Infective Endocarditis 2008; Should We Operate More?

박 승 우

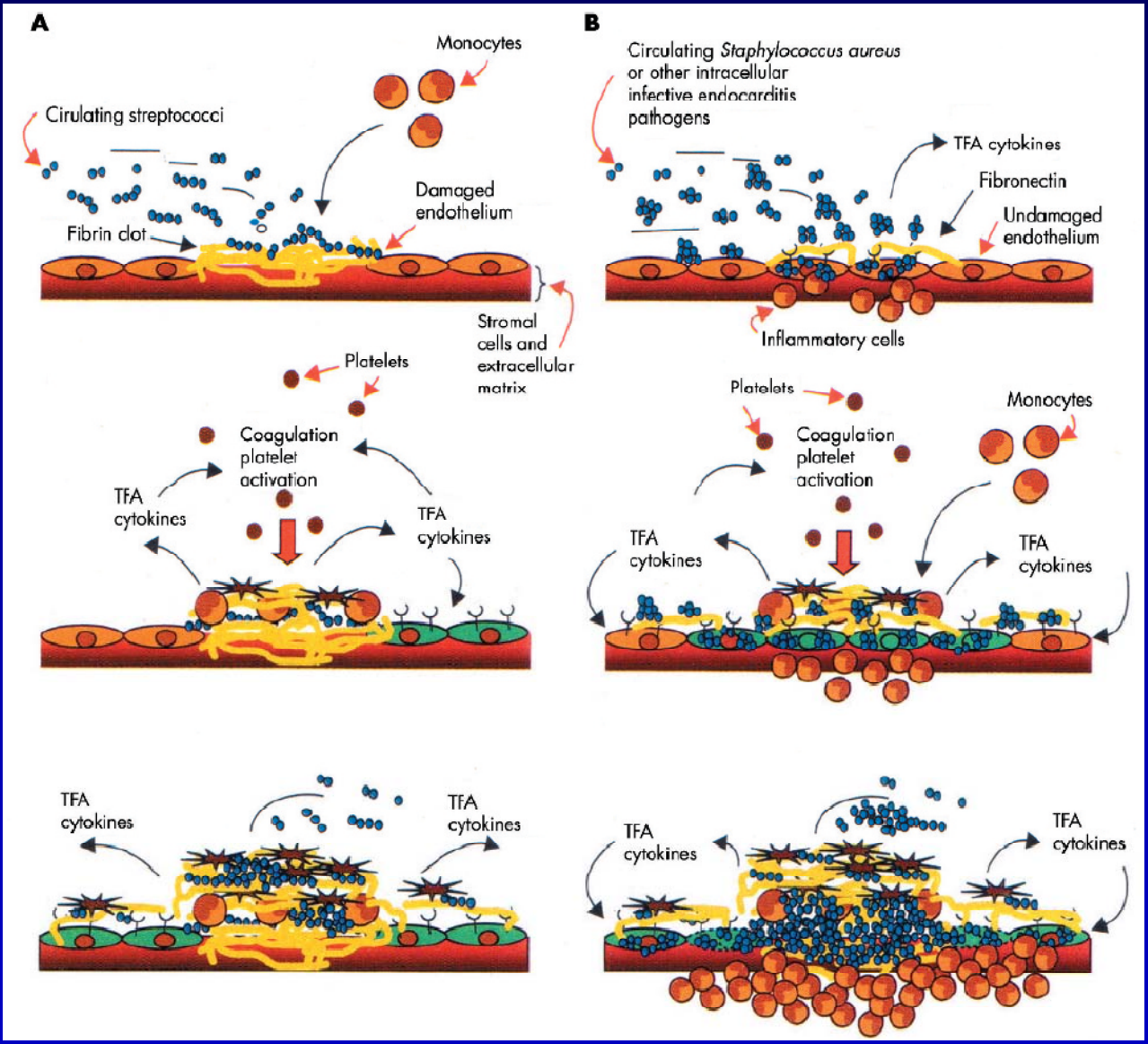
성균관의대 삼성서울병원

Endocarditis

- In pre-antibiotics era, largely fatal disease
- 1885 – Sir William Osler in Gulstonian lectures referred to IE as the "malignant endocarditis"
- 1940's – PCN revived hope for a cure of IE, however morbidity and mortality only partially altered
- Resistant organisms and shifting etiology (IVDA)

Bashore TM et al., Curr Probl Cardiol. 2006

Pathogenesis



Prendergast BD, Heart 2006

Cardiac Pathologic Changes

- Vegetations on valve closure lines
- Destruction and perforation of valve leaflet
- Rupture of chordae tendinae, interventricular septum, papillary muscles
- Valve ring abscess
- Myocardial abscess
- Conduction abnormalities

Modified Duke Criteria

- Major Criteria
  - Positive blood cultures with typical organisms
  - Persistently positive blood cultures
  - Evidence of Endocardial involvement
    - Positive Echocardiogram
      - Oscillating intracardiac mass
      - Abscess
      - Dehiscence of prosthetic valve
    - New Valvular regurgitation

Modified Duke Criteria

- Minor Criteria
  - Predisposition (valvular disease or IDU)
  - Fever
  - Vascular phenomena (Arterial emboli, septic pulmonary infarcts, intracranial hemorrhage, Osler, Janeway)
  - Immunologic phenomena (GN, Osler, Roth spots, Rheumatoid Factor)

Modified Duke Criteria

- Definite IE
  - Pathologic criteria
  - Clinical criteria
    - 2 Major Criteria OR
    - 1 Major and 3 minor Criteria OR
    - 5 Minor Criteria
- Possible IE
    - 1 Major and 1 Minor OR
    - 3 Minor
- Rejected IE

Classification

- OLD
  - Subacute Bacterial Endocarditis
    - Death in 3-6 months
  - Acute Bacterial Endocarditis
    - Death in < 6 weeks
- NEW
  - Native Valve Endocarditis
  - Prosthetic Valve Endocarditis

Surgical Rx

- 1961 – Kay et al. first to report surgical cure of pt with medically resistant IE (fungal TV)
- 1965 Wallace, et al – first report of successful valve replacement in active endocarditis
- Early success in many studies of selected patients led to "paradigm shift" in management of complicated endocarditis

Echo Indication for Surgery

- Vegetation
  - Persistent vegetation after systemic embolism
  - AMVL vegetation, esp. with size > 10mm
  - > 1 embolic events during first 2 weeks of AB
- Valvular dysfunction
  - Acute AR or MR with signs of ventricle failure
  - HF unresponsive to medical therapy
  - Valve perforation or rupture
- Perivalvular extension
  - Valvular dehiscence, rupture, or fistula
  - New heart block
  - Large abscess or extension of abscess in spite of appropriate AB

Baddour LM et al., Circulation 2005

R ns for Surgery

Native valve endocarditis

Class 1

1. Surgery of the native valve is indicated in patients with acute IE who present with HF (level of evidence: B)
2. Surgery of the native valve is indicated in patients with acute IE who present with AR or MR with hemodynamic evidence of elevated LV end-diastolic or left atrial pressures (eg, premature closure of the mitral valve with AR, rapid decelerating MR signal by continuous wave Doppler [v-wave cutoff sign], moderate or severe pulmonary hypertension) (level of evidence: B)
3. Surgery of the valve is indicated in patients with IE caused by fungal or highly resistant organisms (level of evidence: B)
4. Surgery of the native valve is indicated in patients with IE complicated by heart block, anular or aortic abscess, or destructive penetrating lesions (eg, sinus of Valsalva to right atrium, right ventricle, or left atrial fistula, mitral leaflet perforation with aortic valve endocarditis, or infection in anulus fibrosa) (level of evidence: B)

Class 2a

1. Surgery of the native valve is reasonable in patients with IE who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy (level of evidence: C)

Class 2b

1. Surgery of the native valve may be considered in patients with IE who present with mobile vegetations in excess of 10 mm with or without emboli (level of evidence: C)

Prosthetic valve endocarditis

Class 1

1. Consultation with a cardiac surgeon is indicated for patients with IE of a prosthetic valve (level of evidence: C)
2. Surgery is indicated for patients with IE of a prosthetic valve who present with HF (level of evidence: B)
3. Surgery is indicated for patients with IE of a prosthetic valve who present with dehiscence evidenced by cinefluoroscopy or echocardiography (level of evidence: B)
4. Surgery is indicated for patients with IE of a prosthetic valve who present with evidence of increasing obstruction or worsening regurgitation (level of evidence: C)
5. Surgery is indicated for patients with IE of a prosthetic valve who present with complications, eg, abscess formation (level of evidence: C)

Class 2a

1. Surgery is reasonable for patients with IE of a prosthetic valve who present with evidence of persistent bacteremia or recurrent emboli despite appropriate antibiotic treatment (level of evidence: C)
2. Surgery is reasonable for patients with IE of a prosthetic valve who present with relapsing infection (level of evidence: C)

Class 3

1. Routine surgery is not indicated for patients with uncomplicated IE of a prosthetic valve caused by first infection with a sensitive agent (level of evidence: C)

*AR = atrial regurgitation; HF = heart failure; IE = infective endocarditis; LV = left ventricular; MR = mitral regurgitation.

AHA/ACC 2006 guidelines Circulation 2006

Indications for Surgery

- Hemodynamic compromise/ Heart failure
- Persistent bacteremia
- Peripheral embolization
- Extravalvular extension of infection

Heart Failure

- 79/144 pt developed CHF within 6mos of admission
- 60% moderate-severe
- MR – 50% developed CHF, 1/2 severe
- AR – 80% CHF, 2/3 severe
  - 6 month survival with severe CHF/AR
    - medical 7 % vs. med/surgical 64%

Mills J, et al. Chest 1974

Heart Failure

- Early valve replacement in 95 hemodynamically unstable pt – 64% emergent, 88% 48hrs
- Mortality
  - urgent surgery 15% (13/84)
  - elective 18% (2/11)
  - 5 year survival 60%
- Periprosthetic leaks in 13% (10/80) of survivors

Lewis BS, et al. J Thorac Cardiovasc Surg 1982

Heart Failure

- 203 patients with active IE and early valve replacement
- Urgent surgery (<48hrs) in 53%
- Mortality followed 38± 22mos
  - Urgent 7%
  - Overall 4%
  - Long term 6%

Middlemost S, et al. JACC 1991

CHF – Meta-analysis

	Mortality	
	Medical	Med/Surgical
No CHF	15%	11%
CHF	60%	29%

Moon, et al. Prog Cardiovasc Dis. 1997

Persistent Bacteremia

- Nonsterile blood culture 3-5d after diagnosis
- Lack of improvement symptoms after 1wk appropriate AB
- Surgery may eliminate septic focus, but not necessarily improve pt hemodynamic condition unless significant valvular regurgitation

Persistent Bacteremia

- may also be from extracardiac source/emboli
- splenic, renal, cerebral abscesses
- ? proper Rx – surgery?, incidence of recurrent endocarditis in these situations?

Infectious etiology

- S. aureus
- Gram (-)/serratia/pseudomonas
- Fungus

Rubenstein et al., Eur Heart J 1995

Persistent Bacteremia

- Although ↑ complication if blood culture (+), still important to intervene in face of further destruction of valvular/annular tissue
- Operative mortality risk in uncontrolled infection better when operated earlier (within 10d of admit) (17%) than when AB continued for 4-6wks (90%)

Boyd, et al. J Thorac Cardiovasc Surg, 1977

Peripheral Embolization

- Embolic events common 30-40% of IE
  - Brain > limbs, coronary, spleen, kidney
  - directly responsible for ~25% of fatalities[1]
  - recurrence rate 54% within 30d
- Incidence falls after initiation of AB therapy ~ 2wks
- Risk
  - size > 10mm (47% vs 19%)[2]
  - staph, candida, G(-) rod
  - mobile, pedunculated, mitral>aortic

[1]Acar, et al. Eur Heart J 1995, [2]Mugge et al. JACC 1989

Peripheral Embolization

- Recurrent emboli are relative indication for surgery (class IIa) but should not be considered absolute indication

Extravalvular Extension

- annular abscess
  - Extensive tissue necrosis/structural damage including IVS, conduction system, and fibrous skeleton of heart
  - In NVE mitral (1-5%) < aortic (25-50%)
  - Clinically have more valvular regurgitation
  - Operative mortality 19-43% (vs >75% medically treated)
  - High risk (staph/fungal, new heart block, PVE) should undergo TEE (90% detection vs 50% TTE)

Moon, et al. Prog Cardiovasc Dis 1997

Extravalvular Extension

- Conduction disturbances in 30% with abscess vs < 2% if no abscess
- 1st degree > 7d, new 2nd or 3rd degree block requires eval for abscess - TEE

Demographics

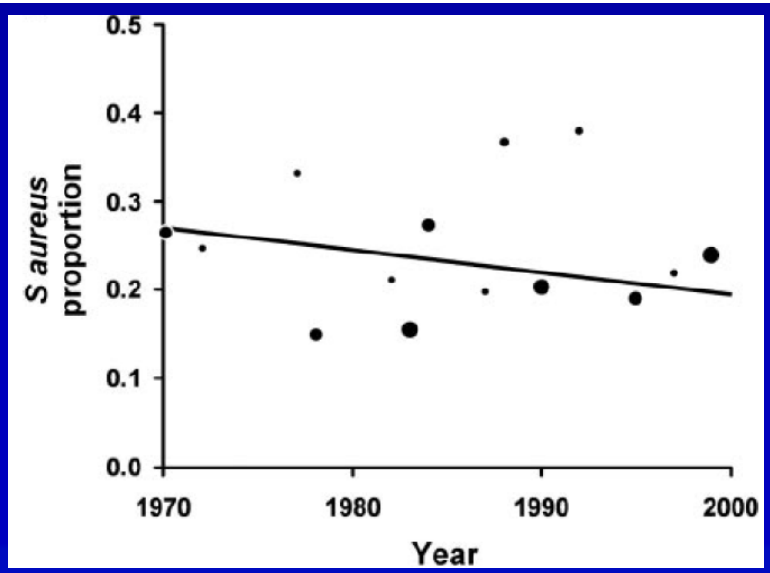
Source	No.	Crude Incidence, /100,000	Demographics: Age Range, yr (Mean or Median)	Demographics: Male/Female Ratio	Risk Factors and Underlying Heart Disease, %: None	RHD	Congenital Heart Disease	Mitral Valve Prolapse	Prosthetic Valve	IVDA
Nolsoe et al[4]	33	1.8	> 15	12/21‖						
Nissen et al[5]	132	1.4	Men (59); women (70)	1.2/1	58	1.5	4.5	0	0	3.0
Benn et al[6]	62	1.7/3.6‡	14–83 (55.4)	1.4/1	34	9.7	11.3	15	14.5	4.8
Foghsgaard et al[7] and Pedersen et al[8]	135	3.5	0–87	2/1	69	2	6	1	16	5
Delahaye et al[9]	415	2.2	0–91 (56)		34		3.1	3.1	22	4.8
Hoen et al[10]	390	3.0	16–95 (59.5)	2.5/1	47		1		16	6
Rossi et al[11]	80	1.6	(48)	1.35/1	21	40	7.5	5	25	2.5
van der Meer et al[12]	438	1.5	2–89		2		12	3	22	7
Hogevik et al[13]	99	6.2	8–88 (69)	1.2/1	43	18	10	7	15	7
Skehan et al[14]	185	1.5	(54.5)		10	18		19	10.2	6.5
Whitby et al[15]	71		17–87 (51.3)	2/1	20	44	4		18	0
Smith et al[16]	78	1.6	15–88	1.3/1	24.4	29.5	6.4		16.7	0
Griffin et al[17]	78		1–90 (58)	1.4/1	14	26	14	17	5.1	0
Steckelberg et al[3]	68	4.2		2.6/1		25	15	15	24	0.3
Tleyjeh et al[18]	107	4.95§	18.8–90.6 (61.5)	2.7/1	32	13	7	17	21	3

*IVDA = IV drug abuse.
†Data on 74 of 80 subjects.
‡1.7 in the first 5 years and 3.6 the next 5 years.
§Average incidence.
‖Male/female gender, No.

Tleyjeh IM et al., Chest. 2007

Change in Proportion per Decade

Parameters	Culture Positive	*S aureus*	Prosthetic Valve	RHD	Surgery
Overall change per decade	0.03 (− 0.03 to 0.08); p = 0.32	0.01 (− 0.04 to 0.05); p = 0.77	0.04 (− 0.02 to 0.11); p = 0.16	− 0.12 (− 0.21 to − 0.03); p = 0.01	0.09 (0.03 to 0.16); p = 0.01
Overall change per decade, adjusted for country	0.02 (− 0.02 to 0.07); p = 0.27	− 0.03 (− 0.09 to 0.04); p = 0.40	0.07 (− 0.01 to 0.16); p = 0.07	− 0.03 (− 0.12 to 0.06); p = 0.40	0.07 (− 0.004 to 0.14) p = 0.06
Denmark	0.83 (0.72 to 0.93)	0.31 (0.17 to 0.46)	0.08 (− 0.23 to 0.08)	0.09 (− 0.09 to 0.27)	0.08 (− 0.09 to 0.24)
France	0.86 (0.74 to 0.98)	0.28 (0.11 to 0.46)	0.005 (− 0.22 to 0.23)	NA	0.22 (0.02 to 0.42)
Italy	0.68 (0.52 to 0.84)	0.18 (0.03 to 0.33)	0.18 (− 0.05 to 0.42)	0.43 (0.19 to 0.67)	0.29 (0.08 to 0.50)
the Netherlands	0.94 (0.85 to 1.03)	0.23 (0.09 to 0.33)	0.09 (− 0.11 to 0.29)	NA	NA
Sweden	0.84 (0.70 to 0.98)	0.40 (0.22 to 0.57)	0.03 (− 0.20 to 0.27)	0.24 (0.00 to 0.47)	0.04 (− 0.16 to 0.24)
United Kingdom	0.85 (0.77 to 0.93)	0.20 (0.11 to 0.29)	0.08 (− 0.05 to 0.20)	0.37 (0.21 to 0.54)	0.12 (0.01 to 0.24)
United States	0.96 (0.87 to 1.04)	0.30 (0.17 to 0.43)	0.05 (− 0.09 to 0.19)	0.15 (− 0.04 to 0.34)	0.02 (− 0.11 to 0.15)
p Value for country (F test)	0.01	0.20	0.16	0.05	0.06



Tleyjeh IM et al., Chest. 2007

국내 심내막염 임상상

발표연도	기 간	환자수	평균연령	심질환 과거력(%)	수술율(%)
1975	1965 -1974	33	28	73	NA
1983	1979 -1983	42	15-67	90	0.02
1984	1972 -1984	36	29	83	NA
1984	1975 -1984	87	25	92	NA
1985	1972 -1984	34	17-72	71	NA
1989	1984 -1988	116	38	78	34
1998	1979 -1984	46	32	NA	30
	1979 -1996	40	38	NA	63
1999	1989 -1998	156	48	46	44
2005	1995 -2003	152	46	50	53

김민규 등, 대한내과학회지 2000, 손준성 등, 감염과 화학요법 2005

국내 심내막염 임상상

발표연도	기 간	환자수	수술율(%)	사망율(내과/내외과%)
1989	1984 -1988	116	34	23 (31/8)
1999	1989 -1998	156	44	17 (21/12)
2005	1995 -2003	152	53	11 (23/3)

김민규 등, 대한내과학회지 2000, 손준성 등, 감염과 화학요법 2005

국내 심내막염 수술 결과

- 67례 (12 PVE, 54 NVE, 1 Mural E)
- 수술 적응증
  - vegetation with embolization 26
  - on-going CHF 22
  - uncontrolled infection 21
  - annular or myocardial abscesss 14
  - large vegetation w/o embolization 13
  - recurred infection 8
  - prosthesis instability 3
  - fungal infection 2

성기익 등, 대한흉부외과학회지 2002

국내 심내막염 수술 결과

- 수술 종류

	repair	replacement			total
		mechanical	tissue	homograft	
mitral	3	20	5		28
aortic		11	2	6 (6)*	19
mitral+aortic		8 (2)*	4		12
tricuspid	3	3			6
others	2				2
total	8	42 (2)	11	6 (6)	67

* Bentall operation

성기익 등, 대한흉부외과학회지 2002

국내 심내막염 수술 결과

- Mortality
  - Early or in-hospital mortality : 2/67 (3.0%)
  - Late mortality : 4/67 (6%)
    - M / 59 : ICH with meningitis pt. → SDH (3months)
    - M / 30 : MDS pt. → sepsis after BMT (16months)
    - M / 20 : ALL pt. → sepsis after reinduction chemo (20months)
    - M / 64 : CRF pt. → recurred infection & medical Tx. (4months)

- Morbidity
  - PPM insertion (1), SDH (2), ICH or hemorrhagic infarction (4), recurred infection and reop (2)

성기익 등, 대한흉부외과학회지 2002

국내 심내막염 수술 결과

- 23례 (2 PVE, 21 NVE)
- 수술 적응증 – ACC/AHA guideline
- 수술 종류
  - 13 MV replacement, 10 MV repair
  - 6 AVR, 2 TV repair, 1 VSD colsure
- Mortality
  - Early (<수술 후 30일); none
  - Late; 수술 후 31개월에 뇌출혈로 1명 사망(4.3%)
- Morbidity
  - 재수술 2례, 종격동염 1례, 저심박출증 1례, 폐렴 1례

안병희 등, 대한흉부외과학회지 2004

MV Repair vs. MV Replacement

Feringa H, et al. Ann Thorac Surg 2007

Clinical Characteristics

	Studies Including Mitral Valve Repair (n = 13)	Studies Including Mitral Valve Replacement (n = 17)	*p* Value
Number of patients with mitral valve repair	470		
Number of patients with mitral valve replacement		724	
Men (%)	74.3% [13]	74.2% [17]	0.98
Mean age (years)	50.7 ± 8.4 [13]	49.5 ± 9.1 [17]	0.62
Surgical acuity			
Acute	66.3% [12]	77.8% [14]	< 0.0001
Chronic	33.7% [12]	22.2% [14]	< 0.0001
Time interval between start of antibiotic treatment and surgery in acute cases	21.9 ± 3.8 [9]	20.3 ± 10.6 [12]	0.66
Indications for surgery			
Congestive heart failure	55.2% [9]	62.8% [11]	0.020
Embolization	11.5% [10]	14.3% [13]	0.11
Large/mobile vegetation	32.9% [9]	28.7% [6]	0.24
Uncontrolled sepsis	15.8% [10]	37.4% [11]	< 0.0001
Abscess	0.0% [9]	11.0% [4]	< 0.0001
Microorganism			
Streptococcus sp	42.6% [12]	42.1% [16]	0.89
Staphylococcus sp	24.0% [12]	31.0% [16]	0.0031
Other	12.5% [12]	7.1% [16]	0.00029
Culture negative/unknown	20.9% [11]	19.8% [15]	0.63

Feringa H, et al. Ann Thorac Surg 2007

Clinical Outcome

	Mitral Valve Repair (n = 470 patients)	Mitral Valve Replacement (n = 724 patients)	*p* Value
Mortality			
Early (< 30 days)	11/470 (2.3%) [13]	104/724 (14.4%) [17]	< 0.0001
Late (≥ 30 days)	24/307 (7.8%) [10]	137/338 (40.5%) [8]	< 0.0001
Morbidity			
Early			
Reoperation	7/319 (2.2%) [9]	26/205 (12.7%) [5]	< 0.0001
Recurrent endocarditis	1/217 (0.5%) [8]	3/253 (1.2%) [8]	0.63
Thromboembolism	2/130 (1.5%) [4]	0/17 (0.0%) [2]	0.20
Cerebrovascular event	7/150 (4.7%) [5]	19/165 (11.5%) [4]	0.045
Late			
Reoperation	20/430 (4.7%) [12]	26/298 (8.7%) [9]	0.039
Recurrent endocarditis	6/328 (1.8%) [11]	28/386 (7.3%) [9]	0.0013
Thrombo-embolism	6/185 (3.2%) [6]	0/7 (0.0%) [1]	0.15
Cerebrovascular event	3/188 (1.6%) [5]	11/45 (24.4%) [2]	< 0.0001

Feringa H, et al. Ann Thorac Surg 2007

Summary

- Potentially lethal disease with varying etiologic agents and different clinical situations (NVE vs PVE, etc).
- No “cookbook” approach to proper therapy, esp. when considering surgery.
- Tendency for surgical treatment has been increased with better result in selected patients.
- Combined medical/surgical Rx of selected populations offers substantial morbidity and mortality benefit.

Summary

- Careful attention to hemodynamic status, infecting organism (staph aureus, fungi, GNR), clinical manifestations (emboli, abscess, conduction abn, CHF), and findings on imaging (TTE/TEE, etc) allow a tailored approach to proper Rx in each patient to minimize morbidity and mortality.

- However, surgery carries risk and decision on whether or not to operate must be carefully thought out with good communication between surgical and medical teams.