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Original Paper

Predictors and Outcomes Associated with Rescue Therapy in SWIFT

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for the SWIFT investigators

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Key Words
Acute stroke · Endovascular therapy · Intravenous tissue plasminogen activator · Recanalization · Rescue therapy · SWIFT trial

Abstract
Introduction: In the Solitaire With the Intention For Thrombectomy (SWIFT) trial, rescue therapy was used when the Solitaire or Merci device was unable to restore vessel patency. Markers for nonrecanalization in acute stroke have been reported for intravenous tissue plasminogen activator; however, similar predictors are not known for endovascular therapy. We sought to identify predictors and outcomes associated with rescue therapy in the SWIFT trial. ***Methods:*** Rescue therapy included the use of an alternative device, agent, or maneuver following failure to recanalize with three retrieval attempts using the initial device. Clinical, angiographic, and demographic data was reviewed. ***Results:*** Among a total of 144 patients enrolled, 43 (29.9%) required rescue therapy. We used the same baseline demographics for patients with and without rescue therapy. Rescue therapy was used in a higher percentage of patients randomized to the Merci group compared with the Solitaire group (43 vs. 21%, $p = 0.009$). Patients with rescue therapy experienced a longer recanalization time ($p < 0.001$), a lower percentage of successful recanalization ($p < 0.001$), and a lower percentage of good outcome ($p = 0.009$). In multivariate analysis, patients randomized to the Merci group (OR 3.99, 95% CI 1.58, 10.10) and age >80 years (OR 3.51, 95% CI 1.06, 11.64) were predictors of rescue therapy. ***Conclusions:*** Merci treatment group and age were predictors of rescue therapy, while a trend toward an increased need of rescue therapy was observed with hypertension and proximal clot location. Rescue therapy was associated with fewer good outcomes. These findings may reflect targets for improvement in endovascular therapy.

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Introduction

In acute ischemic stroke treatment, there is a strong correlation between recanalization and good functional outcome at 3 months when compared with nonrecanalized patients [1]. The greatest benefit to restoring blood flow in acute ischemic stroke occurs with early recanalization, specifically within 90 min [2]. Markers for nonrecanalization after intravenous tissue plasminogen activator (i.v. tPA) include time to treatment, a high National Institutes of Health Stroke Scale (NIHSS) score, thrombus size, location of arterial occlusion, atrial fibrillation, and diabetes [3–6]. Similar predictors are not known for endovascular revascularization therapy.

In the Solitaire With the Intention For Thrombectomy (SWIFT) trial, the Solitaire FR device was compared with the Merci retrieval system in a multicenter Investigational Device Exemption (IDE), randomized, noninferiority trial for the treatment of ischemic stroke due to large intracranial vessel occlusions within 8 h of symptom onset [7]. A total of 113 patients (58 patients in the Solitaire group and 55 patients in the Merci group) were enrolled from 18 sites. The primary endpoint was recanalization [Thrombolysis In Myocardial Infarction (TIMI) scale 2 or 3 flow)] without symptomatic intracranial hemorrhage after up to three passes with the assigned device. A prespecified efficacy stopping rule triggered an early stop to the trial after higher rates of primary outcome were achieved in the Solitaire FR group compared with the Merci group (61 vs. 24%; $p < 0.0001$).

In this post hoc analysis of SWIFT, we aimed to investigate the predictors and outcomes associated with rescue therapy in the SWIFT trial. Identifying these markers may contribute to improved patient selection for mechanical thrombectomy therapies and future clinical trial design.

Methods

Patients were randomized to either the Solitaire group or the Merci group in the SWIFT trial, which was designed to establish the noninferiority of the Solitaire device. A total of 144 patients were enrolled [31 roll-in phase Solitaire patients and 113 randomized patients (58 from the Solitaire group and 55 from the Merci group)] from 18 centers (17 in the USA and 1 in France) during 2010 and 2011. Patients were eligible if they had clinical signs consistent with an acute ischemic stroke, an NIHSS score ≥8 and <30, were either ineligible or failed i.v. tPA, had an angiographic TIMI 0 or 1 occlusion in the M1 or M2 of the middle cerebral artery, internal carotid artery, basilar artery, or vertebral artery that was accessible to the Solitaire FR or Merci device, and could be treated within 8 h from symptom onset. The primary efficacy endpoint of the study was successful recanalization with the assigned study device (no use of rescue treatment) and with no symptomatic intracranial hemorrhage. Successful recanalization was defined as a TIMI scale 2 or 3 flow in all treatable vessels. The SWIFT trial was approved by all appropriate regulatory bodies of the participating centers. All patients provided written, informed consent for participation in the trial before enrollment. A detailed description of the SWIFT trial is available elsewhere [7].

In the trial, the study patients were randomly assigned in a 1:1 ratio to receive either Solitaire FR or Merci as the initial thrombectomy intervention. The neurointerventionalist selected the proper study device size per device-specific instructions for use. He used the assigned device to attempt recanalization until successful recanalization was achieved, or until three passes were performed with the study group device. The primary endpoint angiogram was then performed. 'Rescue therapy' was defined per SWIFT study protocol and included the use of an alternative device, agent, or maneuver following failure to recanalize with three retrieval attempts using the initial device. For this analysis, we reviewed the SWIFT data and compared baseline demographics and outcomes between those patients who received rescue therapy and those who did not receive rescue therapy. Statistical analysis was performed using the t test or Wilcoxon methods and multivariate logistic regression analyses.

All SWIFT investigators had access to all data in the study and had final responsibility for the development and submission of the data for publication.

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Table 1. Baseline demographics by rescue therapy

Baseline demographics	Rescue therapy (n = 43)	No rescue therapy (n = 101)	p value
Age, years	68±12	66±12	0.43
Male gender	44	50	0.59
NIHSS score	17±5	18±5	0.23
Median prestroke mRS (IQR)	0 (0–1)	0 (0–1)	0.61
BMI	30±8	29±7	0.35
i.v. tPA failure	43	48	0.59
Hypertension	77	63	0.13
Diabetes mellitus	28	29	1.00
Hyperlipidemia	53	54	1.00
Smoker	35	41	0.58
Atrial fibrillation	56	50	0.59
Myocardial disease	35	34	1.00
Peripheral artery disease	5	6	1.00

Values are means ± SD or percentages, except where indicated otherwise. mRS = Modified Rankin Scale; BMI = body mass index.

Table 2. Outcomes by rescue therapy

Outcomes	Rescue therapy	No rescue therapy	p value
Solitaire cases, n	19	70	
Merci cases, n	24	31	
Solitaire patients, %	44	69	0.008
Mean time to clot visualization ± SD, min	49±513	154±433	0.21
Mean time to recanalization ± SD, min	93±38	37±23	<0.001
Median number of passes (IQR)	3 (2–3)	1 (1–2)	<0.001
Secondary territory embolization, %	2	4	1.00
Successful recanalization, %	5	72	<0.001
Good Neurologic Outcome – mRS, %	19	44	0.009
Good Neurologic Outcome – mRS or NIHSS, %	32	57	0.02
Symptomatic ICH, %	7	4	0.43

mRS = Modified Rankin Scale; ICH = intracranial hemorrhage.

Results

A total of 144 patients were enrolled [31 roll-in phase Solitaire patients and 113 randomized patients (58 from the Solitaire group and 55 from the Merci group)]. Among these patients, 43 (29.9%) required rescue therapy. We used the same baseline demographics for patients with and without rescue therapy (table 1). Rescue therapy was used in a higher percentage of patients randomized to the Merci group compared with the Solitaire group (43 vs. 21%, p = 0.009). Patients who underwent rescue therapy experienced a longer recanalization time (p < 0.001), a lower percentage of successful recanalization (p < 0.001), and a lower percentage of good outcome (p = 0.009; table 2).

In multivariate analysis, patients randomized to the Merci group (OR 3.99, 95% CI 1.58, 10.10) and age >80 years (OR 3.51, 95% CI 1.06, 11.64) were predictors of rescue therapy. Nonsignificant trends toward an increased need for rescue therapy were observed in patients with hypertension (p = 0.09), and occlusions of the carotid terminus and M1 MCA compared with other locations (p = 0.10). No association was observed with rescue therapy and atrial fibrillation (p = 0.47) or i.v. tPA failure (p = 0.49), and rescue therapy was not associated with symptomatic ICH (p = 0.43).

Discussion

In this post hoc analysis of the SWIFT trial, we considered the Merci treatment group and age to be predictors of rescue therapy, while a trend toward an increased need of rescue therapy was observed with hypertension and proximal clot location. We did not observe an association with many of the markers previously correlated with nonrecanalization in i.v. tPA. The association between rescue therapy and the Merci treatment group likely reflects the differences in device performance. Age was observed as a predictor of rescue therapy, which may have a multifactorial etiology for association. Increased age is associated with vessel tortuosity, atherosclerosis, and diminished endothelial health [8]. Overall, reduced vessel health in the aged population may contribute to the findings.

Markers for nonrecanalization after i.v. tPA include time to treatment, NIHSS, atrial fibrillation, and diabetes; however, our results did not show a similar association for rescue therapy in the SWIFT trial [3–6]. Although nonsignificant, there was a trend toward an increased need for rescue therapy in patients with occlusions of the carotid terminus and M1 MCA compared with other locations. This is similar to findings of poor recanalization in the proximal large and medium size vessels after tPA administration [9]. This is consistent with the broad recognition of larger clots in the proximal vasculature posing the most challenge for recanalization. Several of the markers of nonrecanalization after i.v. tPA were not observed in this analysis, which may support the notion that large vessel occlusions are poorly recanalized with i.v. tPA alone. A long time interval between occlusion and treatment might represent more advanced thrombus organization or progression in size, and therefore the limitation of i.v. tPA recanalization. A high NIHSS score may be due to a large vessel occlusion, which is associated with a limited recanalization success with i.v. tPA. Acute stroke in patients with atrial fibrillation can be due to thromboembolism of a well-organized thrombus that may be amenable to mechanical thrombectomy and not systemic thrombolysis. Nonrecanalization after i.v. tPA in patients with diabetes might represent pial collateral supply, which may be a more important factor in large vessel occlusions, and thus the findings in the present analysis might be different than with i.v. tPA. Rescue therapy was not associated with symptomatic intracranial hemorrhage, which may be an important observation suggesting that persistent attempts and use of more than one device may not substantially increase the risk of hemorrhage.

A limitation of this analysis is the use of rescue therapy as a surrogate marker to identify factors of nonrecanalization. The decision to pursue rescue therapy followed an angiographic evaluation that did not show TIMI 2 or 3 flow in all treatable vessels. The small sample size in this analysis also limits interpretation. Further investigations with larger series might offer better insight into patient selection for endovascular therapy. In particular, patients aged 22–85 years were eligible for inclusion in the SWIFT trial, similar to the age criteria for other acute stroke intervention trials. Identifying the reasons for the increased use of rescue therapy in the older population might contribute to patient selection.

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