Neurology, Psychiatry and Brain Research 22 (2016) 119–126

Contents lists available at ScienceDirect

Neurology, Psychiatry and Brain Research

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

Review

Current status of endovascular treatment for acute ischemic stroke

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ARTICLE INFO

Article history:
Received 2 July 2015
Accepted 2 February 2016
Available online 28 May 2016

Keywords:
Thrombectomy
Ischemic stroke
Endovascular

ABSTRACT

Endovascular therapy is now considered as the standard treatment for acute ischemic stroke in the setting of large vessel occlusion. However, it took time to come to this setting. In this review, first briefly the evolution and actual status of endovascular therapy for acute ischemic stroke are presented. The second part focuses on the daily clinical practice at the authors' institution with respect to the endovascular stroke therapy. While doing this, different aspects will be briefly discussed.

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1. Introduction

The short history of endovascular therapy (ET) for acute ischemic stroke (AIS) can be divided into two eras with the turning point in October 2014. First came the time of pessimism with prospective randomized controlled trials which did not show any additional benefit of emergency ET over the intravenous tissue plasminogen activator (t-PA) alone (Broderick et al., 2013; Ciccone et al., 2013; Kidwell et al., 2013). However, presentation of preliminary results of the MRCLEAN study (Berkhemer et al., 2015) at the 9. World Stroke Congress, which was held in October 2014 in Istanbul (Dippel et al., 2014), marked the beginning of the era of optimism. Other prospective randomized controlled trials shortly followed which all showed the superiority of ET over intravenous t-PA alone in carefully selected patients, especially in patients with large vessel occlusions (LVO) (Goyal et al., 2015; Jovin et al., 2015; Campbell et al., 2015; Saver et al., 2015). In this review, first briefly the evolution and actual status of ET for AIS are presented. The second part focuses on the daily clinical practice at the authors' institution with respect to the AIS therapy. While doing this,

Abbreviations: ET, endovascular therapy; AIS, acute ischemic stroke; LVO, large vessel occlusions; IVT, intravenous thrombolysis; IA, intraarterial; CTP, CT-Perfusion; CTA, CT-Angiography; MTT, Mean transit time.

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http://dx.doi.org/10.1016/j.npbr.2016.02.003
0941-9500/

different aspects of endovascular stroke therapy are briefly discussed.

2. Evolution of emergency endovascular therapy for acute ischemic stroke

Based on the result of The National Institute of Neurological Disorders and Stroke t-PA study (The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995), the FDA approved the intravenous use of t-PA within 3 h of ischemic stroke onset in 1996. Following trials have supported to extend this time window to 4.5 h in appropriately selected patients (Hacke et al., 2008; Wahlgren et al., 2008). Nevertheless, only few patients (<10%) are eligible for application of systemic thrombolytics (Chalouhi et al., 2013; de Los Ríos la Rosa et al., 2012; Hassan, Chaudhry, Grigoryan, Tekle, & Qureshi, 2012). Besides, successful recanalization rates of LVO with intravenous thrombolysis (IVT) alone range only from 10% to 30% (Brommer and van Bockel, 1992; Bhatia et al., 2010; Fulgham et al., 2004; Linfante et al., 2002; Riedel et al., 2011; Saqqur et al., 2007). The first attempts to treat AIS endovascularly mainly based on local intraarterial (IA) application of fibrinolytic agents via microcatheters, which were brought close to the thrombus. Thus, a higher local dose of the drugs could be injected and better recanalisation rates could be achieved. Although since the introduction of intraarterial thrombolysis many case studies and small retrospective studies showed a benefit, Prolyse in Acute Cerebral Thromboembolism Trial (PROACT) I and II (del Zoppo et al., 1998; Furlan et al., 1999), with the only difference between them being including higher number of patients in the PROACT II and of which results were published in 1998 and 1999, respectively, were the first prospective randomized trials investigating the safety and efficacy of IA recombinant prourokinase (r-proUK) and heparin vs. saline placebo and heparin. They showed higher rates of recanalization (57,7% and 66%, respectively) and better 90-day clinical outcome in patients treated with IA r-proUK. However, intracranial hemorrhage rates were high. But the question of superiority of ET over IVT remained unanswered. This led to further improvement of endovascular devices and designing of clinical trials.

3. First generation mechanical thrombectomy devices

3.1. MERCI retriever and the PENUMBRA system

The motto 'Time is brain' gave way to the development of mechanical thrombectomy devices to achieve faster and better arterial recanalisation. Two main methods of endovascular mechanical thrombectomy for LVO are: (1) jailing, dislodging and removal of thrombi with retrievers and (2) aspiration of occlusive thrombi via suction.

Evidence for the effectiveness of mechanical thrombectomy began to mount with the introduction of Mechanical Embolus Removal in Cerebral Ischemia (MERCI) retriever (Stryker Neurovascular, Mountain View, CA, USA) which was used in prospective trials. The rates of recanalization (48%) and chance of good clinical outcome were higher when MERCI retriever used within a time window of 8 h in the MERCI & Multi MERCI trials (Smith et al., 2005; Smith et al., 2008).

The Penumbra Stroke System (Penumbra, Almeda, USA), which works by removing of thrombus with continuous aspiration was a major development as well. Better recanalisation rates could be achieved ranging from 67 to 82% (Penumbra Pivotal Stroke Trial Investigators, 2009; Menon et al., 2011).

The Merci Retriever and the Penumbra System were authorized by the FDA for use in 2004 and 2007, respectively, in the revascularization of patients with AIS secondary to intracranial LVO within 8 h of symptom onset.

4. Second generation mechanical thrombectomy devices

4.1. Stent retrievers

Stent retrievers employ a retrievable stent to jail, disloge and take out the thrombus. The stent is advanced within a microcatheter through the clot with passing it a few millimeters and then deployed which allows partly compressing the clot radially to the vascular wall and partly grasping it with the stent struts. The microcatheter and stent are then carefully removed under continuous proximal aspiration with a syringe (Figs. 1 and 2).

4.2. Solitaire FR and Trevo Pro

Non randomized case series with the Solitaire FR (eV3 Endovascular, Irvine, CA) demonstrated high rates of recanalization (89–96%) and improved rates of favorable clinical outcome compared to earlier devices (Castaño et al., 2010; Hann et al., 2013; Machi et al., 2012; Miteff et al., 2011; Roth et al., 2010).

The Trevo Pro (Stryker Neurovascular, Kalamazoo, MI) is a stent retriever system which, similar to the Solitaire FR, was also found to be superior to the Merci Retriever (Mendonça et al., 2014; Nogueira et al., 2012). Both of the stent retrievers were approved by the FDA for use in acute LVO in 2012.

4.3. Combined suction embolectomy and mechanical retrieval

The "A Direct Aspiration, First Pass Technique (ADAPT)", first introduced by Turk et al. (2014a) is an increasingly utilized approach which combines the two successful methods. The MAX reperfusion catheters, simply the advanced versions of the former Penumbra catheter with larger lumens (Penumbra, Almeda, USA) and Sofia distal access catheters (Micro Vention, Tustin, CA, USA) allowed for the development of this technique (Stampfl et al., 2015; Turk et al., 2014a). In this procedure, the catheter is advanced to the thrombus and direct suction applied. The catheter is then removed along with the thrombus, while applying continuous aspiration. In cases of failure it can be combined with the stent retrievers because of its large lumen. A recent retrospective series of 98 patients by Turk et al. (2014b) reported revascularization in 78% of cases. When used in combination with stent retrievers, this rate rose to 95%, a previously unparalleled result. However, none of the above mentioned catheters have a FDA approval for use in AIS treatment yet.

The Penumbra 3D Separator (Penumbra, Almeda, USA) belongs to the newest generation PS devices which combines the two techniques into a single device. Early results showed promise for safe and effective revascularization (Behme et al., 2014; Mpotsaris, Bussmeyer, & Weber, 2013).

Stentrievers and large bore aspiration catheters have become the dominant endovascular devices used to treat AIS in modern practice.

There are other modern treatment strategies regarding the LVO, such as emergency extracranial internal carotid artery (ICA) stenting or utilization of intracranial stents for persisting occlusions which are nowadays combined in complex individual acute stroke pathologies. Extracranial carotid stents can be employed in cases of acute occlusions due to rupture of a preexisting plaque at the carotid bifurcation, due to severe cardioembolic occlusions of the extracranial ICA or due to dissections. Deployment of intracranial stents find their usage mainly in the persisting acute occlusions after thrombectomy due to a preexisting plaque, in intracranial dissections or in patients