RESEARCH ARTICLE

The Benefit of a Complete over a Successful Reperfusion Decreases with Time

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Objective: Time from stroke onset to reperfusion (TSOR) is strongly associated with outcomes after endovascular treatment. A near-to-complete or complete reperfusion (modified Treatment in Cerebral Ischemia [mTICI] 2c–3) is associated with improved outcomes compared with a successful reperfusion (mTICI 2b). However, it is unknown whether this association remains stable as TSOR increases. Therefore, we sought to investigate the association between TSOR and outcomes according to the reperfusion status.

Methods: We analyzed data from the Endovascular Treatment in Ischemic Stroke registry, a prospective, observational, multicentric study of acute ischemic stroke patients treated with endovascular treatment in 21 centers in France. We included patients with anterior occlusions (M1, internal carotid artery, tandem), with a known time of symptom onset. Outcomes were early neurological improvement at 24 hours and favorable outcome (modified Rankin Scale between 0 and 2) at 90 days.

Results: Overall, 4,444 patients were analyzed. Compared with a mTICI 2b, a mTICI 2c-3 at 1 hour was associated with higher mean marginal probabilities of early neurological improvement (25.6%, 95% CI 11.7–39.5, $p = 0.0003$) and favorable outcome (15.2%, 95% CI 3.0–27.4, $p = 0.0143$), and progressively declined with TSOR. The benefit of a mTICI 2c-3 over a mTICI 2b was no longer significant regarding the rates of early neurological improvement and favorable outcome after a TSOR of 414 and 344 minutes, respectively.

Interpretation: The prognostic value of a complete over a successful reperfusion progressively declined with time, and no difference regarding the rates of favorable outcome was observed between a complete and successful reperfusion beyond 5.7 hours.

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Introduction

Endovascular therapy (EVT) has revolutionized the treatment and prognosis of acute ischemic stroke (AIS) patients due to an anterior large vessel occlusion (LVO).[1] Among the numerous factors associated with functional outcomes is time from symptom onset to reperfusion (TSOR).[2,3] In a meta-analysis of individual data from 5 randomized controlled trials, the probability of functional independence at 90 days declined from 64.1% to 46.1% for a TSOR of 180 minutes and 480 minutes, respectively.[3] In addition, a time from symptom onset to arterial puncture beyond 7 hours and 18 minutes was not significantly associated with improved functional outcomes, compared with medical management alone.[3] These data coming from randomized controlled trials, with strict inclusion and exclusion criteria, and possibly the selection of patients with favorable imaging criteria, Mulder et al assessed the prognostic significance of TSOR in the prospective, observational Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in The Netherlands (MR CLEAN) registry.[2] Similarly, the probability of functional independence at 90 days declined by 7.7% per each hour increase for the TSOR, with 62.7% patients being functionally independent at 90 days for a TSOR of 120 minutes, and only 24.4% patients at 420 minutes.[2] In the aforementioned studies, reperfusion was defined by a modified or extended Thrombolysis in Cerebral Ischemia (mTICI, eTICI) ≥2b, but the effect of the final reperfusion score (ie, TICI 2b, 2c, or 3) was not specifically addressed according to the TSOR. A great deal of evidence has consistently shown the benefit in terms of increased functional independence of a near-to-complete (mTICI 2c) or complete (mTICI 3) reperfusion at the end of EVT over an incomplete, but still successful, reperfusion (mTICI 2b).[4–7] However, it is unknown whether the effect of a near-to-complete or complete reperfusion on functional outcomes remains stable as TSOR increases. This point is of importance for several reasons: (1) from a clinical practice perspective, as it could guide the interventionist to avoid excessive risks of seeking a complete reperfusion according to the TSOR, if a successful reperfusion is already achieved, and (2) from a research perspective, especially for the design of future randomized clinical trials.

With this as a background, we sought to investigate, in a real-life prospective registry, the effect of TSOR on functional outcome at 90 days, according to the final reperfusion status at the end of EVT.

Methods

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

Study Population

We used data from the Endovascular Treatment in Ischemic Stroke (ETIS) registry (NCT03776877), which is an ongoing, multicenter, prospective, observational study evaluating patients suffering from an AIS due to an anterior or posterior LVO treated with EVT in 21 comprehensive stroke centers in France (Supplementary Table S1). Data of the ETIS registry were collected and analyzed according to the recommandations of the "*Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé*." The present study was approved by the ethical committee (ID RCB 2017-A03457-46). Written informed consent was obtained from all patients or their legal representatives. Details regarding data collection and materials have been previously published.[8]

For the present study, we included adult patients (aged ≥18 years) with an anterior LVO (intracranial internal carotid artery, M1 segment of the middle cerebral artery, tandem occlusions) treated by EVT between January 1, 2015 to December 31, 2021, with a known symptom onset (ie, witnessed onset in all patients). Patients with unknown onset time or unwitnessed onset, such as "wake-up" stroke, M2 occlusions, posterior LVO, or isolated extracranial internal carotid artery occlusions, for whom EVT was not performed, and with successful (≥mTICI 2b) reperfusion at the beginning of EVT were excluded.

Clinical Definitions and Time Metrics

Patients' clinical, radiological, and treatment characteristics were collected prospectively. Most patients preferentially underwent brain magnetic resonance imaging (MRI) at baseline or brain computed tomography (CT) scan with CT angiography in cases of MRI contraindication. The Alberta Stroke Program Early CT score (ASPECTS) was assessed on the baseline CT or diffusion weighted imaging. Patients were treated in a dedicated neuroangiography suite with up-to-date equipment under conscious sedation or general anesthesia. Successful, near-to-complete, and complete reperfusion were defined as a mTICI score of 2b, 2c–3, and 3, respectively. The final mTICI score were assessed by one neuroradiologist for each center (>10 years of experience), prospectively, blinded to the results of clinical outcome. CT scan or brain MRI were performed systematically 24 hours after EVT, and also analyzed by one neuroradiologist (>10 years of experience) of each center blinded to the procedure and clinical outcome. Functional outcome was assessed by certified neurologists or research nurses with the modified Rankin Scale (mRS) at 90 days, during face-to-face interviews or phone calls with the patient or their relatives. Time from symptom onset to

EVT start was defined as the time from symptom onset to arterial puncture in the angio suite, and time from symptom onset to reperfusion was defined as the time from symptom onset to successful reperfusion (mTICI ≥2b) for patients in whom EVT was performed, as previously published.[2] In case of EVT failure (mTICI ≤2a), we considered the time from symptom onset to arterial closure (ie, end of the procedure).

Clinical and Radiological Outcomes

Early neurological improvement at 24 hours was defined as a National Institutes of Health Stroke Scale (NIHSS) between 0 and 1 at 24 hours or a reduction of at least 8 points on the NIHSS. Favorable outcome was defined as a mRS between 0 and 2 at 90 days. Safety outcomes included symptomatic intracranial hemorrhage, defined as any intracranial hemorrhages on the 24-hour brain CT associated with an increase of ≥4 points on the NIHSS within 24 hours attributable to the ICH,[9] and all-cause mortality at 90 days.

Statistical Analysis

Quantitative variables were expressed as mean (SD) for normally distributed parameters or median (interquartile range [IQR]) otherwise. Categorical variables were expressed as numbers (percentage). Baseline characteristics were compared using the Student's *t*-test for Gaussian continuous variables, Mann–Whitney *U*-test for non-Gaussian continuous variables, or the χ^2-test (or Fisher's exact test when the expected cell frequency was <5) for categorical variables, as appropriate.

The relationship of outcome variables (early neurological improvement, mRS 0–2, mRS 0–1, and mortality) with reperfusion grades (mTICI 0-2a, mTICI 2b, and mTICI 2c-3) and time from onset to recanalization were assessed with mixed multiple logistic regression models, with center as the random effect and adjustment for prespecified confounding factors (age, sex, baseline ASPECTS, and NIHSS, use of intravenous thrombolysis [IVT]) to reduce the residual imbalances. Furthermore, interaction terms were tested and were retained in the models when significant. The relationship of complete or near complete (mTICI 2c–3) and successful (mTICI 2b) reperfusion with TSOR was further assessed in the subgroup of patients who had received and the subgroup who had not received IVT. Statistical analyses were conducted at a two-tailed α level of 0.05. The data were analyzed using Stata version 17 (StataCorp, College Station, TX).

Results

From January 1, 2015 to December 31, 2021, 4,964 patients presenting with an AIS due to an anterior LVO (M1, internal carotid artery, or tandem occlusions) with a known symptom onset were included in the ETIS registry. Among these patients, 502 were excluded for the following reasons: age under 18 years (n = 5), EVT procedure not realized (n = 431), and recanalization status was not recorded (n = 66). Altogether, 4,444 were included in the present study (Figure 1).

Baseline characteristics of the included patients are shown in Table . The mean age was 70 ± 15 years, and the baseline NIHSS score and ASPECTS were 17 (IQR 9) and 8 (IQR 3), respectively. Overall, 2,188 patients were transferred from a primary stroke center (50.5%), 65.8% (n = 2,923) patients had an M1 occlusion, 19.1% (n = 847) an intracranial internal carotid artery occlusion, and 15.2% (n = 674) had a tandem occlusion. mTICI 2b was achieved in 24.1% (n = 1,071) patients, a mTICI 2c-3 in 64.1% (n = 2,849), and 11.8% (n = 524) had an EVT failure (mTICI 0-2a). At 24 hours, 50.7% (n = 2,255) experienced an early neurological improvement, and 43% (n = 1,697) a favorable outcome at 90 days.

In the overall population, the median time from stroke onset to arterial puncture was 253 minutes (IQR 123 minutes), and 301 (IQR 147 minutes) for stroke onset to reperfusion. Patients with a mTICI 2c–3 had shorter median times from symptom onset to reperfusion (294 vs 310 vs 342 minutes for mTICI 2c-3, mTICI 2b, and mTICI 0-2a, respectively, $p < 0.001$; Table). The number of patients treated with EVT according to TSOR is shown in Table S2.

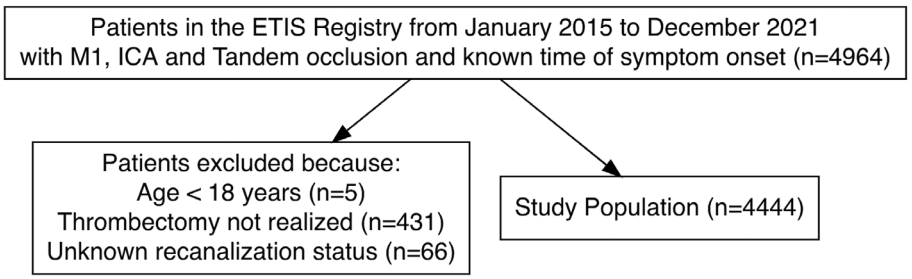

FIGURE 1: Study flow chart. ETIS = Endovascular Treatment in Ischemic Stroke; ICA = internal carotid artery.

TABLE. Baseline Characteristics and Main Outcomes in the Overall Cohort and According to the Final Modified Treatment in Cerebral Ischemia Score

	Total (n = 44,444)	mTICI 0-2a (n = 524, 11.8%)	mTICI 2b (n = 1,071, 24.1%)	mTICI 2c-3 (n = 2,849, 64.1%)	*p*
Age, mean (SD)	70 (15)	70 (15)	69 (15)	71 (14)	0.001
Sex (female), n (%)	2,165 (48.8)	258 (49.3)	490 (45.9)	1,417 (49.8)	0.088
Hypertension, n (%)	2,537 (58.4)	317 (61.3)	568 (54.0)	1,652 (59.6)	0.003
Hypercholesterolemia, n (%)	1,292 (30.2)	159 (31.2)	281 (27.4)	852 (31.1)	0.077
Smoking, n (%)	778 (18.8)	99 (20.4)	198 (19.9)	481 (18.1)	0.295
Diabetes, n (%)	736 (17.1)	72 (14.1)	164 (15.9)	500 (18.1)	0.041
Prior stroke, n (%)	616 (15.4)	82 (18.1)	121 (13.3)	413 (15.6)	0.056
Pre-stroke mRS 0–2, n (%)	3,984 (94.1)	477 (94.8)	956 (94.7)	2,551 (93.8)	0.442
Antiplatelet therapy, n (%)	926 (21.6)	100 (19.8)	191 (18.7)	635 (23.0)	0.010
Anticoagulation, n (%)	776 (23.7)	97 (24.6)	147 (18.0)	532 (25.8)	0.000
Baseline SBP (mmHg), mean (SD)	147 (26)	149 (26)	147 (26)	146 (26)	0.127
Baseline DBP (mmHg), mean (SD)	82 (18)	85 (20)	82 (16)	81 (17)	0.000
Baseline NIHSS, median (IQR)	17 (9)	17 (9)	17 (9)	17 (9)	0.608
Baseline ASPECTS, median (IQR)	8 (3)	8 (4)	8 (3)	8 (3)	0.000
Etiology, n (%)					
Atherothrombosis	630 (15.4)	92 (18.9)	164 (16.8)	374 (14.3)	0.001
Cardioembolic	1902 (46.6)	208 (42.6)	424 (43.4)	1,270 (48.5)	
Dissection	167 (4.1)	30 (6.1)	54 (5.5)	83 (3.2)	
Other/unknown	1,385 (31.2)	158 (30.2)	334 (31.2)	893 (31.3)	
Site of occlusion on invasive imaging, n (%)					
M1	2,923 (65.8)	310 (59.2)	658 (61.4)	1955 (68.6)	0.000
Intracranial ICA	847 (19.1)	117 (22.3)	190 (17.7)	540 (19.0)	
Tandem occlusion	674 (15.2)	97 (18.5)	223 (20.8)	354 (12.4)	
Intravenous thrombolysis, n (%)	2,545 (57.4)	256 (48.9)	644 (60.2)	1,645 (57.9)	0.000
Transfer from primary stroke center, n (%)	2,188 (50.5)	263 (51.9)	577 (55.7)	1,348 (48.3)	0.001
Time from symptom onset to puncture, median (IQR)	253 (139)	256 (150)	255 (134)	250 (139)	0.439
Time from symptom onset to recanalization, median (IQR)	301 (147)	342 (160)	310 (148)	294 (146)	0.000
Early neurological improvement at 24 h, n (%)	2,255 (50.7)	146 (27.9)	484 (45.2)	1,625 (57.0)	0.000
Favorable outcome (mRS 0–2) at 90 days, n (%)	1,697 (43.0)	63 (13.6)	393 (41.9)	1,241 (48.9)	0.000
Excellent outcome (mRS 0–1) at 90 days, n (%)	1,138 (28.9)	39 (8.4)	259 (27.6)	840 (33.1)	0.000
All-cause mortality at 90 days (yes), n (%)	855 (21.7)	194 (41.8)	217 (23.1)	444 (17.5)	0.000
Any ICH, n (%)	1,673 (44.7)	214 (49.0)	445 (49.2)	1,014 (42.2)	0.000
Symptomatic ICH, n (%)	328 (8.8)	61 (14.0)	103 (11.4)	164 (6.9)	0.000

Abbreviation: ASPECTS = Alberta Stroke Program Early CT Score; DBP = diastolic blood pressure; ICA = internal carotid artery; ICH = intracranial hemorrhage; IQR = interquartile range; mRS = modified Rankin Scale; mTICI = modified Treatment in Cerebral Ischemia; NIHSS = National Institutes of Health Stroke Scale; SBP = systolic blood pressure; SD = standard deviation.

Clinical Outcomes According to the Reperfusion Status and Time

Early Neurological Improvement at 24 Hours. At 1 hour after symptom onset, a mTICI 2c–3 was associated with a higher mean marginal probability of early neurological improvement at 24 hours, by an average of 25.6% (95% CI 11.7 to 39.5, $p < 0.001$) compared with a mTICI 2b (Figure 2). At 3 hours after symptom onset, this difference dropped to 18.7% (95% CI 11.7 to 25.7, $p < 0.001$), and dropped further to 7.7% (95% CI 3.0 to 12.4, $p = 0.001$) at 6 hours. This difference became insignificant at 414 minutes (mean marginal probability difference 5.5%, 95% CI −0.1 to 11.1, $p = 0.052$).

Favorable Outcome at 90 Days. At 1 hour after symptom onset, patients with mTICI 2c–3 had a higher mean marginal probability of favorable functional outcome (mRS 0–2) by an average of 15.2% (95% CI 3.0 to 27.4, $p = 0.014$) compared with patients with a mTICI 2b (Figure 3). At 3 hours after symptom onset, the difference dropped to 10.9% (95% CI, 4.1–17.7, $p = 0.002$), and became insignificant after 344 minutes (mean marginal probability difference 4.25%, 95% CI −0.04 to −8.54, $p = 0.052$). When the time from symptom onset to arterial puncture was considered, the mean marginal probability difference of a favorable outcome became insignificant at 327 minutes (mean marginal probability difference 4.5%, 95% CI −0.1 to −9.1, $p = 0.053$; Figure 4).

In addition, the mean marginal probability difference of a favorable outcome between patients with a mTICI 2c-3 and mTICI 2b became insignificant at 250 minutes (OR 0.07, 95% CI 0–0.13, $p = 0.051$) for patients who did not receive IVT before EVT, and at 329 minutes (OR 0.05, 95% CI, 0–0.1, $p = 0.051$) for patients who received IVT before EVT.

All-Cause Mortality at 90 Days. The mean marginal probability difference between a mTICI 2b and a mTICI 2c–3 was stable as TSOR increased (−5.3%, 95% CI −8.5 to −2.2, $p = 0.001$; Figure 5). For both mTICI 2b and mTICI 2c–3, the mean marginal probability increased every hour by 3.5% (95% CI 2.6 to 4.3, $p < 0.001$; Figure 5).

Discussion

In the present study, we showed that the effect of the angiographic reperfusion status (mTICI 2b versus mTICI 2c-3) on ENI at 24 hours and favorable outcome at 90 days was not stable as TSOR increased. The benefit of a mTICI 2c-3 progressively declined with TSOR, until 414 minutes (6.9 hours), at which point there was no longer any prognostic value of a mTICI 2c–3 over a mTICI 2b at the end of EVT for ENI. We found similar results for favorable functional outcome, for which beyond 344 minutes (5.7 hours), the mean marginal probability difference of functional independence at 90 days between mTICI 2b and mTICI 2c–3 patients was not statistically significant.

Due to the increasing expertise of endovascular techniques and important technological developments in the field, the current aim of EVT procedures is to reach the best possible reperfusion score,[4–7] as quickly as possible,[2,3] with the fewest possible thrombectomy passes.[10,11] These goals apply to nearly all EVT procedures, especially regardless of time, as several previous works have shown the prognostic value of a near-to-complete or complete reperfusion (mTICI 2c–3) over a successful reperfusion (mTICI 2b),[5–7,12] obtained after only one pass of thrombectomy.[13,14] In this search for perfection, it is increasingly common that the procedure continues despite having reached a mTICI 2b, unfortunately at the cost of increased procedural risks sometimes. In this context, several studies have indeed underscored the feasibility of treating distal occlusions,[15,16] and randomized controlled trials are currently being performed. That being said, it is still unclear whether the benefit of a near-to-complete or complete reperfusion (mTICI 2c-3) is stable as TSOR increases, and whether the prevailing management described above should apply to all EVT procedures. The present results suggest that the prognostic value of a complete reperfusion over a successful reperfusion progressively declined over time, until it was no longer significant. A possible explanation for these results could be a progressive decrease of the salvageable penumbra over time (ie, infarct growth), such that the reperfusion of the

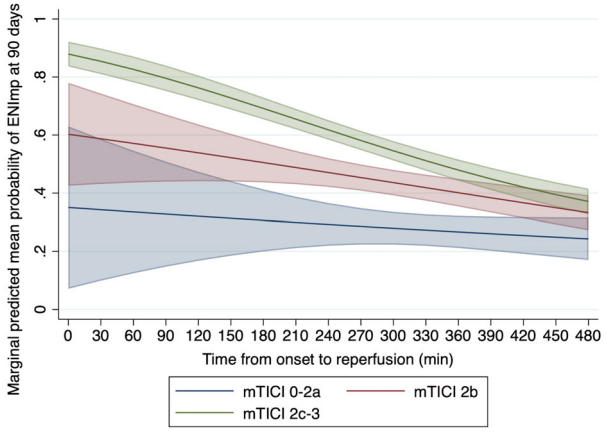

FIGURE 2: Association between early neurological improvement at 24 hours and time from symptom onset to reperfusion according to the reperfusion status. ENImp = early neurological improvement; mTICI = modified Treatment in Cerebral Ischemia.

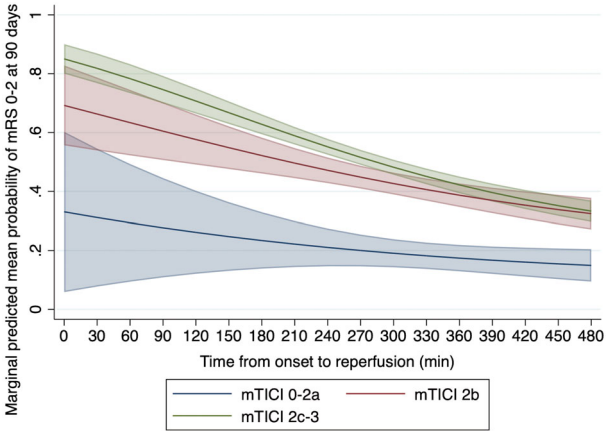

FIGURE 3: Association between favorable outcome at 90 days and time from symptom onset to reperfusion according to the reperfusion status. mRS = modified Rankin Scale; mTICI = modified Treatment in Cerebral Ischemia.

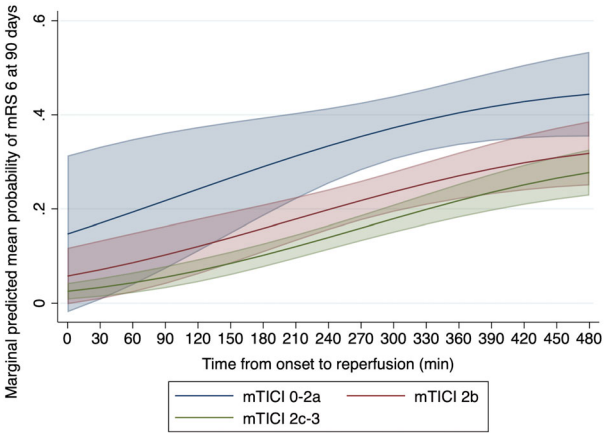

FIGURE 5: Association between all-cause mortality at 90 days and time from symptom onset to reperfusion according to the reperfusion status. mRS = modified Rankin Scale; mTICI = modified Treatment in Cerebral Ischemia.

occluded branches responsible for the mTICI 2b over mTICI 2c–3 would not translate into an improved clinical outcome. This hypothesis is reinforced by the fact that 50.5% of the patients were transferred from a primary stroke center, where the initial brain imaging used for EVT selection was performed and not repeated at the comprehensive stroke center (ie, straight to the angio suite after transfer).[17] Importantly, the present results do not suggest to solely rely on the timeframes presented in this study to define the endovascular strategy (mTICI 2b vs 2c–3), as we only present mean marginal probabilities. Interestingly, we found that the mean marginal probability difference of a favorable outcome between mTICI 2c–3 and mTICI 2b patients became insignificant after 250 minutes and 329 minutes in no-IVT and IVT patients, respectively. It is therefore possible that IVT had a local effect on the microcirculation, allowing local

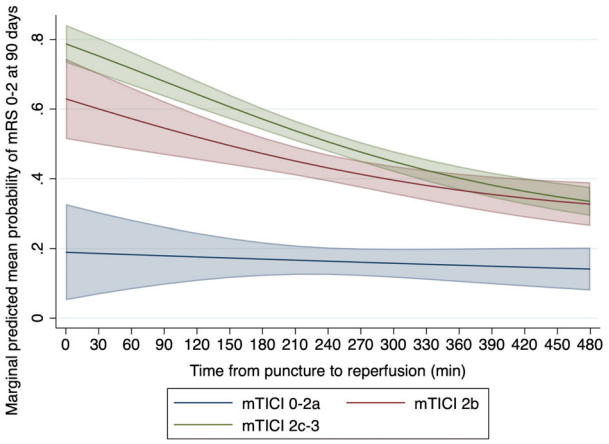

FIGURE 4: Association between favorable outcome at 90 days and time from symptom onset to arterial puncture according to the reperfusion status. mRS = modified Rankin Scale; mTICI = modified Treatment in Cerebral Ischemia.

reperfusion before recanalization with EVT has occurred, hence favoring the maintenance of the salvageable penumbra as TSOR increases. Indeed, the prognostic significance of reperfusion with IVT despite the lack of recanalization has already been reported to be strongly associated with favorable outcomes at 3 months and may explain this result.[18–20] However, perfusion imaging between IVT and recanalization with EVT would be required to confirm this hypothesis. In addition, the decision to use IVT was not randomized in the present study, and several cofounders may also explain this result.

One of our main inclusion criteria for the present study was that patients had a known symptom onset, and multimodal imaging, such as perfusion imaging, was not systematically used for EVT selection. These points are of importance, as our results do not apply to patients with unknown symptom onset or selection based on perfusion imaging. Indeed, late-window patients with an indication for EVT have usually a slow-progressor profile with low ischemic core growth rate,[21–23] with a large salvageable penumbra volume, and may potentially benefit more from a complete reperfusion. As the present patients were not selected using perfusion imaging, it is plausible that the study population includes both patients with slow and fast progressor profiles and varying early infarct growth rates.[24–26] Therefore, we can speculate that (1) patients with a fast progressor profile on the baseline imaging may not benefit from a complete reperfusion over a successful reperfusion before 414 minutes, and (2) patients with a slow progressor profile may benefit from a complete over successful reperfusion after 414 minutes. Indeed, the French Acute Multimodal Imaging Study to Select Patients for Mechanical Thrombectomy (FRAME) study recently highlighted the prognostic value of the mismatch

for the identification of patients more likely to benefit from reperfusion, and showed that the absence of mismatch was an independent predictor of worse outcome in reperfusers even in the early time window.[24] Nevertheless, our results highlight the dynamic of AIS evolution from the baseline imaging to reperfusion, and suggest that additional parameters could be considered before going further into the procedure after obtaining a successful reperfusion. New tools are required to provide a multimodal assessment of the brain parenchyma in the angio suite, such as cone-beam computed tomography perfusion imaging.[27–29] This could be important for the design of future trials in the field, aiming at proving the prognostic value of targeting a complete reperfusion over a successful reperfusion in different settings.

In 2018, the MR CLEAN investigators assessed the association of time to EVT with functional outcome. In that study, Mulder et al showed that time from onset to EVT and reperfusion were strongly associated with functional outcome.[2] Interestingly, the MR CLEAN registry also included AIS patients without strict inclusion and exclusion criteria for EVT selection (ie, no perfusion or collateral assessment), and found stronger associations between time and functional outcome compared with the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials (HERMES) meta-analysis.[3] However, the effect of the reperfusion status (mTICI 2b versus 2c–3) was not specifically considered in these studies. As an additional analysis, Mulder et al assessed the effect of TSOR on functional independence for varying definitions of reperfusion, and found that the strongest association with outcome was for an extended TICI (eTICI) 2c and eTICI 3.[2] Interestingly, the results were not statistically different for an eTICI 2b.[2] Differences with the present study include a larger population, allowing subgroup analyses, particularly in the TICI 2b subgroup (239 patients vs 1,071 patients in the present analysis). Recently, Olivot et al evaluated the relationship between TSOR and the occurrence of PH with functional outcome, and found that parenchymal hemorrhage (PH) rate is strongly associated with TSOR and affects functional outcome (ie, "time is bleeding").[30] It is therefore possible that the relationship between TSOR and functional outcome according to the reperfusion status is also mediated by PH occurrence. Further studies will be needed to confirm these findings.

The present study had several strengths, which included its large population and its prospective design. In addition, and similarly to the MR CLEAN registry,[2] these findings could be more generalizable to real-life clinical practice given the pragmatic design of the ETIS registry, including AIS with a LVO regardless of the collateral or perfusion parameters.

However, several limitations must be acknowledged. First, the present analysis is observational, potentially leading to confounding biases in the analysis. Second, although our sample size was significantly large (n = 4,444), final angiographies after EVT were not reviewed by an independent central core laboratory, and mTICI were adjudicated by the operator in charge, at the end of EVT. Third, the final infarct volume was not systematically assessed in the ETIS registry, limiting the interpretation of our results. Fourth, and as stated previously, our results do not come from a randomized controlled study and do not support the conclusion that there is no benefit of aiming at a complete reperfusion after a certain threshold of time. Our results only suggest that the TSOR seems to play an important role in this relationship, and support the need for future randomized controlled studies to formally answer this question.

Conclusion

The time of symptom onset to reperfusion is associated with worse outcomes. A near-to-complete and complete reperfusion is associated with higher probabilities of favorable outcomes, but this benefit progressively declined over time until there was no difference between a perfect and a successful reperfusion beyond 5.7 hours. The present study underscores the need for new tools to reassess the brain parenchyma in the angio suite to tailor the endovascular strategy.

Acknowledgement

None.

Author Contributions

B.M., S.F., M.M., B.G., and J.M.O. contributed to the conception and design of the study. B.M., S.F., M.M., B.L., G.M., I.S., S.R., A.V., C.C., B.G., and J.M.O. contributed to the acquisition and analysis of data. B.M., S.F., B.G., M.M., and J.M.O. contributed to drafting the text, and preparing the figures.

Potential Conflict Of Interest

J.M.O. declares consulting activities with Abbvie, Acticor, and Bioxodes; speaking fees from BMS and Boerhinger Ingelheim. S.F. is the author of a patent (US20200085454A1). B.M. declares a grant from the French Health Ministry and is the primary investigator of the DETERMINE trial. B.G. has received grants from the French Ministry of Health, is the primary investigator of the TITAN, DIRECT ANGIO, and IA-RESCUE trial, and has received consulting fees from Air Liquide, MIVI, Medtronic, Microvention, and Penumbra.

M.M. declares consulting fees from Boerhinger Ingelheim, Air Liquide, Acticor Biotech, and Amgen. S.R. declares contracts from Boerhinger Ingelheim France, Bristol-Myers Squibb, and Pfizer SAS.

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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