XIV curso

Gestión Integral de los Medicamentos en los servicios de URgencias

GIMUR

CÓDIGO ICTUS

Fisiopatología, diagnóstico y tratamiento agudo

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Sabadell, 20 de Octubre de 2022

ORGANIZA:

sefh Sociedad Española de Farmacia Hospitalaria · fefh Fundación Española de Farmacia Hospitalaria · redfaster Grupo de trabajo de Atención Farmacéutica en Urgencias de la sefh · Parc Taulí Hospital Universitari

PATOLOGIA VASCULAR CEREBRAL

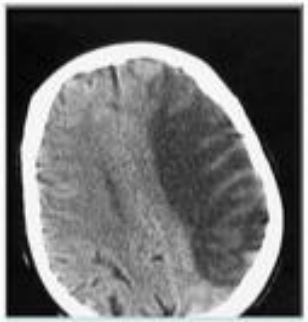
Segunda causa global de muerte, 1ª en mujeres (INE 2012)
Elevada mortalidad: 20% en el primer mes
Principal causa de invalidez
Incidencia: 150-200 casos/100.000 hab y año
Segunda causa de demencia
Primera causa de ingreso en Neurología
2035

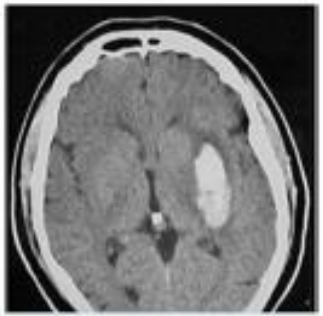
34% ictus
25% pacientes con secuelas de ictus
45% muertes por ictus

ACCIDENTE VASCULAR CEREBRAL / ICTUS

Concepto
Afectación transitoria o permanente de una zona cerebral como consecuencia de una isquemia (oclusión) o una hemorragia (ruptura)

Tipos:
Ictus isquémico (80%) (sinónimos: trombosis, embolia, infarto, etc…)
Ictus hemorrágico (20%): (sinónimos: derrame, sangrado, etc…)





FISIOPATOLOGIA DEL ICTUS

CLASIFICACIÓN TOAST

1- Aterotrombótico

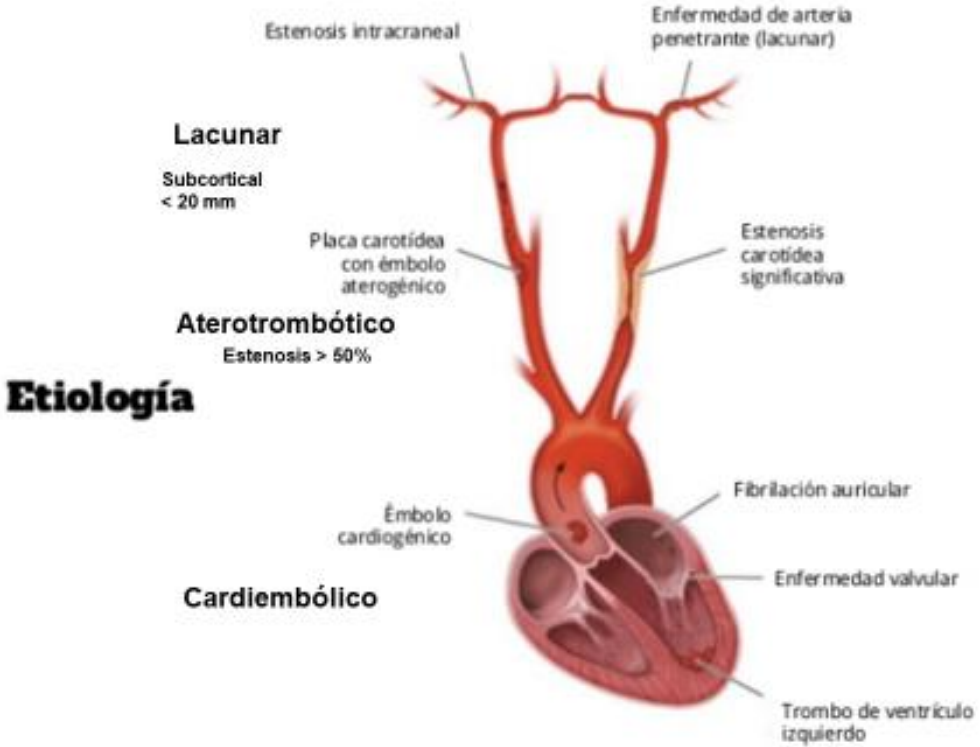
2- Cardioembólico

3- Lacunar (pequeño vaso)

4- Etiología indeterminada (30%)

5- Etiología infrecuente (5%)

Etiología



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: Harrison's *Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

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PREVENCIÓN SECUNDARIA DEL ICTUS

CLASIFICACIÓN TOAST

1- Aterotrombótico Antiagregantes y Revascularización < 15 días

2- Cardioembólico Anticoagulación

3- Lacunar (pequeño vaso) Antiagregación + control HTA

4- Etiología indeterminada (30%) Antiagregación

5- Etiología infrecuente (5%)

Etiologías inusuales

Enf disinmunes y vasculitis

- Angeitis del SNC
- Arteritis temporal
- Vasculopatia virales (herpes y otras)
- PAN y Churg Strauss
- Takayasu
- Enfermdedad de Bürger
- LES
- Síndrome antifosfosfolipidico
- Enf de Behçet
- Enfermedad inflamatoria intestinal

Infecciosas

- Vascultis cerebral asociada a cisticercosis, tuberculosis y micosis

Alteraciones de la coagulación/hematológicas

- CID
- Alteraciones de la coagulación
- Púrpura trombotica trombocitopenica
- Sd de hiperviscosidad

Patología metabólica:

- Calcio, hipercalcemia, magnesio y isquemia cerebral
- Enfermedades metabólicas

Otras

- Sd de vasoconstricción cerebral
- Eclamsia
- Abuso de sustancias
- Sd paraneoplasicos
- Enfermedad de Eales
- Enfermedad de Degos
- Epiteliopatia placoide pigmentada aguda multifocal posterior
- Sd de Sweet
- Sd nefrótico
- Síndrome de Kawasaki
- Síndrome del nevus epidermal
- Fistulas arteriovenosas pulmonares
- Sd de Rendu-Osler
- Disecciones arteriales
- AAC
- Moya Moya
- Sneddon
- CADASIL
- Fabry
- Marfan
- Pseudoxantoma elástico
- Síndrome de Ehrler-Danlos
- Progeria
- Microangiopatias retinianas (SUSAC, SICRET RED-M)
- HERNS
- MELAS
- Síndrome de Sturge-Weber
- Enfermedad de Von-Hippel-Lindau
- Neurofibromatoss
- Enfermedades óseas
- Otras angiopatías inusuales

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DIAGNÓSTICO

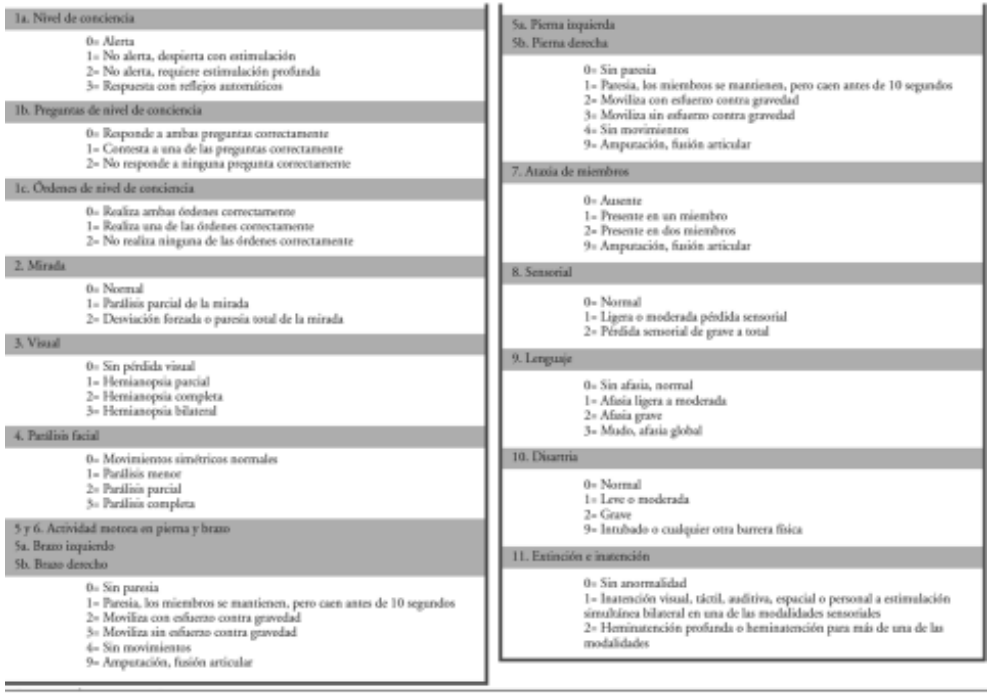
Box de TC craneal:

Enfermería: - **Toma de Constantes**
- **Vía periférica** (en brazo no parético)
- **Analítica** (código ictus)
- **Tóxicos** (jóvenes)
- **ECG** (opcional)

Medicina: **Anamnesis (familia)**
- **Rankin previo**
- **Comorbilidad**
- **Datos: FRCV, medicación, síntomas, etc…**
- **Tiempos:**
  - **Hora de inicio**
  - **Hora de llegada**
  - **Hora de trombolisis**

Exploración física y neurológica
- **Escala NIH**

ESCALA NIH



1a. Nivel de conciencia

0= Alerta
1= No alerta, despierta con estimulación
2= No alerta, requiere estimulación profunda
3= Respuesta con reflejos automáticos

1b. Preguntas de nivel de conciencia

0= Responde a ambas preguntas correctamente
1= Contesta a una de las preguntas correctamente
2= No responde a ninguna pregunta correctamente

1c. Órdenes de nivel de conciencia

0= Realiza ambas órdenes correctamente
1= Realiza una de las órdenes correctamente
2= No realiza ninguna de las órdenes correctamente

2. Mirada

0= Normal
1= Parálisis parcial de la mirada
2= Desviación forzada o paresia total de la mirada

3. Visual

0= Sin pérdida visual
1= Hemianopsia parcial
2= Hemianopsia completa
3= Hemianopsia bilateral

4. Parálisis facial

0= Movimientos simétricos normales
1= Parálisis menor
2= Parálisis parcial
3= Parálisis completa

5 y 6. Actividad motora en pierna y brazo
5a. Brazo izquierdo
5b. Brazo derecho

0= Sin paresia
1= Paresia, los miembros se mantienen, pero caen antes de 10 segundos
2= Moviliza con esfuerzo contra gravedad
3= Moviliza sin esfuerzo contra gravedad
4= Sin movimientos
9= Amputación, fusión articular

5a. Pierna izquierda
5b. Pierna derecha

0= Sin paresia
1= Paresia, los miembros se mantienen, pero caen antes de 10 segundos
2= Moviliza con esfuerzo contra gravedad
3= Moviliza sin esfuerzo contra gravedad
4= Sin movimientos
9= Amputación, fusión articular

7. Ataxia de miembros

0= Ausente
1= Presente en un miembro
2= Presente en dos miembros
9= Amputación, fusión articular

8. Sensorial

0= Normal
1= Ligera o moderada pérdida sensorial
2= Pérdida sensorial de grave a total

9. Lenguaje

0= Sin afasia, normal
1= Afasia ligera a moderada
2= Afasia grave
3= Mudo, afasia global

10. Disartria

0= Normal
1= Leve o moderada
2= Grave
9= Intubado o cualquier otra barrera física

11. Extinción e inatención

0= Sin anormalidad
1= Inatención visual, táctil, auditiva, espacial o personal a estimulación simultánea bilateral en una de las modalidades sensoriales
2= Heminatención profunda o heminatención para más de una de las modalidades

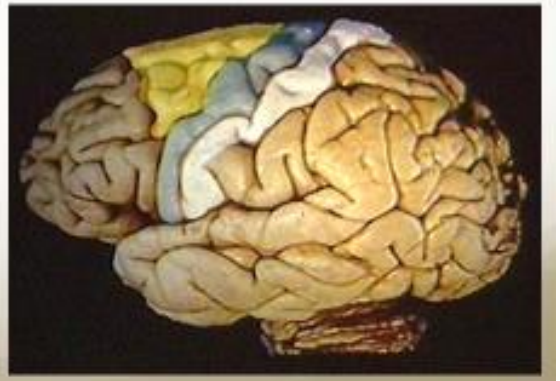
SÍNTOMAS NEUROLÓGICOS I

-**Motor** (hemiparesia/plejia)

-**Sensitivo** (hemihipoestesia/anestesia)

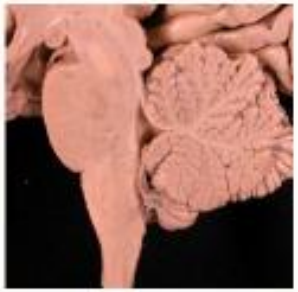
-**Visual** (hemianopsia, ceguera)

-**Lenguaje** (disartria, afasia)



SÍNTOMAS NEUROLÓGICOS II

-**D**ismetría (Incoordinación, ataxia)
-**D**iplopia
-**D**isfagia
-**D**isfonía
-**D**izziness (Vértigo).



- Movimientos involuntarios (corea, balismo)

- Anosognosia
- Asomatognosia
- Apraxia
- Negligencia

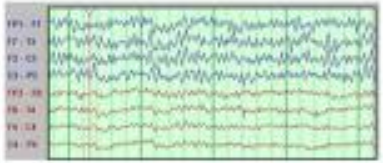
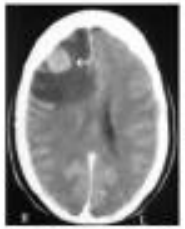
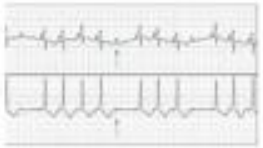
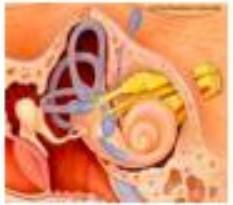
SÍNTOMAS NEUROLÓGICOS III

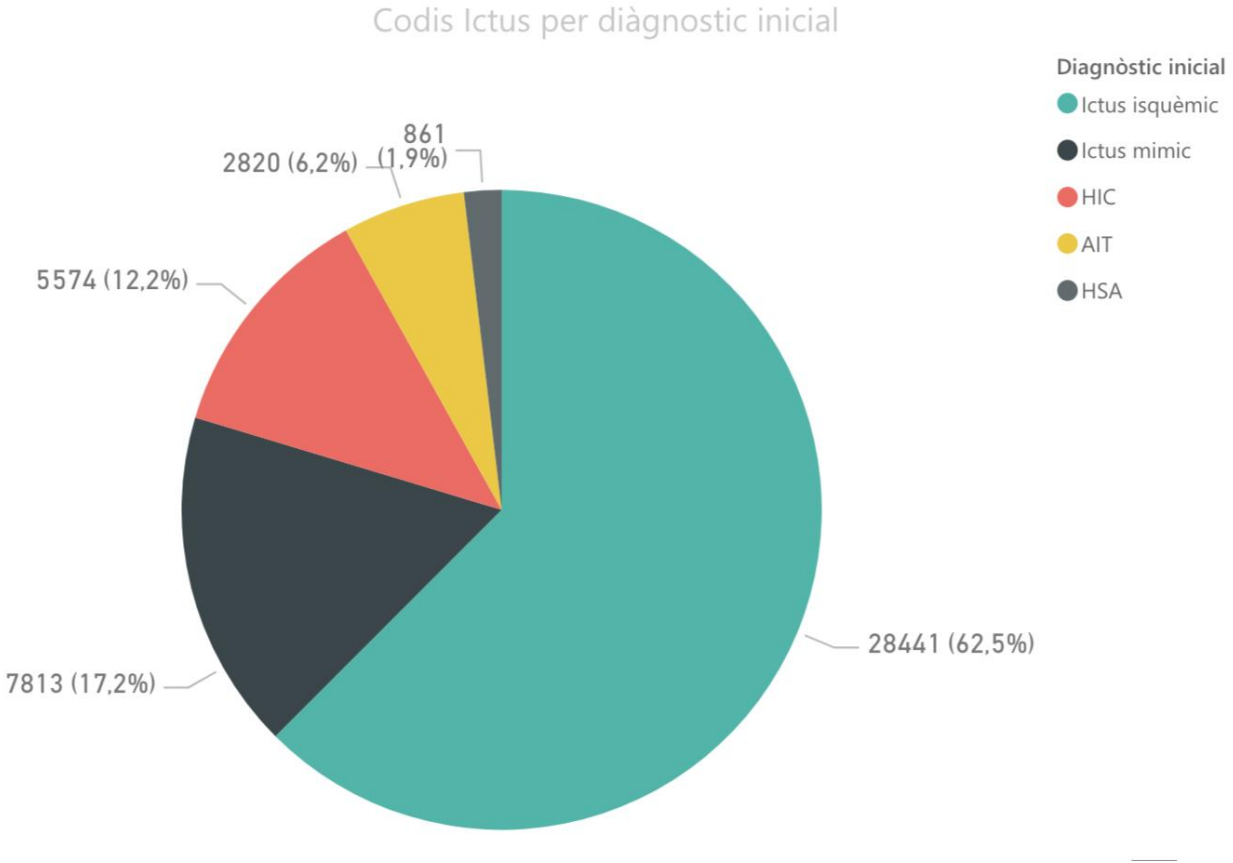
- Déficit mnésico / Sd confusional
- Alucinaciones (visuales, auditivas)
- Simultagnosia (incapacidad de reconocer la globalidad)
- Prosopagnosia (incapacidad de reconocer rostros)
- Palinopsia (persistencia de un estímulo visual)
- Mutismo acinético (apatía extrema)
- Sd del Cautiverio

Diagnóstico diferencial

"Stroke mimic"

- Crisis comiciales
- Tumor cerebral
- Hematoma subdural
- Trastornos metabólicos (hipo/hiperglicemia e hiponatremia)
- Infecciones sistémicas o cerebrales (encefalitis, meningitis...)
- Tóxicos (drogas, alcohol)
- Migraña
- Encefalopatía HTA
- Síncope, vértigo
- Esclerosis múltiple
- Síndrome de conversión


Codis Ictus per diàgnostic inicial
Diagnòstic inicial
Ictus isquèmic
Ictus mimic
HIC
AIT
HSA
861 (1,9%)
2820 (6,2%)
5574 (12,2%)
28441 (62,5%)
7813 (17,2%)

Review > J Clin Neurosci. 2021 Nov;93:174-182. doi: 10.1016/j.jocn.2021.09.025.
Epub 2021 Sep 20.

Ischemic stroke mimics: A comprehensive review

Marietta Pohl [1], David Hesszenberger [2], Krisztian Kapus [1], Janos Meszaros [1], Andrea Feher [3], Imre Varadi [1], Gabriella Pusch [4], Eva Fejes [5], Antal Tibold [1], Gergely Feher [6]

Background: Ischemic stroke is the leading cause of disability and one of the leading causes of death. Ischemic stroke mimics (SMs) can account for a noteble number of diagnosed acute strokes and even can be thrombolyzed.

Methods: The aim of our comprehensive review was to summarize the findings of different studies focusing on the prevalence, type, risk factors, presenting symptoms, and outcome of SMs in stroke/thrombolysis situations.

Results: Overall, 61 studies were selected with 62.664 participants. Ischemic stroke mimic rate was 24.8% (15044/60703). Most common types included peripheral vestibular dysfunction in 23.2%, toxic/metabolic in 13.2%, seizure in 13%, functional disorder in 9.7% and migraine in 7.76%. Ischemic stroke mimic have less vascular risk factors, younger age, female predominance, lower (nearly normal) blood pressure, no or less severe symptoms compared to ischemic stroke patients ($p < 0.05$ in all cases). 61.7% of ischemic stroke patients were thrombolysed vs. 26.3% among SMs ($p < 0.001$). ($p < 0.001$). Overall intracranial hemorrhage was reported in 9.4% of stroke vs. 0.7% in SM patients ($p < 0.001$). Death occurred in 11.3% of stroke vs 1.9% of SM patients ($p < 0.001$). Excellent outcome was (mRS 0-1) was reported in 41.8% ischemic stroke patients vs. 68.9% SMs ($p < 0.001$). Apart from HINTS manouvre or Hoover sign there is no specific method in the identification of mimics. MRI DWI or perfusion imaging have a role in the setup of differential diagnosis, but merit further investigation.

Conclusion: Our article is among the first complex reviews focusing on ischemic stroke mimics. Although it underscores the safety of thrombolysis in this situation, but also draws attention to the need of patient evaluation by physicians experienced in the diagnosis of both ischemic stroke and SMs, especially in vertigo, headache, seizure and conversional disorders.

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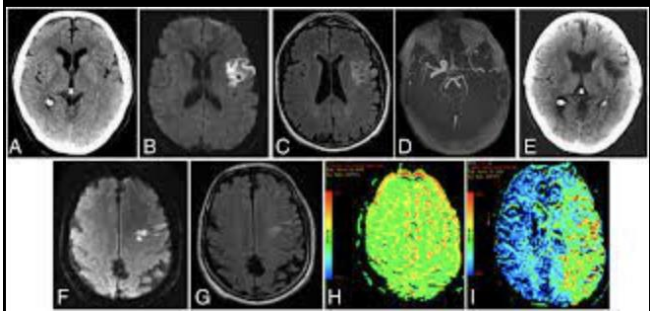
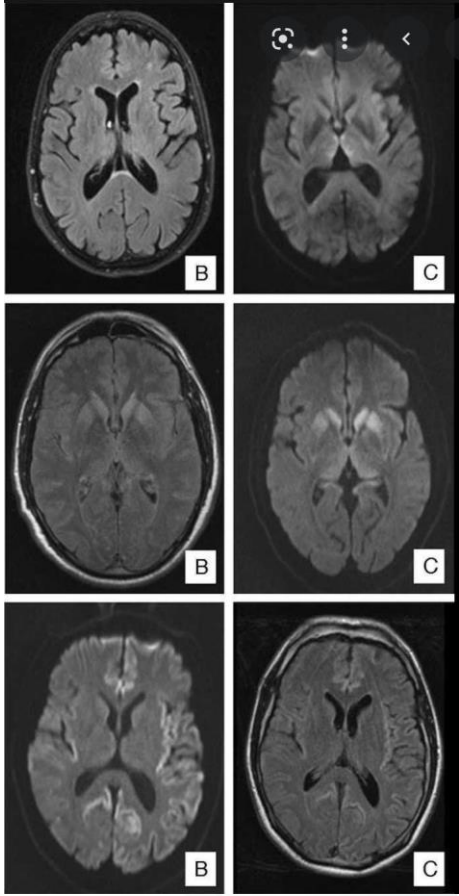


NEUROIMAGEN



TC Simple

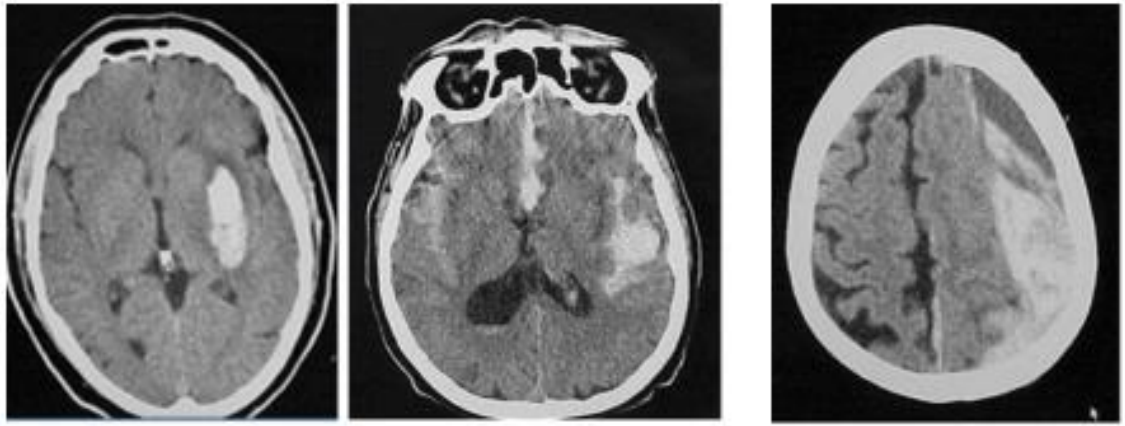
TC perfusión

Angio TC

RM Perfusión/Difusión

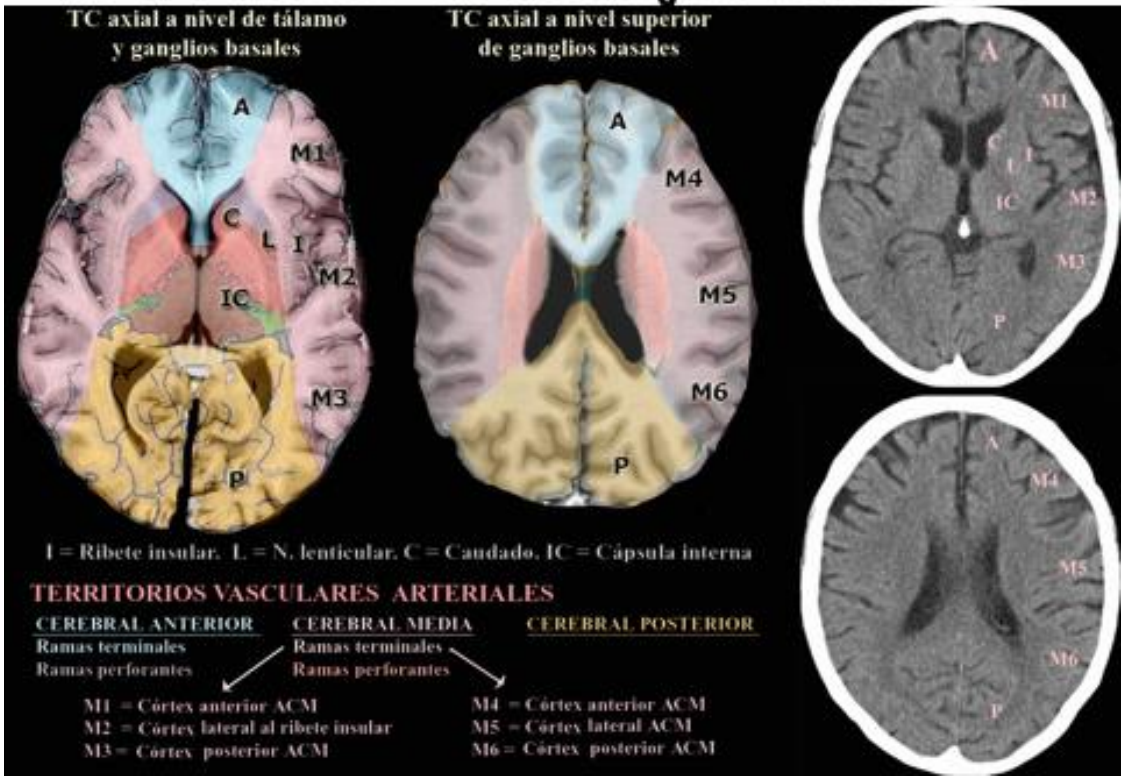
TC simple

Descartar ictus hemorrágico

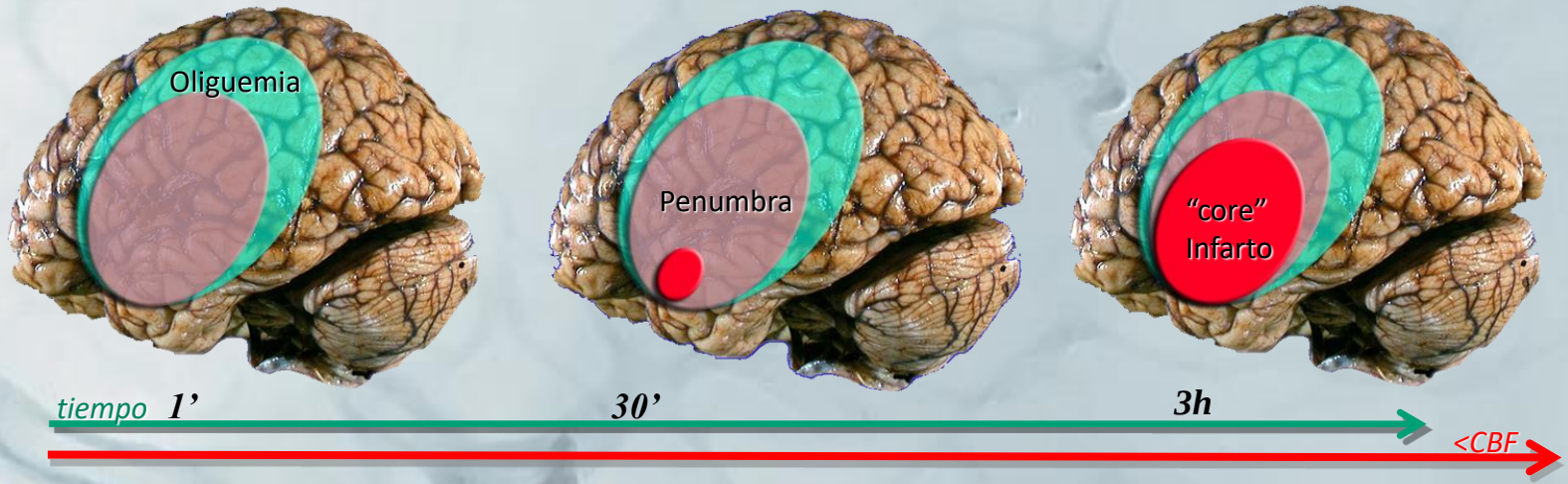


Hematoma cerebral | Hemorragia subaracnoidea | Hematoma subdural

ASPECTS > 5: tejido viable



TC Perfusión



PENUMBRA ISQUÉMICA

Vulnerabilidad selectiva

CBF<18-20 ml/100gr/min

- *parada síntesis proteica neuronal*
- *menor transporte membrana*
- *baja actividad sináptica*
- *reducción potenciales evocados*
- *pérdida conducción eléctrica*
- *parada cortical*

ventana terapéutica

tiempo

<CBF

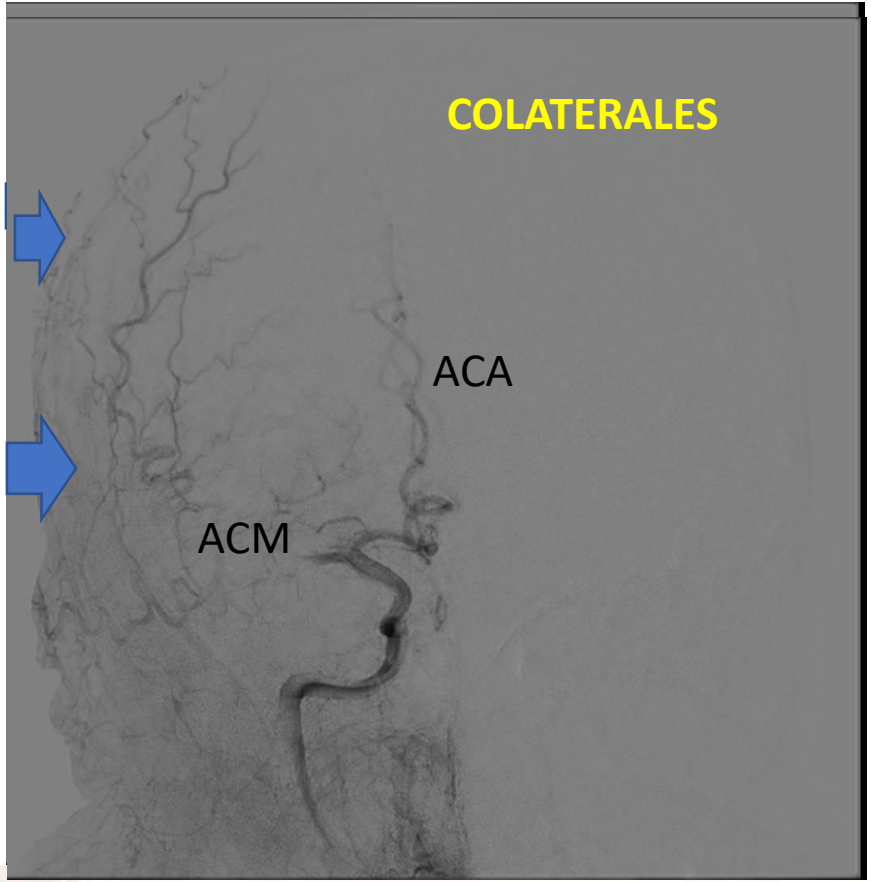
INFARTO

Lesión irreversible

CBF<10-12 ml/100gr/min

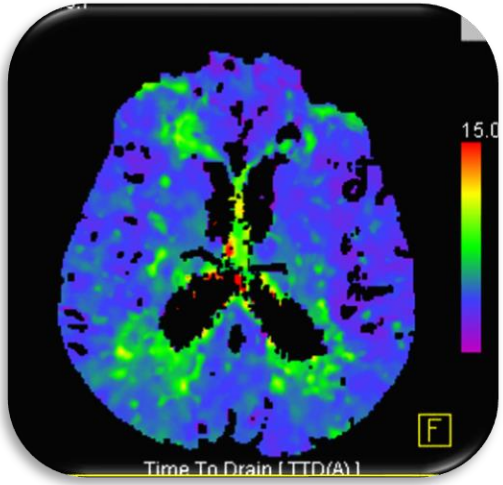
- *supresión potenciales evocados*
- *alteración hidroelectrolítica*
- *disfunción membrana*
- *edema citotóxico*
- *rotura membrana*
- *aumento K extracelular*

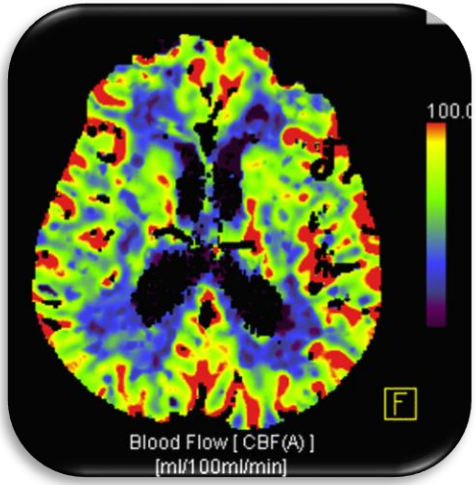
The ischemic penumbra: a dynamic (time+space) concept. Baron J.C. Cerebrovasc Dis 1999;9:193-201

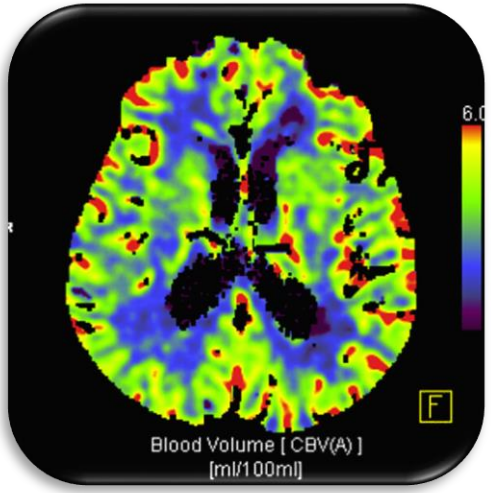

COLATERALES
ACA
ACM

1

PERFUSIÓN NORMAL

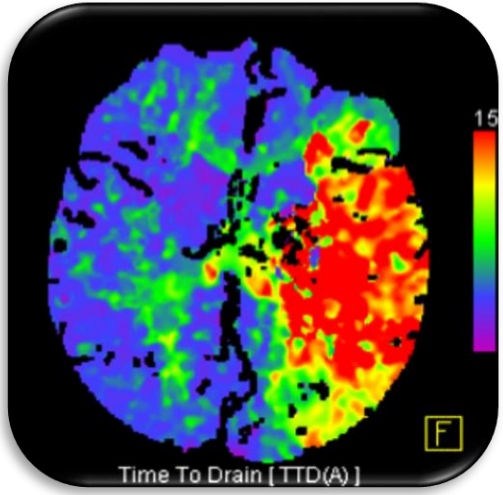


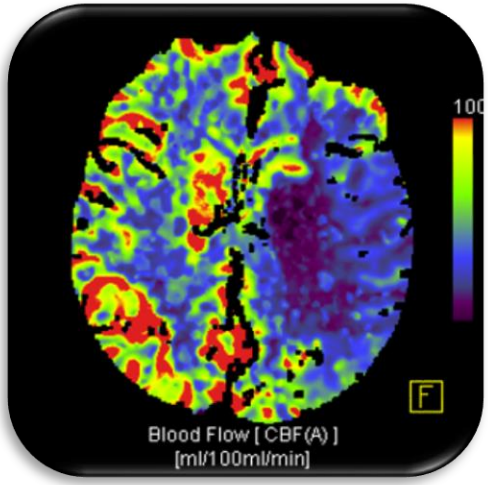


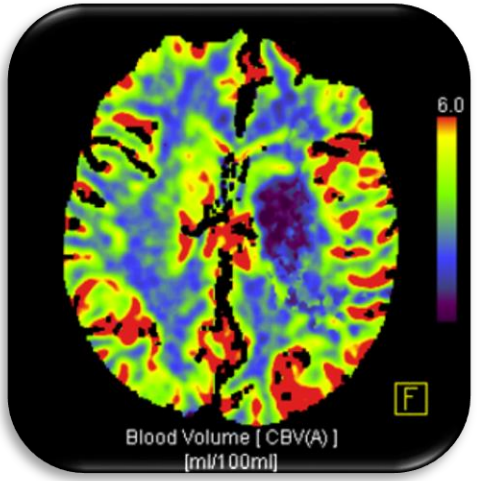


2

PERFUSIÓN DISMINUIDA

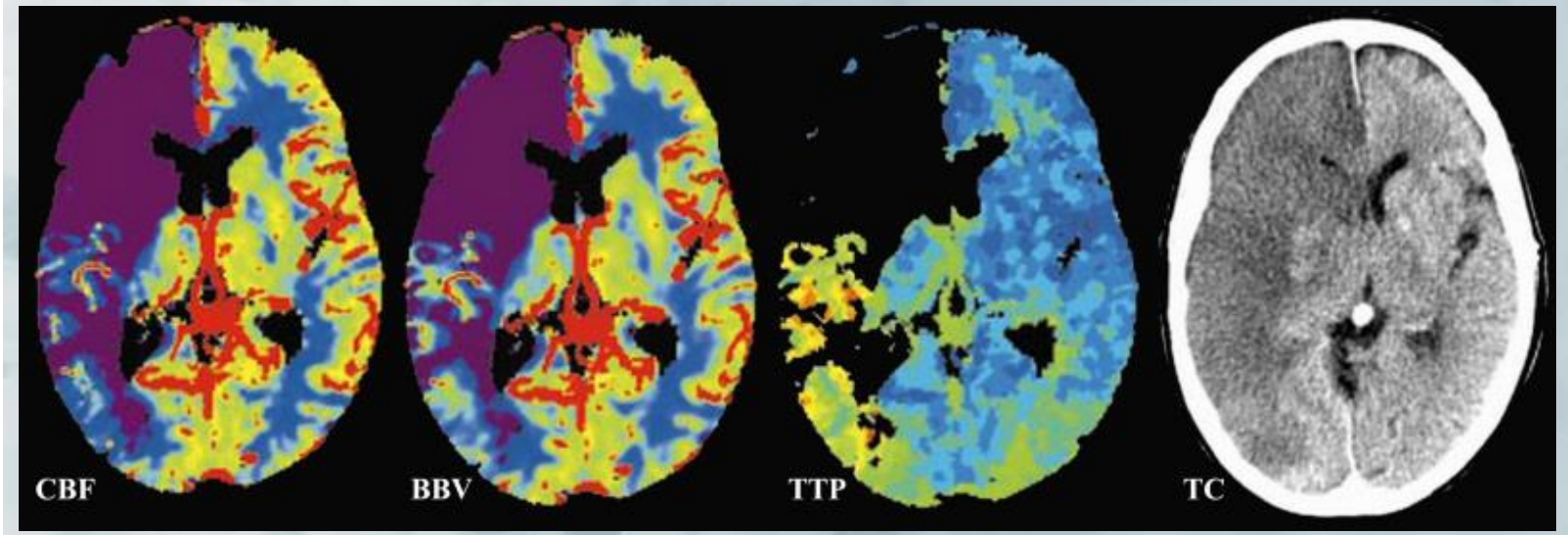






Ausencia de penumbra

pTC

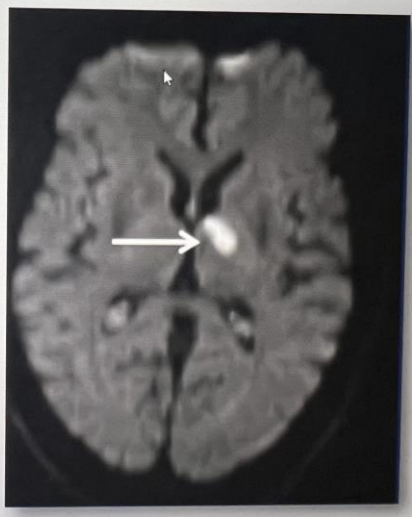


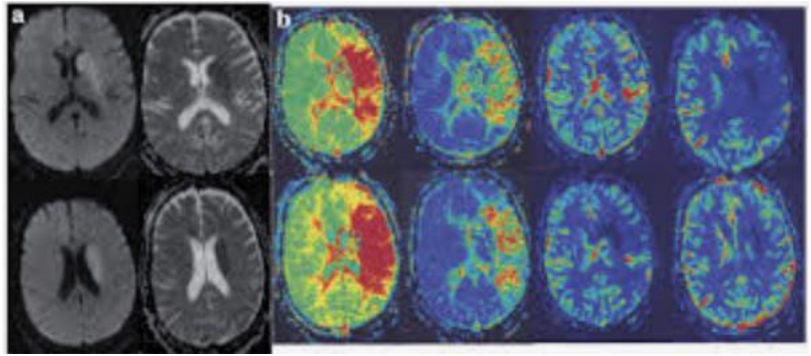
RESONANCIA DIFUSIÓN/PERFUSIÓN

Infarto en RM (secuencia de difusión)

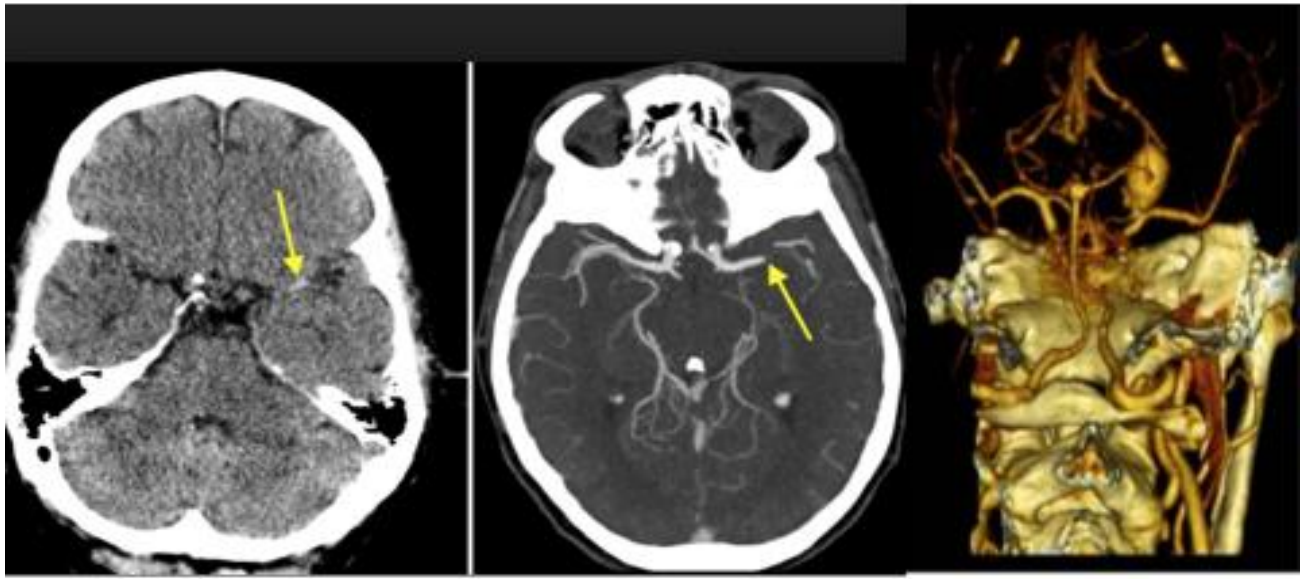
- Fallo de la Bomba Na/K
- Aumento del agua intracelular.
- Edema Citotoxico.

Señal Brillante.



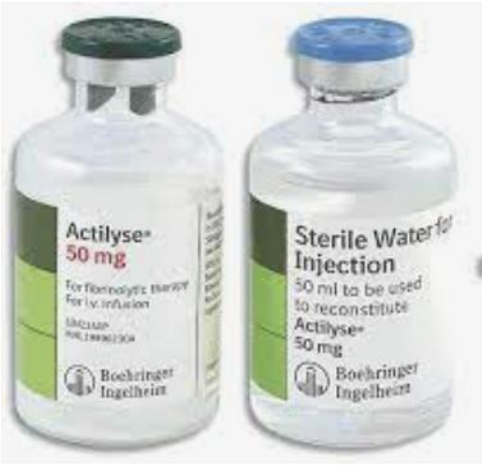


Angio TC: Demostrar oclusión arterial



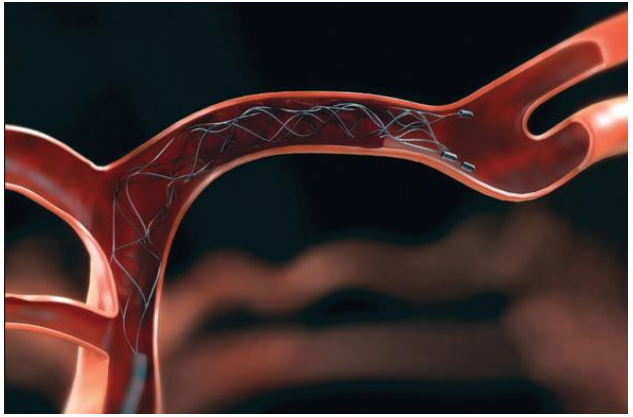
Fibrinolisis (Alteplasa) si < 4.5 h

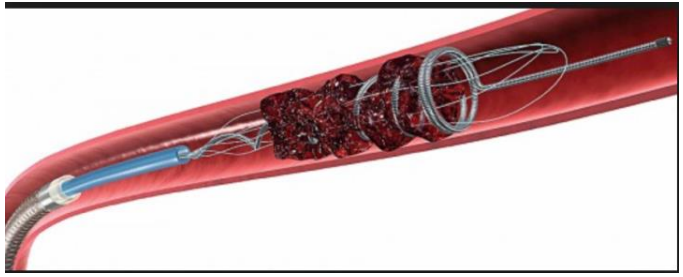
desde el inicio de los síntomas

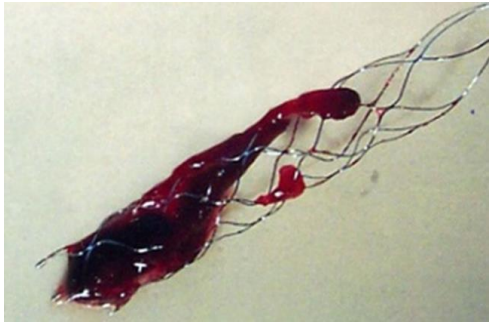


TRATAMIENTO ENDOVASCULAR (< 24 h)

- Punción femoral/radial
- Anestesia opcional
- Dispositivos mecánicos: solitaire / Trevo







Ictus isquémico

Terapia antiHTA en prevención 2aria ≠ beneficio descenso PA manejo agudo[1]

Necesitamos PA elevada -> perfusión cerebral en áreas isquémicas[2]

MAPAS trial[3]

No beneficio claro descenso PA (1as 12 h)
-> Subanálisis[4] **beneficio 161-180 mmHg**

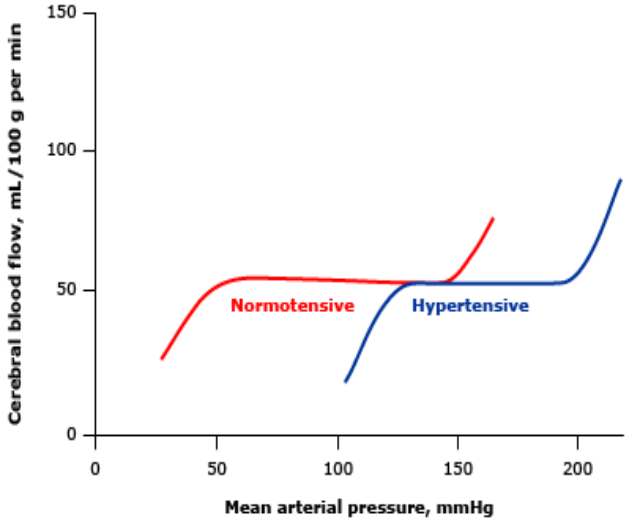
Good outcome -> modified Rankin score 0-2 at 90-days

Pacientes NO FIBRINOLISIS

RIGHT-2 // CATIS // SCAST // COSSACS // ENOS

AIT, HIC, stroke mimics

30 – 48h desde inicio de síntomas



Redrawn from: Kaplan NM. Management of hypertensive emergencies. Lancet 1994; 344:1335.

1. Berge E. Should high blood pressure be lowered in the acute stroke? J Hypertens. 2011 Aug;29(8):1478-9. doi: 10.1097/HJH.0b013e32834a019b. PMID: 21750435. 2. Aiyagari V, Gorelick PB. Management of blood pressure for acute and recurrent stroke. Stroke. 2009 Jun;40(6):2251-6. doi: 10.1161/STROKEAHA.108.531574. Epub 2009 Apr 23. PMID: 19390077. 3. Saver JL. Time is brain--quantified. Stroke. 2006 Jan;37(1):263-6. doi: 10.1161/01.STR.0000196957.55928.ab. Epub 2005 Dec 8. PMID: 16339467. 34. Saver JL. Time is brain-quantified. Stroke. 2006 Jan;37(1):263-6. doi: 10.1161/01.STR.0000196957.55928.ab. Epub 2005 Dec 8. PMID: 16339467.

Ictus isquémico + candidat@ fibrinolisis

PAs ≤ 185 mmHg y PAd ≤ 110 mmHg[4] → **FIBRINOLISIS**

Labetalol 10-20 mg IV en 1-2 min repetible x1
Nicardipino 5 mg/h IV -> + 2.5 mg/h/5-15 min MÁX 15 mg/h
Clevidipino 1-2 mg/h IV -> dosis x2 /2-5 min MÁX 21 mg/h
Otros: **Hidralazina** 10-20 mg/4-6h IV MÁX 40 mg/dosis

FIBRINOLISIS — **1as 24 horas** → **PA 180 - 105 mmHg[4]**

c/15 min 2h – c/30 min 6h – c/1h 16h

Labetalol 10 mg IV + PERF.IV 2-8 mg/min
Nicardipino 5 mg/h IV -> + 2.5 mg/h/5-15 min MÁX 15 mg/h
Clevidipino 1-2 mg/h IV -> dosis x2 /2-5 min MÁX 21 mg/h
Otros: **Hidralazina** 10-20 mg/4-6h IV MÁX 40 mg/dosis

Ictus isquémico + NO candidat@ fibrinolisis

NO TRATAR HTA[4,5]
excepto tensiones extremas
PAs > 220 / PAd > 120 mmHg,
EAC, IC, disección aórtica,
encefalopatía HTA,
pre-eclampsia/eclampsia

15% descenso 1as 24h

4. Powers WJ et al. 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: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019 Dec;50(12):e344-e418. doi: 10.1161/STR.0000000000000211. Epub 2019 Oct 30. Erratum in: Stroke. 2019 Dec;50(12):e440-e441. PMID: 31662037. 5. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL. 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: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019 Dec;50(12):e344-e418. doi: 10.1161/STR.0000000000000211. Epub 2019 Oct 30. Erratum in: Stroke. 2019 Dec;50(12):e440-e441. PMID: 31662037.

FIBRINOLISIS

Diagnóstico ictus isquémico + **déficit neurológico**
< 4.5 horas de inicio de síntomas / estado neurológico basal
Edad ≥ 18 años

Criterios de exclusión

Historia

- ≤ 21 días: hemorragia TGI
- ≤ 3 meses: Cx. SNC, TCE severo
- ≤ 3 meses: Ictus isquémico
- HIC previa
- Neoplasia TGI
- Neoplasia SNC

Clínica

- HSA: náuseas/vómitos
- HTA no controlada
- Sangrado
- Endocarditis
- Sospecha disección aórtica

Hematología

No justifica retraso en fibrinolisis excepto **antecedentes plaquetopenia**

- Plaquetas < 100.000/mm^3
- Anticoagulación + INR > 1.7, TP > 15s, aPTT > 40s
- HBPM a dosis terapéuticas últimas 24h
- NACO con evidencia de actividad (últimas dosis o tiempos de coagulación: TE, TT, actividad Xa, …)

Radiología

- Hemorragia
- Lesión extensa irreversible

Embarazo
MAV en SNC
Aneurisma cerebral
Cx. Mayor, trauma en 2 semanas previas
Historia de sangrado TGI/TGU

FIBRINOLISIS

Diagnóstico ictus isquémico + **déficit neurológico**
< 4.5 horas de inicio de síntomas / estado neurológico basal
Edad ≥ 18 años

Criterios de exclusión

PAs ≤ 185 mmHg y PAd ≤ 110 mmHg[4]

AsSoonAsPossible

2 vías periféricas (buen calibre)

Glucemia

Alteplasa

Dosis: 0.9 mg/kg - **MÁXIMO 90 mg**
- **10%** de la dosis IV BOLUS en 1 min
- **90%** restante en PERF.IV en 60 min

Tenecteplasa

Alternativa eficaz y segura[10-11]
Dosis: 0.25 mg/kg - **MÁXIMO 25 mg**
IV BOLUS en **5 seg**

Post FIBRINOLISIS -> traslado Unidad de Ictus / UCI al menos 24h[4]

1as 24 horas -> c/15 min 2h – c/30 min 6h – c/1h 16h

PA 180 - 105 mmHg[4]

Complicaciones

-> **Hemorragia intracraneal**[6-7]**:** 5-7 %
-> **Sangrado moderado:** equimosis, catéter, encías,…
-> **Angioedema**[8-9]**:** 1-8%, iECAs + riesgo

6. Emberson J et al. Stroke Thrombolysis Trialists' Collaborative Group. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014 Nov 29;384(9958):1929-35. doi: 10.1016/S0140-6736(14)60584-5. Epub 2014 Aug 5. PMID: 25106063; PMCID: PMC4441266. 7. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995 Dec 14;333(24):1581-7. doi: 10.1056/NEJM199512143332401. PMID: 7477192. 36. Hill MD, Buchan AM; Canadian Alteplase for Stroke Effectiveness Study (CASES) Investigators. Thrombolysis for acute ischemic stroke: results of the Canadian Alteplase for Stroke Effectiveness Study. CMAJ. 2005 May 10;172(10):1307-12. doi: 10.1503/cmaj.1041561. PMID: 15883405; PMCID: PMC557101.8. Hurford R, Rezvani S, Kreimei M, Herbert A, Vail A, Parry-Jones AR, Douglass C, Molloy J, Alachkar H, Tyrrell PJ, Smith CJ. Incidence, predictors and clinical characteristics of orolingual angio-oedema complicating thrombolysis with tissue plasminogen activator for ischaemic stroke. J Neurol Neurosurg Psychiatry. 2015 May;86(5):520-3. doi: 10.1136/jnnp-2014-308097. Epub 2014 Jul 12. PMID: 25016564. 9. Myslimi F, Caparros F, Dequatre-Ponchelle N, Moulin S, Gautier S, Girardie P, Cordonnier C, Bordet R, Leys D. Orolingual Angioedema During or After Thrombolysis for Cerebral Ischemia. Stroke. 2016 Jul;47(7):1825-30. doi: 10.1161/STROKEAHA.116.013334. Epub 2016 May 19. PMID: 27197851. 10. Katsanos AH, Safouris A, Sarraj A, Magoufis G, Leker RR, Khatri P, Cordonnier C, Leys D, Shoamanesh A, Ahmed N, Alexandrov AV, Tsivgoulis G. Intravenous Thrombolysis With Tenecteplase in Patients With Large Vessel Occlusions: Systematic Review and Meta-Analysis. Stroke. 2021 Jan;52(1):308-312. doi: 10.1161/STROKEAHA.120.030220. Epub 2020 Dec 4. PMID: 33272127. 11. Burgos AM, Saver JL. Evidence that Tenecteplase Is Noninferior to Alteplase for Acute Ischemic Stroke: Meta-Analysis of 5 Randomized Trials. Stroke. 2019 Aug;50(8):2156-2162. doi: 10.1161/STROKEAHA.119.025080. Epub 2019 Jul 18. PMID: 31318627.

TROMBECTOMÍA MECÁNICA

Horas de inicio de síntomas / estado neurológico basal

< 4.5 horas

FIBRINOLISIS

4.5 horas – 24 h

FIBRINOLISIS

> 24 h

Tratamiento "ESTÁNDAR"

General criteria for MT require all of the following:

- Neuroimaging (eg, CT without contrast or diffusion-weighted MRI) is consistent with a small infarct core (ie, limited signs of early ischemic change) and excludes hemorrhage
- Angiography (eg, CTA or MRA) demonstrates a proximal LAO in the anterior circulation
- Thrombectomy is performed at a stroke center with appropriate expertise in MT
- The patient has a persistent, potentially disabling neurologic deficit
- Treatment can be started within 24 hours of the time last known to be well

Angio – TC / Angio - RMN

Large Artery Occlusión **ESTÁNDAR**

Posterior Large Artery Occlussión **Considerar TROMBECTOMÍA MECÁNICA**

Anterior Large Artery Occlussión

< 6 horas

ASPECTS ≥ 6

6 - 24 horas

DAWN trial
DEFUSE 3 trial

TROMBECTOMÍA MECÁNICA

DAWN trial eligibility require all of the following:

- Treatment (femoral puncture) can start within 6 to 24 hours of time last known to be well
- Failed or contraindicated for IV tPA
- A deficit on the NIHSS of ≥10 points
- No significant prestroke disability: Baseline mRS score ≤1
- Baseline infarct involving <1/3 of MCA territory
- Intracranial occlusion of the ICA or M1 segment of the MCA
- A clinical-core mismatch according to age:
  - Age ≥80 years: NIHSS ≥10 and infarct volume <21 mL
  - Age <80 years: NIHSS 10 to 19 and infarct volume <31 mL
  - Age <80 years: NIHSS ≥20 and infarct volume <51 mL

DEFUSE 3 trial eligibility require all of the following:

- Treatment (femoral puncture) can start within 6 to 16 hours of time last known to be well
- A deficit on the NIHSS of ≥6 points
- Only slight or no prestroke disability: Baseline mRS score ≤2
- Occlusion of the cervical or intracranial ICA (with or without tandem MCA lesions) or the M1 segment of the MCA
- Age 18 to 90 years
- A target mismatch profile on CT perfusion or MRI defined as:
  - An ischemic core volume <70 mL, and
  - A mismatch ratio (the volume of the perfusion lesion divided by the volume of the ischemic core) >1.8, and
  - A mismatch volume (volume of perfusion lesion minus the volume of the ischemic core) >15 mL

Horas de inicio de síntomas / estado neurológico basal → **> 24 h**

TRATAMIENTO ESTÁNDAR

TERAPIA ANTITROMBÓTICA

NIHSS > 5 = ictus moderado-severo

IST trial[12], CAST trial[13]

AAS 100-300 mg/24h

NIHSS ≤ 5 = ictus leve

Meta-análisis 2018[14], Meta-análisis 2021[15], POINT trial, CHANCE trial, THALES trial[21] (Ticagrelor)

AAS 300 mg -> 100 mg/24h

Clopidogrel 300 mg -> 75 mg/24h

DAPT x 21 días

Intracranial Large Artery Atherosclerosis

SAMMPRIS trial[16,17], MATCH trial[18]

AAS 300 mg -> 100 mg

Clopidogrel 300 mg -> 75 mg

DAPT x 90 días

12. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. International Stroke Trial Collaborative Group. Lancet. 1997 May 31;349(9065):1569-81. PMID: 9174558. 13. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. Lancet. 1997 Jun 7;349(9066):1641-9. PMID: 9186381. 14. Hao Q, Tampi M, O'Donnell M, Foroutan F, Siemieniuk RA, Guyatt G. Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke or high risk transient ischaemic attack: systematic review and meta-analysis. BMJ. 2018 Dec 18;363:k5108. doi: 10.1136/bmj.k5108. PMID: 30563866; PMCID: PMC6298178. 15. Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, Wang C, Li H, Meng X, Cui L, Jia J, Dong Q, Xu A, Zeng J, Li Y, Wang Z, Xia H, Johnston SC; CHANCE Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med. 2013 Jul 4;369(1):11-9. doi: 10.1056/NEJMoa1215340. Epub 2013 Jun 26. PMID: 23803136. 16. Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, Janis LS, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Torbey MT, Zaidat OO, Rumboldt Z, Cloft HJ; SAMMPRIS Trial Investigators. Stenting versus aggressive medical therapy for intracranial arterial stenosis. N Engl J Med. 2011 Sep 15;365(11):993-1003. doi: 10.1056/NEJMoa1105335. Epub 2011 Sep 7. Erratum in: N Engl J Med. 2012 Jul 5;367(1):93. PMID: 21899409; PMCID: PMC3552515. 17. Derdeyn CP, Chimowitz MI, Lynn MJ, Fiorella D, Turan TN, Janis LS, Montgomery J, Nizam A, Lane BF, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Lynch JR, Zaidat OO, Rumboldt Z, Cloft HJ; Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial Investigators. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial. Lancet. 2014 Jan 25;383(9914):333-41. doi: 10.1016/S0140-6736(13)62038-3. Epub 2013 Oct 26. PMID: 24168957; PMCID: PMC3971471. 18. Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, Leys D, Matias-Guiu J, Rupprecht HJ; MATCH investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet. 2004 Jul 24-30;364(9431):331-7. doi: 10.1016/S0140-6736(04)16721-4. PMID: 15276392.

Ticagrelor

SOCRATES trial[19]

Beneficio origen aterosclerótico[20]

Monoterapia 90 días

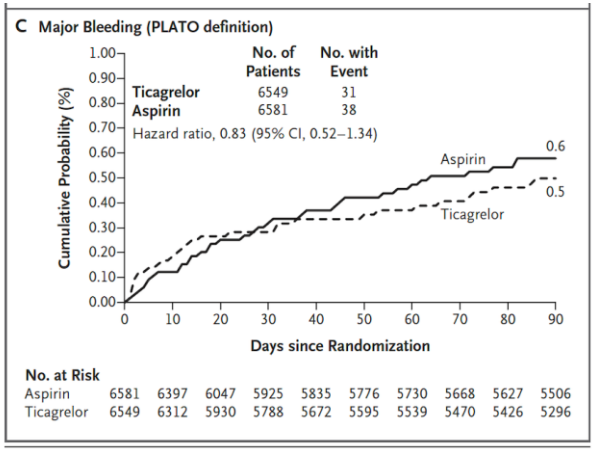
Ictus isquémico NIHSS ≤ 5

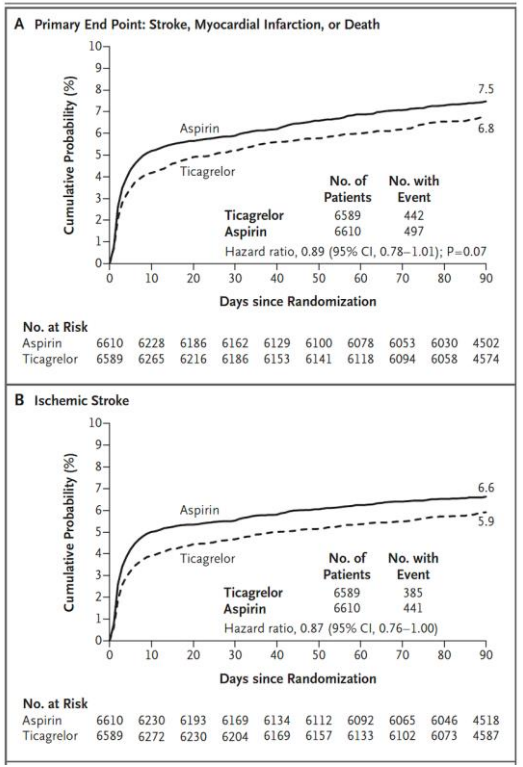
AIT ABCD² score ≥ 4

n=13.199

Exclusión: fibrinolisis, trombectomía, origen cardioembólico

103 (6,7%) of 1542 patients with **ipsilateral stenosis** in the **ticagrelor** group and **147 (9·6%)** of 1539 patients with ipsilateral stenosis in the **aspirin** group had an **occurrence of stroke, myocardial infarction, or death within 90 days** **hazard ratio 0,68 [95% CI 0·53-0·88]; p=0,003)**





19. Johnston SC, Amarenco P, Albers GW, Denison H, Easton JD, Evans SR, Held P, Jonasson J, Minematsu K, Molina CA, Wang Y, Wong KS; SOCRATES Steering Committee and Investigators. Ticagrelor versus Aspirin in Acute Stroke or Transient Ischemic Attack. N Engl J Med. 2016 Jul 7;375(1):35-43. doi: 10.1056/NEJMoa1603060. Epub 2016 May 10. PMID: 27160892. 20. Amarenco P, Albers GW, Denison H, Easton JD, Evans SR, Held P, Hill MD, Jonasson J, Kasner SE, Ladenvall P, Minematsu K, Molina CA, Wang Y, Wong KSL, Johnston SC; SOCRATES Steering Committee and Investigators. Efficacy and safety of ticagrelor versus aspirin in acute stroke or transient ischaemic attack of atherosclerotic origin: a subgroup analysis of SOCRATES, a randomised, double-blind, controlled trial. Lancet Neurol. 2017 Apr;16(4):301-310. doi: 10.1016/S1474-4422(17)30038-8. Epub 2017 Feb 23. PMID: 28238711.

Ticagrelor

THALES trial[21]

Ictus isquémico NIHSS ≤ 5

AIT ABCD² score ≥ 6

Intracranial or extracranial arterial stenosis ≥50%

n=11.016

Exclusión: fibrinolisis, trombectomía, origen cardioembólico

Conclusiones

THALES = CHANCE = POINT con respecto a beneficio DAPT

-> AAS y CLOPIDOGREL no estudiado en NIHSS score 4 - 5, no incluidos en POINT y CHANCE

-> Faltaría comparar AAS + CLOPI frente AAS + TICA

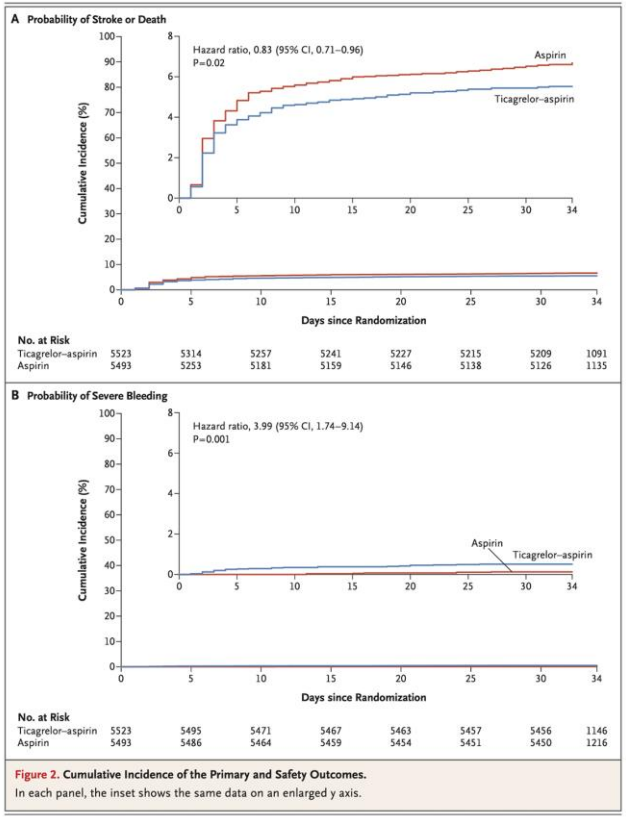


Figure 2. Cumulative Incidence of the Primary and Safety Outcomes.
In each panel, the inset shows the same data on an enlarged y axis.

21. Johnston SC, Amarenco P, Denison H, Evans SR, Himmelmann A, James S, Knutsson M, Ladenvall P, Molina CA, Wang Y; THALES Investigators. Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA. N Engl J Med. 2020 Jul 16;383(3):207-217. doi: 10.1056/NEJMoa1916870. PMID: 32668111.

Pacientes antiagregados "de base" con AAS / Clopidogrel[22-24]

NIHSS > 5 = ictus moderado-severo

Continuar tratamiento previo

NIHSS ≤ 5 = ictus leve

switch

AAS 300 mg -> 100 mg/24h

Clopidogrel 300 mg -> 75 mg/24h

DAPT x 21 días (90 días si aterosclerosis)

22. Groot AE, Vermeij JM, Westendorp WF, Nederkoorn PJ, van de Beek D, Coutinho JM. Continuation or Discontinuation of Anticoagulation in the Early Phase After Acute Ischemic Stroke. Stroke. 2018 Jul;49(7):1762-1765. doi: 10.1161/STROKEAHA.118.021514. Epub 2018 May 23. PMID: 29844030. 50. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, Haeusler KG, Oldgren J, Reinecke H, Roldan-Schilling V, Rowell N, Sinnaeve P, Collins R, Camm AJ, Heidbüchel H; ESC Scientific Document Group. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J. 2018 Apr 21;39(16):1330-1393. doi: 10.1093/eurheartj/ehy136. PMID: 29562325. 24. Paciaroni M, Agnelli G, Micheli S, Caso V. Efficacy and safety of anticoagulant treatment in acute cardioembolic stroke: a meta-analysis of randomized controlled trials. Stroke. 2007 Feb;38(2):423-30. doi: 10.1161/01.STR.0000254600.92975.1f. Epub 2007 Jan 4. PMID: 17204681.

Pacientes anticoagulados "de base"

Evidencia muy limitada sobre mantenimiento/reinicio durante la FASE AGUDA[22-24]

NIHSS ≤ 5 = ictus leve: 24-72h

Déficit neurológico

- **Leve: 3 días**
- **Moderado: 6-8 días**
- **Severo: 12-14 días**

Área infartada extensa / riesgo de transformación hemorrágica / HTA no controlada
+ indicación para ACO

AAS
y switch a
(N)ACO en 1-2 semanas

Meta-análisis 2007 **HBPM / HepNa versus AAS/Placebo**

Recurrencia ictus isquémico similar
3 vs 4,9 % [OR] 0.68, 95% CI 0.44-1.06)

Déficit neurológico / mortalidad similar
74%

Mayor hemorragia intracraneal
2.5 vs 0,7% OR 2.89, 95% CI 1.19-7.01)

22. Groot AE, Vermeij JM, Westendorp WF, Nederkoorn PJ, van de Beek D, Coutinho JM. Continuation or Discontinuation of Anticoagulation in the Early Phase After Acute Ischemic Stroke. Stroke. 2018 Jul;49(7):1762-1765. doi: 10.1161/STROKEAHA.118.021514. Epub 2018 May 29. PMID: 29844030. 23. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, Haeusler KG, Oldgren J, Reinecke H, Roldan-Schilling V, Rowell N, Sinnaeve P, Collins R, Camm AJ, Heidbüchel H; ESC Scientific Document Group. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J. 2018 Apr 21;39(16):1330-1393. doi: 10.1093/eurheartj/ehy136. PMID: 29562325. 24. Paciaroni M, Agnelli G, Micheli S, Caso V. Efficacy and safety of anticoagulant treatment in acute cardioembolic stroke: a meta-analysis of randomized controlled trials. Stroke. 2007 Feb;38(2):423-30. doi: 10.1161/01.STR.0000254600.92975.1f. Epub 2007 Jan 4. PMID: 17204681.

AIT

Tratamiento antitrombótico precoz en AIT

AIT

¿Anticoagulación previa o nueva patología que la indique?

Si → Iniciar o continuar anticoagulación

No → ABCD^2 score

- < 4 → AAS
- ≥ 4 → DAPT 21 días

ABCD^2 score

Edad
PAs/PAd inicial
Clínica
Duración de síntomas
DM2

AAS 300 mg -> 100 mg/24h
Clopidogrel 300 mg -> 75 mg/24h
THALES trial[21] (Ticagrelor, ABCD^2 score 6-7**)**

Evaluación **URGENTE** para conocer el mecanismo isquémico

- Pruebas de imagen
- Cardiología
- Individualizar

Tratamiento antitrombótico precoz en AIT

AIT

Pacientes antiagregados “de base” con **AAS** / **Clopidogrel**

Prasugrel/Ticagrelor: individualizar en función de la patología por la cual se indicó dicho fármaco

switch

AAS 300 mg -> 100 mg/24h

Clopidogrel 300 mg -> 75 mg/24h

DAPT x 21 días

Pacientes **anticoagulados** “de base” o con indicación clara para ello (FA, TVP, válvulas mecánicas)

Anticoagulación

Anticoagulación insuficiente

HBPM - NACO

Anticoagulación correcta + AIT + Aterosclerosis/stent

NACO + antiagregación

Conclusiones - Reflexiones

PHARMACIST IMPACT ON ISCHEMIC STROKE CARE IN THE EMERGENCY DEPARTMENT

Rena A. Gosser, PHARMD, Richard F. Arndt, PHARMD, Kate Schaafsma, PHARMD, MBA, and Cathyyen H. Dang, PHARMD

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Reprint Address: Rena A. Gosser, PHARMD, Department of Pharmacy, University of Wisconsin Hospital and Clinics, 600 Highland Avenue, Madison, WI 53792

tered early to ischemic stroke patients (1,2). A shorter time to treatment is associated with greater benefit, especially if rtPA is initiated within 90 min of symptom onset. In a pooled analysis of six large rtPA studies, the

eligible ischemic stroke patients (4). Pharmacists are in a unique position to enhance Best Practice Strategies 7, 8, and 9, which include mixing rtPA ahead of time, rapid access to i.v. rtPA, and utilizing a team-based approach (4). Froedtert & The Medical College of Wisconsin, a

The proportion of patients in the pharmacist-present group who had a door-to-rtPA time <60 min was nearly two times that of the pharmacist-absent group, however,

Table 1. Target Stroke℠ Ten Best Practice Strategies (4).

Strategy	Best Practice
1	Advance hospital notification by EMS
2	Rapid triage protocol and stroke team notification
3	Single call activation system
4	Stroke tools
5	Rapid acquisition and interpretation of brain imaging
6	Rapid laboratory testing (including point of care testing if indicated)
7	Mix tPA medication ahead of time
8	Rapid access to i.v. tPA
9	Team-based approach
10	Prompt data feedback

EMS = Emergency Medical Services; tPA = tissue plasminogen activator.

There were a few instances in which less than ideal antihypertensive agents (e.g., metoprolol) were chosen to lower blood pressure, prolonging the door-to-rtPA time. This was found most often outside of pharmacist staffing hours of 10:00 AM to 6:30 PM in the pharmacist-absent group (Table 3). The AHA/ASA Early Management of Acute Ischemic Stroke guidelines recommend use of antihypertensive agents, such as i.v. labetalol, nicardipine, and hydralazine (1). The pharmacist-present group had more instances of nicardipine drip utilization after labetalol dose escalation failed to adequately lower blood pressure in a timely manner (Table 3). Pharmacist

Medication Errors in Acute Cardiovascular and Stroke Patients

A Scientific Statement From the American Heart Association

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spective evaluation based on chart review from 234 ischemic and hemorrhagic stroke cases revealed a 19% in-hospital incidence rate of medication errors.[72] Another

technicians, and pharmacists. Failure of communication and coordination appears to be an important source of medication error.[74,75] In addition, there are various factors

Table 4. Common Medications Errors in Patients With Ischemic Stroke

Medication	Type of Error	Reason for Use	Preventable Adverse Event	Guideline Recommendations[74,75]
IV tPA	Underuse; misuse (errors in dosing, patient selection, timing)	Acute stroke treatment	Increased risk of hemorrhagic complications	Administer at the dose of 0.9 mg/kg (maximum 90 mg) within 4.5 hours of onset in patients who qualify for treatment. Rigorous BP control for 24 hours (keep BP <180/105 mm Hg during and after infusion). Avoid anticoagulants and antiplatelet agents within the first 24 hours
Heparin	Overuse; misuse (errors in dosing, monitoring, prescribing, transcribing)	Prevention of early stroke recurrence and stroke progression	Increased risk of hemorrhagic complications	Not recommended, even for those with AF
Warfarin	Underuse; misuse (errors in dosing, monitoring, prescribing)	Primary and secondary stroke prevention in AF	Increased risk of thrombotic and hemorrhagic complications	Commence anticoagulation with adjusted-dose warfarin (target INR 2.0 to 3.0) in patients with ischemic stroke with persistent or paroxysmal AF
Antihypertensive medications	Misuse (excessive BP reduction in the setting of pressure-sensitive stroke)	High BP during the acute period	Possible infarct progression	Lower BP only if >220/120 mm Hg with a goal to reduce by ~15% during the first 24 hours of stroke, except for organ dysfunction that necessitates rapid reduction and fibrinolytic therapy
Combination antiplatelets (aspirin-clopidogrel combination)	Overuse (unproven indication)	Secondary stroke prevention	Increased risk of hemorrhagic complications	Not recommended unless there is a specific indication (stent procedure or ACS)
Corticosteroids	Misuse (unproven indication)	Brain edema	Increased risk of infection and other steroid-related complications	Not recommended
Mannitol	Misuse (errors in dosing, timing, and patient selection)	Brain edema	Acute renal failure, exacerbation of congestive heart failure, electrolyte imbalance	0.25 to 2 g/kg IV administered over 20 minutes unless there is frank congestive heart failure or renal failure
IV infusion of hypotonic solutions (NaCl 0.45%; glucose 5%)	Misuse (error in dosing)	Hydration, hypoglycemia	Brain edema	Not recommended
Gadolinium-based MR contrast agents	Overuse (error in patient selection)	Contrast MRI	Nephrogenic systemic fibrosis	Carefully weigh the benefits and risks in patients with acute renal failure or chronic kidney disease (GFR <30 mL · min^{-1} · 1.73 m^{-2}) or acute renal insufficiency of any severity due to hepatorenal syndrome or in the perioperative liver transplantation period. For patients receiving hemodialysis, consider prompt hemodialysis after administration of the MRI contrast

BP indicates blood pressure; AF, atrial fibrillation; MR, magnetic resonance; MRI, magnetic resonance imaging; and GFR, glomerular filtration rate.

¡Muchas gracias!