Pittsburgh Outcomes After Stroke Thrombectomy Score Predicts Outcomes After Endovascular Therapy for Anterior Circulation Large Vessel Occlusions

Srikant Rangaraju, MBBS; John T.P. Liggins, MSc; Amin Aghaebrahim, MD; Christopher Streib, MD; Chung-Huan Sun, BS; Rishi Gupta, MD; Raul Nogueira, MD; Michael Frankel, MD; Michael Mlynash, MD; Maarten Lansberg, MD; Gregory Albers, MD; Ashutosh Jadhav, MD; Tudor G. Jovin, MD

Background and Purpose—Prognostication tools that predict good outcome in patients with anterior circulation large vessel occlusions after endovascular therapy are lacking. We aim to develop a tool that incorporates clinical and imaging data to predict outcomes after endovascular therapy.

Methods—In a derivation cohort of anterior circulation large vessel occlusion stroke patients treated with endovascular therapy within 8 hours from time last seen well (n=247), we performed logistic regression to identify independent predictors of good outcome (90-day modified Rankin Scale, 0–2). Factors were weighted based on β-coefficients to derive the Pittsburgh Outcomes After Stroke Thrombectomy (POST) score. POST was validated in an institutional endovascular database (University of Pittsburgh Medical Center, n=393) and the Diffusion-Weighted Imaging Evaluation for Understanding Stroke Evolution Study-2 (DEFUSE-2) data set (n=105), as well as in patients treated beyond 8 hours (n=194) and in octogenarians (n=111).

Results—In the derivation cohort, independent predictors (P<0.1) of good outcome included 24- to 72-hour final infarct volume (in cm³, P<0.001), age (years, P<0.001), and parenchymal hematoma types 1 and 2 (H, P=0.01). POST was calculated as age+0.5×final infarct volume+15×H. Patients with POST score <60 had a 91% chance of good outcome compared with 4% with POST score ≥120. POST accurately predicted good outcomes in the derivation (area under the curve [AUC]=0.85) and validation cohorts (University of Pittsburgh Medical Center, AUC=0.81; DEFUSE-2, AUC=0.86), as well as in patients treated beyond 8 hours (AUC, 0.85) and octogenarians (AUC=0.76). POST had better predictive accuracy for good and poor outcome than the ischemic stroke predictive risk score (iSCORE).

Conclusions—POST score is a validated predictor of outcome in patients with anterior circulation large vessel occlusions after endovascular therapy. (Stroke. 2014;45:2298-2304.)

Key Words: cerebrovascular occlusion • endovascular procedures • infarction • ischemia • prognosis • stroke • thrombectomy

Acute large vessel occlusion strokes (LVOS) account for 25% to 40% of all acute ischemic strokes, resulting in significant morbidity and mortality. Data from a natural history study of patients with LVOS with moderate-severe deficits (National Institutes of Health Stroke Scale [NIHSS] ≥10) also suggested low rates of good outcome (modified Rankin Score [mRS], 0–2) in internal carotid artery (14%) and M1 middle cerebral artery (23%) occlusions.1 Proximal occlusions are also less likely to recanalize with intravenous thrombolysis, and clinical trials are underway to determine whether endovascular therapy improves clinical outcome.2,3 In anterior circulation LVOS patients, the final infarct volume (FIV) is a strong and independent predictor of clinical outcome.4,5 After endovascular therapy for LVOS, aggressive medical measures including continuation of life support and surgical therapies (hemicraniectomy, gastrostomy, and tracheostomy) are frequently considered. The decision to pursue aggressive treatment versus de-escalation of care often depends on an estimation of the chance of long-term functional independence. Stroke and critical care physicians are the ones guiding families in this complex decision-making process. Results from the Clinician Judgment vs Risk Score to Predict Stroke Outcomes

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From the Department of Neurology, University of Pittsburgh Medical Center, PA (S.R., A.A., C.S., A.J., T.G.J.); Marcus Stroke and Neuroscience Center, Grady Memorial Hospital, Atlanta, GA (C.-H.S., R.N., M.F.); Wellstar Neurosurgery, Atlanta, GA (R.G.); and Stanford Stroke Center, Stanford University Medical Center, CA (J.T.P.L., M.M., M.L., G.A.).

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Correspondence to Tudor G. Jovin, MD, University of Pittsburgh Medical Center, Pittsburgh, PA 15213. E-mail jovintg@upmc.edu

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(JURASSIC) study suggest that stroke clinicians, compared with the ischemic stroke predictive risk score (iSCORE) prediction tool, perform inferiorly in predicting death or disability in patients with ischemic stroke. This observation argues in favor of developing validated prognostication tools that predict outcomes after ischemic stroke. Many prediction tools that incorporate established clinical and imaging parameters have been developed and validated to predict outcomes in patients with LVOS before endovascular therapy, but the main use of these preintervention scales is to identify patients most likely to benefit from endovascular therapy. These do not incorporate postintervention variables such as FIV or hemorrhagic complications, both major factors that influence outcome after LVOS, thereby limiting their predictive value for clinical outcomes. An outcome prediction tool in LVOS that incorporates postintervention variables has not been developed. Using strong independent predictors of outcome (age, FIV, and presence of parenchymal hematoma types 1 and 2 [PH1/PH2]), we derived the Pittsburgh Outcomes After Stroke Thrombectomy (POST) scale to predict 3-month outcomes in anterior circulation LVOS patients treated within 8 hours from onset and validated the POST score in a large prospective institutional endovascular database and in the Diffusion-Weighted Imaging Evaluation for Understanding Stroke Evolution Study-2 (DEFUSE-2) database. We also compared the predictive power of the POST score with the iSCORE. Last, POST score was validated in patients treated beyond 8 hours from onset and in octogenarians.

Methods

Data Source and Subjects

The derivation cohort was derived from the Grady Memorial Hospital (GMH) endovascular database (2009–2013). Adults (age ≥18 years) with anterior circulation LVOS (internal carotid artery terminus, M1, M2 middle cerebral artery ) who received endovascular therapy within 8 hours from time last seen well were included, and demographic and outcome data were abstracted. Patients lacking mRS at 3 months or follow-up imaging were excluded, and the details are mentioned in Figure I in the online-only Data Supplement. Patients treated within 8 hours were included in the initial analysis to maintain homogeneity. The first validation cohort was derived from the University of Pittsburgh Medical Center (UPMC) endovascular stroke registry (Pittsburgh, PA) where patients were treated at 1 of 3 hospitals, each with endovascular, neurointensive, and rehabilitative services. The second validation cohort was derived from DEFUSE-2. POST was also validated in patients treated beyond 8 hours (GMH, UPMC). Each site had institutional review board approval for the maintenance of endovascular stroke databases. Permission from all 3 centers was sought for use of individual databases.

Measurements

Baseline characteristics (baseline National Institutes of Health Stroke Scale [NIHSS], Alberta Stroke Program Early CT score [ASPECTS], age, sex, hypertension, diabetes mellitus, atrial fibrillation, level of occlusion) were collected. ASPECTS was determined by the stroke physician before intervention. Level of occlusion was confirmed by conventional angiography. Revascularization status (modified thrombolysis in cerebral infarction grade) was determined by the operating physician. FIV (mL) was determined by measuring the area of the infarct on each slice (diffusion-weighted imaging MRI scan within the first 48 hours after treatment or first-available noncontrast head computed tomographic [CT] scan after 24 hours of treatment) and then summing individual slice thicknesses of all outlined areas. Parenchymal hemorrhage was present (H=1) if PH1 (≤30% of the infarcted area with some mild space-occupying effect) or PH2 (>30% of the infarcted area with significant space-occupying effect) hemorrhage was identified on repeating imaging. In 47 patients (UPMC) with 24-hour postintervention brain MRL, as well as CT scans within the next 24 hours, we compared MRI-based and CT-based FIV in a blinded analysis. Strong correlation was observed between MRI-based and CT-based FIV (Figure IA in the Data Supplement; Spearman ρ=0.97; P<0.0001) and in Bland–Altman analysis, no consistent bias of MRI-based versus CT-based FIV calculation was observed (Figure IIB in the Data Supplement). POST score was compared with the iSCORE (UPMC; n=263; 130 patients excluded because of missing data points to calculate the iSCORE).

Statistical Analysis

Categorical variables were compared with Fisher exact test. Continuous variables were compared using unpaired t test (2-tailed) for means and independent samples median test for medians. Variables significantly predictive (P<0.05) of good outcome (90-day mRS, 0–2) in univariate logistic regression analysis were entered in multivariate analysis, and only significant independent predictors of good outcome (P≤0.1) were considered in the final model. These were weighted based on β-coefficients and used in developing the POST scale. Model calibration was assessed in the derivation cohort with the Hosmer–Lemeshow test (P=0.05 considered good calibration). In univariate regression (derivation cohort) with POST score as a predictor of good outcome, we determined the predicted rates of good outcome in different POST score groups and compared these to observed rates (Pearson correlation coefficient was determined). Receiver operating characteristic area under the curve (AUC) was used to assess the discriminative power of POST for good outcome (excellent ≥0.80, very good ≥0.75). Discriminative power of POST for good and very bad outcome (mRS, 5–6) was compared with iSCORE. Statistical analyses were performed using IBM SPSS Statistics Version 20.

Results

Patient Characteristics

Baseline characteristics of the derivation (GMH, n=247) and validation cohorts (UPMC n=393; DEFUSE-2 n=105) are summarized in Table I. Significant differences in baseline NIHSS, ASPECTS, intravenous thrombolysis, median FIV, and PH1/PH2 hemorrhage were observed. Successful recanalization (modified thrombolysis in cerebral infarction, 2B/3) was achieved in 79% (195/247) of GMH patients.

Derivation of the POST Score

In the derivation cohort, univariate analysis identified age (P<0.001), baseline NIHSS (P<0.001), Thrombolysis In Cerebral Infarction 2B/3 recanalization (P<0.001), FIV (P<0.001), PH1/PH2 hemorrhage (H=1 if PH1/PH2 hematoma was present and 0 if absent, P=0.001), female sex (P=0.014), hypertension (P=0.023), and admission glucose (P=0.021) as predictors of good outcome. In multivariate regression analysis, only age (odds ratio=0.94; 95% confidence interval, 0.92–0.97; P<0.001), FIV (odds ratio=0.96; 95% confidence interval, 0.95–0.98; P<0.001), and PH1/PH2 hemorrhage (odds ratio=0.37; 95% confidence interval, 0.25–0.47; P=0.01) were independent predictors of good outcome. These were weighted based on β-coefficients relative to age (Table 2), and the POST score was derived: POST=age+0.5xFIV (mL)+15×H. In the derivation cohort, POST was an excellent predictor of good outcome (AUC=0.85; P<0.001). Calibration
Validation of the POST Score

Rates of good outcome in POST score groups (<60, 60–89, 90–119, ≥120) were determined (Figure 1B). POST ≥120 was associated with 4% chance of good outcome, whereas POST<60 was associated with 91% chance of good outcome. In both validation cohorts, similar rates of good outcome in the POST groups were observed (Figure 1B) except in the POST ≥120 group where the UPMC cohort had higher than expected rate of good outcome. Overall rate of good outcome was similar in all cohorts (P=0.9). Discriminative power of the POST score was excellent in the validation cohorts (UPMC AUC=0.81, P<0.001; DEFUSE-2 AUC=0.86, P<0.001). Excellent correlation between predicted and observed rates of good outcome was observed (UPMC: Pearson correlation coefficient 0.92, P<0.001). In a combined analysis of the GMH and UPMC cohorts, we compared the discriminative power of the POST score for good outcome and found comparable results across tertiles of age, NIHSS, and FIV (Table I in the online-only Data Supplement). Sixty-two of 393 patients (15.8%, UPMC) had early withdrawal of care or hospice measures. After excluding these patients from the analysis, the POST score was still a good predictor of good outcome (AUC, 0.79; P<0.001), and rates of good outcome were similar to those observed without excluding these patients (Figure III in the online-only Data Supplement).

Comparison of POST With iSCORE

The iSCORE is a well-established and validated tool that predicts outcomes in patients with ischemic stroke regardless of stroke pathogenesis.6,7,10 By incorporating FIV and PH1/PH2, we hypothesized that the POST score may be a superior predictor of 3-month outcome in patients with LVOS. In 263 patients (UPMC), POST score was superior to iSCORE in predicting good outcomes (Figure 2A: POST versus iSCORE P=0.019), as well as very bad outcomes (Figure 2B: POST versus iSCORE P=0.04).

POST Score Predicts Outcomes in Patients Treated Beyond 8 Hours

Although time from last seen well to groin puncture was not an independent predictor of good outcome (P=0.16), patients treated beyond 8 hours were not included in the derivation cohort. To determine if the POST score’s ability to predict good outcomes was applicable to patients treated beyond 8 hours, we compared rates of good outcome in patients treated beyond 8 hours with those treated ≤8 hours from time last seen well (UPMC; ≤8 hours: n=393, >8 hours: n=194). The discriminative power of the POST score in predicting good outcomes in the >8 hours group was excellent (Figure 3A; AUC, 0.85; P<0.001), and no differences in rates of good outcome were observed in the 4 POST groups (Figure 3B) compared with the ≤8 hours group.
independence with higher mortality rates compared with younger patients. Medical comorbidities, baseline disabilities, stroke complications, or earlier withdrawal of care could potentially decrease the significance of POST score as an independent predictor of good outcome in these patients. Performance of the POST score in the octogenarians in the UPMC validation cohort was compared with the GMH derivation cohort (Figure 4A). Because patients with age ≥80 years cannot have a POST score <80, younger patients with a POST score <80 were excluded from this analysis. Similar rates of good outcome were observed in the POST score 80 to 89 and ≥120 groups. In the POST score 90 to 119 group, a lower rate of good outcomes was observed in the validation cohort (28%) compared with the derivation cohort (11%), although this was not statistically significant (P=0.17). In a combined analysis (UPMC and GMH, n=111), we found that observed rates of good outcomes were similar in octogenarians compared with younger patients in all POST score groups (Figure 4B). The discriminative power of the POST score for predicting good outcome was good (AUC, 0.76; 95% confidence interval, 0.60–0.92; P=0.008).

Discussion
In the postintervention period after endovascular therapy for LVOS, early and accurate prediction of clinical outcomes can support clinical judgment and may strengthen the surrogate decision maker’s confidence in the clinician’s prognostication. A tool that predicts good outcome after endovascular therapy in patients with LVOS has not been developed. Several preintervention scores have been validated to aid in patient selection for endovascular therapy, but their application to long-term prognostication in patients with LVOS is limited because they do not incorporate postinterventional variables that strongly influence final outcome. Using age, FIV, and PH1/PH2 hemorrhage, we have derived and validated the POST score as a clinical tool to predict 3-month outcomes. The POST score is intended to be used in the postintervention period, that is, ≈24 to 72 hours after endovascular therapy, when a follow-up brain MRI or CT scan is typically performed to assess the infarct burden and any hemorrhagic complication. The POST score reliably predicts 3-month clinical outcomes at a relatively early stage in the patient’s hospital course in a similar manner.
that the functional outcome risk stratification scale (FUNC) score predicts functional outcomes in patients with intracerebral hemorrhage.\textsuperscript{17}

Patients with LVOS who do not make neurological improvement early in the postintervention period often require surgical therapies (gastrostomy or tracheostomy) and admission to nursing facilities. A significant proportion of surrogate decision makers will choose to withdraw care rather than pursue these aggressive measures especially in elderly patients. This decision is often based on the likelihood of achieving functional independence in conjunction with the patient’s expressed wishes or advance directives. Neurologists and critical care physicians are faced with the challenge of providing this prognostication at a relatively early stage after ischemic stroke. The JURASSIC study in patients with ischemic stroke showed that iSCORE-based predictions performed superiorly to clinicians with stroke expertise in predicting death or disability (mRS, 3–6) and that risk scores have a role in decision making after ischemic stroke.\textsuperscript{6} The POST score has excellent discriminative power in predicting 3-month good (mRS, 0–2) and very bad outcomes (mRS, 5–6), is superior to the iSCORE, and can provide objective data to the patient’s families regarding expected outcomes to assist them in medical decision making. A POST score <90 predicts a good outcome in >50\% of patients. However, a POST score ≥120 identifies patients with a very low likelihood of good outcome. In addition, a POST score ≥180 is associated with >75\% chance of a very bad outcome (Figure IVA and IVB in the online-only Data Supplement). If functional independence is the goal, this knowledge may help establish realistic expectations during goals-of-care discussions with surrogate decision makers. Another strength of the POST scale is that it definitively categorizes 74\% of patients with LVOS (474/640 patients in the UPMC and GMH cohorts) in the good outcome (POST<90) or poor outcome (POST≥120) categories, whereas the intermediate POST group (POST, 90–119) accounts for only 26\% (166/640) of all the patients. Whether an accurate prognostication tool such as the POST score can influence medical decision making or stroke-related healthcare costs requires prospective evaluation.

Many traditionally used predictors of outcome in LVOS (ASPECTS, baseline NIHSS, medical comorbidities, modified thrombolysis in cerebral infarction status) were not included in the POST score. ASPECTS on the initial CT scan, a surrogate of core infarct before endovascular therapy, was excluded. Consistent with previous reports,
we also observed that neither baseline NIHSS nor recanalization status was an independent predictor of outcome when FIV was introduced in a statistical model of outcome predictors. Twenty-four-hour NIHSS is better correlated with FIV and could potentially serve as a surrogate of infarct volume, but we were unable to study the relationship between 24-hour NIHSS and 90-day outcome because these data were not consistently available. Furthermore, because a significant proportion of patients are still being treated under general anesthesia, a 24-hour postintervention NIHSS may be significantly distorted in patients who remain intubated. Prospective validation studies should investigate whether 24-hour NIHSS improves the predictive value of the POST score. Medical comorbidities (congestive heart failure, end-stage renal disease, hyperglycemia, cancer, premorbid disabilities) have been used in prognostic tools such as iSCORE, and although these are independent predictors of outcome, these variables may have a smaller impact on clinical outcome compared with age and FIV in the LVOS population. Not surprisingly, the POST score is superior to the iSCORE in predicting outcomes. Premorbid disability (mRS, 3–5) and cancer were not included in the scoring system because of the inherent bias of excluding these patients from endovascular therapy in our patient cohorts, as well as in endovascular stroke practice in general.

There is also a recognized need for surrogate markers of outcome after endovascular therapy in clinical practice, as well as in phase 2 clinical trials. A valid and highly predictive prognostic score such as the POST score could be used as an early surrogate of outcome in clinical trials and in comparative analyses of different patient cohorts. Prospective validation studies in broad populations are necessary to establish the POST score as a surrogate marker of outcome. Validation of the POST score as a predictor of better outcomes based on other quality-of-life metrics and measures of physical disability, other than mRS, should also be considered.

There are several limitations to our study. First, 20% of patients in the derivation cohort and 8% in a validation cohort (UPMC) were excluded because of missing data points (Figure I in the online-only Data Supplement). A significant proportion of patients were also excluded in analyses comparing POST with iSCORE. The retrospective nature of the study may also have introduced selection and ascertainment biases. We observed significant differences in baseline characteristics in the derivation and validation cohorts, which may reflect demographic disparities and differences in patient-selection approaches for endovascular treatment adopted at different institutions. Our derivation cohort was derived from the state of Georgia, located in the stroke belt in southeastern United States where significant racial differences and higher stroke incidence and stroke-related mortality have been observed. Black patients accounted for 38% (94/247) of our derivation cohort as opposed to a predominantly white population in the UPMC validation cohort. Despite these differences, the POST score predicted outcomes comparably in all the study cohorts except for the POST ≥120 group where some differences in performance were observed. All 3 cohorts in this study included patients from the United States, whereas DEFUSE-2 includes some patients from Austria. Because of potential racial and stroke-related differences in other countries, it may be necessary that the POST score be recalibrated before generalizing our results to non-US populations. We did not validate the POST score in patients not treated with endovascular therapy and advise caution when using the POST score in these patients until formal validation is performed. The predictive power of the POST score to predict outcomes beyond 3 months was not assessed. We also did not assess the impact of poststroke medical complications on outcome. The impact of eloquence and infarct topology on outcome was not assessed in our study. Last, patients who underwent early withdrawal of care could potentially lead to an underestimation of the rate of good outcomes, especially in the intermediate POST score range (90–179). In the UPMC cohort, the POST score retained its excellent predictive power for good outcome after excluding patients who underwent inpatient withdrawal of care but this did result in a higher, although statistically insignificant, observed rate of good outcome in the POST ≥120 group.

In conclusion, we have derived and validated the POST score as the first infarct volume–based predictor of 3-month outcomes after endovascular therapy in patients with acute anterior circulation LVOS. The POST score incorporates 3 robust independent predictors of outcome: age, FIV, and PH1/PH2 hemorrhage. The predictive power of the POST score is independent of time from presumed symptom onset to treatment and is not significantly altered in octogenarians. The POST score may be used as a clinical tool to assist medical decision making in anterior circulation LVOS patients after endovascular therapy.

Disclosures

Dr Albers has equity interest (iSchemaView) and has worked as a consultant (Covidien, Lundbeck, iSchemaView). Dr Gupta is a consultant for Stryker Neurovascular, Covidien, and Rapid Medical; receipt of Royalties: UpToDate; and associate editor of Journal of Neuroimaging and Interventional Neuroroom. Dr Nogueira is a member of Stryker Neurovascular (principle investigator for Thrombectomy Revascularization of Large Vessel Occlusions in Acute Ischemic Stroke–2 [TREVO-2] and Diffusion-Weighted Imaging/Perfusion-Weighted Imaging and CT Perfusion Assessment in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention [DAWN] Trials), Covidien (Steering Committee–Solitaire Device Versus the Merci Retriever in Patients With Acute Ischaemic Stroke [SWIFT] Trials; Core Lab–Solitaire FR Thrombectomy for Acute Revascularization [STAR] Trial), and Penumbra (Executive Committee–3D Separator Trial). Dr Jovin received consulting and speaker fees from Co-Axial, ev3, Concentric Medical, and Micrus. The other authors report no conflicts.

References

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http://stroke.ahajournals.org/content/45/8/2298

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http://stroke.ahajournals.org/content/suppl/2014/07/08/STROKEAHA.114.005595.DC1

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SUPPLEMENTAL MATERIAL

The POST Score Predicts Outcomes after Endovascular Therapy for Anterior Circulation Large Vessel Occlusions

Srikant Rangaraju, MBBS;¹ John T.P. Liggins, MD;⁴ Amin Aghaebrahim, MD;¹ Christopher Streib, MD;¹ Chung-Huan Sun, BS;² Rishi Gupta, MD;³ Raul Nogueira, MD;² Michael Frankel, MD;² Michael Mlynash, MD;⁴ Maarten Lansberg, MD;⁴ Gregory Albers, MD;⁴ Ashutosh Jadhav, MD;¹ Tudor Jovin, MD¹

¹Department of Neurology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

²Marcus Stroke & Neuroscience Center, Grady Memorial Hospital, Atlanta, GA, USA

³Wellstar Neurosurgery, Atlanta, GA

⁴Stanford Stroke Center, Stanford University Medical Center, CA, USA

Corresponding author: Tudor Jovin, MD

Email address: jovintg@upmc.edu

Phone number: 1-412-647-3030 Fax number: 1-412-647-8445
Table SI

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Discriminative power (AUC) of the POST score to predict good outcome (mRS 0-2 at 3 months) was assessed in tertiles of Age, baseline NIHSS and FIV. AUC: Area Under the ROC Curve
Figure SI Patient selection for the derivation and validation cohorts. Patients were excluded if any of the following were missing: (1) mRS at 3 months; (2) Unable to calculate FIV or determine PH1/PH2 status due to lack of follow-up imaging for any reason.
Figure SII (A) Strong correlation between MRI-based and CT-based infarct volume calculation. (B) Bland and Altman Plot of the data obtained from 47 paired samples analyzed for infarct size by MRI DWI and CT imaging modalities. Correlation R = 0.238 (P=0.12). Slope = -0.027 (P=0.124). Intercept = 2.606 (p=0.18).
Figure SIII Effect of withdrawal-of-care (WOC) on prediction of good outcome by the POST score. In the UPMC cohort, 62 patients underwent early WOC. Rates of good outcome after excluding WOC patients (White, N=331) was similar to that observed after including WOC patients (Grey, N=393).
Figure SIV POST Score thresholds for good (A) and very bad outcomes (B). In a combined analysis of GMH and UPMC cohorts, POST score ≤90 (A, dotted red line) was associated with favorable chances of a good outcome (mRS 0-2) while POST score ≥180 (B, dotted red line) was associated with a very high chance of death or severe disability (mRS 5-6). Best-fit trendlines (Good outcome: Order 3 polynomial; Very bad outcome: Linear) and $R^2$ for each analysis is shown.