Mechanical Thrombolysis and Stenting in Acute Ischemic Stroke

Jan Gralla, MD, MSc; Caspar Brekenfeld, MD; Pasquale Mordasini, MD; Gerhard Schroth, MD

Acute ischemic stroke is one of the major sources of morbidity and mortality in the industrialized countries. The lifetime risk of stroke is estimated to be 1 in 5 for middle-aged women and 1 in 6 for men according to the Framingham Study. Outcome depends on the length of time between onset of symptoms and revascularization, the recanalization rate, and on whether or not intracranial hemorrhage occurs. A meta-analysis of 52 studies on thrombolysis outcome in 2066 patients showed that the chance of an independent life after stroke increases 4.4 times for patients with successful recanalization compared with patients without recanalization; mortality rate decreases 4-fold.

Intravenously administered tissue plasminogen activator (IV tPA) and local intra-arterial thrombolysis (IAT) have both been shown to improve patient outcome. However, the time window for treatment and the recanalization rate of both approaches are limited, and the application of thrombolytic drugs increases the risk of symptomatic intracranial hemorrhage (sICH). The success of recanalization, furthermore, depends on the occlusion site; proximal occlusions of large vessels such as the internal carotid artery have a poor recanalization rate after either IV tPA or IAT.

Recent studies have examined whether mechanical recanalization techniques can accelerate the process of recanalization, increase the recanalization rate, and even expand the window of opportunity. This article describes the evolution of the different mechanical thrombolysis and stenting techniques and their working principles for endovascular vessel recanalization and reviews the data on the outcome after acute stroke treatment.

Mechanical Thrombolysis

The various techniques and approaches for mechanical thrombolysis (MT) can be divided into 3 categories: thrombus disruption, immediate flow restoration with self-expandable stents, and thrombectomy.

Thrombus Disruption

According to Pro-Urokinase for Acute Cerebral Thromboembolism-2 (PROACT II), IAT consists of local application of the fibrinolytic drug at the proximal surface of the thrombus. Mechanical clot disruption was not allowed according to the study protocol.

Various techniques for thrombus fragmentation have been advocated. The most common is probing the thrombus with the microwire and/or advancing the microcatheter into or beyond the thrombus. This simple mechanical procedure during IAT has been shown to improve the rate of successful recanalization (here defined as Thrombolysis in Myocardial Infarction score ≥2 or Thrombolysis in Cerebral Infarction score ≥2b). In middle cerebral artery occlusions, successful recanalization has reported in 79% compared with the PROACT II data showing a recanalization rate of 66%.

Various studies have shown the efficacy of percutaneous balloon angioplasty at increasing the thrombus surface and achieving recanalization.

The largest study compared 34 patients with M1 occlusions receiving percutaneous balloon angioplasty as the first-line treatment to 36 patients treated with IAT alone (mean National Institutes of Health Stroke Scale [NIHSS], 16). Sufficient recanalization was achieved in 91.2% (versus 63.9%) with a favorable clinical outcome (here defined as modified Rankin Scale at 90-day follow-up ≤2) in 73.5% versus 50%, respectively. After percutaneous balloon angioplasty, however, 64.5% of patients required additional IAT to resolve distal emboli that occurred during treatment.

A modification of this technique is percutaneous balloon angioplasty using low-pressure remodeling balloons. A recent study reports on the use of this technique in conjunction with low-dose eptifibatide and/or IAT. Treatment of 12 consecutive patients (mean NIHSS, 17) produced successful recanalization in 91.6% and a favorable clinical outcome in 41.6%.

Due to the risk of periprocedural complications and distal emboli associated with percutaneous balloon angioplasty, this technique has not emerged as a first-line technique and is reserved rather for patients in whom more conservative methods have failed.

More sophisticated intraluminal clot disruption devices apply ultrasound or laser technology. The EKOS system (EKOS, Bothell, WA) uses a 2.5-Fr microcatheter (MicroLysUS infusion catheter) with a 2.1-MHz piezoelectric sonography element at its distal tip. Local application of ultrasonic vibrations is intended to increase fluid permeation within the...
thrombus so as to enhance the effect of IAT. The initial clinical study on 14 patients with anterior and posterior circulation strokes (mean NIHSS, 18) showed a successful recanalization in 57% with a favorable clinical outcome in 43% of patients. The rate of sICH was increased to 14% (compared with the 10% rate in PROACT II). The device has subsequently been investigated in the Interventional Management of Stroke (IMS)-II trial in which its application in 34 patients resulted in a recanalization rate of 73%. Currently, the EKOS system is one of the 3 mechanical approaches being used in the IMS-III trial.

Laser-based technology is used by the EPAR system (EPAR; Endovasix, Belmont, CA), which aims to emulsify the clot by the application of microcavitation bubbles at the tip of the microcatheter. The clinical study enrolled 34 patients (mean NIHSS, 19) with occlusion sites in the anterior and posterior circulation. In 18 of the 34 patients (53%), the device could be applied as intended with a recanalization rate of 61.1% in this subgroup. The study documented 1 severe adverse event (vessel rupture) and 5.9% of sICH with an overall mortality rate of 38.2%.

Approaches requiring adjuvant thrombolysis are prone to increase the rate of sICH, which is a potential disadvantage compared with techniques applying MT alone.

**Stenting**

Stent placement promises immediate flow restoration without repetitive passing and retrieval attempts and may render unnecessary the application of thrombolytic drugs. Instead of mechanical retrieval, intracranial stenting achieves recanalization by compressing the thrombus to the vessel wall and avoids the risk of proximal thrombus dislocation. However, intracranial stent placement in general, but especially in the setting of acute stroke, has some disadvantages. The compressed thrombus is likely to cause permanent side branch and perforator occlusion. Furthermore, the implant can cause short-term complications such as in-stent thrombosis and reocclusion of the vessel, requiring antiplatelet aggregation medication. However, this preventive medication regime might increase the risk of sICH in the stroke population. Furthermore, the up to 32% restenosis rate reported for bare metal stents at intracranial stenosis in a 9-month follow-up period is matter for concern.

Different stent designs have been successfully applied to the clinical setting of acute stroke; self-expandable stents (SESs) are preferentially used over balloon-mounted stents. Preliminary data on the use of SES in the treatment of acute intracranial vessel occlusion is limited to case reports and small case series.

Levy et al reported successful recanalization in 79% in 18 patients (mean NIHSS, 18) who presented with acute stroke. The placement of SES in the study, however, was accompanied by various other endovascular techniques. Moderate clinical outcome (here defined as modified Rankin Scale at 90-day follow-up ≤3) was achieved in 33.3%.

Brekenfeld et al treated 12 patients (mean NIHSS, 14) with acute ischemic stroke using SES; IAT and/or mechanical thrombolysis failed in 7 patients before stent deployment. Successful recanalization was achieved in 92% of cases; moderate clinical outcome was reported in 50%; no sICH occurred.

Similarly, Linfante et al reported on the use of SES in 19 patients with stroke (mean NIHSS, 19) as a rescue therapy after failure of arterial thrombolysis and/or mechanical thrombectomy. Successful recanalization was achieved in 95% of occlusions. Favorable clinical outcome was achieved in 42%. No intraprocedural complications were encountered; sICH occurred in 16%.

The Stent-Assisted Recanalization in Acute Ischemic Stroke (SARIS) trial is the first Food and Drug Administration-approved prospective trial investigating stenting for the treatment of acute stroke. It reports on 20 patients with stroke (mean NIHSS, 14) treated within the 6-hour window. In all cases (100%), the target vessel was recanalized after treatment. Adjuvant therapies including angioplasty, IAT, and IV tPA were used in 63.2%. At 1-month and 6-month moderate clinical outcome was achieved in 60% of patients.

Although the recanalization rate in all studies on the application of SES in patients with stroke is generally very high, it is debatable whether stenting in acute ischemic stroke has a future role as a first-line treatment due to the risks associated with intracranial stent placement and the recent success of thrombectomy. Stenting does, however, have clear value in selected cases of rescue therapy.

**Mechanical Thrombectomy**

All mechanical thrombectomy devices are delivered by endovascular access proximal to the occlusion site. The various devices can be divided into 3 major groups according to where they apply force on the thrombus.

Proximal devices apply force to the proximal base of the thrombus; this group includes various aspiration catheters and systems.

Distal devices approach the thrombus proximally but then are advanced by a microcatheter past the thrombus to be unsheathed behind it, where force is applied to the distal base of the thrombus; this group includes brush-like, basket-like, or coil-like devices.

The most recently developed devices include stent-like devices that are placed across the occlusion side, deployed within the thrombus, and then retrieved; this group includes various self-expandable stent retrievers (SRs).

**Thrombus Aspiration and Proximal Thrombectomy**

The first reports on mechanical thrombectomy in acute stroke treatment included the use of aspiration catheters. A large microcatheter (4–5 Fr) is advanced to the proximal surface of the clot and suction force is applied using a 60-mL syringe. Entrapment of the thrombus is indicated by the absence of backflow. The catheter is then retrieved with constant negative pressure to avoid loss of thrombus. After each retrieval of clot fragments, the procedure is repeated.

Although widely applied, few data have been published on this approach so far. A recent single-center study reported on 22 consecutive patients (mean NIHSS, 18) treated with aspiration thrombectomy alone. Sufficient recanalization was...
achieved in 81.9% and a favorable clinical outcome in 45.5%.30

The method is technically simple, fast to apply, and inexpensive. It is widely used, especially in proximal occlusions (eg, distal cervical internal carotid artery, internal carotid artery terminus) when the target vessel has a large diameter and an anatomy favorable for device navigation.

**Penumbra System**

The Penumbra system (Penumbra, Alameda, CA) is a refinement of the proximal thrombectomy technique. It applies continuous aspiration in conjunction with mechanical fragmentation and was approved by the Food and Drug Administration for clot removal in stroke treatment in 2007.

Reperfusion catheters of various sizes (0.26–0.51 inch) are advanced to the proximal surface of the thrombus and connected to an aspiration pump providing continuous aspiration (H11002 700 mm Hg). To avoid the obstruction of the aspiration catheter, additional clot fragmentation is achieved with a teardrop-shaped separator mounted at the distal end of the microwire (Figure 1). This setting allows cleaning of the catheter tip of clot fragments at the same time as keeping the device in place during recanalization. The aim of this setting is to debulk the clot from proximal to distal; small catheter sizes should facilitate thrombectomy even in distal branches such as M2 segments.

The Penumbra system has been investigated in numerous single-center and multicenter trials. The Penumbra Pivotal Stroke Trial prospectively examined the results in 125 stroke patients (mean NIHSS, 18) within a window of 8 hours after onset of symptoms. Recanalization of the target vessel was achieved in 81.6%. The study did not state the percentage of patients that received IV tPA before mechanical recanalization. Despite the convincing recanalization rate, clinical outcome was poor; favorable clinical outcome was achieved in only 25% of all patients and in 29% of patients with successful recanalization. The rate of sICH was 11.2% and overall mortality was 32.8%.31 Serious adverse events occurred in 3.2% of cases.

The high recanalization rate in correlation to the poor clinical results in this trial sparked the discussion on the value of recanalization using MT. However, some single-center studies reported better clinical results with the Penumbra system than those of the Pivotal Trial. Kulcsar et al32 reported on a series of 27 patients (mean NIHSS, 14) with large vessel occlusions. The mean procedural time was rather long (1.6 hours). Successful recanalization was achieved in 93% of patients, favorable clinical outcome was found in 48%, and all-cause mortality was reduced to 11%.

The Penumbra system is one of the devices currently being investigated in the IMS-III trial.19

**Distal Thrombectomy**

Due to the technical disadvantages associated with large-diameter aspiration catheters as well as the low retrieval rate of aspiration, a novel generation of distal thrombectomy devices was developed. The microcatheter (0.18–0.27 inch) for the deployment of distal devices is usually easy to navigate even in tortuous vessel anatomy to the intracranial occlusion side. After passing the clot, the device is deployed distally to the thrombus. This approach shifts the application of force to the distal base of the thrombus, which has been shown to increase the efficacy of thrombectomy in vivo. However, vasospasm and vessel wall damage have been more frequently described in association with distal devices. Furthermore, during retrieval, the loose engagement of the clot with the distal device is prone to cause thromboembolic events. For most distal devices, therefore, proximal balloon occlusion and aspiration from the guide catheter (flow reversal) during retrieval are recommended.

Various distal devices have been advocated in the past (eg, Phenox, Bochum, Germany; Catch, Balt, Montmorency, France), most of them available in Europe only. Large clinical experience has been reported on the Merci devices, the first device of this group to receive Food and Drug Administration approval (in 2004).

**Merci Devices**

The essential component of the Merci Retrieval System (Concentric Medical, Mountain View, CA) is the Merci retriever (Figure 2). The initial Mechanical Embolus Removal in Cerebral Ischemia (MERCI) trial evaluated the...
safety and efficacy of the Merci system in the setting of acute stroke within 8 hours of onset in 151 patients (mean NIHSS, 20) who were ineligible for IAT. The trial included patients with anterior circulation (90%) and posterior circulation (10%) stroke. Successful recanalization was achieved in 46% of the treated patients, significantly higher compared with the control group, the spontaneous recanalization rate of 18% of the PROACT II trial. Favorable clinical outcome was achieved in 27.7% of patients. The mean procedure duration was 2.1 hours; clinically significant procedural complications occurred in 7.1% of patients; the sICH rate was 7.8%.

The Multi-MERCI trial was an international, single-arm trial that investigated 164 patients (mean NIHSS, 19) within an 8-hour window after symptom onset. The primary end point was target vessel recanalization. In contrast to the MERCI trial, prior treatment with IV tPA, IAT, or other mechanical techniques was allowed and new generations of the Merci device were included. Successful recanalization was achieved in 57.3% using the retriever alone and in 69.5% in conjunction with other treatment modalities. A favorable clinical outcome was achieved in 36% of patients. Mean procedure duration was 1.6 hours and therefore again remarkably long for a mechanical approach. Clinically significant procedural complications occurred in 5.5% of patients; the sICH rate was 9.8%.

The introduction of the device was a landmark of mechanical recanalization in stroke treatment. Both MERCI trials demonstrated a significantly better clinical outcome in patients with successful recanalization. The group of Merci devices is currently being assessed within the IMS-III trial.

Stent Retriever
The most recently introduced mechanical devices for acute stroke treatment are self-expandable, stent-like thrombectomy devices. Combining the advantages of temporary stenting with immediate flow restoration without the need for permanent implantation plus thrombectomy with definitive thrombus removal, SR devices offer a promising new treatment option for acute ischemic stroke. The devices are applied in a manner comparable to that of intracranial stents. After passing the occlusion site with a microcatheter (0.21–0.27-inch inner diameter), the SR is deployed covering the entire thrombus. The radial force of the SR can immediately generate a channel compressing the thrombus and restore flow to the distal territory. Adjuvant IAT can be applied at this point. After an embedding time of 3 to 10 minutes, the deployed stent is slowly retrieved. As for distal devices, proximal balloon occlusion and flow reversal by aspiration at the guide catheter during retrieval is recommended.

Numerous variants of this device type are currently under development or in first clinical trials (TREVO, Concentric Medical, Mountain View, CA; PULSE, Penumbra, Alameda, CA; ReVive, Micrus, CA).

The first dedicated combined flow restoration and thrombectomy device for acute stroke treatment was the Solitaire FR (ev3, Irvine, CA; Figure 3). The device is a modification of the Solitaire AB Neurovascular Remodeling Device, originally developed for stent-assisted treatment of wide-neck intracranial aneurysms. Within a short period of time, numerous studies have reported on the in vivo and clinical application of the Solitaire FR for stroke treatment.

Castano et al reported in 2010 on their initial experience in 20 patients with acute stroke within an 8-hour time window. Successful recanalization was achieved in 90% of cases with a mean procedural time of 50 minutes. A favorable clinical outcome was attained in 45%; the sICH rate was 9.8%. Other small case series using SR have shown similar successful recanalization rates (88%–91%) and fast procedural times (42–55 minutes) with comparable rates of favorable clinical outcome (42%–54%).

Figure 3. Angiogram showing an acute MCA occlusion (A) and the immediate flow restoration after SR placement (B). Complete recanalization after retrieval (C); the thrombus is encaged in the Solitaire FR. MCA indicates middle cerebral artery; SR, stent retriever.
The largest study to date summarizes these findings. The retrospective collection of cases from 6 large European stroke centers reports on outcome in 141 patients with acute patients (mean NIHSS, 18) treated for occlusions in the anterior (internal carotid artery: 27%, middle cerebral artery: 59%) and posterior circulation (14%). Mean recanalization time was 45 minutes; Thrombolysis in Cerebral Infarction \( \geq 2 \) was achieved in 86% of target vessels. A favorable outcome was found in 55% of patients. Overall mortality was 20.5%.39

The results of 2 larger trials are expected. The SWIFT trial (Solitaire FR with the Intention for Thrombectomy) is a randomized trial comparing the efficacy and safety of the Solitaire FR system with that of the Merci device. Patients included in the trial may be ineligible for or have failed IV tPA within an 8-hour window. The primary outcome is recanalization of an occluded target vessel to Thrombolysis in Myocardial Infarction \( \geq 2 \). Secondary outcomes are recanalization time and modified Rankin Scale at 90-day follow-up. The SWIFT study was halted by the data monitoring board early in 2011 after 126 patients of the anticipated 250 had been enrolled. The results have not been published yet but favorable results for Solitaire FR can be assumed.

The Solitaire FR is currently being evaluated in the STAR Trial (Solitaire FR Thrombectomy for Acute Revascularization). This prospective, international single-arm study has an enrolment goal of 200 consecutive patients with anterior circulation occlusion treated within a window of 8 hours. The study includes patients ineligible for or with failed IV tPA after bridging therapy or thrombectomy as initial treatment. The primary outcomes are recanalization rate of the target vessel to Thrombolysis in Cerebral Infarction \( \geq 2 \) and safety. Secondary outcomes are recanalization time and modified Rankin Scale at 90-day follow-up. First results can be expected mid-2012.

The promising advances in SR compared with previous MT approaches is its reported high recanalization rate and marked reduction in recanalization time. Furthermore, it appears that the high recanalization rate ultimately correlates with a marked elevation in the rate of favorable clinical outcomes.

**Discussion**

Rapid restoration of cerebral blood flow is the principle goal of ischemic stroke therapy and is associated with better clinical outcome and reduced mortality rate after acute stroke. MT is performed using a variety of endovascular recanalization techniques, which have undergone rapid evolution in recent years. Nevertheless, current endovascular stroke treatment remains a multimodal approach combining the advantages of different MT techniques often in conjunction with IAT. Concerning the severity of intracranial complications, endovascular recanalization techniques should be reserved to dedicated stroke centers.

The introduction of mechanical approaches has undoubtedly expanded the time window for stroke treatment and broadened the treatment to patients in whom IV tPA or IAT failed or is contraindicated. The future role and true clinical value of MT is hard to predict and even difficult to investi-


gate. The latest results indicate that MT can achieve high recanalization rates in conjunction with short recanalization times and a low-risk device-related severe adverse event. More importantly, recent data show that the increased recanalization rate of MT improves clinical outcome.

Considering the poor recanalization rate and clinical outcome of patients with proximal vessel occlusions and large thrombus burden (eg, tandem occlusions and internal carotid artery termination), MT is likely to become a first-line treatment. On the other hand, due to the delicate intracranial anatomy and the convincing results of IV tPA in peripheral and M2 occlusions, MT is unlikely to expand into this territory.

More large multicenter series are necessary to elucidate the clinical role of MT in the majority of patients with stroke with proximal middle cerebral artery and basilar artery occlusions. Although likely to influence the clinical outcome of the patient after endovascular stroke treatment, to data no commonly accepted peri intervensional protocol exists. Therefore, the use of proximal protection in case of thrombectomy, the application of local anaesthesia versus general anaesthesia as well as additional use of thrombolytic drugs during MT is up to the center’s preferences. Some relevant results will be available soon and to define the peri intervensional protocol (eg, IMS III, SWIFT, and STAR). Unfortunately, due the rapid rate of evolution, the multimodal approach as well as the many different devices introduced to date, any randomized study will be difficult to conduct and is prone to remain incomplete.

**Disclosures**

J.G. is global principal investigator of the STAR trial and a consultant for ev3.

**References**


급성 혈전체증의 가시적 혈전용해와 스테н트 삽입술

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Jan Gralla, MD, MSc; Caspar Brekenfeld, MD; Pasquale Mordasini, MD; Gerhard Schrot, MD

급성 혈전체증은 산업과의 이환율과 사망률의 주된 원인 중 하나이다. 생애 중 뇌졸중이 발생할 위험도는 Framingham 연구에서 따르면 중년의 남성 6명 중 1명, 여성 5명 중 1명에 달한다.1 그 예후는 증상발생부터 혈관재개통(reaten-}
cularization)까지 걸리는 시간, 재관행정(recanalization) 비율, 두개내혈출(intracranial hemorrhage)의 발생 여부 등에 의해 결정된다.2 2,066명의 환자들의 혈전용해 예후를 조사한 52개 연구를 메타분석한 결과에서, 뇌졸중 이후 독립적인 생활을 유지할 확률은 재관행성이 되지 않은 환자에 비해 성공적으로 재관행성이 된 환자에서 4.4배 증가했고, 사망률은 4배 감소했다.3

정맥내 조직플라스미노거렌활성제(IV tPA) 치료는 국소적 동맥내 혈전용해(intra-arterial thrombolysis, IAT)치료는 두 가지 모두 환자의 예후를 증가하는 것으로 확인되었다. 그러나 치료의 시간적 제한이 있으며, 두 가지 치료의 재관행성 비율 또한 제한적이다.4,5 그리고 혈전용해제의 투여는 증상성 두개내혈출(symptomatic intracranial hemorrhage, sICH)의 위협을 증가시킨다.2 재관행성의 성공은 폐색 부위가 어딘지에 영향을 받는데, 내경동맥과 같은 대혈관의 근위 폐색은 IV tPA나 IAT를 시행해도 재관행성이 줄지 않다.6,7

최근에는 기계적 재관행성 기술이 재관행성 과정을 가속화하고, 재관행성률을 증가시키고, 심지어 치료방법을 기회를 넓힐 수 있는지 여부에 대한 연구들이 진행되고 있다. 본 논문에서는, 각각 다른 기계적 혈전용해(mechanical thrombolysis, MT)와 스테н트 삽입술 그리고 이러한 혈관내 시술을 통해 재관행성을 시도할 때의 작업 원칙의 발전에 대해 기술하고, 급성 뇌졸중 치료 이후의 예후 결과를 검토하였다.

기계적 혈전용해

기계적 혈전용해(MT)에는 다양한 방법과 접근방법이 있으
며 이는 3가지로 분류할 수 있다: 이는 혈전을 부수는 것, 자가
팽창스테트를 사용하여 즉각적으로 혈류를 복구시켜 주는 것, 그리고 혈전제거술이다.

Thrombus disruption

Pro-Urokinase for Acute Cerebral Thromboembolism-2 (PROACT II) 연구에서, IAT는 혈전의 근위부 표면에 섬유소
소용해 약물은 국소적으로 투여하는 것으로 이루어졌으며, 기
계적으로 혈전을 부수는 것은 연구프로토콜에서 금지했다.

혈전을 부수기 위한 방법으로 여러 다양한 방법이 제시되어
았다. 가장 혼란 된 것은 미세웨어(microwire), 미세카테터(mi-
crocatheter)를 혈전 속으로 또는 혈전 내로 통과시키는 것
이다.6 IAT 중에 시행되는 이 간단한 기계적 시술은 Throm-
bolysis in Myocardial Infarction score≥26 또는 Throm-
bolysis in Cerebral Infarction score≥26의 상당한
재관행성 비율을 증가시킨 것으로 나타났다. 증매동맥 폐
색의 경우, 79%에서 성공적으로 재관행성이 일어났다고 보고
되었으며,10 이에 반해 PROACT II 연구결과에서는 재관행성
율이 66%였다.11

다양한 연구에서 경피적 풍성관관절이동술이 혈전의 표면을
던지고 재관행성을 증가시킬 때 효과가 있음을 보였다.11,12
최대 규모의 연구는 M1 폐색을 보인 환자에서 경피적 풍성
관관절이동술을 일차치료로 받은 34명의 환자6와 IAT만 시행 받
은 36명의 환자를 비교한 연구이다(평균 National Institutes
of Health Stroke Scale (NIHSS), 16). 91.2%에서 충분한
정도의 재관행성이 이루어졌고 (versus 63.9%), 90일 후 mod-
ified Rankin Scale (mRS)가 2점 미만으로 좋은 임상적 예후
급성 혈관 폐쇄와 관련된 시술 중 혈종과 외부 부재 발생을 위한 이 방법은 단순 투명한 영역으로서, 다양한 디자인의 스테트가 급성 뇌혈증에서 성공적으로 임상적 문제를 해결했다. 자가행성 스테트(self-expendable stents, SES) 중 일류인 스테트(ballon-mounted stents)보다 더 선호된다. 급성 두개혈관 폐쇄 치료 시 스테트를 사용한 에비리 연구결과는 증례보고와 구구부 중증시리즈에 있다.

Levy 등은 급성 뇌졸중 화자 18명에서(평균 NIHSS, 18) 79%의 성공적인 재판정성을 보고했다. 그리고 이 연구에서 SES의 삽입은 다른 다양한 혈관 내 치료 간섭과 함께 사용되어 33.3%에서 90일 mRS ≤ 2의 중간 정도 임상예후를 보였다. Brekenfeld 등은 12명의 급성 혈관 복구 증후군 화자(평균 NIHSS, 14)를 SES로 치료하되, 이들 중 7명은 스테트 삽 입 이전에 IAT의 기계적 혈전제거가 실패한 경우였다. 92%에서 성공적으로 재판정성을 이루었으며, 50%에서 중간 정도의 임상 예후를 나타내었고, sICH은 없었다.

비슷하게, Linfrante 등은 19명의 뇌졸중 화자에서(평균 NIHSS, 19) 동맥내혈전제거, 기계적 혈전제거술이 실패한 이후 SES를 적용하였다. 95%에서 페쇄부위가 성공적으로 재판정 되었고, 좋은 임상예후는 42%에서 확인되었다. 시술 중 혈종과 발생하지 않았고, sICH은 16%에서 나타났다.

Stent-Assisted Recanalization in Acute Ischemic Stroke (SARIS) 시험은 급성 뇌졸중 치료에서 스테트 삽입술을 시험하는 연구로, 처음으로 미국 심장학의 출판을 받은 간호적 시험이다. 뇌졸중 화자 20명(평균 NIHSS, 14)에 증상발 생 6시간 이내에 치료를 받았다. 모든 화자에서 치료 후 대사 혈관이 재판정되었다. 혈관형성, IAT, 그리고 IV tPA를 포함한 추가적 치료가 63.2%에서 받아졌다. 60%의 화자에서 1개월, 6개월 이후 중간 정도의 임상 예후를 보인 것으로 보고되었다. 25, 27

뇌졸중 화자에서 SES를 적용한 모든 연구에서 재판정율이 대개 매우 높았지만, 급성 혈관 복구에서 스테트 삽입술이 임상치료법으로서 사용될 수 있지만 일부에 대해서는 두개내 스테트 삽입술과 관련된 위험과 최근 혈전제거술의 성 공적 사례보고 등으로 인해 논란의 여지가 있다. 그러나 스테트 삽입술이 일부 선택적 증례에서는 효과가 있음을 분명히 하였다.
전체 혈전 제거술
모든 기계적 혈전제거술 기구는 혈관내 치료를 통해 폐색부위의 원위부로 접근하게 됩니다. 다양한 기구들은 혈전의 어느 부분에서 작용되느냐에 따라 3가지로 분류됩니다.

근위부기구는 혈전의 근위부에 적용됩니다. 이 종류에는 다양한 혈인 카테터와 시스템이 포함됩니다.

원위부기구는 혈전의 원위부에 도달한 다음 미세카테터를 혈전을 통과한 후 혈전의 원위부에 영향을 주는 것이다. 이 종류에는 brush-like, basket-like, coil-like 기구들이 포함됩니다.

장기 근위부에 개발된 기구에는 stent-like 기구가 포함되는 데, 이는 폐색된 부위를 관통하여 혈전내에 위치시킨 다음 다시 회수하는 것으로, 여러 종류의 자가 평창성 스텔트 혈전제거기(self-expandable stent retrievers, SRs)가 있다.

혈전 흡인과 근위부 혈전제거술
급성 뇌졸중 치료에서 처음으로 보고된 기계적 혈전제거술은 혈전 카테터를 사용한 것이었다. 공수 미세 카테터(4~5 Fr)를 혈전의 근위부 표면까지 접근시킨 후 60~180 μm 주사기를 이용하여 흡인력을 적용시킨다. 혈전이 압박되는 여부는 역류가 없는 것으로 확인된다. 이후 지속적으로 응압(negative pressure)을 주어 혈전이 다시 빠져나가는 것을 막으면서 도관을 빼낸다. 혈전조각을 회수하는 과정이 반복된다.

혈전 제거하기 쉽게 쉽고, 빠르고, 비용도 적게 든다. 이 방법인 혈전 내장이 넓고 해부학적으로 가구의 조장이 용이할 때, 특히 근위부 폐색(예를 들어 정 박 내경동맥의 원위부나 내경동맥의 끝부분) 시에 널리 사용된다.

반응형 시스템
반응형 시스템(Penumbra, Alameda, CA)은 근위부 혈전제거기술이 개량된 것이다. 기계적 혈전을 부수면서 지속적으로 혈착하는 방법이며, 2007년에 뇌졸중 치료 시 혈전제거방법으로 미국 심약청의 승인을 받았다.

다양한 크기(0.26~0.51 inch)의 재판류 카테터를 혈전의 근위부 표면에 위치시킨 후 지속적으로 혈진을 할 수 있도록 혈관 펌프로 연결시킨다(-700 mm Hg). 혈관 카테터의 막히는 것을 방지하기 위해, 물방울 모양의 분리기물의 대부분에 장착된 미세와이어에 의해 추가적으로 혈전을 부수는 과정이 진행된다(Figure 1). 이러한 설정은 재판류형 시술을 시행하는 동안에 카테터의 끝부분의 혈전조각을 제거할 수 있게 한다.

이의 목적은 근위부부터 원위부에 이르기까지 혈전의 부피를 줄여는데 있으며, 이로 인해 작은 도관으로 M2 분절과 같은 원위부 분지에서도 혈전제거술을 시행할 수 있다.

반응형 시스템은 많은 단일기관연구 및 다기관임상연구에서 시험이 이루어졌다. Penumbra Pivotal Stroke Trial은 125 명의 뇌졸중환자(평균 NIHSS, 18)에서 중상발생 이후 8시간내에 치료를 시행한 전향적 연구이다. 대상 혈관의 재판류성률은 81.6%였다. 이 연구에서는 기계적 재판류형 방법인 IV tPA를 부여받은 환자의 비율은 연급하지 않았다. 성공적인 재판류형에도 불구하고 임상 예후는 낮았는데, 좋은 임상예후가 단지 전체 환자의 25%, 성공적으로 재판류형이 이루어진 환자의 29%에서 확인되었다. siCH의 비율은 12.2%였고, 전체 사망률은 32.8%였다. 이상의 부작용이 증례의 3.2%에서 발생했다.

이 연구에서 나타난 높은 재판류성률과 나은 임상 예후는 기계적 혈전제거술의 가치에 대한 논의로 이어졌다. 그러나 일부 단일기관 연구에서는 반응형 시스템을 사용해서 Pivotal Trial에서보다 더 좋은 임상 결과를 보고하였다. Kulcsar 등은 27명의 대혈관폐색 환자(평균 NIHSS, 14) 증례시리즈를 보고하였다. 평균 시술시간은 60분이었으며(16 시간), 93%에서
영어로의 번역을 제공할 수 없습니다.
devices는 IMS-III 연구에서 현재 시험중이다. 39

Stent Retriever
기구 원치에 소개된 급성 뇌출혈 치료를 위한 기계적 혈전제거 기구는 자기가재적, stent-like 혈전제거기구이다. 영구적으로 스테인트를 삽입해놓을 필요 없이 즉각적인 혈류개선과 혈중구의 확실한 혈전제거의 이득을 얻을 수 있도록 일시적 스테인트 삽입과 확실한 혈전제거의 장점과 함께, SR device가 급성 허혈뇌졸중의 새로운 유망한 치료방법으로 제시되었다. 이 기구는 두개내 스테인트와 비슷한 방법으로 적용된다. 미세카테터(내경 0.21-0.27-inch)가 패착부위를 통과한 후, SR이 혈전체를 담겨 된다. SR의 방사력(radial force)가 즉시 혈전을 압박하고 동료를 만들어 원위부로의 혈류를 복원시킨다. 이 시점에서 추가적인 IAT가 시도될 수 있다. 3~10분간의 스테인트를 넣은 후, 서서히 스테인트를 빼낸다. 원위부 기구와 마찬가지로, 스테인트를 빼는 동안 근위부를 풍선을 이용하여 패색시키고 가이드카테터를 사용해서 흉유함으로써 혈류를 역행시키는 것이 가능한 것이다.

이를 변형한 많은 기구들이 현재 개발 중이나 첫 임상 시험중에 있다(TREVO, Concentric Medical, Mountain View, CA; PULSE, Penumbra, Alameda, CA; ReVive, Micrus, CA).

급성 뇌출혈 치료를 위해 혈류 복원 및 혈전제거 전용으로 개발된 기구는 Solitaire FR (ev3, Irvine, CA: Figure 3)이다. 이는 두개내 광경동맥류(wide-neck intracranial aneurysms)의 스테인트 보조 치료를 위해 개발된 Solitaire AB Neurovascular Remodeling Device를 보완한 것이다. 빠른 기간 동안, 뇌졸중 치료를 위해 Solitaire FR를 생애내 실험, 또는 임상에 적용시킨 많은 연구들이 보고되었다.

Castano 등은 2010년에 증상발생 8시간 이내의 급성 뇌졸중 환자 20명에서 초기 경과를 보고하였다. 90%에서 성공적으로 재활원성이 이루어졌고, 평균 시술시간은 50분이었다. 48%에서 좋은 임상 예후를 나타내었고, siICH는 10%에서 발생했다. SR을 사용한 다른 소규모 증례연구에서도 비슷한 정도의 성공적인 재활원성을 보였으며(88-91%), 빠른 시술시간(42-55분), 그리고 비슷한 정도의 좋은 예후(42-54%) 보였다.16,39

지금까지 시행된 것 중 최대 규모의 연구는 이러한 결과를 요약한 결과를 보였다. 유럽의 6개 대형 뇌졸중센터의 증례를 후향적으로 모아, 실질환부(경도경색 27%, 중단뇌경색 59%)와 후속환부(14%) 폐색으로 인한 급성 뇌졸중 환자 141명(평균 NIHSS, 18)의 치료결과를 보고했다. 재활원성까지 걸린 평균 시간은 45분이었고, 대상 환자의 86%에서 Thrombolysis in Cerebral Infarction ≥2b의 결과를 보였다. 좋은 임상 예후는 환자의 55%에서 관찰되었고, 전체 사망률은 20.5%였다. 39

현재 두 개의 대규모 임상연구결과를 기대하는 증례이다. SWIFT trial(Solitaire FR with the Intention for Thrombectomy)은 Solitaire FR system을 MERCI device와 비교하여 효과와 안정성 비교를 연구한다. 연구에 포함된 환자들은 IV tPA가 불가능하거나 실패한, 증상발생 8시간 이내의 환자들이다. 임차결과자료는 박리 혈전이 Thrombolysis in Myocardial Infarction ≥2로 재활원성되는 것이다. 이차결과자료는 재활원성까지 시간, 추적관찰 90일제의 mRS 점수이다. SWIFT 연구는 예정된 250명의 환자가 포함되기 전, 126명의 환자가 연구에 포함된 2011년에 자료관리위원회(data monitoring board)에 의해 조기종료되었다. 아직 결과는 발표되지 않았으나 Solitaire FR의 좋은 결과가 기대되고 있다.

Solitaire FR는 현재 STAR Trial (Solitaire FR Thrombectomy for Acute Revascularization)에서 연구되고 있다. 이는 전형적, 국제적, 단일군 시험으로 증상발생 8시간 이내에 치료가 시행될 수 있는 200여의 전신환부 뇌출혈 환자를 포함하는 것을 목표로 한다. 초기치료로서 IV tPA가 불가능하거나 연계치료후 IV tPA에 실패했거나, 기계적 혈전제거술에 실패한 환자를 포함한다. 임차 결과자료는 대상 환간 Thrombolyis in Cerebral Infarction ≥2b로 재활원성 되는 것과 안전성이다. 이차결과자료는 재활원성까지 걸리는 시간과 추적검사 90일 이내의 mRS 점수이다. 첫 결과가 2012년 중반에 나오는 것으로 기대하고 있다.

이전의 기계적 혈전용해와 비교하여 SR의 유망한 발전방향은 높은 재활원성률을 보이는 것과 재활원성 시간이 주목할 만큼 감소했다는 점이다. 또한, 높은 재활원성률이 과학적으로 좋은 임상 예후를 나타내는 비율의 두桁한 증가와 연관한다는 것이다.

토의

avicon은 환혈뇌졸중 치료의 주된 목표이며, 이는 좋은 임상 예후와 연관되고 급성 뇌졸중 이후의 사망률을 감소시킨다. 기계적 혈전용해는 다양한 혈관내 재활원성 기술을 사용해서 이루어지며, 최근 수년간 빠른 발전이 이루어져왔다. 그럼에도 불구하고, 현재의 혈관내 뇌졸중 치료는 여전히 각기 다른 기계적 혈전용해의 이점을 중합한 다각적 방법으로 이루어지고 중증 IAT와 함께 사용된다. 두개내 혈관내의 심각성을 고려할 때, 혈관내 치료를 통한 재활원성율은 특정 뇌졸중센터에 국한되어 시행되어야 한다.

기계적 접근방법의 시도는 뇌졸중 치료에 있어서 시간적 제한을 넘어서고, IV tPA나 IAT가 실패했거나 불가능한 환자의 치료가능도 늘려줄 수 있다는 점에는 의심할 여지가 없다. 기계적 혈전용해의 미래의 역할과 실제 임상에서의 가치는 예측

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Disclosures
J.G. is global principal investigator of the STAR trial and a consultant for ev3.

References


KEY WORDS: acute stroke ■ angioplasty & ■ stenting ■ endovascular treatment ■ interventional neuroradiology ■ mechanical thrombectomy ■ stroke management ■ thrombolysis