**ORIGINAL ARTICLE** 



# Stentriever Thrombectomy Failure: A Challenge in Stroke Management

Claudio Baracchini<sup>1</sup>, Filippo Farina<sup>1</sup>, Matteo Soso<sup>1</sup>, Federica Viaro<sup>1</sup>, Silvia Favaretto<sup>1</sup>, Anna Palmieri<sup>1</sup>, Caterina Kulyk<sup>1</sup>, Enzo Ballotta<sup>2</sup>, Lorena Nico<sup>3</sup>, Giacomo Cester<sup>3</sup>, Francesco Causin<sup>3</sup>

BACKGROUND AND OBJECTIVE: Stentriever thrombectomy failure in patients with acute ischemic stroke caused by anterior circulation large artery occlusion is not a rare event. The purpose of this study was to investigate whether other procedures (tirofiban, permanent stenting) are able to recanalize the occluded vessel and determine a better outcome without increasing mortality and intracranial hemorrhage rates.

■ METHODS: Among 513 patients consecutively admitted with anterior circulation stroke, 109 underwent stentriever thrombectomy. Modified Thrombolysis in Cerebral Ischemia (mTICI) 2b-3 recanalization was achieved in 60 patients (55.0%, group 1). Only 3 of 19 patients (group 2) obtained additional recanalization with intra-arterial infusion of tirofiban. The remaining 46 either underwent permanent stenting (n = 23, group 3) or were left nonrecanalized (n = 23, group 4). The rate of mTICI 2b-3 and clinical outcomes were analyzed in the different groups.

RESULTS: A successful recanalization (mTICl 2b-3) was achieved in 17 patients of group 3 (73.9%). A significantly better outcome was observed in group 3 (modified Rankin Scale [mRS] score, 0–2) than in group 4 at 3 months (56.5% vs. 17.4%). Symptomatic intracranial hemorrhage rates were not different between group 3 and group 4 (4.3% vs. 4.3%), whereas there was a significantly higher mortality in group 4 than in group 3 (39.1% vs. 4.3%). On multivariate analysis, permanent stenting was the only factor independently associated with favorable outcome and mortality. CONCLUSIONS: Permanent stenting might be a feasible solution in patients with acute large artery occlusion after stentriever thrombectomy failure.

# **INTRODUCTION**

ndovascular mechanical thrombectomy combined with intravenous thrombolysis has recently been shown to be superior to thrombolysis alone in the treatment of patients with acute ischemic stroke with large artery occlusion (LAO) of the anterior circulation.<sup>1</sup> In particular, stentriever thrombectomy has been recommended as a first-line method for intra-arterial recanalization, although other thrombectomy or aspiration devices approved by local health authorities may be used at the discretion of the neurointerventionist if rapid, complete, and safe revascularization of the target vessel can be achieved.<sup>2</sup> Stentriever thrombectomy does not guarantee a successful recanalization (modified Thrombolysis in Cerebral Ischemia [mTICI], 2b-3) in all patients as already reported.3 In these cases, additional treatment with glycoprotein IIb/IIIa antagonists such as tirofiban and/or permanent stenting might represent a possible solution to achieve a better prognosis, because recanalization is known to be a strong predictor of good outcome in cerebral ischemia secondary to LAO.<sup>4</sup> Glycoprotein IIb/IIIa inhibitors have been associated with increased risk of fatal intracerebral hemorrhage (ICH) and poor outcome,<sup>5</sup> but not in all studies,<sup>6</sup> and it has been shown that mechanical thrombectomy with stentrievers does not cause relevant endothelial damage.7 Permanent stenting has been suggested as another primary approach or as

# Key words

- Mechanical thrombectomy
- Stent
- Stroke
- Tirofiban

#### Abbreviations and Acronyms

CT: Computed tomography CTA: Cerebral tomography angiography CTp: Perfusion computed tomography DSA: Digital subtraction angiography ICA: Internal cerebral artery ICH: Intracerebral hemorrhage LAO: Large artery occlusion MRI: Magnetic resonance imaging mRS: modified Rankin Scale mTICI: Modified Thrombolysis in Cerebral Ischemia NIHSS: National Institutes of Health Stroke Scale rt-PA: Recombinant tissue plasminogen activator

From the <sup>1</sup>Department of Neuroscience, <sup>2</sup>Vascular Study Group, Department of Surgical, Oncological and Gastroenterological Sciences, and <sup>3</sup>Neuroradiology Unit, University of Padua School of Medicine, Padua, Italy

To whom correspondence should be addressed: Claudio Baracchini, M.D., F.E.S.O. [E-mail: claudiobaracchini@gmail.com]

Citation: World Neurosurg. (2017) 103:57-64. http://dx.doi.org/10.1016/j.wneu.2017.03.070

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/\$ - see front matter © 2017 Elsevier Inc. All rights reserved.

a rescue tool for recanalization of acute intracranial LAO,<sup>8-ro</sup> even though safety is an important issue here as well, because these procedures might increase the rates of symptomatic ICH and death. For this reason, we decided to conduct an observational study in patients with acute stroke caused by an anterior circulation LAO with the aim of investigating whether tirofiban and/or permanent stenting after mechanical thrombectomy failure are able to recanalize the occluded vessel and determine a better outcome without increasing mortality and ICH rates.

### **METHODS**

#### **General Study Protocol**

Patients consecutively admitted to the Stroke Unit of the University Hospital of Padua (Italy) from January 2014 to July 2016 for their first-ever acute ischemic stroke caused by anterior circulation LAO (defined as occlusion of the intracranial internal carotid artery [ICA] and/or middle cerebral artery [MI segment and/or proximal M2 segment]) were prospectively assessed according to standardized diagnostic and therapeutic procedures as recommended by the European Stroke Organization,<sup>11</sup> including treatment with intravenous recombinant tissue plasminogen activator (rt-PA) and/or mechanical thrombectomy in eligible patients. All patients details were entered in a computerized database, recording their demographic characteristics, routine blood tests, and vascular risk factors such as arterial hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure  $\geq 90$  mm Hg or current/past use of antihypertensive medication), diabetes mellitus [fasting serum glucose level ≥7.0 mmol/L (≥126mg/dL), nonfasting serum glucose level ≥11.1 mmol/L (≥200mg/dL), glycated hemoglobin (HbA<sub>1C</sub>) level  $\geq$ 48 mmol/mol or the use of glucose-lowering drugs], hypercholesterolemia [total cholesterol level >6.2 mmol/L (>240 mg/dL) or use of lipid-lowering drugs], smoking (current or stopped within 5 years), cardiac disease [history of angina pectoris, myocardial infarction, coronary treatment (angioplasty/stenting, or bypass surgery), any cardiac arrhythmia such as atrial fibrillation], peripheral arterial disease, or previous transient ischemic attack. Clinical and functional status was assessed with the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS), respectively, both on admission and at discharge. Territorial distribution was evaluated in all patients with magnetic resonance imaging (MRI) or repeat computed tomography (CT) and with the Oxfordshire Community Stroke Project classification system.<sup>12</sup> In all patients, the extracranial and intracranial vessel status was assessed by noninvasive imaging and specifically the diagnosis of anterior circulation LAO was made by transcranial color-coded Doppler sonography<sup>13</sup> and confirmed by CT angiography (CTA) or magnetic resonance angiography if CTA was contraindicated and also by digital subtraction angiography (DSA) for patients undergoing endovascular treatment. Further diagnostic workup included standard blood tests, routine electrocardiography, transthoracic echocardiography, and 24-hour electrocardiography monitoring, plus coagulation studies, and transesophageal echocardiography, if appropriate. Patients with anterior circulation LAO as a result of intracranial dissection were excluded from this study.

## **Interventional Protocol**

Endovascular treatment was decided on the basis of a direct cerebral CT scan (ASPECT [Alberta Stroke Program Early CT] score >5), CTA (anterior circulation LAO), and clinical characteristics (NIHSS score >6 or evolution of stroke symptoms) and was performed within 6 hours of symptom onset, under conscious sedation or general anesthesia depending on clinical neurologic conditions by 2 experienced neuroradiologists (F.C. and G.C.), who shared the same interventional protocol.

The occluded target vessel was the first vessel to be studied with DSA when perfusion CT (CTp) and CTA guaranteed an adequate information on the collateral circulation; otherwise, contralateral carotid and vertebral arteries were studied before reaching the occluded site.

Until 2015, an 8-F balloon guiding catheter (Merci 8F, Penumbra, Alameda, California, USA) or a peripheral guiding sheath (Destination 6F, Terumo, Elkton Maryland, USA) was positioned in the common carotid artery or, if possible, in the cervical ICA. The arterial occlusion was crossed with a 0.53 mm microcatheter (Prowler sel 2.3 F, Codman J&J, Raynham, Massachusetts, USA) and a stentriever thrombectomy was performed; this procedure was attempted for a maximum of 3 times, to minimize the time to recanalization (each attempt lasts about 10–15 minutes) and to reduce the risk of endothelial damage with possible hemorrhagic complications.

Since 2015, an 8-F guiding catheter (Destination 6F Terumo, Elkton, Maryland, USA or Neuron Max Penumbra 2,24 mm, Alameda, California, USA) has been positioned in the cervical ICA and a distal aspiration catheter (5Max Penumbra, Alameda, California, USA; Catalyst 6F Strycker, Freemont, California, USA; Sofia Plus Microvention 2,1 mm, Tustin, California, USA) was advanced to the occlusion site. A distal aspiration was then attempted; in case of failure, a stentriever thrombectomy with distal aspiration was performed.

In all cases of stentriever thrombectomy failure, we evaluated the opportunity to deploy a permanent stent in the occluded segment. The main indications for permanent stenting were: 1) Effectiveness of stentriever bypass when the device was in place but reocclusion or severe stenosis occurred immediately after its retrieval. In such cases, perfusion status is partially or completely recovered immediately after deployment but stops when the device is withdrawn. This situation happened in cases of an underlying stenosis as a result of atherosclerotic plaque, or clots that extended to the M2 segment and could not be completely removed, or in cases of a hard clot that did not penetrate the retriever struts. Extent and burden of the clot can be assessed by CTA and superselective angiography, and the quality of the clot or mural plaque is evaluated on the basis of the degree of hardness detected by a microguidewire and microcatheter, while passing through the thrombus, and observing opened struts after 3-5 minutes from deployment. 2) Presence of a calcified plaque or a distal occlusion that contraindicated multiple retrieve maneuvers. The detection of a calcified plaque visible on CT and CTA or the presence of a clot in an M<sub>2</sub> segment contraindicates thrombectomy by means of stentriever, which might cause endothelial damage, dissection, or perforation and retriever encasement. In such cases, the delivery of a stent might be effective in restoring distal perfusion. Distal aspiration if possible



could be also attempted. 3) ASPECT score  $\geq 6$  with a good mismatch on CTp. Because we believe that stent delivery in an acute setting is a rescue strategy to restore an adequate perfusion, we based our decision on ischemic core extension and site, to achieve the best clinical result and a lower hemorrhagic risk. In all cases, the implanted stent was a Solitaire AB stent (ev3, Irvine California, USA), because it is often used as a first-line or second-line device and therefore in several cases is already on target; this means reducing costs and time for procedure. Prestenting or poststenting balloon angioplasty was performed only in case of

an underlying carotid siphon, MI-segment atherosclerotic stenosis. During the procedure, if not yet administered, an intraarterial bolus (25  $\mu$ g/kg in 3 minutes) of glycoprotein IIb/IIIa (tirofiban) was injected, followed by 12 hours intravenous infusion (0.1  $\mu$ g/kg) before switching to double antiplatelet therapy, which was maintained for 3 months.

A CT scan was performed on a rotational angiographer XperCT (Philips, The Netherlands) at the end of the procedure and a control CT scan was repeated at 4-6 hours to exclude hemorrhagic complications. Twenty-four-hour control DSA was

MANAGEMENT OF THROMBECTOMY FAILURE

Table 1. Demographic and Clinical Characteristics of the Study Population at Admission							
	Total (n = 109)	Group 1 (n = 60)	Group 2 (n $=$ 3)	Group 3 (n = 23)	Group 4 (n = 23)		
Mean age, years ( $\pm$ standard deviation)	65 (±15.3)	64 (±15.4)	62 (±21)	70 (±16.9)	74 (±8.3)		
Male	59 (54.1)	31 (51.7)	0 (0)	15 (65.2)	12 (52.2)		
Hypertension	79 (72.5)	43 (71.2)	2 (66.6)	13 (56.5)	21 (91.3)*		
Diabetes mellitus	17 (15.5)	10 (16.7)	1 (33.3)	1 (4.34)	5 (21.7)		
Hypercholesterolemia	36 (15.6)	16 (26.7)	1 (33.3)	10 (43.4)	9 (39.1)		
Smoking	30 (27.5)	17 (28.3)	1 (33.3)	5 (21.7)	7 (30.4)		
Coronary syndromes	20 (18.3)	8 (13.3)	0 (0)	5 (21.7)	7 (30.4)		
Atrial fibrillation	32 (29.3)	16 (26.7)	1 (33.3)	7 (30.4)	8 (34.8)		
Antiplatelet therapy at admission	51 (46.8)	29 (48.3)	1 (33.3)	9 (39.1)	12 (52.2)		
Anticoagulant therapy at admission	12 (11.0)	6 (10.0)	1 (33.3)	2 (8.7)	3 (13.0)		
Antihypertensive therapy at admission	70 (64.2)	40 (66.7)	2 (66.6)	9 (39.1)	19 (82.6)*		
Lipid-lowering therapy at admission	27 (24.8)	15 (25.0)	1 (33.3)	3 (13.0)	8 (34.8)		
Median National Institutes of Health Stroke Scale at admission (range)	16 (2—26)	16 (2—26)	15 (12—20)	16 (4—26)	18 (5—20)		
Median modified Rankin Scale score at admission (range)	0 (0—4)	0 (0—4)	0 (0—2)	0 (0—2)	0 (0—3)		

Values are number (%) except where indicated otherwise. Group 1 is defined as patients who underwent successful reperfusion with mechanical thrombectomy. Group 2 is defined as patients who underwent successful reperfusion with infusion of tirofiban as rescue treatment after failure of mechanical thrombectomy. Group 3 is defined as patients who failed mechanical thrombectomy and underwent intracranial stenting procedure. Group 4 is defined as patients who failed mechanical thrombectomy and did not undergo intracranial stenting procedure. \*P value < 0.05 between groups 3 and 4.

performed to verify stent patency and distal recanalization. Successful recanalization was defined when mTICI 2b-3 recanalization was persistent on at least a 10-minute delayed angiogram.

#### **Clinical and Neuroradiologic Follow-Up**

All patients underwent 24-hour brain CT, and brain MRI was performed just before hospital discharge. In case of a neurologic deterioration (an increase in NIHSS score  $\geq$ 4), immediate CT or MRI was obtained to check for ICH.<sup>14</sup>

Clinical and functional status was assessed with the NIHSS and mRS, respectively, at discharge and at 1, 3, 6, and 12 months. Vessel patency and stent patency were evaluated by transcranial color-coded Doppler at discharge, and at 1, 3, 6, and 12 months; in case of restenosis, the diagnosis was confirmed by CTA/magnetic resonance angiography.

#### **Statistical Analyses**

The statistical analysis was performed with the SSPS statistical software (SPSS version 13.0 for Windows [SPSS Inc., Chicago, Illinois, USA]). Patients' demographic and clinical characteristics are given as means  $\pm$  standard deviations, as medians and ranges, or as percentages. Mean values were compared with Student t test or analysis of variance test as appropriate. Frequencies and categorical data were compared with  $\chi^2$  or Fisher exact tests. Significance was assumed at P < 0.05. Cox proportional hazard analysis

was used to see which statistically significant factors at univariate analysis could influence outcomes, calculating the odds ratio with 95% confidence intervals.

#### **Standard Protocol Approval and Patient Consent**

The study was approved by our local ethics committee and informed consent was obtained for all patients.

#### RESULTS

During the study period, a total of 513 patients were hospitalized for their first-ever acute anterior circulation ischemic stroke, comprising 315 men (61.4%) and 198 women (38.6%), with a mean age of 71.5  $\pm$  11.4 years. Among those with an anterior circulation LAO, 109 underwent stentriever thrombectomy either alone or in combination with intravenous thrombolysis, and a successful recanalization was achieved in 60 patients (55.0%). An intraarterial infusion of tirofiban was administered after mechanical thrombectomy failure in 19 patients and it determined a successful vessel recanalization in only 3 cases (2.8%). Overall, 46 patients (42.2%) remained nonrecanalized, 6 of whom had an underlying intracranial (MI-segment) atherosclerotic stenosis: 23 of these underwent permanent stenting, including 3 with intracranial atherosclerotic stenosis (group 3), whereas 23 were left nonrecanalized (group 4). A successful recanalization was achieved in 17/23 patients (73.9%) of group 3 and only a partial recanalization in the remaining 6 (Figure 1). Therefore, of the original patients

# **Table 2.** Demographic and Clinical Characteristics of Stented Versus Nonstented Patients and Their Association with OutcomeMeasures (modified Rankin Scale Score <3 at 3 Months and Mortality)</td>

	Group 3 (n = 23)	Group 4 (n = 23)	P1 Value	P2 Value Odds Ratio (95% Confidence Interval)	P3 Value Odds Ratio (95% Confidence Interval)	
Mean age, years ( $\pm$ standard deviation)	70 (±16.9)	74 (±8.3)	NS	-	_	
Male	15 (65.2)	12 (52.2)	NS	—	—	
Hypertension	13 (56.5)	21 (91.3)	<0.01	1.08 (0.91-1.34); NS	1.22 (0.89—1.60); NS	
Diabetes mellitus	1 (4.34)	5 (21.7)	NS	—	—	
Hypercholesterolemia	10 (43.4)	9 (39.1)	NS	—	—	
Smoking	5 (21.7)	7 (30.4)	NS	—	—	
Coronary syndromes	5 (21.7)	7 (30.4)	NS	—	—	
Atrial fibrillation	7 (30.4)	8 (34.8)	NS	—	—	
Antiplatelet therapy at admission	9 (39.1)	12 (52.2)	NS	—	—	
Anticoagulant therapy at admission	2 (8.7)	3 (13.0)	NS	—	—	
Antihypertensive therapy at admission	9 (39.1)	19 (82.6)	< 0.01	1.28 (0.82-1.55); NS	1.05 (0.78—1.80); NS	
Lipid-lowering therapy at admission	3 (13.0)	8 (34.8)	NS	—	—	
Median National Institutes of Health Stroke Scale score at admission (range)	16 (4—26)	18 (5—20)	NS	—	—	
Median modified Rankin Scale score at admission (range)	0 (0—2)	0 (0—3)	NS	—	—	
Location						
ICA	2	2	NS	—	—	
MCA	18	19	NS			
ICA + MCA	3	2	NS			
Systemic thrombolysis	4 (17.4)	10 (43.5)	NS	—	—	
Onset-to-puncture time (minutes)	$206.1\pm56.4$	196.1 ± 48.1	NS	—	<u> </u>	

Values are number (%) except where indicated otherwise. Group 3 is defined as patients who failed mechanical thrombectomy and underwent intracranial stenting procedure. Group 4 is defined as patients who failed mechanical thrombectomy and did not undergo intracranial stenting procedure. *P* values < 0.05 are reported, otherwise they are defined as NS (not significant). P1 is the result of a univariate analysis, and P2 and P3 are the results of a multivariate analysis on the association between demographic and clinical characteristics of the study groups with modified Rankin Scale score <3 at 3 months and mortality, respectively.

ICA, internal carotid artery; MCA, middle cerebral artery.

with acute anterior LAO, 80 (73.4%) obtained an mTICI 2b-3 recanalization after applying different recanalization procedures. Only 1 of these patients had a vessel reocclusion at the 24-hour angiogram; he had been successfully treated with thrombectomy and tirofiban but he died as a result of cerebral herniation.

Demographic and clinical characteristics of the study population are reported in Table 1.

Patients in group 4 were more frequently hypertensive than those in group 3; these patients consequently received more antihypertensive treatment with respect to other patients. No differences in initial NIHSS score, location of anterior circulation LAO, administration of rt-PA and onset-to-puncture time between groups were observed between groups 3 and 4 (Table 2). With regard to prognosis in thrombectomy failures, a better outcome (mRS score, o-2) was more frequently observed in group 3 than in group 4 at 3 months (56.5% vs. 17.4%; P < 0.05) (Figure 2). Symptomatic ICH rates were not different between group 3 and group 4 (4.3% vs. 4.3%), and there was a significantly higher mortality in group 4 compared with group 3 (39.1% vs. 4.3%); P < 0.05) (Tables 3 and 4).

No difference was found in terms of outcome between male and female patients (Table 5).

Arterial hypertension does not seem to influence clinical outcome, as shown by a multivariate analysis (Table 2). When thrombectomy fails, permanent stenting is the only factor independently associated with favorable outcome and mortality.



# DISCUSSION

The main result of our study is that in patients with acute stroke with anterior circulation LAO refractory to stentriever thrombectomy, permanent stenting determined mTICI 2b-3 recanalization in 73.9% of cases with a better clinical outcome and a reduced mortality compared with the nonstent group, without an increase in symptomatic ICH.

Many (45%) of the patients in this study with acute ischemic stroke caused by anterior circulation LAO did not recanalize after stentriever thrombectomy either alone or combined with rt-PA, confirming previous reports.<sup>3</sup>

These results are comparable with the primary rate of recanalization achieved in large randomized trials with similar inclusion criteria such as MR CLEAN (a multicenter randomized

Table 3. Clinical Outcome and Follow-Up							
	Total (n = 109), n (%)	Group 1 (n = 60), n (%)	Group 2 (n = 3), n (%)	Group 3 (n = 23), n (%)	Group 4 (n = 23), n (%)		
Reperfusion rate, patients with modified Thrombolysis In Cerebral Ischemia grade 2b or 3	80 (73.4)	60 (100)	3 (100)	17 (73.9)	0 (0)		
Death	17 (15.6)	6 (10)	1 (33.3)	1 (4.3)	9 (39.1)*†		
Symptomatic hemorrhages	5 (4.6)	3 (5)	0 (0)	1 (4.3)	1 (4.3)		
Patients with modified Rankin Scale score $<3$ at 3 months	53 (48.6)	34 (56.7)	2 (66.6)	13 (56.5)	4 (17.4)*†		
Stroke recurrence	5 (4.6)	2 (3.3)	0 (0)	1 (4.3)	2 (8.7)		

Group 1 is defined as patients who underwent successful reperfusion with mechanical thrombectomy. Group 2 is defined as patients who underwent successful reperfusion with infusion of tirofiban as rescue treatment after failure of mechanical thrombectomy. Group 3 is defined as patients who failed mechanical thrombectomy and underwent intracranial stenting procedure. Group 4 is defined as patients who failed mechanical thrombectomy and did not undergo intracranial stenting procedure.

\**P* value < 0.05 between group 3 and 4.

 $\dagger P$  value < 0.05 between group 1 and 4.

Table 4. Modified Thrombolysis in Cerebral Ischemia Scores   After Intervention in Stenting Group and Nonstenting Group					
Modified Thrombolysis in Cerebral Ischemia Grade	Stenting Group (n = 23), n (%)	Nonstenting Group $(n = 23), n (\%)$			
0	0 (0)	11 (47.8)			
1	1 (4.3)	7 (30.4)			
2A	5 (21.7)	5 (21.7)			
2B	12 (52.2)	0 (0)			
3	5 (21.7)	0 (0)			

clinical trial of endovascular treatment for acute ischemic stroke in The Netherlands)<sup>15</sup> (58.7%), whereas it is lower than in other trials such as SWIFT PRIME (Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment)<sup>16</sup> and EXTEND-IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial),<sup>17</sup> which have reached complete recanalization in  $8_3\%-8_9\%$  of cases. However, in the latter trials, those patients who could not undergo intravenous thrombolysis or had worse radiologic findings on CTp were excluded. Therefore, our results seem to better represent the real clinical practice of a stroke center.

The management of stentriever-failed patients with acute anterior circulation LAO is still unclear. Usually, these patients remain nonrecanalized; their outcome is based on their collaterals and the prognosis is poor in most cases. Additional modalities might be used to achieve recanalization in these patients: intraarterial infusion of rt-PA, intra-arterial infusion of glycoprotein IIb/IIIa inhibitor, or permanent stenting.

Glycoprotein IIb/IIIa inhibitors such as tirofiban are often used in endovascular treatment to prevent thromboembolic complications and early reocclusion because of endothelial damage. According to our study, tirofiban does not seem to be an effective solution because only a small percentage of cases (2.8%) obtained successful recanalization with intra-arterial infusion of tirofiban. Similar to other studies,<sup>6</sup> we did not observe a significant increase of fatal and symptomatic ICH; however, a reocclusion occurred in 1 of the 3 recanalized patients with subsequent cerebral herniation and death.

Before the advent of stentriever thrombectomy, several studies<sup>18-22</sup> assessed efficacy and safety of permanent stenting for recanalization of acute stroke, with some promising results. These studies led to the present study and the application of permanent stenting in a group of selected patients who failed mechanical thrombectomy and with otherwise poor prognosis. One major concern of permanent stenting is that it requires antiplatelet medication during or immediately after the treatment in the acute stage of a stroke and this might increase the risk of symptomatic ICH. In our study, permanent stenting achieved a successful (mTICI 2b-3) recanalization in 73.9% of patients and at least a partial recanalization in the remaining patients. The stenting group had a significantly better outcome than did the control nonstenting group, as shown by a lower disability (mRS score, <3; 56.5% vs. 17.4%; P < 0.05) and mortality (4.3% vs. 39.1; P < 0.05) at 3 months, with the same ICH rate (4.3%). A recent retrospective study<sup>23</sup> seems to confirm our results on the safety of permanent stenting after stentriever failure, despite dual antiplatelet therapy required in the postintervention period. Both studies show that the achievement of a successful recanalization has a significant impact on functional outcome, but only our study showed reduced mortality.

With regard to gender, despite some reports highlighting a worse outcome among female patients with stroke,<sup>24</sup> we have not observed gender differences for safety or for efficacy of mechanical thrombectomy and permanent stenting.

The positive effect of a successful recanalization obtained by permanent stenting was confirmed in patients of all ages, including the elderly; no significant difference of mortality and outcome were observed when stenting and nonstenting patients were stratified by age. These results are consistent with those observed in other studies on mechanical thrombectomy. In the MR CLEAN study,<sup>15</sup> 16% of patients were older than 80 years and obtained a significant improvement at 3 months (odds ratio, 3.24; 95% confidence interval, 1.21–8.62), comparable with that of patients of other age classes. Accordingly, stenting after stentriever thrombectomy failure should be considered an option even in older patients.

This study has some limitations because it was conducted in a single center and the sample size is small, yet it has the advantage of a consolidated diagnostic and interventional protocol performed in a large university hospital. These limitations do

Table 5. Comparison Between Male and Female Patients								
	Male (n = 58), n (%)	Female (n = 51), n (%)	Male Stent (n = 15), n (%)	Female Stent (n = 8), n (%)	Male Nonstent (n = 12), n (%)	Female Nonstent $(n = 11), n (\%)$	<i>P</i> Value	
Modified Thrombolysis in Cerebral Ischemia 2B or 3	42 (72.4)	38 (74.5)	11 (73.3)	6 (75.0)	0 (0)	0 (0)	NS	
Modified Rankin Scale score 3 months <3	25 (43.1)	28 (54.9)	8 (53.3)	5 (62.5)	1 (8.3)	3 (27.3)	NS	
Death	8 (13.8)	9 (17.6)	1 (6.7)	0 (0)	4 (33.3)	5 (45.5)	NS	
Stroke recurrence	4 (6.9)	1 (2.0)	0 (0)	1 (12.5)	2 (16.7)	0 (0)	NS	
NS, not significant.								

warrant a collaborative study among stroke centers with a larger sample size.

#### **CONCLUSIONS**

According to our study, in patients with acute ischemic stroke caused by anterior circulation LAO and refractory to stentriever thrombectomy, permanent stenting seems to lead to a better

#### **REFERENCES**

- I. Mokin M, Snyder KV, Siddiqui AH, Levi EI, Hopkins N. Recent endovascular stroke trials and their impact on stroke systems of care. J Am Coll Cardiol. 2016;67:2645-2655.
- Wahlgren N, Moreira T, Michel P, Steiner T, Jansen O, Cognard C, et al. Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN. Int J Stroke. 2016;11:134-147.
- Campbell BC, Hill MD, Rubiera M, Menon BK, Demchuk A, Donnan GA, et al. Safety and efficacy of Solitaire stent thrombectomy: individual patient data metaanalysis of randomized trials. Stroke. 2016;47:798-806.
- 4. Nogueira RG, Liebeskind DS, Sung G, Duckwiler G, Smith WS. Predictors of good clinical outcomes, mortality, and successful revascularization in patients with acute ischemic stroke undergoing thrombectomy: pooled analysis of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) and Multi MERCI. Trials Stroke. 2009;40:3777-3783.
- Kellert L, Hametner C, Rohde S, Bendszus M, Hacke W, Ringleb P, et al. Endovascular stroke therapy: tirofiban is associated with risk of fatal intracerebral hemorrhage and poor outcome. Stroke. 2013;44:1453-1455.
- Bogdahn U, Schlachetzki F, Schuierer G. Letter by Schlachetzki et al regarding article, "endovascular stroke therapy: tirofiban is associated with risk of fatal intracerebral hemorrhage and poor outcome". Stroke. 2013;44:112.
- Singh P, Doostkam S, Reinhard M, Ivanovas V, Taschner CA. Immunohistochemical analysis of thrombi retrieved during treatment of acute ischemic stroke: does stent-retriever cause intimal damage? Stroke. 2013;44:1720-1722.
- Linfante I, Samaniego EA, Geisbüsch P, Dabus G. Self-expandable stents in the treatment of acute ischemic stroke refractory to current thrombectomy devices. Stroke. 2011;42: 2636-2638.
- 9. Natarajan SK, Sonig A, Mocco J, Dumont TM, Thind H, Hartney ML, et al. Primary stenting for

acute ischemic stroke using the Enterprise intracranial stent: 2-year results of a phase-1 trial. J Vasc Interv Neurol. 2015;8:62-67.

- 10. Gao F, Lo WT, Sun X, Mo DP, Ma N, Miao ZR. Combined use of mechanical thrombectomy with angioplasty and stenting for acute basilar artery occlusions with underlying severe intracranial vertebrobasilar stenosis: preliminary experience from a single Chinese center. AJNR Am J Neuroradiol. 2015;36:1947-1952.
- II. European Stroke Organisation (ESO) Executive Committee, ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis. 2008;25: 457-507.
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet. 1991;337:1521-1526.
- Baumgartner RW, Mattle HP, Schroth G. Assessment of ≥50% and <50% intracranial stenoses by transcranial color-coded duplex sonography. Stroke. 1999;30:87-92.
- 14. Wahlgren N, Ahmed N, Davalos A, Ford GA, Grond M, Hacke W, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SIST-MOST): an observational study. Lancet. 2007;369:275-282.
- Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2015;372:11-20.
- 16. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med. 2015;372: 2285-2295.
- **17.** Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015;372:1009-1018.
- 18. Levy EI, Mehta R, Gupta R, Hanel RA, Chamczuk AJ, Fiorella D, et al. Self-expanding stents for recanalization of acute cerebrovascular

clinical outcome and reduced mortality without an increase in ICH rate. Moreover, our results suggest that permanent stenting as a rescue treatment might be a therapeutic option also for elderly patients, given the positive impact of vessel recanalization in all age groups. In conclusion, permanent stenting might be a feasible solution in patients with acute LAO after stentriever thrombectomy failure.

occlusions. AJNR Am J Neuroradiol. 2007;28: 816-822.

- 19. Zaidat OO, Wolfe T, Hussain SI, Lynch JR, Gupta R, Delap J, et al. Interventional acute ischemic stroke therapy with intracranial selfexpanding stent. Stroke. 2008;39:2392-2395.
- 20. Brekenfeld C, Schroth G, Mattle HP, Do DD, Remonda L, Mordasini P, et al. Stent placement in acute cerebral artery occlusion: use of a selfexpandable intracranial stent for acute stroke treatment. Stroke. 2009;40:847-852.
- 21. Levy EI, Siddiqui AH, Crumlish A, Snyder KV, Hauck EF, Fiorella DJ, et al. First Food and Drug Administration-approved prospective trial of primary intracranial stenting for acute stroke: SARIS (Stent-Assisted Recanalization In Acute Ischemic Stroke). Stroke. 2009;40:3552-3556.
- 22. Mocco J, Hanel RA, Sharma J, Hauck EF, Snyder KV, Natarajan SK, et al. Use of a vascular reconstruction device to salvage acute ischemic occlusions refractory to traditional endovascular recanalization methods. J Neurosurg. 2010;112: 557-562.
- Baek JH, Kim BM, Kim DJ, Heo JH, Nam HS, Yoo J. Stenting as a rescue treatment after failure of mechanical thrombectomy for anterior circulation large artery occlusion. Stroke. 2016;47: 2360-2363.
- 24. Arboix A, Cartanyà A, Lowak M, García-Eroles L, Parra O, Oliveres M, et al. Gender differences and woman-specific trends in acute stroke: results from a hospital-based registry (1986–2009). Clin Neurol Neurosurg. 2014;127:19-24.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 30 December 2016; accepted 16 March 2017

Citation: World Neurosurg. (2017) 103:57-64. http://dx.doi.org/10.1016/j.wneu.2017.03.070

Journal homepage: www.WORLDNEUROSURGERY.org

#### Available online: www.sciencedirect.com

1878-8750/\$ - see front matter © 2017 Elsevier Inc. All rights reserved.