Journal of Neuroradiology xxx (2017) xxx–xxx

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Review

Primary versus secondary mechanical thrombectomy for anterior circulation stroke in children: An update

Q1 Manuel Cappellari [a,*], Giuseppe Moretto [a], Andrea Grazioli [b], Giuseppe Kenneth Ricciardi [b], Paolo Bovi [a], Elisa Francesca Maria Ciceri [b]

[a] USD Stroke Unit, DAI di Neuroscienze, Azienda Ospedaliera Universitaria Integrata, Piazzale A. Stefani 1, 37126 Verona, Italy
[b] UOC Neuroradiologia, DAI Patologia e Diagnostica, Azienda Ospedaliera Universitaria Integrata, Verona, Italy

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Stroke
Childhood
Pediatric
Thrombectomy
Endovascular
Intra-arterial

ABSTRACT

This review of the literature on the use of mechanical thrombectomy (MT) in children with acute ischemic stroke from occlusion of the internal carotid artery and the proximal middle cerebral artery (MCA) compares the efficacy and safety of primary and secondary MT. We analyzed the data reported for 24 case reports from 20 relevant articles published up to 31 December 2016 and the data of a patient treated at our institution. Eighteen cases received primary MT and 7 received secondary MT. The proportions of complete MCA recanalization, small infarcts, and asymptomatic intracranial hemorrhage were similar in both MT groups (73% [11/15] vs. 67% [4/6], 58% [7/12] vs. 60% [3/5], and 15% [2/13] vs. 17% [1/6], respectively). The proportion of favorable neurological outcomes was higher for the primary MT group (69% [11/16] vs. 43% [3/7]). We found no substantial differences in efficacy and safety between primary and secondary MT for anterior circulation stroke in children.

Introduction

Pediatric ischemic stroke, while uncommon, is one of the ten leading causes of death in infancy [1]. More than half of childhood stroke survivors have long-term physical disabilities and cognitive impairment [2]. As occurs in adult stroke patients, the most commonly affected vessels are the distal internal carotid artery (ICA) and the proximal middle cerebral artery (MCA) [3].

Intravenous thrombolysis (IVT) with Alteplase (0.9 mg/kg; maximum dose 90 mg) initiated within 4.5 hours after symptom onset is now standard treatment for acute ischemic stroke (AIS) in adult patients [4]. Intra-arterial thrombolysis (IAT) has not been found to offer advantages over IVT [5]. Techniques of mechanical thrombectomy (MT) are recommended in adult patients with occlusion of the ICA terminus, the middle cerebral artery (M1–M2) or the anterior cerebral artery (A1) within 6 hours after symptoms onset and who do not respond to, or cannot be treated with, IVT (Grade B) [4]. Based on the results of the MR CLEAN, ESCAPE, and REVASCAT trials, which involved a total of 188 adults not eligible for IVT [6–8], current guidelines on revascularization treatment for AIS suggest that primary intra-arterial MT may be considered only when several exclusion criteria for IVT are met [4]. Age less than 18 years is not listed as option for MT, however.

The role of revascularization treatment in childhood stroke is highly controversial. Data on IVT with Alteplase in pediatric patients are extremely limited. The fibrinolytic system is not yet mature in children [9]. Baseline free tissue plasminogen activator (tPA) concentration is lower and the level of plasminogen activator inhibitor 1 (PAI-1), an inhibitor of tPA, is higher than in adults [10]. In addition, the volume of distribution is larger and hepatic clearance is faster in children, suggesting that they can clear Alteplase more quickly [11]. These observations raise the question whether a higher dose of Alteplase may be needed to promote thrombolysis in children with AIS. However, published data on the use of thrombolysis for systemic clots indicate that the risk of hemorrhagic complications appears to be generally higher in children than in adults, when the therapeutic regimen was different from currently approved IV Alteplase dose of 0.9 mg/kg over 1 hour [12].

The use of IV or IA Alteplase for childhood stroke was evaluated in a large international cohort study of childhood stroke (International Pediatric Stroke Study [IPSS]) [13]. Nine of the 687 children with AIS enrolled in the study received IV Alteplase and 5 received IA Alteplase. Although no Alteplase-related deaths or symptomatic intracranial hemorrhage (ICH) events were reported, poor neurological outcome was common. Accordingly, current guidelines

* Corresponding author.
E-mail address: manuel.cappellari@libero.it (M. Cappellari).

https://doi.org/10.1016/j.neurad.2017.11.005
0150-9861/

suggest that the use of Alteplase in children should be limited to the confines of a clinical trial. In December 2013, the National Institutes of Health (NIH) stopped the Thrombolysis in Pediatric Stroke (TIPS) trial due to lack of accrual. The TIPS study was the first prospective treatment trial in pediatric AIS designed to determine the safety, best dose, and feasibility of IVT in children presenting with AIS [14]. Ultimately, only 1 patient among the 93 children screened was enrolled into the study, whereas nearly half had received an alternate diagnosis and the majority of those with ischemic stroke presented a contraindication to treatment.

Following on the remarkable results obtained with the use of modern thrombectomy devices in adult stroke, MT has been extended to and successfully attempted in AIS from large-vessel occlusion also in pediatric patients. However, formal guidelines are currently lacking and endovascular treatments are translated from adult practice. The first review on endovascular therapy for pediatric AIS published in 2012 reported a 28% (5/18) asymptomatic hemorrhage rate in children treated with IAT for anterior circulation AIS. In one of these cases, MT was used in addition to IAT [15]. A more recent review of the literature published between 2008 and 2015 identified a total of 29 pediatric patients who underwent MT [16]. Surprisingly, nearly half had presented a basilar artery (BA) occlusion. Occlusion of the BA is an extremely rare event with a very high mortality rate. There are no data from randomized controlled trials (RCTs) on BA occlusion in adults.

Here, we present an overview of the published literature on the use of MT in AIS children with ICA and/or MCA occlusion, and we compare the efficacy and safety of primary and secondary MT.

Materials and methods

Two of the authors independently searched the PubMed and Embase databases for studies published in English up to December 31, 2016 on the use of MT in pediatric stroke patients with internal ICA and/or MCA occlusion. We used the following search terms: “stroke” and/or “thrombectomy” and/or “thrombolysis” and/or “endovascular” and/or “intra-arterial” and/or “pediatric” and/or “child”. Reference lists in all relevant articles were perused to identify additional data sources. Case series or case reports on the use of MT in pediatric patients with AIS, whatever the etiology, were included [17–36]. In addition, we identified in our hospital’s database files 1 pediatric stroke patient who had been recently treated with MT at the Neuroradiology Units, Department of Diagnostics and Pathology, in Verona University Hospital.

Patients with ICA and/or MCA occlusion plus vertebro-basilar occlusion, and patients who were treated with IAT alone were excluded from the analysis, including 1 patient treated with guidewire clot fragmentation [37].

From the data reported and extrapolated from the radiological report at the end of the angiographic procedure, we detected the following outcome measures: no or complete ICA and MCA recanalization, distal embolism, device-related procedural complication including the transient artery spasm, and thrombectomy device efficacy based on complete/partial MCA recanalization rates.

From the data reported and extrapolated from the clinical findings at the first and last clinical follow-up, we detected the favorable neurological outcomes (NIH Stroke Scale [NIHSS] ≤ 4) at the first and last clinical follow-up.

From the data reported and extrapolated from the radiological description of CT or MRI findings at the radiological follow-up, we detected the following outcome measures: small infarcts (< 1/3 MCA territory), and symptomatic (NIHSS ≥ 1 point from baseline NIHSS in the presence of ICH) or asymptomatic ICH according to the European Cooperative Acute Stroke Study [ECASS] definitions.

Results

The electronic database search retrieved 20 relevant articles published as case reports. We analyzed the data reported for 24 cases of pediatric strokes treated with MT for ICA and/or MCA occlusion. Table 1 presents the data of a patient treated at our institution and an overview of case reports describing MT for pediatric stroke from occlusion of the ICA and/or MCA. Two patients experienced AIS on two separate occasions, and both underwent two MT procedures (case nos. 9, 10, 17, and 18).

Eighteen of the 23 patients (78%) were males. The mean age was 12 ± 5 years. Six (26%) patients were younger than 8 years of age. Advanced neuroimaging with diffusion/perfusion-weighted magnetic resonance imaging (DW/PW MRI) or perfusion computed tomography (pCT) defined an area of tissue mismatch before MT in all 7/25 (28%) cases. Neurological deterioration before MT was present in 5/25 (20%) cases (case nos. 3, 11, 14, 19, and 22).

MT was the primary revascularization procedure in 18/25 (72%) cases, and the secondary revascularization procedure in 7/25 (28%) cases. None of the cases treated with primary MT (primary MT group, case nos. 1–18) received fibrinolytic drugs; IA Alteplase was administered after the procedure in 1 patient (case no. 18). Four of the cases treated with secondary MT (secondary MT group, case nos. 19–25) received MT after IVT (Alteplase), 2 after IAT (Alteplase), and 1 case after IVT (Alteplase) and IAT (Reteplase). Stent retriever devices were used in 16/25 (64%) cases, either alone or in combination with thrombo-aspiration: Solitaire™ (Medtronic) in 11 cases, Trevo Retriever® (Stryker) in 4, and pREset thrombectomy device (Phenox) in 1 case. Merci Retriever® (Concentric Medical Inc.) was used in 4/25 (16%) cases, either alone or in combination with thrombo-aspiration. A Penumbra System® (Penumbra Inc.) was used in 9/25 (36%) cases. Successful revascularization of the occluded vessel was achieved with deployment of a Wingspan® stent (Stryker Neurovascular) after an ineffective MT procedure in 1 case (case no. 3).

Complete ICA and MCA recanalization was achieved in 8/9 (89%) and 15/24 (63%) cases, respectively. No ICA recanalization was required in 1/9 (11%) cases and no MCA recanalization was required in 2/24 (8%) cases. Distal embolism occurred in 4/24 (17%) cases (case nos. 6, 11, 17, and 19). Device-related procedural complication, in which a Merci device fractured during clot retrieval, was reported in 1 case (case no. 20). Transient spasm occurred in the MCA where a Trevo device had been deployed in 2 cases (case nos. 17 and 18).

Favorable neurological outcomes at the first and last clinical follow-up were achieved in 15/25 (60%) and 22/25 (88%) cases, respectively.

Small infarcts were present in 11/19 (58%) cases and ICH (hemorrhagic infarct type 2 [HI-2] as defined by the ECASS) in 3/21 (14%) cases. None of the patients developed symptomatic ICH.

The clinico-radiological characteristics and outcome measures for the primary and secondary MT groups are provided in the online-only Data Supplement. The mean baseline and pre-MT NIHSS scores were higher for the secondary MT group (12 [± 7] vs. 17 [± 6] and 14 [± 5] vs. 19 [± 5] points, respectively). Because recanalization was achieved utilizing different endovascular approaches after unsuccessful primary MT, we considered case nos. 3 and 16 as being “ineffective MT” for the recanalization outcome measures, defined as ICA and MCA recanalization rates, and thrombectomy device efficacy based on complete/partial MCA recanalization rates. The complete ICA recanalization rate was higher for the secondary MT group (100% [2/2] vs. 83% [5/6]), while the complete MCA recanalization rate was similar for both MT groups (73% [11/15] vs. 67% [4/6]). The no ICA recanalization rate was higher for the primary MT group (17% [1/6] vs. 0 [0/2]), while the no MCA recanalization rate was similar between the

Please cite this article in press as: Cappellari M, et al. Primary versus secondary mechanical thrombectomy for anterior circulation stroke in children: An update. J Neuroradiol (2017), https://doi.org/10.1016/j.neurad.2017.11.005