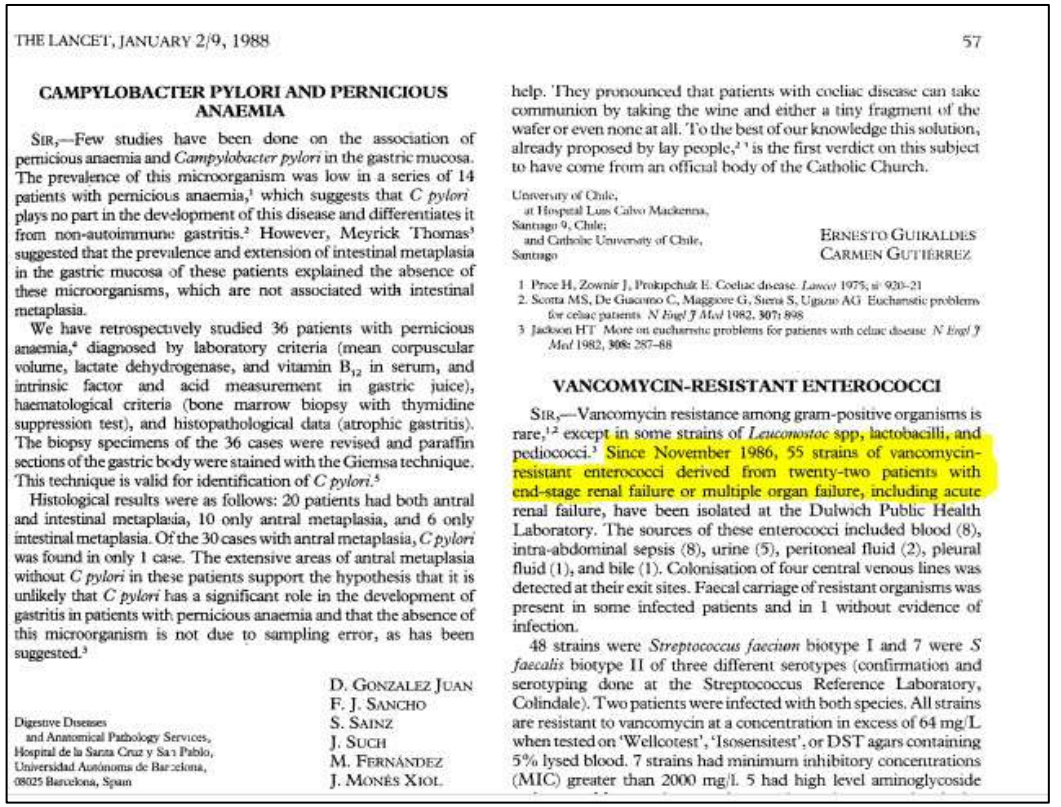
Ne Yapıyoruz? Ne Yapalım? «Hastanın Klinik Örneklerinde VRE Üredi»

Dr. Öğr. Üyesi Sibel YILDIZ KAYA
Cerrahpaşa Tıp Fakültesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD
Mart 2023

VRE Tarihçesi

- 1980'li yıllarda Avrupa ve Amerika'dan bildirilmiş.
- Kısa sürede hastane epidemileri tanımlanmış.
- 1999 Türkiye – Akdeniz Üniversitesi



THE LANCET, JANUARY 2/9, 1988 57

CAMPYLOBACTER PYLORI AND PERNICIOUS ANAEMIA

SIR,—Few studies have been done on the association of pernicious anaemia and *Campylobacter pylori* in the gastric mucosa. The prevalence of this microorganism was low in a series of 14 patients with pernicious anaemia,[1] which suggests that *C pylori* plays no part in the development of this disease and differentiates it from non-autoimmune gastritis.[2] However, Meyrick Thomas[3] suggested that the prevalence and extension of intestinal metaplasia in the gastric mucosa of these patients explained the absence of these microorganisms, which are not associated with intestinal metaplasia.

We have retrospectively studied 36 patients with pernicious anaemia,[4] diagnosed by laboratory criteria (mean corpuscular volume, lactate dehydrogenase, and vitamin B_{12} in serum, and intrinsic factor and acid measurement in gastric juice), haematological criteria (bone marrow biopsy with thymidine suppression test), and histopathological data (atrophic gastritis). The biopsy specimens of the 36 cases were revised and paraffin sections of the gastric body were stained with the Giemsa technique. This technique is valid for identification of *C pylori*.[5]

Histological results were as follows: 20 patients had both antral and intestinal metaplasia, 10 only antral metaplasia, and 6 only intestinal metaplasia. Of the 30 cases with antral metaplasia, *C pylori* was found in only 1 case. The extensive areas of antral metaplasia without *C pylori* in these patients support the hypothesis that it is unlikely that *C pylori* has a significant role in the development of gastritis in patients with pernicious anaemia and that the absence of this microorganism is not due to sampling error, as has been suggested.[3]

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D. GONZALEZ JUAN
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S. SAINZ
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M. FERNÁNDEZ
J. MONÉS XIOL

help. They pronounced that patients with coeliac disease can take communion by taking the wine and either a tiny fragment of the wafer or even none at all. To the best of our knowledge this solution, already proposed by lay people,[2,3] is the first verdict on this subject to have come from an official body of the Catholic Church.

University of Chile, at Hospital Luis Calvo Mackenna, Santiago 9, Chile; and Catholic University of Chile, Santiago

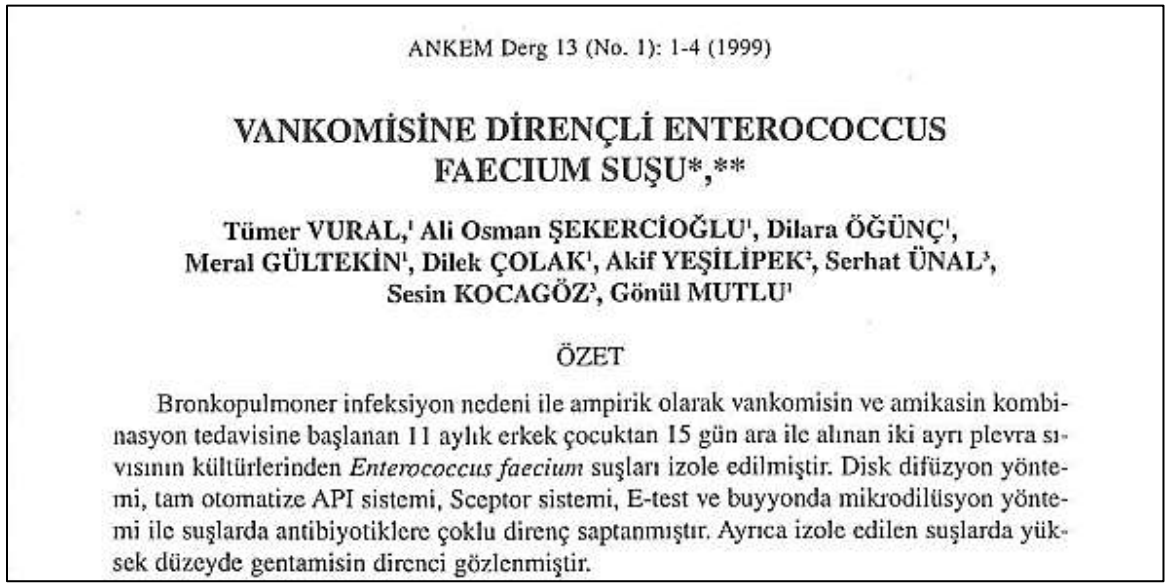
ERNESTO GUIRALDES
CARMEN GUTIÉRREZ

1 Price H, Zowmir J, Prokipchuk E. Coeliac disease. *Lancet* 1975; ii: 920–21
2 Scotta MS, De Giacomo C, Maggiore G, Siena S, Ugazio AG. Eucharistic problems for celiac patients. *N Engl J Med* 1982; 307: 898
3 Jackson HT. More on eucharistic problems for patients with celiac disease. *N Engl J Med* 1982; 308: 287–88

VANCOMYCIN-RESISTANT ENTEROCOCCI

SIR,—Vancomycin resistance among gram-positive organisms is rare,[1,2] except in some strains of *Leuconostoc* spp, lactobacilli, and pediococci.[3] Since November 1986, 55 strains of vancomycin-resistant enterococci derived from twenty-two patients with end-stage renal failure or multiple organ failure, including acute renal failure, have been isolated at the Dulwich Public Health Laboratory. The sources of these enterococci included blood (8), intra-abdominal sepsis (8), urine (5), peritoneal fluid (2), pleural fluid (1), and bile (1). Colonisation of four central venous lines was detected at their exit sites. Faecal carriage of resistant organisms was present in some infected patients and in 1 without evidence of infection.

48 strains were *Streptococcus faecium* biotype I and 7 were *S faecalis* biotype II of three different serotypes (confirmation and serotyping done at the Streptococcus Reference Laboratory, Colindale). Two patients were infected with both species. All strains are resistant to vancomycin at a concentration in excess of 64 mg/L when tested on 'Wellcotest', 'Isosensitest', or DST agars containing 5% lysed blood. 7 strains had minimum inhibitory concentrations (MIC) greater than 2000 mg/L. 5 had high level aminoglycoside



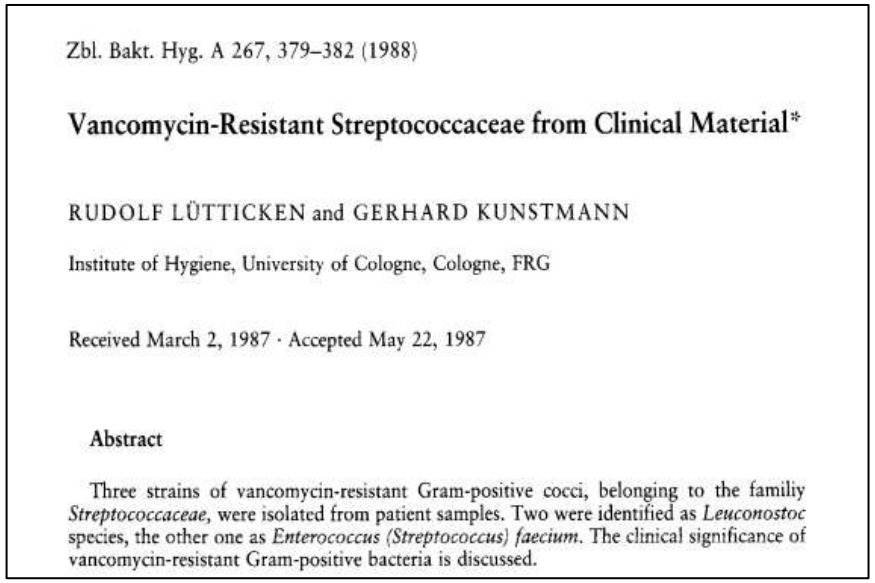
ANKEM Derg 13 (No. 1): 1-4 (1999)

VANKOMİSİNE DİRENÇLİ ENTEROCOCCUS FAECIUM SUŞU*,**

Tümer VURAL,[1] Ali Osman ŞEKERCİOĞLU[1], Dilara ÖĞÜNÇ[1], Meral GÜLTEKİN[1], Dilek ÇOLAK[1], Akif YEŞİLİPEK[2], Serhat ÜNAL[3], Sesin KOCAGÖZ[2], Gönül MUTLU[1]

ÖZET

Bronkopulmoner infeksiyon nedeni ile ampirik olarak vankomisin ve amikasin kombinasyon tedavisine başlanan 11 aylık erkek çocuktan 15 gün ara ile alınan iki ayrı plevra sıvısının kültürlerinden *Enterococcus faecium* suşları izole edilmiştir. Disk difüzyon yöntemi, tam otomatize API sistemi, Sceptor sistemi, E-test ve buyyonda mikrodilüsyon yöntemi ile suşlarda antibiyotiklere çoklu direnç saptanmıştır. Ayrıca izole edilen suşlarda yüksek düzeyde gentamisin direnci gözlenmiştir.



Zbl. Bakt. Hyg. A 267, 379–382 (1988)

Vancomycin-Resistant Streptococcaceae from Clinical Material*

RUDOLF LÜTTICKEN and GERHARD KUNSTMANN

Institute of Hygiene, University of Cologne, Cologne, FRG

Received March 2, 1987 · Accepted May 22, 1987

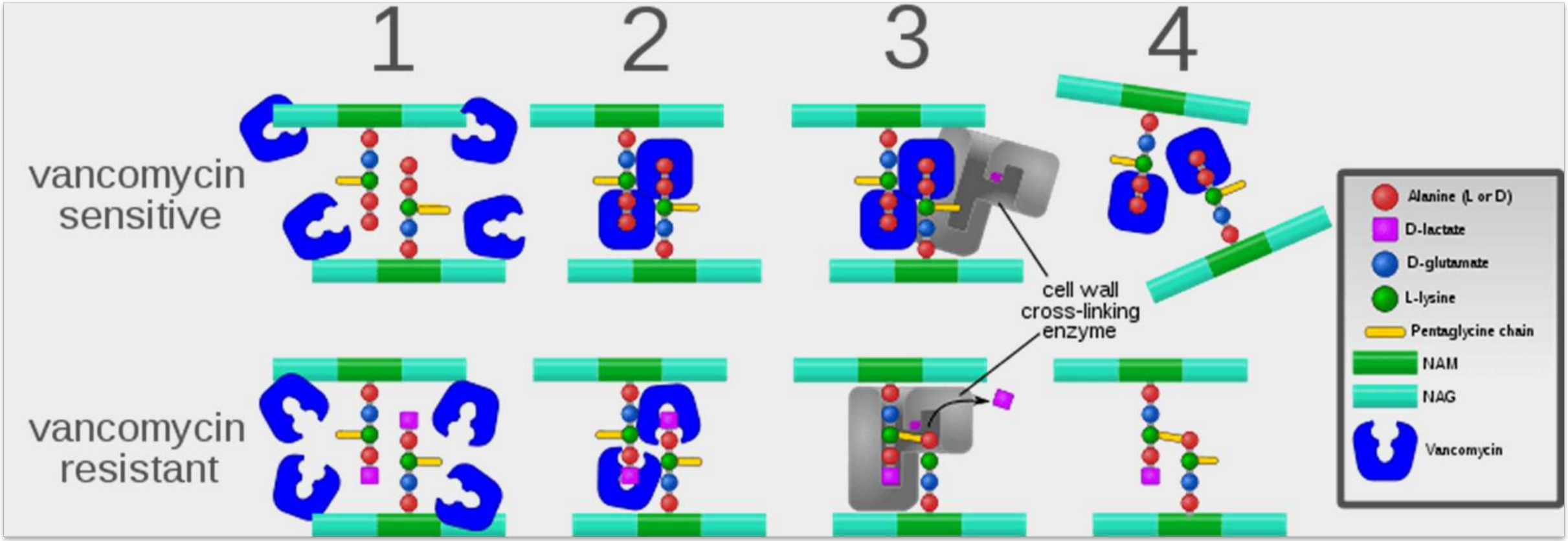
Abstract

Three strains of vancomycin-resistant Gram-positive cocci, belonging to the familiy *Streptococcaceae*, were isolated from patient samples. Two were identified as *Leuconostoc* species, the other one as *Enterococcus (Streptococcus) faecium*. The clinical significance of vancomycin-resistant Gram-positive bacteria is discussed.

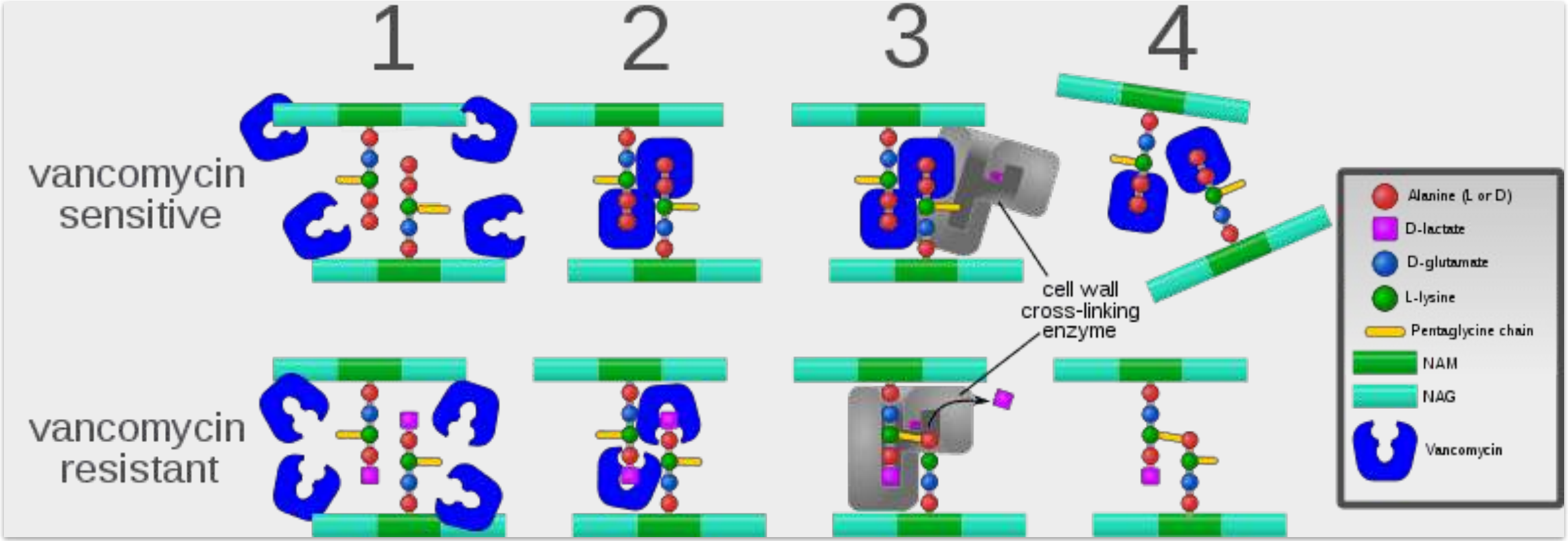
- Avrupa’da çiftlik hayvanlarında ve sağlıklı insanlarda VRE ile gastrointestinal kolonizasyon sık
  - Hayvan yemlerine **avoparsin** eklenmesi
  - Avoparsin yaklaşık 20 yıl kullanılmış, sonrasında ise 1997’de kullanımı yasaklanmıştır.

- Amerika’da ise hospitalize hastalarda gastrointestinal kolonizasyon daha sık

- Vankomisin, hücre duvarı öncüllerinin D-alanil-D-alanin (D-Ala-D-Ala) ucuna bağlanarak hücre duvarı sentezini bloke eder ve enterokokları inhibe eder.



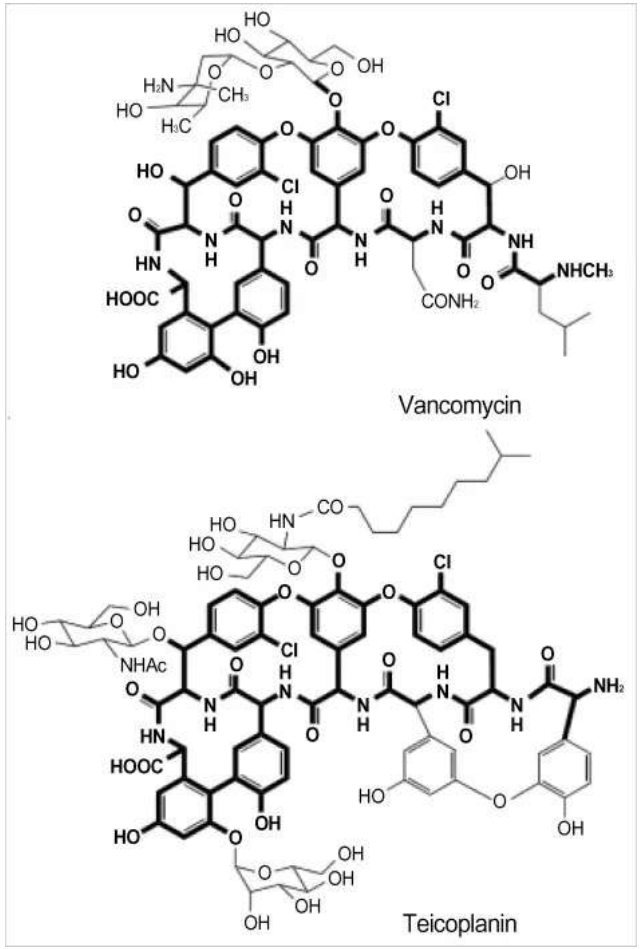
Enterokoklarda VA Direnci



D-Alanin → D-laktat : VanA, VanB, VanD, VanM
D-Alanin → D-serin : VanC, VanE, VanG, VanL, VanN

VanA: D-alanin'in D-laktat ile yer değiştirmesi, vankomisinin minimum inhibitör konsantrasyonunu (MIC) neredeyse 1000 kat artırır.

Vankomisin (glikopeptit) direnci



- Enterokoklarda vankomisin direnci kazanılmış veya intrinsik olabilir.
- Ayrıca hem düşük düzey hem de yüksek düzey vankomisin direnci görülebilir.

- Kazanılmış Direnç

VanA, B, D, E, G, L (En sık *E. faecium* ve *E. faecalis*)

- İntrinsik Direnç

VanC; *E. gallinarum* (vanC1 genotipi) ve *E. casseliflavus* (vanC2 ve vanC3 genotipleri)

Phenotypes of vancomycin-resistant enterococci (VRE)

Phenotype	Ligase gene	Ending of peptidoglycan*	MIC vancomycin (mcg/mL)	MIC teicoplanin (mcg/mL)	Transferability between strains	Species
VanA	*vanA*	D-Ala-D-Lac	64 to 1000	16 to 512	YES	*E. faecium, E. faecalis, E. durans, E. hirae, E. gallinarum, E. casseliflavus, E. raffinosus, E. avium, E. mundtii*
VanB	*vanB*	D-Ala-D-Lac	4 to 32	0.5 to 1	YES	*E. faecium, E. faecalis, E. durans, E. gallinarum*
VanC	*vanC*	D-Ala-D-Ser	8 to 32	0.5 to 1	NO	*E. gallinarum, E. casseliflavus*
VanD	*vanD*	D-Ala-D-Lac	64 to 128	4 to 64	NO	*E. faecium, E. faecalis, E. raffinosus*
VanE	*vanE*	D-Ala-D-Ser	8 to 32	0.5 to 1	NO	*E. faecalis*
VanG	*vanG*	D-Ala-D-Ser	8 to 16	0.5 to 1	YES	*E. faecalis*
VanL	*vanL*	D-Ala-D-Ser¶	8	0.5	NO	*E. faecalis*
VanM	*vanM*	D-Ala-D-Lac¶	>256	64 to >256	YES	*E. faecium*
VanN	*vanN*	D-Ala-D-Ser¶	8	0.5	YES	*E. faecium*

- 9 adet direnç fenotipi tanımlanmıştır.
- Direnç mekanizması tüm fenotiplerde benzerlik gösterip, vankomisinin hedefine daha düşük afinite ile bağlanmasıyla sonuçlanır.

- VanA tipi dirençte;
  - Vankomisin ve teikoplanine yüksek düzey direnç vardır
  - Direnç transfer edilebilir
- VanB tipi dirençte;
  - Vankomisin dirençli, teikoplanin ise duyarlıdır.
  - Direnç transfer edilebilir.

Phenotypes of vancomycin-resistant enterococci (VRE)

Phenotype	Ligase gene	Ending of peptidoglycan*	MIC vancomycin (mcg/mL)	MIC teicoplanin (mcg/mL)	Transferability between strains	Species
VanA	*vanA*	D-Ala-D-Lac	64 to 1000	16 to 512	YES	*E. faecium, E. faecalis, E. durans, E. hirae, E. gallinarum, E. casseliflavus, E. raffinosus, E. avium, E. mundtii*
VanB	*vanB*	D-Ala-D-Lac	4 to 32	0.5 to 1	YES	*E. faecium, E. faecalis, E. durans, E. gallinarum*
VanC	*vanC*	D-Ala-D-Ser	8 to 32	0.5 to 1	NO	*E. gallinarum, E. casseliflavus*
VanD	*vanD*	D-Ala-D-Lac	64 to 128	4 to 64	NO	*E. faecium, E. faecalis, E. raffinosus*
VanE	*vanE*	D-Ala-D-Ser	8 to 32	0.5 to 1	NO	*E. faecalis*
VanG	*vanG*	D-Ala-D-Ser	8 to 16	0.5 to 1	YES	*E. faecalis*
VanL	*vanL*	D-Ala-D-Ser¶	8	0.5	NO	*E. faecalis*
VanM	*vanM*	D-Ala-D-Lac¶	>256	64 to >256	YES	*E. faecium*
VanN	*vanN*	D-Ala-D-Ser¶	8	0.5	YES	*E. faecium*

- VanC tipi direnç;
  - *E. gallinarum* ve *E. casseliflavus* suşlarında görülür.
  - İntrinsik dirençtir.
  - Direnç geni transfer edilmez.
  - İzolasyon önerilmez.

- Teikoplanin direnci varsa VanA tipi direnç olabileceği akla gelmeli ve izolasyon uygulanmalıdır.

VA MIC

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

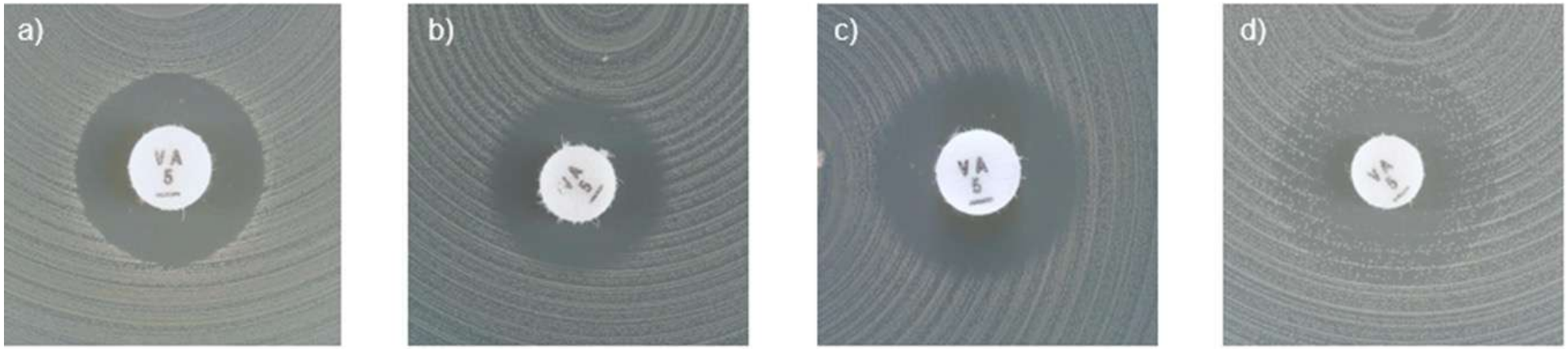
CLINICAL AND LABORATORY STANDARDS INSTITUTE®

- Vankomisine duyarlı – ≤4 mcg/mL
- Vankomisine dirençli – >4 mcg/mL

- Vankomisine duyarlı – ≤4 mcg/mL
- Vankomisine dirençli – ≥32 mcg/mL

Glycopeptides and lipoglycopeptides	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)		
	S ≤	R >	ATU		S ≥	R <	ATU
Dalbavancin	IE	IE			IE	IE	
Oritavancin	IE	IE			IE	IE	
Teicoplanin	2	2		30	16	16	
Telavancin	IE	IE			IE	IE	
Vancomycin	4	4		5	12[A]	12[A]	

Duyarlılık 24 saatlik inkübasyonun ardından okunmalıdır.



VRE risk faktörleri

- Önceki antimikrobiyal tedavi
  - Vankomisin ve sefalosporin kullanımı
  - Geniş spektrumlu antibiyotik kullanımı ile GİS florasının bozulması
  - Anaerobik antibiyotiklerin kullanılması
- VRE ile kolonizasyon durumu
- VRE ile kolonize yüzeylere temas
  - Özellikle ortak kullanılan medikal aletler: tansiyon aleti, ekg probu vb.
  - VRE olgusunun yakınında yatma (ortak eşya kullanımı - günlük malzemeler)

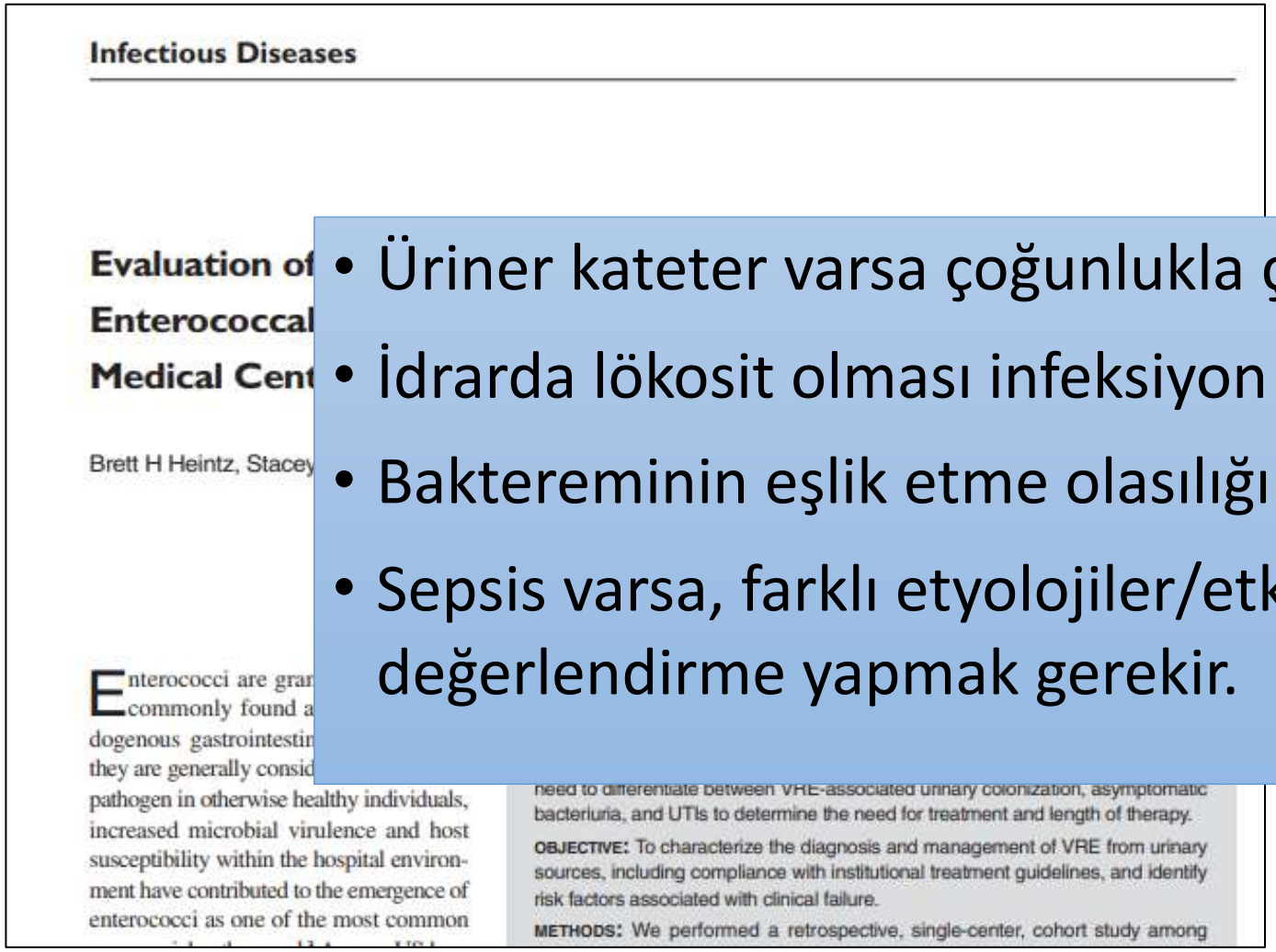
- 72 saatten uzun hastanede kalış
- Uzun süre bakım merkezinde yatma
- Altta yatan önemli tıbbi durumlar (diyaliz gerektiren SDBH, malignite, transplant alıcısı)
- Yoğun bakım gereksinimi
- Proton pompa inhibitörü kullanımı
- İnvazif cihazlar/kateterler

VRE infeksiyonlarına yaklaşım

- İdrar yolu infeksiyonu
- Karın içi infeksiyon (karın içi abseler)
- Bakteremi
- Endokardit
- Deri yumuşak doku infeksiyonları
- Menenjit

İdrar yolu infeksiyonu

- İdrar enterokokların en sık üretildiği klinik örnektir.
  - Üriner kolonizasyon
  - Sistit
  - Piyelonefrit
  - Perinefrik apse
  - Prostatit kaynak olabilir.


Infectious Diseases

Evaluation of
Enterococcal
Medical Cent

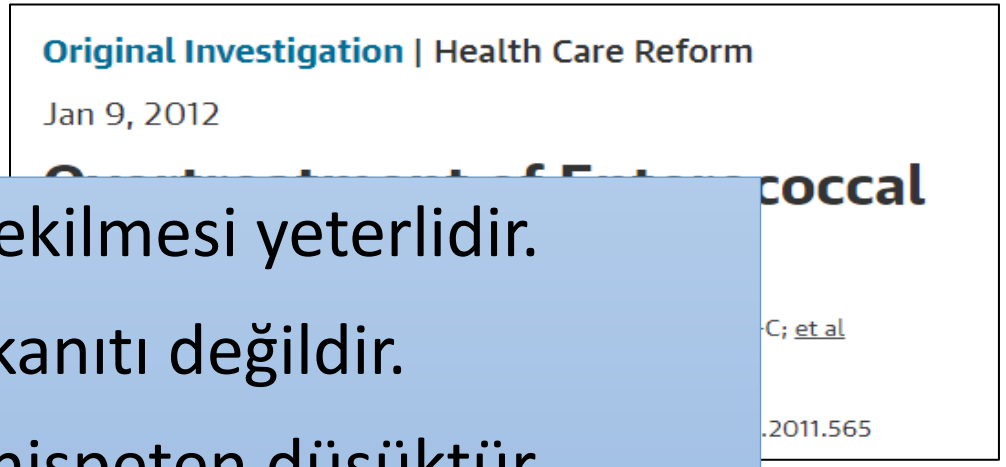
Brett H Heintz, Stacey

Enterococci are gran
commonly found a
dogenous gastrointestin
they are generally consid
pathogen in otherwise healthy individuals,
increased microbial virulence and host
susceptibility within the hospital environ-
ment have contributed to the emergence of
enterococci as one of the most common

need to differentiate between VRE-associated urinary colonization, asymptomatic bacteriuria, and UTIs to determine the need for treatment and length of therapy.

OBJECTIVE: To characterize the diagnosis and management of VRE from urinary sources, including compliance with institutional treatment guidelines, and identify risk factors associated with clinical failure.

METHODS: We performed a retrospective, single-center, cohort study among


Original Investigation | Health Care Reform

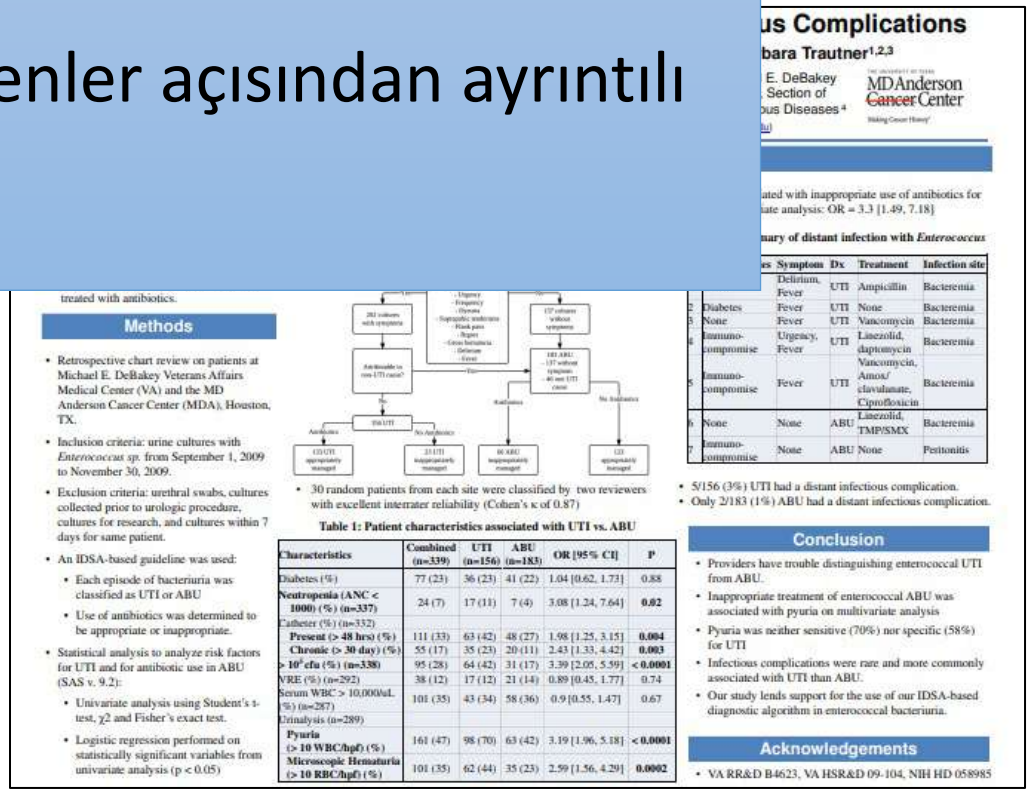
Jan 9, 2012

coccal

C; et al

.2011.565

- Üriner kateter varsa çoğunlukla çekilmesi yeterlidir.
- İdrarda lökosit olması infeksiyon kanıtı değildir.
- Bakterenimin eşlik etme olasılığı nispeten düşüktür.
- Sepsis varsa, farklı etyolojiler/etkenler açısından ayrıntılı değerlendirme yapmak gerekir.


us Complications

bara Trautner[1,2,3]

E. DeBakey
Section of
ous Diseases[4]

MD Anderson Cancer Center

ated with inappropriate use of antibiotics for
ate analysis: OR = 3.3 [1.49, 7.18]

nary of distant infection with *Enterococcus*

	Symptom	Dx	Treatment	Infection site
	Delirium, Fever	UTI	Ampicillin	Bacteremia
Diabetes	Fever	UTI	None	Bacteremia
None	Fever	UTI	Vancomycin	Bacteremia
Immuno-compromise	Urgency, Fever	UTI	Linezolid, daptomycin	Bacteremia
Immuno-compromise	Fever	UTI	Vancomycin, Amox/clavulanate, Ciprofloxicin	Bacteremia
None	None	ABU	Linezolid, TMP/SMX	Bacteremia
Immuno-compromise	None	ABU	None	Peritonitis

- 5/156 (3%) UTI had a distant infectious complication.
- Only 2/183 (1%) ABU had a distant infectious complication.

treated with antibiotics.

Methods

- Retrospective chart review on patients at Michael E. DeBakey Veterans Affairs Medical Center (VA) and the MD Anderson Cancer Center (MDA), Houston, TX.
- Inclusion criteria: urine cultures with *Enterococcus sp.* from September 1, 2009 to November 30, 2009.
- Exclusion criteria: urethral swabs, cultures collected prior to urologic procedure, cultures for research, and cultures within 7 days for same patient.
- An IDSA-based guideline was used:
  - Each episode of bacteriuria was classified as UTI or ABU
  - Use of antibiotics was determined to be appropriate or inappropriate.
- Statistical analysis to analyze risk factors for UTI and for antibiotic use in ABU (SAS v. 9.2):
  - Univariate analysis using Student's t-test, $\chi 2$ and Fisher's exact test.
  - Logistic regression performed on statistically significant variables from univariate analysis ($p < 0.05$)

- 30 random patients from each site were classified by two reviewers with excellent interrater reliability (Cohen's κ of 0.87)

Table 1: Patient characteristics associated with UTI vs. ABU

Characteristics	Combined (n=339)	UTI (n=156)	ABU (n=183)	OR [95% CI]	P
Diabetes (%)	77 (23)	36 (23)	41 (22)	1.04 [0.62, 1.73]	0.88
Neutropenia (ANC < 1000) (%) (n=337)	24 (7)	17 (11)	7 (4)	3.08 [1.24, 7.64]	**0.02**
Catheter (%) (n=332)					
Present (> 48 hrs) (%)	111 (33)	63 (42)	48 (27)	1.98 [1.25, 3.15]	**0.004**
Chronic (> 30 day) (%)	55 (17)	35 (23)	20 (11)	2.43 [1.33, 4.42]	**0.003**
> 10^5 cfu (%) (n=338)	95 (28)	64 (42)	31 (17)	3.39 [2.05, 5.59]	**< 0.0001**
VRE (%) (n=292)	38 (12)	17 (12)	21 (14)	0.89 [0.45, 1.77]	0.74
Serum WBC > 10,000/uL (%) (n=287)	101 (35)	43 (34)	58 (36)	0.9 [0.55, 1.47]	0.67
Urinalysis (n=289)					
Pyuria (> 10 WBC/hpf) (%)	161 (47)	98 (70)	63 (42)	3.19 [1.96, 5.18]	**< 0.0001**
Microscopic Hematuria (> 10 RBC/hpf) (%)	101 (35)	62 (44)	35 (23)	2.59 [1.56, 4.29]	**0.0002**

Conclusion

- Providers have trouble distinguishing enterococcal UTI from ABU.
- Inappropriate treatment of enterococcal ABU was associated with pyuria on multivariate analysis
- Pyuria was neither sensitive (70%) nor specific (58%) for UTI
- Infectious complications were rare and more commonly associated with UTI than ABU.
- Our study lends support for the use of our IDSA-based diagnostic algorithm in enterococcal bacteriuria.

Acknowledgements

- VA RR&D B4623, VA HSR&D 09-104, NIH HD 058985

- Hastaların %58'i gereksiz tedavi alıyor.

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Voided Midstream Urine Culture and Acute Cystitis in Premenopausal Women

Thomas M. Hooto

BACKGROUND

The cause of acute uncomp
voided midstream urine, b
pecially when gram-positiv

METHODS

Women from 18 to 49 yea
of midstream urine, after
for culture (catheter urine).
paired specimens. The primary outcome was a comparison of positive predictive values and negative predictive values of organisms grown in midstream urine, with the presence or absence of the organism in catheter urine used as the reference.

N Engl J Med 2013;369:1883-91.
DOI: 10.1056/NEJMoa1302186
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- Premenopozal kadınlarda komplike olmayan sistit vakalarındaki üremeler değerlendirilmiş.
- Orta akım idrar kültüründen

Sistit semptomları olan kişilerinin idrarında enterokokların yanında başka bir üropatojen mevcutsa, enterokok tedavisi gerekmeyebilir.

Krieger JN. J Infect Dis. 1983 Jul;148(1):57-62.

er idrar

nış ve

öngörmediği gösterilmiş.

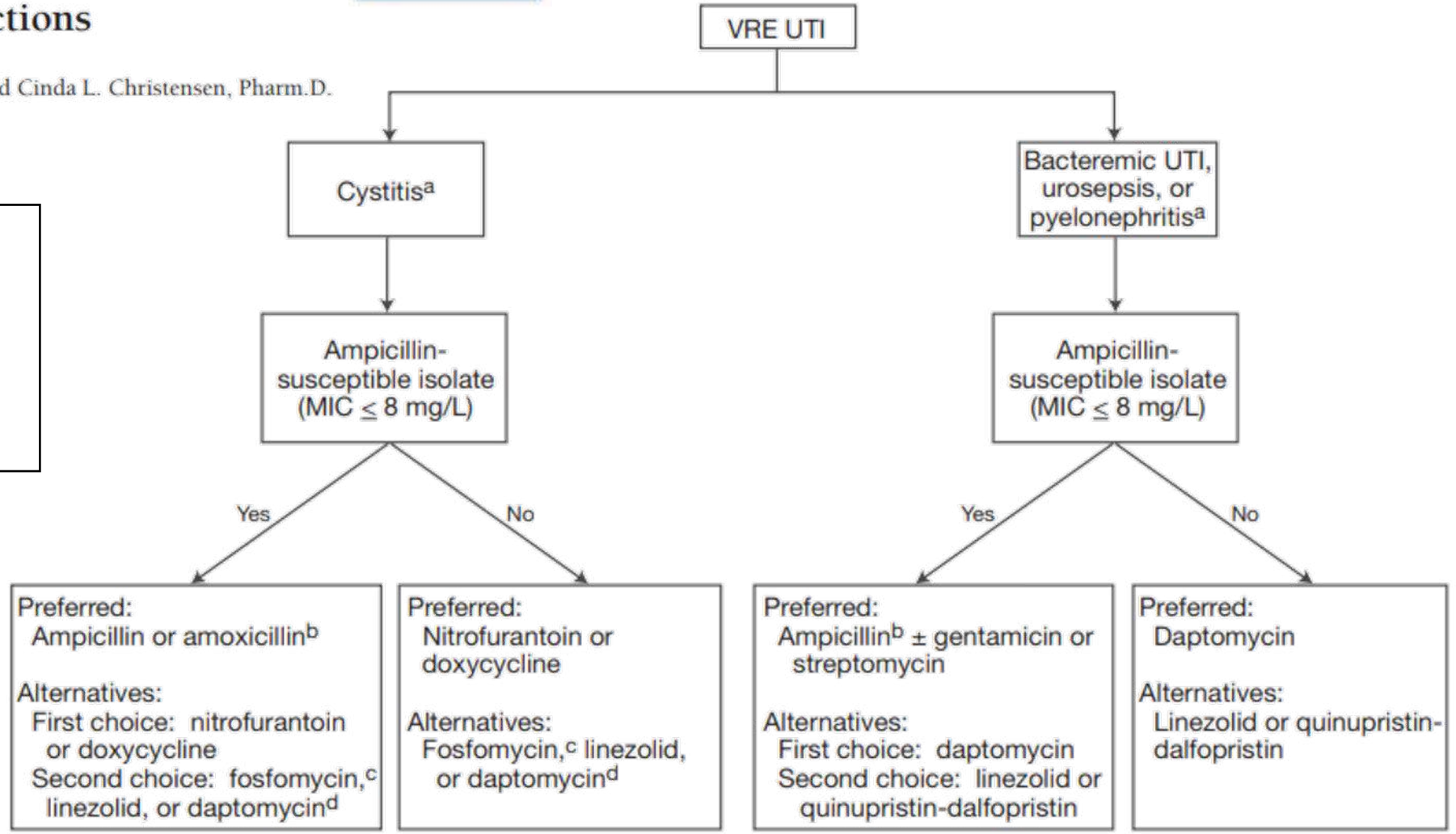
- 20 hastanın (%10) orta akım idrarında enterokok +
  - Sadece 2 hastanın kateter kültüründe enterokok üremesi+
- 16 hastanın (16/20) orta akım idrarında *E. coli* +
  - 11 hastanın kateter kültüründe *E. coli* +

REVIEWS OF THERAPEUTICS

Vancomycin-Resistant Enterococcal Urinary Tract Infections

Brett H. Heintz, Pharm.D., Jenana Halilovic, Pharm.D., and Cinda L. Christensen, Pharm.D.

Fosfomisin ve Nitrofurantoin VRE sistiti tedavisinde önemli alternatiflerdir.



Karın içi infeksiyonlar

SURGICAL INFECTIONS
Volume 21, Number X, 2020
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DOI: 10.1089/sur.2020.001

Systematic Review and Meta-Analysis of the Efficacy of Appropriat
fo

Jian Zhang,[1–3]
Jing-Y

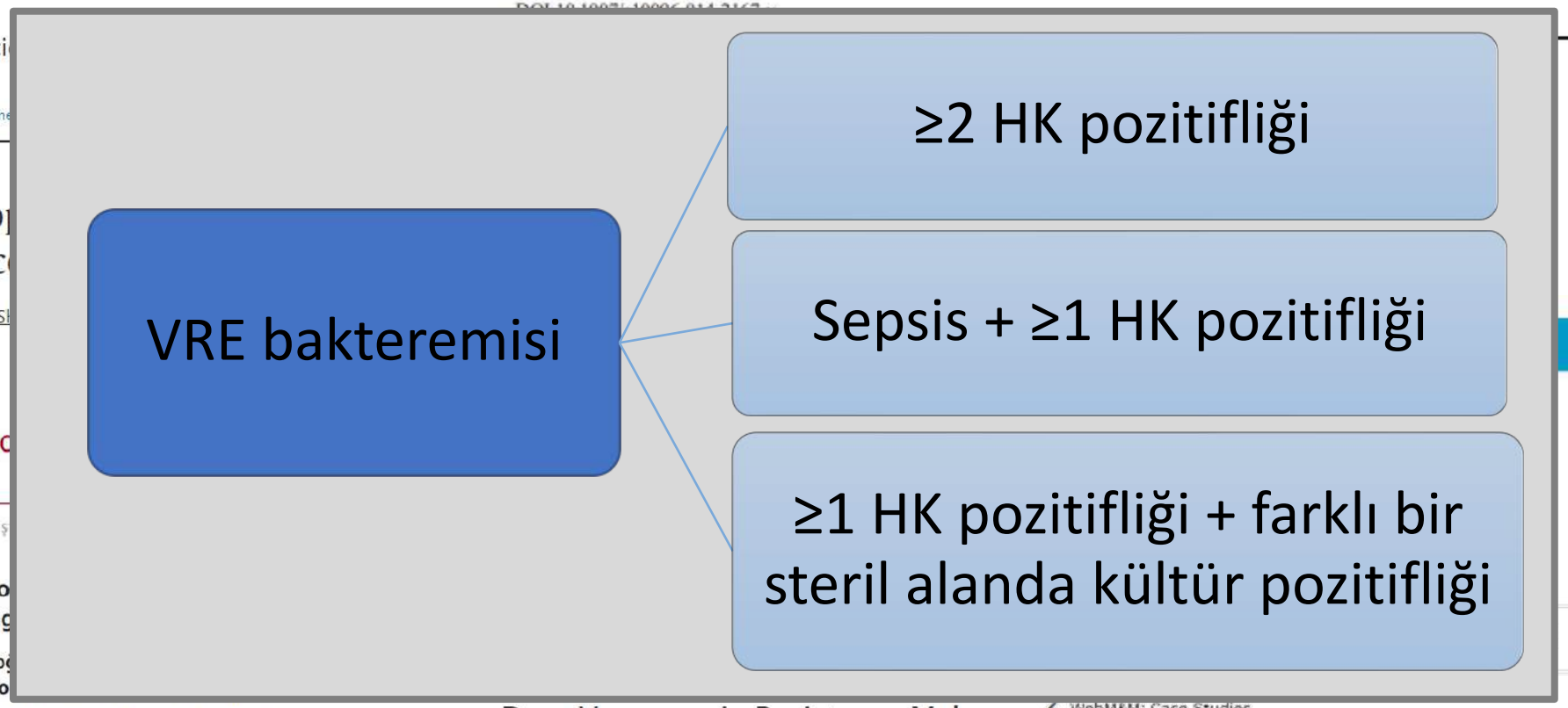
Toplum kökenli, kritik olmayan hastalarda tedavide enterokokların kapsanması gereksizdir.

Abstract

Background: Delayed treatment of seriously infected patients results in increased mortality. However, antimicrobial therapy for the initial 24 to 48 hours is mostly empirically provided, without evidence regarding the causative pathogen. Whether empiric anti-enterococcal therapy should be administered to treat intra-abdominal infection (IAI) before obtaining culture results remains unknown. We performed a meta-analysis to explore the effects of empiric enterococci covered antibiotic therapy in IAI and the risk factors for enterococcal infection in IAI.
Methods: We searched multiple databases systematically and included 23 randomized controlled trials (RCTs) and 13 observational studies. The quality of included studies was assessed, and the reporting bias was evaluated. Meta-analysis was performed using random effects or fixed effects models according to the heterogeneity. The risk ratio (RR), odds ratio (OR), and 95% confidence interval (CI) were calculated.
Results: Enterococci-covered antibiotic regimens provided no improvement in treatment success compared with control regimens (RR, 0.99; 95% CI, 0.97–1.00; p = 0.15), with similar mortality and adverse effects in both arms. Basic characteristic analysis revealed that most of the enrolled patients with IAI in RCTs were young, lower risk community-acquired intra-abdominal infection (CA-IAI) patients with a relatively low APACHE II score. Interestingly, risk factor screening revealed that malignancy, corticosteroid use, operation,

- Enterokokları kapsayan tedavilerin, enterokokların kapsanmadığı tedavilere bir üstünlüğü gösterilememiş.
  - Mortalite ve ilaç yan etkileri benzer bulunmuş.
  - Alt grup analizlerinde de benzer sonuçlar
- n mikroorganizmaların
  ruyor.
- Çalışmaların çoğunda enterokokların oranı %20'nin altında.
- Hastane kaynaklı karın içi infeksiyonlarda enterokokların izolasyonu 2-5 kat daha fazla bulunmuş.

VRE bakteremisi



CDC definitions for nosocomial infections, 1988.

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY JANUARY 2016, VOL. 37, NO. 1

ORIGINAL ARTICLE

VRE and VSE Bacteremia Outcomes in the Era of Effective VRE Therapy: A Systematic Review and Meta-analysis

Chatura Prematunge, MSc;[1] Colin MacDougall, MSc;[1] Jennie Johnstone, MD, PhD;[1,2,3] Kwaku Adomako, MSc;[1] Freda Lam, MPH;[1] Jennifer Robertson, PhD;[1] Gary Garber, MD[1,3,4,5]

BACKGROUND. Prior data suggest that vancomycin-resistant *Enterococcus* (VRE) bacteremia is associated with worse outcomes than vancomycin-sensitive *Enterococcus* (VSE) bacteremia. However, many studies evaluating such outcomes were conducted prior to the availability of effective VRE therapies.

OBJECTIVE. To systematically review VRE and VSE bacteremia outcomes among hospital patients in the era of effective VRE therapy.

METHODS. Electronic databases and grey literature published between January 1997 and December 2014 were searched to identify all primary research studies comparing outcomes of VRE and VSE bacteremias among hospital patients, following the availability of effective VRE therapies. The primary outcome was all-cause, in-hospital mortality, while total hospital length of stay (LOS) was a secondary outcome. All meta-analyses were conducted in Review Manager 5.3 using random-effects, inverse variance modeling.

RESULTS. Among all the studies reviewed, 12 cohort studies and 1 case control study met inclusion criteria. Similar study designs were combined in meta-analyses for mortality and LOS. VRE bacteremia was associated with increased mortality compared with VSE bacteremia among cohort studies (odds ratio [OR], 1.80; 95% confidence interval [CI], 1.38–2.35; $I^2 = 0\%$; $n = 11$); the case-control study estimate was similar, but not significant (OR, 1.93; 95% CI, 0.97–3.82). LOS was greater for VRE bacteremia patients than for VSE bacteremia patients (mean difference, 5.01 days; 95% CI, 0.58–9.44]; $I^2 = 0\%$; $n = 5$).

CONCLUSIONS. Despite the availability of effective VRE therapy, VRE bacteremia remains associated with an increased risk of in-hospital mortality and LOS when compared to VSE bacteremia.

Infect. Control Hosp. Epidemiol. 2016;37(1):26–35

- 2575 bakteremi
- 1863 VSE bakteremisi
- 712 VRE bakteremisi

Mortalite VRE bakteremisinde daha yüksek bulunmuş.

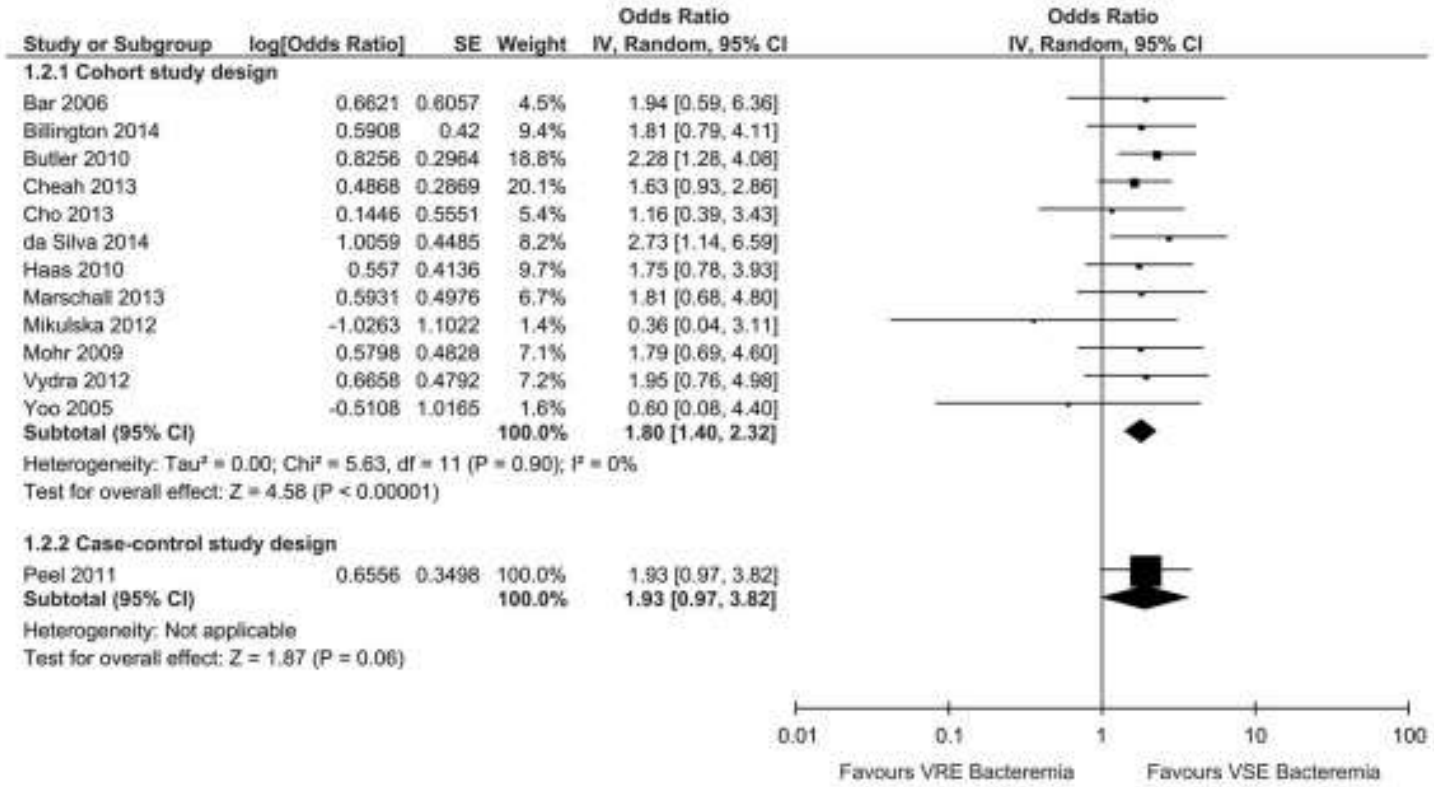


FIGURE 2. VRE and VSE bacteremia unadjusted in-hospital mortality risk by study design. Results of included studies for VRE and VSE bacteremia unadjusted in-hospital mortality risk stratified by study design. Abbreviations: 95% CI, 95% confidence interval; SE, standard error; IV, random, inverse-variance, random-effects method.

Toplam hastane yatışı VRE bakteremisinde daha yüksek bulunmuş.

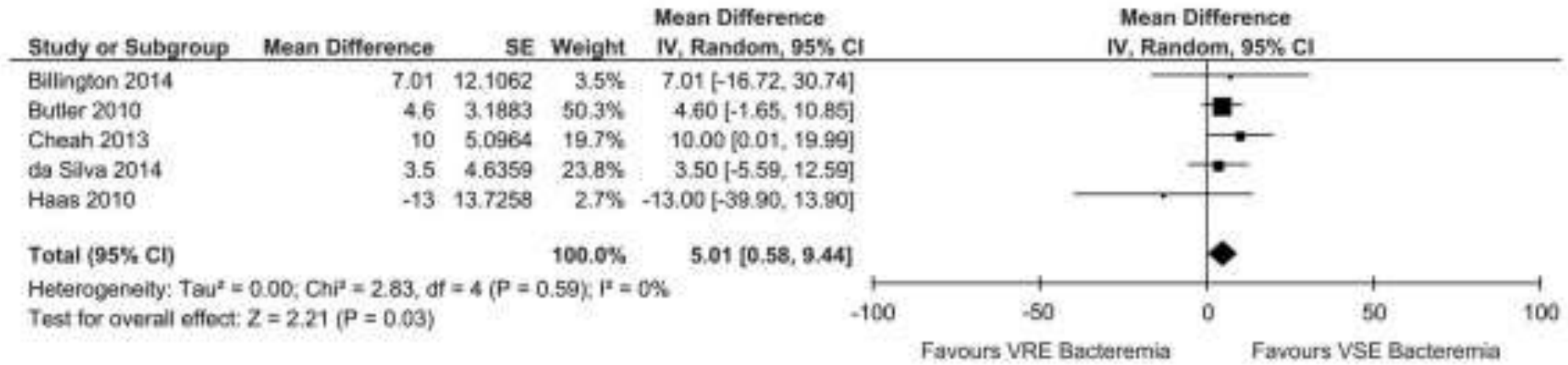


FIGURE 3. VRE and VSE bacteremia total hospital LOS mean difference. Results of studies reporting on VRE and VSE bacteremia total hospital LOS. Abbreviations: LOS, length of stay; 95% CI, 95% confidence interval; SE, standard error; IV, random, inverse-variance, random-effects method.

Bakteremi sonrası hastanede kalış süresi VSE & VRE bakteremilerinde benzer bulunmuş.

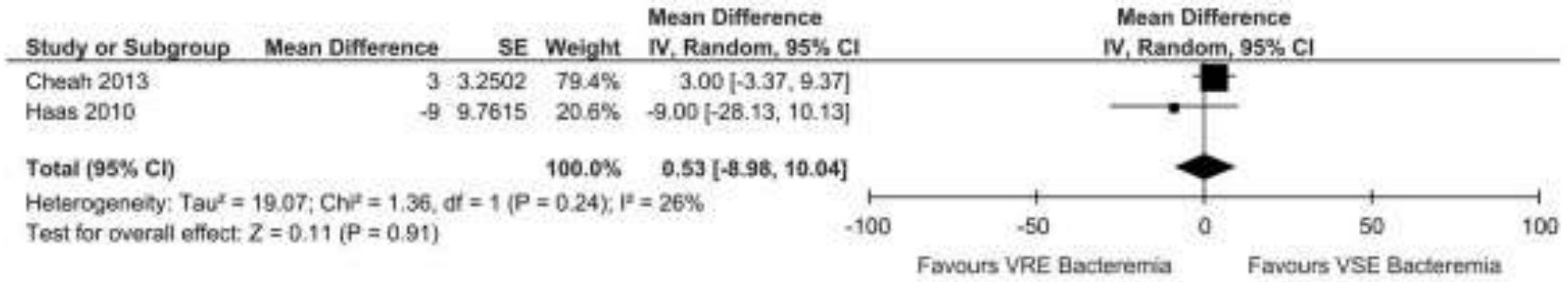
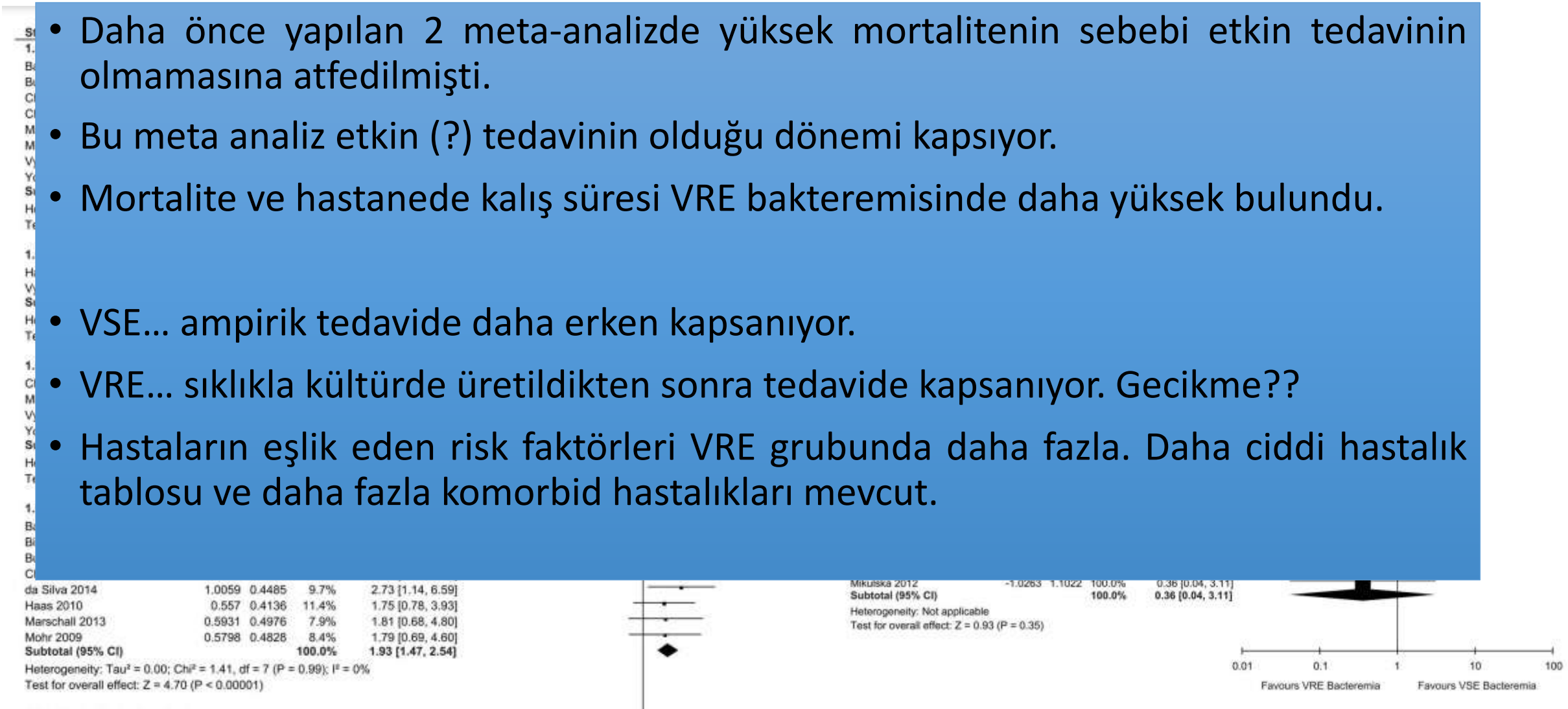


FIGURE 4. VRE and VSE post-bacteremia total hospital LOS mean difference. Results of studies reporting on VRE and VSE post-bacteremia hospital LOS. Abbreviations: LOS, length of stay; 95% CI, 95% confidence interval; SE, standard error; IV, random, inverse-variance, random-effects method.

Alt grup analizlerinde de (yaş, bağışıklık, çalışma grubu ve kalitesi) VRE bakteremisinde mortalite daha yüksek bulunmuş.

- Daha önce yapılan 2 meta-analizde yüksek mortalitenin sebebi etkin tedavinin olmamasına atfedilmişti.
- Bu meta analiz etkin (?) tedavinin olduğu dönemi kapsıyor.
- Mortalite ve hastanede kalış süresi VRE bakteremisinde daha yüksek bulundu.

- VSE… ampirik tedavide daha erken kapsanıyor.
- VRE… sıklıkla kültürde üretildikten sonra tedavide kapsanıyor. Gecikme??
- Hastaların eşlik eden risk faktörleri VRE grubunda daha fazla. Daha ciddi hastalık tablosu ve daha fazla komorbid hastalıkları mevcut.



VRE endokarditi

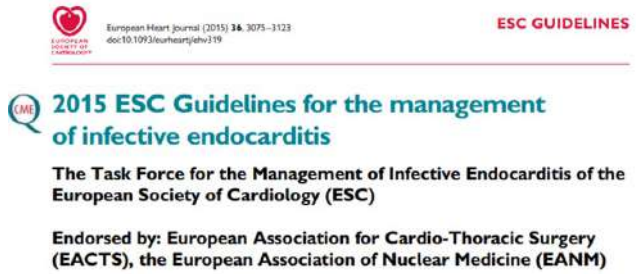
«Hangi VRE bakteremisinde endokardit düşünelim?»

DENOVA skoru

- **D**uration of symptoms ≥7 days;
- Evidence of **e**mbolization;
- **N**umber of positive blood cultures (two or more);
- Unknown **o**rigin of bacteremia;
- Prior heart **v**alve disease;
- **A**uscultation of a heart murmur.

- 3'ün altındaki skorlar endokardit açısından çok düşük riski gösterir.
  - %100 hassasiyet
  - %85 özgüllük

VRE endokarditi


European Heart Journal (2015) 36, 3075–3123
doi:10.1093/eurheartj/ehv319

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)


Circulation
Volume 132, Issue 15, 13 October 2015; Pages 1435-1486
https://doi.org/10.1161/CIR.0000000000000296

AHA SCIENTIFIC STATEMENT

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

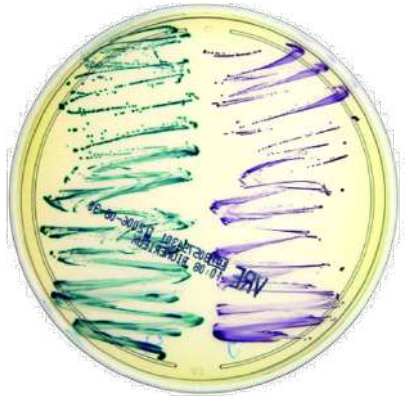
A Scientific Statement for Healthcare Professionals From the American Heart Association

Enterokok endokarditlerinin;

E.faecalis…Olguların %90-97'sinden sorumlu.

E.faecium…Olguların %1-5'inden sorumlu.

Ancak VRE endokarditlerinden sıklıkla *E.faecium* sorumludur.



Enterococcus faecalis

- Daha virülandır
- Bakteremisine endokardit eşlik etme ihtimali daha yüksektir
- Sıklıkla genitoüriner anomalilere eşlik eder
- Mitral kapak tutulumu daha sık

Enterococcus faecium

- Sıklıkla santral kateter veya gastrointestinal odak kaynaklıdır
- Triküspit kapak tutulumu ön planda
- Kolaylaştırıcı faktörler;
  - Öncesinde antibiyotik kullanımı
  - Transplantasyon
  - Siroz

Table 15. Therapy for Endocarditis Involving a Native or Prosthetic Valve or Other Prosthetic Material Resulting From *Enterococcus* Species Caused by Strains Resistant to Penicillin, Aminoglycosides, and Vancomycin

Regimen	Dose* and Route	Duration, wk	Strength of Recommendation	Comments
Linezolid	600 mg IV or orally every 12 h	>6	*Class IIb; Level of Evidence C*	Linezolid use may be associated with potentially severe bone marrow suppression, neuropathy, and numerous drug interactions. Patients with IE caused by these strains should be treated by a care team including specialists in infectious diseases, cardiology, cardiac surgery, clinical pharmacy, and, in children, pediatrics. Cardiac valve replacement may be necessary for cure.
Or				
Daptomycin	10–12 mg/kg per dose	>6	*Class IIb; Level of Evidence C*	

IE indicates infective endocarditis, and IV, intravenous.
*Doses recommended are for patients with normal renal and hepatic function

Linezolid

- Bakteriostatik
- Enterokok infeksiyonları için FDA onayı var.
- Ancak enterokok endokarditi için FDA onayı yok.
- Uzun dönem kullanımda toksisite artmaktadır.
  - Nötropeni, trombositopeni
  - Periferal ve optik nöropati (kalıcı olabilir)
  - İlaç etkileşimleri (SSRI)
- Tedavi sırasında direnç gelişebilir.

Daptomisin

- Bakterisidal
- Enterokok infeksiyonları için FDA onayı yok.
- Çalışmalar daptomisin monoterapisi için yeterli değildir.
- Eğer tercih edilecekse 10-12mg/kg/gün dozunun tercih edilmesi önerilir.
- Daptomisin + ampisilin (ertapenem/seftarolin) kombinasyonu düşünülebilir.
  - Persistan bakteremi varsa veya
  - Daptomisin MIC yüksek ise
- *E. faecium* tedavisi sırasında daptomisin direnci gelişebilir.

VRE infeksiyonu tedavisi

- En uygun tedavi yaklaşımı net değildir.

- Vankomisine dirençli *E. faecium* izolatları sıklıkla eş zamanlı olarak beta-laktamlara ve aminoglikozitlere karşı yüksek düzeyde dirence sahiptir.
- Vankomisine dirençli *E. faecalis* ise penisilin ve ampisiline duyarlı olabilir.

- Kinupristin-dalfopristin : *E. faecalis* izolatları dirençli, *E. faecium* izolatları ise duyarlı saptanır.

- Kinupristin-dalfopristin: FDA onayı kaldırılmıştır.

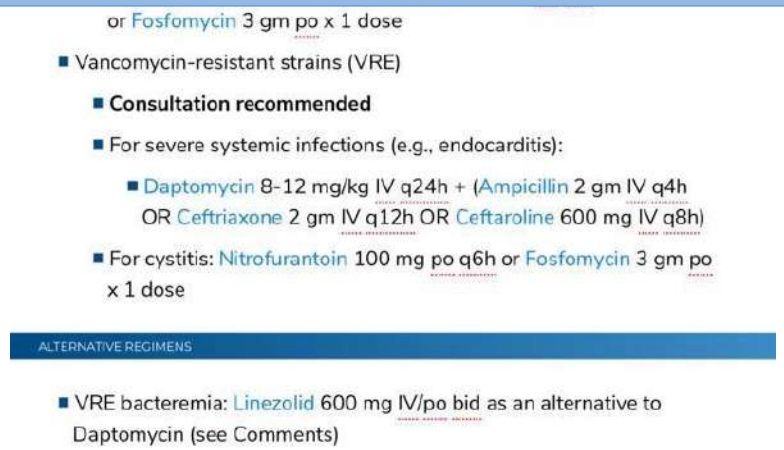
- Daptomisin: Enterokok infeksiyonları için FDA onayı yoktur.

- Linezolid: Enterokok infeksiyonları için FDA onayı vardır.
- Tigesiklin: Enterokok infeksiyonları için FDA onayı vardır.

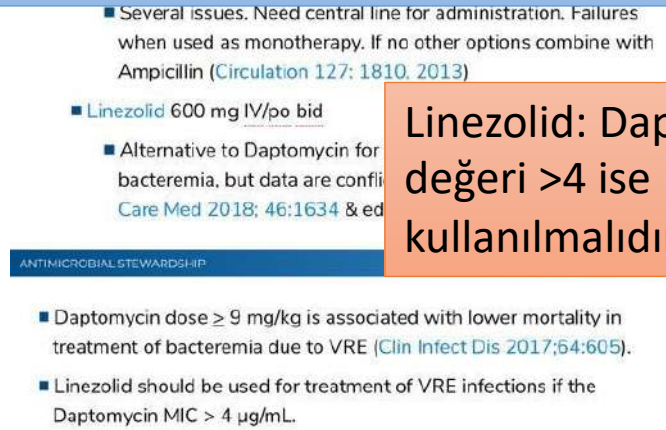
Monotherapy regimens for treatment of bacteremia due to resistant enterococci in adults*

Regimen	Dose and route
Isolate is ampicillin susceptible and vancomycin resistant	
Preferred agents	
Ampicillin	1 to 2 g IV every 4 to 6 hours
Penicillin G[¶]	18 to 30 million units IV per 24 hours either continuously or in 6 equally divided doses
Alternate agents	
Daptomycin[Δ]	8 to 12 mg/kg IV every 24 hours
Linezolid (alternative agent to daptomycin)	600 mg IV every 12 hours
Isolate is ampicillin resistant and vancomycin susceptible	
Preferred agents	
Vancomycin[◇]	Initially 15 mg/kg/dose IV every 12 hours, not to exceed 2 g per dose; subsequent dosing guided by serum trough concentration or AUC monitoring[§]
Daptomycin[Δ] (alternative agent to vancomycin)	8 to 12 mg/kg IV every 24 hours
Linezolid (alternative agent to daptomycin)	600 mg IV every 12 hours
Alternate agents	
High-dose ampicillin (if ampicillin MIC is ≤32 mcg/mL)	3 to 4 g IV every 4 hours
Ampicillin-sulbactam (if ampicillin resistance is due to beta-lactamase production)	3 g IV every 6 hours
Isolate is ampicillin resistant and vancomycin resistant	
Preferred agents	
Daptomycin[Δ]	8 to 12 mg/kg every 24 hours
Linezolid (alternative agent to daptomycin)	600 mg IV every 12 hours
Alternate agents	
High-dose ampicillin (if ampicillin MIC is ≤32 mcg/mL)	18 to 30 g per day
Ampicillin-sulbactam (if ampicillin resistance is due to beta-lactamase production)	3 g IV every 6 hours

- Ciddi sistemik infeksiyon (endokardit vb);
  - Daptomisin (8-12 mg/kg) + (ampisilin / seftriakson / seftarolin)
  - Linezolid (alternatif)
- Sistit;
  - Nitrofurantoin
  - Fosfomisin



- Ciddi sistemik infeksiyon (bakteremi vb);
  - Daptomisin (10-12mg/kg) + (ampisilin / seftriakson / seftarolin)
  - Linezolid (alternatif)
- Sistit;
  - Nitrofurantoin
  - Fosfomisin



Linezolid: Daptomisin MIC değeri >4 ise kullanılmalıdır.

AAC
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Systematic Review and Meta-Analysis of Linezolid versus Daptomycin for Treatment of Vancomycin-Resistant Enterococcal Bacteremia

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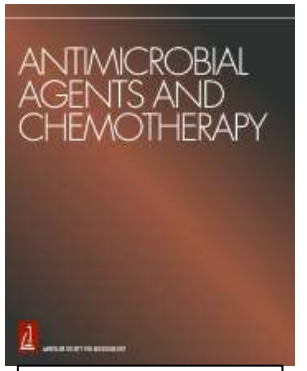
Limited therapeutic options exist for the treatment of vancomycin-resistant *Enterococcus* (VRE) bacteremia; the most commonly used are daptomycin and linezolid. We attempted a systematic review and meta-analysis of the comparative efficacy of those two agents. Studies comparing daptomycin to linezolid treatment for VRE bacteremia, published until August 2012, were identified from the MEDLINE, EMBASE, CENTRAL, ISI Web of Science, and SCOPUS databases. All comparative studies on patients older than 18 years of age that provided mortality data were considered eligible for this systematic review and meta-analysis. The primary outcome of the meta-analysis was 30-day all-cause mortality. Ten retrospective studies including 967 patients were identified. Patients treated with daptomycin had significantly higher 30-day all-cause mortality (odds ratio [OR], 1.61; 95% confidence interval [CI], 1.08 to 2.40) and infection-related mortality (OR, 3.61; 95% CI, 1.42 to 9.20) rates than patients treated with linezolid. When data from all 10 studies were combined, overall mortality was also significantly increased among patients treated with daptomycin (OR, 1.41; 95% CI, 1.06 to 1.89). These findings were confirmed when odds ratios adjusted for potential confounders were pooled. Relapse rates among patients treated with daptomycin were also higher (OR, 2.51; 95% CI, 0.94 to 6.72), although this difference did not reach statistical significance. Adverse event rates were not significantly different between the two groups. Notwithstanding the absence of randomized prospective data, available evidence suggests that mortality rates may be higher with daptomycin than with linezolid among patients treated for VRE bacteremia.



2014; 58(2)

10 çalışma
967 hasta

30 günlük mortalite; daptomisin alan hastalarda daha yüksek bulundu.

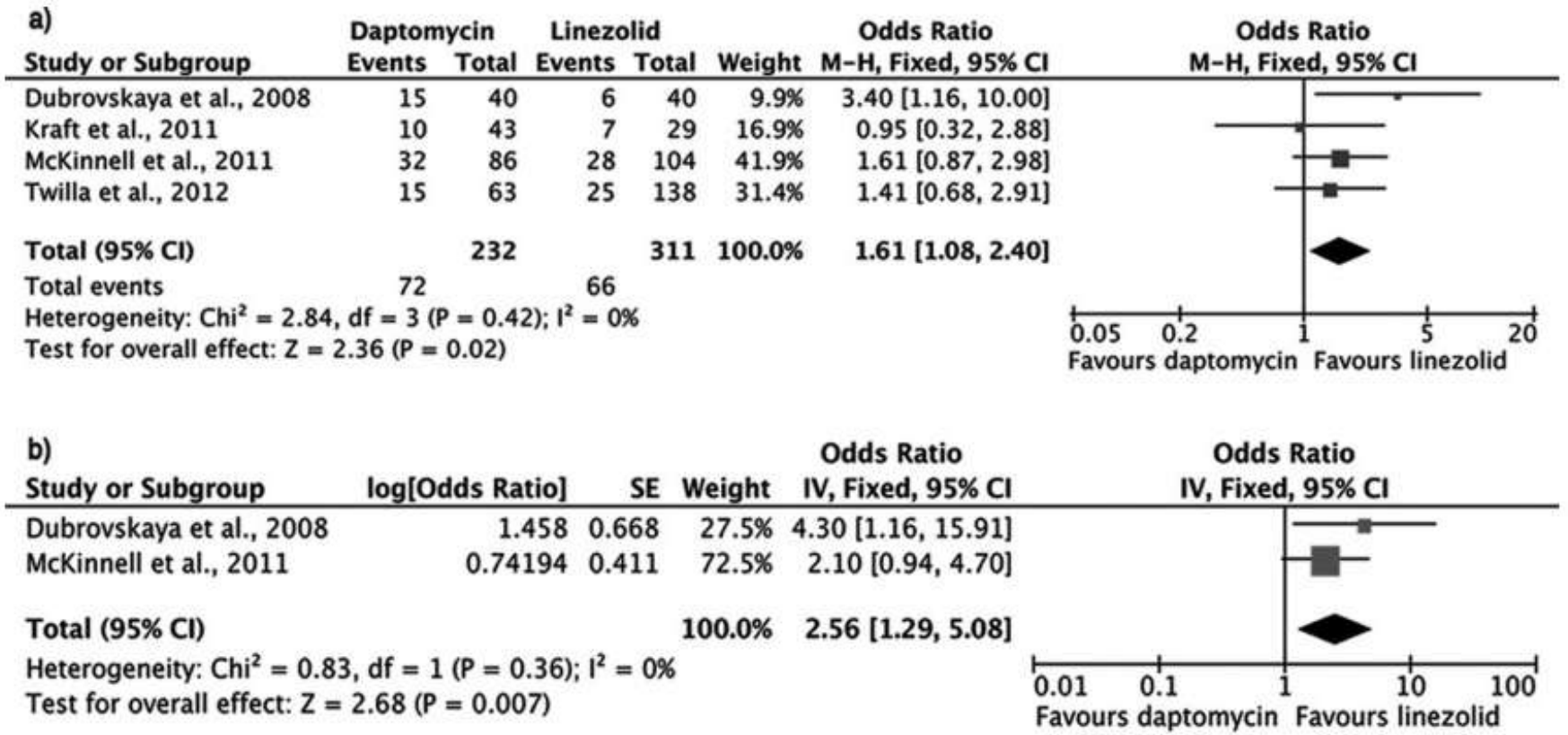


FIG 1 Forest plots (using Mantel-Haenszel [M-H] analysis) of unadjusted (a) and adjusted (b) odds ratios for 30-day all-cause mortality among patients treated with linezolid or daptomycin for VRE bacteremia. CI, confidence interval; SE, standard error; IV, Inverse variance.

İnfeksiyon ilişkili mortalite (a) ve hastane içi mortalite (b): Daptomisin alanlarda daha yüksek bulundu.

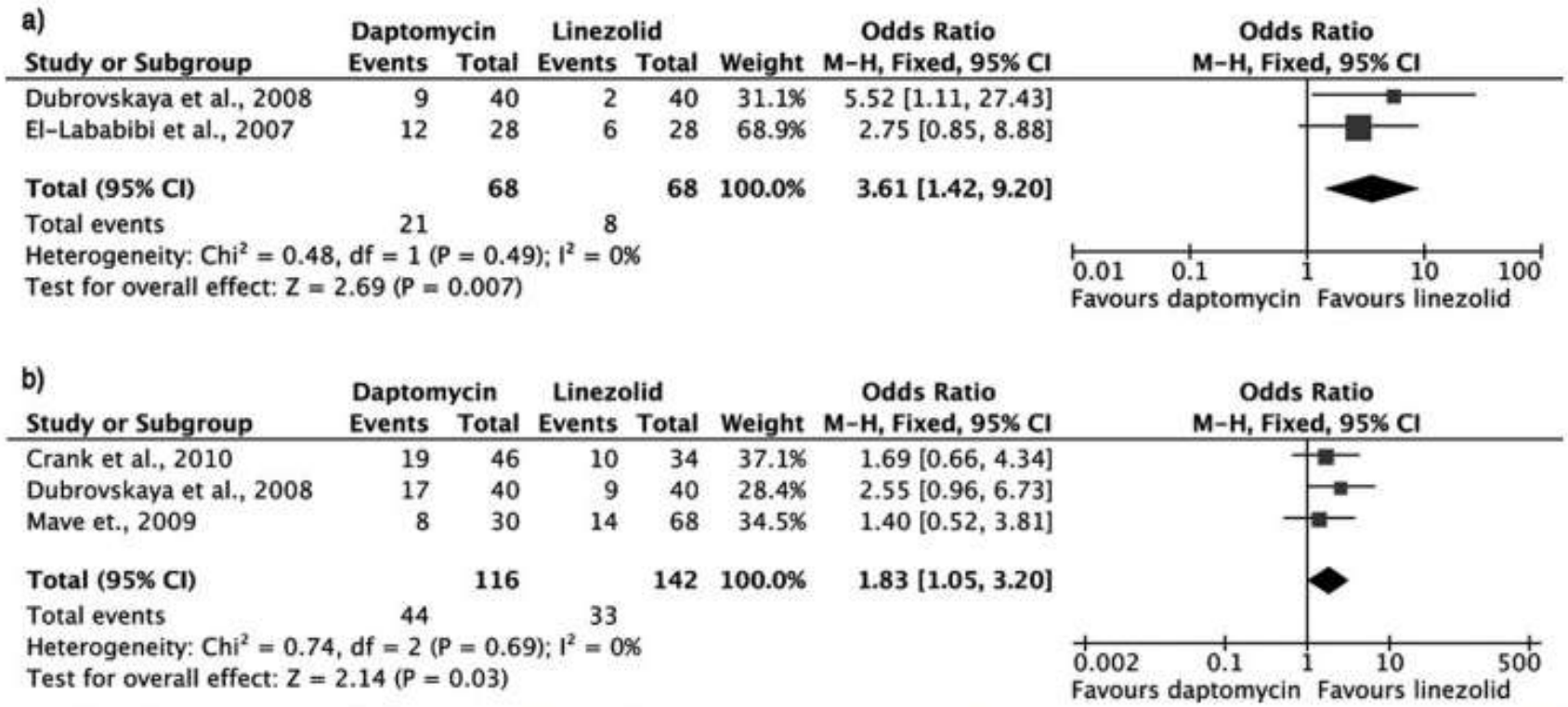


FIG 2 Forest plots (using Mantel-Haenszel [M-H] analysis) of odds ratios for infection-related mortality (a) and in-hospital mortality (b) among patients treated with linezolid or daptomycin for VRE bacteremia.

Genel mortalite: Daptomisin alanlarda daha yüksek bulunmuş.

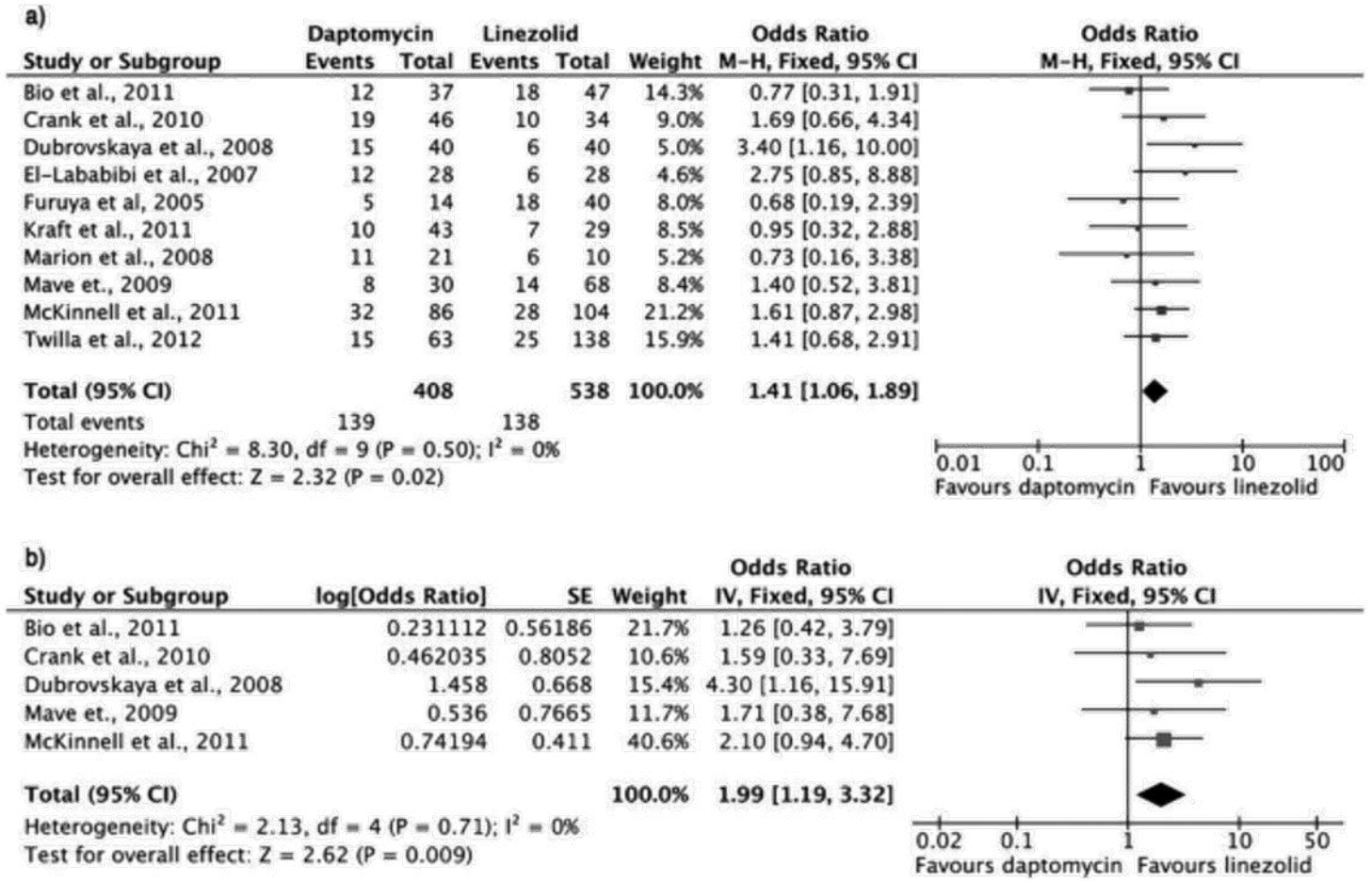


FIG 3 Forest plots (using Mantel-Haenszel [M-H] analysis) of unadjusted (a) and adjusted (b) odds ratios for overall mortality among patients treated with linezolid or daptomycin for VRE bacteremia.

Mikrobiyolojik kür ve bakteremi rekürrensi açısından iki ilaç arasında anlamlı fark yok.

- Daptomisin ile daha fazla tedavi başarısızlığı?
  - Bakterisidal ajan? & Bakteriostatik ajan?
- Daptomisin direnci?
- Daptomisin için uygun ilaç dozu ayarlanamıyor mu?
  - 6mg/kg/gün & 12mg/kg/gün

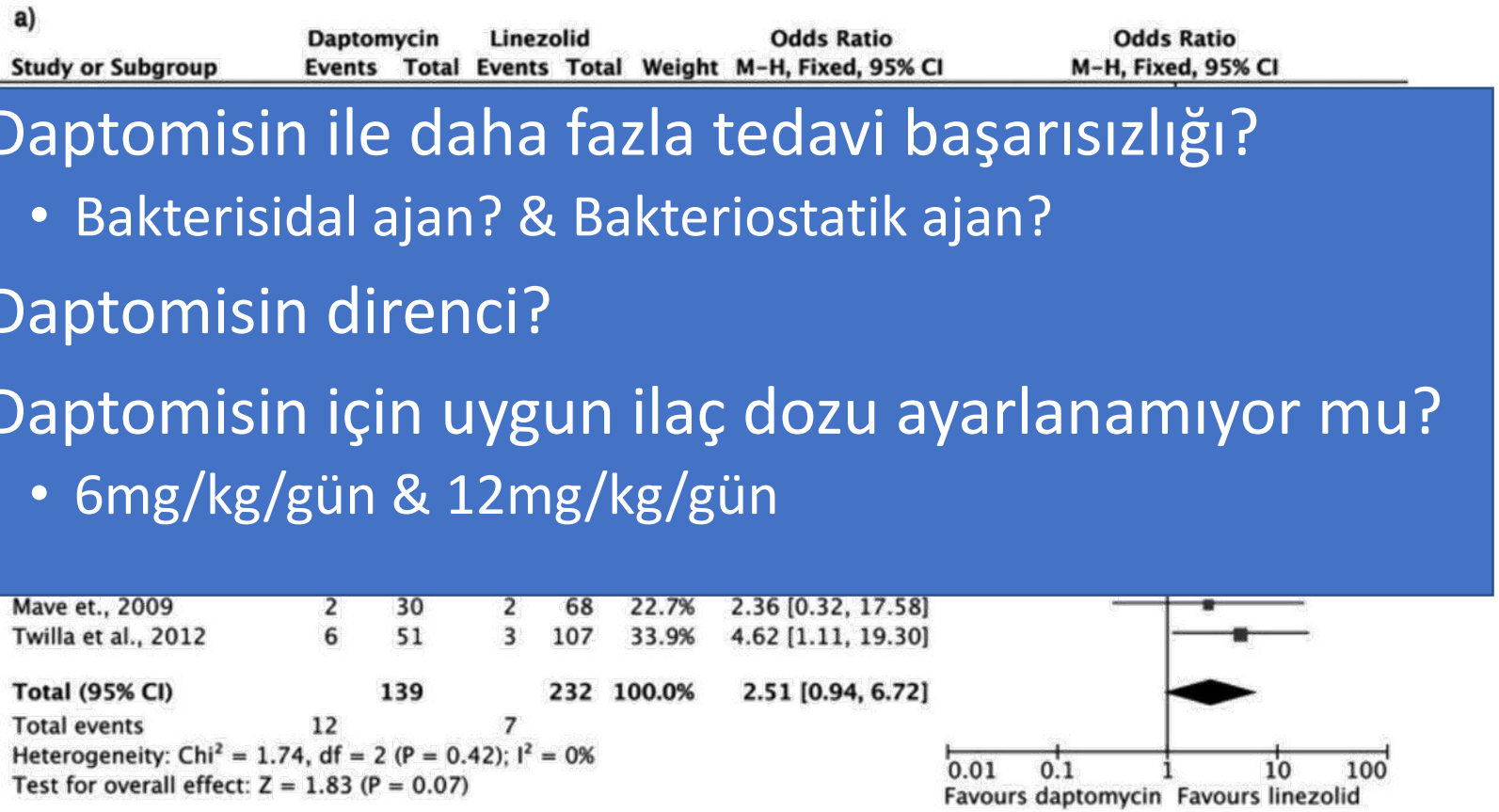


FIG 4 Forest plots (using Mantel-Haenszel [M-H] analysis) of odds ratios for microbiological cure (a) and bacteremia recurrence (b) in patients treated with daptomycin or linezolid for VRE bacteremia.

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Efficacy and safety of daptomycin versus linezolid treatment in patients with vancomycin-resistant enterococcal bacteraemia: An updated systematic review and meta-analysis

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Meta-analysis
Daptomycin

ABSTRACT

Objectives: A systematic review and meta-analysis were conducted to re-assess the efficacy and safety of daptomycin compared with linezolid treatment for vancomycin-resistant enterococcal (VRE) bacteraemia and to explore whether high-dose daptomycin is beneficial.

Methods: PubMed, EMBASE, the Cochrane Library, and meeting abstracts were searched from inception to February 2019. Studies evaluating daptomycin and linezolid treatment for VRE bacteraemia were included.

Results: Twenty-two observational studies were identified. A non-significant higher mortality (OR 1.27; 95% CI 0.99–1.63) and significantly lower risk of thrombocytopenia (OR 0.78; 95% CI 0.61–0.99) were found with daptomycin compared with linezolid treatment. Clinical response (OR 0.88; 95% CI 0.59–1.33), microbiological cure (OR 0.82; 95% CI 0.53–1.28), recurrence of bacteraemia (OR 0.96; 95% CI 0.70–

- 22 çalışma
- 3987 hasta

Klinik cevap açısından iki grup arasında fark görülmedi.

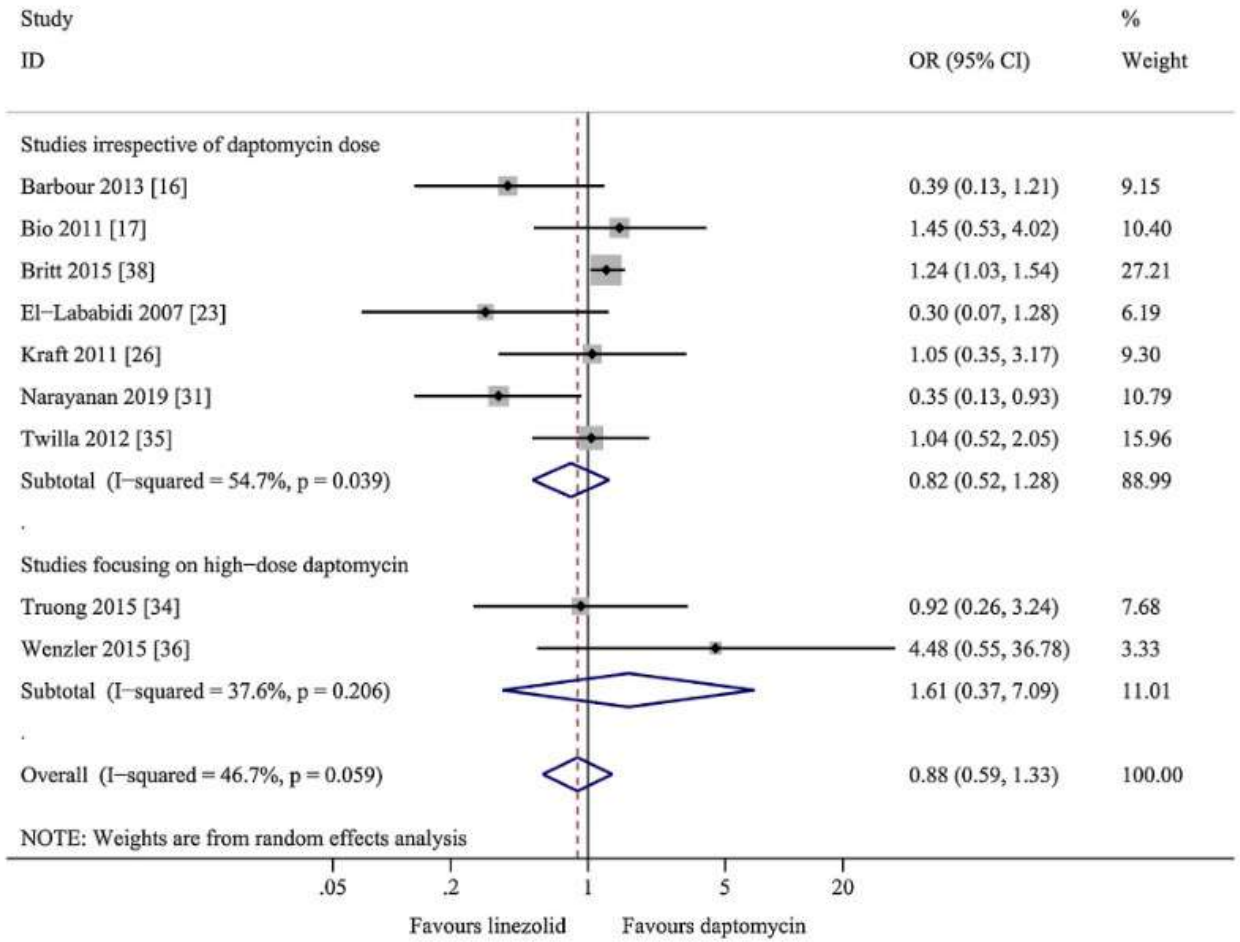

Fig. 3. Forest plots of odds ratios for clinical response.

Mikrobiyolojik kür açısından iki grup arasında fark görülmedi.

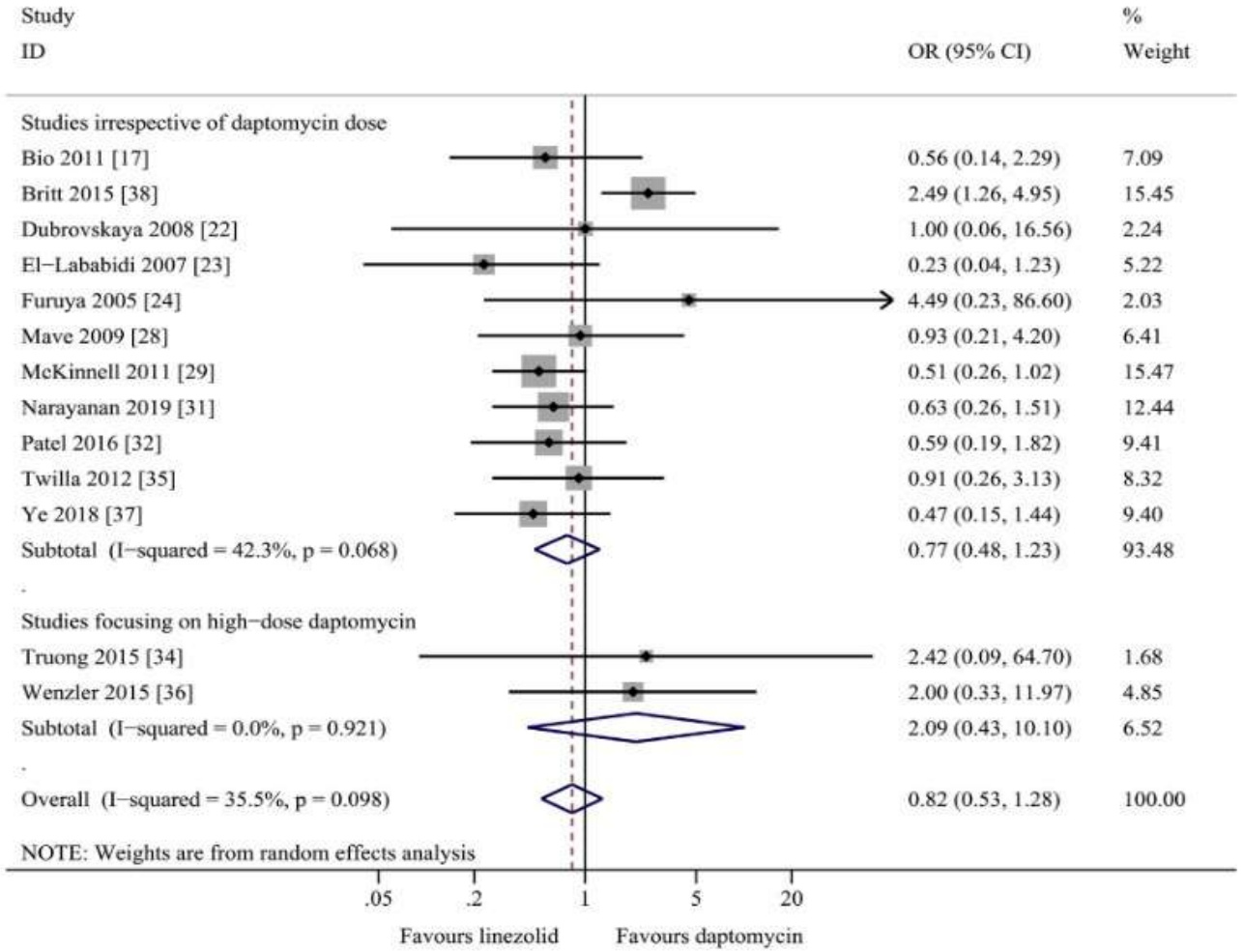

Fig. 4. Forest plots of odds ratios for microbiological cure.

Bakteremi rekürrensi açısından iki grup arasında fark görülmedi.

- Önceki 3 meta-analiz linezolid lehine sonuçlanmıştı.
- Ancak daptomisin dozuna göre yorum yapılmamıştı.
- Daptomisin dozu yüksek tutulduğunda linezolid üstün değil.
- Daptomisin tercih edilen hastaların hastalık ciddiyetleri ve altta yatan hastalıkları genelde daha ağır, sonuçları etkiliyor olabilir.
- Daptomisin ile trombositopeni riski daha düşük, CPK'da yükseklik daha sık.

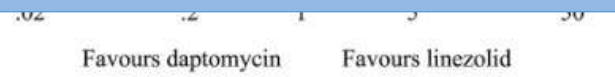

Fig. 5. Forest plots of odds ratios for recurrence of bacteraemia.

Kolonizasyon & Bakteremi

original article

Wien Klin Wochenschr
https://doi.org/10.1007/s00508-020-01733-7

Wiener klinische Wochenschrift
The Central European Journal of Medicine

Risk factors for development of vancomycin-resistant enterococcal bacteremia among VRE colonizers

A retrospective case control study

Abdurrahman Kaya · Sibel Yıldız Kaya · Ilker Inanç Balkan · Osman Faruk Bayramlar · Bilgül Mete · Neşe Saltoglu · Gökhan Aygün · Ömer Fehmi Tabak

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Table 2 Multivariate analysis of risk factors for developing VRE bacteremia

Variables	*P* value	OR (95% CI)
Carbapenem	0.022	6.67 (1.30–34)
Cephalosporin	0.022	4.32 (1.23–15)

OR odds ratio, *CI* confidence interval

- 409 VRE kolonize hasta
- 1 yıl boyunca takip edildi
- 17 VRE bakteremisi
- %4,1

- Risk faktörleri;
  - Karbapenem kullanımı
  - Sefalosporin kullanımı

- Bakteremi gelişen hastalarda yatış süresi daha uzun saptanmış.

Table 3 Studies reporting VRE bacteremia rates among VRE colonized patients

Study	Year	Patient population	Colonized/bacteremia patients	Bacteremia (%)
Oliver et al. [5]	2008	All inpatients	768/*31*	4
Özkaya et al. [15]	2014	All pediatric inpatients	342/*4*	1.1
Zaas et al. [6]	2002	Cancer patients	179/*24*	13.7
Kara et al. [16]	2015	All pediatric inpatients	193/*3*	1.55
Habip et al. [17]	2014	Hematologic cancer	50/*2*	4
Ford et al. [18]	2015	Transplant patients	36/*9*	25
Bossaer et al. [19]	2010	Neutropenic cancer patients	53/*14*	26
Lisboa et al. [20]	2015	Transplant patients	100/*14*	14
MacAllister et al. [21]	2018	Transplant patients	294/*32*	10.8
Mutters et al. [14]	2013	All inpatients	560/*19*	3.4
Kamboj et al. [22]	2010	Transplant patients	68/*23*	33.8
Sütçü et al. [23]	2015	Pediatric patients in ICU	108/*6*	5.5
Aktürk et al. [24]	2016	Pediatric hematolo-oncology	72/*5*	6.9
Matar et al. [25]	2006	Cancer patients	99/*29*	29.2
Kapur et al. [7]	2000	Transplant patients	15/*4*	26
McNeil et al. [9]	2006	Transplant patients	142/*32*	22
Roghmann et al. [8]	1997	Cancer patients	56/*10*	17.8
Patel et al. [26]	2001	Transplant patients	52/*2*	3.8
Montecalvo et al. [27]	1994	Cancer patients	413/*7*	1.7
Brennen et al. [12]	1998	Long-term care residents	36/*0*	0

Farklı çalışmalarda VRE kolonize hastalarda bakteremi gelişme ihtimali % 0-33,8 arasında bulunmuş.

Transplant Infectious Disease, ISSN 1398-2273

Evaluation of risk factors for vancomycin-resistant *Enterococcus* bacteremia among previously colonized hematopoietic stem cell transplant patients

Y. Kang, M. Vicente, S. Parsad, B. Brielmeier, J. Pisano, E. Landon, N.N. Pettit. Evaluation of risk factors for vancomycin-resistant *Enterococcus* bacteremia among previously colonized hematopoietic stem cell transplant patients.
Transpl Infect Dis 2013: **15**: 466–473. All rights reserved

Abstract: *Background.* Hematopoietic stem cell transplantation (HSCT) recipients colonized with vancomycin-resistant *Enterococcus* (VRE) may have an increased risk of developing VRE bacteremia. Identification of risk factors for the development of subsequent VRE

Y. Kang[1], M. Vicente[2], S. Parsad[2], B. Brielmeier[2], J. Pisano[3], E. Landon[3], N.N. Pettit[2]

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Risk faktörleri:

- VRE kolonizasyonu saptandıktan sonra vankomisin kullanımı
- Uzamış nötropeni
- İmmünsüpresyon
- Hastane yatışının ilk haftası VRE pozitifleşmesi

- Önceki yatışlarında VRE ile kolonize olmak ise bağımsız risk faktörü olarak saptanmadı.

- 152 VRE kolonize Kİ nakil hastası
- 23 hastada (%15) VRE infeksiyonu
  - 19 bakteremi (%82,5)
  - 1 idrar yolu infeksiyonu (%4)
  - 2 yumuşak doku infeksyonu (%8,5)
  - 1 menenjit (%4)
- Bakteremi oranı **%13** (19/152)

- Kolonizasyonun saptanması ve HK pozitifliği arasında geçen ortalama zaman **67,2 gün**.

Received: 11 November 2019 | Revised: 18 January 2020 | Accepted: 11 March 2020
DOI: 10.1111/tid.13280

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SHORT COMMUNICATION

WILEY

Daptomycin perioperative prophylaxis for the prevention of vancomycin-resistant *Enterococcus* infection in colonized liver transplant recipients

Sajed Sarwar | Alan Koff | Maricar Malinis | Marwan M. Azar

- Karaciğer nakli yapılan VRE kolonize 25 hastaya, nakil sırasında başlayan ve sonrasında 3-5 gün daptomisin profilaksisi verilmiş.
- 90 günlük takipte bu hastaların hiç birinde VRE bakteremisi gelişmemiş.
- 2 hasta farklı nedenlerden dolayı daptomisin kullanmamış. Her iki hastada da VRE bakteremisi gelişmiş. Ancak her iki hastada birden fazla risk faktörü taşıyan hastalarmış.

TABLE 2 Presence of risk factors for vancomycin-resistant *Enterococcus* infection post-transplantation

Risk factor, within 90 d post-liver transplantation	Number of recipients (n = 25)
Renal replacement therapy	15 (60%)
Need for reoperation	6 (24%)
Hemorrhage	8 (32%)
Roux-en-Y anastomosis	2 (8%)
Biliary leak	1 (4%)
Biliary stricture	1 (4%)
Cytomegalovirus donor seropositivity	8 (32%)
Admission to intensive care unit	25 (100%)
Number of risk factors present	
1	7 (28%)
2	5 (20%)
3	6 (24%)
4	4 (16%)
5	3 (12%)

Ancak farklı çalışmalar uzamış daptomisin kullanımının (>18 gün) daptomisine direnç riskini arttırdığını göstermiş.

Lewis JD. Transpl Infect Dis. 2018;20(3):e12856
Lellek H. Int J Med Microbiol. 2015;305(8):902.

İnfeksiyon Kontrol Önlemleri

- Sürveyans yapılması
- Eğitim (temizlik personeli, sağlık çalışanları, hasta ve hasta yakınları)
- El hijyeni
- Koruyucu ekipman kullanımı (eldiven, önlük)
- Temas izolasyonu + standart önlemler (tek kişilik oda)
- Antibiyotiklerin uygun kullanımı
  - Vankomisinin uygun kullanımı

- VRE çevrede 5-7 gün, ellerimizde ise saatlerce canlı kalabilir.
- Alkolle el hijyeni sağlanması veya ellerin yıkanması ile kolayca uzaklaştırılır.
- Havadan bulaş olmaz.

- 45 oda - 1,023 çevre örneği
- VRE kolonizasyonu olan hastaların çevre kontaminasyonu, VRE infeksiyonu olan hastalardan daha fazla saptanmış.

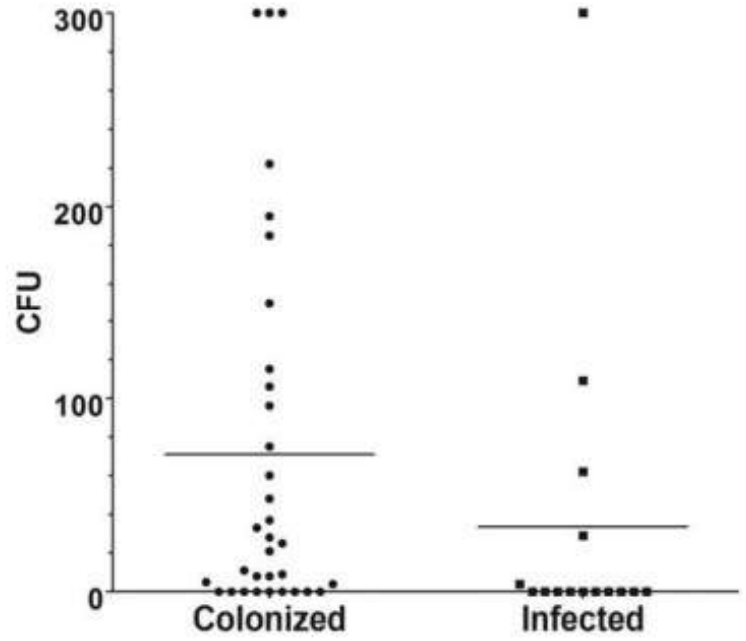

FIGURE 1.
Room contamination with methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci by colonized versus infected patients. Target colony-forming units (CFU) were capped at 300 CFU in this figure.

Published in final edited form as:
Infect Control Hosp Epidemiol. 2014 July ; 35(7): 872–875. doi:10.1086/676861.

A Comparison of Environmental Contamination by Patients Infected or Colonized with Methicillin-Resistant *Staphylococcus aureus* or Vancomycin-Resistant Enterococci: A Multicenter Study

Lauren P. Knelson, MSPH[1], David A. Williams, RN, BSN, IP[2], Maria F. Gergen, MT(ASCP)[2], William A. Rutala, PhD, FSHEA[2], David J. Weber, MD, MPH, FIDSA, FSHEA[2,3], Daniel J. Sexton, MD, FIDSA[1,4], and Deverick J. Anderson, MD, MPH[1,4] on behalf of the Centers for Disease Control and Prevention Epicenters Program

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[3]Division of Infectious Diseases, Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina

[4]Duke Infection Control Outreach Network, Duke University Medical Center, Durham, North Carolina

Abstract

A total of 1,023 environmental surfaces were sampled from 45 rooms with patients infected or colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE) before terminal room cleaning. Colonized patients had higher median total target colony-forming units (CFU) of MRSA or VRE than did infected patients (median, 25 CFU [interquartile range, 0–106 CFU] vs 0 CFU [interquartile range, 0–29 CFU]; $P = .033$).

Healthcare-associated infections (HAIs) represent a substantial cause of morbidity, cost, and increased length of stay in the United States.[1] The contaminated hospital environment has

Enterococci cause a range of illnesses, mostly among patients receiving healthcare, but include bloodstream infections, surgical site infections, and urinary tract infections.

RESISTANCE OF CONCERN

- *Enterococcus* often cause infections among very sick patients in hospitals and other healthcare-settings.
- Some *Enterococcus* strains are resistant to vancomycin, an antibiotic of last resort, leaving few or no treatment options.
- About 20,000 (or 30%) of *Enterococcus* healthcare-associated infections are vancomycin resistant.

PUBLIC HEALTH THREAT

An estimated 66,000 healthcare-associated *Enterococcus* infections occur in the United States each year. The proportion of infections that occur with a vancomycin resistant strain differs by the species of *Enterococcus;* overall 20,000 vancomycin-resistant infections occurred among hospitalized patients each year, with approximately 1,300 deaths attributed to these infections.

	Percent of all *Enterococcus* healthcare-associated infections resistant to vancomycin	Estimated number of infections	Estimated number of deaths attributed
Vancomycin-resistant *Enterococcus faecium*	77%	10,000	650
Vancomycin-resistant *Enterococcus faecalis*	9%	3,100	200
Vancomycin-resistant *Enterococcus* (species not determined)	40%	6,900	450
Totals		20,000	1,300

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

1. AMAÇ

Vankomisine dirençli enterekok infeksiyonlarını önlemek, gerekli kontrol önlemlerini belirlemek ve olası salgınları önlemek için standart bir yöntem belirlemektir.

2. KAPSAM

Cerrahpaşa Tıp Fakültesi Hastanesi'nin tüm birimleri.

3.SORUMLULAR

Cerrahpaşa Tıp Fakültesi Hastanesi'nin tüm çalışanları.

4. KISALTMALAR

HEKK: Hastane Enfeksiyon Kontrol Komitesi

VRE: Vankomisine Dirençli Enterekok

5. UYGULAMA

- Rutin veya başka amaçlı kültürlerde vankomisine dirençli enterekok üremesi durumunda, HEKK haberdar edilir.
- Başka bir hastanede veya serviste uzun süre yatan ve geniş spektrumlu antibiyotik kullanım öyküsüne sahip her hasta mümkünse tek yataklı odaya alınarak, VRE ve diğer dirençli mikroorganizmalar açısından araştırılır.
- VRE saptanması ya da şüphelenilmesi durumunda **"İzolasyon Önlemleri Talimatı"**na uygun olarak temas izolasyonu uygulanır, mümkünse hasta tek kişilik odaya alınır, tek kişilik oda mevcut değilse yalnız yatırılabileceği bir odaya alınır (eğer fazla sayıda VRE saptanan hasta varsa aynı odada yatırılabilir).
- Kolonize çocuk hastaların oyun odası gibi ortak kullanım alanlarına girişi engellenmelidir.
- Odada hastaya özel steteskop, tansiyon aleti, termometre gibi malzemeler bulundurulur, eğer bu malzemelerin/aletlerin dışarı çıkışı gerekiyorsa ***mutlaka*** dezenfekte edilir.
- Odaya girişte, hastaya yakın temasta önlük giyilir ve önlüğün odada kalması sağlanır.
- Hasta odasına giriş ve çıkışta eller alkol bazlı hızlı el dezenfektanı ile dezenfekte edilir.
- Hasta ve enfekte materyal ile temasta steril olmayan eldiven giyilir, odadan çıkmadan eldiven çıkartılır ve eller **"El Hijyeni ve Eldiven Kullanımı Talimatı"**na göre yıkanır.
- Hasta yatak takımları, yıkamaya gönderilecek kumaş materyal özel bir torbada toplanır ve çamaşırhane eşyaların yüksek derecede yıkanması konusunda uyarılır.
- Hastanın çıkartıları ve çöpleri **"Atık Yönetimi Talimatı"**na uygun olarak kırmızı renkli enfekte atık torbasında toplanır, daha sonra ilgili personel tarafından atık merkezine götürülür.
- Odanın temizliği %1'lik çamaşır suyu gibi dezenfektanlar ile her gün yaptırılır. Bu odada kullanılan

temizlik malzemesi ***asla*** başka bir yerde kullanılmaz, eğer temizlik amacıyla yıkama makinesi kullanılacaksa işlem sonrası aletin yüzey fırçası değiştirilir.

- VRE üremiş olan hastalardan HEKK'in belirleyeceği sıklıkta kültür için kontrol örnekleri alınır. HEKK gerekli görürse tüm hastalar ve personelden tarama kültürleri yapılabilir. Temas önlemlerinin sonlandırılması için haftada bir olmak üzere peş peşe yapılan üç rektal sürüntü kültürünün negatif çıkması gerekir. Temas önlemleri, ancak HEKK çalışmalarına ve onların kararına göre sonlandırılır.
- Hasta başka bir bölüme/servis/kuruma sevk edilecek ise mutlaka izolasyon kurallarına nakil sürecinde de uyum gösterilir, hasta servisten ayrılmadan önce yatak takımları ve giysileri değiştirilir, varsa mevcut lezyonların üzeri kapatılır, hasta ile giden kişilere önlük giydirilir ve ilgili bölüm/servis/kurum uyarılır.

6. İLGİLİ DOKÜMANLAR

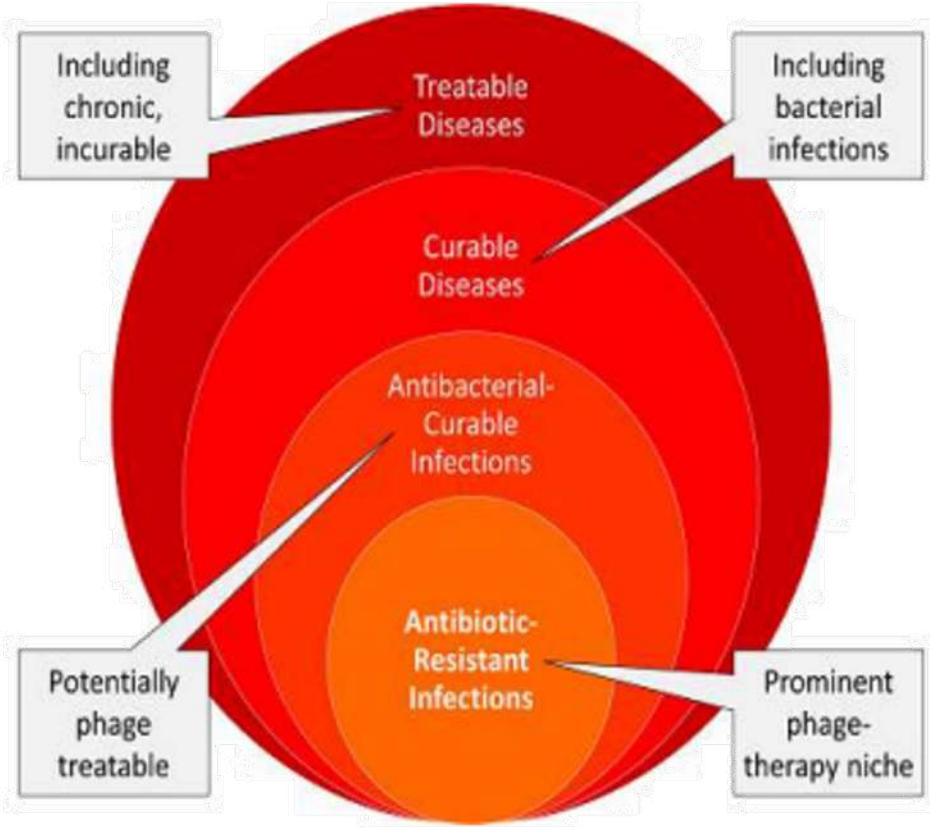
İzolasyon Önlemleri Talimatı

El Hijyeni ve Eldiven Kullanımı Talimatı

Atık Yönetimi Talimatı

Bakteriyofaj tedavisi

- Hastanede yatan hastalarda VRE dekolonizasyonu için alternatif yöntem
- Antibiyotik duyarlılığından bağımsız etkinlik göstermesi ve spesifik konak özelliğine sahip olmasıyla giderek önem kazanmaktadır.
- Bakteriyofaj (faj) sadece bakterileri enfekte eden bir virüs grubudur.
- Her 48 saatte dünyadaki bakterilerin yaklaşık yarısının fajlar tarafından yok edildiği öngörülmektedir.



http://www.phage-therapy.org/

viruses

MDPI

Article

Eradication of Vancomycin-Resistant Enterococci by Combining Phage and Vancomycin

Mor Shlezinger [1,2], Shunit Coppenhagen-Glazer [2], Daniel Gelman [2], Nurit Beyth [1,†] and Ronen Hazan [2,*,†]

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† N.B. and R.H. contributed equally to this work.

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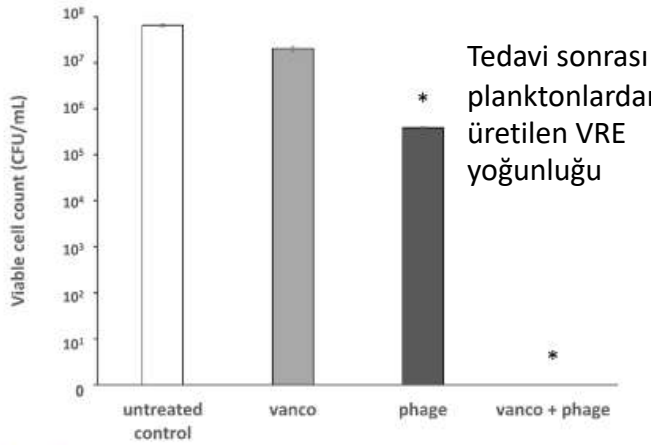
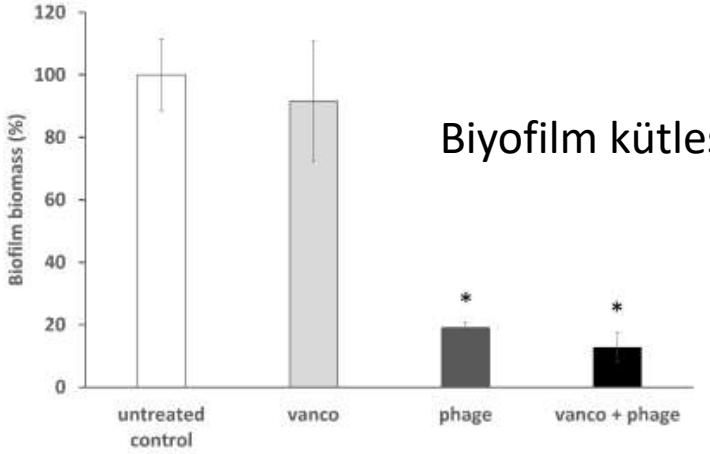
- EFLK1 fajı kullanılmış.
  - *Spounavirinae* subfamily
- Planktonlar VRE ile enfekte edilmiş ve 4 grupta incelenmiş.
  - A. Tedavi verilmeyen grup
  - B. Vankomisin verilen grup
  - C. Bakteriyofaj verilen grup
  - D. Vankomisin + bakteriyofaj verilen grup



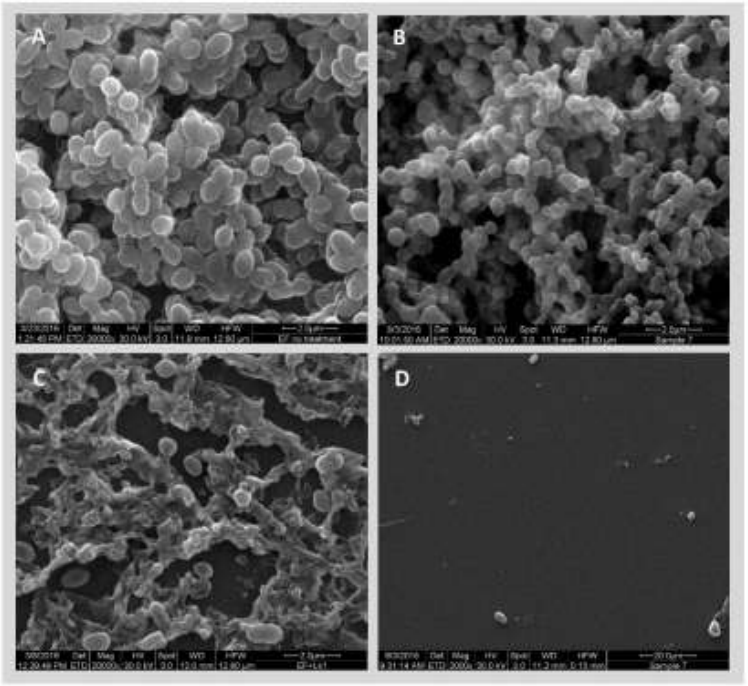
Tedavi sonrası planktonlardan üretilen VRE yoğunluğu

Figure 3. Viable counts of planktonic vancomycin-resistant *E. faecalis* following a combined treatment of phage EFLK1 and vancomycin. The colony forming units (CFU)/mL of VRE treated with 0.015 mg/mL vancomycin combined with phage EFLK1 1.2×10^8 PFU/well is presented. Bacteria were below the limit of detection after treating the cells by combining phage EFLK1 and vancomycin. Bacteria treated only with vancomycin showed survival scores like those of the untreated bacteria; cells treated with phage EFLK1 showed medium survival rates. Combining vancomycin and phage EFLK1 caused seven log reductions in CFU/mL. Light gray = vancomycin-treated bacteria, dark gray = phage EFLK1 treatment, black = phage EFLK1 + vancomycin. Statistically significant ($p < 0.01$) compared to the untreated control. The results are mean ± SD based on three independent biological replicates.



Biyofilm kütlesi

Figure 4. *E. faecalis* biofilm biomass following treatment with phage EFLK1 (1.2×10^8 PFU/well) and vancomycin (0.015 mg/mL). Treatment with combinations of phage EFLK1 and vancomycin significantly decreased bacterial biomass (87% reduction) as evaluated by crystal violet staining. The results are presented as percentages, normalized to the biofilm biomass controls. Light gray = vancomycin-treated bacteria, dark gray = phage EFLK1 treatment served as the control, black = phage EFLK1 + vancomycin treatment. Statistically significant ($p < 0.05$) compared to the untreated control. The results are mean ± SD based on three independent biological replicates.



İzolasyonu ne zaman sonlandıralım?

- 1995 HICPAC: birer haftalık aralarla 3 kez bakılan rektal sürüntü negatif saptandığında izolasyonun bitirilebileceği yönündeydi.

- Ancak sonrasındaki çalışmalar kolonizasyonun (persistan veya intermitant) 1 yıldan uzun sürebileceğini gösterdi.
- Ayrıca taramalar kolonizasyonu saptamada başarısız olabiliyordu.

Altta yatan ciddi hastalığı olanlarda
İnvazif cihazları veya kateteri olanlarda
Tekrarlayan antibiyotik kullanımı olanlarda

Kolonizasyon aylarca devam edebiliyor.

MAJOR ARTICLE

High Rate o
of the Recta
in D
with

Erika M. C.

[1]Department o
School of Med

Table 4. Stool density of vancomycin-resistant *Enterococcus faecium* (VRE) and antibiotic exposure during the 7 days before

Duration of antibiotic exposure, days		≤.001
0	10 (29)	4.2 ± 2.5
1–2	2 (6)	4.8 ± 2.4
3–4	3 (9)	4.9 ± 2.0
≥5	20 (57)	7.6 ± 0.8

Rektal sürüntü ile taramalar VRE kolonizasyonunu saptamada yetersiz kalıyor

The diagnostic accuracy o
with vancomycin-resistant
and RS cultures were perf
and the prevalence of skin
A total of 35 stool sample
ranged from 100%, at VR
densities of ≤4.5 $\log_{10}$ cfu
but it was more common
with higher VRE stool den
continued increase in the prevalence of VRE.

nization
cultures,
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58%; it
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Table 2. Sensitivity of the rectal swab culture method for the detection of vancomycin-resistant *Enterococcus faecium* (VRE) at decreasing stool densities.

VRE stool density, $\log_{10}$ cfu/g of stool	Rectal swab culture			Skin culture	
	No. of samples[a]	VRE not detected, no.	Sensitivity (95% CI)	No. of samples[b]	VRE detected, no. (%)
		5	0 (0–52)	5	0 (0)
		7	0 (0–41)	8	1 (13)
		8	0 (0–37)	10	1 (10)
		0	9 (0–41)	12	2 (17)
		0	23 (5–53)	13	3 (23)
		1	45 (23–68)	21	9 (43)

ki yoğunluğu
abilme ihtimali

rectal swab culture method for the detection of vancomycin-resistant *Enterococcus faecium* (VRE) at increasing stool densities.

VRE stool density, $\log_{10}$ cfu/g of stool	Rectal swab culture			Skin culture	
	No. of samples	VRE not detected, no.	Sensitivity (95% CI)	No. of samples	VRE detected, no. (%)
≥2.5	26	11	58 (37–77)	28	15 (54)
≥3.5	19	4	79 (54–94)	20	15 (75)
≥4.5	18	3	83 (56–96)	18	14 (78)
≥5.5	15	1	93 (68–100)	16	13 (81)
≥6.5	13	1	92 (64–100)	15	12 (80)
≥7.5	6	0	100 (54–100)	7	6 (86)

Kullanılan antibiyotik sayısı ve süresi ile gaytadaki VRE yükü arasında ilişki bulunmuş.

İzolasyonu ne zaman sonlandıralım?

- VRE ile kolonize hastaları taburcu olana kadar kolonize kabul edelim ve
- Temas izolasyonunu sonlandırmayalım.

https://www.cdc.gov/infectioncontrol/guidelines/isolation/precautions.html

Daha öncesinde VRE kolonize olduğu bilinen bir hastanın yeniden hastaneye yatışında izolasyon uygulayalım mı?

- 6-12 ay boyunca,
  - Hastane yatışı olmayan
  - Antibiyotik kullanmayan
  - Vücutta yabancı cisim olmayan

hastalarda rektal sürüntü alınması,

sonucun negatif olması halinde izolasyonun sonlandırılması öneriliyor.

https://www.cdc.gov/infectioncontrol/guidelines/isolation/precautions.html

Sonuç olarak;

- Bir klinik örneğin kültüründe VRE ürediğinde tedavi planlamadan önce etken – kolonizan ayrımının iyi yapılması gerekir.
- Dekübit yarası gibi yüzeyel yaralarda, idrarda ya da karın içi abselerde VRE üremesi, tedavi gerektirmeyebilir.

- Hastane salgınları tek bir kökenden kaynaklanabilir.
- Eğitim ve izolasyon önlemleri VRE kontrolünde çok önemlidir.

- VRE üremesi olan hastaları taburcu olana kadar kolonize kabul etmek gerekir.


TEŞEKKÜR EDERİM