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ORIGINAL ARTICLE

Mechanical thrombectomy failure in anterior circulation strokes: Outcomes and predictors of favorable outcome

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Abstract

Background and purpose: Despite continuous improvement and growing knowledge in the endovascular therapy of large vessel occlusion stroke (LVOS), mechanical thrombectomy (MT) still fails to obtain satisfying intracranial recanalization in 10% to 15% of cases. However, little is known regarding clinical and radiological outcomes among this singularly underexplored subpopulation undergoing failed MT. We aimed to investigate the outcome after failed MT and identify predictive factors of favorable outcome despite recanalization failure.

Methods: We conducted a retrospective analysis of consecutive patients prospectively included in the ongoing observational multicenter Endovascular Treatment in Ischemic

[†]See Appendix S1

Stroke registry from January 2015 to September 2020. Patients presenting with anterior circulation LVOS treated with MT but experiencing failed intracranial recanalization defined as final modified Thrombolysis In Cerebral Infarction (mTICI) score of 0, 1 and 2a were included. Clinical and radiological outcomes were assessed along with the exploration of predictive factors of Day-90 favorable outcome.

Results: The study population comprised 533 patients. Mean age was 68.8 ± 16 years, and median admission National Institutes of Health Stroke Scale (NIHSS) and Alberta Stroke Program Early Computed Tomography Score (ASPECTS) were 17 (IQR 12–21) and 7 (IQR 5–8), respectively. Favorable outcomes were observed in 85 patients (18.2%) and 186 died (39.0%). The rate of symptomatic intracranial hemorrhage was 14.1%. In multivariable analysis, younger age (odds ratio [OR] 0.96, 95% CI 0.94–0.98, $p < 0.001$), a lower admission NIHSS (OR 0.87, 95% CI 0.83–0.91, $p < 0.001$), a lower number of MT passes (OR 0.77, 95% CI 0.77–0.87, $p < 0.001$), a lower delta ASPECTS between initial and Day-1 imaging (OR 0.83, 95% CI 0.71–0.98, $p = 0.026$) and stroke etiology [significant difference among etiological subtypes ($p = 0.024$) with a tendency toward more favorable outcomes for dissection (OR 2.01, 95% CI 0.71–5.67)] were significantly associated with a 90-day favorable outcome.

Conclusions: In this large retrospective analysis of a multicenter registry, we quantified the poor outcome after MT failure. We also identified factors associated with favorable outcome despite recanalization failure that might influence therapeutic management.

KEYWORDS
mechanical thrombectomy, prognosis, recanalization, reperfusion failure

INTRODUCTION

Since the publication of several randomized trials demonstrating the benefit of mechanical thrombectomy (MT) in the treatment of large vessel occlusion stroke (LVOS) [1], indications are continuously broadening. MT allows satisfying intracranial recanalization in nearly 85% of cases at the end of the procedure with the remaining considered as failures since sufficient reperfusion is not reached [1–3].

The literature available about outcomes in this population experiencing unsuccessful revascularization is scarce [4–8]. In these patients with failed MT, the endovascular procedure itself might be the source of impaired outcome. Numerous factors can be hypothesized such as repeated endovascular MT maneuvers, in situ contrast media injections associated with multiple MT passes, anesthetic management, and blood pressure variability or multiple patient transfers. In cases of MT failure, rescue therapies such as intracranial stenting or angioplasty or pharmacological adjuvant therapies (in situ thrombolysis or intravenous antiplatelet agents such as GpIIb-IIIa inhibitors or cangrelor) are increasingly being considered with promising results [4, 5, 9–11]. Hence, recognizing factors associated with subsequent clinical outcome can improve decision making to tailor the rescue strategy in the context of MT failure. In addition, an improved knowledge of MT failure outcomes may also have an application in the development of neuroprotective or neuroreparative drugs [12, 13].

In the present study our aim was to assess the outcomes after MT failure in patients with anterior circulation LVOS as well as predictors of favorable functional outcome.

METHODS

The data used in this study are available from the corresponding author upon reasonable request.

Study population

We conducted a retrospective analysis of consecutive patients included in the prospective ongoing multicenter Endovascular Treatment in Ischemic Stroke registry (ETIS; ClinicalTrials.gov Identifier: NCT03776877). The study period was January 2015 to September 2020. At the time of the study, eight centers participated in the registry. Local ethical committees had approved data collection and analysis. Inclusion criteria were as follows: (i) LVOS of the anterior circulation (M1, M2 intracranial internal carotid artery [ICA] and tandem occlusions) and (ii) MT performed but ending with intracranial recanalization failure defined as a final modified Thrombolysis In Cerebral Infarction (mTICI) score of 0, 1 or 2a. Exclusion criteria were favorable intracranial reperfusion defined as final mTICI ≥ 2b, posterior circulation stroke and isolated ICA occlusion without intracranial occlusion.

Treatment

The indications for MT were based on the timeframes, imaging data including perfusion imaging if available, global comorbidities and standard guidelines [14, 15]. MT procedure was performed in accordance with the patient's condition and local protocol. Prior intravenous thrombolysis (IVT) was administered according to international guidelines, using recombinant tissue plasminogen activator (0.9 mg/kg) in the absence of contraindications.

Collected data

Clinical, imaging, timeline and angiographic data were recorded. Trained research nurses independently assessed the modified Rankin Scale (mRS) score at 90 days, during face-to-face interviews or via telephone conversations with the patients, their relatives or their general practitioners. Angiographic and imaging data were assessed locally by senior neuroradiologists. Collateral status was quantified when assessable using the ASITN classification: grades 3 and 4 were considered as favorable collateral scores. MT failure was defined as a final mTICI score of 0, 1 or 2a. The primary outcome was favorable outcome defined as a 90-day mRS score of 0–2 or equal to pre-stroke mRS. Preoperative adjuvant therapies were also recorded: pharmacological (aspirin, GpIIb/IIIa inhibitor, heparin and vasodilator) and/or mechanical (cervical or intracranial stenting or angioplasty). Procedural complications (dissection, embolism in a new territory and arterial perforation) and 90-day mortality rates were recorded. Intracranial hemorrhage (ICH) was assessed according to the ECASS II classification. Symptomatic intracranial hemorrhage (sICH) was defined as neurological deterioration (NIHSS worsening ≥ 4 points or death) together with ICH.

Statistical analysis

See Appendix S2.

RESULTS

Study population

Among 5076 patients treated with MT and included in the ETIS registry, 533 patients finally met the inclusion exclusion criteria (see study flowchart, Figure 1). Baseline characteristics are presented in Table 1. Briefly, mean age was 68.8 ± 16 years and 48.0% were male. A history of high blood pressure and stroke or transient ischemic attack were observed in, respectively, 57.7% and 15.2%. Two hundred patients (38.9%) were under prior antithrombotic therapy: antiplatelet in 28.0% and anticoagulant in 15.8%. Median admission National Institutes of Health Stroke Scale (NIHSS) and Alberta Stroke Program Early Computed Tomography Score (ASPECTS) were, respectively, 17 (IQR 12–21) and 7 (IQR 5–8). The time of stroke onset was unclear in 33.9%. IVT was administered in 46.2%. Eighty-nine patients (17.0%) were treated under general anesthesia. Median time from stroke onset to arterial puncture was 261 min. Baseline characteristics of the study population in comparison with patients with favorable recanalization with MT are provided in 1.

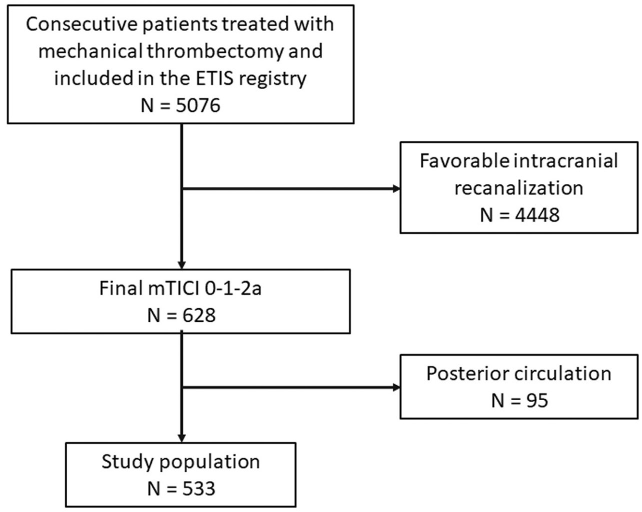

FIGURE 1 Study flowchart. ETIS, endovascular treatment in ischemic stroke; mTICI, modified Thrombolysis In Cerebral Infarction

Clinical and radiological outcomes

Favorable outcome was achieved in 85 patients (18.2%) and 186 died (39.0%). Symptomatic ICH, Parenchymal hematoma (PH) and any ICH were observed in, respectively, 14.1%, 14.0% and 52.9%.

Predictors of favorable outcome

In univariate analysis, younger age, the absence of history of high blood pressure, a lower initial NIHSS score, arterial site of occlusions, IVT prior to MT, a lower number of MT passes, a lower delta ASPECTS between initial and Day-1 imaging and stroke etiology were associated with favorable functional outcome (Table 2). In multivariable analysis, younger age (OR 0.96, 95% CI 0.94 to 0.94, p <0.001), lower initial NIHSS score (OR 0.87, 95% CI 0.83 to 0.91, p <0.001), lower number of MT passes (OR 0.77, 95% CI 0.77 to 0.87, p <0.001), lower delta ASPECT score between initial and Day-1 imaging (OR = 0.83, 95% CI: 0.71 to 0.98, p = 0.026) and stroke etiology (significant difference according to etiology: using cardioembolic stroke as reference, OR = 0.70 [95% CI: 0.28 to 1.75] for large artery atherosclerosis, OR = 2.01 [95% CI: 0.71 to 5.67] for dissection, OR = 0.50 [95% CI: 0.24 to 1.05] for others or undetermined cause, p = 0.024) remained significantly associated with 90-day favorable outcome (Table 2).

TABLE 1 Baseline characteristics of study participants ($N = 533$)

Characteristic	*n*	Value (%)
Baseline demographics and medical history		
Age, years, mean ± SD	533	68.8 ± 16.0
Men	531	255 (48.0)
Hypertension	520	300 (57.7)
Diabetes	519	80 (15.4)
Dyslipidemia	518	158 (30.5)
Current smoking	493	113 (22.9)
Previous stroke or TIA	415	63 (15.2)
Previous ischemic heart disease	409	63 (15.4)
Antithrombotic medications	514	200 (38.9)
Antiplatelet	514	144 (28.0)
Anticoagulant	514	81 (15.8)
Current stroke event		
Systolic BP, mmHg, mean ± SD	446	148.8 ± 26.2
Diastolic BP, mmHg, mean ± SD	445	84.2 ± 18.1
Admission NIHSS score, median (IQR)	516	17 (12–21)
Admission ASPECTS, median (IQR)	506	7 (5–8)
Wake-up stroke or unknown onset	522	177 (33.9)
Pre-stroke mRS < 2	515	454 (88.2)
Site of occlusion		
M1-MCA	533	256 (48.0)
M2-MCA	533	70 (13.1)
Intracranial ICA	533	99 (18.6)
Tandem	533	108 (20.3)
Favorable cortical collateral score	371	202 (54.4)
Stroke etiology		
Large artery atherosclerosis	485	83 (17.1)
Cardioembolic	485	200 (41.2)
Dissection	485	41 (8.5)
Others/undetermined	485	161 (33.2)
Intravenous thrombolysis	524	242 (46.2)
First-line strategy		
Stent retriever	510	110 (21.6)
Contact aspiration	510	228 (44.7)
Combined	510	172 (33.7)
General anesthesia	523	89 (17.0)
Number of passes, median (IQR)	475	4 (2–5)
Adjuvant treatment	498	151 (30.3)
Pharmacological	151	76 (50.3)
Mechanical	151	49 (32.5)
Combined	151	26 (17.2)
Procedural times, min, median (IQR)		
Onset to puncture	500	261 (193–339)
Outcomes		
Favorable outcome (90-day mRS 0–2)	468	85 (18.2)

TABLE 1 (Continued)

Characteristic	*n*	Value (%)
Poor outcome (90-day mRS 4–6)	477	344 (72.1)
90-day death	477	186 (39.0)
Procedural complication	470	101 (21.5)
Any ICH	454	240 (52.9)
sICH	454	64 (14.1)
PH 1–PH 2	449	63 (14.0)
Decompressive craniectomy	345	37 (10.7%)

Note: Values expressed as number (percentage) unless otherwise indicated.

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; BP, blood pressure; CAD, coronary artery disease; ICA, internal carotid artery; ICH, intracranial hemorrhage; IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; sICH, symptomatic intracranial hemorrhage; TIA, transient ischemic attack.

TABLE 2 Multivariable regression analysis of predictors of favorable outcome at 90 days

Predictor of favorable outcome	OR (95% CI)	*p* value*
Age	0.96 (0.94 to 0.98)	<0.001
Admission NIHSS	0.87 (0.83 to 0.91)	<0.001
Number of passes	0.77 (0.67 to 0.87)	<0.001
Delta ASPECTS Day 0–Day 1	0.83 (0.71 to 0.98)	0.026
Stroke etiology		
Cardioembolic	1.00 (Ref.)	0.024
Large artery atherosclerosis	0.70 (0.28 to 1.75)	
Dissection	2.01 (0.71 to 5.67)	
Others or undetermined	0.50 (0.24 to 1.05)	

Note: Values expressed as number (percentage) unless otherwise indicated.

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; Ref., reference.

**p* values calculated using backward multivariable mixed logistic regression model including center as random effect. Descriptive parameters, OR and *p* values were calculated after handling missing values using multiple imputation procedure (m = 10).

DISCUSSION

In the present study, we found that 18.2% of patients with MT failure (defined by final mTICI 0, 1 or 2a) had a favorable outcome at 90 days. We identified factors significantly associated with favorable outcome despite unsuccessful recanalization: younger age, lower initial NIHSS score, fewer MT passes, a limited infarct core extension at Day-1 and stroke etiology.

Unsurprisingly, if the MT procedure failed to recanalize the intracranial target artery, our results confirmed that patient prognosis was poor with a low likelihood of favorable outcome and a high mortality risk. At the time of expanding indications of rescue strategy after first-line standard MT failure, these findings are of interest as they confirm the poor prognosis if sufficient intracranial reperfusion is not achieved. An improved knowledge of what is at stake if reperfusion fails is essential to clarify the role of rescue techniques such as intracranial stenting, intra-arterial thrombolysis or acute antiplatelet therapies (GpIIb-IIIa inhibitors, cangrelor) [4, 5, 9–11].

We also observed that the rate of PH and sICH was quite high in this subgroup of patients with respective rates of 14.1% and 14.0%. This might seem higher than the usual published rates among overall MT patients (namely considering patients recanalized and those that were not) [1, 16]. This point probably has to be taken into account in postoperative antithrombotic and blood pressure management.

We have searched for factors associated with favorable outcome despite reperfusion failure. Younger age and lower initial NIHSS were associated with better functional outcome. Admission NIHSS is a well-established prognostic factor. Interestingly, younger age was also associated with more favorable outcomes despite the risk of malignant infarction in young patients [17]. This is in line with the identified significant prognosis of heterogeneity among stroke etiologies with a statistical tendency favoring dissection in comparison with cardioembolic and large artery atherosclerosis. This may also be explained by the singularly younger population involved in cervical dissection-related ischemic strokes.

Fewer MT passes was also found to be significantly associated with favorable outcome and an increased number of MT passes with mortality risk. The association between number of passes and poorer prognosis has already been reported [6, 18–20]. However, this point may be considered with caution. Indeed, the number of MT passes may actually be a reflection of important confounding factors such as more proximal occlusions sites, complex underlying occlusion etiology, operator's decision or more severe occlusion leading to more MT attempts [18]. Furthermore, the question of whether to stop MT after three or more passes could be a matter of debate [21]. Indeed, it has been reported that whatever the number of passes, recanalization has to be reached to ensure a better clinical outcome than without recanalization [18]. Therefore, based on our results, we cannot recommend interrupting the MT procedure for fear of worst outcome in case of final MT failure.

We also observed that a lower delta ASPECT score between initial and Day-1 imaging was associated with a better outcome despite MT failure. In other words, the absence of infarct core extension or a limited progression of cerebral infarction between the acute phase and Day-1 imaging was associated with a favorable outcome among patients experiencing insufficient intracranial recanalization. Several potential mechanisms explaining such a finding can be discussed including persistency of efficient durable cortical collaterals, delayed spontaneous intracranial arterial recanalization or specific intracranial occlusion etiology and thrombus composition. Interestingly, an initial ASPECT score > 8 was not associated with an improved outcome in this specific population. Only a limited progression of cerebral infarction between initial and Day-1 imaging was associated with clinical prognosis.

Our study has some limitations. First, even though it was derived from our prospectively maintained and ongoing registry, our study was retrospective. The absence of comparison to a control group may be considered as a weakness. However, rather than analyzing the natural history of MT failure in patients with anterior circulation LVOS, here we aim to search for potential factors associated with favorable functional outcome within this population. We use self-adjudication of the final recanalization to include patients. Indeed, over-rating is a common ground in final TICI score by non-external core-laboratory evaluators and this could have led to selection bias [22]. However, we are focusing here on poor recanalization: it is very likely that poor final mTICI scores are reliably assessed. An over-rating phenomenon might be more frequent when declaring higher mTICI scores. Collateral status suffers from missing data limiting its interpretation. This was mostly explained by the impossibility in daily practice of exploring these cortical collaterals in many frequent angiographic presentations such as intracranial internal carotid artery, tandem occlusions or circle of Willis variations limiting its exploration during MT procedure. Contrast media used volumes were not available to explore their influence. However, the contrast media quantity is supposed to be closely related to endovascular procedure duration and repeated MT passes. Similarly, admission glucose level and postprocedural blood pressure values, which are previously identified factors influencing clinical prognosis, were not available. Lastly, we were unable to analyze the arterial patency at 24 or 48 h after MT. This would have been of interest in investigating a link between spontaneous delayed recanalization and clinical outcome [23, 24].

CONCLUSIONS

Failed intracranial reperfusion after MT in anterior circulation LVOS was associated with a low rate of favorable outcome and a high mortality rate. Lower initial NIHSS, younger age, fewer MT passes, lower delta ASPECT score between initial and Day-1 imaging, and stroke etiology were associated with increased likelihood of favorable functional outcome.

AUTHOR CONTRIBUTIONS

Gaultier Marnat: Conceptualization (lead); data curation (lead); formal analysis (lead); investigation (lead); methodology (lead); supervision (lead); validation (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). **Benjamin Gory:** Conceptualization (equal); data curation (equal); methodology (equal); validation (equal); writing – review and editing (equal). **Igor Sibon:** Conceptualization (equal); investigation (equal); writing – review and editing (equal). **Maeva Kyheng:** Data curation (equal); formal analysis (lead); methodology (equal); software (lead); validation (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). **Julien Labreuche:** Formal analysis (lead); software (equal); writing – review and editing (equal). **GrE;goire BOULOUIS:** Data curation (equal); writing – review and editing (equal). **Jean-SE;bastien Liegey:** Writing – review and editing (equal). **Jildaz Caroff:** Data curation (equal); writing – review and editing (equal). **Francois Eugene:** Data curation (equal); writing – review and editing (equal). **Olivier Naggara:** Data curation (equal); writing – review and editing (equal). **Arturo Consoli:** Data curation (equal); writing – review and editing (equal). **Mikael Mazighi:** Writing – review and editing (equal). **Benjamin Maier:** Writing – review and editing (equal). **SE;bastien Richard:** Writing – review and editing (equal). **Christian Denier:** Writing – review and editing (equal). **Guillaume Turc:** Writing – review and editing (equal). **Bertrand Lapergue:** Conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); validation (equal); writing – review and editing (equal). **Romain Bourcier:** Conceptualization (equal); data curation (equal); formal analysis (lead); investigation (equal); methodology (lead); supervision (equal); validation (equal); writing – original draft (supporting); writing – review and editing (lead).

CONFLICT OF INTEREST

All the authors declare that they have no conflicts of interest related to this study.

DATA AVAILABILITY STATEMENT

The data used in this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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