When to operate in Infective Endocarditis?

Earlier is the must !!!

Gilbert Habib
La Timone Hospital
Marseille - France

October 24th 2014

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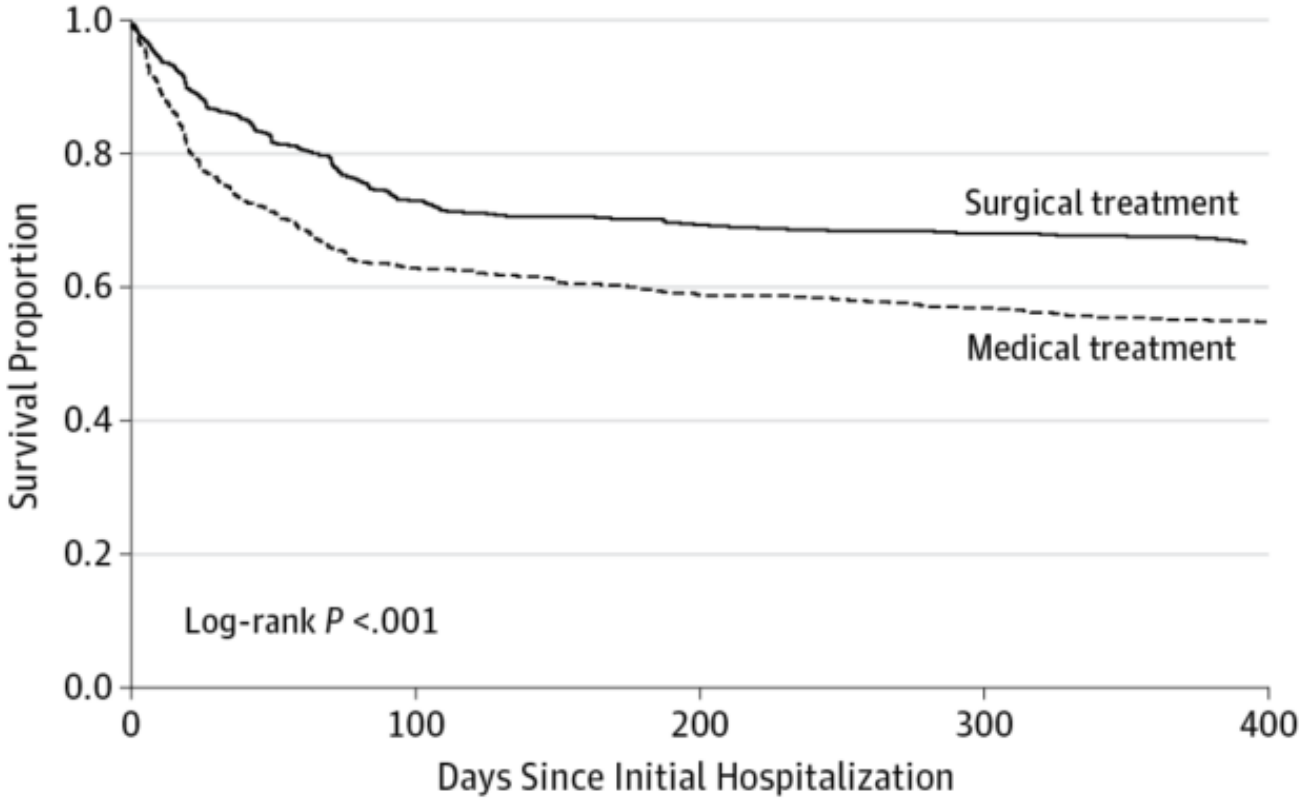
Endocarditis: still a deadly disease!!

Lalani T– JAMA 2013

- unacceptably high (20-50%)



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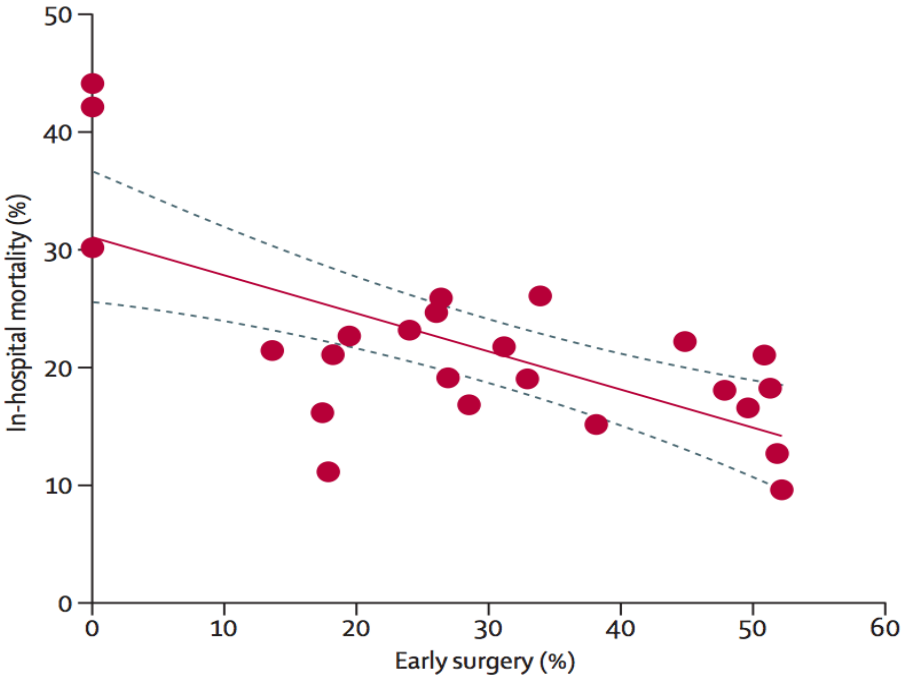
Endocarditis: still a deadly disease!!

Thuny F, Habib G . Lancet 2012;10;379:965-75

Meta-analysis from 24 studies including 8539 patients



- still high mortality
- benefit of early surgery

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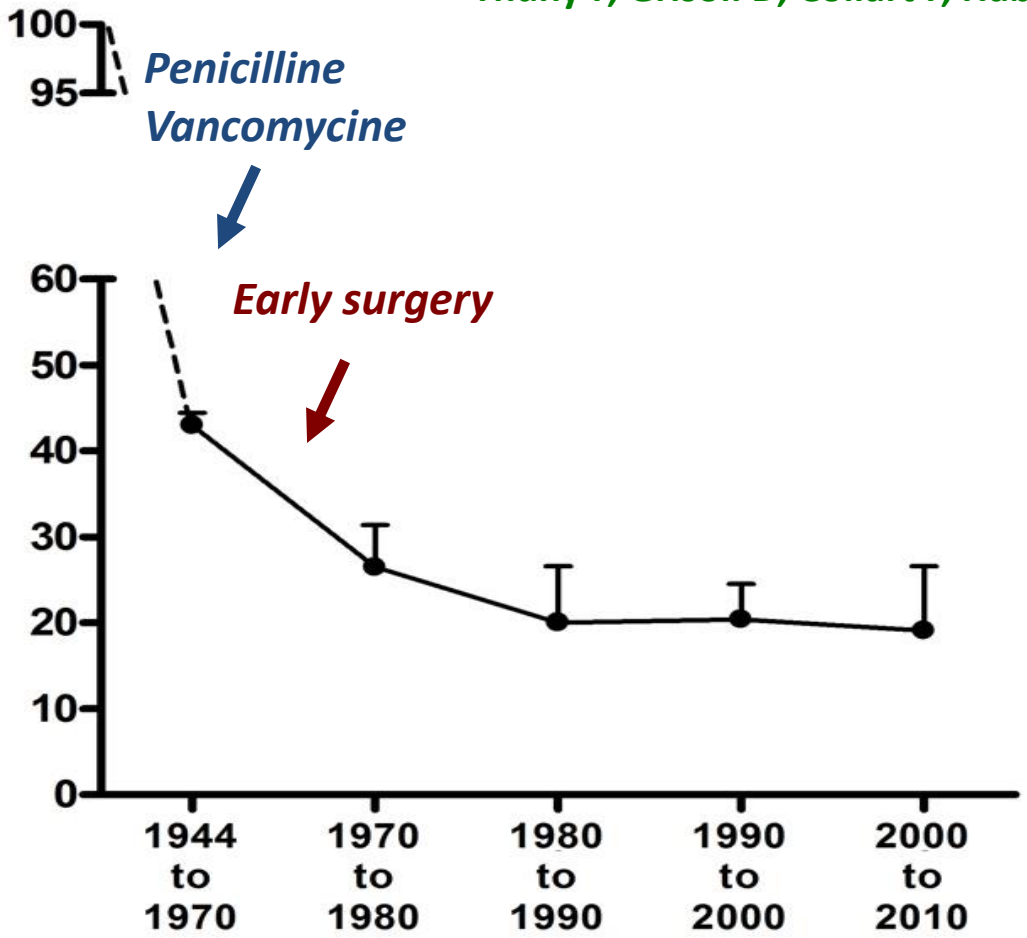
INTRODUCTION

Influence of therapy

Thuny F, Grisoli D, Collart F, Habib G, Raoult D. Lancet 2012;10;379:965-75;



24 largest series (8589 cases)

In-hospital mortality

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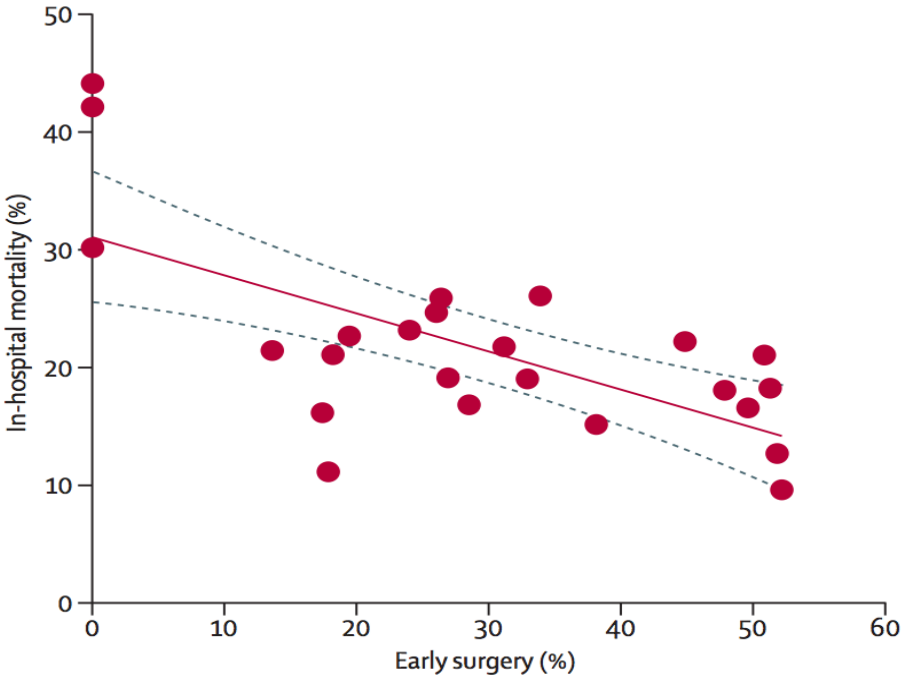

WE NEED

- **early diagnosis**
- **early ATB therapy**
- **early surgery**

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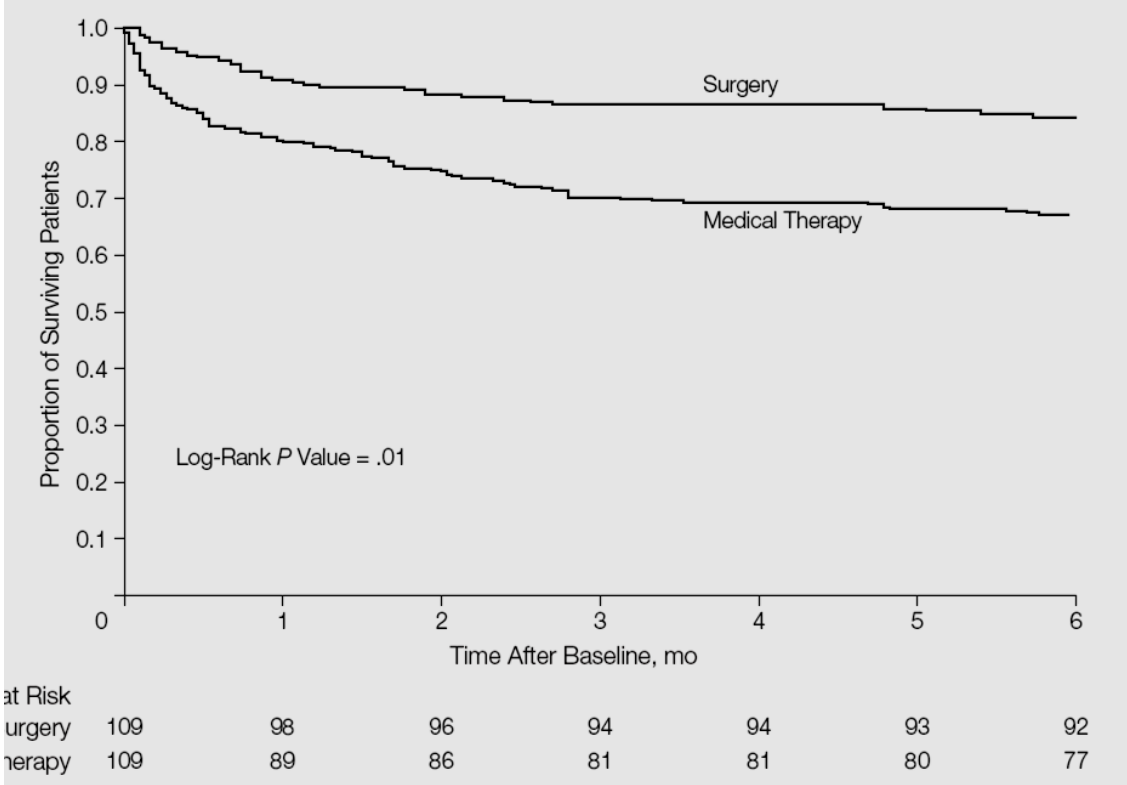
Impact of surgery on mortality

- 513 patients with complicated IE
- 230 (40%) surgical therapy

Vikram– JAMA 2003 ; 290 : 3207



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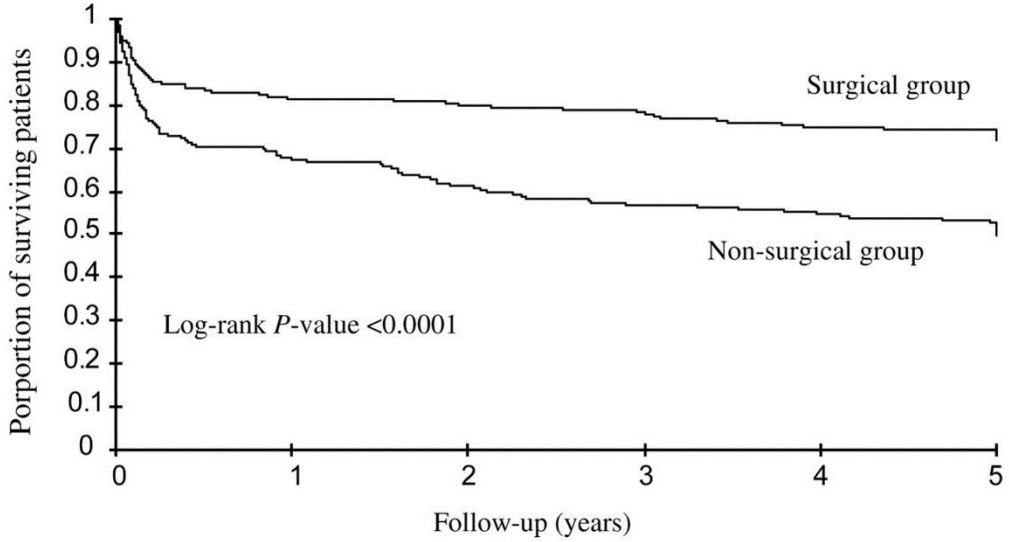
Impact of surgery on mortality

Bannay A et al. Eur Heart J 2011;32:2003-2015

- **449 patients with left-sided IE**
- **240 (53%) surgical therapy**

- increase in short-term mortality
- decrease in long-term mortality



Overall 5-year survival according to the treatment group (Kaplan–Meier curves).

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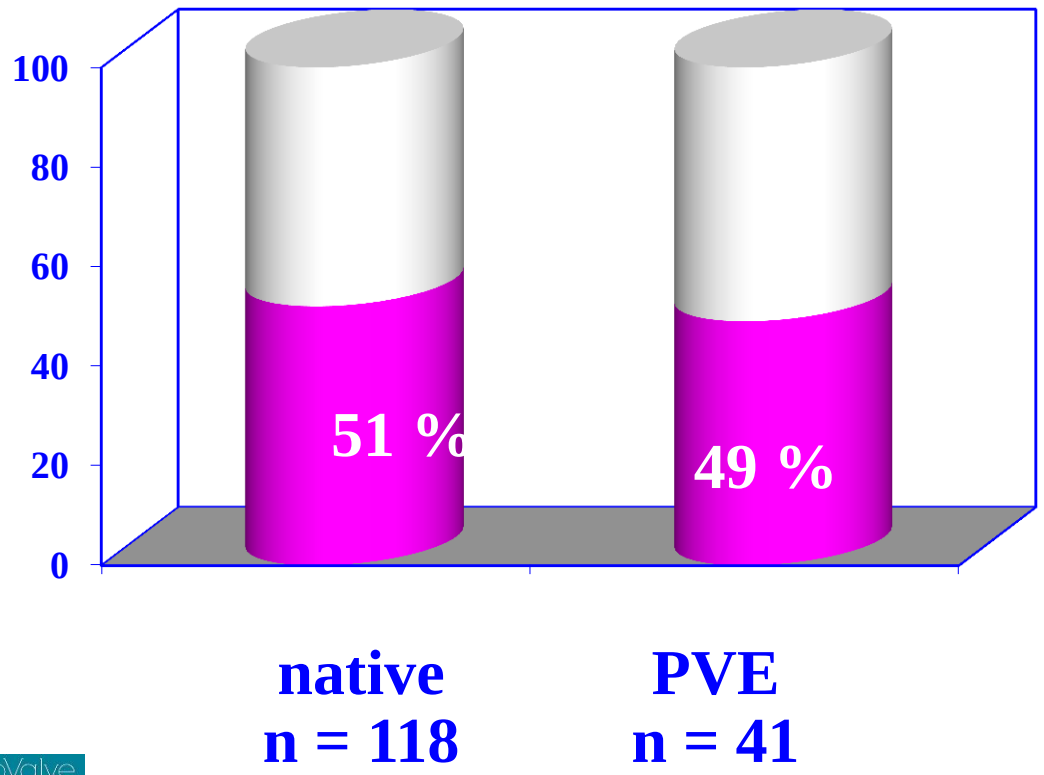
Surgery in IE : Euro Heart Survey

Tornos P – Heart 2005 ; 91 : 571-5



Reasons for surgery

- *CHF: 65%*
- *persistent sepsis: 45%*
- *embolism: 20%*

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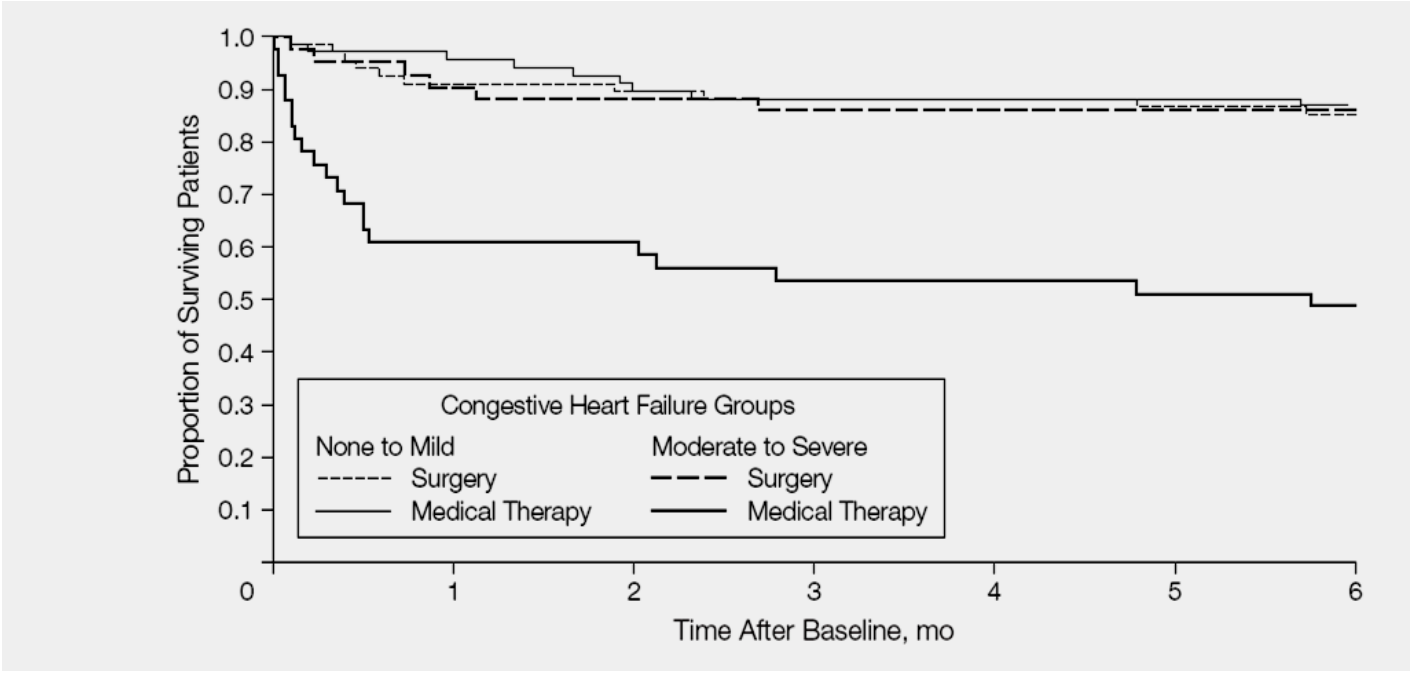
Impact of surgery on mortality

Vikram– JAMA 2003 ; 290 : 3207

- **513 patients with complicated IE , 230 (40%) surgical therapy**
- **6 month mortality**



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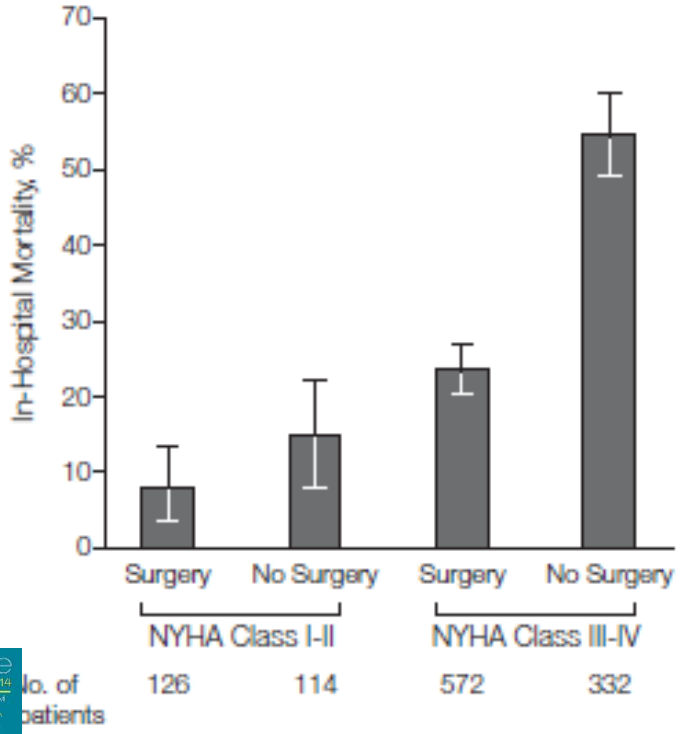
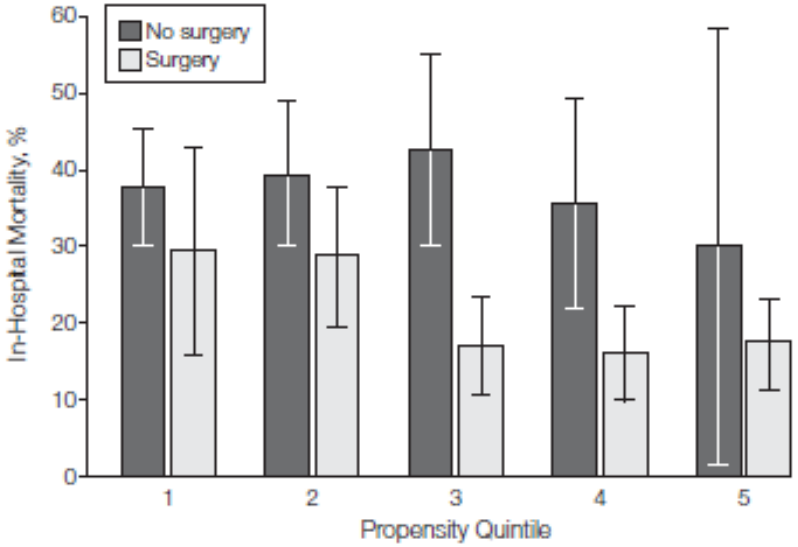
Impact of surgery on mortality

Kiefer T– JAMA 2011 ; 306 : 2239-47

- 1359 patients with IE and CHF , 839 (62%) surgical therapy
- in-hospital mortality = 20.6% vs 44.8%





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Is surgery beneficial ?

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Is surgery beneficial ?

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~~Is surgery beneficial ?~~

1. **In which patient is early surgery necessary ?**

2. **What is the optimal timing for surgery ?**

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European Heart Journal
doi:10.1093/eurheartj/ehp285

Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009)

Chairperson
Prof. Gilbert Habib
Service de Cardiologie
C.H.U. la Timone, Bd Jean Moulin
13005 Marseille - France

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3. Catherine Després, Sophia Antipolis, France

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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

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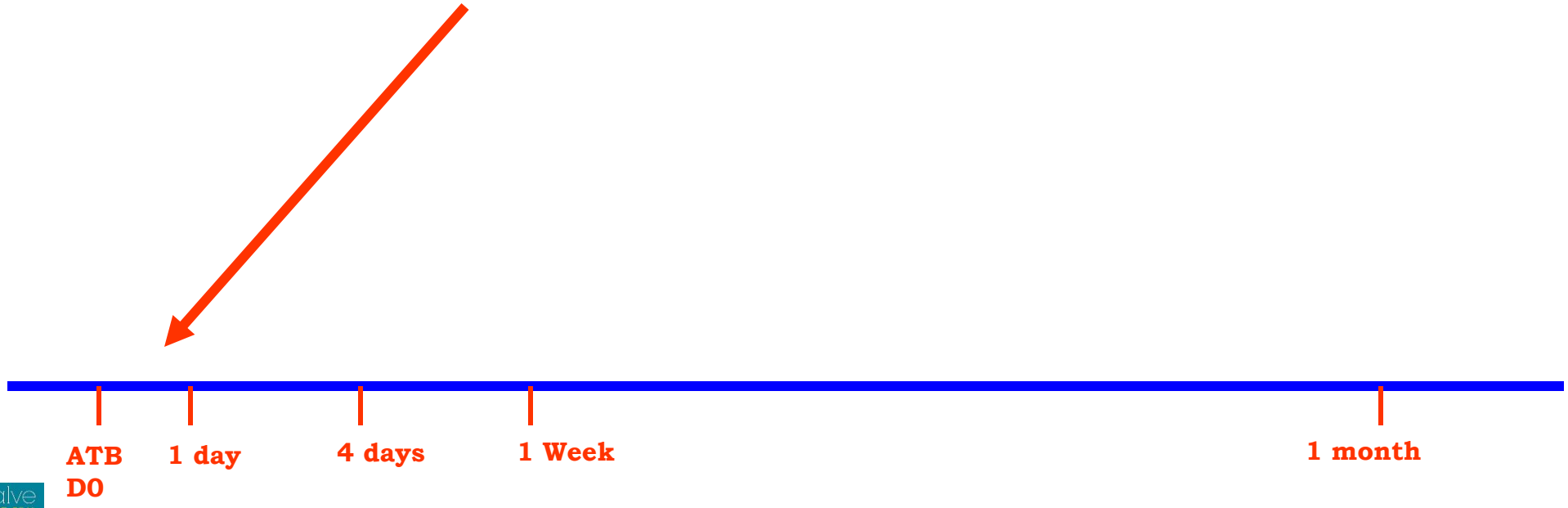
Emergency surgery ?

Emergency surgery (within 24h)



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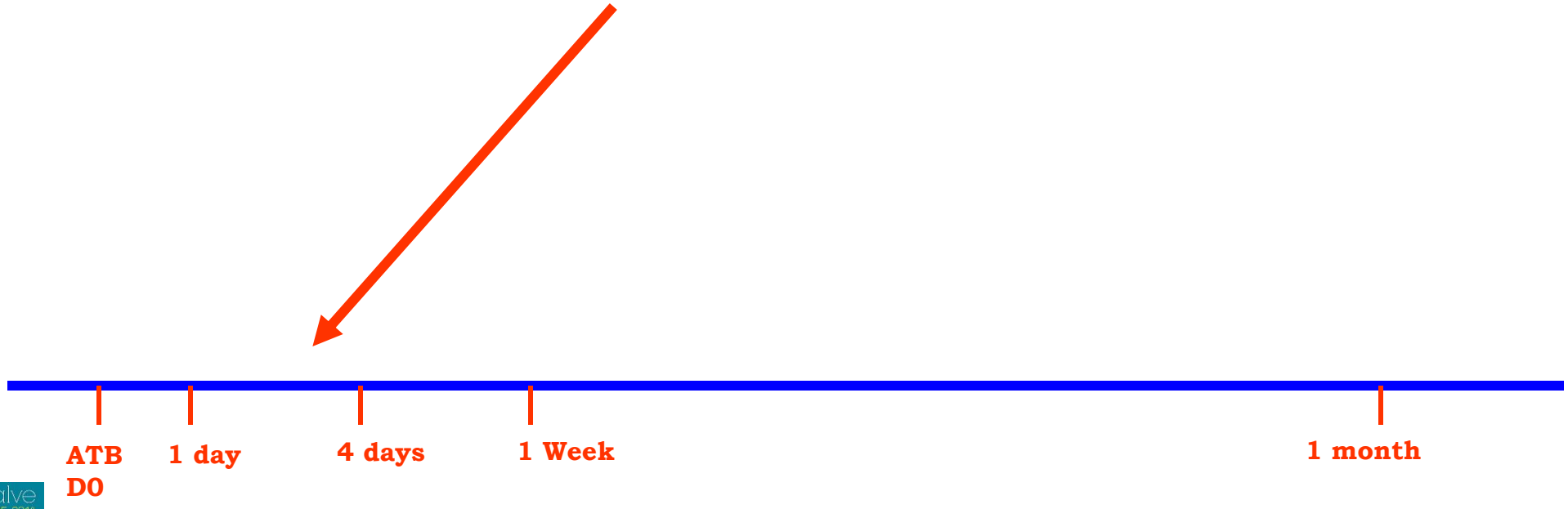
Urgent surgery ?

Urgent surgery (within few days)



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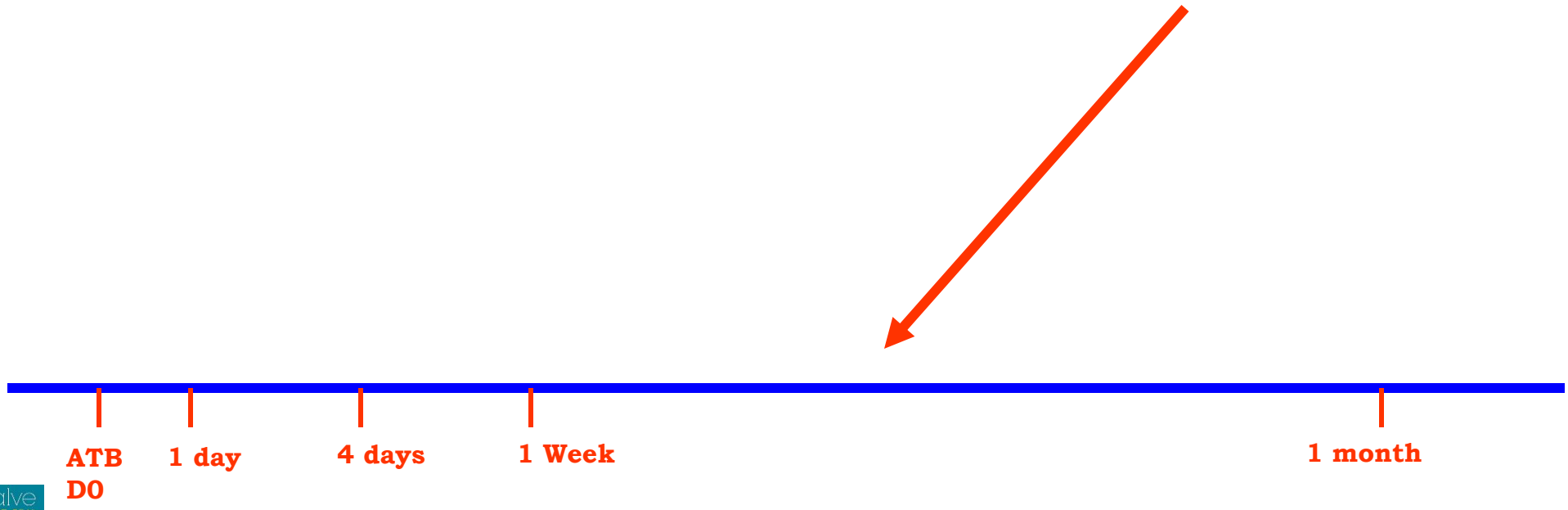
Early surgery ?

Elective surgery (after 2 weeks)



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1. **Is early surgery necessary ?**

2. **What is the optimal timing for surgery ?**

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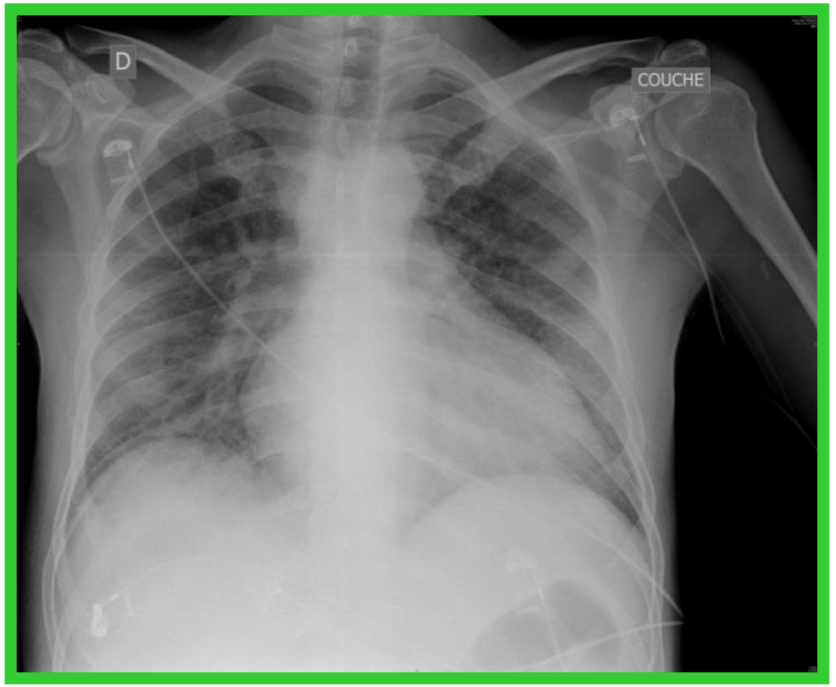
Patient 1: Heart failure

History of the disease

- 52 year-old man,
- fever and lombalgia
- no previous known cardiac disease
- weight loss



Clinical examination

- **severe CHF**
- fever = 38°5
- aortic diastolic murmur 3/6
- **arterial pressure: 90 / 40 mmHg**

Blood cultures:

streptococcus gallolyticus (group D)

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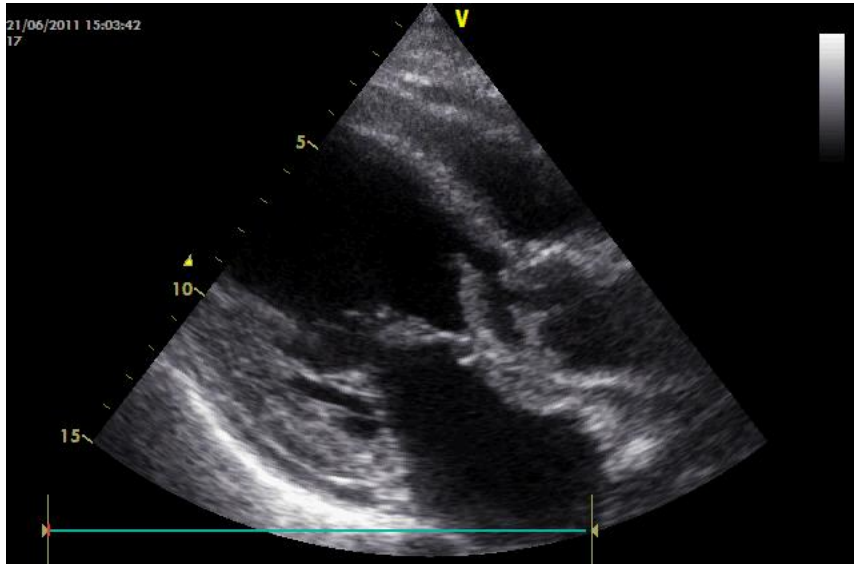

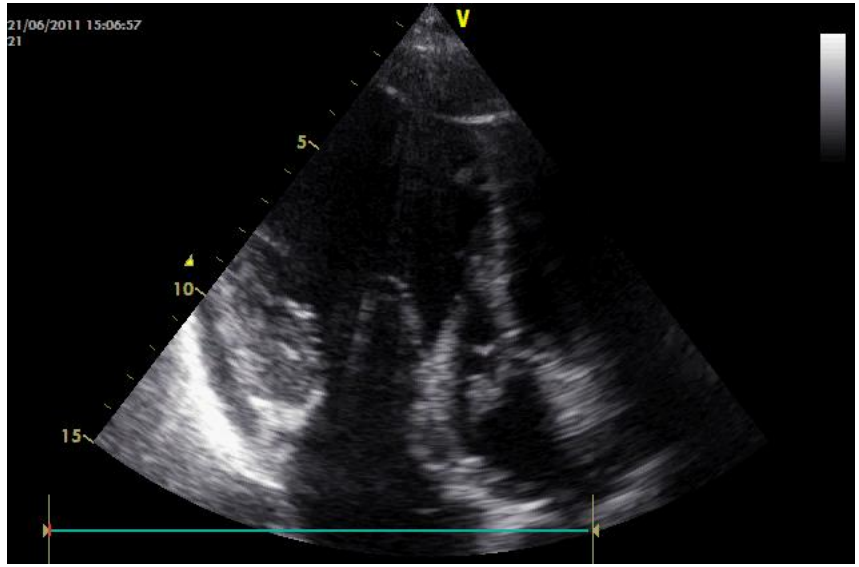

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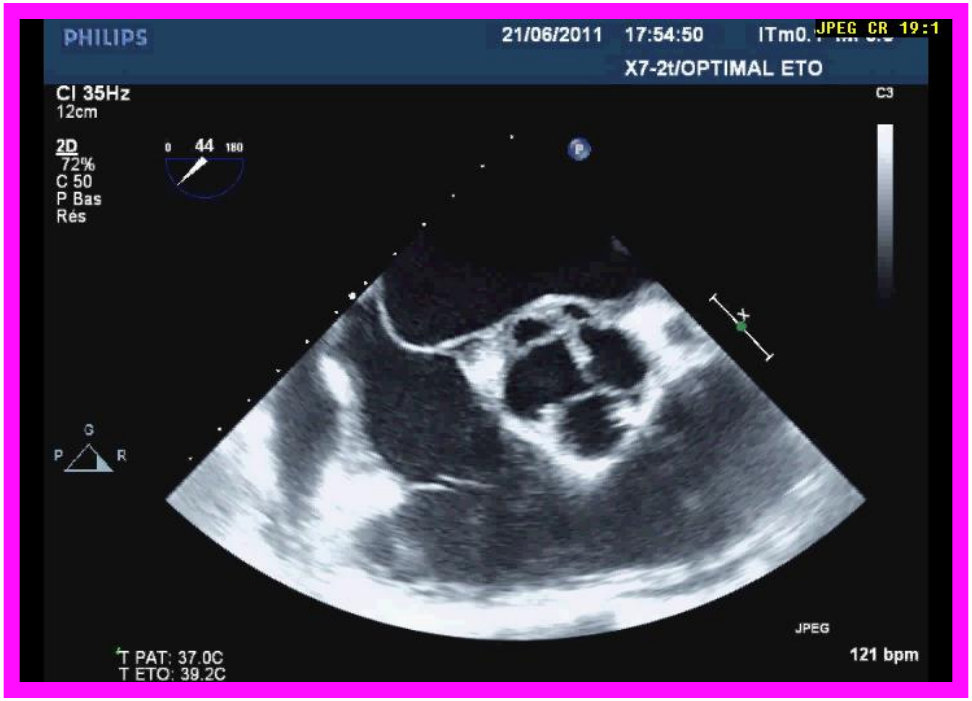

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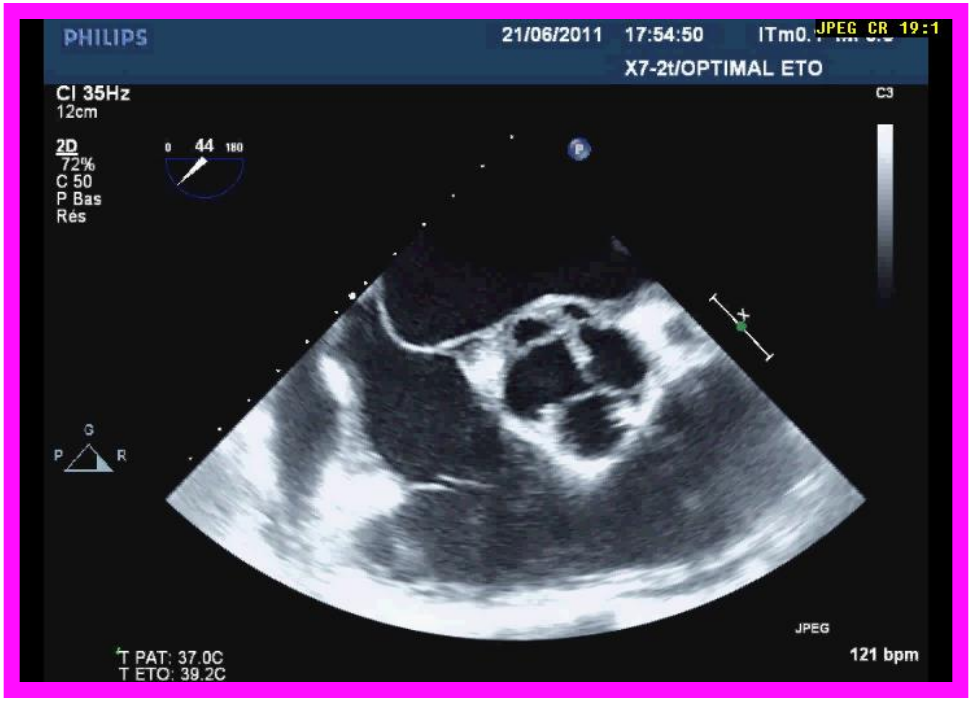

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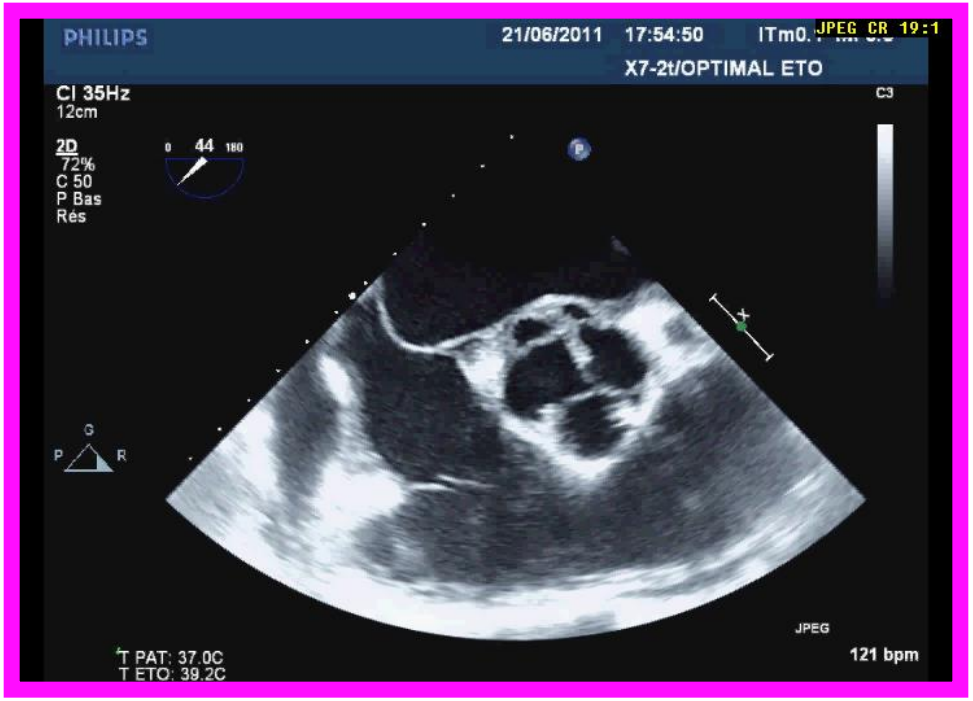

- Severe heart failure
- Abscess

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Indication 1: heart failure

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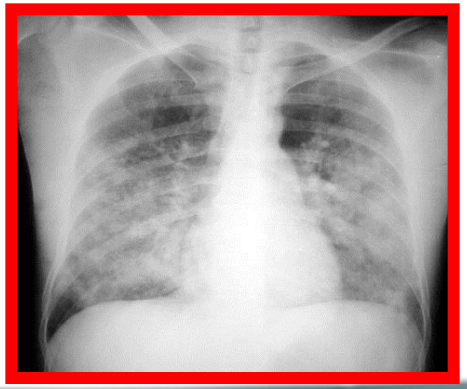
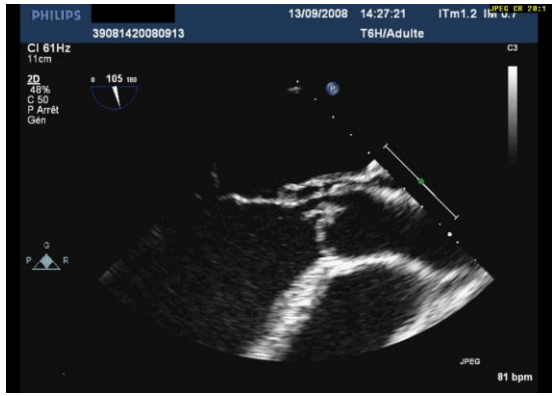
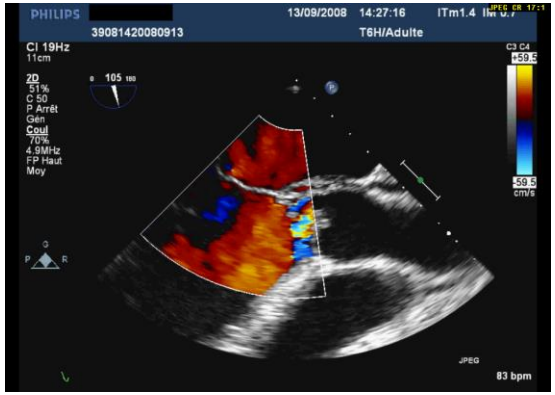


Indication 2: uncontrolled infection

Recommendations: Indications for surgery	Timing*	Class[a]	Level[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





Patient 1: abscess + CHF

Is early surgery necessary ?

YES

- severe valve destruction
- heart failure
- abscess

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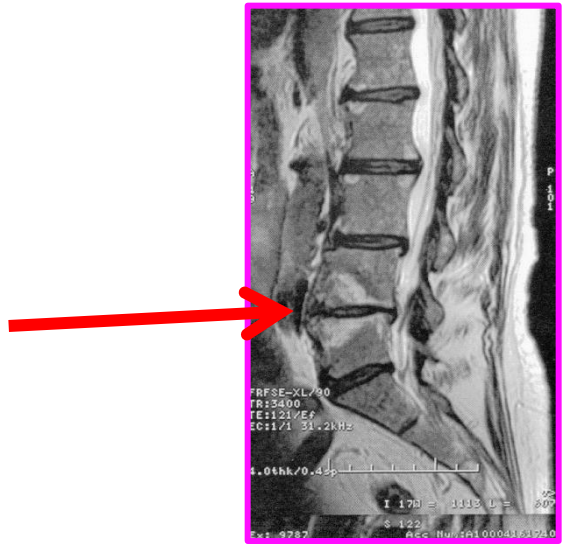
Patient 2: large vegetation

History of the disease

- 52 year-old woman,
- march 2009 : fever and lombalgia
- diagnosis of **spondylitis**
- no previous known cardiac disease



Clinical examination

- **no sign of CHF**
- fever = 38°5
- mitral systolic murmur 2/6
- arterial pressure: 120 / 70 mmHg

Blood cultures:

streptococcus gallolyticus (group D)

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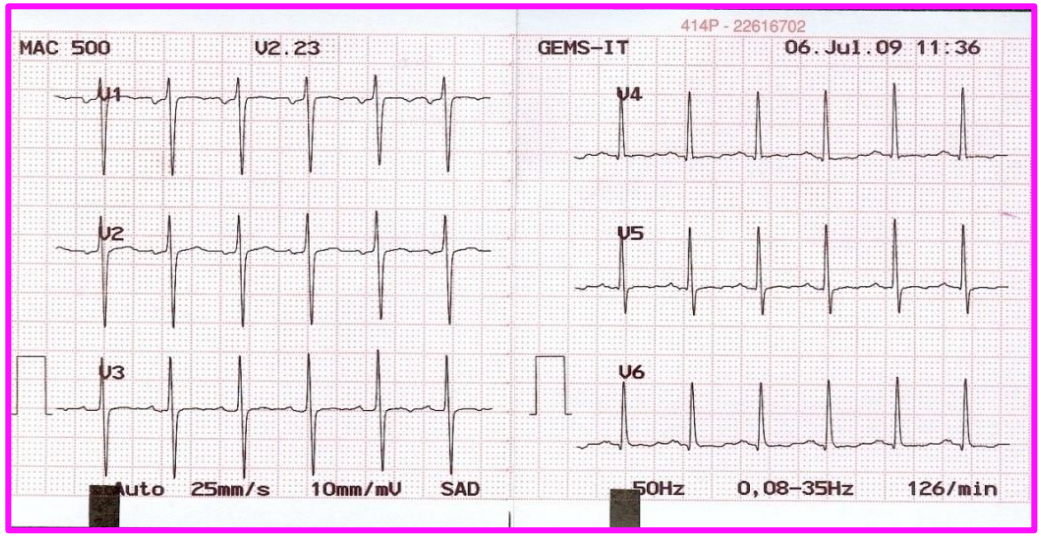
Case report

Laboratory data

- haemoglobin: 8.5 g / dl
- white blood cell count: 11,000 / mm^3
- sedimentation rate: 60 mm
- CRP = 136 mg/l
- creatinin = 60 mg



Blood cultures:

streptococcus bovis (group D)

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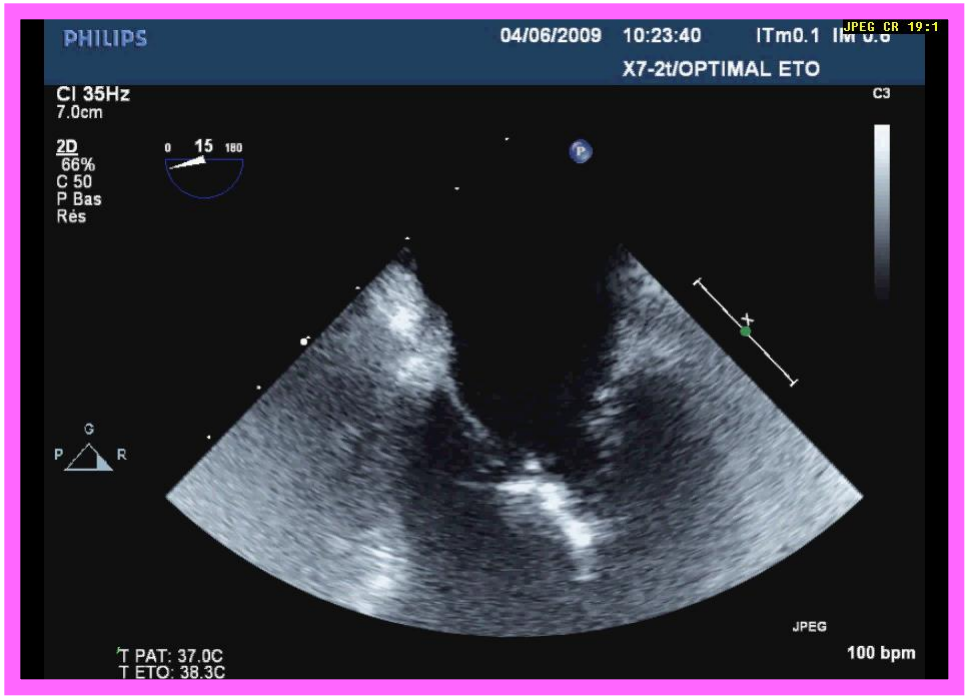
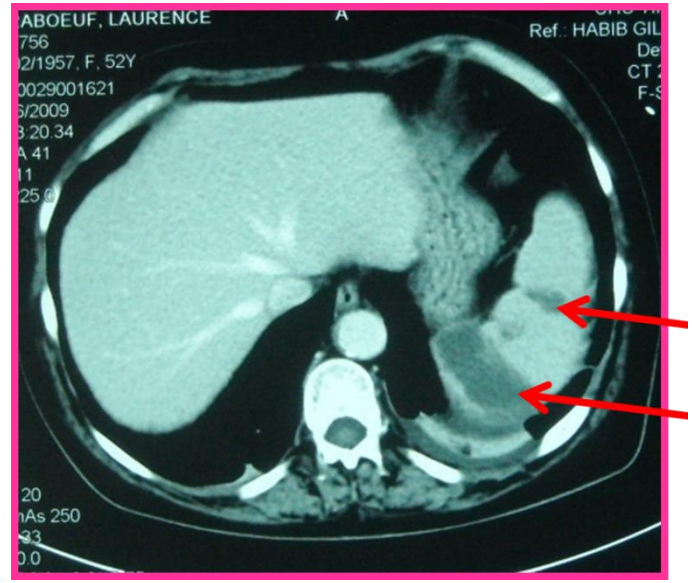
Patient 2





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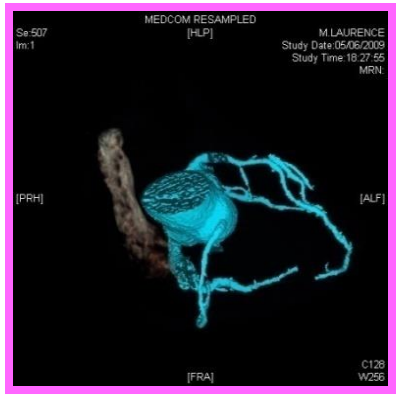
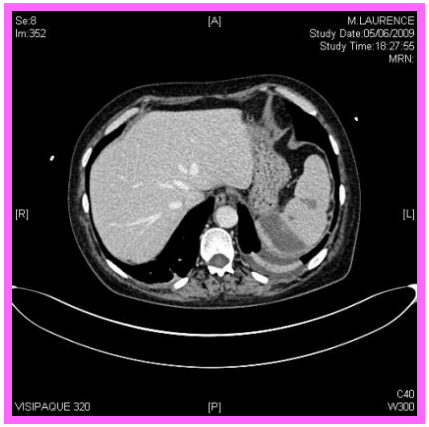
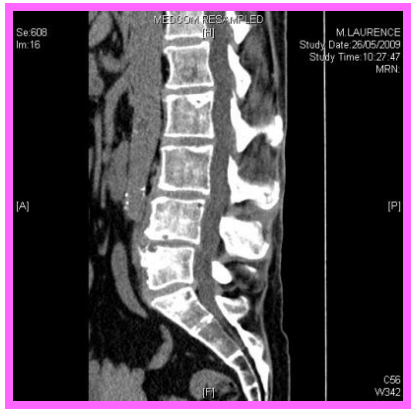
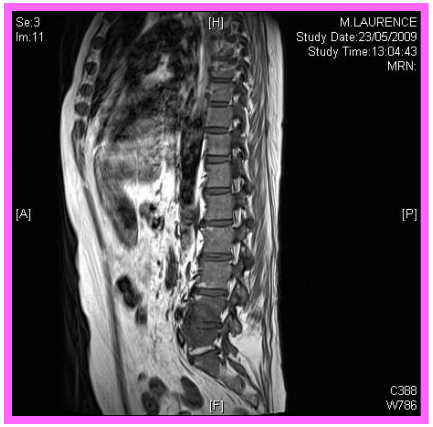
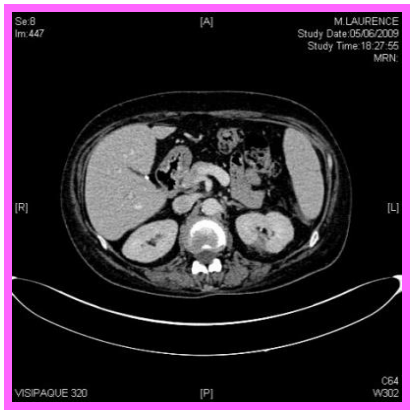
CT-scan imaging











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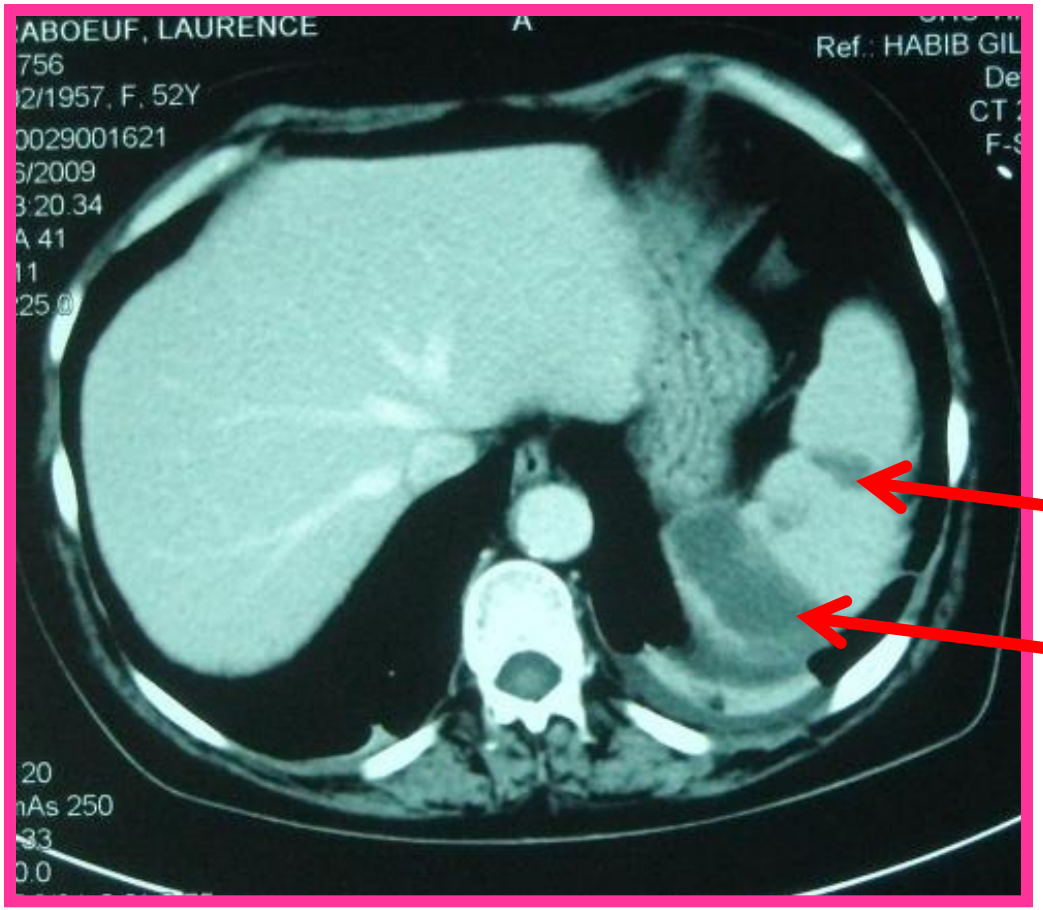
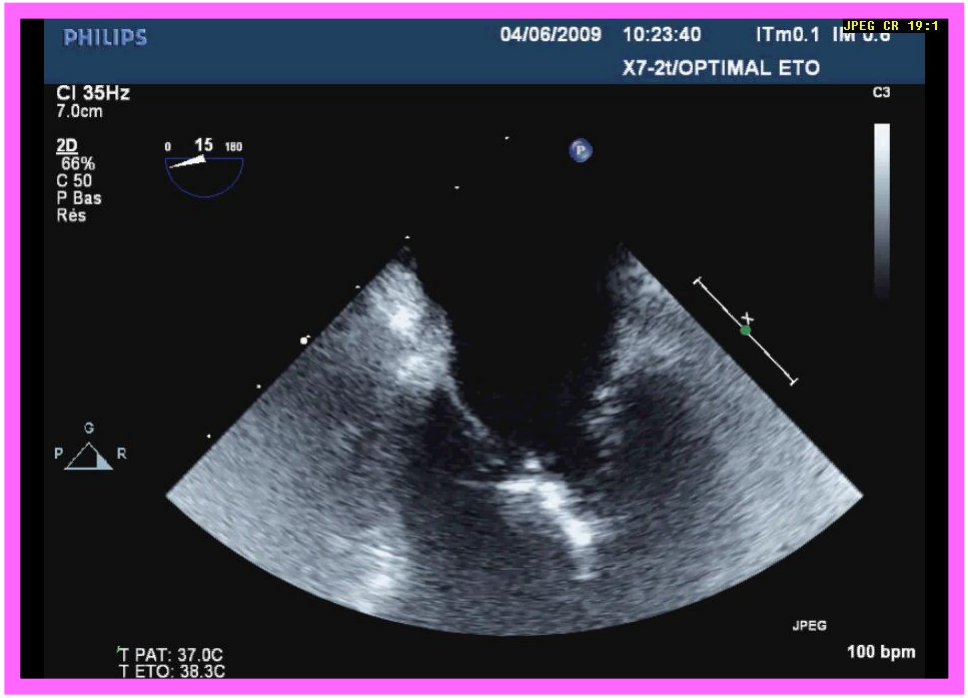
CT-scan imaging



Patient 2: summary

- No heart failure
- Asymptomatic splenic embolism
- Isolated large (26 mm) vegetation



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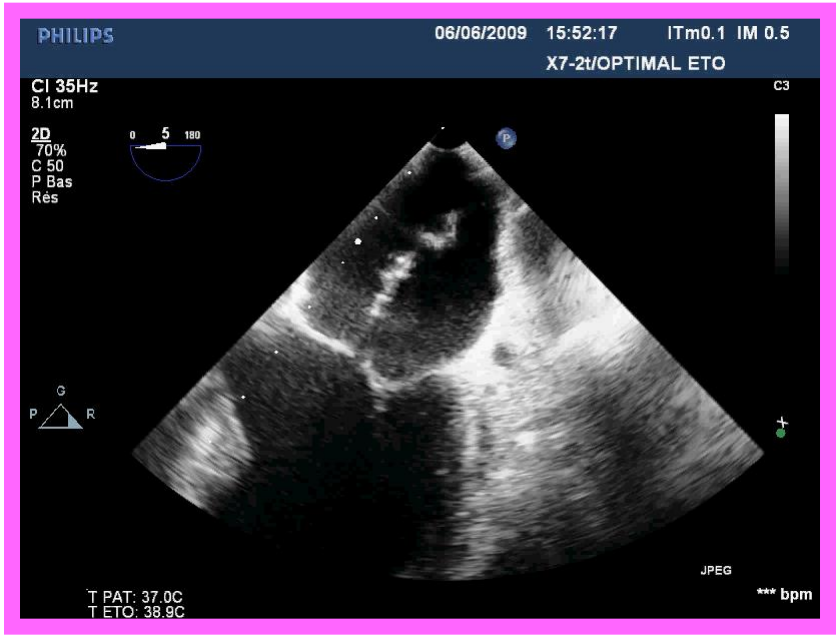
Embolic events in IE

1. are frequent and severe
2. are related to the vegetation size
3. occur early in the course of IE

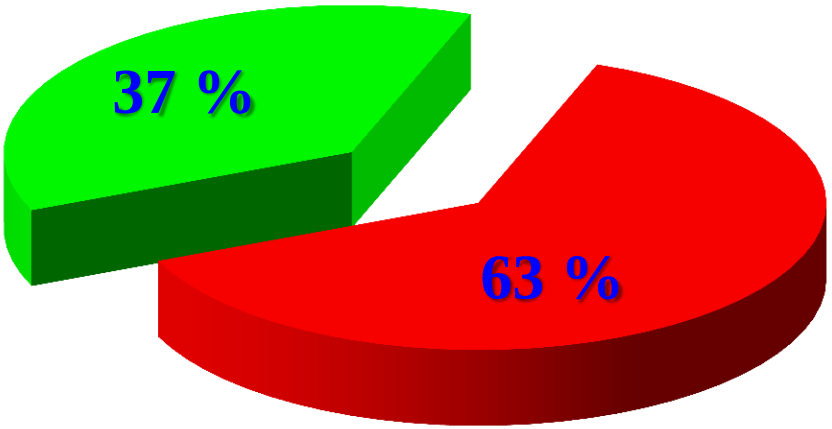


TEE and embolic risk

178 patients, definite IE

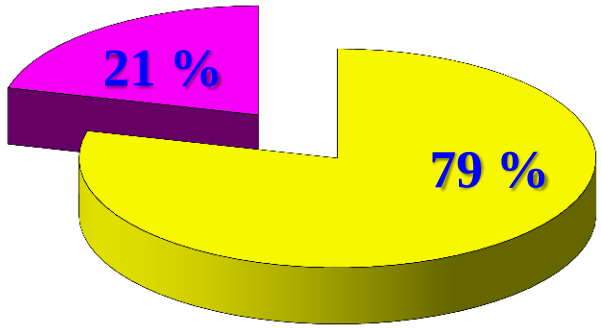
Di Salvo - JACC – 2001; 37 : 1069-76

With embolism



Without embolism

silent embolism



clinical embolism

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TEE and embolic risk

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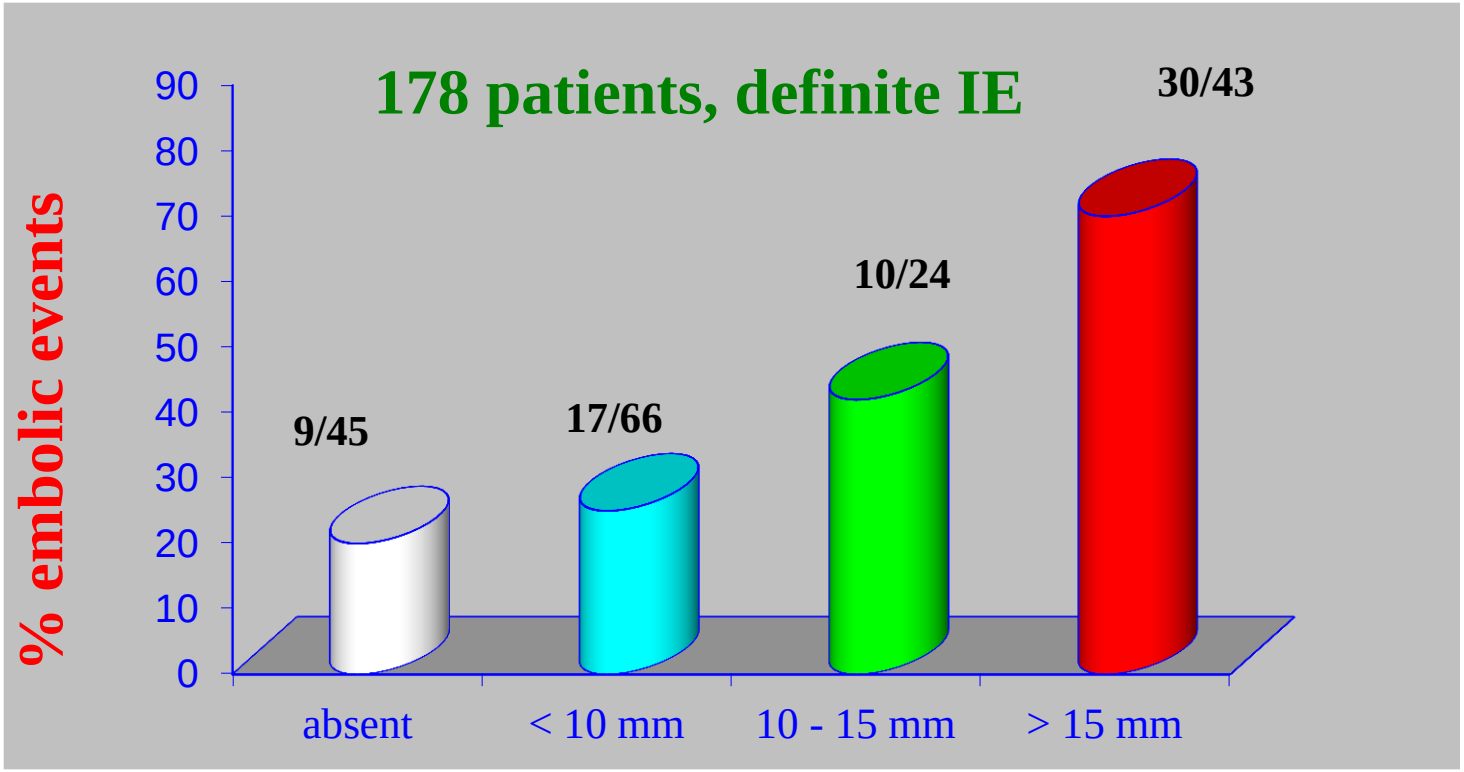

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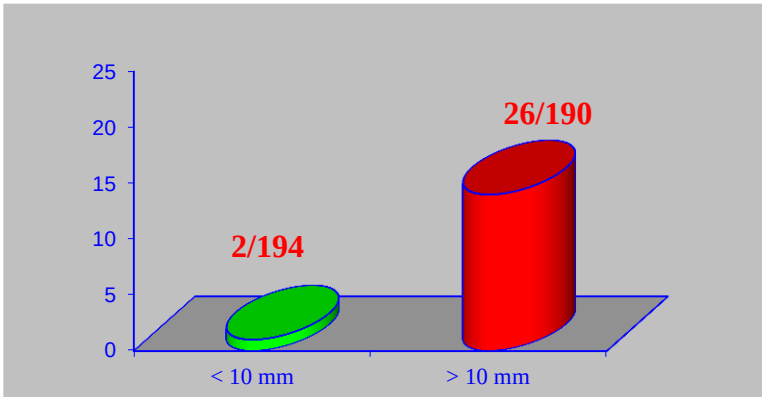
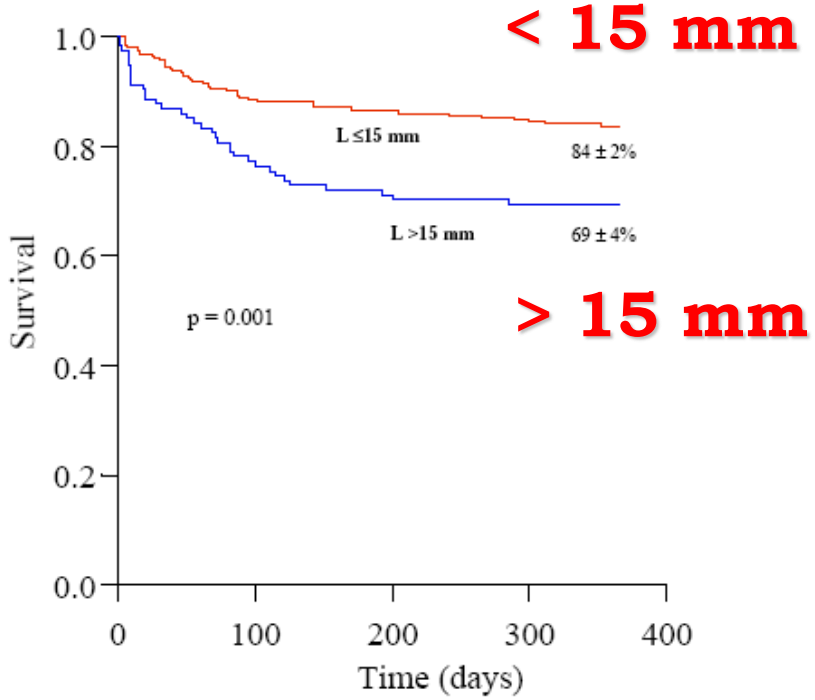
Embolic risk under therapy

F Thuny – Circulation 2005 : 112:69-75

- 384 IE , multicentre European study
- 131 (34%) EE, 28 (7.3%) EE under therapy
- 20 (71.4%) during the first 15 days





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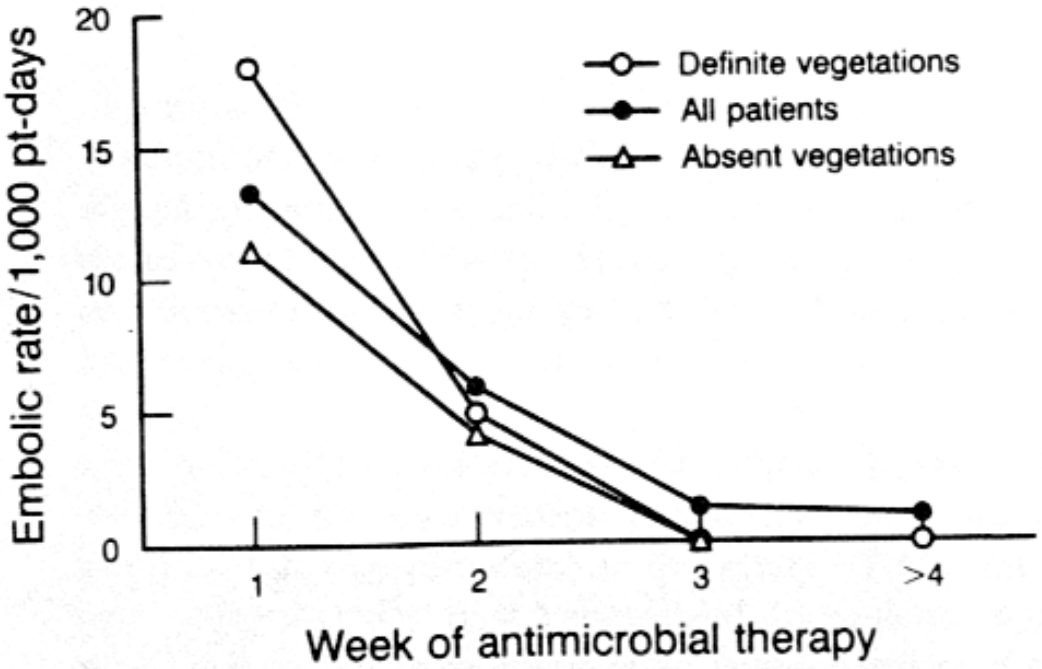
Embolic risk under therapy

Steckelberg - Ann Int Med 1991



- 207 IE
- 13 % embolic events

- 13/1000 pt/d during the 1st week
- 1.2/1000 pt/d after the 2nd week

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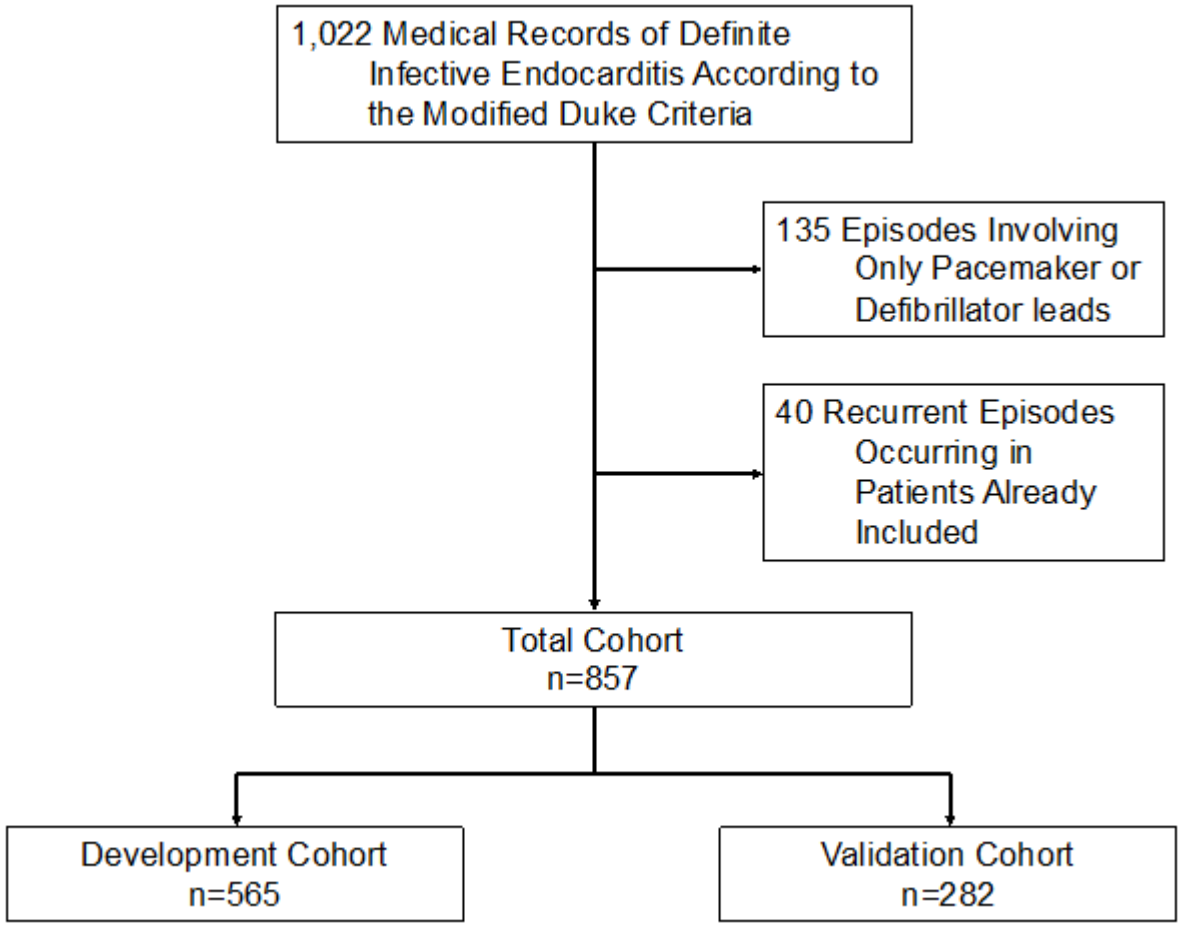
The embolic risk in 2014

Hubert S- J Am Coll Cardiol 2013;62:1384–92



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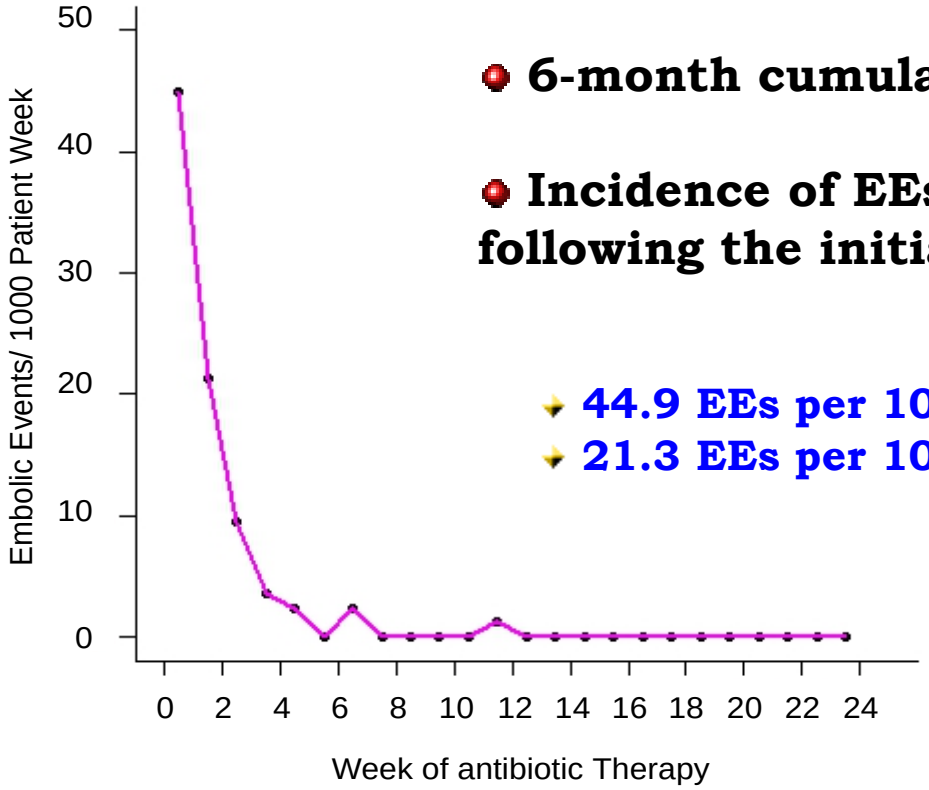

- **6-month cumulative incidence of new EEs: 8.5%**
- **Incidence of EEs highest during the first two weeks following the initiation of antibiotic therapy**
  - **44.9 EEs per 1000 patient-weeks the first week**
  - **21.3 EEs per 1000 patient-weeks the second week**

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Can we predict the embolic risk ?

Hubert S- J Am Coll Cardiol 2013;62:1384–92

	Univariate Analysis ***P* Value**	*Multivariate Analysis* **Hazard Ratio 95% CI**
Age	**0.15**	**1.01 (0.99–1.03)**
Diabetes	**0.05**	**1.29 (0.60–2.77)**
Previous EE	**0.04**	**1.39 (0.73–2.64)**
Atrial fibrillation	**0.07**	**1.66 (0.81–3.39)**
Mitral localization	**0.18**	**1.09 (0.59–2.01)**
Vegetation*		
≤10 mm	**0.35**	**1.27 (0.24–6.73)**
> 10 mm	**0.02**	**4.50 (1.06–19.07)**
Oral streptococci	**0.20**	**0.64 (0.25–1.63)**
Staphylococcus aureus	**0.07**	**1.64 (0.77–3.50)**

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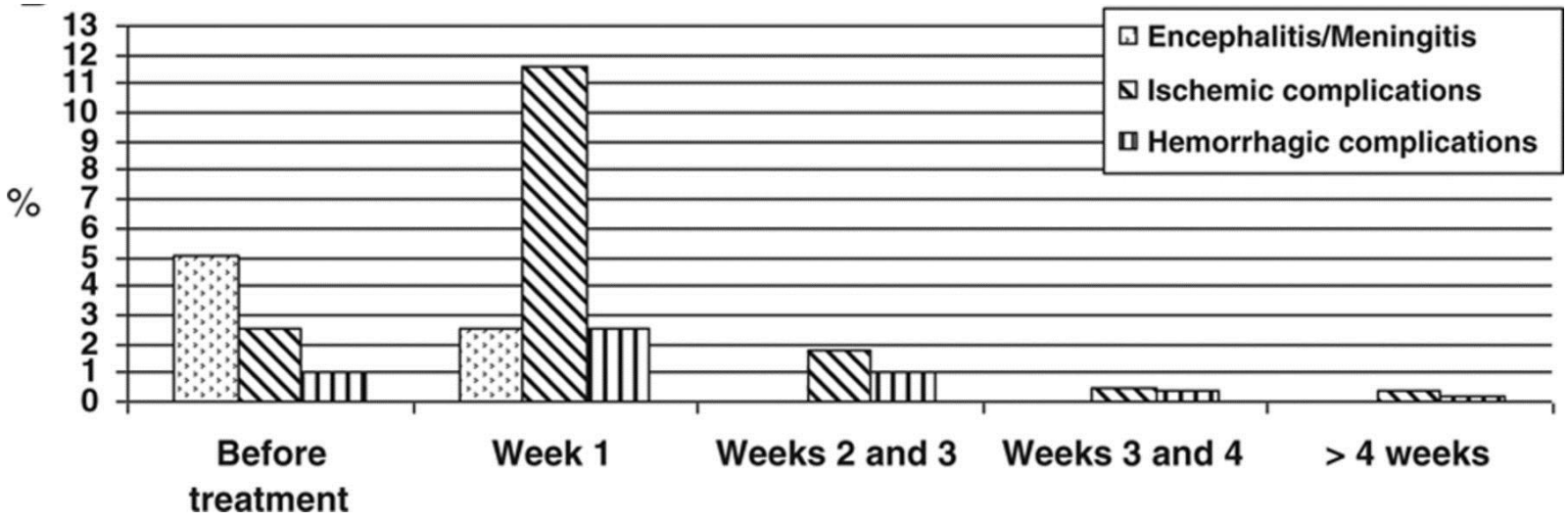
Can we predict the risk of stroke?

García-Cabrera E Circulation. 2013;127:2272-84

- 1345 consecutive episodes of left-sided infective endocarditis from 8 centers in Spain
- 340 neurological events.
- factors associated with neurological events
  - vegetation size ≥3 cm (hazard ratio [HR] 1.91
  - Staphylococcus aureus HR 2.47
  - mitral valve involvement HR 1.29
  - anticoagulant therapy HR 1.31



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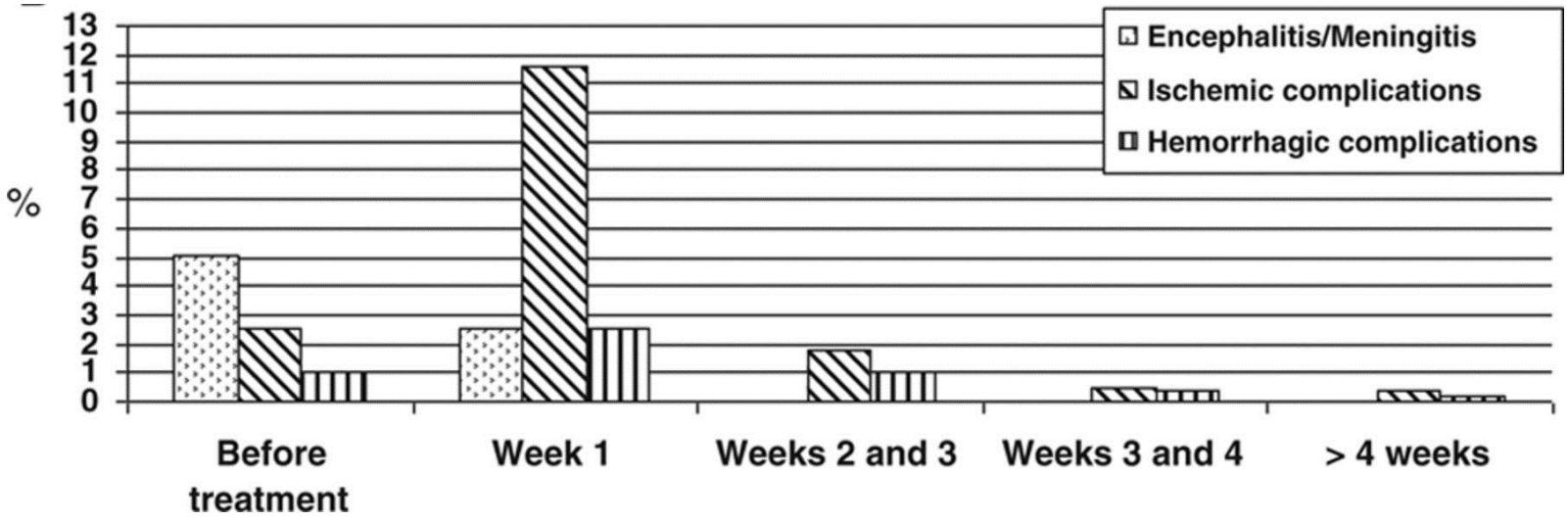
Can we predict the risk of stroke?

García-Cabrera E Circulation. 2013;127:2272-84

- the majority of ischemic strokes occurred during the first week of ATB therapy
- very large (> 3 cm) vegetations are associated with high embolic risk (20%) even after the first week



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Embolic risk under therapy

The risk of new embolism

1. **Dramatically decreases after initiation of ATB**
2. **Is still high during the first 2 weeks of ATB**
3. **Is related to the size and mobility of the vegetation**
4. **Is also related to other than echocardiographic factors**
5. **Can be reduced by very early surgery ?**

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Can we prevent embolic events?

- **Early diagnosis**
- **Early initiation of antibiotic therapy**
- **Early surgery**

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis

Duk-Hyun Kang, M.D., Ph.D., Yong-Jin Kim, M.D., Ph.D.,
Sung-Han Kim, M.D., Ph.D., Byung Joo Sun, M.D., Dae-Hee Kim M.D., Ph.D.,
Sung-Cheol Yun, Ph.D., Jong-Min Song, M.D., Ph.D.,
Suk Jung Choo, M.D., Ph.D., Cheol-Hyun Chung, M.D., Ph.D.,
Jae-Kwan Song, M.D., Ph.D., Jae-Won Lee, M.D., Ph.D.,
and Dae-Won Sohn, M.D., Ph.D.

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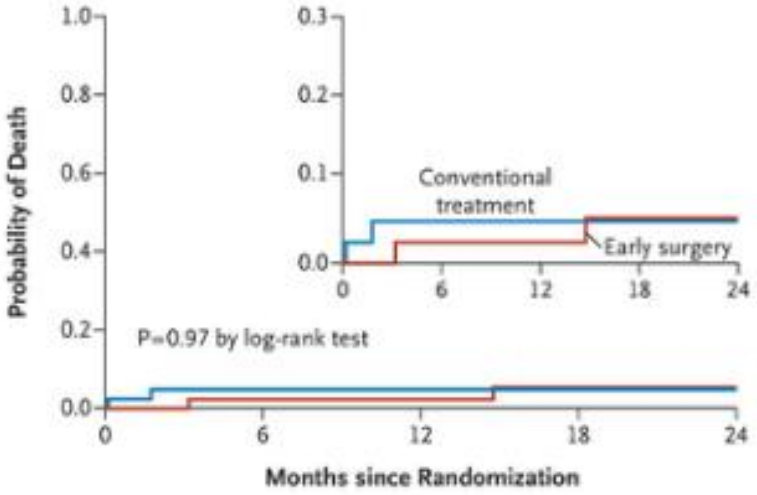
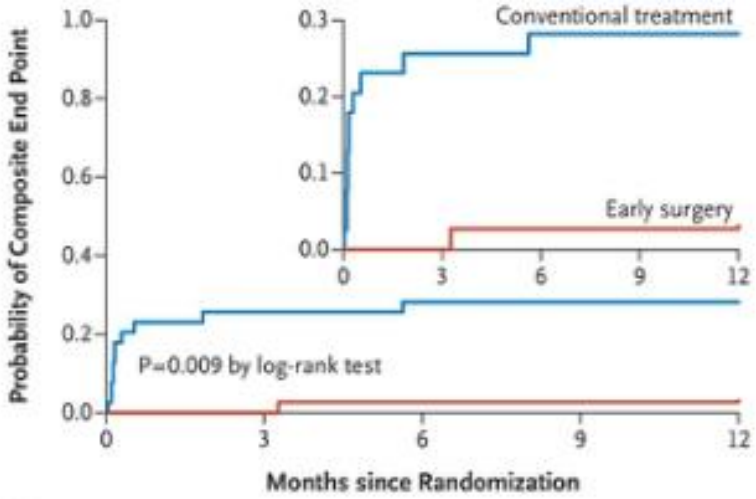
Embolic risk under therapy

Kang DH – N Eng J Med 2012: 366:2466-73



No. at Risk					
Early surgery	37	36	33	28	21
Conventional treatment	39	37	31	27	23



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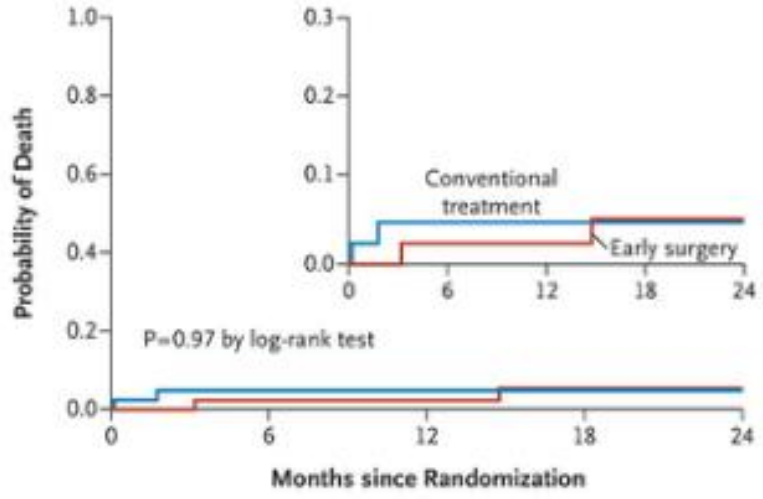
Embolic risk under therapy

Kang DH – N Eng J Med 2012: 366:2466-73

Surgery performed within 48h after randomization !!!



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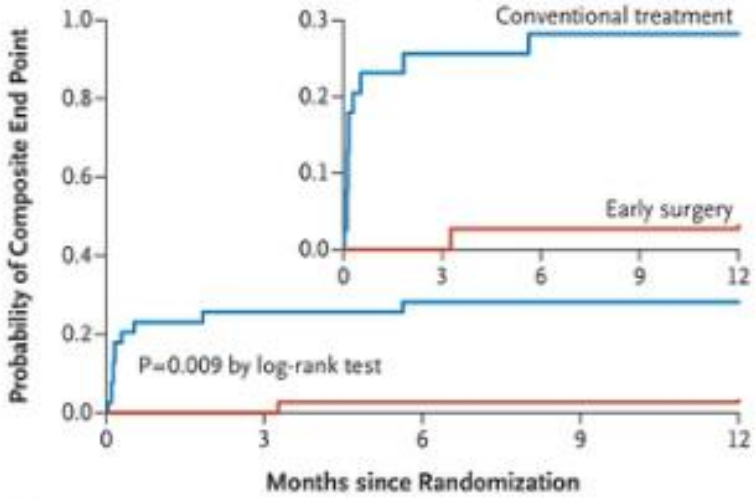

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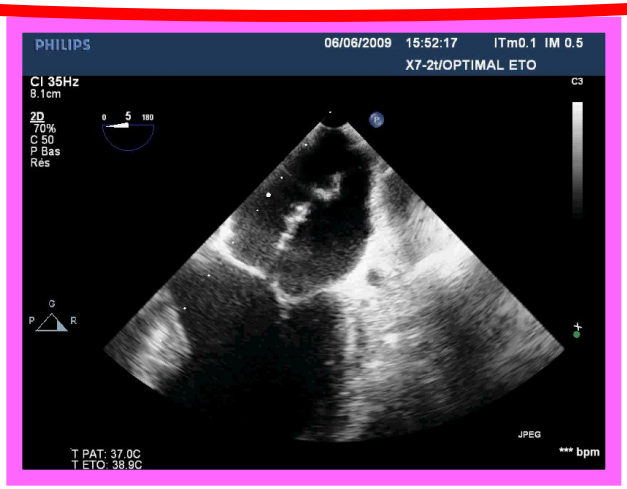
Indication 3: embolic events

Recommendations: Indications for surgery	Timing*	Class[a]	Level[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

Surgery may be preferred if procedure preserving the native valve is feasible



Indication 3: embolic events

Recommendations: Indications for surgery	Timing*	Class[a]	Level[b]
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Aortic or mitral IE with large vegetations (> 10 mm) following one or more embolic episodes despite appropriate antibiotic therapy	Urgent	I	B
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Isolated very large vegetations (> 15 mm)[#]	Urgent	IIb	C

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

Do not delay surgery !!!!

Aix*Marseille université

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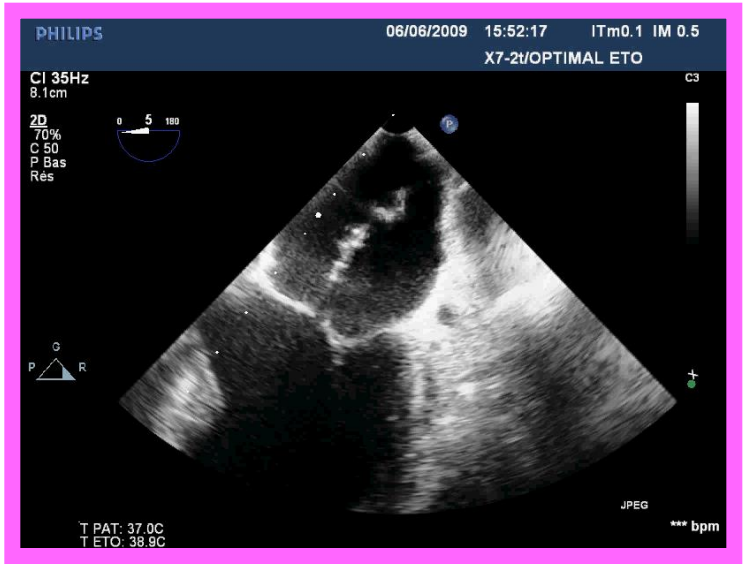
Decision: urgent surgery

ATB (amoxicillin 12g IV / day + gentamycin 3 mg/kg/day)

- previous embolism
- high embolic risk
- high probability of valve repair



Urgent surgery planned

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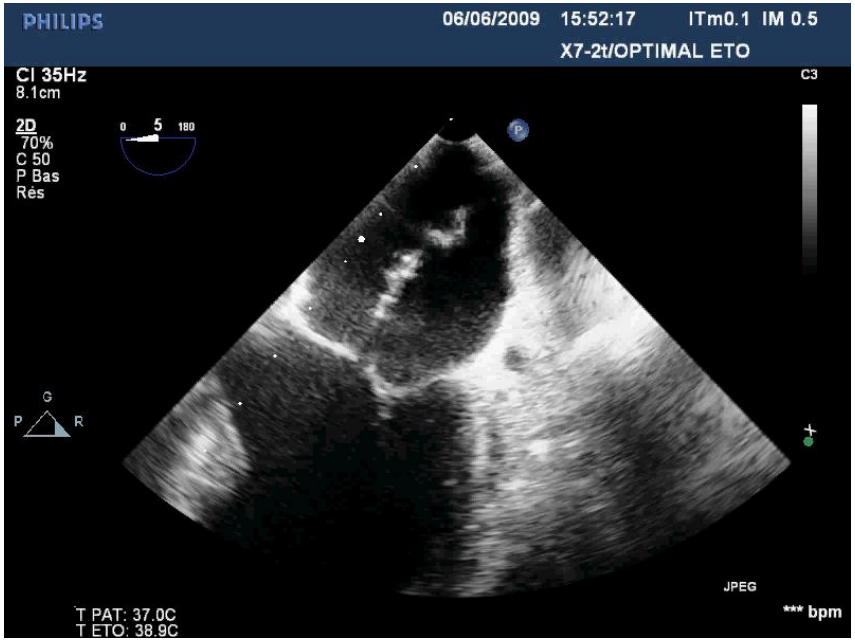
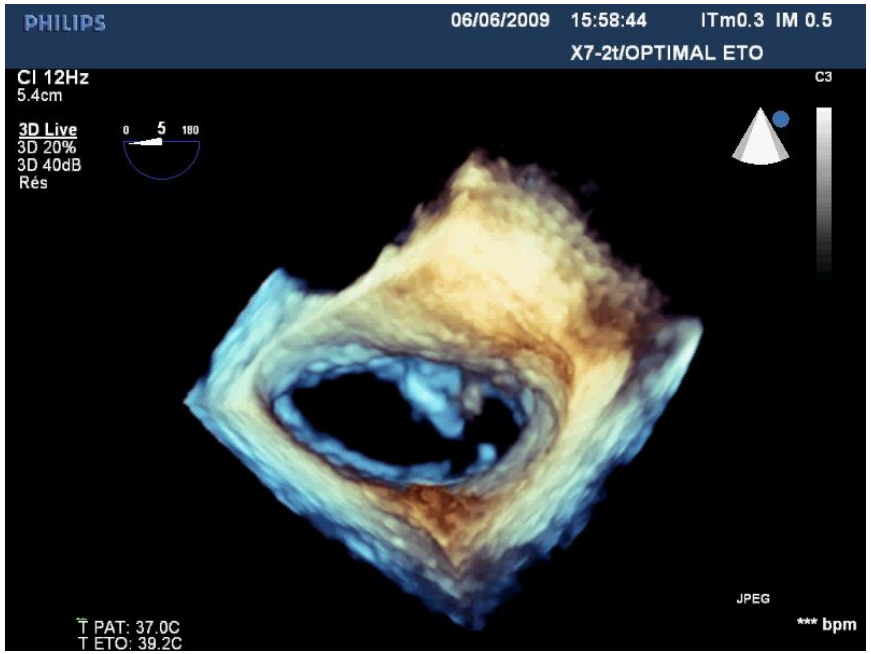
Peroperative TEE





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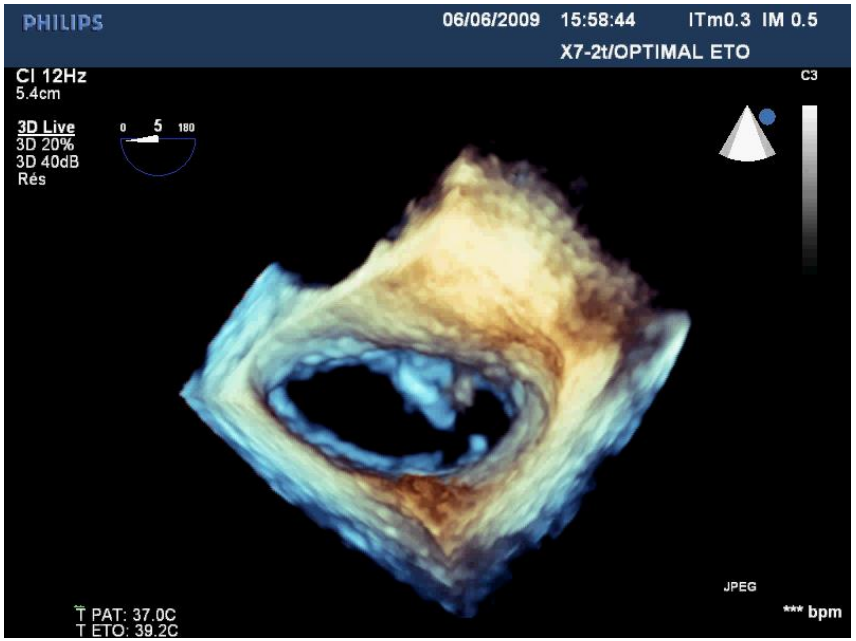

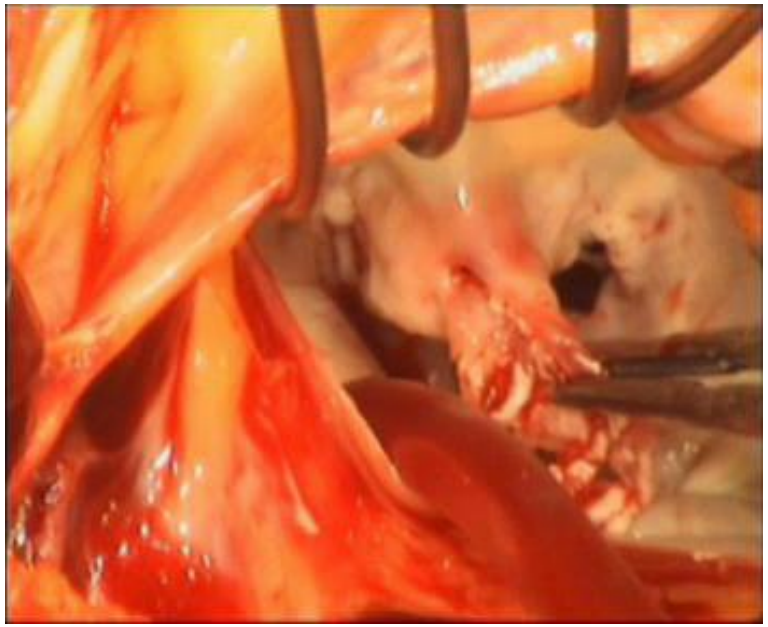

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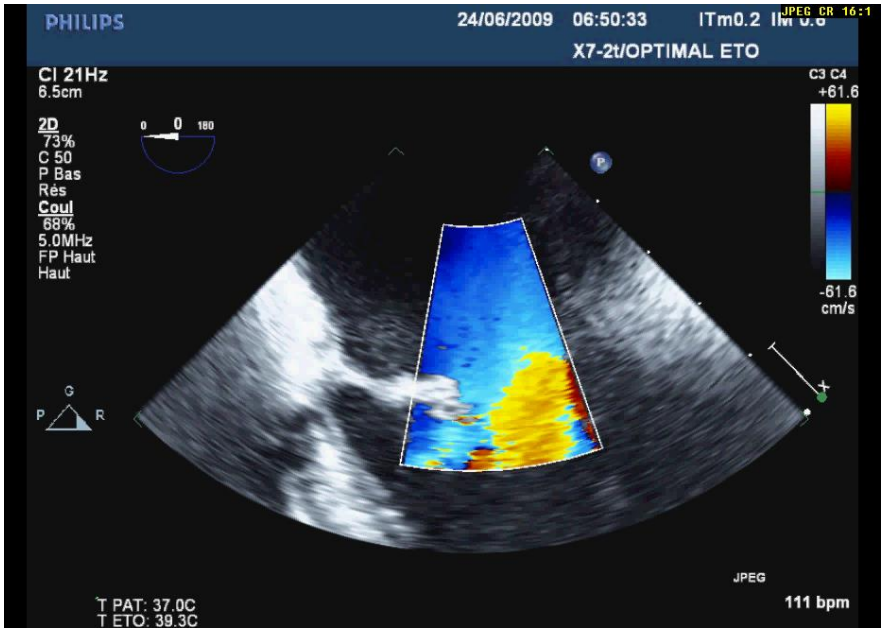
Postoperative TEE



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Conclusion: embolic risk in IE

the risk of embolism

1. Is very high in IE (1/3 patients overall)
2. Dramatically decreases after initiation of ATB
3. Is still high during the first 2 weeks of ATB
4. Is related to the size and mobility of the vegetation
5. Needs an early (surgical) decision by a multidisciplinary team

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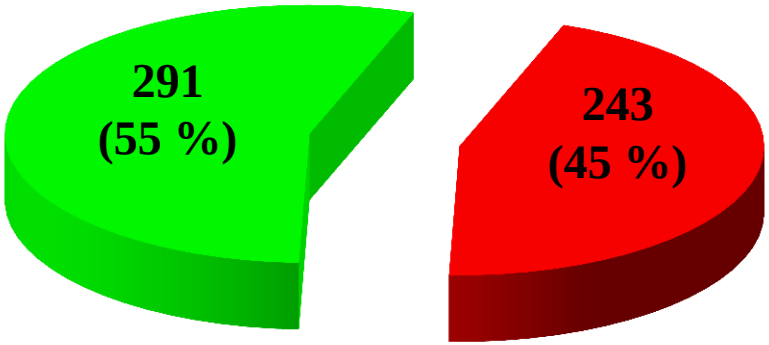
Timing of surgery in IE

534 patients, definite IE

Thuny F, Habib G, EHJ 2009

Early surgery



Medical therapy

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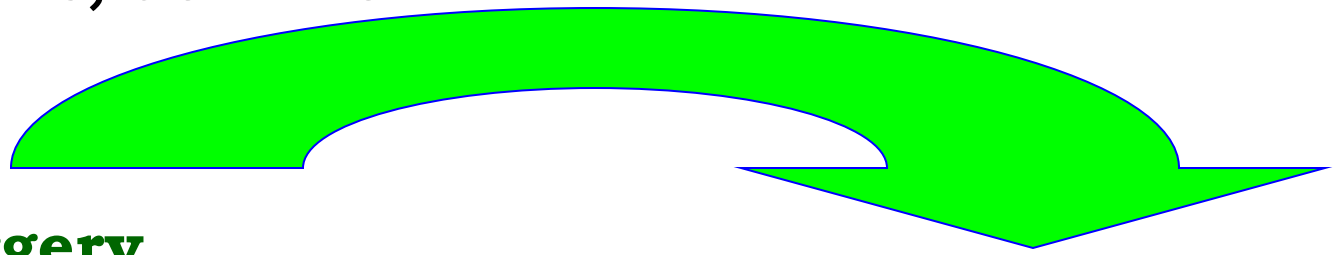
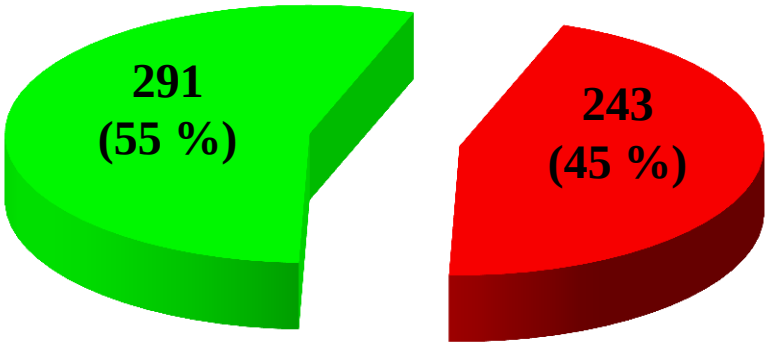
534 patients, definite IE

Thuny F, Habib G, EHJ 2009

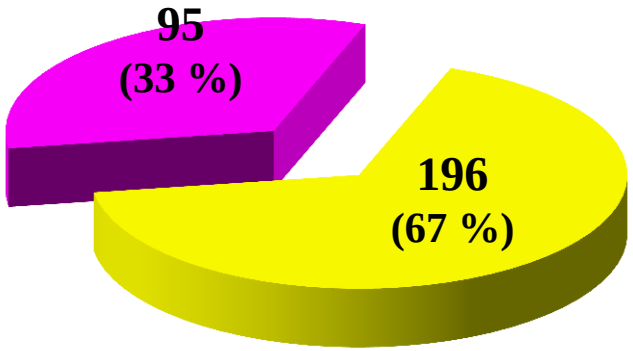


Early surgery



Medical therapy

< 7 days



> 7 days

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Timing of surgery in IE

Thuny F, Habib G, Eur Heart J 2011

	≤1st week surgery group (n=95)	>1st week surgery group (n=196)	*P* Value
6-month mortality	14 (15)	23 (12)	0.47
Relapses	8 (8)	4 (2)	0.02
Postop valv dysfunction	7 (7)	3 (2)	0.02

- similar 6-month mortality
- more frequent relapse ?

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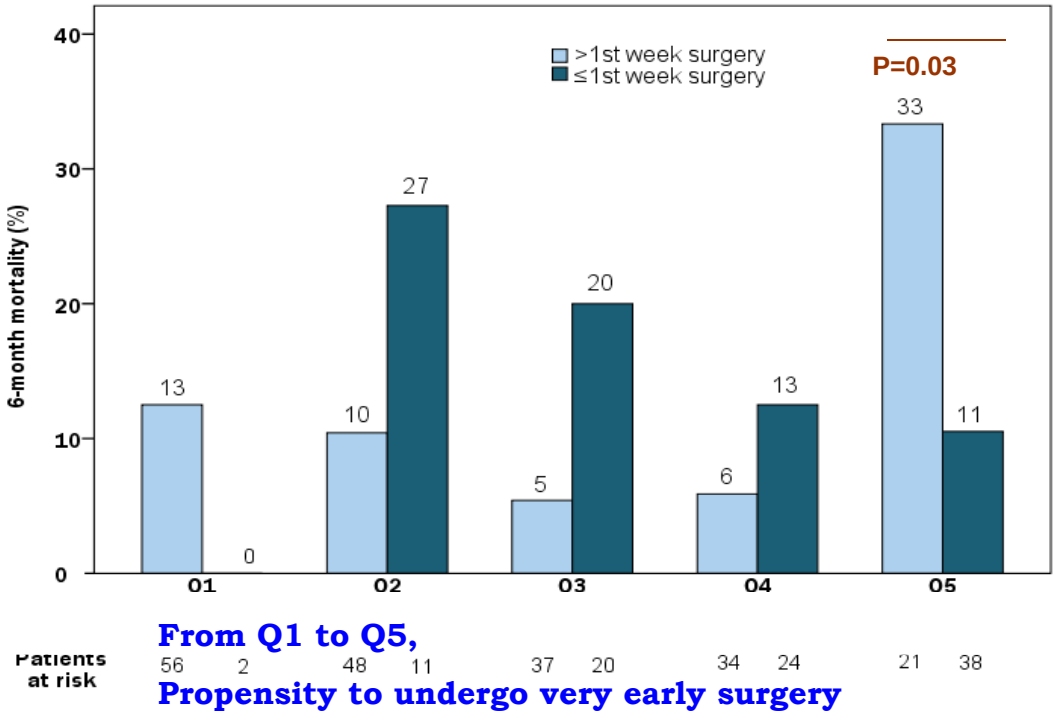
Timing of surgery in IE

Thuny F, Habib G, Eur Heart J 2011

The benefit of surgical therapy was the highest in patients with the most severe and complicated IE

291 operated consecutive patients



From Q1 to Q5,
Propensity to undergo very early surgery

- **≥ 2 indications of surgery in 75% of pts**
- **S.aureus**
- **Larger vegetations**

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Conclusion: infective endocarditis

1. **decision to operate is difficult, timing of surgery is even more**

2. **need for an early prognostic assessment**
   - **hemodynamic risk**
   - **infectious risk**
   - **embolic risk**

3. **decision adapted to the individual patient**

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