AEPEI

lame UMR 1137
Infection, Antimicrobien
Modelisation Evolution

Instituts thématiques Inserm
Institut national
de la santé et de la recherche médicale

"Role of Imaging techniques in endocarditis and vascular infections"

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"Role of Imaging techniques in endocarditis and vascular infections”

Endocarditis

Vascular infections

"Role of Imaging techniques in endocarditis and vascular infections”

Endocarditis	Vascular infections
Diagnosis Prognosis	Therapeutic Therapeutic FU

Infective Endocarditis

- **IE incidence France: stable 25 /10^6 ind/year**
  relatively uncommon : 1 300 cases/year

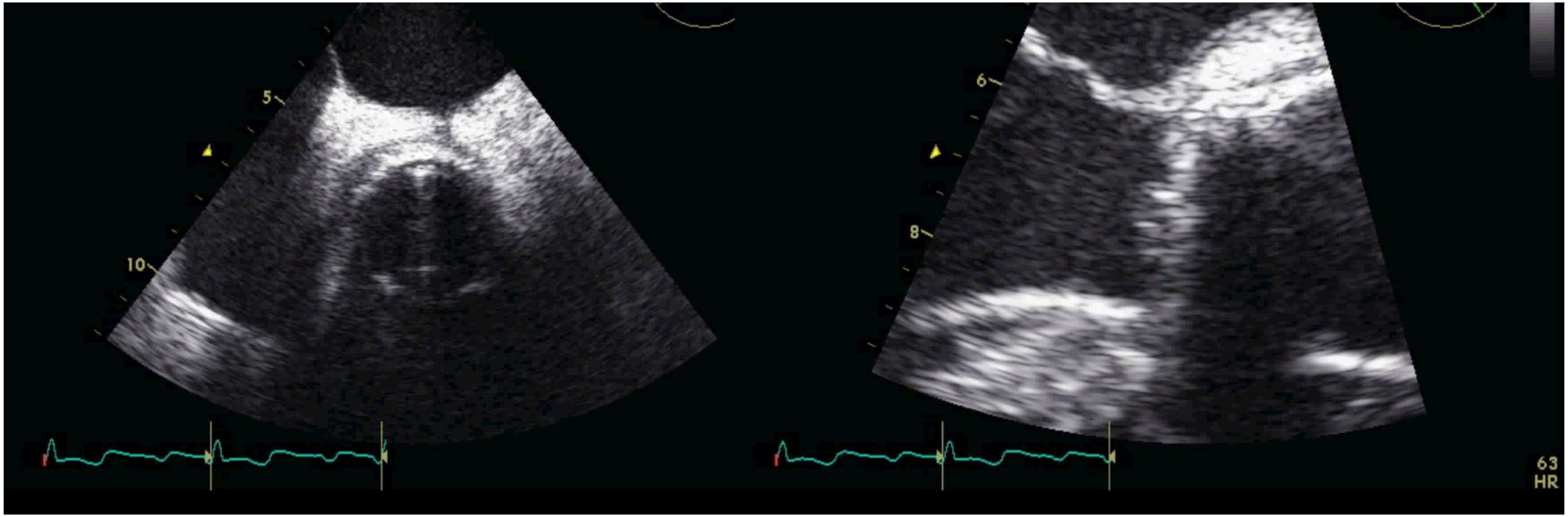
- **Elderly** **70 % > 50 years old**
- **Surgery** **50 %**
- **Mortality** **20 %**

- **Role of cardiac imaging clearly identified in surgical decision-making**

Selton Suty C, CID 2012; 54:1230-1239; Duval X, JACC 2012 ;59:1968-76

Case History

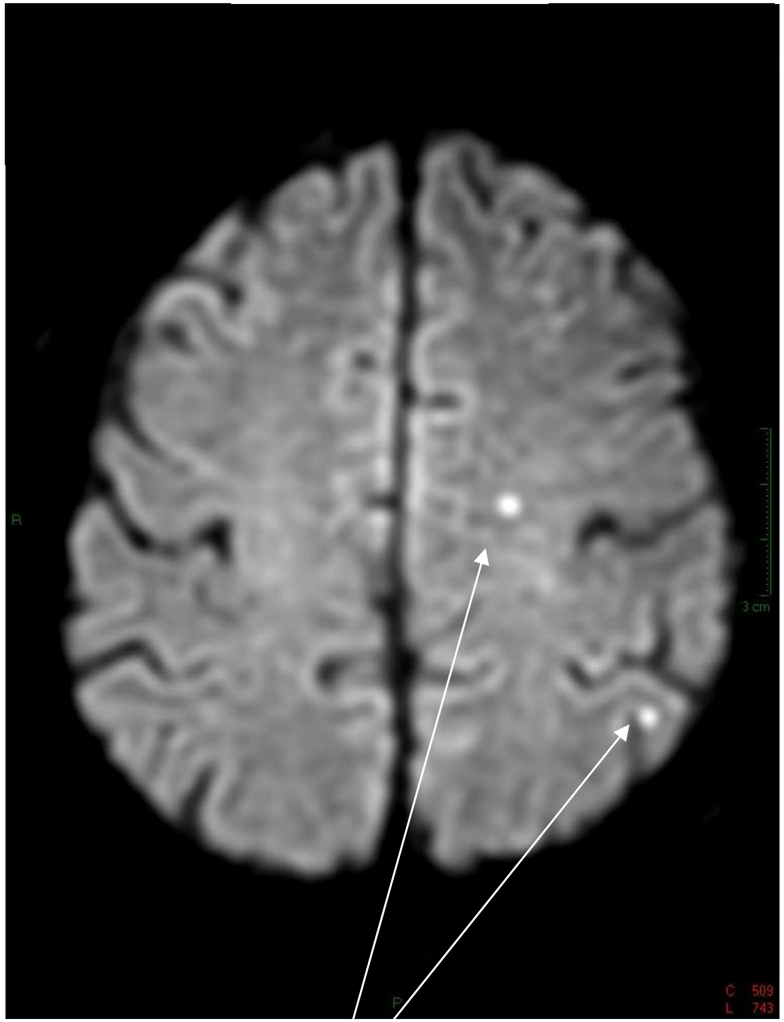
- **62-year old man**
- Bentall intervention in 2005 for severe AR on a bicuspid aortic valve + aortic aneurysm
- Hospitalized
  - persisting fever for 3 weeks
  - amoxicillin treatment for one week
  - normal clinical examination
  - INR = 2
- WBC 13 500 leuco / ml, CRP 185 mg/l
- Negative blood cultures

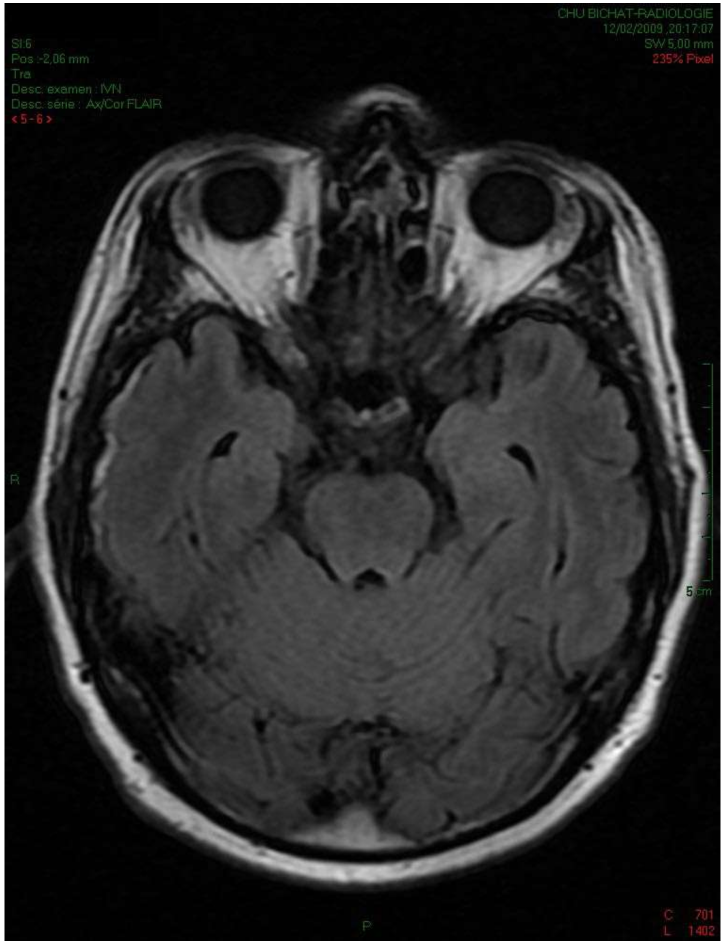


TTE / TEE

- no evidence of abscess
- no regurgitation
- aortic valve: mobile mass 8 mm (thrombus ?, vegetation ?)
- no prosthesis dysfunction

Cerebral MRI





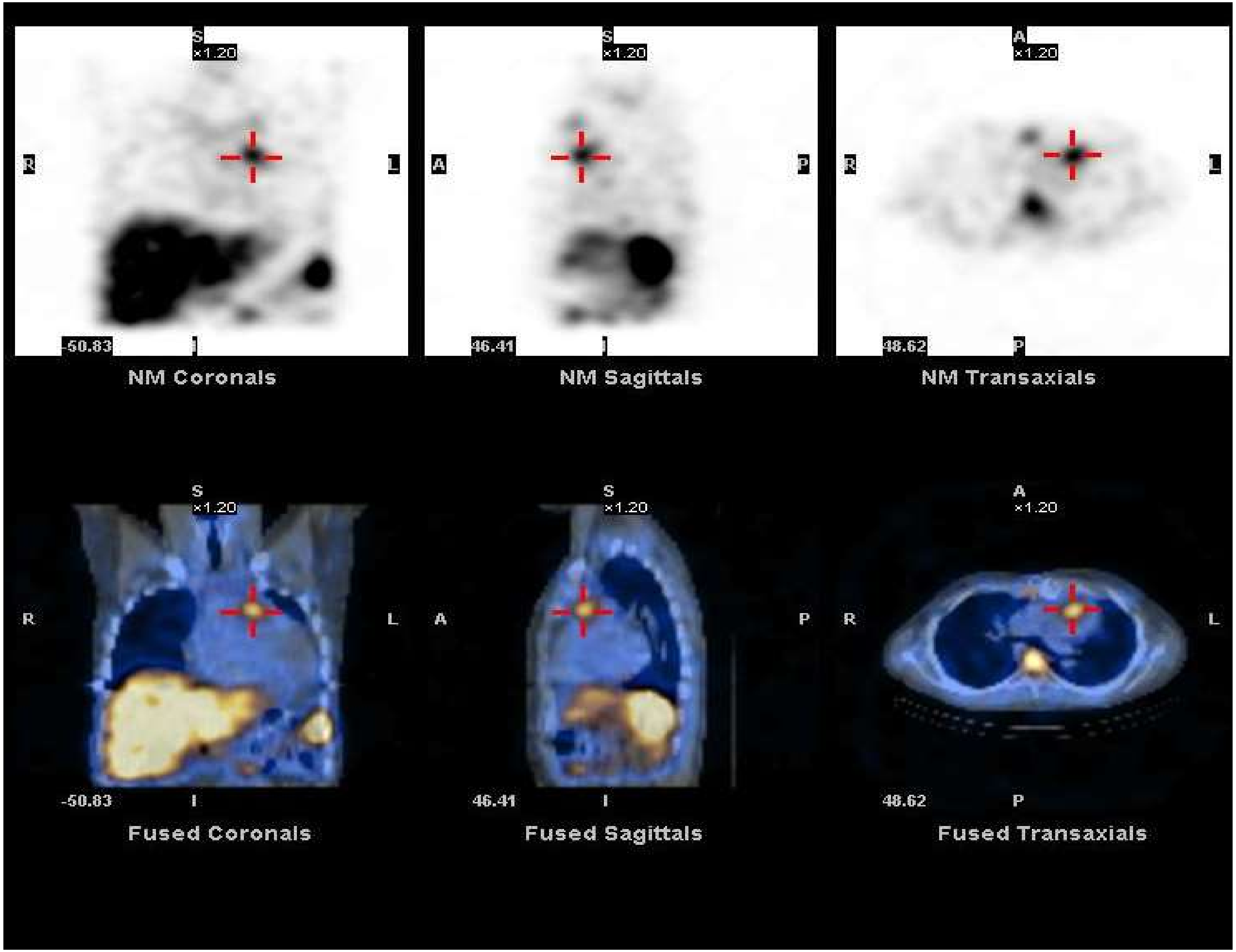
Summary

- **Major Duke criteria** : vegetation ?
- **Minor Duke criteria**
  - Valve prosthesis
  - Fever
  - + 2 small recent asymptomatic strokes

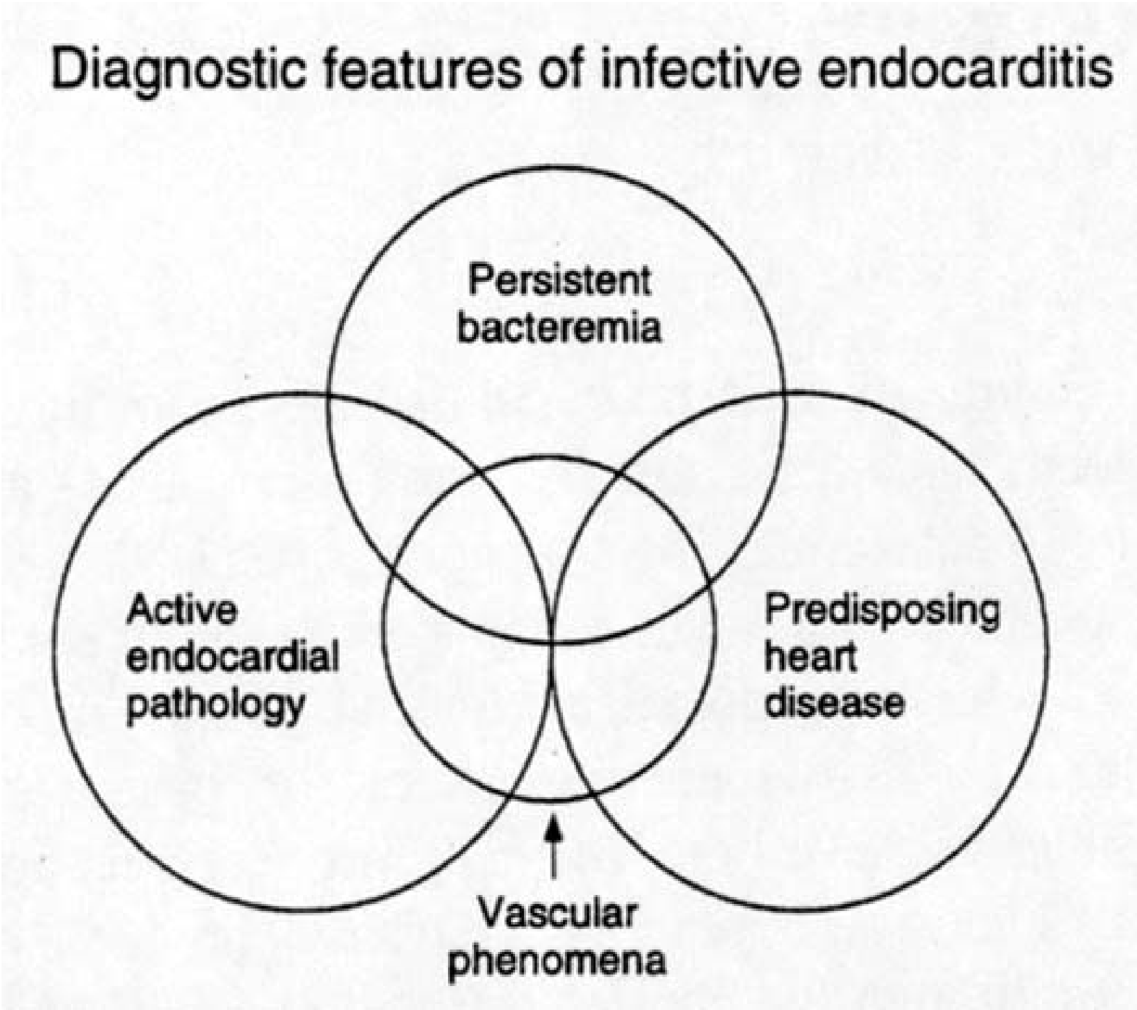
- After cerebral MRI

  possible IE $\rightarrow$ definite IE

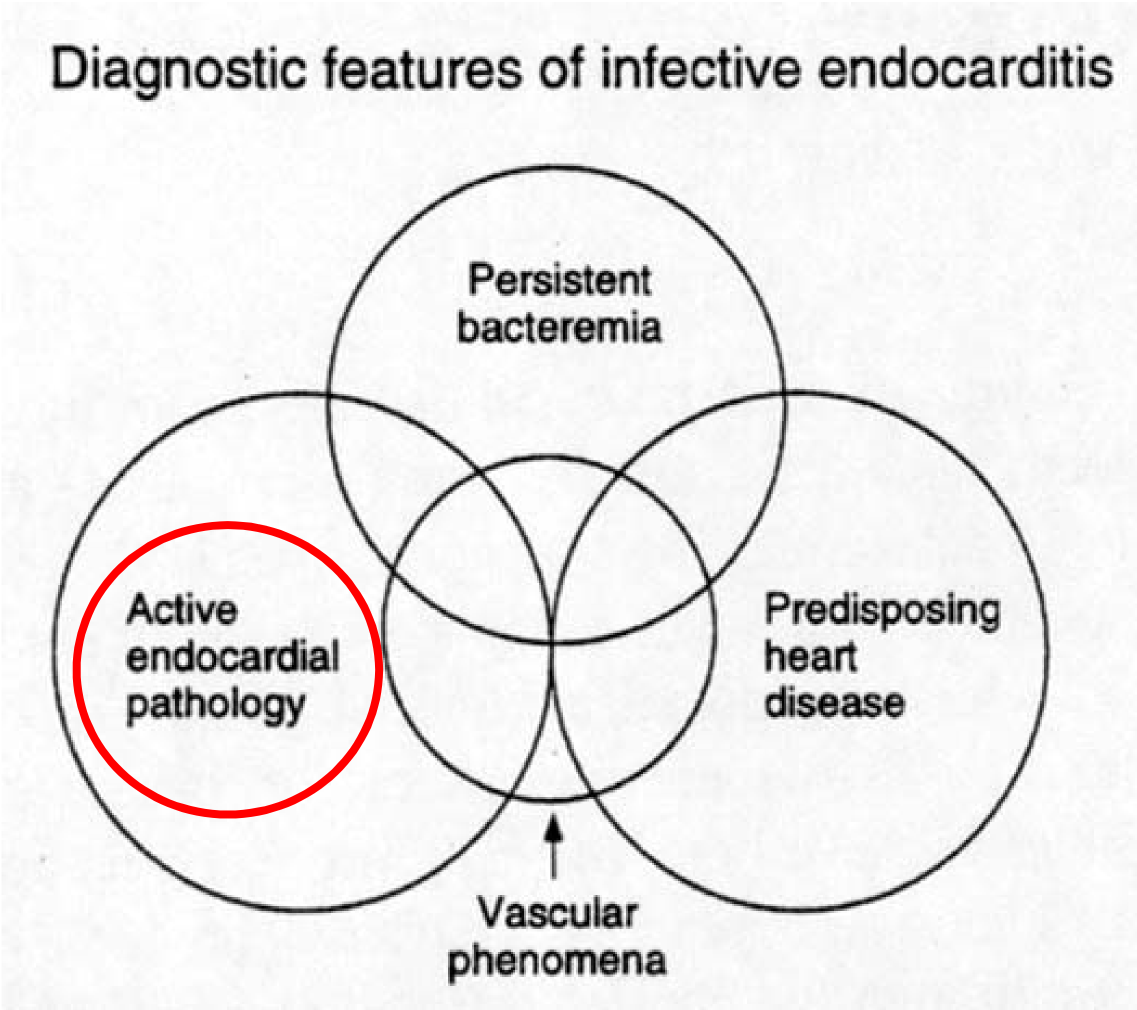
Radionuclide Labelled Leucocytes



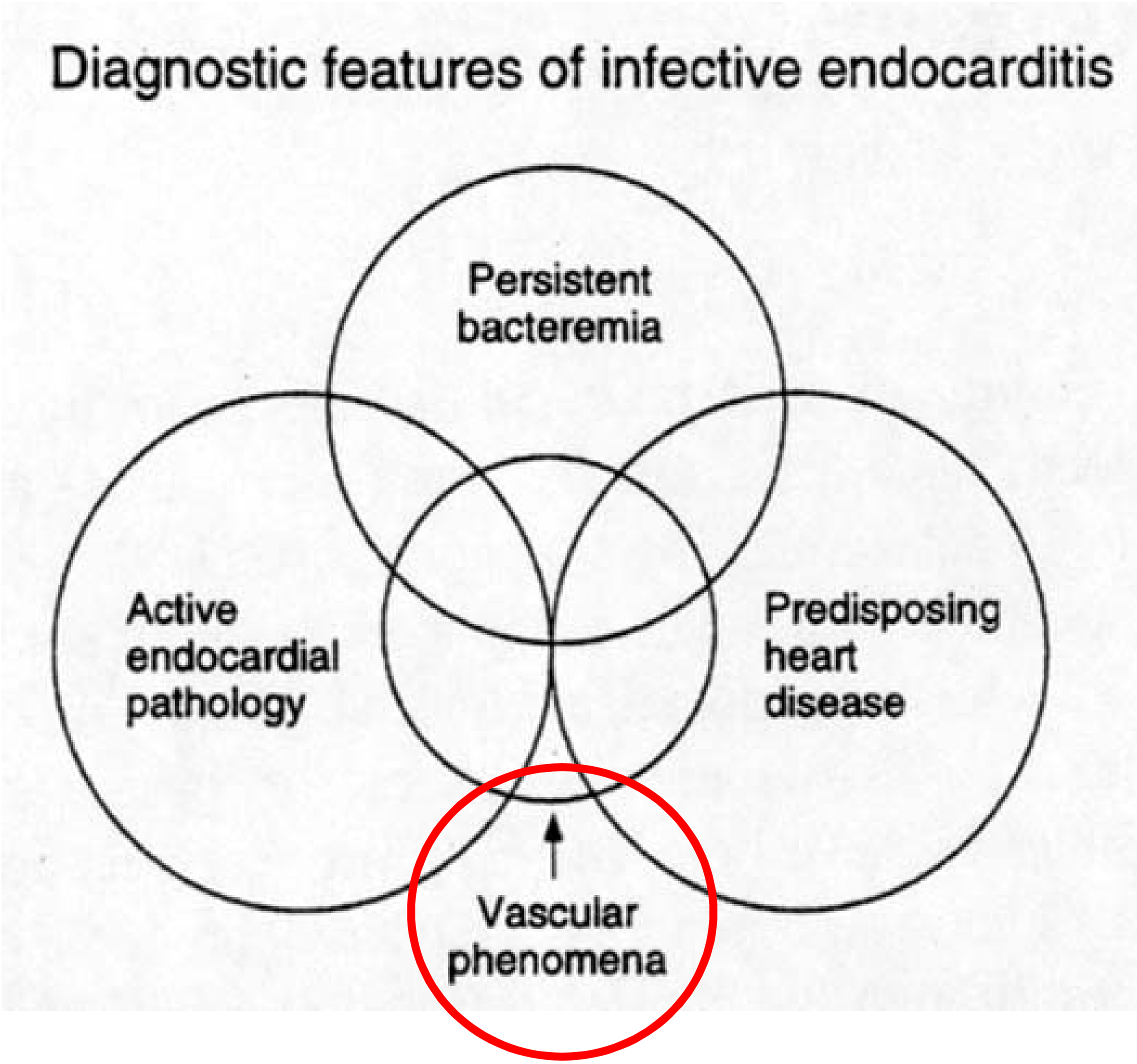
Diagnosis of Endocarditis



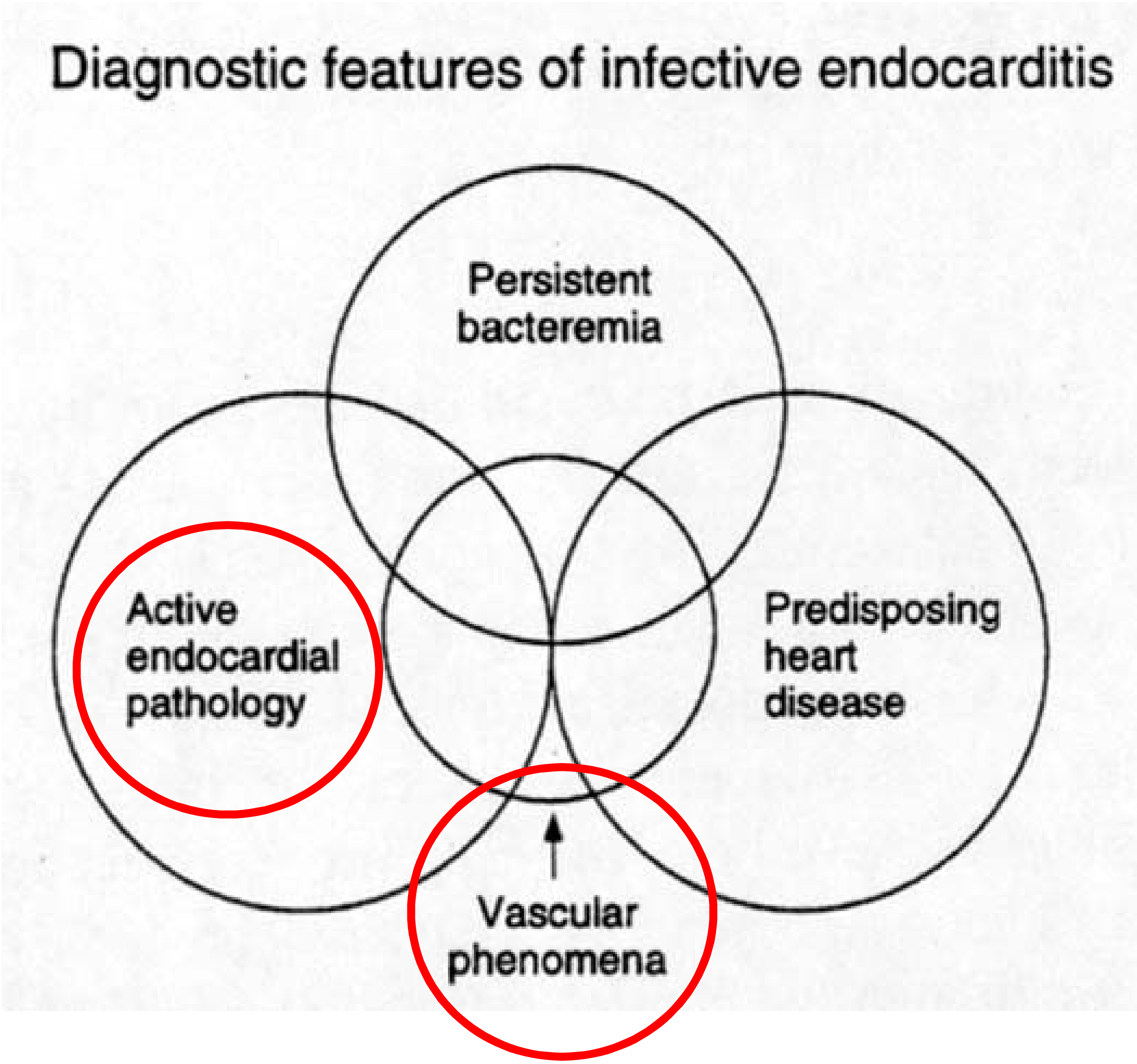
Diagnosis of Endocarditis



Diagnosis of Endocarditis



Diagnosis of Endocarditis



Cardiac echo

Cardiac echography

- Diagnostic of infectious anatomic lesions
- Consequences of these lesions on
  - Valve function
  - Cardiac chambers
  - Pulmonary artery pressures

Endocardial Involvement

- **Major Duke criteria:**
  - ~~New regurgitation murmur~~ (ESC 2015 classification)
  - Echocardiography
    - Vegetation (presence, size, mobility)
    - Abscess (frequency PVE>>NVE; Aortic position >> Mitral)
    - New dehiscence on a prosthetic valve
- **Improved sensitivity of TEE vs. TTE**
  - Native valve 70% → >90%
  - Prosthetic valve 50% → >90%
- The diagnostic value of TEE should be interpreted according to patient characteristics and the probability of endocarditis

Anatomic and echo definitions

	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

Eur Heart J 2015

An isolated periprosthetic regurgitation has a low positive predictive value for the diagnosis of IE

Echo and Cardiac chambers

- **Even in case of severe regurgitation**
  - Acute regurgitations in IE → limited or absent left ventricular enlargement
  - Severe acute regurgitations → rapid increase
    - In filling pressures
    - In systolic pulmonary artery pressures
      (Doppler analysis of tricuspid regurgitant flow)

Echo and embolic risk assessment

Three distinct predictors :

- *Microorganism: S. aureus*
- IE location: Mitral valve IE
- Vegetation length > 10 mm

Dickermann SA and ICE Investigators. Am Heart J. 2007

Thuny F et al. Eur Heart J. 2007

Snygg-Martin U et al. Clin Inf Dis 2008

Valvular surgery_ 2009 ESC indications

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

Valvular surgery_ 2015 ESC indications

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	B	9,58,72, 113,222
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent	IIa	B	9
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent	IIa	B	113
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery[e]	Urgent	IIb	C	

Discrepancies TTE / TEE

105 with suspected endocarditis (TTE and TEE)

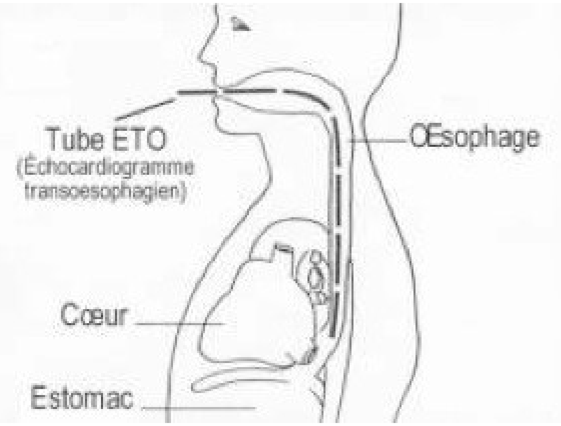
- **10 patients /** Intermediate probability with TTE
  - 7 reclassified at high probability after TEE
- **False positives with TTE**
  - 8 patients
  - non-specific valvular thickening
- **Increased diagnostic value with TEE if:**
  - Intermediate probability after TTE
  - Sub-optimal imaging with TTE
  - Heart valve prosthesis

→ ***no contribution of TEE if low probability***

Prosthetic Endocarditis

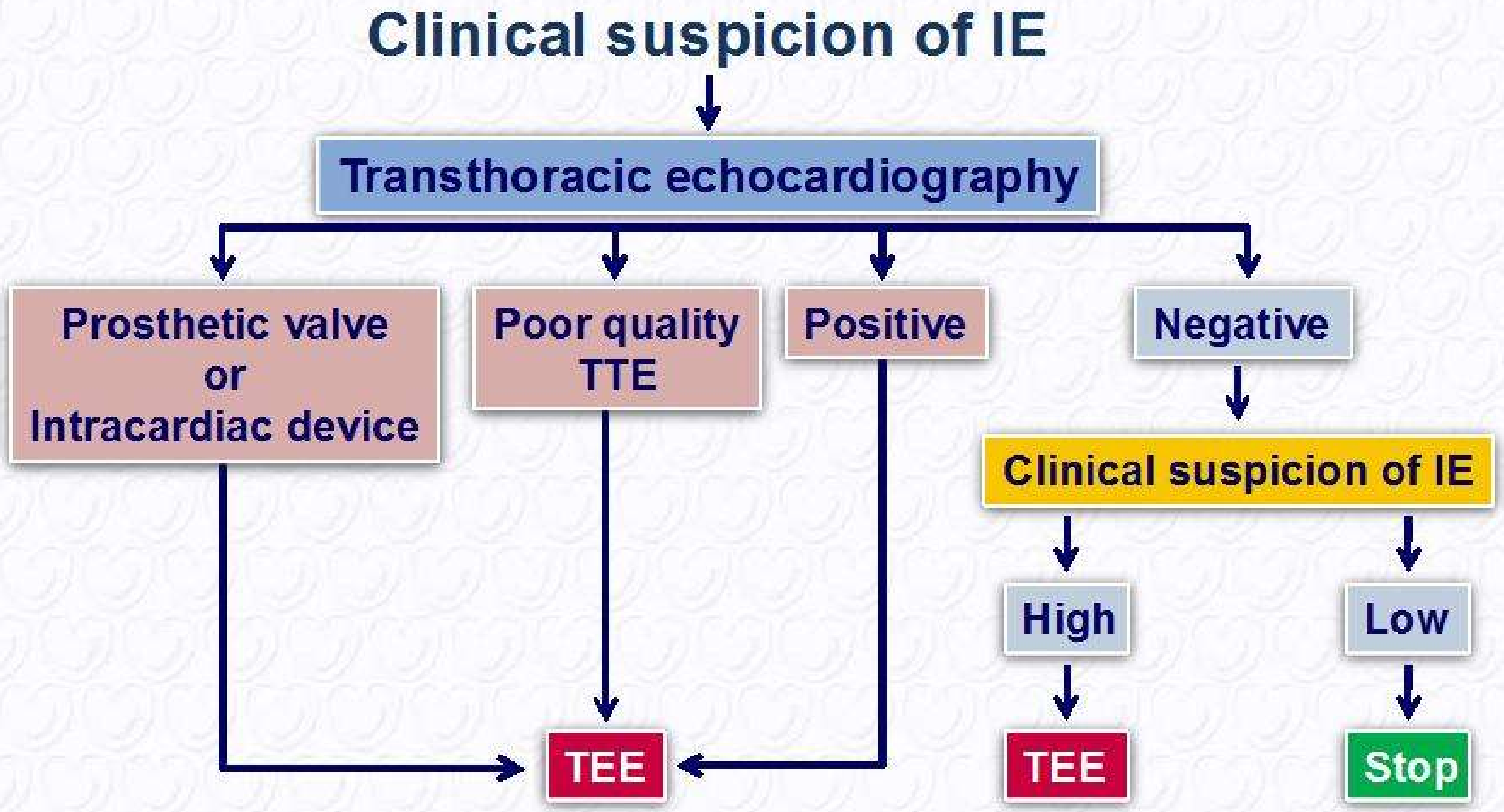
Limitations of Echocardiography

- **Shadowing :** attenuation of ultrasound by prosthetic material → ***false -***
- **Image artifacts** → ***false -, false +***
- Aortic prostheses
  - Posterior part poorly visualised in TTE
  - Anterior part poorly visualised in TEE
- Other artifacts (sutures ..)



➢Importance of high resolution (TEE)

Indications for echocardiography



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

Eur Heart J 2015

Diagnosis Follow-up

Imaging techniques

Echocardiography

Table 10 Role of echocardiography in infective endocarditis

Recommendations	Class[a]	Level[b]	Ref.[c]
A. Diagnosis			
• TTE is recommended as the first-line imaging modality in suspected IE.	I	B	64,65
• TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.	I	B	64, 68–71
• TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.	I	B	64,71
• Repeat TTE and /or TOE within 5–7 days is recommended in case of initially negative examination when clinical suspicion of IE remains high.	I	C	
• Echocardiography should be considered in *Staphylococcus aureus* bacteraemia.	IIa	B	66,67
• TOE should be considered in patients with suspected IE, even in cases with positive TTE, except in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.	IIa	C	
B. Follow-up under medical therapy			
• Repeat TTE and/or TOE are recommended as soon as a new complication of IE is suspected (new murmur, embolism, persisting fever, HF, abscess, atrioventricular block).	I	B	64,72
• Repeat TTE and/or TOE should be considered during follow-up of uncomplicated IE, in order to detect new silent complications and monitor vegetation size. The timing and mode (TTE or TOE) of repeat examination depend on the initial findings, type of microorganism, and initial response to therapy.	IIa	B	64,72
C. Intraoperative echocardiography			
• Intraoperative echocardiography is recommended in all cases of IE requiring surgery.	I	B	64,73
D. Following completion of therapy			
• TTE is recommended at completion of antibiotic therapy for evaluation of cardiac and valve morphology and function.	I	C	

HF = heart failure; IE = infective endocarditis; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.

Cardiac multislice computed tomography (MSCT)

Cardiac multislice computed tomography MSCT

- Mainly used to diagnose **perivalvular lesions**
  - abscesses, fistulae and pseudoaneurysms
- May complete TEE to assess
  - the topography and extension of abscesses, fistulae and pseudoaneurysms.
- Sensitivity and specificity of MSCT:
  > 95% as compared with surgical findings

Cardiac multislice computed tomography MSCT

- **Aortic prosthetic tubes**:
  - Superior to TTE and TEE to diagnose abscesses and/or pseudoaneurysms around.
- **Coronary MSCT**
  - To assess coronary anatomy
  - Mainly considered in pts at low risk of coronary artery disease, due to its high negative predictive value.

Multislice Computed Tomography in Infective Endocarditis

Comparison With Transesophageal Echocardiography and Intraoperative Findings

Gudrun M. Feuchtner, MD, PD,* Paul Stolzmann, MD,§ Wolfgang Dichtl, MD, PHD, PD,†
Thomas Schertler, MD,§ Johannes Bonatti, MD, FECTS,‡ Hans Scheffel, MD,§
Silvana Mueller, MD,† André Plass, MD,‖ Ludwig Mueller, MD,‡ Thomas Bartel, MD, PD,†
Florian Wolf, MD,¶ Hatem Alkadhi, MD, PD§

Innsbruck and Vienna, Austria; and Zurich, Switzerland

37 patients consécutifs suspects cliniquement d'EI

TEE et 64 coupes TDM

29 pts avec EI certaines

Comparaison ETO:

Sensibilité: 97%, spécificité: 88%, VPP: 97%, VPN 88%

Concordance interobservateur: 0.84

JACC 2009 ;53:436-444

Multislice Computed Tomography in Infective Endocarditis

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Comparaison ETO:

Sensibilité: 97%, spécificité: 88%, VPP: 97%, VPN 88%

Concordance interobservateurs: 0.84

Comparaison chirurgie:

Végétation: Sensibilité: 96%, spécificité: 97%, VPP: 97%, VPN 97%

Abcès: Sensibilité: 100%, spécificité: 100%, VPP: 100%, VPN 100%

Mobilité végétation correctement évaluée

Ne diagnostique pas les perforations

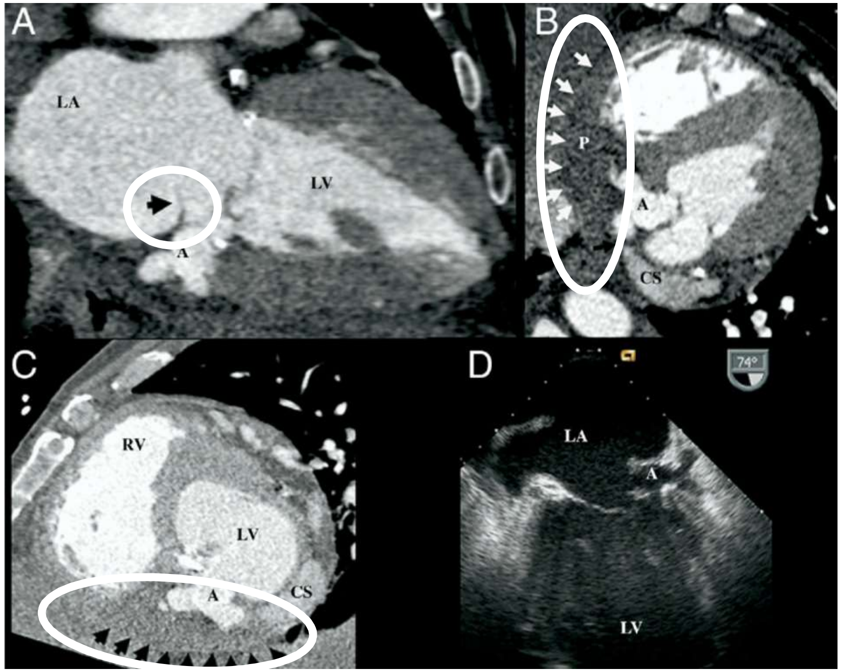
Meilleure évaluation de l'étendue des abcès périvalvulaires

JACC 2009 ;53:436-444

Multislice Computed Tomography in Infective Endocarditis

Comparison With Transesophageal Echocardiography and Intraoperative Findings

Végétation mobile



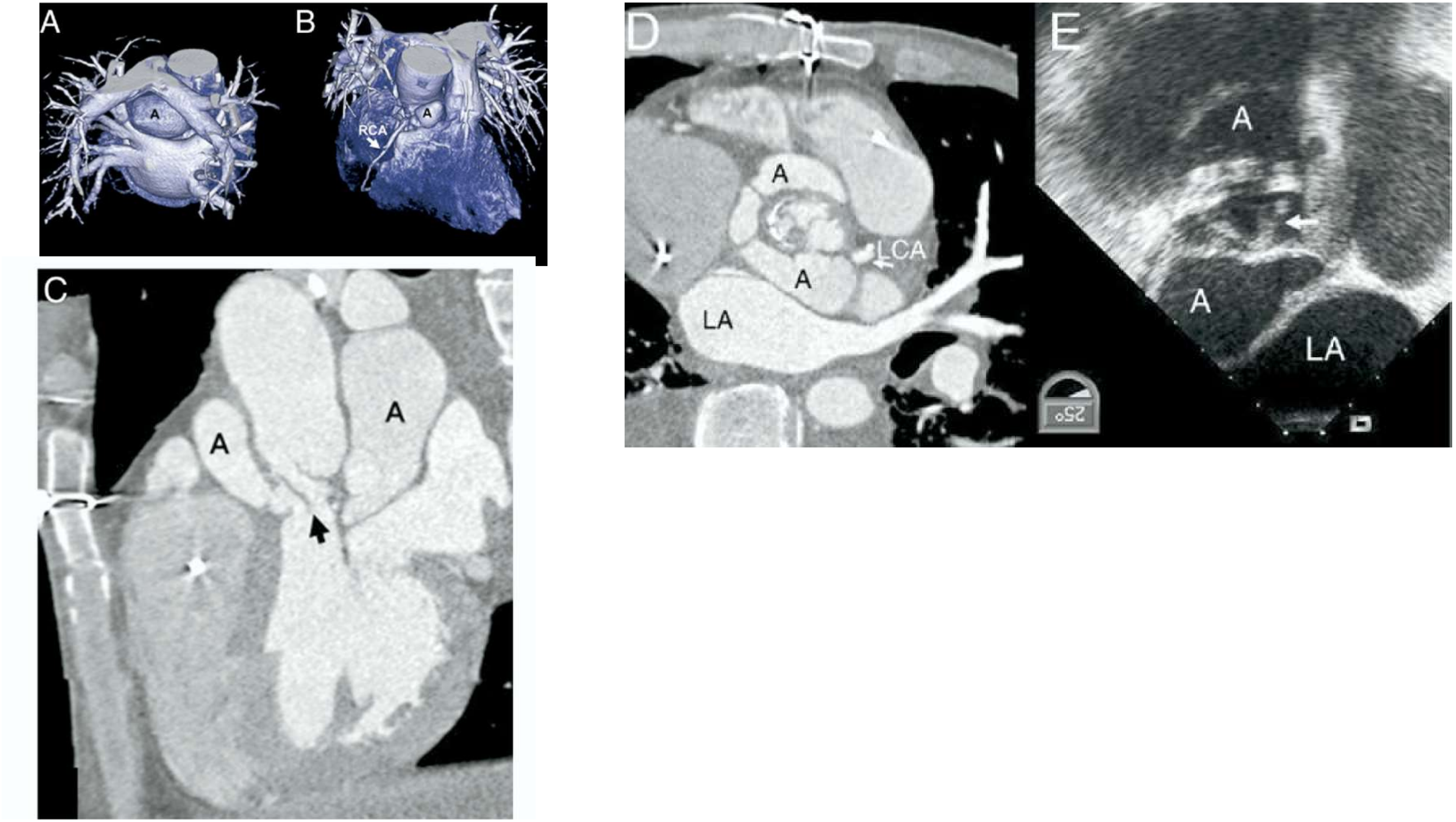
Abcès

ETO: Abcès

Moins bonne visualisation de l'abcès à l'ETO

Multislice Computed Tomography in Infective Endocarditis

Comparison With Transesophageal Echocardiography and Intraoperative Findings



Nuclear Imaging
[18F]FDG PET/CT

Nuclear Imaging

[18F]FDG PET/CT

- **^{18}F-FDG PET/CT:**
  - Reveal glucose consuming cells : tumoral, inflammation..
  - widely used in oncology for staging and evaluation of treatment response
- Introduced more recently for imaging of infection
- Gram positive bacteremia: cost-effective method for detection of metastatic infection
- High physiological cardiac and cerebral ^{18}F-FDG uptake: unsuitable for detecting cardiac and cerebral infectious lesions ?

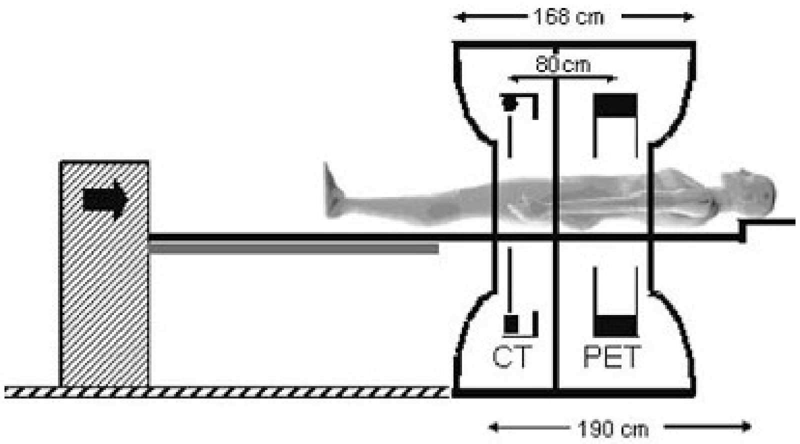
Nuclear Imaging

[18F]FDG PET/CT

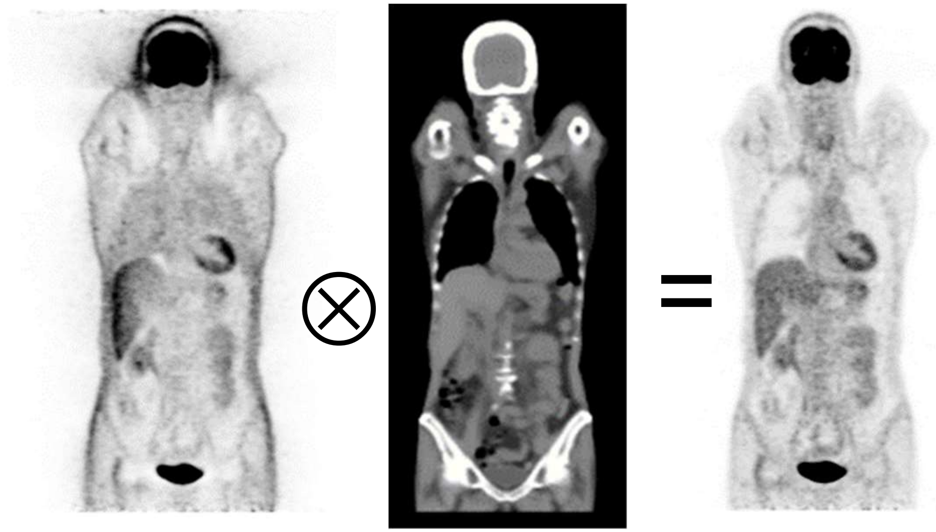
- Suppression of Cardiac ^{18}F-FDG uptake
  - Carbohydrate-restricted diet
  - Patient fasts for at least 12 hours
- Improvement of images using correction for attenuation
- Semi-quantitative analysis of the intensity of FDG uptake
  - maximal standardized uptake value (SUV_{max})
  - valve-to-background ratio: valve SUV_{max} /atrial blood SUV_{max}

^{18}FDG PET/CT

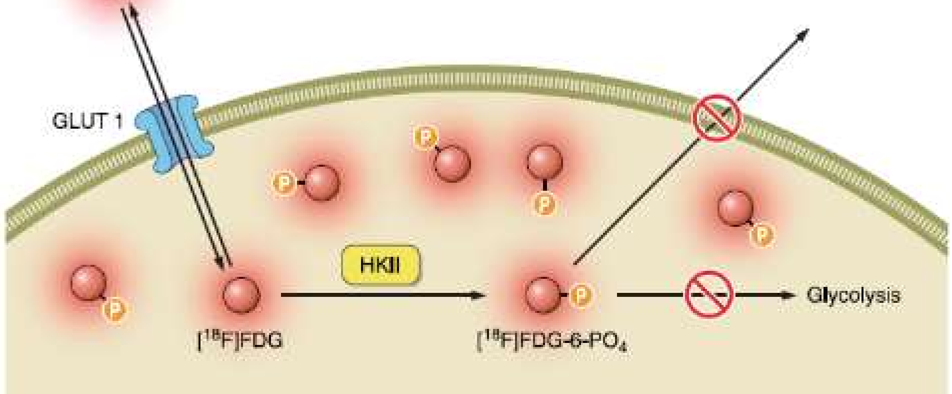
1. **High sensitivity**
2. **Absolute quantification**

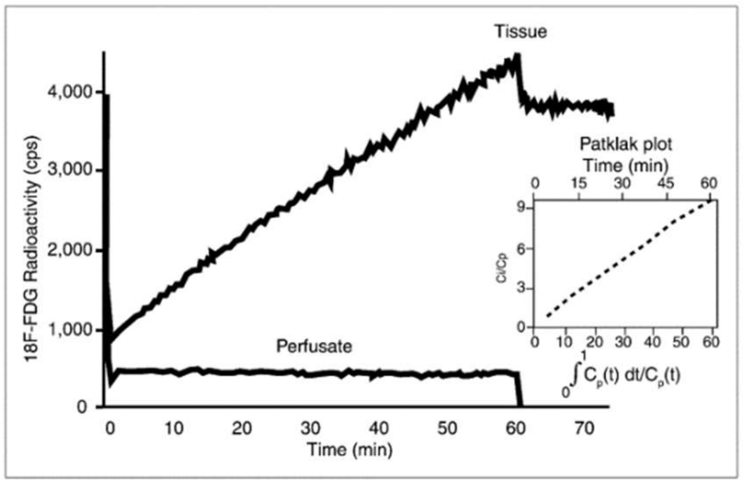


PET CT



18 F-deoxyglucose (FDG)

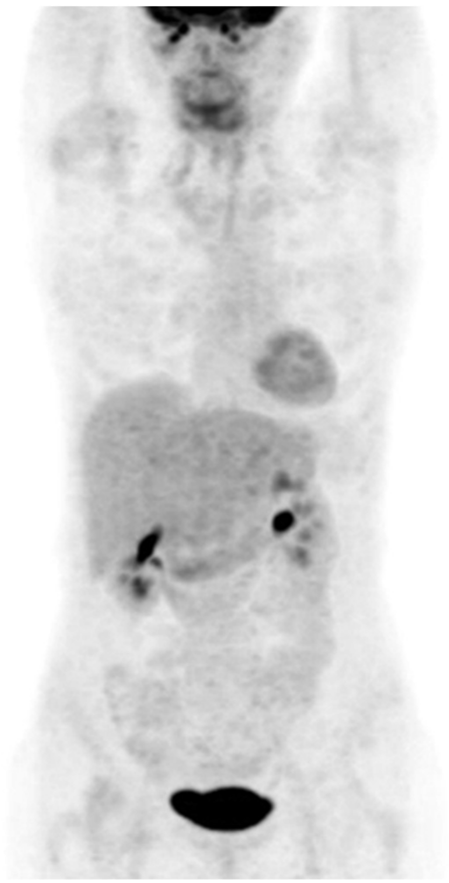




Nguyen et al., Am J Physiol 1990

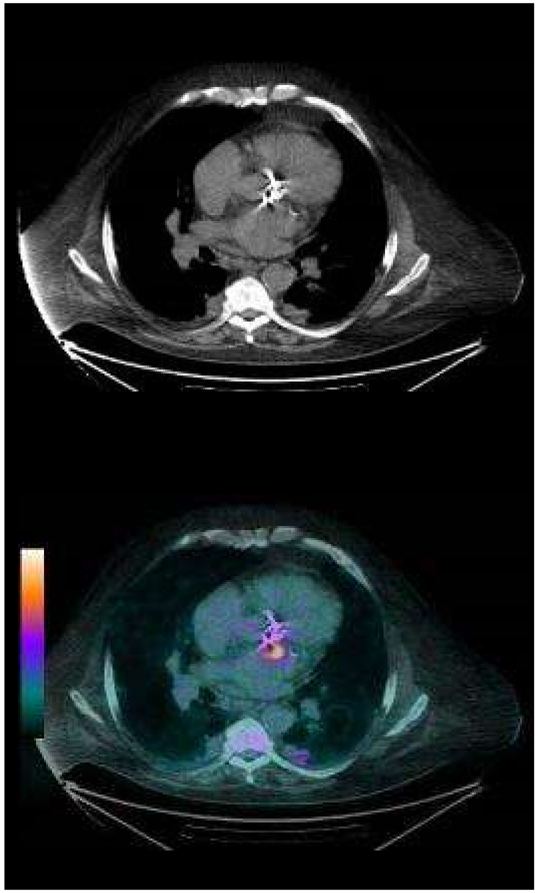
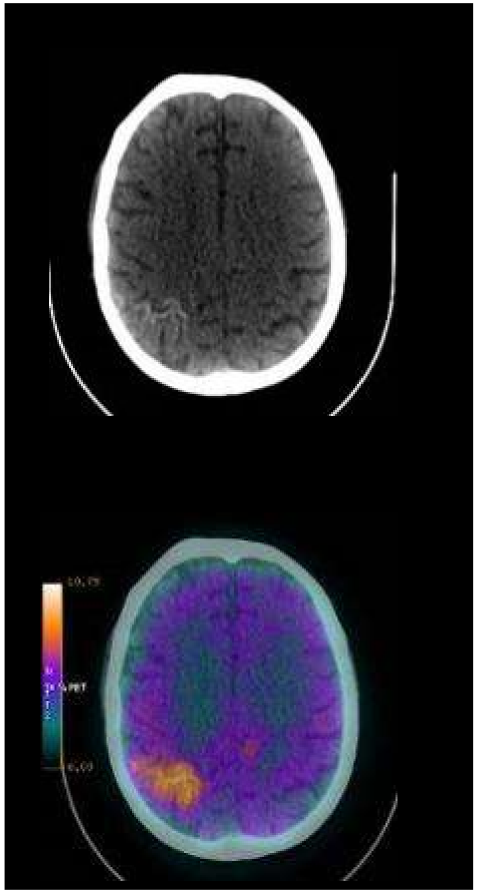
“True” whole-body acquisition

Oncology-derived field of acquisition:
skull base to upper thighs

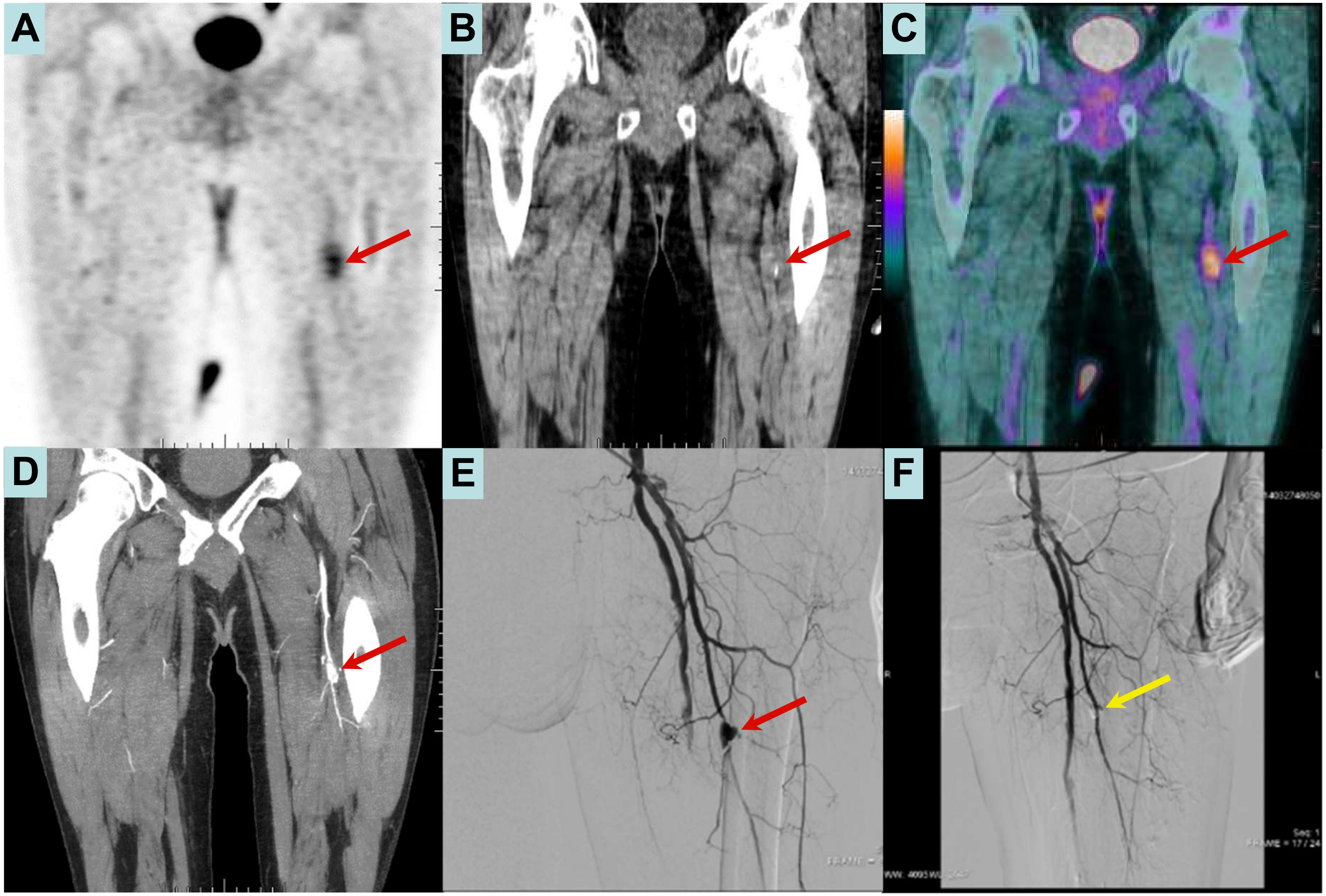


Brain imaging

Trans Arterial Valve Implantation

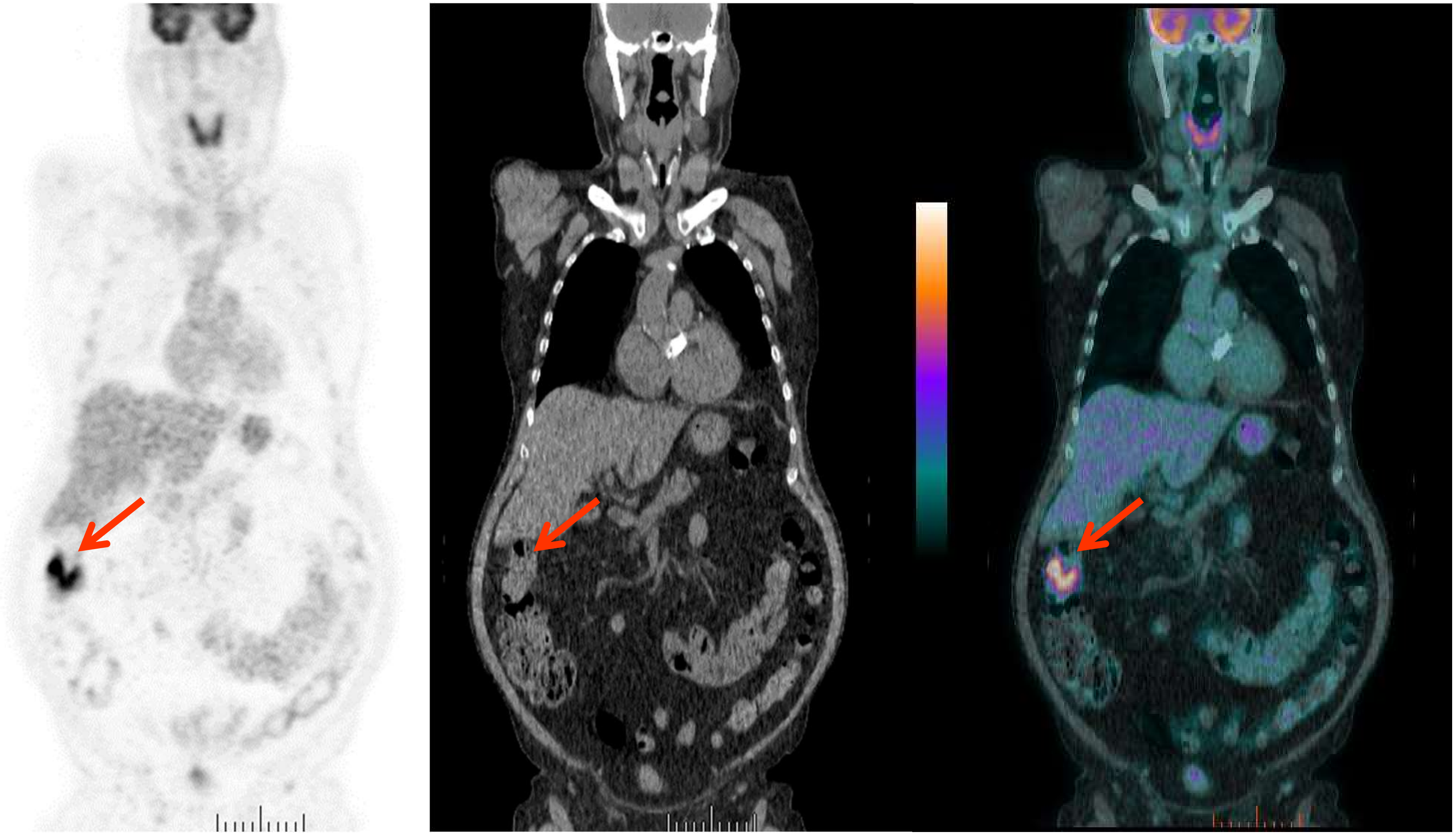




Mycotic aneurysms

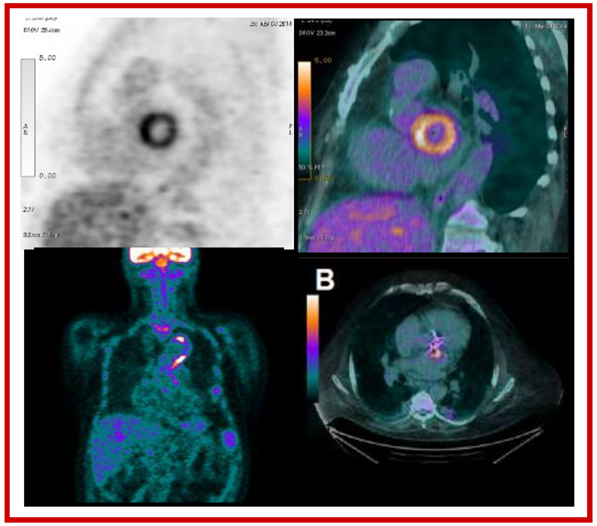


Portal of entry

- Recurrent chills, fever, and positive blood cultures (*E. faecalis*)
- Suspicion of aortic prosthetic valve infection



Diagnostic of valvular involvement



Diagnostic of valvular involvement

Patients with definite IE

	Clinical situations	Total Nb pts Prosthetic V/ PM/native V	Definite EI / total	sensitivity	specificity	PPV False +	NPV False -
Van Riet 2010 *	Definite IE	25 pts 10/0/15	all	12% (3/25)	NA	NA	NA
Kestler M 2014	Definite IE	47pts 15/11/24	all	9.5% (4/47) 4/15 PVE (27%)	NA	NA	NA

0/24 (0%) native valve

* NO carbohydrate-restricted diet

Diagnostic of valvular involvement

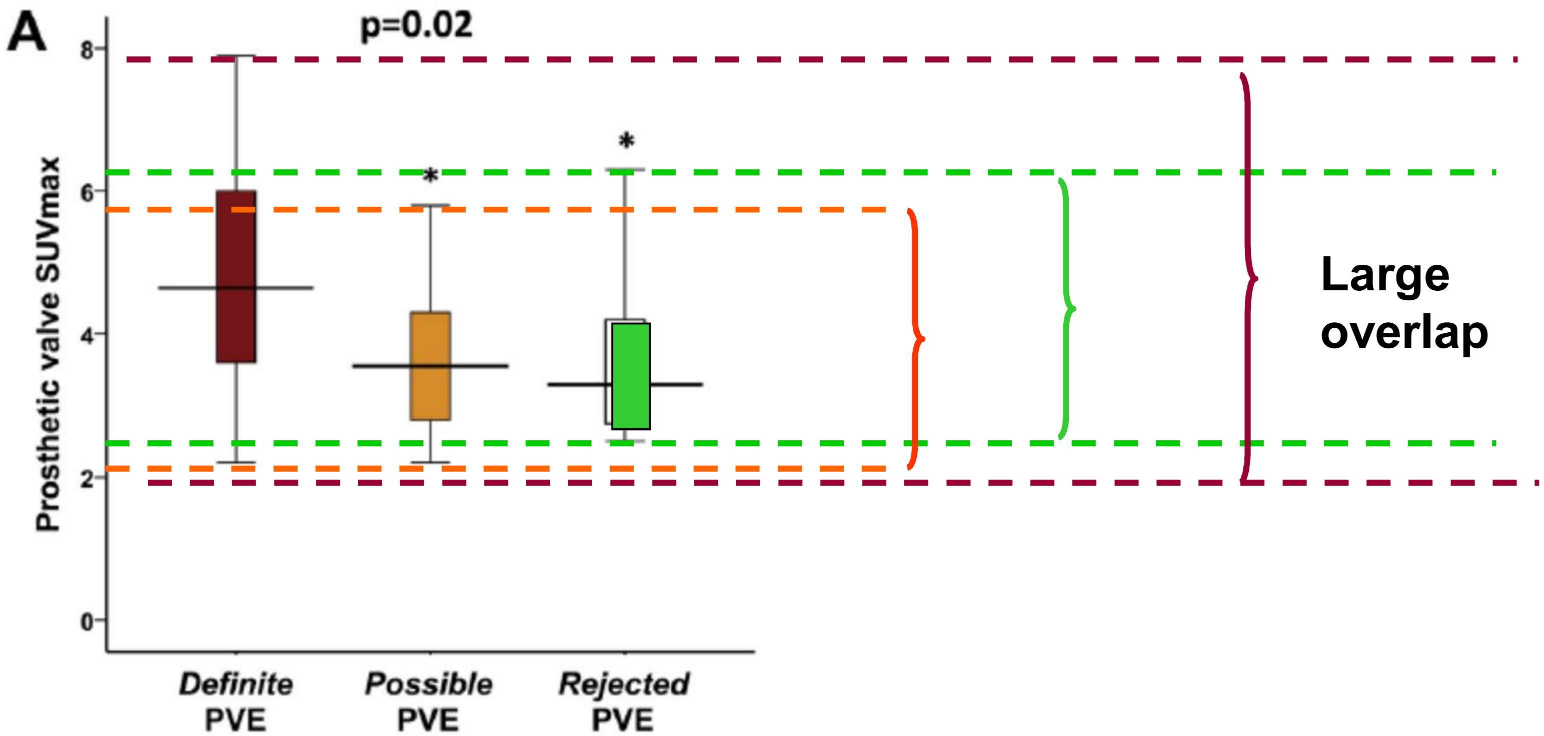
Patients with suspected IE

	Clinical situations	Total Nb pts Prosthetic V/ PM/native V	Definite EI / total	sensitivity	specificity	PPV False +	NPV False -
Kouijzer 2013 *	Gram + bacteremia	72 pts 6/5/61	18/72	39% (7/18)	93%	64% 36%	82% 18%
Saby 2013	Prosthetic valve AND Fever or crp > 10 mg, or bacteremia or + serology or echo pos	72pts 72/0/0	30/72	73% (22/30)	80%	85% 15%	67% 33%

* NO carbohydrate-restricted diet

SUVmax value to improve PET diagnosis performance

Results of the Prosthetic Valve SUV_{max} and Prosthetic Valve-to-Background SUV_{max} Ratio According to the Final Diagnosis



The SUV_{max} was significantly higher in patients with *definite* PVE in comparison with the 2 other groups **(A)**, whereas the prosthetic valve-to-background SUV_{max} ratio was not significantly higher **(B)**. *$p < 0.05$. Abbreviations as in Figures 1 and 2.

L. Saby JACC 2013

False positive results in patients with valvular prosthesis

Subject of concern ?

^{18}F-FDG uptake pattern in non-infected prosthetic heart valves

- Bichat Hospital PET/CT database (Jan-Dec 2013)

- Inclusion criteria:

  Prosthetic heart valve
  - biological and/or mechanical
  - aortic and/or mitral positions

- Exclusion criteria:
  - Infection (bacteremia)
  - Antibiotic regimen: 2 weeks before / 6 weeks after PET/CT

Characterization of ^{18}F-Fluorodeoxyglucose Uptake Pattern in Noninfected Prosthetic Heart Valves

Cédric Mathieu, MD; Nidaa Mikaïl, MD; Khadija Benali, MD; Bernard Iung, MD; Xavier Duval, MD, PhD; Patrick Nataf, MD; Guillaume Jondeau, MD, PhD; Fabien Hyafil, MD, PhD; Dominique Le Guludec, MD, PhD; François Rouzet, MD, PhD

Circ Cardiovasc Imaging. 2017

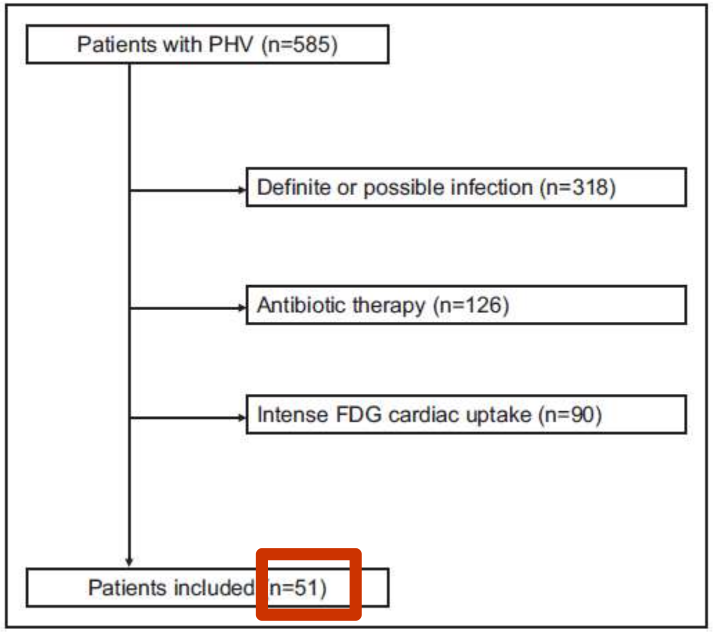


Figure 1. Study flow chart. PHV indicates prosthetic heart valve.

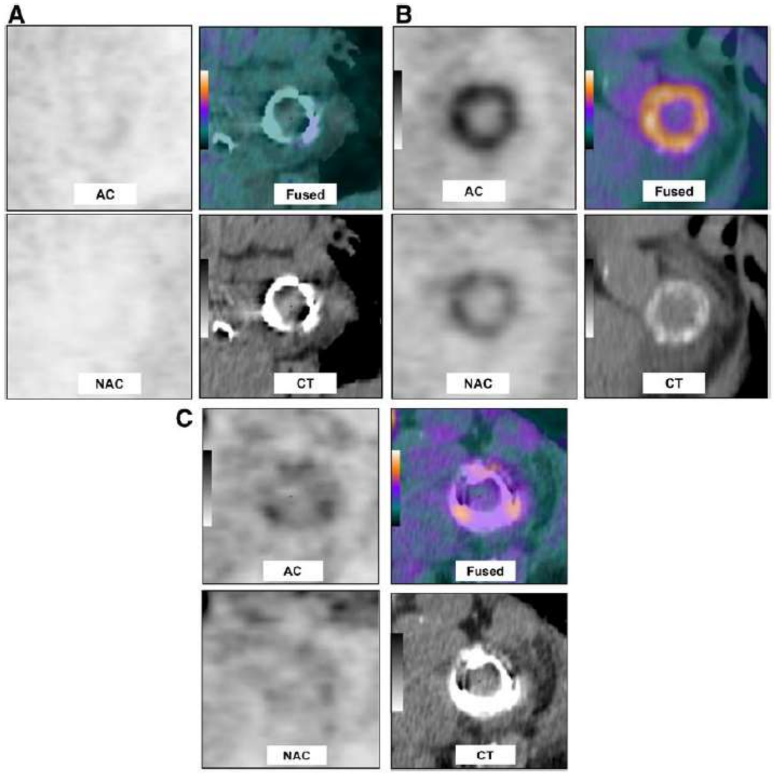
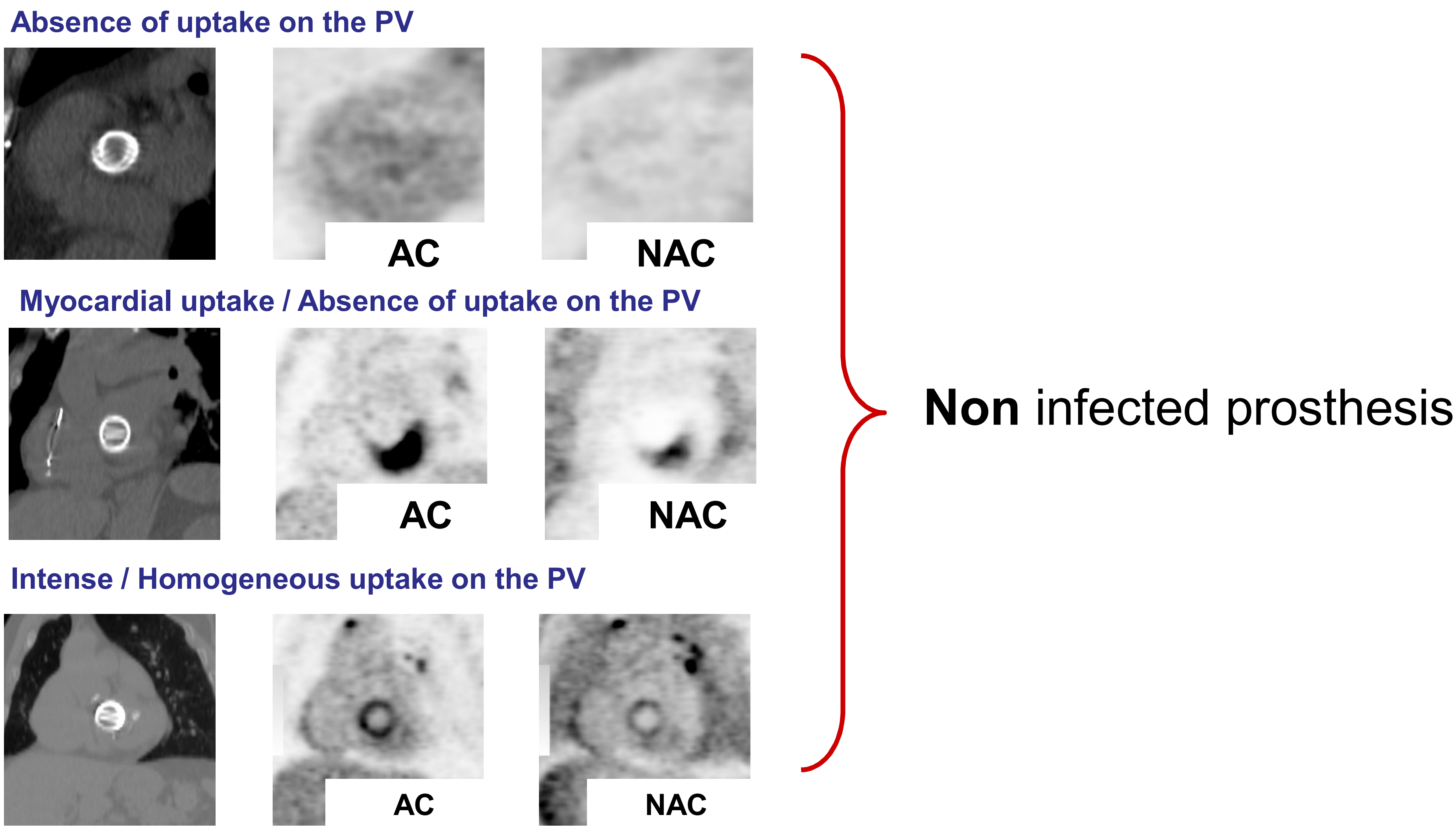
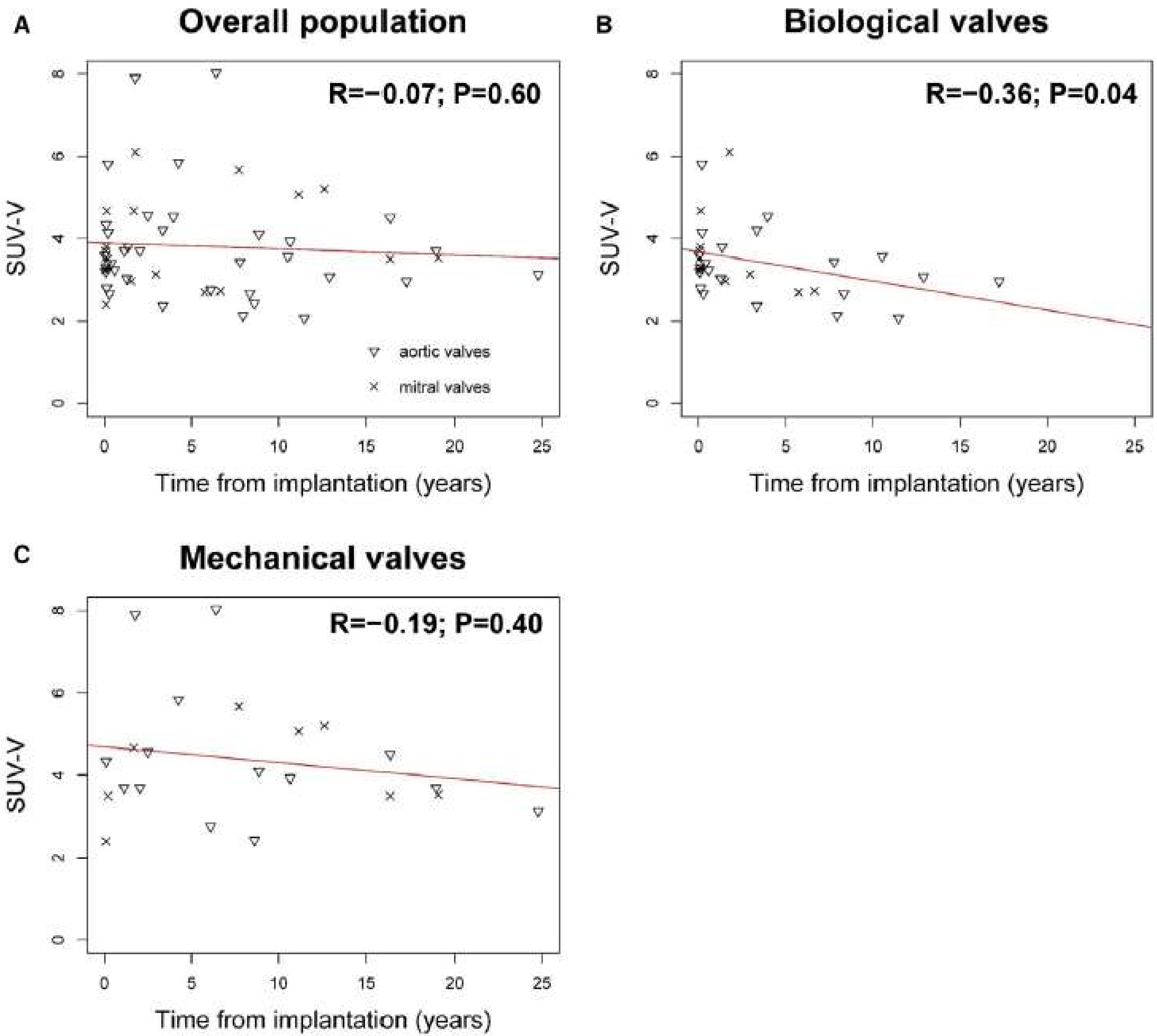


Figure 2. Examples of ^{18}F-FDG perivalvular uptake in noninfected patients.

Results: patients & valves

- **Patients**
  - 51 patients with **54 prosthetic valves**
  - Sex: male 29 (57%)
  - Age: mean 66±15 years [range: 25 – 85]
- **Cardiac valve type**
  - biological (n=32) – mechanical (n=22) prosthesis
- **Indication**
  - Oncology (n=26); Inflammatory syndrome (n=15); Vasculitis (n=10)
- **Time interval between valve implantation and PET/CT**
  - Median: 2.7 years [9 days – 25 years]
  - <2 months: 12 patients


Absence of uptake on the PV
AC
NAC
Myocardial uptake / Absence of uptake on the PV
AC
NAC
Intense / Homogeneous uptake on the PV
AC
NAC
Non infected prosthesis



A
Overall population
R=−0.07; P=0.60
aortic valves
mitral valves
SUV-V
Time from implantation (years)
B
Biological valves
R=−0.36; P=0.04
SUV-V
Time from implantation (years)
C
Mechanical valves
R=−0.19; P=0.40
SUV-V
Time from implantation (years)

Perivalvular uptake in No-IE patients

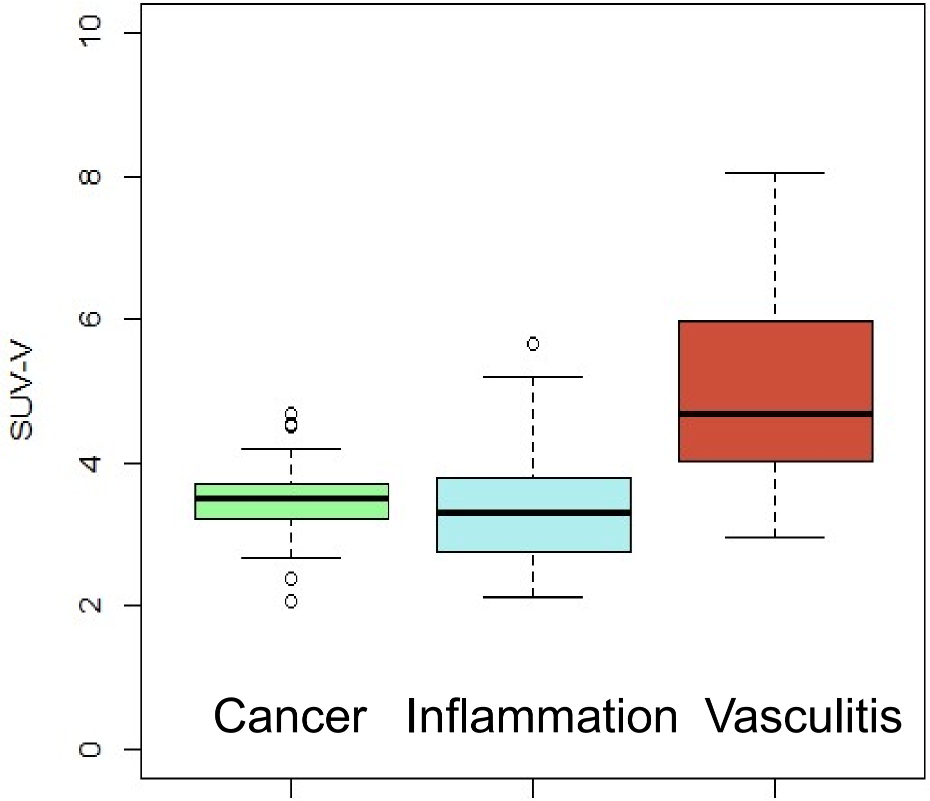
- **Visual analysis of perivalvular uptake**
  - Uptake:
    - AC: **n=50 /54 (93%), Homogeneous in all**
- **Quantitative analysis (SUV-V)**
  - Mechanical: 4.4±1.5
  - Biological: 3.4±0.9 (p=0.01)

SUV: standardized uptake value

Perivalvular uptake

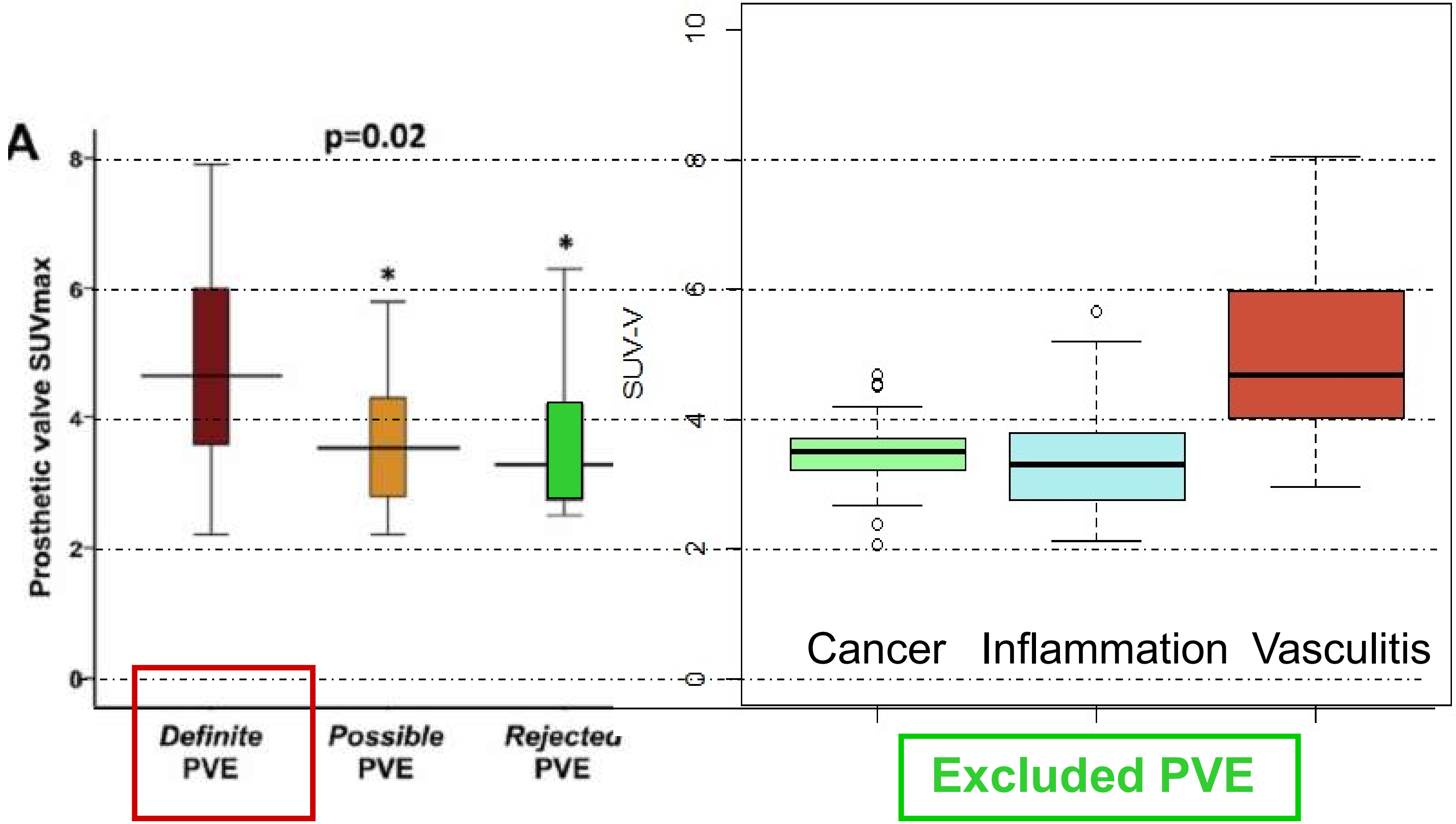
- **Visual analysis of perivalvular uptake**
  - Uptake:
    - AC: n=50 /54 (93%), Homogeneous in all
- **Quantitative analysis (SUV-V)**
  - Mechanical: 4.4±1.5
  - Biological: 3.4±0.9 (p=0.01)

Uptake according to the indications



SUV: standardized uptake value

Perivalvular uptake in pts with <u>valvular prosthesis</u> IE versus NON-IE

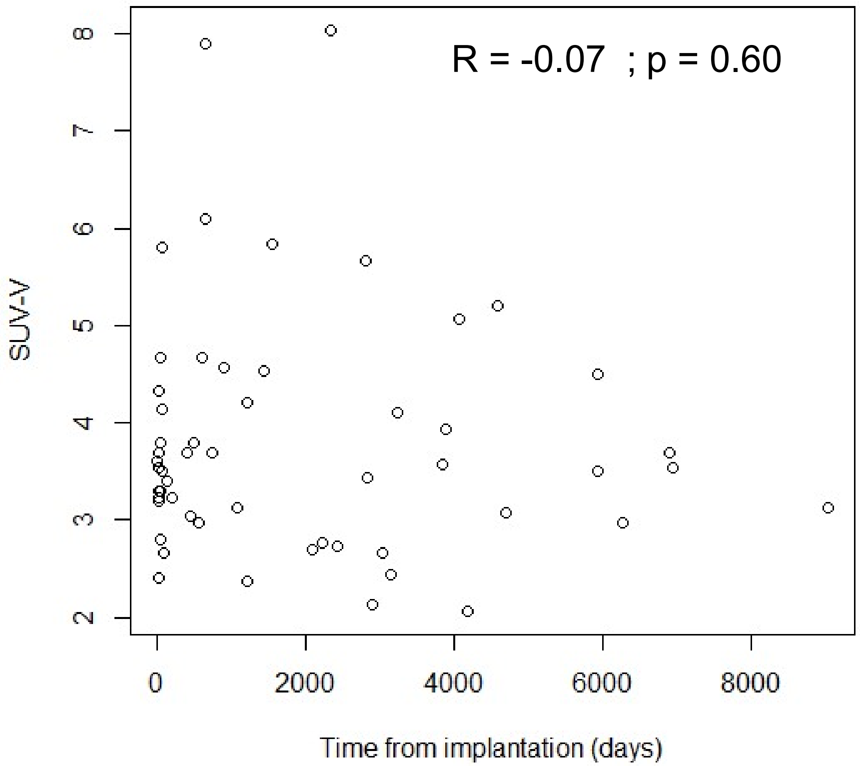


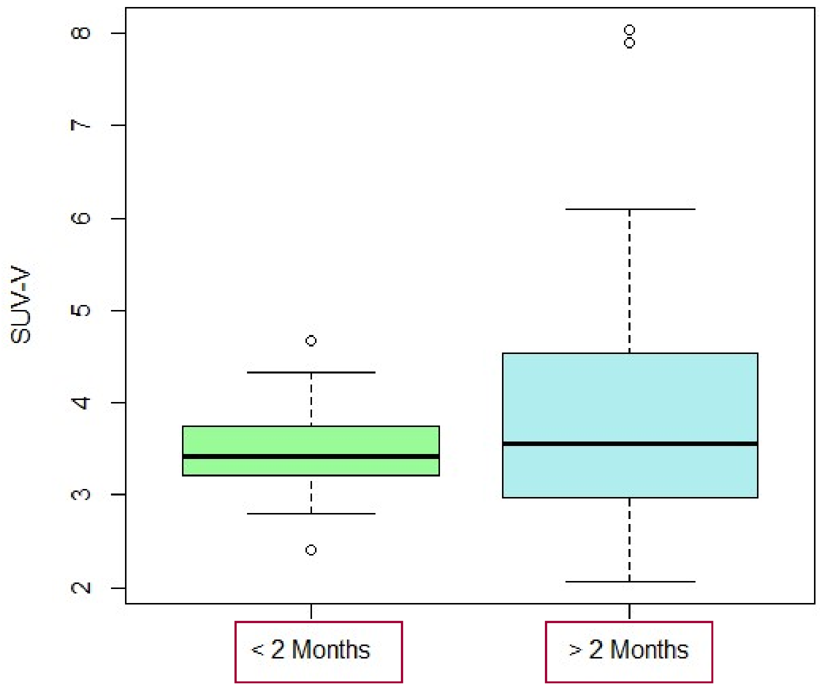
L. Saby JACC 2013

Perivalvular uptake in NON-IE patients

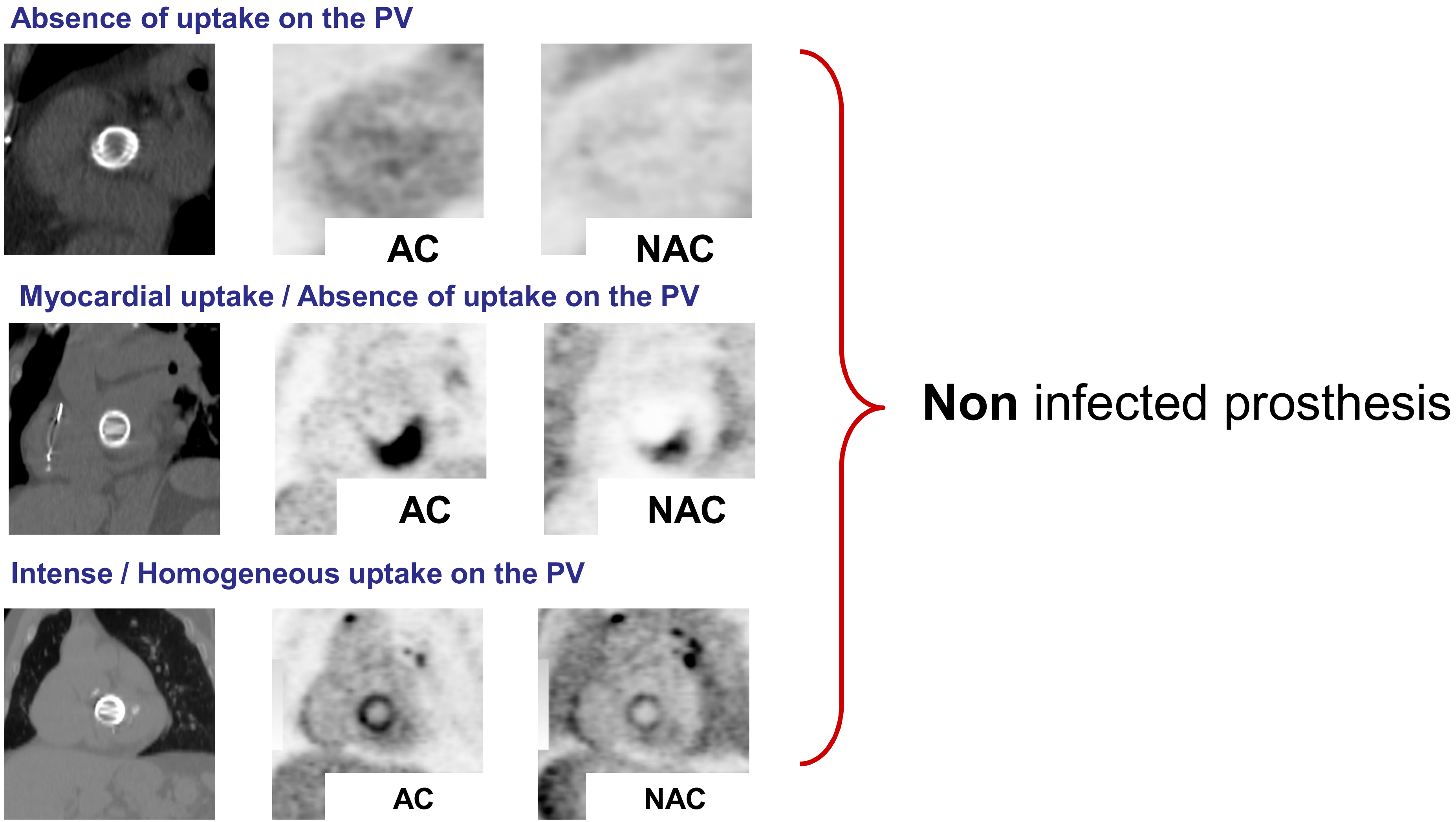
According to time from implantation

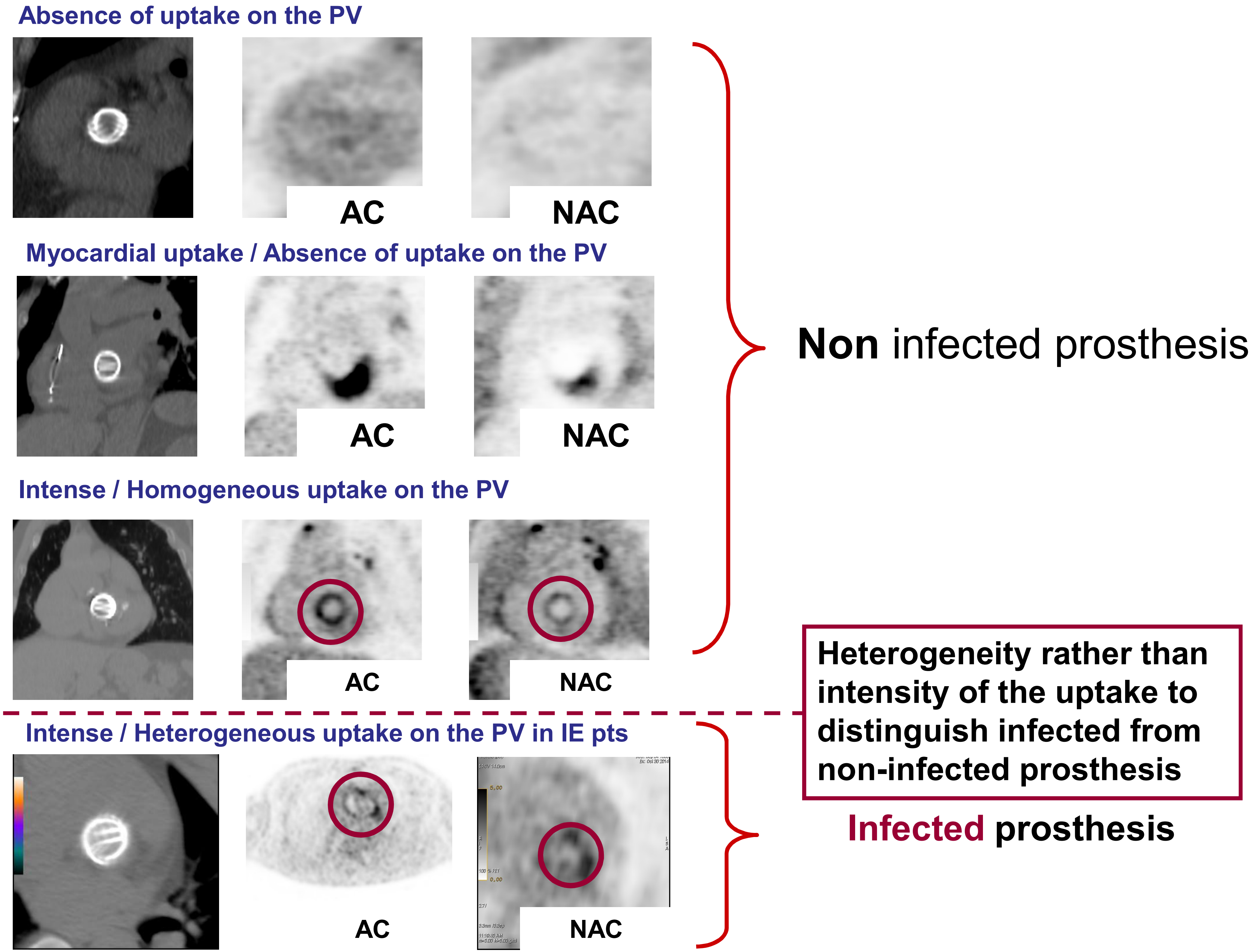
All patients (n=51)





Uptake is not different


Absence of uptake on the PV
AC
NAC
Myocardial uptake / Absence of uptake on the PV
AC
NAC
Intense / Homogeneous uptake on the PV
AC
NAC
Non infected prosthesis



Absence of uptake on the PV
AC
NAC
Myocardial uptake / Absence of uptake on the PV
AC
NAC
Intense / Homogeneous uptake on the PV
AC
NAC
Non infected prosthesis
Intense / Heterogeneous uptake on the PV in IE pts
AC
NAC
Heterogeneity rather than intensity of the uptake to distinguish infected from non-infected prosthesis
Infected prosthesis

CLINICAL PERSPECTIVE

to assess the diagnostic utility of FDG positron emission tomography/computed tomography. The present study shows that noninfected prosthetic heart valves often display a homogeneous FDG uptake. This pattern is present even years after valve implantation and should not be considered, per se, as a marker of prosthetic material infection. In addition, the intensity of the FDG uptake did not decrease according to time from valve surgery and seemed to be greater in patients with a history of vasculitis.

Incremental value of iodure CT scan

Improving the Diagnosis of Infective Endocarditis in Prosthetic Valves and Intracardiac Devices With ^{18}F-Fluordeoxyglucose Positron Emission Tomography/Computed Tomography Angiography

Initial Results at an Infective Endocarditis Referral Center

María N. Pizzi, MD; Albert Roque, MD; Nuria Fernández-Hidalgo, MD, PhD;

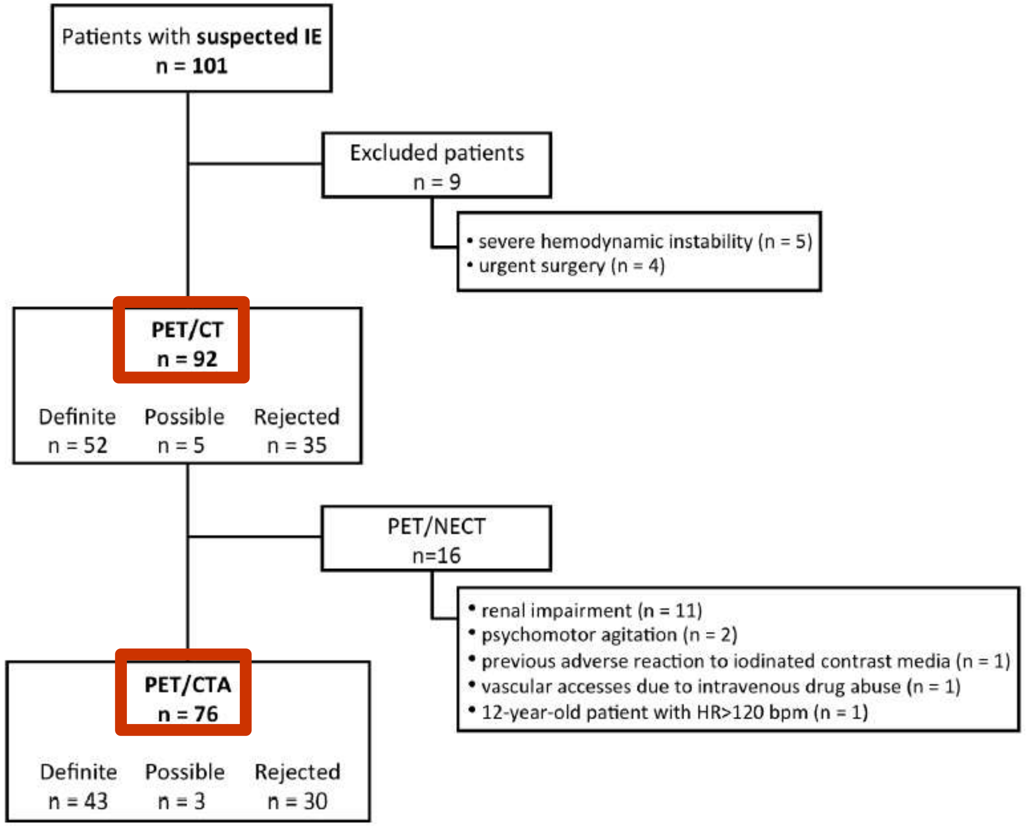
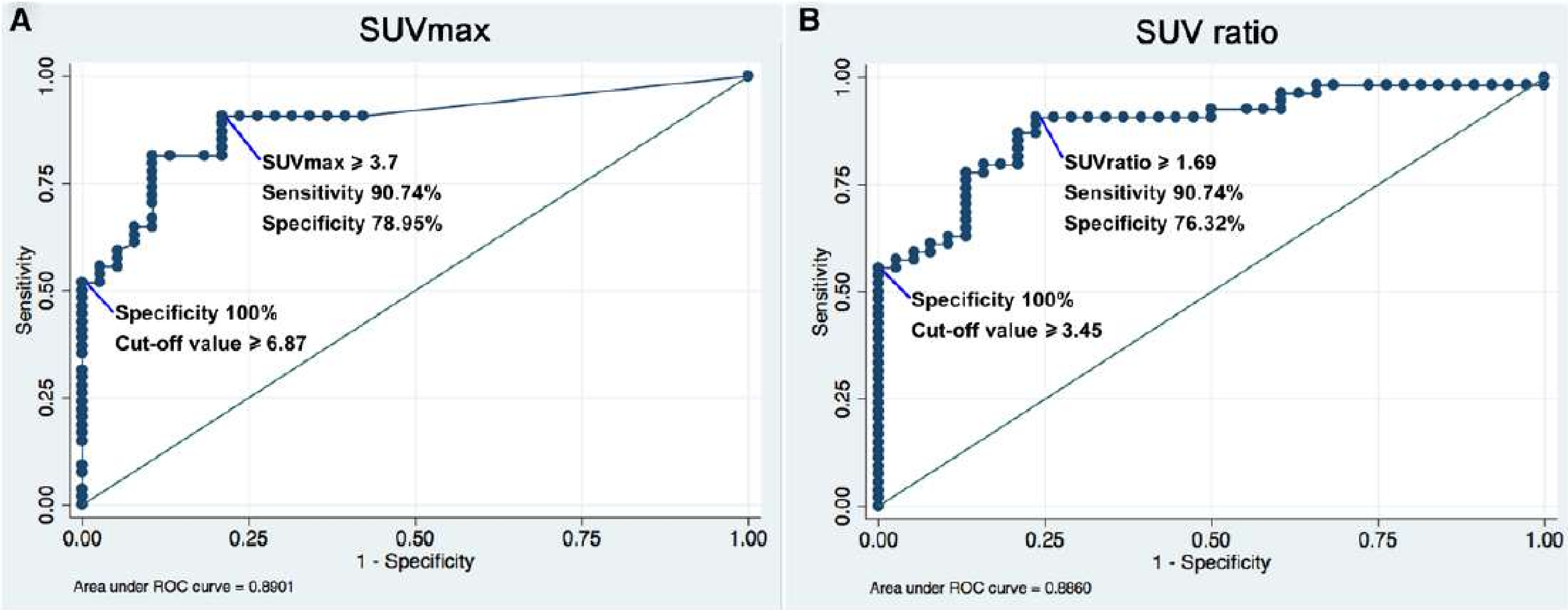
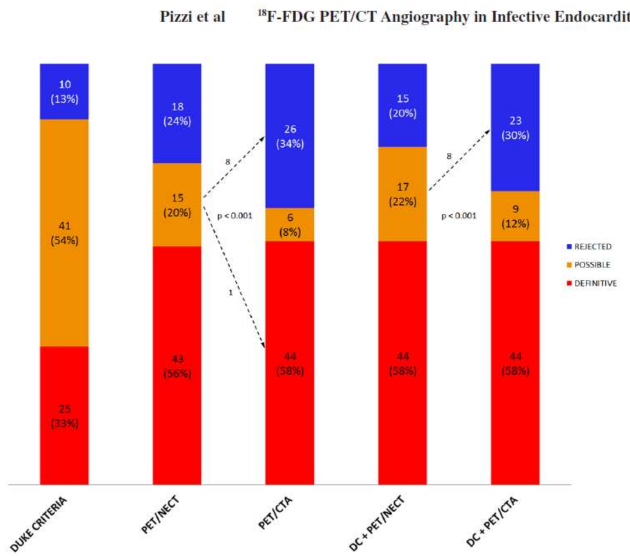
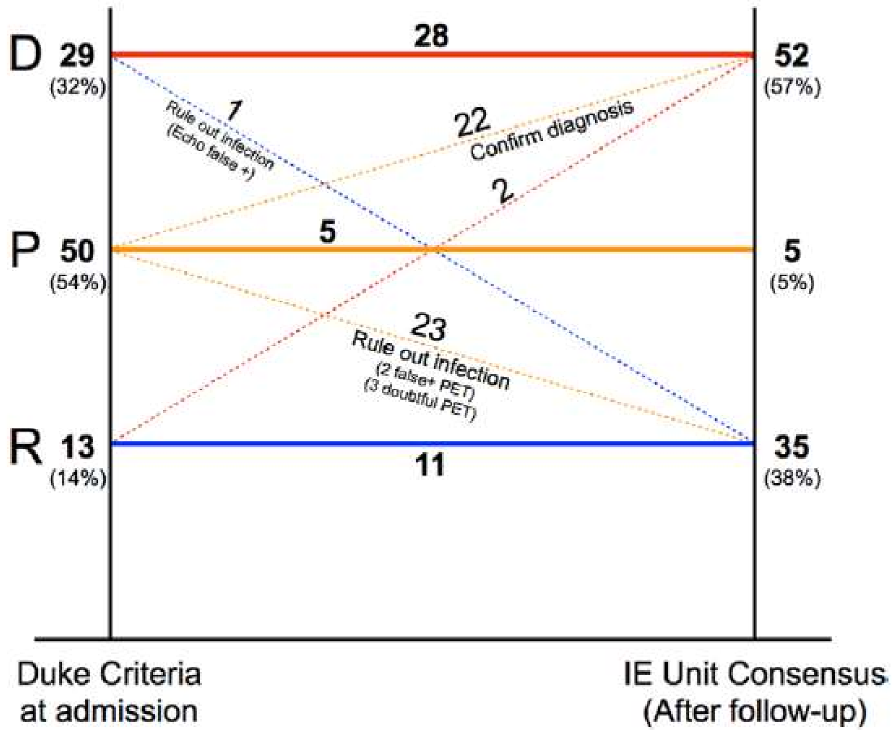


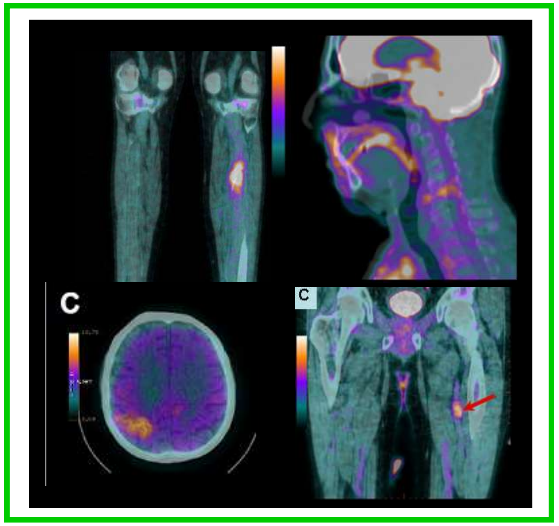
Figure 1. Flowchart of patient progress through the study. CT indicates computed tomography; CTA, computed tomography angiography; HR, heart rate; IE, infective endocarditis; NECT, nonenhanced computed tomography; and PET, ^{18}F-fluorodeoxyglucose positron emission tomography.


A
SUVmax
Sensitivity
1 - Specificity
SUVmax ≥ 3.7
Sensitivity 90.74%
Specificity 78.95%
Specificity 100%
Cut-off value ≥ 6.87
Area under ROC curve = 0.8901
B
SUV ratio
SUVratio ≥ 1.69
Sensitivity 90.74%
Specificity 76.32%
Specificity 100%
Cut-off value ≥ 3.45
Area under ROC curve = 0.8860


Pizzi et al
18F-FDG PET/CT Angiography in Infective Endocarditis
10 (13%)
41 (54%)
25 (33%)
18 (24%)
15 (20%)
43 (56%)
26 (34%)
6 (8%)
44 (58%)
15 (20%)
17 (22%)
44 (58%)
23 (30%)
9 (12%)
44 (58%)
8
1
p < 0.001
8
p < 0.001
REJECTED
POSSIBLE
DEFINITIVE
DUKE CRITERIA
PET/NECT
PET/CTA
DC + PET/NECT
DC + PET/CTA


D 29 (32%)
P 50 (54%)
R 13 (14%)
52 (57%)
5 (5%)
35 (38%)
28
5
11
7
Rule out infection (Echo false +)
22
Confirm diagnosis
2
23
Rule out infection
(2 false+ PET)
(3 doubtful PET)
Duke Criteria at admission
IE Unit Consensus (After follow-up)

Diagnosis of peripheral complications



Diagnosis of peripheral complications

Patients with definite IE

	Clinical situations	Total Nb pts ProstheticV/ PM/native V	Definite EI / total	Peripheral localisations	sensitivity	specificity	PPV False +	NPV False -
Van Riet 2010 **	Definite IE	25 pts 10/0/15	25/25	11/25 (44%) 58% silent	100%	91%	91% 9%	
Kestler M 2014	Definite IE	47pts 15/11/24	47/47	31/47 (66%)	100%	80%	90% 10%	100% 0%

Cf Article Asmar 2014
Pizi Circulation 2015 detection of 14 cases (15%) of peripheral emboli, 10 of which asymptomatic

Kestler M: Cases/controls study; peripheral localisations detected in **57.4%** of cases (TEP) vs **18%** in control (without TEP) p=0.0001

Diagnosis of peripheral complications

Patients with suspected IE

	Clinical situations	Total Nb pts ProstheticV/ PM/native V	Definite EI / total	Peripheral localisations	sensitivity	specificity	PPV False +	NPV False -
Vos 2010 **	Gram pos bacteremia *	115 pts	21/115	11/21 (50%) 50% silent	?	?	?	?
Saby 2013	Prosthetic valve AND Fever or crp > 10 mg, or bacteremia or positive serology or echo pos	72 pts 72/0/0	30/72	8/30 (25%)	?			
Bonfiglioli 2013	Clinical suspicion	71 pts 38/0/33	29/71	17/29 (?) 74%		94%		

*Pts with at least one risk factor for complicated bacteremia (community acquisition, signs of infection more than 48 h before initiation of appropriate treatment, fever more than 72 h after initiation of appropriate treatment, and positive blood cultures more than 48 h after initiation of appropriate treatment

Impact on Duke classification

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

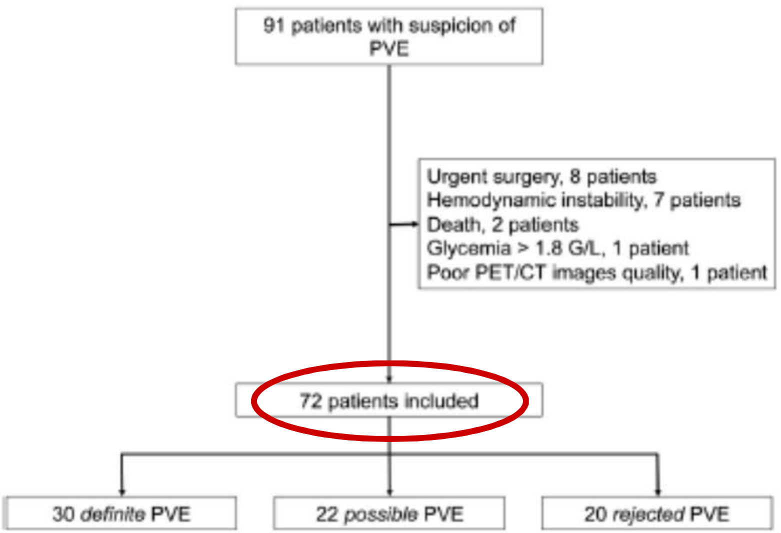


Figure 1 Study Flow Chart

Of the 91 patients with suspicion of prosthetic valve endocarditis (PVE), 72 were included and classified according to the final diagnosis determined using the modified Duke criteria established after a 3-month follow-up. PET/CT = positr emission tomography/computed tomography.

Table 5 Diagnostic Value of the Modified Duke Criteria at Admission With (Duke-PET/CT) and Without the Implementation of the PET/CT Results

	Final Diagnosis		
	Definite PVE	*Possible PVE*	*Rejected PVE*
Duke			
Definite PVE	21 (70)	0 (0)	0 (0)
Possible PVE	8 (27)	22 (100)	10 (50)
Rejected PVE	1 (3)	0 (0)	10 (50)

30 definite IE

Values are n (% of each final diagnosis).
Abbreviations as in Tables 1 and 2.

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Marseille, France

Duke classification upgraded due to

- cardiac uptake in 7/8

- peripheric uptake in 1/8

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Rejected PVE	1 (3)	0 (0)	10 (50)
Duke-PET/CT			
Definite PVE	29 (97)	10 (45)	2 (10)
Possible PVE	1 (3)	12 (55)	10 (50)
Rejected PVE	0	0	8 (40)

Values are n (% of each final diagnosis).
Abbreviations as in Tables 1 and 2.

30 definite IE

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Rejected PVE	0	0	8 (40)

Values are n (% of each final diagnosis).
Abbreviations as in Tables 1 and 2.

30 definite IE

Interobserver variability

Subject of concern ?

Interobserver variability

- Harmonization strategy conducted before a multicenter protocol on PET
- 17 clinical cases of IE suspected pts (PET images)
- Read by 8 nuclear medicine specialists originating in 8 different hospitals
- Interpretation: IE probable; doubtful, excluded

Interobserver variability

- Harmonization strategy conducted before a multicenter protocol on PET
- 17 clinical cases of IE suspected pts (PET images)
- Read by 8 nuclear medicine specialists originating in 8 different hospitals
- Interpretation: IE probable; doubtful, excluded
- **Agreement among the 8 readers:**
  - **3/17** clinical cases: **total agreement**
  - **14/17** clinical cases: **disagreement**
    - Minor (excluded versus doubtful or doubtful versus definite) **n=4**
    - Major (at least 2 readers with extreme disagreement (excluded versus definite) **n=10**

➡ **Training session**

TEPvENDO

140 patients with high suspicion of IE

- 70 prosthetic valve patients
- 70 native valve patients

TEPvENDO

140 patients with high suspicion of IE

- 70 prosthetic valve patients
- 70 native valve patients

	Prosthetic valve pts (n=70)	**Native valve pts (n=70)**
Classified definite IE before PET/CT	34	46
Abnormal cardiac uptake	47 (67.2%)	17 (24.3%)
C. uptake considered related to IE	42.9%	15.7 %
Extracardiac uptake	44.3%	51.4%
Duke classification modifications	24.3%	5.7%
NRI	20%	4.3%,
Therapeutic plans modification	21.4%	31.4%

Taken together, patients who benefited from PET/CT had more frequently

- negative echocardiography or perinanular complication ($p<0.001$)
- and/or possible IE at inclusion ($p=0.037$).

The nature of the cardiac valve was not a determinant of the benefit.

CIED infection diagnosis

CIED: cardiovascular intra cardiac electronic device

CIED infection diagnosis

- 42 pts suspected of CIED infection

CIED: cardiovascular intra cardiac electronic device

CIED infection diagnosis

- 42 pts suspected of CIED infection

	Group A Suspected CIED inf^{ion} N=42
Confirmed infection	35 (83%)
18F-FDG PET/CT uptake	32/42 1 false pos 3 false neg
SUVmax	4.4 ± 1.6
ETOveg^{tion}	12/42

CIED: cardiovascular intra cardiac electronic device

Sarrazin JF et al. JACC 2012

CIED infection diagnosis

- 42 pts suspected of CIED infection

	Group A Suspected CIED inf^{ion} N=42	Group B Controls 6 Weeks post implantation N=12
Confirmed infection	**35 (83%)**	**0**
18F-FDG PET/CT uptake	**32/42** **1 false pos** **3 false neg**	**No or mild uptake**
SUVmax	**4.4 ± 1.6**	**1.2 ± 1.4**
ETOveg^{tion}	**12/42**	**0**

CIED: cardiovascular intra cardiac electronic device

sensitivity	specificity
0.886	0.857

Sarrazin JF et al. JACC 2012

CIED infection diagnosis

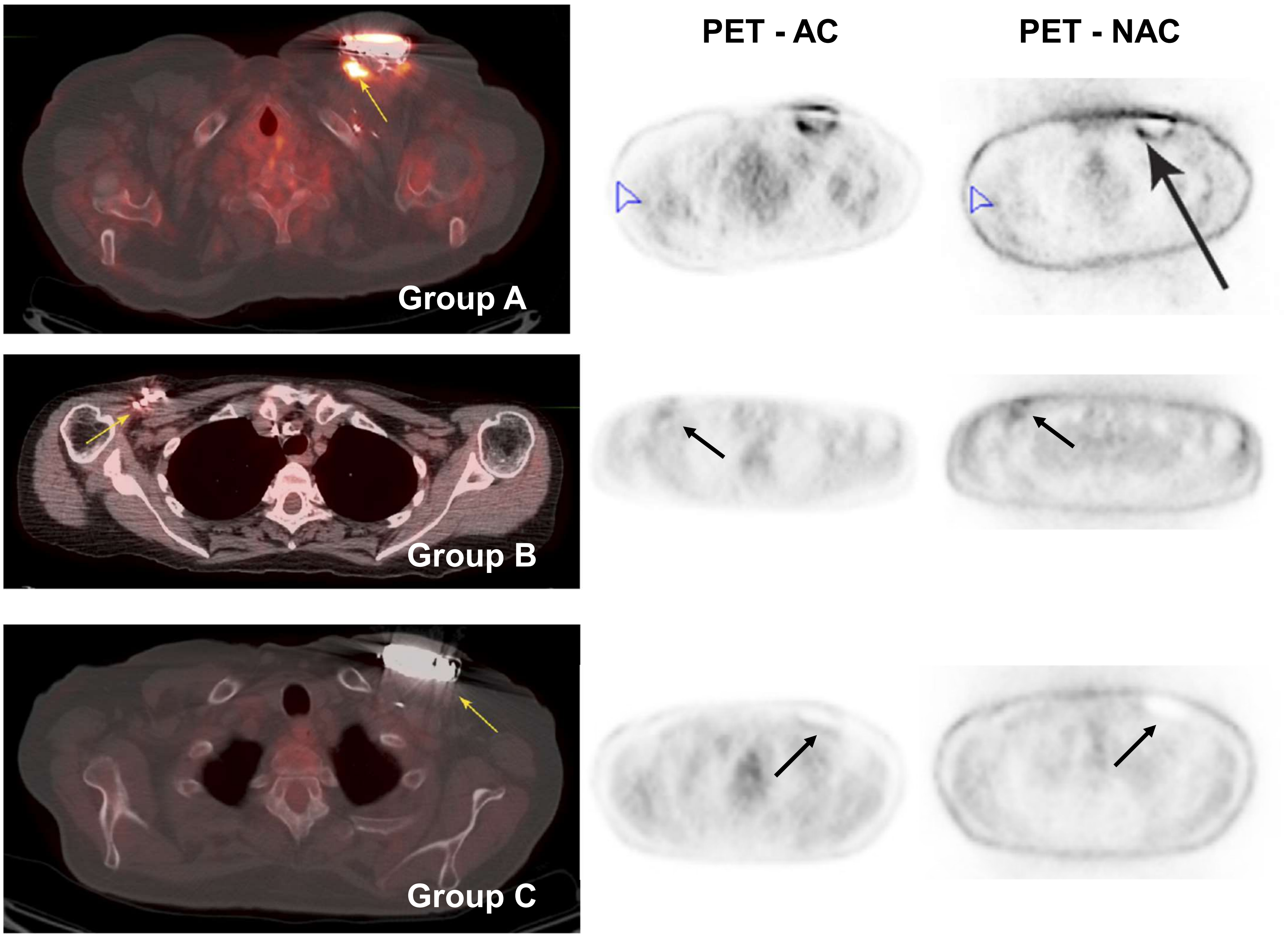
- 42 pts suspected of CIED infection

	Group A Suspected CIED inf^{ion} N=42	Group B Controls 6 Weeks post implantation N=12	Group C Controls > 6 M^{ths} post implantation N=12	
Confirmed infection	35 (83%)	0	0	<0.001
18F-FDG PET/CT uptake	32/42 1 false pos 3 false neg	No or mild uptake	0	
SUVmax	4.4 ± 1.6	1.2 ± 1.4	0	<0.001
ETOveg^{tion}	12/42	0	0	

CIED: cardiovascular intra cardiac electronic device

sensitivity	specificity
88 %	86 %

Sarrazin JF et al. JACC 2012


PET - AC
PET - NAC
Group A
Group B
Group C

CIED infection diagnosis

- 27 pts suspected of CIED infection

CIED: cardiovascular intra cardiac electronic device

CIED infection diagnosis

- 27 pts suspected of CIED infection

	Group A CIED infection N=11	Group B No CIED infection N=16
18F-FDG PET/CT uptake	**7/11** **4 false neg**	**3/16** **2 false pos**
ETO vegetation	**?**	

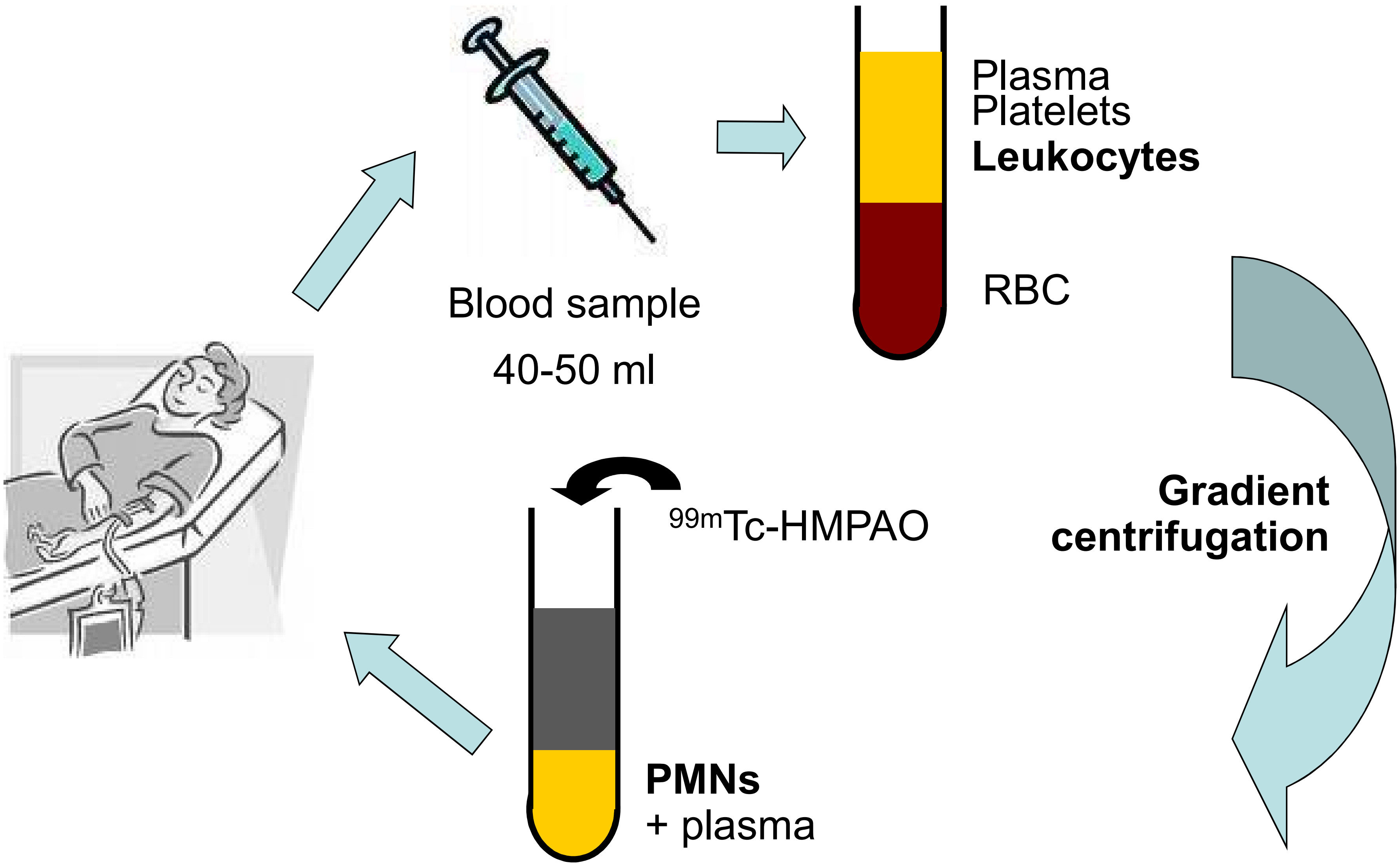
sensitivity	specificity	PPV	NPV
63%	86%	77%	76%

CIED: cardiovascular intra cardiac electronic device

Graziosi M et al. Eur J Nucl Med Mol Imaging 2014

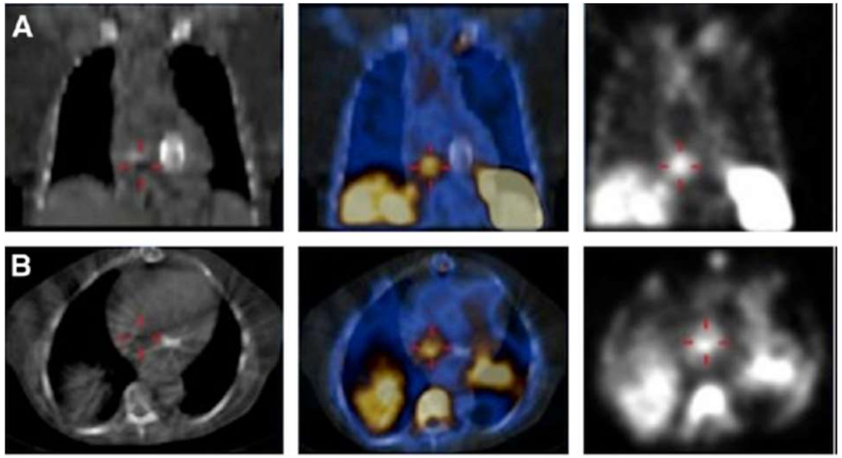
Nuclear Imaging
Labelled leukocytes

Radiolabelled leukocytes: methods



Added Value of ^{99m}Tc-HMPAO–Labeled Leukocyte SPECT/CT in the Characterization and Management of Patients with Infectious Endocarditis

Erba PA et al, J Nucl Med 2012



- 131 pts with suspected IE (prosthetic IE)
- Final Diagnosis of EI 51/131 (39%) patients
  Sensitivity : 90%
  Specificity : 100%

Results of ^{99m}Tc-HMPAO-WBC Scintigraphy in the 51 Patients with Final Diagnosis of IE, Stratified According to Duke Criteria

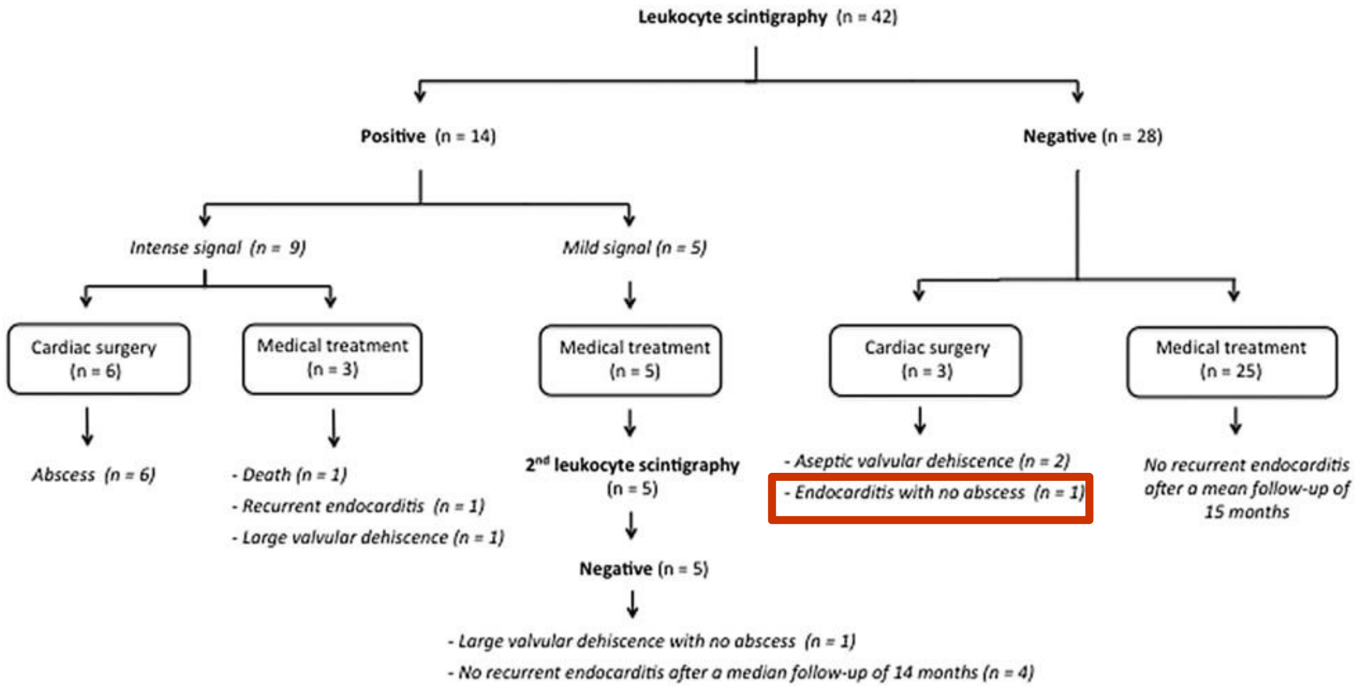
Duke criterion	Positive results			Negative results
	Cardiac only	Cardiac and extracardiac	Extracardiac only	
Definite IE (n = 24)	9	11*	0	4
Possible IE (n = 25)	13	11†	1*	0
Rejected IE (n = 2)	1	1*	0	0

*Septic embolism consequent to IE.

†Eight patients with septic embolism, 1 with vasculitis, and 2 false-positive scans due to vertebral crush and metastasis from prostate cancer.

Labelled leukocytes and infective endocarditis

- 42 pts with suspected prosthetic IE (valve prosthesis / aortic tube / patch)
- **Non-conclusive TTE/TEE in all cases**
- 14 (33%) positive uptake (intense in 9, mild in 5)



(Hyafil et al. Eur Heart J Cardiovasc Imaging 2013;34:1597-606)

Nuclear Imaging
[18F]FDG PET/CT versus Labelled leukocytes

FDG PET *vs.* WBC SPECT

- Single-centre prospective study (Bichat Hospital, Paris)
- **39 patients** (males: 22), aged 62±17 years
- Suspected of **prosthetic valve endocarditis** (PVE)
- Time between FDG PET and WBC SPECT: 7±7 days
- Diagnosis after ≥3-months follow-up (Duke-Li):
  - Definite, n=14 (36%)
  - Possible, n=3
  - Rejected, n=21

Rouzet F et al, J Nucl Med 2014

FDG PET *vs.* WBC SPECT

	Final diagnosis after ≥3 mo follow-up		
	Definite (n=14)	**Possible (n=4)**	**Rejected (n=21)**
FDG PET +	13 (93)	1	6
FDG PET -	1	2	15 (71)
WBC SPECT +	9 (64)	0	0
WBC SPECT -	5	3	22 (100)

- FDG PET false positive <2 months after valve implantation (n=6)
- WBC SPECT false negative (n=5): Coxiella (n=2), Candida (n=1), no abscess (n=2)

FDG PET: Higher sensitivity
WBC SPECT: Higher specificity

Perspectives: FDG PET

Remains to be determined

- Cost-effectiveness
- Diagnostic value, impact on patients' management and outcomes in multicentre trials

Perspectives: FDG PET

Remains to be determined

- Cost-effectiveness
- Diagnostic value, impact on patients' management and outcomes in multicentre trials

- **NCT01916005** - *F. Thuny, Marseille, France*

Diagnostic Value of 18F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Prosthetic Valve Endocarditis.

- **TEPvENDO** - *X. Duval, Bichat, Paris, France*

Diagnostic and therapeutic impact of FDG PET at the acute phase of infective endocarditis (8 centres).

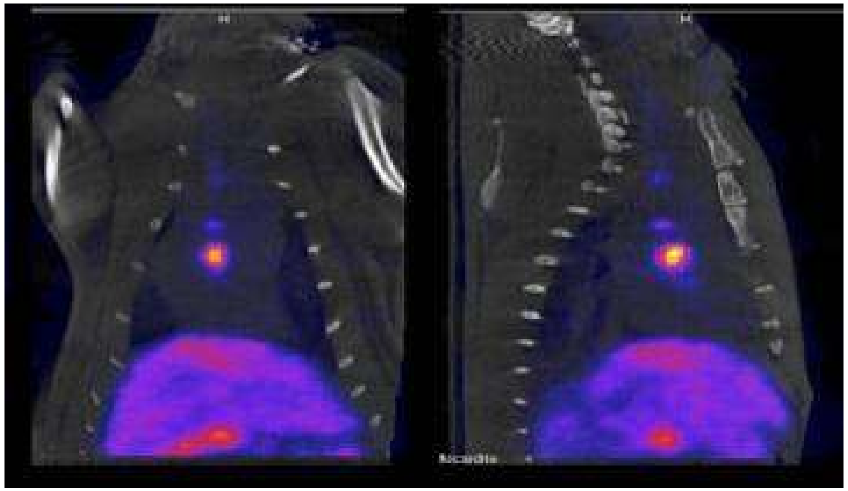
Perspectives: new imaging agents

Leukocytes labelled with positron emitters (PET)

- Requires a long half-life isotope (^{64}Cupper = 12.7 hours)
- *Bhargava et al. NMB 2009*

^{99m}Tc-Annexin A5

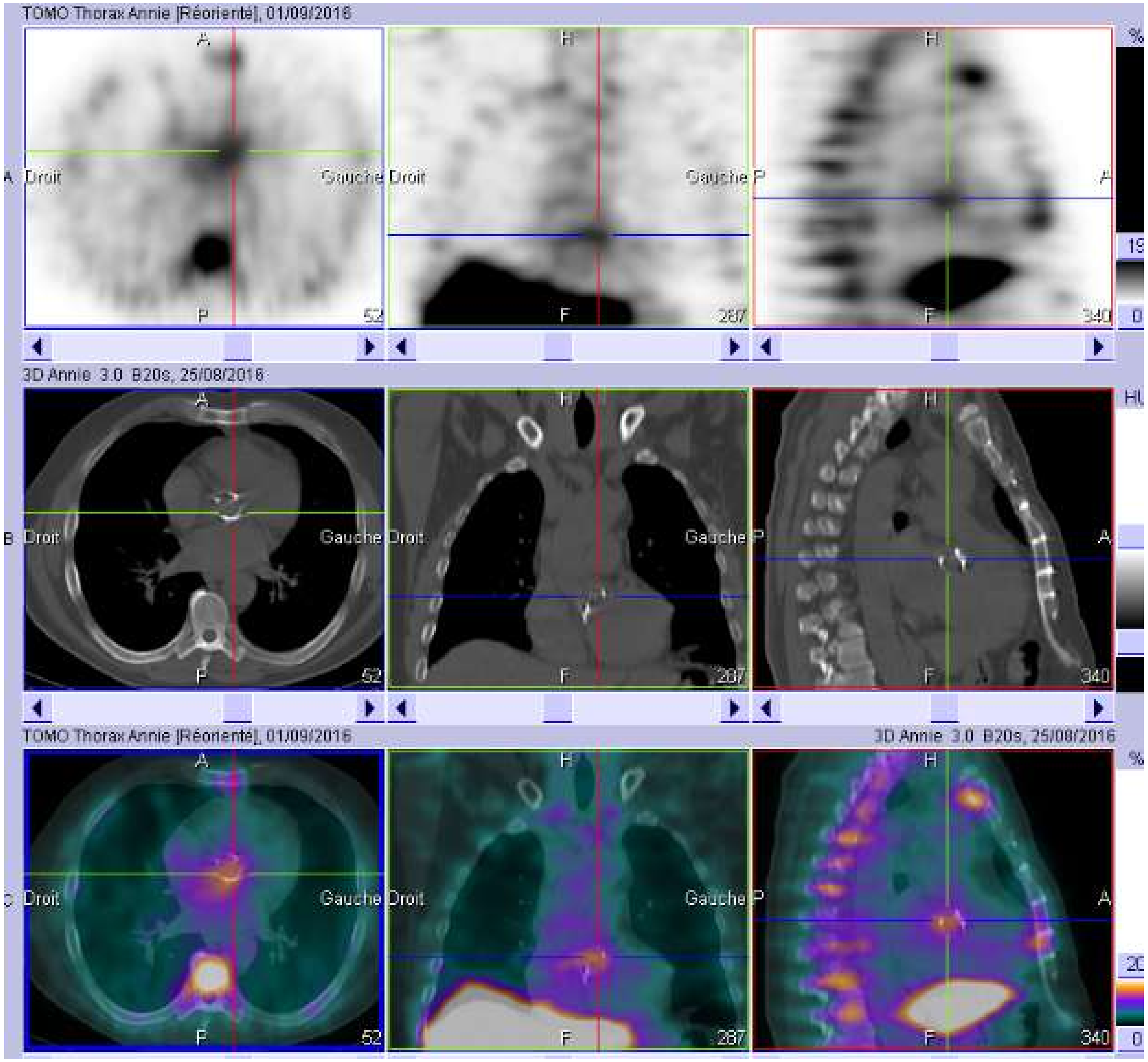
- Target: vegetations (phosphatidylserine expressed by activated platelets)
- No physiological uptake in heart and brain



AnnIE
Sponsor: Inserm
Proof-of-concept study
Patients suspected of IE
Kick off: 2015

Rouzet et al., Circulation 2008
Benali et al., Mol Imaging 2014

SPECT/CT à la ^{99m}Tc-Annexine (Etude AnnIE)
Endocardite streptococcique sur bioprothèse aortique



Cerebral complications of IE

Cerebral complications of IE

Symptomatic neurological complications

- 9 to 40 % according to series
- associated with poor prognosis

Detection of asymptomatic cerebral lesions

- Help to establish IE diagnosis
- Better assessment of
  - Embolic risk
  - Surgery indications
  - IE prognosis (short and long term prognosis)
- Initiation of specific treatment of cerebral com^{tions}
- Improvement of IE prognosis ?

Cerebral complications of IE

Which cerebral complications could be detected ?

Vascular

- Ischemic events
  - Stroke
  - Transient ischemic attack (TIA)
  - Silent embolism
- Hemorrhagic events
  - H. stroke
  - Microbleeds
  - Sub arachnoidal H
- Aneurysms

Infectious

- Meningitis
- Abscess

Cerebral complications of IE

Which imaging to detect cerebral complications ?

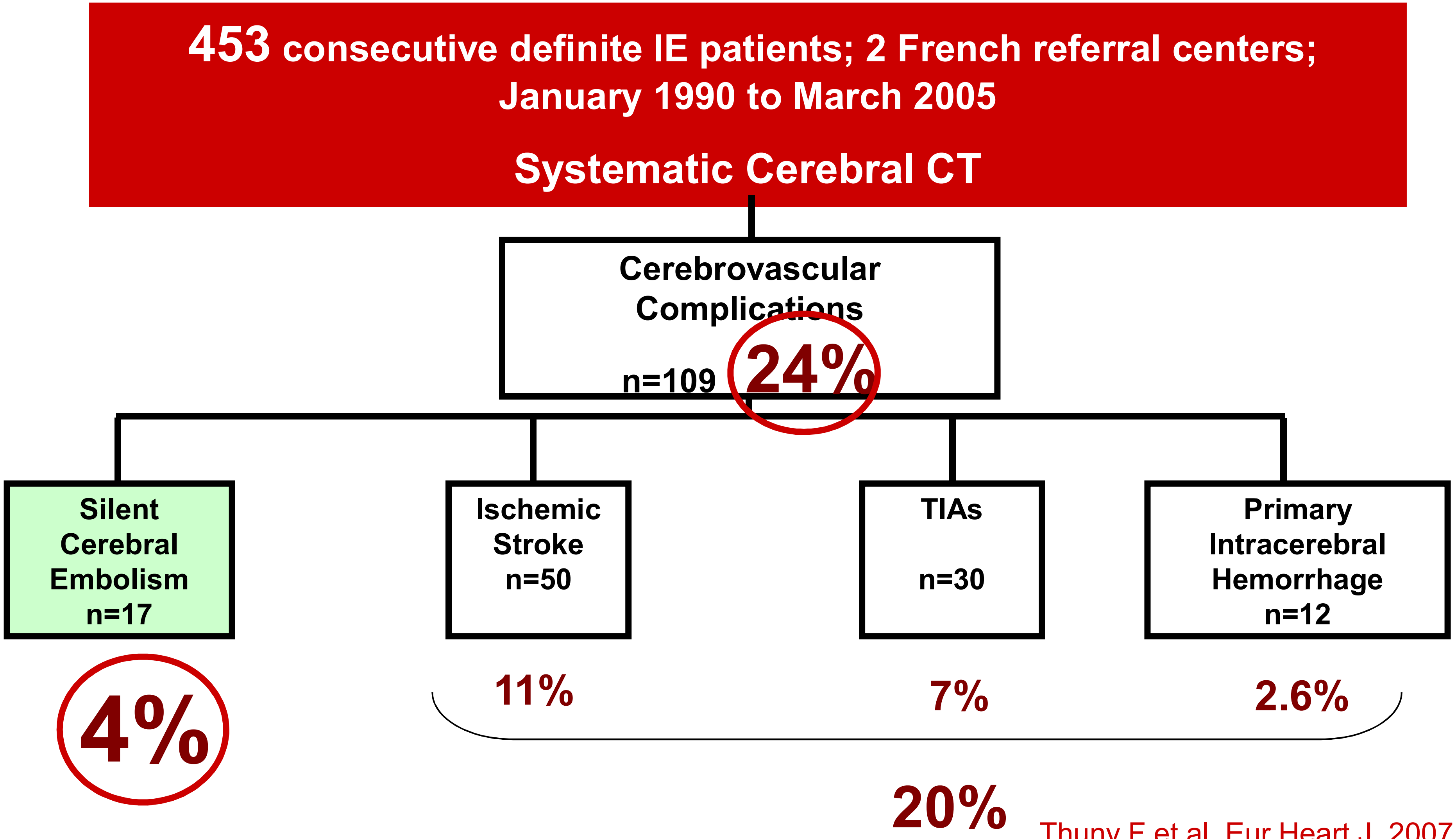
Cerebral

- CT scan
- CT scan with angiography
- MRI
- MRI with angiography
- Conventional 4 vessel angiography

Findings of systematic cerebral imaging studies

- **Findings of systematic cerebral imaging studies**
  - **CT scanner**

Neurological complications incidence
Systematic cerebral CT



Thuny F et al. Eur Heart J. 2007

Findings of systematic cerebral imaging studies

- CT scanner
- CT scanner with angiography

PLOS | ONE Marwa Sayed Meshaal[1]*, Hussein Heshmat Kassem[1], Ahmad Samir[1], Ayman Zakaria[2], Yasser Baghdady[1], Hussein Hassan Rizk[1] April 2015

Systematic cerebral CT with angiography

81 consecutive definite IE patients;

Systematic Cerebral CT with angiography

Cerebrovascular Complications

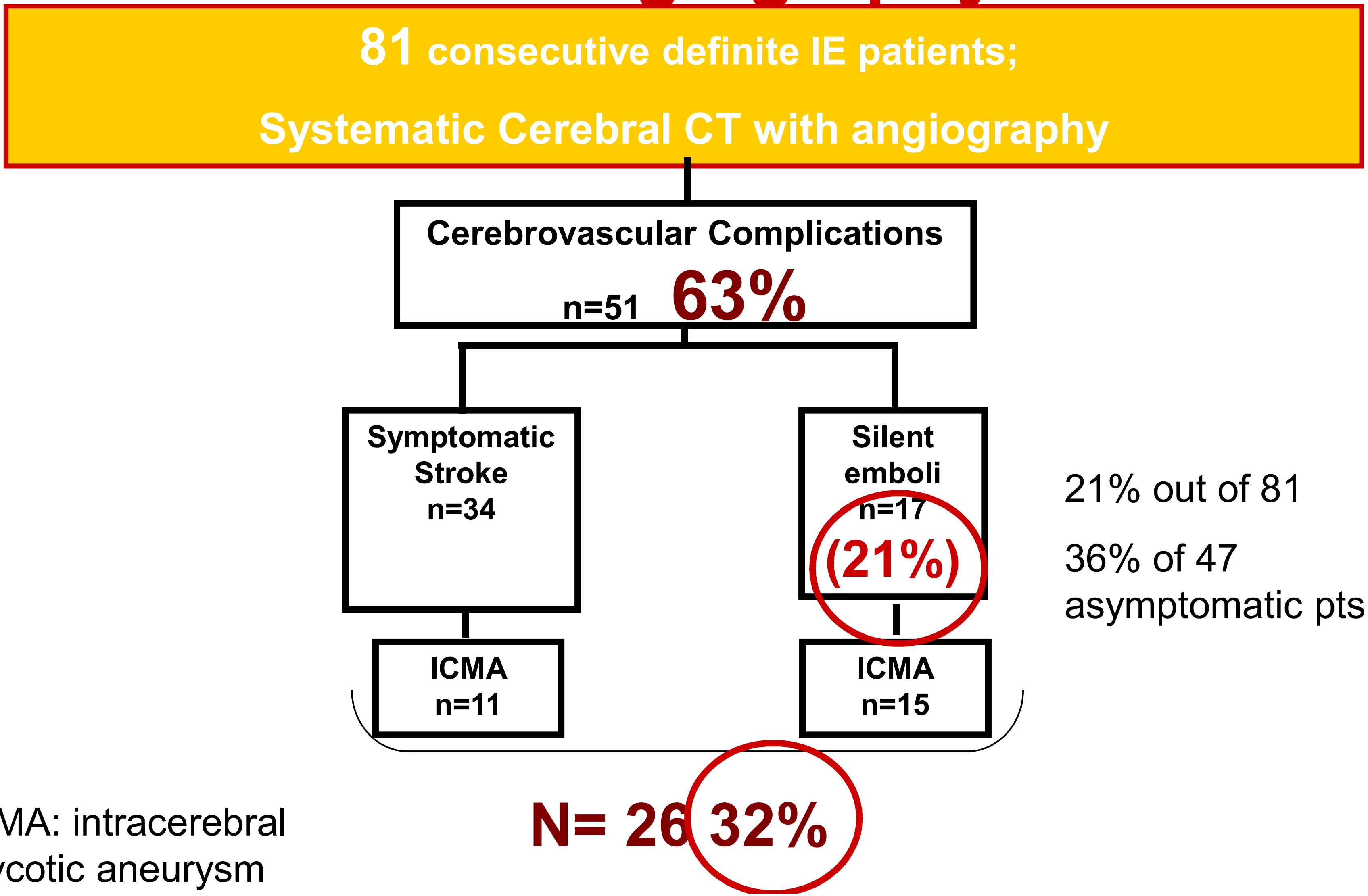
n=51 63%

Symptomatic Stroke n=34

Silent emboli n=17 (21%)

PLOS | ONE Marwa Sayed Meshaal[1]*, Hussein Heshmat Kassem[1], Ahmad Samir[1], Ayman Zakaria[2], Yasser Baghdady[1], Hussein Hassan Rizk[1] April 2015

Systematic cerebral CT with angiography



ICMA: intracerebral mycotic aneurysm

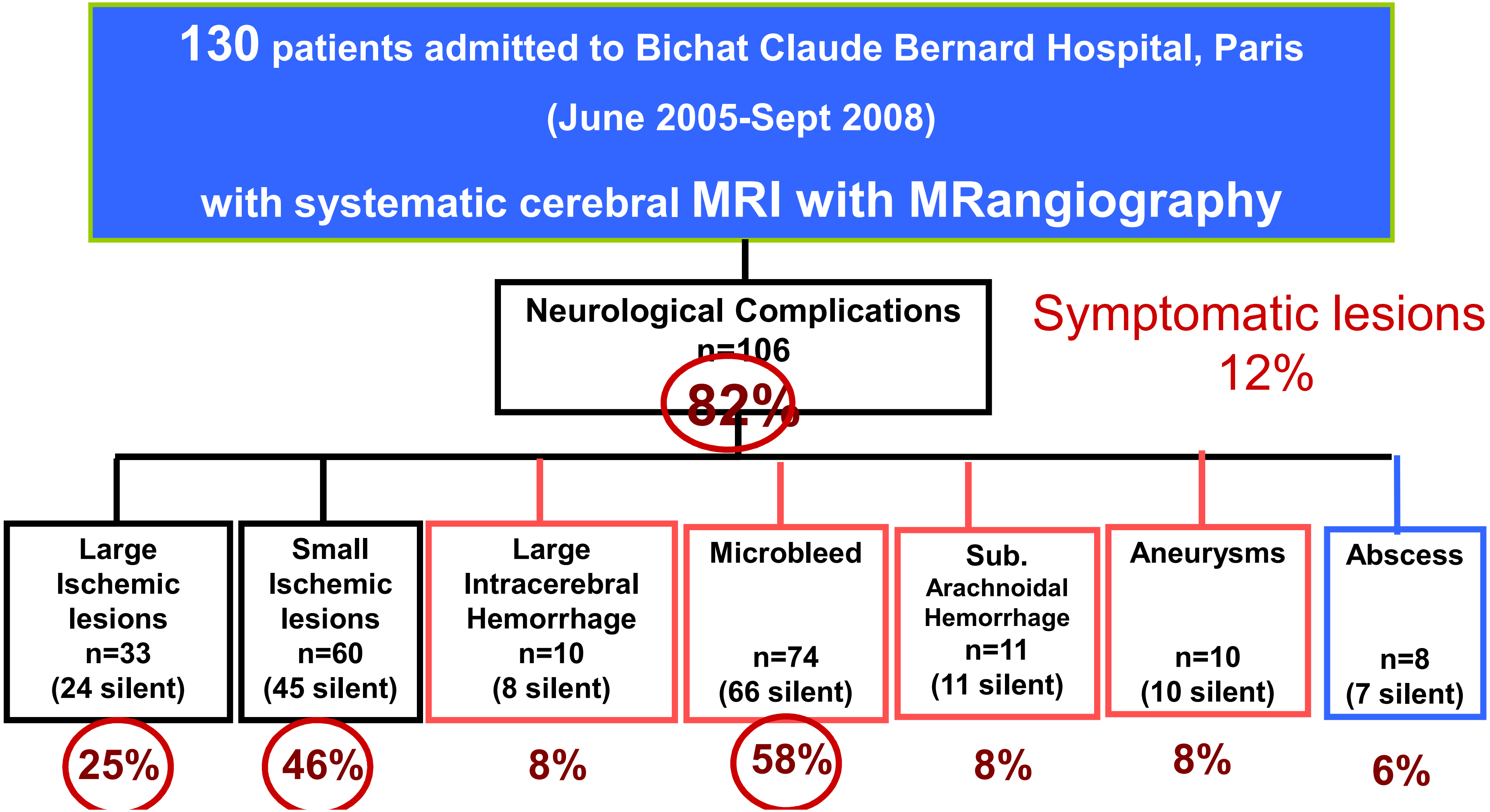
Findings of systematic cerebral imaging studies

- CT scanner
- CT scanner with angiography
- MRI with angiography

Annals of Internal Medicine | ARTICLE

Effects of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis, the IMAGE study

Xavier Duval , Bernard Iung , Isabelle Klein , Eric Brochet , Gabriel Thabut , Florence Arnoult , Laurent Lepage ,
Jean Pierre Laissy , Michel Wolff and Catherine Leport and the IMAGE study group.



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Jean Pierre Laissy , Michel Wolff and Catherine Leport and the IMAGE study group.

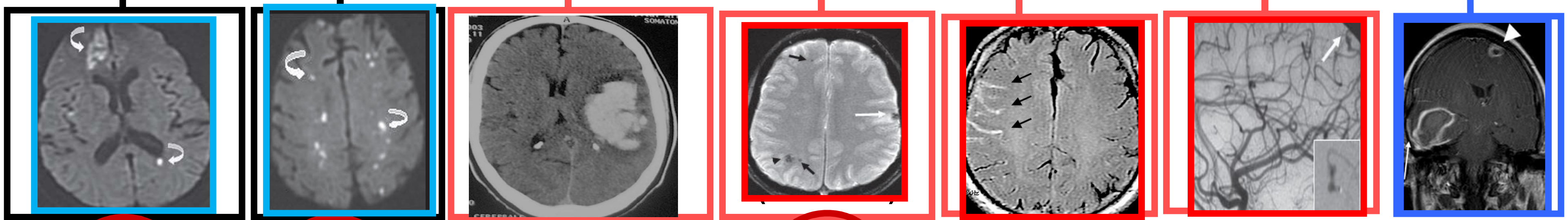
130 patients admitted to Bichat Claude Bernard Hospital, Paris

(June 2005-Sept 2008)

with systematic cerebral MRI with MRangiography

Neurological Complications
n=106
82%

Symptomatic lesions
12%



25% **46%** **8%** **58%** **8%** **8%** **6%**

Annals of Internal Medicine | Article

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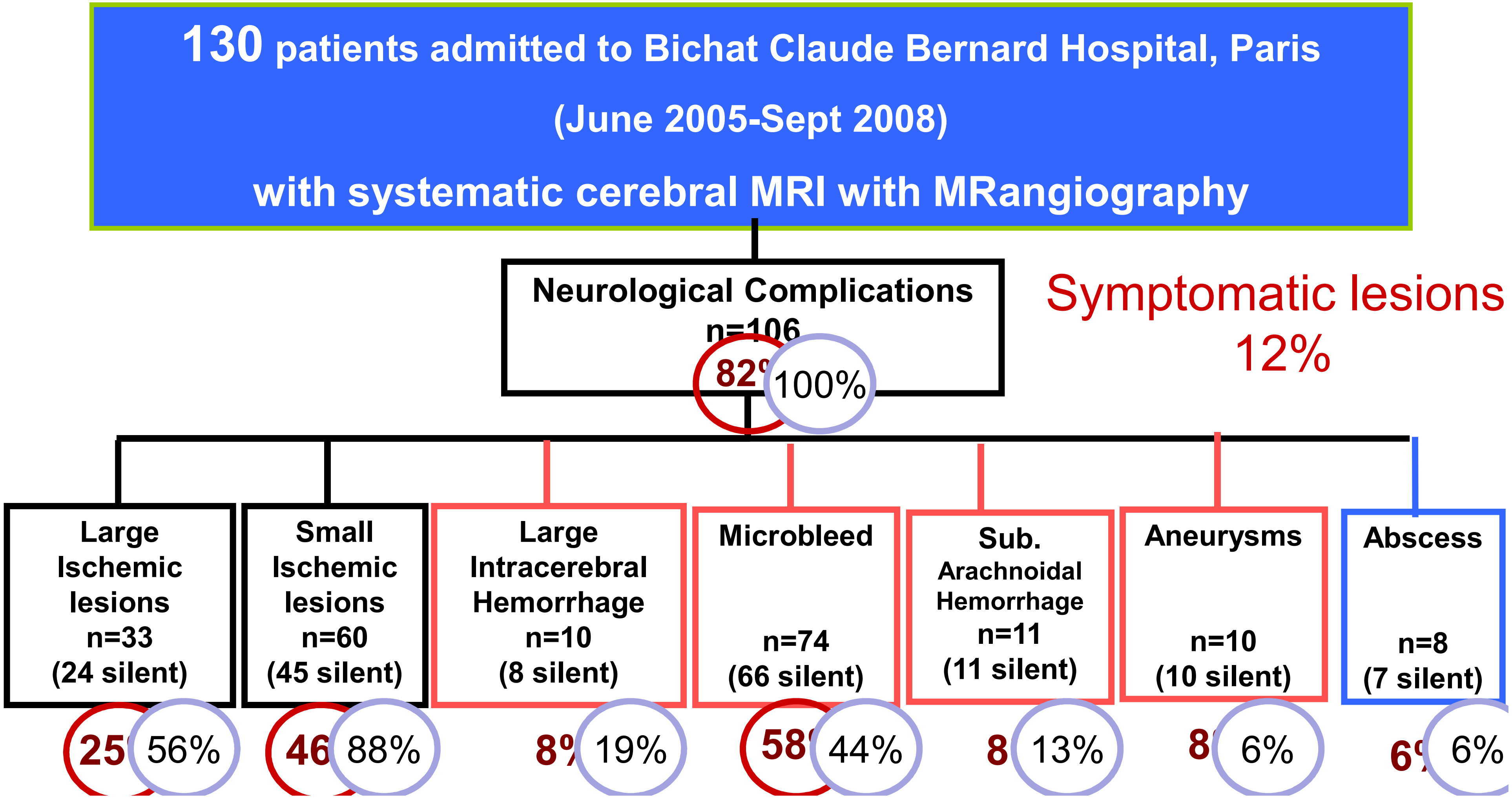


Findings of systematic cerebral imaging studies

- CT scanner
- CT scanner with angiography
- MRI with angiography
- **Conventional 4 vessel angiography**

Conventional cerebral angiography

- **No prospective studies with systematic angiography**
- Retrospective study of **168 pts who underwent cerebral angiography:**
  - **15/**168 pts (**8.9%**) had mycotic aneurysms;
    - 93.3% (14/15) of those had CNS hemorrhage
    - 66.7% (10/15) had acute ischemic findings
- Retrospective study of **151 pts who underwent cerebral angiography before surgery:**
  - 7/151 (**4.6%**) had mycotic aneurysm
  - absence of intracranial bleed on MRI: (NPV) of 0.98

Hui FK, J Neurointerv Surg. 2015 / Monteleone PP, Vasc Med. 2014

Symptomatic and Asymptomatic Neurologic Events

Prospective Series with Systematic Imaging

	n	Imaging	Symptomatic Events (%)	Asymptomatic Embolism (%)
Thuny et al.	453	CT	22	4
Meshaal et al	81	CT + angio	43	21
Snygg-Martin et al.	49	MRI	35	30
Cooper et al.	40	MRI	32	48
Duval et al.	130	MRI	12	47

Thuny et al. Eur Heart J 2007;28:1155-61 / Snygg-Martin et al. Clin Infect Dis 2008;47:23-30
Cooper et al. Circulation 2009;120:585-91 / Duval et al. Ann Intern Med 2010;152:497-504
Meshaal et al Plos one 2015

Diagnostic impact of detected lesions

ESC modified diagnostic criteria

Major criteria

1. Blood cultures positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
- *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or
- Community-acquired enterococci, in the absence of a primary focus; or

b. Microorganisms consistent with IE from persistently positive blood cultures:
- ≥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 and last samples drawn ≥1 h apart); or

c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

2. Imaging positive for IE

a. Echocardiogram positive for IE:
- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

c. Definite paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only) major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

Diagnotic impact of detected lesions

- May account for a minor criteria

  arterial emboli, mycotic aneurysm, intracranial haemorrhage

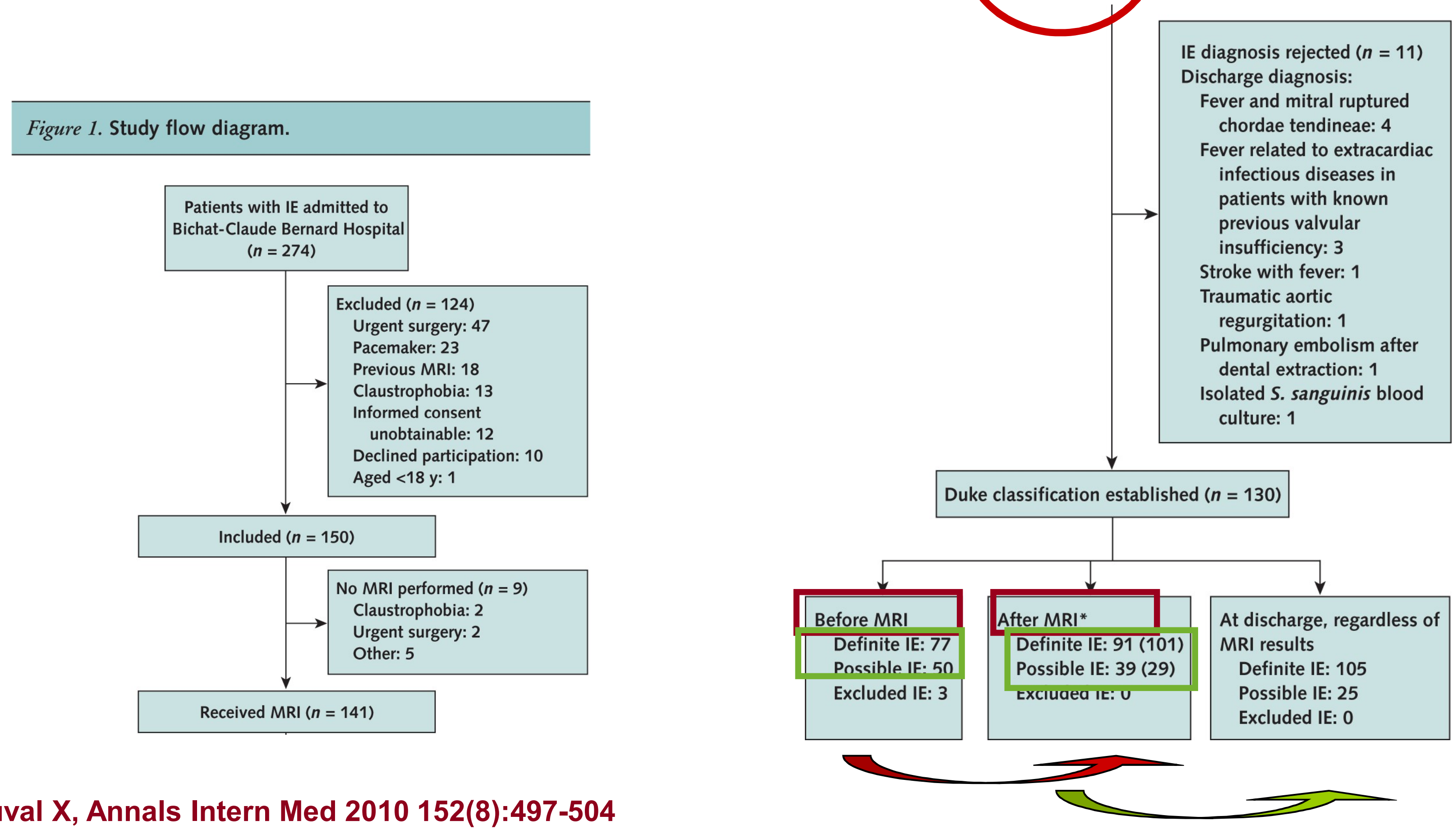
- Only assessed for MRI in the IMAGE study

Annals of Internal Medicine | ARTICLE

Effects of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis, the IMAGE study

• Impact of cerebral lesion detection on IE diagnosis

– Modified-Duke classification upgraded in **32%**

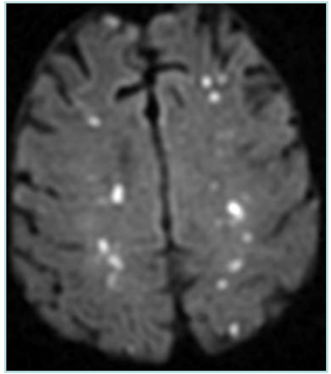


Duval X, Annals Intern Med 2010 152(8):497-504

Prognostic impact of asymptomatic cerebral lesions

Cerebral ischemic spot risk factors

- **Risk factors for Symptomatic cerebral emboli**
  - Vegetation length > 10 mm
  - Staphylococcus aureus IE
  - Mitral valve
  - History of emboli …,



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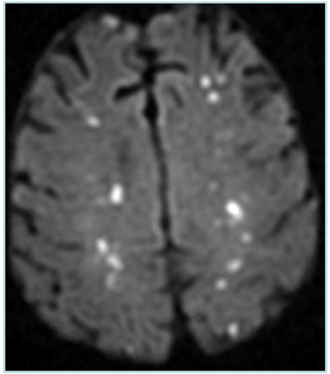


- **Risk factors for Asymptomatic cerebral emboli detected by MRI**

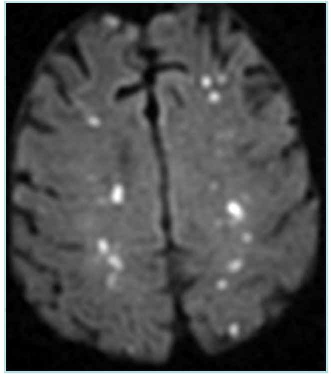
Lesion Characteristic	All Patients (*n* = 130), *n* (%)
Ischemic lesion	68 (52)
Large systematized ischemic lesion*	33 (25)
Small ischemic lesion	60 (46)

Determinants of asymptomatic ischemic lesions

	OR	IC 95%	p
- Vegetation length	1.1 per mm	1.03-1.16	p=0.003
- Staph aureus IE	2.65	1.01-6.96	p=0.05

Duval X, Annals Intern Med 2010 152(8):497-504 / Iung B, Stroke 2013; 44(11):3056-62

Cerebral ischemic spot risk factors



- **Risk factors for Symptomatic cerebral emboli**
  - Vegetation length > 10 mm
  - Staphylococcus aureus IE, mitral valve
  - History of emboli …,
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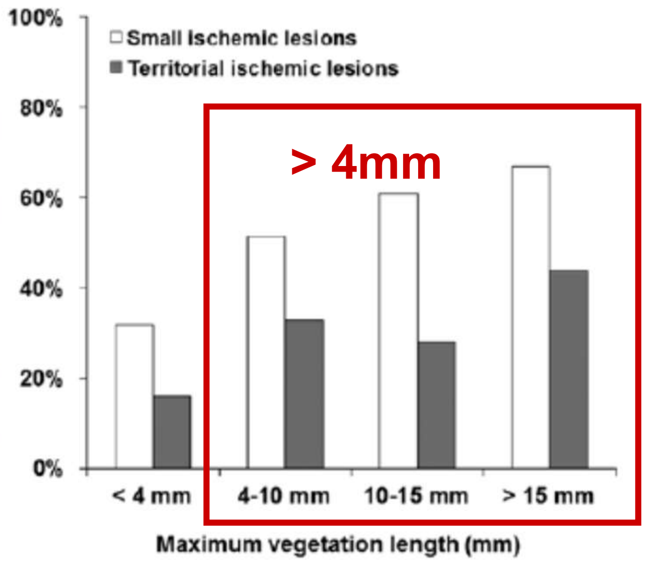
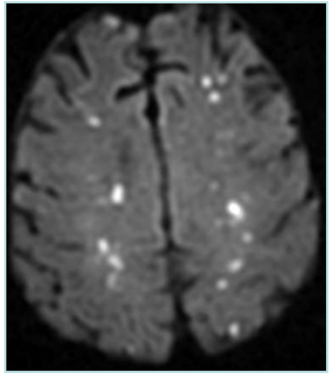


Figure 3. Distribution of territorial and small cerebral ischemic lesions according to vegetation length.

Duval X, Annals Intern Med 2010 152(8):497-504 / Iung B, Stroke 2013; 44(11):3056-62

Cerebral ischemic spot risk factors

- **Risk factors for Symptomatic cerebral emboli**
  - Vegetation length > 10 mm



Same risk factors for symptomatic and asymptomatic emboli

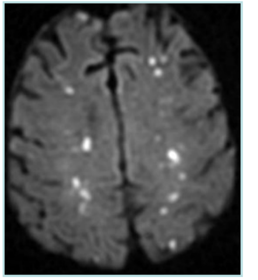
Ischemic spot may be a risk factor for symptomatic emboli ?

Currently no arguments presented in the literature

Figure 3. Distribution of territorial and small cerebral ischemic lesions according to vegetation length.

Duval X, Annals Intern Med 2010 152(8):497-504

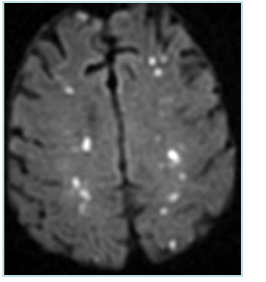
Iung B, Stroke 2013; 44(11):3056-62



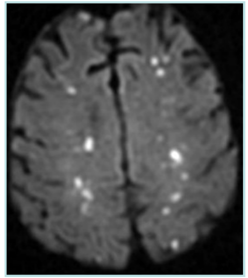
- Impact of ischemic spot on short-term prognosis ?

  Difficult to assess as their discovery may have induced a modification of IE treatment

Cerebral ischemic spot and IE
Long-term prognosis ?



Cerebral ischemic spot and IE Long-term prognosis



- **Outside the IE context**
  - **Cerebral ischemic spots** associated with lower cognition and higher odds of dementia

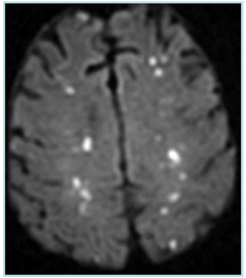
Microinfarct Pathology, Dementia, and Cognitive Systems

Zoe Arvanitakis, MD, MS; Sue E. Leurgans, PhD; Lisa L. Barnes, PhD; David A. Bennett, MD; Julie A. Schneider, MD, MS

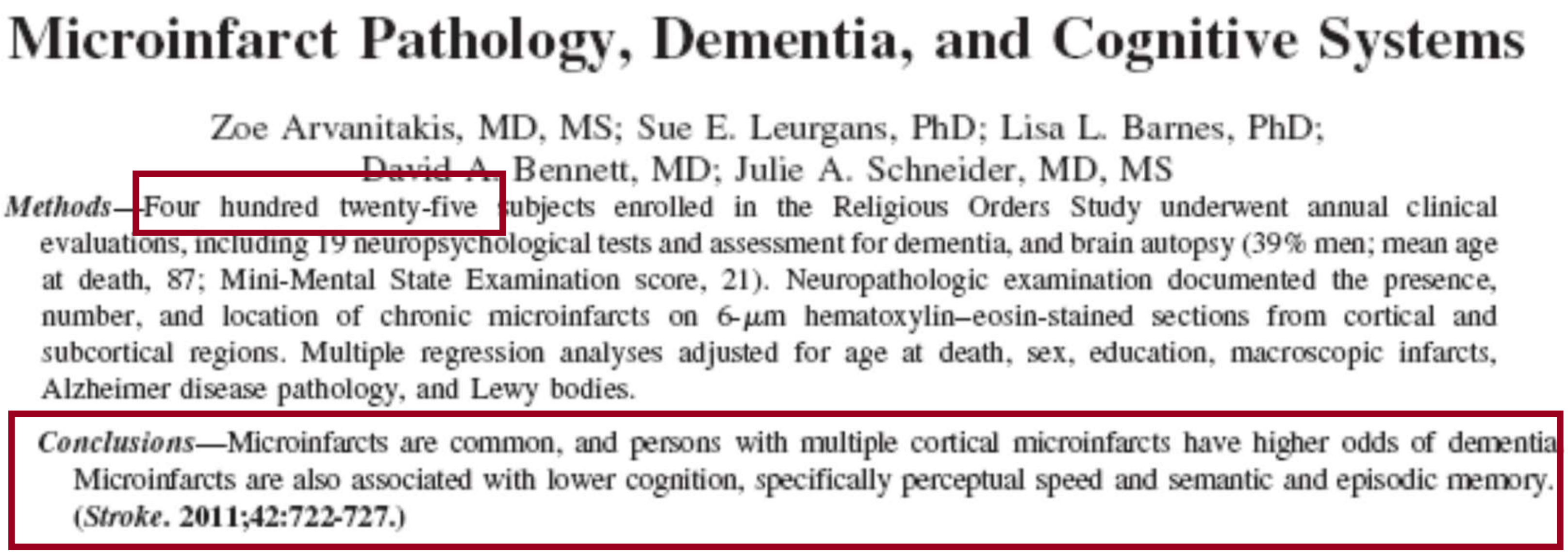
Methods—Four hundred twenty-five subjects enrolled in the Religious Orders Study underwent annual clinical evaluations, including 19 neuropsychological tests and assessment for dementia, and brain autopsy (39% men; mean age at death, 87; Mini-Mental State Examination score, 21). Neuropathologic examination documented the presence, number, and location of chronic microinfarcts on 6-μm hematoxylin–eosin-stained sections from cortical and subcortical regions. Multiple regression analyses adjusted for age at death, sex, education, macroscopic infarcts, Alzheimer disease pathology, and Lewy bodies.

Conclusions—Microinfarcts are common, and persons with multiple cortical microinfarcts have higher odds of dementia. Microinfarcts are also associated with lower cognition, specifically perceptual speed and semantic and episodic memory. (*Stroke*. **2011;42:722-727.**)

Cerebral ischemic spot and IE
Long-term prognosis



- Outside the IE context
  - Cerebral ischemic spots **associated with lower cognition and higher odds of dementia**



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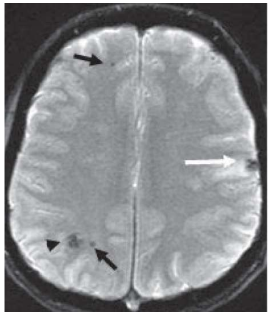
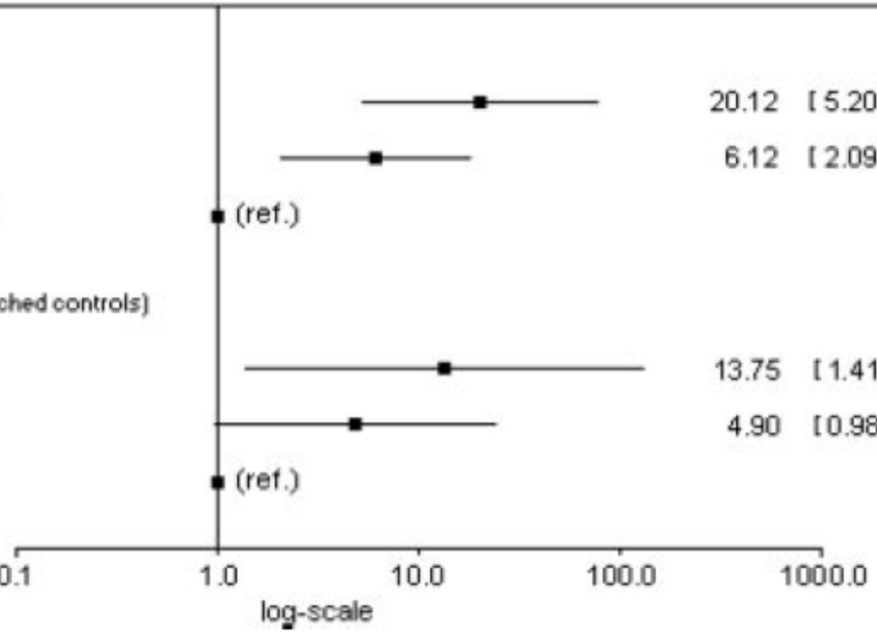
- Impact unknown in IE patients

Microbleeds and IE ?

Cerebral microbleeds
Case-control study



Microbleeds	Cases n (%)	Controls n(%)	OR 95% CI
All study sample (60 cases and 120 matched controls)			
>3	19 (31.7)	5 (4.2)	20.12 [5.20 , 77.80]
1-3	15 (25.0)	13 (10.8)	6.12 [2.09 , 17.94]
None	26 (43.3)	102 (85.0)	(ref.)
Non-anticoagulant-treated patients (43 cases and 43 matched controls)			
>3	10 (23.3)	3 (7.0)	13.75 [1.41 , 134.14]
1-3	10 (23.3)	5 (11.6)	4.90 [0.98 , 24.63]
None	23 (53.5)	35 (81.4)	(ref.)

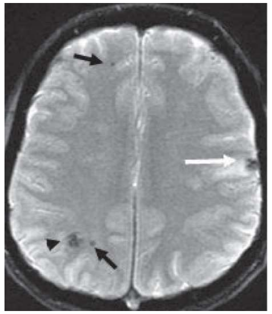


OR increase with the increase in the number of microbleeds suggesting a causal relationship

Klein I Stroke 2009

Cerebral microbleed risk factors

- **Risk factors for microbleeds**
  - not reported in the literature
  - in the IMAGE study



Lesion Characteristic	All Patients (n = 130), n (%)
Hemorrhagic lesion	79 (61)
Intraparenchymal hemorrhagic lesion	10 (8)
Microhemorrhage	74 (58)
Subarachnoidal hemorrhage	11 (8)

Determinants of microhemorrages

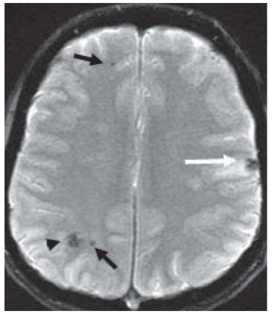
	OR	IC 95%	p
Prosthetic valve	8.01 per mm	2.58-24.90	P<0.001
Anticoagulation therapy			p=0.67

Microbleeds: 86.8% of pts with prosthetic IE vs 47.6% with native valve IE (*P*<0.001)

Microbleed and ischemic lesions: distinct mecanisms

Duval X, Annals Intern Med 2010 152(8):497-504 / Iung B, Stroke 2013; 44(11):3056-62

Cerebral microbleeds and IE short-term prognosis



- **In individuals without endocarditis**
  – Associated with cerebral hemorrhagic risk

- **In IE patients**

Japanese study

– **26 patients** with cerebral MRI

– Cerebral microbleeds: 54%

– **Intracerebral hemorrhage** occurred in 8 patients within 3 months (31%)

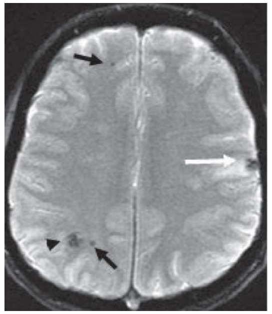
– Number of microbleeds associated with ICH

Determinants of impending ICH

	OR	IC 95%
Preceding ICH	40.0	2.5–2,870
CMB ≥ 1	34.0	1.3-17000
CMB ≥ 2	42.1	
CMB ≥ 3	70.1	

Shuhei Okazaki, Cerebrovasc Dis 2011;32:483–488

Cerebral microbleeds and IE Long-term prognosis



- **Outside the IE context, associated with**
  - Dementia
  - Cognitive decline
  - Chronic cerebrovascular diseases
  - Subarachnoidal hemorrhages

- **Long-term impact Unknown in IE patients**

Lei C; J Neurol Neurosurg Psychiatry. 2013

Cerebral asymptomatic lesions and long-term prognosis

Clinical and MRI follow-up of the IMAGE cohort is ongoing

- Evolution of cerebral lesions diagnosed during the acute phase
- Consequences on neurologic and cognitive status

Therapeutic impact of asymptomatic cerebral lesions

Annals of Internal Medicine | ARTICLE

Effects of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis, the IMAGE study

- **In 29/130 pts (22%): experts modified IE treatment plans based on MRI results**
  - Modification of anticoagulation level n= 6
  - Modification of antibiotics n= 5
  - Modification of surgery plan n=18
    - Surgery date postponed 6
    - Surgery date advanced 6
    - Type of valvular prosthesis 1
    - Reasons for surgery 1
    - Cancellation of surgery 2
    - Indication for surgery 2
  - Embolisation of aneurysm n = 4

However, it is not clear whether silent neurological complications are associated with a poor prognosis

81 consecutive definite IE patients;

Systematic Cerebral CT with angiography

Modification of treatment in 21 pts with ICMA (25.6%) (more than one change in 11 pts)

- **15 pts** : invasive treatment of ICMA (13 endovasc)
  No procedure-related complication
- Anticoagulation stopped in 3 pts with prosthetic v
- Modification of the cardiac surgery type in 17 pts
- Regression of ICMA in 3/11 not treated pts

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

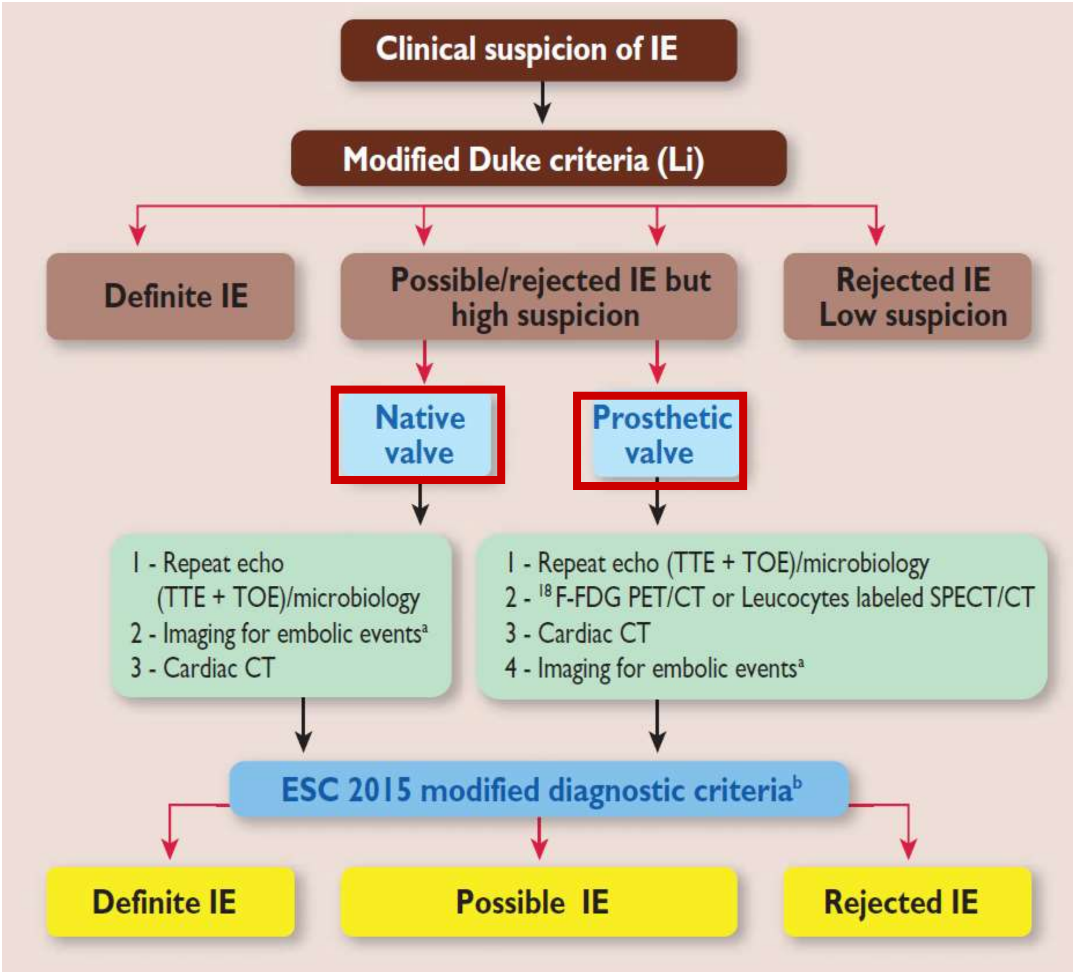
Imaging techniques in IE

Diagnosis

Diagnosis

Imaging techniques

Nuclear imaging



ESC modified diagnostic criteria

Major criteria

1. Blood cultures positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
- *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or
- Community-acquired enterococci, in the absence of a primary focus; or

b. Microorganisms consistent with IE from persistently positive blood cultures:
- ≥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 and last samples drawn ≥1 h apart); or

c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

2. Imaging positive for IE

a. Echocardiogram positive for IE:
- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

c. Definite paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only) major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
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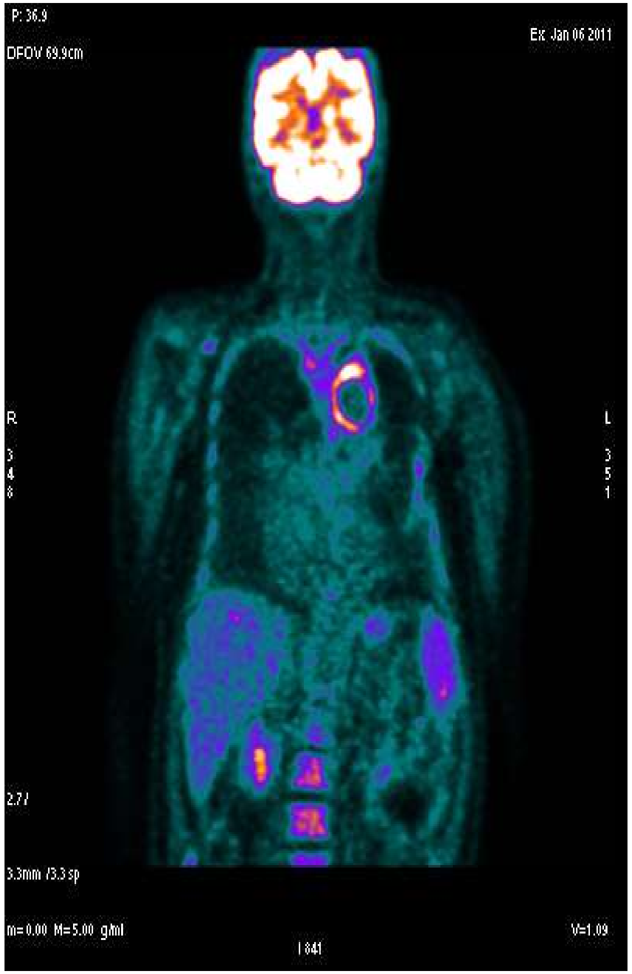
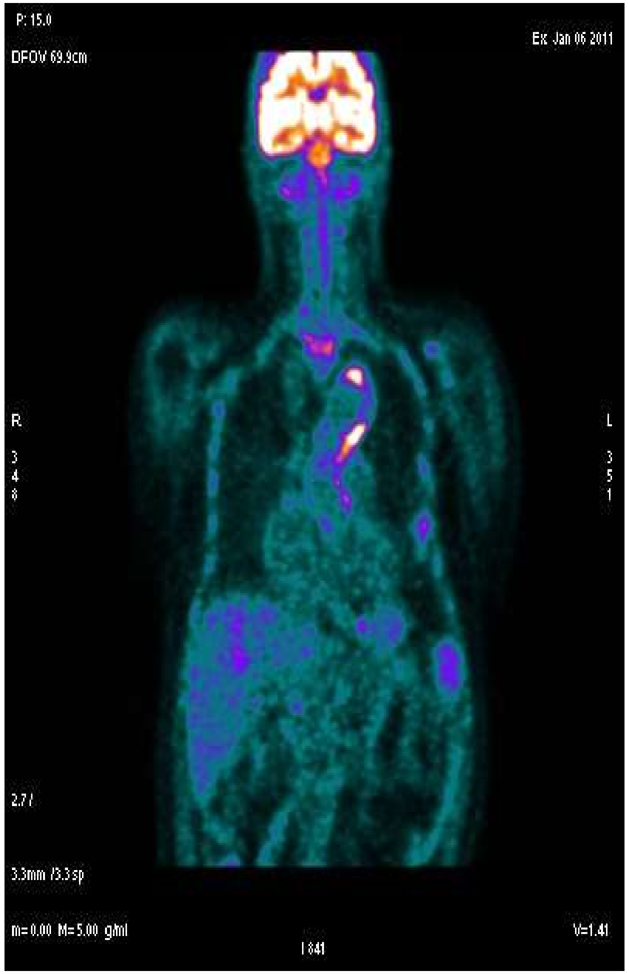
More study is needed to define the utility of ^{18}F-fluorodeoxyglucose positron emission tomography/CT in the diagnosis and management of IE.

American Heart Association®

ACC/AHA 2015

Nuclear imaging in suspected PVGs infection





Diagnostic value of FDG PET/CT in PVGs infection

Mutiple small sample studies

TABLE 1: Summary of literature data regarding the use of ^{18}F-FDG PET imaging requested in suspected vascular graft infection.

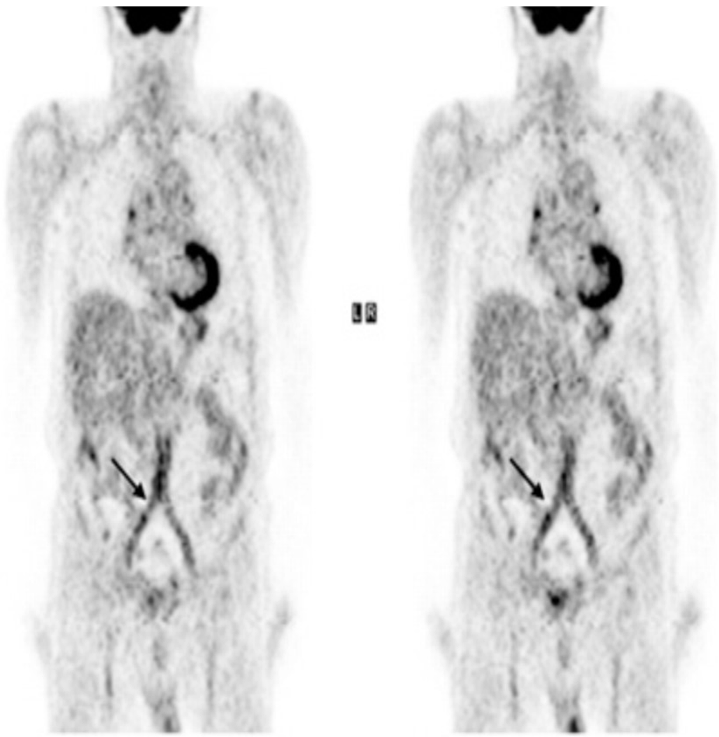
Study	Year	Study Design	Number of patient's	Imaging modality	Interpretation criteria	TP[1]	TN[2]	FP[3]	FN[4]	Sens* %	Spec** %
Fukuchi et al. [10]	2005	prospective	33	PET	Semiquantitative[a]	10	14	8	1	91	64
Keidar et al. [13]	2007	prospective	39	PET/CT	Visual	14	22	2	1	93	91
Lauwers et al. [14]	2008	case series	4	PET	Visual	3	0	1	0	—	—
Spacek et al. [15]	2009	prospective	76	PET/CT	Semiquantitative[b]	54	31	10	1	78.2	92.7
Bruggink et al. [16]	2010	retrospective	25	PET and PET/CT	Semiquantitative[c]	15	10	0	0	93[†]	70[†]
Tokuda et al. [17]	2013	retrospective	9	PET/CT	Semiquantitative[d]	4	5	0	0	—	—

- Good sensitivity, variable specificity

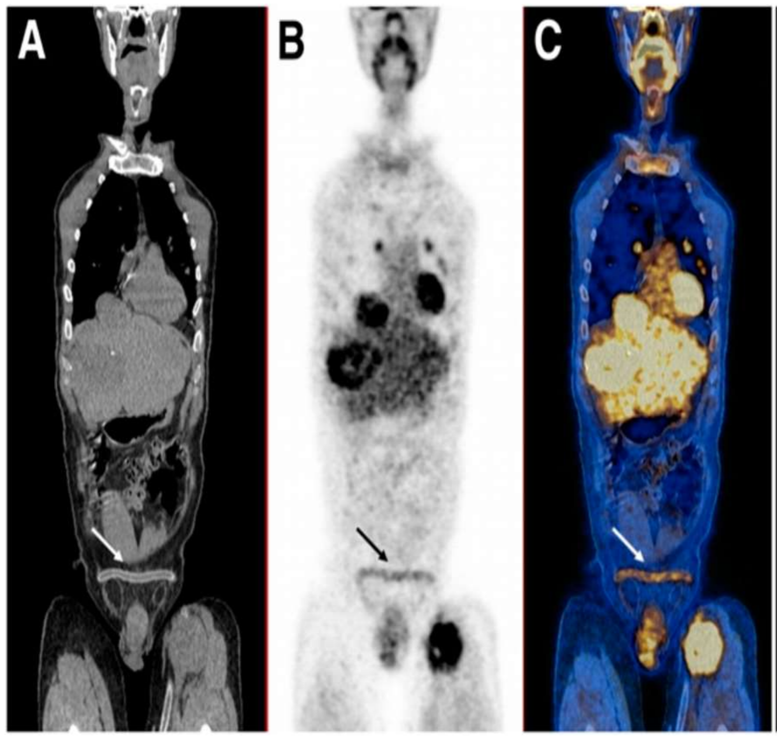
Saleem BR et al, Biomed Res Int 2014

FDG Uptake in **Non**-infected Prosthetic Vascular Grafts

Incidence, Patterns, and Changes over Time



16 years after implant of aorto-bifemoral Dacron graft

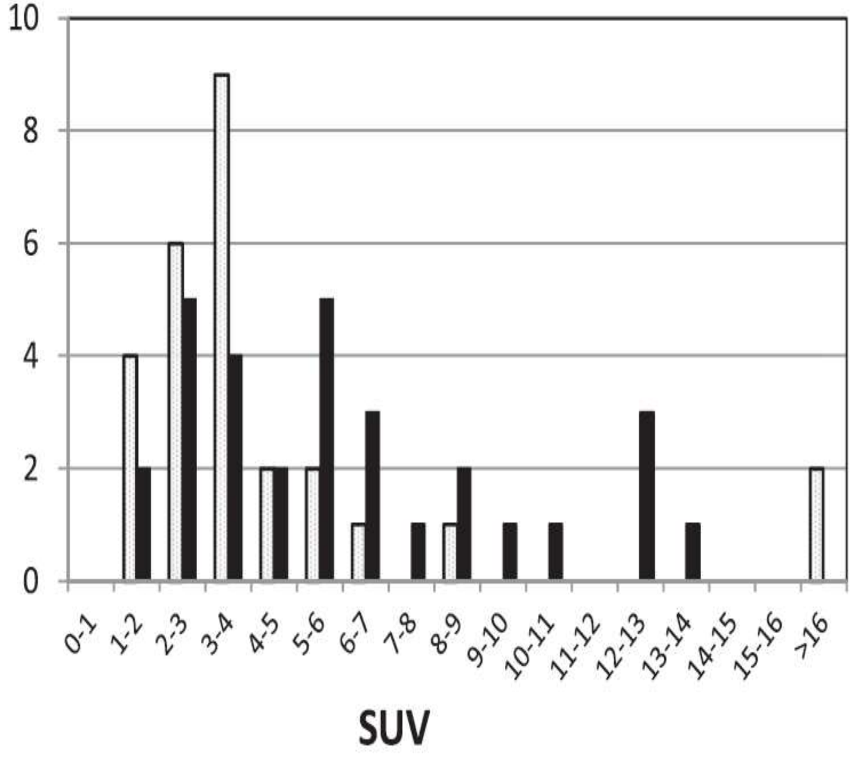


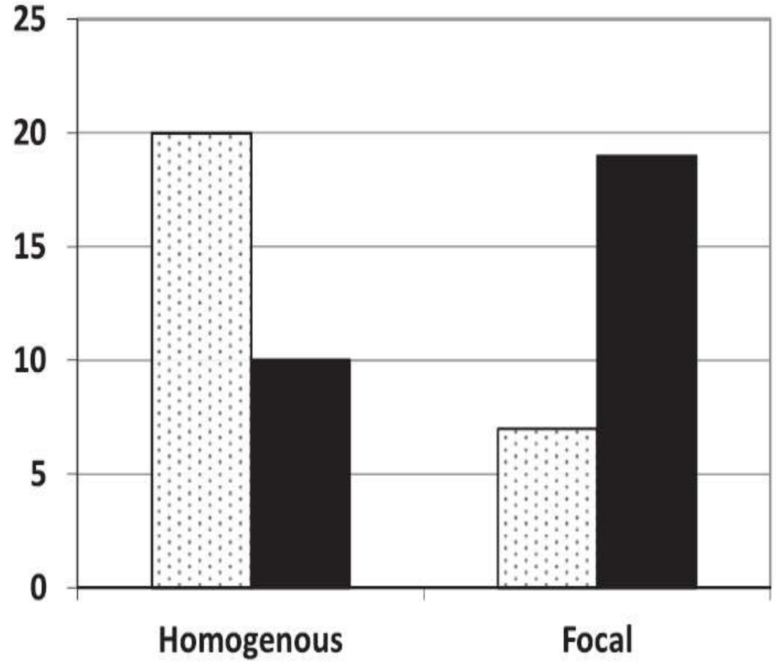
3 years after insertion of femoro-femoral Gore-Tex graft

Keidar Z et al, J Nucl Med 2014

Diagnostic value of FDG PET/CT in PVGs infection

Differential FDG-PET Uptake Patterns in Uninfected and Infected PVGs





Patter
n

☐ Uninfected grafts

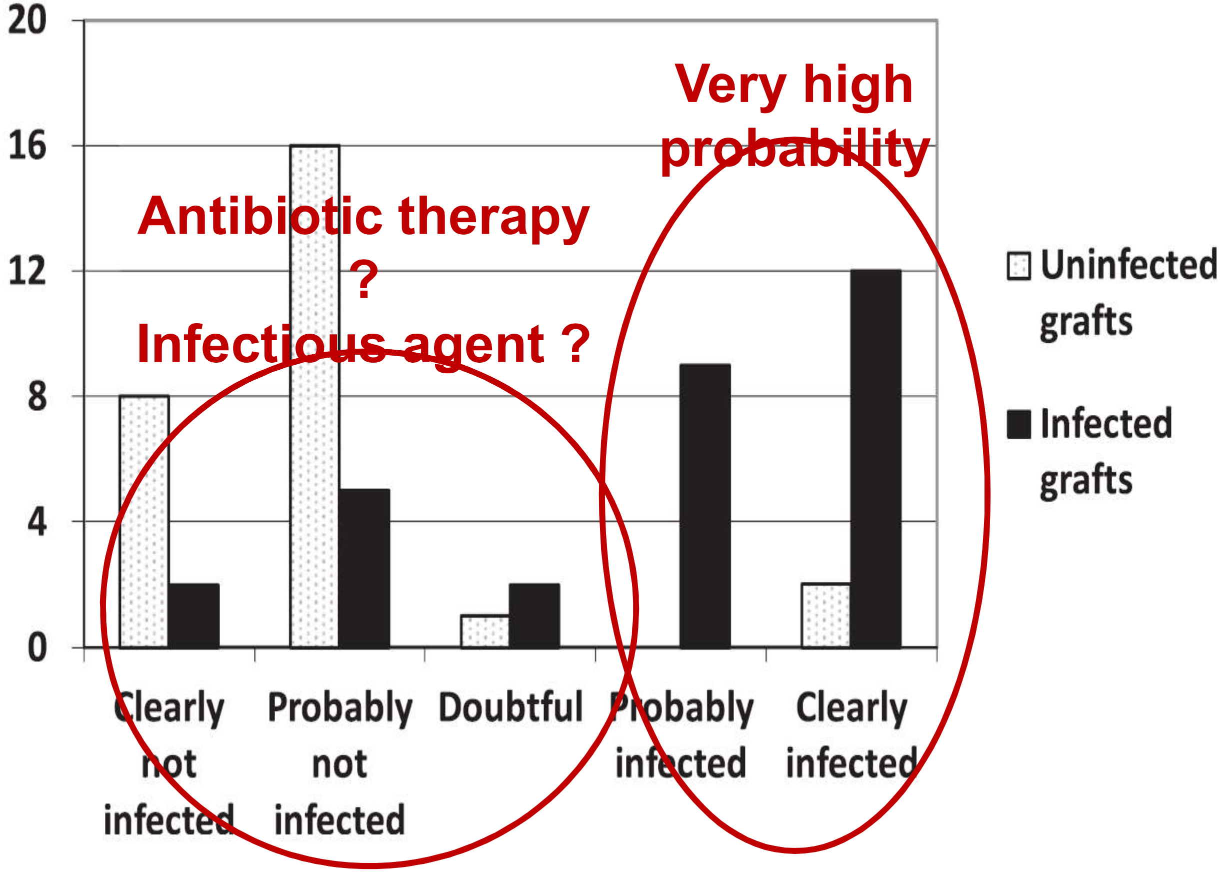
■ Infected grafts

Berger P et al, Eur J Vasc Endovasc Surg 2015

Diagnostic value of FDG PET/CT in PVGs infection

Differential FDG-PET Uptake Patterns in Uninfected and Infected PVGs

Final conclusion of the PET/CT scan



- **FDG uptake patterns in uninfected PVGs largely overlap with those of infected PVGs**

Berger P et al, Eur J Vasc Endovasc Surg 2015

Diagnostic value of WBC SPECT/CT in PVGs infection

Selected studies using ^{99m}Tc-WBCs SPECT

- Liberatore et al. J Nucl Med 1998: 129 pts
  - ***Sensitivity 100%, specificity 92% et accuracy 97%***
- Fiorani et al J Vasc Surg 1993: 37 pts
  - ***Sensitivity 100%, specificity 94% et PPV 90% ar***
- Insall et al. Br J Surg 1990. 17 pts, 8 infected pts.
  - ***8 true positive, 1 false positive, no false negativ***
- Prats et al. J Nucl Med 1994: 36 pts, 20 infected pts
  - ***Sensitivity 100%, specificity 100%***

Imaging modalities in PVG infections

Table 1 Advantages vs. Disadvantages for Different Imaging Modalities in Diagnosing Vascular Prosthetic Graft Infection

Imaging Modality	Advantages	Disadvantages
Ultrasound	No radiation exposure. No contrast-nephrotoxicity Easy and quick to perform	Interference with several artifacts Less differentiating ability compared to other modalities No data on sensitivity and specificity available and interobserver variability
CT	High specificity, relative high sensitivity, fast acquisition procedure Availability in most centres, less invasive Possibility for needle aspiration for microbiological analysis Three-dimensional reconstruction	Decreased sensitivity in low-grade infections Interference with normal postoperative findings in first 6 weeks after surgery
MRI	No radiation exposure. No contrast-nephrotoxicity Could differentiate in small perigraft fluid collections or surrounding inflammatory changes Less invasive and allows tissue characterization Comparable sensitivity and specificity rates to CT	Metal artifacts Diagnostic value for vascular graft infection less investigated compared to other modalities
FDG PET	At least comparable sensitivity and specificity rates to CT Can be fused with CT imaging (or PET-CT) Higher diagnostic rates compared to other modalities in case of low-grade vascular graft infections	Time-invasive investigation Less exact anatomical localization
SPECT	Specificity	Lower resolution and sensitivity compared to FDG PET

Modified from Bruggink JJ *et al,* Semin Vasc Surg 2011

Conclusions (I)

- The diagnosis of IE and VG relies on the conjunction of different criteria which all have limitations.
- Imaging plays a key role in the diagnosis of endocardial involvement and vascular phenomena.
- Indications and pitfalls of echocardiography are well addressed in guidelines.
- Radionuclide imaging (PET/CT, labeled leucocytes) has an incremental diagnostic value in difficult cases (PVE > NV, Vascular graft Infection).
- Impacts on diagnosis and on therapeutic choice may be different according to IE patients (NV/PV)

Conclusions (II)

- Systematic imaging reveals a high incidence of asymptomatic embolic events during acute endocarditis.

- The detection of silent cerebral embolism using cerebral MRI has an impact on diagnosis and therapeutic management.

- Need for further analyses of:
  - Usefulness of systematic multimodality imaging
    - Diagnosis, therapeutic choice, follow-up, prognosis
  - Prognostic assessment of asymptomatic embolism
  - Indications for radionuclide imaging
- Imaging indications must be discussed on an individual basis by a multidisciplinary team

Acknowlegments

- Dr F. Rouzet, Nuclear imaging Bichat, Paris
- Pr B. Iung, Cardiology, Bichat, Paris
- Dr I. Klein, Radiology, Bichat, Paris

Chirurgie valvulaire _ Indications 2015

Table 22 Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)

Indications for surgery	Timing[a]	Class[b]	Level[c]	Ref.[d]
1. Heart failure				
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B	111,115, 213,216
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	I	B	37,115, 209,216, 220,221
2. Uncontrolled infection				
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B	37,209, 216
Infection caused by fungi or multiresistant organisms	Urgent/ elective	I	C	
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	Urgent	IIa	B	123
PVE caused by staphylococci or non-HACEK gram-negative bacteria	Urgent/ elective	IIa	C	
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	B	9,58,72, 113,222
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, $\boxed{\text{and low operative risk}}$	Urgent	IIa	B	9
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent	IIa	B	113
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery[e]	Urgent	IIb	C	

Chirurgie valvulaire _ Indications 2015

Table 22 **Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)**

Indications for surgery	Timing[a]	Class[b]	Level[c]	Ref.[d]
1. Heart failure				
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B	111,115, 213,216
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	I	B	37,115, 209,216, 220,221

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Table 22 Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)

Indications for surgery	Timing[a]	Class[b]	Level[c]	Ref.[d]
1. Heart failure				
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B	111,115, 213,216
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	I	B	37,115, 209,216, 220,221
2. Uncontrolled infection				
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B	37,209, 216
Infection caused by fungi or multiresistant organisms	Urgent/ elective	I	C	
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	Urgent	IIa	B	123
PVE caused by staphylococci or non-HACEK gram-negative bacteria	Urgent/ elective	IIa	C	

Indications for surgery for Heart failure or Uncontrolled infection
NOT MODIFIED