

Role of cardiovascular PET Imaging in Clinical Practice

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European Association of Cardiovascular Imaging & European Association of Nuclear Medicine



EACVI
European Association of
Cardiovascular Imaging

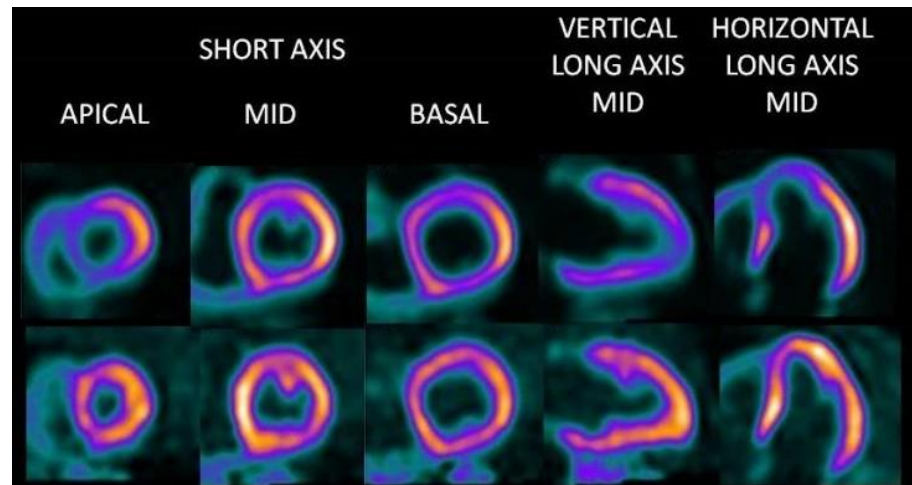
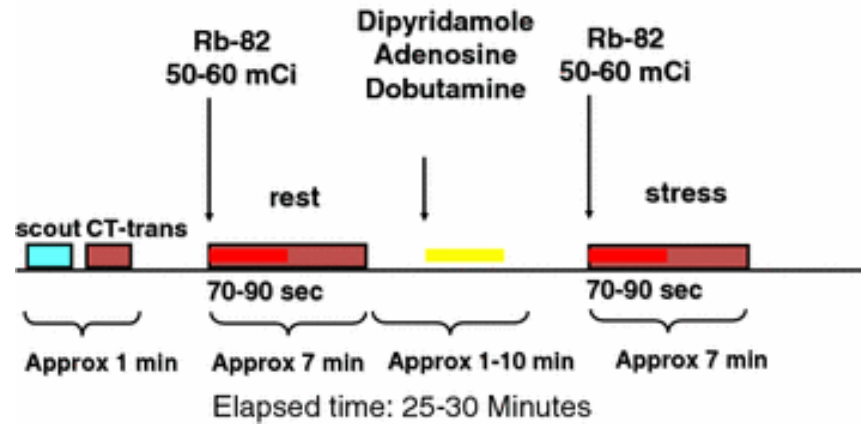


Role of PET Imaging in Clinical Practice

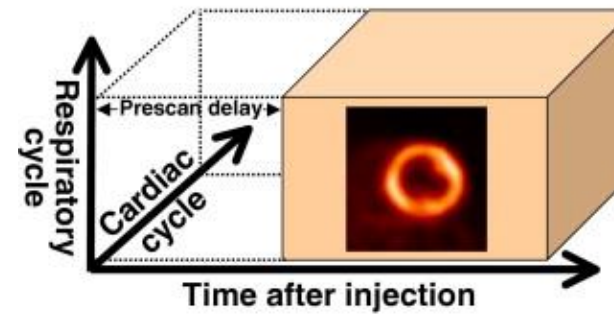
- Myocardial perfusion
- Myocardial Viability-hibernation
- Myocardial inflammation-sarcoidosis
- Vascular Inflammation
- Infective endocarditis
- Device Infections
- Conclusions-Key points

PET Perfusion Study

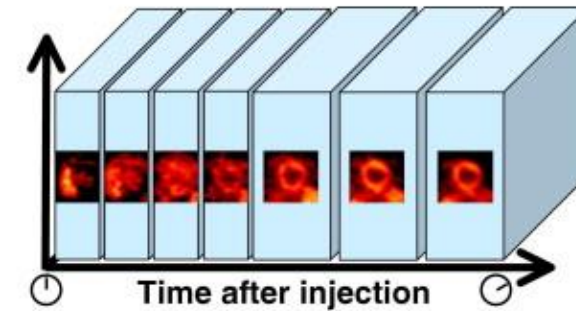
PET/CT Protocol: Pharmacologic



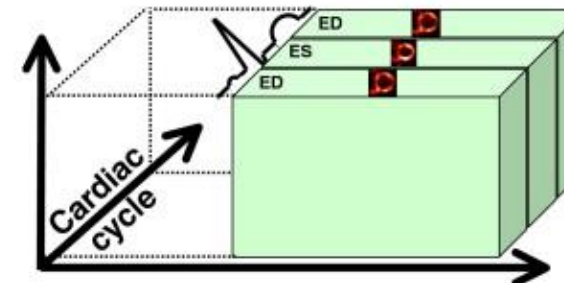
A Static



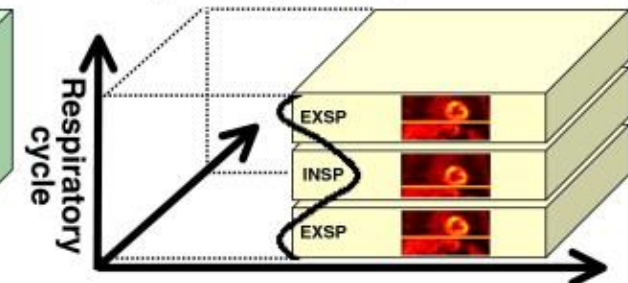
B Dynamic



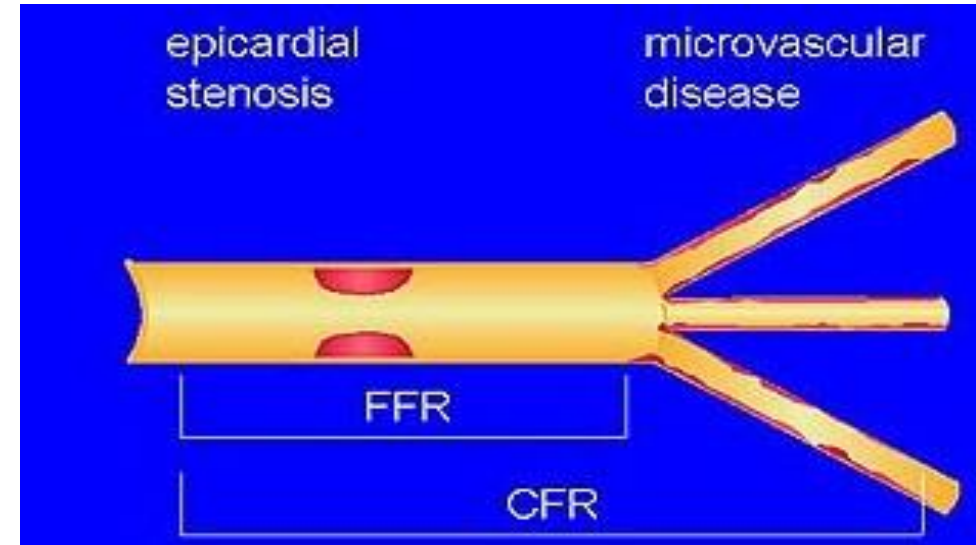
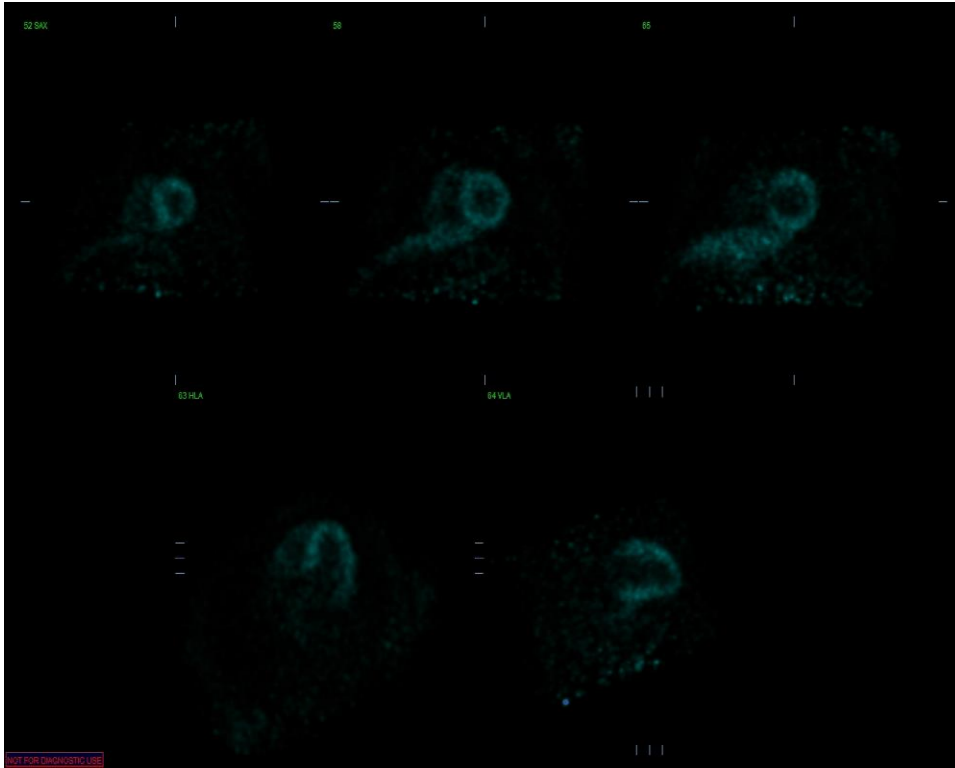
C ECG-Gated



D Respiratory Gating



Myocardial perfusion-PET – Flow quantification

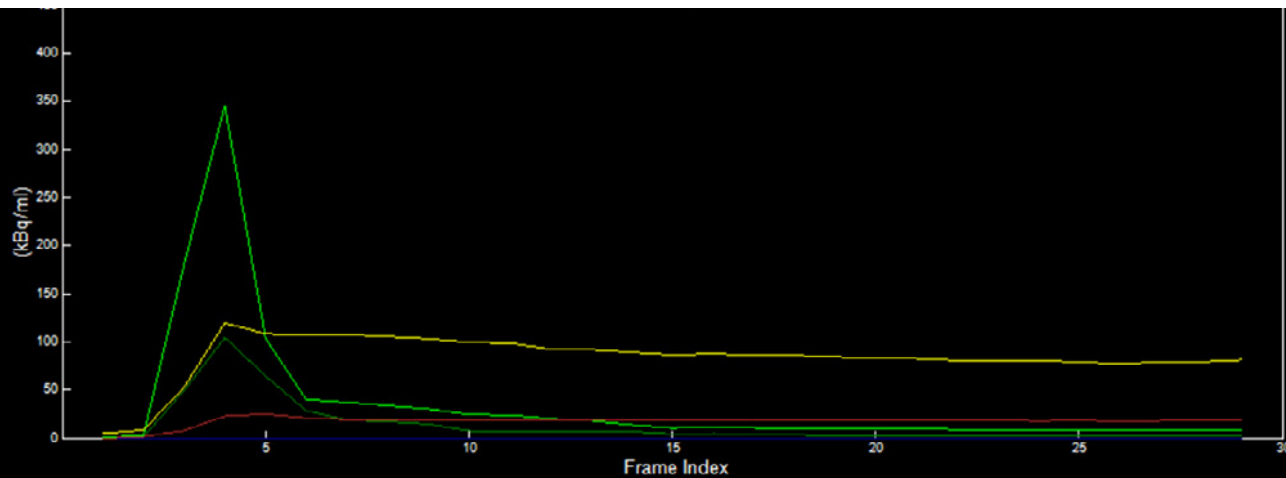


A normal stress MBF and flow reserve (>2.0) has a very high negative predictive value and reliably excludes high-risk obstructive CAD

CFR: 1.7-2 Mildly abnormal

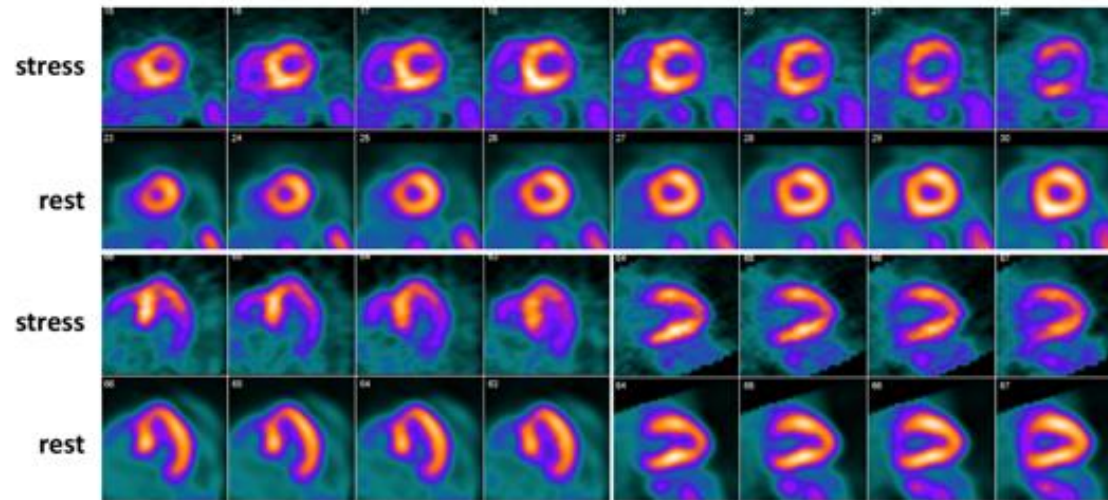
CFR: 1.2–1.7 Abnormal

PET: An excellent technique for assessing the function of microcirculation when obstructive CAD has been excluded

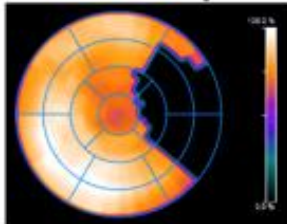


Utility of quantification of myocardial perfusion by PET in CAD detection

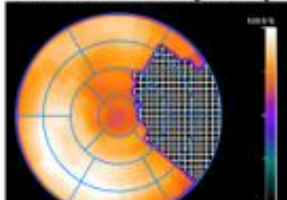
68-year-old male with dyslipidemia, diabetes and HTN presenting with atypical angina



Stress map

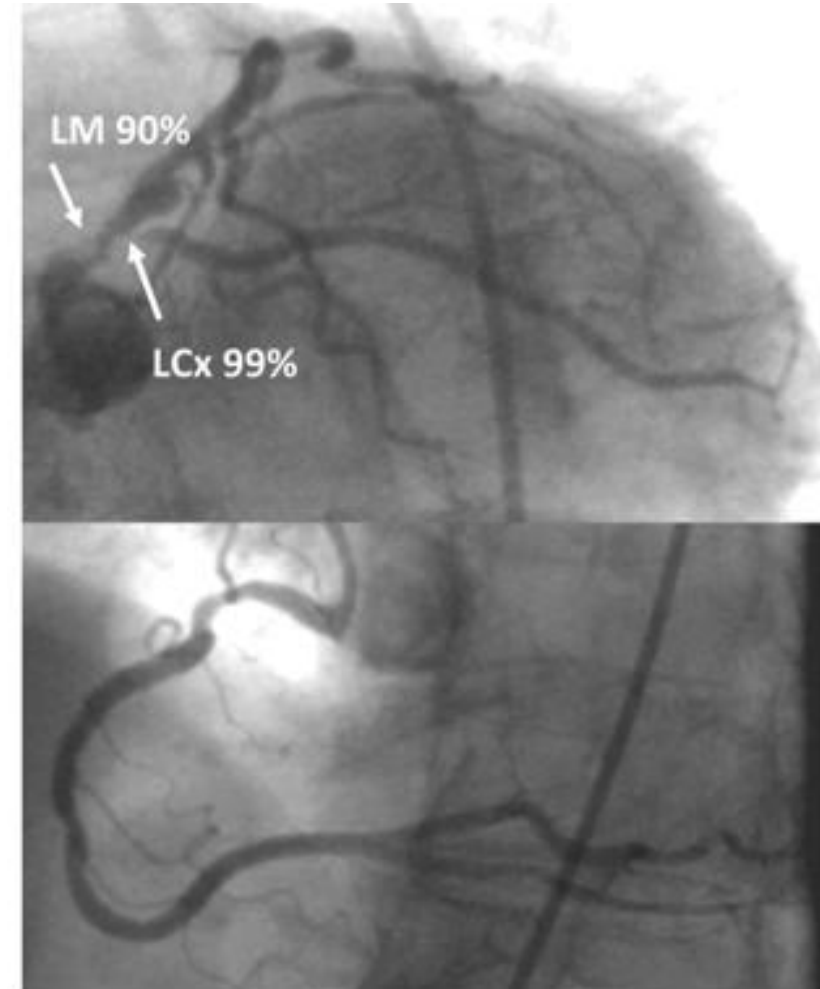


Reversibility map



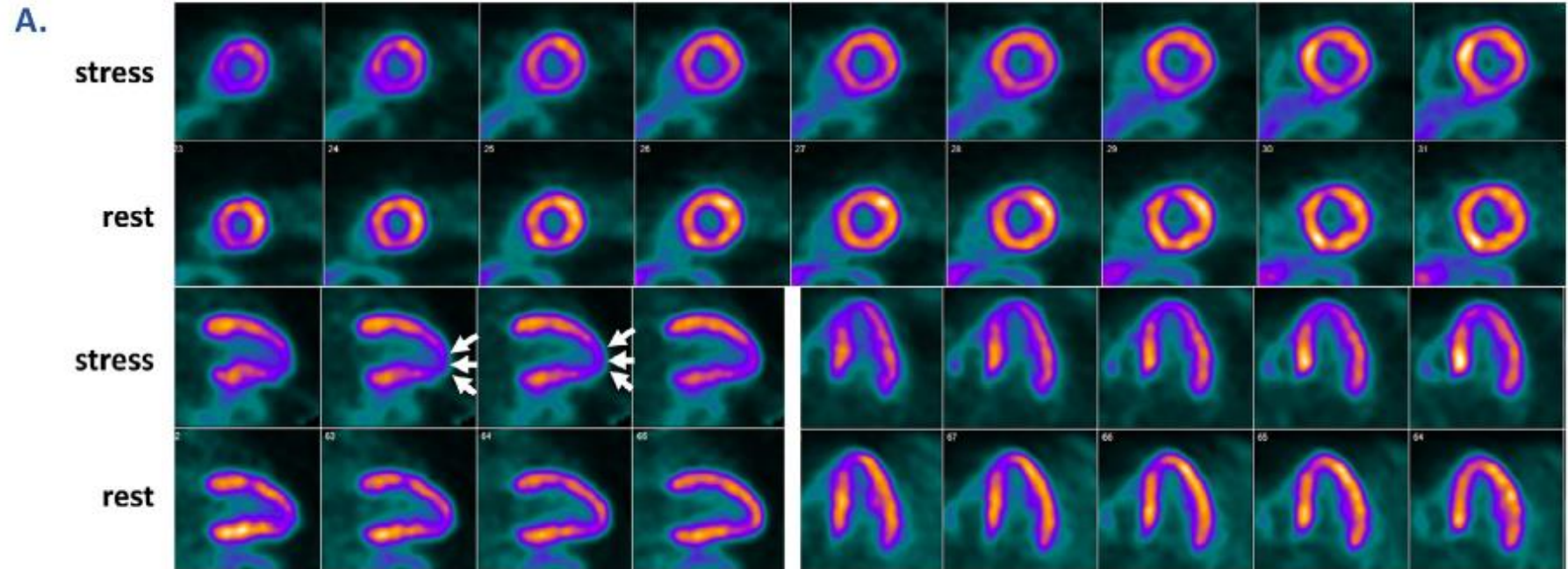
Quantitative myocardial blood flow and CFR

	Rest	Stress	CFR
LAD	1.21	1.19	0.99
LCX	1.16	0.82	0.71
RCA	1.30	1.73	1.33
Global LV	1.22	1.22	1.00

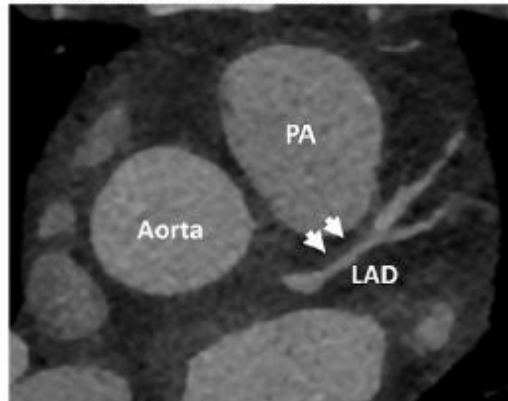


Example of myocardial ischemia from nonobstructive atherosclerosis and Chronic Microvascular Disease

44-year-old female
with a history of
dyslipidemia
and rheumatoid
arthritis presenting
with atypical
chest pain
Resting ECG: normal



B. Coronary CT Angiography



C.

Myocardial blood flow (mL/min/g) and MFR

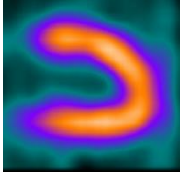
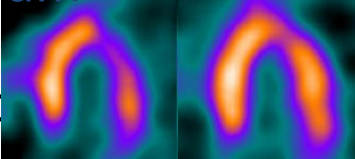
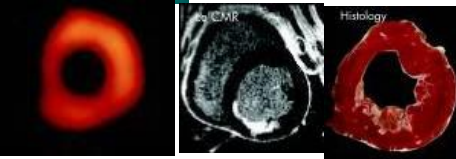
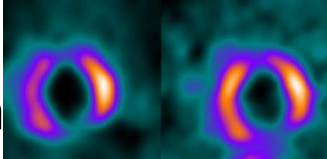
	Rest	Stress	MFR
LAD	0.74	1.24	1.67
LCX	0.76	1.46	1.92
RCA	0.73	1.33	1.82
Global LV	0.75	1.35	1.80

Courtesy M F Di Carli

Indications for PET perfusion imaging

- First line test:
 - Younger patients
 - Higher-risk patients (e.g. advanced chronic kidney disease, diabetes mellitus), or when extensive CAD is known such as in patients with multivessel disease to confirm or exclude balanced ischaemia
 - Patients who may be prone to artifact that could lead to an equivocal result on another test, such as obese patients
- Second line test:
 - PET MPI for the diagnosis of CAD and/or risk stratification of patients who have non-diagnostic, noninvasive imaging tests, or when such a test does not agree with clinical diagnosis

Myocardial Viability-Definitions

- Normal 
- Myopathic Myocardium
- Reversible ischaemic 
- Partial thickness infarction 
- Partial thickness infarction + ischaemia 

Viable= alive

Different types of viable myocardium often co-exist in the same patient and even in the same segment

- **Stunned myocardium**
- Form of contractile dysfunction of viable myocardium caused by a brief episode of ischaemia followed by restoration of perfusion (it can become chronic)
- **Hibernating myocardium**
 - Alive, reduced resting perfusion and function (chronic), recovery after revascularisation

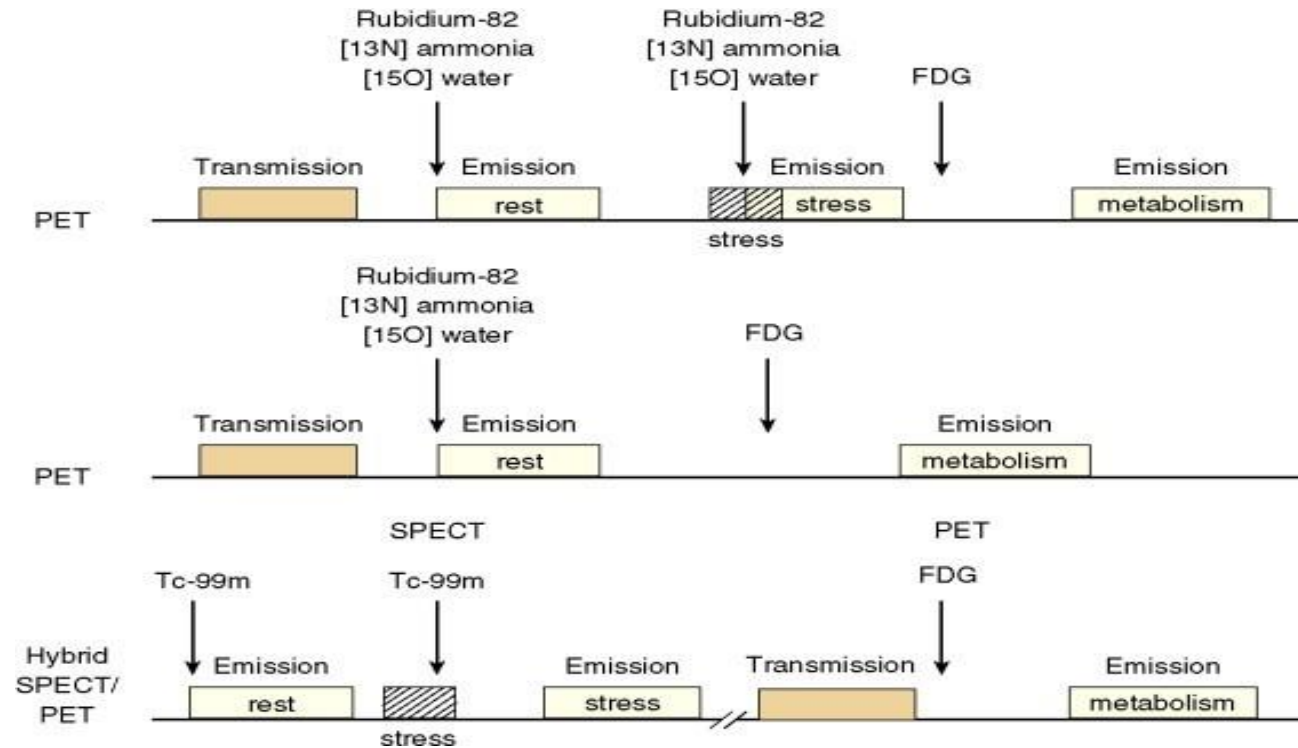
Surrogate definition

Hibernating myocardium is:

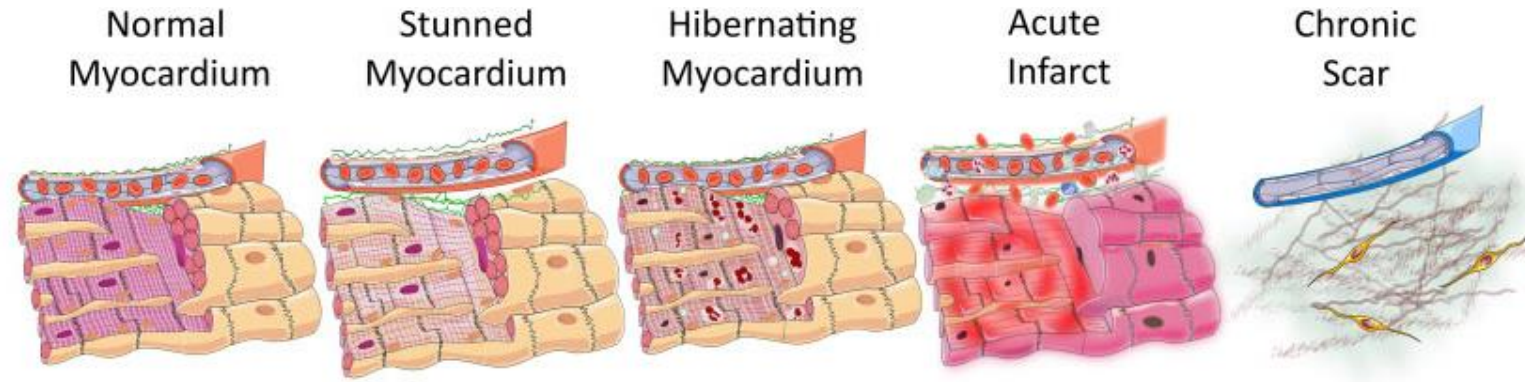
1. akinetic
2. Viable
3. susceptible to ischaemia

Assessment of viability by PET imaging

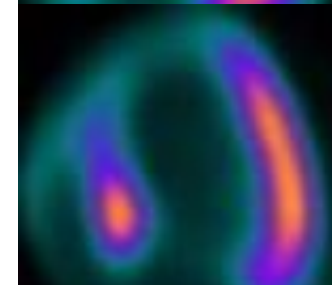
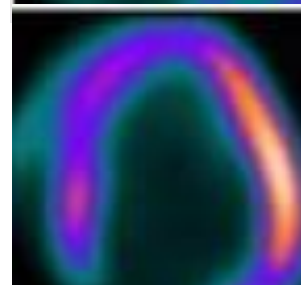
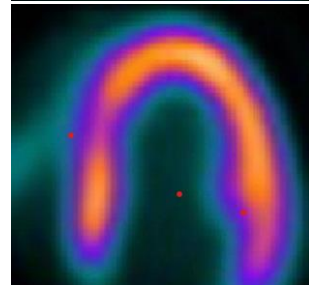
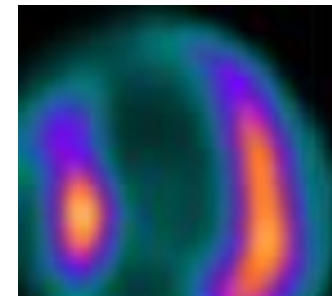
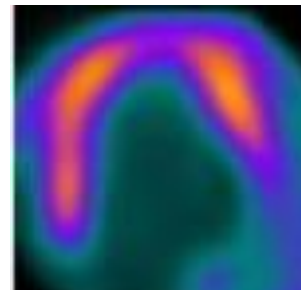
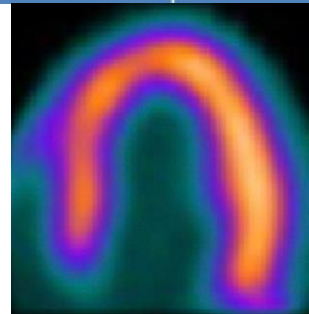
- Dedicated PET NH_3 or Rb, or H_2O + FDG (gated)
- Hybrid MIBI/Tf + FDG



Assessment of viability by PET imaging



Histopathology	Normal Myocardium	Stunned Myocardium	Hibernating Myocardium	Acute Infarct	Chronic Scar
	Normal morphology Normal metabolism Normal contraction	Normal morphology Reduced Ca sensitivity of Contractile proteins Intra and Extracellular Edema	Dedifferentiation of cardiomyocytes Increased Glycogen Reduced Myofibrils Altered Metabolism	Contraction band necrosis. Destruction of membranes, mitochondria, metabolism. Interstitial edema. Infiltration by inflammatory cells	Replacement by Fibrotic tissue



Diagnostic accuracy of non-invasive imaging for detection of myocardial hibernation- Systematic review

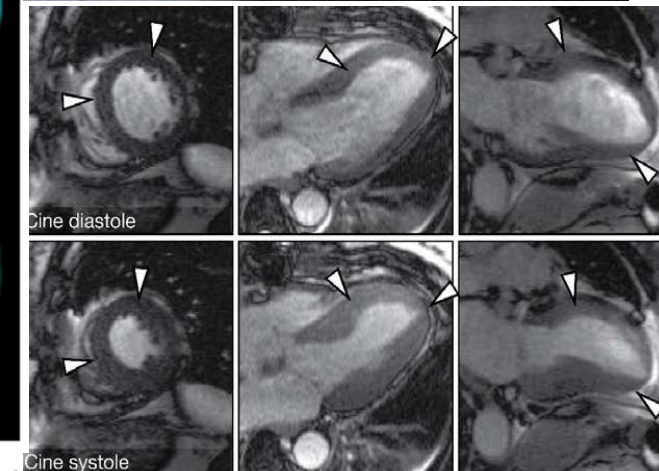
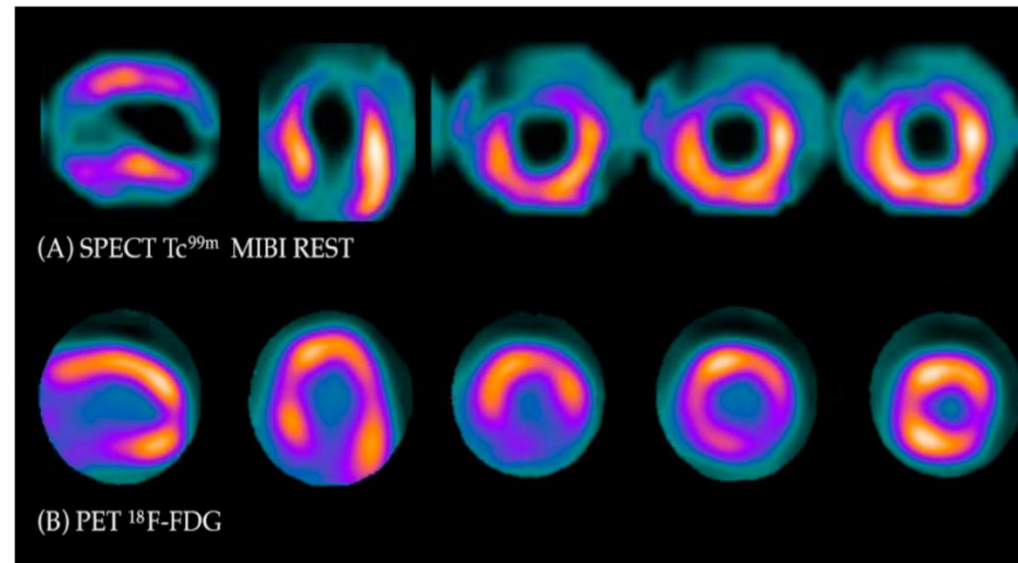
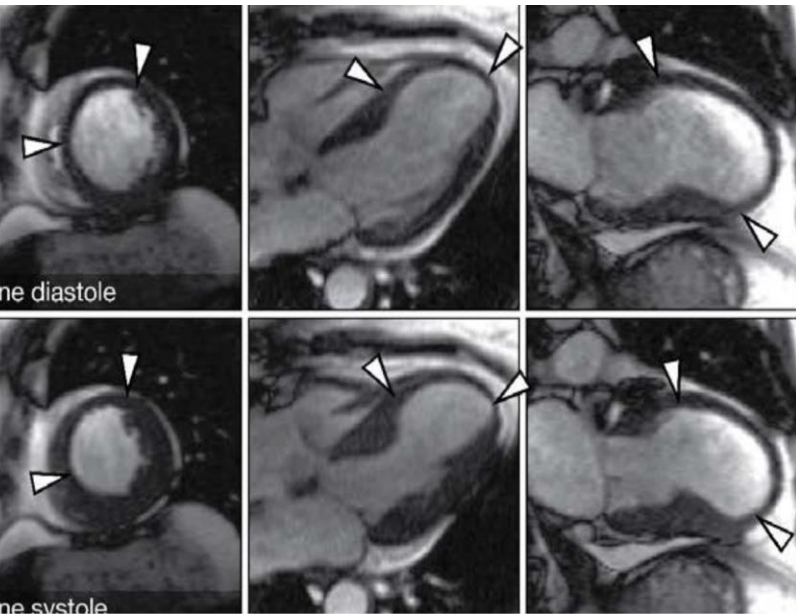
Test	Number of studies	Sensitivity (95% CI)	Specificity (95% CI)	Pooled DOR (95% CI)
CE CMR	14	95.5 (94.1 to 96.7)	53.0 (40.4 to 65.2)	24.33 (11.6 to 51.1)
Stress CMR	12	82.2 (73.2 to 88.7)	87.1 (80.4 to 91.7)	31.2 (15.7 to 61.9)
SPECT	13	85.1 (78.1 to 90.2)	62.1 (52.7 to 70.7)	9.41 (5.05 to 17.5)
PET	4	94.7 (90.3 to 97.2)	68.8 (50.0 to 82.9)	39.9 (21.1 to 75.6)
Echo	12	77.6 (70.7 to 83.3)	69.6 (62.4 to 75.9)	7.96 (5.31 to 11.9)

Detection of Myocardial Hibernation in a 77 year old man

Severe SOBOE

History of ischemic Heart Disease-LV dilatation & dysfunction and prior PCI to the RCA coronary artery.

Follow-up coronary angiography demonstrated persistent good result of the RCA stent and a severe lesion of the proximal LAD



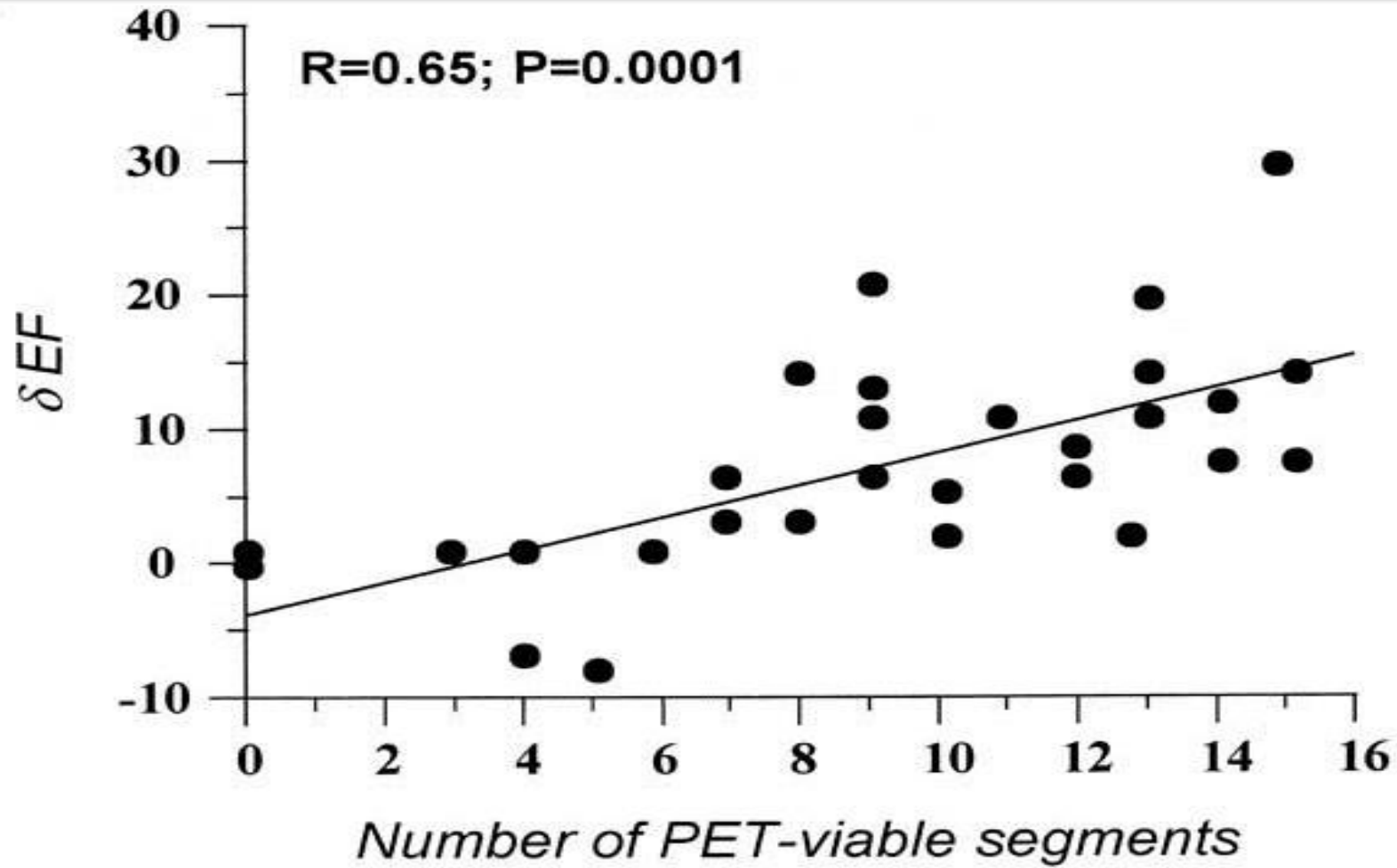
Mismatch between perfusion and metabolism

Ischaemia

Anaerobic metabolism,
glucose ↑

Post-bypass

Viable segments by PET and change in LVEF after Revascularization



Heart failure of ischaemic aetiology -The issues

- Does hibernation assessment improve selection of patients with LV dysfunction for revascularization
- Does revascularization improve survival of patients with hibernating myocardium compared to the results of medical therapy?

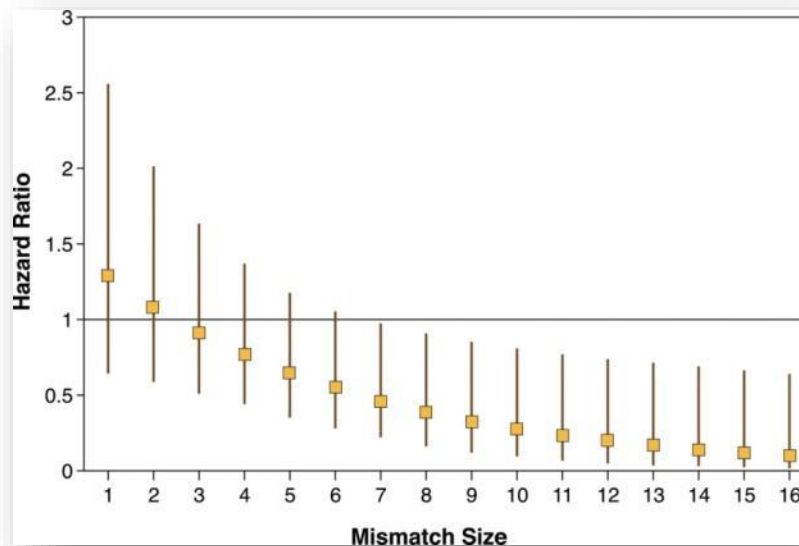
Revasc benefit with extensive hibernation

PARR2 sub-study: PET And Recovery Following Revascularization (PARR 2) Trial-sub-study

Composite end point: death, MI admission

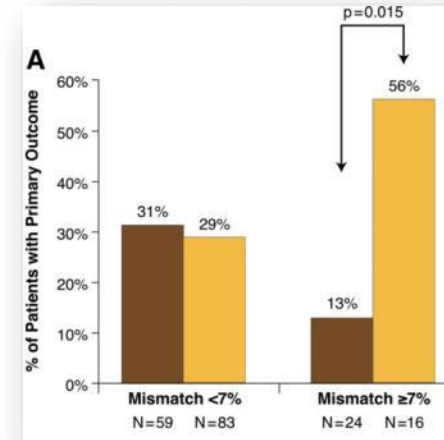
IHD and LVEF <35%

182 patients randomised to PET arm

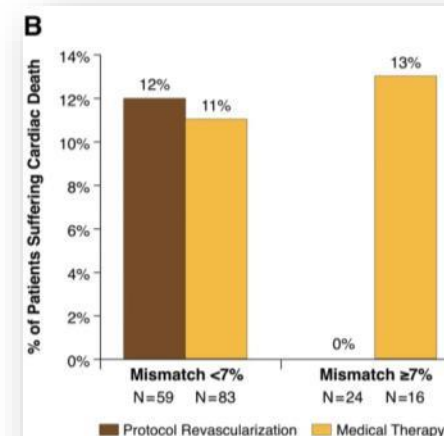


>7% hibernation
benefit from revascularisation

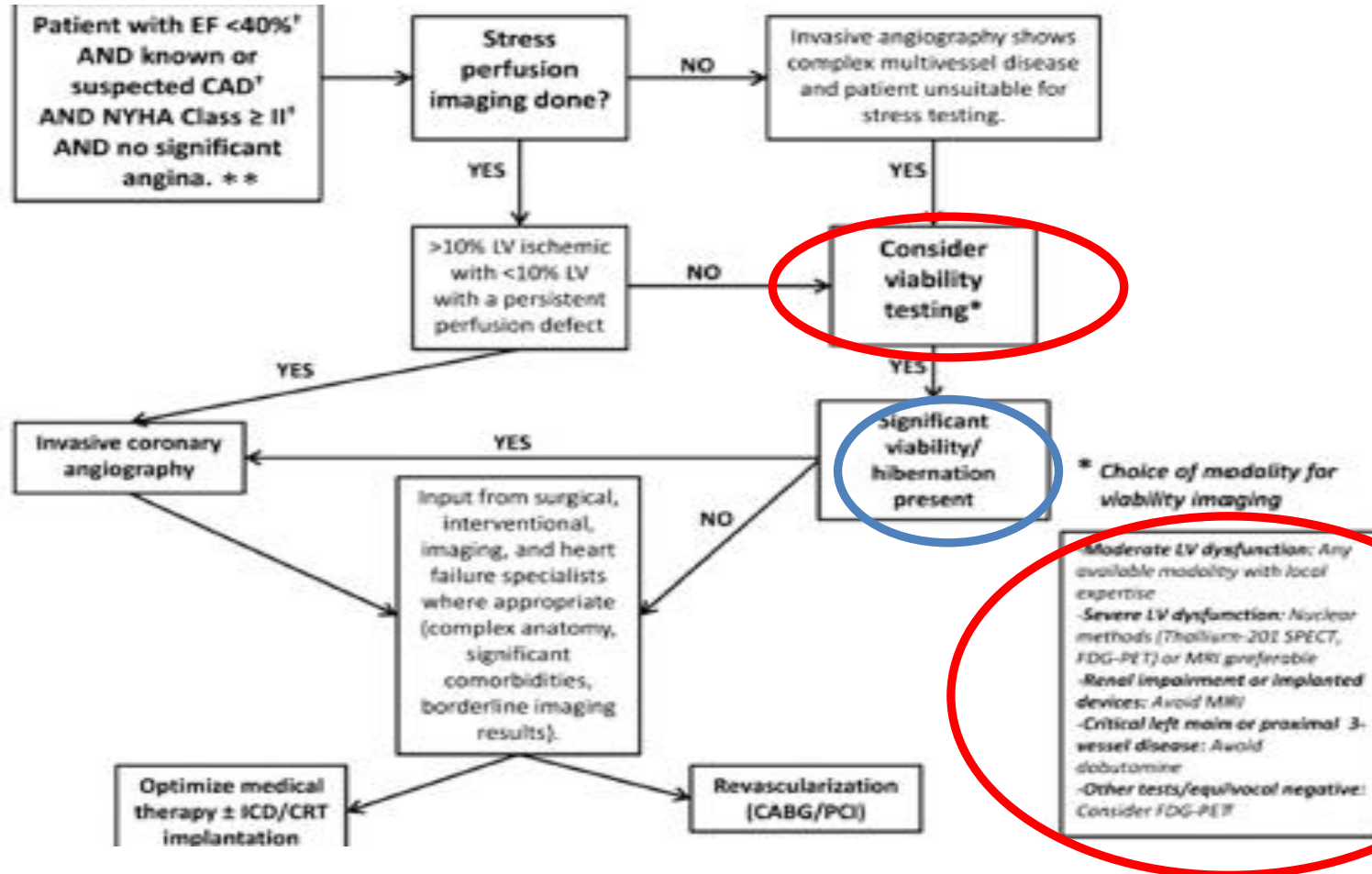
Death, MI, admission



Cardiac death



Myocardial viability: Whom, what, why, which, and how?



When not to do a viability study

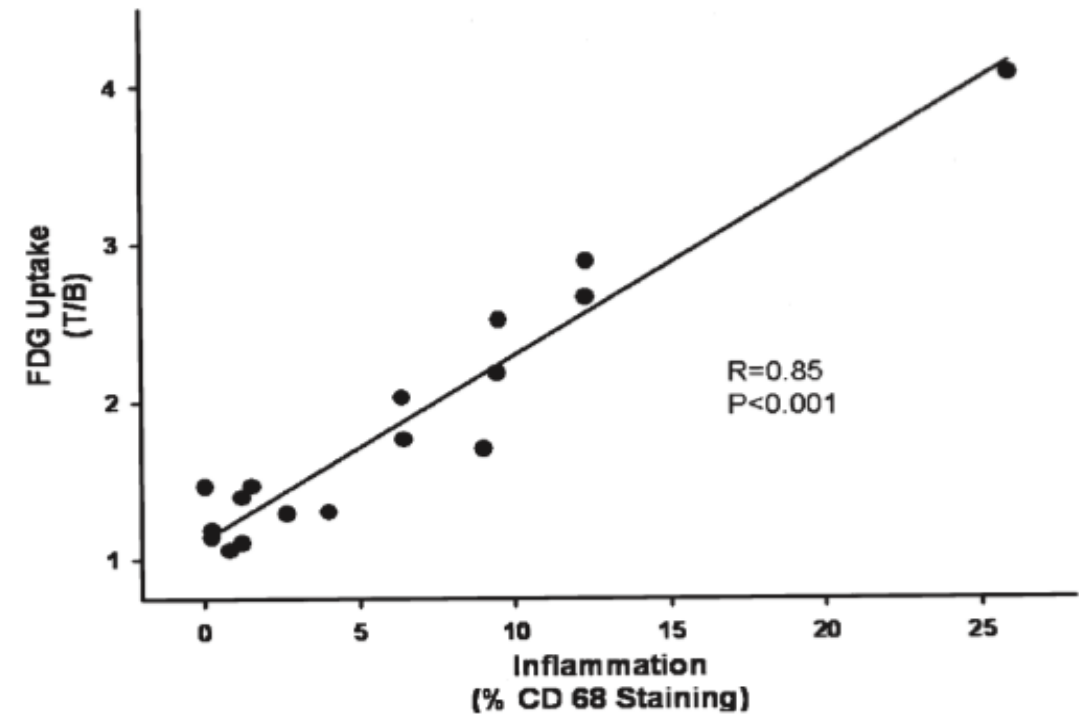
- Predominantly angina CCS- II
- Normal or mild LV dysfunction
- Critical left mainstem coronary disease
 - Good targets
- Documented moderate or severe ischemia
- Minimal or no comorbidities

Cardiac Sarcoidosis

- - Multi-system inflammatory disorder of unknown aetiology
- - Cardiac involvement clinically evident in 10%, although rates are at least double on autopsy studies (20-50%)
 - Affects the septum, LV free wall, papillary muscles, right ventricle
- - Cardiac sarcoid can present as conduction abnormalities, ventricular arrhythmias, systolic or diastolic heart failure, mitral regurgitation
- - Cardiac involvement is the most important predictor of patient prognosis
- - Treatment of cardiac sarcoid is prolonged high dose steroids (important to get diagnosis correct)

18F-FDG PET

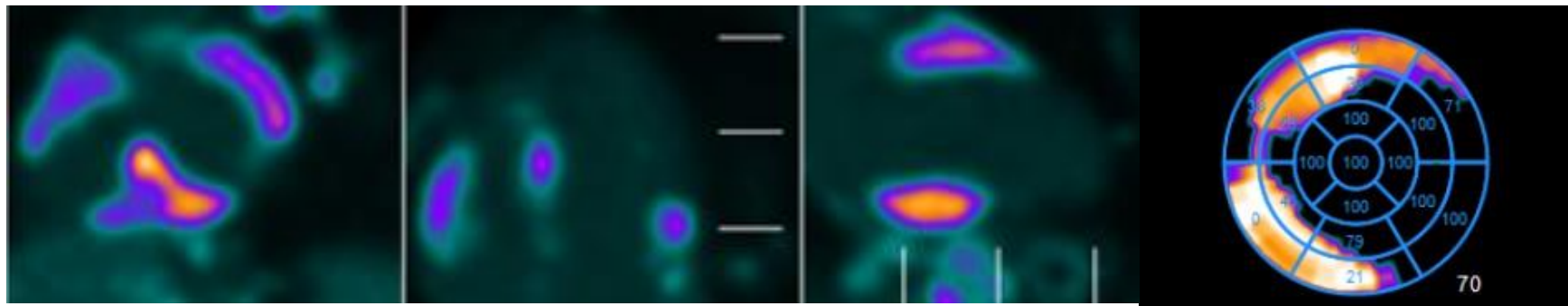
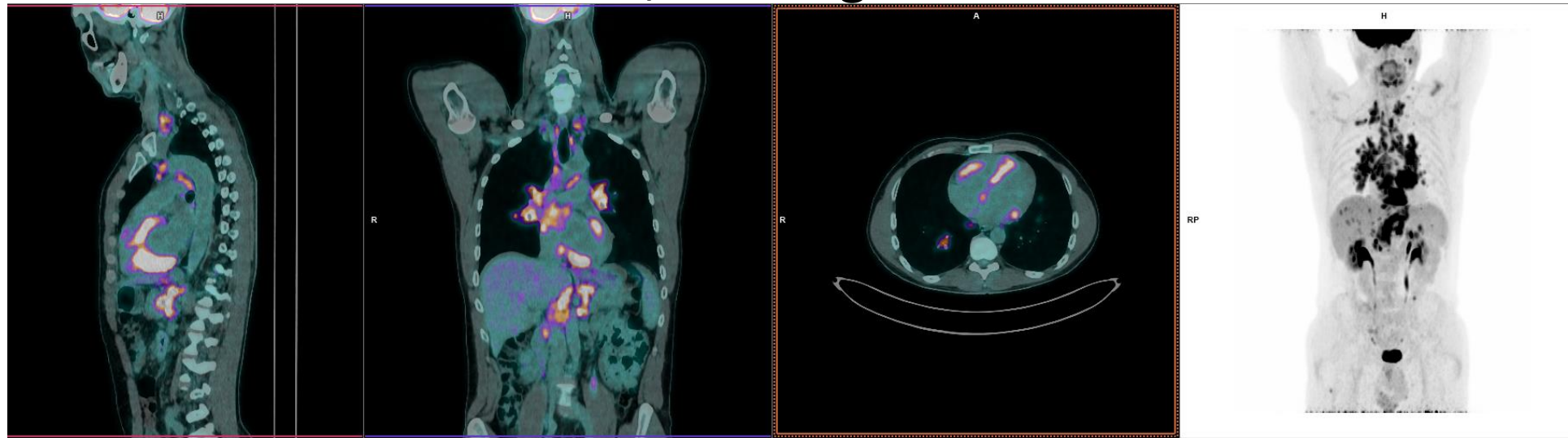
It is established as a marker of inflammation



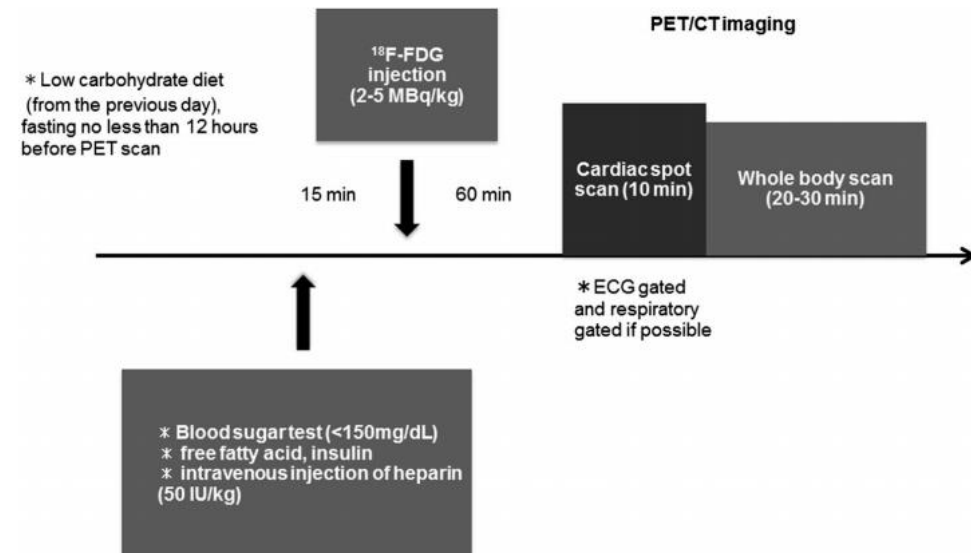
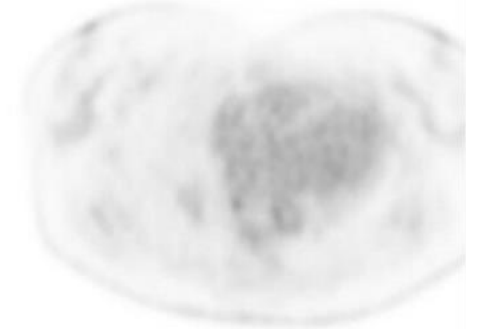
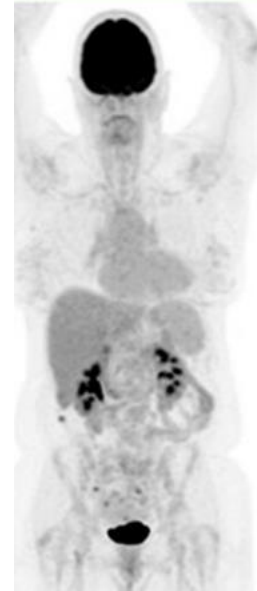
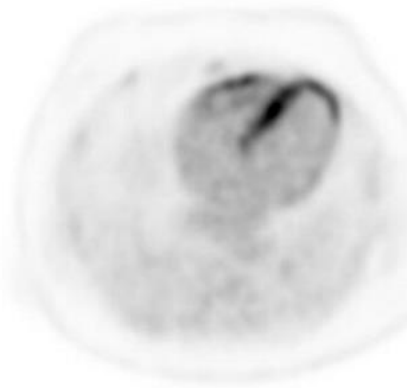
Case- 44 year old man

Asymptomatic, ex smoker, -ve for ischaemia stress MPI, 1st degree atrioventricular block without RBBB, 24-hour Holter: 1st degree atrioventricular block and RBBB
CMR: Strong suspicion of edema with concomitant thickening in the interventricular septum

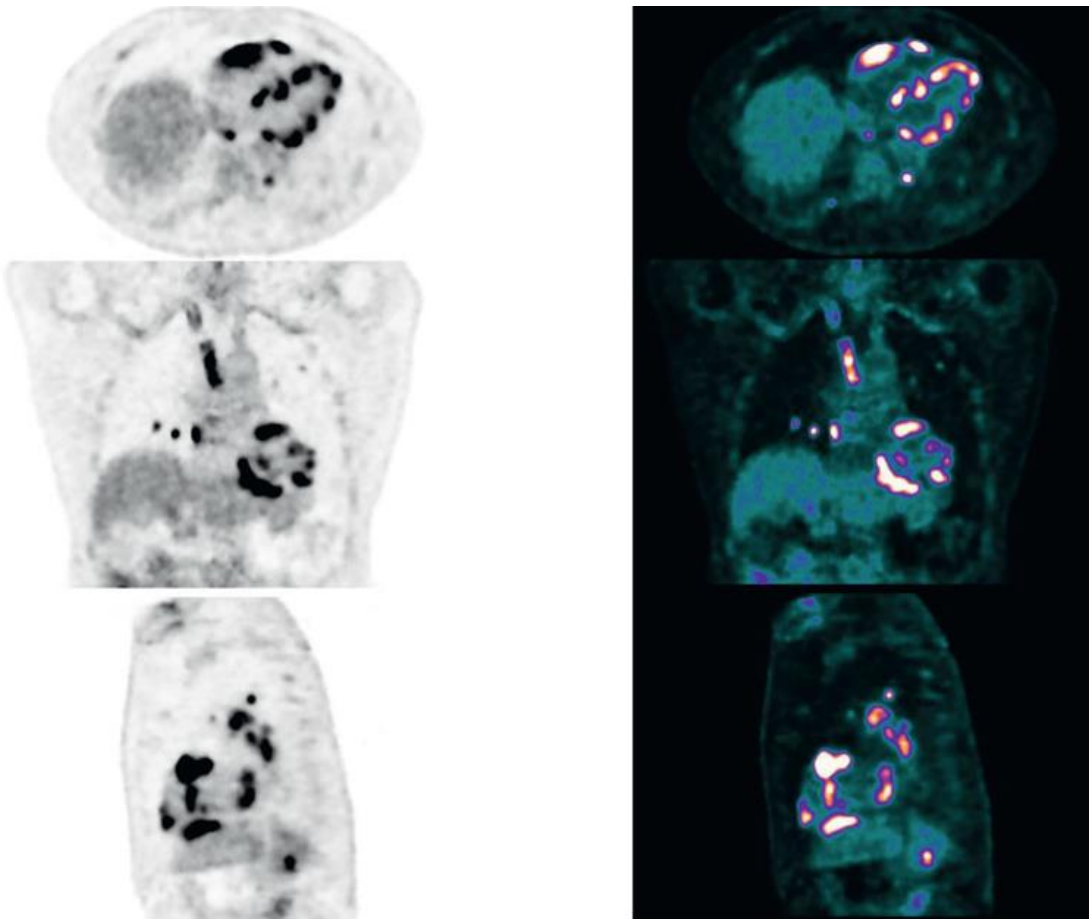
PET/CT Images



18F-fluorodeoxyglucose positron emission tomography imaging for detection of myocardial inflammation



Sarcoidosis-Myocardial Inflammation

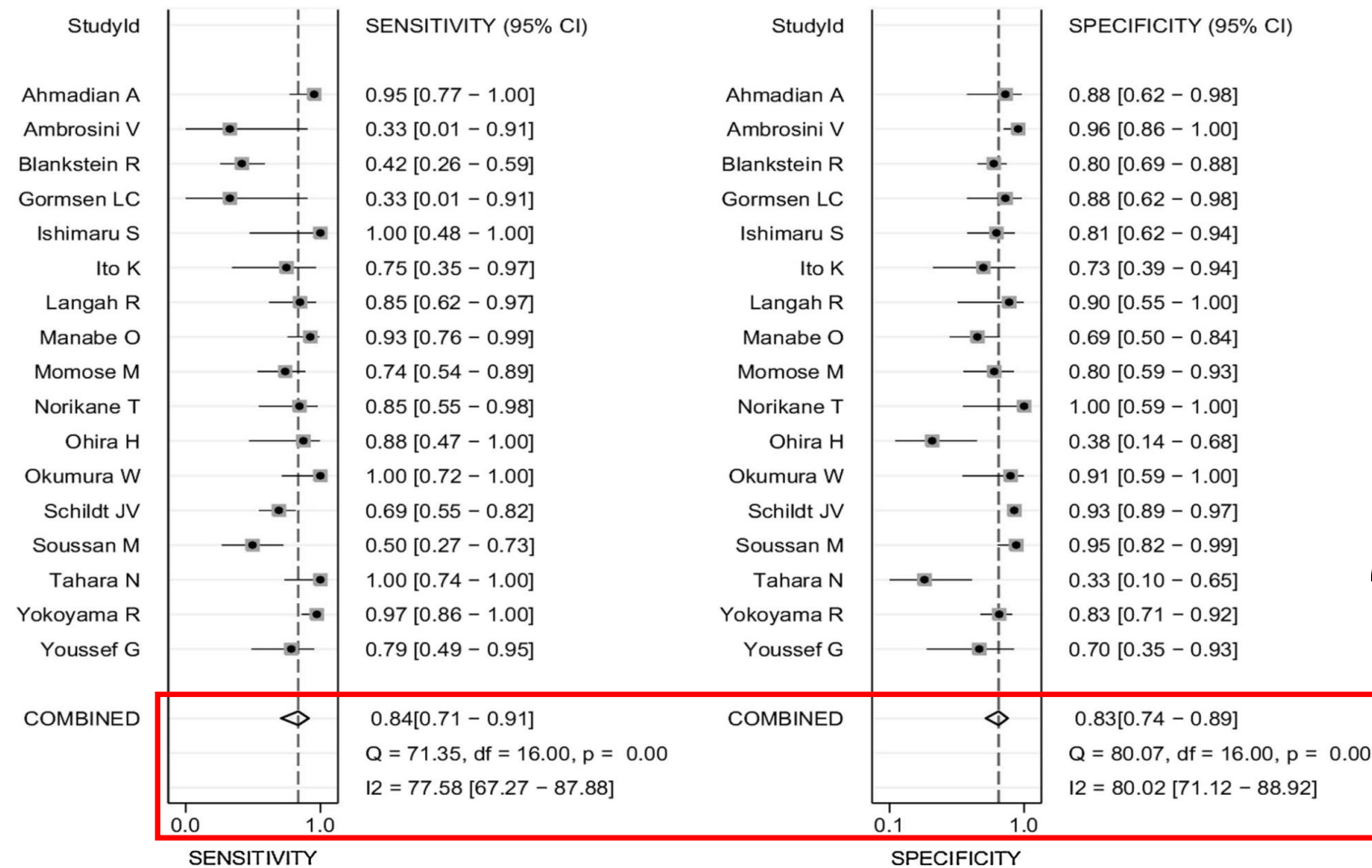


Advantages of ^{18}F -FDG PET:

- biologic nature of the imaging signal,
- potential to identify also extracardiac sarcoidosis involvement,
- feasibility of imaging patients with electrical devices

Diagnostic performance of F-18 FDG PET for detection of cardiac sarcoidosis

A systematic review and meta-analysis



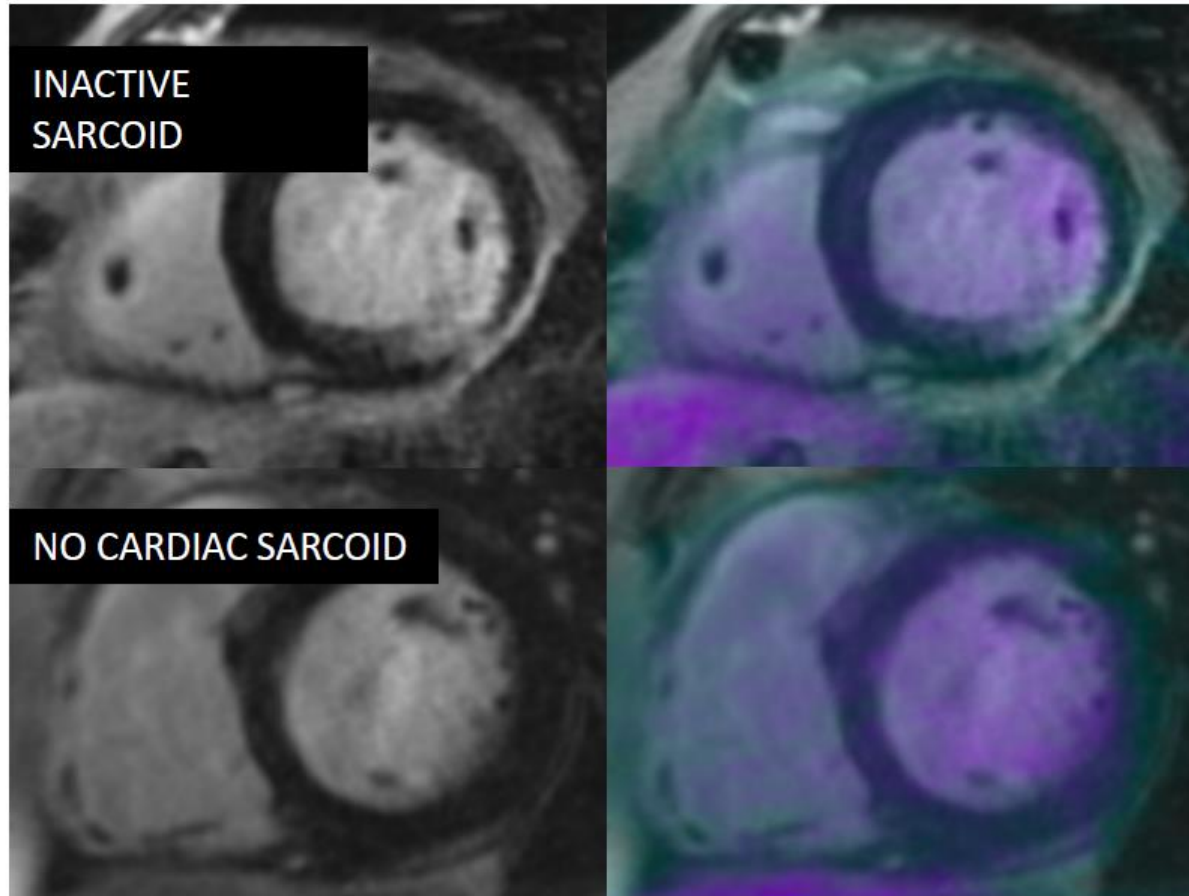
Kim SJ et al., J Nucl Cardiol , 2019

Perfusion and FDG imaging of Cardiac sarcoidosis

	Spectrum of disease by PET/CT to evaluate rest perfusion and metabolism					
	Normal perfusion and metabolism		Abnormal metabolism		Abnormal perfusion and/or metabolism	
Perfusion						
	Normal	Normal	Normal	Abnormal	Abnormal	Abnormal
FDG						
	Normal (Negative)	Diffuse (non-specific)	Focal increase	Focal increase	Focal increase (different areas)	Normal (Negative)
Interpretation	Normal	Non-specific*	Early Disease	Mismatch Pattern	Scar and Inflammation	Scar

*Likely failure to suppress FDG uptake by normal myocardium although rarely can also be seen with diffuse disease

PET/MRI in Cardiac Sarcoidosis

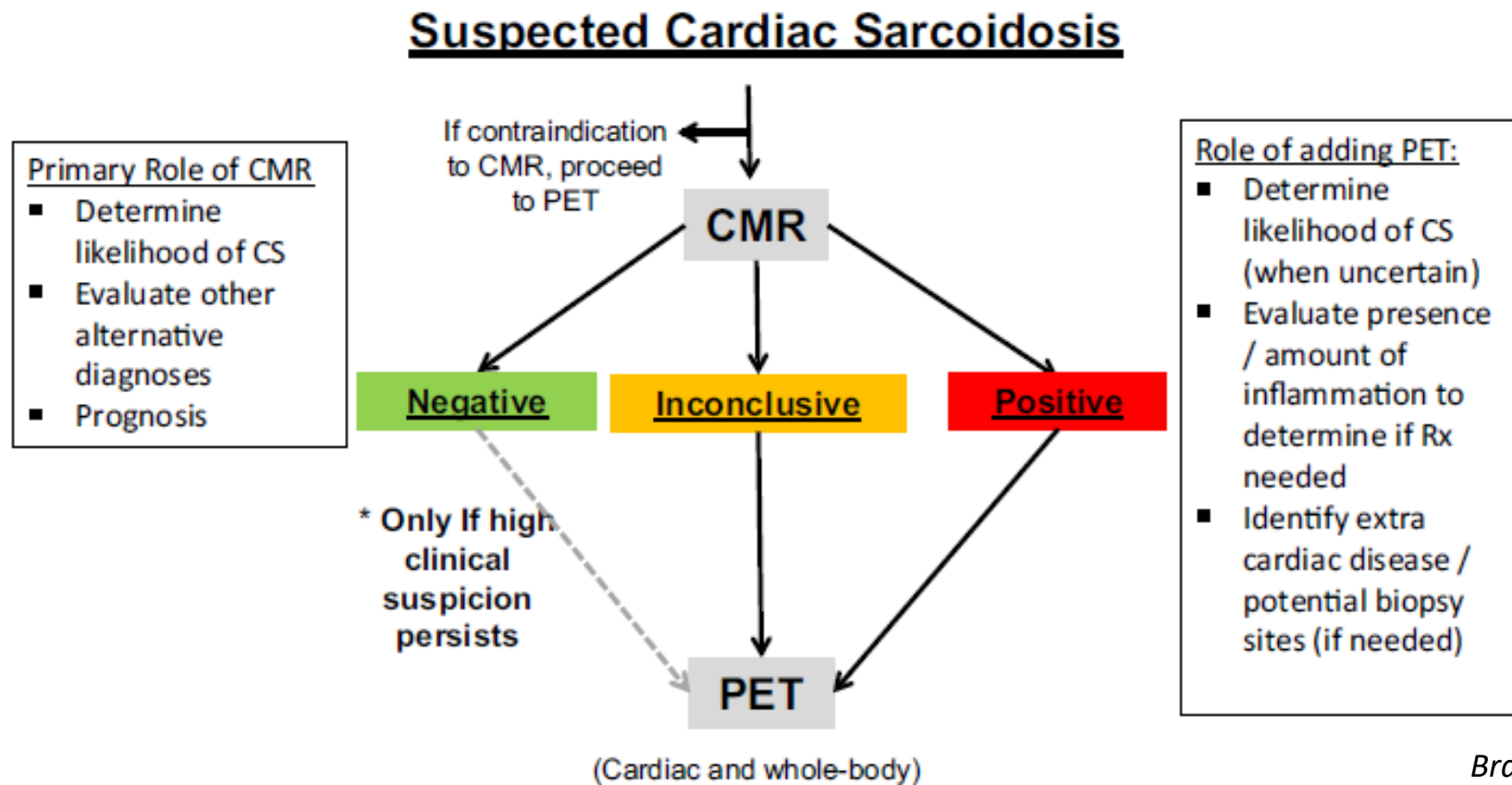


Dweck JACC CVS Imaging 2017



IIBEAA

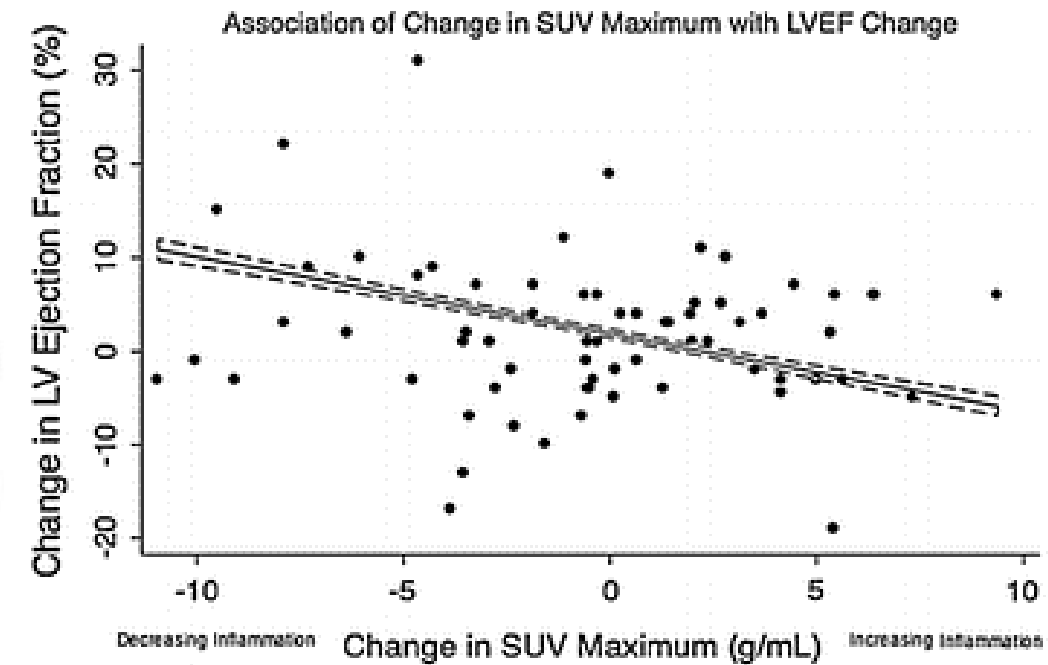
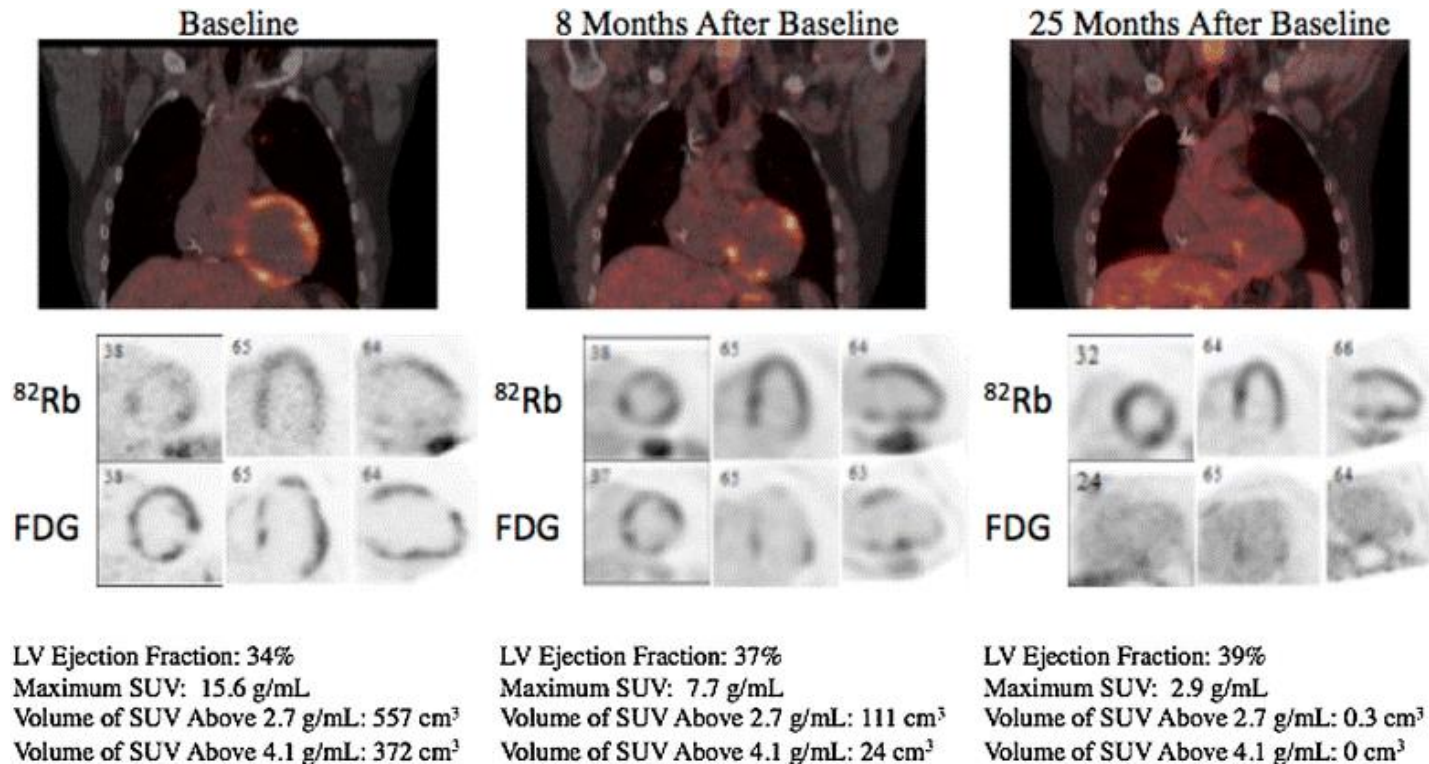
PET vs. CMR in patients with cardiac sarcoidosis



Bravo PE et al., J Nucl Cardiol, 2018

Reduction in ^{18}F -fluorodeoxyglucose uptake on serial cardiac positron emission tomography is associated with improved left ventricular ejection fraction in patients with cardiac sarcoidosis

23 patients with CS, a total of 90 serial PET exams (median 4 per patient)



2023 ESC Guidelines for the management of cardiomyopathies

Recommendations	Class ^a	Level ^b
DPD/PYP/HMDP bone-tracer scintigraphy is recommended in patients with suspected ATTR-related cardiac amyloidosis to aid diagnosis. ^{166–168}	I	B
Contrast-enhanced cardiac CT should be considered in patients with suspected cardiomyopathy who have inadequate echocardiographic imaging and contraindications to CMR. ^{169,170}	IIa	C
In patients with suspected cardiomyopathy, CT-based imaging should be considered to exclude congenital or acquired coronary artery disease as a cause of the observed myocardial abnormality. ¹⁷¹	IIa	C
18F-FDG-PET scanning should be considered for the diagnostic work-up in patients with cardiomyopathy in whom cardiac sarcoidosis is suspected. ^{164,172,173}	IIa	C

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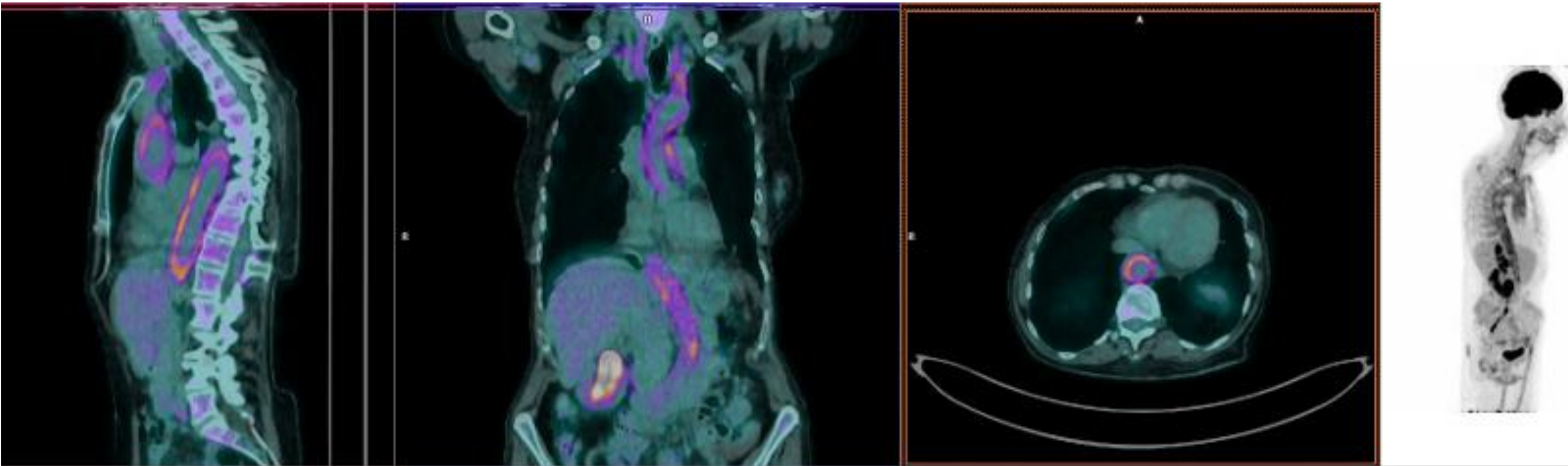
18F-FDG-PET, 18F-fluorodeoxyglucose positron emission tomography; ATTR, transthyretin amyloidosis; CMR, cardiac magnetic resonance; CT, computed tomography; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; HMDP, hydroxymethylene diphosphonate; PYP, pyrophosphate.

^aClass of recommendation.

^bLevel of evidence.

Whole body ^{18}F -FDG- PET/CT imaging for detection of vasculitis

Injection of ^{18}F -FDG, uptake at least 60 minutes, EDE aprox 5 mSv

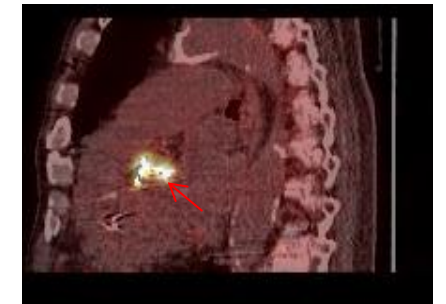
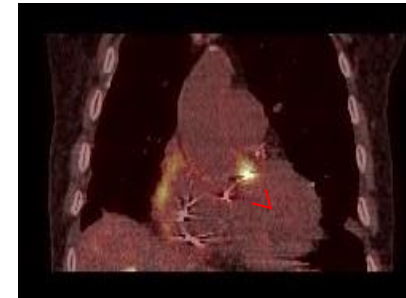
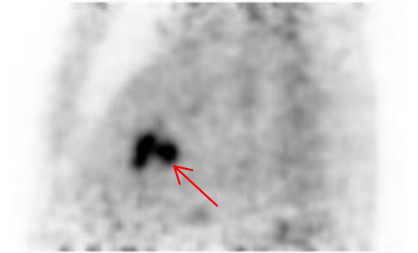
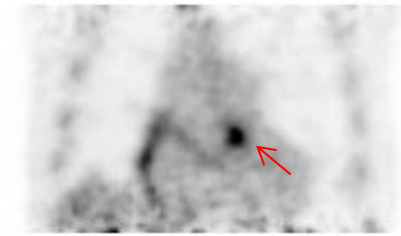
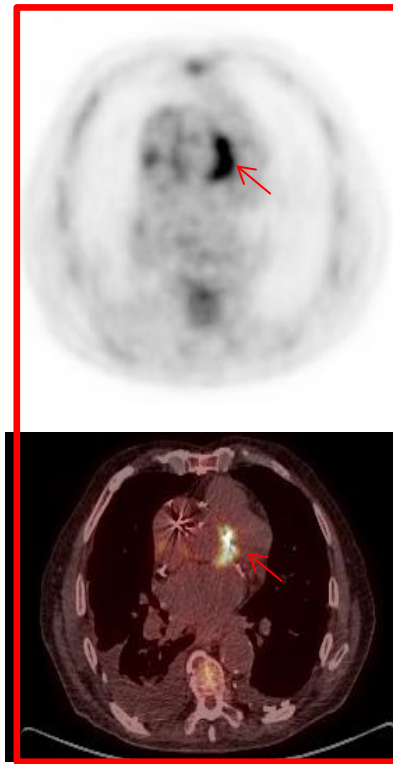
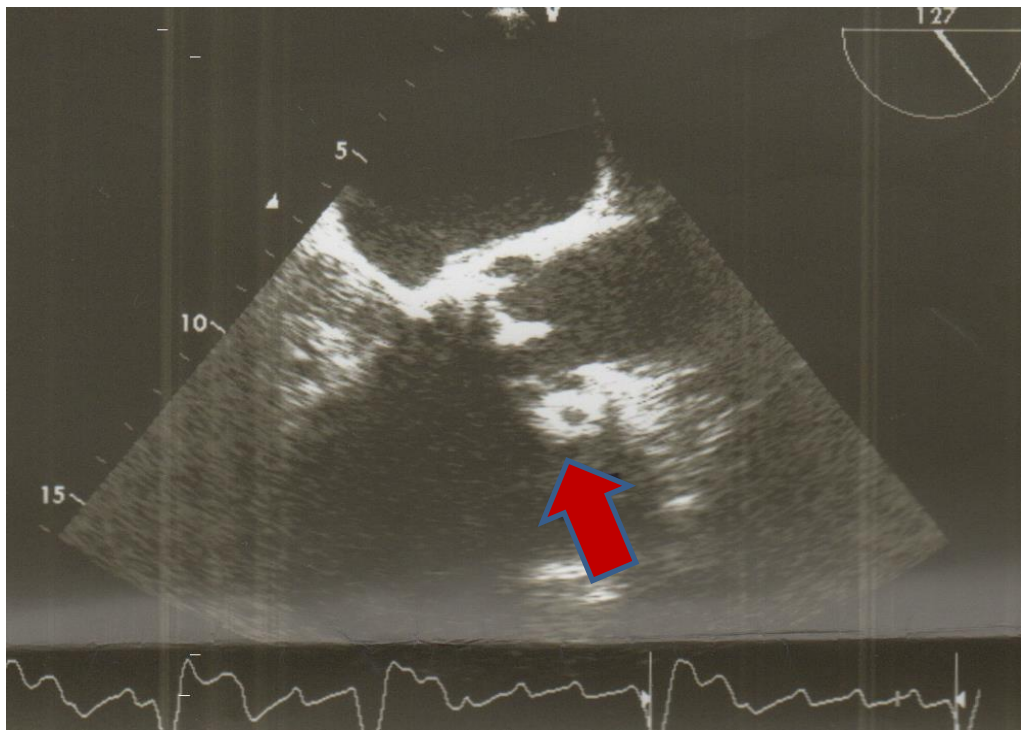


Detection of infective prosthetic valve endocarditis (PVE)

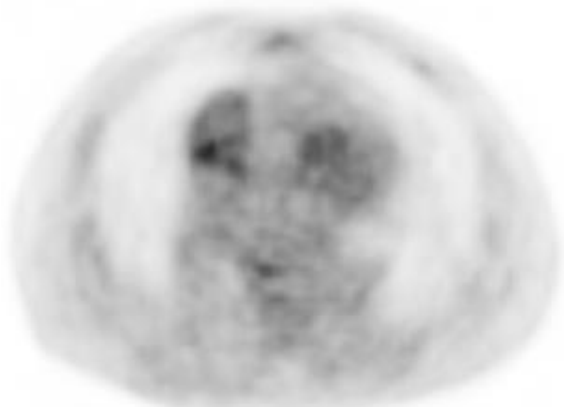
89 year old male patient, with a prior history CABG, AVR and pacemaker, was admitted to hospital because of fever, chills and cough with bloody sputum of 10 days duration, despite administration of ciprofloxacin, 500mg bid, (initially) and moxifloxacin, 400mg od, later on

Laboratory testing: elevated inflammatory markers, cultures of sputum and urine: negative

A strain of *Pseudomonas aeruginosa* (PA), susceptible to all antipseudomonal antibiotics was isolated from three sets of blood cultures

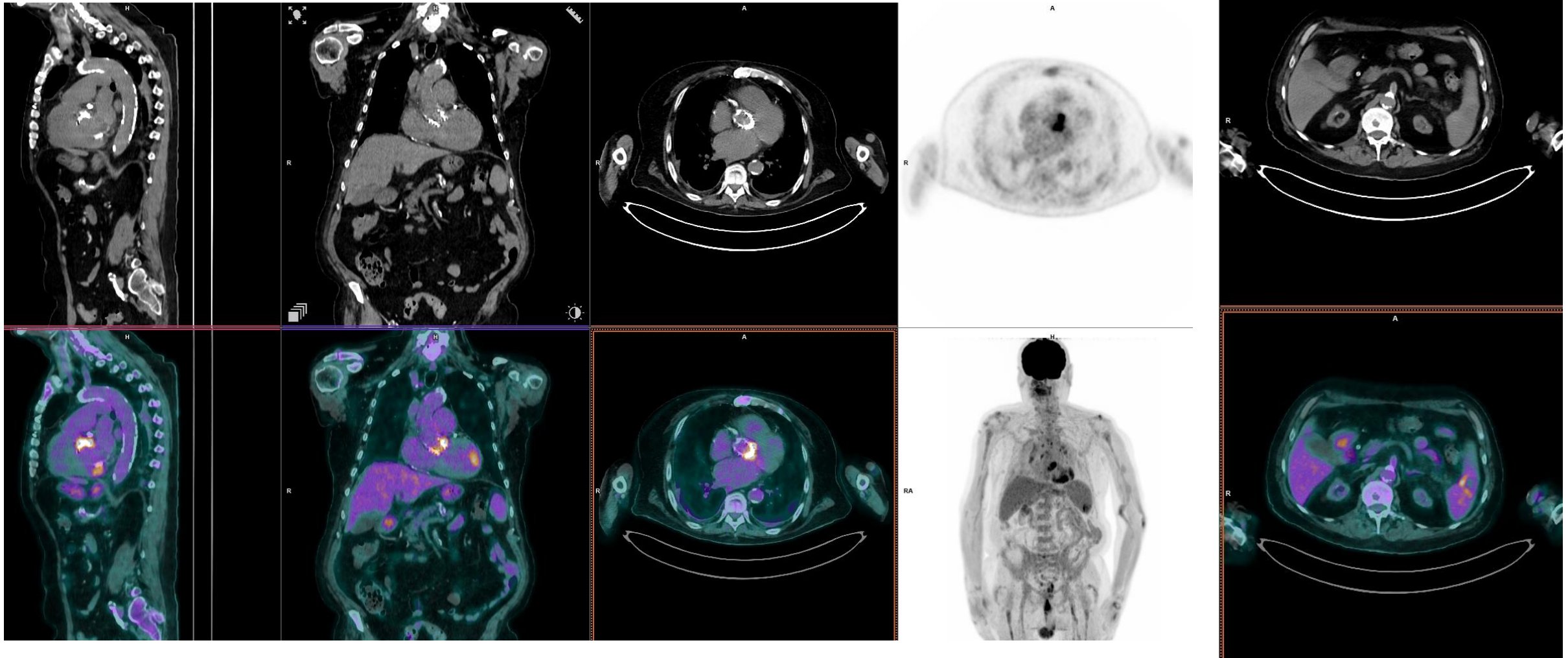


IV treatment with ceftazidime and amikacin, for a total of six weeks followed by oral administration of ciprofloxacin



Example of infective prosthetic valve endocarditis (PVE)

73 year old patient with AVR, was admitted to hospital with symptoms of endocarditis, elevated PCR, TOE non diagnostic, -ve blood cultures



Benefits of ^{18}F -FDG-PET/CT imaging for Diagnosis of infective endocarditis (IE)

- Identification of the presence and extent of cardiac Infection
- Detection of extra-cardiac foci of infection
- Extra-cardiac PET/CT findings lead to a change in management in over one third of patients including prolongation of antibiotic therapy and surgical intervention
- PET/CT can also identify
 - a potential source of entry for infection (e.g dental abscess, deep infection...)
 - or
 - an alternative source of the patient's symptoms (different infectious or inflammatory process, or malignancy)

DIAGNOSTIC ACCURACY OF PET/CT

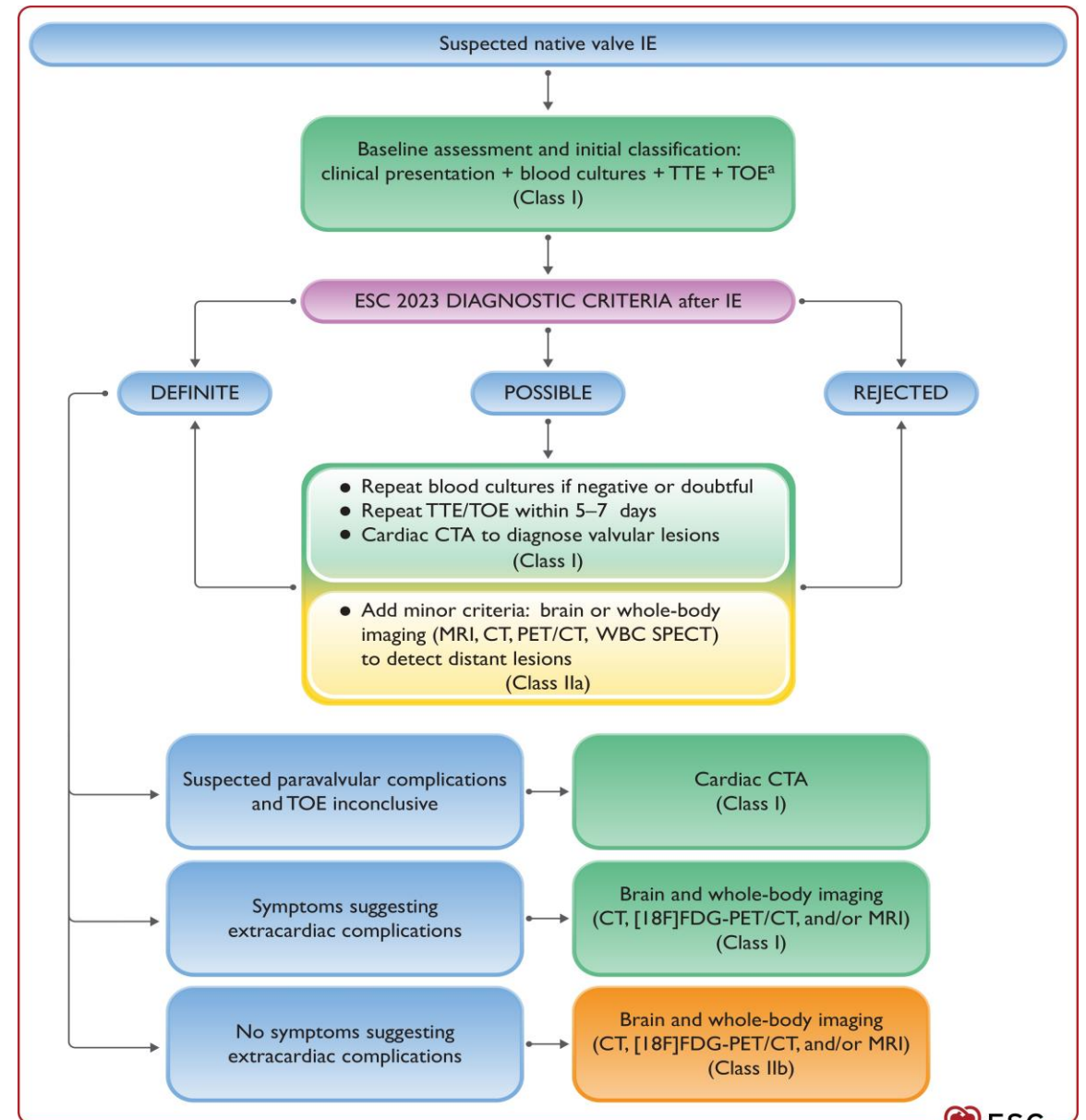
Native valve endocarditis	Prosthetic valve endocarditis
Indications FDG-PET/CT Evaluation disseminated disease	Indications FDG-PET/CT Evaluation disseminated disease Evaluation intracardiac lesions
Intracardiac lesion detection Sensitivity 36% Specificity 98%	Intracardiac lesion detection Sensitivity 86% Specificity 84%

Because of its low sensitivity, negative intracardiac findings in FDG-PET/ CT cannot be used to rule out the diagnosis in Native Valve Endocarditis (NVE)

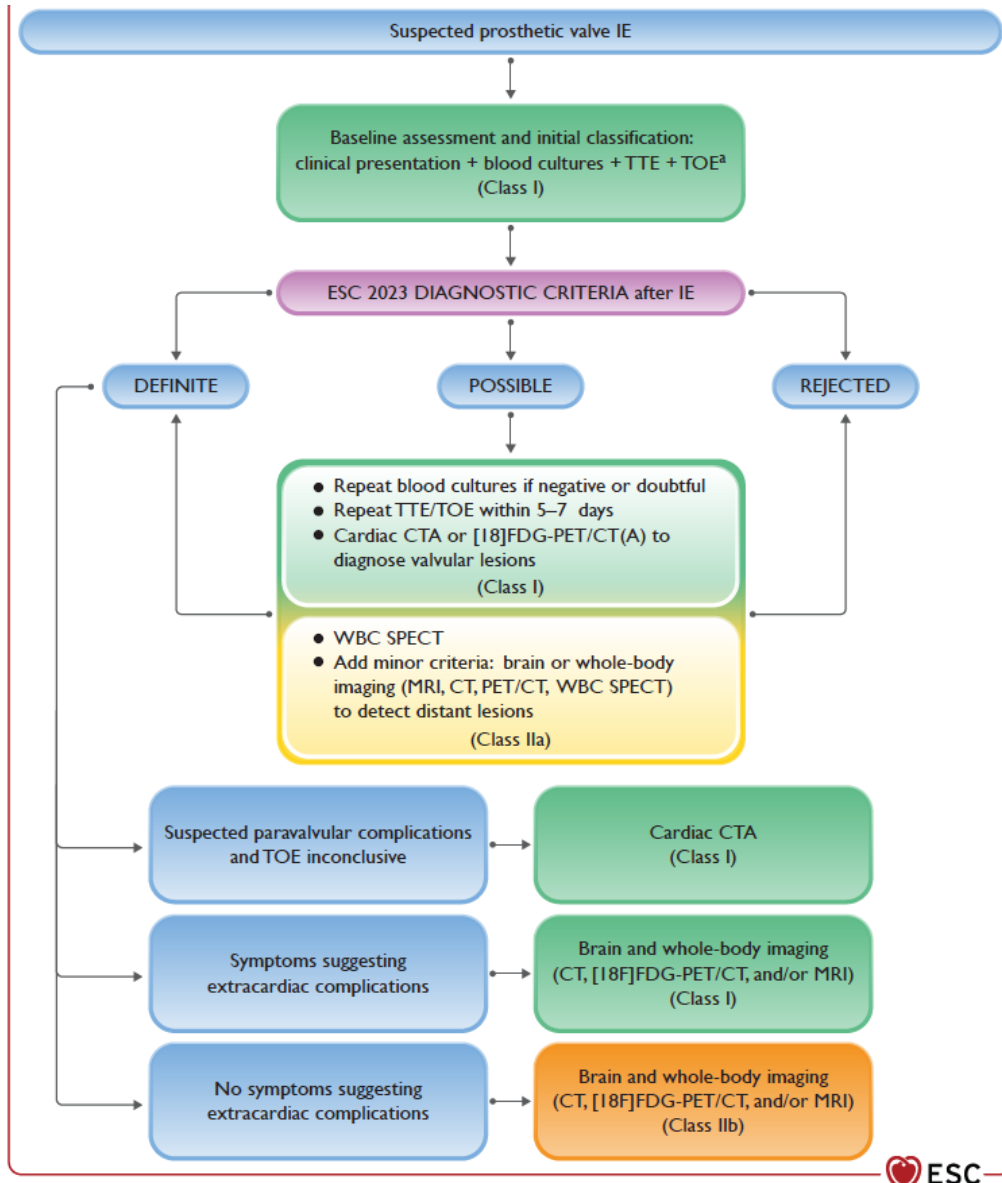
For many patients, there is an indication to perform FDG-PET/ CT for detection of disseminated disease, as distant foci can help establishing the diagnosis

Infective Endocarditis - ESC Guidelines 2023

Major criteria
(i) Blood cultures positive for IE (a) Typical microorganisms consistent with IE from two separate blood cultures: Oral streptococci, <i>Streptococcus gallolyticus</i> (formerly <i>S. bovis</i>), HACEK group, <i>S. aureus</i> , <i>E. faecalis</i> (b) Microorganisms consistent with IE from continuously positive blood cultures: • ≥ 2 positive blood cultures of blood samples drawn >12 h apart. • All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last samples drawn ≥ 1 h apart). (c) Single positive blood culture for <i>C. burnetii</i> or phase I IgG antibody titre $>1:800$.
(ii) Imaging positive for IE: Valvular, perivalvular/periprosthetic and foreign material anatomic and metabolic lesions characteristic of IE detected by any of the following imaging techniques: • Echocardiography (TTE and TOE). • Cardiac CT. • $[^{18}\text{F}]\text{-FDG-PET/CT(A)}$. • WBC SPECT/CT.
Minor criteria
(i) Predisposing conditions (i.e. predisposing heart condition at high or intermediate risk of IE or PWIDs)^a (ii) Fever defined as temperature $>38^{\circ}\text{C}$ (iii) Embolic vascular dissemination (including those asymptomatic detected by imaging only): • Major systemic and pulmonary emboli/infarcts and abscesses. • Haematogenous osteoarticular septic complications (i.e. spondylodiscitis). • Mycotic aneurysms. • Intracranial ischaemic/haemorrhagic lesions. • Conjunctival haemorrhages. • Janeway's lesions. (IV) Immunological phenomena: • Glomerulonephritis. • Osler nodes and Roth spots. • Rheumatoid factor. (V) Microbiological evidence: • Positive blood culture but does not meet a major criterion as noted above. • Serological evidence of active infection with organism consistent with IE.
IE Classification (at admission and during follow-up)
Definite: • 2 major criteria. • 1 major criterion and at least 3 minor criteria. • 5 minor criteria. Possible: • 1 major criterion and 1 or 2 minor criteria. • 3–4 minor criteria. Rejected: • Does not meet criteria for definite or possible at admission with or without a firm alternative diagnosis.



Multimodality Imaging for investigating patients with suspected PVE



TIMING OF IMAGING: FDG-PET/CT results can be accurate as early as 1 month after heart valve replacement

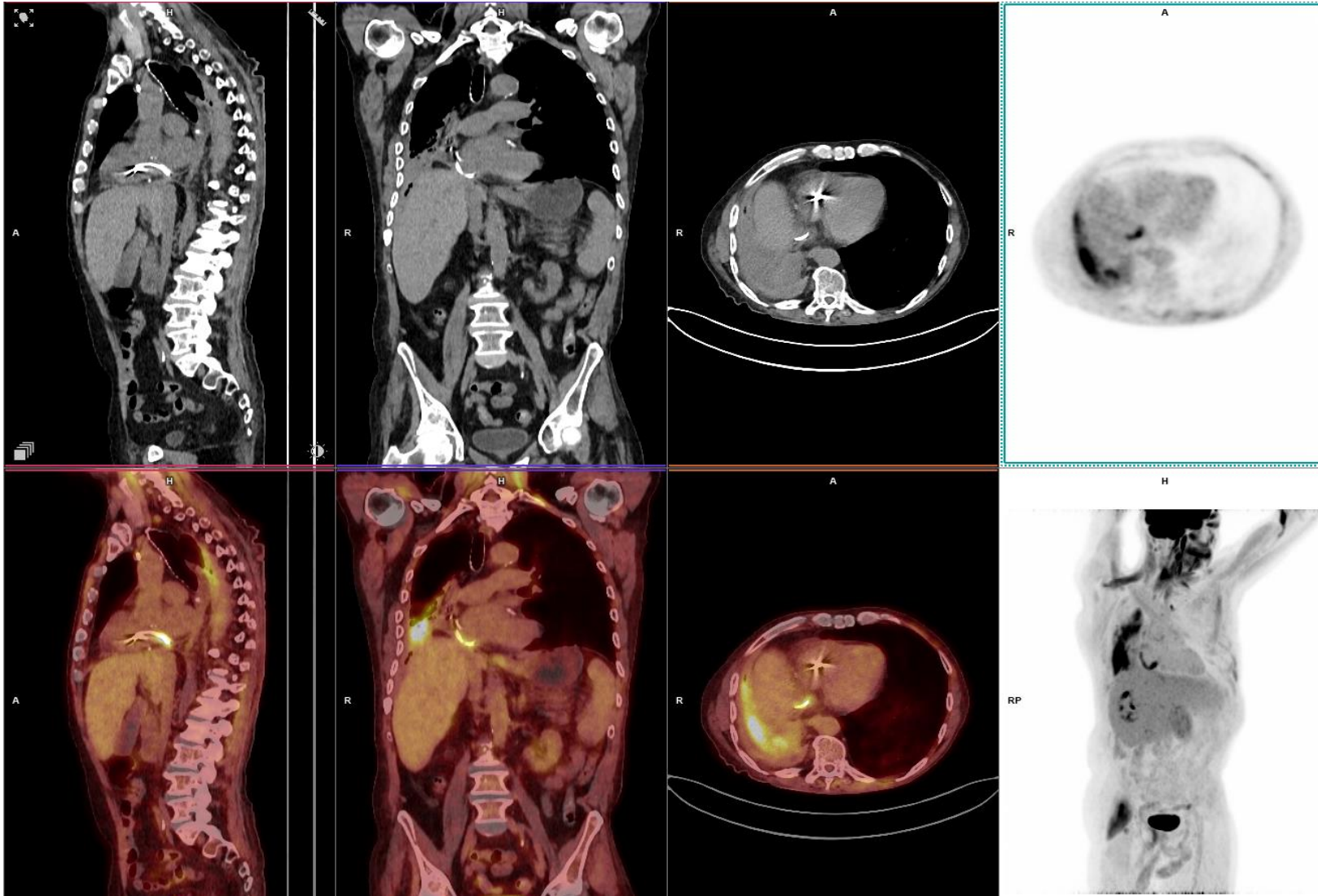
Perform FDG-PET/CT before antibiotic treatment is initiated or as soon as possible promptly after, without delaying the start of antibiotic treatment

Challenges in Diagnosis of Cardiac Implanted Electronic Device (CIED) Infection

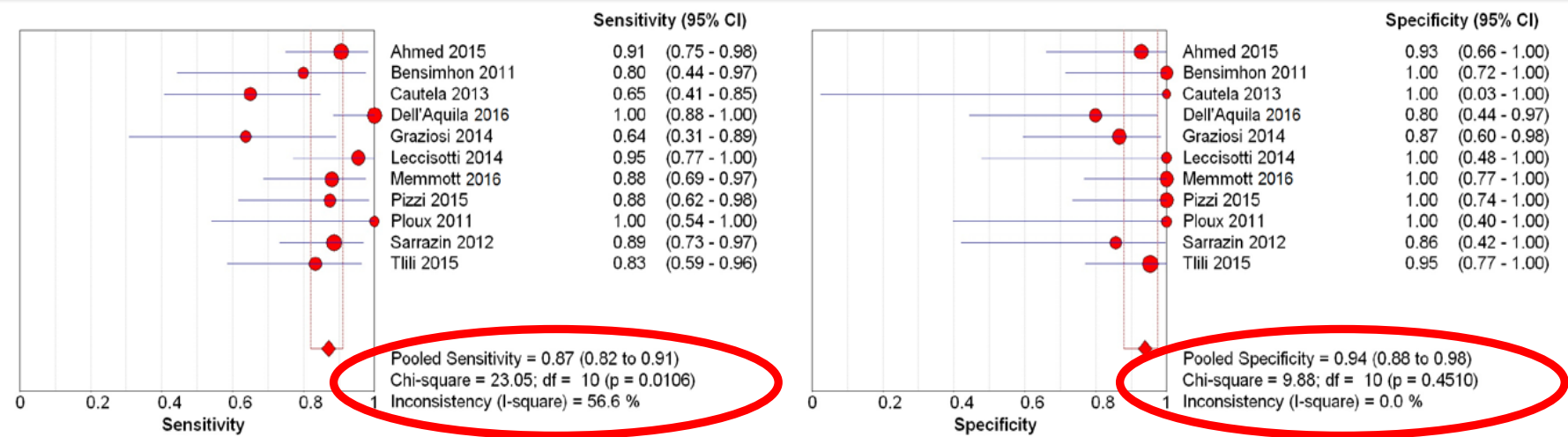
- To differentiate a superficial incisional infection from a true generator pocket infection
- CIED lead infection or endocarditis can be the most challenging
- Challenging to discern the difference between a sterile thrombus and infected vegetation on either TTE or TEE
- A negative echocardiogram does not exclude CIED lead endocarditis, as the extra-cardiac portion of the CIED leads cannot be visualized
- Additional imaging such as CT or ^{18}F -FDG PET/CT can be useful

Infective endocarditis affecting cardiac implantable electronic devices

69 year-old male with history of Ca of the Right lung treated with chemotherapy, radiotherapy and immunotherapy until 2019, Pacemaker in 2020, Episodes of febrile infections in 2023

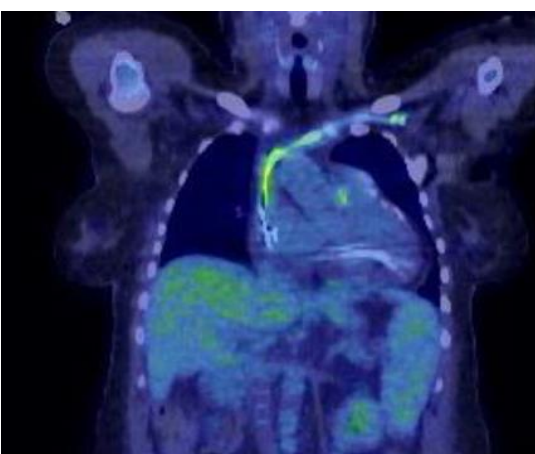


PET/CT imaging in diagnosis of cardiac implantable electronic device infection

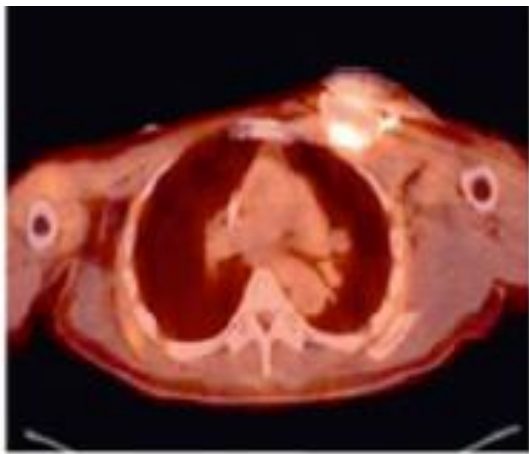
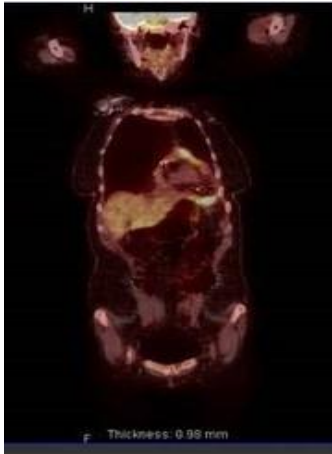


Forrest plots of individual PET/CT studies for diagnosis of cardiac implantable electronic device infection studies

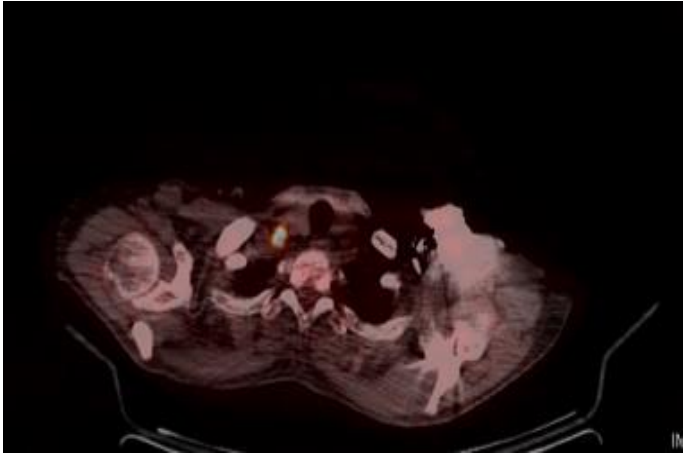
Juneau et al. Circ Cardiovasc Imaging 2017



Sensitivity 76%, specificity 83%



Sensitivity 96%, specificity of 97%



Conclusions

- PET perfusion with quantification is the ideal technique for detecting balanced ischemia, multi-vessel disease and microvascular dysfunction
- PET perfusion in combination with FDG imaging is an excellent technique for assessment of myocardial viability- hibernation in patients with severe LV dysfunction
- PET is a powerful imaging technique to assess patients with:
 - Suspicion of cardiac sarcoidosis as well as those with known disease, providing important information on disease activity (should we start steroids?)
 - Suspicion of prosthetic valve endocarditis or infection of cardiac implanted electronic devices
 - providing Incremental value over echocardiography for the early detection of infection with high sensitivity
 - Identifying distant foci (e.g septic emboli) and alternative causes of infection other than endocarditis

And remember....
Multidisciplinary team approach



Thank you