Acute ischemic stroke with cervical internal carotid artery steno-occlusive lesion: multicenter analysis of endovascular approaches

Luigi Cirillo (luigi.cirillo2@unibo.it)
University of Bologna https://orcid.org/0000-0002-0424-3400

Daniele Giuseppe Romano
University Hospital 'San Giovanni di Dio e Ruggi d'Aragona': Azienda Ospedaliera Universitaria 'San Giovanni di Dio e Ruggi d'Aragona'

Gianfranco Vornetti
University Hospital of Bologna Sant'Orsola-Malpighi Polyclinic: Azienda Ospedaliero-Universitaria di Bologna Policlinico Sant'Orsola-Malpighi https://orcid.org/0000-0001-6409-7962

Giulia Frauenfelder
University Hospital 'San Giovanni di Dio e Ruggi d'Aragona': Azienda Ospedaliera Universitaria 'San Giovanni di Dio e Ruggi d'Aragona'

Chiara Tamburrano
University Hospital of Bologna Sant'Orsola-Malpighi Polyclinic: Azienda Ospedaliero-Universitaria di Bologna Policlinico Sant'Orsola-Malpighi

Francesco Taglialatela
Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi

Salvatore Isceri
Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi

Renato Saponiero
University Hospital 'San Giovanni di Dio e Ruggi d'Aragona': Azienda Ospedaliera Universitaria 'San Giovanni di Dio e Ruggi d'Aragona'

Rosa Napoletano
University Hospital 'San Giovanni di Dio e Ruggi d'Aragona': Azienda Ospedaliera Universitaria 'San Giovanni di Dio e Ruggi d'Aragona'

Mauro Gentile
Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi

Michele Romoli
Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi

Ciro Princiotta
IRCCS Istituto Delle Scienze Neurologiche di Bologna

Luigi Simonetti

Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi
Andrea Zini
Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi

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Abstract

Background

Occlusions of internal carotid artery (ICA), whether isolated or in tandem lesions (TL) have a poor response to treatment with intravenous thrombolysis. Previous studies have demonstrated the superiority of mechanical thrombectomy in the treatment of acute ischemic stroke (AIS) following large vessel occlusion, compared to standard intravenous fibrinolysis. The aim of our study was to describe endovascular treatment (EVT) in AIS due to ICA occlusion, whether isolated or in TL.

Methods

we assessed the association between 90-day outcome and clinical, demographic, imaging and procedure data in 51 consecutive patients with acute isolated ICA or TL occlusion who underwent endovascular treatment (EVT). We evaluated baseline NIHSS and mRS, ASPECTS, type of occlusion, stent placement, use of stent retrievers and/or thromboaspiration, duration of the procedure, mTICI, procedural therapy and complications.

Results

A favorable 90-day outcome (mRS 0–2) was achieved in 34 patients (67%) and was significantly associated with the use of dual antiplatelet therapy after the procedure ($p = 0.008$), shorter procedure duration ($p = 0.031$), TICI 2b-3 ($p < 0.001$) and lack of post-procedural hemorrhagic transformation ($p = 0.001$). Four patients did not survive, resulting in a mortality rate of 8%

Conclusions

EVT in the treatment of AIS due to ICA occlusion is safe and effective; mortality rates are in agreement with the current literature. The use of the stent is safe and promotes good angiographic results, as well as therapy with a GpIIb / IIIa inhibitor immediately after stent release which is also associated with better 3-month outcome and good revascularization.

Background

Ischemic stroke is a devastating condition with a high burden of neurologic disability and death [1]. Timely and effective reperfusion is necessary to reverse the ischemic penumbra and to increase the chance of a favorable clinical outcome [1].

There are different Acute ischemic stroke (AIS) subtypes and several factors may influence the response to therapy, such as time-to-treatment, size, and location of arterial occlusion. The major reason for the limited efficacy of alteplase is the modest rate of early reperfusion among patients with a large-vessel occlusion [2, 3], for example when the internal carotid artery (ICA) is involved. Two types of AIS involving the ICA, that have a worse prognosis for poor response to systemic treatment, are:

a. complete occlusion of ICA due to atheromatous plaque or dissection.
b. tandem occlusions, defined as proximal anterior circulation intracranial occlusion and an ipsilateral cervical ICA high-grade stenosis or occlusion [4]

Acute ICA occlusion is one of the most devastating events, which represents 6–15% of AIS [5] and is associated with a significant level of morbidity and mortality. For this type of lesion, treatment with standard intravenous thrombolysis alone leads to a good clinical outcome in only 17% of cases, with a death rate as high as 55% [6]. Also, for tandem occlusion the response rates to intravenous thrombolysis are low and the prognosis is often poor [7, 8, 9].

Since 2015, many trials [1,10,11,12,13,] assessed the superiority of mechanical thrombectomy in the treatment of AIS due large vessel occlusion, in comparison with standard intravenous fibrinolysis (IV-FL). However, the efficacy of endovascular treatment in tandem lesions as well as the choice of emergency carotid stenting is not yet clearly defined.

We report in this study a multicenter experience in the endovascular treatment (EVT) of AIS due to ICA occlusion, either single or associated with occlusion of a downstream vessel (tandem lesion, TL).

Methods

Patient Selection

Data collection was carried out from May 2018 to March 2020 at the Hub Centers for ischemic stroke in in Bologna (Ospedale Maggiore Carlo Alberto Pizzardi) and in Salerno (Ospedali Riuniti San Giovanni di Dio and Ruggi d'Aragona).

All patients who arrived in the two centers with symptoms of AIS, within 6 hours of onset, were evaluated with CT angiography and CT perfusion according to the stroke protocol. We included in this study all patients (n = 51) diagnosed with ICA occlusion (both on an atheromatous basis or due to dissection) or tandem-type lesions.

Ethical approval was waived by the review boards of our institutions (Ospedale Maggiore Carlo Alberto Pizzardi and Ospedali Riuniti San Giovanni di Dio and Ruggi d'Aragona) in view of the retrospective nature of the study. All procedures being performed were in accordance with the 1964 Helsinki Declaration and its later amendments and were part of approved integrated care pathways (PDTAI 017 and PDTA 234 resolution no. 321 of June 18,2018).

Patients data

We collected the following clinical and demographic data: NIHSS (National Institute of Health Stroke Scale), pre-treatment modified Rankin Scale (mRS), previous antiplatelet therapy, comorbidity (hypertension, diabetes, hypercholesterolemia, and atrial fibrillation), age, and gender.

Neuroimaging features

We evaluated baseline Alberta Stroke Program Early CT Score (ASPECTS), type of occlusion (whether exclusively at the level of the ICA or TL), and the cause of the occlusion (either atheromatous or secondary to dissection) evaluated with angio-CT study and TC perfusion.

Procedure data

We collected data on stent placement, use of stent-retriever and/or thromboaspiration, use of double antiplatelet therapy during the procedure, procedure time, angiographic result using the modified Thrombolysis in Cerebral Infarction score (mTICI): mTICI 0 / 2A = recanalization of the vascular territory < 50% and mTICI 2B / 3 = recanalization of the vascular territory > 50%

Outcome

A good clinical outcome was defined as a mRS of 0–2 at 90 days (as assessed by an examiner independent of the interventional physician), while a mTICI score of 2b-3 was considered as successful reperfusion. Any procedural related complications such as hemorrhagic infarction (HI) or parenchymal hematoma (PH) were classified according to the European Cooperative Acute Stroke Study II criteria [9] and post-discharge NHISS score was regarded as: minor stroke (0–4), moderate stroke (5–15), moderate to severe stroke 16–20 and severe stroke > 20.

Statistical Analysis

Categorical variables were compared using Fisher's exact test, while Wilcoxon rank-sum test was computed for continuous variables. At multivariate analysis, ORs and 95% CIs were estimated with a logistic regression model. Categorical variables were summarized by absolute and relative (%) frequency, numerical variables were described as median and interquartile range (IQR). All tests were two sided, and $p < 0.05$ was considered significant. Statistical analysis was performed using R version 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria, 2019).

Results

Clinical, neuroimaging and procedure data are summarized in Table 1.

Study Population

Between May 2018 and March 2020, 51 consecutive patients (63% males, median age 68 years) with AIS were admitted to our two institutions within 6 hours of the onset of symptoms and underwent EVT. Of these, 9 patients had complete occlusion of the ICA, and 42 had a TL. Baseline ASPECTS was 8-10 in 27 patients (53%) and ≤ 8 in 24 (47%). Median baseline NIHSS was 12 (IQR = 4.0-20.0). Twenty-one patients (41%) were on antiplatelet therapy (ASA or ASA + clopidogrel) prior to the stroke event.

Clinical and Angiographic Outcomes

At 3 months a favorable outcome (mRS 0–2) was achieved in 34 patients (67%), 3 patients (25%) had an mRS > 2 and 4 patients did not survive, resulting in a mortality rate of 8%. TICI 2B-3 (successful intracranial recanalization) was achieved in 42 patients (82%), TICI 0-2A in 9 (18%).

A stent was deployed in 21 patients (41%) and 95% of these had a post-treatment TICI 2B-3, while among patients who did not undergo stent placement 73% achieved successful recanalization (p = 0.064).

Ten patients (19,6%) experienced post-procedural hemorrhagic transformations, in particular, the rate of post interventional parenchymal hematoma was 1,9% for PH1 and 1,9% for PH2 while the rate of post interventional petechial hemorrhages was 9,8% for HI1 and 5,8% for HI2, in the absence of symptomatic bleeding.

The comparison of patients with successful and unsuccessful intracranial recanalization is reported in Table 2.

Management of ICA occlusion and TL in emergency

Nine patients (18%) had complete occlusion of the ICA and 42 (82%) had a TL. Thirty-eight patients (75%) were diagnosed with an atheromatous lesion and 13 (25%) with a dissection of the cervical ICA.

Antiplatelet therapy was administered in 18 patients (35%), aspirin in 6 (12%) and GpIIb/IIIa inhibitors in 11 (22%), only 1 patient (1%) received heparin 2000UI during the procedure.

A stent was employed in 21 patients (41%). Among patients who underwent intracranial mechanical thrombectomy (80.4%), ADAPT was employed in 28 (54.9%), Solumbra in 11 (21.6%) and retriever in 2 (3.9%). The procedure median time was 69 minutes (IQR, 46 – 90 minutes).

Factors Influencing Outcome and Recanalization:

The comparison of patients with favorable and unfavorable outcome at 3 months of follow-up is shown in Table 3.

Factors significantly associated with a favorable 90-day outcome were:

a. the use of double antiplatelet therapy after the procedure: 78.8% of patients who received ASA + clopidogrel had a mRS of 0-2 at 90 days compared to 53.3% of those who received only ASA (p = 0.008)
b. A shorter procedure time: median procedure time was 60 minutes in patients with favorable outcome compared to 86 minutes in patients with 90-day mRS > 2 (p = 0.031)

c. lack of post-procedural hemorrhagic transformation: only 2 patients (20%) among those who had this complication (even though asymptomatic) reached a mRS of 0-2 at 90 days (vs 78% of those without hemorrhagic transformation, p = 0.001)

Notably, patients with favorable outcome were those who had a satisfactory degree of revascularization. In fact, 81% of patients with a TICI of 2b-3 had a mRS at 90 days of 0-2, while in the group with a TICI of 0-2a none had a 90-day mRS of 0-2 ($p < 0.001$). At multivariate analysis, a TICI of 2b-3 was the strongest predictor of favorable outcome (Table 4). Furthermore, this factor affects the mortality rate (2% in patients with TICI 2b-3 vs 33% in those with TICI 0-2a, p = 0.015).

While the presence of diabetes was not significantly associated with the clinical outcome, 56% of those suffering from this condition had a mRS of 0-2 at 3 months, compared to 71% among those without diabetes. In addition, diabetes also affects the mortality rate (19% in patients with diabetes vs 3% in patients without diabetes, p = 0.085).

We did not detect a significant association between a good clinical outcome and the type of occlusion (66 % among occlusions with an atheromatous basis and 69% among those caused by dissection, p = 1). Additionally, we did not find a significant correlation between the degree of severity on the NIHSS scale and the mRS at 3 months.

Good recanalization (TICI 2B-3) was achieved in 95% of patients who underwent stent placement and in 94% of patients who were given double antiplatelet therapy. Among the latter a rate of bleeding of 17% was found, compared with 21% in patients who did not receive double antiplatelet therapy.

Discussion

Timely and effective reperfusion is necessary to reverse the ischemic penumbra and to increase the chance of a favorable clinical outcome [1]. Previously published studies suggested that mechanical treatment methods—particularly stenting in extracranial occlusions— achieve better recanalization, higher favorable outcome rates, and lower death rates than IAT only in patients with AIS resulting from occlusion of the ICA [14, 15]. Acute treatment for ischemic stroke has been rapidly evolving over the past 5 years resulting in a drastic improvement of functional outcome after ischemic stroke in selected patients [16].

The use of a post-procedural dual antiplatelet agent had a significant correlation (p = 0.008) with the outcome at 3 months: 78.8% of patients who underwent this treatment had a 90-day mRS of 0–2 vs 53.3% of those who used only one antiplatelet agent or heparin. This variable is also associated with good revascularization, in fact a TICI score 2B-3 was found in 90.9% of patients who received dual antiplatelet therapy vs 8% of those who did not (p = 0.001).

The choice of post-procedural antiplatelet therapy (single or double) was established as follows:

• Dual therapy: patient with stent implantation, a patient already on ASA therapy before the ischemic event but who nevertheless developed an AIS.

• Single therapy: a patient who was not implanted with a stent and who was not on ASA therapy before the ischemic event, patient with an indication for dual therapy but who developed a hemorrhagic transformation

• No therapy: Patient with single therapy indications who developed a hemorrhagic transformation

EVT can cause endothelial damage resulting in vessel stenosis, dissections and reocclusions [17, 18]. Antiplatelets might prevent thrombus formation and vessel reocclusion in damaged vessel. Furthermore, administration of antiplatelets is required to prevent reocclusion of stents [19, 20]. However, previous studies showed an increase in bleeding complications in bridging patients who receive additional antiplatelet therapy during endovascular intervention: The ARTIS trial was stopped early because of an increased rate of sICH in the patient group in which infusion of 300 mg aspirin was started within 90 minutes of intravenous thrombolysis with alteplase, with no improvement in outcome. [21]

Fisher et al. did not detect an increase in rates of sICH, aICH or any bleeding complications, neither in patients receiving aspirin acutely nor in patients pretreated with antiplatelets [22], in particular sICH (5.6% without ASA vs 6.1% with ASA) and aICH (20% without ASA vs 18.8% with ASA). This data supports our results: we found hemorrhagic transformation in only 19% of patients treated with antiplatelet agents after EVT (not distinguishing between single and double anti-aggregation). Furthermore, none of these hemorrhagic transformations manifested themselves with symptoms and just 1 patient had parenchymal hematoma type 2 (PH2) (> 30% of infarct zone, substantial mass effect attributable to the hematoma) who died before the follow-up at 3 months. Therefore, based on our experience, antiplatelet therapy after EVT is appropriate and safe. No comparison was possible between patients who received antiplatelet therapy and those who did not, since antiplatelet therapy was administered to all but 3 patients (2 were given LMWH and had no bleeding, 1 was not given any therapy and had H2 hemorrhagic transformation).

A similar result is found when evaluating the association between post-procedural hemorrhagic transformation and the outcome at 3 months. In fact, patients who did not present it have an mRS 0–2 at 3 months in 90.2% of cases vs 50% of those who presented it ($p = 0.009$). Similarly, patients who do not have hemorrhagic transformation have a TICI score 2B-3 in 90.2% of cases while only 50% of patients who present with post-procedural hemorrhage have a TICI score 2B-3.

A significant association is observed between 90-day mRS and the degree of vascularization obtained at the end of the treatment defined as successful intracranial recanalization (TICI 2B-3); in fact, 81% of patients who had a TICI 2B-3 had a 90 day MRS < 2 while none of the patients with a TICI of 0-2A had a 90-day mRS of 0–2 ($p < 0.001$). Furthermore, this factor affects the mortality rate, which was 2% in the first group and 33% in the second group ($p = 0.015$). This data is in accordance with a previous study which found a correlation between recanalization and outcome in acute ischemic stroke: recanalization is strongly associated with improved functional outcome and reduced mortality [19, 33].

In our study, we analyzed both patients with single ICA occlusion and patients who presented with TL, who underwent EVT. At 3 months a favorable outcome was achieved in 34 patients (67%), while a mRS > 2 was found in 13 patients (25%) and 4 patients did not survive, resulting in a mortality rate of 8%. These data are in accordance with a previous study [19] which found that the occurrence of recanalization is associated with a 4- to 5-fold increase in the odds of good final functional outcome and a 4- to 5-fold reduction in the odds of death.

Importantly, early NIHSS scores have a strong prognostic value for long-term functional outcome after stroke [23–24]. In fact, in all 4 cases of death, the pre-treatment NHISS was higher than 12. However, the strong correlation between NIHSS and mRS scores does not ensure that the NIHSS is a valid surrogate endpoint [25]: we did not find a relevant correlation between the degree of severity on the NIHSS scale and MRS at 3 months: all patients who presented a "severe" NIHSS at discharge at 3 months had an mRS of 0–2.

Emergency carotid artery stent placement is expected to reopen an extracranial ICA occlusion with reduction of intracerebral blood flow in the affected hemisphere. Also, early flow restoration across the tandem lesion in the MCA and/or distal ICA after extracranial ICA stent placement would aim to reverse the ischemic process by stopping the expansion of the ischemic core into the penumbra. The use of stents certainly allows immediate flow restoration but also increases the technical complexity of the procedure. TICI 2B-3 was reported in 95% of patients in which a stent was deployed vs 73 % among those a stent was not employed (p = 0.064). Stents were used both on isolated ICA lesion and in TL, with a TICI 2B-3 of 100% in the first group and 94% in the second group. Therefore, stent placement led to a good angiographic result even in the TL group even though they have a less favorable prognosis.

In our study, antiplatelet therapy with a glycoprotein IIb / IIIa inhibitor immediately after stent release was used in 18 patients (35%). No acute stent thrombosis was observed while the occurrence of clinically symptomatic bleeding was 17% in patients who received antiplatelet therapy vs 21% in patients in whom it was not administered. Therefore, in our series this therapy was not associated with a greater risk of hemorrhagic transformation than in patients in which it was not used. Pre-treatment antiplatelet therapy was used in 21 patients (41%), of these 17 patients (81%) had a 90-day mRS 0–2 vs 57% among those who did not use antiplatelet therapy (p = 0.081). This result is in accordance with the study by Valente et al. who showed that prior use of antiplatelet therapy improves successful recanalization rate and does not increase the risk of intracranial bleeding in patients affected by AIS due to LVO and treated with EVT [26]. In patients who received pre-treatment antiplatelet therapy, a TICI score of 2B-3 was found in 86% of patients, slightly higher than that found in patients in whom pre-treatment antiplatelet therapy was not administered (80%).

Among the comorbidities we have considered (diabetes, hypercholesterolemia, hypertension and atrial fibrillation) only atrial fibrillation showed a correlation with worse outcome with a trend towards significance. In fact, only 57.1% of patients with atrial fibrillation had a TICI score 2B-3 vs 86% of those who had not this condition (p = 0.095). Furthermore, considering the Outcome of mRS < 1 at 90 days, the presence of diabetes showed a trend towards significance. In fact, in patients not suffering from diabetes, 54.3% had an mRS < 1 while in the group of diabetic patients this value dropped to 25% ($p = 0.07$). This data contrasts with a previous study [27] which showed that the mRS score at discharge did not differ between patients with and without diabetes. There is, however, a paucity of studies that assessed the relationship between type 2 DM and functional outcome at discharge in acute ischemic stroke [28, 29, 30]. It is also relevant to note that 3 out of 4 patients who died before the 3-month follow-up belonged to the group of diabetic patients. Less impactful but still worth noting is that a TICI score of 2B-3 is found in 86% of patients without diabetes and in 75% of those affected by this disease, without however reaching statistical significance ($p = 0.43$). These data can be supported by the observation that diabetes, in addition to being a systemic pathology that affects the patient's performance, is also related to greater arteriosclerosis and stiffness of the vessels, that significantly affect endovascular technical difficulties.

There were no serious procedure-related complications such as dissection or vessel rupture in our study. Ten patients (19.6%) experienced post-procedural hemorrhagic transformation (all asymptomatic), without a significant increase in mortality.

Similarly to what was shown in a previous study [31] we observed a lower mortality rate in our series (8%) compared to Nedeltchev et al. (20%) [32] We hypothesize that the use of new devices in our study and technical advances that have occurred since the time of the study by Nedeltchev et al, such as mechanical clot disruption and the mechanical thrombectomy device, most likely contributed to this difference [31].

Limitations

The present study had several limitations. First, it was observational retrospective, so it was prone to selection and other biases. Second, we used multiple thrombectomy techniques for the treatment of tandem occlusions, such as pharmacologic thrombolysis, mechanical clot disruption, or a mechanical thrombectomy device, making it difficult to determine the effect of the different techniques. Third, we did not have a control group with which to compare outcome rates. Last, since the main focus of this study is the treatment technique, we did not analyze perfusion imaging to quantify the ischemic area before revascularization.

Conclusions

Our study has shown that EVT in the treatment of AIS due to ICA occlusion (both on an atheromatous basis and due to dissection) is feasible, safe, and effective in determining a good functional outcome at 90 days; mortality rates were not higher than in the current literature, resulting in a mortality rate of 8%.

In our experience, stent deployment has proved to be particularly safe and has led to good angiographic results, additionally therapy with a glycoprotein IIb / IIIa inhibitor immediately after stent release did not result in a greater risk of hemorrhagic transformation. The use of post-procedural double antiplatelet therapy was significantly associated with favorable outcome at 3 months and with good revascularization.

Abbreviations

AIS: acute ischemic stroke, ICA: internal carotid artery, IV-FL: intravenous fibrinolysis, EVT: endovascular treatment, mRS: modified Rankin Scale, mTICI: modified Thrombolysis In Cerebral Infarction, TL: tandem lesion.

Declarations

Ethics approval and consent to participate

Ethical approval was waived by the review boards of our institutions (Ospedale Maggiore Carlo Alberto Pizzardi and Ospedali Riuniti San Giovanni di Dio and Ruggi d'Aragona) in view of the retrospective nature of the study. All procedures being performed were in accordance with the 1964 Helsinki Declaration and its later amendments and were part of approved integrated care pathways (PDTAI 017 and PDTA 234 resolution no. 321 of June 18,2018).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

LC, DGR and GV contributed to the study conception and design. Data collection and analysis were performed by LC, GV, CT and AZ. The first draft of the manuscript was written by LC, GV, CT and AZ and all authors reviewed and edited previous versions of the manuscript. All authors read and approved the final manuscript.

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References

1. Labeyrie M-A, Turc G, Hess A, Hervo P, Mas J-L, Meder J-F, Baron J-C, Emmanuel Touzé, e Catherine Oppenheim. Diffusion Lesion Reversal After Thrombolysis: A MR Correlate of Early Neurological Improvement *Stroke* 2012;43(11):2986–91. https://doi.org/10.1161/STROKEAHA.112.661009.
2. del Zoppo GJ, Poeck K, Pessin MS, Wolpert SM, Furlan AJ, Ferbert A, Alberts MJ, Zivin JA, Wechsler L, Busse O, et al. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. Ann Neurol 1992;32(1):78–86. doi: 10.1002/ana.410320113. PMID: 1642475.
3. Bhatia R, Hill MD, Shobha N, Menon B, Bal S, Kochar P, Watson T, Mayank Goyal, e Andrew M. Demchuk. Low Rates of Acute Recanalization With Intravenous Recombinant Tissue Plasminogen Activator in Ischemic Stroke: Real-World Experience and a Call for Action *Stroke* 2010;41(10): 2254–58. https://doi.org/10.1161/STROKEAHA.110.592535.
4. Zhu F, Bracard S, Anxionnat R, Derelle A-L, Tonnelet R, Liao L, Mione G, et al. Impact of Emergent Cervical Carotid Stenting in Tandem Occlusion Strokes Treated by Thrombectomy: A Review of the TITAN Collaboration. Frontiers in Neurology. 2019;10:206. https://doi.org/10.3389/fneur.2019.00206.
5. Rubiera M, Ribo M, Delgado-Mederos R, Santamarina E, Delgado P, Montaner J, José Alvarez-Sabín, e Carlos A. Molina. Tandem Internal Carotid Artery/Middle Cerebral Artery Occlusion: An Independent Predictor of Poor Outcome After Systemic Thrombolysis. *Stroke* 2006;37(9): 2301–5. https://doi.org/10.1161/01.STR.0000237070.80133.1d.
6. Papanagiotou P, Roth C, Walter S, Behnke S, Grunwald IQ, Viera J, Politi M, et al. Carotid Artery Stenting in Acute Stroke. J Am Coll Cardiol. 2011;58(23):2363–69.
7. Blassiau A, Gawlitza M, Manceau P-F, Bakchine S, Serre I. Sébastien Soize, e Laurent Pierot. Mechanical Thrombectomy for Tandem Occlusions of the Internal Carotid Artery—Results of a Conservative Approach for the Extracranial Lesion. Frontiers in Neurology. 2018;9:928. https://doi.org/10.3389/fneur.2018.00928.
8. Meves SH, Muhs A, Federlein J, Büttner T, Przuntek H. e T. Postert. Recanalization of Acute Symptomatic Occlusions of the Internal Carotid Artery. J Neurol. 2002;249(2):188–92. https://doi.org/10.1007/PL00007863.
9. Adams HP, Bendixen BH, Leira E, Chang KC, Davis PH, Woolson RF, Clarke WR. M.D. Hanse Antithrombotic treatment of ischemic stroke among patients with occlusion or severe stenosis of the internal carotid artery A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology. 1999;53(1):122. doi:10.1212/WNL.53.1.122.
10. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, Roy D, et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. N Engl J Med. 2015;372(11):1019–30. https://doi.org/10.1056/NEJMoa1414905.

11. Berkhemer OA, Puck SS, Fransen D, Beumer, Lucie A, van den Berg HF, Lingsma AJ, Yoo WJ, Schonewille, et al. A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke. N Engl J Med. 2015;372(1):11–20. https://doi.org/10.1056/NEJMoa1411587.
12. Saver JL, Goyal M, Bonafe A, Diener H-C, Elad I, Levy VM, Pereira GW, Albers, et al. Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke. N Engl J Med. 2015;372(24):2285–95. https://doi.org/10.1056/NEJMoa1415061.
13. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Alex Rovira, Luis San Román, et al. Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke». *New England Journal of Medicine* 2015;372(24): 2296–2306. https://doi.org/10.1056/NEJMoa1503780.
14. Kappelhof M, Marquering HA, Olvert A. Berkhemer, e Charles B L M Majoie. Intra-Arterial Treatment of Patients with Acute Ischemic Stroke and Internal Carotid Artery Occlusion: A Literature Review *Journal of NeuroInterventional Surgery* 2015;7(1).
15. Mokin M, Kass-Hout TKass-Hout,O, Dumont TM, Kan P, Snyder KV, Nelson L, Hopkins AH Siddiqui, e Elad I. Levy Intravenous Thrombolysis and Endovascular Therapy for Acute Ischemic Stroke With Internal Carotid Artery Occlusion: A Systematic Review of Clinical Outcomes *Stroke* 2012;43(9): 2362–68. https://doi.org/10.1161/STROKEAHA.112.655621.
16. Chalos V, van der Ende NAM, Lingsma HF, Mulder MJHL, Venema E, Dijkland SA, Berkhemer OA, Yoo AJ, Broderick JP, Palesch YY, et al. MR CLEAN Investigators. National Institutes of Health Stroke Scale: an alternative primary outcome measure for trials of acute treatment for ischemic stroke. Stroke. 2020;51:282–90. doi:10.1161/STROKEAHA.119.026791.
17. Kurre W, Pérez MA, Horvath D. Elisabeth Schmid, ansjörg Bäzner, e Hans Henkes. Does Mechanical Thrombectomy in Acute Embolic Stroke Have Long-Term Side Effects on Intracranial Vessels? An Angiographic Follow-up Study. CardioVascular Interventional Radiology. 2013;36(3):629–36. https://doi.org/10.1007/s00270-012-0496-8.
18. Almekhlafi MA, Davalos A, Bonafe A, Chapot R, Gralla J, Pereira VM, Goyal eM. Impact of Age and Baseline NIHSS Scores on Clinical Outcomes in the Mechanical Thrombectomy Using Solitaire FR in Acute Ischemic Stroke Study. American Journal of Neuroradiology. 2014;35(7):1337–40. https://doi.org/10.3174/ajnr.A3855.
19. Enomoto Y, Yoshimura S. Antiplatelet Therapy for Carotid Artery Stenting. Intervent Neurol. 2012;1(3–4):151–63. doi:10.1159/000351686.
20. Chaturvedi S, e Jay S Yadav. The Role of Antiplatelet Therapy in Carotid Stenting for Ischemic Stroke Prevention. *Stroke* 2006;37(6): 1572–77. https://doi.org/10.1161/01.STR.0000221298.43117.be.
21. Zinkstok SM, e Yvo B, Roos. Early Administration of Aspirin in Patients Treated with Alteplase for Acute Ischaemic Stroke: A Randomised Controlled Trial». The Lancet. 2012;380(9843):731–37. https://doi.org/10.1016/S0140-6736(12)60949-0.
22. Broeg-Morvay A, Mordasini P, Slezak A, Liesirova K, Meisterernst J, Schroth G, Arnold M, et al. Does Antiplatelet Therapy during Bridging Thrombolysis Increase Rates of Intracerebral Hemorrhage in

Stroke Patients? A cura di Rudolf Kirchmair. PLOS ONE. 2017;12(1):e0170045. https://doi.org/10.1371/journal.pone.0170045.

23. Rangaraju S, Frankel M, Tudor e, Jovin G. Prognostic Value of the 24-Hour Neurological Examination in Anterior Circulation Ischemic Stroke: A Post Hoc Analysis of Two Randomized Controlled Stroke Trials. Interventional Neurology. 2015;4(3–4):120–29. https://doi.org/10.1159/000443801.
24. Saver JL. e Hernan Altman. Relationship Between Neurologic Deficit Severity and Final Functional Outcome Shifts and Strengthens During First Hours After Onset. *Stroke* 2012;43(6): 1537–41. https://doi.org/10.1161/STROKEAHA.111.636928.
25. Fleming TR. «Surrogate End Points in Clinical Trials: Are We Being Misled? Ann Intern Med. 1996;125(7):605. https://doi.org/10.7326/0003-4819-125-7-199610010-00011.
26. Merlino G, Sponza M, Gigli G, Lorenzut S, Vit A, Gavrilovic V, Pellegrin A. Daniela Cargnelutti, e Mariarosaria Valente. Prior Use of Antiplatelet Therapy and Outcomes after Endovascular Therapy in Acute Ischemic Stroke Due to Large Vessel Occlusion: A Single-Center Experience. Journal of Clinical Medicine. 2018;7(12):518. https://doi.org/10.3390/jcm7120518.
27. Tziomalos K. Type 2 Diabetes Is Associated with a Worse Functional Outcome of Ischemic Stroke. World Journal of Diabetes. 2014;5(6):939. https://doi.org/10.4239/wjd.v5.i6.939.
28. Tuttolomondo A, Pinto A, Salemi G, Raimondo DD, Sciacca RD, Fernandez P, Ragonese P. Giovanni Savettieri, e Giuseppe Licata. Diabetic and Non-Diabetic Subjects with Ischemic Stroke: Differences, Subtype Distribution and Outcome». Nutrition Metabolism Cardiovascular Diseases. 2008;18(2):152–57. https://doi.org/10.1016/j.numecd.2007.02.003.
29. Spratt N, Wang Y, Levi C, Ng K. Malcolm Evans, e Janet Fisher. A Prospective Study of Predictors of Prolonged Hospital Stay and Disability after Stroke. Journal of Clinical Neuroscience. 2003;10(6):665–69. https://doi.org/10.1016/j.jocn.2002.12.001.
30. Arboix A, Rivas A. Luis García-Eroles, Lourdes de Marcos, Joan Massons, e Montserrat Oliveres. Cerebral Infarction in Diabetes: Clinical Pattern, Stroke Subtypes, and Predictors of in-Hospital Mortality. BMC Neurology. 2005;5(1):9. https://doi.org/10.1186/1471-2377-5-9.
31. Kwak HS, Hwang SB, Jin GY, Hippe DS, Chung eGH. Predictors of Functional Outcome after Emergency Carotid Artery Stenting and Intra-Arterial Thrombolysis for Treatment of Acute Stroke Associated with Obstruction of the Proximal Internal Carotid Artery and Tandem Downstream Occlusion. American Journal of Neuroradiology. 2013;34(4):841–46. https://doi.org/10.3174/ajnr.A3304.
32. Nedeltchev K, Brekenfeld C, Remonda L, Ozdoba C, Do D-D, Arnold M. Heinrich P. Mattle, e Gerhard Schroth. Internal Carotid Artery Stent Implantation in 25 Patients with Acute Stroke: Preliminary Results. Radiology. 2005;237(3):1029–37. https://doi.org/10.1148/radiol.2373041537.
33. Sallustio F, Saia V, Marrama F, et al. Mechanical Thrombectomy for Acute Intracranial Carotid Occlusion with Patent Intracranial Arteries. Clin Neuroradiol. 2020. https://doi.org/10.1007/s00062-020-00980-5.

Tables

Table 1 Clinical, neuroimaging and procedure data	
Sex (Female)	19 (37.2%)
Age	68.3 (61.4 – 76)
Diabetes	16 (31.3%)
Hyperlipidemia	24 (47.1%)
Hypertension	36 (70.6%)
Atrial fibrilation	7 (13.7 %)
ASPECTS	10 (7 – 10)
9-10	27 (52.9%)
8 or less	24 (47.1%)
Occlusion type	
Atherosclerotic	38 (74.5%)
Dissection	13 (25.5%)
Tandem lesion	42 (82.3%)
Preprocedural therapy	21 (41.1%)
Intraprocedural therapy	18 (35.3%)
Postprocedural therapy	
ASA	15 (29.4%)
ASA + Clopidogrel	33 (64.7%)
Heparin/none	3 (5.9%)
Hemorragic transformation	10 (19.6%)
Procedure time	69 (46 – 90)
Extracranial technique	
PTA	18 (35.3%)
Stent	6 (11.8%)
PTA + Stent	15 (29.4%)
None/other	12 (23.5%)

Intracranial technique	
ADAPT	28 (54.9%)
Solumbra	11 (21.6%)
Retriever	2 (3.9%)
None	10 (19.6%)
Stent placement	21 (41.1%)

Table 2 Comparison of patients with successful and unsuccessful intracranial recanalization

Variable	Total n = 51	TICI 0-2A n = 9	TICI 2B-3 n = 42	p
Sex				1
Male	32	6 (66.6%)	26 (61.9%)	
Female	19	3 (33.3%)	16 (38.1%)	
Age	68.3 (61.4 – 76)	72 (63 – 69.5)	67.9 (58.4 – 77.2)	0.692
Diabetes				0.436
Yes	16	4 (44.4%)	12 (28.6%)	
No	35	5 (55.5%)	30 (71.4%)	
Hyperlipidemia				1
Yes	24	4 (44.4%)	20 (47.6%)	
No	27	5 (55.5%)	22 (52.4%)	
Hypertension				0.709
Yes	36	7 (77.7%)	29 (69.0%)	
No	15	2 (22.2%)	13 (31.0%)	
Atrial fibrilation				0.095
Yes	7	3 (33.3%)	4 (9.5%)	
No	44	6 (66.6%)	38 (90.5%)	
ASPECTS				0.718
9-10	27	4 (44.4%)	23 (54.8%)	
8 or less	24	5 (55.5%)	19 (45.2%)	
Occlusion type				0.417
Atherosclerotic	38	8 (88.8%)	30 (71.4%)	
Dissection	13	1 (11.1%)	12 (28.6%)	
Occlusion location				1
Tandem	42	8 (88.8%)	34 (81.0%)	

Extracranial	9	1 (11.1%)	8 (19.0%)	
Preprocedural therapy				0.720
Yes	21	3 (33.3%)	18 (42.9%)	
No	30	6 (66.6%)	24 (57.1%)	
Intraprocedural therapy				0.134
Yes	18	1 (11.1%)	17 (40.5%)	
No	33	8 (88.8%)	25 (59.5%)	
Postprocedural therapy				0.001
ASA	15	3 (33.3%)	12 (28.6%)	
ASA + Clopidogrel	33	3 (33.3%)	30 (71.4%)	
Heparin/none	3	3 (33.3%)	0 (0%)	
Hemorrhagic transformation				0.009
Yes	10	5 (55.5%)	5 (11.9%)	
No	41	4 (44.4%)	37 (88.1%)	
Procedure time	69 (46 – 90)	70 (55 – 90)	68.5 (45.5 – 90)	0.683
Extracranial technique				0.081
PTA	18	4 (44.4%)	14 (33.3%)	
Stent	6	1 (11.1%)	5 (11.9%)	
PTA + Stent	15	0 (0%)	15 (35.7 %)	
None/other	12	4 (44.4%)	8 (19.0%)	
Intracranial technique				0.791
ADAPT	28	5 (55.5%)	23 (54.8%)	
Solumbra	11	0 (0%)	2 (4.8%)	
Retriever	2	3 (33.3%)	8 (19.0%)	
None	10	1 (11.1%)	9 (21.4%)	

Stent				0.064
Yes	21	1 (11.1%)	20 (47.6%)	
No	30	8 (88.8%)	22 (52.4%)	

Table 3 Comparison of patients with 90-day mRS 0-2 and mRS >2

Variable	**Total** **n = 51**	**mRS 0-2** **n = 34**	**mRS >2** **n = 17**	**p**
Sex				0.365
Male	32	23 (67.6%)	9 (52.9%)	
Female	19	11 (32.4%)	8 (47.1%)	
Age	68.3 (61.4 – 76)	67.6 (55.6 – 74.5)	69 (63.1 – 77)	0.374
TICI				<0.001
0-2A	9	0 (0%)	9 (52.9%)	
2B-3	42	34 (100%)	8 (47.1%)	
Diabetes				0.345
Yes	16	9 (26.5%)	7 (41.2%)	
No	35	25 (73.5%)	10 (58.8%)	
Hyperlipidemia				0.569
Yes	24	15 (44.1%)	9 (52.9%)	
No	27	19 (55.9%)	8 (47.1%)	
Hypertension				0.745
Yes	36	23 (67.7%)	13 (76.5%)	
No	15	11 (32.3%)	4 (23.5%)	
Atrial fibrilation				0.673
Yes	7	4 (11.8%)	3 (17.6%)	
No	44	30 (88.2%)	14 (82.3%)	
ASPECTS				0.254
9-10	27	20 (58.9%)	7 (41.2%)	

8 or less	24	14 (41.2%)	10 (58.8%)	
Occlusion type				1
Atherosclerotic	38	25 (73.5%)	13 (76.5%)	
Dissection	13	9 26.5%)	4 (23.5%)	
Occlusion location				0.241
Tandem	42	26 (76.5%)	16 (94.1%)	
Extracranial	9	8 (23.5%)	1 (5.9%)	
Preprocedural therapy				0.081
Yes	21	17 (50.0%)	4 (23.5%)	
No	30	17 (50.0%)	13 (76.5%)	
Intraprocedural therapy				0.757
Yes	18	13 (38.2%)	5 (26.5%)	
No	33	21 (61.8%)	12 (70.6%)	
Postprocedural therapy				0.008
ASA	15	8 (23.5%)	7 (41.2%)	
ASA + Clopidogrel	33	26 (76.5%)	7 (41.2%)	
Heparin/none	3	0 (0%)	3 (17.6%)	
Hemorrhagic transformation				0.001
Yes	10	2 (5.9%)	8 (47.1%)	
No	41	32 (94.1%)	9 (52.9%)	
Procedure time	69 (46 – 90)	60 (45 – 76.8)	86 (55-119)	0.031
Extracranial technique				0.597
PTA	18	11 (32.3%)	7 (41.2%)	
Stent	6	4 (11.8%)	2 (11.8%)	
PTA + Stent	15	12 (35.3%)	3 (17.6%)	
None/other	12	7 (20.6%)	5 (26.5%)	
Intracranial technique				0.098

ADAPT	28	20 (58.8%)	8 (47.1%)	
Solumbra	11	4 (11.8%)	7 (41.2%)	
Retriever	2	2 (5.9%)	0 (0%)	
None	10	8 (23.5%)	2 (11.8%)	
Stent				0.366
Yes	21	16 (47.1%)	5 (26.5%)	
No	30	18 (52.9%)	12 (70.6%)	

Table 4 Multivariate model for mRS 0-2 vs mRS >2 by TICI score, postprocedural therapy and hemorrhagic transformation.

	OR	95% CI	p-value
TICI			< 0.001
0-2A	Ref.	Ref.	
2B-3	1.76	1.32 – 2.34	
Postprocedural therapy			0.040
ASA/heparin/none	Ref.	Ref.	
ASA + Clopidogrel	1.25	1.02 – 1.54	
Hemorrhagic transformation			0.008
Yes	Ref.	Ref.	
No	1.45	1.11 – 1.88	