[Endokardit: Son Durum] Tedavide Yenilikler

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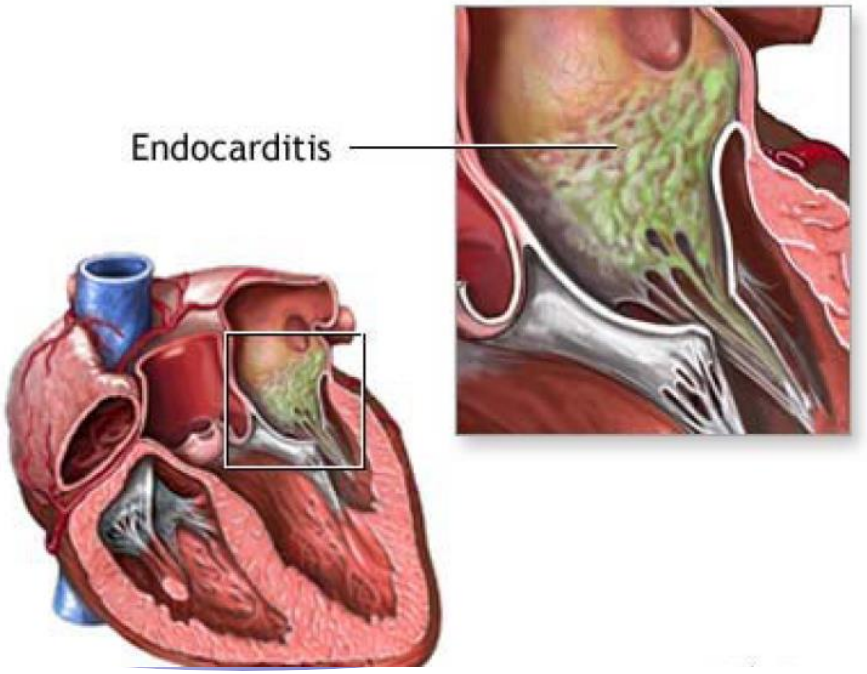
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji ABD

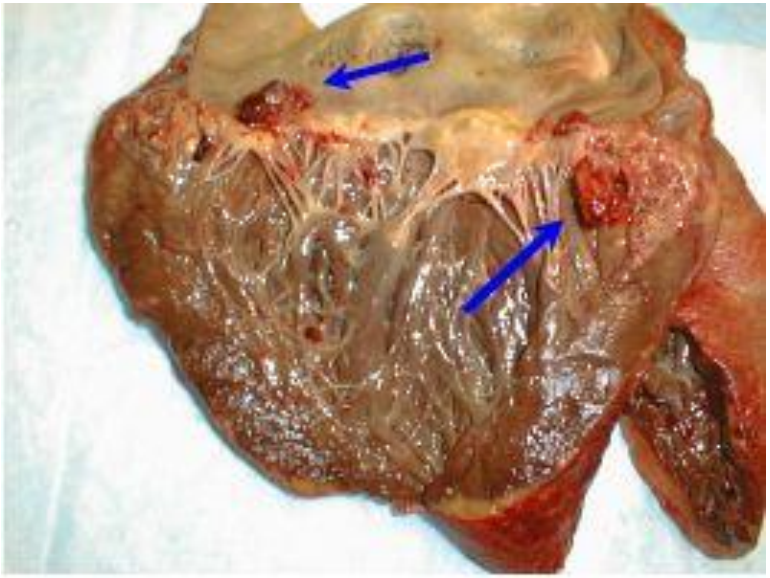
Endokardit

- Kalbin endokardiyal yüzeyinin infeksiyonu
- 2 Tip:
  - *Subakut*
  - *Akut*



Fizyopatoloji

Kalpte kan akımı türbülansının daha önceden zedelenmiş kapaklara veya endokardiyal yüzeylere etken mikroorganizmanın yerleşmesine olanak tanıması ile meydana gelir.



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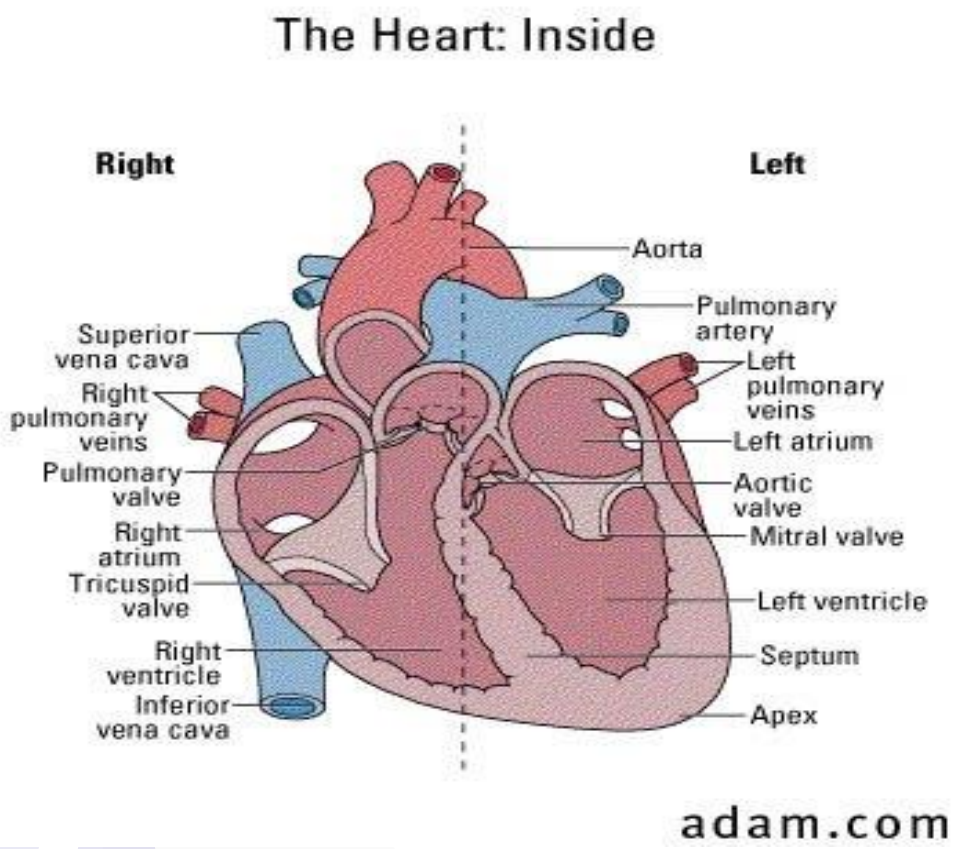


Endoteliyal zedelenme

↓

Platelet-fibrin trombüs

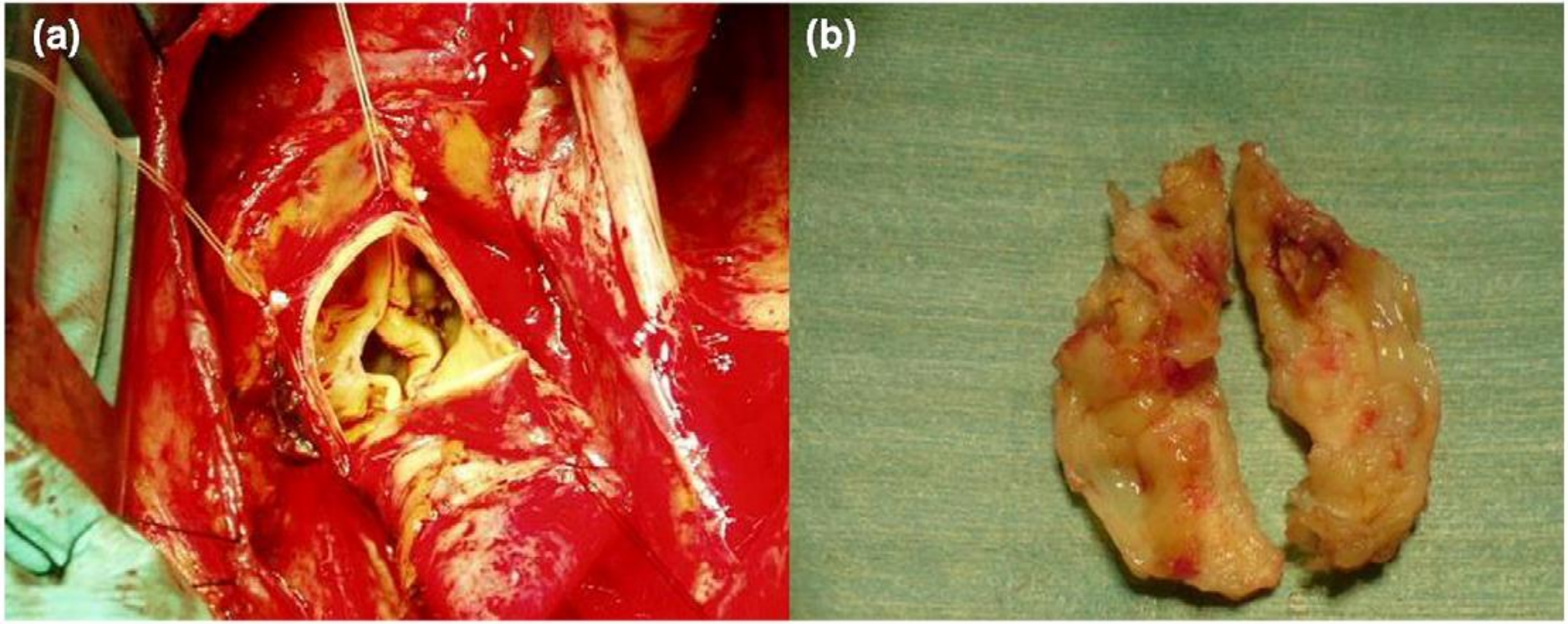
↓

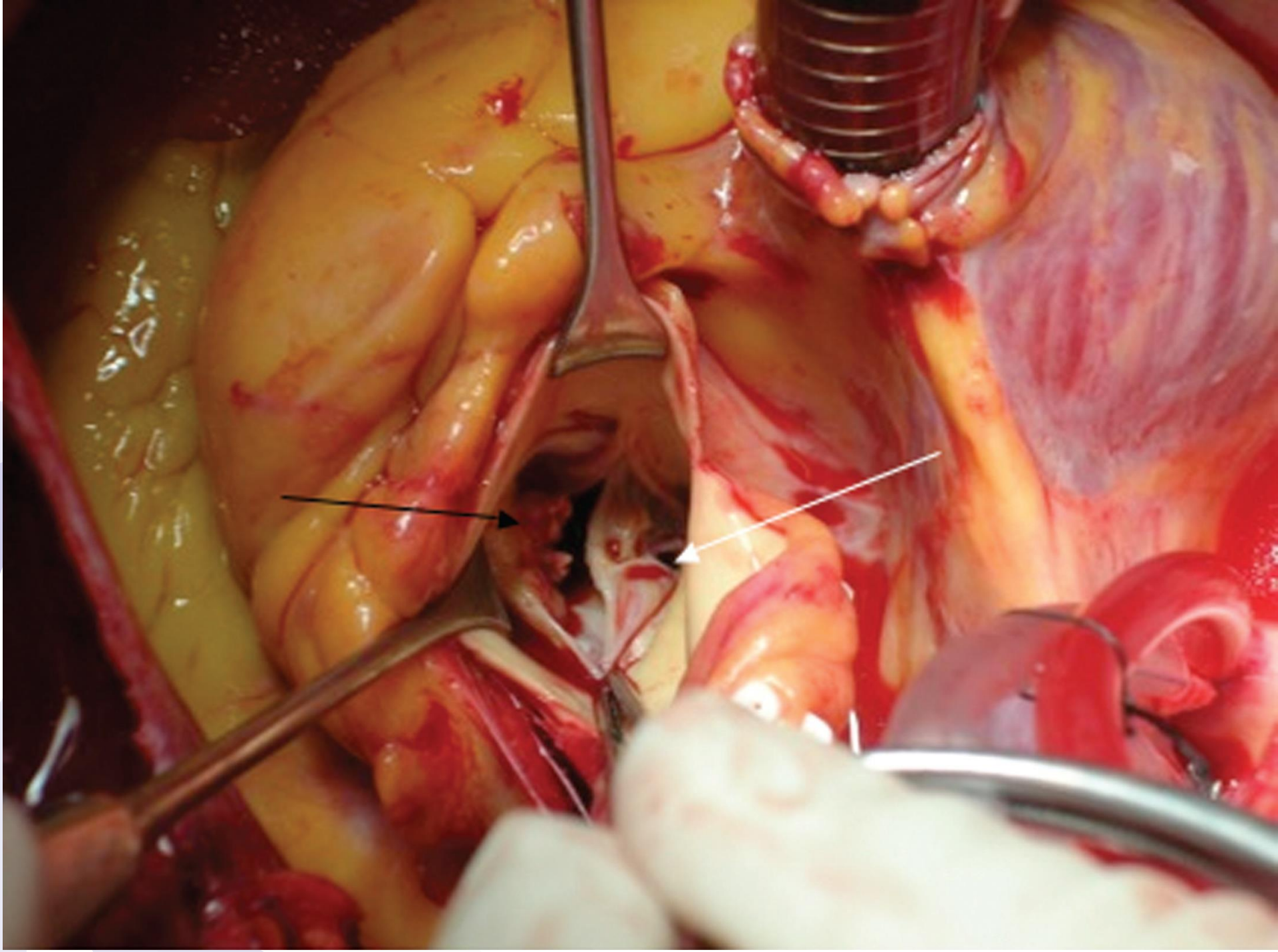
Bakteriyemi

↓

Mikroorganizmaların yerleşmesi

Wilson W, et al. Circulation. 2007;115.


(a)
(b)



Fizyopatoloji

- Klinik bulgular
  - Direk
    - İnfeksiyonun konstitüsyonel semptomları (sitokin)
  - Indirek
    - İnfeksiyonun lokal zedeleyici etkileri
    - Emboli
    - Hematojen yayılım
    - Immun cevap
      - » Immun kompleks veya kompleman aracılı

Tanı
Modifiye Duke Kriterleri

- **Major Kriterler**
  - Pozitif kan kültürü (IE'e özgün mikroorganizma)
  - Persistan pozitif kan kültürü
  - Endokardiyal tutulum varlığı
    - Pozitif Ekokardiyografi
      - İntrakardiyak hareket eden kitle
      - Apse
      - Prostetik kapağın bozulması
    - Yeni üfürüm

Modifiye Duke Kriterleri

- **Minör Kriterler**
  - Predispozisyon (kapak hastalığı ve intrakardiyal araç)
  - Ateş > 38.0° C
  - Vasküler fenomen (Arteriyel emboli, septik pulmoner infarkt, mikotik anavrizma, intracraniyal kanama, Osler, Janeway)
  - İmmunolojik fenomen (GN, Osler nodülü, Roth lekeleri, Romatoid Faktör)
  - Mikrobiyolojik kanıt: Major kriteri karşılamayan kan kültürü pozitifliği veya IE ile uyumlu mikroorganizma ile aktif infeksiyonu gösteren serolojik kanıt

Modifiye Duke Kriterleri

- **Kesin IE**
  - Patolojik Kriter

    -Vejetasyondan alınan kültürden üreme veya histojojik incelemede mikroorganizma görülmesi

    veya

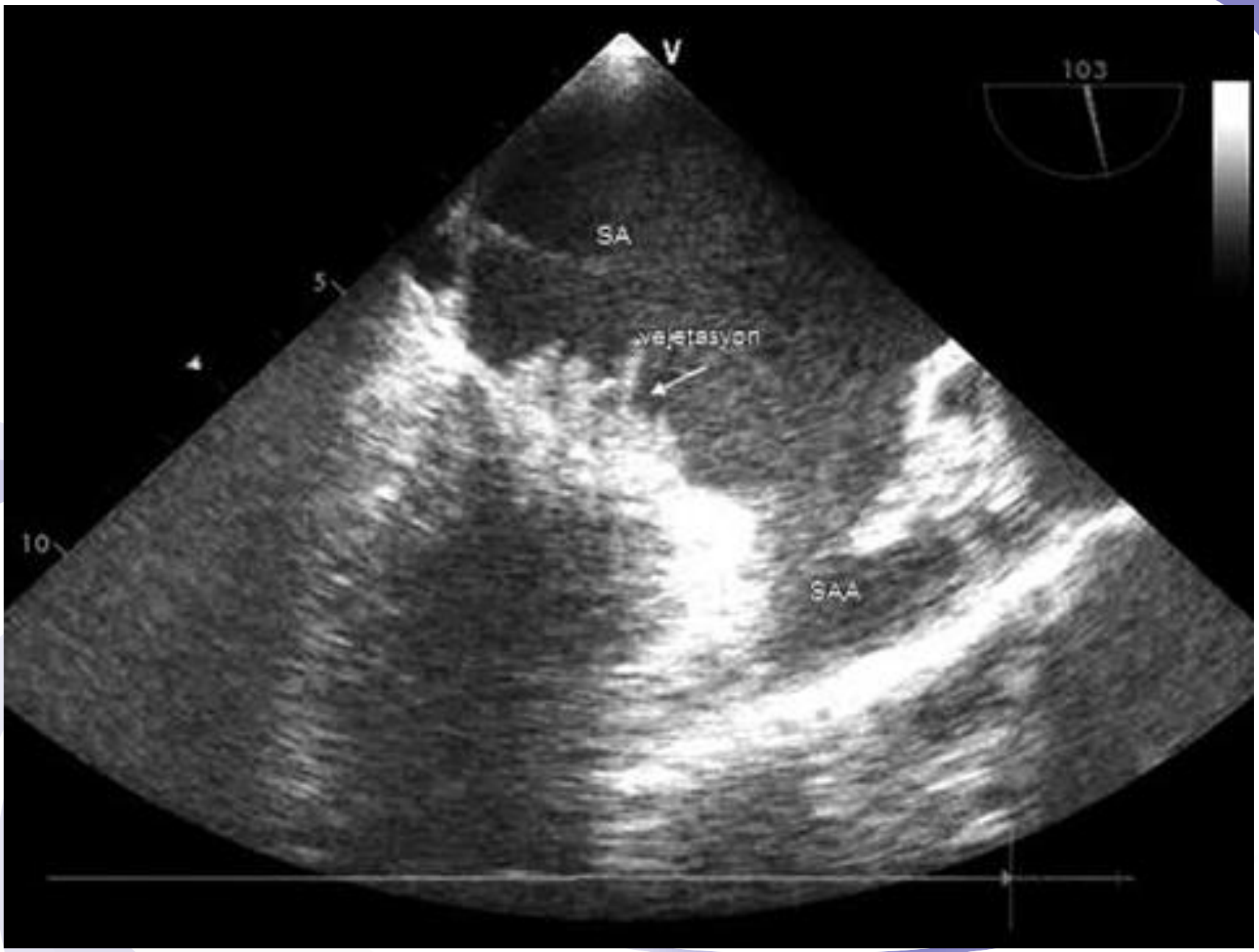
    -Vejetasyon veya intrakardiyak apsenin histopatolojik incelemesi sonucu aktif IE tanısı
  - Klinik Kriterler

    - 2 major kriter; veya

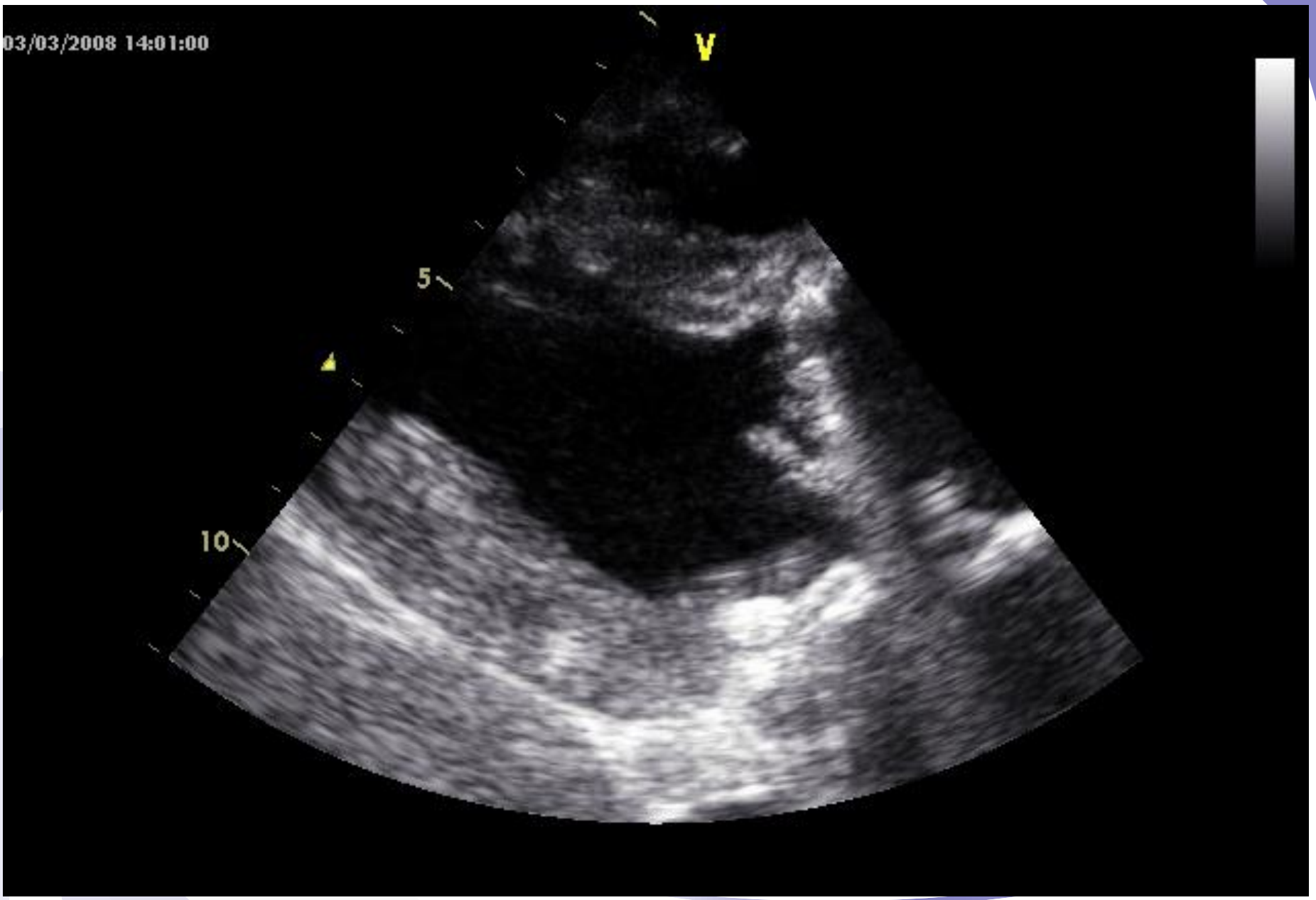
    - 1 major kriter + 3 minör kriter; veya

    - 5 minör kriter
- Olası IE
  - 1 major kriter + 1 minör kriter; veya
  - 3 minör kriter

Ekokardiyografi	Sensitivite
TTE	60%
TEE	80 – 95%



TEE, vegetation on mitral valve



TTE, vegetation on prostetic aortic valve

Etken

Organism	Percentage of Cases							
	Native Valve Endocarditis		Prosthetic Valve Endocarditis at Indicated Time of Onset (Months) after Valve Surgery			Endocarditis in Injection Drug Users		
	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	—	—	—	—	—	—	—
Enterococci	9	13	8	12	11	2	24	9
Staphylococcus aureus	**28**	**53**[c]	**22**	**12**	18	**77**	**23**	**57**
Coagulase-negative staphylococci	5	12	**33**	**32**	11	—	—	—
Fastidious gram-negative coccobacilli (HACEK group)[d]	3	—	—	—	6	—	—	—
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

Karchmer, **Infective Endocarditis, Harrison's Principles of Internal Medicine, 18e**

Infective Endocarditis Epidemiology Over Five Decades: A Systematic Review

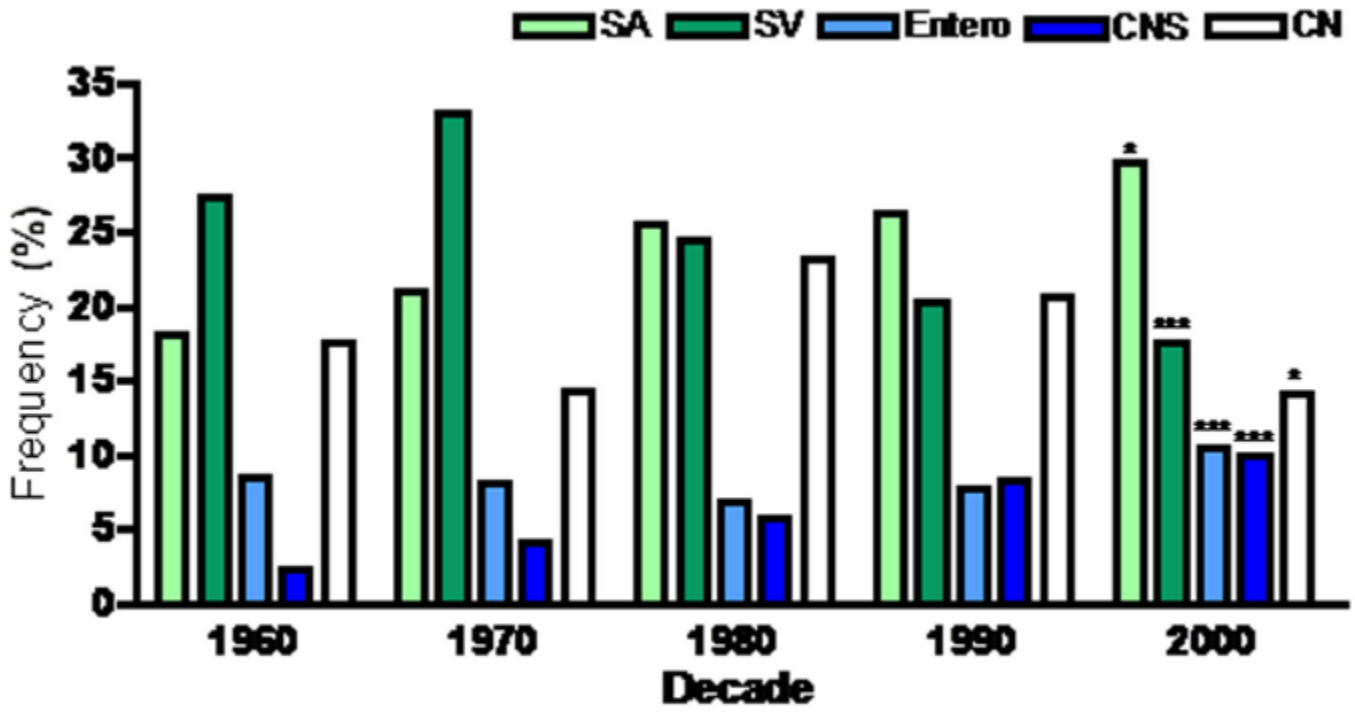


Figure 3. Summary of Worldwide Microbiology of Infective Endocarditis. Bars represent percentage of *Staphylococcus aureus* (SA) (light green), Streptococcus viridans (SV, dark green), enterococci (Entero, light blue), coagulase-negative staphylococcus (CNS, dark blue), and Culture negative (CN, white) endocarditis in each decade. *= $p<0.05$; **=$p<0.01$; ***=$p<0.001$.

Etken

- 107 IE, %66 kültür pozitif

Kan kültürü	Sayı (%)
Koagülaz negatif stafilokok	19 (26.8)
S. aureus	12 (16.9)
S.viridans	9 (12.7)
Diğer streptokoklar	10 (14.1)
Brucella melitensis	8 (11.3)
Gram negatif basil	7 (9.9)
Enterococcus spp.	4 (5.6)
Candida albicans	2 (2.8)

- Kültür negatif hastaların %8'inde Wright agg. testi pozitif
- Bruselloz için serolojik tanı veya kan kültürü pozitifliği tüm hasta gurubunda %10

Erbay, et al. J Heart Valve Dis. 2010;19(2):216-24.

TEDAVİNİN AMACI

1. İnfeksiyonun eradikasyonu

2. İntrakardiak ve ekstrakardiyak lezyonların tedavisi

TEDAVİ

- Medikal
- Medikal+cerrahi

TEDAVİ

- Gecikmiş veya yetersiz antibiyotik tedavisi prognozda etkili
- Erken antibiyotik tedavisi sepsisi, çoklu organ yetmezliğini, ve ani ölümleri önleyebilmekte
- 1 hafta etkin antibiyotik tedavisi sonrası embolik olaylar %65 ⬇
- İlk basamak tedavide halen ESKİ ama ETKİLİ antibiyotikler kullanılmakta
- IE etkenlerinin çoğu halen duyarlı

Canadian Journal of Cardiology 30 (2014) 1046–1057

AHA Scientific Statement

Infective Endocarditis

Diagnosis, Antimicrobial Therapy, and Management of Complications

(*Circulation*. 2005;111:3167-3184.)

Practice Guideline: Focused Update

ACC/AHA 2008 Guideline Update on Valvular Heart Disease: Focused Update on Infective Endocarditis

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

(*Circulation*. 2008;118:887-896.)

AHA/ACC Guideline

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

(*Circulation*. 2014;129:2440-2492.)

European Heart Journal (2009) **30**, 2369–2413
doi:10.1093/eurheartj/ehp285

ESC GUIDELINES

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

Tablo 17 **Enfektif endokarditin ilk ampirik tedavisi için önerilen antibiyotik rejimleri (patojenin tanımlanmasından önce ya da patojen tanımlanmaksızın)**

Antibiyotik	Doz ve uygulama yolu	Süre (hafta)	Kanıt düzeyi	Yorumlar
Doğal kapaklar				
Ampisilim-Sulbaktam, *ya da*	12 g/gün i.v. 4 doz halinde	4–6	IIb C	Kan kültürü negatif EE'li hastalar, bir enfeksiyon hastalıkları uzmanına danışılarak tedavi edilmelidir
Amoksisilin-Klavulanat *ile*	12 g/gün i.v. 4 doz halinde	4–6	IIb C	
Gentamisin[a]	3 mg/kg/gün i.v. ya da i.m. 2 ya da 3 doz halinde	4–6		
Vankomisin[b] *ile*	30 mg/kg/gün i.v. ya da i.m. 2 doz halinde	4–6	IIb C	β-laktamları tolere edemeyen hastalar için
Gentamisin[a] *ile*	3 mg/kg/gün i.v. ya da i.m. 2 ya da 3 doz halinde	4–6		
Siprofloksasin	1000 mg/gün oral yoldan 2 doz ya da 800 mg/gün i.v. 2 doz halinde	4–6		Siprofloksasin, *Bartonella* türleri üzerinde her zaman aynı şekilde etkili değildir. *Bartonella* türleri olasılığı yüksekse, doksisiklin ekleme seçeneği vardır (bakınız *Tablo 16*)
Protez kapaklar (erken, ameliyattan <12 ay sonra)				
Vankomisin[b] *ile*	30 mg/kg/gün i.v. ya da i.m. 2 doz halinde	6	IIb C	Klinik yanıt yoksa, cerrahi ve belki antibiyotik spektrumunun Gram negatif patojenleri kapsayacak şekilde genişletilmesi düşünülmelidir
Gentamisin[a] *ile*	3 mg/kg/gün i.v. ya da i.m. 2 ya da 3 doz halinde	2		
Rifampin	1200 mg/gün oral yoldan 2 doz			
Protez kapaklar (geç, ameliyattan ≥12 ay sonra)				
Doğal kapaklardaki gibi				

Tablo 13 Oral streptokoklar ve D grubu streptokoklara[a] bağlı enfektif endokarditte antibiyotik tedavisi

Antibiyotik	Doz ve uygulama yolu	Süre (hafta)	Kanıt düzeyi
Penisiline tam duyarlı suşlar (MİK <0.125 mg/L)			
Standart tedavi			
Penisilin G[b]	12–18 milyon U/gün i.v. 6 doz halinde	4[c]	I B
ya da			
Amoksisilin[d]	100–200 mg/kg/gün i.v. 4–6 doz halinde	4[c]	I B
ya da			
Seftriakson[e]	2 g/gün i. v. ya da i.m. 1 doz	4[c]	I B
	Pediyatrik dozlar[f]		
	Penisilin G 200,000 U/kg/gün i.v. bölünmüş 4-6 doz.		
	Amoksisilin 300 mg/kg/gün i.v. eşit olarak bölünmüş 4-6 doz.		
	Seftriakson 100 mg/kg/gün i.v. ya da i.m. 1 doz.		
İki haftalık tedavi (g)			
Penisilin G	12–18 milyon U/gün i.v. 6 doz halinde	2	I B
ya da			
Amoksisilin[d]	100–200 mg/kg/gün i.v. 4–6 doz halinde	2	I B
ya da			
Seftriakson[e]	2 g/gün i. v. ya da i.m. 1 doz	2	I B
ile			
Gentamisin[h]	3 mg/kg/gün, i.v. ya da i.m. 1 doz	2	I B
ya da			
Netilmisin	4–5 mg/kg/gün i.v. 1 doz	2	I B
	Pediyatrik dozlar[f]		
	Penisilin, amoksisilin ve seftriakson yukarıdaki gibi.		
	Gentamisin 3 mg/kg/gün i.v. ya da i.m., 1 doz ya da eşit olarak bölünmüş 3 doz.		
Beta-laktama alerjisi olan hastalarda			
Vankomisin[i]	30 mg/kg/gün, i.v. 2 doz halinde	4[c]	I C
	Pediyatrik dozlar [f]		
	Vankomisin 40 mg/kg/gün, i.v. eşit olarak bölünmüş 2-3 doz.		

ESC GUIDELINES, European Heart Journal (2009) 30, 2369–2413

TABLE 4. Therapy of Native Valve Endocarditis Caused by Strains of Viridans Group Streptococci and *Streptococcus bovis* Relatively Resistant to Penicillin

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Aqueous crystalline penicillin G sodium	24 million U/24 h IV either continuously or in 4–6 equally divided doses	4	IB	Patients with endocarditis caused by penicillin-resistant (MIC >0.5 μg/mL) strains should be treated with regimen recommended for enterococcal endocarditis (see Table 8)
or				
Ceftriaxone sodium	2 g/24 h IV/IM in 1 dose	4	IB	
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 1 dose *Pediatric dose*‡: penicillin 300 000 U/24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose; gentamicin 3 mg/kg per 24 h IV/IM in 1 dose or 3 equally divided doses	2		
Vancomycin hydrochloride‡	30 mg/kg per 24 h IV in 2 equally divided doses not to exceed 2 g/24 h, unless serum concentrations are inappropriately low *Pediatric dose*: 40 mg/kg 24 h in 2 or 3 equally divided doses	4	IB	Vancomycin§ therapy recommended only for patients unable to tolerate penicillin or ceftriaxone therapy

(*Circulation*. 2005;111:3167-3184.)

TABLE 5. Therapy for Endocarditis of Prosthetic Valves or Other Prosthetic Material Caused by Viridans Group Streptococci and *Streptococcus bovis*

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Penicillin-susceptible strain (minimum inhibitory concentration ≤0.12 μg/mL)				
Aqueous crystalline penicillin G sodium	24 million U/24 h IV either continuously or in 4–6 equally divided doses	6	IB	Penicillin or ceftriaxone together with gentamicin has not demonstrated superior cure rates compared with monotherapy with penicillin or ceftriaxone for patients with highly susceptible strain; gentamicin therapy should not be administered to patients with creatinine clearance of <30 mL/min
or				
Ceftriaxone	2 g/24 h IV/IM in 1 dose	6	IB	
with or without				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 1 dose *Pediatric dose*‡: penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg IV/IM once daily; gentamicin 3 mg/kg per 24 h IV/IM, in 1 dose or 3 equally divided doses	2		
Vancomycin hydrochloride§	30 mg/kg per 24 h IV in 2 equally divided doses *Pediatric dose*: 40 mg/kg per 24 h IV or in 2 or 3 equally divided doses	6	IB	Vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone
Penicillin relatively or fully resistant strain (minimum inhibitory concentration >0.12 μg/mL)				
Aqueous crystalline penicillin sodium	24 million U/24 h IV either continuously or in 4–6 equally divided doses	6	IB	
or				
Ceftriaxone	2 g/24 h IV/IM in 1 dose	6	IB	
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 1 dose *Pediatric dose*: penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses	6		
Vancomycin hydrochloride	30 mg/kg per 24 h IV in 2 equally divided doses *Pediatric dose*: 40 mg/kg per 24 h IV in 2 or 3 equally divided doses	6	IB	Vancomycin therapy is recommended only for patients unable to tolerate penicillin or ceftriaxone

(*Circulation*. 2005;111:3167-3184.)

Tablo 14 Staphylococcus türlerine bağlı enfektif endokarditte antibiyotik tedavisi.

Antibiyotik	Doz ve uygulama yolu	Süre (hafta)	Kanıt düzeyi
	Doğal kapak		
	Metisiline duyarlı suşlar:		
(Flu)kloksasilin *ya da* Oksasilin *ile*	12 g/gün i.v. 4–6 doz halinde	4–6	I B
Gentamisin[a]	3 mg/kg/gün i. v. ya da i.m. 2 ya da 3 doz halinde **Pediyatrik dozlar**[b] Oksasilin ya da (Flu)kloksasilin 200 mg/kg/gün i.v. eşit olarak bölünmüş 4-6 doz halinde. Gentamisin 3 mg/kg/gün i.v. ya da i.m. eşit olarak bölünmüş 3 doz halinde.	3–5 gün	
	Penisiline alerjisi olan hastalar ya da metisiline dirençli stafilokoklar:		
Vankomisin[c] *ile*	30 mg/kg/gün i.v. 2 doz halinde	4–6	I B
Gentamisin[a]	3 mg/kg/gün i. v. ya da i.m. 2 ya da 3 doz halinde **Pediyatrik dozlar**[b] Vankomisin 40 mg/kg/gün i.v. eşit olarak bölünmüş 2-3 doz halinde	3–5 gün	

TABLE 6. Therapy for Endocarditis Caused by Staphylococci in the Absence of Prosthetic Materials

Regimen	Dosage* and Route	Duration	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin†	12 g/24 h IV in 4–6 equally divided doses	6 wk	IA	For complicated right-sided IE and for left-sided IE; for uncomplicated right-sided IE, 2 wk (see full text)
with				
Optional addition of gentamicin sulfate‡	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	3–5 d		
	Pediatric dose§: Nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			Clinical benefit of aminoglycosides has not been established
For penicillin-allergic (nonanaphylactoid type) patients:				Consider skin testing for oxacillin-susceptible staphylococci and questionable history of immediate-type hypersensitivity to penicillin
Cefazolin	6 g/24 h IV in 3 equally divided doses	6 wk	IB	Cephalosporins should be avoided in patients with anaphylactoid-type hypersensitivity to β-lactams; vancomycin should be used in these cases§
with				
Optional addition of gentamicin sulfate	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	3–5 d		Clinical benefit of aminoglycosides has not been established
	Pediatric dose: cefazolin 100 mg/kg per 24 h IV in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Oxacillin-resistant strains				
Vancomycin‖	30 mg/kg per 24 h IV in 2 equally divided doses	6 wk	IB	Adjust vancomycin dosage to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see full text for vancomycin alternatives)
	Pediatric dose: 40 mg/kg per 24 h IV in 2 or 3 equally divided doses			

(*Circulation*. 2005;111:3167-3184.)

Staphylococcus türlerine bağlı enfektif endokarditte antibiyotik tedavisi.

Protez Kapak			
Metisiline duyarlı suşlar:			
(Flu)kloksasilin *ya da* Oksasilin *ile*	12 g/gün i.v. 4–6 doz halinde	≥6	I B
Rifampin[d] *ve*	1200 mg/gün i.v. ya da oral yoldan 2 doz halinde	≥6	
Gentamisin[e]	3 mg/kg/gün i. v. ya da i.m. 2 ya da 3 doz halinde **Pediyatrik dozlar[b]** Oksasilin ya da (Flu)kloksasilin yukarıdaki gibi. Rifampin 20 mg/kg/gün, i.v. ya da oral yoldan eşit olarak bölünmüş 3 doz halinde.	2	
Penisiline alerjisi olan hastalar ya da metisiline dirençli stafilokoklar:			
Vankomisin[c] *İle*	30 mg/kg/gün i.v. 2 doz halinde	≥6	I B
Rifampin[d] *ve*	1200 mg/gün i.v. ya da oral yoldan 2 doz halinde	≥6	
Gentamisin[e]	3 mg/kg/gün i. v. ya da i.m. 2 ya da 3 doz halinde *Pediyatrik dozlar[b]* Yukarıdaki gibi.	2	

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TABLE 7. Therapy for Prosthetic Valve Endocarditis Caused by Staphylococci

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin	12 g/24 h IV in 6 equally divided doses	≥6	IB	Penicillin G 24 million U/24 h IV in 4 to 6 equally divided doses may be used in place of nafcillin or oxacillin if strain is penicillin susceptible (minimum inhibitory concentration ≤0.1 μg/mL) and does not produce β-lactamase; vancomycin should be used in patients with immediate-type hypersensitivity reactions to β-lactam antibiotics (see Table 3 for dosing guidelines); cefazolin may be substituted for nafcillin or oxacillin in patients with non–immediate-type hypersensitivity reactions to penicillins
plus				
Rifampin	900 mg per 24 h IV/PO in 3 equally divided doses	≥6		
plus				
Gentamicin†	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	2		
	Pediatric dose‡: nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Oxacillin-resistant strains				
Vancomycin	30 mg/kg 24 h in 2 equally divided doses	≥6	IB	Adjust vancomycin to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see full text for gentamicin alternatives)
plus				
Rifampin	900 mg/24 h IV/PO in 3 equally divided doses	≥6		
plus				
Gentamicin	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	2		
	Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses (up to adult dose); gentamicin 3 mg/kg per 24 h IV or IM in 3 equally divided doses			

(*Circulation*. 2005;111:3167-3184.)

Tablo 15 Enterococcus spp.'ye (Enterekok türlerine) bağlı enfektif endokarditte antibiyotik tedavisi

Antibiyotik	Doz ve uygulama yolu	Süre (hafta)	Kanıt düzeyi
Beta-laktam ve gentamisine duyarlı suşlar (dirençli izolatlar için bkz.[a,b,c])			
Amoksisilin *ile* Gentamisin[e]	200 mg/kg/gün i.v. 4–6 doz halinde 3 mg/kg/gün i.v. ya da i.m 2 ya da 3 doz halinde *Pediyatrik dozlar*[f] Amoksisilin 300 mg/kg/gün i.v. eşit olarak bölünmüş 4-6 doz halinde. Gentamisin 3 mg/kg/gün i.v. ya da i.m. eşit olarak bölünmüş 3 doz halinde.	4–6[d] 4–6	I B
YA DA			
Ampisilin *ile* Gentamisin[e]	200 mg/kg/gün i.v. 4–6 doz halinde 3 mg/kg/gün i.v. ya da i.m. 2 ya da 3 doz halinde *Pediyatrik dozlar*[f] Ampisilin 300 mg/kg/gün i.v. eşit olarak bölünmüş 4-6 doz halinde. Gentamisin yukarıdaki gibi.	4–6[d] 4–6	I B
YA DA			
Vankomisin[g] *ile* Gentamisin[e]	30 mg/kg/gün i.v. 2 doz halinde 3 mg/kg/gün i.v. ya da i.m. 2 ya da 3 doz halinde *Pediyatrik dozlar*[f] Vankomisin 40 mg/kg/gün i.v. eşit olarak bölünmüş 2-3 doz halinde. Gentamisin yukarıdaki gibi.	6 6	I C

TABLE 11. Therapy for Native or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Resistant to Penicillin, Aminoglycoside, and Vancomycin

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
E faecium				
Linezolid	1200 mg/24 h IV/PO in 2 equally divided doses	≥8	IIaC	Patients with endocarditis caused by these strains should be treated in consultation with an infectious diseases specialist; cardiac valve replacement may be necessary for bacteriologic cure; cure with antimicrobial therapy alone may be <50%; severe, usually reversible thrombocytopenia may occur with use of linezolid, especially after 2 wk of therapy; quinupristin-dalfopristin only effective against *E faecium* and can cause severe myalgias, which may require discontinuation of therapy; only small no. of patients have reportedly been treated with imipenem/cilastatin-ampicillin or ceftriaxone + ampicillin
or				
Quinupristin-dalfopristin	22.5 mg/kg per 24 h IV in 3 equally divided doses	≥8		
E faecalis				
Imipenem/cilastatin	2 g/24 h IV in 4 equally divided doses	≥8	IIbC	
plus				
Ampicillin sodium	12 g/24 h IV in 6 equally divided doses	≥8		
or				
Ceftriaxone sodium	2 g/24 h IV/IM in 1 dose	≥8	IIbC	
plus				
Ampicillin sodium	12 g/24 h IV in 6 equally divided doses *Pediatric dose*†: Linezolid 30 mg/kg per 24 h IV/PO in 3 equally divided doses; quinupristin-dalfopristin 22.5 mg/kg per 24 h IV in 3 equally divided doses; imipenem/cilastatin 60–100 mg/kg per 24 h IV in 4 equally divided doses; ampicillin 300 mg/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM once daily	≥8		

(*Circulation*. 2005;111:3167-3184.)

Tablo 16 Kan kültürü negatif enfektif endokarditte antibiyotik tedavisi

Patojenler	Önerilen tedavi[a]	Tedavi sonucu
***Brucella* türleri**	Doksisiklin (200 mg/24 saat) artı Kotrimoksazol (960 mg/12 sa.) artı Rifampin (300–600 mg/24 sa.) ≥3 ay[b] boyunca, oral yoldan	Tedavi başarısı antikor titresinin <1:60 olması şeklinde tanımlanmıştır
***Coxiella burnetti* (Q ateşi etkeni)**	Doksisiklin (200 mg/24 sa.) artı Hidroksiklorokin (200–600 mg/24 sa.)[c] oral yoldan ***ya da*** Doksisiklin (200 mg/24 sa.) artı Kinolon (Ofloksasin, 400 mg/24 sa.) oral yoldan (>18 aylık tedavi)	Tedavi başarısı anti-faz I IgG titresinin <1:200 ve IgA ve IgM titrelerinin <1:50 olması şeklinde tanımlanmıştır.
***Bartonella* türleri**	Seftriakson (2 g/24 sa.) ya da Ampisilin (ya da Amoksisilin) (12 g/24 sa.) i.v. ***ya da*** Doksisiklin (200 mg/24 sa.) oral yoldan 6 hafta boyunca ***artı*** Gentamisin (3 mg/24 sa.) ya da intravenöz olarak Netilmisin (3 hafta boyunca)[d]	Hastaların ≥%90'ında tedavi başarısı beklenmektedir
***Legionella* türleri**	Eritromisin (3 g/24 sa.) i.v. 2 hafta boyunca, sonra oral yoldan 4 hafta boyunca ***artı*** Rifampin (300–1200 mg/24 sa.) ya da Siprofloksasin (1.5 g/24 sa.) oral yoldan 6 hafta boyunca	Optimum tedavi bilinmemektedir. Yüksek duyarlılık nedeniyle muhtemelen kinolonlar dahil edilmelidir
***Mycolasma* türleri**	Yeni fluorokinolonlar[e] (>6 aylık tedavi)	Optimum tedavi bilinmemektedir
***Tropheryma whipplei*[f] (Whipple hastalığının etkeni)**	Kotrimoksazol Penisilin G (1.2 MU/24 sa.) ve Streptomisin (1 g/24 sa.) i.v. 2 hafta boyunca, sonra Kotrimoksazol oral yoldan 1 yıl boyunca ***ya da*** Doksisiklin (200 mg/24 sa.) artı Hidroksiklorokin (200–600 mg/24 sa.) oral yoldan ≥18 ay boyunca	Uzun süreli tedavi, optimum süre bilinmemektedir

ESC GUIDELINES, European Heart Journal (2009) 30, 2369–2413

Tedavide Yenilikler

- Vankomisin MİK değerlerinin ≥2 mcg/mL olması durumunda alternatif ajanlar kullanılmalıdır.

Daptomisin

- 6 mg/kg/gün sağ kalp IE'de ruhsatlıdır

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Médecine et maladies infectieuses
Médecine et maladies infectieuses (2014) 25–31

Original article

A retrospective study of daptomycin use in a Paris teaching-hospital

- 6 sol kalp endokarditi
- Doz 6-10 mg/kg/gün
- Gentamisin veya rifampisin kombinasyonu ile
- %50 hastada tedavi başarısız
- Yüksek dozda tedavi başarısı elde edilmiş

J Infect Chemother (2013) 19:698–702
DOI 10.1007/s10156-012-0546-9

ORIGINAL ARTICLE

Treatment of Gram-positive left-sided infective endocarditis with daptomycin

Selçuk Kaya · Gürdal Yilmaz · Ahmet Kalkan · Barış Ertunç · İftihar Köksal

- 14 hasta
- Etken MRSA (%71.5), *S. mutans* (%21.5), MSSA (%7)
- Doz 6 mg/kg/gün
- 13 hastada tedavi başarılı
- *Önemli yan etki yok*

International Journal of Antimicrobial Agents 38 (2011) 365–370

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International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Review

Clinical utility of daptomycin in infective endocarditis caused by Gram-positive cocci☆

- MSSA ve MRSA da kullanılabildiği için iyi bir seçenek
- İkinci basamak tedavi
- Deneysel modelde vejetasyonların steril olması vankomisine göre daha fazla
- Sol kalp veya PV IE'de yüksek doz (10 mg/kg/gün) daha başarılı
- KNS ve enterokok IE'de kullanım için yeterli veri yok
- Avantaj: Oral kullanım
- Dezavantaj: Tedavi sırasında direnç gelişme riski

International Journal of Infectious Diseases 17 (2013) e1076–e1077

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International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

In vivo acquired daptomycin resistance during treatment of methicillin-resistant *Staphylococcus aureus* endocarditis

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ARTICLE INFO

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SUMMARY

This clinical case reports the emergence of a daptomycin-resistant *Staphylococcus aureus* isolate during daptomycin treatment in a patient with right-sided infective endocarditis who had never been treated with vancomycin.

- Tedavi başarısızlığı
- Kültür negatifliği sağlanamamış
- 16 günlük tedavi sonrası, Daptomisin MİK: 0.75, 3 kat artış

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High-Dose Daptomycin plus Fosfomycin Is Safe and Effective in Treating Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus* Endocarditis

José M. Miró,[a] José M. Entenza,[b] Ana del Río,[a] Maria Velasco,[c] Ximena Castañeda,[a] Cristina Garcia de la Mària,[a] Marlyse Giddey,[b] Yolanda Armero,[a] Juan M. Pericàs,[a] Carlos Cervera,[a] Carlos A. Mestres,[a] Manuel Almela,[a] Carlos Falces,[a] Francesc Marco,[a] Philippe Moreillon,[b] Asuncion Moreno,[a] and the Hospital Clinic Experimental Endocarditis Study Group

Hospital Clínic—IDIBAPS, University of Barcelona, Barcelona, Spain[a]; Department of Fundamental Microbiology, University of Lausanne, Lausanne, Switzerland[b]; and Hospital Universitario Fundación Alcorcón, Madrid, Spain[c]

We describe 3 patients with left-sided staphylococcal endocarditis (1 with methicillin-susceptible *Staphylococcus aureus* [MSSA] prosthetic aortic valve endocarditis and 2 with methicillin-resistant *S. aureus* [MRSA] native-valve endocarditis) who were successfully treated with high-dose intravenous daptomycin (10 mg/kg/day) plus fosfomycin (2 g every 6 h) for 6 weeks. This combination was tested *in vitro* against 7 MSSA, 5 MRSA, and 2 intermediately glycopeptide-resistant *S. aureus* isolates and proved to be synergistic against 11 (79%) strains and bactericidal against 8 (57%) strains. This combination deserves further clinical study.

Antimicrob Agents Chemother. 2012 Aug;56(8):4511-5.

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High-Dose Daptomycin Therapy for Left-Sided Infective Endocarditis: a Prospective Study from the International Collaboration on Endocarditis

- Çok merkezli çalışma
- Daptomisin ile tedavi edilmiş 29 IE
- Standart tedavi alan 149 IE
- Daptomisin dozu 7.7-10 mg/kg/gün (median 9.2)
- *S.aureus* ve *E.fecalis* IE'de daptomisin alanlarda hastanede kalış süresi daha kısa
- Hastane sürecinde ve 6 aylık takipte mortalitede fark yok
- Daptomisin dozun <8 mg/kg/gün veya > 8 mg/kg/gün olmasıyla mortalite, klinik-laboratuvar iyileşme, yan etki açısından fark yok

Antimicrob Agents Chemother. 2013 Dec;57(12):6213-22.

Curr Infect Dis Rep (2014) 16:429
DOI 10.1007/s11908-014-0429-6

High-Dose Daptomycin Therapy for Staphylococcal Endocarditis and When to Apply It

Table 1 Selected studies evaluating the safety and utility of high-dose daptomycin

Authors	Type of study	Patient population	Number of patients	Daptomycin therapy	Results and major conclusions	Reference
Moise PA et al. 2009	Retrospective, observational	Subset of patients 18 years or older from the Cubicin Outcomes Registry and Experience (CORE) database with any site of infection	Total=94 IE=15	Median daily dose of 8 mg/kg for 15 days (1–90 days)	Clinically evaluable subset of 74 patients. Clinical cure or improvement in 89 % of all patients. Clinical cure or improvement in IE of 69 %. Two patients discontinued daptomycin secondary to adverse events	[51]
Kullar R et al. 2011	Retrospective, observational	Patients 18 years or older with confirmed or suspected Gram-positive infections (S. aureus or enterococci) at any site	Total=250 IE=31	Median daily dose of daptomycin was 8.9 mg/kg (IQR 8.0–10.0 mg/kg) for 10–13 days (IQR 5–18 days) depending on organism	Clinically evaluable subset of 227 patients. Clinical cure or improvement in 83.6 %. Clinical failure in 5 IE patients	[52]
Carugati et al. 2013	Prospective, cohort	Subset of patients 16 years or older from the International Collaboration on Endocarditis Daptomycin Study (ICE-DS) database with left-sided endocarditis	Total (IE)=178 Daptomycin-treated=29	Median daily dose of 9.2 mg/kg (range, 7.7 to 10.0 mg/kg) for 39 days (range, 25.0 to 43.0 days)	Time to clearance of bacteremia was significantly faster with daptomycin (1 vs. 5 days). Higher dose daptomycin was not associated with an increase in adverse events	[28]
Durante-Mangoni et al. 2012	Case series	Patients with staphylococcal infective endocarditis on a cardiac implantable electronic device	Total=25	Median daily dose of 8.3 mg/kg (6.4–10.7) for 20 days (8–52)	All patients were clinically evaluable. Clinical success of 80 %. No serious adverse events related to high-dose daptomycin	[54]
Murray KP et al. 2013	Matched retrospective, cohort	Patients with MRSA bacteremia on vancomycin or daptomycin matched according to age, Pitt bacteremia score, and source of bacteremia	Total=170 Daptomycin IE=20	Median daily dose of 8.4 mg/kg (IQR 6.3–9.9 mg/kg)	Clinical failure at 30 days was significantly lower in the daptomycin-treated patients. Daptomycin treatment was associated with reduced mortality compared to vancomycin (3.5 % vs. 12.9 %, p=0.047).	[16]
Kullar R et al. 2013	Retrospective, observational	Patients with definitive or possible RS and/or LS IE	Total=70 RS IE=33 LS IE=35 LS/RS=2	Median daily dose of daptomycin was 9.8 mg/kg (IQR 8.2–10.0 mg/kg) for	Clinically evaluable subset of 64 patients. Clinical success in 85.9 % of patients. Two patients experienced adverse events secondary to daptomycin	[55]

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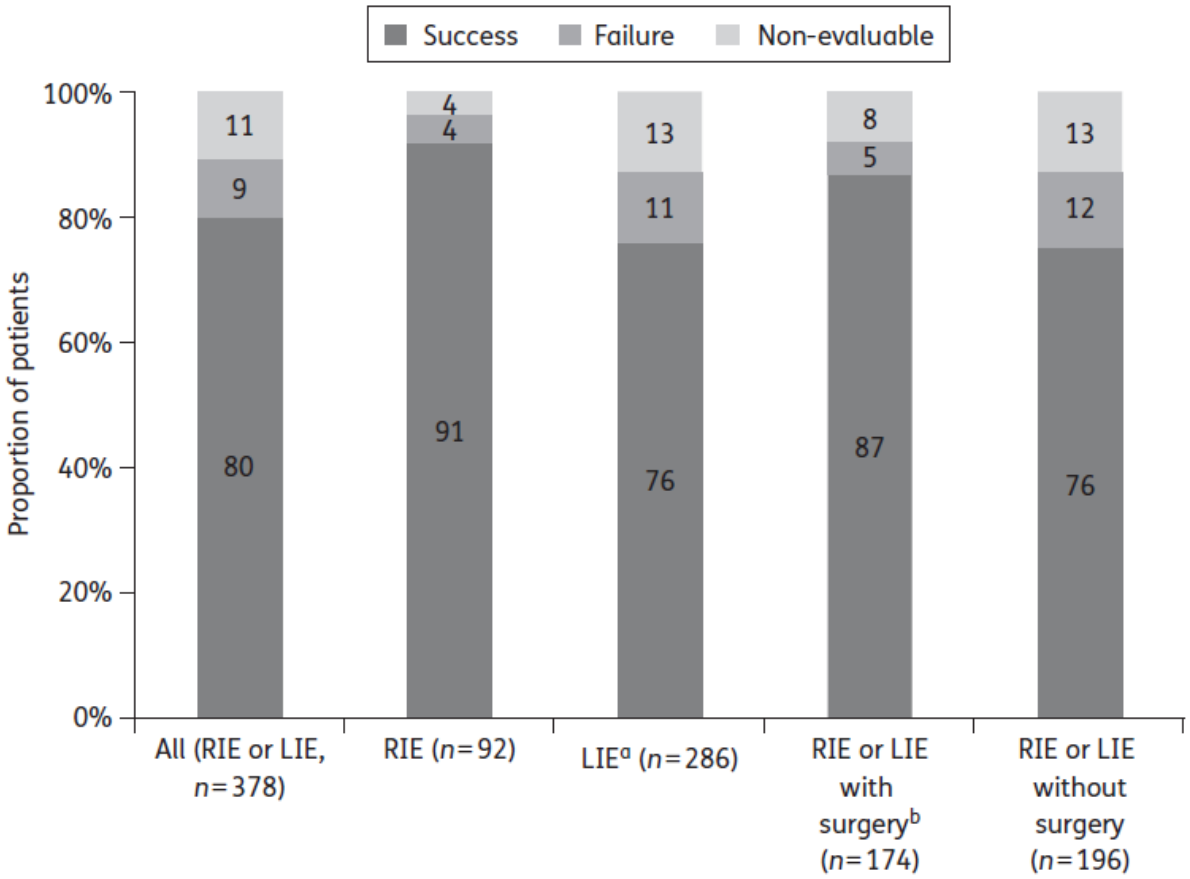
doi:10.1093/jac/dks467 Advance Access publication 28 November 2012

Journal of Antimicrobial Chemotherapy

Daptomycin for the treatment of infective endocarditis: results from a European registry



>8mg/kg/gün dozda başarı %90

DAPTOMYCIN AS AN OPTION IN LEFT-SIDE INFECTIVE ENDOCARDITIS

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Objectives: To evaluate the effectiveness of daptomycin in left-side infective endocarditis (IE).
Methods: Patients with left-side IE according to modified Duke criteria between May 2010 and May 2012 and receiving daptomycin as monotherapy were included.
Results: Fourteen patients were included in the study. Mitral valve was involved in 10 and aortic valve in 4 patients. Eight patients had prosthetic valves. Cardiac abscess was detected in 5 patients. Blood cultures were positive in 13 patients. The most common isolated microorganisms were staphylococci. Early cardiac surgery was required in 5 cases due to congestive heart failure secondary to valvular dysfunction. Daptomycin was used in initial treatment in 4 patients with high MIC values or creatinine levels, while treatment was subsequently modified to daptomycin in 10 patients, because of persistence of infection in 7 patients, drug side-effects in 2 patients and high MIC values in 1 patient. In 10 patients daptomycin was used at a dosage of 6 mg/kg/day and in 4 patients 8 mg/kg/day. In 6 patients daptomycin-related side effects such as increase in serum CPK levels, peripheral neuropathy and myopathy were seen. Daptomycin was not prematurely withdrawn in any of these cases, and side effects returned to normal after the treatment. Clinical improvement was observed at 8.7±3.2 days. Microbiological eradication was observed in 12 cases at 11.1±3.6 days. Relapse was not seen in any patient. Duration of daptomycin treatment was 40.6±4.4 days. Four patients died due to multi-organ failure and heart failure. Ten patients were discharged healthy, with successful surgical treatment in two of them. The four patients in whom daptomycin was used at a dosage of 8 mg/kg/day recovered and no side effects were seen.
Conclusion: Daptomycin has the potential to be an option in left-side IE. Larger sample size studies are needed to confirm the effectiveness of daptomycin in left-side IE.

J Antimicrob Chemother 2012; **67**: 269–289
doi:10.1093/jac/dkr450 Advance Access publication 14 November 2011

Journal of Antimicrobial Chemotherapy

Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy

Table 2. Empirical treatment regimens for endocarditis (pending blood culture results)

Antimicrobial	Dose/route	Comment
1. NVE—indolent presentation		
Amoxicillin[a] AND (optional)	2 g q4h iv	If patient is stable, ideally await blood cultures. Better activity against enterococci and many HACEK microorganisms compared with benzylpenicillin. Use Regimen 2 if genuine penicillin allergy.
gentamicin[a]	1 mg/kg ABW	The role of gentamicin is controversial before culture results are available.
2. NVE, severe sepsis (no risk factors for Enterobacteriaceae, *Pseudomonas*)		
Vancomycin[a] AND	dosed according to local guidelines	In severe sepsis, staphylococci (including methicillin-resistant staphylococci) need to be covered. If allergic to vancomycin, replace with daptomycin 6 mg/kg q24h iv.
gentamicin[a]	1 mg/kg IBW q12h iv	If there are concerns about nephrotoxicity/acute kidney injury, use ciprofloxacin in place of gentamicin[a].
3. NVE, severe sepsis AND risk factors for multiresistant Enterobacteriaceae, *Pseudomonas*		
Vancomycin[a] AND	dosed according to local guidelines, iv	Will provide cover against staphylococci (including methicillin-resistant staphylococci), streptococci, enterococci, HACEK, Enterobacteriaceae and *P. aeruginosa*.
meropenem[a]	2 g q8h iv	
4. PVE pending blood cultures or with negative blood cultures		
Vancomycin[a] AND	1 g q12h iv	
gentamicin[a] AND	1 mg/kg q12h iv	Use lower dose of rifampicin in severe renal impairment.
rifampicin[a]	300–600 mg q12h po/iv	

Table 3. Summary of treatment recommendations for staphylococcal endocarditis

Agent	Dose/route	Duration (weeks)	Comment
NVE, methicillin-susceptible *Staphylococcus* spp.			
Flucloxacillin	2 g every 4–6 h iv	4	Use q4h regimen if weight >85 kg.
NVE, methicillin-resistant, vancomycin-susceptible (MIC ≤2 mg/L) rifampicin-susceptible *Staphylococcus* or penicillin allergy			
Vancomycin AND	1 g iv q12h	4	or dose according to local guidelines. Modify dose according to renal function and maintain pre-dose level 15–20 mg/L.
Rifampicin	300–600 mg q12h po	4	Use lower dose of rifampicin if creatinine clearance <30 mL/min.
NVE, methicillin-resistant, vancomycin-resistant (MIC >2 mg/L), daptomycin-susceptible (MIC ≤1 mg/L) *Staphylococcus* spp. or patient unable to tolerate vancomycin			
Daptomycin AND	6 mg/kg q24h iv	4	Monitor creatine phosphokinase weekly. Adjust dose according to renal function.
Rifampicin OR	300–600 mg q12h po	4	Use lower dose of rifampicin if creatinine clearance <30 mL/min.
Gentamicin	1 mg/kg iv, q12h	4	
PVE, methicillin, rifampicin-susceptible *Staphylococcus* spp.			
Flucloxacillin AND	2 g every 4–6 h iv	6	Use q4h regimen if weight >85 kg.
Rifampicin AND	300–600 mg q12h po	6	Use lower dose of rifampicin if creatinine clearance <30 mL/min.
Gentamicin	1 mg/kg iv, q12h	6	
PVE, methicillin-resistant, vancomycin-susceptible (MIC ≤2 mg/L), *Staphylococcus* spp. or penicillin allergy			
Vancomycin AND	1 g iv q12h	6	or dose according to local guidelines. Modify dose according to renal function and maintain pre-dose level 15–20 mg/L.
Rifampicin AND	300–600 mg q12h po	6	Use lower dose of rifampicin if creatinine clearance <30 mL/min.
Gentamicin	1 mg/kg q12h iv	≥2	Continue gentamicin for the full course if there are no signs or symptoms of toxicity.
PVE, methicillin-resistant, vancomycin-resistant (MIC >2 mg/L), daptomycin-susceptible (MIC ≤1 mg/L) *Staphylococcus* spp. or patient unable to tolerate vancomycin			
Daptomycin AND	6 mg/kg q24h iv	6	Increase daptomycin dosing interval to 48 hourly if creatinine clearance <30 mL/min.
Rifampicin AND	300–600 mg q12h po	6	Use lower dose of rifampicin if creatinine clearance <30 mL/min.
Gentamicin	1 mg/kg q12h iv	≥2	Continue gentamicin for the full course if there are no signs or symptoms of toxicity.

Table 8. Summary of treatment recommendations for fungal endocarditis

Antifungal agent	Dose/route	Serum levels required?	Role in treating *Candida* endocarditis	Role in treating *Aspergillus* endocarditis
Fluconazole	400 mg daily, only reduced in severe renal failure/dialysis	no	long-term suppressive therapy	none
Voriconazole	intravenous therapy preferred initially, licensed doses	yes, with dose modification important	long-term suppressive therapy for fluconazole-resistant, voriconazole-susceptible isolates	first-line therapy with long-term suppression
Amphotericin B	3 mg/kg/24 h (AmBisome) 5 mg/kg/day (Abelcet) 1 mg/kg/day (Fungizone)	no	second-line therapy	second-line therapy, or first line if azole resistance; should not be used for *A. terreus* or *A. nidulans* infection
Micafungin	200 mg daily	no	first-line therapy	third- or fourth-line therapy
Caspofungin	70 mg loading, 50–100 mg daily	no	first-line therapy	no role
Anidulafungin	licensed doses	no	first-line therapy	no role
Posaconazole	400 mg twice daily	yes	no role	third- or fourth-line therapy, long-term suppressive therapy
Flucytosine	100 mg/kg/day in three doses, reduced with renal dysfunction	yes, with dose modification important	as combination therapy with amphotericin B	as combination therapy with amphotericin B
Itraconazole	NA	NA	no role	no role

Tigesiklin

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Efficacy of Tigecycline Alone and in Combination with Gentamicin in the Treatment of Experimental Endocarditis Due to Linezolid-Resistant *Enterococcus faecium*

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We evaluated the efficacy of tigecycline in a rabbit model of experimental endocarditis caused by a linezolid-resistant clinical strain of *Enterococcus faecium*. Tigecycline-treated animals had a 2.8-$\log_{10}$-CFU/g reduction in microbial counts in excised vegetations compared with controls. Addition of gentamicin caused a further arithmetical reduction in colony counts. The therapeutic effect was sustained 5 days after completion of treatment, as shown by relapse studies performed in treatment groups.

Antimicrob Agents Chemother. 2013 Jul;57(7):3392-4.

Linezolid

Eur J Clin Microbiol Infect Dis (2012) 31:2567–2574
DOI 10.1007/s10096-012-1597-7

ARTICLE

Linezolid as rescue treatment for left-sided infective endocarditis: an observational, retrospective, multicenter study

- Danimarka'da Çok merkezli çalışma
- Linezolid ile tedavi edilmiş 38 IE (8 monoterapi, 30 rifam kombinasyonu
- Standart tedavi alan 512 IE
- Tedavi başarısı, hastanede ve 12 aylık izlemde mortalite benzer
- >28 gün linezolid 10 hasta
- Yan etki 4 hastada anemi

J Antimicrob Chemother 2011
doi:10.1093/jac/dkq506
Advance Access publication 11 January 2011

Linezolid for endocarditis: a case series of 14 patients

- Tedaviye yanıt: MRSA (%67), MSSA (%80)
- 7 doğal kapak İE , tedavi yanıtı %87.5
- 4 lead IE, tedavi yanıtı %75
- 6 aylık izlemde relaps yok
- 1 hastada trombositopeni
- 2 hastada meropenem ile kombinasyon, diğerleri ?

Teikoplanin

Treatment of infective endocarditis caused by methicillin-resistant Staphylococcus aureus: Teicoplanin versus vancomycin in a retrospective study

2008, Vol. 40, No. 6-7 , Pages 462-467 (doi:10.1080/00365540701837126)

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Infective endocarditis caused by methicillin-resistant Staphylococcus aureus (MRSA) is increasing. Vancomycin and teicoplanin are 2 intravenous glycopeptides appropriate for its treatment. There is no human study comparing teicoplanin and vancomycin for the treatment of MRSA endocarditis. Between 1996 and 2006, 51 MRSA endocarditis patients were treated at the authors' hospital. There were 29 patients with nosocomial infection; 15 were treated with teicoplanin. Teicoplanin was used as the first therapeutic agent in 3 patients because of renal insufficiency. Vancomycin was used as the first therapeutic agent in 12 patients. Treatment was changed to teicoplanin because of adverse reactions in 10 and persistent bacteremia in 2 patients. Early operation was performed in 2 patients because of persistent MRSA bacteremia. Overall, 7 patients died in hospital. There was no statistically significant difference in hospital mortality rate (42% vs 47%) and bacteriologic failure rate (34% vs 40%) between 36 patients treated with vancomycin and 15 patients treated with teicoplanin. Teicoplanin can be an alternative therapy of MRSA infective endocarditis.

Failure of treatment with teicoplanin at 6 milligrams/kilogram/day in patients with Staphylococcus aureus intravascular infection.
Gilbert DN, et al. Antimicrob Agents Chemother 1991;35:79–87

- Teikoplanin 12mg/kg yükleme dozunu takiben 6m/kg/gün,
- Vankomisin 30 mg/kg/gün
- Teikoplanin gurubunda yüksek başarısızlık oranı nedeniyle hasta alımı 12. hastada durdurulmuş
- Çalışma iptal edilmiş.

International Journal of Infectious Diseases 14S4 (2010) S23–S38

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journal homepage: www.elsevier.com/locate/ijid

Consensus document on controversial issues in the diagnosis and treatment of bloodstream infections and endocarditis

GISIG (Gruppo Italiano di Studio sulle Infezioni Gravi) Working Group on Bloodstream Infections

- Sağ kalp endokarditi tedavisinde teikoplanin vankomisin ile benzer etkiye sahiptir.
- Sol kalp endokarditinde teikoplaninin (6 mg/kg/gün) tedavi başarısı vankomisinden düşüktür.
- Sol kalp endokarditinde teikoplaninin daha yüksek dozda kullanıma ilişkin klinik veri bulunmamaktadır.

J Antimicrob Chemother 2013; **68**: 1650–1654
doi:10.1093/jac/dkt046 Advance Access publication 8 March 2013

Journal of Antimicrobial Chemotherapy

Risk factors for failure of outpatient parenteral antibiotic therapy (OPAT) in infective endocarditis

Objectives: To identify risk factors for failure of outpatient antibiotic therapy (OPAT) in infective endocarditis (IE).

Patients and methods: We identified IE cases managed at a single centre over 12 years from a prospectively maintained database. 'OPAT failure' was defined as unplanned readmission or antibiotic switch due to adverse drug reaction or antibiotic resistance. We analysed patient and disease-related risk factors for OPAT failure by univariate and multivariate logistic regression. We also retrospectively collected follow-up data on adverse disease outcome (defined as IE-related death or relapse) and performed Kaplan–Meier survival analysis up to 36 months following OPAT.

Results: We identified 80 episodes of OPAT in IE. Failure occurred in 25/80 episodes (31.3%). On multivariate analysis, cardiac or renal failure [pooled OR 7.39 (95% CI 1.84–29.66), $P=0.005$] and teicoplanin therapy [OR 8.69 (95% CI 2.01–37.47), $P=0.004$] were independently associated with increased OPAT failure. OPAT failure with teicoplanin occurred despite therapeutic plasma levels. OPAT failure predicted adverse disease outcome up to 36 months ($P=0.016$ log-rank test).

Conclusions: These data caution against selecting patients with endocarditis for OPAT in the presence of cardiac or renal failure and suggest teicoplanin therapy may be associated with suboptimal OPAT outcomes. Alternative regimens to teicoplanin in the OPAT setting should be further investigated.

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Oral antibiotic therapy for the treatment of infective endocarditis: a systematic review

- Amoksisilin, ampisilin, siprofloksasin+ rifampin, oral linezolid
- Başarı oranları %10-100 arasında
- ?

SONUÇ

- Vankomisin kullanılamayan hastalarda veya vankomisin direnci durumunda seçenekler : Linezolid veya daptomisin
- Yüksek doz daptomisin (8-12 mg/kg/gün) daha etkili
- Daha önce vankomisin kullanmış hastalarda daptomisin direnci gelişme riski daha fazla