Journal of the Neurological Sciences 372 (2017) 300–304

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Bridging-therapy with intravenous recombinant tissue plasminogen activator improves functional outcome in patients with endovascular treatment in acute stroke☆

Ilko L. Maier [a,*], Daniel Behme [b], Marlena Schnieder [a], Ioannis Tsogkas [b], Katharina Schregel [b], Alexander Kleinknecht [a], Katrin Wasser [a], Mathias Bähr [a], Michael Knauth [b], Marios Psychogios [b], Jan Liman [a]

[a] Department of Neurology, University Medicine Göttingen, Germany
[b] Department of Neuroradiology, University Medicine Göttingen, Germany

ARTICLE INFO

Article history:
Received 25 July 2016
Received in revised form 21 November 2016
Accepted 1 December 2016
Available online 5 December 2016

Keywords:
Ischemic stroke
Thrombolysis
Endovascular treatment
Acute stroke outcome

ABSTRACT

Background: Although endovascular treatment for proximal cerebral vessel occlusion is very effective, it remains controversial if intravenous thrombolysis (IVT) prior to endovascular treatment is superior compared to endovascular treatment alone. In this study we compared functional outcomes and recanalization rates of endovascularly treated stroke patients with and without bridging IVT.

Methods: Patients with acute large artery occlusion within the anterior and posterior cerebral circulation eligible for intraarterial revascularization with and without prior IVT were included in this monocentric, prospective observational study. Modified Rankin Scale (mRS) and National Institute of Health Stroke Scale (NIHSS) were determined at baseline, discharge and 90-days follow up after stroke. Successful reperfusion was defined as a Thrombolysis in Cerebral Infarction (TICI) scale 2b-3.

Results: Of the 109 patients included, 81 (74%) received bridging therapy with i.v.-rtPA prior to endovascular treatment, 28 (26%) received endovascular treatment alone. There was no difference in groin-to-reperfusion time between the groups (54 vs 50 min; $p = 0.657$), but a trend towards a higher reperfusion rate in patients with bridging therapy (69 vs 15 patients, $p = 0.099$). Mean improvement of the NIHSS during hospitalization was 8 points (SD; ±8) in the bridging-group and 2 points (SD, ±7) in the non-bridging-group ($p = 0.001$). Number of patients with discharge mRS 0–2 (34 vs 5; $p = 0.024$) and 90-days mRS 0–2 (35 vs 6; $p = 0.061$) was higher in the bridging-group compared to the non-bridging-group.

Conclusions: This study provides evidence that bridging therapy with i.v.-rtPA improves functional outcome in patients eligible for endovascular treatment. Further studies are needed to confirm our findings and to identify patients most likely benefitting from bridging therapy.

1. Introduction

Endovascular treatment has been shown to be effective in large artery occlusion in acute ischemic stroke compared to standard medical treatment in five large, randomized prospective trials [1–5]. In these trials, five out of six patients received intravenous thrombolysis (IVT) prior to endovascular treatment following the bridging approach in acute stroke treatment, which has been shown to be save not leading to increased rates of intracranial hemorrhages (ICH) during or after the intervention [3–6]. Three of these five trials, the MR CLEAN, ESCAPE and REVASCAT trials, included patients with and without prior IVT and showed no significant additional effects of IVT in individual subgroup analysis [1–2,4]. This finding was confirmed by a recently published meta-analysis with a pooled analysis of these five, randomized thrombectomy trials [7].

However, recent studies specifically investigating the additional effects of IVT demonstrated that bridging therapy facilitates mechanical thrombectomy. A study by Behme et al. showed that thrombus length and prior IVT predicted successful recanalization in acute M1-occlusion and mechanical thrombectomy [8]. A study by Guedin et al. moreover showed a shorter groin to reperfusion time and a trend towards lower numbers of passes of the thrombectomy device per patient in 68 cases with proximal MCA occlusion [9]. This was associated with an early improvement of National Institution of Health Stroke Scale (NIHSS), but did not reach statistical significance with respect to a favorable outcome at 90 days (defined as modified Rankin Scale (mRS) ≤ 2). However, this study is limited by small number of patients, sole use of the solitaire-device and was restricted to patients with distal carotid and M1-occlusions.

☆ Financial disclosures: none to declare for all authors.

* Corresponding author at: Department of Neurology, University Medicine Göttingen, Robert-Koch-Str. 40, 37075 Göttingen, Germany.
E-mail address: ilko.maier@med.uni-goettingen.de (I.L. Maier).

http://dx.doi.org/10.1016/j.jns.2016.12.001

In contrast to the aforementioned studies, we aimed to investigate the additional effect of prior IVT to endovascular treatment (including combinations and sole use of mechanical thrombectomy and intraarterial (i.a.) thrombolysis) on recanalization rates, groin-to-reperfusion time and functional outcome in patients presenting with acute occlusions of various intracranial cerebral arteries eligible for endovascular revascularization.

2. Material and methods

2.1. Patients and treatment

Clinical and neuroradiological data was analyzed from a prospectively derived, monocentric database including neuroradiological and neurological information on the interventional treatment and clinical outcome of patients presenting with acute ischemic stroke and receiving endovascular treatment between January 2014 and November 2015. In detail, periods and imaging characteristics were recorded by a stroke-experienced senior neuroradiologist while clinical data like prior medical history and medication, NIHSS and mRS have been evaluated and recorded by an experienced, stroke-trained neurologist. NIHSS was recorded on initial presentation of the patient in the emergency department and on discharge. mRS was recorded on initial presentation, discharge and on 90 days follow-up (face-to-face or by telephone interview).

Patient selection for endovascular treatment was performed using a standard operating procedure. Endovascular therapy was performed if patients presented within 6 h after symptom onset, cranial computer tomography (cCT)-based Alberta Stroke Program Early CT score (ASPECTS) were >5, large vessel occlusion was found in CT-angiography (CTA) and ICH had been ruled out. I.v.-rtPA was administered right after the native CT-scan if ICH had been ruled out (0.9 mg/kg over 1 h with 10% of initial bolus) in accordance with the indications and contraindications described in the European Cooperative Acute Stroke Study [ECASS] III trial [10] and endovascular therapy had been performed without delay (bridging therapy with IVT). Patients not receiving i.v.-rtPA prior to endovascular treatment were considered as bridging-therapy negative and patients with prior i.v.-rtPA as bridging-therapy positive.

The endovascular approach (direct aspiration, stent retrieval, i.a.-thrombolysis and combinations of these approaches) was based on the judgement of the treating neuroradiologist and is described in supplementary Table 1. Symptom-to-groin time was defined as period between first appearance of focal neurological deficit attributable to the index ischemic stroke to groin puncture. Groin-to-successful reperfusion time was defined as period from groin puncture to first series of Thrombolysis in Cerebral Infarction perfusion scale (TICI) 2b-3 on digital subtraction angiography. Collateralization of middle cerebral artery strokes at baseline has been quantified using the Pial Arterial Filling Score from Menon et al., derived by single phase contrast CTA [11]. This score ranges from 0 (no vessels visible within the ischemic territory compared with the asymptomatic contralateral hemisphere) to 5 points (increased or normal prominence and extent of pial vessels within the ischemic territory in the symptomatic hemisphere) for collateralization from the anterior- and posterior artery respectively. Total collateralization score consequently ranged from 0 to 10 points. Symptomatic, post-interventional ICH was defined as ICH within 48 h after the endovascular therapy which was attributable to a deterioration of ≥4 points on the NIHSS. Data acquisition for this observational study was incorporated in a database and approved by the ethics committee of the University Medical Center Göttingen.

2.2. Statistical analysis

Statistical analysis was performed using SPSS 20 (IBM SPSS Statistics, Armonk, NY, USA). Characteristics of all patients are shown as mean ± standard deviation (SD) if normally distributed and as median interquartile range (IQR) if not. Comparisons between the bridging- and the non-bridging group were performed using Mann-Whitney-*U* test, Fischer's exact-test, Pearson Chi square (χ^2) and linear regression models as appropriate. p-Values below 0.05 were considered statistically significant.

Table 1
Baseline characteristics (n = 109).

	Bridging-group (n = 81)	Non-bridging-group (n = 28)	p-Value[a]
Demographics and clinical data			
Age (median, IQR)	75 (62–80)	76 (62.8–79.8)	0.827
Sex (n, % male)	40 (59.4)	12 (42.9)	0.354
NIHSS on admission (median points, IQR)	17 (10.5–20.5)	12.5 (8.3–18)	**0.013**
mRS on admission (median points, IQR)	5 (4–5)	4 (3.3–5)	0.165
In hospital days (median, IQR)	10 (6–20.5)	10 (5.3–17.8)	0.445
Medical history			
Art. hypertension (n, %)	61 (75.3)	23 (82.1)	0.604
Diabetes mellitus (n, %)	23 (28.4)	9 (32.1)	0.810
History of AF (n, %)	30 (36.6)	15 (51.7)	0.120
Hyperlipoproteinemia (n, %)	36 (44.4)	10 (35.7)	0.508
PAD (n, %)	8 (9.9)	1 (3.6)	0.442
Smoking (n, %)	18 (22.2)	7 (25)	0.797
CAD (n, %)	13 (16)	9 (32.1)	0.099
Chronic kidney failure (n, %)	11 (13.6)	4 (14.3)	1.000
Procedural and imaging data			
Symptom to groin time (median minutes, IQR)	153 (120–212.5)	173.5 (119.8–252.5)	0.365
Thrombus length (mm; n = 82; median, IQR)	12 (9–20)	9 (7.5–17)	0.224
ASPECTS on baseline imaging (IQR)	8 (7.5–9)	8 (6.8–9)	0.443

IQR: interquartile range, NIHSS: National Institute of Health Stroke Scale, mRS: modified Rankin Scale, AF: atrial fibrillation, PAD: peripheral artery disease, CAD: coronary artery disease, ASPECTS: Alberta Stroke Program Early CT score.
[a] Mann-Whitney-*U* test and Fischer's exact-test as appropriate.

3. Results

3.1. Baseline clinical, procedural and imaging characteristics

Data from 109 patients with endovascular treatment after acute ischemic stroke were included. Baseline NIHSS was significantly higher in the bridging group (17 vs 12.5 points; p = 0.013) and there was a non-significant trend towards a higher number of patients with coronary artery disease in the non-bridging group (Table 1). Median period between symptom onset and groin puncture was not different between the groups (153 vs 173 min; p = 0.365) and the median period between start of i.v.-rtPA to groin puncture was 35 (IQR, 30–45) min in patients with bridging therapy. The median period between symptom onset to the start of i.v.-rtPA was 102 (IQR, 80–137.8) min in the bridging-group. Thrombus-length could be determined in 65 (80.2%) cases in the bridging-group and in 17 (60.7%) cases in the non-bridging-group and revealed no significant difference (bridging-group 12 mm, non-bridging-group 9 mm; p = 0.224). Median ASPECTS was 8 (IQR, bridging-group 7.5–9; non-bridging group 6.8–9) in both groups on baseline imaging.

Sole treatment with i.a.-rtPA (9.9% vs 0%) and combined treatment of i.a.-rtPA and mechanical thrombectomy (51.9% vs 21.4%) was more frequent in the bridging-group compared to the non-bridging group (p = 0.001). There was no significant difference in the use of endovascular devices (Supplementary Table 1).

Kind of endovascularly treated vessel-occlusions did also not differ between groups (p = 0.320; Supplementary Table 2). The middle