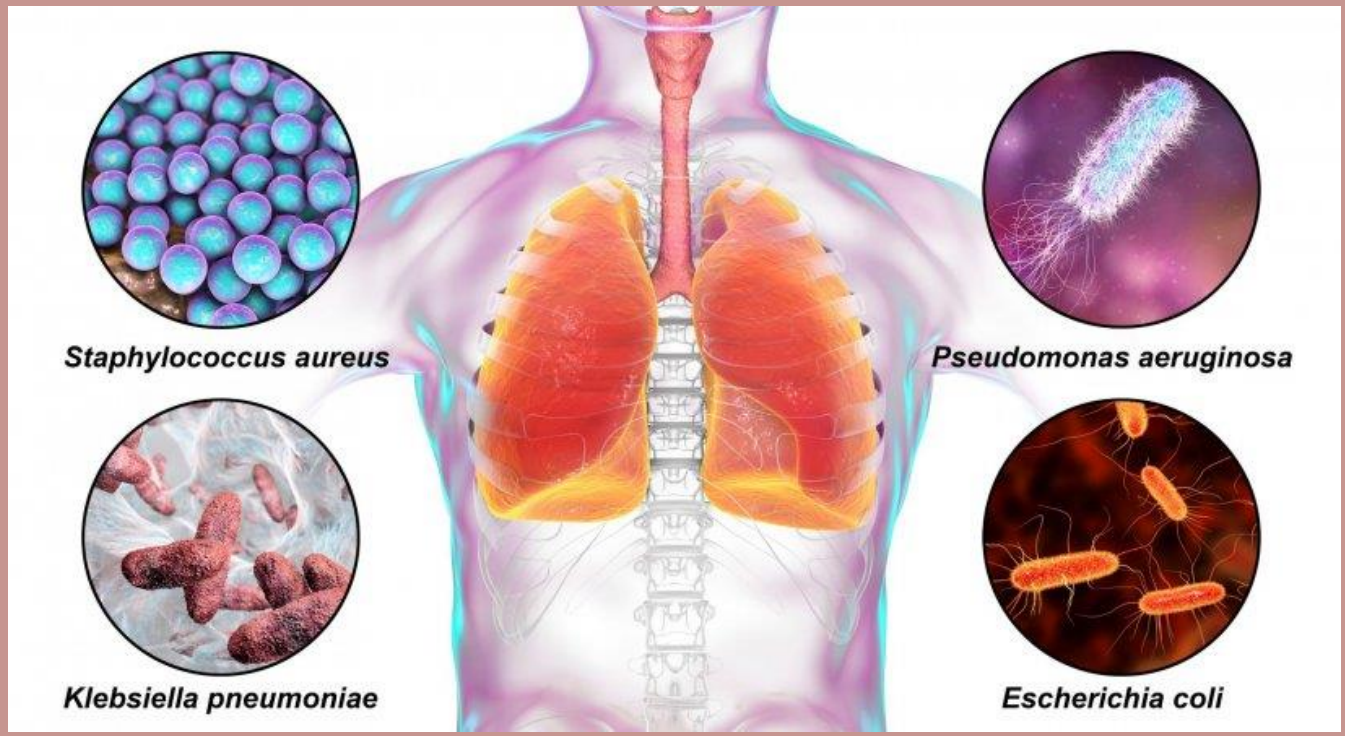
Hastanede Gelişen Pnömoniler



Prof Dr Zekaver Odabaşı - Marmara Ü Tıp F

Clinical Infectious Diseases

IDSA GUIDELINE

Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

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TÜRK TORAKS DERNEĞİ
ERİŞKİNLERDE HASTANEDE GELİŞEN PNÖMONİ TANI VE TEDAVİ UZLAŞI RAPORU
2018

TTD bu rehberi Klimik, Klimud, Ekmud ve TDCY derneklerinin katkılarıyla hazırlamıştır.

International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia

2017

Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT)

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Tanımlar

- **Hastanede Gelişen Pnömoni (HGP)**;
  - Hastaneye **yatıştan 48 saat sonra** gelişen ve yatışında inkübasyon döneminde **olmadığı** bilinen pnömoni
  - Hastaneden **taburcu olduktan sonra 48 saat içinde** ortaya çıkan pnömoni

Tanımlar

- **Ventilatörle İlişkili Pnömoni (VİP)**
  - **Entübasyon sırasında pnömonisi olmayan**, invazif MV desteğindeki hastada **entübasyondan 48 saat sonra** gelişen pnömoni
- **Ventilatörle İlişkili Trakeobronşit (VİTB):**
  - 48-72 saattir MV ‘e bağlı hastada akciğer **grafisinde infiltrasyon olmaksızın** başka nedene bağlı olmayan,
    - **>38°C ateş**
    - **Pürülan balgam**
    - **Lökositoz ya da lökopeni** kriterlerinden **ikisinin** olması

HGP tanı, tedavi ve izleminde…

- Göğüs hastalıkları
- Enfeksiyon hastalıkları ve klinik mikrobiyoloji
- Radyoloji
- Yoğun bakım
- Mikrobiyoloji uzmanları ve
- Hastane enfeksiyon kontrol komitesi

Multidisipliner yaklaşım gerekir

HGP, VİP: bu tanımların amacı ne?

- **Dirençli ya da çoğul ilaç dirençli baktrilerle enfeksiyon riski olan hastaları** belirlemek
- Ancak
- **Bu sınıflamalar duyarlı olmakla birlikte gereksiz geniş spektrum antibiyotik kullanımına** yolaçtığı da unutulmamalıdır
- **2016 IDSA rehberinde;**
  - Sağlık bakım ilişkili pnömoninin (SBİP) **çoğul ilaç direnci taşıyan patojenler açısından yüksek risk taşımadığı** !

- **Multidrug resistant (MDR) (Çok ilaca dirençli, ÇİD):**
  - **Üç veya daha fazla antibiyotik sınıfından en az birer antibiyotiğe direnç** olması
- **Extensively drug resistant (XDR) (Aşırı ilaç direnci):**
  - **1-2 sınıf hariç** hemen **tüm** antibiyotik sınıflarında en az bir antibiyotiğe **direnç** vardır
- **Pandrug resistant (PDR):**
  - **Tüm antibiyotik sınıflarına** direnç olması

HGP genel bilgiler

- Hastanede yatan hastalarda **%0.2 - 2**
- **Hastane enfeksiyonları içerisinde %15 – 22**
- Hastanede gelişen enfeksiyonlar içinde **en sık ölüm nedeni**
- Hastaneye yatışın ilk 48 saatinde, hastanın üst solunum yolları florası hastanedeki dirençli bakteriler ile yer değiştirmeye başlar ve
- **Yatıştan 48 saat sonra** hastane florası ile kolonizasyon oranları belirgin olarak artmaktadır.

- **Çok ilaca dirençli (ÇİD) olmayan bakteriler**
  - S pneumoniae, H influenzae, Enterobacteriaceae (E coli, Klebsiellla, Proteus ve Serratia sp), Metisiline duyarlı Staphylococcus aureus (MSSA), Legionella pneumophila
- **Çok ilaca dirençli (ÇİD) bakteriler**
  - **Pseudomonas aeruginosa**
  - **E coli ve diğer Enterobacteriaceae (GSBL ve/veya karbapenemaz üreten)**
  - **Klebsiella pneumoniae GSBL, karbapenemaz üreten**
  - **Acinetobacter spp**
  - **Stenotrophomonas maltophilia**
  - **Metisiline dirençli Staphylococcus aureus (MRSA)****

HGP/VİP tanısı: klinik kriterler

- **Yeni gelişen akciğer infiltrasyonu + ve bunun enfeksiyöz orijinli olduğunu destekleyen bulgular (2/3)**
  - **1. Ateş**
  - **2. Lökositoz**
  - **3. Pürülan sekresyon**

Klinik Kriter

Duyarlılık %60-70

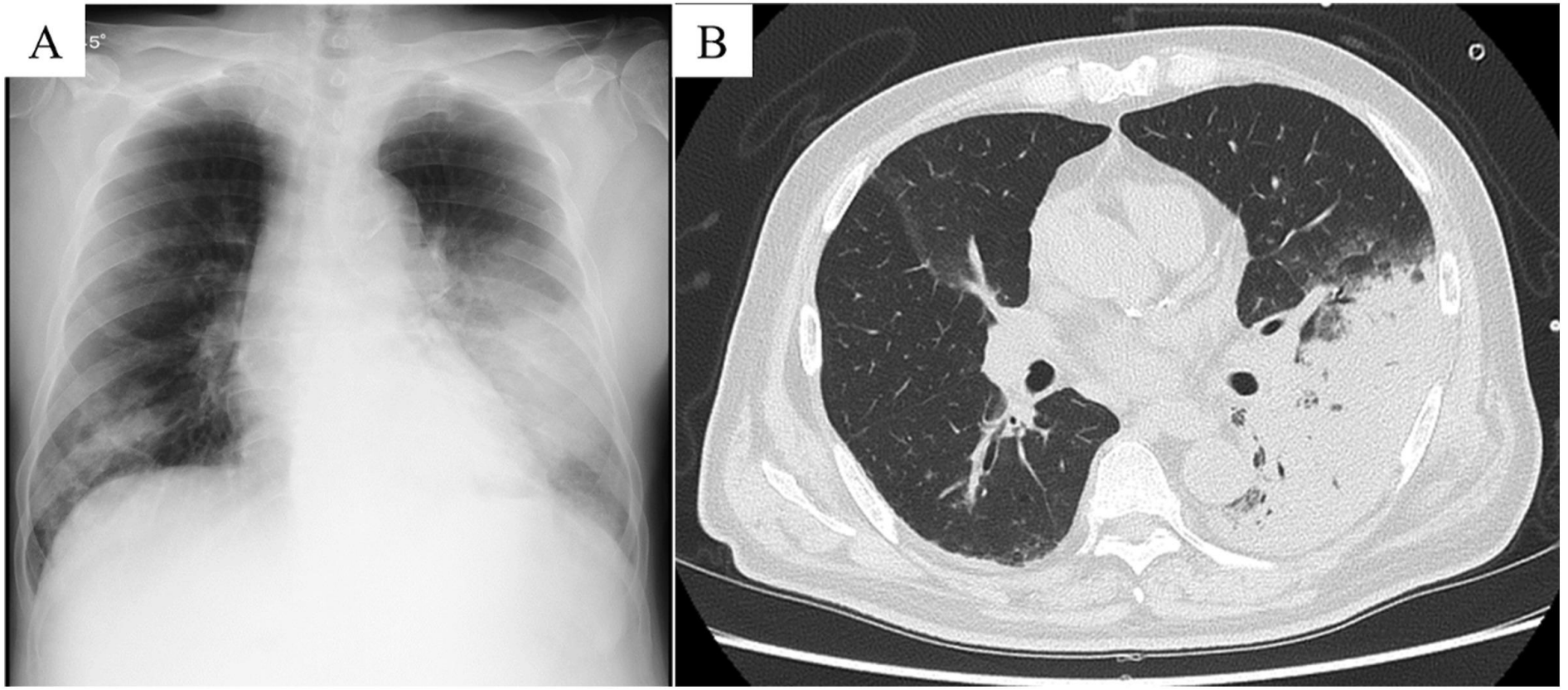
Özgüllük %75

- **Solunum örneği kültürü**
  - **ETA≥ 10^5 cfu/ml (non-kantitatif)**
  - BAL ≥10^4 cfu/ml (kantitatif)
  - Bronkoskopik korunmuş fırça ≥ 10^3 cfu/ml (kantitatif)
- **(CPIS) (Klinik pulmoner enfeksiyon skoru)**
  - **>6 olması pnömoniyi destekler**

Klinik pulmoner enfeksiyon skoru (CPIS)	
Kriter	**Skor**
Ateş	
≥38.5 ama ≤38.9	1
>39 veya <36	2
Lökositoz	
<4,000 veya > 11,000/µL	1
Çomak > 50%	1 (ek olarak)
Oksijenizasyon	
PaO_2 / FiO_2 > 250 ve ARDS yok	2
Akciğer grafisi	
Lokalize infiltrat	2
Yamalı veya diffüz infiltrat	1
İnfiltratların ilerlemesi (ARDS veya kalp yetmezliği yok)	2
Trakeal aspirat	
Orta - yüksek yoğunlukta üreme	1
Üreyen izolat morfolojisi direk incelemede de var	1 (ek olarak)
Maksimum skor 12: tanı anında infiltratta ilerleme ve kültür sonucu olmadığından başlangıçta maksimum skor 8-10 olur.	

Duyarlılık ve özgüllüğü %65 civarında

- 70 yaşında kadın hasta bir haftadır **kontrolsüz diyabet** nedeni ile dahiliye servisinde takip edilirken **ateş, üşüme titreme** gelişmesi nedeni ile değerlendiriliyor.
- Öyküsünde son **3 ayda hastane yatışı ya da intravenöz antibiyotik kullanımı yok**. Son iki gündür **hafif öksürük** tarifliyor, **balgam çıkarmıyor**.
- Fizik muayenede **ateşi 38.4 ^{o}C**, tansiyonu: 130/80 mmHg, solunum sayısı 20/dk, nabzı 90/dk. Solunum muayenesinde **sol akciğer orta - alt bölgelerde krepitan raller** duyuluyor.
- Hemogramında **lökosit sayısı 17.000/mm3**, %80 PMNL
- **CRP 130 mg/L**
- **Prokalsitonin (PCT) 12 ng/L**
- Kreatinin, ALT ve AST normal sınırlarda



İki set periferik kan kültürü alınıyor

- Bu hastada **en uygun** ampirik antibiyotik tedavi seçeneği aşağıdakilerden hangisidir?

A. Seftriakson
B. Seftriakson + siprofloksasin
C. Sefepim veya piperasilin tazobaktam monoterapi
D. Pip/tazo + siprofloksasin
E. Pip/Tazo + siprofloksasin + vankomisin
F. Sefepim + linezolid

Table 4. Recommended Initial Empiric Antibiotic Therapy for Hospital-Acquired Pneumonia (Non-Ventilator-Associated Pneumonia)

Not at High Risk of Mortality[a] and no Factors Increasing the Likelihood of MRSA[b,c]	Not at High Risk of Mortality[a] but With Factors Increasing the Likelihood of MRSA[b,c]	High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d[a,c]
One of the following:	One of the following:	Two of the following, avoid 2 β-lactams:
Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h
OR	OR	OR
Cefepime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h
OR	OR	OR
Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily
	Ciprofloxacin 400 mg IV q8h	Ciprofloxacin 400 mg IV q8h
	OR	OR
Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h
	OR	OR
	Aztreonam 2 g IV q8h	Amikacin 15–20 mg/kg IV daily
		Gentamicin 5–7 mg/kg IV daily
		Tobramycin 5–7 mg/kg IV daily
		OR
		Aztreonam[e] 2 g IV q8h
	Plus:	Plus:
	Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg IV × 1 for severe illness)
	OR	OR
	Linezolid 600 mg IV q12h	Linezolid 600 mg IV q12h
		If MRSA coverage is not going to be used, include coverage for MSSA. Options include: Piperacillin-tazobactam, cefepime, levofloxacin, imipenem, meropenem. Oxacillin, nafcillin, and cefazolin are preferred for the treatment of proven MSSA, but would ordinarily not be used in an empiric regimen for HAP.
If patient has severe penicillin allergy and aztreonam is going to be used instead of any β-lactam–based antibiotic, include coverage for MSSA.		

HGP mortalite ve ÇİD risk faktörleri

Mortaliteyi artıran risk faktörleri

- **Ventilatör tedavisi gerektiren HGP**
- **Septik şok**

ÇİD Pseudomonas ve diğer gram negatif basil ve MRSA risk faktörü

- İV antibiyotik kullanım öyküsü – **son 90 gün içerisinde**

ÇİD Pseudomonas ve diğer gram negatif basil enfeksiyonu risk faktörü

- **Yapısal akciğer hastalığı** (kistik fibroz, bronşektazi)
- Solunum örneğinde yoğun gram negatif bakteri varlığı
- Daha önceden gram negatif enfrksiyon veya kolonizasyon olması

MRSA risk faktörleri

- Ünitede S aureus izolatlarının **>%20 metisilin dirençli** olması
- Ünitede MRSA sıklığı bilinmiyorsa
- Hasta MRSA ile kolonize ise

Table 4. Recommended Initial Empi

Not at High Risk of Mortality[a] and no Factors Increasing the Likelihood of MRSA[b,c]
One of the following:
Piperacillin-tazobactam[d] 4.5 g IV q6h
OR
Cefepime[d] 2 g IV q8h
OR
Levofloxacin 750 mg IV daily
Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h

Mortalite risk faktörü yok

MRSA risk faktörü yok

Not at High Risk of Mortality[a] but With Factors Increasing the Likelihood of MRSA[b,c]
One of the following:
Piperacillin-tazobactam[d] 4.5 g IV q6h
OR
Cefepime[d] or ceftazidime[d] 2 g IV q8h
OR
Levofloxacin 750 mg IV daily
Ciprofloxacin 400 mg IV q8h
OR
Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h
OR
Aztreonam 2 g IV q8h
Plus:
Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)
OR
Linezolid 600 mg IV q12h

Mortalite risk faktörü yok

Ama

MRSA risk faktörü var

High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d[a,c]
2 Two of the following, avoid 2 β-lactams:
Piperacillin-tazobactam[d] 4.5 g IV q6h
OR
Cefepime[d] or ceftazidime[d] 2 g IV q8h
OR
Levofloxacin 750 mg IV daily
Ciprofloxacin 400 mg IV q8h
OR
Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h
OR
Amikacin 15–20 mg/kg IV daily
Gentamicin 5–7 mg/kg IV daily
Tobramycin 5–7 mg/kg IV daily
OR
Aztreonam[e] 2 g IV q8h
Plus:
Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg IV × 1 for severe illness)
OR
Linezolid 600 mg IV q12h
If MRSA coverage is not going to be used, include coverage for MSSA. Options include: Piperacillin-tazobactam, cefepime, levofloxacin, imipenem, meropenem. Oxacillin, nafcillin, and cefazolin are preferred for the treatment of proven MSSA, but would ordinarily not be used in an empiric regimen for HAP.

Mortalite risk faktörü var

Veya

Son 90 günde İV

antibiyotik kullanımı var

Çok ilaca dirençli *Pseudomonas, Acinetobacter* ve diğer gram negatif'lerin etken olduğu HGP için risk faktörleri	• Ağır altta yatan hastalık varlığı • Önceki 90 gün içinde İV antibiyotik kullanımı • Geniş spektrumlu antibiyotik kullanımı • Yapısal akciğer hastalığı (bronşektazi, kistik fibrozis) • Kortikosteroid tedavi • Gram negatif izolatların en az %10'unun monoterapiye dirençli olduğu bir ünitede tedavi* • Solunum sekresyonu gram boyamasında çok sayıda ve predominant gram negatif basil*

***Legionella* için risk faktörleri**	• Hastaneden kullanılan su hazneleri • Önceden hastane kökenli Legionellozis öyküsü
Anaeroblar için risk faktörleri	• Gingivit veya periodontal hastalık • Yutma bozukluğu • Bilinçte bozulma • Orotrakeal girişim
MRSA'nın etken olduğu HGP/VİP için risk faktörleri	• Önceki 90 gün içinde İV antibiyotik kullanımı

*MRSA ülkemizde nadir görülen bir HGP/VİP nedenidir. Özellikle önceden kolonize olan hastalarda ve prevelansı yüksek ünitelerde takip edilen hastalarda düşünülmelidir [5,32,48].

- Hastada HGP/VAP **tedavisinin başlanmasında klinik kriterler yeterli mi** yoksa **klinik kriterlerin yanında PCT** de kullanılmalı mı?

IV. In Patients With Suspected HAP/VAP, Should Procalcitonin (PCT) Plus Clinical Criteria or Clinical Criteria Alone Be Used to Decide Whether or Not to Initiate Antibiotic Therapy?

Recommendation

1. For patients with suspected HAP/VAP, we recommend using clinical criteria alone, rather than using serum PCT plus clinical criteria, to decide whether or not to initiate antibiotic therapy *(strong recommendation, moderate-quality evidence).*

- Aynı şekilde **tedavi başlanmasında CRP** nin de klinik **kriterler üzerine** ekstra etkisi yok

VI. In Patients With Suspected HAP/VAP, Should C-Reactive Protein (CRP) Plus Clinical Criteria, or Clinical Criteria Alone, Be Used to Decide Whether or Not to Initiate Antibiotic Therapy?

Recommendation

1. For patients with suspected HAP/VAP, we recommend using clinical criteria alone rather than using CRP plus clinical criteria, to decide whether or not to initiate antibiotic therapy *(weak recommendation, low-quality evidence)*.

- Aynı şekilde **tedavi başlanmasında CPIS skorunun** da **klinik kriterler üzerine** ekstra etkisi yok

VII. In Patients With Suspected HAP/VAP, Should the Modified Clinical Pulmonary Infection Score (CPIS) Plus Clinical Criteria, or Clinical Criteria Alone, Be Used to Decide Whether or Not to Initiate Antibiotic Therapy?

Recommendation

1. For patients with suspected HAP/VAP, we suggest using clinical criteria alone, rather than using CPIS plus clinical criteria, to decide whether or not to initiate antibiotic therapy *(weak recommendation, low-quality evidence).*

- Ampirik tedavi verilen HGP hastasında **MRSA** riski **olmasada MSSA (metisilin duyarlı S aureus) kapsanmalıdır**.

1. For patients being treated empirically for HAP, we recommend prescribing an antibiotic with activity against *S. aureus* *(strong recommendation, very low-quality evidence)*. (See below for recommendations regarding empiric coverage of MRSA vs MSSA.)
   i. For patients with HAP who are being treated empirically and have either a risk factor for MRSA infection (ie, prior intravenous antibiotic use within 90 days, hospitalization in a unit where >20% of *S. aureus* isolates are methicillin resistant, or the prevalence of MRSA is not known, or who are at high risk for mortality, we suggest prescribing an

- Ampirik tedavi verilen HGP hastasında **Pseudomonas aeruginosa ve diğer gram negatifler kapsanmalıdır**

2. For patients with HAP who are being treated empirically, we recommend prescribing antibiotics with activity against *P. aeruginosa* and other gram-negative bacilli *(strong recommendation, very low-quality evidence).*

i. For patients with HAP who are being treated empirically and have factors increasing the likelihood for *Pseudomonas* or other gram-negative infection (ie, prior intravenous antibiotic use within 90 days; also see Remarks) or a high risk for mortality, we suggest prescribing antibiotics from 2 different classes with activity against *P. aeruginosa (weak recommendation, very low-quality evidence).* (Risk factors for mortality include need for ventilatory support due to HAP and septic shock). All other patients with HAP who are being treated empirically may be prescribed a single antibiotic with activity against *P. aeruginosa.*

- **Pseudomonas aeruginosa üredi:** ikili vs tekli antipseudomonal? (**duyarlılık bilinyor**)
- **Septik şok veya artmış mortalite riski varsa: ikili tx**

XVII. Should Monotherapy or Combination Therapy Be Used to Treat Patients With HAP/VAP Due to *P. aeruginosa*?

Recommendations

1. For patients with HAP/VAP due to *P. aeruginosa* who are not in septic shock or at a high risk for death, and for whom the results of antibiotic susceptibility testing are known, we recommend monotherapy using an antibiotic to which the isolate is susceptible rather than combination therapy *(strong recommendation, low-quality evidence).*
2. For patients with HAP/VAP due to *P. aeruginosa* who remain in septic shock or at a high risk for death when the results of antibiotic susceptibility testing are known, we suggest combination therapy using 2 antibiotics to which the isolate is susceptible rather than monotherapy *(weak recommendation, very low-quality evidence).*

Optimal tedavi süresi 7 gün

XXII. What Is the Optimal Duration of Antibiotic Therapy for HAP (Non-VAP)?

Recommendation

1. For patients with HAP, we recommend a 7-day course of antimicrobial therapy *(strong recommendation, very low-quality evidence).*

Remarks: There exist situations in which a shorter or longer duration of antibiotics may be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters.

Hastanede gelişen pnömonide etken **MRSA** ise, önerilen optimal antibiyotik tedavi süresi **14 gündür**. Benzer şekilde ***Pseudomonas aeruginosa, Acinetobacter baumannii*** **ve** ***Stenotrophomonas*** **spp. gibi nonfermentatif bakterilerin** neden olduğu HGP'li hastalarda da tedavi süresi 14 güne uzatılabilir (**TTD uzlaşı raporu**)

- **Antibiyotik kesilmesinde klinik kriterler + PCT kullanılması öneriliyor**

XXIV. Should Discontinuation of Antibiotic Therapy Be Based Upon PCT Levels Plus Clinical Criteria or Clinical Criteria Alone in Patients With HAP/VAP?

Recommendation

1. For patients with HAP/VAP, we suggest using PCT levels plus clinical criteria to guide the discontinuation of antibiotic therapy, rather than clinical criteria alone *(weak recommendation, low-quality evidence)*.

Remarks: It is not known if the benefits of using PCT levels to determine whether or not to discontinue antibiotic therapy exist in settings where standard antimicrobial therapy for VAP is already 7 days or less.

Başlangıç PCT değerinin > %80 düşmesi ya da < 0.5 ng/L olması antibiyotik kesilmesi konusunda yol göstericidir

- 75 yaşında kadın hasta serebrovasküler olay nedeni ile yaklaşık **3 gündür entübe olarak MV desteği altında** yoğun bakım ünitesinde takip ediliyor.
- Hastanın son 2 **gündür sekresyonlarında artış** ve **oksijen ihtiyacında artışla** birlikte **38.8 ^{o}C ateşi** oluyor, tansiyonu 115/75 mmHg.
- Öyküde son 3 ayda **hastane yatışı, İV antibiyotik yok.**
- AC-PA grafi: **sağ alt zonda yeni gelişen infiltrasyon**
- Hemogram **lökosit sayısı: 11.500/mm3**
- **CRP son 3 gün 70 → 180 → 290 mg/L**
- **Prokalsitonin 4 ng/L**
- DTA ve periferik kan kültürleri alınıyor

Table 3. Suggested Empiric Treatment Options for Clinically Suspected Ventilator-Associated Pneumonia in Units Where Empiric Methicillin-Resistant *Staphylococcus aureus* Coverage and Double Antipseudomonal/Gram-Negative Coverage Are Appropriate

A. Gram-Positive Antibiotics With MRSA Activity	+	B. Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents	+	C. Gram-Negative Antibiotics With Antipseudomonal Activity: Non-β-Lactam–Based Agents
Glycopeptides[a] Vancomycin 15 mg/kg IV q8–12h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)		Antipseudomonal penicillins[b] Piperacillin-tazobactam 4.5 g IV q6h[b]		Fluoroquinolones Ciprofloxacin 400 mg IV q8h Levofloxacin 750 mg IV q24h
OR		OR		OR
Oxazolidinones Linezolid 600 mg IV q12h		Cephalosporins[b] Cefepime 2 g IV q8h Ceftazidime 2 g IV q8h		Aminoglycosides[a,c] Amikacin 15–20 mg/kg IV q24h Gentamicin 5–7 mg/kg IV q24h Tobramycin 5–7 mg/kg IV q24h
		OR		OR
		Carbapenems[b] Imipenem 500 mg IV q6h[d] Meropenem 1 g IV q8h		Polymyxins[a,e] Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12h (maintenance dose) [135] Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV doses
		OR		
		Monobactams[f] Aztreonam 2 g IV q8h		

Table 3. Suggested Empiric Trea
***Staphylococcus aureus* Coverage a**

A. Gram-Positive Antibiotics With MRSA Activity
Glycopeptides[a] Vancomycin 15 mg/kg IV q8–12h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)
OR
Oxazolidinones Linezolid 600 mg IV q12h

B. Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents

Antipseudomonal penicillins[b]
- Piperacillin-tazobactam 4.5 g IV q6h[b]

OR

Cephalosporins[b]
- Cefepime 2 g IV q8h
- Ceftazidime 2 g IV q8h

OR

Carbapenems[b]
- Imipenem 500 mg IV q6h[d]
- Meropenem 1 g IV q8h

OR

Monobactams[f]
- Aztreonam 2 g IV q8h

C. Gram-Negative Antibiotics With Antipseudomonal Activity: Non-β-Lactam–Based Agents

Fluoroquinolones

Ciprofloxacin 400 mg IV q8h

Levofloxacin 750 mg IV q24h

OR

Aminoglycosides[a,c]

Amikacin 15–20 mg/kg IV q24h

Gentamicin 5–7 mg/kg IV q24h

Tobramycin 5–7 mg/kg IV q24h

OR

Polymyxins[a,e]

Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12h (maintenance dose) [135]

Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV doses

VİP - ÇİD risk faktörleri

(1) ÇİD risk faktörleri (Pseudomonas, diğer gr (-) basiller ve MRSA)

- **Son 90 gün içerisinde İV antibiyotik kullanımı**
- **Septik şok** (VİP ile birlikte)
- VİP öncesi ARDS olması
- **VİP öncesi ≥ 5 gün hastane yatışı**
- VİP öncesi akut renal replasman tedavisi uygulanması

A + B + C

(2) ÇİD Pseudomonas ve diğer gram negatif basiller için risk faktörü

- YBÜ 'deki gram negatiflerde **monoterapide kullanılacak ajana > %10 direnç olması**
- ÇİD Pseudomonas ve diğer gram negatiflerle kolonize olması
- YBÜ deki direnç paterninin bilinmemesi

(3) MRSA risk faktörü

- Ünitedeki S. ureus izolatlarının >10-20 metisilin dirençli olması
- MRSA ile kolonizasyon olması
- Ünitede MRSA sıklığının bilinmemesi

- IDSA – ATS **VİP tampirik edavi önerileri**
- **S aureus (MSSA), Pseudomonas aeruginosa** ve diğer gram negatifler tüm ampirik rejimlerde kapsanıyor olmalı
- **MRSA** risk faktörü varsa (tablo, madde 3) vankomisin veya linezolid
- **ÇİD riski varsa ikili anti-pseudomonal ajan** kullanılmalı (tablo, madde 1 veya 2)
- Üreyen etkene karşı etkili alternatif tedavi ajanları mevcutsa **aminoglikozit ve polimiksin grubundan kaçınılmalı**
- Pseudomonas aeruginosa direnç oranı <%10 ve başka direnç riski yoksa **monoterapi** kullanılabilir.
- **Tedavi süresi 7 gün** (MRSA ve non-fermenter gram negatiflerde klinik ve lab bulgularına göre uzatılzbilir).

MICROBIOLOGIC METHODS TO DIAGNOSE VAP AND HAP

I. Should Patients With Suspected VAP Be Treated Based on the Results of Invasive Sampling (ie, Bronchoscopy, Blind Bronchial Sampling) With Quantitative Culture Results, Noninvasive Sampling (ie, Endotracheal Aspiration) With Quantitative Culture Results, or Noninvasive Sampling With Semiquantitative Culture Results?

Recommendation

1. We suggest noninvasive sampling with semiquantitative cultures to diagnose VAP, rather than invasive sampling with quantitative cultures and rather than noninvasive sampling with quantitative cultures *(weak recommendation, low-quality evidence)*.
   Remarks: Invasive respiratory sampling includes bronchoscopic techniques (ie, bronchoalveolar lavage [BAL], protected specimen brush [PSB]) and blind bronchial sampling (ie, mini-BAL). Noninvasive respiratory sampling refers to endotracheal aspiration.

ROLE OF INHALED ANTIBIOTIC THERAPY

XIV. Should Patients With VAP Due to Gram-Negative Bacilli Be Treated With a Combination of Inhaled and Systemic Antibiotics, or Systemic Antibiotics Alone?

Recommendation

1. For patients with VAP due to gram-negative bacilli that are susceptible to only aminoglycosides or polymyxins (colistin or polymyxin B), we suggest both inhaled and systemic antibiotics, rather than systemic antibiotics alone *(weak recommendation, very low-quality evidence)*.

XIX. Which Antibiotic Should Be Used to Treat Patients With HAP/VAP Due to *Acinetobacter* Species?

Recommendations

1. In patients with HAP/VAP caused by *Acinetobacter* species, we suggest treatment with either a carbapenem or ampicillin/sulbactam if the isolate is susceptible to these agents *(weak recommendation, low-quality evidence)*.
2. In patients with HAP/VAP caused by *Acinetobacter* species that is sensitive only to polymyxins, we recommend intravenous polymyxin (colistin or polymyxin B) *(strong recommendation, low-quality evidence)*, and we suggest adjunctive inhaled colistin *(weak recommendation, low-quality evidence)*.

XX. Which Antibiotic Should Be Used to Treat Patients With HAP/VAP Due to Carbapenem-Resistant Pathogens?

Recommendation

1. In patients with HAP/VAP caused by a carbapenem-resistant pathogen that is sensitive only to polymyxins, we recommend intravenous polymyxins (colistin or polymyxin B) *(strong recommendation, moderate-quality evidence)*, and we suggest adjunctive inhaled colistin *(weak recommendation, low-quality evidence)*.

- Hastaya **Piperasilin / Tazobaktam** (4x4.5 gram)
- **+ siprofloksasin (2x400mg)** başlandı
- **Ateş yanıtı alındı**
- CRP ve PCT yavaş da olsa düşme eğiliminde
- Oksijen ihtiyacı henüz azalmadı
- **DTA Üreme**: **10^6 cfu/ml Pseudomonas aeruginosa,**
  - **Meropenem duyarlı**
  - **İmipenem orta duyarlı**
  - **Siprofloksasin orta duyarlı**
  - **Sefepim orta duyarlı**
  - **Piperasilin tazobaktam orta duyarlı**
  - **Seftazidim orta duyarlı**

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 11.0, valid from 2021-01-01

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 11.0, 2021. http://www.eucast.org."

S (susceptible) standart ilaç dozunda duyarlı
I (orta duyarlı) demek değil
I – yüksek dozda ilaç maruziyetinde duyarlı

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 11.0, valid from 2021-01-01

Notes

1. The EUCAST clinical breakpoint tables contain clinical MIC breakpoints (determined or revised during 2002-2019) and their inhibition zone diameter correlates. The EUCAST breakpoint table version 10.0 includes corrected typographical errors, clarifications, breakpoints for new agents and/or organisms, revised MIC breakpoints and revised and new zone diameter breakpoints. Changes are best seen on screen or on a colour printout since cells containing a change are yellow. New or revised comments are underlined. Removed comments are shown in strikethrough font style.

2. PK-PD (Non-species related) breakpoints are listed separately.

3. Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.

4. Antimicrobial agent names in blue are linked to EUCAST rationale documents. MIC and zone diameter breakpoints in blue are linked to the search page of the EUCAST MIC and zone diameter distribution database.

5. The document is released as an Excel® file suitable for viewing on screen and as an Acrobat® pdf file suitable for printing. To utilize all functions in the Excel® file, use Microsoft™ original programs only. The Excel® file enables users to alter the list of agents to suit the local range of agents tested. The content of single cells cannot be changed. Hide lines by right-clicking on the line number and choose "hide". Hide columns by right-clicking on the column letter and choose "hide".

6. EUCAST breakpoints are used to categorise results into three susceptibility categories:
S - Susceptible, standard dosing regimen: A microorganism is categorised as *Susceptible, standard dosing regimen,* when there is a high likelihood of therapeutic success using a standard dosing regimen of the agent.
I - Susceptible, increased exposure: A microorganism is categorised as *Susceptible, increased exposure* * when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
R - Resistant: A microorganism is categorised as *Resistant* when there is a high likelihood of therapeutic failure even when there is increased exposure.
*Exposure is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

7. For an agent and a species, the ECOFF (epidemiological cut-off value) is the highest MIC (or the smallest inhibition zone diameter) for organisms devoid of phenotypically detectable acquired resistance mechanisms. Breakpoints in brackets are based on ECOFF values for relevant species. They are used to distinguish between organisms with and without acquired resistance mechanisms. ECOFFs do not predict clinical susceptibility but in some situations and/or when the agent is combined with another active agent, therapy may be considered.

Carbapenems	Standard dosage	High dosage
Doripenem	0.5 g x 3 iv over 1 hour	1 g x 3 iv over 1 hour
Ertapenem	1 g x 1 iv over 30 minutes	None
Imipenem	0.5 g x 4 iv over 30 minutes	1 g x 4 iv over 30 minutes
Imipenem-relebactam	(0.5 g imipenem + 0.25 g relebactam) x 4 iv over 30 minutes	None
Meropenem	1 g x 3 iv over 30 minutes	2 g x 3 iv over 3 hours
Meropenem-vaborbactam	(2 g meropenem + 2 g vaborbactam) x 3 iv over 3 hours	

* HAP/VAP = hospital-acquired pneumonia/ventilator-associated pneumonia

Ceftazidime	1 g x 3 iv	2 g x 3 iv or 1 g x 6 iv
Ceftazidime-avibactam	(2 g ceftazidime + 0.5 g avibactam) x 3 iv over 2 hours	
Ceftibuten	0.4 g x 1 oral	None
Ceftobiprole	0.5 g x 3 iv over 2 hours	None
Ceftolozane-tazobactam (intra-abdominal infections and UTI)	(1 g ceftolozane + 0.5 g tazobactam) x 3 iv over 1 hour	None
Ceftolozane-tazobactam (hospital acquired pneumonia, including ventilator associated pneumonia)	(2 g ceftolozane + 1 g tazobactam) x 3 iv over 1 hour	None
Ceftriaxone	2 g x 1 iv	2 g x 2 iv or 4 g x 1 iv
Cefuroxime iv	0.75 g x 3 iv	1.5 g x 3 iv

		by extended 3-hour infusion
Piperacillin-tazobactam	(4 g piperacillin + 0.5 g tazobactam) x 4 iv or x 3 by extended 4-hour infusion	(4 g piperacillin + 0.5 g tazobactam) x 4 iv by extended 3-hour infusion

Fluoroquinolones	Standard dosage	High dosage
Ciprofloxacin	0.5 g x 2 oral or 0.4 g x 2 iv	0.75 g x 2 oral or 0.4 g x 3 iv
Delafloxacin	0.45 g x 2 oral or 0.3 g x 2 iv	None
Levofloxacin	0.5 g x 1 oral or 0.5 g x 1 iv	0.5 g x 2 oral or 0.5 g x 2 iv
Moxifloxacin	0.4 g x 1 oral or 0.4 g x 1 iv	None
Norfloxacin	None	None
Ofloxacin	0.2 g x 2 oral or 0.2 g x 2 iv	0.4 g x 2 oral or 0.4 g x 2 iv

Teşekkürler