimic	52.7	93.6	55.4	92.9

aLVO indicates anterior circulation large-vessel occlusion; ICH, intracranial hemorrhage; NPV, negative predictive value; PPV, positive predictive value; RACE, Rapid Arterial oCclusion Evaluation; and TIA, transient ischemic attack.

presented to a PSC had a positive RACE score and would have benefited from direct allocation to a CSC. Thirty-nine patients with other diagnoses had a positive RACE score and would have unnecessarily bypassed a closer PSC for transport to a CSC, including 18 patients with non-aLVO stroke who received intravenous thrombolysis.

In multivariable analyses, male sex, higher mean arterial pressure, and higher RACE scores were significantly associated with ICH or aLVO stroke (Table 3 and Figure S1). A positive RACE score had the strongest association with ICH or aLVO stroke (adjusted OR, 10.11 [95% CI, 6.84–14.93]) (Table 3).

DISCUSSION

Our findings show that a positive RACE score is associated with both ICH and aLVO stroke, whereas the predictive value of other demographic characteristics and EMS observations is limited. The promising future treatment options for ICH and increasing use of EVT emphasize the growing need for adequate identification of patients with stroke who require direct transportation to a CSC.[11–14,35,36] This study demonstrates the potential of the RACE for optimizing prehospital triage and subsequently minimizing treatment delays and improving outcomes for patients with ICH in addition to aLVO stroke.

Although outcomes of patients with ischemic stroke have significantly improved because of the impact of reperfusion therapies, treatment options for hemorrhagic stroke have remained limited and prognosis has not clearly changed over the past 20 years.[37] However, results of recent studies investigating minimally invasive surgery in the immediate phase are encouraging, and multiple trials are ongoing (NCT02880878; NCT03608423; NCT03342664; NCT02654015).[11–14] This stresses the importance of prehospital identification of patients with ICH alongside patients with aLVO stroke. Previous studies that aimed to distinguish patients with ICH from patients with other diagnoses based on clinical findings have been disappointing.[22–26] However, our study suggests that the RACE score could help identify these patients. Its sensitivity was lower for ICH than for aLVO stroke (46% versus 58%), which may be caused by patients with smaller hemorrhages and concomitantly fewer deficits having a false-negative RACE score. Furthermore, the limited prevalence of ICH and aLVO strokes in our cohort may well explain the relatively low PPV (55%). Although its diagnostic accuracy is not optimal, the added value for identification of patients with ICH is a beneficial effect of the RACE, which is cheap and can be easily implemented. New triage modalities, such as costly

TABLE 3. Multivariable Regression Analysis for Diagnosis of ICH or aLVO Stroke Versus Other Diagnoses

Variable	aOR for ICH or aLVO stroke (95% CI)*	*P* value
Multivariable Analysis With Dichotomized RACE Score		
Age, per year increase	1.00 (0.99–1.01)	0.72
Male sex	1.75 (1.30–2.35)	<0.01
History of atrial fibrillation	1.49 (0.92–2.41)	0.10
Use of oral anticoagulation	1.02 (0.64–1.63)	0.93
Mean arterial pressure, per 10 mm Hg increase	1.14 (1.07–1.22)	<0.01
Glucose level, per 1 mmol/L increase†	1.04 (0.99–1.10)	0.16
Abnormal AVPU score (verbal/pain/unresponsive)	0.98 (0.56–1.71)	0.94
Glasgow Coma Scale score, per point decrease from 15	1.02 (0.93–1.12)	0.73
Abnormal pupillary assessment	1.83 (0.87–3.85)	0.11
Nausea/vomiting	1.14 (0.67–1.94)	0.64
Positive RACE score (≥5 points)	10.11 (6.84–14.93)	<0.01
Multivariable Analysis With Categorical RACE Score		
Age, per year increase	1.00 (0.99–1.01	0.90
Male sex	1.86 (1.37–2.54)	<0.01
History of atrial fibrillation	1.49 (0.90–2.48)	0.12
Use of oral anticoagulation	1.04 (0.63–1.71)	0.89
Mean arterial pressure, per 10 mm Hg increase	1.15 (1.08–1.23)	<0.01
Glucose level, per 1 mmol/L increase†	1.03 (0.98–1.09)	0.22
Abnormal AVPU score (verbal/pain/unresponsive)	0.81 (0.47–1.39)	0.44
Glasgow Coma Scale score, per point decrease from 15	0.97 (0.89–1.06)	0.53
Abnormal pupillary assessment	1.79 (0.82–3.89)	0.14
Nausea/vomiting	1.26 (0.70–2.26)	0.47
RACE score‡		
1	1.51 (0.85–2.67)	0.16
2	2.56 (1.44–4.57)	<0.01
3	2.65 (1.10–6.35)	0.04
4	7.92 (4.08–15.39)	<0.01
5	9.83 (4.98–19.42)	<0.01
6	14.80 (6.96–31.47)	<0.01
7	34.88 (17.15–70.92)	<0.01
8	43.60 (21.29–89.29)	<0.01
9	40.74 (16.30–101.84)	<0.01

aLVO indicates anterior circulation large-vessel occlusion; aOR, adjusted odds ratio; AVPU, alert/verbal/pain/unresponsive; ICH, intracranial hemorrhage; and RACE, Rapid Arterial oCclusion Evaluation.

*Intercept of multivariable analysis with dichotomized RACE score: 0.008 (95% CI, 0.002–0.027); intercept multivariable analysis with categorical RACE score: 0.004 (95% CI, 0.001–0.014).

†Serum glucose SI conversion: 1 mmol/L = 18.02 mg/dL.

‡Compared with a RACE score of 0.

mobile stroke units, should be compared with this background.

In our cohort, use of the RACE would have hypothetically implicated that 18 patients with non-aLVO stroke treated with intravenous thrombolysis bypassed a closer PSC, whereas 15 EVT-treated patients with aLVO stroke and 9 patients with ICH would have been directly allocated to a CSC. Set aside the possible benefit for patients with ICH, this may well have led to improved outcomes because the additional time required for an interhospital transfer is generally much higher than the additional transport time to a CSC.[7,8,38,39] This hypothetical example was slightly hampered because a positive or negative RACE score could not be determined in ≈21% of patients. In addition, in our study in a densely populated urban region, the proportions of CSCs (3 versus 4) and of patients primarily presenting to a CSC (61%) were high compared with studies in, for example, the United States, in which up to 90% of stroke centers are PSCs and up to 80% of patients with stroke primarily present to a PSC.[40] Consequently, the example in our cohort may well underestimate the impact of implementation of the RACE for other regions.

In multivariable analysis, most other variables were not significantly associated with ICH or aLVO

stroke and may be of limited use for triage in clinical practice. This is in line with previous studies that reported poor results of scoring systems that tried to identify patients with ICH based on demographic characteristics and clinical observations, which often also included atrial fibrillation, level of consciousness, and nausea/vomiting.[22–26] Surprisingly, a decreased consciousness (verbal/pain/unresponsive on the alert/verbal/pain/unresponsive score or decrease in points on the Glasgow Coma Scale) was not associated with ICH or aLVO stroke in multivariable analysis, whereas this was more common in these patients. However, we found that this was because of its strong correlation with the RACE score, which overshadowed and inversed the effect of a decreased consciousness.

Strengths of this study include the large sample size, number of characteristics assessed, and prospective collection of data. Because of this, the overall amount of missing data was limited, and extensive evaluation of characteristics was possible. Furthermore, the study design was pragmatic, including all patients with a stroke code, using clinical observations from paramedics on-site, and analyzing the whole group of patients with ICH and aLVO stroke, which represents all patients who require direct transportation to a CSC. This makes results well generalizable and useful for routine practice.

However, our study has some limitations. First, some patients were excluded because the application was not used or hospital or transport records were missing. Those excluded had a slightly higher incidence of ICH, which may have underestimated the PPV and the hypothetical implications of use of the RACE score in our cohort. Second, it was not possible to reconstruct the RACE score in ≈20% of patients because of ≥1 missing observations of its 6 clinical items. This may also have reduced the implications of the RACE in our hypothetical example, and we used multiple imputation by chained equations for completing data for the multivariable analyses. Third, a possible history of atrial fibrillation was not routinely documented in EMS transport records and, therefore, extracted from hospital records. In practice, it may be difficult to obtain this information in an emergency setting, although information on use of anticoagulation is generally well known by EMS. Fourth, data on neuroimaging, including the presence, location, and size of ICH and occlusions, were also collected from hospital records and not reviewed by an independent core laboratory. Last, although we focused on patients with ICH and aLVO stroke, other patients may also benefit from direct transportation to a CSC, such as patients with a posterior circulation occlusion.[41] However, this was beyond the scope of the current study.

CONCLUSIONS

Our study shows that a positive RACE score is strongly associated with both ICH and aLVO stroke, whereas other demographic characteristics and prehospital observations have limited value for distinguishing these patients. This highlights the potential of the RACE for optimizing prehospital triage and subsequent allocation of patients with stroke, and emphasizes the importance of its implementation in routine practice.

ARTICLE INFORMATION

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Author Contributions

I.v.d.W. and N.K. conceptualized the study. L.D. and D.D. acquired data. E.v.Z. consulted in statistical analyses, and L.D., V.G., J.H., and E.v.Z. performed analyses. L.D. had full access to all the data in the study and takes responsibility for their integrity and the data analysis. L.D. drafted the manuscript. All authors critically revised the manuscript and approved the final version.

Ethics Statement

The institutional review boards of the Leiden University Medical Center and of the participating hospitals approved the original LPSS (Leiden Prehospital Stroke Study). The need for obtaining informed consent was waived because the extent of effort required by the large number of health care providers was disproportionate compared with the relatively limited sensitivity of the collected data and intrusion to the personal privacy. The original study was registered with ClinicalTrials.gov (identifier: NCT04442659).

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Supplemental Materials

supplementary information

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