# Embolic Risk in Infective Endocarditis

Pr. Patrizio LANCELLOTTI





# 2015 Guidelines for the Management of Infective Endocarditis

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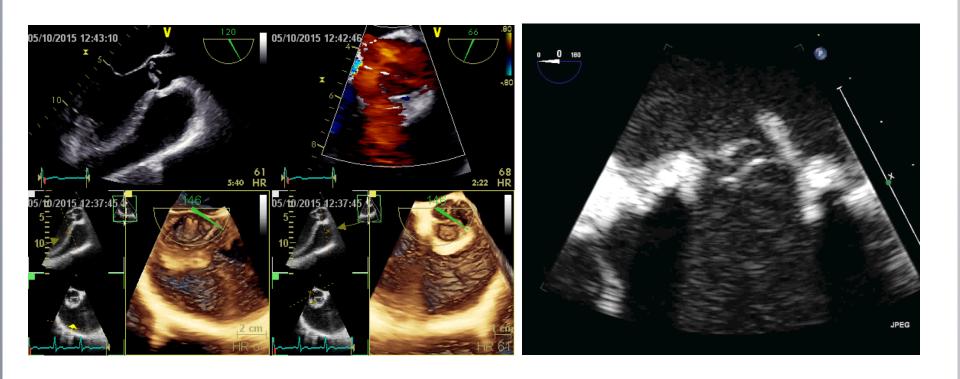
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# **Imaging Diagnosis Clinical Context**

Native valve IE

Prosthetic valve IE



When to operate?

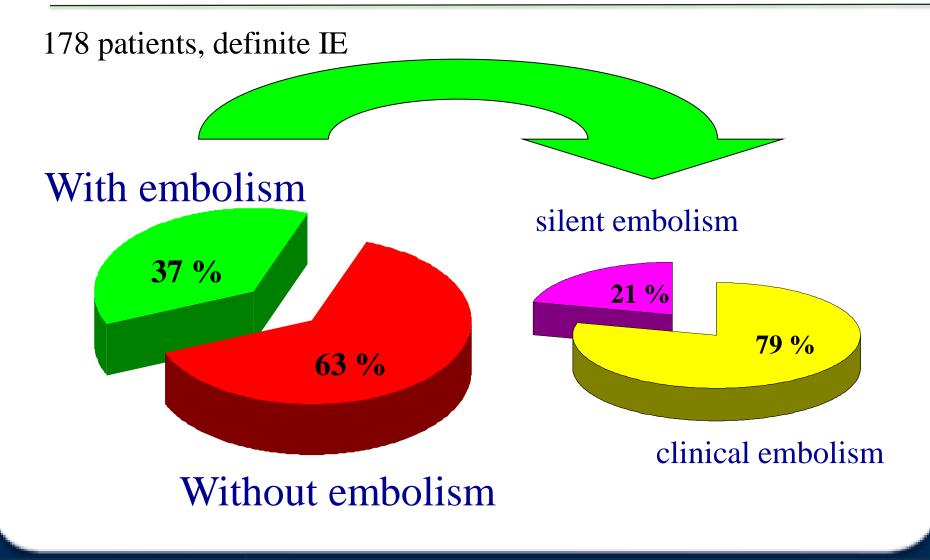
#### **Embolic risk in IE**

- 1. What is the risk of embolism in IE?
- 2. Can we predict the risk of embolism?
- 3. Can we prevent embolic events?
- 4. What to do in neurological complication?

#### **Embolic risk in IE**

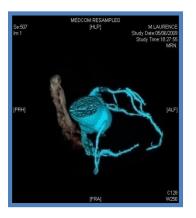
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#### **TEE and embolic risk**



### « Endocarditis » CT-scan

















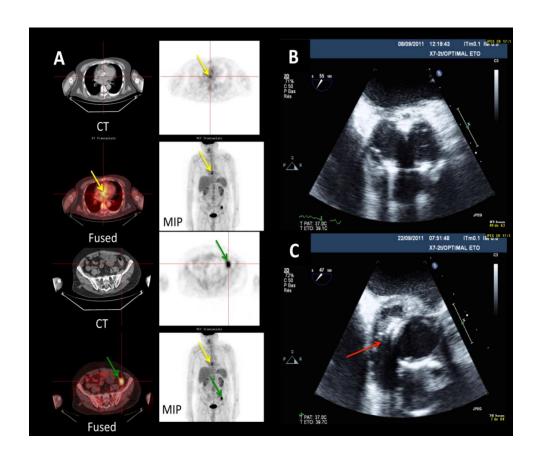
# **CT-scan imaging**

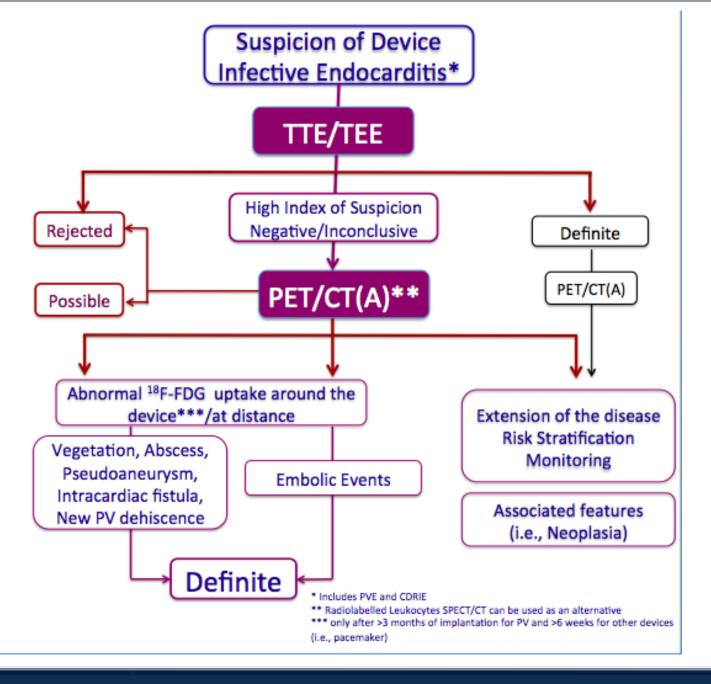


# **18FDG-PET-CT in endocarditis**

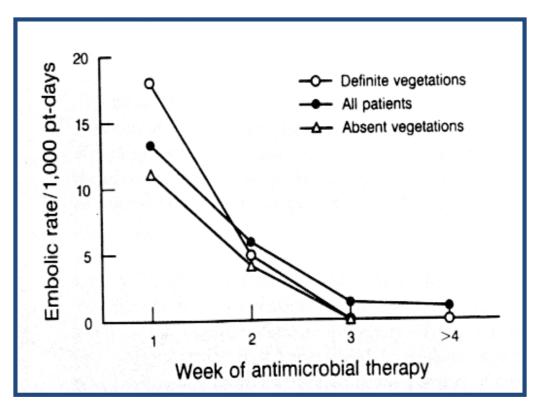
1. Early diagnosis of perivalvular lesions

2. Detection of secondary lesions





## **Embolic risk under therapy**



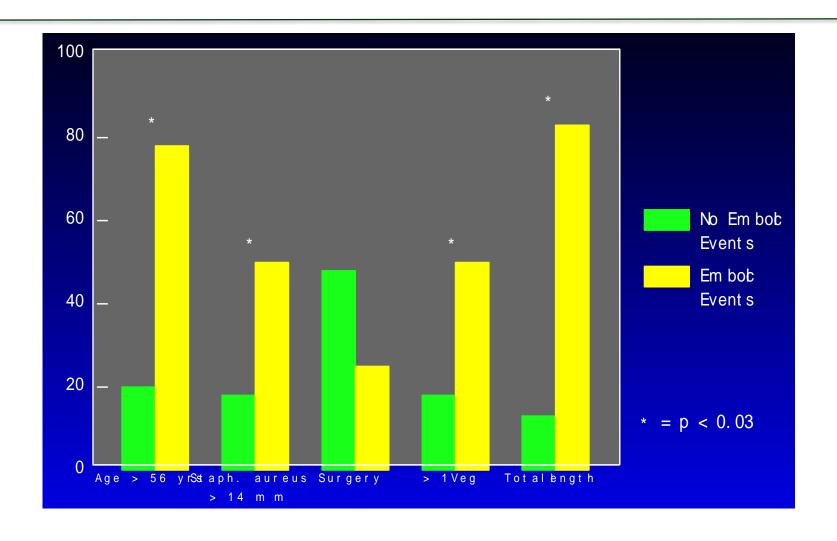
- 207 IE
- 13 % embolic events

- → 13/1000 pt/d during the 1st week
- → 1.2/1000 pt/d after the 2<sup>nd</sup> week

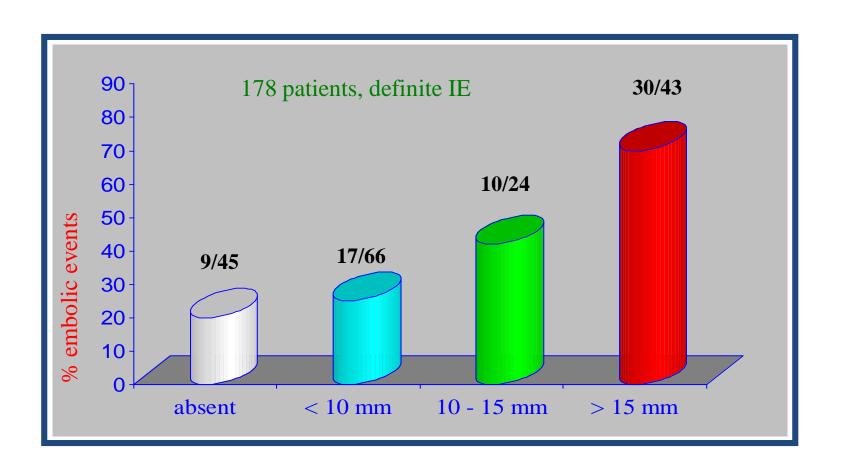
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#### **TEE and embolic risk**

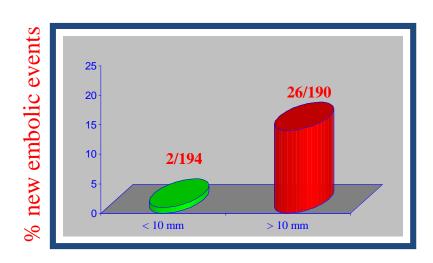


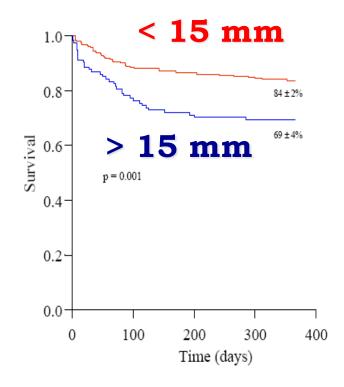
### **TEE and embolic risk**



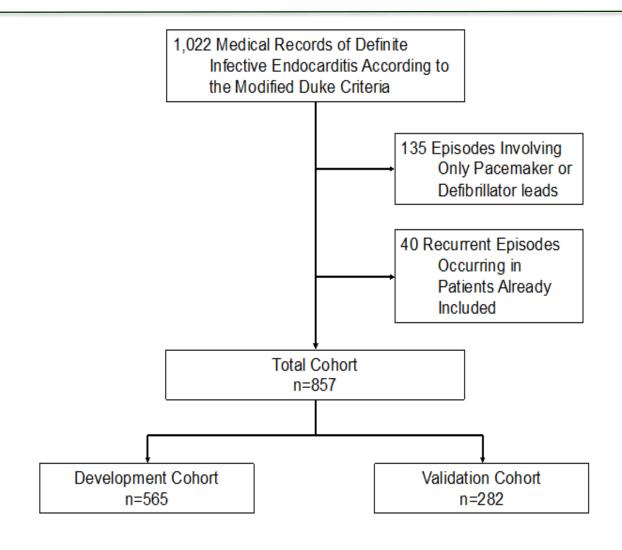
# **Embolic risk under therapy**

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





#### The embolic risk in IE

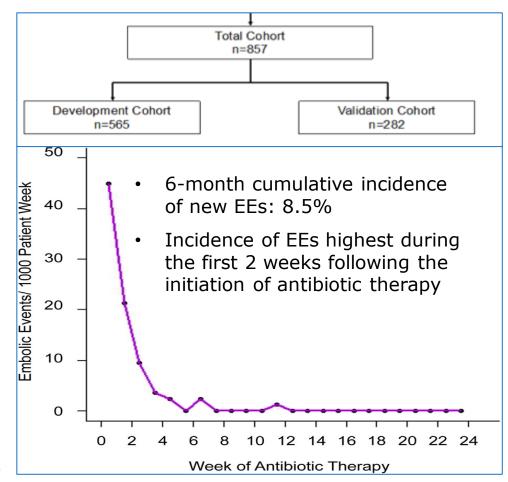


#### The embolic risk in IE





- 44.9 EEs per 1000 patient-weeks the first week
- 21.3 EEs per 1000 patient-weeks the second week



# Can we predict the embolic risk?

Confirmation that EE are related to the vegetation size

		Multivariate Analysis			
Variable	Univariate Analysis p Value	Hazard Ratio (95% Confidence Interval)	p Value		
Age	0.15	1.01 (0.99-1.03)	0.18		
Diabetes	0.05	1.30 (0.61-2.80)	0.50		
Previous embolism	0.04	1.40 (0.74-2.65)	0.30		
Atrial fibrillation	0.07	1.66 (0.81-3.41)	0.17		
Vegetation length (mm) (stratified)*	0.001				
>0 to ≤10		1.26 (0.24-6.69)	0.79		
>10		4.46 (1.06-18.88)	0.04		
Staphylococcus aureus	0.07	1.78 (0.85-3.76)	0.13		

# Can we predict the embolic risk?

Confirmation that EE are related to the vegetation size

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#### Can we calculate the embolic risk?

#### The embolic risk calculator

#### Risk Calculator for 6-Month Embolic Risk for Infective Endocarditis

Collect the following clinical, echocardiographic, and microbiological variables at admission of patient with infective endocarditis.

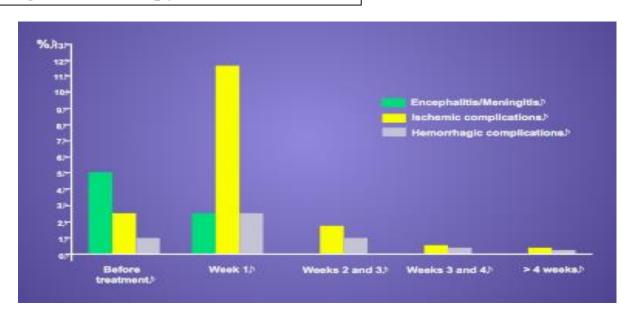
Then, the predicted embolic risk is automatically calculated at different times.

PREDICTED EMBOLIC RISK CALCULATION			
Time (Days)	Predicted Embolic Risk		
1	4%		
2	6%		
3	9%		
4	12%		
5	13%		
6	14%		
7	14%		
10	16%		
11	17%		
12	18%		
13	21%		
14	22%		
18	22%		
19	23%		
23	24%		
28	25%		
35	25%		
47	26%		
48	26%		
180	27%		

## Can we predict the risk of stroke?

- 1345 consecutive episodes of left-sided IE from 8 centers in Spain
- 340 neurological events.
- Factors associated with neurological events
  - Vegetation size ≥3 cm HR 1.91
  - Staphylococcus aureus HR 2.47
  - Mitral valve involvement HR 1.29
  - Anticoagulant therapy HR 1.31

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



### **Embolic risk under therapy**

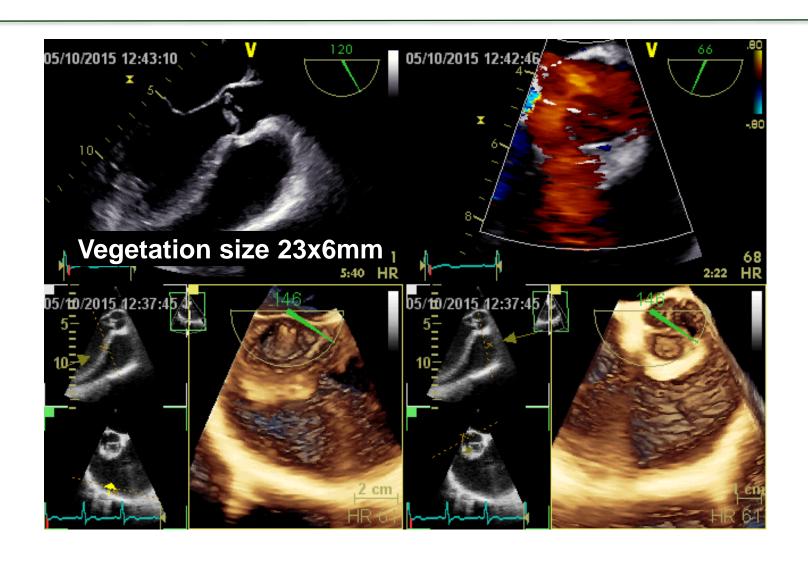
#### The risk of new embolism

- 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?

#### **Embolic risk in IE**

- 1. What is the risk of embolism in IE?
- 2. Can we predict the risk of embolism?
- 3. Can we prevent embolic events?
- 4. What to do in neurological complication?

## When to operate to prevent EE?



#### 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.

## **Study Patients**

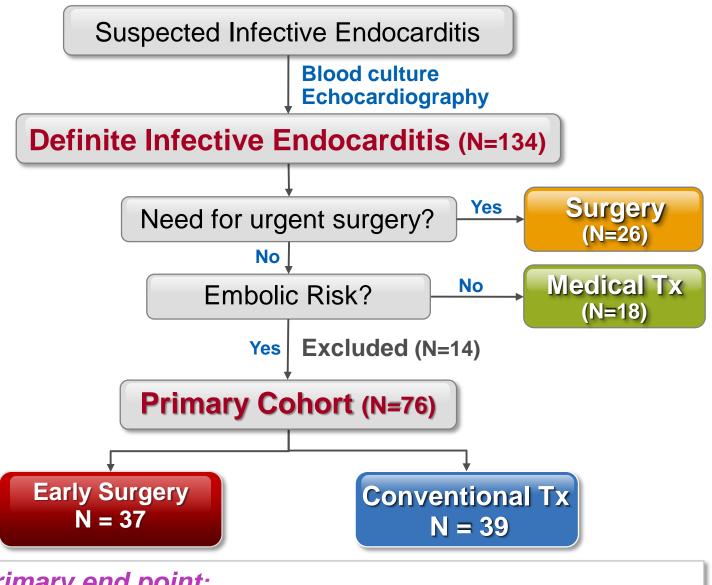
 All patients suspected of IE underwent blood cultures and echocardiography within 24 hrs after hospitalization

#### **Inclusion Criteria**

- Age: 15-80 years
- Definite left-sided native valve IE according to Duke criteria
- Severe mitral or aortic valve disease
- Vegetation length > 10mm

#### **Exclusion Criteria**

- Pts with urgent indication of surgery moderate to severe CHF, heart block, annular or aortic abscess, penetrating lesions, fungal endocarditis
- Pts not candidates for early surgery age
   80 yrs, coexisting major embolic
   stroke or poor medical status
- Prosthetic valve IE
- Right-sided vegetations
- Small vegetations ≤ 10mm



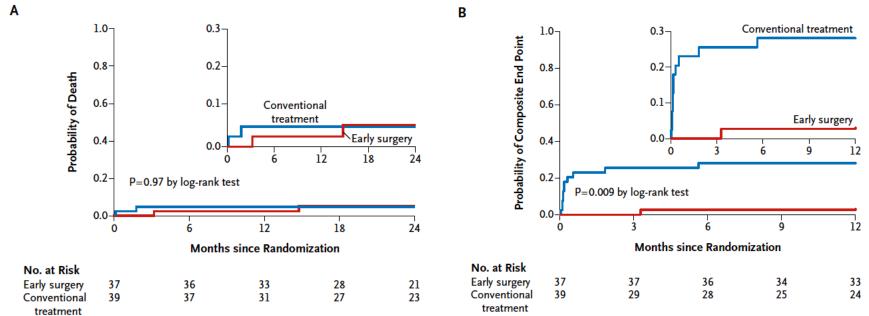
#### **Primary end point:**

In-hopital death and clinical embolic events at 6 weeks

# **Embolic risk under therapy**

Randomization of pts. with severe valve disease, and large vegetations to early surgery (37 patients) or conventional treatment (39)

Primary EP: in hospital death, EE, recurrence of IE, repeat hospitalization due to the development of CHF



# **Indications and timing of surgery**

Indications for surgery	Timing	Class	Level
1. Heart Failure			
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock.	Emergency	ı	В
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance.	Urgent	1	В
2. Uncontrolled infection			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation).	Urgent	I	В
Infection caused by fungi or multiresistant organisms.	Urgent/elective	1	С
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci.	Urgent	lla	В
PVE caused by staphylococci or non-HACEK Gram negative bacteria.	Urgent/elective	lla	С
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after one or more embolic episode despite appropriate antibiotic therapy.	Urgent	I	В
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk.	Urgent	lla	В
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm).	Urgent	lla	В
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery.	Urgent	IIb	С

## Indications and timing of surgery in leftsided valve IE: Prevention of embolism

Indications for surgery	Timing	Class	Level
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after ≥1 embolic episodes despite appropriate antibiotic therapy.	Urgent	ı	В
Aortic or mitral NVE with <b>vegetations &gt;10 mm</b> , associated <b>with severe</b> valve stenosis or regurgitation, and <b>low operative risk</b> .	Urgent	lla	В
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm).	Urgent	lla	В
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery.	Urgent	IIb	С

<sup>&</sup>quot;Surgery may be preferred if procedure preserving the native valve is feasible

# **Early Surgery for IE Prevention of Embolism**

#### 2014 AHA/ACC guidelines

#### **Class IIa indication**

 Recurrent emboli and persistent vegetation despite antibiotic Tx

#### **Class IIb indication**

 Mobile large vegetations in excess of 10 mm

#### 2015 ESC guidelines

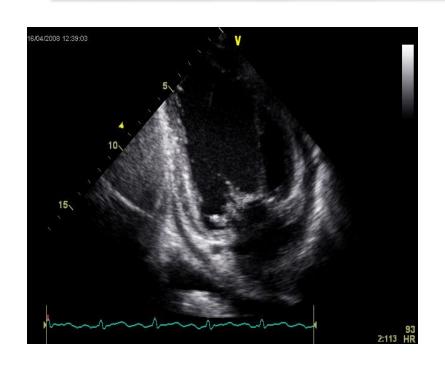
#### **Class I indication**

Large vegetations (> 10mm)
 following <u>one</u> or more embolism
 despite antibiotic Tx

#### **Class IIb indication**

 Isolated very large vegetations in excess of 15 mm

### When to operate to prevent EE?



- Large vegetation
- High embolic risk
- High probability of valve repair



Surgical therapy

Native valve IE

## Indications and timing of surgery in leftsided valve IE: Prevention of embolism

Indications for surgery	Timing	Class	Level
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after ≥1 embolic episodes despite appropriate antibiotic therapy.	Urgent	1	В
Aortic or mitral NVE with <b>vegetations &gt;10 mm</b> , associated <b>with severe</b> valve stenosis or regurgitation, and <b>low operative risk</b> .	Urgent	lla	В
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm).	Urgent	lla	В
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery.	Urgent	IIb	С

Do not delay surgery !!!!

# **Early Surgery for IE Prevention of Embolism**

#### 2014 AHA/ACC guidelines

#### **Early Surgery**

during the initial
 hospitalization before
 completion of a full course
 of antibiotics

#### 2015 ESC guidelines

#### **Urgent Surgery**

Within a few days, <7 days</li>

#### **Embolic risk in IE**

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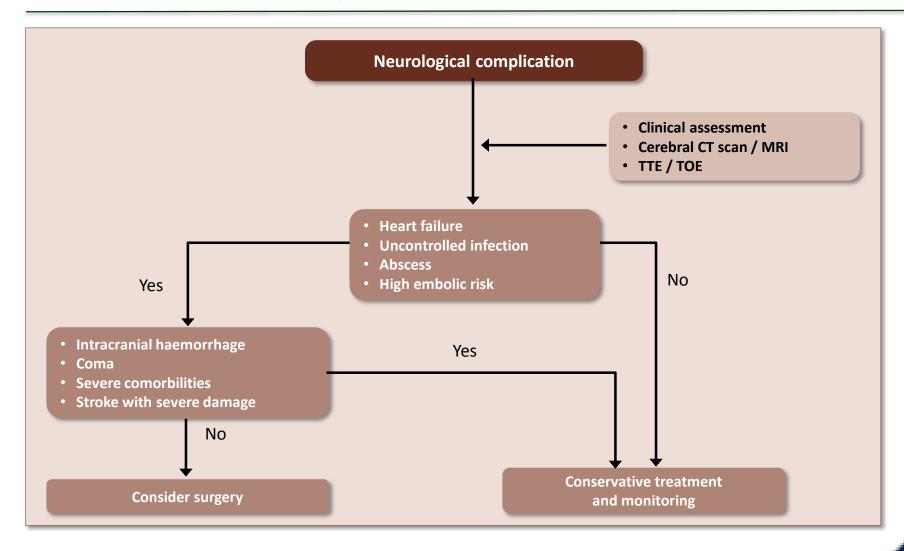
# Therapeutic strategy for patients with IE and neurological complications

- Symptomatic in 15–30% vs. Silent in 35–60% of IE
- Consequence of embolism from vegetations



### Cerebral MRI Diffusion T2\* MR angiography Infectious **Ischemic** Microbleeds **Emboli** aneurysms No Minor Minor criteria criteria

# Therapeutic strategy for patients with IE and neurological complications



# Management of neurological complications of IE

Recommendations	Class	Level
After a silent embolism or transient ischaemic attack, cardiac surgery, if indicated, is recommended without delay.		В
Neurosurgery or endovascular therapy is indicated for very large, enlarging or ruptured intracranial infectious aneurysms.	_	С
Following intracranial haemorrhage, surgery should generally <b>be postponed</b> for ≥1 month.	lla	В
After a stroke, surgery indicated for HF, uncontrolled infection, abscess, or persistent high embolic risk should be considered without any delay as long as coma is absent and the presence of cerebral haemorrhage has been excluded by cranial CT or MRI.	lla	В
Intracranial infectious aneurysms should be looked for in patients with IE and neurological symptoms. CT or MR angiography should be considered for diagnosis. If non-invasive techniques are negative and the suspicion of intracranial aneurysm remains, conventional angiography should be considered.		В

# Conclusion: 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