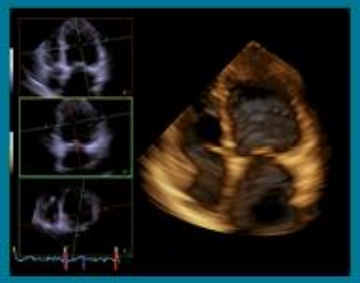


EuroValve

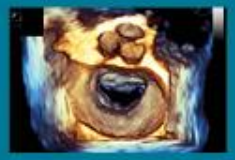
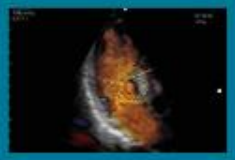
October 24-25, 2014

When to Operate in Infective Endocarditis: Always Late?

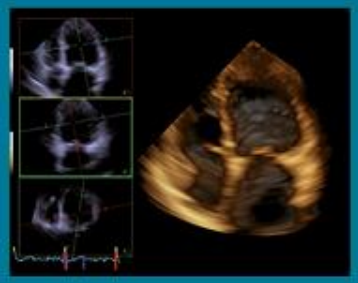
Dr Bernard Prendergast DM FRCP FESC

John Radcliffe Hospital, Oxford, UK



www.eurovalvecongress.com



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October 24-25, 2014

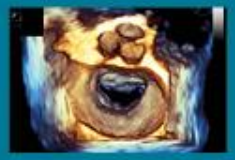
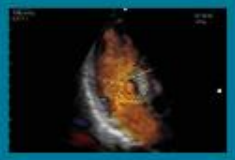
Faculty disclosure

Bernard PRENDERGAST

I disclose the following financial relationships:

Paid speaker for Edwards Lifesciences



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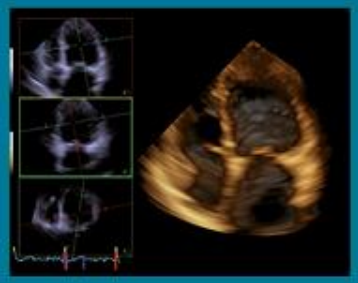

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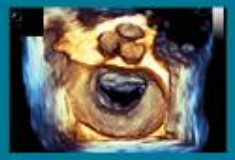
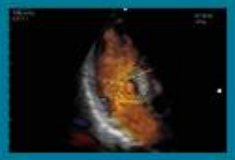
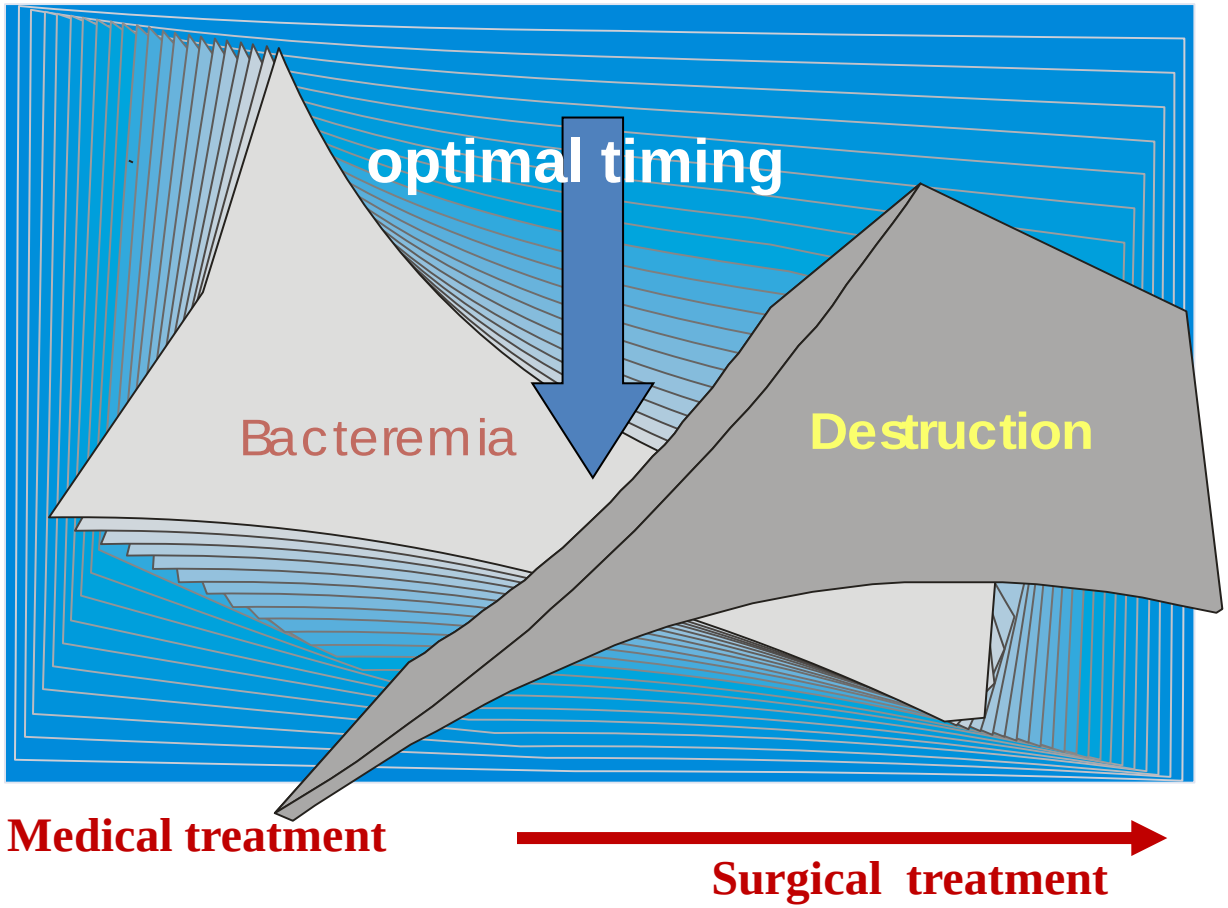



Optimal Timing of Surgery: Destructive IE



Surgery in infective endocarditis

- Major changes over the last 3 decades
  - 1970s/1980s: defer surgery to allow healing
  - Increasing role of early surgery: 20% --> > 50%
- Perioperative mortality no higher and persisting or recurrent infection no more frequent with early surgery
- "Cancer" surgery (wide excision margins)
- Repair easier when performed early
- >15 observational studies (case selection bias):
  - Single centre, retrospective, small numbers
  - Virulent organisms/complications over-represented
  - Elderly/comorbid cases under-represented
  - Surgery only available to early survivors
  - 5 recent propensity matched studies with conflicting results

Infective Endocarditis: The Right Time for Surgery

WHO?

WHEN?

European Heart Journal
doi:10.1093/eurheartj/ehp285

ESC GUIDELINES

Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009)

The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and by the International Society of Chemotherapy (ISC) for Infection and Cancer

Authors/Task Force Members: Gilbert Habib (Chairperson) (France)*, Bruno Hoen (France), Pilar Tornos (Spain), Franck Thuny (France), Bernard Prendergast (UK), Isidre Vilacosta (Spain), Philippe Moreillon (Switzerland), Manuel de Jesus Antunes (Portugal), Ulf Thilen (Sweden), John Lekakis (Greece), Maria Lengyel (Hungary), Ludwig Müller (Austria), Christoph K. Naber (Germany), Petros Nihoyannopoulos (UK), Anton Moritz (Germany), Jose Luis Zamorano (Spain)

Eur Heart J 2009 ;30:2369-2413.

Guidelines of the ESC Task Force on IE

Recommendations: indications for surgery			
A - HEART FAILURE			
Aortic or mitral IE with severe acute regurgitation or valve obstruction causing pulmonary oedema or cardiogenic shock	Emergency	I	B
Aortic or mitral IE with fistula into a cardiac chamber or pericard pulmonary oedema or shock	Emergency	I	B
Aortic or mitral IE with severe acute regurgitatio failure or echocardiographic signs of poor h pulmonary hypertension)	Urgent	I	B
Aortic or mitral IE with sev	Elective	IIa	B
B - UNCON			
Lo tion)	Urgent	I	B
	Urgent	I	B
	Urgent/elective	I	B
C - PROPHYLAXIS			
uons (> 10 mm) following one or more embolic episodes therapy	Urgent	I	B
with large vegetations (> 10 mm) and other predictors of complicated course persistent infection, abscess)	Urgent	I	C
ated very large vegetations (> 15 mm)*	Urgent	IIb	C

Emergency: <24 hours
Urgent: within a few days
Elective: >1-2 weeks of antibiotic therapy

Habib G et al. Eur Heart J 2009 ;30:2369-2413.

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.

N Engl J Med 2012;366:2466-2473.

ORIGINAL ARTICLE

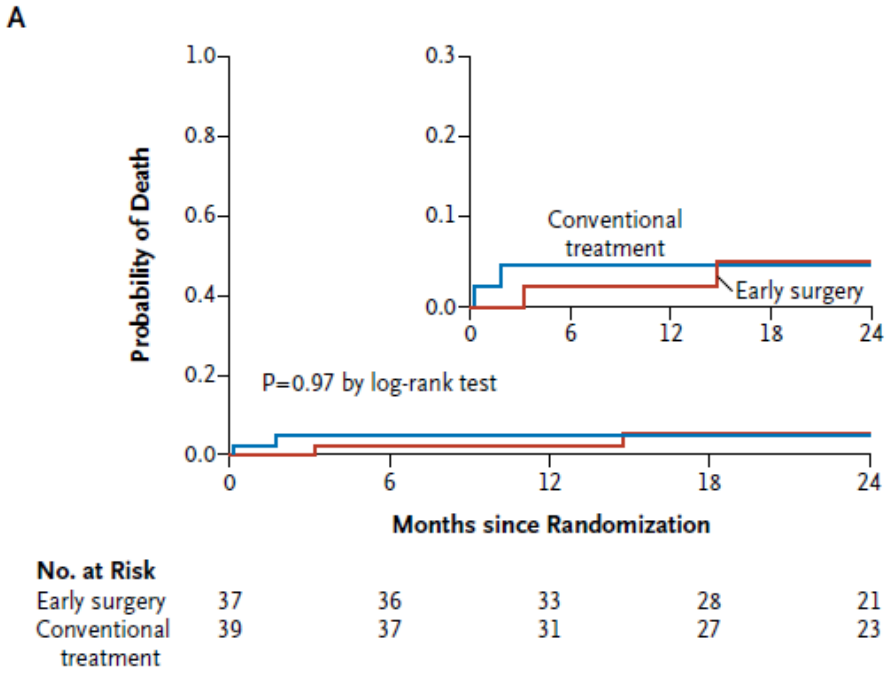
Early Surgery versus Conventional Treatment for Infective Endocarditis

- Inclusion Citeria: Left sided IE, severe valve disease (predominantly MR/AR), large vegetations >1cm
- Exclusion criteria: IE with CHF, >7 days since diagnosis
- Mean age 47 yrs, 67% male, *Staph. aureus* 12%, mean vegetation size 12mm
- Early surgery (<48 hrs, n=37) vs. conventional therapy (AHA guidelines, n=39) (surgery during hospitalisation, n=27; during FU, n=3)
- Antibiotic therapy matched, MV repair more frequent in delayed surgical group
- Primary end-point: in-hospital death and/or major embolic event (imaging confirmed) within 6/52 of randomisation (silent emboli excluded)

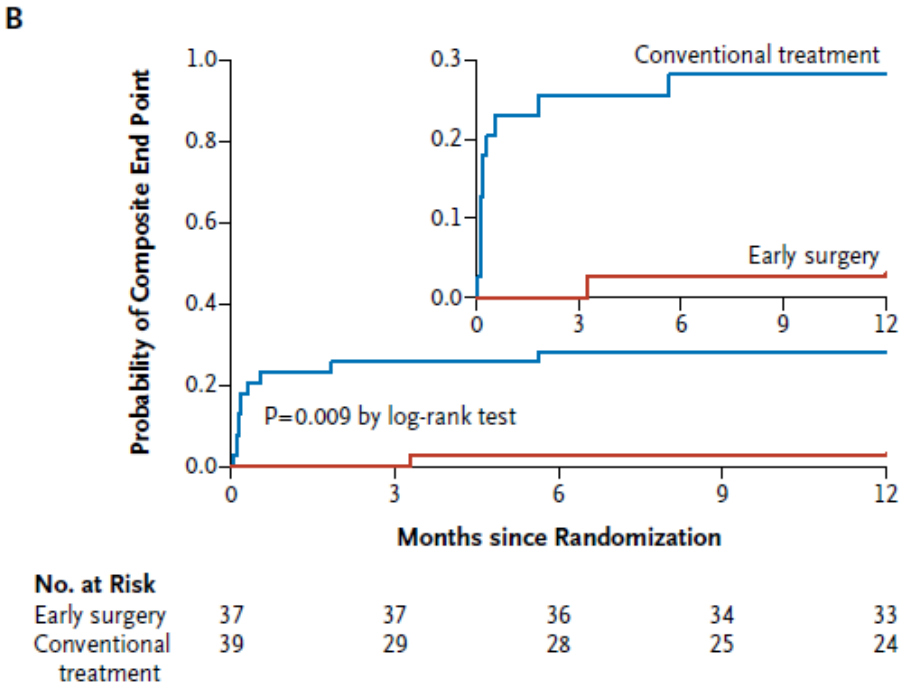
N Engl J Med 2012;366:2466-2473.

ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis



DEATH



DEATH/EMBOLISM

NB:

- All primary end points in conventional treatment group occurred **before** surgery
- Inclusion of secondary endpoints (CHF, recurrent IE, hospitalisation) widened benefits

N Engl J Med 2012;366:2466-2473.

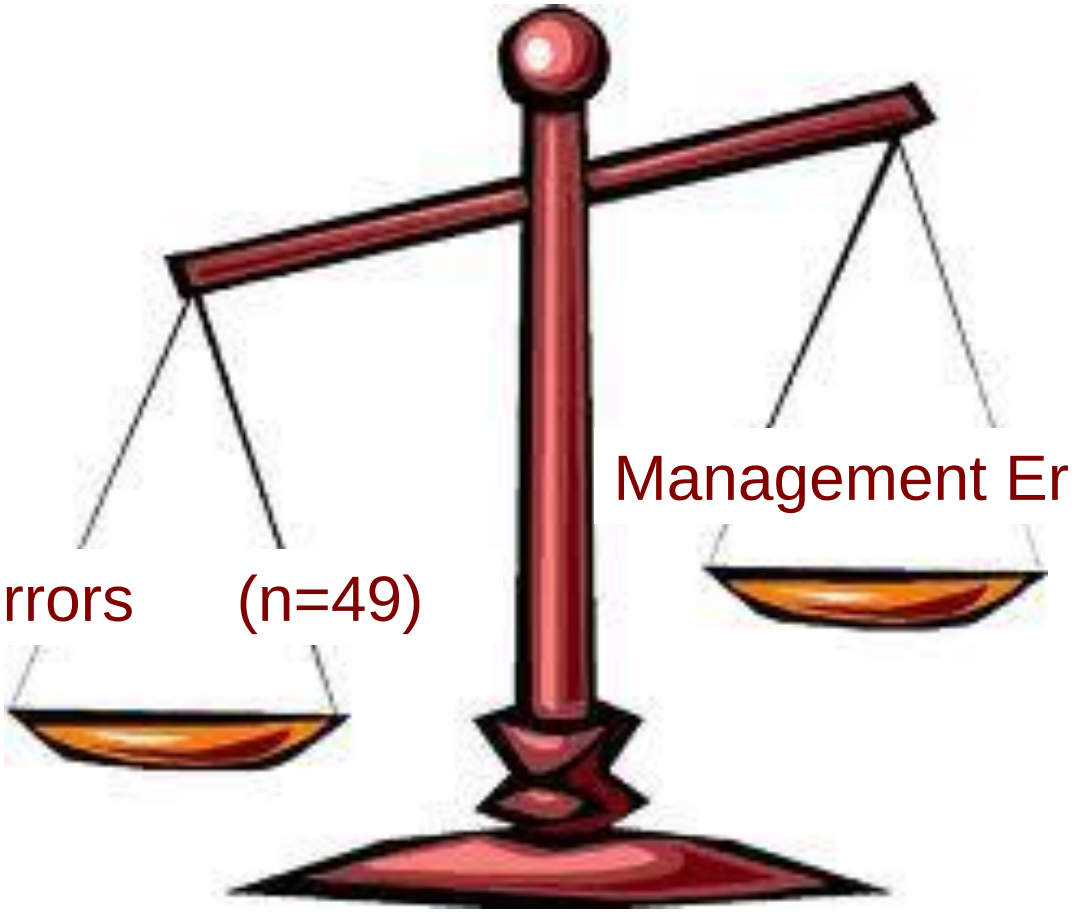
Native-Valve Infective Endocarditis — When Does It Require Surgery?

Steven M. Gordon, M.D., and Gösta B. Pettersson, M.D., Ph.D.

The work of Kang and colleagues provides
data to help define
domized studies to
gery are reasonable
tion of this study f
and raises the bar
who do not have u
valve dysfunction
underscores the po
tis is a dangerous
fits of timely surg
with large vegetati
function, even if t
heart failure, outw
surgery in patients with active infection. In this
sitivity to prescribed antibiotics. Because it is difficult to identify patients who might benefit from early surgery, we would argue that early referral to medical centers with the necessary cardiac surgical experience and resources is warranted for all patients with left-sided, native-valve infective endocarditis who have important valve dysfunction, large vegetations, or invasive disease beyond the cusps or leaflets — not just for those patients with urgent indications. The

N Engl J Med 2012;366:2519-2521.

Main Litigation Cause



Diagnosis Errors (n=49)

Management Errors (n=17)

75%

25%

Medicolegal Case Vignette (1)

- 43 year old
- Fit and Well
- Day 1 A&E

  Fever, night sweats

  CRP 64

  Malaria screen , sent home

Medicolegal Case Vignette (1)

- Day 3 GP:
  - Fever, headaches, Temp 38C
  - Heart murmur noted
  - Blood tests suggested infection – no blood cultures
  - Prescribed clarithromycin
  - Started to feel better

Medicolegal Case Vignette (1)

Day 150 ENT:

- Headaches
- CT head → ? Sinusitis, deviated septum, operated
- Neurology headache due to tension headaches
- Recurrent fever / night sweats
- Multiple courses of antibiotics "seems to clear things"
- Symptoms recurred as soon as he stopped them

Medicolegal Case Vignette (1)

- Day 360 A&E:
  - Headache, temperature 38C, back pain
  - Blood tests suggested infection – no blood cultures
  - CT sinuses again (no sinusitis)
  - Intravenous antibiotics
  - Blurring of vision → ophthalmology ? Panuveitis / posterior uveieitis
  - Discharged home on antibiotics

Medicolegal Case Vignette (1)

Day 390 A&E:

- 18 months of fever, night sweats
- Weight loss
- Headaches
- 20 courses of antibiotics with partial improvement
- Pansystolic murmur
- Echo : mitral regurgitation, vegetation
- Negative blood cultures
- Valve surgery

Contemporary diagnosis of IE

Keystones

- Appropriate clinical suspicion
- Microbiology
  - Polymerase chain reaction
  - Other new diagnostic tools
  - Pathological techniques
- Imaging
- Inflammatory markers

Diagnostic Delay – Days, median (range)

All IE patients

Staph Aureus IE patients

Infective Endocarditis – A Dangerous Disease

- In-hospital mortality 15-20%
- One year mortality 30-40%
- Non-fatal complications
  - Acute stroke 15%
  - CHF 30%
  - Thromboembolic events >20%
- Valve surgery 50%

Chu VH et al. Circulation 2004;109:1745-1749.
Tleyjeh IM et al. JAMA 2005;293:3022-3028.
Tornos P et al. Heart 2005;91:571-575.
Tornos MP et al. Ann Intern Med 1992;117:567-572.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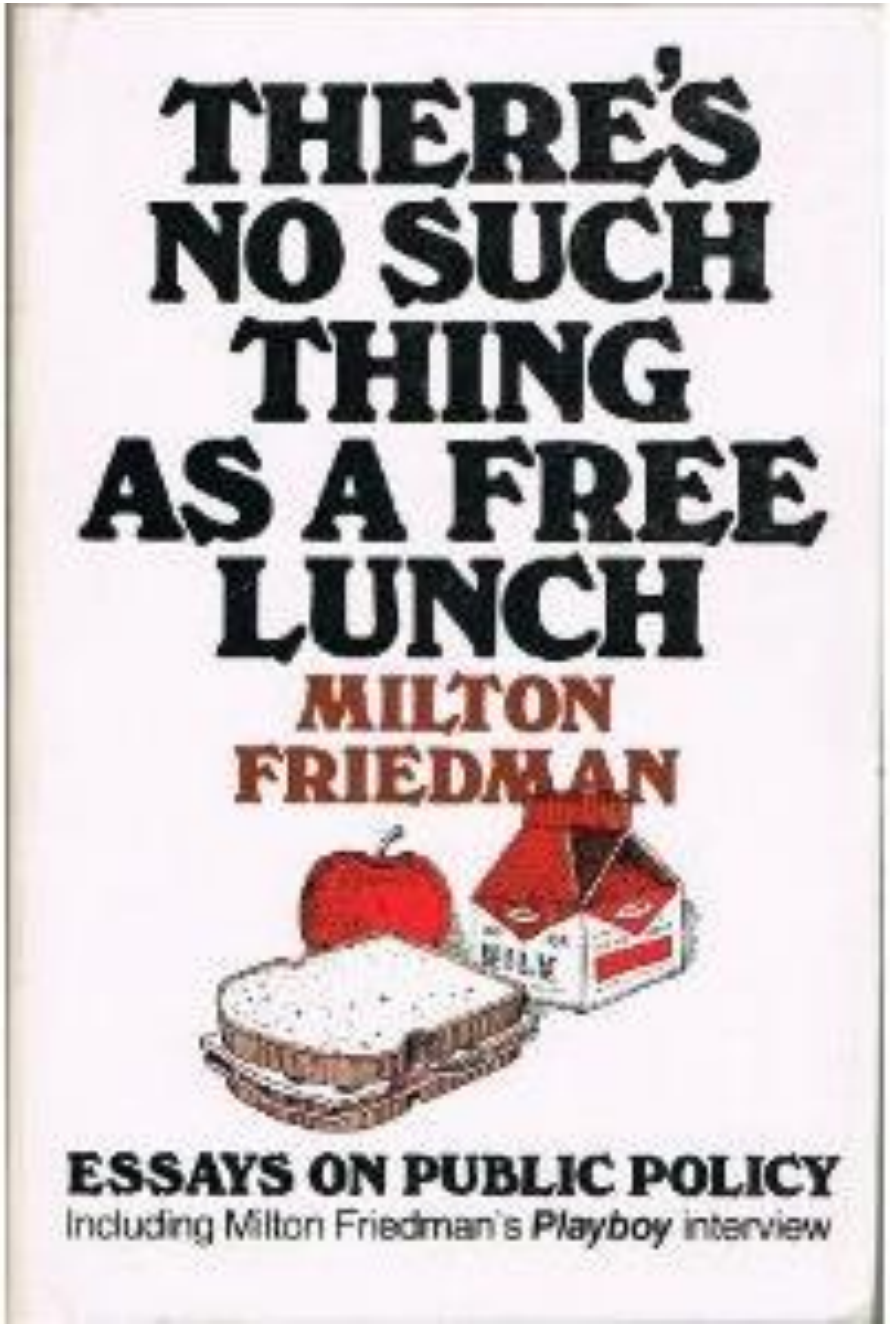
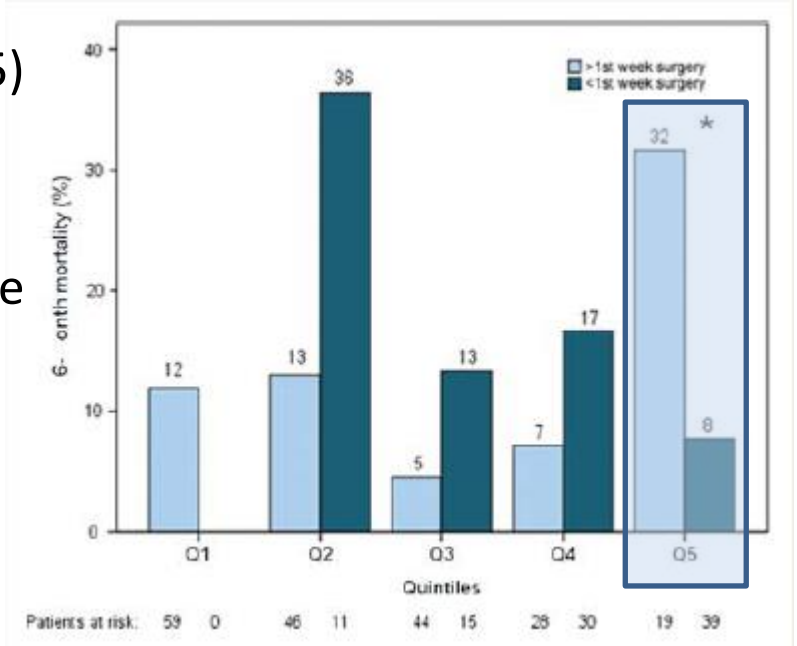

THERE'S NO SUCH THING AS A FREE LUNCH
MILTON FRIEDMAN
ESSAYS ON PUBLIC POLICY
Including Milton Friedman's Playboy interview

European Heart Journal (2011) **32**, 2027–2033
doi:10.1093/eurheartj/ehp089

The timing of surgery influences mortality and morbidity in adults with severe complicated infective endocarditis: a propensity analysis

- 291 pts, surgery for IE, early (<1/52, n=95) vs. late (>1/52, n=191)
- 6/12 mortality by propensity analysis
- Benefits of early surgery in sickest quintile
  - Younger
  - More *Staphylococcus aureus*
  - Congestive heart failure
  - Large vegetations

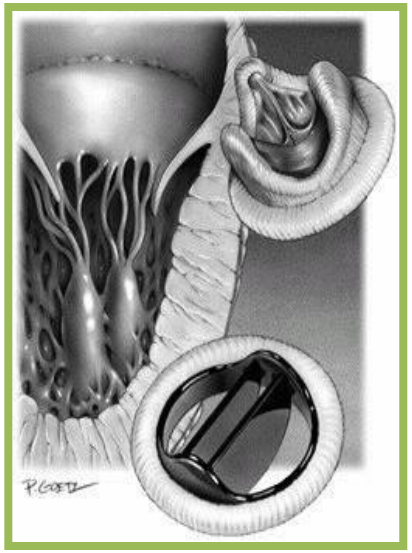


"Surgery performed very early improves survival in severe complicated IE.....
.....but is associated with higher risk of relapse and prosthetic dehiscence."

Thuny F et al

Prosthetic Valve IE

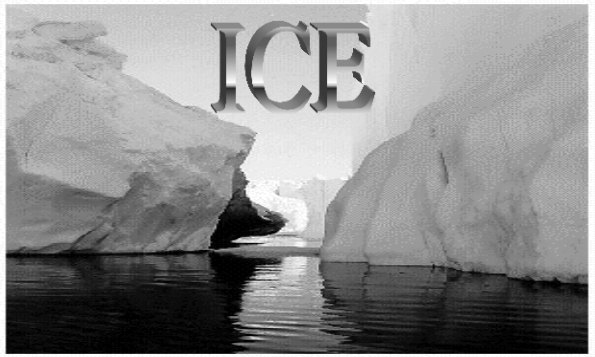
- Most dangerous < 12 months after valve replacement
  - *Staphylococcus*
  - Severe lesions (abscess, prosthetic dehiscence)
  - Redo surgery
    - Lower mortality than medical treatment alone
    - Usually required (urgent indication)
    - Often technically difficult
- Medical treatment may be sufficient if
  - late infection > 12 months
  - sensitive organism (streptococci, HACEK)
  - no perivalvular infection



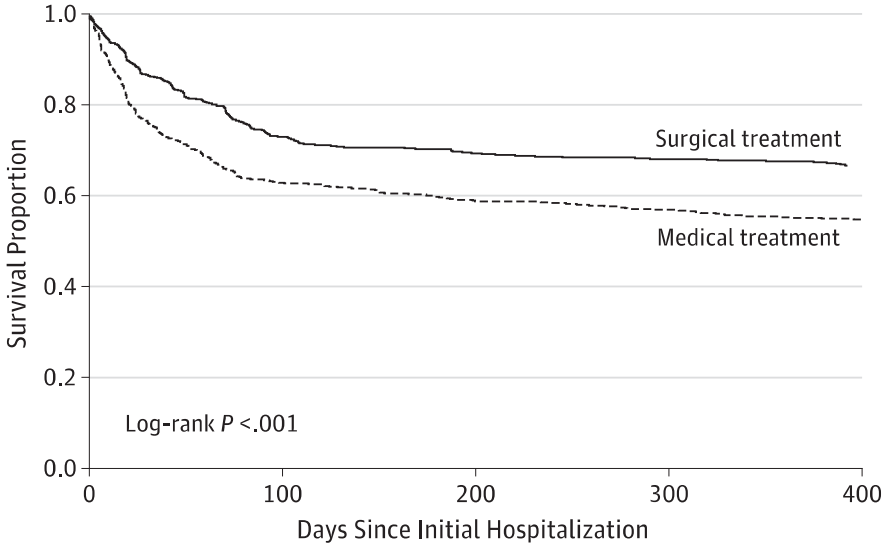
Original Investigation

In-Hospital and 1-Year Mortality in Patients Undergoing Early Surgery for Prosthetic Valve Endocarditis

Tahaniyat Lalani, MD, MHS; Vivian H. Chu, MD, MHS; Lawrence P. Park, PhD; Enrico Cecchi, MD; G. Ralph Corey, MD; Emanuele Durante-Mangoni, MD; Vance G. Fowler Jr, MD, MHS; David Gordon, MBBS, PhD, FRCPA, FRACP, FFoSc; Paolo Grossi, MD, PhD; Margaret Hannan, MD; Bruno Hoen, MD, PhD; Patricia Muñoz, MD, PhD; Hussien Rizk, MD; Souha S. Kanj, MD; Christine Selton-Suty, MD; Daniel J. Sexton, MD; Denis Spelman, MD; Veronica Ravasio, MD; Marie Françoise Tripodi, MD; Andrew Wang, MD; for the International Collaboration on Endocarditis–Prospective Cohort Study Investigators



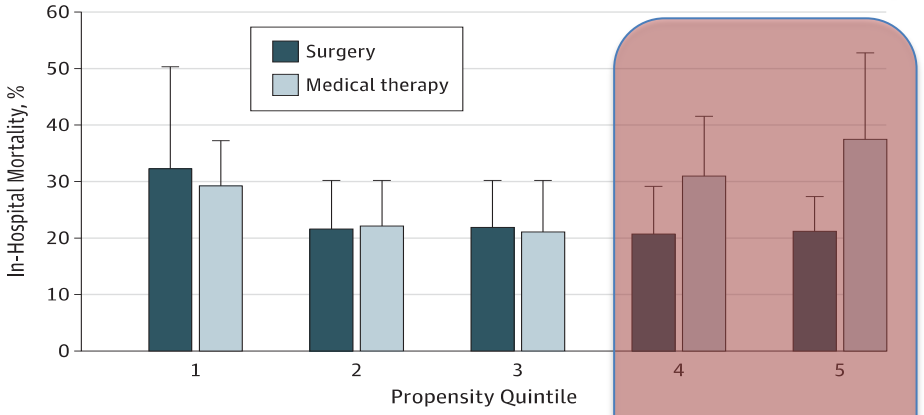
- 1025 patients, worldwide registry
  - 490 early surgery
  - 535 medical therapy
- Analyses
  - Unadjusted outcomes
  - Correction for survival bias
  - Quintiles of disease severity



No. at risk				
Surgery	490	287	255	239
Medical therapy	535	275	250	224

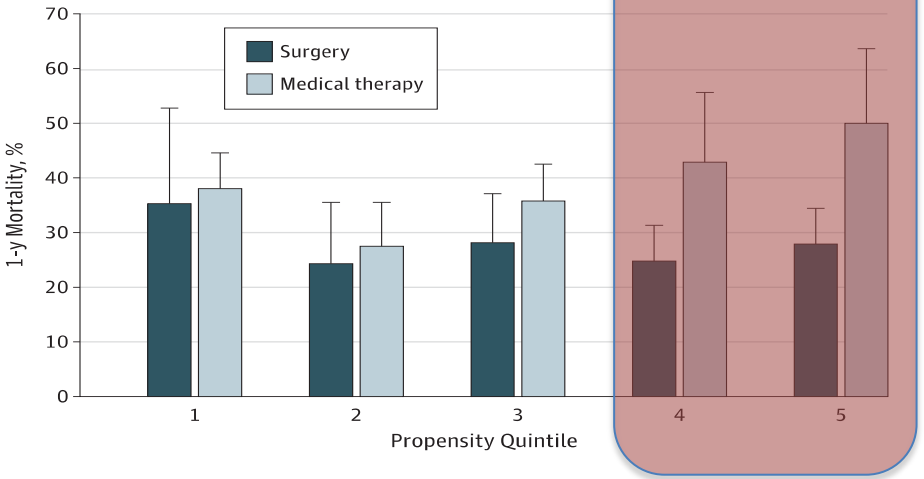
JAMA 2013

IN-HOSPITAL MORTALITY



Propensity, mean (range)	0.20 (0.05-0.28)	0.34 (0.28-0.40)	0.46 (0.40-0.53)	0.61 (0.53-0.69)	0.79 (0.69-0.98)
No. of patients					
Medical therapy	171	131	109	84	5
Surgery	34	74	96	121	5
P value[a]	.72	.93	.89	.09	.03

ONE YEAR MORTALITY

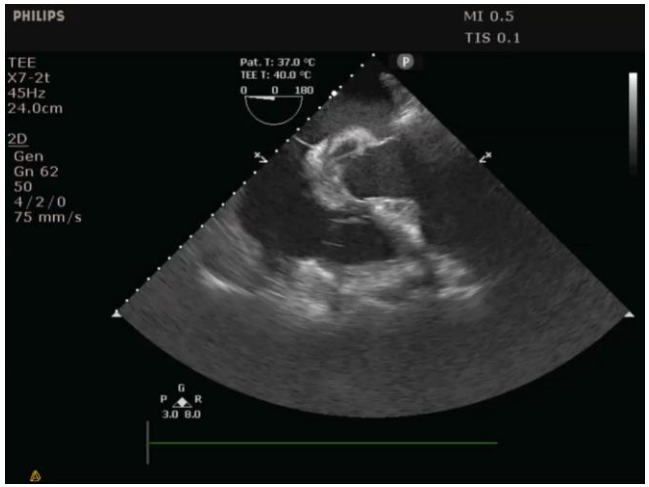


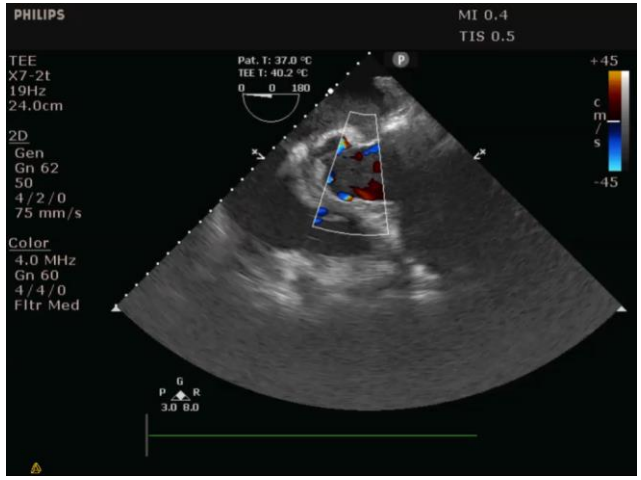
Propensity, mean (range)	0.20 (0.05-0.28)	0.34 (0.28-0.40)	0.46 (0.40-0.53)	0.61 (0.53-0.69)	0.79 (0.69-0.98)
No. of patients					
Medical therapy	171	131	109	84	40
Surgery	34	74	96	121	165
P value[a]	.77	.62	.24	.007	.007

JAMA 2013

A Typical Upper Quintile Patient?

- 59 year old male
- Bioprosthetic AVR & CABG x3 2002
- September 2014: admission with CHF – no echocardiogram
- October 2014: readmission with CHF & left cerebral infarct
- TOE: severe AR with root abscess

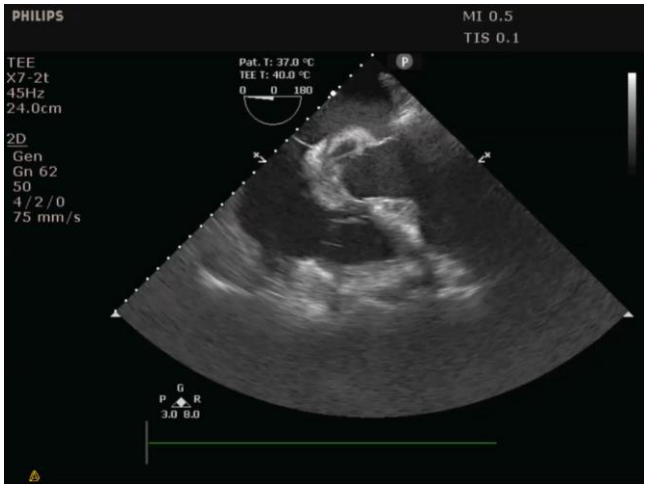


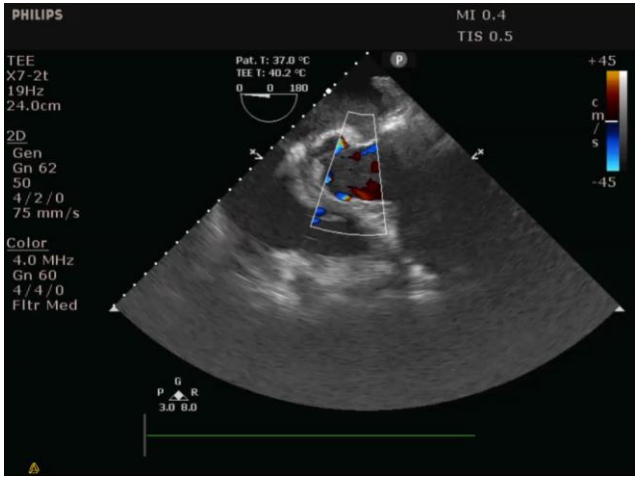


THERE ARE TWO SIDES TO EVERY STORY

A Typical Upper Quintile Patient?

- 59 year old male
- Unemployed
- Bioprosthetic AVR & CABG x3 2002
- Morbid obesity (190kgs)
- Chronic leg oedema
- Turned down for gastric banding
- Immobile
- Sleeps in chair





Conclusions

- The available evidence supports a role for early surgery in IE, especially in the sickest patients
- ESC guidelines endorse this approach and provide recommended timelines
- In reality, these may be difficult to meet
  - Delayed diagnosis
  - Surgical dogma
  - Organisational issues
- In the real world, IE patients are frequently complex and a careful tailored approach is often required
- Efforts should be focussed on speedier diagnosis, access to expert advice, early transfer to a surgical centre and improved models of IE healthcare delivery