ד"ר איילת רז-פסטר
מחלקת פנימית א'
רמב"ם


How much do you like your pet?

Patient no. 1

- 90 years old, Male
- Normal functional and mental status
- Comorbidities: hypertension, severe aortic stenosis (recently diagnosed planned to TAVI..)
- One month before- underwent coronary catheterization - non significant disease

Patient no. 1

- Current admission: fever for 3 weeks, loss of weight
- Physical exam- stable, systolic heart murmur
- Lab- WBC 13,150/µl, HGB-8.0 gr/dl, CR-2.4 mg/dl, CRP- 19 mg/dl

- Chest X ray- pulmonary congestion
- Blood culture taken and started ceftriaxone for “suspected pneumonia”
- Echocardiography (TTE)- severe AS with calcifications
- Blood cultures – *Corynebacterium amycolatum* (1/6) m/p contamination
- Fever continued

Patient no. 1

- ID consultation- a patient with Fever of Unknown Origin
  - stop antibiotics
  - take
  - perfo

What is the contribution of FDG PET/CT in the diagnosis of infectious etiologies in FUO?

Fever of Unknown Origin: The Role of ^{18}F-FDG PET/CT

Zohar Keidar[1,2], Alexandra Gurman-Balbir[3], Diana Gaitini[2,4], and Ora Israel[1,2]

[1]Department of Nuclear Medicine, Rambam Health Care Campus, Haifa, Israel; [2]B. and R. Rappaport Faculty of Medicine, Technion—Israel Institute of Technology, Haifa, Israel; [3]B. Shine Department of Rheumatology, Rambam Health Care Campus, Haifa, Israel; and [4]Department of Diagnostic Imaging, Rambam Health Care Campus, Haifa, Israel

THE JOURNAL OF NUCLEAR MEDICINE • Vol. 49 • No. 12 • December 2008

TABLE 1
Clinical and Imaging Findings in 22 Patients with FUO and Positive Contributory PET/CT Studies

Patient no.	PET/CT findings	Results of additional relevant diagnostic procedures	PET/CT contribution	Final diagnosis
1	Focus in liver	Inconclusive CT	Diagnosis and guiding surgical drainage	Liver abscess
2	Abdominal focus localized to renal cyst	None	Diagnosis and guiding surgical approach	Renal abscess
3	Pelvic focus localized to right ovary	Inconclusive CT	Diagnosis and guiding surgical approach	Ovarian abscess
4	Abdominal focus localized to surgical scar	Inconclusive CT (history of abdominal surgery)	Diagnosis and guiding surgical approach	Abdominal wall abscess
5	Pelvic foci localized to pararectal region and iliac and inguinal lymph nodes	CT (suspected pelvic abscess) and normal gynecologic examination	Diagnosis and guiding surgical approach	Pararectal abscess and reactive lymph nodes
6	Focus in left maxilla	None	Guiding dental evaluation and treatment	Dental abscess
7	Thoracic focus localized to proximal clavicle, sternoclavicular joint, and soft tissues	Inconclusive CT (renal failure and pacemaker; contraindication for intravenous contrast and MRI)	Diagnosis and guiding drainage of abscess. Determining the need for further antibiotic treatment	Osteomyelitis of clavicle and soft-tissue abscess
8	Abdominal focus localized to porta hepatis	None	Diagnosis and guiding surgical approach	Ascending cholangitis
			Diagnosis and guiding therapeutic procedure (removal of catheter)	Infected intravenous catheter
			Guiding biopsy	Giant cell arteritis
			Guiding biopsy	Giant cell arteritis
			Leading criteria to final diagnosis	Aortitis
			Leading criteria to final diagnosis	Idiopathic pericarditis
			Leading criteria to final diagnosis	Idiopathic pericarditis
			Leading criteria to final diagnosis	Idiopathic pericarditis
			Leading criteria to final diagnosis	Sarcoidlike disease
			Leading criteria to final diagnosis	Sarcoidlike disease
			Guiding biopsy	Sarcoidosis
	axillary lymphadenopathy		Leading criteria to final diagnosis	Still disease
20	Thoracic and inguinal foci localized to axillary and inguinal lymphadenopathy	None	Guiding biopsy	Follicular cell lymphoma
21	Abdominal foci localized to both adrenals	CT (hepatosplenomegaly, enlarged left adrenal)	Guiding biopsy	Diffuse large-cell lymphoma
22	Diffuse skeletal uptake	CT (pleural effusion)	Guiding biopsy	Metastatic adenocarcinoma

- 45 cases of FUO (>1wk inpatient investigation)
- 27 positive test
- 9 with infectious etiology
- Deep-seated abscesses

European Journal of Internal Medicine 22 (2011) 112–116

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original article

Diagnostic value of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in patients with fever of unknown origin ☆

Ji-Fang Sheng [a,*], Zi-Ke Sheng [a], Xiao-Min Shen [a], Sheng Bi [a], Jun-Jie Li [a], Guo-Ping Sheng [a], Hai-Ying Yu [a], Hai-Jun Huang [a], Jun Liu [a], Dai-Rong Xiang [a], Meng-Jie Dong [b], Kui Zhao [b,*], Lan-Juan Li [a]

[a] *Department of Infectious Diseases, State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, the First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China*

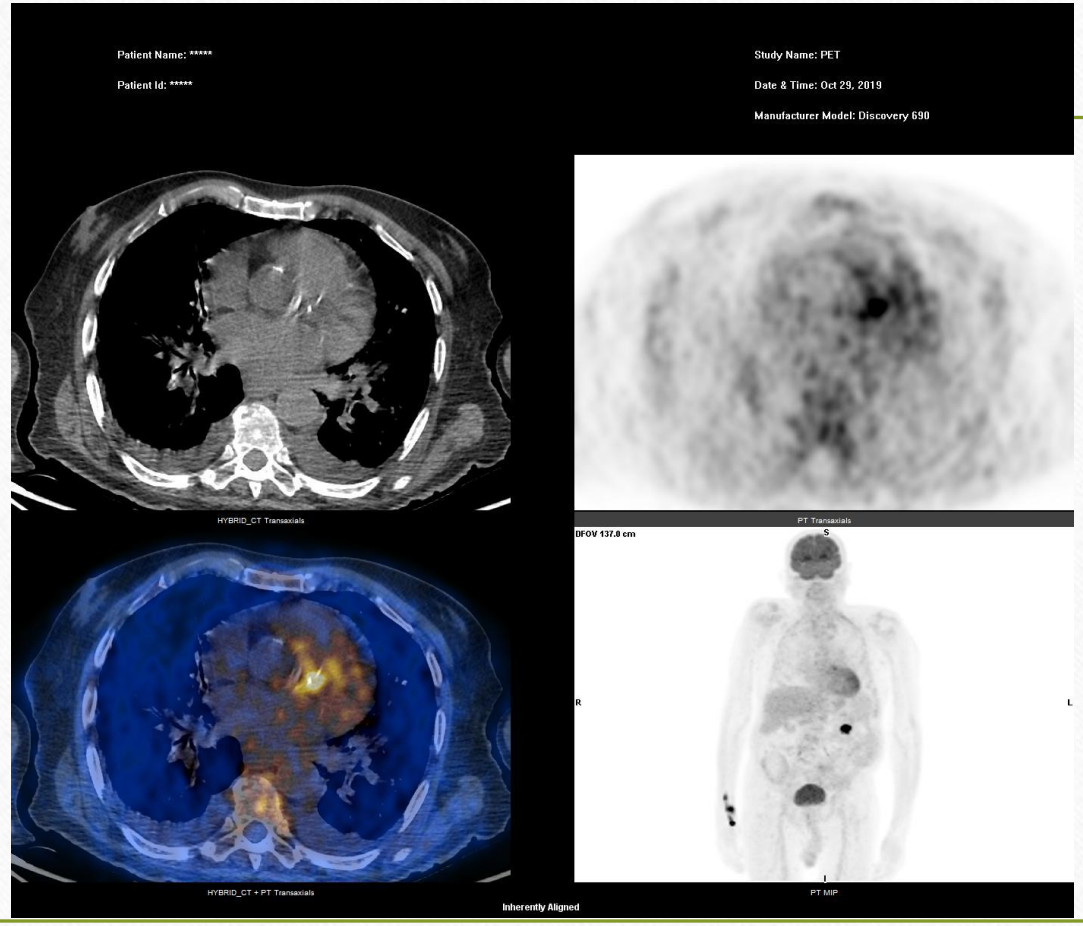
[b] *PET Center, the First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China*

Table 3
Final diagnosis of patients with FUO and contribution of PET/CT to FUO.

Categories	Final diagnosis, No.(%) of cases	PET/CT results		
		Normal	Abnormal	
			Helpful	Noncontrib
Infection	15(31%)	3	12	0
Pulmonary infection	6	1	5	0
Upper respiratory tract infection	1	1	0	0
Tuberculosis	2	0	2	0
Subacute thyroiditis	1	0	1	0
Abdominal infection	2	0	2	0
Viral hepatitis	1	1	0	0
Biliary tract infection	1	0	1	0
Chronic pancreatitis	1	0	1	0
Neoplasm	12(25%)	0	12	0
Malignant lymphoma	8	0	8	0
Lung cancer	2	0	2	0
Relapse of gastric cancer	1	0	1	0
Myelodysplastic syndrome	1	0	1	0
Non-infectious inflammatory disease	9(19%)	1	8	0
Adult-onset Still's disease	5	1	4	0
Sjogren syndrome	1	0	1	0
Systemic lupus erythematosus	1	0	1	0
Vasculitis	1	0	1	0
Sarcoidosis	1	0	1	0
No diagnosis	12(25%)	4	0	8
Total (%)	48(100%)	8	32	8

- Infections were diagnosed in 15/48 cases (31%)
- PET/CT was positive in 12/15 of infections
- Pulmonary and intra-abdominal infections

Back to patient no. 1



Focal pathological FDG uptake on aortic valve

Clinical Infectious Diseases

MAJOR ARTICLE

The Role of ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in the Diagnosis of Left-sided Endocarditis: Native vs Prosthetic Valves Endocarditis

Raphael Abegão de Camargo,[1] Marcio Sommer Bitencourt,[2,3] José Claudio Meneghetti,[4] Jose Soares Jr,[4] Luís Fernando Tonello Gonçalves,[4] Carlos Alberto Buchpiguel,[1] Milena Ribeiro Paixão,[5] Marilia Francesconi Felicio,[6] Alexandre de Matos Soeiro,[7] Tania Mara Varejão Strabelli,[6] Alfredo Jose Mansur,[8] Flavio Tarasoutchi,[5] Mucio Tavares de Oliveira Jr,[7] Jussara Bianchi Castelli,[9] Danielle Menosi Gualandro,[10] Lucas Zoboli Pocebon,[6] Ron Blankstein,[11] Abass Alavi,[12] John Edmund Moore,[13] Beverley Cherie Millar,[13] and Rinaldo Focaccia Siciliano[6]

[1]Department of Nuclear Medicine, University of São Paulo Medical School, [2]Center for Clinical and Epidemiological Research, University Hospital, University of São Paulo School of Medicine, [3]Hospital Israelinta Albert Einstein, [4]Nuclear Medicine and Molecular Imaging Department, [5]Valvular Heart Disease Unit, [6]Infection Control Team, [7]Emergency Unit, [8]Department of Cardiology, [9]Department of Pathology, and [10]Interdisciplinary Medicine in Cardiology Unit, Heart Institute (InCor), Hospital das Clínicas, University of São Paulo Medical School, Brazil; [11]Cardiovascular Division and Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [12]Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia; and [13]Northern Ireland Public Health Laboratory, Department of Bacteriology, Belfast City Hospital, Co. Antrim, United Kingdom

Clinical Infectious Dis, April 2019

FDG PET/CT in diagnosis of IE

- Evaluated prospectively the accuracy of FDG-PET/CT in the diagnosis of IE in a broad, unselected population of individuals with suspected native valve and prosthetic valve endocarditis

- Suspected left sided IE

(1) patients with risk factors for IE and any of following:

  - (a) fever or high inflammatory markers
  - b) new embolic event
  - (c) acute heart failure due to valve regurgitation;

(2) FUO with new heart murmur or embolic event

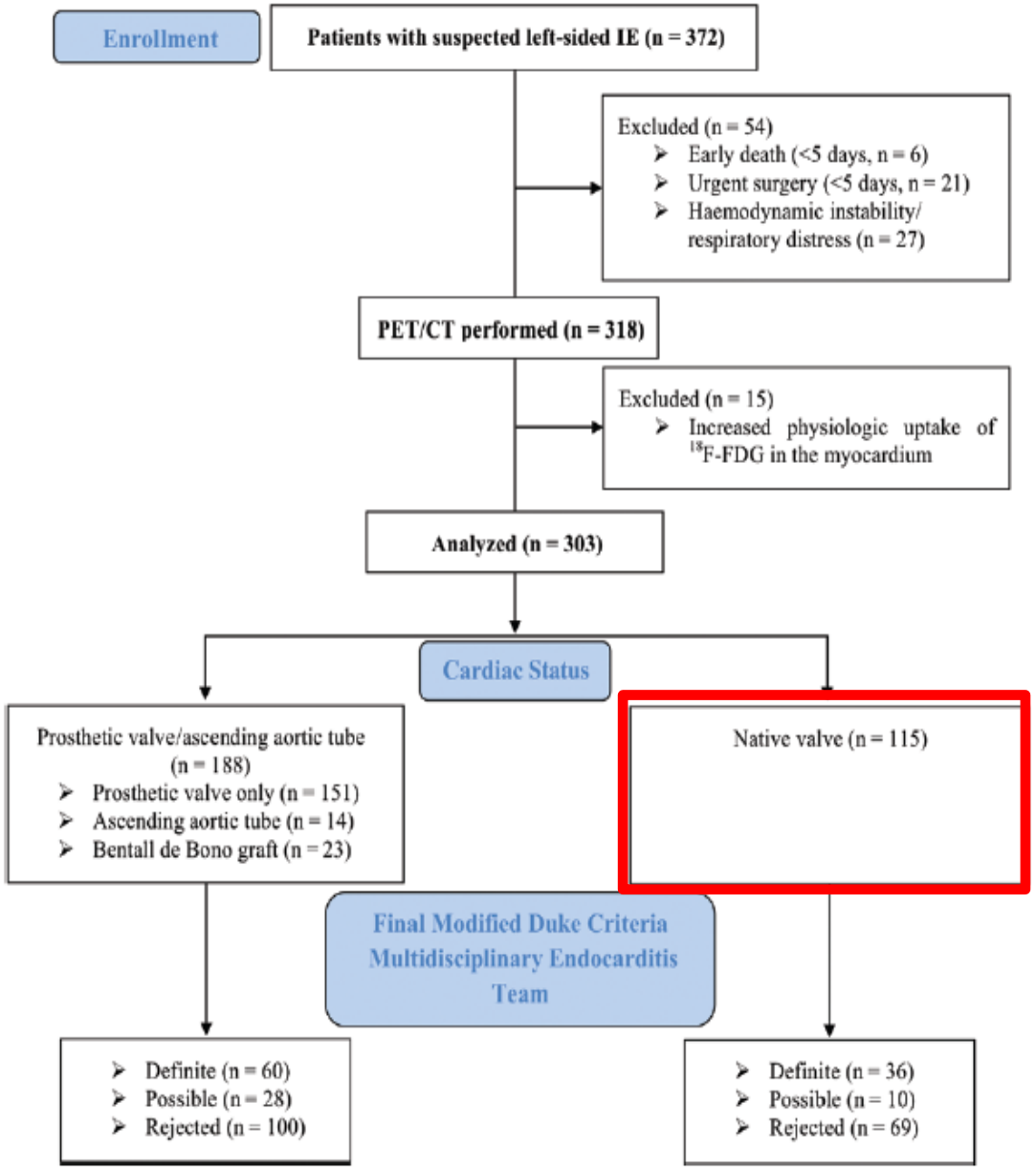


Figure 1. Flow chart showing the classification of episodes of infective endocarditis. Abbreviations: ^{18}F-FDG-PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; IE, infective endocarditis.

Table 2. ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography, Echocardiogram, and Modified Duke Criteria for Detection of Infective Endocarditis

Characteristics	n	SE, %	SP, %	PPV, %	NPV, %	AC, %
Prosthetic valves only						
Admission echocardiography	151	60	95	91	75	79.5
PET/CT cardiovascular focal uptake	151	91	94	92	93	92.7
Admission mDC[a]	151	42	88	74	65	67.5
Admission mDC[a] + PET/CT major criteria	151	91	88	86	93	89.4
Prosthetic valves/ascending aortic prosthesis						
Admission echocardiography	188	59	96	93	73	78.7
PET/CT cardiovascular focal uptake	188	93	90	89	94	91.5
Admission mDC[a]	188	41	90	78	63	67
Admission mDC[a] + PET/CT major criteria	188	93	90	89	94	91.5
Ascending aortic prosthesis only						
Admission echocardiography	37	57	100	100	64	75.7
PET/CT cardiovascular focal uptake	37	100	69	81	100	86.5
Admission mDC[a]	37	38	100	100	55	64.9
Admission mDC[a] + PET/CT major criteria	37	100	100	100	100	100
Native valves						
Admission echocardiography	115	70	93	86	82	83.5
PET/CT cardiovascular focal uptake	115	22	100	100	66	68.7
Admission mDC[a]	115	54	91	81	75	76.5
Admission mDC[a] + PET/CT major criteria	115	65	91	83	80	80.9
Admission mDC[a] + PET/CT major criteria + emboli[b]	115	78	91	86	86	86

Abbreviations: AC, accuracy; CT, computed tomography; mDC, modified Duke criteria; NPV, negative predictive value; PET, positron emission tomography; PPV, positive predictive value; SE, sensitivity; SP, specificity.

[a]Admission mDC definite/reject.

[b]Emboli detected by PET/CT (minor mDC).

Back to patient no. 1

- One week after stopping antibiotics a second blood culture grew..

  Corynebacterium amycolatum

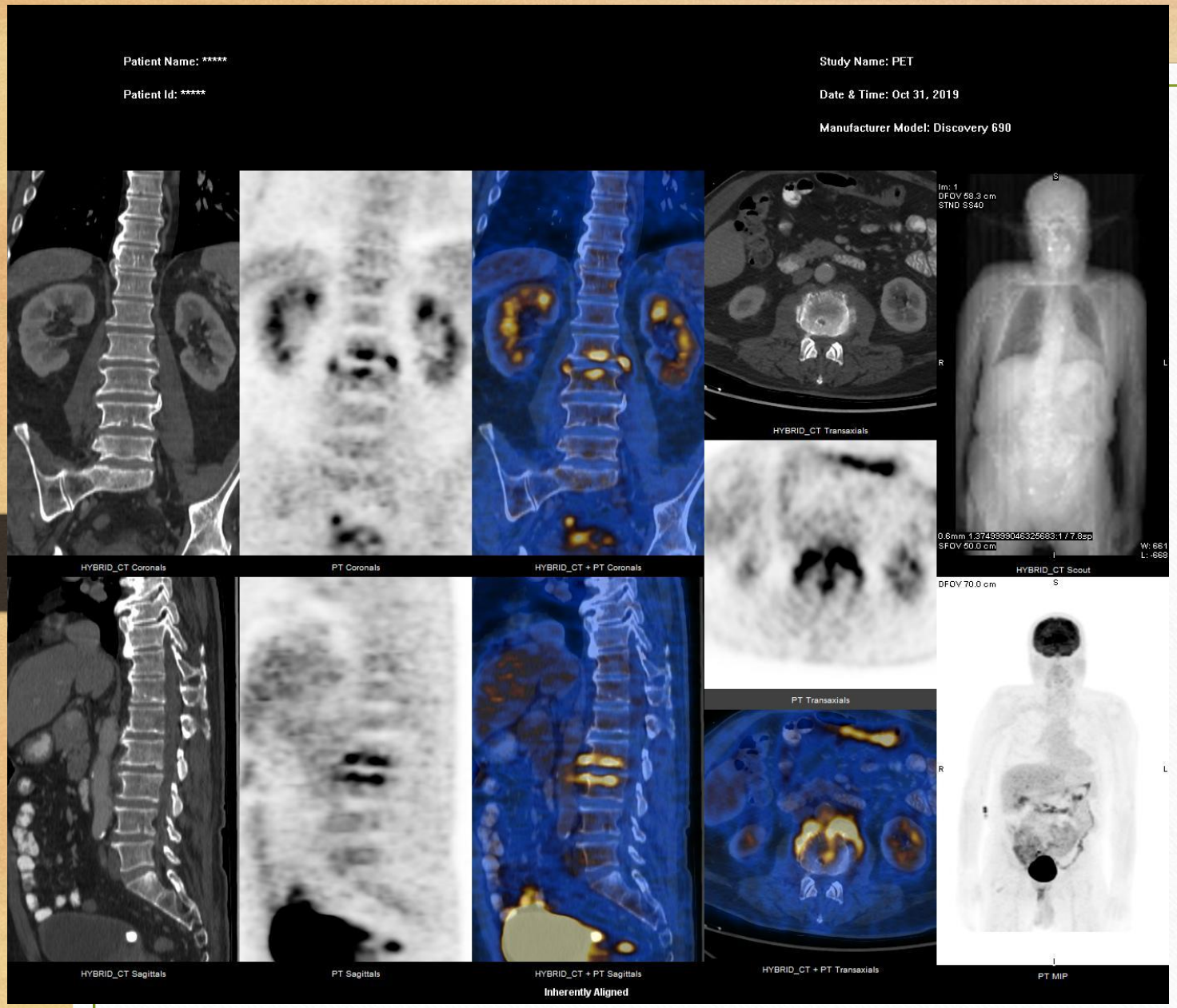
- TEE- a mass suspected as vegetation corresponding to anatomic focal FDG uptake detected by PET/CT
- The patient was diagnosed with definite IE and treated with antibiotics

Patient no.2

- A healthy 74 year old male
- Fever and back/flank pain for 2 weeks
- CTU for suspected nephrolithiasis- SOL of kidney?
- Blood and urine cultures were taken and antimicrobials were started for suspected urinary tract infection

Blood cultures grew???

- *Brucella meletensis*
- Antimicrobials (doxycycline and gentamicin) were started
- Duration of treatment ?? Complicated vs. non-complicated disease?
- Brucellosis with back pain
- Lumbar MRI- no signs of diskitis/osteomyelitis
- The patient continued to complain of back pain (as expected..)
- FDG PET/CT was performed one week after MRI



Pathological FDG uptake in L2-L3 suspected for diskitis/osteomyelitis

)

FDG PET/CT versus MRI for *vertebral* osteomyelitis

2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults[a]

- We recommend a spine MRI in patients with suspected Native Vertebral Osteomyelitis

- We suggest a combination spine gallium /Tc99 bone scan, or computed tomography scan or a positron emission tomography scan in patients with suspected Native Vertebral Osteomyelitis when MRI cannot be obtained (eg, implantable cardiac devices).

FDG PET is a robust tool for the diagnosis of spondylodiscitis: a meta-analysis of diagnostic data.
Prodromou ML, et al. Clin Nucl Med. 2014

PATIENTS AND METHODS:

- We implemented a patient-based meta-analysis of diagnostic data for FDG PET (the index test) against clinical, laboratory, and/or radiologic evidence of disease (the reference standard).

RESULTS:

- **12 studies** provided the diagnostic data on FDG PET and spondylodiscitis, comprising **224 patients**.
- **The combined sensitivity across studies was 0.97 [95% confidence interval (CI), 0.83-1.00], the specificity was 0.88 (95% CI, 0.74-0.95), and the area under the curve was 0.98 (95% CI, 0.96-0.99).**

CONCLUSIONS:

- FDG PET is a robust diagnostic test when spondylodiscitis is suspected and is excellent for exclusion of infectious spondylodiscitis given its low likelihood ratio negative (<0.1).
- Importantly, this diagnostic test is unaffected by other confounders, including the presence of implants, when PET/CT is used.

MRI for suspected vertebral osteomyelitis

Advantages

High sensitivity

Excellent anatomy discrimination: detection of abscesses, cord compression..

Disadvantages

Time consuming 

Need to localize the level

Contraindications with metals

Lower sensitivity on early stages of infection

FDG PET/CT for suspected vertebral osteomyelitis

Advantages

High sensitivity including the early stages of infection

Detection of other metastatic foci

Shorter than MRI

Can be used with metals

No need accurate localization of spine level.

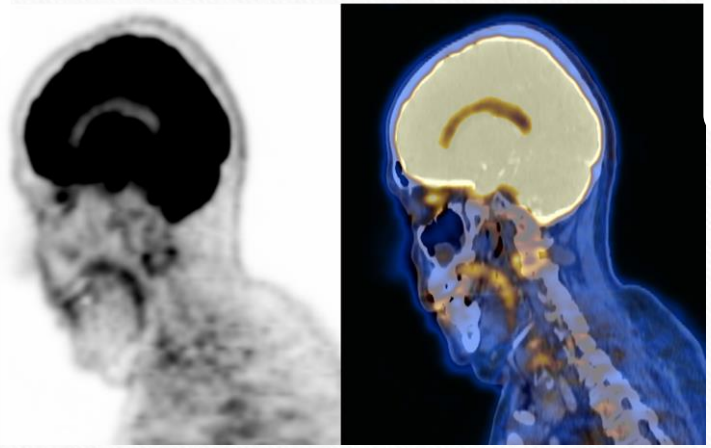
Disadvantages

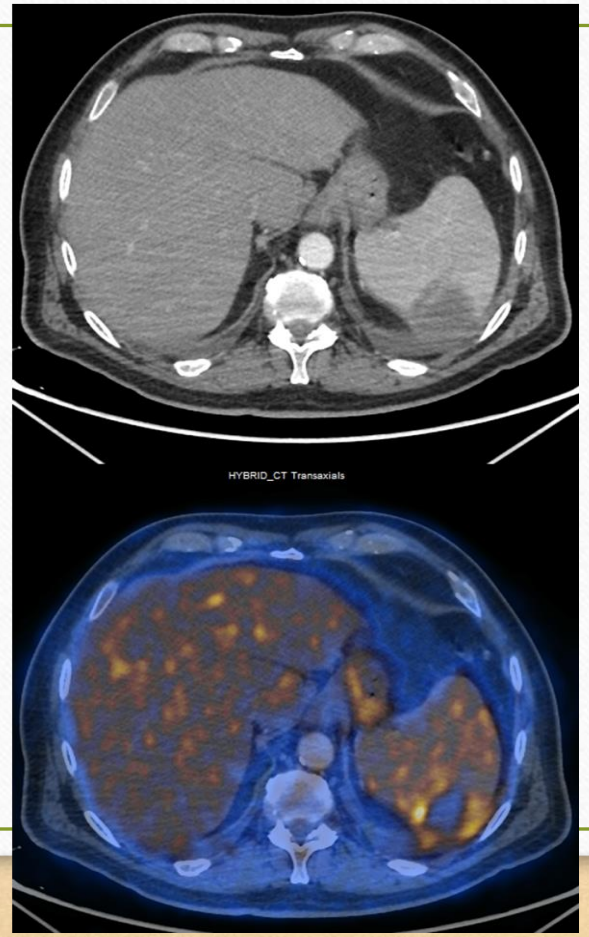
Lower sensitivity for spinal cord (abscess, compression..)

Patient no.3

- A 72-years old patient
- Presented with community-acquired primary staphylococcus aureus bacteremia (SAB)
- Had a fever duration of 10 days on appropriate antimicrobial treatment
- Trans-esophageal echocardiography was normal
- FDG PET/CT was performed

Patient no. 3





Pathological uptake in soft tissues surrounding C1-C2 vertebrae and the left sacroiliac region

Increased uptake at the periphery of a hypodense spleen lesion consistent with infarct.

Clinical Infectious Diseases 2020

Integration of FDG-PET/CT in the Diagnostic Workup for *Staphylococcus aureus* Bacteremia: A Prospective Interventional Matched-cohort Study

Nesrin Ghanem-Zoubi, Olga Kagna, Jawad Abu-Elhija, Mona Mustafa-Hellou, Majd Qasum, Zohar Keidar, and Mical Paul

FDG PET/CT in *staphylococcus aureus* bacteremia

Patients characteristics	PET CT N=46	Controls N=46
Age years	63.5 [51.2, 72.5]	64 [51.2, 75]
Charlson' score	4 [2, 6]	5 [1.25, 8]
MRSA	8 (17.4%)	8 (17.4%)
Poor cognitive status	3 (6.5%)	3 (6.5%)
Any implanted device	9 (19.5%)	4 (8.7%)
Pitt score	1 [0,2]	1 [0,2]
Definite IE	5 (10.8%)	5 (10.8%)
Days of fever after appropriate treatment	3.04 ± 5.96	0.77 ±1.76
Duration of bacteremia (days)	5±10	3±3

FDG PET/CT in *staphylococcus aureus* bacteremia

Patients outcome	PET CT N=46	Controls N=46
Mortality 90 day	6 (13%)	11 (23.9%)
Mortality 30 day	1 (2.17%)	2 (4.3%)
Days of hospital stay after bacteremia onset	21 [15, 39]	16 [10, 26]
Relapse	2 (4.3%)	2 (4.3%)

P= 0.002

P=0.004

FDG PET/CT in infectious diseases

- Fever of Unknown Origin (FUO)
- Native valve infective endocarditis
- Prosthetic valve infective endocarditis
- Vertebral osteomyelitis
- *Staphylococcus aureus* bacteremia
- Vascular infections- native and prosthetic
- Cardiac implanted electrical devices (CIED) infection
- Prosthetic joint infection
- Bacteremia of unknown origin

THE END