"Role of Imaging techniques in endocarditis and vascular infections”

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"Role of Imaging techniques in endocarditis and vascular infections"
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- Endocarditis
- Vascular infections
- Diagnosis
- Prognosis
- Therapeutic
- Therapeutic FU
Infective Endocarditis

• IE incidence France: stable 25 /10⁶ 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

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 → definite IE
Radionuclide Labelled Leucocytes
Diagnosis of Endocarditis

Diagnostic features of infective endocarditis

- Persistent bacteremia
- Active endocardial pathology
- Predisposing heart disease
- Vascular phenomena
Diagnosis of Endocarditis

Diagnostic features of infective endocarditis

- Persistent bacteremia
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Active endocardial pathology
Diagnosis of Endocarditis

Diagnostic features of infective endocarditis

- Persistent bacteremia
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Vascular phenomena
Diagnosis of Endocarditis

Diagnostic features of infective endocarditis

- Persistent bacteremia
- Predisposing heart disease
- Vascular phenomena
- Active endocardial pathology
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
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

## Valvular surgery_ 2009 ESC indications

### C. Prevention of Embolism

<table>
<thead>
<tr>
<th>Indication</th>
<th>urgency</th>
<th>Class</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic or mitral IE with large vegetations (&gt; 10 mm) following one or more embolic episodes despite appropriate antibiotic therapy</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Aortic or mitral IE with large vegetations (&gt; 10 mm) and other predictors of complicated course (heart failure, persistent infection, abscess)</td>
<td>Urgent</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Isolated very large vegetation (&gt; 15 mm)</td>
<td>Urgent</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

## Valvular surgery_ 2015 ESC indications

### 3. Prevention of embolism

<table>
<thead>
<tr>
<th>Indication</th>
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<th>Evidence</th>
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<tbody>
<tr>
<td>Aortic or mitral NVE or PVE with persistent vegetations &gt;10 mm after one or more embolic episode despite appropriate antibiotic therapy</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Aortic or mitral NVE with vegetations &gt;10 mm, associated with severe valve stenosis or regurgitation, and low operative risk</td>
<td>Urgent</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with isolated very large vegetations (&gt;30 mm)</td>
<td>Urgent</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with isolated large vegetation (&gt;15 mm) and no other indication for surgery</td>
<td>Urgent</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>
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

Clinical suspicion of IE

- Transthoracic echocardiography
  - Prosthetic valve or Intracardiac device
  - Poor quality TTE
  - Positive
  - Negative

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**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• TTE is recommended as the first-line imaging modality in suspected IE.</td>
<td>I</td>
<td>B</td>
<td>64.65</td>
</tr>
<tr>
<td>• TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.</td>
<td>I</td>
<td>B</td>
<td>64, 68–71</td>
</tr>
<tr>
<td>• TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.</td>
<td>I</td>
<td>B</td>
<td>64.71</td>
</tr>
<tr>
<td>• Repeat TTE and/or TOE within 5–7 days is recommended in case of initially negative examination when clinical suspicion of IE remains high.</td>
<td>I</td>
<td>C</td>
<td>66.67</td>
</tr>
<tr>
<td>• Echocardiography should be considered in Staphylococcus aureus bacteraemia.</td>
<td>IIa</td>
<td>B</td>
<td>66.67</td>
</tr>
</tbody>
</table>

**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).  

**C. Intraoperative echocardiography**

- **Intraoperative echocardiography** is recommended in all cases of IE requiring surgery.  

**D. Following completion of therapy**

- **TTE** is recommended at completion of antibiotic therapy for evaluation of cardiac valve morphology and function.  

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HF = heart failure; IE = infective endocarditis; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.  
*Class of recommendation.  
*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
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 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
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
• **$^{18}$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 ($\text{SUV}_{\text{max}}$)
  – valve-to-background ratio: valve $\text{SUV}_{\text{max}}$ /atrial blood $\text{SUV}_{\text{max}}$
18FDG PET/CT

1. High sensitivity
2. Absolute quantification

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

<table>
<thead>
<tr>
<th>Clinical situations</th>
<th>Total Nb pts</th>
<th>Definite EI / total</th>
<th>sensitivity</th>
<th>specificity</th>
<th>PPV False +</th>
<th>NPV False -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Riet 2010 *</td>
<td>Definite IE</td>
<td>25 pts 10/0/15</td>
<td>all</td>
<td>12% (3/25)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Kestler M 2014</td>
<td>Definite IE</td>
<td>47 pts 15/11/24</td>
<td>all</td>
<td>9.5% (4/47)</td>
<td>4/15 PVE (27%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

* NO carbohydrate-restricted diet
## Diagnostic of valvular involvement

### Patients with suspected IE

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

* NO carbohydrate-restricted diet
SUV$_{\text{max}}$ value to improve PET diagnosis performance

Results of the Prosthetic Valve SUV$_{\text{max}}$ and Prosthetic Valve-to-Background SUV$_{\text{max}}$ Ratio According to the Final Diagnosis

The SUV$_{\text{max}}$ was significantly higher in patients with definite PVE in comparison with the 2 other groups (A), whereas the prosthetic valve-to-background SUV$_{\text{max}}$ 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 Mkaïîl, 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_

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**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

Myocardial uptake / Absence of uptake on the PV

Intense / Homogeneous uptake on the PV

Non infected prosthesis
A) Overall population

\[ R = -0.07; P = 0.60 \]

B) Biological valves

\[ R = -0.36; P = 0.04 \]

C) Mechanical valves

\[ R = -0.19; P = 0.40 \]
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

Uptake according to the indications

- **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 in pts with valvular prosthesis 
IE versus NON-IE

L. Saby JACC 2013
Perivalvular uptake in NON-IE patients

According to time from implantation

All patients (n=51)

\[ R = -0.07 \ ; \ p = 0.60 \]

Uptake is not different
Absence of uptake on the PV

Myocardial uptake / Absence of uptake on the PV

Intense / Homogeneous uptake on the PV

Non infected prosthesis
Absence of uptake on the PV

Myocardial uptake / Absence of uptake on the PV

Intense / Homogeneous uptake on the PV

Intense / Heterogeneous uptake on the PV in IE pts

Non infected prosthesis

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-Fluorodeoxyglucose 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.
Diagnosis of peripheral complications
## Diagnosis of peripheral complications

### Patients with **definite IE**

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

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

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<th>specificity</th>
<th>PPV False +</th>
<th>NPV False -</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vos 2010</strong> <strong>Gram pos bacteremia * 115 pts</strong></td>
<td>21/115</td>
<td>11/21 (50%)</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>Saby 2013 Prosthetic valve AND Fever or crp &gt; 10 mg, or bacteremia or positive serology or echo pos</strong> 72 pts</td>
<td>30/72</td>
<td>8/30 (25%)</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>Bonfiglioli 2013 Clinical suspicion</strong> 71 pts</td>
<td>29/71</td>
<td>17/29 (?) (74%)</td>
<td>94%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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

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

<table>
<thead>
<tr>
<th></th>
<th>Definite PVE</th>
<th>Possible PVE</th>
<th>Rejected PVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite PVE</td>
<td>21 (70)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Possible PVE</td>
<td>8 (27)</td>
<td>22 (100)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Rejected PVE</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>10 (50)</td>
</tr>
</tbody>
</table>

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

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 = positron emission tomography/computed tomography.

30 definite IE
Duke classification upgraded due to
- cardiac uptake in 7/8
- peripheric uptake in 1/8

30 definite IE
Duke classification upgraded due to
- cardiac uptake in 7/8
- peripheric uptake in 1/8

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

Minor (excluded versus doubtful or doubtful versus definite) n=4
Major (at least 2 readers with extreme disagreement (excluded versus definite) n=10
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
140 patients with high suspicion of IE
- 70 prosthetic valve patients
- 70 native valve patients
140 patients with high suspicion of IE

- 70 prosthetic valve patients
- 70 native valve patients

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

Taken together, patients who benefited from PET/CT had more frequently
• negative echocardiography or perianular 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

<table>
<thead>
<tr>
<th>Group A</th>
<th>Suspected CIED infection</th>
<th>N=42</th>
</tr>
</thead>
</table>

- Confirmed infection: 35 (83%)

- 18F-FDG PET/CT uptake:
  - 32/42 true positive
  - 1 false positive
  - 3 false negative

- SUVmax: 4.4 ± 1.6

- ETOveg: 12/42

CIED: cardiovascular intra-cardiac electronic device

Sarrazin JF et al. JACC 2012
### CIED infection diagnosis

- **42 pts suspected of CIED infection**

<table>
<thead>
<tr>
<th>Group A (Suspected CIED infection N=42)</th>
<th>Group B (Controls 6 Weeks post implantation N=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confirmed infection</strong></td>
<td><strong>No or mild uptake</strong></td>
</tr>
<tr>
<td>35 (83%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>18F-FDG PET/CT uptake</strong></td>
<td></td>
</tr>
<tr>
<td>32/42</td>
<td></td>
</tr>
<tr>
<td>1 false pos</td>
<td></td>
</tr>
<tr>
<td>3 false neg</td>
<td></td>
</tr>
<tr>
<td><strong>SUVmax</strong></td>
<td></td>
</tr>
<tr>
<td>4.4 ± 1.6</td>
<td>1.2 ± 1.4</td>
</tr>
<tr>
<td><strong>ETOveg</strong></td>
<td></td>
</tr>
<tr>
<td>12/42</td>
<td>0</td>
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</tbody>
</table>

**CIED**: cardiovascular intra cardiac electronic device

Sarrazin JF et al. JACC 2012

<table>
<thead>
<tr>
<th>sensitivity</th>
<th>specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.886</td>
<td>0.857</td>
</tr>
</tbody>
</table>
## CIED infection diagnosis

- 42 pts suspected of CIED infection

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<tr>
<th></th>
<th>Group A Suspected CIED infection N=42</th>
<th>Group B Controls 6 Weeks post implantation N=12</th>
<th>Group C Controls &gt; 6 Mths post implantation N=12</th>
</tr>
</thead>
<tbody>
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**CIED:** cardiovascular intra-cardiac electronic device

*Sarrazin JF et al. JACC 2012*
CIED infection diagnosis

- 27 pts suspected of CIED infection

CIED: cardiovascular intra cardiac electronic device
CIED infection diagnosis

- 27 pts suspected of CIED infection

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<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CIED infection</td>
<td>No CIED infection</td>
</tr>
<tr>
<td>N=11</td>
<td></td>
<td>N=16</td>
</tr>
<tr>
<td><strong>18F-FDG PET/CT uptake</strong></td>
<td>7/11 (4 false neg)</td>
<td>3/16 (2 false pos)</td>
</tr>
<tr>
<td><strong>ETO vegetation</strong></td>
<td>?</td>
<td></td>
</tr>
</tbody>
</table>

**Sensitivity, Specificity, PPV, NPV**

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>63%</td>
<td>86%</td>
<td>77%</td>
<td>76%</td>
</tr>
</tbody>
</table>

CIED: cardiovascular intra cardiac electronic device

Nuclear Imaging
Labelled leukocytes
Radiolabelled leukocytes: methods

1. Blood sample 40-50 ml
2. Centrifugation
3. Plasma, Platelets, Leukocytes, RBC
4. Radiolabelled leukocytes: $^{99m}$Tc-HMPAO
5. PMNs + plasma

Gradient centrifugation
• 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

<table>
<thead>
<tr>
<th>Duke criterion</th>
<th>Positive results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiac only</td>
</tr>
<tr>
<td>Definite IE ($n = 24$)</td>
<td>9</td>
</tr>
<tr>
<td>Possible IE ($n = 25$)</td>
<td>13</td>
</tr>
<tr>
<td>Rejected IE ($n = 2$)</td>
<td>1</td>
</tr>
</tbody>
</table>

$^*$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*
### Final diagnosis after ≥3 mo follow-up

<table>
<thead>
<tr>
<th></th>
<th>Definite (n=14)</th>
<th>Possible (n=4)</th>
<th>Rejected (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG PET +</td>
<td>13 (93)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>FDG PET -</td>
<td>1</td>
<td>2</td>
<td>15 (71)</td>
</tr>
<tr>
<td>WBC SPECT +</td>
<td>9 (64)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>WBC SPECT -</td>
<td>5</td>
<td>3</td>
<td>22 (100)</td>
</tr>
</tbody>
</table>

- 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 vs. WBC SPECT**

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 ($^{64}$Cu, half-life = 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 complications
• Improvement of IE prognosis?
### Cerebral complications of IE

#### Which cerebral complications could be detected?

<table>
<thead>
<tr>
<th>Vascular</th>
<th>Infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ischemic events</td>
<td>• Meningitis</td>
</tr>
<tr>
<td>– Stroke</td>
<td>• Abscess</td>
</tr>
<tr>
<td>– Transient ischemic</td>
<td></td>
</tr>
<tr>
<td>attack (TIA)</td>
<td></td>
</tr>
<tr>
<td>– Silent embolism</td>
<td></td>
</tr>
<tr>
<td>• Hemorrhagic events</td>
<td></td>
</tr>
<tr>
<td>– H. stroke</td>
<td></td>
</tr>
<tr>
<td>– Microbleeds</td>
<td></td>
</tr>
<tr>
<td>– Sub arachnoidal H</td>
<td></td>
</tr>
<tr>
<td>• Aneurysms</td>
<td></td>
</tr>
</tbody>
</table>
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

453 consecutive definite IE patients; 2 French referral centers; January 1990 to March 2005
Systematic Cerebral CT

Cerebrovascular Complications
n=109
24%

Silent Cerebral Embolism
n=17
4%

Ischemic Stroke
n=50
11%

TIA's
n=30
7%

Primary Intracerebral Hemorrhage
n=12
2.6%

Findings of systematic cerebral imaging studies

- CT scanner
- CT scanner with angiography
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%)
Cerebrovascular Complications

- Symptomatic Stroke: n=34
  - ICMA: n=11
  - N=26, 32%
- Silent emboli: n=17
  - (21%)
  - ICMA: n=15, 36% of 47 asymptomatic pts

81 consecutive definite IE patients;

ICMA: intracerebral mycotic aneurysm
Findings of systematic cerebral imaging studies

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

130 patients admitted to Bichat Claude Bernard Hospital, Paris
(June 2005-Sept 2008)
with systematic cerebral MRI with MRangiography

Neurological Complications
n=106

Symptomatic lesions
12%

Large Ischemic lesions
n=33 (24 silent)
25%

Small Ischemic lesions
n=60 (45 silent)
46%

Large Intracerebral Hemorrhage
n=10 (8 silent)
8%

Microbleed
n=74 (66 silent)
58%

Sub. Arachnoidal Hemorrhage
n=11 (11 silent)
8%

Aneurysms
n=10 (10 silent)
8%

Abscess
n=8 (7 silent)
6%
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n=10
(10 silent)

Abscess
n=8
(7 silent)
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

# Symptomatic and Asymptomatic Neurologic Events

Prospective Series with Systematic Imaging

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Imaging</th>
<th>Symptomatic Events (%)</th>
<th>Asymptomatic Embolism (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thuny et al.</td>
<td>453</td>
<td>CT</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>Meshaal et al</td>
<td>81</td>
<td>CT + angio</td>
<td>43</td>
<td>21</td>
</tr>
<tr>
<td>Snygg-Martin et al.</td>
<td>49</td>
<td>MRI</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Cooper et al.</td>
<td>40</td>
<td>MRI</td>
<td>32</td>
<td>48</td>
</tr>
<tr>
<td>Duval et al.</td>
<td>130</td>
<td>MRI</td>
<td>12</td>
<td>47</td>
</tr>
</tbody>
</table>

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 galolyticus* (*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 1 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 ¹⁸F-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 embolii, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Serological phenomena: high anti-streptolysin O antibodies, Rheumatoid factor,
   - 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.
Diagnostic impact of detected lesions

– May account for a minor criteria arterial emboli, mycotic aneurysm, intracranial haemorrhage

– Only assessed for MRI in the IMAGE study
Impact of cerebral lesion detection on IE diagnosis

- Modified-Duke classification upgraded in 32%
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 …,
Cerebral ischemic spot risk factors

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

- Risk factors for Asymptomatic cerebral emboli detected by MRI

<table>
<thead>
<tr>
<th>Lesion Characteristic</th>
<th>All Patients</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(n = 130), n (%)</td>
</tr>
<tr>
<td>Ischemic lesion</td>
<td>68 (52)</td>
</tr>
<tr>
<td>Large systematized ischemic lesion*</td>
<td>33 (25)</td>
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Determinants of asymptomatic ischemic lesions

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>IC 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Vegetation length</td>
<td>1.1</td>
<td>1.03-1.16</td>
<td>p=0.003</td>
</tr>
<tr>
<td>- Staph aureus IE</td>
<td>2.65</td>
<td>1.01-6.96</td>
<td>p=0.05</td>
</tr>
</tbody>
</table>

Cerebral ischemic spot risk factors

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

- Risk factors for Asymptomatic cerebral emboli detected by MRI

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<tbody>
<tr>
<td>Vegetation length</td>
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</tr>
<tr>
<td>Staph aureus IE</td>
<td>2.65</td>
<td>1.01-6.96</td>
</tr>
</tbody>
</table>

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

• 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
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.)*

• **Impact unknown in IE patients**
Microbleeds and IE?
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

<table>
<thead>
<tr>
<th>Lesion Characteristic</th>
<th>All Patients (n = 130), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhagic lesion</td>
<td>79 (61)</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhagic lesion</td>
<td>10 (8)</td>
</tr>
<tr>
<td>Microhemorrhage</td>
<td>74 (58)</td>
</tr>
<tr>
<td>Subarachnoidal hemorrhage</td>
<td>11 (8)</td>
</tr>
</tbody>
</table>

Determinants of microhemorrhages

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>IC 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic valve</td>
<td>8.01 per mm</td>
<td>2.58-24.90</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Anticoagulation therapy</td>
<td></td>
<td>p=0.67</td>
<td></td>
</tr>
</tbody>
</table>

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

Microbleed and ischemic lesions: distinct mechanisms

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

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>IC 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preceding ICH</td>
<td>40.0</td>
<td>2.5–2,870</td>
</tr>
<tr>
<td>CMB ≥ 1</td>
<td>34.0</td>
<td>1.3–17000</td>
</tr>
<tr>
<td>CMB ≥ 2</td>
<td>42.1</td>
<td></td>
</tr>
<tr>
<td>CMB ≥ 3</td>
<td>70.1</td>
<td></td>
</tr>
</tbody>
</table>

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
• 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

Clinical suspicion of IE

Modified Duke criteria (Li)

Definite IE

Possible/rejected IE but high suspicion

Rejected IE Low suspicion

Native valve

Prosthetic valve

1 - Repeat echo (TTE + TOE)/microbiology
2 - Imaging for embolic events
3 - Cardiac CT

1 - Repeat echo (TTE + TOE)/microbiology
2 - 18F-FDG PET/CT or Leucocytes labeled SPECT/CT
3 - Cardiac CT
4 - Imaging for embolic events

ESC 2015 modified diagnostic criteria

Definite IE
Possible IE
Rejected IE
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 galolyticus* (*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 ¹⁸F-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. Serological phenomena such as cardiolipin antibody, anti-β-2-glycoprotein I antibodies, Protein S, 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.
**ESC modified diagnostic criteria**

<table>
<thead>
<tr>
<th>Major criteria</th>
</tr>
</thead>
<tbody>
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</tr>
<tr>
<td>• Community-acquired enterococci, in the absence of a primary focus; or</td>
</tr>
<tr>
<td>b. Microorganisms consistent with IE from persistently positive blood cultures:</td>
</tr>
<tr>
<td>• ≥2 positive blood cultures of blood samples drawn &gt;12 h apart; or</td>
</tr>
<tr>
<td>• All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or</td>
</tr>
<tr>
<td>c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre &gt;1:800</td>
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</table>

| 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.

More study is needed to define the utility of $^{18}$F-fluoro-deoxyglucose 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

Multiple small sample studies

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

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

➢ 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

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

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

Final conclusion of the PET/CT scan

- Very high probability
- Antibiotic therapy?
- Infectious agent?

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

  - Sensitivity 100%, specificity 92% et accuracy 97%

- Fiorani et al J Vasc Surg 1993: 37 pts
  - Sensitivity 100%, specificity 94% et PPV 90% and NPV 100%

  - 8 true positive, 1 false positive, no false negative

  - Sensitivity 100%, specificity 100%
# Imaging modalities in PVG infections

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

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>ultrasound</td>
<td>No radiation exposure. No contrast-nephrotoxicity. Easy and quick to perform.</td>
<td>Interference with several artifacts. Less differentiating ability compared to other modalities. No data on sensitivity and specificity available and interobserver variability.</td>
</tr>
<tr>
<td>CT</td>
<td>High specificity, relative high sensitivity, fast acquisition procedure. Availability in most centres, less invasive. Possibility for needle aspiration for microbiological analysis. Three-dimensional reconstruction.</td>
<td>Decreased sensitivity in low-grade infections. Interference with normal postoperative findings in first 6 weeks after surgery.</td>
</tr>
<tr>
<td>MRI</td>
<td>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.</td>
<td>Metal artifacts. Diagnostic value for vascular graft infection less investigated compared to other modalities.</td>
</tr>
<tr>
<td>FDG PET</td>
<td>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.</td>
<td>Time-invasive investigation. Less exact anatomical localization.</td>
</tr>
<tr>
<td>SPECT</td>
<td>Specificity</td>
<td>Lower resolution and sensitivity compared to FDG PET.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Indications for surgery</th>
<th>Timing</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock</td>
<td>Emergency</td>
<td>I</td>
<td>B</td>
<td>111,115, 213,216</td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>37,115, 209,216, 220,221</td>
</tr>
<tr>
<td>2. Uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>37,209, 216</td>
</tr>
<tr>
<td>Infection caused by fungi or multiresistant organisms</td>
<td>Urgent/elective</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci</td>
<td>Urgent</td>
<td></td>
<td></td>
<td>123</td>
</tr>
<tr>
<td>PVE caused by staphylococci or non-HACEK gram-negative bacteria</td>
<td>Urgent/elective</td>
<td>I</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>3. Prevention of embolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with persistent vegetations &gt; 10 mm after one or more embolic episode despite appropriate antibiotic therapy</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>9,58,72, 113,222</td>
</tr>
<tr>
<td>Aortic or mitral NVE with vegetations &gt; 10 mm associated with severe valve stenosis or regurgitation, and low operative risk</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>9</td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with isolated very large vegetations (&gt;30 mm)</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>113</td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with isolated large vegetations (&gt; 15 mm) and no other indication for surgery°</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td></td>
</tr>
</tbody>
</table>

° Note: The indication for surgery in patients with isolated large vegetations (> 15 mm) and no other indication for surgery should be considered in the context of individual patient characteristics and the specific clinical situation.
### Table 22: Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)

<table>
<thead>
<tr>
<th>Indications for surgery</th>
<th>Timing</th>
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<th>Level</th>
<th>Ref.</th>
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</thead>
<tbody>
<tr>
<td>Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula</td>
<td>Emergency</td>
<td>I</td>
<td>B</td>
<td>111,115, 213,216</td>
</tr>
<tr>
<td>causing refractory pulmonary oedema or cardiogenic shock</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>37,115, 209,216, 220,221</td>
</tr>
<tr>
<td>of HF or echocardiographic signs of poor haemodynamic tolerance</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
### Indications for surgery for Heart failure or Uncontrolled infection

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

<table>
<thead>
<tr>
<th>Indications for surgery</th>
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<td>I</td>
<td>B</td>
<td>37,115, 209,216, 220,221</td>
</tr>
<tr>
<td><strong>2. Uncontrolled infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)</td>
<td>Urgent</td>
<td>I</td>
<td>B</td>
<td>37,209, 216</td>
</tr>
<tr>
<td>Infection caused by fungi or multiresistant organisms</td>
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<td>Urgent/elective</td>
<td>IIa</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

NOT MODIFIED