Infective endocarditis

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Definition and classification

- ? Infection most commonly involves heart valves (either native or prostatic) but may also occur on the low-pressure side of a VSD, damaged mural endocardium or on intra-cardiac devices.
- ? Classification
 - ? Temporal acute, sub acute
 - ? Site of infection right Vs left, Valvular Vs non valvular
 - ? Cause of infection bacterial, fungal, rickettsial, culture negative
 - ? Predispostion congenital defects, prostatic valves, drug abuse

Epidemiology

- ? Incidence 2.6-7:100,000 in the western world. Increasing among elderly.
- ? Predisposition congenital heart disease, rheumatic heart disease, IV drug abuse, intra-cardiac devices.
- ? 16-30% of all cases involve prostatic valves.
- ? The risk for IE on prostatic valve is greatest during the first 6-12 month after surgery.

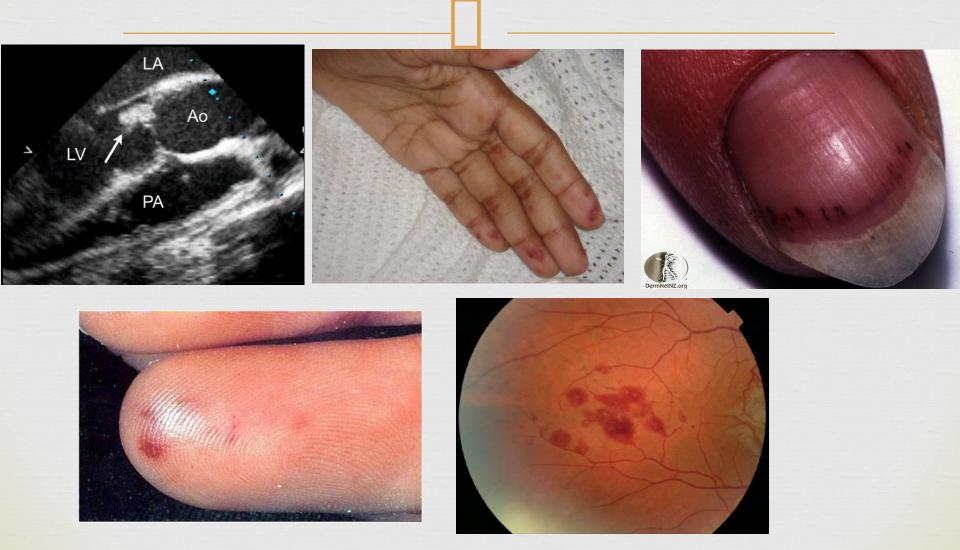
Clinical manifestation

- ? Cardiac manifestations
 - ? Murmur 80-85%
 - ? CHF 30-40%
 - ? Arrhythmia
 - ? Pericarditis
 - ? Coronary emboli
- ? Non cardiac manifestations
 - ? Fever 80-90%
 - ? Chills 40-75%
 - ? Anorexia, weight loss, malaise 25-50%
 - ? Back pain 7-15%
 - ? Arterial emboli 20-50%
 - ? Splenomegaly 15-50%
 - ? Clubbing 10-20%
 - ? Neurologic manifestations 20-40%
 - ? Peripheral manifestations 2-15%
 - ? Petechiae 10-40%

? Laboratory manifestations

- ? Anemia 70-90%
- ? Leukocytosis 20-30%
- ? Microscopic hematuria 30-50%
- ? Elevated ESR 60-90%
- ? Elevated CRP >90%
- ? Elevated RF 50%
- ? Decreased complement 5-40%

Clinical manifestations



Diagnosis - Duke criteria

Major Criteria

1. Positive blood culture

Typical microorganism for infective endocarditis from two separate blood cultures

Viridans streptococci, Streptococcus gallolyticus, HACEK group, Staphylococcus aureus, or

Community-acquired enterococci in the absence of a primary focus, or

Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:

Blood cultures drawn >12 h apart; or

All of 3 or a majority of ≥4 separate blood cultures, with first and last drawn at least 1 h apart

Single positive blood culture for *Coxiella bumetii* or phase I IgG antibody titer of >1:800

2 Evidence of endocardial involvement

Positive echocardiogram^b

Oscillating intracardiac mass on valve or supporting structures or in the path of regurgitant jets or in implanted material, in the absence of an alternative anatomic explanation, or Abscess. or

New partial dehiscence of prosthetic valve, or

New valvular regurgitation (increase or change in preexisting murmur not sufficient)

Minor Criteria

- 1. Predisposition: predisposing heart condition or injection drug use
- 2. Fever ≥38.0°C (≥100.4°F)
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor
- Microbiologic evidence: positive blood culture but not meeting major criterion as noted previously or serologic evidence of active infection with organism consistent with infective endocarditis

<u>Definite IE:</u> Histology or culture of a cardiac vegetation, an embolized vegetation, or intracardiac abscess from the heart finds microorganisms.

Active endocarditis: One of these combinations of clinical criteria

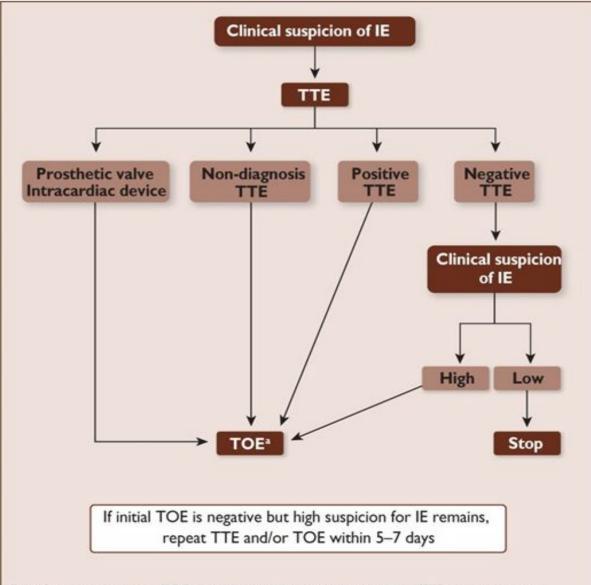
- 2 major clinical criteria
- 1 major and 3 minor criteria
- 5 minor criteria

Possible IE:

- 1 major and 1 minor criteria
- 3 minor criteria

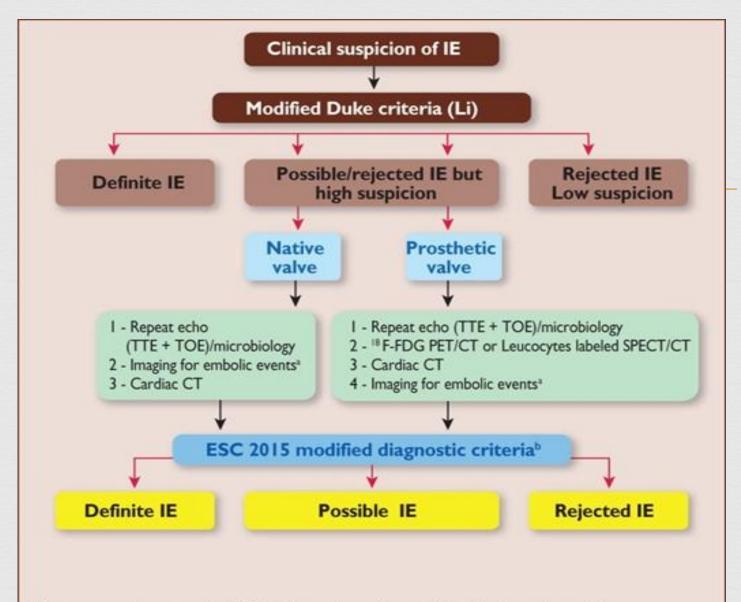
Re	commendations	Classa	Levelb	Ref.c
A.	Diagnosis			
•	TTE is recommended as the first-line imaging modality in suspected IE.	ı	В	64,65
•	TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.		В	64, 68–71
•	TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.	Ī	В	64,71
•	Repeat TTE and /or TOE within 5–7 days is recommended in case of initially negative examination when clinical suspicion of IE remains high.	ı	C	
•	Echocardiography should be considered in Staphylococcus aureus bacteraemia.	lla	В	66,67
•	TOE should be considered in patients with suspected IE, even in cases with positive TTE, except in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.	IIa	O	

•	Repeat TTE and/or TOE are recommended as soon as a new complication of IE is suspected (new murmur, embolism, persisting fever, HF, abscess, atrioventricular block).	1	В	64,72
•	Repeat TTE and/or TOE should be considered during follow-up of uncomplicated IE, in order to detect new silent complications and monitor vegetation size. The timing and mode (TTE or TOE) of repeat examination depend on the initial findings, type of microorganism, and initial response to therapy.	lla	В	64,72
c.	Intraoperative echocardiography			
•	Intraoperative echocardiography is recommended in all cases of IE requiring surgery.	1	В	64,73
D.	Following completion of therapy		9	
•	TTE is recommended at completion of antibiotic therapy for evaluation of cardiac and valve morphology and function.	1	С	



IE = infective endocarditis; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

^aTOE is not mandatory in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.



CT = computed tomography; FDG = fluorodeoxyglucose; IE = infective endocarditis;
PET = positron emission tomography; SPECT = single photon emission computerized tomography;
TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

*May include cerebral MRI, whole body CT, and/or PET/CT.

*See Table 14.

Etiology

TABLE 124-1 Organisms Causing Major Clinical Forms of Endocarditis

Percentage of Cases								
	Native Valve	e Endocarditis	Prosthetic Valve Endocarditis at Indicated Time of Onset (Months) after Valve Surgery			Endocarditis in Injection Drug Users		
Organism	Community- Acquired (n =1718)	Health Care– Associated (n =788)	<2 (n = 144)	2–12 (n = 31)	>12 (n = 194)	Right-Sided (n = 346)	Left-Sided (n = 204)	Total (n = 675) ^a
Streptococci ^b	(40)	9	1	9	(31)	5	15	12
Pneumococci	2	-	_	2 -		-	_	
Enterococci	9	13	8	12	11	2	24	9
Staphylococcus aureus	28	(53°)	22	12	18	(77)	23	(57)
Coagulase-negative staphylococci	5	12	33	(32)	11	_	_	_
Fastidious gram-negative coccobacilli (HACEK group) ^d	3	_	 -	-	6	· 	1 1	·
Gram-negative bacilli	1	2	13	3	6	5	13	7
Candida spp.	<1	2	8	12	1	_	12	4
Polymicrobial/miscellaneous	3	4	3	6	5	8	10	7
Diphtheroids	-	<1	6	_	3	_	_	0.1
Culture-negative	9	5	5	6	8	3	3	3

Treatment

Microorganism	ABX
Strep – penicillin susceptible	 Penicillin G 4 weeks Ceftriaxone 4 weeks Vancomycin 4 weeks
Strep – relatively resistant to pen	 Penicillin G or ceftriaxone 4 weeks plus gentamycin for 2 weeks Vancomycin for 4 weeks
Strep – mod resistant to penicillin	 Penicillin G or ceftriaxone plus gentamycin for 6 weeks Vancomycin fir 4 weeks
Enterococci	 Penicillin G plus gentamycin for 4-6 weeks Ampicillin plus gentamycin for 4-6 weeks Vancomycin plus gentamycin 4-6 weeks
Staph – methicillin susceptible, native valves	 Nafcillin or oxacillin 4-6 weeks Cefazolin 4-6 weeks Vancomycin 4-6 weeks
Staph - methicillin resistant, native valves	1. Vancomycin 4-6 weeks
Staph - meticillin susceptible prostatic valves	1. Nafcillin or oxcillin 6-8 weeks plus gentamycin 2 weeks plus rifampin 6-8 weeks
Staph - methicillin resistant, prostatic valves	1. Vancomycin 6-8 weeks plus gentamycin 2 weeks plus rifampin 6-8 weeks
HACEK	 Ceftriaxone 4 weeks Ampi-sulbactam 4 weeks

Bartonella endocarditis

- ? B. quintana and B. henselae are the most common bartonella spp. implicated in endocarditis.
- ? Native valves > prostatic valves
- ? 60% aortic valve
- ? Sub-acute endocarditis, mild non specific symptomes lasting for months to years,
- ? Positive blood cultures 25% (6 weeks of incubation)
- ? Diagnosis sierology, PCR
- ? Treatment aminoglycosides for at least 2 weeks

Q fever

- ? C. brunetti
- ? Gram neg cocco-bacillus
- ? Primary sources cattle, sheep and goats
- ? Incidence 24-54 cases per years in the USA. 70% male, April June.
- ? Acute Q fever
 - ? Incubation 3 30 days
 - Proposition (40%), pneumonia (17%), pneumonia + hepatitis (20%), isolated fever (14%), CNS involvement (2%), pericarditis or myocarditis (1%).
 - ? Symptoms: fatigue, photophobia, headache, sweats, nausea, vomiting, diarrhea, cough, rash.
 - ? Lab: normal WBC, thrombocytosis during recovery.
 - ? CXR: rounded opacities
- ? Chronic Q fever
 - ? Almost always implies endocarditis usually in patients with previous valvular disease, immunosuppression or CRF
 - ? Valvular vegetations 12% in TTE
 - ? Hepatomegaly, splenomegaly, elevated RF, elevated ESR, elevated CRP.
- ? Diagnosis: PCR, Sierology (IgG >1:800 phase I = chronic disease. IgG >1:800 phase II = acute disease).
- ? Treatment
 - ? Acute disease doxycycline 100mg bid for 14 days
 - ? Chronic disease doxycycline 100mg bid + hydroxychloroquine 200mg bid for 18 mo. second line rifampin + doxycycline or ciproxin

Main complications of left-sided valve infective endocarditis and their management

Heart failure in infective endocarditis

HF is the most frequent complication of IE and represents the most common indication for surgery in IE. HF is observed in 42–60% of cases of NVE and is more often present when IE affects the aortic rather than the mitral valve.

Valvular regurgitation in native IE may occur as a result of mitral chordal rupture, leaflet rupture (flail leaflet), leaflet perforation or interference of the vegetation mass with leaflet closure. A particular situation is infection of the anterior mitral leaflet secondary to an infected regurgitant jet of a primary aortic IE.

Clinical presentation of HF may include dyspnea, pulmonary edema and cardiogenic shock. Echocardiography is also useful to evaluate the hemodynamic consequences of valvular dysfunction, measurement of pulmonary artery pressure, detection of pericardial effusion and assessment and monitoring of left ventricular systolic function and left and right heart filling pressures.

B-type natriuretic peptide has potential use in the diagnosis and monitoring of HF in IE. Both elevated levels of cardiac troponins and HF is the most frequent and among the most severe complications of IE. Unless B-type natriuretic peptide are associated with adverse outcomes in severe complication for early surgery in NVE and PVE to severe HF is the most important predictor of in hospital, by and PVE even in patients with cardiogenic shock.

Uncontrolled infection

Persisting infection

Perivalvular extension in infective endocarditis

- Perivalvular extension of IE is the most frequent cause of uncontrolled infection and is associated with a poor prognosis and high likelihood of the need for surgery. Perivalvular complications include abscess formation, pseudoaneurysms and fistulae
- ? Pseudoaneurysms and fistulae are severe complications of IE and are frequently associated with very severe valvular and perivalvular damage. The frequency of fistula formation in IE has been reported to be 1.6%, with *S. aureus* being the most commonly associated organism (46%).
- ? Despite high rates of surgery in this population (87%), hospital mortality remains high (41%). Other complications due to major extension of infection are less frequent and may include ventricular septal defect, third-degree atrio-ventricular block and acute coronary syndrome.
- Perivalvular extension should be suspected in cases with persistent unexplained fever or new atrio-ventricular block. Therefore an electrocardiogram should be performed frequently during continuing treatment, particularly in aortic IE. TOE, MSCT and PET/CT are particularly useful for the **Embolic eyents in infective endocardities** he sensitivity of TTE is <50%. Embolic events are a frequent and life-threatening complication of IE related to the migration of cardiac vegetations. The brain and spleen are the most frequent sites of embolism in left-sided IE, while pulmonary embolism is frequent in native right-sided and pacemaker lead IE. Stroke is a severe complication and is associated with increased morbidity and mortality. Conversely, embolic events may be totally silent in 20–50% of patients with IE, especially those affecting the splenic or cerebral circulation, and can be diagnosed by non-invasive imaging. Thus systematic abdominal and cerebral CT scanning may be helpful. However, contrast media should be used with caution in patients with renal impairment or hemodynamic instability because of the risk of worsening renal impairment in combination with antibiotic nephrotoxicity.

Overall, embolic risk is very high in IE, with embolic events occurring in 20-50% of patients. However, the risk of new events (occurring after initiation of antibiotic therapy) is only 6-21%. A study from the ICE group demonstrated that the incidence of stroke in patients receiving appropriate antimicrobial therapy was 4.8/1000 patient-days in the first week of therapy, falling to 1.7/1000 patient-days in the second week, and further thereafter.

Other complications of infective endocarditis

- ? Neurological complications
- ? Symptomatic neurological events develop in 15–30% of all patients with IE and additional silent events are frequent. Stroke (ischaemic and haemorrhagic) is associated with excess mortality. Rapid diagnosis and initiation of appropriate antibiotics are of major importance to prevent a first or recurrent neurological complication. After a first neurological event, cardiac surgery, if indicated, is generally not contraindicated, except when extensive brain damage or intracranial haemorrhage is present.
- ? <u>Infectious aneurysms</u>

Splenic complications

Myocarditis and pericarditis

Heart rhythm and conduction disturbances

Musculoskeletal manifestations

Acute renal failure

Surgery

TABLE 124-6 Timing of Cardiac Surgical Intervention in Patients With Endocarditis

	Indication for Su	rgical Intervention
Timing	Strong Supporting Evidence	Conflicting Evidence, but Majority of Opinions Favor Surgery
Emergent (same day)	Acute aortic regurgitation plus preclosure of mitral valve Sinus of Valsalva abscess ruptured into right heart Rupture into pericardial sac	
Urgent (within 1–2 days)	Valve obstruction by vegetation Unstable (dehisced) prosthesis Acute aortic or mitral regurgitation with heart failure (New York Heart Association class III or IV) Septal perforation Perivalvular extension of infection with/without new electrocardiographic conduction system changes Lack of effective antibiotic therapy	Major embolus plus persisting large vegetation (>10 mm in diameter)
Elective (earlier usually preferred)	Progressive paravalvular prosthetic regurgitation Valve dysfunction plus persisting infection after ≥7–10 days of antimicrobial therapy Fungal (mold) endocarditis	Staphylococcal PVE Early PVE (≤2 months after valve surgery) Fungal endocarditis (<i>Candida</i> spp.) Antibiotic-resistant organisms

Patient characteristics

- · Older age
- Prosthetic valve IE
- Diabetes mellitus
- Comorbidity (e.g., frailty, immunosuppression, renal or pulmonary disease)

Clinical complications of IE

- Heart failure
- Renal failure
- >Moderate area of ischaemic stroke
- Brain haemorrhage
- Septic shock

Microorganism

- Staphylococcus aureus
- Fungi
- Non-HACEK Gram-negative bacilli

Echocardiographic findings

- · Periannular complications
- Severe left-sided valve regurgitation
- · Low left ventricular ejection fraction
- · Pulmonary hypertension
- Large vegetations
- · Severe prosthetic valve dysfunction
- Premature mitral valve closure and other signs of elevated diastolic pressures

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ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis

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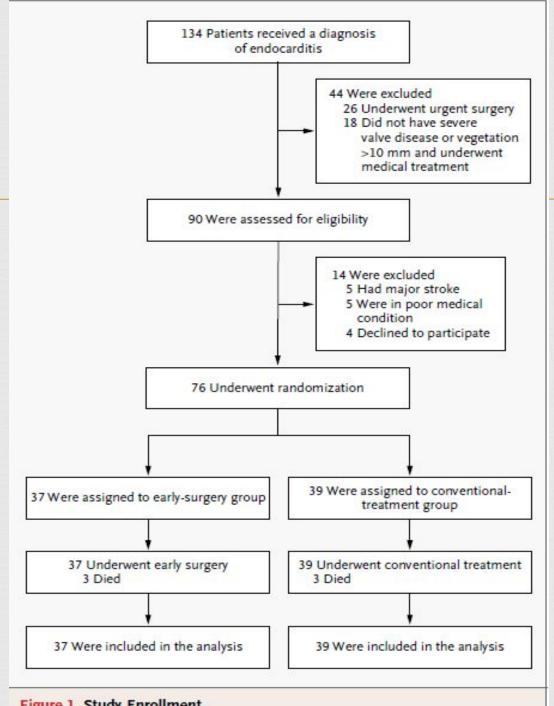


Figure 1. Study Enrollment.

Table 1. Clinical and Echocardiographic Characteristics of the Patients at Baseline, According to Treatment Group.*

Characteristic	Conventional Treatment (N=39)	Early Surgery (N = 37)
Age — yr	47.8±17.5	45.5±14.9
Male sex — no. (%)	27 (69)	24 (65)
Diabetes — no. (%)	4 (10)	8 (22)
Hypertension — no. (%)	7 (18)	11 (30)
Coronary artery disease — no. (%)	1 (3)	3 (8)
Immunocompromised state — no. (%)†	1 (3)	2 (5)
Underlying valve disease — no. (%)	39 (100)	35 (95)
Serum creatinine — mg/dl	0.90±0.67	1.28±1.85
EuroSCORE value‡	6.7±1.7	6.4±1.6
Embolism on admission — no. (%)	17 (44)	19 (51)
Cerebral	11 (28)	11 (30)
Renal	7 (18)	6 (16)
Splenic	9 (23)	14 (38)
Left ventricular ejection fraction — %	60.7±7.2	61.7±5.1
Valve involved — no. (%)		
Mitral	23 (59)	22 (59)
Aortic	11 (28)	11 (30)
Aortic and mitral	5 (13)	4 (11)

Vegetation diameter	14.1±3.5	13.5±3.2
>10-15 mm — no. (%)	26 (67)	26 (70)
>15 mm — no. (%)	13 (33)	11 (30)
Valvular disease — no. (%)		
Severe stenosis	3 (8)	1 (3)
Severe regurgitation	36 (92)	36 (97)
Blood microorganism — no. (%)		
Viridans streptococci	13 (33)	10 (27)
Other streptococci	12 (31)	11 (30)
Staphylococcus aureus	5 (13)	3 (8)
Enterococcus	1 (3)	2 (5)
Other§	1 (3)	1 (3)
Negative culture¶	7 (18)	10 (27)

Table 2. Characteristics of Antibiotic Therapy, According to Treatment Group.

Characteristic	Conventional Treatment (N = 39)	Early Surgery (N = 37)	P Value
Control of the underlying infection			
Defeverescence — days			
Median	2	2	0.21
Interquartile range	1–6	1-3	
Persistence of bacteremia — no. (%)*	1 (3)	0	1.00
Antibiotic regimen			
Beta-lactam-based therapy — no. (%)	39 (100)	37 (100)	1.00
Beta-lactam antibiotic alone	26 (67)	27 (73)	0.62
Beta-lactam antibiotic with amino- glycoside†	13 (33)	10 (27)	0.62
Duration — days			
Median	35	35	0.93
Interquartile range	28-42	28-42	

^{*} Persistence of bacteremia was defined as positive blood cultures 1 week after antibiotic therapy was initiated.

[†] An aminoglycoside was administered for 2 or more weeks.

Table 3. Clinical End Points.

Outcome	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

CONCLUSIONS

As compared with conventional treatment, early surgery in patients with infective endocarditis and large vegetations significantly reduced the composite end point of death from any cause and embolic events by effectively decreasing the risk of systemic embolism. (EASE ClinicalTrials.gov number, NCT00750373.)

Points for discussion

- ? <u>Patient population</u>: relatively **young**, low rate of **comorbidities**.
- ? <u>Microbiology</u>: high rate of **Streptococcal** infections, low rate of **Staphylococcal**.
- ? In real-life: patients are older, more comorbidities, and more virulent bacteria, higher rate of complications are expected.
- ? Rate of embolism: ~30% (60% cerebral).
 - ? Higher risk during first wk after diagnosis.

Prophylaxis

TABLE 124-8 High-Risk Cardiac Lesions for Which Endocarditis Prophylaxis Is Advised Before Dental Procedures

Prosthetic heart valves

Prior endocarditis

Unrepaired cyanotic congenital heart disease, including palliative shunts or conduits

Completely repaired congenital heart defects during the 6 months after repair

Incompletely repaired congenital heart disease with residual defects adjacent to prosthetic material

Valvulopathy developing after cardiac transplantation

TABLE 124-7 Antibiotic Regimens for Prophylaxis of Endocarditis in Adults With High-Risk Cardiac Lesions^{a,b}

- A. Standard oral regimen
 - 1. Amoxicillin: 2 g PO 1 h before procedure
- B. Inability to take oral medication
 - 1. Ampicillin: 2 g IV or IM within 1 h before procedure
- C. Penicillin allergy
 - Clarithromycin or azithromycin: 500 mg PO 1 h before procedure
 - 2. Cephalexinc: 2 g PO 1 h before procedure
 - 3. Clindamycin: 600 mg PO 1 h before procedure
- D. Penicillin allergy, inability to take oral medication
 - Cefazolin^c or ceftriaxone^c: 1 g IV or IM 30 min before procedure
 - 2. Clindamycin: 600 mg IV or IM 1 h before procedure

Non-specific prevention measures to be followed in high-risk and intermediate-risk patients

These measures should ideally be applied to the general population and particularly reinforced in high-risk patients:

- Strict dental and cutaneous hygiene. Dental follow-up should be performed twice a year in high-risk patients and yearly in the others.
- · Disinfection of wounds.
- Eradication or decrease of chronic bacterial carriage: skin, urine.
- Curative antibiotics for any focus of bacterial infection.
- · No self-medication with antibiotics.
- Strict infection control measures for any at-risk procedure.
- Discourage piercing and tattooing.
- Limit the use of infusion catheters and invasive procedure when possible. Favour peripheral over central catheters, and systematic replacement of the peripheral catheter every 3–4 days. Strict adherence to care bundles for central and peripheral cannulae should be performed.

Recommendations for prophylaxis of infective endocarditis in the highest-risk patients according to the type of at-risk procedure

Re	commendations	Classa	Levelb
A.	Dental procedures		
•	Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	lla	C
•	Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces or following the shedding of deciduous teeth or trauma to the lips and oral mucosa	ш	С
в.	Respiratory tract procedures ^c		
•	Antibiotic prophylaxis is not recommended for respiratory tract procedures, including bronchoscopy or laryngoscopy, or transnasal or endotracheal intubation	m	С
c.	Gastrointestinal or urogenital procedure	s or TO	DE ^c
•	Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE	ш	C
D.	Skin and soft tissue procedures ^c		
•	Antibiotic prophylaxis is not recommended for any procedure	ш	c

Recommendations for antibiotic prophylaxis for the prevention of local and systemic infections before cardiac or vascular interventions

Recommendations	Classa	Level ^b	Ref.c
Preoperative screening of nasal carriage of Staphylococcus aureus is recommended before elective cardiac surgery in order to treat carriers	ı	A	46,47
Perioperative prophylaxis is recommended before placement of a pacemaker or implantable cardioverter defibrillator	î	В	45
Potential sources of sepsis should be eliminated ≥2 weeks before implantation of a prosthetic valve or other intracardiac or intravascular foreign material, except in urgent procedures	lla	C	
Perioperative antibiotic prophylaxis should be considered in patients undergoing surgical or transcatheter implantation of a prosthetic valve, intravascular prosthetic or other foreign material	lla	С	
Systematic local treatment without screening of S. aureus is not recommended	ш	С	

Case

- ? 49y male
- ? Staphylococcus aureus NVE
- ? 3 weeks of IV antibiotics
- ? Undergoing MVR due to ruptured chorda and CHF
- ? How long will you treat following the surgery?

How do you count the duration of therapy?

- ? It is reasonable that the counting of days for the duration of antimicrobial therapy begin on the first day on which blood cultures are negative
- ? If operative tissue cultures are positive, antimicrobial course is reasonable after valve surgery



Any questions?