



Akut İskemik İnmede Endovasküler Tedavi Yönetimi

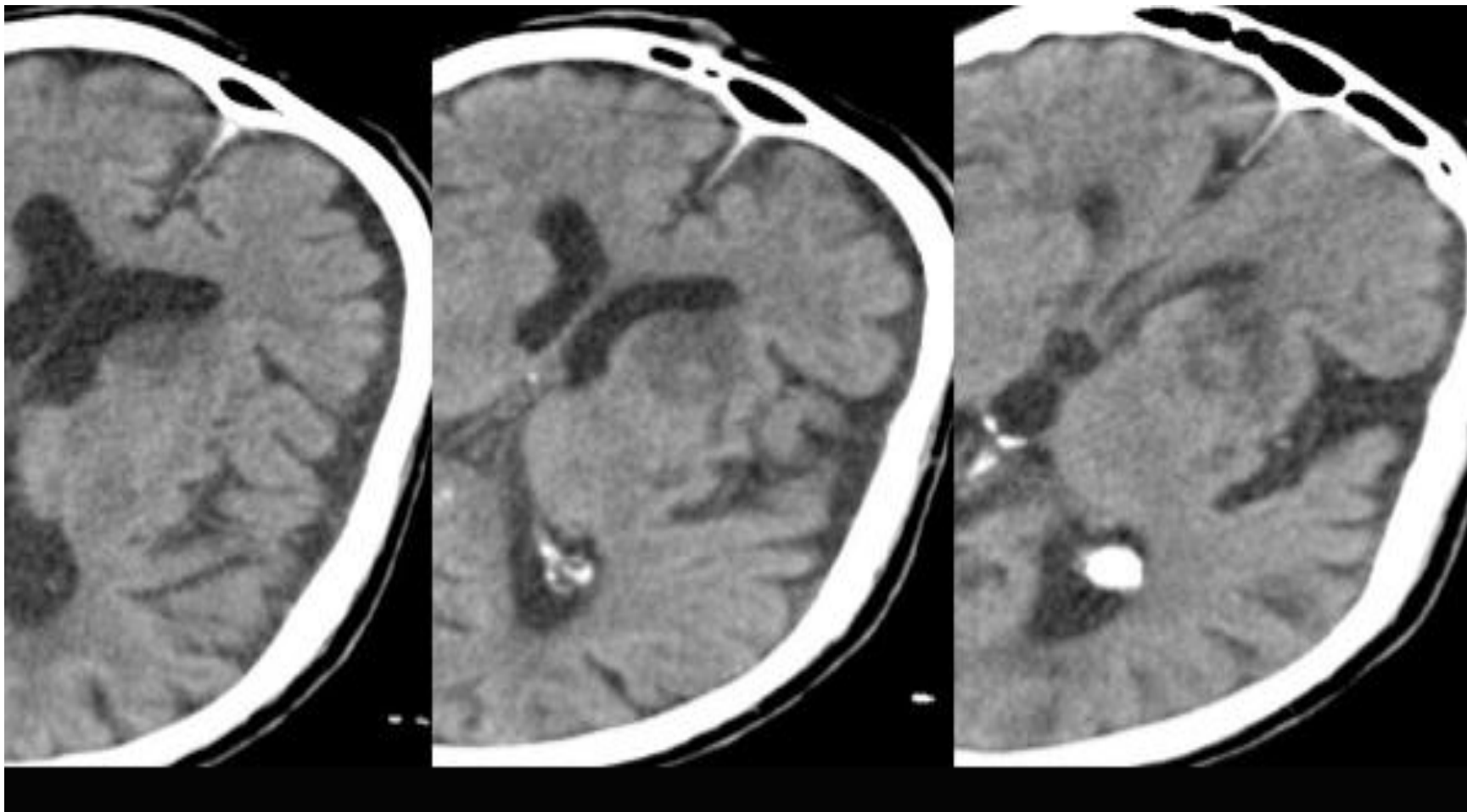
DR. OKAN YILDIRIM

TURGUT ÖZAL TIP MERKEZİ RADYOLOJİ ABD.

Vaka (video)

- 82 Yaşında erkek hasta
- Olay- Kapı: 80 dk
- Kapı-İlaç: 60 dk
- Endovasküler kasık girişi: 210. dk
- Kasık giriş- rekanalizasyon: 65 dk.
- Geliş NIHSS: 18
- ASPECT: 7

Kaudat nukleus-Lentiform nukleus-İnsular korteks hipodansite: ASPECT 7

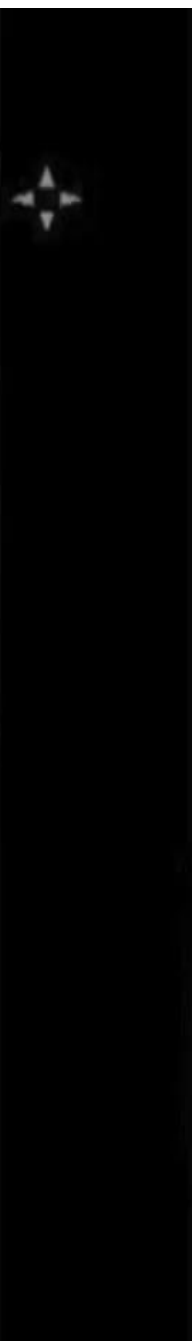


İnternal karotis arterde preokluziv darlık, MCA total okluzyon



97
2018
2018

0.0







- Trombektomi sonrası 1. gün MCA sulama alanlarında hipodansite yok. Posteriopariatel düzeyde asemptomatik hiperdens SAK ile uyumlu dansite artışı

İnme neden önemli?



- Türkiye’de 3. sıradaki ölüm sebebi-1. sıradaki sakatlık nedeni
- DSÖ(2004- nüfus 69 milyon) mevcut hasta sayısı 1.2 milyon
- Yıllık yeni hasta sayısı 152 bin
- Türkiye’de minör inme için kişi başı 200 TL, majör inme geçiren bir hasta için ise yaklaşık maliyet 20-40 bin TL
- Sosyal problem ve iş gücü kaybı



Time Is Brain—Quantified

Jeffrey L. Saver, MD



Stroke: Time is brain

Background and Purpose—The phrase “time is brain” emphasizes that human nervous tissue is rapidly lost as stroke progresses and emergent evaluation and therapy are required. Recent advances in quantitative neurostereology and stroke neuroimaging permit calculation of just how much brain is lost per unit time in acute ischemic stroke.

Methods—Systematic literature-review identified consensus estimates of number of neurons, synapses, and myelinated fibers in the human forebrain; volume of large vessel, supratentorial ischemic stroke; and interval from onset to completion of large vessel, supratentorial ischemic stroke.

Results—The typical final volume of large vessel, supratentorial ischemic stroke is 54 mL (varied in sensitivity analysis from 19 to 100 mL). The average duration of nonlacunar stroke evolution is 10 hours (range 6 to 18 hours), and the average number of neurons in the human forebrain is 22 billion. In patients experiencing a typical large vessel acute ischemic stroke, 120 million neurons, 830 billion synapses, and 714 km (447 miles) of myelinated fibers are lost each hour. In each minute, 1.9 million neurons, 14 billion synapses, and 12 km (7.5 miles) of myelinated fibers are destroyed. Compared with the normal rate of neuron loss in brain aging, the ischemic brain ages 3.6 years each hour without treatment. Altering single input variables in sensitivity analyses modestly affected the estimated point values but not order of magnitude.

Conclusions—Quantitative estimates of the pace of neural circuitry loss in human ischemic stroke emphasize the time urgency of stroke care. The typical patient loses 1.9 million neurons each minute in which stroke is untreated. (Stroke. 2006;37:263-266.)

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Table 5. ED-Based Care

	Action	Time
William	Door to physician	≤10 minutes
Nicholas	Door to stroke team	≤15 minutes
Michael	Door to CT initiation	≤25 minutes
	Door to CT interpretation	≤45 minutes
Thomas	Door to drug (≥80% compliance)	≤60 minutes
	Door to stroke unit admission	≤3 hours

David L. Tirsch
CT indicates computed tomography; and ED, emergency department.
Source: Bock.⁹⁶

- Kapı-hekim ≤10 dk
- Kapı-inme takımı ≤15 dk.
- Kapı-BT çekilmesi ≤25 dk.
- Kapı-BT yorumlanması ≤45 dk.
- Kapı-ilaç (≥%80 uyum) ≤60 dk
- Kapı-inme ünitesine yatış ≤3 sa

Reperfüzyona tedavisine karar verme



- Hasta en son iyi olduğu zaman (IV r-tPA verebilir miyim?)
- Nörolojik muayene (NIHSS)
- Herhangi bir ciddi hastalık öyküsü (IV r-tPA verebilir miyim?)
- Kan şekeri seviyesi (hipoglisemik atak olabilir mi?)
- Kan basıncı(IV r-tPA verebilir miyim?)
- Beyin Bt görüntüleme (IV r-tPA verebilir miyim?)

İV r-tPA endikasyon-kontrendikasyonları

IV tPA Verilmez

Daima dışlama kriteri

- ☐ Tedaviye semptom başlamasından sonraki 4,5 saat içinde başlanamayacak ise
- ☐ Görüntülemede herhangi bir tip akut (intraserebral, subaraknoid, subdural) kanama
- ☐ BT'de demarke ve geniş hipodansite
- ☐ Sistolik kan basıncı >185 mmHg veya diastolik kan basıncı >110 mmHg
- ☐ Trombositopeni (<100 bin/mm³)
- ☐ INR $>1,7$
- ☐ aPTT >40 sn

İV r-tPA endikasyon-kontrendikasyonları

Göreceli (Bazı şart/durumlarda) dışlama kriteri ama hastaların çoğu için IV tPA uygundur.

- ☐ Başlangıç zamanının belirlenememiş olması
- ☐ Uyanma esnasında farkedilen inme
- ☐ Son 3 ay içinde kraniyo/spinal cerrahi
- ☐ Son 3 ay içinde kraniyo/spinal travma
- ☐ Son 3 ay içinde iskemik inme
- ☐ Son 3 hafta içinde gastrointestinal kanama
- ☐ Son 3 hafta içinde genitoüriner kanama
- ☐ Son 3 hafta içinde majör cerrahi
- ☐ Son 2 hafta içinde majör sistemik travma
- ☐ Son 1 hafta içinde komprese edilemeyecek arterlere ponksiyon
- ☐ İntrakraniyal kanama öyküsü

- ☐ NOAK (non-Vitamin K antagonisti oral anti koagülan) kullanımı (son 48 saatte)
- ☐ Son evre böbrek yetmezliği, diyaliz
- ☐ İleri karaciğer yetmezliği, siroz
- ☐ Aort diseksiyonu
- ☐ İnfektif endokardit
- ☐ Sistemik malignite
- ☐ İntrakraniyal intraaksiyel tümör veya kitle
- ☐ İntrakraniyal AVM
- ☐ Yaygın ön duvar ST elevasyonlu miyokard infarktüsü
- ☐ Perikardit
- ☐ Son 7 gün içinde dural ponksiyon

İV r-tPA endikasyon-kontrendikasyonları

IV tPA Verilir

Dışlama kriteri değildir.

- ☐ BT'de hiperdens arter işareti
- ☐ Minör inme (NIHSS <5)
- ☐ Majör inme (NIHSS >22)
- ☐ Hızlı düzelen hasta
- ☐ İnsidental intrakraniyal anevrizma
- ☐ Ekstra-aksiyel intrakraniyal tümör
- ☐ Serviko-kraniyal arter diseksiyonu
- ☐ İleri yaş (>80 yıl)
- ☐ Demans
- ☐ Epileptik nöbet

- ☐ İnme öncesi mobilitayı engellemeyen özürllük
- ☐ Hiperglisemi
- ☐ Hipoglisemi
- ☐ Menstrüel kanama
- ☐ Hamilelik
- ☐ Akut miyokard infarktüsü (non-STEMI, posterior veya inferior STEMI)
- ☐ İntrakardiyak trombus
- ☐ Son 7 gün içinde dural ponksiyon
- ☐ Son 7 gün içinde aspirin ve/veya klopidoğrel kullanımı
- ☐ IV heparin kullanımı (son 24 saatte, aPTT <40 sn)
- ☐ Düşük molekül ağırlıklı heparin kullanımı (son 24 saatte, aPTT <40 saniye, anti-faktör Xa normal)

Radyolojik Değerlendirme

- Genel kabul olarak, orta serebral arter sulama sahasının 1/3'ünden daha fazla bölgede hipodansite saptanması yüksek kanama riski nedeniyle revaskülarizasyon için kontrendikedir.

Markers of Increased Risk of Intracerebral Hemorrhage After Intravenous Recombinant Tissue Plasminogen Activator Therapy for Acute Ischemic Stroke in Clinical Practice

The Multicenter rt-PA Acute Stroke Survey

David Tanne, MD; Scott E. Kasner, MD; Andrew M. Demchuk, MD; Nira Koren-Morag, PhD; Sandra Hanson, MD; Martin Grond, MD; Steven R. Levine, MD; and the Multicenter rt-PA Stroke Survey Group*

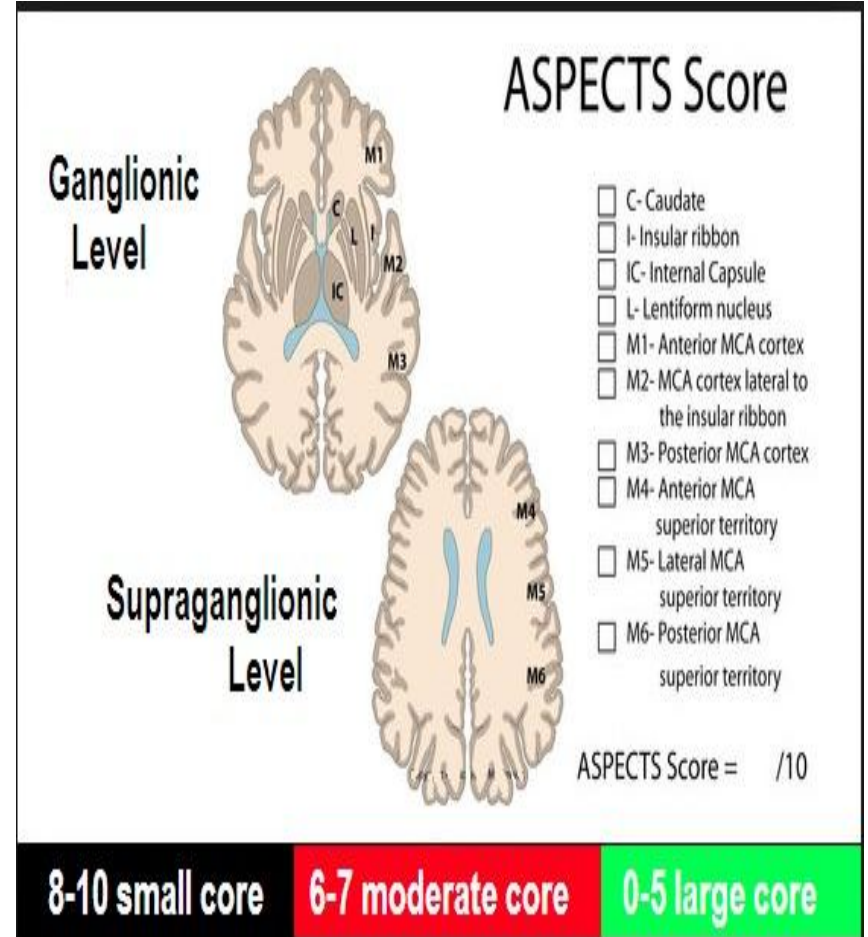
Background—Intravenous recombinant tissue plasminogen activator (rtPA) is an effective therapy for acute ischemic stroke, but it is associated with risk of intracerebral hemorrhage (ICH). Our aim was to identify, in a large cohort of patients, readily available baseline factors that are associated with thrombolysis-related ICH.

Methods and Results—In a multicenter retrospective and prospective investigation of individual data from 1205 patients treated in routine clinical practice with intravenous rtPA within 3 hours of stroke symptom onset, 72 patients (6%) developed symptomatic ICH and 86 additional patients (7%) had ICH. The rate of symptomatic ICH was more than doubled in patients with minor (<33% of MCA territory) early ischemic changes and more than 4-fold higher in patients with major (>33%) changes compared with those without early ischemic changes. Higher levels of serum glucose and lower platelet counts were associated with increasing rate of ICH (Figure 1).

1679-1685.)

ASPECT

- İskemik inmede erken BT bulgularının değerlendirmesinde oluşabilecek bu karışıklıkları önlemek ve objektif değerlendime yapabilmek için Alberta Stroke Programme Early CT (ASPECT) skoru hesaplanması kullanılır.
- Bu skor hesaplanırken BT incelemesi üzerinde orta serebral arter sulama alanı 2 aksiyel kesitte değerlendirilir.



Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy

THE LANCET • Vol 355 • May 13, 2000

Philip A Barber, Andrew M Demchuk, Jinjin Zhang, *et al*

Test	Functional outcome					Symptomatic haemorrhage				
	Independent	Dependent or dead	Sensitivity	Specificity	Odds ratio (95% CI)	Yes	No	Sensitivity	Specificity	Odds ratio (95% CI)
NIHSS										
≤15 (n=81)	56	25	0.69	0.76	6.8 (3.4-14)	6	75	0.40	0.52	0.7 (0.2-2.7)
>15 (n=73)	18	55				4	69			
ASPECTS										
≤7 (n=89)*	71	18	0.78	0.96	82 (23-290)	1	90	0.90	0.62	14 (1.8-117)
>7 (n=65)	3	62				9	56			
MCA rule										
≤1/3 (n=89)*	67	22	0.73	0.91	25 (10-63)	1	90	0.90	0.62	14 (1.8-117)
>1/3 (n=65)	7	58				9	56			

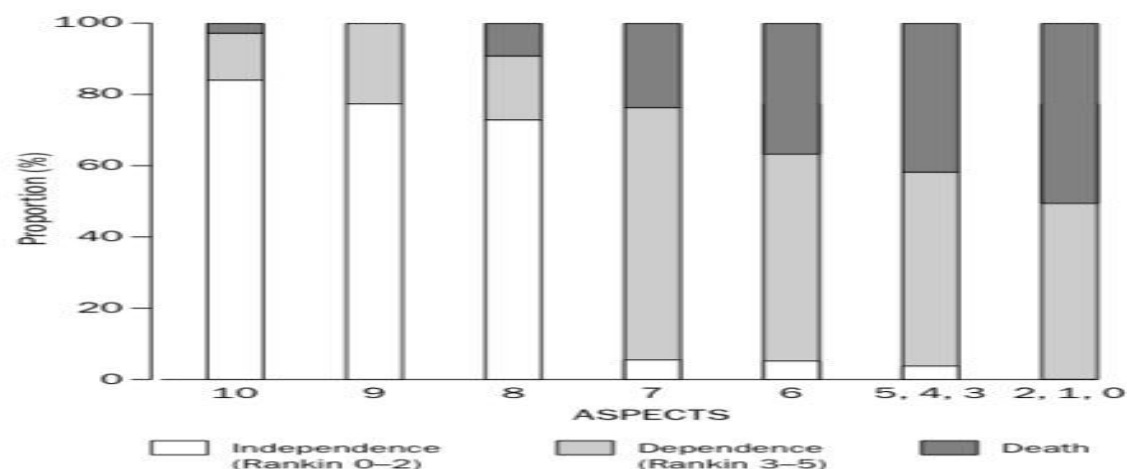


Figure 2: ASPECTS and functional outcome
Spearman correlation coefficient -0.69 , $p < 0.001$.

κ statistic for agreement between two observers

	Stroke neurologists	Radiology trainees	Experienced neuroradiologists
Without knowledge of clinical information			
Evidence of early ischaemia	0.25	0.52	0.20
Side of lesion	0.34	0.58	0.35
Evidence of focal brain swelling	0.25	0.41	0.36
≤1/3 vs >1/3 MCA	0.49	0.14	0.37
ASPECTS ≤7 vs >7	0.69	0.39	0.47

With knowledge of affected hemisphere

Evidence of early ischaemia	0.45	0.34	0.33
Evidence of focal brain swelling	0.24	0.23	0.42
≤1/3 vs >1/3 MCA	0.61	0.64	0.52
ASPECTS ≤7 vs >7	0.85	0.71	0.89

Table 2: Assessment of agreement between observers

İskemik İnmede İv-r tPA Etkinliği

Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials

Jonathan Emberson*, Kennedy R Lees*, Patrick Lyden*, Lisa Blackwell, Gregory Albers, Erich Bluhmki, Thomas Brodt, Geoff Cohen, Stephen Davis,

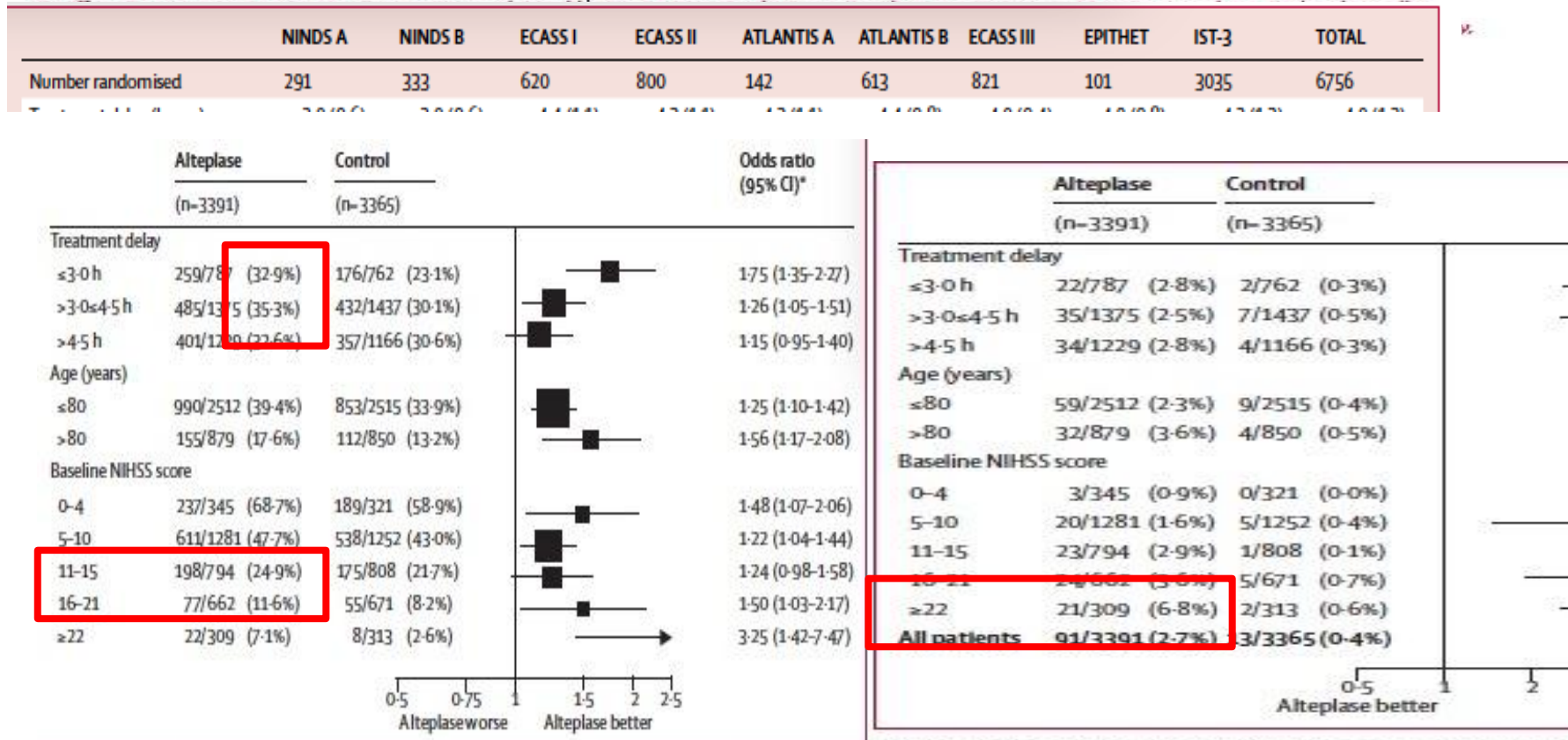


Figure 2: Effect of alteplase on good stroke outcome (mRS 0-1), by treatment delay, age, and stroke severity

Figure 4: Effect of alteplase on fatal intracranial haemorrhage

The Importance of Size

Successful Recanalization by Intravenous Thrombolysis in Acute Anterior Stroke Depends on Thrombus Length

Christian H. Riedel, MD; Philip Zimmermann, MD; Ulf Jensen-Kondering, MD; Robert Stinge, MD; Günther Deuschl, MD; Olav Jansen, MD

Background and Purpose—We hypothesize that in acute middle cerebral artery stroke, thrombus lengths measured in thin-slice nonenhanced CT images define a limit beyond which systemic thrombolysis will fail to recanalize occluded arteries.

Methods—In 138 patients who presented with acute middle cerebral artery stroke and who were treated with intravenous thrombolysis (IVT), we measured lengths of thrombotic clots depicted as arterial hyperdensities in admission nonenhanced CT images with 2.5-mm slice width. Vascular recanalization was investigated after thrombolysis and recanalization results were related to thrombus lengths by logistic regression.

Results—In 62 patients, IVT resulted in recanalization; among these patients, no thrombus length exceeded 8 mm. The median modified Rankin scale score at hospital discharge was 2. In the remaining 76 patients, thrombus lengths mostly exceeded 8 mm and IVT failed in recanalization. These patients were discharged with a median modified Rankin scale score of 5.

Conclusions—This study shows that in acute middle cerebral artery stroke, IVT has nearly no potential to recanalize occluded vessels if thrombus length exceeds 8 mm. (*Stroke*. 2011;42:1775-1777.)

The Benefits of Intravenous Thrombolysis Relate to the Site of Baseline Arterial Occlusion in the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET)

Deidre A. De Silva, MBBS, MRCP, FAMS; Caspar Brekenfeld, MD; Martin Ebinger, Dr Med, Dr Phil; Søren Christensen, PhD; P. Alan Barber, PhD, FRACP; Kenneth S. Butcher, MD, PhD, FRCPC; Christopher R. Levi, FRACP; Mark W. Parsons, PhD, FRACP; Christopher F. Bladin, MD, FRACP; Geoffrey A. Donnan, MD, FRACP; Stephen M. Davis, MD, FRACP; for the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET) Investigators

Background and Purpose—In ischemic stroke, the site of arterial obstruction has been shown to influence recanalization and clinical outcomes. However, this has not been studied in randomized controlled trials, nor has the impact of arterial obstruction site on reperfusion and infarct growth been assessed. We studied the influence of site and degree of arterial obstruction patients enrolled in the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET).

Methods—EPITHET was a prospective, randomized, placebo-controlled trial of intravenous tissue plasminogen activator (tPA) in the 3- to 6-hour time window. Arterial obstruction site and degree were rated on magnetic resonance angiography blinded to treatment allocation and outcomes.

Results—In 101 EPITHET patients, 87 had adequate quality magnetic resonance angiography, of whom 54 had baseline arterial obstruction. Infarct growth attenuation was greater in those with tPA treatment compared to placebo among patients with middle cerebral artery (MCA) obstruction ($P=0.037$). The treatment benefit of tPA over placebo in attenuating infarct growth was greater for MCA than internal carotid artery (ICA) obstruction ($P=0.060$). With tPA treatment, good clinical outcome was more likely with MCA than with ICA obstruction ($P=0.005$). Most patients with ICA obstruction did not achieve good clinical outcome, whether treated with tPA (100%) or placebo (77%). The study was underpowered to prove any treatment benefit of tPA among patients with any or severe degree of arterial obstruction.

Conclusions—Arterial obstruction site strongly predicts outcomes. ICA obstruction carries a uniformly poor prognosis whereas good outcomes with MCA obstruction are associated with tPA therapy. (*Stroke*. 2010;41:295-299.)

Key Words: arterial obstruction ■ ischemic stroke ■ myocardial infarction ■ thrombolysis

Site of Arterial Occlusion Identified by Transcranial Doppler Predicts the Response to Intravenous Thrombolysis for Stroke

TABLE 1. Clinical Outcomes at 24 Hours and 3 Months and the Recanalization Rates After IV t-PA Treatment

Factors	Proximal MCA	Distal MCA	Tandem ICA/MCA	Terminal ICA	Basilar Artery	P Value
No. (%)	166 (51%)	116 (35%)	22 (7%)	17 (5%)	10 (3%)	
Age (mean ± SD)	69 ± 14	69 ± 13	64 ± 12	70 ± 14	75 ± 10	0.3‡
Baseline NIHSS median (range)	18 (6–32)	13 (3–29)	19 (6–29)	20 (11–28)	27 (7–35)	<0.001†
Complete recanalization ≤2 hours of rt-PA bolus	49/163 (30%)	50/113 (44%)	6/22 (27%)	1/17 (6%)	3/10 (33%)	0.007*
24 hours NIHSS ≤2; no. (%)	24/155 (15.5%)	35/107 (33%)	5/21 (24%)	0/14 (0%)	2/8 (25%)	0.004*
3 months modified Rankin Scale score ≤1; No. (%)	33/131 (25%)	50/96 (52%)	3/14 (21%)	2/11 (18%)	2/8 (25%)	<0.001*
Mortality at 3 months	31/131 (24%)	16/96 (17%)	2/14 (14%)	5/11 (45%)	6/8 (75%)	0.0024*
Symptomatic intracranial hemorrhage	20/166 (12%)	5/116 (4%)	1/22 (5%)	2/17 (12%)	3/9 (33%)	0.018*

İskemik İnmede İv-r tPA Etkinliği

Assessment and Improvement of Figures to Visually Convey Benefit and Risk of Stroke Thrombolysis

Jigneshkumar Gadhia, MD; Sidney Starkman, MD; Bruce Ovbiagele, MD; Latisha Ali, MD; David Liebeskind, MD; Jeffrey L. Saver, MD

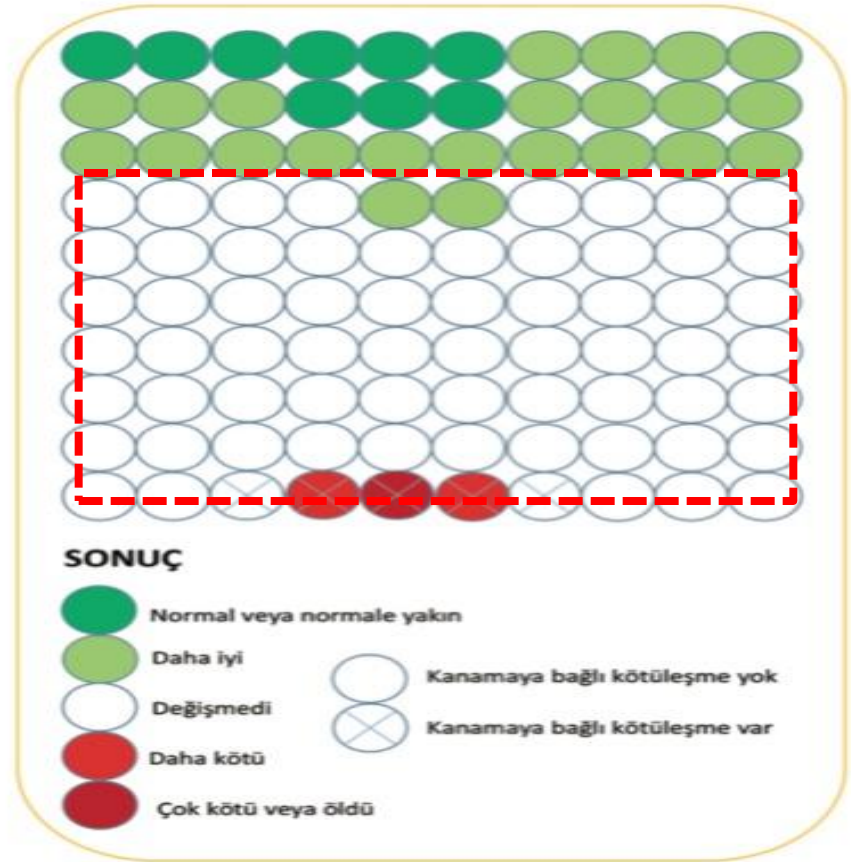
Background and Purpose—Deciding whether to use intravenous fibrinolytic therapy for acute cerebral ischemia within 3 hours of onset is challenging for patients, family members, and health care providers. Visual displays can permit individuals to rapidly understand response patterns to therapy. This study sought to evaluate, refine, and improve existing visual aids for stroke fibrinolytic decision-making.

Methods—Existing visual aids were identified by Medline search and querying of national guideline organizations, pharmaceutical manufacturers, and stroke specialists, and were rated on a formal 8-point quality rating scale (0, lowest; 8, highest). Based on available instruments, new visual displays were developed to improve informed decision-making in routine practice.

Results—Two existing visual aids were identified, one from an emergency medicine society and one from a pharmaceutical company. Both were comparison visual displays of outcomes with and without treatment; no decision matrix visual aid was found. Both scored 4.0 on the quality scale, showing defects of effect size distortion, privileging less salient outcomes, dissimilar representation by treatment group, and limited stakeholder participation in generation. Revised versions of these graphics were developed with higher quality scores (6.75 and 7.75). In addition, a new decision matrix display with quality score 8.0 was developed that complements the numeric text of a national patient education tool developed jointly by US neurology, emergency medicine, and stroke patient organizations.

Conclusion—Existing visual aids for stroke fibrinolysis decision-making have deficiencies. New visual displays are now available to convey the health benefits and risks of fibrinolytic stroke therapy efficiently and informatively to patients and family members. (*Stroke*. 2010;41:300-306.)

İlk 3 saat içinde verilebilen İV tPA'nın sonuçlara olan etkisi



Endovasküler işlemler

- Her ne kadar iv r-tPA akut iskemik inme için en etkili medikal tedavi olsada yeterli rekanalizasyon sağlayamaması tedavi penceresinin darlığı, endovasküler tedavilerin önünü açmıştır.
 1. Lokal İA trombolitik ajan kullanımı
 2. İV ve İA kombine trombolitik ajan kullanımı
 3. Mekanik trombektomi

Lokal İA trombolitik ajan infüzyonu

JAMA. 1999 Dec 1;282(21):2003-11.

Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism.

Furlan A¹, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, Pessin M, Ahuja A, Callahan F, Clark WM, Silver F, Rivera F.

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Abstract

CONTEXT: Intravenous tissue-type plasminogen activator can be beneficial to some patients when given within 3 hours of stroke onset, but many patients present later after stroke onset and alternative treatments are needed.

OBJECTIVE: To determine the clinical efficacy and safety of intra-arterial (IA) recombinant prourokinase (r-proUK) in patients with acute stroke of less than 6 hours' duration caused by middle cerebral artery (MCA) occlusion.

DESIGN: PROACT II (Prolyse in Acute Cerebral Thromboembolism II), a randomized, controlled, multicenter, open-label clinical trial with blinded follow-up conducted between February 1996 and August 1998.

SETTING: Fifty-four centers in the United States and Canada.

PATIENTS: A total of 180 patients with acute ischemic stroke of less than 6 hours' duration caused by angiographically proven occlusion of the MCA and without hemorrhage or major early infarction signs on computed tomographic scan.

INTERVENTION: Patients were randomized to receive 9 mg of IA r-proUK plus heparin (n = 121) or heparin only (n = 59).

MAIN OUTCOME MEASURES: The primary outcome, analyzed by intention-to-treat, was based on the proportion of patients with slight or no neurological disability at 90 days as defined by a modified Rankin score of 2 or less. Secondary outcomes included MCA recanalization, the frequency of intracranial hemorrhage with neurological deterioration, and mortality.

RESULTS: For the primary analysis, 40% of r-proUK patients and 25% of control patients had a modified Rankin score of 2 or less (P = .04). Mortality was 25% for the r-proUK group and 27% for the control group. The recanalization rate was 66% for the r-proUK group and 18% for the control group (P<.001). Intracranial hemorrhage with neurological deterioration within 24 hours occurred in 10% of r-proUK patients and 2% of control patients (P = .06).

CONCLUSION: Despite an increased frequency of early symptomatic intracranial hemorrhage, treatment with IA r-proUK within 6 hours of the onset of acute ischemic stroke caused by MCA occlusion significantly improved clinical outcome at 90 days.

Lokal İA trombolitik ajan infüzyonu

Analysis of the Safety and Efficacy of Intra-Arterial Thrombolytic Therapy in Ischemic Stroke

Rejane C. Lisboa, MD; Borko D. Jovanovic, PhD; Mark J. Alberts, MD

Background and Purpose—Intra-arterial thrombolytic therapy (IAT) may be a treatment option for patients with ischemic stroke. We analyzed the safety and efficacy of IAT on the basis of published data.

Methods—We searched computerized databases for studies using IAT in ≥ 10 patients with ischemic stroke. Some studies had control patients for comparison. Data were collected on age, stroke territory, time to treatment, medication, site of arterial occlusion and recanalization on angiogram, outcomes, and symptomatic intracranial hemorrhage (SICH).

Results—The analysis included 27 studies with 852 patients who received IAT and 100 control subjects. There were more favorable outcomes in the IAT than in the control group (41.5% versus 23%, $P=0.002$), with a lower mortality rate for IAT (IAT, 27.2%; control group, 40%, $P=0.004$). The IAT group had an odds ratio of 2.4 (95% CI, 1.45 to 3.85) for favorable outcome. SICH was more frequent in the IAT group compared with the control group (9.5% versus 3%, $P=0.046$). The subgroup of patients receiving a combination of intravenous thrombolytic therapy and IAT had more favorable outcomes than the IAT alone subgroup, but this trend did not reach statistical significance (53.6% versus 41.5%, $P=0.1$). Among the patients treated with IAT, those who had supratentorial strokes were more likely to have favorable outcomes than those with infratentorial strokes (42.2% versus 25.6%; $P=0.001$; odds ratio, 2.0; 95% CI, 1.33 to 3.0).

Conclusions—IAT for ischemic stroke appears efficacious but carries an increased risk of SICH. Further prospective studies are needed to prove the safety and efficacy of IAT in stroke. (*Stroke*. 2002;33:2866-2871.)

Outcomes	IAT (n=852), %	Control Subjects (n=100), %	OR (95% CI)	P
Favorable outcome	41.5	23	2.4 (1.45–3.85)	0.002
SICH	9.5	3	3.4 (1.05–11.1)	0.046
Death	27.2	40	0.56 (0.36–0.87)	0.004

İV ve İA kombine trombolitik ajan kullanımı

Combined Intravenous and Intra-Arterial Recanalization for Acute Ischemic Stroke: The Interventional Management of Stroke Study

The IMS Study Investigators

Background and Purpose—To investigate the feasibility and safety of a combined intravenous (IV) and intra-arterial (IA) approach to recanalization in patients with ischemic stroke.

Materials and Methods—Subjects ages 18 to 80 with an NIH Stroke Scale (NIHSS) ≥ 10 at baseline had IV recombinant tissue plasminogen activator (rt-PA) started (0.6 mg/kg, 60 mg maximum over 30 minutes) within 3 hours of onset. Additional rt-PA was then administered via microcatheter at the site of the thrombus up to a total dose of 22 mg over 2 hours of infusion or until thrombolysis. Primary comparisons were with similar subsets of placebo and rt-PA-treated subjects from the NINDS rt-PA Stroke Trial.

Results—The 80 subjects had a median baseline NIHSS score of 18. The median time to initiation of IV rt-PA was 140 minutes as compared with 108 minutes for placebo and 90 minutes for rt-PA-treated subjects in the NINDS rt-PA Stroke Trial. The 3-month mortality in Interventional Management Study (IMS) subjects (16%) was numerically lower but not statistically different than the mortality of placebo (24%) and rt-PA-treated subjects (21%) in the NINDS rt-PA Stroke Trial. The rate of symptomatic intracerebral hemorrhage (6.3%) in IMS subjects was similar to that of rt-PA-treated subjects (6.6%) but higher than the rate in placebo-treated subjects (1.0%, $P=0.018$) in the NINDS rt-PA Stroke Trial. IMS subjects had a significantly better outcome at 3 months than NINDS placebo-treated subjects for all outcome measures (odds ratios ≥ 2).

Conclusions—A randomized trial of standard IV rt-PA as compared with a combined IV and IA approach is needed. (Stroke. 2004;35:1004-1012)

TABLE 4. Three-Month Outcome: IMS and NINDS rt-PA Trial Cohorts (Ages 18–80 and Baseline NIHSS ≥ 10)

	IMS Study	NINDS Placebo	Odds Ratio* (95% CI)	NINDS rt-PA	Odds Ratio† (95% CI)
mRS (0–1) at 90 days	24/80 (30%)	38/211 (18%)	2.26 (1.15, 4.47)	59/182 (32%)	1.00 (0.51–1.96)
NIHSS ≤ 1 at 90 days	22/80 (28%)	31/211 (15%)	2.51 (1.21, 5.18)	45/182 (25%)	1.45 (0.73, 2.90)
Barthel (95–100) at 90 days	37/80 (46%)	63/211 (30%)	2.17 (1.20, 3.91)	76/182 (42%)	1.39 (0.76, 2.54)
Glasgow 91 at 90 days	27/80 (34%)	47/211 (22%)	1.91 (1.01, 3.60)	63/182 (35%)	1.12 (0.59, 2.14)
Global test	—	—	2.36‡ (1.35, 4.14)	—	1.35§ (0.78, 2.37)
mRS (0–2) at 90 days	34/80 (43%)	59/211 (28%)	2.18 (1.20, 3.99)	71/182 (39%)	1.28 (0.70, 2.33)
NIHSS ≤ 2 at 90 days	25/80 (31%)	42/211 (20%)	2.11 (1.08, 4.13)	60/182 (33%)	1.08 (0.57, 2.06)
NIHSS ≤ 2 at 24 hours	11/80 (14%)	7/211 (3%)	5.39 (1.80, 16.19)	26/182 (14%)	1.77 (0.71, 4.39)

*From logistic regression model for favorable outcome adjusted by baseline NIHSS score and time to treatment (continuous)

- IMS çalışmasında kombine tedavi protokolü
- İlk önce İV olarak 0,6 mg/kg (max 60 mg) rt-PA verilir. Bu dozun %15'i bolus şeklinde geri kalanı infüzyon şeklinde 30 dakika içerisinde verilir. Bir taraftan da hasta anjiyografi ünitesine transfer edilir.
- İA tedaviye atağın en geç 5. saatinde başlanmalıdır. 2 mg rt-PA 2 dakika içerisinde trombüsün distali ne enjekte edilir. Kateter trombüsün içerisine çekilerek, 2 mg rt-PA 2 dakika süresince trombüsün içerisine verilir. Daha sonra kateter trombüsün proksimaline çekilir 9 mg/st rt-PA, infüzyon ya da manuel pulse şeklinde maksimum iki saat boyunca verilir.

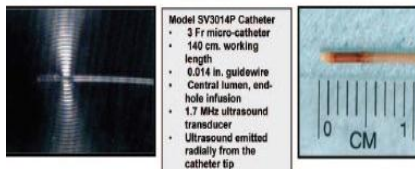
iv ve iA kombine trombolitik kullanımı

The Interventional Management of Stroke (IMS) II Study

The IMS II Trial Investigators

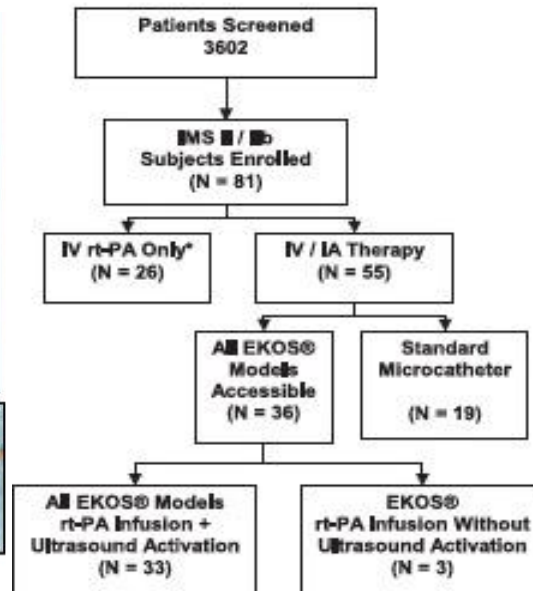
Background and Purpose—The purpose of this study was to further investigate the feasibility and safety of a combined intravenous and intra-arterial approach to recanalization for ischemic stroke.

Methods—Subjects, ages 18 to 80, with a baseline NIHSS ≥ 10 had intravenous recombinant tissue plasminogen activator (rt-PA) started (0.6 mg/kg over 30 minutes) within 3 hours of onset. For subjects with an arterial occlusion at angiography, additional rt-PA was administered via the **EKOS micro-infusion catheter or a standard microcatheter** at the site of the thrombus up to a total dose of 22 mg over 2 hours of infusion or until thrombolysis.



Model SV3014P Catheter

- 3 Fr micro-catheter
- 140 cm. working length
- 0.014 in. guidewire
- Central lumen, end-hole infusion
- 1.7 MHz ultrasound transducer
- Ultrasound emitted radially from the catheter tip



3-Month Outcome	IMS II n=81	NINDS Placebo n=211	OR* (95% CI)	NINDS rt-PA n=182	OR* (95% CI)
mRS 0-1	33%	18%	2.78 (1.46, 5.31)	32%	1.36 (0.72, 2.56)
mRS 0-2	46%	28%	2.82 (1.54, 5.16)	39%	1.74 (0.95, 3.19)
NIHSS ≤ 1	27%	15%	2.84 (1.40, 5.73)	25%	1.85 (0.92, 3.70)
NIHSS ≤ 2	33%	20%	2.66 (1.38, 5.12)	33%	1.47 (0.78, 2.77)
BI 95-100	53%	30%	3.24 (1.80, 5.85)	42%	2.29 (1.24, 4.23)
Global Test Statistic	NA	NA	2.88 (1.66, 4.99)	NA	1.85 (1.06, 3.23)
NIHSS 0-2 at 24 hours	19%	3%	7.07 (2.54, 19.63)	14%	2.27 (0.996, 5.16)

*Adjusted for age, baseline NIHSS, and time to treatment

Endovasküler tedavi & İV trombolitik tedavi

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MARCH 7, 2013

VOL. 368 NO. 10

Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke

Joseph P. Broderick, M.D., Yuko Y. Palesch, Ph.D., Andrew M. Demchuk, M.D., Sharon D. Yeatts, Ph.D., Pooja Khatri, M.D., Michael D. Hill, M.D., Edward C. Jauch, M.D., Tudor G. Jovin, M.D., Bernard Yan, M.D., Frank L. Silver, M.D., Rüdiger von Kummer, M.D., Carlos A. Molina, M.D., Bart M. Demaerschalk, M.D., Ronald Budzik, M.D., Wayne M. Clark, M.D., Osama O. Zaidat, M.D., Tim W. Malisch, M.D., Mayank Goyal, M.D., Wouter J. Schonewille, M.D., Mikael Mazighi, M.D., Ph.D., Stefan T. Engelke, M.D., Craig Anderson, M.D., Ph.D., Judith Spilker, R.N., B.S.N., Janice Carrozzella, R.N., B.A., R.T.(R.), Karla J. Ryckborst, R.N., B.N., L. Scott Janis, Ph.D., Renée H. Martin, Ph.D., Lydia D. Foster, M.S., and Thomas A. Tomsick, M.D., for the **Interventional Management of Stroke (IMS) III Investigators**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke

Chelsea S. Kidwell, M.D., Reza Jahan, M.D., Jeffrey Gornbein, Dr.P.H., Jeffrey R. Alger, Ph.D., Val Nenov, Ph.D., Zahra Ajani, M.D., Lei Feng, M.D., Ph.D., Brett C. Meyer, M.D., Scott Olson, M.D., Lee H. Schwamm, M.D., Albert J. Yoo, M.D., Randolph S. Marshall, M.D., Philip M. Meyers, M.D., Dileep R. Yavagal, M.D., Max Wintermark, M.D., Judy Guzy, R.N., Sidney Starkman, M.D., and Jeffrey L. Saver, M.D., for the **MR RESCUE Investigators***

Endovascular Treatment for Acute Ischemic Stroke

Alfonso Ciccone, M.D., Luca Valvassori, M.D., Michele Nichelatti, Ph.D., Annalisa Sgoifo, Psy.D., Michela Ponzio, Ph.D., Roberto Sterzi, M.D., and Edoardo Boccardi, M.D., for the **SYNTHESIS Expansion Investigators***

CONCLUSIONS

The trial showed similar safety outcomes and no significant difference in functional independence with endovascular therapy after intravenous t-PA, as compared with intravenous t-PA alone. (Funded by the National Institutes of Health and others; ClinicalTrials.gov number, NCT00359424.)

CONCLUSIONS

A favorable penumbral pattern on neuroimaging did not identify patients who would differentially benefit from endovascular therapy for acute ischemic stroke, nor was embolectomy shown to be superior to standard care. (Funded by the National Institute of Neurological Disorders and Stroke; MR RESCUE ClinicalTrials.gov number, NCT00389467.)

CONCLUSIONS

The results of this trial in patients with acute ischemic stroke indicate that endovascular therapy is not superior to standard treatment with intravenous t-PA. (Funded by the Italian Medicines Agency, ClinicalTrials.gov number, NCT00640367.)

Endovasküler tedaviler bitiyor mu?

News > Medscape Medical News > Conference News > International Stroke Conference (ISC) 2013

IMS-III: No Benefit of Endovascular Therapy After Thrombolysis

Çalışma	Dahil edilme Kriterleri		İV r-tPA	Endovasküler yöntem	Ort Kasık giriş süre	Ort. Yaş	Ortanca NIHSS Skoru	90 Gün mRS 0-2	90 Gün mortalite	TICI 2b/3	Semp. Intrakraniyal kanama
IMS-III	*İv r-tPA başlangıç zamanı ≤3 saat *Endovasküler başlama ≤5 s *NIHSS ≥10 veya BTA oklüzyon ≥8	434	%100	r-tPA (%60) EKOS(%5) MERCİ(%22), Penumbra(%12) Soliter (%1) Diğer(%4)	208 dk	69	17	%42	%20	%41	%6
		222	%100	-	Raporlanmamış	68	16	%40	%22	Raporlanmamış	%6
MR-RESCUE	*Anjiyografide ICA, M1 veya M2 Okl. *Endovasküler başlangıç ≤8 sa *NIHSS Skor ≥6	64	%44	MERCİ Penumbra	381 dk	64	18	%19	%19	%27	%5
		54	%30	-		68	18	%20	%24	Raporlanmamış	%3
SYNTHESIS Expansion	*İv-r tPA Başlangıç zamanı ≤4.5 Endovasküler tedavi başlangıç ≥6 saat	181	%0	r-tPA(%91), MERCİ(%3), Penumbra(%5), Solitaire(%10) Diğer(%13)	225 dk	66	13	%42	%14	Raporlanmamış	%6
		181	%100		Raporlanmamış	67	13	%46	%10	Raporlanmamış	%6

IMS III, MR RESCUE, SYNTHESIS EXPANSION ELEŞTİRİLERİ

Endovascular treatment for acute ischemic stroke patients: implications and interpretation of IMS III, MR RESCUE, and SYNTHESIS EXPANSION trials: a report from the Working Group of International Congress of Interventional Neurology

Adnan I. Qureshi, MD^{*}, Foad Abd-Allah, MD, Aitziber Aleu, MD, John J. Connors, MD, Ricardo A. Hanel, MD, Ameer E. Hassan, MD, Haitham M. Hussein, MD, Nazli A. Janjua, MD, Rakesh Khatri, MD, Jawad F. Kirmani, MD, Mikael Mazighi, MD, Heinrich P. Mattle, MD, Jefferson T. Miley, MD, Thanh N. Nguyen, MD, Gustavo J. Rodriguez, MD, Qaisar A. Shah, MD, Adnan H. Siddiqui, MD, Jose I. Suarez, MD, M. Fareed K. Suri, MD, and Reha Tolun, MD

Abstract

Objective: The results of Interventional Management of Stroke (IMS) III, Magnetic Resonance and REcanalization of Stroke Clots Using Embolectomy (MR RESCUE), and SYNTHESIS EXPANSION trials are expected to affect the practice of endovascular treatment for acute ischemic stroke. The purpose of this report is to review the components of the designs and methods of these trials and to describe the influence of those components on the interpretation of trial results.

Dose of IA thrombolytics

Lack of third generation IA thrombolytic use

Limited use of new generation thrombectomy devices (stent retrievers)

Critique of patient selection in the IMS III, MR RESCUE, and SYNTHESIS EXPANSION trials

Lack of confirmation of arterial occlusion prior to endovascular treatment

Low enrollment rate of patients with atrial fibrillation related ischemic stroke in SYNTHESIS EXPANSION trial

Low enrollment rate of patients with basilar artery distribution ischemic stroke

2015; Endovasküler Mekanik Trombektomi Yılı

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A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

O.A. Berkhemer, P.S.S. Fransen, D. Beumer, L.A. van den Berg, H.F. Lingsma, A.J. Yoo, W.J. Schonewille, J.A. Vos, P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Walderveen, J. Staals, J. Hofmeijer, J.A. van Oostayen, G.J. Lycklama à Nijeholt, J. Boiten, P.A. Brouwer, B.J. Emmer, S.F. de Bruijn, L.C. van Dijk, L.J. Kappelle, R.H. Lo, E.J. van Dijk, J. de Vries, P.L.M. de Kort, W.J.J. van Rooij, J.S.P. van den Berg, B.A.A.M. van Hasselt, L.A.M. Aarden, R.J. Dallinga, M.C. Visser, J.C.J. Bot, P.C. Vroomen, O. Eshghi, T.H.C.M.L. Schreuder, R.J.J. Heijboer, K. Keizer, A.V. Tielbeek, H.M. den Hertog, D.G. Gerrits, R.M. van den Berg-Vos, G.B. Karas, E.W. Steyerberg, H.Z. Flach, H.A. Marquering, M.E.S. Sprengers, S.F.M. Jenniskens, L.F.M. Beenen, R. van den Berg, P.J. Koudstaal, W.H. van Zwam, Y.B.W.E.M. Roos, A. van der Lugt, R.J. van Oostenbrugge, C.B.L.M. Majoie, and D.W.J. Dippel, for the **MR CLEAN Investigators***

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

M. Goyal, A.M. Demchuk, B.K. Menon, M. Eesa, J.L. Rempel, J. Thornton, D. Roy, T.G. Jovin, R.A. Willinsky, B.L. Sapkota, D. Dowlatshahi, D.F. Frei, N.R. Kamal, W.J. Montaner, A.Y. Poppe, K.J. Ryckborst, F.L. Silver, A. Shuaib, D. Tampieri, D. Williams, O.Y. Bang, B.W. Baxter, P.A. Burns, H. Choe, J.-H. Heo, C.A. Holmstedt, B. Jankowitz, M. Kelly, G. Linares, J.L. Mandzia, J. Shankar, S.-I. Sohn, R.H. Swartz, P.A. Barber, S.B. Coutts, E.E. Smith, W.F. Morrish, A. Weill, S. Subramaniam, A.P. Mitha, J.H. Wong, M.W. Lowerison, T.T. Sajobi, and M.D. Hill for the **ESCAPE Trial Investigators***

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

B.C.V. Campbell, P.J. Mitchell, T.J. Kleinig, H.M. Dewey, L. Churilov, N. Yassi, B. Yan, R.J. Dowling, M.W. Parsons, T.J. Oxley, T.Y. Wu, M. Brooks, M.A. Simpson, F. Miteff, C.R. Levi, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, M. Priglinger, T. Ang, R. Scroop, P.A. Barber, B. McGuinness, T. Wijeratne, T.G. Phan, W. Chong, R.V. Chandra, C.F. Bladin, M. Badve, H. Rice, L. de Villiers, H. Ma, P.M. Desmond, G.A. Donnan, and S.M. Davis, for the **EXTEND-IA Investigators***

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

T.G. Jovin, A. Chamorro, E. Cobo, M.A. de Miquel, C.A. Molina, A. Rovira, L. San Román, J. Serena, S. Abilleira, M. Ribó, M. Millán, X. Urra, P. Cardona, E. López-Cancio, A. Tomasello, C. Castaño, J. Blasco, L. Aja, L. Dorado, H. Quesada, M. Rubiera, M. Hernández-Pérez, M. Goyal, A.M. Demchuk, R. von Kummer, M. Gallofré, and A. Dávalos, for the **REVASCAT Trial Investigators***

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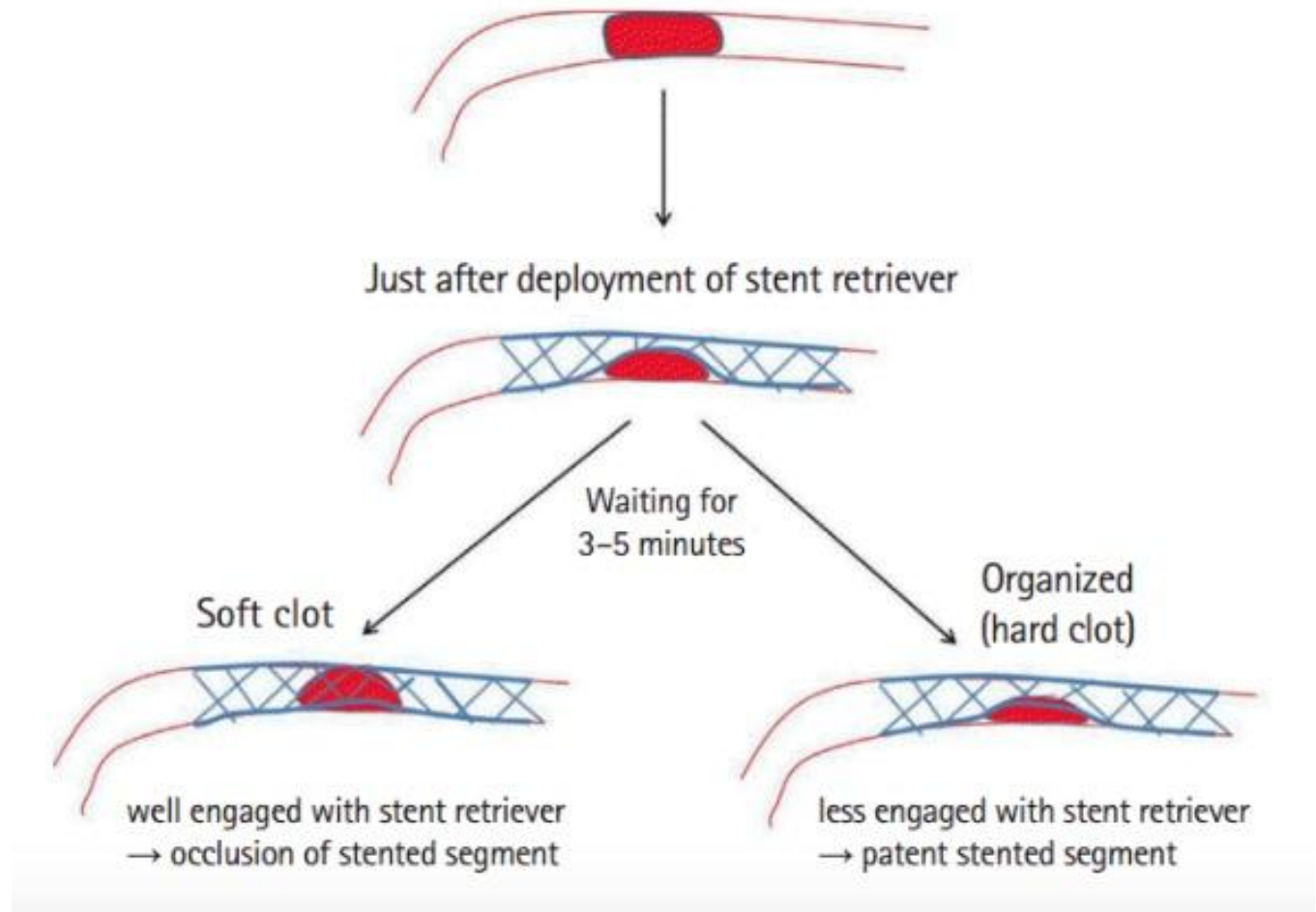
JUNE 11, 2015

VOL. 372 NO. 24

Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

Jeffrey L. Saver, M.D., Mayank Goyal, M.D., Alain Bonafe, M.D., Hans-Christoph Diener, M.D., Ph.D., Elad I. Levy, M.D., Vitor M. Pereira, M.D., Gregory W. Albers, M.D., Christophe Cognard, M.D., David J. Cohen, M.D., Werner Hacke, M.D., Ph.D., Olav Jansen, M.D., Ph.D., Tudor G. Jovin, M.D., Heinrich P. Mattle, M.D., Raul G. Nogueira, M.D., Adnan H. Siddiqui, M.D., Ph.D., Dileep R. Yavagal, M.D., Blaise W. Baxter, M.D., Thomas G. Devlin, M.D., Ph.D., Demetrius K. Lopes, M.D., Vivek K. Reddy, M.D., Richard du Mesnil de Rochemont, M.D., Oliver C. Singer, M.D., and Reza Jahan, M.D., for the **SWIFT PRIME Investigators***

Stent Retriever Mekanik Trombektomi



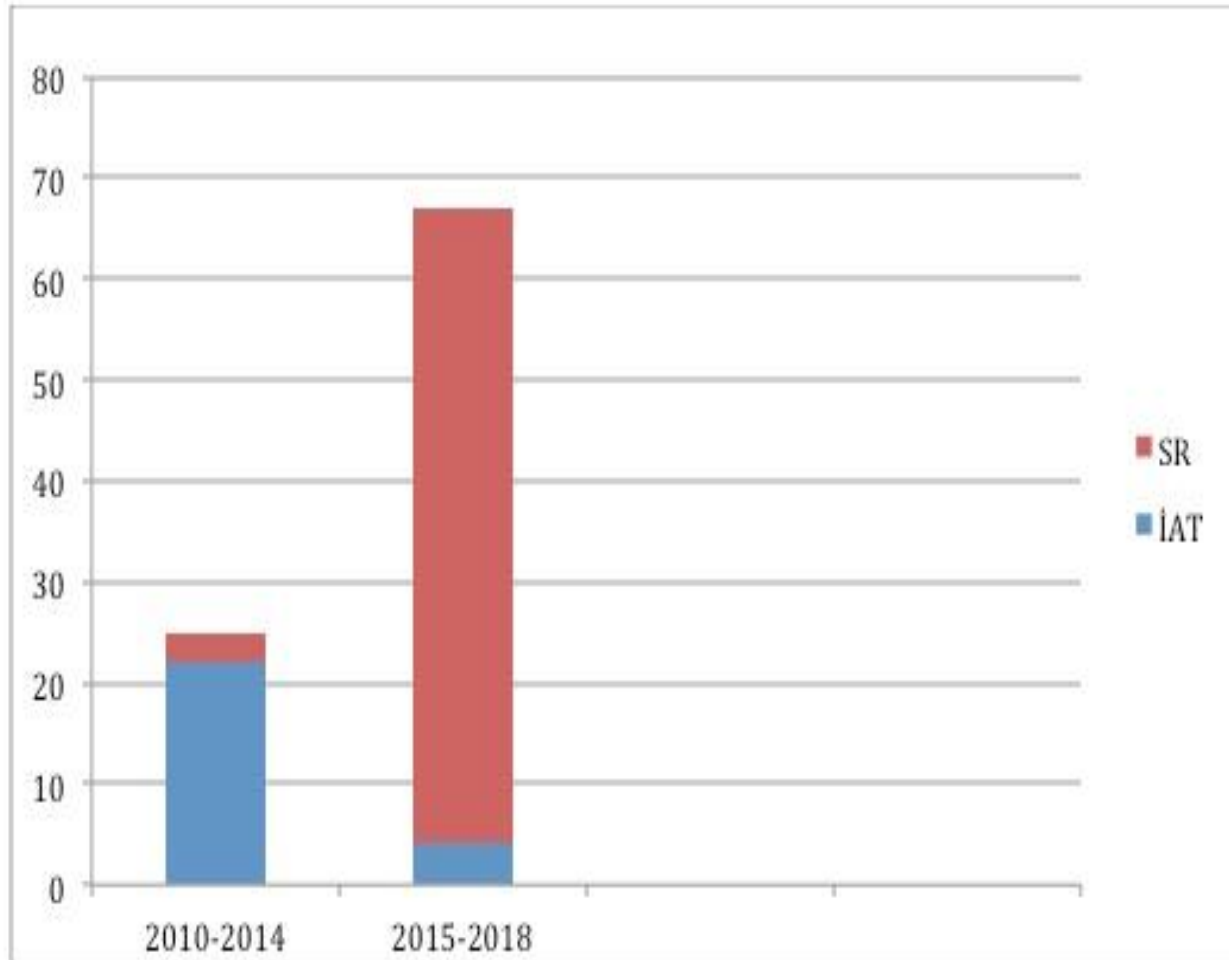
Stent Retriever Mekanik Trombektomi

Çalışma	Dahil Edilme Kriteri		iv r- tPA	Endovasküler tedavi yöntemi	Ortalama başlangıç- kasık girişi süresi	Ortalama Yaş (yıl)	Ortanca NIHSS skoru	90 gün mRS 0-2	90 gün mortalite	TICI 2b/3	Semptomatik İntrakraniyel Kanama
MR CLEAN	- Anjiyografide ICA, M1, M2, A1 veya A2 oklüzyonu - Endovasküler tedavi başlangıç zamanı ≤6 saat - NIHSS skoru ≥2	Aktif Tedavi (n=233)	%87	r-tpA, ürokinaz, EKOS, MERCI, Penumbra, Solitaire (%82)	260 dakika	66 (ortanca)	17	%33	%21	%59	%8
		Kontrol Tedavi (n=267)	%91	-	-	66 (ortanca)	18	%19	%22	-	%6
ESCAPE	- BT ASPECTS ≥6 - BTA'da yeterli kollateral - BTA'da ICA, M1 veya M2 oklüzyonu - Endovasküler tedavi başlangıç zamanı ≤12 saat - NIHSS skoru ≥6	Aktif Tedavi (n=165)	%73	Solitaire (%61), Diğer Stent (%18) Diğer trombektomi	208 dakika	71 (ortanca)	16	%53	%10	%72	%4
		Kontrol Tedavi (n=150)	%79	-	-	70 (ortanca)	17	%29	%19	-	%3
EXTEND IA	- iv r-tpA başlangıç zamanı ≤4,5 saat - BTA'da ICA, M1 veya M2 oklüzyonu - BTP'de yeterli penumbra dokusu - Endovasküler tedavi başlangıç zamanı ≤6 saat	Aktif Tedavi (n=35)	%100	Solitaire	210 dakika	69	17	%71	%9	%86	%0
		Kontrol Tedavi (n=35)	%100	-	-	70	13	%40	%20	-	%6

Stent Retriever Mekanik Trombektomi

SWIFT PRIME	- iv r-tPA başlangıç zamanı ≤4,5 saat - BT ASPECTS ≥7 - BTA'da ICA veya M1 oklüzyonu - Endovasküler tedavi başlangıç zamanı ≤6 saat - NIHSS skoru ≥8 ve <30	Aktif Tedavi (n=98)	%100	Solitaire	224 dakika	65	17	%60	%9	%88	%0
		Kontrol Tedavi (n=98)	%100	-	-	66	17	%36	%12	-	%3
REVASCAT	- BT ASPECTS ≥7 veya MR ASPECTS ≥6 - BTA'da ICA veya M1 oklüzyonu - Endovasküler tedavi başlangıç zamanı ≤8 saat - NIHSS skoru ≥6	Aktif Tedavi (n=103)	%68	Solitaire	269 dakika	66	17	%44	%18	%66	%2
		Kontrol Tedavi (n=103)	%78	-	-	67	17	%28	%16	-	%2

Kliniğimizdeki Değişim



**Amerikan Kalp Birliđi/ Amerikan İnme Birliđi
Klavuzu(2015)**



1-İv. r-tPA için uygun hastalar, endovasküler tedavi düşünülse bile iv. r-tPA almalıdır (Sınıf I; Kanıt düzeyi A). (2013 klavuzu ile aynı)

Amerikan Kalp Birliđi/ Amerikan İnme Birliđi Klavuzu(2015)



Aşağıdaki kriterlerin tamamını karşılıyorsa geri toplanabilir stentler kullanılarak endovasküler tedavi yapılmalıdır. (Sınıf I; Kanıt Düzeyi A). (Yeni tavsiye)

- a) İnme öncesi mRS skoru 0-1,
- b) Başlangıcından itibaren 4,5 saat içinde profesyonel medikal derneklerin uygun gördüğü şekilde iv. r-tPA alan akut iskemik inme,
- c) Neden olan ICA veya proksimal MCA (M1) oklüzyonu,
- d) Yaş ≥ 18 yıl,
- e) NIHSS skoru ≥ 6 ,
- f) ASPECTS ≥ 6 ,
- g) Semptom başlangıcından itibaren 6 saat içinde (kasık ponksiyonu) tedavinin başlayabilmeli

Amerikan Kalp Birliđi/ Amerikan İnme Birliđi Klavuzu(2015)



Ön sirkülasyon oklüzyonu olan ve iv. r-tPA'nın kontrendike olduđu, özenle seçilmiş hastalarda inme başlangıcından sonra 6 saat içinde tamamlanmış geri toplanabilir stentler ile endovasküler tedavi makuldur (Sınıf IIa; Kanıt Düzeyi C) (Yeni tavsiye).

İnternal karotis arterde preokluziv darlık, MCA total okluzyon



- Teşekkür ederim...