Nefrolog Gözüyle İnfektif Endokardit Tedavisi:

Antimikrobik tedavi, dozlar, PK ve PD

Dr. Ayşe Zeynep BAL

SBÜ Ankara Eğitim ve Araştırma Hastanesi

Nefroloji Kliniği

KRONİK BÖBREK HASTALIĞI TANIMI

En az 3 ay süren

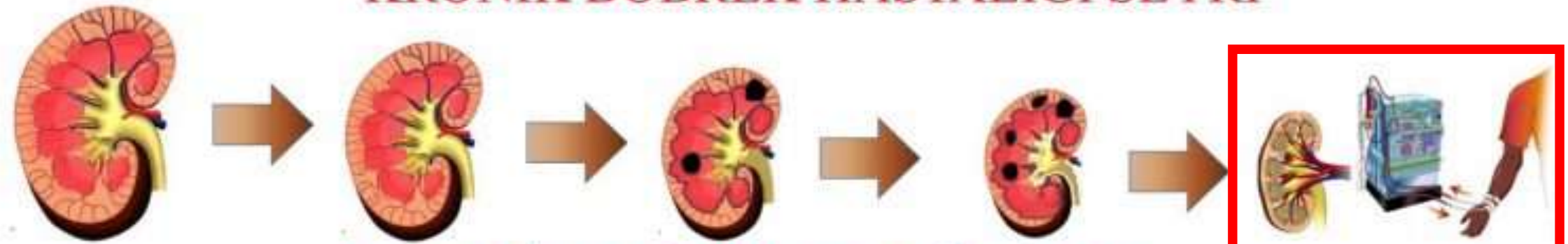
BÖBREK HASARI GÖSTERGELERİ	Albuminüri > 30 mg/gün İdrar sedimentinde anormallikler Tubuler bozukluğa bağlı elektrolit bozukluğu Histolojik olarak saptanan bozukluk Görüntüleme ile saptanan bozukluk Böbrek nakli öyküsü
GLOMERULAR FİLTRASYON HIZINDA AZALMA	GFR <60 ml/min/1.73 m2

KBH PROGRESYON RİSKİ
2012 KDIGO KLAVUZU

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g < 3 mg/mmol	30–300 mg/g 3–30 mg/mmol	> 300 mg/g > 30 mg/mmol
	G1	Normal or high	≥ 90	Düşük risk		
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29		Yüksek risk	
	G5	Kidney failure	< 15			

www.nefroloji.org

KRONİK BÖBREK HASTALIĞI SEYRİ



GLOMERÜLER FİLTRASYON DEĞERİ (GFD)

120 ml/dk — 90 ml/dk — 60 ml/dk — 30 ml/dk — 15 ml/dk — 0 ml/dk

Evre 1

- Normal GFD ile birlikte böbrek hasarı (Proteinüri, polikistik böbrek hastalığı gibi)
- Kan basıncı kontrolü (<130/80), kan şekeri kontrolü (A1C<6.5), kilo kontrolü

Evre 2

- GFD de hafif azalma ile birlikte böbrek hasarı
- Kan basıncı kontrolü (<130/80), kan şekeri kontrolü (A1C<6.5), kilo kontrolü

Evre 3

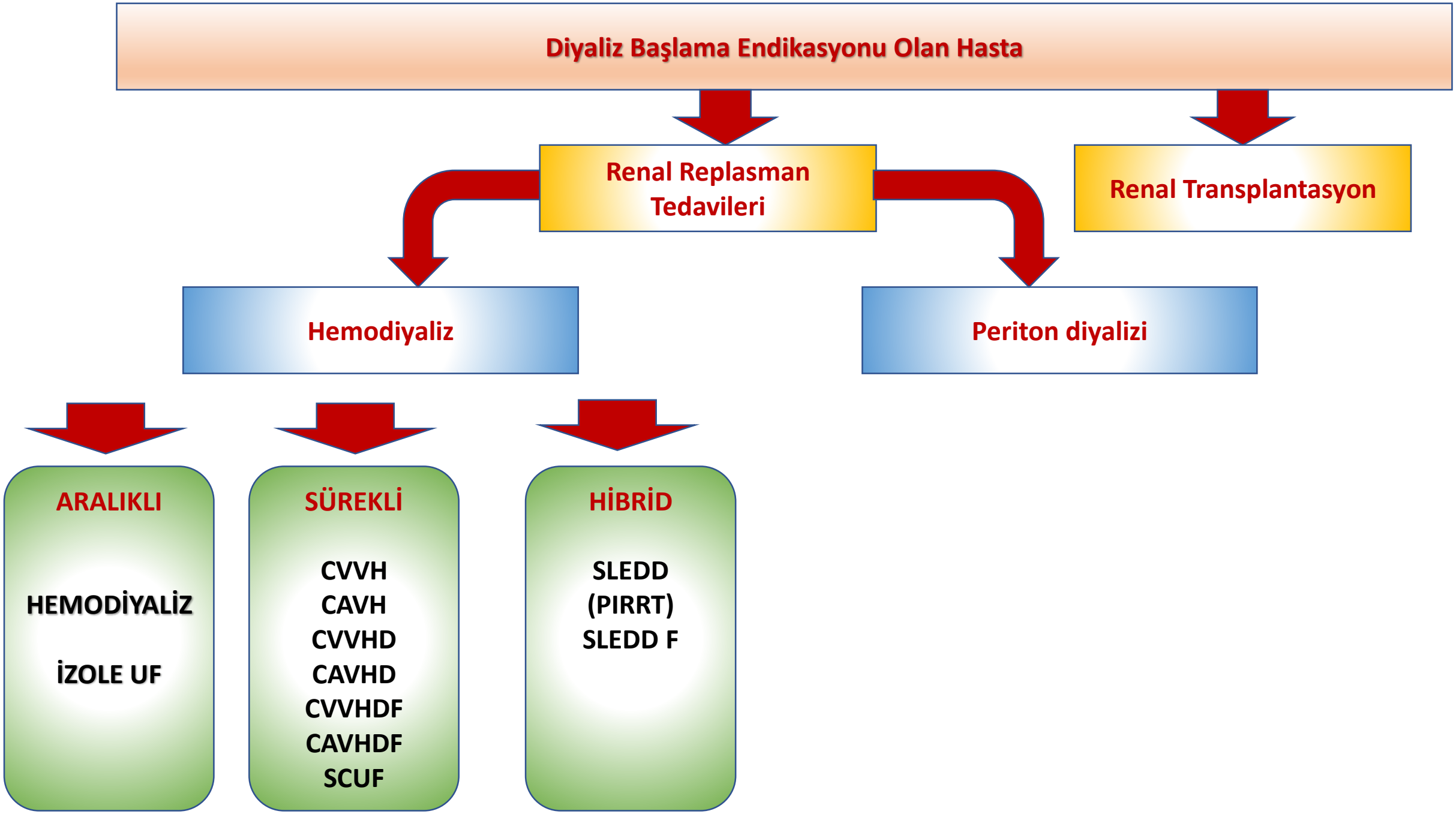
- Orta derecede böbrek hasarı ile birlikte anemi, kemik hastalığı başlar
- Nefroloji uzmanı tarafından yakın takip gereklidir
- Özel diyet ve tedavi gerekli olabilir

Evre 4

- Ciddi böbrek hasarı ile birlikte anemi, kemik hastalığı
- Fosfor ve potasyumda yükselme
- Evre 2-3 teki öneriler
- Renal replasman tedavileri hakkında bilgilendirme yapılmalı

Evre 5

- Son dönem böbrek yetmezliği
- Hemodiyaliz için damar giriş yolu veya karın diyalizi için katater takılmalı
- GFD 10 ml/dk nın altında renal replasman tedavisine başlanmalı


Diyaliz Başlama Endikasyonu Olan Hasta
Renal Replasman Tedavileri
Renal Transplantasyon
Hemodiyaliz
Periton diyalizi
ARALIKLI
HEMODİYALİZ
İZOLE UF
SÜREKLİ
CVVH
CAVH
CVVHD
CAVHD
CVVHDF
CAVHDF
SCUF
HİBRİD
SLEDD
(PIRRT)
SLEDD F

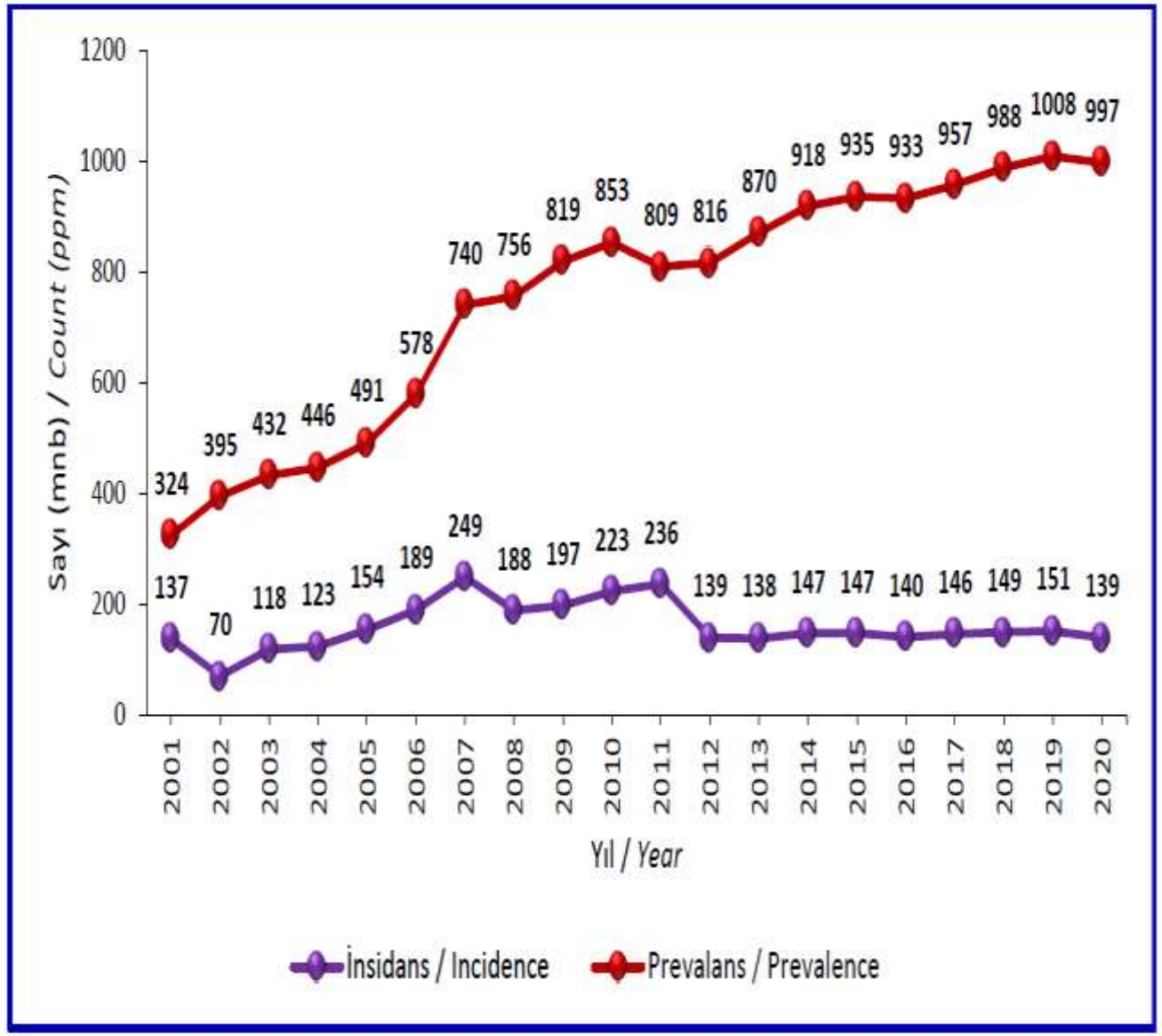
TÜRKİYE'DE NEFROLOJİ, DİYALİZ VE TRANSPLANTASYON

REGISTRY OF THE NEPHROLOGY, DIALYSIS AND TRANSPLANTATION IN TURKEY

REGISTRY 2020

T.C. SAĞLIK BAKANLIĞI VE TÜRK NEFROLOJİ DERNEĞİ ORTAK RAPORU

MINISTRY OF HEALTH AND TURKISH SOCIETY OF NEPHROLOGY JOINT REPORT



ŞEKİL 1. Türkiye'de RRT gerektiren son dönem böbrek hastalığının insidansı ve prevalansı.

TABLO 2. 2020 yılı sonu itibariyle RRT ile izlenmekte olan hastaların (çocuk hastalar dahil) RRT tipine göre dağılımı.

TABLE 2. *Distribution of prevalent RRT patients (including pediatric patients) by RRT type as of the end of 2020.*

	n	%
Hemodiyaliz / *Hemodialysis*	60.558	72.66
Periton diyalizi / *Peritoneal dialysis*	3.387	4.06
Transplantasyon / *Transplantation* *	19.405	23.28
Toplam / *Total*	83.350	100.00

* **Yaklaşık sayı** / *Approximate number*

TABLO 1. 2020 yılı içinde ilk renal replasman tedavisi (RRT) olarak hemodiyalize (HD) başlayan hastaların HD tipine göre dağılımı.

TABLE 1. *Distribution of patients who started hemodialysis (HD) as the first renal replacement therapy (RRT) in 2020 by HD type.*

	n	%
Merkezde standart HD / *Standard HD in center*	8.989	98.99
Evde HD / *Home HD*	39	0.43
Hemodiyafiltrasyon / *Hemodiafiltration*	34	0.37
Hemofiltrasyon / *Hemofiltration*	0	0.00
Tipi belli değil / *Unknown type*	19	0.21
Toplam / *Total*	9.081	100.00

TABLO 7. 2020 yılı sonu itibariyle prevalan HD hastalarının HD tipine göre dağılımı.

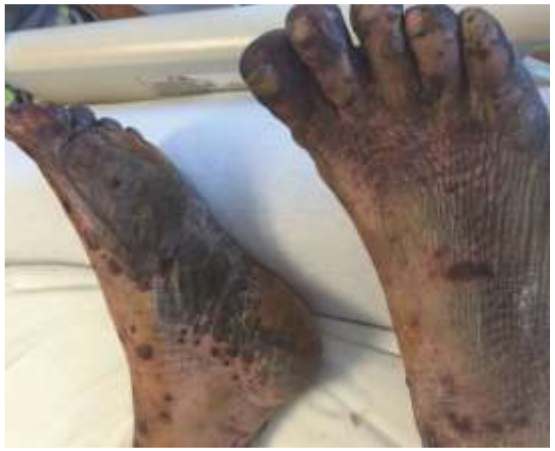
TABLE 7. *Distribution of prevalent HD patients by HD type as of the end of 2020.*

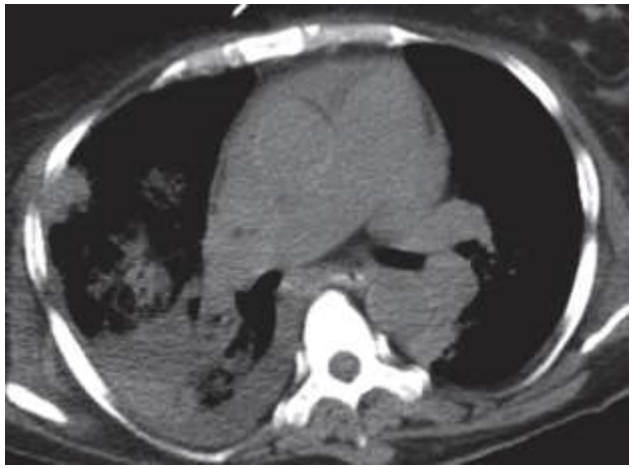
	n	%
Merkezde standart HD / *Standard HD in center*	57.920	95.64
Hemodiyafiltrasyon / *Hemodiafiltration*	1.576	2.60
Evde HD / *Home HD*	895	1.48
Hemofiltrasyon / *Hemofiltration*	5	0.01
Tipi belli değil / *Unknown type*	162	0.27
Toplam / *Total*	60.558	100.00

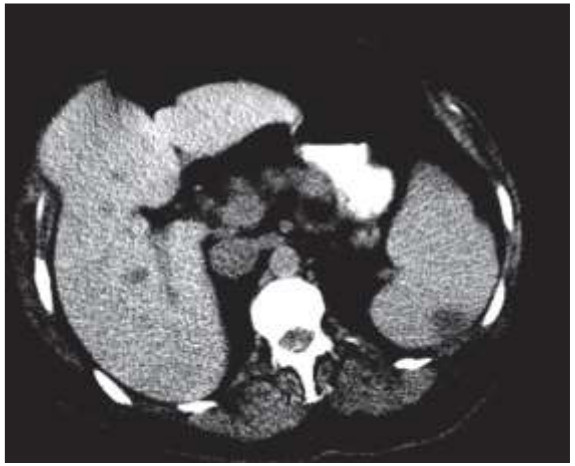
Hindawi
Case Reports in Nephrology
Volume 2017, Article ID 9460671, 7 pages
https://doi.org/10.1155/2017/9460671

Case Report

Nephrologists Hate the Dialysis Catheters: A Systemic Review of Dialysis Catheter Associated Infective Endocarditis







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Infective Endocarditis in Patients on Chronic Hemodialysis

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ABSTRACT

BACKGROUND Infective endocarditis (IE) is a common and serious complication in patients receiving chronic hemodialysis (HD).

OBJECTIVES This study sought to investigate whether there are significant differences in complications, cardiac surgery, relapses, and mortality between IE cases in HD and non-HD patients.

METHODS Prospective cohort study (International Collaboration on Endocarditis databases, encompassing 7,715 IE episodes from 2000 to 2006 and from 2008 to 2012). Descriptive analysis of baseline characteristics, epidemiological and etiological features, complications and outcomes, and their comparison between HD and non-HD patients was performed. Risk factors for major embolic events, cardiac surgery, relapses, and in-hospital and 6-month mortality were investigated in HD-patients using multivariable logistic regression.

RESULTS A total of 6,691 patients were included and 553 (8.3%) received HD. North America had a higher HD-IE proportion than the other regions. The predominant microorganism was *Staphylococcus aureus* (47.8%), followed by enterococci (15.4%). Both in-hospital and 6-month mortality were significantly higher in HD versus non-HD-IE patients (30.4% vs. 17% and 39.8% vs. 20.7%, respectively; $p < 0.001$). Cardiac surgery was less frequently performed among HD patients (30.6% vs. 46.2%; $p < 0.001$), whereas relapses were higher (9.4% vs. 2.7%; $p < 0.001$). Risk factors for 6-month mortality included Charlson score (hazard ratio [HR]: 1.26; 95% confidence interval [CI]: 1.11 to 1.44; $p = 0.001$), CNS emboli and other emboli (HR: 3.11; 95% CI: 1.84 to 5.27; $p < 0.001$; and HR: 1.73; 95% CI: 1.02 to 2.93; $p = 0.04$, respectively), persistent bacteremia (HR: 1.79; 95% CI: 1.11 to 2.88; $p = 0.02$), and acute onset heart failure (HR: 2.37; 95% CI: 1.49 to 3.78; $p < 0.001$).

CONCLUSIONS HD-IE is a health care-associated infection chiefly caused by *S. aureus*, with increasing rates of enterococcal IE. Mortality and relapses are very high and significantly larger than in non-HD-IE patients, whereas cardiac surgery is less frequently performed. (J Am Coll Cardiol 2021;77:1629-40) © 2021 by the American College of Cardiology Foundation.

5591 hasta 2000-2006 64 merkez , 24 ülke

2124 hasta 2008-2012 34 merkez , 18 ülke

HD ve HD dışı grup karşılaştırılması

KAYNAK: HASTANE DIŞI SAĞLIK HİZMETİ
ANA PREDİSPOZON RF : KALICI KATATER
EN SIK MO: S. Aureus
MORTALİTE ve RELAPS FAZLA
CERRAHİ ORANI AZ

HİJYEN KURALLARINA ve ÖNLEME KLAVUZLARINA KOŞULSUZ UYUM

TABLE 2 Comparison of Etiologic, Echocardiographic, and Treatment Characteristics; Complications; and Outcomes Between Hemodialysis and Nonhemodialysis Populations in the ICE Cohort

	Nonhemodialysis (n = 6,138)	Hemodialysis (n = 553)	p Value
Causative microorganisms	5,743	527	
Staphylococcus aureus	1,600 (27.9)	252 (47.8)	<0.001
MRSA	346/1,600 (21.6)	95/252 (37.7)	<0.001
Coagulase-negative staphylococci	619 (10.8)	78 (14.8)	0.012
Viridans group streptococci	1,087 (18.9)	16 (3.0)	<0.001
Enterococci	630 (11.0)	81 (15.4)	0.007
Bovis group streptococci	380 (6.6)	7 (1.3)	<0.001
Other streptococci	357 (6.2)	8 (1.5)	<0.001
HACEK	82 (1.4)	0	<0.001
Non-HACEK Gram negative	183 (3.2)	20 (3.8)	0.481
Fungi/yeast	106 (1.8)	17 (3.2)	0.081
Polymicrobial	71 (1.2)	14 (2.7)	0.047
Blood culture negative	482 (8.4)	28 (5.3)	0.003
Other	154 (2.7)	6 (1.1)	0.002

TABLE 2 Comparison of Etiologic, Echocardiographic, and Treatment Characteristics; Complications; and Outcomes Between Hemodialysis and Nonhemodialysis Populations in the ICE Cohort

	Nonhemodialysis (n = 6,138)	Hemodialysis (n = 553)	p Value
Complications			
Stroke	1,018 (16.6)	95 (17.2)	0.723
Systemic embolization (nonstroke)	1,414 (23.0)	104 (18.8)	0.015
Congestive heart failure	1,826 (29.7)	143 (25.9)	0.046
Persistent bacteremia	516 (8.4)	124 (22.4)	<0.001

ASLINDA ERKEN FARK EDİLİYOR
FAKAT KATATER ÇEKİMİNDE
GECİKMELER BAKTERİYEMİYİ
ARTTIRIYOR

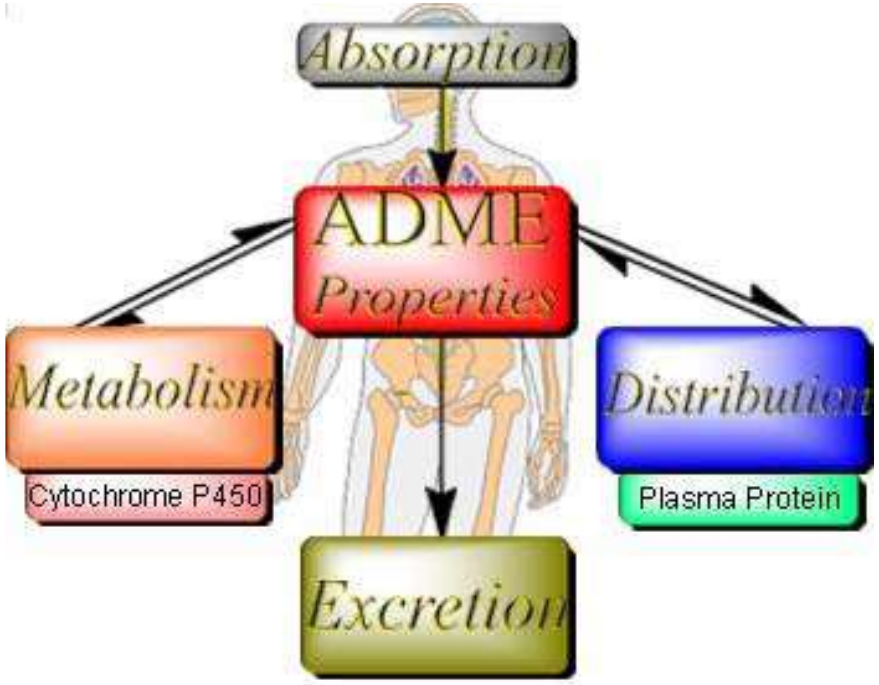
TABLE 2 Comparison of Etiologic, Echocardiographic, and Treatment Characteristics; Complications; and Outcomes Between Hemodialysis and Nonhemodialysis Populations in the ICE Cohort

	Nonhemodialysis (n = 6,138)	Hemodialysis (n = 553)	p Value
Antibiotic treatment	3,525	351	
Beta-lactams	799 (22.7)	69 (19.7)	0.178
Glycopeptides	326 (9.2)	82 (23.4)	<0.001
Aminoglycosides	91 (2.6)	14 (4.0)	0.192
Beta-lactams + aminoglycosides	1498 (42.5)	52 (14.8)	<0.001
Glycopeptides + aminoglycosides	248 (7.0)	63 (17.9)	<0.001
Glycopeptides + beta-lactams	113 (3.2)	16 (4.6)	0.240
Glycopeptides + beta-lactams + aminoglycosides	193 (5.5)	23 (6.6)	0.433
Other	257 (7.3)	32 (9.1)	0.253

İSTENMEYEN İLAÇ ETKİLERİNDEN KAÇINMA

OPTİMUM TEDAVİYİ SAĞLAMAK

Kronik Böbrek Hastalarında İlaçların Farmokinetiği



Dağılım

Hipervolemi varlığında suda çözünen antibiyotiklerin dağılım hacmi artar, aynı etkiyi alabilmek için *doz artırmak* gerekebilir.

Hipovolemi durumunda da, ilacın aynı etkisi için, daha *düşük doz* gerekebilir

Table I. Protein binding of antibacterials commonly used in critically ill patients and of antibacterials in development (all protein binding data have been adapted from Donnelly et al.[26] and MIMS Australia[27]). We have also included data on antifungal agents for the reader's reference

Highly bound (>70%)	Moderately bound (70–30%)	Minimally bound (<30%)
Amphotericin B (90%)	Azithromycin (7–51%)	Amikacin (0–11%)
Anidulafungin (>99%)	Aztreonam (60%)	Amoxicillin (17–20%)
Caspofungin (97%)	Cefotaxime (40%)	Ampicillin (15–25%)
Cefazolin (75–85%)	Cefuroxime (33–50%)	Cefepime (16–19%)
Cefonicid (98%)	Cephalothin (55–75%)	Ceftazidime (17%)
Cefoperazone (90%)	Ciprofloxacin (20–40%)	Ceftobiprole (22%)
Cefoxitin (80–50%)	Clarithromycin (42–50%)	Cefpirome (9%)
Ceftriaxone (85–95%)	Chloramphenicol (60%)	Colistin (<10%)
Clindamycin (90% bound to α_1-acid glycoprotein)	Levofloxacin (50%)	Doripenem (8%)
Cloxacillin (94%)	Linezolid (31%)	Ethambutol (20–30%)
Dalbavancin (93%)	Moxifloxacin (30–50%)	Fluconazole (11–12%)
Daptomycin (90–93%, 30% to α_1-acid glycoprotein)	Nitrofurantoin (40%)	Fosfomycin (0%)
Dicloxacillin (97%)	Benzylpenicillin [penicillin-G] (65%)	Gentamycin (<30%)
Doxycycline (93%)	Piperacillin (30%)	Imipenem (20%)
Ertapenem (85–95%)	Sulfamethoxazole (68%)	Isoniazide (0–10%)
Erythromycin (73–81%)	Ticarcillin (55%)	Meropenem (2%)
Faropenem (96–99%)	Trimethoprim (45%)	Metronidazole (<20%)
Flucloxacillin (95%)	Vancomycin (30–60%)	Norfloxacin (10–15%)
Fusidic acid (95–97%)	Voriconazole (58%)	Polymyxin B (<10%)
Iclaprim (93%)		Quinupristin/dalfopristin (11–26%)
Itraconazole (99.8%)		Tobramycin (<30%)
Lincomycin (80–90%)		
Minocycline (75%)		
Nafcillin (90%)		
Oxacillin (93%)		
Posaconazole (>97%)		
Rifampicin [rifampin] (80%)		
Sulfisoxazole (92%)		
Teicoplanin (90–95%)		
Telavancin (92–94%)		
Tigecycline (71–89%)		

Am J Transl Res , 2019
Med Mal Infect , 2019

Metabolizma

İlaç metabolizmasında sitokrom p450 sistemi rol alır. Ancak, KBH'lı hastalarda, sitokrom enzim sisteminin aktivitesinde azalma olur, bu da ilaçların metabolizmasını etkiler.

Ekskresyon

Kronik Böbrek Hastalığında Antibiyoterapi Önerileri

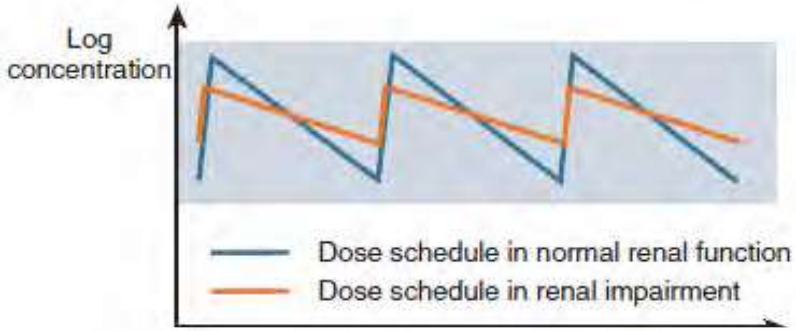
DOZ AZALTILMASI

Uygulama aralığı değişmeden doz azaltması yapılabilir 24 saat boyunca MIC üzerindeki konsantrasyonları mümkün olduğunca uzun süre korumak için.

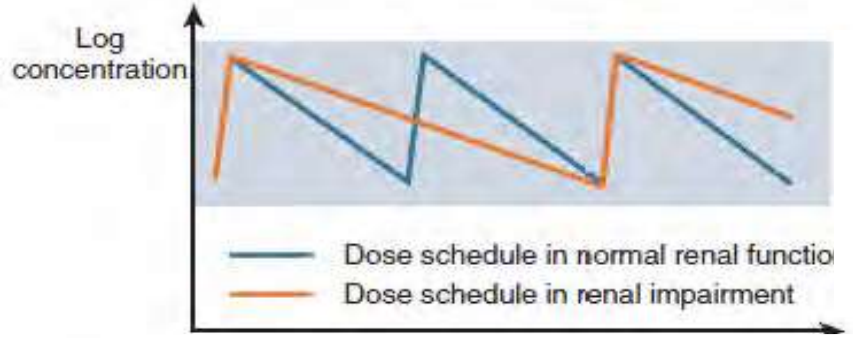
İNTERVAL UZATILMASI

İdame dozların devamı ve uygulama aralığının azaltılması. Konsantrasyona bağlı AB Cmax ana PK parametre

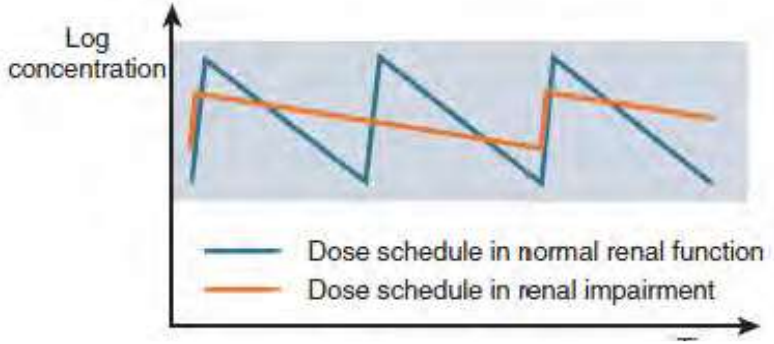
KOMBİNASYON



Time-dependent antibiotics
- Beta lactams
  - Penicillins[20,22,23]
  - Carbapenems[20,22,23]
  - Cephalosporins[20,22,23]
  - Monobactam[23,24]
- Macrolides[20,25]
- Clindamycin[20]
- Linezolid[20]
- Tetracyclines[20]
- Tigecycline[20,22]



Concentration-dependent antibiotics
- Aminoglycosides[18-20]
- Fluoroquinolones[19-21]
- Polymyxin[19,20,22]



Concentration and time dependent
- Daptomycin[19,20,26]
- Vancomycin[20,22]

Adv Chronic Kidney Dis. 2019

KBH'da Glomerüler Filtrasyon Hızında Hangi Formül ?

Table 1. Comparison of Cockcroft-Gault, MDRD, and CKD-EPI Equations

Equation characteristics	Cockcroft-Gault[11]	MDRD[12]	CKD-EPI[13]
Renal function estimate	Creatinine clearance	Estimated glomerular filtration rate	Estimated glomerular filtration rate
Units	mL/min	mL/min/1.73 m^2	mL/min/1.73 m^2
Equation variables	Serum creatinine concentration Age Gender Weight	Serum creatinine concentration Gender Age Race	Serum creatinine concentration Gender Age Race
Patient population used to generate equation	Male $N = 505$ Average renal function = creatinine clearance 73 mL/min by 24-h urinary creatinine clearance	Patients with known kidney disease $N = 1628$ Average renal function = 40 mL/min/1.73 m^2 by ^{125}I-iothalamate renal clearance	Diverse population $N = 12,150$ Average renal function = 68 mL/min/1.73 m^2 by ^{125}I-iothalamate renal clearance

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; MDRD, Modification of Diet in Renal Disease.

Adv Chronic Kidney Dis. 2019

Médecine et maladies infectieuses 50 (2020) 323–331

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Review

Antibiotics and chronic kidney disease: Dose adjustment update for infectious disease clinical practice☆

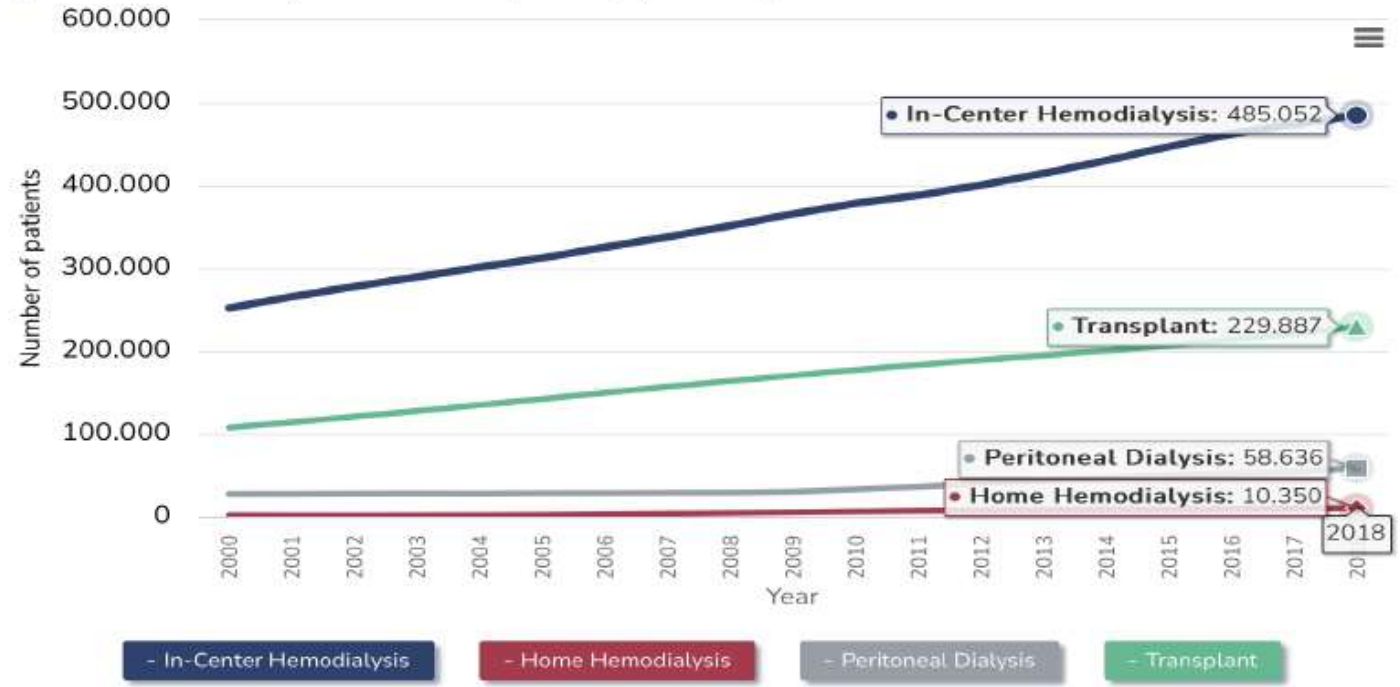
Table 1
List of drugs for which recommendations were made by the working group and consequences on dosing adjustment.
Liste des médicaments pour lesquels le groupe de travail a émis des recommandations et conséquences sur l'adaptation posologique des médicaments.

Antibiotics (INN)	Recommendations	Dosing adjustment in CKD patients
Aminoglycosides		
Amikacin	Depending on clinical severity: 20 to 30 mg/kg as a 30-minute infusion [22–24]	There is no established regimen that ensures both the good efficacy and tolerability of aminoglycosides in case of renal failure. When the prescription of aminoglycosides is clinically required, the unit dosage should not be decreased as aminoglycosides are concentration-dependent antibiotics. A single infusion is most often sufficient. If several infusions are needed, the residual concentration should be monitored and dose administration should be spaced accordingly [25]
Gentamicin	Gram-positive cocci infections: 3 to 5 mg/kg Gram-negative bacilli infections: 5 to 8 mg/kg [23]	
Tobramycin	Gram-positive cocci infections: 3 to 5 mg/kg Gram-negative bacilli infections: 5 to 8 mg/kg [23]	
Cephalosporins		
Cefaclor	Indications are limited to tonsillitis due to *Streptococcus pyogenes* and lower urinary tract infections. Little PK/PD data is available; thus, this oral cephalosporin cannot be recommended for use in other indications [26,27]	Dosing adjustment if GFR < 30 mL/min [28]
Cefalexin	The use of cefalexin should be avoided because its PK/PD profile is not compatible with oral administration	Dosing adjustment if GFR < 60 mL/min [28]
Cefadroxil	Indications are limited to tonsillitis due to *Streptococcus pyogenes* and lower urinary tract infections. Cefadroxil is not mentioned in the recent guidelines for urinary tract or upper respiratory tract infections [26,27]	Dosing adjustment if GFR < 40 mL/min [29]

101 AB
57 si için öneriler yenilenmiş

Renal Replasman Tedavileri

Figure 1.6 Number of prevalent ESRD patients, by modality, 2000-2018



Data source: USRDS ESRD database. ESRD prevalence was identified on December 31 of each year.

Renal Replasman Tedavileri Sırasında Antimikrobiyal Uzaklaştırmayı Belirleyen Ana Faktörler

Hastaya Ait Özellikler

İlaç İlişkili Faktörler

RRT ile İlişkili Faktörler

Renal Replasman Tedavileri Sırasında Antimikrobiyal Uzaklaştırmayı Belirleyen Ana Faktörler

Hastaya Ait Özellikler
Rezidüel Renal Fonksiyonu
Böbrek dışı klirenste değişiklikler
Dağılım volümündeki varyasyon
Diğer ilaçlarla etkileşim
Kan pH
Hipoalbüminemi

AACN Adv Crit Care. 2017

Renal Replasman Tedavileri Sırasında Antimikrobiyal Uzaklaştırmayı Belirleyen Ana Faktörler

İlaç İlişkili Faktörler	
Proteine bağlanma	PROTEİNE BAĞLANMA ORANI (>80%)
Dağılım hacmi	GENİŞ DAĞILIM HACMİ (>1 L/kg)
Moleküler Ağırlık	BÜYÜK MOLEKÜL AĞIRLIĞI
Moleküler boyut ve yapı	
Suda çözünürlük	LİPOFİLİK
Elektriksel yük	YENİ MEMBRANLAR İÇİN GEÇERLİ DEĞİL

AACN Adv Crit Care. 2017

RRT sırasında ilaç Farmakokinetiği

Proteine bağlanma

Dağılım hacmi

Moleküler Ağırlık

İLAÇ KLİRENSİ

- Dağılım hacmi, vücuttaki toplam ilaç miktarı ile plazma konsantrasyonları arasındaki orantılılık sabitleridir
- Dağılım hacmi > 2 lt/kg ise damar dışı dağılıyor ve /veya dokuya yoğun dağılıyor
- **Dağılım hacmi < 1 lt/kg hepsi plazmada ve RRT ile tamamına yakını temizlenebilir**

- Bir maddenin birim zamanda plazmadan temizlenen miktarı
  - Elimine edilme oranı/Konsantrasyon
- Bir ilacın idame dozu hesaplanması için kullanılır
- Toplam vücut klirensi: metabolizma + ekskresyon
- **RRT DEVREYE GİRDİĞİNDE**
  - **EXTRACORPOREAL KLİRENS göz önünde bulundurulmalı**

RRT sırasında ilaç Farmakokinetiği

Proteine bağlanma

Dağılım hacmi

Moleküler Ağırlık

+

İLAÇ KLİRENSİ

Serbest fraksiyon (f): Proteine bağlı olmayan ilaç RRT'den elimine olabilir

Eleklenme katsayısı (SC): ultrafiltrattaki ilaç konsantrasyonu/plazma ilaç konsantrasyonu

→ Konvektif

Saturasyon koefficient (SA): diyalizattaki ilaç konsantarasyonu/plazma ilaç konsantarasyonu

→ Difüzyon

- **Sonuç: SA < SC ve diffusif CL < convektif CL**

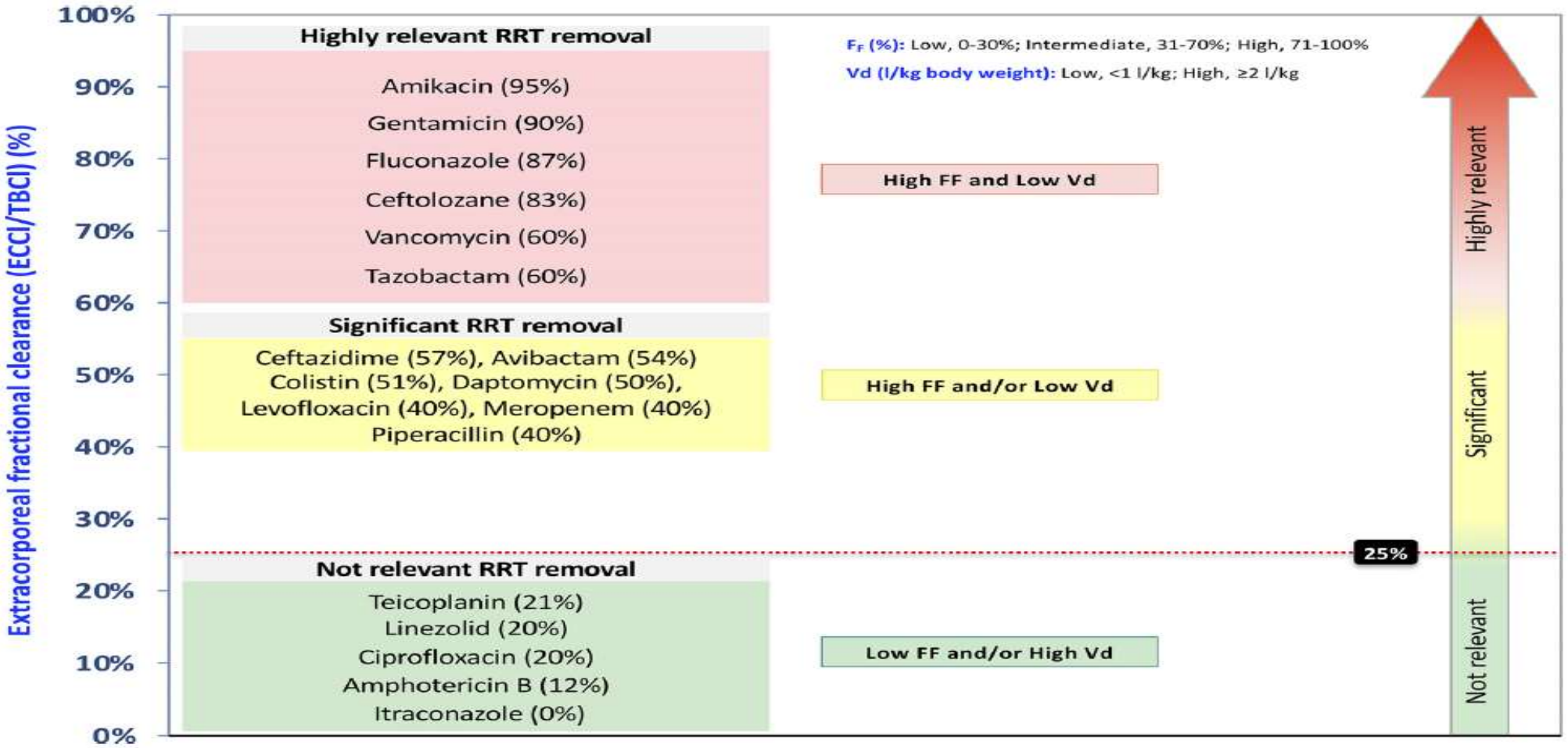


FIG 2 The extracorporeal fractional clearance (CL_{EC}/CL_{TB} [percentage]) of a given antimicrobial during renal replacement therapy derives from the ratio of extracorporeal clearance (CL_{EC}) to total body clearance (CL_{TB}) (shown here as "ECCl/TBCl") and indicates the relative contribution of CL_{EC} to CL_{TB}. As displayed above, the variability of *V* and *f* (here "Vd" and "F_F") results in a substantially different impact of CRRT on CL_{TB} of antimicrobials, while an MW up to 1,000 to 1,500 Da (e.g., vancomycin or colistin) does not represent *per se* a limit to extracorporeal removal across the membranes commonly used in CRRT. MW, molecular weight; *V*, distribution volume.

AACN Adv Crit Care. 2017

Renal Replasman Tedavileri Sırasında Antimikrobiyal Uzaklaştırmayı Belirleyen Ana Faktörler

RRT ile İlişkili Faktörler
RRT modalitesi
Solut uzaklaştırılma şekli
Diyaliz dozu
Membran özellikleri
Tedavi süresi
Vasküler yol resirkülasyonu

Renal Replasman Modaliteleri

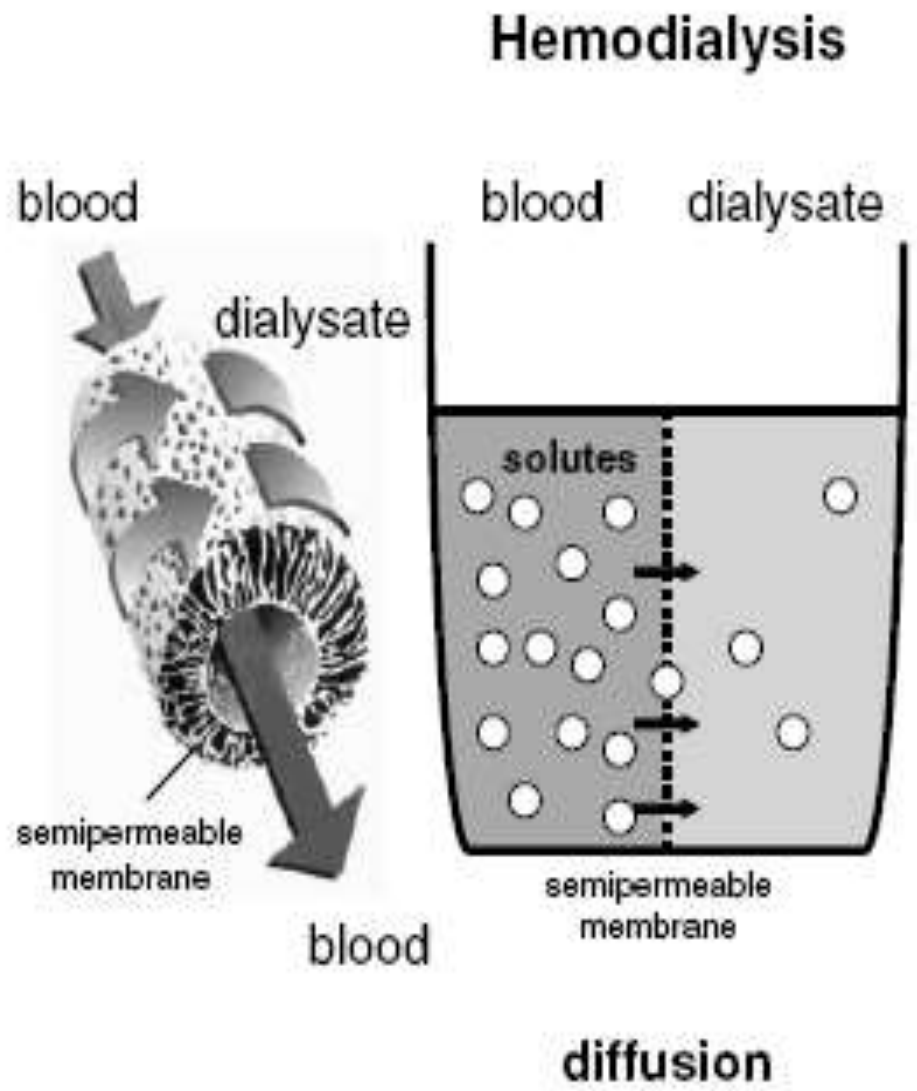
Aralıklı hemodiyaliz (IHD)

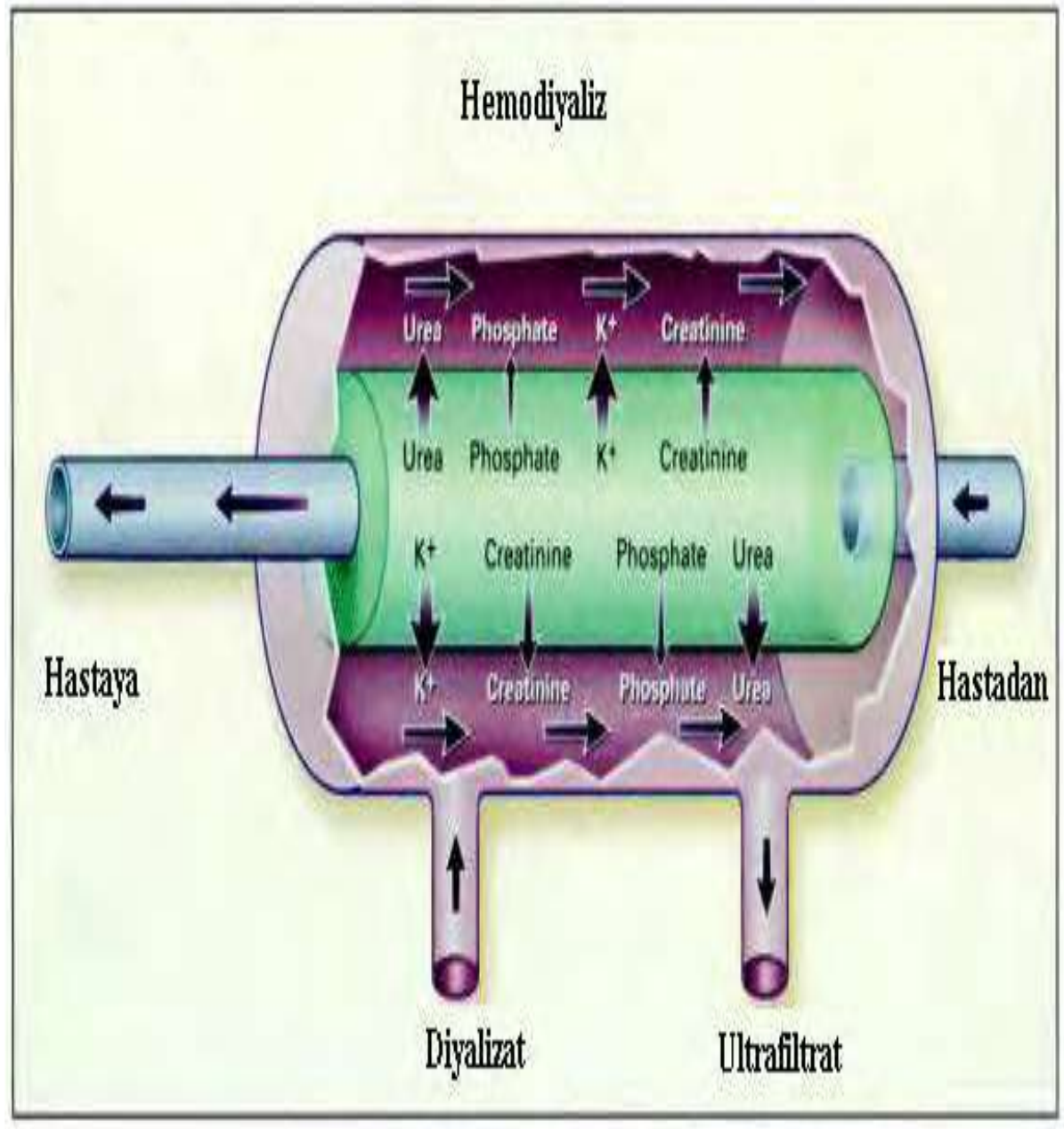
- Günlük Kısa Süreli HD
- Nokturnal HD
- PIRRT
- İzole UF
- Expanded HD

Sürekli renal replasman tedavileri (SRRT)

- Devamlı venövenöz hemofiltrasyon (CVVH)
- Devamlı venövenöz hemodiyaliz (CVVHD)
- Devamlı venövenöz hemodiafiltrasyon (CVVHDF)

DİFÜZYON


Hemodialysis
blood
dialysate
blood
dialysate
solutes
semipermeable membrane
blood
semipermeable membrane
diffusion


Hemodiyaliz
Urea
Phosphate
K+
Creatinine
Urea
Phosphate
K+
Creatinine
K+
Creatinine
Phosphate
Urea
K+
Creatinine
Phosphate
Urea
Hastaya
Hastadan
Diyalizat
Ultrafiltrat

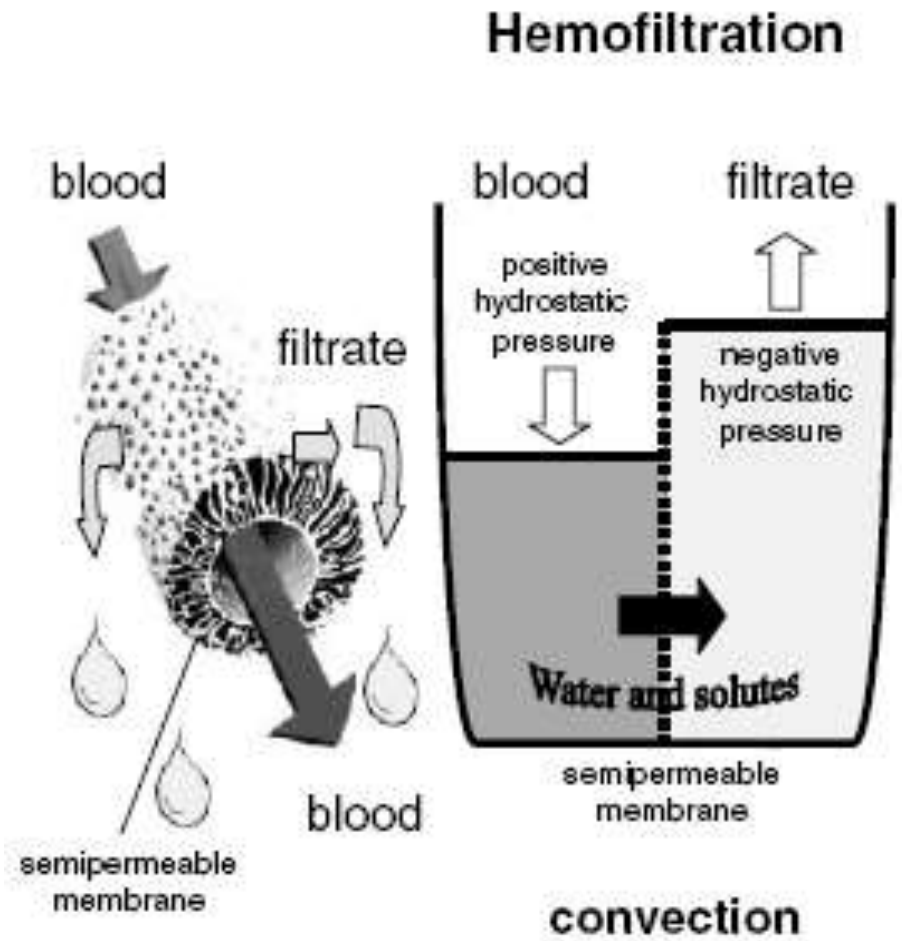
Aralıklı Hemodiyaliz

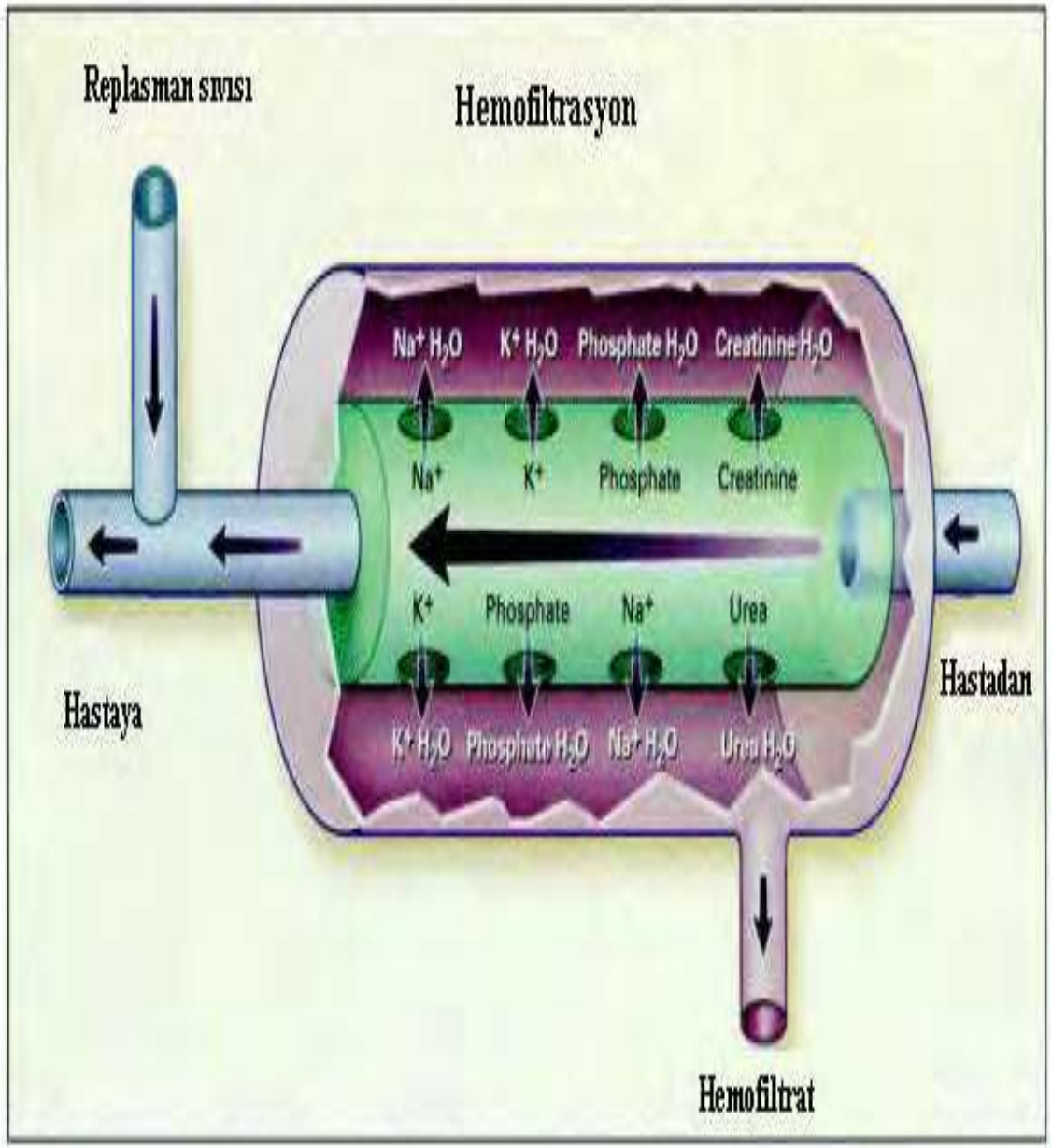
- Düşük/yüksek permeabilitesi olan membran aracılığıyla, kanın **difüzyonla** purifikasyonu sağlanır
- Diyalizat solusyonunun akımı ters yöndedir
- Replasman sıvısı kullanılmaz
- Qb: 50-200 mL/dk Qf: 8-25 mL/dk
  Qd: 10-20 mL/dk K: 14-36 L/24 saat
- Sadece düşük molekül ağırlıklı moleküller süzülür

Klirens :

- ✓ kan akımına bağlıdır
- ✓ membran özelliklerine (alanı/kalınlığı),
- ✓ diyalizat akımına (500ml/dk),
- ✓ solütün molekül ağırlığına,
- ✓ diffüzyon katsayısına,
- ✓ sıvının ısısına

KONVEKSİYON





Sürekli Renal Replasman Tedavileri

Hemofiltrasyon

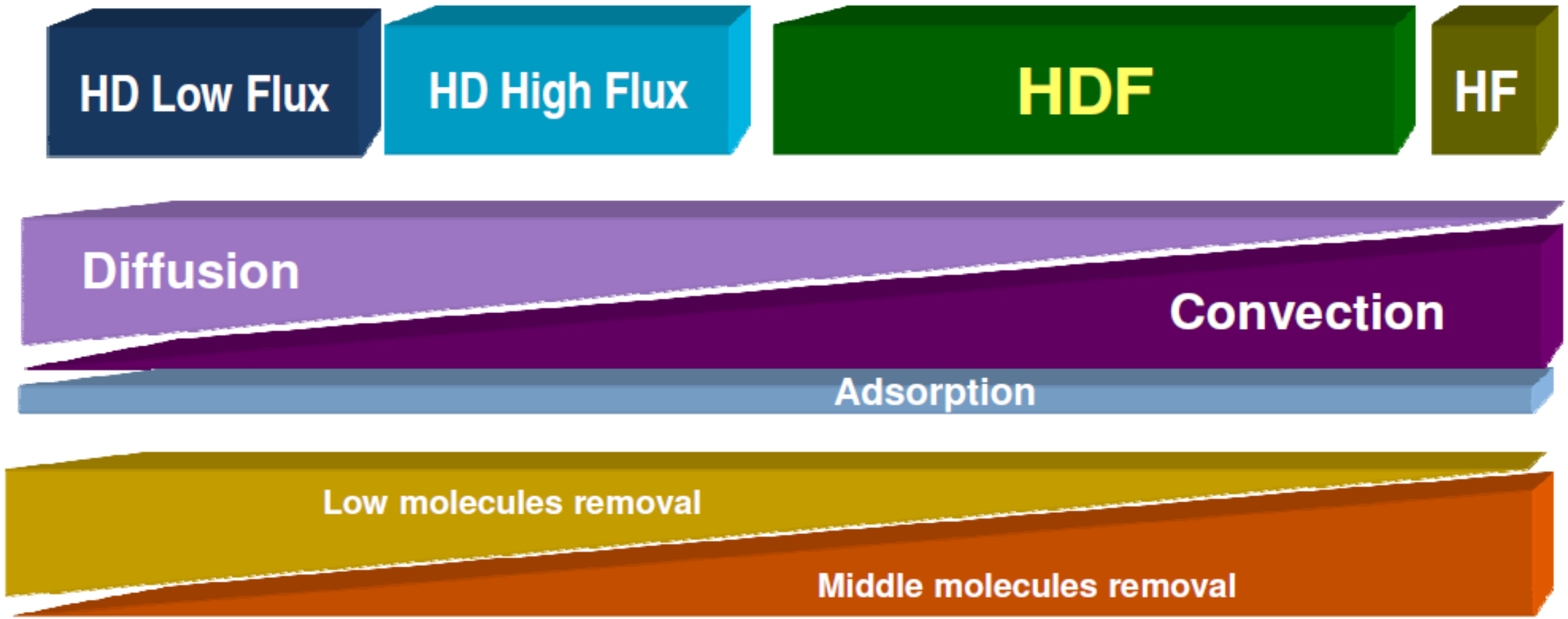
- **Yüksek permeabilitesi** olan membran aracılığıyla, kanın **konvektiv** olarak purifikasyonu sağlanır
- Ultrafiltrasyon kontrol altındadır
- Ultrafiltrat replasman solusyonuyla yer değiştirir
- Qb: 50-200 mL/dk Qf: 8-25 mL/dk
  K: 12-36 L/24 saat

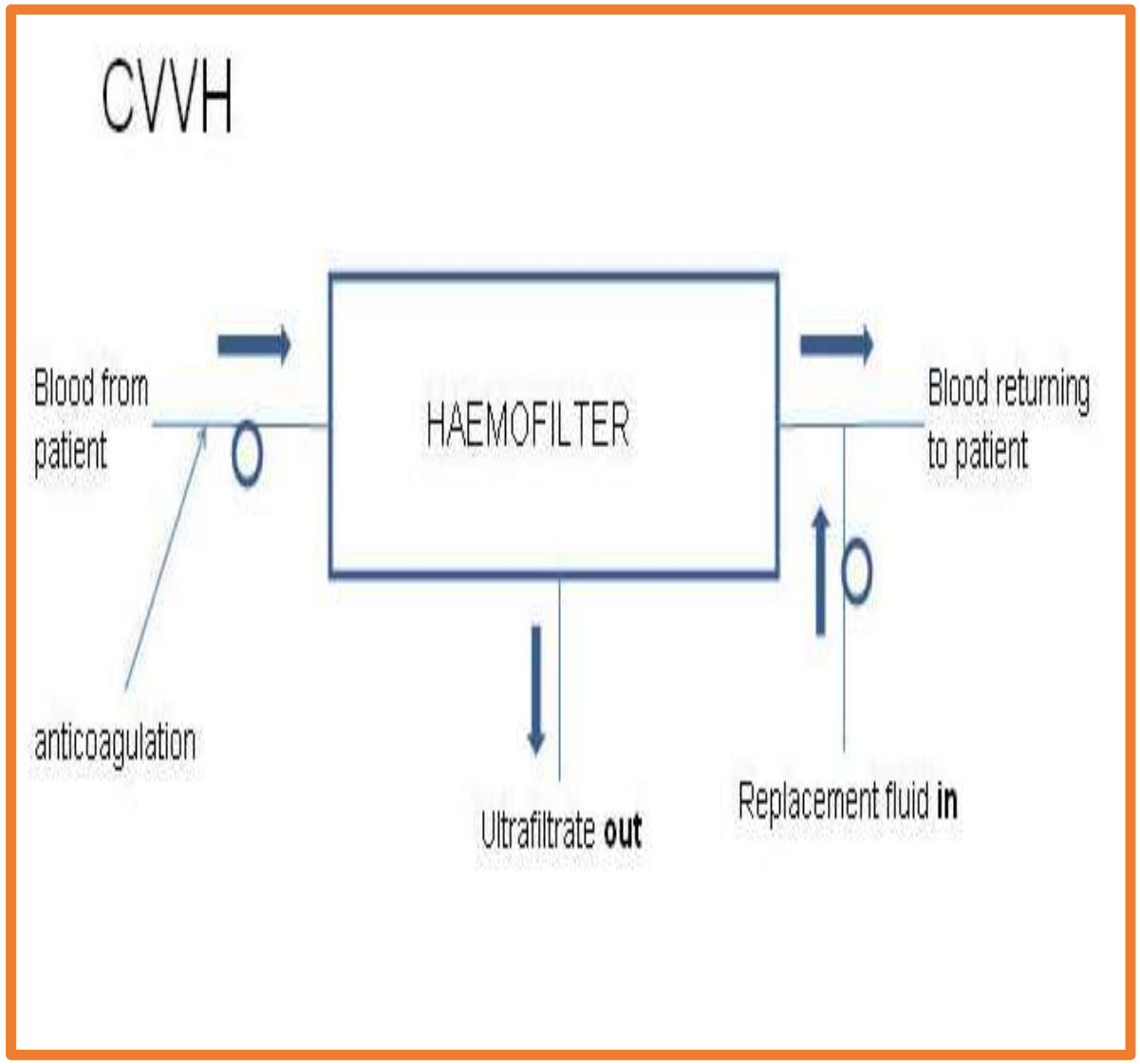
Hemodiafiltrasyon

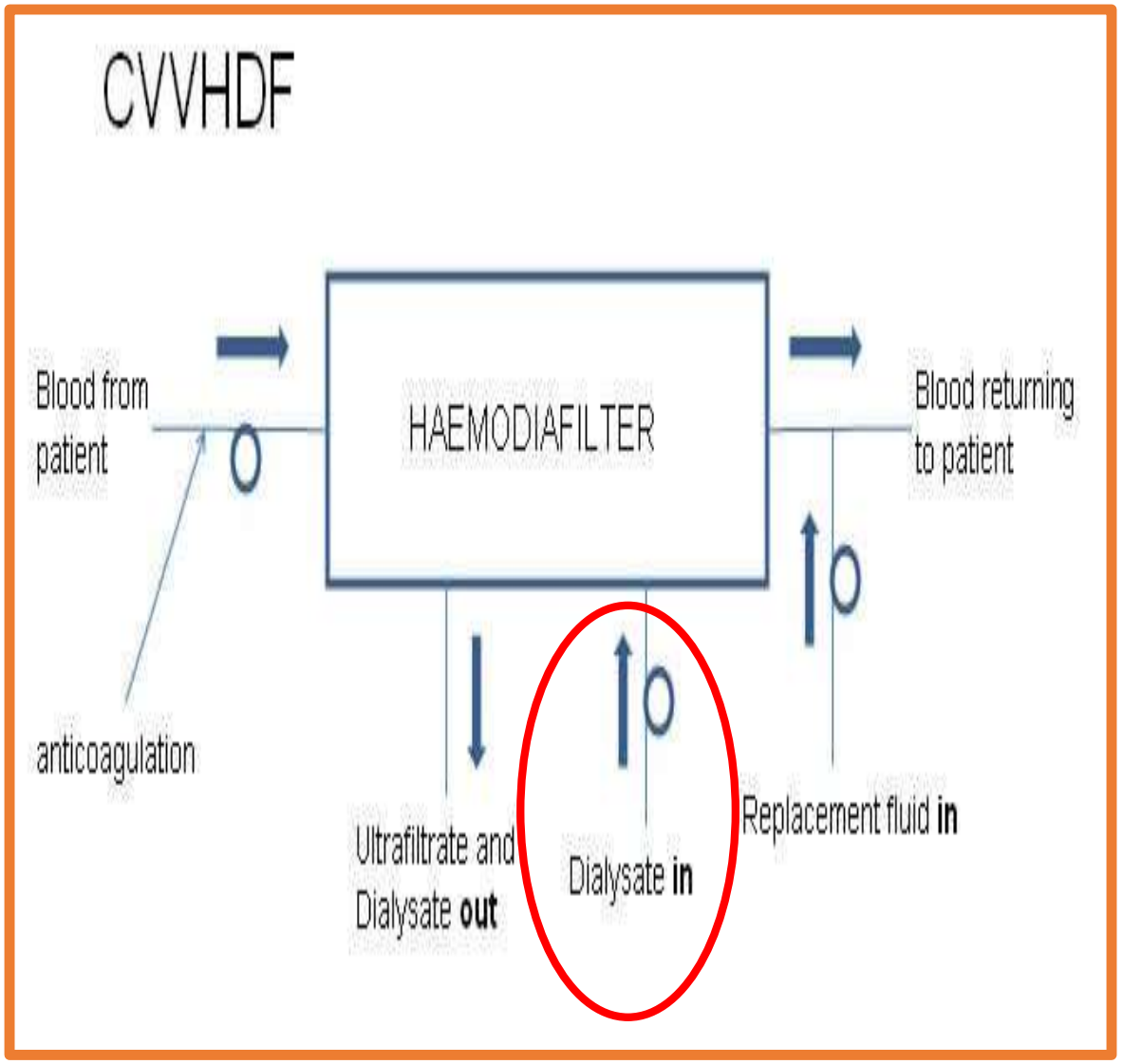
- **Difüziv - konvektiv** kan purifikasyonu
- Ters akımlı diyalizat
- **Yüksek permeabilitesi** olan membranla küçük ve orta büyüklükte moleküllerin uzaklaştırılması sağlanabilir
- Qb: 50-200 mL/dk Qf: 8-12 mL/dk
  Qd: 10-20 mL/dk K: 20-40 L/24 saat

Klirens :

- ✓ Ultrafiltre edilen plazma miktarına
- ✓ Membran özelliklerine (alanı/kalınlığı)

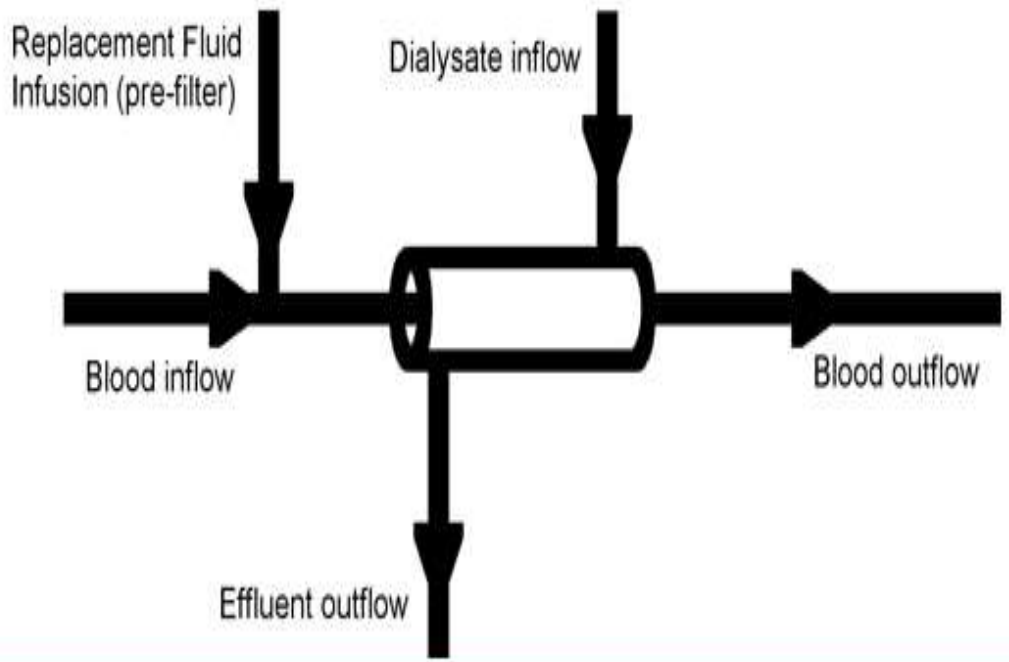

HD Low Flux
HD High Flux
HDF
HF
Diffusion
Convection
Adsorption
Low molecules removal
Middle molecules removal


CVVH
Blood from patient
HAEMOFILTER
Blood returning to patient
anticoagulation
Ultrafiltrate **out**
Replacement fluid **in**


CVVHDF
Blood from patient
HAEMODIAFILTER
Blood returning to patient
anticoagulation
Ultrafiltrate and Dialysate **out**
Dialysate **in**
Replacement fluid **in**

Schematic of CVVHDF with pre-filter infusion of replacement fluid

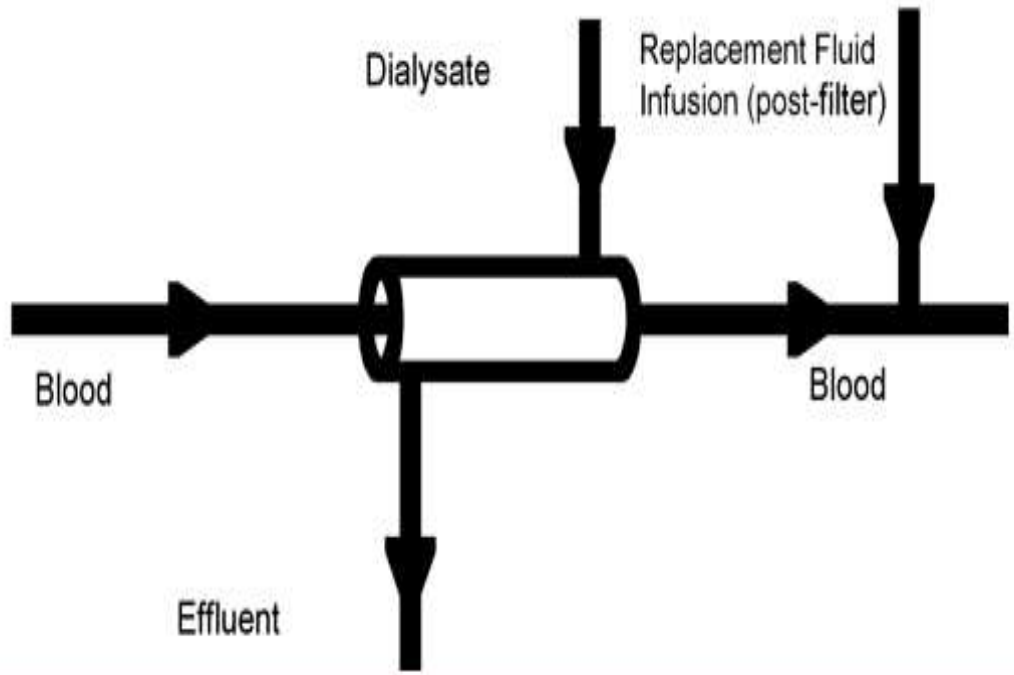
Schematic of CVVHDF with pre-filter infusion of replacement fluid



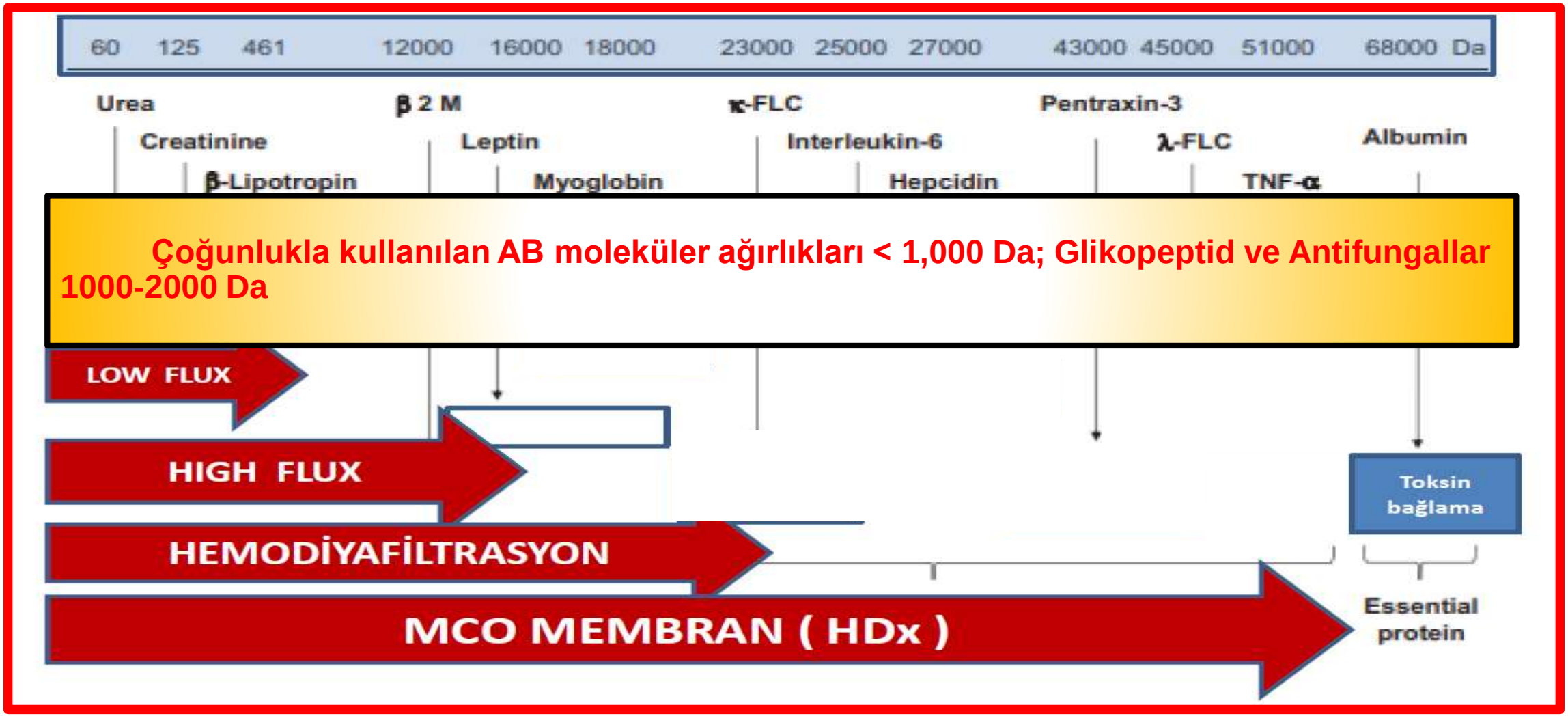
CVVHDF: continuous venovenous hemodiafiltration.

Schematic of CVVHDF with post-filter infusion of replacement fluid

Schematic of CVVHDF with post-filter infusion of replacement



CVVHDF: continuous venovenous hemodiafiltration.


60 125 461 12000 16000 18000 23000 25000 27000 43000 45000 51000 68000 Da
Urea
β 2 M
κ-FLC
Pentraxin-3
Creatinine
Leptin
Interleukin-6
λ-FLC
Albumin
β-Lipotropin
Myoglobin
Hepcidin
TNF-α
Çoğunlukla kullanılan AB moleküler ağırlıkları < 1,000 Da; Glikopeptid ve Antifungallar 1000-2000 Da
LOW FLUX
HIGH FLUX
HEMODİYAFİLTRASYON
MCO MEMBRAN (HDx)
Toksin bağlama
Essential protein

	İHD	CVVHD	CVVH	CVVHDF
Membran geçirgenliği	değişken	yüksek	yüksek	yüksek
Kan akım hızı (ml/dk)	250-400	100-200	200-300	100-200
Diyalizat akım (ml/dk)	500-800	15-45	-	16-34
Filtrat (L/gün)	0-4	2-7	25-95	25-50
Replasman sıvısı (L/gün)	-	-	22-90	22-45
Solüt klirensi	difüzyon	difüzyon	konveksiyon	Her ikisi
Üre klirensi (ml/dk)	180-200	22	16-67	30-60
Süre (saat)	3-4	>24	>24	>24

CVVHDF > CVVHD > CVVH > IHD

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MAIN TEXT ARTICLE

WILEY Artificial Organs

Vancomycin hemodialysis: Clearance differences between high-flux hemodialysis and on-line hemodiafiltration

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TABLE 1 Demographic data

Patient	Age (years)	Sex	HD vintage (mo)	Dry weight (kg)	Hb (g/dL)	Albumin (g/L)	Vancomycin use	Vascular access
1	70	M	24	64	12	47	Fever	Catheter
2	63	M	34	77	12.3	33	Soft tissue infection	Fistula
3	59	M	61	55.7	11.7	33	Soft tissue infection	Fistula
4	66	M	58	60	9.2	30	Sepsis	Catheter
5	49	F	16	52.5	11	43	Fever	Catheter
6	76	M	66	55	8.7	35	Vascular access infection	Fistula
7	58	M	4	91.5	10.4	46	Vascular access infection	Catheter
8	82	M	70	78	8.9	36	Fever	Catheter
9	65	M	24	55.5	10.5	37	Vascular access infection	Catheter

HD çıkışı 1 gr yükleme ; HD bitimi 0.5 gr ek doz.
Kan örnekleri arter ve venöz setten her saat başı alınmış.
Ayrıca diyaliz bitimi 15. 30. ve 45. dakikalarda da ek örnekler alınmış.

TABLE 2 Hemodialysis characteristics

	HFHD				OL-HDF				
	BVP (L)	*Kt* (L)	Vancomycin at start of HD (μg/mL)	Vancomycin at end of HD (μg/mL)	BVP (L)	*Kt* (L)	*Qi* (mL/min)	Vancomycin at start of HD (μg/mL)	Vancomycin at end of HD (μg/mL)
1	71.1	49.7	18.4	9.8	69.9	47.6	86.5	12.4	4.8
2	70.8	47.2	10.6	4.1	71.9	53.1	77.2	9.4	1
3	105.8	60.9	8.5	4.2	104.6	57.7	110	9.7	4.4
4	65.1	48.8	8.7	4.3	91.4	61.4	100	15.7	6.5
5	73	45.1	14.2	5.7	68.2	46	97	19.1	9.3
6	92.9	52.9	10.4	4.8	83.2	59.1	110	11.8	3.6
7	95.7	60.4	13.4	6.6	94.6	68.3	136	7.8	2.9
8	94.5	58.5	14.8	7.5	82.8	65.4	102	22.8	7.7
9	96.9	51.5	13.1	7.1	86.9	48.9	100	12	4.8
Mean	85 ± 15	52.7 ± 5.8	12.4 ± 3.2	6.0 ± 1.9	85.4 ± 30.5	56.3 ± 7.9	102 ± 16.4	13.4 ± 4.9	5 ± 2.5

TABLE 3 Dialyzer clearance of vancomycin, BUN, creatinine, and β_2-microglobulin in HFHD and OL-HDF

	HFHD				OL-HDF			
	Kd_{dc} (mL/min)				Kd_{dc} (mL/min)			
Patient	Vancomycin	BUN	Creatinine	β_2-m	Vancomycin	BUN	Creatinine	β_2-m
1	75.7	138.6	123.4	45.2	153.5	178.7	156.6	120.8
2	104.2	160.5	127.5	70.1	122	165.8	126.4	95.4
3	119.9	208.4	190.2	96	132.8	220.1	183.5	99.8
4	116.1	181.6	147.3	88.9	150.7	172.7	153.6	111.6
5	102.2	184	168.2	60.5	149.4	240.8	200.6	156
6	119.9	194.2	147.2	70.3	154.1	220.4	89	103.9
7	121.4	200.6	178	70.2	146.9	19.2	178.2	113.8
8	122.7	201.1	187.7	67.5	170.4	240	215	141
9	115	191.1	175.7	84.5	141	217.7	182	96
Mean	110.8 ± 15	184 ± 22.1	160.6 ± 25	72.6 ± 15.4	146.8 ± 13.8	204.1 ± 37.2	170.7 ± 40.2	113.4 ± 24.2

P=0.025

TABLE 3 Intravenous antimicrobial dosing in critically ill patients with acute kidney injury[a]

Antimicrobial	Conventional IHD	PIRRT	CRRT
Glyco-, glycolipo-, and lipopeptides			
Dalbavancin	No adjustment	No data	No adjustment
Daptomycin	4–6 mg/kg q48h (after dialysis on dialysis day) + 50% additional dose after IHD session preceding 72-h interdialytic period	6 mg/kg q24h	6 mg/kg q24h
Oritavancin	No adjustment	No adjustment	No adjustment
Telavancin	No data	No data	No data
Teicoplanin	6–12 mg/kg q72h	No data	6–12 mg/kg q48h
Vancomycin	7.5–15 mg/kg q48h–q72h (after dialysis on dialysis day)	15 mg/kg (after PIRRT session)	10–15 mg/kg q24h–q48h or continuous infusion
Ampicillin/sulbactam	1.5 g q12h (after dialysis on dialysis day)	No data	1.5–3 g q6h–q8h
Piperacillin/tazobactam	2.25 g q8h–q12h + 0.75 g after dialysis	2.25–3.375 g q6h–q8h or continuous infusion	2.25–3.375 g q6h–q8h or continuous infusion
Oxacillin	No adjustment	No adjustment	No adjustment
Cefazolin	0.5–1 g q24h or 1–2 g q48h–q72h + 0.5–1 g after dialysis	No data	1 g q8h or 2 g q12h
Cefotetan	1–2 g q48h + 1 g after dialysis	No data	0.75 g q12h
Cefoxitin	2 g q24h–q48h + 1 g after dialysis	No data	2 g q8h–q12h
Cefuroxime	0.75–1.5 g q24h (after dialysis on dialysis day)	No data	0.75–1.5 g q8h–q12h
Cefepime	0.5–1 g q24h + 1 g after dialysis	1 g q6h	1 g q8h or 2 g q12h
Cefotaxime	2 g q24h + 1 g after dialysis	No data	1–2 g q12h–q24h
Ceftaroline	0.2–0.4 g q12h (after dialysis on dialysis day)	No data	0.4 to 0.6 g q12h
Ceftazidime	2 g q24h–q48h + 1 g after dialysis	2 g q12h	1g q8h or 2 g q12h or continuous infusion
Ceftazidime/avibactam	0.94 g q48h (after dialysis on dialysis day)	No data	1.25 g q8h
Ceftizoxime	2 g q24h + 1 g after dialysis	No data	2 g q12h–q24h
Ceftolozane/tazobactam	0.15 g q8h (after dialysis on dialysis day)	No data	No data
Ceftriaxone	No adjustment	No adjustment	No adjustment
Ceftobiprole	0.25 g q24h (after dialysis on dialysis day)	No data	No data
Doripenem	0.25 g q12h–q24h	0.5 g q8h	0.5–1 g q8h–q12h
Ertapenem	0.5 g q24h + 0.15 g after dialysis (if dose is given within 6 h pre-IHD)	1 g q24h	0.5–1 g q24h
Imipenem/cilastatin	0.25 g q12h (after dialysis on dialysis day)	0.5 g q6h	0.25–0.5 g q6h–q8h
Meropenem	0.5–1 g q24h (after dialysis on dialysis day)	0.5 g q8h	0.75 g q8h or 1.5 g q12h or continuous infusion
Meropenem/vaborbactam	0.5/0.5 g q12h	No data	No data

Seminars in Dialysis

MISTAKES WE MAKE IN DIALYSIS

Dosing: Antimicrobial Dosing in Intermittent & Continuous Hemodialysis

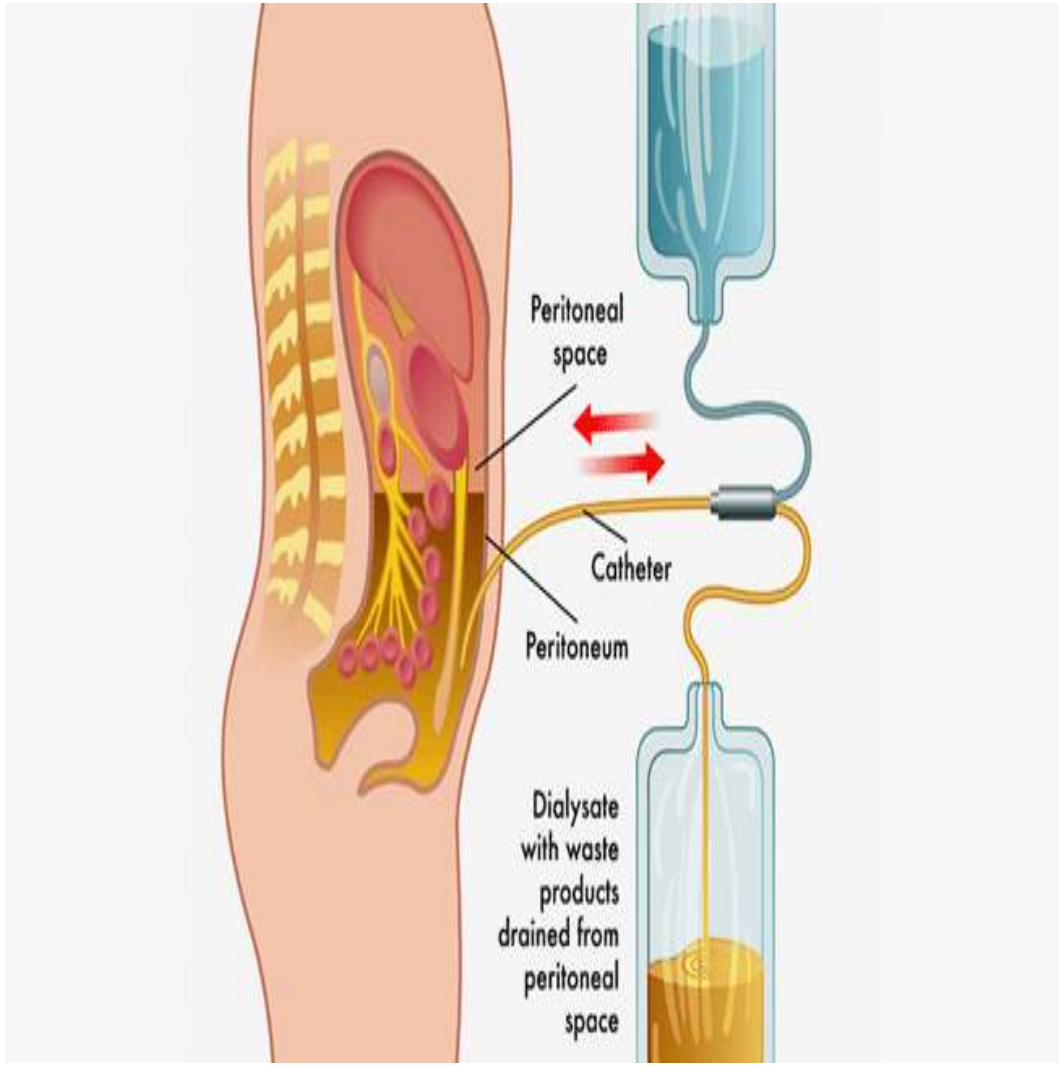
Indication	Intermittent Hemodialysis	Continuous Hemodialysis
All Indications	2 g IV x1 now and post-HD Alternative dosing for patients not on stable hemodialysis schedule: 1 g x1 now, then qPM	1 g IV q8h

P. aeruginosa Minimum Inhibitory Concentration (mg/L)

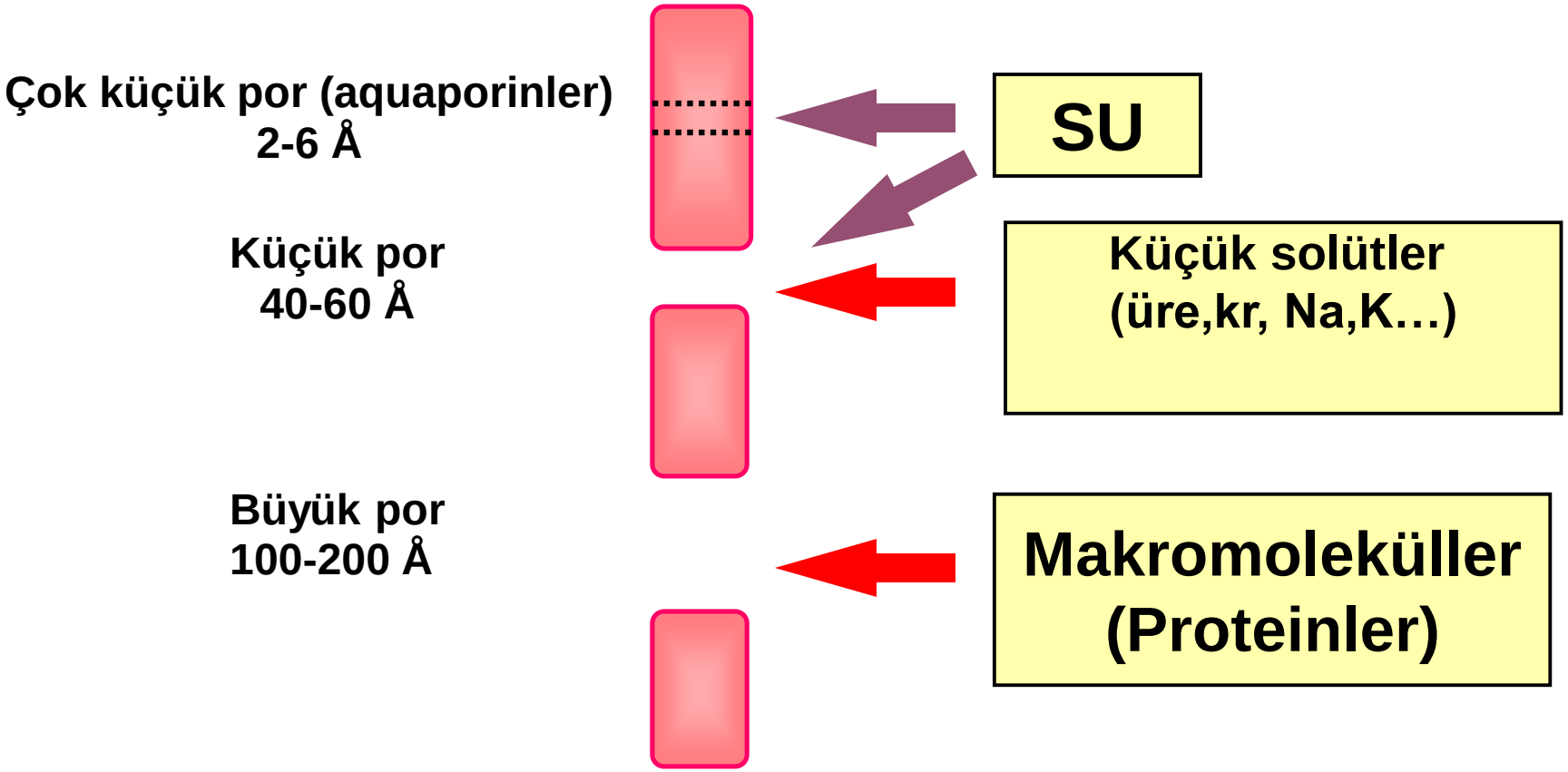
Öneri: Antibiyotik tdv hedefine ulaşmak için agresif davranma (daha yüksek doz)

CRTT Antibiyotik rejimlerinin hiçbirinde farmakodinamik hedeflere ulaşılmadı

Periton Diyalizi



Solüt ve Su Transportu Üç Por Modeli



Solüt Transport Mekanizmaları

DİFFÜZYON

- Konsantrasyon gradienti ile doğru orantılı
- Solütün büyüklüğü ile ters orantılı

KONVEKSİYON

- Ultrafiltrasyon ile doğru orantılı
- Refleksiyon katsayısı ile ters orantılı

HD ⇔ PD
Solüt ve Su Transportundaki Farklılıklar

- **Küçük molekül ağırlıklı üremik toksinler HD ile daha iyi temizlenir.**
- **Orta ve büyük molekül ağırlıklı üremik toksinler PD ile daha iyi temizlenir.**
- **UF HD'de hidrostatik basınç gradienti, PD'de ozmotik basınç gradienti ile sağlanır.**
- **Fazla miktarda sıvının kısa sürede uzaklaştırılmasında HD PD'den daha etkindir.**

Periton Diyalizinde İlaç Klirensi

- Proteine bağlanma oranı
- Dağılım
- Moleküler ağırlık
- Hidrofilisite/liposolubilite

- Periton geçirgenliği
- APD/CAPD
- Periton yüzey alanı
- Kan akımı
- PD süresi
- Diyalizat glukoz miktarı

Table 4. Automated Peritoneal Dialysis Antibiotic Pharmacokinetic Studies

Drug, Dose, and Patients Studied	Peritoneal Dialysis Prescription	Pharmacodynamic Results	Author's Conclusion	ISPD Guideline Recommendations for Intermittent dosing[61]
Cefazolin,[64,65] $N = 10$ without peritonitis (3 anuric, 7 patients with RRF 2-3 mL/min/1.73 m^2); cefazolin 15 mg/kg IV actual body weight	Three cycles of 2.5%, 2 L cycler assisted exchange (dwells 1 to 3) for 8 h, followed by two 2.5%, 2-L ambulatory dwells (dwells 4 and 5) of about 8 h each	Cefazolin 15 mg/kg IP during second ambulatory exchange would provide adequate serum and dialysate concentrations (>8 mg/L) for all dwells. Cefazolin 20 mg/kg IP during the first ambulatory exchange would be needed to provide adequate serum and dialysate concentrations throughout	Cefazolin 20 mg/kg IP every 24 h in first or second ambulatory dwell [long dwell]	15-20 mg/kg IP every 24 h
Ceftazidime,[66] $N = 11$ without peritonitis (2 anuric; RRF mean 4.4 ± 1.6 mL/min/1.73 m^2); ceftazidime 15 mg/kg IV actual body weight	Three cycles of 2.5%, 2-L cycler-assisted exchange (dwells 1 to 3) for 8 h, followed by two 1.5%, 2-L ambulatory dwells (dwells 4 and 5) of about 8 h each	Serum and dialysate concentrations remained greater than MIC 8 mg/L (sensitive organisms) for the entire 24-h interval	Ceftazidime 15 mg/kg IV or 20 mg/kg IP every 24 h in long dwell	1000-1500 mg IP every 24 h
Meropenem,[67] $N = 6$ without peritonitis (RRF median 3 mL/min); meropenem 500 mg IV (infusion over 30 min) or IP	15-h long dwell with 7.5% icodextrin, 1.5 L, followed by six 2-L cycles over 9 h with average glucose concentrations 1.36 to 2.72%	Target 40% T > MIC; IP meropenem 0.5 g resulted in T > MIC serum levels adequate to treat organisms up to MIC ≤ 4 mg/L in 5 of 6 patients and resulted T > MIC in dialysate concentration for bacteria with MIC up to 8 mg/L; IV meropenem 0.5 g resulted in adequate serum level to treat organisms up to MIC 4 mg/L but failed to reach adequate T > MIC for clinically relevant pathogens in dialysate.	Intermittent dosing with meropenem 0.5 g IP once daily; meropenem 0.5 g IV once daily resulted in poor IP exposure	1 g IP every 24 h
Fosfomycin,[68] $N = 8$ without peritonitis (RRF median 3 mL/min/1.73 m^2); fosfomycin 4 g IV or IP	15-h long dwell with 7.5% icodextrin, 2 L, followed by six 2.5-L cycles over 9 h with Dianeal PD 4	50% T > MIC up to 64 mg/L in serum and dialysate observed after IP administration; 50% T > MIC up to 64 mg/L in serum but not dialysate after IV administration	Intermittent dosing with fosfomycin 4 g IP every 24 h; fosfomycin 4 g IV resulted in insufficient fosfomycin concentrations in the peritoneal fluid	No recommendation
Piperacillin,[69] $N = 8$ noninfected (RRF median 1.2 mL/min/1.73 m^2); piperacillin 35 mg/kg IV actual body weight	Three cycles of 2.5%, 2-L cycler-assisted exchange (dwells 1 to 3) for 8 h, followed by two 2.5%, 2-L ambulatory dwells (dwells 4 and 5) of about 8 h each	Piperacillin end of dwell concentrations remained above the MIC for sensitive organisms (8 mg/L)	Piperacillin 4000 mg IV q12 h; intermittent piperacillin 4000 mg IP is not recommended as this dosing scheme would not result in adequate serum and dialysate concentrations	No recommendation

(Continued)

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Peritoneal Dialysis
Suzuki H (ed): Home Dialysis in Japan.
Contrib Nephrol. Basel, Karger, 2012, vol 177, pp 30–37

Appropriate Drug Dosing in Patients Receiving Peritoneal Dialysis

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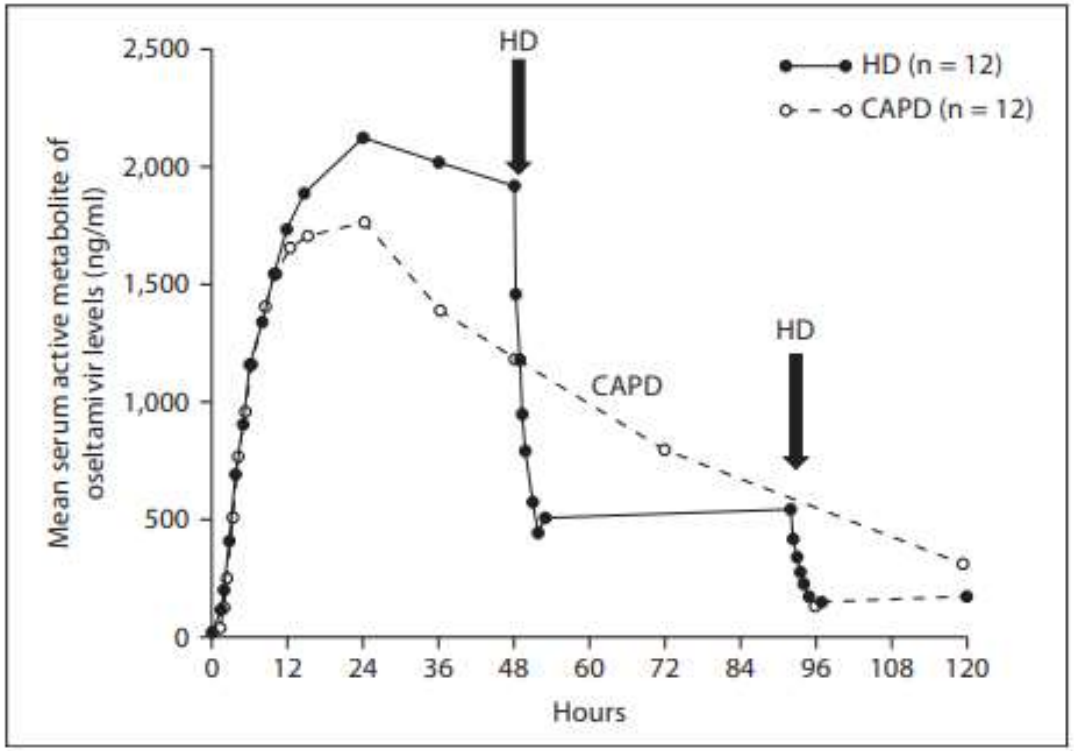

Fig. 2. Consecutive change in mean serum levels of active metabolite of patients undergoing CAPD and HD [7].

- Antibiyotik düzeyleri HD'e göre periton diyalizinde daha uzun süre sabit seyredebilir
- Proteine az bağlanan ve dağılım hacmi düşük olan antibiyotikler PD ile uzaklaştırılabilir.

Perit Dial Int. 2016
Contrib Nephrol. 2012

Table 1. PK-PD parameters and antibiotic dosing recommendation for HD, CAPD and APD patients [8]

	Cefazolin	Cefepim	Tobramycin	Vancomycin
PK-PD parameters				
Urinary excretion rate	85%	80%	80%	90%
Protein binding rate	80%	12%	Less than 5%	34–55%
Volume of distribution	0.22 L/kg	0.25 L/kg	0.28 L/kg	0.9–1.0 L/kg
Molecular weight	566.6 Da	571.5 Da	467.5 Da	1485.7 Da
PK-PD parameters which quantify the activity of an antibiotic	Time above MIC (time dependent)	Time above MIC (time dependent)	Cmax/MIC (concentration dependent)	AUC/MIC
Dosing recommendation				
Hemodialysis	500–1000 mg after HD	1000 mg after HD	5 mg/kg after HD	LD 20 mg/kg, MD 10 mg/kg after HD
CAPD Intermittent (once daily)	15 mg/kg	1 g	0.6 mg/kg	15–30 mg/kg every 5–7 days
CAPD Continuous (mg/L, all exchabges)	LD 500 mg/L, MD 125 mg/L IP	LD 500 mg/L, MD 125 mg/L IP	LD 8 mg/L, MD 4 mg/L IP	LD 1000 mg/L, MD 25 mg/L IP
APD Intermittent (mg/kg)	20 mg/kg IP once per day, in long day dwell	1 g IP one exchange per day	LD 1.5 mg/kg IP in long dwell, then 0.5 mg/kg IP each day in long day dwell	LD 30 mg/kg in long dwell, repeat dosing 15 mg/kg IP in long dwell every 3–5 days, following levels

PK-PD = Pharmacokinetics-pharmacodyamics; MIC = minimum inhibitory concentration; AUC = Area Under the serum concentration time Curve; Cmax = peak serum level; LD = loading dose, MD = maintenanc dose in mg; IP = intraperitoneal administration.
Residual renal function (defined as >100 mL/day urine output) should be empirically increased by 25%.

Contrib Nephrol. Basel, Karger, 2012.

Take home notes

- ***Renal replasman tedavi şekli mutlaka bilinmeli***
- ***Renal replasman tedavi şekilleri arasındaki geçişler yakın takip edilmeli***
- ***Hastanın rezidüel renal fonksiyonu olup olmadığı dikkate alınmalı ; RRF olan hastalarda daha yüksek antibiyotik dozlarına ihtiyaç olabileceği***
- ***RRT şekline göre AB için öneriler takip edilmeli fakat***
  - ***Hastanın klinik iyilik hali***
  - ***Laboratuvar, görüntüleme ve mikrobiyolojik tetkikler***

Teşekkürler