ACC Middle East Conference 2018

In partnership with:

جمعية القلب السعودية
Saudi Heart Association

Endocarditis : Current State of Management

Hassan Chamsi-Pasha
FRCP,FACC

Declaration of Interest

- **Nothing to declare.**

Case

- A 35 year old female who had bioprosthetic AVR and MVR 4 months earlier.
- Presented with fever for one month associated with chills and fatigue.
- A diagnosis of culture-negative endocarditis was made.
- Treated with Teicoplanin & Meropenem for 6 weeks and discharged well.

- Readmitted 6 weeks later with 5 days history of fever and malaise.
- O/E : she was febrile (39.6 C)
- New systolic murmur 3/6.
- WBC = 7.3 CRP = 177 ESR = 70 .
- Blood cultures were negative .
- ECG :sinus rhythm , and chest X ray demonstrated cardiomegaly.


FR 52Hz
9.0cm
M4
2D
57%
C 47
P Off
Gen
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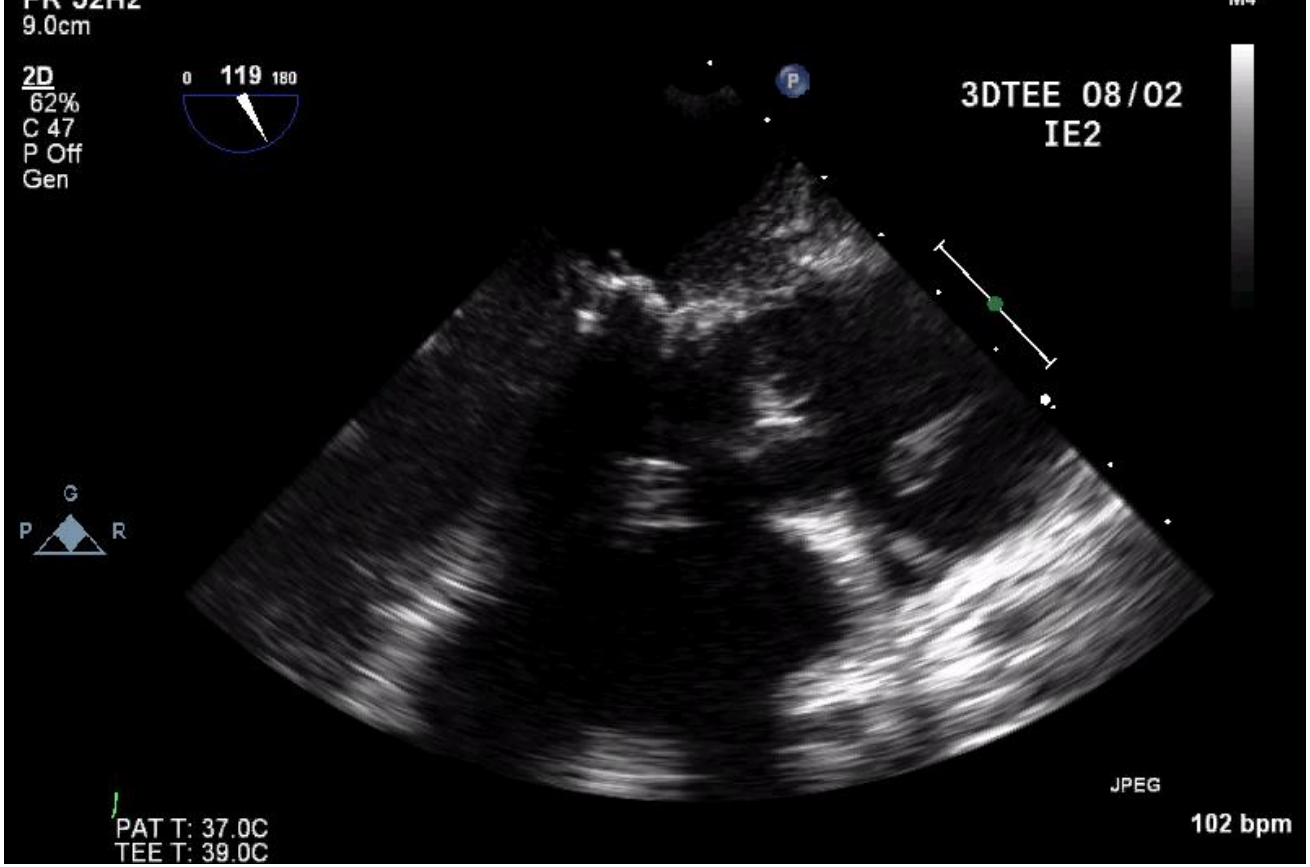
JPEG
PAT T: 37.0C
TEE T: 39.6C
109 bpm


9.0cm
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62%
C 47
P Off
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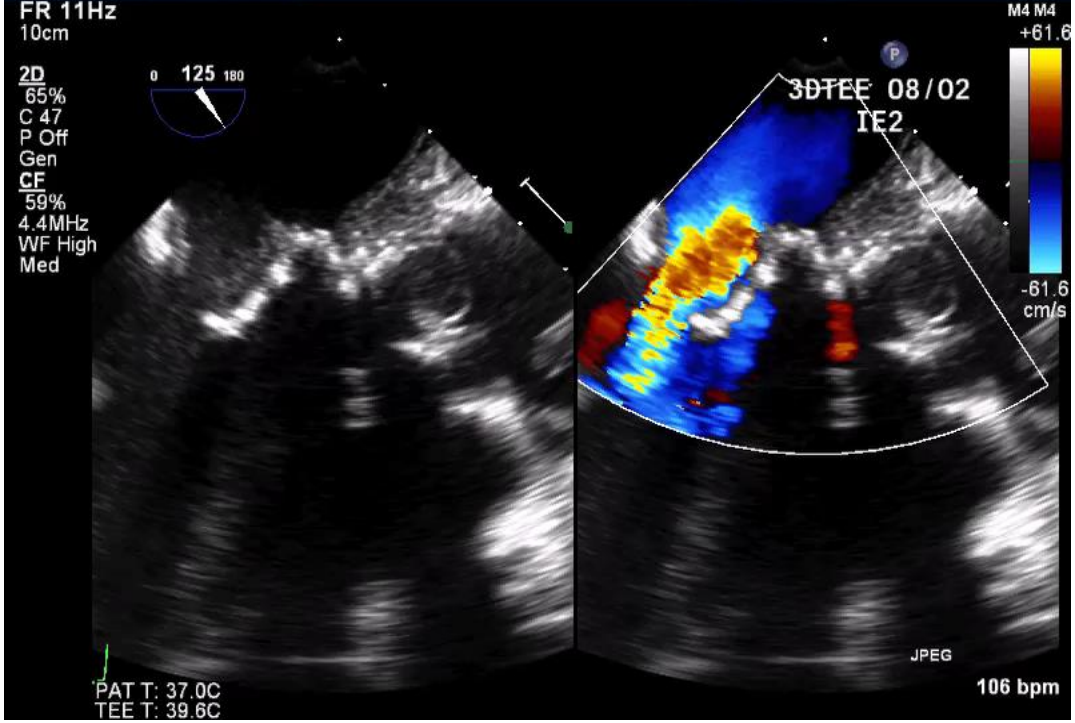
PAT T: 37.0C
TEE T: 39.0C
102 bpm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-61.6
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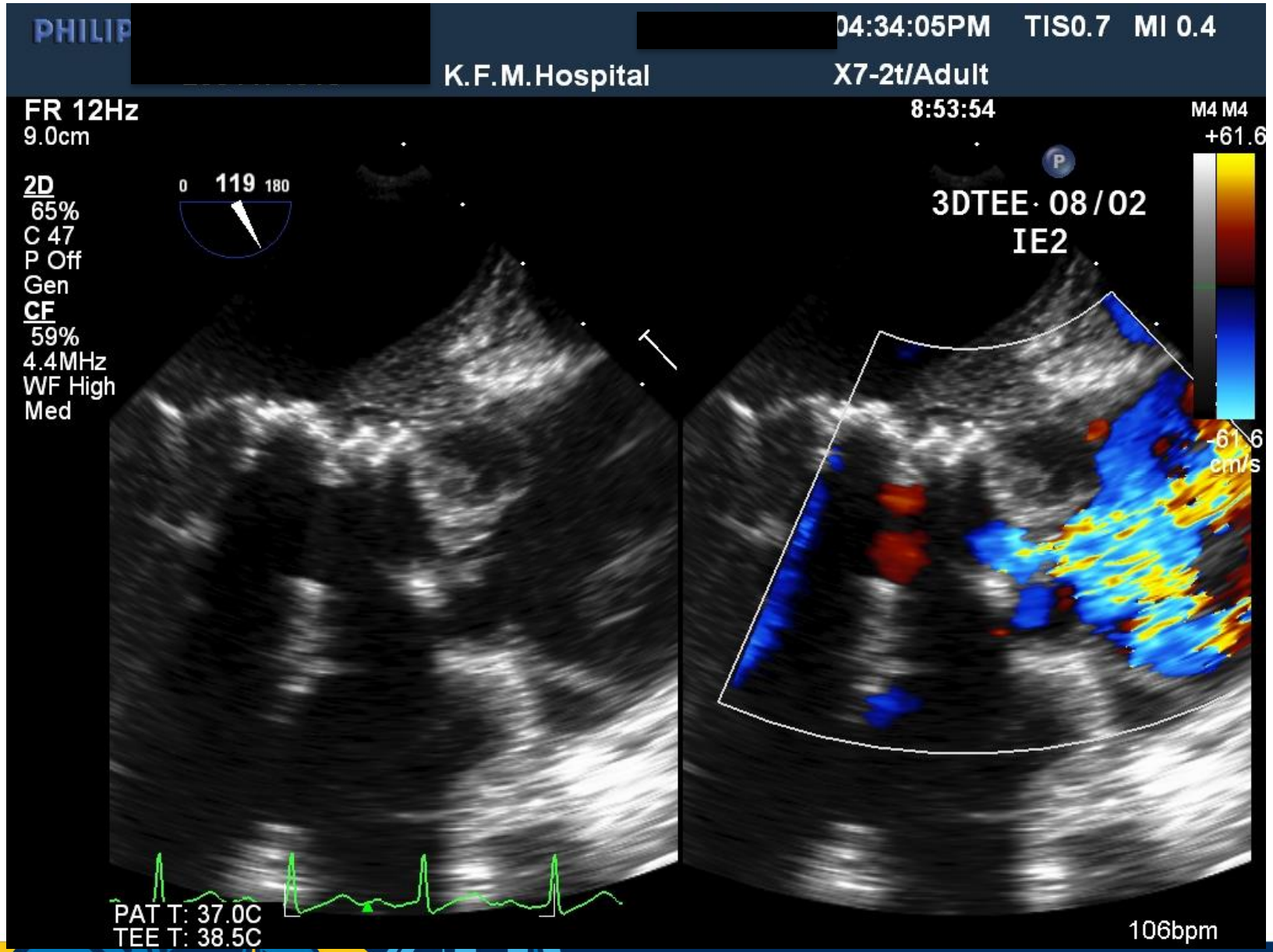
TEE T: 39.6C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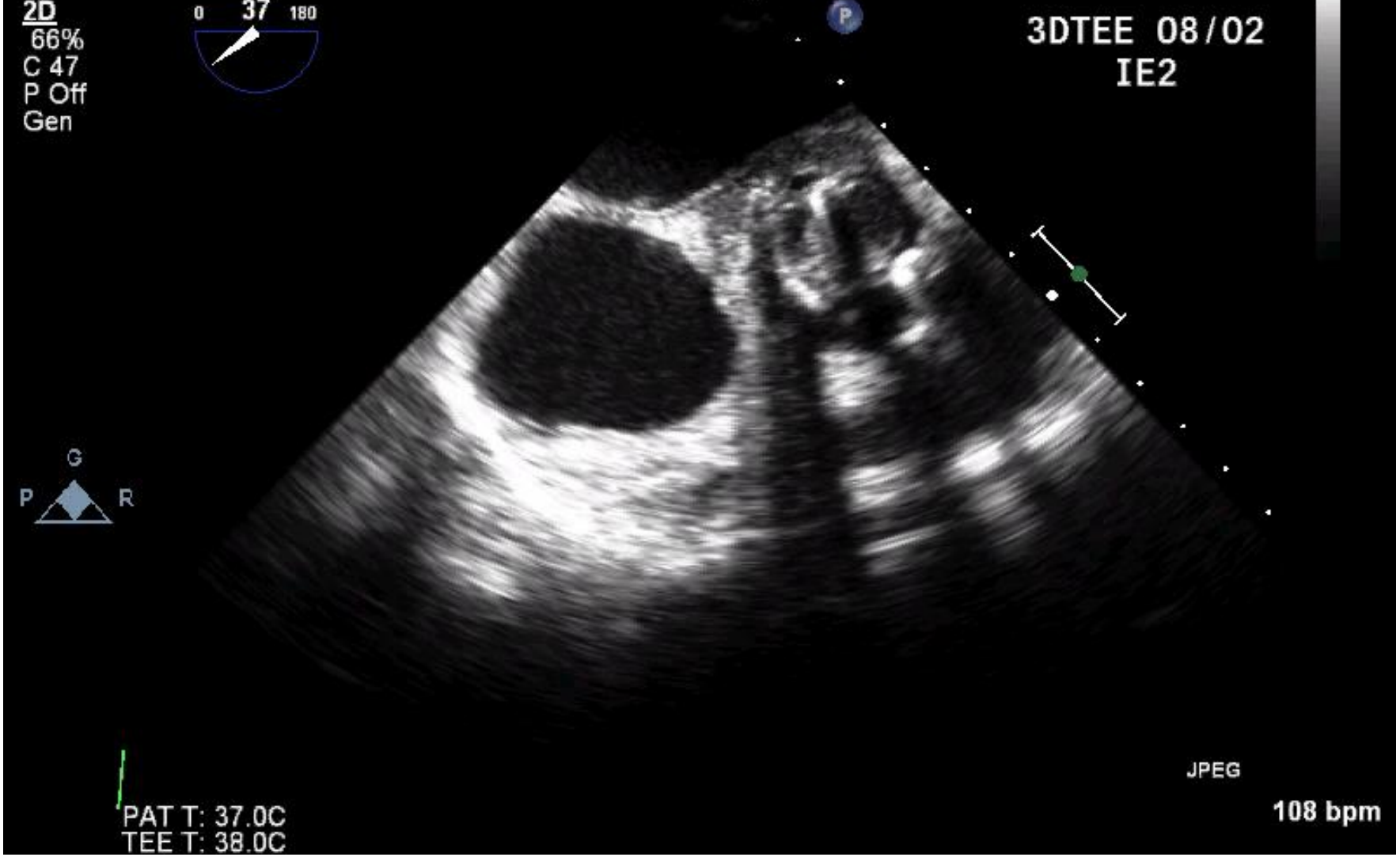
cm/s
PAT T: 37.0C
TEE T: 38.5C
106bpm


2D
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C 47
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Gen
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3DTEE 08/02
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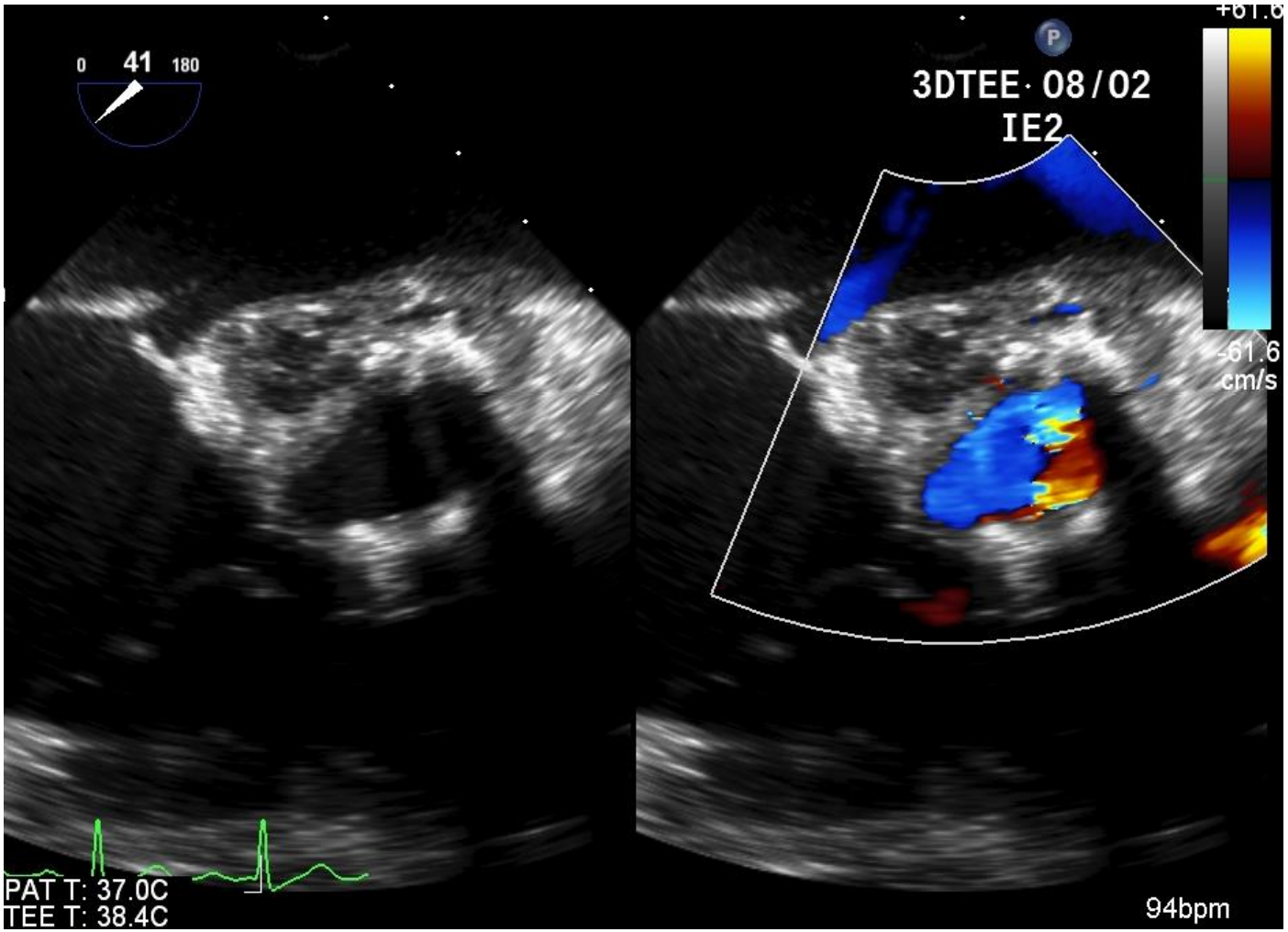
PAT T: 37.0C
TEE T: 38.0C
108 bpm

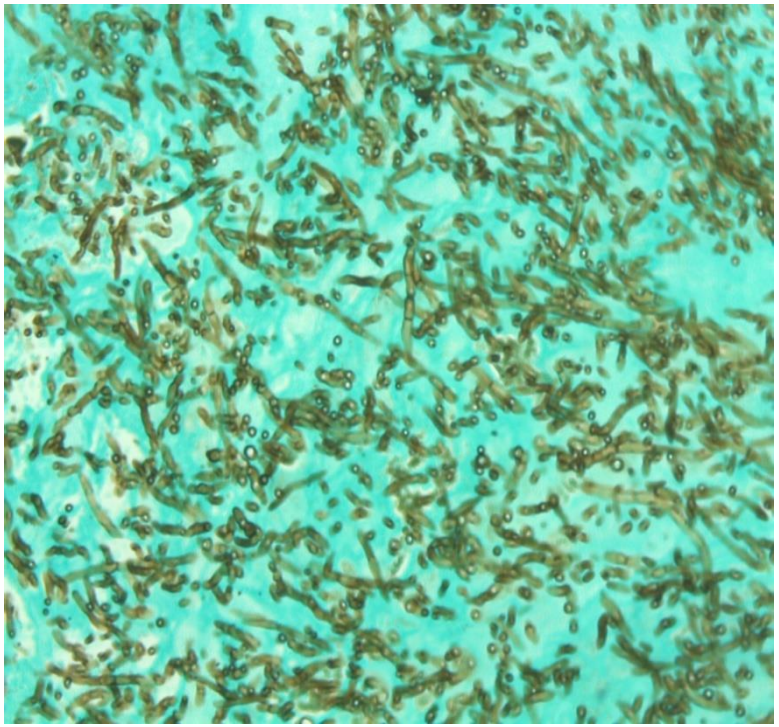

0
41
180
3DTEE · 08/02
IE2
-61.6
cm/s
PAT T: 37.0C
TEE T: 38.4C
94bpm

In Theatre

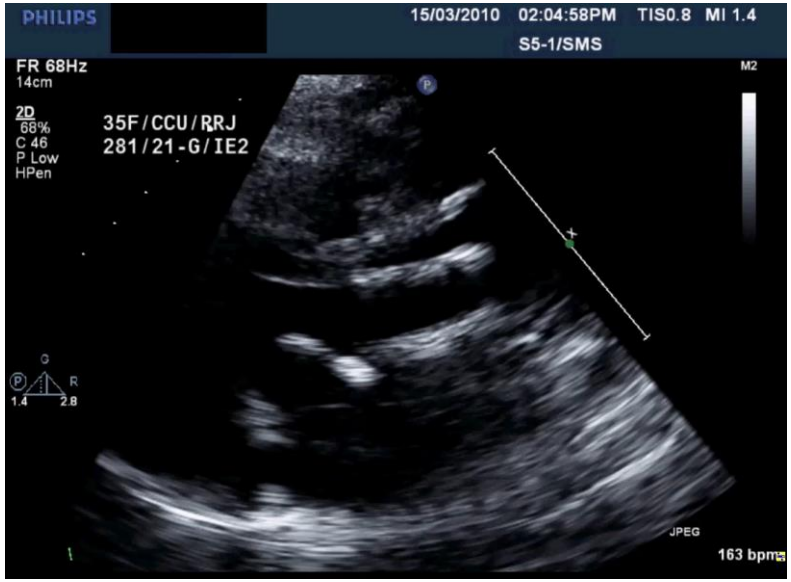
- An extensive abscess cavity extending from right coronary artery ostium to LCA ostium.
- Vegetations were seen on the bioprosthetic aortic valve and a cystic globular mass (1.3 cm in diameter) was seen attached to the bioprosthesis.
- A bovine pericardial patch of aortic root was implanted and the aortic bioprosthesis was replaced with porcine valve.

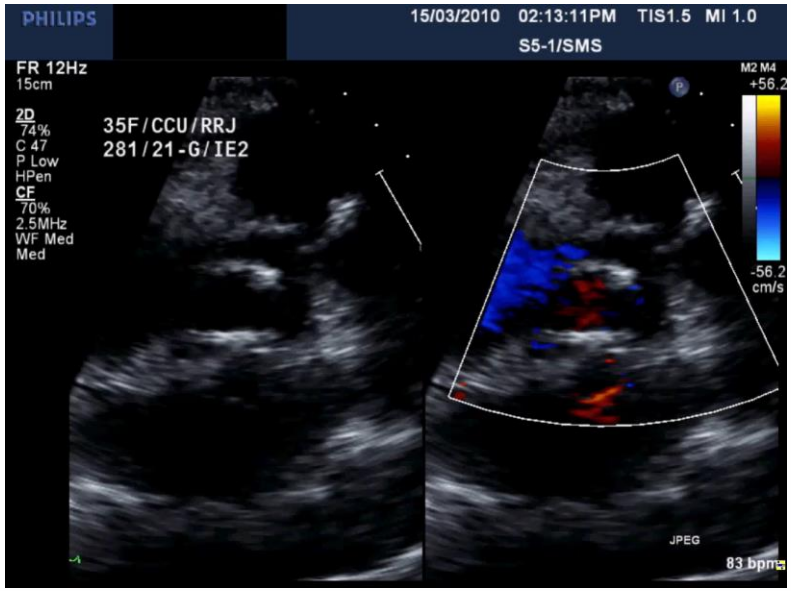
- Histopathological examination: heavy growth of

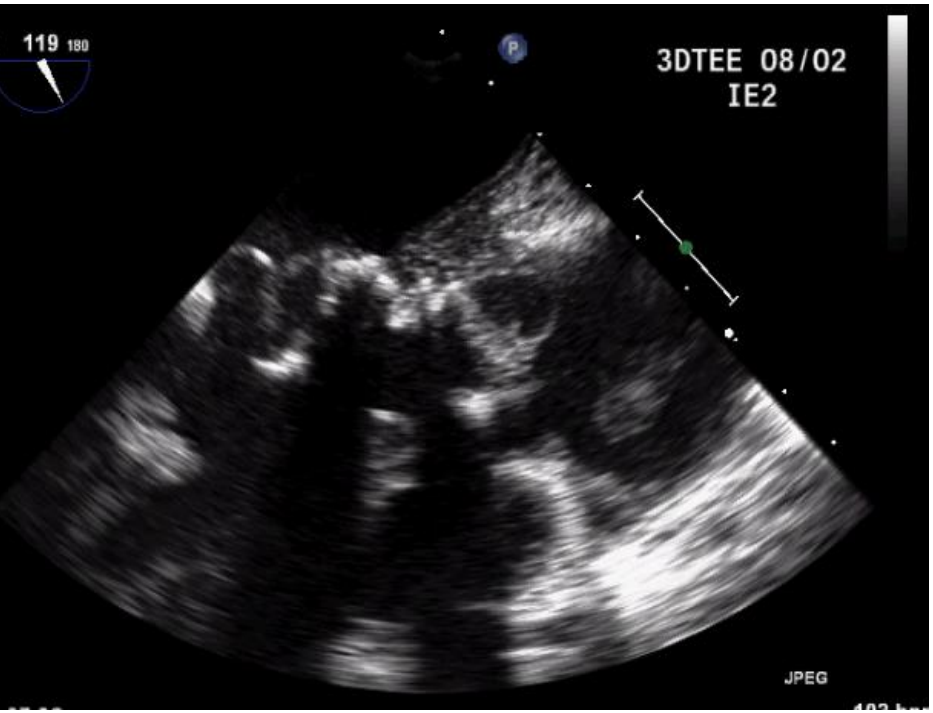
  Aspergillus fumigatus.
- Tissue cultures: no bacterial growth.
- Started on Liposomal Amphotericin B.
- Post-operative recovery was initially satisfactory.



- 5 weeks later:
  she became febrile and hypotensive.
- TTE showed an aortic abscess.
- Patient refused any kind of intervention.
- She suddenly went into shock and expired on the same day.






119 180
3DTEE 08/02
IE2
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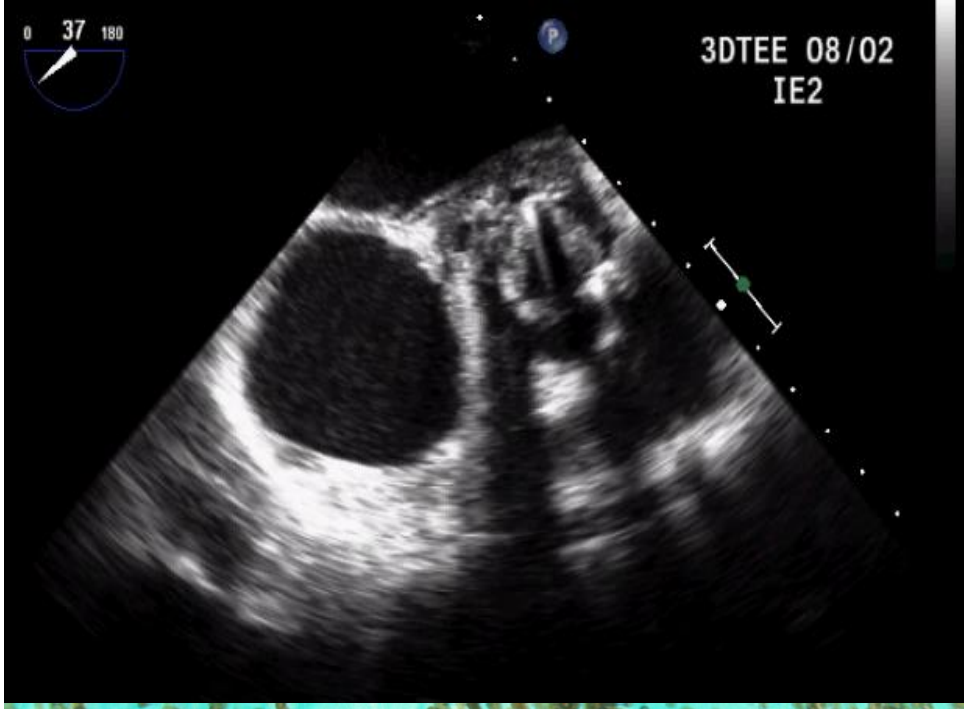
0 37 180
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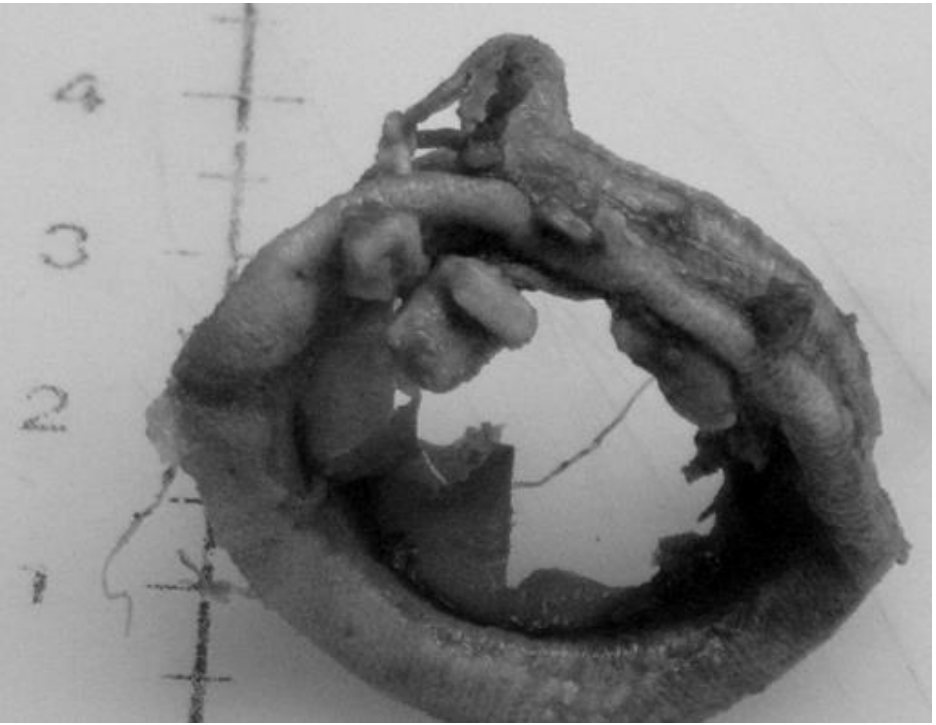
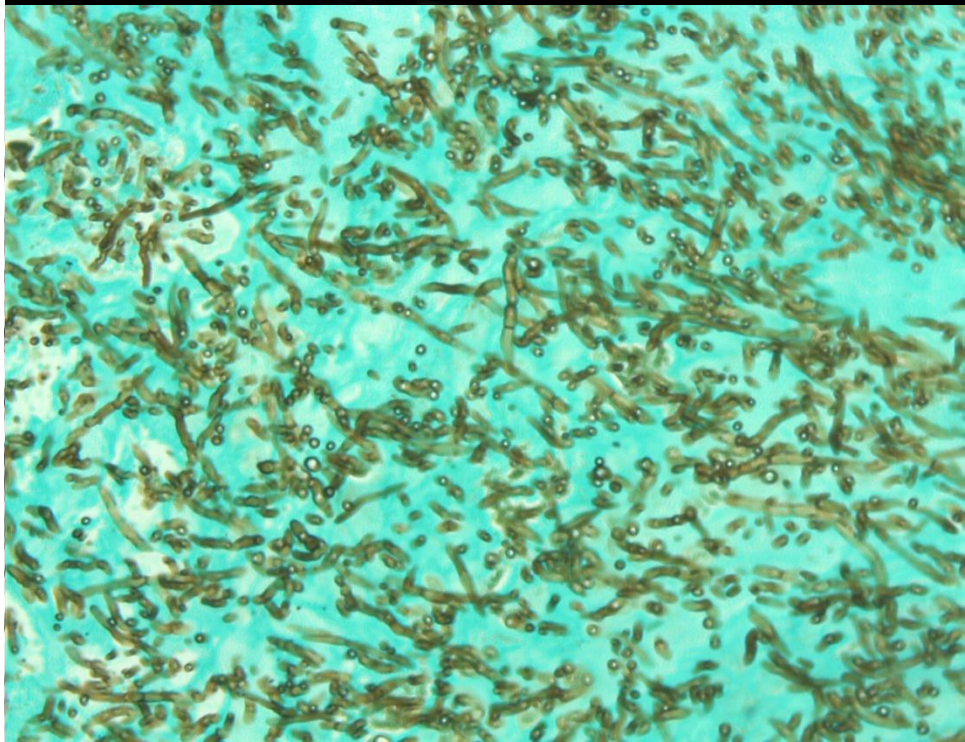




Aspergillous Endocarditis

- An ominous condition with increasing prevalence in the hospital population.
- Detection of source, establishing diagnosis, and treatment remain highly challenging.
- Even with aggressive medical and surgical treatment, the outcomes for patients with prosthetic valve endocarditis due to Aspergillus species have been extremely poor.

Infective Endocarditis: what's new?

Increased high risk subgroups

- IVDA
- Intracardiac devices
- Hemodialysis
- Congenital heart disease
- Nosocomial diseases

New imaging techniques

New therapeutic strategies

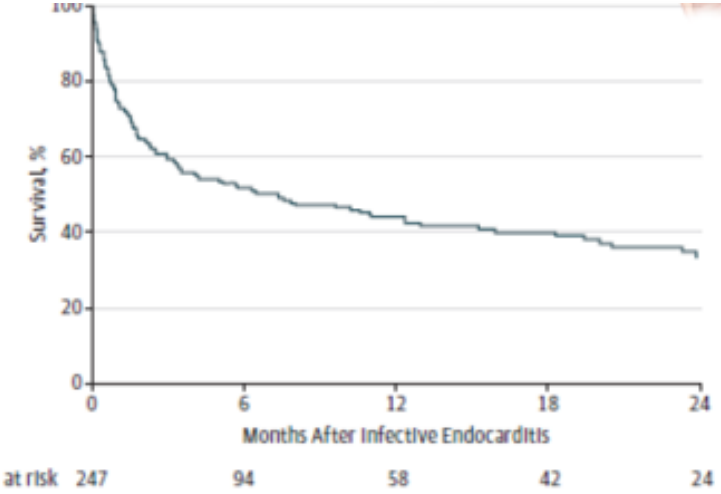
Endocarditis post TAVR

Original Investigation JAMA. 2016;316(10):1083-1092.
September 13, 2016

Association Between Transcatheter Aortic Valve Replacement and Subsequent Infective Endocarditis and In-Hospital Death

Ander Regueiro, MD[1]; Axel Linke, MD[2]; Azeem Latib, MD[3]; et al

- 20006 patients between 2005-2015
- 250 IE
- incidence, 1.1%per person-year
- median age, 80 years; 64%men
- Enterococci species and Staphylococcus aureus the most frequent microorganisms (24.6% and 23.3%)
- in-hospital mortality: 36% (90 deaths; 160 survivors)
- Surgery performed in 14.8%



EDITORIAL

American Heart Association | American Stroke Association

Infective Endocarditis After Transcatheter Aortic Valve Replacement: The Worst That Can Happen

Gilbert Habib, MD, PhD

Journal of the American Heart Association. Sept. 2018

2017 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease (2014 guideline with 2017 focused update incorporated)

Developed in Collaboration with the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

AHA Scientific Statement

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

2015

Endorsed by the Infectious Diseases Society of America

Larry M. Baddour, MD, FAHA, Chair; Walter R. Wilson, MD; Arnold S. Bayer, MD; Vance G. Fowler, Jr, MD, MHS; Imad M. Tleyjeh, MD, MSc; Michael J. Rybak, PharmD, MPH; Bruno Barsic, MD, PhD; Peter B. Lockhart, DDS; Michael H. Gewitz, MD, FAHA; Matthew E. Levison, MD; Ann F. Bolger, MD, FAHA; James M. Steckelberg, MD; Robert S. Baltimore, MD; Anne M. Fink, PhD, RN; Patrick O'Gara, MD, FAHA; Kathryn A. Taubert, PhD, FAHA; on behalf of the American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council

European Heart Journal (2015) **36**, 3075–3123
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

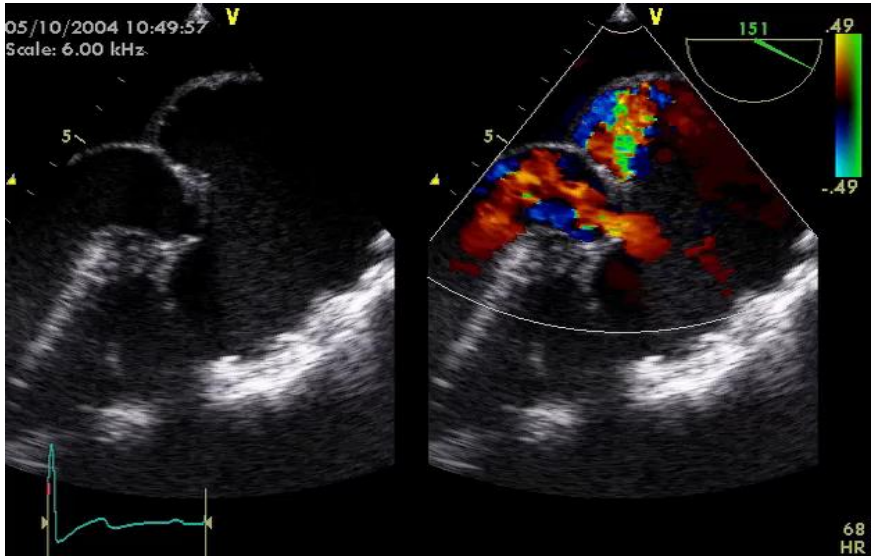
The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

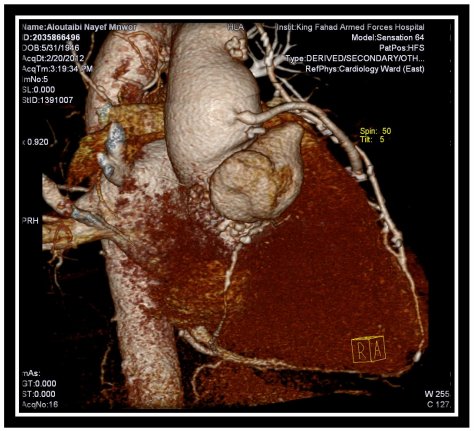
Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

Multimodality Imaging In Endocarditis

TEE

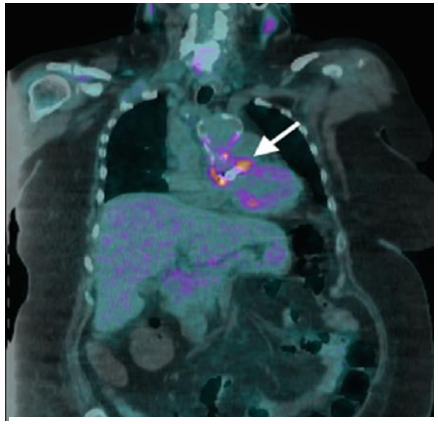
Morphology





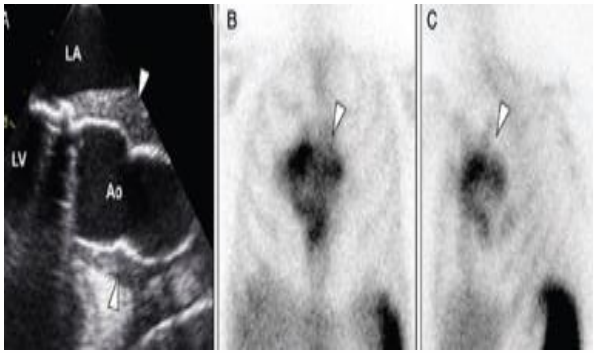
Cardiac CT

Perivalvular lesions

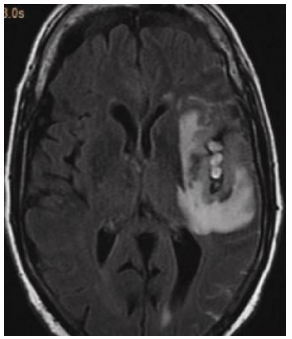


PET CT

Inflammation/Infection



Radiolabeled leucocyte SPECT



MRI

Echocardiography

Sensitivity

- 70% for native valve and 50% for prosthetic valve with TTE.
- 96% and 92% for TEE.

Specificity

- 90% for both TTE and TEE

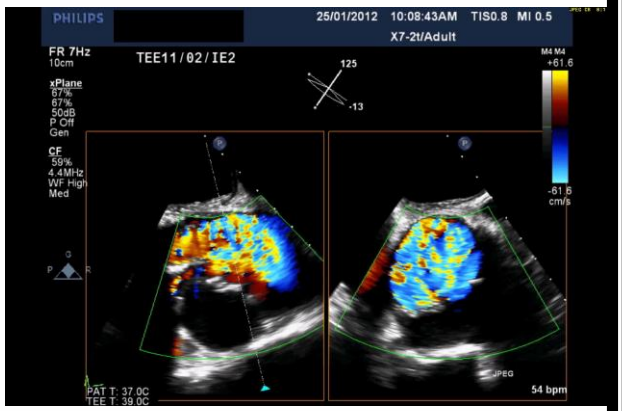
BUT NOT 100%

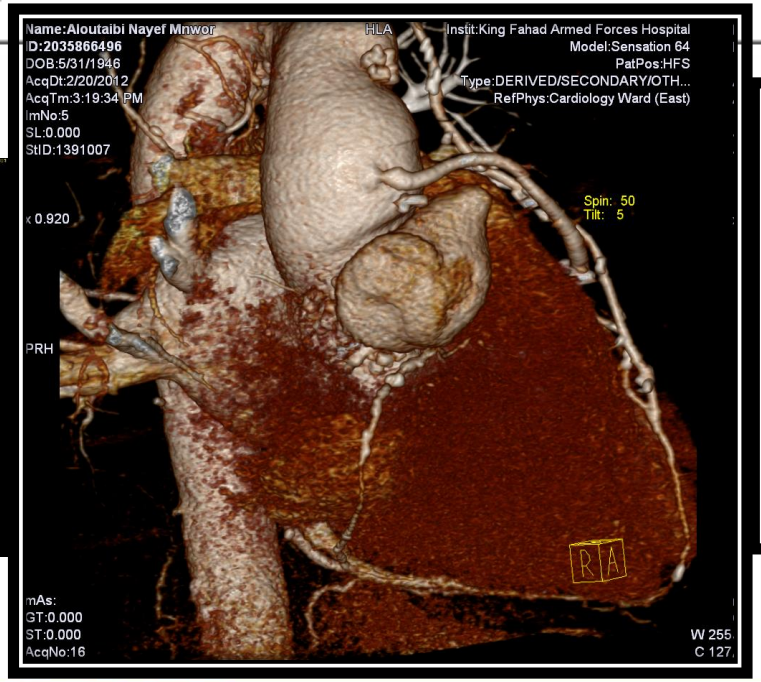
TTE is recommended in patients with suspected IE to identify vegetations, characterize the hemodynamic severity of valvular lesions, assess ventricular function and pulmonary pressures, and detect complications	I	B

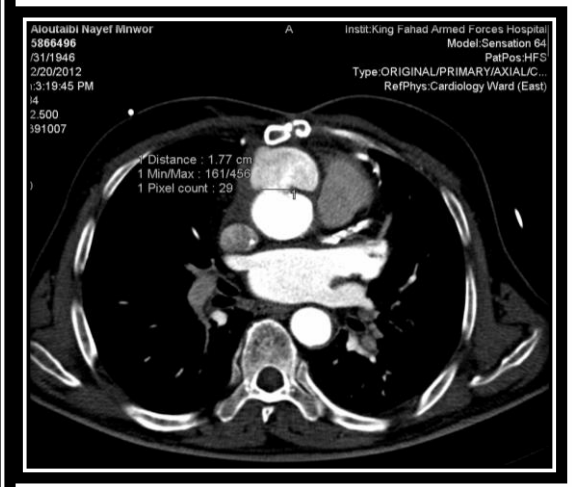
Recommendations	COR	LOE
TEE is recommended in all patients with known or suspected IE when TTE is nondiagnostic, when complications have developed or are clinically suspected, or when intracardiac device leads are present	I	B
TTE and/or TEE are recommended for reevaluation of patients with IE who have a change in clinical signs or symptoms (e.g., new murmur, embolism, persistent fever, HF, abscess, or atrioventricular heart block) and in patients at high risk of complications (e.g., extensive infected tissue/large vegetation on initial echocardiogram or staphylococcal, enterococci, or fungal infections)	I	B

Cardiac CT

Recommendations	COR	LOE
Cardiac CT is reasonable to evaluate morphology/anatomy in the setting of suspected paravalvular infections when the anatomy cannot be clearly delineated by echocardiography	IIa	B





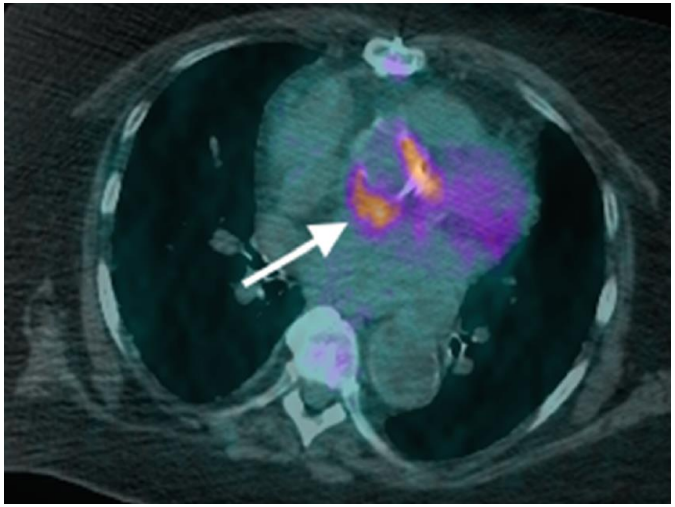


Courtesy of Dr. M Alasnag

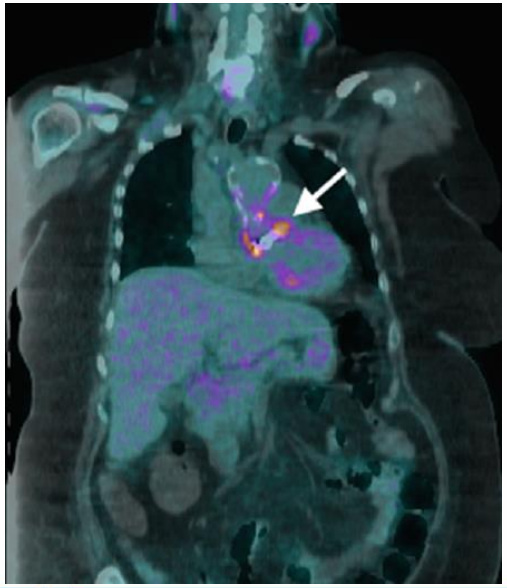
18 FDG PET/CT

(fluorodeoxyglucose positron emission tomography)

- Foci of active infection are often metabolically active, and will avidly take up glucose.
- Major role of 18 FDG PET/CT currently in equivocal cases of suspected aortic prosthetic infections.



Insights Imaging (2016) 7:801–818



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ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.01.092

Cardiac Imaging in Endocarditis

Positron Emission Tomography/Computed Tomography for Diagnosis of Prosthetic Valve Endocarditis

Increased Valvular ^{18}F-Fluorodeoxyglucose Uptake as a Novel Major Criterion

72 consecutive patients suspected of having PVE.

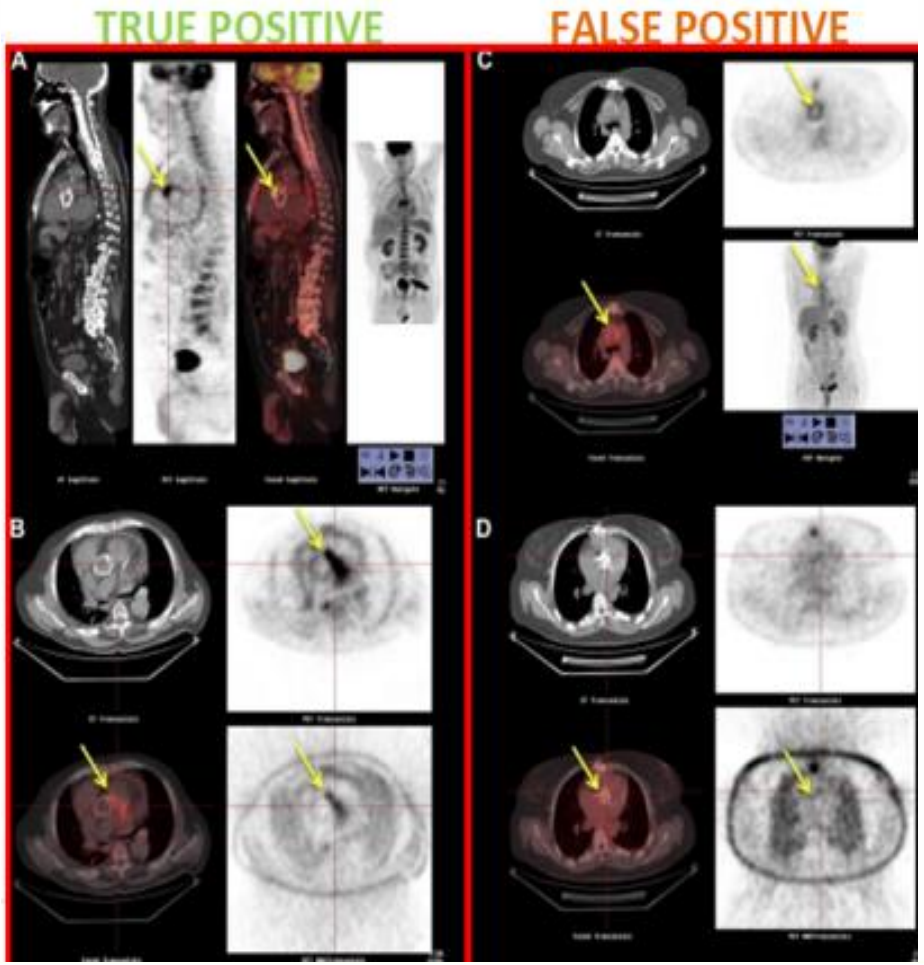
Ludivine Saby, MD,* Olivia Laas, MD,† Gilbert Habib, MD,* Serge Cammilleri, MD, PhD,†
Julien Mancini, MD, PhD,‡ Laetitia Tessonnier, MD,† Jean-Paul Casalta, MD,§
Frederique Gouriet, MD, PhD,§ Alberto Riberi, MD,‖ Jean-Francois Avierinos, MD,*
Frederic Collart, MD,‖ Olivier Mundler, MD, PhD,† Didier Raoult, MD, PhD,§
Franck Thuny, MD, PhD*§¶

PET CT SCAN

- Better sensitivity for detection of prosthetic IE.
- Sensitivity:97%
- Specificity: 80%

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

	Final Diagnosis		
	Definite PVE	*Possible* PVE	*Rejected* PVE
Duke			
Definite PVE	21 (70)	0 (0)	0 (0)
Possible PVE	8 (27)	22 (100)	10 (50)
Rejected PVE	1 (3)	0 (0)	10 (50)
Duke-PET/CT			
Definite PVE	29 (97)	10 (45)	2 (10)
Possible PVE	1 (3)	12 (55)	10 (50)
Rejected PVE	0	0	8 (40)



Nuclear Imaging

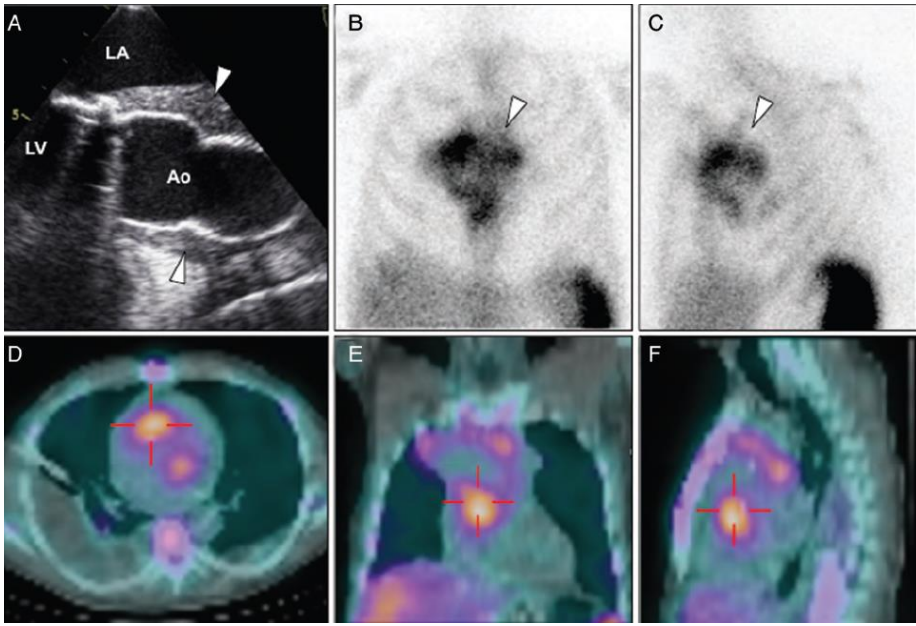
Radiolabelled leucocyte SPECT

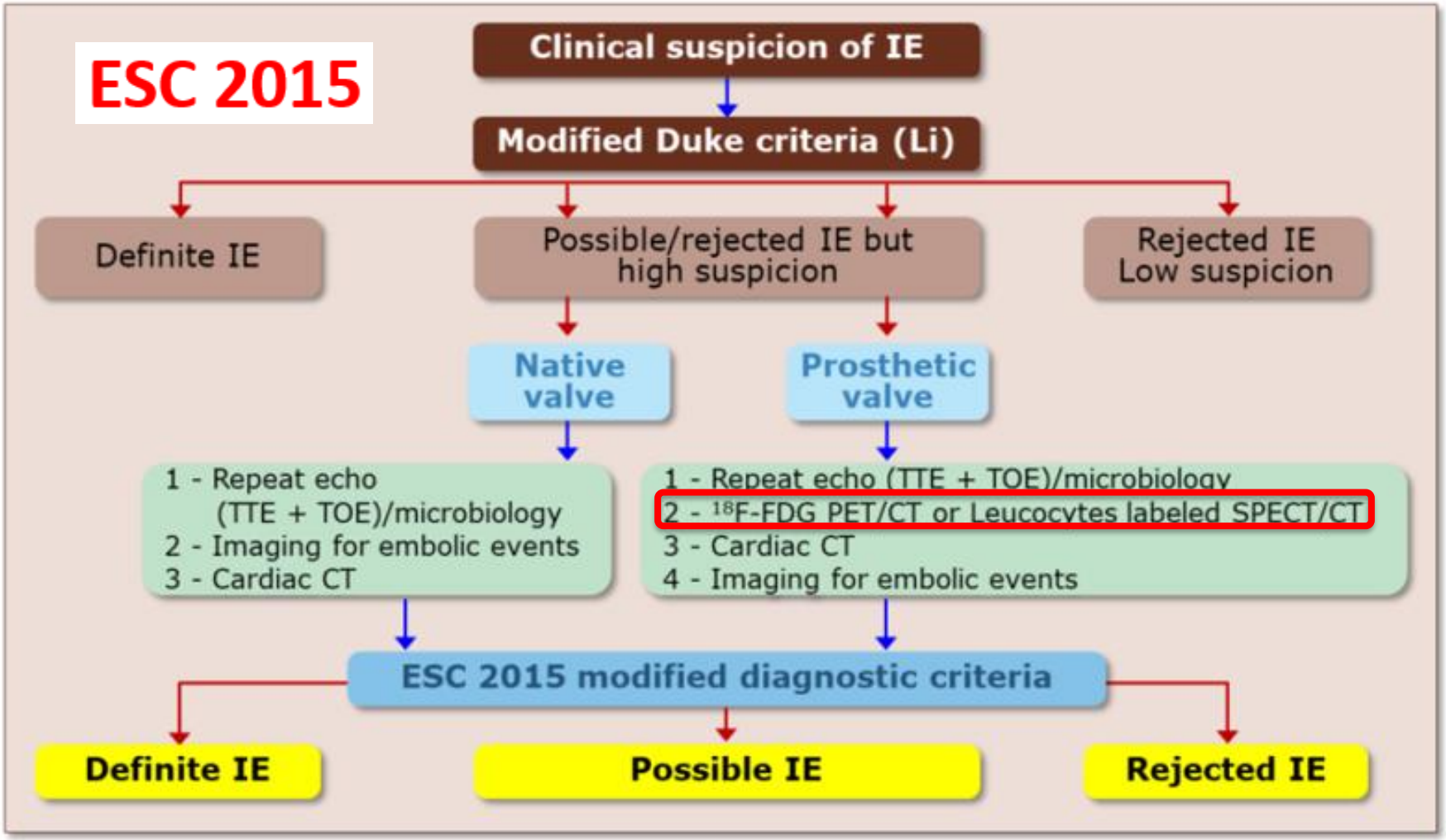
- Retrospective study of 42 patients for detection of perivalvular infection in patients with a suspicion of PVE and inconclusive TEE.
- High specificity: almost 100%
- Useful in post operative IE suspicion.
- But more time consuming.
- Lower spatial resolution.

EUROPEAN SOCIETY OF CARDIOLOGY®
European Heart Journal – Cardiovascular Imaging (2013) **14**, 586–594
doi:10.1093/ehjci/jet029

Role of radiolabelled leucocyte scintigraphy in patients with a suspicion of prosthetic valve endocarditis and inconclusive echocardiography

Fabien Hyafil[1]*, François Rouzet[1], Laurent Lepage[2], Khadija Benali[1], Richard Raffoul[2], Xavier Duval[3], Ulrik Hvass[2], Bernard Iung[4], Patrick Nataf[2], Rachida Lebtahi[5], Alec Vahanian[4], and Dominique Le Guludec[1]

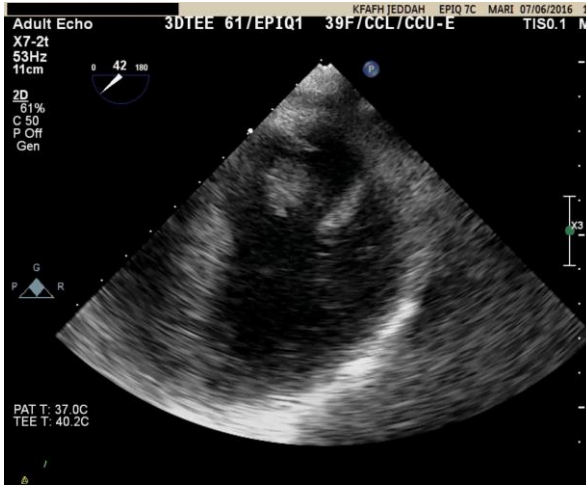




Recommendations on nuclear and multimodality imaging in IE and CIED infections

Eur J Nucl Med Mol Imaging 2018 Sep;45(10):1795-1815

Endocarditis TEAM



- IE is NOT a single disease.
- High level of expertise.
- Early discussion with the surgery team.
- The prognosis depends on an early management.

Recommendations	COR	LOE
Patients with IE should be evaluated and managed with consultation of a multispecialty Heart Valve Team including an infectious disease specialist, cardiologist, and cardiac surgeon. In surgically managed patients, this team should also include a cardiac anesthesiologist	I	B

Recommendations	Class	Level
Patients with complicated IE should be evaluated and managed at an early stage in a reference centre, with immediate surgical facilities and the presence of a multidisciplinary "Endocarditis Team" including an ID specialist, a microbiologist, a cardiologist, imaging specialists, a cardiac surgeon, and if needed a specialist in CHD.	IIa	B
For patients with non-complicated IE managed in a non-reference centre, early and regular communication with the reference centre and, when needed, with visit to the reference centre, should be made.	IIa	B

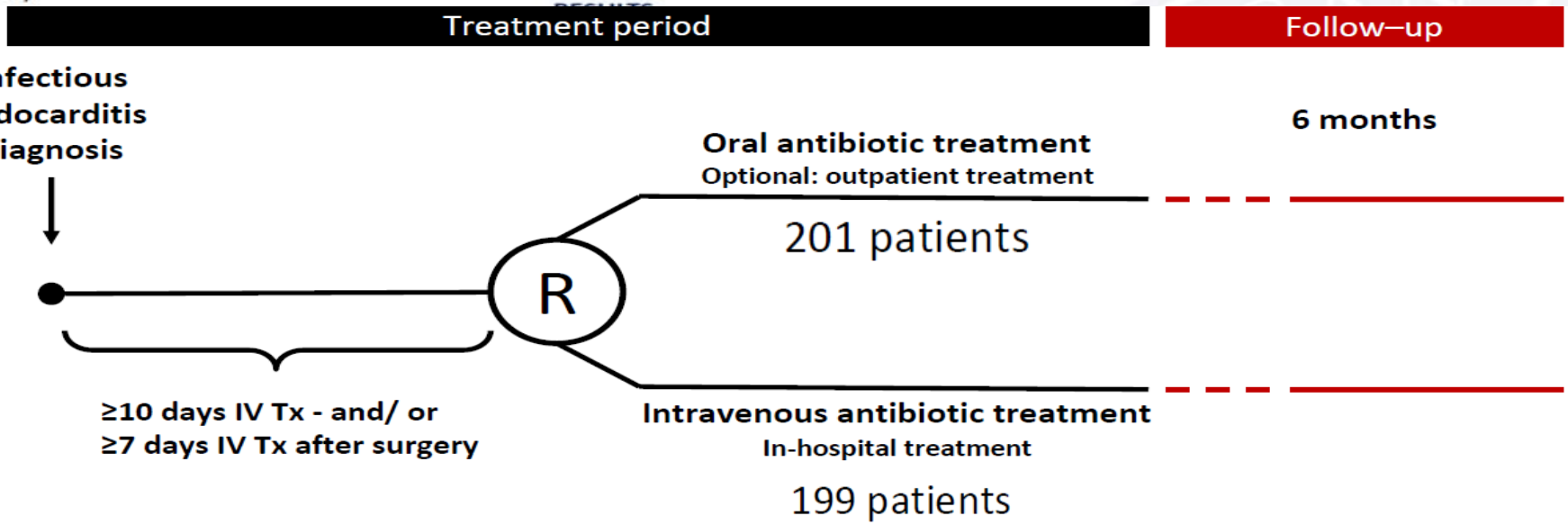
Infective Endocarditis: Medical Therapy

Recommendations	COR	LOE
Appropriate antibiotic therapy should be initiated and continued after blood cultures are obtained with guidance from antibiotic sensitivity data and infectious disease consultants	I	B

- 4 to 6 weeks in-hospital
- iv antibiotics (iv lines)

Partial oral treatment of left-sided infectious endocarditis: The POET Trial

Trial design: Patients with infective endocarditis on the left side of the heart and stabilized with intravenous antibiotics were randomized to oral antibiotic therapy (n = 201) vs. continuation of intravenous antibiotic therapy (n = 199).



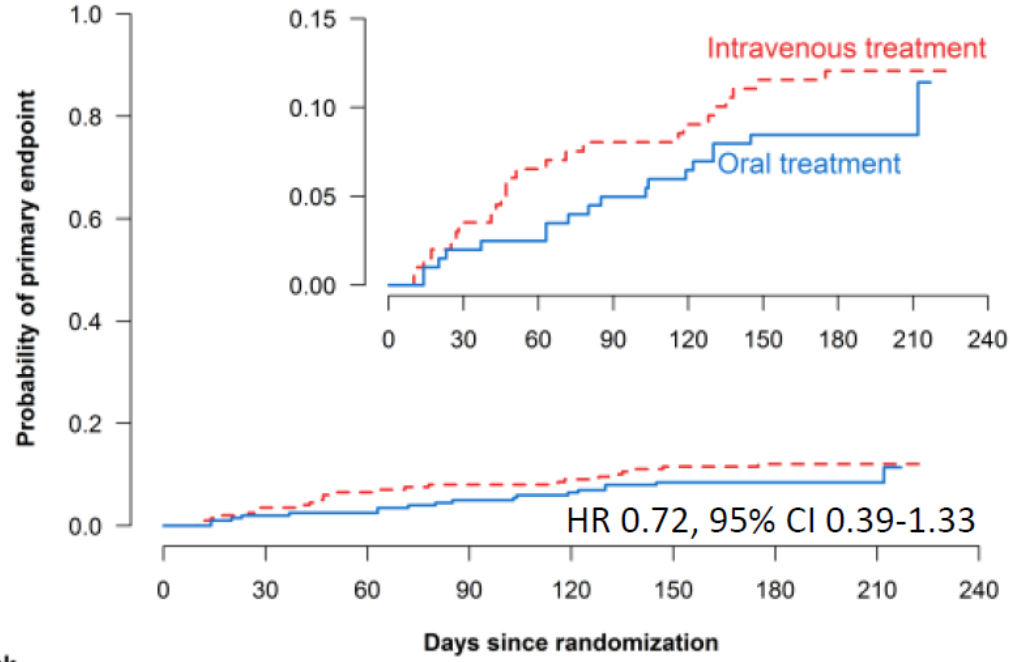
- T <38.0 °C >2 days
- C-reactive protein fall to ≤25% of peak value or <20 mg/L
- White blood cell count <15 x 10^9/L
- By transesophageal echocardiography ≤48 h prior to randomization: No sign of abscess formation or valve abnormalities requiring surgery

Iversen K, et al. N Engl J Med 2018;Aug 28:[Epub]

Primary endpoint

(All cause mortality, unplanned cardiac surgery, embolic events or relapse of bacteremia)

Difference 3.1%, 95% CI: -3.4% - 9.6%, Non-inferiority met



No. at Risk									
Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Infective Endocarditis: Intervention

Recommendations	COR	LOE
Decisions about timing of surgical intervention should be made by a multispecialty Heart Valve Team of cardiology, cardiothoracic surgery, and infectious disease	I	B
Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with IE who present with valve dysfunction resulting in symptoms of HF	I	B

Infective Endocarditis: Intervention

Recommendations	COR	LOE
Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with left-sided IE caused by *Staphylococcal aureus*, fungal, or other highly resistant organisms	I	B
Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) is indicated in patients with IE complicated by heart block, annular or aortic abscess, or destructive penetrating lesions	I	B

Infective Endocarditis: Intervention

Recommendations	COR	LOE
Early surgery (during initial hospitalization before completion of a full therapeutic course of antibiotics) for IE is indicated in patients with evidence of persistent infection as manifested by persistent bacteremia or fevers lasting longer than 5 to 7 days after onset of appropriate antimicrobial therapy	I	B
Surgery is recommended for patients with prosthetic valve endocarditis and relapsing infection (defined as recurrence of bacteremia after a complete course of appropriate antibiotics and subsequently negative blood cultures) without other identifiable source for portal of infection	I	C

Indications and Timing of Surgery

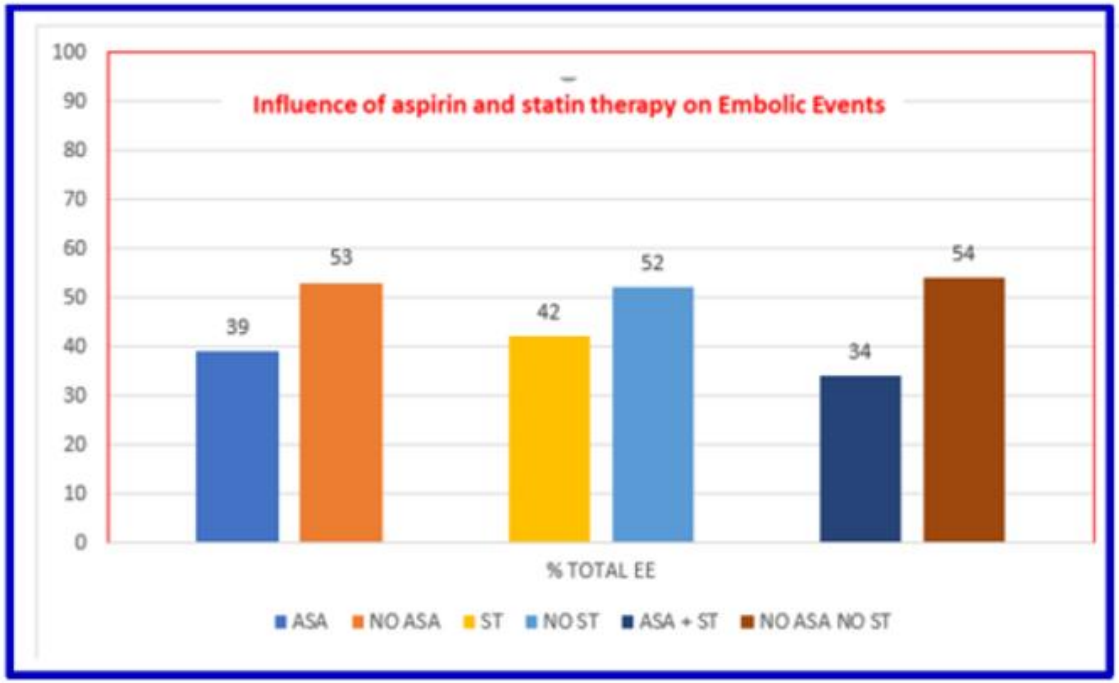
ESC 2015

Indications for surgery	Timing	Class	Level
1. Heart Failure			
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock.	Emergency	I	B
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance.	Urgent	I	B
2. Uncontrolled infection			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation).	Urgent	I	B
Infection caused by fungi or multiresistant organisms.	Urgent/elective	I	C
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci.	Urgent	IIa	B
PVE caused by staphylococci or non-HACEK Gram negative bacteria.	Urgent/elective	IIa	C
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after one or more embolic episode despite appropriate antibiotic therapy.	Urgent	I	B
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk.	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm).	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery.	Urgent	IIb	C

Embolic Risk: Role of Aspirin & Statins

Veyrier et al. ESC 2018

- ✓ 529 patients, 135 (25%) were treated by Aspirin 130 (24%) were treated with Statins
- ✓ The 135 patients treated by Aspirin presented with less frequent EE [53 (39%) vs 211 (53%) p= 0.01] and similar hemorrhagic complications (8 (5.9%) vs 45 (11%) p=NS)
- ✓ The 130 patients treated by Statins presented with less frequent EE [55 (42%) vs 209 (52%) p= 0.04] and similar hemorrhagic complications (9 (7%) vs 44 (11%) p=NS).
- ✓ By multivariate analysis, only Aspirin therapy (OR 0.6 [0.4; 0.92]) and combined therapy (OR 0.5 [0.28; 0.89]) were protective against EE



Daily combined ASA and STATIN therapy prior to IE diagnosis is associated with decreased incidence of embolic events and cerebral hemorrhage.

Both aspirin and statin therapy reduce embolic events in patients with infective endocarditis

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PURPOSE

To evaluate prior Aspirin (ASP) and/or Statin (ST) therapy on embolic risk in Infective Endocarditis (EI)

METHODS

A retrospective observational study including all adult patients hospitalized from 01/01/2010 to 31/12/2106 for EI. During hospitalization, all patients were observed daily in the cardiology unit and patients were systematically reviewed at one month after discharge for a follow-up consultation. From the medical records, data on pre-existing comorbidities, prior use of ASP and ST, pathogens, clinical, laboratory and echocardiographic findings, embolic events, hemorrhagic complications and 30 days mortality were record.

PRIMARY END POINT

Embolic events occurring before or during hospitalization for EI.

SECONDARY END POINTS

Occurrence of an hemorrhagic event and 30 days mortality.

EXCLUSIONS

All patients with left-sided, right-sided, prosthetic valve or intracardiac device associated IE were included.

OUTCOMES

Blood cultures, serological assessment, transthoracic and transesophageal echocardiography and cerebrothoracoabdominal CT scans were systematically performed. Diagnosis of EE was based on clinical, CT scans and/or magnetic resonance data. CT scans was performed the first week of hospitalization and were subsequently repeated if clinically indicated.

RESULTS

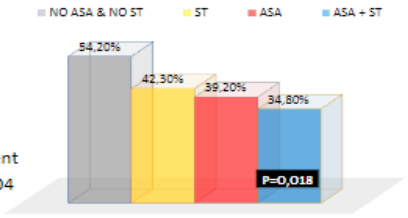
Population (n=529)

478 (88.7%) left sided EI, vegetation in 417 patients (78.8 %), vegetation length > 10mm in 252 patients (46.7%), 135 patients treated by Aspirin (ASP), 130 treated by Statin (ST) and 66 with combined therapy ASA + ST.

Embolic Events (n=264 - 50%)

- Prior ASP therapy was associated with less frequent EE 53 (39%) vs 211 (54%) : OR 0.56 [0.38;0.83] P=0.004
- Prior ST therapy was associated with less frequent EE 55 (42%) vs 209 (52%) : OR 0.67 [0.45;0.99] p= 0.04
- Prior combined therapy was associated with less frequent EE : 23 (35%) vs 179 (54%) : OR 0.46 [0.26;0.78] p=0.004

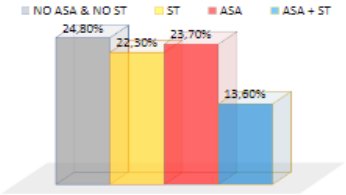
By multivariate analysis, only combined therapy were protective : OR 0.5 [0.28; 0.89] p=0.018



EMBOLIC EVENTS

Cerebral embolisms (CE) (n=134 - 25,3%)

Only the combined therapy was associated with less CE 9 (13,6%) vs 82 (24,2%) OR 0.50 [0.23;0.99] p=0.046

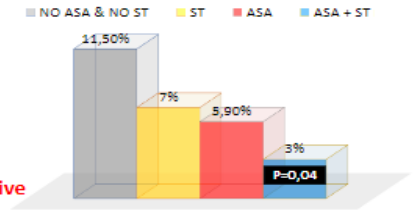


CEREBRAL EMBOLISM

Cerebral hemorrhages (n=53 - 10%)

- ASP therapy presented a trend toward a rate reduction 8 (5.9%) vs 45 (11.4%) : OR 0.51 [0.22;1.04] p=0.06
- ST therapy had similar hemorrhagic complications 9 (7%) vs 44 (11%) : OR 0.62 [0.28;1.24] p=0.19

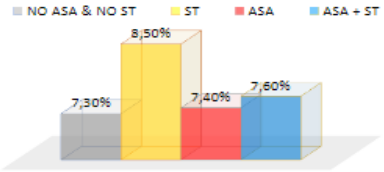
By multivariate analysis, combined therapy were protective 2 (3%) vs 38 (11.5%) : OR 0.31 [0.06;0.96] p=0.04



CEREBRAL HEMORRHAGES

30 days mortality (n=40 - 7,6%)

No significant association with prior ASA therapy OR 1.00 [0.46;2.01] p=0.99, prior ST therapy OR 1.21 [0.57;2.40] p=0.6 or combined therapy OR 1.08 [0.38;2.56] p=0.87



30D MORTALITY

CONCLUSION

Daily combined ASA and ST therapy prior to EI diagnosis is associated with an decreased incidence of embolic events and cerebral hemorrhages

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Conclusion

- A change in clinical and microbiological epidemiology (older people, more prosthetic valve, more staphylococci).
- New imaging tools exist but experience is needed.
- A multidisciplinary approach is mandatory.
- Difficult cases should be sent to reference center.

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