II CONGRESO
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BILBAO 2013
Palacio Euskalduna
27/28 de septiembre

MANEJO INTERVENCIONISTA DE LA ENDOCARDITIS INFECCIOSA

Vegetación y cirugía. ¿Importa el tamaño?

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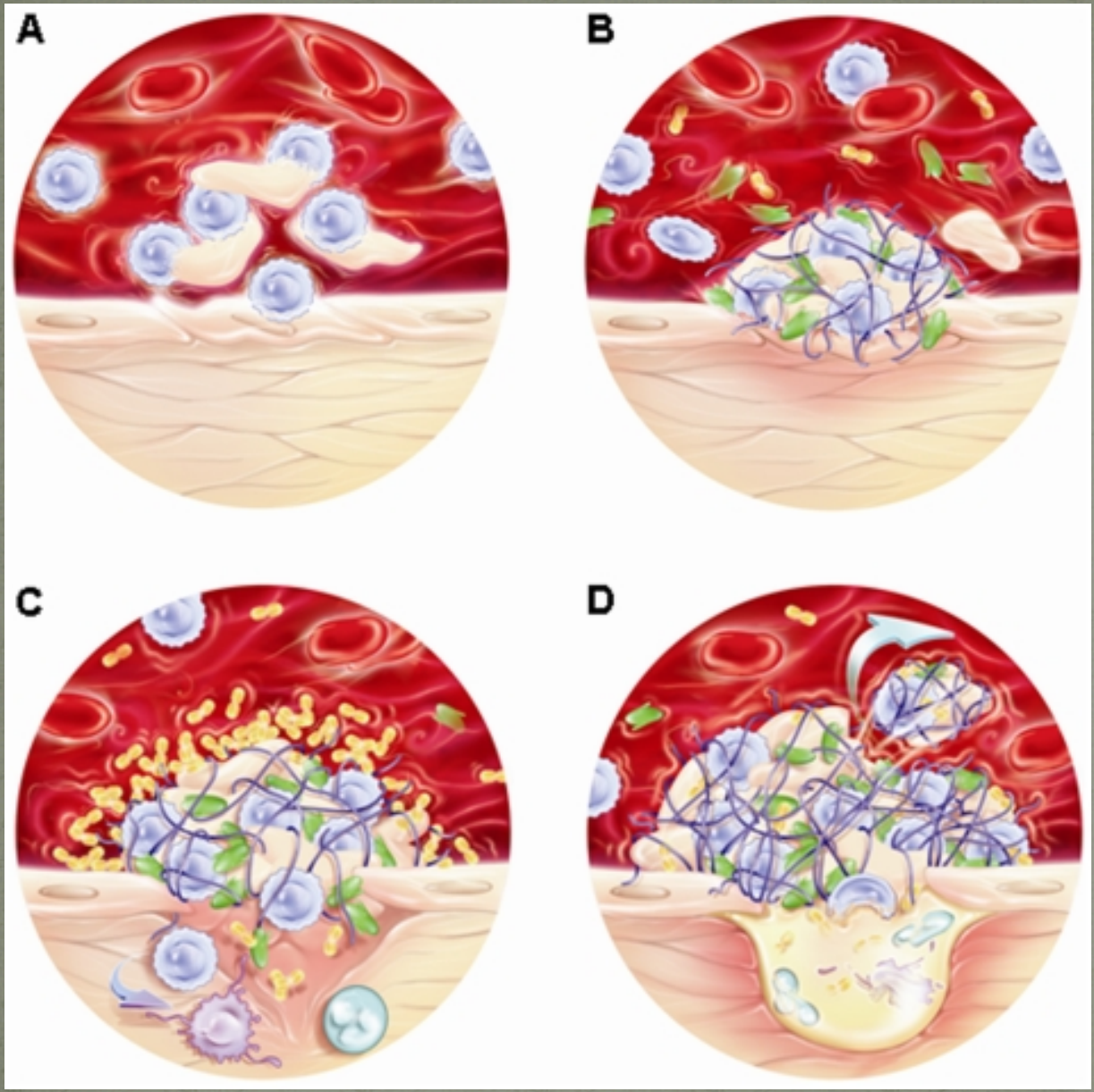
SEICAV
Sociedad Española de Infecciones Cardiovasculares

Mi mujer es rara de cojones...
Por favor
Mea sentado



EVENTO EMBÓLICO:

- ✓ **Hemodinámico:**
  - **Fragmentación Vegetación.**
- ✓ **Protrombosis.**
- ✓ **Bioenzimático:**
  - **Fragilidad vegetación.**
  - **Destrucción tisular.**

Eventos Embólicos en EI

- 20 - 80 % pacientes.
- Elevada morbi-mortalidad.
- Asintomáticos 20 % pacientes.
- Dos tipos:
  - A-AB: Mas frecuentes. Previenen con diagnóstico precoz.
  - D-AB (New EE): 6 - 21 % pacientes s/t primera semana. Previenen con cirugía precoz.

Predicción Riesgo "Nuevo EE"

1. Tamaño y movilidad de la vegetación.
2. Vegetación mitral.
3. Variación tamaño vegetación en terapia antibiótica.
4. Microorganismos: Staph. Strep. Cand.
5. Embolia previa.
6. EI multivalvular.
7. Marcadores biológicos.

Predicción Riesgo "Nuevo EE" para EI nativa:

1. **Tamaño y movilidad de la vegetación:**
   - vegetaciones de longitud > 10 mm.
   - Impacto en supervivencia a 1 año vegetaciones muy grandes (> 15 mm) y móviles.

Risk of Embolism and Death in Infective Endocarditis: Prognostic Value of Echocardiography

A Prospective Multicenter Study

Thuny et al (*Circulation*. 2005;112:69-75.)

Predicción Riesgo "Nuevo EE" para EI nativa:

Embolic Events During Antibiotic Therapy

New-EE occurred in 28 patients (7.3%). Sites of embolization were central nervous system (14 cases), spleen (9 cases), kidney (5 cases), peripheral arteries (5 cases), eye (2 cases), coronary circulation (2 cases), and pulmonary circulation (2 cases). These events occurred at a median time of 7 days (range, 1 to 38) after institution of adequate antibiotic therapy (20 [71.4%] in the first 15 days).

Thuny et al Prognosis of Infective Endocarditis

(*Circulation*. 2005;112:69-75.)

TABLA 19. **Indicaciones y momento de cirugía en la endocarditis infecciosa sobre válvula nativa izquierda**

Recomendaciones: indicaciones para la cirugía	Momento[a]	Clase[b]	Nivel[c]
C. Prevención de embolias			
El aórtica o mitral con vegetaciones grandes (> 10 mm) con uno o más episodios embólicos a pesar de la terapia antibiótica adecuada	Urgencia	I	B
El aórtica o mitral con vegetaciones grandes (> 10 mm) y otros indicadores de evolución complicada (insuficiencia cardiaca, infección persistente, absceso)	Urgencia	I	C
Vegetaciones muy grandes aisladas (> 15 mm)[d]	Urgencia	IIb	C

[a]Cirugía de emergencia: cirugía llevada a cabo en las primeras 24 h, cirugía de urgencia: en unos pocos días, cirugía electiva: después de al menos 1 o 2 semanas de terapia antibiótica.
[b]Clase de recomendación.
[c]Nivel de evidencia.
[d]La cirugía será la mejor opción si el procedimiento que protege la válvula nativa es factible.

Habib G et al. Guía de práctica clínica para prevención, diagnóstico y tratamiento de la endocarditis infecciosa (nueva versión 2009)

Rev Esp Cardiol. 2009;62(12):1465.e1-.e54

Predicción Riesgo Embólico: Marcadores biológicos (I)

Circulating Matrix Metalloproteinases in Infective Endocarditis: A Possible Marker of the Embolic Risk

Results: MMP-9 serum level was significantly higher in patients with new-EE compared to controls (median [interquartile range]; 250 ng/mL [175–455] *vs.* 111 ng/mL [70–144], respectively; $p<0.0001$) and patients with no new-EE (250 ng/mL [175–455] *vs.* 138 ng/mL [95–232]; $p<0.01$). A higher MMP-9 activity in patients who experienced new-EE was further confirmed by gelatin zymography analysis. Circulating MMP-9 remains a predictor of new-EE after adjustment for vegetation length and other potential confounders. This parameter provided incremental predictive value over vegetation measurements.

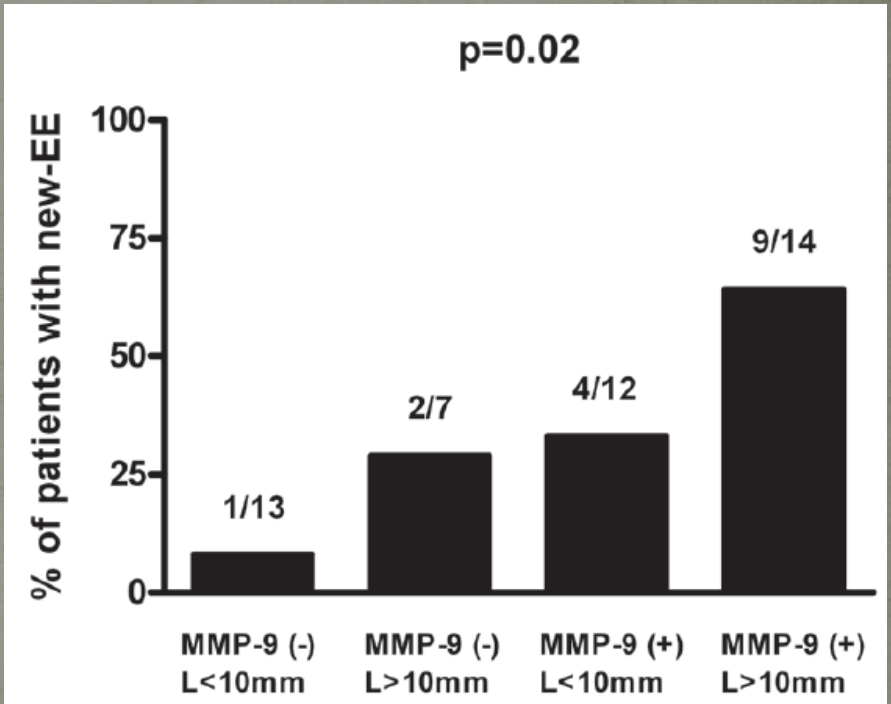
Conclusions: MMP-9 serum level is associated with the risk of embolism during IE. This marker might help physicians in the management of the disease, but further propspective studies are need to confirm these preliminary results.

Thuny F. PloS one 2011;6:e18830.

Predicción Riesgo Embólico: Marcadores biológicos (II)

Table 3. Predictive Values of The Different Risk Stratification Strategies.

	PPV (%)	NPV (%)	OR (95% CI)	p
Vegetation length >10 mm	43	78	4.4 (1.2 to 16.2)	0.03
MMP-9>167 ng/mL	50	85	5.7 (1.3 to 24.1)	0.02
Vegetation length >10 mm and MMP-9>167 ng/mL	64	78	6.4 (1.6 to 25.5)	0.008



Thuny F. PloS one 2011;6:e18830.

Extensión de la Indicación Quirúrgica para prevenir "Nuevo EE" en EI

Early Surgery versus Conventional Treatment for Infective Endocarditis

N Engl J Med 2012;366:2466-73.

Prediction of Symptomatic Embolism in Infective Endocarditis: Construction and Validation of a Risk Calculator in a Multicenter Cohort

Hubert S. J Am Coll Cardiol (2013), doi: 10.1016/j.jacc.2013.07.029

Early Surgery versus Conventional Treatment for Infective Endocarditis

STUDY END POINTS

The primary end point was a composite of in-hospital death or clinical embolic events that occurred within 6 weeks after randomization. An specified secondary end points, at 6 months of follow-up, included death from any cause, embolic events, recurrence of infective endocarditis, and repeat hospitalization due to the development of congestive heart failure.

N Engl J Med 2012;366:2466-73.

Early Surgery versus Conventional Treatment for Infective Endocarditis

Selección de Pacientes

- **Endocarditis izquierda nativa**, según criterios de DuKe modificados, que en el **momento del diagnóstico** presentan **Valvulopatía severa sin complicaciones** y alto riesgo embólico por **Vegetación > 10 mm.**

N Engl J Med 2012;366:2466-73.

TABLA 19. **Indicaciones y momento de cirugía en la endocarditis infecciosa sobre válvula nativa izquierda**

Recomendaciones: indicaciones para la cirugía	Momento[a]	Clase[b]	Nivel[c]
A. Insuficiencia cardiaca			
El aórtica o mitral con regurgitación aguda grave u obstrucción de la válvula que causa edema pulmonar persistente o shock cardiogénico	Emergencia	I	B
El aórtica o mitral con fístula en cámara cardiaca o pericardio que causa edema pulmonar persistente o shock	Emergencia	I	B
El aórtica o mitral con regurgitación aguda grave u obstrucción de la válvula e insuficiencia cardiaca persistente o signos ecocardiográficos de mala tolerancia hemodinámica (cierre mitral precoz o hipertensión pulmonar)	Urgencia	I	B
El aórtica o mitral con regurgitación grave y sin insuficiencia cardiaca	Electiva	IIa	B
B. Infección incontrolada			
Infección localmente incontrolada (absceso, seudoaneurisma, fístula, vegetación en aumento)	Urgencia	I	B
Fiebre persistente y hemocultivos positivos > 7-10 días	Urgencia	I	B
Infección causada por hongos u organismos multirresistentes	Urgencia/electiva	I	B
C. Prevención de embolias			
El aórtica o mitral con vegetaciones grandes (> 10 mm) con uno o más episodios embólicos a pesar de la terapia antibiótica adecuada	Urgencia	I	B
El aórtica o mitral con vegetaciones grandes (> 10 mm) y otros indicadores de evolución complicada (insuficiencia cardiaca, infección persistente, absceso)	Urgencia	I	C
Vegetaciones muy grandes aisladas (> 15 mm)[d]	Urgencia	IIb	C

[a]Cirugía de emergencia: cirugía llevada a cabo en las primeras 24 h, cirugía de urgencia: en unos pocos días, cirugía electiva: después de al menos 1 o 2 semanas de terapia antibiótica.
[b]Clase de recomendación.
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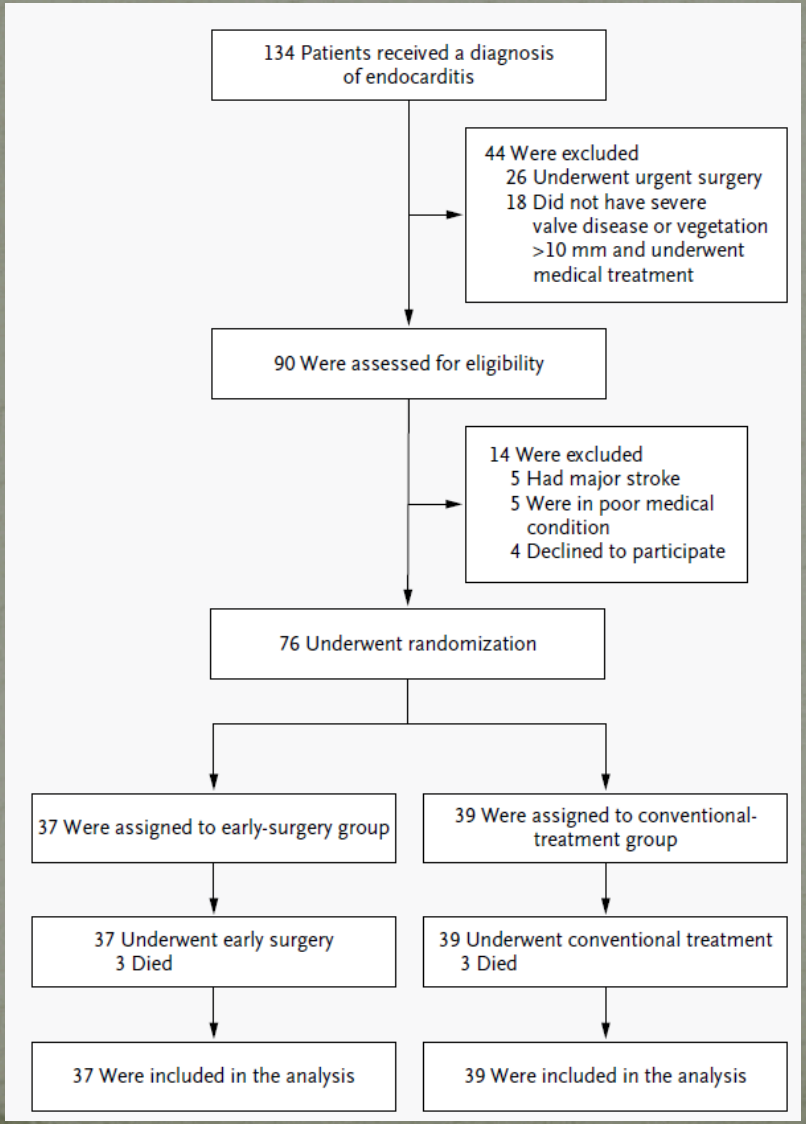
Rev Esp Cardiol. 2009;62(12):1465.e1-.e54

Early Surgery versus Conventional Treatment for Infective Endocarditis

carditis,[9] patients were excluded if they had moderate-to-severe congestive heart failure, infective endocarditis complicated by heart block, annular or aortic abscess, destructive penetrating lesions requiring urgent surgery, or fungal endocarditis. Other exclusion criteria were an age of more than 80 years, coexisting major embolic stroke with a risk of hemorrhagic transformation at the time of diagnosis, and a serious coexisting condition (e.g., cancer) (Fig. 1). Patients were also excluded if they had infective endocarditis involving a prosthetic valve, right-sided vegetations, or small vegetations (diameter, ≤10 mm)

N Engl J Med 2012;366:2466-73.

Early Surgery versus Conventional Treatment for Infective Endocarditis



N Engl J Med 2012;366:2466-73.

Early Surgery versus Conventional Treatment for Infective Endocarditis

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)

N Engl J Med 2012;366:2466-73.

Early Surgery versus Conventional Treatment for Infective Endocarditis

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

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Early Surgery versus Conventional Treatment for Infective Endocarditis

SURGICAL PROCEDURES

All patients in the early-surgery group underwent valve surgery within 48 hours after randomization; the median time between randomization and surgery was 24 hours (interquartile range, 7 to 45). Of the 22 patients with involvement of the mitral valve, 8 patients underwent mitral-valve repair and 14 underwent mitral-valve replacement with a mechanical valve. Of the 15 patients with involvement of the aortic valve or both the mitral and aortic valves, 14 underwent mechanical-valve replacement and 1 underwent valve replacement with a biologic prosthesis. Concomitant coronary-artery bypass grafting at the time of valve surgery was performed in 2 patients (5%).

Of the 39 patients assigned to the conventional-treatment group, 30 (77%) underwent surgery during the initial hospitalization (27 patients) or during follow-up (3). The surgical procedures included 11 mitral-valve repairs, 6 mitral-valve replacements (with 5 patients receiving a mechanical valve and 1 a biologic prosthesis), 11 aortic-valve replacements (with 9 patients receiving a mechanical valve and 2 a biologic prosthesis), and 2 combined aortic-valve replacements (with 1 patient receiving a mechanical valve and 1 a biologic prosthesis) and mitral-valve repairs. In 8 patients (21%), indications for urgent surgery

N Engl J Med 2012;366:2466-73.

Early Surgery versus Conventional Treatment for Infective Endocarditis

Our study has several limitations. The trial was limited in scope, in that it included patients with severe valvular disease and large vegetations and excluded those with major stroke, infective endocarditis involving a prosthetic valve, or aortic abscess. Our exclusion criteria also affected the relative frequencies of causative microorganisms, and the incidence of infective endocarditis due to *S. aureus* was lower than that in previous studies.[1,21] The risk–benefit ratio of early surgery over conventional treatment may differ according to the type of high-risk situation and the causative organism. The rate of death within 30 days after

In conclusion, early surgery, as compared with conventional treatment, significantly reduced the composite end point of death from any cause or embolic events by effectively reducing the risk of systemic embolism among patients with infective endocarditis and large vegetations.

- EI estreptococicas.
- Afectación valvular severa sin ICC.
- Bajo riesgo quirúrgico.
- < probabilidad reparación mitral.

N Engl J Med 2012;366:2466-73.

Prediction of Symptomatic Embolism in Infective Endocarditis: Construction and Validation of a Risk Calculator in a Multicenter Cohort

Table 1. Baseline Characteristics of Patients with Infective Endocarditis

	Total Cohort (n=847)	Development Sample (n=565)	Validation Sample (n=282)	p Value *
Center				
Marseille	598 (70.6)	401 (71.0)	197 (69.9)	
Amiens	249 (29.4)	164 (29.0)	85 (30.1)	0.73
Clinical data				
Age (years)	62.3 ± 15	62.7 ± 15	61.6 ± 15.6	0.31
Male gender	606 (71.6)	402 (71.2)	204 (72.3)	0.72
Diabetes	140 (16.5)	95 (16.8)	45 (16.0)	0.75
History of Cancer	126 (14.9)	87 (15.4)	39 (13.8)	0.54
Intravenous drug use	42 (5.0)	27 (4.8)	15 (5.3)	0.80
Previous heart disease	493 (58.2)	331 (58.6)	162 (57.5)	0.75
Atrial fibrillation	121 (14.3)	80 (14.2)	41 (14.5)	0.88
Heart failure	317 (37.4)	221 (39.1)	96 (34.0)	0.15
* Previous embolism	318 (38.2)	212 (38.3)	106 (38.0)	0.93
Ischemic stroke	180 (21.3)	117 (20.7)	63 (22.3)	0.58
Cerebral hemorrhage	47 (5.6)	28 (5.0)	19 (6.7)	0.28
Charlson score index	3.2 ± 2.4	3.3 ± 2.4	3.1 ± 2.4	0.19
Aspirin	10.8 (12.8)	72 (12.8)	36 (12.8)	0.99
Anticoagulant therapy	155 (18.3)	108 (19.1)	47 (16.7)	0.39

MANUSCRIPT

* 134 (42%) EE sintomáticos

Hubert S. J Am Coll Cardiol (2013), doi: 10.1016/j.jacc.2013.07.029

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	Total Cohort (n=847)	Development Sample (n=565)	Validation Sample (n=282)	p Value *
Localization				
Prosthetic valve	226 (26.7)	149 (26.4)	77 (27.3)	0.77
Multivalvular	172 (20.3)	119 (21.1)	53 (18.8)	0.44
Aortic	517 (61.0)	351 (62.1)	166 (58.9)	0.36
Mitral	474 (56.0)	318 (56.3)	156 (55.3)	0.79
Tricuspid	22 (2.6)	15 (2.7)	7 (2.5)	0.88
Echocardiography				
Vegetation length (mm)	11.7 ± 9	11.6 ± 8.9	11.9 ± 9.3	0.64
Vegetation length (stratified)				0.86
Absence of vegetation	136 (16.0)	88 (15.6)	48 (17.0)	
Vegetation ≤10 mm	220 (26.0)	148 (26.2)	72 (25.5)	
Vegetation >10 mm	491 (58.0)	329 (58.2)	162 (57.5)	
Periannular complications	224 (26.5)	157 (27.8)	67 (23.8)	
Left ventricle ejection fraction< 45%	67 (7.9)	47 (8.3)	20 (7.0)	0.53
Severe regurgitation	423 (49.9)	294 (52.0)	129 (45.7)	0.08

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Table 1. Baseline Characteristics of Patients with Infective Endocarditis

	Total Cohort (n=847)	Development Sample (n=565)	Validation Sample (n=282)	p Value *
Causative microorganism				
Oral streptococci	135 (15.9)	96 (17.0)	39 (13.8)	0.23
Streptococcus bovis	148 (17.5)	91 (16.1)	57 (20.2)	0.14
Staphylococcus aureus	145 (17.1)	99 (17.5)	46 (16.3)	0.66
Coagulase negative staphylococci	72 (8.5)	42 (7.4)	30 (10.6)	0.12
Enterococci	105 (12.4)	72 (12.7)	33 (11.7)	0.66
Fungi	9 (1.1)	6 (1.1)	3 (1.1)	0.99
Others	104 (12.3)	73 (12.9)	31 (11.0)	0.42
No identification	129 (15.2)	86 (15.3)	43 (15.3)	0.34

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Prediction of Symptomatic Embolism in Infective Endocarditis: Construction and Validation of a Risk Calculator in a Multicenter Cohort

TRATAMIENTO QUIRÚRGICO

- 493 (58%) pacientes tras 10 días de media (IQR 3-27) de tratamiento antibiótico:
  - 227 (46%) con ICC.
  - 173 (35%) con complicaciones perianulares.
  - 185 (36%) con vegetación grande +/- EE previo.
  - 89 (18% operados y 11% total) único criterio vegetación grande +/- EE previo.

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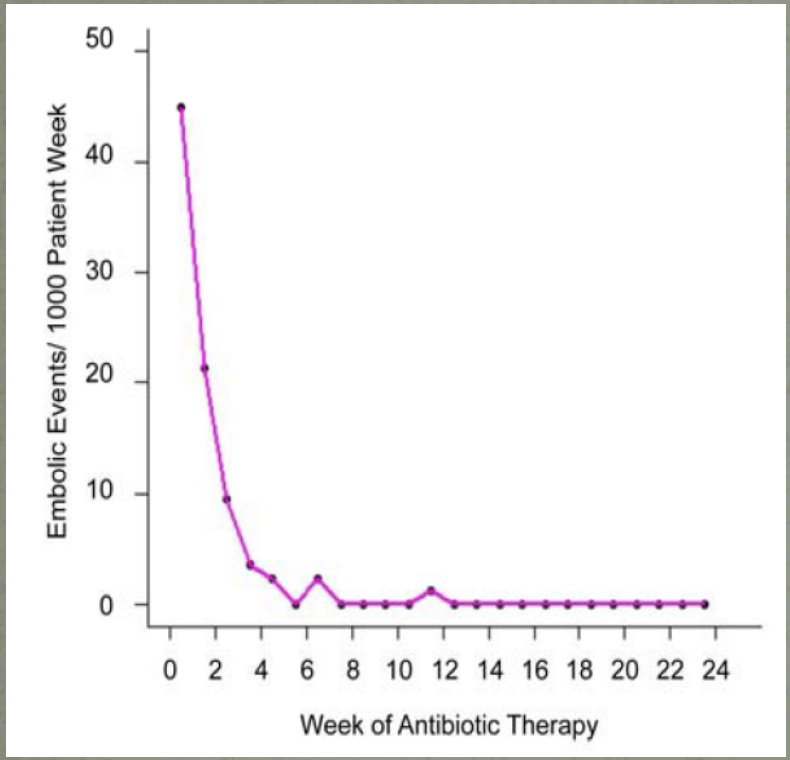
Prediction of Symptomatic Embolism in Infective Endocarditis: Construction and Validation of a Risk Calculator in a Multicenter Cohort

Incidence of Embolic Events According to Competing Risks



- **72 (8,9 %) pacientes:**
  - SNC 36
  - Periféricas 16
  - Bazo 10
  - Riñón 4
  - Ojo 2
  - Coronarias 2
  - Mesentéricas 2

- **Cirugía 61,7 %.**
- **Muerte 20 %.**

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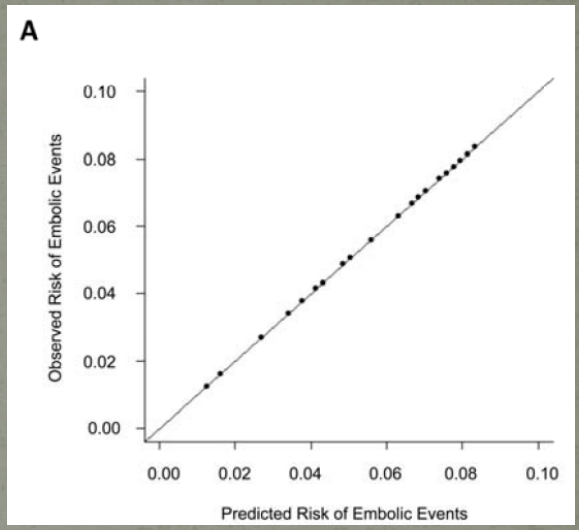
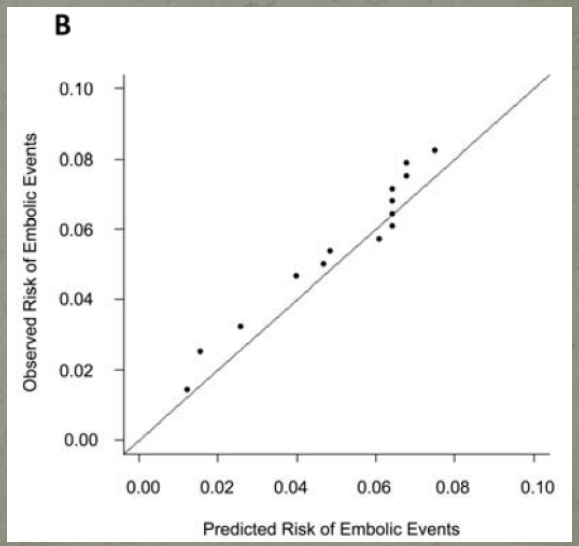
Prediction of Symptomatic Embolism in Infective Endocarditis: Construction and Validation of a Risk Calculator in a Multicenter Cohort

Table 2 Predictive Variables for Embolic Events (Development Sample).

Age	0.01315524
Diabetes	0.26509903
Previous embolism	0.33690184
Atrial fibrillation	0.50552733
Vegetation length (stratified)*	
>0 to ≤10 mm	0.23113278
> 10 mm	1.49626773
Staphylococcus aureus	0.57917495





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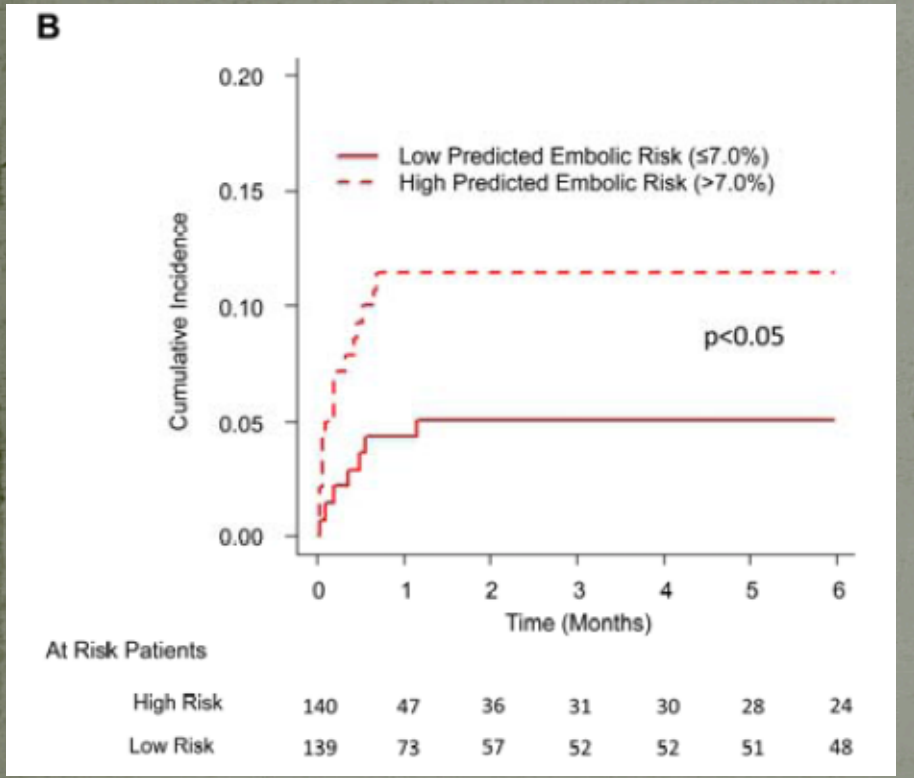

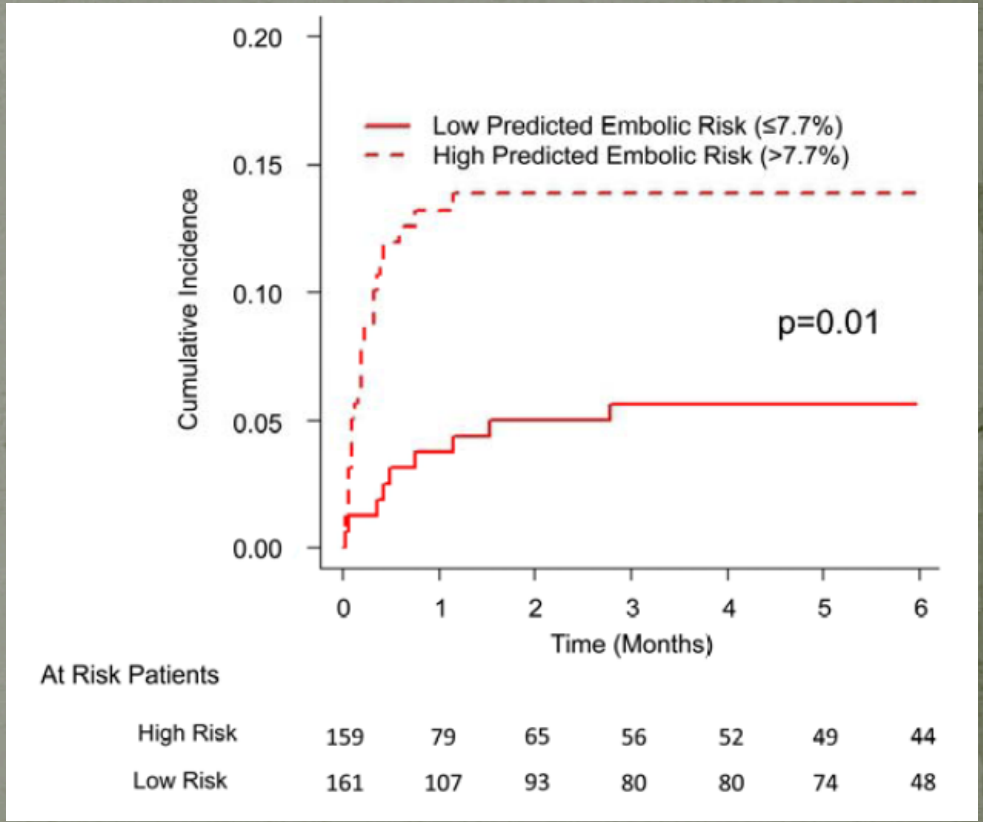

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Prediction of Symptomatic Embolism in Infective Endocarditis: Construction and Validation of a Risk Calculator in a Multicenter Cohort

Risk Calculator for 6-Month Embolic Risk for Infective Endocarditis

Google: Embolic Risk French Calculator

DATA AT ADMISSION

Clinical Data	Age (years)	75
	Diabetes (0: no ; 1: yes)	1
	Previous embolism (0: no ; 1: yes)	1
	Atrial fibrillation (0: no ; 1: yes)	0
Echocardiography		
	Vegetation >0 to ≤10 mm (0: no ; 1: yes)	0
	Vegetation >10 mm (0: no ; 1: yes)	1
Microorganism		
	Staphylococcus aureus (0: no ; 1: yes)	1

PREDICTED EMBOLIC RISK CALCULATION

Time (Days)	Predicted Embolic Risk
1	5%
2	6%
3	10%
4	13%
5	14%
6	15%
7	16%
10	18%
11	18%
12	20%
13	22%
14	24%
18	24%
19	25%
23	26%
28	27%
35	27%
47	28%
48	28%
180	29%

Clinical Data	Age (years)	70
	Diabetes (0: no ; 1: yes)	0
	Previous embolism (0: no ; 1: yes)	0
	Atrial fibrillation (0: no ; 1: yes)	0
Echocardiography		
	Vegetation >0 to ≤10 mm (0: no ; 1: yes)	0
	Vegetation >10 mm (0: no ; 1: yes)	0
Microorganism		
	Staphylococcus aureus (0: no ; 1: yes)	0

PREDICTED EMBOLIC RISK CALCULATION

Time (Days)	Predicted Embolic Risk
1	0%
2	0%
3	1%
4	1%
5	1%
6	1%
7	1%
10	1%
11	1%
12	1%
13	2%
14	2%
18	2%
19	2%
23	2%
28	2%
35	2%
47	2%
48	2%
180	2%

Conclusions: The risk of embolism during infective endocarditis can be quantified at admission by a simple and accurate calculator. It might be useful for facilitating therapeutic decisions.

ACCEPTED MANUSCRIPT

TABLA 19. **Indicaciones y momento de cirugía en la endocarditis infecciosa sobre válvula nativa izquierda**

Recomendaciones: indicaciones para la cirugía	Momento[a]	Clase[b]	Nivel[c]
C. Prevención de embolias			
EI aórtica o mitral con vegetaciones grandes (> 10 mm) con uno o más episodios embólicos a pesar de la terapia antibiótica adecuada	Urgencia	I	B
EI aórtica o mitral con vegetaciones grandes (> 10 mm) y otros indicadores de evolución complicada (insuficiencia cardiaca, infección persistente, absceso)	Urgencia	I	C
Vegetaciones muy grandes aisladas (> 15 mm)[d]	Urgencia	IIb	C

[a]Cirugía de emergencia: cirugía llevada a cabo en las primeras 24 h, cirugía de urgencia: en unos pocos días, cirugía electiva: después de al menos 1 o 2 semanas de terapia antibiótica.
[b]Clase de recomendación.
[c]Nivel de evidencia.
[d]La cirugía será la mejor opción si el procedimiento que protege la válvula nativa es factible.

EI aórtica o mitral con valvulopatía severa en el diagnóstico , vegetación > 10 mm y bajo riesgo quirúrgico	Emergencia (< 48 h)	I	A
EI mitral con IM severa, RS, alta probabilidad de reparación, vegetación > 10 mm y bajo riesgo quirúrgico	Electiva	IIa	A
Predicción alto riesgo embólico con bajo-intermedio riesgo quirúrgico	Urgencia	IIb	C

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