New imaging techniques in the diagnosis of infective endocarditis

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Paris, France
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Disclosures

Bernard Iung, MD

Consultancy for Edwards Lifesciences

Speaker’s fee from Boehringer Ingelheim and Novartis
Diagnostic features of infective endocarditis

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

- Mobile mass implanted on upstream side of the valve
  - Location
  - Number
  - Maximal length
  - Mobility

- Diagnostic value
  - Sensitivity: TTE 50-70%, TEE >90%
  - Specificity > 90%

- Histology: septic thrombus

- Major criterion in Duke classification
Destructive Valvular Lesions

- Perforations or tears
  - Direct visualisation of the defect (TEE)
  - Regurgitant jet originating from the leaflet
- Valve prolapse (chordal rupture, commissural lesion)
- Abscess / valvular aneurysms
  - Leaflet thickening ± deformation
  - Isolated or adjacent to a vegetation
  - Evolution toward perforation
Perivalvular lesions

- Abscess
  - Perivalvular neocavity
  - May cause regurgitation or fistulae
  - Initially limited to perivalvular thickening
  - Sensitivity: TTE 30-50%, TEE 80-90%

- New paraprosthetic dehiscence
  - Paraprosthetic regurgitation
  - Check if it was not previously diagnosed
  - Major criterion in Duke classification
3D-TEE
Regurgitations

- Valvular (valve destruction)

- Perivalvular
  - Fistulised abscess in upstream and downstream cavities
  - Paraprosthetic regurgitation

- Pitfalls in quantification of regurgitations
  - Eccentric jets
  - Acute regurgitations (concern on the validity of severity criteria)
# Modified diagnostic criteria for infective endocarditis

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Echocardiography of Valve Prostheses

Bioprostheses: lesions on leaflets / ring, perivalvular abscesses
Mechanical prostheses: vegetations on ring, perivalvular abscesses

• Limitations of echocardiography
  – artifacts: false +, false – (more frequent with TTE)
  – shadowing : false –
  – Aortic valve
    • Poor visualization of posterior part with TTE
    • Poor visualization of anterior part with TEE

• Aortic tube (partial, Bentall)
  Frequent false – in peritubular area
Echocardiography for suspected infective endocarditis

If initial TOE is negative but high suspicion for IE remains, repeat TTE and/or TOE within 5–7 days.

IE = infective endocarditis; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

*TOE is not mandatory in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.
Cardiac CT Scan / MRI

In particular for IE on prosthetic valves and/or prosthetic tubes when TTE and TEE are inconclusive.

Sensitivity of CT scan > 90% vs. surgical findings

(Feuchtner et al. J Am Coll Cardiol 2009; 53:436-44
$^{18}$F FDG PET Scan

Incorporation of $^{18}$F FDG by activated leukocytes, monocyte-macrophages, and CD4+ T lymphocytes
**18F FDG PET Scan**

- 72 pts with suspected prosthetic endocarditis
  - ↑ sensitivity of Duke criteria from 70 to 97%
  - ↓ possible IE from 53 to 32%
  

- 92 pts with suspected IE on prosthesis or cardiac devices
  - ↑ sensitivity of Duke criteria from 52 to 91%
  - Reclassification of 90% of possible IE
  - 95% definite rejected IE after PET-CT
  - Better performance when combined with CT angiography

  *(Pizzi et al. Circulation 2015;132:1113-26)*
16 patients referred for TAVR IE suspicion

Final diagnosis (expert-team at 3 months FU):
- definite-IE in 10
- possible-IE in 1
- rejected-IE in 5.

Echocardiography = major criteria in 5 patients (5 vegetations, 2 paravalvular lesions) and new regurgitation in only 1 of them.

Leaflet thickening/increased mean gradient in 70% and 80% of definite-IE.

(Salaun et al. JACC Cardiovasc Imaging 2018;11:143-6)
$^{18}$F FDG PET Scan
Limitations of $^{18}$F FDG PET CT

- Availability, need for specific expertise in cardiac imaging
- Radiation
- High myocardial uptake: need for specific diet
- Lower sensitivity in IE on native valves
  - Resolution (4 mm)
  - Valve mobility
- False negatives due to prolonged prior antibiotic therapy
  (Swart et al. Circulation 2018; 138:1412-27)
Limitations of $^{18}\text{F} \text{FDG PET CT}$

- False positives due to inflammation (3 post-operative months)
- False positive periprosthetic uptake years after surgery
- Importance of uptake pattern (heterogenity)
  
  \[ \text{(Mathieu et al. Circ Cardiovasc Imaging 2017;10:e005585)} \]

- Artifacts from pacing/defibrillation leads (need for specific correction)
- Diagnostic performance can be improved
  - CT scan with iodine injection
    
    \[ \text{(Pizzi et al. Circulation 2015; 132:1113-26)} \]
  - Visual and quantitative assessment of $^{18}\text{F} \text{FDG uptake}$
    
    \[ \text{(Swart et al. Circulation 2018; 138:1412-27)} \]
Radiolabelled Leucocyte Scintigraphy

- Autologous leucocytes are radiolabelled with 99mTc and injected
- Radiolabelled leucocytes accumulate at the site of active infection
- Differentiation between inflammation and infection
18F FDG PET CT and Leucocyte Scintigraphy

• 39 pts with suspected prosthetic IE and inconclusive echo

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<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Pred. Value (%)</th>
<th>Negative Pred. Value (%)</th>
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<tr>
<td>PET CT</td>
<td>93</td>
<td>71</td>
<td>68</td>
<td>97</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>64</td>
<td>100</td>
<td>100</td>
<td>81</td>
</tr>
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• Discrepancies in 12 pts (31%)
  – False – leucocyte scintigraphy (non-pyogenic microorganisms)
  – False + PET CT (< 2 months after surgery)

• Complementarity → possibility of a sequential approach

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<td><strong>2. Imaging positive for IE</strong></td>
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<td>a. Echocardiogram positive for IE:</td>
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<td>• Vegetation;</td>
</tr>
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<td>• Abscess, pseudoaneurysm, intracardiac fistula;</td>
</tr>
<tr>
<td>• Valvular perforation or aneurysm;</td>
</tr>
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<td>• New partial dehiscence of prosthetic valve;</td>
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<td>b. Abnormal activity around the site of prosthetic valve implantation detected by $^{18}$F-FDG PET/CT (only if the prosthesis was implanted for &gt;3 months) or radiolabelled leukocytes SPECT/CT;</td>
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<td>c. Definite paraavalvular lesions by cardiac CT.</td>
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Algorithm for the diagnosis of infective endocarditis

**Clinical suspicion of IE**

**Modified Duke criteria (Li)**

- **Definite IE**
  - Native valve
    - 1 - Repeat echo (TTE + TOE)/microbiology
    - 2 - Imaging for embolic events
    - 3 - Cardiac CT
  - Prosthetic valve
    - 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**

CT = computed tomography; FDG = fluorodeoxyglucose; IE = infective endocarditis; PET = positron emission tomography; SPECT = single photon emission computerized tomography; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

May include cerebral MRI, whole body CT, and/or PET/CT.

See Table 14.
# Neurologic Events

Prospective Series with Systematic Imaging 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>Snygg-Martín et al.</td>
<td>49</td>
<td>MRI</td>
<td>35</td>
<td>48</td>
</tr>
<tr>
<td>Cooper et al.</td>
<td>40</td>
<td>MRI</td>
<td>32</td>
<td>37</td>
</tr>
<tr>
<td>Duval et al.</td>
<td>130</td>
<td>MRI</td>
<td>12</td>
<td>47</td>
</tr>
</tbody>
</table>

*Thuny et al. Eur Heart J 2007;28:1155-61*
*Cooper et al. Circulation 2009;120:585-91*
Cerebral MRI in IE: IMAGE study

Systematic angio-MRI in 130 patients with acute infective endocarditis

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Symptoms</th>
<th>No symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=130</td>
<td>n=16</td>
<td>n=114</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Total</th>
<th>Symptoms</th>
<th>No symptoms</th>
</tr>
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<tbody>
<tr>
<td>≥ 1 lesion</td>
<td>106 (82%)</td>
<td>16 (100%)</td>
<td>90 (79%)</td>
</tr>
<tr>
<td>Ischaemic lesions</td>
<td>68 (52%)</td>
<td>14 (88%)</td>
<td>54 (47%)</td>
</tr>
<tr>
<td>Large systematized lesions</td>
<td>33 (25%)</td>
<td>9 (56%)</td>
<td>24 (21%)</td>
</tr>
<tr>
<td>Small ischaemic lesions</td>
<td>60 (46%)</td>
<td>14 (88%)</td>
<td>46 (40%)</td>
</tr>
<tr>
<td>Haemorrhagic lesions</td>
<td>79 (61%)</td>
<td>10 (63%)</td>
<td>69 (61%)</td>
</tr>
<tr>
<td>Intra-parenchymal haemorrhage</td>
<td>10 (8%)</td>
<td>3 (19%)</td>
<td>7 (6%)</td>
</tr>
<tr>
<td>Microbleeds</td>
<td>74 (58%)</td>
<td>7 (44%)</td>
<td>67 (59%)</td>
</tr>
<tr>
<td>Subarachnoidal haemorrhage</td>
<td>11 (8%)</td>
<td>2 (13%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Unruptured aneurysms</td>
<td>10 (8%)</td>
<td>1 (6%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Cerebral abscess</td>
<td>8 (6%)</td>
<td>1 (6%)</td>
<td>7 (6%)</td>
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Impact of Cerebral MRI on Diagnosis

Change of diagnosis for 17 / 53 non-definite endocarditis (32%) Microbleeds were not taken into account for diagnosis

<table>
<thead>
<tr>
<th>Diagnostic before MRI</th>
<th>Definite n=77</th>
<th>Possible n=50</th>
<th>Excluded n=3</th>
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<tr>
<td>Diagnostic after MRI</td>
<td></td>
<td></td>
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<tr>
<td>Definite n=91</td>
<td>77</td>
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Impact of Cerebral MRI on Therapy

24 patients (18%)

- Anticoagulant therapy only  n=1
- Antibiotic therapy only  n=5
- Change in valvular surgery  n=18
  - Change in date  n=12 (6 delayed, 6 earlier)
  - Contra-indication  n=2
  - Indication  n=2
  - Type of indication  n=1
  - Valvular substitute  n=1
  - (associated to change in medical therapy in 3 patients)

Embolisation of mycotic aneurysm in 3 patients before surgery

Abdominal Imaging

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Spleen</th>
<th>Kidneys</th>
<th>Liver</th>
<th>Vessels</th>
</tr>
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<tr>
<td>4 European centres</td>
<td>384</td>
<td>13</td>
<td>6</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>AEPEI French survey</td>
<td>497</td>
<td>17</td>
<td>9</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Asymptomatic patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Image Abdo *</td>
<td>58</td>
<td>26</td>
<td>9</td>
<td>0</td>
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* Systematic MRI

Thuny et al. Circulation 2005;112:69-75
Impact of Systematic Abdominal Imaging

- 58 patients from the IMAGE study who underwent both cerebral and abdominal MRI
- $\geq 1$ abdominal lesion in 20 patients (34%)
- MRI led to upgrade Duke classification in 8 patients:
  - Due to cerebral MRI in 4 patients
  - Due to both cerebral and abdominal MRI in 4
  - Never exclusively due to abdominal MRI
- Changes in therapeutic decisions in 11 patients (19%):
  - Due to cerebral MRI in 4 patients
  - Due to both cerebral and abdominal MRI in 7
  - Never exclusively due to abdominal MRI

Impact of Systematic Abdominal Imaging

Systematic thoraco-abdomino-pelvic CT scan in 522 patients with suspected IE

- 217 (42%) had ≥ IE-related lesion
- Upgrade to definite IE in 0.8% of patients
- No impact on medical or surgical therapy
- Specific treatment needed in 1.9% of asymptomatic patients
- 15% acute renal failure within 5 days

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Detection of Extra-Cardiac Lesions by $^{18}$F FDG PET CT

- Cardiac and extra-cardiac imaging in a single whole-body acquisition
- May detect portal of entry and/or embolic events
- Limited value of cerebral imaging due to high physiological uptake of $^{18}$F-FDG by the brain
Impact of systematic $^{18}$F FDG PET CT TEPVENDO Multicentre Prospective Study

Systematic $^{18}$F FDG PET SCAN in 140 patients treated for IE (80 definite IE): 70 IE on native valves, 70 prosthetic IE

- Cardiac uptake in 24% of native IE and 67% of prosthetic IE
- Extra-cardiac uptake in 51% of native IE and 44% of prosthetic IE
- Change in Duke classification in 6% of native IE and 24% of prosthetic IE
- Changes in diagnosis or therapy with PET scan in patients with
  - Possible IE
  - Negative echocardiography
  - Peri-valvular lesions

(Duval et al. submitted)
Infective Endocarditis on CIED

- 6-13% of cases of endocarditis  
  (Athan et al. JAMA 2012;307:1727-35)

- Difficulties of diagnosis  
  Frequent lead infection without vegetation (Klug et al. Circulation 2007;116:1349-55)

- Usefulness of nuclear imaging  
  PET CT  
  (Ploux et al. Heart Rhythm 2011;8:1478-81)  
  Leucocyte scintigraphy (Erba et al. JACC Cardiovasc Imaging 2013;6:1075-86)

- Indication of device removal
IE on CIED

Visualisation of all parts of pacing leads and device pocket

Conclusions

• Echocardiography remains the cornerstone of the diagnosis of cardiac injury in IE. Its sensitivity is greatly increased with TEE.

• Multimodality imaging improves the diagnosis when echocardiography is doubtful or not conclusive:
  – Cardiac CT scan/MRI,
  – $^{18}$F FDG PET CT, possibly completed by leucocyte scintigraphy, particularly for IE on foreign material.
Conclusions

• Non-cardiac imaging frequently detects non-cardiac embolism which impacts diagnosis and therapeutic management:
  – Impact of cerebral imaging (in particular MRI),
  – Limited impact of abdominal imaging,
  – Promising perspectives of $^{18}$F FDG PET CT.

• Need for:
  – Tailored approach according to clinical context and results of investigations.
  – Specific expertise in imaging of infective endocarditis.
The Endocarditis Team

Clinician/Cardiologist
- Patient History
- Fulfilment of Duke Criteria
- Overall responsibility for in-patient & out-patient management

Primary care physician
- Patient History
- Symptoms
- Referral

Specialists
- Infectious disease specialist
- Renal physician
- Haematologist
- Rheumatologist
- Orthopaedic surgeons

Microbiologist
- Identification of aetiological agent
- Guidance on antimicrobial therapy

Histopathologist
- Microscopy of excised valve tissue/emboli/vegetation

Cardiac imaging specialist
- TTE
- TEE

Nuclear Physician (PET/CT)
- Echo inconclusive
- Surgical intervention (ICED)
- Monitoring embolic events & metastatic infection

Cardiac Surgeon
- Removal/replacement of valves and ICED
- Cardiac repair

CT/MRI specialists
- Monitoring embolic events & metastatic infection in cases of secondary complications

(Millar, Habib and Moore  Heart 2016;102:796-807)