Journal of the American Heart Association

ORIGINAL RESEARCH

CLEAR Thrombectomy Score: An Index to Estimate the Probability of Good Functional Outcome With or Without Endovascular Treatment in the Late Window for Anterior Circulation Occlusion

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BACKGROUND: With the expanding eligibility for endovascular therapy (EVT) of patients presenting in the late window (6–24 hours after last known well), we aimed to derive a score to predict favorable outcomes associated with EVT versus best medical management.

METHODS AND RESULTS: A multinational observational cohort of patients from the CLEAR (Computed Tomography for Late Endovascular Reperfusion) study with proximal intracranial occlusion (2014–2022) was queried (n=58 sites). Logistic regression analyses were used to derive a 9-point score for predicting good functional outcome (modified Rankin Scale score 0–2 or return to premorbid modified Rankin Scale score) at 90 days, with sensitivity analyses for prespecified subgroups conducted using bootstrapped random forest regressions. Secondary outcomes included 90-day functional independence (modified Rankin Scale score 0–2), poor outcome (modified Rankin Scale score 5–6), and 90-day survival. The score was externally validated with a single-center cohort (2014–2023). Of the 3231 included patients (n=2499 EVT), a 9-point score included age, early computed tomography ischemic changes, and stroke severity, with higher points indicating a higher probability of

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This article was sent to Neel S. Singhal, MD, PhD, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Preprint posted on Research Gate February 5, 2024. https://doi.org/10.2139/ssrn.4711611.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.124.034948

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

a good functional outcome. The areas under the curve for the primary outcome among EVT and best medical management subgroups were 0.72 (95% CI, 0.70–0.74) and 0.87 (95% CI, 0.84–0.90), respectively, with similar performance in the external validation cohort (area under the curve, 0.71 [95% CI, 0.66–0.76]). There was a significant interaction between the score and EVT for good functional outcome, functional independence, and poor outcome (all $P_{interaction}$<0.001), with greater benefit favoring patients with lower and midrange scores.

CONCLUSIONS: This score is a pragmatic tool that can estimate the probability of a good outcome with EVT in the late window.

REGISTRATION: URL: https://www.Clinicaltrials.gov; Unique identifier: NCT04096248.

Key Words: acute stroke ■ endovascular therapy ■ late window ■ prognosis ■ score ■ thrombectomy

CLINICAL PERSPECTIVE

What Is New?

- With as many as half of patients undergoing endovascular therapy for large vessel occlusion stroke outside of guideline recommendations, the prognosis for a good functional outcome is unclear.
- In the heterogeneous, multinational CLEAR (Computed Tomography for Late Endovascular Reperfusion) cohort, we developed and externally validated a simple score that can be used to prognosticate functional improvement associated with endovascular therapy in the late window.

What Are the Clinical Implications?

- The 9-point score (inclusive of age, stroke severity, and early infarct volume) is strongly associated with functional recovery.
- Lower scores—representing older patients, more severe deficits, and larger infarct volumes—were associated with poor outcomes, but a favorable outcome was more likely if endovascular therapy was pursued.

Nonstandard Abbreviations and Acronyms

ASPECTS	Alberta Stroke Program Early CT Score
BMM	best medical management
CLEAR	Computed Tomography for Late Endovascular Reperfusion
EVT	endovascular therapy
LKW	last known well
LVO	large vessel occlusion
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
sICH	symptomatic intracranial hemorrhage

When compared with best medical management (BMM), endovascular therapy (EVT) for acute large vessel occlusion (LVO) is associated with significant clinical benefit, with a number needed to treat to reduce long-term disability between 2 and 8 for select patients treated 6 to 24 hours after time last known well (LKW).[1] This benefit has been confirmed for a highly specific, homogeneous population of patients without preexisting disability, with proximal occlusions, and minimal evidence of ischemic injury on baseline neuroimaging.[2] However, growing evidence from secondary analyses of randomized clinical trials and observational cohorts shows that patients with moderate preexisting disability,[3–5] distal occlusions,[6–13] and larger regions of early infarction[14–20] may also benefit from reperfusion treatment. By contrast, patients with milder presenting deficits[21] and those with completed infarctions on baseline neuroimaging in the late window[22] may not achieve better functional outcomes with EVT over BMM. One limitation of these studies is the homogeneity of clinical and imaging features among patients included in clinical trials, which precludes a more granular analysis of EVT treatment effect among "trial-ineligible" patients.[23]

In the absence of randomized clinical trial data that would establish the efficacy of EVT in complex clinical scenarios, and given the high proportion of patients treated beyond current guideline criteria,[24–26] a more precise estimate of favorable outcomes with EVT for late window patients with LVO is needed. We modeled outcomes associated with EVT versus BMM across a large, heterogeneous cohort to predict a favorable response to treatment using a pragmatic numerical scale. We also sought to determine at which thresholds EVT may not be associated with better outcomes (or higher risk) than BMM.

METHODS

Deidentified data from this investigation may be made available upon reasonable request of the corresponding author. These results are presented in accordance with the Transparent Reporting of a Multivariable Prediction

Model for Individual Prognosis or Diagnosis Initiative[27] and Prediction Model Risk of Bias Assessment Tool (Table S1).[28] This study was approved by the local institutional review board of participating sites.

Patient Population

The CLEAR (Computed Tomography for Late Endovascular Reperfusion) study includes consolidated patient-level data of consecutive adult patients >18 years of age treated between January 2014 and May 2022 with and without EVT primarily presenting between 6 and 24 hours after LKW (NCT04096248).[29–31] Given the 8-year window for inclusion in CLEAR, EVT and BMM practices may have changed over time (particularly following 2018 trials[32,33]). Patients were primarily recruited for CLEAR if they underwent EVT or BMM within 6 to 24 hours of LKW; however, a minority had missing data regarding treatment times or LKW or may have been treated outside of this window (<5%).

Patients treated at any of 66 participating sites in the CLEAR study were screened for inclusion if they had complete data regarding the following required covariates for model derivation: age, sex, prestroke modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS) score, Alberta Stroke Program Early Computed Tomography Score (ASPECTS), and intracranial occlusion of the internal carotid artery or middle cerebral artery (M1 or M2) determined on noninvasive vascular imaging. Patients with a prestroke mRS score 0 to 4 were included. Due to the low proportion of patients with available perfusion imaging data (<50%), perfusion estimates were not used to build the model. Patients were excluded if 90-day mRS scores were unavailable (Figure 1).

In the external validation cohort, consecutive adult patients from the University of Pittsburgh Medical Center treated with EVT (January 2014–October 2023) who otherwise met the aforementioned criteria were included.

Statistical Analysis

The primary outcome was a "good functional outcome," defined as 90-day mRS score of 0 to 2, or return to prestroke mRS score, as described previously.[3,5,34] This outcome was selected due to inclusion of patients with preexisting disability, who would have been unlikely to improve to a mRS score of 0 to 2 by 90 days, and for whom a return to a baseline level of disability is a desirable outcome. Secondary outcomes included functional independence (90-day mRS score 0–2), symptomatic intracranial hemorrhage (sICH, defined by the European Cooperative Acute Stroke Study III as an intracranial hemorrhage associated with a deterioration in NIHSS score ≥4 points),[35] poor outcome (90-day mRS score 5–6), and mortality at 90 days. Functional independence was evaluated in patients with prestroke mRS score 0 to 2. Poor outcome was selected to suggest futility in EVT when compared with the natural history observed in these patients (BMM). Descriptive statistics were used to illustrate differences between groups in clinical, imaging, and outcome measures.

In addition to analyzing continuous data measures, patients were categorized into prespecified subgroups: prestroke mRS scores 0 to 2 and 3 to 4[5]; age ≤50 years, 51 to 75 years, and >75 years; NIHSS scores of 0 to 5, 6 to 12, 13 to 18, and >18[33]; ASPECTS of 0 to 5 and 6 to 10; and intracranial occlusion of the internal carotid artery, middle cerebral artery (M1), and branch middle cerebral artery (M2).

Prespecified covariates (eg, age, sex, occlusion location, hypertension, diabetes, atrial fibrillation, ASPECTS, NIHSS score, intravenous thrombolysis, prestroke mRS score, and EVT versus BMM) were added to a multivariable logistic regression model for the primary outcome of a good 90-day functional outcome. To yield a practical model balancing adequate performance with minimum required predictor variable input, the multivariable regression ("comprehensive model") was optimized using a forward stepwise approach with the greatest minimization of the Bayesian information criterion; appropriate variable selection was checked by repeating the forward stepwise approach with greatest minimization of corrected Akaike information criterion and assessing agreement in the covariables identified with both strategies. The whole model test characterized model significance. Integer subscores for each qualifying predictor in the model were assigned by dividing each significant covariate's adjusted odds ratio (aOR) by the smallest OR and rounding to the nearest increment of 0.5.[36]

To ensure the appropriateness of scoring transformation, random forest regressions with 2500 sample bootstrapping for internal validation were performed to illustrate comparable predictive performance across the comprehensive model (incorporating all prespecified covariates), abbreviated model (incorporating covariates identified in stepwise regression), and the CLEAR score-transformed model.[37] A multiplicative interaction term for CLEAR score×EVT versus BMM was also calculated for the primary and secondary outcomes.

For sensitivity analyses, the scored model was also tested among patients meeting ("trial-eligible") and not meeting ("trial-ineligible") adapted inclusion criteria for DAWN (Diffusion-Weighted Imaging or Computed Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention With Trevo),[32] DEFUSE-3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke),[33] or MR CLEAN-LATE

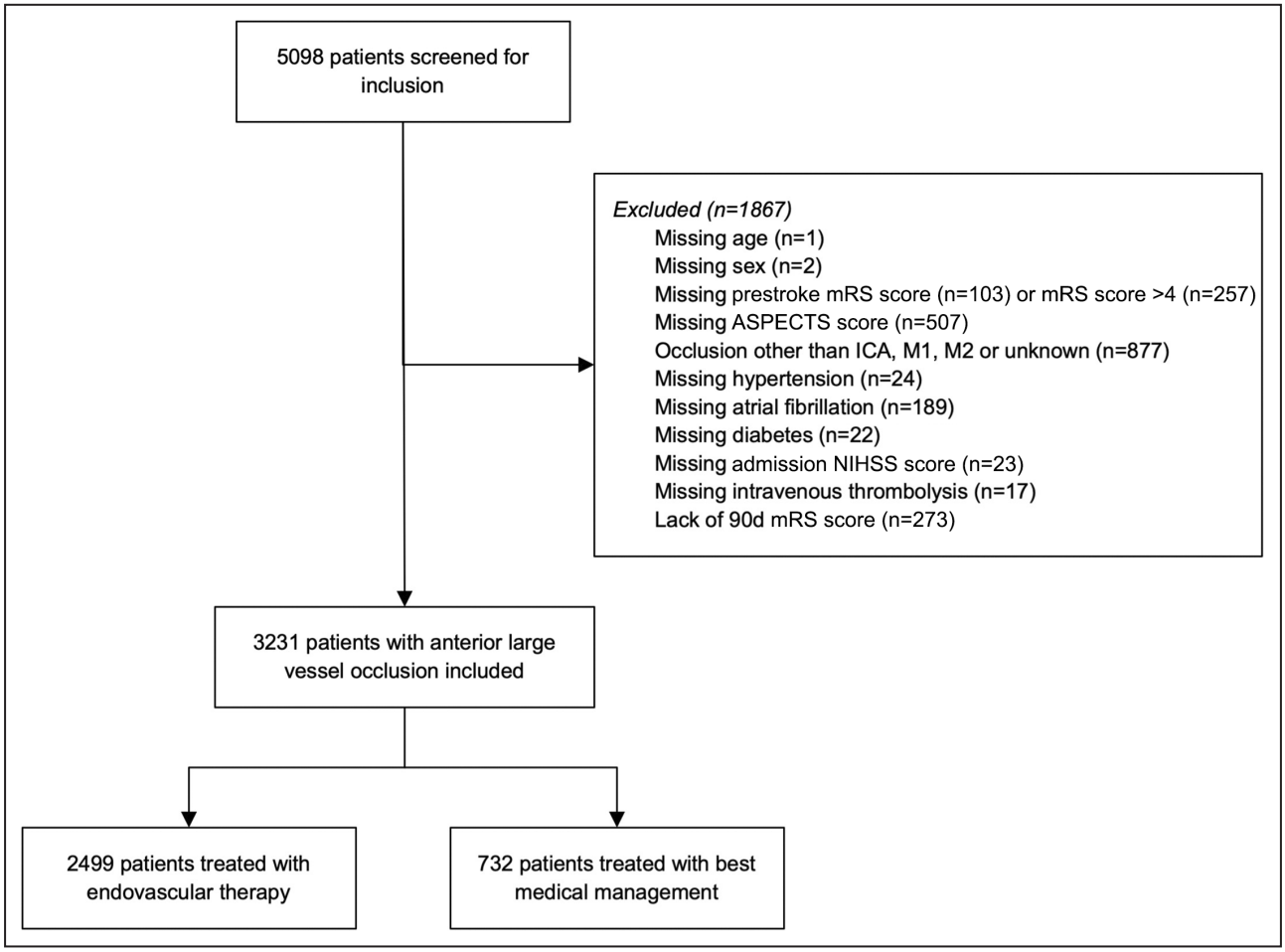

Figure 1. Patient inclusion flow chart.
ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; BMM, best medical management; ICA, internal carotid artery; M1, M1 segment of the middle cerebral artery; M2, M2 segment of the middle cerebral artery; mRS, modified Rankin score; and NIHSS, National Institutes of Health Stroke Scale

(Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands for LATE Arrivals)[38] trials (Table S2), and for patients without known time from LKW to treatment. The scored model was also tested among patient subgroups stratified by premorbid mRS and admission ASPECTS.[3-10] Models were derived for the primary outcome, and were subsequently tested against secondary outcomes. Model discrimination was characterized by the area under the curve (AUC) with 95% CIs.

There was no adjustment for multiple hypothesis testing. All tests were performed at the 2-sided level, with P values ≤0.05 considered statistically significant. Missing data were not imputed. No variables were missing for primary outcome analysis. For secondary outcomes analyses, patients with missing data in the variables of interest were excluded. Data analyses were performed using JMP Pro v. 17.0.0 (SAS Institute Inc, Cary, NC, USA) and R v. 4.2.2 with packages: "randomForest,"[39] "pROC," "dplyr," and "rms."

RESULTS

Of the 5098 patients from CLEAR, 3231 (63.4%) patients from 58 sites (8 sites did not meet inclusion criteria) were included (Figure 1). The median age was 73 years (interquartile range 62–82), NIHSS score was 16 (interquartile range 10–20) and 2499 (77.3%) were treated with EVT (Table 1). A good functional outcome was achieved in 1237 (38.3%) patients, with 174 (5.5%) experiencing sICH, and 2479 (76.7%) patients surviving at 90 days (Table 1). Of participants in this cohort, 1690 (52.3%) would have been eligible for the DAWN, DEFUSE-3, or MR CLEAN-LATE trials (Table 1; Table S2), with 1492/2499 (58.7%) patients undergoing EVT meeting trial criteria.

CLEAR Score Derivation

A combined multivariable logistic regression model for good functional outcome was derived using prespecified inputted variables (eg, age, sex, occlusion location, hypertension, diabetes, atrial fibrillation, ASPECTS, admission NIHSS score, intravenous thrombolysis, prestroke mRS score, and EVT versus BMM; "Comprehensive Model" in Table S3). A stepwise regression analysis yielded an abbreviated multivariable model with age, ASPECTS, admission NIHSS score, and EVT versus BMM treatment approach ("Abbreviated Model" in Table S2). Lower age, higher ASPECTS, lower NIHSS score, and EVT were independently associated with greater likelihood of good functional outcome in all models (Table S3). The aORs from the stepwise abbreviated model yielded the 9-point CLEAR score composed of age (2 points: ≤50, 1 point 51–75, 0 points >75), ASPECTS (1 point: 6–10, 0 points 0–5), and admission NIHSS score (5 points: 0–5, 3 points: 6–12, 1 point: 13–18, 0 points: >18), with higher scores indicating higher probability of a good functional outcome (Table 2).

Regression Performance and Sensitivity Analyses

For 90-day good functional outcome, the CLEAR score fitted for the EVT and BMM subgroups yielded AUCs of 0.72 (95% CI, 0.70–0.74) and 0.87 (95% CI, 0.84–0.90), respectively (Table S4). The sensitivity of the CLEAR score model in the EVT cohort was 72.1% (95% CI, 69.4%–74.8%), and specificity was 62.6% (95% CI, 60.1%–65.1%) whereas the sensitivity in the BMM cohort was 78.7% (95% CI, 72.6%–84.7%), and specificity was 80.7% (95% CI, 77.4%–84.0%). The predicted probability of a good outcome was higher for EVT than for BMM for CLEAR scores of 0 to 6, with a range of absolute benefit increase with EVT from 4.3% (score=6) to 22.2% (score=3) (Table 3). The probability of a good functional outcome was no different for EVT versus BMM with CLEAR scores of 7 or 8. Score performance for secondary outcomes (eg, functional independence, sICH, poor outcome, and mortality) and additional sensitivity analyses (eg, substratifying the cohort by trial eligibility, ASPECTS, prestroke mRS score, and LKW-to-puncture time intervals) are described in Table S4.

External Validation

Demographic data for the external validation cohort are described in Table S5. The CLEAR score was similarly predictive of a good functional outcome at 90 days in the validation cohort (n=470; AUC, 0.71 [95% CI, 0.66–0.76]). The score was also predictive of secondary end points including functional independence at 90 days (AUC, 0.72 [95% CI, 0.67–0.77]), poor outcome (AUC, 0.72 [95% CI, 0.67–0.77]), and 90-day survival (AUC, 0.73 [95% CI, 0.68–0.78]) but was not predictive of sICH (AUC, 0.51 [95% CI, 0.47–0.56], Table S6). Calibration plots showed that the observed proportion of patients achieving a good functional outcome was similar to the proportions predicted by the CLEAR score (Spiegelhalter z=−0.05, P=0.96, Figure S1). Calibration accuracy was similar for secondary outcomes: functional independence (z=−0.04, P=0.97), sICH (z=0.0, P=1.0), poor outcome (z=−0.01, P=0.99), and survival (z=0.10, P=0.92).

EVT Versus BMM

There was a significant interaction between the CLEAR score and EVT versus BMM for the primary outcome ($P_{interaction}$<0.001) indicating a difference in the odds of a good outcome with EVT when stratified by CLEAR score. The CLEAR score yielded separate predicted probability curves for this outcome across each CLEAR score, with a higher probability of better outcomes with EVT among lower and midrange CLEAR scores (Table 3; Figure 2A). For CLEAR scores of 7 or 8, both EVT-treated and BMM-treated patients had >80% likelihood of good functional outcome and functional independence (Table 3; Figure 2A and 2B).

EVT-treated patients had a higher absolute risk for sICH than BMM-treated patients for every CLEAR score, with no significant interaction between treatment and CLEAR score ($P_{interaction}$=0.64), indicating no difference in sICH with EVT according to CLEAR score (Table 3; Figure 2C). A significant interaction between EVT and BMM with the CLEAR score was also observed for poor outcome ($P_{interaction}$<0.001; Table 3; Figure 2D). However, there was no significant interaction between CLEAR score and EVT versus BMM for the outcome 90-day survival ($P_{interaction}$=0.20; Figure 2E).

DISCUSSION

We developed a pragmatic prognostic score that can predict a good outcome following EVT for anterior circulation LVO treated predominantly in the extended time window. The key elements comprising this score were distilled from universally available information (age, NIHSS score, and ASPECTS), which could permit widespread generalizability of the tool in aiding decision-making and prognostication. In spite of its simplicity, the score showed good internal and external validation. In the early window, EVT is consistently and strongly associated with clinical benefit over medical management irrespective of age, preexisting disability, and across a wide range of ASPECTS (including ASPECTS 2–5).[18] However, when combinations of poor clinical and imaging predictors were considered in prior

Table 1. Patient Characteristics

	All (n=3231)	EVT (n=2499)	BMM (n=732)
Demographics			
Age, median y (IQR)	73 (62–82)	72 (61–82)	76 (65–85)
Age category, no. (%)			
≤50 y	319 (9.9%)	253 (10.1%)	66 (9.0%)
51–75 y	1473 (45.6%)	1186 (47.5%)	287 (39.2%)
>75 y	1439 (44.5%)	1060 (42.4%)	379 (51.8%)
Female sex, no. (%)	1472 (45.6%)	1134 (45.4%)	338 (46.2%)
Hypertension, no. (%)	2230 (69.0%)	1753 (70.1%)	477 (65.2%)
Atrial fibrillation, no. (%)	1143 (35.4%)	880 (35.2%)	263 (35.9%)
Diabetes, no. (%)	715 (22.1%)	583 (23.3%)	132 (18.0%)
Stroke characteristics			
Prestroke mRS score, no. (%)			
0–2	2765 (85.6%)	2200 (88.0%)	565 (77.2%)
3–4	466 (14.4%)	299 (12.0%)	167 (22.8%)
Admission NIHSS score, median (IQR)	16 (10–20)	15 (10–20)	16 (10–21)
Admission NIHSS score category, no. (%)			
0–5	300 (9.3%)	199 (8.0%)	101 (13.8%)
6–12	838 (25.9%)	687 (27.5%)	151 (20.6%)
13–18	1027 (31.8%)	833 (33.3%)	194 (26.5%)
>18	1066 (33.0%)	780 (31.2%)	286 (39.1%)
Alberta Stroke Program Early Computed Tomography Score, no. (%)			
6–10	2798 (86.6%)	2328 (93.2%)	470 (64.2%)
0–5	433 (13.4%)	171 (6.8%)	262 (35.8%)
Occlusion location, no. (%)			
Internal carotid artery	585 (18.1%)	444 (17.8%)	141 (19.3%)
M1 segment of the middle cerebral artery	1869 (57.9%)	1498 (59.9%)	371 (50.7%)
M2 segment of the middle cerebral artery	777 (24.0%)	557 (22.3%)	220 (30.0)
Intervention and outcomes			
DAWN (Diffusion-Weighted Imaging or Computed Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention With Trevo)/DEFUSE-3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke)/MR CLEAN-LATE trial eligibility, no. (%)	1690 (52.3%)	1492 (59.7%)	198 (27.0%)
Intravenous thrombolysis, no. (%)	625 (19.3%)	565 (22.6%)	60 (8.2%)
Symptomatic intracranial hemorrhage, no. (%)	174 (5.5%), n=3179	154 (6.2%), n=2469	20 (2.8%), n=710
Good 90-day functional outcome (return to prestroke mRS score or mRS score 0–2), no. (%)	1237 (38.3%)	1059 (42.4%)	178 (24.3%)
Functional independence (90-day mRS score 0–2), no. (%)	1144 (35.4%)	987 (39.5%)	157 (21.4%)
mRS score at 90 d, no. (%)			
0	252 (7.8%)	220 (8.8%)	32 (4.4%)
1	433 (13.4%)	373 (14.9%)	60 (8.2%)
2	459 (14.2%)	394 (15.8%)	65 (8.9%)
3	497 (15.4%)	403 (16.1%)	94 (12.8%)
4	524 (16.2%)	387 (15.5%)	137 (18.7%)
5	314 (9.7%)	192 (7.7%)	122 (16.7%)
6	752 (23.3%)	530 (21.2%)	222 (30.3%)

BMM indicates best medical management; EVT, endovascular therapy; IQR, interquartile range; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

Table 2. CLEAR Score

Characteristic	Score value*
Age	
≤50 y	2
51–75 y	1
>75 y	0
Alberta Stroke Program Early Computed Tomography Score	
6–10	1
0–5	0
Admission National Institutes of Health Stroke Scale score	
0–5	5
6–12	3
13–18	1
>18	0
Total	0–8

CLEAR indicates Computed Tomography for Late Endovascular Reperfusion.

*Derived by rounding to the nearest 0.5 increment after dividing adjusted odds ratios by the smallest odds ratio value.

studies (eg, older age *and* poorer ASPECTS), there was less clear benefit or no advantage of EVT over medical management.[40] In this analysis, we found that lower CLEAR scores (corresponding to older age and poorer ASPECTS) were associated with a *higher* probability of a good functional outcome with EVT as opposed to BMM. In our experience, patients who are elderly with significant neurological deficits and extensive infarct burden (who would have a lower CLEAR score) are often *not* considered for EVT due to suspected futility. Although the natural history of stroke in these patients is poor—when compared with the natural history of stroke in younger patients with more favorable neuroimaging—the odds of a good outcome are greater with EVT than with medical management. The higher probability of a good functional outcome with EVT in patients with lower CLEAR scores may be related to the significant benefit of acute reperfusion therapy even when there is less tissue amenable to salvage, or patients may have limited functional reserve. The natural history of infarct progression without attempted reperfusion in these patients is devastating; however, even in these patients, there may be a benefit with EVT.

Conversely, better outcomes with EVT over BMM were *not* observed in patients with higher CLEAR scores (younger patients with milder symptoms). For patients with the highest CLEAR scores (7 or 8), which corresponds to younger patients, milder deficits, and more favorable ASPECTS, there is a high probability of good outcomes even without EVT. For many of these patients, EVT may not sufficiently augment cerebral perfusion and improve functional outcomes. The findings presented here would support the equipoise in randomizing these patients to EVT or BMM in ongoing clinical trials (eg, NCT04167527, NCT03796468). Although the CLEAR score may be useful to prognosticate outcomes with anterior circulation LVO, it has greater utility in identifying patients likely to benefit (or not likely to benefit) from EVT.

In this study, we also observed better outcomes across a range of prespecified subgroups, such as prestroke mRS or ASPECTS. Each of these features likely influences clinical outcomes, and some characteristics such as more distal occlusion location and history of diabetes were independently predictive of a good functional outcome in the comprehensive model. However, the abbreviated model (which excluded some covariates) performed similarly to the comprehensive model. Moreover, the CLEAR score showed similar performance for predicting a good functional outcome at 90 days with EVT irrespective of late-window trial eligibility, very low ASPECTS of 3 to 5, and moderate prestroke disability. Other clinical and imaging elements have been strongly tied to outcomes in anterior LVO, including collateral status, presence of diffusion-weighted imaging and T2 mismatch, and advanced perfusion imaging findings. Many of these imaging features are not widely used or require expensive software that may not be available at many institutions.[41-43] We have also previously shown that clinical outcomes are no different for patients selected for EVT based on perfusion imaging, magnetic resonance imaging, or computed tomography in routine clinical practice.[29,44] That said, fewer than half of the patients in this cohort underwent perfusion imaging, so these metrics were not included in the model.

This study builds on previously published prediction models in that we report outcomes in routine practice using effective, second-generation (and later) stent-retrievers and aspiration catheters, as opposed to earlier studies which reported thrombectomy outcome scores using less effective devices.[45] Our population was also treated predominantly beyond >6 hours, which prior studies excluded (Table S7). Because of differences in tissue vulnerability to infarction across treatment windows, it is unclear if this score would perform similarly for patients treated in the early time window, and if prior scores would outperform the CLEAR score in this late window cohort. Similar to the CLEAR thrombectomy score, the interactive, web-based MR PREDICTS[46] tool (http://www.mrpredicts.com/) allows for precision outcome estimation using only a few key clinical variables. However, this score was derived from a more homogeneous population from one country including a smaller proportion with preexisting disability (19% with a prestroke mRS maximum score of 2 versus 25.9% with a mRS score of 2–4 in CLEAR). Furthermore, there was no representation of patients treated beyond 6.5 hours of time last seen well (which comprised the majority of patients in CLEAR).

Table 3. Probability of Each Outcome According to Treatment Across CLEAR Scores

CLEAR* score value	Good functional outcome, probability (95% CI)			Functional independence, probability (95% CI)			sICH, probability (95% CI)			Poor outcome, probability (95% CI)			Survival, probability (95% CI)		
	EVT	BMM	ABI	EVT	BMM	ABI	EVT	BMM	ARI	EVT	BMM	ARI	EVT	BMM	ABI
0	14.5 (12.4 to 17.0)	2.1 (1.3 to 3.5)	12.4 (10.7 to 14.1)	14.3 (12.0 to 17.0)	2.1 (1.2 to 3.7)	12.2 (10.3 to 14.1)	5.8 (4.2 to 7.9)	3.0 (1.5 to 6.0)	2.8 (1.3 to 4.3)	59.0 (54.5 to 63.4)	84.0 (79.5 to 87.6)	−25.0 (−28.3 to −21.7)	52.4 (47.5 to 57.3)	41.2 (35.0 to 47.6)	11.2 (7.1 to 15.3)
1	21.1 (18.9 to 23.6)	4.5 (3.0 to 6.6)	16.6 (14.4 to 18.8)	21.0 (18.5 to 23.6)	4.4 (2.8 to 6.8)	16.6 (14.2 to 19.0)	5.9 (4.6 to 7.5)	3.0 (1.7 to 5.1)	2.9 (1.4 to 4.4)	48.1 (44.8 to 51.4)	72.2 (67.6 to 76.4)	−24.1 (−27.9 to −20.3)	63.0 (59.7 to 66.3)	54.0 (49.2 to 58.8)	9.0 (4.9 to 13.1)
2	29.7 (27.5 to 32.0)	9.2 (6.9 to 12.1)	20.5 (17.7 to 23.3)	29.6 (27.3 to 32.1)	8.9 (6.4 to 12.3)	20.7 (17.7 to 23.7)	6.1 (5.0 to 7.3)	2.9 (1.8 to 4.5)	3.2 (1.7 to 4.7)	37.3 (35.1 to 39.6)	56.3 (51.9 to 60.6)	−19.0 (−23.1 to −14.9)	72.5 (70.4 to 74.5)	66.4 (62.4 to 70.1)	6.1 (2.3 to 9.9)
3	40.0 (37.9 to 42.1)	17.8 (14.5 to 21.6)	22.2 (18.8 to 25.6)	40.1 (37.9 to 42.3)	17.3 (13.7 to 21.7)	22.8 (19.1 to 26.5)	6.2 (5.3 to 7.2)	2.8 (1.8 to 4.3)	3.4 (1.9 to 4.9)	27.7 (25.8 to 29.6)	39.0 (34.6 to 43.7)	−11.3 (−15.2 to −7.4)	80.3 (78.6 to 82.0)	76.9 (72.9 to 80.4)	3.4 (0.0 to 6.8)
4	51.2 (48.9 to 53.6)	31.7 (27.2 to 36.5)	19.5 (15.6 to 23.4)	51.5 (49.0 to 54.1)	31.0 (26.1 to 36.3)	20.5 (16.2 to 24.8)	6.4 (5.4 to 7.5)	2.7 (1.6 to 4.5)	3.7 (2.2 to 5.2)	19.7 (17.8 to 21.8)	24.1 (19.7 to 29.1)	−4.4 (−7.9 to −0.9)	86.3 (84.5 to 88.0)	84.8 (80.7 to 88.1)	1.5 (−1.4 to 4.4)
5	62.3 (59.4 to 65.2)	49.8 (43.8 to 55.9)	12.5 (8.4 to 16.6)	62.8 (59.7 to 65.9)	49.0 (42.5 to 55.5)	13.8 (9.2 to 18.4)	6.5 (5.3 to 8.0)	2.7 (1.4 to 4.9)	3.8 (2.3 to 5.3)	13.6 (11.7 to 15.8)	13.6 (10.1 to 18.2)	0 (−2.8 to 2.8)	90.7 (88.9 to 92.3)	90.4 (86.5 to 93.2)	0.3 (−2.1 to 2.7)
6	72.3 (68.8 to 75.5)	68.0 (60.9 to 74.4)	4.3 (0.5 to 8.1)	72.9 (69.2 to 76.2)	67.3 (59.5 to 74.2)	5.6 (1.3 to 9.9)	6.7 (5.1 to 8.8)	2.6 (1.2 to 5.6)	4.1 (2.6 to 5.6)	9.2 (7.5 to 11.3)	7.3 (4.8 to 10.8)	1.9 (−0.3 to 4.1)	93.8 (92.1 to 95.2)	94.0 (90.7 to 96.2)	−0.2 (−2.2 to 1.8)
7	80.4 (76.9 to 83.6)	82.0 (75.3 to 87.2)	−1.6 (−4.8 to 1.6)	81.0 (77.3 to 84.2)	81.5 (74.1 to 87.2)	−0.5 (−4.1 to 3.1)	6.8 (4.8 to 9.6)	2.5 (1.0 to 6.5)	4.3 (2.8 to 5.8)	6.1 (4.7 to 8.0)	3.7 (2.2 to 6.3)	2.4 (0.7 to 4.1)	95.9 (94.4 to 97.0)	96.4 (93.7 to 97.9)	−0.5 (−2.1 to 1.1)
8	86.6 (83.3 to 89.4)	90.7 (85.5 to 94.2)	−4.1 (−6.6 to −1.6)	87.1 (83.7 to 89.9)	90.4 (84.5 to 94.2)	−3.3 (−6.1 to −0.5)	7.0 (4.6 to 10.6)	2.4 (0.8 to 7.5)	4.6 (3.1 to 6.1)	4.0 (2.9 to 5.6)	1.9 (1.0 to 3.5)	2.1 (0.8 to 3.4)	97.3 (96.1 to 98.2)	97.8 (95.8 to 98.9)	−0.5 (−1.7 to 0.7)

ABI indicates absolute benefit increase (EVT vs BMM); ARI, absolute risk increase (EVT vs BMM); BMM, best medical management; CLEAR, Computed Tomography for Late Endovascular Reperfusion; EVT, endovascular therapy; and sICH, symptomatic intracranial hemorrhage.

*Using this score, higher points indicate a higher probability of achieving a good functional outcome.

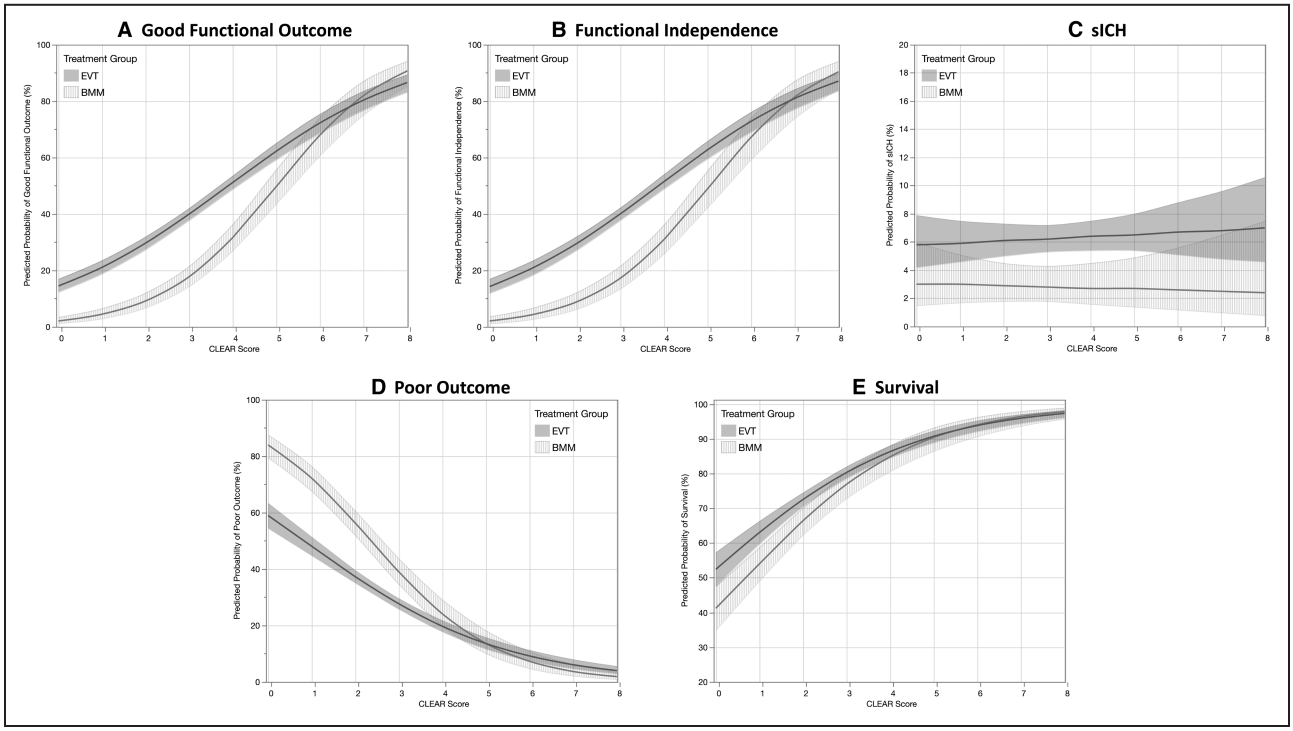

Figure 2. Predicted probability of primary and secondary outcomes in the main cohort according to treatment with EVT or BMM regressed over CLEAR scores.
Margins plots shown for the predicted probability with 95% CI by treatment with EVT of BMM regressed over CLEAR scores for (**A**) good functional outcome (eg, 90-day mRS score 0–2 or return to premorbid mRS score), (**B**) functional independence (90-day mRS score 0–2), (**C**) sICH, (**D**) poor outcome (90-day mRS score 5–6), and (**E**) 90-day survival. BMM indicates best medical management; CLEAR, Computed Tomography for Late Endovascular Reperfusion; EVT, endovascular therapy; mRS, modified Rankin score; and sICH, symptomatic intracranial hemorrhage.

Limitations

Although this study included a diverse population of patients with anterior circulation LVO treated in the extended window, the treatment allocation was nonrandomized. The patients included in this analysis were evaluated during a period of rapidly evolving interventional paradigms for the treatment of LVO (2014–2022) when EVT was not universally recommended, or recommended for only select subgroups based on emerging trial results.[32,33] Over time, we learned that the benefit of EVT extended to patients who presented beyond 6 hours and in patients with poor ASPECTS.[14,15,17-19] By nature of being a multisite retrospective data set spanning multiple years, there is inherent site-to-site variability in data capture and reporting, both in methodology and accuracy. Further, the performance of the models presented had high sensitivity and specificity on a population level, but they may not perform as well in certain individuals with unique scenarios (eg, patients with multiple LVOs or those with significant mass effect due to infarct). Due to the limitations in the original design of the CLEAR data collection instrument, we did not capture other variables used in previous prediction models (eg, serum glucose, perfusion imaging parameters, and collateral grade). Therefore, we are unable to compare the performance of the CLEAR score against other scores used for prognostication in early window EVT (Table S7). Although one primary inclusion criterion for the CLEAR study was EVT between 6 and 24 hours after LKW, some patients had undocumented treatment times or may have been treated outside this window. These patients comprised <5% of the cohort in this analysis and were excluded as part of one sensitivity analysis, which was nearly identical to the model including the primary cohort. Another limitation was the site-level adjudication of ASPECTS, which was reported by vascular neurologists or interventional neuroradiologists as part of the study design. Moreover, the observed outcomes in this study reflect what is observed in routine clinical practice for patients with a wide range of clinical and imaging characteristics. Finally, although these data were derived from patients treated at 58 sites and diverse practice patterns, external validation of this score in other cohorts (eg, those with exclusively "large core") should be performed.

CONCLUSIONS

The CLEAR score is a simple, pragmatic tool that can estimate the probability of a good clinical outcome in patients with acute LVO in the extended window. Although the score was not adapted from randomized clinical trial data, the heterogeneous, multinational cohort permits widespread generalizability and application of these findings. Whether this score outperforms other scores generated for prognostication in the early treatment window is unclear and warrants further exploration. That said, the CLEAR score remains valid in an external cohort, patients with moderate disability, and in patients who would not have been eligible for inclusion in late-window EVT trials. This simple score provides prognostic information regarding outcomes related to EVT or BMM in patients that can be useful in preintervention counseling to manage patient and family expectations in the setting of clinical or imaging extremes.

ARTICLE INFORMATION

Received February 9, 2024; accepted June 7, 2024.

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Acknowledgments

The authors would like to thank Oscar Bolanos, Medtronic. Conceptualization by James E. Siegler, Manisha Koneru, Thanh N. Nguyen; Data curation (all authors); Formal analysis Manisha Koneru, Muhammad M. Qureshi; Funding acquisition Thanh N. Nguyen; Investigation James E. Siegler, Manisha Koneru, Muhammad M. Qureshi, Adnan Mujanovic, Jean Raymond, Thanh N. Nguyen; Methodology Manisha Koneru, Muhammad M. Qureshi, Adnan Mujanovic, Jean Raymond; Supervision Thanh N. Nguyen; Validation Manisha Koneru, Muhammad M. Qureshi, Mohamed Doheim, Alhamza R. Al-Bayati; Writing original draft James E. Siegler, Manisha Koneru; Review/editing (all authors).

Sources of Funding

The CLEAR study was supported by Medtronic and the Society of Vascular and Interventional Neurology pilot grant.

Disclosures

James E. Siegler reports research support from Viz.ai, Medtronic, Philips, and is supported by R61NS135583 from the National Institutes of Health, unrelated to the present work. Diogo C. Haussen reports compensation from Vesalio, Cerenovus, Chiesi USA, Inc., Brainomix, Stryker, Poseydon Medical for consultant services; stock options in Viz AI; compensation from Jacobs institute for data and safety monitoring services. Daniel Strbian reports employment by Helsingin ja Uudenmaan Sairaanhoitopiiri. Simon Nagel reports compensation from Brainomix for consultant services. Hiroshi Yamagami reports compensation from Otsuka Pharmaceutical Co., Ltd. for other services; compensation from Medtronic for other services; grants from Bristol-Myers Squibb; compensation from Daiichi Sankyo Company LTD, Bristol-Myers Squibb, Johnson and Johnson, Bayer, Stryker for other services. Hilde Henon reports grants from SANOFI-AVENTIS U.S. LLC. Sunil A. Sheth reports compensation from motif neurosciences for other services; compensation from Viz.ai, Imperative Care, Inc, Penumbra, Inc. for consultant services; grants from National Institutes of Health; employment by UTHealth McGovern Medical School. Santiago Ortega-Gutierrez reports compensation from Medtronic, MicroVention, Inc., Stryker for consultant services; grants from Stryker, National Institute of Health, methinks, Siemens, MicroVention, Inc.; employment by Carver College of Medicine-University of Iowa. J. Kaesmacher reports grants from Swiss National Science Foundation to other. Alicia C. Castonguay reports employment by Medtronic. Ajit S. Puri reports compensation from Medtronic for consultant services; compensation from Stryker for consultant services; compensation from Johnson & Johnson Health Care Systems Inc. for consultant services; and compensation from MicroVention, Inc. for consultant services. Patrik Michel reports grants from Swiss National Science Foundation (other); grants from Swiss Heart Foundation (other); grants from University of Lausanne (other). Markus A. Möhlenbruch reports grants from Medtronic (other); grants from MicroVention, Inc. (other); grants from Stryker (other). Daniel Kaiser reports grants from Joachim Herz Stiftung. Peter A. Ringleb reports compensation from Daiichi Sankyo Company for consultant services; employment by Heidelberg University Hospital; compensation from Boehringer Ingelheim for consultant services; travel support from Bristol-Myers Squibb; travel support from Bayer Healthcare. O.O. Zaidat reports grants from Medtronic (other); grants from Penumbra, Inc. to other; grants from Johnson and Johnson (other); compensation from Medtronic for consultant services; grants from Stryker to other; compensation from Stryker for consultant services; compensation from Johnson & Johnson Health Care Systems Inc. for consultant services; stock holdings in Penumbra, Inc.; compensation from Penumbra, Inc. for consultant services. Marc Ribo reports compensation from Philips for consultant services; stock holdings in Anaconda Biomed, Methinks; compensation from AptaTargets, Stryker Corporation, Cerenovus, Medtronic MiniMed, In, Inc., for consultant services; stock holdings in Nora. Raul G. Nogueira reports compensation from Philips, Corindus Inc., Biogen, Inc., Prolong Pharmaceuticals, Ceretrieve, Viz-AI, Imperative Care, Inc, NeuroVasc Technologies, Inc., RapidPulse, Genentech, Brainomix, Cerenovus, Vesalio, Perfuze, Hybernia, Stryker Corporation, Phenox, Astrocyte, Corindus Vascular Robotics, Medtronic USA, Cerebrotech, Shanghai Wallaby, Anaconda Biomed for consultant services; stock holdings in Quantanosis AI; compensation from Synchron for data and safety monitoring services; stock holdings in Piraeus Medical; stock options in Viseon, Inc., Brainomix, Ceretrieve,Viz-AI, Reist/Q'Apel Medical, Vesalio, Cerebrotech, Perfuze, Viz-AI, Corindus Inc., Truvic; grants from Cerenovus; grants from Stryker; stock holdings in Brain4Care. Thanh N. Nguyen reports grants from Society of Vascular and Interventional Neurology; Medtronic to institution; advisory board for Brainomix and Idorsia; associate editor of *Stroke*.

Supplemental Material

Tables S1–S7
Figure S1

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