Managing Complex Endocarditis
Echo's Vital Role

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Case. IE with Heart Failure

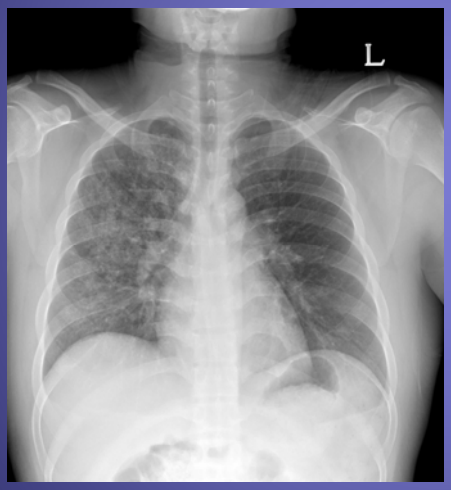
32 year-old male with high fever

BP: 109/78 mmHg, PR 112, BT 39.1°C
ABGA: 7.48-33-66-25 (8 PM at ER)
Portable Echo: MV vegetation with MR

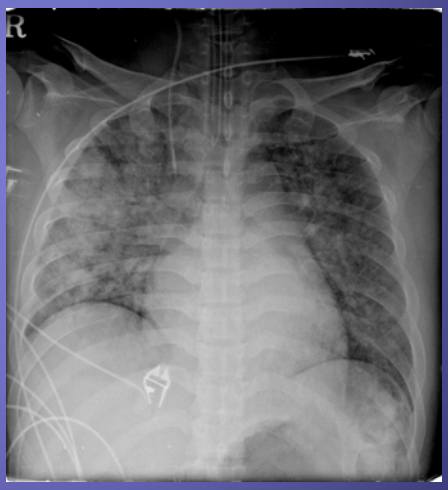
ABGA: 7.42-34-47-22 (2 AM at CCU)

Rapid Progression of Pulmonary Edema

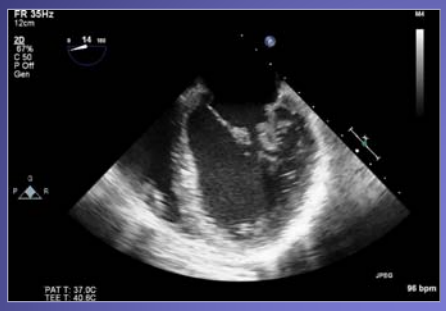
6 PM at ER

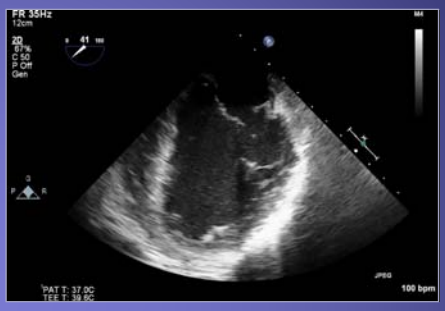


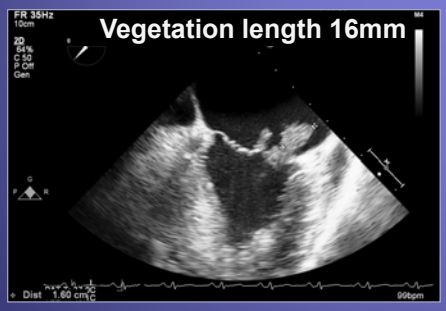
2 AM on the next day at CCU



Case. IE with Pulmonary Edema







2015 ESC Guidelines for Left-sided IE Indications and Timing of Surgery

Indications for surgery	Timing[a]	Class[b]	Level[c]
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[e]	Urgent	IIb	C

IE with Heart Failure

- **Emergency Surgery (within 24 hours)**

  IE with ***refractory pulmonary edema or cardiogenic shock*** caused by

  acute valvular regurgitation or obstruction

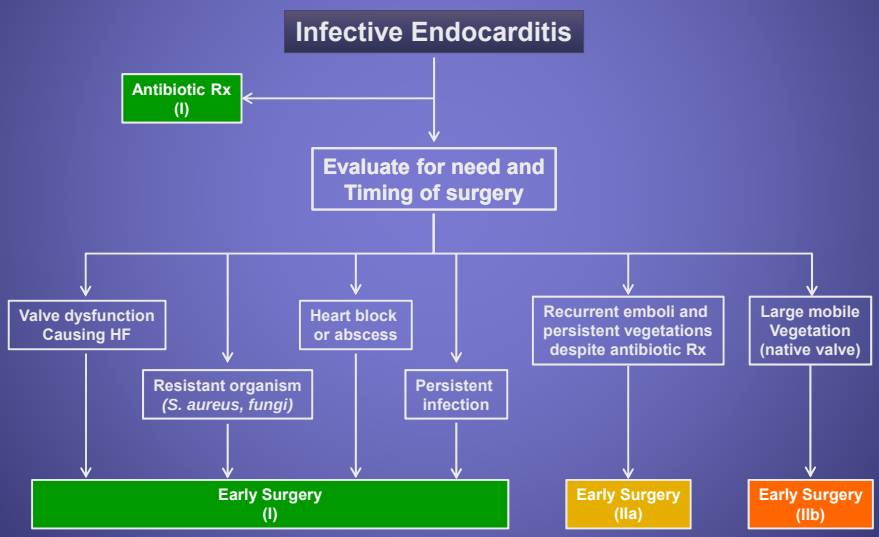
  fistula into cardiac chamber or the pericardium

- **Urgent Surgery (within a few days)**

  IE with ***persisting heart failure, early MV closure or significant pulmonary hypertension***

2014 AHA/ACC Guideline

Treatment of IE



2014 AHA/ACC Guideline

- **Definition of Early Surgery**

  Surgery during the initial hospitalization before completion of a full therapeutic course of antibiotics

- **Timing of Surgery**

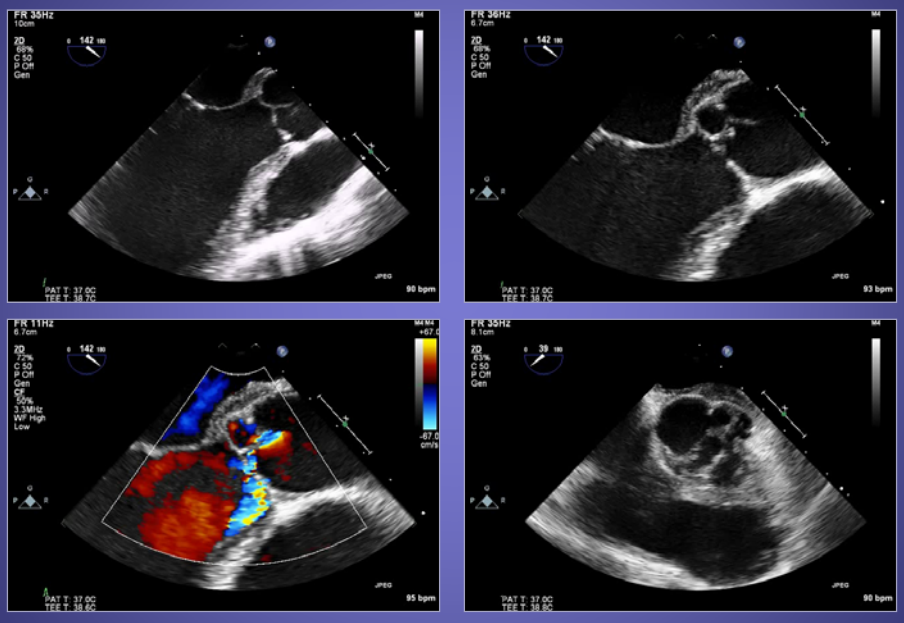
  Decisions should be made by a Heart Valve Team of cardiology, cardiac surgery and infectious disease specialists

Urgent Surgery for IE

Uncontrolled Infection

- Locally Uncontrolled Infection
  - Abscess, Fistula, False aneurysm
  - Enlarging vegetations
- Persisting fever and positive blood cultures > 7-10 days
- Infection caused by fungi or multiresistant organisms

Case. 29 year-old male: IE with aortic abscess



Embolism in Infective Endocarditis

- Embolism is a frequent and serious complication of IE due to migration of vegetations
- Embolic events occur in 20-50% of IE cases, but the risk of new events is 6-21%
- The brain is the most frequent site of embolism

Neurologic Complications in IE

- Among 1345 left-sided IE, neurologic complications occurred to 340 (25%) patients, in whom overall mortality was 45% vs. 24% in those without these complications (P<0.01)
- Appropriate antimicrobial treatment considerably reduced neurologic complications after 1 week

García-Cabrera E, et al. Circulation 2013;127:2272-2284

How to Prevent Embolism

- Early diagnosis of IE and prompt institution of antibiotic therapy
- Surgical removal of vegetations

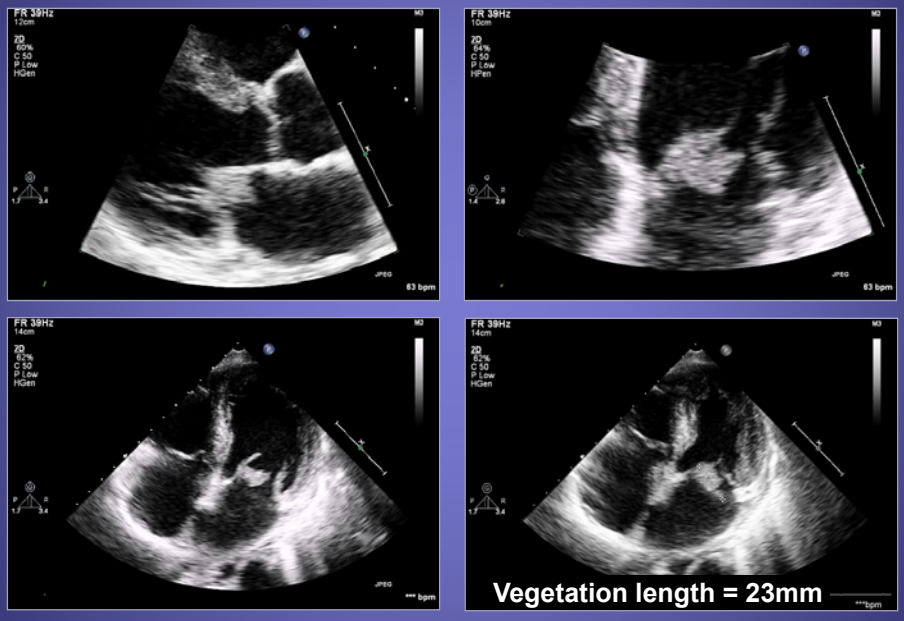
Case. IE with Large Vegetations

70 year-old male with fever

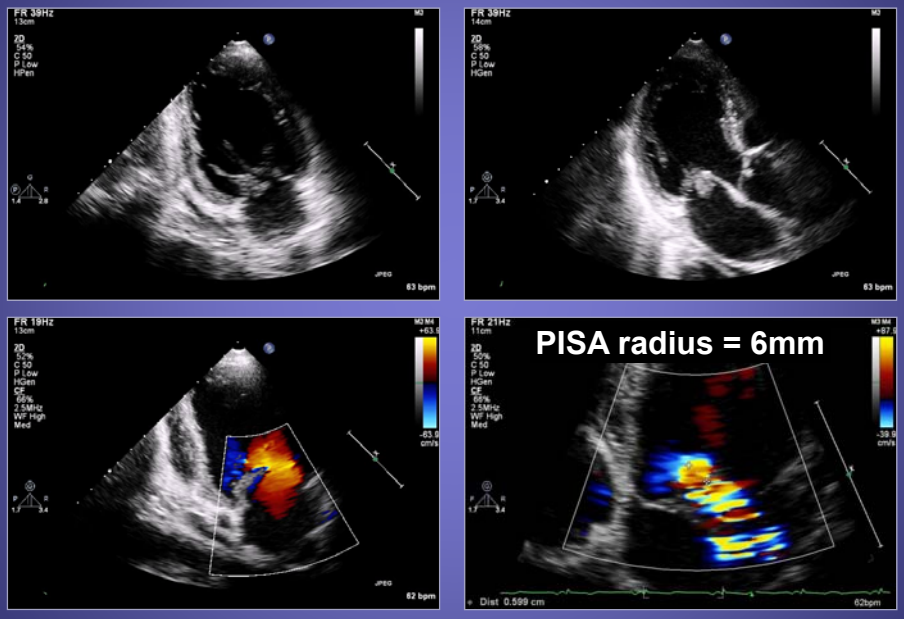
- He noted intermittent fevers for 3 weeks
- Pansystolic murmur was heard on cardiac examination

→ *Echo and blood cultures were done immediately after transfer to ER*

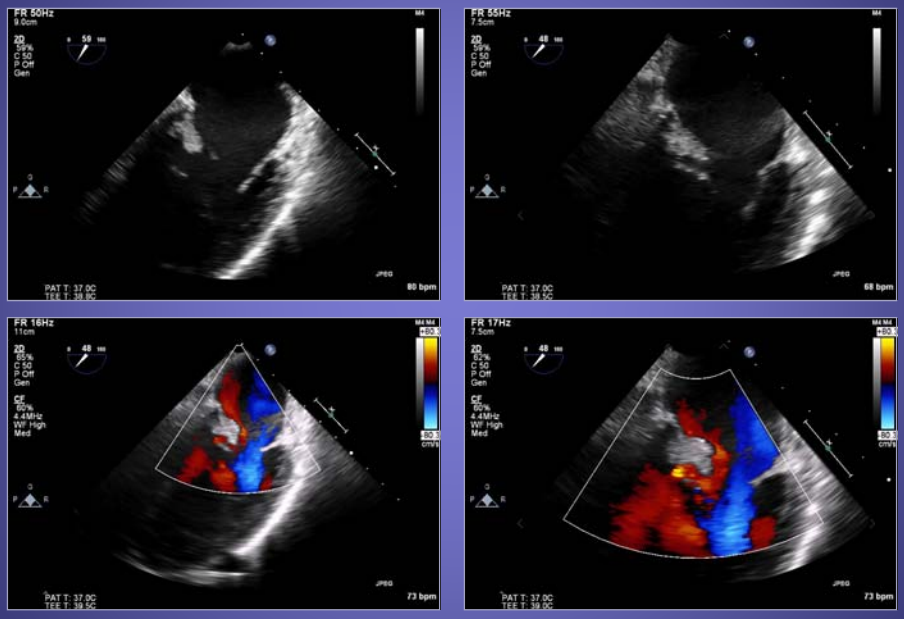
Case. IE with Large Vegetations



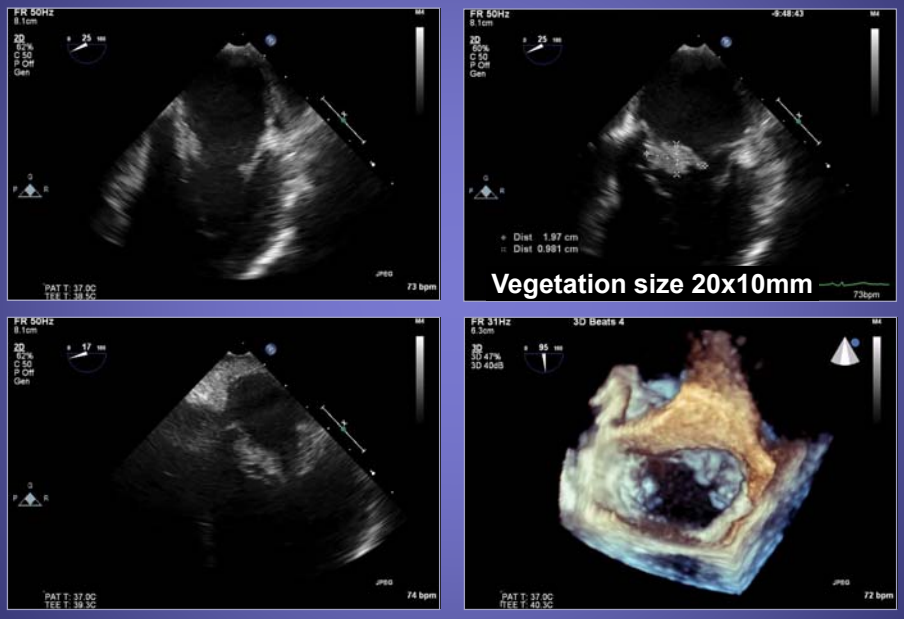
Case. IE with Large Vegetations



Case. IE with Large Vegetations



Case. IE with Large Vegetations



Case. IE with large vegetations

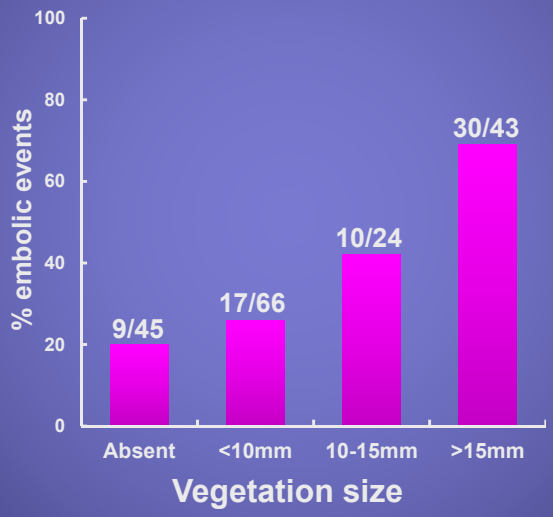
Is embolic risk greater than operative risk in this patient?

1) Yes
2) No

Echo Predicts Embolism in IE

- Echocardiography plays a key role in predicting embolic events
- The size and mobility of vegetation are the most potent independent predictors
- Patients with large vegetations (> 10mm) have a higher risk of embolism

Echo Predicts Embolism



Di Salvo G, et al. JACC 2001;37:1069-76

Predictors for Embolic Events

Variable	Univariate analysis	Multivariate analysis	
	p value	Hazard Ratio	p value
Age	0.15	1.01	0.18
Diabetes	0.05	1.30	0.50
Previous embolism	0.04	1.40	0.30
Atrial fibrillation	0.07	1.66	0.17
Vegetation length (mm)	0.01		
0 - 10		1.26	0.79
> 10		4.46	0.04
Staphylococcus aureus	0.07	1.78	0.13

Hubert S, et al. J Am Coll Cardiol 2013;62:1384-92

Operative risk assessment

	Low Risk	Intermediate Risk	High Risk
STS PROM	**<4%**	**4-8%**	**> 8%**
	AND	OR	OR
Frailty	**None**	**1 Index (mild)**	**≥ 2 Indicies (moderate to severe)**
	AND	OR	OR
Major organ system compromise	**None**	**1 Organ system**	**2 Organ systems**
	AND	OR	OR
Procedure-specific impediments	**None**	**Possible**	**Possible**

2014 AHA/ACC Valvular Heart Disease Guideline

Case. IE with Large Vegetations

Operative Risk

- **EuroSORE**
  - Age: 70
  - Active endocarditis
  - Preserved LV function
  - No pulmonary HTN
  - Intervention: Single non CABG
    - ✓Logistic EuroSCORE: **8.73%**
    - ✓EuroSCORE II: **1.37 %**

- **STS PROM**
  - Isolated MV replacement
  - Diabetes
  - Infective endocarditis
  - Moderate MR/TR

  ✓Risk of mortality: **5.87%**

Case. IE patient at embolic risk

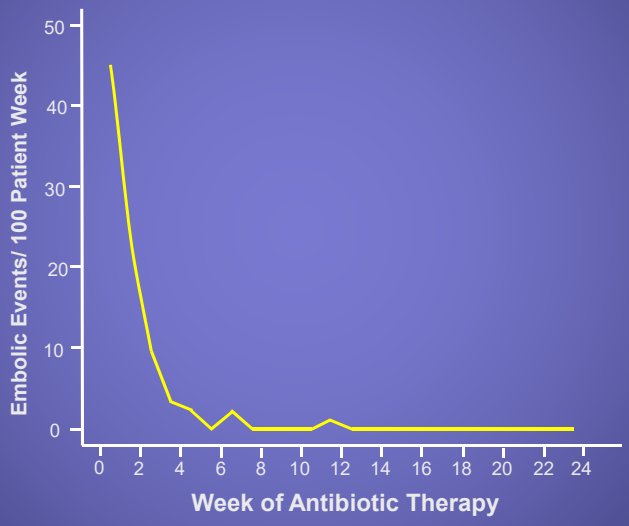
Does this patient need valve surgery?

1) Yes, urgent surgery
2) Yes, elective surgery
3) No, antibiotic therapy alone

Surgery to Prevent Embolism

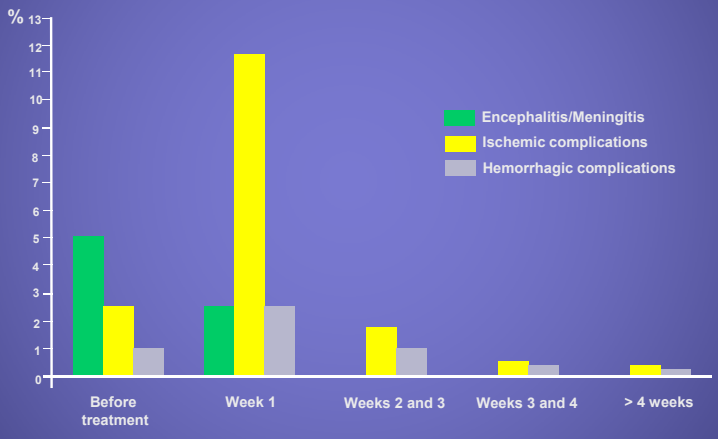
Timing of Surgery

Incidence of Embolic Events



Hubert S, et al. J Am Coll Cardiol 2013;62:1384-92

Incidence of Neurologic Complications



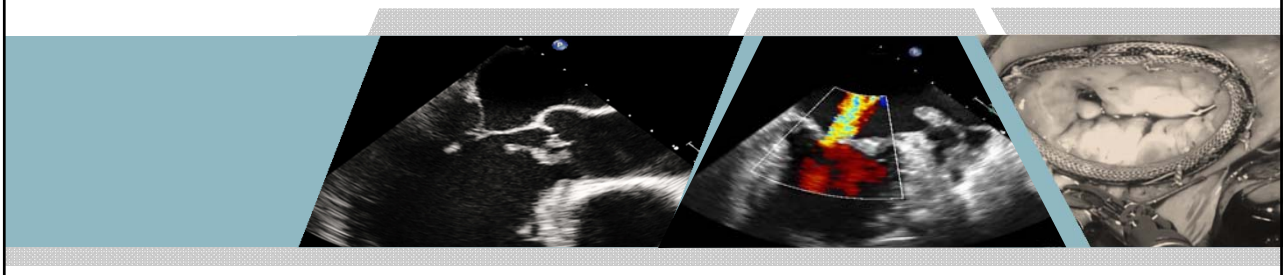
Gracia-Cabrera E, et al. Circulation. 2013;127:2272-2284

Surgery for Infective Endocarditis

- Previous observational studies comparing surgery with medical therapy have been subject to the limitations imposed by baseline differences, treatment selection and survivor biases
- Data supporting early surgery from randomized controlled trials are scarce due to ethical concerns about withholding surgery in control patients

Prendergast BD. Circulation 2010;1141
Lalani T, et al. Circulation 2010;1005

Randomized Trial of *Ea*rly *S*urgery Versus Conventional Treatment for Infective *E*ndocarditis *(EASE)*



Duk-Hyun Kang, MD, PhD
on behalf of The EASE Trial Investigators
Asan Medical Center, Seoul, Korea
UNIVERSITY OF ULSAN COLLEGE OF MEDICINE
Asan Medical Center

Study Patients

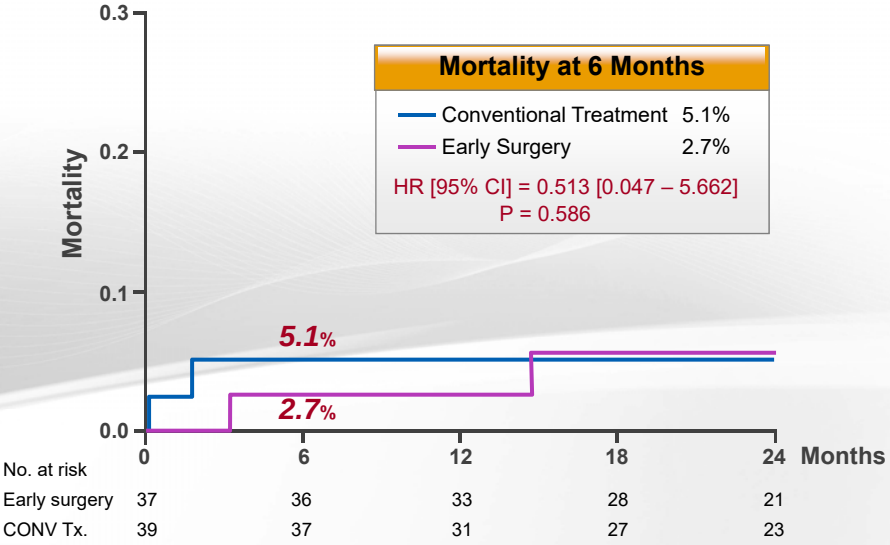
- All patients suspected of IE underwent blood cultures and echocardiography within 24 hrs after hospitalization

Inclusion Criteria	Exclusion Criteria
▪ Age: 15-80 years ▪ Definite left-sided native valve IE according to Duke criteria ▪ Severe mitral or aortic valve disease ▪ Vegetation length > 10mm	▪ Pts with urgent indication of surgery moderate to severe CHF, heart block, annular or aortic abscess, penetrating lesions, fungal endocarditis ▪ Pts not candidates for early surgery age > 80 yrs, coexisting major embolic stroke or poor medical status ▪ Prosthetic valve IE ▪ Right-sided vegetations ▪ Small vegetations ≤ 10mm

Study Procedures

- All pts screened for eligibility underwent transesophageal echo and CT
- Pts were randomly assigned on a 1:1 basis to **early surgery** or **conventional treatment** using an interactive web response system
- **In the early surgery group**, surgery was performed **within 48 hours** of randomization
- **Pts in the conventional treatment group** were treated according to the current guidelines

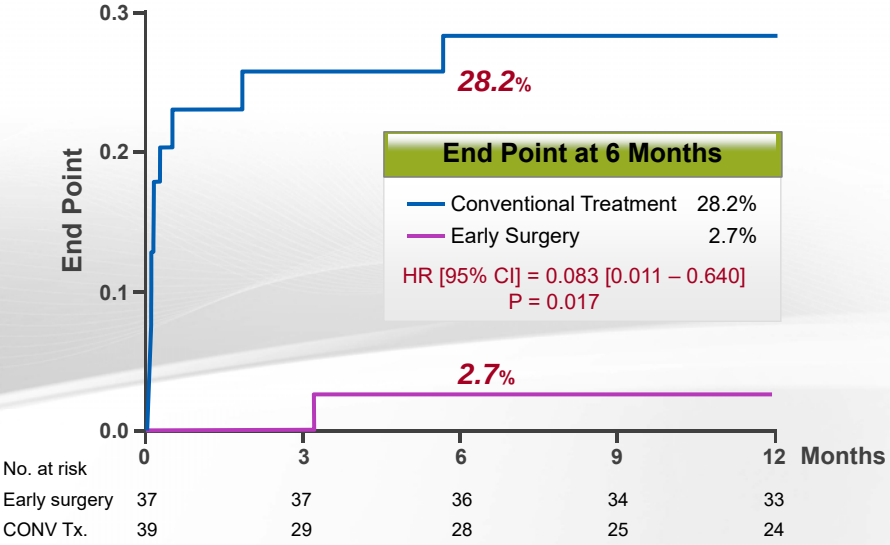
All Cause Mortality



No. at risk					
Early surgery	37	36	33	28	21
CONV Tx.	39	37	31	27	23

Kang DH, et al. N Engl J Med 2012;366:2466-73

End Point



No. at risk					
Early surgery	37	37	36	34	33
CONV Tx.	39	29	28	25	24

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis

Duk-Hyun Kang, M.D., Ph.D., Yong-Jin Kim, M.D., Ph.D., Sung-Han Kim, M.D., Ph.D., Byung Joo Sun, M.D., Dae-Hee Kim M.D., Ph.D., Sung-Cheol Yun, Ph.D., Jong-Min Song, M.D., Ph.D., Suk Jung Choo, M.D., Ph.D., Cheol-Hyun Chung, M.D., Ph.D., Jae-Kwan Song, M.D., Ph.D., Jae-Won Lee, M.D., Ph.D., and Dae-Won Sohn, M.D., Ph.D.

NEJM 2012;366:2466-73

2015 ESC Guidelines for Left-sided IE
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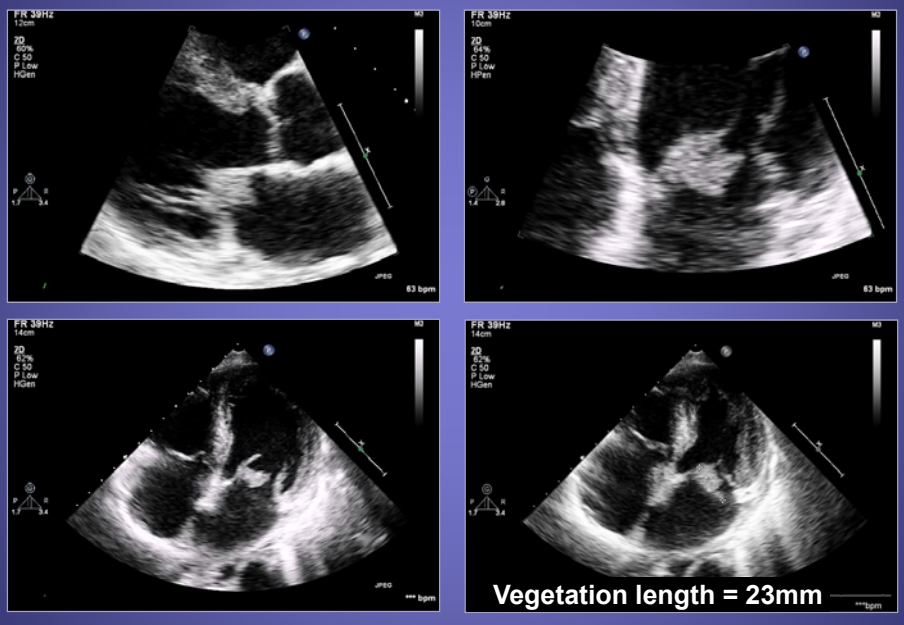
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery[e]	Urgent	IIb	C

Early Surgery for IE

Prevention of Embolism

2009 ESC guidelines	2015 ESC guidelines
Class I indication ▪ Large vegetations (> 10mm) following **one** or more embolism despite antibiotic Tx	**Class I indication** ▪ Large vegetations (> 10mm) following **one** or more embolism despite antibiotic Tx **Class IIa indication** ▪ Large vegetations (> 10mm) with severe valve disease and low operative risk ▪ Isolated very large vegetations in excess of 30 mm

Case. IE with Large Vegetations

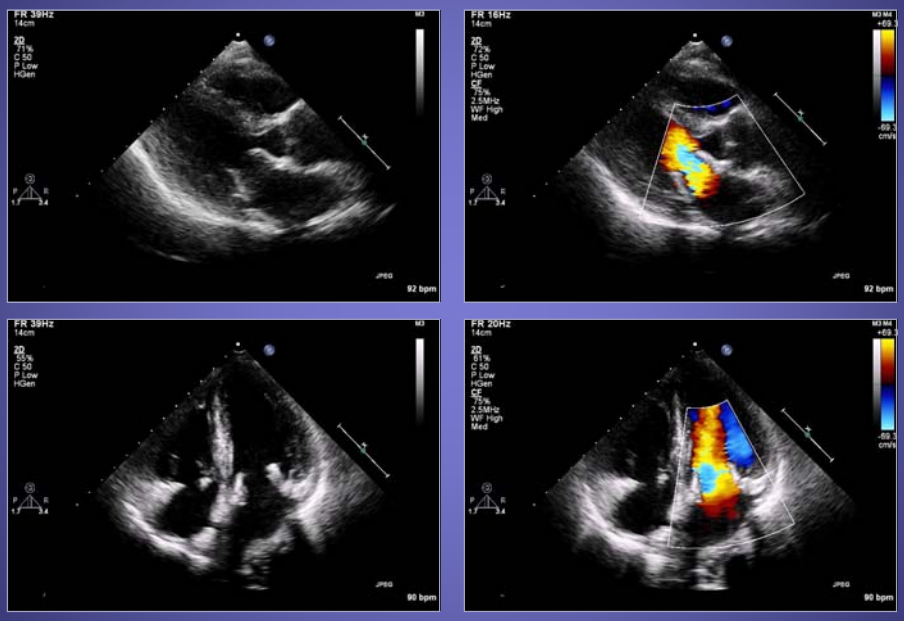


Case. IE patient at embolic risk

Does this patient need valve surgery?

1) Yes, urgent surgery
2) Yes, elective surgery
3) No, antibiotic therapy alone

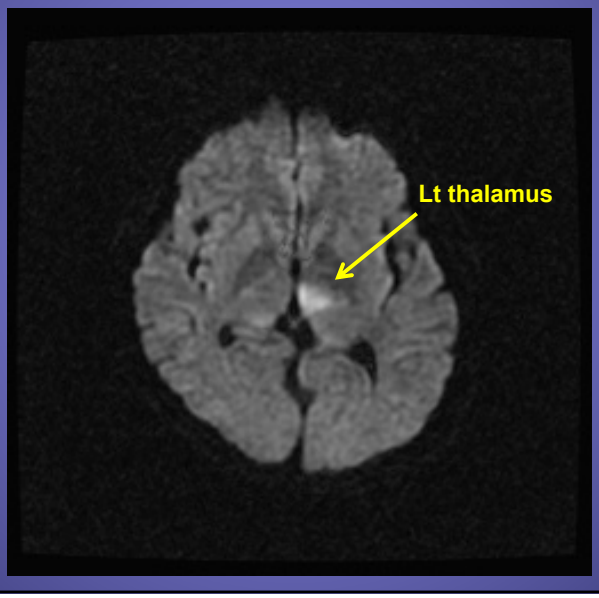
Case. 70-year-old male with large vegetations



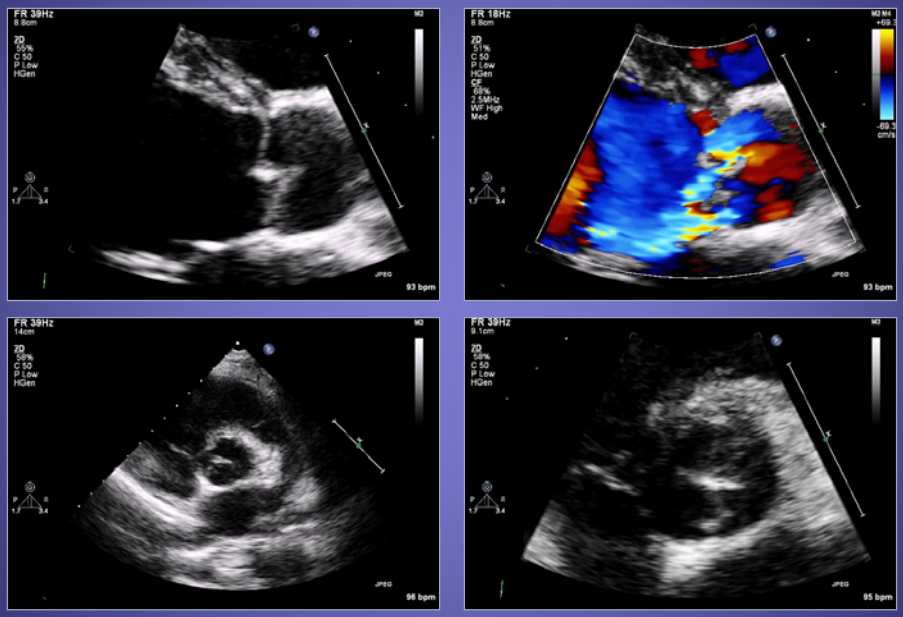
Surgical Timing after Neurologic Complication

- Early surgery may pose significant risks for neurologic deterioration and perioperative cerebral bleeding in patients with a neurologic complication
- Timing of surgery is challenging in the event of large cerebral infarction or intracranial hemorrhage

33 year old female
Right hemiparesis and Drowsy mentality



Case. 33 yr-old female with infective endocarditis



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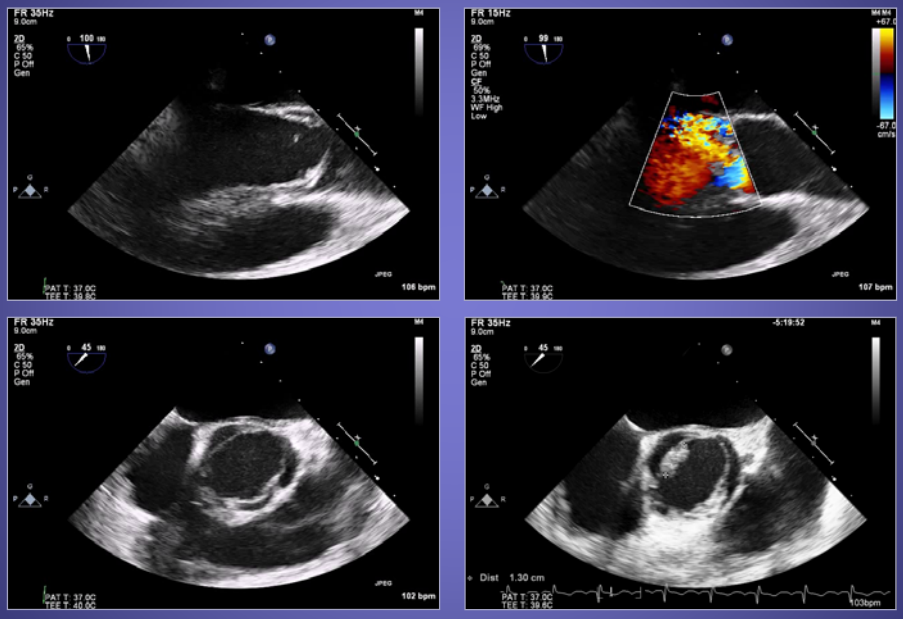
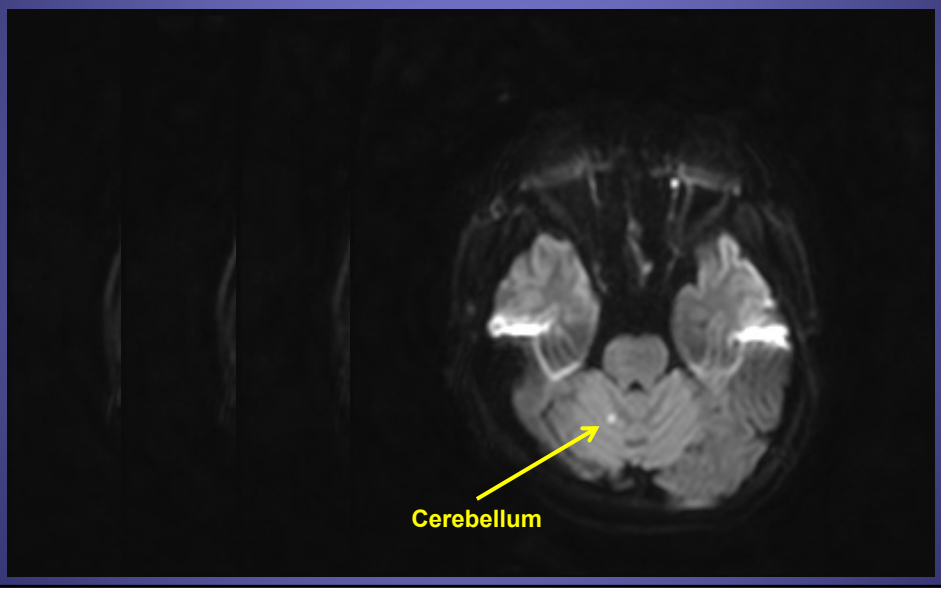
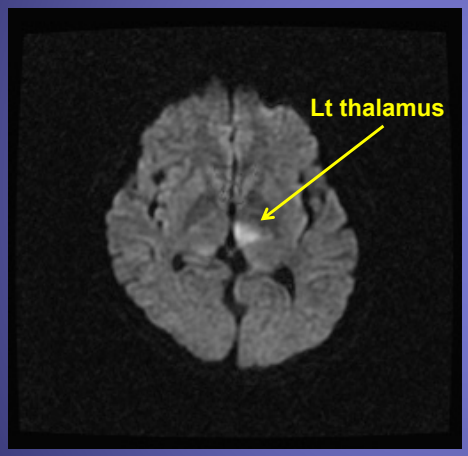


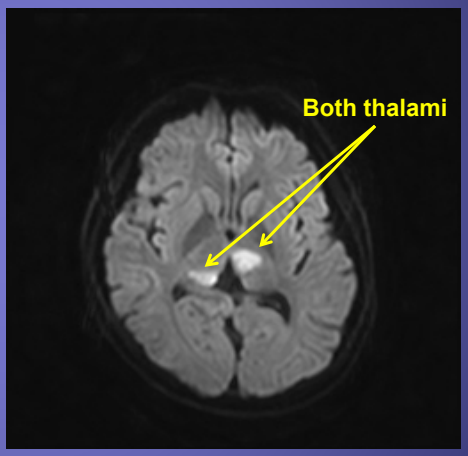
Mentality aggravation to semicoma
MRI at 9 PM on the same day



Drowsy
8 AM MRI



Semicoma
9 PM MRI



Case. IE complicated with Coma

Is embolic risk greater than operative risk in this patient?

1) Yes
2) No

Surgical Timing after Neurologic Complication

- Systematic early MRI of the brain may help clinical decision on timing of surgery
- Surgery should not be delayed in patients with stroke and HF if cerebral hemorrhage has been excluded and coma is absent
- Surgery should be delayed in patients with a large cerebral infarction at risk of hemorrhagic transformation or intracerebral hemorrhage

Case. IE complicated with Coma

Is embolic risk greater than operative risk in this patient?

1) Yes
2) No

Treatment Decision Based on Risk Stratification

Characteristics	Early Surgery	Medical Therapy
Heart failure		
Moderate to severe	(+++)	
Mild	(+)	
Uncontrolled infection		
Abscess	(++)	
Persistent infection	(+)	
Micro-organism	*Staphylococcus aureus* Fungus	
Embolic risk	High	Low
Vegetation size	Large	Small
Antibiotic therapy	<1 week	>2 weeks
Operative risk	Low	High
Likelihood of valve repair	High	Low

Kang DH. Heart 2015;101:1786-1791

Take Home Messages

- Rapid diagnosis of IE by performing blood culture and echo within 24 hours
- TEE is essential for identification and management of complicated IE
- Decision for surgery should be based on individual risk-benefit analysis
- Early surgery is strongly indicated if its benefits exceed operative risks