CLINICAL AND POPULATION SCIENCES



Mechanical Thrombectomy in Prestroke Disability: Data From the Italian Endovascular Stroke Registry

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BACKGROUND: The benefits and safety of mechanical thrombectomy (MT) in patients with prestroke disability, classified as modified Rankin Scale (mRS) score of 3 to 4, and anterior circulation stroke remain uncertain. This study aims to evaluate these factors using data from the Italian Registry of Endovascular Treatment in Acute Stroke.

METHODS: We analyzed data collected between 2015 and 2021, comparing functional outcomes (mRS), symptomatic intracerebral hemorrhage, and recanalization rates (Thrombolysis in Cerebral Infarction) at 90 days post-MT in patients with prestroke mRS score of 3 to 4 versus 0 to 2. A good outcome was defined as no change in the mRS score from baseline. Subgroup analysis was stratified by age.

RESULTS: A total of 11.411 (96%) patients with prestroke mRS score of 0 to 2 and 477 (4%) patients with prestroke mRS score of 3 to 4 were included. Compared with patients with a baseline mRS score 0 to 2, those with mRS score 3 to 4 were older (82 versus 75 years; P<0.001) and predominantly female (71.7% versus 53%; P<0.001). The maintenance of the same mRS score after MT was observed in 100 (23.3%) patients with prestroke mRS score 3 to 4, compared with 2332 (22.1%) patients with mRS score 0 to 2 (P=0.556). Mortality was significantly higher in the mRS score 3 to 4 group (n=159 [37.1%] versus n=1939 [18.4%]; P<0.001). Successful recanalization (Thrombolysis in Cerebral Infarction score ≥2b) was lower in the mRS score 3 to 4 group (n=333 [71.6%] versus n=8706 [77.7%]; P=0.002), while no significant differences in symptomatic intracerebral hemorrhage were found. The benefit of MT was maintained in patients aged 80 to 85 and over 85 years with prestroke mRS score 3 to 4, although mortality remained higher.

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CONCLUSIONS: Our data suggest that prestroke disability does not imply less chance of returning to prestroke conditions after MT, even in octogenarians, despite higher mortality and lower recanalization rate. More data are warranted to better understand the benefit of MT in this subgroup of patients.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: cerebral infarction ■ intracranial hemorrhages ■ stroke ■ thrombectomy ■ thrombolytic therapy

Nonstandard Abbreviations and Acronyms

IVT intravenous thrombolysis mRS MT

modified Rankin Scale mechanical thrombectomy

NIHSS National Institutes of Health Stroke

Scale

nternational guidelines recommend mechanical thrombectomy (MT) for acute ischemic stroke caused by large vessel occlusion in the anterior circulation for patients with a modified Rankin Scale (mRS) score of ≤1.^{1,2} In fact, patients with prestroke disability, defined as an mRS score >1, were initially excluded from clinical trials, resulting in a lack of clinical outcome and safety data for this significant subgroup. Nevertheless, it is estimated that over one-third of patients with acute ischemic stroke due to large vessel occlusion have preexisting disabilities, raising questions about the appropriateness of endovascular treatment for these individuals.3,4

Preliminary investigations, mostly single-center studies with limited sample sizes, have suggested potential benefits of MT even in patients with an mRS score >1, though this is accompanied by a significantly increased 90-day mortality rate.^{5,6} The expected benefit quantification, however, depends on the definition of outcomes. The varying inclusion criteria and end points of different studies have complicated the interpretation of results, which remains inconsistent. The standard definition of a favorable outcome, mRS score 0 to 2 at 3 months, is disadvantageous for those with preexisting disabilities (mRS score, 2) and unfeasible for individuals with mRS score of 3 to 4 compared with those with an initial mRS score of 0 to 1.

Moreover, advancements in endovascular techniques, the extension of the treatment window to 24 hours, and broader adoption of these procedures have led to an increasing number of patients undergoing MT. In clinical practice, including patients with an mRS score ≤2 has become routine. Thus, the definition of a favorable outcome requires revision for patients with prestroke disabilities. A recent meta-analysis demonstrated that over a guarter of patients with mRS score 3 to 4 could return to their prestroke condition after MT, indicating potential benefits even for this group.7

Although aggregated data suggest a potential benefit of MT in this population, evidence remains limited, particularly for patients with a prestroke mRS score >2, and the scientific community has called for further high-quality data from larger sample sizes.8,9 Additionally, there is no information on the impact of age in this cohort undergoing thrombectomy. In this study, we examined the benefit and safety of MT in a population of patients with prestroke mRS score 3 to 4, assessing the likelihood of returning to prestroke conditions compared with those with mRS score 0 to 2, using data from the Italian Registry of Endovascular Treatment in Acute Stroke. We also analyzed the effect of age on outcomes in these patients.

METHODS

Study Design

The Italian Registry of Endovascular Treatment in Acute Stroke established in 2010, collects clinical and instrumental data on endovascular treatments for acute ischemic stroke. It includes all consecutive patients undergoing these procedures according to current guidelines, with voluntary participation from both academic and hospital institutions. Initially involving 26 centers, the registry has expanded to 55 sites. However, only those with at least 80% data completeness in the main efficacy and safety measures are considered suitable for statistical analysis. For this study, data from 40 centers were used. Further organizational details and the objectives of this multicenter national registry are described elsewhere.10 Ethical approval for the Italian Registry of Endovascular Treatment in Acute Stroke was approved by the Ministry of Health in 2015. The use of anonymized data for retrospective studies does not require additional approvals. The study adhered to the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) for observational research (Supplemental Material).¹¹ Anonymized data can be provided upon reasonable request to the corresponding author.

The study period spanned from January 2015 to December 2021. We retrospectively included all consecutive patients aged ≥18 years who underwent MT for anterior large vessel occlusion, with or without prior intravenous thrombolysis (IVT). Inclusion criteria for MT aligned with current Italian and international guidelines.^{1,12} Exclusions included posterior circulation strokes, patients lacking a prestroke mRS score, those with a baseline mRS score of 5, and those showing a 90-day mRS improvement of ≥2 points compared with baseline. This exclusion was necessary to account for potential discrepancies in mRS evaluation among operators and transient prestroke

disabilities. Instead, an improvement of 1 point was considered as no change from the baseline mRS in the final outcome. The patient selection criteria flowchart is presented in Figure 1.

Population Characteristics

We collected demographic data (age and sex), clinical information (stroke severity at admission measured by the National Institutes of Health Stroke Scale [NIHSS]), patients' medical history (vascular risk factors and pre-event medications), radiological features (Alberta Stroke Program Early CT Score, ranging from 0 to 10 where a lower score indicates a larger ischemic area), site of vessel occlusion, recanalization rate measured by the Thrombolysis in Cerebral Infarction scale, and key time intervals for imaging and endovascular procedures. 13,14

Outcome Measures

Prestroke and poststroke disability was assessed using the mRS score, defined as follows: 0, no symptoms; 1, no significant disability despite symptoms; 2, slight disability; 3, moderate disability; 4, moderate-to-severe disability; 5, severe disability; and 6, death. Patients were categorized into 2 groups: prestroke mRS score 0 to 2 (absent/minor disability) and mRS score 3 to 4 (moderate/severe disability), with comparisons made between variables. Functional outcomes were measured by the 90-day mRS, obtained through follow-up visits or neurologistconducted phone calls. Primary outcomes were defined as a good clinical outcome at 90 days (no change in mRS score compared with prestroke) and 90-day mortality (mRS score, 6). Secondary outcomes included the technical success and safety of MT. Safety variables included the rate of symptomatic intracerebral hemorrhage, defined according to the ECASS III criteria as any cerebral hemorrhage accompanied by clinical deterioration, with an increase of ≥4 points on the NIHSS, as

well as post-thrombectomy complications such as distal embolization from thrombus fragmentation, inguinal hematoma of any size requiring surgery, and vessel dissection during treatment.¹⁵ Technical efficacy was assessed by the recanalization rate, based on Thrombolysis in Cerebral Infarction scale values of 2b-3 (successful recanalization with complete filling/ perfusion) versus 0-2a (ranging from no perfusion to partial filling). Finally, the effect of age on the primary outcomes was assessed.

Statistical Analysis

Statistical analysis was performed with the IBM SPSS Statistics (version 29.0) software package. We reported counts and percentages for categorical variables, and median and interquartile range for other variables. For the comparison between groups (mRS score 0-2 versus 3-4), we used 2-tailed Fisher exact test for categorical variables and Mann-Whitney U test for other variables. When needed, we estimated effect sizes using adjusted standardized residuals for categorical variables and Hodges-Lehmann median differences for other variables. We used logistic regression analysis to evaluate the relationship between various predictor variables and binary outcome variables reporting P, B with SE, and odds ratio (exp(B)) with 95% Cls. As independent variables, we used age, sex, NIHSS, vascular risk factors, successful recanalization, combined IVT+endovascular therapy, and door-to-groin time. For modeling the relationship between age and mRS or mortality, we binned the sample in 20 age-classes, using 5% centiles bins, then we computed the mean of age, mortality, and mRS recovering frequency for every class. We used adjusted R2 model selection for choosing the best regression model (among linear, polynomial, or exponential). P<0.05 was chosen as the statistical significance threshold.

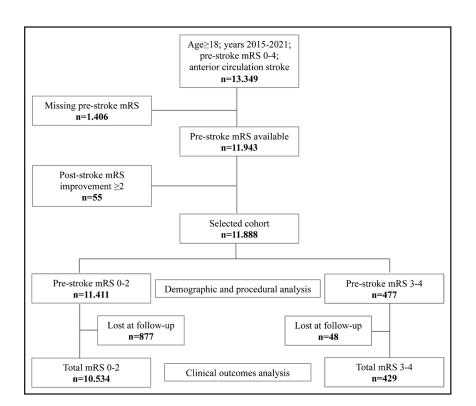


Figure 1. Patient selection flowchart. mRS indicates modified Rankin Scale.

RESULTS

Population Characteristics

For clinical, demographic, and radiological characteristics, 11411 patients with prestroke mRS score 0 to 2 (96%) were compared with 477 patients with prestroke mRS score 3 to 4 (4%). Of these, 414 (87%) patients presented with prestroke mRS score of 3, while 63 (13%) had a prestroke mRS score of 4. After excluding missing 90-day mRS data, the outcome analysis was conducted between 10534 (mRS score, 0–2) and 429 (mRS score, 3–4) individuals.

Patients with moderate-to-severe disability were older (82 versus 75 years; P<0.001), more frequently female (71.7% versus 53%; P < 0.001), and had higher presenting NIHSS scores (18 versus 16; P<0.001). Additionally, those with prestroke mRS score 3 to 4 exhibited a significantly higher vascular risk profile and greater use of antithrombotic medications (both antiplatelets and anticoagulants), antihypertensives, and statins. No significant differences were noted in radiological parameters, including the Alberta Stroke Program Early CT Score and the site of vascular occlusion, between the groups. Patients with prestroke mRS score 3 to 4 were less likely to receive IVT compared with those with prestroke mRS score 0 to 2 (32% versus 51.1%; P<0.001). Regarding MT, there was a significant increase in door-to-imaging and door-to-groin times for patients with greater disability (32 versus 28 and 84 versus 77 minutes, respectively; both P<0.001). A nonsignificant trend of shorter procedure duration was observed in patients with prestroke mRS score 3 to 4 (55 versus 60 minutes; P=0.058). Detailed clinical, demographic, and radiological analyses with respective significances are provided in Table 1.

Outcomes

The primary and secondary outcomes are presented in Table 1. The proportion of patients maintaining the same mRS score as their baseline was 23.3% for those with a prestroke mRS score of 3 to 4, compared with 22.1% for patients with a prestroke mRS score of 0 to 2 (*P*=0.556). In contrast, mortality was significantly lower in the group with less prestroke disability (18.4% versus 37.1%; *P*<0.001). After adjusting for age, sex, NIHSS score, vascular risk factors, successful recanalization, IVT+EVT, and door-togroin time, the odds ratio for mortality was 1.59 for patients with a prestroke mRS score of 3 to 4 (odds ratio, 1.59 [CI, 1.26−2.01]; *P*<0.001). Changes in mRS and mortality relative to baseline disability are detailed in Figure 2.

Regarding secondary outcomes, the rate of successful recanalization (Thrombolysis in Cerebral Infarction score ≥2b) was lower in patients with a prestroke mRS score of 3 to 4 compared with those with mild or no disability (71.6% versus 77.7%; *P*=0.002). MT demonstrated a similar safety profile between groups, with symptomatic intracerebral hemorrhage rates of 8.4% in the mRS

Table 1. Demographic, Clinical, and Radiological Features, and Outcomes of Patients With Prestroke mRS Scores of 0 to 2 and 3 to 4 Treated With Mechanical Thrombectomy

_					
N=11888					
mRS score 0-2 (n=11411)	mRS score 3-4 (n=477)	P value			
75 (17)	82 (11)	<0.001*			
6053 (53%)	342 (71.7%)	<0.001*			
16 (9)	18 (8)	<0.001*			
365 (3.4%)	30 (6.6%)	<0.001*			
3626 (33.9%)	231 (50.7%)	<0.001*			
1695 (15.8%)	124 (27.2%)	<0.001*			
7053 (65.9%)	342 (75%)	<0.001*			
1083 (10.1%)	74 (16.2%)	<0.001*			
608 (5.3%)	40 (8.4%)	0.005*			
682 (6.4%)	78 (17.1%)	<0.001*			
1715 (16%)	34 (7.5%)	<0.001*			
2657 (24.8%)	118 (25.9%)	0.621			
461 (4%)	22 (4.6%)	0.561			
99 (0.9%)	37 (8.1%)	<0.001*			
578 (5.4%)	26 (5.7%)	0.762			
1	ı				
2975 (26.1%)	178 (37.3%)	<0.001*			
1834 (16.1%)	154 (32.3%)	<0.001*			
5610 (40.2%)	285 (59.7%)	<0.001*			
1795 (15.7%)	97 (20.3%)	0.008*			
	1	1			
10 (2)	10 (2)	0.454			
1					
4209 (41.4%)	169 (39.8%)				
2299 (22.7%)	104 (25.1%)				
1089 (10.7%)	57 (13.7%)	0.170			
934 (9.2%)	37 (8.9%)				
526 (5.2%)	13 (3.3%)				
1102 (10.8%)	36 (8.8%)				
J					
5594 (51.1%)	148 (32%)	<0.001*			
J.					
1448 (14.4%)	55 (13.5%)				
4298 (42.7%)	177 (43.6%)	0.899			
3903 (38.8%)	160 (39.4%)				
414 (4.1%)	14 (3.4%)				
8706 (77.7%)	333 (71.6%)	0.002*			
3823 (43%)	170 (41.3%)	0.248			
3823 (43%)	170 (41.3%)	0.248			
	N=11888 mRS score 0-2 (n=11411) 75 (17) 6053 (53%) 16 (9) 365 (3.4%) 3626 (33.9%) 1695 (15.8%) 7053 (65.9%) 1083 (10.1%) 608 (5.3%) 682 (6.4%) 1715 (16%) 2657 (24.8%) 461 (4%) 99 (0.9%) 578 (5.4%) 2975 (26.1%) 1834 (16.1%) 5610 (40.2%) 1795 (15.7%) 10 (2) 4209 (41.4%) 2299 (22.7%) 1089 (10.7%) 934 (9.2%) 526 (5.2%) 1102 (10.8%) 5594 (51.1%) 1448 (14.4%) 4298 (42.7%) 3903 (38.8%) 414 (4.1%)	mRS score 0-2 (n=11411) 75 (17) 82 (11) 6053 (53%) 342 (71.7%) 16 (9) 18 (8) 365 (3.4%) 30 (6.6%) 3626 (33.9%) 231 (50.7%) 1695 (15.8%) 124 (27.2%) 7053 (65.9%) 342 (75%) 1083 (10.1%) 74 (16.2%) 608 (5.3%) 40 (8.4%) 682 (6.4%) 78 (17.1%) 1715 (16%) 2657 (24.8%) 118 (25.9%) 461 (4%) 22 (4.6%) 99 (0.9%) 37 (8.1%) 578 (5.4%) 2657 (26.1%) 178 (37.3%) 1834 (16.1%) 154 (32.3%) 5610 (40.2%) 285 (59.7%) 10 (2) 4209 (41.4%) 10 (2) 4209 (41.4%) 169 (39.8%) 2299 (22.7%) 104 (25.1%) 1089 (10.7%) 57 (13.7%) 934 (9.2%) 37 (8.9%) 526 (5.2%) 13 (3.3%) 1102 (10.8%) 5594 (51.1%) 148 (32%) 448 (14.4%) 55 (13.5%) 4298 (42.7%) 177 (43.6%) 3903 (38.8%) 160 (39.4%) 414 (4.1%) 14 (3.4%)			

(Continued)

Table 1. Continued

	N=11888							
	mRS score 0-2 (n=11411)	mRS score 3-4 (n=477)	P value					
Subarachnoid hemorrhage	346 (3%)	14 (2.9%)	0.999					
Dissection	177 (1.6%)	5 (1%)	0.565					
Distal embolization	834 (7.3%)	28 (5.9%)	0.280					
Retroperitoneal/puncture site growing hematoma	83 (0.7%)	4 (0.8%)	0.780					
Time intervals, min; median (IQR)								
Door to imaging	28 (25)	32 (32)	<0.001*					
Door to groin puncture	97 (77)	110 (84)	<0.001*					
Door to recanalization	162 (101)	178 (102)	<0.001*					
Procedure time	60 (53)	55 (55)	0.058					
Clinical outcomes, n (%)								
90-d return to prestroke mRS	2332 (22.1%)	100 (23.3%)	0.556					
90-d mortality	1939 (18.4%)	159 (37.1%)	<0.001*					

Missing data: ASPECTS (n=1841), site of occlusion (n=1378), endovascular treatment (n=1419), TICI (n=218), and sICH and safety (n=591). ASPECTS indicates Alberta Stroke Program Early CT Score; carotid TL, T-shape or L-shape clot occlusion; EVT, endovascular treatment; ICA, internal carotid artery; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SICH, symptomatic intracerebral hemorrhage; TIA, transient ischemic attack; and TICI, Thrombolysis in Cerebral Infarction. "Statistically significant.

score 3 to 4 group versus 7.6% in the mRS score 0 to 2 group (P=0.595). Procedural complication rates did not differ significantly between the groups.

Annually, the proportion of patients with a prestroke mRS score of 3 to 4 undergoing thrombectomy averaged 4%, with no significant variation over the 7-year period analyzed (data not shown).

Age stratification revealed that the probability of maintaining the same mRS poststroke as baseline was similar between the 2 groups for patients <80 years of age. Interestingly, this probability increased significantly for patients aged 80 to 85 years and those >85 years of age with a prestroke mRS score of 3 to 4 (Table 2). Conversely, mortality rates remained consistently higher for the prestroke mRS score 3 to 4 group, regardless of age.

The intersection of 2 models relating age and the risk of death (blue line), and age and the probability of returning to the same prestroke mRS (orange line), regardless of baseline mRS, is shown in Figure 3.

DISCUSSION

This study analyzes the largest cohort of patients with preexisting disabilities (mRS score, 3-4) and acute ischemic stroke due to large vessel occlusion who underwent MT. The findings indicate that this subgroup has a similar likelihood of maintaining their baseline disability level compared with those with mild or no prestroke disability. However, the mortality rate is significantly higher in this population. MT was proven to be safe, showing no increased risk of symptomatic intracerebral hemorrhage or procedural complications across the groups analyzed. Notably, we observed a lower recanalization rate in patients with higher baseline disabilities, along with increased times to access imaging and initiate MT in these patients, which correlated with a trend toward shorter duration of the endovascular procedure.

With our criterion for a good outcome established, the favorable clinical outcomes documented are consistent with a recent meta-analysis, showing nearly overlapping return rates to the same initial mRS score (20% versus

Post Pre	0	1	2	3	4	5	6
0	23.4%	16.6%	13.9%	12.4%	12.8%	5.7%	15.1%
1	24%		13.7%	14.7%	14.5%	7.1%	26.1%
2	-	23.7% 18.2		18.2%	14.8%	8.5%	34.8%
3	-	-	29.6%		20.5%	13.6%	36.3%
4	1			33.	4%	24.1%	42.6%

Figure 2. Changes in modified Rankin Scale (mRS) score and mortality relative to baseline disability (prestroke mRS on the vertical axis, poststroke mRS on the horizontal axis).

Green: no mRS changes compared with baseline disability. Yellow: 1-point worsening shift in mRS. Orange: 2-point worsening shift in mRS. Red: ≥3-point worsening shift in mRS. Dark red: 3-month mortality.

0.010*

0.021*

1.610 (1.120-2.313)

1.524 (1.066-2.181)

90-d mRS equal 90-d mortality Prestroke mRS Prestroke mRS Prestroke mRS Prestroke mRS score 0-2 score 3-4 P value score 0-2 score 3-4 P value <79 y (n=7070) 25.7% 21.6% 0.247 13.4% 33.3% < 0.001* 0.795 (0.539-1.173) 3.219 (2.284-4.537)

1.639 (1.097-2.448)

2.015 (1.321-3.074)

23.5%

35.4%

Table 2. Three-Month Probability of Maintaining the Same mRS Score and Mortality Stratified by Age in Patients With Prestroke mRS Scores of 0 to 2 and 3 to 4

0.016*

0.001

mRS indicates modified Rankin Scale.

16.1%

14.0%

23.9%

24.6%

80-85 y (n=2426)

>85 y (n=1467)

23.7% for an mRS score of 2; 27% versus 29.6% for an mRS score of 3; 31% versus 33.6% for an mRS score of 4), while our mortality rates were lower (36% versus 34.8% for an mRS score of 2; 45% versus 36.3% for an mRS score of 3; 61% versus 42.6% for an mRS score of 4).7 Interestingly, the clinical benefit appears to be greater in patients with higher prestroke disability, a finding that is consistent with other studies. 16,17 A possible explanation for this phenomenon is 2-fold: from a clinical perspective, the transition from 0 to 1 or 1 to 2 on the mRS is more nuanced and seemingly easier to achieve compared with the transition from 3 to 4, which more clearly defines a loss of autonomy. Second, patients with mRS score 3 to 4 included in the analysis may represent a hyperselected group by the treating physicians, indicating a selection bias. In fact, a favorable neuroimaging pattern (including perfusion studies) or specific clinical characteristics (such as the type of preexisting disability) may have guided patient selection. These reasons may also explain the observed net benefit in our age-stratified analysis, showing a significant benefit in maintaining the same baseline mRS score in patients with moderate-severe preexisting

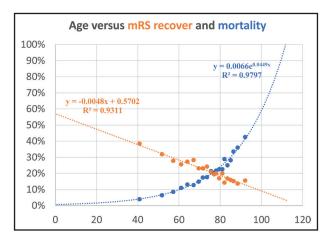


Figure 3. Relationship between age and the risk of death (blue line), and age and the probability of maintaining the same prestroke modified Rankin Scale (mRS) score after stroke treated with mechanical thrombectomy (orange line), independently of baseline mRS.

disability compared with those with mild or no disability as age increases. Taken together, these findings appear particularly notable given the higher burden of comorbidities and increased procedural time intervals observed in the group with prestroke mRS score 3 to 4. Despite these factors, the proportion of patients returning to their premorbid mRS was similar to those with milder or no prestroke disability. This suggests that, although this population presents with additional risk factors, they do not necessarily translate into poorer functional outcomes post-thrombectomy. However, this must be interpreted with caution, as the mechanisms underlying this result remain unclear and may reflect—at least in part—a combination of careful patient selection and effective treatment protocols. This interpretation may also apply to octogenarians, although no conclusive data can be drawn in this regard. Nevertheless, while further studies are needed to confirm our findings and better delineate the predictors of functional recovery in this group, this result holds significant relevance given the aging population and the increasing number of elderly individuals undergoing MT, with potential implications for socioeconomic costs.4

33.1%

45.5%

The mortality data are also consistent. In agreement with previous studies, mortality in patients with greater prestroke disability is significantly increased at 3 months.¹⁸⁻²⁰ Conversely, patients with such disabilities appear to benefit from thrombectomy compared with medical therapy in terms of reduced final mortality, particularly in cases of effective recanalization.721-24

MT was found to be safe, with nonsignificant rates of procedural complications and symptomatic intracerebral hemorrhage in the analyzed populations. We documented a lower recanalization rate in the mRS score 3 to 4 group, aligning with prior observations by Florent et al²⁰ but contrasting with other studies that reported no differences in recanalization rates. 5,9,19,21 This finding was associated with increased times to access imaging and start treatment. We speculate that the longer door-to-imaging and doorto-treatment times may be partially due to the need for more extensive anamnesis on prestroke conditions during patient selection. Physicians likely required additional time to assess the overall prognosis, comorbid conditions, and

^{*}Stastically significant.

potential benefits of MT in these patients, which contributed to the delays. Moreover, obtaining a thorough medical history and consulting family members or caregivers for patients with preexisting disabilities may have also played a role in extending these time intervals. Similarly, we observed a trend toward shorter treatment duration in the angiography suite, possibly due to fewer thrombectomy passes being performed in patients with preexisting disabilities, which consequently reduces recanalization rates. Certainly, we cannot exclude that other factors not systematically available from the registry data (such as more complex vascular anatomy or a greater clot burden) may have contributed to this result. Nevertheless, favorable outcome results were comparable between groups, suggesting that the early termination of MT in case of failure should not be justified in this population and also highlighting the importance of optimizing workflow efficiency in this subgroup.

Our study has several limitations. The first is the retrospective design. As registry data, outcome measures may vary between centers due to the absence of centralized adjudication. Additionally, we lack a control group for comparison. Furthermore, patients with preexisting disability undergoing treatment may represent a highly selected group, excluding those deemed too frail or at higher risk of complications, while including those with favorable advanced neuroimaging features. However, with the available registry data, it was not possible to identify patients who may have been selected based on perfusion imaging. This selection bias could result in an overestimation of good outcomes in the group with greater preexisting disability. Moreover, we do not have details on which kind of disability, whether neurological or orthopedic, was responsible for the prestroke mRS. We also lack data concerning the type of rehabilitation between discharge and 90-day follow-up and differences in the quality of rehabilitation in different regions of Italy. Finally, we cannot rule out interference in outcomes, including bleeding complications, due to the different proportions of patients undergoing IVT in the analyzed groups.

We also clarify that, although the principles of patient selection, procedural safety, and the role of MT in prestroke disability populations likely extend beyond regional differences, the results of this study pertain to a specific national health care system with distinct access to acute stroke treatment and poststroke rehabilitation pathways. Therefore, the generalizability of the results and their applicability to other health care systems must be further investigated.

Despite all limitations, these real-world data suggest the unavoidable need to pay careful selection of patients with relevant prestroke disability based on a detailed medical history and neuroimaging predictors. Our data suggest the efficacy and safety of MT in selected patients with moderate-to-severe prestroke disability (mRS score, 3–4) and also in association with advanced age. Although careful patient selection is mandatory, prestroke disability alone does not seem to be a sufficient

criterion to exclude patients from endovascular treatment. Randomized controlled trials are needed to assess the outcomes and safety of MT in patients with prestroke disability, providing insights to refine clinical practice and patient selection. We encourage future research to address this important gap and guide decision-making in this complex population.

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Supplemental Material

STROBE Checklist

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