İnfektif Endokardit
(Yeni Rehberler)

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İnfektif Endokardit (İE)

- Yıllık insidans: 3-9/100.000
- Yaşamı tehdit eden infeksiyon hastalıkları içinde sepsis, pnömoni ve intraabdominal apselerin ardından dördüncü sırada
- Ciddi komplikasyonlar
- Yüksek mortalite
- Kompleks bir hastalık

Neden yeni rehber?

Değişen epidemiyolojik özellikler:

- *Staphylococcus aureus*' a bağlı İE vakalarında artış
- Sağlık bakımı ile ilgili vakalarda artış
- Ortalama hasta yaşının yükselmesi
- Romatizmal kapak hastalığına bağlı vaka sayısında düşme
- Prostetik kapak ve diğer alet kullanım oranında artış,
- Cerrahi tedavi uygulanan hasta sayısının artması

Neden yeni rehber?

- Yeni çalışmalar: Geniş İE serilerinin yayınlanması (İE'de cerrahi tedavi ile ilgili ilk randomize çalışma)
- Görüntüleme yöntemlerindeki gelişmeler (Üç boyutlu ekokardiyografi, multi-slice CT, kardiyak MRI, PET/CT, SPECT/CT)
- Mortalite ve morbidite ölçümü ve cerrahi endikasyonu için yeni risk skalaları
- Yeni antibiyotikler

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ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

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AHA Scientific Statement

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Endorsed by the Infectious Diseases Society of America

Larry M. Baddour, MD, FAHA, Chair; Walter R. Wilson, MD; Arnold S. Bayer, MD; Vance G. Fowler, Jr, MD, MHS; Imad M. Tleyjeh, MD, MSc; Michael J. Rybak, PharmD, MPH; Bruno Barsic, MD, PhD; Peter B. Lockhart, DDS; Michael H. Gewitz, MD, FAHA; Matthew E. Levison, MD; Ann F. Bolger, MD, FAHA; James M. Steckelberg, MD; Robert S. Baltimore, MD; Anne M. Fink, PhD, RN; Patrick O'Gara, MD, FAHA; Kathryn A. Taubert, PhD, FAHA; on behalf of the American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council

(*Circulation*. 2015;132:00-00. DOI: 10.1161/CIR.0000000000000296.)

2015 ESC rehberi

1. Profilaksi
2. Endokardit ekibi
3. Tanı
4. Tedavi
5. Özel durumlar

2015 ESC rehberi

1. **Profilaksi**
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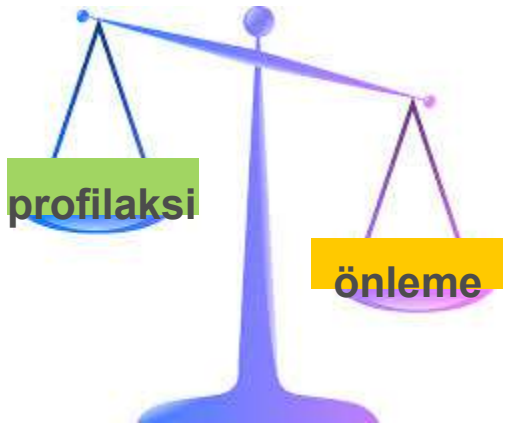
2015 ESC rehberi (profilaksi)



- Profilaksinin yararını gösteren gerçek bilimsel veri yok, hatta riskleri var
- Profilaksi yalnızca **yüksek riskli hastalara** **yüksek riskli dental işlem** uygulandığında

Table 3 Cardiac conditions at highest risk of infective endocarditis for which prophylaxis should be considered when a high-risk procedure is performed

Recommendations	Class[a]	Level[b]
Antibiotic prophylaxis should be considered for patients at highest risk for IE: (1) Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair. (2) Patients with a previous episode of IE. (3) Patients with CHD: (a) Any type of cyanotic CHD. (b) Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.	IIa	C
Antibiotic prophylaxis is not recommended in other forms of valvular or CHD.	III	C

2014 AHA/ACC(American College of Cardiology/American Heart Association) Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

- **Yüksek riskli hastalar:**
  - Prostetik kapak veya kalp kapağı tamiri için kullanılmış herhangi bir prostetik materyal varlığı
  - Geçirilmiş İE hikayesi
  - Siyanotik konjenital kalp hastalıkları, rezidüel defekt kalmış opere konjenital kalp hastalıkları ve rezidüel defekt kalmamış konjenital kalp hastalıklarının ilk altı ayıdır.
  - Transplante kalpte kapaktaki yapısal anormalliğe bağlı kapak regürjitasyonu

İE profilaksi

- 2015 ESC rehberinde kapak tamiri için kullanılan prostetik materyal varlığı, profilaksi için **endikasyon,**
- 2014 AHA/ACC rehberinde MitraClip benzeri bir prostetik materyalin varlığı profilaksi için **endikasyon değil**

Table 5 Recommendations for prophylaxis of infective endocarditis in the highest-risk patients according to the type of at-risk procedure

Recommendations	Class[a]	Level[b]
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	IIa	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	III	C

National Institute for Health and Clinical Excellence (NICE) 2008

En yüksek riskli kardiyak durumlar dahil hiçbir durumda antimikrobik **profilaksi yok**

- dental veya dental olmayan bir işlemle İE gelişimi arasında kesin olarak kanıtlanmış bir ilişki yok
- düzenli diş fırçalama, oral florayla sürekli yineleyen bakteriyemilere, tek bir dental işleme göre daha fazla neden oluyor;
- antibiyotik profilaksisinin klinik etkinliği kanıtlanamamış
- antibiyotik profilaksisinde kullanılan antibiyotikler,özellikle anafilaksi nedeniyle ölüm nedeni
- maliyet

2015 ESC rehberi (Profilaksi)

DURUM	ANTİBİYOTİK	İşlemden 30-60 dakika önce tek doz	
		Yetişkin	Çocuk
Penisilin veya ampisilin alerjisi yok	Amoksisilin veya ampisilin*	2 g oral veya i.v.	50 mg/kg oral veya i.v.
Penisilin veya ampisilin alerjisi var	Klindamisin	600 mg oral veya i.v.	20 mg/kg oral veya i.v.

* Alternatif olarak sefaleksin yetişkinde 2g i.v, çocukta 50 mg/kg i.v., sefazolin veya seftriakson yetişkinde 1 g, çocukta 50 mg/kg i.v.

2015 ESC rehberi

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2015 ESC rehberi (endokardit ekibi)

- Birçok bölümü ilgilendiren uzman görüşü gerekir. Kardiyologlar, kalp cerrahları, infeksiyon hastalıkları uzmanları, mikrobiyologlar, nörologlar, beyin cerrahları, KKH' da uzmanlaşmış olanlar, radyologlar ve diğer uzmanlar

2014 AHA/ACC Valvular Heart Disease Guideline

Benzer şekilde İE hastalarının takip ve tedavisinde takım çalışması:

- **Kardiyolog**
- **Kalp cerrahı**
- **İnfeksiyon hastalıkları uzmanı**
- **Anesteziyolog**

2015 ESC rehberi (endokardit ekibi)

Referans merkezi

- Transtorasik ekokardiyografi (TTE), Transözefajiyal ekokardiyografi (TÖE), multislice CT, MRI ve nükleer görüntüleme de dahil diyagnostik işlemlere **acil erişim** imkanı
- Acil kardiyak cerrahi imkanı
- Ekibi oluşturacak yeterli sayıda uzman hekim
- Nörocerrahi ve girişimsel nöroradyoloji gibi imkanlar

2015 ESC rehberi

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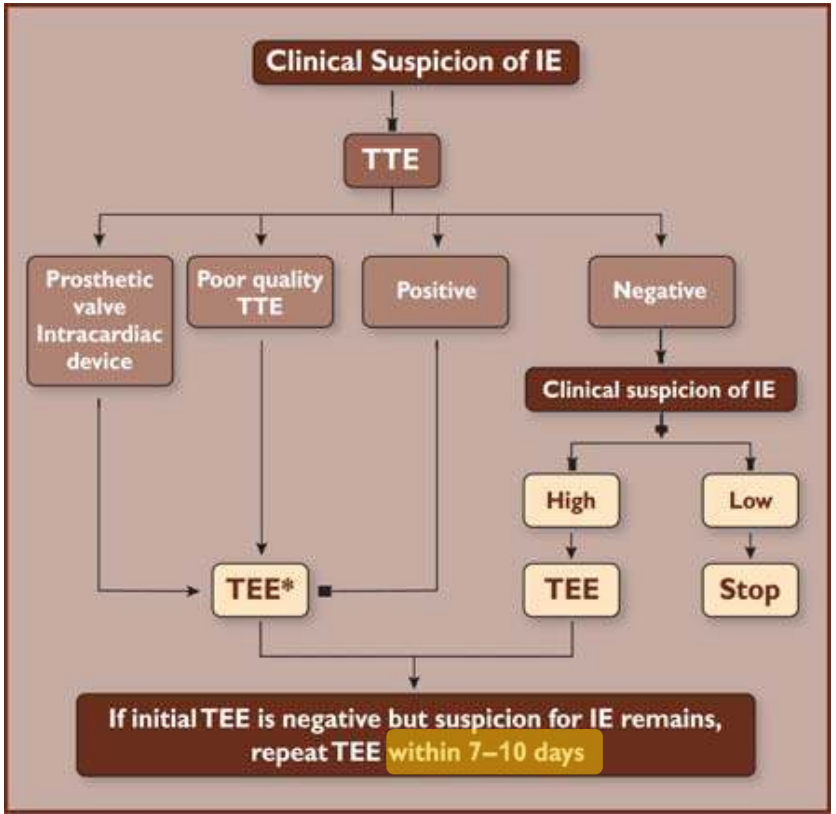
2015 ESC rehberi (tanı)

2009 rehberi



2015 rehberi

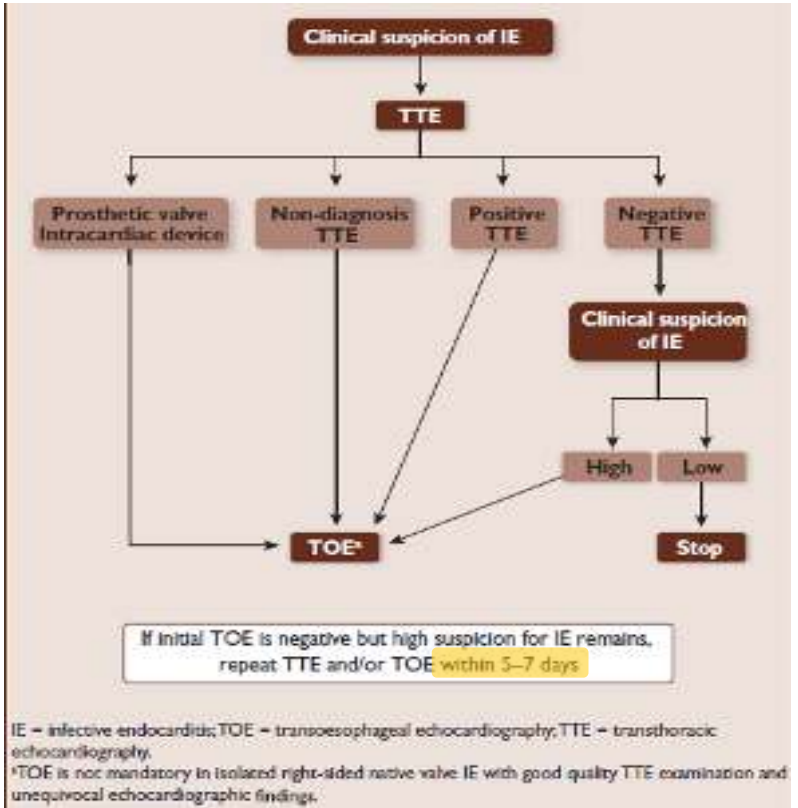


Table 13 Definition of infective endocarditis according to the modified Duke criteria (adapted from Li *et al.*[87])

Definite IE
Pathological criteria • Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or • Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis **Clinical criteria** • 2 major criteria; or • 1 major criterion and 3 minor criteria; or • 5 minor criteria
Possible IE
• 1 major criterion and 1 minor criterion; or • 3 minor criteria
Rejected IE
• Firm alternate diagnosis; or • Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or • No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or • Does not meet criteria for possible IE, as above

2015 ESC rehberi (tanı)

Major criteria

1. Blood cultures positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
- *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or
- Community-acquired enterococci, in the absence of a primary focus; or

b. Microorganisms consistent with IE from persistently positive blood cultures:
- ≥2 positive blood cultures of blood samples drawn >12 h apart; or
- All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or

c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

2. Imaging positive for IE

a. Echocardiogram positive for IE:
- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

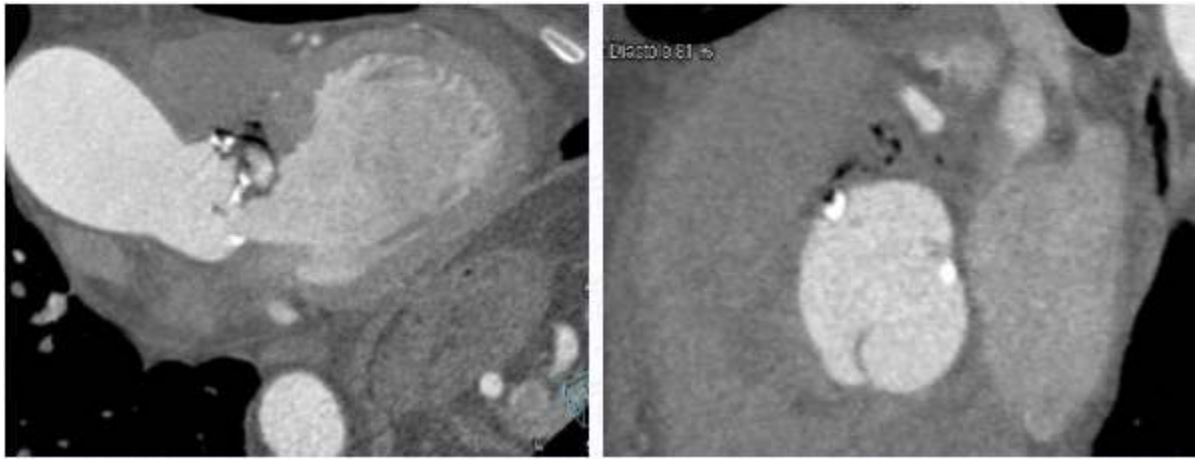
c. Definite paravalvular lesions by cardiac CT.

Major kriterler

b- 18F-FDG PET/CT (sadece prostetik kapak uygulanmasından sonraki süre>3 ay ise) veya radyoaktif işaretlenmiş lökosit SPECT/CT ile implantasyon bölgesinde anormal aktivite tesbit edilmesi

c- Kardiyak CT ile paravalvüler lezyonların gösterilmesi

Kardiyak CT



Cardiac imaging in infectious endocarditis

Niels Eske Bruun[1]*, Gilbert Habib[2]*, Franck Thuny[2], and Peter Sogaard[1]

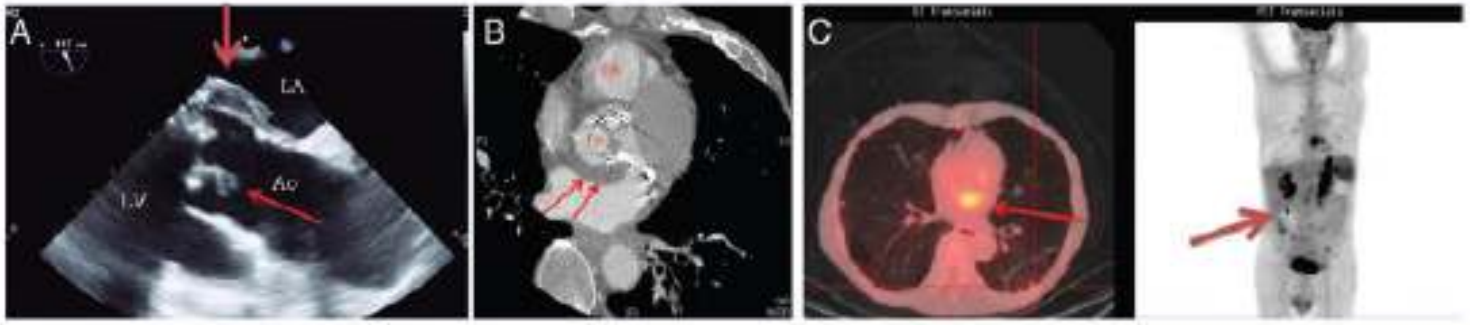


Figure 9 Multimodality imaging of a bioprosthetic aortic valve endocarditis. (*A*) Transoesophageal echocardiography: vegetation on a bioprosthetic leaflet (thin arrow) and posterior aortic root abscess (thick arrow). (*B*) Posterior aortic root abscess visualized by CT-scan (arrows). (*C*) PET-CT showing increased 18F-Fluorodeoxyglucose uptake on both the aortic prosthesis (left panel, arrow) and on a colonic tumour (right panel, arrow). LA, left atrium; LV, left ventricle; Ao, aorta; PA, pulmonary artery; Pr, prosthesis.

European Heart Journal (2014) **35**, 624–632

Cardiac imaging in infectious endocarditis

Niels Eske Bruun[1*], Gilbert Habib[2*], Franck Thuny[2], and Peter Sogaard

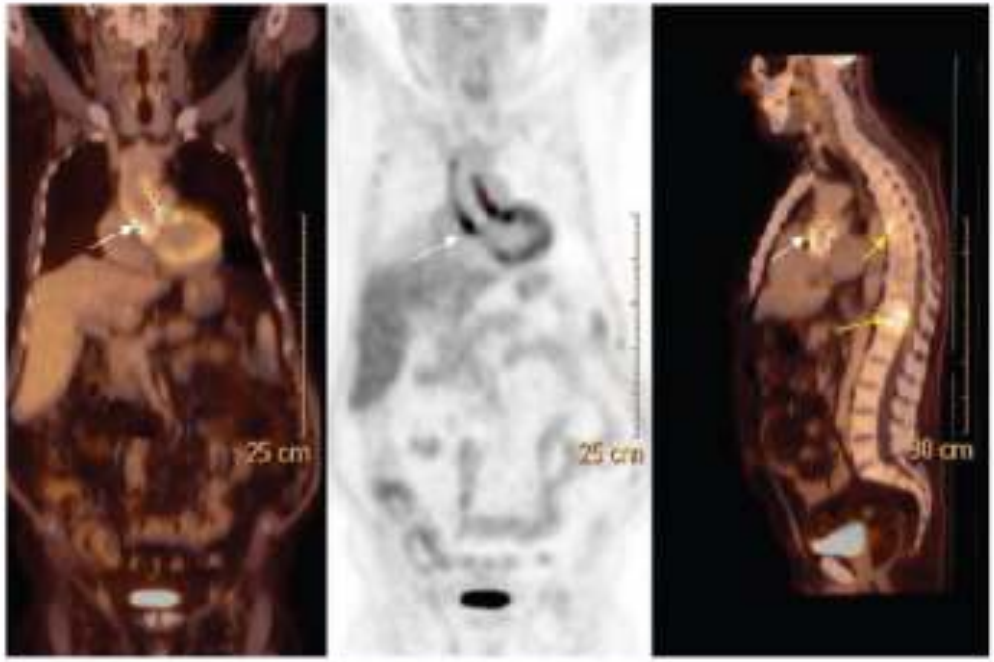
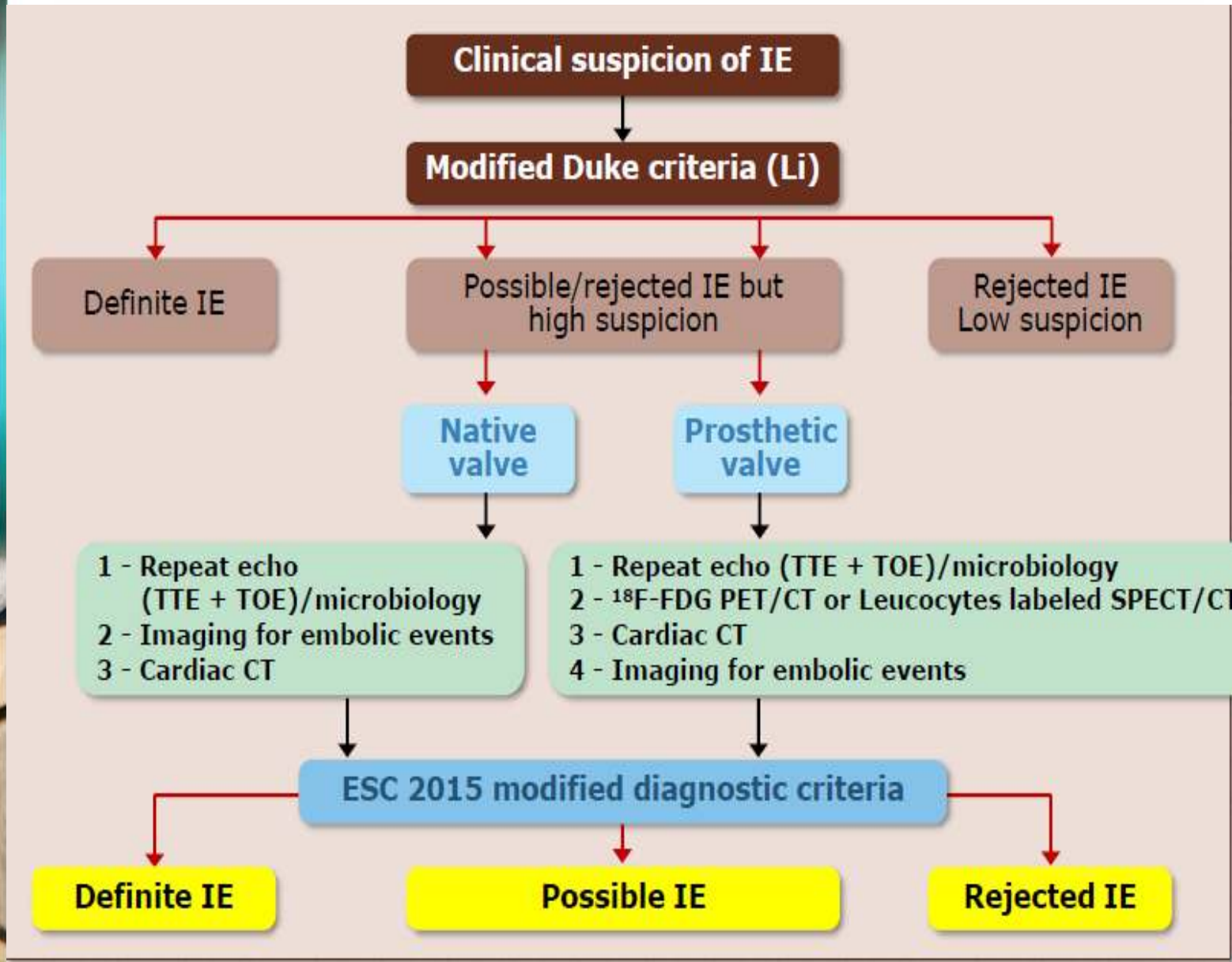


Figure 10 PET-CT of infected composite aorta graft (white arrows) inserted 16 years previously. Note the two foci in the thoracal columna

Minor criteria
1. Predisposition such as predisposing heart condition, or injection drug use. 2. Fever defined as temperature >38°C. 3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions. 4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor. 5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

2015 ESC rehberi (tanı algoritması)



2015 ESC rehberi

1. Profilaksi
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5. Özel durumlar

2015 ESC rehberi (ampirik tedavi)

Table 20 Proposed antibiotic regimens for initial empirical treatment of infective endocarditis in acute severely ill patients (before pathogen identification)[a]

Antibiotic	Dosage and route	Class[b]	Level[c]	Comments
Community-acquired native valves or late prosthetic valves (≥12 months post surgery) endocarditis				
Ampicillin with (Flu)cloxacillin *or* oxacillin with Gentamicin[d]	12 g/day i.v. in 4–6 doses 12 g/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 1 dose	IIa	C	Patients with BCNIE should be treated in consultation with an ID specialist.
Vancomycin[d] with Gentamicin[d]	30–60 mg/kg/day i.v. in 2–3 doses 3 mg/kg/day i.v. or i.m. in 1 dose	IIb	C	For penicillin-allergic patients
Early PVE (<12 months post surgery) or nosocomial and non-nosocomial healthcare associated endocarditis				
Vancomycin[d] with Gentamicin[d] with Rifampin	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 1 dose 900–1200 mg i.v. or orally in 2 or 3 divided doses	IIb	C	Rifampin is only recommended for PVE and it should be started 3–5 days later than vancomycin and gentamicin has been suggested by some experts. In healthcare associated native valve endocarditis, some experts recommend in settings with a prevalence of MRSA infections >5% the combination of cloxacillin plus vancomycin until they have the final S. aureus identification

İnfektif Endokardit (tedavi)

- Aminoglikozidler, klinik yararları net olarak gösterilemediğinden ve renal toksisiteyi artırabileceklerinden stafilokokal NVE'de artık tavsiye edilmemekte
- Kullanıldıklarında nefrotoksisiteyi azaltmak için **günde tek doz** önerilmekte

Treatment regimens for native valve endocarditis due to penicillin-susceptible viridans streptococci and *Streptococcus bovis* (MIC ≤0.12 mcg/mL)*

American Heart Association (AHA)		European Society of Cardiology (ESC)	British Society for Antimicrobial Chemotherapy (BSAC)
Adult	**Pediatric**		
4-week regimens[¶]:	**4-week regimens:**	**4-week regimens[Δ]:**	**4- to 6-week regimens:**
Aqueous penicillin G 12 to 18 million units per 24 hours IV either continuously or in four or six divided doses **or (if penicillin is unavailable)** Ampicillin 2 g IV every 4 hours **or** Ceftriaxone 2 g per 24 hours IV or IM in one dose **Beta-lactam-intolerant patients:** Vancomycin° 30 mg/kg per 24 hours IV in two divided doses	Aqueous penicillin G 200,000 to 300,000 units/kg per 24 hours IV in six divided doses (maximum dose: 24 million units per 24 hours) **or (if penicillin is unavailable)** Ampicillin 200 to 300 mg/kg per 24 hours IV divided in four or six divided doses (maximum dose: 12 g per 24 hours) **or** Ceftriaxone 100 mg/kg per 24 hours IV[‖] in two divided doses or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) **Beta-lactam-intolerant patients:** Vancomycin° 40 mg/kg per 24 hours IV in two or three divided doses (maximum dose: 2 g per 24 hours)	Aqueous penicillin G[¶] 12 to 18 million units per 24 hours IV in four or six divided doses or continuous infusion **or** Amoxicillin 100 to 200 mg/kg per 24 hours IV in four to six divided doses **or** Ampicillin 12 g per 24 hours (or 100 to 200 mg/kg per 24 hours) IV in six divided doses **or** Ceftriaxone[¶ǁ] 2 g per 24 hours IV or IM in one dose **or** Vancomycin° 30 mg/kg per 24 hours IV in two divided doses	Benzylpenicillin[#] 1.2 g every 4 hours IV **or** Ceftriaxone 2 g per 24 hours IV/IM
2-week regimens[†]:	**2-week regimens[†]:**	**2-week regimens[Δ†]:**	**2-week regimens[†]:**
Either Aqueous penicillin G 12 to 18 million units per 24 hours IV either continuously or in six divided doses **or** Ceftriaxone 2 g per 24 hours IV or IM in one dose **plus** Gentamicin[**] 3 mg/kg per 24 hours IV or IM in one dose (preferred) or in three divided doses	Not recommended for children due to lack of data	**Either** Aqueous penicillin G 12 to 18 million units per 24 hours IV in four to six divided doses or continuous infusion **or** Amoxicillin 100 to 200 mg/kg per 24 hours IV in four to six divided doses **or** Ampicillin 12 g (or 100 to 200 mg/kg) per 24 hours IV in six divided doses **or** Ceftriaxone[¶ǁ] 2 g per 24 hours IV or IM in one dose **plus** Gentamicin[**,¶¶] 3 mg/kg per 24 hours IV or IM in one dose	**Either** Benzylpenicillin[#] 1.2 g every 4 hours IV **or** Ceftriaxone 2 g per 24 hours IV or IM **plus** Gentamicin[**] 1 mg/kg every 12 hours IV

Treatment regimens for native valve endocarditis due to strains of viridans streptococci and *Streptococcus bovis* relatively resistant to penicillin G (MIC >0.12 mcg/mL and <0.5 mcg/mL)*

American Heart Association (AHA)		European Society of Cardiology*¶ (ESC)	British Society for Antimicrobial Chemotherapy (BSAC)
Adult	**Pediatric**		
Combination: **Either** Aqueous penicillin G 24 million units per 24 hours IV either continuously or in four or six divided doses for four weeks **or** Ampicillin 2 g IV every 4 hours for four weeks **plus** Gentamicin[Δ] 3 mg/kg per 24 hours IV or IM in one dose for first two weeks **or** **Monotherapy:** **Either** Vancomycin[◇] 30 mg/kg per 24 hours IV in two divided doses for four weeks **or** Ceftriaxone 2 g per 24 hours IV or IM in one dose for four weeks	**Combination:** **Either** Aqueous penicillin G 200,000 to 300,000 units/kg per 24 hours IV in six divided doses (maximum dose: 24 million units per 24 hours) for four weeks **or** Ampicillin 200 to 300 mg/kg per 24 hours IV divided in four or six divided doses (maximum dose: 12 g per 24 hours) for four weeks **or** Ceftriaxone 100 mg/kg per 24 hours IV[‡] in two divided doses or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) for four weeks **plus** Gentamicin[Δ] 3 to 6 mg/kg per 24 hours IV in three divided doses for first two weeks **Beta-lactam-intolerant patients:** Vancomycin[◇] 40 mg/kg per 24 hours IV in two or three divided doses (maximum dose: 2 g per 24 hours unless levels are inappropriately low) **plus** gentamicin (dosing as above) for four weeks	**Combination:** **Either** Aqueous penicillin G 24 million units per 24 hours IV in four or six divided doses or continuous infusion for four weeks **or** Amoxicillin 200 mg/kg per 24 hours IV in four or six divided doses for four weeks **or** Ampicillin 12 g per 24 hours (200 mg/kg per 24 hours) in six divided doses for four weeks **or** Ceftriaxone[§] 2 g per 24 hours IV or IM in one dose for four weeks **plus** Gentamicin[Δ§] 3 mg/kg per 24 hours IV or IM in one dose for two weeks **OR** Vancomycin[◇] 30 mg/kg per 24 hours IV in two divided doses for four weeks **plus** Gentamicin[Δ] 3 mg/kg per 24 hours IV or IM in one dose for first two weeks	**Combination:** Benzylpenicillin[¥] 2.4 g every 4 hours IV for four to six weeks **plus** Gentamicin[Δ] 1 mg/kg every 12 hours IV for two weeks

Suggested regimens for therapy of native or prosthetic valve endocarditis due to enterococcal strains susceptible to penicillin and gentamicin*

American Heart Association (AHA)		European Society of Cardiology (ESC)	British Society for Antimicrobial Therapy (BSAC)
Adult dose	**Pediatric dose¶**	**Adult dose△**	**Adult dose**
Aminoglycoside combination regimen◇		**Aminoglycoside combination regimen**	**Aminoglycoside combination regimen**
Aqueous penicillin G 18 to 30 million units per 24 hours IV continuously or in six divided doses for four to six weeks§ **or** Ampicillin 2 g IV every 4 hours for four to six weeks§ **plus** Gentamicin‡ 3 mg/kg per 24 hours IV or IM in three divided doses for four to six weeks§	Aqueous penicillin G 200,000 to 300,000 units/kg per 24 hours IV in six divided doses (maximum dose: 24 million units per 24 hours) for four to six weeks§ **or** Ampicillin 200 to 300 mg/kg per 24 hours IV divided in four or six divided doses (maximum dose: 12 g per 24 hours) for four to six weeks§ **plus** Gentamicin‡ 3 to 6 mg/kg per 24 hours IV in two or three divided doses for four to six weeks§	Amoxicillin 200 mg/kg per 24 hours IV in four or six divided doses for four to six weeks **or** Ampicillin 12 g per 24 hours (200 mg/kg per 24 hours) IV in four or six divided doses for four to six weeks **plus** Gentamicin‡ 3 mg/kg per 24 hours IV or IM in one dose for four to six weeks	Amoxicillin 2 g every 4 hours IV for four to six weeks **or** Penicillin 2.4 g every 4 hours IV for four to six weeks **plus** Gentamicin‡ 1 mg/kg every 12 hours IV for four to six weeks
Beta-lactam combination regimen◆†		**Beta-lactam combination regimen†**	
Ceftriaxone 2 g IV every 12 hours for six weeks **plus** Ampicillin 2 g IV every 4 hours for six weeks	Ceftriaxone 100 mg/kg per 24 hours IV in two divided doses or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) for six weeks **plus** Ampicillin (dosing as above) for six weeks	Ceftriaxone 2 g IV every 12 hours for six weeks **plus** Ampicillin (dosing as above) for six weeks	

Suggested regimens for therapy of native or prosthetic valve endocarditis due to enterococcal strains resistant to penicillin and susceptible to vancomycin and aminoglycosides*

American Heart Association (AHA)[¶]		European Society of Cardiology (ESC)	British Society for Antimicrobial Therapy (BSAC)
Adult dose	**Pediatric dose**	**Adult dose**	**Adult dose**
Strains with intrinsic penicillin resistance[Δ]			
Vancomycin[◊] 30 mg/kg per 24 hours IV in two divided doses for six weeks **plus** Gentamicin[§] 3 mg/kg per 24 hours IV or IM in three divided doses for six weeks	Vancomycin[◊] 40 mg/kg per 24 hours IV (maximum dose: 2 g per 24 hours unless levels are inappropriately low) in two or three divided doses for six weeks **plus** Gentamicin[§] 3 to 6 mg/kg per 24 hours IV in three divided doses for six weeks	Vancomycin[◊] 30 mg/kg per 24 hours IV in two divided doses for six weeks **plus** Gentamicin[§] 3 mg/kg per 24 hours IV or IM in one dose for six weeks	Vancomycin[◊] 1 g IV every 12 hours for four to six weeks[†] **or** Teicoplanin[¥] 10 mg/kg IV once daily for four to six weeks[†] **plus** Gentamicin[§] 1 mg/kg IV every 8 to 12 hours for four to six weeks[†]
Beta-lactamase-producing strains			
Ampicillin-sulbactam[•] 3 g every 6 hours IV for six weeks **or** Vancomycin[◊] 30 mg/kg per 24 hours IV in two divided doses for six weeks **plus** Gentamicin[§] 3 mg/kg per 24 hours IV or IM in three divided doses for six weeks	See above	Ampicillin-sulbactam[•] 12 g per 24 hours (or 300 mg/kg per 24 hours) IV in four equally divided doses for four to six weeks[†] **or** Amoxicillin-clavulanate[•] 200 mg/kg (amoxicillin component) per 24 hours IV in six equally divided doses for four to six weeks[†] **or** Vancomycin[◊] 30 mg/kg per 24 hours IV in two divided doses for six weeks **plus** Gentamicin[§] 3 mg/kg per 24 hours IV or IM in one dose for four to six weeks[†]	

The doses in this table are intended for patients with normal renal function. The doses of many of these agents must be adjusted in the

Suggested regimens for therapy of native or prosthetic valve endocarditis due to enterococcal strains susceptible to penicillin and resistant to gentamicin*

American Heart Association (AHA)		European Society of Cardiology (ESC)	British Society for Antimicrobial Therapy (BSAC)
Adult dose	**Pediatric dose**	**Adult dose**	**Adult dose**
Aminoglycoside combination regimen[1]		**Aminoglycoside combination regimen**[1]	**Aminoglycoside combination regimen**[1]
Ampicillin 2 g IV every 4 hours for four to six weeks[Δ] **or** Aqueous penicillin G 18 to 30 million units per 24 hours continuously or in six divided doses for four to six weeks[Δ] **plus** Streptomycin[◊] 15 mg/kg per 24 hours IV or IM in two divided doses for four to six weeks[Δ]	Consultation with a pediatric infectious disease expert is recommended in all cases of enterococcal infective endocarditis	Amoxicillin 200 mg/kg/day in four to six doses for four to six weeks[Δ] **or** Ampicillin 12 g per day (200 mg/kg per day) in four or six doses for four to six weeks[Δ] **plus** Streptomycin[◊] 15 mg/kg per 24 hours IV or IM in two divided doses for four to six weeks[Δ]	Amoxicillin 2 g every 4 hours IV for four to six weeks[Δ] **with or without** Streptomycin[◊] 15 mg/kg per 24 hours IM in two divided doses for four to six weeks[Δ]
Beta-lactam combination regimen[§]			
Ceftriaxone 2 g IV every 12 hours for six weeks **plus** Ampicillin 2 g IV every 4 hours for six weeks	Ceftriaxone 100 mg/kg per 24 hours IV in two divided doses or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) for six weeks **plus** Ampicillin 200 to 300 mg/kg per 24 hours IV divided in four to six divided doses (maximum dose: 12 g per 24 hours) for six weeks	Ceftriaxone 2 g IV every 12 hours for six weeks **plus** Ampicillin 2 g IV every 4 hours for six weeks	

Suggested regimens for therapy of native or prosthetic valve endocarditis due to to enterococcal strains resistant to penicillin, aminoglycosides, and vancomycin*

American Heart Association (AHA)		European Society of Cardiology (ESC)
Adult dose	**Pediatric dose**	**Adult dose**
Linezolid¶ 600 mg IV or orally every 12 hours for >6 weeks **or** Daptomycin$^{\Delta}$ 10 to 12 mg/kg IV every 24 hours for >6 weeks **or** Alternative regimens (ie, daptomycin plus ampicillin, or ceftaroline) may be reasonable in patients with persistent bacteremia or strains with daptomycin MIC at high end of susceptible range	Consultation with a pediatric infectious disease specialist is recommended	Daptomycin 10 mg/kg per 24 hours IV once per day for ≥8 weeks **plus** Ampicillin 12 g per 24 hours (or 200 mg/kg per 24 hours) IV in six divided doses for ≥8 weeks **OR** Linezolid¶ 1200 mg per 24 hours IV or orally in two divided doses for ≥8 weeks **OR** Quinupristin-dalfopristin$^{\diamond}$ 22.5 mg/kg per 24 hours IV in three divided doses for ≥8 weeks **OR** Combinations of antibiotics according to in vitro susceptibility§ (eg, daptomycin plus ertapenem or ceftaroline)

İnfektif Endokardit (tedavi)

Daptomisin

- Henüz bütün Avrupa ülkelerinde kullanılabilir durumda değil
- Stafilokokal endokardit tedavisinde **alternatif tedavi**

Optimal stafilokokal İE tedavisi hala tartışmalı

Suggested regimens for therapy of native valve endocarditis due to staphylococcus

American Heart Association		British Society for Antimicrobial Chemotherapy	European Society of Cardiology*
Adult (for patients with normal renal function)	**Pediatric (not to exceed dose of normal adult)**		
Oxacillin-susceptible strains•Δ	**Oxacillin-susceptible strains•**	**Methicillin-sensitive**	**Methicillin-susceptible strains**
Nafcillin or oxacillin 12 g per 24 h IV in 4 or 6 equally divided doses for 6 wks, **or** Cefazolin§ 6 g per 24 h IV in 3 equally divided doses for 6 wks,	Nafcillin or oxacillin 200 mg/kg per 24 h IV in 4 or 6 equally divided doses for 6 wks **or** Cefazolin§ 100 mg/kg per 24 h IV in 3 equally divided doses for 6 wks	Flucloxacillin 2 g IV every 4 to 6 hours for 4 wks	Oxacillin or cloxacillin or flucloxacillin 12 g per 24 h IV in 4-6 equally divided doses for 4 to 6 wks Vancomycin¥ 30 mg/kg per 24 h IV in 2 equally divided doses for 4 to 6 wks
Oxacillin-resistant strains	**Oxacillin-resistant strains**	**Methicillin resistant**	**Methicillin resistant strains**
Vancomycin¥ 30 mg/kg per 24 h IV in 2 equally divided doses for 6 wks; not to exceed 2 g per 24 h unless concentrations in serum are inappropriately low	Vancomycin¥ 40 mg/kg per 24 h IV in 2 or 3 equally divided doses for 6 wks	Vancomycin¥ 1 g IV every 12 h for 4 wks **plus** Rifampin 300 to 600 mg PO every 12 h for 4 wks	Vancomycin¥ 30 mg/kg per 24 h IV in 2 doses for 4 to 6 wks

Treatment regimens for native valve endocarditis due to *Staphylococcus*

American Heart Association (AHA)		European Society of Cardiology* (ESC)	British Society for Antimicrobial Chemotherapy (BSAC)
Adult	**Pediatric**		
Methicillin-susceptible strains¶	**Methicillin-susceptible strains**	**Methicillin-susceptible strains△**	**Methicillin sensitive**
Nafcillin or oxacillin 12 g per 24 hours IV in four or six divided doses for 6 weeks **or** Cefazolin° 6 g per 24 hours IV in three divided doses for 6 weeks	Nafcillin or oxacillin 200 mg/kg per 24 hours IV (maximum dose: 12 g per 24 hours) in four or six divided doses for 4 to 6 weeks **or** Cefazolin° 100 mg/kg per 24 hours IV (maximum dose: 12 g per 24 hours) in three divided doses for 4 to 6 weeks	Oxacillin or cloxacillin or flucloxacillin 12 g per 24 hours IV in four or six divided doses for 4 to 6 weeks **or** Cefazolin° 6 g per 24 hours IV in three divided doses for 6 weeks **or** Cefotaxime° 6 g per 24 hours in three divided doses	Flucloxacillin 2 g IV every 4 to 6 hours for 4 weeks
Methicillin-resistant strains	**Methicillin-resistant strains§**	**Methicillin-resistant strains△**	**Methicillin resistant**
Vancomycin¥ 30 mg/kg per 24 hours IV in two divided doses for 6 weeks **or** Daptomycin ≥8 mg/kg† per 24 hours IV once daily for 6 weeks	Vancomycin¥ 40 mg/kg per 24 hours IV (maximum dose: 2 g per 24 hours unless levels are inappropriately low) in two or three divided doses for 6 weeks	Vancomycin¥ 30 to 60 mg/kg per 24 hours IV in two or three divided doses for 4 to 6 weeks **or** Daptomycin† 10 mg/kg per 24 hours IV once daily for 4 to 6 weeks	Vancomycin¥ 1 g IV every 12 hours for 4 weeks **plus** Rifampicin 300 to 600 mg orally every 12 hours for 4 weeks **OR** Daptomycin 6 mg/kg IV every 24 hours for 4 weeks **plus** Rifampicin 300 to 600 mg orally every 24 hours for 4 weeks **or** Gentamicin 1 mg/kg IV every 12 hours for 4 weeks

YENİ

İnfektif Endokardit(tedavi)

Rifampisin

- Yabancı cisim varlığında
- Etkili antistafilokokal antibiyotik tedavisi verildikten 3-5 gün sonra
- Yüksek bakteri yoğunluğunda, rifampisine dirençli subpopulasyonlarla karşılaşılabilir.

Suggested regimens for therapy of prosthetic valve endocarditis due to *Staphylococcus* species

American Heart Association (AHA)		European Society of Cardiology (ESC)
Adult	**Pediatric***	**Adult**
Methicillin-susceptible strains	**Methicillin-susceptible strains**	**Methicillin-susceptible strains**
One of the following¶: Nafcillin or oxacillin 12 g per 24 hours IV in six divided doses for ≥6 weeks **or** Cefazolin△ 6 g per 24 hours IV in three divided doses for ≥6 weeks **plus** Rifampin◇ 900 mg per 24 hours IV or orally in three divided doses for ≥6 weeks **plus** Gentamicin§¥ 3 mg/kg per 24 hours IV or IM in two or three divided doses for 2 weeks	**One of the following¶:** Nafcillin or oxacillin 200 mg/kg per 24 hours IV (maximum dose: 12 g per 24 hours) in four or six divided doses for ≥6 weeks **or** Cefazolin△ 100 mg/kg per 24 hours IV (maximum dose: 12 g per 24 hours) in three divided doses for ≥6 weeks **plus** Rifampin◇ 20 mg/kg per 24 hours IV (maximum dose: 900 mg per 24 hours) in three divided doses for ≥6 weeks **plus** Gentamicin§¥ 3 to 6 mg/kg per 24 hours IV or IM in three divided doses for first 2 weeks	**One of the following¶:** Oxacillin or cloxacillin or flucloxacillin 12 g per 24 hours IV in four or six divided doses for ≥6 weeks **or** Cefazolin△ 6 g per 24 hours IV in three divided doses for ≥6 weeks **or** Cefotaxime△ 6 g per 24 hours IV in three divided doses for ≥6 weeks **plus** Rifampin◇ 900 to 1200 mg per 24 hours IV or orally in two or three divided doses for ≥6 weeks **plus** Gentamicin§ 3 mg/kg per 24 hours IV or IM in one or two doses for the first 2 weeks
Methicillin-resistant strains	**Methicillin-resistant strains**	**Methicillin-resistant strains**
Vancomycin* 30 mg/kg per 24 hours IV in two divided doses for ≥6 weeks **plus** Rifampin◇ 900 mg per 24 hours IV or orally in three divided doses for ≥6 weeks **plus** Gentamicin§¥ 3 mg/kg per 24 hours IV or IM in two or three divided doses for 2 weeks	Vancomycin* 40 mg/kg per 24 hours IV (maximum dose: 2 g per 24 hours) in two or three divided doses for ≥6 weeks **plus** Rifampin◇ (see dosing above) for ≥6 weeks **plus** Gentamicin§¥ (see dosing above) for first 2 weeks	Vancomycin* 30 to 60 mg/kg per 24 hours IV in two or three divided doses for ≥6 weeks **plus** Rifampin◇ 900 to 1200 mg per 24 hours IV or orally in two or three divided doses for ≥6 weeks **plus** Gentamicin§ 3 mg/kg per 24 hours IV or IM in one or two divided doses for first 2 weeks

Suggested regimens for therapy of prosthetic valve endocarditis due to penicillin-susceptible viridans streptococci and *Streptococcus gallolyticus* (*bovis*) (MIC ≤0.12 mcg/mL)*

American Heart Association (AHA)		European Society of Cardiology (ESC)
Adult	**Pediatric (not to exceed dose of normal adult)**	**Adult**
Either Aqueous penicillin G 24 million units per 24 hours IV either continuously or in four or six divided doses for six weeks **or** Ampicillin 2 g IV every 4 hours for six weeks **or** Ceftriaxone[¶] 2 g per 24 hours IV in one dose for six weeks **with or without** Gentamicin[Δ◇] 3 mg/kg per 24 hours IV or IM in one dose for first two weeks **Beta-lactam-intolerant patients:** Vancomycin[§] 30 mg/kg per 24 hours IV in two divided doses for six weeks	**Either** Aqueous penicillin G 200,000 to 300,000 units/kg per 24 hours IV in six divided doses (maximum dose: 24 million units per 24 hours) for six weeks **or** Ampicillin 200 to 300 mg/kg per 24 hours IV divided in four or six divided doses (maximum dose: 12 g per 24 hours) for six weeks **or** Ceftriaxone 100 mg/kg per 24 hours IV in two divided doses or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) for six weeks **plus** Gentamicin[Δ◇] 3 to 6 mg/kg per 24 hours IV in three divided doses for first two weeks **Beta-lactam-intolerant patients:** Vancomycin[§] 40 mg/kg per 24 hours IV in two or three divided doses (maximum dose: 2 g per 24 hours unless levels are inappropriately low) for six weeks **plus** gentamicin (dosing as above) for first two weeks	**Either** Aqueous penicillin G 12 to 18 million units per 24 hours IV in four or six divided doses or continuously for six weeks **or** Amoxicillin 100 to 200 mg/kg per 24 hours IV in four or six divided doses for six weeks **or** Ampicillin 12 g per 24 hours (or 100 to 200 mg/kg per 24 hours) IV in four or six divided doses for six weeks **or** Ceftriaxone[¶] 2 g per 24 hours IV in one dose for six weeks **or** Vancomycin[§] 30 mg/kg per 24 hours IV in two divided doses for six weeks

Suggested regimens for therapy of prosthetic valve endocarditis due to strains of viridans streptococci and *Streptococcus gallolyticus* (*bovis*) relatively or fully resistant to penicillin G (MIC >0.12 mcg/mL)*

American Heart Association (AHA)		European Society of Cardiology* (ESC)
Adult	**Pediatric**	**Adult**
Combination: **Either** Aqueous penicillin G 24 million units per 24 hours IV either continuously or in four or six divided doses for six weeks **or** Ampicillin 2 g IV every 4 hours for six weeks **or** Ceftriaxone¶ 2 g/24 hours IV in one dose for six weeks **plus** Gentamicin$^{\Delta}$ 3 mg/kg per 24 hours IV or IM in three divided doses for two to six weeks **Monotherapy:** Vancomycin◇ 30 mg/kg per 24 hours IV in two divided doses for six weeks	**Combination:** **Either** Aqueous penicillin G 200,000 to 300,000 units/kg per 24 hours IV in six divided doses (maximum dose: 24 million units per 24 hours) for six weeks **or** Ampicillin 200 to 300 mg/kg per 24 hours IV divided in four or six divided doses (maximum dose: 12 g per 24 hours) for six weeks **or** Ceftriaxone 100 mg/kg per 24 hours IV in two divided doses or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) for six weeks **plus** Gentamicin$^{\Delta}$ 3 to 6 mg/kg per 24 hours IV in three divided doses for six weeks **Beta-lactam-intolerant patients:** Vancomycin◇ 40 mg/kg per 24 hours IV in two or three divided doses (maximum dose: 2 g per 24 hours unless levels are inappropriately low) for six weeks **plus** gentamicin (dosing as above) for first two weeks	**Combination:** **Either** Aqueous penicillin G 24 million units per 24 hours IV in four or six divided doses or continuously for six weeks **or** Amoxicillin 200 mg/kg per 24 hours IV in four or six divided doses for six weeks **or** Ceftriaxone¶ 2 g per 24 hours IV in one dose for six weeks **or** Ampicillin 12 g per 24 hours (or 200 mg/kg per 24 hours) in four or six divided doses for six weeks **or** Vancomycin◇ 30 mg/kg per 24 hours IV in two doses for six weeks **plus** Gentamicin$^{\Delta}$ 3 mg/kg per 24 hours IV or IM in one dose for six weeks

Suggested regimens for therapy of native or prosthetic valve endocarditis due to HACEK* microorganisms

American Heart Association (AHA)		European Society of Cardiology (ESC)
Adult	**Pediatric**	**Adult**
One of the following: Ceftriaxone¶ 2 g per 24 hours IV in one dose for 4 weeks$^{\Delta}$ **or** Ampicillin$^{\diamond}$ 2 g IV every 4 hours for 4 weeks$^{\Delta}$ **or** Ciprofloxacin§ 1000 mg per 24 hours orally in two divided doses or 800 mg per 24 hours IV in two divided doses for 4 weeks$^{\Delta}$	**Monotherapy:** Ceftriaxone¶ 100 mg/kg per 24 hours IV in two divided doses, or 80 mg/kg in one daily dose (maximum dose: 4 g per 24 hours; if dose is >2 g per 24 hours, use divided dosing every 12 hours) for 4 weeks$^{\Delta}$ **or** Cefotaxime 200 mg/kg per 24 hours IV in four divided doses (maximum dose: 12 g per 24 hours) for 4 weeks$^{\Delta}$ **Combination therapy:** Ampicillin$^{\diamond}$ 200 to 300 mg/kg per 24 hours IV divided in four or six divided doses (maximum dose: 12 g per 24 hours) for 4 weeks$^{\Delta}$ **plus** Gentamicin¥ 3 to 6 mg/kg per 24 hours IV in three divided doses for 4 weeks$^{\Delta}$	**One of the following:** Ceftriaxone¶ 2 g per 24 hours IV in one dose for 4 weeks$^{\Delta}$ **or** Combination therapy with: Ampicillin$^{\diamond}$ 12 g per 24 hours IV in six divided doses **plus** Gentamicin¥ 3 mg/kg per 24 hours IV or IM in two or three divided doses for 4 to 6 weeks$^{\Delta}$ **or** Ciprofloxacin§ 750 mg every 12 hours orally or 400 mg every 8 or 12 hours IV for 4 weeks$^{\Delta}$

*Haemophilus spp,Aggregatibacter(Actinobacillus actinomycetemcomitans), Cardiobacterium hominis, Eikenella corrodens, Kingella kingae

Kültür negatif İE

- En yaygın ajanlar müşkülpesent mikroorganizmalar
  - Zoonotik ajanlar(*Coxiella burnetii*,*Bartonella* spp)
  - Mantarlar,
  - Antibiyotik kullanmış hastalarda streptokoklar
- Akut semptomlar ➡ *S. aureus*, beta-hemolitik streptokoklar ve gram-negatif basiller ➡ vankomisin ve sefepim
- Subakut semptomlar ➡ *S. aureus*, viridans streptokoklar, HACEK grubu ve enterokoklar ➡ vankomisin ve ampisilin-sulbaktam

Kültür negatif İE tedavisi

Table 19 Antibiotic treatment of blood culture-negative infective endocarditis (adapted from Brouqui *et al.*[193])

Pathogens	Proposed therapy[a]	Treatment outcome
Brucella spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600/24 h) for ≥3–6 months[b] orally	Treatment success defined as an antibody titre <1:60. Some authors recommend adding gentamicin for the first 3 weeks.
C. burnetii (agent of Q fever)	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally (>18 months of treatment)	Treatment success defined as anti-phase I IgG titre <1:200, and IgA and IgM titres <1:50.
Bartonella spp.[d]	Doxycycline 100 mg/12 h orally for 4 weeks plus gentamicin (3 mg/24 h) i.v. for 2 weeks	Treatment success expected in ≥90%.
Legionella spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 weeks or clarithromycin (500 mg/12 h) i.v. for 2 weeks, then orally for 4 weeks plus rifampin (300–1200 mg/24 h)	Optimal treatment unknown.
Mycoplasma spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 months[e]	Optimal treatment unknown.
T. whipplei (agent of Whipple's disease)[f]	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally for ≥18 months	Long-term treatment, optimal duration unknown.

İnfektif Endokardit (Cerrahi tedavi)

İki primer objektif cerrahi müdahale:

1. İnfekte dokuların çıkarılması
2. Kalp anatomisinin rekonstrüksiyonu (İnfekte kapakların tamiri veya replasmanı dahil)

Sol kapak endokarditinde cerrahi indikasyonları ve zamanı

Table 22 Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)

Indications for surgery	Timing[a]	Class[b]	Level[c]	Ref.[d]
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	111,115, 213,216
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	37,115, 209,216, 220,221
2. Uncontrolled infection				
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B	37,209, 216
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	123
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	9,58,72, 113,222
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent	IIa	B	9
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent	IIa	B	113
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery[e]	Urgent	IIb	C	

Sağ kapak endokarditi cerrahi indikasyonları

Table 26 Indications for surgical treatment of right-sided infective endocarditis

Recommendation	Class[a]	Level[b]
Surgical treatment should be considered in the following scenarios: • Microorganisms difficult to eradicate (e.g. persistent fungi) or bacteraemia for > 7 days (e.g. *S. aureus*, *P. aeruginosa*) despite adequate antimicrobial therapy or • Persistent tricuspid valve vegetations > 20 mm after recurrent pulmonary emboli with or without concomitant right heart failure or • Right HF secondary to severe tricuspid regurgitation with poor response to diuretic therapy	IIa	C

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1. Profilaksi
2. Endokardit ekibi
3. Tanı
4. Tedavi
5. **Özel durumlar**

Özel durumlar

- Yoğun Bakım'da İE
- Kanser ilişkili İE
- Marantik (nonbakteriyel) İE
- Gebelikte İE
- İmplante elektronik alet
- Sağ taraf İE
- Kongenital kalp hastalığı
- Antitrombotik tedavi


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