Interventional Neurology

Intervent Neurol 2016;5:101–110
DOI: 10.1159/000445809
Received: November 23, 2015
Accepted: February 3, 2016
Published online: May 27, 2016

1664–9737/16/0054–0101$39.50/0
www.karger.com/ine

Original Paper

Rescue Thrombectomy in Large Vessel Occlusion Strokes Leads to Better Outcomes than Intravenous Thrombolysis Alone: A 'Real World' Applicability of the Recent Trials

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Key Words
Rescue thrombectomy · Large vessel occlusion · Intravenous thrombolysis · Interventional Management of Stroke III trial

Abstract
Background: The Interventional Management of Stroke III (IMS-III) trial demonstrated no benefit for intravenous recombinant tissue plasminogen activator (IV rt-PA) followed by endovascular therapy versus IV rt-PA alone. However, IMS-III mostly included earlier generation devices.

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Intervent Neurol 2016;5:101–110
DOI: 10.1159/000445809

The recent thrombectomy trials have incorporated the stent-retriever technology, but their generalizability remains unknown. ***Methods:*** The North American Solitaire Acute Stroke (NASA) registry recruited patients treated with the Solitaire FR™ device between March 2012 and February 2013. The NASA-IMS-III-Like Group (NILG baseline NIHSS score ≥10 who received IV rt-PA) was compared to the IV rt-PA and IV + intra-arterial (IA)-IMS-III groups and the MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trial controls to assess the stent-retriever treatment in the 'real-world' setting. The NILG was also compared to non-IV rt-PA NASA patients to evaluate the impact of IV rt-PA on thrombectomy. ***Results:*** A total of 136 of the 354 NASA patients fulfilled criteria for the NILG. Baseline characteristics were well balanced across groups. Time from onset to puncture was higher in NILG than IV+IA-IMS-III patients (274 ± 112 vs. 208 ± 47 min, $p < 0.0001$). Occlusions involving the intracranial ICA, MCA-M1, or basilar arteries were more common in NILG than IV+IA-IMS-III patients (91.2 vs. 47.2%, $p < 0.00001$). Modified thrombolysis in cerebral infarction ≥2b reperfusion was higher in NILG than IV+IA-IMS-III patients (74.3 vs. 39.6%, $p < 0.00001$). A 90-day modified Rankin Scale score ≤2 was more frequent in the NILG than IV+IA-IMS-III patients (51.9 vs. 40.8%, $p = 0.03$) and MR CLEAN (51.9 vs. 19.1%, $p < 0.00001$), ESCAPE (51.9 vs. 29.3%, $p = 0.0002$), SWIFT Prime (51.9 vs. 35.5%, $p = 0.02$), and REVASCAT (51.9 vs. 28.2%, $p = 0.0003$) controls. Symptomatic intracranial hemorrhage definitions varied across the different studies with rates ranging from 2.7% (ESCAPE) to 11.9% (NILG). The NILG 90-day mortality (24.4%) was higher than in SWIFT Prime but comparable to all other groups. IV rt-PA was an independent predictor of good outcome in NASA (OR = 2.3, 95% CI 1.2–4.7). ***Conclusion:*** Our results support the 'real-world' applicability of the recent thrombectomy trials.

Introduction

The Interventional Management of Stroke III (IMS-III) trial demonstrated no significant difference between treatments with intravenous recombinant tissue plasminogen activator (IV rt-PA) alone and IV rt-PA followed by endovascular therapy [1]. However, this trial utilized mostly earlier generations of devices and did not evaluate the efficacy of newer devices now known to have higher rates of reperfusion [2]. The subsequent thrombectomy trials including MR CLEAN, ESCAPE, EXTEND-IA, SWIFT Prime, and REVASCAT incorporated the newer stent retriever technology as the only or main endovascular reperfusion strategy and clearly demonstrated a strong benefit of mechanical thrombectomy over medical treatment alone [3–7]. However, these trials were highly selective about which patients and treatment centers they include, and the generalizability of their results in the 'real-world' setting remains unknown. Here, we present data on an 'IMS-III-Like Group' from the North American Solitaire Acute Stroke (NASA) registry, a repository database of the Solitaire FR™ stent retriever. An exploratory analysis was performed to compare these results to the IMS-III IV rt-PA and combined IV/IA groups to investigate how the stent retriever technology would have influenced the IMS-III trials. We also analyzed how these patients compare to the control groups from the recent trials using the newer technology as an attempt to demonstrate the superiority of stent-retriever thrombectomy over medical treatment alone in a setting outside the clinical trial environment.

Methods

The NASA registry was an investigator-initiated registry that recruited 24 clinical sites within North America to submit retrospective demographic, clinical presentation, site-adjudicated angiographic, procedural, and clinical outcome data (90-day modified Rankin Scale, mRS, score) on consecutive patients treated

with the Solitaire device from March 2012 to February 2013. The overall NASA results and detailed methodology have been published elsewhere [8–10]. Essentially, patients presenting within 8 h from symptom onset of an anterior circulation large vessel occlusion or within 12 h of a vertebrobasilar occlusion were included. The thrombolysis in myocardial infarction (TIMI) and modified thrombolysis in cerebral infarction (mTICI) reperfusion scales were defined according to the Solitaire With the Intention for Thrombectomy (SWIFT) and Trevo versus Merci Retrievers for Thrombectomy Revascularization of Large Vessel Occlusions in Acute Ischemic Stroke (TREVO 2) clinical trial definitions with successful reperfusion defined as mTICI/TIMI ≥2 [11, 12]. The time from stroke onset to reperfusion was defined as the time the patient was last seen well to successful reperfusion or the end of the procedure in cases for which reperfusion was not achieved. Symptomatic intracranial hemorrhage (sICH) was defined as any parenchymal hematoma, subarachnoid hemorrhage, or intraventricular hemorrhage associated with a worsening of the National Institutes of Health Stroke Scale (NIHSS) score of ≥4 within 24 h. Good functional outcome was defined as a 90-day mRS score ≤2. Adjuvant therapy was defined as any additional drug (i.e. intra-arterial, IA, lytic) or mechanical device modality used other than the Solitaire FR stent retriever. Reperfusion, angiographic data, hemorrhage type, and clinical outcome were adjudicated by each individual center. There was no industry sponsorship or funding for the registry. Institutional review board approval was obtained from each institution's review board; only de-identified information was submitted to the coordinating center.

For the primary aim of the current study, we identified the cohort of NASA patients who would have met inclusion criteria for the IMS-III trial [i.e. received IV rt-PA and had a NIHSS score of ≥10 on presentation – NASA-IMS-III-Like Group (NILG)] and compared their baseline characteristics and outcomes to the results of the IV rt-PA and the combined IV rt-PA and IA treatment groups from the IMS-III trial as well as to the control groups from the MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials. Additionally, we compared the outcomes of the NILG to those NASA patients not receiving IV rt-PA as an attempt to establish whether IV rt-PA could have any beneficial or deleterious effect in patients treated with stent retriever.

Statistical Analysis

For the comparisons between NILG and the IMS-III, MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials, dichotomous outcomes were analyzed by using the number of events in each group and the total number of participants in order to calculate the risk ratio. For continuous variables, the means and standard deviations from each study were used to calculate the mean difference. A random-effects model was utilized. Analyses were performed with RevMan (Review Manager, version 5.3., Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

For the NASA registry data, descriptive, univariate, and multivariate statistics were performed using the JMP 10 software (SAS Institute, Cary, N.C., USA). Baseline and outcomes variables of the NILG patients were compared to the non-IV rt-PA NASA patients using the Fisher exact test and χ^2 test for categorical variables and the Student t test and unpaired t test for continuous variables. Additionally, we performed a univariate analysis of predictors of good outcomes in the NASA registry. Then, variables with a p value of <0.10 were entered into the multivariate binary logistic regression model to determine the independent predictors of good clinical outcomes. Statistical significance was set at $p < 0.05$.

Results

A total of 354 patients were enrolled in the NASA registry across the 24 participating centers with 136 patients fulfilling the inclusion criteria for NILG (i.e. treatment with IV rt-PA, baseline NIHSS score ≥10, known 90-day mRS score). Table 1 displays the comparison of the baseline characteristics between the NILG (n = 136) versus the combined IV+IA (n = 434) and IV rt-PA only (n = 222) IMS-III arms and the control groups of the MR CLEAN (n = 267), ESCAPE (n = 150), SWIFT Prime (n = 98), and REVASCAT (n = 103) trials. The baseline variables were in general well balanced in terms of age, gender, and comorbidities with the exception of higher rates of atrial fibrillation and diabetes in NILG than MR CLEAN and higher rates of hypertension in NILG than SWIFT Prime. The mean/median NIHSS score on presentation was nominally higher in the NILG as compared to the other groups. The mean time from stroke onset to groin puncture (TOG) was significantly higher in the NILG as compared to the

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Table 1. Baseline characteristics in the NILG compared to the IMS-III trial treatment and control groups and the MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials control groups

Baseline variable	NILG[a] reference (n = 136)	IMS-III IV rt-PA+IA[a] (n = 434)	IMS-III control (n = 222)	p[a]	MR CLEAN control (n = 267)	p	ESCAPE control (n = 150)	p	SWIFT Prime control (n = 98)	p	REVASCAT control (n = 103)	p	p
Age, years													
Mean ± SD	67.3±16	66.3±12	65.5±13	0.50	n.a.	n.a.	n.a.	n.a.	66.3±11.3	0.60	67.2±9.5	0.95	0.60
Median	70	69	68		65.7		70.0		n.a.				
Range	28–100	23–89	23–84										
Male gender	47.8% (65)	50.2% (218)	55.0% (122)	0.62	58.8% (157)	*0.04*	47.3% (71)	0.94	46.9% (45)	0.78	52.4% (54)	0.48	0.78
Baseline NIHSS score[b]													
Mean ± SD	18.5±7	17.3±5	17.0±5	0.06	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Median	19	17	16		18		17		17		17		
Range	1–40	7–40	8–30		4–38		n.a.		n.a.				
Atrial fibrillation	39.7% (54)	35.3% (153)	31.5% (70)	0.35	25.8% (69)	*0.004*	40.0% (60)	0.96	39.2% (38/97)	0.93	35.9% (37)	0.55	0.93
Hypertension	72.8% (99)	73.5% (319)	77.0% (171)	0.87	n.a.	n.a.	72.0% (108)	0.88	57.7% (56/97)	*0.02*	69.9% (72)	0.62	*0.02*
Diabetes mellitus	22.8% (31)	21.7% (94)	24.3% (54)	0.78	12.7% (34)	*0.01*	26.0% (39)	0.53	15.5% (15/97)	0.17	18.4% (19)	0.41	0.17
Coronary artery disease	28.7% (39)	23.5% (102)	32.4% (72)	0.22	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Mean systolic blood pressure ± SD, mm Hg	142.9±27	148±21	147.3±24	*0.04*	145±24.4	0.45	146 (median)	n.a.	n.a.	n.a.	144 (median)	n.a.	n.a.
Mean TOG ± SD, min	274±112	208±47	n.a.	*<0.00001*	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Occlusion					(266)		(147)		(94)		(101)		
None	0% (0)	19.3% (84)	n.a.	*0.005*	0% (0)	1.00	0% (0)	1.00	0% (0)	1.00	0% (0)	1.00	1.00
ICA	26.5% (36)	15.0% (65)		*0.002*	29.3% (78)	0.55	26.5% (39)	0.99	16.0% (15)	0.06	27.7% (28)	0.83	0.06
MCA-M1	55.2% (75)	31.1% (135)		*<0.00001*	62.0% (165)	0.18	71.4% (105)	*0.005*	76.6% (72)	*0.001*	64.4% (65)	0.15	*0.001*
MCA-M2/M3[c]	8.8% (12)	23.7% (103)		*0.0003*	7.9% (21)	0.75	2.0% (3)	*0.02*	6.4% (6)	0.50	7.9% (8)	0.80	0.50
Basilar	9.6% (13)	1.1% (5)		*<0.0001*	0% (0)	*0.005*	0% (0)	*0.02*	0% (0)	*0.04*	0% (0)	*0.03*	*0.04*

Values in parentheses are numbers except where otherwise indicated. Values in italics indicate statistical significance. n.a. = Not available.

[a] Comparison between NASA IV rt-PA+Solitaire and IMS-III IV rt-PA+IA. [b] The NIHSS score was obtained prior to endovascular treatment in NASA and prior to IV rt-PA in IMS-III.

[c] Multiple M2 occlusion patients were included.

Table 2. Clinical and imaging outcomes in the NILG vs. the IMS-III trial treatment and control groups and the MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials control groups

	NILG[a] reference (n = 136)	IMS-III IV rt-PA+IA[a] (n = 434)	IMS-III IV rt-PA only (n = 222)	p[a]	MR CLEAN control (n = 267)	p	ESCAPE control (n = 150)	p	SWIFT prime control (n = 98)	p	REVASCAT control (n = 103)	p
mTICI ≥2b	74.3% (101)	39.6% (126/318)	n.a.	*<0.00001*	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
sICH[b]	11.9%[b] (9)	6.2%[b] (27)	5.9% (13)	0.87	5.9%[b] (16)	0.81	2.7%[b] (4/150)	0.12	7.2%[b] (7/97)	0.86	5.8%[b] (6)	0.80
90-day mRS score ≤2	51.9% (70)	40.8% (169/415)	38.7% (83/215)	*0.03*	19.1% (51/267)	*<0.00001*	29.3% (43/147)	*0.0002*	35.5% (33/93)	0.02	28.2% (29/103)	*0.0003*
90-day mortality	24.4% (33)	19.1% (83)	21.6% (48)	0.19	22% (59)	0.62	19% (28/147)	0.29	12.4% (12/97)	*0.03*	15.5% (16/103)	0.10

Values in parentheses are numbers. Values in italics indicate statistical significance.
[a] Comparison between NASA IV rt-PA+Solitaire vs. IMS-III IV rt-PA+IA. [b] Different definitions for sICH were applied.

combined IV+IA-IMS-III group (274 ± 112 vs. 208 ± 47 min, p < 0.00001). Notably, there were significant differences in the presence and severity of intracranial occlusions amongst the NASA and IMS-III patients. Occlusions involving the intracranial ICA, MCA-M1, or basilar arteries were present in 91.2% of the NILG but only in 47.2% of the combined IV+IA-IMS-III group patients (p < 0.00001). NILG had more basilar and relatively less MCA-M1 occlusions as compared to the newer thrombectomy trials (table 1).

Table 2 summarizes the clinical and imaging outcomes across the different study groups. There were significantly higher rates of optimal reperfusion (mTICI ≥2b) in the NILG than the combined IV+IA-IMS-III group patients (74.3 vs. 39.6%, p < 0.00001). sICH definitions varied across the different studies with rates ranging from 2.7% (ESCAPE) to 11.9% (NILG). The rates of functional independence at 90 days (mRS score ≤2) were significantly higher in the NILG compared to the combined IV+IA-IMS-III group (51.9 vs. 40.8%, p = 0.03) and the IV rt-PA IMS-III group (51.9 vs. 38.7%, p = 0.02) as well as to the MR CLEAN (51.9 vs. 19.1%, p < 0.00001), ESCAPE (51.9 vs. 29.3%, p = 0.0002), SWIFT Prime (51.9 vs. 35.5%, p = 0.02), and REVASCAT (51.9 vs. 28.2%, p = 0.0003) controls. The NILG 90-day mortality was higher than in SWIFT Prime (24.4 vs. 12.4%, p = 0.03) but comparable to all the other groups.

Logistic regression analysis including all NASA patients with available 90-day mRS outcome demonstrated that the use of IV rt-PA was an independent predictor of good outcomes at 90 days (OR = 2.3, 95% CI 1.2–4.7, p = 0.02). Interestingly, this effect on clinical outcomes was not mediated by differences in recanalization rates as the prior usage of IV rt-PA did not influence the rates of reperfusion (tables 3–5).

Discussion

Our study supports the 'real-world' applicability of the recent thrombectomy trials, as in a large cohort of patients treated outside clinical trials, endovascular treatment with stent retrievers also seems to result in better outcomes as compared to medical treatment alone. We made this finding despite greater baseline stroke severity, longer time from stroke onset

Table 3. NILG vs. NASA non-IV rt-PA baseline characteristics and outcomes

Characteristic	NASA non IV rt-PA (n = 179)	NASA IV rt-PA+Solitaire (n = 136)	p
Mean age ± SD, years	67.7±14	67.3±16	0.8
Males	47.8%	47.8%	1.0
Mean baseline NIHSS score ± SD	17.8±6	18.5±7	0.3
Atrial fibrillation	44.7%	39.7%	0.4
Hypertension	79.3%	72.8%	0.2
Diabetes mellitus	25.7%	22.8%	0.6
Coronary artery disease	35.8%	28.7%	0.2
Mean systolic blood pressure ± SD, mm Hg	147±28	142.9±27	0.2
Mean TOG ± SD, min	436.7±289	274±112	*<0.001*
Angiographic occlusion site			
ICA	22.4% (40)	26.5% (36)	0.2
MCA-M1	54.2% (97)	55.2% (75)	0.9
MCA-M2/M3	11.7% (21)	8.8% (12)	0.4
Basilar	11.7% (21)	9.6% (13)	0.5
IA lytics	27.4%	30.9%	0.5
Rescue therapy	26.3%	24.3%	0.7
Balloon guide catheter	37.1%	48.5%	*0.06*
General anesthesia	69.6%	68.4%	0.9
mTICI ≥2b-3	74.7%	74.3%	1.0
mTICI 3	41%	41.2%	1.0
sICH	9.0%	11.9%	0.5
90-day mRS score ≤2	34.6%	51.9%	*0.003*
90-day mortality	34.1%	24.4%	0.08

Values in parentheses are numbers. Values in italics indicate statistical significance.

to treatment, and more proximal location of arterial occlusions in the NASA patient cohort as compared to the IMS-III patients. A similar benefit was suggested by the comparison with the control groups of the MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials.

The IMS-III trial was limited by the use of earlier generation devices and does not reflect current practice. Patients undergoing mechanical thrombectomy in IMS-III were treated with what is now considered an obsolete technology (e.g. the Merci retriever, 28.4% patients, and the first generation of the Penumbra thromboaspiration system, 16.2% patients). Only 5 of the 334 IMS-III patients (1.5%) treated with endovascular therapy received stent-retriever treatment. More remarkably, almost half of the endovascular allocated IMS-III patients were treated with IA rt-PA alone [2]. In contrast, the MR CLEAN, ESCAPE, EXTEND-IA, SWIFT Prime, and REVASCAT trials utilized stent retrievers as the sole or main reperfusion treatment in the vast majority of their patients [3–7]. By achieving faster and better (both quantitatively and qualitatively) reperfusion, these trials demonstrated a remarkable benefit of thrombectomy over medical treatment alone.

A potential criticism to the aforementioned trials is the one of over-selection – raising questions about how generalizable their results are in a larger and less controlled setting. While, due to their uncontrolled nature, registries have a clear disadvantage in definitely proving an intervention, they have an advantage when it comes to the evaluation of how applicable a new therapy is in a broader and more liberal environment. The NASA registry encompassed over 20 different centers with a wider variation in practice patterns, imaging selection paradigms, and treatment algorithms than what is observed in any of the recent

Table 4. NASA univariate analysis of predictors of 90-day functional outcomes

	mRS score ≤2 (n = 132)	mRS score >2 (n = 183)	p
Demographics			
Mean age ± SD, years	65.0±15.1	69.2±14.4	*0.02*
Females	69 (52.7)	95 (51.9)	0.89
Mean baseline NIHSS (range)	15 (12–20)	19 (16–24)	*<0.0001*
White ethnicity	101 (77.7)	132 (72.5)	0.54
Comorbidities			
Hypertension	95 (72.0)	146 (79.8)	0.11
Atrial fibrillation	52 (39.4)	83 (45.4)	0.29
Diabetes mellitus	27 (20.5)	50 (27.3)	0.16
Hyperlipidemia	63 (47.7)	101 (55.2)	0.19
Smoking history	42 (32.1)	53 (29.3)	0.60
Coronary artery disease	40 (30.3)	63 (34.4)	0.44
Clinical presentation			
Occlusion site			0.06
MCA-M1	81.0 (61.4)	90.0 (49.5)	
ICA	23.0 (17.4)	53 (29.1)	
Vertebrobasilar	12 (9.1)	22 (12.1)	
Mean initial systolic blood pressure ± SD, mm Hg	140.3±25.5	148.6±28.6	*0.01*
Mean initial diastolic blood pressure ± SD, mm Hg	76.7±15.6	79.9±18.8	0.10
IV rt-PA	70 (53.0)	65 (35.7)	*0.002*
Procedural factors			
Mean TOG ± SD, min	338.7±229.1	384.6±251.6	0.10
Mean time to revascularization or end of procedure ± SD, min	59.4±70.5	79.9±79.8	*0.03*
General anesthesia	62.0 (60.2)	113 (75.8)	*0.008*
IA rt-PA	34.0 (25.8)	56.0 (30.6)	0.35
Use of balloon guide catheter	65.0 (51.2)	61.0 (35.5)	*0.007*
Mean number of passes ± SD	1.5 (0.84)	2.0 (1.1)	*<0.0001*
Use of rescue therapy	16.0 (12.1)	65.0 (35.5)	*<0.0001*
Imaging outcomes			
mTICI ≥2a	127 (96.2)	153.0 (83.6)	*0.0004*
mTICI ≥2b	118.0 (89.4)	115.0 (63.2)	*<0.0001*
sICH	3.0 (2.3)	29.0 (16.0)	*<0.0001*

Values are n (%) unless otherwise indicated. Values in italics indicate statistical significance.

Table 5. NASA multivariate analysis of predictors of good 90-day functional outcomes

	Good outcome, OR (95% CI)	p
mTICI ≥2b	5.8 (2.2–12.6)	*0.0002*
Baseline NIHSS score	0.91 (0.89–0.96)	*0.001*
sICH	0.1 (0.02–0.4)	*0.01*
General anesthesia	0.4 (0.2–0.8)	*0.01*
Rescue therapy	0.4 (0.2–0.8)	*0.01*
Use of IV rt-PA	2.3 (1.2–4.7)	*0.02*
Balloon guide catheter	2.2 (1.1–4.3)	*0.03*
Age	0.98 (0.96–1.0)	0.11
TOG	0.99 (0.99–1.0)	0.45

Values in italics indicate statistical significance.

thrombectomy trials. Despite that, similar rates of recanalization and good outcomes were seen, supporting the notion that as long as the procedure is done by experienced operators and centers, the benefit of early thrombectomy seem to be generalizable. Our results are further supported by a recent study from the REVASCAT investigators demonstrating that their trial patients treated with endovascular therapy had similar outcomes to patients treated in a parallel population-based endovascular stroke reperfusion registry [13].

Another important finding in our analysis is that the use of IV rt-PA was found to be an independent predictor of good outcome in the NASA registry. Notably, we could not find an association between TOG and outcomes. Therefore, IV rt-PA does not seem to be a confounder for time to treatment. However, there might have been unaccounted differences between patients who received IV rt-PA and those who did not. Notably, we could not adjust for differences in baseline ASPECTS across the two groups since ASPECTS was not collected in the NASA registry. Interestingly, there was no difference in the rates of mTICI ≥2b or TICI 3 reperfusion between NASA patients treated with IV rt-PA and those not treated with IV rt-PA. Thus, any potential benefit of IV rt-PA in this setting appears to be unrelated to its reperfusion mechanism. This finding is consistent with a recent study demonstrating lower rates of infarct growth in fully reperfused patients who received IV rt-PA prior to thrombectomy than in those who did not and supports the recent experimental data suggesting a neuroprotective effect to rt-PA [14, 15]. Our study also adds to the increasing body of evidence demonstrating the safety of rescue endovascular therapy following intravenous thrombolysis, as no difference in the rates of sICH were seen amongst NASA patients who did and those who did not receive IV rt-PA (11.9 vs. 9.0%, p = 0.5) [1, 3–6, 16]. Given the safety of thrombectomy before IV rt-PA and its potential benefit in the clinical outcomes, our results favor the combined IV+IA approach rather than the IV or IA approaches in isolation. However, a prospective clinical trial is needed to confirm these findings.

There are important limitations to our study with many of them being related to its retrospective nature. The comparison with the IMS-III, MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials was not performed at a patient level. However, baseline NIHSS score, age, comorbidities, and vascular occlusion sites were either similar across groups or adversely affected the NILG. The NILG had a slightly lower baseline systolic blood pressure than IMS-III patients. Lower systolic blood pressure has been linked to higher recanalization rates, so it is possible that this small imbalance may have favored the NILG outcomes [17]. Moreover, NASA did not collect baseline ASPECTS which is one of the strongest determinants of outcomes after endovascular therapy [18]. However, it is unlikely that IMS-III patients had higher stroke burden on presentation than NILG patients given the higher baseline NIHSS score, longer TOG, and higher frequency of ICA, MCA-M1, and basilar occlusions observed in NILG than IMS-III patients. Similarly, the control groups of the MR CLEAN, ESCAPE, SWIFT Prime, and REVASCAT trials had high median ASPECTS (9, 9, 9, and 8, respectively), so it is unlikely that the NILG would have significantly better ASPECTS mostly when considering the nominal differences in the median baseline NIHSS score across the different groups. Mortality in the NILG was comparable to most studies but was higher than in SWIFT Prime, potentially due to a higher stroke severity and the inclusion of basilar occlusions in the NILG. Finally, adjudication of reperfusion and clinical outcomes was performed locally at each site, without a core laboratory or requirement of an independent adjudicator. This lack of central adjudication may be biased toward better outcomes in NASA than in the randomized trials. Ongoing prospective registries involving the Solitaire and Trevo devices should overcome these limitations and provide a more definite proof of the generalizability of stent-retriever thrombectomy.

Conclusion

In agreement with the recent trials, stent-retriever bridging therapy for large vessel occlusion strokes seems to result in better outcomes than intravenous thrombolysis alone even when performed outside the more rigid and selective clinical trial environment.

Disclosure Statement

Dr. Nogueira, Dr. Zaidat, and Dr. Gupta are consultant/advisory board members of Covidien and Stryker Neurovascular. Dr. Malisch is a member of the DSMB SWIFT Trial. Dr. Linfante is a consultant for Covidien. Dr. Rai is a consultant/advisory board member of Stryker Neurovascular. Dr. English is a consultant for Stryker Neurovascular. Dr. Abraham is a consultant of Stryker Neurovascular and a member of the speaker's bureau for Boehringer Ingelheim. The other authors have no conflicts of interest to disclose.

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