



Achieving complete recanalization is the best predicting factor of good outcome for thrombectomy in the elderly. Results from a prospective monocentric study

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Abstract

Background and aims Little is known about predicting factors for a good outcome (GO) after endovascular treatment (EVT) performed for acute ischemic stroke (AIS) related to large vessel occlusion (LVO) in the over-80s population. We evaluate demographic and procedural predictors of GO from our prospective registry of patients treated during the acute phase of an LVO-related AIS.

Methods GO was defined as a 3-month modified Rankin scale (mRS) ≤ 3 or equivalent to pre-stroke mRS. Univariate (UVA) and multivariate (MVA) analysis were performed to assess the factors' independent effect on the outcome. The magnitude of the between-group differences was assessed by calculating the standardized differences (StD). Variables with StD $>0,2$ were included in the MVA.

Results From 182 patients aged ≥ 80 , 3-month GO was observed in 31.3% (57/182). The proportion of $\text{TICI} \geq 2\text{c-}3$ was significantly lower in the poor outcome (PO) group compared to the GO group (52% versus 78.9%, $\text{StD}=0.591$). In univariate logistic regression model, $\text{TICI} \geq 2\text{c-}3$ is associated with a 277% increase in the chances of a GO ($\text{OR}=3.77$, 95%CI 1.79–7.97, $P<0.001$). This association remained significant in multivariate logistic regression model ($\text{aOR}=0.77$, 95%CI 0.66–0.89, $P=0.000501$) even when a hemorrhagic transformation (HT) occurs ($p_{\text{het}}=0.57948$).

Conclusions We show that achieving a TICI score of 2c-3 seems to be the best predictive factor for the outcome in the elderly population. In this group, every effort should be made to achieve excellent recanalization.

Keywords Aged · Endovascular therapy · Ischemic stroke · Clinical outcome

Abbreviations

AIS Acute ischemic stroke
aOR Adjusted odds ratio
ASPECT Alberta Stroke Program Early CT score
CT Computed tomography

CI Internal carotid artery
ECASS European Cooperative Acute Stroke Study
EQ-5D EuroQol 5 Dimension
EVT Endovascular treatment
FLAIR Fluid Attenuation Inversion Recovery
FPE First pass effect
GO Good outcome
HT Hemorrhagic transformation
IVT Intravenous thrombolysis
LVO Large vessel occlusion
MCA Middle cerebral artery
MLR Multilevel logistic regression
MRI Brain magnetic resonance imaging
mRS Modified Rankin scale
mTICI Modified Thrombolysis in Cerebral Infarction
MVA Multivariate analysis

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PH	Parenchymal hemorrhage
NIHSS	National Institutes of Health Stroke Scale
OR	Odds ratio
PO	Poor outcome
RCT	Randomized controlled trial
SD	Standard deviation
StD	Standardized difference
sICH	Symptomatic intracranial hemorrhage
SWI	Susceptibility weighted imaging sequences
TOAST	Trial of ORG 10172 in Acute Stroke Treatment
TOF	3D time-of-flight
UVA	Univariate analysis

Introduction

Stroke patients over 80 years of age make up 30% of all stroke patients [1]. In the wake of several randomized controlled trials (RCTs) published since 2015, endovascular treatment (EVT) is the reference procedure in acute ischemic stroke (AIS) related to a large vessel occlusion (LVO), up to 24 h after symptoms onset [2, 3]. The generalizability of these studies to the group of elderly patients is often limited due to a lack of representation of this group in main RCTs and the lack of RCT dedicated to this population, specifically when it comes to people aged 80 years and more [4]. Many conclusions about the efficacy and safety of EVT in the elderly have thus been deduced from sub-group analysis of RCTs or retrospective studies [5, 6]. At one hand, EVT has been proposed to be an effective intervention for the elderly population, with a 40% decrease of the mortality in the EVT group [6] but at the other hand, advanced age has also been identified as a significant predictor of poor outcome [7], mortality [8] and hemorrhagic transformation [9] following EVT. This discrepancy seems to be partly related to an important heterogeneity in the patients' characteristics analyzed among different studies [10].

Thus, to better predict the patients' clinical outcome, we proposed to seek for the prognostic factors of good clinical outcome (GO) in the elderly population undergoing EVT, with a special interest in common pre and per-EVT characteristics that may be easily assessed during the acute phase management.

Methods

Data collection and outcome

We retrospectively analyzed prospectively collected data of patients who were treated with EVT for an AIS related to a LVO at a comprehensive stroke center integrated into a

network of 6 referring hospitals between January 2013 and December 2023. Methods and data collected are presented in detail in the Supplementary materials.

The primary clinical outcome was dichotomized into GO, defined as a mRS score ≤ 3 at 3 months or a 3-months mRS score equivalent to pre-stroke mRS, and poor clinical outcome (PO - mRS score at 3 months >3 or mRS score at 3 months $>$ pre-mRS score). The local ethics committee approved this research protocol and waived the need for the patient's consent (Ethics Approval Reference: study n°24/41/1305).

Results

Patients' cohort characteristics and outcomes

From 2012 to 2023, 182 patients underwent endovascular recanalization (supplemental Fig. 1). All basic demographic, clinical data, radiologic and procedural characteristics are summarized in Table 1.

Reperfusion status and clinical outcome

GO were observed in 31.3% (57/182) of patients at 3 months.

As shown in Fig. 1, the proportion of modified treatment in cerebral infarction (mTICI) score $\geq 2c-3$ differed significantly between the GO and PO groups. The proportion of mTICI $\geq 2c-3$ was significantly lower in PO group (52%) compared to GO group (78.9%), with a medium effect size (StD=0.591).

In univariate logistic regression model, the presence of mTICI $\geq 2c-3$ is associated with a 277% increase in the chances of a GO (OR=3.77, 95% CI 1.79–7.97; $P<0.001$).

In multivariate logistic regression model, as shown on Fig. 2, the association remained independently significant after adjustment on significant baseline differences (age, diabetes, current smoking, NIHSS on admission, ASPECT score, M2 stroke or internal carotid artery (CI) termination LVO, IVT, number of passes, first pass effect, time from onset to recanalization between 6 and 12 h and 12–24 h) with an aOR of GO of 4.36 (95% CI 1.17–18.54; $P=0.035$). As illustrated in Fig. 3, achieving an excellent reperfusion (mTICI $\geq 2c-3$) significantly enhances the number of excellent outcome (mRS 0–1) at 3 months, while maintaining similar distribution across other categories (aOR: 1.52; 95% CI: 1.20–1.99; $P<0.01$). Furthermore, for each unit increase in the mTICI score, there was a 51.7% increase in the probability of a GO (aOR=1.5165368; $P<0.01$).

These results differ significantly from the lower age group, where the occurrence of excellent recanalization had

Table 1 Baseline characteristics and procedural results of the cohort compared by rates of clinical outcome

	Overall (N= 182)	Clinical outcome		Standardized differences
		Poor (N = 125)	Good (N = 57)	
Demographic characteristics				
• Age, mean	85.94 ± 4.29	86.29 ± 4.56	85.18 ± 3.57	0.272*
• Men	31.9 (58/182)	30.4 (38/125)	35.1 (20/57)	0.100
Medical history				
Cardiovascular risk factors				
• Hypertension	79.7 (145/182)	79.2 (99/125)	80.7 (46/57)	0.038
• Diabetes	18.1 (33/182)	15.2 (19/125)	24.6 (14/57)	0.236*
• Hypercholesterolemia	53.8 (98/182)	51.2 (64/125)	59.6 (34/57)	0.171
• Current smoking	10.4 (19/182)	8 (10/125)	15.8 (9/57)	0.242*
Previous antithrombotic medication				
• Antiplatelet agents	65.4 (119/182)	66.7 (84/125)	62.5 (35/57)	0.179
• Anticoagulant agents	42.9 (78/182)	45.6 (57/125)	36.8 (21/57)	0.070
• Antiplatelet + anticoagulant agents	22.5 (41/182)	21.6 (27/125)	24.6 (14/57)	0.121
• Antiplatelet + anticoagulant agents	65.4 (119/182)	67.2 (84/125)	61.4 (35/57)	0.121
Current stroke event				
• NIHSS score ^c	16 (10.25,20)	17 [13.00, 21]	11 [6.00, 17]	0.756*
• Pre-stroke mRS ^d	0 [0,2]	0 [0, 2]	0 [0, 2.5]	0.023
• ASPECTS ^b	10 [8,10]	10 [8, 10]	10 [8, 10]	0.208*
Imaging				
• CT-scan ^a	97.3(177/182)	97.6 (122/125)	96.5 (55/57)	0.175
• MRI ^a	14.8(27/182)	13.6 (17/125)	17.5 (10/57)	0.165
Site of occlusion				
Anterior circulation				
• MCA - M1	50 (91/182)	52 (65/125)	45.6 (26/57)	0.128
• MCA - M2	19.8 (36/182)	16 (20/125)	28.1 (16/57)	0.294*
• Tandem	6.6 (12/182)	5.6 (7/125)	8.8 (5/57)	0.123
• Extracranial and/or intracranial carotid	18.1 (33/182)	20.8 (26/125)	12.3 (7/57)	0.231*
Posterior circulation				
• Vertebral and Basilar	3.8 (7/182)	4 (5/125)	3.5 (2/57)	0.026
Cardioembolic etiology				
Multiple territory	58.2 (106/182)	56.8 (71/125)	61.4 (35/57)	0.094
• Multiple territory	1.6 (3/182)	1.6 (2/125)	1.8 (1/57)	0.012
Treatment characteristics				
• IVT	41.2 (75/182)	37.6 (47/125)	49.1 (28/57)	0.234*
• General anesthesia	100 (182/182)	100 (125/125)	100 (57/57)	0.0
Front-line procedure^f				
• Stent retriever	54.4 (99/182)	52.8 (66/125)	57.9 (33/57)	0.107
• Contact aspiration	1.6 (3/182)	1.6 (2/125)	1.8 (1/57)	
• Stent retriever and contact aspiration	38.5 (70/182)	40 (50/125)	35.1 (20/57)	
Other EVT characteristics				
• Number of passes ^h	2 [1, 3]	2 [1, 3]	1 [1, 2]	-0.598*
• First pass effect ^g	33.5 (61/182)	26.4 (33/125)	49.1 (28/57)	0.487*
• Onset to admission, min	163 [60, 240]	162 [60, 240]	171 [54, 240]	0.051
• Onset to recanalization, min	270 [215.5, 345.5]	266 [216.5, 360]	271.5 [209.5, 318.25]	0.219*
• Onset to recanalization between 6-12h ⁱ	20.9 (38/182)	22.4 (28/125)	17.5 (10/57)	0.479*
• Onset to recanalization between 12-24h ⁱ	9.3 (17/182)	7.2 (9/125)	14 (8/57)	0.453*
Treatment outcomes				
Final recanalization grade (TICI)				
• TICI ≥ 2c	60.4 (110/182)	52 (65/125)	78.9 (45/57)	0.591*
• 24-hours NIHSS ^k	8 [2, 16]	14 [9, 20]	2 [0, 4.25]	-1.994*
Hemorrhagic transformation				
• Any ^e	30.2 (55/182)	37.6 (47/125)	14 (8/57)	0.709*
• Symptomatic ^j	4.9 (9/182)	6.4 (8/125)	1.8 (1/57)	0.320*
Parenchymal^g				
• PH-1	7.1 (13/182)	10.4 (13/125)	0 (0/57)	0.777*
• PH-2	8.8 (16/182)	12.8 (16/125)	0 (0/57)	

Values are no./total.no. (%) or median (25th to 75th percentiles). Good outcome is defined as a mRS 0-3 at 3 months or equal to pre-stroke mRS. (*) indicates variables with StD superior to 0.2. ^aOne missing value, ^b Three missing values, ^c Four missing values, ^d Five missing values, ^e Seven missing values, ^f Ten missing values, ^g Eighteen missing values, ^h Twenty missing values, ⁱ Twenty-three missing values, ^j Thirty-five missing values, ^k Forty-five missing values. Abbreviations: ASPECT: Alberta Stroke Program Early CT score; CT: computed tomography; EVT: endovascular treatment; IVT: intravenous thrombolysis; MCA: middle cerebral artery; MCA-M1: M1 segment of middle cerebral artery; MCA-M2: M2 segment of middle cerebral artery; MRI: brain magnetic resonance imaging; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale; PH: parenchymal hemorrhage; TICI: Thrombolysis in Cerebral Infarction score.

no effect on 3-month GO in MVA (aOR 0.41; 95% CI: 0.15 to 1.17), see Table S3.

When it comes to hemorrhages, as shown in Fig. 4, although HT is significantly associated with PO (aOR: 0.06;

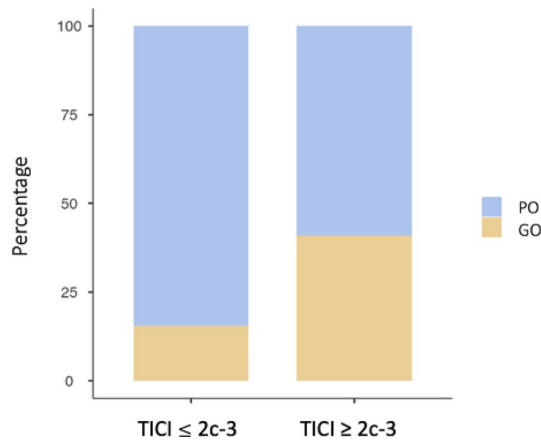


Fig. 1 Percentage of good or bad outcome in each TICl category. *Abbreviations:* Good outcome is defined as a mRS 0-3 at 3 months or equal to pre- stroke mRS.GO good outcome, PO poor outcome, TICl Thrombolysis in Cerebral Infarction score

95% CI 0.01–0.2; $P=0.0003$), there is no association with the extent of reperfusion ($P>0.05$). HT is also significantly associated with the number of passages (OR: 1.34; 95% CI 1.07–1.7; $P=0.01$).

Discussion

Our study shows that (1) GO at 3 months is significantly associated with an excellent reperfusion either obtained in one or multiple passes, in the elderly population undergoing

EVT; (2) through this excellent reperfusion score, the number of 0–1 mRS increases significantly without any change in other categories.

The effect of recanalization grade on clinical outcome is probably mediated mainly by its effect on final infarct volume, often reported to be reduced in patients with a good reperfusion score [11] and to be positively associated with 3-month mRS score [12].

As it significantly enhances the rate of excellent clinical outcome (mRS 0 to 1), achieving excellent reperfusion is crucial, in view of the major impact of the 3-month mRS score on long-term functional outcome [13], mortality [14] and quality of life [15] in the elderly.

In our series, in contrast to the hypothesis of reperfusion-related HT [16], we found no significant association between reperfusion and HT. This suggests that bleeding may not be related to the reperfusion extend. In contrast, some factors like ischemic lesion volume or leukoaraiosis have not been studied in our series and may be involved [17, 18].

The present study is limited by its retrospective and observational design potentially leading to confounding biases in the analysis. Secondly, our study was monocentric with a moderate sample size, resulting in potential other bias. Thirdly, due to the lack of sufficient imaging available, the role of collaterals could not be assessed to the same extent as the impact of postoperative antithrombotic therapy and blood pressure management.

Nevertheless, achieving a mTICl score of 2c-3 now seems to be the best predictive factor for the outcome in

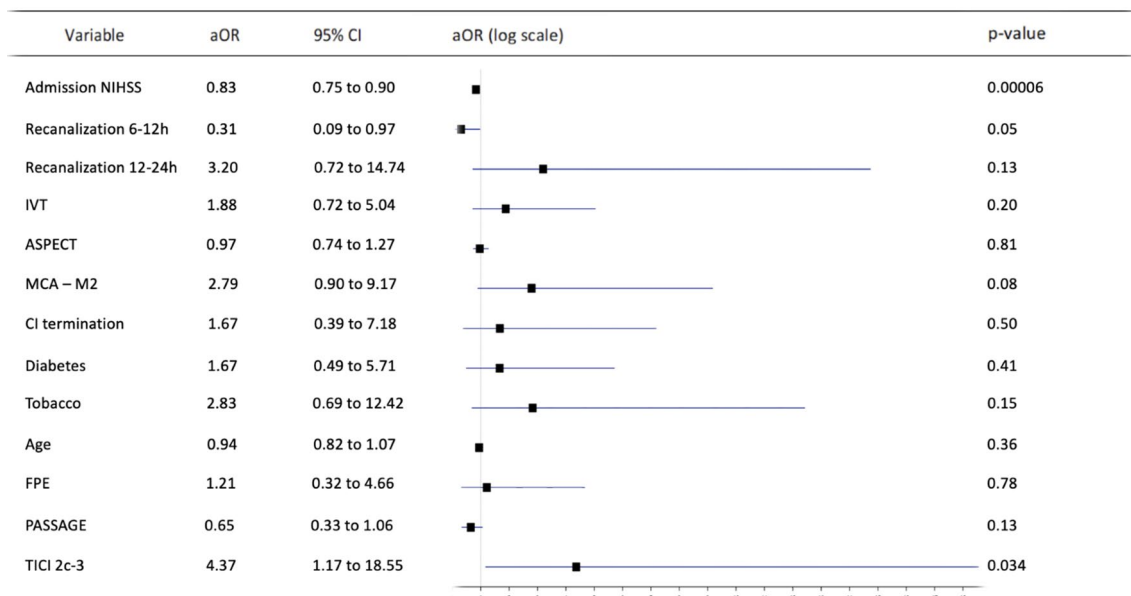


Fig. 2 Forest plot showing association between good outcome and prespecified variables by calculating adjusted odds ratio (aOR) with their 95% confidence intervals (CIs) and P values for heterogeneity across variables. *Abbreviations:* ASPECTS Alberta Stroke Program Early CT score, CI termination internal carotid artery termination, CI

internal carotid artery, IVT intravenous thrombolysis, FPE First pass effect, MCA-M2 M2 segment of middle cerebral artery, mRS modified Rankin Scale, NIHSS National Institutes of Health Stroke Scale, TICl Thrombolysis in Cerebral Infarction score.

Fig. 3 Percentage of patients in each mRS at 3 months by TICI category variables. *Abbreviations:* mRS Modified Rankin Score, mRS 0: No disability, mRS 1: No significant disability despite symptoms, mRS 2: Slight disability, mRS 3: Moderate disability, mRS 4: Moderately severe disability, mRS 5: Severe disability, mRS 6: Dead, TICI: Thrombolysis in Cerebral Infarction score

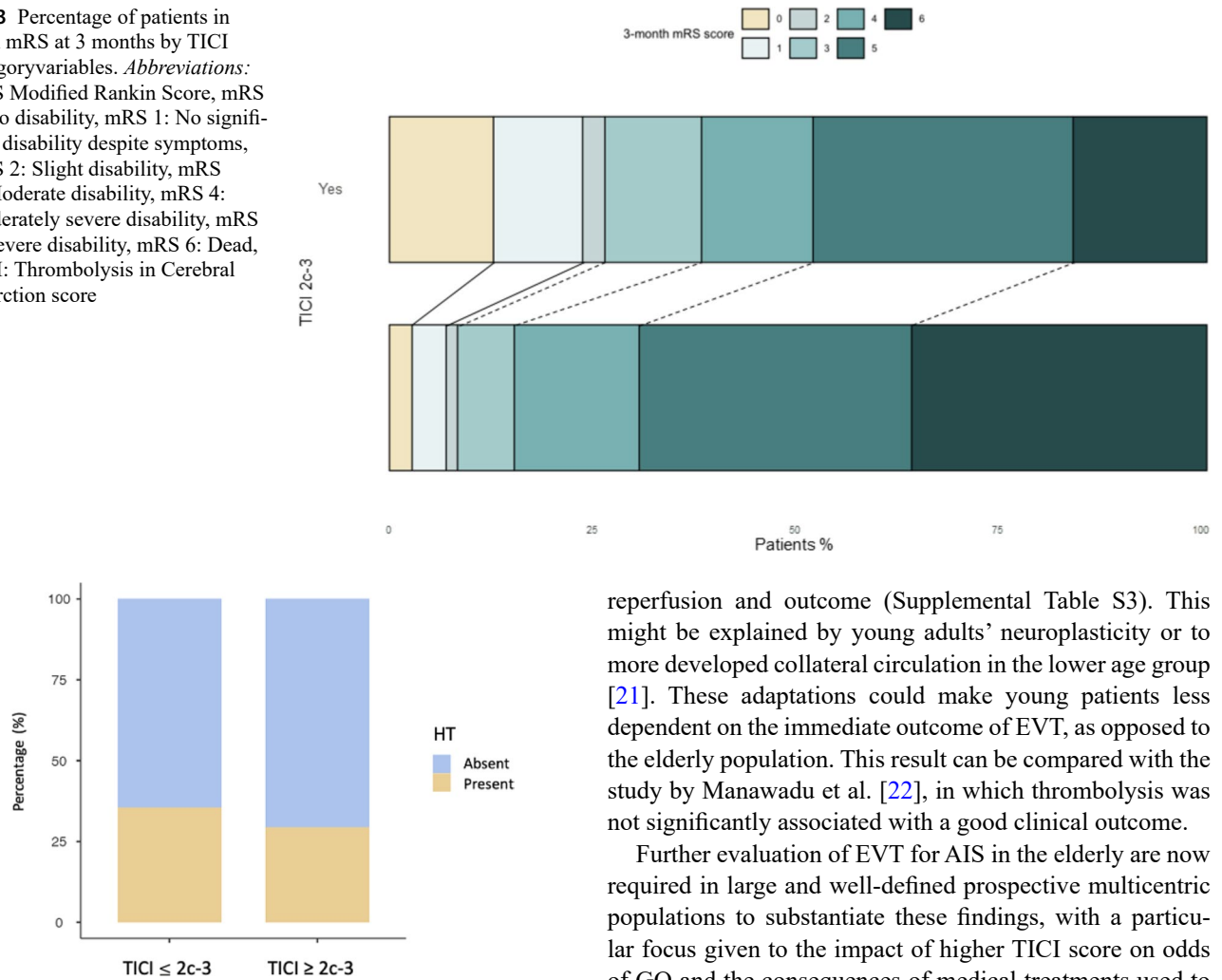
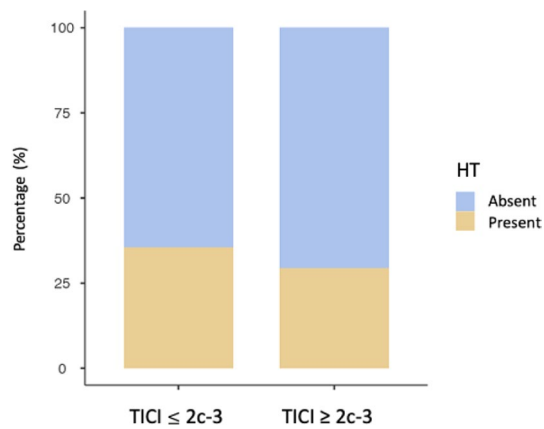


Fig. 4 Percentage of hemorrhage in dichotomized TICI categories. *Abbreviations:* HT: hemorrhagic transformation, TICI: Thrombolysis in Cerebral Infarction score



the elderly population. Our findings indicate that patients who underwent mTICI 2c–3 reperfusion exhibited significantly higher rates of GO compared to those who underwent mTICI 0–2b reperfusion. This advocates for the achievement of the greatest recanalization threshold in order to maximize the chance of a GO after AIS related to LVO. Our study confirms, in a different demographic area and healthcare system, the results previously reported by Chen, Huanwen et al. on the significant association between TICI 2c–3 score and good outcome [19]. However, in contrast, our study shows that the number of passages is significantly associated with hemorrhagic transformation. In line with previous studies on the association of a higher rate of hemorrhagic transformation with the number of passages [20]. This finding was particularly interesting when compared to the results of a similar analysis on under-80s population, which showed no significant association between excellent

reperfusion and outcome (Supplemental Table S3). This might be explained by young adults' neuroplasticity or to more developed collateral circulation in the lower age group [21]. These adaptations could make young patients less dependent on the immediate outcome of EVT, as opposed to the elderly population. This result can be compared with the study by Manawadu et al. [22], in which thrombolysis was not significantly associated with a good clinical outcome.

Further evaluation of EVT for AIS in the elderly are now required in large and well-defined prospective multicentric populations to substantiate these findings, with a particular focus given to the impact of higher TICI score on odds of GO and the consequences of medical treatments used to achieve this aim in case of complex EVT [23, 24], which have not been evaluated in our population.

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Author contributions Author contributions: Study concept and design: MA, FD, PD. Acquisition of data: MA, CC, FD, PD, DB, OC, FDI. Analysis and interpretation of data: MA, FD. Drafting of the manuscript: MA, FD. Critical revision of the manuscript for important intellectual content: MA, FD, CC, PD. Administrative, technical or material support: PD. Study supervision: FD. All authors read and approved the final manuscript. MA: Manar Abomulay FD: François Delvoye PD: Philippe Desfontaines CC: Carla Ciobanu DB: Denis Brisbois OC: Olivier Cornet FDI: François Dister.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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