

Original research

# Early neurological deterioration in patients with minor stroke due to isolated M2 occlusion undergoing medical management: a retrospective multicenter study

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## ABSTRACT

**Background** Patients with minor stroke and M2 occlusion undergoing best medical management (BMM) may face early neurological deterioration (END) that can lead to poor long-term outcome. In case of END, rescue mechanical thrombectomy (rMT) seems beneficial. Our study aimed to define factors relevant to clinical outcome in patients undergoing BMM with the possibility of rMT on END, and find predictors of END.

**Methods** Patients with M2 occlusion and a baseline National Institutes of Health Stroke Scale (NIHSS) score $\leq$ 5 that received either BMM only or rMT on END after BMM were extracted from the databases of 16 comprehensive stroke centers. Clinical outcome measures were a 90-day modified Rankin Scale (mRS) score of 0–1 or 0–2, and occurrence of END.

**Results** Among 10 169 consecutive patients with large vessel occlusion admitted between 2016 and 2021, 208 patients were available for analysis. END was reported in 87 patients that were therefore all subjected to rMT. In a logistic regression model, END (OR 3.386, 95% CI 1.428 to 8.032), baseline NIHSS score (OR 1.362, 95% CI 1.004 to 1.848) and a pre-event mRS score=1 (OR 3.226, 95% CI 1.229 to 8.465) were associated with unfavorable outcome. In patients with END, successful rMT was associated with favorable outcome (OR 4.549, 95% CI 1.098 to 18.851). Among baseline clinical and neuroradiological features, presence of atrial fibrillation was a predictor of END (OR 3.547, 95% CI 1.014 to 12.406).

**Conclusion** Patients with minor stroke due to M2 occlusion and atrial fibrillation should be closely monitored for possible worsening during BMM and, in this case, promptly considered for rMT.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with minor stroke and isolated M2 occlusion undergoing best medical management may face early neurological deterioration that can lead to poor long-term outcome.

## WHAT THIS STUDY ADDS

⇒ Our retrospective study shows that early worsening during best medical management can affect long-term outcome, that can be ameliorated by a rescue mechanical thrombectomy. Presence of atrial fibrillation appears to be a main determinant of early neurological deterioration.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study suggests that patients with minor stroke due to isolated M2 occlusion and concomitant atrial fibrillation should be closely monitored for possible worsening and, in such case, promptly considered for mechanical thrombectomy.

## INTRODUCTION

Patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO) and a baseline National Institutes of Health Stroke Scale (NIHSS) score $\leq$ 5 represent a challenge concerning the most appropriate emergent treatment. Indeed, the benefit of mechanical thrombectomy (MT) is controversial as very few patients with a minor stroke were enrolled

in the main trials to draw meaningful conclusions and inconsistent evidence comes from retrospective studies.<sup>1–5</sup> In real-world practice, the possibility of immediate MT is considered on a case-by-case basis after careful evaluation of clinical and radiologic features. Therefore, the presence of an isolated occlusion of the M2 segment of the middle cerebral artery may elicit skepticism in consideration of the risks of an invasive procedure not counterbalanced by the possible benefits in patients with minimal impairment. Conversely, patients with LVO and a minor stroke that do not receive effective recanalization therapies may experience an early neurological deterioration (END) due to the expansion of the hypoperfused area, possibly leading to poor long-term functional outcome.<sup>3,5</sup> Although an early worsening has been documented in up to one-third of patients with minor stroke and LVO, these patients may still benefit from a rescue MT.<sup>2,6,7</sup> We have recently suggested that patients with minor stroke and isolated M2 occlusion should receive best medical management (BMM), with intravenous thrombolysis when applicable, as first option during the acute management and possibly be considered for a rescue MT (rMT) in case of END.<sup>8</sup> Hence, the search of baseline features for the identification of patients that are at risk for END during medical management is relevant.

Here we report a retrospective multicenter analysis on consecutive patients with minor AIS due to isolated occlusion of the M2 segment that received BMM only or that initially received BMM but were then subjected to rMT following an early worsening of symptoms. The primary purpose of this study was to define predictors of clinical outcome in these patients. The secondary aim was to identify baseline predicting factors of END.

## METHODS

### Patients and treatment

The prospective databases of 16 comprehensive stroke centers were screened for consecutive patients with AIS due to LVO admitted between January 2016 and December 2021. All patients were diagnosed with a non-contrast CT scan for determination of the Alberta Stroke Program Early CT Score (ASPECTS), followed by a neck and head multiphase CT angiography (mCTA) to locate the site of occlusion and assess the leptomeningeal collateral circulation using the Menon score.<sup>9,10</sup> The identification of M2 segment involvement was done on CT angiograms and defined as an occlusion located from the genu of the middle cerebral artery on to the proximal part of one of the first order branches. Caliber dominance was considered present when one division had a larger caliber than the other(s).<sup>11,12</sup> An example of occlusion of a M2 dominant division is provided in online supplemental figure 1. Patients with an occlusion site other than the isolated M2 segment, a baseline NIHSS score  $\geq 6$  or a pre-event mRS score  $> 1$  were excluded. Patients with missing data regarding 90-day clinical outcome were also excluded. Among patients with isolated M2 occlusion and a baseline NIHSS score  $\leq 5$ , those subjected to immediate MT, already described in a previous report,<sup>8</sup> were excluded for the purpose of this study. This led to a group of patients with isolated M2 occlusion and a baseline NIHSS score  $\leq 5$  that were either subjected to BMM only (including intravenous thrombolysis when applicable) or that received rMT on END during BMM. END was defined as an increase of the NIHSS score of at least four points from baseline leading to a NIHSS score  $\geq 6$ , that occurred within 24 hours from the onset of symptoms and was not due to intracranial hemorrhage.<sup>13</sup>

MT was performed with a stent-retriever and proximal guide catheter aspiration, direct contact aspiration or a combination

of stent-retriever and distal aspiration, at the discretion of each individual interventionalist. Flow restoration at the end of the procedure was graded using the modified Treatment In Cerebral Infarction (mTICI) scale and based on the percentage reperfusion of the territory supplied by M2, with successful MT corresponding to a score of 2b–3.<sup>14,15</sup> In each participating center, two neuroradiologists with more than 5 years of experience reviewed the diagnostic radiological and angiographic data of all patients. In cases of doubt or disagreement, Digital Imaging and Communications in Medicine (DICOM) images were sent to two expert neuroradiologists of the coordinating center for re-evaluation and adjudication.

### Clinical variables and measures of outcome

Demographic data (age and sex), cerebrovascular risk factors, baseline clinical and imaging data as well as therapeutic procedures of the acute phase were collected.

In regard to the first aim of the study, clinical outcome was measured with the modified Rankin Scale (mRS) score acquired at 90 days either in person or on the telephone. A 90-day mRS score of 0–1 (excellent neurological outcome) was chosen as the primary clinical outcome measure given the baseline minor symptoms of patients. The secondary clinical outcome measure was a 90-day mRS score of 0–2 (functional independence). Safety outcome measures were (1) intraparenchymal brain bleeding events after recanalization therapies, assessed by CT scan or MRI at 72 hours and classified according to previously established criteria,<sup>16</sup> and (2) death of any cause within 90 days after stroke.

In regard to the second aim of our study, occurrence of END during BMM was used as the outcome measure.

### Statistical analysis

To identify predictors of neurological outcome we used Mann–Whitney U test/Student's t-test and Pearson's chi square test as appropriate to assess differences in demographics, baseline clinical and neuroradiological features, occurrence of END, rate of thrombolysis and brain bleeding events after recanalization treatments between patients with 90-day excellent outcome or functional independence and patients with the corresponding unfavorable outcome (mRS 2–6 or 3–6, respectively). Significance threshold was set at P value  $< 0.05$ . Variables with P value  $\leq 0.1$  at univariate analysis or with a clinically meaningful role were entered in a multivariate analysis. This was performed with a logistic regression model using the chosen outcome measure as dependent variable.

The same statistical approach was used to identify possible predictors of END. We used Mann–Whitney U test/Student's t-test and Pearson's chi square test as appropriate to assess differences between patients with and patients without END, respectively. Thereafter, to adjust the effect size for potential confounders, a multivariate binary logistic regression analysis was performed, using END as dependent variable and a set of covariates selected for having a P value  $\leq 0.1$  in univariate analysis or for being clinically meaningful.

The goodness of fit for any logistic regression model was evaluated with the Hosmer–Lemeshow test. All analyses were performed using SPSS software (IBM).

## RESULTS

A total of 10 169 consecutive patients with AIS due to LVO were screened and 208 patients with isolated M2 occlusion, a baseline NIHSS score  $\leq 5$  and a pre-event mRS score  $\leq 1$  intended

for initial BMM were available for analysis. A flow diagram of patient selection is provided in online supplemental figure 2. The study population included 121 patients that received only BMM because they did not experience END (BMM group) and 87 patients (41.8%) initially receiving BMM but that later underwent END and were therefore all subjected to rMT (BMM+rMT group). In the latter group of patients, clinical deterioration occurred at a median (IQR) time of 245 (186–359) minutes from

the onset of symptoms. The rate of successful reperfusion after rMT was 83.7%.

In univariate analysis of the entire study sample, higher baseline NIHSS score, a pre-event mRS score=1 and occurrence of END were associated with an unfavorable 90-day outcome (table 1). In a logistic regression model that used these variables along with other clinically meaningful ones (age, left-side stroke, involvement of a dominant M2 division, thrombolysis

**Table 1** Univariate analysis of predicting factors for clinical outcome in the entire cohort of patients

Parameter	mRS score 0–1	mRS score 2–6	P value*
Patients, number/total (%)	163/208 (78.4)	45/208 (21.6)	
Demographics			
Females, number/total (%)	81/163 (49.7)	21/45 (46.7)	0.719
Age in years, median (IQR)	71 (61–79)	75 (68–82)	0.277
Clinical features and medical therapy			
Atrial fibrillation, number/total (%)	50/140 (35.7)	14/34 (41.2)	0.554
Diabetes, number/total (%)	29/131 (22.1)	10/33 (30.3)	0.325
Dyslipidemia, number/total (%)	74/139 (53.2)	20/38 (52.6)	0.947
Coronary artery disease, number/total (%)	35/131 (26.7)	10/36 (27.8)	0.899
Carotid atherosclerosis, number/total (%)	55/133 (41.3)	13/35 (37.1)	0.652
Previous stroke, number/total (%)	26/129 (20.1)	10/34 (29.4)	0.247
Baseline NIHSS score, median (IQR)	3 (2–4)	4 (3–5)	<b>0.008</b>
Pre-event mRS score=1, number/total (%)	22/163 (13.5)	15/45 (33.3)	<b>0.002</b>
END, number/total (%)	61/163 (37.4)	26/45 (57.8)	<b>0.014</b>
Current antiplatelet therapy, number/total (%)	41/132 (31.1)	17/38 (44.7)	0.117
Current anticoagulant therapy, number/total (%)	29/136 (21.3)	10/34 (29.4)	0.316
Thrombolysis, number/total (%)	108/163 (66.2)	25/45 (55.5)	0.182
Baseline imaging data			
Left-side stroke, number/total (%)	103/163 (63.2)	24/45 (53.3)	0.230
Dominant M2 division, number/total (%)	86/163 (52.8)	22/45 (48.9)	0.645
ASPECT, median (IQR)	10 (9–10)	10 (9–10)	0.708
Menon score, median (IQR)	4 (4–5)	4 (4–4)	0.668
Brain bleeding events			
IPH, number/total (%)			0.871
No IPH	121/131 (92.4)	36/40 (90.0)	
IPH type 1	8/131 (6.1)	3/40 (7.5)	
IPH type 2	2/131 (1.5)	1/40 (2.5)	
<b>Multivariate logistic regression for predicting factors of unfavorable clinical outcome (mRS score 2–6)</b>			
Parameter	OR	95% CI	P value*
Age	1.014	0.979 to 1.050	0.426
Pre-event mRS score=1	<b>3.226</b>	<b>1.229 to 8.465</b>	<b>0.017</b>
Baseline NIHSS score	<b>1.362</b>	<b>1.004 to 1.848</b>	<b>0.047</b>
END	<b>3.386</b>	<b>1.428 to 8.032</b>	<b>0.006</b>
Left-side stroke	1.061	0.480 to 2.345	0.883
Dominant M2 division	0.592	0.267 to 1.314	0.198
No thrombolysis	1.836	0.782 to 4.311	0.163
IPH			
IPH type 1	1.006	0.209 to 4.836	0.994
IPH type 2	0.885	0.053 to 14.752	0.932

\*Figures in bold type denote statistical significance (considered at P<0.05).

ASPECTS, Alberta Stroke Program Early CT Score; CI, confidence interval; END, early neurological deterioration; IPH, intraparenchymal hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.

**Table 2** Outcome and safety data of patients in the best medical management+rescue mechanical thrombectomy and best medical management groups

Parameter	BMM+rMT	BMM	P value*
Number of patients/total (%)	87/208 (41.8)	121/208 (58.2)	
Clinical outcome			
90-day mRS score 0–1, number/total (%)	61/87 (70.1)	102/121 (84.3)	<b>0.014</b>
90-day mRS score 0–2, number/total (%)	70/87 (80.4)	118/121 (97.5)	<b>&lt;0.001</b>
Mortality of any cause, number/total (%)	7/87 (8.0)	1/121 (0.8)	<b>0.008</b>
Brain bleeding events			
IPH, number/total (%)			<b>0.017</b>
No IPH	74/86 (86.0)	83/85 (97.6)	
IPH type 1	10/86 (11.6)	1/85 (1.2)	
IPH type 2	2/86 (2.3)	1/85 (1.2)	

\*Figures in bold type denote statistical significance (considered at P<0.05).  
BMM, best medical management; IPH, intraparenchymal hemorrhage; mRS, modified Rankin Scale; rMT, rescue mechanical thrombectomy.

and brain bleeding events), END (OR 3.386, 95% CI 1.428 to 8.465, P=0.006), a pre-event mRS score=1 (OR 3.226, 95% CI 1.229 to 8.465, P=0.017) and higher baseline NIHSS score (OR 1.362, 95% CI 1.004 to 1.848, P=0.047) were associated with unfavorable outcome (table 1). After dichotomization of the mRS score 0–2 versus 3–6, age (OR 1.054, 95% CI 1.010 to 1.099, P=0.047), a higher baseline NIHSS score (OR 1.791, 95% CI 1.058 to 3.033, P=0.030) and END (OR 12.723, 95% CI 2.416 to 67.006, P=0.003) were associated with unfavorable outcome in multivariate analysis (online supplemental table 1).

In the BMM+rMT group, 70.1% of patients achieved a 90-day excellent neurological outcome, whereas this rate was significantly higher in patients of the BMM group (84.3%, P=0.014). Similar results were observed for rates of functional independence (mRS 0–2, 80.4% in patients of the BMM+rMT group vs 97.5% in patients of the BMM group, P<0.001). The rate of non-symptomatic parenchymal hemorrhage (intraparenchymal hemorrhage type 1) was significantly higher in patients of the BMM+rMT group (11.6% vs 1.2%, P=0.017), as well as the rate of mortality (8.0% in the BMM+rMT group vs 0.8% in the BMM group, P=0.008; table 2).

In univariate analysis of patients of the BMM+rMT group, we found a tendency towards lower baseline NIHSS score, thrombolysis and successful recanalization after rMT being associated with a 90-day mRS score 0–1, that however remained below the threshold of significance (P=0.061, P=0.069 and P=0.059, respectively). Interestingly, the time elapsed from the onset of symptoms to the moment of clinical deterioration was not a factor associated with the 90-day outcome (median (IQR) onset-to-worsening (minutes)=235 (180–359) in patients with 90-day mRS score 0–1 vs 261 (230–360) in patients with 90-day mRS score 2–6, P=0.134). In multivariate analysis that used variables with a P value≤0.1 in univariate analysis along with other clinically meaningful ones (age, pre-event mRS score=1, left-side stroke and involvement of a dominant M2 division), lower baseline NIHSS score (OR 0.562, 95% CI 0.347 to 0.910, P=0.019) and successful recanalization after rMT (OR 4.549, 95% CI 0.098 to 18.851, P=0.037) were associated with a favorable 90-day clinical outcome (table 3). After dichotomization of the mRS score 0–2 versus 3–6, lower age (OR 0.939, 95% CI 0.884 to 0.996, P=0.036), baseline NIHSS score (OR 0.470, 95% CI 0.242 to 0.913, P=0.026) and successful recanalization after rMT (OR 5.290, 95% CI 1.050 to 26.650, P=0.043) were associated with a favorable outcome (online supplemental table 2).

As an early clinical worsening during BMM constitutes a relevant factor for 90-day unfavorable outcome, we looked for possible baseline predictors of END. Among baseline clinical, radiological and pharmacologic data that were measured, the rates of atrial fibrillation (AF), current antiplatelet or anticoagulant therapy and involvement of a dominant M2 division were significantly higher (P<0.001, P=0.009, P=0.020 and P=0.002, respectively) in patients experiencing END in univariate analysis. However, AF resulted as the only independent predictor of END in a logistic regression model (OR 3.547, 95% CI 1.014 to 12.406, P=0.048; table 4).

## DISCUSSION

Our retrospective study confirms that END is a frequent event in patients with a minor stroke due to involvement of the M2 segment of the middle cerebral artery and represents the most important predictor of long-term poor outcome in patients that are initially intended for medical therapy. In case of END, rMT represents a feasible treatment option that can improve, at least in part, the clinical outcome.<sup>2 5 8 17</sup>

Patients with a minor stroke due to isolated M2 occlusion pose a two-fold problem during the acute management, that is the presence of a distal and less easily accessible site of occlusion and minimal symptoms, eliciting skepticism about the appropriateness of immediate thrombectomy as the preferred recanalization treatment. Moreover, we have recently reported that in such a scenario, immediate mechanical thrombectomy has no clear benefit over a therapeutic approach based on BMM with the possibility of rMT on END.<sup>8</sup> The results of the present study further corroborate the evidence that rMT is indeed beneficial when END occurs. Conversely, in our analysis thrombolysis neither seems to prevent the occurrence of END nor is associated with long-term favorable outcome after END. Following this line of evidence, there is a need to define baseline clinical or instrumental criteria to identify patients with M2 occlusion and minor symptoms that might be at higher risk for clinical deterioration despite BMM.

Clear-cut predictive factors of END are still missing but a more proximal site of occlusion, thrombus length and extension, diabetes and atrial fibrillation probably play a role.<sup>2 5 17–19</sup> It is conceivable that putative mechanisms of END result in reduction of cerebral perfusion pressure, possibly mediated by poor patency of the leptomeningeal collateral network.<sup>20</sup> However, in our study the pial arterial filling status, assessed with the Menon

**Table 3** Univariate analysis of possible predicting factors of 90-day modified Rankin Scale score 0–1 in patients in the best medical management+rescue mechanical thrombectomy group

Parameter	mRS score 0–1	mRS score 2–6	P value*
Number of patients/total (%)	61/87 (70.1)	26/87 (29.9)	
Demographics			
Females, number/total (%)	33/61 (54.1)	13/26 (50.0)	0.726
Age, median (IQR)	69 (59–79)	74 (66–83)	0.773
Baseline clinical features			
Atrial fibrillation, number/total (%)	24/38 (63.1)	9/15 (60.0)	0.831
Diabetes, number/total (%)	10/29 (34.5)	2/14 (14.3)	0.166
Dyslipidemia, number/total (%)	19/37 (51.3)	11/19 (57.9)	0.642
Coronary artery disease, number/total (%)	10/29 (34.5)	6/17 (35.3)	0.956
Carotid atherosclerosis, number/total (%)	9/31 (29.0)	6/16 (37.5)	0.555
Previous stroke, number/total (%)	9/27 (33.3)	3/15 (20.0)	0.359
Baseline NIHSS score, median (IQR)	3 (2–4)	4 (3–5)	0.061
Pre-event mRS score=1, number/total (%)	6/61 (9.8)	6/26 (23.0)	0.101
Baseline imaging data			
Left-side stroke, number/total (%)	37/61 (60.6)	14/26 (53.8)	0.555
ASPECTS, median (IQR)	10 (9–10)	10 (9–10)	0.940
Dominant M2 division, number/total (%)	40/61 (65.6)	16/26 (61.5)	0.719
Menon score, median (IQR)	4 (4–5)	4 (4–4)	0.975
Medical therapy and procedural parameters			
Current antiplatelet therapy, number/total (%)	14/30 (46.7)	10/19 (52.6)	0.684
Current anticoagulant therapy, number/total (%)	13/34 (38.2)	4/15 (26.7)	0.433
Thrombolysis, number/total (%)	45/61 (73.8)	14/26 (53.8)	0.069
OTW time, minutes (IQR)	235 (180–359)	261 (230–360)	0.134
mTICI 2b-3, number/total (%)	54/61 (88.5)	18/25 (72.0)	0.059
Brain bleeding events			
IPH, number/total (%)			0.827
No IPH	52/60 (86.7)	22/26 (84.6)	
IPH type 1	7/60 (11.6)	3/26 (11.5)	
IPH type 2	1/60 (1.6)	1/26 (3.8)	
<b>Multivariate logistic regression for predicting factors of 90-day mRS score 0–1 in patients of the BMM+rMT group</b>			
Parameter	OR	95% CI	P value*
Age	0.971	0.929 to 1.015	0.131
Pre-event mRS score=1	0.844	0.191 to 3.727	0.823
Left-side stroke	0.692	0.223 to 2.143	0.523
Dominant M2 division	1.708	0.563 to 5.188	0.345
Baseline NIHSS score	<b>0.562</b>	<b>0.347 to 0.910</b>	<b>0.019</b>
Thrombolysis	2.873	0.914 to 9.030	0.071
mTICI 2b-3	<b>4.549</b>	<b>1.098 to 18.851</b>	<b>0.037</b>

\*Figures in bold type denote statistical significance (considered at P<0.05).

. ASPECTS, Alberta Stroke Program Early CT Score; BMM, best medical management; CI, confidence interval; IPH, intraparenchymal hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; mTICI, modified Treatment In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; OTW, onset-to-worsening; rMT, rescue mechanical thrombectomy.

score, was not predictive of END. Conversely, we must consider that the Menon score was acquired when patients had minor symptoms and were initially intended for medical management only, but we do not know whether it was different at the time of END.

In our cohort, AF was associated with early worsening. AF has been already described as a predictive factor of poor 90-day outcome after stroke. Indeed, AF is frequently associated with

ischemic heart disease, valvular disease or sick sinus syndrome, with a consequent decreased heart function. Moreover, the evidence that elevated serum cardiac troponin levels are associated with END in patients with AF-related stroke supports the close connection between heart dysfunction and poor outcome.<sup>21</sup> This can explain the increased rate of mortality that was observed in our patients with END. Furthermore, the relatively frequent occurrence of AF in our cohort possibly justifies also the high

**Table 4** Univariate analysis of baseline clinical, neuroimaging and medical therapy data between patients with and without early neurological deterioration

Parameter	Patients with END	Patients without END	P value*
Number of patients/total (%)	87/208 (41.8)	121/208 (58.2)	
Demographics			
Females, number/total (%)	46/87 (52.9)	56/121 (46.3)	0.348
Age in years, median (IQR)	70 (61–80)	71 (64–79)	0.256
Clinical features and medical therapy			
Atrial fibrillation, number/total (%)	33/53 (62.3)	31/121 (25.6)	<0.001
Diabetes, number/total (%)	12/43 (27.9)	27/121 (22.3)	0.459
Dyslipidemia, number/total (%)	30/56 (53.6)	64/121 (52.9)	0.933
Coronary artery disease, number/total (%)	16/46 (34.8)	29/121 (24.0)	0.159
Carotid atherosclerosis, number/total (%)	15/47 (31.9)	53/121 (43.8)	0.159
Previous stroke, number/total (%)	12/42 (28.6)	24/121 (19.8)	0.240
Baseline NIHSS score, median (IQR)	3 (2–4)	3 (2–4)	0.420
Pre-event mRS score=1, number/total (%)	12/87 (13.8)	25/121 (20.7)	0.201
Current antiplatelet therapy, number/total (%)	24/49 (49.0)	34/121 (28.1)	<b>0.009</b>
Current anticoagulant therapy, number/total (%)	17/49 (34.7)	22/121 (18.2)	<b>0.020</b>
Thrombolysis, number/total (%)	59/87 (67.8)	74/121 (61.1)	0.324
Baseline imaging data			
ASPECTS, median (IQR)	10 (9–10)	10 (9–10)	0.876
Left-side stroke, number/total (%)	51/87 (58.6)	76/121 (62.8)	0.541
Menon score, median (IQR)	4 (4–4)	4 (3–5)	0.082
Dominant M2 division, number/total (%)	56/87 (64.4)	52/121 (43.0)	<b>0.002</b>
<b>Multivariate logistic regression for predicting factors of END</b>			
Parameter	OR	95% CI	P value*
Age	0.978	0.923 to 1.038	0.479
Atrial fibrillation	<b>3.547</b>	<b>1.014 to 12.406</b>	<b>0.048</b>
No current antiplatelet therapy	2.507	0.643 to 9.775	0.186
No current anticoagulant therapy	1.232	0.120 to 12.601	0.861
Dominant M2 division	1.835	0.058 to 5.806	0.302
Menon score	0.693	0.366 to 1.312	0.260
No thrombolysis	0.691	0.142 to 3.365	0.647

\*Figures in bold type denote statistical significance (considered at  $P < 0.05$ ).

.ASPECTS, Alberta Stroke Program Early CT Score; CI, confidence interval; END, early neurological deterioration; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.

rate of patients undergoing clinical deterioration, compared with what was previously described in cases of minor stroke with isolated M2 occlusion.<sup>19 22</sup> In these patients, mechanisms of END may include an overall reduction of cerebral blood flow in conjunction with a less effective deployment of leptomeningeal collaterals.<sup>23–25</sup> However, previous studies focused on a putative difference of collateral circulation between cardioembolic and non-cardioembolic stroke have led to uneven conclusions.<sup>26 27</sup> Finally, recanalization rates after medical management have been reported to be lower in AIS patients with AF, possibly in relation to a different clot composition.<sup>28 29</sup>

Regardless of the underlying mechanism and from a practical standpoint, the results of our study suggest that minor stroke patients with isolated M2 occlusion and concomitant AF should be closely monitored for possible worsening during BMM and considered for rMT immediately after the beginning of clinical deterioration.

The main limitation of our study derives from its retrospective nature and non-controlled design, making it prone to a selection

bias. Although clinical records were carefully reviewed, the results could have been affected by the quality of data not collected within the more rigid criteria of a randomized trial. Several variables that may be predictive of 90-day clinical outcome were not available in our analysis, such as the admission to an intensive care unit or a stroke unit, or the time elapsed from clinical worsening to the moment of groin puncture in patients experiencing END. We are also aware that other potential predictors of END were missing in our analysis. These include, for example, blood pressure and thrombus length and extension.<sup>19</sup> Also, a group of patients suffering END but not receiving rMT was not available for analysis to verify whether this treatment approach is indeed beneficial. This aspect can be relevant given the overall high rate of favorable outcome associated with this specific condition, that leaves limited space to validate the effectiveness of an invasive recanalization procedure. Conversely, our results derive from a relatively large population of patients with minor stroke and isolated M2 occlusion initially intended for medical therapy, in consideration of the rarity of the two conditions combined.

Nonetheless, for the same considerations that were reported above, our sample size may still not be large enough to detect significant baseline clinical or neuroradiological features that have a role in the occurrence of END or in long-term outcome.

## CONCLUSIONS

In patients with M2 occlusion and minimal baseline symptoms undergoing medical management, END can affect long-term outcome that, however, can be ameliorated by effective rMT. Among baseline clinical features, presence of atrial fibrillation appears to be a predictor of END.

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