Original research

Early technique switch following failed passes during mechanical thrombectomy for ischemic stroke: should the approach change and when?

Pedro N Martins ,[1,2] Raul G Nogueira,[1,2,3] Mohamed A Tarek,[1,2] Jaydevsinh N Dolia,[1,2] Sunil A Sheth,[4] Santiago Ortega-Gutierrez ,[5] Sergio Salazar-Marioni,[4] Ananya Iyyangar,[4] Milagros Galecio-Castillo ,[5] Aaron Rodriguez-Calienes ,[5,6] Aqueel Pabaney,[1,2] Jonathan A Grossberg ,[1,2] Diogo C Haussen[1,2]

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[1]Department of Neurology, Emory University School of Medicine, Atlanta, Georgia, USA
[2]Grady Memorial Hospital, Atlanta, Georgia, USA
[3]UPMC, Pittsburgh, Pennsylvania, USA
[4]Department of Neurology, University of Texas Health Science Center, Houston, Texas, USA
[5]Department of Neurology, Neurosurgery and Radiology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA
[6]Grupo de Investigacion Neurociencia, Efectividad Clinica y Salud Publica, Universidad Cientifica del Sur Facultad de Ciencias de la Salud, Lima, Peru

Correspondence to
Dr Diogo C Haussen; diogo.haussen@emory.edu

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ABSTRACT

Background Fast and complete reperfusion in endovascular therapy (EVT) for ischemic stroke leads to superior clinical outcomes. The effect of changing the technical approach following initially unsuccessful passes remains undetermined.

Objective To evaluate the association between early changes to the EVT approach and reperfusion.

Methods Multicenter retrospective analysis of prospectively collected data for patients who underwent EVT for intracranial internal carotid artery, middle cerebral artery (M1/M2), or basilar artery occlusions. Changes in EVT technique after one or two failed passes with stent retriever (SR), contact aspiration (CA), or a combined technique (CT) were compared with repeating the previous strategy. The primary outcome was complete/near-complete reperfusion, defined as an expanded Thrombolysis in Cerebral Infarction (eTICI) of 2c–3, following the second and third passes.

Results Among 2968 included patients, median age was 66 years and 52% were men. Changing from SR to CA on the second or third pass was not observed to influence the rates of eTICI 2c–3, whereas changing from SR to CT after two failed passes was associated with higher chances of eTICI 2c–3 (OR=5.3, 95% CI 1.9 to 14.6). Changing from CA to CT was associated with higher eTICI 2c–3 chances after one (OR=2.9, 95% CI 1.6 to 5.5) or two (OR=2.7, 95% CI 1.0 to 7.4) failed CA passes, while switching to SR was not significantly associated with reperfusion. Following one or two failed CT passes, switching to SR was not associated with different reperfusion rates, but changing to CA after two failed CT passes was associated with lower chances of eTICI 2c–3 (OR=0.3, 95% CI 0.1 to 0.9). Rates of functional independence were similar.

Conclusions Early changes in EVT strategies were associated with higher reperfusion and should be contemplated following failed attempts with stand-alone CA or SR.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Fast and complete reperfusion in mechanical thrombectomy for stroke leads to superior clinical outcomes. However, whether early changes in reperfusion strategies after failed passes lead to earlier or greater reperfusion is not clear.

WHAT THIS STUDY ADDS

⇒ In this cohort of patients treated with stent retriever, contact aspiration, or combined technique as the first-line strategy for acute ischemic stroke treatment, we observed higher chances of reperfusion when changing to the combined technique after one or two failed contact aspiration passes, as well as after two failed stent retriever passes. Switching from the combined technique to contact aspiration after two failed combined technique passes was associated with lower chances of reperfusion.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Neurointerventionists should contemplate very early technique switches following failed passes during thrombectomy.

INTRODUCTION

The clinical benefits of endovascular therapy (EVT) have been shown strongly dependent on the degree of reperfusion in several randomized controlled trials.[1 2] Achieving faster recanalization is associated with better outcomes[3], however, no technique has been shown to lead to higher rates of reperfusion with fewer passes. The Contact Aspiration versus Stent Retriever for Successful Revascularization (ASTER) and the Aspiration thrombectomy versus stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS) trials[4 5] showed similar rates of reperfusion among participants randomized to three consecutive attempts with either contact aspiration or stent retriever (SR) with or without combined aspiration. The Combined Use of Contact Aspiration and the Stent Retriever Technique versus Stent Retriever Alone for Recanalization in Acute Cerebral Infarction (ASTER 2) trial did not show a significant difference in final reperfusion rates between participants randomized to SR or combined technique, although

higher rates of successful reperfusion with up to three combined technique attempts were reported.[6] It is common for operators to change devices or techniques after failed device passes,[7 8] however this practice may increase procedural complexity and costs despite having an undetermined benefit.[9] We aim to identify whether switching thrombectomy strategies is associated with higher reperfusion rates and to evaluate how early the potential benefit may be observed.

METHODS

Design, setting, and participants

This was a retrospective analysis of prospectively maintained databases from three comprehensive stroke centers in the United States. We included consecutive patients who presented with intracranial internal carotid artery (ICA), middle cerebral artery (MCA) M1/M2, or basilar/vertebrobasilar artery occlusion strokes and underwent EVT using either SR, catheter aspiration (contact aspiration (CA)) or a combined technique (CT: SR plus CA) for the first pass strategy. Passes employing other techniques (eg, remote balloon guide catheter aspiration, stenting, angioplasty, microwire maceration, intra-arterial thrombolysis, or a combination of those) or targeting at any other vessel (eg, anterior cerebral artery, MCA M3) were excluded. The study period spanned January 2015 (or the date on which each center started prospectively collecting thrombectomy data) to August 2023.

Patients were included for the per-pass analysis if they did not respond to the previous pass. For the third pass, patients who had undergone two passes with repeated strategies were included. Reperfusion rating was based on the expanded thrombolysis in cerebral ischemia (eTICI) scoring system.[2] For analyses evaluating eTICI 2c–3 reperfusion as outcome, the lack of response for each pass was defined as eTICI < 2c or eTICI 2c–3 with subsequent reocclusion. For analyses involving eTICI 2b–3, the lack of response was defined as eTICI < 2b. The choice of device and technique was at the treating neurointerventionists' discretion.

Outcomes

The primary endpoint was complete or near-complete recanalization (eTICI 2c–3) per pass for both the second and third passes. The secondary outcomes were successful recanalization (eTICI 2b–3) for the second and third passes, the cumulative incidences of recanalization at pass 3 according to different technique sequences, as well as the first pass effect (FPE, first pass eTICI 2c–3), functional independence (modified Rankin Scale (mRS) score ≤2) at day 90, subarachnoid hemorrhage, and parenchymal hematoma according to European Cooperative Acute Stroke Study III criteria.[10]

Endeavors to address bias

Since no specific reperfusion strategy has been demonstrated to outperform others, the decision to initiate or switch techniques was not expected to be significantly influenced by clinical or demographic characteristics. Rather, the decision on which strategy to employ is probably to be explained by the previous reperfusion grade achieved, occlusion location, resource availability, and operator preference.

Statistical analysis

Variables of interest were described as median (quartiles) or means (SD), when numeric, or absolute and relative frequencies, when discrete or ordinal. Logistic regression models with prespecified adjustments for age, occlusion location, use of balloon-guide catheter, pre-attempt eTICI, and center were used in the strategy modification analysis. Missing covariates data were handled using multiple imputation. Complications were compared via Fisher's exact test, the X^2 test, or the Kruskal-Wallis test as appropriate. Aspiration catheter sizes were compared between CT and CA using Mann-Whitney's test.

We estimated the cumulative incidences of reperfusion across different sequences of techniques using the Kaplan-Meier method. All participants with a sequence compatible with the one of interest were considered (online supplemental figure S2). We compared groups according to the technique for the three first passes for patients who underwent passes using the same technique (SR vs CA vs CT) using Cox regression adjusting for age, occlusion location, use of balloon guide catheter, and site. A two-tailed α of 0.05 was considered. All analyses were conducted using R Software v4.3.1.

RESULTS

Descriptive data

3748 procedures from three comprehensive stroke centers were assessed for eligibility, of which 2968 met inclusion criteria (online supplemental figure S1). Patients had a median (IQR) age of 66 (56–77) years and 52% were male. Strokes were predominantly due to MCA M1 occlusions, followed by MCA M2, ICA terminus, basilar artery, and petrous/cavernous ICA occlusions. Baseline characteristics for all patients included are described in online supplemental table S1. Descriptions of baseline characteristics for patients included in each pass are also detailed in the appendix (online supplemental tables S2–S4). Isolated SR was the most frequent first pass approach, followed by CT and CA, with notable between-center differences (online supplemental table S6). Strategy changes over successive passes are depicted in figure 1. Median (IQR) of passes to 2c–3 and 2b–3 reperfusion were 2 (1–4), and 1 (1–2), respectively.

Outcome data

Reperfusion with the second pass

Following a failed first pass with stand-alone SR, changing to either CT or CA was not associated with significantly different rates of eTICI 2c-3 compared with repeating another SR pass, while changing to CA was associated with lower rates of 2b–3 reperfusion. Following a failed first pass with CA, switching the second pass strategy to CT was associated with higher chances of eTICI 2c–3 as well as 2b–3 reperfusion as compared with repeating a second CA pass; switching from CA to SR was not associated with significantly different eTICI 2c–3, or 2b–3. Following a failed first pass with CT, no significant differences were observed in the chances of eTICI 2c–3 or eTICI 2b–3 after the second pass with either SR or CA alone. All analyses were adjusted for age, occlusion location, first pass eTICI score, use of balloon guide catheter, and center. The findings and the magnitude of associations are displayed in table 1 and figure 2A–C. eTICI 2c–3 and 2b–3 rates for the second pass are shown in online supplemental tables S2 and S3.

Reperfusion with the third pass

Among participants for whom SR was employed in the first and second passes, changing to the combined technique in the third pass was associated with higher rates of eTICI 2c–3 but not eTICI 2b-3, while switching to CA did not show a significant difference for either of the outcomes (table 1; figure 2D). For patients with no response to two CA passes, changing to the combined technique was associated with higher chances

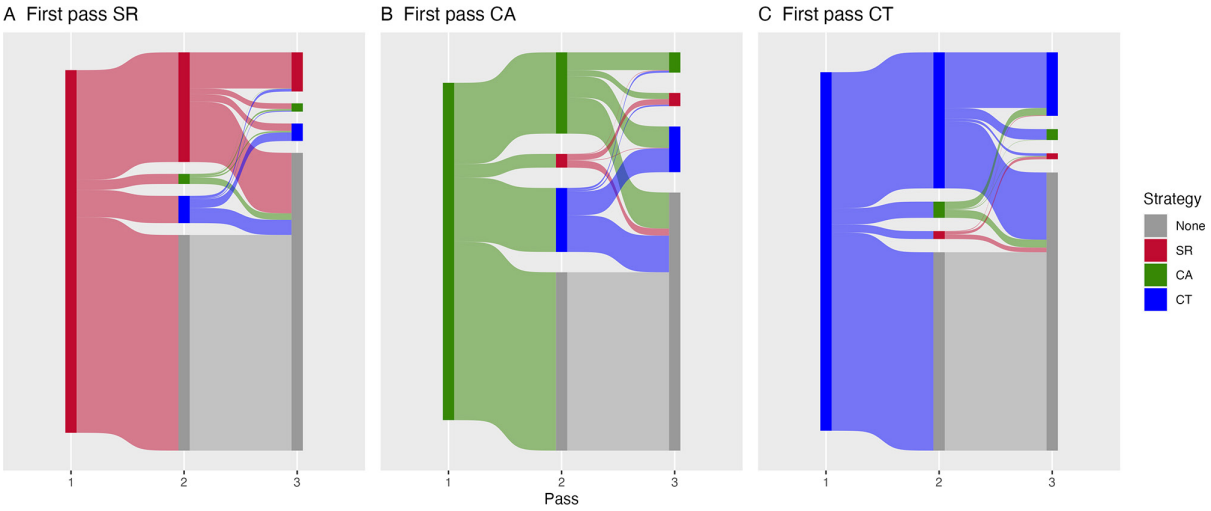

Figure 1 Sankey plot of strategy transitions over passes. 'None' refers to patients who did not undergo the corresponding pass. SR, stent retriever; CA, contact aspiration; CT, combined technique.

of eTICI 2c–3 reperfusion compared with repeating a third CA pass, with a consistent eTICI 2b–3 estimate and 95% CI although not statistically significant; changing from CA to SR was not associated with changes in the chances of eTICI 2c-3 or 2b–3 (table 1; figure 2E). After two CT passes with no response, changing to CA was associated with lower eTICI 2c-3 chances as compared with a further CT attempt, while the association for eTICI 2b–3 was not significant; switching to SR was not associated with a significant difference in the chances of either 2c–3 or 2b–3 reperfusion (table 1; figure 2F). eTICI 2c–3 and 2b–3 rates for the second pass are shown in online supplemental tables S2 and S3.

Three repeated passes

CT was associated with earlier eTICI 2c–3 reperfusion when compared with CA (adjusted hazard ratio (aHR)=1.3, 95% CI 1.0 to 1.7, P=0.014). No significant differences were observed between CT and SR (aHR=1.1, 95% CI 0.9 to 1.3; P=0.337) or SR and CA (aHR=1.2, 95% CI 1.0 to 1.5; P=0.087) (figure 3A). Consistent results were observed for eTICI 2b–3 (online supplemental figure S3).

First pass effect

After adjusting for age, occlusion location, balloon guide catheter use, and center, the combined technique outperformed aspiration alone for first pass effect (aOR=1.3, 95% CI 1.0 to 1.6; P=0.027) but its difference versus SR was not statistically significant (aOR=1.1, 95% CI 0.9 to 1.3; P=0.296). Stent retriever and aspiration were not significantly different (aOR=1.2, 95% CI 0.9 to 1.5; P=0.166). Of note, first pass strategies differed across sites (online supplemental table S6). The inner diameter of aspiration catheters used for CA and CT in the first and second passes is described in online supplemental table S7.

Modified Rankin Scale at day 90

Neither univariate nor multivariate analysis of day 90 independence rates showed significant differences across strata change in the second pass, although estimates and 95% confidence intervals were consistent with the reperfusion rate findings (online supplemental table S8). Ordinal analyses of the mRS for missing 90-day mRS scores also yielded non-significant results (online supplemental table S9).

Table 1 Logistic regression models for 2c–3 and 2b-3 reperfusion following one or two failed passes

First pass strategy	Stent retriever				Contact aspiration				Combined			
Second pass outcome (eTICI)	2c–3		2b–3		2c–3		2b–3		2c–3		2b–3	
Strategy	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value
Stent retriever	—		—		1.9 (0.6 to 6.3)	0.272	3.9 (0.8 to 18.0)	0.080	1.3 (0.5 to 3.7)	0.579	1.0 (0.3 to 3.5)	0.951
Contact aspiration	0.5 (0.2 to 1.3)	0.142	0.3 (0.1 to 0.9)	**0.028**	—		—		0.4 (0.2 to 1.0)	0.064	0.5 (0.2 to 1.1)	0.072
Combined	1.1 (0.7 to 1.9)	0.620	0.9 (0.5 to 1.6)	0.767	2.9 (1.6 to 5.5)	**<0.001**	3.3 (1.7 to 6.3)	**<0.001**	—		—	
Two first passes strategy	**2 x Stent retriever**				**2 x Contact aspiration**				**2 x Combined**			
Third pass outcome (eTICI)	**2c–3**		**2b–3**		**2c–3**		**2b–3**		**2c–3**		**2b–3**	
Strategy	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**
Stent retriever	—		—		0.5 (0.1 to 3.2)	0.425	1.4 (0.2 to 11.7)	0.735	1.1 (0.3 to 3.7)	0.571	3.0 (0.3 to 28.7)	0.340
Contact aspiration	0.7 (0.2 to 2.9)	0.665	0.8 (0.3, 2.4)	0.698	—		—		0.3 (0.1 to 0.9)	**0.032**	0.8 (0.3 to 2.3)	0.676
Combined	5.3 (1.9 to 14.6)	**0.001**	1.8 (0.7, 4.3)	0.210	2.7 (1.0 to 7.4)	**0.048**	2.6 (0.8 to 9.0)	0.124	—		—	

Models adjusted for age, occlusion location, previous pass eTICI, balloon guide catheter use, and center.
eTICI, extended Thrombolysis in Cerebral Infarction.

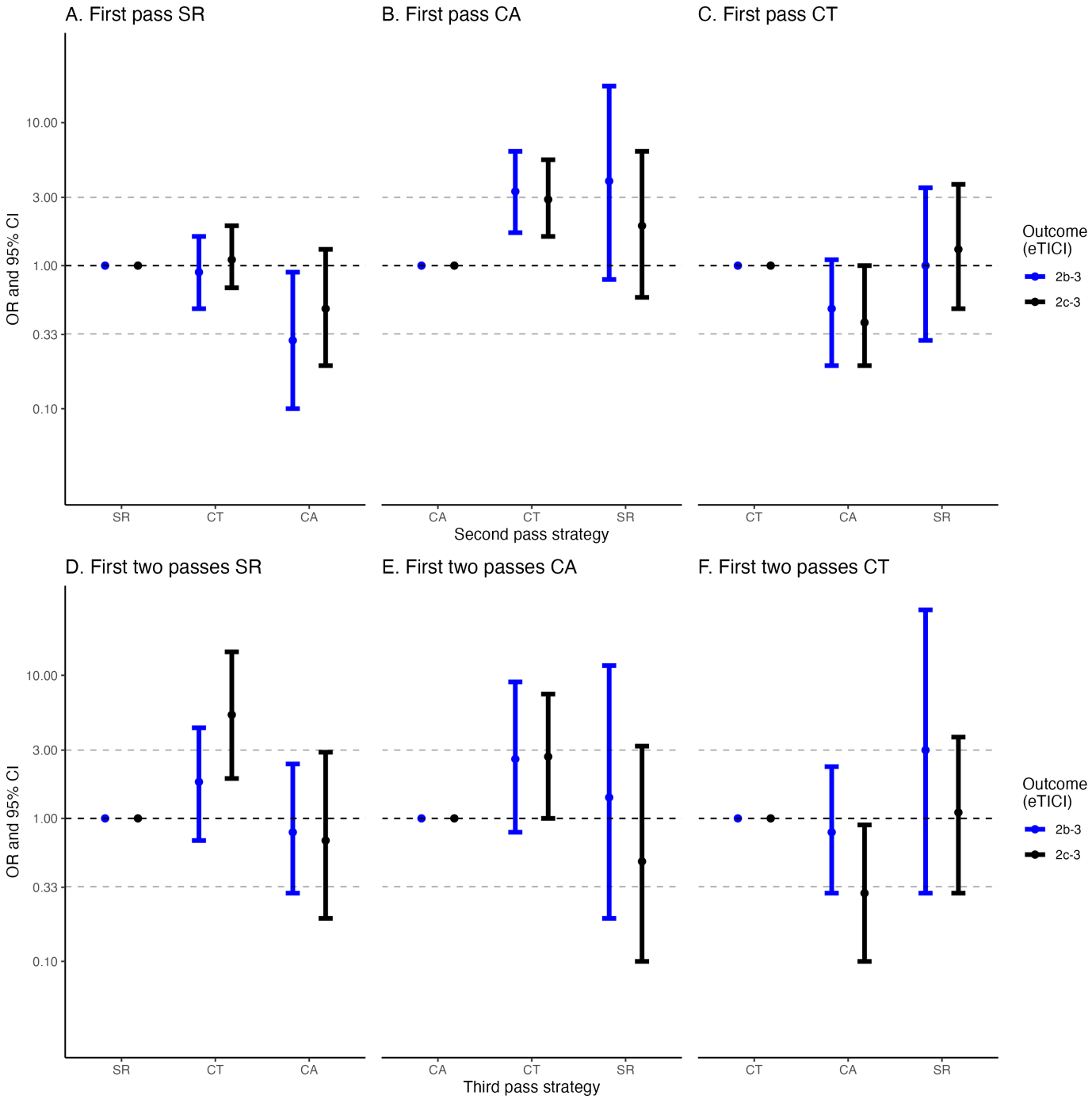

Figure 2 Association between changes in technique and reperfusion outcomes. SR, stent retriever; CA, contact aspiration; CT, combined technique; eTICI, expanded Thrombolysis in Cerebral Infarction; OR: Odds Ratio; CI: Confidence Interval.

Procedural time

Overall procedural time was lower for patients undergoing first-line CA when compared with SR or CT (median 39 vs 49 vs 50 min, P<0.001, online supplemental table S1). Switching strategies after a failed first pass with SR or CA was not associated with longer procedures (online supplemental tables S2–S4), whereas changing from CT to CA was associated with a longer procedural time (online supplemental table S2). No differences in procedural duration were observed if changes were made or not for pass 3.

Complications

No differences were observed among strategies in relation to the rates of subarachnoid hemorrhage or parenchymal hematoma according to first and second pass techniques (online supplemental table S10).

DISCUSSION

In this cohort of patients undergoing mechanical thrombectomy in three comprehensive stroke centers in the United States, switching to the combined technique after as early as one failed contact aspiration pass or two failed stent retriever passes was associated with higher full/near-full reperfusion rates, whereas changing to contact aspiration after two failed combined technique passes was found to be associated with lower chances of eTICI 2c–3 reperfusion.

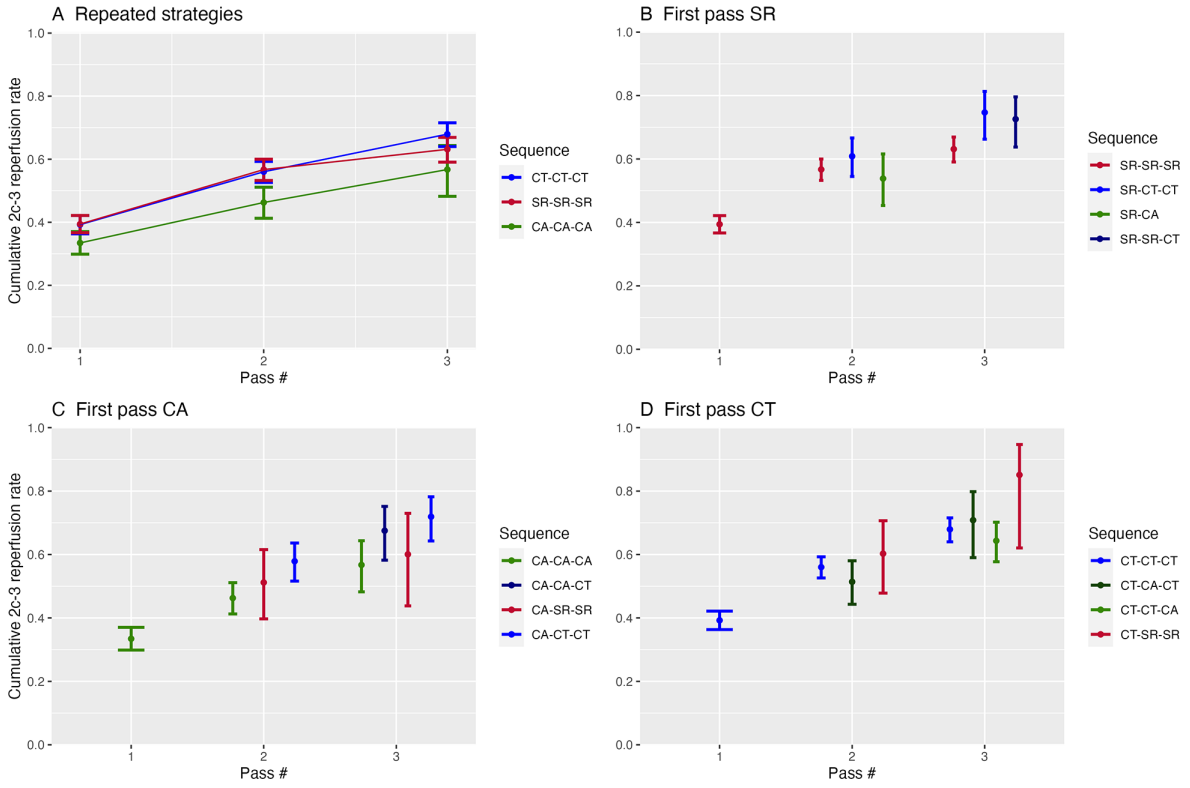

Figure 3 Cumulative incidences of eTICI 2c–3 according to reperfusion strategies. Final eTICI 2c–3 proportions (95% CIs): 63.1% (59.1% to 63.9%) for SR; 56.7% (48.2% to 64.3%) for CA and 67.9% (64.0% to 71.5%) for CT. CA, contact aspiration; CT, combined technique; eTICI, expanded Thrombolysis in Cerebral Infarction; SR, stent retriever. Bars represent the 95% confidence intervals.

The extent and speed of reperfusion has a substantial impact on clinical outcomes, and first pass eTICI 2c–3 is the primary angiographic goal of mechanical thrombectomy since it has been unequivocally associated with the highest rates of functional independence. The HERMES meta-analysis demonstrated that, compared with eTICI 0, the adjusted odds of mRS 0-2 at 90 days increased along with the degree of reperfusion (eTICI 2a: OR=1.4; eTICI 2b50: OR=2.4; eTICI 2b67: OR=5.1; eTICI 2c: OR=5.2; eTICI 3: OR=7.3).[2] Additionally, as the number of required passes increases, the odds of a favorable clinical outcome decrease while the risk of intracranial hemorrhage rises.[1 3 11–14] Although final eTICI 2c–3 rates as high as 65% have been reported in clinical trials, the FPE was only achieved in 23–41% of patients with proximal large vessel occlusions in contemporary series and randomized trials.[1 6 14–20] Incorporating practice patterns that lead to faster and more complete reperfusion is therefore essential for improving clinical outcomes.

Randomized studies comparing MT strategies include the ASTER trial,[4] which showed no difference in angiographic outcomes between up to three contact aspiration versus stent retriever passes in 189 patients, with a cumulative eTICI 2c–3 proportion of 56.6% for SR versus 56.3% for CA in the intention-to-treat analysis (P=0.82) and cumulative eTICI 2b–3 proportions of 83.1% (SR) and 85.4% (CA). A secondary analysis showed similar rates of first pass effect between SR and CA (31.3% vs 26.3%, P=0.44).[20] Our findings compare favorably, as our hazard ratios for complete or near-complete reperfusion were approximately 1 when comparing stand-alone CA against SR after adjusting for age, occlusion location, balloon-guide catheter use and center. In addition, the present data suggest a potential negative impact of transitioning to CA after one failed SR pass for eTICI 2b–3 when compared with repeating the initial strategy. The COMPASS trial randomized 270 patients and reinforced the hypothesis of similar performance between SR and CA for eTICI 2c–3 within 45 min of access and first pass eTICI 2b–3, although CA outperformed SR for eTICI 3 within 45 min and time to eTICI 2b–3.[5] The study compared time to outcome rather than number of passes and did not disclose first pass eTICI 2c-3 data, limiting comparisons. Of note, 85% of the patients randomized to SR had distal aspiration combined with SR thrombectomy at some point during their procedure.

The ASTER 2 study[6] did not observe significant differences between the CT and SR alone among 405 patients for the prespecified primary outcome of eTICI 2c–3 with up to three passes (65% vs 58%, OR=1.33, 95% CI 0.88 to 1.99; P=0.17). The present findings are consistent with ASTER 2, as the comparison between up to three successive CT passes and up to three isolated SR also showed a higher, but not significantly different proportion of eTICI 2c–3 in the CT group (67.9% vs 63.2%, aHR=1.1, 95% CI 1.0 to 1.3; P=0.103) (figure 3). Estimates for first pass effect were also comparable between the ASTER 2 trial and this study. Whereas the trial estimated an OR for FPE of 1.4 (95% CI 0.9 to 2.1; P=0.12), the present study found an adjusted OR of 1.1 (95% CI 0.9 to 1.3; P=0.296).

Studies directly comparing CA with CT are more scarce. The Penumbra Separator 3D trial[21] supported the similarity of both techniques for cumulative mTICI 2–3 and 2b–3, although the 3D Separator device was not designed for, and has not been demonstrated to function by itself as, a reperfusion device. Preliminary data presented at the European Stroke Organization Conference 2023 on the Adaptive endovascular strategy to the CloT MRI in large intracranial vessel occlusion (VECTOR) trial demonstrated earlier reperfusion was accomplished with the CT than with CA, with an absolute difference of 11% in FPE favoring the combined

technique, although the final rates or eTICI 2c–3, defined as the primary endpoint, were not significantly different between groups.[22 23] Our analyses also showed a benefit for earlier reperfusion with the combined technique when compared to contact aspiration alone (aHR 1.3, 95% CI 1.0 to 1.7, P=0.014) which may be attributable to first pass effect, for which a difference in favor of CT was also noted (aOR=1.3, 95% CI 1.0 to 1.6; P=0.027). Contact aspiration techniques have had a remarkable evolution and increasing use in the past years, which was also observed in our study (online supplemental figure S4), and a part of the lower reperfusion rates in our study could be explained by successive changes in device characteristics over time as well as operator experience with the technique. The discrepancy in cumulative reperfusion with three passes between the studies may reside in the fact that VECTOR included solely subjects with a positive susceptibility vessel sign (indicating red-cell-rich thrombi) on MRI, while the present series did not take clot characteristics into consideration.

The responsiveness of patients to given strategies might vary due to several factors. Clot composition may play a significant role, with red-cell-rich thrombi potentially being more responsive to SR than to CA[24 25]. However, biomarkers for determining clot composition and data supporting device/technique-specific benefits related to preprocedural thrombus profiling are scarce. A failed pass might also contribute to responsiveness to further passes and to specific techniques through its impact on the vessel wall and clot structure.[26] The responsiveness to a specific technique might influence the chances of reperfusion in subsequent passes,[3] supporting the concept that very early modification of the thrombectomy technique may be desirable, and that the lack of difference in cumulative reperfusion observed in trials might relate to the less substantial benefit with repeated passes using the same technique. Vessel angulation at the site of occlusion has been demonstrated to affect the performance of the Merci retriever,[27] as well as SR[28] and CA[29] thrombectomy. It is possible that the combined technique might allow for a synergistic effect by (1) straightening the artery and allowing for the aspiration catheter to engage the clot following its main longitudinal axis and (2) attenuating the effect of clot adhesiveness by minimizing the area of thrombus exposed to the endothelium and decreasing the magnitude of breakaway force required for clot dislodgement.

Our study has several limitations, including weaknesses inherent to the study design such as unmeasured confounders. A propensity for certain first pass techniques in different centers was noted, which led to a between-center exploratory analysis that ultimately showed no significant interactions. Sample size limitations precluded the comparison of effects between anterior and posterior circulation occlusions. The selection of techniques based on the neurointerventionist's discretion and experience with diverse techniques might have introduced bias. This study was not designed to evaluate the impact of changes in reperfusion strategies on clinical outcomes. There was no central adjudication for reperfusion scoring. There was substantial heterogeneity in device types and sizes; device stratification would lead the analysis to limited subgroup sample sizes. Although SR sizing and length were not controlled for, the size of aspiration catheter inner diameter was comparable between CA and CT for the second pass and minimally larger for CA as compared to CT for the first pass, therefore not explaining the observed benefit of CT. The analysis related to procedural times is exploratory and did not consider potential confounders.

CONCLUSION

Very early changes to the combined technique after failed standalone CA or SR passes were associated with higher chances of reperfusion and should be contemplated. Additional studies are warranted to validate the benefit associated with switching strategies in mechanical thrombectomy.

Correction notice Since this article first published, the authors identified errors in the results for the secondary outcome (eTICI 2b-3) presented in Table 1 and Figure 2. These and the results section were updated. This correction has no impact on the conclusions.

X Santiago Ortega-Gutierrez @CerebrovascLab, Milagros Galecio-Castillo @mili_galecio, Aaron Rodriguez-Calienes @AaronCalienes, Jonathan A Grossberg @JAGrossbergMD and Diogo C Haussen @diogohaussen

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ORCID iDs
Pedro N Martins http://orcid.org/0000-0002-5760-6869
Santiago Ortega-Gutierrez http://orcid.org/0000-0002-3408-1297
Milagros Galecio-Castillo http://orcid.org/0000-0002-8107-9632
Aaron Rodriguez-Calienes http://orcid.org/0000-0002-8413-6954
Jonathan A Grossberg http://orcid.org/0000-0002-1152-8826

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