

IV. Girişimsel Nöroloji Eğitim Toplantısı

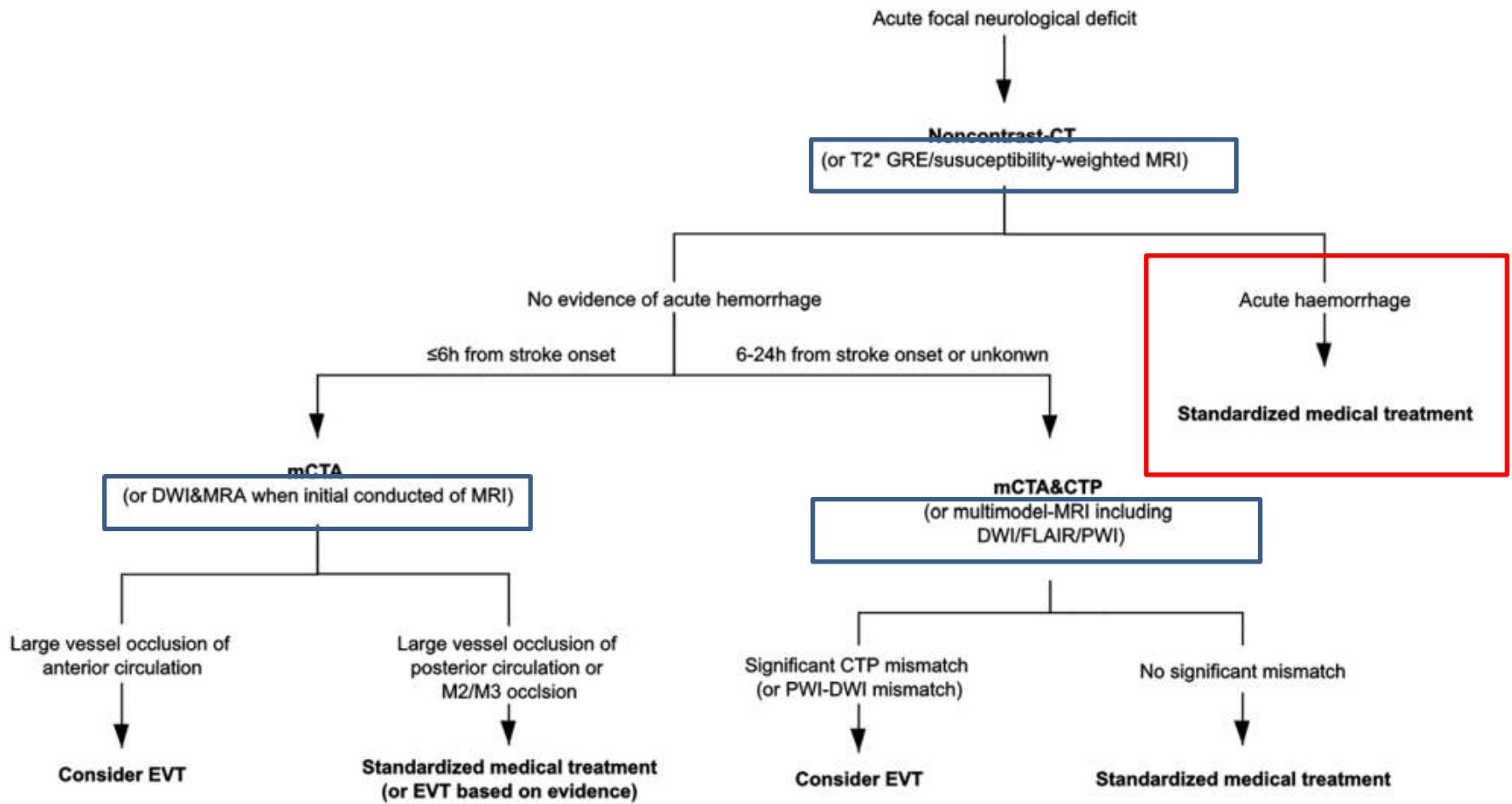
Patofizyoloji ve Nörogörüntüleme

Akut İnmede MRI

21-22 Mayıs 2022, Gaziantep

Anıl Tanburoğlu
Beyin Damar Hastalıkları ve İnceleme Merkezi





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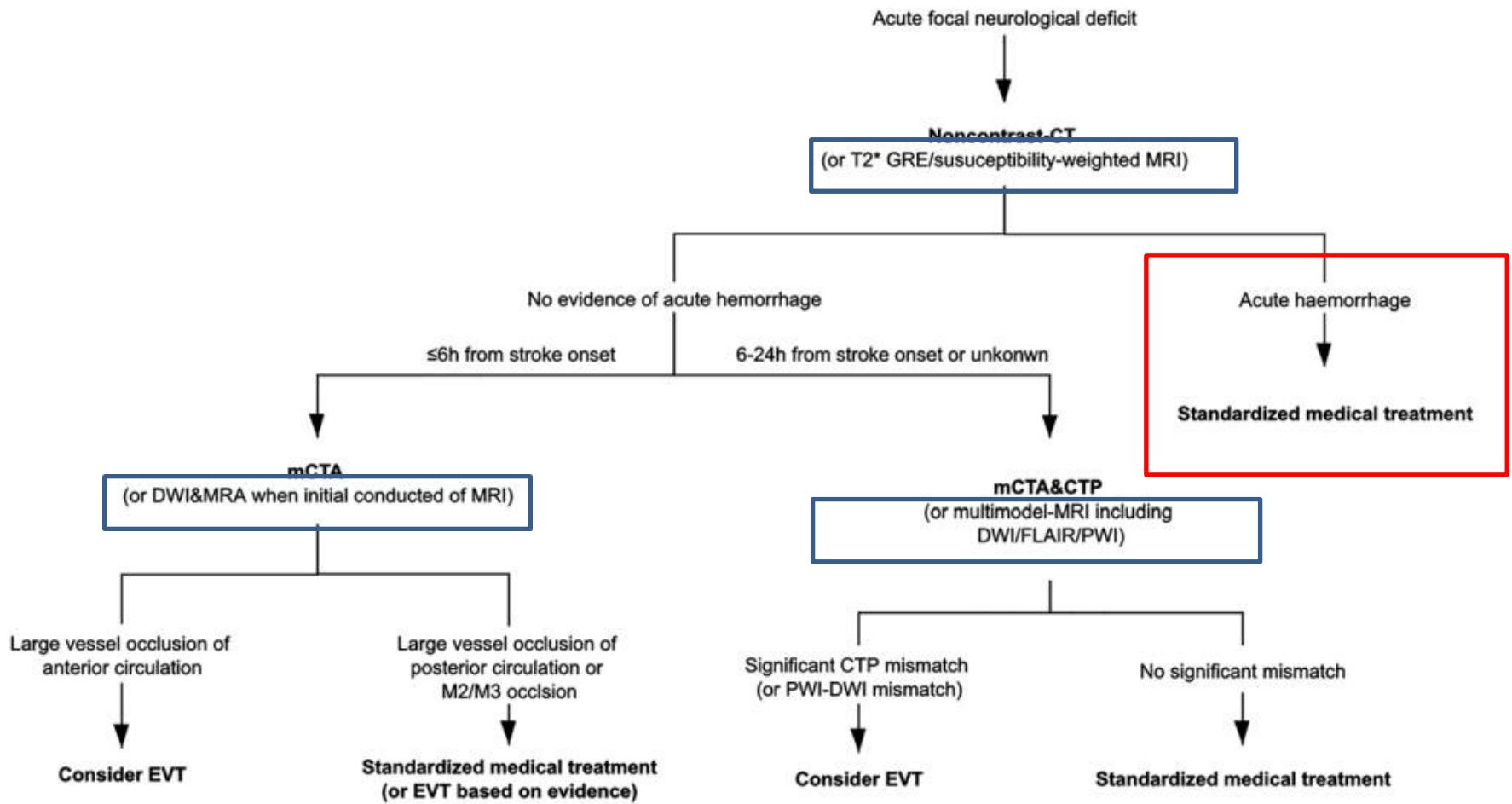
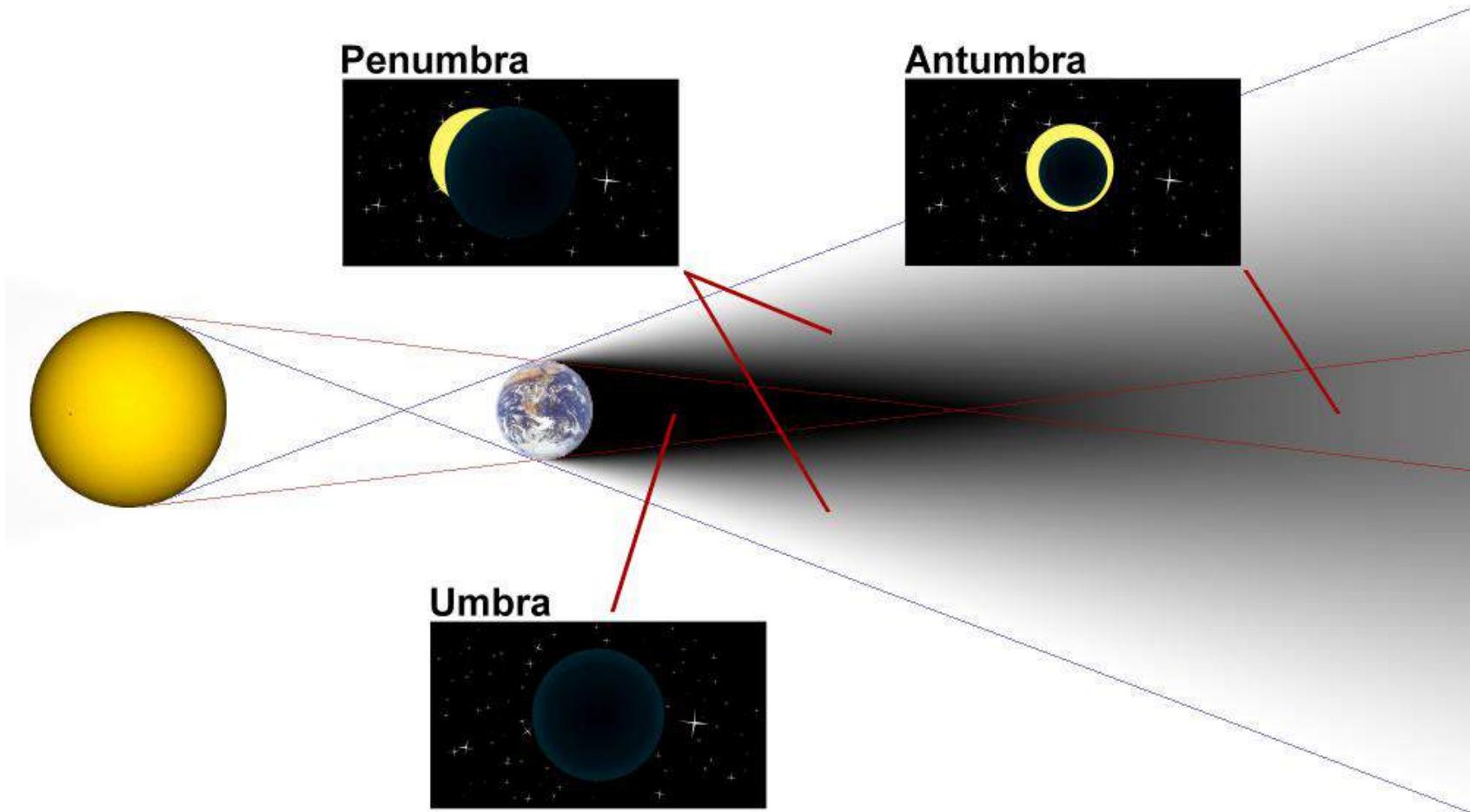


Table 1: Advantages and limitations of CT and MR imaging.

| Imaging characteristics | CT | MRI |
|--|----|-----|
| Availability in primary health care institutions | ++ | - |
| Lower cost | + | - |
| Rapid image acquisition | ++ | + |
| Lack of vulnerability to motion artifacts | + | - |
| Lower signal-to-noise ratio | ++ | + |
| Less ionizing radiation | - | ++ |
| Feasibility and safety for patients with metallic implants | ++ | - |
| Less time for postprocessing of multimodal imaging | - | - |
| Renal toxicity associated with contrast administration | + | + |
| Ability to assess causes of ICH while in the scanner | + | + |
| Detection of intracranial hemorrhage including microbleeds | + | ++ |

Patofizyoloji

- Kor-penumbra modeli?
 - Tüm modeller yanlıştır ama bazıları yararlıdır
 - KOR:
 - PENUMBRA: elektriksel aktivite kaybı,potansiyel düzelmeye
 - akım eşikleri yaklaşaktır, kor ise ana oyuncudur
- Zamanın sayısallığı ve mekansallığı(doku penceresi)
- Bireysel farklar(precision medicine)



The **penumbra** is the part of a shadow where the light source is only partially blocked.

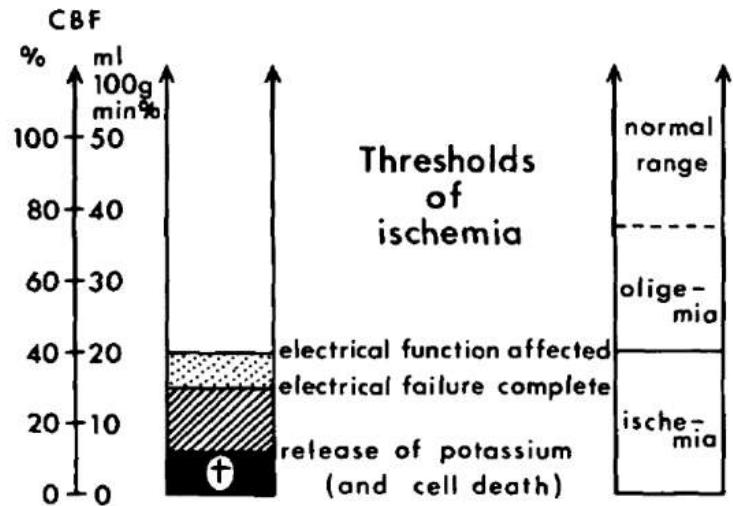
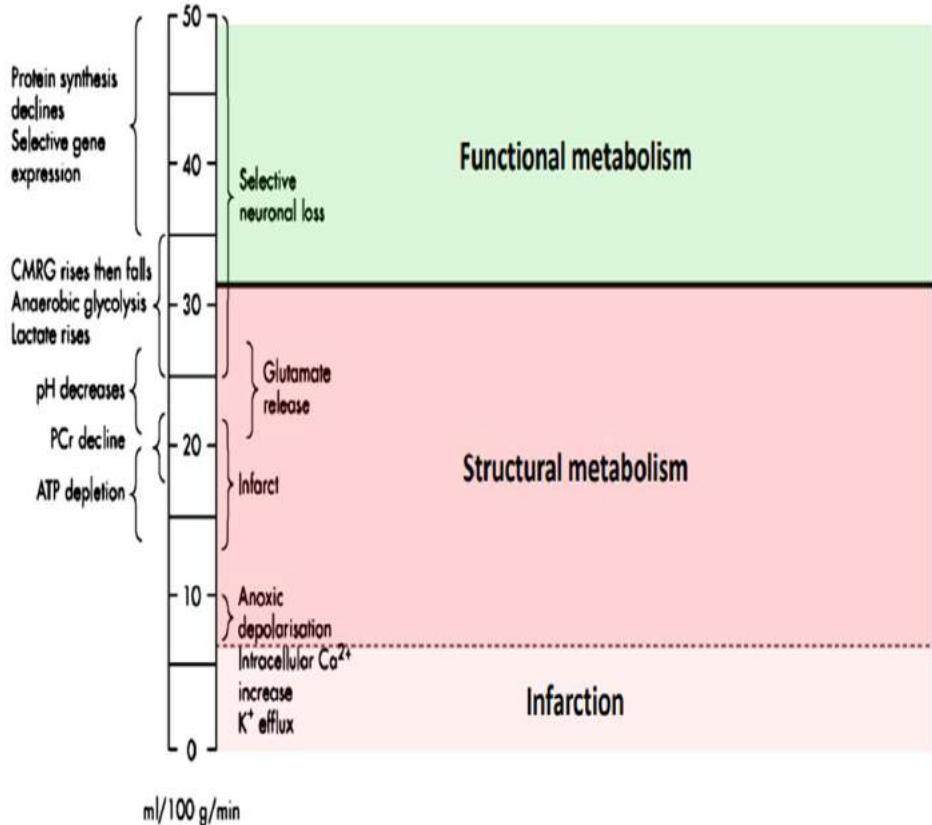


FIGURE 5. Ischemic thresholds for electrical failure and for release of cellular K^+ . For further details see text.

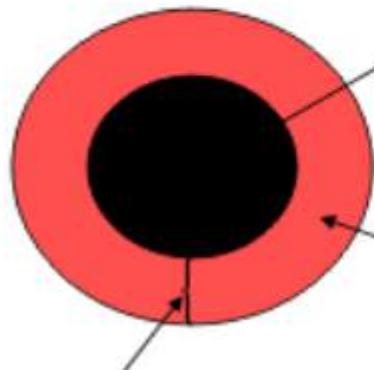


Astrup J, Symon L, Branston NM, Lassen NA. Stroke. 1977 Jan-Feb;8(1):51-7.

- Ortalama beyin akımı; 56 ml/dk'nın üzeri
- 30-50 ml/dk oligemi
– geçici iskemi
- 20-30 ml/dk..... iskemi
– serebral disfonksiyon
- 10-15 ml/dk altı..... hücre ölümü
- Kan akımı tamamen kesildiği zaman
– 3 dk içerisinde hücre ölümü

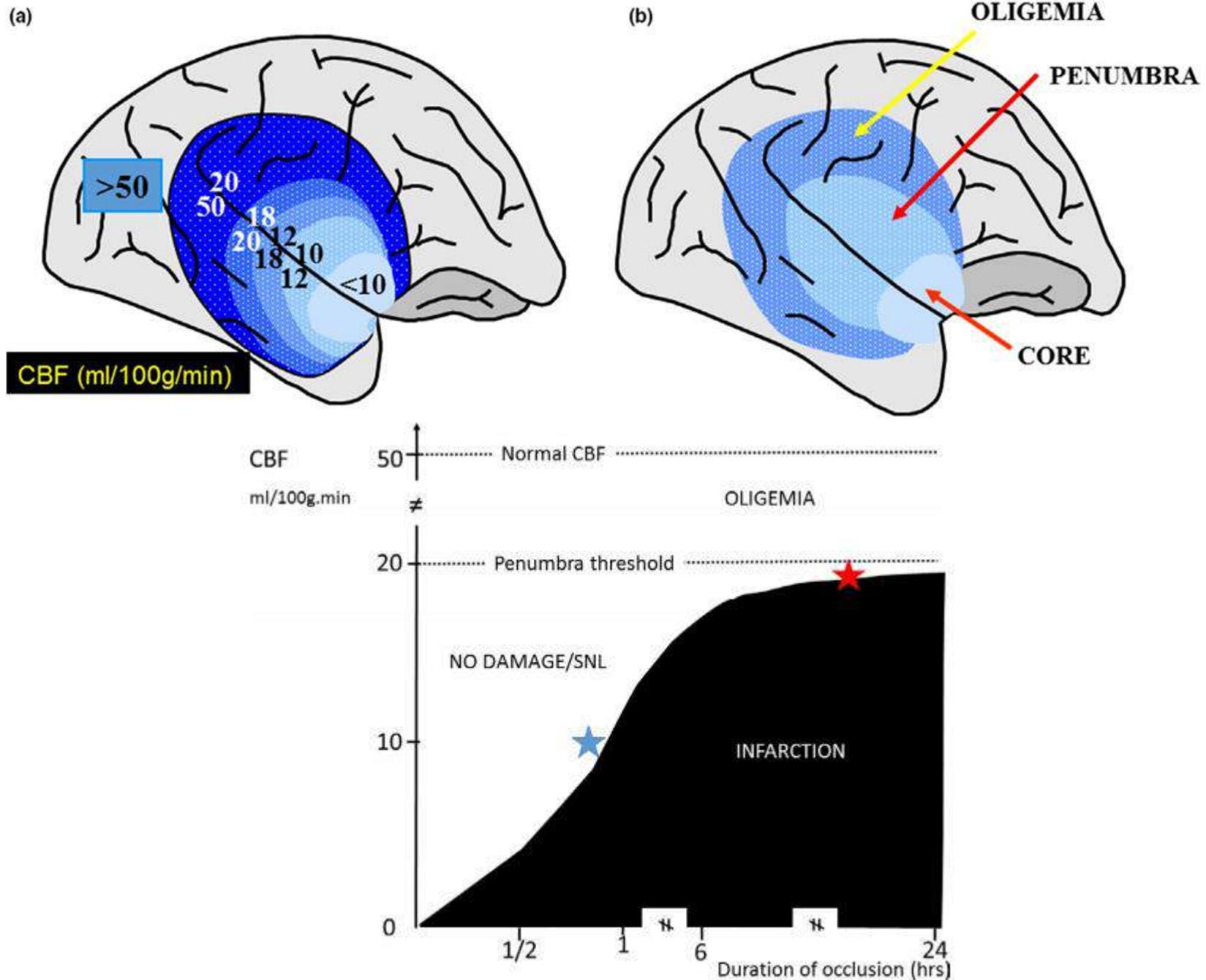
Ischemic Penumbra

DWI / PWI Mismatch



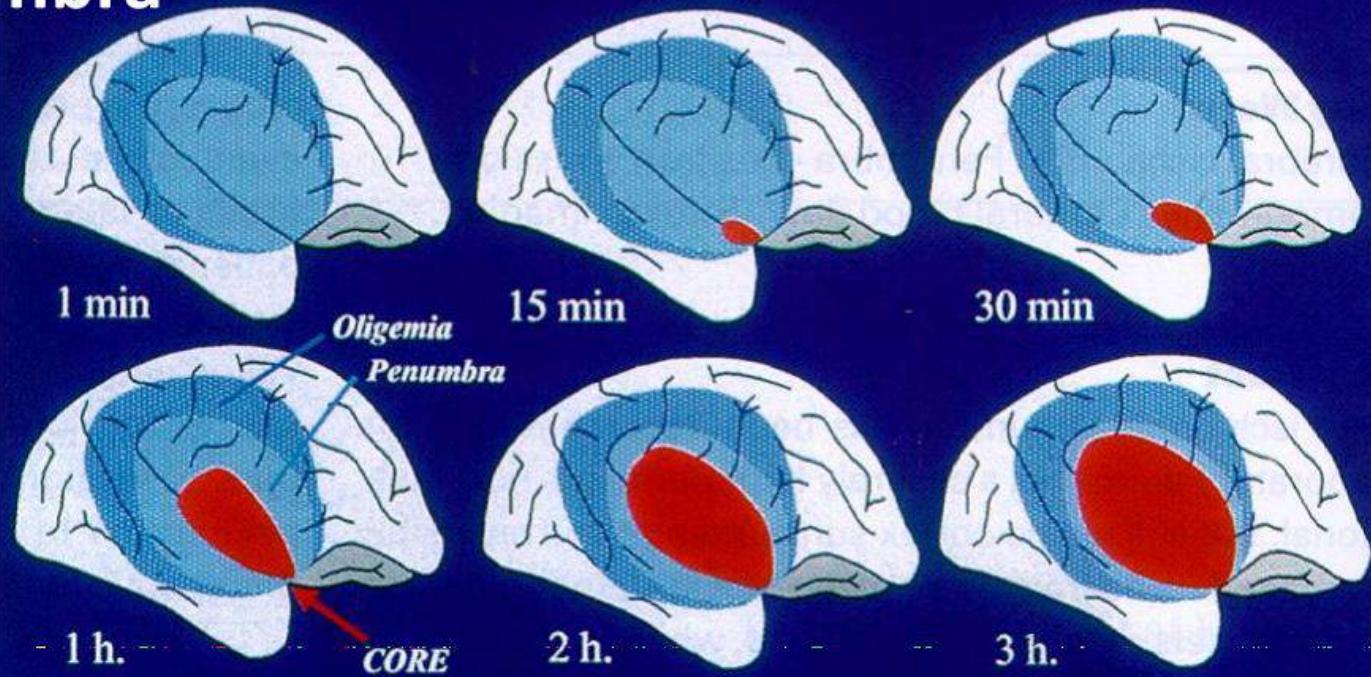
- Diffusion Abnormality
- CBF < 10 ml/100g/min
- Cytotoxic edema
- Irreversible ischemia

- Perfusion Abnormality
- CBF = 10-18 ml/100g/min
- Neuronal paralysis
- Reversible ischemia



KOLLATERAL dokunun yaşayabilmesi için zorunludur!

Penumbra



Baron JC Cerebrovasc Dis. 2001;11:2-8.

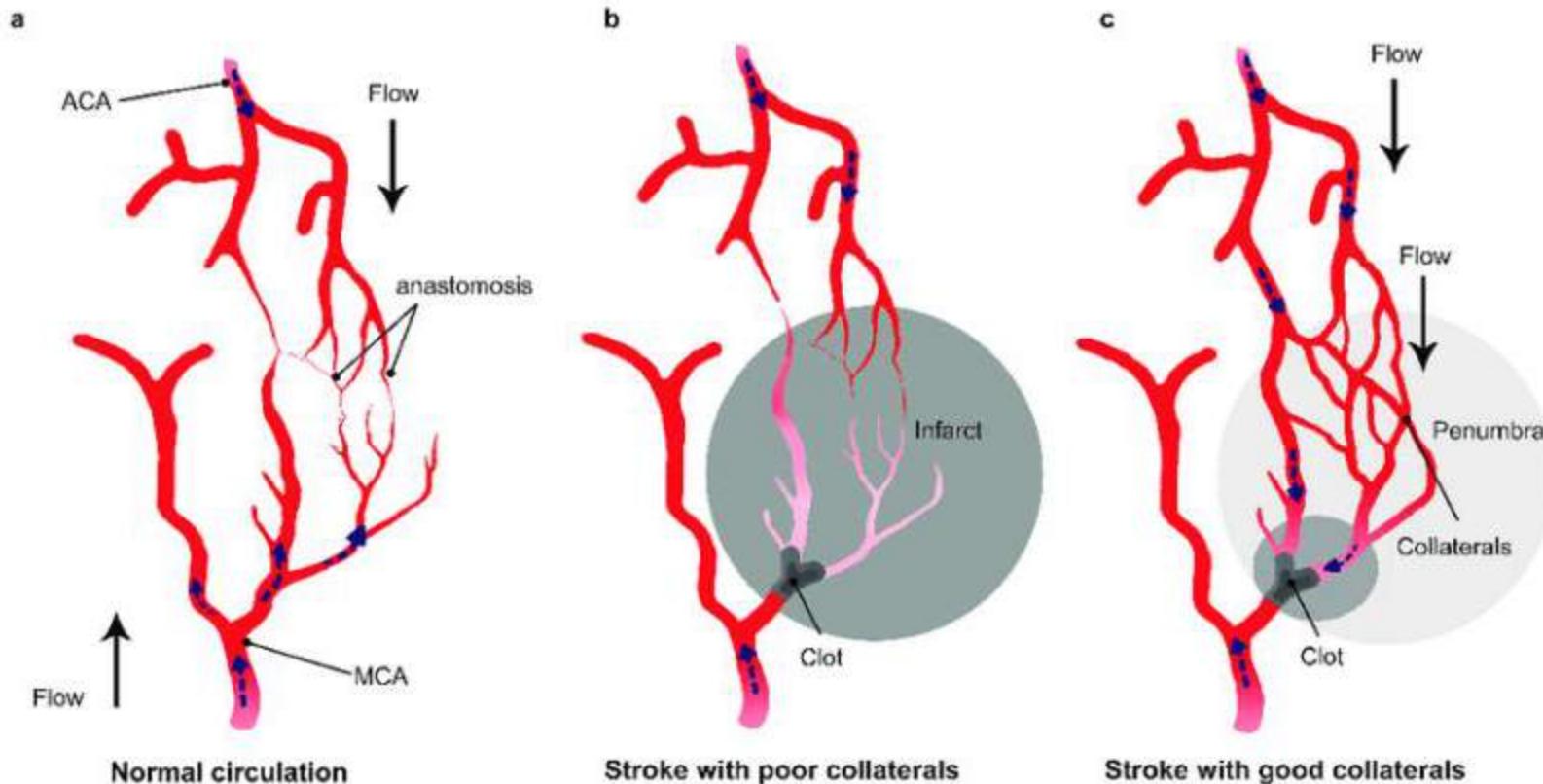
Loss of electrical function with intact cell membranes¹

„fundamentally reversible“²

¹ Astrup J et al. Stroke. 1981;12:723-725

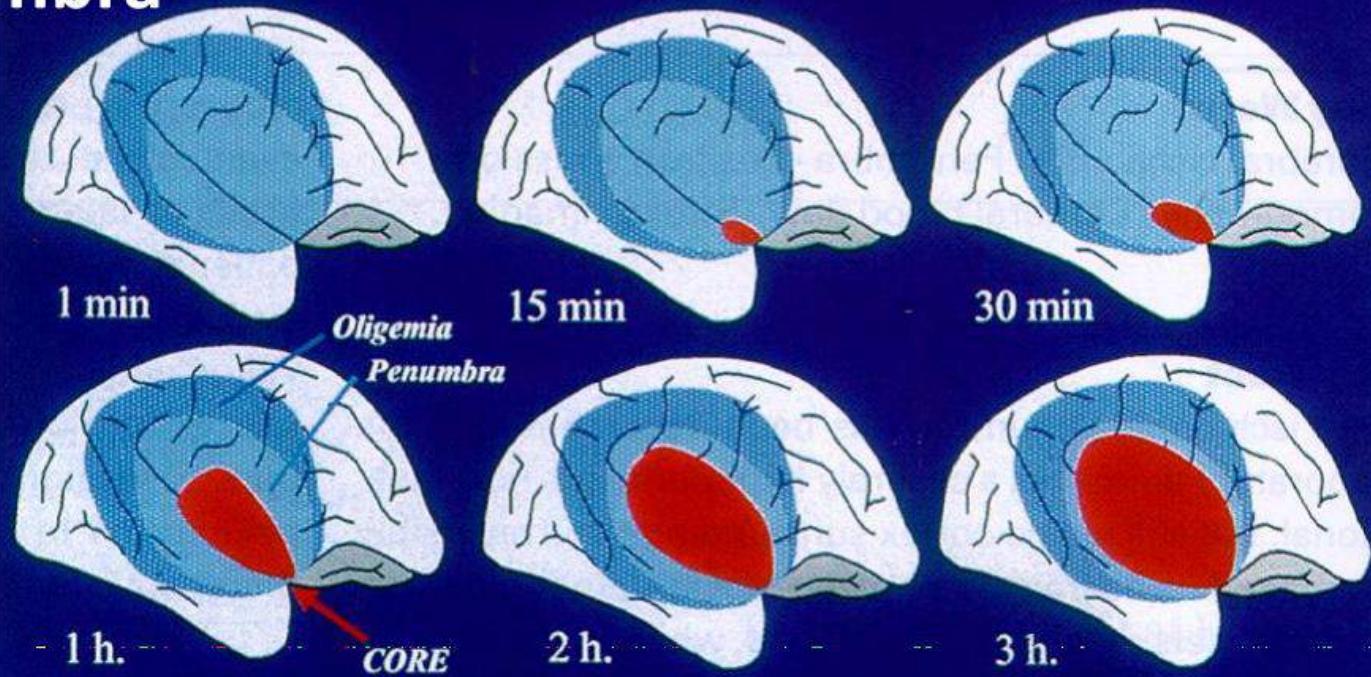
² Hakim AM et al. JCBFM. 1989;9:523-534

Collaterals



KOLLATERAL dokunun yaşayabilmesi için zorunludur!

Penumbra



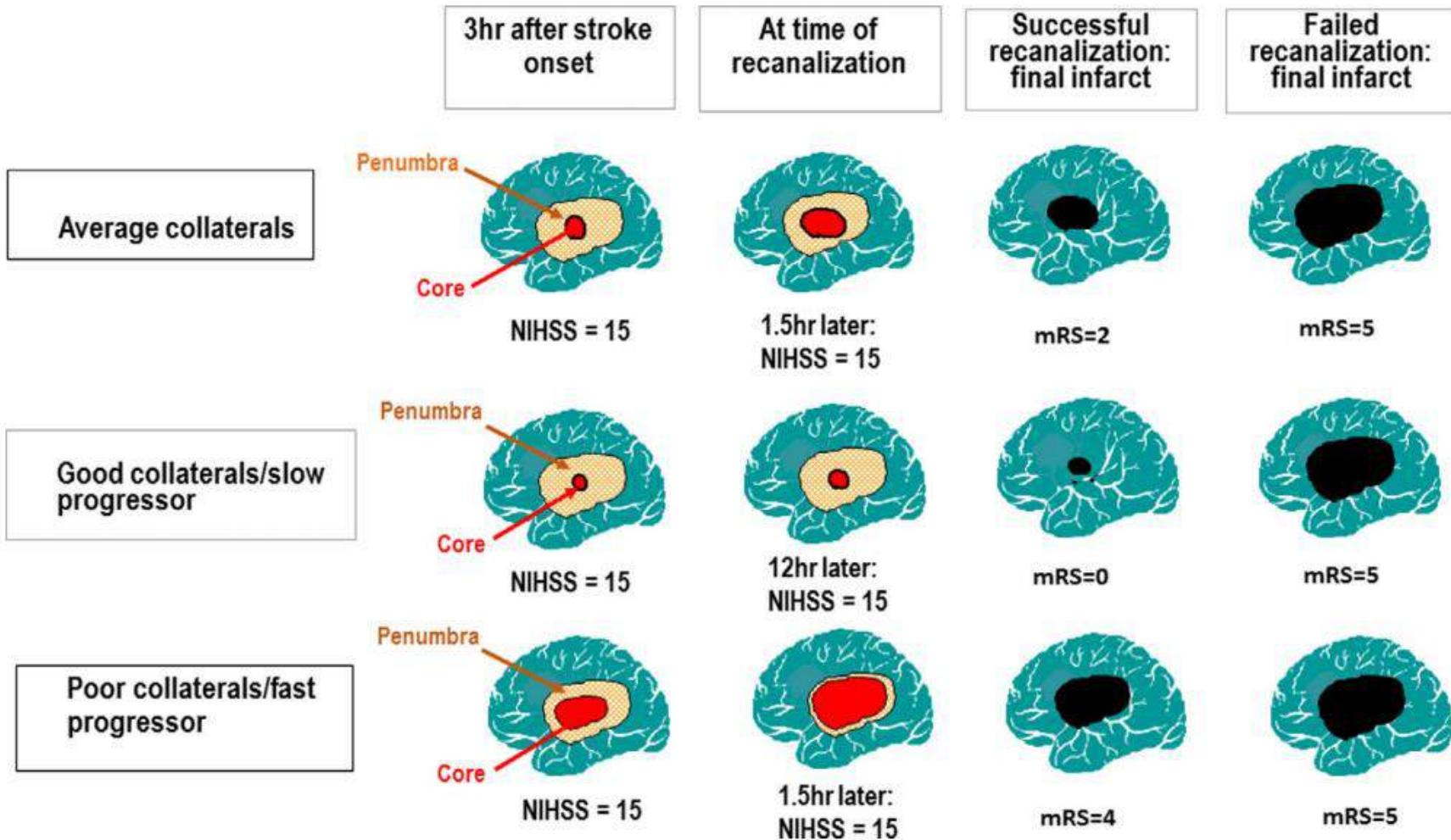
Baron JC Cerebrovasc Dis. 2001;11:2-8.

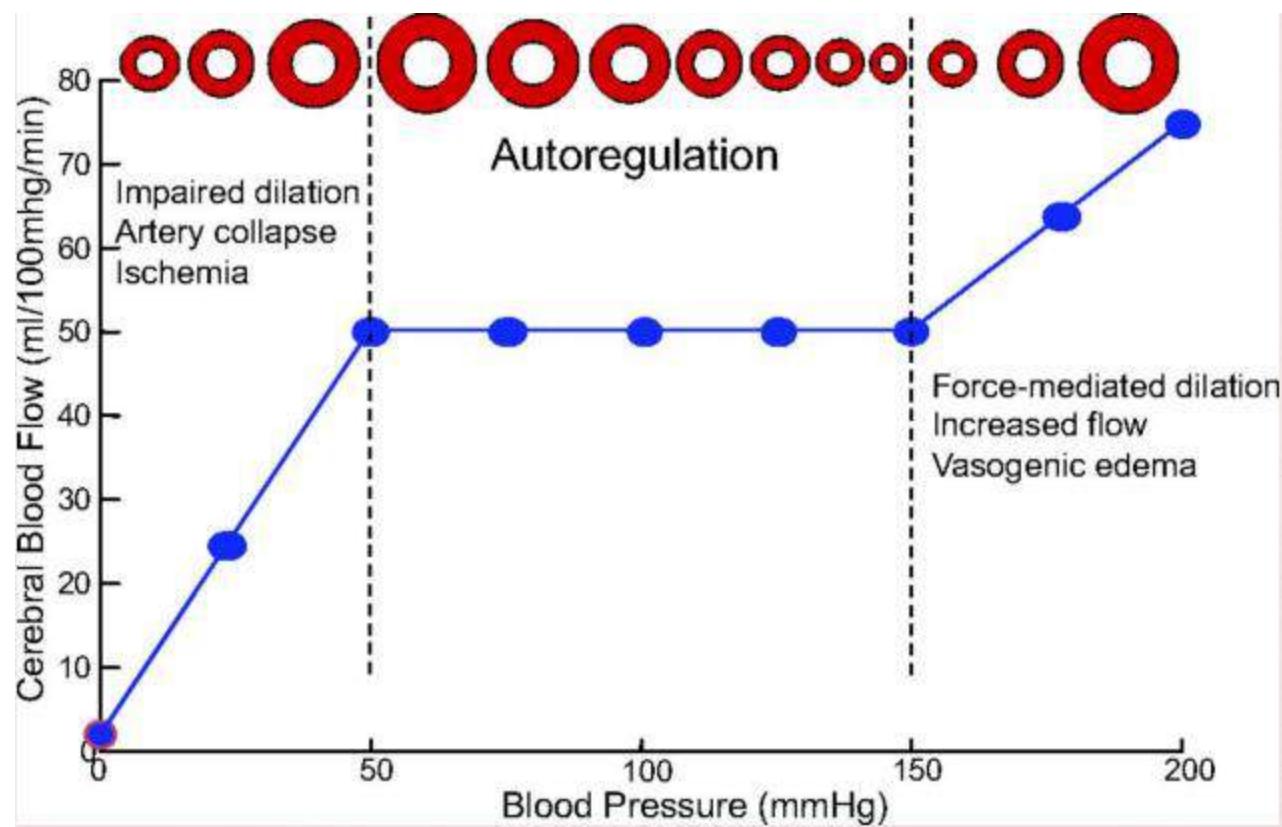
Loss of electrical function with intact cell membranes¹

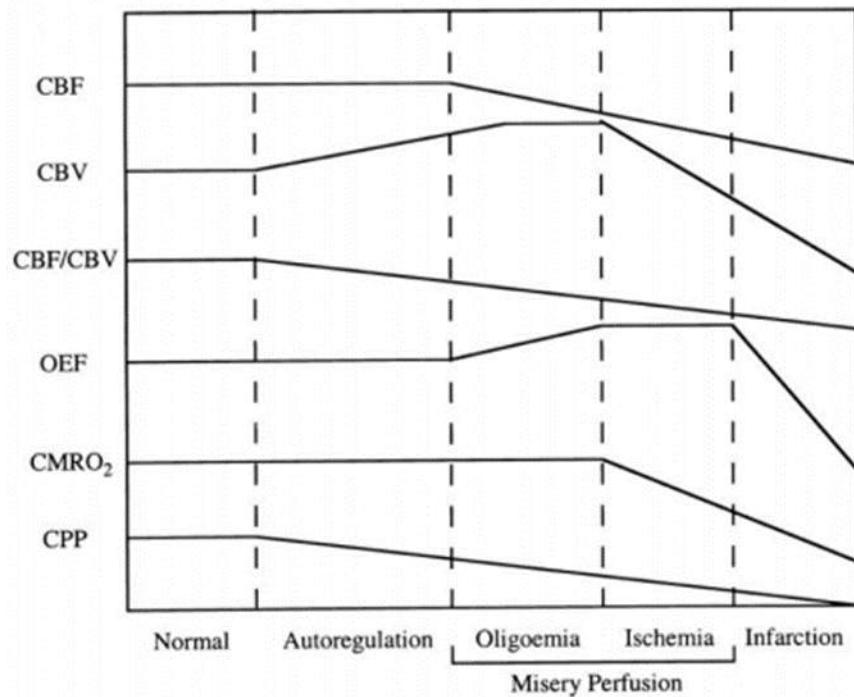
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¹ Astrup J et al. Stroke. 1981;12:723-725

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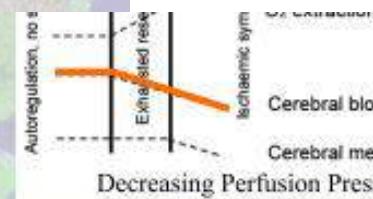
Evre 1 Vasodilatasyon Evre 2 OEF Artışı

CBV

- Cerebral Blood Volume
- 'Percentage of blood vessels in a specific volume of tissue'
- Higher in cortex and basal ganglia
- Changes with autoregulation and dilatation or constriction of vessels
- CBV in core ↓, in penumbra =↑

CBF

- Cerebral Blood Flow
- Normal: 50-80 ml/100g braintissue/min
- Higher energy demand: cortex, basal ganglia: 2-3x white matter
- autoregulation: diameter change vessels
- In case of max. dilatation and decrease perfusion pressure: CBF ↓



CBF↓

core en penumbra

MTT↑

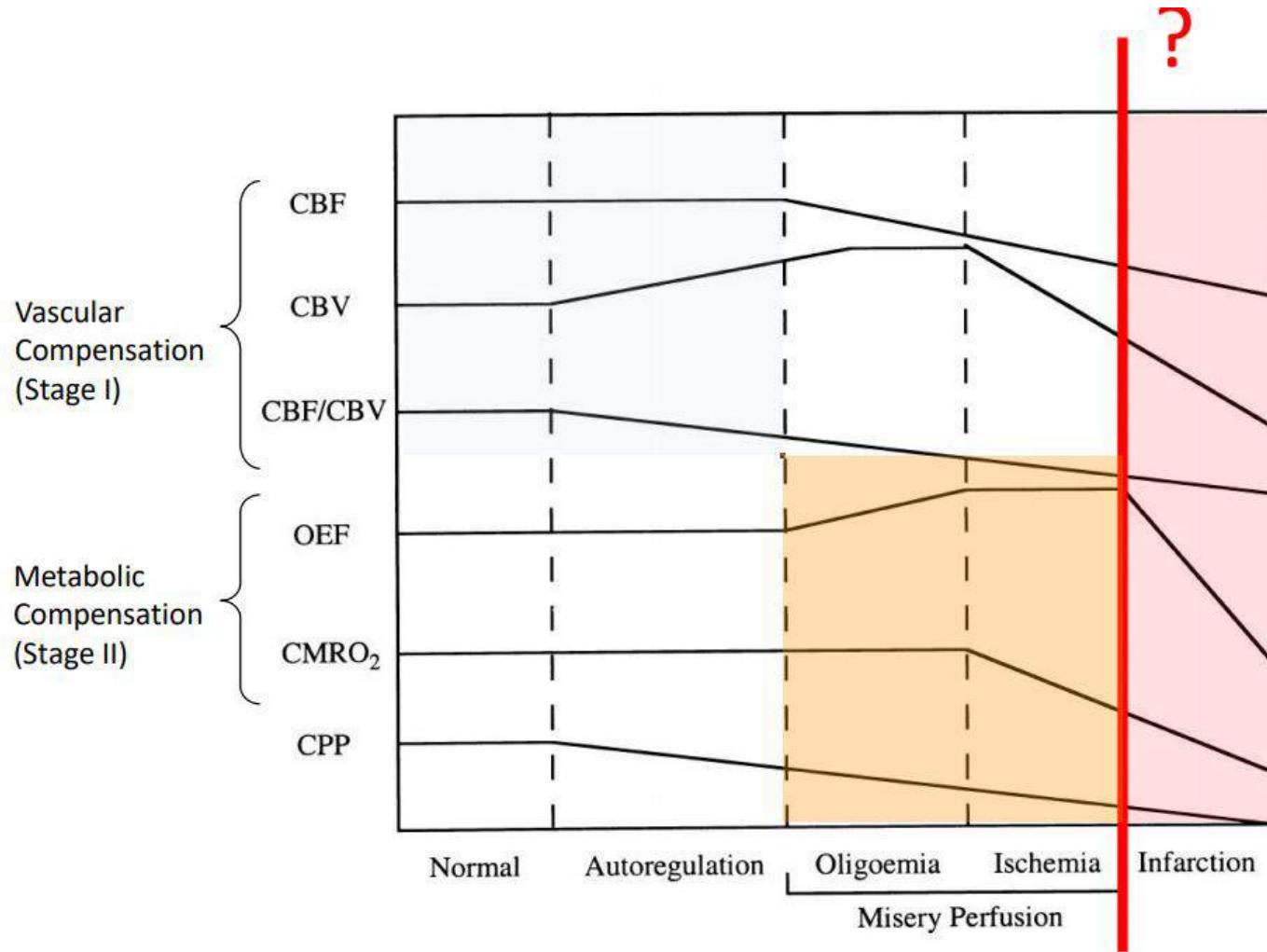
core, penumbra
luxury perfusion

↓CBV

infarct core

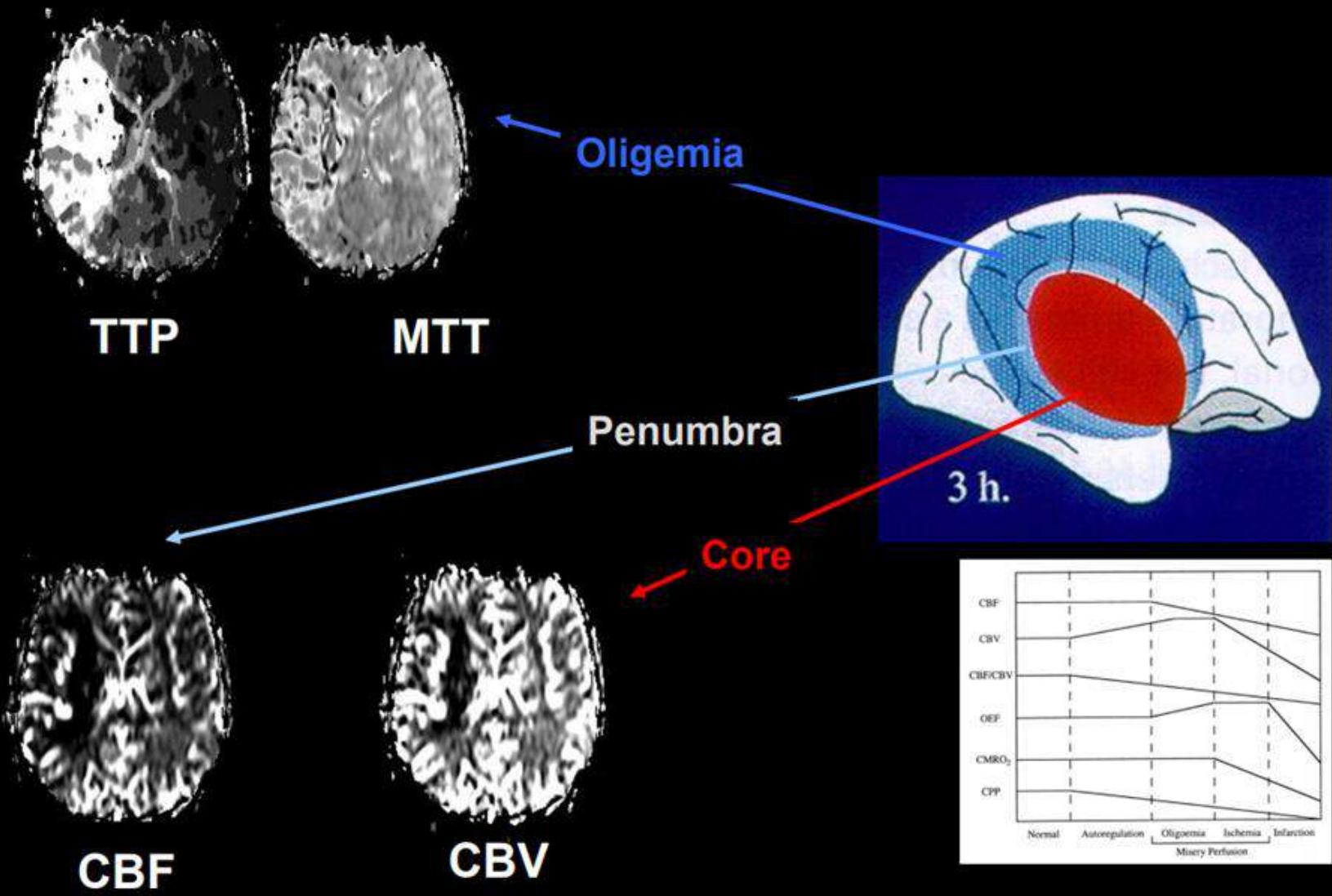
=/ ↑ CBV

penumbra



Gibbs J, Wise R, Leenders K, Jones T. Evaluation of cerebral perfusion reserve in patients with carotid-artery occlusion. *Lancet*. 1984;310-314

Pathophysiology: Perfusion parameters



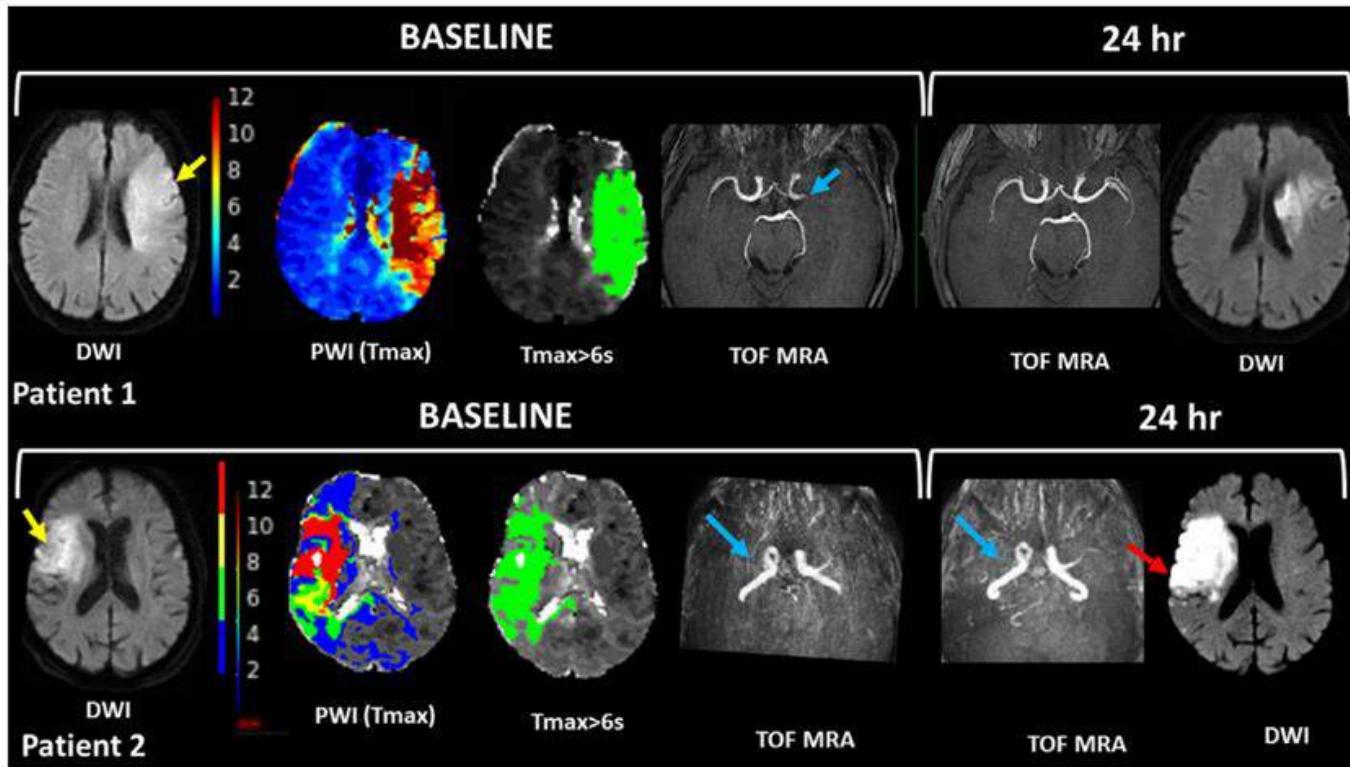


FIGURE 4 Set of serial MRI images (shown for one illustrative cut only) obtained on admission in two patients with acute proximal MCA occlusion ('baseline') and at the 24 h follow-up session ('24 h'), illustrating the widely divergent fate of the penumbra depending on occurrence of early recanalization. Patient 1 had severe neurological deficit on admission (NIHSS = 21) and DWI showed an already extensive ischaemic lesion with faint borders (yellow arrow). Perfusion-weighted imaging (PWI) generated T_{\max} images showed a markedly delayed perfusion lesion with $T_{\max} > 6$ s, that is, the penumbra threshold, involving the entire MCA territory well beyond the DWI lesion (a 'mismatch'). The automated perfusion software generated a map of $T_{\max} > 6$ s (green blob). Time-of-flight magnetic resonance angiography (TOF-MRA) demonstrated proximal left MCA occlusion (blue arrow). The patient was thrombolysed and immediately taken to the angio suite for thrombectomy, which resulted in complete recanalization 4 h 25 min after stroke onset. The 24 h follow-up DWI showed partial reversal of the lesion, and the MRA showed persistent complete recanalization. The 24 h NIHSS was down to 3. In patient 2 (same layout), there was proximal left MCA occlusion with marked DWI-PWI mismatch. NIHSS was 18. The patient received bridging therapy (i.e., thrombolysis followed by thrombectomy), which unfortunately was unsuccessful. Accordingly, the proximal right MCA occlusion was unchanged on 24 h MRA. Note the marked posterior extension of the DWI lesion encompassing part of the initial penumbra at the 24 h time point (red arrow). NIHSS was unchanged. Courtesy: Professor Catherine Oppenheim and Dr Wagih Ben Hassen [Colour figure can be viewed at wileyonlinelibrary.com]

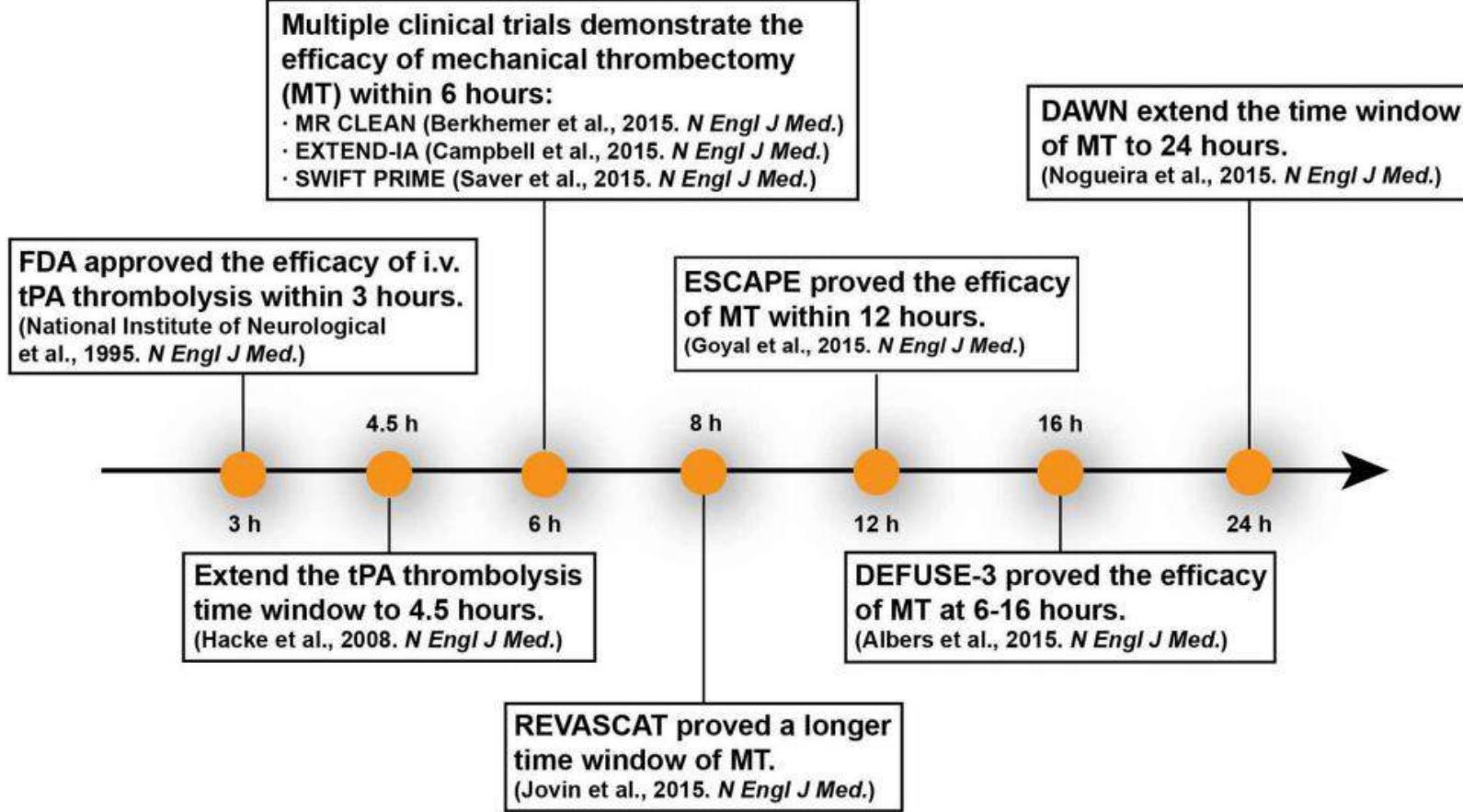


TABLE 1 | Imaging modalities used in the key clinical trials to expand the therapeutic window of ischemic stroke.

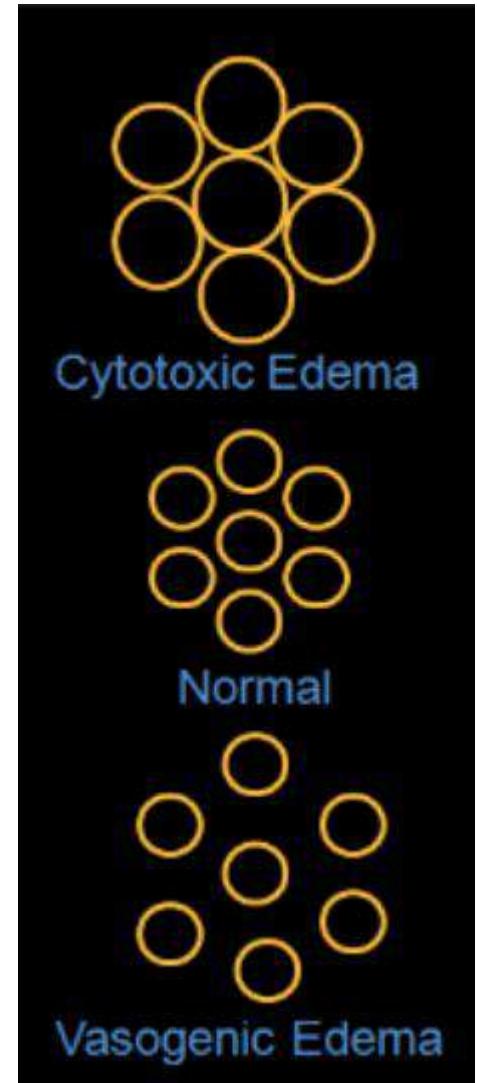
| Study | Sample size | Time window | Imaging modalities | Treatment | Implications |
|-------------|-------------|--------------------------------|--------------------|--|---|
| EPITHET | 101 | 3–6 h after onset | PWI/ DWI | Alteplase or placebo | Alteplase increased reperfusion and neurological outcome at 90 days |
| ECASS III | 821 | 3–4.5 h after onset | CT or MRI | Alteplase or placebo | Alteplase improved neurological outcome at 90 days |
| MR CLEAN | 500 | 6 h after onset | CTA or MRA | Intraarterial treatment or standard care alone | Intraarterial treatment improved neurological outcome at day 90 |
| EXTEND-IA | 70 | 6 h after onset | CTP | Alteplase with thrombectomy or alteplase alone | Thrombectomy improved reperfusion, early neurologic recovery, and functional outcome |
| SWIFT PRIME | 833 | 6 h after onset | CTP, or PWI/DWI | tPA, or tPA with endovascular thrombectomy | Thrombectomy showed more effective recanalization than tPA alone |
| REVASCAT | 206 | 8 h after onset | CT, DWI | Thrombectomy or standard care alone | Thrombectomy reduced the severity of disability |
| ESCAPE | 316 | 12 h after onset | CT, CTA | Thrombectomy plus standard care or standard care alone | Endovascular thrombectomy benefited the patients with moderate-to-severe ischemic stroke. |
| DEFUSE-3 | 182 | 6–16 h after onset | CTP, PWI/DWI | Thrombectomy plus standard care or standard care alone | Thrombectomy resulted in better functional outcomes than standard medical therapy alone |
| DOWN | 206 | 6–24 h after onset | DWI, CTP | Thrombectomy plus standard care or standard care alone | Thrombectomy improved the outcomes at 90 days |
| WAKE UP | 503 | 4.5 h to unknown time of onset | DWI, FLAIR | Alteplase or placebo | Alteplase improved functional outcome at 90 days |

İnmede Nörogörüntüleme

- AHA/ASA 2018/9 guideline: DWI daha sensitif ama rutin kullanımı maliyet-etkin değil
- DWI,MR perfüzyon: 6-24 saat arası anterior sirkulasyon LVO'larda seçili hastalarda önerilir
- Stroke protokolü:
 - DWI/ADC, T2 flair, T2*/SWI, MRA, MRP
 - Hemorajiyi dışlama
 - Erken iskemik değişiklikleri saptama
 - Susceptibility vessel sign varlığı
 - Okluzyonu lokalize etme
 - Kurtarılabilir dokuyu tanımlama

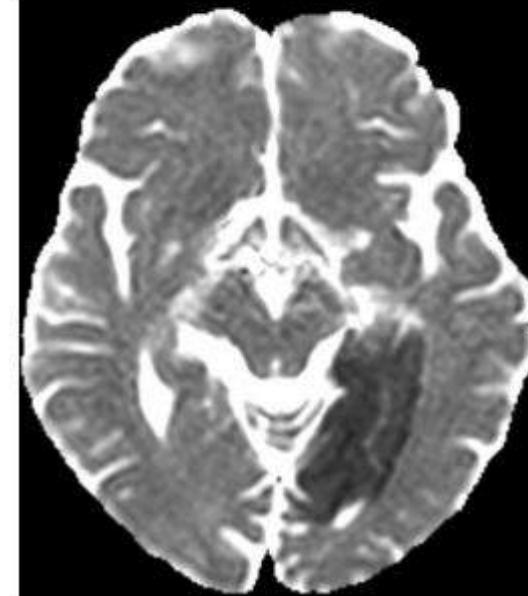
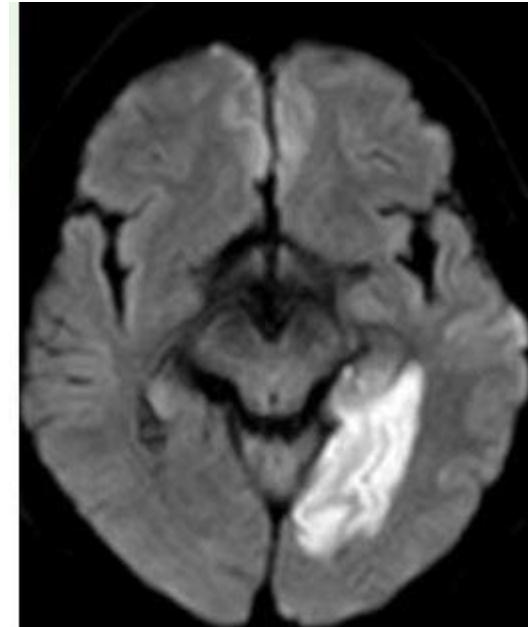
MRI DWI/ADC

- Voxeldeki su moleküllerinin Random Brownian hareketine dayanır
 - Yüksek hücre içeriği ve hücresel ödem düşük difüzyon gösterir
- Beyin iskemisi=sitotoksik ödem
 - Na^+/K^+ pompası çalışmaması sonucu $\rightarrow \text{Na}$ hücre içine $\rightarrow \text{Cl}^-$ eşlik ederek osmotik gradient ile suyun hücre içine girişi
- BT ile kıyasla çok küçük ve erken enfarktlara daha sensitif
 - Dakikalar içinde yüksek sinyal
 - 3-30 dk içinde pozitif
- ADC-DWI' den hesaplanan difüzyon büyüğlük ölçümüdür, aslında difüzyon derecesini gösteren bir parametrik haritadır



DWI/ADC-İskeminin Zamansallığı

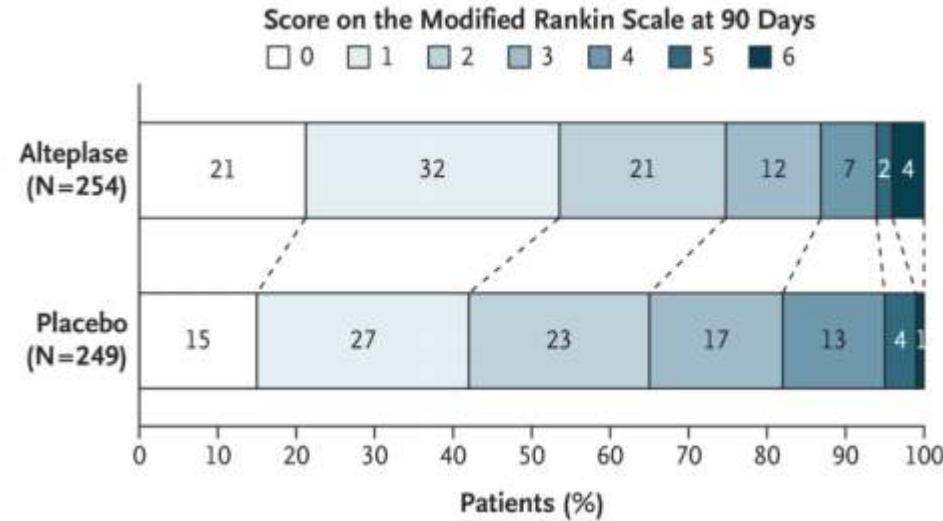
- Akut(0-7 g)
 - ADC 1-4 gün maksimal azalma
- Subakut (1-3 h)
- Kronik(>3 h)



T2 FLAIR

- BOS dan sinyalleri kaldırarak oluşan görüntü
- 6-12 saat içinde pozitif sinyaller(DWI/FLAIR mismatch)
- Yavaş akım flow void kaybı olarak görülebilir

DWI/FLAIR mismatch



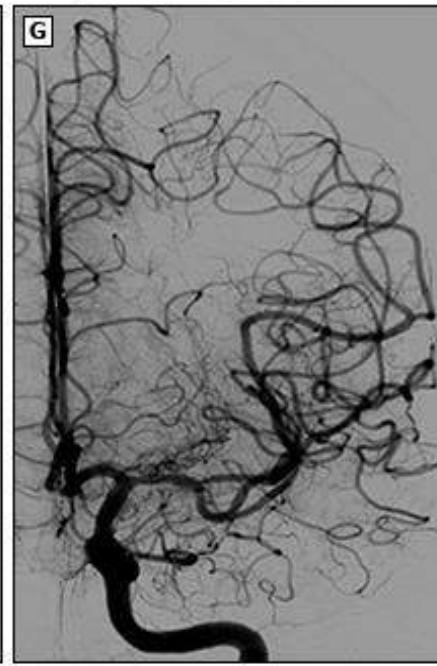
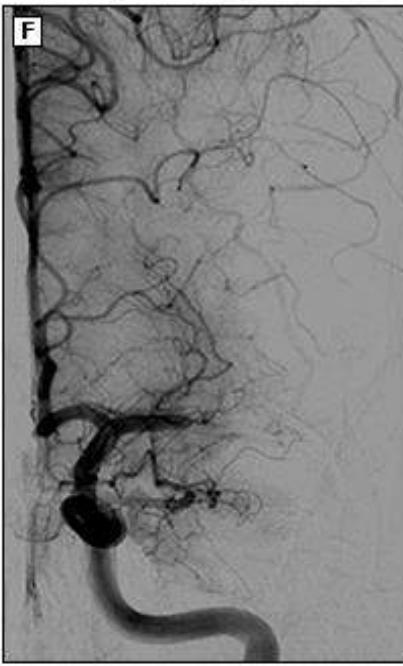
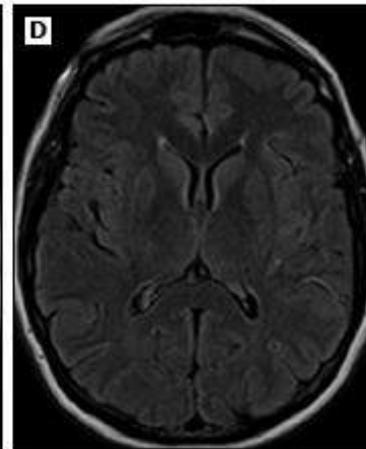
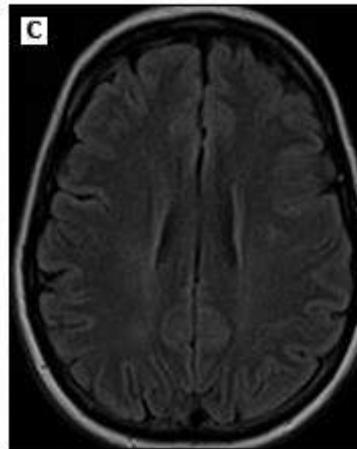
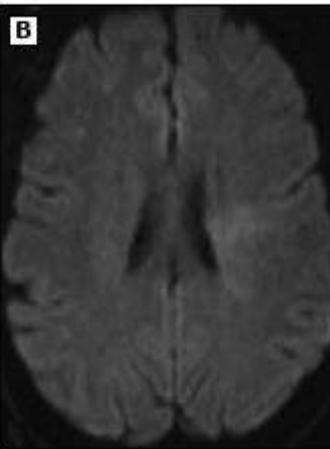
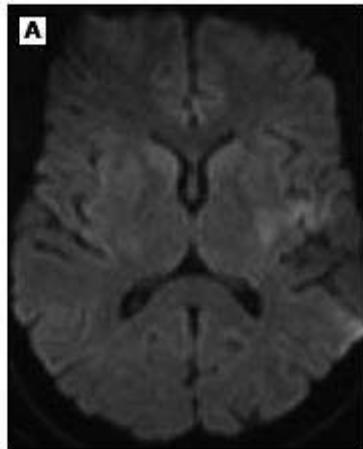
- WAKE-UP çalışması
 - Multisenter, randomize, placebo kontrollü
 - Başlangıç zamanı bilinmeyen inmlerde alteplazin tedavi etkisi
 - 90. gün mRS 0-1 %53 vs %42
 - Sayısal daha fazla ölüm (10/3) ve anlamlığa ulaşan PH2 (10/1)
- DWI/FLAIR=doku penceresi(tissue window)

3. In patients with AIS who awake with stroke symptoms or have unclear time of onset > 4.5 hours from last known well or at baseline state, MRI to identify diffusion-positive FLAIR-negative lesions can be useful for selecting those who can benefit from IV alteplase administration within 4.5 hours of stroke symptom recognition.

IIa

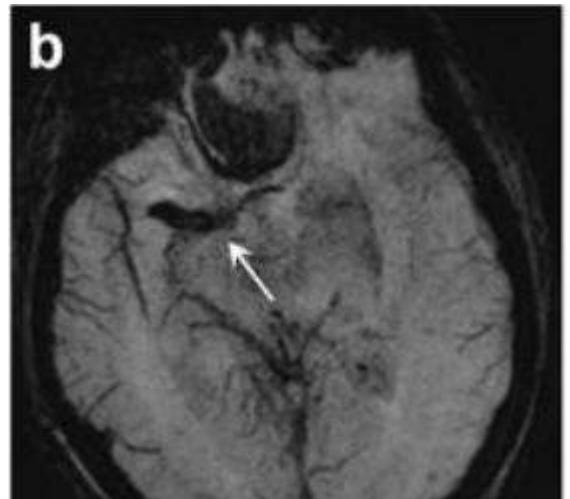
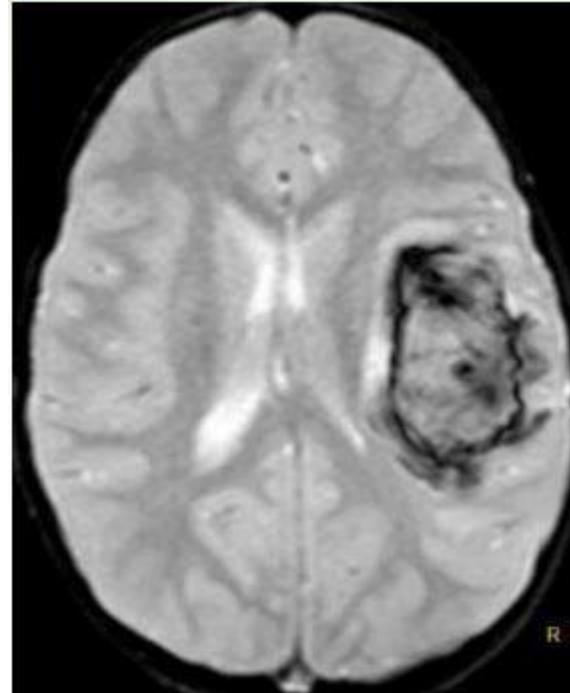
B-R

The WAKE-UP trial (Efficacy and Safety of MRI-based Thrombolysis in Wake-Up Stroke) randomized 503 patients with AIS who awoke with stroke or had unclear time of onset >4.5 hours from last known well and could be treated with IV alteplase within 4.5 hours of stroke symptom recognition. Eligibility required MRI mismatch between abnormal signal on DW-MRI and no visible signal change on FLAIR. DW-MRI lesions larger than one-third of the territory of the middle cerebral artery (MCA), NIHSS score >25, contraindication to treatment with alteplase, or planned thrombectomy were all exclusions. The trial was terminated early for lack of funding before the designated 800 patients were randomized. Ninety-four percent were wake-up strokes. Median NIHSS score was 6. Median time from last known well was slightly over 10 hours. At baseline, one-third of the patients had vessel occlusion on time-of-flight MRA, and three-quarters of the FLAIR lesions were <9 mL. The end point of an mRS score of 0 to 1 at 90 days was achieved in 53.3% of the IV alteplase group and in 41.8% of the placebo group ($P=0.02$).⁸⁸



T2*/GRE/SWI

- lokal manyetik alana etkileri olan bileşikler nedeni ile ortaya çıkan sekanslar
- Kan ürünleri, kalsiyum ve para/dia/ferro -manyetik bileşikler
- Trombüs saptanması=Susceptibility vessel sign



4. Magnetic resonance (MR) imaging (MRI) is effective to exclude ICH before IV alteplase administration.

I

B-NR

MRA

- TOF tekniği- kontrastsız, akım yönü ve hızına duyarlı
- Darlık derecesi ve uzunluğunu overestimate
- Faz kontrast anjiografi: venöz trombozda
- CE-MRA- kontrastlı kan akımından etkilenmeyen, yavaş akımda daha az artefakt(VA-CCA/ICA)

MRA/CTA

MRA

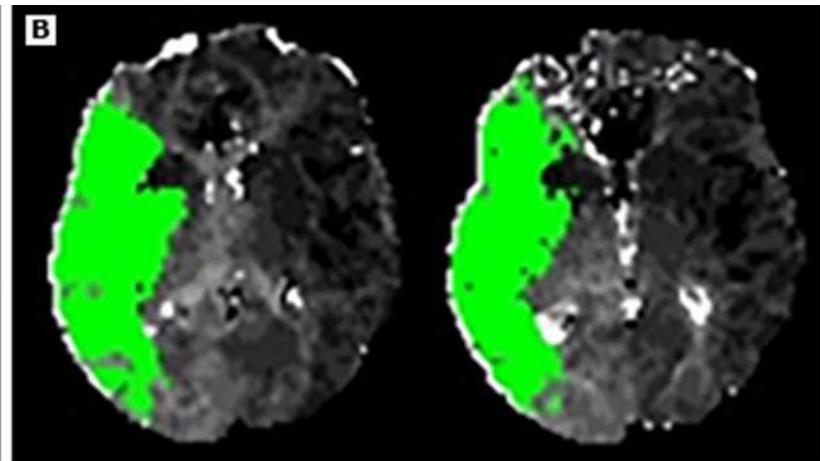
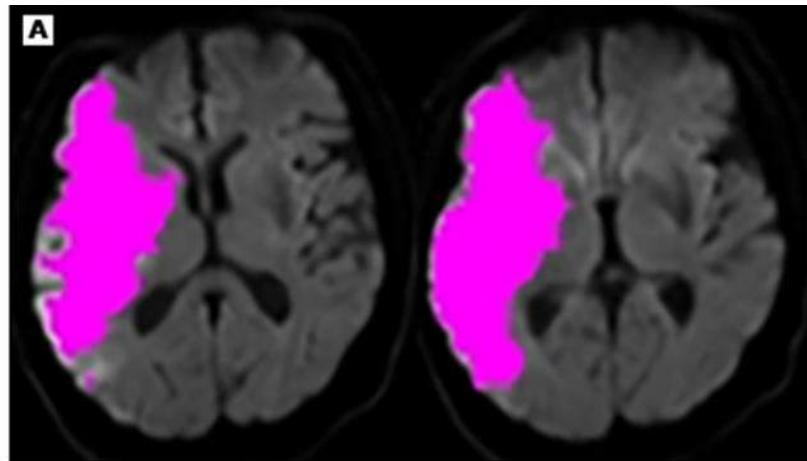
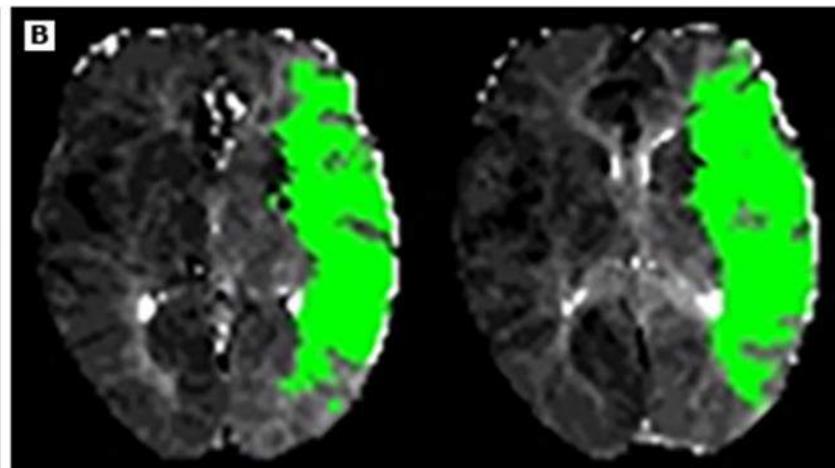
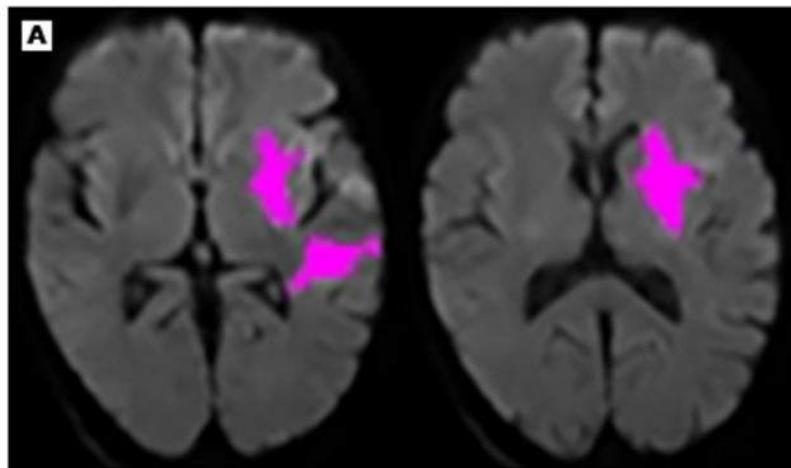
- Kontrastsız
- Hemodinami bilgisi
- Limitli ulaşım
- CE-MRA Artefaktlar

CTA

- Yaygın ulaşım
- Hızlı veri işleme
- Akımdan bağımsız
- DSA ya yakın sonuçlar

Kontrast bağımlı
Radyasyon

MR Perfüzyon



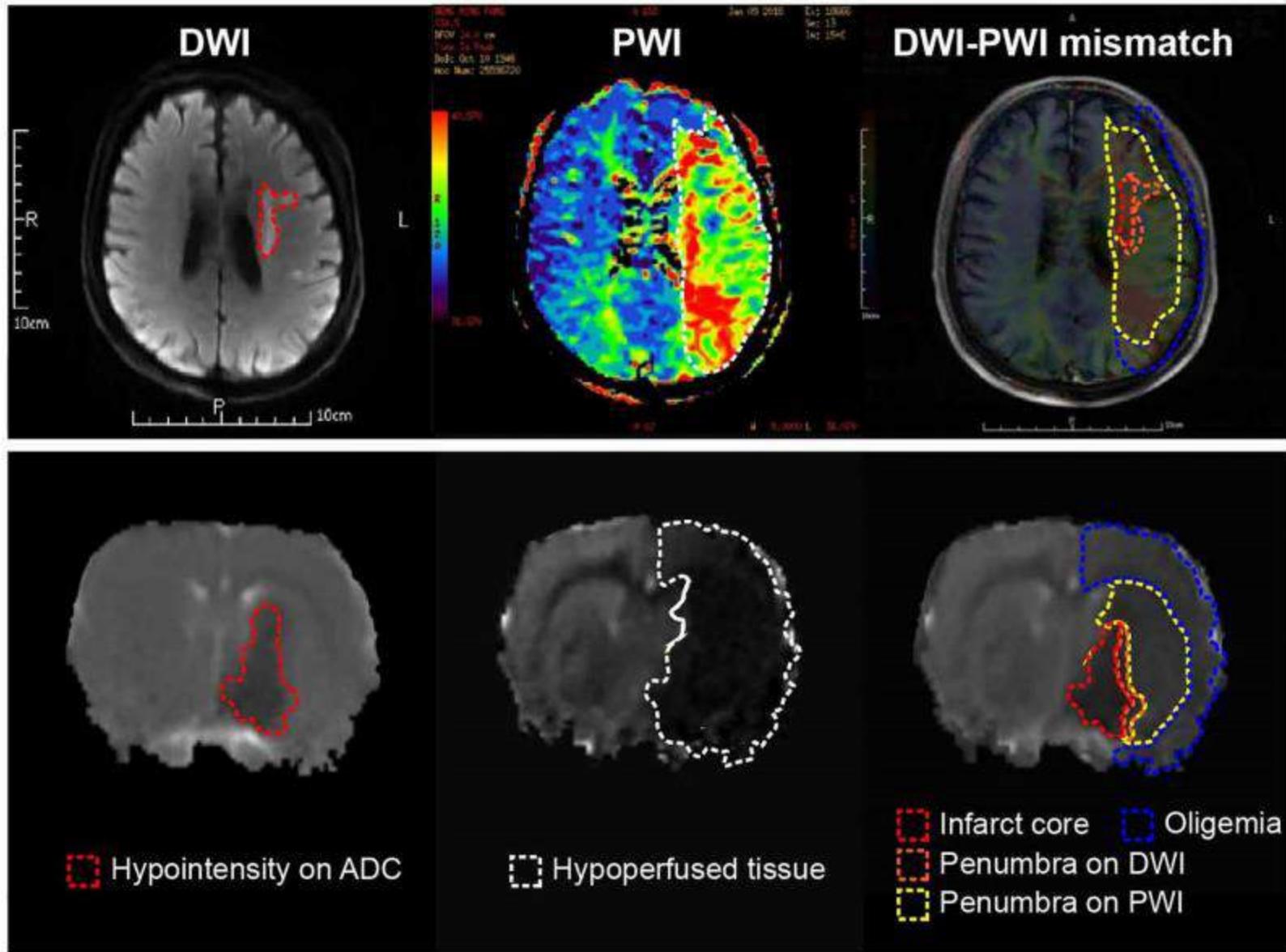


FIGURE 2 | Current concept of the ischemic penumbra. Both clinical (Upper) and experimental (Below) MRI data showed early abnormality on DWI equals the infarct core plus a part of tissue at risk (penumbra), and the perfusion deficiency on PWI includes part of the region of benign oligemia. MRI, magnetic resonance imaging; PWI, perfusion-weighted imaging.

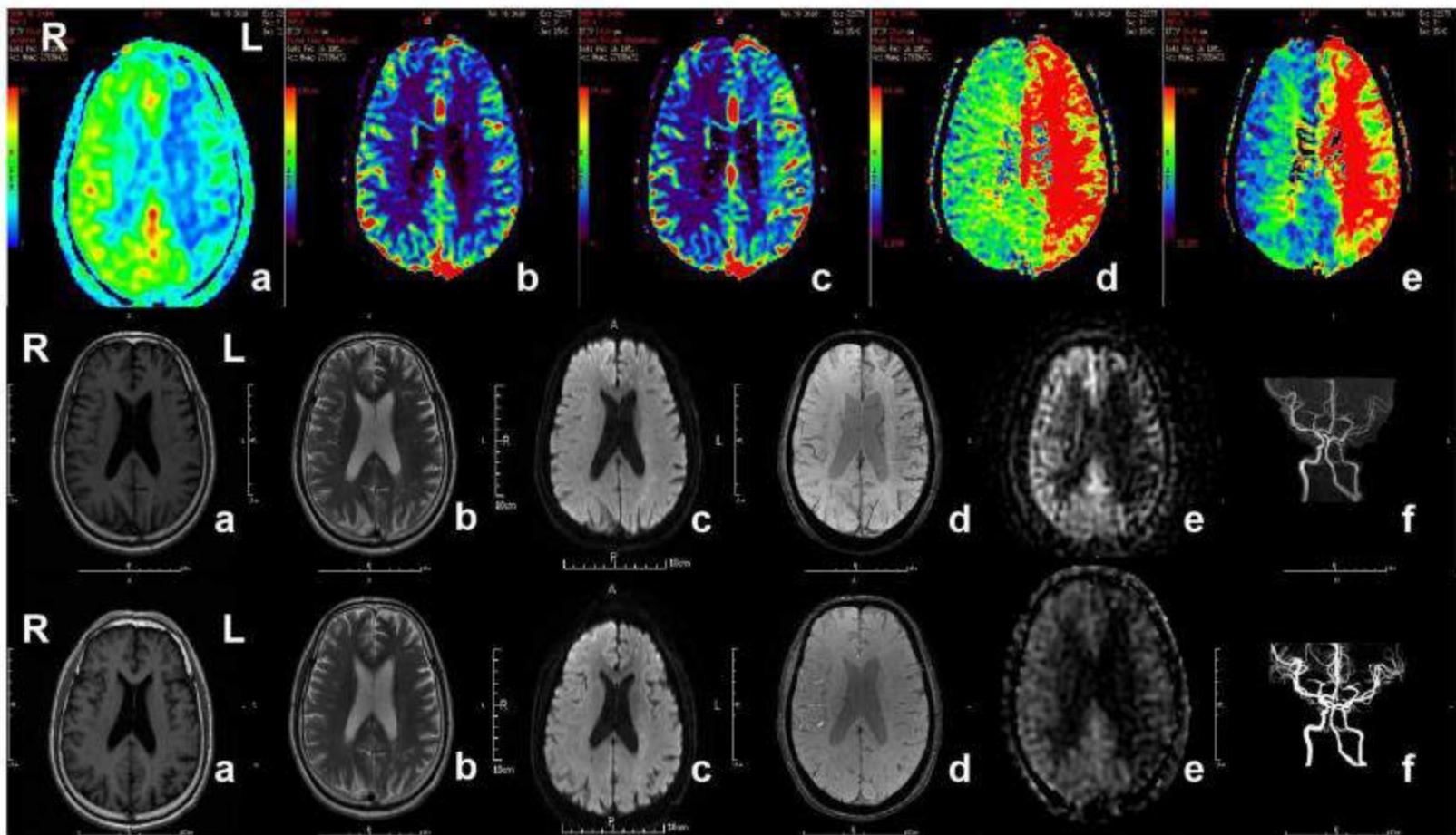
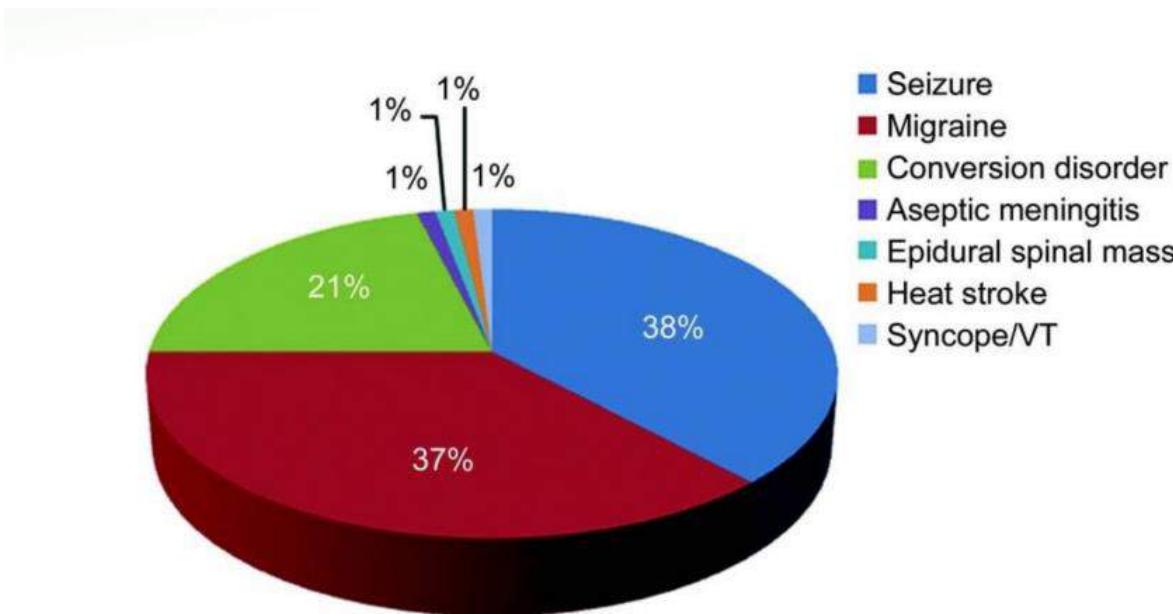


FIGURE 3 | MR imaging of the patient with acute ischemic stroke. The patient, 71-year-old male, suffered from weakness of right limbs, alalia and was unable to walk 3 h prior to the imaging. Medical history included hypertension, diabetes and varicosity of both lower extremities. Physical examination showed right facial palsy, the muscle strength of right limbs was grade I, right Babinski sign (+), Chaddock sign (+), and NIHSS score was 13. The diagnosis of the patient is acute ischemic stroke. The patient was given multimodal MRI and MRA before and after recanalization. The first row showed perfusion-weighted imaging: a and b, Lower CBF in left cerebral hemisphere. c, Higher CBV in left cerebral hemisphere. d, Longer MTT in left cerebral hemisphere. e, Longer TTP in left cerebral hemisphere. The second row and third row showed MRI and MRA before recanalization and after recanalization, respectively. a, b, and c, In the left frontal lobe and lateral ventricle had sporadic dots with slightly longer T1 signal, longer T2 signal higher signal, respectively, in T1WI, T2WI, DWI. d, No cerebral microbleeds in SWI. e, Original ASL. f, MRA showed the intracranial segment of the left internal carotid artery and the left middle cerebral artery were significantly narrow in the second row, while recanalization got in left internal carotid artery and middle cerebral artery. MR, magnetic resonance; MRA, magnetic resonance angiography; SWI, susceptibility weighted imaging; ASL, arterial spin labeling; CBV, cerebral blood volume; CBF, cerebral blood flow; TTP, time to peak; MTT, mean transit time.

Mimikleri dışlama

- 3-10%
- Nöbet,migren,hipoglisemi,konversiyon,senkop,VT.



3 çalışma

- Dawn
- Defuse 3
- Wake-Up

| | | |
|---|---|---|
| 1. When selecting patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining CTP or DW-MRI, with or without MRI perfusion, is recommended to aid in patient selection for mechanical thrombectomy, but only when patients meet other eligibility criteria from one of the RCTs that showed benefit from mechanical thrombectomy in this extended time window. | I | A |
|---|---|---|

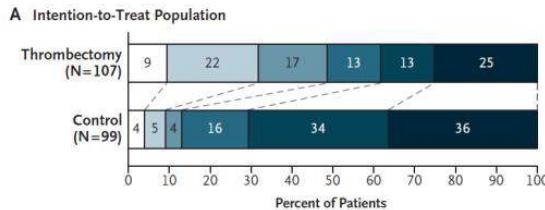
The DAWN trial (Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) used clinical-core mismatch (a combination of age-adjusted NIHSS score and age-adjusted core infarct size on CTP or DW-MRI) as an eligibility criterion to select patients with large anterior circulation vessel occlusion for mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in functional outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33% [95% CI, 21–44]; posterior probability of superiority >0.999).⁵¹ The DEFUSE 3 trial (Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution) used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67 [95% CI, 1.60–4.48]; $P<0.0001$).⁵² Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from one or the other of these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN or DEFUSE 3 eligibility should be strictly adhered to in clinical practice.^{51,52}

>6 saat MTx

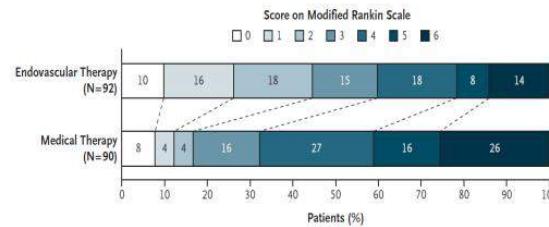
- DAWN DWI ya da CTP /klinik mismatch



N Engl J Med. 2018 Jan 4;378(1):11-21



N Engl J Med. 2018 Feb 22;378(8):708-718



- DEFUSE.3 otomatize kor/perfüzyon mismatch

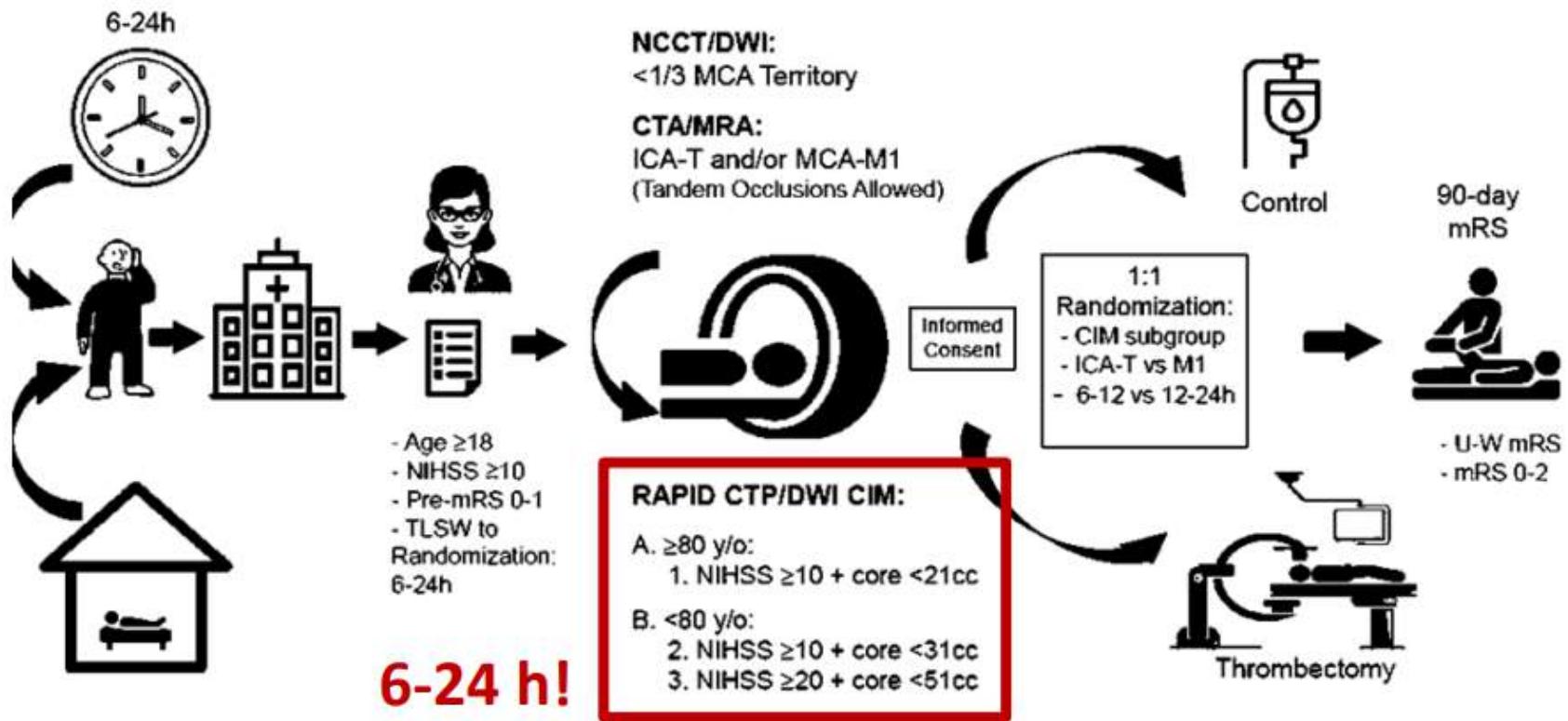


DWI or CTP – clinical mismatch

- - 0-<21 cc core infarct and NIHSS ≥ 10 (and age ≥ 80 years old)
- - 0-<31 cc core infarct and NIHSS ≥ 10 (and age < 80 years old)
- - 31 cc to <51 cc core infarct and NIHSS ≥ 20 (and age < 80 years old)
- NIHSS ≥ 10

CTP or DWI

- Core <70 ml,
mismatch ratio ≥ 1.8 ,
mismatch volume ≥ 15 ml
- NIHSS ≥ 6



<20-50 mL ischemic core

Nogueira RG et al. N Engl J Med. 2018;378(1):11-21.

| | | | |
|---|-----|-----|---------------------|
| <p>7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.</p> | I | A | New recommendation. |
| <p>8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.</p> | IIa | B-R | New recommendation. |

The DAWN trial used clinical imaging mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33%; 95% CI, 21–44; posterior probability of superiority >0.999).¹⁰⁸ In DAWN, there were few strokes with witnessed onset (12%). The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67; 95% CI, 1.60–4.48; $P<0.0001$).¹⁰⁹ Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN and DEFUSE-3 eligibility should be strictly adhered to in clinical practice.

3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset >4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the MCA territory and no visible signal change on FLAIR.

IIa

B-R

The WAKE-UP RCT randomized 503 patients with AIS who awoke with stroke or had unclear time of onset and could be treated with IV alteplase within 4.5 hours of stroke symptom recognition. Eligibility required MRI mismatch between abnormal signal on DW-MRI and no visible signal change on FLAIR. DW-MRI lesions larger than one-third of the territory of the MCA, NIHSS score >25, contraindication to treatment with alteplase, or planned thrombectomy were all exclusions. Ninety-four percent were wake-up strokes. Median NIHSS score was 6. Median time from last known well to symptom recognition was ≈7 hours and to alteplase administration slightly over 10 hours. The primary end point of an mRS score 0 to 1 at 90 days was achieved in 53.3% of the alteplase group and in 41.8% of the placebo group ($P=0.02$). Only 20% had LVO of the intracranial internal carotid or proximal middle cerebral arteries.⁸⁸

Wake-up and unknown time of onset

IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) administered within 4.5 h of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset >4.5 h from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the MCA territory and no visible signal change on FLAIR. (COR IIa; LOE B-R)‡

• WAKE-UP

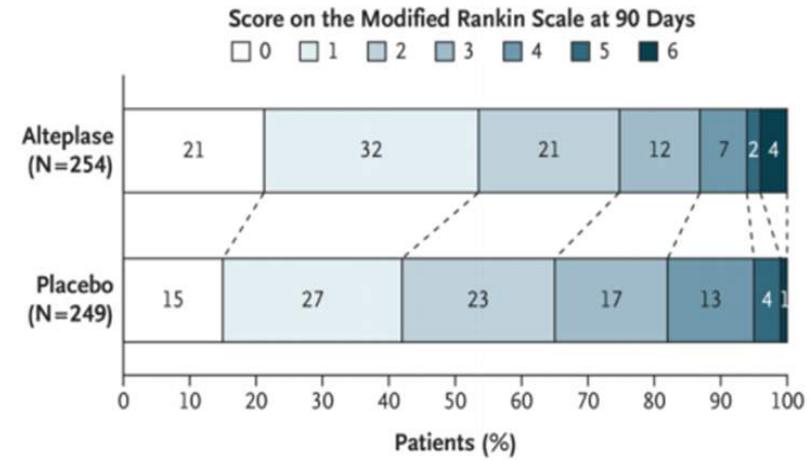


MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators*

Table 3. Safety Outcomes.

| Outcome | Alteplase Group (N=251) | Placebo Group (N=244) | Adjusted Odds Ratio (95% CI) ^a | P Value |
|-------------------------------------|----------------------------|--------------------------|---|---------|
| | no. (%) | | | |
| Primary† | | | | |
| Death or dependency at 90 days | 33 (13.5) | 44 (18.3) | 0.68 (0.39–1.18) | 0.17 |
| Death at 90 days | 10 (4.1) | 3 (1.2) | 3.38 (0.92–12.52) | 0.07 |
| Secondary | | | | |
| Symptomatic intracranial hemorrhage | | | | |
| As defined in SITS-MOST‡ | 5 (2.0) | 1 (0.4) | 4.95 (0.57–42.87) | 0.15 |
| As defined in ECASS II§ | 7 (2.8) | 3 (1.2) | 2.40 (0.60–9.53) | 0.21 |
| As defined in ECASS III¶ | 6 (2.4) | 1 (0.4) | 6.04 (0.72–50.87) | 0.10 |
| As defined in NINDS | 20 (8.0) | 12 (4.9) | 1.78 (0.84–3.71) | 0.13 |
| Parenchymal hemorrhage type 2** | 10 (4.0) | 1 (0.4) | 10.46 (1.32–82.77) | 0.03 |



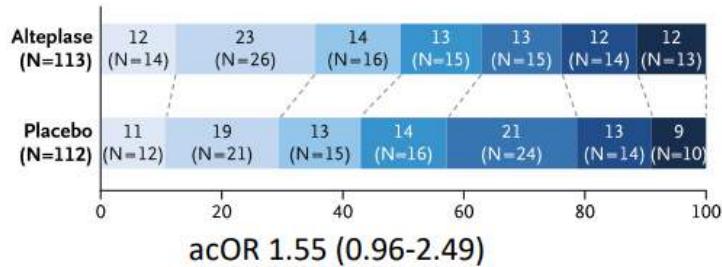
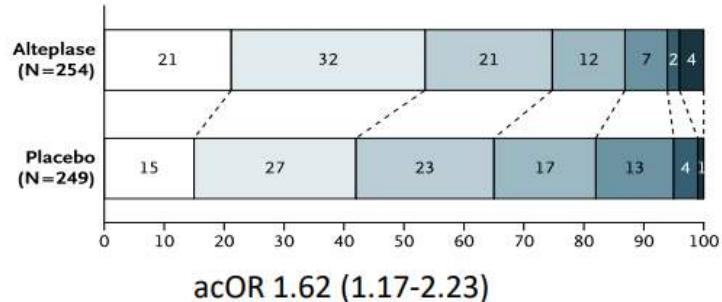
DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4·5 h of symptom onset (PRE-FLAIR): a multicentre observational study

Götz Thomalla, Bastian Cheng, Martin Ebinger, Qing Hao, Thomas Tourdias, Ona Wu, Jong S Kim, Lorenz Breuer, Oliver C Singer, Steven Warach, Soren Christensen, Andras Treszl, Nils D Forkert, Ivana Galinovic, Michael Rosenkranz, Tobias Engelhorn, Martin Köhrmann, Matthias Endres, Dong-Wha Kang, Vincent Dousset, A Gregory Sorensen, David S Liebeskind, Jochen B Fiebach, Jens Fiehler, Christian Gerloff, for the STIR and VISTA Imaging Investigators

Lancet Neurol 2011; 10: 978–86

DWI-FLAIR mismatch identified patients **within 4·5 h** of symptom onset with **62%** (95% CI 57–67) sensitivity

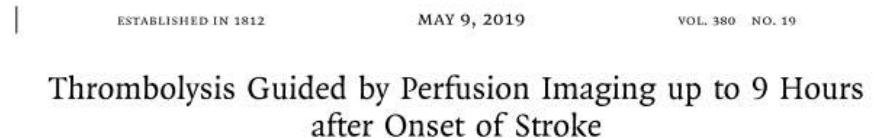
IVT > 4.5 hrs



MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas,

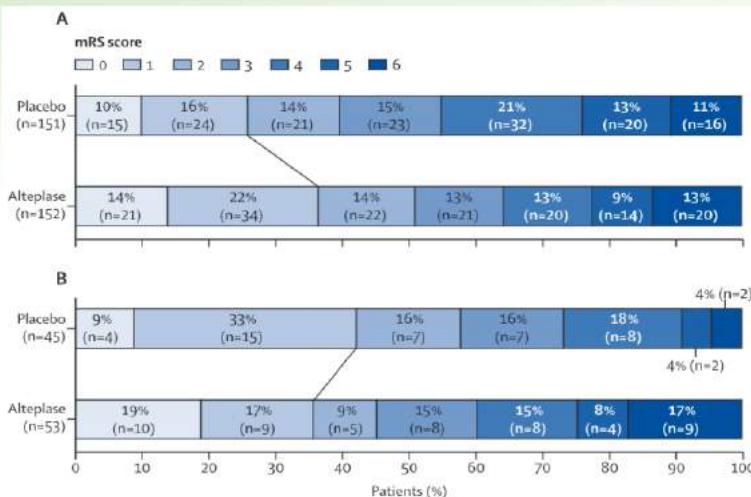
WAKE UP trial



H. Ma, B.C.V. Campbell, M.W. Parsons, L. Churilov, C.R. Levi, C. Hsu, T.J. Kleinig, T. Wijeratne, S. Curtze,

EXTEND trial

Mismatch



No mismatch

Extending thrombolysis to 4·5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data

Bruce C Y Campbell*, Henry Mo*, Peter A Ringden*, Mark W Parsons, Leonid Churilov, Martin Nedenskjöld, Christopher R Levi, Chung Hui, Timothy J Kleinstag, Marc Fuster, Didier Loya, Carlos Molina, Tasso Wijeratne, Sami Curtze, Helen M Drury, P Alan Barber, Kenneth S Butcher, Deside A De Silva, Christopher F Macleod, Naeef Yassie, Johannes A R P Joff, Gagan Sharma, Andrew Blizard, Patricia M Desmond, Stefan Schwab, Peter D Schellinger, Bernhard Yan, Peter J Mitchell, Joaquin Serrador, Danilo Toni, Vincent Thijs, Werner Hacke, Stephen M Davis†, Geoffrey A Donnan‡, on behalf of the EXTEND, ECASS-4, and EPITHET Investigators

Summary

Background Stroke thrombolysis with alteplase is currently recommended 0–4·5 h after stroke onset. We aimed to determine whether perfusion imaging can identify patients with salvageable brain tissue with symptoms 4·5 h or more from stroke onset or with symptoms on waking who might benefit from thrombolysis.

Methods In this systematic review and meta-analysis of individual patient data, we searched PubMed for randomised trials published in English between Jan 1, 2006, and March 1, 2019. We also reviewed the reference list of a previous systematic review of thrombolysis and searched ClinicalTrials.gov for interventional studies of ischaemic stroke. Studies of alteplase versus placebo in patients (aged ≥18 years) with ischaemic stroke treated more than 4·5 h after onset, or with wake-up stroke, who were imaged with perfusion-diffusion MRI or CT perfusion were eligible for inclusion. The primary outcome was excellent functional outcome (modified Rankin Scale [mRS] score 0–1) at 3 months, adjusted for baseline age and clinical severity. Safety outcomes were death and symptomatic intracerebral haemorrhage. We calculated odds ratios, adjusted for baseline age and National Institutes of Health Stroke Scale score, using mixed-effects logistic regression models. This study is registered with PROSPERO, number CRD42019128036.

Findings We identified three trials that met eligibility criteria: EXTEND, ECASS-4-EXTEND, and EPITHET. Of the 414 patients included in the three trials, 213 (51%) were assigned to receive alteplase and 201 (49%) were assigned to receive placebo. Overall, 211 patients in the alteplase group and 199 patients in the placebo group had mRS assessment



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See Online Comment

<https://doi.org/10.1016/j.jtcbe.2019.05.005>

*Contributed equally

†Contributed equally

‡Investigators listed in the appendix

Department of Medicine and Neurology, Melbourne Brain Centre (Prof B C Y Campbell PhD, Prof M W Parsons PhD, Prof L Churilov PhD, N Yan PhD, Prof D Schellinger PhD, Prof J Mitchell PhD, Prof J Serrador PhD, Prof D Toni PhD, Prof V Thijs PhD, Prof W Hacke MD, Prof S M Davis MD).

| Safety outcomes | Placebo (n=152) | Alteplase (n=152) | Odds ratio (95% CI)* | p value |
|--|--------------------|----------------------|-------------------------|---------|
| Death at 3 months | 16/152 (11%) | 20/152 (13%) | 1·28 (0·60–2·73) | 0·52 |
| Symptomatic intracerebral haemorrhage§ | 1/152 (1%) | 7/152 (5%) | 7·29 (0·88–60·18) | 0·07 |

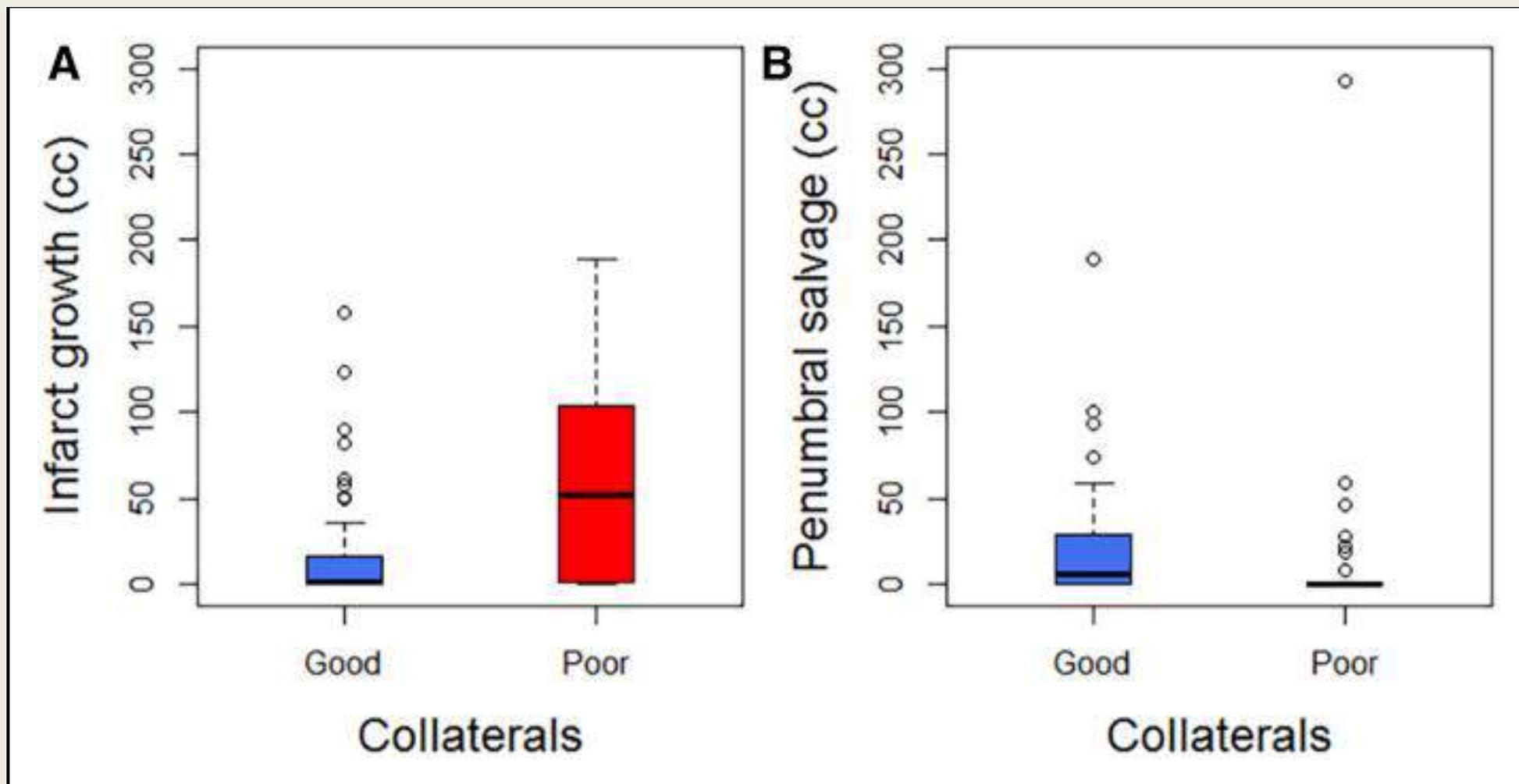
ENDOVASKÜLER TEDAVİ ÖNCESİ KOLLATERAL DEĞERLENDİRME - CTA

Demet Funda Baş

Collateral Clock Is More Important Than Time Clock for Tissue Fate

A Natural History Study of Acute Ischemic Strokes

Achala Vagal, MD, MS; Richard Aviv, MD; Heidi Sucharew, PhD; Mahati Reddy, MD;
Qinghua Hou, MD; Patrik Michel, MD; Tudor Jovin, MD; Thomas Tomsick, MD;
Max Wintermark, MD; Pooja Khatri, MD, MSc
Stroke September 2018

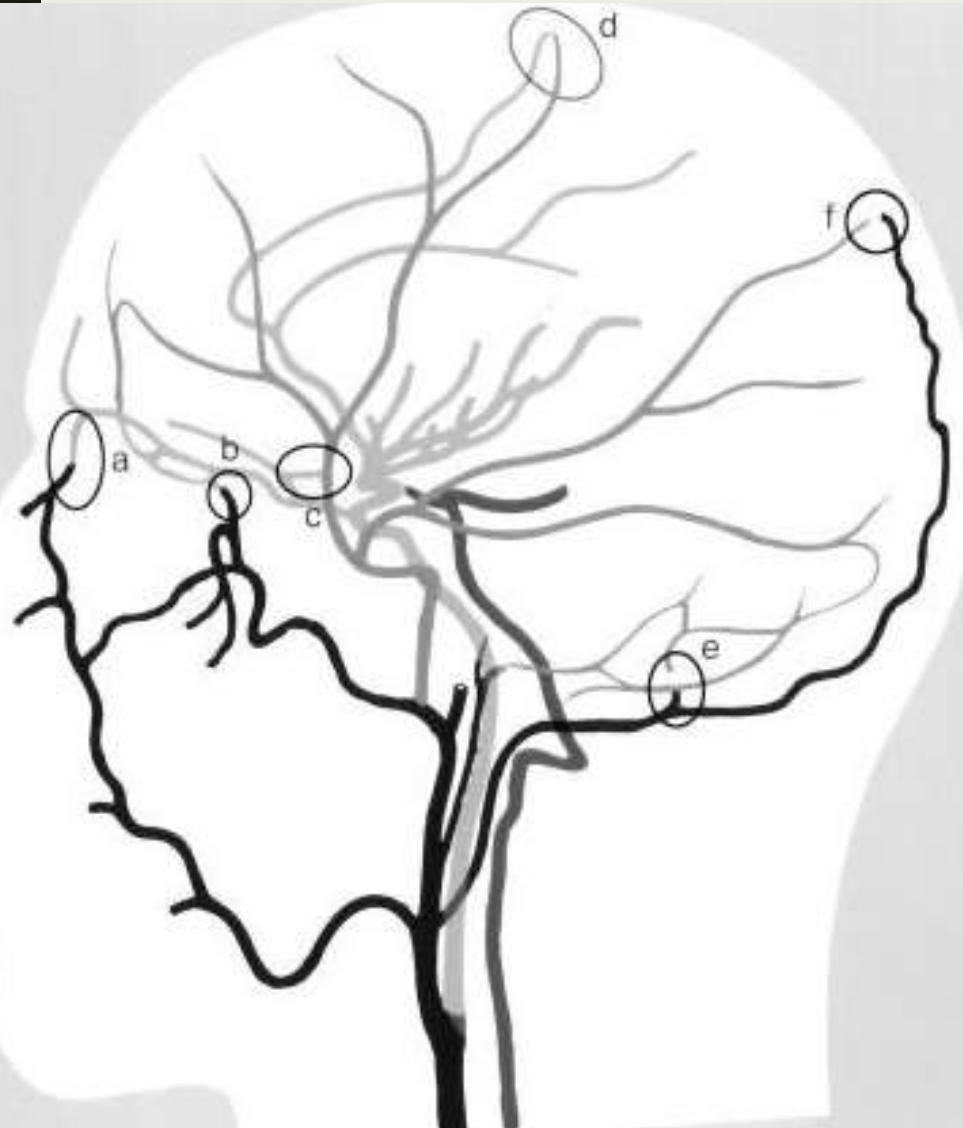


Kollateral Anatomi

- Ekstrakranial & intrakranial
- Circle of Willis
 - *Primer kollateraller*
- Oftalmik a ve leptomeningeal damarlar
 - *Sekonder kollateraller*
- MCA & ACA > MCA & PCA > PCA & ACA terminal anastomozlar

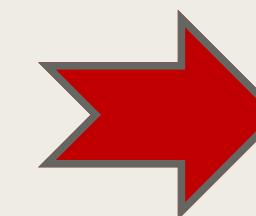
Collateral Circulation

David S. Liebeskind, MD



■ Ekstrakranial arterial kollateral sirkülasyon

- *Facial a (a)*
- *Maxillary a (b)*
- *Middle meningeal a (c)*
- *Dural arteriolar anastomozlar*
 - Middle meningeal a
 - Occipital a (d)



Oftalmik a

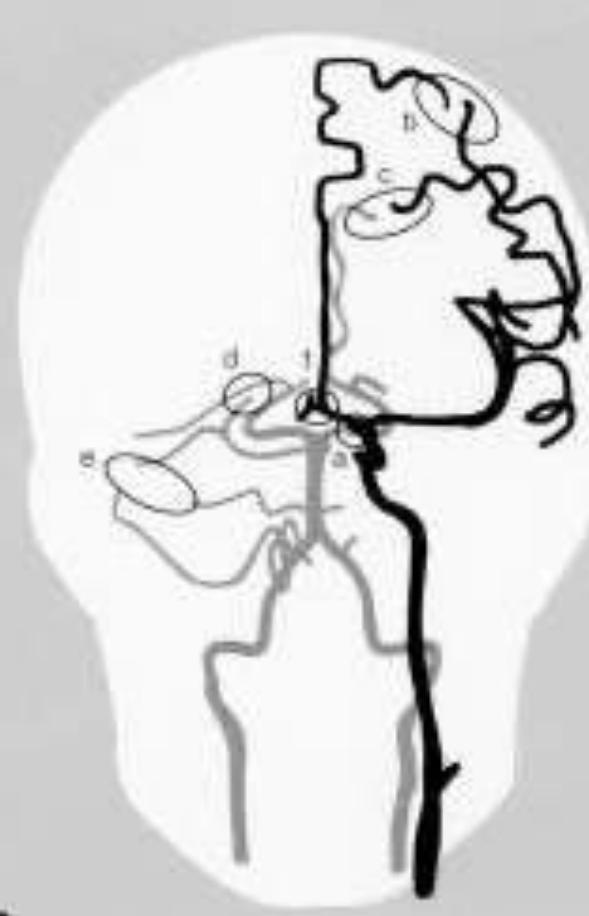
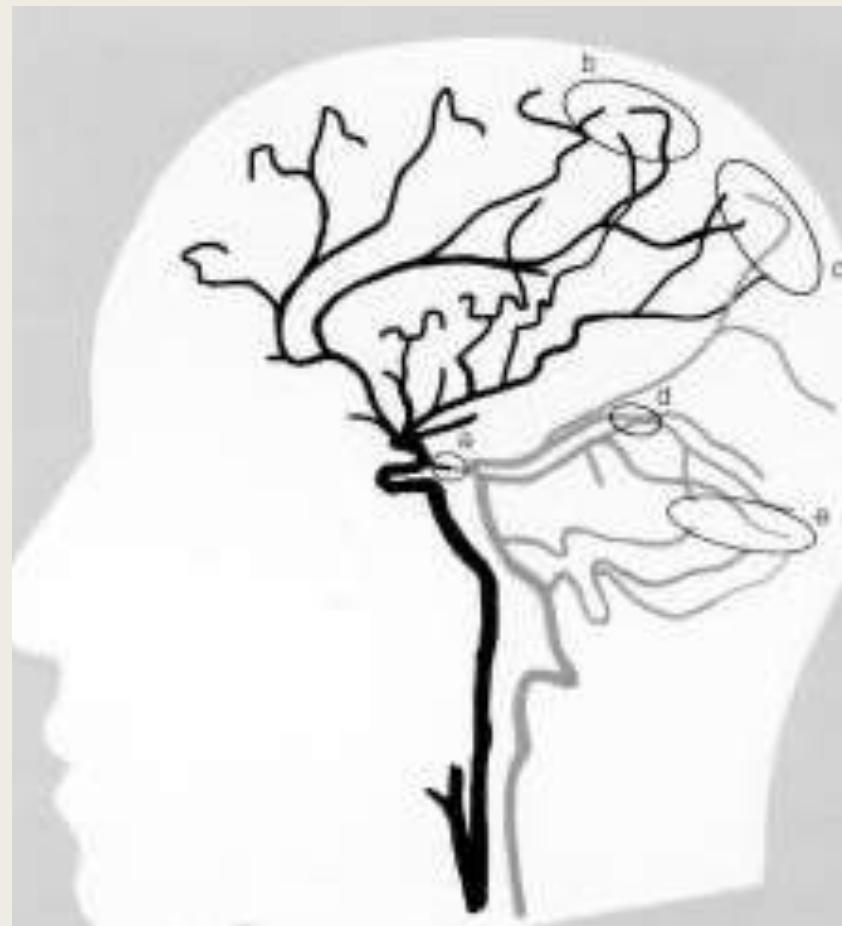
Mastoid foramen (e)
Parietal foramen (f)

Collateral Circulation

David S. Liebeskind, MD

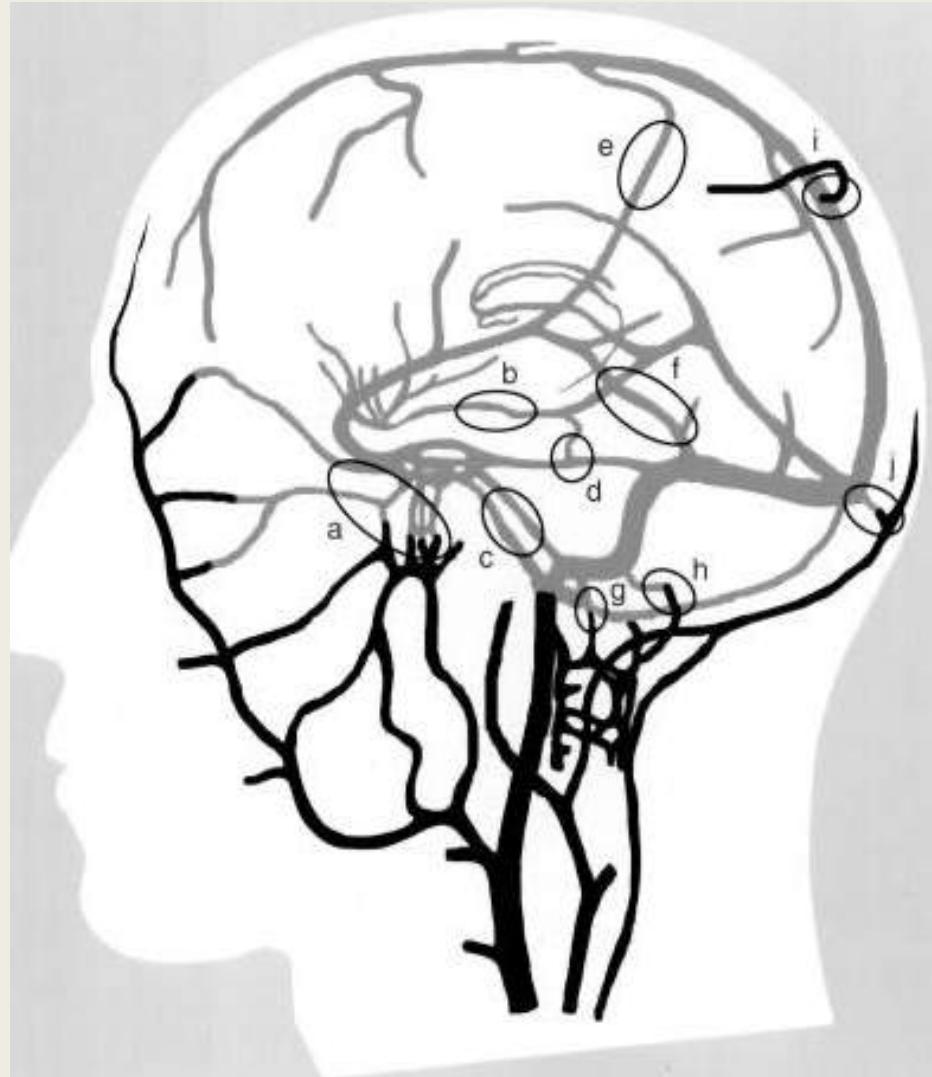
Intrakranial arterial kollateral sirkülasyon

- *Pcomm (a)*
- *Leptomeningeal anastomozlar (ACA & MCA (b) MCA&PCA (c))*
- *Tektal pleksus (PCA & SCA) (d)*
- *Distal serebellar aa (e)*
- *Acomm (f)*



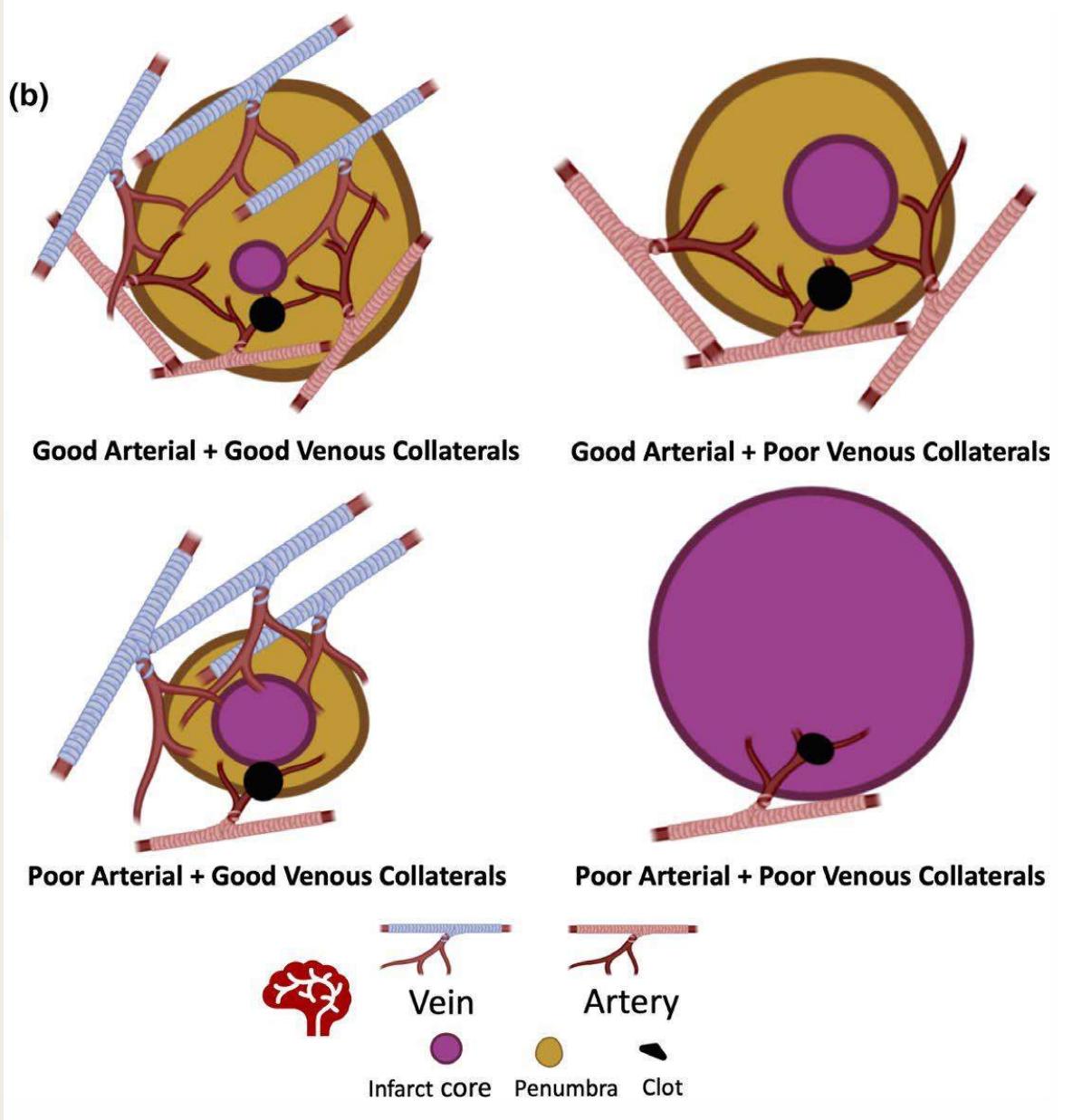
Collateral Circulation

David S. Liebeskind, MD



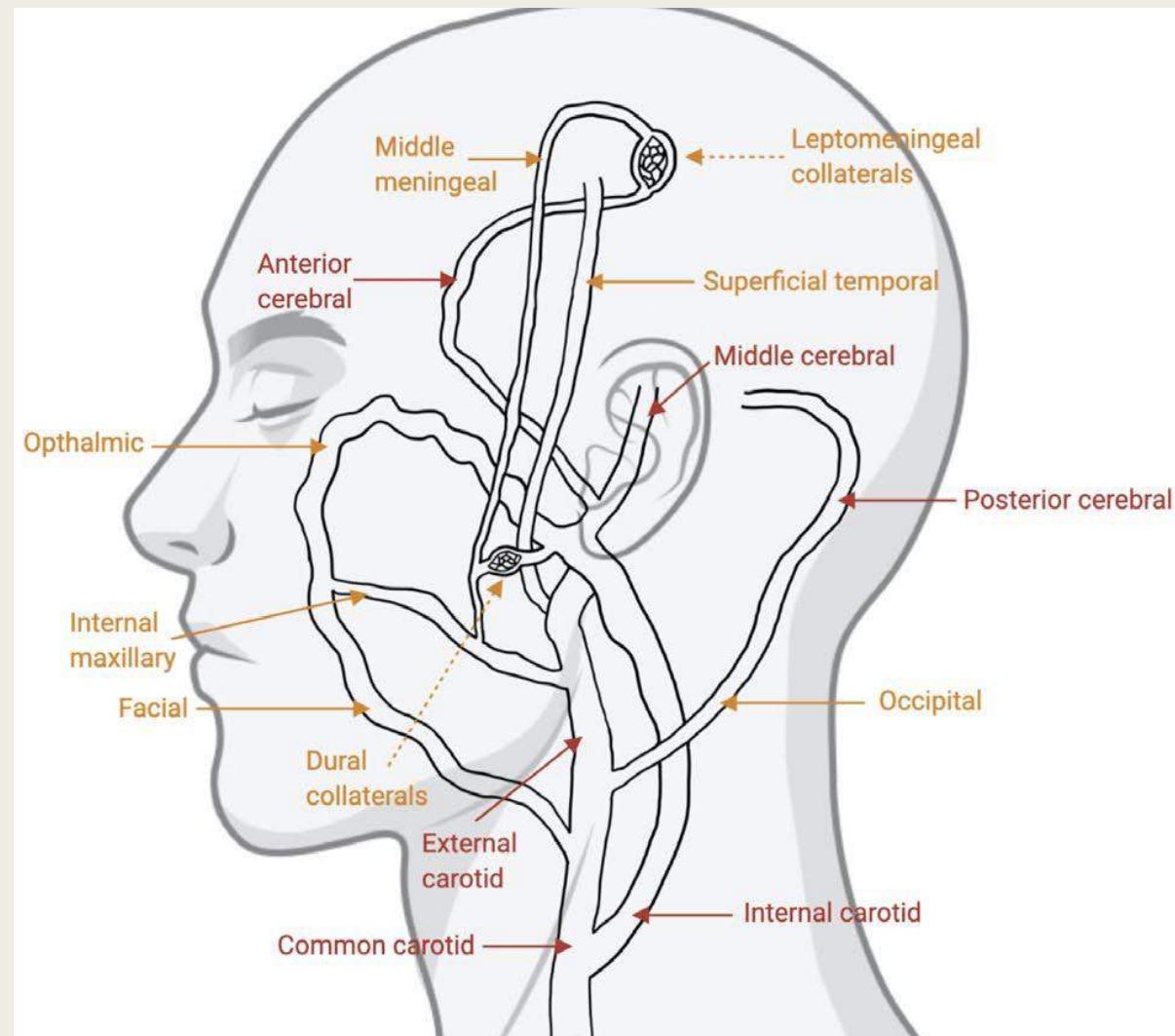
■ Venöz kollateral sirkülasyon

- *Pterygoid plexus (a)*
- *Deep middle cerebral v (b)*
- *Inferior petrosal sinus & basilar plexus (c)*
- *Superior petrosal sinus (d)*
- *Anastomotic v of Trolard (e)*
- *Anastomotic v of Labbe (f)*
- *Condyloid emissary v (g)*
- *Mastoid emissary v (h)*
- *Parietal emissary v (i)*
- *Occipital emissary v (j)*



Cerebral collaterals in acute ischaemia: Implications for acute ischaemic stroke patients receiving reperfusion therapy

Abina Vishni Ravindran^{1,3,6} | Murray C. Killingsworth^{1,5,7} | Sonu Bhaskar^{1,2,3,4,5,6}



Görüntüleme

- Altın standart DSA
 - *Sık bakılmaz*
 - *Kontrast hacmi ve basıncı önemli*
- TCD
 - *Transtemporal pencere*
 - *Serebral vazomotor reaktivite - otoregülasyon & kollateral durum*
 - CO_2 inhalasyonu, asetazolamid enjeksiyonu veya apne
- CTA
- MRA
 - *Willis proksimal arteriyel segmentleri*

Cerebral Collateral Circulation: A Review in the Context of Ischemic Stroke and Mechanical Thrombectomy

Guilherme Santos Piedade^{1,2}, Clemens M. Schirmer¹, Oded Goren¹, Hua Zhang³, Amir Aghajanian³, James E. Faber³, Christoph J. Griessenauer^{1,4,5}

World Neurosurgery, February 2019

Table 1. Comparison of Collateral Scoring Systems

| | | Digital Subtraction Angiography | | | CTA | | |
|-------|---|--|--|--|--|--|--|
| | | Modified Version of ASIV/ SIR Collateral Score for Dynamic CTA | | | ASPECTS-on-Collaterals* | | |
| Grade | ASTIN/SR Collateral Score | Christoforidis et al. ¹⁵ | DynaCTA | ASPECTS-on-Collaterals* | Tan et al. ¹⁶ | Mitoff et al. ¹⁷ | |
| 0 | No collaterals visible to the ischemic site | Collaterals constituted the ischemic site until the late venous phase | Partial collateralization of the ischemic site until the late venous phase | Arteries distal to the occlusion less prominent compared with a but >50% of the occluded MCA territory | Collateral supply filling <50% compared with a matching region in the opposite territory | Contrast opacification is absent collateral supply to the occluded MCA territory | |
| 1 | Slow collaterals to the periphery of the ischemic site with persistence of some of the defect | Collaterals constituted the ischemic site with distal portion of the occluded vessel segment | Arteries distal to the occlusion | Arteries distal to the occlusion | Collateral supply filling <50% compared with a matching region in the opposite territory | Contrast opacification is non-existent or barely visible just during any point of time | |
| 2 | Rapid collaterals to the periphery of ischemic site with persistence of some of the defect and to only a portion of the occluded vessel | Collaterals constituted vessels in the proximal portion of the segment adjacent to the occluded vessel | Partial collateralization of the ischemic site before the venous phase | Arteries distal to the occlusion compared with a matching region in the opposite site | Collateral supply filling >50% compared with a matching region in the opposite site | Vessels can be seen at the distal to the occlusion but <100% of the occluded MCA territory | |
| 3 | (collaterals with slow but complete a geographic defect of the entire ischemic bed by the late venous phase) | Collaterals constituted vessels in the distal portion of the segment adjacent to the occluded vessel | Complete collateralization of the ischemic site by the late venous phase | Arteries distal to the occlusion | Collateral supply filling 100% of the occluded MCA territory | Sylvian fissure | |
| 4 | (complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by the early venous phase) | Collaterals constituted vessels in the distal portion of the segment adjacent to the occluded vessel | Complete collateralization of the ischemic site before the venous phase | Arteries distal to the occlusion | Vessels are constituted distal to the occlusion | Collateral supply filling 100% of vessels are constituted distal to the occlusion | |
| 5 | (no retrograde perfusion) | | | | | | |
| | | Little or no significant reconstitution of the territory of the occluded vessel | | | | | |

Miteff Sistemi

- Single phase CTA
- Sylvian fissürde MCA kollateral dallarına göre 3 puanlı skorlama
 - *3p damarlar oklüzyon distaline kadar yeniden oluşmuş*
 - *2p bazı damarlar Sylvian fissürde görünüyor*
 - *1p kontrastlanma sadece distal süperfisyal damarlarda görünüyor*

Cerebral collaterals in acute ischaemia: Implications for acute ischaemic stroke patients receiving reperfusion therapy

Abina Vishni Ravindran^{1,3,6}  | Murray C. Killingsworth^{1,5,7} | Sonu Bhaskar^{1,2,3,4,5,6} 

Maas Sistemi

- Single phase CTA
- Kontralateral tarafa kıyaslama ile 5 puanlık skorlama sistemi
 - *5p taşkın*
 - *4p kontralateral taraftan daha fazla*
 - *3p kontralateral taraf ile eşit*
 - *2p kontralateral taraftan daha az*
 - *1p damar kontrastlanması yok*

Cerebral collaterals in acute ischaemia: Implications for acute ischaemic stroke patients receiving reperfusion therapy

Abina Vishni Ravindran^{1,3,6}  | Murray C. Killingsworth^{1,5,7} | Sonu Bhaskar^{1,2,3,4,5,6} 

Qureshi dereceleme şeması

- Single phase CTA / MRA
- 6 puanlık bir skala
 - *5p ICA/BA oklüzyonu*
 - *4Ap/4Bp ICA/BA oklüzyonu; kollaterallerle antegrad veya retrograd akım var*
 - *3Ap/3Bp M1 kök oklüzyonu lentikülostriat damarlar korunmuş veya kayıp*
 - *2p iki dal oklüzyonu*
 - *1p bir dal oklüzyonu*
 - *0p oklüzyon yok*

Assessment of Cerebral Collateral Flow With Single-Phase Computed Tomography Angiography-Based Multimodal Scales in Patients With Acute Ischemic Stroke

Haoran He, MD,* Zhong-Ming Qian, MD, PhD,† Yuan Sheng, PhD,† and Yong Liu, MD, PhD*

(J Comput Assist Tomogr 2020;44: 708–713)

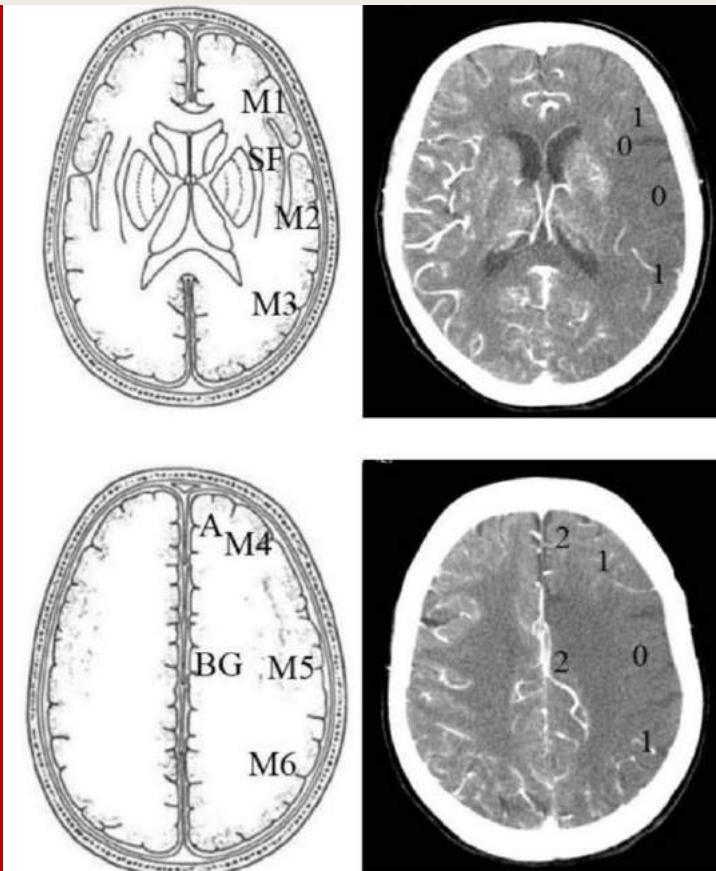
Regional leptomeningeal skor

Single phase CTA

20 puanlık skorlama

ASPECT bölgelerine, ACA bölgесine ve basal gg'a göre yapılır

- 0 lentikülostriat/pial damar yok
- 1 lentikülostriat/pial damar daha az
- 2 lentikülostriat/pial damar kontralateral hemisfere eşit/daha belirgin
- Sylvian fissürde 0-2-4 şeklinde puan verilir



| Region | Score |
|----------------------|-------|
| M1 | |
| M2 | |
| M3 | |
| M4 | |
| M5 | |
| M6 | |
| ACA (A) | |
| BasalGanglia (BG) | |
| Sylvian fissure (SF) | |
| rLMS score | |

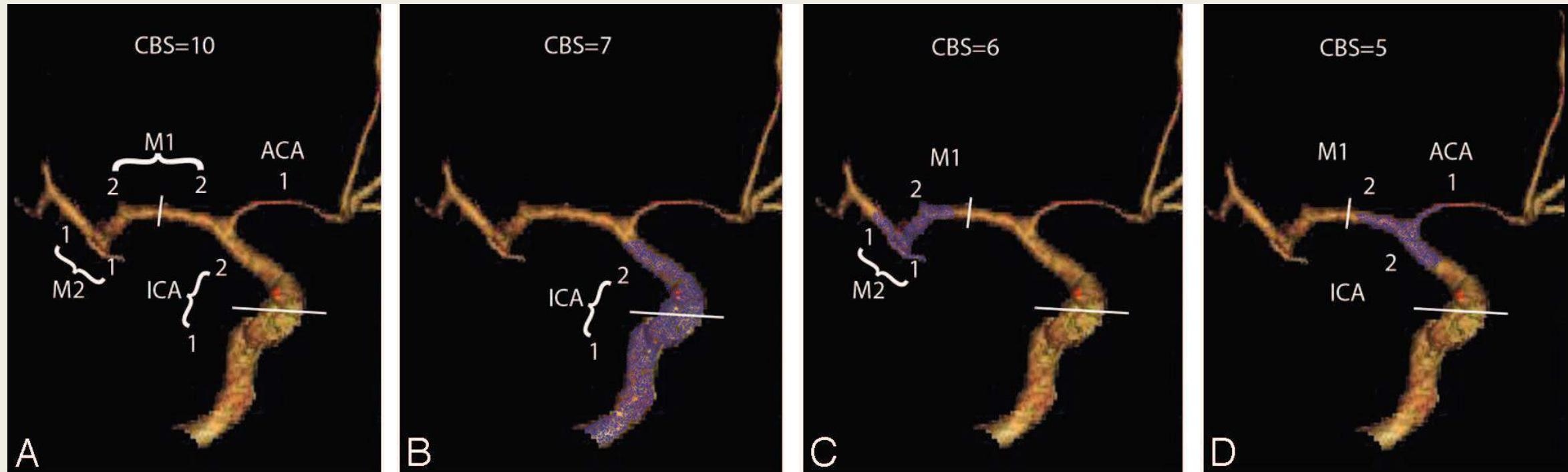
TAN skorlama

ORIGINAL
RESEARCH

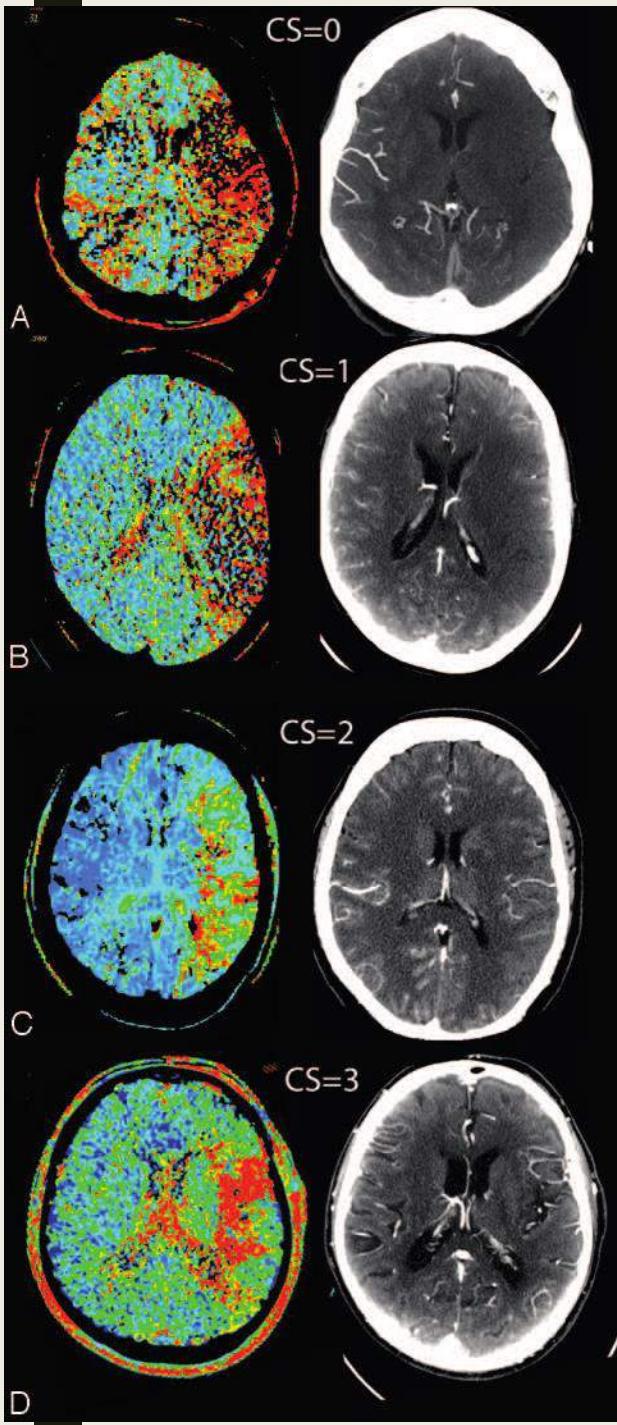
I.Y.L. Tan

CT Angiography Clot Burden Score and Collateral Score: Correlation with Clinical and Radiologic Outcomes in Acute Middle Cerebral Artery Infarct

BACKGROUND AND PURPOSE: Clot extent, location, and collateral integrity are important determinants



A 10-point score is normal, implying absence of thrombus. Two points (as indicated) are subtracted for thrombus found on CTA in the supraclinoid ICA and each of the proximal and distal halves of the MCA trunk. One point is subtracted for thrombus found in the infraclinoid ICA and AI segment and for each affected M2 branch. *B*, Occlusion of infra- and supraclinoid ICAs with a CBS of 7. *C*, Distal M1 and 2 M2 branch occlusions produce a CBS of 6. *D*, Occlusion of the terminal ICA, proximal M1, and AI, with a resultant CBS of 5.



ORIGINAL
RESEARCH

I.Y.L. Tan

CT Angiography Clot Burden Score and Collateral Score: Correlation with Clinical and Radiologic Outcomes in Acute Middle Cerebral Artery Infarct

BACKGROUND AND PURPOSE: Clot extent, location, and collateral integrity are important determinants of outcome in acute middle cerebral artery infarct.

TAN skorlama

- 4 farklı vakanın MTT ve CTA kaynak görüntüleri, her biri sol MCA sulama alanında uzamış MTT
 - A. *Kollateral skor 0; Damar yok*
 - B. *Kollateral skor 1; kollateral kaynak dolumu $\leq\%50$ ama $>\%0$*
 - C. *Kollateral skor 2; kollateral kaynak dolumu $<\%100$ ama $>\%50$*
 - D. *Kollateral skor 3; kollateral kaynak dolumu $\geq\%100$*

Modifiye Tan

- Single phase CTA
- İyi ve kötü
 - *İyi*
 - Kollateraller MCA sulama alanının $\geq\%50$ sinde görülüyor
 - *Kötü*
 - Kollateraller MCA sulama alanının $<\%50$ sinde görülüyor

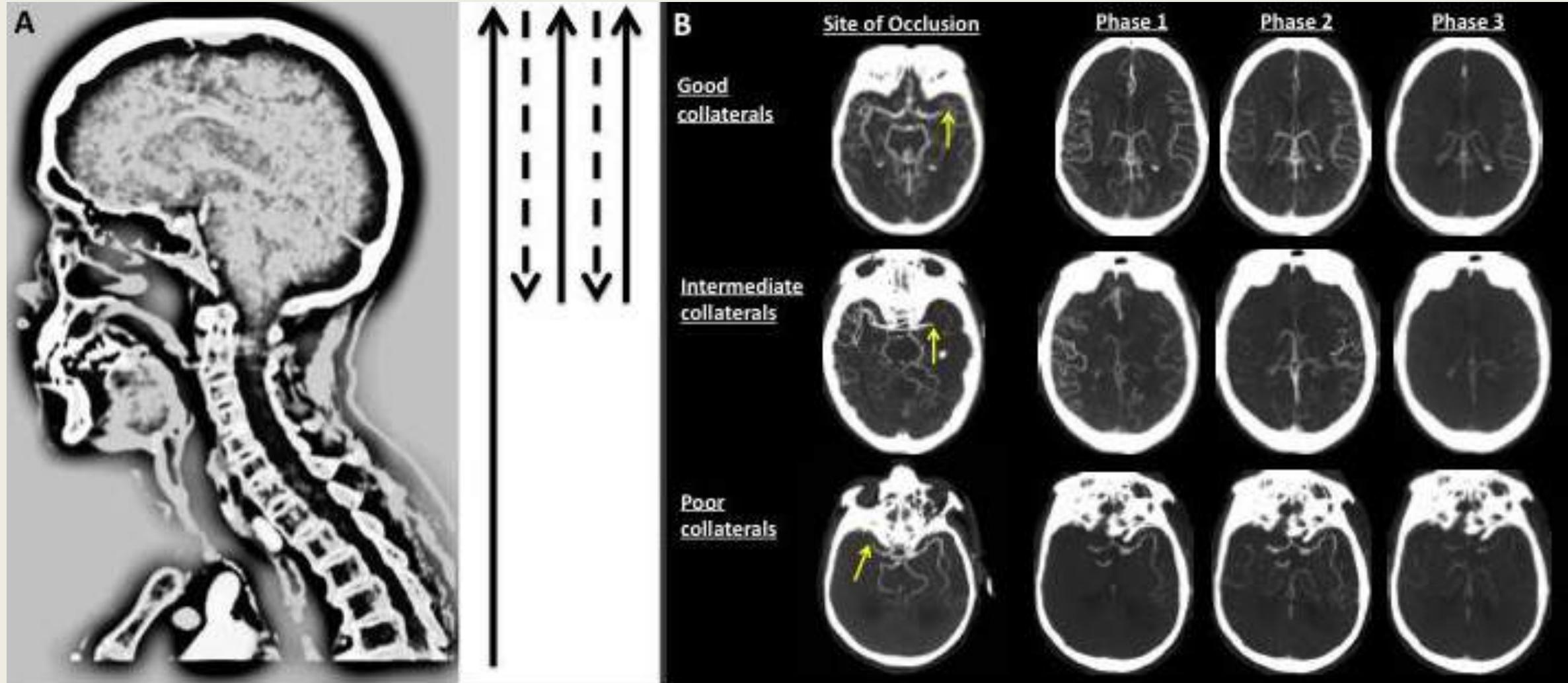
Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019-30. DOI: 10.1056/NEJMoa1414905

(PDF updated March 12, 2015.)

ESCAPE

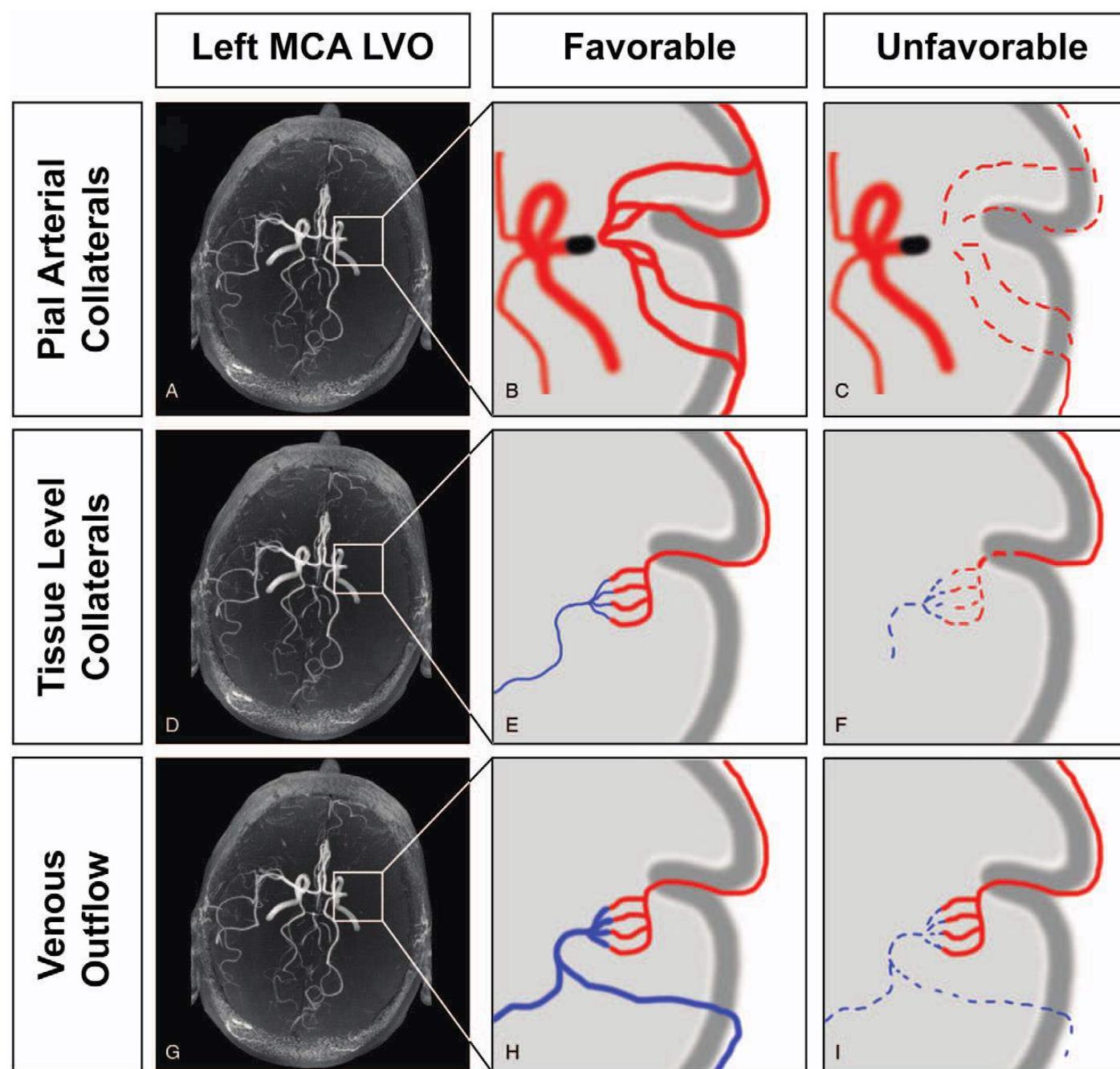


Multifaz CTA kollateral skor

- Multifaz CTA
- Toplam 6p
 - *5p Etkilenen hemisferde dolum gecikmesi yok*
 - *4p Etkilenen hemisferde 1 faz dolum gecikmesi var*
 - *3p Etkilenen hemisferde 2 faz dolum gecikmesi var veya 1 faz gecikme & ciddi oranda azalmış sayıda kollateraller*
 - *2p Etkilenen hemisferde 2 faz dolum gecikmesi var & ciddi oranda azalmış sayıda kollateraller veya 1 faz gecikme & damarların görünmediği alanlar var*
 - *1p Etkilenen hemisferde herhangi bir fazda birkaç damar görünüyor*
 - *0p Etkilenen hemisferde herhangi bir fazda hiç damar görünmüyör*
- ≤3p kötü prognoz ile ilişkili

Cerebral collaterals in acute ischaemia: Implications for acute ischaemic stroke patients receiving reperfusion therapy

Abina Vishni Ravindran^{1,3,6}  | Murray C. Killingsworth^{1,5,7} | Sonu Bhaskar^{1,2,3,4,5,6} 



Rethinking the Collateral Vasculature Assessment in Acute Ischemic Stroke

The Comprehensive Collateral Cascade

Tobias Djamsched Faizy, MD, and Jeremy Josef Heit, MD, PhD

Topics in Magnetic Resonance Imaging, August 2021

- Comprehensive collateral cascade

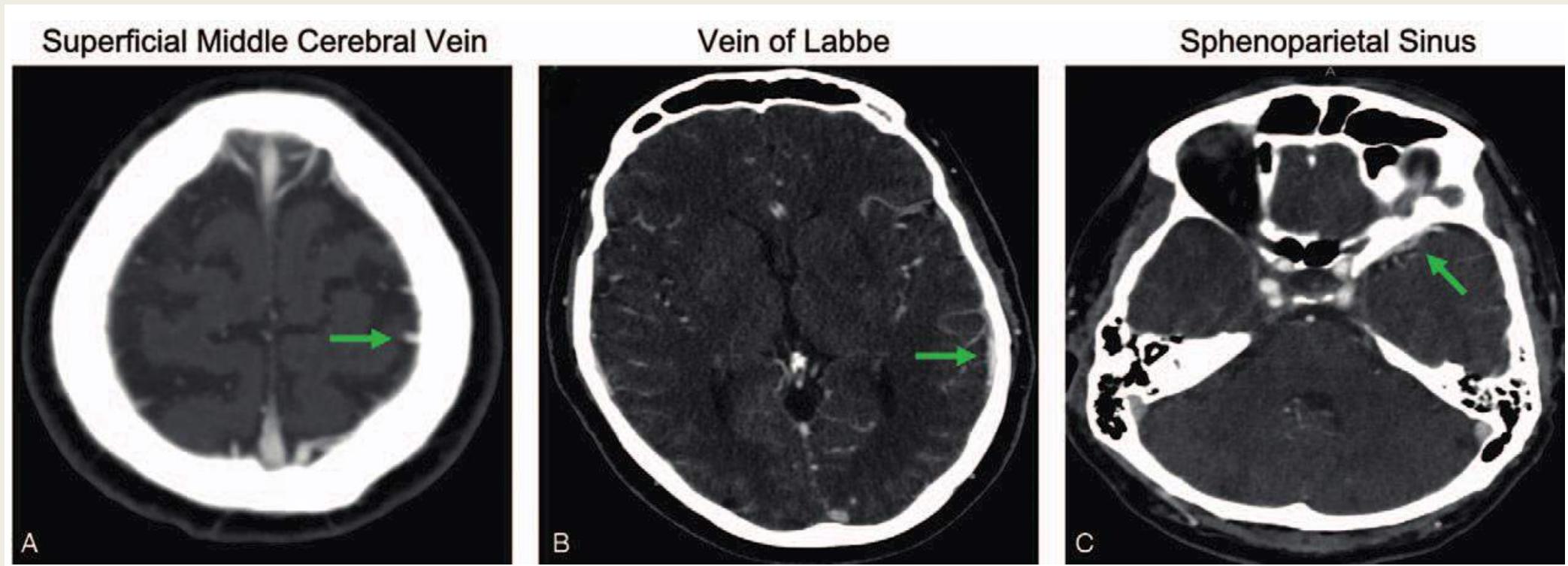
- COVES skorlama
- MCA sulama alanındaki ana venlerin değerlendirmesi – kortikal venöz drenaj
 - *Superficial Middle Cerebral v*
 - *Labbe v*
 - *Sphenoparietal sinüs*
- COVES ≥ 1 daha iyi kollateral profil & bazal ASPECT skor

Rethinking the Collateral Vasculature Assessment in Acute Ischemic Stroke

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Topics in Magnetic Resonance Imaging, August 2021



Prognostic Evaluation based on Cortical vein score difference In Stroke score

PRECISE

- Single phase CTA
- Hemisferler arası fark
 - *Superficial Middle Cerebral v*
 - *v of Labbe (VOL)*
 - *v of Trolard (VOT)*
 - *Basal v of Rosenthal (BVR)*
 - *2p tam dolum*
 - *1p kısmi dolum*
 - *0p dolum yok*
- Kompozit Skor : etkilenmeyen hemisfer puanı – etkilenen hemisfer puanı

CRISP

Combined aRterial and venous grading Scale to Predict outcome in anterior circulation ischemic stroke

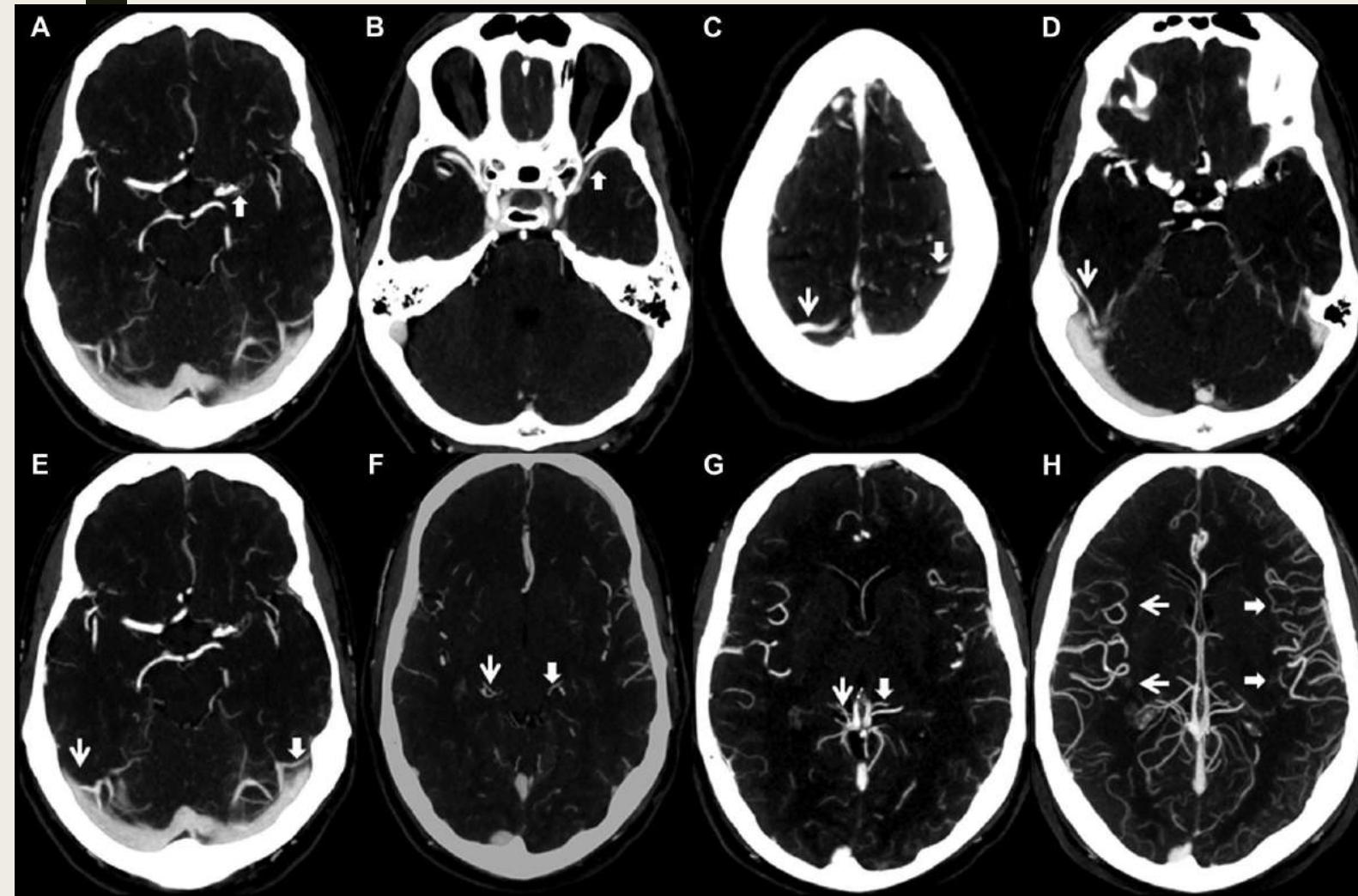
- Arterial ve PRECISE skorlamadan daha iyi 90. gün sonlanım öngörüsü
- CRISP sınıf-1 (kötü) : “kötü” venöz derece (<2 venöz dolum) ve “azalmış” kollateral derece
- CRISP sınıf-2 (ara) : “kötü” venöz derece ve “iyi” kollateral derece
- CRISP sınıf-3 (ara) : “iyi” venöz derece (≥ 2 venöz dolum) ve “azalmış” kollateral derece
- CRISP sınıf-4 (iyi) : “iyi” venöz derece ve “iyi” kollateral derece

A Combined Arterial and Venous Grading Scale to Predict Outcome in Anterior Circulation Ischemic Stroke

Rajsrinivas Parthasarathy, Sung-II Sohn, Thomas Jeerakathil, Mahesh P. Kate, Sachin M. Mishra, Vivek K. Nambiar, Aftab Ahmad, Bijoy K. Menon, Ashfaq Shuaib

From the Department of Medicine, University of Alberta, Edmonton, Alberta (RP, TJ, MPK, AA, AS); Department of Neurology, Institute for Brain Research, Keimyung University School of Medicine, Daegu, South Korea (SIS); and Department of Neurosciences, Foothills Medical Centre, University of Calgary, Calgary, Alberta (SMM, VKN, BKM).

J Neuroimaging 2015



- A. Sol MCA oklüzyonu
- B. Sol Superficial Middle Cerebral v kisman dolum (skor 1)
- C. v of Trolard kontralat ile eşit (skor 2)
- D. v of Labbe sağ hemisfer
- E. v of Labbe karşı taraf ile eşit (skor 2)
- F. Basal v of Rosenthal (BVR) karşı taraf ile eşit (skor 2)
- G. Basal v of Rosenthal (BVR) girişi
- H. İyi kollateraller

Kompozit skor 7

CRISP sınıf 4

Collateral Scores in Acute Ischemic Stroke

A retrospective study assessing the suitability of collateral scores as standalone predictors of clinical outcome

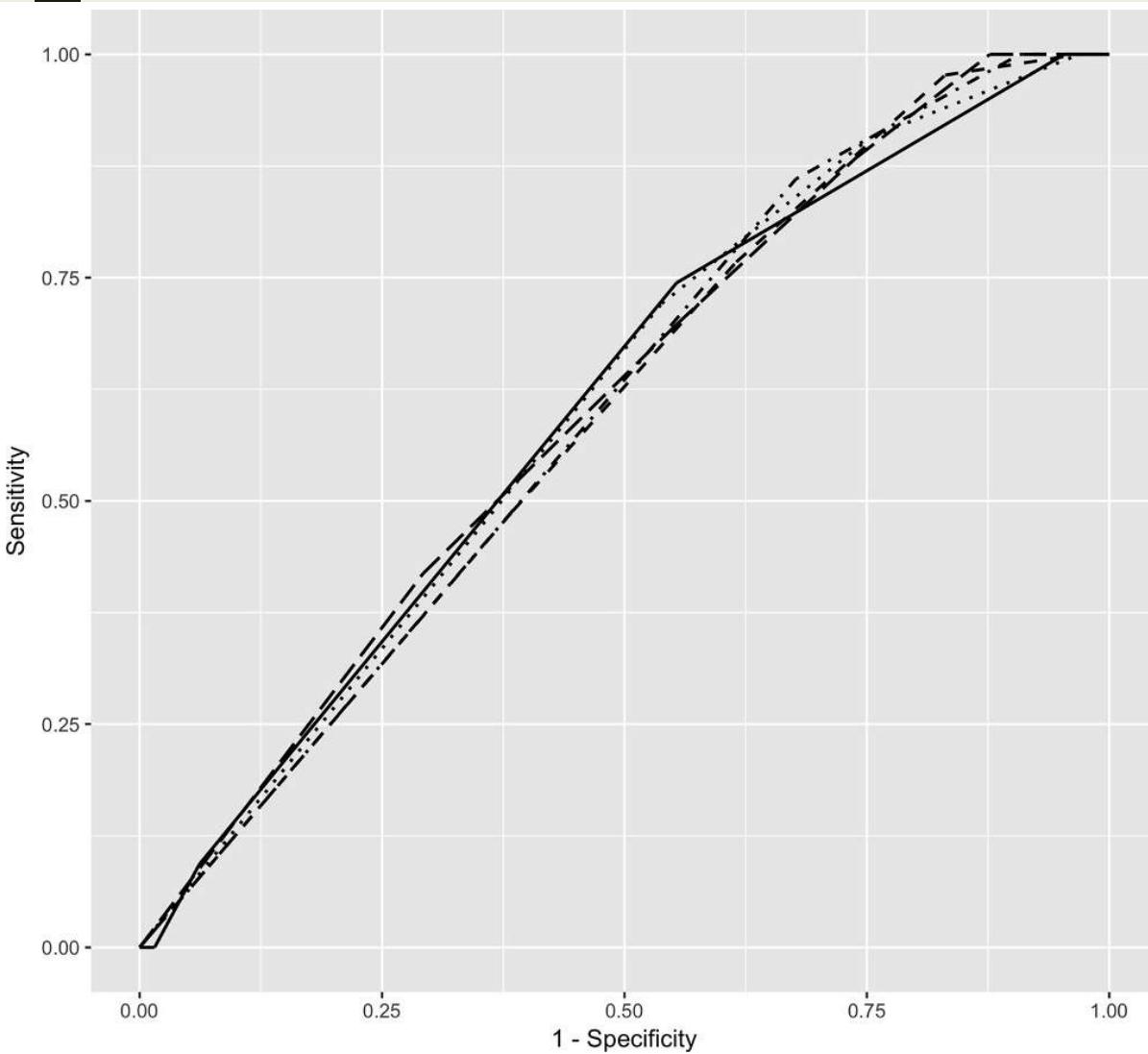
Fatih Seker¹ · Benjamin Pereira-Zimmermann² · Johannes Pfaff¹ · Jan Purrucker³ · Christoph Gumbinger³ · Silvia Schönenberger³ · Martin Bendszus¹ · Markus A. Möhlenbruch¹ 

| | AUC (95% CI) | Optimum cut-off | Sensitivity | Specificity | PPV | NPV |
|-----------|------------------|-----------------|-------------|-------------|------|------|
| Maas | 0.60 (0.51–0.70) | 2.5 | 0.74 | 0.45 | 0.47 | 0.73 |
| Miteff | 0.60 (0.52–0.68) | 2.5 | 0.86 | 0.32 | 0.46 | 0.78 |
| Tan | 0.61 (0.51–0.70) | 2.5 | 0.72 | 0.46 | 0.47 | 0.71 |
| ASITN/SIR | 0.59 (0.49–0.70) | 2.5 | 0.77 | 0.39 | 0.45 | 0.71 |
| mCTA | 0.61 (0.50–0.71) | 2.5 | 0.88 | 0.26 | 0.44 | 0.77 |

Collateral Scores in Acute Ischemic Stroke

A retrospective study assessing the suitability of collateral scores as standalone predictors of clinical outcome

Fatih Seker¹ · Benjamin Pereira-Zimmermann² · Johannes Pfaff¹ · Jan Purrucker³ · Christoph Gumbiner³ · Silvia Schönenberger³ · Martin Bendszus¹ · Markus A. Möhlenbruch¹ 



- Kollateral skorlamanın klinik sonlanım üzerinde etkisi gösterilmiştir
- Analiz edilen kollateral skorlama sistemlerinin hiçbirini klinik sonlanımı tek kriter olarak yeterli öngörmemiş
- Kollateral skorlama trombektomi hasta seçiminde tek görüntüleme kriteri olarak kullanılmamalı

BRIEF REPORT**Which Acute Ischemic Stroke Patients Are Fast Progressors?**

Results From the ESCAPE Trial Control Arm

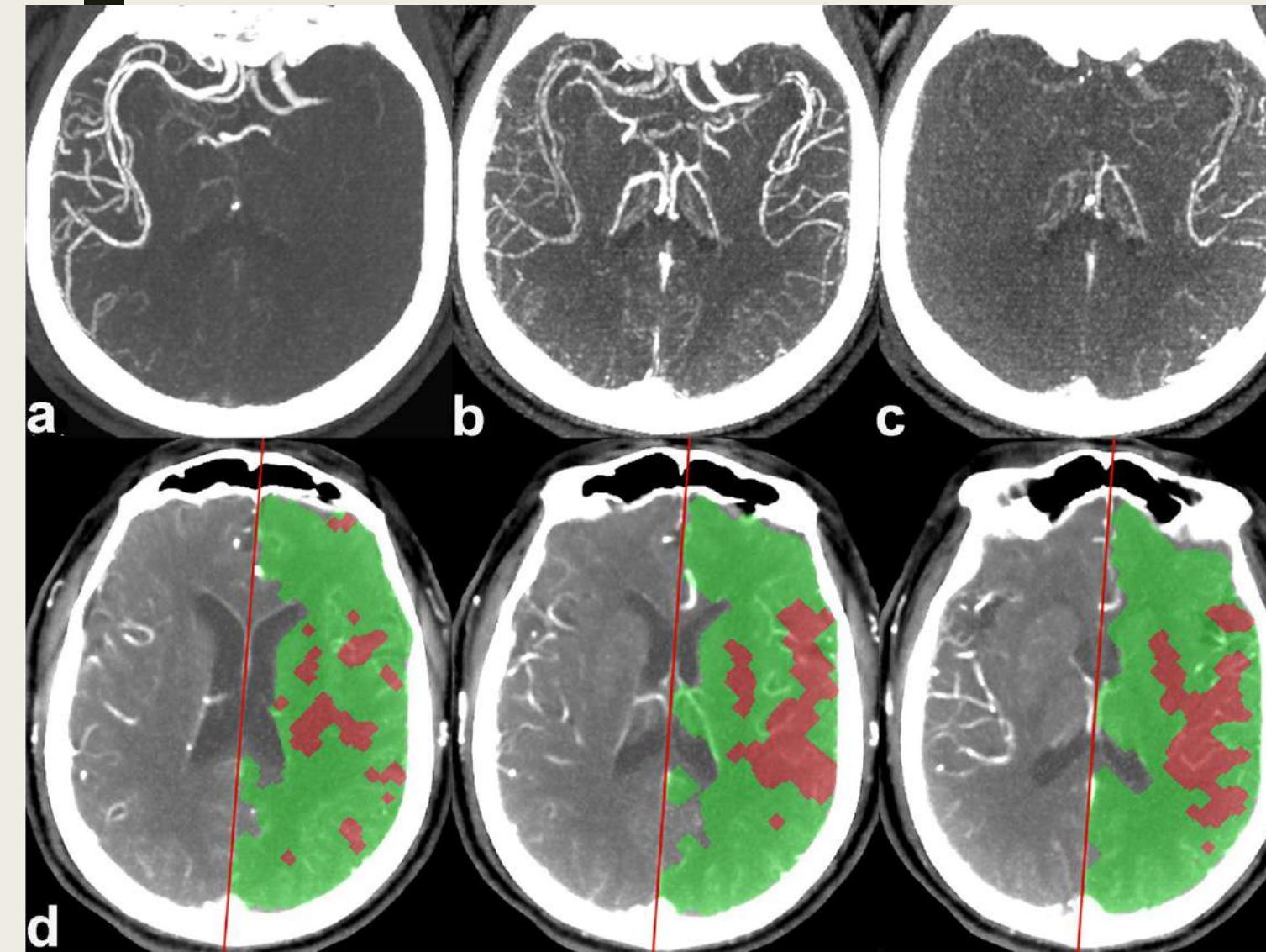
Johanna M. Ospe, MD; Michael D. Hill, MD; Manon Kappelhof, MD; Andrew M. Demchuk, MD;
 Bijoy K. Menon, MD; Arunv Mayank; Dar Dowlatshahi, MD; Don Frei, MD; Jeremy L. Rempel, MD; Blaise Baxter, MD;
 Mayank Goyal, MD, PhD

| | All (n=43) | Fast progressors (n=15) | Other patients (n=28) | P value |
|---|---------------------|----------------------------|--------------------------|---------|
| Clinical baseline characteristics | | | | |
| Age in years, median (IQR) | 75.5 (62.9–84.0) | 70.2 (64.7–84.0) | 78.2 (61.8–84.1) | 0.760 |
| Female sex, n (%) | 21 (48.8) | 6 (40.0) | 15 (53.6) | 0.526 |
| Medical history, n (%) | | | | |
| Diabetes | 14 (32.6) | 5 (33.3) | 9 (32.1) | 1.000 |
| Atrial fibrillation | 19 (44.2) | 6 (40.0) | 13 (46.4) | 0.755 |
| Baseline NIHSS, median (IQR) | 14 (11–19) | 18 (14–20) | 12 (9–17.5) | 0.003 |
| Imaging baseline characteristics | | | | |
| Occlusion location on baseline CTA, n (%) | | | | 0.021 |
| ICA-T* | 9 (20.9) | 7 (46.7) | 2 (7.1) | |
| ICA-L† | 2 (4.7) | 1 (6.7) | 1 (3.6) | |
| ICA-I‡ | 2 (4.7) | 0 | 2 (7.1) | |
| Proximal M1 | 7 (16.3) | 3 (20.0) | 4 (14.3) | |
| Mid M1 | 10 (23.3) | 1 (6.7) | 9 (32.1) | |
| Distal M1 | 13 (30.2) | 3 (20.0) | 10 (35.7) | |
| Ipsilateral cervical ICA occlusion, n (%) | 3 (7.0) | 1 (6.7) | 2 (7.1) | 1.000 |
| Collateral Status, n (%) | | | | 0.021 |
| Poor | 3 (7.1) | 3 (20.0) | 0 | |
| Intermediate | 2 (4.8) | 1 (6.7) | 1 (3.7) | |
| Good | 37 (88.1) | 11 (73.3) | 26 (96.3) | |
| Treatment and time | | | | |
| Intravenous alteplase, n (%) | 33 (76.7) | 14 (93.3) | 19 (67.9) | 0.127 |
| Onset-to-imaging time, min, median (IQR) | 101 (66–156) | 75 (59–115) | 101.5 (74.5–190.5) | 0.090 |
| Imaging-to-repeat CTA time, min, median (IQR) | 312 (239–360), n=41 | 312 (252–347) | 297 (219–378), n=26 | 0.705 |
| Clinical and imaging outcomes | | | | |
| 24-h NIHSS, median (IQR) | 13.5 (9–18), n=42 | 18 (14–24) | 10 (6–15), n=27 | 0.001 |
| mRS score 0–2 at 90 d, n (%) | 11 (25.6) | 2 (13.3) | 9 (32.1) | 0.276 |
| 24-h ASPECTS, median (IQR) | 8 (4–9) | 4 (0–5) | 8 (7–9) | <0.001 |
| 24-h infarct, mL, median (IQR) | 33 (12–105) | 146 (58–258) | 16 (7–46.5) | <0.001 |
| 24-h parenchymal hemorrhage, n (%) | 7 (16.3) | 2 (13.3) | 5 (17.9) | 1.000 |

- Karotid Terminal oklüzyon
- Kollateral akım
 - ACA&PCA'dan

Comparison of CT angiography collaterals for predicting target perfusion profile and clinical outcome in patients with acute ischemic stroke

Shan-shan Lu¹ · Xuan Zhang¹ · Xiao-quan Xu¹ · Yue-zhou Cao² · Lin-bo Zhao² · Qiang-hui Liu³ · Fei-yun Wu¹ · Sheng Liu² · Hai-bin Shi² 

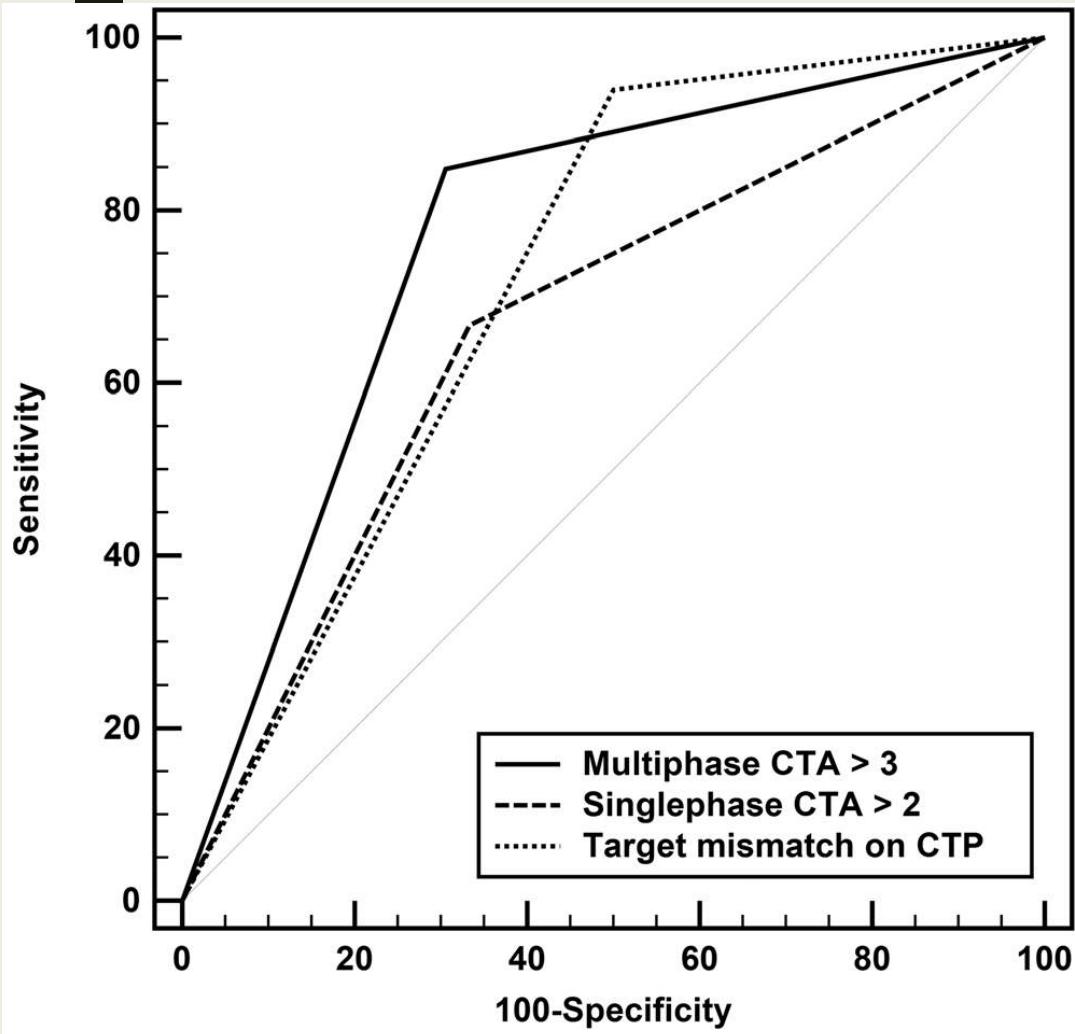


- a. sCTA kötü kollateraller (derece 1)
- a-c mCTA iyi kollateraller (derece 4)
- CTP mismatch oranı 7.19

Comparison of CT angiography collaterals for predicting target perfusion profile and clinical outcome in patients with acute ischemic stroke

Shan-shan Lu¹ • Xuan Zhang¹ • Xiao-quan Xu¹ • Yue-zhou Cao² • Lin-bo Zhao² • Qiang-hui Liu³ • Fei-yun Wu¹ • Sheng Liu² • Hai-bin Shi² 

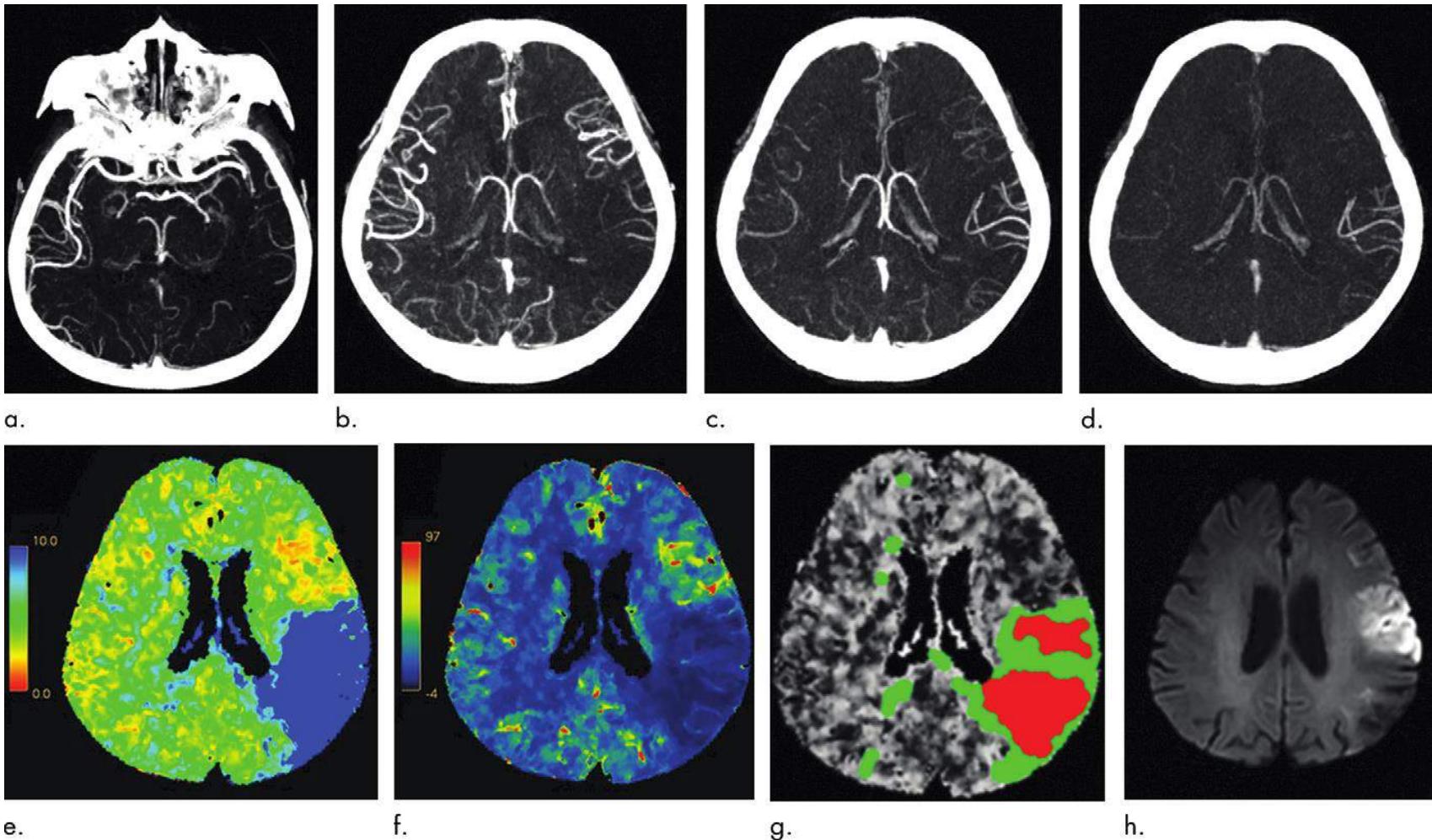
- AIS 5-15 saat ve semptom zamanı bilinmeyen
 - Daha iyi kollateraller daha küçük iskemik kor hacmi ve daha büyük mismatch oranı ile ilişkili
- sCTA pial arteriel dolumu mCTA'dan daha az öngörmüş
- mCTA > sCTA
 - CTP'da hedef mismatch belirleme
 - 90. gün mRS 0-2 öngörme
- mCTA eşik değer 3



mRS 0-2

Collateral Status at Single-Phase and Multiphase CT Angiography versus CT Perfusion for Outcome Prediction in Anterior Circulation Acute Ischemic Stroke

2020; 296:393–400



- a. M2 oklüzyonu
b. Single phase CTA (tepe arterial faz);
parietal lobda azalmış pial damarlar
b-d Multi phase CTA; perifer damarların
dolumunda 1 faz gecikme.

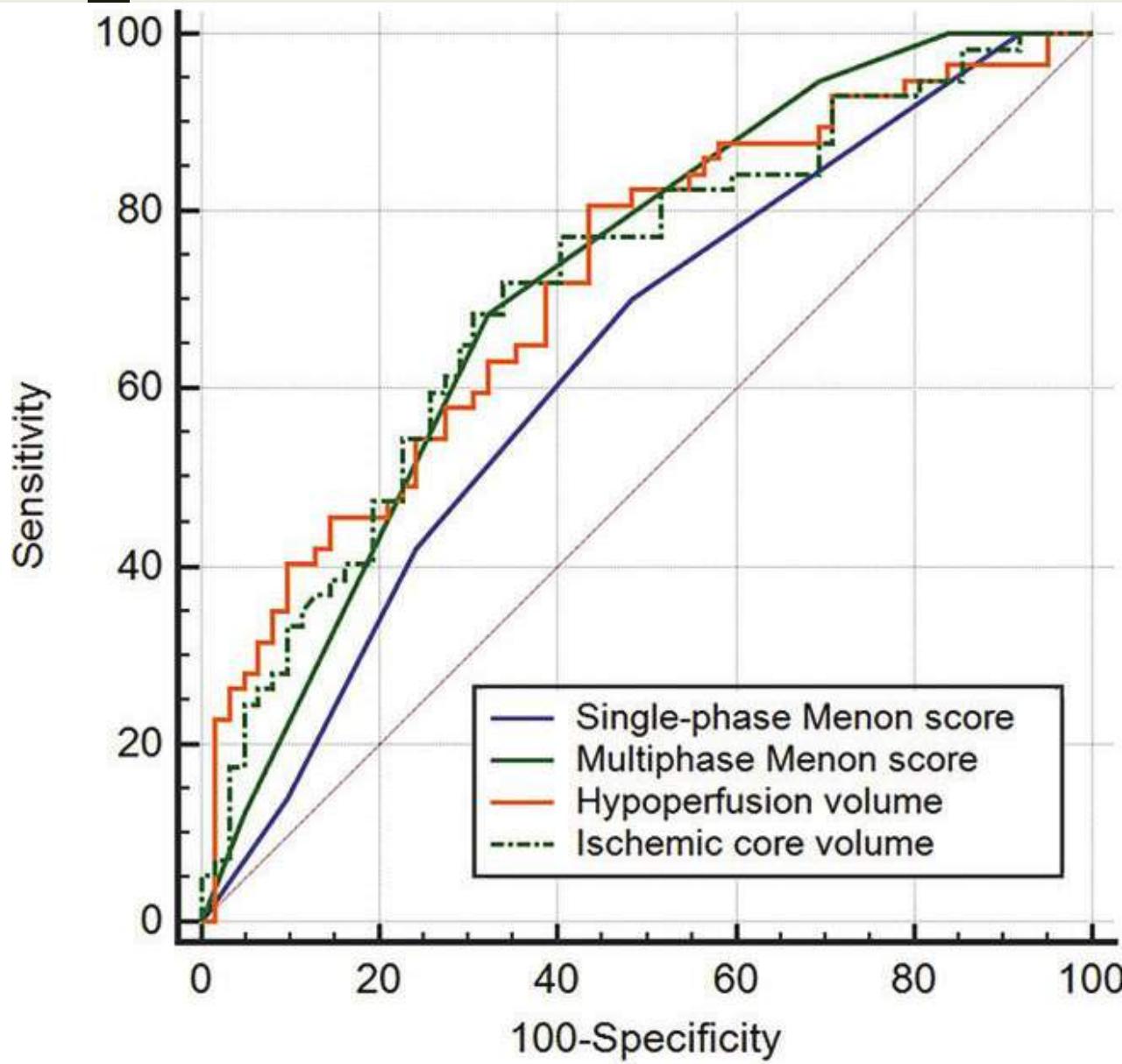
Geç fazda kollateral damarların
tam olmayan boşalımı

- e-f time to max ve CBF haritaları
g. iskemik kor (kırmızı) hipoperfüze alan
(yeşil)
h. iv tromboliz sonrası final enfarkt alanı

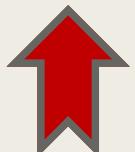
Table 4: Criterion Values and Coordinates of the Receiver Operating Characteristic Analysis Regarding a Favorable Clinical Outcome

| Variable | AUC | 95% CI | Youden Index | Associated Criterion | Sensitivity (%) | 95% CI (%) | Specificity (%) | 95% CI (%) |
|--------------------------|------|------------|--------------|----------------------|-----------------|------------|-----------------|------------|
| Single-phase Menon score | 0.64 | 0.54, 0.72 | 0.22 | >2 | 70.2 | 56.6, 81.6 | 51.6 | 38.6, 64.5 |
| Multiphase Menon score | 0.72 | 0.63, 0.80 | 0.36 | >3 | 68.4 | 54.8, 80.1 | 67.7 | 54.7, 79.1 |
| Hypoperfusion volume | 0.72 | 0.63, 0.80 | 0.37 | <150.2 mL | 80.7 | 68.1, 90.0 | 56.5 | 43.3, 69.0 |
| Ischemic core volume | 0.71 | 0.62, 0.79 | 0.38 | <8.4 mL | 71.9 | 58.5, 83.0 | 66.1 | 53.0, 77.7 |

Note.—AUC = area under the curve, CI = confidence interval.

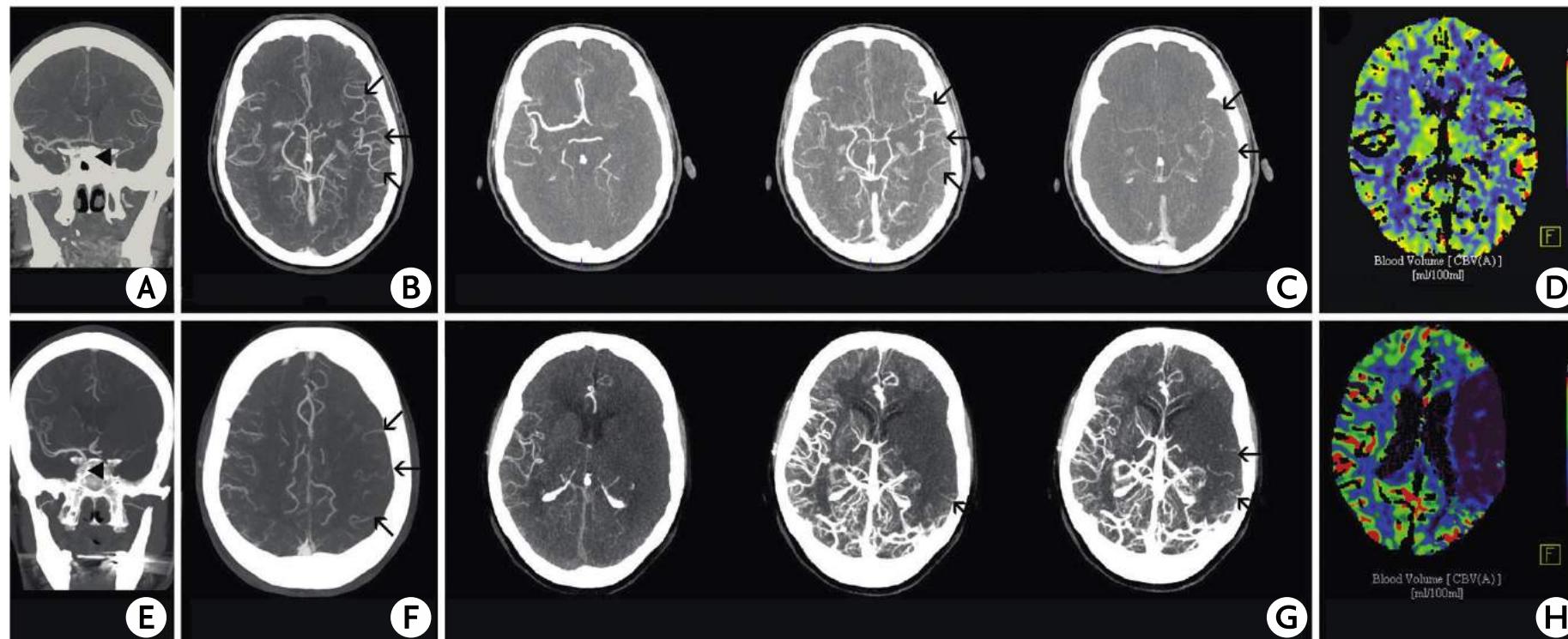


- Single & multi faz CTA kollateral skorları ile final infarkt hacmi arasında orta derecede negatif korelasyon
 - Pihti uzunluğu $>8\text{mm}$
 - Erken reperfüzyon olmayanlarda
- 90. gün iyi klinik sonlanımı öngörmede
 - $mCTA > sCTA$
 - $mCTA \approx CTP$



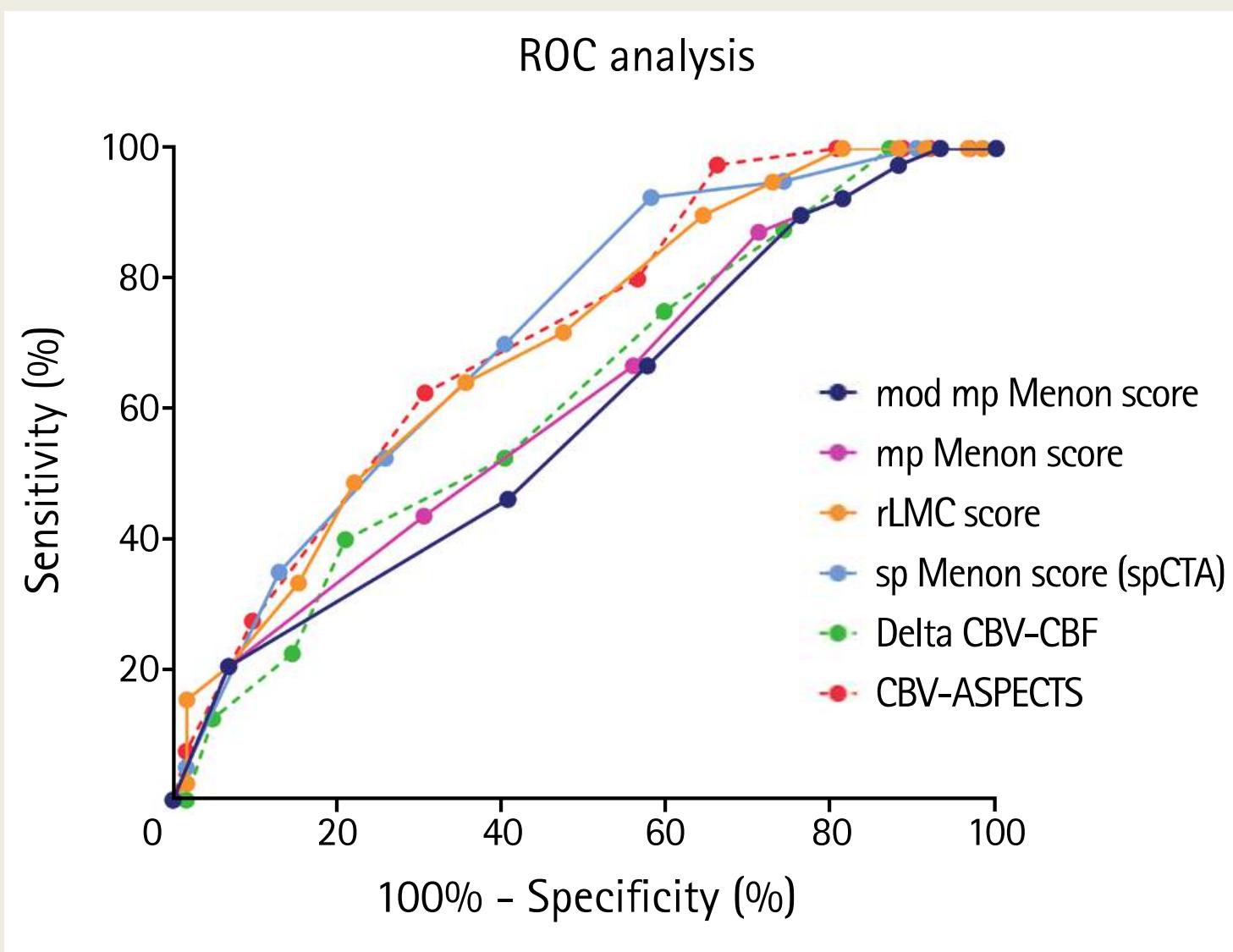
Outcome Prediction Using Perfusion Parameters and Collateral Scores of Multi-Phase and Single-Phase CT Angiography in Acute Stroke: Need for One, Two, Three, or Thirty Scans?

| Region | Score | 0 [Normal score (4)] | 1 [Mild score (3)] | 2 [Moderate score (2)] | 3 [High score (1)] |
|---|---------------------|---|---|---|---|
| AICH-MC-region | Description | Beyond the occluded artery within the symptomatic and compared with the asymptomatic contralateral hemisphere, there is no loss of perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. |
| MCA-PC-region | | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. |
| ASPECTS region | | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. |
| MCA-S region | | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. | No loss of normal increased perfusion. |
| ASPECTS region MCA-S region MCA-S region MCA-S region MCA-S region MCA-S region | Region | Region | Region | Region | Region |
| ASPECTS region MCA-S region MCA-S region MCA-S region MCA-S region MCA-S region | Description | When compared to a matching region in the contralateral hemisphere, there is: | When compared to a matching region in the contralateral hemisphere, there is: | When compared to a matching region in the contralateral hemisphere, there is: | When compared to a matching region in the contralateral hemisphere, there is: |
| loss of perfusion | | loss of perfusion | loss of perfusion | loss of perfusion | loss of perfusion |
| Vessels | | Vessels | Vessels | Vessels | Vessels |
| Normal vessels | | Normal vessels | Normal vessels | Normal vessels | Normal vessels |
| and extent of perfusion | | and extent of perfusion | and extent of perfusion | and extent of perfusion | and extent of perfusion |
| No vessels visible | Region | Region | Region | Region | Region |
| No vessels visible | Description | Normal vessels | Normal vessels | Normal vessels | Normal vessels |
| No vessels visible | | No vessels visible | No vessels visible | No vessels visible | No vessels visible |
| No vessels visible | Vessels | Vessels | Vessels | Vessels | Vessels |
| No vessels visible | Extent of perfusion | Extent of perfusion | Extent of perfusion | Extent of perfusion | Extent of perfusion |
| No vessels visible | Score | Score | Score | Score | Score |
| No vessels visible | 0 | 1 | 2 | 3 | 4 |
| Maximum score | 0 | 1 | 2 | 3 | 4 |
| Used for scoring of MPR-CTA | 0 | 1 | 2 | 3 | 4 |
| Used for scoring of S-CTA | 0 | 1 | 2 | 3 | 4 |
| Used for scoring of Dp-CTA | 0 | 1 | 2 | 3 | 4 |
| Used for scoring of S-CTA | 0 | 1 | 2 | 3 | 4 |



Outcome Prediction Using Perfusion Parameters and Collateral Scores of Multi-Phase and Single-Phase CT Angiography in Acute Stroke: Need for One, Two, Three, or Thirty Scans?

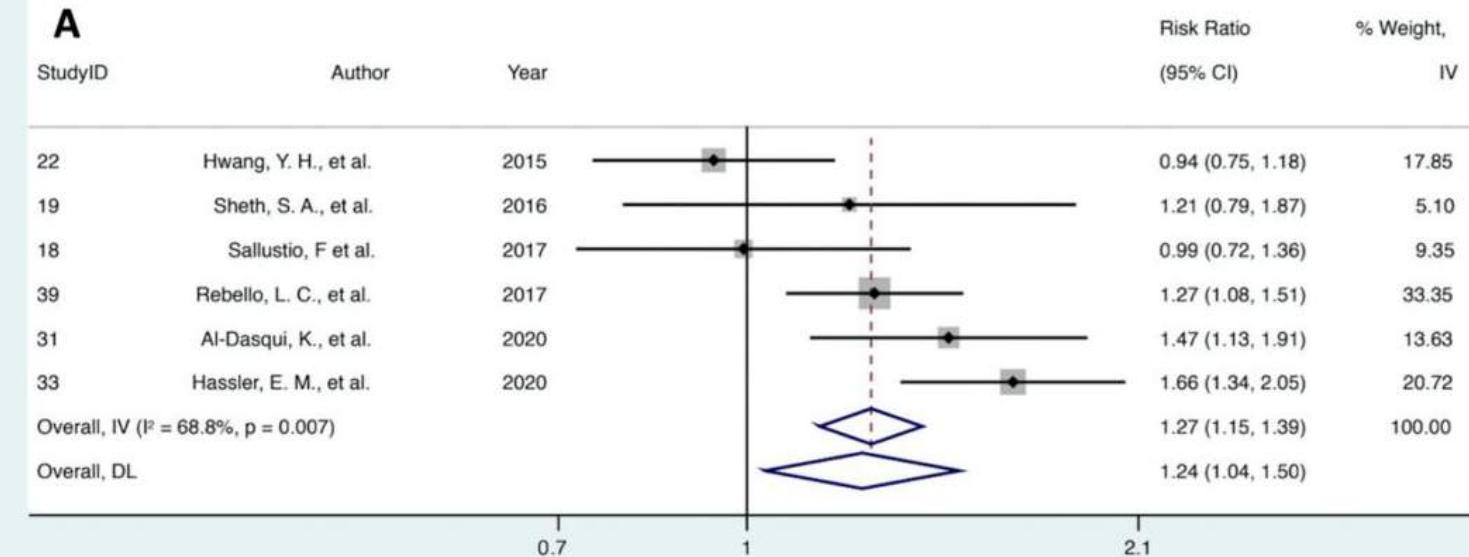
- Sol terminal karotid a. oklüzyonu olan iki hasta; iyi kollateraller (A-D) ve kötü kollateraller (E-H)
- Single faz kollateral akım değerlendirme (B,F) (sp Menon skor)
 - hasta A skor 10, hasta B skor 2
- Multi faz kollateral akım değerlendirme (C,G)
 - ilk görüntüler Tepe arteriyal faz
 - 7.5 saniyelik zamansal rezolüsyon ile takip eden fazlar
 - Hasta A; 1 faz gecikme ancak yayılım ve belirginlik benzer; mp Menon skor 8
 - Hasta B; 1 faz gecikme ve damarların görünmediği bazı iskemik bölgeler; mp Menon skor 2
- CBV haritaları (D&H)
 - Hasta A CBV-ASPECT skor 7; Hasta B CBV-ASPECT skor 0



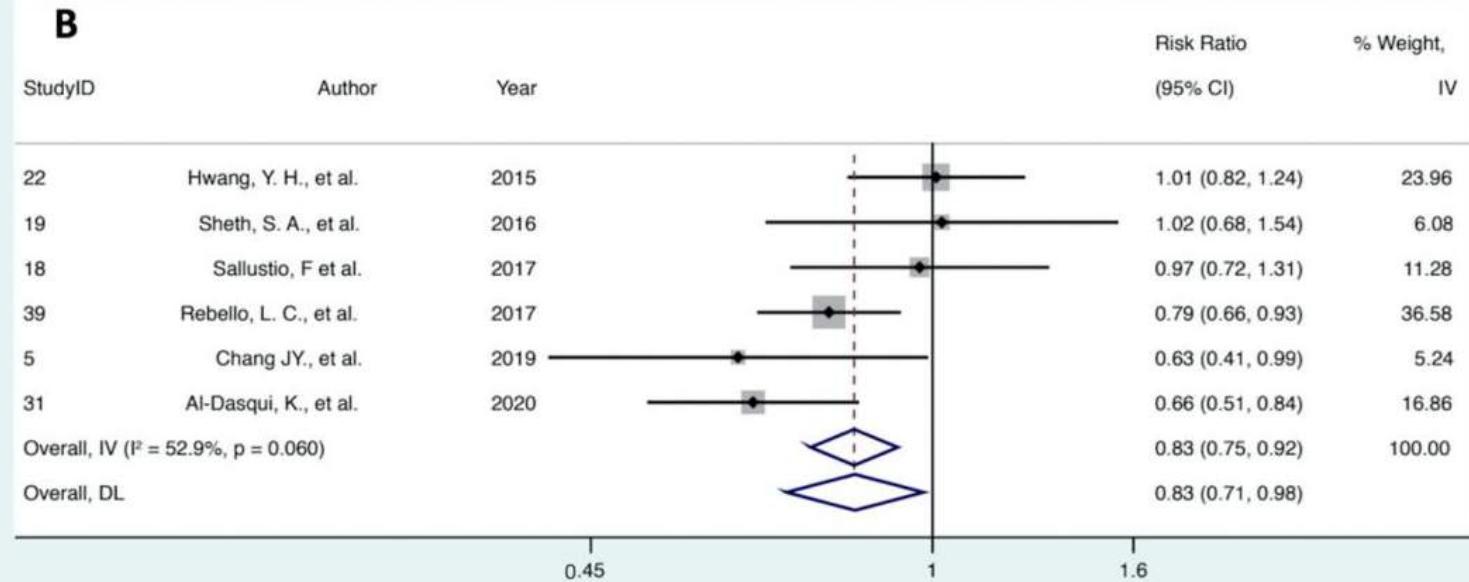
Outcome Prediction Using Perfusion Parameters and Collateral Scores of Multi-Phase and Single-Phase CT Angiography in Acute Stroke: Need for One, Two, Three, or Thirty Scans?

- iyi klinik sonlanım 90.gün mRS ≤2
- mpCTA klinik sonlanım öngörüsü spCTA'dan daha iyi bulunmamış
- Trombektomi için NCCT ve spCTA'dan fazlasına ihtiyaç yok

Association of large artery atherosclerosis with pre-intervention collateral status

A


Association of cardioembolism with pre-intervention collateral status

B


Article

Published: 16 November 2021

Stroke Aetiology and Collateral Status in Acute Ischemic Stroke Patients Receiving Reperfusion Therapy—A Meta-Analysis

Akansha Sinha ^{1,2}, Peter Stanwell ³ , Roy G. Beran ^{1,2,4,5,6,7}, Zeljka Calic ^{1,2,5}, Murray C. Killingsworth ^{1,2,4,8}  and Sonu M. M. Bhaskar ^{1,4,5,*} 

- Büyük arter aterosklerozu işlem öncesi daha iyi kollaterallerle
- Kardiyoemboli işlem öncesi daha kötü kollaterallerle
 - ilişkili bulunmuş

Eveline J.A. Wiegers[●], BSc; Maxim J.H.L. Mulder, MD, PhD; Ivo G.H. Jansen, MD, PhD; Esmee Venema, MD; Kars C.J. Compagne, BSc; Olvert A. Berkhemer, MD, PhD; Bart J. Emmer, MD, PhD; Henk A. Marquering, PhD; Adriaan C.G.M. van Es, MD, PhD; Marieke E. Sprengers, MD, PhD; Wim H. van Zwam, MD, PhD; Robert J. van Oostenbrugge, MD, PhD; Yvo B.W.E.M. Roos, MD, PhD; Charles B.L.M. Majoie, MD, PhD; Bob Roozenbeek, MD, PhD; Hester F. Lingsma, PhD; Diederik W.J. Dippel, MD, PhD; Aad van der Lugt, MD, PhD; on behalf of the MR CLEAN Trial and MR CLEAN Registry Investigators*

MR CLEAN

- TAN skorlama
- Kötü kollateraller &
 - *Daha ileri yaş*
 - *Erkek*
 - *Yüksek başvuru kan şekeri*
 - *ICA-T oklüzyonu*

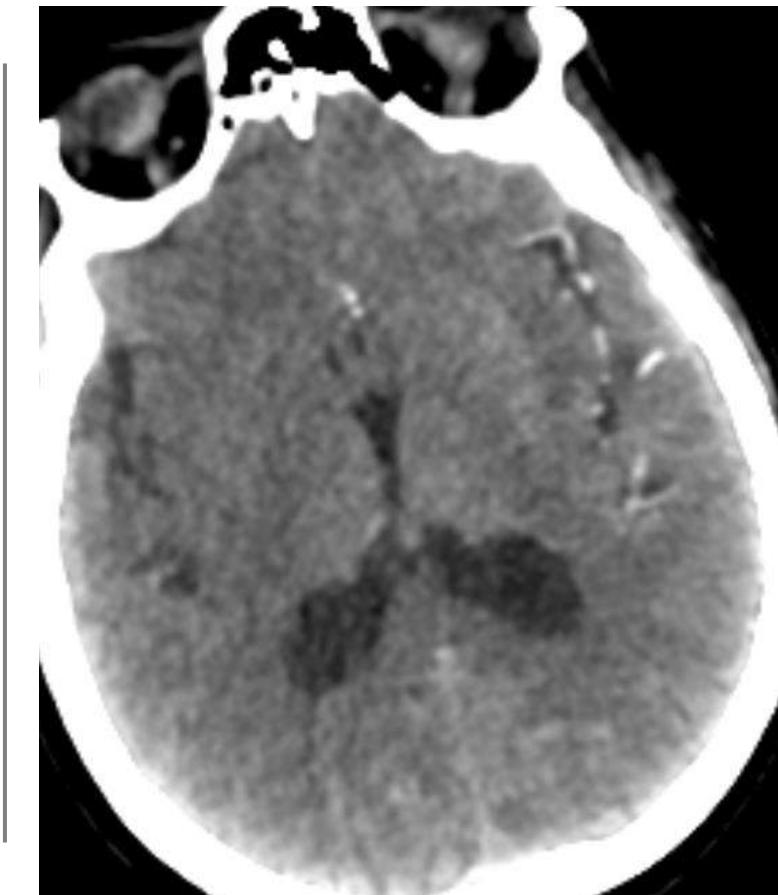
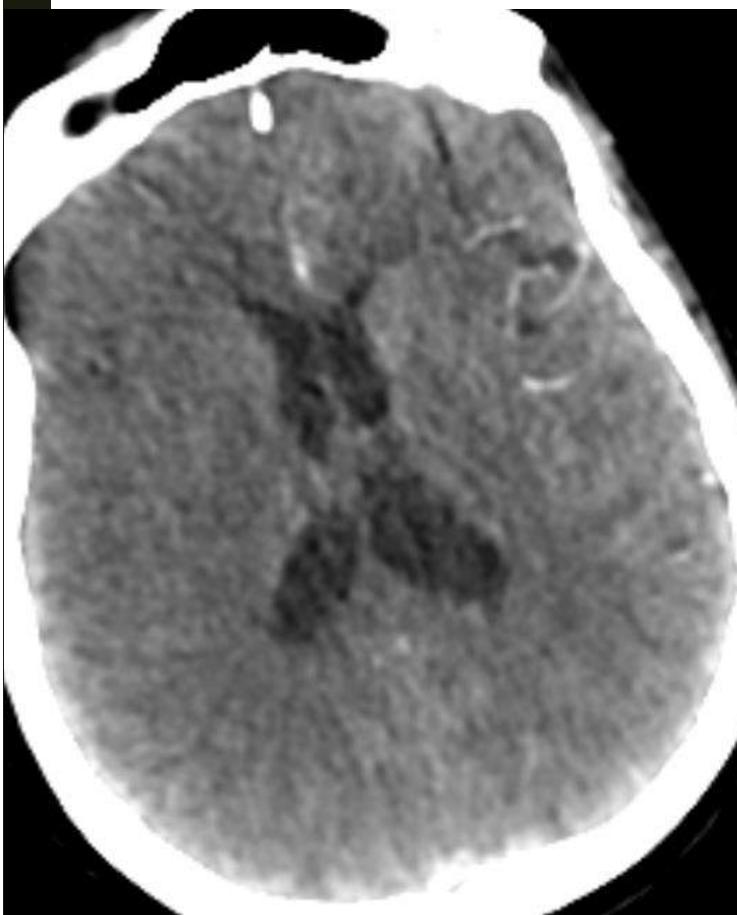
Clinical and Imaging Determinants of Collateral Status in Patients With Acute Ischemic Stroke in MR CLEAN Trial and Registry

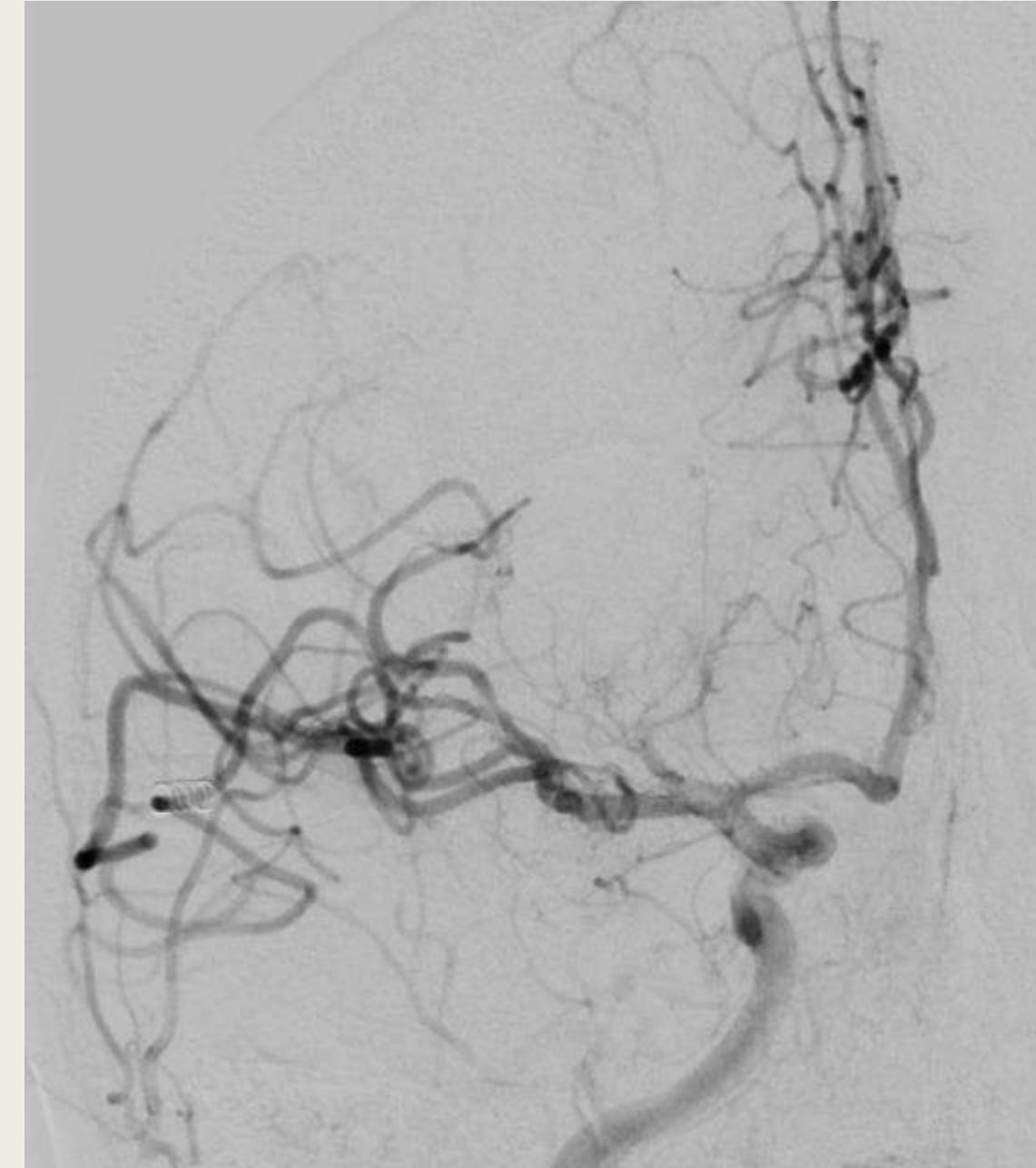
Eveline J.A. Wiegers¹, BSc; Maxim J.H.L. Mulder, MD, PhD; Ivo G.H. Jansen, MD, PhD; Esmee Venema, MD; Kars C.J. Compagne, BSc; Olvert A. Berkhemer, MD, PhD; Bart J. Emmer, MD, PhD; Henk A. Marquering, PhD; Adriaan C.G.M. van Es, MD, PhD; Marieke E. Sprengers, MD, PhD; Wim H. van Zwam, MD, PhD; Robert J. van Oostenbrugge, MD, PhD; Yvo B.W.E.M. Roos, MD, PhD; Charles B.L.M. Majoie, MD, PhD; Bob Roozenbeek, MD, PhD; Hester F. Lingsma, PhD; Diederik W.J. Dippel, MD, PhD; Aad van der Lugt, MD, PhD; on behalf of the MR CLEAN Trial and MR CLEAN Registry Investigators*

| | Total (n=1988) | Grade 0 (n=123) | Grade 1 (n=596) | Grade 2 (n=734) | Grade 3 (n=422) | P Value |
|---|----------------|-----------------|-----------------|-----------------|-----------------|---------|
| Clinical | | | | | | |
| Age, y; median (IQR) | 69 (58–79) | 72 (60–79) | 71 (61–80) | 68 (58–78) | 67 (56–77) | <0.001 |
| Men, no. (%) | 1086 (55) | 81 (66) | 355 (60) | 392 (53) | 199 (47) | <0.001 |
| NIHSS; median (IQR) | 16 (12–20) | 19 (15–23) | 18 (14–22) | 16 (12–19) | 14 (10–18) | <0.001 |
| SBP, mm Hg; mean (SD) | 149 (25) | 154 (25) | 149 (25) | 148 (25) | 148 (24) | 0.04 |
| DBP, mm Hg; mean (SD) | 82 (15) | 85 (15) | 82 (16) | 81 (15) | 81 (16) | 0.01 |
| Glucose at baseline, mmol/L; median (IQR) | 6.7 (5.9–8.0) | 7.1 (6.0–8.5) | 6.8 (6.0–8.1) | 6.7 (5.8–7.9) | 6.5 (5.8–7.8) | 0.01 |
| Atrial fibrillation, n (%) | 462 (24) | 34 (28) | 134 (23) | 180 (25) | 87 (21) | 0.24 |
| Hypercholesterolemia, n (%) | 560 (29) | 35 (29) | 185 (32) | 192 (27) | 111 (27) | 0.19 |
| Hypertension, n (%) | 973 (49) | 59 (48) | 315 (53) | 334 (46) | 199 (48) | 0.06 |
| Diabetes mellitus, n (%) | 323 (16) | 26 (21) | 91 (15) | 120 (16) | 61 (15) | 0.33 |
| Myocardial infarction, n (%) | 302 (15) | 19 (16) | 100 (17) | 107 (15) | 54 (13) | 0.34 |
| Peripheral artery disease, n (%) | 159 (8.1) | 8 (6.6) | 66 (11) | 58 (8.0) | 22 (5.3) | 0.01 |
| Ischemic stroke, n (%) | 304 (15) | 21 (17) | 108 (18) | 104 (14) | 54 (13) | 0.08 |
| Prestroke modified Rankin Scale score, n (%) | | | | | | 0.10 |
| 0 | 1395 (71) | 81 (68) | 409 (69) | 524 (72) | 302 (73) | |
| 1 | 240 (12) | 19 (16) | 64 (11) | 90 (12) | 51 (12) | |
| 2 | 135 (6.9) | 10 (8) | 47 (8) | 46 (6) | 24 (6) | |
| >2 | 190 (10) | 10 (8) | 69 (12) | 65 (9) | 39 (9) | |
| Current smoking, n (%) | 481 (29) | 27 (22) | 146 (25) | 180 (25) | 113 (27) | 0.50 |
| Statin use, n (%) | 666 (34) | 44 (36) | 232 (40) | 221 (30) | 128 (31) | <0.01 |
| Antiplatelet use, n (%) | 638 (32) | 37 (30) | 235 (40) | 209 (29) | 121 (29) | <0.001 |
| Antihypertensive medication use, n (%) | 1004 (51) | 59 (50) | 338 (57) | 353 (49) | 194 (47) | <0.01 |
| Intravenous alteplase treatment, n (%) | 1607 (81) | 95 (77) | 485 (81) | 598 (81) | 338 (80) | 0.52 |
| Imaging | | | | | | |
| Level of occlusion on noninvasive vessel imaging, n (%) | | | | | | <0.001 |
| ICA | 86 (4.5) | 2 (1.6) | 21 (3.5) | 31 (4.3) | 27 (6.4) | |
| ICA-T | 447 (23) | 46 (37) | 176 (30) | 157 (22) | 64 (15) | |
| M1 | 1144 (60) | 63 (51) | 333 (56) | 452 (61) | 271 (64) | |
| M2 | 214 (11) | 12 (10) | 60 (10) | 88 (12) | 52 (12) | |
| ASPECTS on NCCT—median (IQR) | 9 (7–10) | 8 (6–10) | 8 (7–10) | 9 (7–10) | 9 (8–10) | <0.001 |
| Other | | | | | | |
| Time from onset to CTA—median (IQR) | 105 (72–171) | 106 (66–183) | 99 (72–160) | 104 (72–174) | 115 (80–189) | 0.23 |

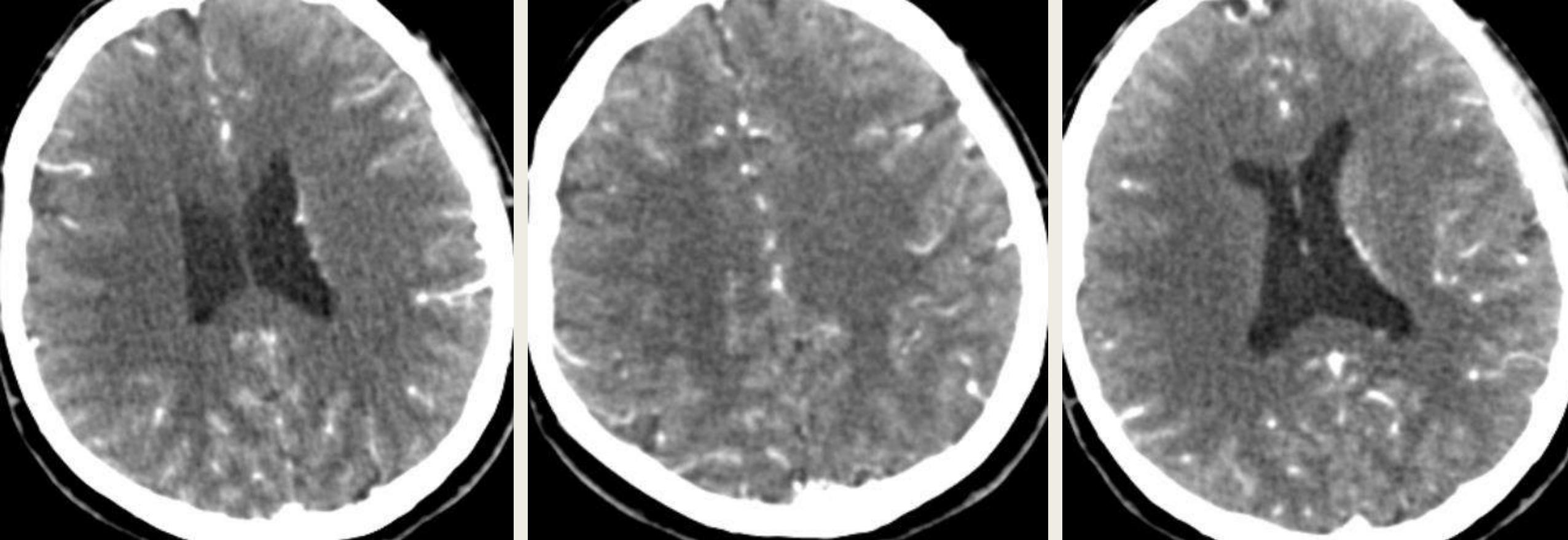


VAKA 1

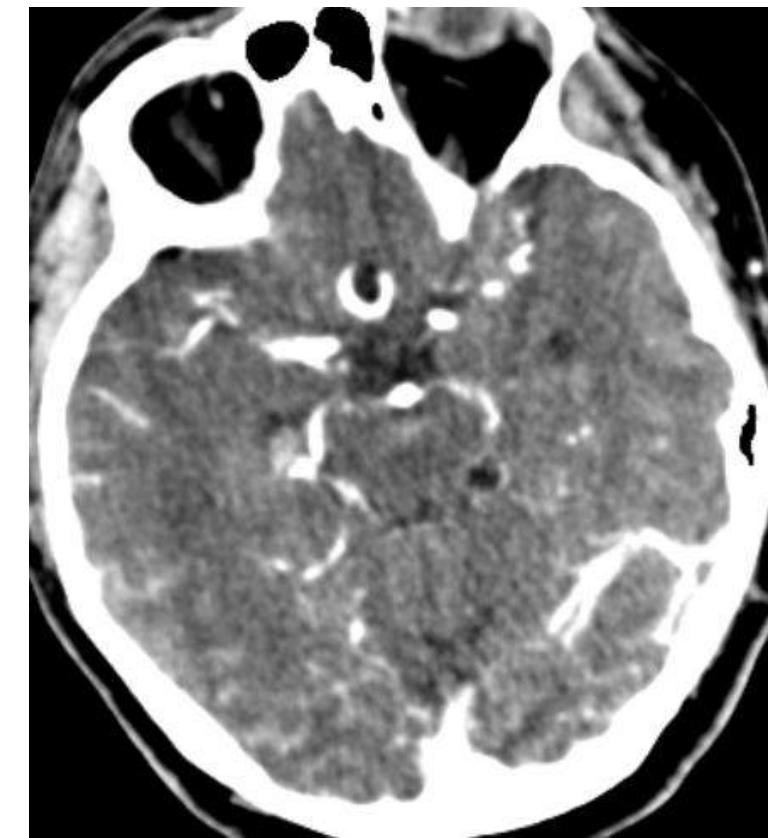
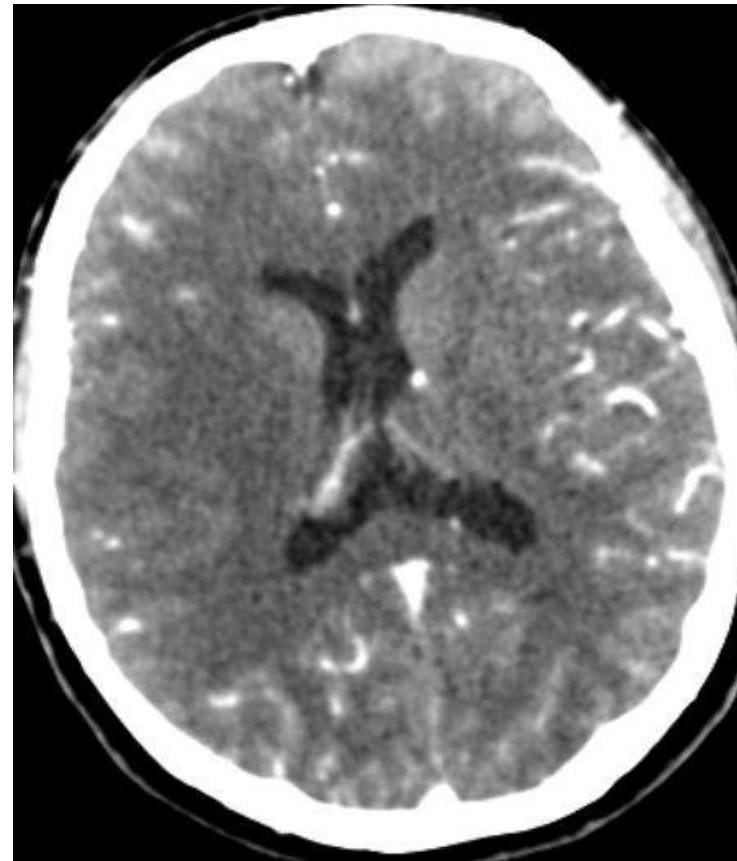
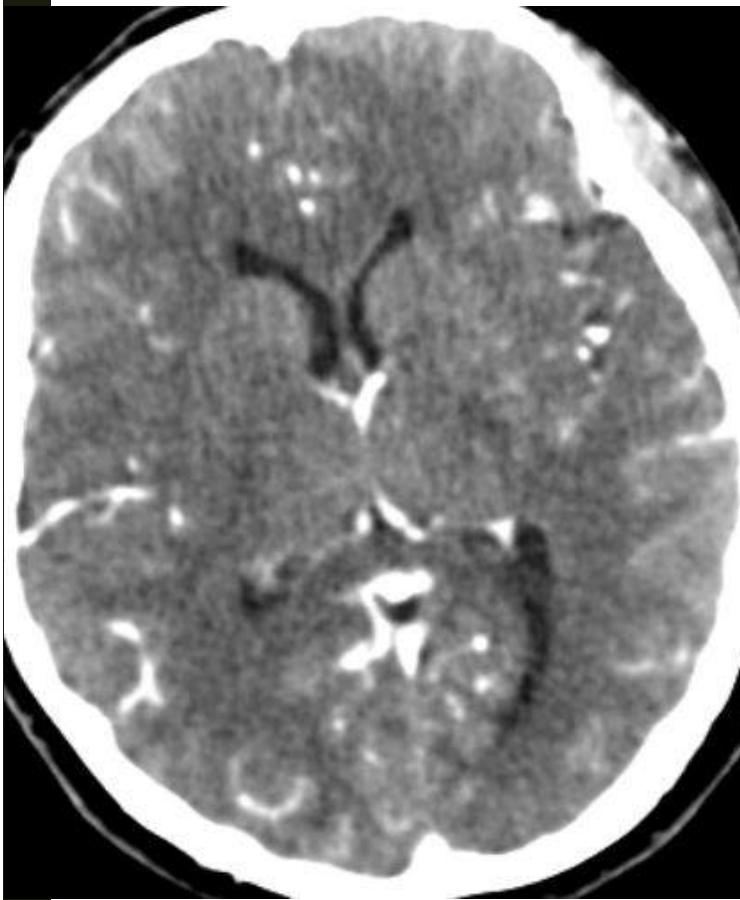


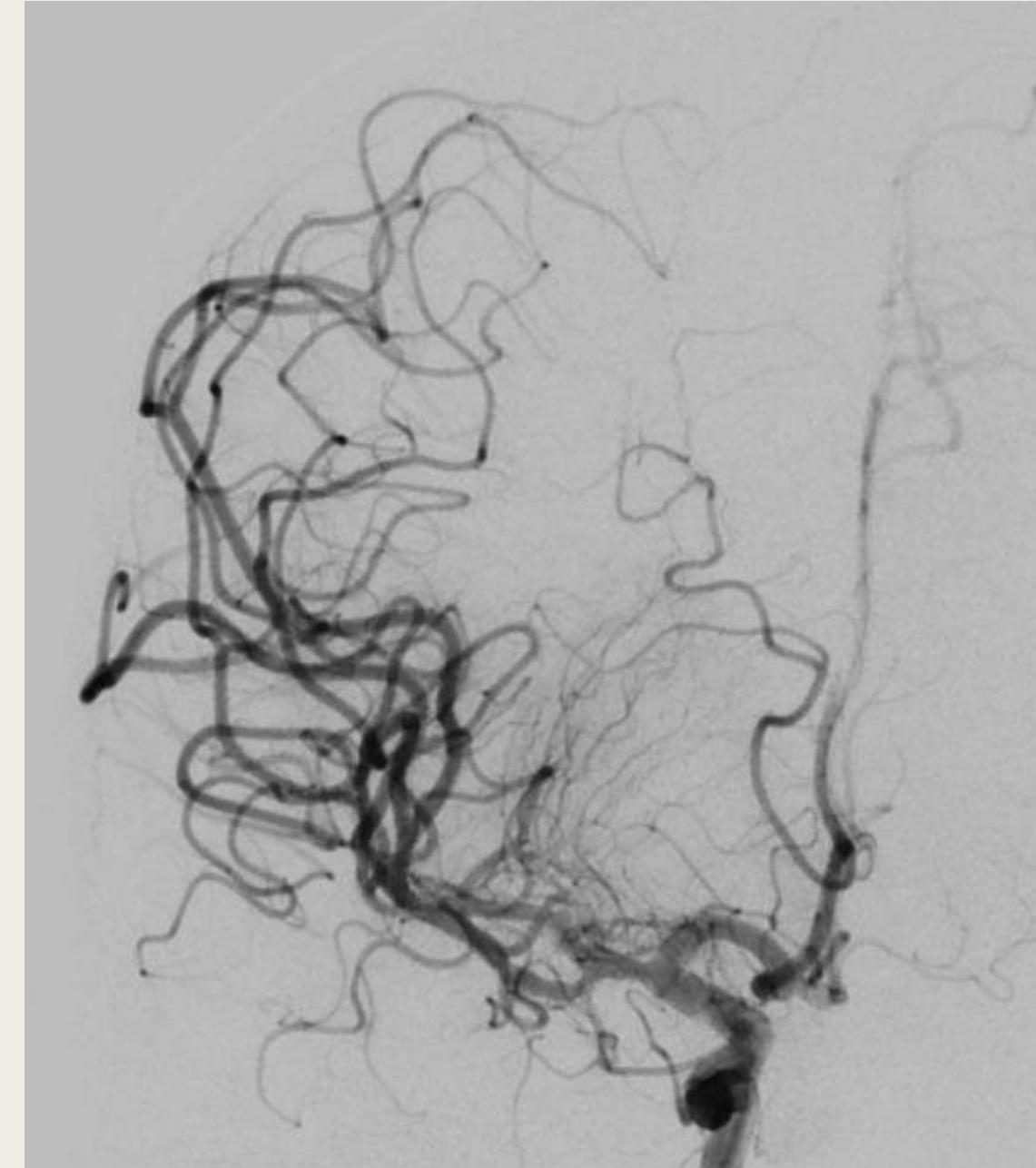


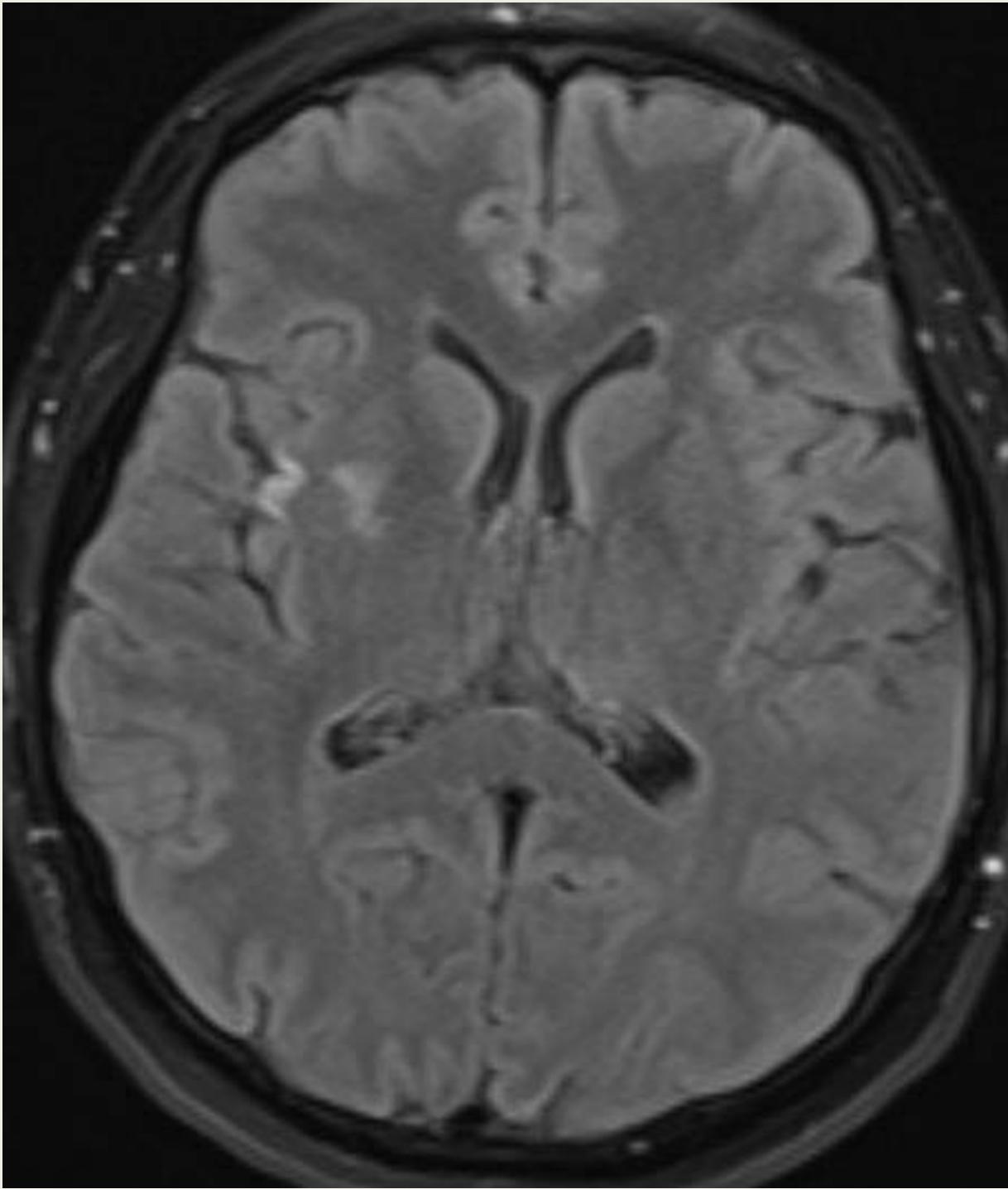


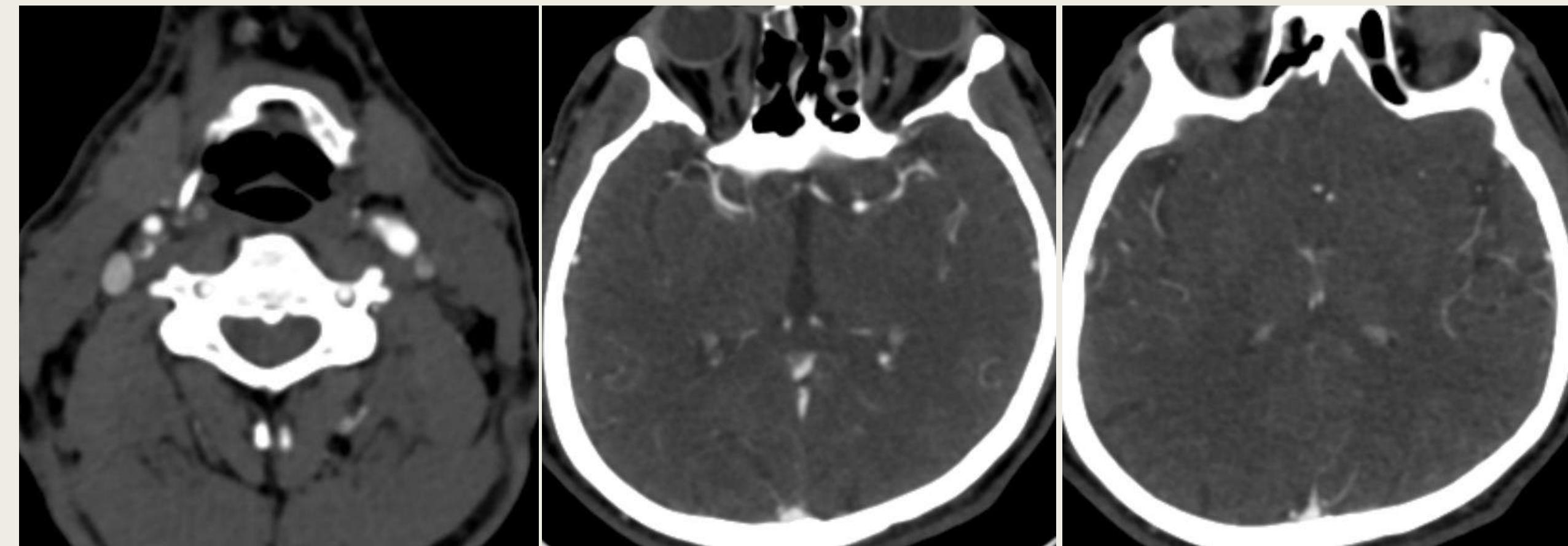


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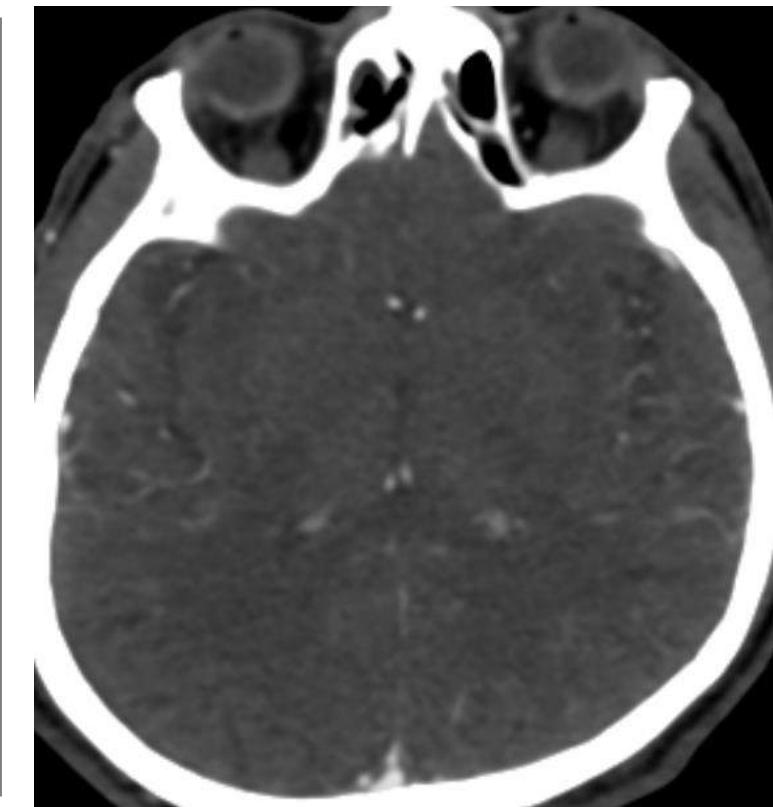
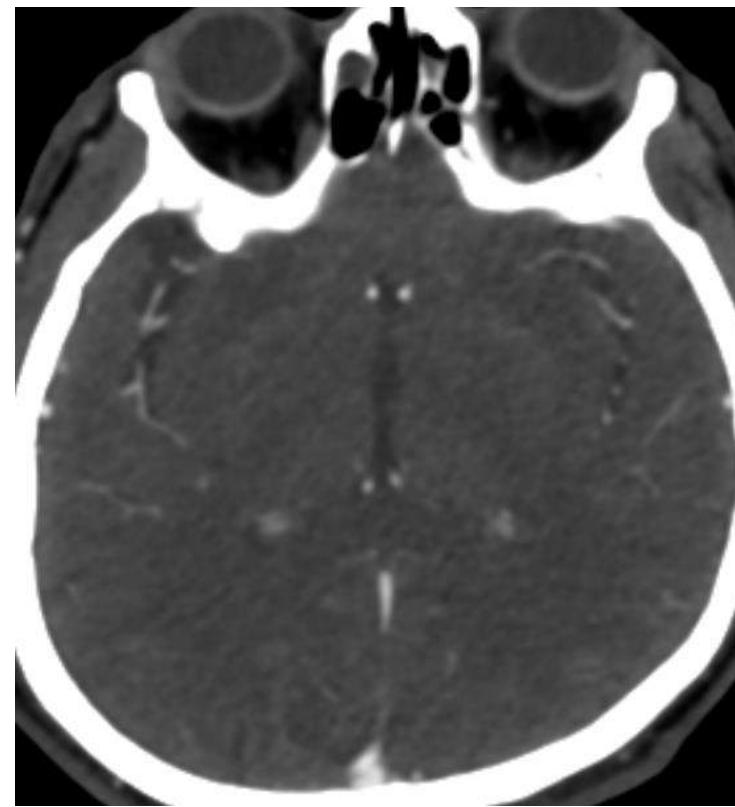
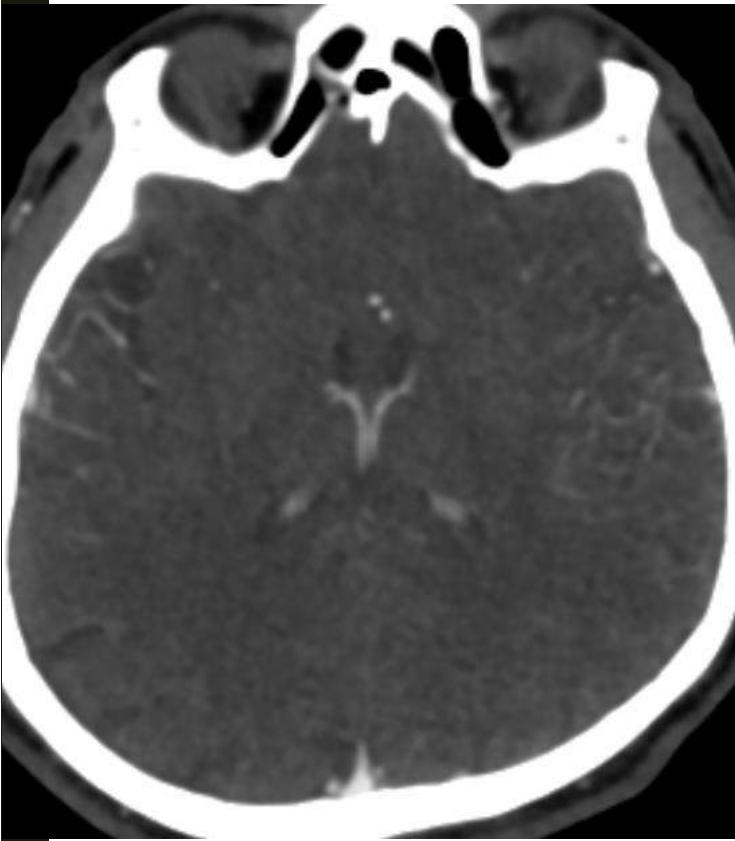


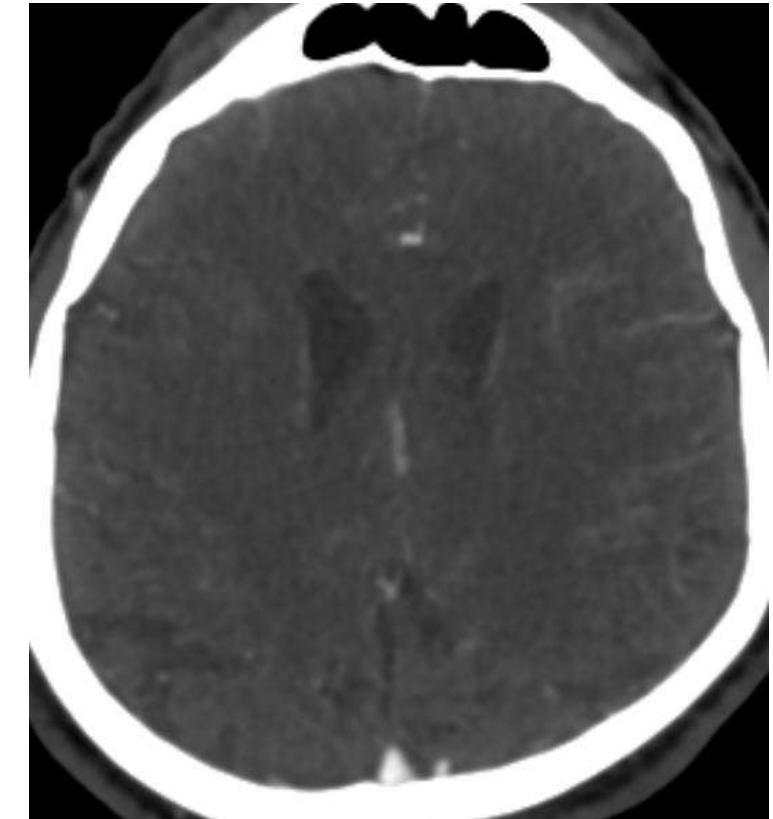
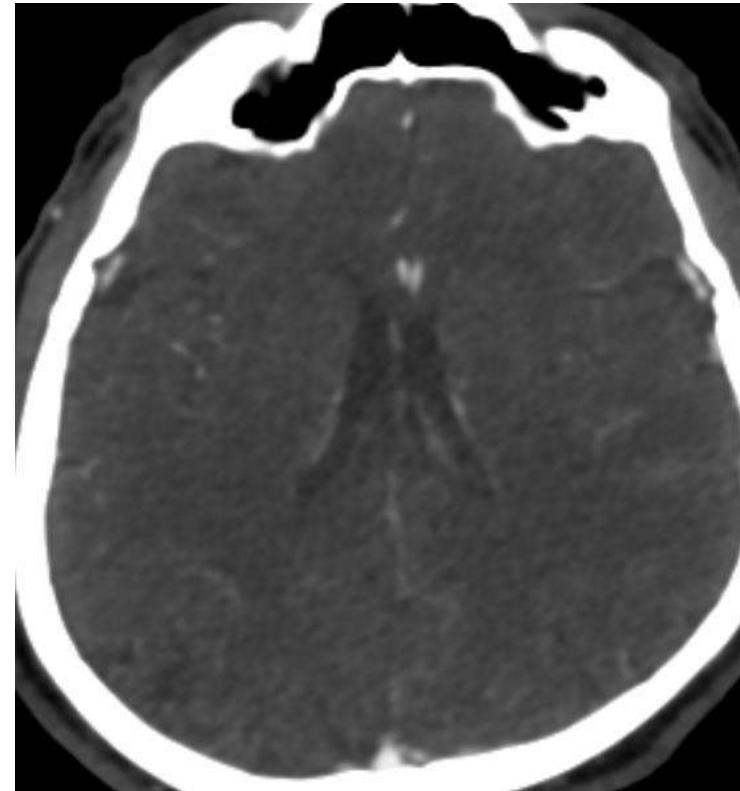
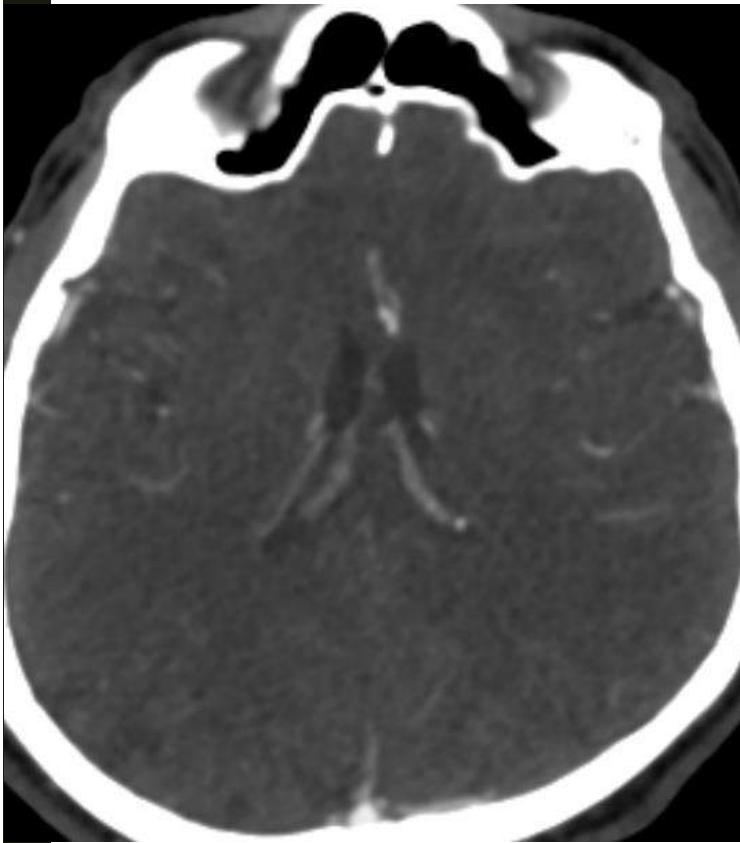


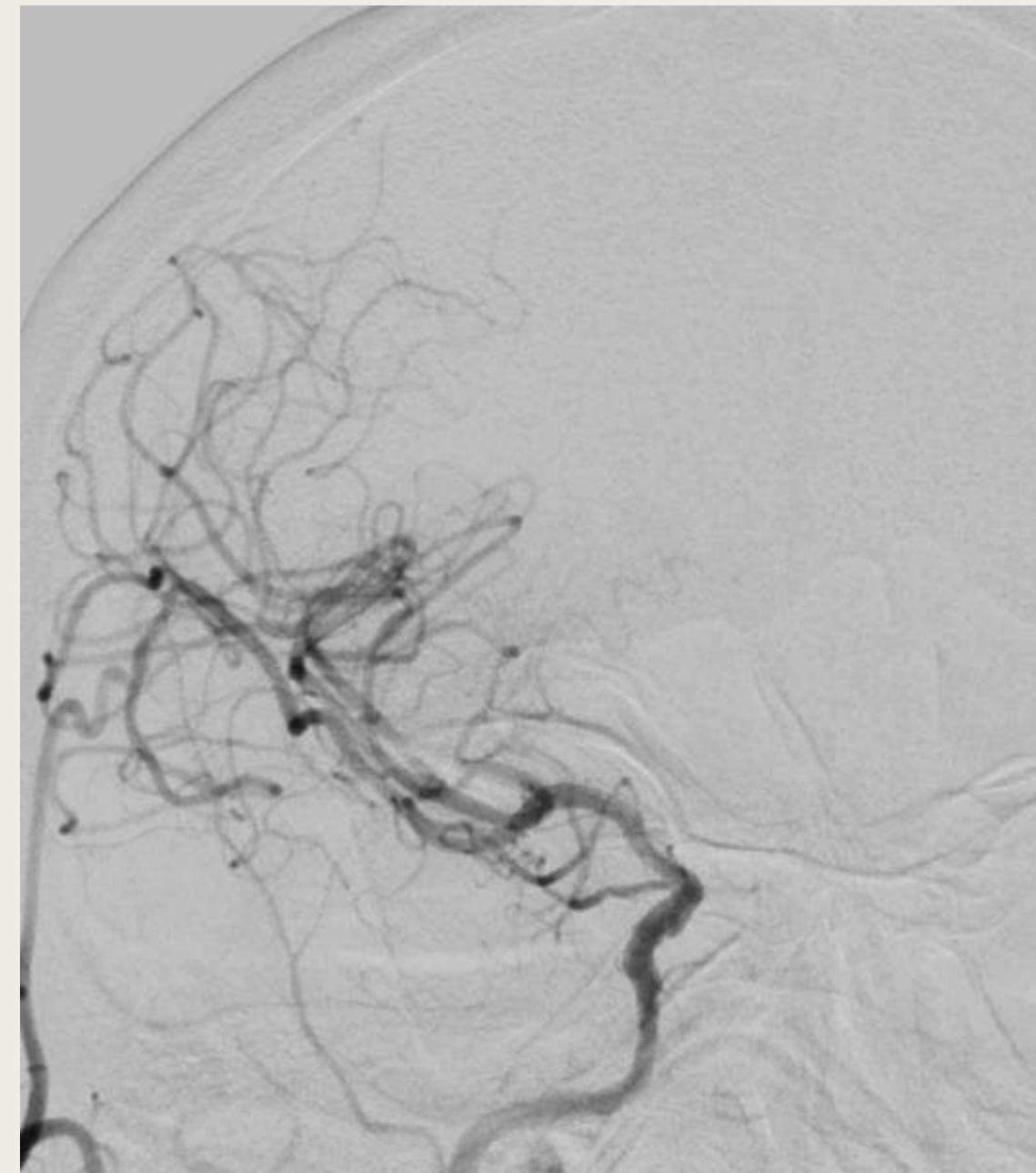
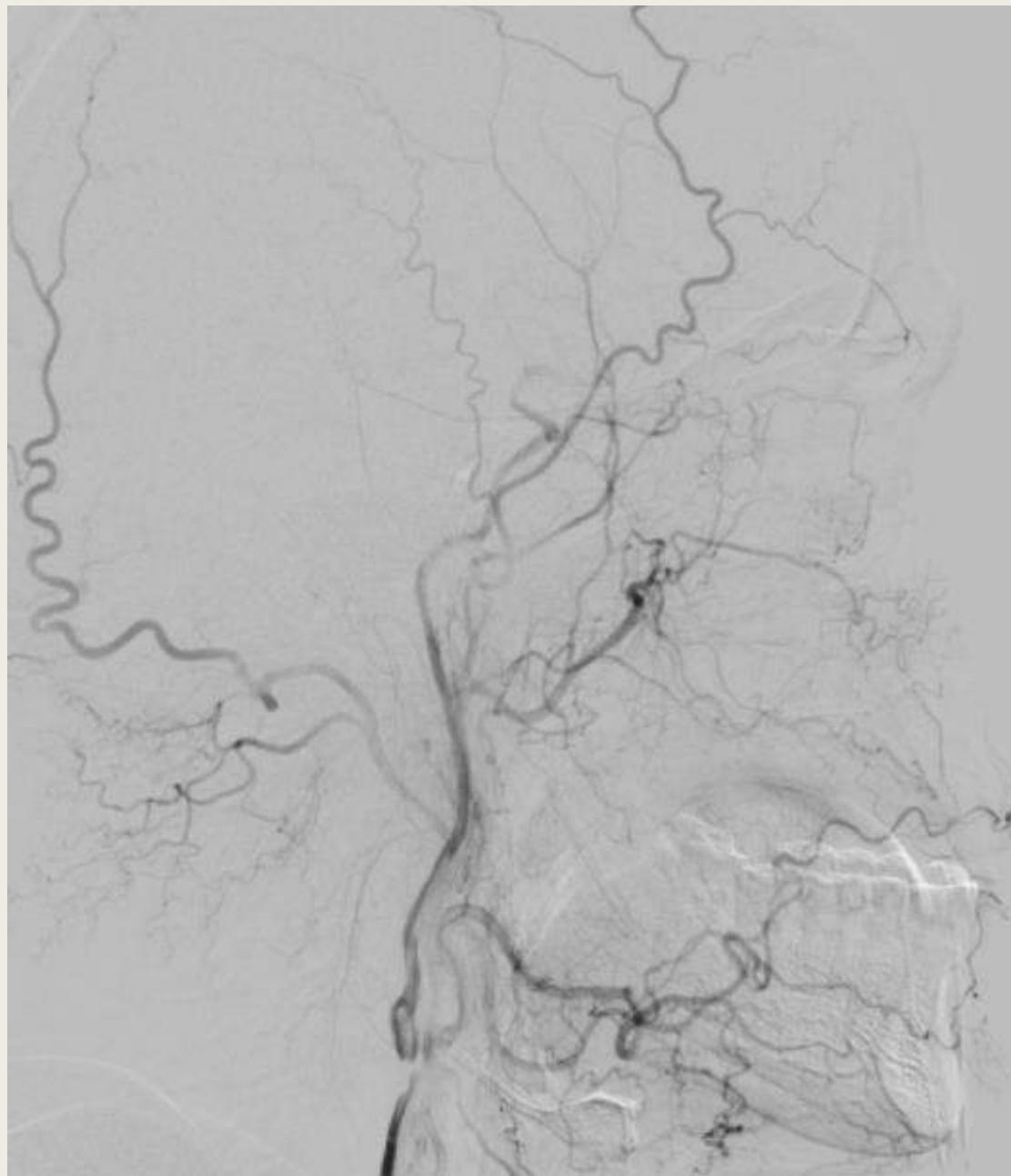


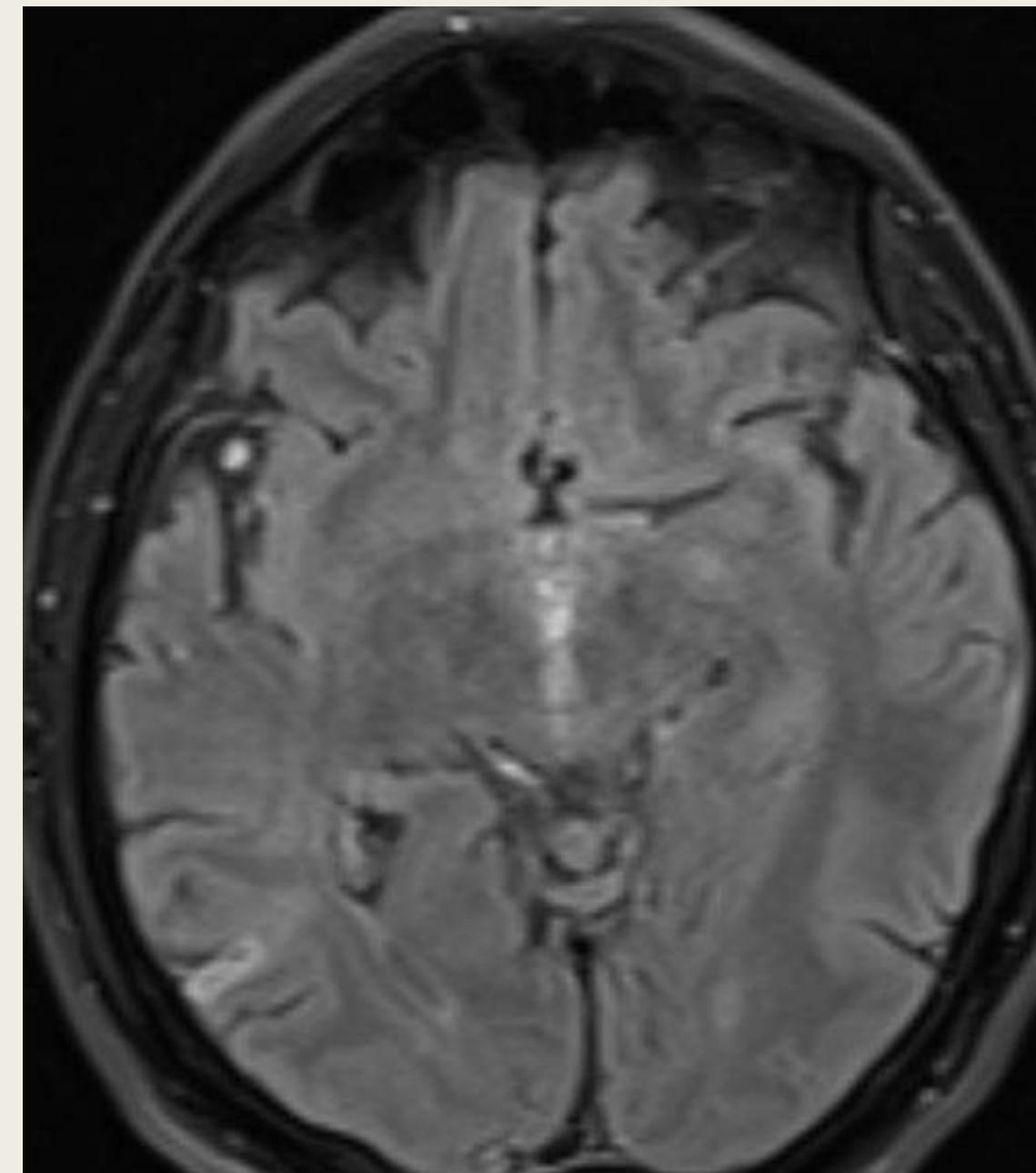
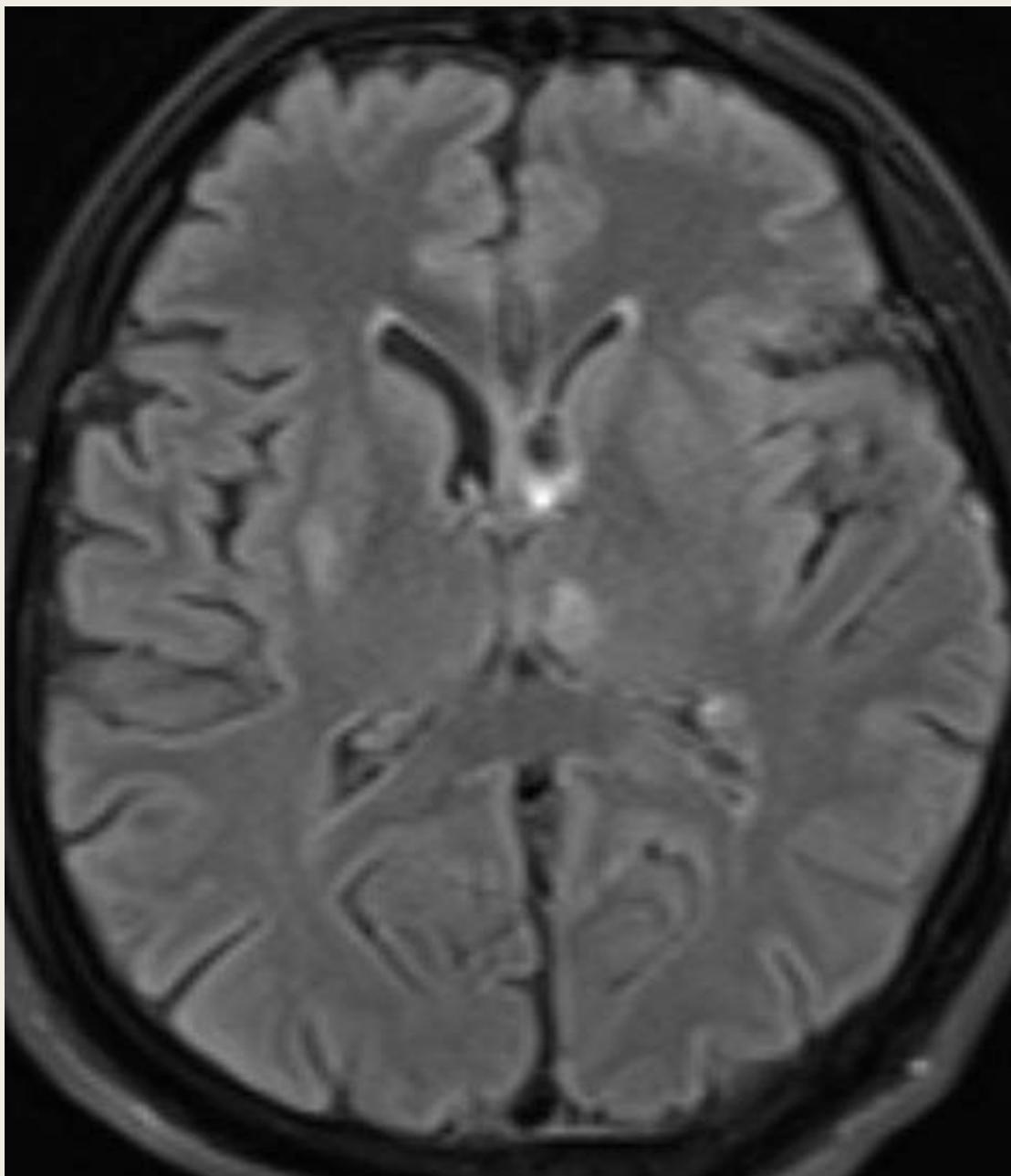


VAKA 3









Akut Inmede BT, BT Angio ve BT Perfuzyon

Talip Asil

Memorial Hizmet Hastanesi
Inme Unitesi

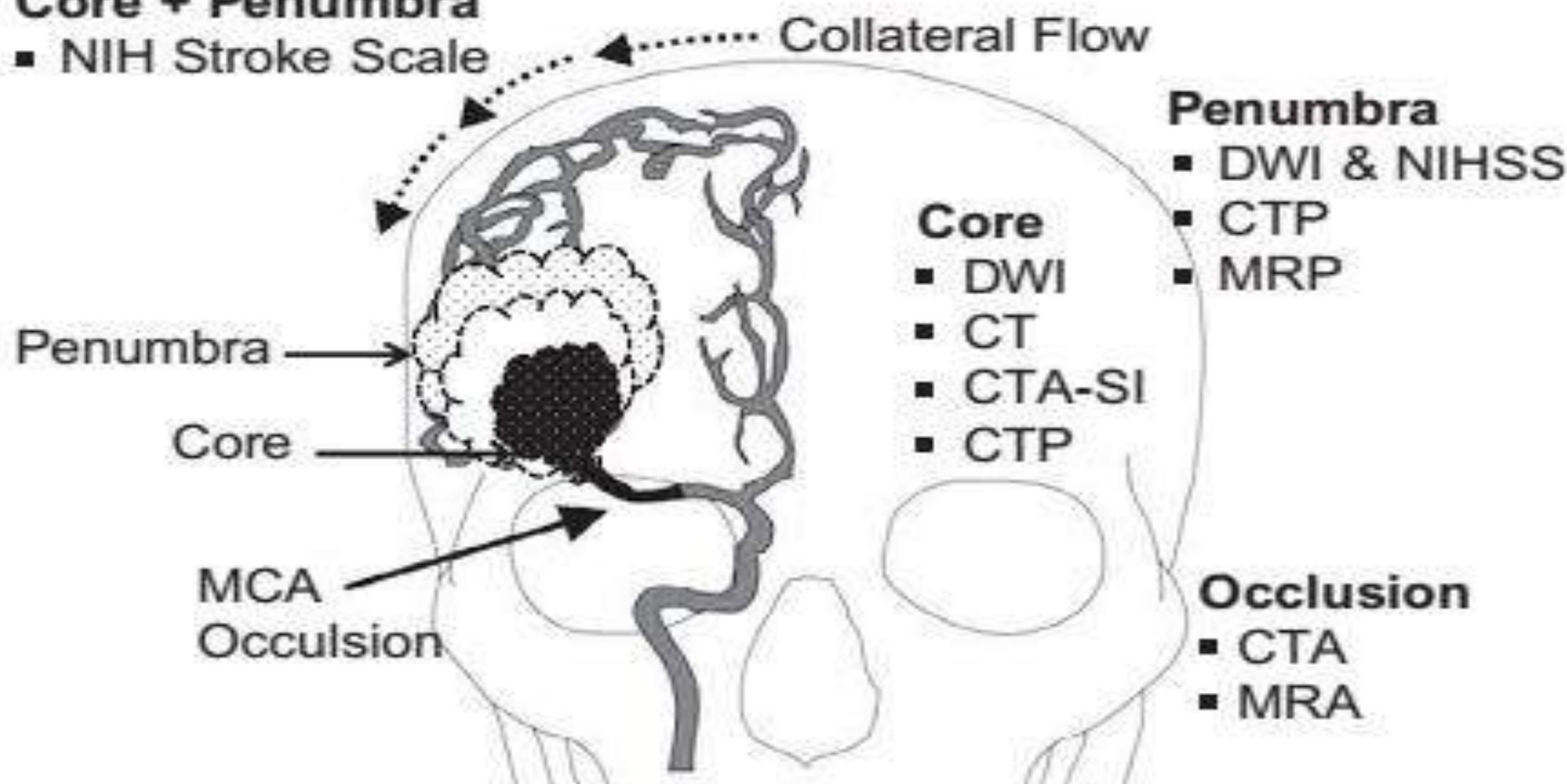
Tedavi etmeden once

- **Clinical**
 - Inme Baslangic zamani
 - Inme Siddeti
- **Goruntuleme**
 - Clot lokalizasyonu
 - Core ve Kurtarilabilir doku (penumbra tahmini)
 - Colleteral skorlama
- **4C Kurali**

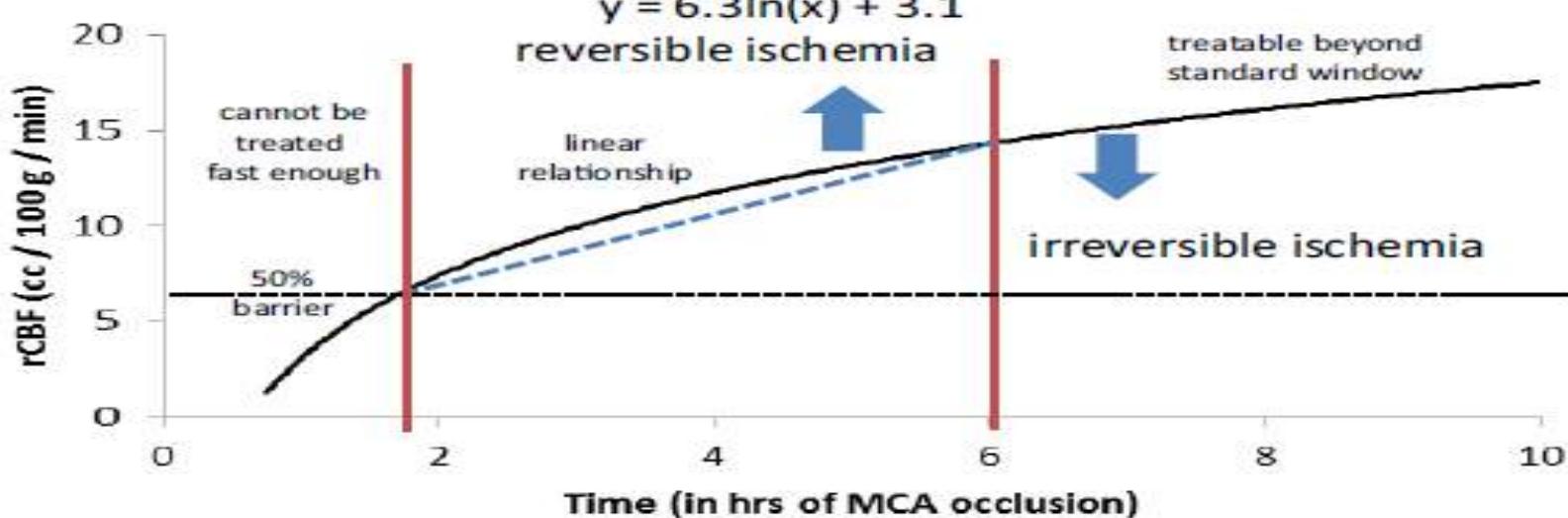
Stroke Physiology & Imaging Methods

Core + Penumbra

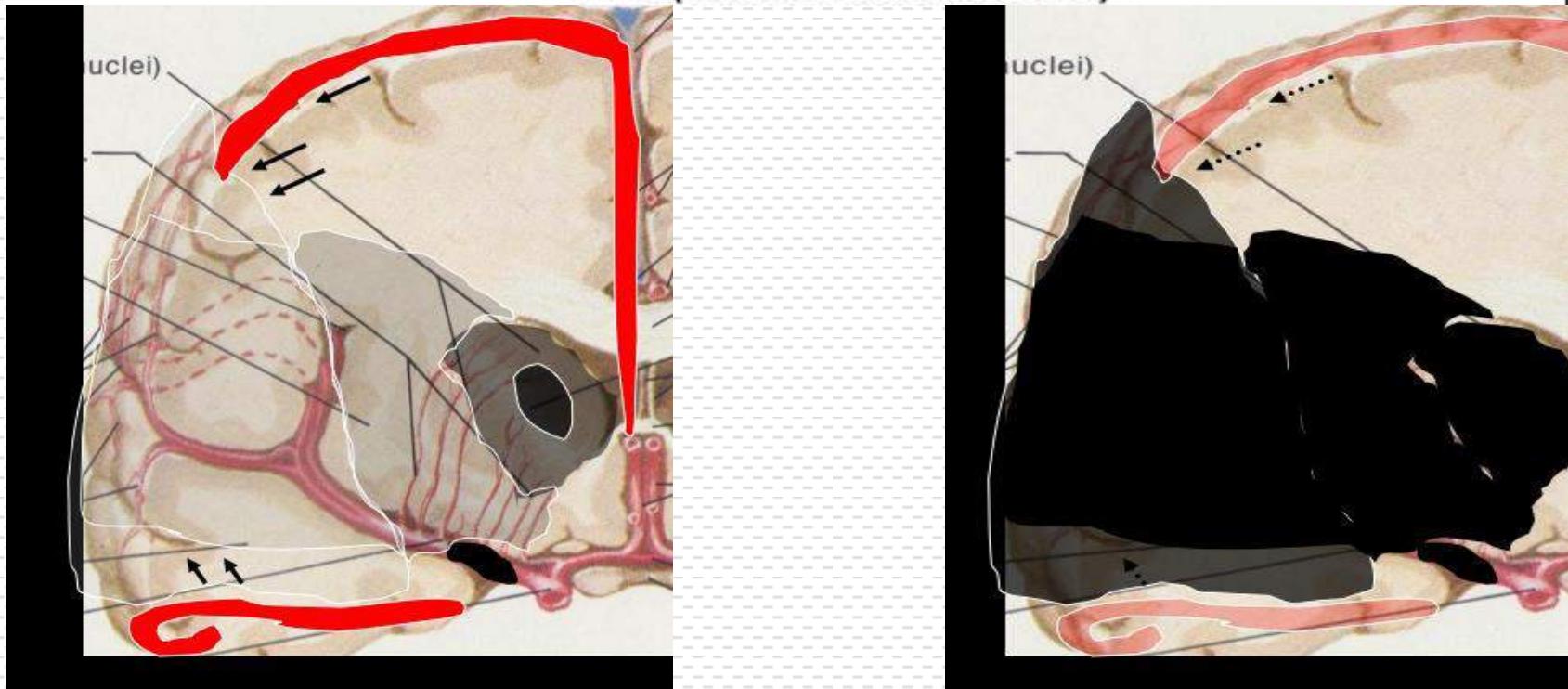
- NIH Stroke Scale

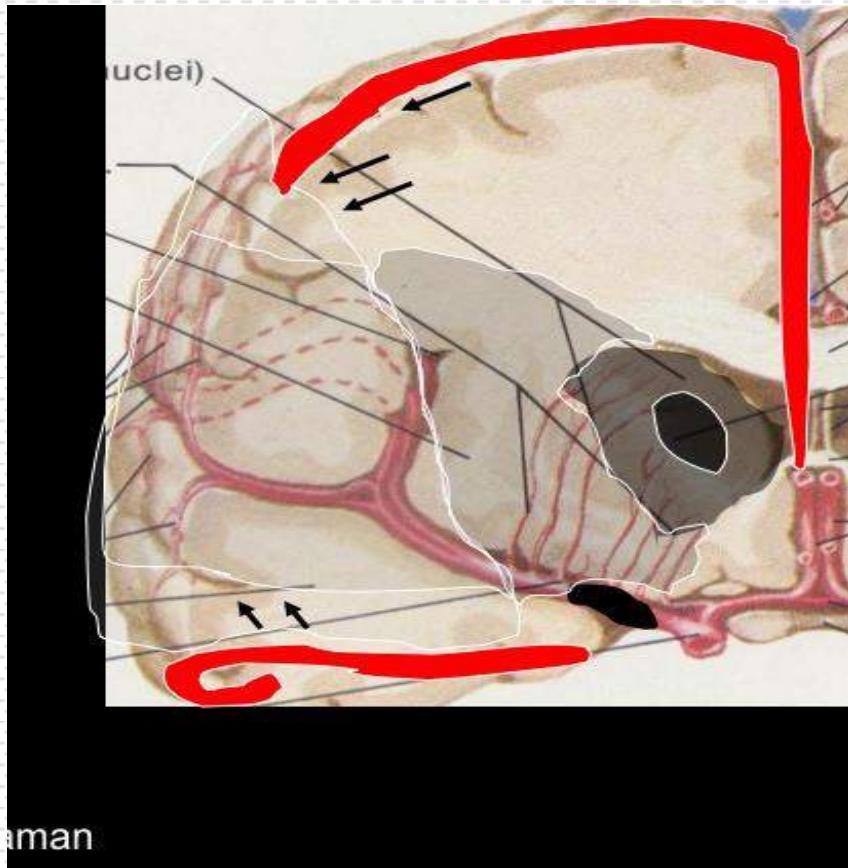


Logarithmic Time Curve to Irreversible Ischemia



Al Ali 2015





NIH Score = NIH Score

Klinik-Goruntuleme Mismatch

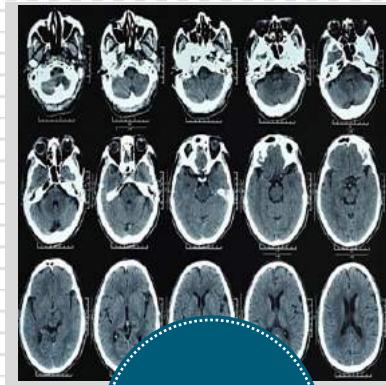


Nuts and Bolts of NIH Stroke scale

1. Tool used by healthcare providers to objectively quantify impairment caused by stroke.
1. Initially designed as a research tool and then incorporated into Acute stroke evaluation.
1. A trained provider administers the NIHSS which usually takes about 10 min.
1. Scale consists of 11 items and each item ranges from 0-5 where 0 is normal and 5 means severely affected.
1. Maximum possible score is 42.

| Score | Stroke severity |
|------------------------|-----------------|
| 0 symptoms | No stroke |
| 1-4 Stroke | Minor |
| 5-15 Stroke | Moderate |
| 16-20 to severe Stroke | Moderate |
| 21-42 Severe | Severe |

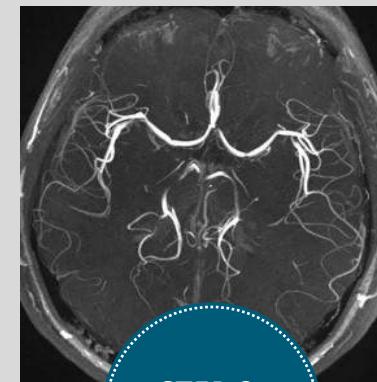
İlk 4.5-6 Saat



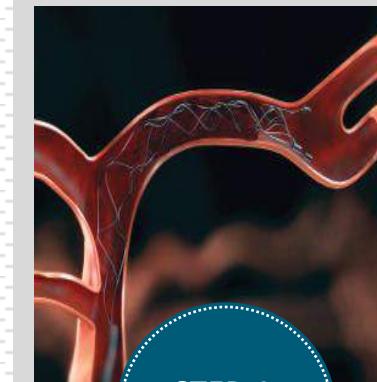
STEP 1:
Plain CT



STEP 2:
rt-PA

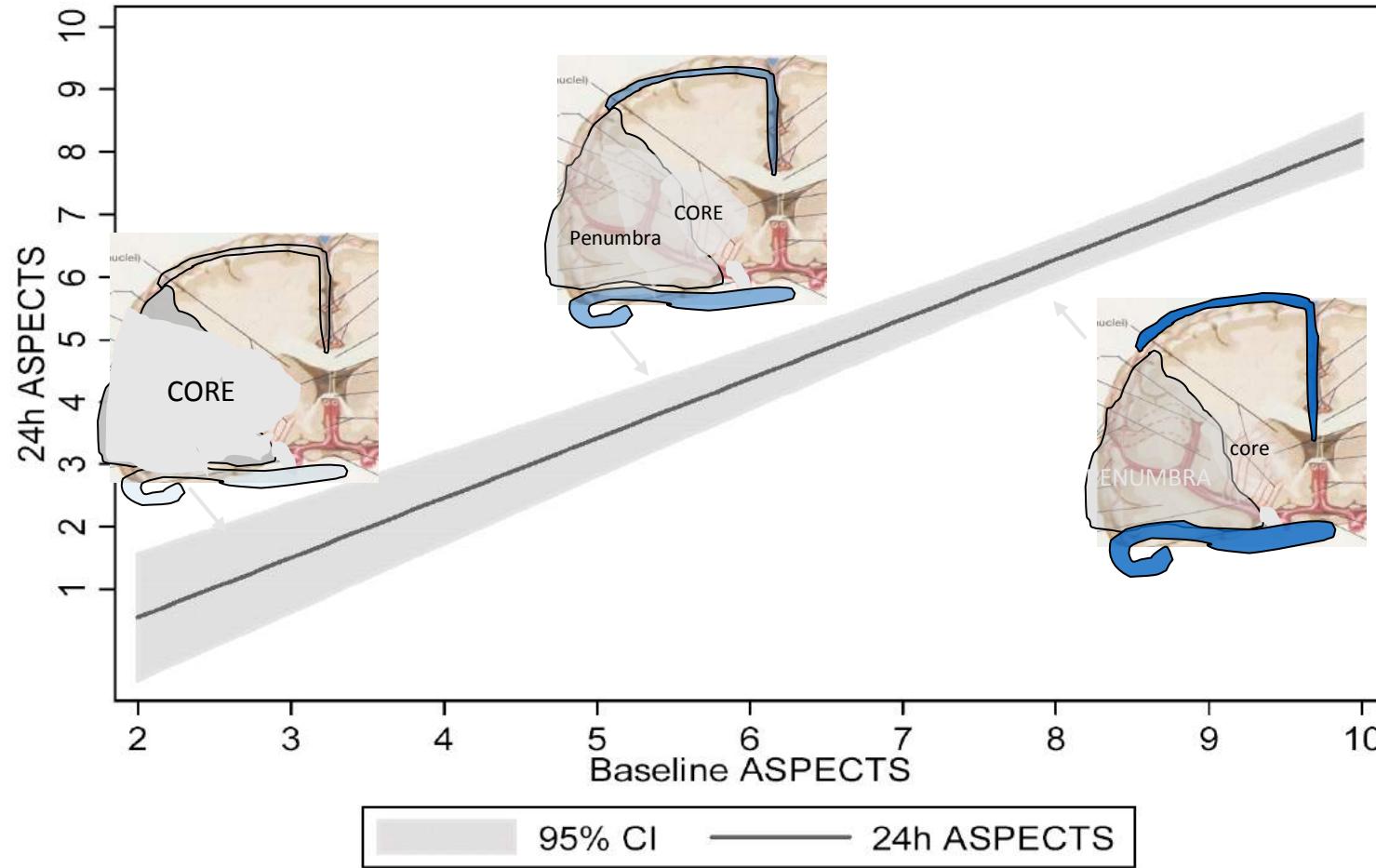


STEP 3:
CT Angio



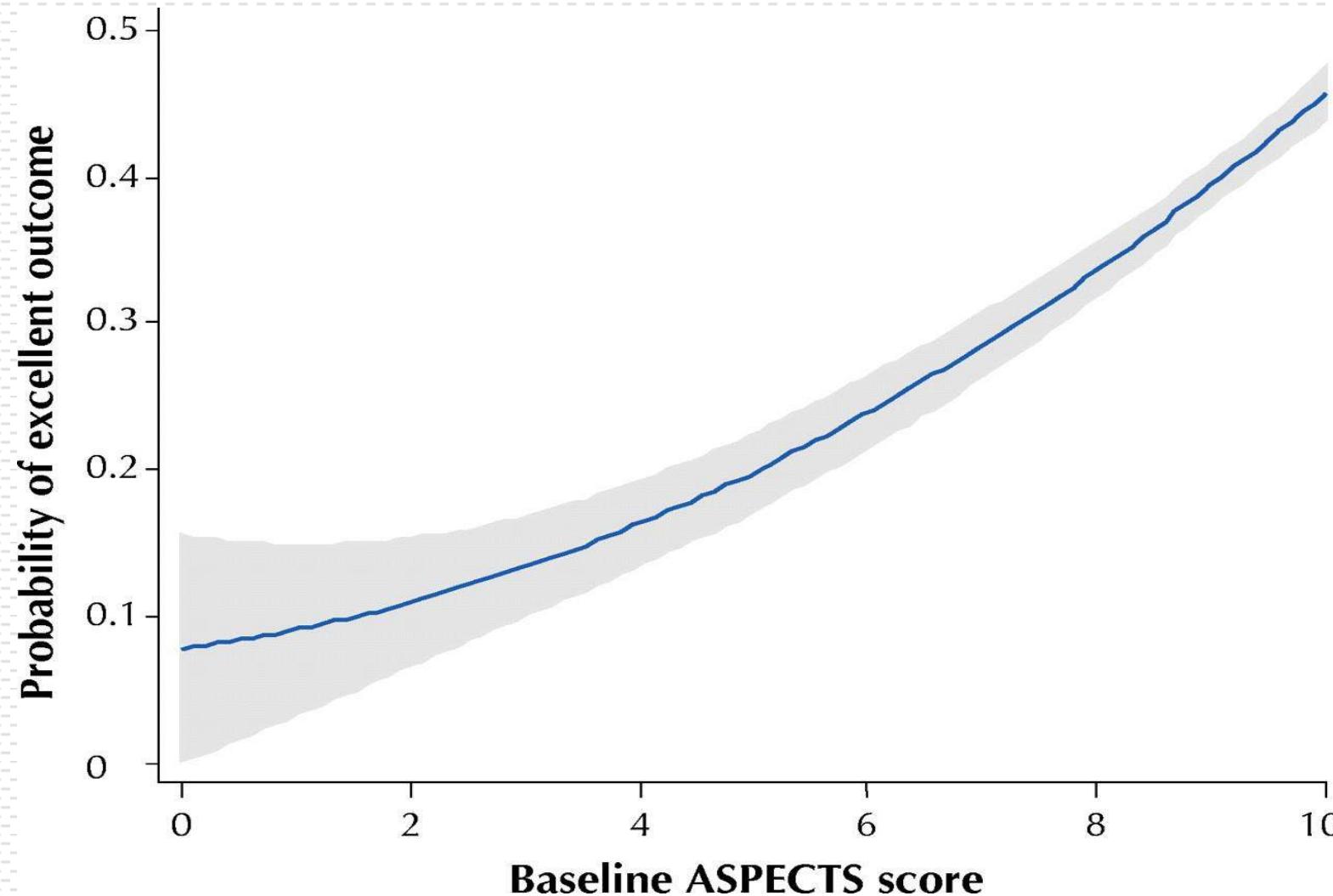
STEP 4:
Endovascular

Dzialowski I et al. ASPECTS ECASS-2. Stroke

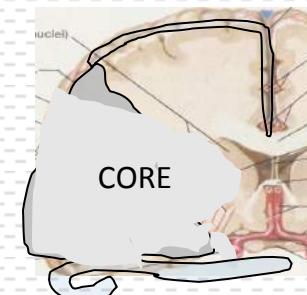
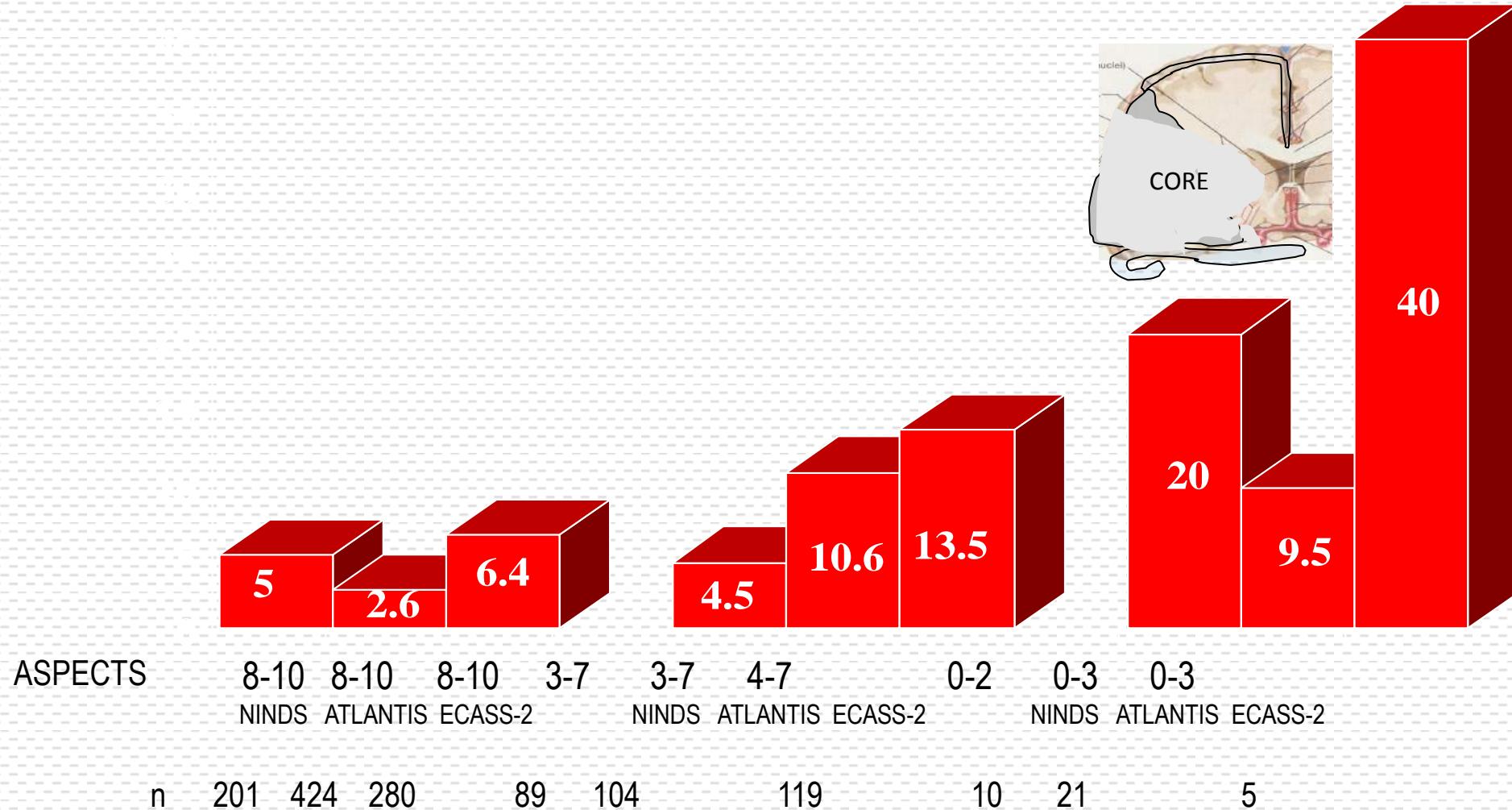


ASPECTS clinical outcome

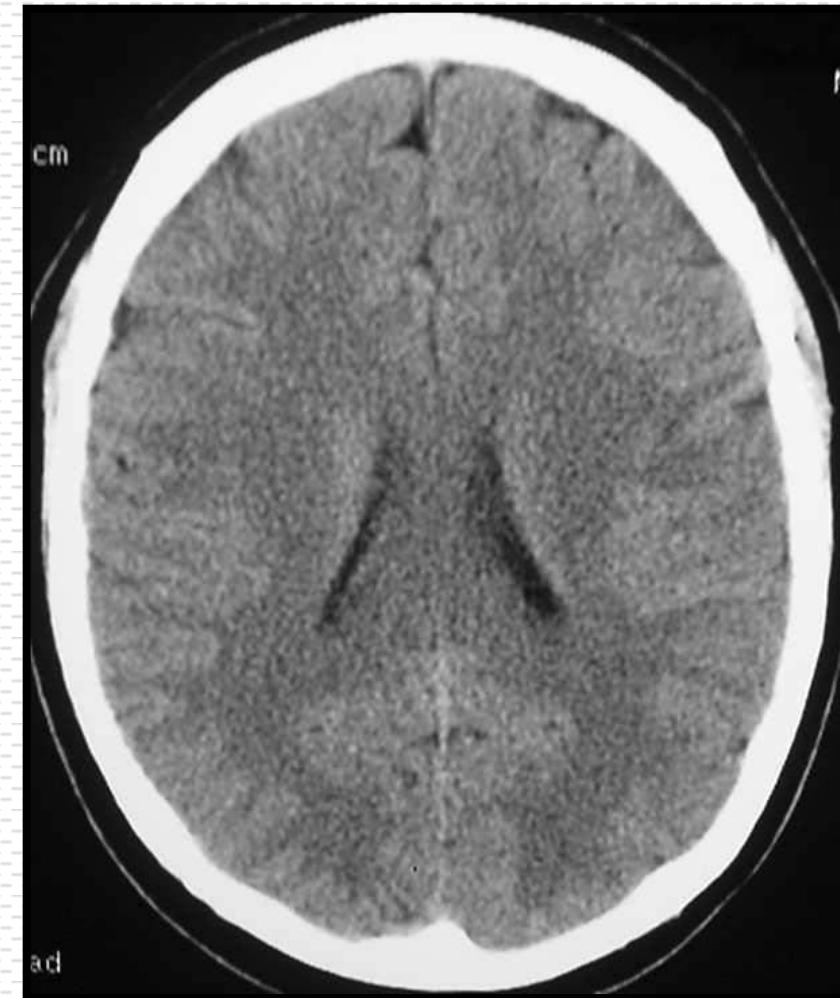
Hill MD et al. CASES. CMAJ 2005

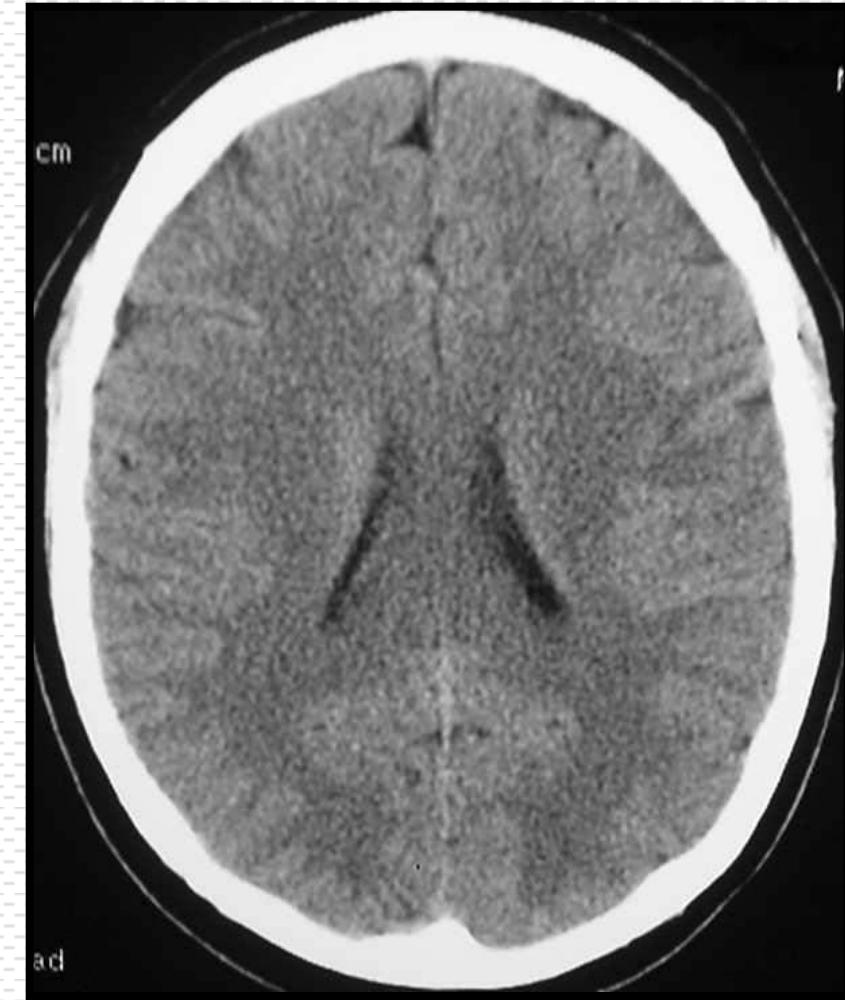
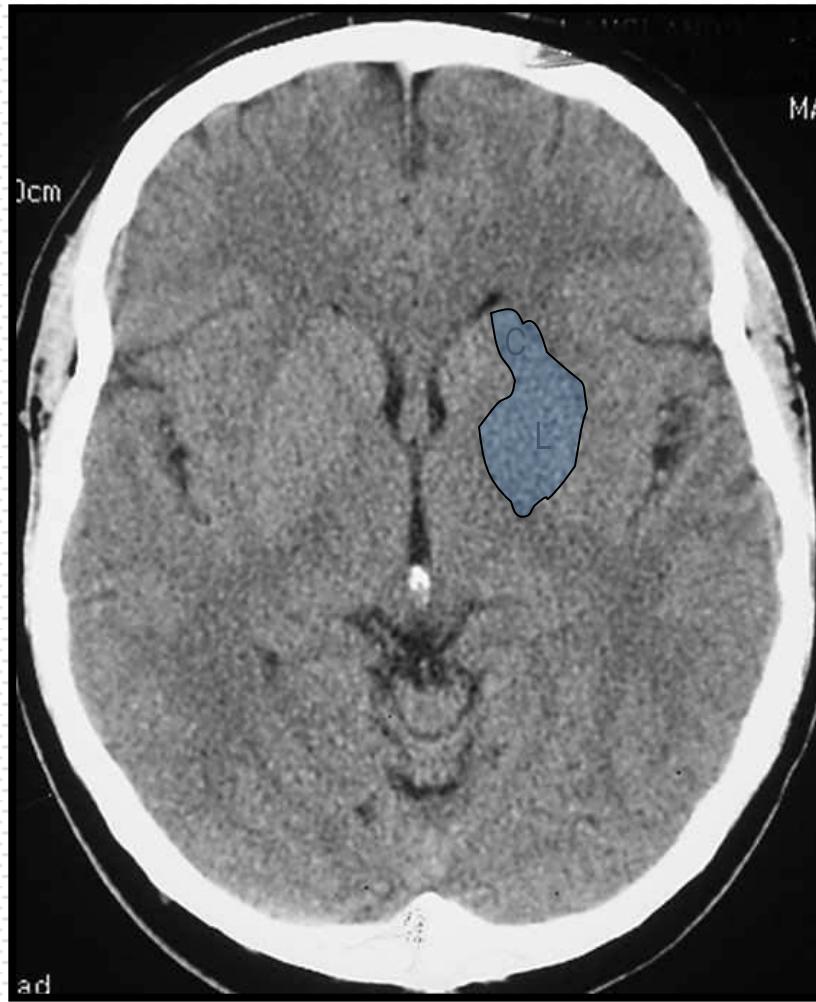


ASPECT Skoru- sICH İliskisi



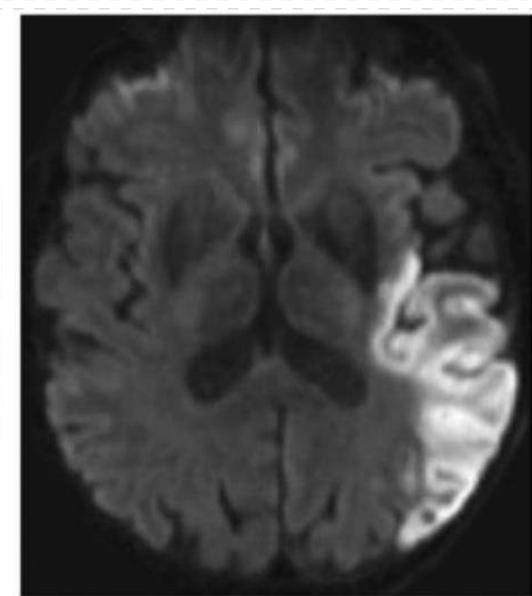
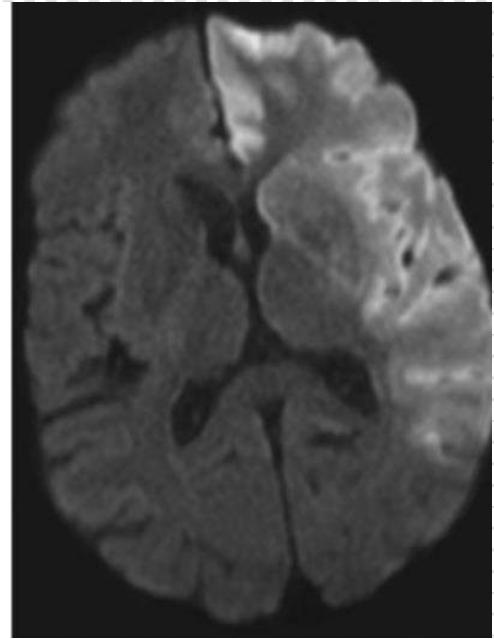
1Saatlik Sağ Hemiparezi



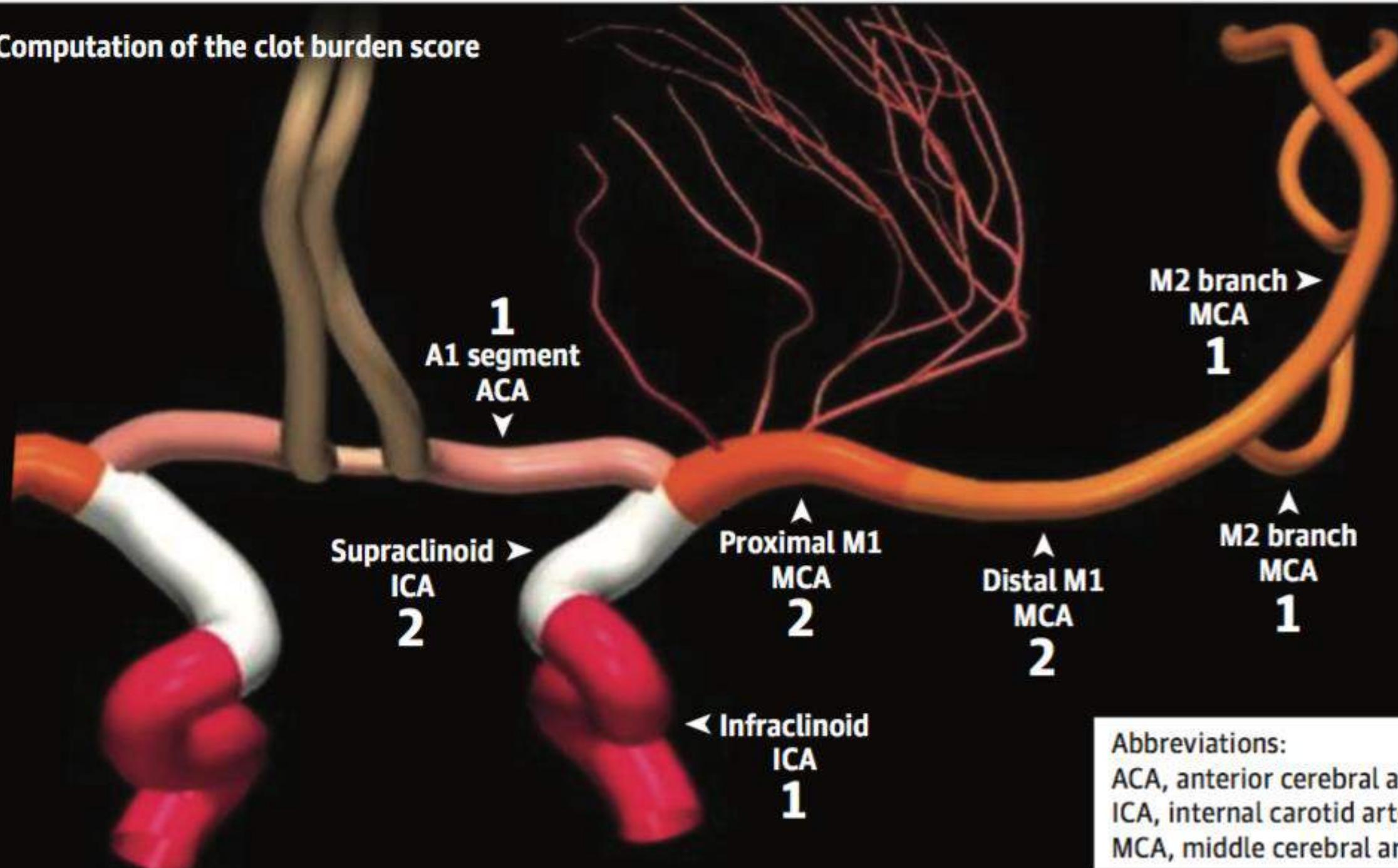


24. saat



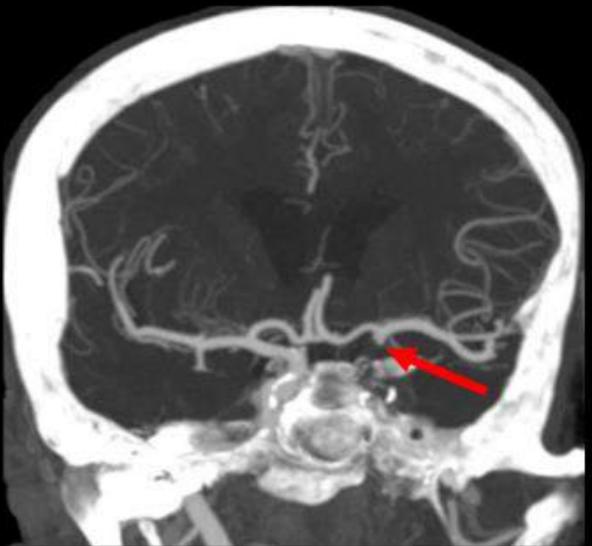


A Computation of the clot burden score

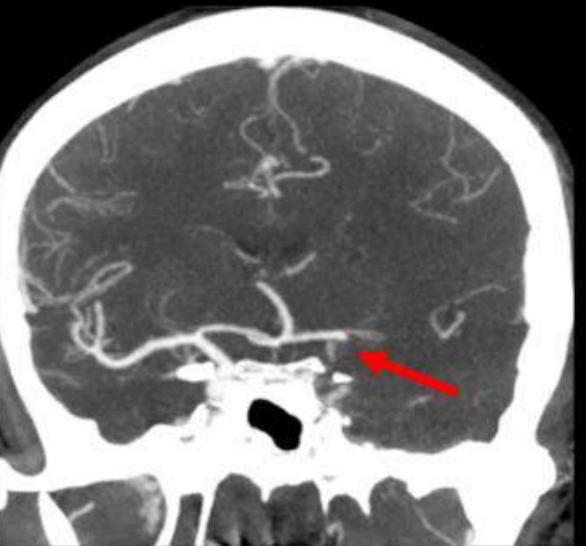


Abbreviations:
ACA, anterior cerebral artery
ICA, internal carotid artery
MCA, middle cerebral artery

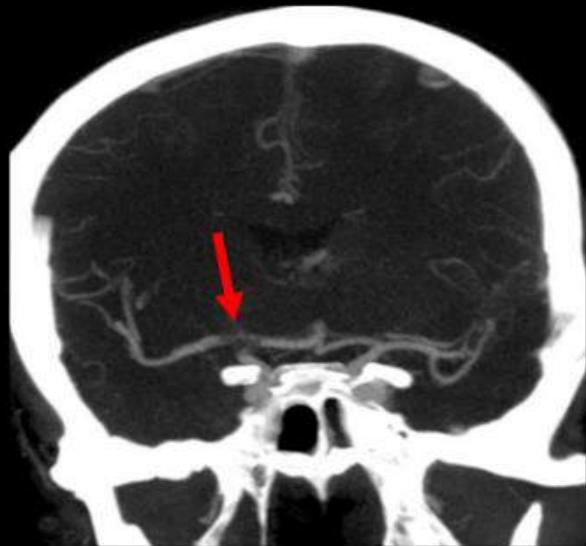
Terminal ICA I Occlusion



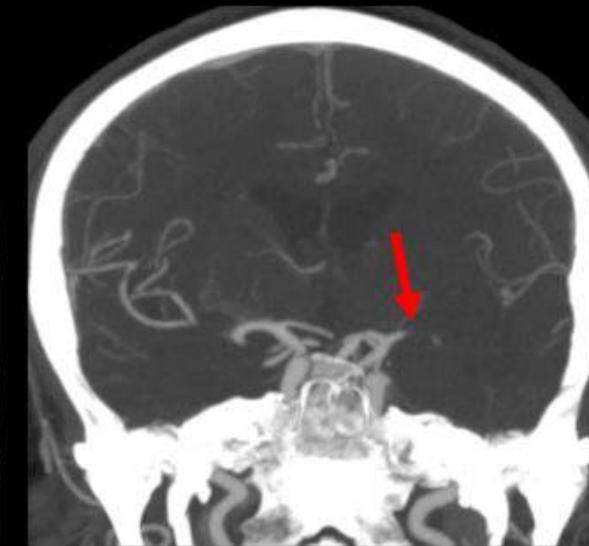
Terminal ICA L Occlusion



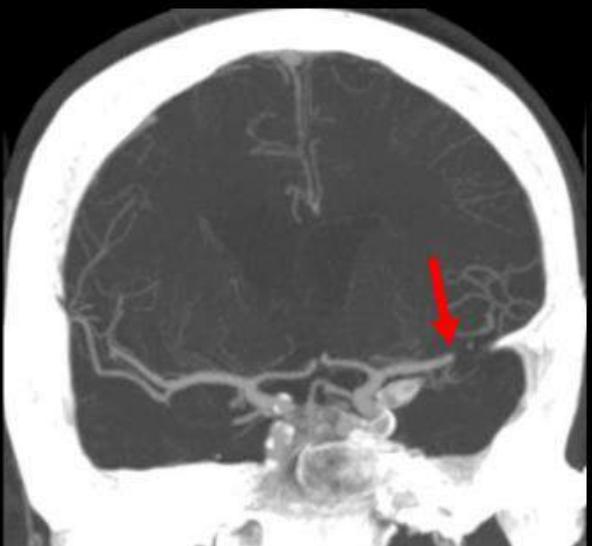
Terminal ICA T Occlusion



Proximal M1 Occlusion



Distal M1 Occlusion



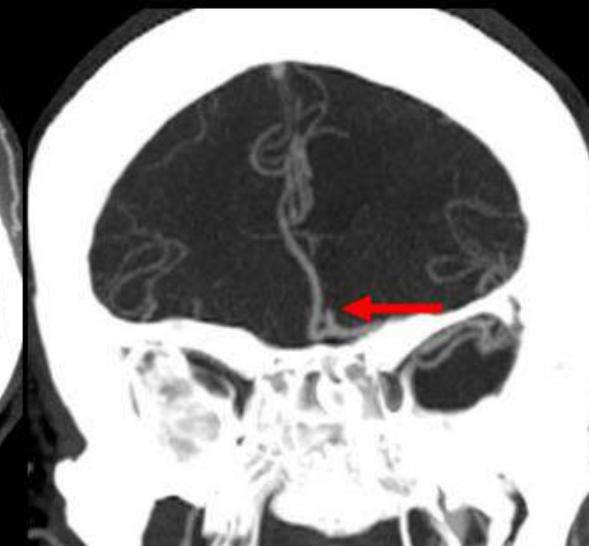
Proximal M2 Occlusion



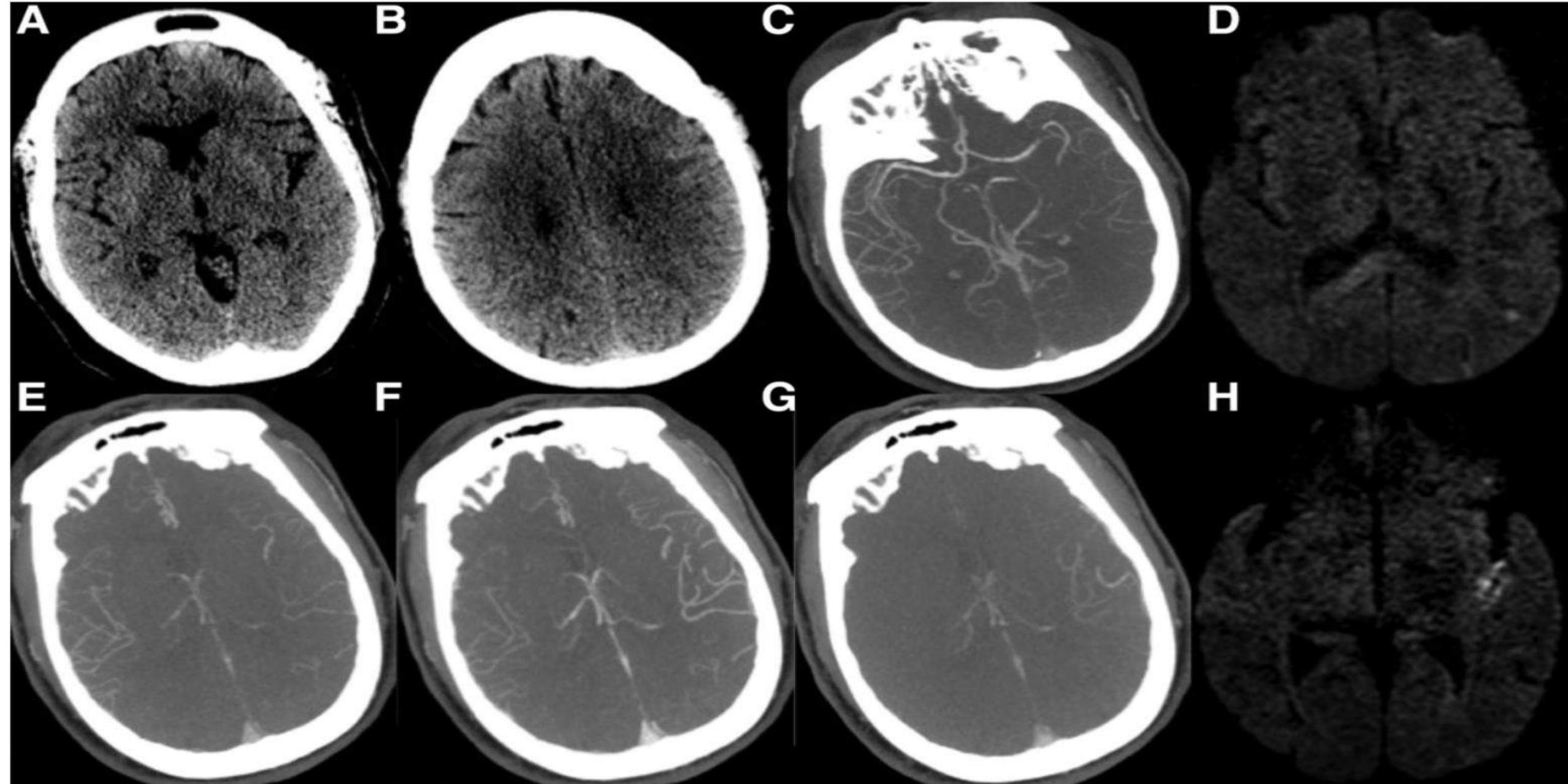
Distal M2 Occlusion



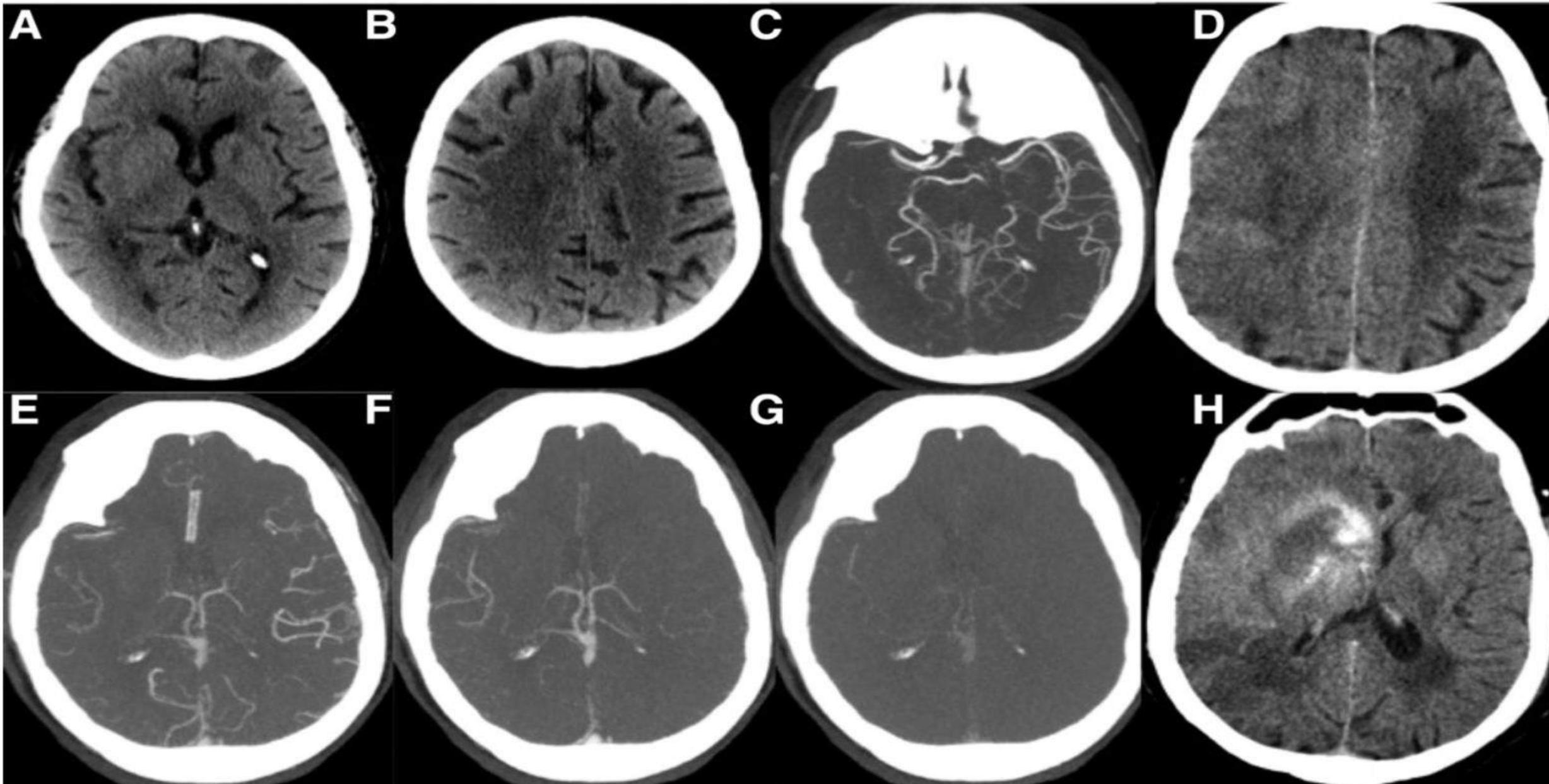
ACA A2 Occlusion

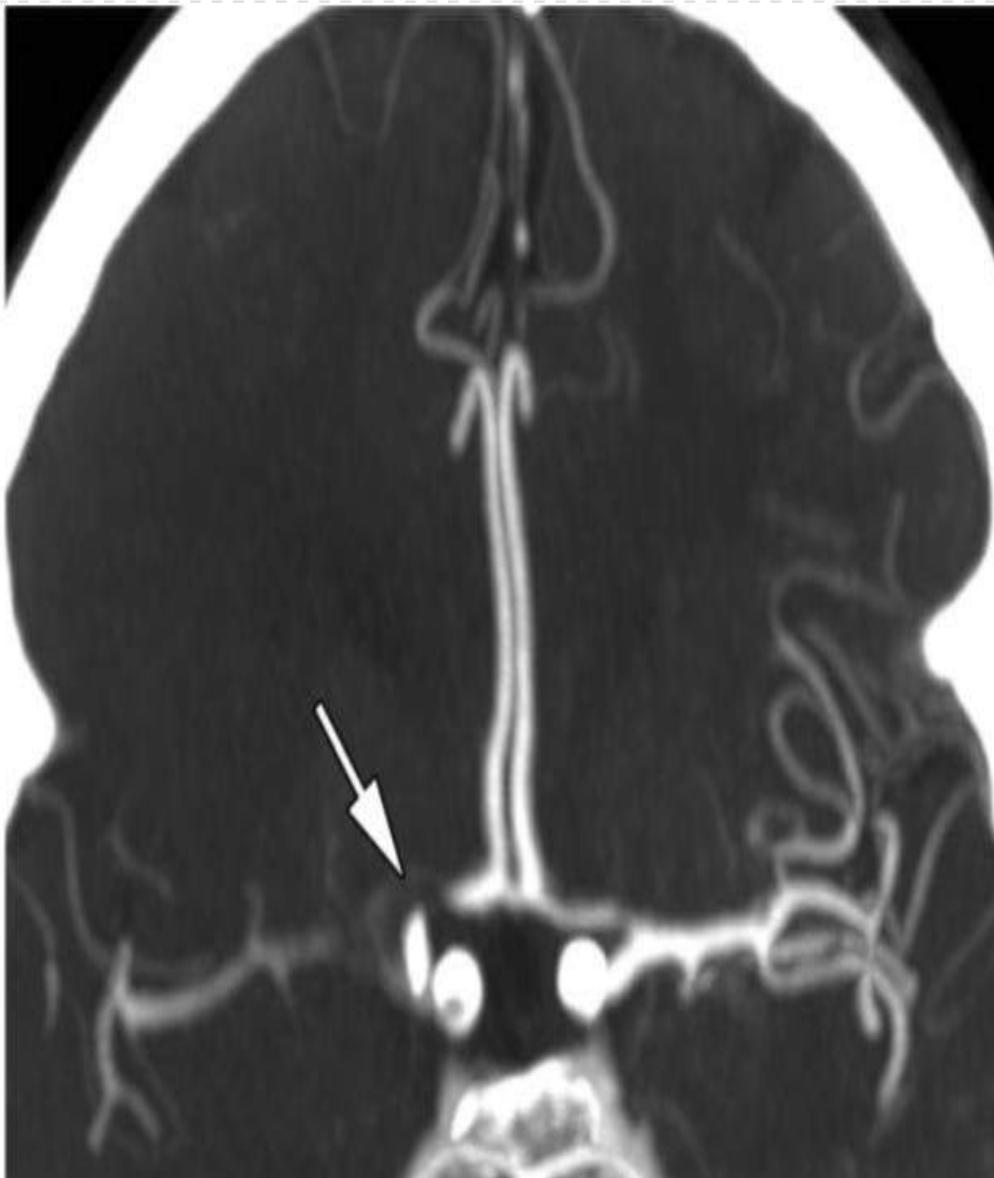


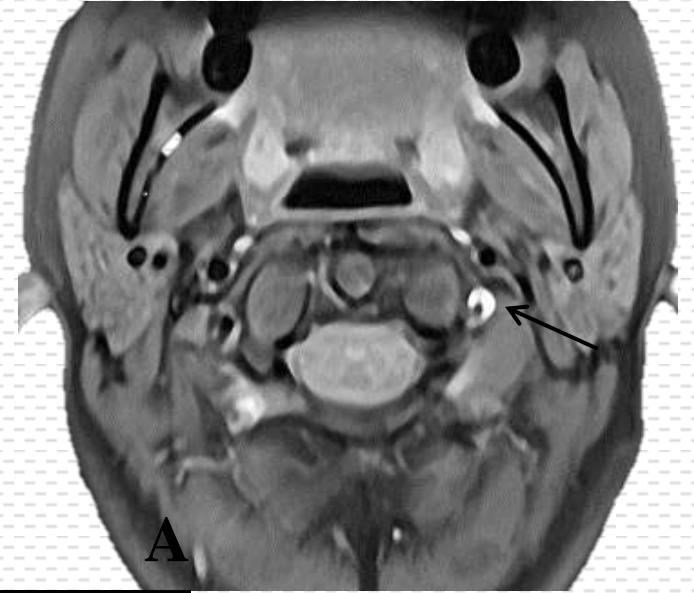
Iyi Kolleteral



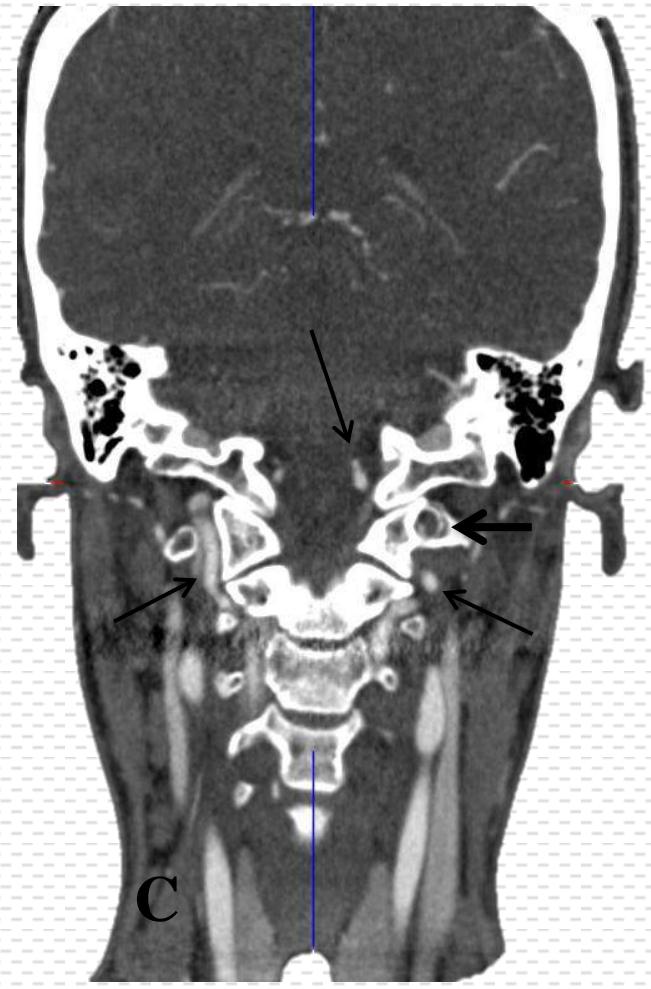
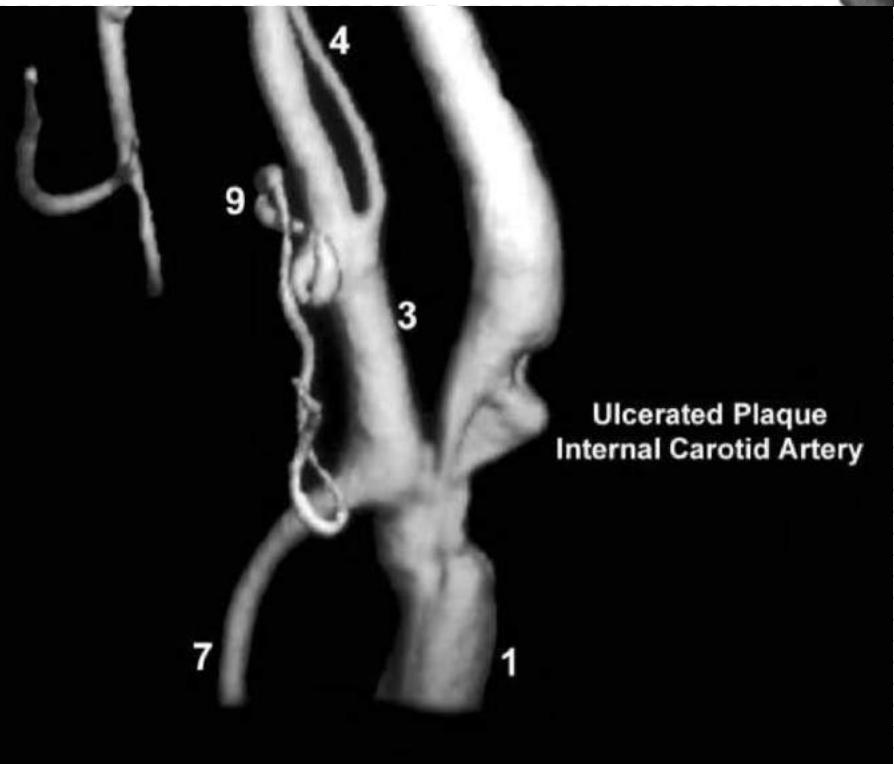
Kotu Kolleteral





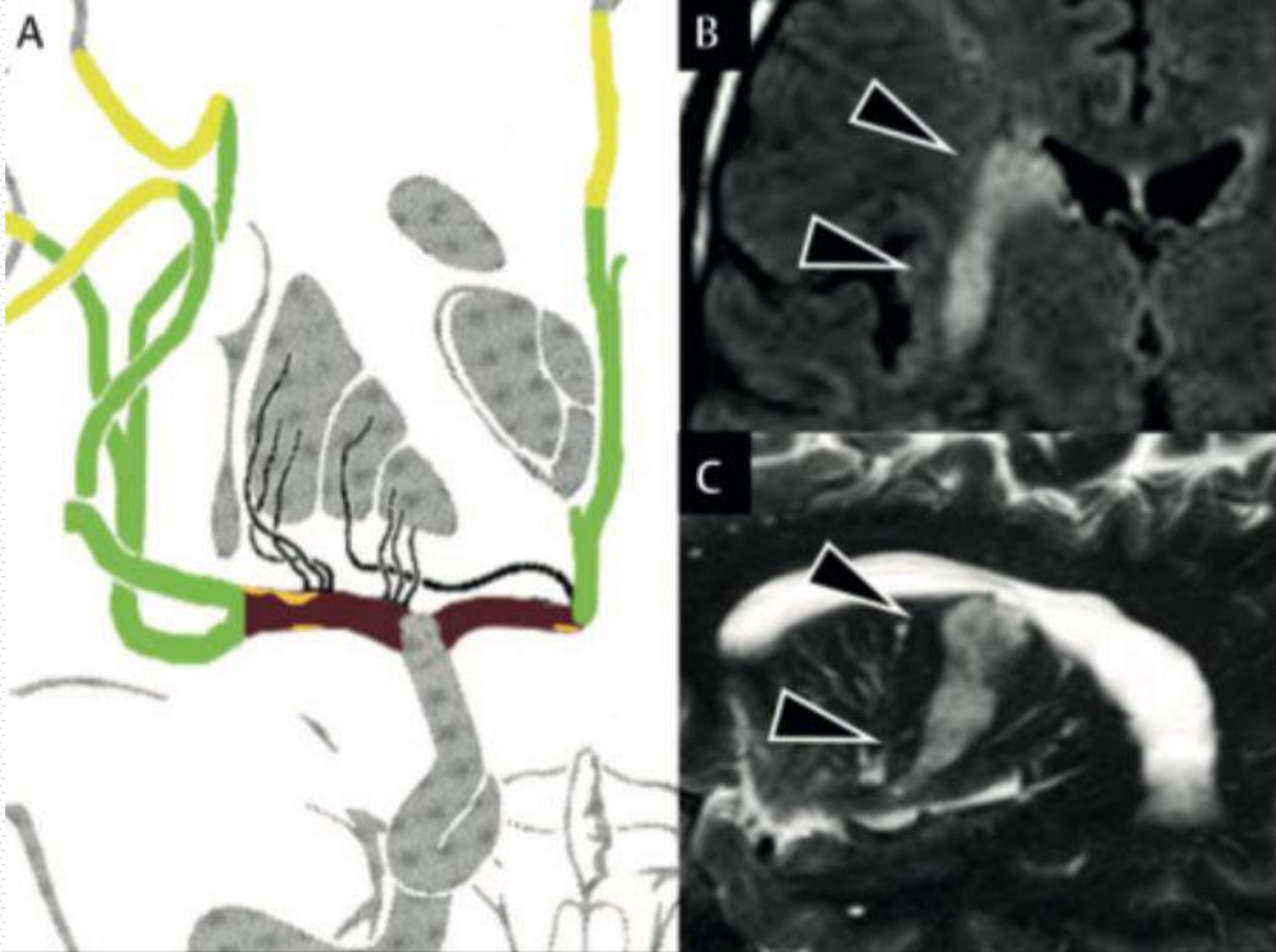


A

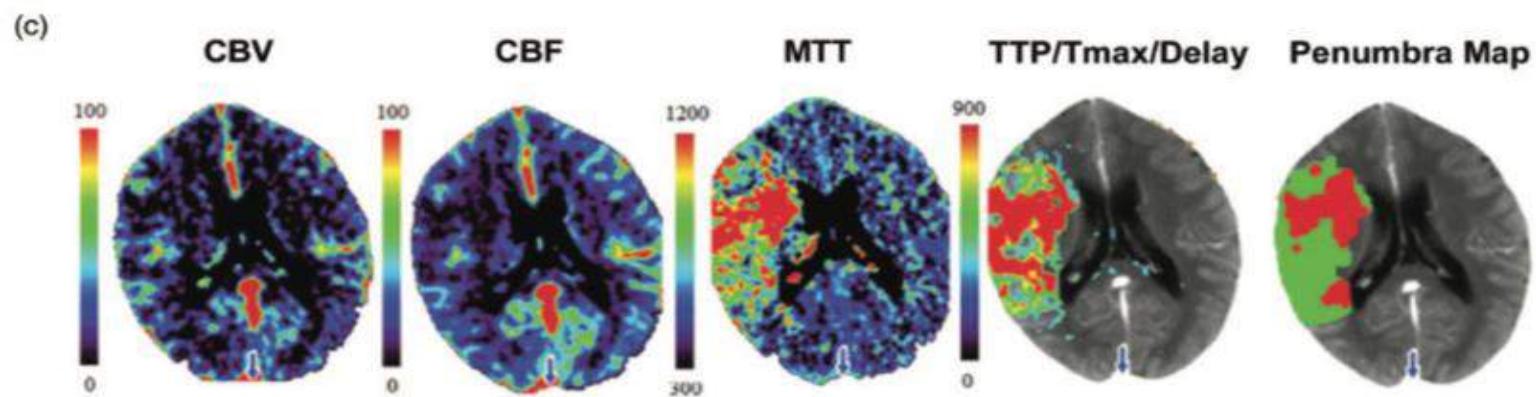
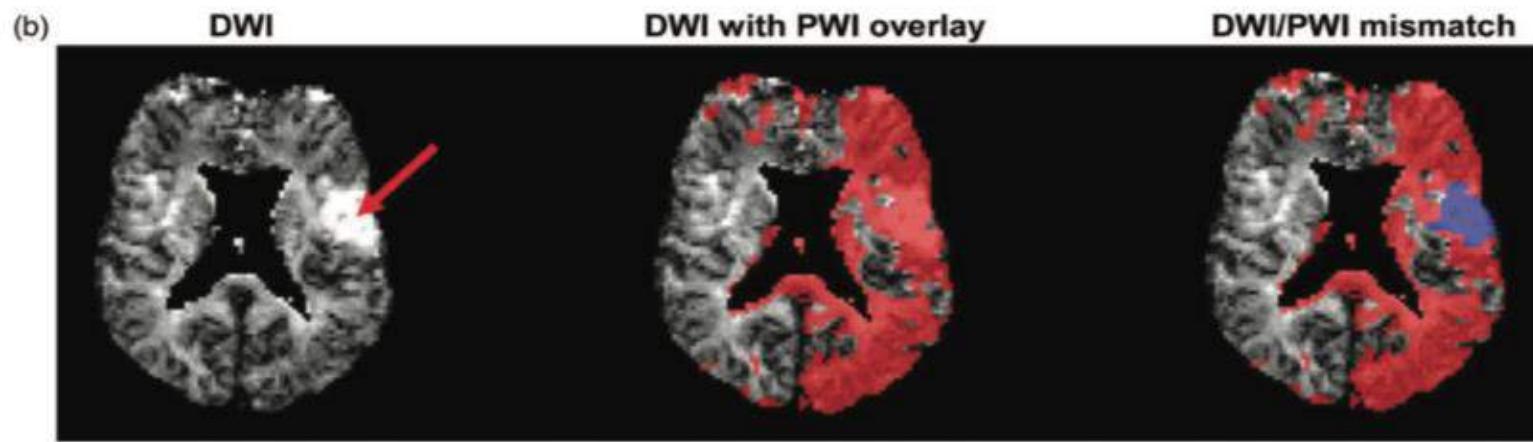
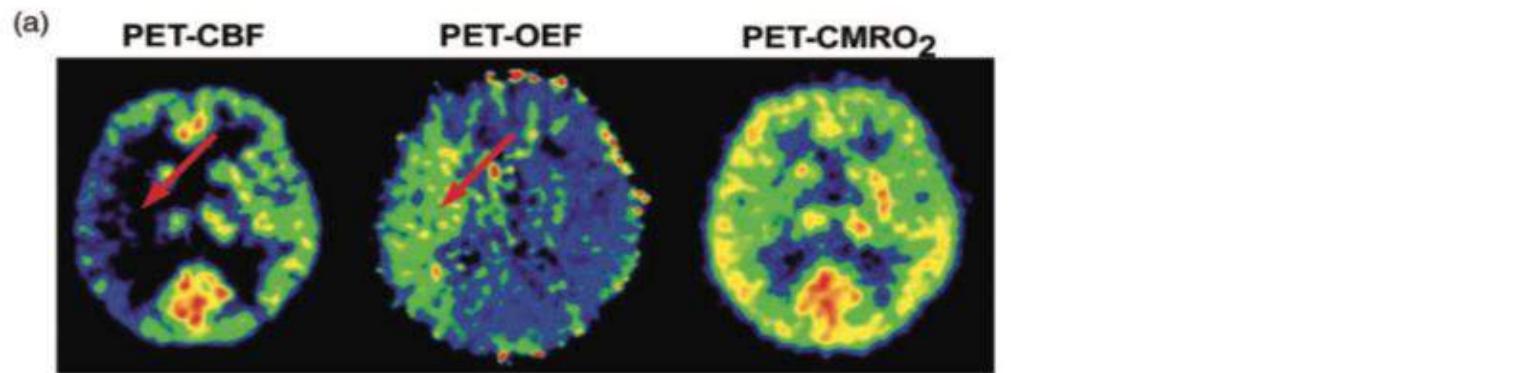


C

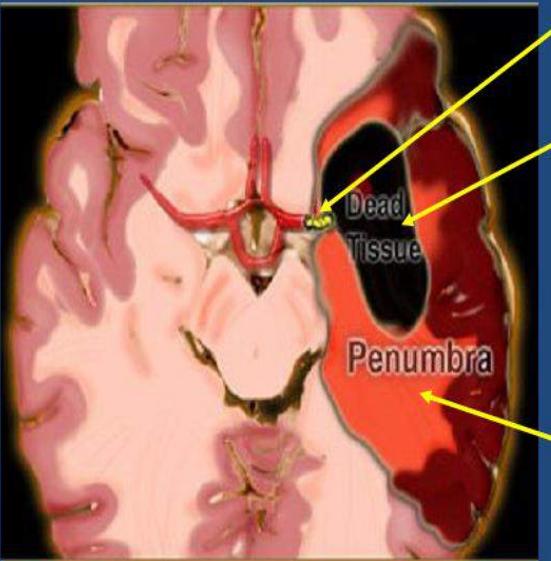




| Techniques | Ischemic core | Ischemic penumbra | Advantages | Disadvantages |
|--|--|---|---|--|
| PET | Very low CBF ^a and CMRO ₂ and variable OEF | CBF <20 ml/100 g/min, increased OEF, but relatively preserved CMRO ₂ | Accuracy thanks to quantitative measures of both perfusion and metabolism | Technically challenging Expensive Radiation Limited availability |
| SPECT | >70% reduction in tracer signal compared to the contralateral side | 40–70% reduction of tracer signal compared to contralateral side | Lower cost Good availability | Use of radioactive agents Difficult data analysis Coarse spatial resolution Inaccurate in case of partial reperfusion |
| MRI: “Perfusion–diffusion mismatch” | DWI lesion = hyperintensity | PWI lesion (Tmax > 6 s or delay time > 3 s) – DWI lesion <i>(MTT less precise than delay measures)</i> | Most accurate way to map the penumbra and core in the clinical setting | Limited access to MRI Contraindications (e.g. pacemakers, claustrophobia) |
| MRI: “ASL–DWI mismatch” | DWI lesion | ASL–CBF threshold of 40%—DWI lesion | Rapid Non-invasive Quantitative measures | Poor spatial resolution Loss of signal due to low perfusion Artifacts due to slow collateral flow |
| CTP | Low CBF (<30%) | Tmax > 6 s or delay time > 3 s <i>(MTT less precise than delay measures)</i> | Low cost Good availability | Less reliable than MRI Radiation exposure Artifacts in case of low cardiac ejection fraction |



Infarct Core and Penumbra

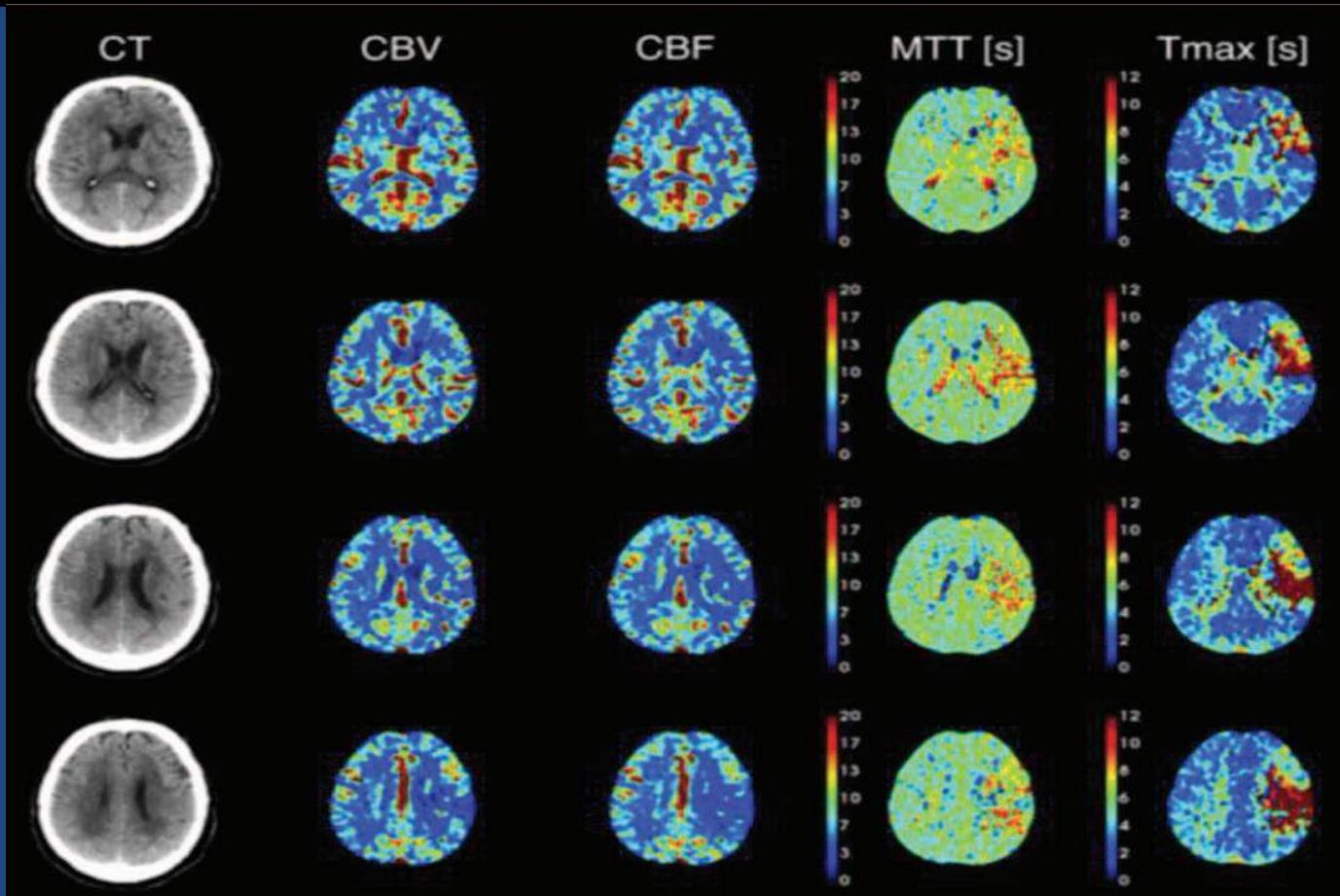


Occluded MCA

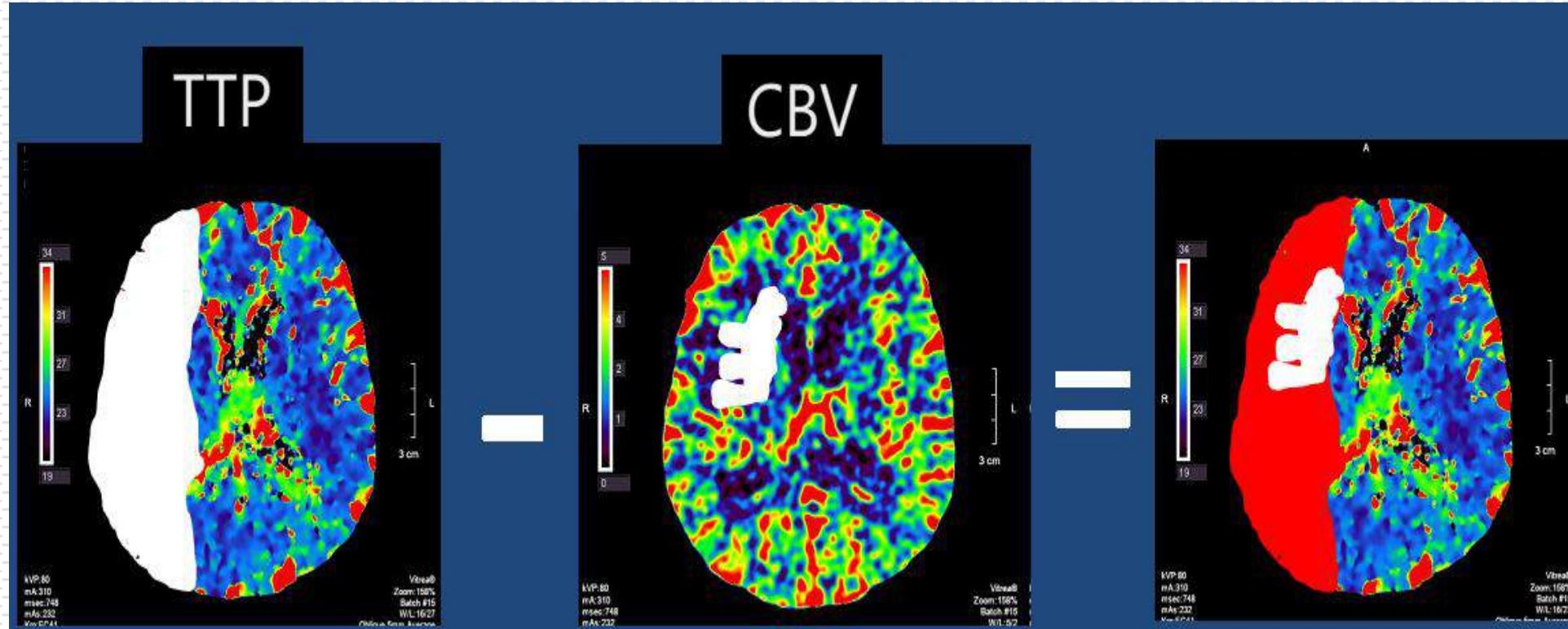
Infarct Core – irreversible damage

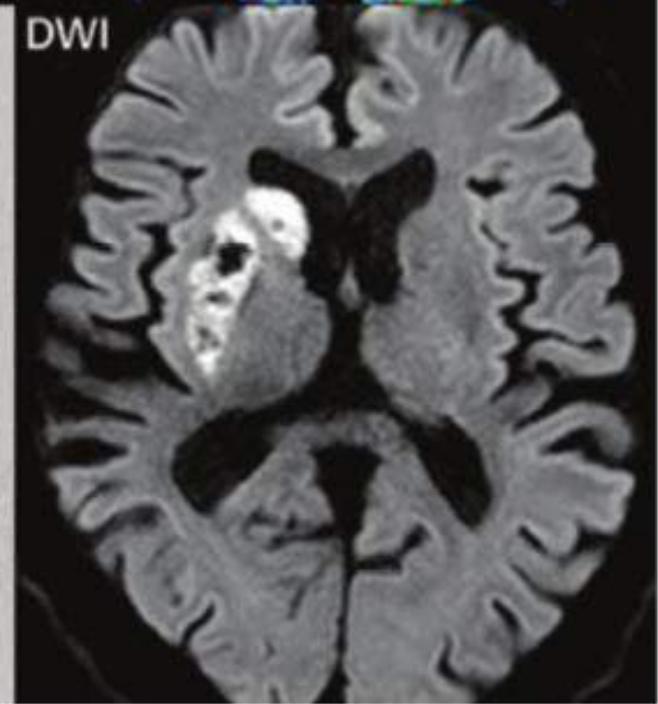
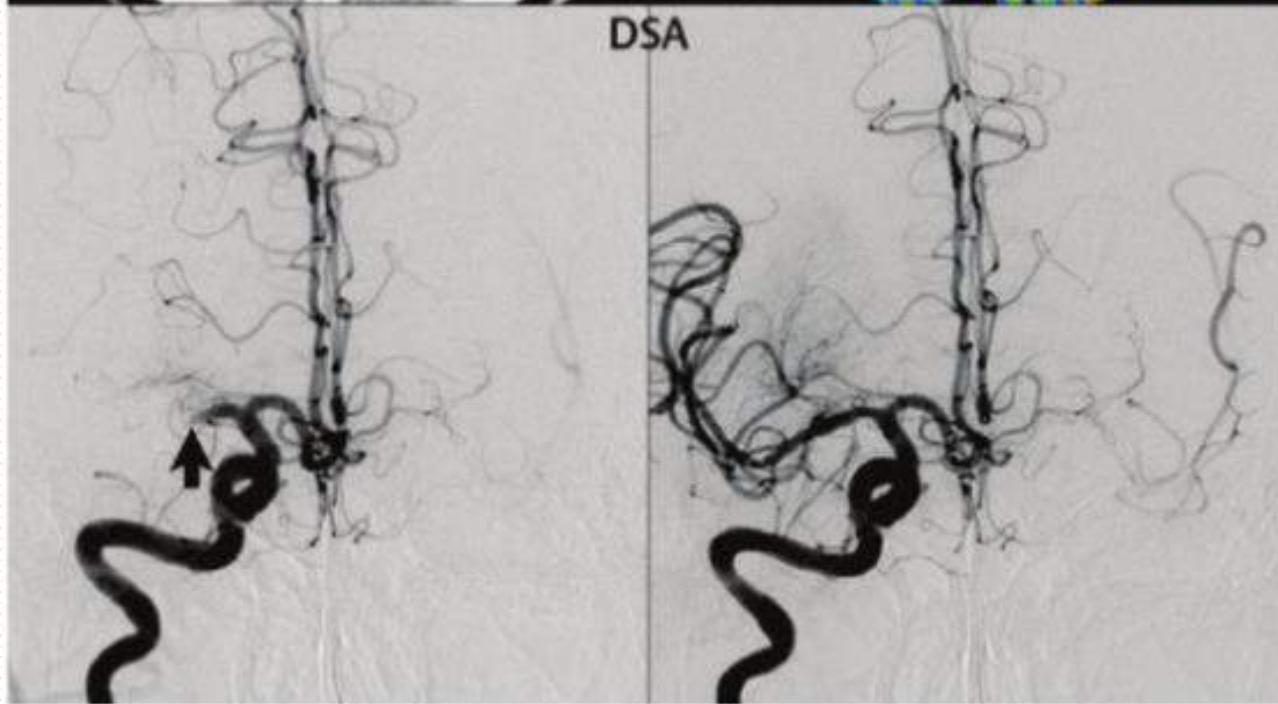
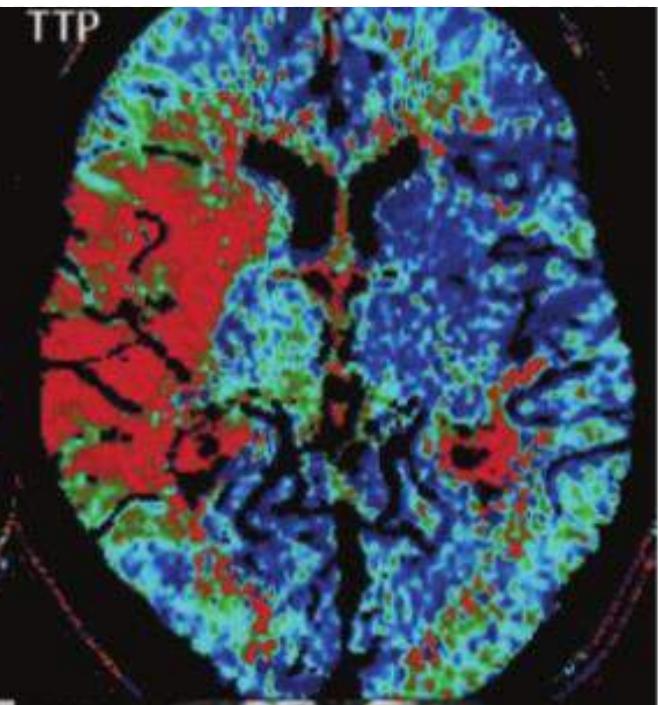
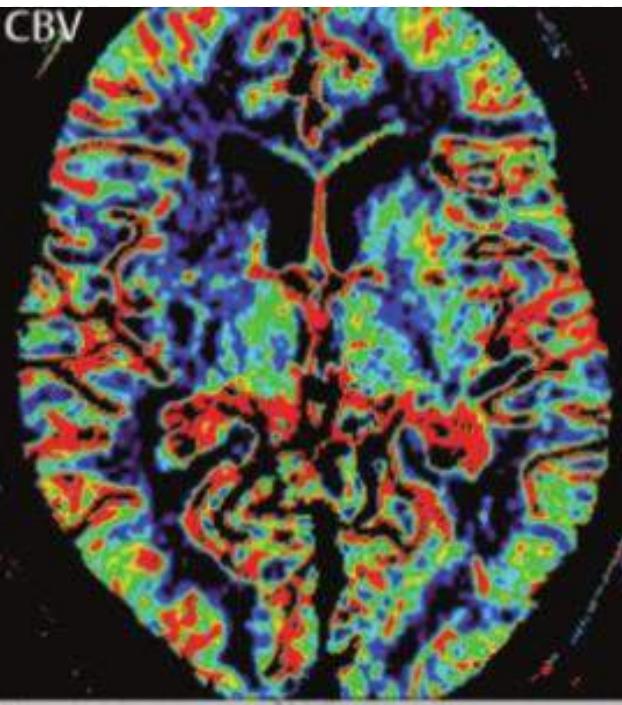
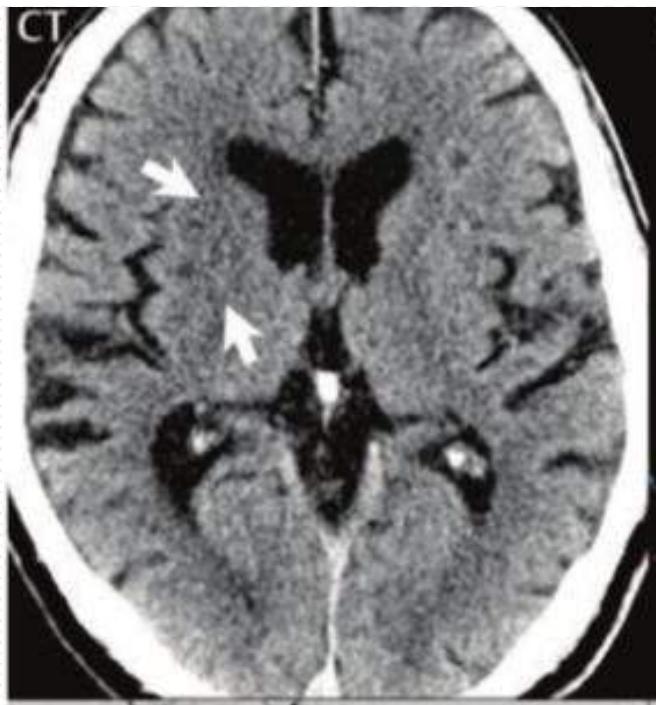
Penumbra – tissue at risk

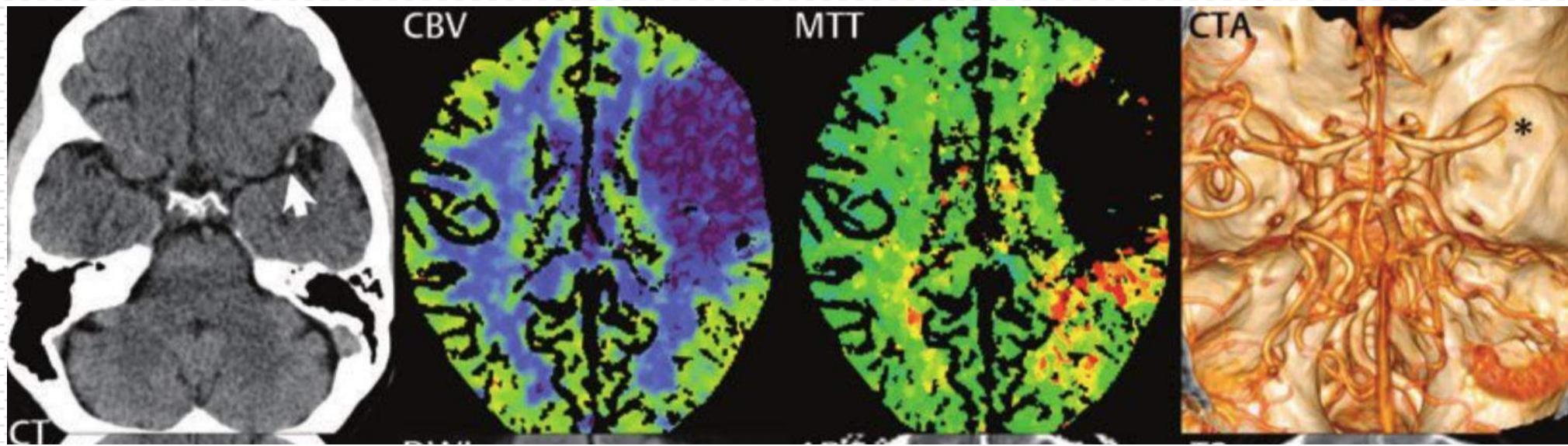
Without treatment the infarction will expand to include penumbra



Perfusion Imaging







Fast Versus Slow Progressors of Infarct Growth in Large Vessel Occlusion Stroke

Clinical and Research Implications

Marcelo Rocha, MD, PhD; Tudor G. Jovin, MD

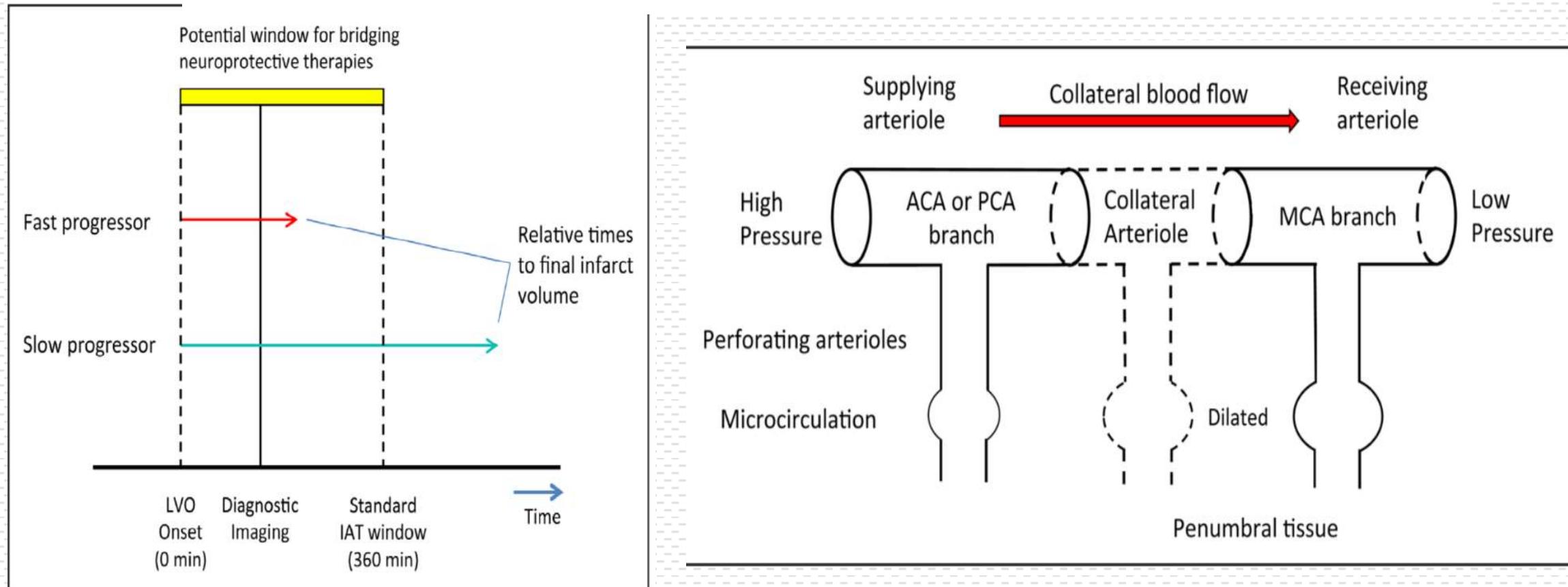
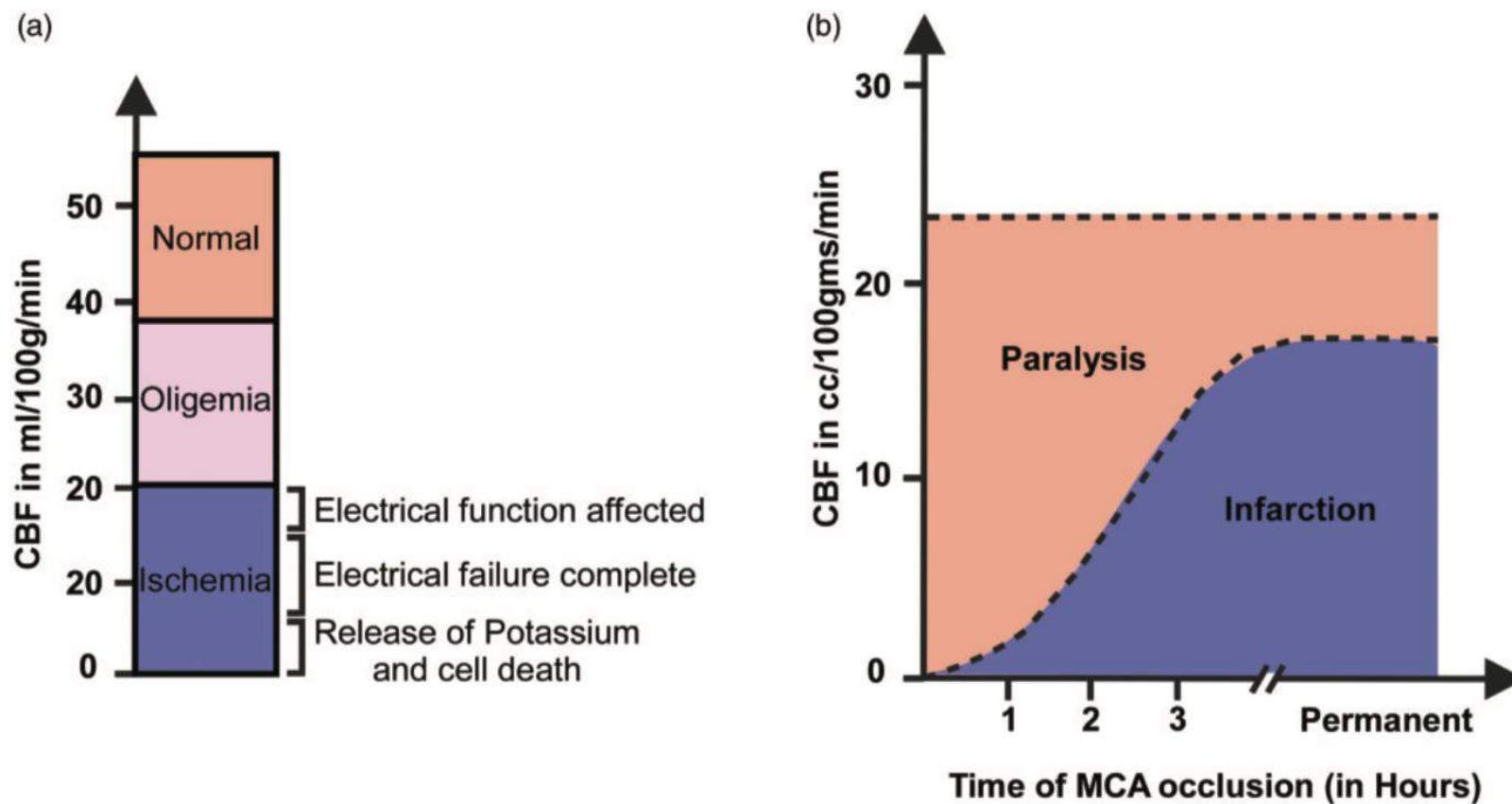


Figure 1. Representation of the ischaemic thresholds from two studies: (a) Figure modified from Astrup et al. (1977), represents ischaemic thresholds for electrical failure and K⁺ release. (b) Cartoon modified from Jones et al. (1981), illustrating the CBF x Time interaction, where paralysis represents the ischaemic penumbra and infarction representing the core.
Source: reproduced with permission from Astrup et al., 1977⁴ and Jones et al., 1981.⁷

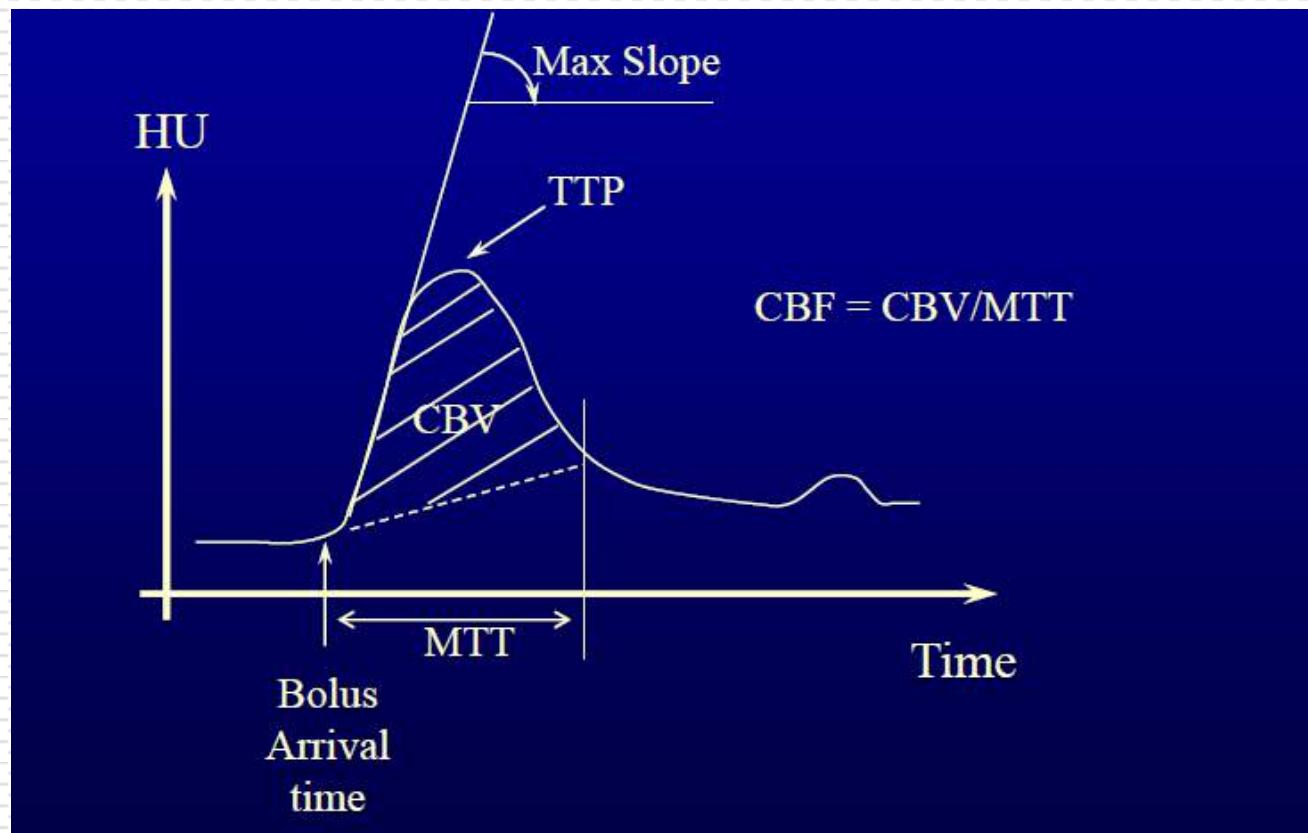


Penumbra Reversible Perfusion Deficit

OtoregULATOR mekanizma intakt

Vasodilatasyon mevcut

Serebrovasküler reserv kapasite düşük (CVR)



MTT
 (Deconvolution)
 \downarrow
 \downarrow
CBV

$$\text{CBF} = \frac{\text{CBV}}{\text{MTT}}$$

MTT mean transit time (sn): arteriyel input ile venöz output arasındaki zaman

TTP time to peak (sn): kontrastın maksimum değerine ulaşincaya kadar geçen zaman

CBV cerebral blood volume (ml/100 g): birim miktardaki beyin parankimindeki kan volümü

CBF cerebral blood flow (ml/100 g/min): birim miktardaki beyin parankiminden dakikada geçen kan volümü

Beyin perfusion

Normal

Oligemi

Penumbra

İnfarkt

Cerebral blood flow

>50–60 ml/100 g/min

30–60 ml/100 g/min

20–30 ml/100 g/min

< 10 ml/100 g/min

Gri Cevher CBV ~ 4 mL/100 g/min,
Beyaz Cevher CBV ~ 2 mL/100 g/min

Gri Cevher CBF ~ 40–60 mL/100 g/min,
Beyaz Cevher CBF ~ 20–30 mL/100 g/min

CBF = CBV/MTT

Normal perfüzyon parametreleri

Gri cevher

MTT: 4 s

CBF: 60 ml/100 g/min

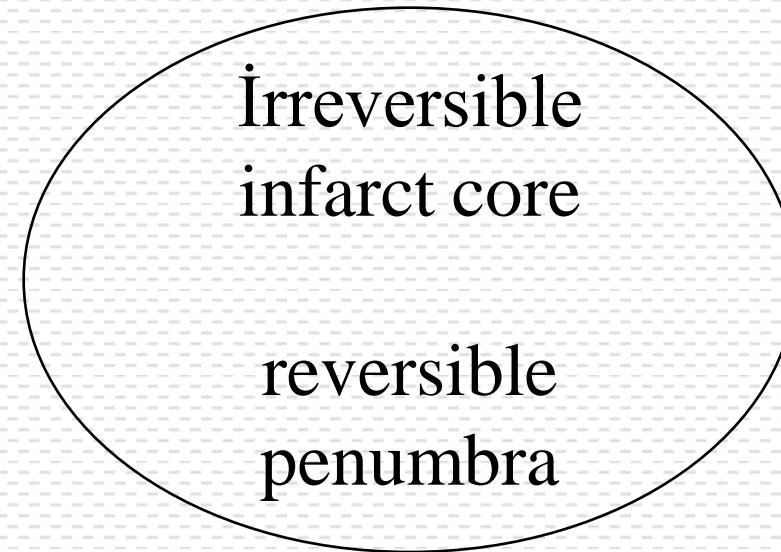
CBV: 4 ml/100 g

Beyaz cevher

MTT: 4.8 s

CBF: 25 ml/100 g/min

CBV: 2 ml/100 g



INFARKT

$\text{CBF} < 25 \text{ mL} \times 100 \text{ g}^{-1} \times \text{min}^{-1}$.

$\text{CBV} < 2 \text{ mL} \times 100 \text{ g}^{-1}$

PENUMBRA

Artmış MTT (>6.4 sn)

>60% CBF

Normal yada artmış CBV (80%–100% veya daha yüksek) (2-2.2 ml/100 mg)

Artmış MTT (>6.4 sn)

>30% CBF

>60% CBV,

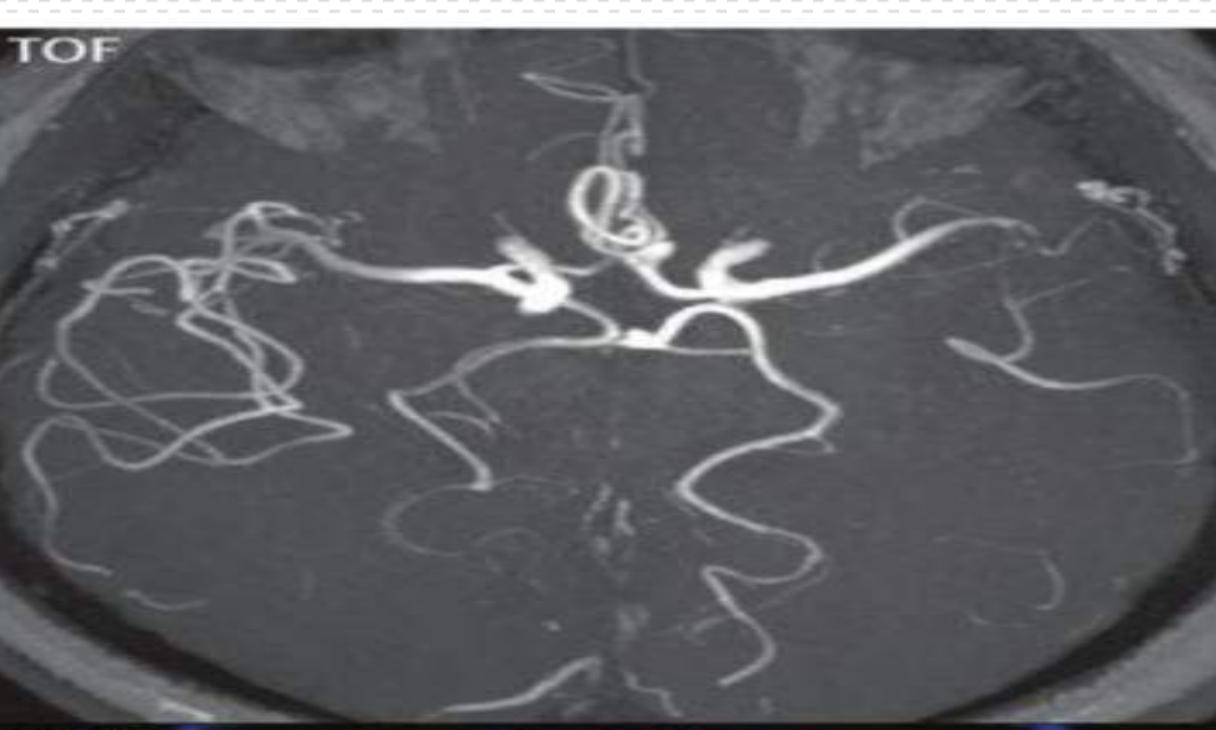
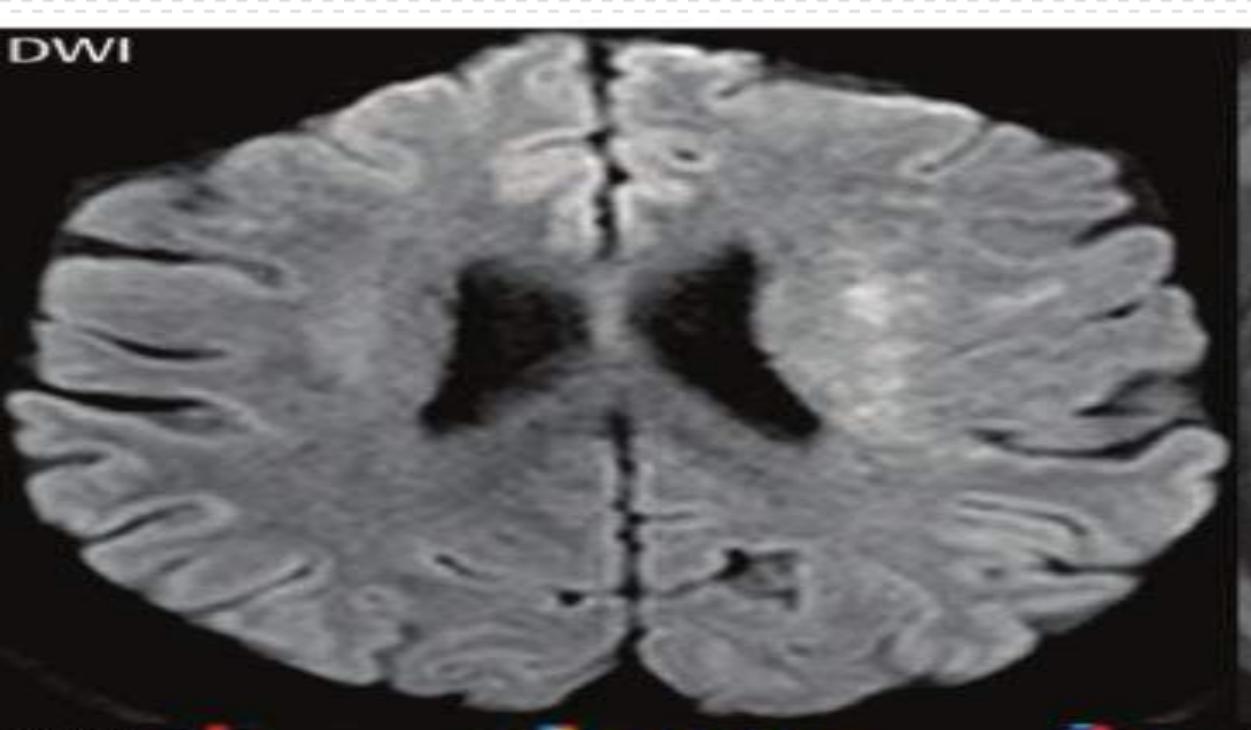
İNFARKT

<30% CBF

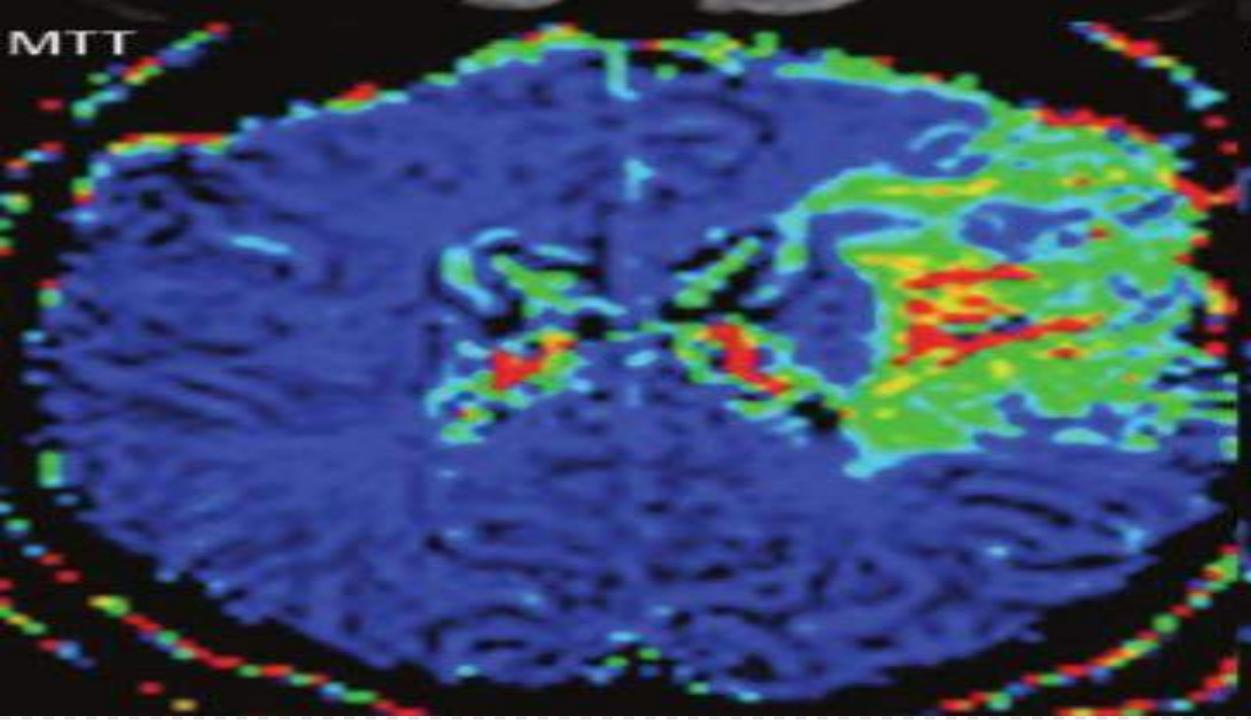
<40% CBV

artmış MTT (%145 & 6.4 sn)

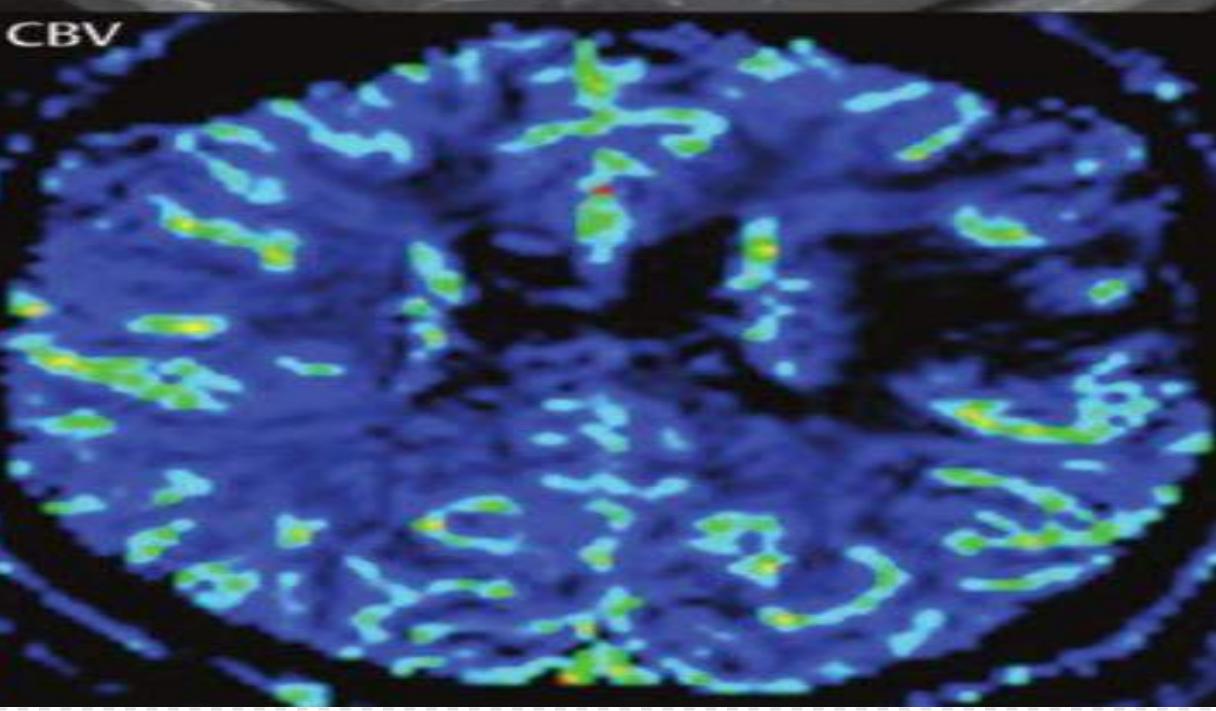
DWI

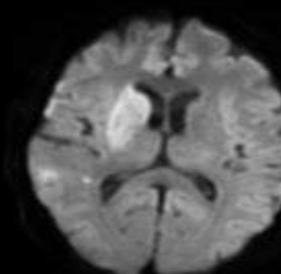
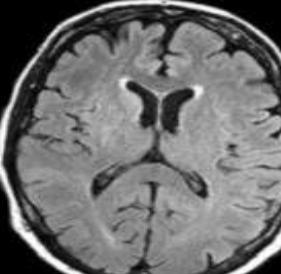
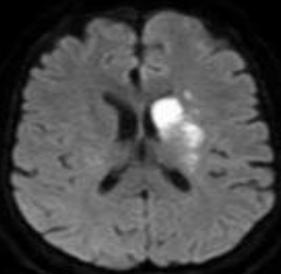
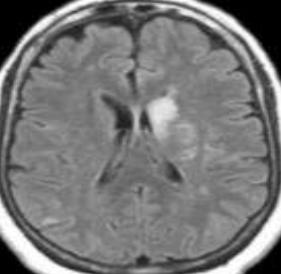
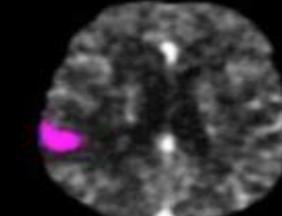
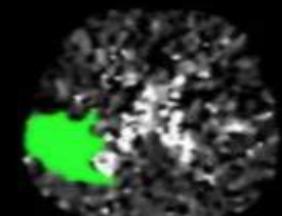
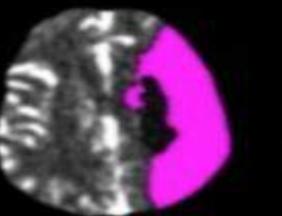
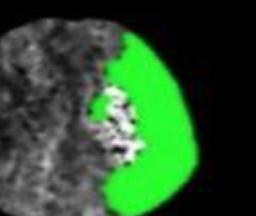
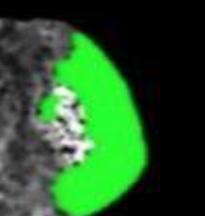
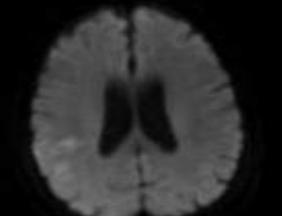
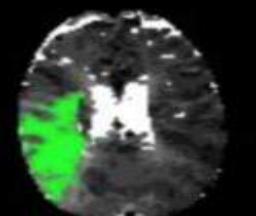
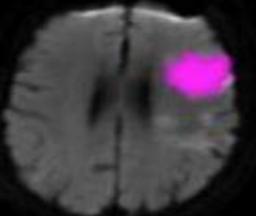
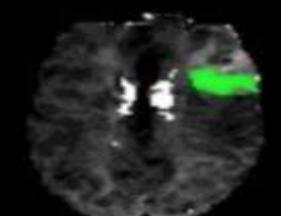


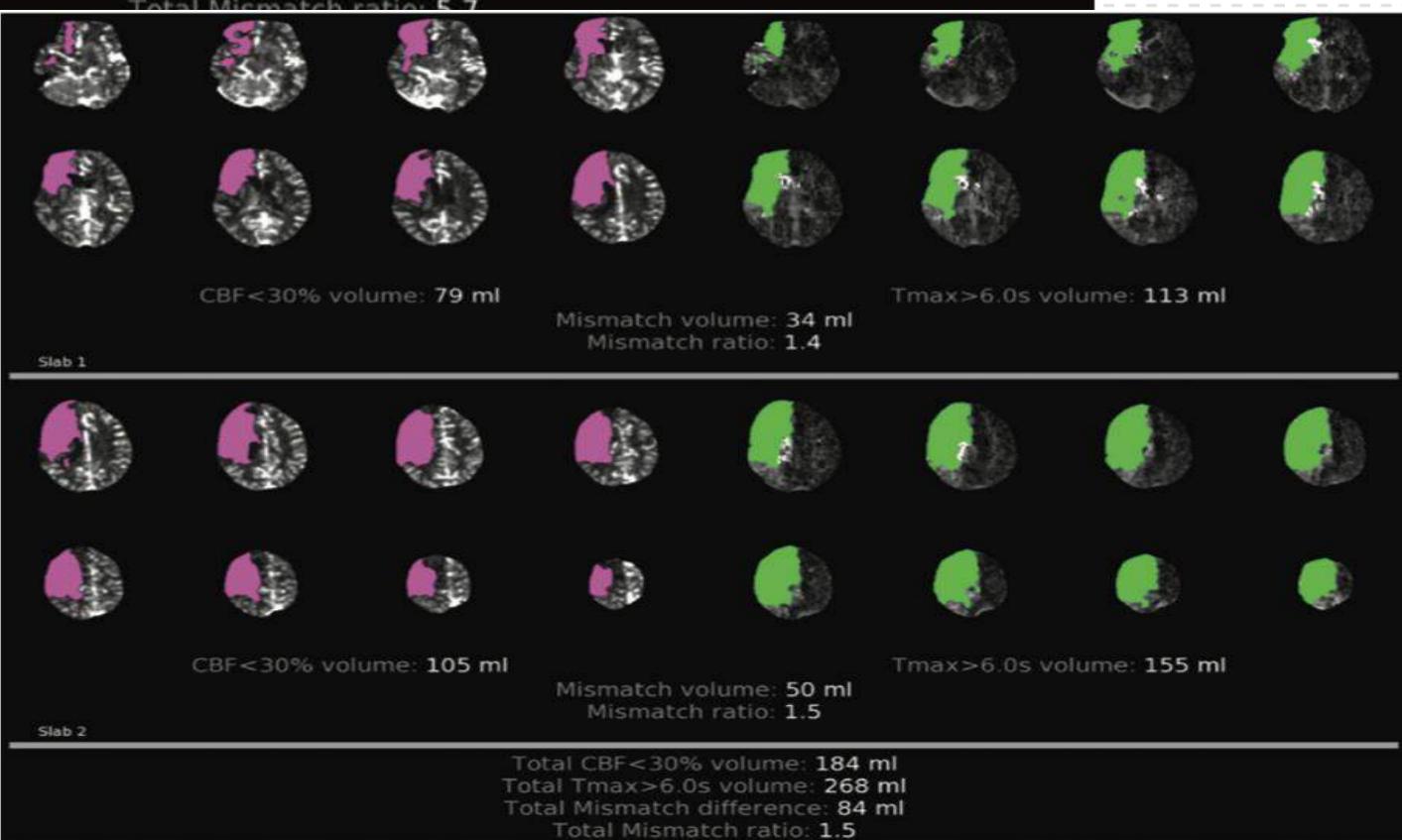
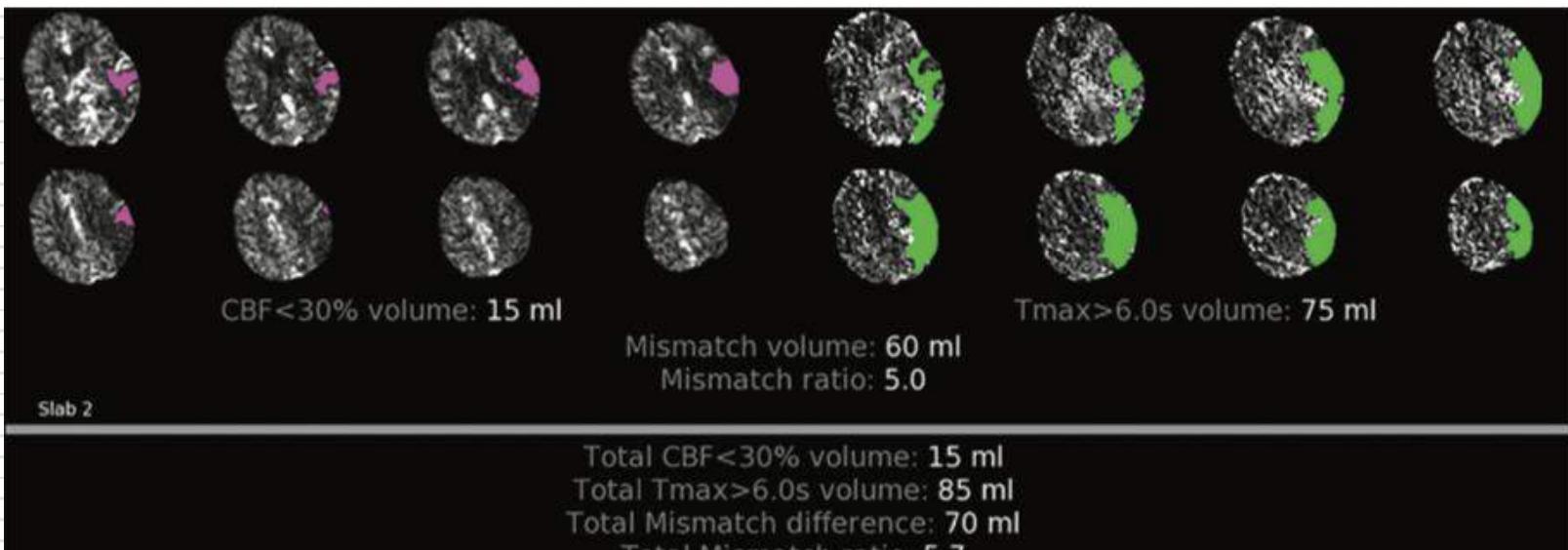
MTT



CBV



| | Clinical Criteria | Advanced Imaging Criteria | Candidate by Imaging | | Not a Candidate by Imaging | |
|----------------|--|--|--|--|---|---|
| WAKE-UP | <ul style="list-style-type: none"> • Age 18-80 • NIHSS < 25 • LKW > 4.5 h | <ul style="list-style-type: none"> • DWI/FLAIR mismatch • DWI lesion < 1/3 MCA territory. |  |  |  |  |
| EXTEND | <ul style="list-style-type: none"> • Age > 18 • NIHSS 4-26 • LKW 4.5-9 h | <ul style="list-style-type: none"> • Penumbra – core mismatch ratio > 1.2 • Penumbra – core absolute difference > 10 ml • Core < 70 ml | <p>CT</p>  <p>CBF</p>  <p>Tmax</p>  <p>CBF</p>  <p>Tmax</p>  | <p>MRI</p>  <p>DWI</p>  <p>DWI</p>  <p>Tmax</p>  | | |



DAWN Trial

- Infarkt alani < 1/3 MCA territory (CT veya MRI)
- MRA veya BTA da MCA M1 veya terminal ICA okluzyonu
- Klinik Imaging Mismatch (CIM) RAPID Software
- DWI veya CTP-rCBF maps:
 - a. 0-20 cc kor infarkt ve NIHSS ≥ 10 (yas ≥ 80)
 - b. 0-30 cc kor infarkt ve NIHSS ≥ 10 (yas < 80)
 - c. 31 cc -< 50 cc kor infarkt ve NIHSS ≥ 20 (yas< 80)

DEFUSE 3 Trial

| Inclusion criteria | DEFUSE-3 ¹⁰ |
|------------------------------------|--|
| Time window | 6–16 hours since time last known well |
| Age | 18–90 years |
| mRS score before qualifying stroke | ≤2; life expectancy ≥6 months |
| NIHSS score | ≥6 |
| Arterial occlusion | ICA and/or M1 * |
| Mismatch definition | Target mismatch based on CT or MR perfusion imaging, as determined by an automated image postprocessing system Infarct core volume <70 mL† AND mismatch volume >15 mL (Tmax>6 s‡) AND mismatch ratio (penumbra/core) >1.8 |

*Carotid occlusions could be cervical or intracranial, with lesions in DEFUSE-3.

†Based on CT perfusion or MRI diffusion.

‡The size of the penumbra was estimated from the volume of delayed arrival of an injected tracer agent (time to

CLEAR Study

- 1604 Hasta
- 5 ülke, 15 merkez
- 6-24 saatte trombektomi yapılan hastalar
- Görüntüleme
 - BT
 - BT perfüzyon
 - MRI
- 1604 hasta değerlendirilmiş 534 hastaya sadece BT ile trombektomi uygulanmış

CLEAR Study

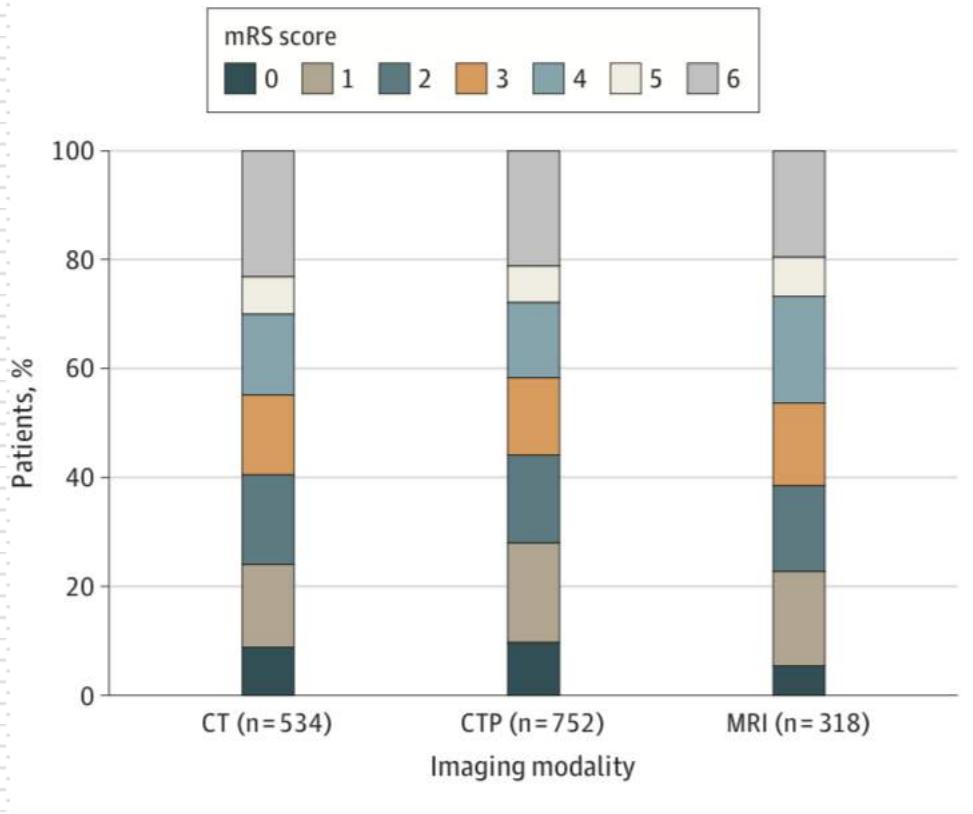


Table 1. Baseline Characteristics, Metrics, and Outcomes of Patients in the 6-24-Hour Window, According to Imaging Modality Selection for Thrombectomy (continued)

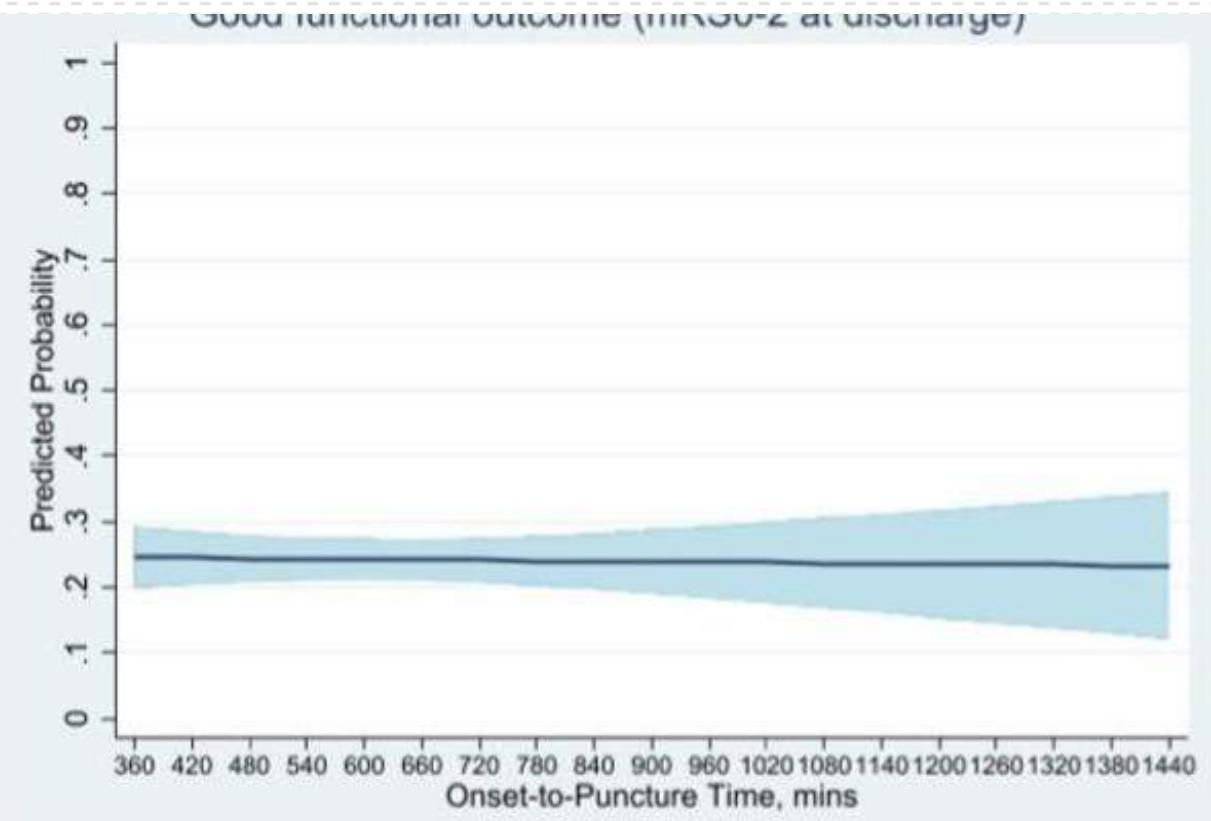
| Characteristic | Patients, No. (%) | | | | <i>P</i> value |
|--|-------------------|----------------------------------|-------------------------------|----------------------------|----------------|
| | Overall | Computed tomography ^a | Computed tomography perfusion | Magnetic resonance imaging | |
| 90-d mRS score | | | | | .21 |
| 0-2 | 676 (42.1) | 220 (41.2) | 333 (44.3) | 123 (38.7) | |
| 3-6 | 928 (57.9) | 314 (58.8) | 419 (55.7) | 195 (61.3) | |
| Symptomatic intracranial hemorrhage ^b | | | | | .11 |
| No | 1478 (93.7) | 476 (91.9) | 700 (94.2) | 302 (95.3) | |
| Yes | 100 (6.3) | 42 (8.1) | 43 (5.8) | 15 (4.7) | |
| Mortality, 90 d | | | | | .38 |
| No | 1258 (78.4) | 409 (76.6) | 593 (78.9) | 256 (80.5) | |
| Yes | 346 (21.6) | 125 (23.4) | 159 (21.1) | 62 (19.5) | |

Association between Time to Treatment and Clinical Outcomes in Endovascular Thrombectomy Beyond 6 hours Without Advanced Imaging Selection

- 3278 hasta, 2610 (79.6%) ilk 6 saat ve 668(20.4%) hasta 6-24 saat
- Sadece BT ve BT angio ile seçilen hastalar
- 5 yıllık sure İngiliz Ulusal Registry

| Feature | < 6 hours n (%) median (IQR) or mean±SD | 6 – 24 hours n (%) median (IQR) or mean±SD | P value |
|------------------------------------|--|--|---------|
| Socio-demographics | | | |
| Sample size | 2610 | 668 | <0.001 |
| Sex (male) | 1450 (55.3) | 366 (54.8) | |
| <60 years | 646 (24.8) | 220 (32.9) | |
| 60-69 | 534 (20.5) | 128 (19.2) | |
| 70-79 | 785 (30.1) | 177 (26.5) | |
| 80-89 | 573 (21.9) | 130 (19.5) | |
| >90 years | 72 (2.8) | 13 (1.9) | |
| Baseline characteristics | | | |
| NIHSS on admission | 18(13-22) | 16(9-20) | <0.001 |
| Rankin before Stroke | 0(0-1) | 0(0-1) | 0.06 |
| IV Thrombolysis | 1835 (70.3) | 226 (33.8) | <0.001 |
| Witnessed Stroke Onset | 1742 (66.7) | 454 (67.9) | 0.54 |
| General Anesthesia | 1345 (51.5) | 411 (61.5) | <0.001 |
| ThromboAspiration | 1861 (71.3) | 480 (71.2) | 0.77 |
| StentRetriever | 1405 (53.8) | 412 (61.9) | <0.001 |
| ThromboAspiration & StentRetriever | 969 (37.1) | 300 (44.9) | <0.001 |
| Proximal Balloon Flow Arrest | 477 (18.3) | 139 (20.8) | 0.13 |

| measures | Onset To Puncture | | Early vs Late Window | |
|-------------------------------|------------------------------------|-------------------------------------|----------------------|--------------|
| | Early Window (<6 hours) n/N (%) | Late Window (6-24 hours) n/N (%) | aOR (95% CI)** | P val |
| charge (Ordinal) | N=2610 | N=668 | 0.65 (0.55 – 0.77) | 0.000 |
| | 521/2610 (19.9) | 98/668 (14.6) | 0.58 (0.44 – 0.76) | 0.000 |
| | 879/2610 (33.6) | 166/668 (24.8) | 0.56 (0.45 – 0.70) | 0.000 |
| months (Ordinal) ^δ | N=725 | N=207 | 0.66 (0.49 – 0.90) | 0.009 |
| | 439/725 (60.5) | 112/207 (54.1) | 0.67 (0.47 – 0.97) | 0.034 |
| | 2113/2610 (80.9) | 523/668 (78.3) | 0.82 (0.65 – 1.03) | 0.09 |
| | 1284/2610 (49.2) | 324/668 (48.5) | 0.95 (0.79 – 1.14) | 0.58 |
| ualization | 1372/2610 (52.5) | 436/668 (65.2) | 1.84 (1.50 – 2.25) | 0.000 |
| | 1596/2497 (63.9) | 335/632 (53.0) | 0.73 (0.60 – 0.89) | 0.002 |
| | 221/2497 (8.8) | 105/632 (16.6) | 1.70 (1.28 – 2.25) | 0.000 |
| | 281/1781 (15.7) | 74/503 (14.7) | 1.02 (0.76 – 1.37) | 0.86 |
| | 58/1665 (3.4) | 20/431 (4.6) | 1.19 (0.67 – 2.09) | 0.54 |
| Mortality | 338/2610 (12.9) | 98/668 (14.6) | 1.14 (0.87 – 1.49) | 0.31 |



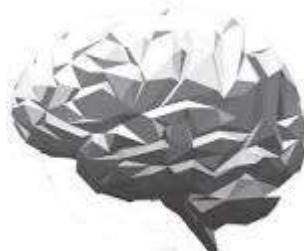
İlginiz için teşekkürler





6 saat Sonrası İnme ve Uyanma İnmeleri: Vaka Seçimi

Dr. Vedat Ali YÜREKLİ
Süleyman Demirel Üniversitesi Tıp
Fakültesi Nöroloji Ana Bilim Dalı



IV. Girişimsel Nöroloji Eğitim Toplantısı
21 - 22 MAYIS 2022
SHIMALL DELUXE OTEL, GAZİANTEP

- Uyanma inmeleri ve 6 saat sonrası başvuran akut inmeler, tüm inmelerin %14-27'sini oluşturur.

G. Thomalla et al. N Engl J Med 379;7 nejm.org August 16, 2018

- DAWN ve DEFUSE-3 çalışmaları **geç başvuran anterior sistem büyük damar oklüzyonlarına** bağlı akut iskemik inmelerde endovasküler trombektominin etkinliğini göstermiştir

Nogueira RG, DAWN Trial Investigators Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. N Engl J Med 2018;378:11-21.

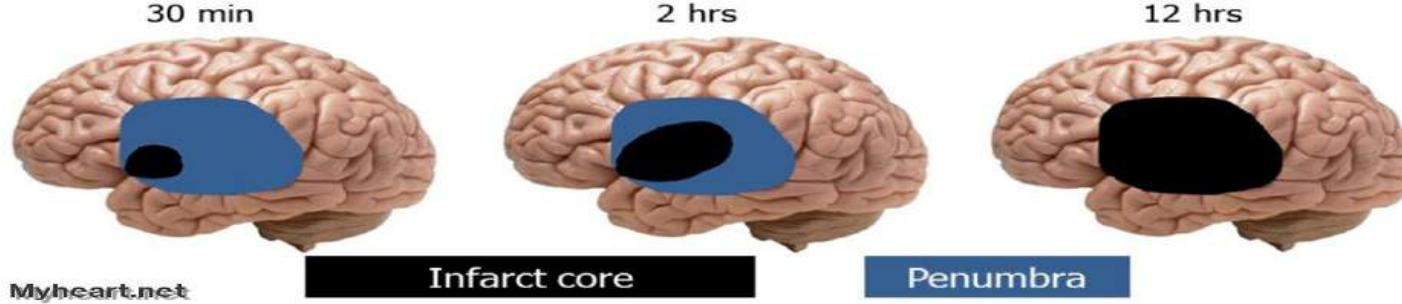
- Son randomize kontrollü çalışmalar, akut iskemik inmede
 - hem IVT
 - hem de EVT için terapötik zaman penceresini genişletti,

Ancak;

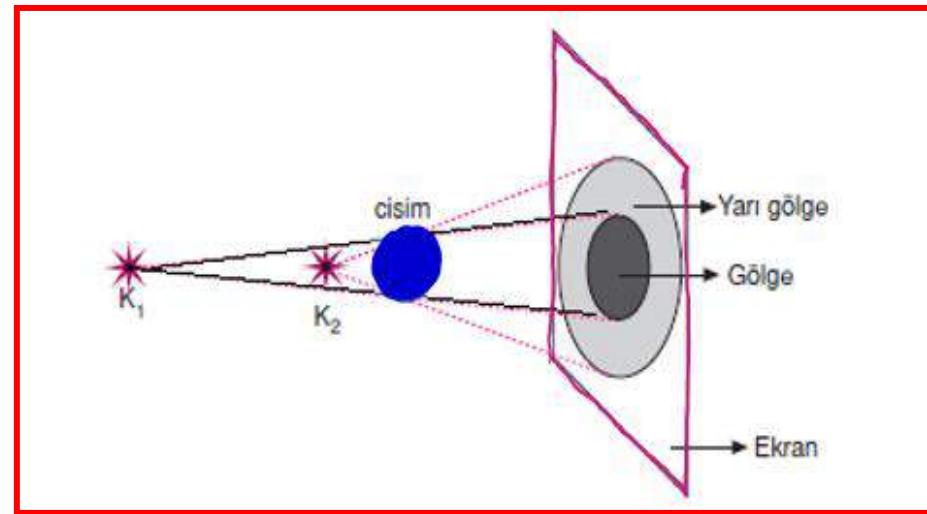
aynı zamanda tedavi algoritması karmaşıklığını da artırdı

- Bu çalışmalarla artık "**zaman temelli**" hasta seçimi, yerini "**doku temelli**" hasta seçimine bırakmıştır.
- Büyük damar tıkanıklıklarına bağlı akut iskemik inmeli hastalarda;
 - rekanalizasyonda 30 dakikalık gecikme,
 - **iyi klinik sonlanım olasılığında %16'lık bir azalmaya** yol açar.

- Geç başvuran inmelerle birlikte uyanma inme hastalarında aslında reperfüzyon tedavilerine uygun olabilecek bir çok hasta grubu bulunabilmektedir.
- DAWN ve DEFUSE-3 çalışmalarında;
- Gerek dahil edilme kriterlerinin karışık olması
- Gerekse hasta seçimi için kullanılan yazılımların her merkezde bulunmaması,
 - hasta seçimi ile ilgili yeni çalışmalar gerektiğini ortaya koymaktadır.



- Nöro-görüntülemede önemli olan kısım, küçük bir iskemik çekirdeğe ve **büyük bir penumbraya sahip** hastayı yakalayabilmektir.



- Büyük olasılıkla bu hastalar hızlı hareket edilirse reperfüzyon tedavilerinden fayda görecektir.

Umbra; tam gölge
Penumbra; yarı gölge

TABLO 1: DAWN ve DEFUSE-3 çalışmalarının ana metodolojik karakteristikleri.

| DAWN | DEFUSE-3 |
|--|--|
| Son normal görülme zamanına göre 6-24 saat | Son normal görülme zamanına göre 6-16 saat |
| Intrakraniyal IKA veya proksimal OSA oklüzyonu | Ekstrakranial veya Intrakranial IKA veya proksimal OSA oklüzyonu |
| Grup A: >80 yaş, NIHSS >10; enfarkt hacmi <21 ml | Enfarkt hacmi <70 ml ve iskemik doku hacminin başlangıç enfarkt hacmine oranı >1.8 |
| Grup B: <80 yaş, NIHSS >10; enfarkt hacmi <31 ml | |
| Grup C: <80 yaş, NIHSS >20; enfarkt hacmi 31-51 ml | |
| BT veya MR temelli görüntüleme | BT veya MR temelli görüntüleme |
| RAPID yazılım (Görüntü analizi için) | RAPID yazılım (Görüntü analizi için) |
| Sadece TREVO cihazı kullanılmıştır | Tüm FDA onaylı Trombektomi cihazlarına izin verilmiştir |
| Enfarkt hacminin hesaplanması diffüzyon ağırlıklı MR görüntüleme veya perfüzyon BT ile alınan görüntülerin otomatize yazılım (RAPID, iSchemaView) yardımı ile yapılmıştır. | |

Gürkaş E. Uyanma inmeleri ve 6 saat sonrası başvuran akut inmelerde endovasküler tedavi.
Müngen B, Özdemir AÖ, editörler. Akut İskemik İnmede Endovasküler Revaskülarizasyon. 1. Baskı.
Ankara: Türkiye Klinikleri; 2019. p.7-10.

| 3.7. Mechanical Thrombectomy (Continued) | COR | LOE | New, Revised, or Unchanged |
|---|-----|-----|----------------------------|
| 7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended. | I | A | New recommendation. |
| 8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable. | IIa | B-R | New recommendation. |

- Bu çalışmalar sonucunda, AHA/ASA 2018 kılavuzu 6-16 saat dilimi içerisinde yer alan ve DAWN ve/veya DEFUSE 3 çalışma kriterlerini sağlayan hastalarda trombektomiyi Klas 1A
- 16-24 saat dilimi içerisinde yer alan ve DAWN çalışma kriterlerini sağlayan hastalar için de Klas 2A olarak önerileri arasına almıştır

| 3.7. Mechanical Thrombectomy (Continued) | COR | LOE | New, Revised, or Unchanged |
|---|-----|-----|----------------------------|
| 7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended. | I | A | New recommendation. |
| 8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable. | IIa | B-R | New recommendation. |

The DAWN trial used clinical imaging mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33%; 95% CI, 21–44; posterior probability of superiority >0.999).¹⁰⁸ In DAWN, there were few strokes with witnessed onset (12%). The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67; 95% CI, 1.60–4.48; $P<0.0001$).¹⁰⁹ Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. **DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset.** Therefore, only the eligibility criteria from one or the other of these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN or DEFUSE-3 eligibility should be strictly adhered to in clinical practice.

MEKANİK TROMBEKTOMİ-DAWN ÇALIŞMASI

90 gün sonunda fonksiyonel bağımsızlık;
trombektomi grubunda % 49,
kontrol grubunda %13 saptanmış(p<0.001)

Erken klinik yanıt;

Trombektomi grubunda %48,
kontrol grubunda %19(p<0.001),

DWI-ASPECT

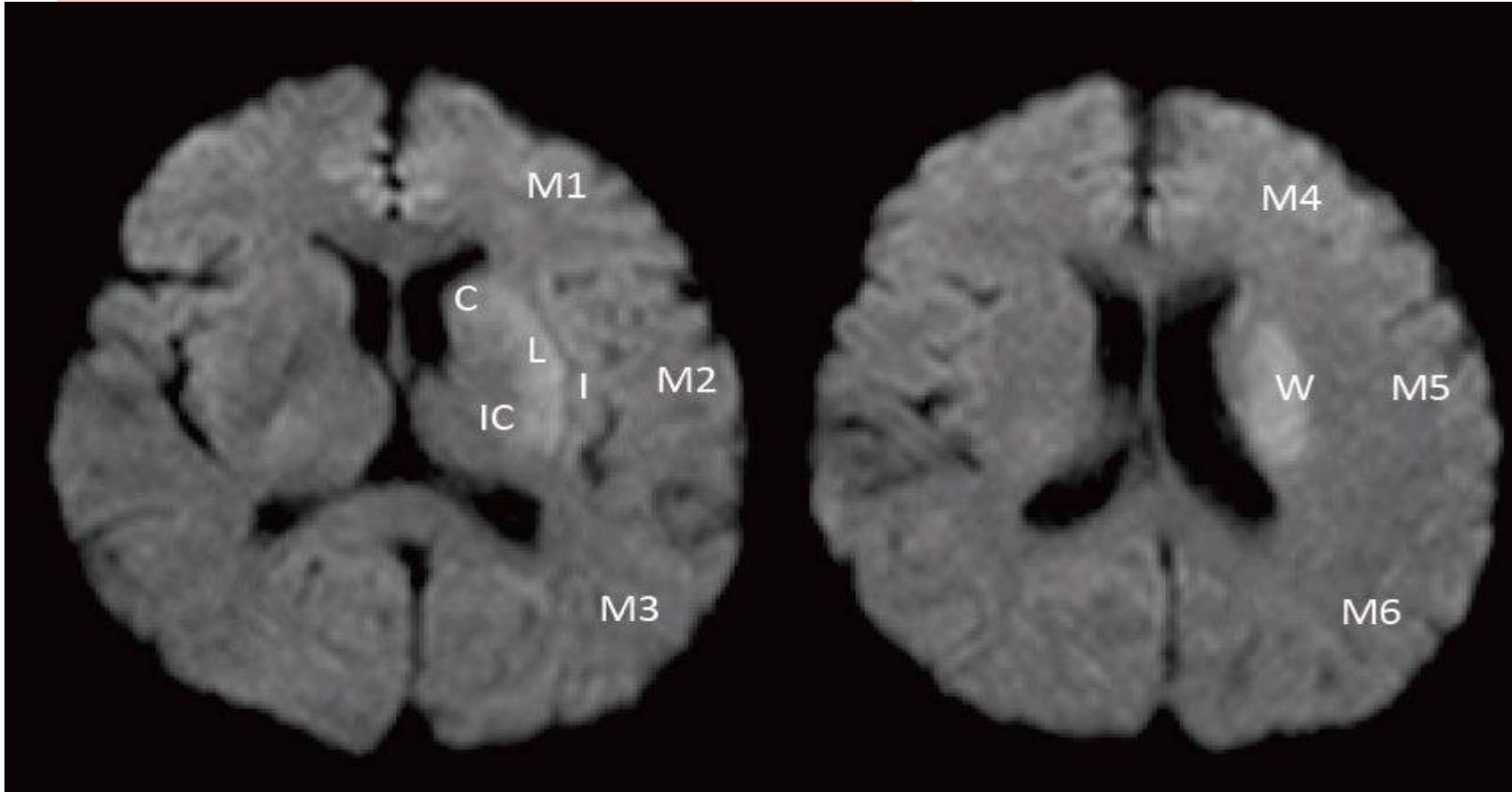


Figure 1 : DWI ASPECTS is evaluated in 11 regions: 10 ASPECTS (Alberta stroke programme early CT score) sites and a white matter (W) lesion. If abnormal signals due to infarction are detected, the count is 0; if they are not detected, the count is 1. If no infarctions are ultimately observed, the total score is 11; if infarction is observed in all target regions, the total score is 0. C: caudate.; L: lentiform.; IC: internal capsule.; I: insular ribbon.; M1: anterior middle cerebral artery (MCA) cortex.; M2: MCA cortex lateral to the insular ribbon.; M3: posterior MCA cortex.; M4, M5, and M6 are anterior, lateral, and posterior MCA territories, respectively, immediately superior to M1, M2, and M3, respectively, rostral to basal ganglia.; W: white matter (corona radiate).

DWI-ASPECT ile iskemik kor volumü arasında korelasyon vardır

| DWI ASPECT | CORE VOLUME |
|------------|-------------|
| ≥7 | ≤25 |
| ≥5 | ≤70 |
| ≥3 | ≤100 |

SPECIAL TOPIC

doi: 10.2176/nmc.st.2020-0357

Neurol Med Chir (Tokyo) 61, 163–192, 2021

Online February 11, 2021

Guidelines for Mechanical Thrombectomy in Japan, the Fourth Edition, March 2020: A Guideline from the Japan Stroke Society, the Japan Neurosurgical Society, and the Japanese Society for Neuroendovascular Therapy

Guidelines for Mechanical Thrombectomy in Japan, the Fourth Edition, March 2020: A Guideline from the Japan Stroke Society, the Japan Neurosurgical Society, and the Japanese Society for Neuroendovascular Therapy

Hiroshi YAMAGAMI,¹ Mikito HAYAKAWA,² Manabu INOUE,³ Koji IIHARA,⁴

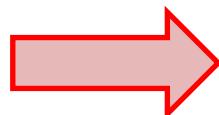
- NIHSS skoru ≥ 10 ise
- iskemik kor hacmi ≤ 25 mL ise (bu, ≥ 7 DWI-ASPECTS'e karşılık gelir)
- ICA veya MCA M1 oklüzyonu olan
- 6-16 saat içindeki hastalara

MT güçlü bir öneri olarak tavsiye edilir.

Vaka Seçiminde;

- DAWN ve DEFUSE çalışmaları之外 bahsedeceğim çalışmalarından ilki:
- WAKE-UP protokolü olarak da bilinen

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset.



Yani başlangıcını bilmediğimiz inme hastalarına MRG kılavuzluğunda trombolitik versek nasıl olur?

The NEW ENGLAND JOURNAL of MEDICINE

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AUGUST 16, 2018

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MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas,

- Çok merkezli bir çalışmada,
- İnme başlangıç zamanı bilinmeyen hastalar
 - intravenöz alteplaz alan
 - placebo
 - Olmak üzere 2 gruba rastgele seçilmiş.
- Mekanik trombektomi planlanan hastalar çalışma dışı bırakılmış.
- Tüm hastalarda, MRG difüzyon ağırlıklı görüntülemede görünen ancak FLAIR sekanslarında herhangi bir parankim hiperintensitesi olmayan hastalar çalışmaya alınmış.

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennericci, A. Kemmling, J. Marstrand, B. Modrau, L. Neub, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators*

RESULTS

The trial was stopped early owing to cessation of funding after the enrollment of 503 of an anticipated 800 patients. Of these patients, 254 were randomly assigned to receive alteplase and 249 to receive placebo. A favorable outcome at 90 days was reported in 131 of 246 patients (53.3%) in the alteplase group and in 102 of 244 patients (41.8%) in the placebo group (adjusted odds ratio, 1.61; 95% confidence interval [CI], 1.09 to 2.36; $P=0.02$). The median score on the modified Rankin scale at 90 days was 1 in the alteplase group and 2 in the placebo group (adjusted common odds ratio, 1.62; 95% CI, 1.17 to 2.23; $P=0.003$). There were 10 deaths (4.1%) in the alteplase group and 3 (1.2%) in the placebo group (odds ratio, 3.38; 95% CI, 0.92 to 12.52; $P=0.07$). The rate of symptomatic intracranial hemorrhage was 2.0% in the alteplase group and 0.4% in the placebo group (odds ratio, 4.95; 95% CI, 0.57 to 42.87; $P=0.15$).

CONCLUSIONS

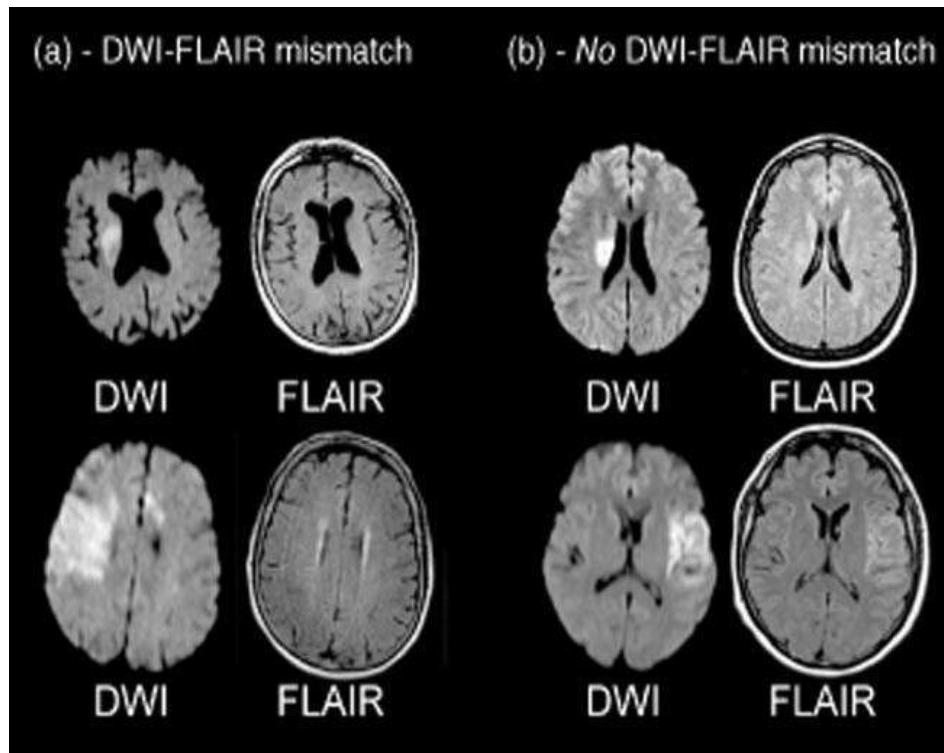
In patients with acute stroke with an unknown time of onset, intravenous alteplase guided by a mismatch between diffusion-weighted imaging and FLAIR in the region of ischemia resulted in a significantly better functional outcome and numerically more intracranial hemorrhages than placebo at 90 days. (Funded by the European Union Seventh Framework Program; WAKE-UP ClinicalTrials.gov number, NCT01525290; and EudraCT number, 2011-005906-32.)

| | Alteplase Group (N = 254) % | Placebo Group (N = 249) | P değeri |
|--------------------------------|--------------------------------|----------------------------|----------|
| İyi klinik sonlanım - 90 günde | 131/246 (53.3) | 102/244 (41.8) | 0.02 |
| Median infarkt hacmi | 3.0 (0.8–17.7) | 3.3 (1.1–16.6) | 0.32¶ |
| Parenchymal hemorrhage type 2 | 10 (4.0) | 1 (0.4) | 0.03 |

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thromalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators*

- Başlangıç zamanı bilinmeyen, iskemi bölgesinde **difüzyon pozitif / FLAIR negatif** hastalarda **intravenöz alteplaz**,
- 90 içinde placebo göre anlamlı ölçüde daha iyi bir fonksiyonel sonuç ve sayısal olarak daha fazla intrakraniyal kanama ile sonuçlanmıştır.



Difüzyon lezyonu olan ama FLAIR lezyonu olmayan alanın geniş olması ["Difüzyon Pozitif FLAIR Negatif" veya kısaca "DPFN" kriteri]

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

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Diff MRG de iskemi gözlenen



FLAIR MRG de iskemik alan olmayan



inmenin yaklaşık olarak önceki 4.5 saat
içinde meydana geldiğini gösterir.

- Ayrıca, hiperintens FLAIR lezyonlarının varlığı,
 - geç evre inmelerin olası bir göstergesi olmasının yanı sıra,
 - 3 saat içinde tedavi edilen hastalarda da **semptomatik intrakraniyal kanama (sICH) riskinin** artmasıyla bağlantılıdır.
- Dolayısıyla ilk **3 saat içinde akut FLAIR lezyonu olanlarda hemoraji riski yüksektir.**

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MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas,

- WAKE-UP çok merkezli çalışmasında IVT zaman penceresi uzamasa da;
 - Uyanma İnmeli veya GBİ'li hastaların 0-4,5 saatlik zaman penceresinde olup olmadıklarına dair bilgi vermesi açısından
 - DWI/FLAIR mismatch yönteminin kullanımı konusunda önemli bir çalışma olmuştur.

Aoki ve ark. Tarafından 2010 yılında

- DWI FLAIR uyumsuzluğunun
 - %78'lik bir duyarlılık ve
 - %83'lük pozitif prediktif değeri
 - ile <4.5 saatte inme başlangıcını öngördüğü gösterilmiştir.
 - Aoki J, Kimura K, Iguchi Y, et al. FLAIR can estimate the onset time in acute ischemic stroke patients. *J Neurol Sci* 2010; 293: 39–44.

- ESO IVT kılavuzları, Uyanma inmelerinde;
- DWI/FLAIR disosiyasyonu olan hastalarda trombolitik tedaviyi önermektedir.
 - kanıt kalitesi>>>yüksek;
 - öneri gücü>>>güçlü

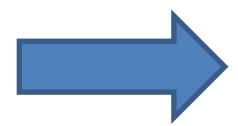
Guideline

**European Stroke Organisation
(ESO) – European Society for
Minimally Invasive Neurological Therapy
(ESMINT) guidelines on mechanical
thrombectomy in acute ischaemic stroke**

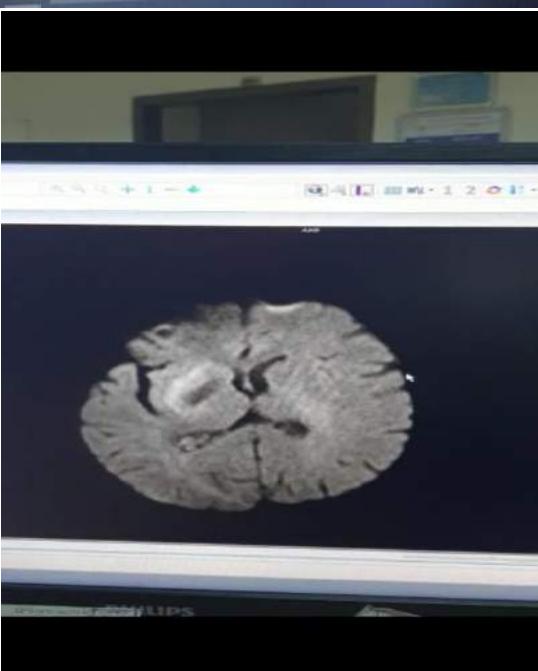
**EUROPEAN
STROKE JOURNAL**

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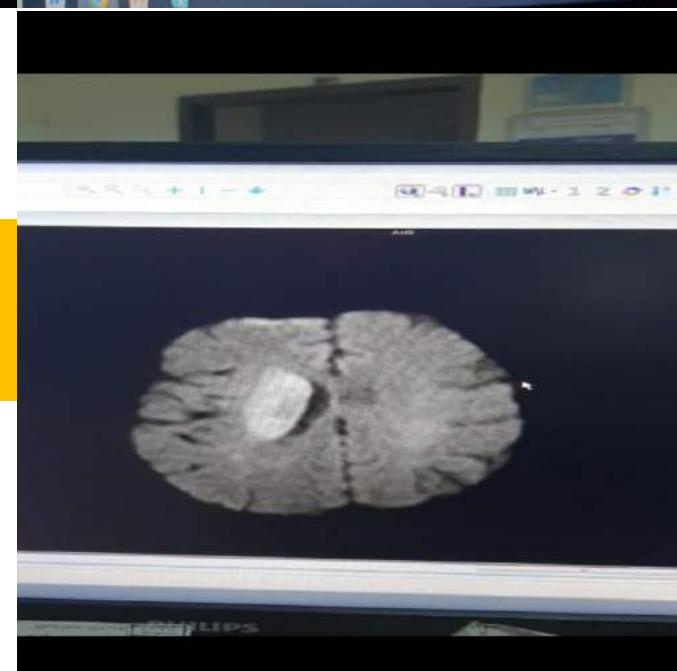
Olgı Örneği

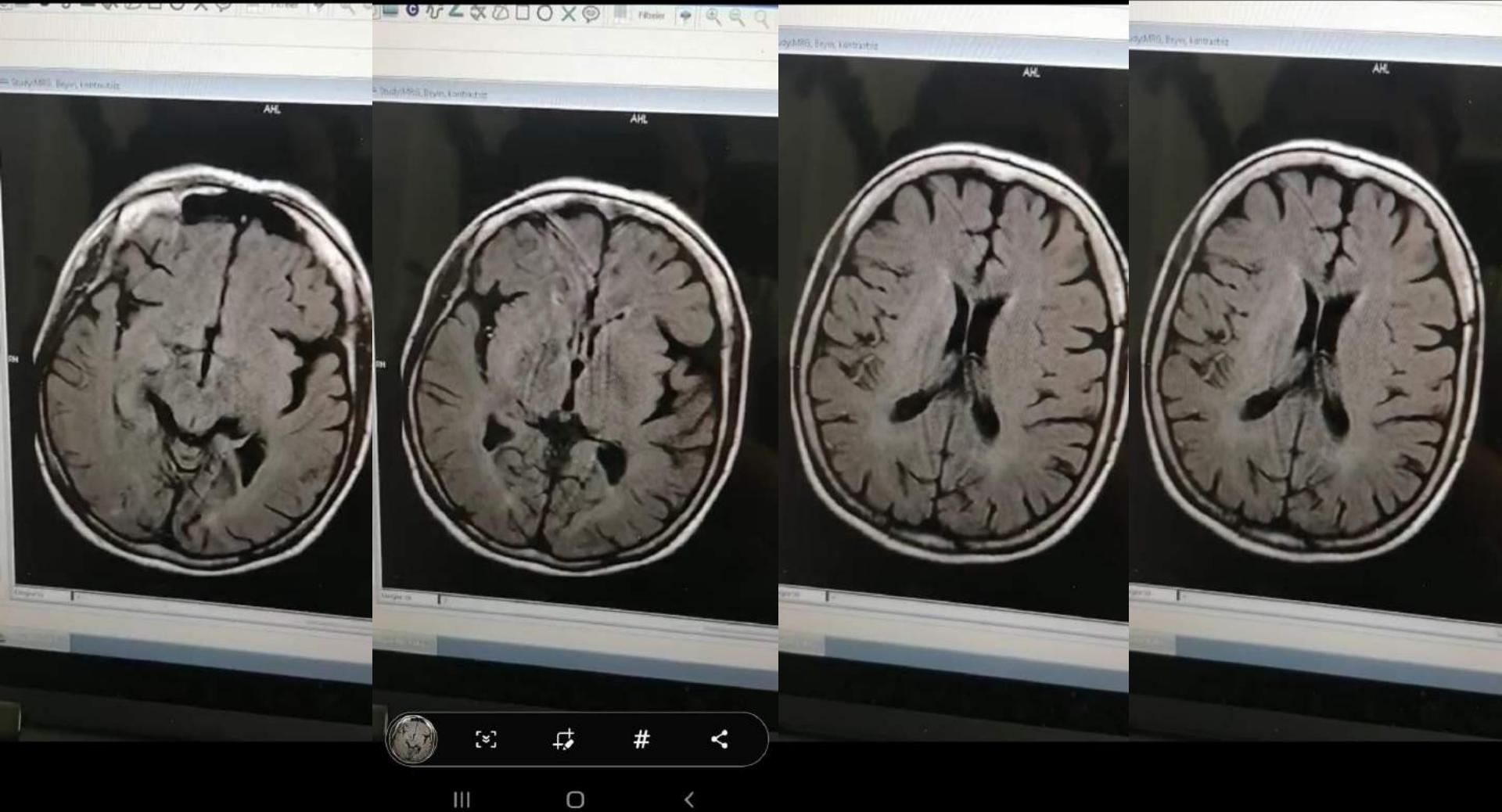


- 66 y K hasta
- Geliş NIHS skoru 10
- Gece 3 gibi yataktan düşmüş
- Biliç letarjik
- Sol hemiparezi üst 2/5 alt 1 /5

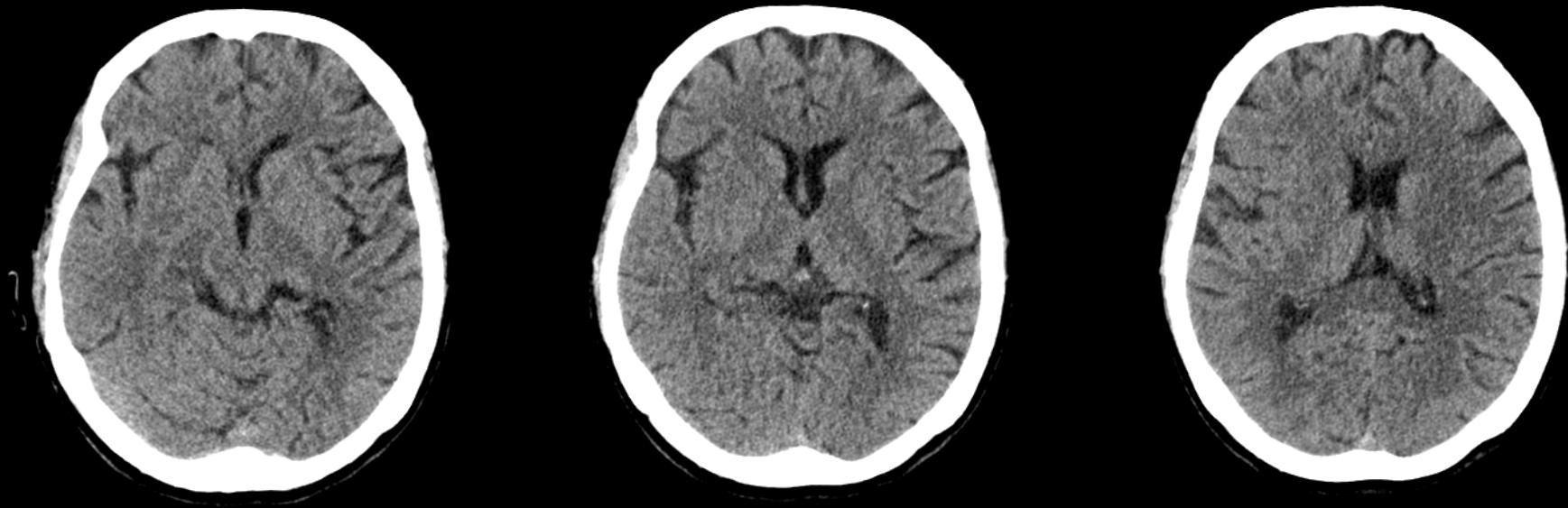


Diffüzyon ve ADC Görüntüleri

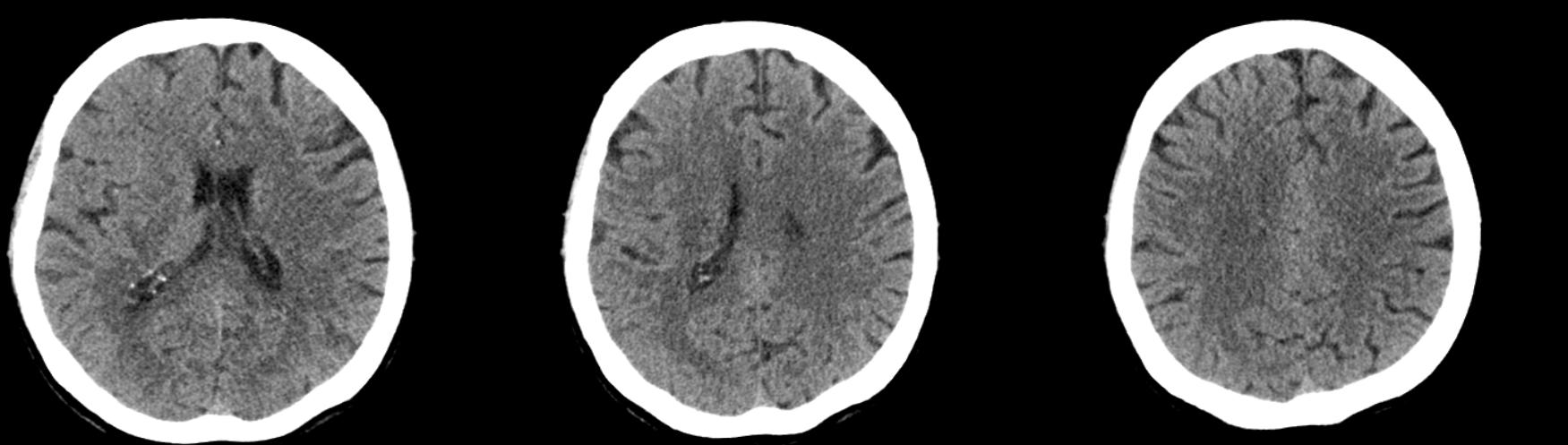




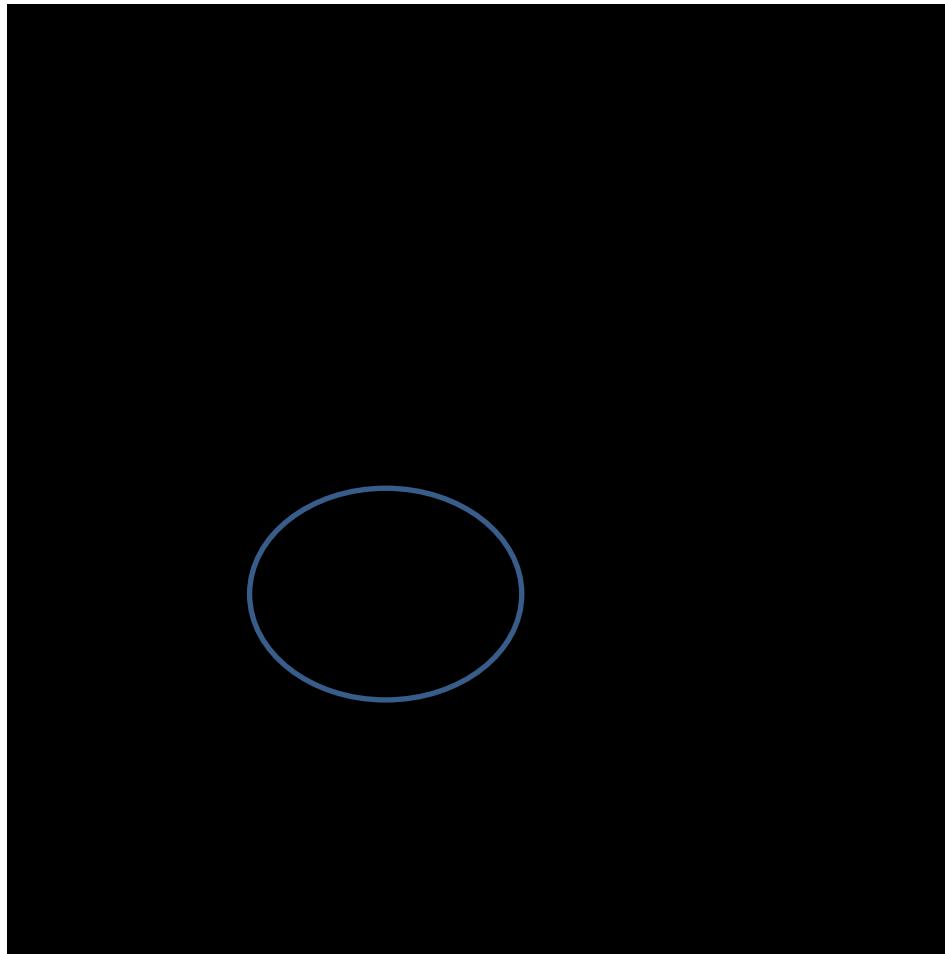
FLAIR görüntüler



Başvuru ASPECT :10

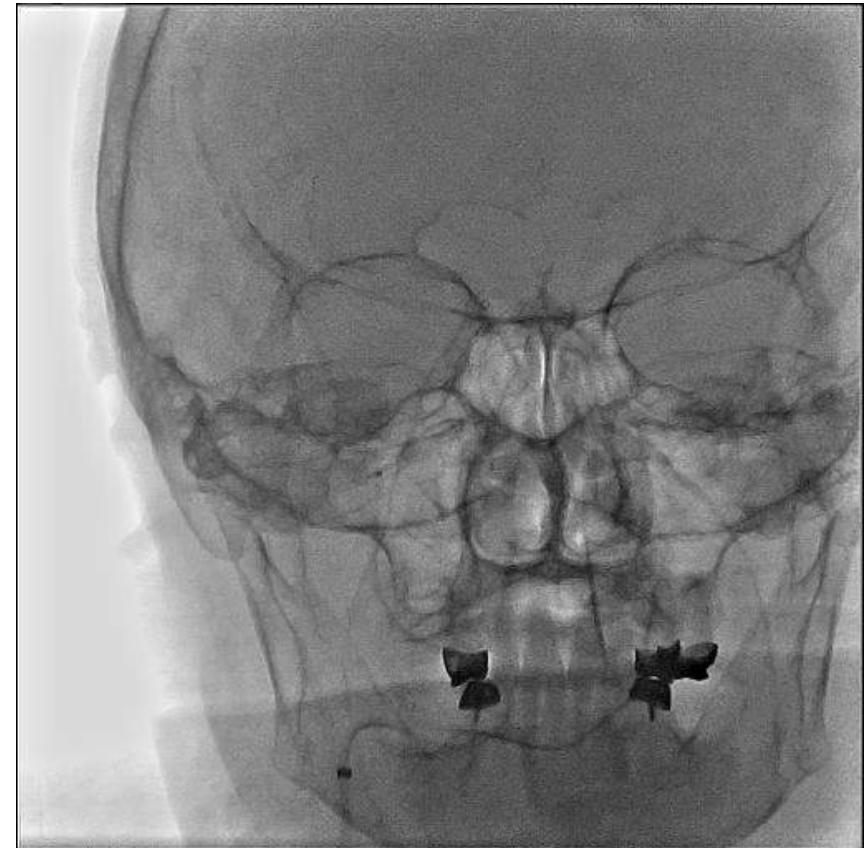
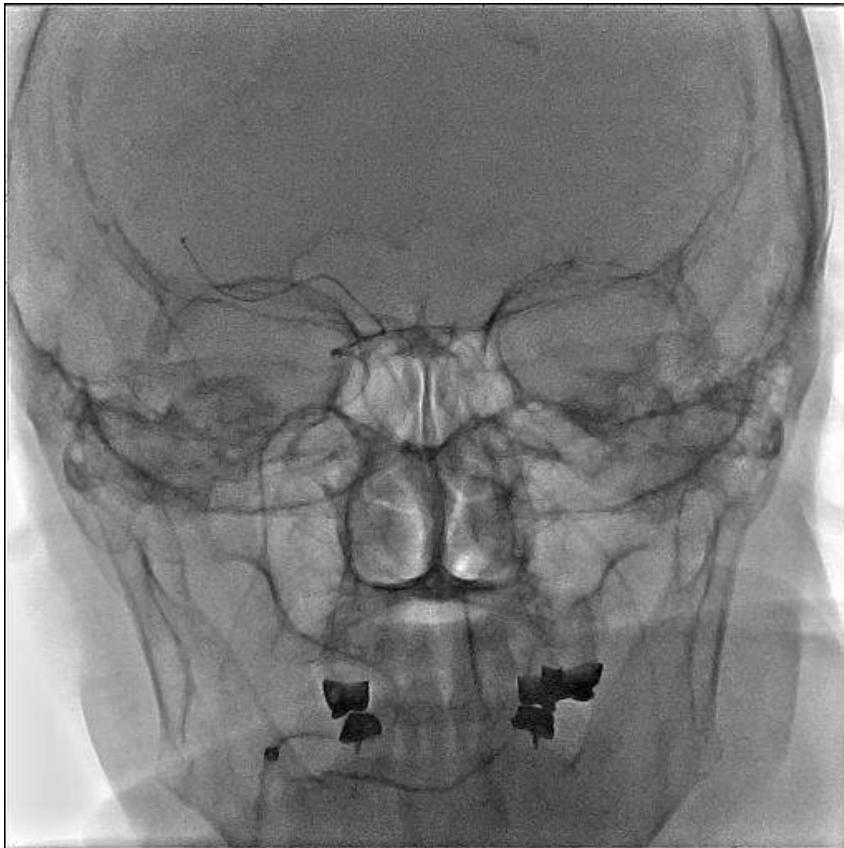


Sağ MCA M1 oklude



1. Pass

Stent retriever



1. pass

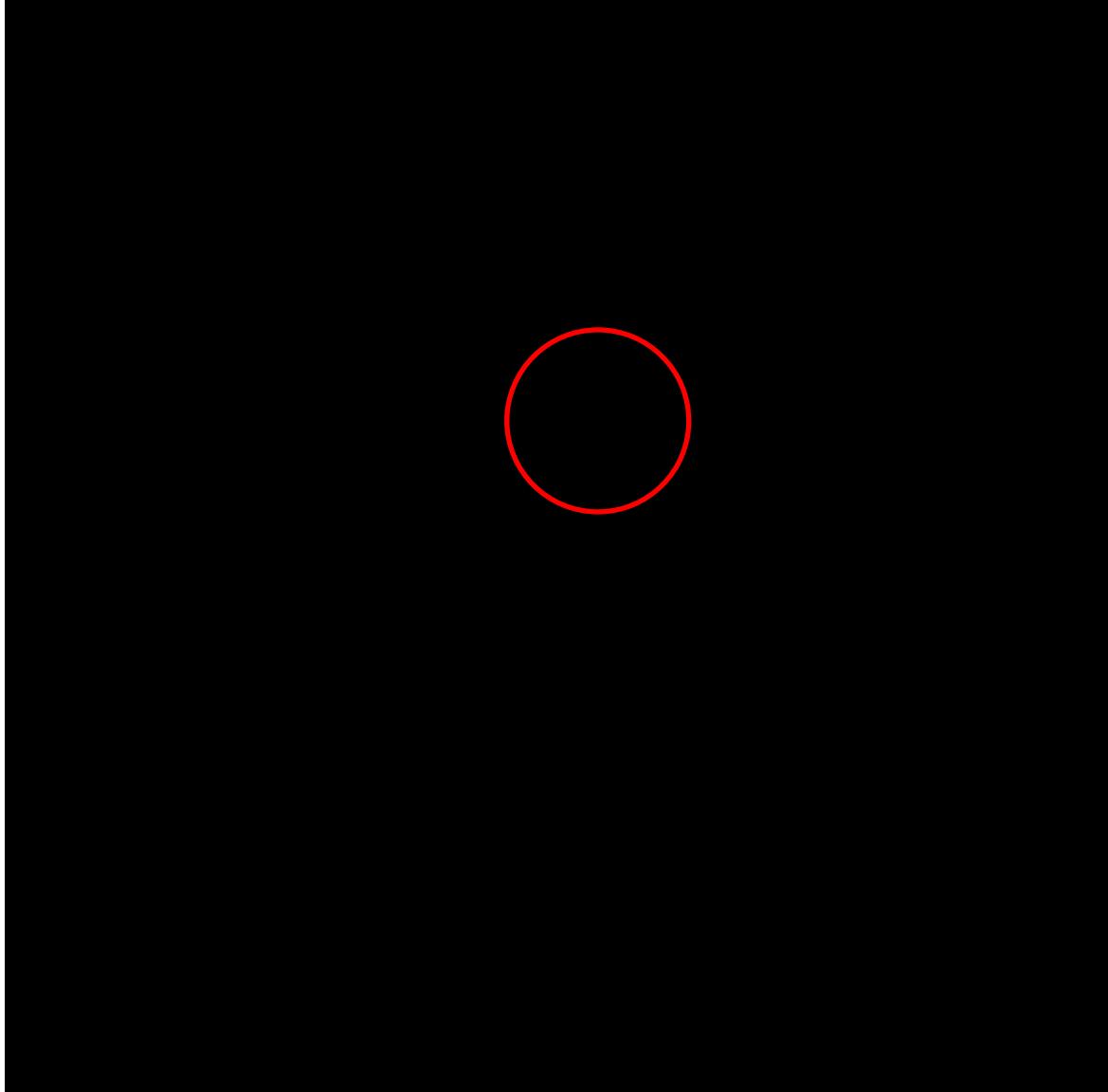


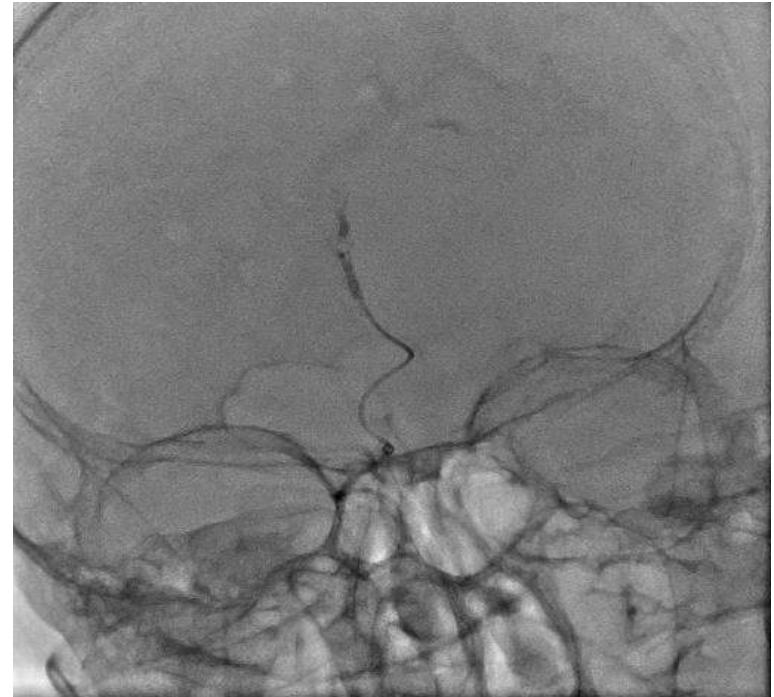
2. pass



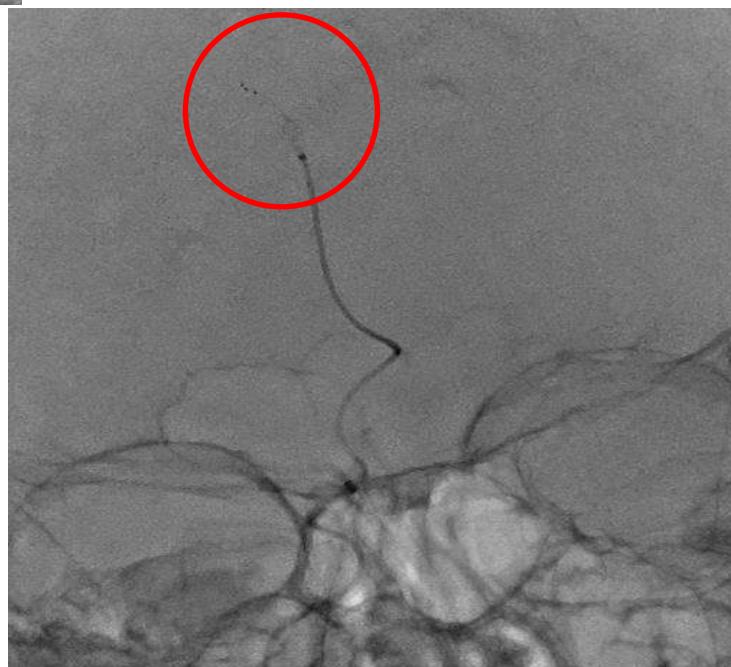
Sağ ACA A2 de distal
emboli

3. pass

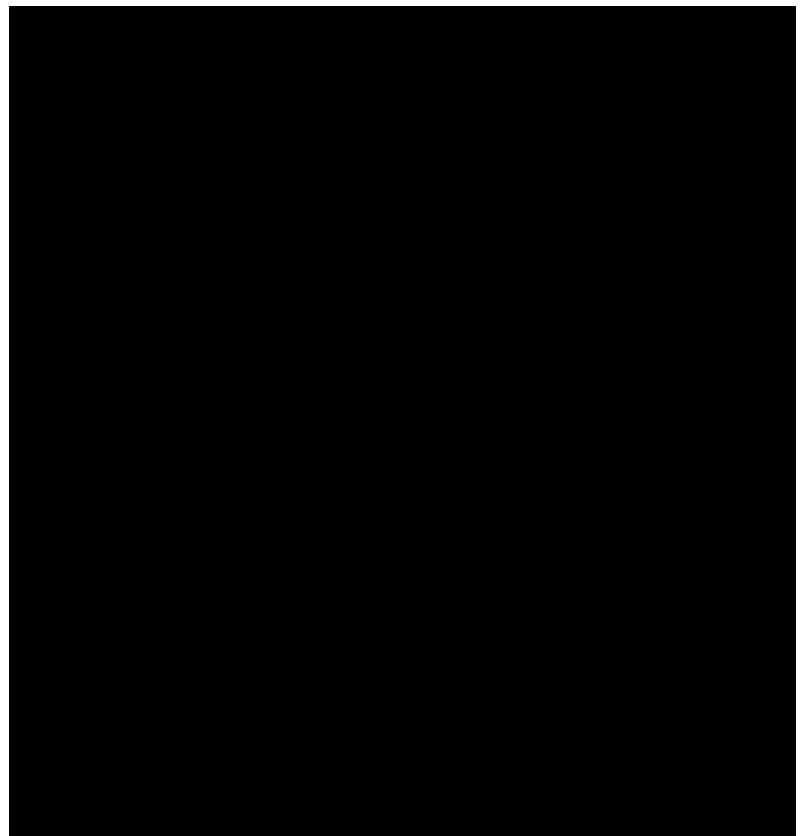
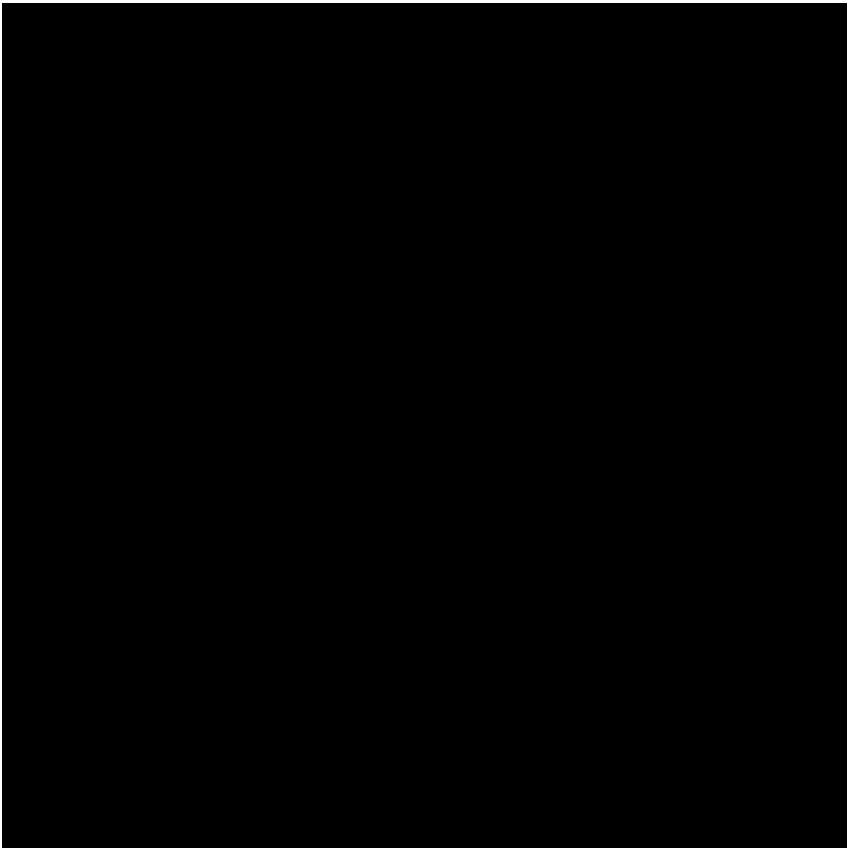


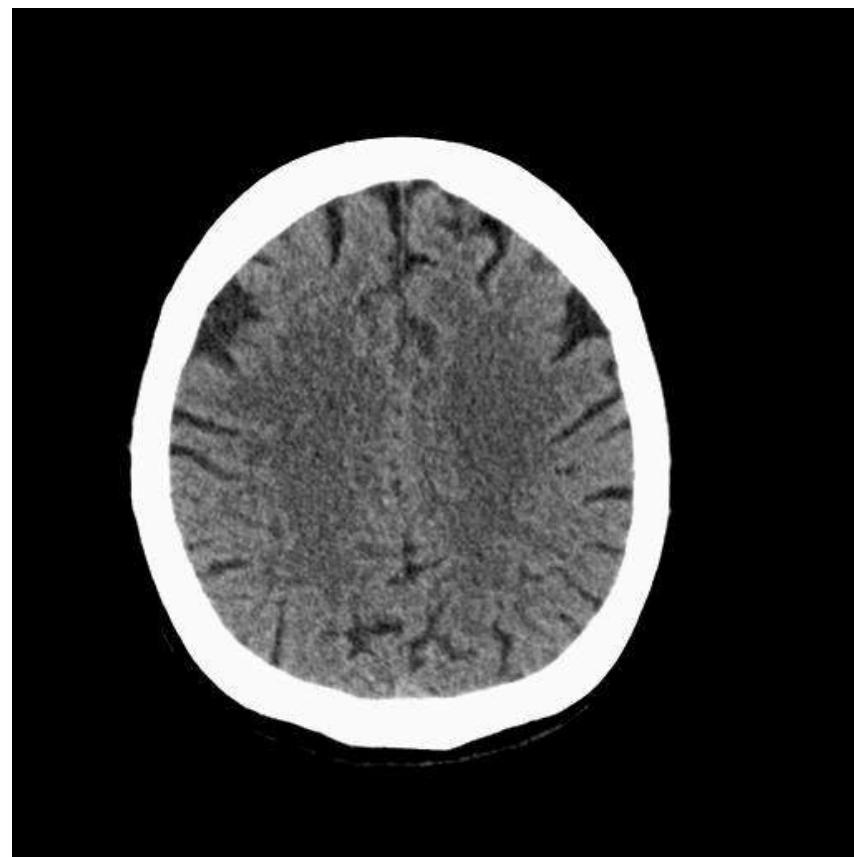


ACA A2 4x40
Stent retriever



ACA A2 tek pass rekonalizasyon





Çıkış Muayenesi

- SOL ÜST EKSTREMİTE KAS GÜCÜ
 - PROKSİMAL 1/5 DISTAL 0.
- SOL ALT EKSTREMİTE KAS GÜCÜ
 - KALÇA FLEKSİYONU 1+/5
 - DİZ FLEKSİYONU 0
 - DİZ EKSTANSİYONU 2/5
 - AYAK DORSİFLEKS VE PLANTAR FLEKS 0

Intravenous Thrombolysis in Unwitnessed Stroke Onset: MR WITNESS Trial Results

Lee H. Schwamm, MD,^{1*} Ona Wu, PhD,^{2*} Shlee S. Song, MD,³

Methods: Patients aged 18 to 85 years with AIS of unwitnessed onset at 4.5 to 24 hours since they were last known to be well, treatable within 4.5 hours of symptom discovery with intravenous alteplase (0.9mg/kg), and presenting with qDFM were screened across 14 hospitals. The primary outcome was the risk of symptomatic intracranial hemorrhage (sICH) with preplanned stopping rules. Secondary outcomes included symptomatic brain edema risk, and functional outcomes of 90-day modified Rankin Scale (mRS).

Results: Eighty subjects were enrolled between January 31, 2011 and October 4, 2015 and treated with alteplase at median 11.2 hours (IQR = 9.5–13.3) from when they were last known to be well. There was 1 sICH (1.3%) and 3 cases of symptomatic edema (3.8%). At 90 days, 39% of subjects achieved mRS = 0–1, as did 48% of subjects who had vessel imaging and were without large vessel occlusions.

- 80 hasta ... 18-85 yaş arası
- 4.5-24 saat içinde başvuran
- Quantative-DWI -FLAIR mismatch saptanan hastalar
- 0.9 mg / kg IV tpa
- Hastalar ortalama 11.2 saat içinde IV tpa almış
- 1 hasta.....% 1.3 sICH;
- 3 hasta.....% 3.8 semptomatik ödem
- % 39 hastada mRS..0-1 arası

ANN NEUROL 2018;83:980–993

- Uyanma İnmesi ve GBI'li hastalarda
 - Yalnızca Kontrastsız BBT kullanarak vaka seçimi yapılan ikinci çalışma:



Thrombolysis in Stroke With Unknown Onset Based on Non-Contrast Computerized Tomography (TRUST CT)

Marek Sykora, MD, PhD, MSc; Lars Kellert, MD; Patrik MD; Stefan Krebs, MD; Wilfried Lang, MD; Wolfgang Benjamin Bender, MD; Annerose Mengel, MD; Khoulda

errari,
, MD;

Background—Intravenous thrombolysis (IVT) in w
proven to be safe and effective using advanced
perfusion) for patient selection. However, in most
We hypothesize that pragmatic non-contrast comp

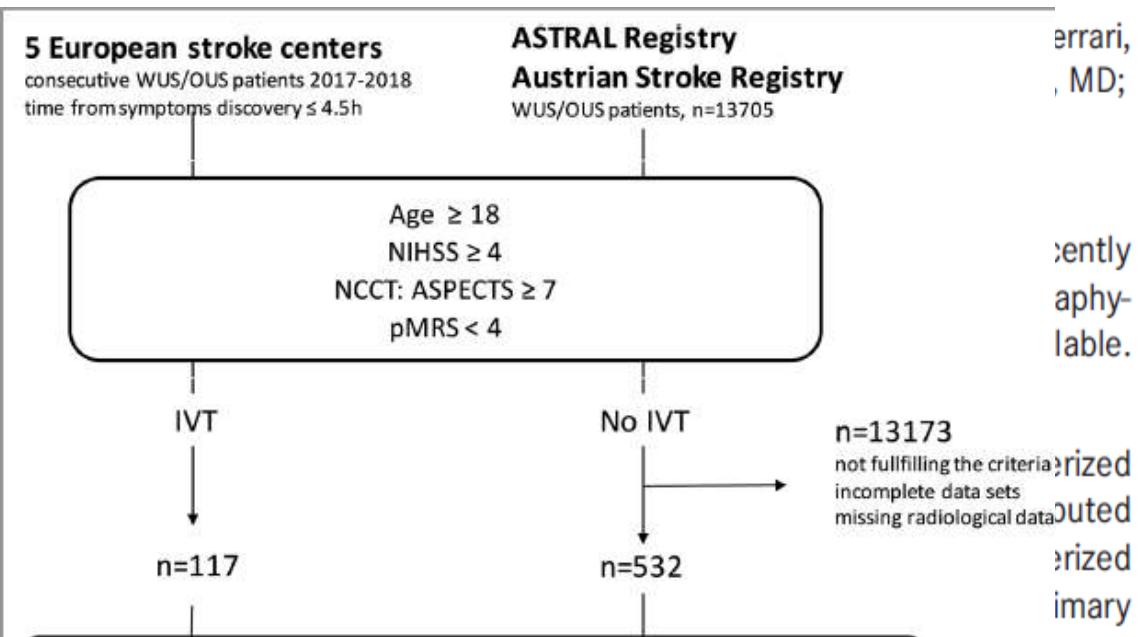
cently
aphy-
able.

Methods and Results—TRUST-CT (Thrombolysis
Tomography) is an international multicenter reg
tomography-based IVT with National Institute of H
Tomography score ≥ 7 were included and compared

imary

end point was the incidence of symptomatic intracranial hemorrhage; secondary end points included 24-hour National Institute of Health Stroke Scale improvement of ≥ 4 and modified Rankin Scale at 90 days. One hundred and seventeen WUS/SUO patients treated with non-contrast computed tomography-based IVT were included. As compared with 112 controls, the median admission National Institute of Health Stroke Scale was 10 and the median Alberta Stroke Program Early Computerized Tomography score was 10 in both groups. Four (3.4%) IVT patients and one control patient (0.9%) suffered symptomatic intracranial hemorrhage (adjusted odds ratio 7.9, 95% CI 0.65–96, $P=0.1$). A decrease of ≥ 4 National Institute of Health Stroke Scale points was observed in 67 (57.3%) of IVT patients as compared with 25 (22.3%) in controls (adjusted odds ratio 5.8, CI 3.0–11.2, $P<0.001$). A months, 39 (33.3%) IVT patients reached a modified Rankin Scale score of 0 or 1 versus 23 (20.5%) controls (adjusted odds ratio 1.94, CI 1.0–3.76, $P=0.05$).

Conclusions—Non-contrast computed tomography-based thrombolysis in WUS/SUO seems feasible and safe and may be effective. Randomized prospective comparisons are warranted.



- ESO kılavuzları,
 - 4,5-9 saatlik zaman aralığında
 - kontrastsız BT'ye dayalı IVT'nin etkinliğini
kanıt kalitesi, orta;
öneri gücü, güçlü
olarak önermektedir.



NCCT and CTA-based imaging protocol for endovascular treatment selection in late presenting or wake-up strokes

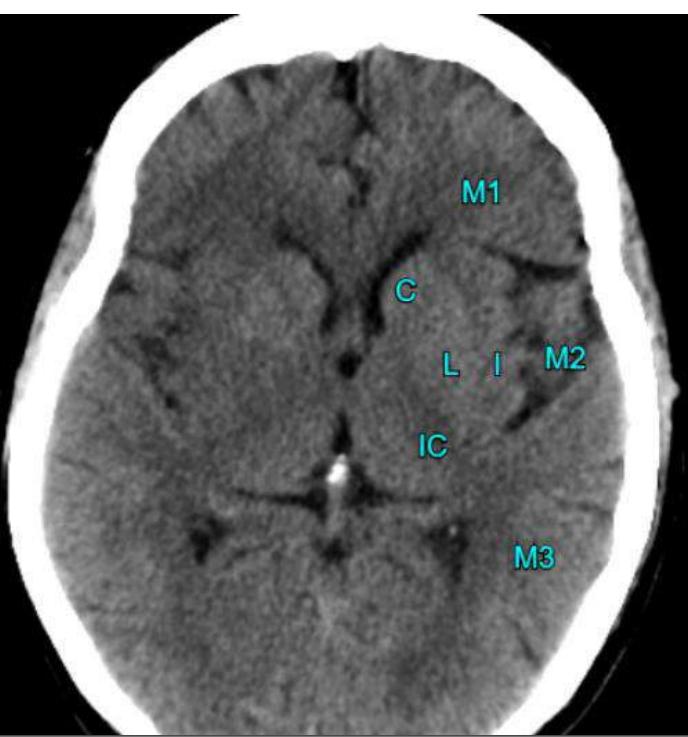
Telma Santos,¹ Andreia Carvalho,¹ André Almeida Cunha,² Marta Rodrigues,² Tiago Gregório,³ Ludovina Paredes,³ Henrique Costa,^{1,3} José Mário Roriz,⁴ João Pinho,⁵ Miguel Veloso,^{1,3} Sérgio Castro,² Pedro Barros,^{1,3} Manuel Ribeiro²

Santos T, et al. J NeuroIntervent Surg 2018;0:1–5.

Methods An observational study was performed, which included consecutive patients with anterior circulation ischemic stroke with large vessel occlusion treated with EVT. Patients presenting within 6 hours were treated if their NIH Stroke Scale (NIHSS) score was ≥ 6 and Alberta Stroke Program Early CT score (ASPECTS) was ≥ 6 , while patients presenting with WUS or 6–24 hours after last seen well (WUS/LPS) were treated if their NIHSS score was ≥ 12 and ASPECTS was ≥ 7 .

Uyanma inmeleri ve Geç Başvuran İnme hastalarında

- 18 yaş ve üzeri,
- basal mRS skoru 2'nin altında,
- NIH inme skalası skoru 12 ve üzeri
- kontrastsız BT'de Alberta Stroke Programme Early CT Score (ASPECTS) skoru 7 ve üzeri olan
- BTA'da büyük damar oklüzyonu olan hastalar çalışmaya dahil edilmiştir.



Calculating the ASPECTS Score:

Each area of grey white loss constitutes 1 deduction point

Subganglionic Nuclei:

| | |
|-------------------------------------|----|
| <u>M1</u> - Frontal operculum | -1 |
| <u>M2</u> - Anterior temporal lobe | -1 |
| <u>M3</u> - Posterior temporal lobe | -1 |

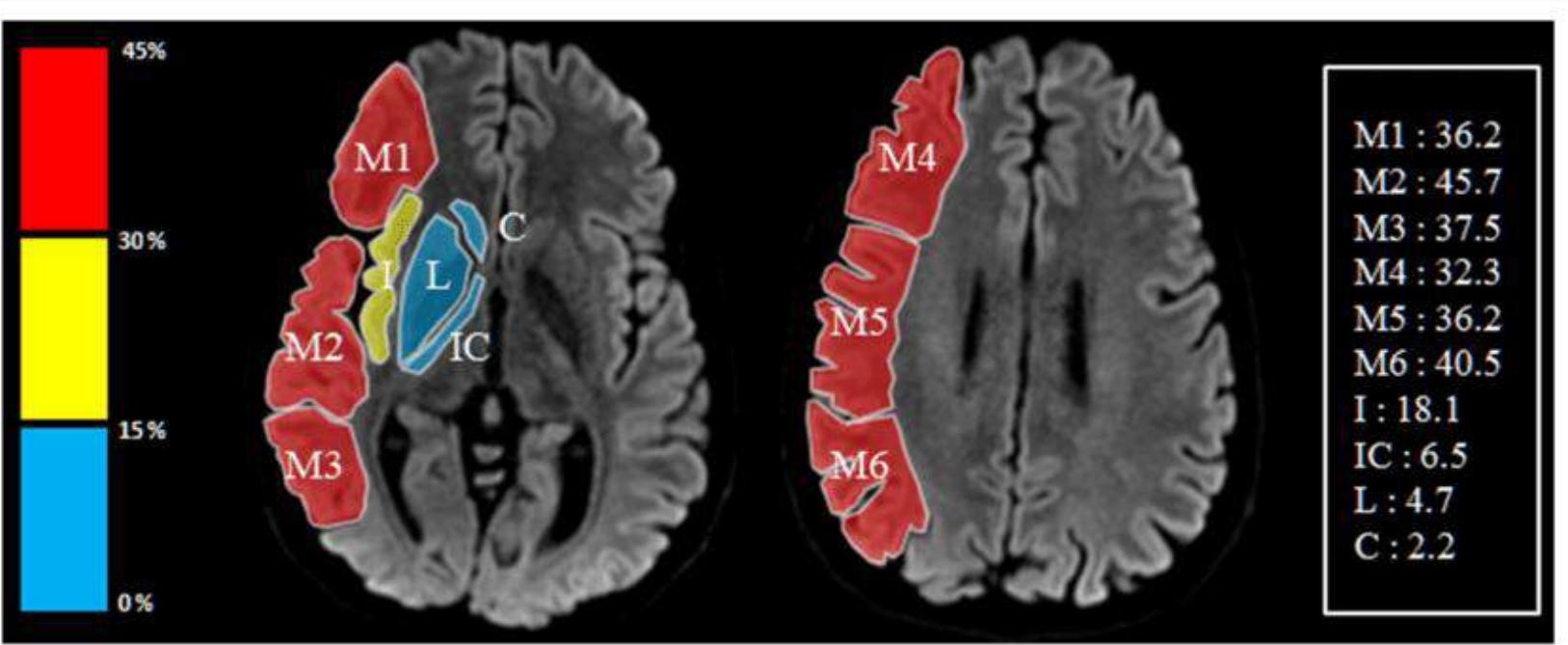
Supraganglionic Nuclei:

| | |
|---------------------------|----|
| <u>M4</u> - Anterior MCA | -1 |
| <u>M5</u> - Lateral MCA | -1 |
| <u>M6</u> - Posterior MCA | -1 |

Basal Ganglia:

| | |
|--------------------------------|----|
| Caudate (C) | -1 |
| Lentiform Nucleus (L) | -1 |
| Insula (I) | -1 |
| Internal Capsule (IC) any part | -1 |

Total ASPECTS Score. /10



| |
|-----------|
| M1 : 36.2 |
| M2 : 45.7 |
| M3 : 37.5 |
| M4 : 32.3 |
| M5 : 36.2 |
| M6 : 40.5 |
| I : 18.1 |
| IC : 6.5 |
| L : 4.7 |
| C : 2.2 |

NCCT and CTA-based imaging protocol for endovascular treatment selection in late presenting or wake-up strokes

Telma Santos,¹ Andreia Carvalho,¹ André Almeida Cunha,² Marta Rodrigues,² Tiago Gregório,³ Ludovina Paredes,³ Henrique Costa,^{1,3} José Mário Roriz,⁴ João Pinho,⁵ Miguel Veloso,^{1,3} Sérgio Castro,² Pedro Barros,^{1,3} Manuel Ribeiro²

252 EVT uygulanan hastalardan 63 (%25.3) hasta 6 saatlik pencere dışında tedavi edilmiş.
 Uyanma İnmesi..34 hasta
 GBI...29 hasta

Table 2 Baseline characteristics, interventional procedure data, and outcomes in patients treated 6–24 hours after last seen well

Santos T, et al. J NeuroIntervent Surg 2018;0:1–5.

| | Wake-up stroke (n=34) | Late presenting stroke (n=29) | P value |
|---------------------------------------|-----------------------|-------------------------------|---------|
| Successful recanalization (mTICI ≥2b) | 33 (97.1) | 27 (93.1) | 0.59 |
| NIHSS at 24 hours | 8 (3–13) | 7 (3–15) | 0.825 |
| mRS ≤2 at 3 months | 21 (61.8) | 20 (69.0) | 0.55 |
| Mortality at 3 months | 4 (11.8) | 1 (3.4) | 0.363 |
| Symptomatic ICH | 1 (2.9) | 1 (3.4) | 1 |
| Peri-procedural complications† | 3 (8.8) | 1 (3.4) | 0.618 |
| Tandem occlusion | 9 (26.5) | 7 (24.1) | 0.832 |

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Results 249 patients were included, 63 of whom were in the WUS/LPS group. Baseline characteristics were similar between groups, except for longer symptom-recanalization time, lower admission NIHSS (16 vs 17, $P=0.038$), more frequent tandem occlusions (25.4% vs 11.8%, $P=0.010$), and large artery atherosclerosis etiology (22.2% vs 11.8%, $P=0.043$) in the WUS/LPS group. No differences in symptomatic intracranial hemorrhage, peri-procedural complications or mortality were found between groups. Three-month functional independence was similar in both groups (65.1% in WUS/LPS vs 57.0% in ≤ 6 hours, $P=0.259$) and no differences were found after adjustment for confounders.

- Sonuçlara bakıldığında
- **3. ay mortalite oranlarında**
 - %15.6 ilk 6 saat grubunda,
 - %7.9, uyanma ve GBİ grubunda, $p=0.126$) ve
- **3. ay iyi klinik sonlanım**,
 - ilk 6 saatte başvuran hastalarda %57.0 iken
 - uyanma ve GBİ grubunda % 65.1 olarak raporlanmıştır ($p=0.259$).
- Ek olarak uyanma ve GBİ hastaları arasında sonlanım noktaları açısından istatistiksel anlamlı fark gözlenmemiştir.

NCCT and CTA-based imaging protocol for endovascular treatment selection in late presenting or wake-up strokes

Telma Santos,¹ Andreia Carvalho,¹ André Almeida Cunha,² Marta Rodrigues,² Tiago Gregório,³ Ludovina Paredes,³ Henrique Costa,^{1,3} José Mário Roriz,⁴ João Pinho,⁵ Miguel Veloso,^{1,3} Sérgio Castro,² Pedro Barros,^{1,3} Manuel Ribeiro²

Conclusions This real-world observational study suggests that EVT may be safe and effective in patients with WUS and LPS selected using clinical-core mismatch (high NIHSS/high ASPECTS in NCCT).

Sonuç →

- Yüksek NIHSS (12 ve üzeri)
- Kontrastsız BT'de yüksek ASPECTS (7 ve üzeri)
 - kullanılarak seçilen Uyanma inmeleri ve Geç Başvuran İnme hastalarında;
 - EVT'nin güvenli ve etkili olabileceğini düşündürmektedir.

Original research

Endovascular thrombectomy for anterior circulation stroke beyond 6 hours of onset in Sweden 2015 to 2020: rates and outcomes in a nationwide register-based study

Teresa Ullberg  ^{1,2} Mia von Euler,³ Per Wester,^{4,5} Fabian Arnberg,⁶ Bo Norrving,² Tommy Andersson,^{6,7} Johan Wassélius¹

Results Late window EVT increased from 0.3% of all IS in 2015 to 1.8% in 2020, and from 17.4% of all anterior circulation EVTs in 2015 to 32.9% in 2020. Of 2199 patients, 76.9% (n=1690) were early window EVTs and 23.1% late window EVTs (n=509; 141 known onset, 368 LSW). Median age was 73 years, and 46.2% were female, with no differences between groups. Favorable outcome did not differ between groups (early window 42.4%, late window known onset 38.9%, late window LSW 37.3% ($p=0.737$)) and remained similar when adjusted for baseline differences. sICH rates did not differ (early window 4.0%, late window known onset 2.1%, late window LSW 4.9% ($p=0.413$)).

Conclusion Late window EVTs have increased substantially over time, and currently account for one third of anterior circulation treatments. Early and late window patients had similar outcomes.

Patient selection

We included all patients with anterior circulation large vessel occlusion acute IS, defined as occlusion of the intracranial portion of the internal carotid artery or the M1 or M2 segment of the middle cerebral artery on digital subtraction angiography (DSA), who were registered in both Riksstroke and EVAS from January 1, 2015 to December 31, 2020 and had groin puncture with the intention of EVT, were pre-stroke independent defined as modified Rankin Scale (mRS) score of 0–2, and had registered onset-to-groin (OTG) times.

Original research

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Table 1 Patient characteristics in 2199 patients with anterior circulation LVO stroke treated in the early (<6 hours) and late (6–24 hours) time windows. Missing data were <2% for all variables

| Variable | Early window reference n=1690, % (n) | Late window known onset n=141, % (n) | Late window LSW n=368, % (n) | P value |
|-----------------------------------|---|---|---------------------------------|---------|
| Stroke characteristics | | | | |
| Median NIHSS (IQR) | 16 (11–20) | 12 (7–17) | 15 (11–19) | <0.001 |
| Wake-up stroke | 3.2% (54) | 0% (0) | 61.1% (225) | <0.001 |
| MCA, M2 | 29.4% (497) | 39.0% (55) | 25.0% (92) | |
| Reperfusion rate | | | | 0.141 |
| mTICI 2b–3 | 84.9% (1418) | 80.6% (112) | 87.5% (321) | |
| Early neurological outcome | | | | |
| 24 hours NIHSS, median (IQR) | 6 (2–14) | 7 (3–15) | 8 (3–16) | 0.002 |
| Adverse events | | | | |
| sICH | 4.0% (67) | 2.1% (3) | 4.9% (18) | 0.413 |

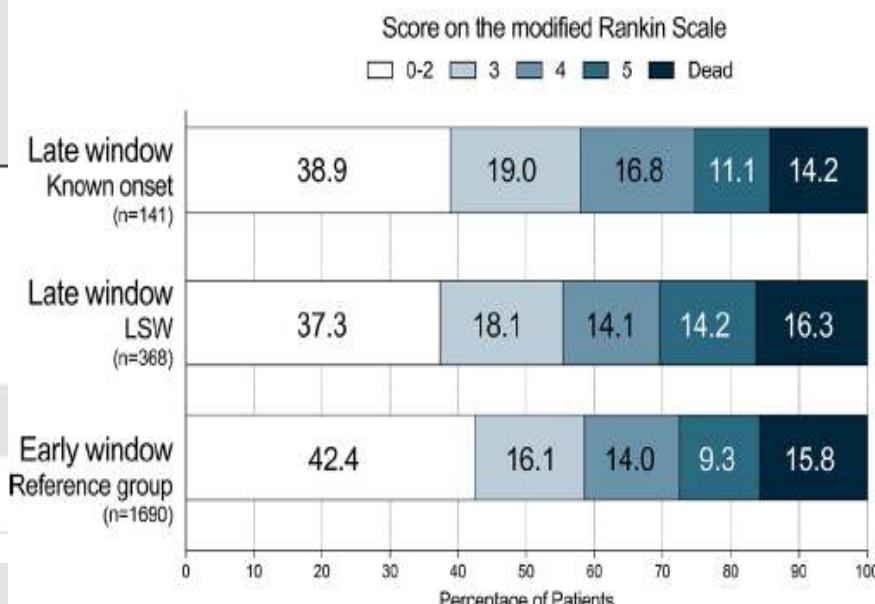


Figure 3 90-day functional outcome stratified by time window. There was no significant difference between groups ($p=0.737$). Loss to follow-up (19.6%) were replaced by imputed values. LSW, last seen well.

Mechanical thrombectomy beyond 6 hours in acute ischaemic stroke with large vessel occlusion in the carotid artery territory: experience at a tertiary hospital[☆]

E. Natera-Villalba^{a,*}, A. Cruz-Culebras^a, S. García-Madrona^a, R. Vera-Lechuga^a,

NEUROLOGÍA 2020

- 59 hasta.....%55.9 kadın; yaş ortalaması 71
- 33 olguda Uyanma İnmesi
- Medyan başlangıç NIHSS skoru 16
- Medyan ASPECTS skoru 8
- Hastaların %94.9'u kurtarılabilir doku nun > %50'sini gösteriyordu.
- Başlangıçtan 24 saat sonra MT uygulanan 5 hastanın %88.1'inde, kaydadeğer rekanalizasyon sağlandı.

Mechanical thrombectomy beyond 6 hours in acute ischaemic stroke with large vessel occlusion in the carotid artery territory: experience at a tertiary hospital[☆]

E. Natera-Villalba^{a,*}, A. Cruz-Culebras^a, S. García-Madrona^a, R. Vera-Lechuga^a,

NEUROLOGÍA 2020

Table 5 Logistic regression analysis of the variables showing a statistically significant association with poorer functional prognosis.

| | OR | 95% CI | P |
|---------------------------------|------|------------|------|
| Age | 0.93 | 0.81-1.07 | .317 |
| Atrial fibrillation | 0.12 | 0.004-2.82 | .187 |
| Baseline NIHSS score | 0.72 | 0.47-1.12 | .144 |
| Puncture-to-recanalisation time | 1.03 | 0.95-1.13 | .455 |
| NIHSS score at discharge | 0.44 | 0.204-0.95 | .036 |

Daha kötü prognos ile ilişkili değişkenler

- Yaş
- Atriyal fibrilasyon
- Yüksek NIHSS skorları (Başvuru ve Taburculukta)
- Daha uzun ponksiyon-rekanalizasyon süresi

- 41 hastadan>>>22 si MT işlemine alınmış
- Dahil edilme kriterleri
 - ASPECT >6
 - 6-24 saat aralığı
 - DWI lesion volume 70 mL veya az
 - Penumbra volume 15 mL veya daha fazla
 - Mismatch oranı 1.8 veya fazla
 - T max >10 sn olan Perfüzyon lezyon hacminin 100 mL den az olması

Table 2. Functional outcome of patients in our study compared to endovascular trials

| | RIH study cohort | RIH study cohort & DEFUSE-2 | HERMES cohort | Extend IA cohort |
|--|------------------|-----------------------------|-----------------|------------------|
| Good functional outcome (mRS 0-2) | 14/22 (63.6%) | 28/46 (60.8%) | 291/633 (46.0%) | 25/35 (71.0%) |
| Excellent functional outcome (mRS 0-1) | 9/22 (40.9%) | N/A | 170/633 (26.9%) | 18/35 (51.0%) |
| Symptomatic hemorrhage | 0/22 (0%) | N/A | 28/634 (4.4%) | 0/35 (0%) |

- Mechanical Embolectomy for Acute Ischemic Stroke Beyond Six Hours from Symptom Onset Using MRI based perfusion imaging Ryan A. Et al. *Journal of the Neurological Sciences* 2017

Kollateral Değerlendirmeye göre hasta seçimi

- Akut inmeli hastalarda intrakraniyal kollateral dolasımının penumbrayı koruduğu ve enfarktüs büyümesini sınırladığı bilinmektedir.
- BT anjiyografi, intrakraniyal kollaterallerin değerlendirilmesi için sıkılıkla uygulanan invaziv olmayan bir yöntemdir.

Kollateral Değerlendirmeye göre hasta seçimi

- Günümüzde kollateral değerlendirmesinde kullanılan metodlar kalitatif ve semikantitatif metodlardır ve birbirlerine üstünlükleri kanıtlanmamıştır.
- Basitçe oklüzyon distalinde normal olan karşı tarafla aynı veya daha fazla, ya da orta serebral arter için vasküler sulama alanının %50'den fazlasında kollateral vasküler yapı varlığı '**iyi kollateral**',
- Aksine distalde hiç vasküler yapı izlenmemesi ya da orta serebral arter için vasküler sulama alanının %50'den azında vasküler yapı olması distalde **kötü kollateral** akıma işaret eder

TAN Kollateral Skorlamasi

- **0:** absent collateral supply to the occluded MCA territory
- **1:** collateral supply filling $\leq 50\%$ but $>0\%$ of the occluded MCA territory
- **2:** collateral supply filling $>50\%$ but $<100\%$ of the occluded MCA territory
- **3:** 100% collateral supply of the occluded MCA territory

Collateral Circulation in Thrombectomy for Stroke After 6 to 24 Hours in the DAWN Trial

90 gün sonunda

| Kollateral Durumu | mRS 0-2 arası |
|-------------------|---------------|
| İyi | % 43.7 |
| Zayıf | % 30.8 |
| Kötü | % 17.7 |

Kollateral skorlaması..

BTA'da TAN skorlama
DSA'da ASITN grade ile
yapılmış.

(American Society of Interventional and
Therapeutic Neuroradiology collateral score)

David S.et al.

doi.org/10.1161/STROKEAHA.121.034471

Stroke. 2022;53:742–748

- Role of modified TAN score in predicting prognosis in patients with acute ischemic stroke undergoing endovascular therapy
- Recep Baydemir¹, Özlem Aykaç², Bilgehan Atilgan Acar³, Zehra Uysal Kocabas⁴, Aysel Milanlioğlu⁵, Ezgi Sezer Eryildiz⁶, Atilla Özcan Özdemir² Clin Neurol Neurosurg 2021 Nov;210:106978

- 101 hasta çalışmaya dahil edilmiş
- % 50 sinde kötü kollateral saptanmış
- Kötü kollateralı olan bu hastaların
 - geliş NIHSS ve 24 saat sonraki NIHSS değerleri
 - Mortalite
 - Futil rekanalizasyon oranları ...yüksek bulunmuş.
 - mRSları düşük bulunmuş.

CT angiography collateral scoring: Correlation with DWI infarct size in proximal middle cerebral artery occlusion stroke within 12 h onset

Mahmoud M. Higazi * , Enas A. Abdel-Gawad

The Egyptian Journal of Radiology and Nuclear Medicine (2016) 47, 991–997

Table 1 Demographic, clinical and imaging data.

| | All patients (n = 30) | CS ≤ 50% (n = 14) | CS ≥ 50% (n = 16) | p value |
|------------------------------|--------------------------|--------------------------|-------------------------|--------------|
| Age, y, median (IQR) | 70 (55–83) | 78 (68–83) | 62 (52–80) | 0.102 |
| Sex, male, no. (%) | 20 (67%) | 9 (64%) | 11 (69%) | |
| NIHSS, mean ± (SD) | 13 ± (7) | 17 ± (5) | 9 ± (6) | 0.001 |
| Lag time, h, mean ± (SD) | 5.34 ± (2.29) | 5.96 ± (2.59) | 5.03 ± (2.04) | 0.448 |
| DWI volume, mL, median (IQR) | 24.317 (14.049–117.747) | 119.381 (28.556–154.470) | 15.4590 (12.772–24.318) | 0.009 |

IQR: interquartile range and SD: standard deviation.

- **Kollateral skorlaması < % 50 ise**
 - DWI volume ortalama = 119
 - NIHSS ortalama=17
- **Kollateral skorlaması > % 50 ise**
 - DWI volume ortalama=15
 - NIHSS ortalama=17

Extending thrombolysis to 4·5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data

Bruce C V Campbell*, Henry Ma*, Peter A Ringleb*, Mark W Parsons, Leonid Churilov, Martin Bendszus, Christopher R Levi, Chung Hsu, Timothy J Kleinig, Marc Fatar, Didier Leys, Carlos Molina, Tissa Wijeratne, Sami Curtze, Helen M Dewey, P Alan Barber, Kenneth S Butcher, Deidre A De Silva, Christopher F Bladin, Nawaf Yassi, Johannes A R Pfaff, Gagan Sharma, Andrew Bivard, Patricia M Desmond, Stefan Schwab, Peter D Schellinger, Bernard Yan, Peter J Mitchell, Joaquín Serena, Danilo Toni, Vincent Thijs, Werner Hacke, Stephen M Davist, Geoffrey A Donnan†, on behalf of the EXTEND, ECASS-4, and EPITHET Investigators‡

Findings We identified three trials that met eligibility criteria: EXTEND, ECASS4-EXTEND, and EPITHET. Of the 414 patients included in the three trials, 213 (51%) were assigned to receive alteplase and 201 (49%) were assigned to receive placebo. Overall, 211 patients in the alteplase group and 199 patients in the placebo group had mRS assessment data at 3 months and thus were included in the analysis of the primary outcome. 76 (36%) of 211 patients in the alteplase group and 58 (29%) of 199 patients in the placebo group had achieved excellent functional outcome at 3 months (adjusted odds ratio [OR] 1·86, 95% CI 1·15–2·99, $p=0\cdot011$). Symptomatic intracerebral haemorrhage was more common in the alteplase group than the placebo group (ten [5%] of 213 patients vs one [<1%] of 201 patients in the placebo group; adjusted OR 9·7, 95% CI 1·23–76·55, $p=0\cdot031$). 29 (14%) of 213 patients in the alteplase group and 18 (9%) of 201 patients in the placebo group died (adjusted OR 1·55, 0·81–2·96, $p=0\cdot66$).

Interpretation Patients with ischaemic stroke 4·5–9 h from stroke onset or wake-up stroke with salvageable brain tissue who were treated with alteplase achieved better functional outcomes than did patients given placebo. The rate of symptomatic intracerebral haemorrhage was higher with alteplase, but this increase did not negate the overall net benefit of thrombolysis.

Extending thrombolysis to 4·5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data

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| | Placebo (n=201) | Alteplase (n=213) | Odds ratio* (95% CI) | p value |
|---|--------------------|----------------------|-------------------------|---------|
| Primary outcome | | | | |
| Excellent functional outcome (mRS score 0–1) at 3 months | 58/199 (29%) | 76/211 (36%) | 1·86 (1·15–2·99) | 0·01 |
| Secondary outcomes | | | | |
| Functional improvement in mRS score at 3 months† | NA | NA | 1·60 (1·12–2·27) | 0·009 |
| Functional independence (mRS score 0–2) at 3 months | 87/199 (44%) | 103/211 (49%) | 1·74 (1·08–2·81) | 0·02 |
| Early neurological improvement at 72 h‡ | 31/197 (16%) | 58/206 (28%) | 2·54 (1·51–4·27) | <0·0001 |
| Safety outcomes | | | | |
| Death at 3 months | 18/201 (9%) | 29/213 (14%) | 1·55 (0·81–2·97) | 0·19 |
| Symptomatic intracerebral haemorrhage§ | 1/201 (<1%) | 10/213 (5%) | 9·70 (1·23–76·55) | 0·03 |

Tenecteplase in Stroke Patients Between 4.5 and 24 Hours (TIMELESS)

- Actual Study Start Date : March 2, 2019
- Estimated Primary Completion Date : September 1, 2022
- Estimated Study Completion Date : September 1, 2022

Tenecteplase in Stroke Patients Between 4.5 and 24 Hours (TIMELESS)

- Nörogörüntüleme:
- Manyetik rezonans anjiyografi (MRA)
- veya bilgisayarlı tomografi anjiyografi (BTA)
 - ile ICA veya M1, M2 oklüzyonu (karotis oklüzyonları servikal veya intrakraniyal olabilir, tandem MCA lezyonları olsun veya olmasın)

BT perfüzyon veya MR perfüzyonda
İskemik kor hacmi < 70 mL,
mismatch oranı ≥ 1.8 ve
Mismatch hacmi ≥ 15 mL)

- Geç Başvuran İnme (GBİ) ve Uyanma İnmeli (UI) hastalarda EVT gerekliliği için daha basit ve daha hızlı protokoller gerekliliği aşikardır.
- Ancak, bu hastaları seçmek için en uygun görüntüleme protokolü hala tartışma konusudur.
 - Barber PA, Hill MD, Eliasziw M, et al. Imaging of the brain in acute ischaemic stroke: comparison of computed tomography and magnetic resonance diffusion-weighted imaging. *J Neurol Neurosurg Psychiatry* 2005;76:1528-33.
 - von Kummer R, Bourquain H, Bastianello S, et al. Early prediction of irreversible brain damage after ischemic stroke at CT. *Radiology* 2001;219:95-100.

6 saat Sonrası İnme ve Uyanma İnmelerinde vaka Seçiminde -ÖZETLE -DİKKAT EDİLECEK HUSUSLAR

- BT'de hipodansite olmaması
- Normal veya normale yakın BT bulguları olan hastada BT anjiyografide majör damar/dal oklüzyonu olması
- BT perfüzyon yapılan olgularda hipo-perfüze alanının geniş ama hipodansitenin küçük olması
- MCA sulama alanının %50'den fazlasında kollateral vasküler yapı varlığı **'iyi kollateral olması'**
- DWI lezyon hacminin 70 mL veya az olması
- Penumbra volume 15 mL veya daha fazla olması
- DWI/FLAIR mismatch olması

Teşekkürler