Infective Endocarditis, Improving Diagnosis

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- IE is a disease of multisystem involvement, master of disguise
- Despite high achievements in medicine and antibiotics, disease is getting more and aggressive and complicated
- At the same time its incidence is increasing

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Diagnosing IE

Definite:
Pathological
Clinical; 2 major, 1 major & 3 minor, 5 minor

Possible:
1 major criterion and 1 minor criterion; or
3 minor criteria

Definite, Possible, Rejected
Clinical diagnosis &
Pathological diagnosis

Rejected:
Firm alternative diagnosis explaining evidence of IE; or
Resolution of IE syndrome with antibiotic therapy for 4 days; or
No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for 4 days; or
Does not meet criteria for possible IE as above

Definition of infective endocarditis according to the modified Duke criteria (adapted from Li *et al.*[87])

Definite IE
Pathological criteria • Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or • Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis
Clinical criteria • 2 major criteria; or • 1 major criterion and 3 minor criteria; or • 5 minor criteria
Possible IE
• 1 major criterion and 1 minor criterion; or • 3 minor criteria
Rejected IE
• Firm alternate diagnosis; or • Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or • No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or • Does not meet criteria for possible IE, as above

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Major criteria

1. Blood cultues positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
- *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* 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 Coxiella burnetii 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.

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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.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

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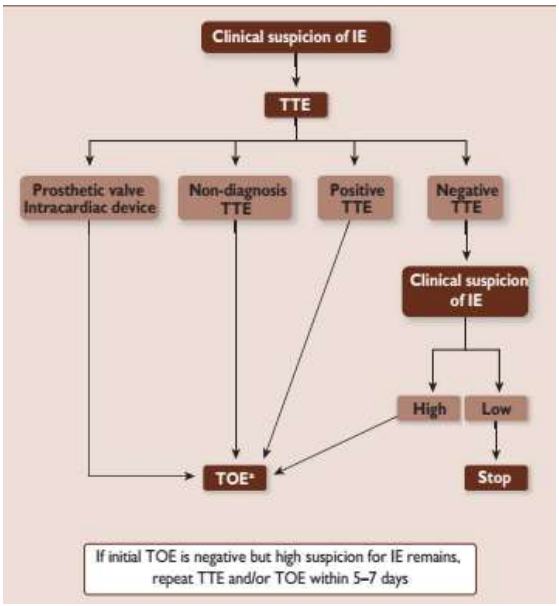
- So diagnosis is based on:
  - Clinical Features
  - Imaging Techniques
  - Laboratory work-up

1. *Cardiac Imaging*
2. *Non Cardiac Imaging*

I. Cardiac Imaging

2D TTE & TEE



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3D Echocardiography

- 3D TEE have demonstrated advantages over 2-dimensional TEE to better detect and delineate vegetations and to identify IE Complications
- Allows the analysis of 3D volumes of cardiac structures in any possible plane
- Better analysis of vegetation morphology and size may lead to better prediction of the embolic risk

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- Particularly useful in the assessment of perivalvular extension of the infection, prosthetic valve dehiscence and valve perforation

- ***Conventional 2D TTE and TEE will remain the corner stone to diagnose IE and its complications***

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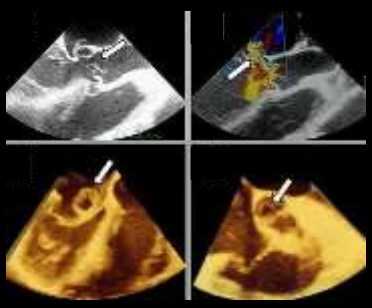
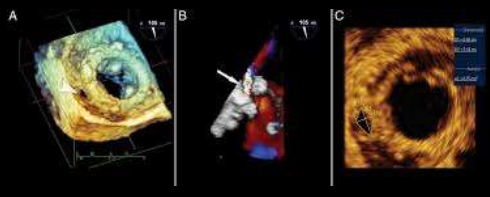
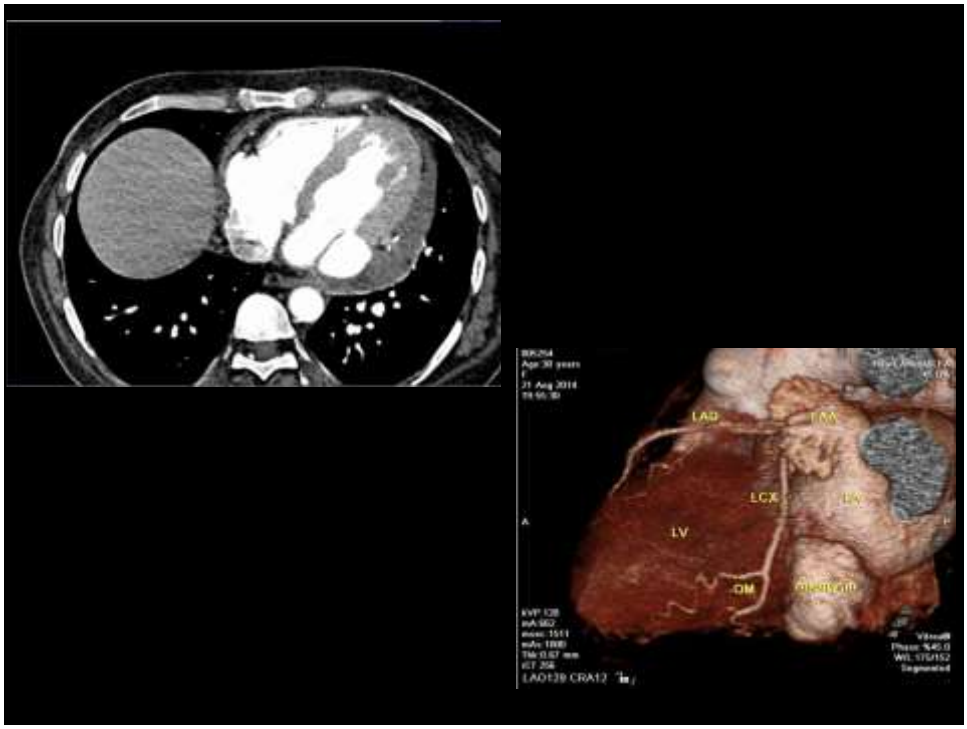




MSCT Cardiography

- Detection of ***perivalvular extension*** especially in PVE & with extensive calcifications
- Superior in information regarding the extent and consequences of perivalvular extension, including the anatomy of pseudoaneurysms, abscesses and fistulae
- Use of CT in IE is the ***non-invasive assessment of the coronaries*** prior to surgery, esp. in AV IE, where coronary angiography is associated with risk of systemic embolization & aortic wall perforation

- NVE & PVE results of *MSCT* are comparable to intra-operative findings, and with no significant difference to TTE & TEE
- ***Cerebral*** & ***Abdominal*** CT could be performed in the same setting


LAD
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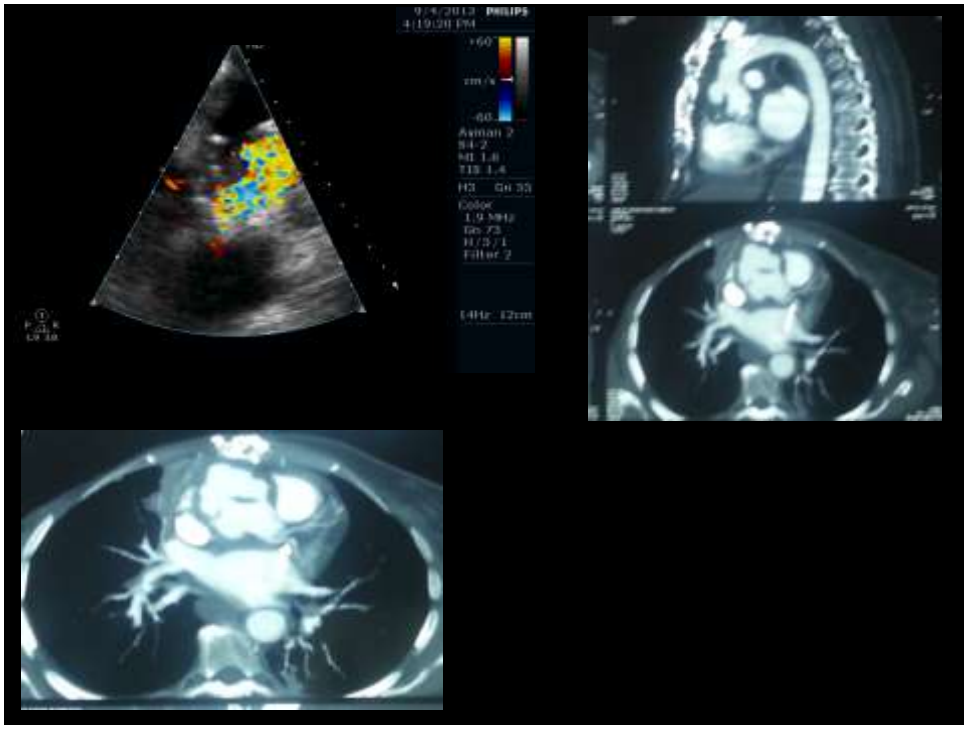
PHILIPS

F-fluorodesoxyglucose (F-FDG) PET-CT

- Few reports are existing, mainly in PVE, where abnormal FDG uptake around cardiac prosthesis may help in early diagnosis
- Helpful to differentiate active IE from old healed infection
- Less valuable in NVE, however might be helpful in detecting perivalvular extension
- Extracardiac spread of infection

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II. Non Cardiac Imaging

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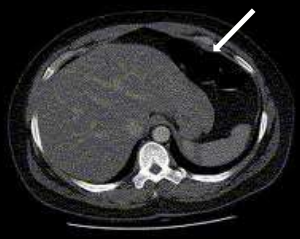
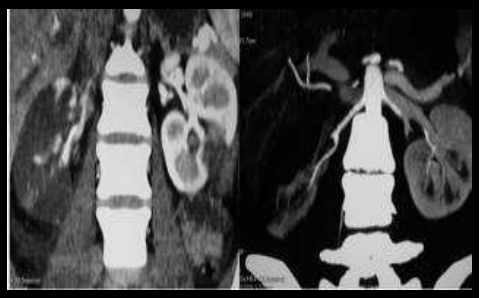
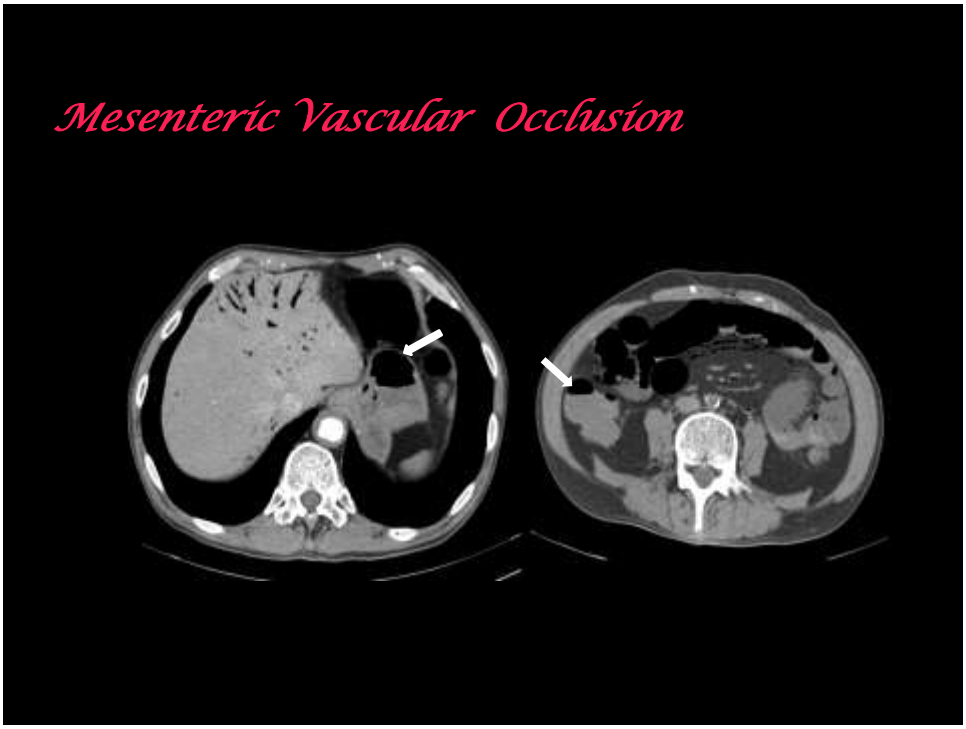
Abdominal U/S and CT

- Systemic embolization occurs in 22% to 50% of cases of IE
- Splenic infarction is a common complication of left-sided IE (40% of cases)
- About 5% of patients with splenic infarction will develop splenic abscess
- Acute renal failure is a common complication of IE, occurs in about 30% of patients:
  - *Immune complex* and vasculitic glomerulonephritis
  - *Renal infarctions*

Solid Organ Embolization







CNS Imaging

- CNS gets a major share (65%) of the embolic events
- Neurologic complications, dramatically change the prognosis & affect ttt plan
- Such complications are clinically apparent in 20% -40% of cases
- True incidence of acute brain embolization is not actually known

- In one study, findings of cerebral MRI upgraded the diagnosis of IE in 25% of patients presenting initially with non-definite IE

Annals of Internal Medicine | ARTICLE

Effect of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis

A Prospective Study

Xavier Duval, MD, PhD; Bernard Iung, MD; Isabelle Klein, MD, PhD; Eric Brochet, MD; Gabriel Thabut, MD, PhD; Florence Arnaulf, MD; Laurent Lepage, MD; Jean-Pierre Laissy, MD, PhD; Michel Wolff, MD; and Catherine Leport, MD, PhD, for the IMAGE (Resonance Magnetic Imaging at the Acute Phase of Endocarditis) Study Group*

Background: Neurologic complications of endocarditis can influence diagnosis, therapeutic plans, and prognosis.

Objective: To describe how early cerebral magnetic resonance imaging (MRI) affects the diagnosis and management of endocarditis in hospitalized adults.

Design: Single-center prospective study between June 2005 and October 2008. (ClinicalTrials.gov registration number: NCT00144885)

Setting: Tertiary care university hospital in France.

Patients: 130 patients with endocarditis.

Intervention: Cerebral MRI with angiography performed up to 7 days after admission and before any surgical intervention.

Measurements: 2 experts jointly established the endocarditis diagnostic classification (according to Duke-modified criteria) and therapeutic plans just before and after MRI and then compared them.

Results: Endocarditis was initially classified as definite in 77 patients and possible in 50 and was excluded in 3. Sixteen patients (12%) had acute neurologic symptoms. Cerebral lesions were detected by MRI in 106 patients (82% [95% CI, 75% to 89%]), including ischemic lesions in 68, microhemorrhages in 74, and silent aneurysms in 10. Solely on the basis of MRI results and excluding microhemorrhages, diagnostic classification of 37 of 53 (32%) cases of nondefinite endocarditis was upgraded to either definite (34 patients) or possible (3 patients). Endocarditis therapeutic plans were modified for 24 (18%) of the 130 patients, including surgical plan modifications for 18 (14%). Overall, early MRI led to modifications of diagnosis or therapeutic plan in 36 patients (28% [CI, 20% to 36%]).

Limitation: Investigators did not assess whether the MRI-related changes in diagnosis and therapeutic plans improved patient outcomes or led to unnecessary procedures and increased costs.

Conclusion: Cerebral lesions were identified by MRI in many patients with endocarditis but no neurologic symptoms. The MRI findings affected both diagnostic classifications and clinical management plans.

Primary Funding Source: French Ministry of Health.

Ann Intern Med. 2010;152:497-504. www.annals.org

For author affiliations, see end of text.

* For members of the IMAGE Study Group, see the Appendix (available at www.annals.org).

Subclinical Brain Embolization in Left-Sided Infective Endocarditis

Results From the Evaluation by MRI of the Brains of Patients With Left-Sided Intracardiac Solid Masses (EMBOLISM) Pilot Study

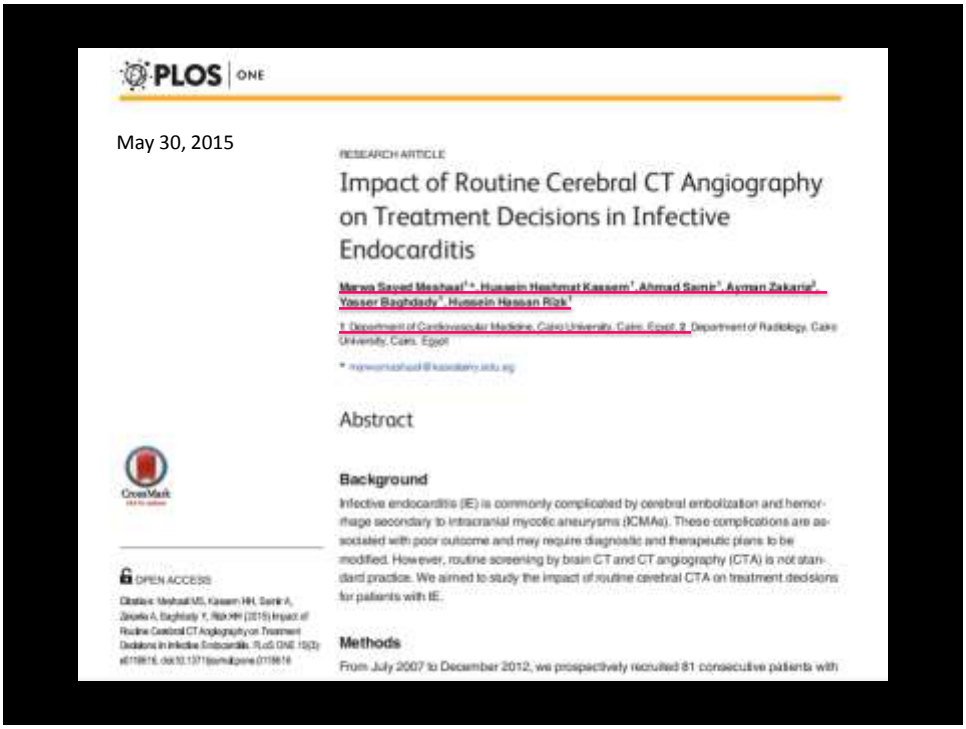
Howard A. Cooper, MD; Elissa C. Thompson, MD; Robert Laureno, MD; Arthon Fisisz, MD; Alexander S. Mark, MD; Mark Lin, MD; Steven A. Goldstein, MD

***Background*—**Acute brain embolization (ABE) in left-sided infective endocarditis has significant implications for clinical decision making. The true incidence of ABE, including subclinical brain embolization, is unknown.

***Methods and Results*—**We prospectively studied 56 patients with definite left-sided infective endocarditis. Patients were examined by a study neurologist, and those without contraindication had magnetic resonance imaging of the brain. Patients without clinical evidence of acute stroke but with magnetic resonance imaging evidence of ABE were considered to have subclinical brain embolization. Clinical stroke was present in 14 of 56 patients (25%). Among 40 patients undergoing magnetic resonance imaging, the incidence rates of subclinical brain embolization and any ABE were 48% and 80%, respectively. ABE was present in 18 of 19 patients (95%) with *Staphylococcus aureus* infection. At 3 months, mortality was similar among patients with clinical stroke and subclinical brain embolization (62% versus 53%; $P=NS$) and was higher among patients with any ABE than among those without ABE (56% versus 12%; $P=0.046$). Valvular surgery was performed in 25 patients (45%), including 16 with ABE, at a median of 4 days. No patient suffered a postoperative neurological complication. Surgery was independently associated with a lower risk of mortality at 3 months (odds ratio, 0.1; 95% confidence interval, 0.03 to 0.6; $P=0.016$).

***Conclusions*—**Magnetic resonance imaging detected subclinical brain embolization in a substantial number of patients with left-sided infective endocarditis, suggesting that the incidence of ABE may be significantly higher than reports based on clinical and computed tomography findings have indicated. Brain magnetic resonance imaging may play a role in the complex decision about surgical intervention in infective endocarditis. (*Circulation*. 2009;120:585-591.)

Key Words: infective endocarditis ■ magnetic resonance imaging ■ stroke ■ surgery



PLOS ONE

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RESEARCH ARTICLE

Impact of Routine Cerebral CT Angiography on Treatment Decisions in Infective Endocarditis

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Abstract

Background

Infective endocarditis (IE) is commonly complicated by cerebral embolization and hemorrhage secondary to intracranial mycotic aneurysms (ICMAs). These complications are associated with poor outcome and may require diagnostic and therapeutic plans to be modified. However, routine screening by brain CT and CT angiography (CTA) is not standard practice. We aimed to study the impact of routine cerebral CTA on treatment decisions for patients with IE.

Methods

From July 2007 to December 2012, we prospectively recruited 81 consecutive patients with

OPEN ACCESS

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- July 2007 to Dec. 2012 carried out by IE working group Kasr El-Ainy
- 81 consecutive patients had lt side IE
- Patients underwent CTA within 1 wk
- 34 patients had symptomatic CNS embolization
- ICMA occurred in 26(32%) patients; 15(18.5%) were silent
- CTA findings changed treatment plan in 21patients (25.6%); 11 were neurologically free

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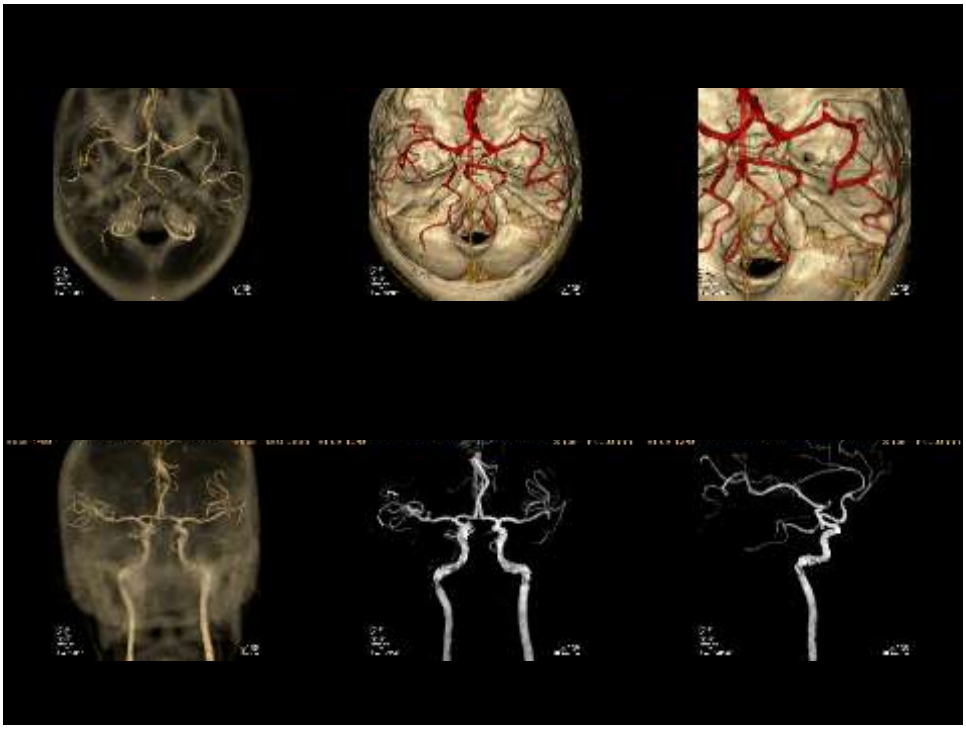
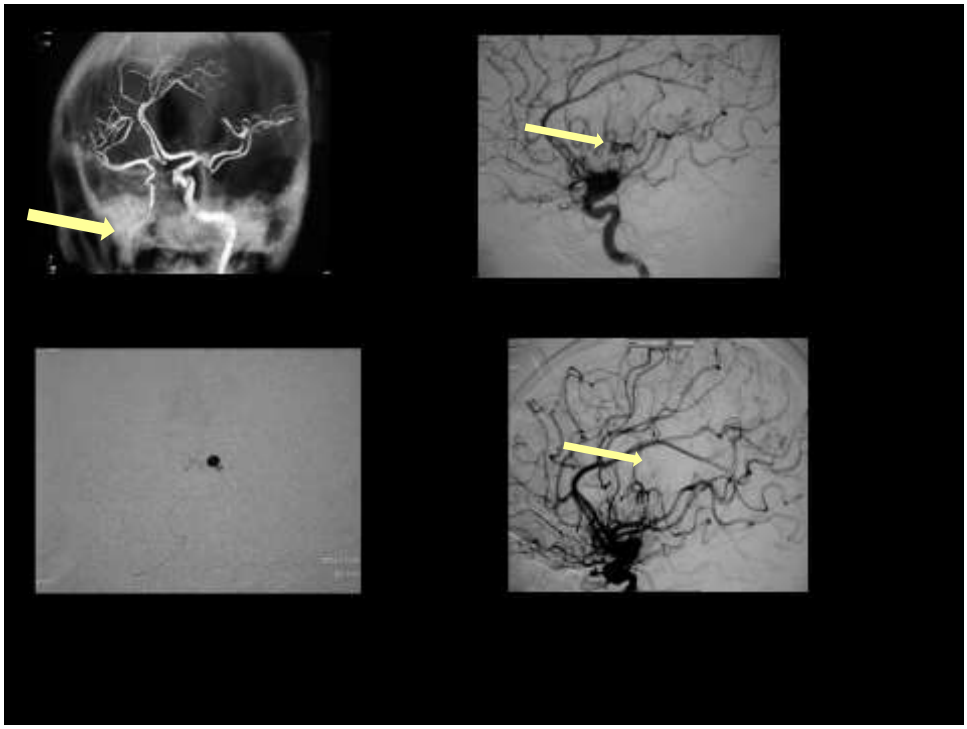
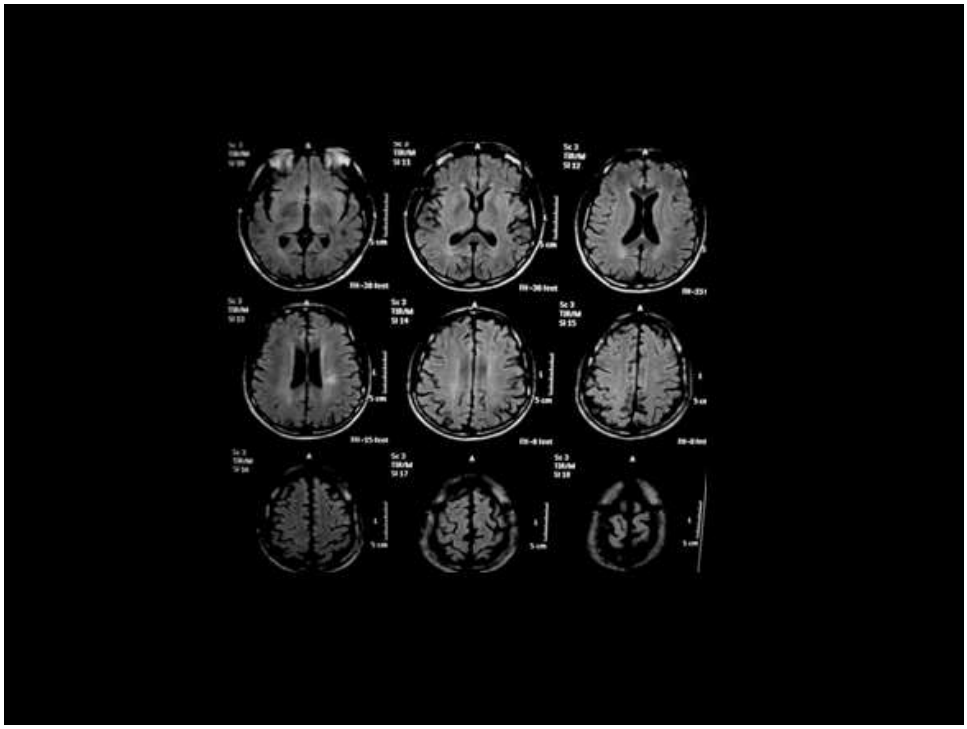
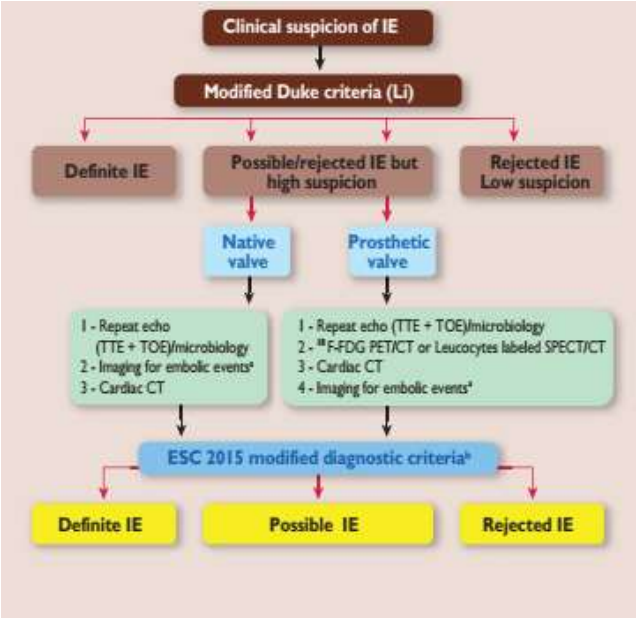
Brain CT & CT angiography









Laboratory Techniques

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- Positive blood cultures remain the cornerstone of diagnosis
- 3 sets are taken at 30-min intervals, each containing 10 mL of blood
- Incubated in both aerobic and anaerobic atmospheres
- Sampling should be obtained from a peripheral vein rather than from a central venous catheter
- Using a meticulous sterile technique
- Withdraw Bl cultures prior to any antibiotic use

Investigation for blood culture negative infective endocarditis

Pathogen	Diagnostic procedures
Brucella spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Coxiella burnetii	Serology (IgG phase I >1:800), tissue culture, immunohistology, and PCR of surgical material.
Bartonella spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Tropheryma whipplei	Histology and PCR of surgical material.
Mycoplasma spp.	Serology, culture, immunohistology, and PCR of surgical material.
Legionella spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Fungi	Blood cultures, serology, PCR of surgical material.

Thank you