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Risk factors and predictors of intracranial hemorrhage after mechanical thrombectomy in acute ischemic stroke: insights from the Stroke Thrombectomy and Aneurysm Registry (STAR)

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Abstract

Background—Reducing intracranial hemorrhage (ICH) can improve patient outcome in acute ischemic stroke (AIS) intervention. We sought to identify ICH risk factors after AIS thrombectomy.

Methods—This is a retrospective review of the Stroke Thrombectomy and Aneurysm Registry (STAR) database. All patients who underwent AIS thrombectomy with available ICH data were included. Multivariable regression models were developed to identify predictors of ICH after thrombectomy. Subgroup analyses were performed stratified by symptom status and European Cooperative Acute Stroke Study (ECASS) grade.

Results—The study cohort comprised 6860 patients. Any ICH and symptomatic ICH (sICH) occurred in 25% and 7% of patients, respectively. Hemorrhagic infarction 1 (HI1) occurred in 36%, HI2 in 24%, parenchymal hemorrhage 1 (PH1) in 22%, and PH2 in 17% of patients classified by ECASS grade. Intraprocedural complications independently predicted any ICH (OR 3.8083, P<0.0001), PH1 (OR 1.9053, P=0.0195), and PH2 (OR 2.7347, P=0.0004). Race also independently predicted any ICH (black: OR 0.5180, P=0.0017; Hispanic: OR 0.4615, P=0.0148), sICH (non-white: OR 0.4349, P=0.0107), PH1 (non-white: OR 3.1668, P<0.0001), and PH2 (non-white: OR 1.8689, P=0.0176), with white as the reference. Primary mechanical thrombectomy technique also independently predicted ICH. ADAPT (A Direct Aspiration First Pass Technique) was a negative predictor of sICH (OR 0.2501, P<0.0001), with stent retriever as the reference.

Conclusions—This study identified ICH risk factors after AIS thrombectomy using real-world data. There was a propensity towards a reduced sICH risk with direct aspiration. Procedural complications and ethnicity were predictors congruent between categories of any ICH, sICH, PH1, and PH2. Further investigation of technique and ethnicity effects on ICH and outcomes after AIS thrombectomy is warranted.

INTRODUCTION

After several independent randomized controlled trials found mechanical thrombectomy (MT) to be superior to medical management alone in acute ischemic stroke (AIS) patients with large vessel occlusion, it has been adopted as the standard of care treatment.[1–3] Recently, investigations have focused on improving treatment efficiency by reducing time to revascularization, optimizing patient selection with the use of advanced imaging technologies, and evaluating the design of novel thrombectomy devices.[1] Both thrombectomy and thrombolysis carry associated risks of hemorrhage due to mechanical trauma to the vessel wall, blood–brain barrier disruption, and reperfusion-related free radical production.[4] Identifying modifiable risk factors for treatment-related complications is an avenue for investigation that may enhance outcomes in AIS patients.

The risk of any post-thrombectomy intracranial hemorrhage (ICH) and symptomatic ICH (sICH) has been estimated to range from 15.2–36.0% and 2.3–13.8%, respectively.[2 5–7] When compared with the major clinical trials, there is a higher reported risk of hemorrhage among real-world data. [5 8] This has been attributed to the use of stricter patient selection criteria and greater technical homogeneity in the clinical trials setting.[8] The European Cooperative Acute Stroke Study (ECASS) radiographic criteria has been used in AIS thrombectomy clinical trials to estimate ICH severity.[9] We hypothesized that the risk factors for ICH after AIS thrombectomy may vary depending on ECASS grade. The aims of this multicenter retrospective study were to identify potentially modifiable ICH risk factors after AIS thrombectomy in the real-world patient setting, and to assess for differences in these risk factors based on the presence or absence of symptoms and the ECASS grade.

METHODS

Study design

We retrospectively reviewed a database of AIS patients who underwent MT at 33 stroke centers participating in the Stroke Thrombectomy and Aneurysm Registry (STAR) from January 2013 to December 2020. The study was approved by the institutional review board (IRB) at each individual institution and follows the guidelines set forth by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[10] Patient consent was waived by the IRB. The data were obtained retrospectively and collected according to a standardized protocol. Verification, de-identification, and attestation of data accuracy were performed by investigators at each contributing institution. Individual patient data from each contributing institution were pooled by investigators at the Medical University of South Carolina and these pooled data were analyzed by an independent statistician.

Patient identification and selection

The inclusion criteria for the present study were (1) age ≥18 years, (2) underwent MT for AIS, and (3) available ICH data. Patient selection for MT and post-procedural stroke cares were performed according to participating institutional standards. At most institutions, AIS treatment standards followed the guidelines set forth by the American Heart Association/ American Stroke Association.[11]

Baseline data and variables

Baseline data collected by the consortium included patient, clinical, and AIS treatment parameters. Patient variables comprised age, sex, and race. Clinical data comprised medical history data (history of diabetes mellitus, hypertension, atrial fibrillation, hyperlipidemia, congestive heart failure and/or prior stroke), pre-stroke smoking status (non-smoker, former smoker, and current smoker), pre-stroke modified Rankin Scale (mRS) score, primary vessel occlusion location (anterior or posterior circulation), National Institutes of Health Stroke Scale (NIHSS) score at presentation, and the Alberta Stroke Program Early CT Score (ASPECTS). Clinical assessments and interpretation of radiographic studies at presentation and throughout the hospital stay were performed independently by neuroradiologists, neurologists, and neurointerventionalists according to participating institutional standards.

AIS treatment parameters included administration of intravenous tissue plasminogen activator (IV-tPA), balloon guide catheter use, primary MT technique (A Direct Aspiration First Pass Technique (ADAPT) vs no ADAPT (comprising Solumbra, stent retriever, and other)), time from onset to groin puncture, time from puncture to clot engagement, time from puncture to reperfusion, total procedure time, and post-MT reperfusion grade. The post-MT reperfusion grade was reported using the revised modified Thrombolysis In Cerebral Infarction (mTICI) system. This was assessed by the treating neurointerventionalist by comparing the initial (pre-MT) to the final (post-MT) catheter digital subtraction angiography.[12] Successful reperfusion was defined as mTICI grade 2b or greater.
AIS treatment-related complications included distal embolization and intraprocedural complications. Intraprocedural complications comprised access site complications, vessel

injury, patient agitation or neurological instability during the procedure. Modern MT devices, comprising stent retrievers and aspiration catheters, were used in all procedures. The technique was reported according to the first recanalization attempt.

Outcomes

The primary outcome was any ICH after MT for AIS. This was assessed by neuroradiologists at each participating center and defined as blood at any site in the brain on the post-procedure CT and/or MRI studies. Secondary outcomes included sICH, the ECASS grade, and good neurological outcome. sICH was defined as any ICH with concurrent documentation of a clinical deterioration according to any one of the following criteria: (1) increase in the NIHSS score of 4 or more points, (2) increase in the NIHSS score of 2 or more points in one category, or (3) need for intubation, hemicraniectomy, external ventricular drain placement, or other major medical or surgical intervention.[8 9] The ECASS grade was assigned by neuroradiologists at each participating center according to established CT criteria whereby hemorrhagic infarction 1 (HI1) was defined as small petechiae along the margins of the infarct, hemorrhagic infarction 2 (HI2) as confluent petechiae within the infarcted area without mass effect, parenchymal hemorrhage 1 (PH1) as blood in 30% or less of the infarcted area with mild mass effect, and parenchymal hemorrhage 2 (PH2) as blood in more than 30% of the infarcted area with significant mass effect.[9] Good neurological outcome was defined as mRS score 0–2 at 90 days.[13]

Statistical analysis

Statistical analyses were performed using JMP PRO (version 16.2, SAS Institute, Cary, NC) and Microsoft Excel (Redmond, WA). Baseline patient, clinical, and AIS treatment characteristics were compared between groups dichotomized by the primary and secondary outcomes using univariable logistic and multinomial regression analyses, as appropriate. Odds ratios (OR) and 95% confidence intervals (95% CI) were reported. For categorical variables at more than two levels, reference levels were established as the basis for odds ratios. Independent predictors of any ICH and sICH were identified using multivariable logistic regression analyses. For any ICH and good outcome, multivariable model 1 included each of the predictors with $P<0.05$ from the univariable analysis, and multivariable model 2 included each of the predictors with $P<0.05$ from model 1. For sICH, multivariable model 1 included each of the predictors with $P<0.05$ from the univariable analysis, and multivariable model 2 used an ad hoc adaptation of forward stepwise regression for predictor variables with $P<0.05$. Interactions with technique (ADAPT vs not ADAPT) and subgroup predictors of interest were tested separately in the derived multivariable models. Subgroup predictors included final mTICI score (≤2a vs >2a), time from onset to groin puncture (6 hours vs 6–24 hours vs ≥24 hours), time from puncture to clot engagement (≤10 min vs >10 min), and time from puncture to reperfusion (≤60 min vs >60 min). For the outcomes of any ICH and sICH, multivariable logistic regression interaction models included respective predictors from model 2 and the interaction term ADAPT×subgroup-defining variable. Groups were then stratified by the ECASS grade, using HI1 as the reference variable. Univariable predictors of each ECASS grade were identified using multinomial logistic regression analyses. Several multivariable multinomial regression models were fitted for the outcome of ECASS grade. The goodness of fit was determined by the Akaike information criterion curve (AICc)

using model comparison methods, and the model with the best fit was selected for the final analysis. Statistical significance was defined as P<0.05, and all tests were two-tailed. Missing data were not imputed.

RESULTS

Predictors of the primary outcome

From the STAR registry, 6860 patients were eligible and categorized by the primary outcome of ICH (n=1728) versus no ICH (n=5132) after MT for AIS. Table 1 outlines the univariable and multivariable predictors of the primary outcome. Prior history of diabetes (P=0.0273), former smoker (P=0.0008; with non-smoker as the reference category), anterior circulation occlusion (P<0.0001), higher admission NIHSS (P<0.0001), lower ASPECTS (P<0.0001), use of IV-tPA (P=0.0148), use of balloon angioplasty (P=0.0143), use of ADAPT (P<0.0001; with stent retriever as the reference category), longer time from onset to groin puncture (P<0.0001), shorter time from puncture to clot engagement (P<0.0001), longer time from puncture to reperfusion (P=0.0164), distal embolization (P<0.0001), and intraprocedural complications (P<0.0001) were positive univariable predictors of the primary outcome. Race (black: P=0.0144; Hispanic: P<0.0001; non-white: P<0.0001; white as reference), use of other MT technique (P<0.0001; stent retriever as reference), and higher final mTICI score (P<0.0001) were negative univariable predictors of the primary outcome.

In both multivariable models, higher admission NIHSS (model 1: OR 3.7699, P=0.0022; model 2: OR 1.0385, P<0.0001), use of IV-tPA (model 1: OR 1.9390, P=0.0003; model 2: OR 1.7000, P=0.0005), use of balloon angioplasty (model 1: OR 2.8566, P=0.0007; model 2: OR 1.6232, P=0.0314), longer time from onset to groin puncture (model 1: OR 33.3044, P<0.0001; model 2: OR 1.0007, P=0.0002), shorter time from puncture to clot engagement (model 1: OR 0.0762, P=0.0046; model 2: OR 0.9753, P<0.0001), distal embolization (model 1: OR 1.8155, P=0.0083; model 2: OR 1.6455, P=0.0103), and intraprocedural complications (model 1: OR 4.8303, P<0.0001; model 2: OR 3.8083, P<0.0001) were positive independent predictors of the primary outcome. In both multivariable models, Hispanic race (model 1: OR 0.3409, P=0.0084; model 2: OR 0.4615, P=0.0148; white as reference) was a negative independent predictor of the primary outcome. In model 1 only, black race (model 1: OR 0.5180, P=0.0017; white as reference) was a negative independent predictor of the primary outcome. In model 2 only, higher final mTICI score (model 2: P=0.0460) was a negative independent predictor of the primary outcome. Primary MT technique did not independently predict the primary outcome in either model.

Subgroup analyses for the primary outcome

Exploratory subgroup analyses did not show a difference in the odds of the primary outcome for patients treated with ADAPT MT technique among the subgroups of final mTICI score (≤2a vs >2a; $P_{interaction}$=0.4444), time from onset to groin puncture (6 hours vs 6–24 hours vs ≥24 hours; $P_{interaction}$=0.1413), time from puncture to clot engagement (≤10 min vs >10 min; $P_{interaction}$=0.1696), and time from puncture to reperfusion (≤60 min vs >60 min; $P_{interaction}$=0.3049).

Predictors of symptomatic ICH

Data on symptom status was available for 1696 of 1728 patients who experienced ICH and they were dichotomized into sICH (n=474) and no sICH (n=1222). Table 2 outlines the univariable and multivariable predictors of sICH. Prior history of congestive heart failure (P=0.0105), Hispanic race (P<0.0001; with white as the reference category), lower ASPECTS (P=0.0131), lower admission NIHSS (P=0.0230), use of IV-tPA (P=0.0425), shorter time from onset to groin puncture (P=0.0270), longer time from puncture to reperfusion (P<0.0001), longer total procedure time (P=0.0003), and intraprocedural complications (P<0.0001) were positive univariable predictors of sICH. ADAPT technique (P<0.0001) was a negative univariable predictor of sICH.

In both multivariable models, non-white race (model 1: OR 0.2344, P=0.0017; model 2: OR 0.4349, P=0.0107; white as reference) and ADAPT technique (model 1: OR 0.2283, P<0.0001; model 2: OR 0.2501, P<0.0001) were negative independent predictors of sICH. Longer total procedure time was a positive independent predictor of sICH in both models (model 1: OR 1.0099, P=0.0488; model 2: OR 1.0073, P=0.0119).

Subgroup analyses for sICH

Exploratory subgroup analyses did not show a difference in the odds of the primary outcome for patients treated with the ADAPT MT technique among the subgroups of final mTICI score (≤2a vs >2a; $P_{interaction}$=0.6702), time from onset to groin puncture (6 hours vs 6–24 hours vs ≥24 hours; $P_{interaction}$=0.3893), time from puncture to clot engagement (≤10 min vs >10 min; P_{inter}action=0.2065), and time from puncture to reperfusion (≤60 min vs >60 min; $P_{interaction}$=0.7705).

ECASS grades

Data on ECASS grade was available for 1312 of 1728 ICH patients and were categorized as HI1 (n=480, 36.6%), HI2 (n=320, 24.4%), PH1 (n=290, 22.1%) or PH2 (n=222, 16.9%) (table 3). Table 4 outlines the univariable predictors of the ECASS categories, with HI1 as the reference category. Univariable positive predictors of HI2 were distal embolization (P=0.0485) and longer time from puncture to reperfusion (P=0.0137). The univariable negative predictor of HI2 was former smoking status (P=0.0055; non-smoker as reference). Univariable positive predictors of PH1 were admission NIHSS (P=0.0009), longer procedure time (P=0.0036), intraprocedural complications (P=0.0195), and non-white race (P<0.0001; white as reference). Univariable negative predictors of PH1 were prior history of diabetes (P=0.0097) and former smoking status (P=0.0022; non-smoker as reference). Univariable positive predictors of PH2 were longer procedure time (P=0.0004), intraprocedural complications (P=0.0195), and other race (P<0.0001; white as reference).

In the multivariable model, higher admission NIHSS (OR 1.0278, P=0.0383) and longer time from puncture to reperfusion (OR 1.0065, P=0.0054) were positive independent predictors of category) were positive independent predictors of PH1. Prior HI2. Higher admission NIHSS (OR 1.0400, P=0.0034), intrap-history of diabetes was a negative independent predictor of procedural complications (OR 2.0122, P=0.0255), and non-PH1 (OR 0.5879, P=0.0092). Higher admission NIHSS (OR white race (OR 3.0318, P<0.0001;

with white as the reference 1.0314, P=0.0430), intraprocedural complications (OR 2.3290, P=0.0105), and non-white race (OR 1.9144, P=0.0234; with white as the reference category) were positive independent predictors of PH2 (table 5).

Neurological outcome

Data on neurological outcome at 90 days was available for 2938 of 6860 MT patients and they were dichotomized by good (mRS 0–2; n=1167, 39.7%) and poor (mRS 3–6, n=1771, 60.3%) outcome. Univariable positive predictors of good outcome were current smoking status (P<0.0001; non-smoker as reference), higher ASPECTS (P<0.0001), and higher final mTICI score (P<0.0001). Univariable negative predictors of good outcome were older age (P<0.0001), non-white race (P=0.0004; white as reference), prior history of diabetes (P<0.0001), prior history of hypertension (P<0.0001), prior history of atrial fibrillation (P<0.0001), prior history of stroke (P<0.0001), higher pre-morbid mRS (P<0.0001), higher admission NIHSS (P<0.0001), use of IV-tPA (P<0.0001), ADAPT technique (P=0.0130), longer time from onset to groin puncture (P<0.0001), longer time from puncture to reperfusion (P<0.0001), longer procedure time (P<0.0001), distal embolization (P=0.0485), and intraprocedural complications (P<0.0001) (table 6).

In both multivariable models, higher ASPECTS (model 1: OR 15.1704, P<0.0001; model 2: OR 11.7959, P<0.0001) was a positive independent predictor of good outcome. Non-white race (OR 1.9114, P=0.0167; white as reference) was a positive independent predictor of good outcome in model 1 only. In both multivariable models, older age (model 1: OR 0.3619, P<0.0001; model 2: OR 0.0300, P<0.0001), black race (model 1: OR 0.6499, P=0.0395; model 2: OR 0.6284, P=0.0185), higher pre-morbid mRS (model 1: OR 0.0454, P<0.0001; model 2: OR 0.0607, P<0.0001), higher admission NIHSS (model 1: OR 0.0181, P<0.0001; model 2: OR 0.0137, P<0.0001), longer time from onset to groin puncture (model 1: OR 0.0361, P=0.0005; model 2: OR 0.0350, P<0.0001), longer total procedure time (model 1: OR 0.0351, P=0.0329; model 2: OR 0.0036, P<0.0001), and intraprocedural complications (model 1: OR 0.3073, P=0.0013; model 2: OR 0.4160, P=0.0077) were negative independent predictors of good outcome. Primary MT technique did not independently predict good outcome in either model.

DISCUSSION

It is evident that endovascular therapy is associated with improved neurological recovery after AIS.[3 7] However, hemorrhagic transformation after AIS, particularly sICH, is associated with worse clinical outcomes.[14] Major clinical trials have not reported a significant difference in any ICH or sICH rates between AIS patients treated with MT versus without MT.[3 7] However, the risk factors for ICH and sICH may be different among MT-treated patients, and reducing the incidence of hemorrhagic transformation after MT may improve their neurological outcomes. In this study, we sought to identify modifiable risk factors for ICH after MT for AIS among patients treated at 33 stroke centers between 2013 and 2020. We found the rates of any ICH and sICH, which were 25% and 7%, respectively, to be comparable to those reported in the major clinical trials.[3 7] This contrasts with several retrospective studies that reported higher rates of any ICH and sICH.[5 6 8] This may be

due to improvements in thrombectomy technique and periprocedural management over time, including device familiarity, standardization of stroke center certification guidelines, increased efficiency, and higher rates of successful reperfusion.[15]

In the ASTER and COMPASS trials, a difference in the rate of ICH or sICH between the use of aspiration versus stent retriever was not found.[1 2] While we did not find technique-associated differences in the risk of any ICH, technique was an independent predictor of sICH in the STAR registry. Compared with stent retriever use, ADAPT was associated with a lower risk of sICH, suggesting that ADAPT-associated ICHs are predominantly asymptomatic. We did not find any interactions between use of ADAPT and TICI grade, time from onset to puncture, or time from puncture to reperfusion. This suggested that the observed association between thrombectomy technique and risk of sICH was independent of the degree of reperfusion or the efficiency of the procedure. We also found balloon angioplasty to be independently associated with increased risk of any ICH, but not sICH. Our observation of a technique-associated difference in risk of sICH did not translate into a difference in 90-day neurological outcomes between ADAPT and stent retriever. Although the effects of ICH after MT on clinical outcomes were not within the scope of the present study, a recent meta-analysis by Tang *et al* found asymptomatic ICH to be associated with worse 3-month clinical outcome among patients who underwent MT (adjusted OR 1.89, P=0.007).[16] This suggests that efforts to reduce any ICH, asymptomatic or otherwise, are important in the neurological recovery of AIS patients after MT.

The primary molecular driver for hemorrhagic transformation after AIS is thought to be reperfusion injury.[17] Reperfusion activates inflammatory cascades and reactive oxygen species, both of which can damage capillary endothelial cells and lead to increased vascular permeability.[18] A downstream consequence is the activation of matrix metalloproteinases (MMPs), particularly MMP-9, which incite destruction of basal lamina collagen, thereby promoting vasogenic edema formation and injury to the surrounding parenchyma.[19] The combination of poor baseline collaterals and successful recanalization after AIS has been associated with an increased risk of ICH, lending support to the hypothesis for reperfusion injury in patients experiencing ICH after MT.[20] Direct mechanical trauma from the device itself may cause vascular injury, and periprocedural thrombus fragmentation can lead to distal migration, both of which may promote ICH after MT.[21 22] The ECASS group first developed their grading system for hemorrhagic transformation in an attempt to characterize clinically significant ICH after AIS reperfusion.[23 24] Initial emphasis was placed on distinguishing hemorrhagic infarction (HI), from parenchymal hematoma (PH). In the original ECASS trials, only PH2 was found to be associated with neurological deterioration and 3-month mortality after AIS. [9] Although these trials were primarily designed to address the safety and efficacy of thrombolysis for AIS, PH occurrence has also been associated with reduced favorable outcome and increased mortality after MT.[14]

We divided patients by ECASS grade to assess for differences in ICH predictors for each ECASS subtype. In contrast to our any ICH and sICH analyses, we did not find thrombectomy technique to be an independent predictor of ECASS grade, with HI1 as the reference category. MT-related complications were modifiable independent predictors of both PH1 and PH2, which is consistent with studies reporting vessel wall trauma to be a

potential mechanism underlying clinically significant hemorrhage after recanalization for AIS.[21 22] This highlights the importance of the technical aspect in stroke thrombectomy. Shorter time from puncture to clot engagement predicted any ICH, whereas longer time from puncture to reperfusion predicted HI1 but not sICH, PH1 or PH2. Longer total procedure time predicted sICH, PH1, PH2, and poor neurological outcome. It is conceivable that faster intracranial navigation methods using large bore catheters may increase the risk of vessel wall trauma. Taken together, these findings suggest that reducing time to reperfusion and total procedure time is an important goal for MT. Further investigation is needed to identify the mechanism for the observed relationship between shorter time to puncture to clot engagement and any ICH. We also found race to be an independent predictor of both PH1 and PH2. Relationships between race and hemorrhagic complications have been identified among patients receiving thrombolysis for AIS, and proposed mechanisms include differences between genetic risk factors, susceptibility to reperfusion therapies, underlying atherosclerotic disease burden, and mechanical sensitivities of the vessel wall.[25] In our ECASS analysis, non-white race was associated with increased risk of both PH1 and PH2 and concurrently with reduced risk of sICH. The differential effects of race on risk of ICH after MT and the impact of ethnicity on outcomes following post-MT ICH warrant further investigation.

Higher NIHSS score at admission was associated with increased risk of PH1 and PH2 in our ECASS analysis, which is consistent with the established connection between greater stroke burden and risk of hemorrhagic transformation.[26] Concordant with recent clinical trials investigating outcomes after thrombectomy, we did not find differences in the risk of ICH with or without use of adjunctive tPA.[27] Interestingly, we found prior history of diabetes to be a negative independent predictor of PH1. Diabetes is an established risk factor for hemorrhagic transformation after thrombolysis for AIS.[28] Hyperglycemia dysregulates blood–brain barrier hemostasis by altering endothelial cell function.[29] However, the degree of stress hyperglycemia response, when defined as admission serum glucose relative to the baseline glycated hemoglobin (HbA1c), may be a stronger predictor of hemorrhagic transformation than pre-morbid blood glucose levels.[30] Sulfonylurea medications may also have protective effects by dampening the inflammatory response after AIS.[31] Future studies should seek to understand the mechanism by which pre-existing diabetes mellitus modifies the risk and severity of hemorrhagic transformation after MT for AIS.

There are several limitations to the present study, which affect the validity of our results. Importantly, the study protocol was not constructed to investigate specifically the association between AIS MT and risk of ICH. Therefore, our retrospective analysis is subject to confirmation bias as variables were chosen based on data availability and hypothesis generation. Specifically, data on blood pressure parameters, laboratory values including blood glucose levels, use of monitored anesthesia care versus general anesthesia, timing of post-MT neuroimaging studies, location of balloon angioplasty, and presence versus absence of collaterals were not available, and may have been relevant risk factors for post-MT ICH. Our results are also contingent on the accuracy and reliability of reported data, which were primarily based on medical chart abstraction. Data were self-reported and the principal investigators at each participating center were directly responsible for its fidelity and validity. It was not externally adjudicated by an independent data monitoring

board. Therefore, this study is limited by potential heterogeneity in patient selection and data reporting between centers. Additionally, because data were obtained retrospectively, the total number of eligible patients and reasons for exclusion were not readily available. The uncorrected multiple comparisons performed within the study could have elevated the false discovery rate. Outcomes data were not available to test our hypothesis that post-MT hemorrhagic transformation would be associated with worse neurological recovery in the STAR patient cohort. Specifically, we were not able to compare differences in neurological outcomes between patients with any ICH, sICH or each of the ECASS grades. Therefore, we were unable to determine which of the identified modifiable risk factors in the present study is most critical to improving patient outcomes. Future studies should seek to address this limitation by investigating associations between post-MT hemorrhagic transformation risk factors and neurological outcomes in real-world datasets of patients stratified by ICH symptom status and by ECASS grade.

CONCLUSIONS

In this large multicenter retrospective cohort of real-world patient data, this study has identified potentially modifiable factors that may reduce ICH risk after AIS thrombectomy. Contrary to the findings of the ASTER and COMPASS trials, the STAR database indicated a reduced symptomatic hemorrhage risk with direct aspiration, when compared with stent retriever. When stratified by ECASS grade, MT-related complications and race were the risk factors that were congruent predictors between each respective category of overall ICH, symptomatic hemorrhage, PH1, and PH2. The findings of the present study suggest that additional investigation of technique and ethnicity effects on hemorrhagic transformation and patient outcomes after AIS thrombectomy is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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WHAT IS ALREADY KNOWN ON THIS TOPIC

- Mechanical thrombectomy has been adopted as the standard of care treatment for patients with acute ischemic stroke. Hemorrhage after acute ischemic stroke thrombectomy is associated with worse neurological outcomes.

WHAT THIS STUDY ADDS

- This study identified modifiable and unmodifiable risk factors for hemorrhage after acute ischemic stroke thrombectomy using real-world data from a multicenter, multi-national database.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- Thrombectomy technique appeared to affect risk of hemorrhage after acute ischemic stroke thrombectomy. There was a propensity towards an increased overall hemorrhage but reduced symptomatic hemorrhage risk with direct aspiration when compared with stent retriever.

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Table 1

Predictors of intracranial hemorrhage after mechanical thrombectomy for acute ischemic stroke

	Intracranial hemorrhage (n=1728)	No intracranial hemorrhage (n=5132)	Univariable analysis		Multivariable analysis model 1*		Multivariable analysis model 2†	
			OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age, years (SD)	69.7 (14.0)	69.3 (14.9)	1.0018 (0.9980 to 1.0055)	0.3551	–	–	–	–
Female, n (%)	874/1728 (50.6)	2510/5126 (50.5)	1.0666 (0.9564 to 1.1895)	0.2460	–	–	–	–
Race, n (%)				**<0.0001**		**0.0012**		**0.0156**
White	1074/1511 (71.1)	2496/3910 (63.8)	Ref	Ref	Ref	Ref	Ref	Ref
Black	190/1511 (12.6)	518/3910 (13.2)	0.8528 (0.7113 to 1.0215)	**0.0144**	0.5180 (0.3433 to 0.7815)	**0.0017**	0.7147 (0.5047 to 1.0121)	0.0584
Hispanic	45/1511 (3.0)	275/3910 (7.0)	0.3803 (0.2753 to 0.5254)	**<0.0001**	0.3409 (0.1531 to 0.7591)	**0.0084**	0.4615 (0.2479 to 0.8594)	**0.0148**
Non-white	202/1511 (13.4)	621/3910 (15.9)	0.7559 (0.6315 to 0.8997)	**<0.0001**	1.0051 (0.5720 to 1.7662)	0.9859	1.1370 (0.7600 to 1.7010)	0.5323
Diabetes mellitus, n (%)	494/1690 (29.2)	1330/5027 (26.5)	1.149 (1.106 to 1.297	**0.0273**	1.4018 (0.9782 to 2.0088)	0.0658	–	–
Hypertension, n (%)	1236/1691 (73.1)	3695/5036 (73.4)	0.9859 (0.8706 to 1.1164)	0.8226	–	–	–	–
Atrial fibrillation, n (%)	598/1687 (35.4)	1833/5026 (36.5)	0.9566 (0.8525 to 1.0733)	0.4490	–	–	–	–
Hyperlipidemia, n (%)	679/1689 (40.2)	2141/5031 (42.6)	0.9075 (0.8112 to 1.0152)	0.0893	–	–	–	–
Congestive heart failure, n (%)	114/895 (12.7)	299/2329 (12.8)	0.9910 (0.7866 to 1.2485)	0.9389	–	–	–	–
Prior stroke, n (%)	268/1569 (17.1)	680/4294 (15.8)	1.0948 (0.9377 to 1.2782)	0.2539	–	–	–	–
Smoking status, n (%)				**0.0028**		0.3178	–	–
Non-smoker	599/946 (63.3)	1628/2359 (69.0)	Ref	Ref	Ref	Ref	–	–
Former smoker	186/946 (19.7)	359/2359 (22.1)	1.4081 (1.1525 to 1.7204)	**0.0008**	0.9801 (0.6498 to 1.4781)	0.9235	–	–
Current smoker	161/946 (17.0)	372/2359 (15.8)	1.1763 (0.9561 to 1.4472)	0.1247	0.7101 (0.4484 to 1.1246)	0.1445	–	–
Anterior circulation, n (%)	1603/1716 (93.4)	4479/5076 (88.2)	1.89052 (1.5350 to 2.3300)	**<0.0001**	1.4542 (0.2985 to 7.0839)	0.6430	–	–
Pre-morbid mRS, mean (SD)	0.6 (1.1)	0.7 (1.1)	0.976286 (0.9231 to 1.0326)	0.4014	–	–	–	–
Admission NIHSS, mean (SD)	16.3 (6.9)	15.2 (7.1)	1.0235 (1.0156 to 1.0315)	**<0.0001**	3.7699 (1.6122 to 8.9171)	**0.0022**	1.0385 (1.0197 to 1.0580)	**<0.0001**

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	Intracranial hemorrhage (n=1728)	No intracranial hemorrhage (n=5132)	Univariable analysis		Multivariable analysis model 1*		Multivariable analysis model 2†	
			OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
ASPECTS, mean (SD)	7.8 (1.8)	8.3 (1.7)	0.8501 (0.8211 to 0.8802)	**<0.0001**	0.7629 (0.3345 to 1.7546)	0.5222	–	–
IV-tPA, n (%)	769/1712 (44.9)	2454/5079 (48.3)	0.8723 (0.7815 to 0.9737)	**0.0148**	1.9390 (1.3556 to 2.7735)	**0.0003**	1.7000 (1.2594 to 2.2948)	**0.0005**
Angioplasty, n (%)	121/1041 (11.6)	196/2213 (8.9)	1.3535 (1.0651 to 1.7120)	**0.0143**	2.8566 (1.5556 to 5.2456)	**0.0007**	1.6232 (1.0472 to 2.5162)	**0.0314**
ADAPT, n (%)	710/1525 (46.6)	1632/4691 (34.8)	1.7782 (1.5213 to 2.0770)	**<0.0001**	1.4668 (0.9074 to 2.3711)	0.1180	–	–
Time from onset to groin puncture, mean min (SD)	434.4 (449.2)	380.2 (387.5)	1.0003 (1.0002 to 1.0004)	**<0.0001**	33.3044 (7.1428 to 169.1229)	**<0.0001**	1.0007 (1.0003 to 1.0011)	**0.0002**
Time from puncture to occlusion site, min (SD)	11.8 (16.2)	19.9 (27.9)	0.9800 (0.9727 to 0.9874)	**<0.0001**	0.0762 (0.0121 to 0.4302)	**0.0046**	0.9753 (0.9655 to 0.9839)	**<0.0001**
Time from puncture to ≥mTICI 2b, min (SD)	54.1 (45.7)	51.2 (40.2)	1.0016 (1.0003 to 1.0029)	**0.0164**	2.5857 (0.4776 to 13.8528)	0.2684	–	–
Procedure time, min (SD)	51.2 (47.1)	48.7 (42.5)	1.0012 (0.9992 to 1.0033)	0.2377	–	–	–	–
Final mTICI score, n (%)				**<0.0001**		**0.0356**		**0.0002**
0	102/1682 (6.1)	312/4484 (6.4)	Ref	Ref	Ref	Ref	Ref	Ref
1	40/1682 (2.4)	108/4884 (2.2)	1.1330 (0.7398 to 1.7348)	0.8602	1.5577 (0.1843 to 13.1666)	0.6840	0.8085 (0.2367 to 2.7618)	0.7345
2a	172/1682 (10.2)	295/4884 (6.0)	1.7835 (1.3317 to 2.3885)	**<0.0001**	2.1638 (0.7384 to 6.3410)	0.1594	1.3626 (0.6230 to 2.9804)	0.4384
2b	636/1682 (37.8)	1546/4884 (31.7)	1.2584 (0.9880 to 1.6027)	0.1863	1.4976 (0.6600 to 3.3981)	0.3340	1.1064 (0.6037 to 2.0275)	0.7436
2c	156/1682 (9.3)	382/4884 (7.8)	1.2492 (0.9338 to 1.6710)	0.4330	1.5878 (0.6513 to 3.8709)	0.3092	1.0724 (0.5422 to 2.1210)	0.8408
3	576/1682 (34.2)	2241/4884 (45.9)	0.7862 (0.6175 to 1.0010)	**<0.0001**	0.8551 (0.3768 to 1.9406)	0.7082	0.5501 (0.3059 to 0.9895)	**0.0460**
Distal emboli, n (%)	309/1316 (23.5)	585/3704 (15.8)	1.6360 (1.4010 to 1.9104)	**<0.0001**	1.8155 (1.1657 to 2.8276)	**0.0083**	1.6455 (1.1265 to 2.4038)	**0.0103**
Intraprocedural complication, n (%)	194/1481 (13.1)	220/4125 (5.3)	2.6756 (2.1839 to 3.2780)	**<0.0001**	4.8303 (2.6102 to 8.9387)	**<0.0001**	3.8083 (2.4030 to 6.0356)	**<0.0001**

Interactions were explored for the outcome of intracranial hemorrhage between ADAPT and subgroup-defining variable (ADAPT × variable) with no ADAPT as reference adjusting for other covariates in model 2. Subgroup defining variables tested were: final mTICI score (≤2a vs ≥2b; P=0.4444), time from onset to groin puncture (≤6 hours vs 6–24 hours vs ≥24 hours; P=0.1413), time from puncture to occlusion site (≤10 min vs >10 min; P=0.1696), and time from puncture to ≥mTICI 2b (≤1 hour vs >1 hour; P=0.3049).

*Model includes statistically significant variables from univariate analyses.

† Model includes statistically significant variables from model 1.

ADAPT, A Direct Aspiration First Pass Technique; ASPECTS, Alberta Stroke Program Early CT Score; IV-tPA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale.

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Table 2

Predictors of symptomatic intracranial hemorrhage after mechanical thrombectomy for acute ischemic stroke in patients

	Symptomatic hemorrhage (n=474)	Asymptomatic hemorrhage (n=1222)	Univariable analysis		Multivariable analysis model 1*		Multivariable analysis model 2†	
			OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age, years (SD)	70.4 (13.3)	69.4 (14.2)	1.0146 (0.8207 to 1.2543)	0.1761	–	–	–	–
Female, n (%)	238/474 (50.2)	618/1222 (50.6)	0.9856 (0.7972 to 1.2185)	0.8936	–	–	–	–
Race, n (%)				**0.0007**		**0.0115**		0.0698
White	273/400 (68.3)	770/1080 (71.3)	Ref	Ref	Ref	Ref	Ref	Ref
Black	51/400 (12.8)	139/1080 (12.9)	1.0349 (0.7298 to 1.4675)	0.8475	0.8173 (0.4052 to 1.6486)	0.5732	0.9048 (0.5057 to 1.5658)	0.7259
Hispanic	25/400 (6.3)	20/1080 (1.9)	3.5256 (1.9272 to 6.4498)	**<0.0001**	0.7820 (0.1942 to 3.1495)	0.7294	1.3458 (0.4121 to 3.7702)	0.5990
Non-white	51/400 (12.8)	151/1080 (14.0)	0.9526 (0.6739 to 1.3466)	0.7835	0.2344 (0.0949 to 0.5787)	**0.0017**	0.4349 (0.2191 to 0.8283)	**0.0107**
Diabetes mellitus, n (%)	145/467 (31.1)	346/1209 (28.6)	1.1232 (0.8903 to 1.4169)	0.3271	–	–	–	–
Hypertension, n (%)	356/468 (76.1)	871/1209 (72.0)	1.2335 (0.9638 to 1.5786)	0.0955	–	–	–	–
Atrial fibrillation, n (%)	172/467 (36.8)	422/1207 (35.0)	1.0846 (0.8685 to 1.3544)	0.4738	–	–	–	–
Hyperlipidemia, n (%)	175/466 (37.6)	499/1209 (41.3)	0.8557 (0.6869 to 1.0659)	0.1643	–	–	–	–
Congestive heart failure, n (%)	40/224 (17.9)	74/662 (11.2)	1.7274 (1.1364 to 2.6257)	**0.0105**	1.9404 (0.9668 to 3.8946)	0.0622	–	–
Prior stroke, n (%)	72/427 (16.9)	194/1128 (17.2)	0.9764 (0.7257 to 1.3139)	0.8749	–	–	–	–
Smoking status, n (%)				0.927				
Non-smoker	143/223 (64.1)	450/714 (63.0)	Ref	Ref	–	–	–	–
Former smoker	44/223 (19.7)	141/714 (19.8)	0.9820 (0.6667 to 1.4464)	0.9267	–	–	–	–
Current smoker	36/223 (16.1)	123/714 (17.2)	0.9210 (0.6074 to 1.3967)	0.6986	–	–	–	–
Anterior circulation, n (%)	438/473 (92.6)	1134/1211 (93.6)	0.8497 (0.5614 to 1.2862)	0.4413	–	–	–	–
Pre-morbid mRS, mean (SD)	0.7 (1.1)	0.6 (1.1)	1.4861 (0.8812 to 2.5062)	0.1374	–	–	–	–
Admission NIHSS, mean (SD)	15.7 (7.2)	16.6 (6.8)	0.9822 (0.9671 to 0.9976)	**0.0230**	1.0029 (0.9659 to 1.0412)	0.8806	–	–
ASPECTS, mean (SD)	7.6 (2.0)	7.8 (1.8)	0.9192 (0.8601 to 0.9825)	**0.0131**	0.9221 (0.8081 to 1.0522)	0.2296	–	–

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	Symptomatic hemorrhage (n=474)	Asymptomatic hemorrhage (n=1222)	Univariable analysis		Multivariable analysis model 1*		Multivariable analysis model 2†	
			OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
IV-tPA, n (%)	228/469 (48.6)	524/1215 (43.1)	1.2475 (1.0075 to 1.5448)	**0.0425**	1.4328 (0.8373 to 2.4519)	0.1895	–	–
Angioplasty, n (%)	33/275 (12.0)	86/757 (11.4)	1.0640 (0.6939 to 1.6313)	0.7762	–	–	–	–
ADAPT, n (%)	124/397 (31.2)	580/1097 (52.9)	0.3398 (0.2503 to 0.4613)	**<0.0001**	0.2283 (0.1306 to 0.2991)	**<0.0001**	0.2501 (0.1568 to 0.3968)	**<0.0001**
Time from onset to groin puncture, mean min (SD)	392.9 (401.7)	450.6 (466.2)	0.9997 (0.9993 to 0.9999)	**0.0270**	0.2345 (0.0098 to 5.6006)	0.3704	–	–
Time from puncture to occlusion site, min (SD)	14.2 (25.0)	11.2 (13.1)	1.0093 (0.9966 to 1.0222)	0.1508	–	–	–	–
Time from puncture to ≥mTICI 2b, min (SD)	62.5 (48.6)	51.1 (44.4)	1.0050 (1.0028 to 1.0073)	**<0.0001**	1.0003 (0.9885 to 1.0122)	0.9624	–	–
Procedure time, min (SD)	64.7 (50.9)	47.3 (45.5)	1.0070 (1.0032 to 1.0108)	**0.0003**	1.0099 (1.0002 to 1.0197)	**0.0488**	1.0073 (1.0016 to 1.0129)	**0.0119**
Final mTICI score, n (%)				0.0766				
0	29/407 (7.3)	71/1104 (6.4)	Ref	Ref	–	–	–	–
1	16/407 (3.9)	24/1104 (2.2)	1.6322 (0.7588 to 3.5110)	0.2100	–	–	–	–
2a	57/407 (14.0)	111/1104 (10.1)	1.2572 (0.7347 to 2.1513)	0.4036	–	–	–	–
2b	169/407 (41.5)	460/1104 (41.7)	0.8995 (0.5641 to 1.4342)	0.6563	–	–	–	–
2c	45/407 (11.1)	107/1104 (9.7)	1.0296 (0.5912 to 1.7933)	0.9178	–	–	–	–
3	136/407 (33.4)	426/1104 (38.6)	0.7816 (0.4870 to 1.2545)	0.3074	–	–	–	–
Distal emboli, n (%)	70/324 (21.6)	238/976 (24.4)	0.8546 (0.6317 to 1.1561)	0.3081	–	–	–	–
Intraprocedural complication, n (%)	74/382 (19.4)	116/1067 (10.9)	1.9700 (1.4322 to 2.7089)	**<0.0001**	1.7587 (0.8608 to 3.5937)	0.1215	–	–

Interactions were explored for the outcome of symptomatic intracranial hemorrhage between ADAPT and subgroup-defining variable (ADAPT × variable) with no ADAPT as reference adjusting for other covariates in model 2. Subgroup defining variables tested were: final mTICI score (≤2a vs ≥2b; P=0.2934), time from onset to groin puncture (≤6 hours vs 6–24 hours vs ≥24 hours; P=0.3893), time from puncture to occlusion site (≤10 min vs >10 min; P=0.2065), and time from puncture to ≥mTICI 2b (≤1 hour vs >1 hour; P=0.7705).

*Model includes statistically significant variables from univariate analyses.

†Model includes statistically significant variables from model 1.

ADAPT, A Direct Aspiration First Pass Technique; ASPECTS, Alberta Stroke Program Early CT Score; IV-tPA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale.

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Table 3

Distribution of hemorrhage categories by ECASS

ECASS categories	Frequency (%)
HI1	480/1312 (36.6)
HI2	320/1312 (24.4)
PH1	290/1312 (22.1)
PH2	222/1312 (16.9)

ECASS, European Cooperative Acute Stroke Study; HI, hemorrhagic infarction; PH, parenchymal hemorrhage.

Table 4

Univariate predictors of hemorrhage categories using multinomial logistic regression models

ECASS	Variable	Relative OR (95% CI)	P value
HI1			
	Ref	Ref	Ref
HI2			
	Distal embolization	1.4460 (1.0024 to 2.0859)	**0.0485**
	Diabetes mellitus	0.8484 (0.6200 to 1.1609)	0.3041
	Hypertension	1.0015 (0.7282 to 1.3773)	0.9927
	Atrial fibrillation	1.0936 (0.8108 to 1.4751)	
	Hyperlipidemia	1.2419 (0.9276 to 1.6627)	
	Congestive heart failure	0.5307 (0.2656 to 1.0605)	
	Prior stroke	1.2530 (0.8481 to 1.8512)	
	Smoking status		
	Non-smoker	Ref	Ref
	Current smoker	0.7512 (0.4429 to 1.2738)	0.2882
	Former smoker	0.4776 (0.2835 to 0.8045)	**0.0055**
	Admission NIHSS	1.0103 (0.9887 to 1.0324)	0.3513
	Anterior circulation	1.0405 (0.5653 to 1.9152)	0.8984
	Time from onset to groin puncture	0.9998 (0.9994 to 1.0002)	0.2862
	Angioplasty	0.9105 (0.4920 to 1.6847)	0.7651
	ADAPT	1.0053 (0.7394 to 1.3668)	0.9730
	Time from puncture to occlusion site	1.0181 (0.9926 to 1.04540)	0.1685
	Time from puncture to ≥mTICI 2b	1.0039 (1.0008 to 1.0070)	**0.0137**
	Procedure time	1.0032 (0.9965 to 1.0099)	0.3435
	Final mTICI score		
	0	Ref	Ref
	1	1.7789 (0.6447 to 4.9084)	0.2659
	2a	1.6565 (0.7973 to 3.4418)	0.1760
	2b	0.7951 (0.4196 to 1.5066)	0.4818
	2c	0.7861 (0.3685 to 1.6772)	0.5335
	3	0.8440 (0.4447 to 1.3205)	0.6038
	Complications	1.6109 (0.9225 to 2.8129)	0.0936
	Race		
	White	Ref	Ref
	Black	1.0520 (0.6795 to 1.6506)	0.8253
	Hispanic	0.1447 (0.0185 to 1.1300)	0.0652
	Non-white	1.2656 (0.7654 to 2.0927)	0.3585
PH1			
	Distal embolization	0.8361 (0.5576 to 1.2539)	0.3866

ECASS	Variable	Relative OR (95% CI)	P value
	Diabetes mellitus	0.6407 (0.4573 to 0.8977)	**0.0097**
	Hypertension	0.8904 (0.6445 to 1.2300)	0.4811
	Atrial fibrillation	1.0991 (0.8087 to 1.4939)	0.5459
	Hyperlipidemia	0.8286 (0.6088 to 1.1279)	0.2320
	Congestive heart failure	0.8658 (0.4789 to 1.5652)	0.6333
	Prior stroke	1.0489 (0.6920 to 1.5900)	0.8219
	Smoking status		
	Non-smoker	Ref	Ref
	Current smoker	0.6559 (0.3861 to 1.1143)	0.1187
	Former smoker	0.4498 (0.2694 to 0.7510)	**0.0022**
	Admission NIHSS	1.0387 (1.0158 to 1.0623)	**0.0009**
	Anterior circulation	0.9986 (0.5364 to 1.8588)	0.9964
	Time from onset to groin puncture	0.9996 (0.9992 to 1.0000)	0.0678
	Angioplasty	1.1226 (0.6162 to 2.0451)	0.7055
	ADAPT	0.9470 (0.6956 to 1.2894)	0.7296
	Time from puncture to occlusion site	1.0144 (0.9872 to 1.0426)	0.2948
	Time from puncture to ≥mTICI 2b	0.9983 (0.9946 to 1.0018)	0.3485
	Procedure time	1.0088 (1.0030 to 1.0149)	**0.0036**
	Final mTICI score		
	0	Ref	Ref
	1	0.8000 (0.2100 to 3.0473)	0.7436
	2a	1.2632 (0.5456 to 2.9244)	0.5854
	2b	1.2291 (0.6061 to 2.4924)	0.5674
	2c	0.9787 (0.4259 to 2.2492)	0.9596
	3	1.2695 (0.6247 to 2.5796)	0.5095
	Complications	1.9053 (1.1090 to 3.2734)	**0.0195**
	Race		
	White	Ref	Ref
	Black	1.0123 (0.6194 to 1.6545)	0.9609
	Hispanic	0.1841 (0.0235 to 1.4387)	0.1066
	Non-white	3.1668 (2.0317 to 4.9361)	**<0.0001**
PH2			
	Distal embolization	1.0237 (0.6574 to 1.5942)	0.9174
	Diabetes mellitus	1.0106 (0.7169 to 1.4246)	0.9519
	Hypertension	1.1232 (0.7813 to 1.6148)	0.5303
	Atrial fibrillation	0.9754 (0.6963 to 1.3665)	0.8850
	Hyperlipidemia	0.9211 (0.6604 to 1.2847)	0.6281
	Congestive heart failure	0.9738 (0.5134 to 1.8469)	0.9352
	Prior stroke	0.6286 (0.3770 to 1.0481)	0.0750

ECASS	Variable	Relative OR (95% CI)	P value
	Smoking status		
	Non-smoker	Ref	Ref
	Current smoker	0.8030 (0.4395 to 1.4670)	0.4753
	Former smoker	0.8126 (0.4788 to 1.3790)	0.4417
	Admission NIHSS	0.9983 (0.9744 to 1.0227)	0.8876
	Anterior circulation	1.0071 (0.5111 to 1.9841)	0.9838
	Time from onset to groin puncture	0.9996 (0.9991 to 1.000)	0.0734
	Angioplasty	1.6062 (0.9023 to 2.8591)	0.1072
	ADAPT	0.8241 (0.5741 to 1.1830)	0.2942
	Time from puncture to occlusion site	1.0097 (0.9766 to 1.0411)	0.5462
	Time from puncture to ≥mTICI 2b	1.0052 (1.0018 to 1.0085)	**0.0022**
	Procedure time	1.0113 (1.0053 to 1.0179)	**0.0004**
	Final mTICI score		
	0	Ref	Ref
	1	1.6545 (0.5003 to 5.4718)	0.4092
	2a	1.5550 (0.6533 to 3.7014)	0.3183
	2b	1.1488 (0.5425 to 2.4326)	0.7170
	2c	0.9052 (0.3717 to 2.2048)	0.8264
	3	0.9907 (0.4641 to 2.1150)	0.9808
	Complications	2.7347 (1.5588 to 4.7974)	**0.0004**
	Race		
	White	Ref	Ref
	Black	0.8677 (0.5013 to 1.5019)	0.6122
	Hispanic	0.6626 (0.1819 to 2.4133)	0.5325
	Non-white	1.8689 (1.1149 to 3.1329)	**0.0176**

ADAPT, A Direct Aspiration First Pass Technique; HI, hemorrhagic infarction; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; PH, parenchymal hemorrhage.

Table 5

Multivariable multinomial logistic regression model for hemorrhage categories

ECASS	Variables	Relative OR (95% CI)	P value
HI1			
	Ref	Ref	Ref
HI2			
	Complications	1.4690 (0.7750 to 2.7844)	0.2384
	Diabetes mellitus	0.8530 (0.5832 to 1.2469)	0.4111
	Race (non-white)	1.0166 (0.5854 to 1.7653)	0.9535
	Race (Hispanic)	0.1602 (0.020 to 1.2726)	0.0832
	Race (black)	1.2384 (0.7614 to 2.0145)	0.3888
	Admission NIHSS	1.0278 (1.0015 to 1.0548)	**0.0383**
	Time from puncture to ≥mTICI 2b	1.0065 (1.0019 to 1.0112)	**0.0054**
PH1			
	Complications	2.0122 (1.0894 to 3.7167)	**0.0255**
	Diabetes mellitus	0.5879 (0.3943 to 0.8767)	**0.0092**
	Race (non-white)	3.0318 (1.8814 to 4.8855)	**<0.0001**
	Race (Hispanic)	0.1741 (0.0218 to 1.3877)	0.0987
	Race (black)	0.9437 (0.5529 to 1.6107)	0.8318
	Admission NIHSS	1.0400 (1.0130 to 1.0676)	**0.0034**
	Time from puncture to ≥mTICI 2b	0.9988 (0.9938 to 1.0038)	0.6374
PH2			
	Complications	2.3290 (1.2188 to 4.4506)	**0.0105**
	Diabetes mellitus	1.2272 (0.8036 to 1.8741)	0.3432
	Race (other)	1.9144 (1.0917 to 3.3570)	**0.0234**
	Race (Hispanic)	0.7211 (0.1909 to 2.7233)	0.6295
	Race (black)	0.9918 (0.5421 to 1.8147)	0.9787
	Admission NIHSS	1.0314 (1.0010 to 1.0628)	**0.0430**
	Time from puncture to ≥mTICI 2b	1.0041 (0.9987 to 1.0095)	0.1374

AICc = 2448.27.

AICc, Akaike information criterion curve; ECASS, European Cooperative Acute Stroke Study; HI, hemorrhagic infarction; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; PH, parenchymal hemorrhage.

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Table 6

Predictors of good outcome after mechanical thrombectomy for acute ischemic stroke

	Good outcome (n=1167)	Poor outcome (n=1771)	Univariable analysis		Multivariable analysis model 1*		Multivariable analysis model 2†	
			OR (95% CI)	P value	oR (95% CI)	P value	oR (95% CI)	P value
Age, years (SD)	65.6 (0.4)	73.2 (0.3)	0.0387 (0.0240 to 0.0618)	**<0.0001**	0.3619 (0.0118 to 0.1079)	**<0.0001**	0.0300 (0.0114 to 0.0775)	**<0.0001**
Female, n (%)	555/1167 (47.6)	877/1771 (49.5)	0.9244 (0.7973 to 1.0718)	0.2977	–	–	–	–
Race, n (%)				**0.0040**		**0.0085**		**0.0055**
White	553/851 (65.0)	736/1257 (58.6)	Ref	Ref	Ref	Ref	Ref	Ref
Black	132/851 (15.5)	206 (1257 (16.4)	0.8528 (0.6677 to 1.0893)	0.2024	0.6499 (0.4311 to 0.9795)	**0.0395**	0.6284 (0.4269 to 0.9249)	**0.0185**
Hispanic	31/851 (3.6)	41/1257 (3.3)	1.0063 (0.6231 to 1.6252)	0.9795	0.7048 (0.3152 to 1.5758)	0.3941	0.5685 (0.2770 to 1.1671)	0.1239
Non-white	135/851 (15.9)	274 (21.8)	0.6557 (0.5191 to 0.8284)	**0.0004**	1.9114 (1.1246 to 3.2486)	**0.0167**	1.5346 (0.9742 to 2.4175)	0.0647
Diabetes mellitus, n (%)	261/1164 (22.4)	563/1754 (32.1)	0.6114 (0.5157 to 0.7250)	**<0.0001**	0.9432 (0.6653 to 1.3372)	0.7425	–	–
Hypertension, n (%)	783/1164 (67.3)	1393/1761 (79.1)	0.5429 (0.4590 to 0.6422)	**<0.0001**	0.9358 (0.6461 to 1.3555)	0.7258	–	–
Atrial fibrillation, n (%)	376/1159 (32.4)	732/1755 (41.7)	0.6711 (0.5746 to 0.7839)	**<0.0001**	1.2250 (0.8747 to 17157)	0.2368	–	–
Hyperlipidemia, n (%)	540/1163 (46.4)	802/1755 (45.7)	1.0300 (0.8877 to 1.1951)	0.6971	–	–	–	–
Congestive heart failure, n (%)	119/1027 (11.6)	207/1517 (13.7)	0.8294 (0.6519 to 1.0553)	0.1257	–	–	–	–
Prior stroke, n (%)	127/999 (12.7)	286/1501 (19.1)	0.6187 (0.4934 to 0.7759)	**<0.0001**	0.8261 (0.5406 to 1.2623)	0.3762	–	–
Smoking status, n (%)				**<0.0001**		0.4394	–	–
Non-smoker	680/1045 (65.1)	1075/1531 (70.2)	Ref	Ref	Ref	Ref	–	–
Former smoker	166/1045 (15.9)	268/1531 (17.5)	0.9792 (0.7889 to 1.2154)	0.8488	1.0031 (0.6830 to 1.4732)	0.9874	–	–
Current smoker	199/1045 (19.0)	188/1531 (12.3)	1.6734 (1.3412 to 2.0878)	**<0.0001**	1.3224 (0.8489 to 2.060)	0.2166	–	–
Anterior circulation, n (%)	1043/1160 (89.9)	1557/1753 (88.8)	1.1222 (0.8809 to 1.4295)	0.3488	–	–	–	–
Pre-morbid mRS, mean (SD)	0.3 (0.7)	1.0 (1.3)	0.0348 (0.0208 to 0.0569)	**<0.0001**	0.0454 (0.0172 to 0.1133)	**<0.0001**	0.0607 (0.0259 to 0.1356)	**<0.0001**

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	Good outcome (n=1167)	Poor outcome (n=1771)	Univariable analysis		Multivariable analysis model 1*		Multivariable analysis model 2†	
			OR (95% CI)	P value	oR (95% CI)	P value	oR (95% CI)	P value
Admission NIHSS, mean (SD)	12.7 (6.7)	17.2 (6.8)	0.0169 (0.0101 to 0.0278)	**<0.0001**	0.0181 (0.0072 to 0.0443)	**<0.0001**	0.0137 (0.0053 to 0.0345)	**<0.0001**
ASPECTS, mean (SD)	8.5 (1.5)	7.7 (1.9)	15.1704 (9.1126 to 25.5575)	**<0.0001**	11.5580 (4.8282 to 28.3468)	**<0.0001**	11.7959 (5.1502 to 27.6201)	**<0.0001**
IV-tPA, n (%)	582/1166 (49.9)	695/1764 (39.4)	0.6524 (0.5619 to 0.7574)	**<0.0001**	1.0447 (0.7489 to 1.4575)	0.7968	–	–
Angioplasty, n (%)	105/883 (11.9)	147/1306 (11.3)	1.0641 (0.8152 to 1.3889)	0.6481	–	–	–	–
ADAPT, n (%)	422/1081 (39.0)	718/1638 (43.8)	0.8205 (0.7017 to 0.9594)	**0.0130**	0.9693 (0.6669 to 1.4088)	0.8700	–	–
Time from onset to groin puncture, mean min (SD)	363.9 (386.6)	466.7 (523.6)	0.03641 (0.0103 to 0.1187)	**<0.0001**	0.0362 (0.0040 to 0.2498)	**0.0005**	0.0350 (0.0049 to 0.1996)	**<0.0001**
Time from puncture to occlusion site, min (SD)	15.7 (23.0)	18.8 (27.4)	0.3009 (0.0749 to 1.0961)	0.0691	–	–	–	–
Time from puncture to ≥mTICI 2b, min (SD)	36.8 (31.1)	47.7 (36.6)	0.0420 (0.0183 to 0.0938)	**<0.0001**	0.3136 (0.0090 to 11.4607)	0.5253	–	–
Procedure time, min (SD)	39.1 (37.4)	56.8 (49.2)	0.0021 (0.0004 to 0.0107)	**<0.0001**	0.0351 (0.0014 to 0.7661)	**0.0329**	0.0036 (0.0003 to 0.0415)	**<0.0001**
Final mTICI score, n (%)				**<0.0001**		**0.0003**		**<0.0001**
0	39/1148 (3.4)	147/1736 (8.5)	Ref	Ref	Ref	Ref	Ref	Ref
1	6/1148 (0.5)	41/1736 (2.4)	0.5516 (0.2184 to 1.3933)	0.2082	0.8801 (0.0660 to 11.7353)	0.9230	0.7434 (0.1264 to 4.3725)	0.7429
2a	30/1148 (2.6)	140/1736 (8.1)	0.8077 (0.4758 to 1.3712)	0.4290	1.0963 (0.2818 to 4.2648)	0.8945	0.8045 (0.2661 to 2.4322)	0.7000
2b	343/1148 (29.9)	587/1736 (33.8)	2.2025 (1.5102 to 3.2120)	**<0.0001**	3.0485 (0.9704 to 9.5769)	0.0563	3.0038 (1.2166 to 7.4161)	**0.0171**
2c	128/1148 (11.2)	166/1736 (9.6)	2.9064 (1.9065 to 4.4307)	**<0.0001**	3.5746 (1.0664 to 11.9816)	**0.0390**	3.4819 (1.3011 to 9.3174)	**0.0130**
3	602/1148 (52.4)	655/1736 (37.7)	3.4642 (2.3929 to 5.0151)	**<0.0001**	4.9856 (1.5979 to 15.5552)	**0.0057**	4.5460 (1.8365 to 11.2526)	**0.0011**
Distal emboli, n (%)	183/1021 (17.9)	321/1522 (21.1)	0.8170 (0.6677 to 0.9998)	**0.0485**	1.4048 (0.8977 to 2.1984)	0.1368	–	–
Intraprocedural complication, n (%)	46/1028 (4.5)	149/1564 (9.5)	0.4449 (0.3165 to 0.6253)	**<0.0001**	0.3073 (0.1434 to 0.6585)	**0.0013**	0.4160 (0.2182 to 0.7933)	**0.0077**

*Model includes statistically significant variables from univariate analyses.

† Model includes statistically significant variables from model 1.

ADAPT, A Direct Aspiration First Pass Technique; ASPECTS, Alberta Stroke Program Early CT Score; IV-tPA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale.