Endocarditis:
Medical vs. Surgical Treatment

Nabin K. Shrestha, MD, MPH

Infectious Diseases

Cleveland Clinic

Conflicts of interest

- Nothing to disclose

Complications of infective endocarditis

- Local complications
  - Heart failure
  - Heart block
- Embolic complications
  - Stroke
- Metastatic complications
  - Vertebral osteomyelitis
  - Septic arthritis
- Immunologic complications
  - Immune complex glomerulonephritis

Infective endocarditis treatment

- Medical
  - To eliminate the infecting pathogen with antibiotic therapy
- Surgical
  - To eradicate the focus of infection
  - To correct valvular defects caused by the infection

Treatment decision

- Medical versus surgical treatment for infective endocarditis
- Non-surgical versus surgical treatment for infective endocarditis

Non-surgical vs. surgical treatment of infective endocarditis

Figure 1. Kaplan-Meier Curve Relating Valve Surgery to Time to Death Among Propensity-Matched Patients

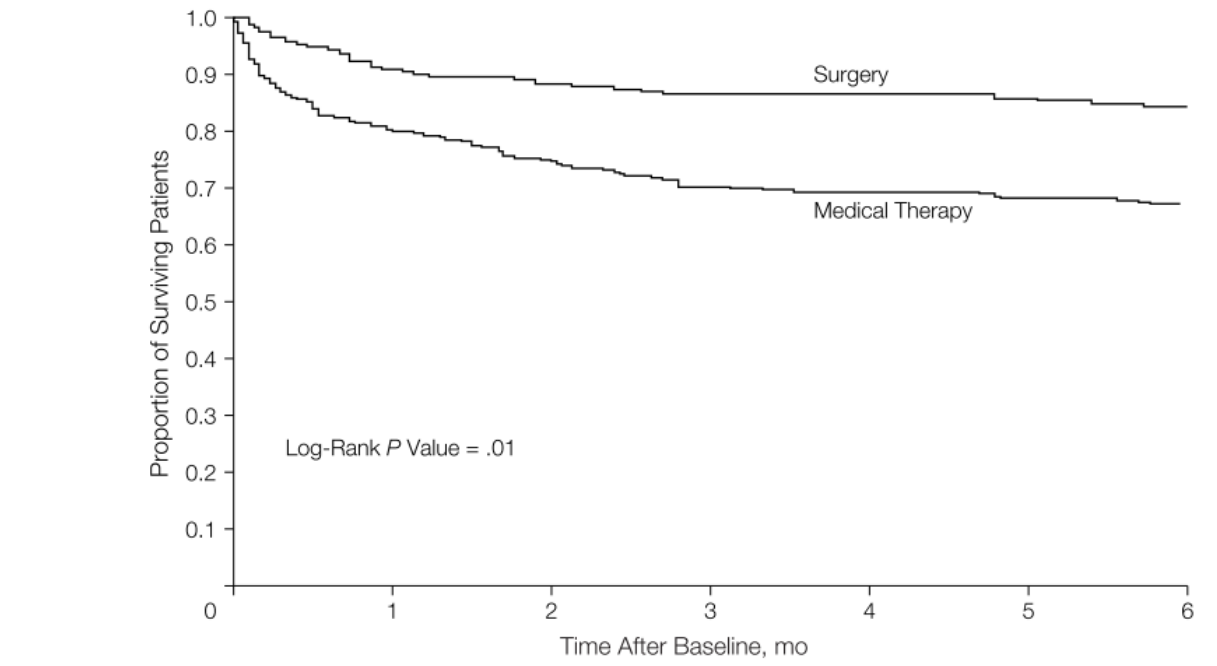


Table 3. Cox Proportional Hazards Analyses of Time to Death Among Patients Undergoing Valve Surgery

Model	Hazard Ratio (95% CI)	*P* Value
Total cohort (n = 513)		
Unadjusted	0.43 (0.29-0.63)	<.001
Heterogeneity adjusted*	0.35 (0.23-0.54)	<.001
Propensity-matched group (n = 218)†		
Unadjusted	0.45 (0.23-0.86)	.02
Adjusted for confounding‡	0.45 (0.24-0.88)	.02
Adjusted for confounding and heterogeneity	0.40 (0.18-0.91)	.03

Vikram HR, et al. JAMA 2003;290:3207-3214

Non-surgical vs. surgical treatment of infective endocarditis

TABLE 2. HR (95% CI) of Valve Surgery Under Different Modeling Conditions

Analysis	Unadjusted	Adjusted for Logit (Propensity)	Adjusted for Logit (Propensity) and Individual Covariates*
Matched cohort 93 pairs, total (n=186)	1.6 (0.8 to 2.9)	1.7 (0.9 to 3.2)	1.3 (0.5 to 3.1)
P	0.16	0.12	0.56
Time-dependent covariate without lag (n=546)	2.1 (1.4 to 3.4)	2.3 (1.4 to 3.8)	1.9 (1.1 to 3.2)
P	0.001	0.001	0.02
Time-dependent covariate with 3-day lag (n=546)	1.8 (1.2 to 2.8)	1.9 (1.2 to 3.0)	1.5 (0.9 to 2.6)
P	0.005	0.009	0.11

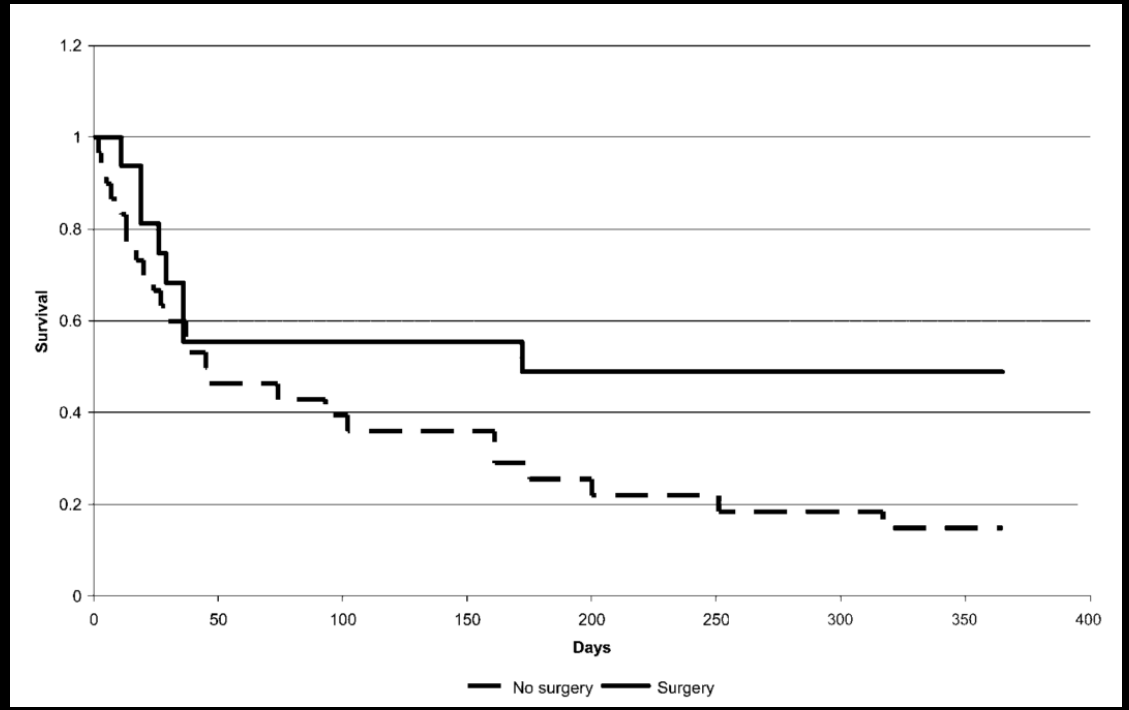
*Covariates included age, sex, Charlson score, *S aureus*, aorta-involved, creatinine, prosthetic (none/within 2 months/>2 months), hemoglobin, white blood cell count, NYHA class III/IV or I/II, stroke and relapse, and any embolic event other than stroke. Because the matched cohort analysis had a smaller sample size, only covariates not already included as part of the propensity score calculation were included in the multivariable model; these variables were creatinine, white blood cell count, stroke, embolic event, and aorta-involved.

Tleyjeh IM, et al. Circulation 2007;115:1721-1728

Non-surgical vs. surgical treatment of infective endocarditis

Table 5. Multivariate analysis of survival of the 102 patients with infective endocarditis (IE) within the matched cohort.

Characteristic	χ^2 test score	Hazard ratio (95% CI)
Surgery	13.01	0.27 (0.13–0.55)
Diabetes mellitus	19.80	4.81 (2.41–9.62)
Chronic indwelling central catheter	7.43	2.65 (1.31–5.33)
Paravalvular complications	4.43	2.16 (1.06–4.44)



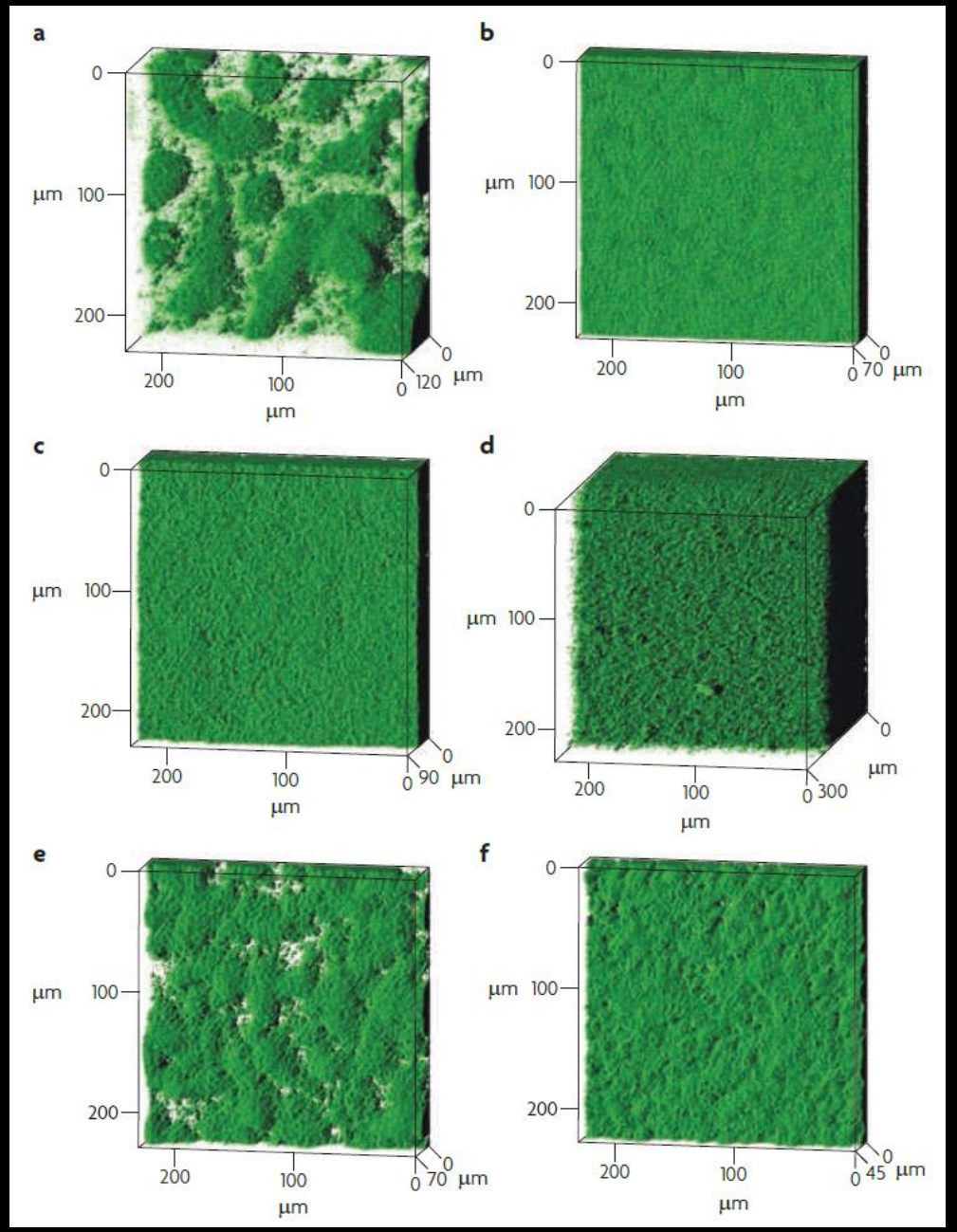
Aksoy O, et al. Clin Infect Dis 2007;44:364-72

Biofilm Infections

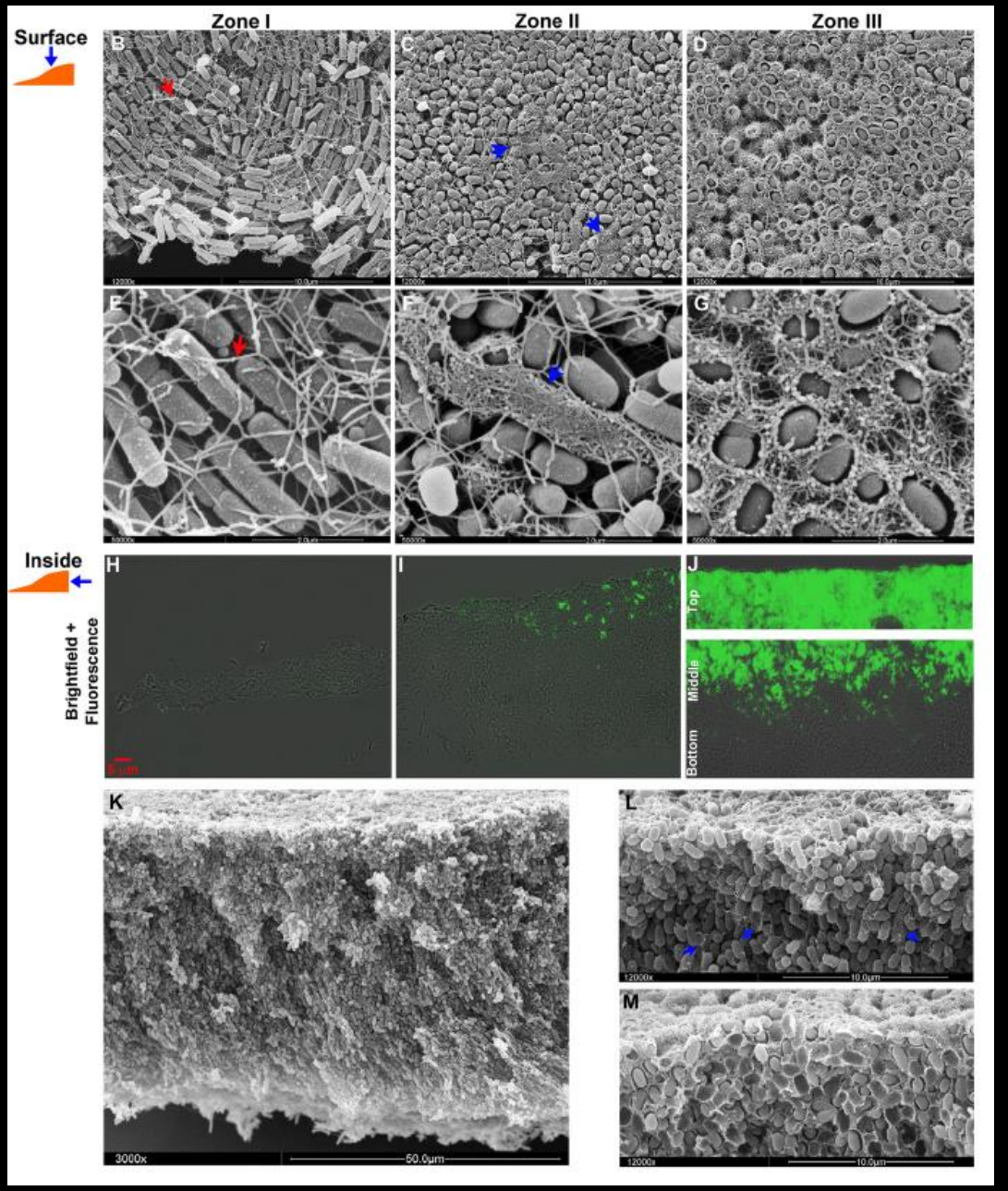
- Infections of prosthetic material are biofilm-associated infections
- Biofilm-associated infections are difficult to eradicate without removing the biofilm

- Prosthetic valve endocarditis (PVE) is an infection of prosthetic material
- One would expect limited success in treating PVE medically

Biofilms



Flemming H-C,, et al. Nature Rev 2010;139:887-93



Serra DO, et al. mBio 2013;4:e00103-13

Non-surgical vs. surgical treatment of prosthetic valve endocarditis

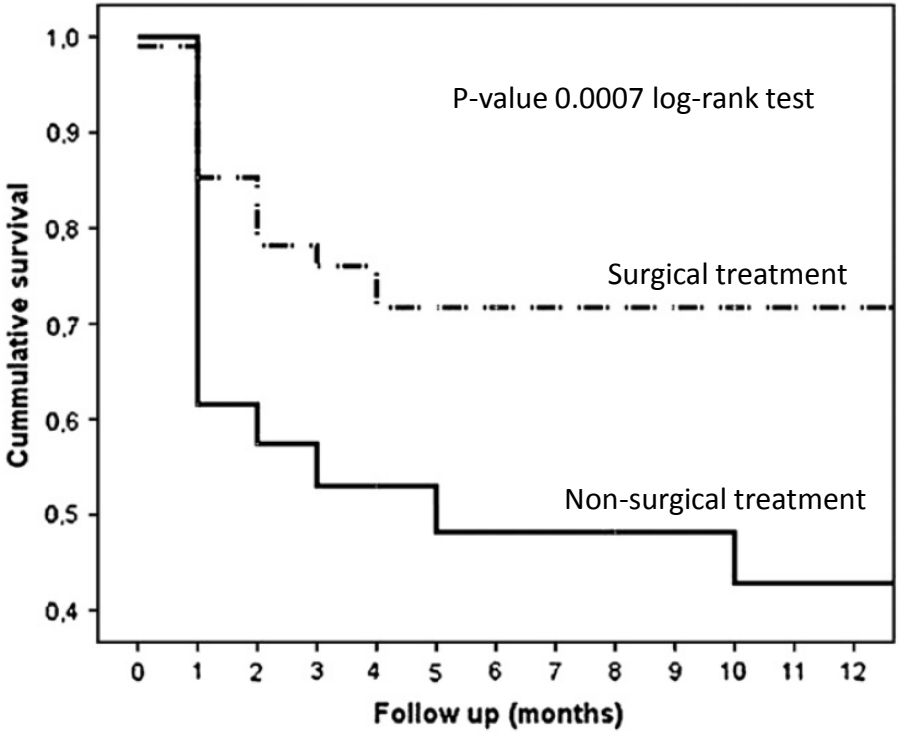


FIGURE 1. Long-term survival of patients with prosthetic valve endocarditis after combined medical and surgical treatment *(upper line)* or medical treatment alone *(lower line)*.

Surgical treatment was a significant predictor of survival on Cox regression analysis :
HR 0.43, 95% CI 0.24 – 0.74, p-value 0.003)
(presumably not controlled for confounders):

Allonse-Valle H, et al. J Thorac Cardiovasc Surg 2010;139:887-93

Non-surgical vs. surgical treatment of prosthetic valve endocarditis

Table IV. Logistic regression analysis of variables independently associated with inhospital mortality in patients with PVIE and matched propensity for surgical treatment

Variable	OR	95% CI	P
S aureus infection	3.67	1.39-9.74	.009
Brain embolization	11.12	4.16-29.73	<.001
Surgery	0.56	0.23-1.36	.198

Area under ROC curve = 0.797.

Note:
58% treated non-surgically
in-hospital mortality 25% vs 23% for surgical vs non-surgical treatment

Wang A, et al. Am Heart J 2005;150:1086-91

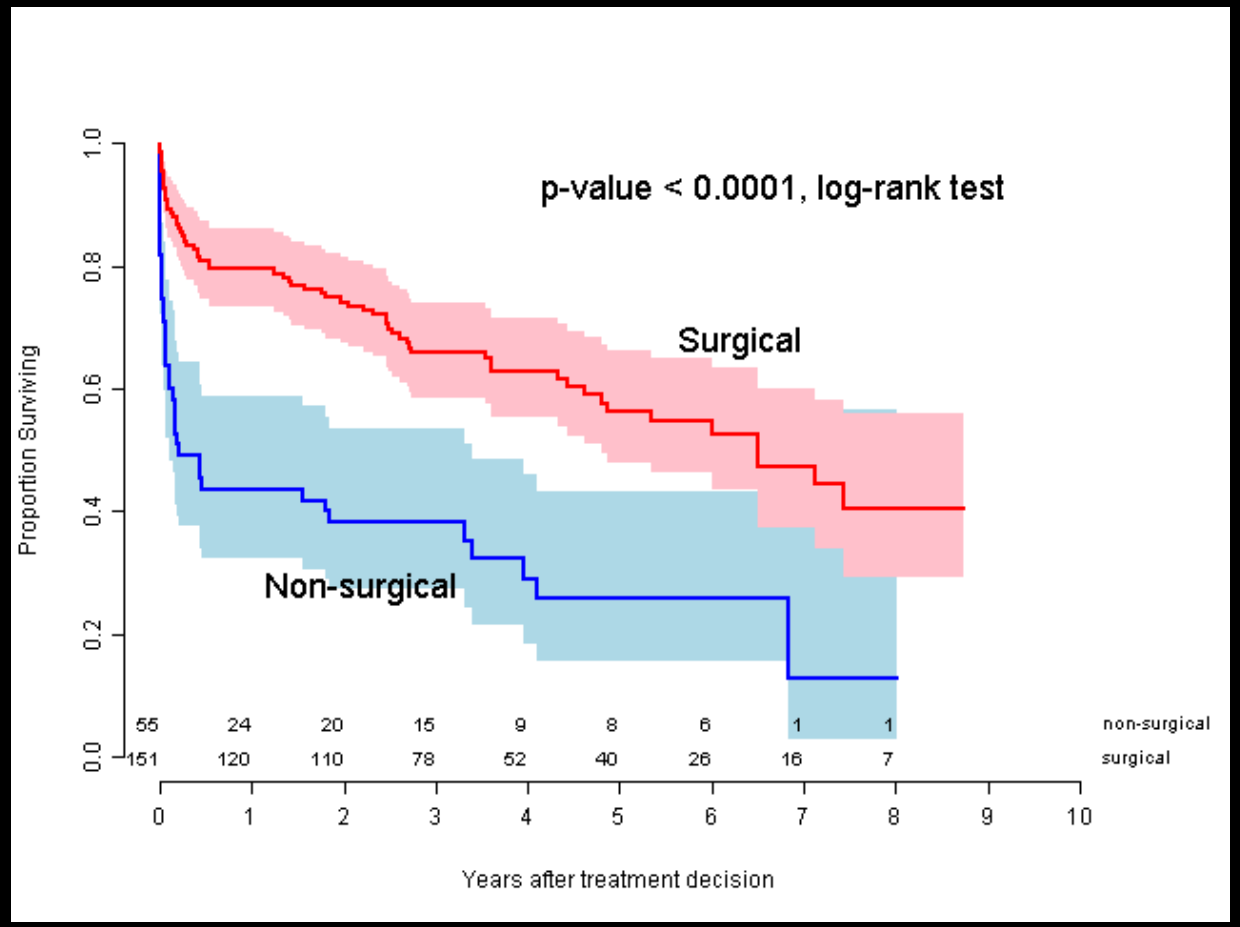
Non-surgical vs. Surgical Treatment of PVE at Cleveland Clinic

- Study period: April 1, 2008 to Mar 31, 2015
- 508 patients with PVE, 24% treated non-surgically, 76% surgically

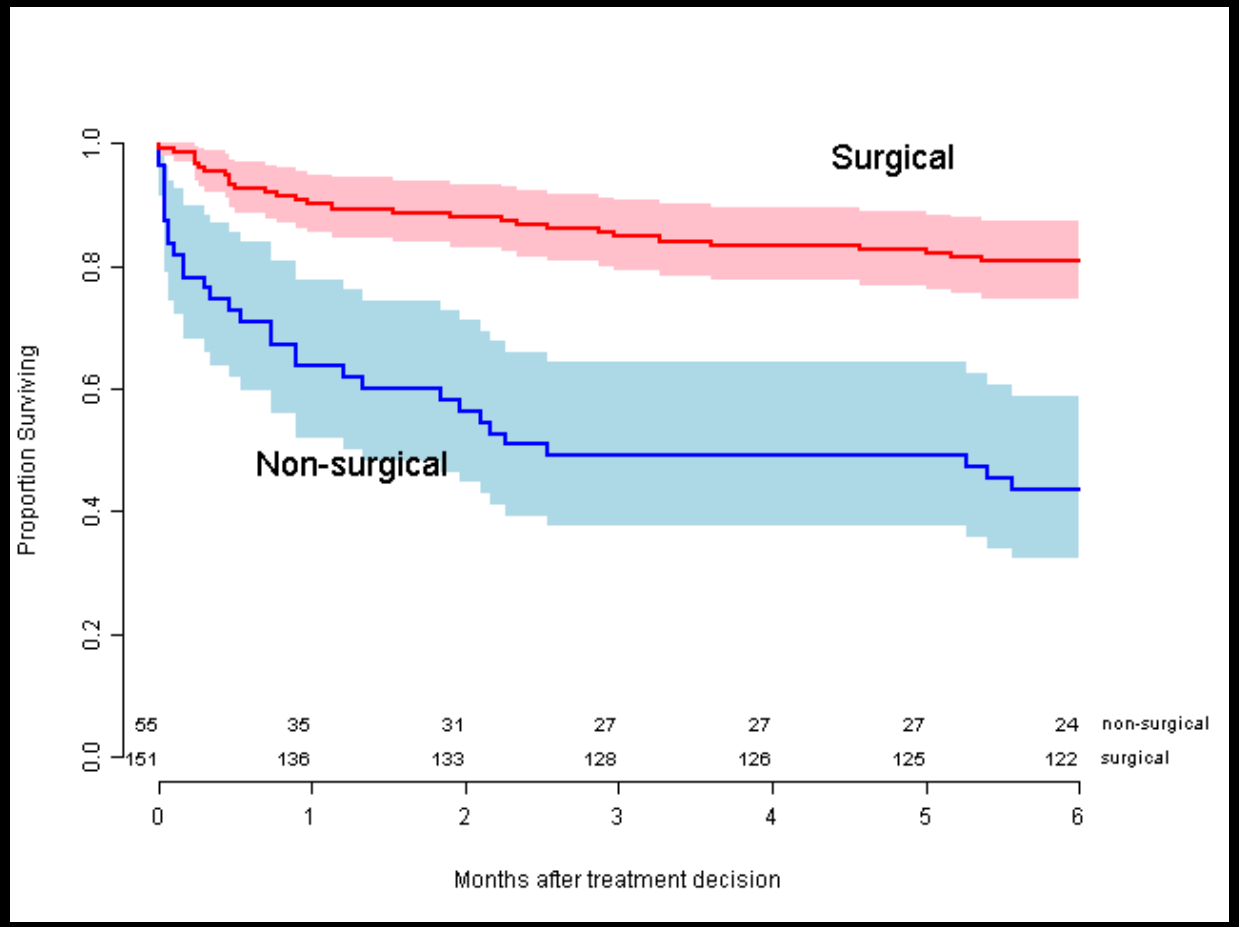
- Propensity to be treated surgically calculated using a logistic regression model

- Propensity score-matched surgically-treated controls obtained for non-surgically treated patients
  - 55 treated non-surgically, 151 treated surgically, in the propensity score matched dataset

Kaplan-Meier plot comparing patient survival after surgical versus medical treatment for PVE



Survival over a few years



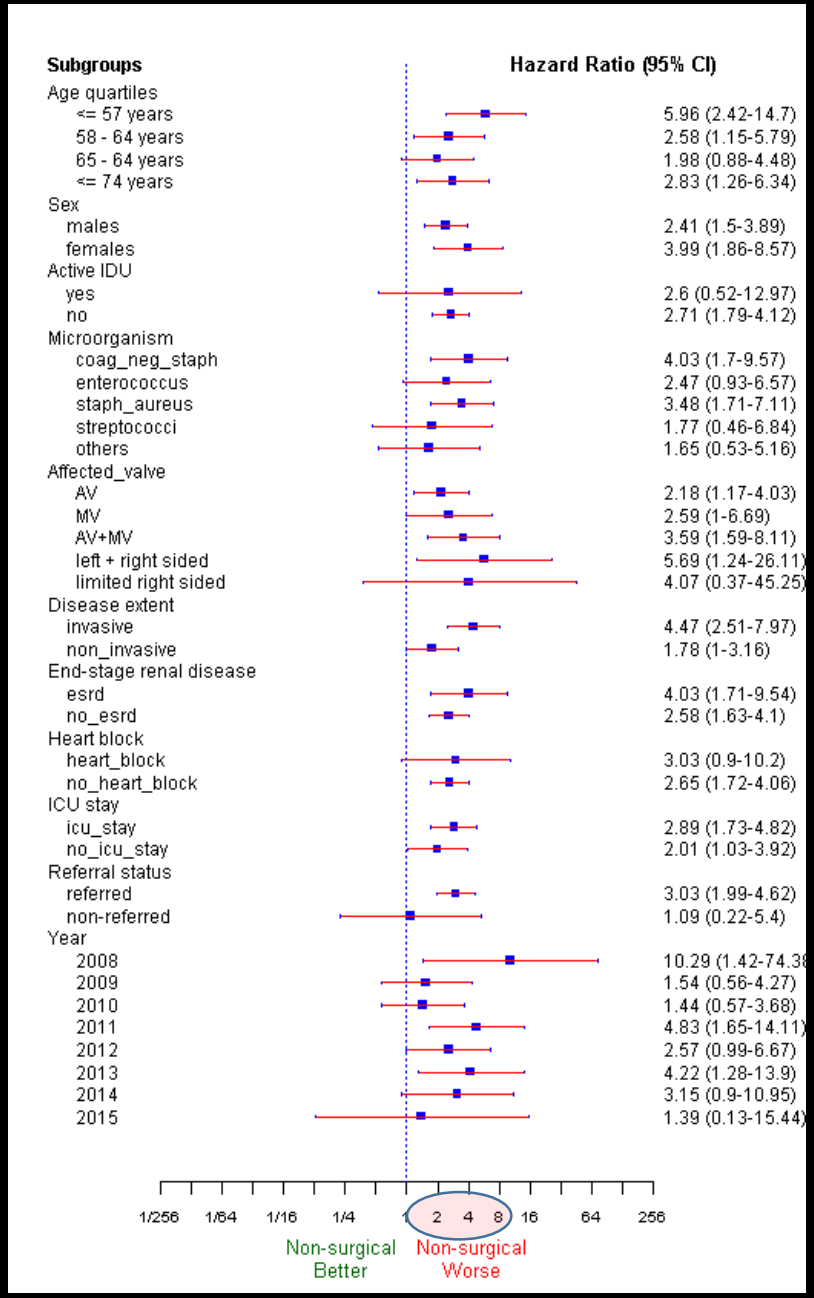
Survival over the first 6 months

Non-surgical vs. surgical treatment for PVE

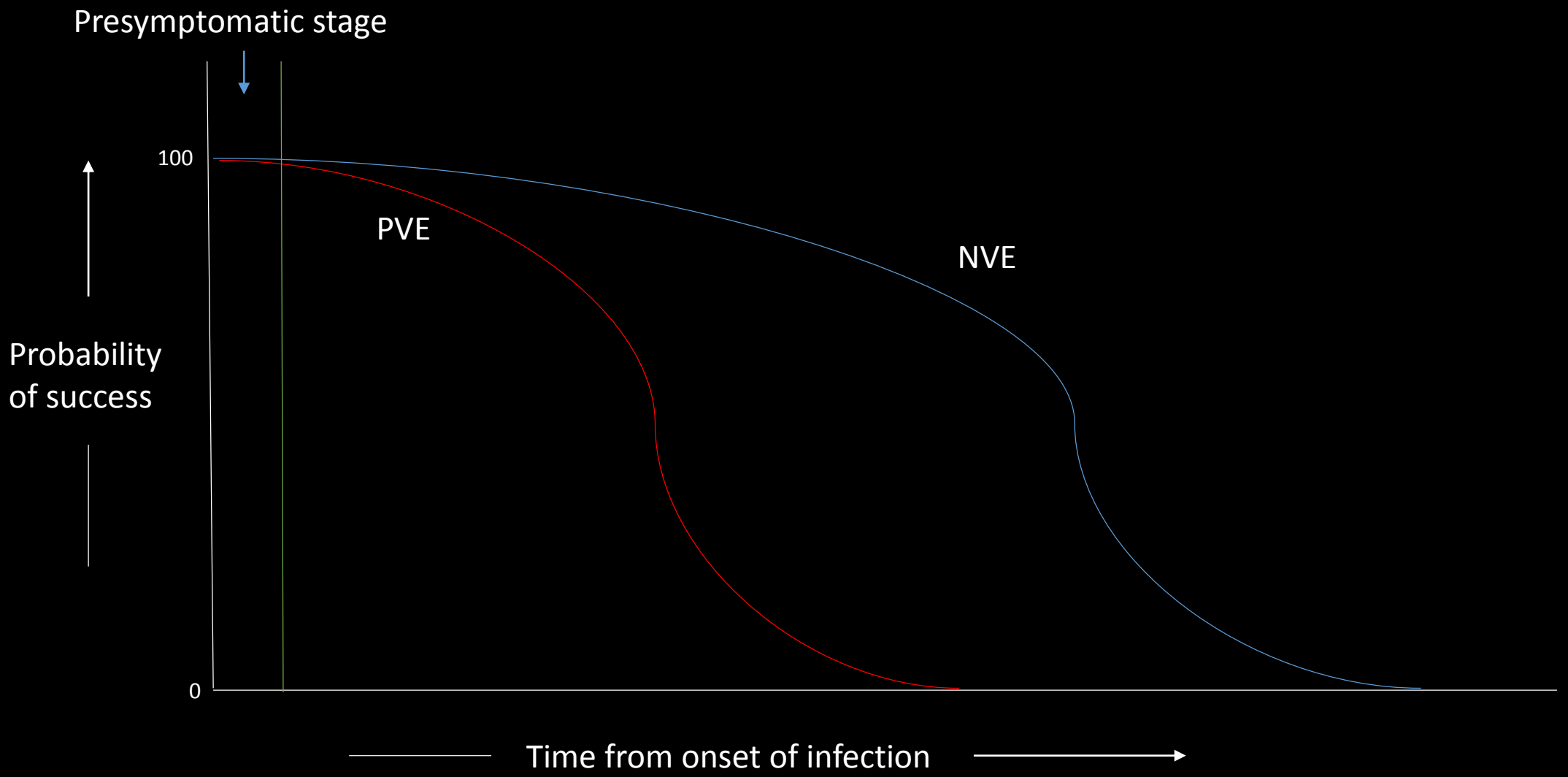
Primary outcome	Hazard Ratio	95% C.I.	P-value
Death	2.72	1.82 – 4.06	<0.0001

Secondary outcomes	Hazard Ratio	95% C.I.	P-value
In-hospital death	5.18	2.57 – 10.44	<0.0001
Death within one year	3.81	2.31 – 6.27	<0.0001
Readmission or death within 90 days	4.85	2.78 – 8.45	<0.0001
Subsequent surgery for IE	12.37	4.59 – 33.37	<0.0001
Subsequent non-IE cardiac surgery	0.93	0.11 – 7.99	0.94

Hazard ratios for death for non-surgical versus surgical treatment for PVE



Probability of success with medical therapy in endocarditis



When is surgery necessary?

- When medical treatment alone will not cure the infection
  - Invasive infection / abscess
  - Large bacterial burden
  - Virulent pathogen
  - Prosthetic valve endocarditis
- Medical treatment alone may cure the infection, but significant valvular defects lead to significant heart failure
  - Acute aortic regurgitation
  - Moderate to severe aortic/mitral insufficiency or stenosis
- There is significant risk of embolism

Early versus late surgery for IE

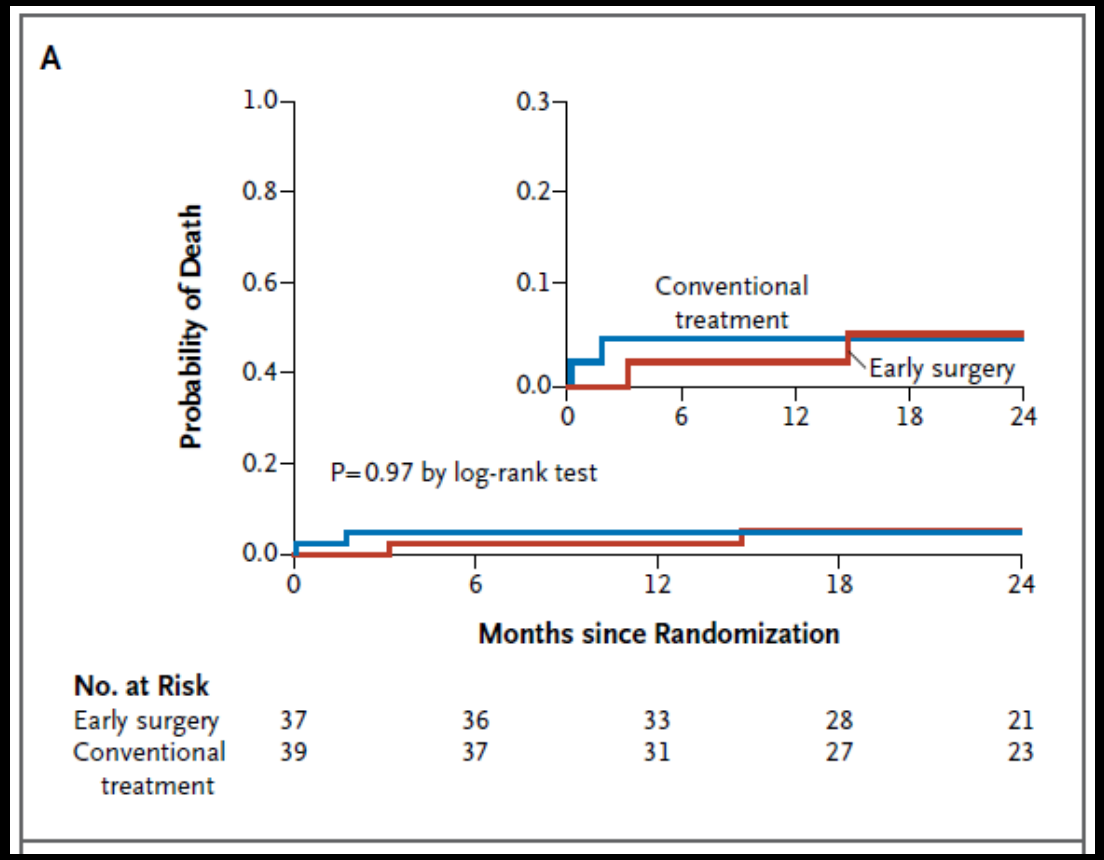
- **Study design:** RCT
- **Study sample:** adults with left-sided NVE with high risk for embolism
- **Early group:** all underwent surgery within 48 h of randomization, median 24 h
- **Conventional group:** 77% surgery during index hospitalization, urgently in 21% (median 6.5 d after randomization), electively in 79% (> 2 wk after randomization)
- **Notable characteristics:** median diameter of vegetations 12 mm; viridans strept (30%), other strept (30%), S. aureus (11%)

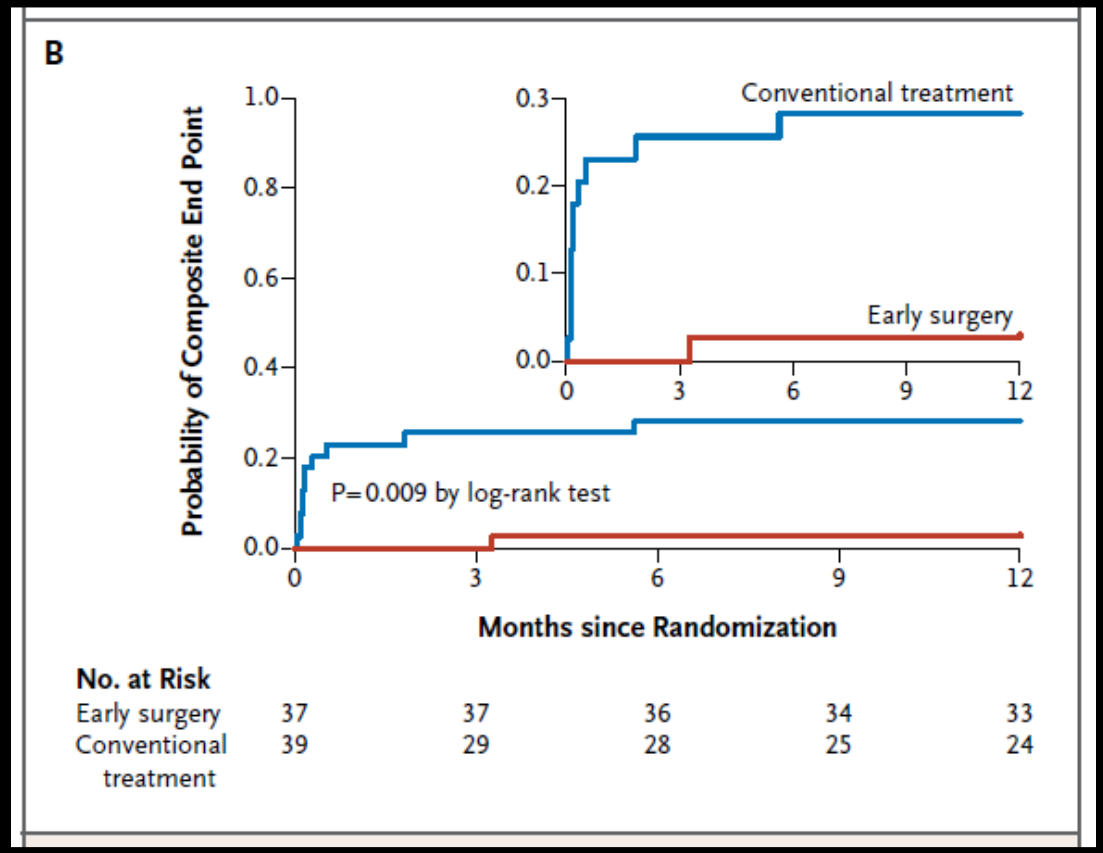
Kang, D-H, et al. Early surgery versus conventional treatment for infective endocarditis. NEJM 2012;366:2466-73

Table 3. Clinical End Points.

Outcome	Conventional Treatment (N=39)	Early Surgery (N=37)	P Value
Primary end point — no. (%)			
In-hospital death or embolic event at 6 wk	9 (23)	1 (3)	0.01
In-hospital death	1 (3)	1 (3)	1.00
Embolic event at 6 wk			
Any	8 (21)	0	0.005
Cerebral	5 (13)	0	
Coronary	1 (3)	0	
Popliteal	1 (3)	0	
Splenic	1 (3)	0	
Secondary end points at 6 mo — no. (%)			
Any	11 (28)	1 (3)	0.003
Death	2 (5)	1 (3)	1.00
Embolic event	8 (21)	0	0.005
Recurrence of infective endocarditis	1 (3)	0	1.00

Early versus late surgery for IE





Kang, D-H, et al. Early surgery versus conventional treatment for infective endocarditis. NEJM 2012;366:2466-73

Main messages

- All patients with infective endocarditis need medical therapy
- A substantial proportion of patients will require surgery
- The longer the patient has endocarditis before it is diagnosed the more likely the need for surgery
- The window of opportunity for success without surgery is smaller for prosthetic valve endocarditis than for native valve endocarditis
- If a decision is made to operate for infective endocarditis, the operation should be performed sooner rather than later