ACCIDENTE CEREBRO-VASCULAR

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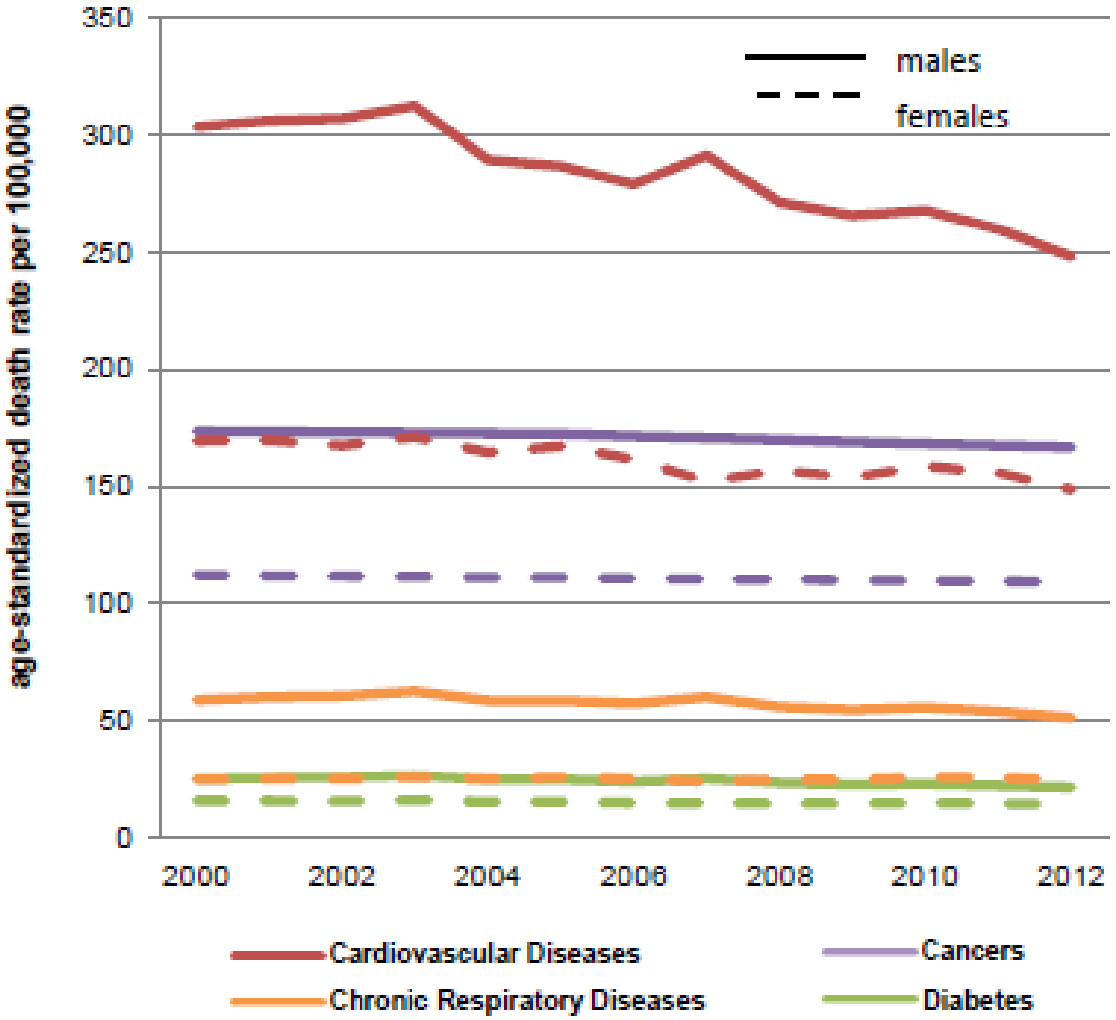
Argentina

World Health Organization - *Noncommunicable Diseases (NCD) Country Profiles*, 2014.

Total population: 41 087 000

Income Group: Upper middle

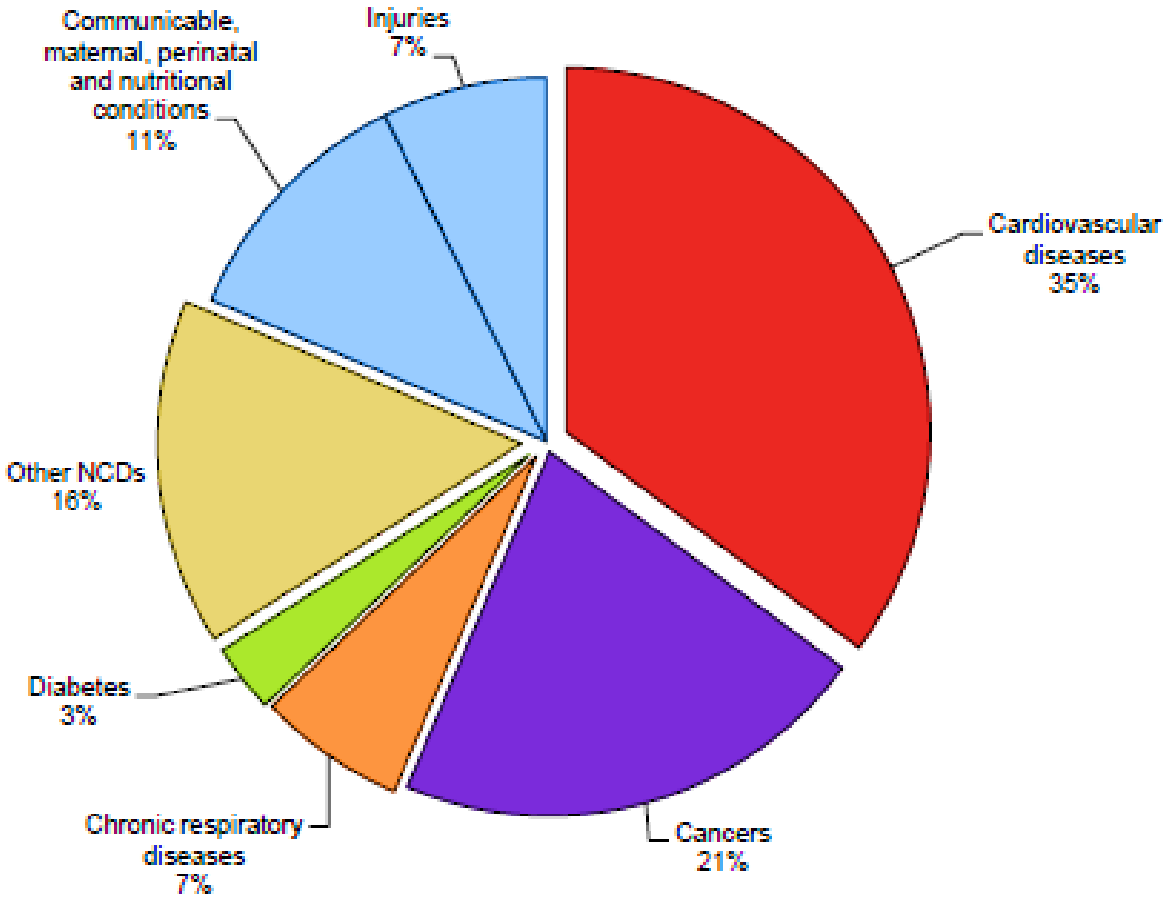
Age-standardized death rates*



World Health Organization - *Noncommunicable Diseases (NCD) Country Profiles*, 2014.

Argentina

Proportional mortality (% of total deaths, all ages, both sexes)*



Total deaths: 314,000
NCDs are estimated to account for 81% of total deaths.

Historia……

- Hippocrates (400 BC): Apoplexy. Injuria cerebral aguda, no traumática (Apoplexia: término Griego: “a striking away”).
- Imhotep, fundador de medicina egipcia, describió el término stroke en un papiro “Edwin Smith papyrus” (~ 3000 BC)
- 1689. *A Physico-Medical Essay Concerning the Late Frequencies of Apoplexies together with a general method of their prevention, and cure. Wiliam Cole*
- Stroke (cerebrovascular): ICD-9 en 1968
- Definición por la WHO: 1871 (1980)
- Nueva defincián propuesta por la AHA-ASA en 2013.

Definición de Ataque cerebral (OMS)

- Sindrome clínico
  - Rápida aparición de síntomas y/o signos focales (en ocasiones globales) de manifestaciones neurológicas que expresan pérdida de función cerebral
  - Manifestaciones neurológicas > 24 hs (o muerte)
  - Con aparente causa de origen vascular

OMS-1970

AIT (Ataque isquémico transitorio)

– *"Disfunción neurológica focal de origen vascular y transtoria de duración variable, comunmente de 2 a 15 minutos pero que ocasionalmente pueden extenderse a 24hs y que no deja déficit neurológico persistente"*

A classification and outline of cerebrovascular diseases, II. *Stroke*. 1975;6:564–616.

AHA/ASA Expert Consensus Document

An Updated Definition of Stroke for the 21st Century

Stroke. 2013;44:2064-2089.

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

Table 1. Definition of Stroke

The term "stroke" should be broadly used to include all of the following:

Definition of CNS infarction: CNS infarction is brain, spinal cord, or retinal cell death attributable to ischemia, based on

1. pathological, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or
2. clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥24 hours or until death, and other etiologies excluded. (Note: CNS infarction includes hemorrhagic infarctions, types I and II; see "Hemorrhagic Infarction.")

Definition of ischemic stroke: An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction. (Note: Evidence of CNS infarction is defined above.)

Definition of silent CNS infarction: Imaging or neuropathological evidence of CNS infarction, without a history of acute neurological dysfunction attributable to the lesion.

Table 1. Definition of Stroke

Stroke. 2013;44:2064-2089.

Definition of intracerebral hemorrhage: A focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma.
(Note: Intracerebral hemorrhage includes parenchymal hemorrhages after CNS infarction, types I and II—see "Hemorrhagic Infarction.")

Definition of stroke caused by intracerebral hemorrhage: Rapidly developing clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma.

Definition of silent cerebral hemorrhage: A focal collection of chronic blood products within the brain parenchyma, subarachnoid space, or ventricular system on neuroimaging or neuropathological examination that is not caused by trauma and without a history of acute neurological dysfunction attributable to the lesion.

Definition of subarachnoid hemorrhage: Bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord).

Definition of stroke caused by subarachnoid hemorrhage: Rapidly developing signs of neurological dysfunction and/or headache because of bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord), which is not caused by trauma.

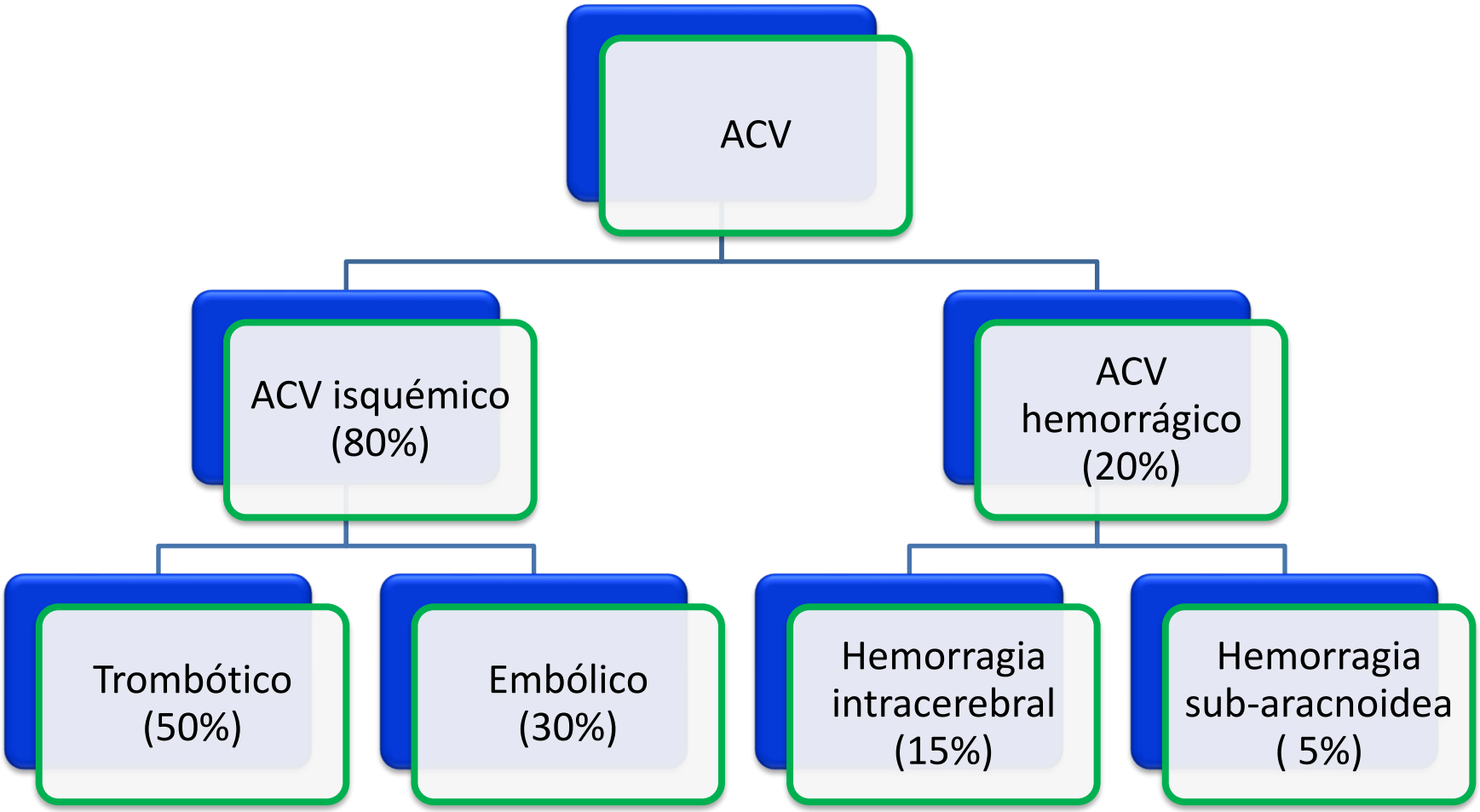
Definition of stroke caused by cerebral venous thrombosis: Infarction or hemorrhage in the brain, spinal cord, or retina because of thrombosis of a cerebral venous structure. Symptoms or signs caused by reversible edema without infarction or hemorrhage do not qualify as stroke.

Definition of stroke, not otherwise specified: An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥24 hours or until death, but without sufficient evidence to be classified as one of the above.

Type of stroke	Description
Ischaemic stroke	Neurological dysfunction due to infarction at cerebral, spinal or retinal sites
Silent CNS infarction	CNS infarction supported by imaging/neuropathological evidence without prior acute neurodysfunction
Intracerebral haemorrhage	Localised collection of blood in the brain parenchyma/ventricular system that is not induced by trauma
Stroke from intracerebral haemorrhage	Non-trauma-induced, rapid development of neurological symptoms of dysfunction due to localised collection of blood in the brain parenchyma/ventricular system
Silent cerebral haemorrhage	Long-term localised collection of blood in the brain parenchyma/subarachnoid space/ventricular system that is not induced by trauma, with no history of acute neurological dysfunction. Detected on neuroimaging and neuroexamination
Subarachnoid haemorrhage	Bleeding into the space between the arachnoid membrane and the pia mater of the brain or spinal cord
Stroke from subarachnoid haemorrhage	Changes to neurological function and incidence of headaches due to bleeding into subarachnoid space that are not induced by trauma
Stroke from cerebral venous thrombosis	Thrombosis in the cerebral venous structure that causes infarction or haemorrhage
Unspecified stroke	Acute neurological dysfunction due to ischaemia or haemorrhage lasting for more than 24 hours or until death, and lacking evidence allowing categorisation

CNS = central nervous system

Source: Adapted from Sacco et al (2013)


ACV
ACV isquémico (80%)
ACV hemorrágico (20%)
Trombótico (50%)
Embólico (30%)
Hemorragia intracerebral (15%)
Hemorragia sub-aracnoidea (5%)

Stroke. 2013;44:2064-2089.

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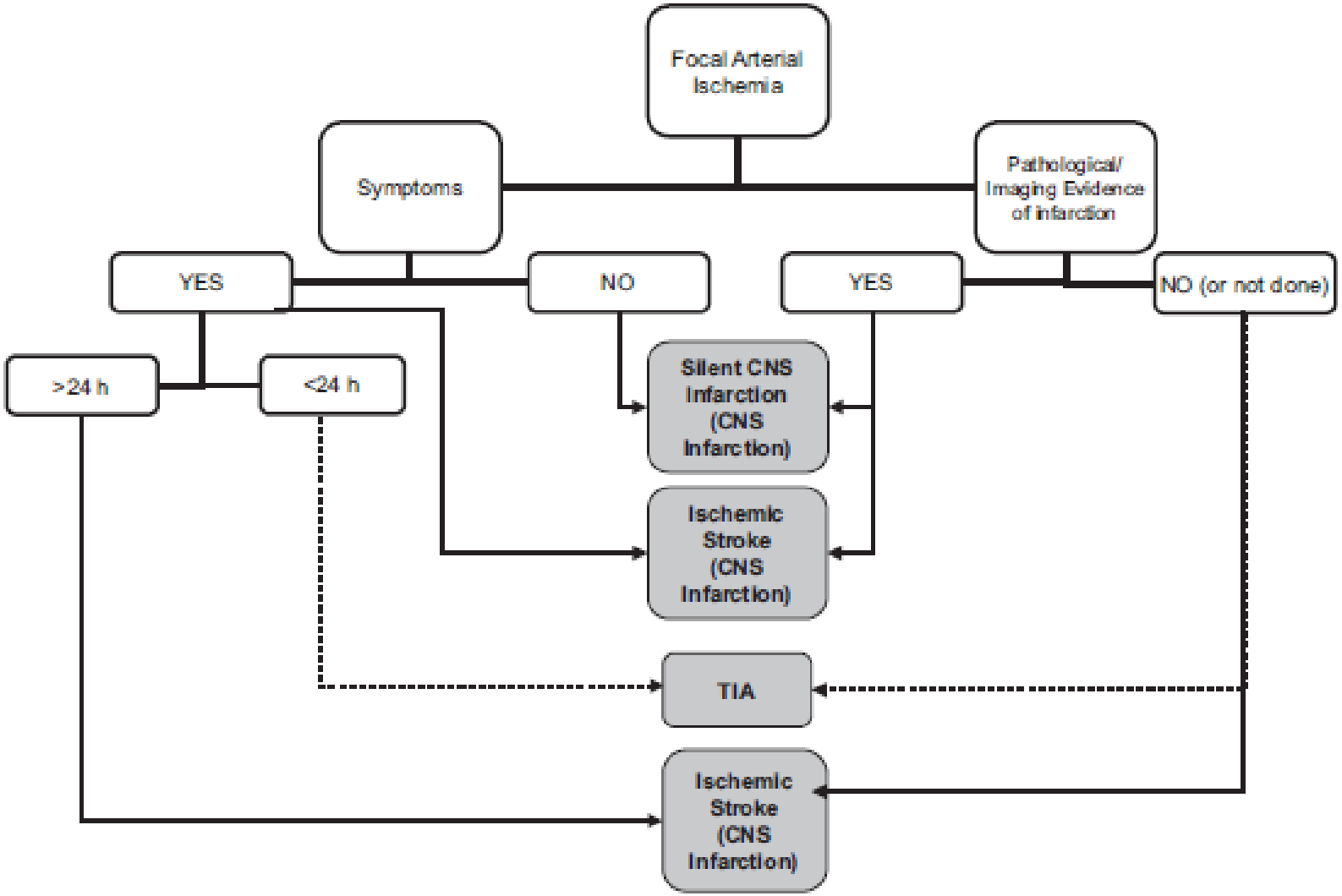

Ataque cerebral (Stroke-ACV)

¿Es una Emergencia Médica?

- Definitivamente SÍ
- (Al igual que un INFARTO de MIOCARDIO)

- ***Por qué es una Emergencia?***
  - Rápida aparición
  - Pobre pronóstico si no hay adecuada recuperación
  - Requerimiento de pronta intervención

Ataque cerebral: ***Pronóstico***

- Tasa de muerte luego de un primer ataque: (todo tipo de ACV):
  - 12% a 7días (por efecto del daño cerebral)
  - 19% a 30 días (por complicaciones médicas)
  - 30% a un año
  - RR muerte en pacientes que tuvieron ACV 2 veces vs población general
- 20% de los supervivientes a un primer ACV: dependencia para actividades de la vida diaria
- 1-16% riesgo de recurrencia dentro del primer año (luego 5% por año)

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Ataque cerebral:
motivos de la intervención médica urgente

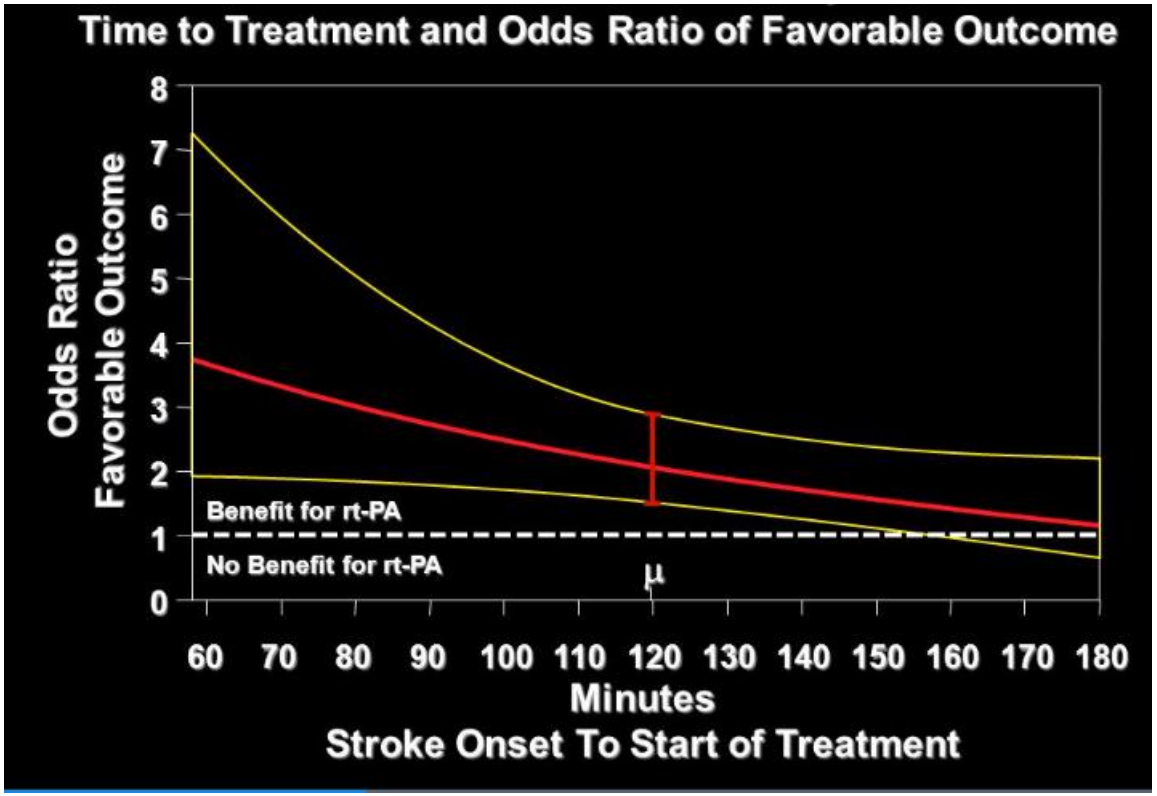
- Problemas médicos en etapa precoz:
  - Obstrucción de vía aérea superior
  - Riesgo de aspiración
  - Complicaciones tromboembólicas
  - Infecciones
  - Hipertensión endocraneana
  - Convulsiones

- Eficaz terapéutica aplicada en forma precoz
  - **"TIEMPO ES CEREBRO"**

“Tiempo es Cerebro”

Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h



Saver JL. *Stroke*. 2006
Lancet 2004

Enfoque ante el paciente:
I.¿Es un evento vascular?

- Historia Clínica: crucial (paciente/ familiar)
  - Edad
  - Inicio de los síntomas
  - Factores de riesgo para ACV

- Manifestaciones neurológicas:
  - Focales o no focales?
  - Síntomas "negativos" >> síntomas "positivos"
  - Aparición súbita?
  - Los síntomas focales alcanzaron su máxima intensidad al inicio (en minutos u horas) o de evolución progresiva (horas a días)

Enfoque ante el paciente:

1.¿Es un evento vascular?

2. Puede ser un "Stroke MIMIC"?

"Stroke mimic" se define como una enfermedad o condición que se presenta con un cuadro clínico semejante al stroke pero no tiene infarto del tejido nervioso.
Son ejemplos de stroke mimic: estados posconvulsivos, síncope, tumores cerebrales, sepsis, hipoglucemia, demencia, intoxicaciones, amnesia global transitoria, crisis de migraña, estado confusional agudo.

- **Enfoque ante el paciente:**
- 3. Si es vascular ¿dónde está localizada la lesión y que vasos son los comprometidos?
- 4. ¿Cuál es el mecanismo de la enfermedad: isquemia o hemorragia?

“Tiempo es Cerebro”

Conducta inicial del paciente con un ataque cerebral en un centro de atención primaria

Escala FAST

Escala FAST

- **Asimetría facial: 1 punto**
- **Parálisis del brazo / pierna: 1 punto**
- **Trastornos del habla: 1 punto**

Total 0 a 3

- **ACV sospechado si el puntaje >0**
- **Sensibilidad para el diagnóstico de ACV 82%**
- **Especificidad para el diagnóstico de ACV 37%**

Propiedades clinométricas de las herramientas que ayudan al reconocimiento y diagnóstico del ACV

ROSIER (Reconocimiento del Stroke en la Sala de Emergencias)

Lancet Neurology 2005

ESCALA ROSIER

¿Ha habido Pérdida conciencia ó sincope?	Si (-1)		No (0)	
¿Ha habido actividad convulsiva?	Si (-1)		No (0)	
¿Ha habido algún nuevo inicio agudo (ó al despertar)				
Debilidad facial asimétrica	Si (+1)		No (0)	
Debilidad asimétrica de brazo	Si (+1)		No (0)	
Debilidad asimétrica de pierna	Si (+1)		No (0)	
Trastorno del habla	Si (+1)		No (0)	
Defecto campo visual	Si (+1)		No (0)	
		Puntaje total	-2 a +5	

- **. Total -2 a +5**
- Posible ACV si el puntaje es >0 en ausencia de hipoglucemia

Escala NIH (National Institutes of Health USA)

Variable	Definición	Puntos		Variable	Definición	Puntos
1A. Nivel de Conciencia	0 = Alerta 1 = Somnolencia 2 = Estupor 3 = Coma			7. Motor MI-Der.	0 = Normal 1 = Desviación del miembro 2 = Algún esfuerzo vs gravedad 3 = Sin esfuerzo vs gravedad 4 = Sin movimiento	
1B. Nivel de Conciencia (preguntas)	0 = Ambas Correctas 1 = Una Correcta 2 = Ambas Incorrectas (se pregunta el mes actual y la edad del paciente)			8. Motor MI-Izq.	Igual al anterior (Prueba con pierna extendida a 30° durante 5 segundos)	
1C. Nivel de Conciencia (órdenes)	0 = Responde ambas 1 = Responde una 2 = No responde (Ordenes: abrir y cerrar los ojos y empuñar la mano no pretética)			9. Ataxia	0 = Ausente 1 = Presente en una extremidad 2 = Presente en 2 o más extremidades	
2. Mirada Conjugada	0 = Normal 1 = Parálisis parcial 2 = Desviación forzada			10. Sensibilidad	0 = Normal 1 = Pérdida parcial, leve 2 = Pérdida densa	
3. Campos Visuales	0 = Normal 1 = Hemianopsia parcial 2 = Hemianopsia completa 3 = Hemianopsia bilateral			11. Lenguaje	0 = Normal 1 = Afasia leve a moderada 2 = Afasia severa 3 = Mutismo	
4. Paresia Facial	0 = Normal 1 = Asimetría menor 2 = Paresia parcial (central) 3 = Parálisis completa			12. Disartria	0 = Articulación Normal 1 = Disartria leve a moderada 2 = Ininteligible	
5. Motor MS-Der.	0 = Normal 1 = Desviación del miembro 2 = Algún esfuerzo vs gravedad 3 = Sin esfuerzo vs gravedad 4 = Sin movimiento			13. Extinción (Inatención) Negligencia	0 = Ausente 1 = Parcial 2 = Completa	
6. Motor MS-Izq.	Igual al anterior (Prueba con brazos extendidos a 90° durante 10 segundos)			PUNTUACION TOTAL		

Escala NIH

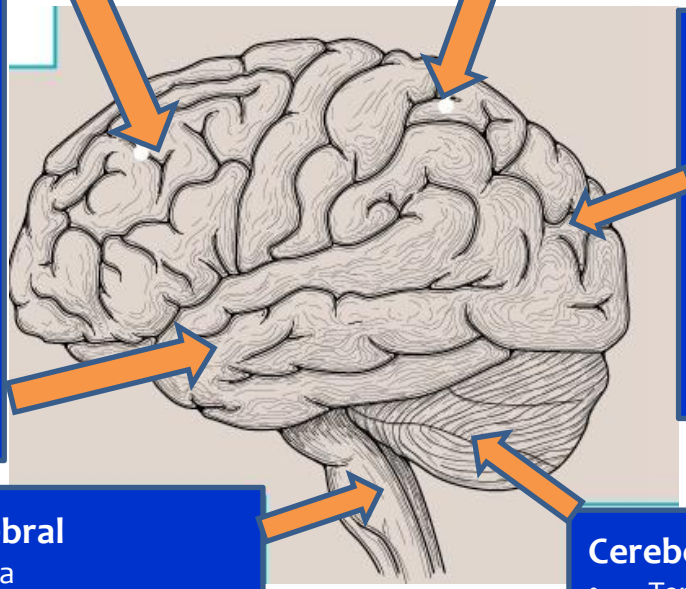
Puntaje: 0-42 puntos

- NIH < 5: ACV leve
- NIH 5-10: ACV leve-moderado
- NIH 11-20: ACV moderado-grave
- NIH > 20: ACV muy grave

Lóbulo frontal
- Paresia
- Trastornos conductuales
- Afasia de Broca

Lóbulo Parietal
- Anomia / agrafia /
- alexia /discalculi a/ apraxia
- Dificultad den dibujar objetos
- Incapacidad de focalizar atención visual
- Dificultad en distinguir
- derecha vs izquierda

Lóbulo temporal
- Afasia de Wernicke
- Alteración atención selectiva
- Prosopagnosia
- Dificultad en identificar y nominar objetos
- Conducta agresiva y hablar persistente
- Hipersexualidad
- Dificultad en categorizar objetos



Lóbulo Occipital
- Defecto campo visual
- Agnosia color y movimiento
- Dificultad en lecto/escritura
- Alucinaciones
- Dificultad en reconocer objetos dibujados
- Dificultad en reconocer palabras

Tallo cerebral
- Disfagia
- Vértigo
- Insomnio
- Sleep apnea
- Dificultad en organizar o comprender el medio ambiente

Cerebelo
- Temblor
- Vértigo
- Alteración coordinación mov finos y para caminar
- Incapacidad para reach out and grab objetos

Clasificación más específica

Oxfordshire Community Stroke Project

Sindrome total de la circulación anterior (Cerebral media; cerebral anterior)

- Disfunción cerebral: disfasia, discalculia, desorden visoespacial
- Defecto campo visual homónimo
- Déficit motor y/o sensitivo ipsilateral con al menos dos de tres: brazo, cara, MI

Sindromes parciales de la circulación anterior:

- Dos de los tres de los anteriores

Sindrome lacunar: ACV subcortical

- Motor puro
- Sensitivo puro
- Sensitivo-motor
- Hemiparesia-atáxica

Sindrome de la circulación posterior

- Parálisis craneal ipsilateral con déficti motor o sensitivo contralateral
- Desorden del movimiento conjugado de los ojos
- Disfunción cerebelar
- Defecto campo visual homónimo

JAMA®

Online article and related content current as of June 22, 2010.

Does This Patient Have a Hemorrhagic Stroke?: Clinical Findings Distinguishing Hemorrhagic Stroke From Ischemic Stroke

Shauna Runchey; Steven McGee

JAMA. 2010;303(22):2280-2286 (doi:10.1001/jama.2010.754)

- **19 estudios prospectivos= 6438 pacientes con 24% de ACV hemorrágicos**

- **Mayor probablilidad de HEMORRAGIA:**
  - coma (likelihood ratio [LR], 6.2; 95% [CI], 3.2-12)
  - Rigidez de nuca (LR, 5.0; 95% CI, 1.9-12.8)
  - Convulsiones (LR, 4.7; 95% CI, 1.6-14)
  - PAD > 110 mmHg (LR, 4.3; 95% CI, 1.4-14)
  - Vómitos (LR, 3.0; 95% CI, 1.7-5.5)
  - Cefalea (LR, 2.9; 95% CI, 1.7-4.8).

- **Menor probabilidad de HEMORRAGIA**
  - Soplo carotídeo (LR, 0.12; 95% CI, 0.03-0.47)
  - Ataque de isquemia cerebral transitoria previo (0.34; 95% CI, 0.18-0.65).

Imágenes en Stroke

- ¿El ACV es isquémico o hemorrágico?
- ¿Cuál es el tamaño y la localización?
- ¿Cuál es la causa del stroke?
- ¿Es el paciente candidato para Trombolisis?

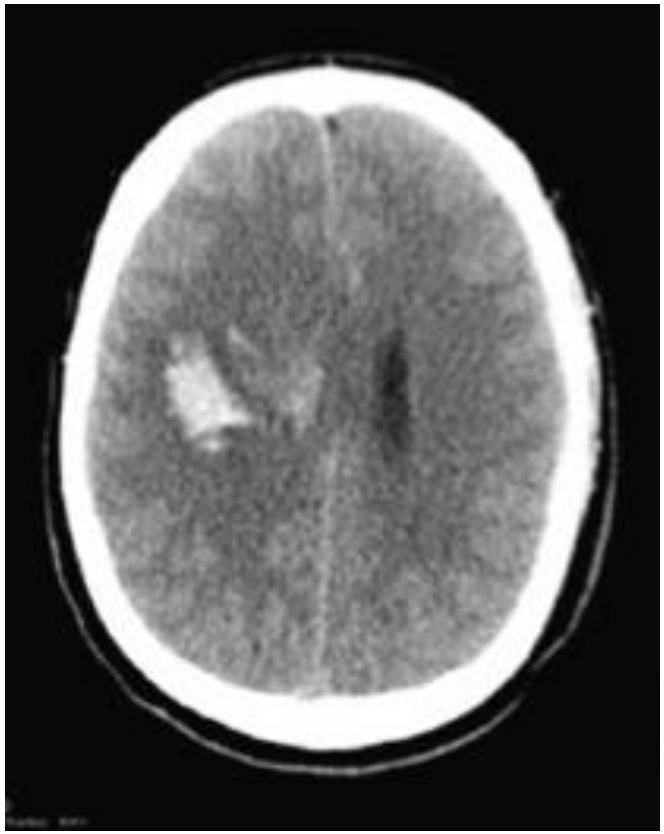
- El objetivo de las imágenes en el stroke agudo es evaluar las 4 P's:
  - Parenchyma
  - Pipes (vasos)
  - Perfusion
  - Penumbra

Table 1 Technique selection for the evaluation of acute stroke with CT and MR imaging

Area to be evaluated	CT	MR imaging
Parenchyma	Unenhanced CT	Conventional MR imaging and diffusion-weighted imaging
Blood vessels (pipes)	CT angiography	MR angiography
Perfusion	CT perfusion imaging	Perfusion-weighted imaging
Penumbra	Mismatch between cerebral blood flow and blood volume	Mismatch between diffusion-weighted and perfusion-weighted imaging findings

TAC sin contraste: ACV hemorrágico

- Sensibilidad: 90% / Especificidad: 99%



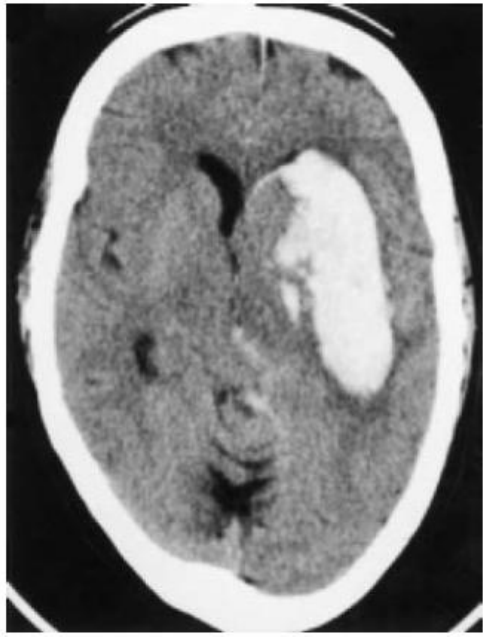
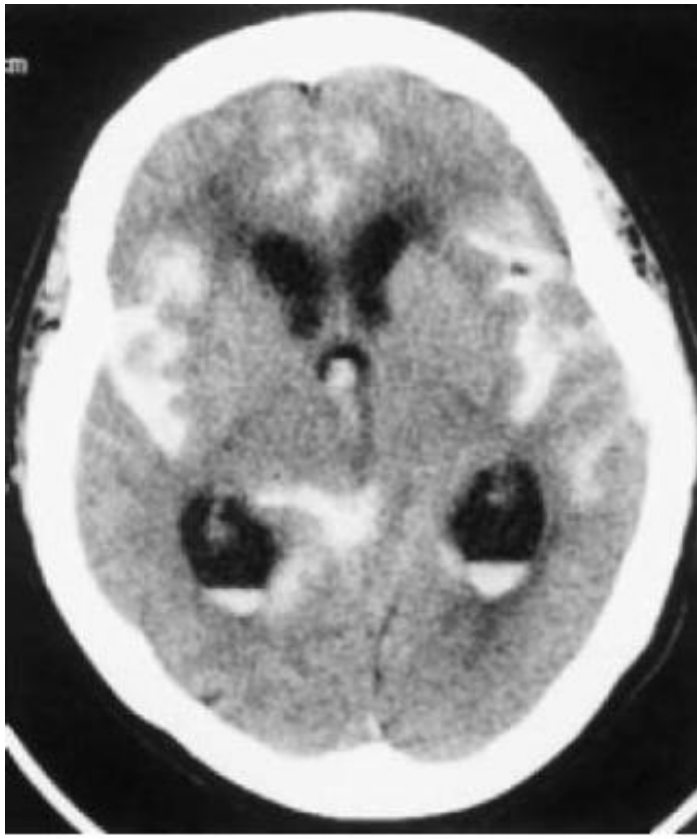
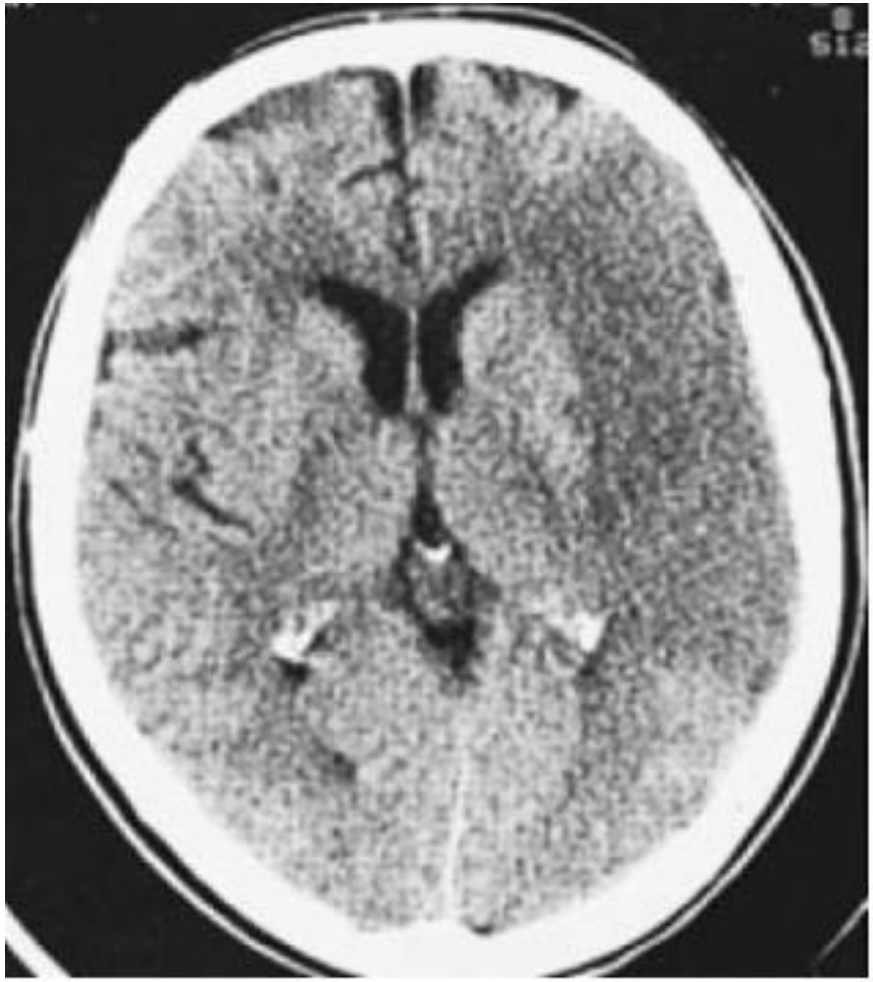


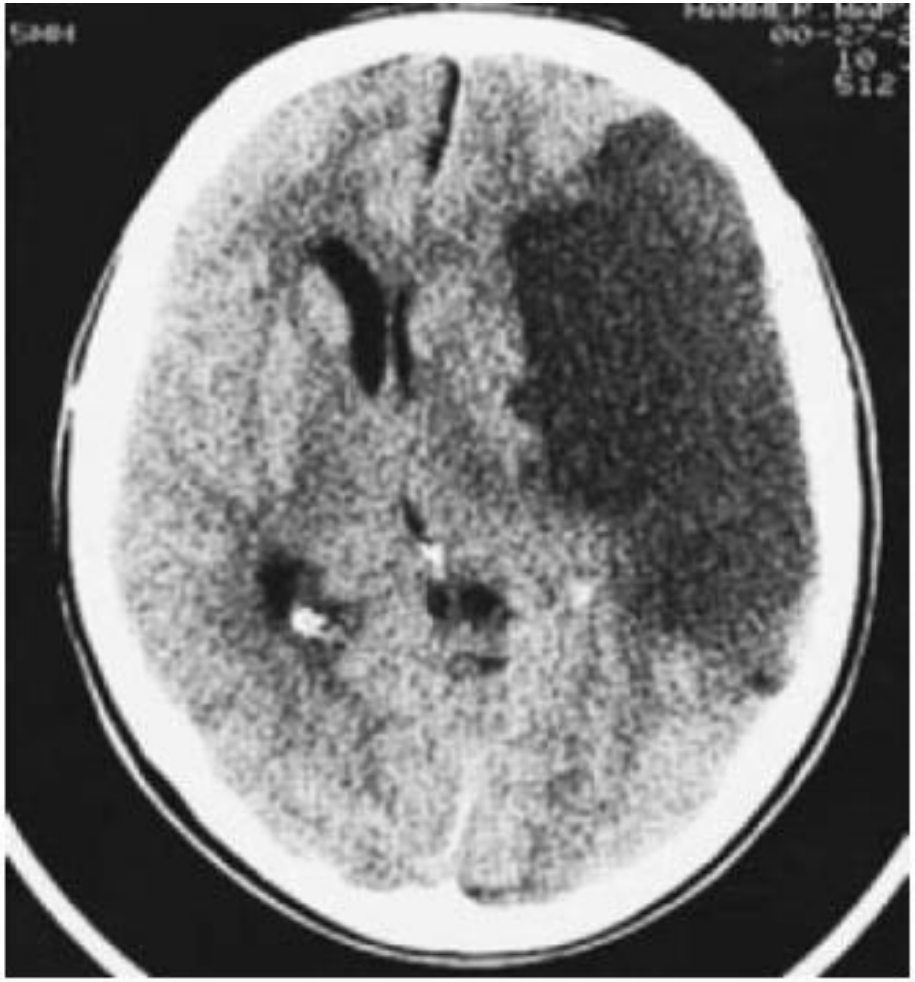
Figure 34-20. An unenhanced CT scan showing the typical picture of a massive primary (hypertensive) hemorrhage in the basal ganglia. The third ventricle and ipsilateral lateral ventricle are compressed and displaced by the expanding mass (12 h after onset of stroke).



Kidwell CS, et al. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. JAMA 2004;292:1823–1830

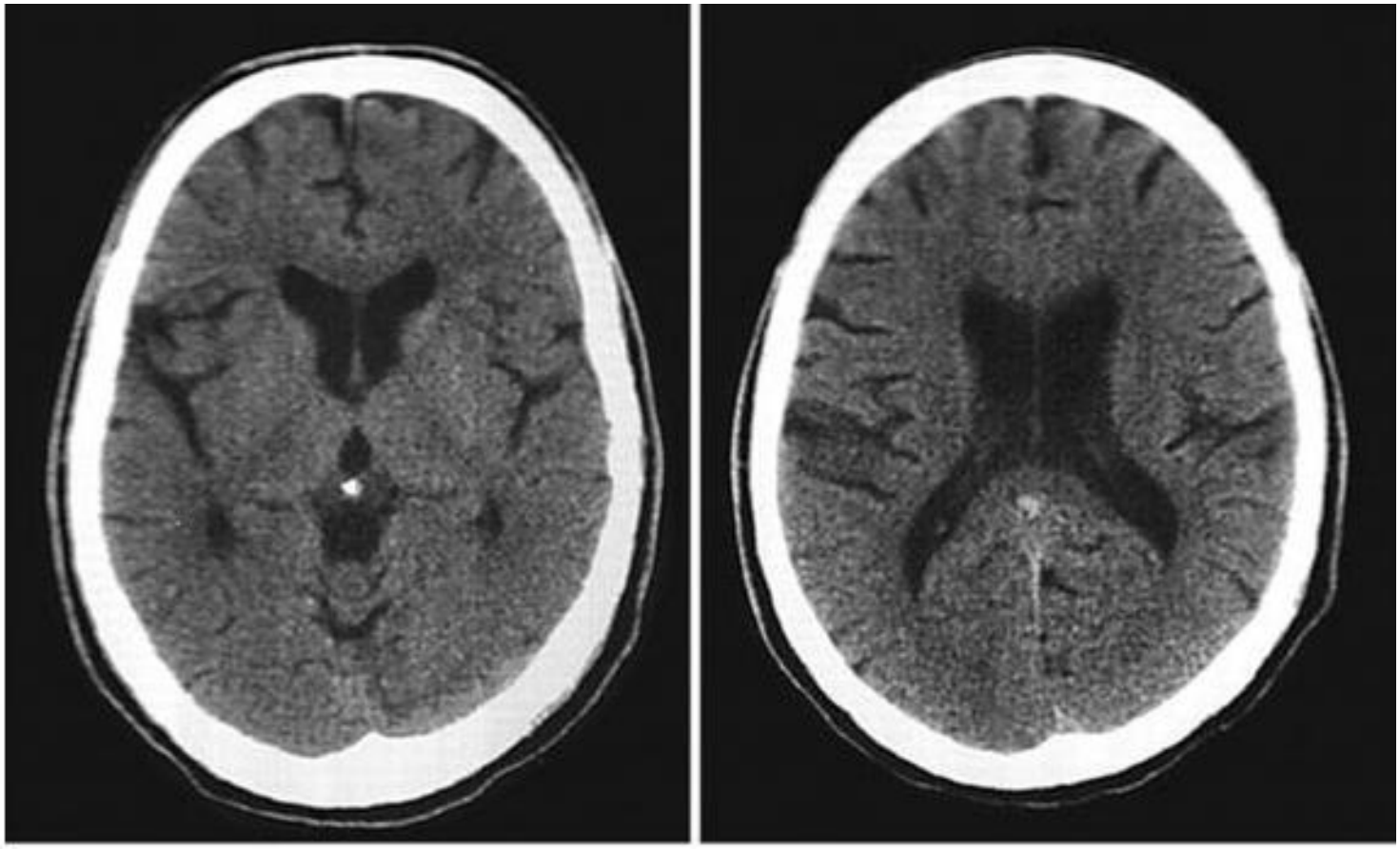
TAC sin contraste: ACV Isquémico



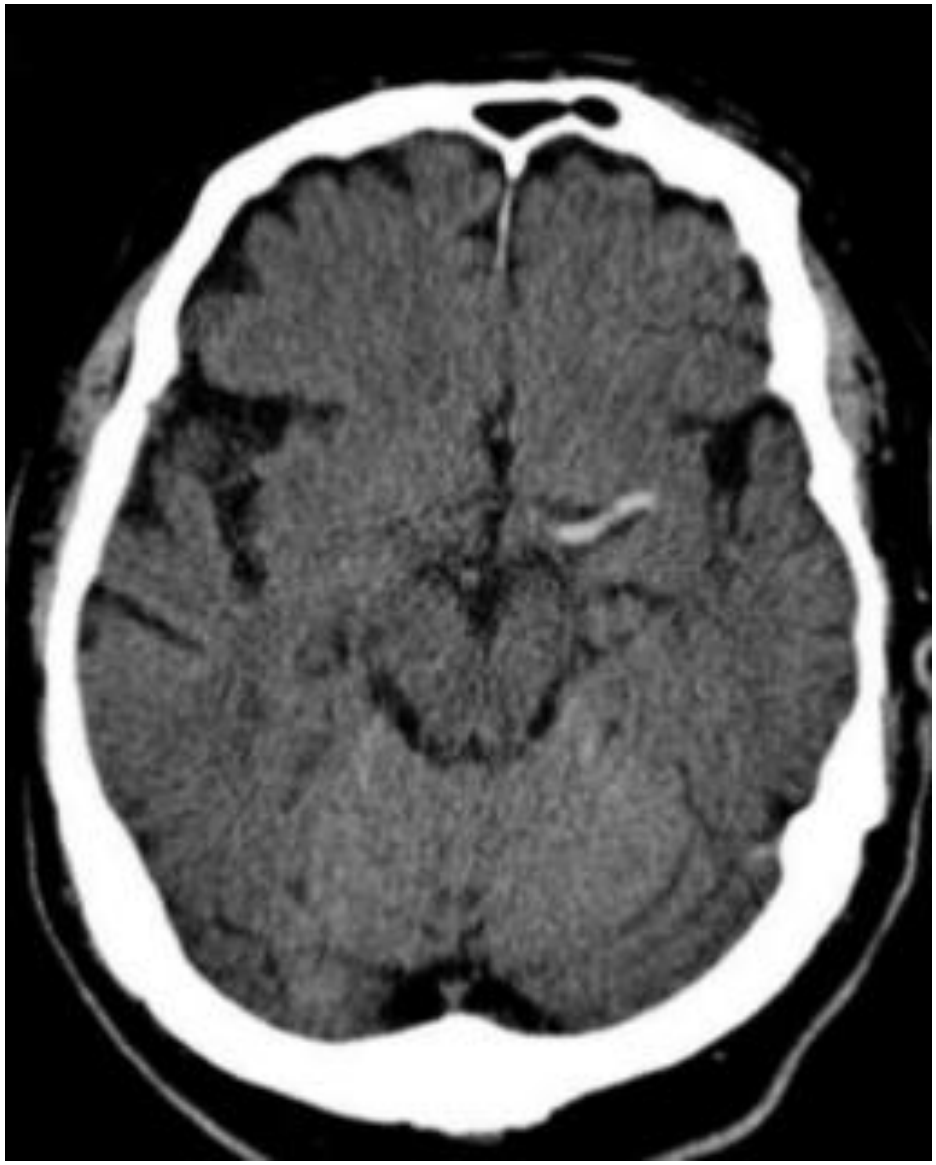


TAC sin contraste: ACV Isquémico

- Especificidad: 56% - 100%
- Sensibilidad: 20-75%
  (ventana de 6 a 8 hs)

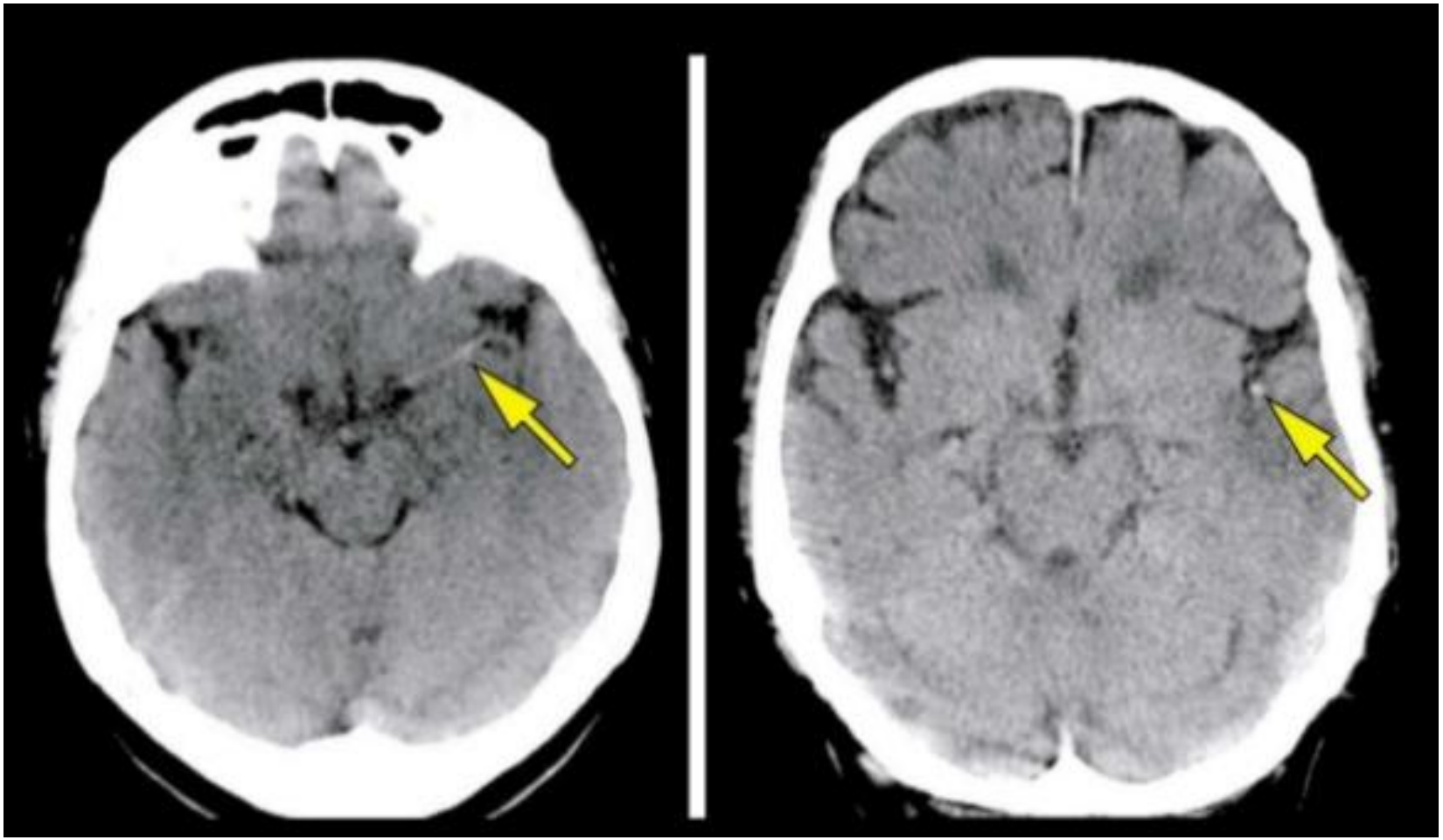


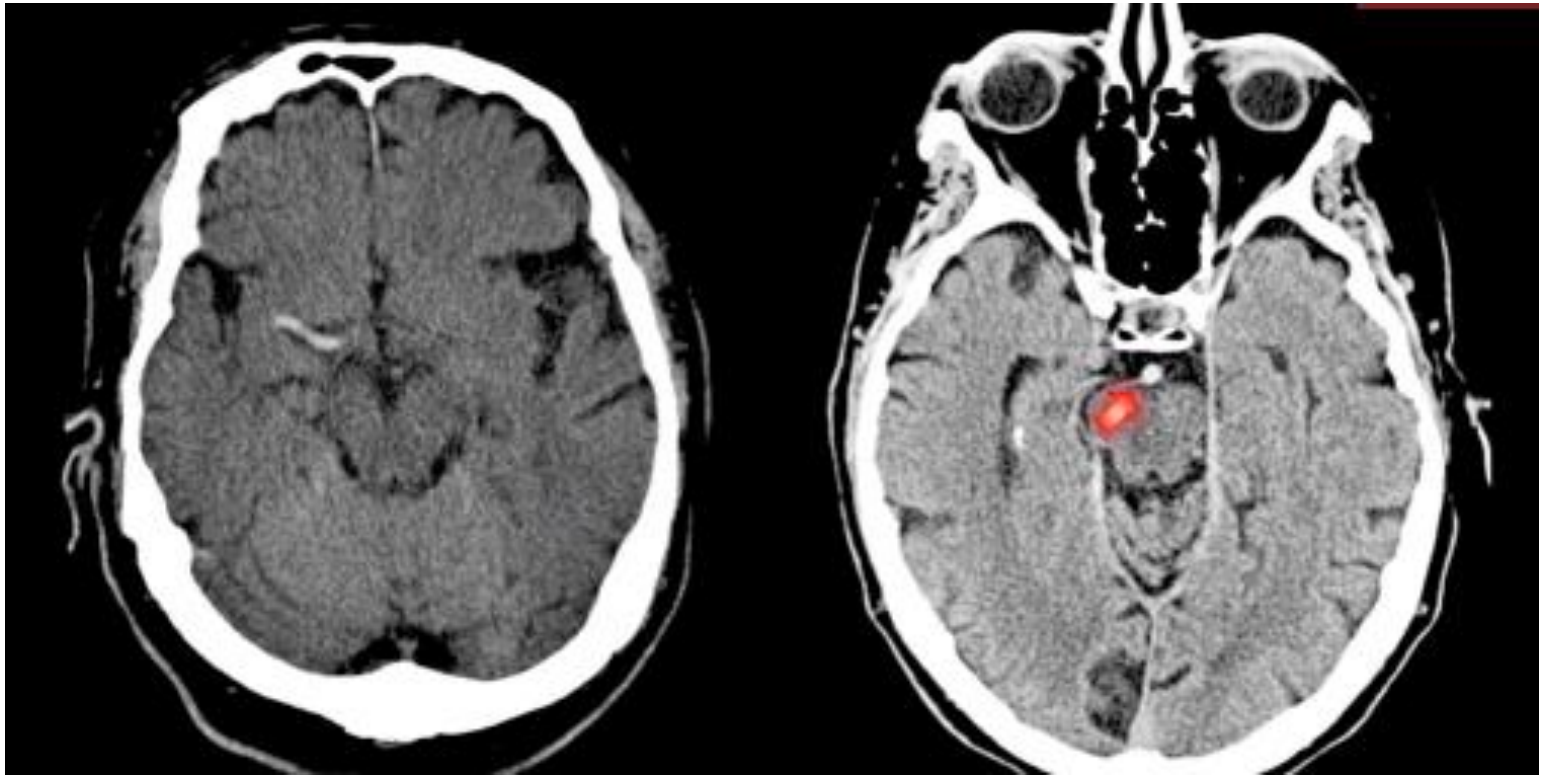
ACV isquémico
Signos precoces en TAC

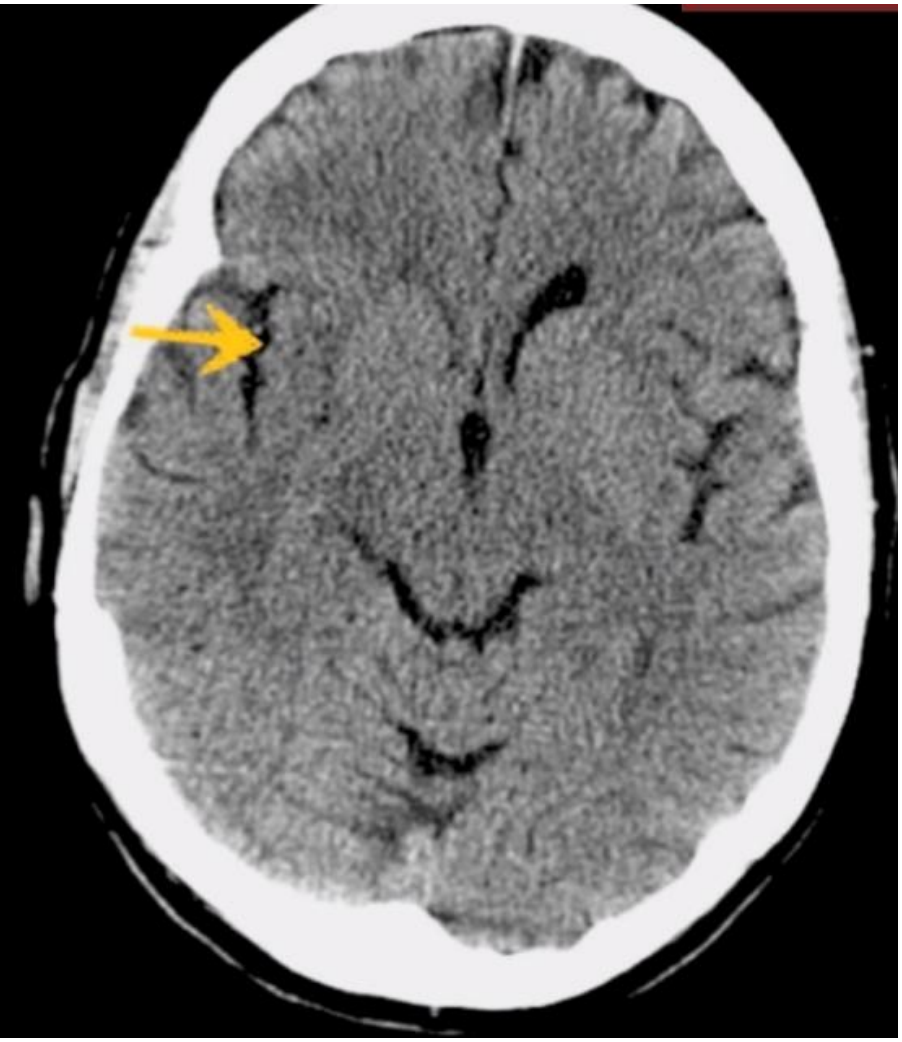


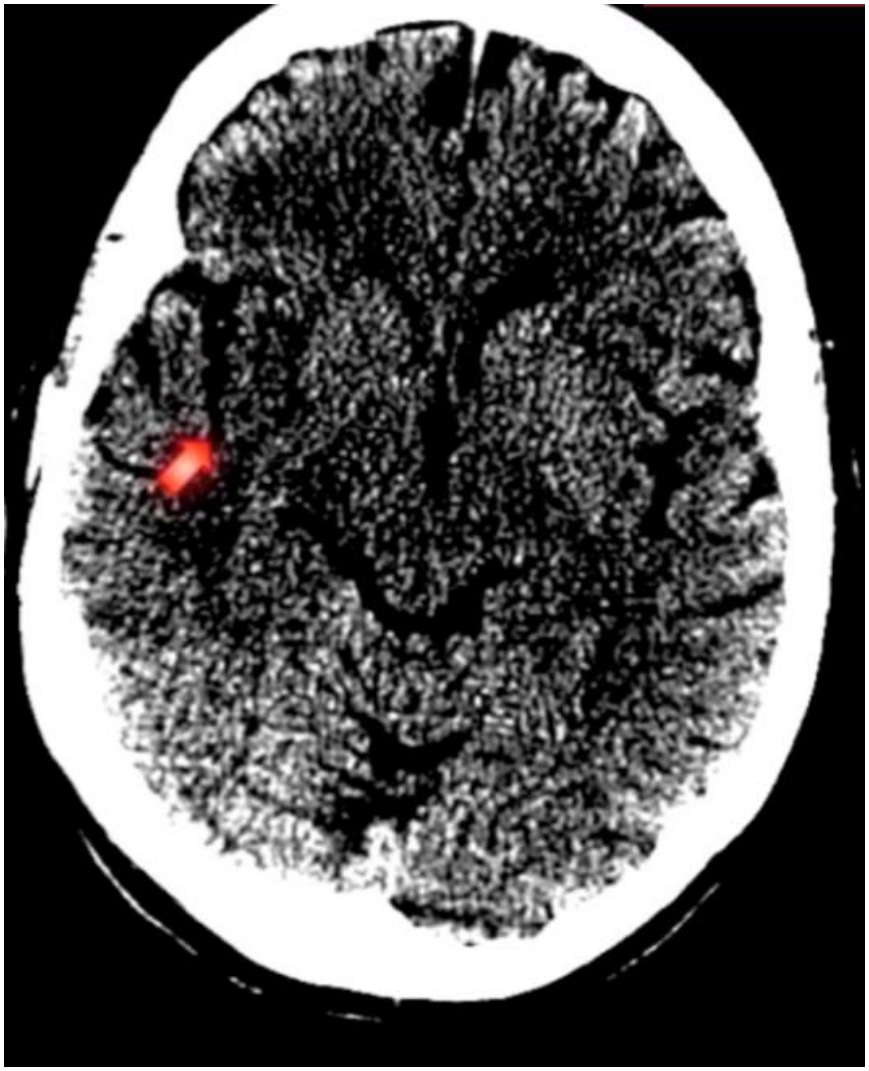
Sensibilidad: 17-50%

Especificidad:~ 100%





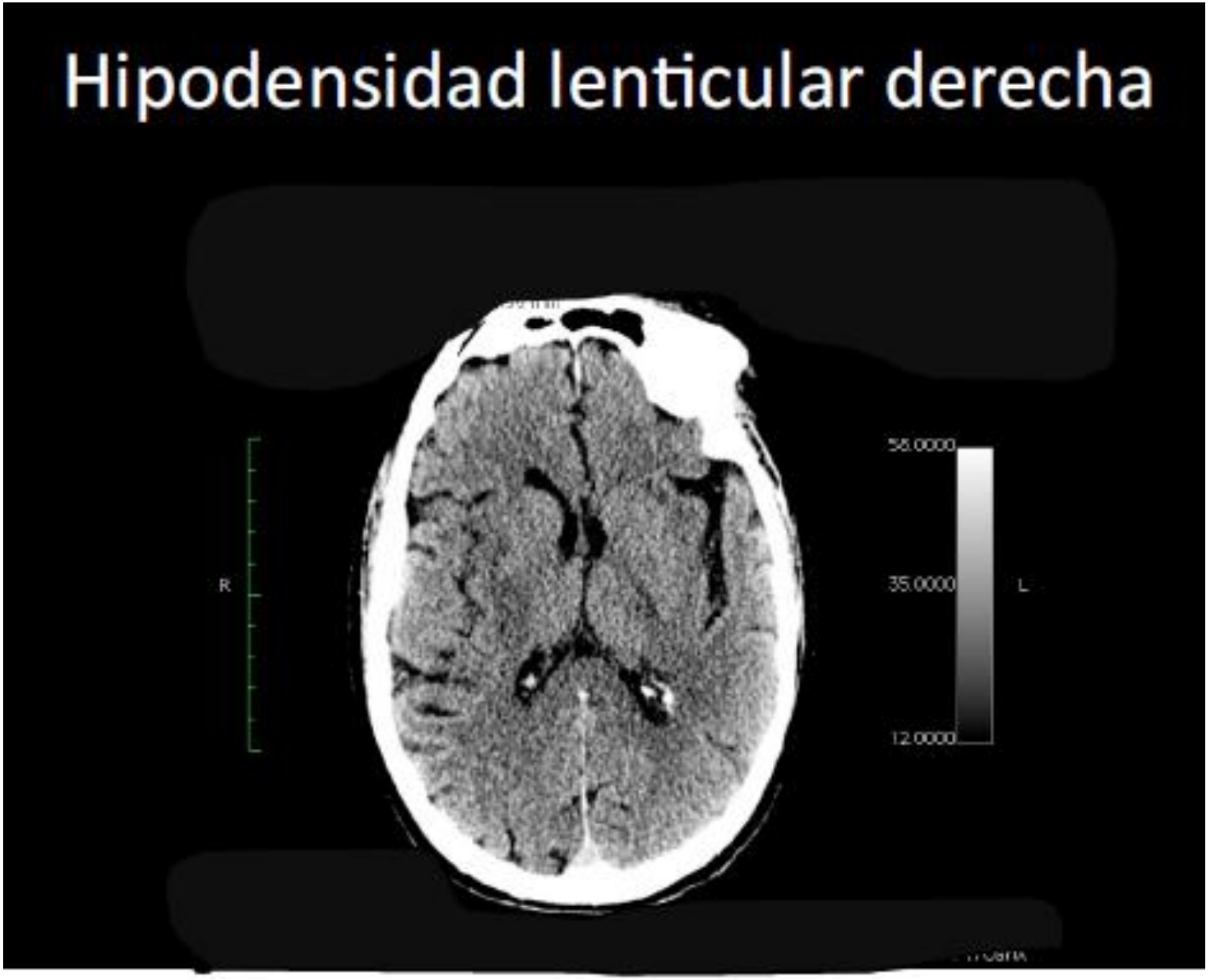




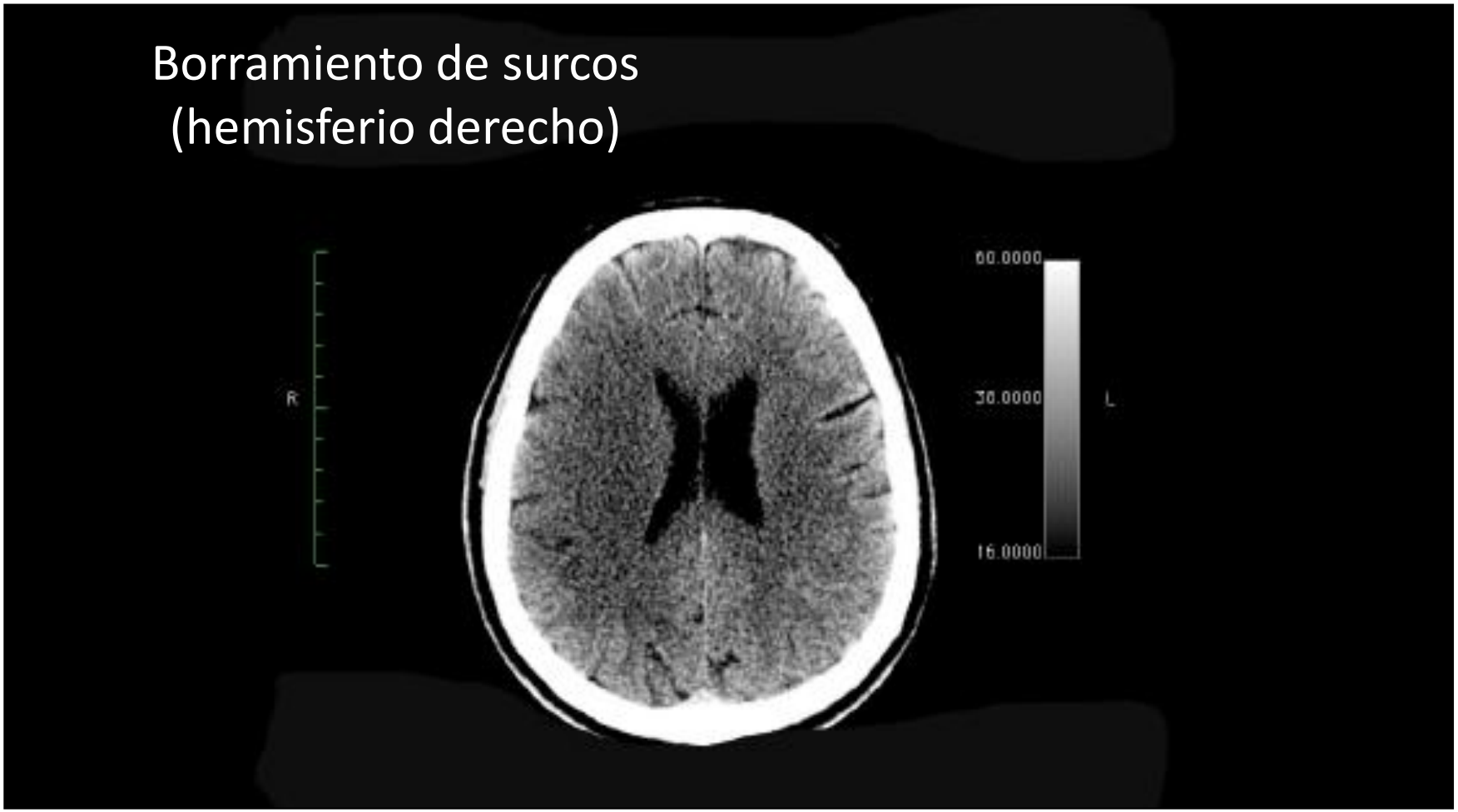
Signos Tomográficos Tempranos en Isquemia Cerebral Aguda

1. Signo arteria cerebral media hiperdensa
2. Hipodensidad nucleo lenticular
3. Borramiento insular
4. Borramiento de surcos de convexidad
5. Perdida interfase sustancia gris / blanca

Hipodensidad lenticular derecha



Borramiento de surcos
(hemisferio derecho)

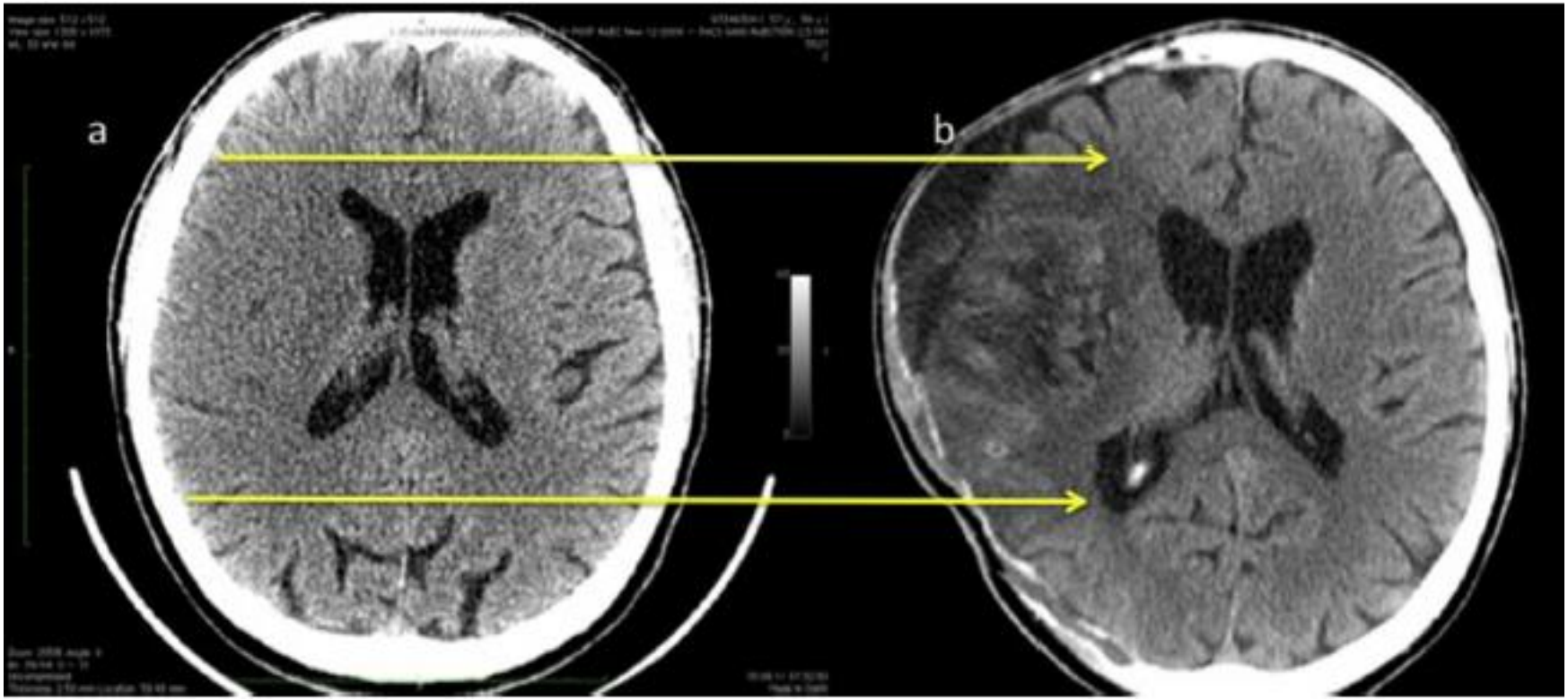


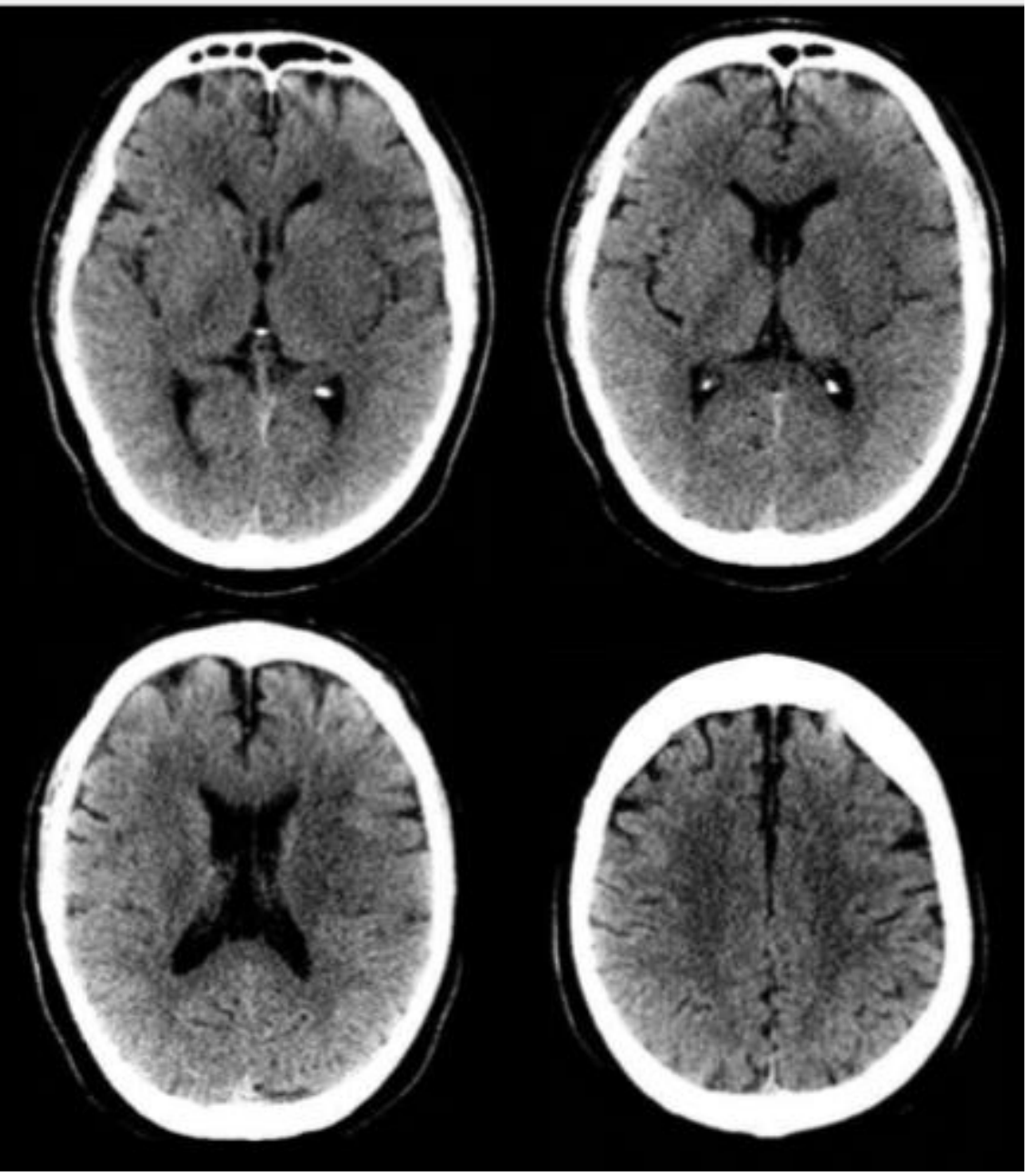
TAC en el ACV isquémico

- Hipodensidad: 3-6hs de la aparición del ACV isquémico
  - 44% presente en TAC (≤ 5hs)
  - 71% (< 6hs) (scan con mejor calidad de imagen + imágenes con mayor contraste)

(Horowitz SH, et al. Computed tomographic–angiographic findings within the first five hours of cerebral infarction. Stroke 1991;22:1245–1253)

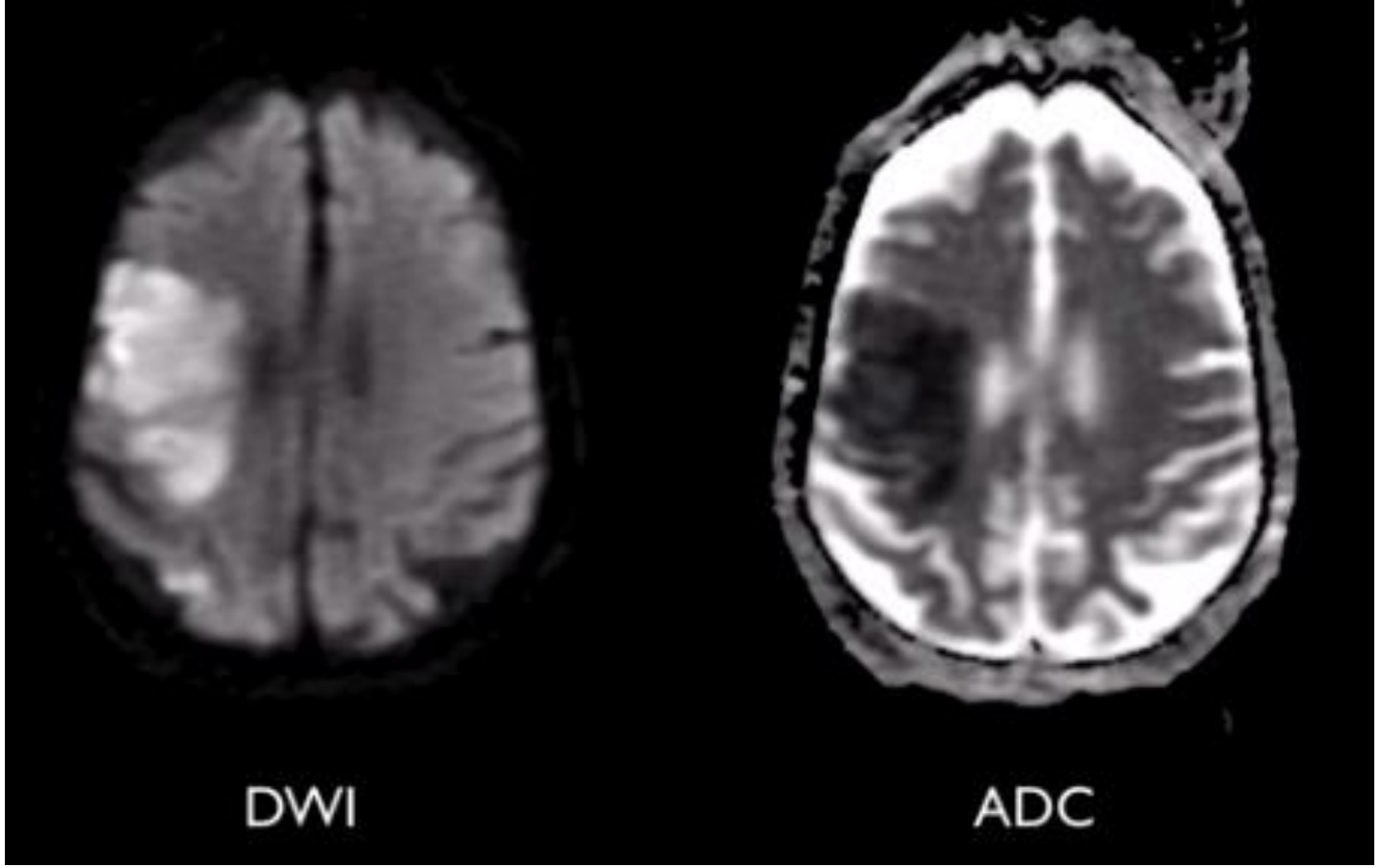
(Lev MH, et al. Acute stroke: improved nonenhanced CT detection—benefits of soft-copy interpretation by using variable window width and center level settings. Radiology 1999;213:150–155)


a
b



ASPECTS = 6

(I, L, C, M2)

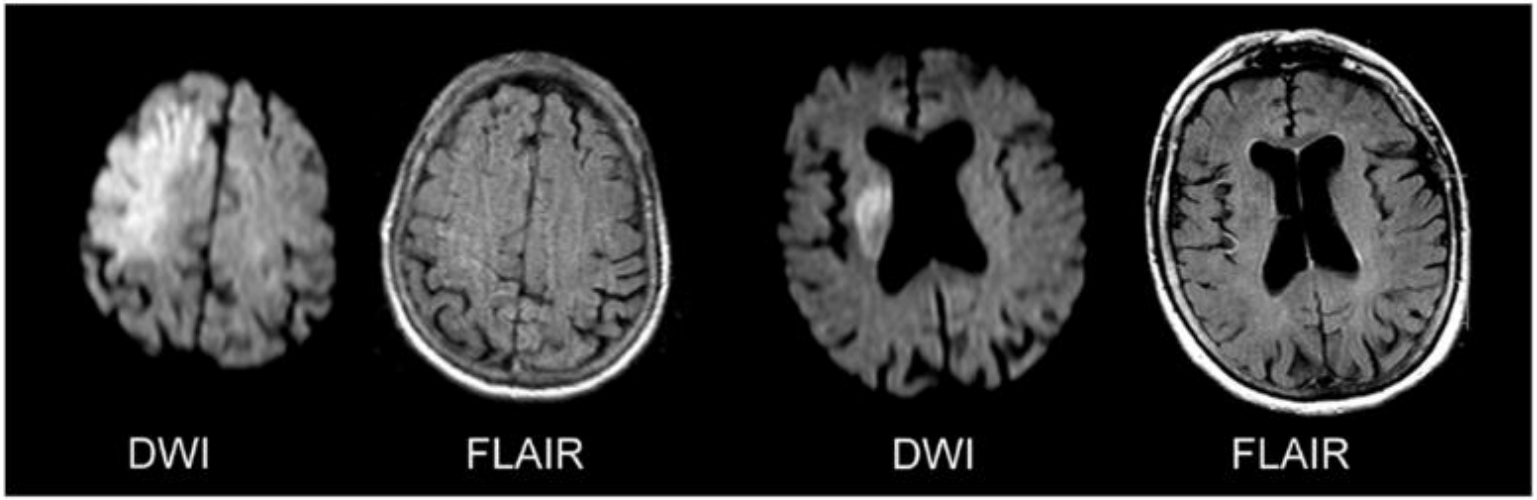


< 3 hs del ACV isquémico
86% Difusión (+)
14% Flair (+)

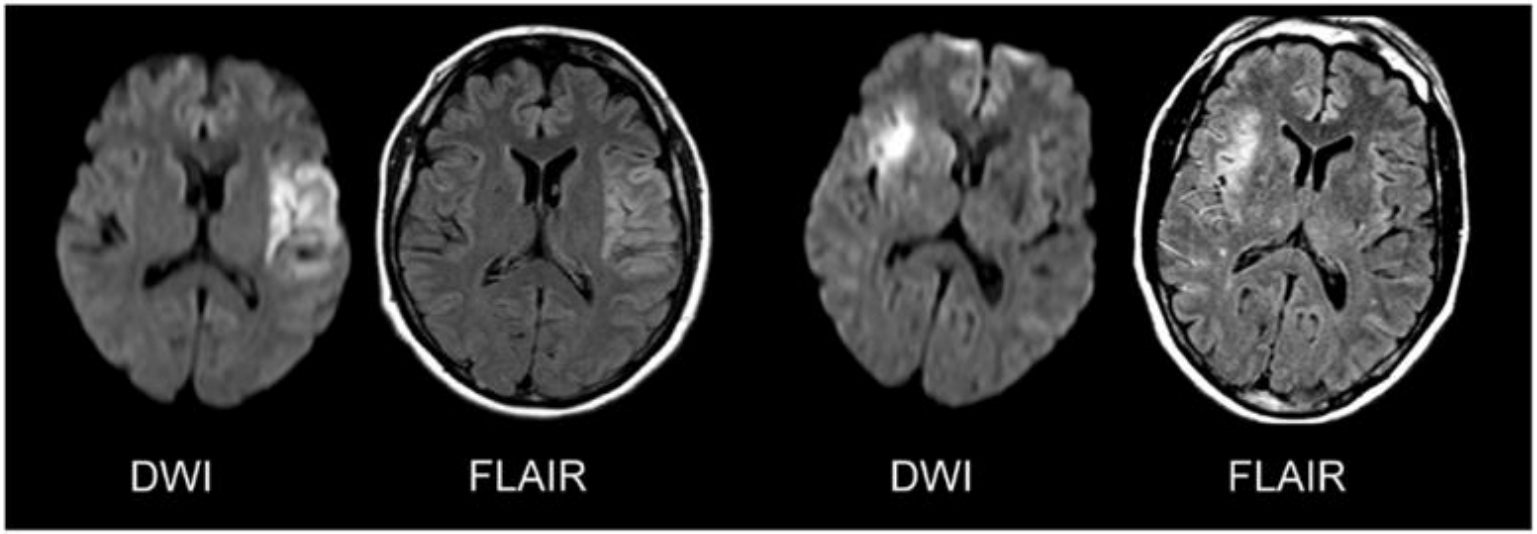
6-24 hs del ACV isquémico
99% Difussión (+)
88% Flair (+)

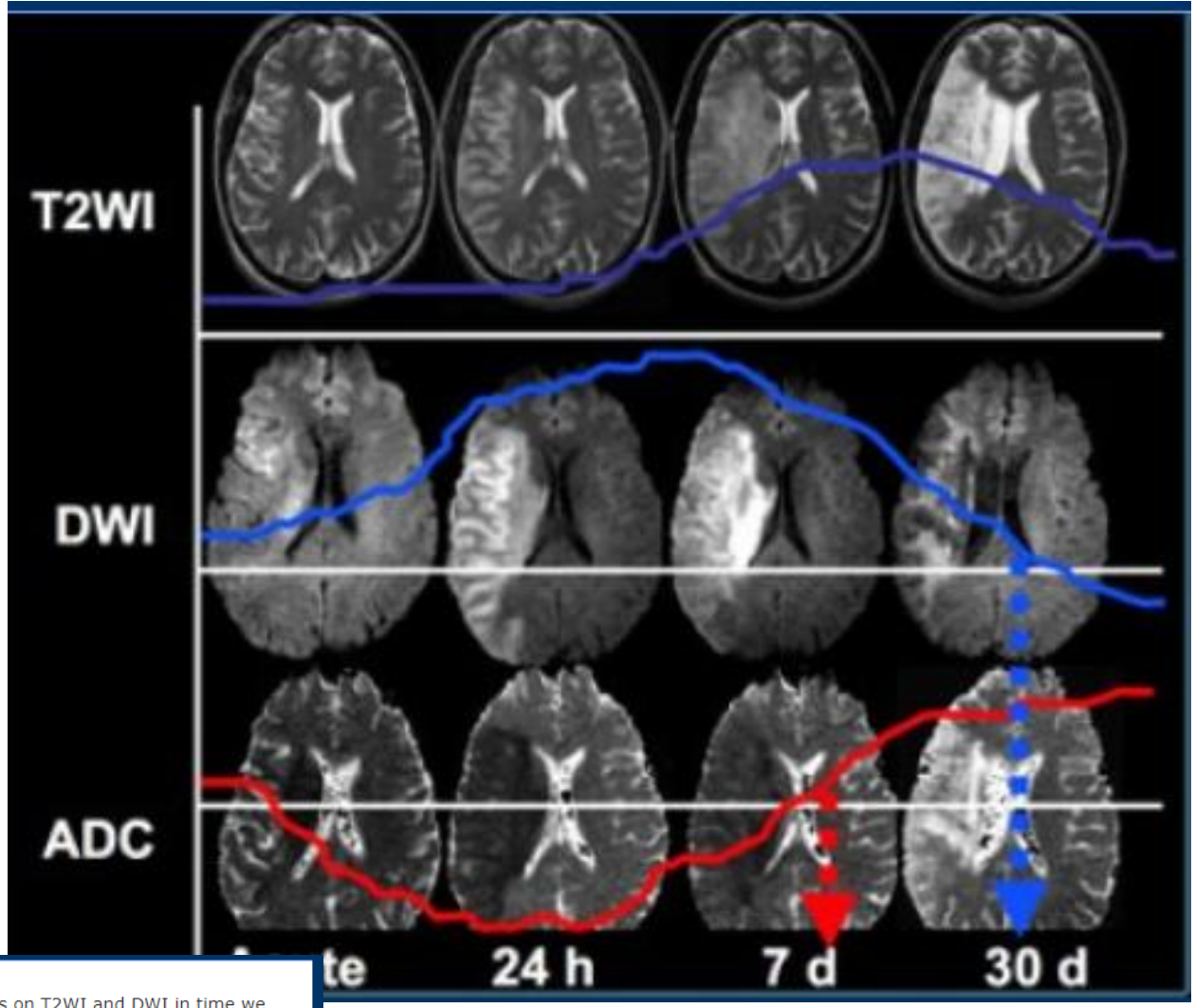
Falsos (-) de DWI
- Infartos pequeños
- Imagen ultra precoz
- Infarto en tallo cerebral

DWI-FLAIR-mismatch



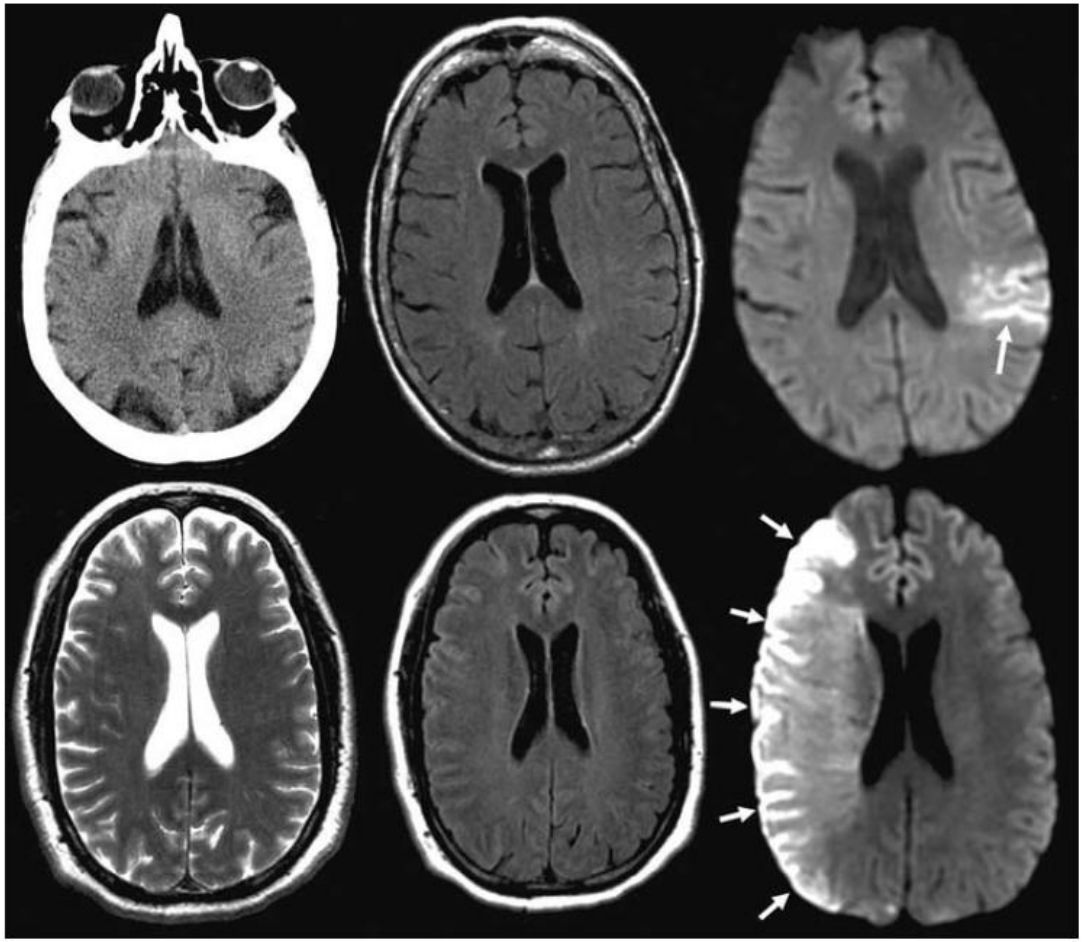
No DWI-FLAIR-mismatch





When we compare the findings on T2WI and DWI in time we will notice the following:

- In the acute phase T2WI will be normal, but in time the infarcted area will become hyperintense.
- The hyperintensity on T2WI reaches its maximum between 7 and 30 days. After this it starts to fade.
- DWI is already positive in the acute phase and then becomes more bright with a maximum at 7 days.
- DWI in brain infarction will be positive for approximately for 3 weeks after onset (in spinal cord infarction DWI is only positive for one week!).
- ADC will be of low signal intensity with a maximum at 24 hours and then will increase in signal intensity and finally becomes bright in the chronic stage.



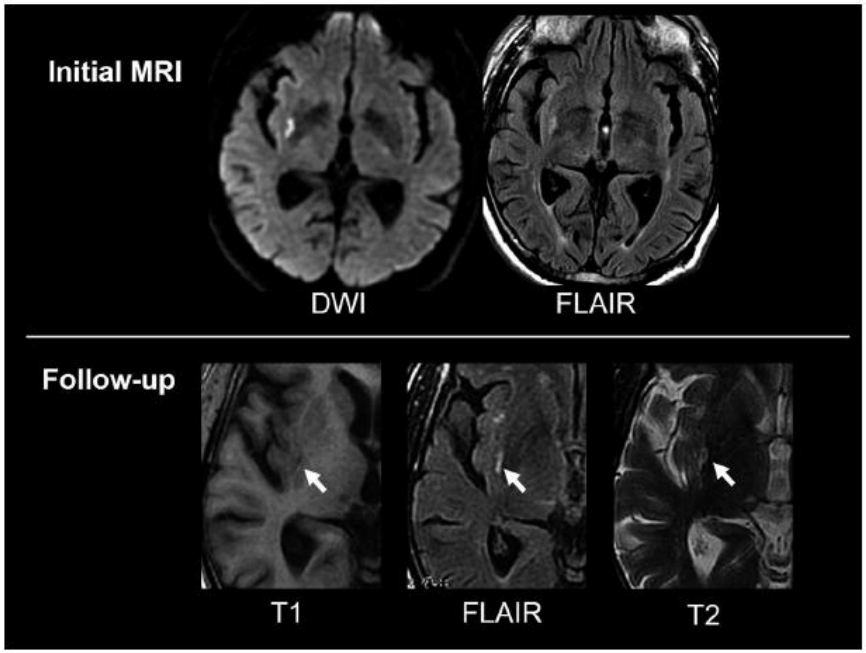
Do Transient Ischemic Attacks with Diffusion-Weighted Imaging Abnormalities Correspond to Brain Infarctions?

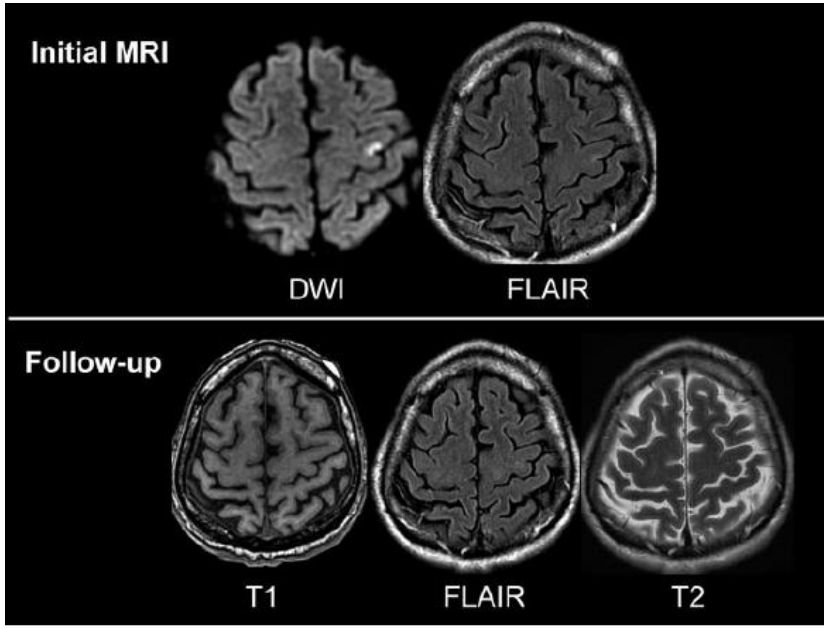
AJNR 27 | Sep 2006

C. Oppenheim
C. Lamy
E. Touzé
D. Calvet
M. Hamon
J.-L. Mas
J.-F. Méder

103 con TIA: 36 (34.9%) DWI (+)
33 pts con follow-up:
80% lesión permanente

7 pts no lesión en follow-up





Do Transient Ischemic Attacks with Diffusion-Weighted Imaging Abnormalities Correspond to Brain Infarctions?

Table 1: Characteristics of transient ischemic attack (TIA) patients with and without infarction on follow-up MR imaging (MRI)

	Reversible ($n = 7$)	Infarction ($n = 26$)	All Patients ($n = 33$)	*P* Value
Male, %	5 (71%)	18 (70%)	23 (69%)	1
Age, y (mean ± SD)	58 ± 15	61 ± 17	60 ± 16	.5
Symptoms				
Duration, min (mean ± SD)	76 ± 85	188 ± 253	201 ± 262	.2

Table 2: Quantitative diffusion-weighted MR imaging (DWI)–derived variables of the 59 transient ischemic attack (TIA) lesions according to imaging outcome

	Reversible ($n = 14$)	Infarction ($n = 45$)	*P* Value
DWI volume, cm^3 (mean ± SD)	0.21 ± 0.21	0.91 ± 1.7	.003
Absolute ADC, 10^{-6} mm^2/s (mean ± SD)	722 ± 118	631 ± 135	.022
rADC (mean ± SD)	91 ± 9%	79 ± 15%	.001

Note:—rADC corresponds to apparent diffusion coefficient (ADC) within the TIA lesion divided by the mirror ADC value.

The New England
Journal of Medicine

Volume 333 DECEMBER 14, 1995 Number 24

TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

Table 5. Outcome at Three Months According to the Classification of the Stroke Subtype at Base Line.

STROKE SUBTYPE*	t-PA		PLACEBO	
	NO. OF PATIENTS	% WITH FAVORABLE OUTCOME†	NO. OF PATIENTS	% WITH FAVORABLE OUTCOME†
Small-vessel occlusive	51		30	
Barthel index		75		50
Modified Rankin scale		63		40
Glasgow outcome scale		63		43
NIHSS		47		33
Large-vessel occlusive	117		135	
Barthel index		49		36
Modified Rankin scale		40		22
Glasgow outcome scale		45		28
NIHSS		33		18
Cardioembolic	136		137	
Barthel index		46		37
Modified Rankin scale		38		28
Glasgow outcome scale		39		31
NIHSS		29		20

Outcome favorable: OR, 1.9; 95% CI 1.2–1.9)
32% más probable que placebo de evolución a NO o mínima discapacidad
(95-100 en la escala de Barthel)
Por cada 8 pacientes tratados, 1 tuvo evolución excelente o recuperación completa

Ensayos clínicos confirmadores

- ECASS (European Cooperative Acute Stroke Study I y II)
- ATLANTIS A y B (Acute Non Interventional Therapy in Ischemic Stroke)

THE LANCET

ARTICLES | VOLUME 363, ISSUE 9411, P768-774, MARCH 06, 2004

Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials

The ATLANTIS, ECASS, and NINDS rt-PA Study Group Investigators*

	Treatment	n	Odds ratio (95% CI)*	
			Adjusted	Unadjusted
Interval (min)				
0–90	rt-PA	161	2·81 (1·75–4·50)	1·96 (1·30–2·95)
	Placebo	150		
91–180	rt-PA	302	1·55 (1·12–2·15)	1·65 (1·23–2·22)
	Placebo	315		
181–270	rt-PA	390	1·40 (1·05–1·85)	1·34 (1·04–1·72)
	Placebo	411		
271–360	rt-PA	538	1·15 (0·90–1·47)	1·04 (0·84–1·29)
	Placebo	508		

3hs

4,5hs

3-month favourable outcomes include Rankin (0–1), Barthel (95–100), and NIHSS (0–1). One, eight, nine, and six patients from NINDS part I, ECASS I, ECASS II, and ATLANTIS B, respectively, were excluded from this analysis since they were randomised after 360 min or OTT was not reported. *Odds ratios calculated from global statistical approach[13] by ITT analysis. Adjusted odds ratios were calculated adjusting for age, baseline glucose concentration, baseline NIHSS, baseline diastolic blood pressure, previous hypertension, and interaction between age and baseline NIHSS.

Table 1: **Odds ratio for a favourable outcome at 3 months after stroke**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 25, 2008 VOL. 359 NO. 13

Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke

End Point	Intention-to-Treat Population			
	Alteplase Group (N=418)	Placebo Group (N=403)	Odds Ratio (95% CI)	P Value
	no. (%)			
Primary end point				
mRS score of 0 or 1 — unadjusted analysis	219 (52.4)	182 (45.2)	1.34 (1.02–1.76)	0.04†
mRS score of 0 or 1 — adjusted analysis‡	—	—	1.42 (1.02–1.98)	0.04§

Outcome favorable:

Alteplase vs placebo

- 52.4% vs. 45.2%; odds ratio, 1.34; 95% confidence interval [CI], 1.02 to 1.76; P = 0.04).

AHA/ASA Scientific Statement

Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke

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

Stroke. Febr 2016

Intravenous alteplase (0.9 mg/kg; maximum dose, 90 mg) is recommended for administration to eligible patients who can be treated in the time period of 3 to 4.5 hours after stroke onset (*Class I; Level of Evidence B*). The eligibility criteria for treatment in this time period are similar to those for people treated at earlier time periods within 3 hours, with the following additional exclusion criteria: patients >80 years old, those taking oral anticoagulants (OACs) regardless of international normalized ratio (INR), those with a baseline NIHSS score >25, those with imaging evidence of ischemic injury involving more than one third of the middle cerebral artery (MCA) territory, or those with a history of both stroke and diabetes mellitus.

AHA/ASA Scientific Statement

Stroke. Feb 2016

Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke

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

Table 4. Inclusion and Exclusion Characteristics of Patients With Ischemic Stroke Who Could Be Treated With Intravenous rtPA Within 3 Hours From Symptom Onset

Inclusion criteria
Diagnosis of ischemic stroke causing measurable neurological deficit
Onset of symptoms <3 h before treatment begins
Age ≥18 y
Exclusion criteria
Significant head trauma or prior stroke in the previous 3 mo
Symptoms suggest SAH
Arterial puncture at noncompressible site in previous 7 d
History of previous intracranial hemorrhage
Intracranial neoplasm, AVM, or aneurysm
Recent intracranial or intraspinal surgery
Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
Active internal bleeding
Acute bleeding diathesis, including but not limited to
Platelet count <100 000/mm³
Heparin received within 48 h resulting in abnormally elevated aPTT above the upper limit of normal
Current use of anticoagulant with INR >1.7 or PT >15 s
Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (eg, aPTT, INR, platelet count, ECT, TT, or appropriate factor Xa activity assays)
Blood glucose concentration <50 mg/dL (2.7 mmol/L)
CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)
Relative exclusion criteria
Recent experience suggests that under some circumstances, with careful consideration and weighting of risk to benefit, patients may receive fibrinolytic therapy despite ≥1 relative contraindications. Consider risk to benefit of intravenous rtPA administration carefully if any of these relative contraindications is present
Only minor or rapidly improving stroke symptoms (clearing spontaneously)
Pregnancy
Seizure at onset with postictal residual neurological impairments
Major surgery or serious trauma within previous 14 d
Recent gastrointestinal or urinary tract hemorrhage (within previous 21 d)
Recent acute myocardial infarction (within previous 3 mo)