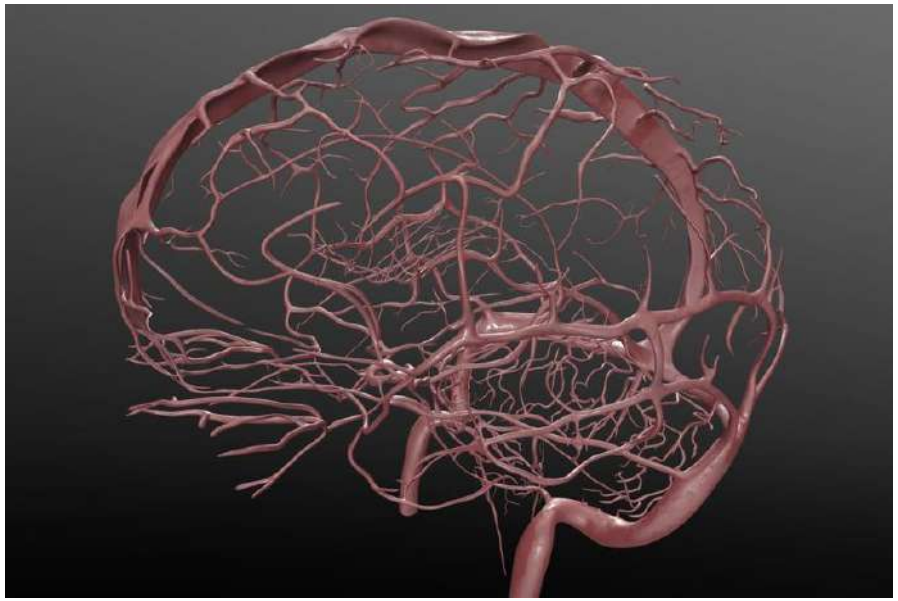

SEREBRAL VENÖZ ANATOMİ

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Atatürk Üniversitesi Nöroloji AD

IV. Girişimsel Nöroloji Eğitim Toplantısı

Mayıs 2022 GAZİANTEP

- **Kraniyal venler** ve **dural venöz sinüsler**, doğrudan veya dolaylı olarak beyni etkileyen birçok farklı olaya eşlik eder.
- Venöz ağın herhangi bir şekilde hasara uğraması hemipleji, koma ve ölümü de içeren ciddi defisitlere neden olabilir.
- Serebral venlerin birbiriyle olan zengin bağlantıları, varyasyon çeşitliliği ve boyutlarındaki farklılıkların fazla olması normal durumlarının tanımlanmasını zorlaştırmıştır.
- **Vücudun geri kalanının çoğundan farklı olarak, serebral arter sistemini uzaktan bile takip etmez.**
- **Kortikal venler, kortikal arterlerin aksine yüzeysel olarak uzanır.**
- **Serebral venlerin kas dokusu olmayan ince duvarları vardır.**
- **Serebral venlerin kapakçıkları yoktur.**

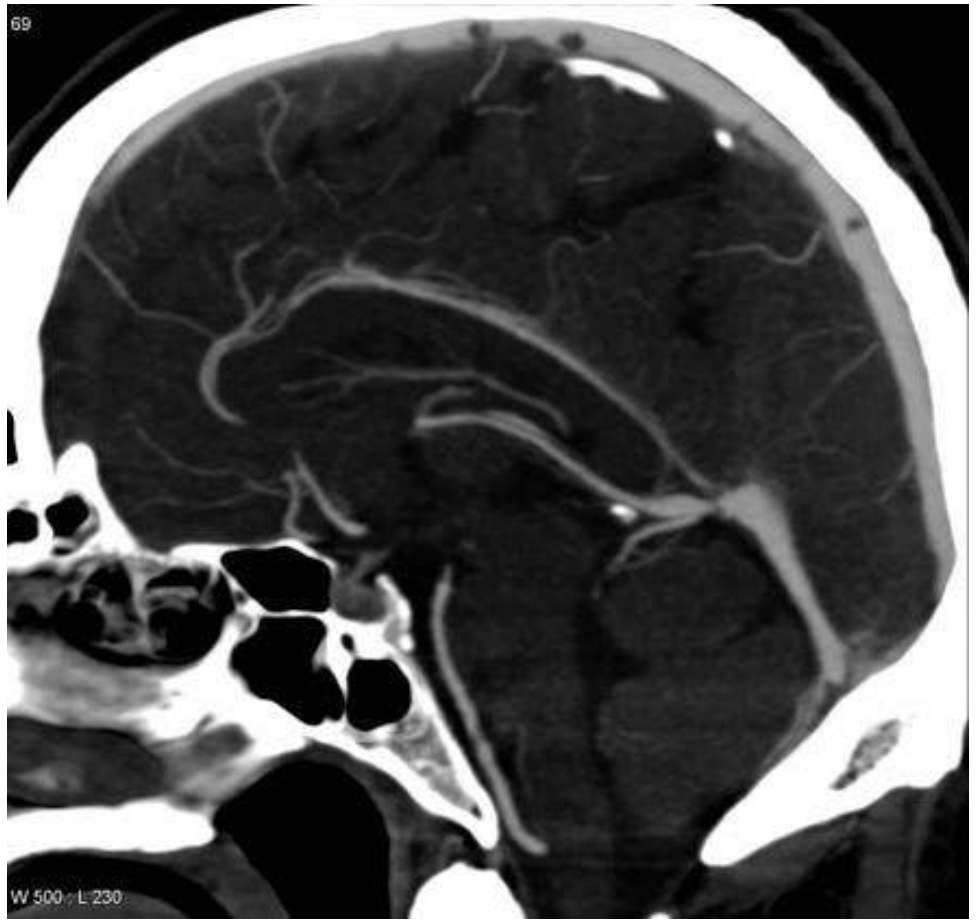
- Kraniyal venöz sistem
  - **Dural venöz sinüsler**
  - **Serebral venler**

Kraniyal dural venöz sinüsler

- Dural sinüsler intrakraniyal venöz kanı toplayan ve drenajını sağlayan venöz kanallar sistemidir.
- Duramaterin dış (periosteal) ve iç (meningeal) yaprakları arasında bulunur.
- Kapak içermezler (lümende düzensiz trabeküller)

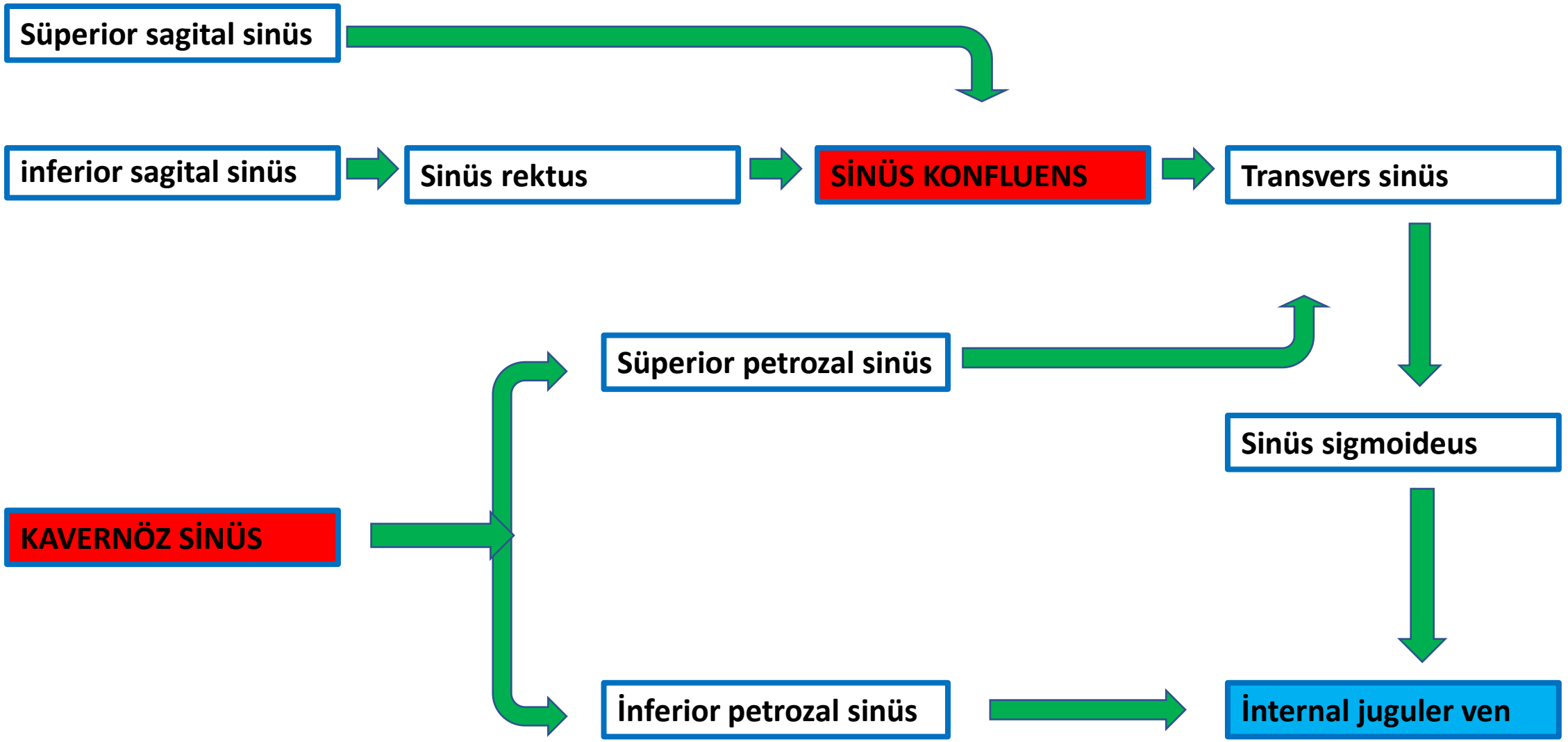
- Dural sinüsler içinde subaraknoid mesafedeki beyin omurilik sıvısını boşaltan **araknoid granülasyonlar** bulunur.
  - Transvers sinüs
  - Süperior sagital sinüs

!!! Trombozu taklit edebilir



Dural sinüsler

- **Süperior grup**
  - Sinüs konfluenste toplanır
- **İnferior (bazal) grup**
  - Kavernöz sinüste toplanır


Süperior sagital sinüs
inferior sagital sinüs
Sinüs rektus
SİNÜS KONFLUENS
Transvers sinüs
Süperior petrozal sinüs
Sinüs sigmoideus
KAVERNÖZ SİNÜS
İnferior petrozal sinüs
İnternal juguler ven

Süperior grup dural venöz sinüsler

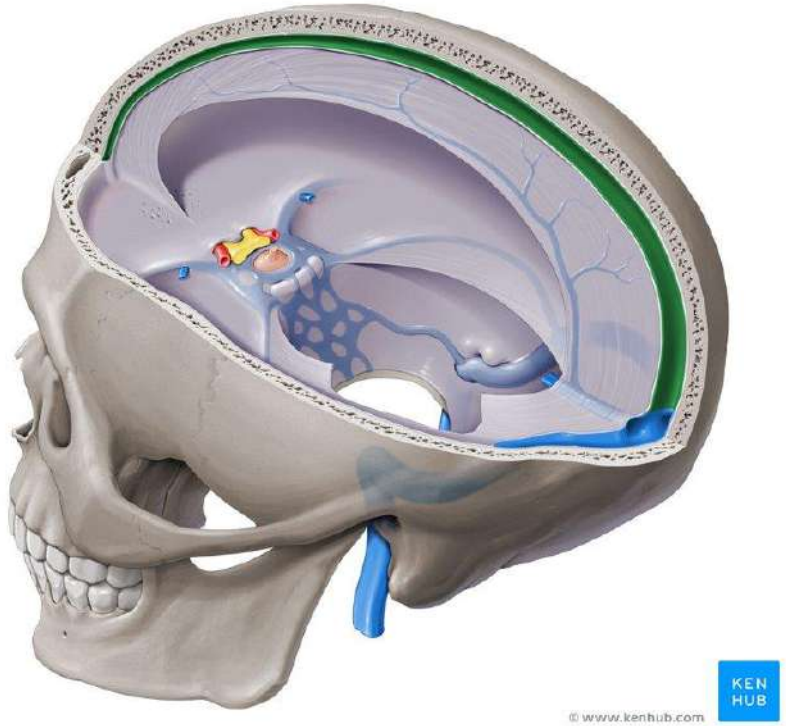
- Süperior sagital sinüs
- İnferior sagital sinüs
- Sinüs rektus
- Falsin sinüs
- Oksipital sinüs
- Sinüs konfluens
- Lateral sinüs
  - Transvers s
  - Sigmoid s

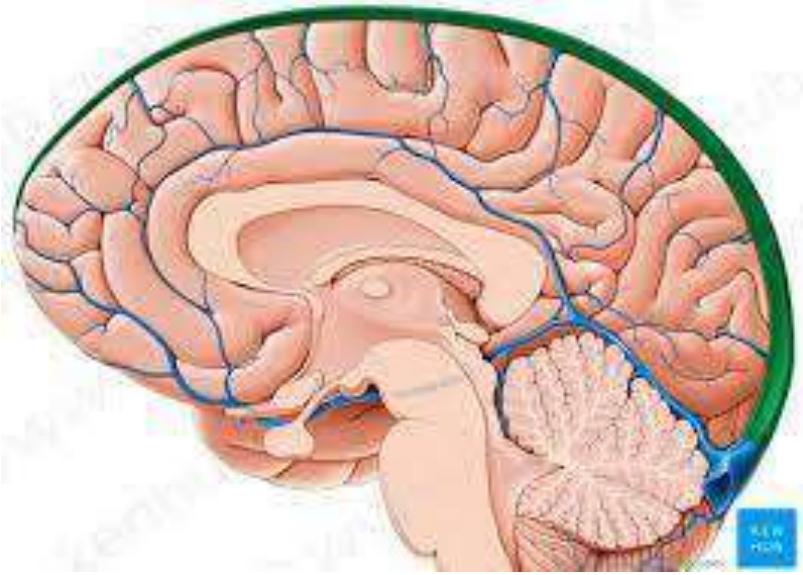
İnferior grup dural venöz sinüsler

- Kavernöz sinüs
- Süperior petröz sinüs
- İnferior petröz sinüs
- Sfenopariyetal sinüs

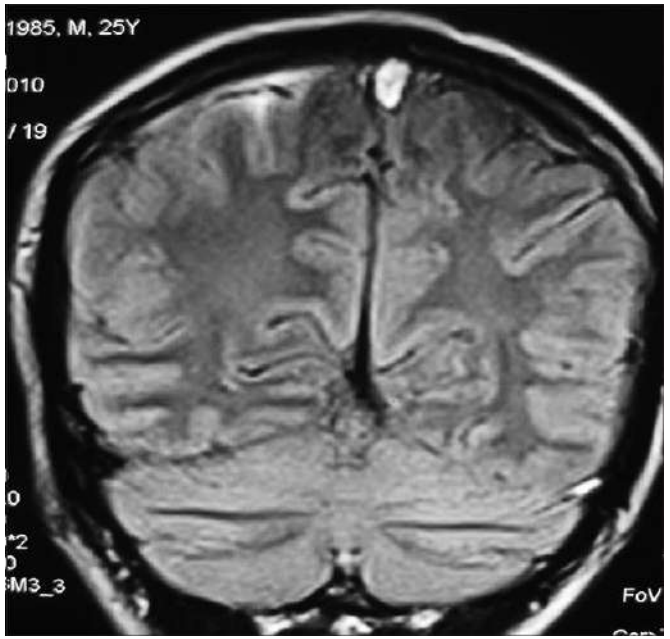
Süperior sagital sinüs (SSS)

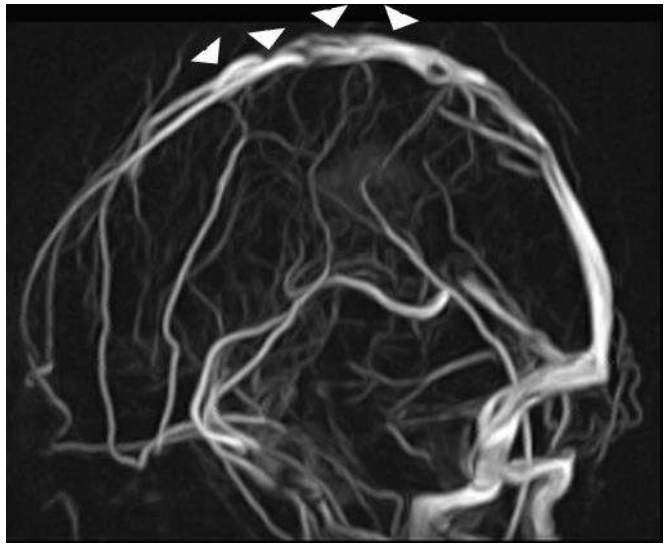
- Krista galli yakınından başlar ve falks serebrinin konveks üst kenarı boyunca arkaya doğru uzanır.
- İnternal oksipital protüberansa yakın bir yerde bir tarafa (genellikle sağ) yönelir ve **transvers sinüs** olarak devam eder.



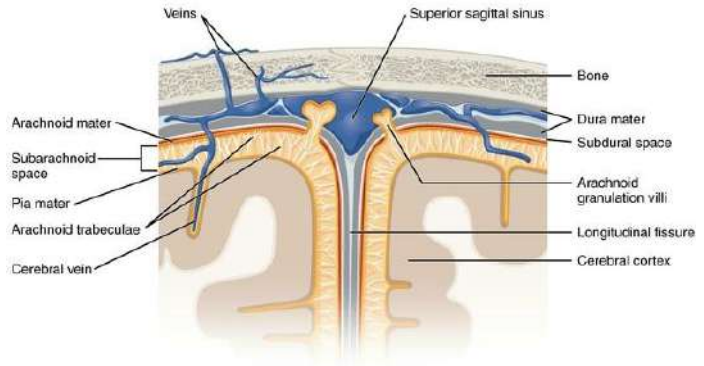


- Arkaya doğru gittikçe genişleyen **SSS** koronal görüntülerde üçgen, sagital görüntülerde yarımay şeklinde görünür.

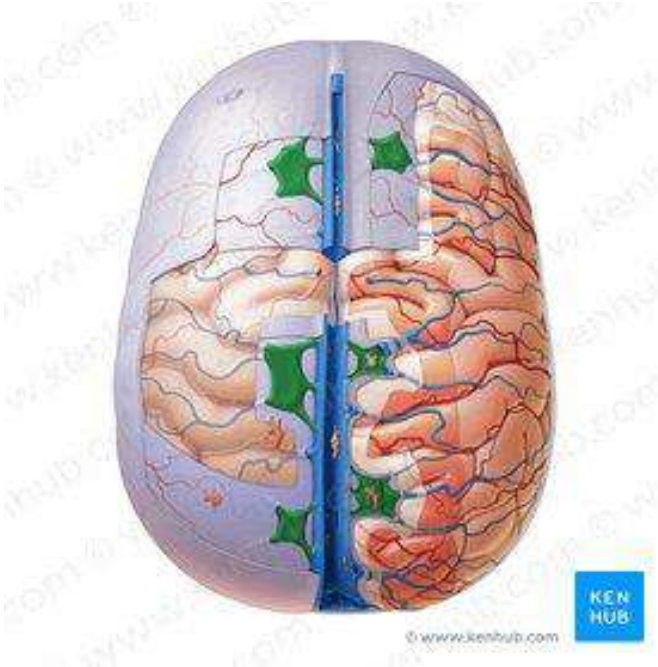




- SSS'ün iç kısmında süperior serebral venlerin sinüse açılma yerleri, **araknoid granülasyonlar** ve inferior kısmında **fibröz bant** yapıları vardır.

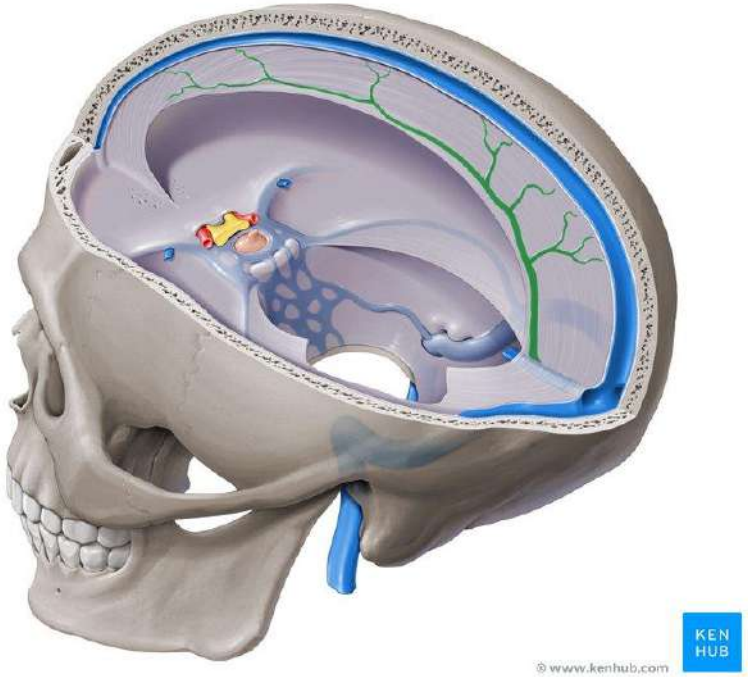


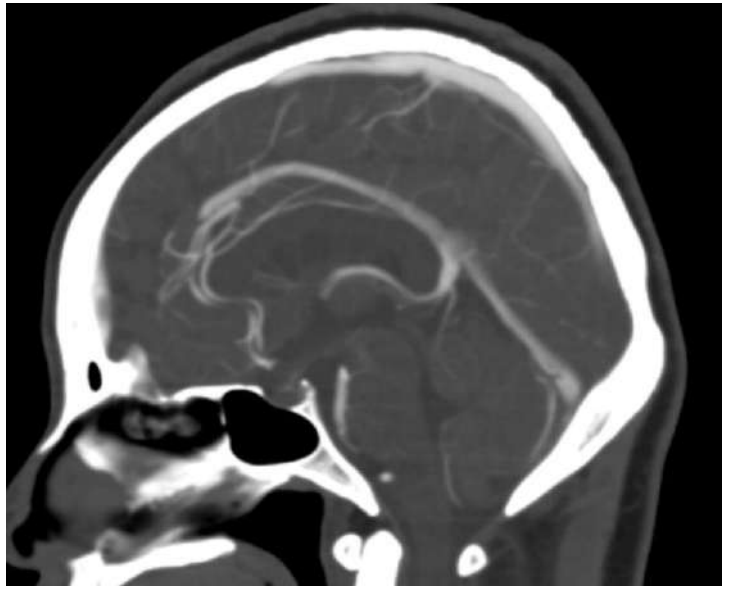
- SSS ayrıca dura mater içerisinde düzensiz şekilli **lateral venöz lakünalarla** da bağlantılıdır.



İnferior sagital sinüs (İSS)

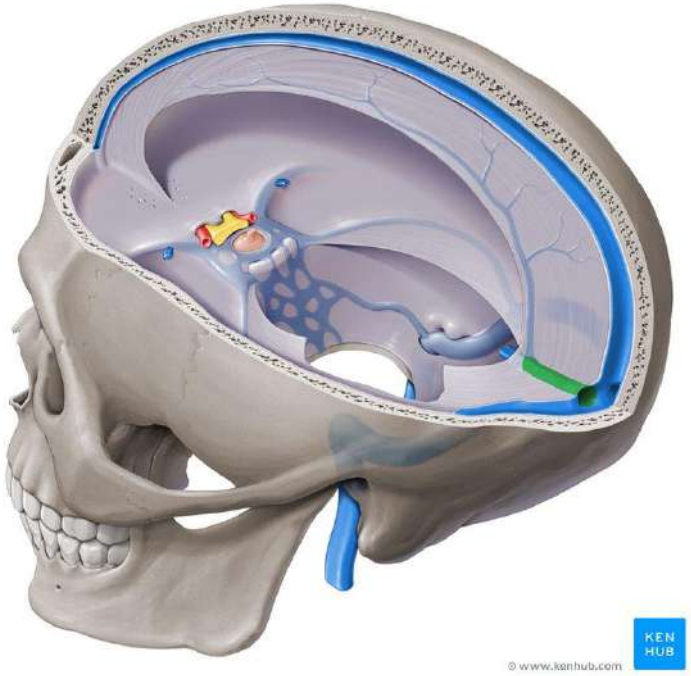
- Falk serebrinin konkav şekilli serbest alt kenarı içerisindedir.
- Korpus kallosumun anterior gövdesi üzerinde başlar.
- Korpus kallosumun splenium kısmının hemen arkasında **Galen veni** ile birleşerek **sinüs rektus**u oluşturur.
- Falks serebri, serebral hemisferlerin medial yüzleri ve korpus kallosumun venöz drenajını sağlar

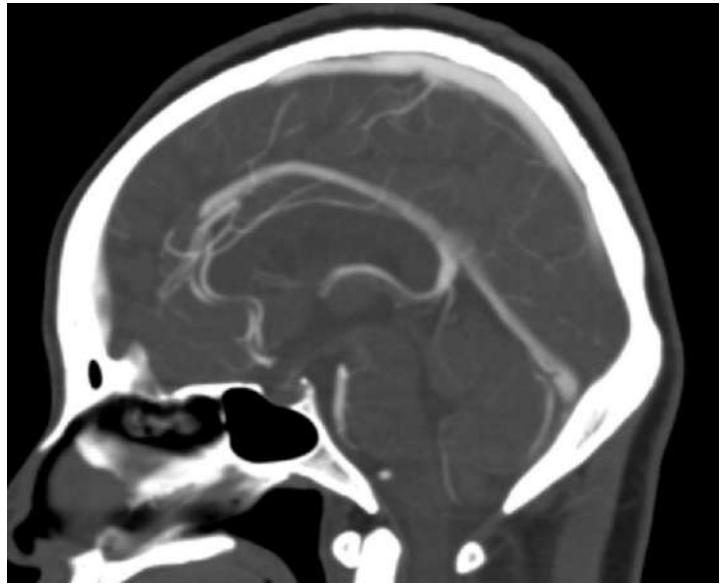




Sinüs rektus

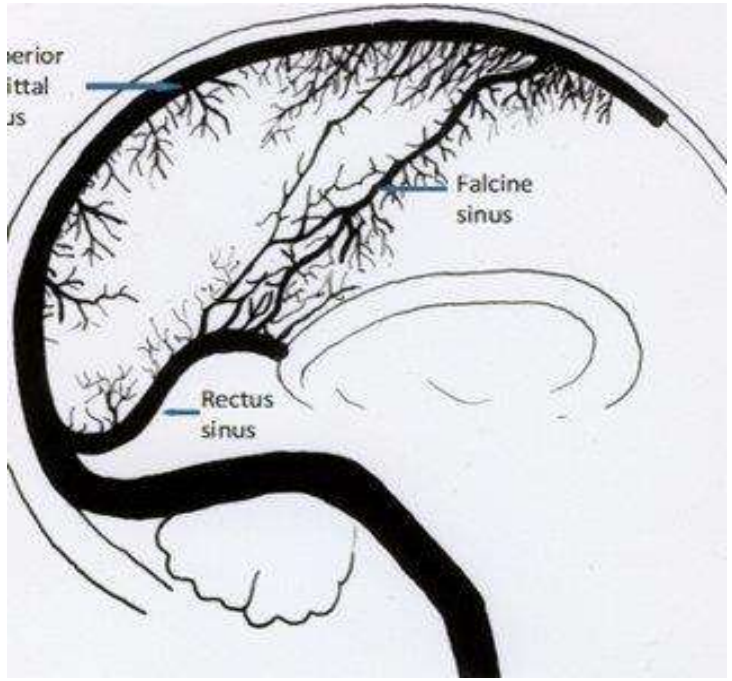
- Falk serebri ve tentorium serebelli bileşkesinde yer alır.
- **İSS** ile **Galen venin**in birleşmesiyle oluşur ve buradan başlayarak posteroinferiora doğru ilerleyerek internal oksipital protuberansa kadar uzanır.
- Burada SSS ile birleşerek **sinüs konfluensi** oluşturur.
- Falk serebri ve tentorium serebelli ve komşu beyin parenkiminden küçük venler alır.

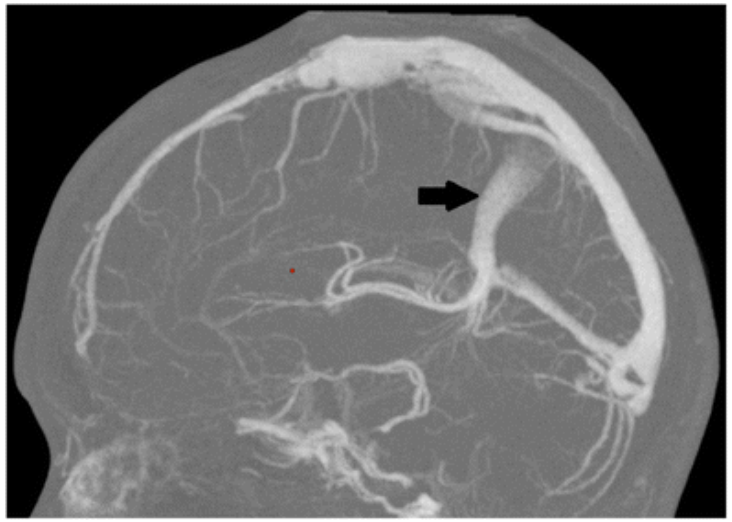




Falsin sinüs

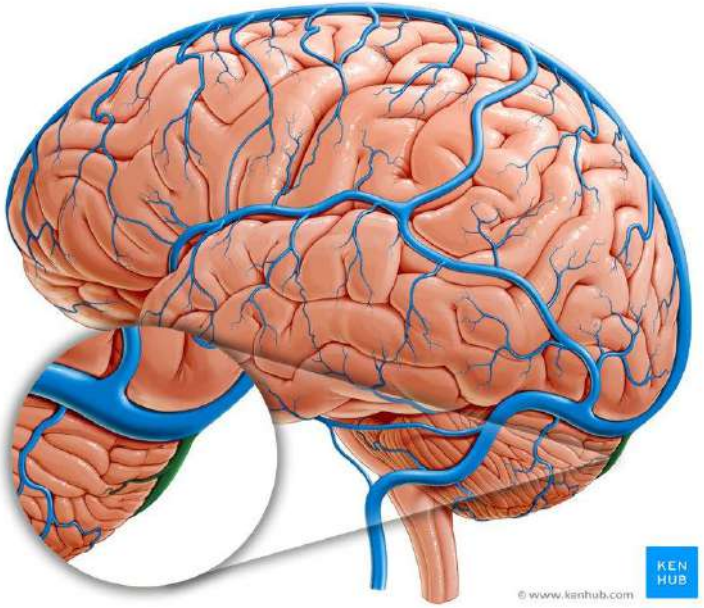
- Falks serebri içinde yerleşen falsin sinüs fetüste normal bir anatomik yapıdır.
- Doğumdan sonra kapanır ve yetişkinlerde nadiren görülür (%2,1).
- Sinüs rektus agenezisi ya da trombozunda persiste edebilir veya rekanalize olabilir.

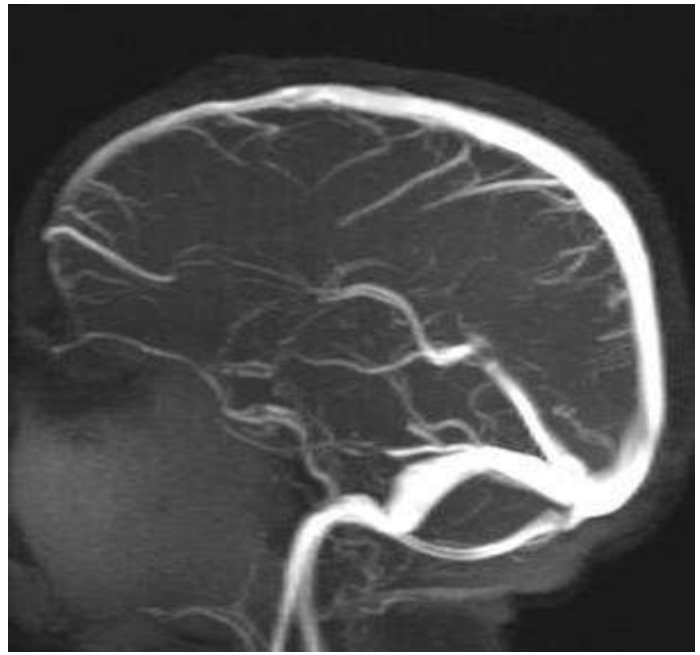




Oksipital sinüs

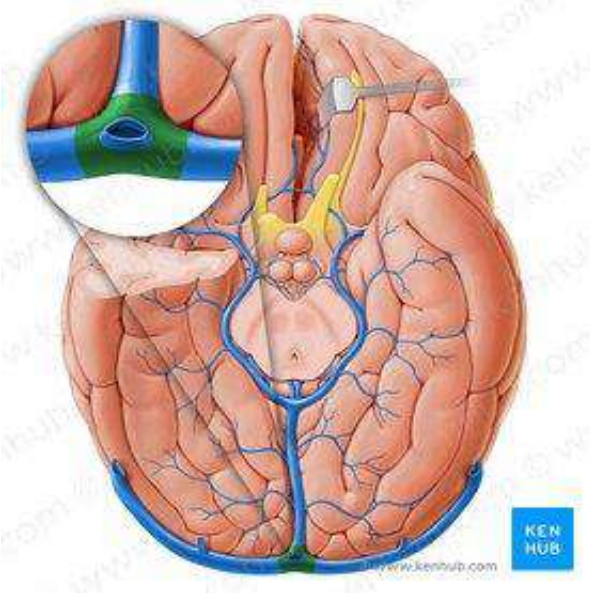
- Foramen magnumdan başlayıp posterosüperiora doğru ilerleyerek (falks serebellinin serbest kenarı boyunca) **sinüs konfluense** dökülür.
- İnferiorda ikiye ayrılıp marjinal sinüs olarak devam eder ve **juguler bulbus**a drene olur.
- Oksipital sinüs her zaman bulunmaz (yetişkin kadavra serilerinde % 64,5-%93).
- Hipoplazik posterior dural sinüslerin varlığında genişleyip esas drenaj yolağı olur.

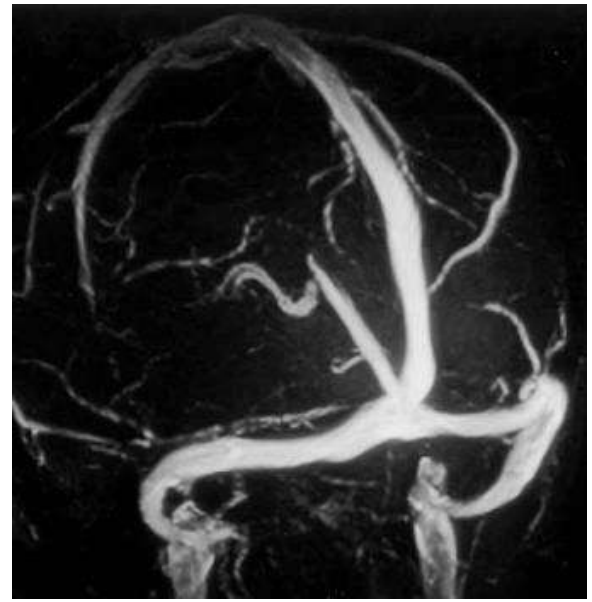




Sinüs konfluens

- **SSS** ile **sinüs rektus**un birleşmesi ile oluşur ya da SSS'ün genişlemiş posterior bölümü tarafından oluşturulur.
- Ayrıca **oksipital sinüs** ve kontrlateral **transvers sinüs**ün birleşim yeridir.
- İnternal oksipital protüberansın sıklıkla sağ tarafına deviye görünümdedir.



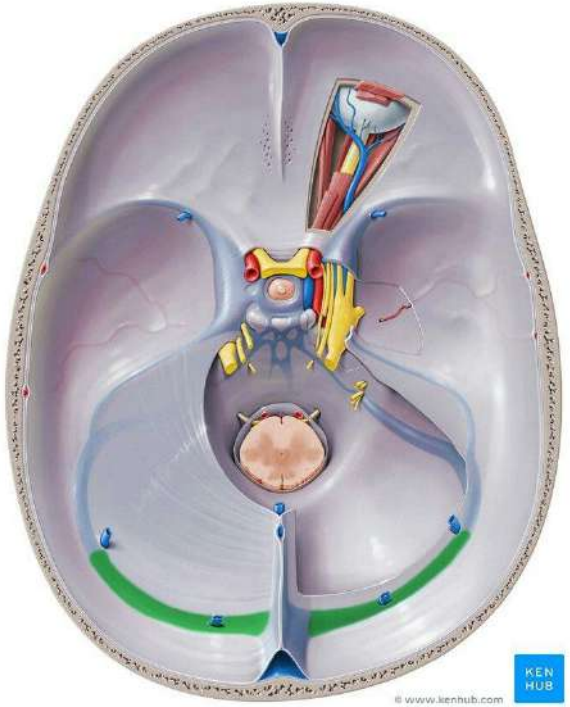


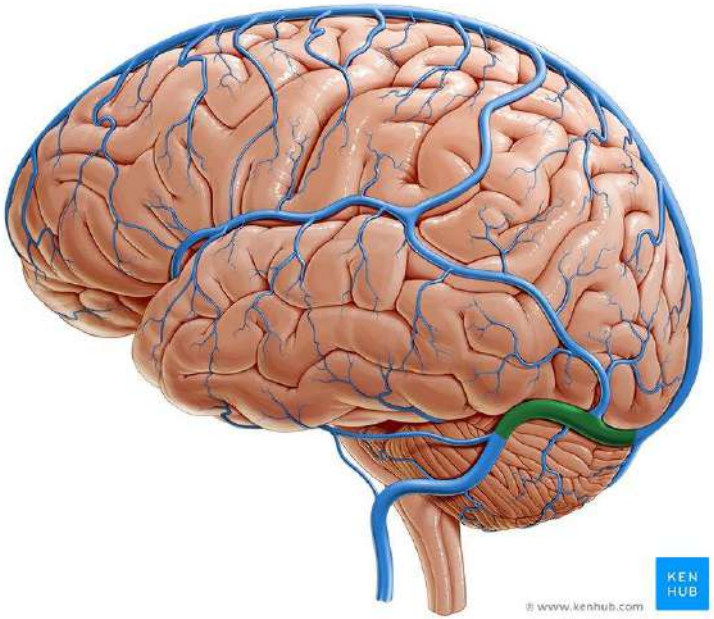
Lateral (transvers ve sigmoid) sinüs

- En büyük dural sinüs

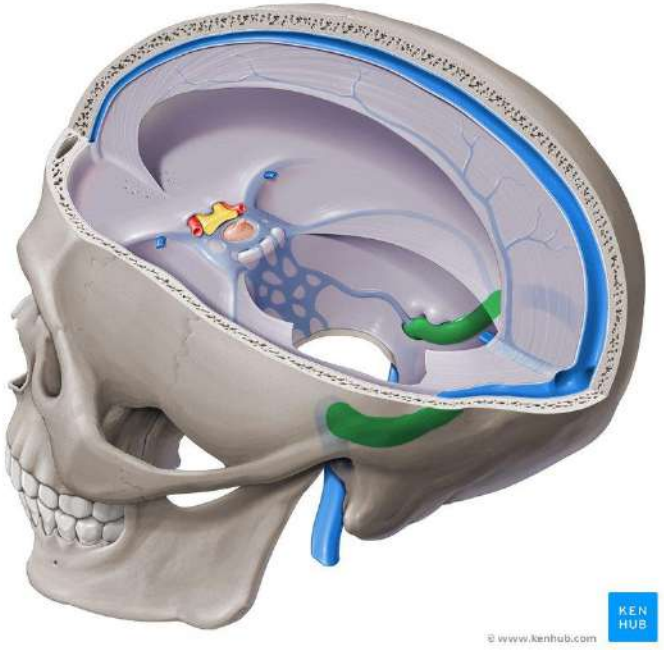
Transvers sinüs

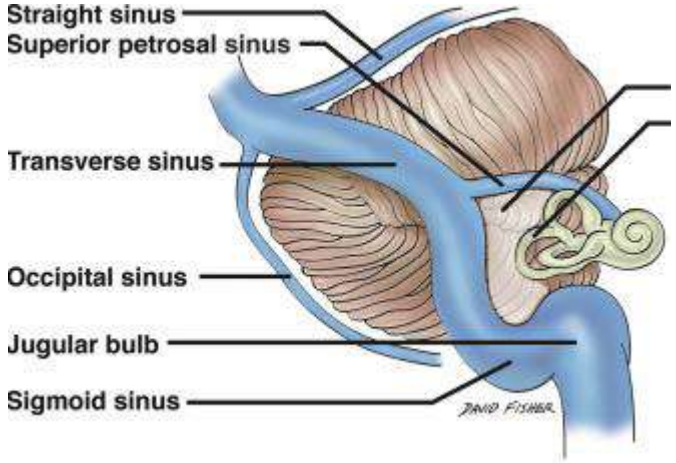
- **Torkular herofili**den başlayıp (oksipital kemiğin **transvers sulkusu** içerisinde) anteroinferiora ve laterale ilerler.
- Süperior petröz sinüs transvers sinüsün terminal kısmına drene olur.





- Transvers sinüs **tentoriumu** geçtikten sonra **sigmoid sinüs** adını alır.
- Mediale ve inferiora doğru uzanır.
- Temporal kemiğin mastoid bölümündeki **sigmoid sulkus** içerisinde S harfi şeklinde seyir gösterir ve **internal juguler vene** ulaşır.
- İnternal juguler venle sigmoid sinüs arasındaki geçiş bölgesine **juguler bulbus** denir.
- **!!! Unilateral aplazi-hipoplazi sık, venöz sinüs trombozu tanısı kayarken dikkat!!**





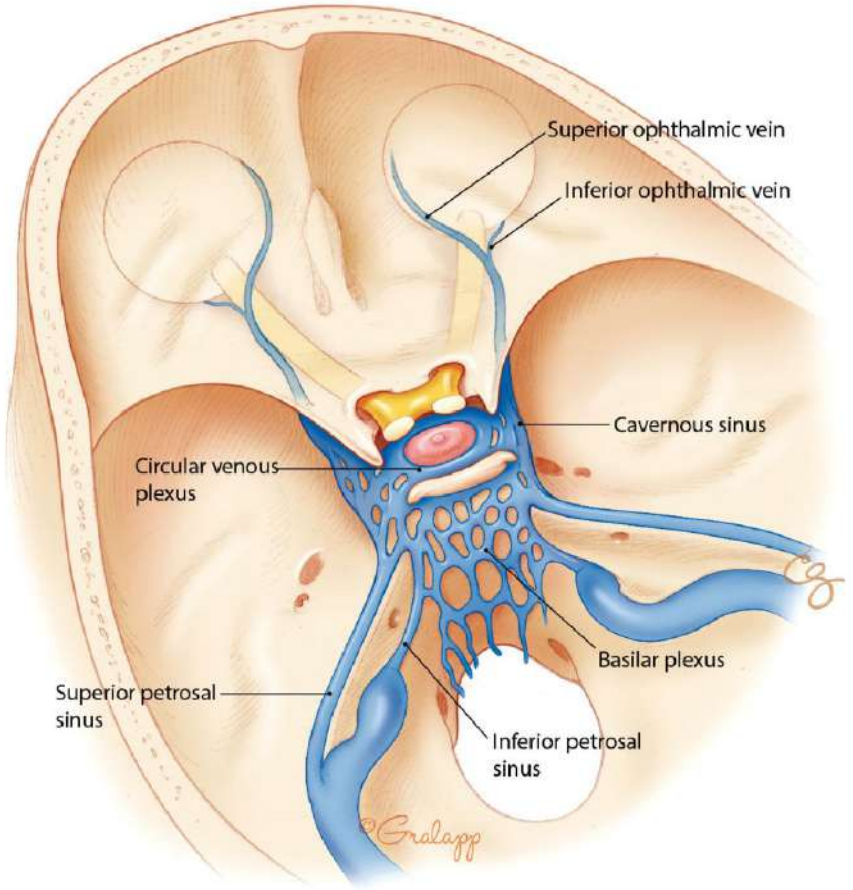
İnferior (bazal) grup dural venöz sinüsler

- Serebrumun alt yüzünde merkezinde **kavernöz sinüs**ün bulunduğu örümcek ağı şeklinde geniş ve oldukça karmaşık bir venöz ağ oluştururlar.

- Kavernöz sinüs
- Süperior petröz sinüs
- İnferior petröz sinüs
- Sfenopariyetal sinüs

Kavernöz sinüs

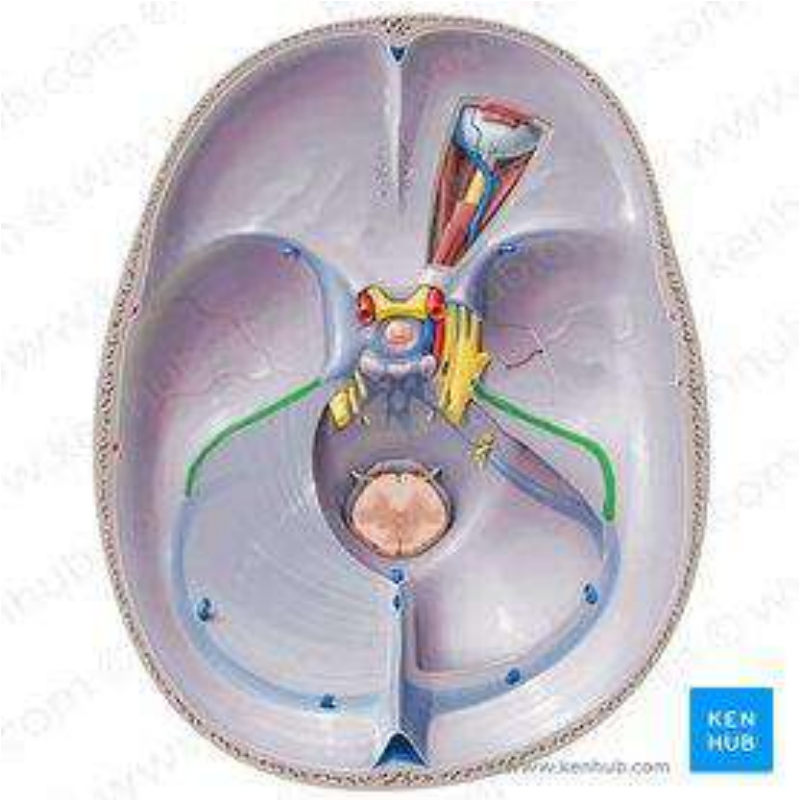
- Sellanın her iki yanında yerleşir ve **interkavernöz sinüsler** aracılığıyla birbirine bağlanır.
- Anterior bölümüne
  - **Sup ve inf oftalmik ven**
  - **Sfenoparietel sinüs** drene olur
- Posterior bölümden
  - **Superior petrozal sinüs**
  - **İnferior petrozal sinüs'e** drene olur.



- **Lateral duvar**
  - Okülomotor sinir
  - Troklear sinir
  - Trigmeninal sinirin oftalmik (V1) maksiller (V2) ve dalları
- **Medial duvar**
  - İnternal karotid arter
  - Abdusens siniri

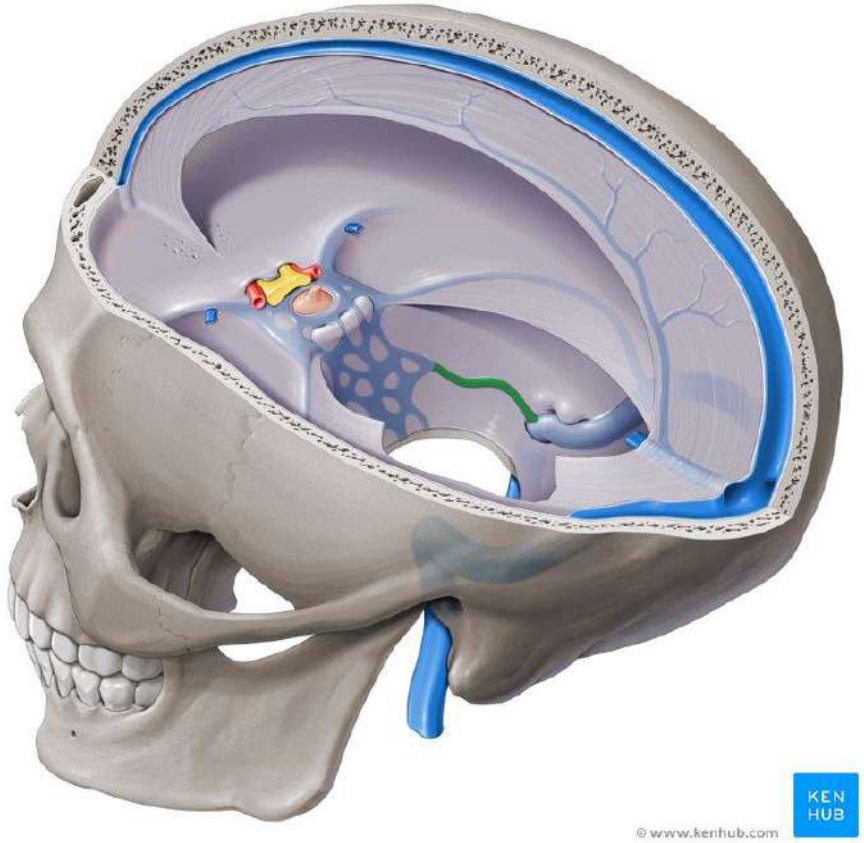
Süperior petröz sinüs

- Kavernöz sinüsün posterior kısmını transvers sinüsün terminal kısmına (kavernöz-sigmoid bileşkesi) bağlar.



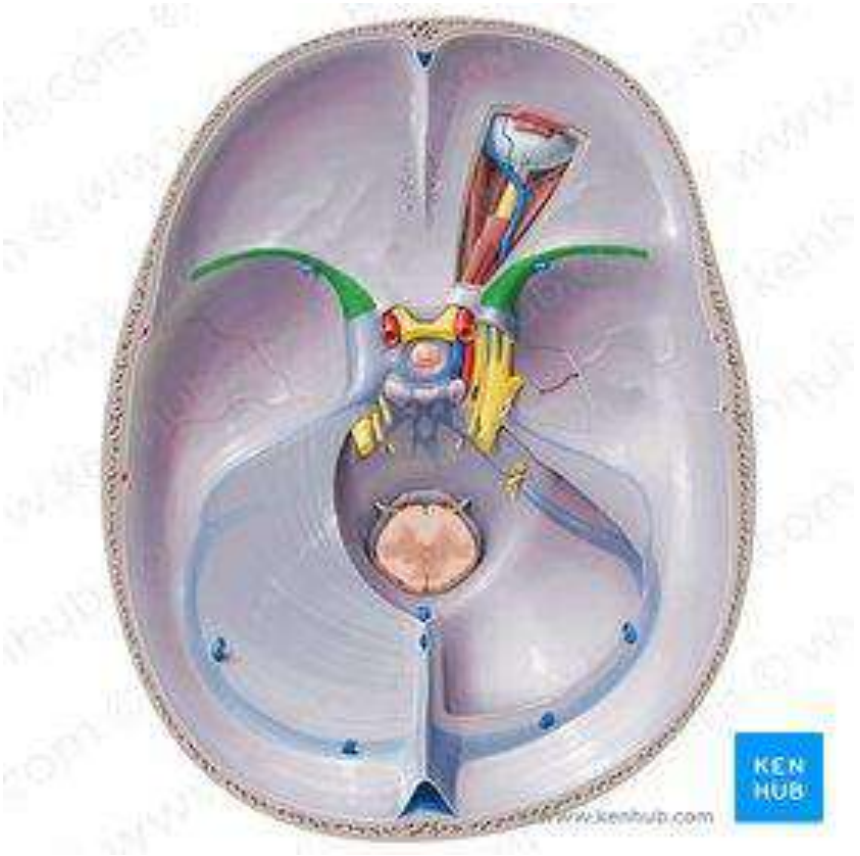
İferior petröz sinüs

- Kavernöz sinüsü internal juguler vene drene eder.



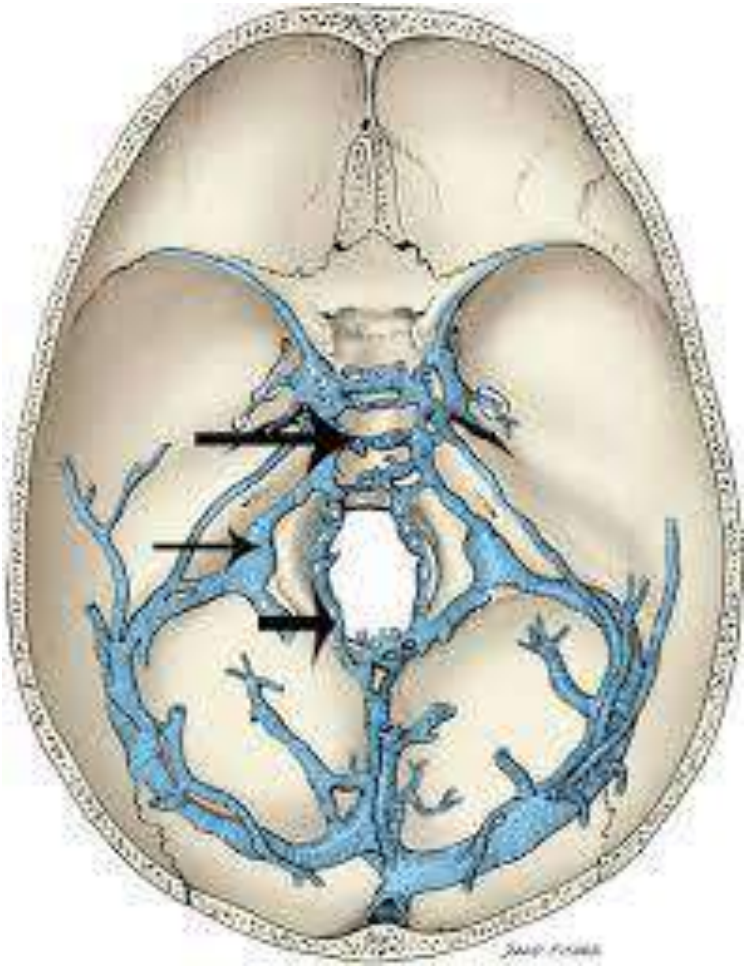
Sfenopariyetal sinüs

- Sfenoid kemiğin küçük kanadının alt yüzü boyunca mediale doğru ilerler.
- Yüzeyel Sylvian venin medialdeki devamıdır.
- Meningeal venler ve frontol lobun orbital girusunu drene eden venler dökülür.
- 3 tipik drenaj paterni vardır
  - Kavernöz sinüse doğru
  - Pterigoid pleksusa doğru
  - İnferior petröz sinüs veya transvers sinüse doğru



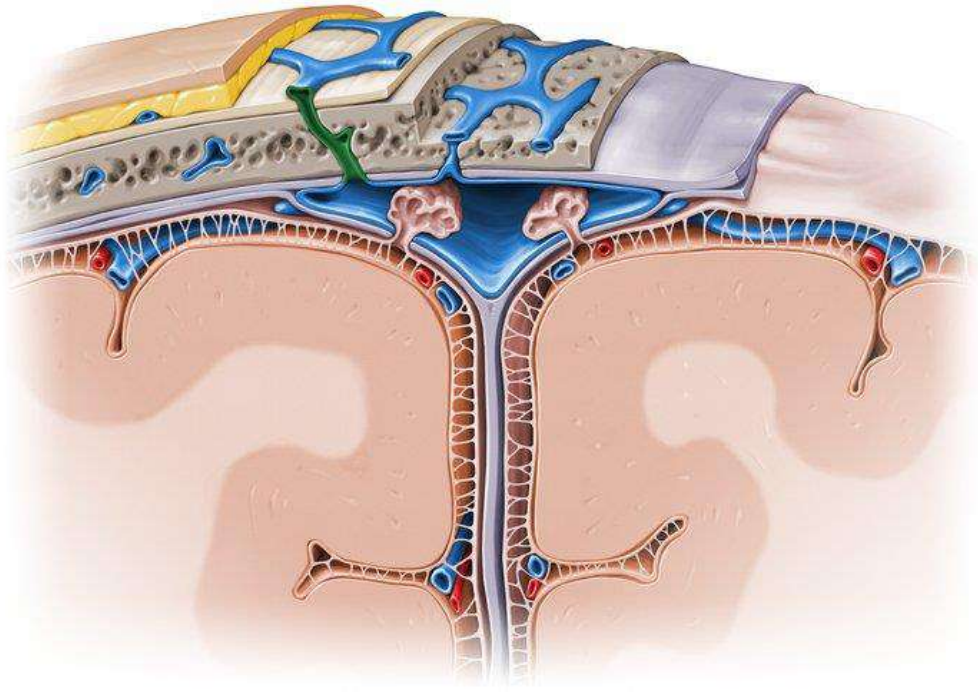
Baziller (oksipital)venöz pleksus

- **Klivus**ta dura içerisinde yerleşmiş birbiri ile iştirakli venöz kanallar ağından oluşur.
- **Kavernöz sinüs** ile **inferior petrozal sinüs** arasında yer alır ve foramen magnuma kadar uzanarak **internal vertebral venöz pleksus** ile devam eder.



Emisser venler

- Dural **venöz sinüslerle ekstrakraniyal venlerin** bağlantı kurmasını sağlar.
- Bu venler , kraniyal kemik yapıları foraminalar aracılığıyla geçerek önemli kollateral yolaklar oluşturur.



Serebral ve serebellar venler

- Araknoid materi ve dura materin iç yaprağını delerek kraniyal venöz sinüslere ulaşırlar.
- Yerleşim yerlerine göre ikiye ayrılırlar
  - **Supratentoryal venler**
    - Serebral hemisferlerin drenajını sağlar
  - **İnfretentoryal venler**
    - Serebellum ve beyin sapını drene eder

Serebral supratentoryal (hemisferik) venler

YÜZEYEL SEREBRAL (KORTİKAL) VENLER

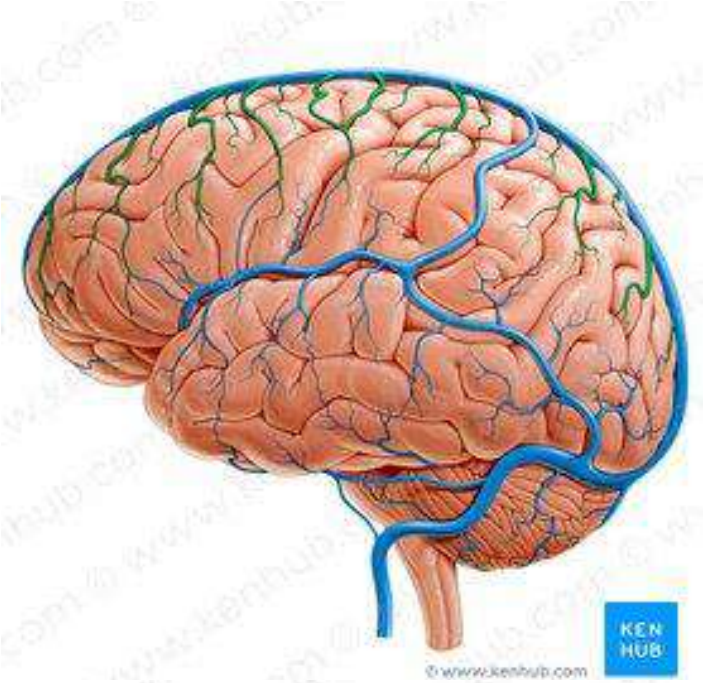
- **Süperior serebral venler**
  - Lateral konveksite venleri
  - Medial taraf venleri
- **Yüzeyel orta serebral (Sylvian) venler**
- **İnferior serebral venler**
  - Lateral konveksite venleri
  - Medial taraf venleri
  - Bazal taraf venleri

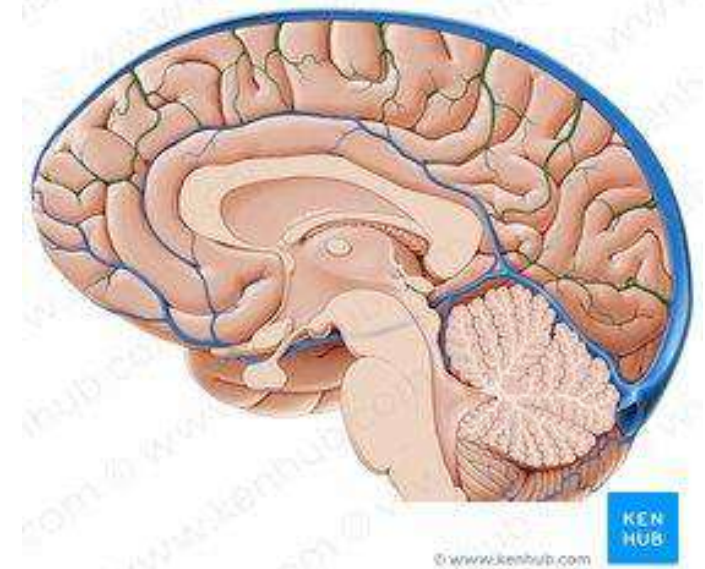
PARANKİMAL VENLER

- **Yüzeyel parankimal venler**
  - İntrakortikal venler
  - Subkortikal venler
  - Yüzeyel medüller venler
- **Derin parankimal venler**
  - Derin medüller venler
  - Subependimal venler
- **Transserebral ve anastomotik venler**

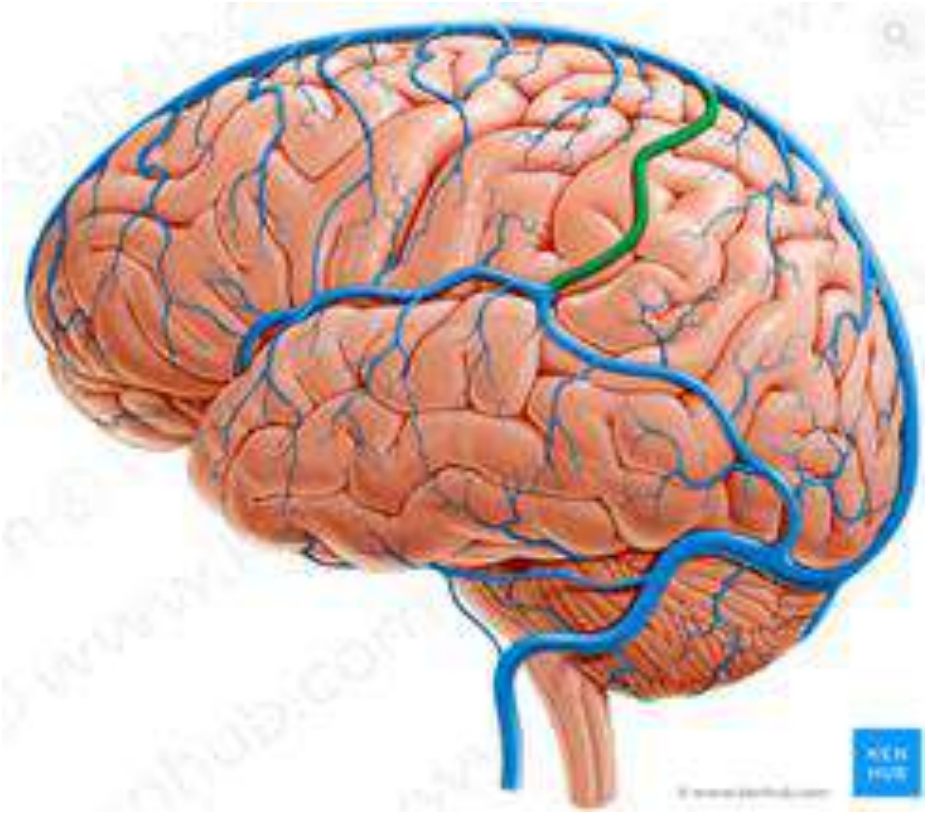
Süperior serebral venler

- **Medial grup venleri** interhemisferik fissür içerisinde, **lateral grup venleri** lateral serebral yüzde ilerleyip araknoid membranı delerek birleşir ve **SSS**'e açılır.
- SSS'e kadar olan bu bölüm **"köprü venleri"** olarak adlandırılır.
- Travmaya bağlı gelişen subdural hematomlarda kanamanın kaynağı bu venlerdir.



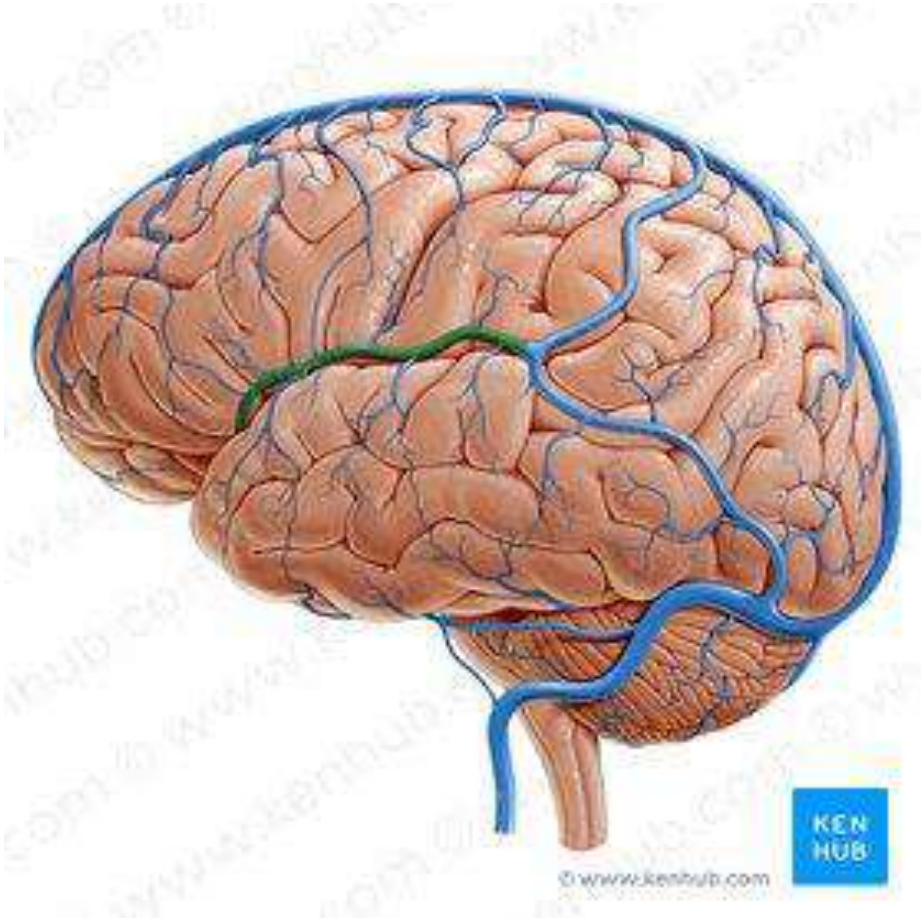


- Parietal bölgede birçok **lateral süperior serebral ven** 2-3 ana trunkus şeklinde veya tek trunkus şeklinde (**Trolard veni – süperior anastomotik ven**) birleşir.
- Trolard veni yetişkinlerin 1/3'ünde bulunur.
- **SSS** ile **yüzeyel orta serebral ven**i (Sylvian ven) birbirine bağlar



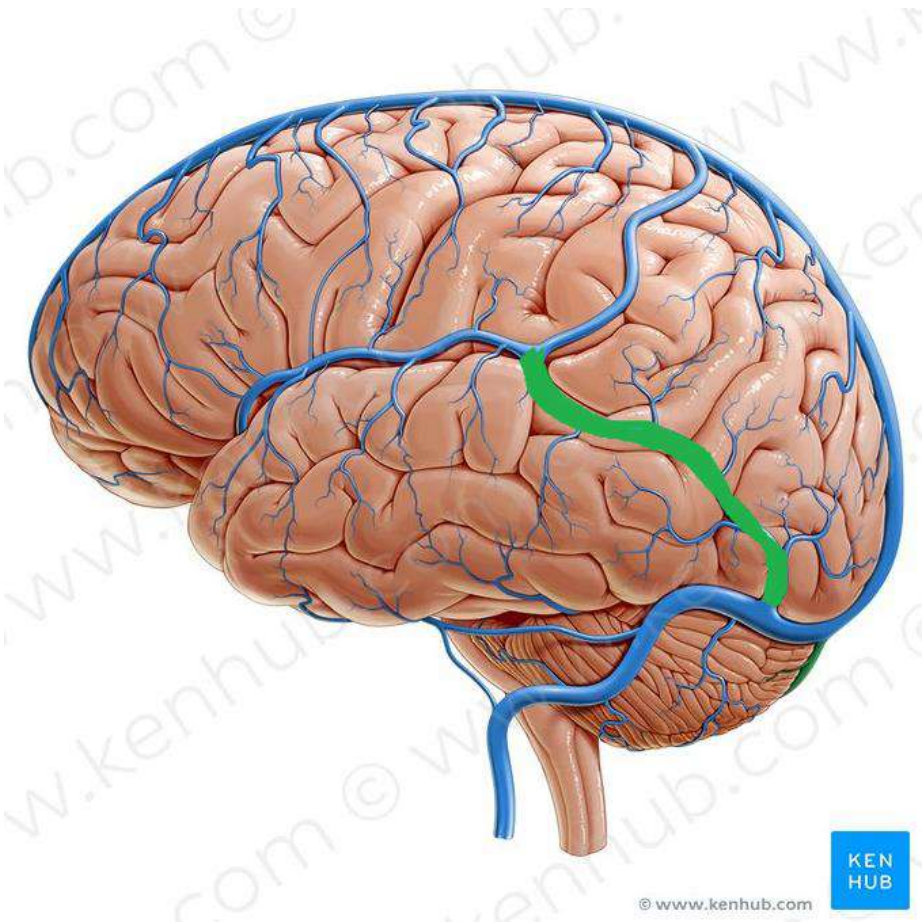
Yüzeyel orta serebral ven (Yüzeyel Sylvian ven)

- Operkulum ve lateral serebral fissür (Sylvian fissür) komşuluğundaki alanları drene eder.



İnferior serebral venler

- **Serebrumun lateral yüzü**nün alt kısımlarını, **oksipital** ve **temporal** lobların alt yüzlerini drene eder.
- Sylvian fissürden inferiora ve posteriora doğru ilerleyerek transvers sinüse ulaşan büyük trunkus **Labbe veni (inferior anastomotik ven)** olarak adlandırılır.
- Labbe veni anjografik olarak % 70 sağda bulunur.
- **!!!** Labbe veni geniş olduğunda Trolard veni ve Sylvian ven oldukça küçük çaplı olur veya hiç izlenmez.



Parankimal venler

Yüzeyel parankimal venler

- Serebral korteks (intrakortikal venler)
- Subkortikal ak madde (subkortikal venler)
- Yüzeyel medüller venleri drene eder

Derin parankimal venler

- Derin ak maddenin drenajını sağlar
- Ak madde içerisinde ventriküler tarafa yakın, derin bir seyir gösterip genellikle lateral ventrikülün süperolateral köşesine doğru konverjans gösterek **subependimal venlere** dökülürler.

Transserebral ve anastomotik venler

Teşekkürler

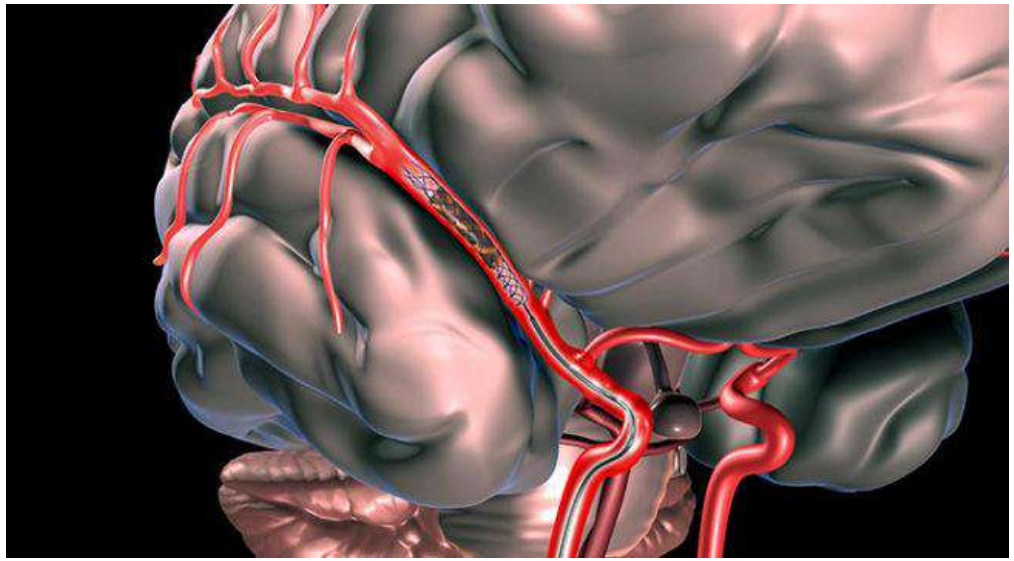
Akut İnme Endovasküler Tedavisi Sırasında Anestezi, Sedasyon, Lokal Anestezi

Dr. Ayşenur Önalan

Kartal Dr. Lütfi Kırdar Şehir Hastanesi

İnme Merkezi

- Akut iskemik inmede oklude olan damarın beslediği alana bağlı olarak hastada nörolojik bulgular belirir ve en önemlisi şuuru etkilenebilir.



Görüntüleme seçimi

Büyük damar okluzyonu iyi klinik

Sınırda büyük core

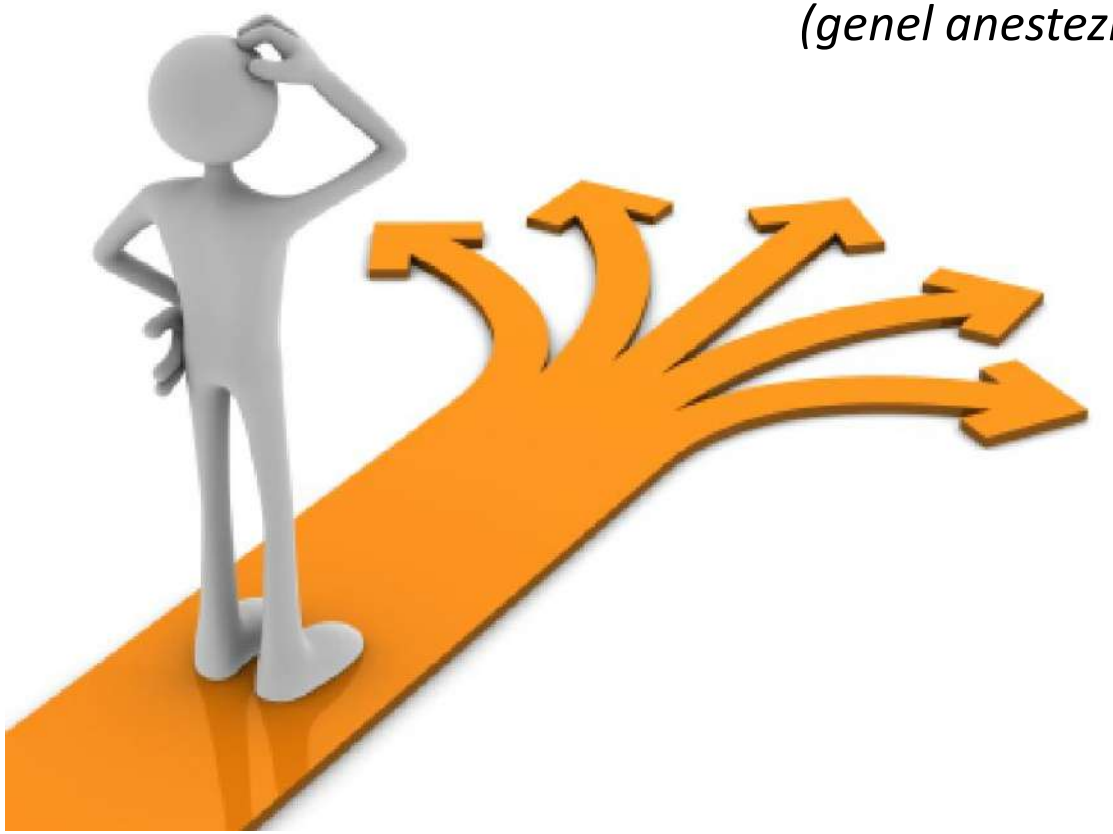
Anestezi seçimi

Uygulanacak teknik

.....

Zaman kaybını en az düzeye indirme ve hemodinamik stabilitenin sağlanması açısından perioperatif anestezi stratejisini iyi belirlemek gerekir!!!

(genel anestezi? bilinçli sedasyon? ilaç seçimi?)



Sedasyon Derinliği

	Hafif sedasyon (anksiyolizis):	Orta sedasyon/analjezi (bilinçli sedasyon):	Derin sedasyon/analjezi:	Genel anestezi:
Yanıt	Verbal uyarana normal yanıt	Verbal veya taktil uyarana anlamlı yanıt	Tekrarlanan veya ağrılı uyarandan sonra anlamlı yanıt	Ağrılı uyaranla bile uyandırılamaz
Havayolu	Etkilenmez	Girişim gerekmez	Girişim gerekebilir	Sıklıkla girişim gerekir
Spontan solunum	Etkilenmez	Yeterli	Yetersiz olabilir	Genellikle yetersiz
Kardiyovasküler fonksiyon	Etkilenmez	Genelde sürdürür	Genelde sürdürür	Bozulmuş olabilir

Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018.A Report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology*. Anesthesiology. 2018;128(3):437-79.

Anestezi Tekniği
Bilinçli Sedasyon

- Hoş olmayan, ağrılı prosedürlerin tolere edilmesine ve prosedürle ilişkili olası istenmeyen anılardan kaçınılmasına yardımcı olur.
- Hastanın ağrı algısını da azaltması amaçladığından sedatifler analjezikler ile kombine edilir.
- İdeal ajan sedatif, analjezik ve amnestik özelliklerin yanı sıra hızlı bir başlangıç ve kısa etki süresine sahip olmalıdır.

Anestezi Tekniği

GENEL ANESTEZİ

- **AVANTAJ:**
- Hava yolu kontrolü
- Ağrı kontrolü
- Hasta immobilitesi, daha iyi görüntüleme
- **DEZAVANTAJ:**
- Revaskülarizasyon süresi uzar
- Hipotansiyon ; daha fazla iskemik hasar

BİLİNÇLİ SEDASYON

- **AVANTAJ:**
- Daha kısa revaskülarizasyon süresi
- Daha az hemodinamik problem
- İşlem boyunca daha iyi nörolojik değerlendirme
- **DEZAVANTAJ:**
- Hasta hareketliliğine bağlı prosedurel komplikasyonlar,
- Daha yüksek doz radyasyon maruziyeti,
- Daha fazla kontrast madde ihtiyacı
- Hava yolu kontrolünün olmaması

Midazolam

Anksiyolitik, Amnestik, Sedatif, Hipnotik, Kas gevşetici ve Antikonvulzan etkileri vardır ancak **Analjezi sağlamaz.**

Solunum depresyonuna ve hipotansiyona neden olabilir.

IV Doz : 2-2.5 mg, 2-5 dk sonra tekrarlanan 1 mg'lık dozlar (genelde 5mg'dan fazla gerekmez)
60 >yaş ve kronik hastalığı olanlarda: başlangıç dozu 0,5-1 mg, ve en az 30 saniyede 1 mg) (genelde 3.5mg'dan fazla gerekmez)
Etki Başlangıcı: 2-3dk, Max etki 5-10 dk,
Yarılanma Ömrü (t½): 1-2.5 saat

Özellikle yaşlı hastalarda rebound ajitasyona yol açabileceği akılda tutulmalıdır.

Antidotu

Ancak ilacın etki süresi sedatif ajandan daha kısa bu nedenle yeniden sedasyona neden olabileceği düşünülerek dikkatli olunmalıdır.

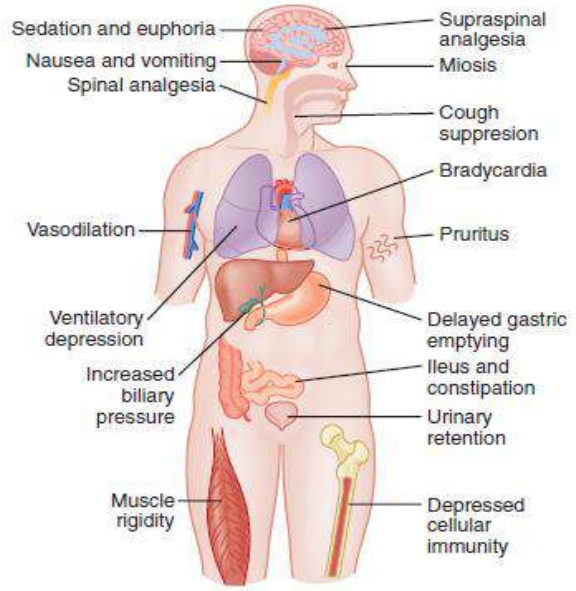
- **IV Doz:** Dakikada 0.2 mg. Max: 20 dakikada bir 1.0 mg
  - Pratikte:
    - **Her 1mg midazolam için 0,1mg flumenazil**
- **Etki Başlangıcı:** 1dk
- **Yarılanma Ömrü (t½):** 45 dk

Fentanil(IV/IM)

Opioid Analjeziktir, anksiyolitik etkisi yoktur

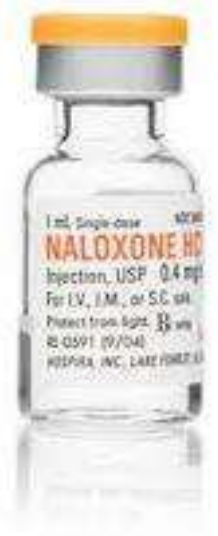
Bulantı, kusma, hipotansiyon, bradikardi ve solunum depresyonu yapabilir.

IV Doz: 1-1.5 mcg/kg başlangıç dozu ve ardından her 3 dakikada bir 1 mcg/kg titre
Etki Başlangıcı: IV: 1-2 dk
Yarılanma Ömrü (t½): 30-60 dk



Özellikle geri çekilen stentlerin çekilme işlemi sırasında hasta ciddi bir başağrısı çekebilir. Bu esnada işlemin konforunu önemli ölçüde arttırır.

- Opioid antidotu



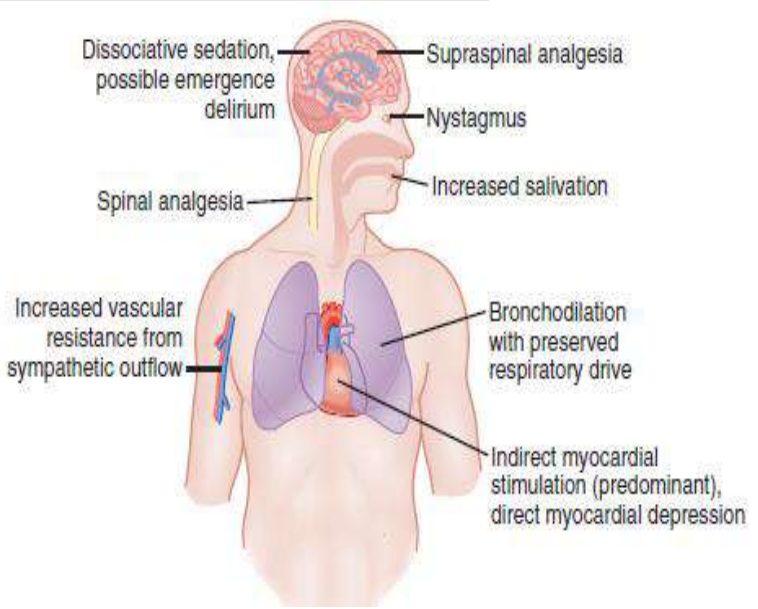
- **IV Doz:** 0.1 ila 2.0 mg
- **Etki Başlangıcı:** 1dk
- **Yarılanma Ömrü (t½):** 15-30 dk

Ketamin (IV/IM)

Kuvvetli analjezik ve hafif hipnotik özellikleri olan ve hızlı etki ortaya koyan anestetik bir ajandır.

Ketaminin tek başına kullanımını takiben kan basıncı ve nabız hızı yükselebilir.

IV Doz: IV: 1-3 mg/kg.
Etki Başlangıcı: 1 dk (ıv)
Yarılanma Ömrü (t½): 5-15 dk



Ajitasyon, laringospazm ve kusma yapabilir. Son doz sırasında benzodiazepin uygulanması bu yan etkileri ortadan kaldırmaya yardımcı olur.

ETOMİDAT(IV)

Amnestik, Sedatif, Hipnotik olup Analjezik etkisi yoktur

Sık yan etki olarak miyoklonusa (1/3 hasta) ve intravenoz enjeksiyon ağrısına neden olmaktadır.

IV Doz: 0,3 mg/kg.
Etki Başlangıcı: IV: 1-2 dk, Süre 5-7 dk
Yarılanma Ömrü (t½): 30-60 dk

Beraberinde fentanil veya midazolam kullanıldığında miyoklonik aktivite, enjeksiyon ağrısının ve postoperatif venoz komplikasyonların azaldığı bildirilmiştir

Deksmedetomidin (IV)

Sedatif, analjezik, anksiyolitik özelliklere sahip bir α-2-agonisttir.

Solunumu baskılamaması ve sempatik tonusu düşürerek cerrahiye stres yanıtı azaltması açısından nöro-girişimsel işlemlerde tercih edilebilecek bir ajandır

Bradikardi ve hipotansiyona yol açabilir.

IV Doz: 1 mcg/kg.
Etki Başlangıcı: 3-5 dk
Yarılanma Ömrü (t½): 15 dk

Dexmedetomidin, benzodiazapine alternatif olarak kullanılabilir.

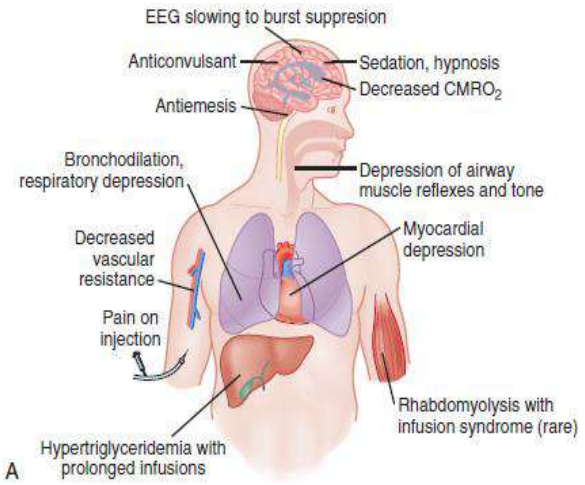
Propofol (IV)

Lipofilitesi yüksek, kan beyin bariyerine geçiş hızlı

Düşük dozlarla sedatif, hipnotik, anksiyolitik ve antiemetik özelliği vardır.
Ancak analjezi sağlamaz.

Sistemik vazodilatasyon etkisinden dolayı hipotansiyon ve solunum depresyonu oluşturur

IV Doz: 1 ila 2 mg/kg. Yetişkin (zayıf): 0,5 ila 1 mg/kg
Etki Başlangıcı: IV: 15-30 sn
Yarılanma Ömrü (t½): 1-3 dk



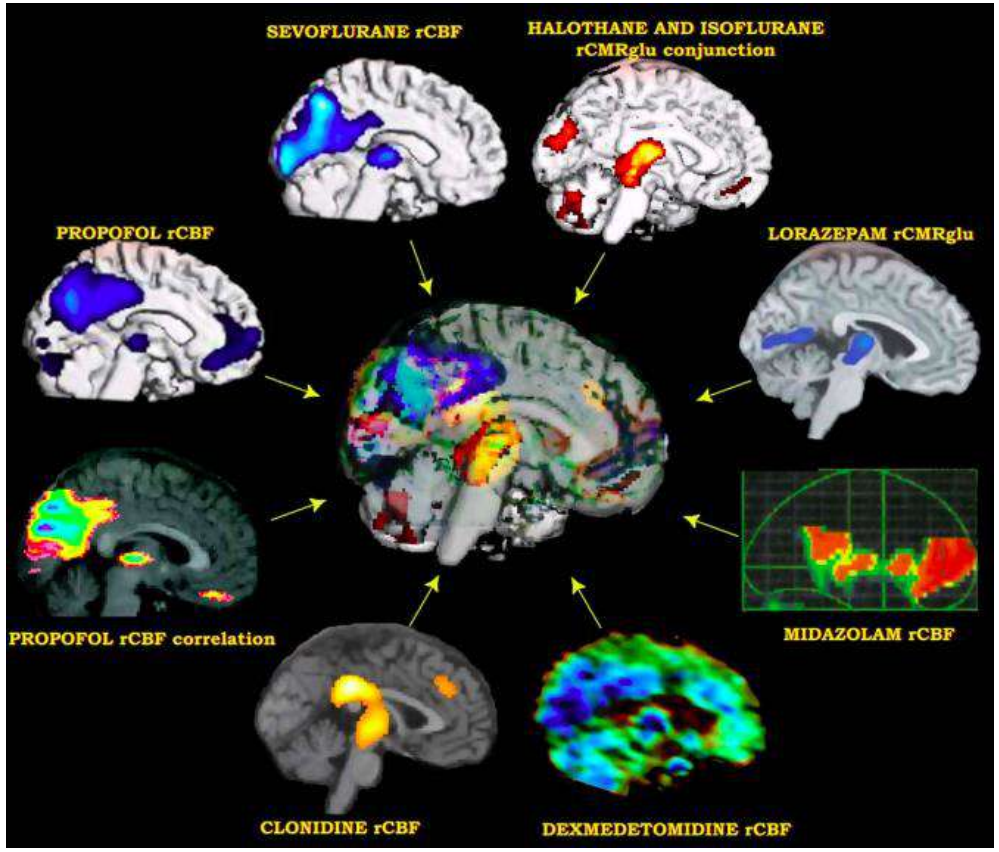
Bazı çalışmalarda propofolün nöroprotektif özelliği olduğu belirtilmiştir.[1]

1-Zwerus R, Absalom A. Update on anesthetic neuroprotection. Current Opinion in Anesthesiology. 2015;28(4):424-30.

Volatil (uçucu) anestezik ajanlar

- Sistemik hemodinamik stabiliteyi sağlar, ancak inhalasyon anestetikleri serebral vazodilatasyonu indükler.
- Beyin kan akımını arttırır ve prosedür sırasında nörofizyolojik takibe izin vermez.
- Tüm volatil anestetiklerin potent olarak serebral vazodilatatör olduğu ve serebral kan akımını artırdığı kabul edilir.

- Genel anestezi uygulaması sırasında volatil (uçucu) anestezik ajanlar *(isofluran, desfluran, sevofluran)* ve/veya iv anestezik ajanlar *(propofol, etomidat, ketamin)* kullanılabilir.

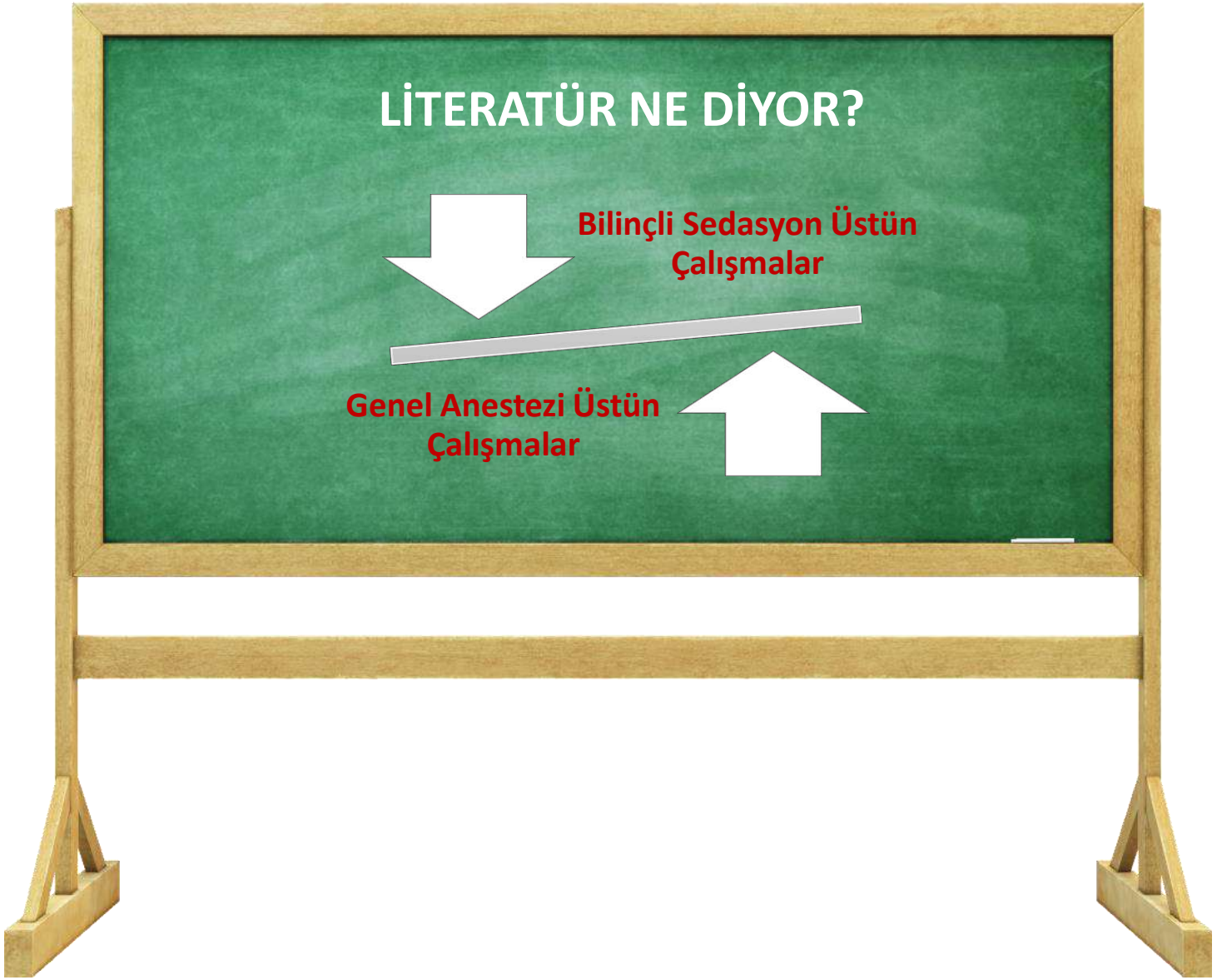


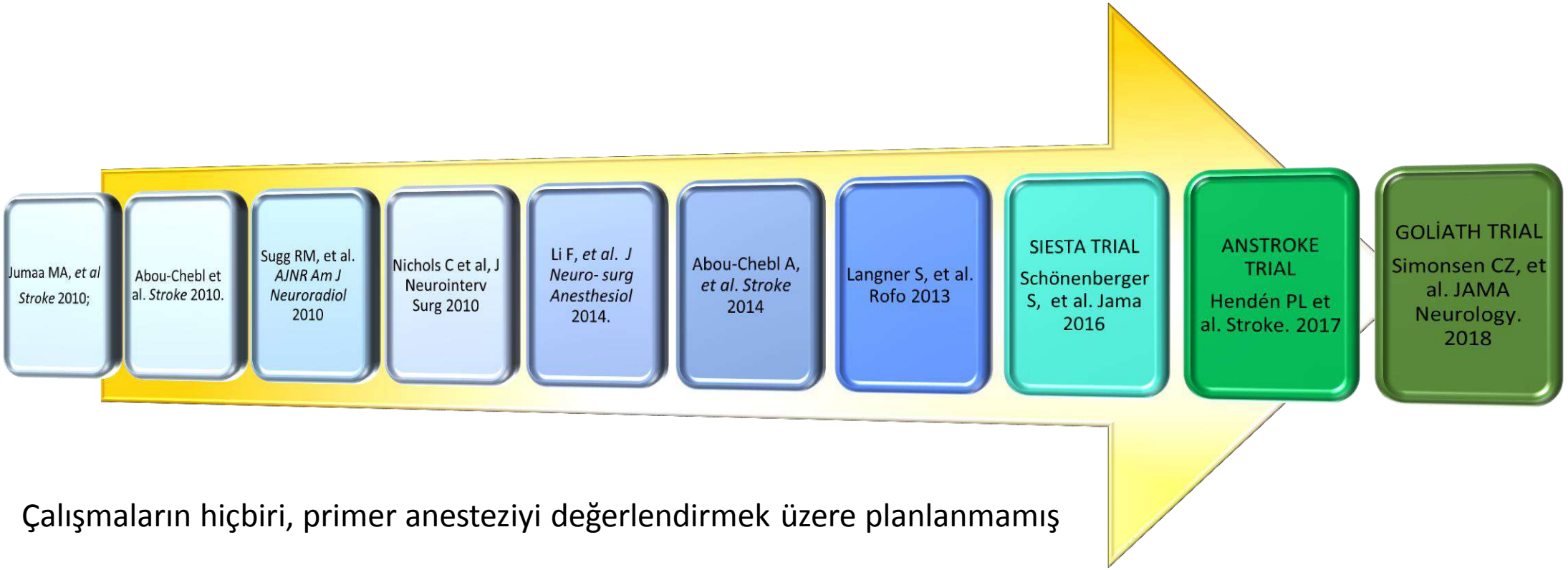
Alkire, M. T., & Miller, J. (2005). *General anesthesia and the neural correlates of consciousness. The Boundaries of Consciousness: Neurobiology and Neuropathology, 229–597.*

- **Fentanil+midazolam kombinasyonu,** en çok benimsenen prosedürlerden biridir, ancak diğer kombinasyonlar da (örneğin, propofol+fentanil veya propofol+ketamin kombinasyonu) benimsenmiştir.[1]
- **Dexmedetomidin,** benzodiazepine alternatif olarak kullanılabilir.[2]
- **Sedatif/analjezikler;** küçük miktarlarda, titre edilerek, artan dozlarda veya infüzyon şeklinde uygulanabilir.[2]
- **Sedatiflerle birlikte uygulanabilecek opioidler:** Fentanil, remifentanil, alfentanil, meperidine, morfin

1-Procedural Sedation. Benzoni T, Cascella M. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.2022 Feb 5. Bookshelf ID: NBK551685

2-Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018A Report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology. Anesthesiology. 2018;128(3):437-79.


LİTERATÜR NE DİYOR?
Bilinçli Sedasyon Üstün Çalışmalar
Genel Anestezi Üstün Çalışmalar



Çalışmaların hiçbiri, primer anesteziyi değerlendirmek üzere planlanmamış

- ✓ Az sayıda çalışma kan basıncındaki değişiklikler, uygulanan anesteziklerin türü ve dozu hakkında ayrıntılı veri sunmuştur.
- ✓ NIHS yüksek hastaların GA altında tedavi edilme olasılığının daha yüksek görünmekte

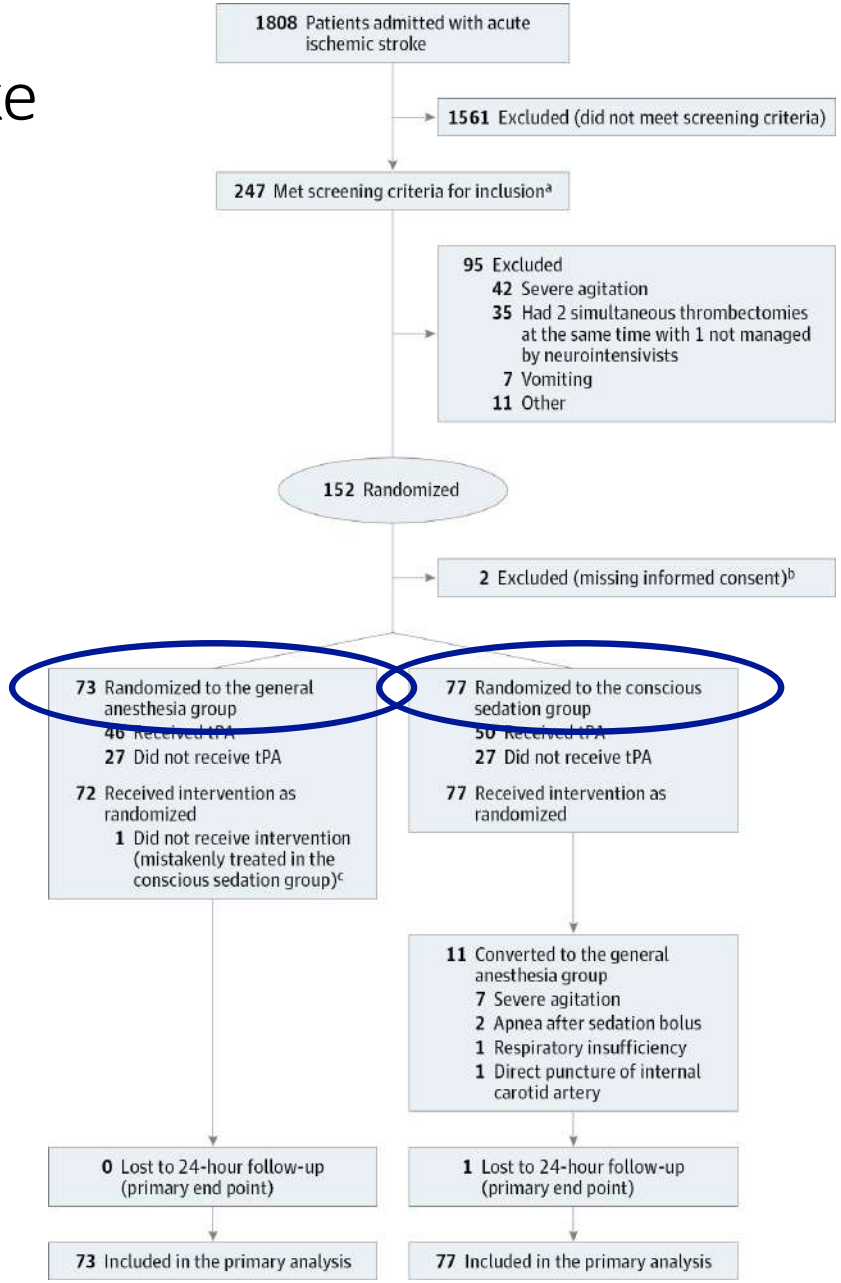
Trial, Year, Author	N	Study population	Mono-/ multicentric	Mode of Sedation	Results
Nichols (31) 2009	81	AIS (anterior circulation)	Monocentric	CS vs. GA	CS associated with: – higher rate of good outcome – lower mortality
Sugg (34) 2010	66	AIS (anterior and posterior circulation)	Monocentric	CS vs. GA	CS associated with: – better outcome – lower complication rate
Abou-Chebl (15) 2010	960	AIS (anterior cirulation)	Multicentric (12 centers)	CS vs. GA	GA independent predictor of: – worse outcome – higher mortality
Brekenfeld (43) 2010	40	AIS	Monocentric	CS vs. GA	GA associated with: – fewer technical failures and complications – higher recanalization rates – better clinical outcomes.
Jumaa (16) 2010	126	AIS (MCA/M1-occlusion)	Monocentric	CS vs. GA	CS associated with: – shorter ICU stay – less complications – reduced mortality – smaller infarcts – better outcome
Davis (17) 2012	129	AIS (anterior and posterior circulation)	Monocentric	LA vs. GA	Independent predictors for good outcome: – local anaesthesia – systolic blood pressure > 140 mmHg – low baseline NIHSS
Langner (33) 2012	131	AIS (anterior and posterior circulation)	monocentric	CS vs. GA	CS feasible, safe and faster than GA
Hassan (19) 2013	907	AIS (anterior and posterior circulation) SAH (Aneurysm occlusion and vasospasm)	Multicentric (2 centers)	CS vs. GA	CS associated with – low rate of conversion to GA – low rate of adverse outcomes
Li (32) 2014	109	AIS (anterior and posterior circulation)	Monocentric	CS vs. GA	GA associated with – higher mortality – longer door-to-recanalization time
Abou-Chebl (35) 2014	281	AIS (anterior and posterior circulation)	Multicentric (18 centers)	LA vs. GA	Higher mortality associated with: – GA – premorbid hypertension – NIHSS – unsuccessful recanalization

CS, conscious sedation; GA, general anesthesia; LA, local anesthesia; NIHSS, National Institute of Health Stroke Scale, AIS, acute ischemic stroke.

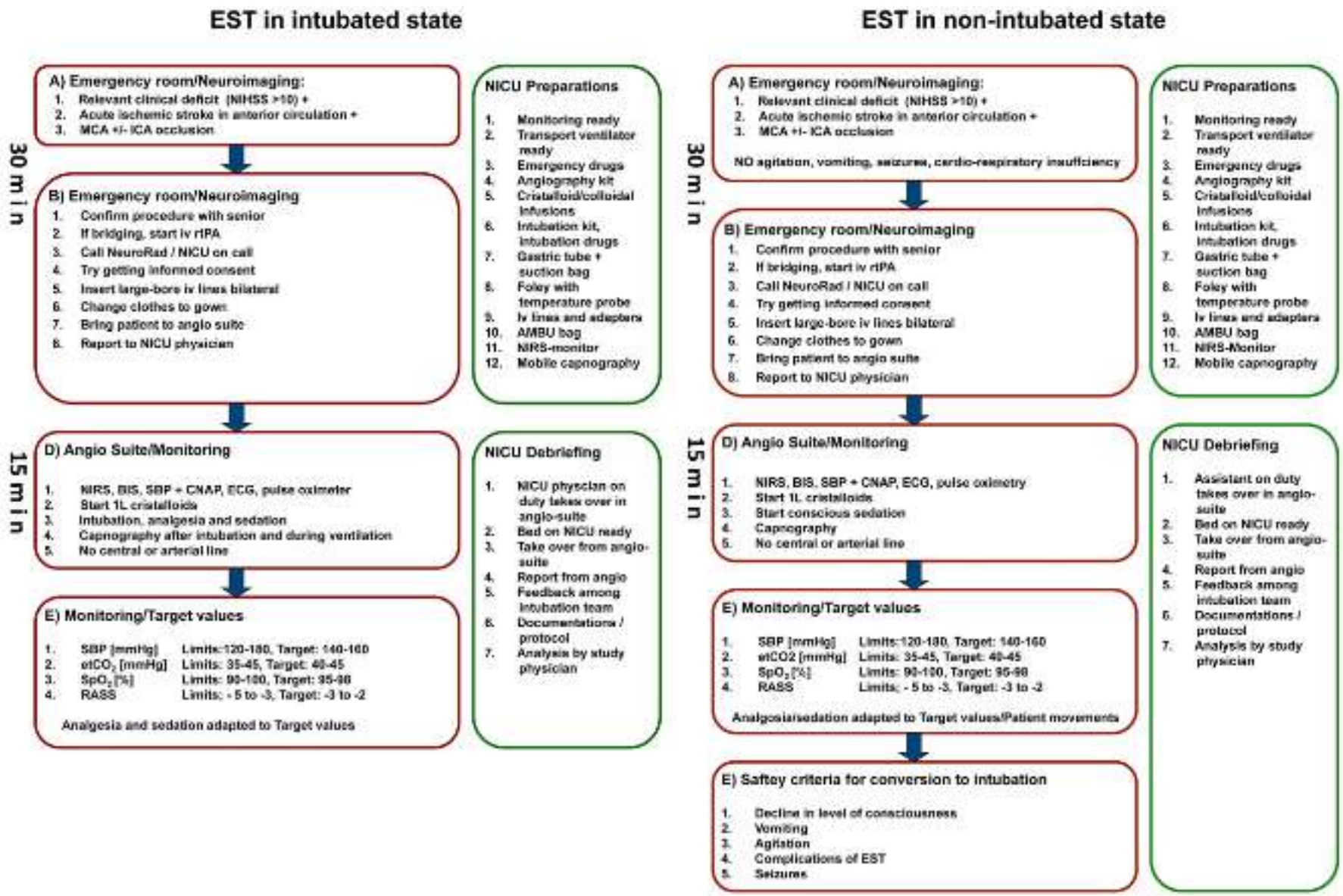
SIESTA TRIAL

(Sedation vs Intubation for Endovascular Stroke Treatment)

- 2014-2016, tek merkezli, randomize kontrollü
- İlk 9 sa, İKA ve/veya MCA M1 oklüzyonu, NIHS>10
- **Primer sonlanım:**24. sa NIHS erken nörolojik iyileşme (4 puan)
- **Sekonder sonlanım:** 90. gün mRS, mortalite, güvenilirlik ve uygulanabilirlik girişimsel parametreleri



JAMA. 2016;316(19):1986-1996. doi:10.1001/jama.2016.16623


EST in intubated state
A) Emergency room/Neuroimaging:
1. Relevant clinical deficit (NIHSS >10) +
2. Acute ischemic stroke in anterior circulation +
3. MCA +/- ICA occlusion
30 min
B) Emergency room/Neuroimaging
1. Confirm procedure with senior
2. If bridging, start iv rtPA
3. Call NeuroRad / NICU on call
4. Try getting informed consent
5. Insert large-bore iv lines bilateral
6. Change clothes to gown
7. Bring patient to anglo suite
8. Report to NICU physician
NICU Preparations
1. Monitoring ready
2. Transport ventilator ready
3. Emergency drugs
4. Angiography kit
5. Cristalloid/colloidal infusions
6. Intubation kit, intubation drugs
7. Gastric tube + suction bag
8. Foley with temperature probe
9. Iv lines and adapters
10. AMBU bag
11. NIRS-monitor
12. Mobile capnography
15 min
D) Angio Suite/Monitoring
1. NIRS, BIS, SBP + CNAP, ECG, pulse oximeter
2. Start 1L cristalloids
3. Intubation, analgesia and sedation
4. Capnography after intubation and during ventilation
5. No central or arterial line
NICU Debriefing
1. NICU physcian on duty takes over in anglo-suite
2. Bed on NICU ready
3. Take over from angio-suite
4. Report from angio
5. Feedback among intubation team
6. Documentations / protocol
7. Analysis by study physician
E) Monitoring/Target values
1. SBP [mmHg] Limits:120-180, Target: 140-160
2. etCO2 [mmHg] Limits: 35-45, Target: 40-45
3. SpO2 [%] Limits: 90-100, Target: 95-98
4. RASS Limits: - 5 to -3, Target: -3 to -2
Analgesia and sedation adapted to Target values
EST in non-intubated state
A) Emergency room/Neuroimaging:
1. Relevant clinical deficit (NIHSS >10) +
2. Acute ischemic stroke in anterior circulation +
3. MCA +/- ICA occlusion
NO agitation, vomiting, seizures, cardio-respiratory insufficiency
30 min
B) Emergency room/Neuroimaging
1. Confirm procedure with senior
2. If bridging, start iv rtPA
3. Call NeuroRad / NICU on call
4. Try getting informed consent
5. Insert large-bore iv lines bilateral
6. Change clothes to gown
7. Bring patient to angio suite
8. Report to NICU physician
NICU Preparations
1. Monitoring ready
2. Transport ventilator ready
3. Emergency drugs
4. Angiography kit
5. Cristalloid/colloidal infusions
6. Intubation kit, intubation drugs
7. Gastric tube + suction bag
8. Foley with temperature probe
9. Iv lines and adapters
10. AMBU bag
11. NIRS-Monitor
12. Mobile capnography
15 min
D) Angio Suite/Monitoring
1. NIRS, BIS, SBP + CNAP, ECG, pulse oximetry
2. Start 1L cristalloids
3. Start conscious sedation
4. Capnography
5. No central or arterial line
NICU Debriefing
1. Assistant on duty takes over in angio-suite
2. Bed on NICU ready
3. Take over from angio-suite
4. Report from angio
5. Feedback among intubation team
6. Documentations / protocol
7. Analysis by study physician
E) Monitoring/Target values
1. SBP [mmHg] Limits:120-180, Target: 140-160
2. etCO2 [mmHg] Limits: 35-45, Target: 40-45
3. SpO2 [%] Limits: 90-100, Target: 95-98
4. RASS Limits: - 5 to -3, Target: -3 to -2
Analgosia/sedation adapted to Target values/Patient movements
E) Saftey criteria for conversion to intubation
1. Decline in level of consciousness
2. Vomiting
3. Agitation
4. Complications of EST
5. Seizures

Variable	General Anesthesia (n = 73)	Conscious Sedation (n = 77)	Difference (95% CI)	*P* Value[a]
Primary Outcome				
Change in NIHSS[b], mean (95% CI)	−3.2 (−5.6 to −0.8)	−3.6 (−5.5 to −1.7)	−0.4 (−3.4 to 2.7)	.82[c]
Change in NIHSS, median (IQR)	−5.0 (−10.0 to 2.0)	−4.0 (−10 to 2.0)		
NIHSS after 24 h, mean (SD)	13.6 (11.1)	13.6 (9.0)	0.0 (−3.3 to 3.3)	>.99[d]

16.8 at admission vs 13.6 after 24H

17.2 at admission vs 13.6 after 24H

Çalışmanın birinci sonlanım noktası olarak belirlenen erken nörolojik iyileşmede (24. saat NIHSS) her iki grup arasında fark saptanmamıştır.

Secondary Outcomes

Variable	General Anesthesia (n = 73)	Conscious Sedation (n = 77)	Difference (95% CI)	*P* Value[a]
Complications during EST				
Critical hypertension or hypotension (>180 mm Hg or <120 mm Hg)	2 (2.7)	0	−2.7 (−6.5 to 1.0)	.14[f]
Critical ventilation or oxygenation disturbance[q]	3 (4.1)	3 (3.9)	−0.2 (−6.5 to 6.1)	.95[f]
Intervention-associated complications	2 (2.7)	2 (2.6)	−0.1 (−5.3 to 5.0)	.96[f]
Complications after EST				
Hypertension or hypotension (>180 mm Hg or <120 mm Hg)	17 (23.3)	10 (13.0)	−10.3 (−22.6 to 2.0)	.10[f]
Hyperthermia or hypothermia (>37.2°C or <36.0°C)	24 (32.9)	7 (9.1)	−23.8 (−36.3 to −11.2)	<.001[f]
Delayed extubation[r]	36 (49.3)	5 (6.5)	−42.8 (−55.5 to −30.1)	<.001[f]
Ventilation-associated complications[s]	10 (13.7)	3 (3.9)	−9.8 (−18.8 to −0.8)	.03[f]

GA'da hasta hareketliliği DAHA AZ ancak
Girişim sonrası komplikasyonlar DAHA FAZLA
hipotermi (%32.9'a karşı %9.1; $P < .001$), gecikmiş ekstübasyon (%49.3'e karşı %6.5; $P < .001$) ve pnömoni (%13.7'ye karşı %3.9; $P = .03$)

Secondary Outcomes

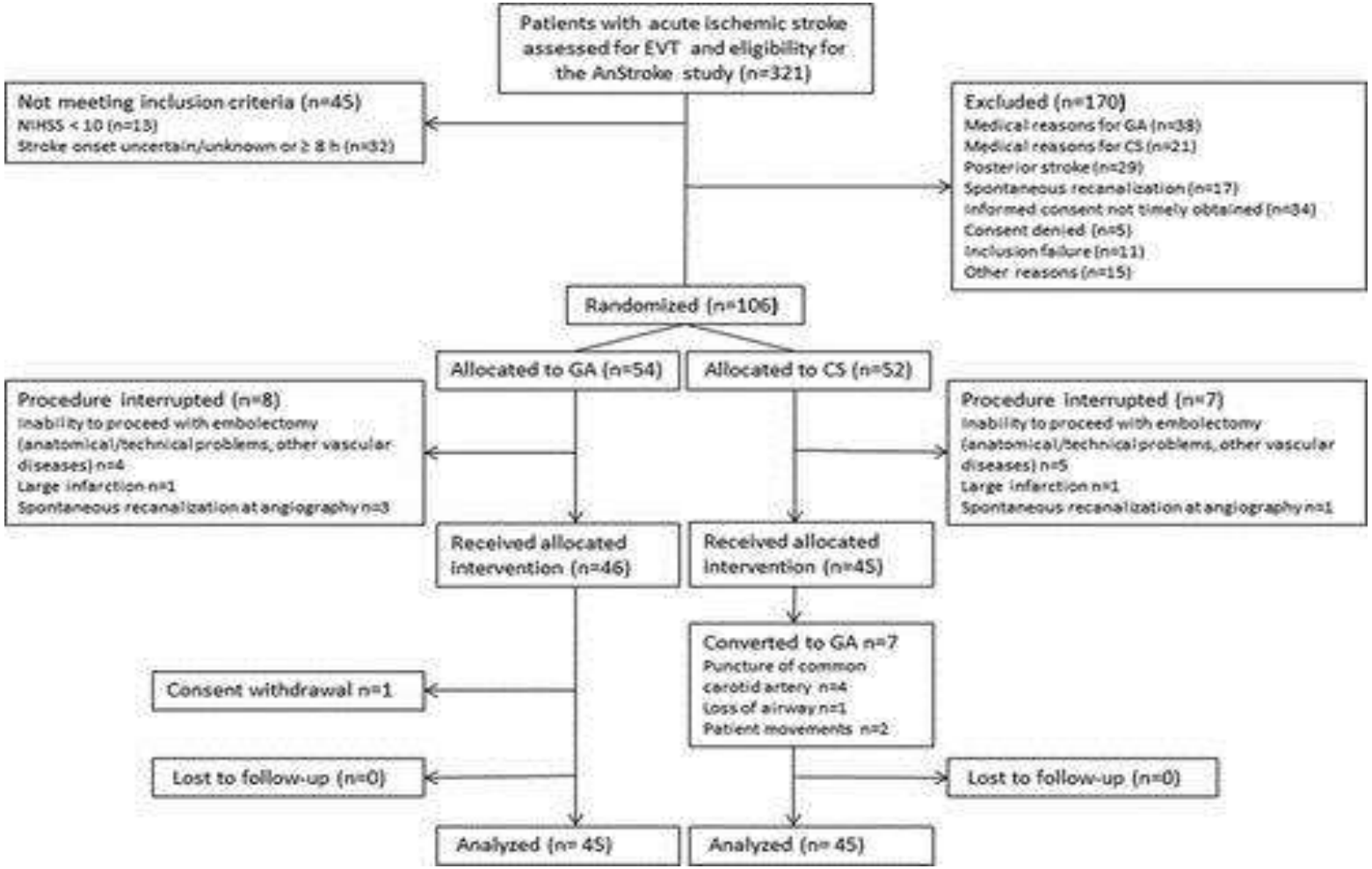
Variable	General Anesthesia (n = 73)	Conscious Sedation (n = 77)	Difference (95% CI)	*P* Value[a]
Clinical				
Modified Rankin Scale after 3 mo, mean (SD)	3.5 (1.9)	3.7 (1.8)	0.2 (3.3 to 3.9)	.41[e]
Modified Rankin Scale after 3 mo, median (IQR)	4 (2 to 5)	4 (3 to 5)		
Modified Rankin Scale 0-2 af… N… No. (%)	27 (37)	14 (18.2)	−18.8 (−32.8to−4.8)	.01[f]
In… m… No. (%)				.83[f]
Mortality after 3 mo, No. (%)	18 (24.7)	19 (24.7)	0.0 (−13.8 to 13.8)	>.99[f]
Substantial reperfusion grade 2b-3 (TICI)	65 (89.0)	62 (80.5)	−8.5 (−19.9 to 2.9)[f]	
Substantial patient movement[m]	0	7 (9.1)	9.1 (2.7 to 15.5)	.01[f]

3. ay mRS ≤ 0-2 bilinçli sedasyon grubunda daha düşük saptanmıştır (p=0.01).

Sonuç:

- Bilinçli sedasyonun genel anesteziye göre herhangi bir avantajı gösterilememiştir.
- Hatta önceki çalışmaların aksine bilinçli sedasyon grubunda 3. ay mRS ≤ 0-2 daha düşük saptanmıştır (p=0.01).

AnSTROKE (Anesthesia During Stroke) TRIAL



Anterior sistem
<8 sa,
NIHSS sağ ≥10/ sol ≥ 14
Toplam 90 hasta

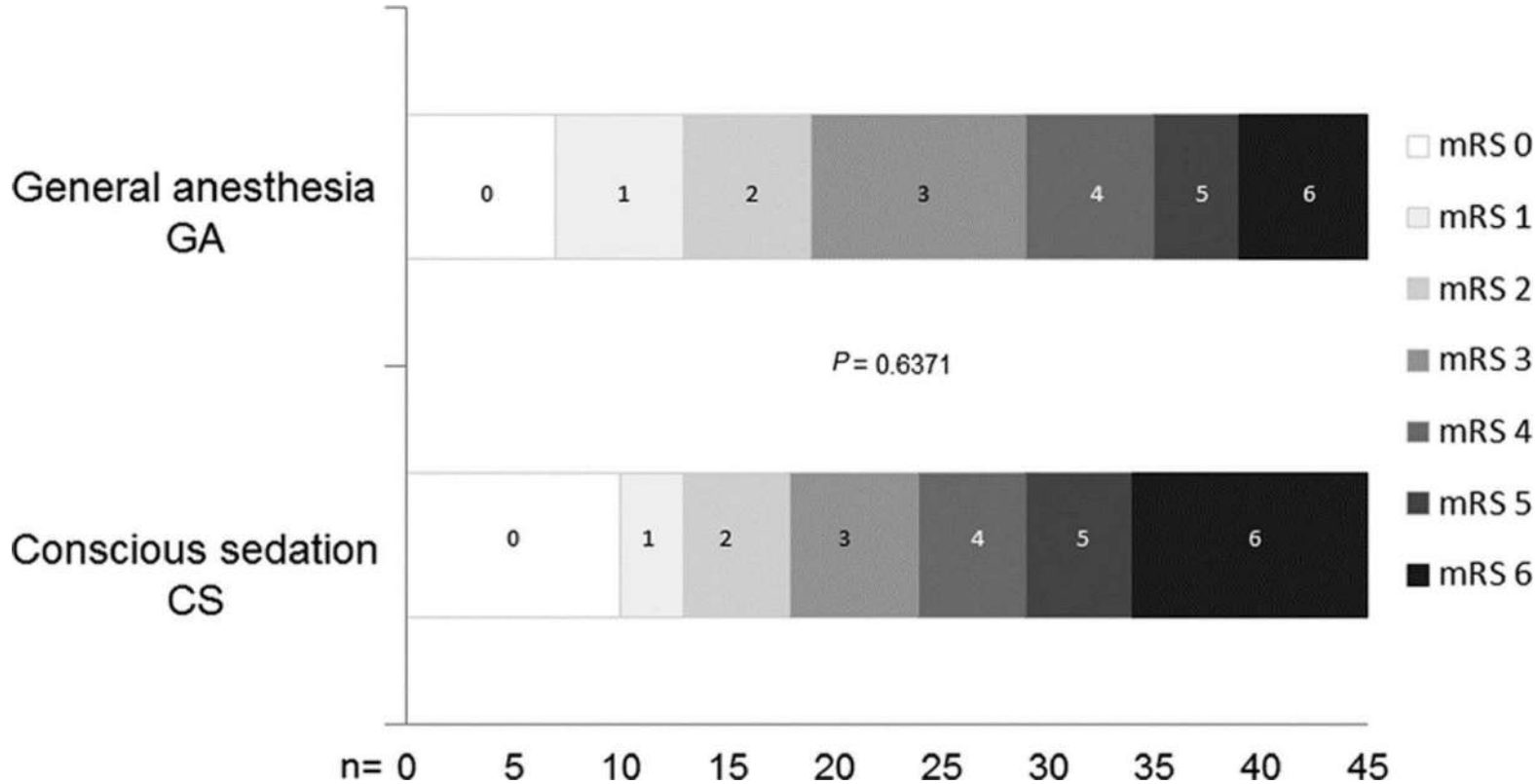
GA:
Propofol+remifentanil
---> sevofluran+remifentanil
BS:
Remifentanil

Pia Löwhagen Hendén. Stroke. General Anesthesia Versus Conscious Sedation for Endovascular Treatment of Acute Ischemic Stroke, Volume: 48, Issue: 6, Pages: 1601-1607, DOI: (10.1161/STROKEAHA.117.016554)

OUTCOME DATA

	GA n=45	CS n=45	*P* Value
mTICI 2b–3=successful recanalization, n (%)	41 (91.1)	40 (88.9)	1.000
NIHSS score after 24 h	8 (3–15)	9 (2–15)	0.5986
Hospital			1.000
mR			01
mRS s			.000
Mortality at 3 mo, n (%)		(24.4)	0.2813
Complications			
Symptomatic intracerebral hemorrhage*	0 (0)	3(6.7)	0.2416
Anesthesiological complications, n (%)	2 (4.4)	4 (8.9)	0.6766
Interventional complications, n (%)	11 (24.4)	6 (13.3)	0.4299

Başarılı rekanalizasyon (modifiye TICI 2b-3), 24. saat NIHSS, hastanede meydana gelen ölüm, 3. Ay (mRS ≤2), girişimsel işlemlere ve anesteziye bağlı komplikasyonlar arasında İKİ GRUP ARASINDA ANLAMLI FARLILIK SAPTANMAMIŞ!!!


General anesthesia
GA
0
1
2
3
4
5
6
P = 0.6371
Conscious sedation
CS
0
1
2
3
4
5
6
mRS 0
mRS 1
mRS 2
mRS 3
mRS 4
mRS 5
mRS 6
n= 0
5
10
15
20
25
30
35
40
45

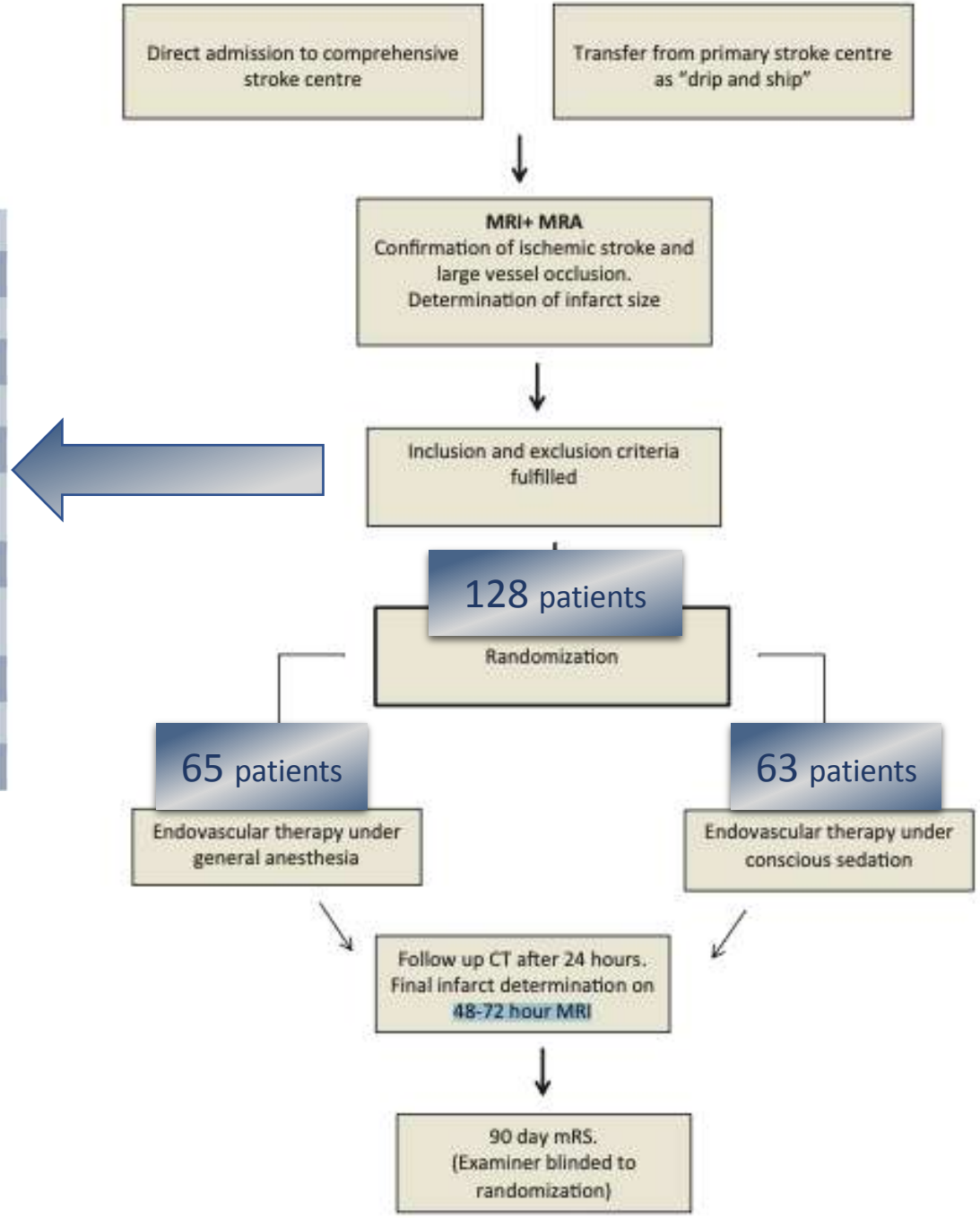
- İlk kez bu çalışmada anjiyografi kalitesini ve işlem sırasında hasta hareketlerini değerlendirmek için bir skorlama yapılmış.

- Bilinçli sedasyon alan hasta grubunda anjiyografi kalitesinin kötü ve hasta haraketlerinin fazla olmasına rağmen; diğer grup ile karşılaştırıldığında komplikasyonlar arasında anlamlı bir fark bulunmamıştır.

GOLIATH TRIAL

(The General or Local Anesthesia in Intra Arterial Therapy)

Inclusion criteria
1. Severe stroke (NIHSS ≥ 10)
2. Modified Rankin Scale ≤ 2 before stroke
3. Groin puncture feasible within 6 hours of symptom onset
4. MRI findings:
a) Clot in a reachable vessel. (ICA, ICA-T, M1, M2)
b) Infarct volume <70 ml on the initial diffusion-weighted MRI scan.
Exclusion criteria
1. MRI contraindications (pacemaker, vomiting, respiratory insufficiency, obesity)
2. Glasgow coma score < 9
3. Patients intubated prior to arrival
4. Previous allergic reactions to anesthetic drugs



Genel anestezi prosedürü:

- Suksametonyum ile hızlı sıralı entübasyon (bolus: 0.5–1 mg/kg), alfentanil (bolus: 0.02–0.03 mg/kg), and propofol (bolus: 1–5 mg/kg followed by infusion of 2–10 mg/kg/h).
- Anestezinin devamı : propofol and remifentanil

Bilinçli sedasyon:

- Fentanyl bolus 25–50 mg (tekrar uygulanabilir)
- Propofol infüzyon: 1–2 mg/kg/h.

- **Birincil sonlanım noktası;** mililitre cinsinden ölçülen enfarktın büyümesi (10 mL'lik bir fark klinik olarak anlamlı kabul edildi)
- **İkincil sonlanım noktası;** 90 gün sonra mRS skorları, zaman ve kan basıncı seviyeleri ve güvenlik son noktaları

Table 2. Primary and Secondary Imaging and Clinical Outcomes

Outcome	General Anesthesia (n = 65)	Conscious Sedation (n = 63)	*P* Value
Successful reperfusion (mTICI 2b-3), No. (%)	50 (76.9)	38 (60.3)	.04
Acute infarct volume, median (IQR), mL	10.5 (2.4-23.6)	13.3 (5.2-31.1)	.26
Final infarct volume, median (IQR), mL	22.3 (8.1-64.5)	38.0 (16.7-128.0)	.04
Infarct volu	GA ve CS kolları arasında enfarkt büyümesi istatistiksel olarak ANLAMLI DEĞİL!		.10
90-d mRS score, median (IQR)	2 (1-3)	2 (1-4)	.04
NIHSS score in 24 h, median (IQR)	6 (3-14)	10 (2-19)	.19
Change in NIHSS score after 24 h, median (IQR)	−10 (−14 to −5)	−7 (−13 to 0)	.11

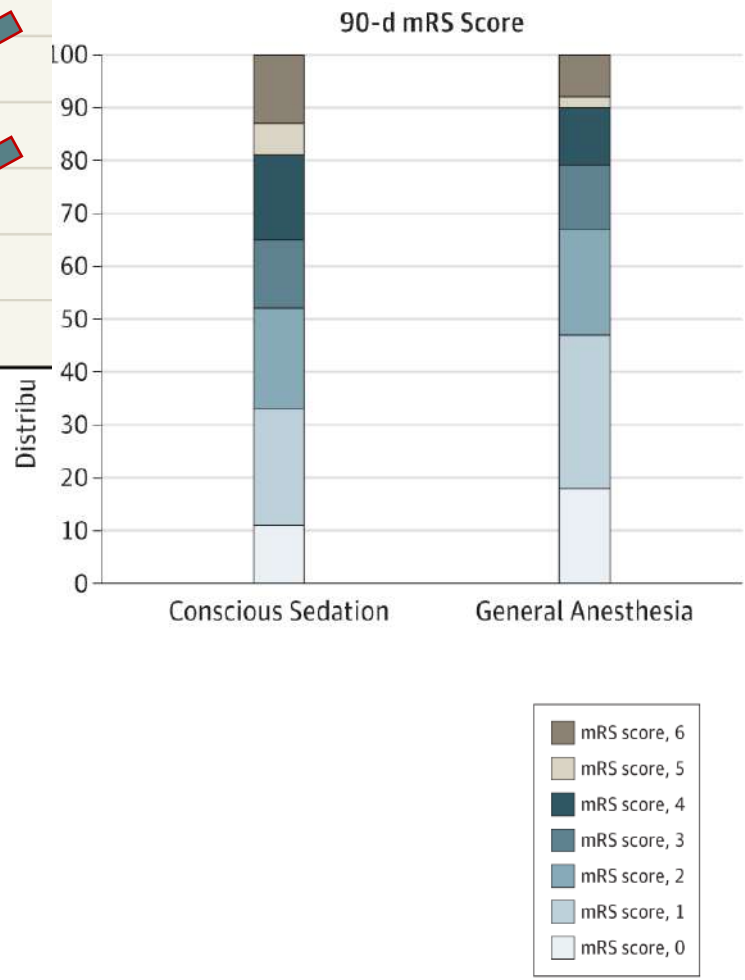


Table 3. Secondary Outcomes Associated With Time and Blood Pressure[a]

Time Interval[b]	General Anesthesia (n = 65)	Conscious Sedation (n = 63)	*P* Value
Time from symptom onset to arrival at neurointerventional	159 (122-230)	145 (113-231)	.55
			<.001
Time from onset to groin puncture, mean (SD), min	262 (71)	180 (72)	.22
Time from imaging to groin puncture, median (IQR), min	61 (48-73)	54 (40-75)	.13
Time from groin puncture to reperfusion, median (IQR), min	34 (21-51)[c]	29 (16-51)[d]	.27
			.63
			<.001
No. (%)	23 (35.4)	10 (15.9)	.01
Median time (IQR), min	2 (1-5.5)	6.5 (2-13)	.09
Phenylephrine hydrochloride, median (IQR), mg	2.2 (1.2-3.0)	0.2 (0.0-1.0)	<.001
Ephedrine sulfate, median (IQR), mg	10 (0-10)	0	<.001

Hastanın anjiyo süitine girişi ve kasık ponksiyonu arasında geçen süre GA grubunda daha uzun saptandı (p=0.001)

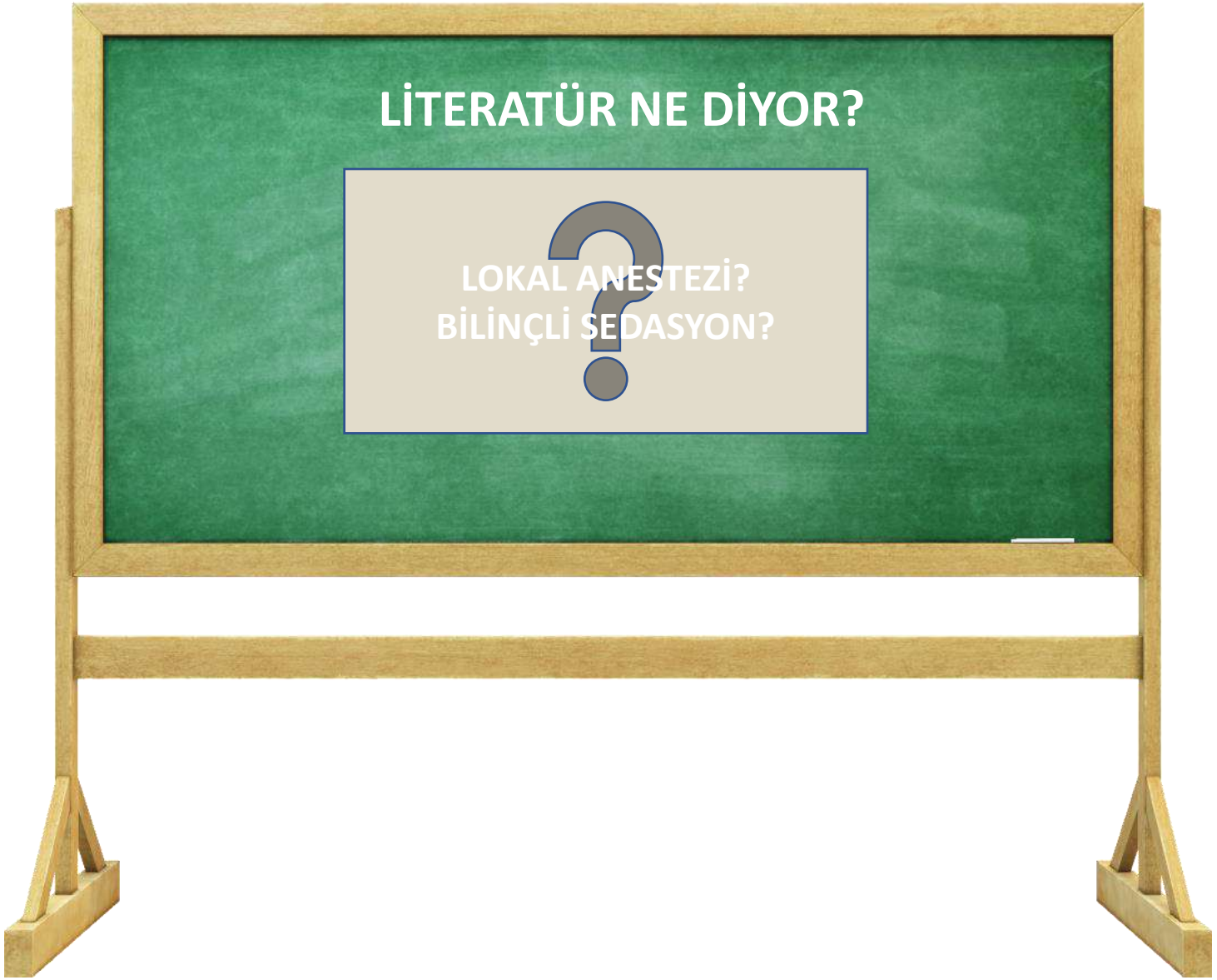
GA grubunda ortalama arter basıncında (MAP) %20'den fazla bir düşüş yaşandı Bununla birlikte, MAP 70 mm Hg'nin altına düştüğünde, süre CS hastaları için GA hastalarına göre anlamlı olmayan şekilde daha uzundu.

Sonuç:

- Final enfarkt volümü, enfarkt alanında ki büyüme, 90. gün mortalite, 24. saat NIHSS de gruplar arası anlamlı fark saptanmazken,
- Genel anestezi grubunda başarılı reperfüzyon (TICI 2b-3) oranı daha yüksek (p=0.04)
- Üçüncü ay fonksiyonel bağımsızlıkta (mRS ≤2) gruplar arası anlamlı fark olmamakla birlikte genel anestezi grubu sayısal olarak daha fazladır.
- Hastanın anjiyo süitine girişi ve kasık ponksiyonu arasında geçen süre ise genel anestezi grubunda daha uzun saptanmıştır (p=0.001)
- GA veya CS altında tedavi edilen hastalar arasında enfarktüs büyümesi hacmindeki fark istatistiksel anlamlılığa ulaşmamıştır (medyan [IQR]büyüme, 8.2 [2.2-38.6]

Sonuç:

- Anterior dolaşımdaki büyük damar tıkanıklıklarının neden olduğu akut iskemik inmede trombektomi uygulanan hastalarda GA, BS ile karşılaştırıldığında daha kötü doku veya klinik sonuçlara yol açmadı.


LİTERATÜR NE DİYOR?
LOKAL ANESTEZİ?
BİLİNÇLİ SEDASYON?

MR CLEAN verilerinin post hoc analizinde, GA'nın olumsuz bir etkisi olduğu (GA uygulananlar ile kompozit LA+BS) gösterilmiştir.[1]

Aynı düşünce HERMES çalışmasında da doğrulanmıştır.[2]

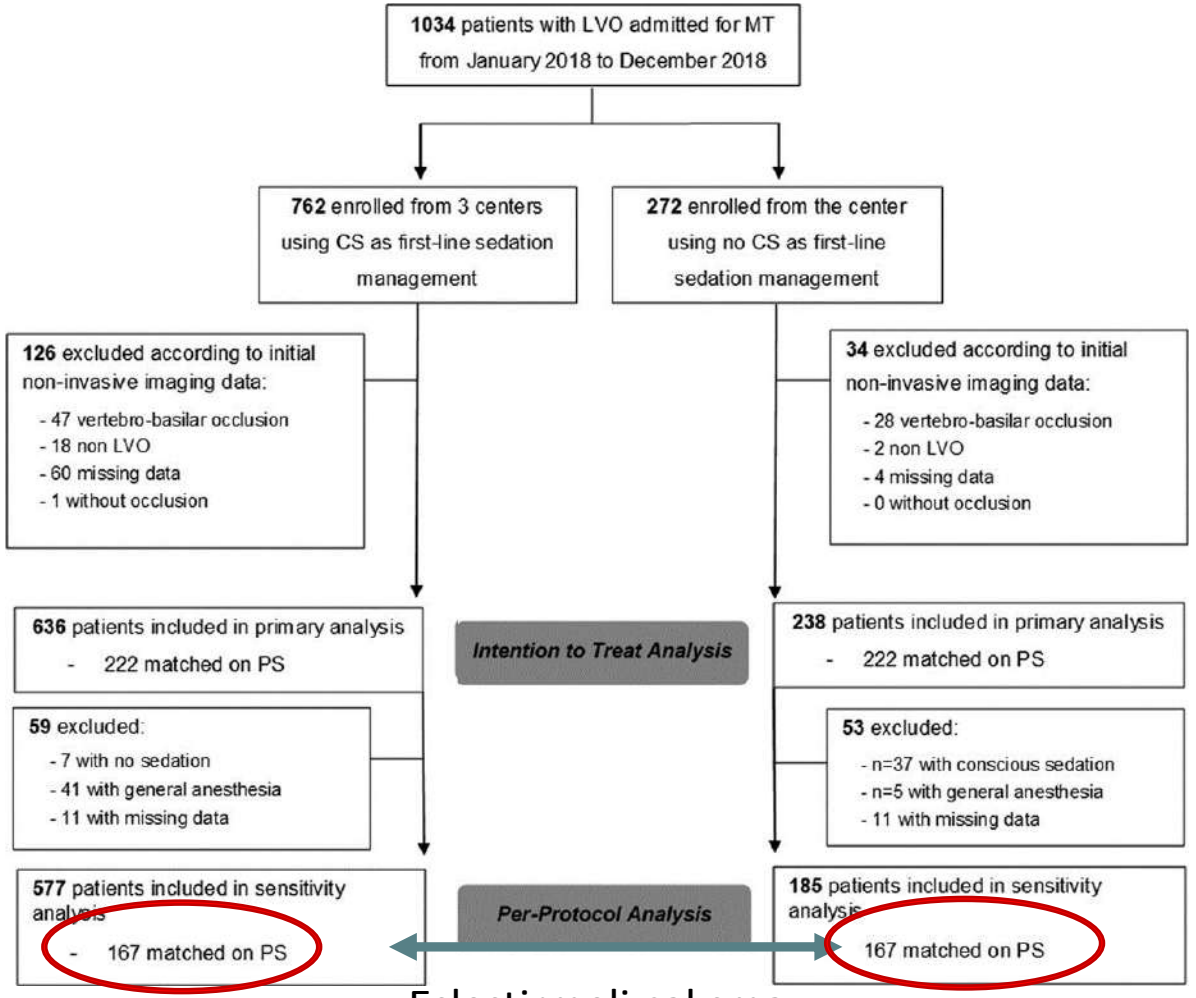
Ancak LA+GA+BS birlikte değerlendiren randomize çalışma yok.

1-Berkhemer OA, van den Berg LA, Fransen PS, et al.. The effect of anesthetic management during intra-arterial therapy for acute stroke in MR CLEAN. *Neurology* 2016;87:656–664.

2- Campbell BCV, van Zwam WH, Goyal M, et al.. Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data. Lancet Neurol 2018;17:47–53.

Stroke
Volume 51, Issue 10, October 2020; Pages 2951-2959
https://doi.org/10.1161/STROKEAHA.120.029194

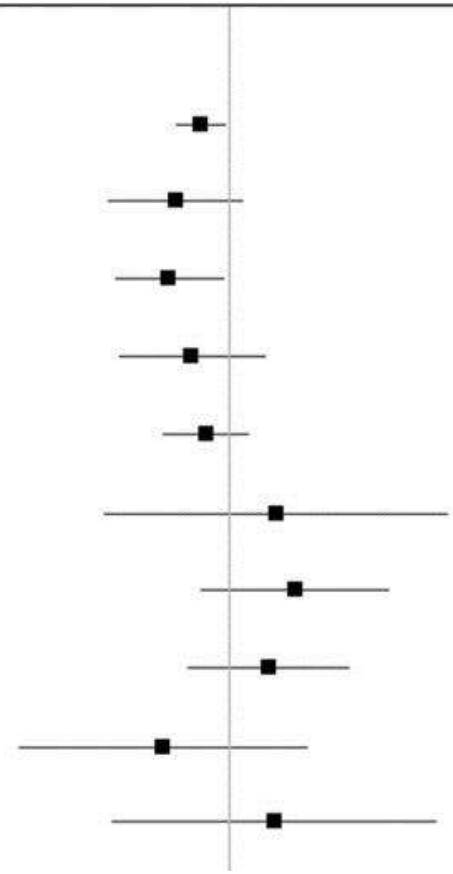
Local Anesthesia Without Sedation During Thrombectomy for Anterior Circulation Stroke Is Associated With Worse Outcome



Eşleştirmeli çalışma

LA :≈10 mL Lidokain
CS :Remifentanil (doz belirtilmemiş)
Her iki grupta da ortalama kan basıncı>100mmHg

Outcomes	CS group	LA group	RR (95%CI)	*P*
Propensity-Score Matched Cohort	**(N=222)**	**(n=222)**		
Successful reperfusion (mTICI 2b-3)	193 (87.1)	170 (76.6)	0.88 (0.79 to 0.98)[2]	0.012
Complete reperfusion (mTICI 3)	70 (35.6)	63 (28.2)	0.79 (0.58 to 1.06)[2]	0.11
Favorable outcome[1]	116 (52.0)	89 (40.0)	0.76 (0.60 to 0.97)[2]	0.028
Excellent outcome	82 (36.8)	69 (31.0)	0.84 (0.61 to 1.17)[2]	0.29
Early neurological improvement	126 (56.5)	112 (50.7)	0.90 (0.74 to 1.08)[2]	0.25
Any procedural complications	19 (8.5)	23 (10.2)	1.23 (0.57 to 2.63)[2]	0.59
90-day all-cause mortality	40 (18.2)	54 (24.3)	1.34 (0.88 to 2.03)[2]	0.17
Any ICH	83 (37.4)	98 (43.9)	1.19 (0.83 to 1.70)[2]	0.34
Parenchymal Hematoma	34 (15.3)	25 (11.1)	0.74 (0.39 to 1.41)[2]	0.36
sICH	19 (8.3)	22 (9.9)	1.22 (0.59 to 2.50)[2]	0.58



Çalışmanın sonucu;

- LA grubu, 90 günde daha düşük bir olumlu fonksiyonel sonuç ve daha düşük başarılı reperfüzyon oranına sahipti.

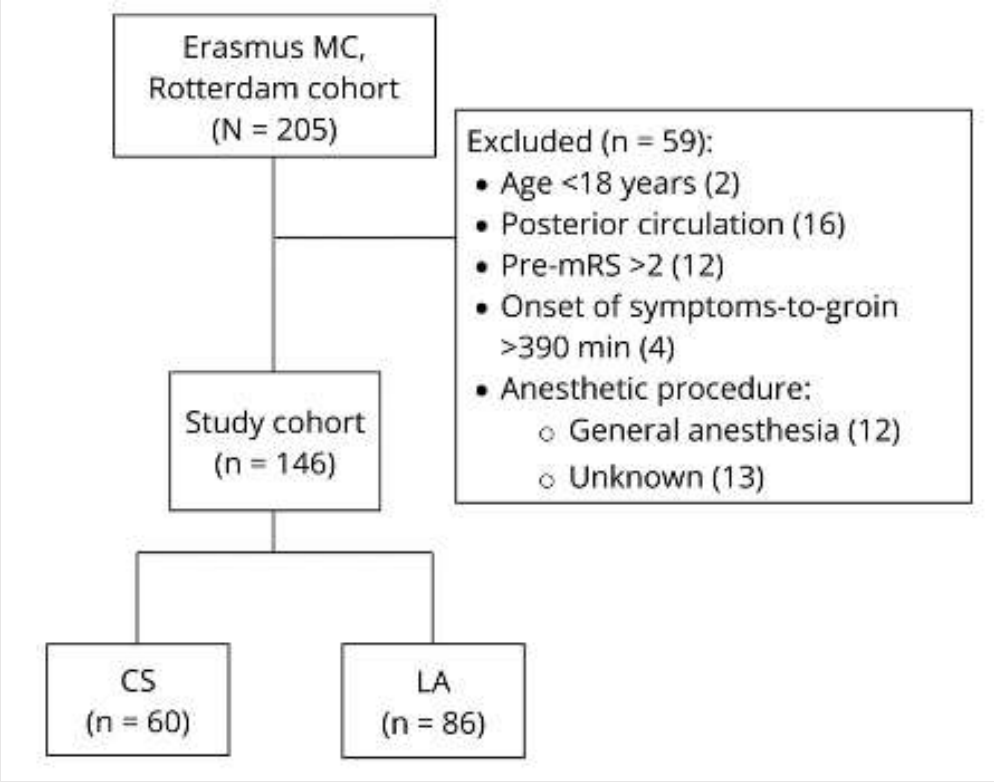
- Ancak, LA yapıldığında MT sırasında herhangi bir anestezi uzmanının bulunmadığı da unutulmamalıdır, bu da LA grubunda daha kötü sonuçlara katkıda bulunmuş olabilir.

Benvegnu F, Richard S, Marnat G, et al. Local anesthesia without sedation during thrombectomy for anterior circulation stroke is associated with worse outcome. Stroke. 2020;51:2951-2959.

Conscious sedation or local anesthesia during endovascular treatment for acute ischemic stroke

Rob A. van de Graaf, MD,* Noor Samuels, MD,* Maxim J.H.L. Mulder, MD, PhD, Ismail Eralp, MD, PhD, Adriaan C.G.M. van Es, MD, PhD, Diederik W.J. Dippel, MD, PhD, Aad van der Lugt, MD, PhD,vand Bart J. Emmer, MD, PhD, for the Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN) Registry Investigators

‘MR CLEAN Registry’ kayıtlı hastalar



İlaç protokolü:
propofol 2-6 mg/kg/sa veya
remifentanil 1 ile 4 µg/kg/sa

Neurology® 2018;91:e19-e25.doi:10.1212/WNL.0000000000005732

BS uygulanan grupta;

- 90. gün mRS skorları daha kötü (acOR 0.4 [%95 GA 0.2-0.7])
- mRS skoru ≤2 olan hasta sayısı daha az (OR 0.4 [%95 GA 0.2-0.8])
- 30 gün içindeki mortalite daha yüksek (17/60'a karşı 10/86, OR 2.6 [%95 GA 1.0–6.4]).
- 90 gün içinde mortalite daha yüksek (21/60) ve %16 (14/86) (OR 2.3 [%95 GA 1.0–5.2]).
- TICI ≥ 2C rekanalizasyon, daha az (OR 0.4 [%95 CI 0.2-0.8])

- İnme başlangıcından reperfüzyona kadar geçen süre [%95 GA -14.0 ve 35.3]
- Toplam işlem süresi,
- İşlemle ilgili komplikasyonlar
- ciddi yan etkiler benzer sonuçlandı.

SONUÇ

- BS LA'ya kıyasla zayıf fonksiyonel sonuç ve daha yüksek mortalite ile ilişkilendirilmiş.
- Reperfüzyon oranları, işlem süresi, işlemle ilgili komplikasyonlar ve ciddi yan etkiler 2 grup arasında farklılık göstermemiş .

- Çalışmanın sınırlaması tek merkezli olması, küçük örneklem büyüklüğü, BS ve LA gruplarının randomize edilmemiş olmasıdır.

2019 AHA/ASA kılavuzu

3.7.4. Technique (Continued)	COR	LOE
5. It is reasonable to select an anesthetic technique during EVT for AIS on the basis of individualized assessment of patient risk factors, technical performance of the procedure, and other clinical characteristics.	IIa	B-R

- Akut iskemik inmenin endovasküler tedavisi sırasında, hastanın risk faktörlerini bireysel olarak değerlendirerek, prosedürün teknik performansına ve diğer klinik özelliklerine göre anestezi tekniğin seçilmesi önerilmiştir (sınıf IIa, kanıt düzeyi B)

EVE GÖTÜRÜLECEK MESAJ

- Endovasküler tedavi esnasında uygulanacak anestezi tekniği hakkında net bir konsensus bulunmamaktadır.
- Her tekniğin kendine ait avantaj ve dezavantajları bulunduğundan hastanın kliniği, hekimin tecrübesi ve merkezin teknik donanımı tercihi belirlemektedir.
- Tedavi stratejisi ne olursa olsun, MT sırasında hipotansiyondan kaçınılmalı mümkün olan en kısa sürede en az komplikasyonla tamamlanmalıdır.

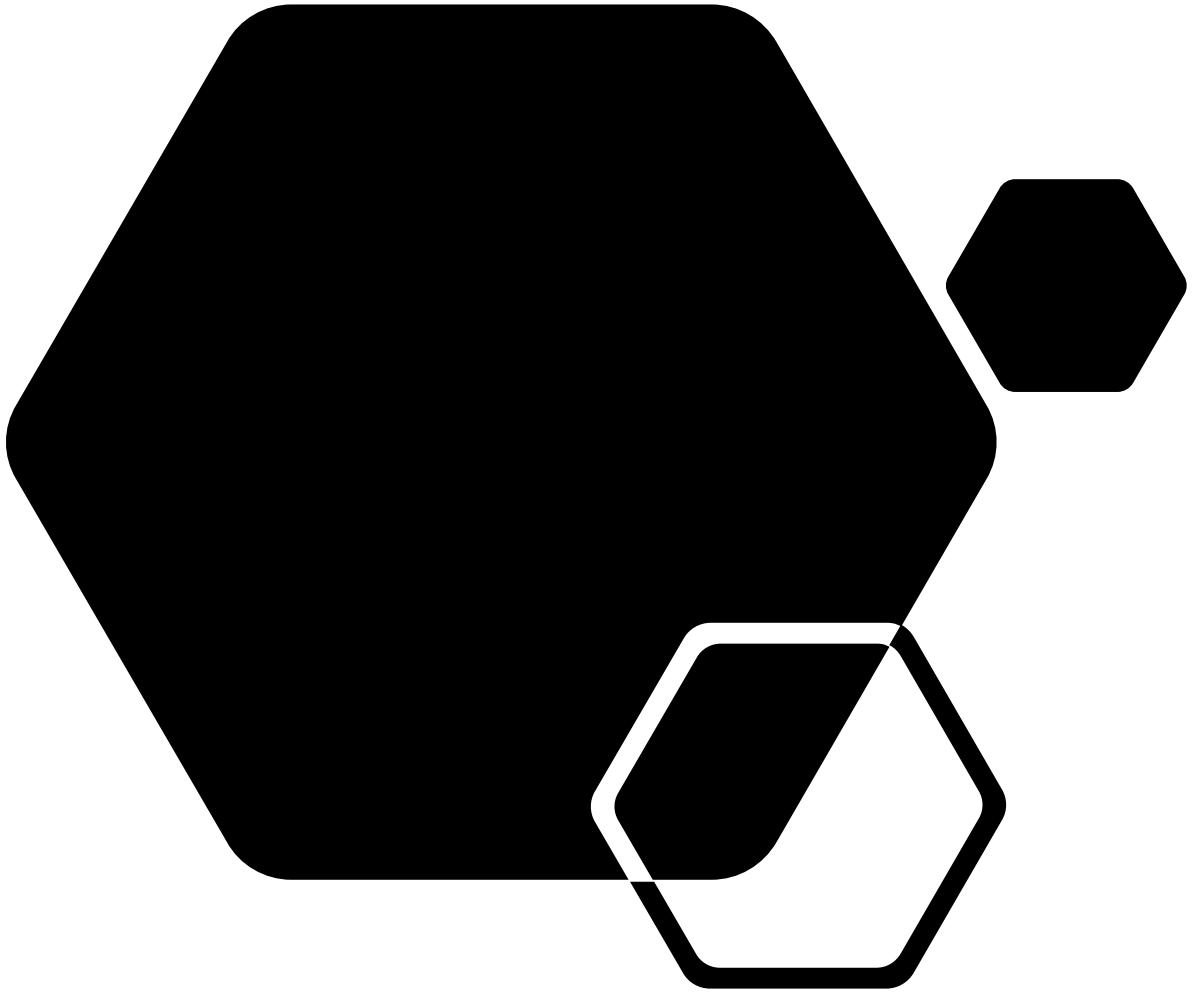
- **“Bir ulusun asker ordusu ne kadar güçlü olursa olsun, kazandığı zafer ne kadar yüce olursa olsun, bir ulus ilim ordusuna sahip değilse, savaş meydanlarında kazanılmış zaferlerin sonu olacaktır. Bu nedenle bir an önce büyük, mükemmel bir ilim ordusuna sahip olma zorunluluğu vardır.’’**

Teşekkürler….

Trombektomi Sonrası İntraarteryal Tromboliz-Güncel Bilgiler

Hasan Hüseyin Karadeli

İstanbul Medeniyet Üniversitesi



- % 60.6 : USA – Rescue Therapy

- Complete Reperfusion
- Near Complete Reperfusion

- 2 times Good Functional Outcome

Intra-Arterial Thrombolysis after Unsuccessful Mechanical Thrombectomy in the STRATIS Registry

S.F. Zaidi, A.C. Castonguay, O.O. Zaidat, N. Mueller-Kronast, D.S. Liebeskind, H. Salahuddin, and M.A. Jumaa

RESULTS: A total of 212/984 (21.5%) patients received rescue therapy, of which 83 (39.2%) and 129 (60.8%) were in the no intra-arterial rtPA and intra-arterial rtPA groups, respectively. Most occlusions were M1, with 43.4% in the no intra-arterial rtPA group and 55.0% in the intra-arterial rtPA group ($P = .12$). The median intra-arterial rtPA dose was 4 mg (interquartile range = 2–12 mg). A trend toward higher rates of substantial reperfusion (modified TICI ≥2b) (84.7% versus 73.0%, $P = .08$), good functional outcome (59.2% versus 46.6%, $P = .10$), and lower rates of mortality (13.3% versus 23.3%, $P = .08$) was seen in the intra-arterial rtPA cohort. Rates of symptomatic intracranial hemorrhage did not differ (0% versus 1.6%, $P = .54$).

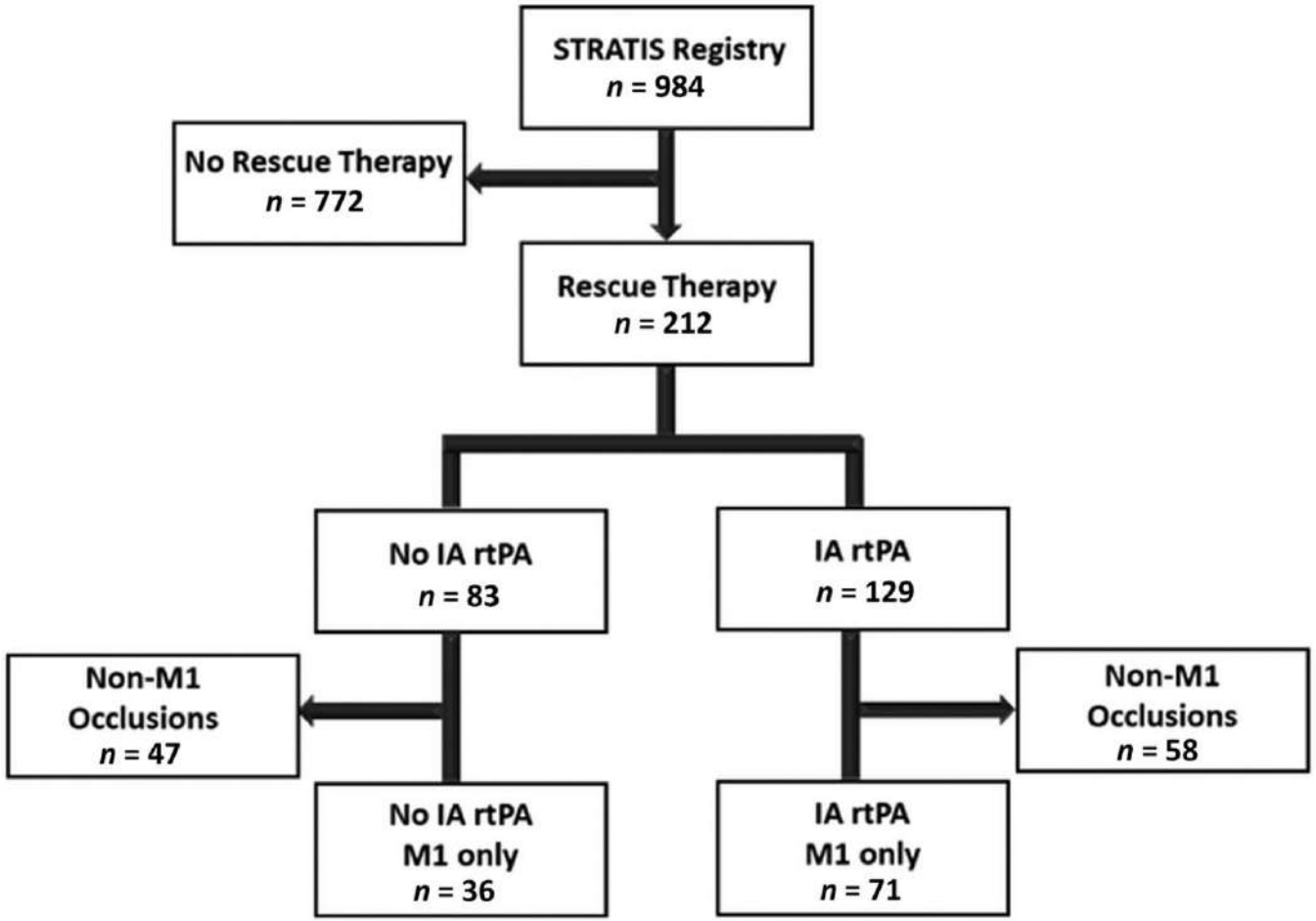
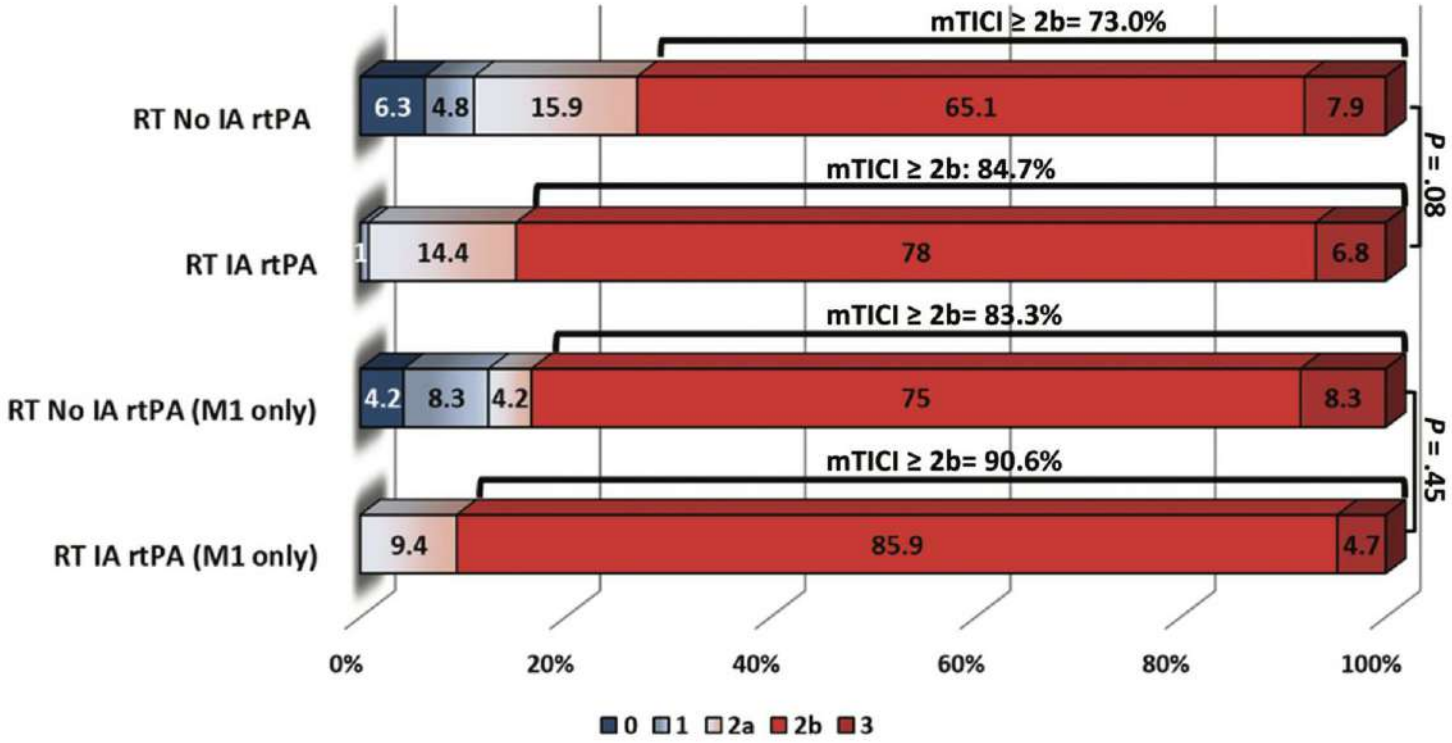
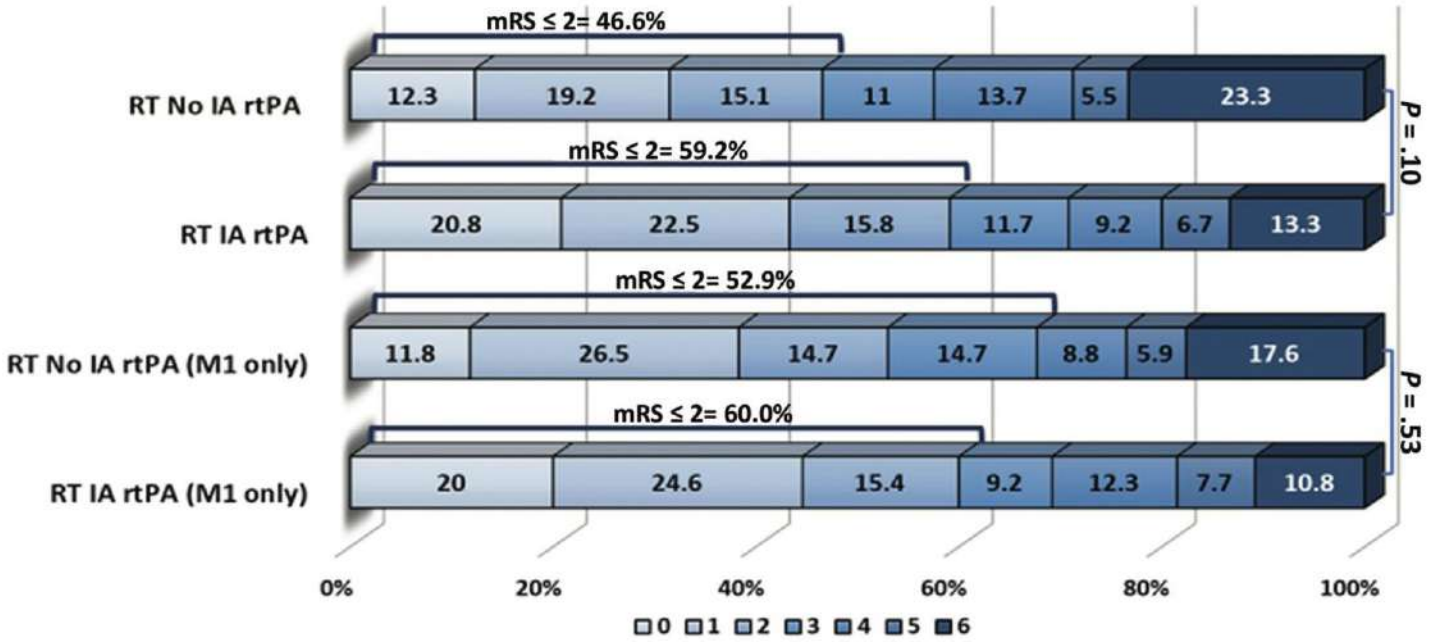


FIG 1. Study flow chart.


mTICI ≥ 2b= 73.0%
RT No IA rtPA
6.3
4.8
15.9
65.1
7.9
P = .08
mTICI ≥ 2b: 84.7%
RT IA rtPA
14.4
78
6.8
mTICI ≥ 2b= 83.3%
RT No IA rtPA (M1 only)
4.2
8.3
4.2
75
8.3
P = .45
mTICI ≥ 2b= 90.6%
RT IA rtPA (M1 only)
9.4
85.9
4.7
0%
20%
40%
60%
80%
100%
0
1
2a
2b
3


mRS ≤ 2= 46.6%
RT No IA rtPA
12.3
19.2
15.1
11
13.7
5.5
23.3
mRS ≤ 2= 59.2%
RT IA rtPA
20.8
22.5
15.8
11.7
9.2
6.7
13.3
P = .10
mRS ≤ 2= 52.9%
RT No IA rtPA (M1 only)
11.8
26.5
14.7
14.7
8.8
5.9
17.6
mRS ≤ 2= 60.0%
RT IA rtPA (M1 only)
20
24.6
15.4
9.2
12.3
7.7
10.8
P = .53
0%
20%
40%
60%
80%
100%
0 1 2 3 4 5 6

Multivariable logistic regression analysis when adjusting for IA rtPA use, history of hyperlipidemia, number of device passes, time from onset to procedure end, time from onset to arterial puncture, M1 vessel location, and ICA vessel location did not show IA rtPA use as an independent predictor of substantial reperfusion (OR = 1.07; 95% CI, 0.44–2.57; $P = .89$), good functional outcome (OR = 0.92; 95% CI, 0.46–1.83; $P = .80$), or mortality (OR = 0.54; 95% CI, 0.22–1.31; $P = .17$) (Online Supplemental Data).

- Dosing of IA İN Rescue Treatment
- 2-12 MG
- 4-6 MG
- 3-10 MG

- Limitataions of STRATİS REGİSTRY:
- PASSES
- ONSET TO GROİN PUNCTURE TİME

JAMA

QUESTION Does the use of adjunct intra-arterial thrombolysis following an angiographically successful thrombectomy improve functional outcomes in patients with large vessel occlusion acute ischemic stroke?

CONCLUSION Among patients with large vessel occlusion acute ischemic stroke and successful reperfusion following thrombectomy, use of adjunct intra-arterial alteplase compared with placebo resulted in a greater likelihood of excellent neurological outcome at 90 days.

POPULATION

61 Men
52 Women

Adults with large vessel occlusion acute ischemic stroke successfully treated with thrombectomy within 24 hours of stroke onset

Mean age: 71 years

LOCATIONS

7
Stroke centers
in Catalonia, Spain

INTERVENTION

121 Patients randomized
113 Patients analyzed

61
Alteplase
Intra-arterial alteplase, 0.225 mg/kg, infused over 15 to 30 minutes

52
Placebo
Intra-arterial placebo infused over 15 minutes

PRIMARY OUTCOME

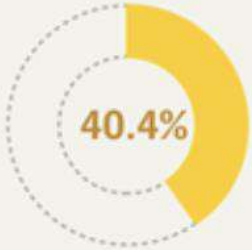
Percentage of patients with a score of 0 or 1 on themodified Rankin Scale (mRS), indicating no disability at 90 days

FINDINGS

Patients with mRS score of 0 or 1

Alteplase
36 of 61 patients

Placebo
21 of 52 patients



The adjusted risk difference was significant:

Risk difference, **18.4%**
(95% CI, 0.3% to 36.4%; *P* = .047)

Renú A, Millán M, San Román L, et al; CHOICE Investigators. Effect of intra-arterial alteplase vs placebo following successful thrombectomy on functional outcomes in patients with large vessel occlusion acute ischemic stroke. *JAMA*. Published online February 10, 2022. doi:10.1001/jama.2022.1645

affected arterial territory, corresponding with an expanded TICI (eTICI) score of 2b50 or greater. Although 71% of patients achieved successful reperfusion scores in previous randomized trials, only 27% of the patients treated were disability free at 90 days.[3] It is possible that a substantial vol-

the microvascular bed.[7] Therefore, it was postulated that thrombi persist within the microcirculation in patients with normal or nearly normal cerebral angiograms at the end of thrombectomy,[8] and it was hypothesized that these smaller thrombi would be more suitable to dissolve than more proximal thrombi because the efficacy of thrombolysis is related to the extent of clot burden.[9]

Table 1. Baseline Characteristics of Patients in the CHOICE Trial of Intra-arterial Alteplase

Characteristics	Alteplase (n = 61)	Placebo (n = 52)
Age, median (IQR), y	73 (71-76)	73 (69-67)
Race and ethnicity, No. (%)		
White	59 (97)	48 (92)
Hispanic	2 (3)	3 (6)
Other[a]	0	1 (2)
Sex, No. (%)		
Female	28 (46)	24 (46)
Male	33 (54)	28 (54)
Medical history, No. (%)		
Hypertension	39 (64)	34 (65)
Diabetes	19 (31)	11 (21)
Atrial fibrillation	10 (16)	9 (17)
Ischemic stroke or transient ischemic attack	5 (8)	4 (8)
NIHSS score at hospital arrival, median (IQR)[b]	14 (8-20)	14 (10-20)
Blood pressure at hospital arrival, median (IQR), mm Hg		
Systolic	139 (121-156)	136 (113-155)
Diastolic	73 (65-83)	70 (61-78)
Glucose level at hospital arrival, median (IQR), mg/dL	134 (108-164)	119 (103-143)
Treatment with intravenous alteplase before randomization, No. (%)[c]	38 (62)	31 (60)
ASPECTS value, median (IQR)[d]	9.0 (9.0-10.0)	10.0 (8.0-10.0)
Baseline modified Rankin Scale score of 1, No. (%)	9 (15)	9 (17)
Location of intracranial occlusion on angiography, No. (%)[e]		
Terminal internal carotid artery	7 (12)	4 (8)
Proximal, middle, or distal M1	19 (31)	20 (39)
Proximal or distal M2	33 (54)	28 (54)
Ipsilateral cervical carotid occlusion, No. (%)	6 (10)	4 (8)
Angiographic eTICI scores according to local investigators at randomization, No. (%)[f]		
2b50/67: 50%-89% reperfusion	34 (56)	31 (60)
2c/3: 90%-100% reperfusion	27 (44)	21 (40)
Workflow times, median (IQR), min		
Time from stroke onset to randomization	306.0 (208.0-672.0)	345.0 (237.0-609.0)
Time from stroke onset to start of study treatment	315.0 (218.0-680.0)	356.0 (260.5-635.0)

Table 2. Primary and Secondary Outcomes of the CHOICE Trial of Intra-arterial Alteplase

Outcomes	Alteplase (n = 61)	Placebo (n = 52)	Absolute risk difference, % (95% CI)	*P* value[a]
Primary outcome				
Score of 0 or 1 on modified Rankin Scale at 90 d, No. (%)	36 (59.0)	21 (40.4)	18.4 (0.3 to 36.4)	.047
Secondary outcomes				
Improved angiographic eTICI score, No. (%) [n = 111][b]	5 (8.5)	4 (7.7)	0.6 (−9.5 to 10.7)	.91
Excluding baseline eTICI scores of 3	5/44 (11.3)	4/43 (9.3)	1.8 (−11.0 to 14.5)	.78
Modified Rankin Scale score at 90 d, No. (%)[c]			1.54 (0.79 to 2.94)[d]	.38[e]
0	21 (34.4)	12 (23.1)		.18[f]
1	15 (24.6)	9 (17.3)		
2	5 (8.2)	12 (23.1)		
3	4 (6.6)	5 (9.6)		
4	8 (13.1)	6 (11.5)		
5-6	8 (13.1)	8 (15.4)		
Infarct expansion ratio, median (IQR) [n = 111][g]	2.0 (0.5-2.03)	4.2 (0.8-46.1)		.27[h]
Patients with infarct expansion, No. (%) [n = 110]	39 (63.9)	38 (74.5)	−8.9 (−25.6 to 7.9)	.31
Infarct volume at 48 h, median (IQR), mL [n = 110]	7.7 (3.7-29.3)	12.7 (3.1-35.5)		.79[h]
Tertiary outcomes				
Barthel Index of 95-100 at 90 d, No. (%) [n = 100][i]	38 (67.9)	27 (61.4)	6.4 (−12.3 to 25.0)	.60
Ischemic worsening, No. (%) [n = 111][j]	1 (1.6)	3 (5.8)	−4.9 (−18.0 to 8.3)	.32
EQ-5D-3L score at 90 d, median (IQR)				
Visual analog scale [n = 97][k]	80 (60-90)	80 (50-90)		.88[h]
Overall [n = 97][l]	0.73 (0.49-1.00)	0.74 (0.51-1.00)		.38[h]

maging. This suggests that the improved functional out-
come may be explained by an amelioration in the microcircu-
atory reperfusion.[18] Recently, perfusion imaging studies per-

Figure 2. Distribution of Functional Scores at 90 Days in the CHOICE Trial of Intra-arterial Alteplase

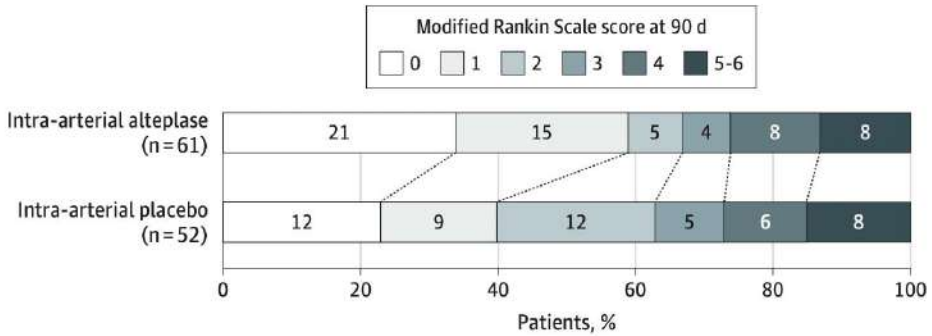


Table 3. Adverse Events in the CHOICE Trial of Intra-arterial Alteplase

Outcomes	No. (%) of participants	
	Alteplase (n = 61)	Placebo (n = 52)
Primary safety outcomes		
Symptomatic intracranial hemorrhage at 24 h	0	2 (3.8)
Death at 90 d	5 (8.2)	8 (15.4)
Additional safety outcomes		
Any serious adverse events[a]	10 (16.4)	15 (28.8)
Any cerebral hemorrhage	19 (31.1)	18 (34.6)
Hemorrhagic infarction		
Type 1[b]	11 (18.0)	8 (15.4)
Type 2[c]	1 (1.6)	0
Parenchymal hematoma		
Type 1[d]	0	0
Type 2[e]	2 (3.2)	4 (7.7)
Remote	1 (1.6)	0
Subarachnoid hemorrhage	4 (6.6)	6 (11.5)

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JOURNAL OF STROKE

Journal of Stroke 2021;23(1):91-102
https://doi.org/10.5853/jos.2020.01788

Original Article

Safety and Angiographic Efficacy of Intra-Arterial Fibrinolytics as Adjunct to Mechanical Thrombectomy: Results from the INFINITY Registry

FREQUENCY

INDİCATİON

SAFETY

EFFİCACY

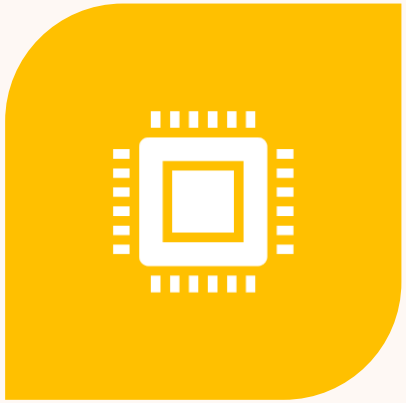
Table 1. Details of participating centers, frequency of MT+IA and typical mode of intra-arterial administration

Center	IA thrombolytic	Median dose (IQR)	Observational period	MT+IA cases	AC MT in study period	%	Typical mode of intra-arterial administration			
							Microcatheter injection	Localization of microcatheter	Speed of injection	Control series (time point)
University Hospital Bochum	tPA	8 (4–18) mg	01/2011–05/2019	11	1,020	1	Yes	As distal as safely possible, usually before clot	1 mL/min	One control run 10 min after final injection
University Hospital Helsinki	tPA	3 (2–5) mg	01/2016–10/2019	31	770	4.0	Yes	As distal as safely possible, usually before clot	Small boluses of 1 mg/5 min	Control run after each 1 mg bolus (usually at 5 min after injection)
University Hospital Bern	UK	250.000 (250.000–500.000) IU	01/2010–12/2018	117	1,195	9.8	Yes	As distal as safely possible, usually before clot	Full dose over 30 min using a syringe infusion pump.	Immediately after infusion is finished, no additional control run
University Hospital Strasbourg	tPA	11 (10–15) mg	01/2018–01/2019	28	142	19.7	Yes	As distal as safely possible	5 mL/min injection by hand using a 5 mL syringe	Immediately after infusion is finished, no additional control run
University Hospital Essen	tPA	10 (5–10) mg	01/2015–09/2019	13	380	3.4	Yes	Proximal infusion (M1) in case of M3/M4 Otherwise as distal as possible	5 mL/min injection by hand using a 5 mL syringe	Immediately after infusion is finished, no additional control run
University Hospital Münster	tPA	10 (7–18) mg	01/2015–12/2016	4	216	1.9	Yes	As distal as safely possible	5 mL/min injection by hand using a 5 mL syringe	Immediately after infusion is finished, no additional control run
University Hospital Köln	tPA	7 (5–10) mg	01/2018–10/2019	76	270	28.1	n=31 (administration via microcatheter) n=45 (administration via distal access catheter)	Microcatheter: As distal as possible usually before clot Distal access: proximal infusion (usually M1 for e.g., residual M3 occlusion)	1 mL/min injection by hand using a 10 mL syringe	Immediately after infusion is finished, no additional control run
University Hospital Göttingen	tPA	11 (9–18) mg	01/2016–08/2019	13	577	2.3	Yes	As distal as safely possible (usually just before clot)	0.5–1 mL/min injection by hand using multiple 1 mL syringes	Immediately after infusion is finished, no additional control run
University Hospital Hamburg	tPA	10 (10–18) mg	01/2015–01/2018	5	762	0.7	Yes	As distal as safely possible (usually just before clot)	1 mL/min injection by hand using multiple 1 mL syringes	Immediately after infusion is finished, no additional control run
University Hospital Rostock	tPA	18 (9–20) mg	10/2015–10/2019	13	280	4–6	Yes	Proximal Infusion (e.g., M1 for an residual M3 occlusion)	5 mL/min injection by hand using a 5 mL syringe	Immediately after infusion is finished, no additional control run
Total				311	5,612	5.5				

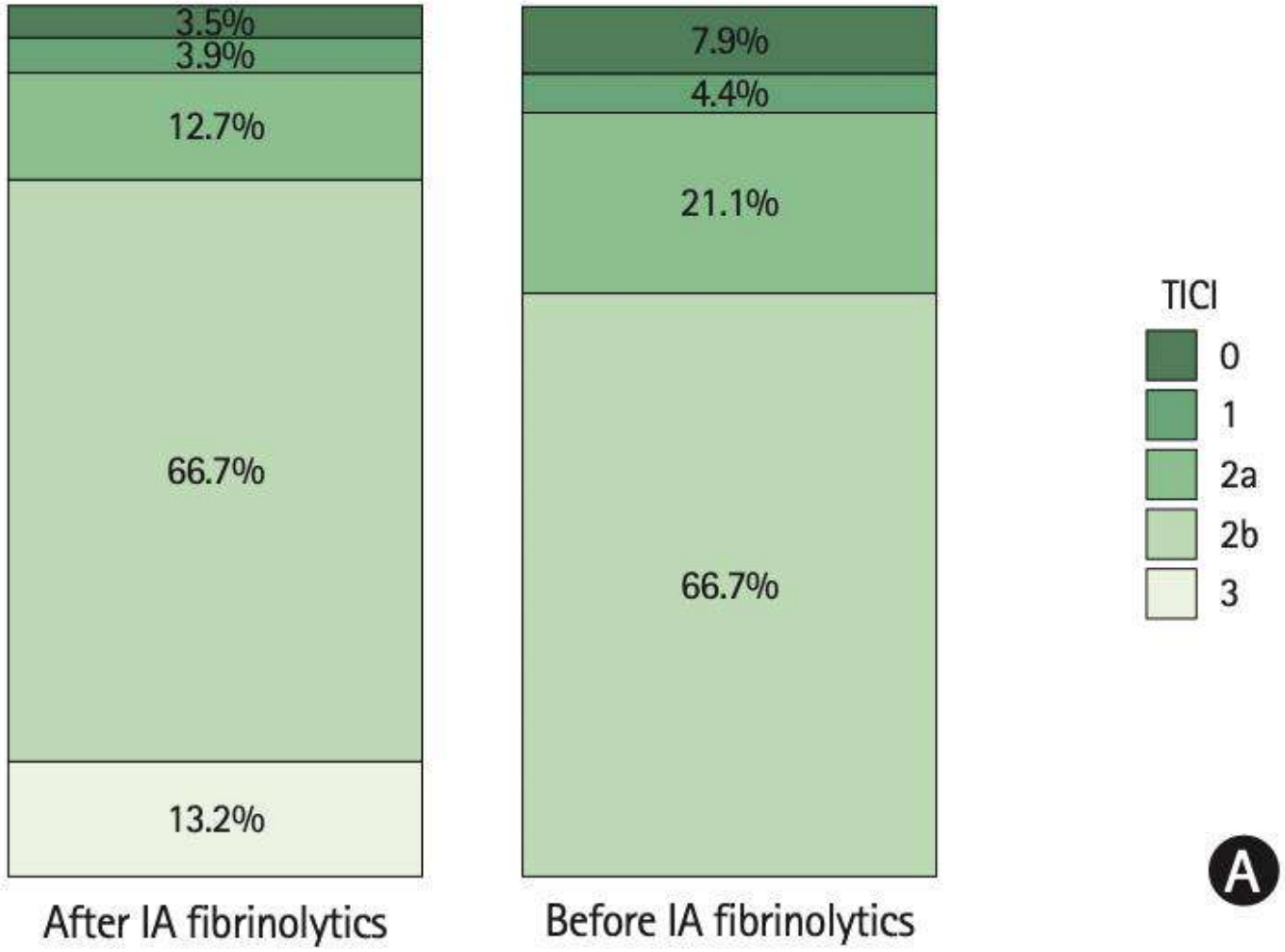
M1, M3, M4, first, third and fourth segment of the middle cerebral artery, respectively.
MT, mechanical thrombectomy; IA, intra-arterial; IQR, interquartile range; AC, anterior circulation; tPA, tissue plasminogen activator; UK, urokinase.

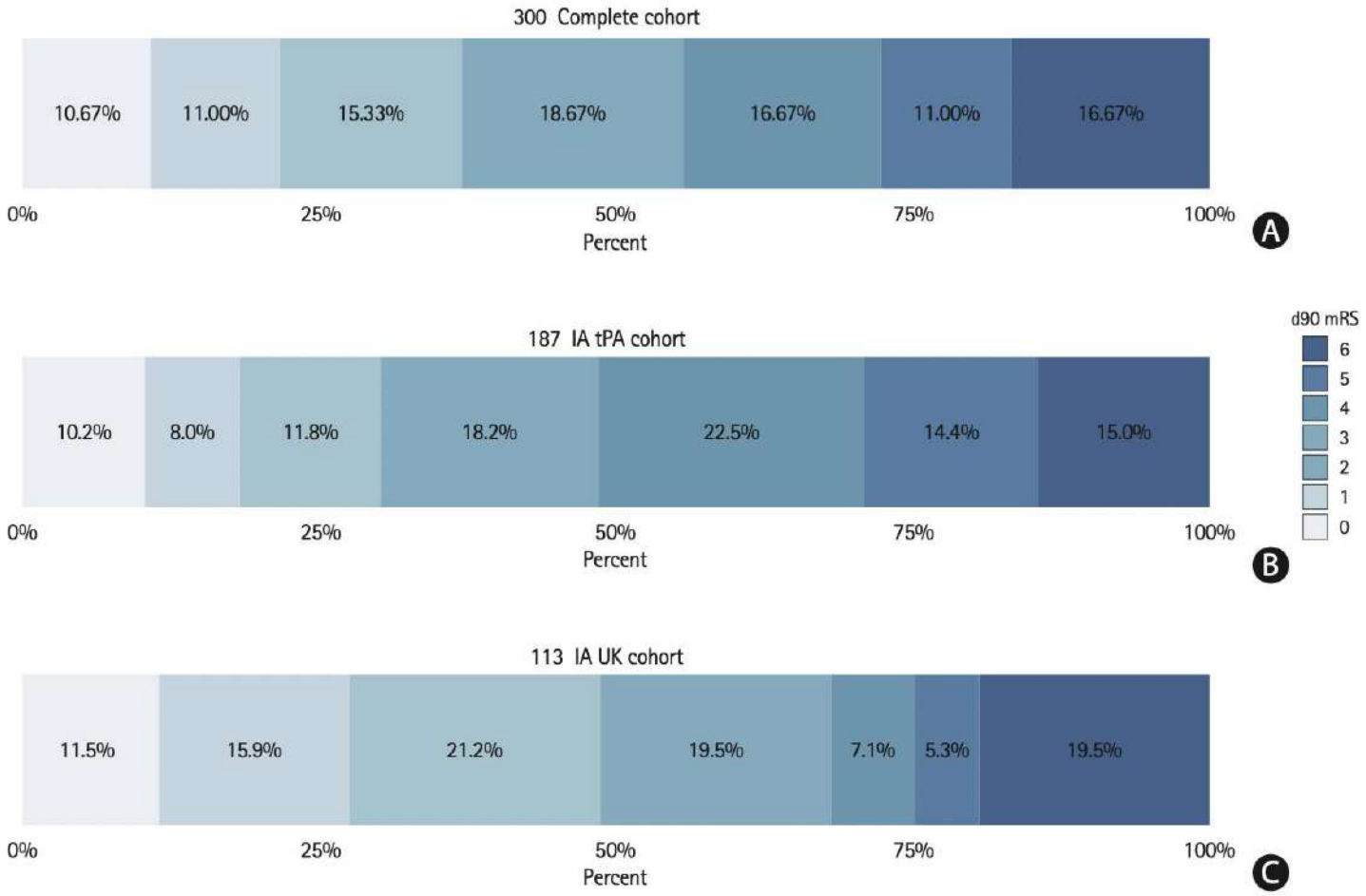
RESCUE OF TICI0-2B RE- PERFUSIONS AFTER MT

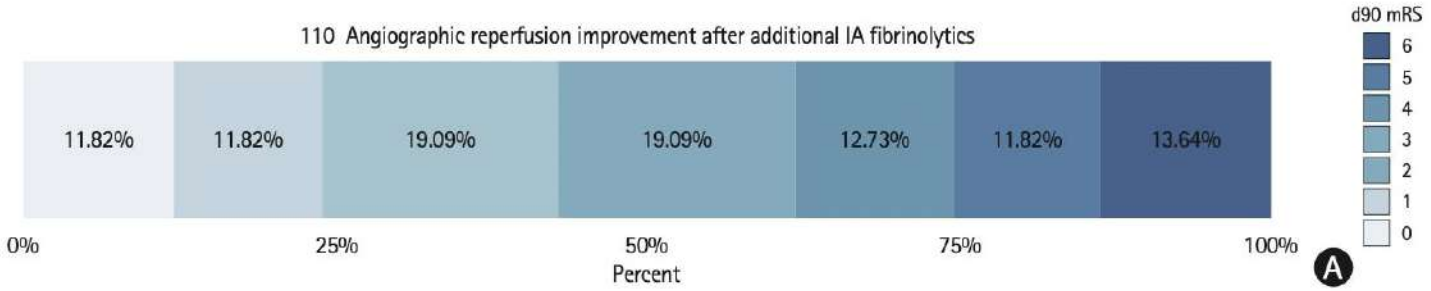
TREATMENT OF EMBOLI IN A NEW TERRITORY



ADMINISTRATION BEFORE OR DURING THE FIRST OR SECOND STENT- RETRIEVER DEPLOYMENT AT THE OPERATOR'S DISCRETION


3.5%
3.9%
12.7%
66.7%
13.2%
After IA fibrinolytics
7.9%
4.4%
21.1%
66.7%
Before IA fibrinolytics
TICI
0
1
2a
2b
3
A


300 Complete cohort
10.67%
11.00%
15.33%
18.67%
16.67%
11.00%
16.67%
0%
25%
50%
75%
100%
Percent
A
187 IA tPA cohort
10.2%
8.0%
11.8%
18.2%
22.5%
14.4%
15.0%
0%
25%
50%
75%
100%
Percent
B
d90 mRS
6
5
4
3
2
1
0
113 IA UK cohort
11.5%
15.9%
21.2%
19.5%
7.1%
5.3%
19.5%
0%
25%
50%
75%
100%
Percent
C


110 Angiographic reperfusion improvement after additional IA fibrinolytics
11.82%
11.82%
19.09%
19.09%
12.73%
11.82%
13.64%
0%
25%
50%
75%
100%
Percent
d90 mRS
6
5
4
3
2
1
0
A

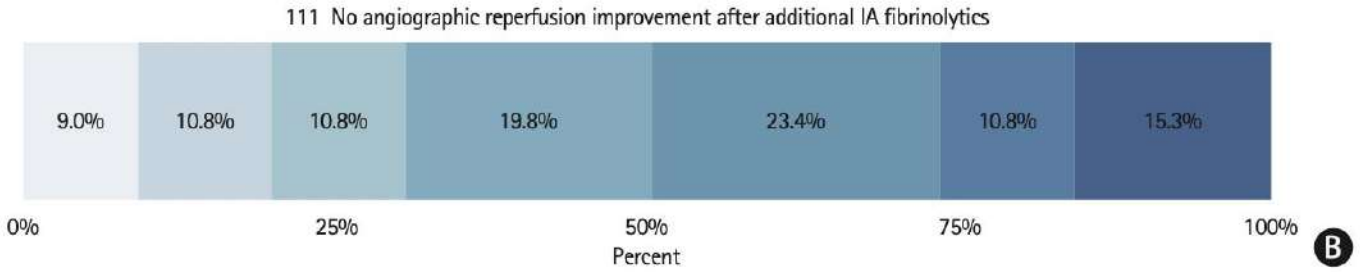

111 No angiographic reperfusion improvement after additional IA fibrinolytics
9.0%
10.8%
10.8%
19.8%
23.4%
10.8%
15.3%
0%
25%
50%
75%
100%
Percent
B

Table 3. Clinical benefit of angiographic reperfusion with strata of TICI grade before administration of IA fibrinolysis

TICI before IA fibrinolytics		mRS		OR
		>2	≤2	
0	ARI−	8 (100)	0 (0)	
	ARI+	6 (66.7)	3 (33.3)	
	Total (TICI0)	14 (82.4)	3 (17.6)	1.50 (0.95–2.38)
1	ARI−	3 (75)	1 (25)	
	ARI+	4 (66.7)	2 (33.3)	
	Total (TICI1)	7 (70)	3 (30)	1.50 (0.09–25.39)
2a	ARI−	14 (77.8)	4 (22.2)	
	ARI+	17 (63.0)	10 (37.0)	
	Total (TICI2a)	31 (68.9)	14 (31.1)	2.06 (0.53–8.00)
2b	ARI−	52 (64.2)	29 (35.8)	
	ARI+	36 (52.9)	32 (47.1)	
	Total (TICI2b)	88 (59.1)	61 (40.9)	1.59 (0.83–3.08)
All TICI	ARI−	77 (69.4)	34 (30.6)	
	ARI+	63 (57.3)	47 (42.7)	
	Total (all TICI)	140 (63.3)	81 (36.7)	cOR 1.83 (1.04–3.22)*

Values are presented as number (%). Calculated using Mantel-Haenszel statistics. *P* for heterogeneity of OR, 0.54 (Breslow-Day test). 95% Confidence intervals of OR were calculated using Woolf's approximation.
TICI, thrombolysis in cerebral infarction; IA, intra-arterial; mRS modified Rankin Scale; OR, odds ratio; ARI−/+, angiographic reperfusion improvement; cOR, common odds ratio.
*$P<0.05$.

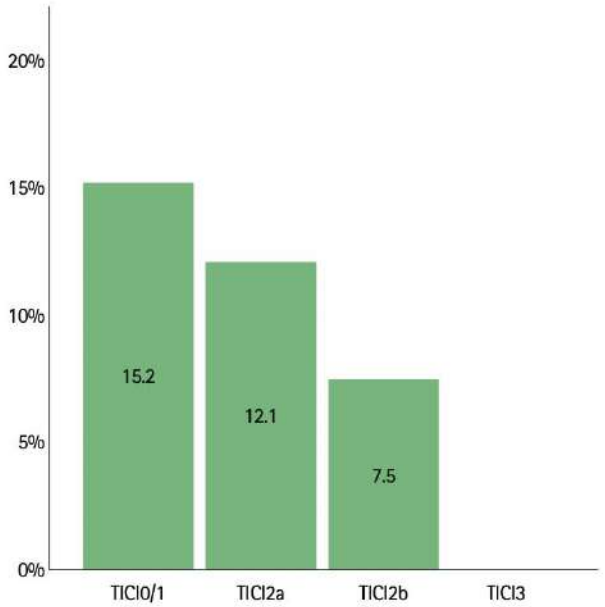


Figure 1. Risk of symptomatic intracranial hemorrhage (sICH) according to thrombolysis in cerebral infarction (TICI). Data on sICH was available in 308/311 patients. SICH occurred in 5/33 patients (15.2%) with TICI0/1, in 8/66 patients (12.1%) with TICI2a, in 14/187 patients (7.5%) with TICI2b and did not occur in 22 patients with TICI3. There was a decreased risk of sICH with higher TICI grade (adjusted odds ratio [aOR] per grade increase derived from logistic regression analysis: aOR, 0.43; 95% confidence interval, 0.20 to 0.94). TICI scores used were before administration of intra-arterial fibrinolytics in cases of rescue of TICI0-2b reperfusions. In other cases (treatment of emboli in new territory or administration during first retrievals at the operator's discretion) final TICI scores were used.

- Majority (>80%) of patients received IA fibrinolytics within 6 hours after symptom-onset.
- Rates of sICH were twice as high compared to rates of sICH reported in the Highly Effective Reperfusion Us- ing Multiple Endovascular Devices (HERMES) collaboration or the Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE-NA1) trial (8.8% vs. 3.9%/4.4%)
- Any angiographic reperfusion improvement was observed in half of the patients with around one-third resulting in a TICI grade change.
- Any angiographic reperfusion improvement after IA fibrinolytics was associated with better outcomes.

- UK upregulates blood brain barrier tight junctions
- More favorable effect on matrix metalloproteinases
- Potentially lowering the risk of bleeding in comparison to tPA

JAMA Neurology | Original Investigation

Safety and Efficacy of Intra-arterial Urokinase After Failed, Unsuccessful, or Incomplete Mechanical Thrombectomy in Anterior Circulation Large-Vessel Occlusion Stroke

Johannes Kaesmacher, MD; Sebastian Bellwald, MD; Tomas Dobrocky, MD; Thomas R. Meinel, MD; Eike I. Piechowiak, MD; Martina Goeldlin, MD; Christoph C. Kurmann, MD; Mirjam R. Heldner, MD; Simon Jung, MD; Pasquale Mordasini, MD; Marcel Arnold, MD; Pascal J. Mosimann, MD; Gerhard Schroth, MD; Heinrich P. Mattle, MD; Jan Gralla, MD, MSc; Urs Fischer, MD, MSc

Figure 1. Study Flowchart

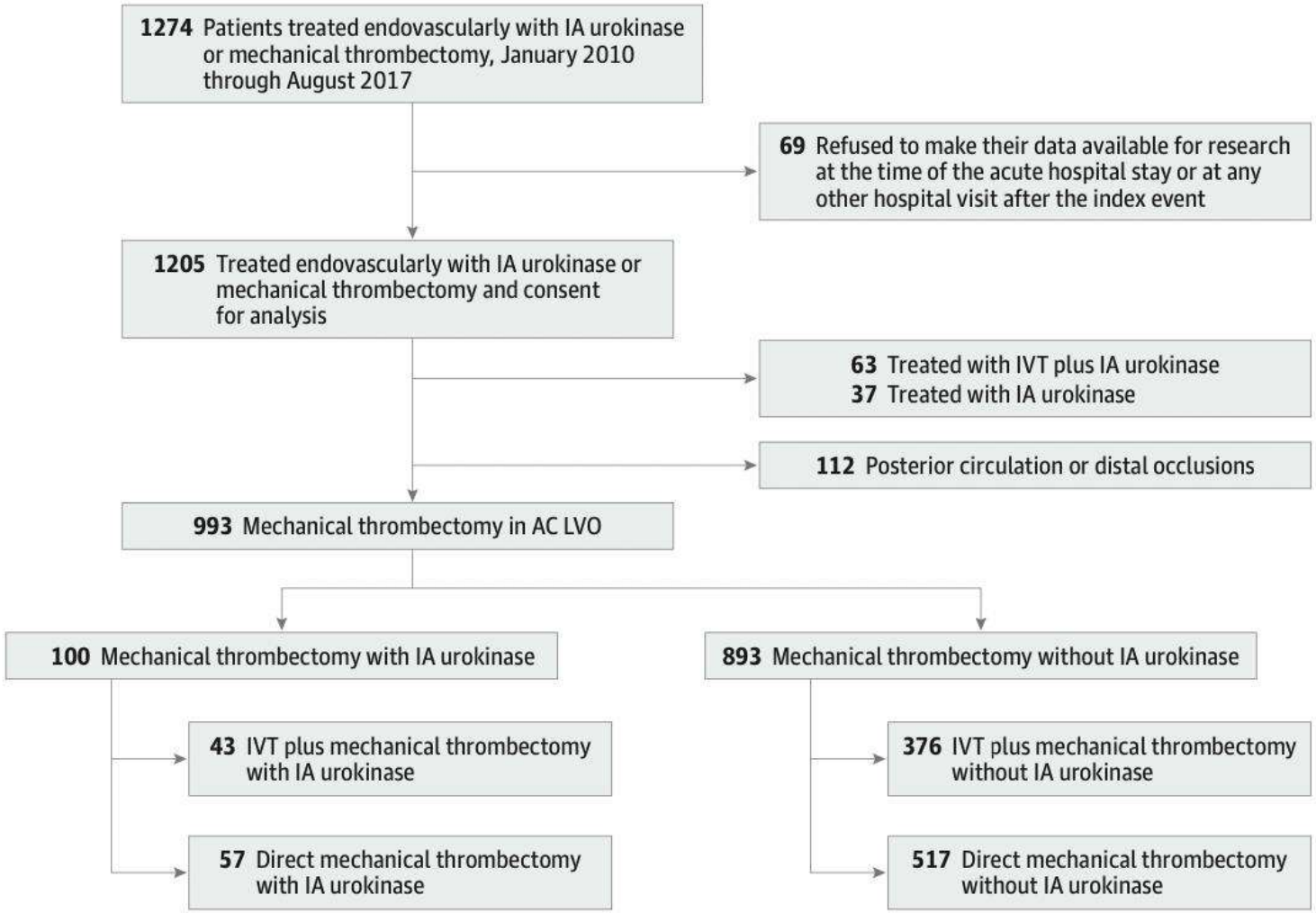


Table 2. Primary and Secondary Outcomes

Outcome	Treatment Group, No./Total No. (%)			P Value	Model A[a]		Model B[b]	
	All (N = 993)	MT Without Intra-arterial Urokinase (n = 893)	MT With Intra-arterial Urokinase (n = 100)		No./Total No.	aOR (95% CI)[c]	No./Total No.	aOR (95% CI)[c]
Poststroke seizures								
None	943/990 (95.3)	845/890 (94.9)	98/100 (98.0)	.80	NA	NA	NA	NA
Focal	19/990 (1.9)	18/890 (2.0)	1/100 (1.0)		NA	NA	NA	NA
Complex focal	5/990 (0.5)	5/890 (0.6)	0/100		NA	NA	NA	NA
Generalized	23/990 (2.3)	22/890 (2.5)	1/100 (1.0)		NA	NA	NA	NA
Systemic bleeding	13/992 (1.3)	13/892 (1.5)	0/100	.63	NA	Did not converge	NA	Did not converge
PROACT-II								
sICH	65/972 (6.7)	60/875 (6.9)	5/97 (5.2)	.67	930/972	0.81 (0.31-2.13)	877/972	0.46 (0.15-1.42)
aICH (excluding sICH)	237/907 (26.1)	222/815 (27.2)	15/92 (16.3)	.02[d]	869/907	0.53 (0.29-0.95)	823/907	0.54 (0.29-0.99)
mRS score 0-2 at 90 d[e]	374/959 (39.0)	329/860 (38.3)	45/99 (45.5)	.19	917/959	1.00 (0.62-1.64)	854/959	1.93 (1.11-3.37)
Mortality at 90 d	254/959 (26.5)	235/860 (27.3)	19/99 (19.2)	.09	917/959	0.78 (0.43-1.40)	854/959	0.48 (0.25-0.92)

Abbreviations: aICH, asymptomatic intracranial hemorrhage; aOR, adjusted odds ratio; IA, intra-arterial; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NA, not applicable; PROACT-II, Prolyse in Acute Cerebral Thromboembolism II trial; sICH, symptomatic ICH.

[a] Indicates baseline model.

[b] Indicates baseline and technical model.

[c] Indicates aOR of intra-arterial urokinase administration.

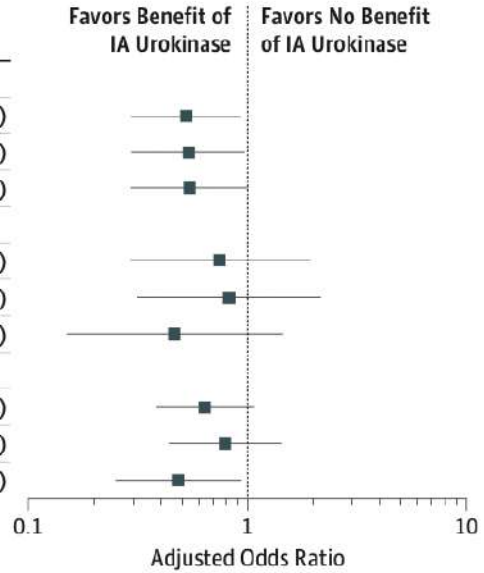
[d] $P < .05$, Fisher exact test.

[e] Scores range from 0 to 6, with higher scores indicating more severe disability (6 indicates death).

Figure 2. Crude and Adjusted Odds Ratio of Intra-arterial (IA) Urokinase and Several Outcomes

A Risk of aICH, sICH, and mortality

Outcome	Adjusted Odds Ratio (95%)
aICH	
Unadjusted	0.52 (0.29-0.92)
Model A	0.53 (0.29-0.95)
Model B	0.54 (0.29-0.99)
sICH	
Unadjusted	0.74 (0.29-1.89)
Model A	0.81 (0.31-2.13)
Model B	0.46 (0.15-1.42)
Mortality	
Unadjusted	0.63 (0.38-1.07)
Model A	0.78 (0.43-1.40)
Model B	0.48 (0.25-0.92)



B Modified Rankin Scale score

Outcome	Adjusted Odds Ratio (95%)
mRS 0-2	
Unadjusted	1.35 (0.89-2.05)
Model A	1.00 (0.62-1.64)
Model B	1.93 (1.11-3.37)

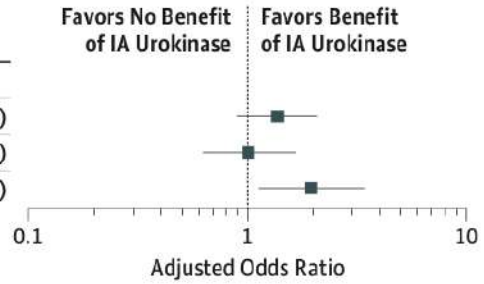
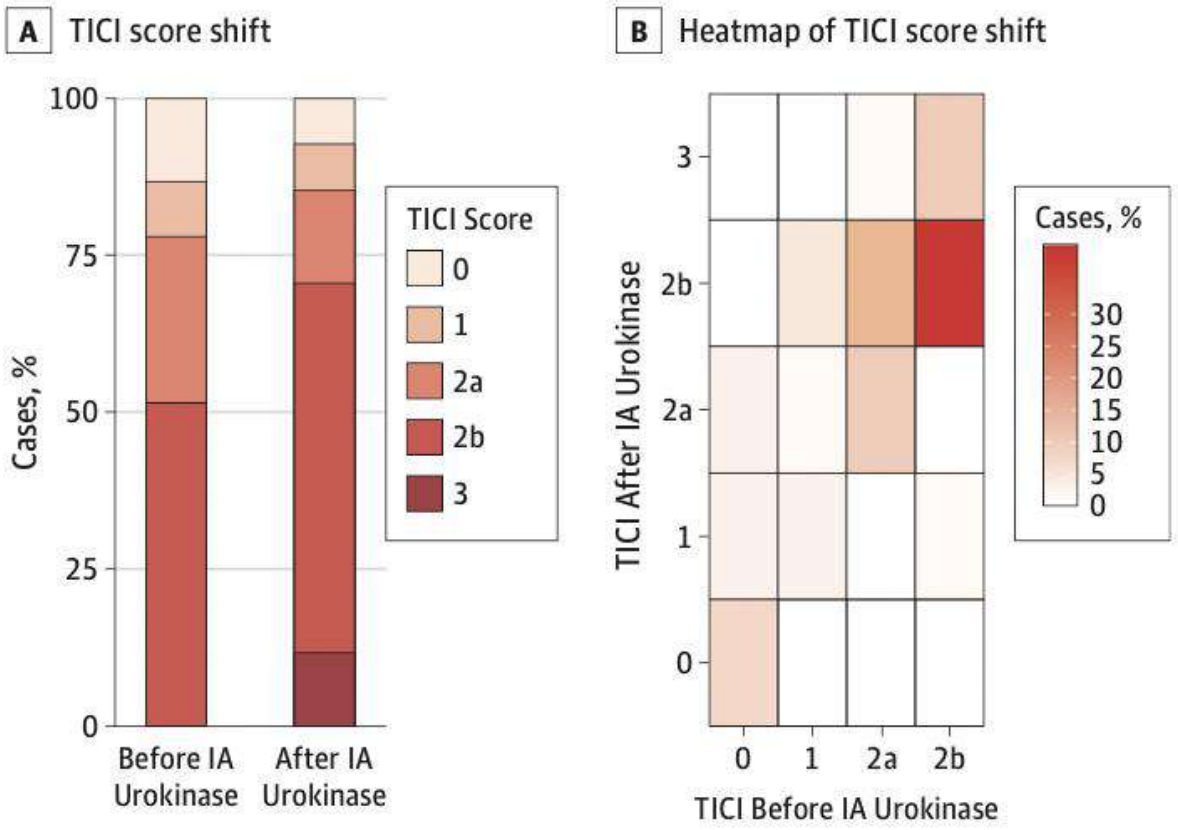


Figure 3. Reperfusion Improvement With Intra-arterial (IA) Urokinase After Failed and Incomplete Mechanical Thrombectomy



TICI indicates Thrombolysis in Cerebral Infarction (TICI) grade. Shifts in grades are shown after administration of IA urokinase.

Before this publication, data regarding intra-arterial thrombolysis during MT were mixed, with some studies suggesting increased risk of hemorrhage. A post hoc analysis of the SWIFT (Solitaire With the Intention For Thrombectomy) trial[4] revealed that in patients treated with MT, receipt of intra-arterial recombinant tissue plasminogen activator (rt-PA) was strongly associated with intracerebral hemorrhage (ICH), although many of the patients in this study were treated with now-outdated devices. On the other hand, thrombolytic in-

nase. Not only was the symptomatic ICH rate not elevated in urokinase-treated patients compared with the non–urokinase cohort (5.2% vs 6.9%; *P* = .67), but the total ICH rate was in fact lower (16.3% vs 27.2%; *P* = .02). Although this difference should be interpreted cautiously owing to the numerous biases associ-

urokinase infusions are addressing a "no-reflow" phenomenon, a finding that has been seen clearly in multiple animal models and cardiac literature but proven difficult to demonstrate definitively in clinical AIS. In a no-reflow state, distal perfusion remains impaired despite large vessel recanalization due to obstructions of the microvasculature, which may be caused by endothelial injury and/or microthrombi. As such, if urokinase is able to improve distal perfusion and minimize infarct expansion, the overall ICH risk could be reduced as well.[8]

ized placebo-controlled fashion. Finally, in the upcoming MOST (Multi-arm Optimization of Stroke Thrombolysis) study,[11] patients with AIS will be randomized to receiving intravenous rt-PA plus intravenous argatroban, eptifibatide, or placebo. Although not all patients in the MOST study will harbor LVOs, the low ICH rates seen in the study by Kaesmacher et al[2] bode well for the safety concerns of such a study in patients undergoing MT.[11]

Intraarterial Thrombolysis as Rescue Therapy for Large Vessel Occlusions

Analysis From the North American Solitaire Stent-Retriever Acute Stroke Registry

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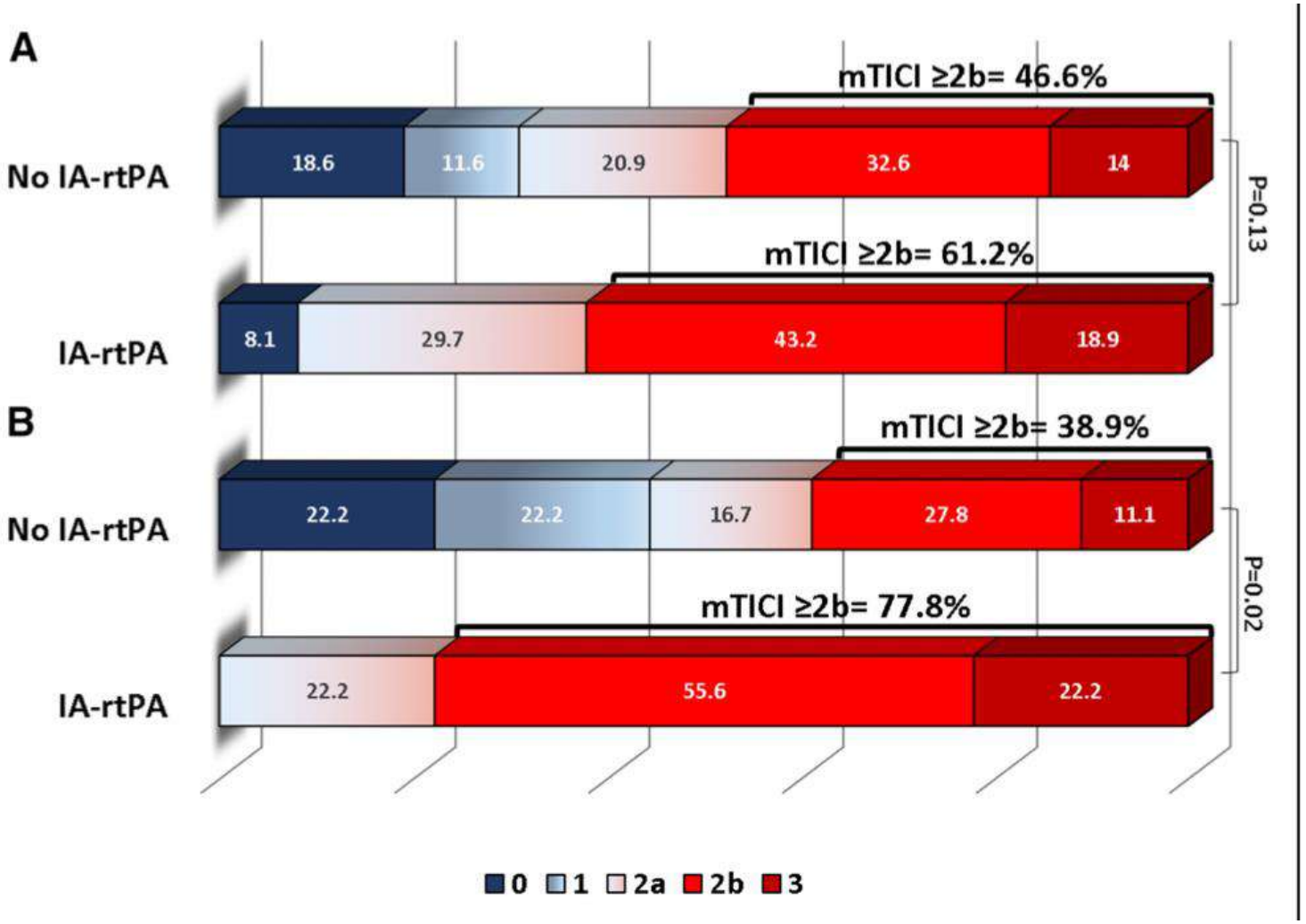
Background and Purpose—Mechanical thrombectomy (MT) devices have led to improved reperfusion and clinical outcomes in acute ischemic stroke patients with emergent large vessel occlusions; however, less than one-third of patients achieve complete reperfusion. Use of intraarterial thrombolysis in the context of MT may provide an opportunity to enhance these results. Here, we evaluate the use of intraarterial rtPA (recombinant tissue-type plasminogen activator) as rescue therapy (RT) after failed MT in the North American Solitaire Stent-Retriever Acute Stroke registry.

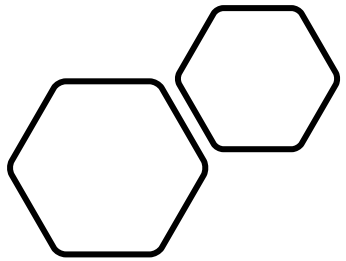
Methods—The North American Solitaire Stent-Retriever Acute Stroke registry recruited sites within North America to submit data on acute ischemic stroke patients treated with the Solitaire device. After restricting the population of 354 patients to use of RT and anterior emergent large vessel occlusions, we compared patients who were treated with and without intraarterial rtPA after failed MT.

Results—A total of 37 and 44 patients was in the intraarterial rtPA RT and the no intraarterial rtPA RT groups, respectively. Revascularization success (modified Thrombolysis in Cerebral Infarction ≥2b) was achieved in more intraarterial rtPA RT patients (61.2% versus 46.6%; P=0.13) with faster times to recanalization (100±85 versus 164±235 minutes; P=0.36) but was not statistically significant. The rate of symptomatic intracranial hemorrhage (13.9% versus 6.8%; P=0.29) and mortality (42.9% versus 44.7%; P=0.87) were similar between the groups. Good functional outcome (modified Rankin Scale score of ≤2) was numerically higher in intraarterial rtPA patients (22.9% versus 18.4%; P=0.64). Further restriction of the RT population to M1 occlusions only and time of onset to groin puncture ≤8 hours, resulted in significantly higher successful revascularization rates in the intraarterial rtPA RT cohort (77.8% versus 38.9%; P=0.02).

Conclusions—Intraarterial rtPA as RT demonstrated a similar safety and clinical outcome profile, with higher reperfusion rates achieved in patients with M1 occlusions. Prospective studies are needed to delineate the role of intraarterial thrombolysis in MT. **(*Stroke*. 2019;50:1003-1006. DOI: 10.1161/STROKEAHA.118.024442.)**

Key Words: occlusion ■ reperfusion ■ standard of care ■ stroke ■ thrombectomy


A
No IA-rtPA
18.6
11.6
20.9
32.6
14
mTICI ≥2b= 46.6%
IA-rtPA
8.1
29.7
43.2
18.9
mTICI ≥2b= 61.2%
P=0.13
B
No IA-rtPA
22.2
22.2
16.7
27.8
11.1
mTICI ≥2b= 38.9%
IA-rtPA
22.2
55.6
22.2
mTICI ≥2b= 77.8%
P=0.02
0 1 2a 2b 3



- EMBOLIC

- ATHEROSKLEROTİC

Efficacy and Safety of Low-Dose Tirofiban for Acute Intracran Atherosclerotic Stenosis Related Occlusion with Residual Stenosis after Endovascular Treatment

Zhizhong Yan, MD,*† Zhonghua Shi, MD,† Yuhai Wang, MD,† Chunlei Zhang, MD,† Jiaming Cao, MD,† Chunlong Ding,† Mirui Qu, MD,‡ Yunbao Xia, MD,‡ Jin Cai, MD,* Xin Zhang, MD,* and Handong Wang, MD*

Background: The optimal treatment strategy for residual stenosis in patients with acute intracranial atherosclerotic stenosis related occlusion (ICAS-O) after endovascular treatment (EVT) is unknown. This study aims to evaluate the efficacy and safety of low-dose tirofiban in patients with residual stenosis after EVT due to acute ICAS-O. *Methods:* Retrospective analysis of prospectively enrolled consecutive patients with residual stenosis after EVT due to acute ICAS-O from March 2015 to May 2019. Patients were divided into EVT alone group or EVT plus tirofiban group. The primary endpoint was the favorable functional outcome (defined as modified Rankin scale score of 0-2) at 90 days. The secondary endpoints were the proportions of reocclusion of recanalized arteries within 72 hours after EVT, symptomatic intracranial hemorrhage (sICH), any ICH, and mortality at 90 days. Logistic regression for predictors of reocclusion and functional outcomes were performed. *Results:* A total of 98 patients, 50 treated with tirofiban and 48 without tirofiban, were enrolled in this study. Compared with patients in EVT alone group, patients in EVT plus tirofiban group had higher favorable functional outcome rate, lower mortality, and a lower reocclusion rate (56.3% versus 30.4%; $P = .014$, 8.3% versus 28.3%; $P = .016$, and 10.4% versus 32.6%; $P = .011$, respectively). The rates of any ICH and sICH were similar between the 2 groups. The use of tirofiban was associated with the favorable functional outcome (odds ratio [OR], 3.417; 95% confidence interval [CI], 1.149-10.163; $P = .027$) and lower reocclusion rate (OR, 0.145; 95% CI, 0.038-0.546; $P = .004$) on multivariate logistic regression analysis. *Conclusions:* In patients with residual stenosis after EVT due to acute ICAS-O, a low-dose of tirofiban is associated with favorable functional outcome and reduced incidence of reocclusion without increasing any ICH and sICH.

Key Words: Acute ischemic stroke—endovascular treatment—glycoprotein IIb/IIIa receptor inhibitor—large vessel occlusion

Table 1. *Demographic and clinical characteristics of patients with and without tirofiban*

Characteristics	Tirofiban (n = 50)	Without tirofiban (n = 48)	*P* value
Age, mean (SD), y	68.1 (13.9)	70.5 (13.8)	.43
Female, n (%)	21 (42)	20 (41.7)	1.0
Vascular risk factors			
Hypertension, n (%)	33 (66)	30 (62.5)	.83
Diabetes mellitus, n (%)	7 (14)	8 (16.7)	.78
Atrial fibrillation, n (%)	9 (18)	8 (16.7)	1.0
History of stroke or TIA, n (%)	12 (30)	6 (12.5)	.14
Baseline NIHSS score, median (IQR)	19 (13-25)	21 (13-30)	.17
Baseline ASPECTS/pc-ASPECTS, median (IQR)	9 (9-10)	9 (8-10)	.76
Site of occlusion			.44
ICA, n (%)	16 (32)	12 (25)	
MCA-M1 segment, n (%)	23 (46)	24 (50)	
MCA-M2 segment, n (%)	5 (10)	9 (18.8)	
BA, n (%)	6 (12)	3 (6.3)	
Intravenous alteplase use, n (%)	43 (86)	34 (70.8)	.09
CS 2-4, n (%)	30 (60)	28 (58.3)	1.0
Time to revascularization, median (IQR)	257.1 (200.5-301)	298.8 (220.4-323)	.12
Procedure time, median (IQR)	52.1 (28.8-65.3)	53.2 (30.4-63.8)	.72
Number of passes, median (IQR)	2 (1-2)	2 (1-2)	.71
Balloon angioplasty, n (%)	4 (8)	5 (10.4)	.74
Residual stenosis>70%, n (%)	22 (44)	16 (33.3)	.28

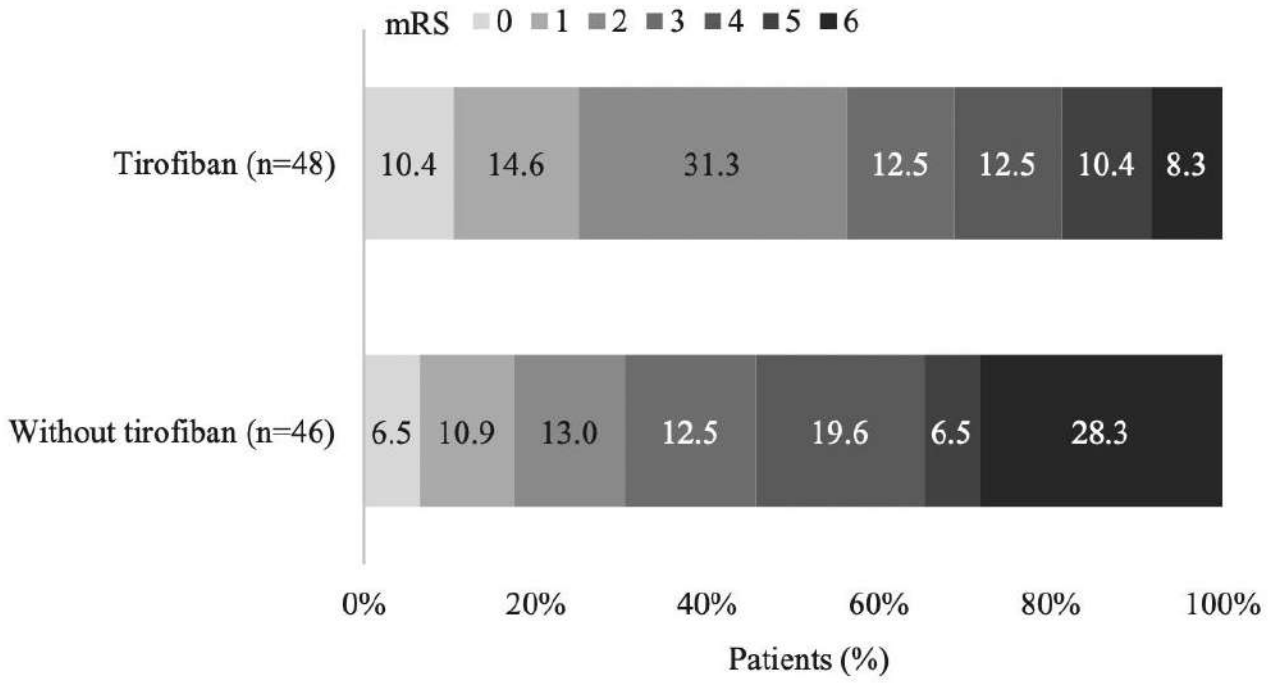


Figure 1. *Scores on the modified Rankin scale at 90 days.*

Table 2. *Functional outcomes at 90 days, reocclusion, any ICH and sICH*

Outcome	All patients (n = 98)			Residual stenosis >70% (n = 38)			Residual stenosis ≤70% (n = 60)		
	Tirofiban (n = 50)	Without tirofiban (n = 48)	*P* value	Tirofiban (n = 22)	Without tirofiban (n = 16)	*P* value	Tirofiban (n = 28)	Without tirofiban (n = 32)	*P* value
mRS score 0-2 no./total no. (%)	27/48 (56.3)	14/46 (30.4)	0.014	12/21 (57.1%)	6/15 (40%)	0.500	15/27 (55.6%)	8/31 (25.8)	.031
mRS score 6 no./total no. (%)	4/48 (8.3)	13/46 (28.3)	0.016	3/21 (14.3)	8/15 (53.3)	0.025	1/27 (3.7)	5/31 (16.1)	.201
Reocclusion no./total no. (%)	5/48 (10.4)	15/46 (32.6)	0.011	4/20 (20)	11/16 (68.8)	0.006	1/28 (3.6)	4/30 (13.3)	.354
Any ICH no./total no. (%)	14/50 (28)	14/48 (29.2)	1.000	5/22 (22.7)	5/16 (31.3)	0.713	9/28 (32.1)	9/32 (28.1)	.783
sICH no./total no. (%)	6/50 (12)	4/48 (8.3)	0.741	3/22 (13.6)	1/16 (6.3)	0.624	3/28 (10.7)	3/32 (9.4)	1.000

Abbreviations: ICH, intracranial hemorrhage; mRS, modified Rankin scale; sICH, symptomatic ICH.

Kwon et al and Ihn et al,[15,16] the use of tirofiban in this study was as follows: a low-dose intra-arterial tirofiban (Lunan Better Pharmaceutical Co., Ltd., China) bolus (standardly, at a rate of 0.05 mg/min; the dose ranged from 0.4 to 0.5 mg) followed by continuous intravenous infusion at 0.4-0.5 mg/h for 24 hours. If follow-up CT

Safety of Intra-Arterial Tirofiban Administration in Ischemic Stroke Patients after Unsuccessful Mechanical Thrombectomy

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ABSTRACT

Purpose: To assess the safety of low-dose intra-arterial (IA) tirofiban bolus after unsuccessful mechanical thrombectomy in patients with ischemic stroke due to large artery occlusion in anterior cerebral circulation.

Materials and Methods: Patients with ischemic stroke who were treated with mechanical thrombectomy were enrolled in a multicenter registry. Low-dose tirofiban was injected into the residual arterial thrombus in patients after unsuccessful mechanical thrombectomy. The major safety measurement was defined as symptomatic intracranial hemorrhage (SICH). The functional outcome at 90 days was assessed with the modified Rankin Scale, and a score of 0–2 was defined as favorable.

Results: Of the 632 enrolled patients, 154 (24.4%) received IA tirofiban treatment. The SICH rate was 13.6% (21/154) in patients with tirofiban and 16.7% (80/478) in patients without tirofiban ($P = .361$). IA tirofiban was not associated with increased risk of SICH (odds ratio [OR], 0.69; 95% confidence interval [CI], 0.36–1.31; $P = .26$). IA tirofiban treatment did not increase the risk of mortality at 90 days of the index stroke (OR, 0.66; 95% CI, 0.36–1.31; $P = .15$). Patients with large artery atherosclerosis stroke who were treated with tirofiban were associated with decreased risk of death (OR, 11.3% vs 23.4%; $P = .042$) compared to patients who were not treated with tirofiban.

Conclusions: Low-dose IA tirofiban administration may be relatively safe in patients with ischemic stroke after unsuccessful recanalization.

ABBREVIATIONS

ACTUAL = endovascular treatment for acute anterior circulation, IA = intra-arterial, ICH = intracranial hemorrhage, LAA = large artery atherosclerosis, mRS = modified Rankin Scale, mTICI = modified Thrombolysis in Cerebral Infarction, rtPA = recombinant tissue plasminogen activator, SICH = symptomatic intracranial hemorrhage

EDITORS' RESEARCH HIGHLIGHTS

- The use of intra-arterial (IA) IIB/IIIA inhibitors as a rescue treatment for failed large artery thrombectomy in the acute stroke patient is controversial due to concerns of an increased risk of symptomatic subarachnoid hemorrhage (SICH). The current study assessed the safety of low-dose (0.25–1.0 mg) IA tirofiban injected through a microcatheter located near the occlusion.
- Of the 632 patients enrolled in the endovascular treatment for acute anterior circulation ischemic stroke (ACTUAL) registry at 21 stroke centers, 154 (24.4%) who failed the initial thrombectomy received IA tirofiban, and 77 (16.1%) who failed the initial thrombectomy did not.
- SICH occurred in 13.6% (21/154) of patients receiving IA tirofiban and in 16.7% (80/478) of those without ($P = .361$). No significant difference was observed in 90-day mortality or functional outcomes between the 2 groups. There was also no significant difference in the occurrence of SICH between patient groups who had and had not received intravenous thrombolysis.
- Low-dose IA tirofiban was safe in treating patients with large artery ischemic stroke who had failed thrombectomy. Further studies are required to corroborate such safety and to establish overall efficacy.

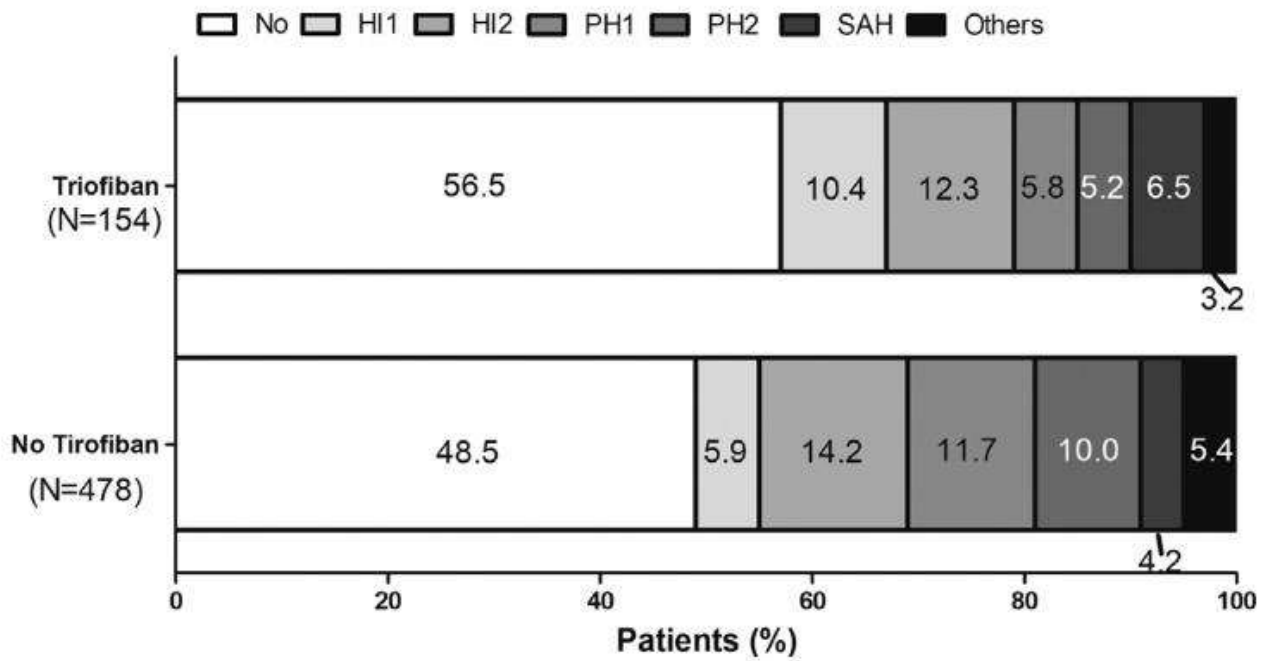


Figure 1. Anatomic distribution of intracranial hemorrhage. Anatomic distribution of intracranial hemorrhage was defined according to the Heidelberg Bleeding Classification. No significant difference was observed concerning overall distribution of ICH between patients with and without IA tirofiban ($P > .05$). HI = hemorrhagic infarction; PH = parenchymal hematoma; SAH = subarachnoid hemorrhage.

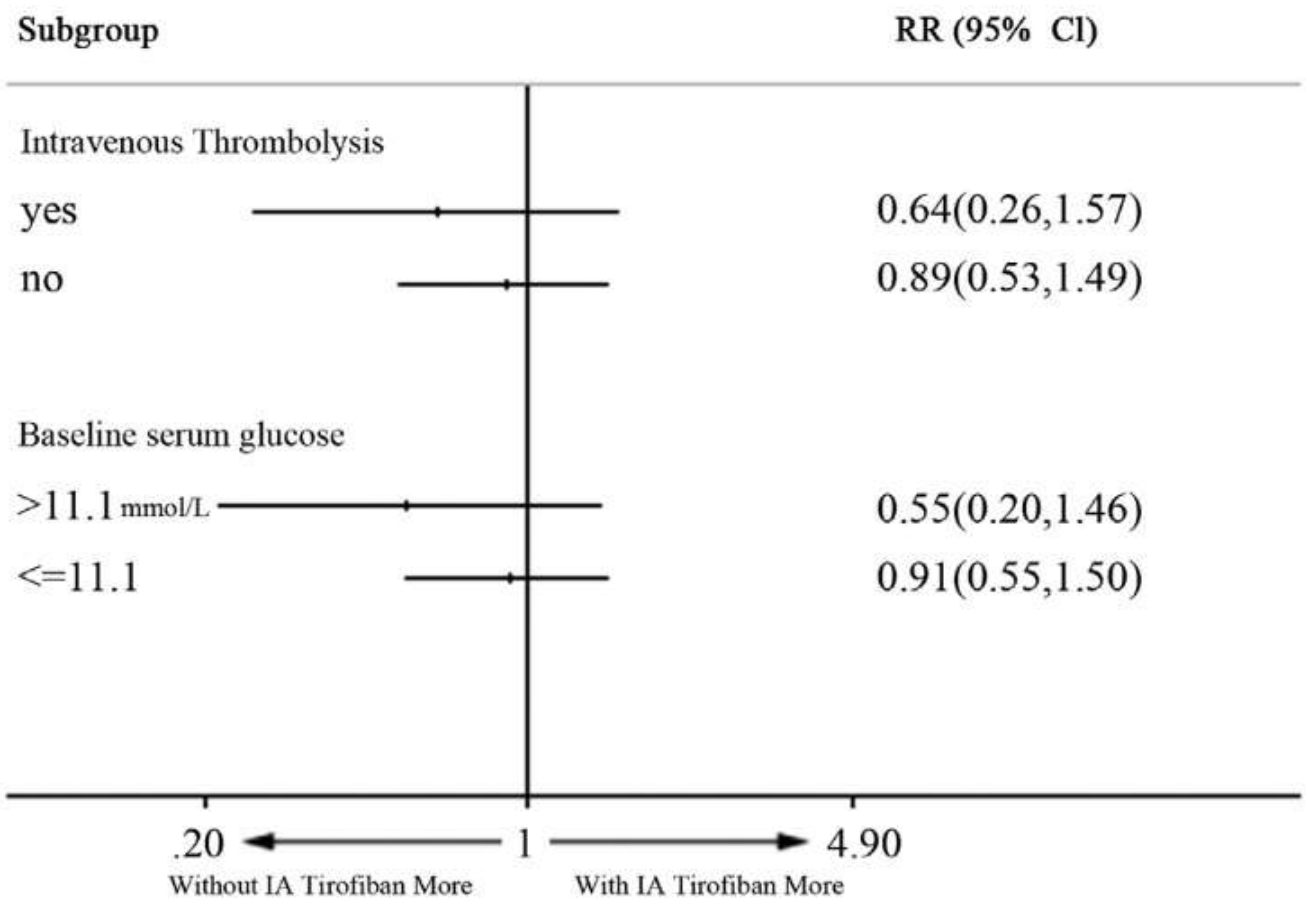


Figure 2. Subgroup analyzation for SICH after intra-arterial (IA) tirofiban treatment. CI = confidence interval; RR = relative risk.

- DİKKATİNİZ İÇİN TEŞEKKÜRLER…

Akut Endovasküler Tedavi sırasında kalıcı stent uyguladım, **anti-agregan** tedavi seçenekleri

Dr. Nihat ŞENGEZE

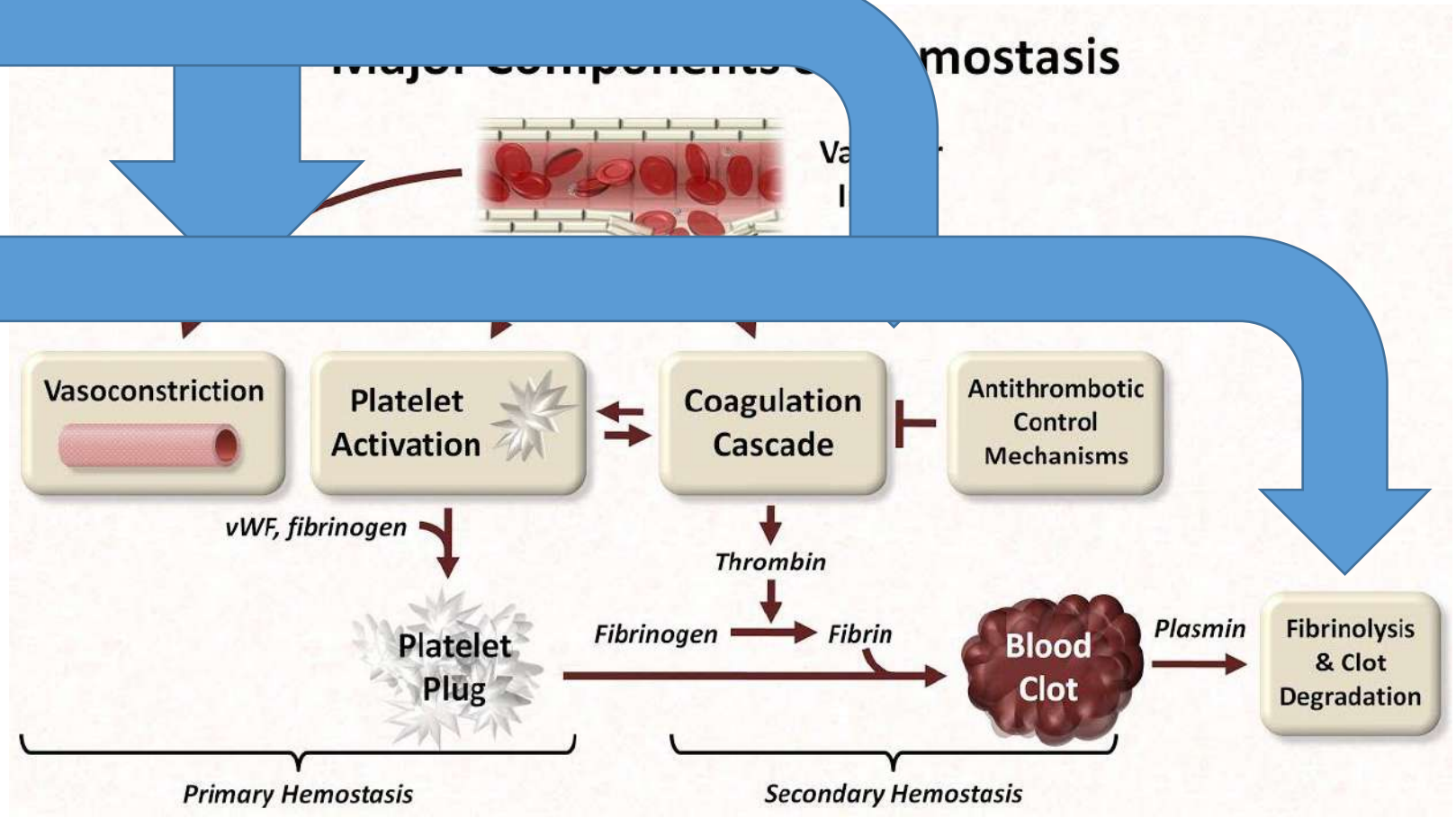
Süleyman Demirel Üniversitesi Nöroloji AD.

IV. Girişimsel Nöroloji Eğitim Toplantısı

22. Mayıs 2022 - GAZİANTEP

Hemostaz mekanizması

- Primer Hemostaz
  - Vazokonstriksiyon
  - Trombosit fazı
- Sekonder hemostaz
  - Koagülasyon faktörleri
  - Fibrin kaskadı
- Tersiyer hemostaz
  - Fibrinolizis



- **Trombosit agregasyon kaskadı;**

Endotel hasarı sonrası;

Adhezyon

Kollagen, vWF
Glikoproteinler (GP)

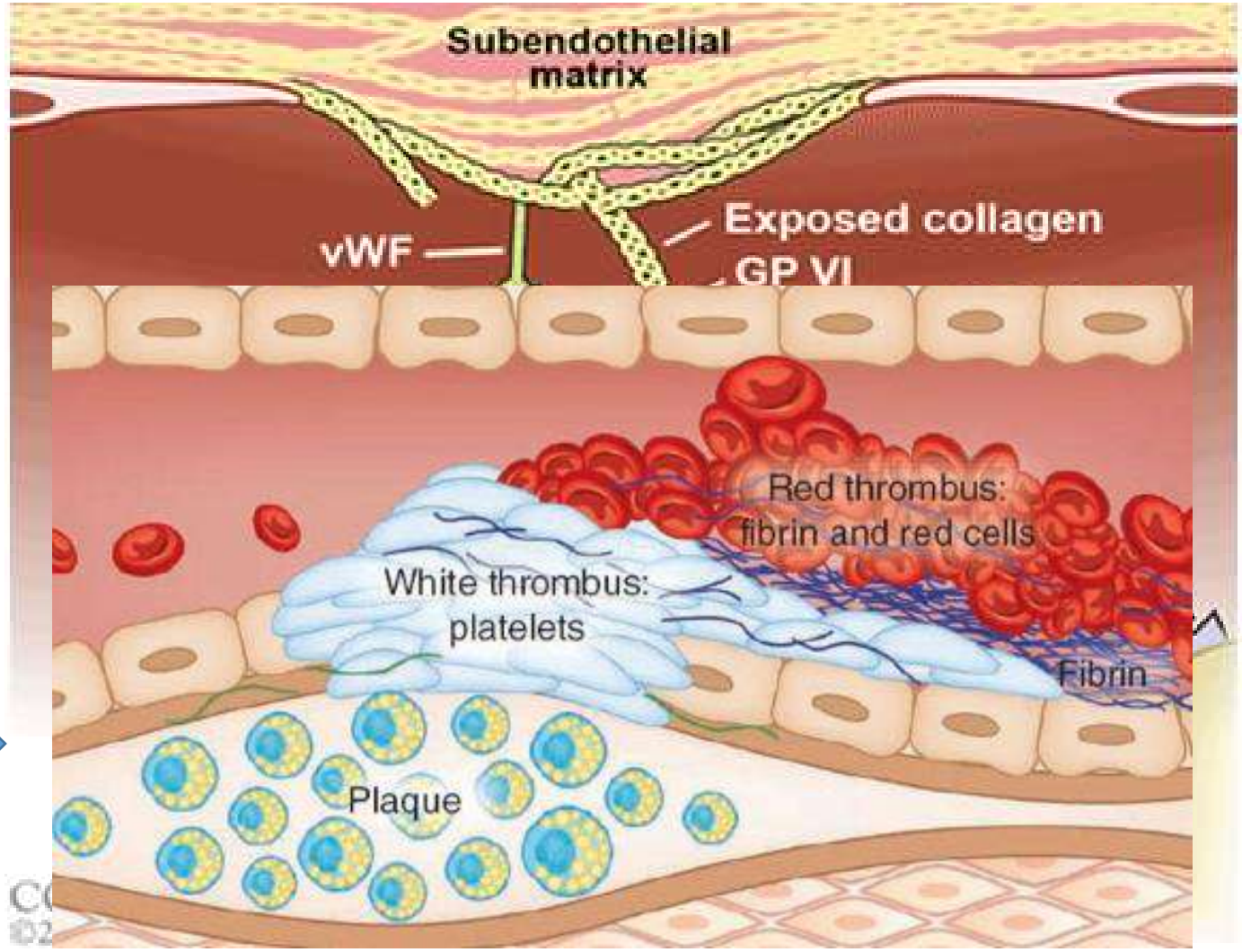
Aktivasyon

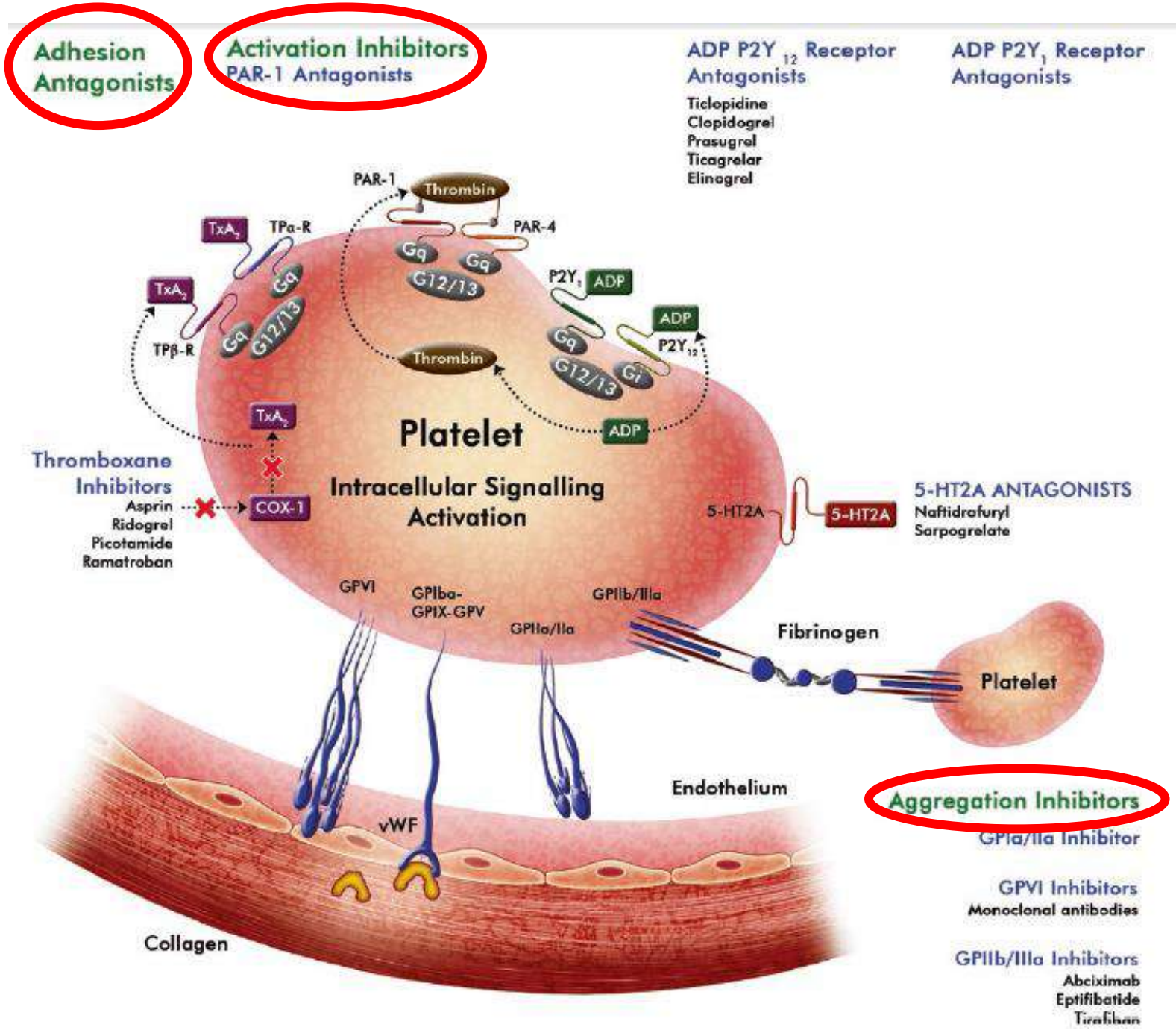
ADP, cAMP
Serotonin
Tromboksan (TxA2)

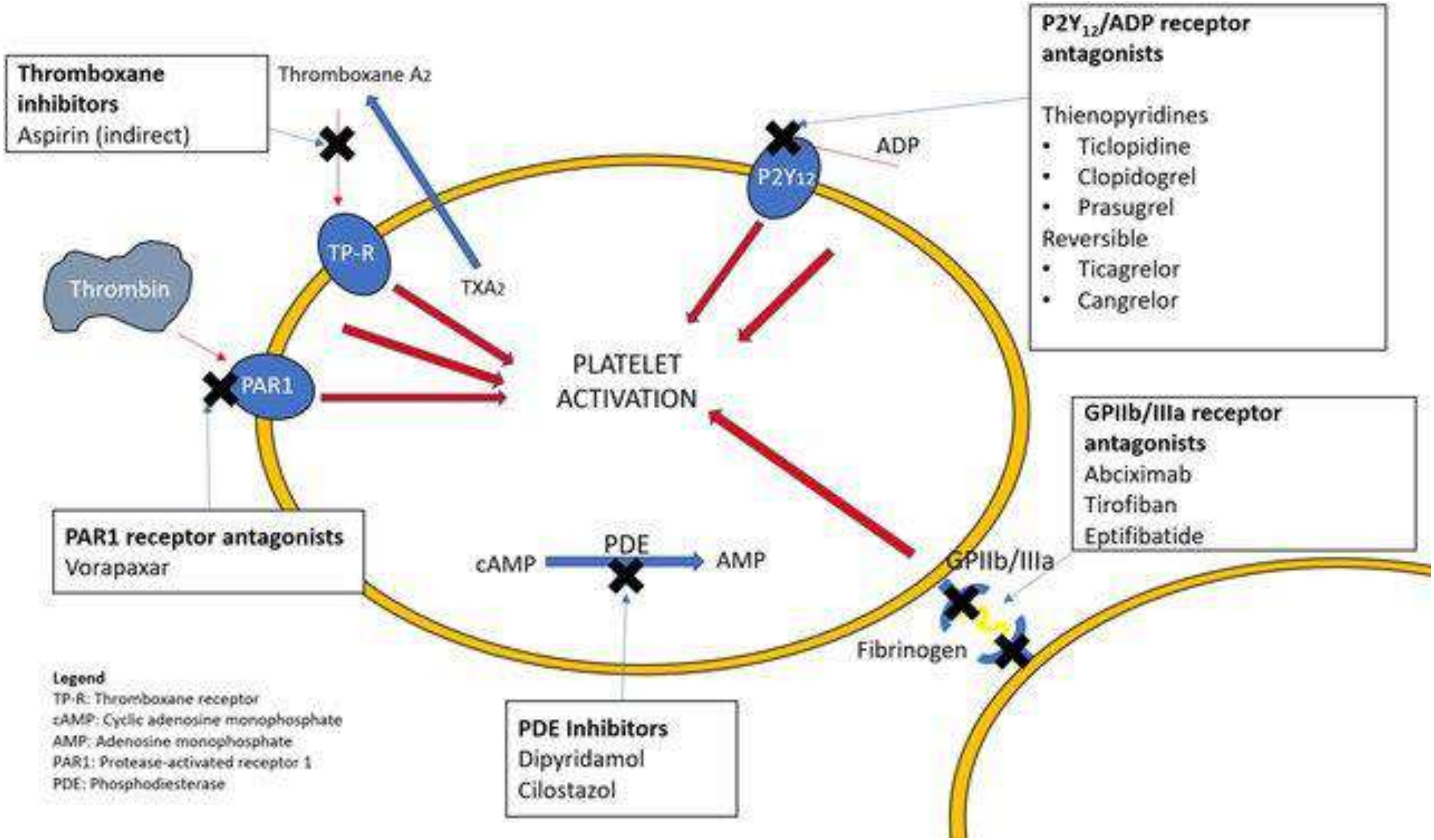
GP IIb/IIIa aktivasyonu

Agregasyon

GP IIb/IIIa
Fibrinojen




Adhesion Antagonists
Activation Inhibitors
PAR-1 Antagonists
ADP P2Y 12 Receptor Antagonists
Ticlopidine
Clopidogrel
Prasugrel
Ticagrelar
Elinogrel
ADP P2Y1 Receptor Antagonists
PAR-1
Thrombin
PAR-4
TxA2
TPα-R
Gq
G12/13
TPβ-R
P2Y1
ADP
P2Y12
Gi
Platelet
Intracellular Signalling Activation
Thromboxane Inhibitors
Asprin
Ridogrel
Picotamide
Ramatroban
COX-1
5-HT2A
5-HT2A ANTAGONISTS
Naftidrofuryl
Sarpogrelate
GPVI
GPIba-GPIX-GPV
GPIIa/IIa
GPIIb/IIIa
Fibrinogen
Platelet
Endothelium
vWF
Collagen
Aggregation Inhibitors
GPIa/IIa Inhibitor
GPVI Inhibitors
Monoclonal antibodies
GPIIb/IIIa Inhibitors
Abciximab
Eptifibatide
Tirofiban


Thromboxane inhibitors
Aspirin (indirect)
Thromboxane A2
P2Y12/ADP receptor antagonists
Thienopyridines
• Ticlopidine
• Clopidogrel
• Prasugrel
Reversible
• Ticagrelor
• Cangrelor
ADP
P2Y12
TP-R
TXA2
Thrombin
PAR1
PLATELET ACTIVATION
PAR1 receptor antagonists
Vorapaxar
cAMP
PDE
AMP
GPIIb/IIIa receptor antagonists
Abciximab
Tirofiban
Eptifibatide
GPIIb/IIIa
Fibrinogen
PDE Inhibitors
Dipyridamol
Cilostazol
Legend
TP-R: Thromboxane receptor
cAMP: Cyclic adenosine monophosphate
AMP: Adenosine monophosphate
PAR1: Protease-activated receptor 1
PDE: Phosphodiesterase

Piyasada kullanılan antiplatelet ilaçlar;

- **Asetilsalisilik asit (ASA)** } Tromboksan inhibitörleri

- **Dipiridamol**
- **Silastazol** } Fosfodiesteraz (PDE) inhibitörleri

- **Klopidogrel**
- **Tiklopidin**
- **Prasugrel** } Geri dönüşsüz
- **Tikagrelor**
- **Kangrelor** } Geri dönüşlü

} P2Y12/ADP reseptör antagonistleri

Glikoprotein IIb/IIIa inhibitörleri;

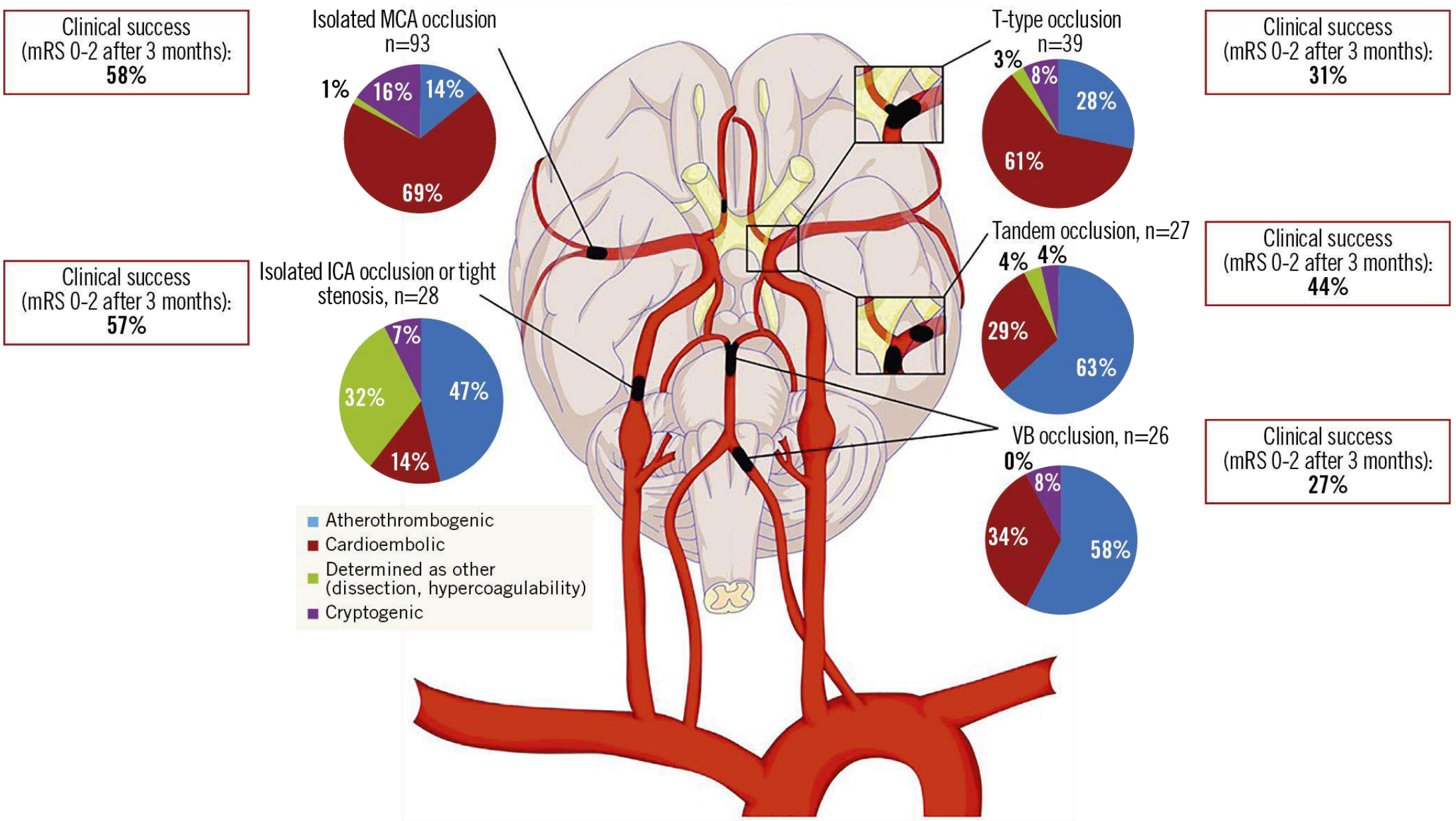
- **Absiksimab**
- **Tirofiban**
- **Eptifibatid**

	COX inhibitör	$P2Y_{12}$ inhibitörleri				GIIb-IIIa inhibitörleri		
	Asetil-salisilikasit	**Klopidogrel**	Prasugrel	Ticagrelor	Cangrelor	Abciximab	Ebtifibatid	Tirofiban
Hedef	Siklo-oksijenaz	$P2y_{12}$	$P2y_{12}$	$P2y_{12}$	$P2y_{12}$	GIIb-IIIa	GIIb-IIIa	GIIb-IIIa
Reversibilite	Irreversible	Irreversible	Irreversible	Reversible	Reversible	Irreversible	Irreversible	Irreversible
Önilaç	Yok	Evet (2 adım)	Evet (1 adım)	Yok	Yok	Monoklonal antikor	Peptid	Non-peptid
Uygulama	Oral iv	Oral	Oral	Oral	iv	iv	iv	iv
Başlangıç etki	75-100mg po: 1st 250mg iv: 15dk	**75mg: 3-7g 300mg: 6st 600mg: 3st**	10mg: 3-5g 20mg: 24st 60mg: 1st	90mg: 2-3g 180mg: 1-2st	30µg/kg bolus + 4ug/kg/dk: 2dk	0,25mg/kg bolus: 10dk	180µg/kg bolus: 15dk	6µg/kg (1dk) 30dk
İdame	75-100mg/gün	75mg/gün	5-10mg/gün	90mg/12st	4µg/kg/dk Periprosedürel	0,125µg/kg/dk (Max 10µg/dk)	2µg/kg (72st'e kadar)	0.1µg/kg/dk (18st'e kadar)
Platelet fonksiyon normalizasyon	5-7 gün	5-7 gün	5-10 gün	3-4 gün	30-60dk	12st	4-6st	4-8st
Yarılanma süresi	15-30dk	6st	7st	8-12st	1st	10-30dk	2.5st	2st

Sorular;

- Akut inme endovasküler tedavisinde **hangi oklüzyonlarda** ve **ne gibi durumlarda kalıcı stent** uygulamak zorunda kalabilirim?
- Hasta **İV TPA** aldı, stent koymak zorundayım nasıl yaklaşalım?
- Kalıcı stent uygulamam gerekiyor, endovasküler tedavide **İA TPA** vereyim mi?
- Akut inme stent uyguladım, Antiagreganların **avantaj** ve **dezavantajları**, birbirine üstünlükleri var mı?
- Stent kullandım oklüde oldu **GP IIb/IIIa inhibitör** (Tirofiban vb.) kullandım, tedaviye nasıl devam edeyim? Antiagregan ne kullanabilirim? Ne zaman başlarım?

- Akut inme endovasküler tedavisinde ***hangi oklüzyonlarda*** ve ***ne gibi durumlarda*** kalıcı stent uygulamak zorunda kalabilirim?



Vavrova J, et al. **Long-term outcomes of thrombectomy for acute ischaemic stroke by occluded artery and stroke aetiology: a PRAGUE-16 substudy**. EuroIntervention. 2021 Jun 11;17(2):e169-e177.

- **Ekstrakranial Stentleme**
  - İnternal Karotid arter proksimal
  - Vertebral arter proksimal
  - Subklavyen arter

- **İntrakranial Stentleme**
  - MCA
  - Baziler
  - Vertebral arter (intrakranial segment)
  - İnternal karotis arter (intrakranial segment)

- Akut stentleme sonrası stent oklüzyonu?

Table 2

Predictors of stent occlusion: multivariate analysis.

Variables	OR (95% CI)	*p*
Use of post-stenting angioplasty (no, *vs* yes)	11.2 (2.49–50.78)	0.002
Residual post-stenting stenosis (per 10% of increase)	2.1 (1.38–3.06)	<0.001
mTICI 0-2a at the end of ET	13.5 (1.97–92.24)	0.008

The variables entered in the initial model were those showing a $p < 0.10$ in univariate analysis. The final model was selected using a backward selection strategy. The Hosmer–Lemeshow test showed an adequate goodness-of-fit of the final model ($X^2 = 8.775$, $p = 0.269$). The model as a whole explained between 37% (Cox and Snell R2) and 56% (Nagelkerke R2) of the variance in carotid stent occlusion and classified correctly a total of 88% of cases.

ET: endovascular therapy; mTICI: modified Thrombolysis in Cerebral Infarction.

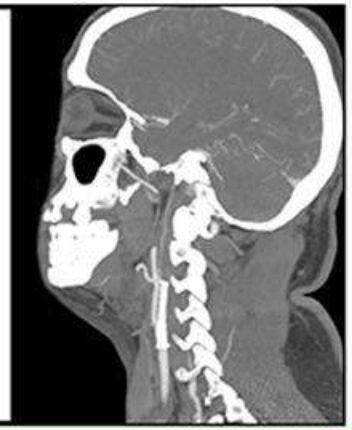
Carotid stent occlusion after emergent stenting in acute ischemic stroke:

incidence, predictors and clinical relevance.

Occluded stent

n = 22

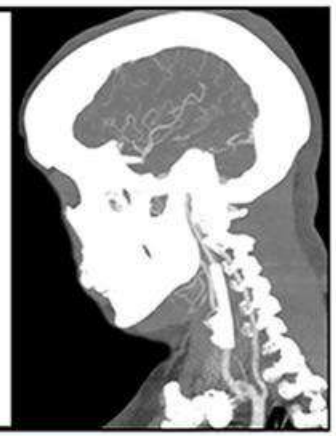
(22%)



Patent stent

n = 77

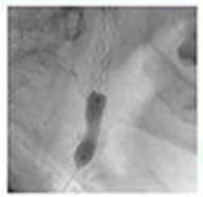
(78%)



PREDICTORS OF EARLY STENT OCCLUSION

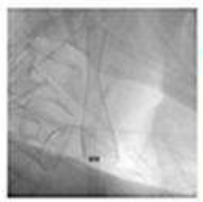
Lower use of post-stenting angioplasty

aOR	*95%CI*	*p*
11.2	2.5-50.8	0.002



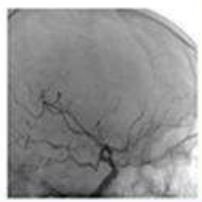
Increased residual intrastent stenosis

aOR	*95%CI*	*p*
2.1	1.4-3.1	<0.001



Unsuccesful intracranial recanalization (mTICI 0-2a)

aOR	*95%CI*	*p*
13.5	2.0-92.2	0.008



CLINICAL OUTCOME AT DAY 90

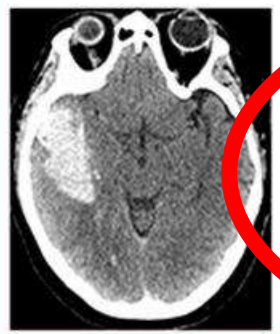
	Occluded stent	Patent stent	p
mRS, median (IQR)	3 (1-4)	2 (1-2)	0.004
mRS 3-6, n (%)	15 (68)	18 (23)	<0.001

Worse mRS shift

aOR	*95%CI*	*p*
3.9	1.3-11.3	0.014

mRS > 2

aOR	*95%CI*	*p*
6.3	1.8-22.7	0.005



sICH AT 24 HOURS

Occluded stent		Patent stent
14%	vs	1%

p = 0.03

Akut endovasküler tedavide **ne gibi durumlarda** kalıcı stent uygulamak zorunda kalınabilir?

- Kateter ile oklüzyon distaline geçilemediğinde
- Balon anjioplasti sonrası re-oklüzyon, ciddi stenoz (>%90)
- Arteriyel diseksiyon (psödo anevrizma vb komplikasyon sonrası)
- Arter darlığı >%70-90 üzeri ve distal akımın yetersiz olduğu
- İntrakranial oklüzyon, birkaç kez trombektomi ile açılamadığında ‘’kurtarıcı stent’’ uygulama

- En çok veri Tandem oklüzyonlar ve proksimal İCA stentleme

- Zevallos CB, et al. Acute Carotid Artery Stenting Versus Balloon Angioplasty for Tandem Occlusions: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2022 Jan 18;11(2)
- Anadani M, et al. Endovascular Therapy of Anterior Circulation Tandem Occlusions: ***Pooled Analysis From the TITAN and ETIS Registries.*** Stroke. 2021 Oct;52(10):3097-3105.
- Marnat G,et al. Safety and Outcome of Carotid Dissection Stenting During the Treatment of Tandem Occlusions: A Pooled Analysis of TITAN and ETIS. Stroke. 2020 Dec;51(12):3713-3718.
- Wilson MP, et al. Management of tandem occlusions in acute ischemic stroke - intracranial versus extracranial first and extracranial stenting versus angioplasty alone: a systematic review and meta-analysis. J Neurointerv Surg. 2018 Aug;10(8):721-728.

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

7. Treatment of tandem occlusions (both extracranial and intracranial occlusions) when performing mechanical thrombectomy may be reasonable.	**IIb**	**B-R**
Tandem occlusions were included in recent endovascular trials that showed benefit of mechanical thrombectomy over medical management alone. In the HERMES meta-analysis, 122 of 1254 tandem occlusions (RR, 1.81 [95% CI, 0.96–3.4]) and 1132 of 1254 nontandem occlusions (RR, 1.71 [95% CI, 1.40–2.09]) were reported compared with medical management.[189] In THRACE, 24 of 196 tandem occlusions (RR, 1.82 [95% CI, 0.55–6.07]) and 172 of 196 nontandem occlusions (RR, 1.34 [95% CI, 0.87–2.07]) were treated compared with IV alteplase alone.[109] In HERMES, there is heterogeneity of treatment methods directed to the proximal extracranial carotid occlusion (no revascularization of the proximal lesion versus angioplasty versus stenting). A retrospective analysis of pooled data from 18 centers examined 395 patients with AIS caused by tandem lesion of the anterior circulation who underwent mechanical thrombectomy (TITAN [Thrombectomy in Tandem Lesions]). mTICI grade 2b/3 was achieved in 76.7% of patients. At 90 days, 52.2% achieved an mRS score of 0 to 2, 13.8% had parenchymal hematoma, and 13.2% were dead.[202] Multiple retrospective reports detail the technical success of mechanical thrombectomy for tandem occlusions but do not provide specifics on comparative approaches. No conclusions about the optimum treatment approach for patients with tandem occlusions are therefore possible.		

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

8. The safety and efficacy of IV glycoprotein IIb/IIIa inhibitors administered during endovascular stroke treatment are uncertain.	**IIb**	**C-LD**
Uncertainty remains about the safety and efficacy of IV glycoprotein IIb/IIIa inhibitors, including abciximab, administered in the setting of endovascular stroke treatment. The published literature is limited primarily to case series and retrospective reviews of single-center databases and focuses largely on administration of IV glycoprotein IIb/IIIa inhibitors to prevent thrombus formation during emergent carotid and vertebrobasilar artery stenting and mechanical thrombectomy.[203–205] Further research is needed comprising multicenter analyses of endovascular stroke therapy necessitating adjunctive antiplatelet therapy for emergent angioplasty and stenting.		

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

9. Use of salvage technical adjuncts, including intra-arterial fibrinolysis, may be reasonable to achieve mTICI grade 2b/3 angiographic results.	IIb	C-LD

Intra-arterial fibrinolytic therapy played a limited role in the recent endovascular trials but was used as rescue therapy, not initial treatment. In MR CLEAN, the EVT method was at the discretion of operator, with 40 of 233 treated with alternative stent retrievers to Trevo and Solitaire or intra-arterial alteplase. Details are not available, but no patients were treated with intra-arterial alteplase alone. Twenty-four of 233 (10.3%) had treatment with a second modality. Treatment method had no impact on outcomes in this trial.[206] In THRACE, an intra-arterial lytic was used to a maximum dose of 0.3 mg/kg and allowed to establish goal reperfusion, only after mechanical thrombectomy was attempted. A mean dose of 8.8 mg was administered in 15 of 141 patients receiving mechanical thrombectomy (11%). There was no effect on outcomes compared with mechanical thrombectomy alone.

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

3.9. Antiplatelet Treatment

3.9. Antiplatelet Treatment	COR	LOE
1. Administration of aspirin is recommended in patients with AIS within 24 to 48 hours after onset. For those treated with IV alteplase, aspirin administration is generally delayed until 24 hours later but might be considered in the presence of concomitant conditions for which such treatment given in the absence of IV alteplase is known to provide substantial benefit or withholding such treatment is known to cause substantial risk.	I	A

3.9. Antiplatelet Treatment (Continued)	COR	LOE
2. In patients presenting with minor noncardioembolic ischemic stroke (NIHSS score ≤3) who did not receive IV alteplase, treatment with dual antiplatelet therapy (aspirin and clopidogrel) started within 24 hours after symptom onset and continued for 21 days is effective in reducing recurrent ischemic stroke for a period of up to 90 days from symptom onset.	I	A

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

3. The efficacy of the IV glycoprotein IIb/IIIa inhibitors tirofiban and eptifibatide in the treatment of AIS is not well established.	**IIb**	**B-R**

Prospective, randomized, open-label phase II trials of tirofiban[217] and eptifibatide[218] have suggested safety for treatment in patients with AIS. Single-arm studies of eptifibatide as adjunctive therapy to IV alteplase support ongoing RCTs to establish safety and efficacy.[173,174] Further trials are necessary to clarify the safety and efficacy of this intervention.

4. Ticagrelor is not recommended over aspirin for treatment of patients with minor acute stroke.	**III: No Benefit**	**B-R**

The recently completed SOCRATES trial (Acute Stroke or Transient Ischaemic Attack Treated With Aspirin or Ticagrelor and Patient Outcomes) was a randomized, double-blind, placebo-controlled trial of ticagrelor versus aspirin begun within 24 hours in patients with minor stroke (NIHSS score ≤5) or TIA (ABCD2 score ≥4). With a primary outcome of time to the composite end point of stroke, MI, or death up to 90 days, ticagrelor was not found to be superior to aspirin (HR, 0.89 [95% CI, 0.78–1.01]; P=0.07).[219] However, because there were no significant safety differences in the 2 groups, ticagrelor may be a reasonable alternative in stroke patients who have a contraindication to aspirin.

5. The administration of the IV glycoprotein IIb/IIIa inhibitor abciximab as medical treatment for AIS is potentially harmful and should not be performed.	**III: Harm**	**B-R**

A recent Cochrane review of IV glycoprotein IIb/IIIa receptor antagonists in the treatment of AIS found that these agents are associated with a significant risk of ICH without a measurable improvement in death or disability.[220] The majority of trial data apply to abciximab, which was studied in the AbESTT trial (A Study of Effectiveness and Safety of Abciximab in Patients With

J Neurointerv Surg. 2022 Apr 15;neurintsurg-2022-018683. doi: 10.1136/neurintsurg-2022-01
Online ahead of print.

Emergent carotid stenting versus no stenting for acute ischemic stroke due to tandem occlusion: a meta-analysis

Francesco Diana [1], Michele Romoli [2], Giada Toccaceli [3], Aymeric Rouchaud [4 5], Charbel Mounayer [4 5], Daniele Giuseppe Romano [6], Francesco Di Salle [7], Paolo Missori [8], Andrea Zini [9], Diana Aguiar de Sousa [10], Simone Peschillo [11 12]

- Sistematik inceleme, PRISMA yönergelerini takip etti.
- 1 Ocak 2004 ile 7 Mart 2022 tarihleri
- Toplam 46 çalışma
  - Üçüncü ay mRS
  - Semptomatik intraserebral kanama (sICH)
  - Tekrarlayan inme
  - Rekanalizasyon başarısı
  - Başka artere embolizasyon
  - Restenoz oranı

- Akut stentleme yapılan vakalarda sICH oranı artmasına rağmen (OR=1.97), daha iyi fonksiyonel sonuç (OR=1.52) ve başarılı rekanalizasyon oranı (OR=1.91) ile ilişkiliydi.
- Restenoz oranı Akut stentleme yapılan grupta stentsiz gruba göre daha düşüktü (%2'ye karşı %9, p=0,001)
- Rekanalizasyon oranı stentleme yapılan grupta retrograd yaklaşımda daha yüksekti.
- Akut stentleme yapılan grupta işlem sırasında;
  - Antiplatelet ilaç kullanılan grupta glikoprotein IIb/IIIa inhibitörlerine kıyasla daha iyi fonksiyonel sonuç oranı (%60'a karşı %46, p=0.016) ve daha düşük sICH oranı (%7'ye karşı %11; p=0.08) saptandı.

Comment > AJNR Am J Neuroradiol. 2021 May;42(5):926. doi: 10.3174/ajnr.A7122.
Epub 2021 Apr 8.

The Challenge of an Acute Antithrombotic Regimen for Treatment of Tandem Lesions Stroke

P Papanagiotou [1], B Gory [2]

- Tandem oklüzyonlarda akut stentleme sonrası stent trombozu %14.5 ile %45 arasında bildirilmiş.
- En yüksek risk ilk 24 saatte
- Merkezlerde antitrombotik tedavi rejimleri arasında farklı yaklaşımlar
- Bazı hastalar, inme öncesi ilaçları ile birlikte antiplatelet ajanlar alırlar.
  - Düşük stent trombozu riski altındadır ve bu nedenle agresif bir antiplatelet stratejisinden kaçınılabilir.
  - Kalan hastalarda stent trombozunu önlemek için akut peri-girişimsel antiplatelet ajanlar uygulanmalıdır.
- Kullanılabilen ajanlar arasında intravenöz aspirin, klopidogrel, tikagrelor ve glikoprotein IIb/IIIa inhibitörleri (GPI'ler) veya yeni ilaç Kangrelor bulunur.
  - ASA ve Klopidogrel etkisi geç başlar
  - GPI açısından kanama riski daha yüksektir.

Meta-Analysis > J Cardiovasc Surg (Torino). 2019 Dec;60(6):693-702.
doi: 10.23736/S0021-9509.18.10312-0. Epub 2018 Jan 23.

Overview of evidence on emergency carotid stenting in patients with acute ischemic stroke due to tandem occlusions: a systematic review and meta-analysis

Andreia Pires Coelho [1 2], Miguel Lobo [3], Ricardo Gouveia [3], Diogo Silveira [3], Jacinta Campos [3], Rita Augusto [3], Nuno Coelho [3], Alexandra Canedo [3]

- Bu meta-analizde, acil ICA stentleme grubunda rekanalizasyona kadar geçen süre önemli ölçüde daha uzundu.
- Eşzamanlı ICA stentlemenin göreceli etkinliğini ve güvenliğini gösteren hiçbir prospektif, randomize kontrollü çalışma bugüne kadar yayınlanmamıştır.
- Tandem oklüzyonlarda akut inmenin erken tedavisinde anjiyoplasti ve ekstrakraniyal karotid arterlere stentlemenin rolünü tanımlamak için ek çalışmalar yapılmalıdır. O zamana kadar akut inmeli hastalarda trombektomi ile birlikte **ICA stentlemeden kaçınılmasını öneriyoruz.**

- Tandem oklüzyonda CAS için tartışmalı veriler varsa, ***Balon anjioplasti*** yapalım ve stent uygulamayalım?

Journal of the American Heart Association
Volume 11, Issue 2, 18 January 2022
https://doi.org/10.1161/JAHA.121.022335

SYSTEMATIC REVIEW AND META-ANALYSIS

Acute Carotid Artery Stenting Versus Balloon Angioplasty for Tandem Occlusions: A Systematic Review and Meta-Analysis

Cynthia B. Zevallos, MD *; Mudassir Farooqui, MD, MPH *; Darko Quispe-Orozco, MD; Alan Mendez-Ruiz, MD; Andres Dajles, MS; Aayushi Garg, MD; Milagros Galecio-Castillo, MD; Mary Patterson, BA; Osama Zaidat, MD, MS; Santiago Ortega-Gutierrez, MD, MSc

- Toplam 1404 çalışma
  - 59 çalışma kriterlere uygun bulunmuş.
  - 34 çalışma kalitatif sentez ile metaanalize dahil edilmiş.
  - Tandem oklüzyon
    - Ekstrakranial İCA oklüzyon veya stenozu (%70-99)
    - Proksimal intrakranial oklüzyon (M1, İCA tepe)

- Tandem oklüzyonu olan hastarda proksimal İCA akut stentlemesi etkili ve güvenlidir
- **Karotis arter stentleme ve retrograd yaklaşım; balon anjioplasti ve anterograd yaklaşıma göre;**
  - **Reperfüzyon başarısı ve üçüncü ayda fonksiyonel sonlanım açısından üstündür.**
- CAS, sICH oranlarında artış olmaksızın IVT alan hastalarda bile güvenli görünmektedir.
- Ancak, değerlendirilen sonuçları etkileyebilecek stent açıklığı ve antitrombotik tedavi hakkında hala yetersiz veri bulunmaktadır.

- Bu meta-analiz,
  - Teknikleri yapılandırılmış**, antitrombotik rejimlerin standartize edildiği** ve güvenlik sonuçlarıyla karşılaştıran randomize kontrollü bir çalışma, tandem oklüzyonlar için tedavinin optimal yönetiminde kesin rehberlik sunacaktır.

Çalışmalardaki sınırlılıklar;

- Aynı grup inme hastaları (oklüzyon yeri, darlık derecesi vs…)
- Hastaların İV-TPA alıp-almadığı
- Endovasküler tedaviye kadar geçen süre
- Kollateral dolaşım, ASPECT skoru
- Endovasküler teknik ve malzeme farklılığı
- Periprosedural ve sonrası sıkı tansiyon takibi
- İşlem sırası heparin, tirofiban, İA litik uygulaması
- Antiagregan standart seçim, dual antiagregan, direnç?

AJNR Am J Neuroradiol. 2020 Dec;41(12):2274-2279. doi: 10.3174/ajnr.A6888. Epub 2020 Oct 29.

Considerations for Antiplatelet Management of Carotid Stenting in the Setting of Mechanical Thrombectomy: A Delphi Consensus Statement

M Goyal [1 2], S Yoshimura [3], G Milot [4], J Fiehler [5], M Jayaraman [6], F Dorn [7], A Taylor [8], J Liu [9], F Albuquerque [10], M E Jensen [11], R Nogueira [12 13], J F Fraser [14], R Chapot [15], L Thibault [16], C Majoie [17], P Yang [9], N Sakai [18], D Kallmes [19], K Orlov [20], A Arthur [21], P Brouwer [22 23], J M Ospel [24 25]

- Karotis arter acil stentlemesinde standart bir antiplatelet tedavi rejimi önermek
- 7 ülkeden 19 nörogirişimselci
- 2010-2020 arası literatür taraması
- Delphi metadolojisi ile algoritm

- EVT sırasında karotis stentleme olasılığı var ise genel görüş IV aspirin 500 mg bolus
  - IV ASA yoksa ortak görüş GPIIb/IIIA inhibitörü

Table 1: Consensus recommendations for the dosage of GPIIb/IIIa receptor inhibitors[a]

Agent	Tirofiban	Eptifibatide	Abciximab
Loading dose (IV or IA bolus)	12 mcg/kg for 30 min[b]	180 mcg/kg for 1–2 min	0.25 mg/kg
Maintenance dose (if necessary, IV infusion for 12–24 h)	0.1 mcg/kg/min	2 mcg/min	125 mcg/kg/min
Trade name	Aggrastat	Integrilin	ReoPro
Duration of antiplatelet effect	4–8 h	4 h	48 h

Note:—IA indicates intra-arterial.

[a] Dosages are suggestions based on the panel consensus and may vary according to local availability of dosages.

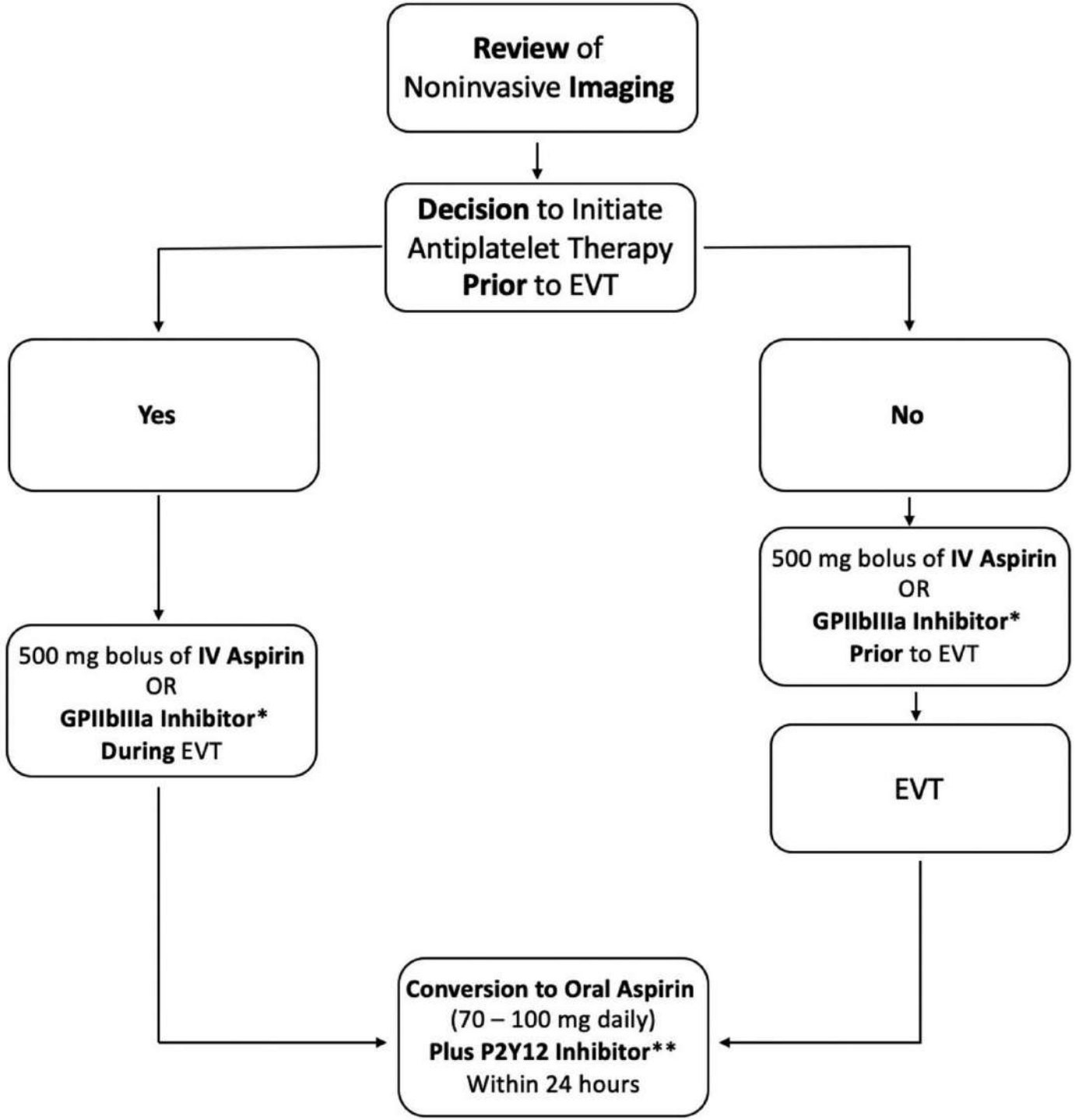
[b] 0.4 mcg/kg/min.

İşlem sonrası antiagregan seçimi

ASA 100 mg + P2Y12 inhibitörü

Table 2: Consensus recommendations for dosing of oral P2Y12 inhibitors in the postprocedural period[a]

Agent	Clopidogrel	Ticagrelor	Prasugrel
Loading dose[b]	600 mg	180 mg	40–60 mg
Maintenance dose	75 mg daily	60–90 mg 2×/day	5–10 mg daily
Trade name	Plavix	Brilinta/Brilique	Effient
Onset of action	2 h	30 min	15–30 min


Review of Noninvasive **Imaging**
Decision to Initiate Antiplatelet Therapy **Prior** to EVT
Yes
No
500 mg bolus of **IV Aspirin** OR **GPIIbIIIa Inhibitor*** **During** EVT
500 mg bolus of **IV Aspirin** OR **GPIIbIIIa Inhibitor*** **Prior** to EVT
EVT
Conversion to Oral Aspirin (70 – 100 mg daily) **Plus P2Y12 Inhibitor**** Within 24 hours

Comparative Study > JACC Cardiovasc Interv. 2018 Jul 9;11(13):1290-1299.
doi: 10.1016/j.jcin.2018.05.036.

Carotid Stenting With Antithrombotic Agents and Intracranial Thrombectomy Leads to the Highest Recanalization Rate in Patients With Acute Stroke With Tandem Lesions

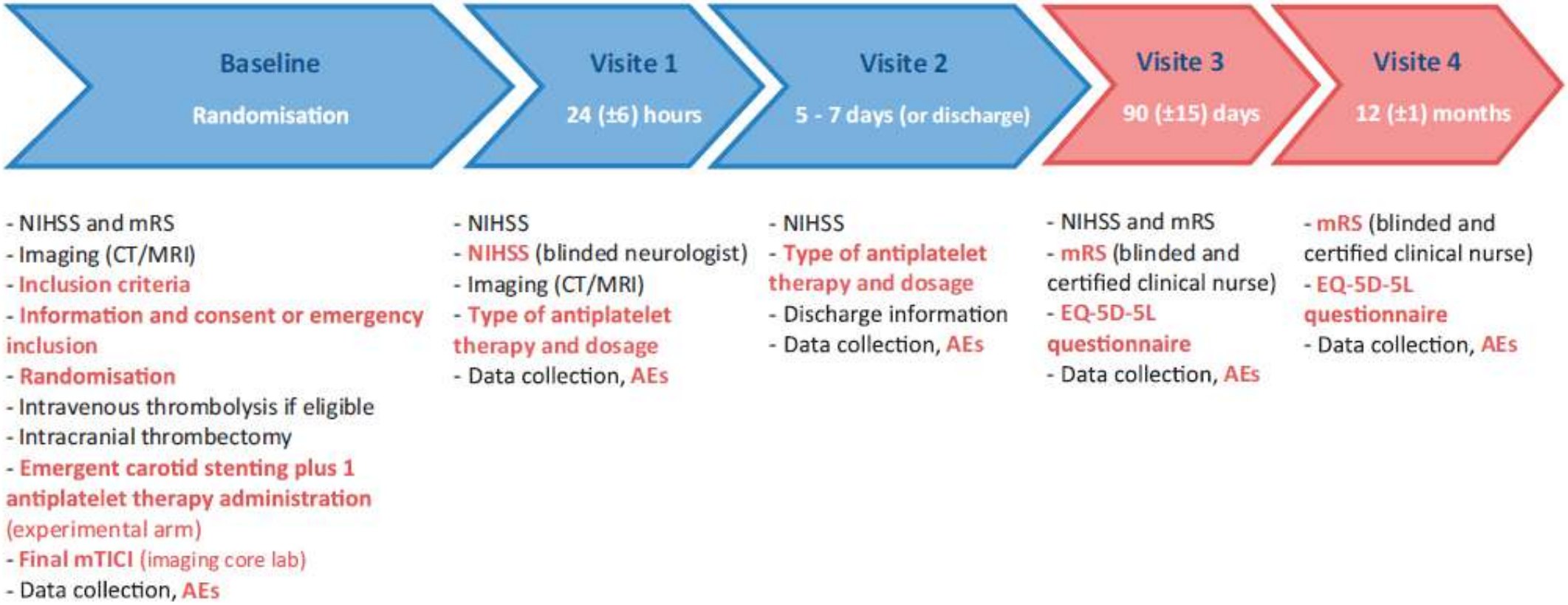
Panagiotis Papanagiotou [1], Diogo C Haussen [2], Francis Turjman [3], Julien Labreuche [4], Michel Piotin [5], Andreas Kastrup [6], Henrik Steglich-Arnholm [7], Markus Holtmannspötter [8], Christian Taschner [9], Sebastian Eiden [9], Raul G Nogueira [2], Maria Boutchakova [10], Adnan Siddiqui [11], Bertrand Lapergue [12], Franziska Dorn [13], Christophe Cognard [14], Monika Killer [15], Salvatore Mangiafico [16], Marc Ribo [17], Marios N Psychogios [18], Alejandro Spiotta [19], Marc Antoine Labeyrie [20], Alessandra Biondi [21], Mikaël Mazighi [5], Sébastien Richard [22], René Anxionnat [23], Serge Bracard [23], Benjamin Gory [23], TITAN Investigators

- 482 tandem oklüzyon hasta
  - Ekstrakranial İCA lezyon
    - Total oklüzyon veya >%90 darlık)
  - Proksimal intrakranial oklüzyon
    - Distal İCA
    - MCA M1
    - Proksimal M2

- 4 gruba ayrılmış
  1. Akut İCA stentleme, antitrombotik kullanım ve mekanik trombektomi (256)
  2. Akut İCA stentleme ve mekanik trombektomi (66)
  3. İCA balon anjioplasti ve mekanik trombektomi (52)
  4. Sadece intrakranial mekanik trombektomi (108)
- Hastaların %61.5 IV-TPA almış ve %74 işlem sırasında antitrombotik tedavi almış

TITAN protokol

Figure 1. Study assessment flow chart.



The red text corresponds to the study's specific acts.

NIHSS: National Institutes of Health Stroke Scale; mRS: modified Rankin Scale; MRI: magnetic resonance imaging; CT: computed tomography; mTICI: modified Thrombolysis In Cerebral Infarction; AEs: adverse events.

- **TITAN**, anterior sirkülasyon tandem oklüzyonu nedeniyle akut iskemik inme hastalarında iki tedavi tipini doğrudan karşılaştıran ve özellikle hastalığın akut fazında en az bir antiplatelet tedavi ile ilişkili akut internal karotid arter stentlemenin güvenliğini ve etkinliğini değerlendiren **ilk randomize çalışmadır**.
- Ekstrakraniyal İKA'nın intrakraniyal trombektomi ile kombinasyon halinde antitrombotik tedavi ile akut stentlenmesi, tandem lezyonları olan akut inmeli hastaların tedavisinde daha yüksek rekanalizasyon oranları ile ilişkilidir.
- IV-TPA köprüleme tedavisi, sadece mekanik trombektomiye göre daha üstündür.
- ‘’Head first’’ yaklaşım daha üstün bulundu.
- **Periprosedürel tek antiagregan kullanımı ile sICH riskinde anlamlı bir artış olmadan, daha iyi fonksiyonel sonlanım elde edildi.**

Tek ya da ikili antiagregan

TABLE 5 Comparison of Efficacy and Safety Outcomes According to the Type of Antithrombotic Therapy in the Thrombectomy and Cervical Internal Carotid Artery Stenting Group

	Thrombectomy and Cervical ICA Stenting With		
	1 Antithrombotic Drug (n = 138)	At Least 2 Antithrombotic Drugs (n = 118)	p Value
Recanalization	112/138 (81)	100/117 (85)	0.454
Early neurological improvement	31/67 (46)	32/68 (47)	1
90-day favorable outcome	77/136 (57)	70/118 (59)	0.758
90-day mortality	10/136 (7)	14/118 (12)	0.312
Symptomatic Hemorrhagic complications	5/137 (4)	8/118 (7)	0.397

- Grup 1 hastalarda tek ya da ikili antiagregan kullanımı açısından
  - Rekanalizasyon başarısı
  - 3. ayda klinik sonlanım
  - Semptomatik intrakranial hemoraji

  Açısından anlamlı bir farklılık saptanmadı.

- IV aspirin, IV glyco-protein IIb/IIIa reseptor antagonist, klopidogrel ve heparin kullanılmış ve standartize bir protokol yok.

- Akut inme endovasküler tedavisinde hangi oklüzyonlarda ve **ne gibi durumlarda** kalıcı stent uygulamak zorunda kalabilirim?

- Akut inme vakalarında kalıcı stent uygulama;
    - Arterin Oklüzyonu
    - Arterin Stenozu
    - Arterin Diseksiyonu

› Int J Stroke. 2021 Apr;16(3):342-348. doi: 10.1177/1747493020929948. Epub 2020 Jun 9.

Effect of emergent carotid stenting during endovascular therapy for acute anterior circulation stroke patients with tandem occlusion: A multicenter, randomized, clinical trial (TITAN) protocol

François Zhu [1], Gabriela Hossu [2], Marc Soudant [3], Sébastien Richard [4 5], Hamza Achit [3], Mélanie Beguinet [3], Vincent Costalat [6], Caroline Arquizan [7], Arturo Consoli [8], Bertrand Lapergue [9], Aymeric Rouchaud [10], Francisco Macian-Montoro [11], Alessandra Biondi [12], Thomas Moulin [13], Gaultier Marnat [14], Igor Sibon [15], Christophe Paya [16], Stéphane Vannier [17], Christophe Cognard [18],

Multicenter Study › Stroke. 2017 Apr;48(4):963-969. doi: 10.1161/STROKEAHA.116.015202. Epub 2017 Feb 24.

Successful Reperfusion With Mechanical Thrombectomy Is Associated With Reduced Disability and Mortality in Patients With Pretreatment Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score ≤6

Jean-Philippe Desilles [1], Arthuro Consoli [2], Hocine Redjem [2], Oguzhan Coskun [2], Gabriele Ciccio [2], Stanislas Smajda [2], Julien Labreuche [2], Cristian Preda [2], Clara Ruiz Guerrero [2], Jean Decroix [2], Georges Rodesch [2], Mikael Mazighi [2], Raphaël Blanc [2], Michel Piotin [2], Bertrand Lapergue [2], ETIS (Endovascular Treatment in Ischemic Stroke) Research Investigators

Observational Study › Stroke. 2021 Oct;52(10):3097-3105. doi: 10.1161/STROKEAHA.120.033032. Epub 2021 Aug 10.

Endovascular Therapy of Anterior Circulation Tandem Occlusions: Pooled Analysis From the TITAN and ETIS Registries

Mohammad Anadani [1 2], Gaultier Marnat [3], Arturo Consoli [4], Panagiotis Papanagiotou [5], Raul G Nogueira [6], Adnan Siddiqui [7], Marc Ribo [8], Alejandro M Spiotta [2], Romain Bourcier [9], Maeva Kyheng [10], Julien Labreuche [10], Adam de Havenon [1], Igor Sibon [11], Cyril Dargazanli [12], Caroline Arquizan [13], Christophe Cognard [14], Jean-Marc Olivot [15], René Anxionnat [16 17], Gérard Audibert [18], Mikaël Mazighi [19], Raphaël Blanc [19], Bertrand Lapergue [20], Sébastien Richard [21 22], Benjamin Gory [16 17], TITAN and ETIS Registry Investigators

Observational Study > Stroke. 2020 Dec;51(12):3713-3718. doi: 10.1161/STROKEAHA.120.030038.
Epub 2020 Nov 10.

Safety and Outcome of Carotid Dissection Stenting During the Treatment of Tandem Occlusions: A Pooled Analysis of TITAN and ETIS

- Toplam 136 tandem oklüzyon ve internal karotis arter **servikal segment diseksiyonu**
  - 65 (%47.8) hasta kalıcı stent
  - 71 (%52.2) stent uygulanmamış

- Standart tedavi prosedürü yok
- Antiagregan tedaviye ilişkin bilgi standartize değil

Table. Comparison in Outcomes Between Patients With and Without CAS

Characteristics	Extracranial CAS		Unadjusted*		Adjusted†	
	No (n=71)	Yes (n=65)	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Angiographic outcomes						
mTICI 2b/3	48 (67.6)	58 (89.2)	3.97 (1.57 to 10.05)	0.004	2.24 (1.33 to 3.77)	0.002
mTICI 3	17 (23.9)	22 (33.9)	1.63 (0.77 to 3.45)	0.20	2.20 (1.70 to 3.22)	0.25
Procedural complications	10 (14.1)	6 (9.2)	0.62 (0.21 to 1.81)	0.38	0.74 (0.42 to 1.31)	0.30
Patency of extracranial carotid artery	37 (52.0)	52 (80.2)	3.79 (1.52 to 9.45)	0.005	1.82 (1.14 to 2.91)	0.013
Clinical outcomes						
90-day favorable outcome‡	44 (61.4)	35 (54.3)	0.75 (0.37 to 1.49)	0.41	0.84 (00.58 to 1.22)	0.36
90-day mortality	4 (5.8)	5 (8.0)	1.42 (0.36 to 5.56)	0.62	1.00 (0.48 to 2.09)	0.99
24 h change in NIHSS, mean (95% CI)§	−2.3 (−4.1 to −0.5)	−2.7 (−4.9 to −0.5)	−0.40 (−3.25 to 2.46)‖	0.78	−0.68 (−3.61 to 2.24)¶	0.65
Hemorrhagic complications						
sICH	4 (5.6)	7 (10.8)	2.02 (0.56 to 7.25)	0.28	1.59 (0.79 to 3.17)	0.19

- Tandem oklüzyonlar için endovasküler tedavi sırasında **disseke servikal karotid** arterin **acil stentlenmesi**, intrakraniyal reperfüzyonun sonucu ne olursa olsun **güvenli** görünmektedir.
- Ancak daha iyi bir klinik sonuçla ilişkili değildir.
- KAS, intrakraniyal reperfüzyondan sonra karotid arterin **yüksek riskli**, **yüksek dereceli stenoz**una neden olan diseksiyonu bağlamında düşünülebilir.

- Tandem oklüzyonda **akut servikal ICA stentleme** ile tedavi edilen hastalarda, daha yüksek intraserebral kanama olasılığına rağmen,
  - üçüncü ayda iyi fonksiyonel sonuç daha yüksekti
  - bununla birlikte, intraserebral kanamaların çoğu **asemptomatik** idi.

- Servikal ***ICA diseksiyonu*** ile ilişkili tandem oklüzyonun tedavisi için;
  - MT'den önce IV-TPA uygulama güvenli
  - Üçüncü ayda iyi fonksiyonel sonuç ile ilişkiliydi.

- Anadani M, et al. Endovascular Therapy of Anterior Circulation Tandem Occlusions: Pooled Analysis From the TITAN and ETIS Registries. Stroke. 2021 Oct;52(10):3097-3105
- Marnat G, et al. Thrombolysis Improves Reperfusion and the Clinical Outcome in Tandem Occlusion Stroke Related to Cervical Dissection: TITAN and ETIS Pooled Analysis. J Stroke. 2021 Sep;23(3):411-419

- Hasta **İV TPA** aldı nasıl yaklaşalım?

Stroke. 2019 Aug;50(8):2250–2252. doi: 10.1161/STROKEAHA.118.024733. Epub 2019 Jun 17.

Emergent Carotid Stenting Plus Thrombectomy After Thrombolysis in Tandem Strokes: Analysis of the TITAN Registry

Mohammad Anadani [1], Alejandro M. Spiotta [1], Ali Alawieh [1], Francis Turjman [2], Michel Piotin [3], Diogo C. Haussen [4], Raul G. Nogueira [4], Panagiotis Papanagiotou [5], Adnan H. Siddiqui [6], Bertrand Lapergue [7], Franziska Dorn [8], Christophe Cognard [9], Marc Ribo [10], Marios N. Psychogios [11], Marc Antoine Labeyrie [12], Mikael Mazighi [13], Alessandra Biondi [14], René Anxionnat [15], Serge Bracard [15], Sébastien Richard [16], Benjamin Gory [15], TITAN (Thrombectomy In TANdem Lesions) Investigators

- Aterosklerotik tandem oklüzyonu olan 205 hasta
- Mekanik trombektomi ve akut karotis arter stentleme

- IV-TPA alan 125 (%60), almayan 80 (%40)

Table. CAS-MT Outcomes After Thrombolysis Versus Without Thrombolysis

Outcome	N	IVT Group (n=125)	No-IVT Group (n=80)	*P* Value
Symptomatic ICH	205	6 (5)	6 (8)	0.544
Parenchymal hematoma type 1–2	173	16 (15)	12 (18)	0.647
90-d mortality	202	10 (8)	16 (20)*	0.017
mTICI 2b–3	205	102 (82)	64 (80)	0.856
mTICI 3	205	43 (34)	30 (38)	0.657
90-d favorable outcome	202	76 (62)	40 (51)	0.145
Procedural complications	199	14 (12)	9 (11)	0.999

- Aterosklerotik Tandem Oklüzyon'lu akut iskemik inme hastalarında, IV-TPA alan hastalarda bile KAS-MT yaklaşımı ile hemorajik komplikasyonda anlamlı artış saptanmadı.

- Sınırlılıklar;
  - Hemorajik komplikasyon oranını etkileyebilecek heterojen antitrombotik protokoller olabilir.
  - Bu çalışma için yalnızca işlem öncesi antitrombotik veriler mevcut.

- Kalıcı stent uygulamam gerekiyor **İA TPA** vereyim mi?

- Bu konuda çalışmalarda veri yok
- IV-TPA kullanımına göre davranılmalı

AJNR Am J Neuroradiol. 2020 Nov; 41(11): 2088–2093.
doi: 10.3174/ajnr.A6768
PMCID: PMC7658830
PMID: 32972953

Carotid Stenting and Mechanical Thrombectomy in Patients with Acute Ischemic Stroke and Tandem Occlusions: Antithrombotic Treatment and Functional Outcome

V. Da Ros,[a] J. Scaggiante,[a] F. Sallustio,[b] S. Lattanzi,[c] M. Bandettini,[d] A. Sgreccia,[e] C. Rolla-Bigliani,[f] E. Lafe,[e] G. Sanfilippo,[e] M. Diomedi,[b] M. Ruggiero,[g] N. Haznedari,[g] M. Giannoni,[h] C. Finocchi,[d] and R. Floris[a]

- Hali hazırda antiplatelet alanlarda ASA 300 mg veya klopidogrel 75 mg
- Antiplatelet almayanlarda IV aspirin 500 mg
- Dual antiplatelet (ASA+klopidogrel veya IV aspirin 1000 mg)

Multivariate analysis of factors influencing symptomatic ICH and functional independence

Factors	Mean	95% CI	*P* Value
Influencing symptomatic ICH			
Intraprocedural heparin ≥3000 IU	3547 ± 588 IU	2377–4718	.01
ASPECTS ≤7	6.6 ± 0.4	5.8–7.4	.001
MT attempts ≥3	3.3 ± 0.3	2.6–4.1	.002
Influencing functional independence (mRS ≤2)			
ASPECTS ≥8	8.4 ± 0.4	7.9–9.2	.001
MT attempts ≤2	1.9 ± 0.3	1.3–2.5	.004

- Acil karotid arter stent yerleştirilmesi ile tedavi edilen hastalar için optimal antitrombotik tedavi değerlendirilmeye devam etmektedir.
- Çalışmanın analizinde, standart intraprosedürel **heparin dozları (≥3000 IU) sICH oranı daha yüksektir**
- Antiplateletler güvenliydi ve **ikili antiagregasyon tedavisi daha iyi fonksiyonel sonuçlarla** ilişkiliydi.

Özetle;

- Tandem oklüzyon akut stentleme sonrası;
  - İşlem sırasında IV aspirin 250-500 mg yükleme
  - IV aspirin yoksa ASA 300 mg ve klopidogrel 300-600 mg yükleme
  - Hastada 24±6 saat sonra BT ile kanama kontrolü
  - Kanama olmayan hastada Dual antiplatelet tedavi
    - 4-12 hafta dual antiplatelet sonrası tek antiagregan
  - IV-TPA alan hasta, acil stentleme → ilk 24 satte anti-platelet kullanımına engel değil
  - İA-TPA ile ilgili yeterli veri yok
  - GPIIb/IIIa inhibitör kullanılmış ise 24 saat idame dozu devam
    - Sonrasında dual antiplatelet seçimi
  - Standart heparin dozuna dikkat (<3000 ü)

Cerebrovasc Dis. 2021;50(2):162-170. doi: 10.1159/000512204. Epub 2021 Jan 20.

Increased Rates of Hemorrhages after Endovascular Stroke Treatment with Emergency Carotid Artery Stenting and Dual Antiplatelet Therapy

Felix Hadler [1], Raveena Singh [2], Martin Wiesmann [2], Arno Reich [3], Omid Nikoubashman [2]

Clin Neuroradiol. 2021 Sep;31(3):737-744. doi: 10.1007/s00062-020-00954-7. Epub 2020 Sep 17.

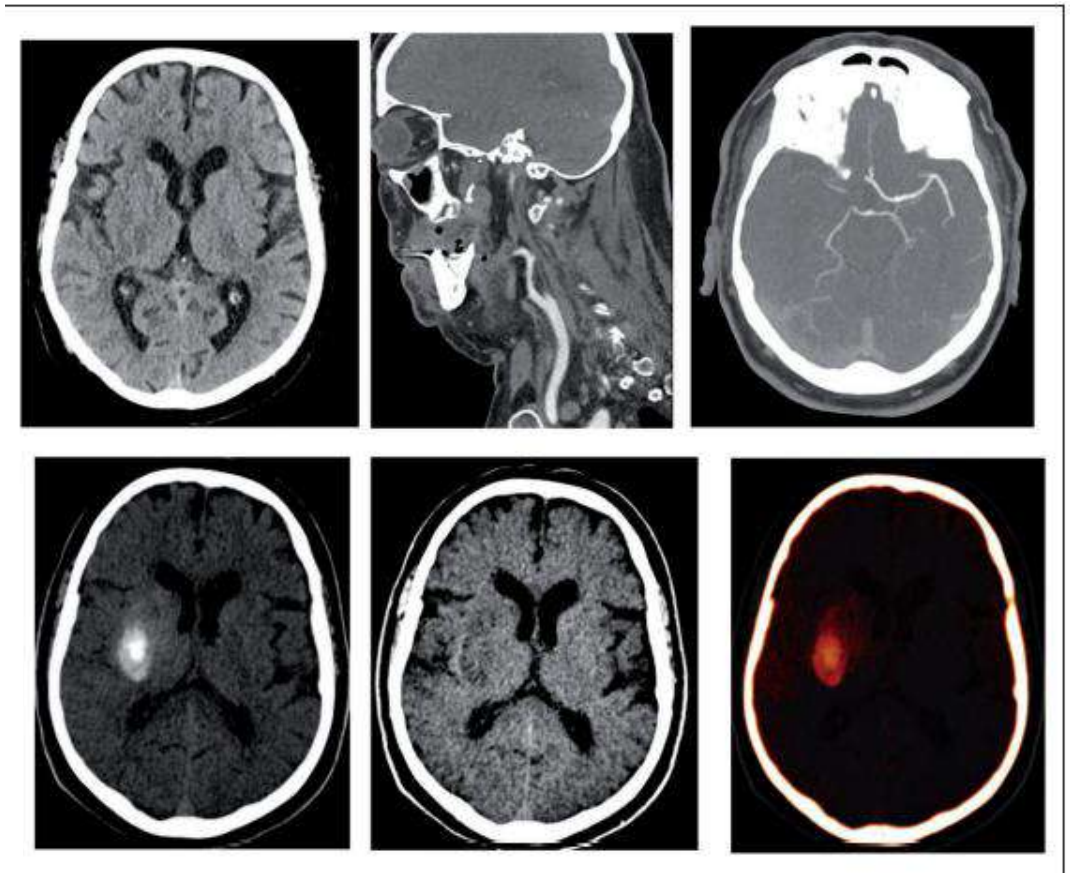
Emergency Carotid Endarterectomy Instead of Carotid Artery Stenting Reduces Delayed Hemorrhage in Thrombectomy Stroke Patients

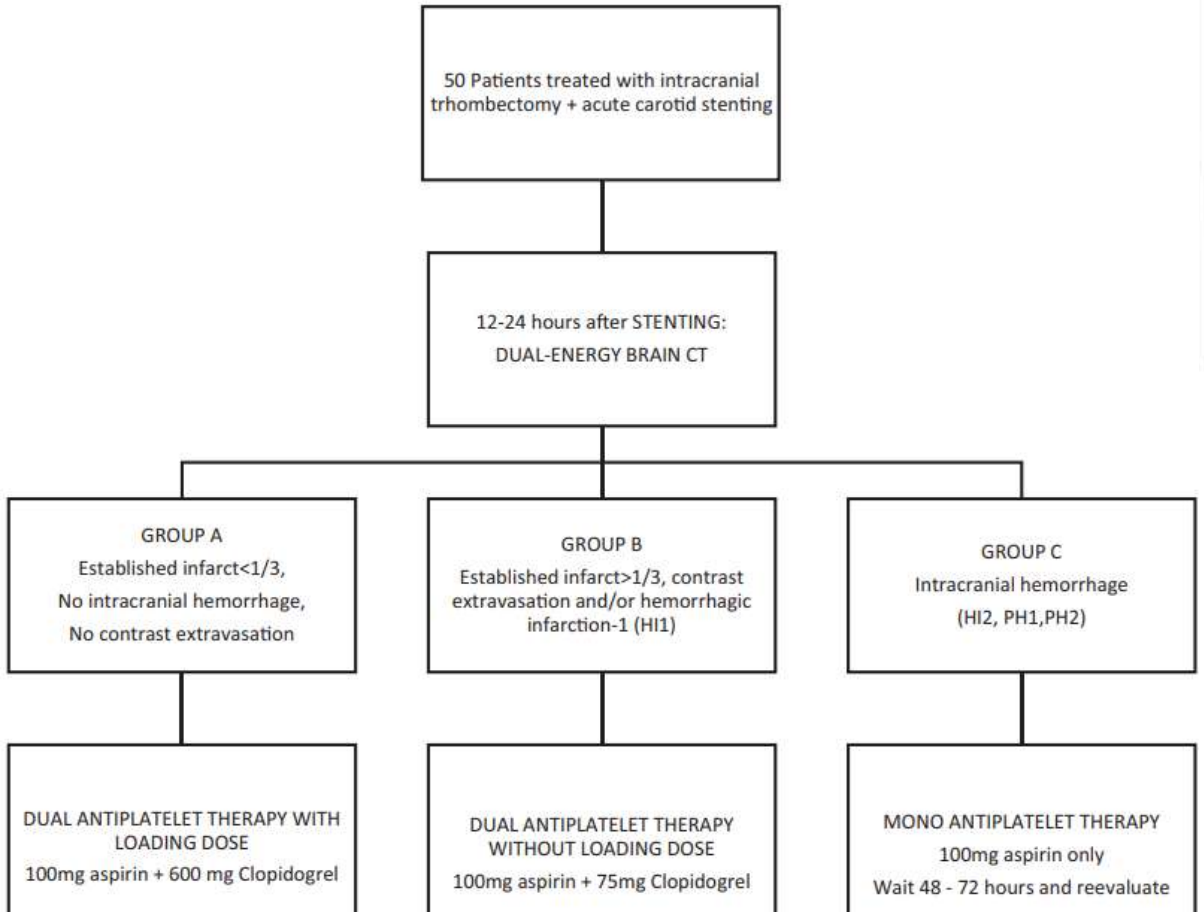
Raveena Singh [1], Sven Dekeyzer [1], Arno Reich [2], Drosos Kotelis [3], Alexander Gombert [3], Martin Wiesmann [1], Omid Nikoubashman [4]

Interv Neuroradiol. 2020 Apr;26(2):222-230. doi: 10.1177/1591019919880425. Epub 2019 Nov 5.

Dual energy CT in the management of antiplatelet therapy in patients with acute ischemic stroke for carotid obstruction

Eduardo Murias [1], Pedro Vega [1], Elena Lopez-Cancio [2], Jorge Peña [1], Edison Morales [1], Lorena Benavente [2], Montserrat González [2], Davinia Larrosa [2], Maria Rico [2], Nuria Riesco [2], Maria Cadenas [1], Jose Maria Jimenez [1], Juan Chaviano [1], Antonio Saiz [1], Sergio Calleja [2], Faustino Arias [1]





Akut endovasküler tedavide **ne gibi durumlarda** kalıcı stent uygulamak zorunda kalınabilir?

- Kateter ile oklüzyon distaline geçilemediğinde
- Balon anjioplasti sonrası re-oklüzyon, ciddi stenoz (>%90)
- Arteriyel diseksiyon (psödo anevrizma vb komplikasyon sonrası)
- Arter darlığı >%70-90 üzeri ve distal akımın etkisiz olduğu
- **İntrakranial oklüzyon, birkaç kez trombektomi ile açılamadığında ‘’kurtarıcı stent’’ uygulama**

Multicenter Study > J Am Heart Assoc. 2020 Mar 3;9(5):e012795. doi: 10.1161/JAHA.119.012795.
Epub 2020 Mar 3.

Emergency Intracranial Stenting in Acute Stroke: Predictors for Poor Outcome and for Complications

Christian Paul Stracke [1 2], Jens Fiehler [2], Lukas Meyer [2], Götz Thomalla [3], Lars Udo Krause [4], Stephan Lowens [5], Jan Rothaupt [5], Byung Moon Kim [6], Ji Hoe Heo [7], Leonard L L Yeo [8 9 10], Tommy Andersson [8 9 11], Christoph Kabbasch [12], Franziska Dorn [13], Rene Chapot [1], Uta Hanning [2]

- Çok merkezli, retrospektif
- Ön sistem ve arka sistem LVO, 4751 hastanın 210
  - 136 (%64.8) ön sistem (2/3 ön sistem, 1/3 arka sistem)
  (İCA tepe, MCA M1,M2 proksimal, ACA A1, Baziler ve intrakranial vertebral)
- Toplam (%4.4) akut intrakranial stentleme
- 22 hasta (%10.5) Semptomatik Intrakranial Hemoraji (SIH)
  - SIH %86.4 ön sistem ($p<0.025$)
- Toplam %31 hastada IV-TPA kullanılmış (İA TPA ile ilgili veri yok)

- Antiplatelet tedavi rejimi için standart bir protokol yok
- Toplam 150 hastada antiagregan ile ilgili veri mevcut
- Tüm hastalara akut olarak
  - En azından monoantiagregasyon veya bir GpIIb/IIIa antagonisti verilmiş
- Bu grupta 124 hasta
  - Eptifibatid 109 vaka (%82)
  - Tirofiban (12 vaka)
  - Abxicimab (3 vaka) olmak üzere bir GpIIb/IIIa antagonisti almıştır.
  - İşlemden 24 saat sonra kontrol bilgisayarlı tomografi taramasına kadar GpIIb/IIIa antagonistlerine devam edildi.
- Daha sonra her merkezin kararına bağlı olarak tek veya çift antiagregasyona devam edildi.

- Mekanik trombektomi başarısızlığından sonra intrakraniyal kurtarma stentlemesinden sonra iyi sonuç oranı,
  - kalıcı oklüzyonları olan hastalarda bildirilenden oldukça yüksektir
- İyi bir sonucun ana belirleyicisi,
  - Stent takmadan önce düşük sayıda trombektomi manevrası yapılmasıydı.
- Gözlenen kanama oranı, normal trombektomi prosedürlerinden daha yüksektir, ancak kabul edilebilir (SIH %10.5)
  - Anterior dolaşımda daha fazla
  - İleri yaş (>74)
  - Kadın cinsiyet
- Sınırlayıcı;
  - **İntrakranial stentleme kararı tamamen nöro-girişimselcinin tercihine göre**
  - **Antiplatelet rejim standart değil**
    - Bu nedenle, GpIIb/IIIa antagonistlerinin diğer antiplatelet ilaçlardan (asetilsalisilik asit, dipiridamol ve klopidogrel) veya Ticagrelor gibi daha yeni, hızlı uygulanabilen ilaçlardan daha üstün olup olmadığı sonucuna varamayız.

- Kalıcı stent uygulayınca antiagregan seçenekleri neler?
- Antiagreganların avantaj ve dezavantajları, birbirine üstünlükleri var mı?

Piyasada kullanılan antiplatelet ilaçlar;

- **Asetilsalisilik asit (ASA)** } Tromboksan inhibitörleri

- **Dipiridamol**
- **Cilastazol** } Prostoglandin E inhibitörleri

- **Klopidogrel**
- **Tiklopidin**
- **Prasugrel** } Geri dönüşsüz
- **Tikagrelor**
- **Cangrelor** } Geri dönüşlü

} P2Y12/ADP reseptör antagonistleri

	COX inhibitör	$P2Y_{12}$ inhibitörleri				GIIb-IIIa inhibitörleri		
	Asetil-salisilikasit	**Klopidogrel**	Prasugrel	Ticagrelor	Cangrelor	Abciximab	Ebtifibatid	Tirofiban
Hedef	Siklo-oksijenaz	$P2y_{12}$	$P2y_{12}$	$P2y_{12}$	$P2y_{12}$	GIIb-IIIa	GIIb-IIIa	GIIb-IIIa
Reversibilite	Irreversible	Irreversible	Irreversible	Reversible	Reversible	Irreversible	Irreversible	Irreversible
Önilaç	Yok	Evet (2 adım)	Evet (1 adım)	Yok	Yok	Monoklonal antikor	Peptid	Non-peptid
Uygulama	Oral iv	Oral	Oral	Oral	iv	iv	iv	iv
Başlangıç etki	75-100mg po: 1st 250mg iv: 15dk	**75mg: 3-7g 300mg: 6st 600mg: 3st**	10mg: 3-5g 20mg: 24st 60mg: 1st	90mg: 2-3g 180mg: 1-2st	30µg/kg bolus + 4ug/kg/dk: 2dk	0,25mg/kg bolus: 10dk	180µg/kg bolus: 15dk	6µg/kg (1dk) 30dk
İdame	75-100mg/gün	75mg/gün	5-10mg/gün	90mg/12st	4µg/kg/dk Periprosedürel	0,125µg/kg/dk (Max 10µg/dk)	2µg/kg (72st'e kadar)	0.1µg/kg/dk (18st'e kadar)
Platelet fonksiyon normalizasyon	5-7 gün	5-7 gün	5-10 gün	3-4 gün	30-60dk	12st	4-6st	4-8st
Yarılanma süresi	15-30dk	6st	7st	8-12st	1st	10-30dk	2.5st	2st

İkili antiagragan mı? Tek antiagregan mı?

- Tek antiagregan iskemik inme rekürrensi %13-22 azaltıyor
- İkili antiagregan (farklı etki mekanizmalarının kombinasyonu)
  - Özellikle erken dönem
  - Özellikle yüksek riskli hastalarda
- Çoğu çalışma ASA+diğer antiagregan
  - Erken dönemde ve en etkili kombinasyon ASA+Klopidogrel (CHANCE 2013, POINT 2018)
  - Diğer Antiagregan kombinasyon çalışmaları olumsuz sonuçlandı
  - ASA+Tikagrelor yeni bir seçenek (THALES 2020)

Aspirin (asetilsalisilik asit)

- ASA IV 500-900 mg yükleme + Klopidogrel 300-600 mg yükleme
  - Sonrası ASA 100 mg + klopidogrel 75 mg (3 ay)
  - Tekli antiagregan ile devam

- Stent kullandım oklüde oldu **GP IIb/IIIa inhibitör** (Tirofiban vb.) kullandım, tedaviye nasıl devam edeyim? Antiagregan ne kullanabilirim? Ne zaman başlarım?

Glikoprotein IIb/IIIa inhibitörleri;

- Mevcut GP IIb/IIIa inhibitörleri arasında
  - **Absiksimab**
  - **Tirofiban**
  - **Eptifibatid**
- Trombositlerinin plazma zarındaki glikoprotein IIb/IIIa reseptörlerini bloke ederek trombosit agregasyonunu önler ve fibrinojen bağlanmasını inhibe eder.
- Sadece IV kullanılabilirler.

- Retrospektif çalışmalarda sıklıkla Tirofiban kullanılmış
  - İşlem sırasında yükleme + saatlik doz idame
  - ASA 300-500 mg + Klopidogrel 300-600 mg yükleme
  - 12-24 saat sonra Dual-antiplatelet tedaviye geçiş (ASA 100+klopidogrel 75)
- Tirofiban ve Eptifibatid şu an için daha güvenli
- Abciximab ile kanama riski daha yüksek

- Zhu X, Cao G. Safety of Glycoprotein IIb-IIIa Inhibitors Used in Stroke-Related Treatment: A Systematic Review and Meta-Analysis. Clin Appl Thromb Hemost. 2020 Jan-Dec;26

ÖZETLE

- Akut stentleme sonrası kanama riski daha yüksek ancak fonksiyonel sonlanımı etkilemiyor (sICH için anlamlı risk artışı yok)
- Standart bir tedavi rejimi henüz yok
- İşlem öncesi antiplatelet alan hastada aynı tedavinin devamı
  - Yükleme doza gerek yok
- ASA + Klopidogrel en sık tercih edilen kombinasyon
- Dual antiplatelet tedavi
  - DWI ASPECT <5 ve CT ASPECT <7 olanlarda → kaçınmak
  - İleri yaş, Diyabet → kanama riski fazla
- Halen sICH açısından antiplatelet tedavi GPIIb/IIIa inh.'ne göre daha güvenli
  - Kanama için yüksek riskli hasta (DM, ASPECT<7, NIHSS>15, yaş>70)
  - Sadece akut stent trombozu durumunda → GPIIb/IIIa inhibitörü kullanmak
  - GPIIb/IIIa kullanılacaksa → Tirofiban ve Eptifibatid

- **Prospektif, randomize, tedavi standardizasyonu yapılmış, çift kör, kontrollü çalışmalara ihtiyaç var**

- Pop R, et al. Postprocedural Antiplatelet Treatment after Emergent Carotid Stenting in Tandem Lesions Stroke: Impact on Stent Patency beyond Day 1. AJNR Am J Neuroradiol. 2021;42(5):921-925

Gerçek hayat !

- 4 saatlik hasta, ileri yaş
- DM, HT, HL, AF
- İV TPA
- İşleme kadar 1 saatte geldi (>5 saat kasık ponksiyonu)
- Tandem oklüzyon (İKA proksimal oklüde + MCA proksimal)
- Kollateral zayıf, Düşük ASPECT skoru
- İCA geçilemedi stent uyguladınız
  - MCA açılması da gecikti
- İntrakranial oklüzyon açıldı ancak Stent oklüde oldu
- Trofiban kullandınız, açıldı…

- **Hangi antiagregan verelim? Ne zaman verelim?**

- Sabrınız için teşekküler