


ORIGINAL RESEARCH

Predicting Recanalization Failure With Conventional Devices During Endovascular Treatment Related to Vessel Occlusion

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BACKGROUND: Among patients with stroke eligible for endovascular treatment, preprocedure identification of those with low chances of successful recanalization with conventional devices (stent-retrievers and/or direct aspiration) may allow anticipating procedural rescue strategies. We aimed to develop a preprocedural algorithm able to predict recanalization failure with conventional devices (RFCD).

METHODS: Observational study. Data from consecutive patients with stroke who received endovascular treatment between 2019 and 2022 in 10 centers were collected from the Catalan Stroke Registry (Codi Ictus Catalunya Registry, CICAT). RFCD was defined as final thrombolysis in cerebral infarction $\leq 2a$ or the use of rescue therapy defined as balloon angioplasty \pm stent deployment. Univariate and multivariate analysis to identify variables associated with RFCD were performed. A gradient boosted decision tree machine learning model to predict RFCD was developed utilizing preprocedure variables previously selected. Clinical improvement at 24 hours was defined as a drop of ≥ 4 points from baseline National Institutes of Health Stroke Scale score or 0–1 at 24 hours.

RESULTS: In total, 984 patients were included; RFCD was observed in 14.3% (n:141) of the cases. Of these, 47.5% (n = 67) received balloon angioplasty \pm stent deployment as rescue therapy. Among patients receiving balloon angioplasty \pm stent deployment, clinical improvement was associated with lower number of attempts with conventional devices (median number of passes 2 versus 3; $P = 0.045$). In logistic regression, the absence of atrial fibrillation (odds ratio [OR]: 2.730, 95%CI: 1.541–4.836; $P = 0.007$) and no-thrombolytic treatment (OR: 1.826, 95%CI: 1.230–2.711; $P = 0.003$) emerged as independent predictors of RFCD. A predictive model for RFCD, based on age, sex, hypertension, wake-up stroke, baseline National Institutes of Health Stroke Scale score, Alberta Stroke Program Early CT [Computed Tomography] Score, occlusion site, thrombolysis, and atrial fibrillation showed an acceptable discrimination (area under the curve: 0.72 ± 0.024 SD) and accuracy (0.75 ± 0.015 SD). Overall performance was moderate (weighted F1-score: 0.77 ± 0.041 SD).

CONCLUSION: In RFCD patients, early balloon angioplasty \pm stent deployment rescue was associated with improved outcomes. A predictive model using affordable preprocedure clinical variables could be useful to identify these patients before intervention.

Key Words: acute stroke ■ endovascular procedure ■ prognosis ■ recanalization

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Currently, endovascular treatment (EVT) based on mechanical thrombectomy using direct aspiration or stent retrievers has become the standard of care for patients with stroke with large vessel occlusion.¹ The benefit of this treatment is highly time sensitive,² and the lower the number of attempts, the higher the degree of reperfusion and good functional outcome.^{3,4}

Conventional clot retrieval modalities, such as direct aspiration, deployment of a stent retriever, or a combined stent retrieval with distal aspiration technique,⁵ represent the first line strategy during EVT. According to most recent studies, rates of recanalization failure (thrombolysis in cerebral infarction [TICI] $\leq 2a$)⁶ with conventional devices (RFCD) range between 15% and 35%.⁷⁻⁹ One of the main reasons of RFCD is the underlying presence of intracranial atherothrombotic disease (ICAD) reported to be responsible of more than 70% of these cases.^{10,11} In cases of RFCD, the interventionalist can decide to suspend the procedure after a given number of failed attempts or adopt a rescue strategy to achieve substantial recanalization that most often includes glycoprotein IIb/IIIa inhibitors, angioplasty, and/or intracranial stenting.¹²

If the underlying cause of stroke is an ICAD, a lower number of initial attempts, limiting endothelial damage and plaque activation, has been associated with best angiographic results.^{4,13} Previous studies suggest that a single stent-retriever pass through the occlusion, aiming to debulk potential overlaying clot at the culprit of the stenosis, should be enough before proceeding with angioplasty and stenting.¹⁴

For this reason, reliable predictors of underlying ICAD or RFCD could be of great interest to guide interventionalist decisions, suggesting early adoption of rescue strategies beyond conventional stent retrievers or aspiration devices.¹²

Preprocedural variables such as longer elapsed time to EVT,^{15,16} thrombus length,¹⁷ or other radiological findings, such as intracranial artery calcification, specific computed tomography (CT) perfusion maps profiles, and leptomeningeal collateral status, have been related to recanalization failure.^{12,18-20} Despite all efforts to effectively recognize those patients with low chances of successful recanalization with conventional devices prior to the EVT initiation, to date there are no available tools able to reliably predict RFCD.^{4,12} Moreover, some selected baseline characteristics and in-hospital variables could play a role in RFCD identification.

We aim to determine preprocedure variables associated with RFCD and develop a multivariable prognostic model using machine learning (based on a classification algorithm previously tested²¹) to identify potential patients with high risk of RFCD.

Nonstandard Abbreviations and Acronyms

A&S	balloon angioplasty and intracranial stenting
EVT	endovascular treatment
ICAD	intracranial atherothrombotic disease
NIHSS	National Institutes of Health Stroke Scale
RFCD	recanalization failure with conventional devices

CLINICAL PERSPECTIVE

What Is New?

- Recanalization failure with conventional devices occurs in almost 15% of endovascular treatment cases. Early implementation of alternative strategies as rescue therapy could be associated with better outcomes.
- The development of a predictive algorithm-based model of recanalization failure with conventional devices using affordable and simple preprocedure variables has shown an acceptable accuracy and discrimination.

What Are the Clinical Implications?

- Optimizing endovascular treatment procedures remains a challenge in clinical practice. A clinical predictive model to detect those patients with high odds of recanalization failure with conventional devices could help to guide interventionalists on procedural strategy.

METHODS

Study Design and Population

The present study adheres to the transparent reporting of a machine learning predictive models for individual prognosis or diagnosis statement according to guidelines.²²

We performed an observational, multicenter study from a prospectively acquired, government-mandated, population-based registry of all stroke codes in Catalonia (Codi Ictus Catalunya Registry). We included patients with stroke from 10 EVT stroke centers who received EVT from January 2019 to March 2022 (flowchart in the Supplemental Material). The study was approved by the local ethics committee (Ref. CEIm:

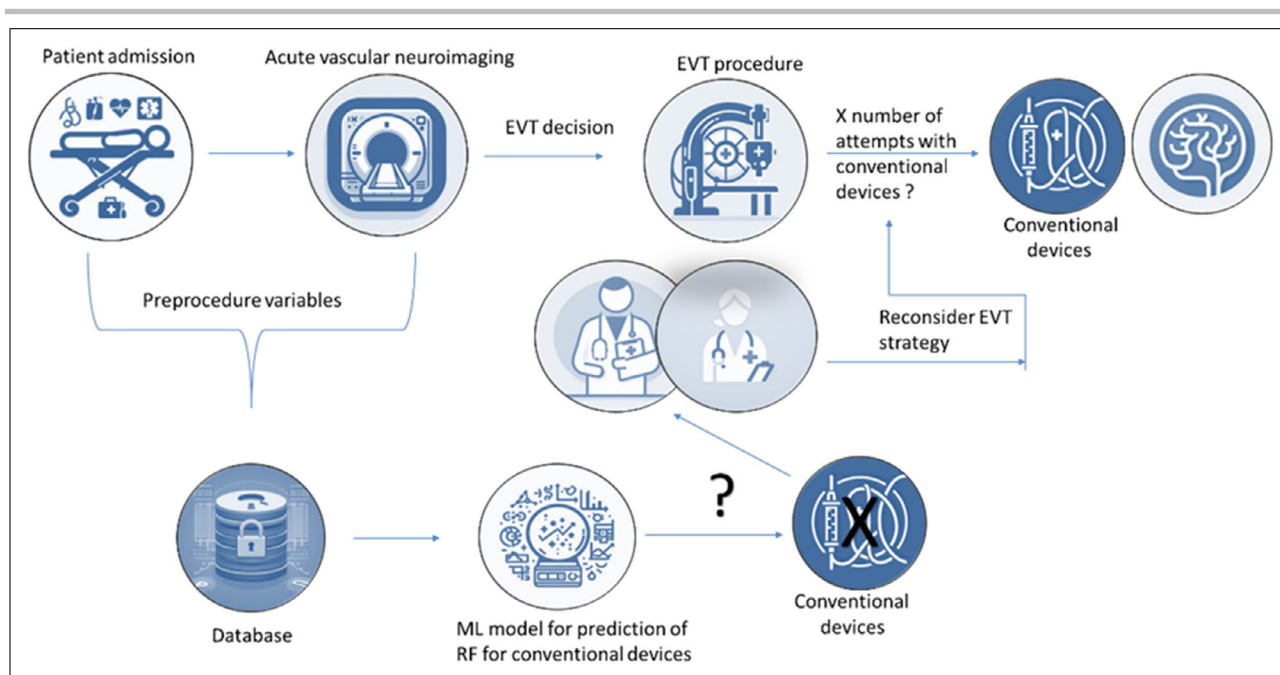


Figure 1. Intended use of the model in the acute stroke phase during EVT procedure. EVT indicates endovascular treatment; ML, machine learning; and RF, recanalization failure.

028/2022). The governmental regional CICAT registry satisfies all legal requirements mandated by the local law of personal data protection. Informed consent was waived by the local ethics committee. Data supporting the findings of this study will be made available to a qualified investigator from the corresponding author on reasonable request. The present study adheres to the observational cohort guideline (Strengthening the Reporting of Observational Studies in Epidemiology).

We performed a descriptive study and statistical analysis evaluating preprocedure variables associated with RFCD. The purpose of the developed prognostic model is the prospective prediction of patients who may present RFCD; it is intended to guide decision making before and during EVT (the intention of the use is graphically presented in Figure 1).

In addition, a subgroup analysis to determine variables associated with favorable outcome after balloon angioplasty±intracranial stenting (A&S) and a comparison between A&S versus non-A&S in RFCD patients were performed.

Radiologic and Angiographic Assessment

The CICAT registry includes radiologic and angiographic evaluation of all patients receiving EVT. Alberta Stroke Program Early CT Score, occlusion location by CT angiography, symptomatic hemorrhagic transformation (according to SITS-MOST [Safe Implementation of Thrombolysis in Stroke-Monitoring] criteria²³), occlu-

sion location on first angiogram, and TICI score after first pass and at the end of the procedure are reported as assessed by the local investigators in each center. Other reported variables related to the EVT are devices used, number of thrombectomy passes, and intracranial A&S rescue. First pass effect²⁴ was defined as TICI 2b-3 after first thrombectomy attempt with conventional thrombectomy devices.

Outcomes, Variable of Interest, and Machine Learning Algorithm

The primary outcome was RFCD, defined by final TICI≤2a or adoption of rescue therapies with A&S. Although the CICAT registry clearly captures the use of intracranial stenting the use of other rescue strategies such as intraarterial infusion of glycoprotein IIb/IIIa inhibitors or angioplasty without stenting may not be as accurately recorded.

The variables of interest obtained for the prognostic model were selected using factor analysis of mixed data and univariate and multivariate analysis, including age, sex, hypertension, diabetes, atrial fibrillation, presentation as wake-up stroke, National Institutes of Health Stroke Scale (NIHSS) score on admission, Alberta Stroke Program Early CT Score on admission CT scan, or occlusion location on first angiogram. Clinical improvement at 24 hours was defined as a drop of ≥4 points from baseline NIHSS score or 0–1 NIHSS score at 24 hours.²⁵

Table 1. Baseline Characteristics, In-Hospital Variables, in RFCD, and Successful Recanalization With Conventional Devices Patients

	RFCD n=141	Successful recanalization with conventional devices n=834	P value
Age, y, mean±SD	69.6 ±12.7	72.3 ±13	0.034
Female sex (%)	59 (36.1)	411 (48.7)	0.076
Atrial fibrillation	16 (11.3)	207 (24.5)	0.001
Wake-up stroke (%)	59 (36.1)	268 (31.7)	0.019
RACE score median (IQR)	6 (3–7)	6 (4–7)	0.63
Dyslipidemia (%)	68 (48.2)	349 (41.3)	0.035
Smoking (%)	28 (19.8)	145 (17.2)	0.08
Diabetes	40 (28.3)	169 (20)	0.01
Hypertension (%)	95 (67.3)	521 (61.8)	0.31
Baseline NIHSS score, median (IQR)	13 (8–20)	16 (10–21)	0.048
ASPECTS score, median (IQR)	9 (8–10)	9 (8–10)	0.36
IV thrombolysis n (%)	44 (31.2)	352 (41.7)	0.018
TICA occ (%)	14 (11.8)	76 (10.4)	0.62
MCA M1 occ (%)	65 (55)	389 (53.4)	0.406
MCA M2 occ (%)	19 (16.1)	174 (23.9)	0.011
Basilar artery occ (%)	11 (9.3)	34 (4.6)	0.001

ASPECTS indicates Alberta Stroke Program Early CT Score; IQR, interquartile range; IV thrombolysis, intravenous thrombolysis; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; RACE, rapid arterial occlusion evaluation; RFCD, recanalization failure with conventional devices; and TICA, terminal internal carotid artery.

An extreme gradient boost model was trained using Python (version 3.12.1) and xgboost (version 2.02).²⁶ From the 984 patients included in the CICAT registry during the study period, 891 had all the variables of interest reported (no imputation was performed) and were used for building the model. An 80%/20% split was carried to search for parameters with hyperopt (version 0.2.7).²⁷ The parameters were `colsample_bytree`, `gamma`, `learning_rate`, `max_depth`, `min_child_weight`, and `scale_pos_weight`. Once the parameters were tuned, a 5-fold cross-validation was performed to determine the performance of the model in different folds.

Statistical Analysis

Descriptive analyses of the population are provided (Table 1). The Shapiro–Wilk test was used to test the normality of continuous variables. Categorical variables are expressed by numbers and percentage, and continuous variables as median (interquartile range [IQR]) or mean (\pm SD) where appropriate. The association with categorical interest variables and clinical outcome was assessed by the Pearson chi-square or Fisher exact test and the Student's *t* or Mann–Whitney *U* test for continuous variables. We performed a multivariate analysis in all EVT patients for RFCD evaluating the association of preprocedure variables selected by univariate analysis. A logistic regression model was performed with the forward stepwise method to identify factors independently associated with RFCD using a *P* value <0.05 in

the univariate analysis to enter each variable and a *P* value >0.1 to remove it from the model. A 2-sided *P* value <0.05 was considered statistically significant. No adjustment for multiple comparisons was performed. Statistical analysis was performed using SPSS Statistics version 23.0 (IBM, Armonk, NY). In addition, we performed the same analysis evaluating the association of A&S with preprocedural variables in the RFCD subgroup.

We report model discrimination and clinical utility. For binary classification with a threshold of *P* = 0.5, we report area under curve, accuracy, true positive, false positive, true negative, false negative, and weighted F1-score. We also report feature importance using xgboost's F score.

RESULTS

Study Population

From the 984 EVT patients included, RFCD occurred in 14.3% (n:141) of the cases. Among these, 47.5% (n = 67) received intracranial A&S as rescue therapy. Overall, the mean age was 71.9 (SD \pm 13.8), 47.8% (n:470) were females and the median baseline NIHSS score was 15 (IQR: 9–21). First pass effect was achieved in 46.9% of cases and successful reperfusion at the end of the procedure was achieved in 874 cases (88.8%). Symptomatic intracranial hemorrhage at 24 hours was observed in 4% (n = 40) of the cases.

Table 2. Performance of the Model for RFCD Prediction

	Fold1	Fold2	Fold3	Fold4	Fold5	Mean	SD±
AUC	0.75	0.74	0.7	0.7	0.7	0.718	0.0248
Accuracy	0.77	0.74	0.74	0.77	0.75	0.754	0.0151
True positive, n	23	22	19	22	18		
False positive, n	31	38	37	25	34		
True negative, n	116	111	113	116	116		
False negative, n	9	8	10	16	11		
Positive predictive value (%)	67	73	65	57	62	64.8	
Negative predictive value (%)	78	74	75	82	77	77.2	
F1-score (weighted)	0.8	0.8	0.77	0.78	0.7	0.77	0.041

AUC indicates area under the curve; and RFCD, recanalization failure with conventional devices.

Outcomes and Predictive Model

As compared with patients in which successful recanalization was achieved with conventional devices, those with RFCD showed the following differences: they were younger (69.9 versus 72.3; $P = 0.034$), had lower baseline NIHSS scores (median 13 versus 16; $P = 0.048$), were less likely to have atrial fibrillation (11.3% versus 24.5%; $P = 0.001$), received intravenous thrombolysis less frequently (31.2% versus 41.7%; $P = 0.018$), and presented middle cerebral artery-M2 occlusions to a lesser degree (16.1% versus 23.9%; $P = 0.011$). In contrast, rates of dyslipidemia (48.2% versus 41.3%; $P = 0.035$), diabetes (28.3% versus 20%; $P = 0.01$), and basilar artery occlusion (9.3% versus 4.6%; $P = 0.001$) were higher among RFCD patients. Baseline characteristics and preprocedure variables according to RFCD outcome are presented in Table 1.

In a logistic regression, adjusted by age, baseline NIHSS score, atrial fibrillation, dyslipidemia, diabetes, thrombolysis treatment, and occlusion site location, the absence of atrial fibrillation (odds ratio [OR]: 2.730, 95% CI: 1.541–4.836; $P = 0.007$) and non-thrombolysis treatment (OR: 1.826, 95% CI: 1.230–2.711; $P = 0.003$) emerged as independent predictors of RFCD.

A predictive extreme gradient boost model based on age, sex, hypertension, atrial fibrillation, wake-up stroke, baseline NIHSS score, Alberta Stroke Program Early CT Score, occlusion site, and intravenous thrombolysis was performed. The overall accuracy for predicting RFCD (0.75 ± 0.015 , SD) and discrimination (area under curve of 0.72 ± 0.024 , SD) were acceptable, and overall performance was moderate (F1-score 0.77 ± 0.041 , SD). Positive predictive value and negative predictive value were 65% and 78%, respectively. Performance and a complete overview of the results are presented in Table 2.

Variable importance expressed as the F score revealed that the most important preprocedure variables were age, baseline NIHSS score, and Alberta

Stroke Program Early CT Score. The feature importances are shown in Figure 2.

Intracranial A&S Versus Non-A&S in the RFCD Patient Subgroup

Baseline characteristics, preprocedures variables, and univariate analysis results comparing intracranial A&S versus no A&S patients in the RFCD subgroup are presented in Table 3. Multivariate analysis adjusted for atrial fibrillation and occlusion site showed that lower age (OR: 0.954, 95% CI: 0.912–0.97; $P = 0.037$) and wake-up stroke (OR: 7.346, 95% CI: 2.412–22.368; $P < 0.001$) were independent predictors of receiving intracranial A&S during the EVT.

Among patients who received A&S ($n = 67$), final complete recanalization (TICI 2c-3) was achieved in 46 cases (68.6%), 15 (22.3%) presented a clinical improvement at 24 hours and 4 cases (5.9%) presented symptomatic hemorrhagic transformation. The median of number of attempts with conventional devices was 3 (IQR: 2–3). Among patients who received intracranial A&S, clinical improvement at 24 hours was associated with lower number of attempts with conventional devices (median number-passes 2 [IQR: 1–3] versus 3 [IQR: 2–4]; $P = 0.045$, Figure 3).

DISCUSSION

The present study based on a regional, mandatory, prospective registry including up to 10 comprehensive stroke centers showed that RFCD occurs in almost 15% of EVT patients. RFCD was significantly associated with absence of atrial fibrillation and no previous intravenous thrombolytic treatment. Commonly available clinical baseline variables were used to develop a logistic regression model able to predict RFCD with an acceptable accuracy. However, the prediction power

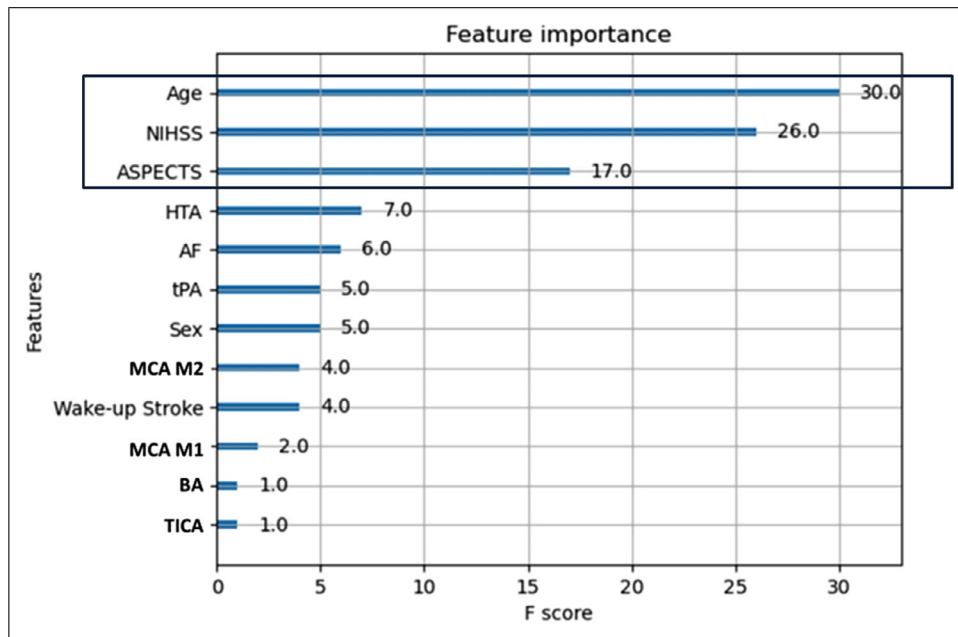


Figure 2. F score values feature importance. Computed for the xgboost (mean values of 5 feature permutations). Frame indicates the 3 most important variables. AF indicates atrial fibrillation; ASPECTS, Alberta Stroke Program Early CT Score; BA, basilar artery; HTA, hypertension; IV thrombolysis, intravenous thrombolysis; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; TICA, terminal internal carotid artery; and tPA, Tissue plasminogen activator.

Table 3. Baseline Characteristics, In-Hospital Variables, in Stenting, and Nonstenting Patients in the RFCD Subgroup

RFCD patients: 141	Stenting patients n=67	No stenting patients n=74	P value
Age, y, mean±SD	65.8 ±12.4	72.7 ±12.1	0.001
Female sex (%)	24 (35.8)	37 (50)	0.134
Atrial fibrillation	4 (5.9)	14 (18.9)	0.023
Wake-up stroke (%)	40 (59.7)	24 (28.3)	<0.001
RACE score median (IQR)	5(2–7)	6(4–7)	0.77
Dyslipidemia (%)	35 (52.2)	35 (47.2)	0.58
Smoking (%)	17 (25.3)	13 (17.5)	0.49
Diabetes	21 (31.3)	21 (28.3)	0.66
Hypertension (%)	47 (70.1)	50 (67.5)	0.43
Baseline NIHSS, median (IQR)	12 (7–17)	16 (9–21)	0.06
ASPECTS score, median (IQR)	9 (8–10)	9 (8–10)	0.99
IV thrombolysis n (%)	17 (25.3)	29 (39.1)	0.08
TICA occ (%)	10 (14.9)	4 (5.4)	0.01
MCA M1 occ (%)	35 (52.2)	31 (41.8)	0.07
MCA M2 occ (%)	7 (10.4)	14 (18.9)	0.005
Basilar artery occ (%)	11 (16.4)	2 (2.7)	0.004
Median number of passes (IQR)	3 (2–3)	3 (2–5)	0.017
Median mRS at 3 mo (IQR)	4 (1–5)	5 (3–6)	0.32

ASPECTS indicates Alberta Stroke Program Early CT Score; IQR, interquartile range; IV thrombolysis, intravenous thrombolysis; MCA, middle cerebral artery; mRS, modified Rankin score; NIHSS, National Institutes of Health Stroke Scale; RACE, rapid arterial occlusion evaluation; and TICA, terminal internal carotid artery.

was substantially improved by a machine learning based algorithm fed with similar baseline variables. To our knowledge, this is the first study exploring a predictive model of RFCD.

RFCD is with no doubt largely mediated by the underlying presence of ICAD²⁸; however, there might

be additional cases in which different etiologies can also be responsible of RFCD. Independently of the responsible cause of RFCD, rescue therapy with intracranial A&S has been proposed as a reasonable alternative to achieve recanalization at the end of the procedure.¹² Moreover, previous data suggest that, in cases in which

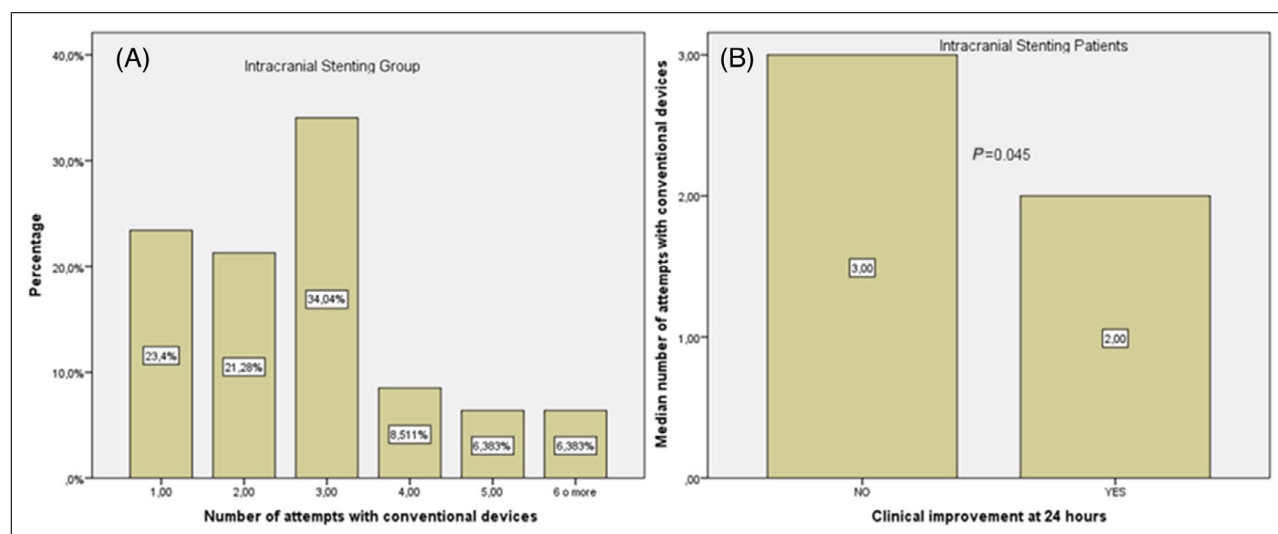


Figure 3. Graphic bars showing data on number of attempts in intracranial stenting patients. The percentage of patients according to number of attempts prior intracranial stenting placement (A) and the median of number of attempts according to clinical improvement at 24 hours in intracranial stenting patients (B).

intracranial A&S was finally adopted, final angiographic success was associated with a lower number of initial failed passes with conventional devices.¹⁴ For this reason, we decided to perform a pragmatical study focusing on predicting RFCD, regardless of the underlying cause or clot composition. Such algorithm should be useful for interventionalists during the procedures guiding the decision about when to switch from conventional thrombectomy devices to a rescue bailout technique such as intracranial stenting. In one hand, the algorithm should be specific enough to avoid conversion to rescue therapy in patients likely to recanalize with additional attempts with conventional thrombectomy devices. In the other hand, it should be sensitive enough to avoid an excessive number of failed passes that would jeopardize sustained recanalization after rescue therapy and increase the risk of complications such as intracranial hemorrhage.

In the present study, the rate of RFCD and A&S were in concordance with prior data.^{11,29} The absence of atrial fibrillation and no thrombolytic treatment before the procedure were the only independent predictors of RFCD. Moreover, some of the most representative clinical variables of the model as the absence of atrial fibrillation could reflect or pointed underlying ICAD etiology, inferring its value as RFCD marker. These findings are in line with prior large vessel occlusion ICAD-related focused studies¹² and trials where intravenous thrombolysis has been tested in EVT patients.³⁰ In our study, the median number of failed attempts before rescue therapy was adopted was 3. In many cases, the number of attempts was substantially higher and included device changing or different combinations. Moreover, lesser number of attempts before intracranial stenting

was associated with clinical improvement at 24 hours. Implementing an algorithm able to efficiently predict RFCD in clinical practice could help optimize and individualize periprocedural decisions such as persevering with conventional devices versus early intracranial A&S bailout, ultimately improving final angiographic results and clinical outcomes.

Previous studies described different variables associated with RFCD or suspected underlying ICAD.^{18–20,31,32} Several imaging surrogate biomarkers such as location of the occlusion, presence of intracranial calcifications, collateral status by CT angiography assessment, or CT-perfusion map patterns have shown a strong association with RFCD. In future studies, these variables could be combined with clinical variables to improve the accuracy of the predicting algorithms. Ideally the radiological features should be automatically detected and extracted from the admission imaging files to seamlessly generate predictions in real time that will not involve time consuming manual segmentations by experienced operators. Until then, algorithms including only commonly available baseline clinical information may be an acceptable and readily applicable solution. In addition, our predictive model includes patients with basilar artery occlusion and could be useful as well in this specific group in which imaging parameters such as CT-perfusion maps are more difficult to interpret.

Otherwise, among the RFCD patients, intracranial A&S was performed in less than half of cases (47.5%) and was associated with lower age and wake-up stroke. The relation between age and receiving intracranial A&S was observed in previous studies²⁹ and is probably related to the willingness to proceed beyond

standard of care in younger patients. The relation with wake-up stroke presentation may be related to the time of the day when the procedure is performed: the morning hours may be associated with favorable logistics and experienced operators more prone to A&S. However, the relation of the presentation mode with the underlying cause deserves further attention in future studies.

Limitations and Strengths

Strengths of this analysis include its relatively large sample size from a prospective mandatory regional registry and the use of variables easily obtained in an emergency setting.

This study has the inherent limitations of an observational study from a prospective registry potentially limiting its generalizability to other settings and regions. Moreover, patients with no reported data related to the use of intracranial A&S were excluded of from the study. The reported use of other rescue therapies such as glycoprotein IIb/IIIa inhibitors and angioplasty alone were scarce and incomplete, potentially affecting the findings of the present study.

The accuracy of the model could vary over time, assuming the progressive implementation in clinical practice of new technologies and devices used as first line strategy³³ that could change the recanalization results observed in this study. Therefore, such algorithms should be recurrently reviewed and rebuilt in order to match the latest technological device developments.

The absence of an external validation cohorts is another limitation; we performed an internal cross validation (20% of the sample) to mitigate this potential frailty. However, our results need to be replicated by other groups and cohorts before adopting the algorithm in routine clinical practice.

CONCLUSION

In the present study, RFCD occurs in 14.3% of cases. Independent variables associated with RFCD were absence of atrial fibrillation and no thrombolysis treatment. A predictive model based on baseline clinical variables could be useful to identify these patients before intervention and guide interventionalist in their decisions during EVT.

ARTICLE INFORMATION

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Supplemental Materials

Figure S1. Study flow chart.

Guidelines for Developing and Reporting Machine Learning Predictive Models in Biomedical Research: A Multidisciplinary View – Checklist
 Guidelines for Developing and Reporting Machine Learning Predictive Models in Biomedical Research: A Multidisciplinary View – Checklist

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