

**Original Paper**

# Stent Retriever-Based Thrombectomy in Octogenarians

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Medical Center, Jerusalem, Israel**Key Words**

Endovascular · Octogenarians · Reperfusion · Stroke · Thrombectomy

**Abstract**

**Background and Aims:** Stent retriever-based thrombectomy (SRT) may be beneficial in patients with large hemispheric stroke. Previous studies concluded that favorable outcomes are far less frequent after endovascular therapy in older patients but have not explored outcomes in the era of newer-generation stent retrievers. **Materials and Methods:** Consecutive patients with large hemispheric stroke treated with SRT were included. We compared neurological and functional outcomes between patients younger and older than 80. **Results:** We included 16 patients older than 80 (22.5%, mean age 84.1 ± 4.4, 56% females) and compared them to 55 patients that were younger than 80 (77.5%, mean age 63.1 ± 12.5, 51% females). Risk factor profile, admission neurological severity, stroke etiology and procedure-related variables including excellent target vessel recanalization did not differ between the groups. Favorable outcome at 90 days (modified Rankin score ≤2) was more common in younger patients (77 vs. 23%; p = 0.031). In contrast, mortality rates were higher in octogenarians (40 vs. 7%; p = 0.01). Logistic regression analysis adjusting for neurological severity and collateral state identified age over 80 (odds ratio, OR 0.15, 95% CI 0.03–0.75; p = 0.02) and reperfusion state (OR 7.4, 95% CI 1.1–49.9; p = 0.04) as significant modifiers of favorable outcome. Similarly, age over 80 was identified as a positive predictor of mortality (OR 8.1, 95% CI 1.8–36.7; p = 0.007). **Conclusions:** Octogenarians have higher chances of mortality and lower probability of achieving functional independence even after SRT. Nevertheless, because some elderly patients do achieve favorable outcomes, the cost-effectiveness of SRT in this population needs to be further studied.

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## Introduction

Large hemispheric ischemic stroke secondary to internal carotid or proximal middle cerebral artery occlusions carries a mortality rate of close to 80% if left untreated [1, 2]. Systemic thrombolysis is of limited benefit in these patients [3–6], but endovascular reperfusion therapy has recently proved effective in several prospective studies [7–12] that used rigorous selection criteria and mandated an independent premorbid state for inclusion. Most previous series evaluating this technique in large hemispheric strokes only included relatively younger patients with 80 being the usual upper age limit [13–16], and studies that did include older patients have shown that the rates of favorable outcome are considerably lower in patients older than 80, despite adequate vessel recanalization [17–19]. However, most of these studies used older techniques for reperfusion, while the advent of newer-generation stent retriever-based thrombectomy (SRT) allows for more rapid and complete target vessel recanalization and tissue reperfusion [20]. Furthermore, the life expectancy in most countries is constantly increasing and clinicians will likely be faced with many more patients presenting with large stroke who are older than 80. Therefore, we aimed to evaluate whether octogenarian patients also benefit from SRT if it would become widely available.

## Patients and Methods

We prospectively recruited consecutive patients presenting with large hemispheric stroke that underwent SRT over the span of 2 years from 2013 to 2015 into our stroke registry and the data was retrospectively analyzed. The institutional review board authorized anonymous inclusion of patients into the consecutive database without getting informed consent.

To be eligible for SRT, patients had to have an initial National Institutes of Health Stroke Scale (NIHSS) score >10 and to be previously independent [modified Rankin score (mRS) <2]. Furthermore, all included patients were treated within 8 h of stroke onset. The diagnosis of internal carotid or proximal middle cerebral artery occlusion was established according to clinical findings that included hemiparesis/hemiplegia, sensory symptoms and evidence for cortical involvement such as aphasia, neglect or hemianopsia in various combinations. The diagnosis of large vessel occlusion had to be proven on computed tomography (CT) angiography (CTA), magnetic resonance angiography or digital subtraction angiography in all patients. Exclusion criteria included evidence of large hemispheric infarction on the admission CT defined as hypodensity covering more than 1/3 of the middle cerebral artery territory, international normalized ratio >3 and existing disease with limited life expectancy (e.g. terminal cancer). Patients with small vessel disease were excluded, as were those presenting in deep coma and those with primary intracerebral or subarachnoid hemorrhage.

In this study, we compared patients that were younger than 80 at the time of presentation to those older than 80. Clinical and demographic characteristics accrued included cerebrovascular risk profile, concomitant medications, time from symptom onset to initiation of endovascular procedure and time from onset to reperfusion. Infarct etiology was classified according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria as cardioembolic, large artery atherothrombotic, other classified (e.g. dissection) or unclassified [21].

All patients were admitted to the intensive care unit for at least 24 h post procedure. Neurological deficits were determined with the NIHSS [22], and functional deficits before admission and at 90 days post infarct were evaluated with the mRS [23]. Favorable outcome was defined as an mRS ≤2.

Radiological parameters were evaluated on entry CT/magnetic resonance imaging and on the diagnostic and therapeutic angiography and follow-up CT/CTA. Flow was classified with the thrombolysis in cerebral infarction (TICI) scale and TICI 2b–3 was considered as favorable recanalization and reperfusion [24]. Collateral flow was classified with the ASITN/SIR Collateral Flow Grading System on pretreatment angiography [24]. The score was dichotomized into poor (grades 0–2; 0 = no collaterals, 1 = slow collaterals to the periphery of the ischemic area, 2 = rapid collaterals to the periphery of ischemic site with persistence of some of the defect and to only a portion of the ischemic territory), and favorable (grades 3–4; 3 = collaterals with slow but complete filling of the ischemic area by the late venous phase, 4 = complete and rapid filling in the entire ischemic territory by retrograde perfusion).

**Table 1.** Univariate analysis of data according to age

Variable/group	Younger than 80 (n = 55)	Older than 80 (n = 16)	p
Age, years	63.1±12.5	84.3±4.1	<0.0001
Gender, male	27 (49)	7 (44)	0.707
Occlusion site			0.655
Proximal ICA	4 (7)	1 (6)	
Proximal M1 MCA	40 (81)	13 (73)	
Distal M1 MCA	6 (11)	2 (12)	
Tandem ICA + MCA	5 (9)	0	
Involved hemisphere, left	30 (55)	6 (38)	0.230
Hypertension	38 (69)	14 (87)	0.143
Ischemic heart disease	29 (53)	8 (50)	0.848
Atrial fibrillation	28 (56)	9 (57)	0.707
Diabetes mellitus	19 (35)	4 (25)	0.473
Hyperlipidemia	27 (49)	7 (44)	0.707
Smoking	14 (26)	3 (19)	0.580
Previous stroke	11 (20)	5 (31)	0.343
Bridging tPA given	21 (38)	7 (44)	0.688
TOAST classification			0.836
Cardioembolic	38 (69)	12 (75)	
Large vessel	9 (16)	3 (19)	
Other	1 (2)	0	
Unknown	7 (13)	1 (6)	
Admission NIHSS	18.2±5.5	18.4±7.3	0.927
Discharge NIHSS	7.9±8.1	12.0±11.2	0.138
Delta NIHSS	10.5±6.0	7.1±7.9	0.084
90-day mRS 0–2	27 (57) <sup>a</sup>	3 (21) <sup>b</sup>	
Mortality	4 (7)	6 (40)	0.001

Figures are means ± SD or n (%). ICA = Internal carotid artery; MCA = middle cerebral artery.

<sup>a</sup>Total number = 47. <sup>b</sup>Total number = 14.

Our standard treatment protocol in patients with large vessel occlusions included in the study suggests going directly to SRT if the treatment is immediately available and to use bridging with tPA if the SRT is not immediately available. All patients underwent SRT with the solitaire device (Medtronic USA). Failure to achieve recanalization led to use of further devices such as the pREset® LITE Thrombectomy Device (Phenox GmbH) or thrombus aspiration. Treatment complications including post-procedure hemorrhage and clinical deterioration without hemorrhage were also documented. Symptomatic hemorrhage was classified according to published criteria [12].

Statistical evaluations were performed using SPSS PASW 22 (IBM). For univariate analysis patients were compared using Student's t test for continuous variables or  $\chi^2$  test for categorical variables. Bivariate logistic regressions models were then used to test the effects of age over 80 on favorable outcome and survival. The models incorporated NIHSS scores, collateral grading and reperfusion status.

## Results

Seventy-one consecutive patients fulfilling entry criteria were recruited into this preliminary study. Of those, 16 were older than 80 and represented the study group (median age 82.5, 28% men). They were compared to the remainder of the patients (55) that were younger than 80 at the time of presentation (median age 62.5, 59% men). The baseline clinical and radiological characteristics are presented in table 1. All patients were independent prior to

**Table 2.** Comparison of procedure- and post-procedure-associated variables

Variable/group	Younger than 80 (n = 55)	Older than 80 (n = 16)	p
Onset to SRT, min	232.0±110.9	239.5±129.9	0.828
Onset to recanalization, min	276.7±114.6	279.5±135.0	0.938
Favorable collaterals (grade 3–4)	16 (31)	2 (13)	0.137
Post-procedure TICI			0.836
0–2a	7 (13)	2 (12)	
2b–3	47 (87)	14 (88)	
Intracerebral hemorrhage			
All	7 (13)	6 (38)	0.029
Symptomatic	1 (2)	2 (13)	0.132

Figures are means ± SD or n (%).

the procedure (mRS ≤2). Octogenarians did not differ in demographics and baseline criteria from younger patients. Of note, procedure-related variables including type and site of vessel occlusion, onset-to-treatment time and time to vessel recanalization, number and types of procedural modalities used and lesion length did not differ between the groups (table 2). Adequate target vessel recanalization (TICI 2b–3) also did not differ between the groups (table 2)

Favorable outcome at 90 days (mRS ≤2) was more common in younger patients (77 vs. 23%; p = 0.031). In contrast, mortality rates were higher in octogenarians (40 vs. 7%; p = 0.01). Fatalities were due to infections or neurological deteriorations in all cases and did not involve withdrawal of life support in any of our patients.

Thirteen of our patients (18%) had hemorrhagic transformation of their infarcts, but only 3 of these (4%) were classified as symptomatic since they had confluent parenchymal hematoma that resulted in neurological worsening. Of these, 2 were in the older than 80 group and 1 in the younger group.

Logistic regression analysis adjusting for neurological severity and collateral state identified age over 80 (odds ratio, OR 0.15, 95% CI 0.03–0.75; p = 0.02) and reperfusion state (OR 7.4, 95% CI 1.1–49.9; p = 0.04) as significant modifiers of favorable outcome. Similarly, age over 80 was identified as a positive predictor of mortality (OR 8.1, 95% CI 1.8–36.7; p = 0.007).

## Discussion

The current preliminary study further expands the existing knowledge regarding the efficacy of SRT in older patients with large and often deadly strokes. This is particularly important as the population in the world grows substantially older and many more octogenarians will likely present with large hemispheric strokes in the upcoming years, leading to the creation of a large burden on intensive care services. Recently, published studies provided further evidence supporting the use of SRT in patients with large proximal vessel occlusions but largely excluded older patients. Nevertheless, prior studies have shown that systemic thrombolysis is generally effective in patients older than 80 despite higher mortality rates [25], and the use of SRT that allows for rapid and more complete recanalization raised hopes for better outcomes in older patients with large strokes as well. However, favorable outcomes

were observed less often and mortality rates were significantly increased in our octogenarian patients despite similar rates of excellent recanalization. Our results are in agreement with those of previous studies [17–19, 26, 27], including some that used stentriever [28], but do show that it is still possible to achieve favorable outcomes even in the very old. Similar results were also seen in a recently published meta-analysis of individual patient data from five recent trials that showed that the odds ratio of favorable outcome were higher in patients older than 80 treated with thrombectomy compared with those treated with tPA [29]. The reason for the discrepancy between our results and this analysis remain unclear but may suggest a more rigorous patient selection process in the trials included in the meta-analysis. Furthermore, only 198 of 1,278 patients in this analysis were older than 80, and whether stroke severity was lower in these patients compared to younger patients is not known. Interestingly, a recent study found that in order for older patients to have favorable outcome, the initial core needs to be much smaller [30]. Furthermore, age was found to be an important modulator of futile recanalization and poor outcome after adjusting for recanalization state in another study [31], suggesting that the impact of age on outcome may be not solely depend on vessel recanalization.

Importantly, in the current study, octogenarians presented with similar stroke severity, etiology, and similar onset-to-treatment and onset-to-recanalization time frames compared to younger patients. Admission to intensive care was a prerequisite of this study and therefore, admission settings are also not responsible for the discrepant results between younger patients and octogenarians. The low symptomatic intracerebral hemorrhage rates obtained in our group of patients is also reassuring that such patients may still be good candidates for therapy and that the rate of symptomatic intracerebral hemorrhage is not responsible for the increased frequency of poor outcome observed in elderly patients. Older patients may have poor outcome more frequently due to higher frequencies of concomitant disease and poor recuperation and rehabilitation capabilities compared to younger patients.

Importantly, several of our elderly patients did reach mRS 2 and several others reached mRS 3, which may still be looked upon as a reasonable outcome in patients with very large stroke since these patients are still able to ambulate. These results do show an improvement over those obtained with prior-generation endovascular techniques attesting to the superiority of SRT. Furthermore, chronological age does not always equal biological age and therefore, some octogenarians will still likely do well with treatment. Hence, we certainly cannot recommend withholding therapy in octogenarians despite the high costs and the low chances for good functional outcome. However, our results and those of others [17–19, 26, 27] suggest that prognosis should be more guarded in older patients.

Our study is limited by a relatively small number of included patients and therefore, we cannot exclude the possibility of missing statistical significance due to low power. Nevertheless, our results can be viewed as hypothesis generating, and larger randomized studies exploring outcome after SRT in younger versus older patients and the cost-effectiveness of this strategy should be carried out in the future. In light of our findings as well as those of others, it will be interesting to explore in the future whether direct SRT may be superior to bridging with tPA in patients with large artery occlusions.

In conclusion, SRT may be beneficial for most patients with large hemispheric strokes and may also improve outcome in older patients. Variables associated with increased chances of survival and good outcome including successful recanalization can only be determined during angiography. Therefore, our results suggest that efforts to recanalize the occluded artery may be considered in all patients with distal internal carotid or proximal middle artery occlusions but that prognostication should be guarded in the very old patients.

## Acknowledgements

This work was supported by the Peritz and Chantal Scheinberg Cerebrovascular Research Fund and by the Sol Irwin Juni Trust Fund.

## Disclosure Statement

All authors hereby declare they had no conflicts of interest.

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