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 L.A. Slater,  J.M. Coutinho,  J. Gralla,  R.G. Nogueira,  A. Bonafé,  A. Dávalos,  R. Jahan,  E. Levy,  B.J. Baxter,  J.L. Saver, and  V.M. Pereira; for the STAR and SWIFT investigators

## ABSTRACT

**BACKGROUND AND PURPOSE:** Previous studies have suggested that advanced age predicts worse outcome following mechanical thrombectomy. We assessed outcomes from 2 recent large prospective studies to determine the association among TICI, age, and outcome.

**MATERIALS AND METHODS:** Data from the Solitaire FR Thrombectomy for Acute Revascularization (STAR) trial, an international multicenter prospective single-arm thrombectomy study and the Solitaire arm of the Solitaire FR With the Intention For Thrombectomy (SWIFT) trial were pooled. TICI was determined by core laboratory review. Good outcome was defined as an mRS score of 0–2 at 90 days. We analyzed the association among clinical outcome, successful-versus-unsuccessful reperfusion (TICI 2b–3 versus TICI 0–2a), and age (dichotomized across the median).

**RESULTS:** Two hundred sixty-nine of 291 patients treated with Solitaire in the STAR and SWIFT data bases for whom TICI and 90-day outcome data were available were included. The median age was 70 years (interquartile range, 60–76 years) with an age range of 25–88 years. The mean age of patients 70 years of age or younger was 59 years, and it was 77 years for patients older than 70 years. There was no significant difference between baseline NIHSS scores or procedure time metrics. Hemorrhage and device-related complications were more common in the younger age group but did not reach statistical significance. In absolute terms, the rate of good outcome was higher in the younger population (64% versus 44%,  $P < .001$ ). However, the magnitude of benefit from successful reperfusion was higher in the 70 years of age and older group (OR, 4.82; 95% CI, 1.32–17.63 versus OR 7.32; 95% CI, 1.73–30.99).

**CONCLUSIONS:** Successful reperfusion is the strongest predictor of good outcome following mechanical thrombectomy, and the magnitude of benefit is highest in the patient population older than 70 years of age.

**ABBREVIATIONS:** AIS = acute ischemic stroke; NASA = North American Solitaire Stent Retriever Acute Stroke; STAR = Solitaire FR Thrombectomy for Acute Revascularization; SWIFT = Solitaire FR With the Intention For Thrombectomy; TIMI = Thrombolysis in Myocardial Infarction

The clinical outcome after acute ischemic stroke is generally worse in the elderly compared with nonelderly populations.<sup>1,2</sup> Poorer outcomes are to be expected in the elderly population in all disease states; however, the effect of a therapy may still

afford a similar magnitude of benefit.<sup>3</sup> Results from the Third International Stroke Trial suggest that the therapeutic effect of IV-tPA is similar or even better in the elderly population.<sup>4,5</sup> With regard to stroke therapy, recanalization has been definitively related to good clinical outcomes.<sup>6–8</sup> However, it has been reported in multiple studies that despite similar rates of recanalization, the elderly have higher mortality rates and poorer outcomes than younger patients following intra-arterial treatment.<sup>7,9–13</sup> These studies were mostly retrospective, single-center series or used older generation devices with suboptimal reperfusion rates.<sup>7,9–13</sup> Recent clinical studies demonstrating the value of mechanical thrombectomy for acute ischemic stroke (AIS) did not include a significant number of elderly patients.<sup>14–17</sup> We performed a post

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**Table 1: Demographics and baseline characteristics**

Characteristic	70 Years or Younger	Older Than 70 Years	P Value
No.	135	134	
Male	49% (66/135)	34% (45/134)	.013
NIHSS (median) (IQR)	18 (14–20)	17 (13–20)	.359
Prestroke mRS (categorical)			<.001
0	81% (95/118)	63% (71/113)	
1	15% (18/118)	17% (19/113)	
2	3% (3/118)	19% (21/113)	
3	2% (2/118)	2% (2/113)	
Occluded vessel			.101
ICA	21% (28/130)	7% (22/132)	
M1	70% (91/130)	64% (84/132)	
M2	8% (10/130)	18% (24/132)	
M3	1% (1/130)	2% (2/132)	
Baseline ASPECTS (mean)	8.1 ± 1.9 (133)	8.4 ± 1.4 (133)	.207
IV-tPA	63% (77/123)	58% (70/121)	.513
Baseline serum glucose level (mean)	127 ± 56 (130)	126 ± 56 (129)	.865
Atrial fibrillation	27% (36/135)	51% (68/134)	<.001
Hypertension	53% (72/135)	74% (99/134)	<.001
Coronary artery disease	21% (29/135)	25% (34/134)	.474
Diabetes	19% (25/135)	19% (25/134)	1
Hyperlipidemia	46% (62/135)	39% (52/134)	.267
Peripheral artery disease	1% (2/135)	0% (0/134)	.498
Smoking	24% (32/135)	4% (5/134)	<.001
Prior stroke or TIA	13% (17/135)	25% (34/134)	.008

Note:—IQR indicates interquartile range.

hoc analysis of 2 prospective core lab–reviewed studies assessing mechanical thrombectomy by using new-generation devices (stent retrievers) for AIS to determine whether the benefit of reperfusion was constant across age groups, including the older population.

## MATERIALS AND METHODS

### Study Design and Patient Selection

We pooled data from the Solitaire FR Thrombectomy for Acute Revascularization (STAR) study and the Solitaire arm of Solitaire FR With the Intention For Thrombectomy (SWIFT) trial. Details of both studies have been previously reported.<sup>18,19</sup> Briefly, STAR was a prospective, multicenter, single-arm study. Key inclusion criteria were presentation within 8 hours of onset of acute ischemic stroke, a proximal occlusion of an anterior circulation vessel, age between 18 and 85 years, and a National Institutes of Health Stroke Scale score of 8–30. All patients were treated in high-volume stroke centers with a Solitaire stent retriever (Covidien, Irvine, California) through a balloon-guided catheter.<sup>19</sup> SWIFT was a randomized open-label trial with blinded end point assessment comparing the Solitaire stent retriever with the Merci retriever (Concentric Medical, Mountain View, California). The study included patients 22–85 years of age with NIHSS scores of 8–30. Patients were either ineligible for or had not responded to intravenous rtPA.<sup>18</sup>

All data in the STAR and SWIFT studies were determined by an independent CT and MR imaging core laboratory, a separate angiography core laboratory, and an independent clinical events committee. The clinical events committee was responsible for the review and validation of all complications that occurred during the course of the studies and the subsequent classification of these complications related to the device or procedure. The study data were independently monitored; study management was provided

by the sponsor, Covidien. Clinical outcome was determined at 90 days with the modified Rankin Scale. Reperfusion results were reported by using the Thrombolysis in Cerebral Infarction score and was defined as ranging from no reperfusion (TICI = 0) to complete reperfusion (TICI = 3), including partial reperfusion of TICI 2, divided into 2a and 2b as less than and greater than 50%, respectively.<sup>20</sup> This definition is different from the original one in which 2a was defined as less than two-thirds perfusion of the distal territory, and 2b, as greater than two-thirds perfusion.<sup>21</sup> Intracranial hemorrhage was reported with the European Cooperative Acute Stroke Study classification.<sup>22</sup> For the current study, we excluded patients from both studies for whom no TICI score or 90-day mRS was available.

### Data Analysis

Based on the distribution of age, patients within the cohort were dichotomized into 2 groups across the median for age. We studied differences in baseline patient characteristics and treatment details between the age groups. For continuous variables, we used a *t* test or Wilcoxon test, and for discrete variables, a Fisher exact test. We then used multivariate logistic regression analysis to assess the effect of successful reperfusion (TICI 2b–3) versus unsuccessful reperfusion (TICI 0–2a) on clinical outcome in each age group. Good clinical outcome at 90 days was defined as a mRS score of 0–2.

We calculated odds ratios, adjusting for the following variables: atrial fibrillation, ASPECTS, NIHSS score at admission, dyslipidemia, sex, hypertension, location of occlusion, use of IV-tPA, prestroke mRS, and smoking.

## RESULTS

A total 269 of the 291 patients treated with the Solitaire device in the STAR and SWIFT trials were included in this analysis. Twenty-two patients were excluded because of missing mRS scores at 90 days ( $n = 7$ ) or missing TICI scores ( $n = 15$ ). The median age for the entire cohort was 70 years (interquartile range, 60–76 years), and the age range was 25–88 years. The mean age for patients 70 years or younger was 59 years, and for those older than 70, it was 77 years. The baseline characteristics are summarized in Table 1. The proportion of men was higher among the younger compared with the older patients (49% versus 34%,  $P = .013$ ). The baseline NIHSS score did not differ between the groups (18 versus 17,  $P = .359$ ). There was a significantly lower rate of atrial fibrillation (27% versus 51%,  $P < .001$ ), hypertension (53% versus 74%,  $P < .001$ ), and prior stroke or TIA (13% versus 25%,  $P = .008$ ) in the younger group, while smoking was more common in the 70 years and younger group (24% versus 4%,  $P < .001$ ). The proportion of patients with a prestroke mRS of zero was lower in

**Table 2: Details of endovascular procedure<sup>a</sup>**

	70 Years or Younger	Older Than 70 Years	P Value
No. of Solitaire passes (mean)	1.8 ± 1.0	1.7 ± 1.0	.420
Time from symptom onset to hospital arrival	178 (98–265)	172 (68–245)	.263
Time from groin puncture to balloon guiding catheter	11 (6–17)	12 (8–17)	.12
Time from symptom onset to groin puncture	253 (205–322)	255 (185–323)	.714
Time from groin puncture to reperfusion	46 (28–68)	42 (32–70)	.714
TICI 2b–3	87% (117/135)	83% (111/134)	.400
General anesthesia	67% (90/135)	65% (87/134)	.763
Conscious sedation	29% (39/135)	28% (38/134)	.763

Note:—IQR indicates interquartile range.

<sup>a</sup>All times are given as median minutes with IQR in parentheses.

**Table 3: Complications and outcome stratified by age**

	70 Years or Younger	Older Than 70 Years	P Value
Complication			
Symptomatic intracerebral hemorrhage	4% (5/135)	1% (2/134)	.447
PH-1 intracerebral hemorrhage	2% (3/135)	1% (2/134)	1
PH-2 intracerebral hemorrhage	2% (3/135)	0% (0/134)	.247
SAH intracerebral hemorrhage	1% (2/135)	2% (3/134)	.684
IVH intracerebral hemorrhage	0% (0/135)	1% (1/134)	.498
Any intracerebral hemorrhage	19% (25/135)	14% (19/134)	.410
Vasospasm	27% (36/135)	17% (23/134)	.077
Device-related AE	16% (21/135)	14% (19/134)	.864
Outcome at 90 days			
All-cause mortality	8% (11/135)	12% (16/134)	.318
mRS 0–2	64% (87/135)	12% (59/134)	0.318

Note:—PH-1 indicates parenchymal hematoma type 1; PH-2, parenchymal hematoma type 2; IVH, intraventricular hemorrhage; AE, adverse events.

**Table 4: Rate of good outcome according to age and TICI score<sup>a</sup>**

Age Groups (yr)	TICI 2b–3	TICI 0–2a	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
70 or younger	67.5% (79/117)	44.4% (8/18)	2.6 (0.95–7.11)	4.82 (1.32–17.63)
Older than 70	49.5% (55/111)	17.4% (4/23)	4.66 (1.49–14.59)	7.32 (1.73–30.99)

<sup>a</sup>The frequency of good clinical outcome is given according to age and TICI scores. For each age group, the OR is provided for good outcome in patients with successful reperfusion (TICI 2b–3) vs unsuccessful reperfusion (TICI 0–2a).

**Table 5: Rates of good outcome according to age quartiles and TICI score**

Age (yr)	TICI 0–2a	TICI 2b–3	P Value
60 or younger	75.0% (9/12)	87.0% (47/54)	.372
61–70	50.0% (3/6)	73.0% (46/63)	.346
71–77	46.7% (7/15)	74.1% (43/58)	.061
78 or older	25.0% (2/8)	67.9% (36/53)	.044

the older than 70 years of age group (81% versus 63%,  $P < .001$ ). Although not reaching statistical significance, the mean baseline ASPECTS was slightly lower in the 70 years and younger group (8.1 versus 8.4,  $P = .207$ ). There was a trend toward a higher proportion of M2 occlusions in the older than 70 years of age group (8% versus 18%,  $P = .101$ ).

There was no significant difference in the proportion of patients who received IV-tPA in the 2 groups (63% versus 58%,  $P = .513$ , Table 1). There was no significant difference in the mechanical thrombectomy and time metrics, with a similar number of Solitaire passes, times of onset to arrival at the hospital and groin punctures, and similar types of anesthesia used and number of TICI 2b–3 reperfusion (Table 2).

Complications including intracranial hemorrhage, vasospasm, and device-related problems are summarized in Table 3. Although not reaching statistical significance, intracranial hemorrhage (19% versus 14%,  $P = .410$ ) and vasospasm (27% versus 17%,  $P = .077$ ) occurred more often in the younger age group. Device-related complications were similar between the 2 groups (16% versus 14%,  $P = .864$ ). There was a trend toward higher overall 90-day mortality in the older group (8% versus 12%  $P = .318$ ). Good clinical outcome was achieved in 64% of the 70 years and younger and 44% of the 70 years and older groups ( $P < .001$ ).

The rates of good outcome according to TICI score and age are summarized in Table 4. Univariate analysis showed that the effect of successful reperfusion on good outcome was more pronounced in the older than 70 years of age group than in the 70 years of age or younger group (OR, 2.6; 95% CI, 0.95–7.11 versus 4.66; 95% CI, 1.49–14.59). The same trend was seen when dividing the patients into quartiles, with overall better outcomes in the younger patients but a greater differential between good outcomes for unsuccessful-versus-successful outcome as age increased (Table 5). After adjustment for potential confounders, the strength of the association between successful reperfusion and outcome increased in both age groups but remained stronger in the age group older than 70

years (OR, 4.82; 95% CI, 1.32–17.63;  $P = .018$  versus OR, 7.32; 95% CI, 1.73–30.99;  $P = .007$ ). Table 6 demonstrates multivariate analysis of the predictors of good outcome following mechanical thrombectomy in patients younger and older than 70 years.

## DISCUSSION

Our post hoc analysis of the STAR trial and the patients from the Solitaire arm of the SWIFT trial, 2 prospective core lab–reviewed studies evaluating these new-generation devices, demonstrates that successful reperfusion, as defined by a TICI score of 2b or 3, after endovascular treatment of AIS, is the most significant variable in achieving good clinical outcome and is more significant in the elderly population. When we dichotomized patients across the age median, similar rates of successful reperfusion (87% versus 83%  $P = .4$ ) were demonstrated in both groups of patients and higher rates of good clinical outcome, given successful reperfusion, were demonstrated in the younger patients (younger than 70 years of age = 67.5%, older than 70 years of age = 49.5%). However, the effect of successful reperfusion was more pronounced in the older patients, with a higher odds ratio of 7.32 for good out-

**Table 6: Predictors of good outcome following mechanical thrombectomy in younger and older patients**

Variable	70 Years or Younger			Older Than 70 Years		
	OR	95% CI	P Value	OR	95% CI	P Value
Afib	0.53	(0.18–1.61)	.265	1.5	(0.58–3.90)	.407
Baseline ASPECTS	1.16	(0.91–1.49)	.222	1.06	(0.73–1.54)	.752
Baseline NIHSS	0.88	(0.78–0.99)	.033	0.86	(0.78–0.96)	.006
Female	1.28	(0.49–3.33)	.617	1.07	(0.39–2.97)	.898
HTN	0.57	(0.20–1.63)	.296	1	(0.34–2.95)	.995
ICA	4.01	(0.88–18.33)	.073	0.35	(0.08–1.44)	.145
IV-tPA	1.06	(0.38–2.96)	.915	2.32	(0.89–6.06)	.086
Prestroke mRS score	0.53	(0.26–1.11)	.092	0.64	(0.38–1.10)	.104
TICI 2b–3	4.82	(1.32–17.63)	.018	7.32	(1.73–30.99)	.007

**Note:**—Afib indicates atrial fibrillation; HTN, hypertension.

come in the patients older than 70 years compared with the younger cohort for whom the odds ratio was 4.8. Recent randomized controlled trials demonstrated the benefit of mechanical thrombectomy by using stent retrievers in the treatment of AIS (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment [SWIFT-PRIME], Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke [ESCAPE], Multicenter Randomized Clinical Trial of Endovascular treatment for Acute Ischemic Stroke in the Netherlands [MR CLEAN], and Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial [EXTEND-IA] trials).<sup>14–17</sup> Patient selection and new treatment guidelines are crucial at this point.

Although there was a trend toward higher 90-day mortality in the older group, this did not reach statistical significance (8% versus 12%,  $P = .318$ ). These mortality rates were lower for both age groups than those reported in previous studies, with the North American Solitaire Stent Retriever Acute Stroke (NASA) registry reporting 27.3% 90-day mortality in the younger group and 43.9% in the older group.<sup>12</sup> Most interesting, Engelter et al<sup>9</sup> in their analysis of IV thrombolysis and Mono et al<sup>10</sup> in their analysis of intra-arterial thrombolysis reported lower rates of 90-day mortality compared with the NASA registry, with 12% and 22% mortality for younger cohorts, respectively, and 32% and 40% mortality in the older cohorts. The Engelter and Mono studies reviewed results using treatment methods with lower recanalization rates than stent retrievers, and the NASA registry had an older patient population. Additionally, in our study, there was no difference in intracranial hemorrhage rates of all types in the younger age group (19% versus 14%,  $P = .410$ ); moreover, hemorrhage did not have a significant impact on differences in clinical outcome or mortality rates between the 2 groups and is in keeping with previously published results.<sup>12</sup>

Singer et al<sup>22</sup> demonstrated the highest rates of good clinical outcome (mRS  $\leq 2$ ) in the youngest quartile (60%) and the lowest in the oldest quartile (17%). They then dichotomized the entire patient cohort into good and poor clinical outcomes and determined the proportion of patients within each group in whom successful reperfusion was achieved. Thrombolysis in Myocardial Infarction (TIMI) 2–3 was achieved in 95% and 75% of those with good and poor clinical outcomes, respectively.<sup>23</sup> Kurre et al<sup>13</sup> analyzed intra-arterial therapy in patients with AIS 80 years of age and older and reported successful recanalization as defined by

TICI 2b–3 in 87.9% of patients; however, only 17.4% of patients achieved functional independence. Castonguay et al<sup>12</sup> evaluated the data from the NASA registry and reported successful recanalization in 73.1% of the patients 80 years of age and younger and 69.2% of patients older than 80 years when evaluated by the TICI score and in 84% of the younger group and 83.3% of the older group when using TIMI, with rates of good outcomes of 45.4% and 27.3% in the younger and older populations,

respectively.

Mono et al<sup>10</sup> assessed treatment of AIS with intra-arterial thrombolysis and measured successful revascularization as TIMI 2–3; this was demonstrated in 71% of the younger patients and 65% of the older patients, with good clinical outcomes in 46% of the younger patients and 28% of the older patients.<sup>7</sup> Luedi et al<sup>7</sup> analyzed outcome in quartiles and demonstrated TIMI 2–3 recanalization achieved in 81.3% and good outcome in 64.7% of the patients in the youngest quartile and TIMI 2–3 achieved in 73.8% and good outcome achieved in 20.3% of the patients in the oldest quartile.<sup>7</sup> Although assessing IV thrombolysis, Engelter et al<sup>9</sup> also demonstrated poorer outcomes in the younger-versus-older groups (37% versus 29%) and revascularization rates were not reported; however, it would be expected that lower rates of successful revascularization would have been achieved given that no intra-arterial therapy was used.

These studies consistently demonstrated lower absolute rates of good outcome in the older age groups; and similar to results of studies using first-generation mechanical thrombectomy devices, high recanalization rates did not always equate to clinical benefit.<sup>21,24,25</sup> Furthermore, previous analysis of the STAR registry by using stratification by the Stroke Prognostication using Age and NIH Stroke Scale (SPAN) demonstrated poorer outcomes in patients with SPAN-100-positive scores, that is, patients with AIS in whom age + presentation NIHSS were  $>100$ .<sup>26</sup> Of note, the baseline NIHSS score did not differ significantly between the older and younger groups in our study or indeed in the other studies comparing outcomes between the 2 age groups. This finding confirms the expectation that poorer outcomes are expected in older age groups unless good reperfusion is achieved.

Although our analysis also demonstrated lower rates of good outcomes in the older patients, the rates of good outcome were higher than those in previous series. The overall better outcomes may be due to faster procedure times, new-generation devices, and criteria for center selection for the trials requiring high volume and experienced stroke centers.<sup>18,19,27</sup> The mean time from symptom onset to groin puncture in the NASA registry was 364.7 minutes for the younger cohort and 358.9 minutes in the older cohort, compared with 253 minutes and 255 minutes in our study; and the mean time from groin puncture to reperfusion was 71.7 minutes and 93.1 minutes within the NASA registry and 46 minutes and 42 minutes in our series for the younger and older cohorts, respectively.<sup>12</sup> Additionally, well-defined imaging

criteria were used to select patients with both a large vessel occlusion and a favorable ASPECTS, and patient selection is likely to play a role in determining good outcome. Improved likelihood of good outcome in patients selected using imaging criteria was highlighted by an assessment of stroke therapy scoring grades performed by Marks et al,<sup>28</sup> in which better clinical outcomes were associated with TICI 2b–3 scores compared with TICI 0–2a and with TIMI 2 or 3 scores only when the patient had a target mismatch, suggesting that good outcome is dependent more on reperfusion than on recanalization. Furthermore, Daniere et al<sup>29</sup> found that despite higher ASPECTSs in the older age groups, they still had significantly poorer outcomes than the younger groups. The authors concluded that the elderly may benefit from thrombectomy when their core volume is small, and they suggested that an age-adjusted ASPECTS should be used to maximize the chance of good clinical outcome postintervention.

To our knowledge, our analysis is the first to use prospective core lab–reviewed data, including patients between 25 and 88 years of age. We have chosen to dichotomize the cohort across the median, reducing the mean age of our younger (59 years of age) and older (77 years of age) cohorts compared with some other series. However, we think that this limitation is somewhat countered by the robust nature of the data, and thus is still sufficient to illustrate the principle that age should not be the sole determinant of whether to treat and that if a patient qualifies for treatment, particularly in the older groups, attempts should be made to achieve TICI 2b–3 reperfusion because these patients are afforded the greatest benefit from successful reperfusion.

The results from the recently published Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) demonstrated the efficacy and safety of intra-arterial therapy for acute stroke; and in addition, in their subgroup analysis, the patients in the 80 years of age and older group showed a greater benefit with intervention than the younger than 80 years of age group.<sup>15</sup> Although this was an assessment of intervention overall rather than reperfusion alone, it further indicates that the elderly should not be denied intra-arterial stroke therapy on the basis of age alone. This finding is similar to those in studies of IV-tPA for AIS in which subgroup analyses have demonstrated that the elderly not only benefit from IV-tPA but may even benefit more than the younger population; therefore, patients presenting with AIS should not be excluded from receiving treatment on the basis of age alone.<sup>4,30</sup>

A limitation of this analysis and indeed from applying the results of the recently published trials to elderly patients is that for the most part, the proportion of patients older than 80 years of age was small, and it is conceivable that the benefit of reperfusion may have a ceiling effect. Now that there is proof of principle for mechanical thrombectomy and there is evidence suggesting that the older patients not only benefit but may benefit more significantly when successful reperfusion is achieved, further evaluation of endovascular therapy for AIS in the older population should be performed with a focus on revascularization. Given the aging population, particular attention should be paid to those older than 80 years of age either

in the form of well-documented registries or randomized controlled trials.

## CONCLUSIONS

Successful reperfusion is the strongest predictor of good outcome following mechanical thrombectomy, and the magnitude of benefit is highest in the patient population older than 70 years of age.

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