

SUPPLEMENTARY MATERIAL

METHODS

Study design, participants, and procedures. Data were prospectively collected and included: age, hypertension, diabetes mellitus, hyperlipidemia, smoke habit, previous stroke or transient ischemic attack, atrial fibrillation, coronary heart disease, congestive heart failure, pre-stroke treatment (i.e., antiplatelet, oral anticoagulant, and/or statin), pre-stroke modified Rankin Scale (mRS) score, baseline National Institutes of Health Stroke Scale (NIHSS) score, baseline Alberta Stroke Program Early Computed Tomography (ASPECT) score, occlusion site (tandem defined as cervical internal carotid artery [ICA] occlusion associated with M1-segment of the middle cerebral artery [MCA] and/or A1-segment of the anterior cerebral artery [ACA] embolic occlusion; carotid T-syphon defined as intracranial ICA occlusion associated with M1-segment and A1-segment occlusion; M1- or M2-segment occlusion; or vertebro-basilar occlusion), clot burden score,¹ poor collateral circulation if Careggi collateral score of 0 (i.e., no flow in both ACA and MCA territory) or 1 (i.e., flow in ACA territory), and good collateral circulation if Careggi collateral score of 2 (i.e., flow in MCA territory, above the insular region), 3 (i.e., flow in MCA territory, including the insular region), or 4 (i.e., flow in M1-segment), mechanical thrombectomy alone [direct] or after IVT [bridging therapy], symptom onset-to-groin puncture time, type of procedure (i.e., aspiration alone, stent retriever alone, or combination of aspiration and stent retriever), angioplasty procedure or extra-cranial stent placement, type of anesthesia (i.e., local only, conscious sedation, or general anesthesia), reperfusion after procedure according to the thrombolysis in cerebral ischemia (TICI) grading system, first pass effect (defined as achieving a complete recanalization with a single thrombectomy device pass),² symptom onset-to-end procedure time (defined as the time to reopening the occluded vessel or the end of procedure in case of failure), NIHSS score at the end of endovascular procedure, and 3-month mRS score.

Statistical analysis. The AUC-ROC values were calculated also in the following subgroups of patients included in the entire cohort with complete data for generating the nomogram: males and females; first (January 2011-December 2014) and last (January 2015-December 2016) study period; pre-stroke mRS score ≤ 1 and 2, NIHSS and ASPECT scores ≥ 6 and < 6 according to the different class of recommendation and level of evidence for mechanical thrombectomy applied by the current American Heart Association/American Stroke Association; tandem, carotid T-syphon, M1-segment, M2-segment, and vertebro-basilar occlusion; clot burden score 0-5, 6-7 and 8-9; 19 good and poor collateral circulation; onset-to-groin puncture time ≤ 180 , 281-270, and 271-360 minutes; mechanical thrombectomy alone (direct) and after IVT (bridging); aspiration, stent retriever, and combination of aspiration and stent retriever; endovascular treatment with and without angioplasty procedure; local anesthesia, conscious sedation, and general anesthesia; first pass effect and no first pass effect.

RESULTS

The points assigned to each predictor on preliminary score of the nomogram were based on their proportions to the points (i.e., 10) assigned to the biggest impact predictor (i.e., baseline NIHSS score) on the probability of 3-months unfavorable outcome. The estimated effect (absolute beta value) of non-categorical variables depended on its unit and regression coefficient, while that of categorical variables depended only on the regression coefficient. Finally, the logistic regression model is: $\text{Log}_e p(x)/[1 - p(x)] = - 8.116 + 0.152 * \text{NIHSS score} + 0.050 * \text{age} + 0.004 * \text{onset-to-end procedure time} + 0.851 * \text{pre-stroke mRS score} + 0.341 * \text{direct mechanical thrombectomy} + 2.729 * \text{TICI0} + 1.814 * \text{TICI1} + 1.434 * \text{TICI2a} + 0.470 * \text{TICI2b}$.

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TABLES

Supplemental Table 1. Registry organization.

Name	Location	Role
Roberto Gasparotti	Spedali Civili, Brescia	Steering Committee
Domenico Inzitari	University of Florence, Firenze	Steering Committee
Salvatore Mangiafico	Ospedale Careggi-University Hospital, Firenze	Steering Committee
Danilo Toni	Sapienza University Hospital, Roma	Steering Committee
Stefano Vallone	Ospedale Civile S. Agostino-Estense- University Hospital, Modena	Steering Committee
Andrea Zini	IRCCS Istituto delle Scienze Neurologiche, Maggiore Hospital, Bologna	Steering Committee
Mauro Bergui	Città della Salute e della Scienza-Molinette, Torino	Scientific Committee
Francesco Causin	Azienda Ospedaliero-Universitaria, Padova	Scientific Committee
Alfonso Ciccone	Carlo Poma Hospital, Mantova	Scientific Committee
Patrizia Nencini	University of Florence, Firenze	Scientific Committee
Andrea Saletti	Arcispedale S. Anna-University Hospital, Ferrara	Scientific Committee
Fabrizio Sallustio	Policlinico Tor Vergata, Roma	Scientific Committee
Rossana Tassi	Ospedale S. Maria delle Scotte-University Hospital, Siena	Scientific Committee
Federico Zappoli Thyron	San Matteo Hospital, Pavia	Scientific Committee
Giovanni Pracucci	University of Florence, Firenze	Data management and coordination unit
Valentina Saia	Ospedale Santa Corona, Pietra Ligure	Data management and coordination unit

Supplemental Table 2. Percentage of patients treated per center.

Center	Percentage of patients treated
Ospedale Careggi-University Hospital, Firenze	6.7
Policlinico Tor Vergata, Roma	6.2
Ospedale Civile S. Agostino-Estense- University Hospital, Modena	5.7
Ospedale S. Maria delle Scotte-University Hospital, Siena	5.2
Città della Salute e della Scienza-Molinette, Torino	5
Policlinico G. Martino, Messina, Italy	4.8
Arcispedale S. Anna-University Hospital, Ferrara	4.7
Spedali Civili, Brescia	4.2

Ospedale Civile Mazzini, Teramo	4
Azienda Ospedaliero-Universitaria, Padova	3.4
IRCCS San Martino-IST, Genova	3
Ospedale Universitario, Parma	2.9
Ospedale San Giovanni Bosco, Torino	2.4
Ospedale Maggiore, Bologna	2.4
Ospedale Centrale, Bolzano	2.3
Ospedale Cisanello, Pisa	2.3
Ospedale Universitario Circolo - ASST Sette Laghi, Varese	2.3
Sapienza University Hospital, Roma	1.9
Ospedale M. Bufalini, Cesena	1.7
Fondazione Policlinico A. Gemelli, UCSC, Roma	1.7
San Matteo Hospital & C. Mondino Foundation, Pavia	1.6
Ospedale Niguarda Cà Granda, Milano	1.6
Azienda Ospedaliera Universitaria Integrata, Verona	1.6
Ospedale SS. Annunziata, Taranto	1.5
Ospedale dell'Angelo -USSL3 Serenissima, Mestre	1.5
Policlinico Bari	1.4
Presidio Ospedaliero SS. Filippo e Nicola, Avezzano	1.3
Azienda Ospedaliera Annunziata, Cosenza	1.3
Ospedale Santa Corona, Pietra Ligure	1.2
IRCCS San Raffaele, Milano	1.2
Ospedali Riuniti Marche, Ancona	1.1
Azienda Ospedaliero-Universitaria Maggiore della Carità, Novara	1
Humanitas Research Hospital, Rozzano	0.9
Ospedale San Camillo-Forlanini, Roma	0.9
Istituto Ospedaliero Fondazione Poliambulanza, Brescia	0.7
Ospedale Regionale U. Parini, Aosta	0.7
Ospedale S. Maria della Misericordia, Rovigo	0.6
Ospedale SS. Antonio e Biagio e Cesare Arrigo, Alessandria	0.6
Ospedale SS. Annunziata, Sassari	0.4
Ospedale Civico-A.R.N.A.S., Palermo	0.4
Ospedale Cardarelli, Napoli	0.4
Ospedale S. Francesco, Nuoro	0.3
Ospedale A. Manzoni, Lecco	0.2
Ospedale S. Bortolo, Vicenza	0.2
Ospedale S. Michele-AO Brotzu, Cagliari	0.1

Supplemental Table 3. Demographics and clinical characteristics of the included and excluded patients.

	Included patients (n=1802)	Excluded patients (n=1912)	P value
Demographics			
Age (years), median (IQR)	72 (61-79)	70 (58-78)	0.002
Male sex, n (%)	919 (51)	1016 (53.1)	0.200
Medical history			
Hypertension, n (%)	970 (62.5) [249]	1029 (65.5) [342]	0.080
Diabetes mellitus, n (%)	240 (15.5) [249]	277 (17.6) [342]	0.102
Hyperlipidemia, n (%)	407 (26.2) [249]	431 (27.5) [342]	0.443
Smoke habit, n (%)	321 (20.7) [249]	352 (22.4) [342]	0.240
Previous stroke/transient ischemic attack, n (%)	72 (4.6) [249]	105 (6.8) [342]	0.011
Atrial fibrillation, n (%)	509 (32.8) [249]	414 (26.4) [342]	<0.001
Coronary heart disease, n (%)	160 (10.3) [249]	138 (8.8) [342]	0.161
Congestive heart failure, n (%)	100 (6.4) [249]	117 (7.5) [342]	0.291
Antiplatelet treatment, n (%)	511 (28.4)	544 (28.5)	0.971
Oral anticoagulant treatment, n (%)	183 (10.2)	153 (8)	0.026
Statin treatment, n (%)	259 (14.4)	290 (15.2)	0.517
Baseline data			
Study period (January 2015-December 2016), n (%)	1206 (66.9)	1051 (55)	<0.001

Pre-stroke mRS score, median (IQR)	0	0 (0-1) [581]	<0.001
NIHSS score, median (IQR)	18 (14-22)	17 (13-21) [191]	<0.001
ASPECT score, median (IQR)	10 (9-10) [156]	10 (8-10) [278]	0.560
<i>Occlusion site</i>			<0.001
Tandem, n (%)	313 (17.5) [13]	303 (16.4) [66]	
Carotid T-syphon, n (%)	281 (15.7) [13]	263 (14.2) [66]	
M1-segment middle cerebral artery, n (%)	852 (47.6) [13]	640 (34.7) [66]	
M2-segment middle cerebral artery, n (%)	204 (11.4) [13]	256 (13.9) [66]	
Vertebro-basilar arteries, n (%)	139 (7.8) [13]	384 (20.8) [66]	
Clot burden score, median (IQR)	6 (5-8) [1248]	6 (4-8) [1400]	0.172
Good collateral circulation, n (%)	633 (69.9) [897]	444 (65) [1229]	0.039
Direct mechanical thrombectomy, n (%)	786 (43.6)	1126 (60.7) [57]	<0.001
Symptom onset-to-groin puncture time (minutes), median (IQR)	230 (180-280)	285 (205-405) [349]	<0.001
<i>Type of procedure</i>			0.309
Aspiration alone, n (%)	452 (36.4) [561]	396 (39.3) [905]	
Stent retriever alone, n (%)	596 (48) [561]	453 (45) [905]	
Combination of aspiration and stent retriever, n (%)	193 (15.6) [561]	158 (15.7) [905]	
Angioplasty procedure or stent placement, n (%)	187 (13.6) [422]	208 (15.4) [565]	0.174
<i>Type of anesthesia</i>			<0.001
Local only, n (%)	475 (29.8) [208]	359 (22.1) [288]	
Conscious sedation, n (%)	419 (26.3) [208]	448 (27.6) [288]	
General anesthesia, n (%)	700 (43.9) [208]	817 (50.3) [288]	
<i>Reperfusion after procedure (TICI)</i>			<0.001
Grade 0, n (%)	145 (8)	132 (7.2) [86]	
Grade 1, n (%)	77 (4.3)	102 (5.6) [86]	
Grade 2a, n (%)	223 (12.4)	304 (16.6) [86]	
Grade 2b, n (%)	303 (16.8)	361 (19.8) [86]	
Grade 3, n (%)	1054 (58.5)	927 (50.8) [86]	
First pass effect, n (%)	469 (36.8) [528]	348 (31.1) [793]	0.003
Symptom onset-to-end procedure time (minutes), median (IQR)	310 (251-360)	375 (293-500) [405]	<0.001
Outcome			
3-month mRS score 3-6, n (%)	946 (52.5)	1007 (58.8) [198]	<0.001

Data are n (%) or median (IQR). Numbers within square brackets indicate number of missing values. mRS = modified Rankin Scale. NIHSS = National Institutes of Health Stroke Scale. ASPECT = Alberta Stroke Program Early Computed Tomography. TICI = Thrombolysis in cerebral infarction.

Supplemental Table 4. Demographics and clinical characteristics of the training and test cohorts.

	Training cohort (n=1219)	Test cohort (n=583)	P value
Demographics			
Age (years), median (IQR)	71 (61-79)	72 (61-80)	0.487
Male sex, n (%)	605 (49.6)	314 (53.9)	0.097
Medical history			
Hypertension, n (%)	663 (62.5) [158]	307 (62.4) [91]	1.000
Diabetes mellitus, n (%)	166 (15.6) [158]	74 (15) [91]	0.821
Hyperlipidemia, n (%)	273 (25.7) [158]	134 (27.2) [91]	0.536
Smoke habit, n (%)	228 (21.5) [158]	93 (18.9) [91]	0.253
Previous stroke/transient ischemic attack, n (%)	50 (4.7) [158]	22 (4.5) [91]	0.897
Atrial fibrillation, n (%)	357 (33.6) [158]	152 (30.9) [91]	0.296
Coronary heart disease, n (%)	115 (10.8) [158]	45 (9.1) [91]	0.325
Congestive heart failure, n (%)	73 (6.9) [158]	27 (5.5) [91]	0.319
Antiplatelet treatment, n (%)	349 (28.6)	162 (27.8)	0.738
Oral anticoagulant treatment, n (%)	127 (10.4)	56 (9.6)	0.618
Statin treatment, n (%)	170 (13.9)	89 (15.3)	0.473
Baseline data			
Study period (January 2015-December 2016), n (%)	809 (66.4)	397 (68.1)	0.487

Pre-stroke mRS score, median (IQR)	0	0	0.732
NIHSS score, median (IQR)	18 (14-22)	18 (14-22)	0.228
ASPECT score, median (IQR)	10 (9-10) [111]	10 (9-10) [45]	0.515
<i>Occlusion site</i>			0.790
Tandem, n (%)	212 (17.5) [9]	101 (17.4) [4]	
Carotid T-syphon, n (%)	193 (16) [9]	88 (15.2) [4]	
M1-segment middle cerebral artery, n (%)	582 (48.1) [9]	270 (46.6) [4]	
M2-segment middle cerebral artery, n (%)	135 (11.2) [9]	69 (11.9) [4]	
Vertebro-basilar arteries, n (%)	88 (7.3) [9]	51 (8.8) [4]	
Clot burden score, median (IQR)	6 (5-8) [843]	6 (5-8) [405]	0.871
Good collateral circulation, n (%)	434 (69.1) [591]	199 (71.8) [306]	0.432
Direct mechanical thrombectomy, n (%)	528 (43.3)	258 (44.3)	0.722
Symptom onset-to-groin puncture time (minutes), median (IQR)	230 (180-280)	230 (180-280)	0.708
<i>Type of procedure</i>			0.708
Aspiration alone, n (%)	315 (37.1) [371]	137 (34.9) [190]	
Stent retriever alone, n (%)	401 (47.3) [371]	195 (49.6) [190]	
Combination of aspiration and stent retriever, n (%)	132 (15.6) [371]	61 (15.5) [190]	
Angioplasty procedure or stent placement, n (%)	120 (12.8) [285]	67(15) [137]	0.275
<i>Type of anesthesia</i>			0.293
Local only, n (%)	307 (28.6) [145]	168 (32.3) [63]	
Conscious sedation, n (%)	290 (27) [145]	129 (24.8) [63]	
General anesthesia, n (%)	477 (44.4) [145]	223 (42.9) [63]	
<i>Reperfusion after procedure (TICI)</i>			0.605
Grade 0, n (%)	104 (8.5)	41 (7)	
Grade 1, n (%)	54 (4.4)	23 (3.9)	
Grade 2a, n (%)	156 (12.8)	67 (11.5)	
Grade 2b, n (%)	206 (16.9)	97 (16.6)	
Grade 3, n (%)	699 (57.3)	355 (60.9)	
First pass effect, n (%)	304 (35.5) [362]	165 (39.6) [166]	0.155
Symptom onset-to-end procedure time (minutes), median (IQR)	310 (251-362)	310 (250-360)	0.664
Outcome			
3-month mRS score 3-6, n (%)	643 (52.7)	303 (52)	0.763

Data are n (%) or median (IQR). Numbers within square brackets indicate number of missing values. mRS = modified Rankin Scale. NIHSS = National Institutes of Health Stroke Scale. ASPECT = Alberta Stroke Program Early Computed Tomography. TICI = Thrombolysis in cerebral infarction.

Supplemental Table 5. Multivariate logistic regression analysis: independent predictors of 3-month unfavorable outcome.

	Regression coefficient (Standard Error)	Odds Ratio (95% Confidence Interval)	P value
Age	0.050 (0.006)	1.052 (1.040-1.064)	<0.0001
Pre-stroke mRS score	0.851 (0.157)	2.341 (1.722-3.182)	<0.0001
Baseline NIHSS score	0.152 (0.014)	1.164 (1.132-1.196)	<0.0001
Symptom onset-to-end procedure time	0.004 (0.001)	1.004 (1.002-1.006)	<0.0001
Mechanical thrombectomy after IVT	0 (Reference)	1.000 (Reference)	-
Mechanical thrombectomy alone	0.341 (0.145)	1.406 (1.059-1.868)	0.0181
TICI 3	0 (Reference)	1.000 (Reference)	-
TICI 2b	0.470 (0.188)	1.600 (1.106-2.314)	0.0131
TICI 2a	1.434 (0.225)	4.194 (2.701-6.513)	<0.0001
TICI 1	1.814 (0.450)	6.137 (2.538-14.828)	<0.0001
TICI 0	2.729 (0.372)	15.313 (7.385-31.752)	<0.0001

mRS = modified Rankin Scale. NIHSS = National Institutes of Health Stroke Scale. TICI = Thrombolysis in cerebral infarction.

Supplemental Table 6. The discriminative performance of the IER-START nomogram in the subgroups of patients.

	3-month mRS score 3-6	AUC-ROC value	95% CI
Male sex, n (%)	489 (53.2)	0.828	0.802-0.854
Female sex, n (%)	457 (51.8)	0.838	0.812-0.864
Study period (January 2015-December 2016), n (%)	628 (52.2)	0.826	0.803-0.849
Study period (January 2011-December 2014), n (%)	318 (53.4)	0.845	0.815-0.875
Pre-stroke mRS score ≤ 1 , n (%)	846 (50.3)	0.824	0.805-0.844
Pre-stroke mRS score 2, n (%)	100 (82.6)	0.843	0.769-0.917
Baseline NIHSS score ≥ 6 , n (%)	940 (53.4)	0.828	0.809-0.847
Baseline NIHSS score < 6 , n (%)	6 (14.6)	0.876	0.705-1.000
ASPECT score ≥ 6 , n (%)	845 (52.8) [156]	0.833	0.813-0.852
ASPECT score < 6 , n (%)	31 (68.9) [156]	0.763	0.624-0.902
Tandem, n (%)	184 (58.8) [13]	0.833	0.789-0.877
Carotid T-syphon, n (%)	173 (61.6) [13]	0.842	0.795-0.888
M1-segment middle cerebral artery, n (%)	409 (48) [13]	0.825	0.797-0.852
M2-segment middle cerebral artery, n (%)	105 (51.5) [13]	0.851	0.799-0.904
Vertebro-basilar arteries, n (%)	66 (47.5) [13]	0.797	0.724-0.870
Clot burden score 0-5, n (%)	92 (55.8) [1248]	0.824	0.761-0.886
Clot burden score 6-7, n (%)	74 (43.5) [1248]	0.852	0.794-0.910
Clot burden score 8-9, n (%)	100 (45.7) [1248]	0.811	0.754-0.868
Good collateral circulation, n (%)	286 (45.2) [897]	0.837	0.806-0.868
Poor collateral circulation, n (%)	189 (69.5) [897]	0.847	0.802-0.893
Symptom onset-to-groin puncture time ≤ 180 min, n (%)	204 (47.1)	0.801	0.760-0.841
Symptom onset-to-groin puncture time 181-270 min, n (%)	463 (55.3)	0.842	0.816-0.868
Symptom onset-to-groin puncture time 271-360 min, n (%)	279 (52.4)	0.847	0.815-0.880
Mechanical thrombectomy alone (direct), n (%)	459 (58.4)	0.826	0.798-0.854
Mechanical thrombectomy after IVT (bridging), n (%)	487 (47.9)	0.831	0.806-0.856
Aspiration, n (%)	225 (49.8) [561]	0.812	0.774-0.851
Stent retriever, n (%)	328 (55) [561]	0.848	0.818-0.878
Combination of aspiration and stent retriever, n (%)	129 (66.8) [561]	0.784	0.716-0.851
Angioplasty procedure or stent placement, n (%)	103 (55.1) [422]	0.845	0.791-0.899
No angioplasty procedure or stent placement, n (%)	652 (54.7) [422]	0.828	0.806-0.851
Local only anesthesia, n (%)	217 (45.7) [208]	0.851	0.818-0.885
Conscious sedation, n (%)	226 (53.9) [208]	0.816	0.776-0.856
General anesthesia, n (%)	390 (55.7) [208]	0.811	0.779-0.842
First pass effect, n (%)	188 (40.1) [528]	0.802	0.762-0.842
No first pass effect, n (%)	512 (63.6) [528]	0.826	0.798-0.855
NIHSS score ≤ 10 at the end of procedure, n (%)	239 (16.1) [975]	0.802	0.737-0.868
NIHSS score 11-20 at the end of procedure, n (%)	209 (59.7) [975]	0.793	0.723-0.853
NIHSS > 20 at the end of procedure, n (%)	171 (89.1) [975]	0.841	0.775-0.908

Data are n (%). Numbers within square brackets indicate number of missing values. mRS = modified Rankin Scale. NIHSS = National Institutes of Health Stroke Scale. ASPECT = Alberta Stroke Program Early Computed Tomography.