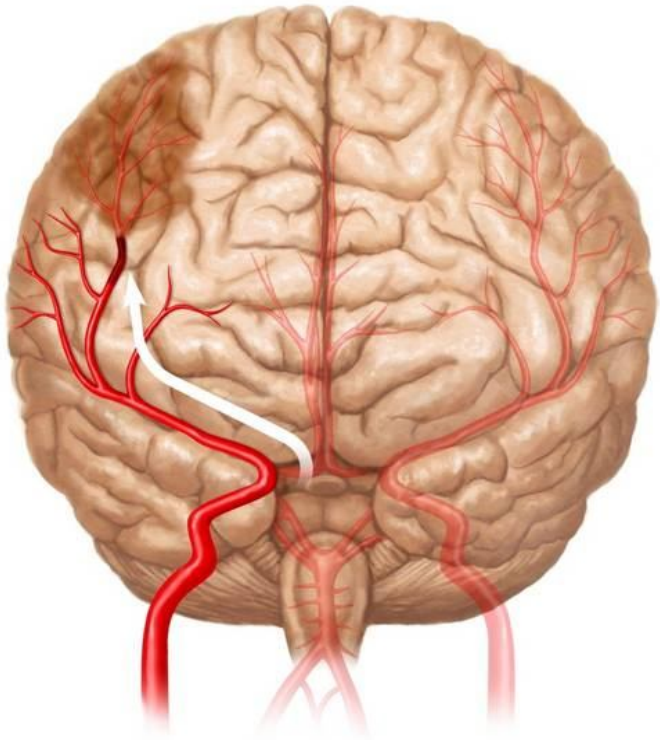
SEICAV

Sociedad Española de Infecciones Cardiovasculares

El Sistema Nervioso Central y la Endocarditis Infecciosa

A. de Alarcón
Servicio de Enfermedades Infecciosas
HU Virgen del Rocío, Sevilla

Guión

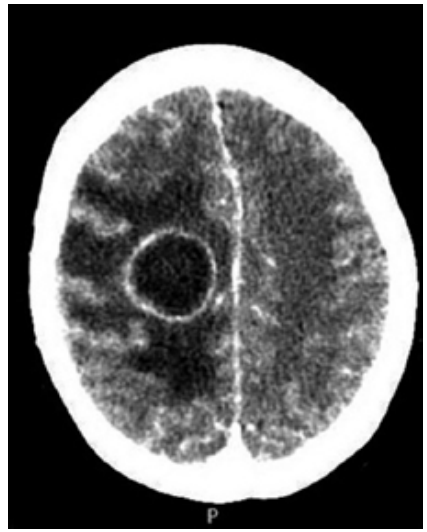


- Incidencia
- Tipos
- Factores de riesgo
- Prevención
  - Tratamiento médico
  - Tratamiento quirúrgico
- Influencia en el pronóstico vital e interacción con la cirugía cardíaca
- Tratamiento anticoagulante

Incidencia

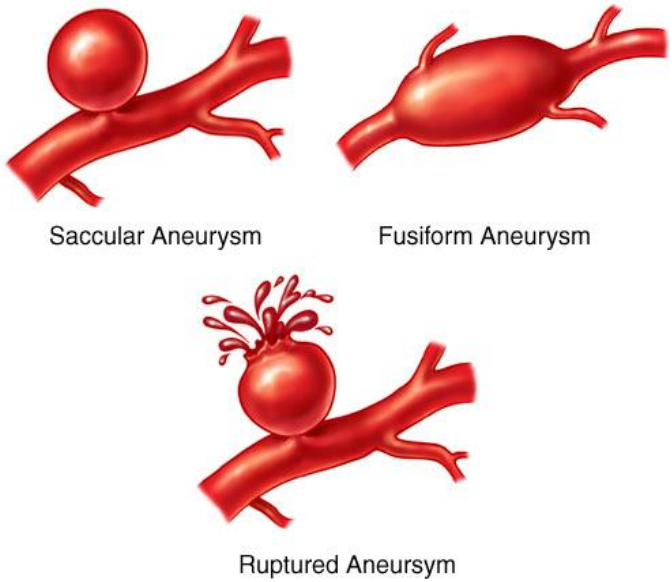
- Literatura: 20 – 40%
- Variabilidad dependiendo de su consideración: ¿Deben incluirse convulsiones?, ¿deterioro del sensorio? ¿cefalea?
- Frecuencia mayor cuando se utilizan mejores pruebas diagnósticas
  - Snigg_Martin *et al*. ***Clin Infect Dis 2008; 47: 23-30*** → 72 pacientes con EI (prospectivo): 65% CNL detectadas en RNM (30% asintomáticas)
  - Cooper *et al*. ***Circulation 2009; 120: 585-591*** → 56 pts (prospectivos), 40 con RNM: 80% de CNL (48% asintomáticas)
  - Hess *et al*. ***AJNR Am J Neuroradiol 2013; 34: 1579-84*** → 109 pts con EI asintomáticos: 71.5% de lesiones en RNM

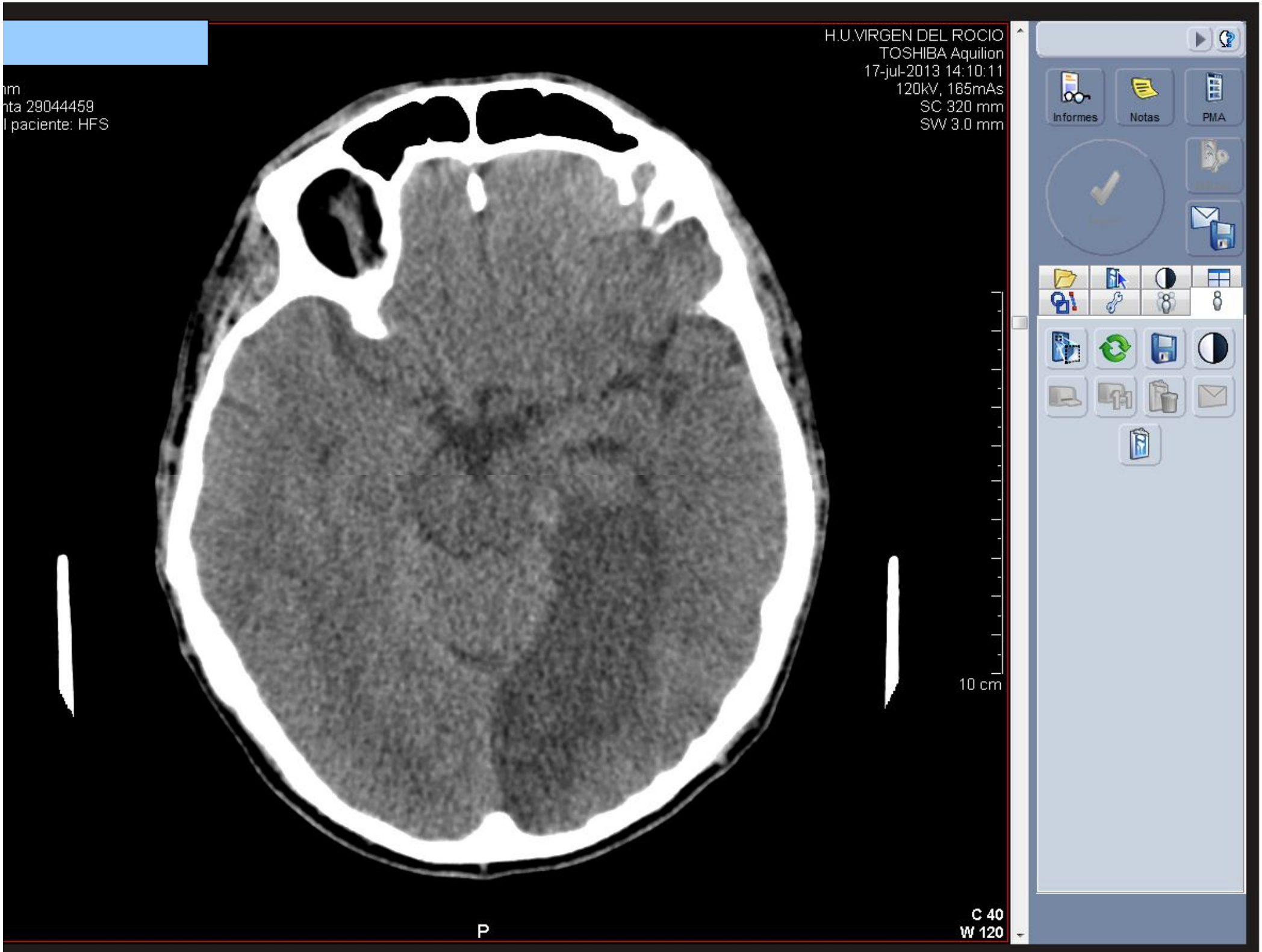
Tipos



- Lesiones no vasculares
  - **Meningoencefalitis**
  - **Absceso cerebral**

- Lesiones vasculares
  - **Embólicas**
    - Isquémicas
    - Hemorrágicas
  - **Sobre pared arterial** –> hemorragia
    - Arteritis infecciosa
    - Aneurisma micótico

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Informes
Notas
PMA
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W 120
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a 29059338

paciente: HFS

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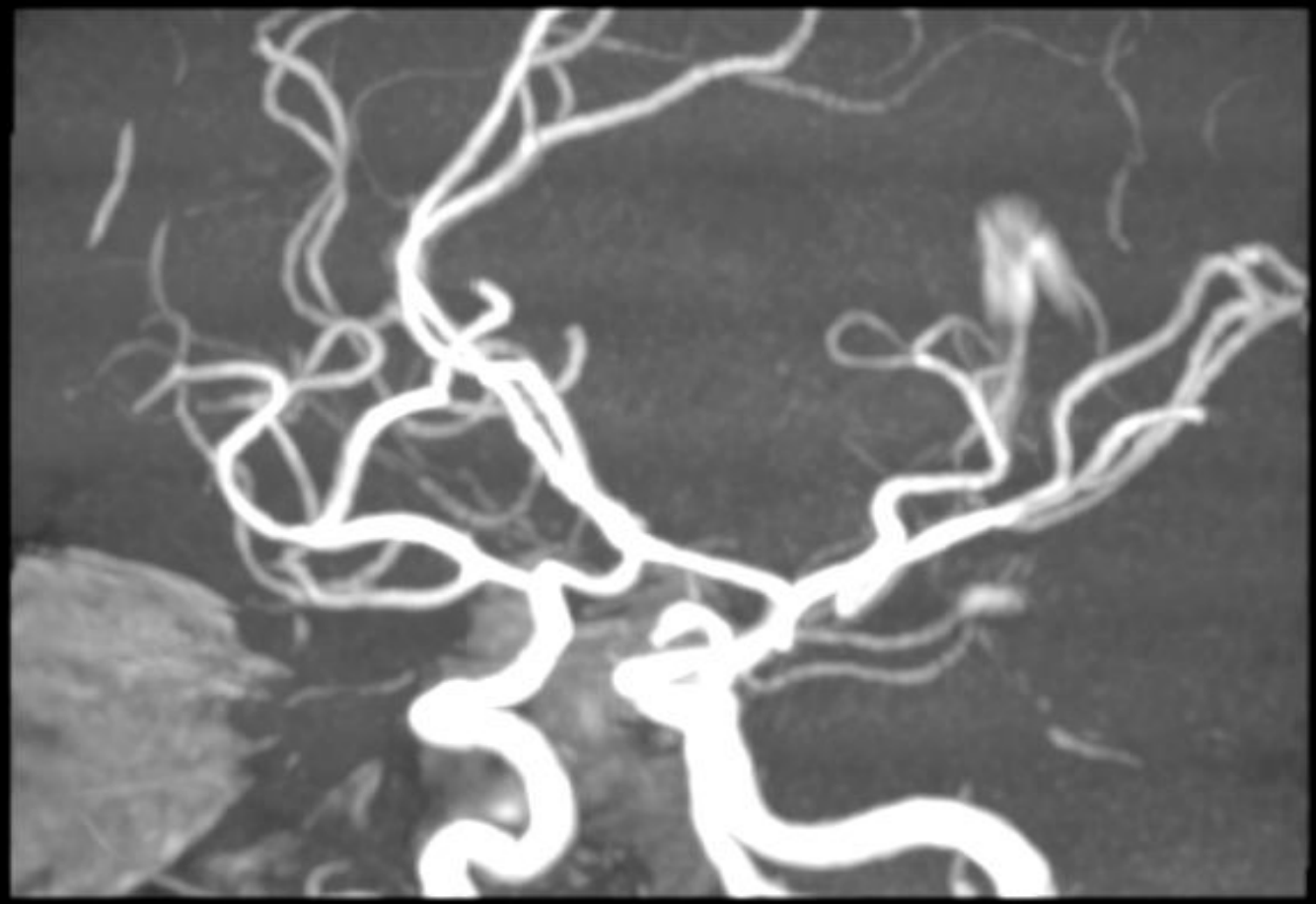

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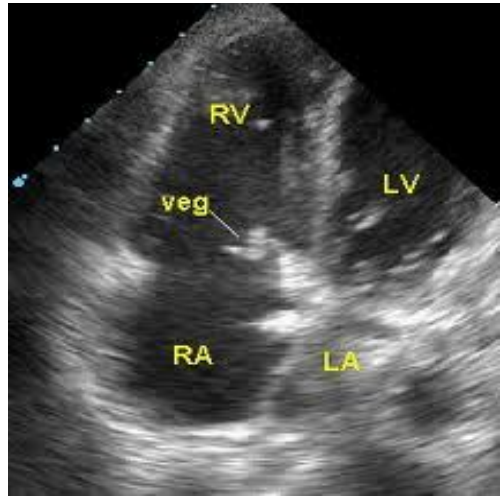
W 256

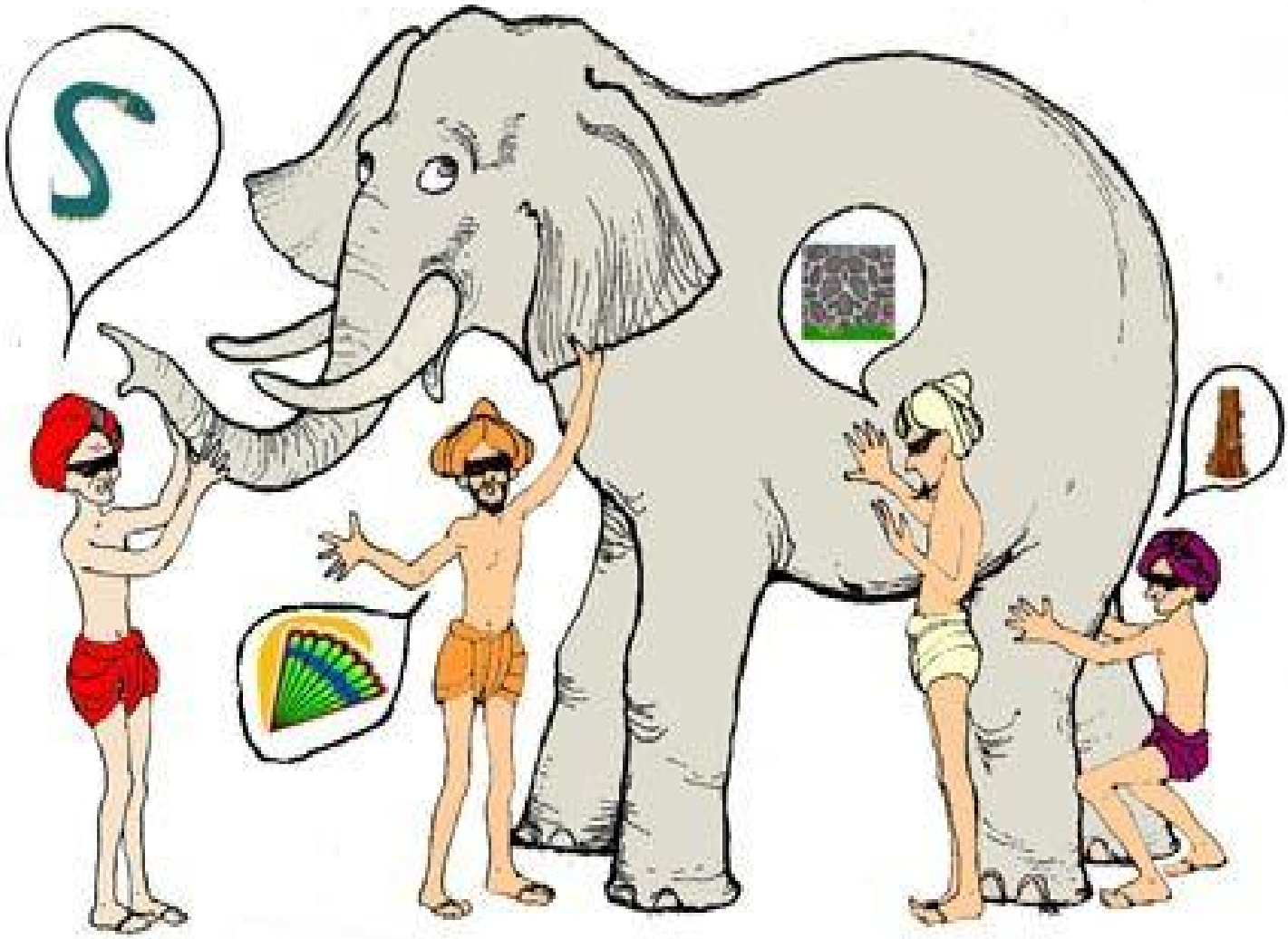
Desc. del estudio: Arteriografía de Arteria Carót
Informes
C 512
W 256

Factores de Riesgo

- Edad → añosos menos CN
- Microorganismo → *S. aureus*
- Válvula mitral → No relación, hasta x 2.5
- Características de la vegetación
  - **No relación**
  - **> 1 cm**
  - **> 1.4 cm**
  - **> 1.8 cm^2**
  - **> 2 cm**



Okonta KE and Adamu YB. What size of vegetation is an indication for surgery in endocarditis? ***Interactive cardiovascular and Thoracic Surgery 2012; 15. 1052-56***



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

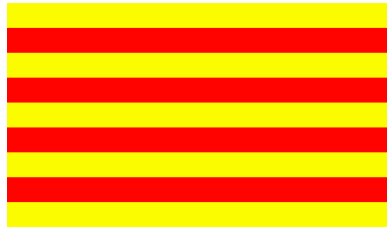
American Heart Association

Neurologic Complications of Infective Endocarditis: Risk Factors, Outcome, and Impact of Cardiac Surgery: A Multicenter Observational Study

Emilio García-Cabrera, Nuria Fernández-Hidalgo, Benito Almirante, Radka Ivanova-Georgieva, Mariam Noureddine, Antonio Plata, José M. Lomas, Juan Gálvez-Acebal, Carmen Hidalgo-Tenorio, Josefa Ruíz-Morales, Francisco J. Martínez-Marcos, Jose M. Reguera, Javier de la Torre-Lima and Aristides de Alarcón González
on behalf of the Group for the Study of Cardiovascular Infections of the Andalusian Society of Infectious Diseases (SAEI) and the Spanish Network for Research in Infectious Diseases (REIPI)

Circulation. published online May 6, 2013;

GEICV - SAEI



H. Vall d´Hebron (Barcelona)

Junts, som més forts !!

(1345 casos)

Table 3. Unadjusted and Adjusted Multivariable Analysis of Hazard Ratio of Risk Factors Associated with Neurological Complications in Infective Endocarditis Patients.

Neurologic Complications	Unadjusted HR (95% CI)	*p*	Adjusted HR (95% CI)	*p*
Global NC				
Elderly (≥ 70 years)	0.87 (0.68-1.11)	0.22		
Aortic valve	1		1	
Mitral valve	1.16 (0.90-1.48)	0.25	1.29 (1.02-1.61)	0.03
Aortic and mitral valve	0.94 (0.61-1.42)	0.94	1.00 (0.70-1.44)	0.99
Staphylococcus aureus	2.43 (1.94-3.05)	<0.001	2.47 (1.94-3.15)	<0.001
Anticoagulant therapy	1.19 (0.92-1.54)	0.184	1.31 (1.00-1.72)	0.048
Vegetation ≥ 30 mm	2.29 (1.28-4.07)	0.005	1.91 (1.07-3.43)	0.029
Enceph/Meningitis				
Staphylococcus aureus	4.50 (2.94-6.88)	<0.001	4.34 (2.84-6.64)	<0.001
Ischemic complications				
Aortic valve	1			
Mitral valve	1.33 (0.98-1.80)	0.069		
Aortic and mitral valve	1.13 (0.71-1.81)	0.604		
Staphylococcus aureus	1.81 (1.32-2.49)	<0.001	1.77 (1.27-2.48)	0.001
Vegetation ≥ 30 mm	2.25 (1.05-4.79)	0.036	2.02 (1.09-4.30)	0.007
Cerebral hemorrhage				
Period 1996-2009	0.71 (0.39-1.28)	0.253	0.55 (0.27-1.07)	0.079
Elderly (≥ 70 years)	0.45 (0.22-0.91)	0.026	0.36 (0.16-0.83)	0.014
Aortic valve	1			
Mitral valve	1.73 (0.99-3.02)	0.054		
Aortic and mitral valve	1.24 (0.52-2.95)	0.62		
Anticoagulant therapy	2.26 (1.33-3.84)	0.002	2.71 (1.54-4.76)	0.001
Staphylococcus aureus	2.27 (1.22-4.25)	0.01	2.35 (1.30-4.23)	0.005
Vegetation ≥ 30 mm	3.49 (0.97-12.64)	0.056	2.93 (0.91-9.49)	0.073

García-Cabrera E et al. Circulation. 2013 Jun 11;127(23):2272-84.

García-Cabrera E et al. Circulation. 2013 Jun 11;127(23):2272-84.

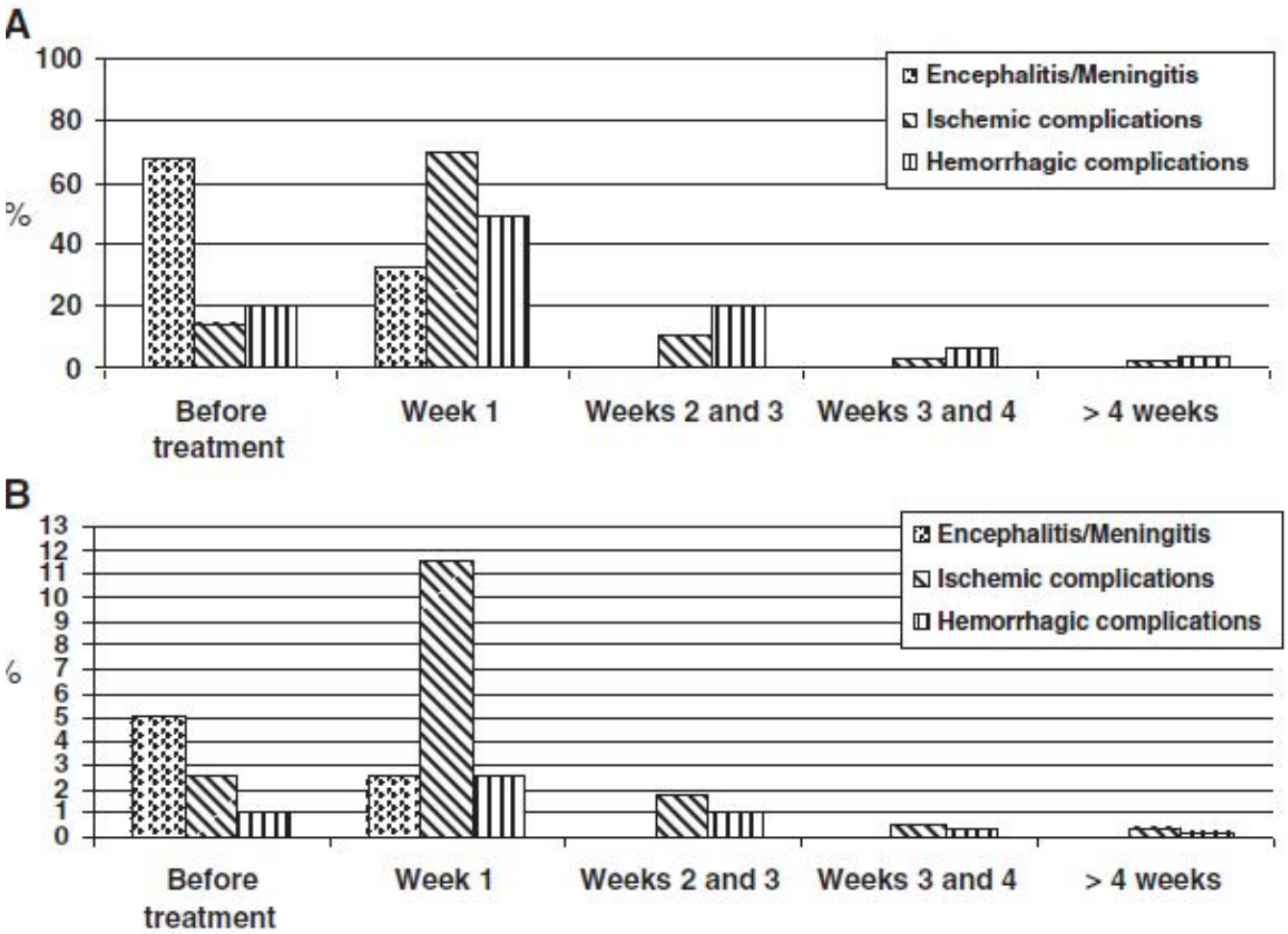


Figure 1. A, Percentage of each neurological complication occurring in patients with these events (n=340) relative to the start of antibiotic treatment. **B**, Percentage of each neurological complication in the total cohort (n=1345) c patients with infective endocarditis relative to the start of antibiotic treatment.

Leer también:

Vilacosta I *et al* . ***J Am Coll Cardiol 2002; 39: 1489-95***

Dikerman SA *et al.* ***Am Heart J 2007; 1086-1094***

Table 4. Changes in the Frequency of Vascular Neurologic Complications Over Time in Patients with Infective Endocarditis

	Antibiotic therapy ≤7 days N=162*	Antibiotic therapy >7 days N=49#	Standardized risk differences (95% CI)**
Type of neurological complication			
Ischemic	133/1216 (10.9)	30/1083 (2.8)	-74.7% (-75.7, -73.7)
Hemorrhagic	29/1216 (2.4)	19/1187 (1.6)	-32.9% (-33.6, -32.2)
Valve affected			
Mitral	76/499 (15.2)	30/423 (7.1)	-53.4% (-55.9, -51.0)
Aortic	69/574 (12.2)	13/495 (2.6)	-78.5% (-80.0, -77.1)
Aortic and mitral	17/143 (19.0)	6/126 (4.8)	-59.9% (-63.7, -56.2)
Causal agent			
VGS¶	30/263 (11.4)	6/233 (2.6)	-77.4% (-79.5, -75.4)
S. aureus	53/221 (25.0)	10/159 (6.3)	-74.8% (-78.7, -71.0)
CNS§	21/167 (12.6)	5/146 (3.4)	-72.8% (-75.8, -69.7)
Enterococcus spp	14/159 (8.8)	10/145 (6.9)	-21.7% (-25.8, -17.5)
Others	33/295 (11.2)	10/262 (3.8)	-65.9% (-67.0, -64.2)
Unknown etiology	11/120 (9.2)	8/109 (7.3)	-19.9% (-24.9, -15.0)
Anticoagulant treatment			
Yes	40/241 (16.5)	18/202 (8.9)	-43.1% (-47.2, -39.0)
No	122/974 (12.5)	31/852 (3.6)	-71.9% (-73.1, -70.6)
Vegetation size			
No vegetation	37/321 (11.5)	11/284 (3.9)	-66.4% (-68.7, -64.1)
<10 mm	82/611 (13.4)	20/529 (3.8)	-71.8% (-73.5, -70.2)
≥10 mm	53/404 (13.1)	25/351 (7.1)	-45.7% (-48.4, -43.0)
≥20 mm	15/118 (12.7)	6/103 (5.8)	-54.2% (-58.8, -49.6)
≥30 mm	7/22 (31.8)	3/15 (20.0)	-37.1% (-58.4, -15.9)

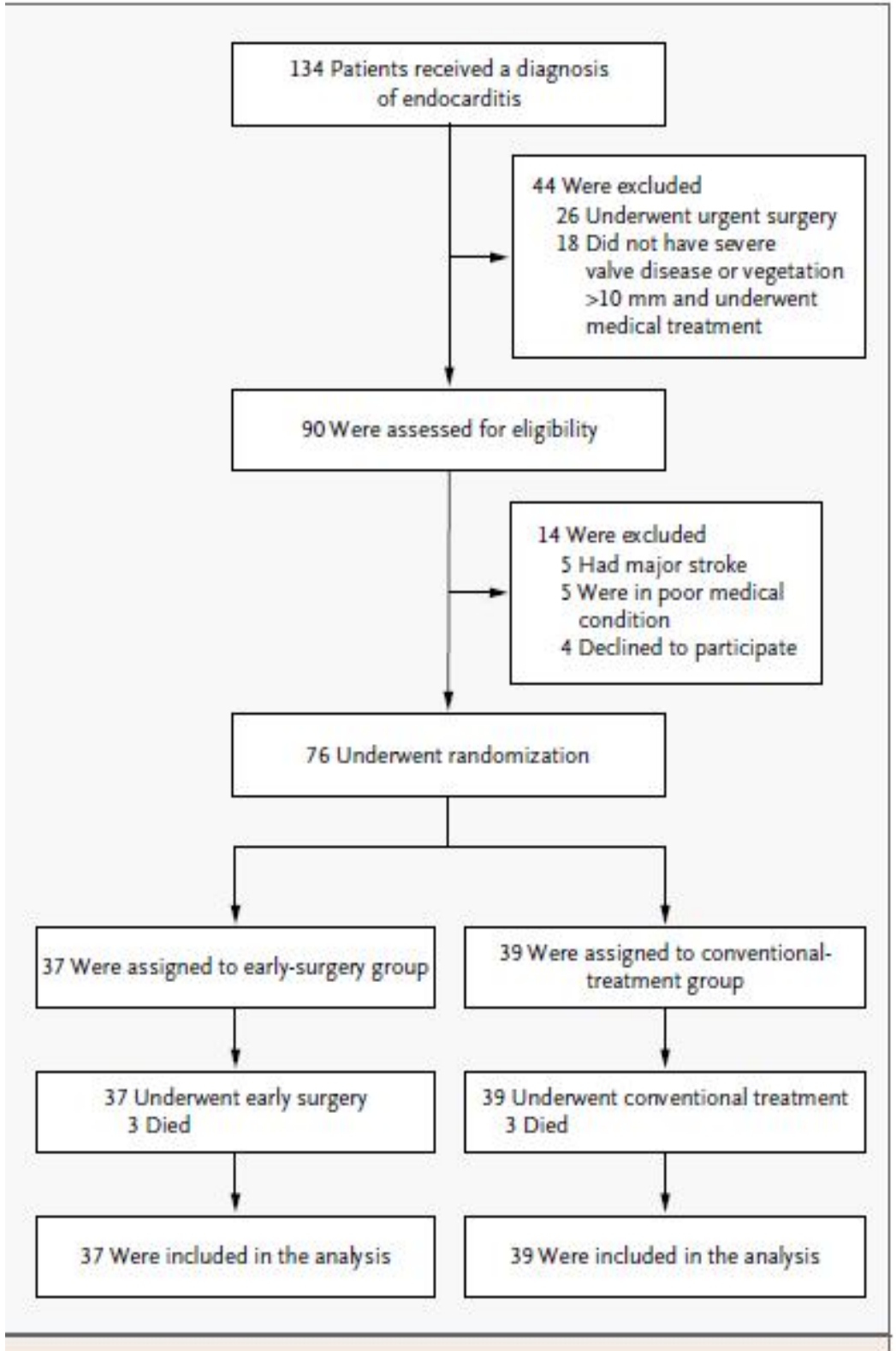


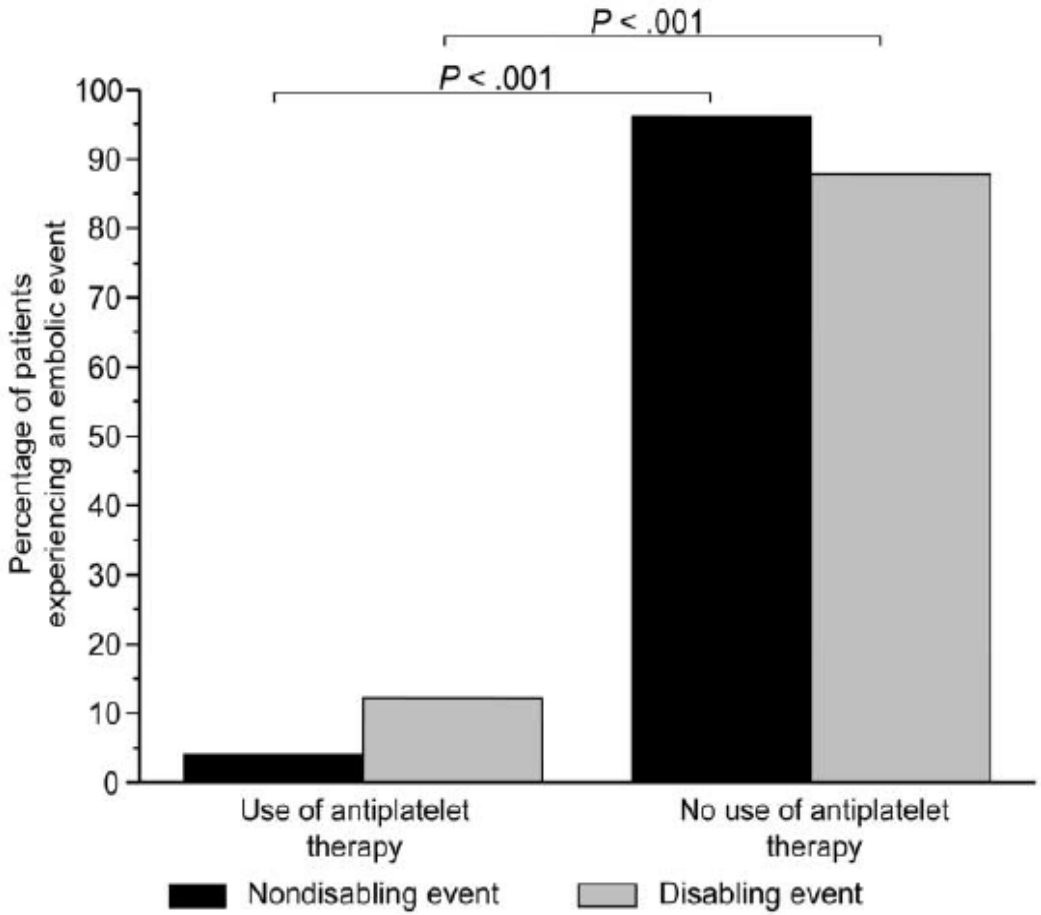
Table 3. Clinical End Points.

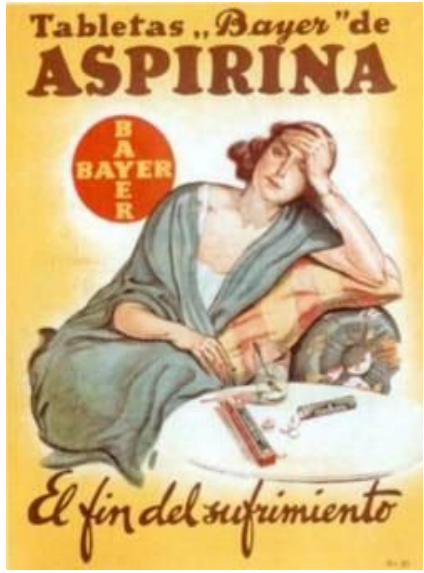
Outcome	Conventional Treatment (N=39)	Early Surgery (N=37)	P Value
Primary end point — no. (%)			
In-hospital death or embolic event at 6 wk	9 (23)	1 (3)	0.01
In-hospital death	1 (3)	1 (3)	1.00
Embolic event at 6 wk			
Any	8 (21)	0	0.005
Cerebral	5 (13)	0	
Coronary	1 (3)	0	
Popliteal	1 (3)	0	
Splenic	1 (3)	0	
Secondary end points at 6 mo — no. (%)			
Any	11 (28)	1 (3)	0.003
Death	2 (5)	1 (3)	1.00
Embolic event	8 (21)	0	0.005
Recurrence of infective endocarditis	1 (3)	0	1.00

Duk-Hyun Kang *et al*. Early surgery versus conventional treatment for infective endocarditis.
N Engl J M 2012; 366: 2466-73

Table 1. Clinical and Echocardiographic Characteristics of the Patients at Baseline, According to Treatment Group.*

Characteristic	Conventional Treatment (N=39)	Early Surgery (N=37)
Age — yr	47.8±17.5	45.5±14.9
Male sex — no. (%)	27 (69)	24 (65)
Diabetes — no. (%)	4 (10)	8 (22)
Hypertension — no. (%)	7 (18)	11 (30)
Coronary artery disease — no. (%)	1 (3)	3 (8)
Immunocompromised state — no. (%)†	1 (3)	2 (5)
Underlying valve disease — no. (%)	39 (100)	35 (95)
Serum creatinine — mg/dl	0.90±0.67	1.28±1.85
EuroSCORE value‡	6.7±1.7	6.4±1.6
Embolism on admission — no. (%)	17 (44)	19 (51)
Cerebral	11 (28)	11 (30)
Renal	7 (18)	6 (16)
Splenic	9 (23)	14 (38)
Left ventricular ejection fraction — %	60.7±7.2	61.7±5.1
Valve involved — no. (%)		
Mitral	23 (59)	22 (59)
Aortic	11 (28)	11 (30)
Aortic and mitral	5 (13)	4 (11)
Vegetation diameter	14.1±3.5	13.5±3.2
>10–15 mm — no. (%)	26 (67)	26 (70)
>15 mm — no. (%)	13 (33)	11 (30)
Valvular disease — no. (%)		
Severe stenosis	3 (8)	1 (3)
Severe regurgitation	36 (92)	36 (97)
Blood microorganism — no. (%)		
Viridans streptococci	13 (33)	10 (27)
Other streptococci	12 (31)	11 (30)
Staphylococcus aureus	5 (13)	3 (8)
Enterococcus	1 (3)	2 (5)
Other§	1 (3)	1 (3)
Negative culture¶	7 (18)	10 (27)





Anavekar NS et al. Impact of prior antiplatelet therapy on risk of embolism in infective endocaritis
Clin Infect Dis 2007:44: 1180-6

Variable	OR (95% CI)	*P*
Embolic events		
Antiplatelet therapy (unadjusted)	0.35 (0.20–0.63)	<.001
Antiplatelet therapy (adjusted)[a]	0.36 (0.19–0.68)	.002
Death within first 6 months[b]		
Antiplatelet therapy (adjusted)[a]	0.29 (0.10–0.81)	.018

[a] Model listed in appendix.
[b] Two hundred one patients died.

600 pacientes (cohorte R)
Toma de antiagregantes 6 meses

Uso de antiagregantes

- Chan KI et al. A randomized trial if aspirin on the risk of embolic events inpatients ith infective endocaritis. ***J Am coll Cardiol 2003; 42; 775-80***
- Chan KL et al. Effect of long-term aspirina use on embolic events in infective endocarditis. ***Clin Infect Dis 2008, 46. 37-41***
  - *No descenso del número de embolismos*
  - *Más tendencia al sangrado*
- Eisen DM et al. Reduced replacement surgery and complication rate in *Staphylococcus aureus* endocarditis patients receiving acetyl-salicylic acid. ***J Infection 2009; 58: 332-338***
  - *No descenso del numero de embolismos ni mas fenómenos hemorrágicos*
  - *Menos tasa de Cia valvular*

¿Influyen las CNL en la mortalidad?

Data in the first 3 columns are expressed as number (percentage). * p<0.05; ** p<0.001;

Table 5. Unadjusted and Adjusted Multivariable Analyses of Risk Factors Related to Early Mortality

	Total Cohort N =1345	Survivors N = 944	Non-survivors N =401	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Complications					
Septic Shock†	154 (12)	41 (27)	113 (74)**	4.65 (3.72-5.80)**	2.24 (1.69-2.95)**
Acute renal failure ¤	424 (32)	222 (52)	202 (48)**	2.56 (2.10-3.13)**	1.65 (1.30-2.10)**
Heart failure‡	675 (51)	394 (58)	281 (42)**	2.63 (2.12-3.27)**	2.35 (1.80-3.07)**
Neurologic complications	340 (25)	188 (55)	152 (45)**	2.05 (1.67-2.51)**	1.58 (1.23-2.02)**
Type of complication#					
Encephalitis-meningitis	86 (6)	44 (50)	43 (50)*	2.10 (1.53-2.88)**	0.94 (0.61-1.45)
Total ischemic	192 (14)	114 (59)	78 (41)**	1.59 (1.24-2.03)**	1.67 (1.27-2.19)**
Small ischemic	138 (10)	82 (59)	56 (41)**	1.42 (0.93-2.19)	
Moderate-severe ischemic	54 (4)	32 (59)	22 (41)	1.59 (1.19-2.10)**	1.63 (1.19-2.22)**
Cerebral hemorrhage	60 (4)	28 (47)	32 (53)**	2.04 (1.42-2.92)**	1.73 (1.10-2.71)*

García-Cabrera E et al. Circulation. 2013 Jun 11;127(23):2272-84.

CNL y Cirugía

Table 3. Indications for surgery and reasons why surgery was not performed, although indicated

Indications	N=523	95% CI
Left ventricular failure	355 (67.9%)	63.7 – 71.7
Intracardiac complications*	140 (26.8%)	23.1 – 30.7
Sepsis	22 (4.2%)	2.8 – 6.3
Repeated embolisms	6 (1.1%)	0.5 – 2.5
Reasons for no surgery	**N=187**	**95% CI**
Neurological complications	24 (12.8%)	8.8 – 18.0
Refused by the patient	22 (11.8%)	7.9 – 17.2
Poor clinical status	91 (48.7%)	41.6 – 55.8
Underlying disease	26 (13.9%)	9.7 – 19.6
Death before scheduled intervention	24 (12.8%)	8.7 – 18.4

García-Cabrera E et al. Circulation. 2013 Jun 11;127(23):2272-84.

¿Cuando operar?

- En infartos isquémicos pequeños o asintomáticos no hay restrición más allá de 72 horas
- En infartos isquémicos extensos el tiempo de espera varia entre 2 – 4 semanas
- En lesiones hemorrágicas debe esperarse al menos 4 semanas
- En aneurismas micóticos:
  - Si hay signos de sangrado → Terapia intravascular o Neurocirugía abierta previa a cirugía y esperar al menos dos semanas si se utiliza este abordaje
  - Si no signos de sangrado:
    - Actitud expectante y controles → 30% desaparecen
    - Intervención si cirugía cardiaca se juzga muy probable

Rossi M, Gallo A, De silva RJ, Sayeed R. What is the optimal timing for surgery in infective endocarditis ith cerebrovascular complications?. ***Interactive Cardiovascular and Thoracic Surgery 2012, 14:72-80***

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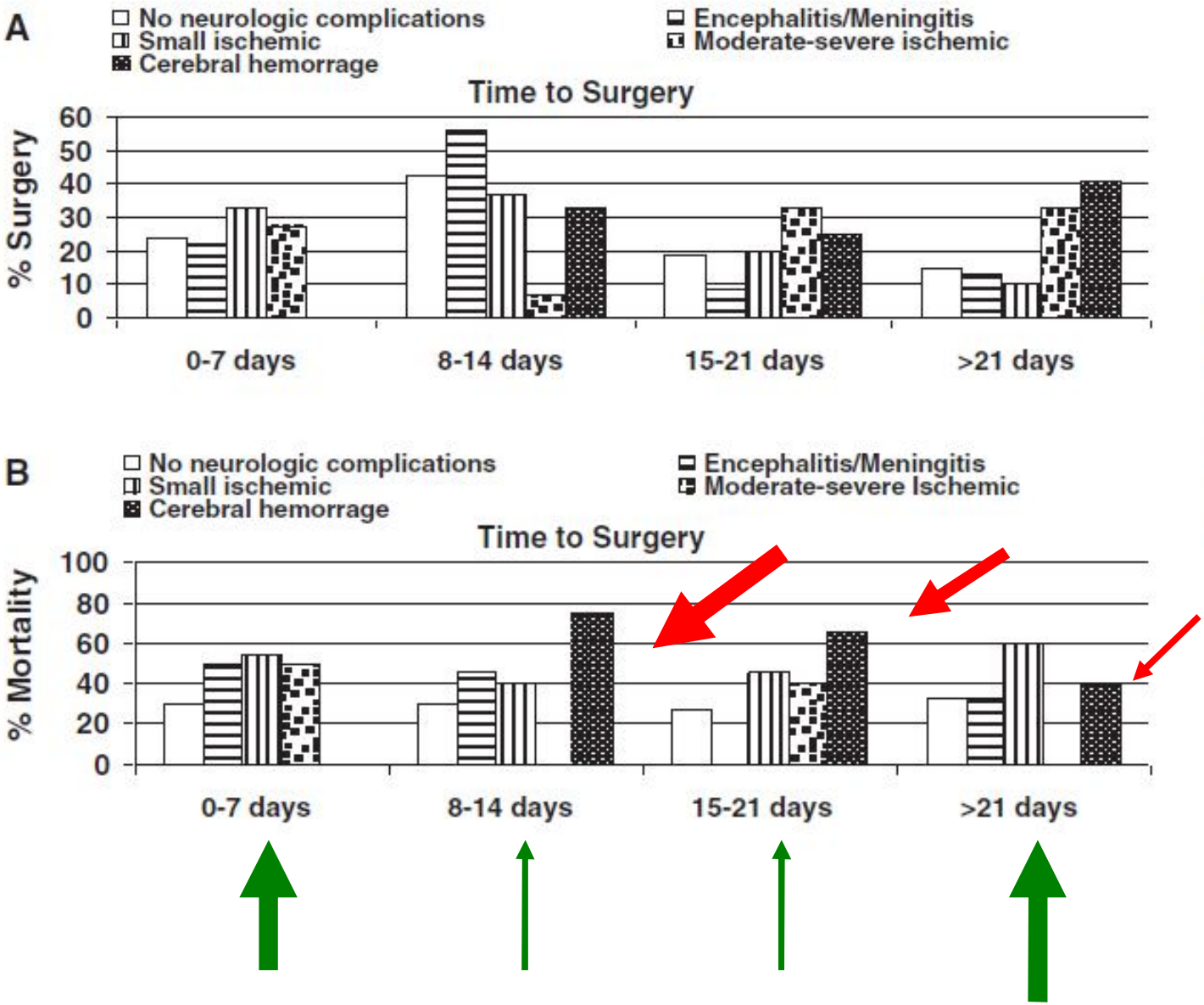
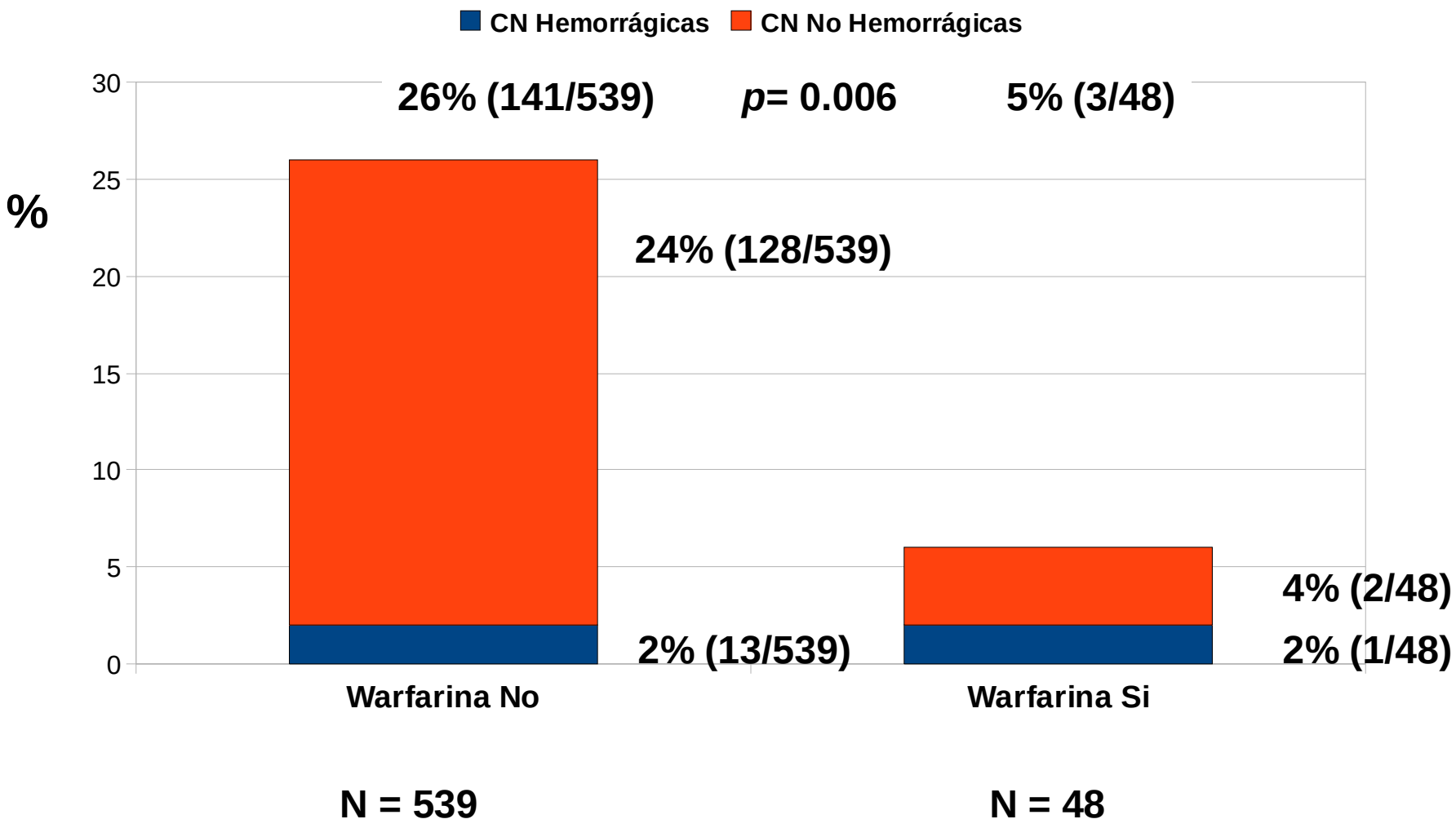


Figure 2. A, Percentage of patients undergoing cardiac surgery and timing of the procedure by type of neurological complication. **B**, Percentage of patients with each neurological complication who had a fatal outcome after cardiac surgery according to the time to surgery (only patients who had operations are included).

¿Anticoagulación?



U. Snygg-Martin et al. Warfarin therapy and incidence of cerebrovascular complications in left-sided native valve Endocarditis. ***Eur J Clin Microbiol Infect Dis 2011;30(2): 151-7***

García-Cabrera E et al. Circulation. 2013 Jun 11;127(23):2272-84.

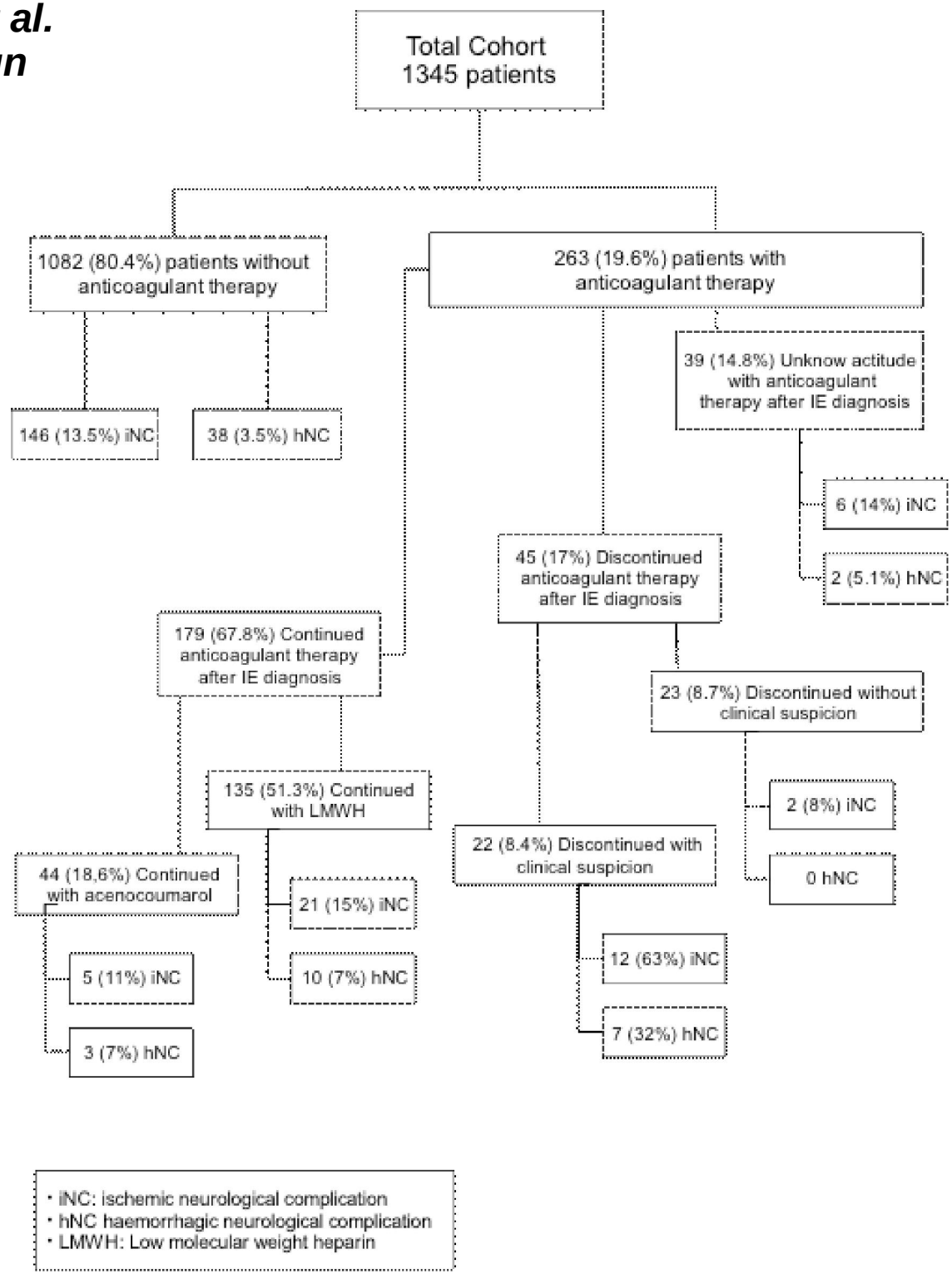


Table 5. Use of anticoagulant therapy and risk of a neurologic complication (NC). Data from the total cohort

	N	Ischemic NC	OR (95% CI)	Hemorrhagic NC	OR (95% CI)
Not anticoagulated	1082	146 (13.5%)	1	38 (3.5%)	1
Anticoagulated	263	46 (17.5%)	1.36 (0.94-1.95)	22 (8.4%)	2.5 (1.45-4.32)
Continued with acenocoumarol	44	5 (11.4%)	0.82 (0.32–1.12)	3 (6.8%)	2.0 (0.59-6.78)
Continued with heparin	135	21 (15.5%)	1.17 (0.71– .92)	10 (7.4%)	2.2 (1.06-4.08)
Discontinued without suspicion	23	2 (8.7%)	0.61 (0.14–2.63)	0	-
Discontinued with suspicion	22	12 (57%)	8.55 (3.54–20.6)	7 (31.9%)	12.8 (4.94-3.2)

Table 6. Use of anticoagulant therapy and risk of a neurologic complication (NC). Data from patients with prosthetic valve infective endocarditis

	N	Ischemic NC	OR (95% CI)	Hemorrhagic NC	OR (95% CI)
Not anticoagulated	124	15 (12%)	1	3 (2.4%)	1
Anticoagulated	201	32 (16%)	1.37 (0.71-2.66)	14 (7%)	3.9 (0.85-10.7)
Continued with acenocoumarol	36	5 (11%)	0.66 (0.18-1.24)	3 (7%)	3.66 (0.71-19)
Continued with heparin	104	15 (14%)	1.21 (0.56-2.61)	7 (6.7%)	2.88 (0.73-11.4)
Discontinued without suspicion	15	1 (6.6%)	0.51 (0.64-4.23)	0	-
Discontinued with suspicion	15	9 (60%)	21.8 (5.3-89.6)	4 (26%)	14.6 (1.98-61)

García-Cabrera E et al. Circulation. 2013 Jun 11;127(23):2272-84.

Conclusiones

- Las CNL son un hecho frecuente en la EI y su incidencia real es probablemente mucho mayor de lo reportado
- Factores especialmente predisponentes son la etiología por *S. aureus* y una vegetación de gran tamaño
- Un diagnóstico precoz y el tratamiento antimicrobiano apropiado son las armas más potentes para evitarlas. No obstante, otras opciones más agresivas (cirugía) son posibles
- A pesar de ello, su influencia negativa en el pronóstico solo ocurre en las más graves y un excesivo temor puede llevar a un retraso no justificado en una cirugía cuando ésta es necesaria
- Una suspensión transitoria de la anticoagulación en las EI más predisponentes a desarrollarlas puede evitar desastres hemorrágicos sin especial riesgo trombótico en válvulas protésicas