ORTOPEDİK PROTEZ İNFEKSİYONLARINA MEDİKAL YAKLAŞIM

Dr. Neşe DEMİRTÜRK
Afyon Sağlık Bilimleri Üniversitesi Tıp Fakültesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD.
Afyonkarahisar, 2020.

EKLEM PROTEZ CERRAHİSİ

- Osteoartrozlu hastalarda yaşam kalitesini arttırmak için giderek artan sıklıkta uygulanıyor

- İnfeksiyöz komplikasyonlar önemli morbidite nedeni
  - Ekonomik yük
  - Uzun süreli antibiyotik tedavisi & antibiyotik direnci

EPİDEMİYOLOJİ

- En sık diz eklem protezlerinde; *eklem ve yumuşak dokuda hareket daha fazla ve koruyucu yumuşak doku daha az.*
  - *%0.5-%2 diz protezlerinde;*
    - İlk yıl için %0.5
    - İlk 10 yıl için %1.4
  - *%0.5-%1 kalça protezlerinde*
  - *<%1 omuz protezlerinde*

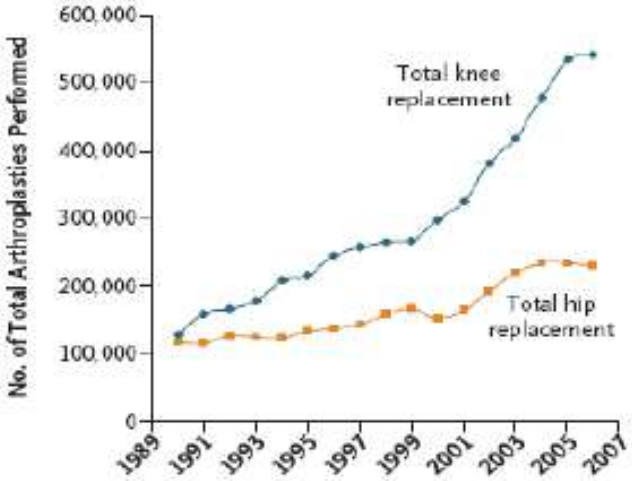
- Ülkemizde görülme sıklığı ???

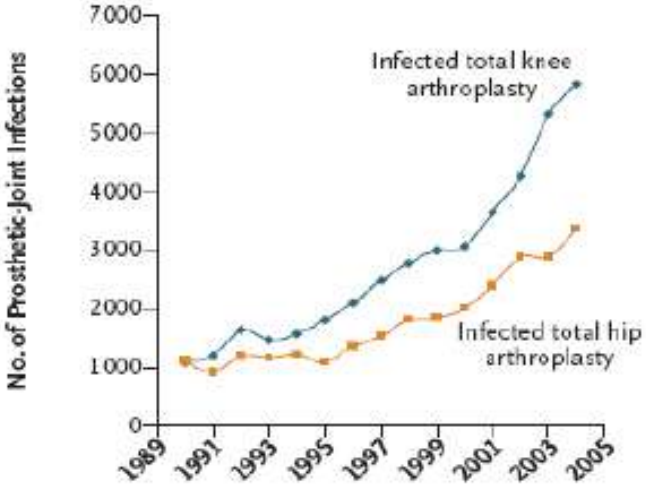
Beam E & Osmon D. Inf Dis Clin N Am, 2018.

Infection Associated with Prosthetic Joints

Jose L. Del Pozo, M.D., Ph.D., and Robin Patel, M.D.

N Engl J Med 2009;361:787-94.





Kimler risk altında ?

- RA, DM, malignite, KBY, obesite ve lenfödem gibi bir komorbiditesi olanlar
- Prednizon, anti-TNF gibi bir romatolojik ilaç kullananlar
- Daha önceden artroplasti ya da aynı cerrahi bölgede infeksiyon geçirenler
- Cerrahi süresi normalden uzun olanlar
- Hematom ya da yarada açılma gibi bir post-op komplikasyon gelişenler

SINIFLAMA

- Erken başlangıçlı
- Gecikmiş başlangıçlı
- Geç başlangıçlı

https://www.uptodate.com/contents/prosthetic-joint-infection-epidemiology-microbiology-clinical-manifestations-and-diagnosis?topicRef=7665&source=see_link

ERKEN BAŞLANGIÇLI

- İmplantasyon sırasında
- Yüksek virulanslı mo; *MRSA, Gram negatifler*

- Hastanın kendi cilt florasından
- Ameliyathane personelinin ellerinden

Ameliyat ortamından

- **Bulgular ilk 3 ayda**

- Ağrı,
- Sıcaklık, eritem,
- İnsizyon yerinde endürasyon veya ödem,
- Yarada açılma ya da prülan akıntı,
- Eklemde efüzyon
- Ateş

GECİKMİŞ BAŞLANGIÇLI

- İmplantasyon sırasında

- Düşük virulanslı mo; *KNS, Enterokok, prorionobacterium*

- **Bulgular ilk 3 -12 ayda**

- Klinik daha silik , tanı zor
- Sebat eden ağrı
- **İmplantta gevşeme**
- Ateş
- Aralıklı drenaj görülen sinus ağzı varlığı ve hafif şişlik

GEÇ BAŞLANGIÇLI

- Hematojen yayılım
- *S aureus, KNS, Gram negatifler*

- Solunum yolu infeksiyonları
- Üriner infeksiyonlar
- Gastrointestinal infeksiyonlar
- Dental infeksiyonlar
- Geçici bakteriyemi

- **Bulgular 12 aydan sonra**
- **Akut başlangıç**
- Sıcaklık
- Eritem
- İnsizyon yerinde ödem ve endürasyon
- Eklemde efüzyon
- Ateş.
- Önceden sorun olmayan eklemde ağrı başlaması ve dislokasyon

Funguslar etken olabilir mi ?

- Görülme sıklığı < %1
  - Daha çok geç başlangıçlı olanlarda
- Genellikle monomikrobiyal etken
  - *Candida albicans , C parapsilosis*
- Riskli grup
  - Revizyon atroplasti
  - Bakteriyel protez infeksiyonu
  - Uzun antimikrobiyal tedavi
  - İmmunosupresyon
  - DM

Beam E & Osmon D. Inf Dis Clin N Am, 2018
L. Escola-Verge et al. J Infect, 2018.
Dutronc H et al Scand J Infect, 2010

TEDAVİ

- *NELER ÖNEMLİ ??*

- İnfeksiyonun başlangıç zamanı
- Etken patojenin virulans ve antibiyotik duyarlılık durumu
- Protez çevresindeki yumuşak dokunun durumu
- Protezin fonksiyonelliği
  - Gevşeme derecesi
- Hastanın genel durumu
- Hastanın tedavi uyumu

Protez çıkarılmadan tedavi şansı

- Protezde fonksiyon kaybı yok
- Sinus traktı yok
- Operasyon sonrası 30 gün içinde ve semptom süresi 3 haftadan kısa
- Etiyolojide kolay tedavi edilebilir bir etken var, oral ab'lere duyarlı ve hasta uyumlu

EVET

- Debridman ve mikrobiyolojik örnekleme
- Takiben sistemik antibiyotik tedavisi
- Başarı şansı %70-%90

HAYIR

- Tek ya da iki aşamalı revizyon cerrahisi
- Sistemik antibiyotik tedavisi

Protez çıkarılmadan yapılan tedavide hangi antibiyotikler ?

- Başlangıçta 2-6 hafta parenteral antibiyotik tedavisi
- Etken stafilokok ise Rifampisin ile kombine olmalı, R alamayan hastalarda pe tedavi süresi 4-6 hafta olmalı.
- Takiben oral tedavi ile antibiyoterapi devamı
  - Kalça protezlerinde total süre 3 ay
  - Diz protezlerinde total süre 6 ay

© 2020 UpToDate, Inc. and/or its affiliates. All Rights Reserved.

Antibiotic therapy for treatment of osteomyelitis or prosthetic joint infection in adults

Infectious agent	Antibiotic regimen	Dosing
Empiric therapy	Vancomycin PLUS a third- or fourth-generation cephalosporin (such as ceftriaxone, ceftazidime, or cefepime)	As summarized below
Pathogen-specific therapy		
Staphylococci, methicillin susceptible*	Nafcillin	2 g IV every 4 hours
	Oxacillin	2 g IV every 4 hours
	Cefazolin	2 g IV every 8 hours
	Flucloxacillin	2 g IV every 6 hours
	Ceftriaxone[¶]	2 g IV every 24 hours
Staphylococci, methicillin resistant*	**Regimen of choice:**	
	Vancomycin[Δ]	20 mg/kg loading dose, then 15 mg/kg/dose IV every 12 hours, not to exceed 2 g per dose initially
	Alternative regimens:[◊]	
	Daptomycin[§]	6 to 10 mg/kg IV once daily
	Teicoplanin (where available)[¥‡]	12 mg/kg IV every 12 hours for 3 to 5 doses, followed by 12 mg/kg once daily
Staphylococci, adjunctive agents*	Rifampin	300 to 450 mg orally twice daily
	Fusidic acid (where available)[¥]	500 mg orally 3 times daily
Gram-negative organisms	Ciprofloxacin[†,**,¶¶]	750 mg orally twice daily or 400 mg IV every 12 hours; for treating Pseudomonas, increase IV dose to 400 mg IV every 8 hours
	Levofloxacin[**,¶¶]	750 mg orally or IV once daily
	Ceftriaxone[ΔΔ]	2 g IV every 24 hours
	Ceftazidime[**]	2 g IV every 8 hours
	Cefepime[**]	2 g IV every 8 to 12 hours
	Ertapenem[ΔΔ]	1 g IV every 24 hours
	Meropenem[**]	1 g IV every 8 hours

© 2020 UpToDate, Inc. and/or its affiliates. All Rights Reserved.

Enterococcus spp, penicillin-susceptible	Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses or Ampicillin sodium 12 g IV q24 h continuously or in 6 divided doses	Vancomycin 15 mg/kg IV q12 h or Daptomycin 6 mg/kg IV q24 h or Linezolid 600 mg PO or IV q12 h	4–6 wk. Aminoglycoside optional Vancomycin should be used only in case of penicillin allergy
Enterococcus spp, penicillin-resistant	Vancomycin 15 mg/kg IV q12 h	Linezolid 600 mg PO or IV q12 h or Daptomycin 6 mg IV q24 h	4–6 wk. Addition of aminoglycoside optional

le-abstract/56/1/e1/4157705 by guest on

Streptococci, penicillin sensitive	**One of the following:**	
	Aqueous crystalline penicillin G	20 to 24 million units IV every 24 hours, either continuously or in 6 equally divided doses
	Ampicillin	12 g IV every 24 hours, either continuously or in 6 equally divided doses
	Ceftriaxone	2 g IV every 24 hours
	Vancomycin[Δ]	20 mg/kg loading dose, then 15 mg/kg/dose IV every 12 hours, not to exceed 2 g per dose, initially
Cutibacterium (formerly *Propionibacterium*) *acnes*[§§]	**One of the following:**	
	Aqueous crystalline penicillin G	20 million units IV every 24 hours, either continuously or in 6 divided doses
	Ceftriaxone	2 g IV every 24 hours

Diagnosis and management prosthetic joint infection IDSA guidelines, 2013.

Treatment of Staphylococcus aureus prosthetic joint infection in adults with retained hardware following debridement and completion of intravenous therapy: Oral antibiotic continuation therapy *¶

Table 3. Common Antimicrobials Used for Chronic Oral Antimicrobial Suppression (B-III Unless Otherwise Stated in Text)[a,b]

Microorganism	Preferred Treatment	Alternative Treatment
Staphylococci, oxacillin-susceptible	Cephalexin 500 mg PO tid or qid or Cefadroxil 500 mg PO bid	Dicloxacillin 500 mg PO tid or qid Clindamycin 300 mg PO qid Amoxicillin-clavulanate 500 mg PO tid
Staphylococci, oxacillin-resistant	Cotrimoxazole 1 DS tab PO bid Minocycline or doxycycline100 mg PO bid	
β-hemolytic streptococci	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	Cephalexin 500 mg PO tid or qid
Enterococcus spp, penicillin susceptible	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	
Pseudomonas aeruginosa	Ciprofloxacin 250–500 mg PO bid	
Enterobacteriaceae	Cotrimoxazole 1 DS tab PO bid	β-lactam oral therapy based on in vitro susceptibilities
Propionibacterium spp	Penicillin V 500 mg PO bid to qid or Amoxicillin 500 mg PO tid	Cephalexin 500 mg PO tid or qid Minocycline or doxycycline 100 mg PO bid

https://www.uptodate.com/contents/image/print?imageKey=ID%2F119914&topicKey=ID%2F7665&search=Prosthetic%20joint%20infection:%20Treatment&rank=1~120&source=see_link

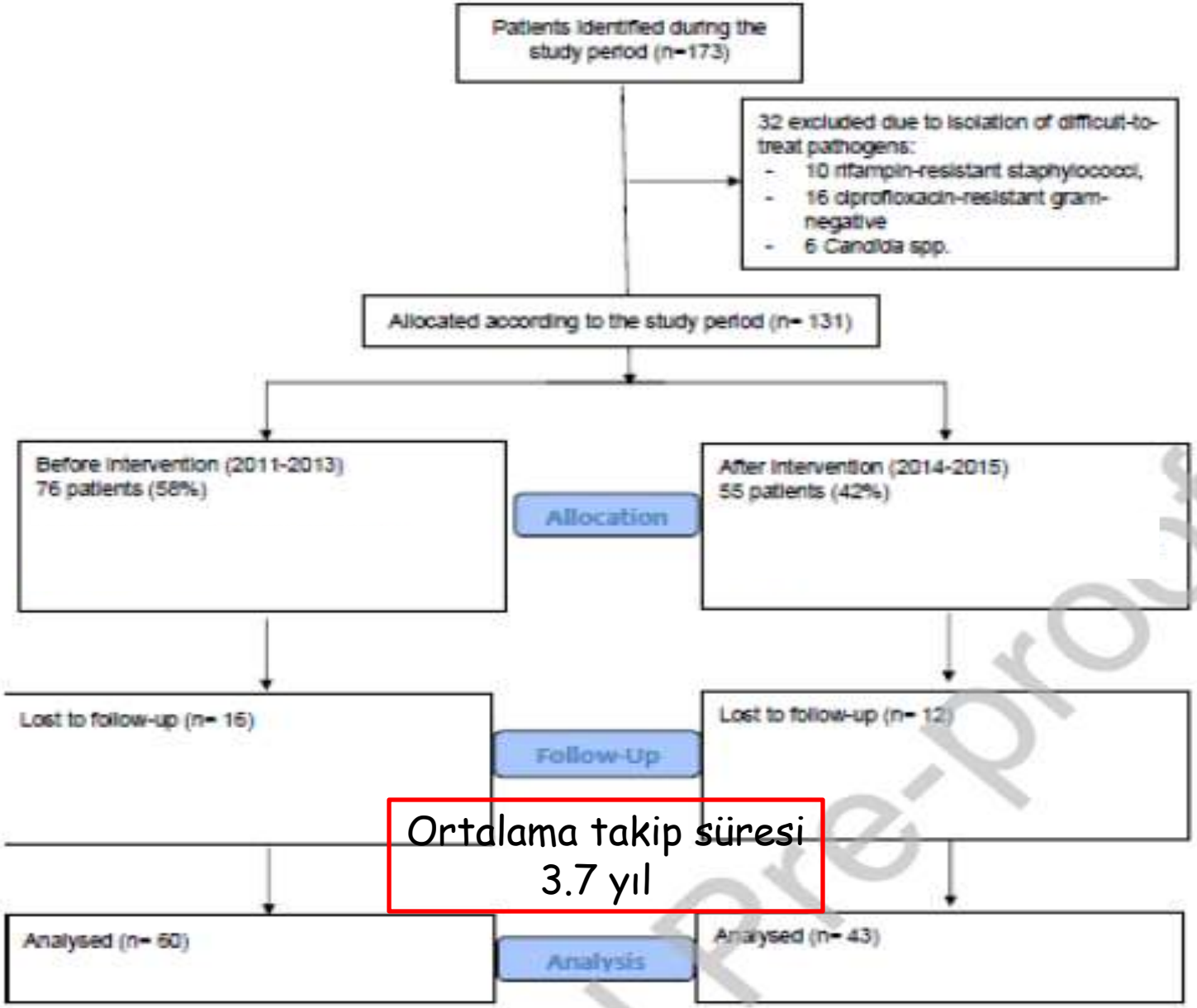
Funguslar etkense….

- Azoller tedavide etkili
  - Flukonazol
  - Vorikonazol
  - Amfoterisin B
- Başarı şansı düşük
- Protezin çıkarılması gerekli

Cobo F, Infect Dis, 2017.
L. Escola-Verge et al. J Infect, 2018.
Dutronc H et al Scand J Infect, 2010.

Rifampisin

- Tedavi için kritik bir antibiyotik.
- Gram pozitif mikroorganizma biyofilmlerine penetrasyonu çok iyi.
- Oral biyoyararlanımı iyi.
- Direnç gelişme olasılığı nedeni ile monoterapide kullanılmamalı.



Ortalama takip süresi
3.7 yıl

Pre-proof

Highlights – International Journal of Antimicrobial Agents

- The infection-free survival after 1 and 2 years was significantly better for patients who received biofilm-active antibiotics than for those who did not.
- In addition, biofilm-active antibiotic treatment was associated with lower pain intensity and better joint function
- The role of biofilm-active antibiotics needs to be validated in larger cohort studies.

after 1 year

(83% vs. 70%, p = 0.040)

after 2 years

(67% vs. 48%, p = 0.038).

Protezin çıkarılması gereken hastalar

- İnfeksiyon operasyondan >30 gün sonra başlamışsa protezi çıkarmadan başarılı tedavi güçtür.

  - Tek aşamalı
  - İki aşamalı
    - İnfeksiyonun nüks olasılığı daha az

    - Hangisi daha başarılı ??

Tek aşamalı revizyon cerrahisi

- Prülan drenaj ve sinüz ağzı yok ise
- Daha önce revizyon cerrahisi yapılmamış ise
- Düşük virulanslı ve oral antibiyotiklerle tedavi edilebilecek bir bakteri etkense
  - *MRSA, Candida, enterokok* ve *GRAM negatifler* etken ise başarı şansı düşük.
- Hasta immün yetkin ise

Tek aşamalı revizyon yapılan hastalarda antibiyoterapi önerileri protez çıkarılmayan hastalarla aynı

- Başlangıçta 2-6 hafta parenteral antibiyotik tedavisi
- Etken stafilokok ise Rifampisin ile kombine olmalı, R alamayan hastalarda pe tedavi süresi 4-6 hafta olmalı.
- Takiben oral tedavi ile antibiyoterapi devamı
  - Kalça protezlerinde total süre 3 ay
  - Diz protezlerinde total süre 6 ay

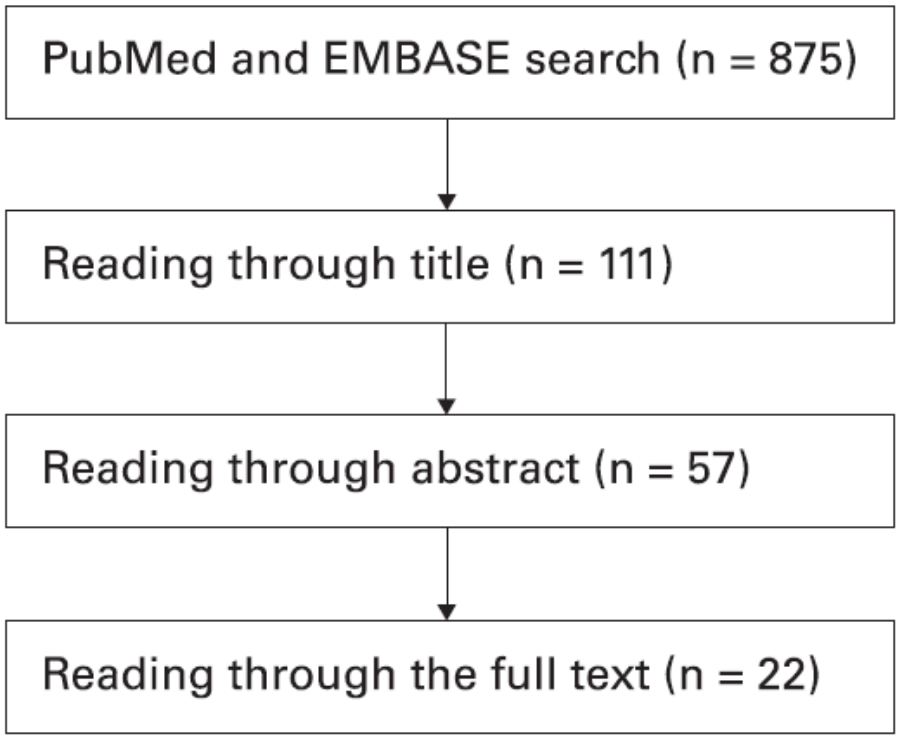
■ JOINT ARTHROPLASTY: OPTIMIZING OUTCOMES

Indications for a single-stage exchange arthroplasty for chronic prosthetic joint infection

A SYSTEMATIC REVIEW

R. R. Thakrar,
S. Horriat,
B. Kayani,
F. S. Haddad

Bone Joint J 2019;101-B(1 Supple A):19–24.



SONUÇLAR

Relaps %0-%18

En sık etken *S epidermidis*

Başarılı sonuç; etkenle, konağın immün durumu ve sinus ağzı varlığı ile direkt ilişkili !!!

İki aşamalı revizyon cerrahisi uygulanan hastalarda antibiyoterapi

- İlk aşama cerrahiden 2 hafta öncesinde antibiyotik tedavileri kesilmeli
- İlk aşama sırasında kültür alınmalı
- Eklem aralığına antibiyotikli sement uygulaması

Sementte hanqi antibiyotikler ???

Table 2 Dosage of antibiotics mixed in antibiotic-loaded bone cement (ALBC)

Situation	Antimicrobial	Fixation cement (prophylactic dose: per 40 g PMMA cement) Simple: industrially admixed antibiotics (italics: manually admixed antibiotics)	Spacer cement (therapeutic dose: per 40 g PMMA cement)
Standard situation			
Susceptible or unknown pathogen(s)	Gentamicin +	1 g	1 g
	Clindamycin	1 g	1 g (+ 2 g *vancomycin*)
Special situations			
Staphylococcus spp. (oxacillin-/methicillin-resistant)	Gentamicin +	0.5 g	0.5 g
	Vancomycin or	2 g	2 g (+ 2 g[a])
	Daptomycin	*2 g*	*3 g*
Vancomycin-resistant enterococci (VRE)	Gentamicin +	0.5 g	0.5–1 g
	Linezolid or	*1 g*	*2 g*
	Daptomycin or	*2 g*	*3 g*
	Fosfomycin sodium[b]	*2 g*	*2-4 g*
Resistant gram-negative pathogens (e.g., *E. coli*, *Klebsiella*, *Enterobacter*, *Pseudomonas* spp.)	Gentamicin +	0.5 g	0.5–1 g
	Colistin[c] or	*2 g (= 60 million U)*	*4 g (= 120 million U)*
	Fosfomycin sodium[b] or	*2 g*	*2-4 g*
	Meropenem or	*2 g*	*3 g*[d]
	Ciprofloxacin	*2 g*	*3 g*
Yeasts (*Candida* spp.) or molds (e.g., *Aspergillus* spp.)	Gentamicin +	0.5 g	0.5–1 g
	Liposomal amphotericin B (Ambisome®) or	*0.2 g*[e]	*0.2 g*[a, e]
	Voriconazole	*0.2 g*	*0.4 g*[a]

[a] These Afb concentrations do not fulfill the mechanical ISO requirements for fixation cement

[b] Fosfomycin sodium is preferred over fosfomycin calcium due to better mechanical properties of PMMA

[c] Available as colistin sodium or colistin sulfate (equal efficacy)

[d] Improved efficacy and antimicrobial release in combination with gentamicin 1 g and clindamycin 1 g

[e] The literature is still controversial regarding minimal effective concentrations

- İkinci cerrahi öncesi interval
  - Kısa ya da uzun
  - 2-4 hafta
  - 4-8 hafta; zor tedavi edilen mo etkense

- Takiben yeni protezin implantasyonu.
  - İkinci aşama öncesinde de hasta 2 hafta antibiyotiksiz bırakılabilir.
    - İmplantasyon sırasında tekrar kültür ??????

Archives of Orthopaedic and Trauma Surgery (2019) 139:295–303
https://doi.org/10.1007/s00402-018-3052-4

ORTHOPAEDIC SURGERY

Outcome of short versus long interval in two-stage exchange for periprosthetic joint infection: a prospective cohort study

	Short-interval group (SI)	Long-interval group (LI)
Microbial spectrum		
Coagulase-negative staphylococci	17	16
Staphylococcus aureus	2	3
Propionibacterium acnes	2	2
E. coli	0	1
Streptococci	0	2
Others	1	5
Culture-negative	5	1

vakomisin
+
ampisilin/sulbaktam

2 hafta

< 4 hafta
> 4 hafta

Biyofilm penetrasyonu olmayan ab ler

olanlara 12 hafta

Uzun intervalli olanlara en az 6 hafta (toplamda en az 12 hafta)

Table 2 Perioperative and follow-up parameters

	Short-interval group (SI)	Long-interval group (LI)
Inpatient parameters[a]		
Interval explantation to implantation (days)	17.9 (7–27)	63.0 (28–204)
Hospital stay (days)	28.0 (21–45)	26.0 (20–57)
Intensive care unit stay (days) (explantation)	0.5 (0–1)	0.5 (0–2)
Follow-up at > 32 months		
Decayed	1	1
Stay in geriatric ward (days)	0	204
Relapse of PJI	0	1
Revision due to infection	1	3
Revision due to aseptic cause	1	2

[a]Values given as mean and range

Conclusions This study suggests that two-stage exchange with short interval has a similar outcome than with long interval, when highly active antibiotic therapy is used. Patient inconvenience and care costs due to immobilization were lower when strategies with a short interval were used.

In one retrospective study including more than 250 patients with PJI who underwent two-stage exchange arthroplasty, the risk of failure was increased among patients with a positive culture at reimplantation (45 vs 21 percent) [45]. In another retrospective study including more than 150 patients with PJI, the presence of positive cultures obtained at the time of new prosthesis implantation was not associated with a worse outcome [46].

Stage two — Stage two consists of new prosthesis implantation. Arthrotomy is performed with operative inspection, collection of cultures and frozen section histology [47]. If frozen section is negative, hardware reimplantation may be performed. If frozen section is positive, then a determination of whether or not to proceed with implantation of new hardware must be made; intraoperative findings are important in such decision-making.

If there are no apparent signs of infection, the new prosthesis may be implanted; many favor the use of antibiotic-impregnated cement to fix the new prosthesis [1]. Empiric antibiotic therapy (guided by culture data obtained at the time of the original resection and at the time of reimplantation) should be administered pending final operative culture results.

Patients with positive cultures at the time of reimplantation should be managed with reinstitution of antimicrobial therapy to complete another treatment course, followed by chronic suppressive antimicrobial therapy. Patients with negative cultures at the time of reimplantation do not require further antimicrobial therapy.

Permanent resection arthroplasty — Permanent resection arthroplasty may be appropriate for patients who must undergo resection for management of infection, but who do not meet criteria for reimplantation or for whom reimplantation does not offer a significant functional improvement (such as patients who are nonambulatory for other reasons) [1]. Such patients may include nonambulatory patients, patients who are poor candidates for major surgery (including those with limited bone stock or soft tissue coverage), patients with infection due to highly resistant organisms, and patients who failed a previous exchange in whom the

Topic Feedback

- İkinci aşama cerrahide alınan kültürde üreme var
- Ya da operasyona kadar antibiyotik tedavisi sürdürüldü
- Re-implantasyondan sonra kalça için 3 ayı, diz için 6 ayı tamamlayacak şekilde tedaviye devam

Trampuz A, Zimmerli W. Swiss Med Wkly, 2005.
Esposito S &Leone S Int J Antimicrobial Agents, 2008.

- Antibiyotik tedavisi re-implantasyona kadar kesilmemeli
- 'Drug *holidays*' ve re-implantasyon öncesi eklem aspirasyonu ve kültür önerilmiyor.
- **Gerekçe**; antibiyotiğin kesildiği dönemde bakteriler yeniden replike olabilir ve re-implante protezi yeniden infekte edebilir.

Li C et al Int Orthopaedics, 2020.

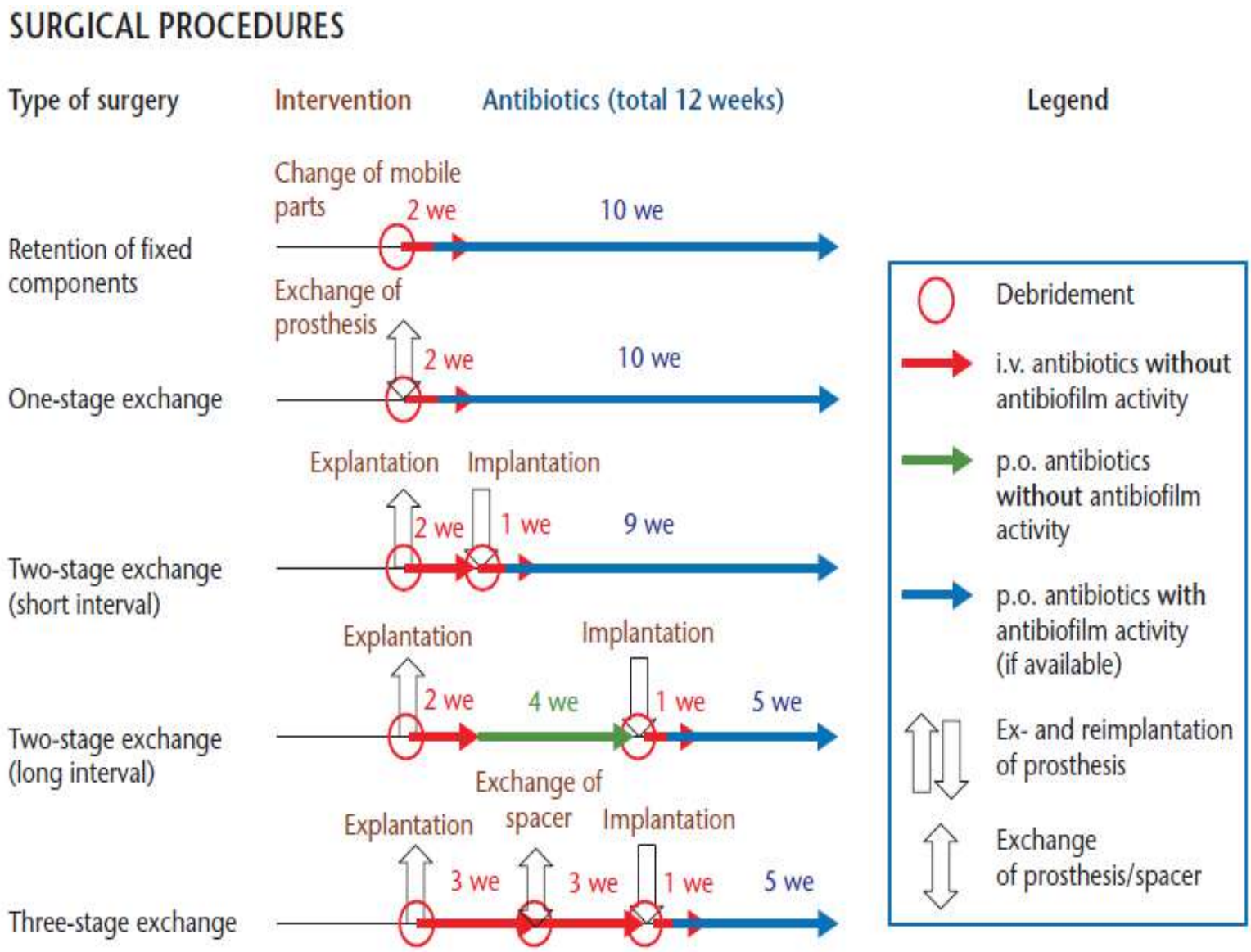


Fig. 3 Overview of surgical procedures for PJI. Reproduced with permission from the Pocket Guide to Diagnosis & Treatment of PJI, PRO-IMPLANT Foundation (version 9, October 2019).

Archives of Orthopaedic and Trauma Surgery (2018) 138:635–642
https://doi.org/10.1007/s00402-018-2886-0

ORTHOPAEDIC SURGERY

Outcome of hip and knee periprosthetic joint infections caused by pathogens resistant to biofilm-active antibiotics: results from a prospective cohort study

Doruk Akgün[1] · Carsten Perka[1] · Andrej Trampuz[1] · Nora Renz[1]

Received: 4 October 2017 / Published online: 19 January 2018
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

Table 1 Patient demographics, clinical and laboratory findings

Variable	All patients ($n=163$)	DTT PJI group ($n=30$)	Non-DTT PJI group ($n=133$)	p value
Patient age at the time of explantation (years)*	70 ± 10	69.5 ± 12.5	69.6 ± 9.8	0.965
Sex[a]				0.978
Male	71 (43.6)	13 (43.3)	58 (43.6)	
Female	92 (56.4)	17 (56.7)	75 (56.4)	
Joint[a]				0.304
Hip	84 (51.5)	18 (60)	66 (49.6)	
Knee	79 (48.5)	12 (40)	67 (50.4)	
Charlson comorbidity index (age adjusted)*	4 ± 2.1	4.5 ± 2.6	3.9 ± 2	0.122
CRP at admission (mg/l)*	39.2 ± 67	41 ± 49.9	38.8 ± 70.5	0.053
Microbiology[a]				
Monomicrobial	79 (48.5)	14 (46.7)	65 (48.9)	0.827
Polymicrobial	61 (37.4)	16 (53.3)	45 (33.8)	0.046
Negative cultures	23 (14.1)	–	23 (17.3)	–
No. of patients with previous septic revisions[a]	82 (50.3)	21 (70)	61 (45.9)	0.025
No. of previous septic revisions*	2.5 ± 1.6	1.8 ± 1.7	1.1 ± 1.7	0.015

*

Table 2 Treatment and outcome characteristics of all patients

Variable	All patients ($n=163$)	DTT PJI group ($n=30$)	Non-DTT PJI group ($n=133$)	p value
Treatment				
Time until reimplantation (days)	63.9 ± 34.5	89.4 ± 50.5	58.1 ± 26.9	< 0.001
CRP prior to reimplantation (mg/l)	11.9 ± 13.1	10 ± 11.8	12.3 ± 13.4	0.164
Total duration of antimicrobial therapy (days)	123.3 ± 57.7	150.8 ± 74.7	117.4 ± 51.7	0.003
Duration of i.v. antimicrobial therapy (days)[a]	32.8 ± 20.2	50.4 ± 31	29 ± 14.7	< 0.001
Duration of oral antimicrobial therapy (days)[a]	84.1 ± 32.2	90.1 ± 47.3	82.8 ± 28.2	0.553
No. of revisions during interval	1.7 ± 1.3	2 ± 1.6	1.5 ± 1	0.324
Duration of hospital stay (days)	31.2 ± 15.9	44.5 ± 26.5	28.2 ± 10.4	< 0.001

Etken tamamen eradike edildi mi? Nasıl anlarım ?

- CRP
- Sedimentasyon
- Diğer biyobelirteçler ????

- Klinik bulgular
  - Ağrı var mı?
  - Eklem fonksiyonel mi?

Seçenek 3:Antimikrobiyal baskılama

- Operasyonu kaldıramayacak hastalar
- Etken düşük virulanslı bir mikroorganizma
- Etken po kullanılabilecek antimikrobiklere duyarlı
- Hasta po antimikrobik kullanabilecek özellikte ve uzun süreli kullanımdan zarar görmeyecek ise
- Sistemik infeksiyon bulguları yok
- Protez intakt, gevşeme ve fonksiyon bozukluğu yok

- Protez çıkarılmadan debridman
- Takiben 4 hafta İV antibiyotik tedavisi
- Uzun süreli po baskılama tedavisi

- Başarı şansı
  - Kalça protezlerinde %60
  - Diz protezlerinde %26-%82

Clinical Microbiology and Infection
Available online 17 September 2019
In Press, Corrected Proof

Original article

Suppressive antibiotic therapy in prosthetic joint infections: a multicentre cohort study

R. Escudero-Sanchez [1], E. Senneville [2], M. Digumber [2], A. Soriano [3], M.D. del Toro [4], A. Bahamonde [5], J.L. del Pozo [6], L. Guio [7], O. Murillo [8], A. Rico [9], M.J. García-País [10], D. Rodríguez-Pardo [11], J.A. Iribarren [12], M. Fernández [13], N. Benito [14], G. Fresco [1], A. Muriel [15], J. Ariza [8], J. Cobo [1]

Show more

https://doi.org/10.1016/j.cmi.2019.09.007

Get rights and conten

- Retrospektif, çok merkezli
- 302 hasta değerlendirilmiş
- Tetrasiklin & kotrimaksazol
- 5 yıl infeksiyon kontrolü %58.6
- <70 yaş, Gram pozitif mo dışında başka bir etken olumsuz sonuçla ilişkili

IVYSPRING INTERNATIONAL PUBLISHER

Journal of Bone and Joint Infection

2019; 4(6): 268-276. doi: 10.7150/jbji.37262

Research Paper

Cl
Pa
Re

Borg

1. D
2. D

- R
- 2
  p
- kotrimaksazol, doksisiklin, siprofloksasin, amoksisilin/klavulonat
- Ortalama ab kullanım süresi 38 ay (1-151 ay)

- 13 hastada (%56.5) başarılı
- Etken S aureus ise başarı şansı düşük (%80 & %33 tedavi yetersizliği)
- Yan etki nedeni ile tedavi kesilen hasta sayısı 2

Vankomisin & Daptomisin

IVYSPRING INTERNATIONAL PUBLISHER

Journal of Bone and Joint Infection

2019; 4(2): 72 -75. doi: 10.7150/jbji.22118

Short Research Paper

Daptomycin versus Vancomycin as Post-Operative Empirical Antibiotic Treatment for Prosthetic Joint Infections: A Case-Control Study

C Joseph[1], O Robineau[2,3], M Titecat[3,4], S Putman[5], N Blondiaux[6], C Loiez[4], M Valette[2], JL Schmit[1], E Beltrand[7], H Dézeque[5], S Nguyen[8], H Migaud[3,5], E Senneville[2,3,5]✉

1. Infectious Diseases Department, University Hospital of Amiens, France
2. Infectious Diseases Department, Gustave Dron Hospital of Tourcoing, France

Table 1. Compared characteristics and outcome of 40 patients treated empirically with either Vancomycin or Daptomycin for a periprosthetic joint infection

	Daptomycin n=20 (%)	Vancomycin n=20 (%)	P
Age, years mean ± SD	65.6 ± 15.8	67.5 ± 13.1	.67
Male	10 (50)	8 (40)	.52
Body weight kg, mean ± SD	77.5 ± 20.4	77.9 ± 16.6	.9
Co-morbidity	3* (15)	4** (20)	.9
Acute PJI	9 (45)	9 (45)	1
Total hip arthroplasty	16 (80)	16 (80)	1
Total knee arthroplasty	4 (20)	4 (20)	1
Debridement-retention	8 (40)	12 (60)	0.20
One-stage exchange	8 (40)	6 (30)	0.51
Two-stage exchange	4 (20)	2 (10)	.38
Time from incision to first administration min, mean ± SD	94.1 ± 36.7	101.1 ± 149.6	.59
Baseline serum creatinine concentration mg/L, mean ± SD	6.56 ± 1.74	6.06 ± 1.81	.52
C-reactive protein mg/L, mean ± SD	32.8 ± 45.8	70.6 ± 68.8	0.09
Combined antibiotics			.34
- cefotaxime	10 (50)	11 (55)	.75
- cefepime	8 (40)	6 (30)	.51
- aztreonam	1 (5)	0	.31
- gentamicin	1 (5)	1 (5)	1
- ciprofloxacin	0	2 (10)	.15
Hospital stay length days, mean ± SD	22.1 ± 23.4	21.8 ± 15.9	.59
Culture-guided antibiotic therapy			
- mean duration, days ± SD	91.1±40.5	102.9±86.2	0.10
- rifampicin-levofloxacin	9 (45%)	8 (40%)	.75
- rifampicin-doxycyclin	2 (10%)	2 (10%)	1
- rifampicin-cotrimoxazole	1 (5%)	2 (10%)	.55
- rifampicin-linezolid	3 (15%)	2 (10%)	.23
- clindamycin-levofloxacin	1 (5%)	1 (5%)	1
- clindamycin-doxycyclin	2 (10%)	2 (10%)	1
- ceftriaxone-levofloxacin	2 (10%)	3 (15%)	.23
Outcome			
- death***	1 (5%)	0	.31
- relapsing infection	2 (10%)	2 (10%)	1
- remission	17 (85%)	18 (90%)	.63

Table 3. Compared tolerance to antibiotic treatment of 40 patients treated empirically for either Vancomycin or Daptomycin

AE episodes	Daptomycin (n=20)	Vancomycin (n=20)	P
Allergy	0	1 (5%)	.31
Thrombophlebitis at the injection site	0	2 (10%)	.15
Nausea	4 (20%)	4 (20%)	1
Diarrhoea	2 (10%)	1 (5%)	.54
Acute renal failure	0	2 (10%)	.15
Myalgia*	1 (5%)	0	.31
Total N° of episodes of adverse events	7 (35%)	10 (50%)	.92
Total N° of patients who experienced adverse events	4 (20%)	6 (30%)	.47
Total N° of patients with discontinuations for adverse events	0	5** (25%)	.02

*: mild, without elevated CPK, **: acute renal insufficiency (n=2) and thrombophlebitis (n=3)

Daptomisin & Linezolid

Linezolid versus daptomycin treatment for periprosthetic joint infections: a retrospective cohort study

Masahiro Sawada, Kenichi Oe*, Masayuki Hirata, Hiroshi Kawamura, Narumi Ueda, Tomohisa Nakamura, Hirokazu Iida and Takanori Saito

Department of Orthopaedic Surgery, Kansai Medical University, 2-5-1 Shinmachi, Hirakata, Osaka 573-1010, Japan

© The Author(s). 2019 **Open Access** T International License (http://creativecor reproduction in any medium, provided the Creative Commons license, and inc (http://creativecommons.org/publicdor

Methods: This study retrospectively evaluated 82 patients between June 2009 and December 2017, to compare the effectiveness of LZD (group L, $n = 39$) and DAP (group D, $n = 43$) for treatment of PJIs harboring gram-positive microorganisms. Surgical options used with LZD or DAP therapy included implant retention, implant removal, and a shift to another appropriate antibiotic. Infection control was defined as not requiring implant removal after the final treatment.

Table 1 Preoperative patient characteristics

Characteristics	Group L	Group D
Number of joints	39	43
Surgical intervention during this therapy, number		
None	18	12
Only debridement	7	12
Debridement and implant removal	0	2
One-stage revision	0	5
Two-stage revision	13	6
Shift to another antibiotic after identification	1	6

[a]Student's *t* test
[b]Pearson's chi-squared test
[c]Mann-Whitney *U* test
[d]Fisher's exact test

Table 2 Prosthetic joint and surgical interventions

Joints	Group L ($n = 39$)			Group D ($n = 43$)		
	Implant retention	Implant removal	Shift to another antibiotic	Implant retention	Implant removal	Shift to another antibiotic
Hip, *n*	11	8	1	10	10	5
Knee, *n*	13	5	0	9	2	1
Shoulder, *n*	0	0	0	3	0	0
Ankle, *n*	1	0	0	2	1	0

n number

Table 3 Microorganisms isolated from PJIs in the current study

Pathogen	Group L, *n* (%)	Group D, *n* (%)
Gram-positive bacterium	28 (72%)	30 (70%)
Methicillin-resistant bacterium	20	13
Other gram-positive bacterium	8	17
Other microorganisms	1 (2%)	6 (14%)
No identification using joint aspiration	5 (13%)	7 (16%)
No culture	5 (13%)	0

n number

Table 4 Reasons for antibiotic discontinuation

Reasons	Group L, *n* (%)	Group D, *n* (%)	*P* value[a]
Continuation for clinical success	17 (44%)	30 (70%)	*0.025*
Clinical failure or not evaluable	3 (8%)	3 (7%)	1.000
Adverse event	12 (31%)	3 (7%)	*0.009*
Shift to another antibiotic after identification or for no efficacy	3 (8%)	6 (14%)	0.487
Fixed administration duration in advance	2 (5%)	1 (2%)	0.602
Unknown	2 (5%)	0 (0%)	0.223

n number
[a]Fisher's exact test

Linezolid pe tedavi sonrası po verilebilir mi?

Linezolid in the treatment of periprosthetic joint infection caused by coagulase-negative staphylococci

Hannah K. Eriksson, David Ahadpour, Nils P. Hailer, Stergios Lazarinis & Josef D. Järhult

To cite this article: Hannah K. Eriksson, David Ahadpour, Nils P. Hailer, Stergios Lazarinis & Josef D. Järhult (2019) Linezolid in the treatment of periprosthetic joint infection caused by coagulase-negative staphylococci, Infectious Diseases, 51:9, 683-690, DOI: 10.1080/23744235.2019.1642510

To link to this article: https://doi.org/10.1080/23744235.2019.1642510

Methods: We conducted a retrospective study of patients with PJI caused by CoNS treated with surgical intervention and orally administrated linezolid during the period 1995–2014 ($n = 28$). Clinical outcomes and adverse events related to linezolid administration were evaluated. Mean time to follow-up was 4.3 years (range: 0.2–12).

Table 2. Susceptibility of CoNS strains.

Antibiotics	Number of strains tested	Number of resistant strains (%)
Isoxazolyl penicillin	28	28 (100)
Clindamycin	28	23 (82)
Quinolone[a]	27	20 (74)
Rifampicin	28	16 (57)
Fusidic acid	28	19 (68)
Co-trimoxazole	26	21 (81)
Vancomycin	28	0 (0)
Gentamicin	26	24 (92)
Tobramycin	28	27 (96)
Linezolid	28	0 (0)
Tigecycline	6	0 (0)
Daptomycin	5	0 (0)

[a]Number tested for ciprofloxacin; 8, 19 for nalidixic acid.

Table 1. Demographic and clinical characteristics of included patients.

Pat. no.	Age (years) /gender	Joint	Indication THA/TKA	Final surgical therapy	Comorbidity/ risk factors	Type of PJI	Indication linezolid	Duration of linezolid therapy (weeks)	Duration of AB therapy (weeks)	Follow-up time (year)	Cure
1	77/M	Hip	OA	2-stage	DM, smoking	Delayed	MDRS	3	32	4.5	No
2	76/F	Hip	Fracture	2-stage	None	Delayed	MDRS	4	25	2	Yes
3	68 y/M	Hip	OA	DAIR	Obesity, Parkinson	Early	MDRS	4	16	2	Yes
4	62 y/M	Hip	OA	DAIR	None	Early	MDRS	1	15	10	Yes
5	73 y/F	Hip	OA	2-stage	Obesity	Delayed	MDRS	3	8	10	Yes
6	70 y/M									4	Yes
7	88 y/M									0.2	Yes
8	80 y/F									0.2	Yes
9	78 y/F									6	Yes
10	84 y/F									5	Yes
11	72 y/M									3.5	Yes
12	68 y/M									5	Yes
13	77 y/F									4	No
14	77 y/M									11	Yes
15	83 y/M									10	Yes
16	80 y/M									1.5	Yes
17	66 y/F									4	No
18	80 y/M	Hip	OA	2-stage	None	Early	MDRS	4	9	0.7	Yes
19	83 y/M	Knee	OA	2-stage	None	Delayed	MDRS	8	11	4	Yes
20	60 y/M	Knee	OA	DAIR	None	Early	MDRS	3	24	12	Yes
21	63 y/M	Knee	Fracture	DAIR	RA, malignancy	Delayed	MDRS	4	158	8	No
22	77 y/M	Knee	OA	DAIR	None	Early	AE	3	20	9.5	Yes
23	67 y/M	Knee	OA	2-stage	None	Delayed	MDRS	6	7	6	Yes
24	77 y/M	Knee	OA	DAIR	None	Delayed	MDRS	8	33	5	No
25	74 y/M	Knee	OA	DAIR	DM, obesity	Delayed	MDRS	4	8	2	No
26	72 y/F	Knee	OA	2-stage	Obesity	Early	AE	6	30	1	Yes
27	63 y/F	Knee	OA	DAIR	Obesity	Early	AE	12	14	9	Yes
28	75 y/F	Knee	OA	2-stage	None	Early	MDRS	2	10	10.5	Yes

Tedavi başarısı 22/28 %78.6

Yan etki 11/28 %39.3

Table 4. Microorganisms and groups of organisms involved in non-hematogenous prosthetic joint infections according to time of infection after surgery (≤1 month, 2–3 months, 4–12 months, >12 months).

Microorganism or Microorganism Group	PJI within 1 Month after Surgery n = 844	PJI 2-3 Months after Surgery n = 243	PJI 4-12 Months after Surgery n = 277	PJI > 12 Months after Surgery n = 619	p-Value
	Total no. (%)*				
Staphylococcus species					
• Coagulase-negative staphylococci	236 (28.2) **	107 (44) ** †	167 (60.3) †	348 (56.2)	<0.001
○ *Staphylococcus epidermidis*	132 (15.6) **	68 (28) ** †	106 (38.3) †	203 (32.8)	<0.001
○ *Staphylococcus lugdunensis*	2 (0.2) **	3 (1.3) **	10 (3.6)	22 (3.6)	<0.001
• *Staphylococcus aureus*	301 (35.7)	60 (24.7)	60 (21.7)	108 (17.4)	<0.001
Streptococcus species	36 (4.3) **	25 (10.3) **	14 (5.1)	49 (7.9)	<0.001
○ *Streptococcus agalactiae*	8 (0.9) **	11 (4.5) **	6 (2.2)	10 (1.6)	0.003
○ Viridans group streptococci not identified to species level	6 (0.7) **	7 (2.9) **	2 (0.7) †	18 (2.9) †	0.003
Enterococcus species	106 (12.6)	23 (9.5)	15 (5.4)	32 (5.4)	<0.001
Aerobic Gram-negative bacilli	396 (46.9) **	50 (20.6) ** †	37 (13.4) †	37 (13.4)	<0.001
• *Enterobacteriaceae*	303 (35.9) **	37 (15.2) ** †	25 (9) †	48 (7.8)	<0.001
○ *Escherichia coli*	129 (15.3)	12 (4.9)	10 (3.6)	21 (3.4)	<0.001
○ *Proteus* spp.	75 (8.9)	7 (2.9)	7 (2.5)	14 (2.3)	<0.001
○ *Enterobacter* spp.	73 (8.6) **	11 (4.5) ** †	2 (0.7) †	6 (1)	<0.001
○ *Klebsiella* spp.	48 (5.7)	2 (0.8)	4 (1.4)	3 (0.5	<0.001
• Non-fermenting Gram-negative bacilli	138 (16.4) **	16 (6.6) **	11 (4)	41 (6.6)	<0.001
○ *Pseudomonas* spp.	128 (15.2) **	17 (7) **	11 (4)	35 (5.7)	<0.001
Aerobic Gram-positive bacilli	16 (1.9)	3 (1.2)	7 (2.5)	23 (3.7)	0.083
Anaerobic Gram-positive bacilli	19 (2.3) **	14 (5.7) **	16 (5.8)	61 (9.7)	<0.001
• *Cutibacterium* spp.	17 (2) **	12 (4.9) **	16 (5.8)	51 (8.2)	<0.001
Anaerobic Gram-positive cocci	8 (0.9)	4 (1.6)	5 (1.8)	13 (2.1)	0.330
Anaerobic Gram-negative bacilli	12 (1.4)	2 (0.8)	1 (0.4)	5 (0.8)	0.409
Mycobacterium species	2 (0.2)	1 (0.9)	4 (1.4)	2 (0.3)	0.068
Fungi	8 (0.9)	3 (1.2)	3 (1.1)	12 (1.9)	0.418
Multidrug-resistant organisms	202 (23.9)	20 (8.2)	20 (7.2)	43 (6.9)	<0.001
• Methicillin-resistant *S. aureus*	93 (11)	14 (5.8)	14 (5.1)	30 (4.8)	<0.001
• Multidrug-resistant Gram-negative bacilli	112 (13.3)	7 (2.5)	5 (1.8)	14 (2.3)	<0.001
• Extended-spectrum beta-lactamases producing *Enterobacteriaceae*	36 (4.3)	1 (0.4)	2 (0.7)	1 (0.3)	<0.001
Ciprofloxacin-resistant Gram-negative bacilli	84 (10)	5 (2.1)	4 (1.4)	11 (1.8)	<0.001
Polymicrobial infections	230 (27.2)	36 (14.7)	32 (11.1)	77 (11.1)	<0.001

International Journal of Antimicrobial Agents 53 (2019) 294–301

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

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

Multidrug-resistant and extensively drug-resistant Gram-negative prosthetic joint infections: Role of surgery and impact of colistin administration

Antonios Papadopoulos[a], Alba Ribera[b], Andreas F Mavrogenis[c], Dolors Rodriguez-Pardo[d], Eric Bonnet[e], Mauro José Salles[f], María Dolores del Toro[g], Sophie Nguyen[h], Antonio Blanco-García[i], Gábor Skaliczki[j], Alejandro Soriano[k], Natividad Benito[l], Sabine Petersdorf[m], Maria Bruna Pasticci[n], Pierre Tattevin[o], Zeliha Kocak Tufan[p], Monica Chan[q], Nuala O'Connell[r], Nikos Pantazis[s], Aikaterini Kyprianou[a], Carlos Pigrau[d], Panayiotis D Megaloikonomos[c], Eric Senneville[h], Javier Ariza[b], Panayiotis J Papagelopoulos[c], Efthymia Giannitsioti[a,*], on behalf of the ESCMID Study Group for Implant-Associated Infections (ESGIAI)[1]

2.2. Data collection and definitions

This retrospective analysis of prospectively collected data referred to all patients aged >18 years with a definite diagnosis of MDR or XDR GNB PJI from 2000–2015 in all collaborative centres.

	Success (*n* = 81; 61.8%)	Failure (*n* = 50; 38.2%)	Total (*n* = 131)	*P*-value
Age (years) (mean ± S.D.)	71.8 ± 13.4	74.9 ± 11.4	73.0 ± 12.7	0.179
Sex				0.091
Male	34 (42.0)	13 (26.0)	47 (35.9)	
Female	47 (58.0)	37 (74.0)	84 (64.1)	
Gram-negative bacterial resistance				**0.018 ***
MDR	72 (88.9)	36 (72.0)	108 (82.4)	
XDR	9 (11.1)	14 (28.0)	23 (17.6)	
Therapy				0.338
Monotherapy	28 (35.0)	13 (26.5)	41 (31.8)	
Combination therapy	52 (65.0)	36 (73.5)	88 (68.2)	
Time from arthroplasty to infection onset				0.700
Early (≤4 weeks)	44 (60.3)	29 (64.4)	73 (61.9)	
Late (>4 weeks)	29 (39.7)	16 (35.6)	45 (38.1)	
Surgery type				**0.001 ***
DAIR	32 (39.5)	35 (70.0)	67 (51.1)	
No-DAIR	49 (60.5)	15 (30.0)	64 (48.9)	

Etken mo	XDR	MDR	Toplam
E coli	1	43	44
P aeruginosa	15	18	33
K pneumonia	4	24	28
E cloacae	1	22	23
A baumanii	3	3	6
P mirabilis	2	2	4
M morganii	0	4	4
P stuartii	0	2	2

- ESBL pozitif
  n=94
- Florokinolon dirençli
  n=43
- Karbapenem dirençli
  n=12
- Kolistin direçli
  n=1
  K pneumonia (PDR)

* 13 olguda polimikrobiyal infeksiyon mevcut

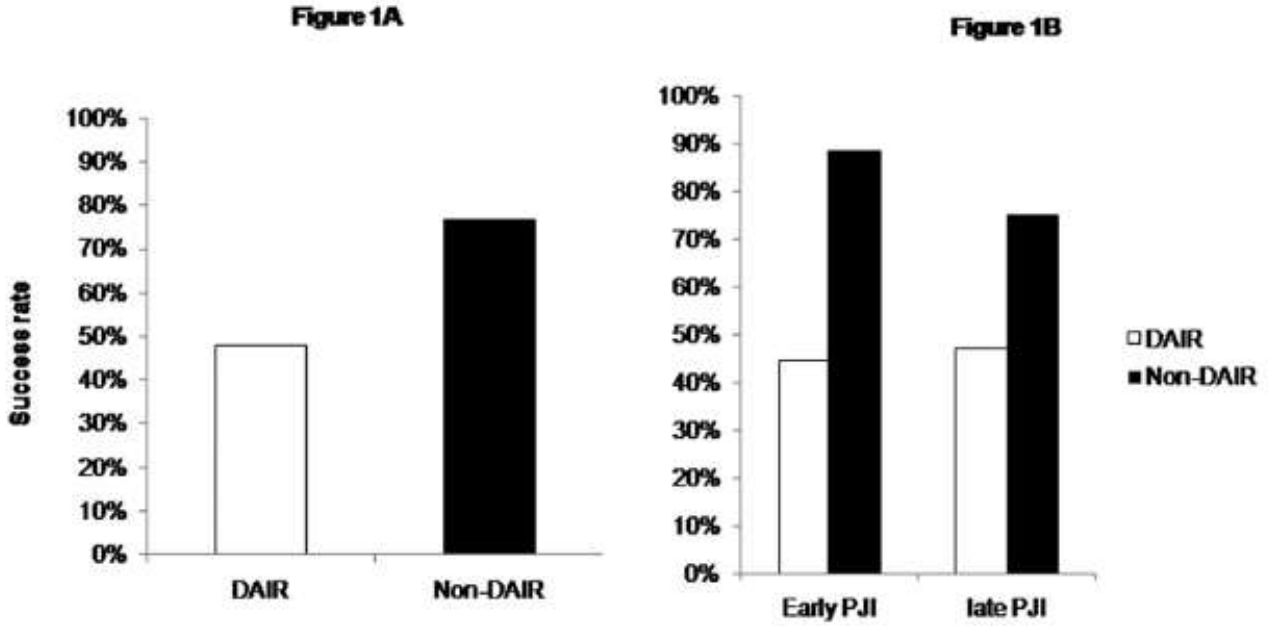
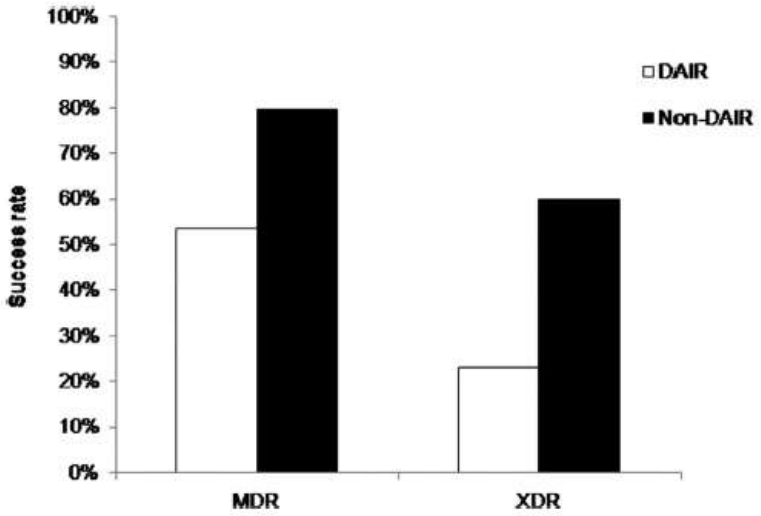


Fig. 1. Proportion of success depending on (A) type of surgery (DAIR versus non-DAIR) and (B) nested within early and late prosthetic joint infection (PJI). DAIR, debridement, antibiotics and implant retention.



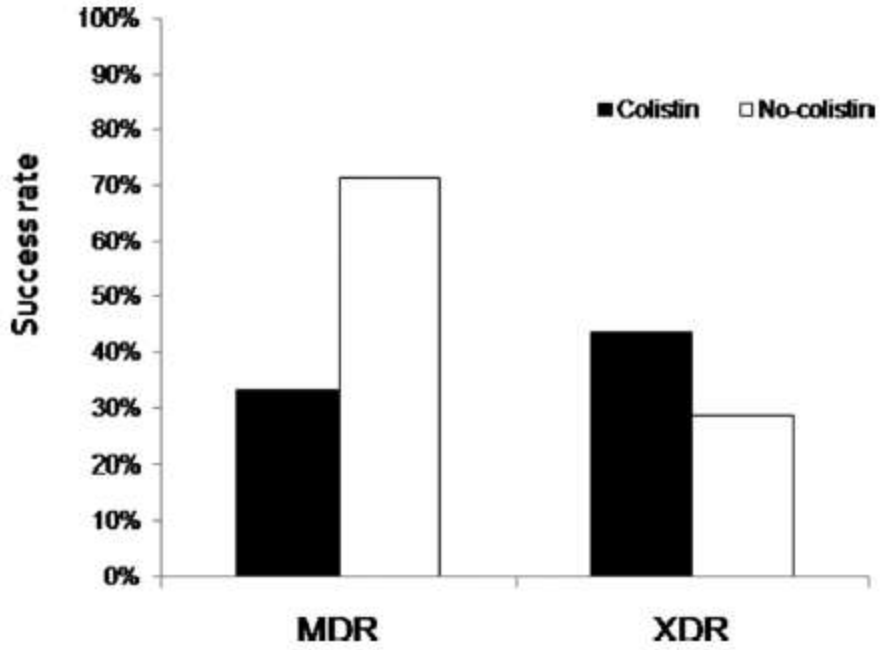
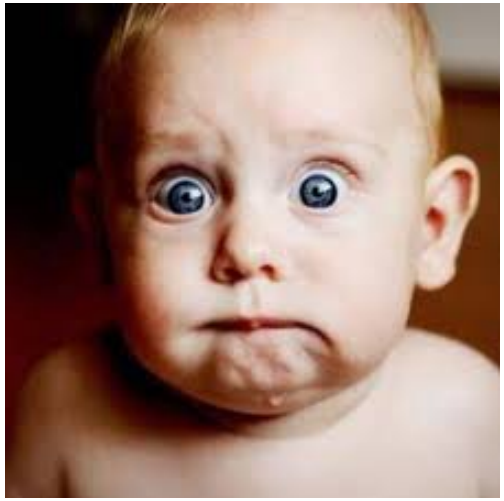


Fig. 4. Proportion of success depending on colistin administration nested within prosthetic joint infections caused by multidrug-resistant (MDR) and extensively drug-resistant (XDR) Gram negative bacteria.

Dirençli Gram negatiflerde…

Klebsiella, P aeruginosa, Acinetobacter

- Karbapenemler
- Kinolonlar
- Kolistin
- Fosfomisin
- Aminoglikozidler
- Tigesiklin



TEŞEKKÜR EDERİM….