



PERCORSO DIAGNOSTICO DELLE INFEZIONI DEL TORRENTE CIRCOLATORIO: FOCUS SULLE ENDOCARDITI

Ruolo della Medicina Nucleare nella diagnosi delle endocarditi

Silvia Morbelli

S.C. Medicina Nucleare

Città della Salute e della Scienza di Torino

Università' di Torino



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FDG PET in inflammation and infections: from a false positive finding to clinical impact

Penicillin Discovery



Alexander Fleming

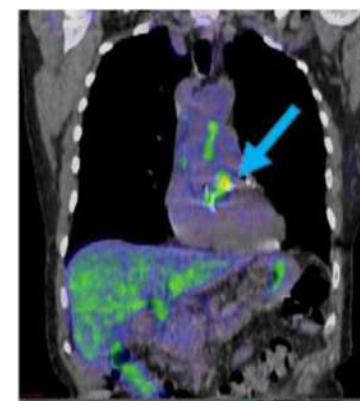
Lung Cancer Staging



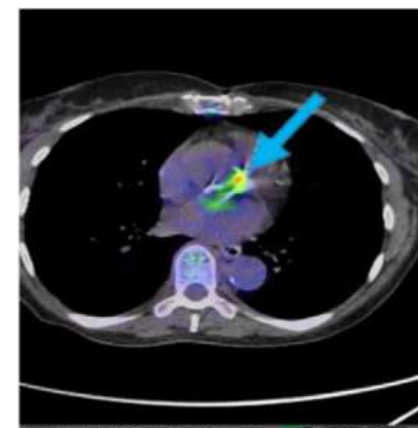
Suspected Recurrence after SBRT



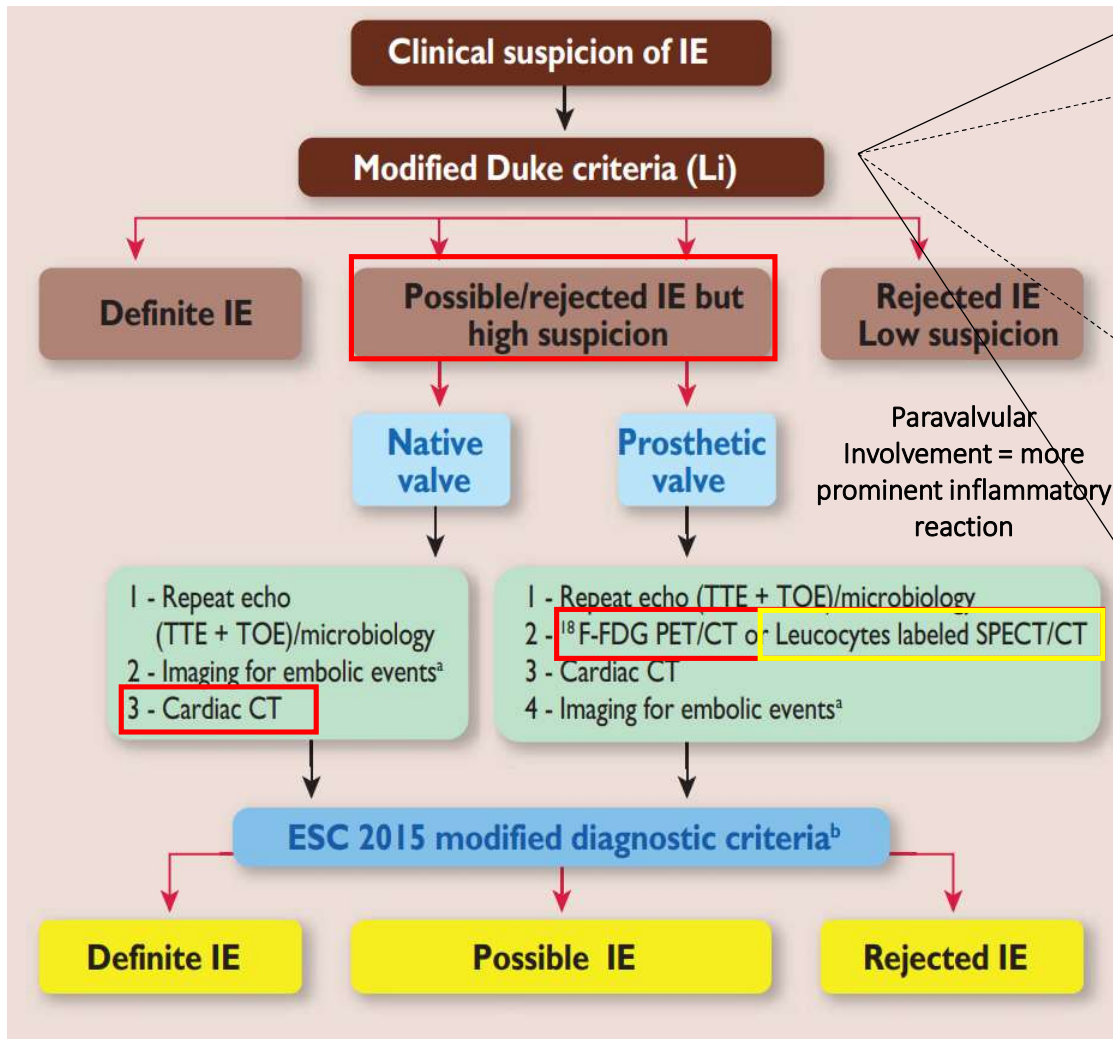
Morbelli et al EJNMMI 2013 Suppl 10



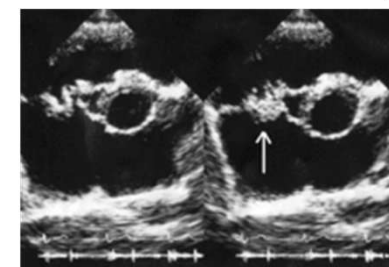
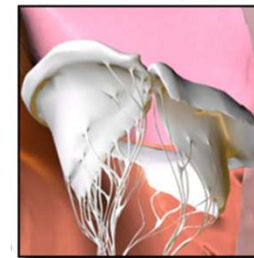
PET in Endocarditis



In 2021 the Centers for Medicare & Medicaid Services (CMS) retired a noncoverage decision for FDG PET for infection, and inflammation imaging and coverage determinations are now made locally



Major criteria
1. Blood cultures positive for IE a. Typical microorganisms consistent with IE from 2 separate blood cultures: • <i>Viridans streptococci</i> , <i>Streptococcus gallolyticus</i> (<i>Streptococcus bovis</i>), <i>HACEK</i> group, <i>Staphylococcus aureus</i> ; 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 <i>Coxiella burnetii</i> 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.

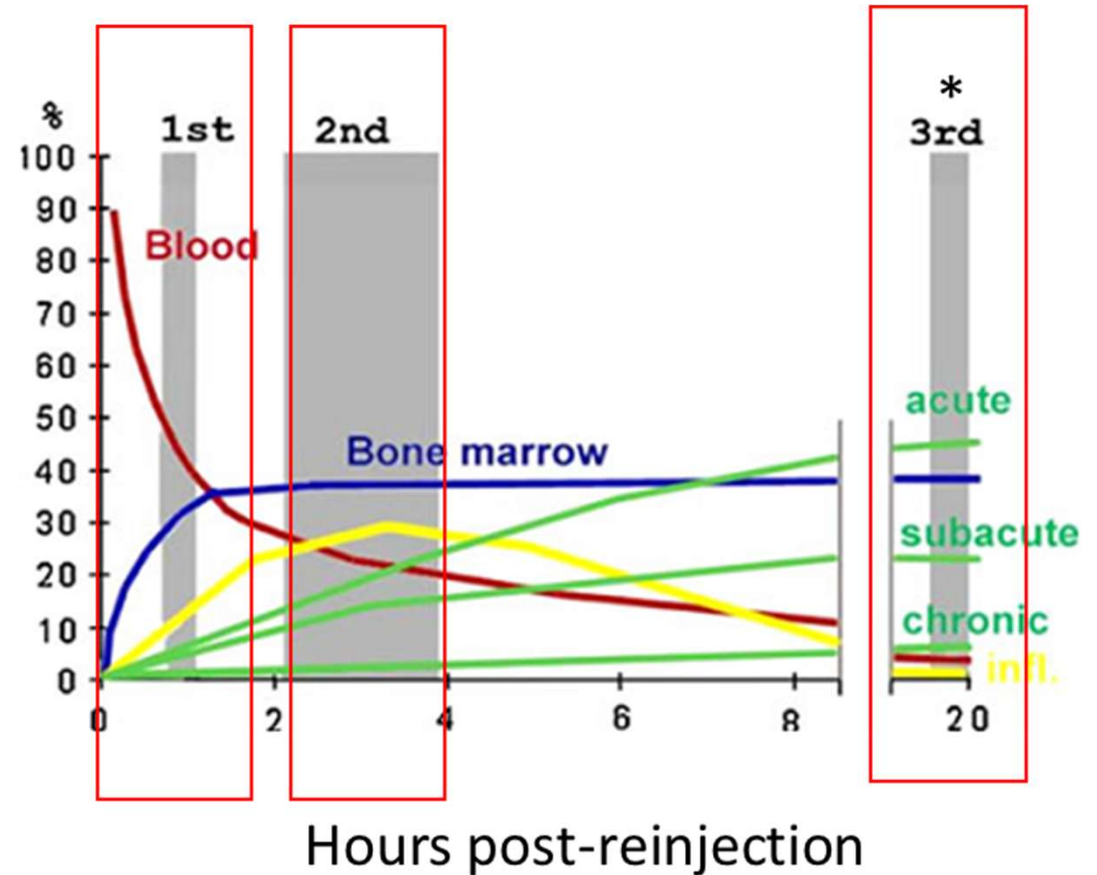


2015 ESC Guidelines Eur Heart Journal 2015

The decreased sensitivity of TTE/TOE for detecting vegetations in prosthetic valves highlights the need for adjunct imaging techniques

Labelled White Blood Cells Scintigraphy:

- Targets a mechanism of disease, not the disease
- Time-consuming (disposable sterile close devices for labelling are now available)
- Requires highly specialized staff (safety consideration)
- Lower Sensitivity for Fungine Infections

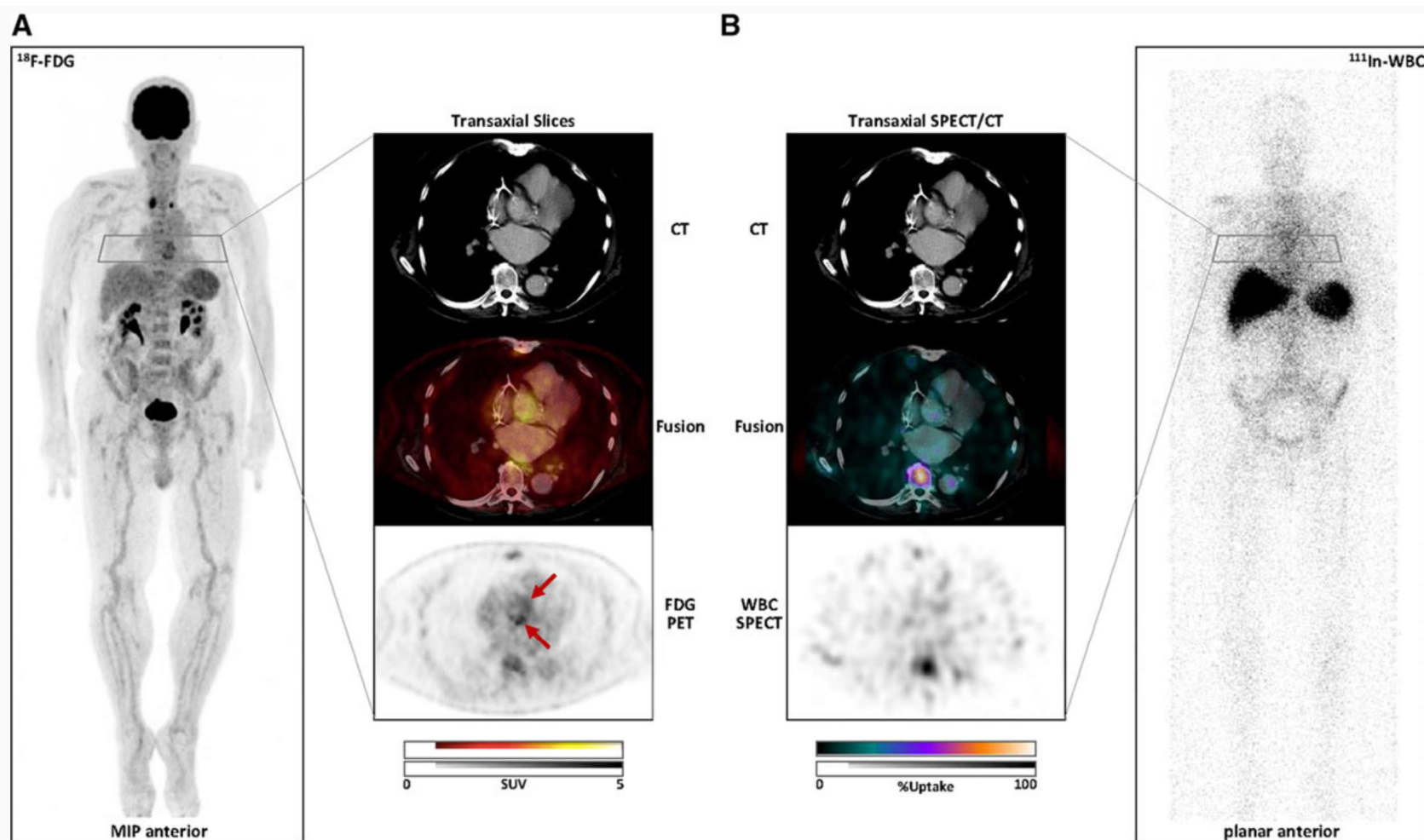


Signore et al 2011

Increasing specificity in suspected IE with WBC-labeled imaging

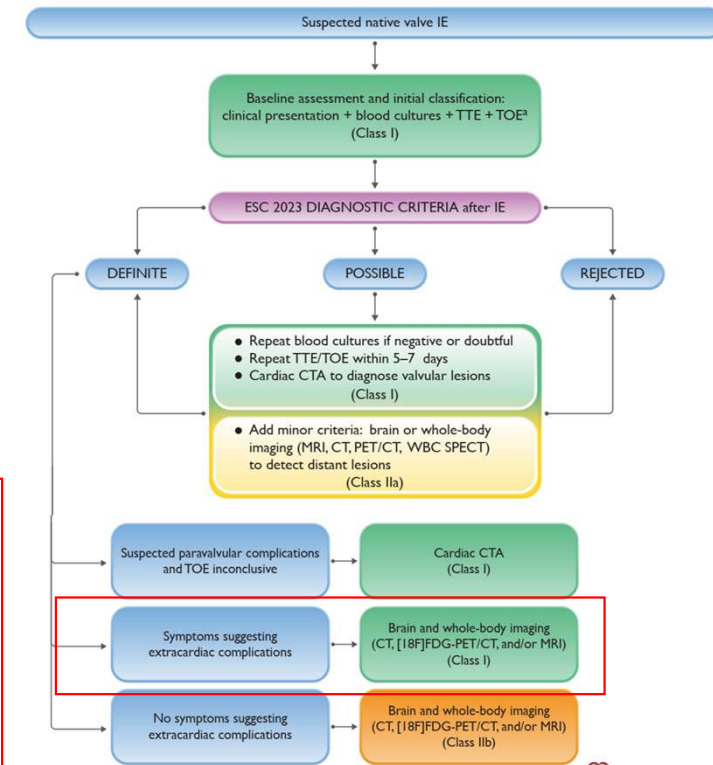
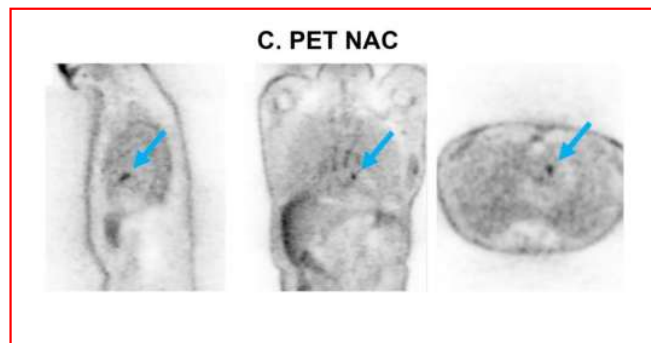
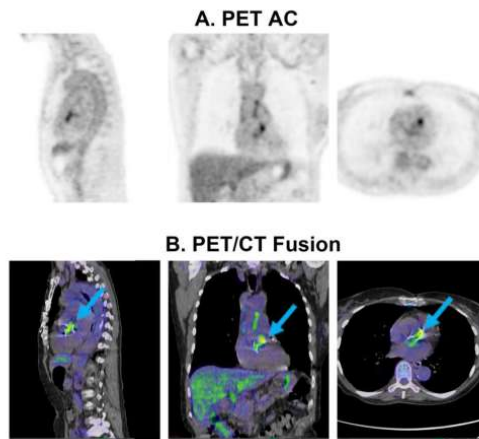
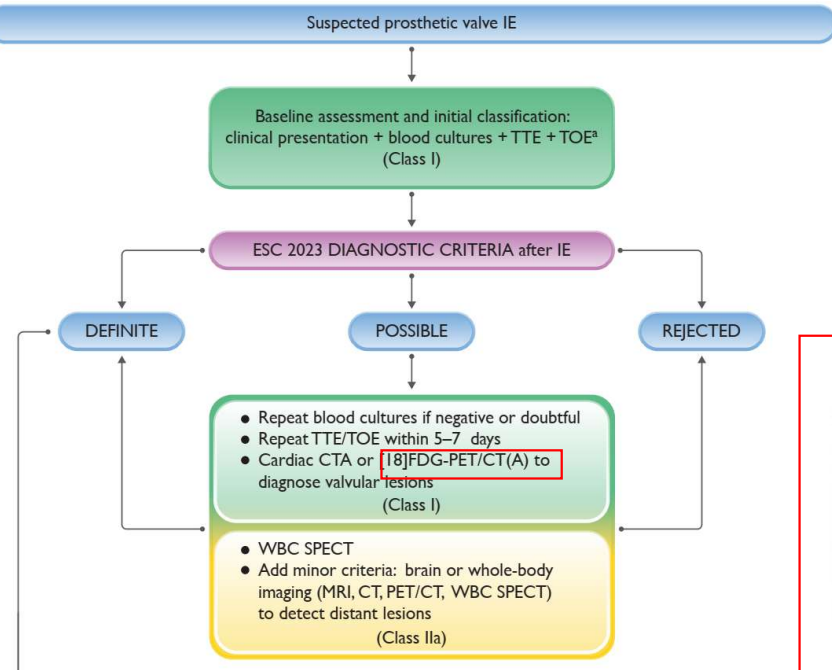
In specific cases WBC-labeled imaging may rule out the occurrence of IE, after inconclusive FDG PET/CT imaging

SPECT/CT may help to reduce the number of misdiagnosed IE cases classified in the 'possible IE' category by the modified Duke criteria



Sohns et al. Circ Cardiovasc Imaging 2017

2023 ESC Guidelines for the management of endocarditis



Meta-analysis showed 86% sensitivity and 84% specificity for [18F]FDG-PET/CT in PVE



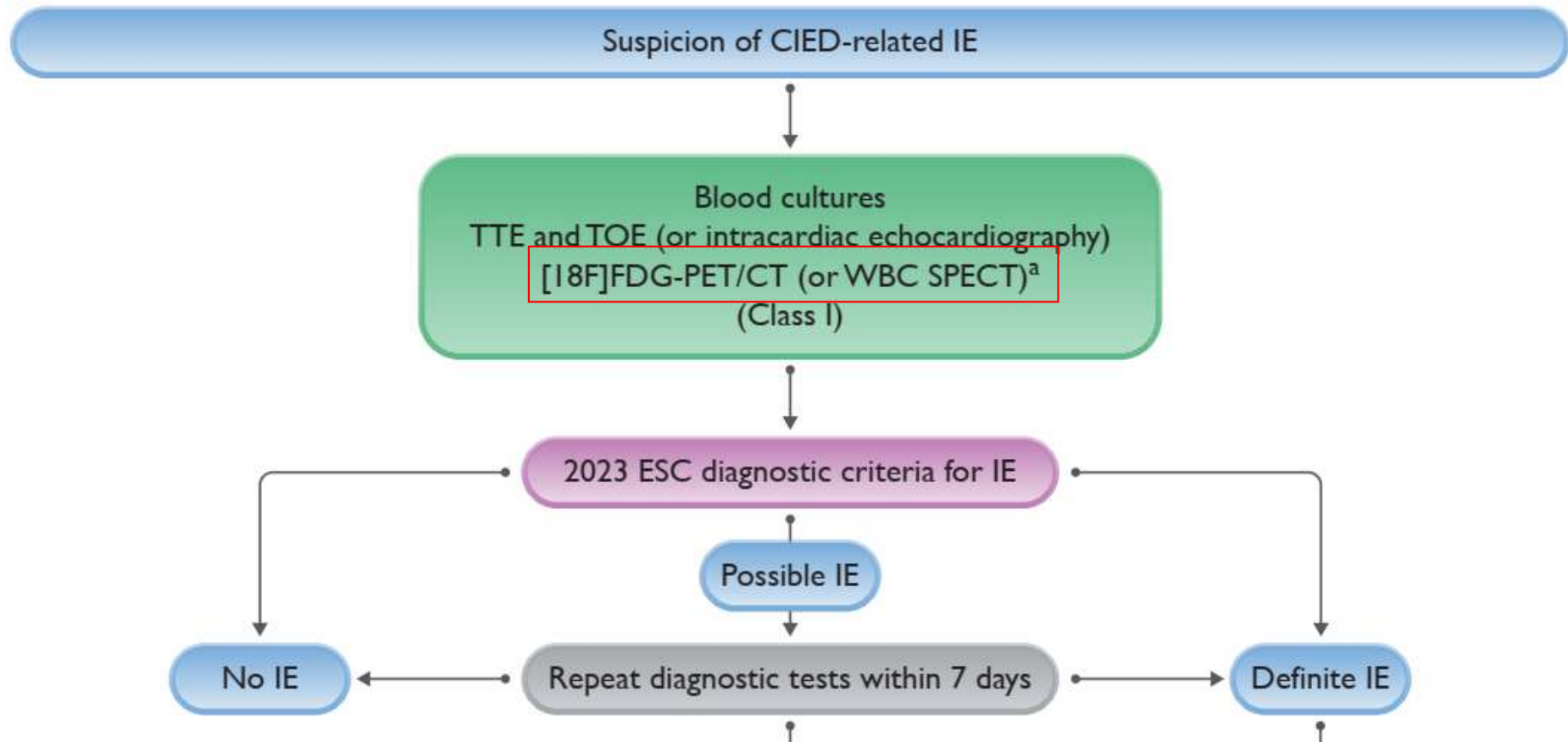
ESC

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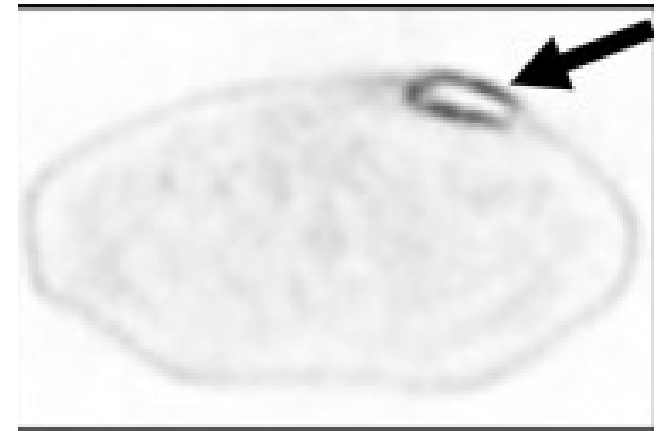
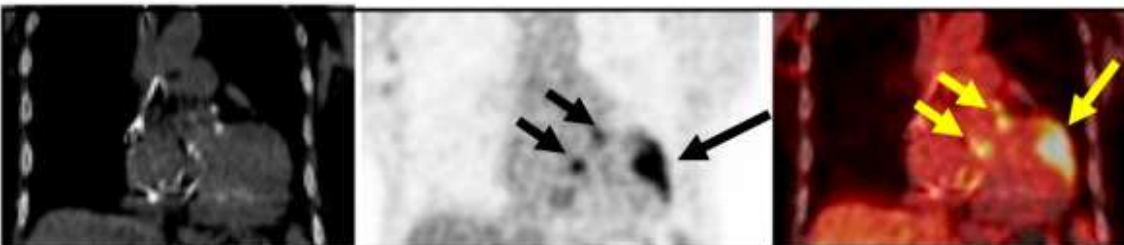
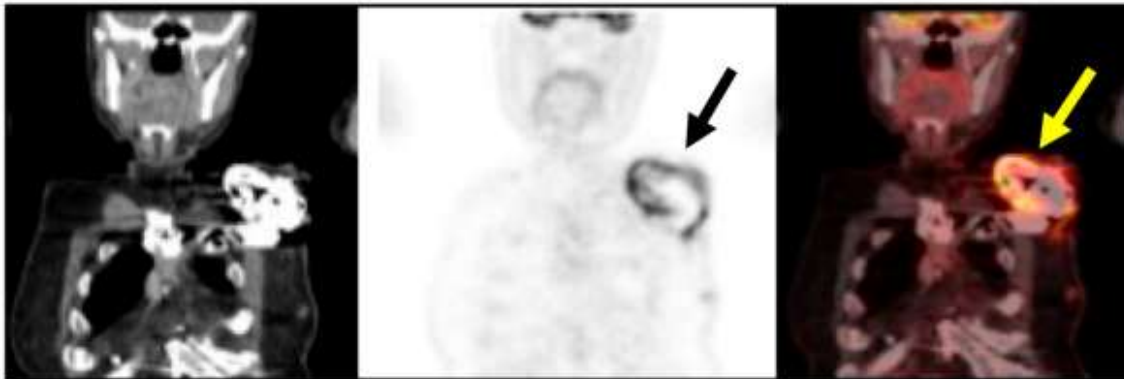
European Heart Journal (2023) 00, 1–95
<https://doi.org/10.1093/eurheartj/ehad193>

ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis



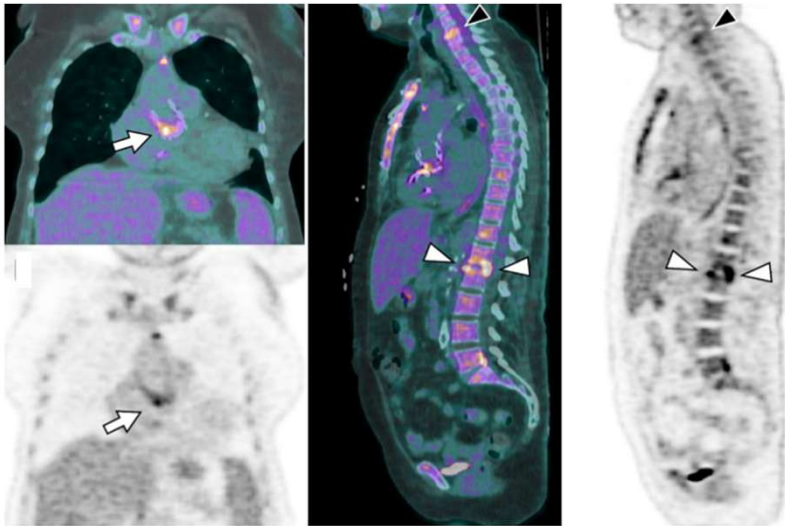
Infection involving the pocket of the device



Multimodal Imaging in IE and the contribution of FDG PET

Table 1. Applications of ¹⁸ F-FDG PET/CT for evaluation of suspected cardiovascular infection.
<ul style="list-style-type: none">• Define extent of infection (e.g., involvement of the ascending aortic root)• Localize infection (particularly with multiple devices/prostheses)• Identify infection in areas not or suboptimally imaged by TEE (prosthetic material, conduits)• Detect abscess• Detect infectious complications• Identify embolic phenomena• Identify portal of entry (to address other areas of infection)• Guide risk assessment• Detect metabolically active lymph nodes• Exclude endocarditis as a source of fever/symptoms, particularly in suspected prosthetic valve endocarditis, and is less reliable for possible native valve endocarditis or CIED-related infection

ASNC Recommendations 2024



Clinical Scenarios	Native Valves		Prosthetic Valves	
	¹⁸ F-FDG PET/CT	Radiolabeled Leukocyte SPECT/CT	¹⁸ F-FDG PET/CT	Radiolabeled Leukocyte SPECT/CT
2. Possible IE or IE Rejected by Modified Duke-Li Criteria but High Clinical Suspicion				
2.1 Gram-positive bacteremia with negative echo—Typical organism for IE**	A (7.5)	M (5)	A (8)	A (7.5)
2.2 Gram-positive bacteremia with negative echo—Atypical organism for IE	A (7.5)	M (5)	A (7.5)	A (7.5)
2.3 Gram-negative bacteremia with negative echo—Typical organism for IE (HACEK) [†]	A (7.0)	M (*)	A (7.5)	M (5.5)
2.4 Gram-negative bacteremia with negative echo—Atypical organism for IE (non-HACEK)	M (5)	M (*)	A (7.5)	M (5)
2.5 Fungemia with negative echo	M (5)	R (2)	A (7.5)	R (1.5)

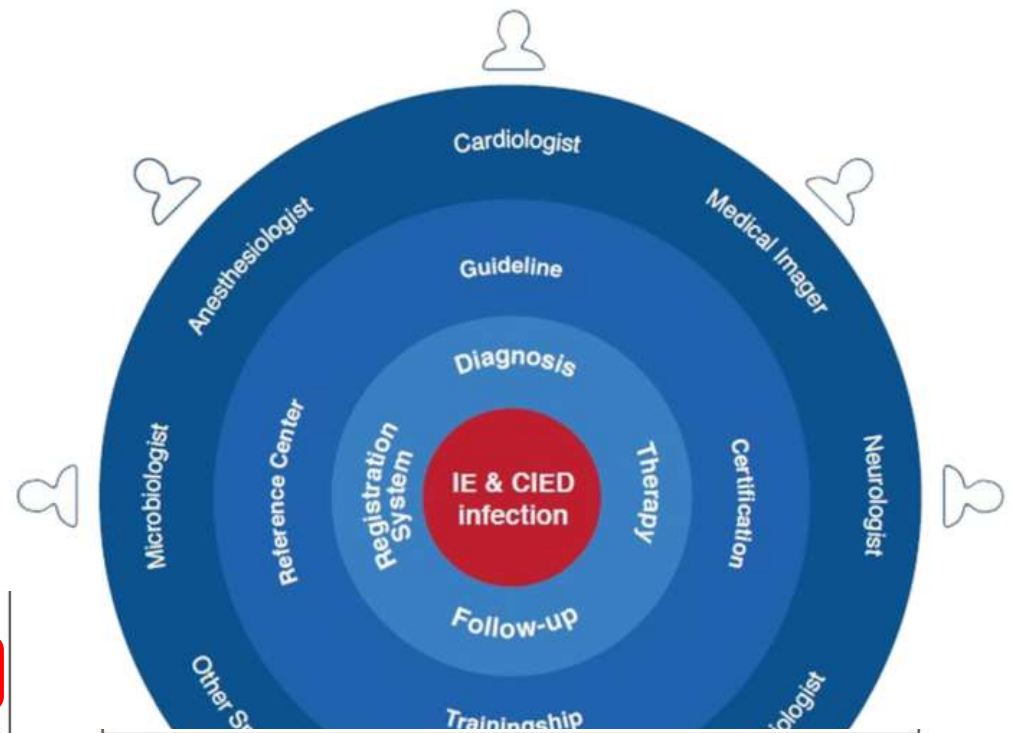
The 'Endocarditis Team'

When to refer a patient with IE to an 'Endocarditis Team' in a reference centre

1. Patients with complicated IE (i.e. endocarditis with HF, abscess, or embolic or neurological complication or CHD), should be referred early and managed in a reference centre with immediate surgical facilities.
2. Patients with non-complicated IE can be initially managed in a non-reference centre, but with regular communication with the reference centre, consultations with the multidisciplinary 'Endocarditis Team', and, when needed, with external visit to the reference centre.

Characteristics of the reference centre

1. Immediate access to diagnostic procedures should be possible including TTE, TOE, multislice CT, MRI, and nuclear imaging.
2. Immediate access to cardiac surgery should be possible during the early stage of the disease, particularly in case of complicated IE (HF, abscess, large vegetation, neurological, and embolic complications).
3. Several specialists should be present on site (the 'Endocarditis Team'), including at least cardiac surgeons, cardiologists, anaesthesiologists, ID specialists, microbiologists and, when available, specialists in valve diseases, CHD, pacemaker extraction, echocardiography and other cardiac imaging techniques, neurologists, and facilities for neurosurgery and interventional neuroradiology.

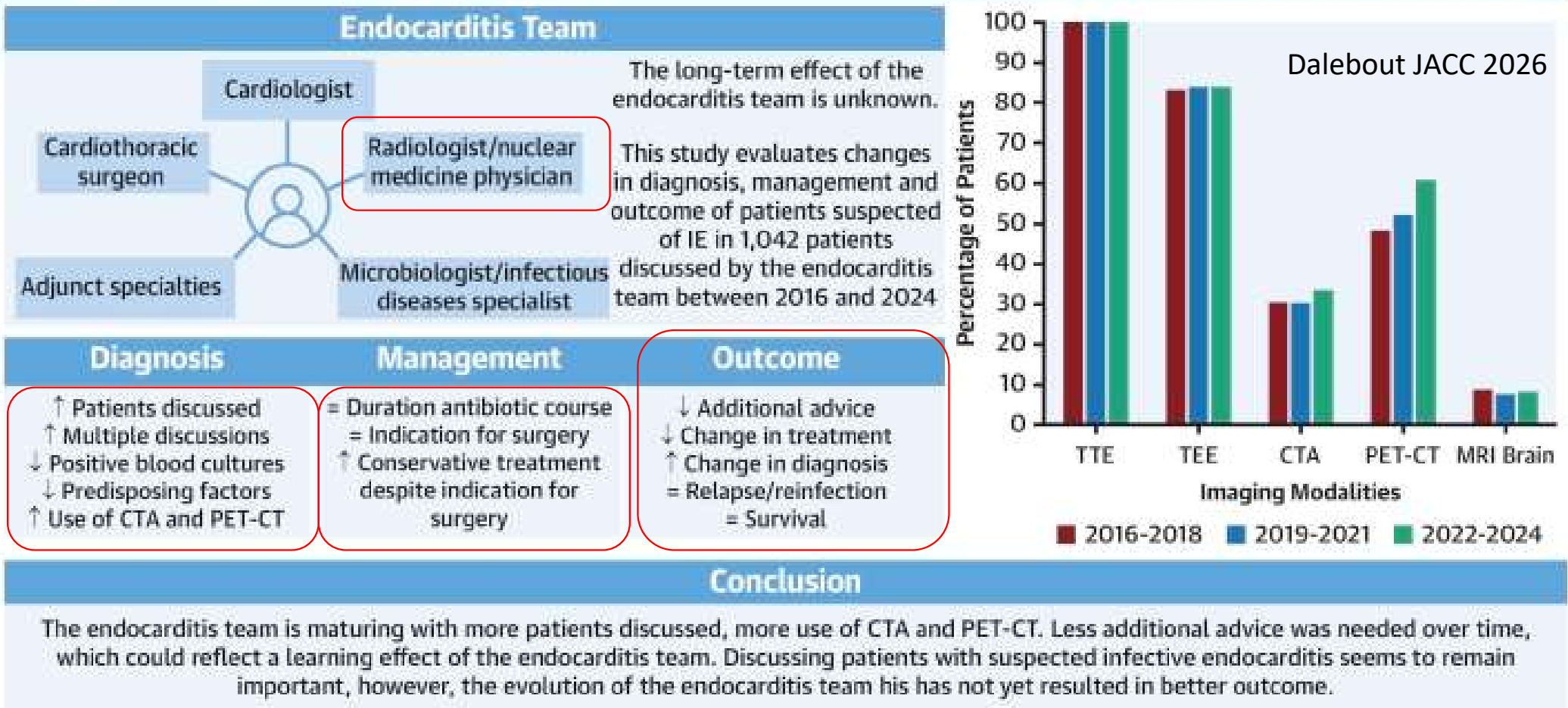


Role of the 'Endocarditis Team'

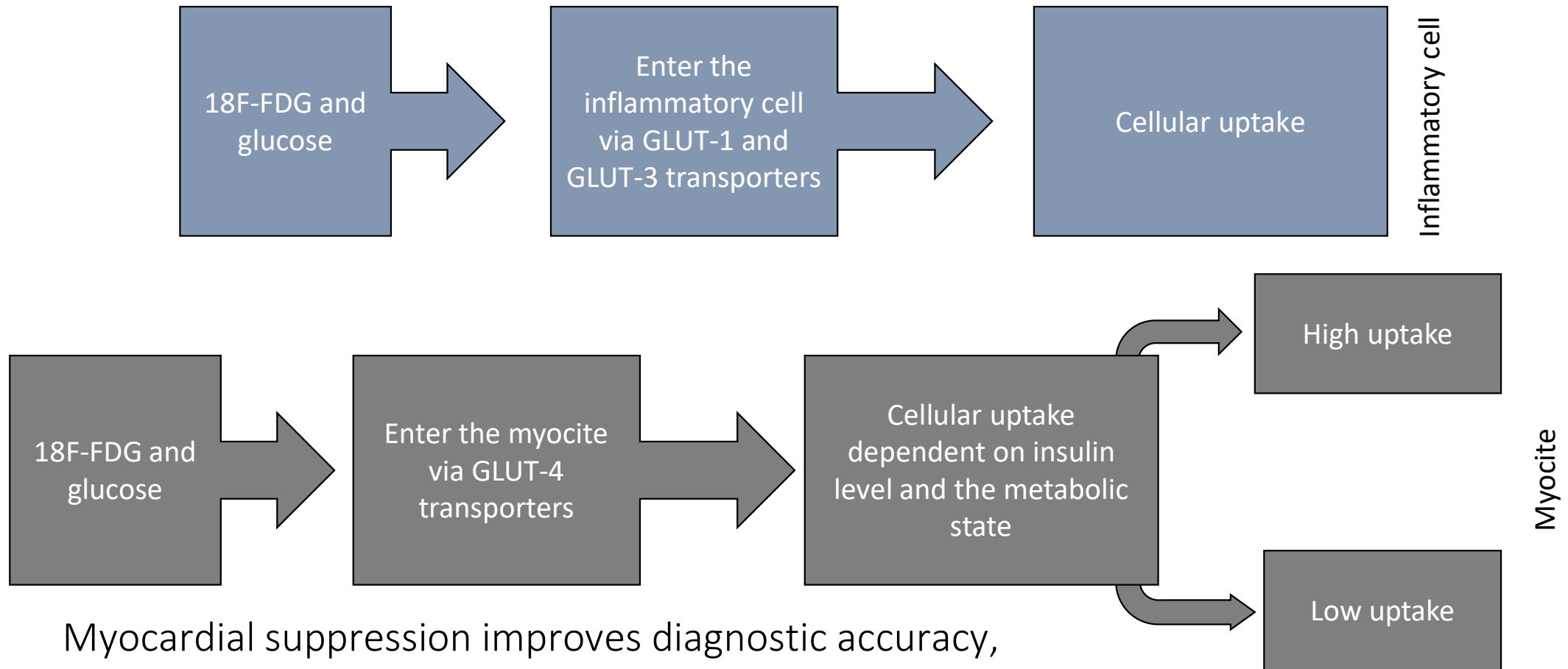
1. The 'Endocarditis Team' should have meetings on a regular basis in order to discuss cases, take surgical decisions, and define the type of follow-up.
2. The 'Endocarditis Team' chooses the type, duration, and mode of follow up of antibiotic therapy, according to a standardized protocol, following the current guidelines.
3. The 'Endocarditis Team' should participate in national or international registries, publicly report the mortality and morbidity of their centre, and be involved in a quality improvement programme, as well as in a patient education programme.
4. The follow-up should be organized on an outpatient visit basis at a

CENTRAL ILLUSTRATION: Changes in Diagnosis, Management, and Outcomes in Patients With Infective Endocarditis from 2016 to 2024

Changes in Diagnosis, Management, and Outcomes in Patients With Infective Endocarditis From 2016 to 2024



FDG PET/CT in Infective Endocarditis: patient preparation



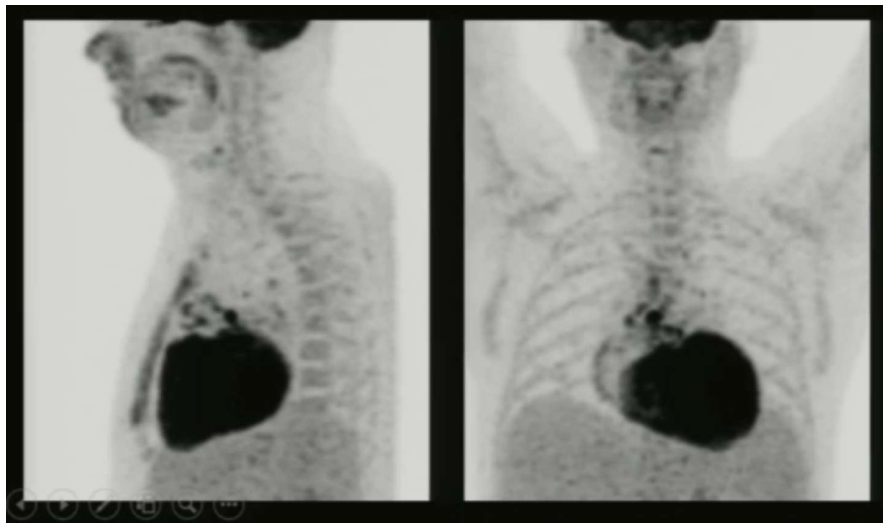
Myocardial suppression improves diagnostic accuracy, particularly for IE assessment, but can be withheld when urgent imaging is required.

Adapted from Osborne et al. J Nucl Cardiol 2016

FDG PET/CT in Infective Endocarditis: patient preparation

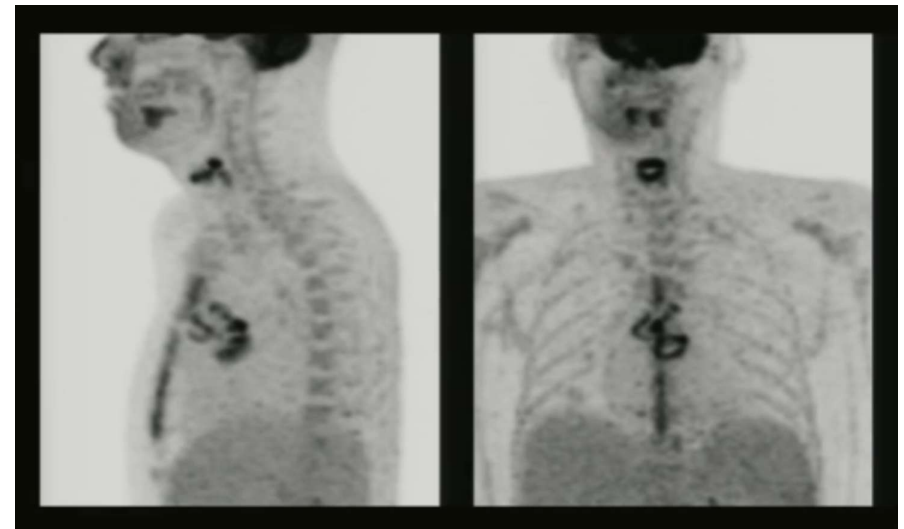
no specific patient preparation

- Variable amount of physiological myocardial uptake
- Lesions may be «lost» in high background



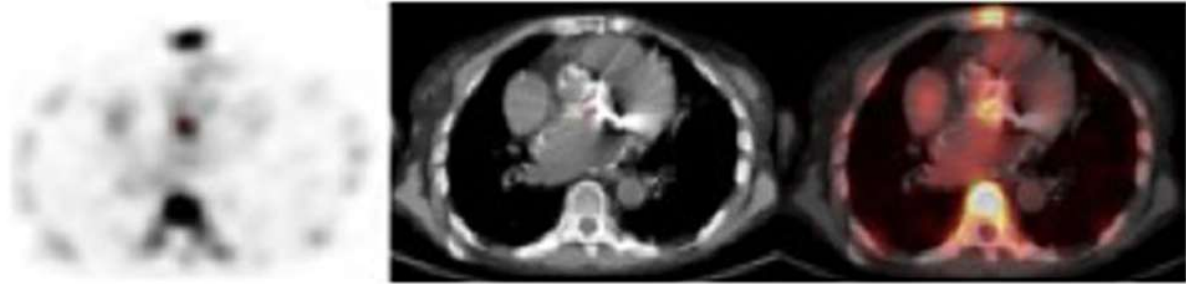
with specific patient preparation

- Physiological myocardial uptake is (ideally) absent
- Lesions are easily identified



Positive FDG PET patterns

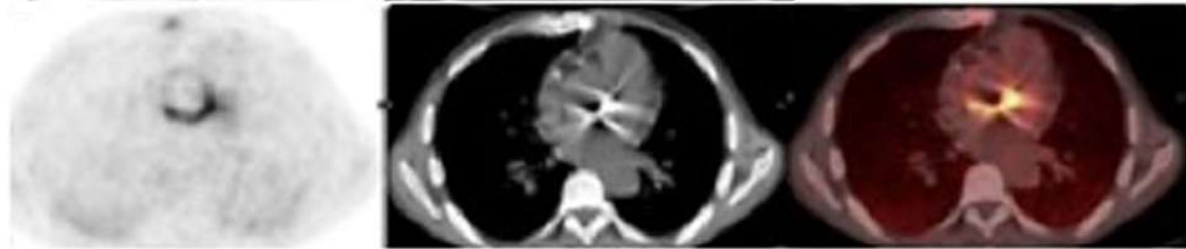
Typical focal pattern at WBC imaging



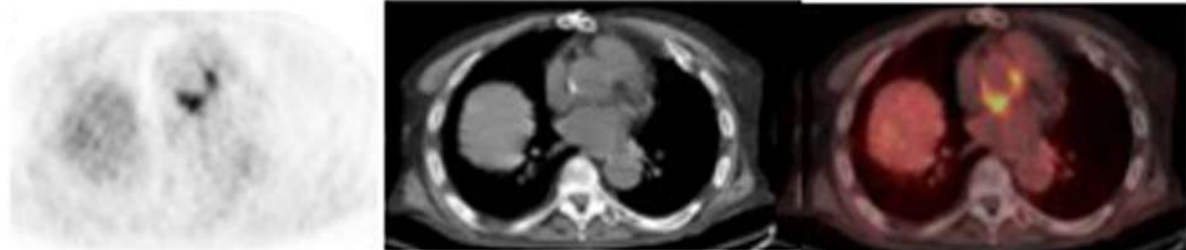
Focal pattern of FDG PET



Diffuse FDG uptake



Focal uptake over an area of diffuse FDG uptake





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European Heart Journal - Cardiovascular Imaging (2020) 21, 34–35

doi:10.1093/ehjci/jez254

Pattern recognition on fluorodeoxyglucose positron emission tomography/computed tomography in infective endocarditis: within the normal limits?

FDG PET/CT in IE and CIED infection

Confounding factors

Pitfalls

Recommendations

False positive

Surgical procedure

- Duration procedure
- Recent valve implantation
- Surgical adhesives
- Complications

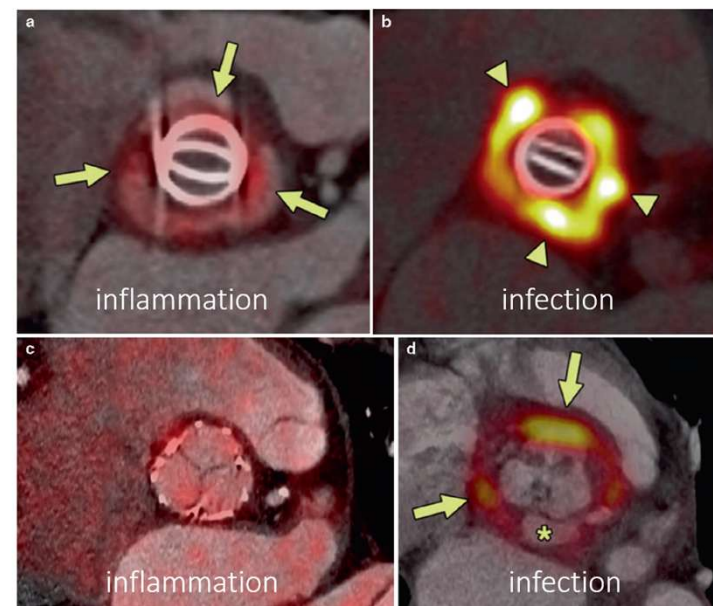
- Information procedure needed

Pathological conditions

- Lipomatous hypertrophy of the interatrial septum, thrombi, vasculitis, tumour metastases, atherosclerotic plaques, and marantic IE

- Excluding non-infectious causes
- Proper use of the combined CT
- Learning curve

Post-operative inflammation vs. infection



Check the time from surgery

PET if >3 months
from surgery

False positive or
false negative

Patient preparation

- Physiological myocardial uptake: false positive or negative (masked)

- Optimal procedural preparation: fasting and low-carbohydrate diet (\pm heparin i.v.)

PET technical procedure

- Motion artefacts
- Metal artefacts (CIED, dense PHV) and over-correction due to beam hardening
- Mismatch PET and CT fusion

- Proper quality check images

PET imaging reading

- No standardized qualitative and quantitative scoring method

- Standard procedures (EANM), reproducibility warranted

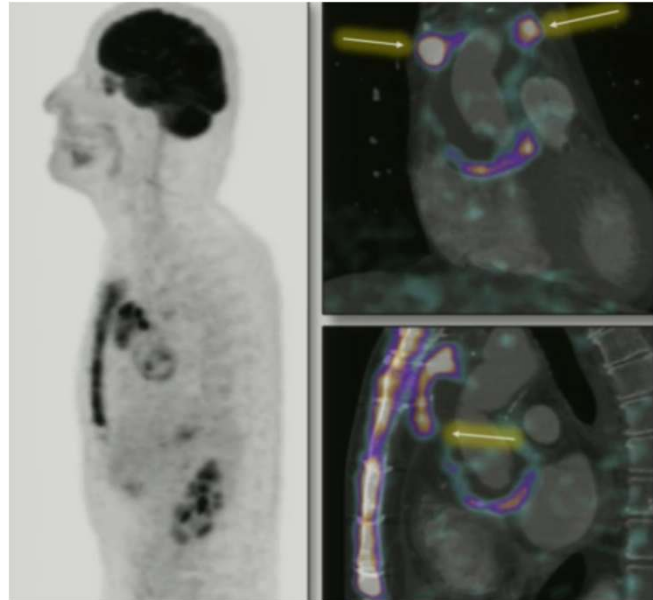
False negative

PET imaging reading

- Isolated, small, or mobile vegetations due to limited temporal and spatial resolution
- NVP

- Need for a multimodality approach in which each imaging modality covers the other's possible shortcomings

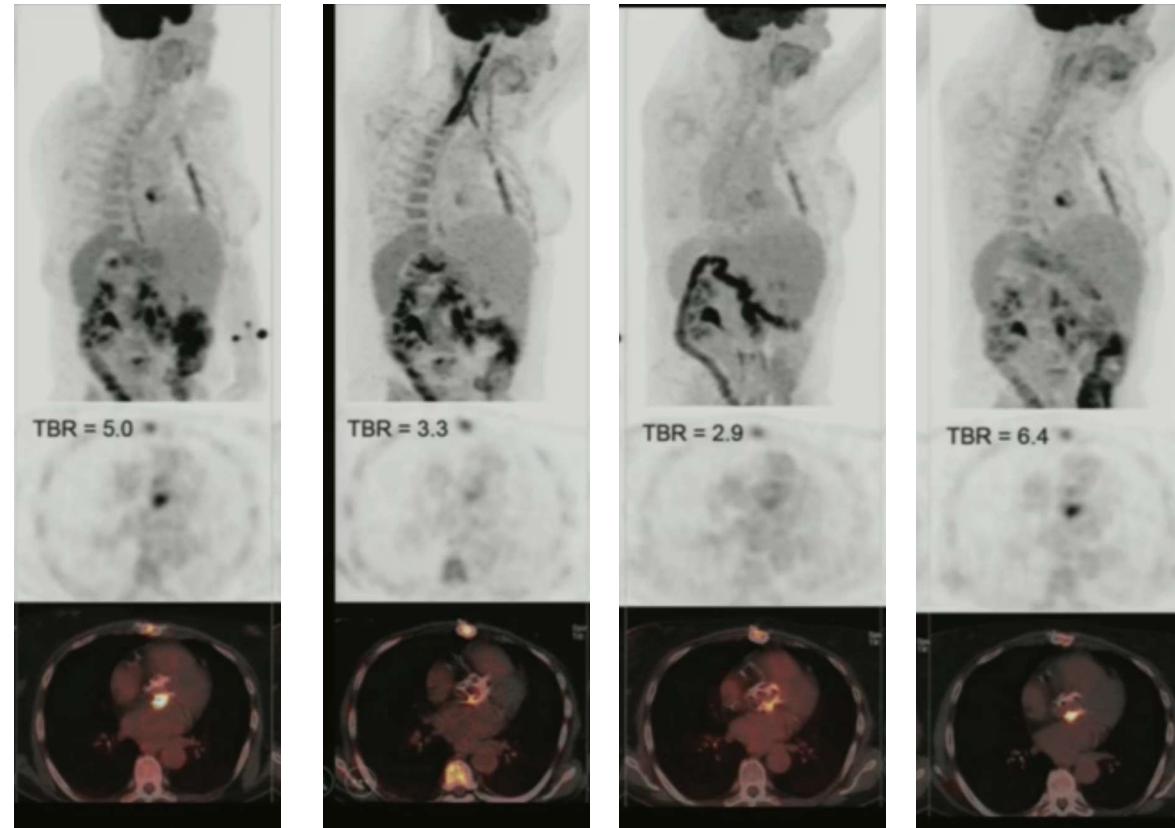
Surgical adhesive



Synthetic and/or protein components
(e.g. bovine serum albumin)

May induce inflammation/foreign
body reactions

Assesment after treatment



FDG PET in Endocarditis

Native valve endocarditis	Prosthetic valve endocarditis	Cardiac device related endocarditis	
		Pocket infections	Lead infections
Indications FDG-PET/CT Evaluation disseminated disease	Indications FDG-PET/CT Evaluation disseminated disease Evaluation intracardiac lesions	Indications FDG-PET/CT Evaluation disseminated disease Evaluation device pocket	Indications FDG-PET/CT Evaluation disseminated disease Evaluation intracardiac lesions
Intracardiac lesion detection Sensitivity 36% Specificity 98%	Intracardiac lesion detection Sensitivity 86% Specificity 84%	pocket lesion detection Sensitivity 93% Specificity 98%	Intracardiac lesion detection Sensitivity 65% Specificity 88%
Key points Cardiac preparation (intracardiac lesions as potential additional findings)	Key points Cardiac preparation Surgery reports: Bioglu, Medtronic Mosaic prosthetic valve (false positives) Confirm findings on NAC images	Key points Cardiac preparation Confirm findings on NAC images	Key points Cardiac preparation Confirm findings on NAC images Possible benefit delayed acquisition (180 minutes)

FDG-PET/CT Standardization (Specific for infective endocarditis. For general recommendations: see EANM guidelines [23,26])	Optional strategies
Preparation High fat - low carbohydrate diet: start 24 hours before scan Fasting: start 12 hours before scan (Optional) Heparin IV 15 minutes before FDG injection. Recommended dose 50 IU/kg If antibiotics indicated: Start treatment without delay, perform FDG-PET/CT as soon as possible	Combined FDG-PET / CT-angiography <i>Pro:</i> Increased sensitivity, information extent of infection, abscess evaluation. <i>Con:</i> Radiation exposure.
Analysis & interpretation Consider both uptake intensity and heterogeneity Confirm findings on non-attenuation corrected images (if cardiac implanted materials)	Recommendations: Weigh risks / benefits. Use CT scanners with high temporal resolution and TOF capable, high sensitive PET/CT system if available. Consider renal protection strategies.
	Semiquantitative PET/CT analysis (SUV) <i>Pro:</i> validated benefit for diagnosis in oncology <i>Con:</i> Limited experience in suspected IE (PVE only). demands standardization to ensure reproducibility of findings across PET/CT systems.
	Recommendations: Can be considered when in doubt after visual assessment. Cut off values for PVE: SUVmax >3.3 and/or SUVratio (bloodpool) >2.0 (best results SUVratio)

- Greater clinical utility and diagnostic accuracy in patients with suspected endocarditis on prosthetic valves or intracardiac devices compared to native valves.

- Pre-examination dietary preparation and standardization of protocols are essential for PET to avoid false negatives.

- Careful integration of PET data with morphological data (multimodal approach), clinical history, and the timing and approach of previous surgery is fundamental.

- PET is inherently a total-body examination with an excellent signal-to-noise ratio, making it suitable for defining the potential "origin" of the infectious process and comprehensively identifying both cardiac and extracardiac sites of infection (also at relapse)

Grazie per l'attenzione ma soprattutto grazie a...



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