

EuroValve 2015

A case of large veg. with neurological complication

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Nice, France. March 2015.

Clinical presentation

- A 69-year-old man presented to a secondary H with fever (40 C⁰), shivers, myalgias, and odynophagia in the last 48 h.
- Past history: Diabetes & hypercholesterolemia.
- In the last 4 months he **had gone to the dentist** several times.
- During the first 4 hours after admission his clinical status deteriorated significantly, he had aphasia, and petechiae appeared in the trunk and the extremities.
- **Ph. Exam.:** Meningismus and fell into a coma.

Clinical presentation & evolution

- Suspicion of meningitis & admission to the ICU.
- **Intubation: mucous & purulent** material in the oropharynx.
- **Cranial CT**: normal; **LP**: non-diagnostic.
- Urine & **BC** were taken & antibiotics started: Ceftriaxone, vancomycin, ampicillin and iv. corticoids.
- **48 h evolution**: acute renal failure, thrombocytopenia, septic shock, hypernatremia, and erysipeloid cutaneous reddish eruption in the extremities.
- Cerebrospinal fl. culture: neg.; BC: **St. pyogenes** (x3).

Clinical evolution

- Clinical status: **progressively improving** with vasoconstriction therapy, fluids, ceftriaxone & clindamycin, and ventilatory support, but..... he had **relapsing peaks of fever**.
 - TTE: normal LV function, LA enlargement, mitral annular calcification & **moderate MR**.
 - TEE: A **15 mm**, mitral veg. with moderate MR.
 - Hemodynamically better, but neurologically slow. New cranial CT: **large left parietoccipital hematoma**.
 - Extubation was delayed, and percutaneous tracheostomy performed. **Surgery was requested**.
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Clinical questions

- **Does the patient have a surgical indication ?**
 - **Should the patient undergo surgery ?**
-

Table 19 Indications and timing of surgery in left-sided native valve infective endocarditis

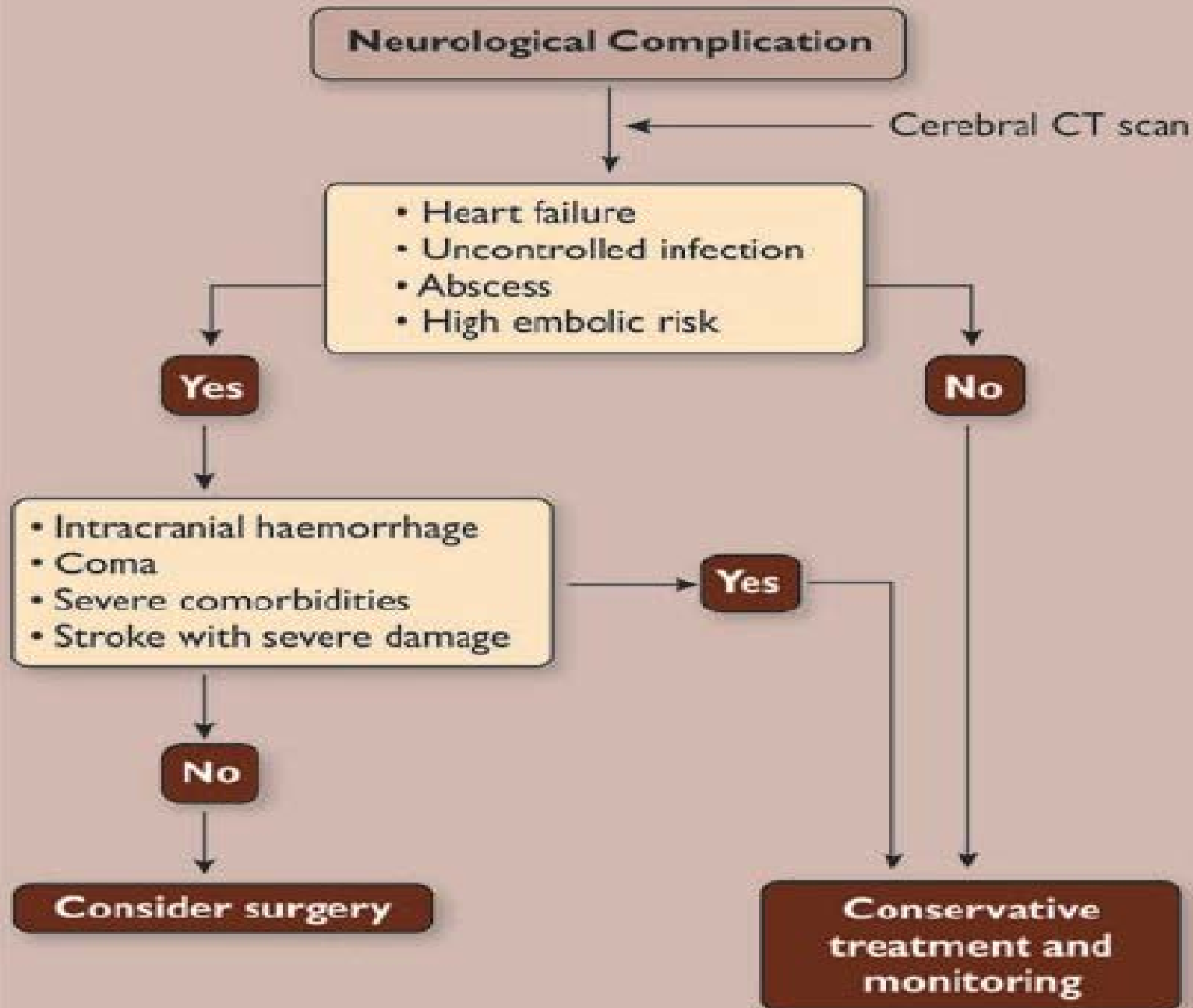
Recommendations: Indications for surgery	Timing*	Class ^a	Level ^b
A - HEART FAILURE			
Aortic or mitral IE with severe acute regurgitation or valve obstruction causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B
Aortic or mitral IE with fistula into a cardiac chamber or pericardium causing refractory pulmonary oedema or shock	Emergency	I	B
Aortic or mitral IE with severe acute regurgitation or valve obstruction and persisting heart failure or echocardiographic signs of poor haemodynamic tolerance (early mitral closure or pulmonary hypertension)	Urgent	I	B
Aortic or mitral IE with severe regurgitation and no HF	Elective	IIa	B
B - UNCONTROLLED INFECTION			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B
Persisting fever and positive blood cultures > 7–10 days	Urgent	I	B
Infection caused by fungi or multiresistant organisms	Urgent/elective	I	B
C - PREVENTION OF EMBOLISM			
Aortic or mitral IE with large vegetations (> 10 mm) following one or more embolic episodes despite appropriate antibiotic therapy	Urgent	I	B
Aortic or mitral IE with large vegetations (> 10 mm) and other predictors of complicated course (heart failure, persistent infection, abscess)	Urgent	I	C
Isolated very large vegetations (> 15 mm) [#]	Urgent	IIb	C

^aClass of recommendation.

^bLevel of evidence.

*Emergency surgery: surgery performed within 24 h, urgent surgery: within a few days, elective surgery: after at least 1 or 2 weeks of antibiotic therapy.

[#]Surgery may be preferred if procedure preserving the native valve is feasible.



Clinical evolution

- Two centers did not consider the patient a surgical candidate so he stayed at the H.
 - Progressive neurologic improvement (2 weeks): he reached a normal level of consciousness, swallow without choking, speak, and finally the tracheal tube could be removed.
 - A **repeat TEE was similar** (large mitral veg. & moderate MR).
 - Referred to our center (40 days after the index admission) as **potential candidate for cardiac surgery**: conscious, temporarily disoriented, with dysarthria & right hemiparesis (2/5), and no fever.
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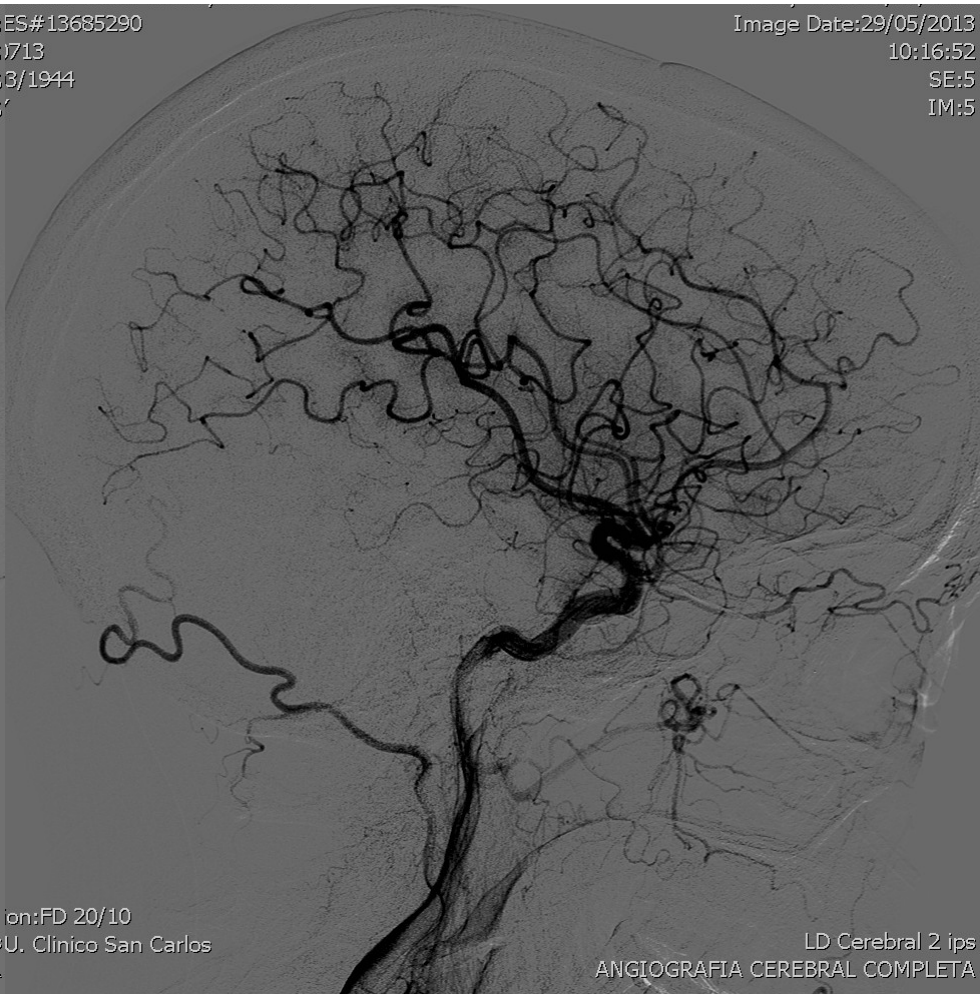
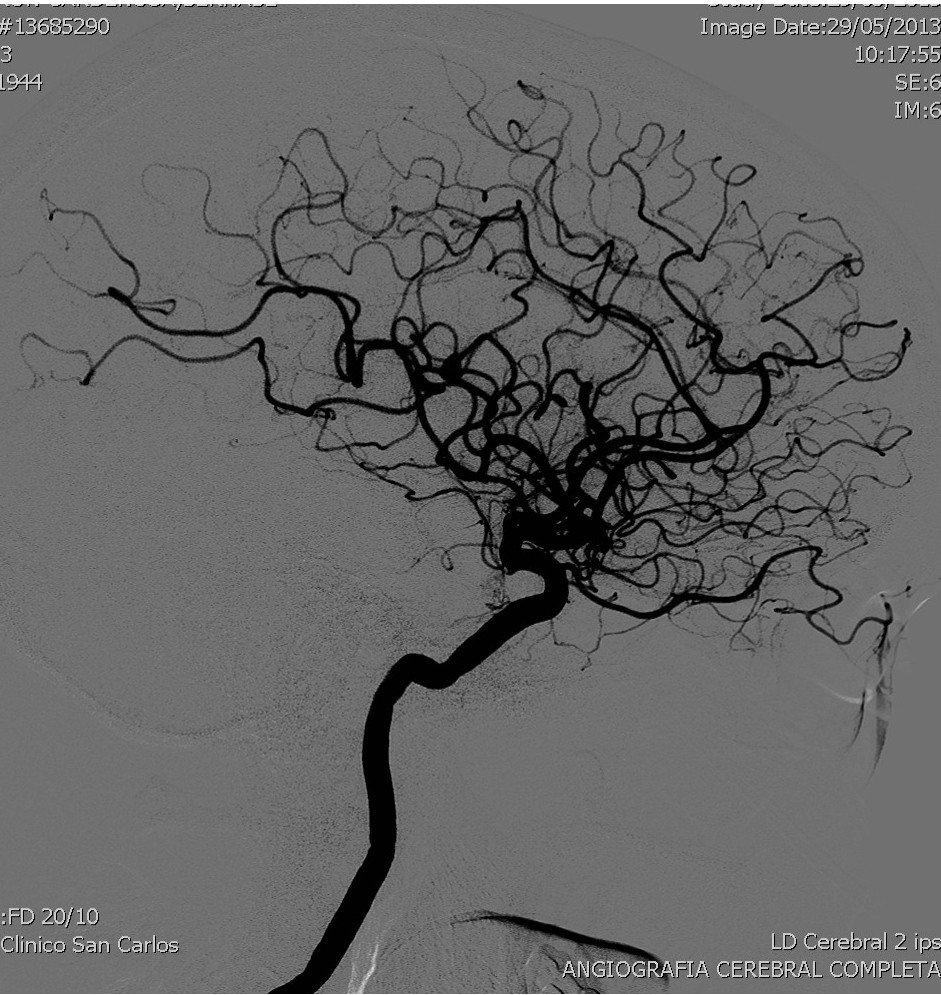
Clinical evolution

- **Ph. Exam:** dysarthria, right hemiparesis, murmur of mitral regurgitation & no signs of HF.
- **Blood analysis:** Hb: 8,8 g/dl, total leukocyte count: 6200 (61,7% N), platelets: 371000.
- Renal & liver function tests. Coagulation studies, serum electrolyte, and blood glucose were within **normal limits**.
- Urine culture & blood cultures were **negative**.
- Chest X-ray was normal (**no signs of HF**).
- **Angio MRI, cerebral angiography, and a TEE.**

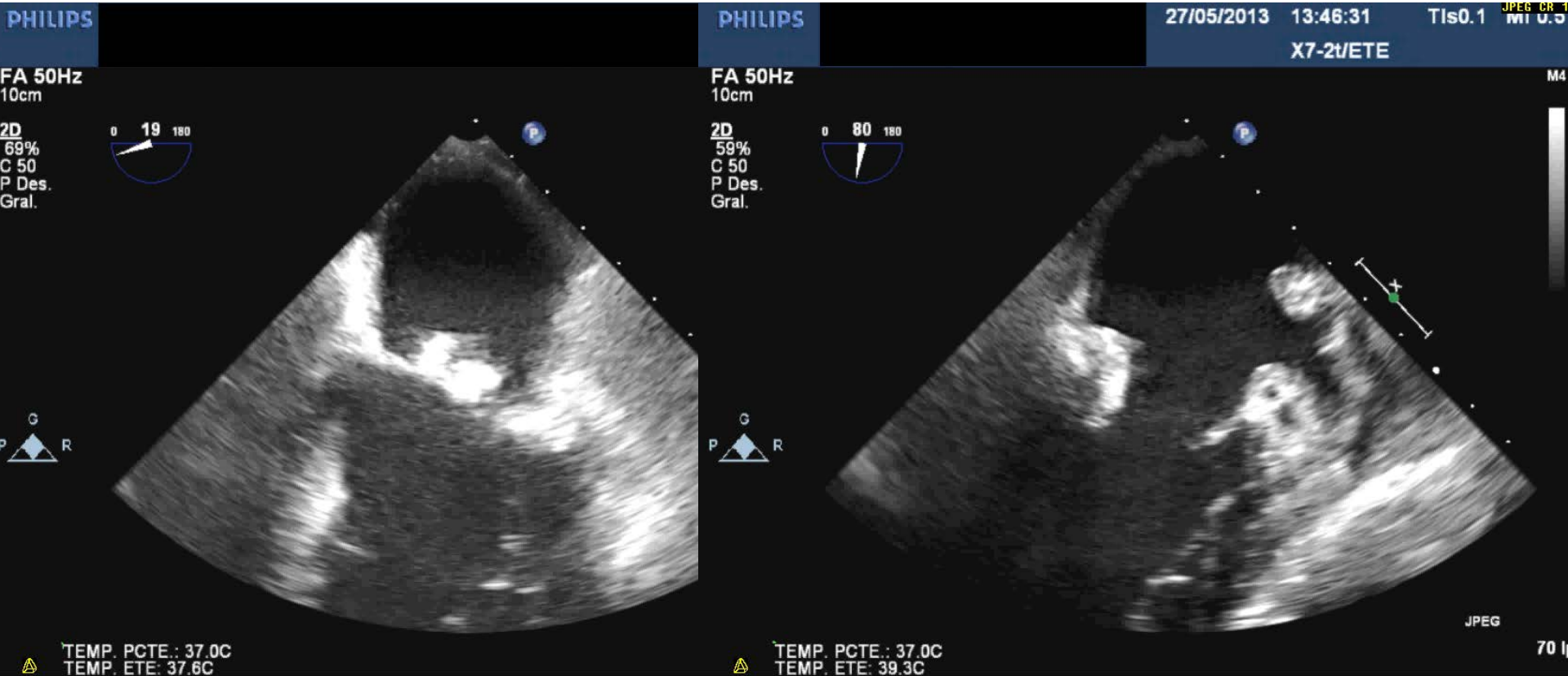
Cerebral M. R. Imaging



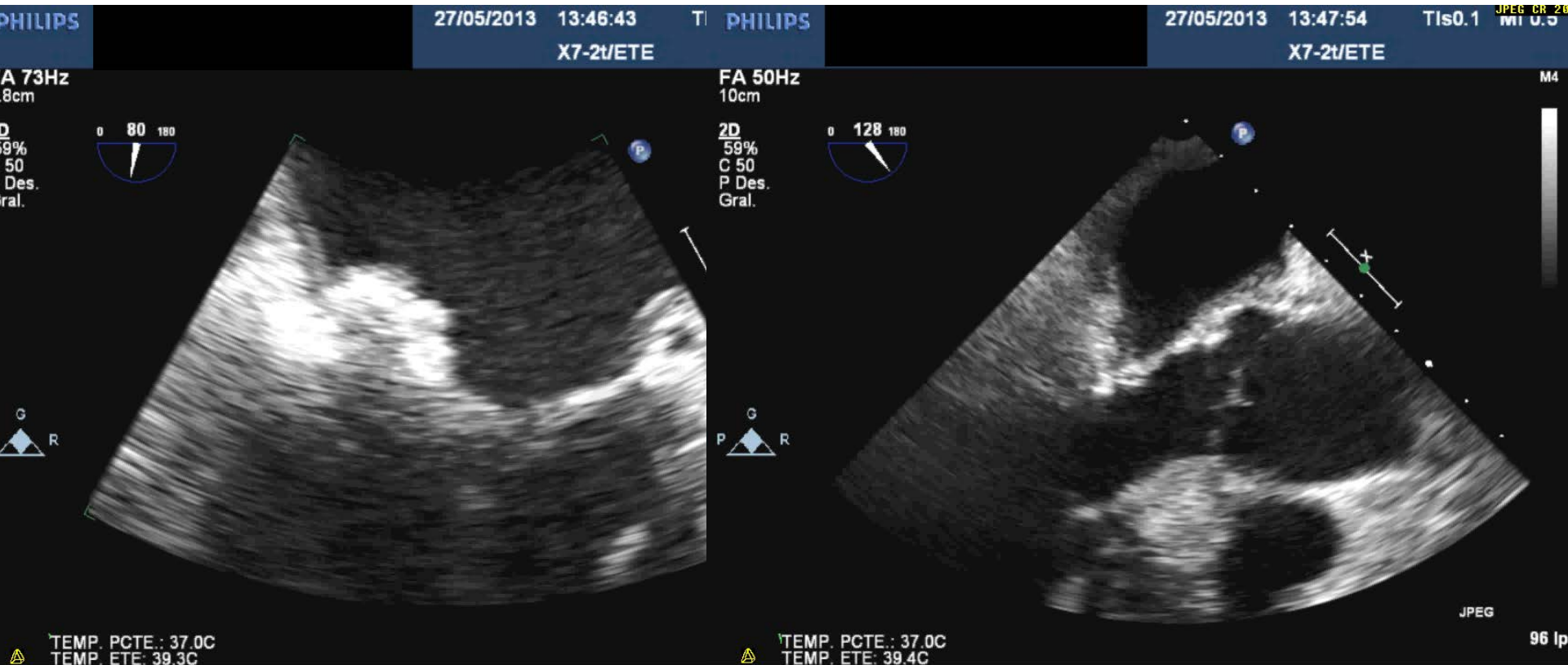
Cerebral angiography



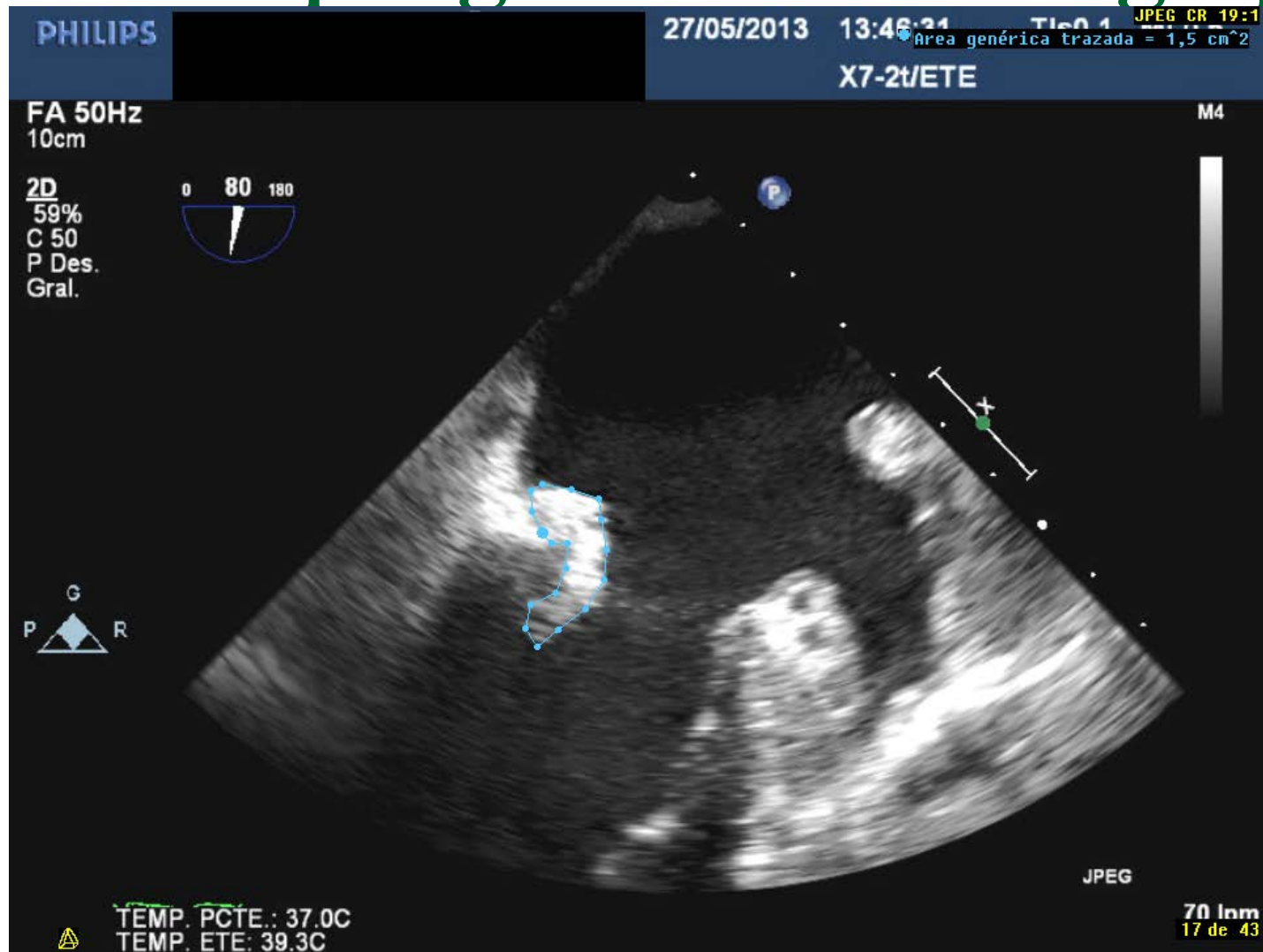
Transesophageal echocardiography



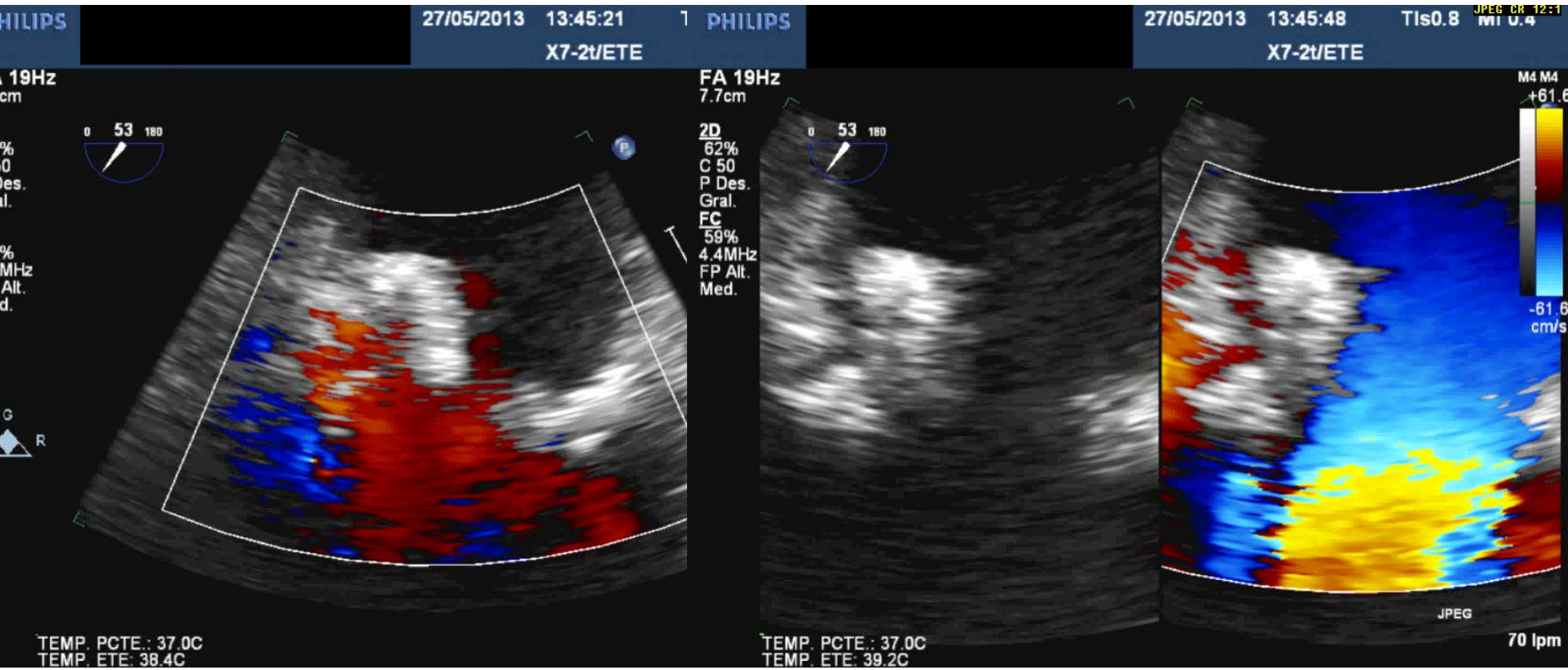
Transesophageal echocardiography



Transesophageal echocardiography



Transesophageal echocardiography



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[#]Surgery may be preferred if procedure preserving the native valve is feasible.

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

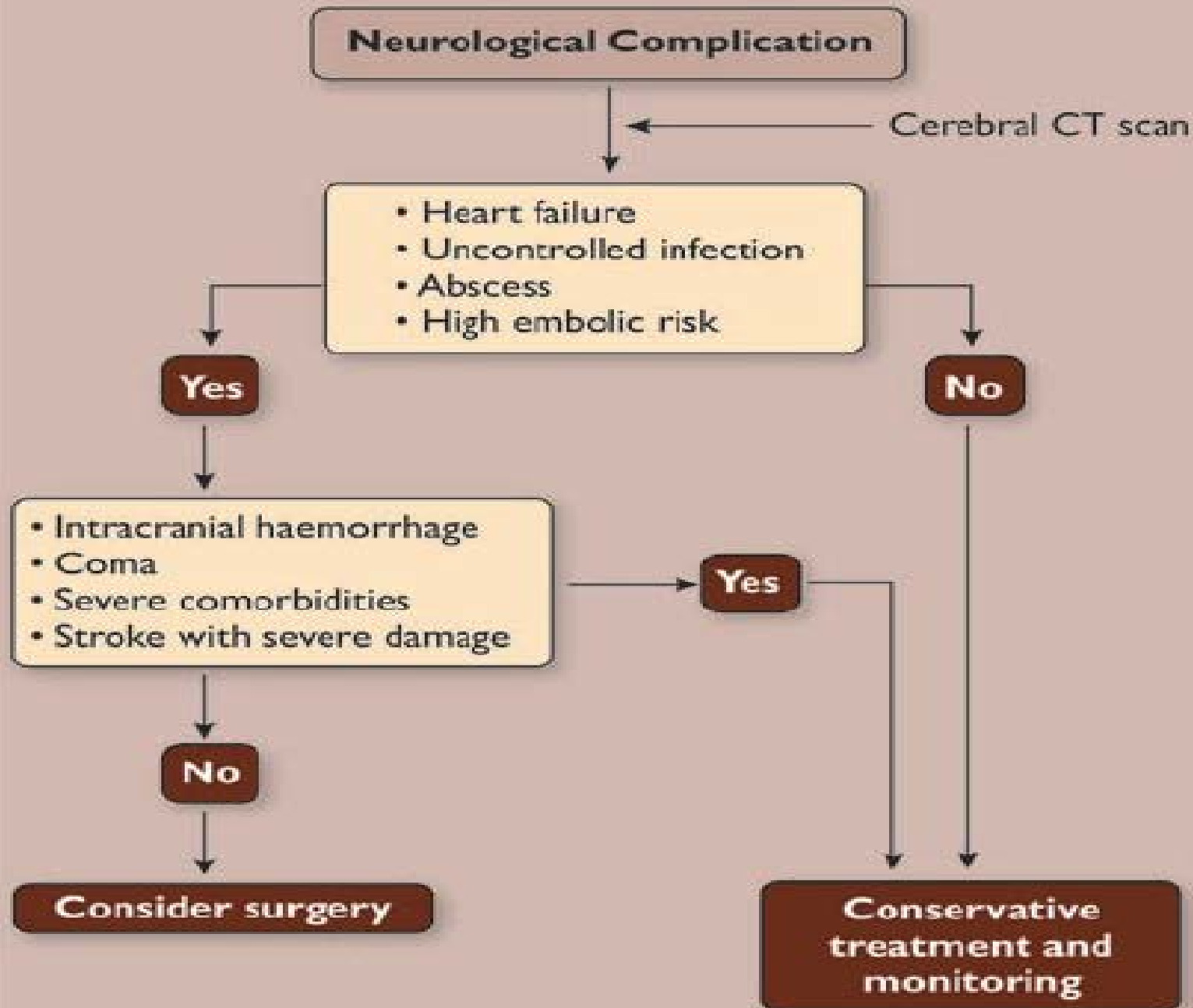
on behalf of the Group for the Study of Cardiovascular Infections of the Andalusian Society of Infectious Diseases (SAEI) and the Spanish Network for Research in Infectious Diseases (REIPI)

Circulation. published online May 6, 2013;

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539



Clinical evolution

- Mitral valve replacement: mechanical prosthesis.
 - Immediate intense rehabilitation after surgery (right hemiparesis).
 - Two years later the patient is on anticoagulants and walking with a cane.
-

Vegetation size & embolism

- Veg. size can be one of the reasons for surgery, but **is rarely the only one**.
 - **Not** all veg. sizes have the **same clinical impact**.
 - **Accuracy of veg. size** depends on the echo technique: TEE (RT3-D TEE). It is not always that easy, length, area or volume ?
 - Although surgery may be effective in reducing the risk of embolism, the **operative risk has to be balanced** against this benefit.
 - Surgical **indications** & surgical **suitability** may **vary** during the evolution of the disease.
-

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)	<i>p</i>	Adjusted HR (95% CI)	<i>p</i>
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
<i>Staphylococcus aureus</i>	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				
<i>Staphylococcus aureus</i>	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		
<i>Staphylococcus aureus</i>	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
<i>Staphylococcus aureus</i>	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

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)
<i>S. aureus</i>	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)
<i>Enterococcus spp</i>	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)

* Patients with meningitis, encephalitis and brain abscesses were excluded. Patients with neurologic complications (NC) before admission or during the first week of antimicrobial treatment were excluded.

Patients who developed NC after one week of appropriate antimicrobial treatment.

** Standardized risk differences =(Risk of NC with 1 week of appropriate antibiotic treatment- Risk of NC during the first 1 week of appropriate antibiotic treatment)/ Risk of NC during the first 1 week of appropriate antibiotic treatment
[¶] VSG *viridans*-group streptococci
[§] CNS coagulase-negative staphylococci

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)
Period					
1984-1995	208 (15)	158 (76)	50 (24)	1	1
1996-2007	1137 (85)	786 (69)	351 (31)*	1.42 (1.05-1.91)*	1.01 (0.73-1.41)
Sex					
Male	911 (67)	649 (71)	262 (29)	1	
Female	434 (33)	295 (68)	139 (32)	1.16 (0.91-1.37)	
Charlson Index, median (range)	2 (0-11)	1 (0-10)	3 (0-11)**	1.12 (1.08-1.16)**	1.06 (1.01-1.12)**
Age					
<70 years	927 (69)	699 (75)	228 (25)		
≥70 years	418 (31)	245 (59)	173 (41)**	1.83 (1.50-2.23)**	1.57 (1.23-2.01)**
Valve					
Native valve	1020 (76)	750 (74)	270 (26)	1	1
Prosthetic valve	325 (24)	194 (60)	111 (40)**		
Early	128 (39)	63 (49)	65 (51)**	2.17 (1.65-2.85)**	1.58 (1.16-2.15)**
Late	197 (61)	131 (66)	66 (33)	1.36 (1.04-1.78)*	1.49 (1.07-2.08)**
Prosthesis					
Mechanical	230 (17)	150 (65)	80 (35)	1	
Biological	95 (7)	64 (68)	31 (32)	1.20 (0.83-1.74)	
Affected valve					
Aortic	628 (47)	456 (73)	172 (27)	1	
Mitral	559 (41)	388 (69)	171 (31)	1.10 (0.89-1.36)	
Aortic and mitral	158 (12)	100 (63)	58 (37)*	1.31 (0.97-1.77)	
Causal agents					
VGS [¶]	280 (21)	241 (86)	39 (14)**	0.38 (0.28-0.54)**	
<i>S. aureus</i>	263 (20)	137 (52)	126 (48)**	2.28 (1.85-2.82)**	2.25 (1.72-2.94)**
CNS [§]	179 (13)	101 (56)	78 (44)**	1.70 (1.32-2.17)**	2.05 (1.50-2.60)**
<i>Enterococcus spp</i>	168 (12)	119 (71)	49 (29)		
Anticoagulant therapy					
Yes	241 (18)	156 (65)	85 (35)**	1.34 (1.07-1.69)**	1.21 (0.88-1.66)
No	1104 (82)	788 (71)	316 (29)	1	1
Vegetation size					
Vegetation <10 mm	669 (50)	508 (76)	161 (24)**	0.70 (0.57-0.87)**	
Vegetation ≥10 mm	447 (33)	301 (67)	146 (33)**	1.29 (1.04-1.60)*	1.25 (0.99-1.57)
Vegetation ≥20 mm	133 (10)	85 (64)	48/133 (36)*	1.35 (0.99-1.83)	
Vegetation ≥30 mm	24 (2)	15 (63)	9 (37)	1.44 (0.74-2.87)	
Surgical intervention					
Yes	523 (39)	359 (69)	164 (31)	1.06 (0.87-1.29)	
No	822 (61)	585 (71)	237 (29)	1	
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)*

Data in the first 3 columns are expressed as number (percentage). * p<0.05; ** p<0.001; ¶ VSG viridans-group streptococci § CNS coagulase-negative staphylococci † analyzed in 1256 patients; □ analyzed in 1336 patients; ‡ analyzed in 1328 patients; # A separate regression analysis was performed for each neurological complication

Table 6. Characteristics and Outcome of Patients with Valve Surgery and Neurologic Complications

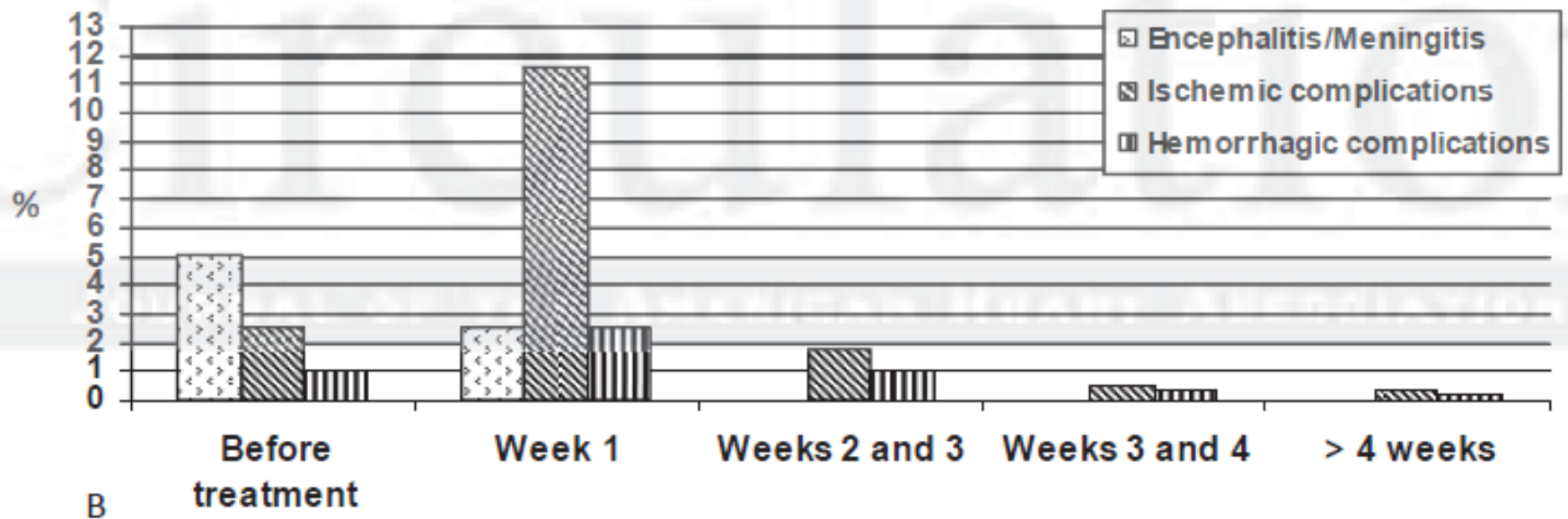
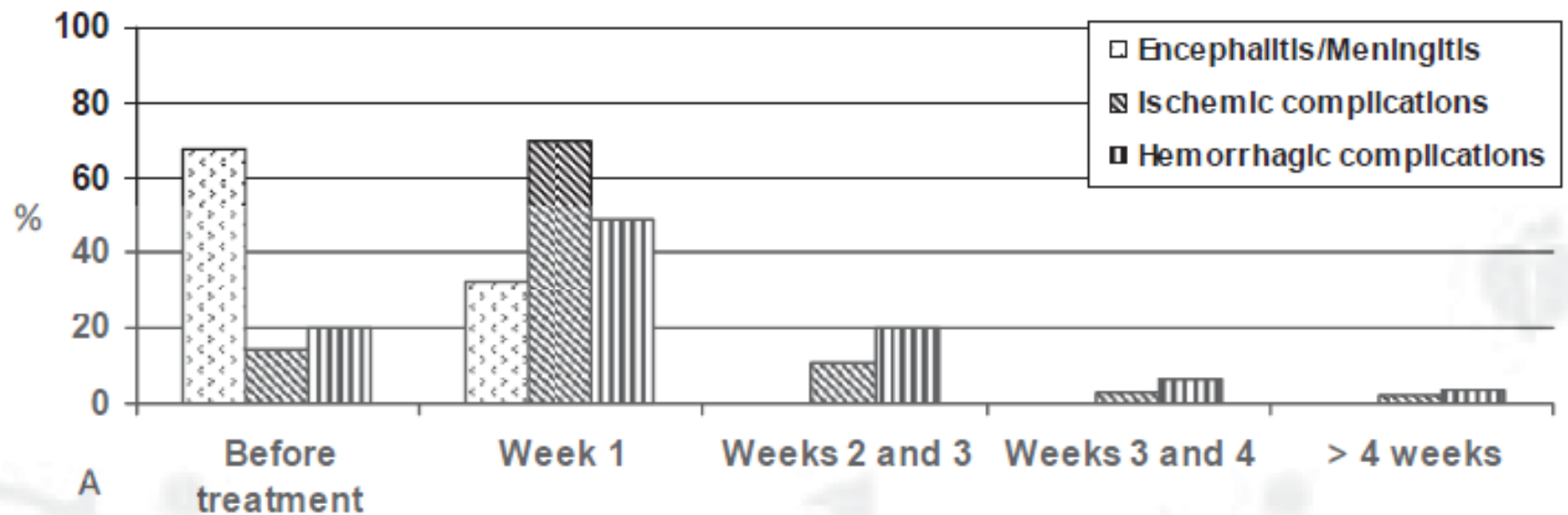
Time from the event to surgery‡	0-7 days	8-14 days	15-21 days	> 21 days	Total
n (%)	120 (24)	202 (40)	97 (20)	78 (16)	497*
EuroSCORE median (p25, p75)	10 (7, 13)	10 (7, 12)	9 (7, 11)	7 (5, 11)	9 (7, 12)
No Neurologic complications	93	164	76	60	393
Encephalitis-meningitis	5	13	2	3	23
Small ischemic	18	20	11	5	54
Moderate-severe ischemic	4	1	5	5	15
Cerebral hemorrhage	0	4	3	5	12
Bleeding/Death due to bleeding/ Total deaths					
No neurologic complications	0/0/28	6/5/49	1/1/21	1/1/14	8/7/112
Encephalitis-meningitis	0/0/3	4/3/6	0/0/0	0/0/1	4/3/10
Small ischemic	2/2/10	2/1/8	3/3/5	0/0/3	7/6/26
Moderate-severe ischemic	1/1/2	0/0/0	1/1/2	0/0/0	2/2/4
Cerebral hemorrhage	0/0/0	2/2/3	1/1/2	1/1/2	4/4/7

‡ In this row, the times indicated refer to time to surgery. *In 26 patients the date of surgery was not recorded

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Moderate-severe ischemic	1/1/2	0/0/0	1/1/2	0/0/0	2/2/4
Cerebral hemorrhage	0/0/0	2/2/3	1/1/2	1/1/2	4/4/7

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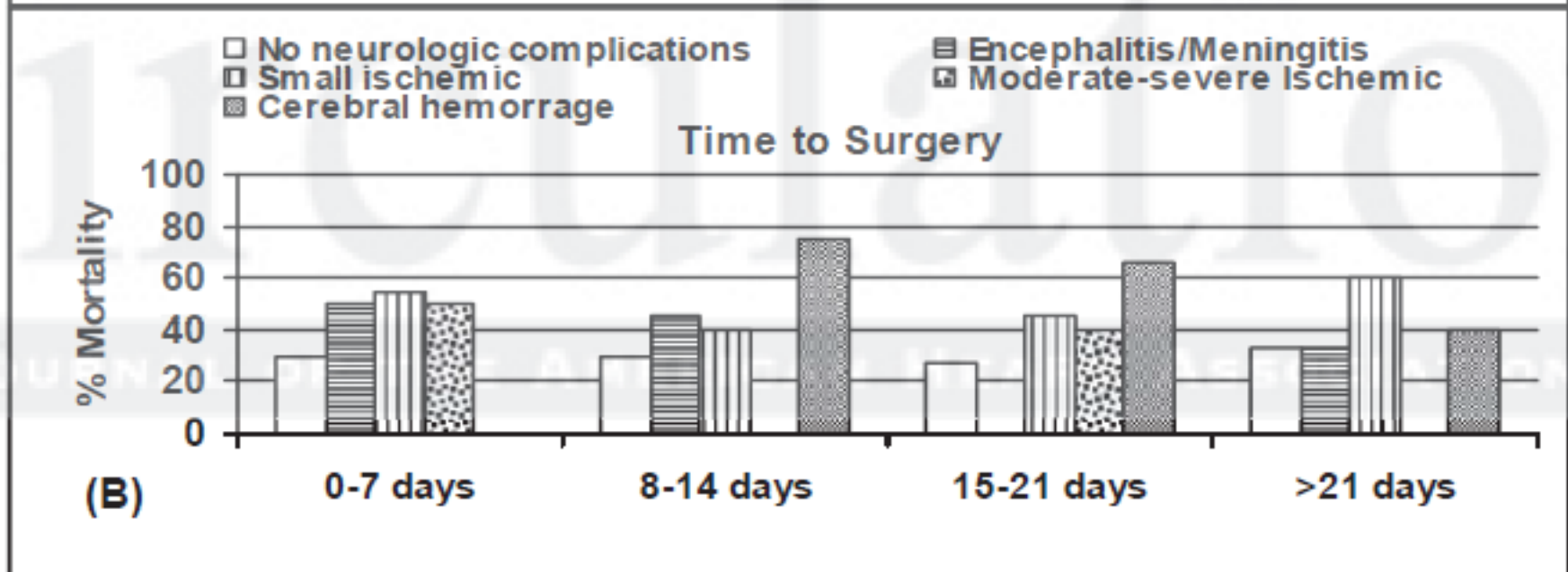
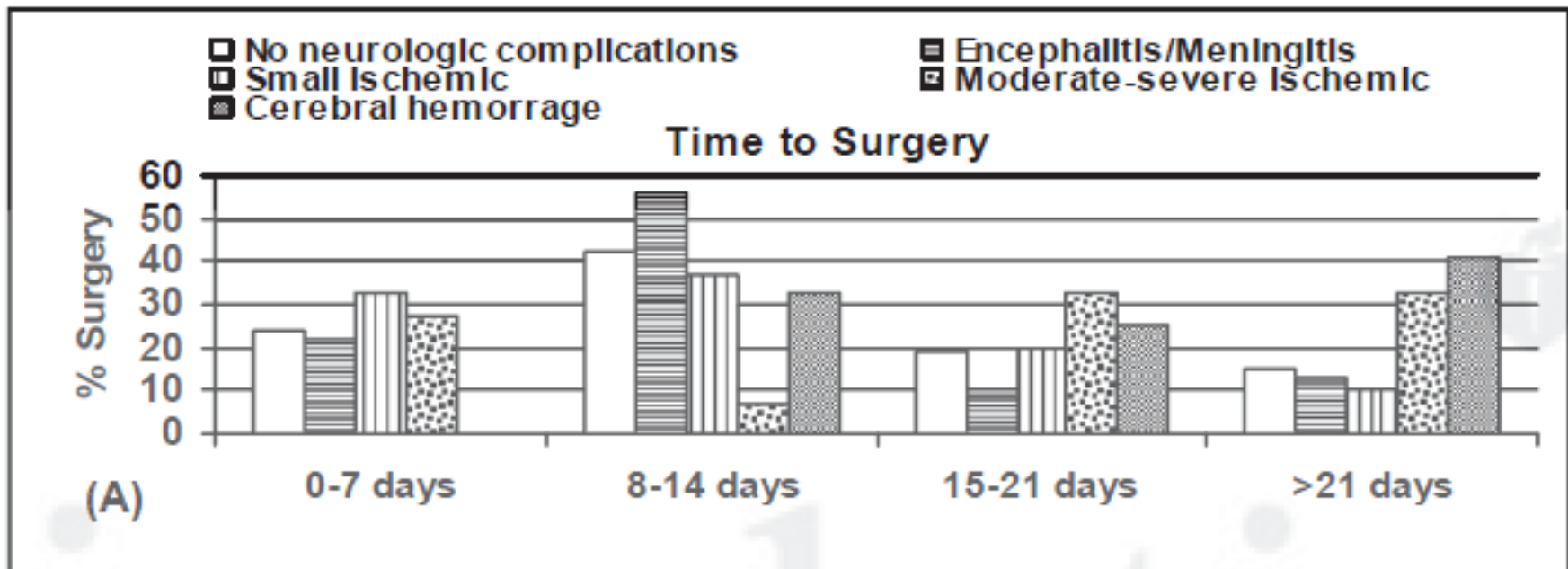


Table 2. Main characteristics of patients in the two registries

Demographic Data	Andalusian hospitals (N=1018) N (%) [95% CI]	Vall d'Hebron Hospital (N=327) N (%) [95% CI]
Male sex	694 (68) [65-71]	217 (66) [61-71]
Age, median (IQR), y	59 (25)	66 (23.5)
Elderly (≥ 70 years)	290 (28) [26-31]	128 (39) [34-45]
Charlson Index, median (range)	1 (0-10)	2 (0-11)
Type of infective endocarditis		
Native valve IE	762 (75) [72-77]	258 (79) [74-83]
Early prosthetic valve IE	99 (10) [8-12]	29 (9) [6-12]
Late prosthetic valve IE	157 (15) [13-17]	40 (12) [9-16]
Affected valve		
Aortic	472 (46) [43-49]	156 (48) [42-53]
Mitral	431 (42) [39-45]	128 (39) [34-44]
Aortic and mitral	115 (11) [9-13]	43 (13) [10-17]
Etiological Agents		
VGS	208 (20) [18-23]	73 (22) [18-27]
<i>Staphylococcus aureus</i>	198 (19) [17-22]	65 (20) [16-25]
CNS	148 (14) [12-17]	31 (9) [7-13]
<i>Enterococcus</i> spp.	120 (12) [10-14]	48 (15) [11-19]
Unknown etiology	108 (11) [9-13]	22 (7) [4-10]
Cardiac surgery	394 (39) [36-42]	129 (39) [34-45]
Early mortality	313 (31) [28-34]	88 (27) [22-32]

VGS, viridans group streptococci; CNS, coagulase-negative staphylococci

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

*Severe valvular regurgitation, abscess, or fistula

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)	<i>p</i>	Adjusted HR (95% CI)	<i>p</i>
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
<i>Staphylococcus aureus</i>	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				
<i>Staphylococcus aureus</i>	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		
<i>Staphylococcus aureus</i>	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
<i>Staphylococcus aureus</i>	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

Endocarditis

Risk of Embolization After Institution of Antibiotic Therapy for Infective Endocarditis

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