Nice
Janvier 2014

Endocardites Infectieuses en 2014

Imagerie et Recommandations

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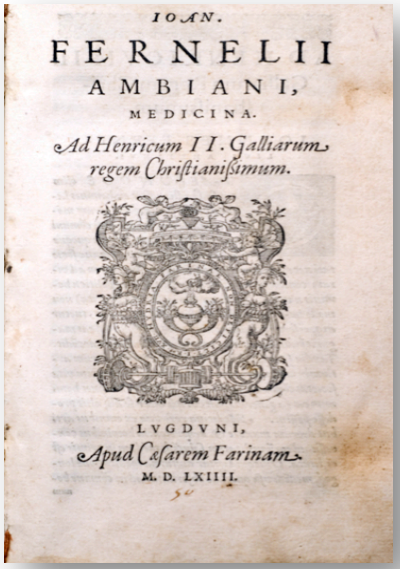
Aix-Marseille Université

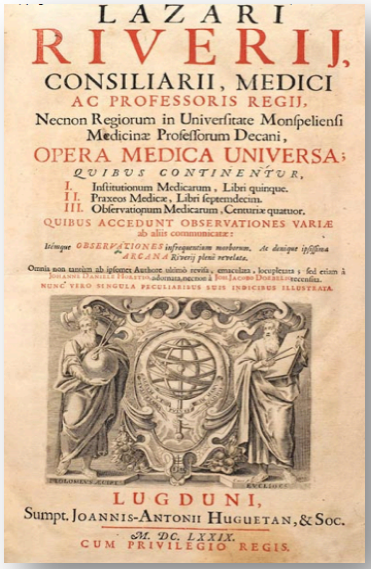
Evolution of knowledge from the early clinical description down to the early days of surgery…

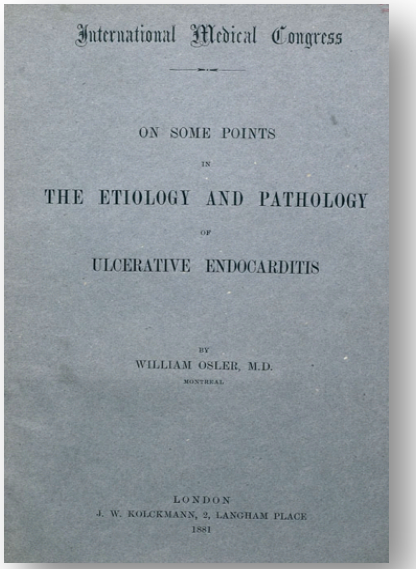
Jean Fernel
(1497-1558)

Lazare Riviere
(1589-1655)

William Osler
(1849-1919)







Evolution of knowledge from the early clinical description down to the early days of surgery…

Evidence of endocardial lesions

- Histology
- New regurgitant murmur
- Predisposing heart disease

TTE

TEE

CT Scan

PET/CT
Leucocytes R. SPECT/CT

1970s-1990s

1990s-2000s

2000s-2010s

years

- Valve culture
- Blood cultures

Serologies

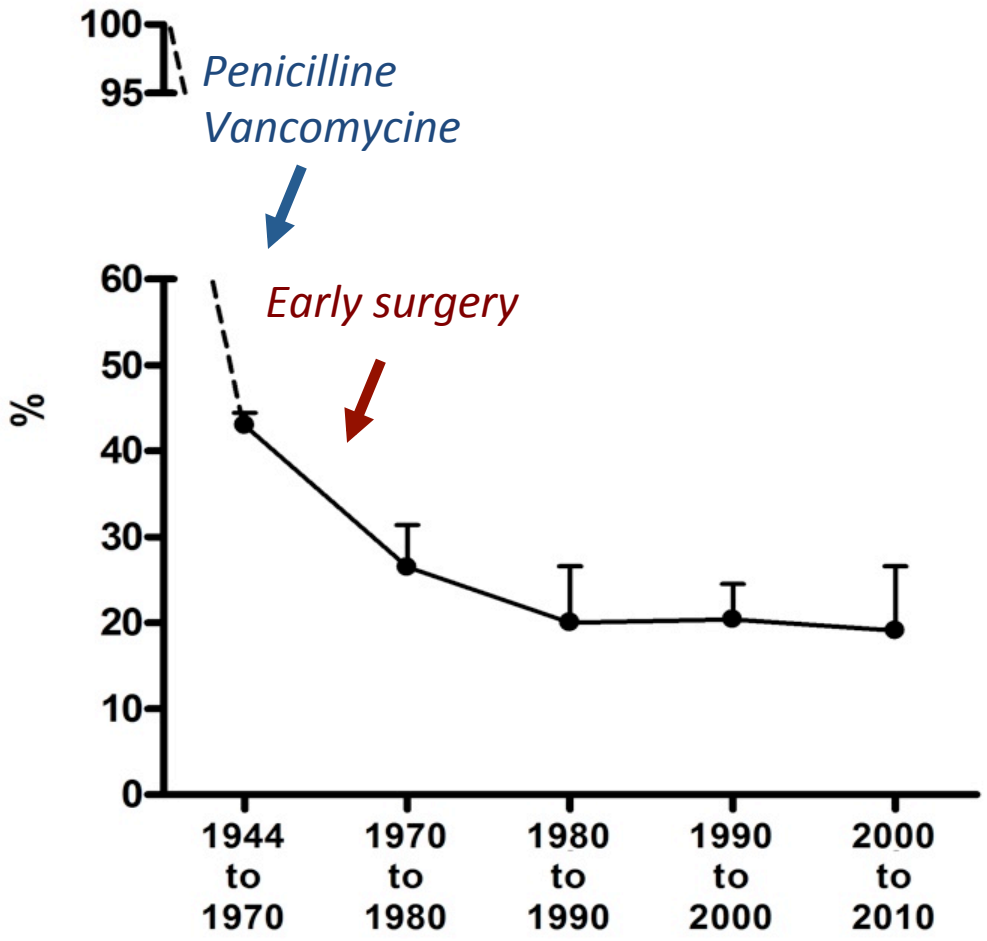
- PCR
- Immunohistochemistry

Mass spectrometry

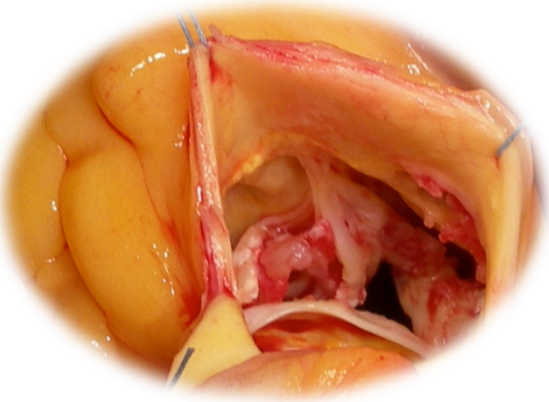
Evidence of infection

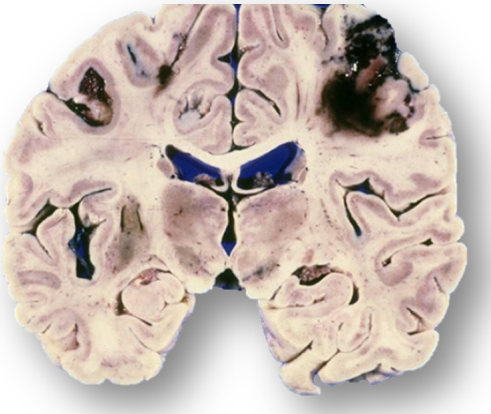
Evolution of knowledge from the early clinical description down to the early days of surgery…

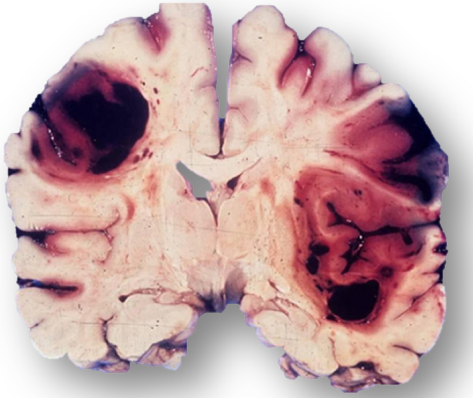
Mortality (%)



Thuny F, et al. *Lancet* 2012;379:965-75





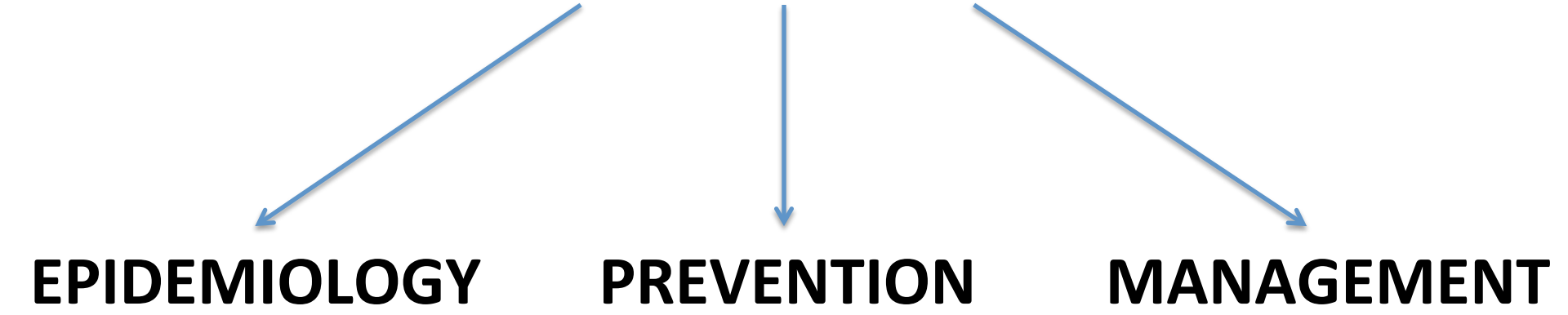


2000 people / year in France
17 000 people / year in USA

1/3 of patients
will die within the 1st year of diagnosis

Research in IE remains very dynamic and offer hope to improve prognosis

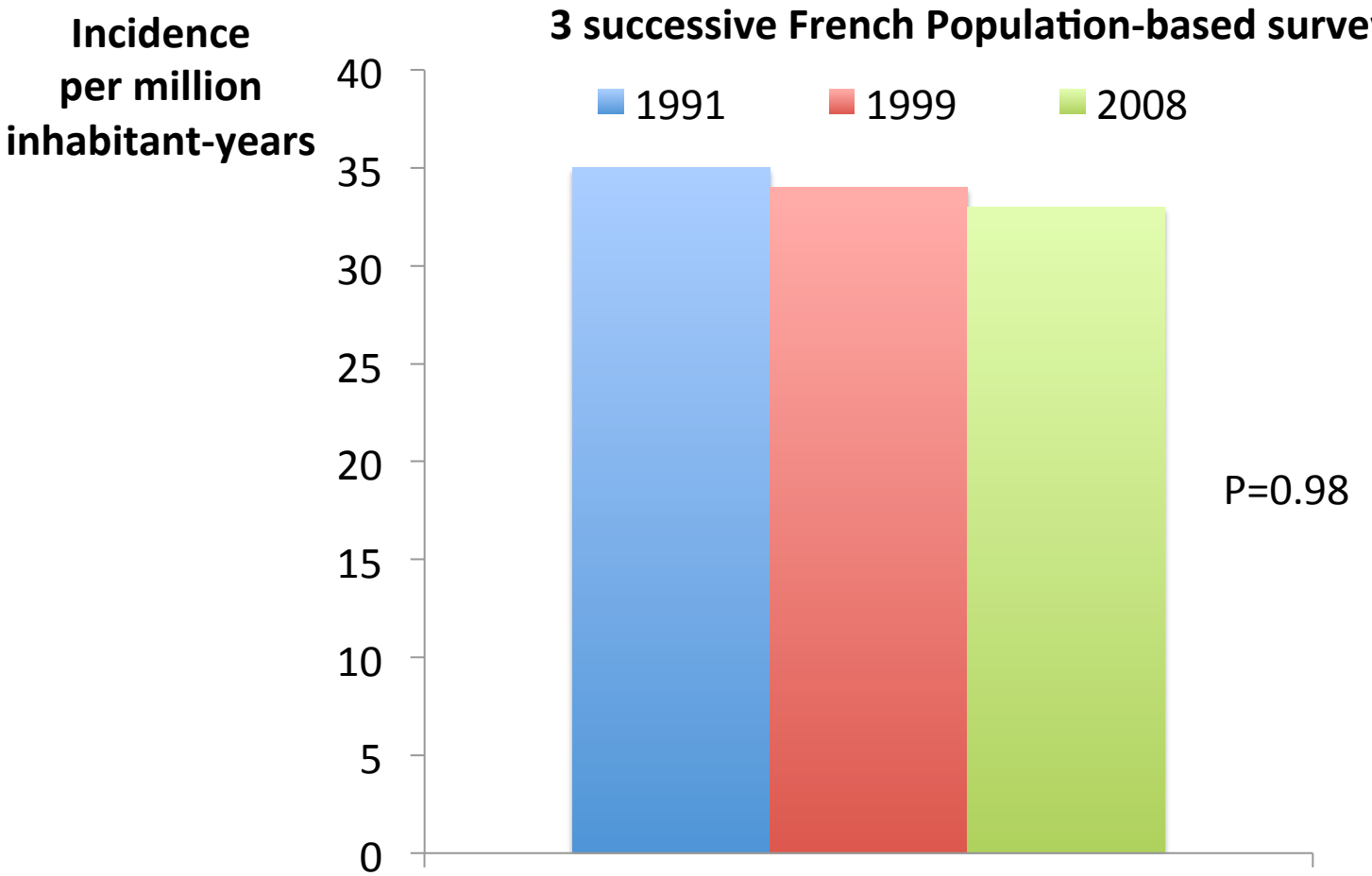
WHAT'S NEW IN ENDOCARDITIS ?



EPIDEMIOLOGY

EPIDEMIOLOGY

Prevention strategies have not lowered the incidence of this life-threatening disease



Duval X, et al. J Am Coll Cardiol 2012;59:1968-76

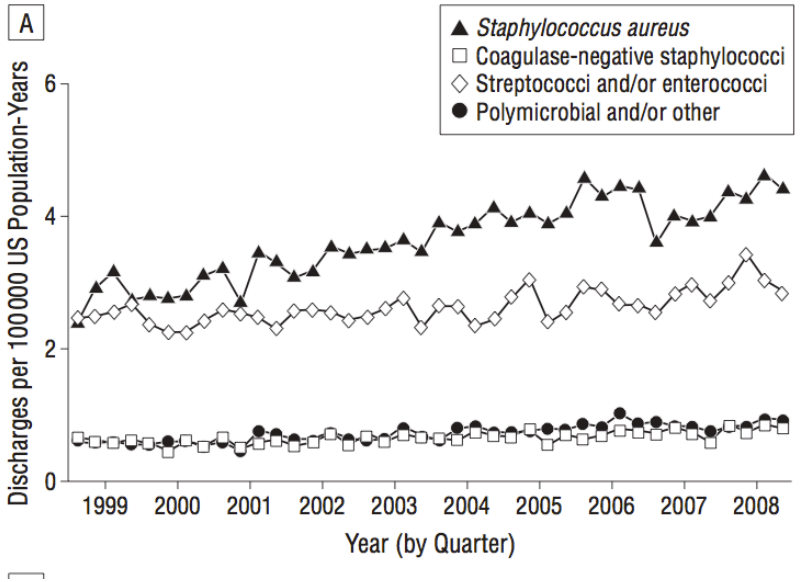
EPIDEMIOLOGY

Epidemiological profile has changed

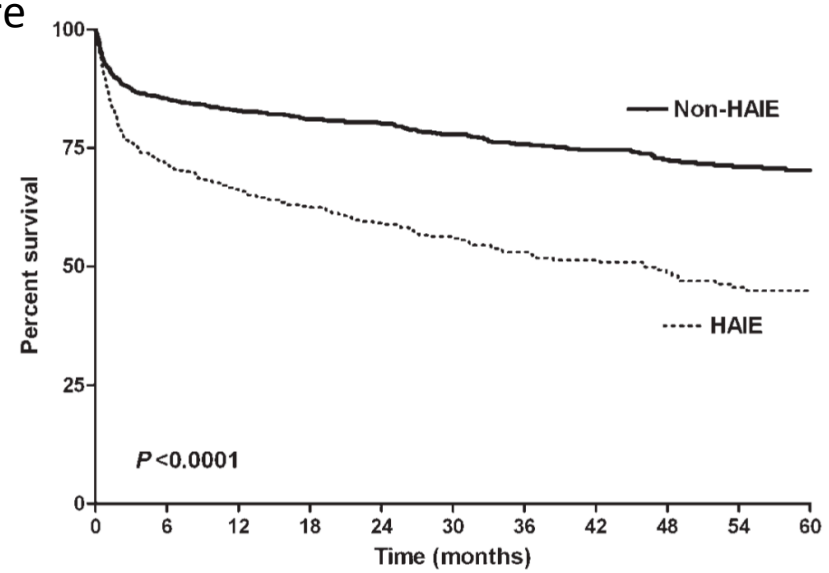
Increasing proportion of «Health care-associated IE»

30% of cases

Nosocomial
Long-term IV therapy
Hemodialysis
Home care

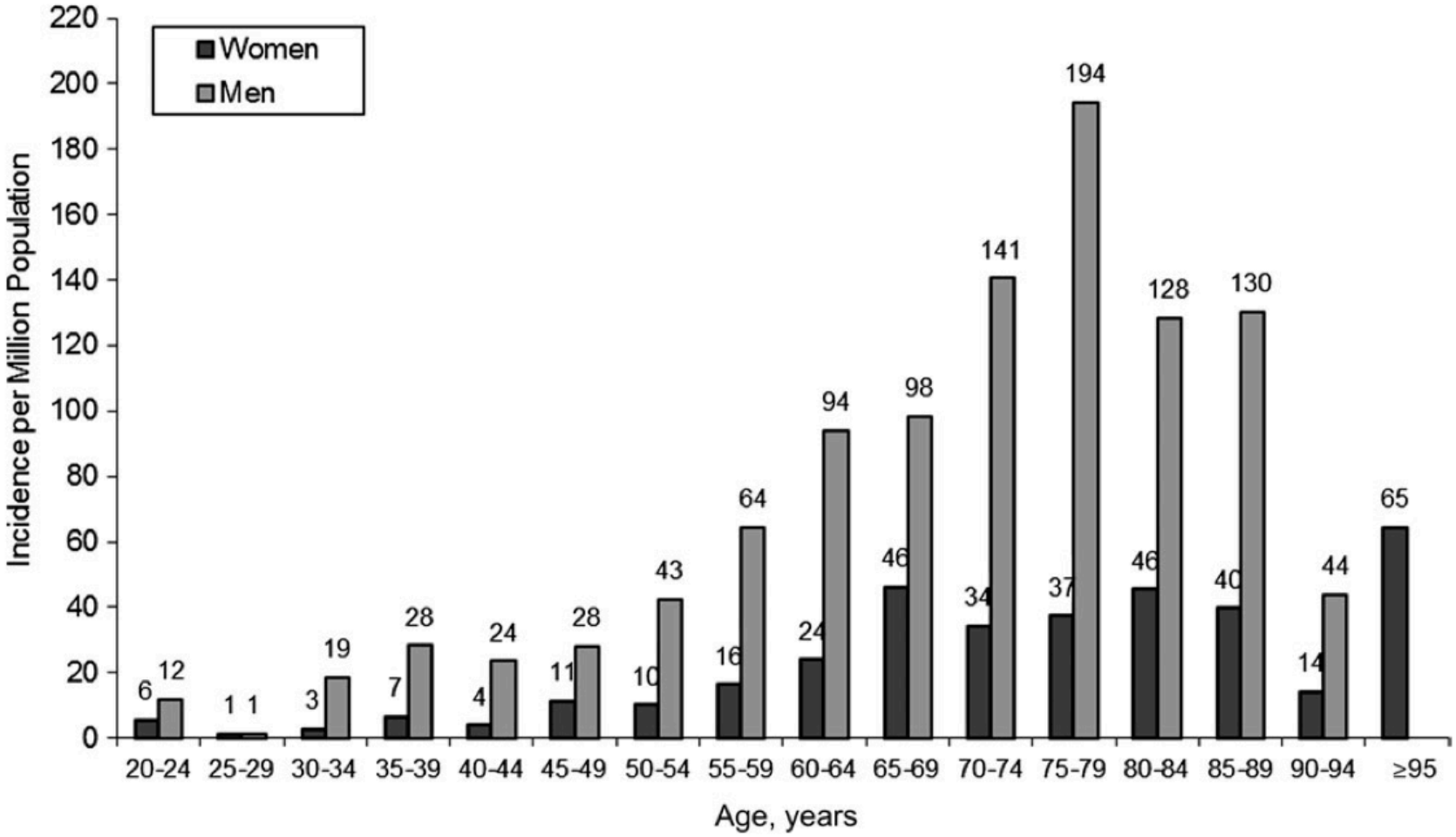


Federspiel JJ et al, et al. *Arch Intern Med* 2012;172:364-365



Sy RW, et al. *Eur Heart J* 2010;31:1890-1897

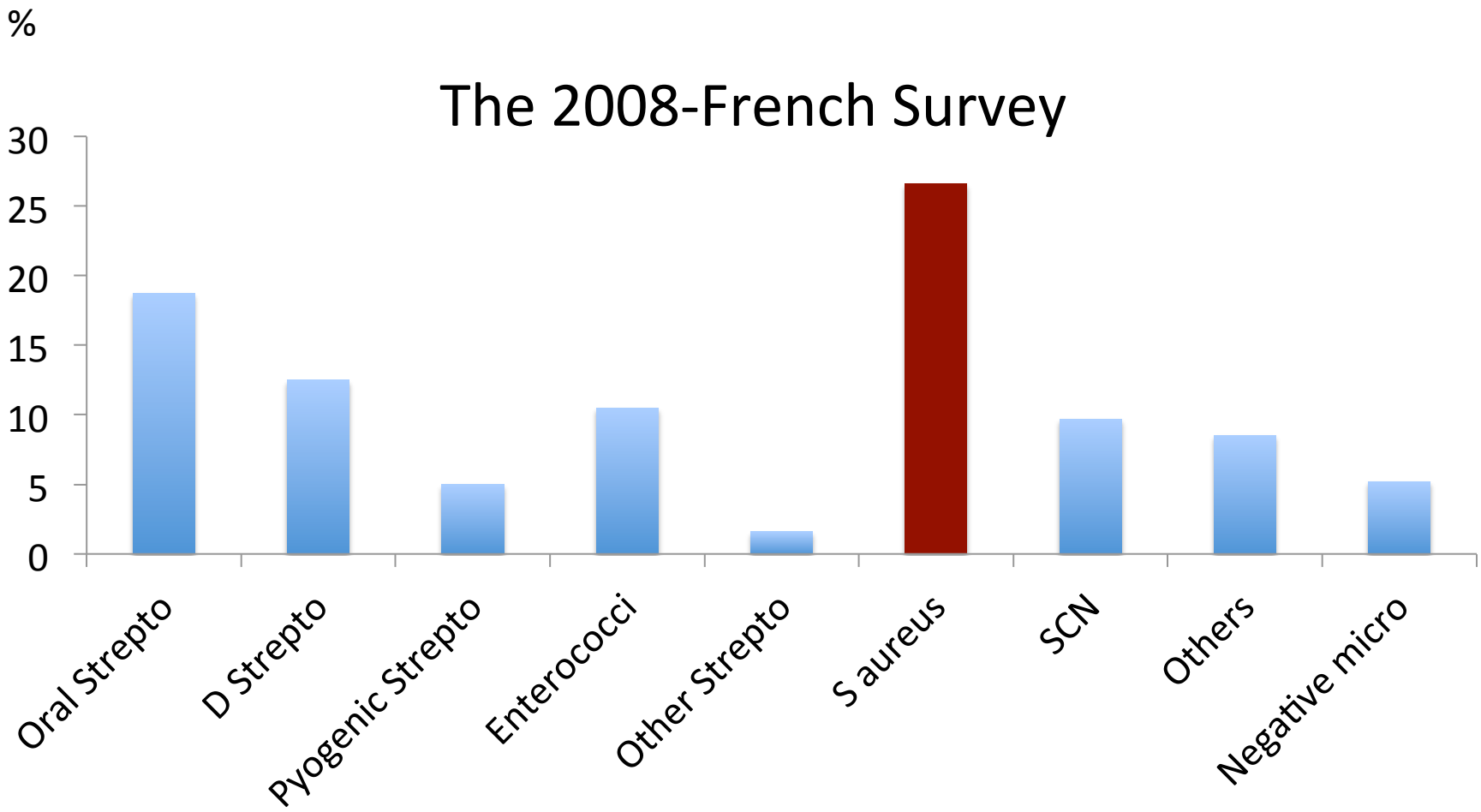
EPIDEMIOLOGY



Selton-Suty C, et al. Clin Infect Dis 2012;54:1230-9

EPIDEMIOLOGY

Epidemiological profile has changed
S aureus is the first causative pathogen



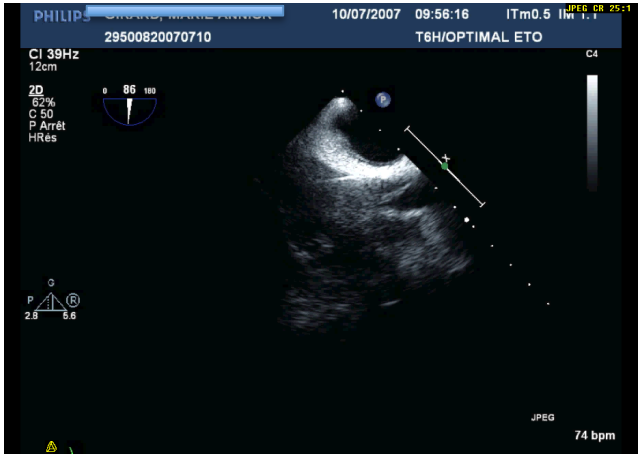
Selton-Suty C, et al. Clin Infect Dis 2012;54:1230-9

EPIDEMIOLOGY

Epidemiological profile has changed

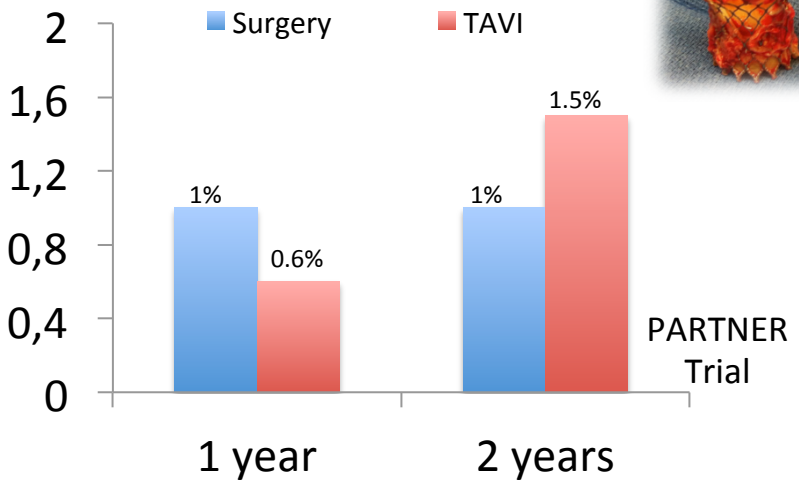
Pacemaker/ICD leads endocarditis

- 2 per 1000 implants/year
- Increasing of the number of implantation
  CDIE=15% of all IE



Prosthetic valve endocarditis

- 1% per patient–year
- Increasing of the number of implantation (plus 5-7% per year)
- PVE=20-30% of all IE
- Emergence of new forms: TAVI++



Uslan DZ, et al. Arch Intern Med 2007;167:669–75

Kodali SK, et al. New Engl J Med 2012;366:1686-95

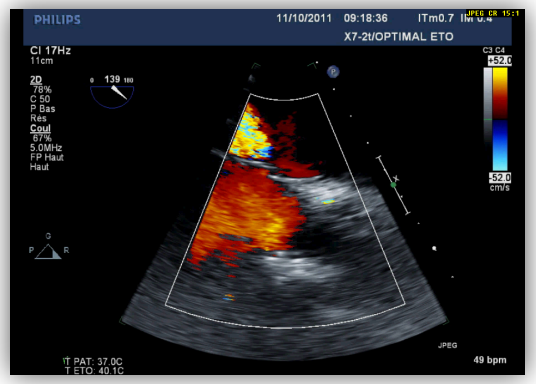
EPIDEMIOLOGY

Epidemiological profile has changed

Post-TAVI endocarditis

➡ Emergence of "TAVI endocarditis": a new type of PVE?

- Paravalvular leaks my be the nidus for infection
- Elderly patients with more comorbidities and more insidious symptoms
- Little experience of TEE-interpretation in post-TAVI-endocarditis
- Surgery may not be a feasible treatment option in the majority of cases
- Intuitively, the prognosis of patients can be expected to be worse

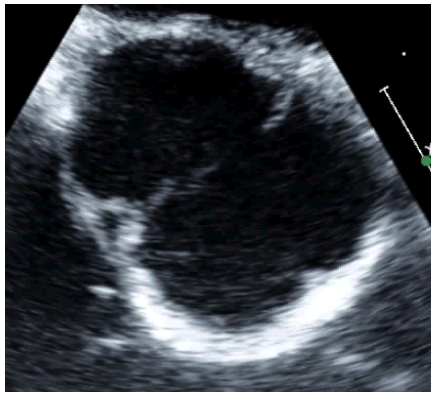


Eisen E, et al. Clin Cardiol 2012;35,E1–E5

PREVENTION

PREVENTION

Cardiac predisposition



Antibiotics

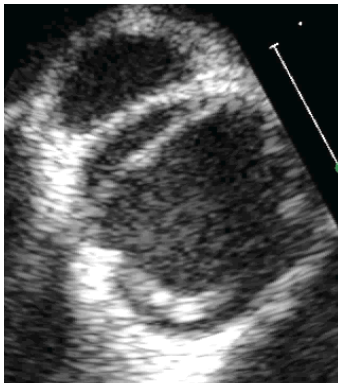
Bacteremia

Hygiene

Porte of entry

- Oral
- Skin
- Digestive
- Urinary

Endocarditis



PREVENTION

The History of antibioprophylaxis

- First recommendations: AHA 1955
- Definitions of moderate- and high- risk patients (cardiac predispositions)
- Definitions of the different procedures (dental, GI, GU…)
- ATB: drugs and doses…

	Procedures listed	Predisposing cardiac conditions*	
		High risk	Moderate risk
Dental procedures			
French (2002)[33,78]	Several dental procedures—eg, dental extraction, scaling	Prophylaxis recommended	Prophylaxis optional
BSAC (2006)[35]	All dental procedures involving dento-gengival manipulation or endodontics	Prophylaxis recommended	Prophylaxis not recommended
AHA (2007)[6]	Any dental procedure that involves manipulation of the oral mucosa	Prophylaxis recommended	Prophylaxis not recommended
Extra-dental procedures			
French (2002)[33,78]	Several procedures—eg, colonoscopy	Prophylaxis recommended or optional (depending on the procedure)	Prophylaxis optional or not recommended (depending on the procedure)
BSAC (2006)[35]	Several procedures—eg, oesophageal laser therapy	Prophylaxis recommended	Prophylaxis recommended
AHA (2007)[6]	..	Prophylaxis not recommended	Prophylaxis not recommended

*See panel. BSAC=British Society of Antimicrobial Chemotherapy. AHA=American Heart Association.

Table 3: **Comparison of recent guidelines that have reduced indications for prophylaxis of infective endocarditis**

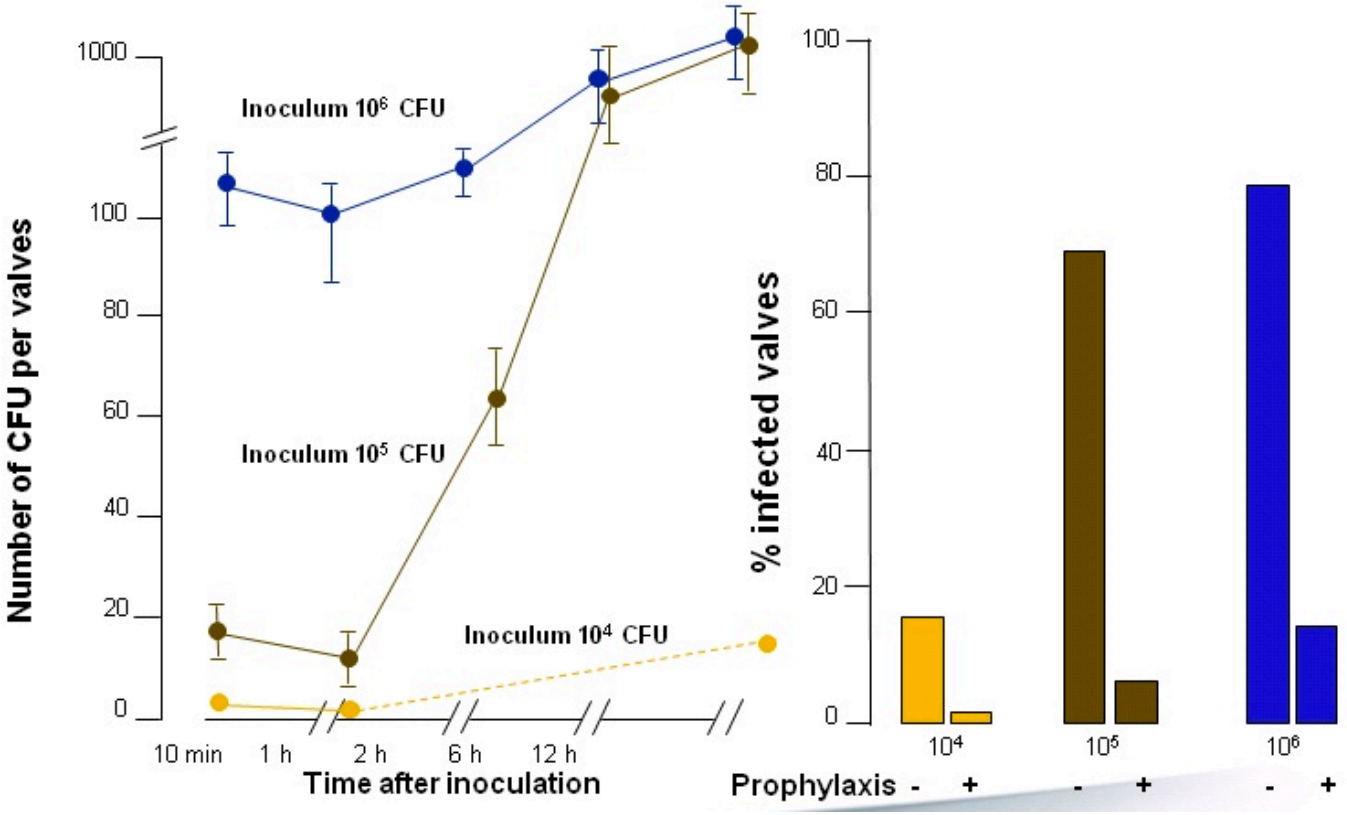
PREVENTION

What are the evidence of antibioprophylaxis?

PREVENTION

The evidences supported antibioprophylaxis are only experimental-based

Single-dose Amoxicillin Prophylaxis in Streptococcal IE



Moreillon P. ESC 2009

PREVENTION

The evidences supported antibioprophylaxis are only experimental-based

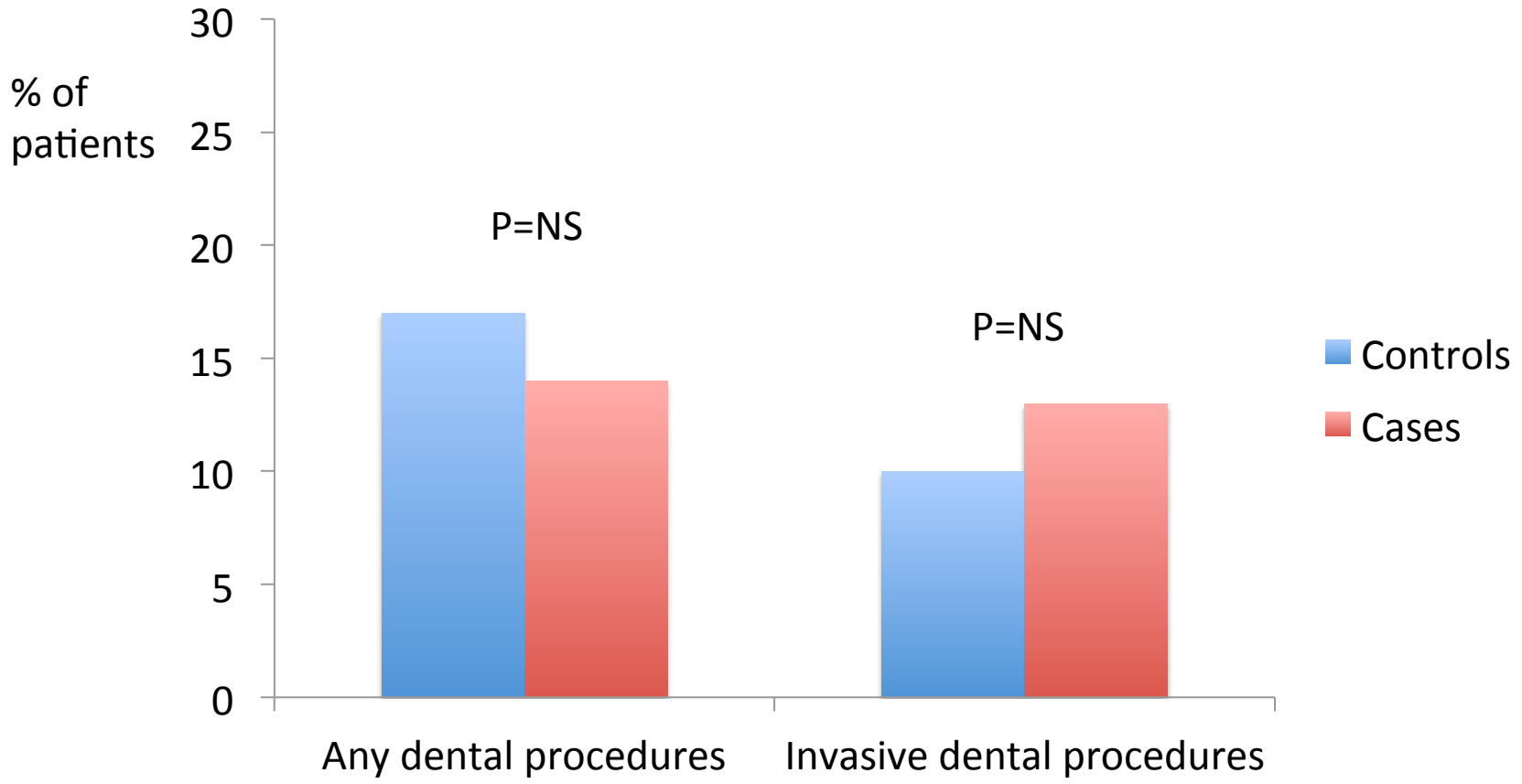
Dans la « vie réelle »: bactériémie rarement équivalente aux modèles expérimentaux

	CFU/mL
• Dose de germes pour EI expérimentale	10^{7-8}
• Extraction dentaire	10

Beeson et al. J Exp Med 1945;81:199
McEntegart et al 1949;2:596

PREVENTION

Dental procedures does not seem to be a risk factor for IE



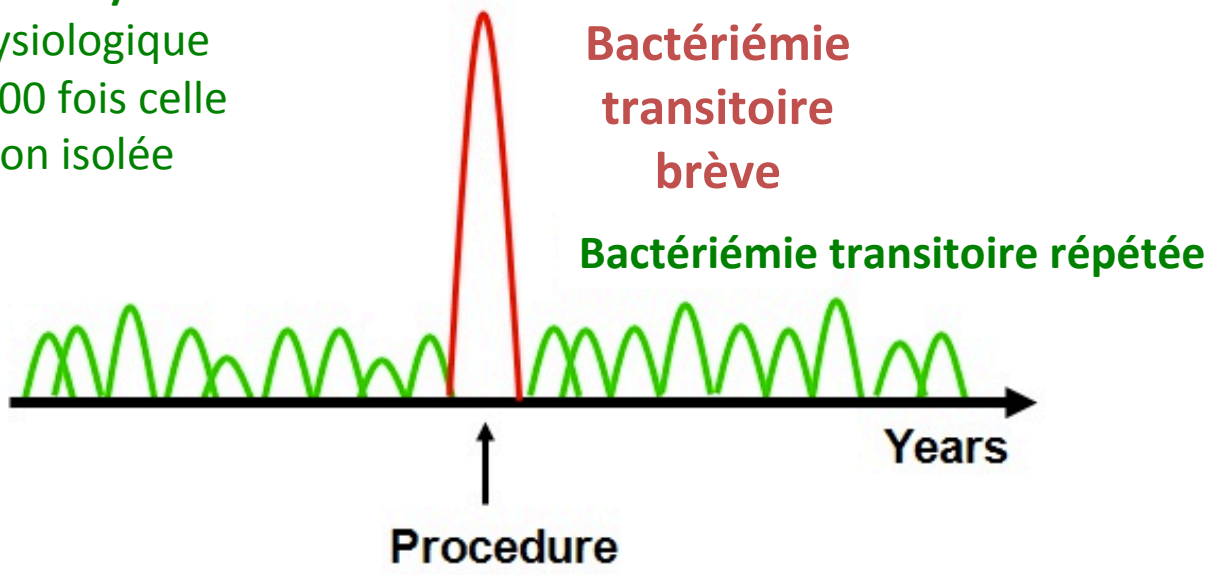
Strom BL, et al. Ann Intern Med 1998;129:761-9

PREVENTION

Dental procedures does not seem to be a risk factor for IE

« Activité normale »: bactériémie transitoire répétée

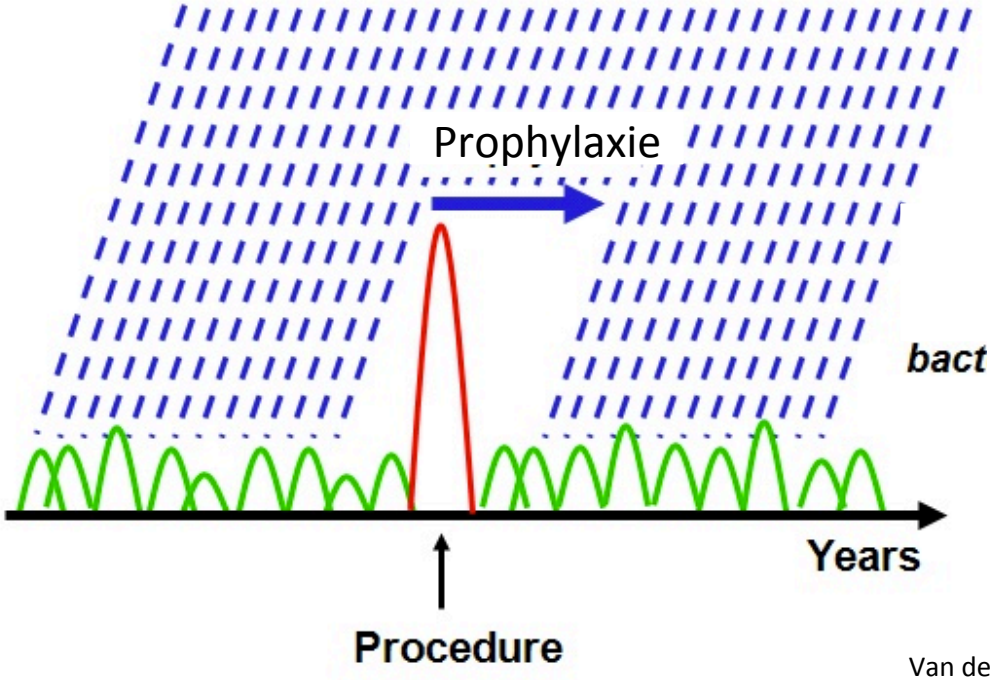
Exposition cumulée/an
Bactériémie physiologique cumulée = 100 000 fois celle d'une extraction isolée



PREVENTION

Dental procedures does not seem to be a risk factor for IE

Donc Intérêt limité de l'Antibioprophylaxie



Van de Meer et al. Lancet 1992:339;135-9

PREVENTION

Dental procedures does not seem to be a risk factor for IE

Donc Intérêt limité de l'Antibioprophylaxie

Simulation du rapport cout-efficacité de l'antibioprophylaxie:

- **10 millions de patients à risque**
- **En supposant que l'antibioprophylaxie soit efficace à 100%**

Protection de 19 cas
Décès de 181 cas par anaphylaxie
+ risques de résistances

Agha Z et al. Med Decis Making 2005;25:308-20

PREVENTION

ESC IE prevention: main changes

1. **A**ntibiotic prophylaxis must be **limited to patients with the highest risk of IE undergoing the highest risk dental procedure**

2. **Good oral hygiene** and regular dental review **are more important** than antibiotic prophylaxis

3. **Aseptic measures** are mandatory during venous catheterization and during invasive procedures

4. **Prospective epidemiological studies** are needed to evaluate if the reduced use of prophylaxis is associated with a change in the incidence of IE.

ESC Guidelines 2009

PREVENTION

ESC IE prevention: main changes

Cardiac Predispositions

	Level of evidence
Antibiotic prophylaxis should only be recommended for patients at highest risk of IE	IIa C
1. Patients with a prosthetic valve or any prosthetic material used for cardiac valve repair	
2. Patients with previous IE	
3. Patients with congenital heart disease (CHD)	
a. Cyanotic CHD with or without previous interventions	
b. CHD with complete repair (surgical or percutaneous) for the next 6 months	
c. When a residual defect persists after cardiac surgery or percutaneous technique	
Antibiotic prophylaxis is <u>no longer</u> recommended in other form of valvular or CHD	III C

ESC Guidelines 2009

PREVENTION

ESC IE prevention: main changes

Dental procedures

	Level of evidence	
AB should be considered only for dental procedures with manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	IIa	C
AB is not recommended for local anaesthetic injections in non infected tissue removal of sutures, dental X-rays	III	C
Placement or adjustment of removable prosthodontic or orthodontic appliances or braces		
After the shedding of deciduous teeth or trauma to the lips and oral mucosa		

ESC Guidelines 2009

PREVENTION

ESC IE prevention: main changes

Single dose 30-60 min before dental procedure

Situation	Antibiotic	Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin or Ampicillin	2 g p.o. or i.v.	50 mg/kg p.o. or i.v.
Allergy to penicillin or ampicillin	Clindamycin	600mg p.o. or i.v.	20 mg/kg p.o. or i.v.

ESC Guidelines 2009

PREVENTION

AHA IE prevention: main changes

TABLE 3. Cardiac Conditions Associat… Risk of Adverse Outcome From Endocard… …is With Dental Procedures Is Rec…

Prosthetic cardiac valve
Previous IE
Congenital he…
Unre… …g palliative shunts and conduits
…ital heart defect with prosthetic material or …d by surgery or by catheter intervention, during the …ter the procedure†
Re… CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
Cardiac transplantation recipients who develop cardiac valvulopathy

≈ IDEM

AHA Guidelines 2007

PREVENTION

British IE prevention (« NICE ») Guidelines : main changes

NEVER !

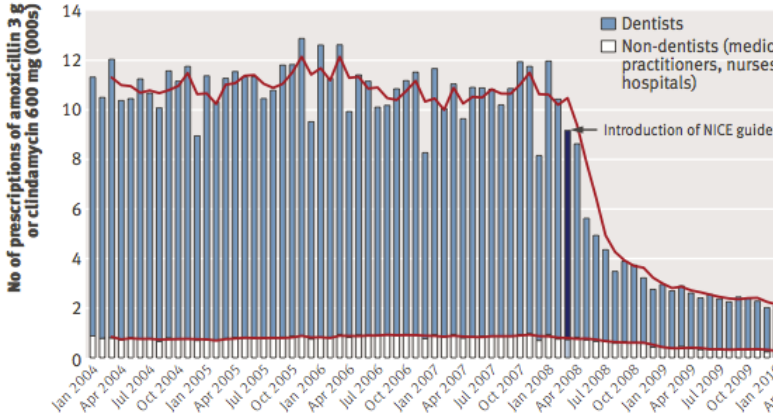
Richey R, el al. BMJ 2008;336:770-1

PREVENTION

British IE prevention (« NICE ») Guidelines : main changes

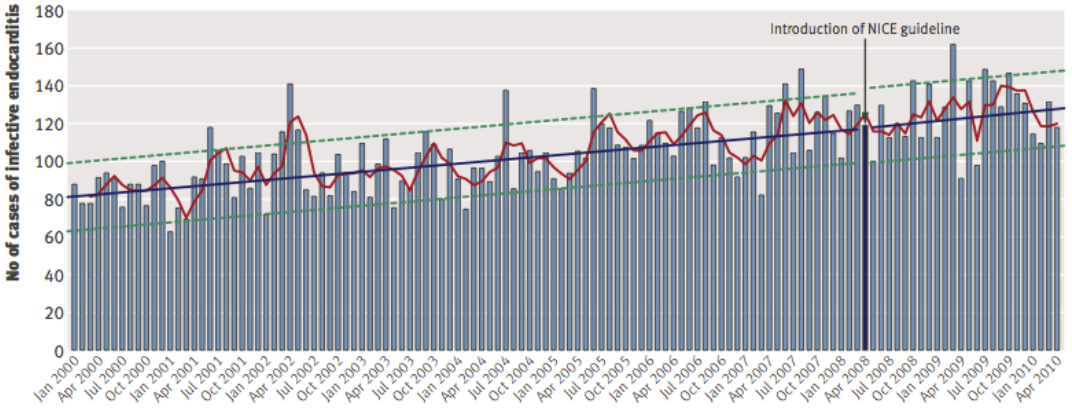
Impact of the NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: before and after study

Antibioprophylaxis presciption



P<0.001

Number of endocarditis cases



P=0.61

Thornhill MH, et al. BMJ 2011;342:d2392

PREVENTION

What to do in France ?

- **Good oral Hygiene + Dentist consultations**
- **Good skin hygiene**
- **Restrict the IV catheter**
- **Restrict tattoo, piercing… in patients at risk**

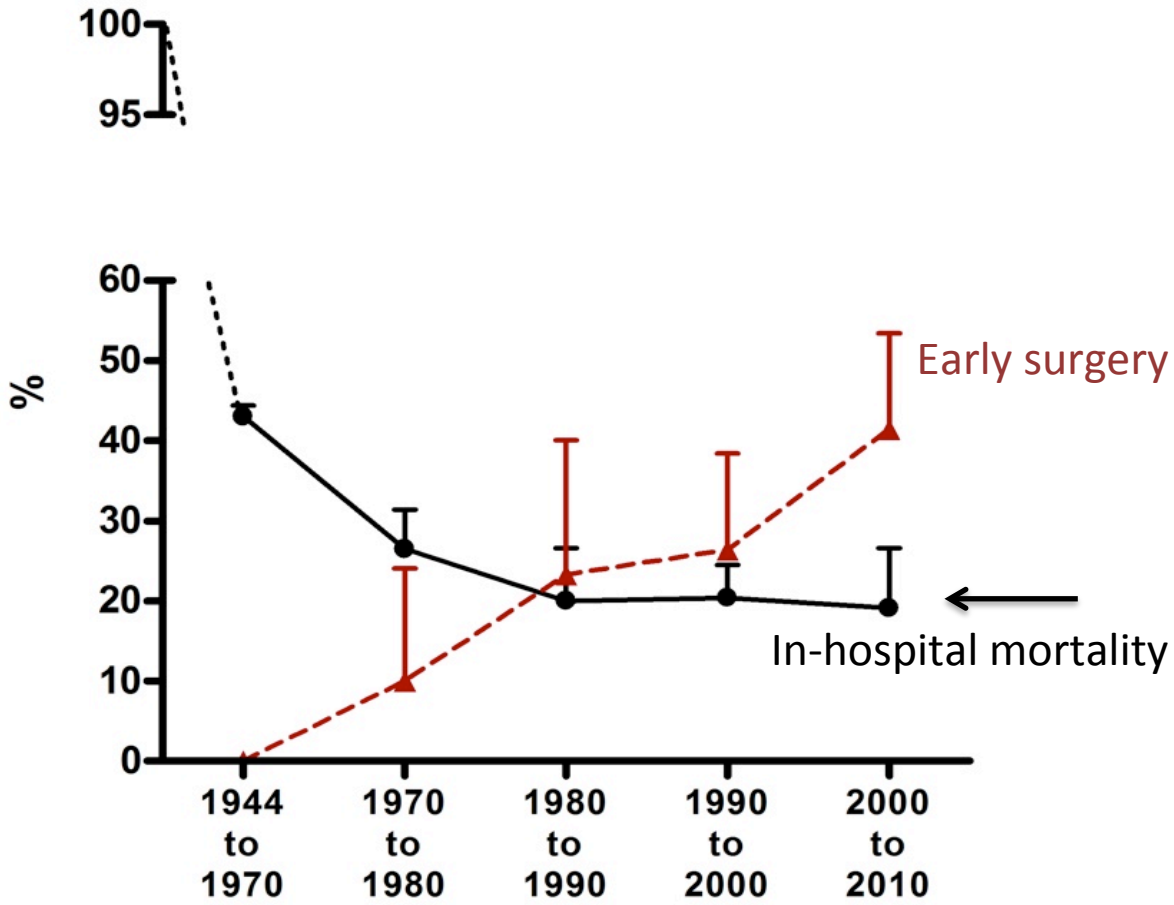
Follow ESC guidelines for the Antibioprophylaxis

MANAGEMENT

MANAGEMENT

Mortality has not decreased since the last decades

« Residual deaths »



Persistence of high in-hospital fatality rate ≈ 10-20%

Thuny F, et al. *Lancet* 2012;379:965-75

MANAGEMENT

« *Residual deaths* »

Causes of death re

The diagnosis is often done too late

Insufficiencies in prognostic assessment

Thuny F, et al. *Am Heart J* 2012;164:94-101

MANAGEMENT

Challenges in the management

1. Improve the **diagnostic** strategies to reduce the delay of the start of appropriate treatment

2. Improve **prognostic** assessment to identify patients requiring close monitoring and urgent surgery

3. Develop new **medico-surgical strategies**

MANAGEMENT

Diagnosis of IE: The Modified Duke Criteria
(adapted from Li & al.)

MAJOR CRITERIA

- ***Blood culture positive for IE***

Typical microorganisms consistent with IE from 2 separate blood cultures:

Viridans streptococcus, Streptococcus bovis, HACEK group, Staphylococcus aureus or community acquired enterococci in the absence of a primry focus

Microorganisms consistent with IE from 2 persistely positive blood cultures

At least 2 positive blood cultures of blood samples drawn > 12 h apart or all of 3 or a majority of ≥ 4 separate cultures of blood with first & last sample drawn at least 1 h apart

Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1:800

- ***Evidence of endocardial involvement***

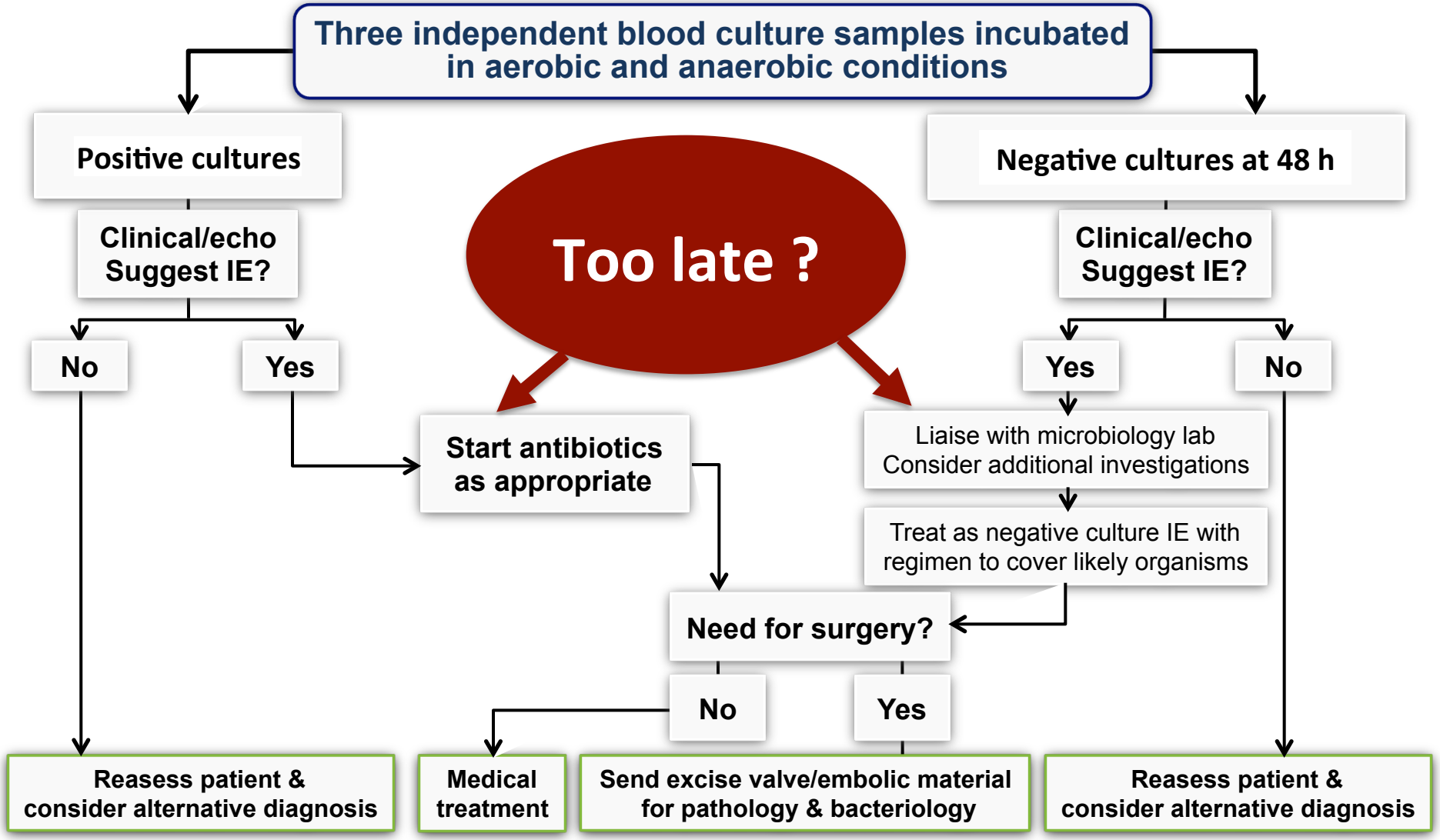
Echocardiogram positive for IE ***(Vegetation, New partial dehiscence of prosthetic valve)***
New valvular regurgitation

MINOR CRITERIA

- ***Predisposition*: Predisposing heart condition, injection drug use**
- ***Fever*: temperature > 38°C**
- ***Vascular phenomena*: major arterial emboli, septic pulmonary infarcts, mycotic aneurysms, Intracranial haemorrhages, conjunctival haemorrhages, Janeway lesions**
- ***Immunologic phenomena*: glomerulonephritis Osler's node, Roth's spot, rheumatoid factor**
- ***Microbiological evidence*: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE**

MANAGEMENT

Current Recommendations in Microbiological Testing



ESC Guidelines 2009

MANAGEMENT

Perspectives in Microbiological Testing:

Obtain a rapid diagnosis and recognition of the causative pathogen

- Systematic ***"Kit endocardite"*** at admission including in 2 hours
  - 1st unit: Blood cultures, serologies, rheumatoid factors, antinuclear antibodies, ± PCR
  - 2nd unit and 3rd unit: Blood cultures

- Valvular Tissue:
  - Broad range PCR (16S rRNA and 18S rRNA)
  - (Auto)immunohistochemistry

MANAGEMENT

Echocardiography for guiding management of IE

Role in the **diagnosis** → Introduce ATB

Role in the **prognostic assessment** → Indicate surgery

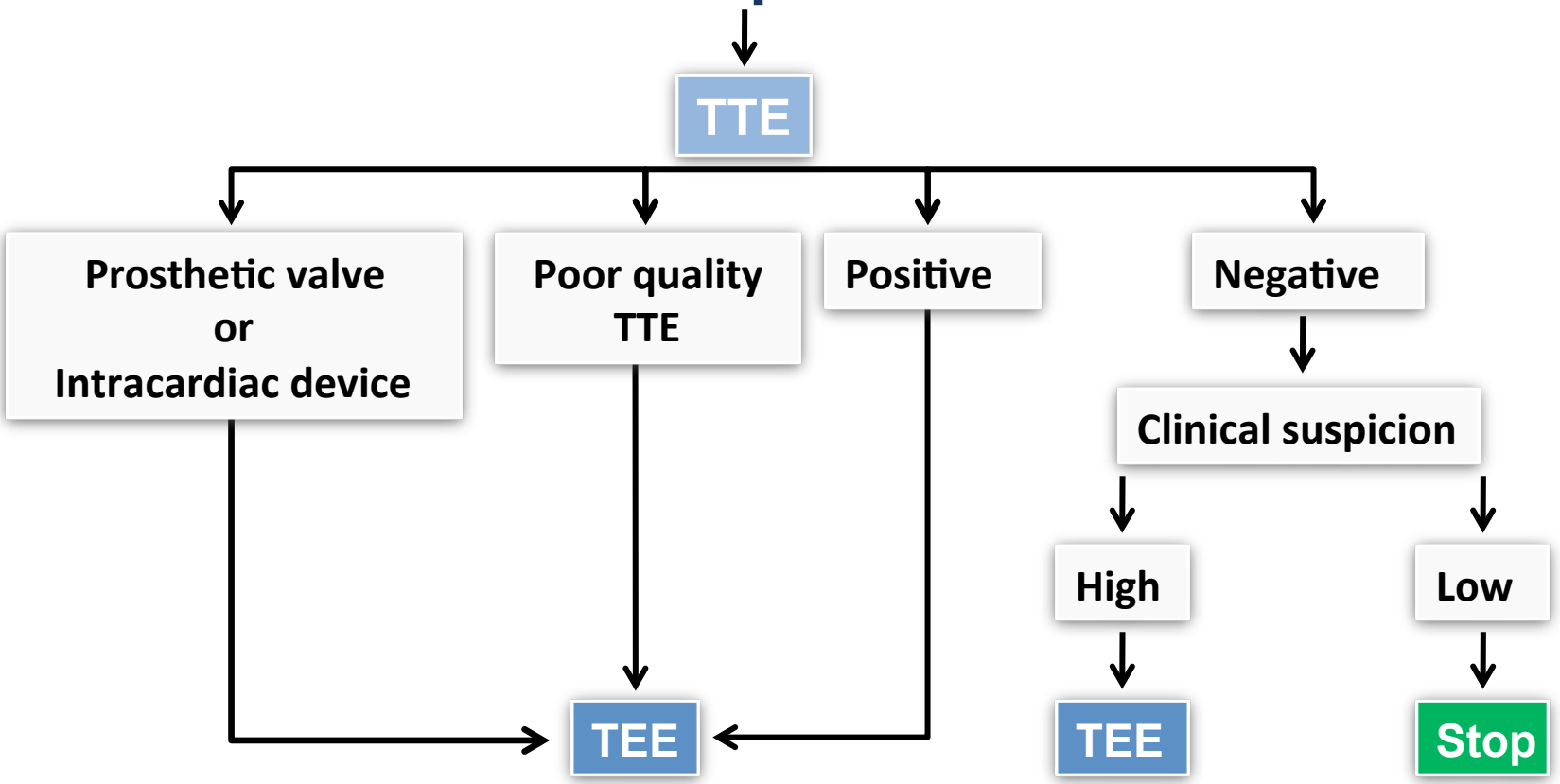
Role in the **follow-up** → Detect late complications

Only Echo is recommended to identify the endocardial lesions of IE in the Guidelines

ESC, ACC/AHA Guidelines

MANAGEMENT

Echocardiography for guiding management of IE



If initial TEE is negative but persistent suspicion of IE: repeat TEE within 7-10 days

ESC Guidelines 2009

MANAGEMENT

Echocardiography for guiding management of IE

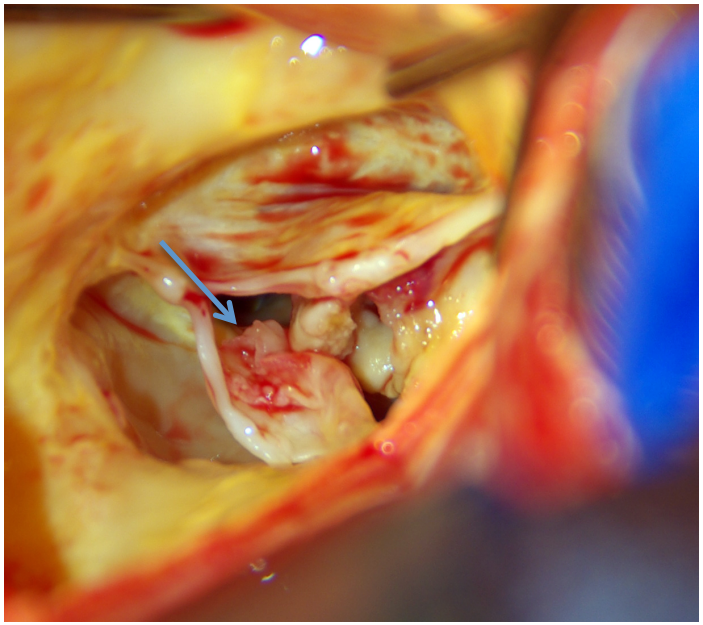
	Surgery / Necropsy	Echocardiography
Vegetation	Infected mass attached to an endocardial structure or an implanted intracardiac material	Oscillating or non oscillating intracardiac mass or other endocardial structures or non implanted intracardiac material
Abscess	Perivalvular cavity with necrosis and purulent material not communicating with the cardiovascular lumen	Thickened non-hogeneous perivalvular area with echodense or echolucent appearance
Pseudoaneurysm	Perivalvular cavity communicating with the cardiovascular lumen	Pulsatile perivalvular echo-free space with colour-Doppler flow detected
Perforation	Interruption of endocardial tissue continuity	Interruption of endocardial tissue continuity traversed by colour Doppler flow
Fistula	Communication between 2 neighbouring cavities through a perforation	Colour-Doppler communication between 2 neighbouring cavities through a perforation
Valve aneurysm	Saccular outpouching of valvular tissue	Saccular bulging of valvular tissue
Dehiscence of a prosthetic valve	Dehiscence of the prosthesis	Paravalvular regurgitation identified by TTE/TTE with or without rocking motion of the prosthesis

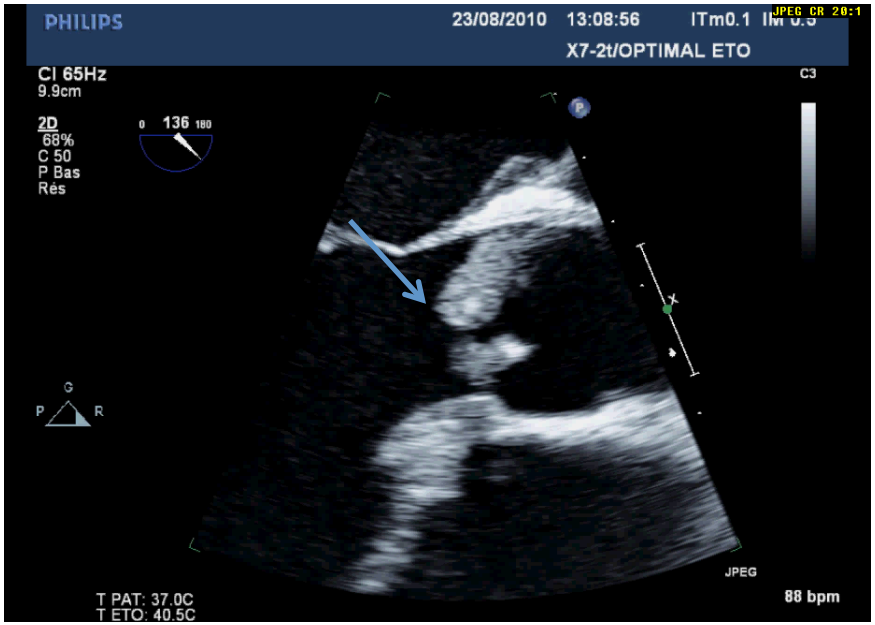
ESC Guidelines 2009

MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Vegetation	**Infected mass attached to an endocardial structure or an implanted intracardiac material**	**Oscillating or non oscillating intracardiac mass or other endocardial structures or non implanted intracardiac material**



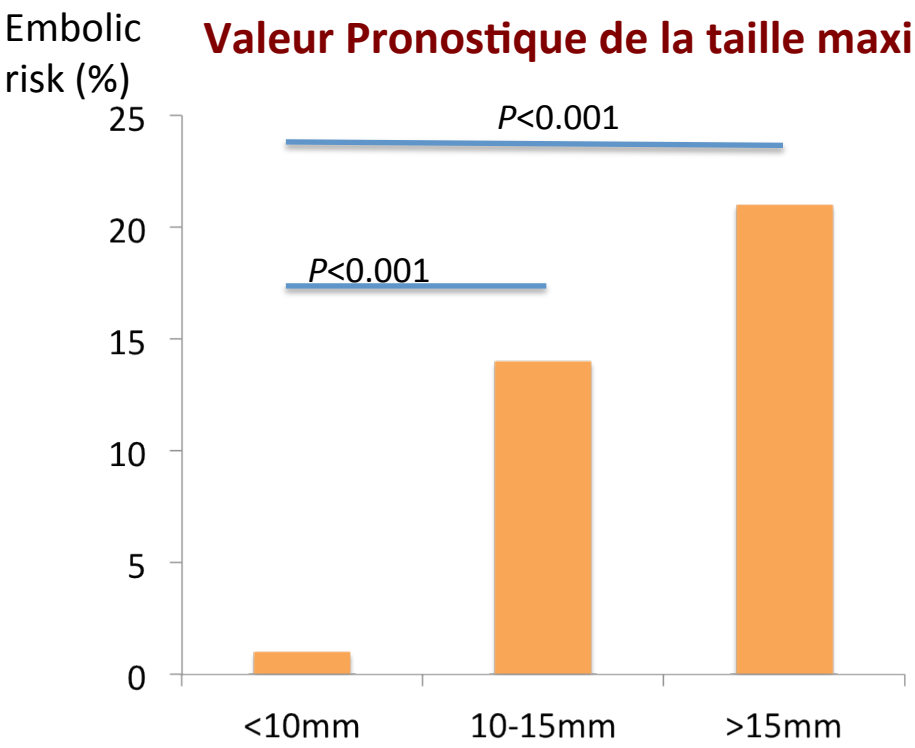


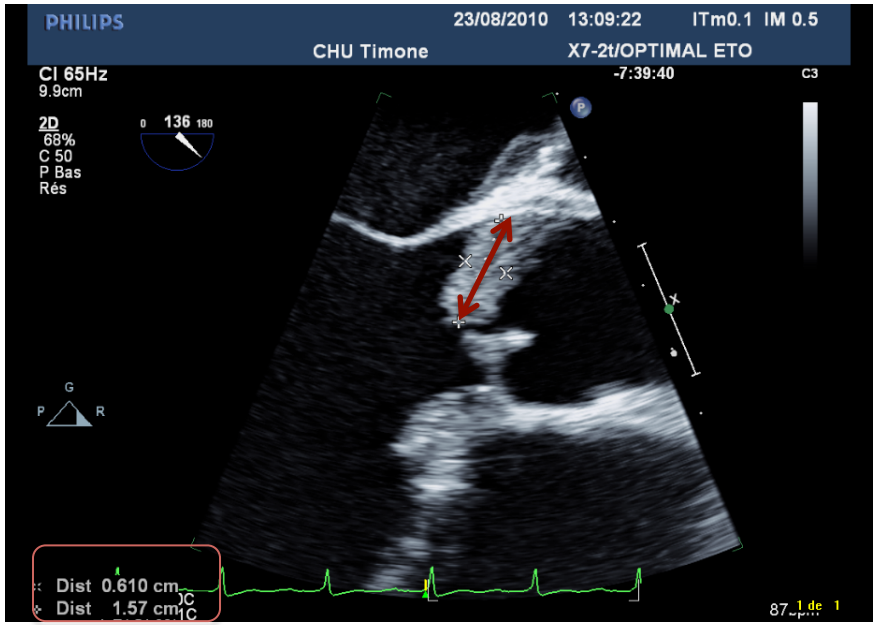
MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Vegetation	**Infected mass attached to an endocardial structure or an implanted intracardiac material**	**Oscillating or non oscillating intracardiac mass or other endocardial structures or non implanted intracardiac material**

Valeur Pronostique de la taille maximale (dans tous les plans) des végétation





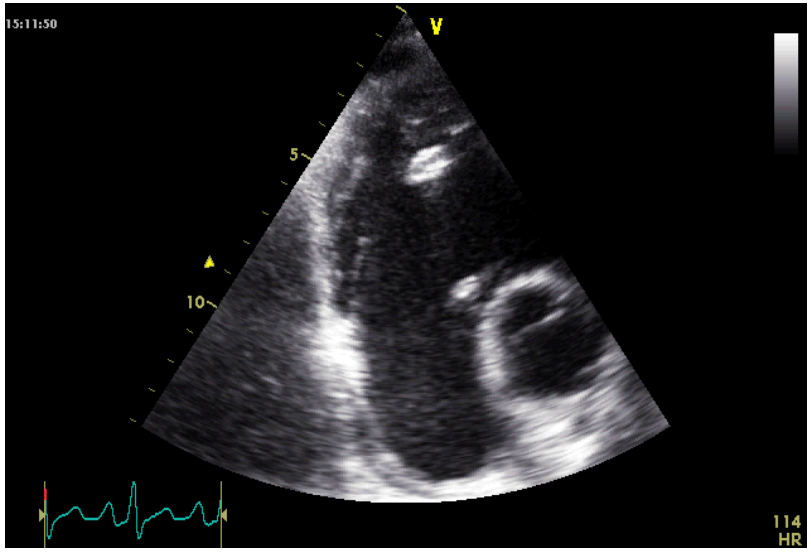
Thuny F. et al. Circulation 2005;112:69-75

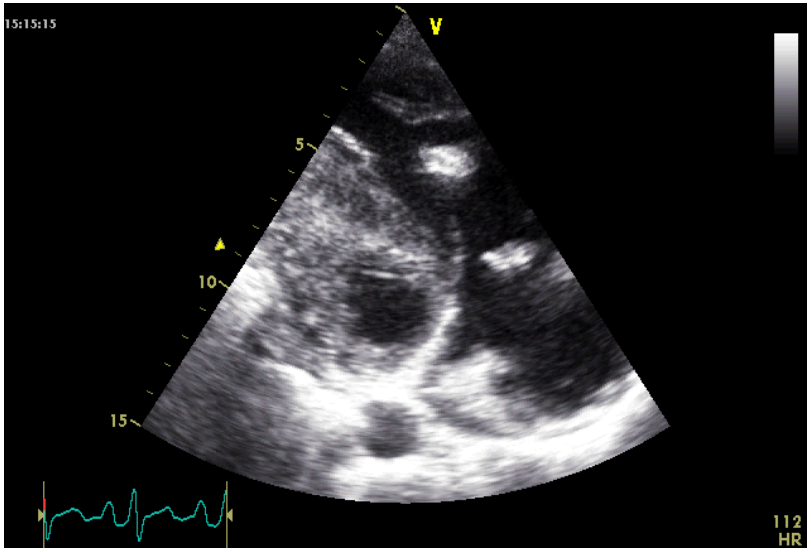
MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Vegetation	**Infected mass attached to an endocardial structure or an implanted intracardiac material**	**Oscillating or non oscillating intracardiac mass or other endocardial structures or non implanted intracardiac material**

Végétation Tricuspidienne (ETT): toxicomane IV





MANAGEMENT

Echocardiography for guiding management of IE

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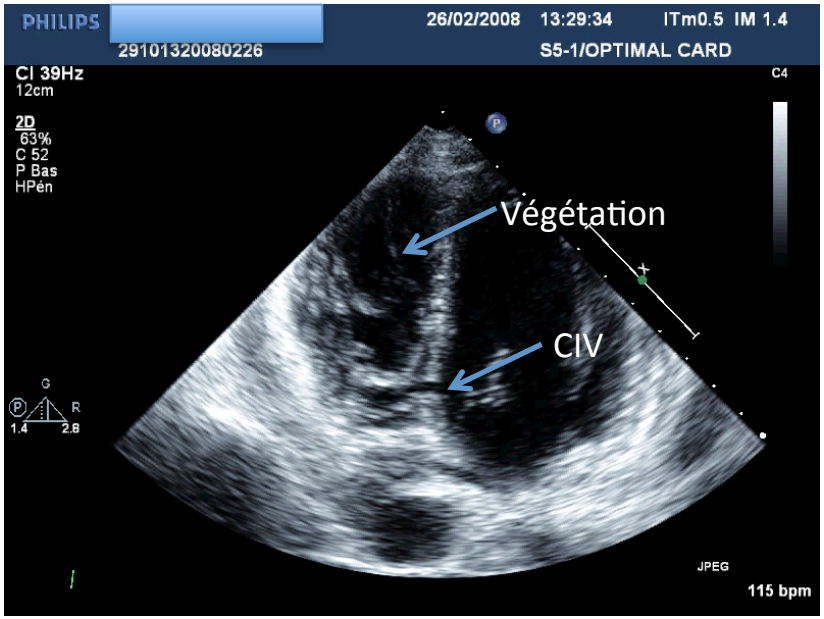
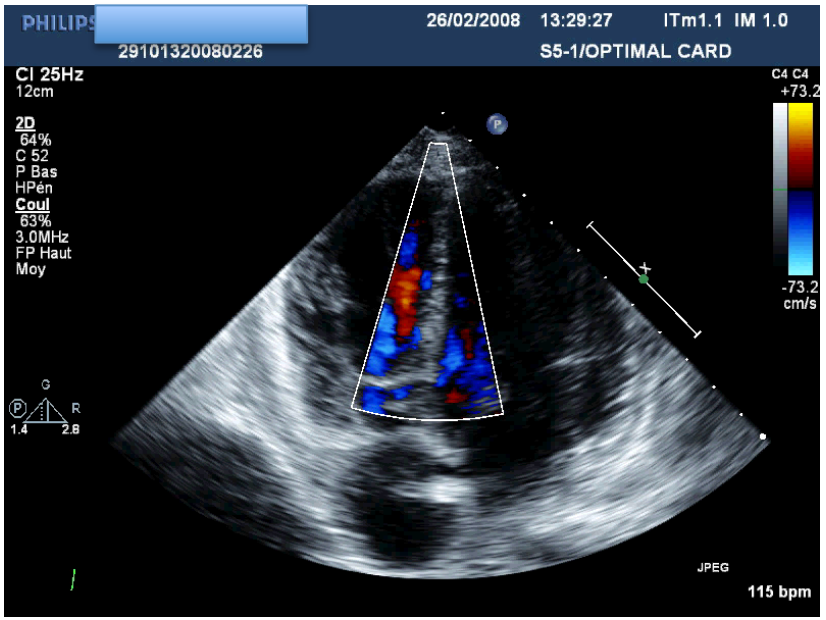
Végétation Tricuspidienne (ETT): CIV congénitale





MANAGEMENT

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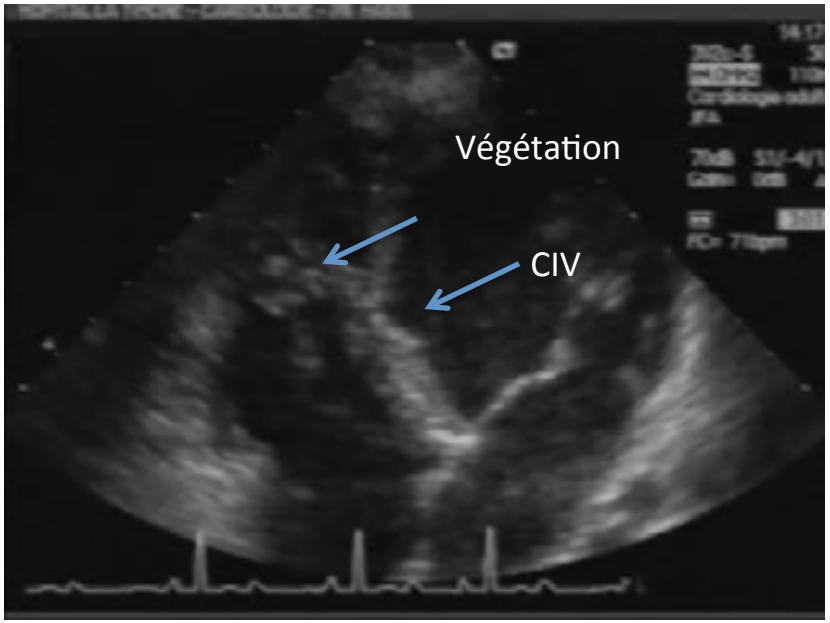

MANAGEMENT

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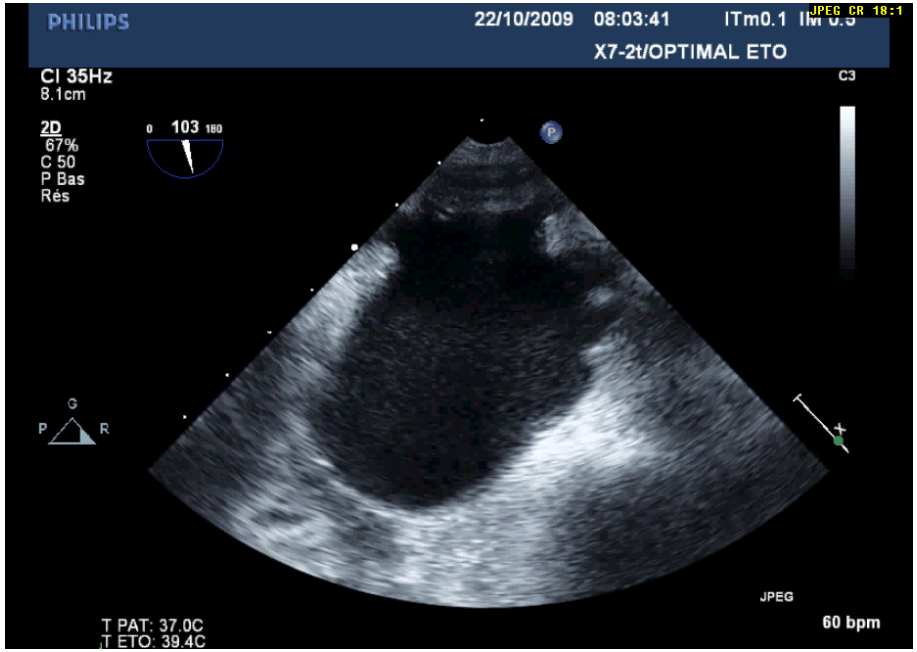
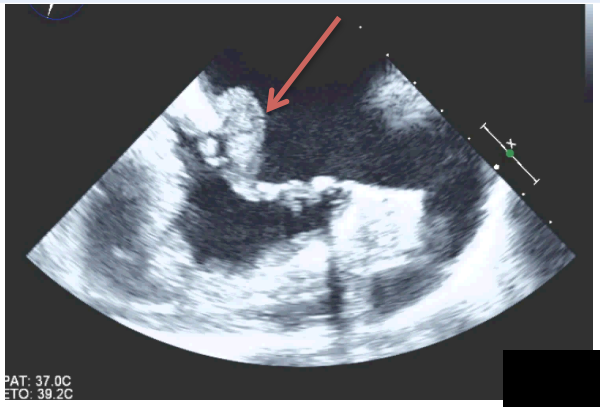
Végétation sur sonde de PMI

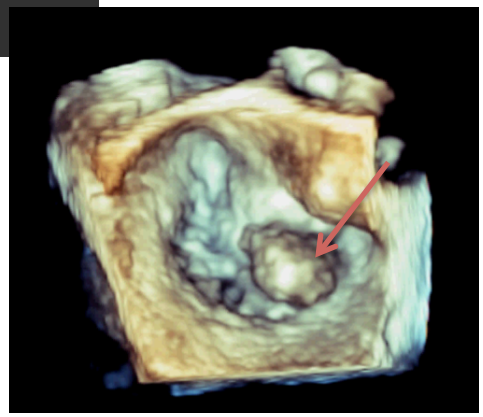


MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Abscess	Perivalvular cavity with necrosis and purulent material not communicating with the cardiovascular lumen	Thickened non-hogeneous perivalvular area with echodense or echolucent appearance





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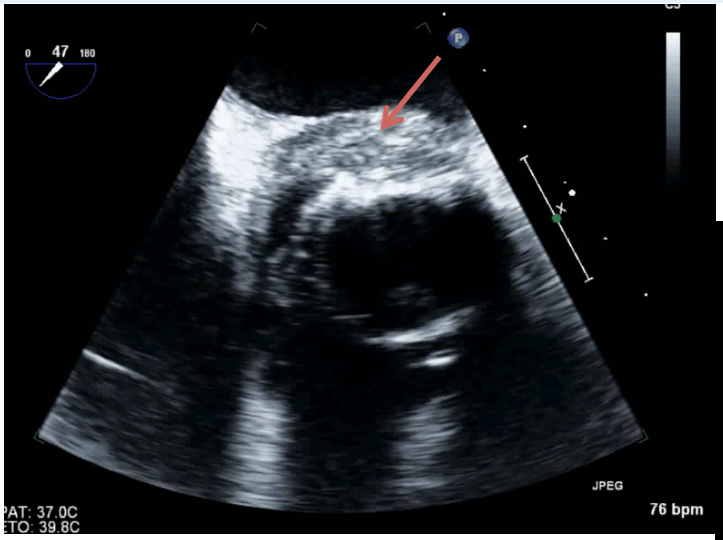
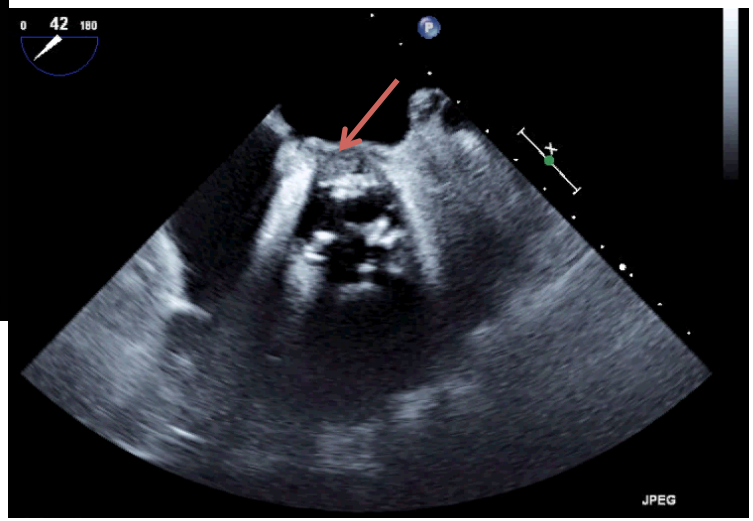
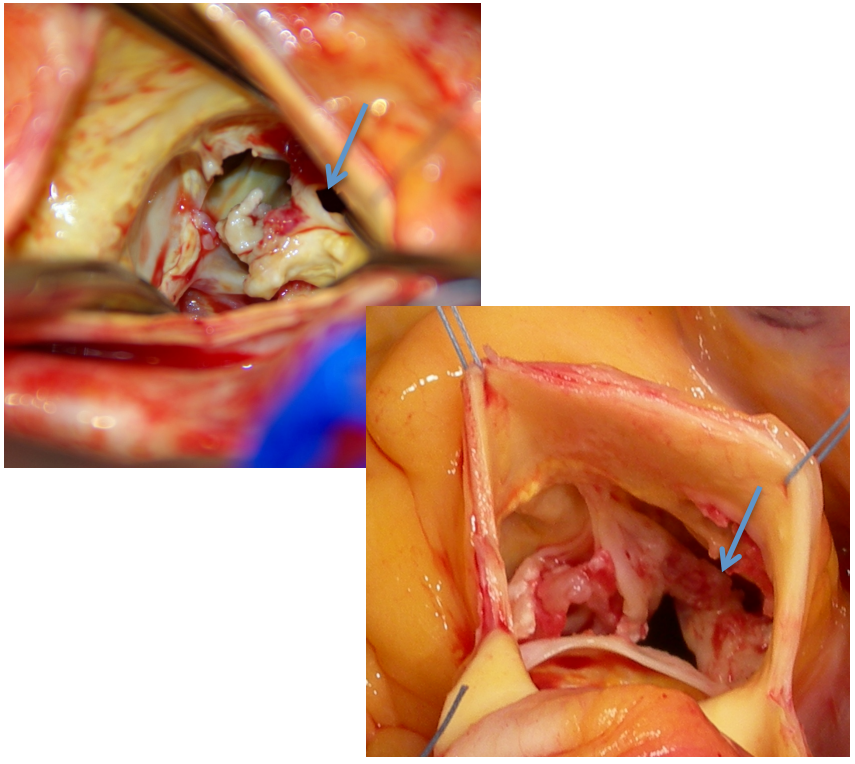


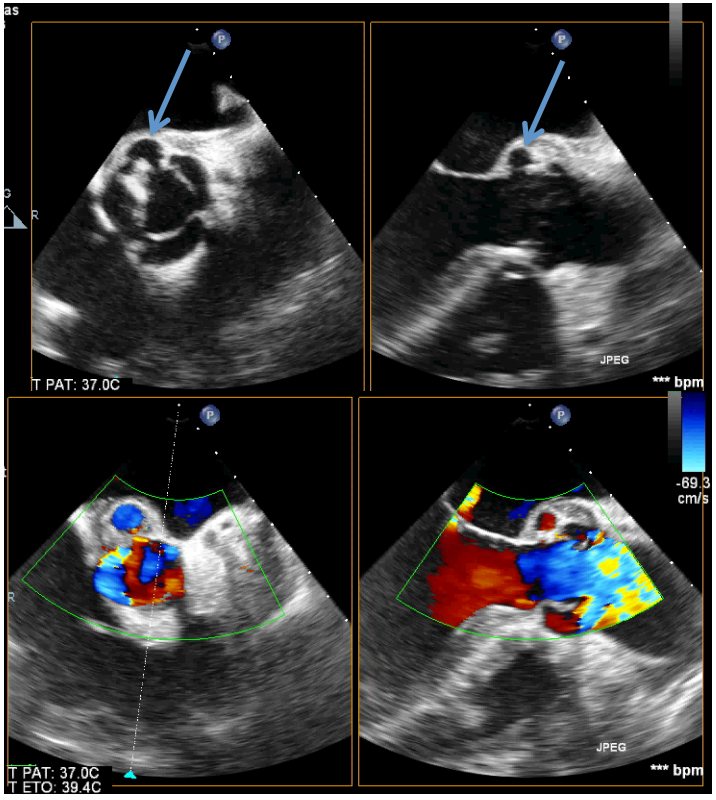


MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Pseudoaneurysm	Perivalvular cavity communicating with the cardiovascular lumen	Pulsatile perivalvular echo-free space with colour-Doppler flow detected





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Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
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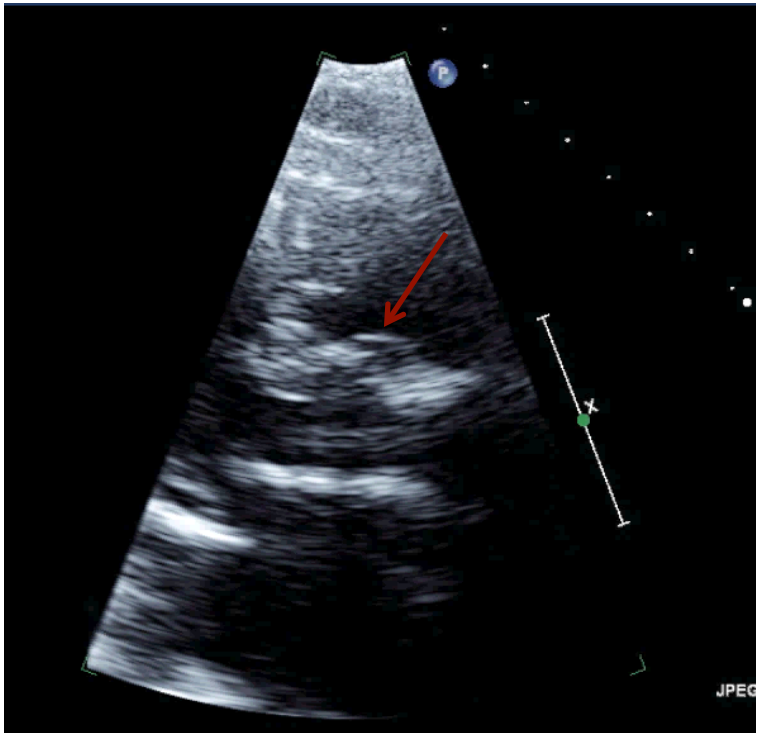
Abcès et Faux-anévrysmes antérieurs
ETT+++



MANAGEMENT

Echocardiography for guiding management of IE

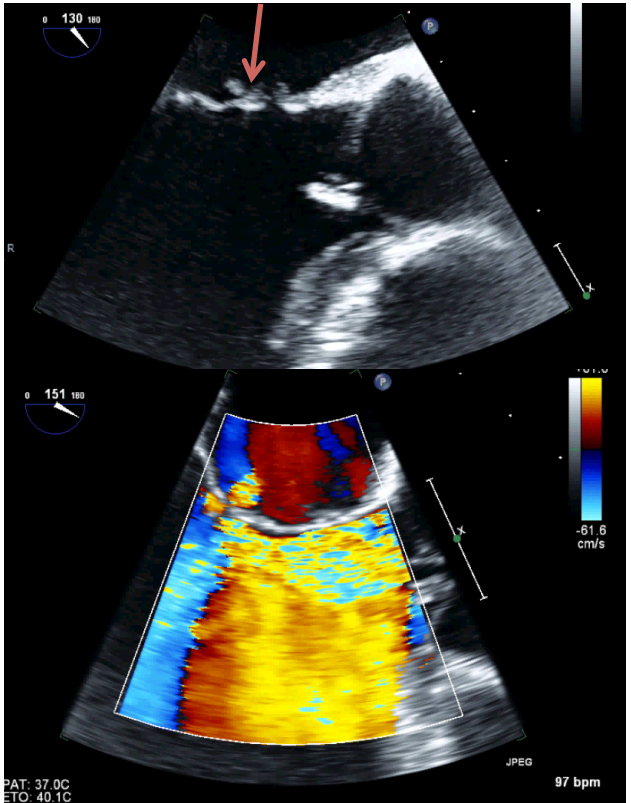
	Surgery / Necropsy	Echocardiography
Fistula	**Communication between 2 neighbouring cavities through a perforation**	**Colour-Doppler communication between 2 neighbouring cavities through a perforation**

Fistule Aorte-OG

MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Perforation	Interruption of endocardial tissue continuity	Interruption of endocardial tissue continuity traversed by colour Doppler flow



MANAGEMENT

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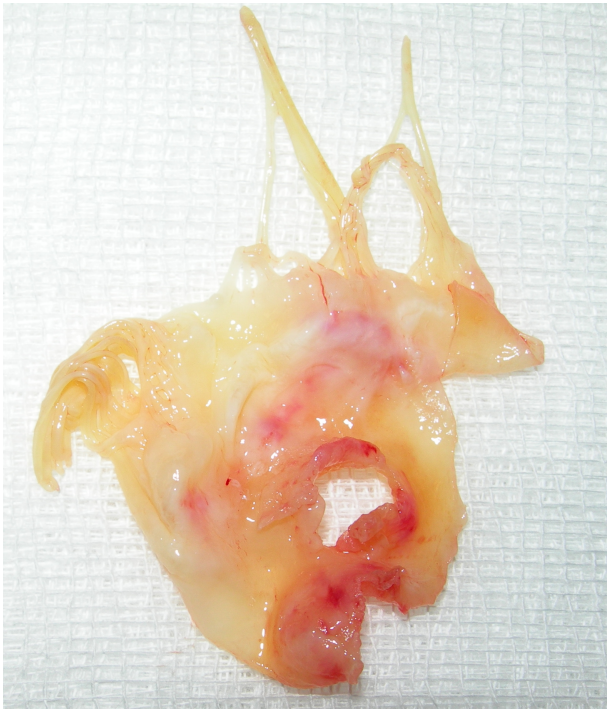
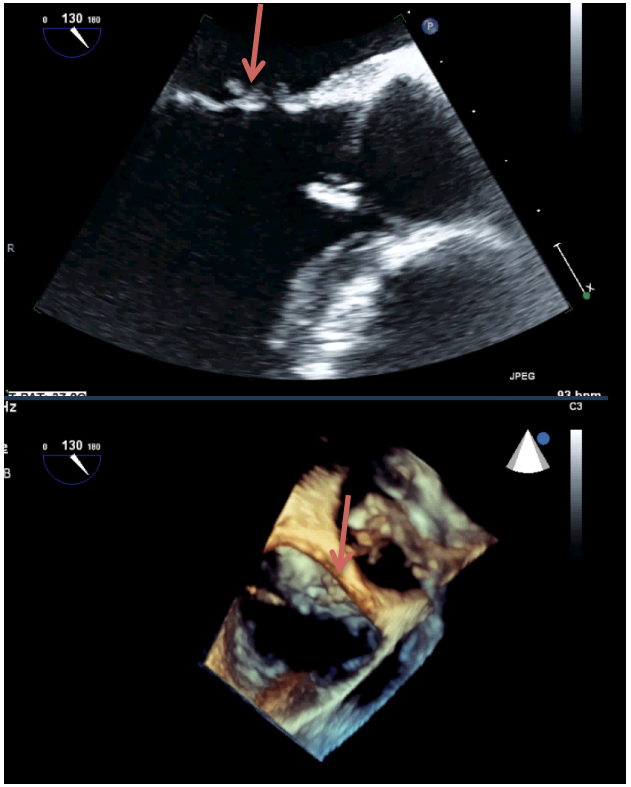
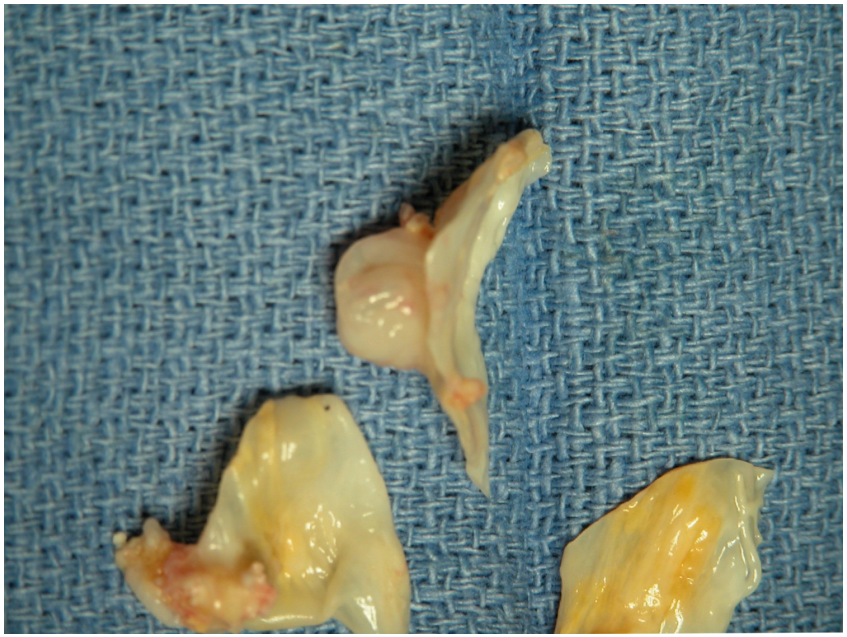




MANAGEMENT

Echocardiography for guiding management of IE

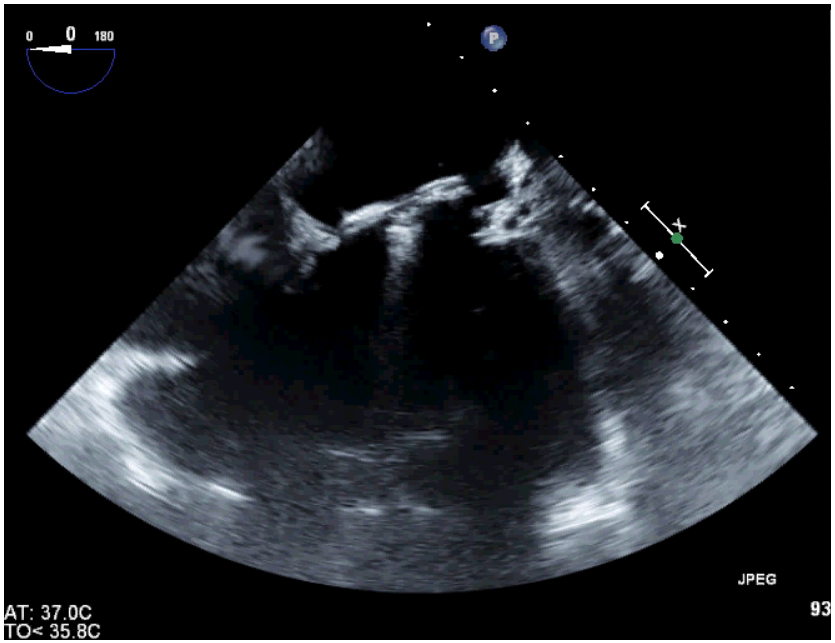
	Surgery / Necropsy	Echocardiography
Valve aneurysm	Saccular outpouching of valvular tissue	Saccular bulging of valvular tissue

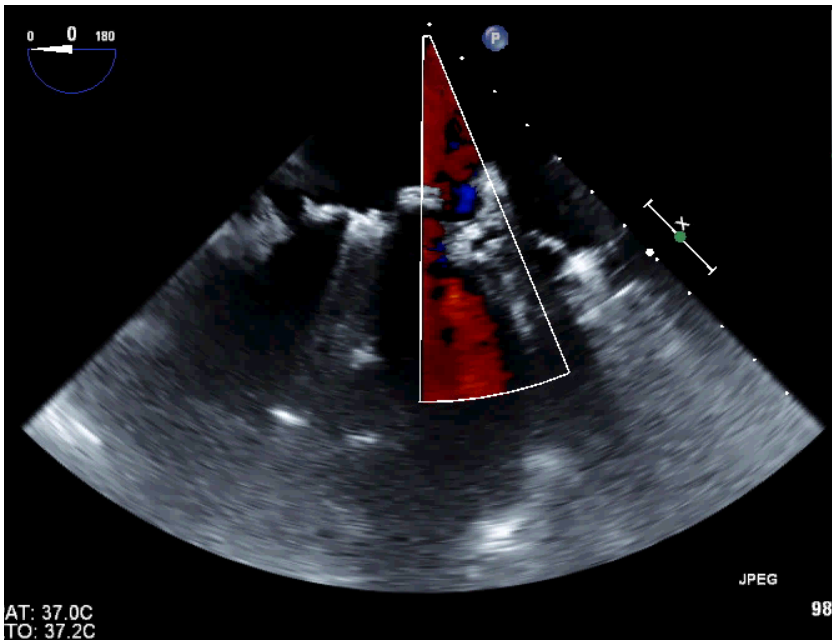


MANAGEMENT

Echocardiography for guiding management of IE

	Surgery / Necropsy	Echocardiography
Dehiscence of a prosthetic valve	**Dehiscence of the prosthesis**	**Paravalvular regurgitation identified by TTE/TTE with or without rocking motion of the prosthesis**





MANAGEMENT

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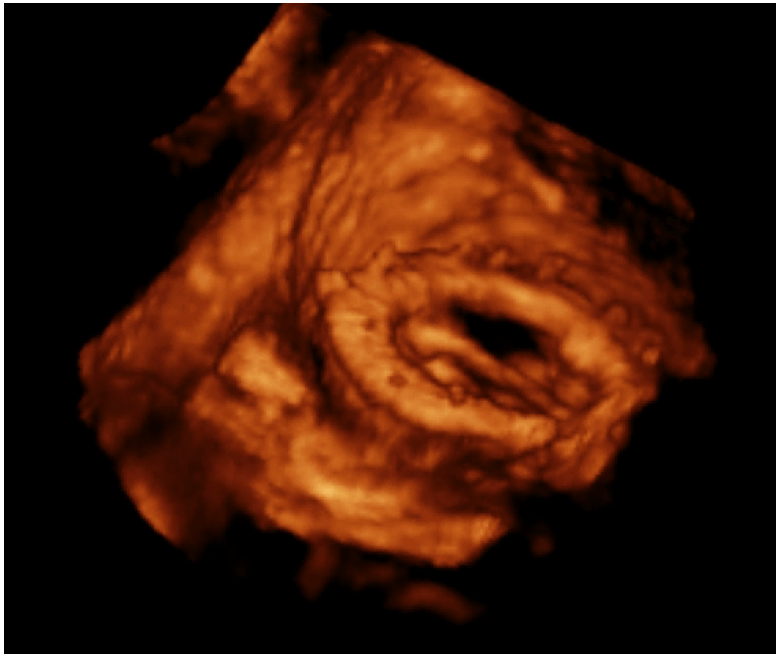
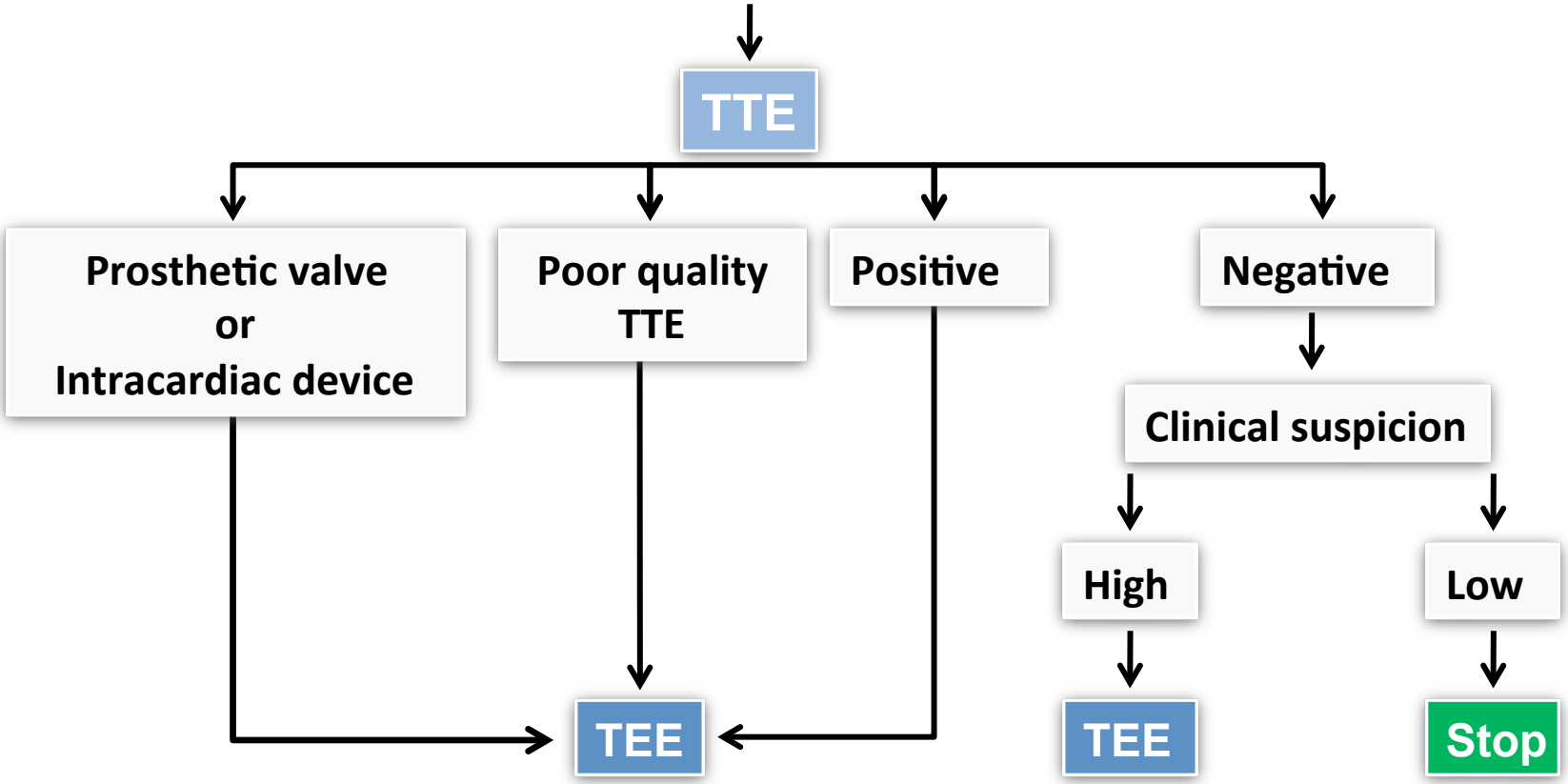


MANAGEMENT

Echocardiography for guiding management of IE



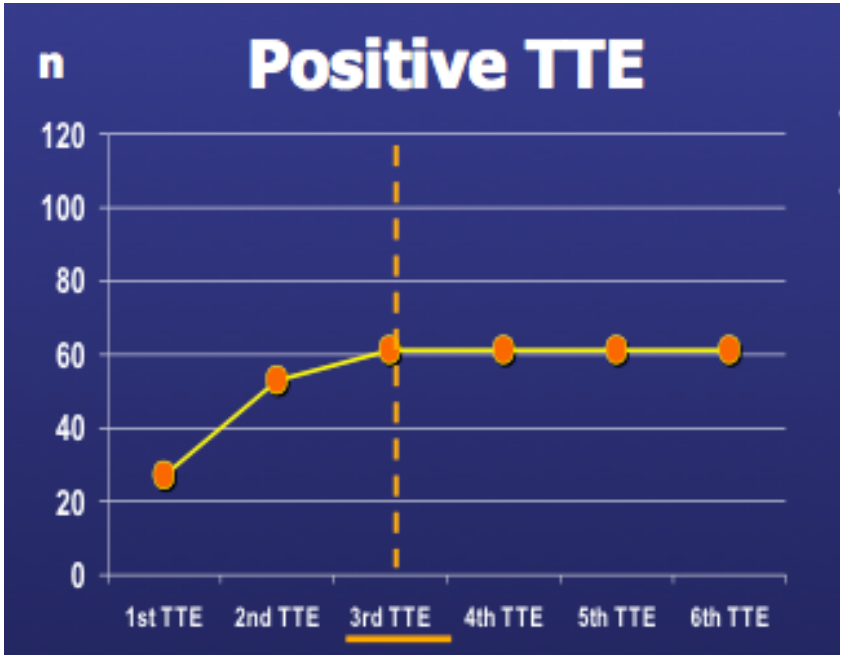
If initial TEE is negative but persistent suspicion of IE: repeat TEE within 7-10 days

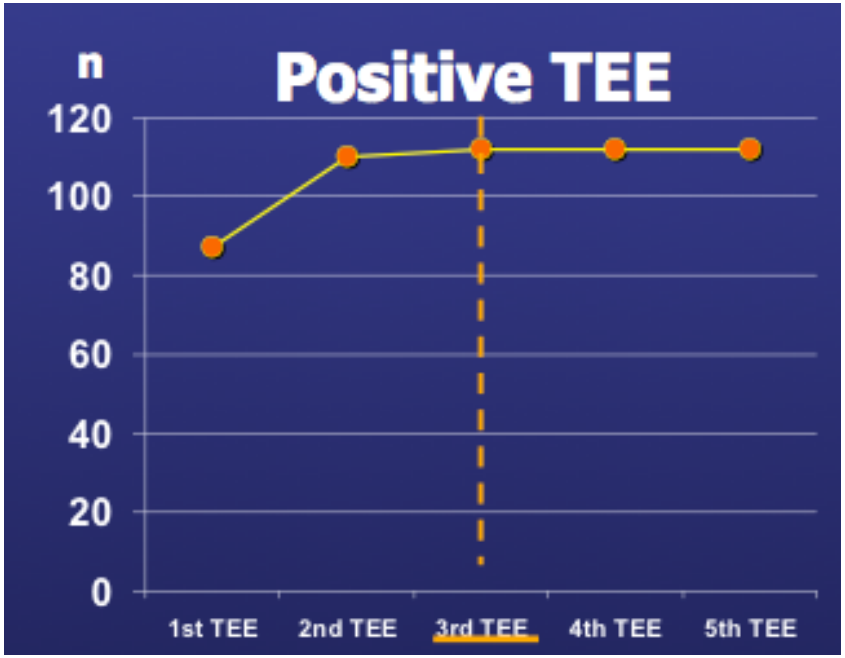
ESC Guidelines 2009

MANAGEMENT

Echocardiography for guiding management of IE

Repeat Echo



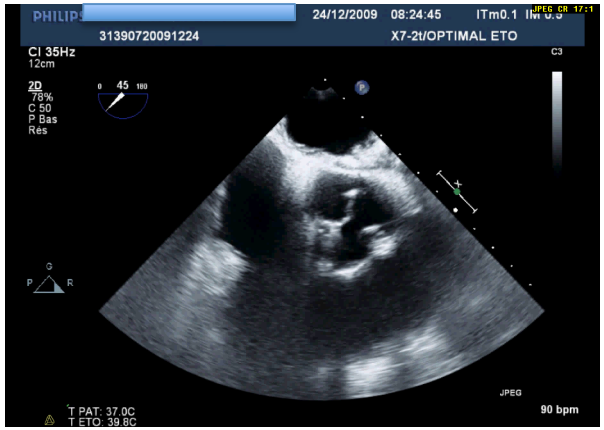


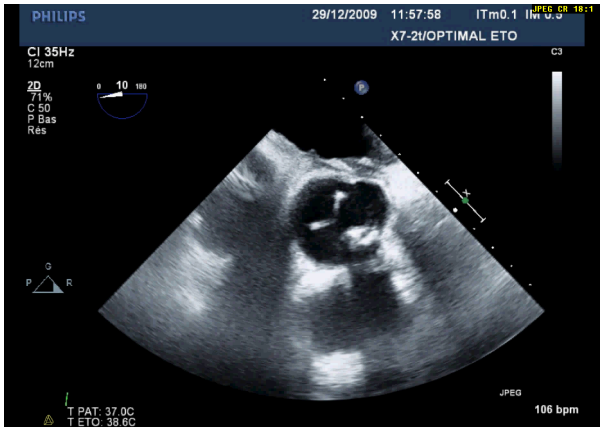
Viera MLC, et al. Heart 2004;90:1020–1024

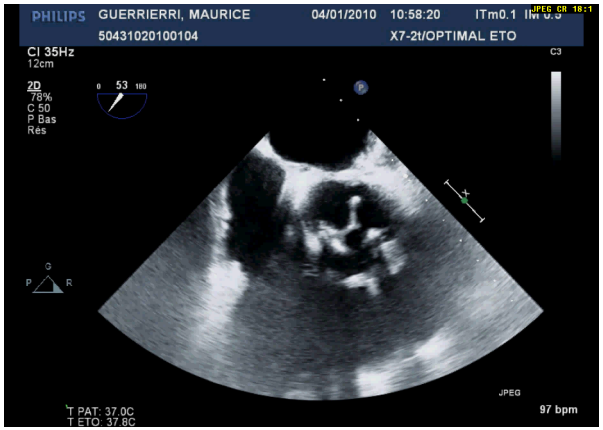
MANAGEMENT

Echocardiography for guiding management of IE

Repeat Echo

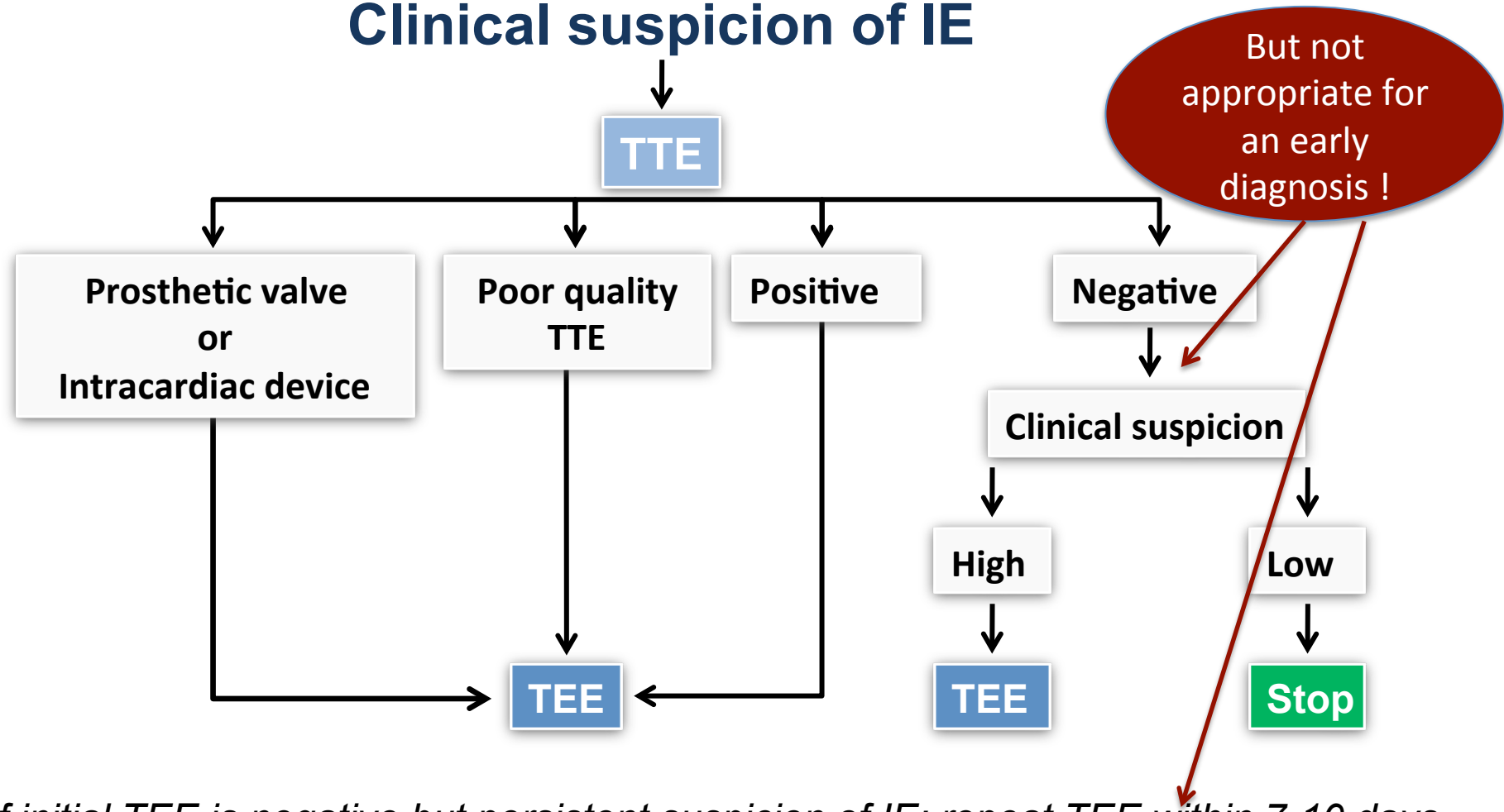






MANAGEMENT

Echocardiography for guiding management of IE



If initial TEE is negative but persistent suspicion of IE: repeat TEE within 7-10 days

ESC Guidelines 2009

MANAGEMENT

Intitial Echo is Negative or Inconclusive in 20%-30%

(prosthetic valves and intracardiac devices)

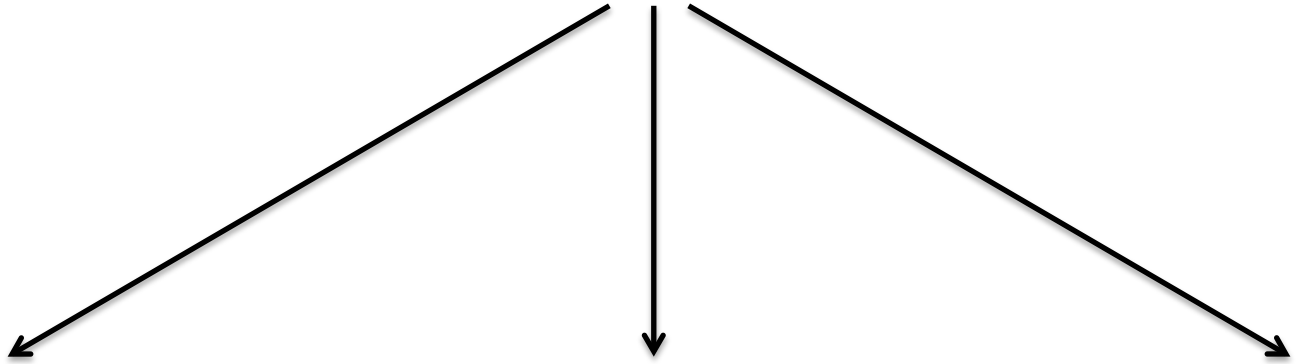
Stop

If initial TEE is negative but persistent [illegible] repeat TEE within 7-10 days

ESC Guidelines 2009

MANAGEMENT

Innovations in the diagnostic strategy have emerged through new imaging methods



Systematic
Cerebral MRI

Cardiac
CT scan

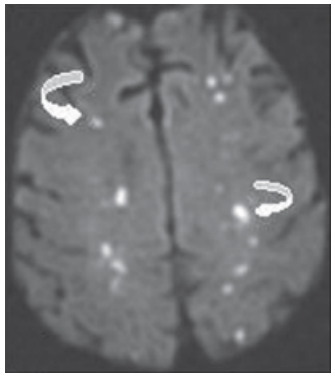
Molecular imaging

Thuny F, et al. Arch Cardiovasc Dis 2013;106:52-62

MANAGEMENT

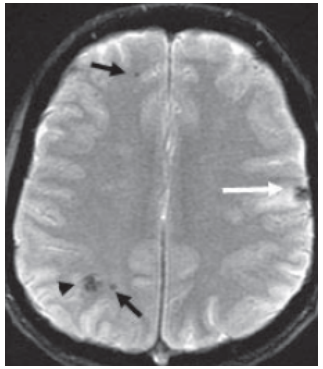
Systematic Cerebral MRI

Diffusion



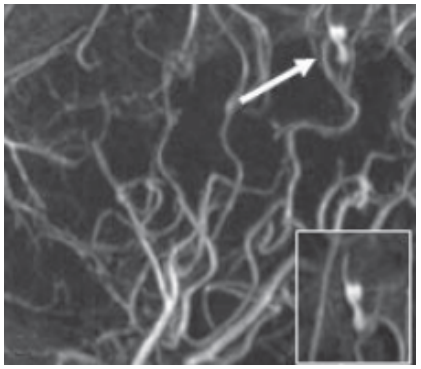
Cerebral infarcts (60%)

T2*



Micro-hemorrhages (60%)

MR angiography



Infectious aneurysms (8%)

- Incidence of neurological events: **65% to 82%**
- Diagnostic reclassification: **32%**
- Therapeutic plans modifications: **18%**

Duval X, et al. Ann Intern Med 2010;152:497-504
Cooper HA, et al. Circulation 2009;120:585-91
Snygg-Martin U, et al. Clin Inf Dis 2008;47:23-30

MANAGEMENT

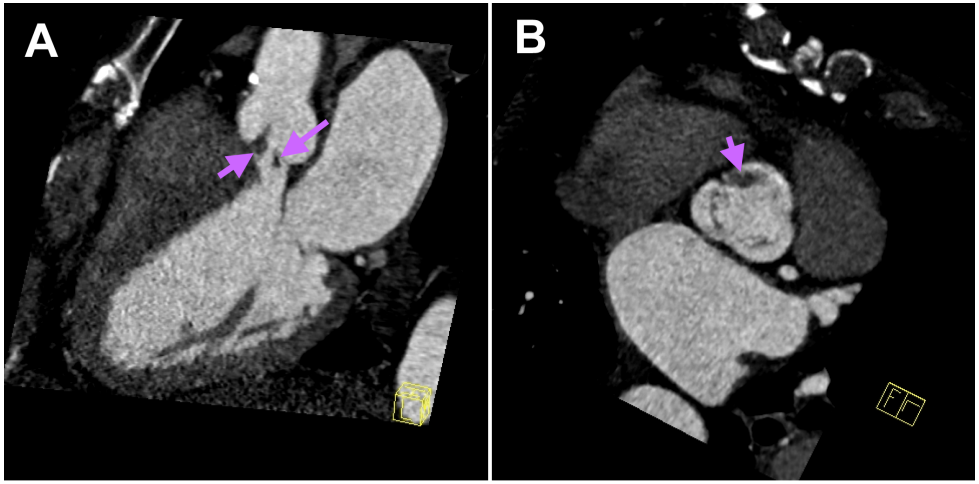
Cardiac ECG-gated CT scan+whole body CT

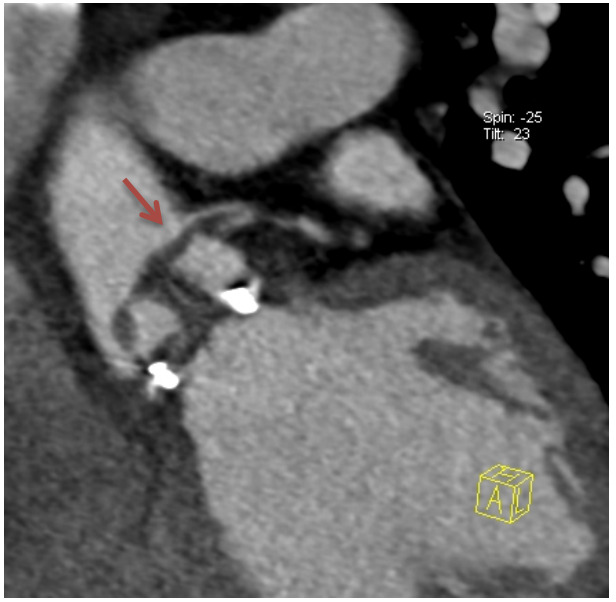
- Good results in detecting valvular abnormalities in IE
- In PVE, could detect **periannular complications** (anterior) not seen by TEE
- Preoperative **exclusion of coronary artery disease**
- Screening of **silent emboli**
- *!! Risk of acute renal failure*

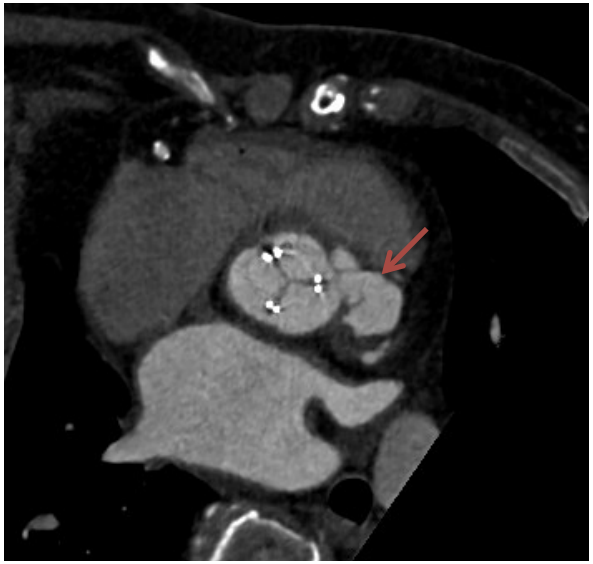
Feuchtner GM, et al. J Am Coll Cardiol 2009;436-44
Fagman E, et al. Eur Radiol 2012;22:2407-14

MANAGEMENT

Cardiac ECG-gated CT scan+whole body CT







MANAGEMENT

18F-FDG PET-CT

- **Echo** provides **morphological imaging** without accurate information on the activity of IE = **insensitive for very early diagnosis**
- **PET/CT** provides **a functional imaging of inflammation** and has been tested in the diagnosis **of vascular graft infections**
- **PET/CT in infection of pacemakers/defibrillators**

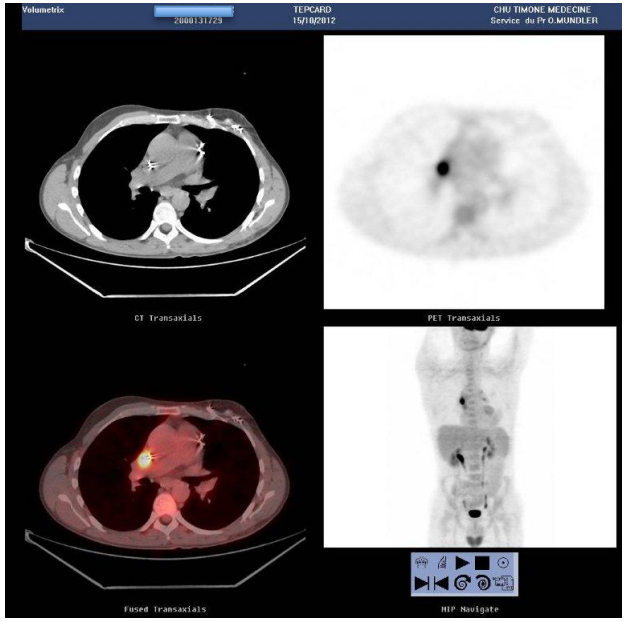


Table 2 Diagnostic value of ^{18}F-FDG PET/CT in cardiovascular implantable electronic device infections.

Study	Material	Sensitivity (%)	Specificity (%)
Bensimhon et al. [54]	Pocket + leads	80	100
	Leads	60	100
Ploux et al. [55]	Leads	100	93
Sarrazin et al. [56]	Pocket + leads	89	86

- Good Se and Sp in pocket infection
- Good Sp in leads infection
- Low Se in leads infection
- The timing after implantation has to be defined

Ploux S et al. *Heart Rhythm* 2011;8:1478-81
Bensimhon L , et al. Clin Microbiol Infect 2011; 17:836-44
Sarrazin JF, et al. J Am Coll Cardiol 2012;59:1616–25
Thuny F, et al. Arch Cardiovasc Dis 2013;106:52-62

MANAGEMENT

18F-FDG PET-CT

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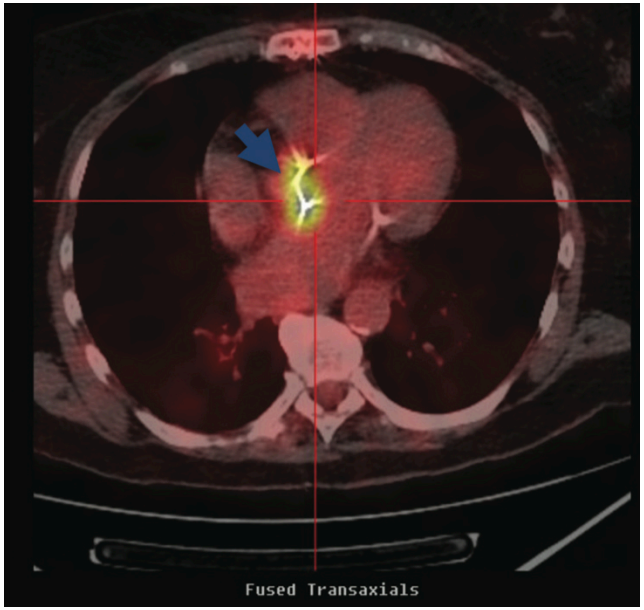
- **Clinical cases on the role of PET/CT in prosthetic valve IE (PVE)**



Saby L, et al. Circulation 2013;126:e217-220
Thuny F, et al. Arch Cardiovasc Dis 2013;106:52-62

MANAGEMENT

18F-FDG PET-CT

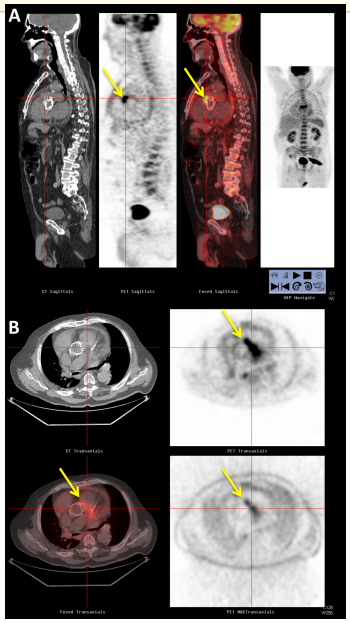
Cardiac Imaging in Endocarditis

Positron Emission Tomography/Computed Tomography for Diagnosis of Prosthetic Valve Endocarditis

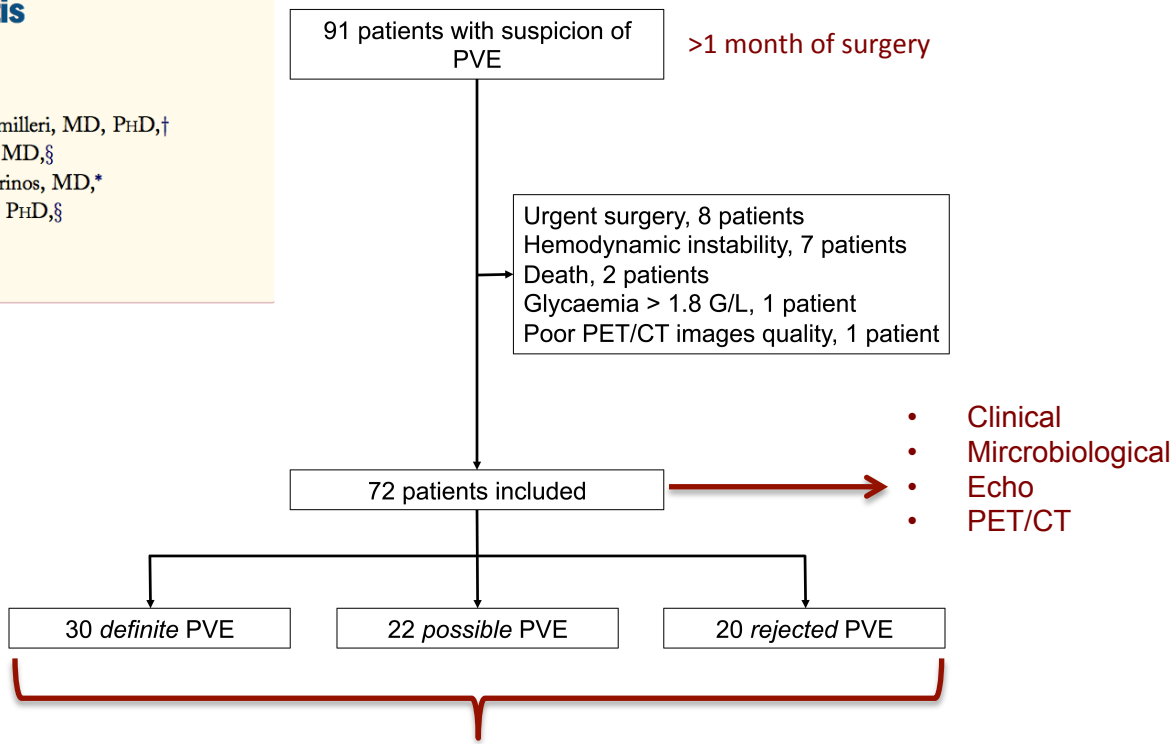
Increased Valvular ^{18}F-Fluorodeoxyglucose Uptake as a Novel Major Criterion

Ludivine Saby, MD,* Olivia Laas, MD,† Gilbert Habib, MD,* Serge Cammilleri, MD, PhD,† Julien Mancini, MD, PhD,‡ Laetitia Tessonnier, MD,† Jean-Paul Casalta, MD,§ Frederique Gouriet, MD, PhD,§ Alberto Riberi, MD,|| Jean-Francois Avierinos, MD,* Frederic Collart, MD,|| Olivier Mundler, MD, PhD,† Didier Raoult, MD, PhD,§ Franck Thuny, MD, PhD*§¶

Marseille, France



Pilot study



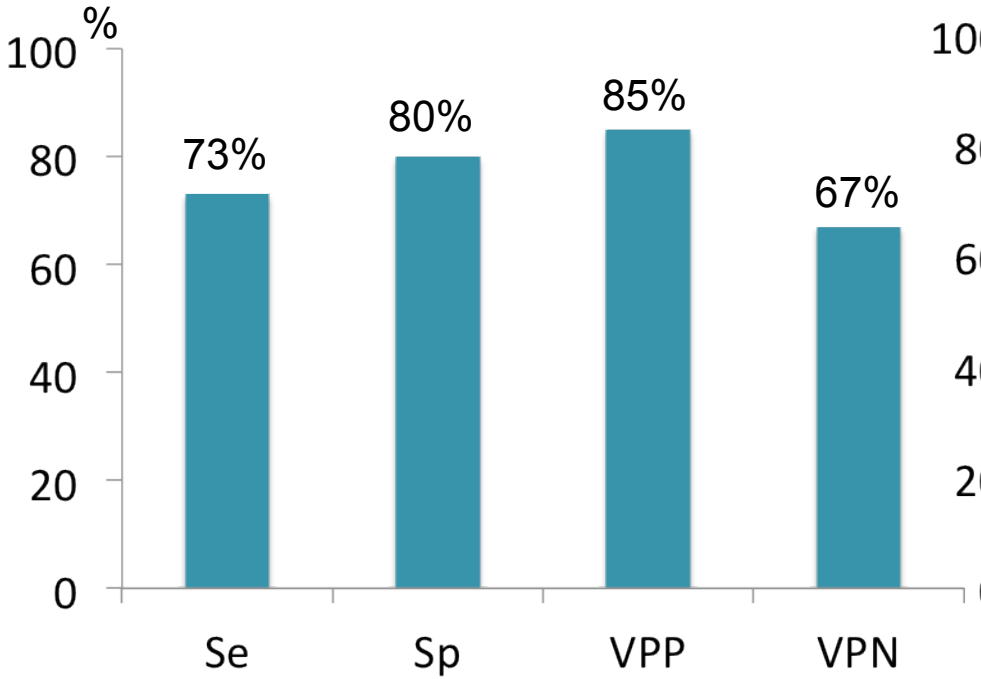
Saby et al, J Am Coll Cardiol 2013;61:2374–82

MANAGEMENT

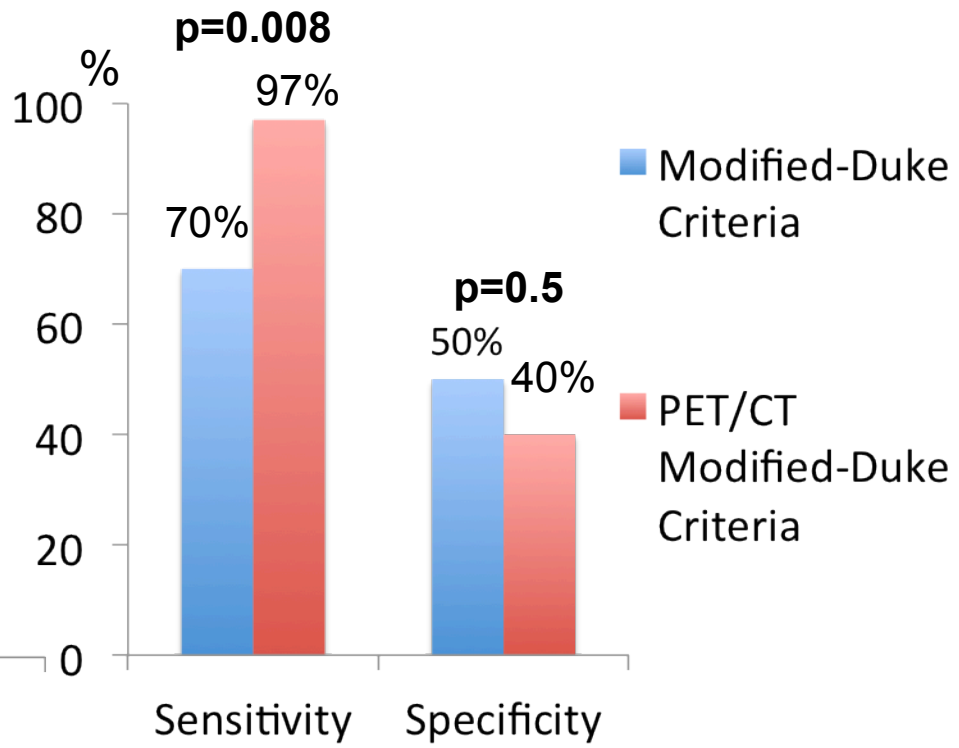
18F-FDG PET-CT

PET/CT median time=6 days after admission and 9 days after ATB

PET/CT diagnostic value



PET/CT as a novel major criterion



Saby et al, J Am Coll Cardiol 2013;61:2374–82

MANAGEMENT

18F-FDG PET-CT

PET/CT 2013-Modified Duke criteria for the diagnosis of IE

MAJOR CRITERIA

- ***Blood culture positive for IE***

Typical microorganisms consistent with IE from 2 separate blood cultures:

Viridans streptococcus, Streptococcus bovis, HACEK group, Staphylococcus aureus or community acquired enterococci in the absence of a primry focus

Microorganisms consistent with IE from 2 persistely positive blood cultures

At least 2 positive blood cultures of blood samples drawn > 12 h apart or all of 3 or a majority of ≥ 4 separate cultures of blood with first & last sample drawn at least 1 h apart

Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1:800

- ***Evidence of endocardial involvement***

Echocardiogram positive for IE *(Vegetation, New partial dehiscence of prosthetic valve)*
New valvular regurgitation

- ***Positive FDG PET/CT***

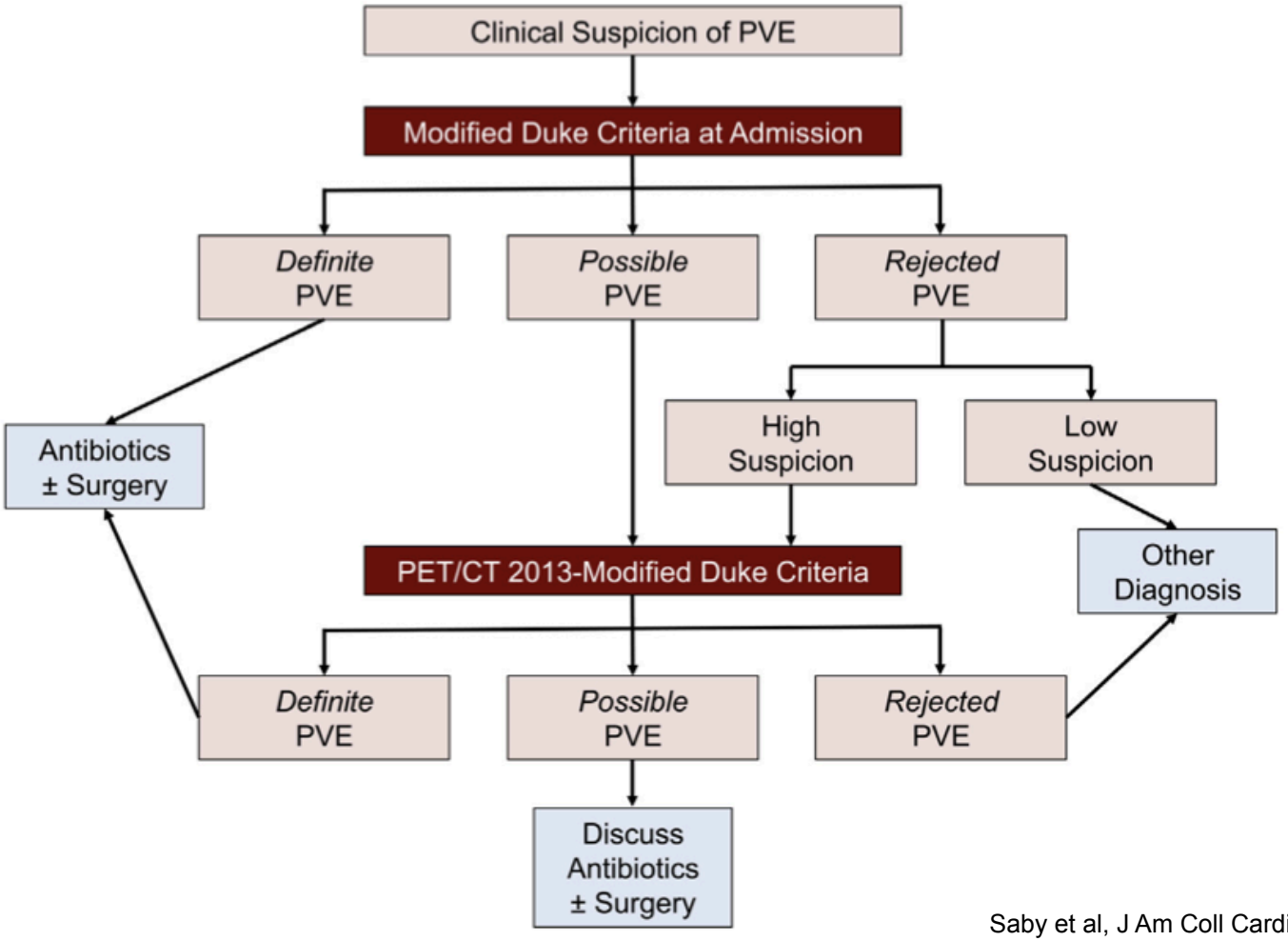
MINOR CRITERIA

- ***Predisposition*: Predisposing heart condition, injection drug use**
- ***Fever*: temperature > 38°C**
- ***Vascular phenomena*: major arterial emboli, septic pulmonary infarcts, mycotic aneurysms, Intracranial haemorrhages, conjunctival haemorrhages, Janeway lesions**
- ***Immunologic phenomena*: glomerulonephritis Osler's node, Roth's spot, rheumatoid factor**
- ***Microbiological evidence*: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE**

Thuny F et al, J Am Coll Cardiol 2013; pii: S0735-1097(13)05542-3

MANAGEMENT

18F-FDG PET-CT

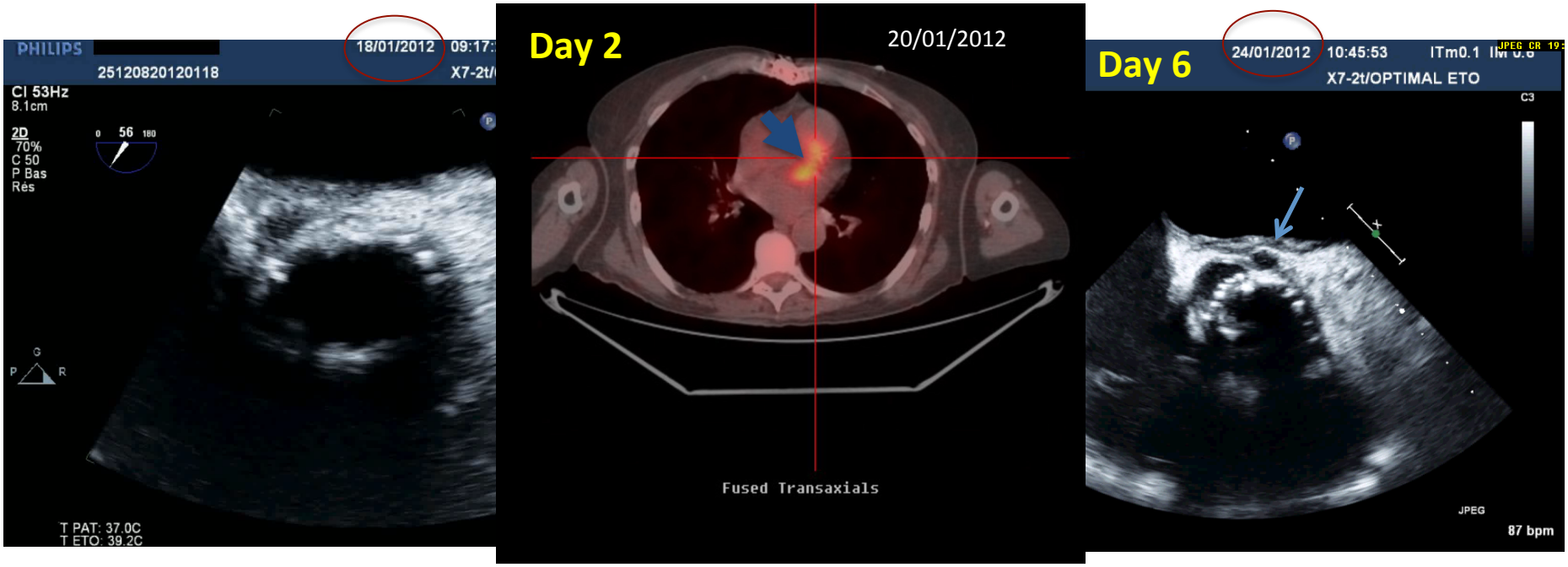


Saby et al, J Am Coll Cardiol 2013;61:2374–82

MANAGEMENT

18F-FDG PET-CT

PET/CT identifies peri-annular abscesses earlier than TTE and TEE in PVE

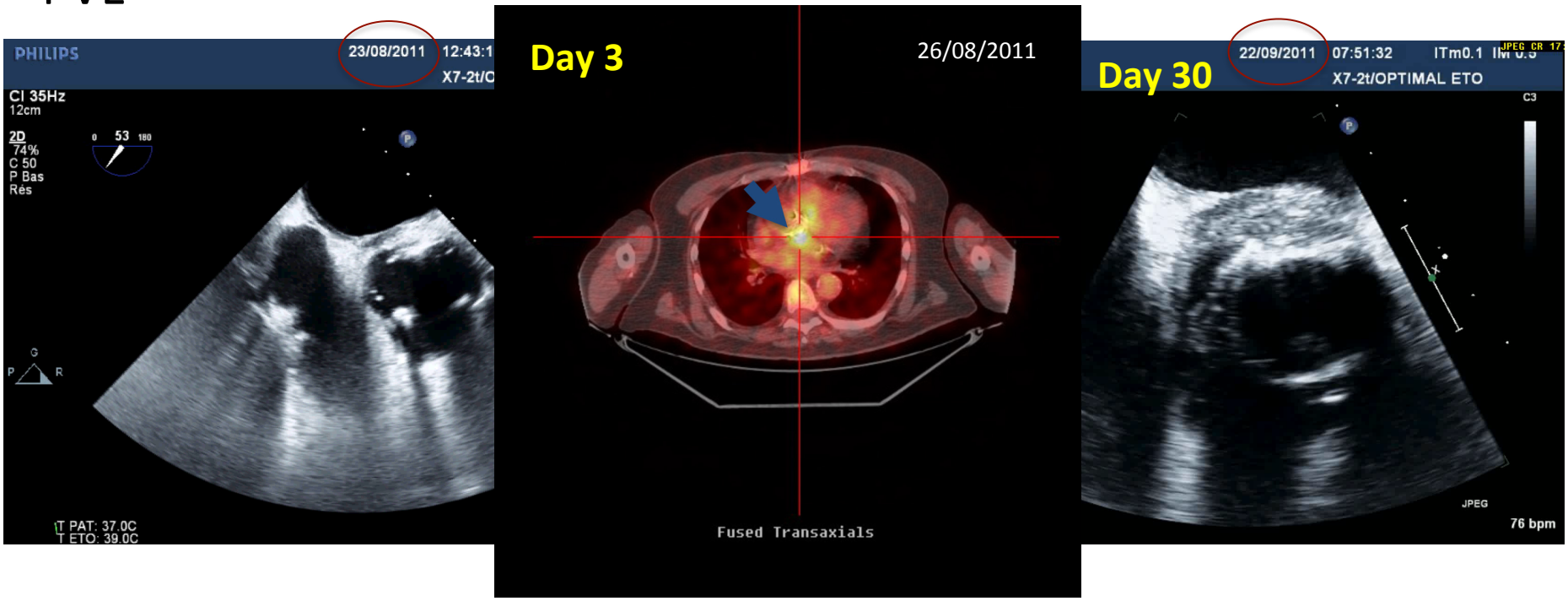


Saby L, et al. Circulation 2013;126:e217-220

Saby L et al. J Am Coll Cardiol 2013;61:2374–82

MANAGEMENT

PET/CT identifies peri-annular abscesses earlier than TTE and TEE in PVE



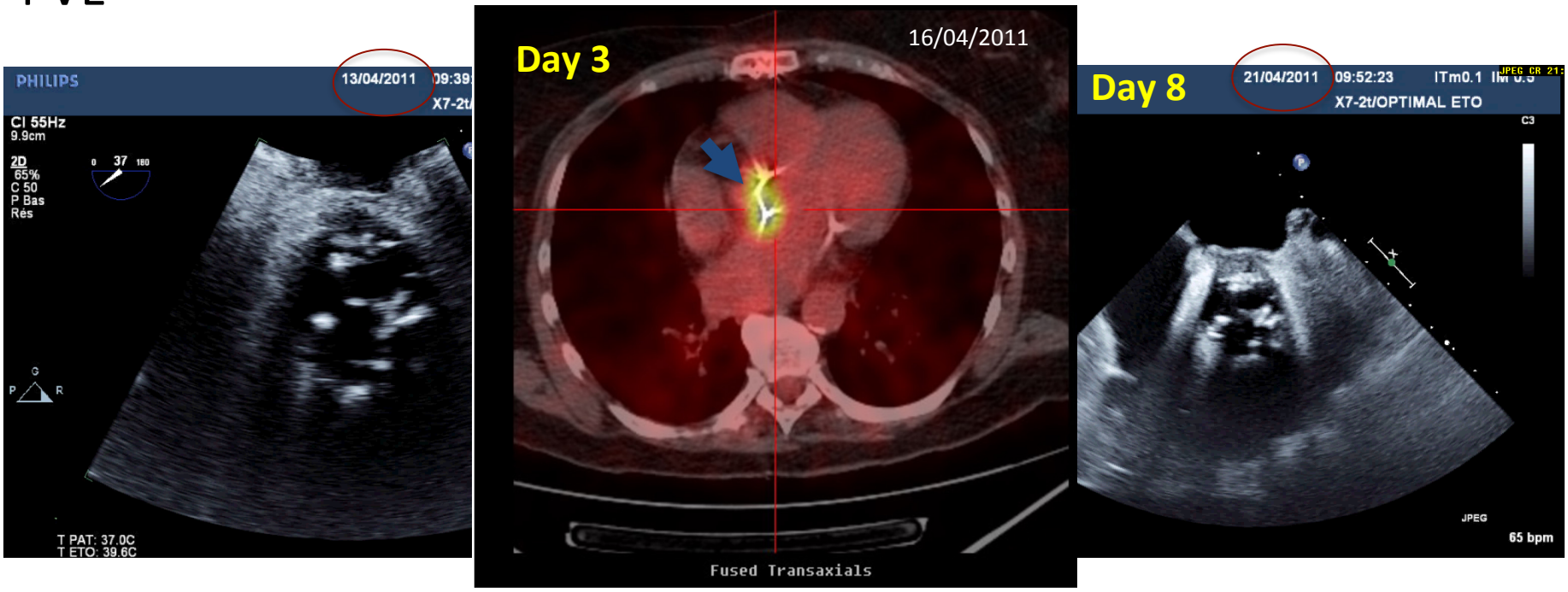
Saby L, et al. Circulation 2013;126:e217-220

Saby L et al. J Am Coll Cardiol 2013;61:2374–82

MANAGEMENT

18F-FDG PET-CT

PET/CT identifies peri-annular abscesses earlier than TTE and TEE in PVE

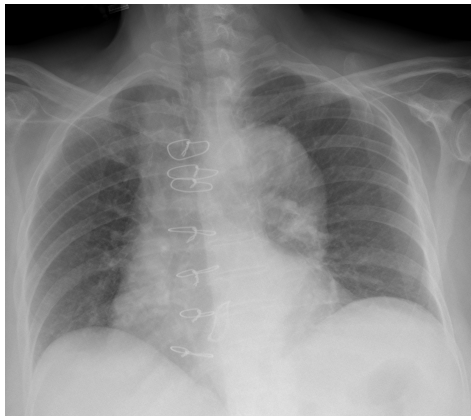


Saby L, et al. Circulation 2013;126:e217-220

Saby L et al. J Am Coll Cardiol 2013;61:2374–82

CLINICAL CASE-1

- 81-year-old-woman

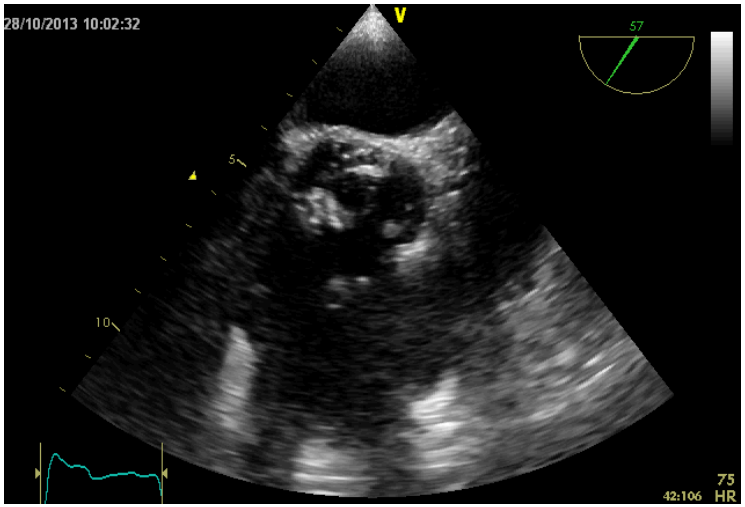


- Aortic bioprosthetic valve

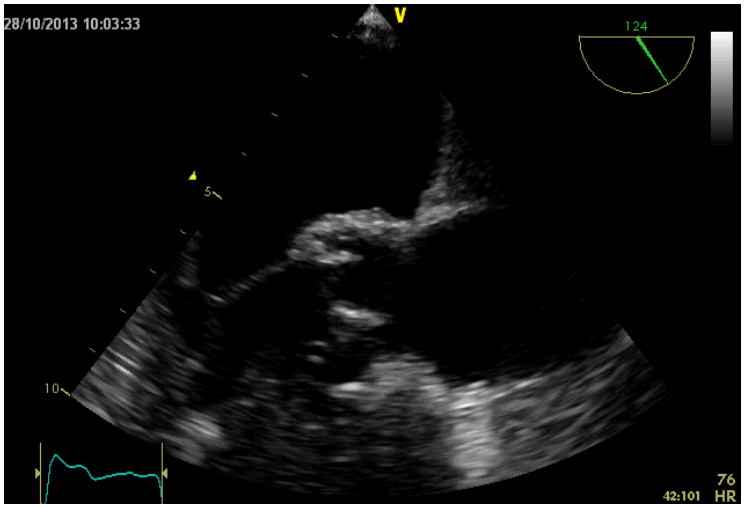
- 5 years later:
  - Fever (38.8°C)
  - 3 positive blood cultures: *Pseudomonas aeruginosa*
  - Known systolic heart murmur, no heart failure
  - WBC=13giga/L, CRP=280 mg/L, Creatinine: 85µmol/L
  - ECG: Normal, TTE: bioprosthetic valve with moderate obstruction (mean gradient=25mmHg)

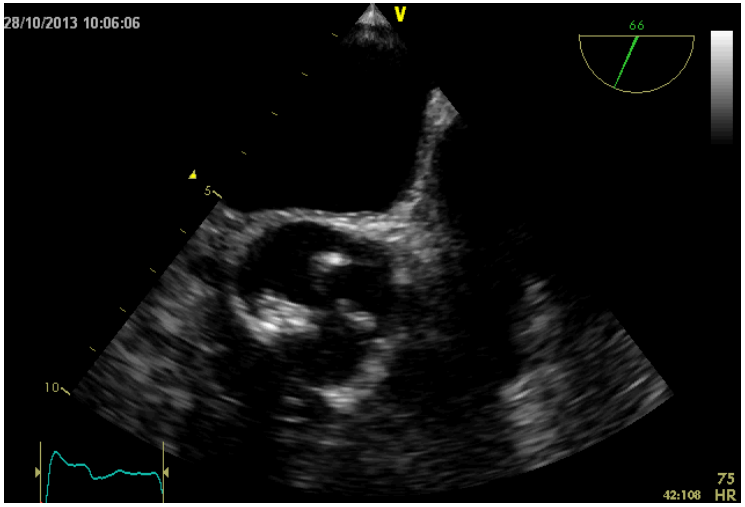
CLINICAL CASE-1

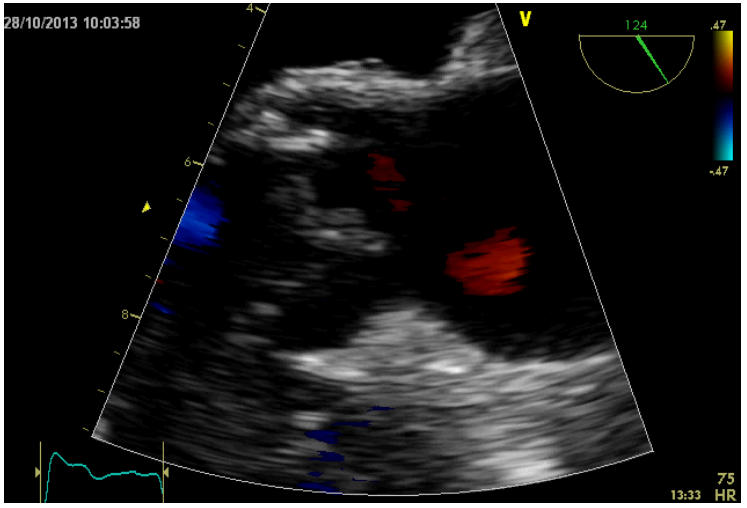
TEE



No vegetation
No abscess
Moderate obstruction

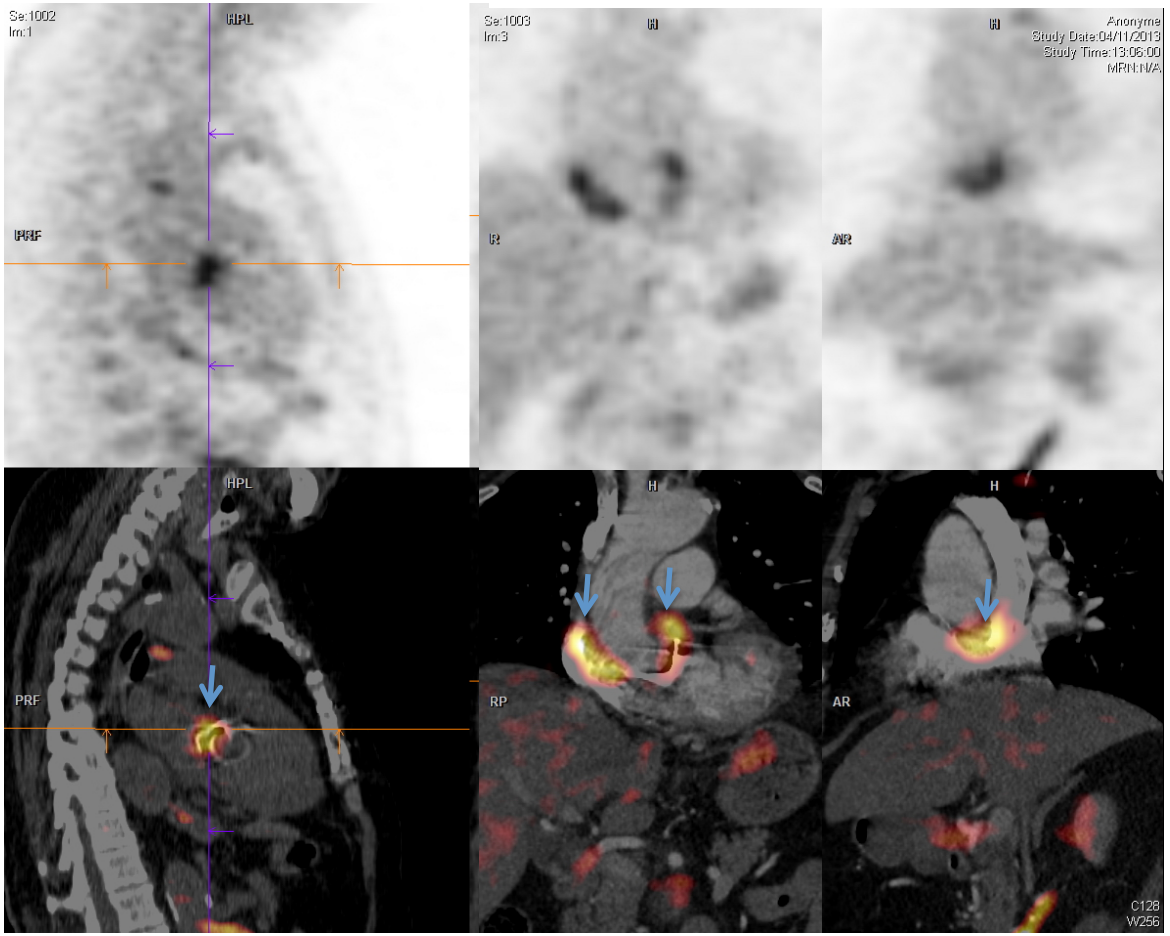






CLINICAL CASE-1

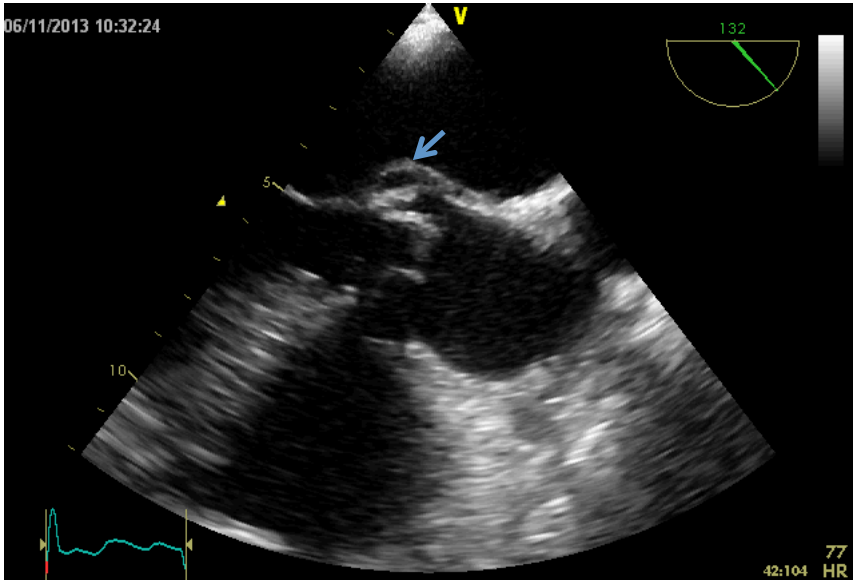
18F-FDG PET-CT

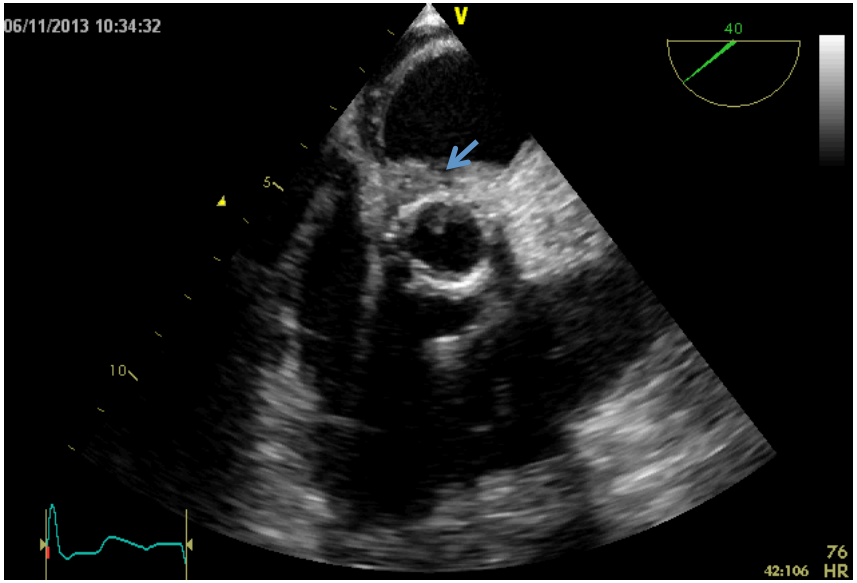


Definite *P.aeruginosa* PVE

CLINICAL CASE-1

New Echo (Day 9)

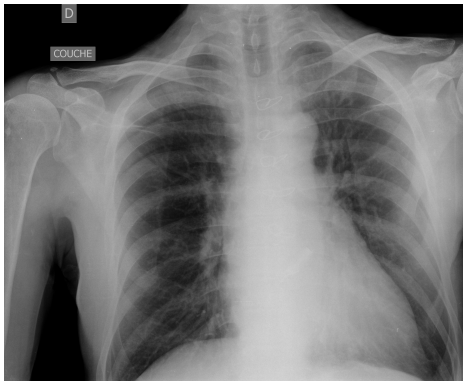




Definite *P.aeruginosa* PVE with abscess:
SURGERY

CLINICAL CASE-2

- 64-year-old-man

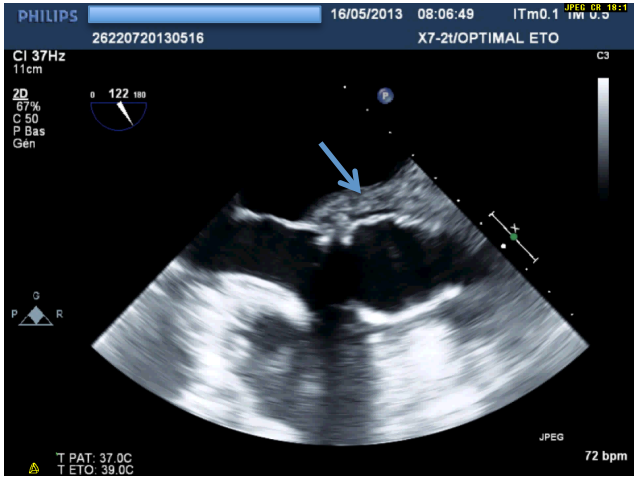


- Composite aortic valve and AA replacement (Bentall procedure)

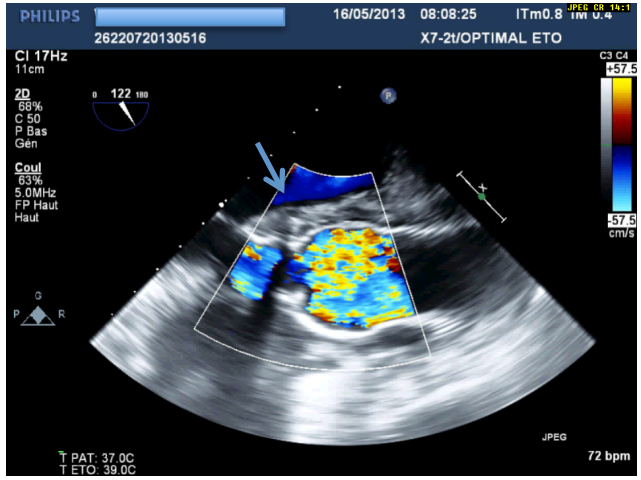
- 2 months later:
  - Fever (39°C)
  - 3 positive blood cultures: *S.aureus* Methi-S
  - No new heart murmur, No heart failure
  - No clinical vascular and immunologic phenomena
  - WBC=17giga/L, CRP=247 mg/L, Creatinine: 90µmol/L
  - ECG: Normal, TTE: poor quality

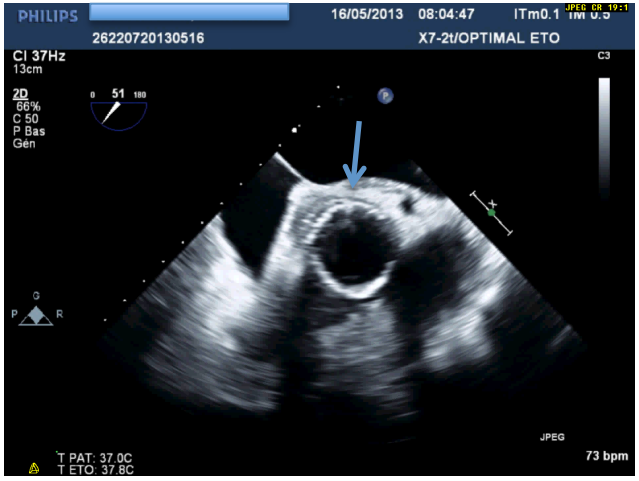
CLINICAL CASE-2

TEE



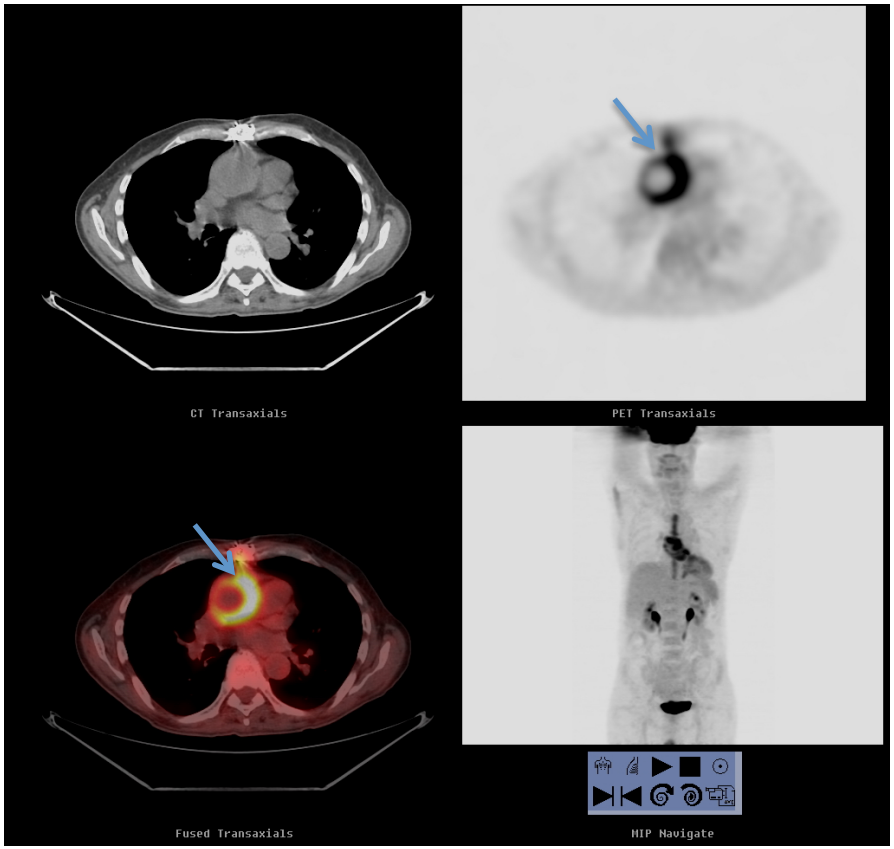
Periprosthetic thickening

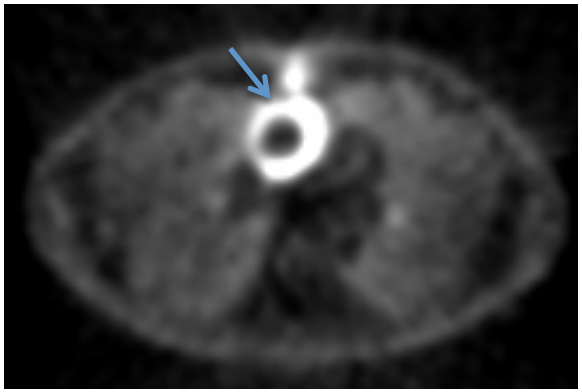


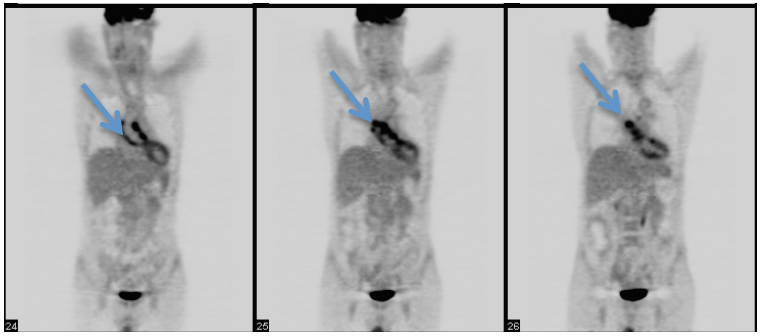


CLINICAL CASE-2

18F-FDG PET-CT

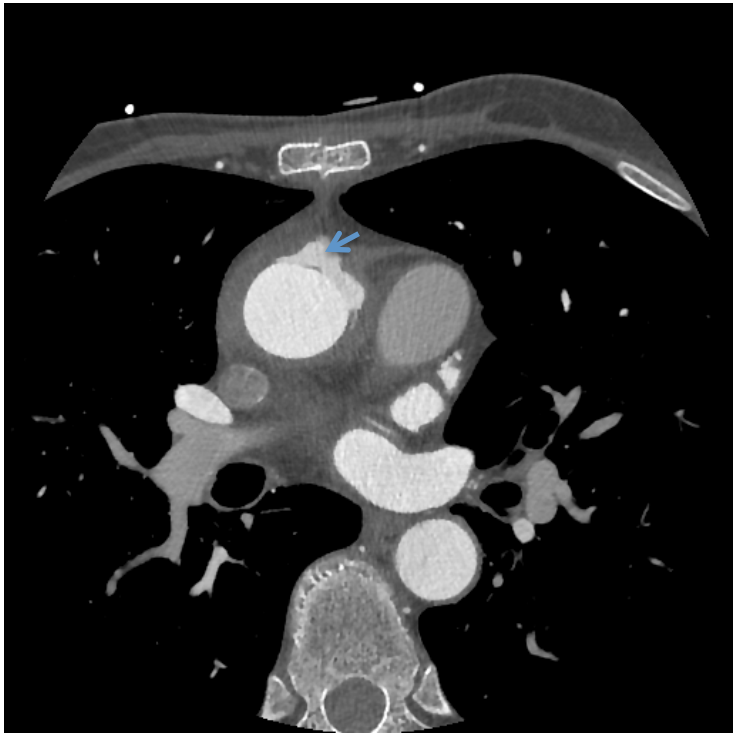






CLINICAL CASE-2

ECG-gated Cardiac CT scan

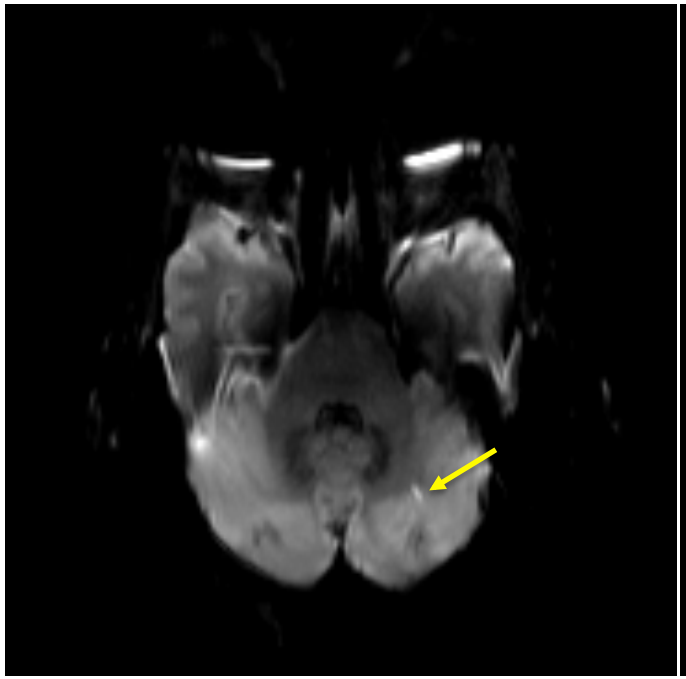


Definite *S aureus* PVE with pseudoaneurysm:
SURGERY

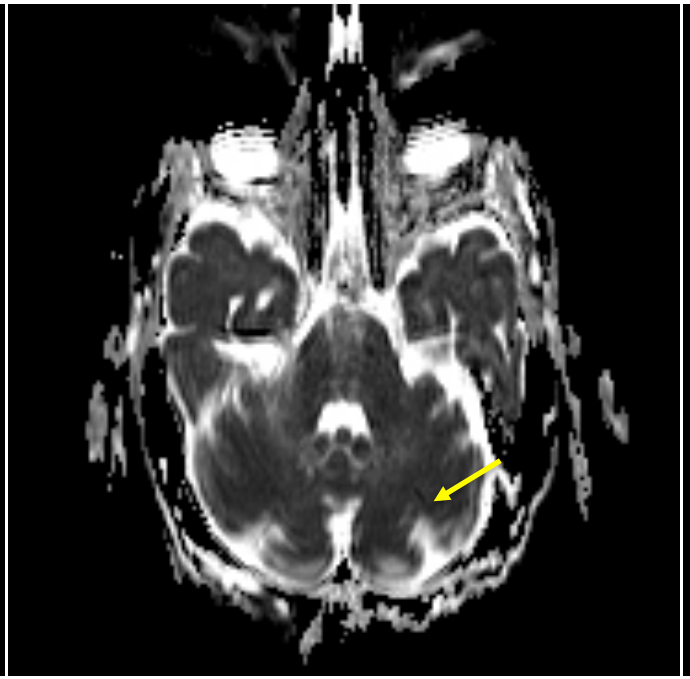
CLINICAL CASE-2

Cerebral MRI

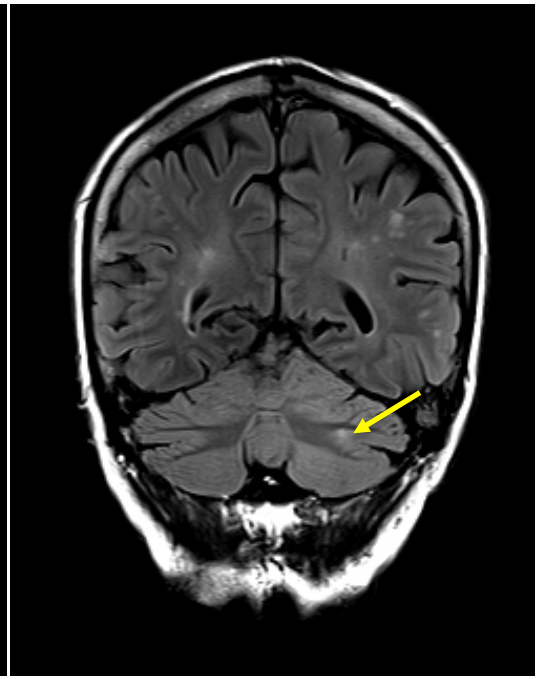
Recent cerebellum embolic event



Diffusion weighted imaging



ADC map

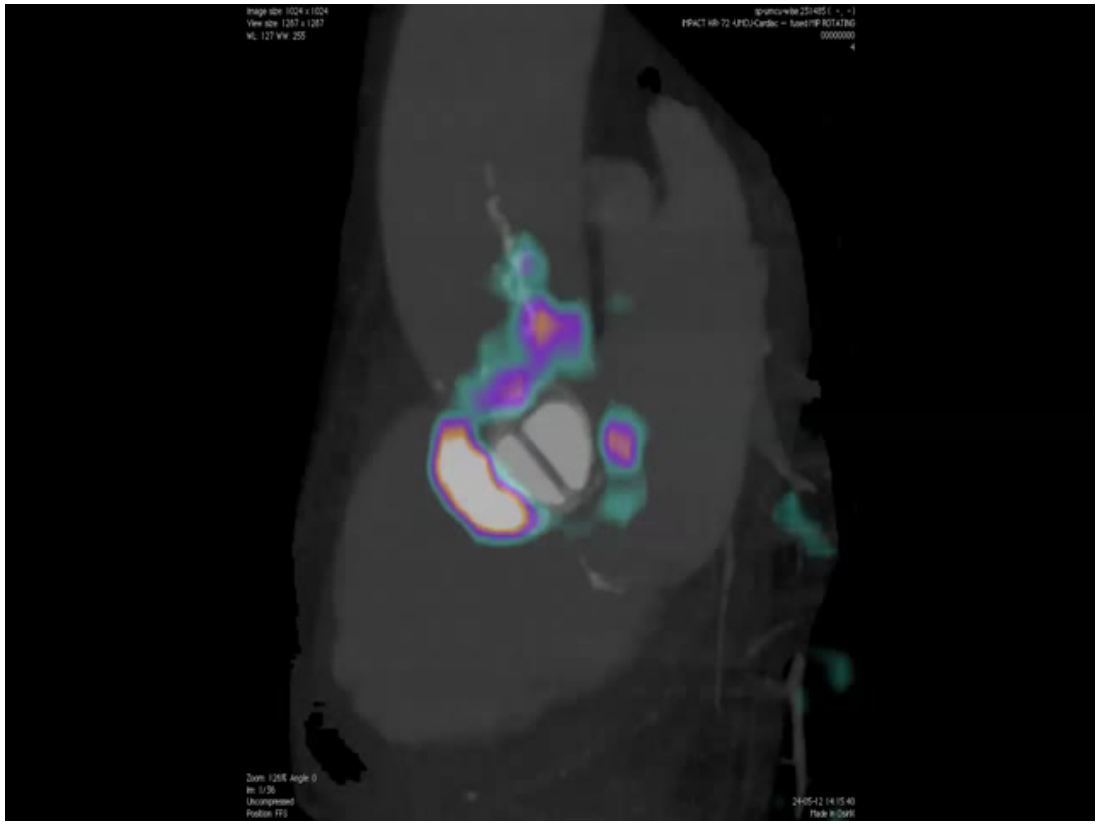


FLAIR

Definite *S aureus* PVE with pseudoaneurysm:
SURGERY

MANAGEMENT

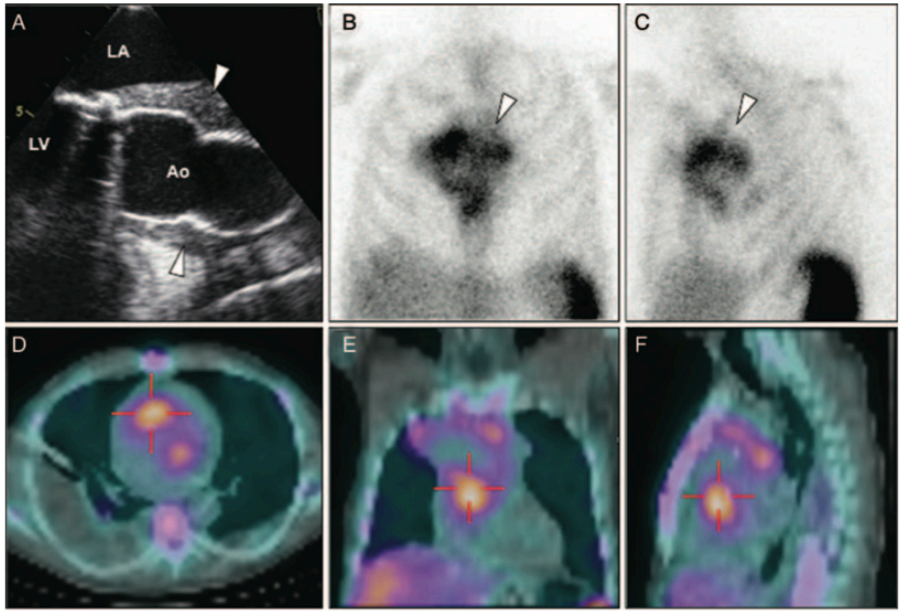
ECG-Gated CARDIAC CT/PET-CT FUSED



Tanis W, et al. JACC Cardiovasc Img 2013

MANAGEMENT

Radiollabeled leucocytes SPECT/CT



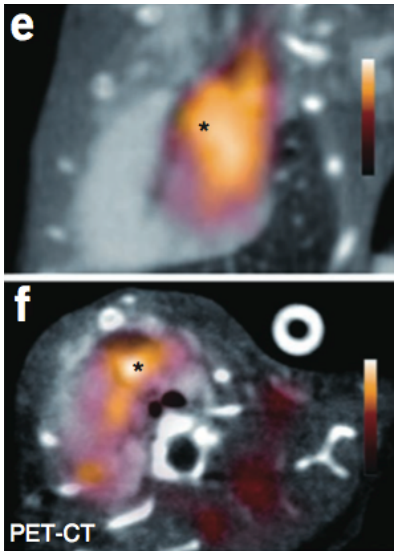
- Better specificity, lower sensitivity than PET/CT
- Time consuming (4-24 hours)
- Interest in “early postoperative PVE”?

Hyafil F, et al. Eur Heart J Cardiovasc Imaging. 2013;14:586-94
Erba PA, et al. J Nucl Med 2012; 53:1235-43

MANAGEMENT

Researches on other molecular imaging

Imaging of *S aureus* via an analog of prothrombin, which binds staphylocoagulase



Panizzi P, et a. Nat Med 2011;17:1142-47

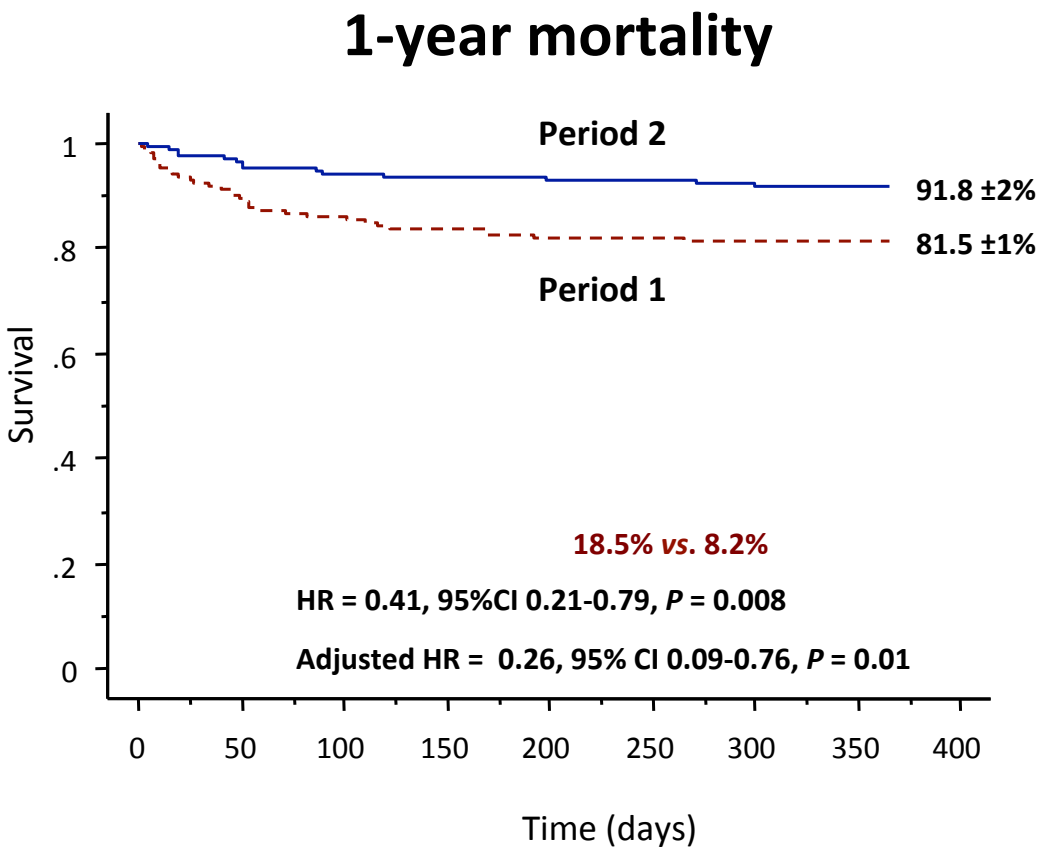
Imaging of as P-Selectin (an agent of Endothelial Activation)

Rozet F, et al. J Nucl Med 2011;52:1433-40

Development of New Medico-Surgical Strategies

Development of New Medico-Surgical Strategies

Impact of a standardized multidisciplinary approach



Botelho-Nevers E, et al. Arch Intern Med 2009;169:1290-1298
Thuny F, et al. Arch Intern Med 2009;170:211-212

Development of New Medico-Surgical Strategies

Very Early Surgery

Recommendations: Indications for surgery	Timing	Level of evidence	
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 cardiogenic shock	Emergency	I	B
• Aortic or mitral IE with severe acute regurgitation and persisting HF or echo-cardiographic signs of poor hemodynamic tolerance (early mitral closure or pulmonary hypertension)	Urgent	I	B
• Aortic or mitral IE with severe acute regurgitation and no HF	Elective	IIa	B
B. UNCONTROLLED INFECTION			
• Locally uncontrolled infection	Urgent	I	B
• Persisting fever and positive blood culture > 7-10 days		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 treatment	Urgent	I	B
• Aortic or mitral IE with large vegetations (10 mm) and other predictors of complicated course (HF, persistent infection, abscess)	Urgent	I	C
• Isolated very large vegetations (>15 mm)	Urgent	IIb	C

ESC 2009

Development of New Medico-Surgical Strategies

Very Early Surgery to Prevent Embolism and Death

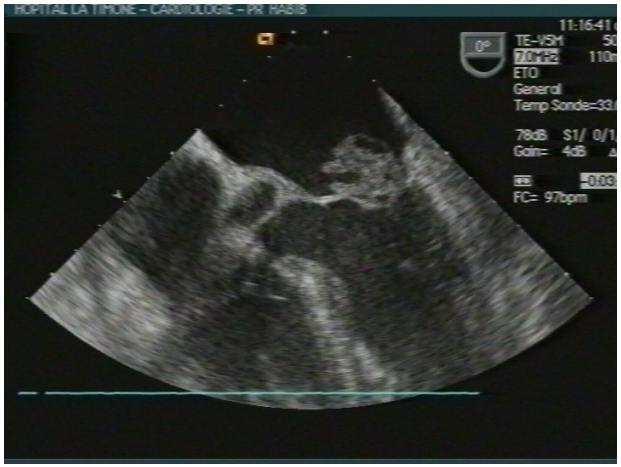
1st Randomized trial

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.



Kang DH, et al. New Engl J Med 2012;366:2466-73

Development of New Medico-Surgical Strategies

Very Early Surgery to Prevent Embolism and Death

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

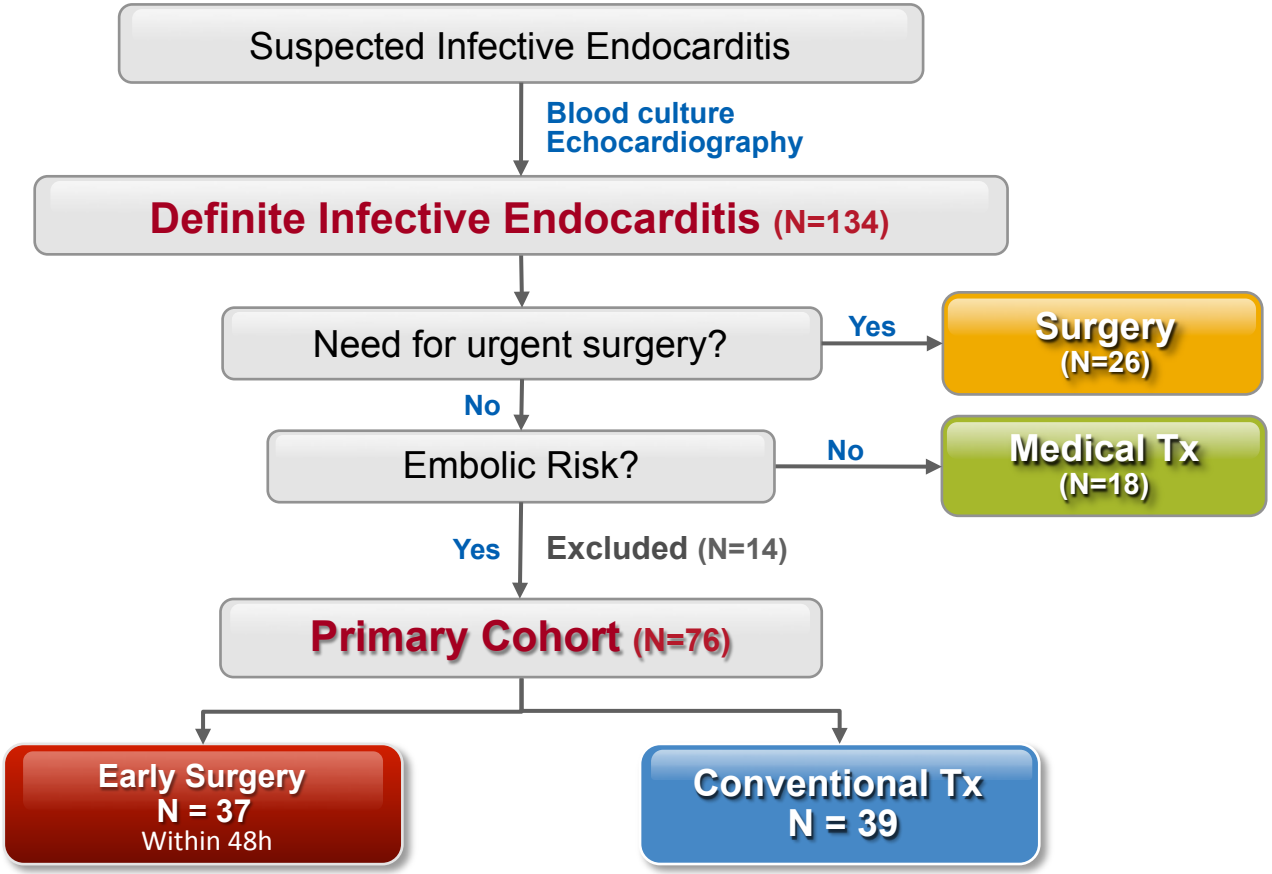
Exclusion Criteria

- 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

Kang DH, et al. New Engl J Med 2012;366:2466-73

Development of New Medico-Surgical Strategies

Very Early Surgery to Prevent Embolism and Death



Primary end point: In-hopital death and clinical embolic events at 6 weeks

Kang DH, et al. New Engl J Med 2012;366:2466-73

Development of New Medico-Surgical Strategies

Very Early Surgery to Prevent Embolism and Death

End Point	CONV Tx (n=39)	Early Surgery (n=37)	p-value
Primary end point	***9 (23%)***	***1 (3%)***	***0.014***
In-hospital death	1 (3%)	1 (3%)	1.000
Embolic event at 6 wks	8 (21%)	0 (0%)	0.005
Cerebral	5	0	
Coronary	1	0	
Popliteal	1	0	
Spleen	1	0	
Secondary end point at 6M	***11 (28%)***	***1 (3%)***	***0.003***
Mortality	2 (5%)	1 (3%)	1.000
Embolic event	8 (21%)	0 (0%)	0.005
Relapse of IE	1 (3%)	0 (0%)	1.000

Kang DH, et al. New Engl J Med 2012;366:2466-73

Development of New Medico-Surgical Strategies

Very Early Surgery to Prevent Embolism and Death

Characteristics	CONV Tx (n=39)	Early Surgery (n=37)	p-value
Age, years	48±18	46±15	0.54
Male sex	27 (69%)	24 (65%)	0.69
Diabetes	4 (10%)	8 (22%)	0.17
Hypertension	7 (18%)	11 (30%)	0.23
Coronary artery disease	1 (3%)	3 (8%)	0.35
Immunocompromised status	1 (3%)	2 (5%)	0.61
Serum creatinine, mg/dL	0.9±0.7	1.3±1.9	0.31
EuroSCORE	6.7±1.7	6.4±1.6	0.49
Embolism on admission	17 (44%)	19 (51%)	0.50
Brain	11 (28%)	11 (30%)	
Kidney	7 (18%)	6 (16%)	
Spleen	9 (23%)	14 (38%)	

But

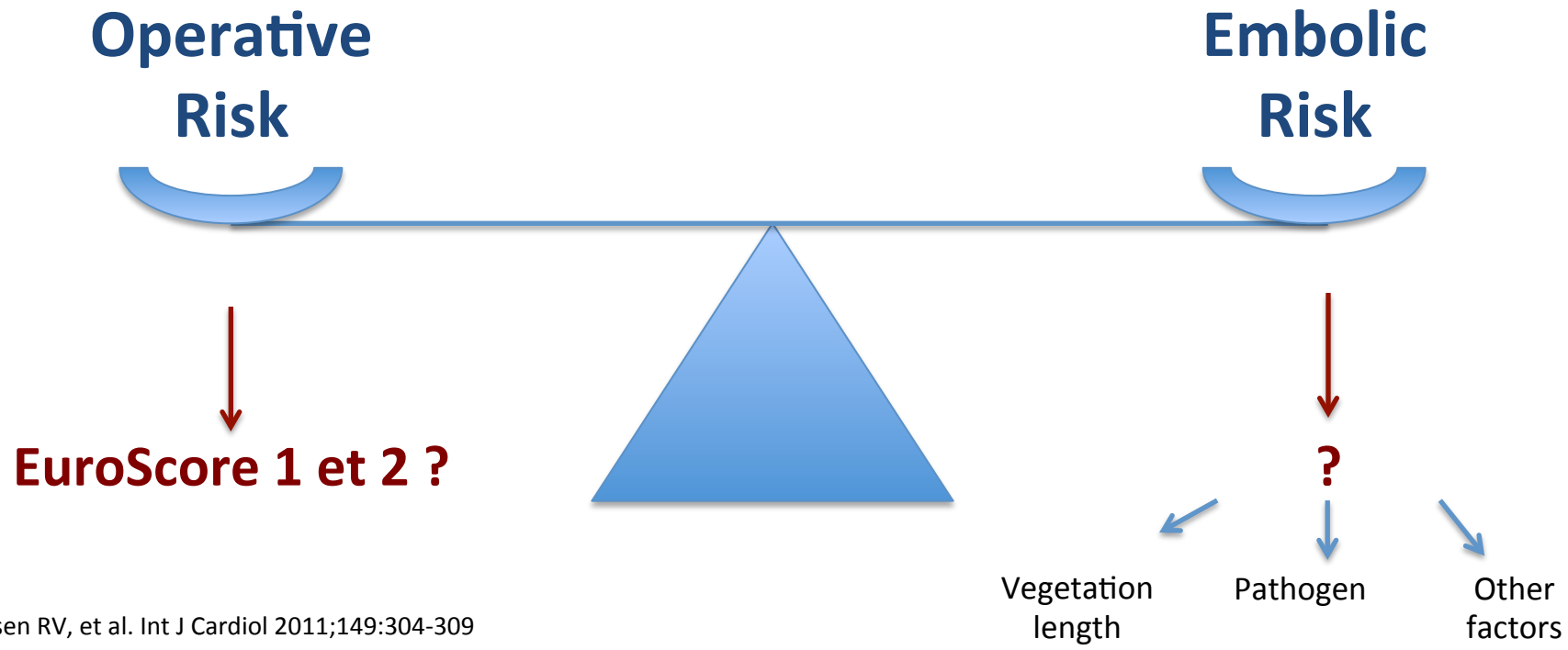
- exclusion of patients with high comorbidities
- Vegetation length is not the only predictor of embolism

Kang DH, et al. New Engl J Med 2012;366:2466-73

Development of New Medico-Surgical Strategies

Prediction of Embolic Risk in Infective Endocarditis

<u>Quantification</u> of Benefit/Risk Ratio for surgery must be evaluated



Rasmussen RV, et al. Int J Cardiol 2011;149:304-309

Development of New Medico-Surgical Strategies

Prediction of Embolic Risk in Infective Endocarditis

Benefit/Risk Ratio <u>Quantification</u>
for surgery must be evaluated

"The Embolic Risk French Calculator"

Heart Valve Disease

Prediction of Symptomatic Embolism in Infective Endocarditis

Construction and Validation of a Risk Calculator in a Multicenter Cohort

Sandrine Hubert, MD,*† Franck Thuny, MD, PHD,*‡§ Noemie Resseguier, MD,‖ Roch Giorgi, MD, PHD,‖ Christophe Tribouilloy, MD, PHD,¶# Yvan Le Dolley, MD,* Jean-Paul Casalta, MD,** Alberto Riberi, MD,† Florent Chevalier, MD,¶ Dan Rusinaru, MD,¶ Dorothée Malaquin, MD,¶ Jean Paul Remadi, MD,†† Ammar Ben Ammar, MD,‡‡ Jean Francois Avierinos, MD,* Frederic Collart, MD,† Didier Raoult, MD, PHD,‡** Gilbert Habib, MD*

Marseille and Amiens, France

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.

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

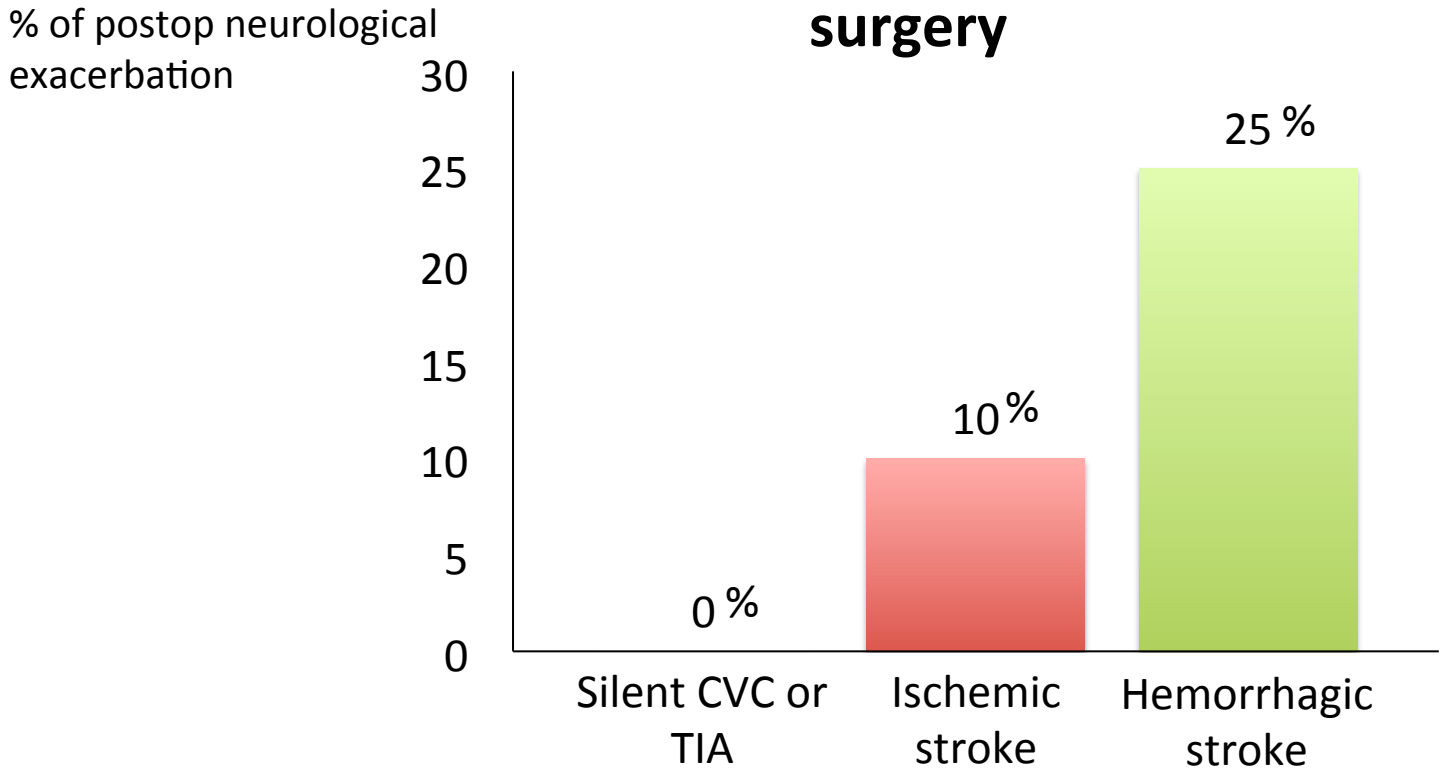
PREDICTED EMBOLIC RISK CALCULATION	
Time (Days)	**Predicted Embolic Risk**
1	5%
2	6%
3	10%
4	13%
5	14%
6	15%
7	16%
10	18%
11	18%
12	20%
13	22%
14	24%
18	24%
19	25%
23	26%
28	27%
35	27%
47	28%
48	28%
180	29%

Hubert S, et al. J Am Coll Cardiol 2013;62:1384–92

Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

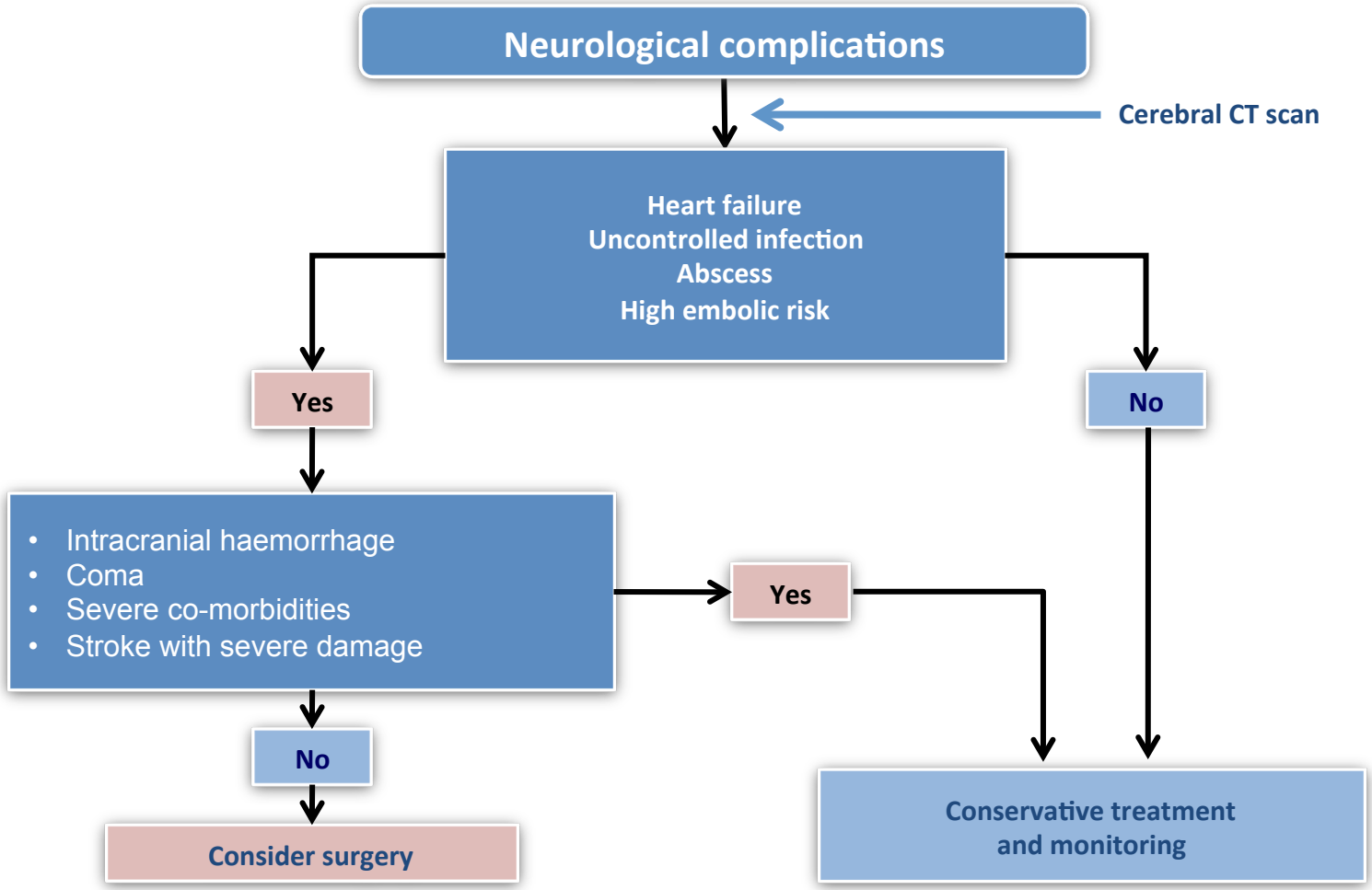
<u>Postoperative neurological exacerbation</u> depends on the severity of the cerebral damage rather than the timing of surgery



Thuny F, et al. Eur Heart J 2005;28:1155-1161

Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

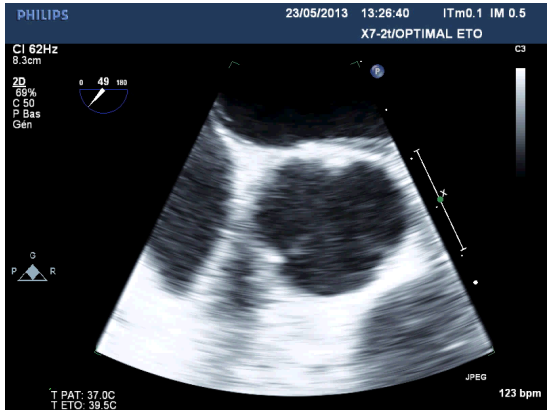


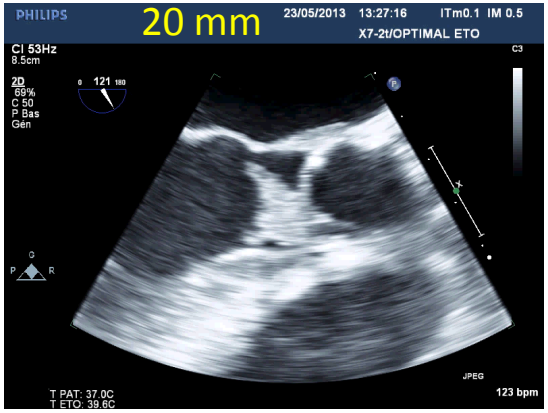
ESC Guidelines 2009

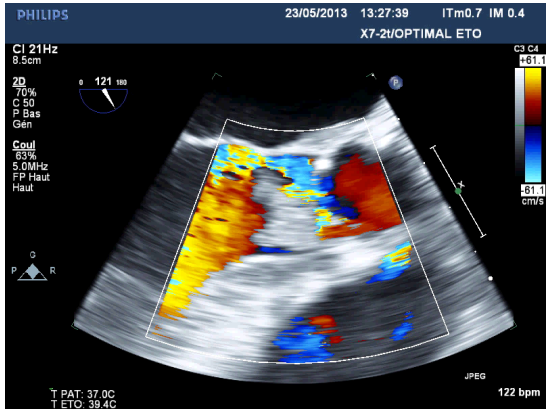
Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

- 55-year old woman, diabetes, history of heart murmur
- Recent skin wound
- Fever (40°), diastolic murmur, no heart failure, normal neurological examination
- ECG: sinus tachycardia
- CRP=375 mg/L, Blood cultures: *Staphylococcus aureus MS (x3)*
- Cerebral MRI: silent EE







Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

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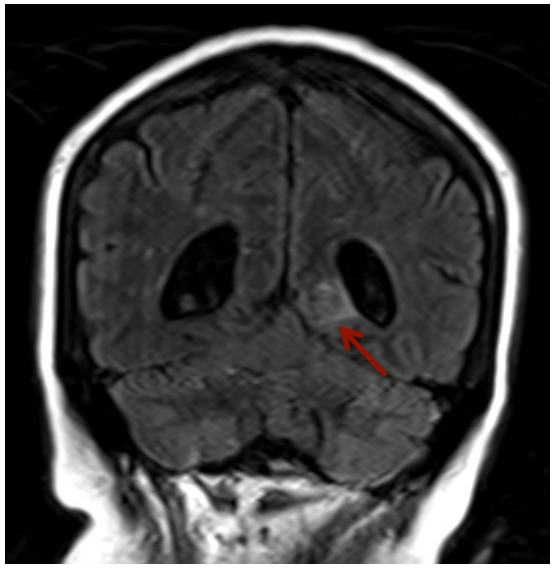
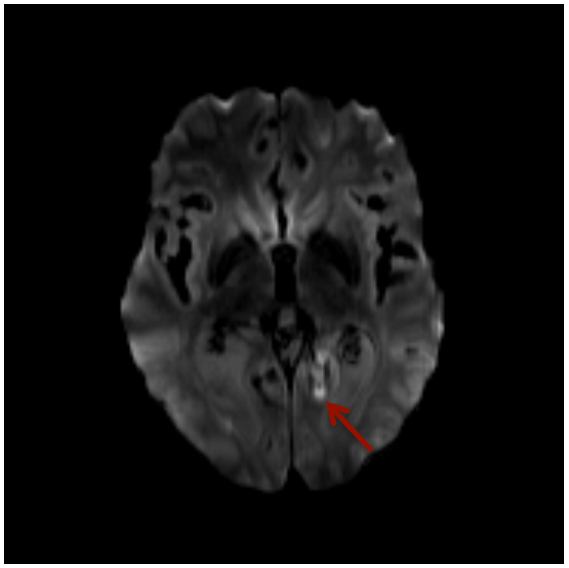
- Cerebral MRI: silent EE

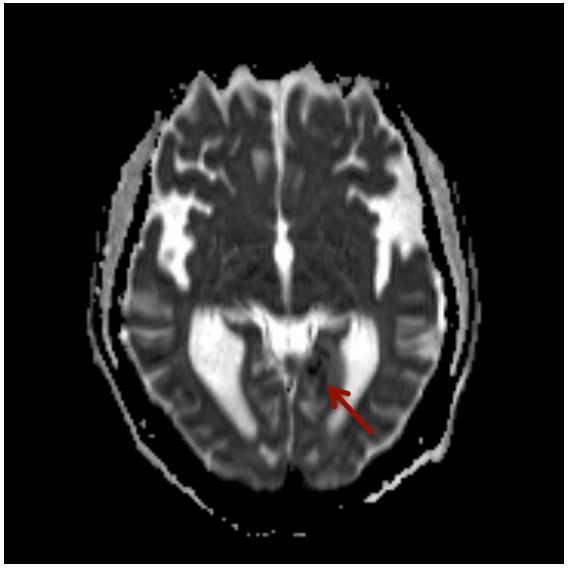
MRI-FLAIR



MRI-DIFFUSION

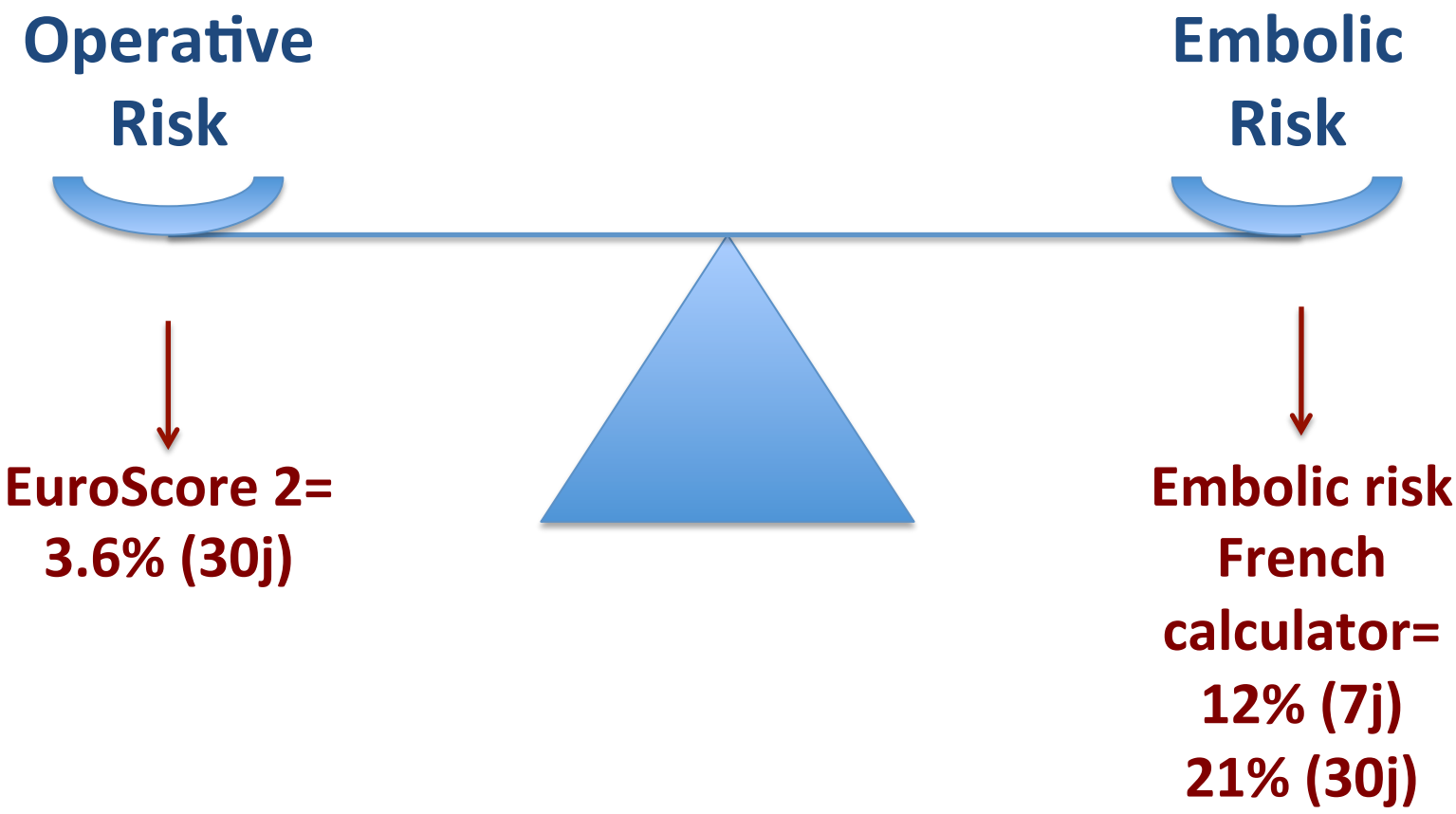


MRI-ADC



Development of New Medico-Surgical Strategies

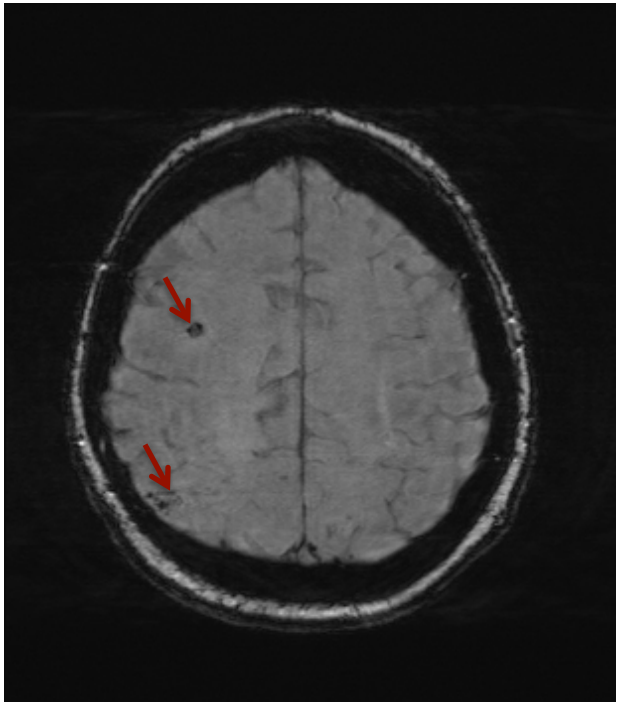
Surgery after Neurological Complications

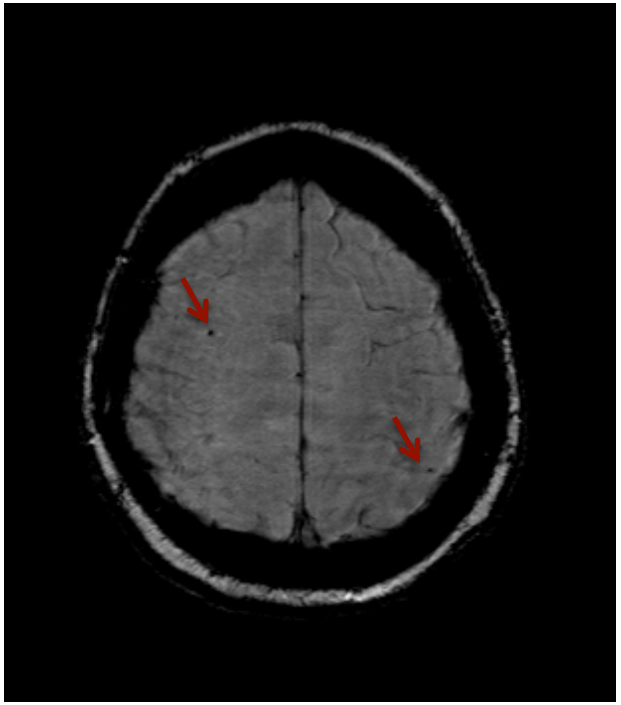


Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

T2*-MRI





Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

Infectious aneurysm

Angio-MRI

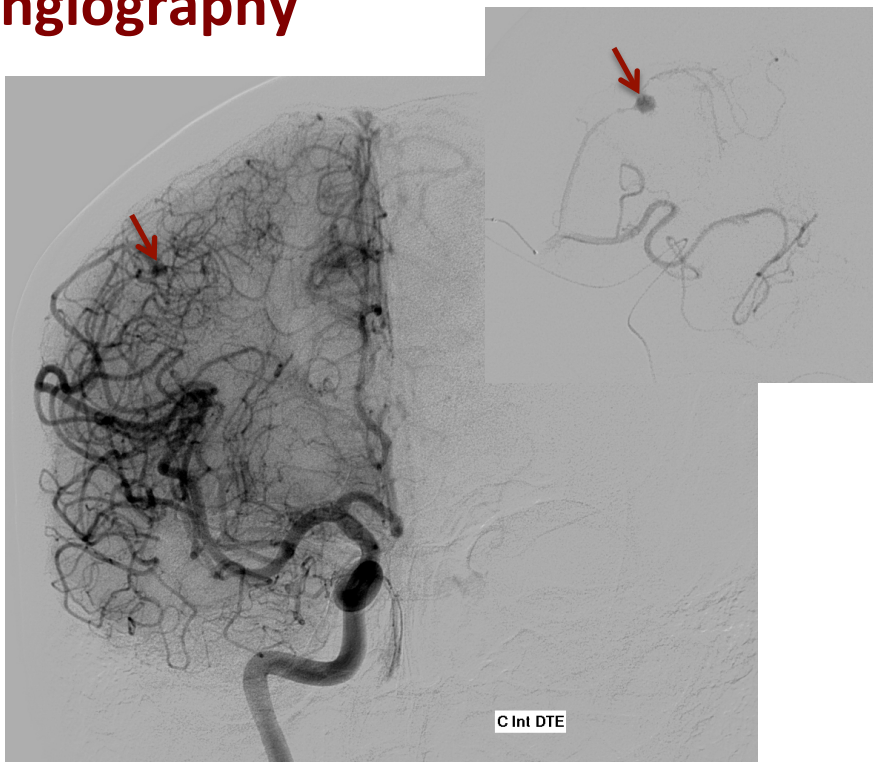
Cerebral-CT with injection

Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

Infectious aneurysm

Angiography

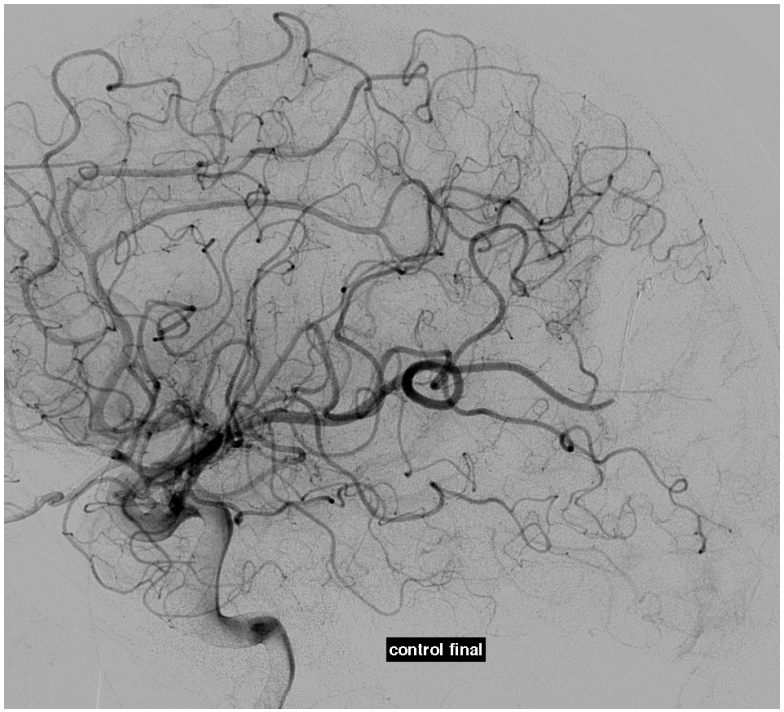


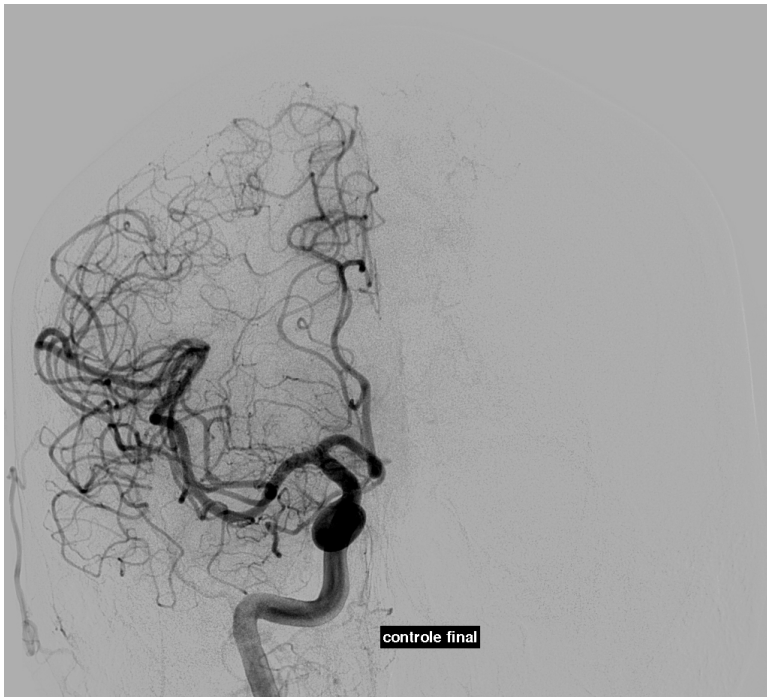
Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

Infectious aneurysm

Angiography + embolization





Development of New Medico-Surgical Strategies

Surgery after Neurological Complications

- 55-year old woman, diabetes, history of heart murmur
- Recent skin wound
- Fever (40°), diastolic murmur, no heart failure, normal neurological examination
- ECG: sinus tachycardia
- CRP=375 mg/L, Blood cultures: *Staphylococcus aureus MS (x3)*
- Cerebral CT: silent EE

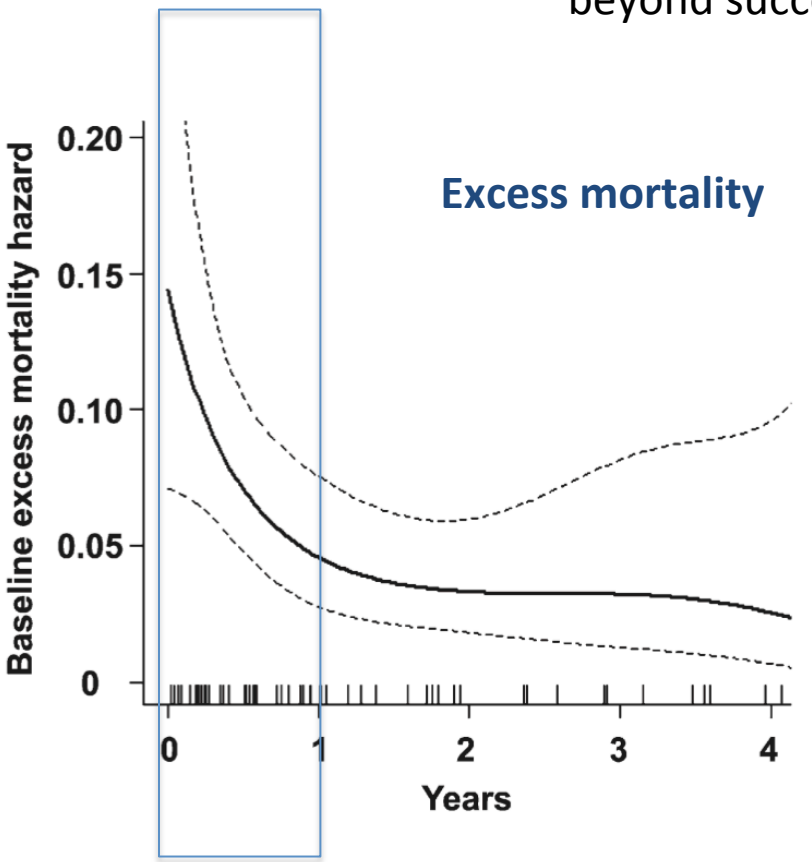
Surgery could be performed at Day 12

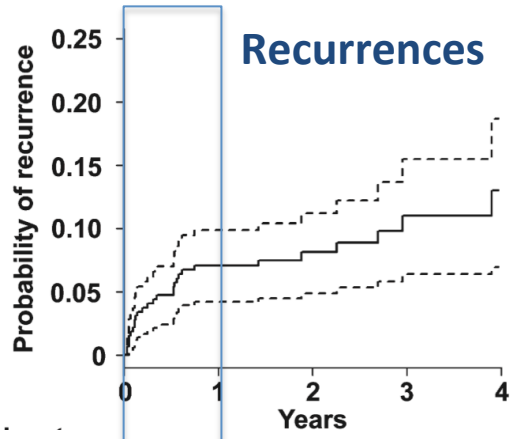
Bioprosthetic valve

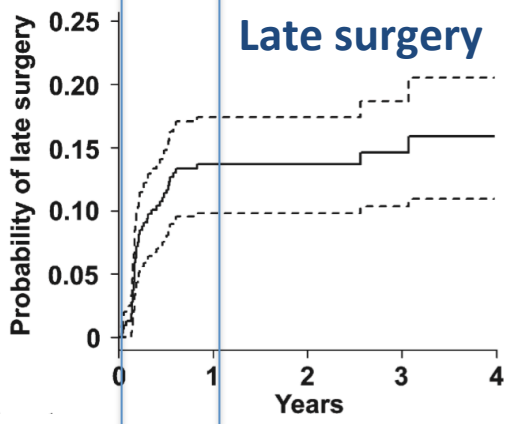
Development of New Medico-Surgical Strategies

Close Follow-up during the 1st Year after diagnosis

Mortality and morbidity may extend beyond successful treatment







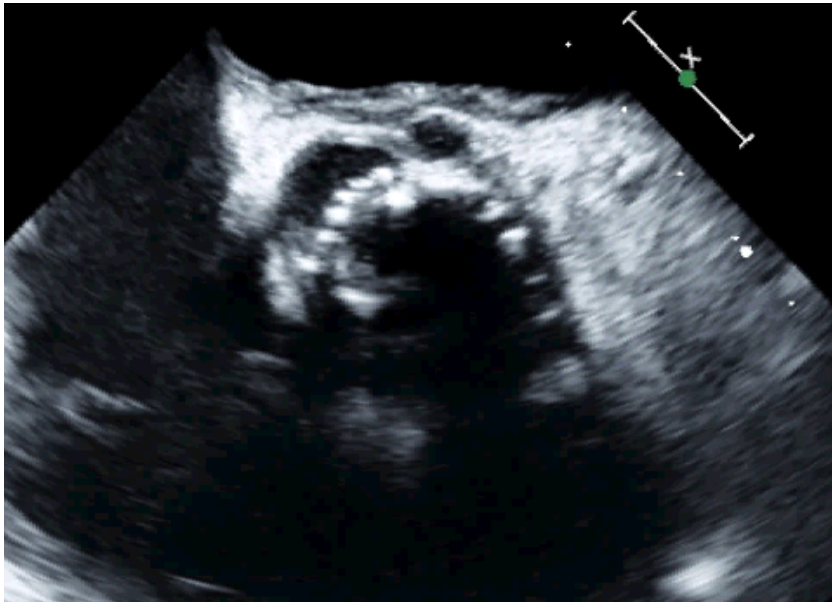
Thuny F, et al. Am Heart J 2012; Am Heart J. 2012;164:94-101

Development of New Medico-Surgical Strategies

Close Follow-up during the 1st Year after diagnosis

Mortality and morbidity may extend
beyond successful treatment

But Echo is limited in the identification of prosthetic valve sterilization at the end of a medical treatment



Is it sterelized?

Development of New Medico-Surgical Strategies

Close Follow-up during the 1st Year after diagnosis

5 patients with positive SPECT/CT on prosthetic valve, medical treatment

← 2nd SPECT/CT after trt

Negative in all the 5 patients

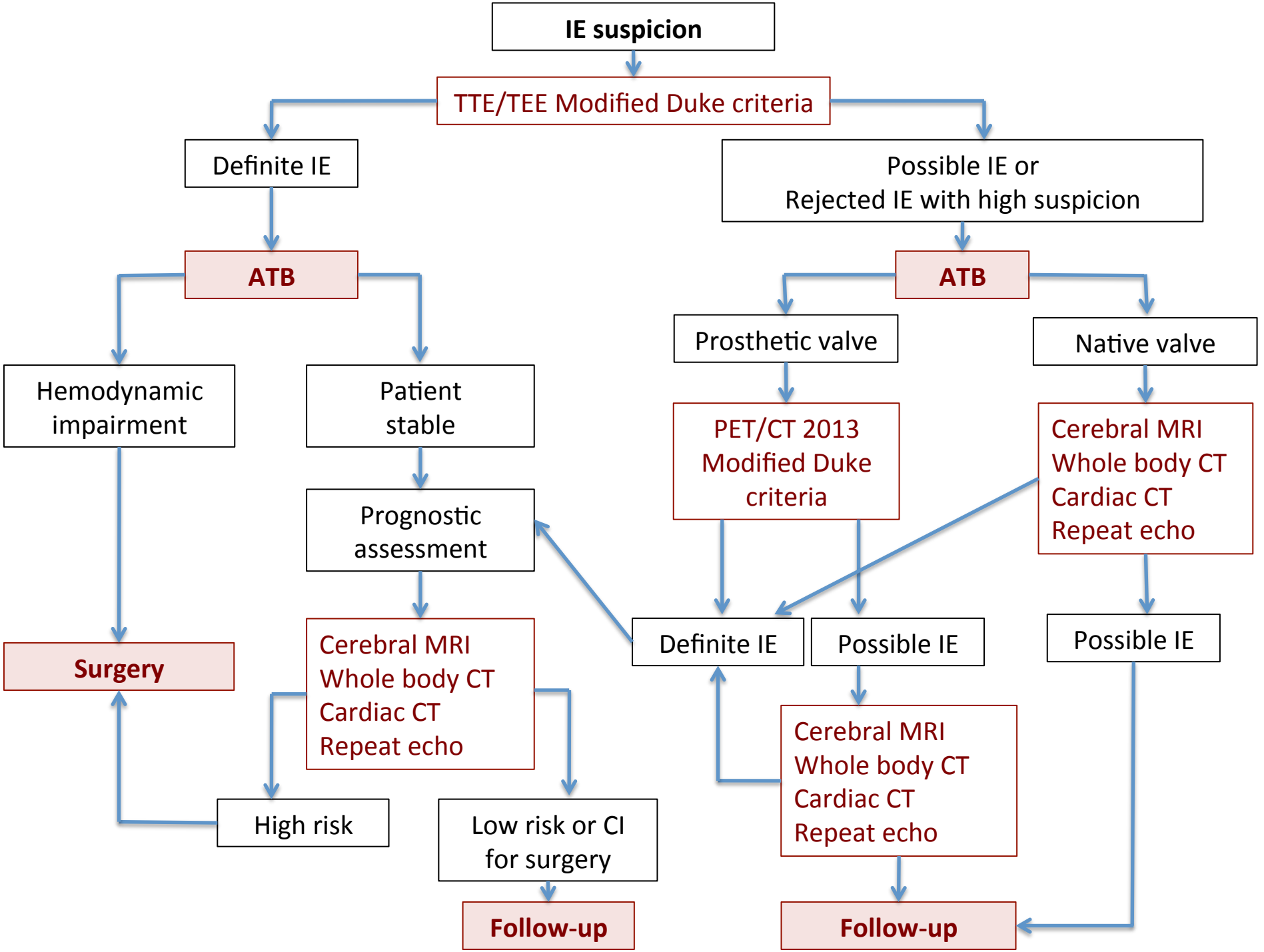
1 patient prosthetic aspetic dehiscence at 56 days
4 patients with no event

Hyafil F, et al. Eur Heart J Cardiovasc Imaging. 2013;14:586-94

CONCLUSION

WHAT'S NEW IN ENDOCARDITIS ?

- The profile of IE is changing but the mortality remains high
- The indication of antibiotic prophylaxis has been restricted
- Novel methods offer hope in decreasing mortality by accelerating the diagnostic process and the risk stratification


IE suspicion
TTE/TEE Modified Duke criteria
Definite IE
Possible IE or
Rejected IE with high suspicion
ATB
ATB
Hemodynamic
impairment
Patient
stable
Prosthetic valve
Native valve
PET/CT 2013
Modified Duke
criteria
Cerebral MRI
Whole body CT
Cardiac CT
Repeat echo
Prognostic
assessment
Surgery
Cerebral MRI
Whole body CT
Cardiac CT
Repeat echo
Definite IE
Possible IE
Possible IE
Cerebral MRI
Whole body CT
Cardiac CT
Repeat echo
High risk
Low risk or CI
for surgery
Follow-up
Follow-up

MERCI

BONNE ANNEE !