Kemik ve Eklem İnfeksiyonlarında Etkene Yönelik Antimikrobiyal Tedavi

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Kemik ve Eklem İnfeksiyonları

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OSTEOMYELİT

SEPTİK ARTRİT

PROTEZ İNFEKSİYONLARI

Osteomyelit

Table 2. Waldvogel's osteomyelitis classification system

Hematogenous osteomyelitis
Contiguous osteomyelitis
Accompanied by systemic vascular diseases
Not accompanied by systemic vascular diseases
Chronic osteomyelitis

- Sosyo-ekonomik ve medikal teknolojideki gelişmelere parelel olarak azaldı
- Ç>E
- Tek patojen etken

- ✓ Travma
- ✓ Komşu inf. odağı
- ✓ Cerrahi…platin,plak vb uygulamalar arttı
- ✓ Artroplasti sayısı arttı
- ✓ E>Ç
- ✓ ≥1 patojen etkendir

Osteomyelit…Anatomik sınıflandırma

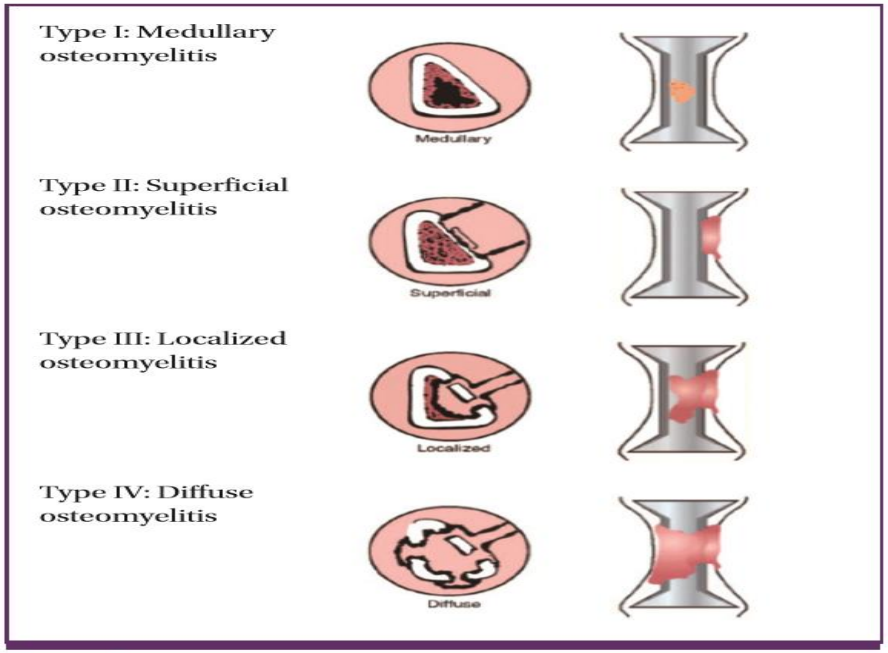


Figure 1. Cierny-Mader classification of osteomyelitis according to the anatomical extent.

Hematojen osteomyelit

Direkt inokülasyon veya komşu enfeksiyon odağı

Kortikal kemik tutulur.
Kemik stabilitesi korunur.

Tüm kemik katmanları tutulur.
Kemik stabilitesi bozulur

Cerrahi yöntem ve antimikrobiyal tedavi süresi bu sınıflamaya göre planlanır

Osteomyelit…etken

- Osteomyelitte etkenin izolasyonu
  - tanıyı doğrulamak
  - etken spesifik tedavileri seçmek için çok önemlidir
- Bakteriyel osteomyelitte patojenlerin dağılımı
  - Hastanın yaşına,
  - Hastalığın yayılma yoluna
    - Hematojen
    - Direkt inokulasyon
    - Komşu yumuşak doku
    - postoperatif
  - Klinik duruma
  - Klinik bulgunun şiddetine göre değişir

Osteomyelit…etkenler

Adult (>17 years)

Staphylococcus aureus

Pseudomonas aeruginosa

Serratia marcescens

Escherichia coli

Coagulase negative staphylococci

- Streptokoklar…ısırık yaraları ve diyabetik ayak infeksiyonlarında sık
- Tüberküloz osteomiyelit hastalarının sayısı AIDS hastalarına paralel olarak artmakta
- fungal enfeksiyon… nadir

Yaşa göre etkenlerin dağılımı

Table 4. Major causative organisms according to patient age

Infants (≤1 year)
Group B streptococci
Staphylococcus aureus
Escherichia coli
Child/youth (1–16 years)
Staphylococcus aureus
Streptococcus pyogenes
Haemophilus influenza
Adult (>17 years)
Staphylococcus aureus
Pseudomonas aeruginosa
Serratia marcescens
Escherichia coli
Coagulase negative staphylococci

Hematojen osteomyelit, tüm osteomyelit vakalarının ~% 20'sini oluşturur;
Genellikle çocuklarda gelişir

Çocuklardaki hematojen osteomyelitin % 90'ından *S. aureus* sorumludur. *Haemophilus influenzae* bağlı hematojen osteomiyelit aşılanmayan çocuklarda yaygındır

Klinik durum göre etkenlerin dağılımı

Table 5. Major causative organisms according to clinical conditions

Clinical situation	Microorganism
Bite wound	Streptococci, anaerobic bacteria, *Pasteurella multocida, Eikenella corrodens*

Türk Mikrobiyol Cem Derg 41(1):46-48, 2011
doi:10.5222/TMCD.2011.046

Olgu Sunumu

Kedi Isırığı Sonrası Gelişen *Pasteurella multocida*'ya Bağlı Osteomyelit Olgusu

Umay BALCI *, Derya SEYMAN **, Nevgün Sepin ÖZEN *, Dilara İNAN ***

Klinik durum göre etkenlerin dağılımı

Klinik durum	mikroorganizma
Vasküler yetmezlik…miks infeksiyon	*S.aureus*, KNS, Enterobacteriaceae, streptococci, enterococci ve anaerobik patojenler
Proteze bağlı	*S. aureus* (en sık), *S.epidermidis, P.aeruginosa, Propionibacterium* spp
SVK(+); geniş spekt.AB kullanım öyküsü ; Candida spp tekrarlayan izolasyonu; diğer patojenlerin yokluğunda	*Candida* spp

Osteomyelit…tanı

- Klinik
  - Akut osteomyelit
    - Semptomlar birkaç gün içinde başlar
    - Lokal semptomlar…ağrı, hassasiyet, ısı artışı, ödem
    - Sistemik semptomlar…ateş, irritabilite
    - Çocuk…metafiz
    - Erişkinde ….diafiz
  - Kronik osteomyelit
    - Yavaş seyirli…haftalar, aylar
    - Sekestre, osteoskleroz, sinüs traktı
    - Sinus traktı tıkanır ise apse ve YDİ mg
- Radyolojik
- Mikrobiyolojik
  - Apse kültürü
  - Cerrahi veya perkütan kemik doku kültürü ve kan kültürü
  - Sürüntü kültürü…sinüs traktından **ANLAMLI DEĞİL**
- Histopatolojik

Osteomyelit tedavide temel prensipler

Antimikrobiyal tedavi (AI)

Hastaya ait faktörler (AIII)

Kr. osteomyelitli hastalarda önemli

- ✓ İyi beslenme
- ✓ Sigara kullanmama
- ✓ Kan şeker düzeyinin regülasyonu
- ✓ Kan akımının sağlanması

Cerrahi tedavi

- Akut osteomyelit (AII)
  - Abse
  - Radyolojik olarak nekroz bulguları (+)
  - Antimikrobiyal tedaviye yanıt Ø ise
- Kronik osteomyelit (AIII)
  - Nekrotik dokunun debritmanı
  - Kemik yapıların stabilizasyonu
  - Ölü alanların yönetimi
  - yumuşak dokunun yönetimi

Clinical guidelines for the antimicrobial treatment of bone and joınt infections. Infect Chemother 2014; 46(2):125-138.

Osteomyelit…tedavi

Apse- Kemik doku kültürleri ve kan kültürleri alınır

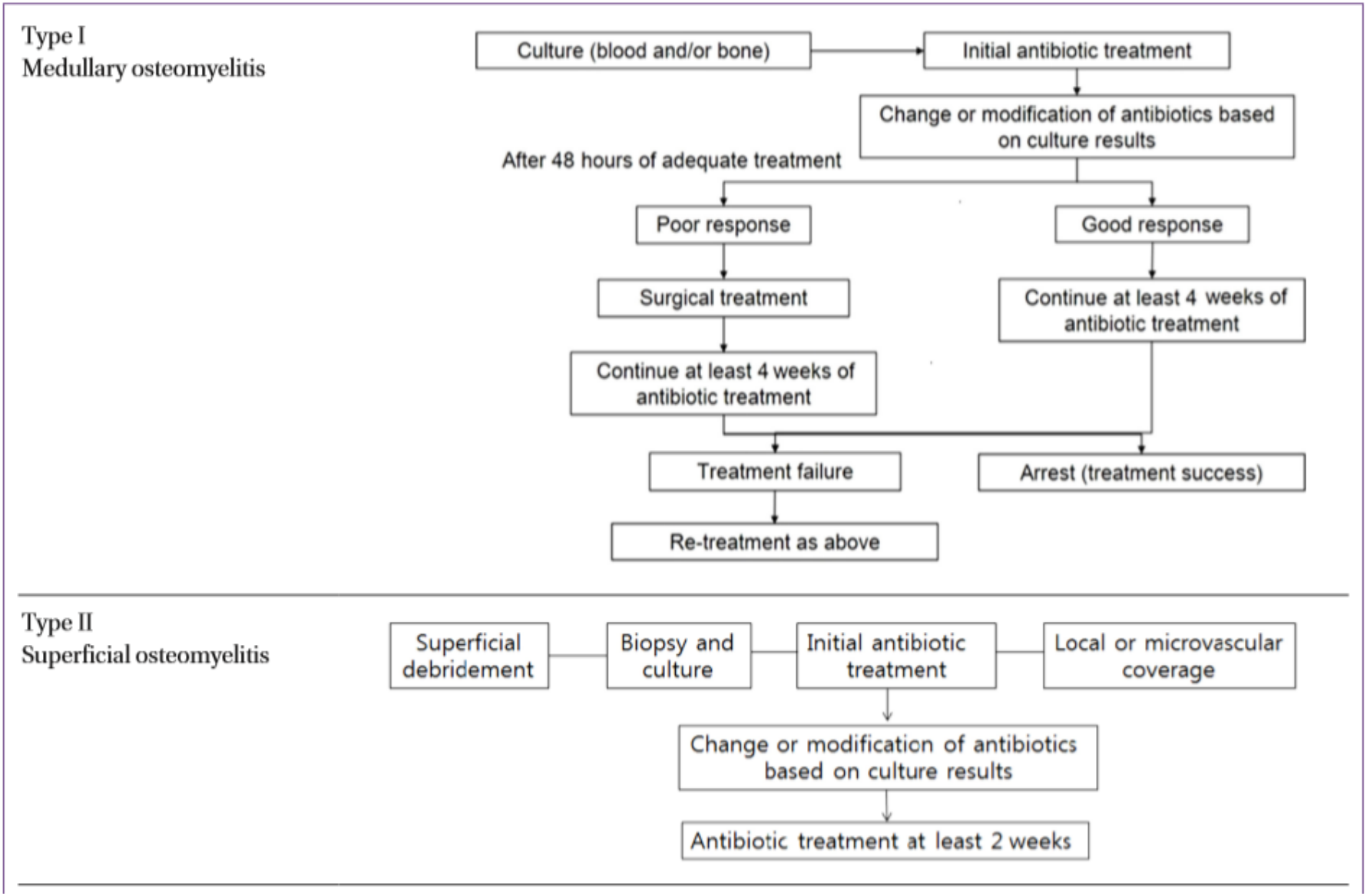
Debritman sonrası cerrahi sınırdan doku kültürü

Ampirik Antibiyotik tedavisi

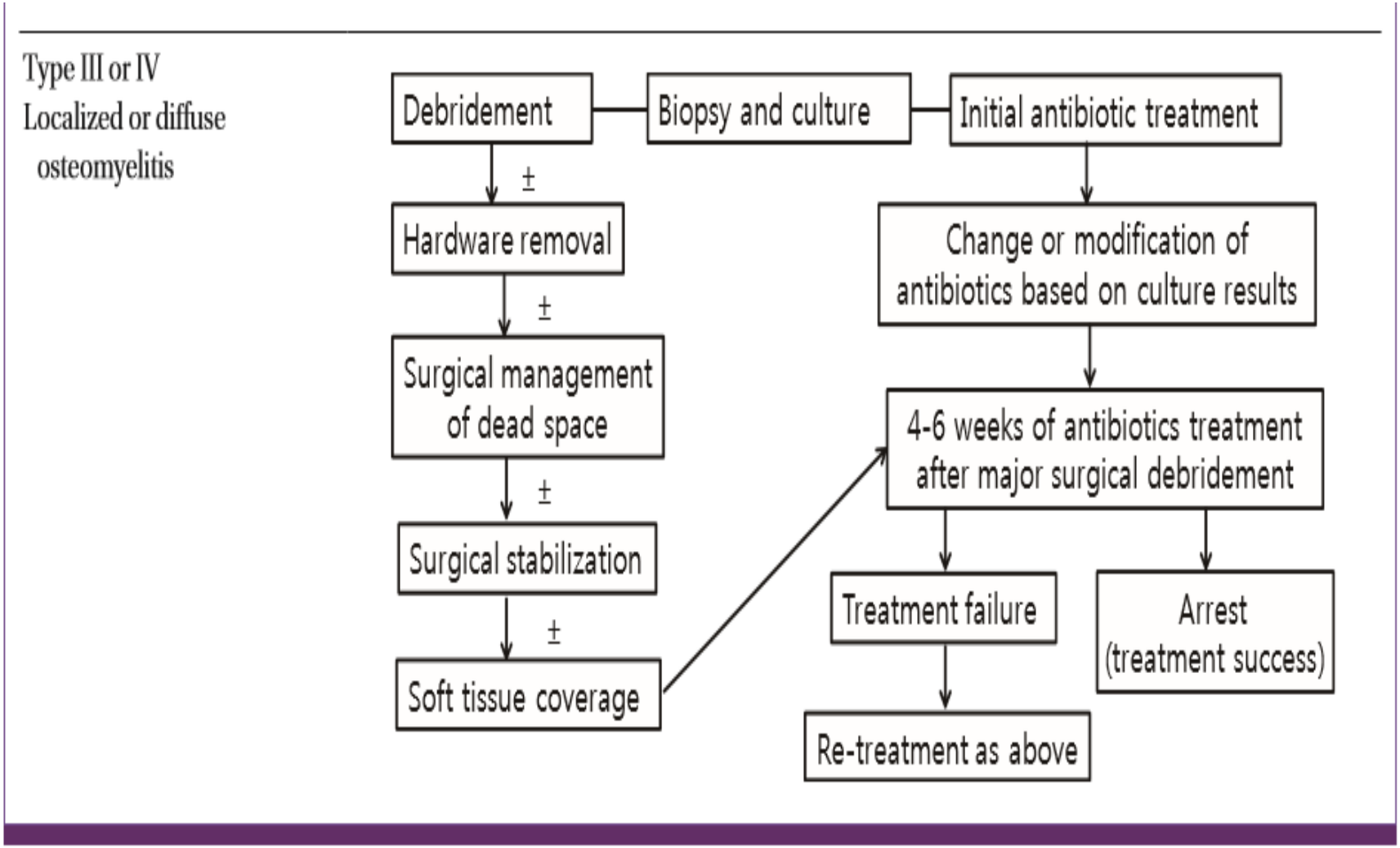
- ✓ Bakterisidal
- ✓ Kemik doku penetrasyonu
- ✓ Gram boyama sonucuna ve
- ✓ Osteomyelitin nedenine; hastanın GD; toplum/hastane kaynaklı; risk faktörlerine göre tedavi planlanır

Kültür sonucuna göre tedavi yönetimi

Osteomyelit…tedavi



Osteomyelit…tedavi



Osteomyelit…ampirik tedavi

	Organism	Preferred	Alternative
Empirical antibiotic therapy	Community onset	2.0 g nafcillin[a] every 4 hours or 2.0 g cefazolin every 8 hours (+[b]/-) 2.0 g ceftriaxone every 24 hours	MSSA
	Nosocomial or healthcare-associated	1.0 g vancomycin[c] every 12 hours or 400 mg teicoplanin every 24 hours (First day every 12 hours) (+[b]/-) 2.0 g ceftazidime or cefepime every 8 hours	MRSA

Gr(-) bakterinin etken olma riski (+) ise

Toplum kaynaklı osteomyelit…. seftriakson

Sağlık bakımı ilişkili osteomyelit… seftazidim/sefepim eklenilmeli

- ✓ ÜSİ /intraabd. kaynaklı bakteriyemi
- ✓ Yaşlı
- ✓ immunkompromize

Osteomyelit…etken spesifik tedavi

Selective antibiotic therapy	Methicillin susceptible *Staphylococcus aureus* or Coagulase-negative staphylococci	2.0 g nafcillin every 4 hours	3.0 g ampicillin/sulbactam every 6 hours hours y 8 hours 2 hours
	Methicillin resistant *Staphylococcus aureus* or Coagulase-negative staphylococci		ours lfopris- y 8 hours mycin npin oxazole + 600 mg rifampin
	Streptococcus spp.	3–4 million units penicillin G every 4–6 hours	2.0 g ceftriaxone every 24 hours
	Enterobacteriaceae, quinolone-susceptible, non–extended-spectrum β-lactamase (ESBL)-producing	500–750 mg ciprofloxacin every 12 hours	2.0 g ceftriaxone every 24 hours
	Enterobacteriaceae, quinolone-resistant, non–ESBL-producing	2.0 g ceftriaxone every 24 hours	
	Enterobacteriaciae, ESBL producer	1.0 g ertapenem every 24 hours or 500 mg imipenem every 6 hours –2.0 g meropenem every 8 hours	
		ceftazidime or cefepime every 8 hours combined with aminoglycoside for eeks) owed by 750 mg oral ciprofloxacin[e] 12 hours	4.5 g piperacillin/tazobactam every 8 hours (+/-) (combined with aminoglycoside for 2–4 weeks) or 500 mg imipenem every 6 hours or 1.0–2.0 g meropenem every 8 hours → followed by 750 mg oral ciprofloxacin every 12 hours
	Mixed anaerobes	3.0 g ampicillin/sulbactam every 6–8 hours 1.2 g amoxicillin/clavulanate every 6–8 hours 4.5 g piperacillin/tazobactam every 8 hours	+500 mg metronidazole every 8 hours +600 mg clindamycin every 8 hours or 500 mg imipenem every 6 hours or 1.0–2.0 g meropenem every 8 hours

MSSA osteomyelitinde Vankomisin kullanılmamalı…rekürrens oranı yüksek(AII)

Rifampisin (BII)

Erken evre kullanılmamalı

Oral tedavide …kombinasyon tedavisi

Rif+siprofloksasin; Rif+levofloksasin; Rif+ TMP-SMX

Pseudomonas osteomyeliti BIII

Siprofloksasin İV monoterapi önerilmez

Yüksek bakteriyel yüke bağlı direnç gelişme riski yüksek

Oral tedaviye geçildiğinde kullanılmalı

Osteomyelit tedavi süresi

Clinical Guidelines for the Antimicrobial Treatment of Bone and Joint Infections in Korea

The Korean Society for Chemotherapy, The Korean Society of Infectious Diseases, and The Korean Orthopaedic Association

SON MAJOR DEBRITMANDAN SONRA 4-6 HAFTA

Osteomyelit…tedavi süresi

2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections[a]

Table 11. Suggested Route, Setting, and Duration of Antibiotic Therapy, by Clinical Syndrome

Bone or joint			
No residual infected tissue (eg, postamputation)	Parenteral or oral	…	2–5 d
Residual infected soft tissue (but not bone)	Parenteral or oral	…	1–3 wk
Residual infected (but viable) bone	Initial parenteral, then consider oral switch	…	4–6 wk
No surgery, or residual dead bone postoperatively	Initial parenteral, then consider oral switch	…	≥3 mo

Osteomyelit…tedavi süresi

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

40. The optimal duration of therapy for MRSA osteomyelitis is unknown. A minimum 8-week course is recommended (**A-II**). Some experts suggest an additional 1–3 months (and possibly longer for chronic infection or if debridement is not performed) of oral rifampin-based combination therapy with TMP-SMX, doxycycline-minocycline, clindamycin, or a fluoroquinolone, chosen on the basis of susceptibilities (**C-III**).

Septik Artrit

Septik artrit için yüksek risk grupları

- Romatoid artrit, dejeneratif osteoartrit gibi eklem hastalıkları
- İV madde kullanımı
- Alkolizm
- ***Pseudomonas aeruginosa* septic arthritis of knee after intra-articular ozone injection**

Derya Seyman[1], Nevgun Sepin Ozen[2], Dilara Inan[3], Gozde Ongut[4], Dilara Ogunc[4]

[1]Antalya Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Antalya, Turkey;
[2]Antalya Hıfzıssıhha Institute,Department of Clinical Microbiology,Antalya, Turkey;
[3]Akdeniz University Medical Faculty, Department of Infectious Diseases and Clinical Microbiology, Antalya, Turkey;
[4]Akdeniz University Medical Faculty, Department of Medical Microbiology, Antalya, Turkey

- >80 yaş
- HIV

Septik Artrit…etkenler

Gram-positive aerobes	**% 60-90**
Staphylococcus aureus	
Streptococci other than pneumococci	
Streptococcus pneumoniae	
Gram-negative bacilli	✓ Tekrarlayan ÜSİ ✓ yeni abd. cerrahi ✓ İmmunsupresyon ✓ İleri yaş
Haemophilus influenzae	
Escherichia coli	
Klebsiella pneumoniae	
Neisseria gonorrhoeae	Genç ve cinsel aktif
Neisseria meningitidis	
Mycobacterium spp.	
Fungi	
Anaerobes	Travma sonrası

Kültür negatiflik %4.5-64

Septik Artrit…klinik

Hassasiyet, ağrı, eritem, ısı artışı, şişme ve hareket kısıtlılığı

- Ateş (%60)
- Akut başlangıç (~ 2 hafta içinde)
  - En sık
  - Akut başlangıçlı protez infeksiyonu
- Yavaş klinik
  - Düşük virülanslı bakteriler
  - tbc
- Tek eklem tutulumu… en sık
  - Diz, kalça
- >1 eklem tutulumu (%20-25)
  - gonokok

Septik Artrit…tanı

Antibiyotik tedavisinden önce yapılacak incelemeler

- Eklem sıvısından tam kan sayımı ve dağılımı
- Eklem sıvısından gram boyama ve kültür
  - Kan kültür şişesine ekim
  - Santrifüj sonrası agar plaklara ekim
- Eklem sıvısından AARB, tbc kültür, tbc PCR
  - Tbc şüphesinde
- Eklem sıvısından mantar kültürü
  - Fungal infeksiyon şüphesinde
- Kan kültürü
- Hemogram, sedimentasyon hızı, CRP

Eklem sıvısından tam kan sayımı ve dağılımı

Table 9. Sensitivity and specificity based on the results of white blood cell (WBC) counts and fractions [37]

	Sensitivity (%)	Specificity (%)	Likelihood ratio (95% CI)	
			Positive	Negative
> 100,000 WBC/mm^3	29	99	28.0 (12.0–66.0)	0.71 (0.64–0.79)
> 50,000 WBC/mm^3	62	92	7.7 (5.7–11.0)	0.42 (0.34–0.51)
> 25,000 WBC/mm^3	77	73	2.9 (2.5–3.4)	0.32 (0.23–0.43)
Polymorphonuclear cells ≥ 90%	73	79	3.4 (2.8–4.2)	0.34 (0.25–0.47)

CI, confidence interval.

Clinical guidelines for the antimicrobial treatment of bone and joınt infections.
Infect Chemother 2014; 46(2):125-138.

Septik Artrit…tanı

- X-ray…tanı değeri Ø
- MR
  - Osteomyelit ve deri ve yumuşak doku infeksiyon varlığını
  - Cerrahi ihtiyaç ±
- Kemik sintigrafisi
- Sinovyal sıvı kültürü ve Doku biyopsisi
  - İrrigasyon veya küretaj sırasında

Septik Artrit…tedavi

Eklem sıvı kültürleri ve kan kültürleri alınır

Yeterli drenaj
- ✓ 24-48 saat içinde
- ✓ ≥1 sayıda eklem aspirasyonu
- ✓ Cerrahi işlem

Ampirik Antibiyotik tedavisi
- ✓ Bakterisidal
- ✓ Gram boyama sonucuna ve risk faktörlerine göre tedavi planlanır

Kültür sonucuna göre tedavi yönetimi

Risk faktörlerine göre ampirik tedavi

Table 10. Selection of empirical antimicrobial agents for the treatment of septic arthritis according to risk factors

Risk factors	Antibiotics
No risk factor	2.0 g cefazolin every 8 hours or 1.0–2.0 g nafcillin every 4 hours or 3.0 g ampicillin/sulbactam every 6 hours *with/without gentamicin (5 mg/kg) *If anaphylactic history with penicillin: 1.0 g vancomycin every 12 hours (trough concentration of vancomycin should be 15–20 μg/mL) or 400 mg teicoplanin every 24 hours (first day 400 mg; every 12-hours loading)
High-risk of gram-negative bacteria infection (elderly, recurrent urinary tract infection, recent abdominal surgery, immunocompromised)	2.0 g ceftriaxone every 24 hours *If allergic to ceftriaxone: 750 mg levofloxacin every 24 hours or 400 mg ciprofloxacin every 12 hours
High risk of methicillin resistant *staphylococcus aureus* (recent admission into a long-term care facility, foot ulcer)	1.0 g vancomycin every 12 hours (trough concentration of vancomycin should be 15–20 μg/mL) or 400 mg teicoplanin every 24 hours (first day 400 mg; every 12-hours loading)
Possible *Neisseria gonorrhoeae* (young adult, recurrent sexually transmitted infections, recent gonococcal infection)	1.0 g ceftriaxone every 24 hours (intravenous or intramuscular route)

Clinical guidelines for the antimicrobial treatment of bone and joınt infections.
Infect Chemother 2014; 46(2):125-138.

Gram boyama sonucuna göre ampirik tedavi

Table 11. Selection of antimicrobial agents based on Gram stain results

Gram stain result		Antibiotics
Gram-positive cocci	Low risk of Methicillin resistant *Staphylococcus aureus*	2.0 g cefazolin every 8 hours or 1.0–2.0 g nafcillin every 4 hours or 3.0 g ampicillin/sulbactam every 6 hours *with/without gentamycin (5 mg/kg) *If anaphylactic history with penicillin: 1.0 g vancomycin every 12 hours (trough concentration of vancomycin should be 15–20 µg/mL) or 400 mg teicoplanin every 24 hours (first day 400 mg; every 12-hours loading)
Gram-positive cocci	High risk of Methicillin resistant *Staphylococcus aureus*	1.0 g vancomycin every 12 hours (trough concentration of vancomycin should be 15–20 µg/mL) or 400 mg teicoplanin every 24 hours (first day 400 mg; every 12-hours loading)
Gram-negative bacilli		2.0 g ceftriaxone every 24 hours *If allergic to ceftriaxone: 750 mg levofloxacin every 24 hours or 400 mg ciprofloxacin every 12 hours
Gram-negative cocci		1.0 g ceftriaxone every 24 hours (intravenous or intramuscular route)

Kültür sonucuna göre tedavi

Table 12. Selection of antimicrobial agents based on the results of bacterial culture and antibiotic susceptibility testing

Major pathogen	Primary	Alternative
Methicillin susceptible *Staphylococcus aureus*	1.0–2.0 g nafcillin every 4 hours or 2.0 g cefazolin every 8 hours	3.0 g ampicillin/sulbactam every 6 hours *with/without gentamicin (5 mg/kg) *If anaphylactic history with penicillin: 1.0 g vancomycin every 12 hours (trough concentration of vancomycin should be 15–20 µg/mL) or 400 mg teicoplanin every 24 hours (first day 400 mg; every 12-hours loading)
Methicillin-resistant *Staphylococcus aureus*	1.0 g vancomycin every 12 hours (trough concentration of vancomycin should be 15–20 µg/mL) or 400 mg teicoplanin every 24 hours (first day 400 mg every 12-hours loading)	600 mg linezolid every 12 hours
Streptococcus spp.	3–4 million units penicillin G every 4–6 hours or 20 million units 24-hours continuous infusion or 2.0 g cefazolin every 8 hours	2.0 g ceftriaxone every 24 hours or 750 mg levofloxacin every 24 hours
Enterobacteriaceae, quinolone-susceptible	400 mg ciprofloxacin every 12 hours or 750 mg levofloxacin every 24 hours	2.0 g ceftriaxone every 24 hours
Enterobacteriaceae, quinolone-resistant	Ceftriaxone 2.0 g every 12 hours	
Enterobacteriaceae, ESBL producer	1.0 g ertapenem every 24 hours or 500 mg imipenem every 6 hours or 1.0 g meropenem every 8 hours	
Neisseria gonorrhoeae	1.0 g ceftriaxone every 24 hours	1.0 g cefotaxime every 8 hours
Pseudomonas aeruginosa	2.0 g ceftazidime every 8 hours	2.0 g cefepime every 12 hours or 4.5 g piperacillin-tazobactam every 8 hours or 500 mg imipenem every 6 hours or 1.0 g meropenem every 8 hours
Mixed anaerobes	3.0 g ampicillin-sulbactam every 6 hours	500 mg metronidazole every 8 hours or 600 mg clindamycin every 8 hours

Tedavi süresi

- Toplam tedavi süresi ortalama 4-6 hafta
  - CRP ve Sedimentasyon
  - Eklem semptomlarındaki düzelme
- En az 2 hafta İV antimikrobiyal tedavi
- Semptomlar düzelir ise oral antibiyotik ile tedavi süresi tamamlanır

Kültür negatif hastalarda tedavi

- Kültür negatif fakat septik artrit bulguları (+)
- Ampirik antibiyotik tedavisi devam edilmeli
  - CRP ve Sedimentasyon
  - Eklem semptomlarında ve klinik düzelme

Protez İnfeksiyonu

SEPTİK ARTRİT **OSTEOMYELİT** **PROTEZ İNFEKSİYONU**

Protez İnfeksiyonu…klinik

Bone Joint J. 2017 Nov;99-B(11):1482-1489. doi: 10.1302/0301-620X.99B11.BJJ-2016-0655.R2.

The unsuspected prosthetic joint infection : incidence and consequences of positive intra-operative cultures in presumed aseptic knee and hip revisions.

Jacobs AME[1], Bénard M[1], Meis JF[2], van Hellemondt G[3], Goosen JHM[3].

RESULTS: The incidence of unsuspected PJI was 27 out of 340 (7.9%) in TKA and 41 out of 339 (12.1%) in THA. Following revision TKA, the rate of infection-free implant survival in patients with an unsuspected PJI was 88% (95% confidence intervals (CI) 60 to 97) at two years compared with 98% (95% CI 94 to 99) in patients without PJI (p = 0.001). After THA, the rate of survival was similar in those with unsuspected PJI (92% (95% CI 73 to 98) at two years) and those without (94% (95% CI 89 to 97), p = 0.31).

CONCLUSION: Following revision of TKA and THA for aseptic diagnoses, around 10% of cases were found to have positive cultures. In the knee, such cases had inferior infection-free survival at two years compared with those with negative cultures; there was no difference between the groups following THA. Cite this article: Bone Joint J 2017;99-B:1482-9.

- İnfeksiyon dışı nedenlerden dolayı revizyon yapılan hastalarda protez infeksiyonu olabilir
- TDP…%7.9 (27/340 vaka)
- TKP…%12.1 (41/339 vaka)

Protez İnfeksiyonu…tanı

- İntraoperatif doku kültürleri alınmadan **en az 2 hafta önce** antimikrobiyal tedavi kesilmeli

Protez İnfeksiyonu…Tanı

- peri-protez doku kültür sayısı kaç olmalı?

5-6 tane doku kültürü

≥2 doku kültüründe aynı mikroorganizmanın üremesi

Protez infeksiyonu

Diagnosis and management of prosthetic joint infection..CID 2013:56;1-25

Protez İnfeksiyonu…tanı

İstisnai durumlar

- Multipl doku kültürünün sadece bir tanesinde veya sinovyal sıvıda üreme var ise?
- *S. aureus*… **Pİ (+)**
- KNS, *Propionibacterium acnes*…

J Clin Microbiol. 2016 Dec 28;55(1):234-243. doi: 10.1128/JCM.01914-16. Print 2017 Jan.

Optimal Periprosthetic Tissue Specimen Number for Diagnosis of Prosthetic Joint Infection.

Peel TN[1,2], Spelman T[3], Dylla BL[1], Hughes JG[1], Greenwood-Quaintance KE[1], Cheng AC[2,4], Mandrekar JN[5], Patel R[6,7].

- 3 periprostetik doku örneğinin

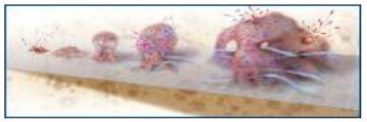
veya

- 4 periprostetik doku örneğinin konvansiyonel yöntemlerle

- Protez infeksiyon tanısının en kesin doğruluğunun elde edildiğini ortaya koymaktadır

Sonikasyon

- Çıkarılan protez hava geçirmez steril konteyner konur
- 48 saat içinde mikrobiyoloji lab. ulaştırılmalı
- Laminar hava akımı olan biyogüvenlik kabini içinde konteyner içine 50-200 cc ringer laktat eklenir
- Vorteks …30 sn
- Sonikasyon için ultrasonik banyo… 1dk
- Vorteks …30 sn
- Besiyerlerine ekim



Sinovyal sıvının analizi

- Tanı kriteri
- Preoperatif dönemde Pİ tanısı konulmuş olsa bile **mutlaka** yapılmalı
- Pİ tanısı için Sinovyal sıvıda lökosit eşik değer nedir???

Ascione T et all. Oral Therapy, Microbiological Findings, and Comorbidity Influence the Outcome of Prosthetic Joint Infections Undergoing 2-Stage Exchange. J Arthroplasty. 2017 Jul;32(7):2239-2243.

J Arthroplasty. 2000 Apr;15(3):301-4.

White blood cell counts and differential in synovial fluid of aseptically failed total knee arthroplasty.

Kersey R[1], Benjamin J, Marson B.

Abstract

A cell count and d ptic failure over a 5-year peri ocyte cells was 87%, and the nts >2,000. Five knees in 4 pa with osteoarthritis as a ve value for the absence of inf rthroplasty.

Bone Joint J. 2013 Ap

Sinovyal sıvı Lökosit sayısı

TDP ≥ 1700 mm³

TKP ≥ 4000 mm³

> %65 PNL hakimiyeti

Synovial flui hetic joint infection.

Dinneen A[1], Guyot A

Cut-off values with curate diagnosis of infection in total knee (TKR) and total hip replacement (THR). All patients undergoing revision TKR or THR for suspected prosthetic joint infection between 2009 and 2011 at two hospitals were identified. A total of 75 patients were included with a mean age of 70.3 years (38 to 89). Synovial fluid was aspirated pre-operatively and peri-prosthetic tissue samples were taken intra-operatively for histological and microbiological examination. Receiver operating characteristic (ROC) plots were constructed for white cell and differential counts in aspirated fluid. The optimal cut-off for TKR and THR was 1590 white cells/μl and 65% neutrophilia. The white cell count cut-off value identified for THR was notably lower than previously quoted in the literature. A cut-off value for white cell count in synovial aspirate in suspected prosthetic joint infection of between 1100 and 1700 white cells/μl is likely to be applicable to both THR and TKR.

Musculoskeletal Infection Social – MSIS PI için standart tanımı

MAJOR KRİTERLER	**1. 2 ayrı periprostetik doku/sıvı kültüründe aynı mikroorganizmanın üremesi** **2. Eklem-protez ile ilişkili sinüs traktı**
MİNOR KRİTERLER	1. Sed ve CRP yüksekliği 2. Sinovyal sıvı lökosit sayımında yükseklik veya lökosit esteraz strip testinin ++ olması 3. Sinovyal sıvı PNL yüzdesinin artması 4. Periprostetik dokuda histopatolojik inceleme pozitifliği 5. Tek bir doku/ sıvı kültürde bir bakterinin izolasyonu

TANI KRİTERİ= 1 MAJOR veya 3 MİNOR KRİTER

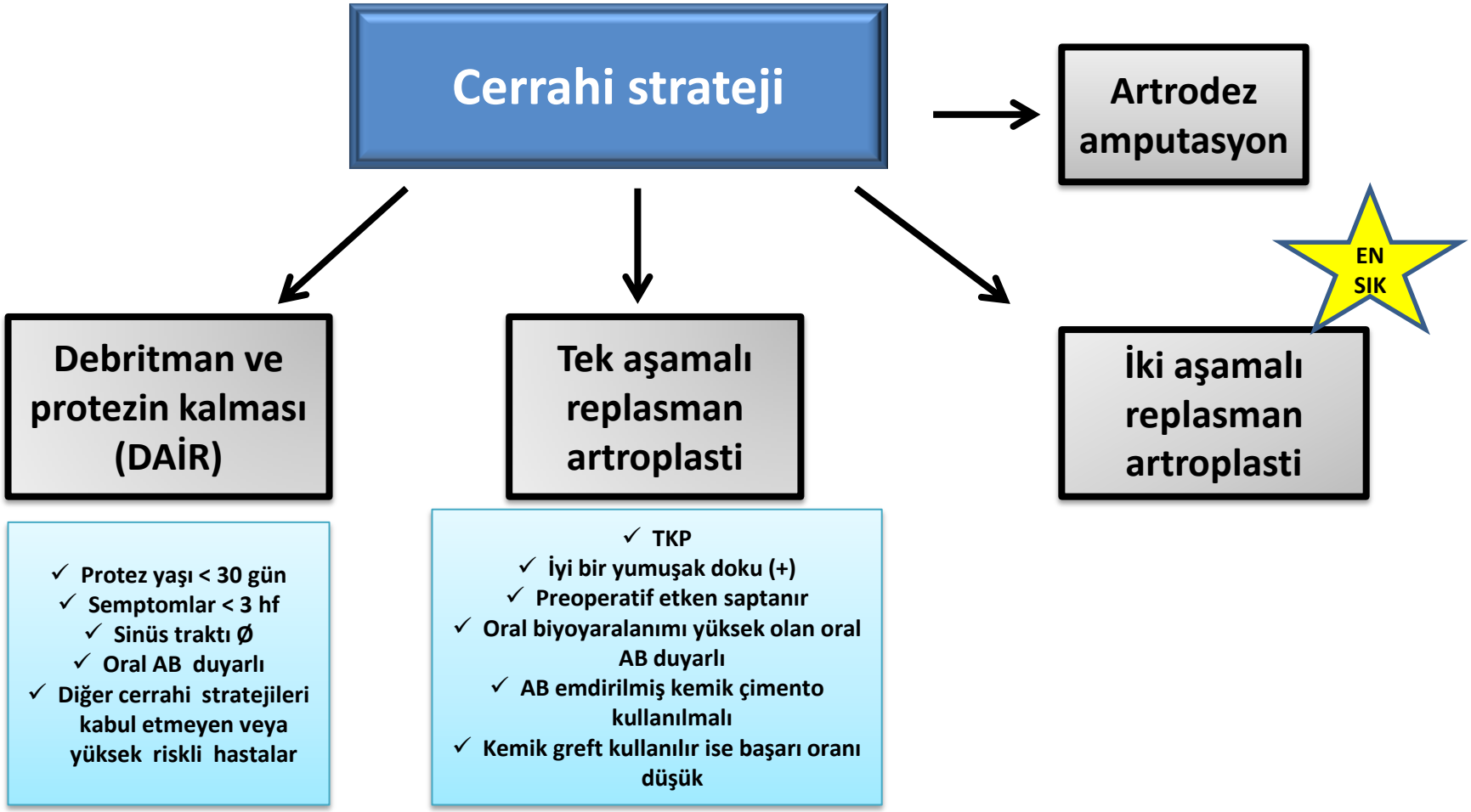
Protez İnfeksiyon tanı kriterleri (Musculoskeletal Infection Social 2014)

Minor Tanı Kriterleri için Eşik Değerler

KRİTERLER	AKUT Pİ (<90 gün)	KRONİK Pİ (>90 gün)
Sedimentasyon Hızı (mm/h)	Eşik değer yok	30
CRP (mg/L)	100	10
Sinovyal sıvı WBC	10000	3000
Sinovyal sıvı PNL %	90	80
Lökosit esteraz	+ veya ++	+ veya ++
Histolojik inceleme	>5 nötrofil her büyük büyütmede (X40)	>5 nötrofil her büyük büyütmede (X40)

Protez İnfeksiyonu…yönetimi

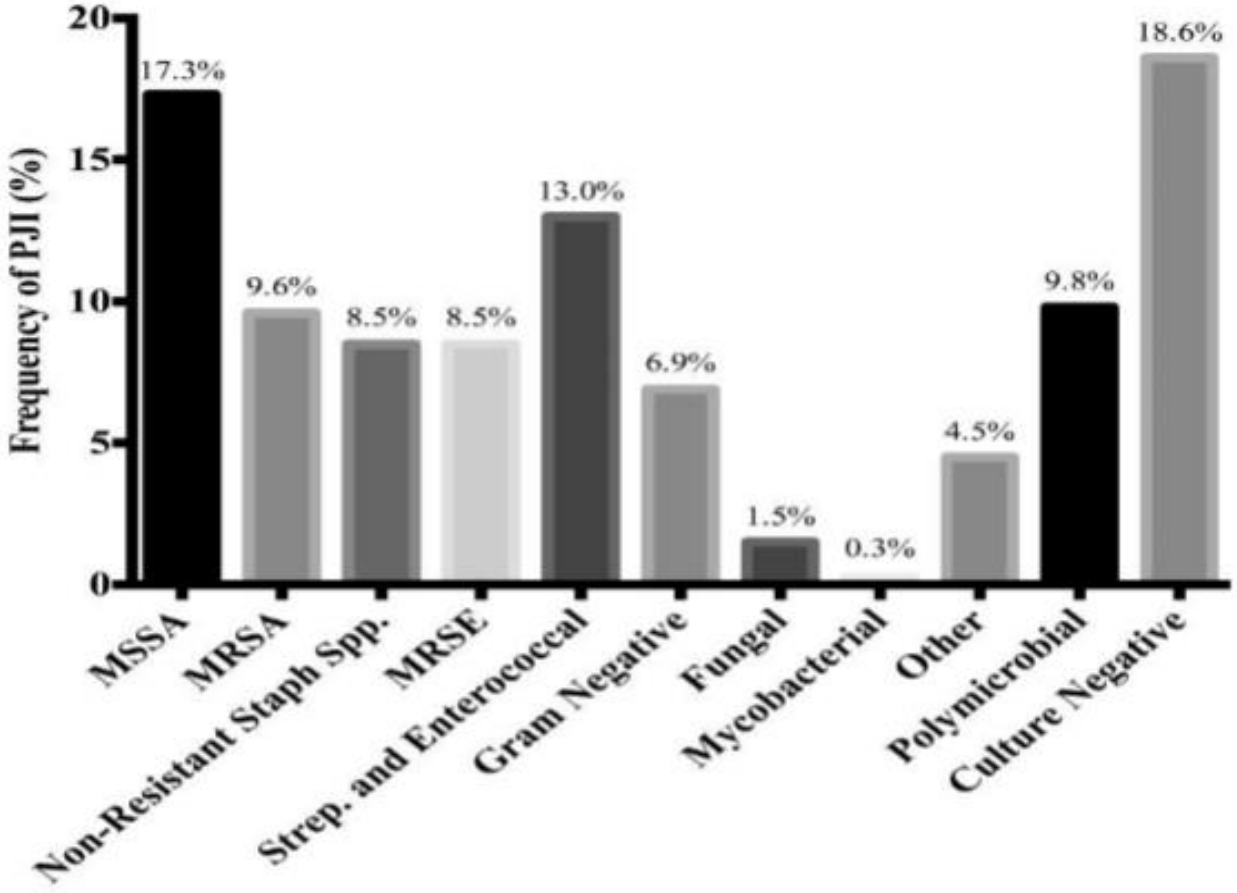
- Tedavi süresini belirleyen en önemli faktör



ARTRODEZ..eklem füzyonu

- Artroplasti için yeterli kemik dokunun olmaması
- Kötü cilt ve cilt altı doku
- Protez replasmanları sonrası tekrarlayan enfeksiyonlar
- Dirençli etkenlere bağlı enfeksiyonlar
- Ağrı dramatik azalır
- Ayak kısalığı
- Hareket kısıtlılığı

Protez İnfeksiyonu… etkenler



A Review of the Literature on Culture-Negative Periprosthetic Joint Infection: Epidemiology, Diagnosis and Treatment

Ta

Author	Year of publication	Study design	No. of cases	Prevalence of CN PJI (%)	Risk factors	Diagnosis	Two-stage revision success rate (%)	Antibiotics (%)	Outcome
Berbari et al.[2]	Sep 2007	Retrospective	60	7	Prior antibiotics use	The presence of purulence surrounding the prosthesis, positive histopathology or cutaneous sinus tract communicating with prosthesis	94	Cephalosporins (82) Vancomycin (12) Other (6)	The outcome of CN PJI is similar to the outcome of PJI due to known pathogens
Bejon et al.[5]	Jan 2010	Retrospective	62	41	More common in knees than hips	Persistent inflammation, wound discharge or implant loosening with bacterial growth or positive histology or persistent sinus tract	83	Glycopeptides (100)	CN PJI was not associated with a poorer outcome
Malekzadeh et al.[7]	Apr 2010	Retrospective	35	10.6	Antibiotics use within the last 3 months prior to diagnosis date, presence of postoperative wound drainage	The presence of purulence surrounding the prosthesis, positive histopathology or cutaneous sinus tract communicating with prosthesis	78	Cefazolin (69) Vancomycin (13) None or other (18)	The demographics and outcome of CP and CN PJI patients were similar
Huang et al.[10]	Jun 2012	Retrospective	48	11.9	N/A	Two positive cultures or sinus tract communicating with prosthesis or 4 of the following: 1) elevated ESR or CRP; 2) elevated synovial fluid WBC; 3) elevated synovial fluid PMN%; 4) one positive culture; and 5) intraoperative purulence	70	Vancomycin (81) Cephalosporins (10) Other (9)	The overall infection control rate was similar between CP and CN PJI cases
Choi et al.[9]	Jun 2013	Retrospective	40	23.0	Previous antibiotics use	The new definition for PJI by the workgroup of the MSIS	85	Vancomycin (70) Other (30)	The success rate of infection control was higher in the CN group, which suggests that CN may not necessarily be a negative prognostic factor for PJI
Kim et al.[11]	Feb 2015	Retrospective	102	42.1	Previous antibiotics use	The new definition for PJI by the workgroup of the MSIS	100	Vancomycin (85) Other (15)	The infection control rates and clinical outcomes were not different between CP and CN groups
Kim et al.[12]	Jul 2015	Retrospective	51	26.7	Prolonged previous intravenous and oral antibiotics treatment	In CN PJI patients, infection was diagnosed when there were following findings: elevated ESR or CRP, elevated synovial WBC, elevated synovial PMN%, presence of pus, and more than 5 neutrophils per high-power field on histologic examination.	92% in early postoperative infection, 96% in the late chronic infection	Vancomycin (86) Other (14)	Overall rates of infection control, successful treatment, and functional outcomes were not different between the CP and CN groups

Debritman, antibiyotik, irrigasyon ve protezin kalması -DAİR

- Stafilokokkal PI

Table 2. Intravenous or Highly Bioavailable Oral Antimicrobial Treatment of Common Microorganisms Causing Prosthetic Joint Infection (B-III Unless Otherwise Stated in Text)

Microorganism	Preferred Treatment[a]	Alternative Treatment[a]	Comments
Staphylococci, oxacillin-susceptible	Nafcillin[b] sodium 1.5–2 g IV q4-6 h or Cefazolin 1–2 g IV q8 h or Ceftriaxone[c] 1–2 g IV q24 h	Vancomycin IV 15 mg/kg q12 h or Daptomycin 6 mg/kg IV q 24 h or Linezolid 600 mg PO/IV every 12 h	See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text
Staphylococci, oxacillin-resistant	Vancomycin[d] IV 15 mg/kg q12 h	Daptomycin 6 mg/kg IV q24 h or Linezolid 600 mg PO/IV q12 h	See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text

2-6 hafta etken spesifik İV tedavi

+

Rifampisin 2x 300-450 mg PO

****Rif. kullanılamaz ise İV tedavi süresi 4-6 hf**

Rifampisin 2x 300-450 mg PO

+

Oral AB

- ✓ **Siprofloksasin/levofloksasin**
- ✓ **trimetoprim sülfametoksazol**
- ✓ **Doksisiklin**
- ✓ **1. Kuşak SS (sefaleksin vb)**

Tedavi süresi

TKP…3 ay

TDP…6 ay

Omuz, dirsek ve ayak bileği …3 ay

Diagnosis and management of prosthetic joint infection..CID 2013:56;1-25

Tedavi
Debritman ve protezin kalması

- Diğer etkenler…etken spesifik tedavi

Microorganism	Preferred Treatment[a]	Alternative Treatment[a]	Comments
Propionibacterium acnes	Penicillin G 20 million units IV q24 h continuously or in 6 divided doses or Ceftriaxone 2 g IV q24 h	Clindamycin 600–900 mg IV q8 h or clindamycin 300–450 mg PO qid or Vancomycin 15 mg/kg IV q12 h	4–6 wk Vancomycin only in case of allergy
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
Pseudomonas aeruginosa	Cefepime 2 g IV q12 h or Meropenem[e] 1 g IV q8 h	Ciprofloxacin 750 mg PO bid or 400 mg IV q12 h or Ceftazidime 2 g IV q8 h	4–6 wk Addition of aminoglycoside optional Use of 2 active drugs could be considered based on clinical circumstance of patient. If aminoglycoside in spacer, and organism aminoglycoside susceptible than double coverage being provided with recommended IV or oral monotherapy
Enterobacter spp	Cefepime 2 g IV q12 h or Ertapenem 1 g IV q24 h	Ciprofloxacin 750 mg PO or 400 mg IV q12 h	4–6 wk.
Enterobacteriaceae	IV β-lactam based on in vitro susceptibilities or Ciprofloxacin 750 mg PO bid		4–6 wk
β-hemolytic streptococci	Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses or Ceftriaxone 2 g IV q24 h	Vancomycin 15 mg/kg IV q12 h	4–6 wk Vancomycin only in case of allergy

Clin Infect Dis. 2013 Jan;56(2):182-94. doi: 10.1093/cid/cis746. Epub 2012 Aug 31.

A large multicenter study of methicillin-susceptible and methicillin-resistant Staphylococcus aureus prosthetic joint infections managed with implant retention.

Lora-Tamayo J[1], Murillo O, Iribarren JA, Soriano A, Sánchez-Somolinos M, Baraia-Etxaburu JM, Rico A, Palomino J, Rodríguez-Pardo D, Horcajada JP, Benito N, Bahamonde A, Granados A, del Toro MD, Cobo J, Riera M, Ramos A, Jover-Sáenz A, Ariza J; REIPI Group for the Study of Prosthetic Infection.

- Tedavi başarı oranı %55

Tedavide başarısızlık tanımı

- **İlk debritmandan 30 gün sonra ekstra debritman ihtiyacının olması**
- **Başlangıç antibiyotik tedavisinde revizyon yapılma ihtiyacının olması**
- Herhangi bir nedenle ilk 2 yıl içinde protezin çıkarılması
- infeksiyonun devam etmesi/tekrarlaması… 2 yıl içinde
- Superinfeksiyon gelişmesi

THE BONE & JOINT JOURNAL

■ HIP

Outcomes following debridement, antibiotics and implant retention in the management of periprosthetic infections of the hip

A REVIEW OF COHORT STUDIES

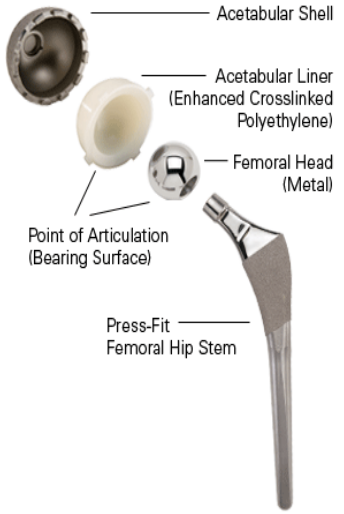
- Semptomların başlangıcı ile debritman arasındaki süre < 7 gün …%72

  > 7 gün …%51.8 başarı *p<0.0001*

- Debritmanda femoral baş veya acetabular liner değiştirilir ise …%73.9

  değiştirilmez ise …%60.7 başarı *p<0.0001*

- Birkaç debritman ile çok sayıda debritm yapmak arasında fark yok *p=0.167*



Tedavi

Tek aşamalı replasman artroplasti

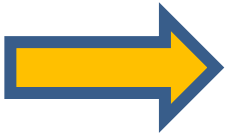
- Stafilokokkal PI

2-6 hafta etken spesifik İV tedavi

+

Rifampisin 2x 300-450 mg PO

****Rif. kullanılamaz ise İV tedavi süresi 4-6 hf**



Rifampisin 2x 300-450 mg PO

+

Oral AB

- ✓ **Siprofloksasin/levofloksasin**
- ✓ **trimetoprim sülfametoksazol**
- ✓ **Doksisiklin**
- ✓ **1. Kuşak SS (sefaleksin vb)**

Tedavi süresi

3 ay

- Diğer etkenler
- 4-6 hf etken spesifik İV veya biyoyararlanımı yüksek PO tedavi

Diagnosis and management of prosthetic joint infection..CID 2013:56;1-25

İki aşamalı replasman artroplasti

- Başarı oranı %65-98
- **Preoperatif sinovyal sıvı kültürü alınmalı**
  - Üreyen etkenin antimikrobiyal duyarlılığı, spacer içine konulacak antibiyotik seçimine rehberlik eder
  - Vankomisin, klindamisin, gentamisin
  - Doz ??? 10 gr vanko. ve genta… sistemik yan etki Ø
  - Statik spacer mi? AB'li spacer mi?
    - Reinfeksiyon oranları arasında fark ±
    - AB2 li spacer…tedavi sonu klinik +hareket hızı çok iyi
- **Protezin çıkarılması ve spacer yerleştirilmesi**

İki aşamalı replasman artroplasti

- **Etken spesifik İV/PO antimikrobiyal tedavi**
  - Klinik bulgular düzelene
  - CRP, Sed normal düzeye gelene kadar
  - Tedavi süresi
    - kişiye göre planlanır
    - **en az 2 hafta İV**
    - **Genelde toplam tedavi süresi 6-12 hafta**

- **Antimikrobiyal tedavi stoplanır**
- **En az 2 hafta beklenir**
  - Antimikrobiyal etki kaybolsun
- **Eklemden kültür için aspirasyon yapılır**
  - Mutlaka kan kültür şişesine de sinovyal sıvı ekilmeli
- **Kültür negatif ise 2.aşama olarak yeni protez takılır**

Etkene göre cerrahi yaklaşım

MRSA
Enterococcus spp
İlaça Dirençli Etkenlerde

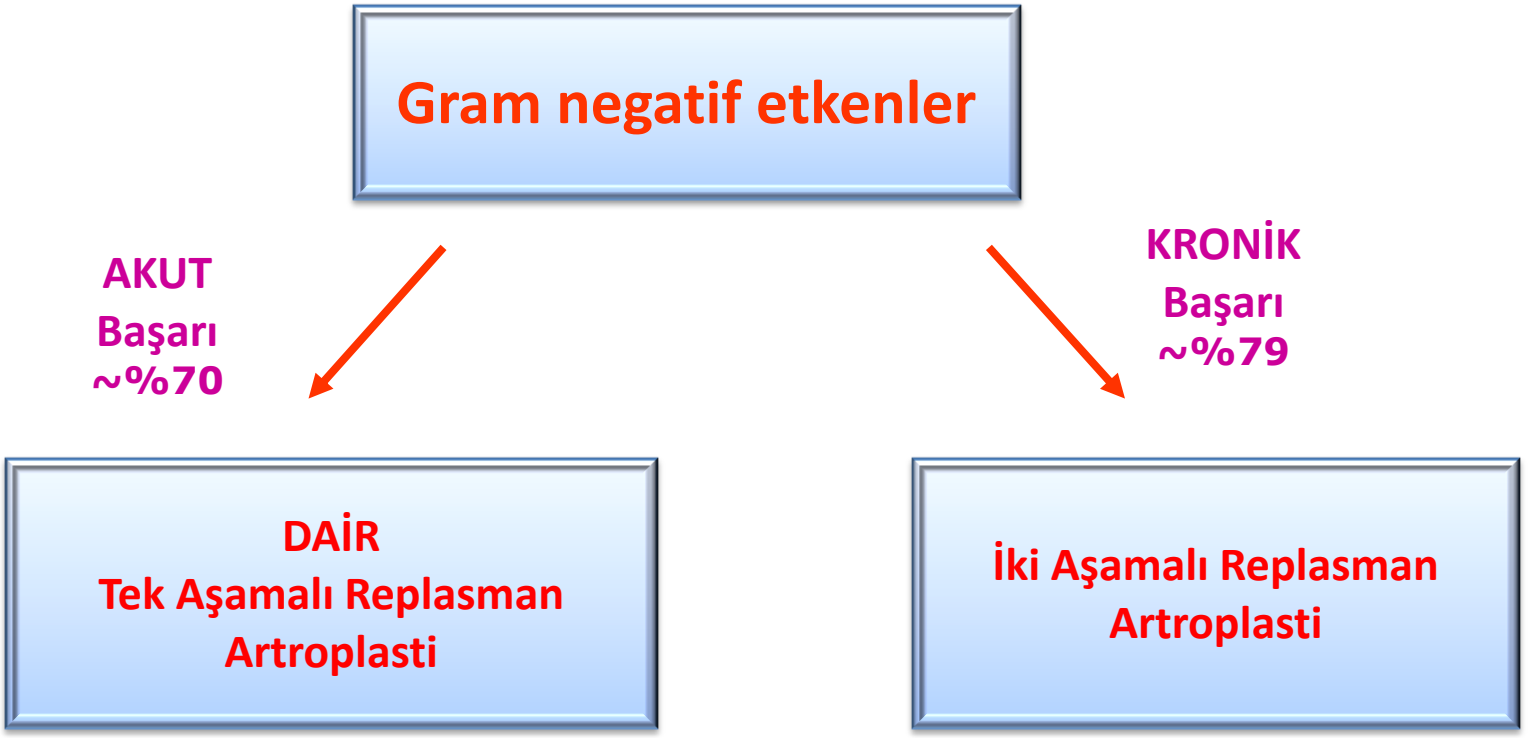
İki Aşamalı Replasman Artroplasti tercih edilmeli

Streptococcus spp

DAİR
Tek Aşamalı Replasman Artroplasti

McLawhorn AS, Nawabi DH et al. Management of resistant, atypical and culture-negative periprosthetic joint infections after hip and knee arthroplasty. Open Orthop J.2016;10:615-632.

Etkene göre cerrahi yaklaşım



Amputasyon

- Enfekte kemik ve yumuşak dokular tamamen uzaklaştırıldı sepsis/bakteriyemi Ø ise
  - Amputasyon sonrası AB tedavisi=24-48 saat
- Rezidü enfekte kemik /yumuşak doku kaldı ise
  - 4-6 hf etken sps. İV/po tedavi

Diagnosis and management of prosthetic joint infection..CID 2013:56;1-25

Protez İnfeksiyonu Önleme

Prevention of periprosthetic joint infection

NEW GUIDELINES

J. Parvizi,
N. Shohat,
T. Gehrke

From Rothman Institute, Philadelphia, United States

The World Health Organization (WHO) and the Centre for Disease Control and Prevention (CDC) recently published guidelines for the prevention of surgical site infection. The WHO guidelines, if implemented worldwide, could have an immense impact on our practices and those of the CDC have implications for healthcare policy in the United States.

Our aim was to review the strategies for prevention of periprosthetic joint infection in light of these and other recent guidelines.

Cite this article: *Bone Joint J* 2017;99-B(4 Supple B):3–10.

Table I. Pre-operative recommendations for the prevention of surgical site infection, according to various guidelines

	ICM[5]	WHO[6]	CDC[7]	SHEA[8]	NICE[9]
Nasal screening and decolonisation	Against universal screening. Mupirocin choice of therapy in known carriers (strong).	Mupirocin 2%, with or without antimicrobial body wash; choice of therapy in known carriers (moderate).	Not covered.	Screen and decolonise before high risk procedures (moderate).	Against routine decolonisation.
Pre-operative skin preparation	Use CHG (or antiseptic soap when unavailable) starting at least the night before surgery (strong).	Shower or bathe (moderate). Unresolved: the efficacy of antimicrobial soap or impregnated cloth.	Shower or bathe with plain or antimicrobial soap or an antiseptic agent at least the night before surgery (IB). Unresolved: best timing, type of wash or anti-microbial impregnated cloth.	Unresolved whether CHG is effective.	Bathe or shower using soap either the day before or the day of surgery, with no evidence showing the efficacy of pre-operative washing. Unresolved whether CHG is effective.
Immunosuppressive therapy	Immunosuppressive therapy should be stopped (strong).	Do not stop immunosup-pressive therapy routinely (very low).	Unresolved: the effect of specific treatments, duration, dose or peri-operative management.	Avoid immuno-suppressive medications in the peri-operative period, if possible (low).	Not covered.
Glycemic control (including peri-operative recommendations)	Glucose level < 200 mg/dl and HbA1C < 7% (strong).	Use protocols for glycemic control in both diabetic and non-diabetic patients (low). No conclusion regarding glucose target levels.	Maintain glucose level < 200 mg/dL (IA) in both diabetic and non-diabetic patients. Unresolved: efficacy of tighter glycemic control, the best timing, duration or method to reduce SSI, or HbA1C target.	Lower haemoglobin A1c ≤ 7% before surgery (high). Immediate post-operative ≤ 180 mg/dL. Against tighter control (≤ 110 mg/dL) (moderate).	Against routine insulin for non-diabetic patients post-operatively.

Table II. Antimicrobial recommendations for the prevention of surgical site infection, according to different guidelines

	ICM[5]	WHO[6]	CDC[7]	SHEA[8]	NICE[9]
Pre-operative					
Timing	Within 1 hr (2 hrs for Vancomycin/Clindamycin) (strong).	Within 2 hrs, while considering its half-life (moderate).	Based on its pharmacokinetics, it reaches bactericidal levels when incision is made (IB).	Within 1 hr (2 hrs for Vancomycin/Fluoroquinolones) (high). Closer to incision more effective. No conclusion on the relation to tourniquet.	Single dose at start of anesthesia, considering its pharmacokinetics. Before inflation of tourniquet.
Weight adjustment	Should be weight adjusted (strong).	Not covered.	No conclusion.	Adjust to patient weight (high). 80 kg ≤ 2 g of cefazolin 120 kg ≤ 3 g.	Not covered.
Intra-operative					
Re-dosing	After two half-lives of the prophylactic antibiotics and in cases of large blood volume loss (> 2000 cc) and fluid resuscitation (> 2000 cc) (strong).	Not covered.	No conclusion.	If the duration of the procedure exceeds two half-lives of the drug or there is excessive blood (high).	After two half-lives of prophylactic antibiotics.
Post-operative					
Timing	No longer than 24 hrs post-operatively (strong).	Against antibiotics after surgical wound is closed (moderate).	Against antibiotics after surgical wound is closed (IA).	No longer than 24 hrs post-operatively (high).	Not covered.
Drain	Do not continue antibiotics (strong).	Do not continue antibiotics (low).	Do not continue antibiotics (IA).	Do not continue antibiotics (high).	Not covered.

ICM, International Consensus Meeting (strength of consensus); WHO, World Health Organization (quality of evidence); CDC, Center for Disease Control and Prevention (strength of recommendation); NICE, The National Institute for Health and Care Excellence; SHEA, Society for Healthcare Epidemiology of America (quality of evidence); IA/IB, strong recommendations; II, weak recommendations

Table III. Intra-operative recommendations for the prevention of surgical site infection (SSI), according to various guidelines[41]

	ICM[5]	WHO[6]	CDC[7]	SHEA[8]	NICE[9]
Laminar air flow	Not necessary (strong).	Against (low to very low).	Not covered.	Follow the American Institute of Architects recommendations (low).[41]	Not covered.
Body exhaust suit	Cannot recommend .	Not covered.	Unresolved.	Not covered.	Not covered.
Operating room traffic	Minimum (strong).	Not covered.	Not covered.	Minimum (low).	Minimum.
Intra-operative skin preparation	Acknowledge the importance of alcohol (strong). Unresolved: optimal solution.	Alcohol-based CHG agent (low to moderate).	Alcohol based antiseptic agent (IA).	Dual agent containing alcohol (unless contraindicated) (high).	Unresolved: optimal solution.
Hair removal	Use clippers if necessary, as close to surgery as possible (strong).	Against hair removal. Use clippers if necessary (moderate).	Not covered.	Against hair removal (moderate). If necessary, use clippers outside the operating room.	Against hair removal. If necessary, use clippers with a single-use head on the day of surgery.
Sealant and drapes	Unresolved.	Against (very low).	Not necessary (II).	Against (high).	Against routine use of non-impregnated incise drapes.
Oxygenation	Not covered.	Recognise the significance in endotracheal intubation. 80% fraction for 2 to 6 hrs post-operatively (moderate).	Recognise the significance in endotracheal intubation and recommend administrating increased FiO_2 intra-operatively and in the immediate post-operative period (IA). Unresolved: other types of anesthesia, duration, target level or delivery method.	Supplemental oxygen during and immediately post-operatively with mechanical ventilation (high).	Maintain saturation rate ≥ 95%. Do not recommend routine supplemental.

Normothermia	Recognise the significance of patient normothermia (strong).	Suggest the use of warming devices in the operating room (moderate).	Recognise the significance (IA). Unresolved: method, timing, and lower limit.	Maintain normothermia during the peri-operative period when anesthesia duration ≥ 1 hr (high).	Recognise the significance and add specific guidelines.
Antibiotic impregnated bone cement	Agree on its effectiveness. Recommend when high-risk PJI (strong).	Not covered.	Unresolved is the effect on biofilm.	Not covered.	Not covered.
Wound irrigation	Agree on irrigation (strong). Unresolved is the optimal solution.	Consider aqueous iodophor solutions. Against antibiotic irrigation (low).	Use aqueous iodophor solutions for deep or subcutaneous tissue irrigation (II). Unresolved: antimicrobial irrigation.	Perform antiseptic wound lavage (moderate).	Against irrigation.
Coated sutures	Unresolved on whether specific sutures or staples prevent infection.	Suggest Triclosan-coated sutures (moderate).	Against the use of antimicrobial coated sutures (II).	Against routine use of antimicrobial coated sutures (moderate).	Unresolved on whether this may reduce the SSI risk. The type of surgery may influence.
Wound dressing	Occlusive dressings with alginated hydrofiber (weak).	Against the use of any kind of advanced dressing (low).	Unresolved.	Not covered.	Unresolved. Suggest silver nylon might be better than gauze.
Topical antimicrobial agents	Not covered.	Not covered.	Against. PRP is not necessary for SSI prevention (II).	Against (moderate).	Against.
Allogeneic blood transfusion	Increases the risk for PJI (strong).	Not covered.	Against withholding transfusion of necessary blood products (IB). Unresolved is whether blood transfusion is an independent risk factor and if there is an association with volume or specific products.	Increases the risk of SSI by decreasing macrophage function. Reduces blood loss and the need for blood transfusion (moderate).	Not covered.

Eve gidecek mesaj

Etken spesifik tedavi

TEŞEKKÜRLER