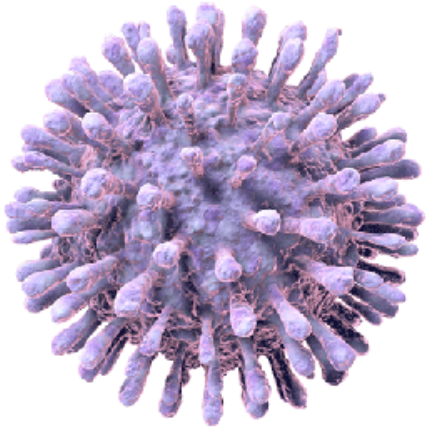
HİV ve Komorbidite
- Renal Sorunlar -



Doç. Dr. Sabahat Alışır Ecder
İstanbul Medeniyet Üniversitesi Tıp Fakültesi
Nefroloji Bilim Dalı

Tremendous progress against AIDS over the past 15 years has inspired a global commitment to end the epidemic by 2030.

36.9 million

People living with HIV (2017)

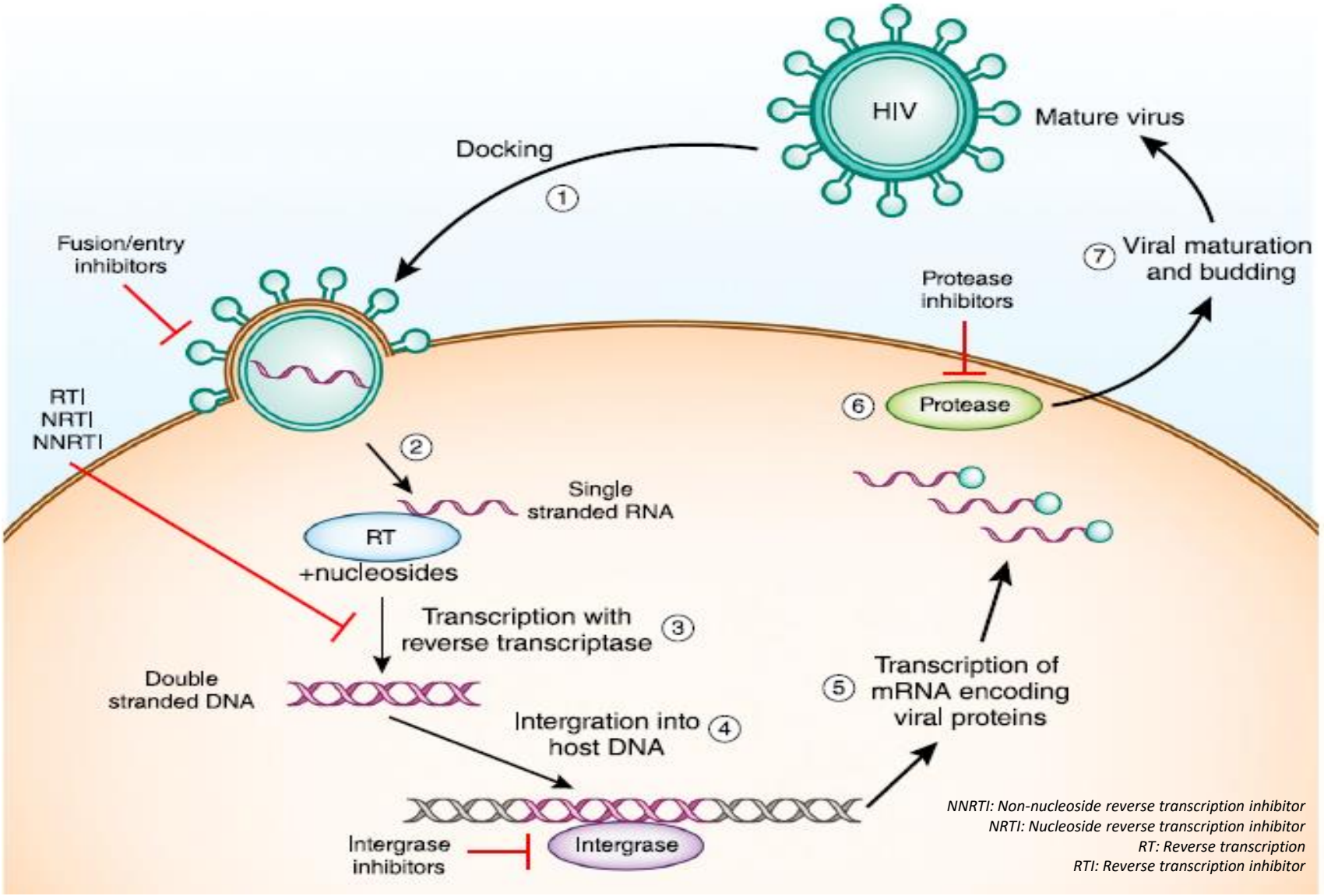
21.7 million

People living with HIV on antiretroviral therapy (2017)

1.8 million

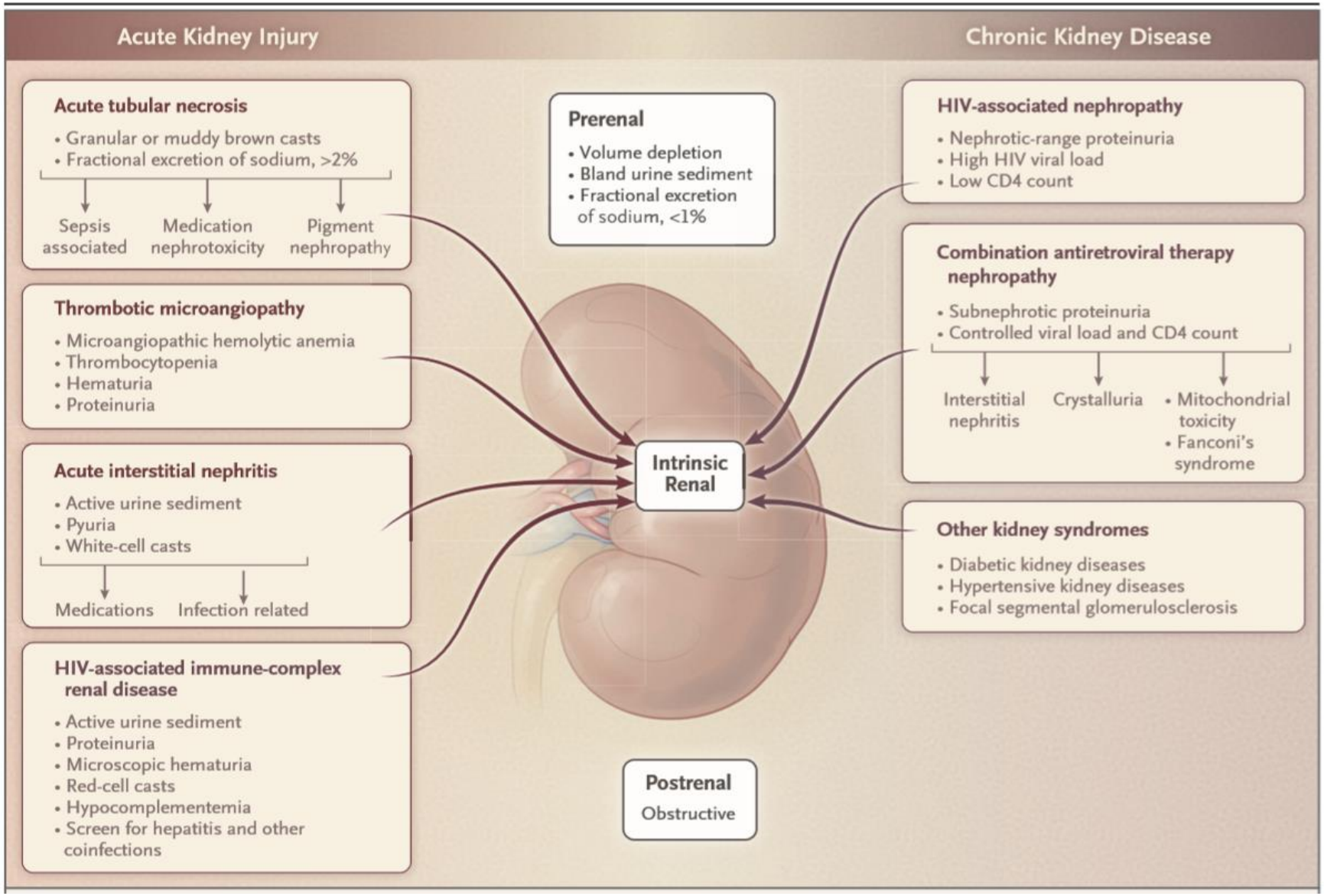
People newly infected with HIV (2017)

HIV Tedavisi – Tarihsel Süreç



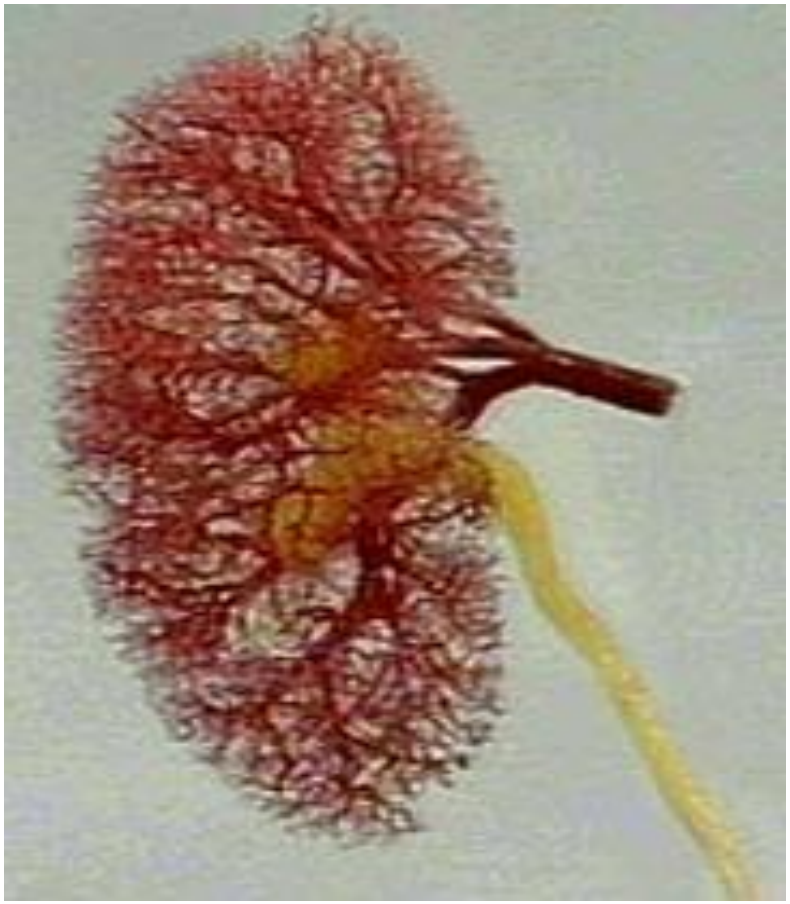
Atta et al: Clin J Am Soc Nephrol 14: 2018

HIV ile İlişkili Böbrek Hastalıkları



Cohen et al: N Engl J Med 2017:377: 2363-2374

Akut Böbrek Hasarı



- 48 saat içinde serum kreatinin konsantrasyonunun ≥0.3 mg/dL (≥26.5 µmol/L) artışı

  veya

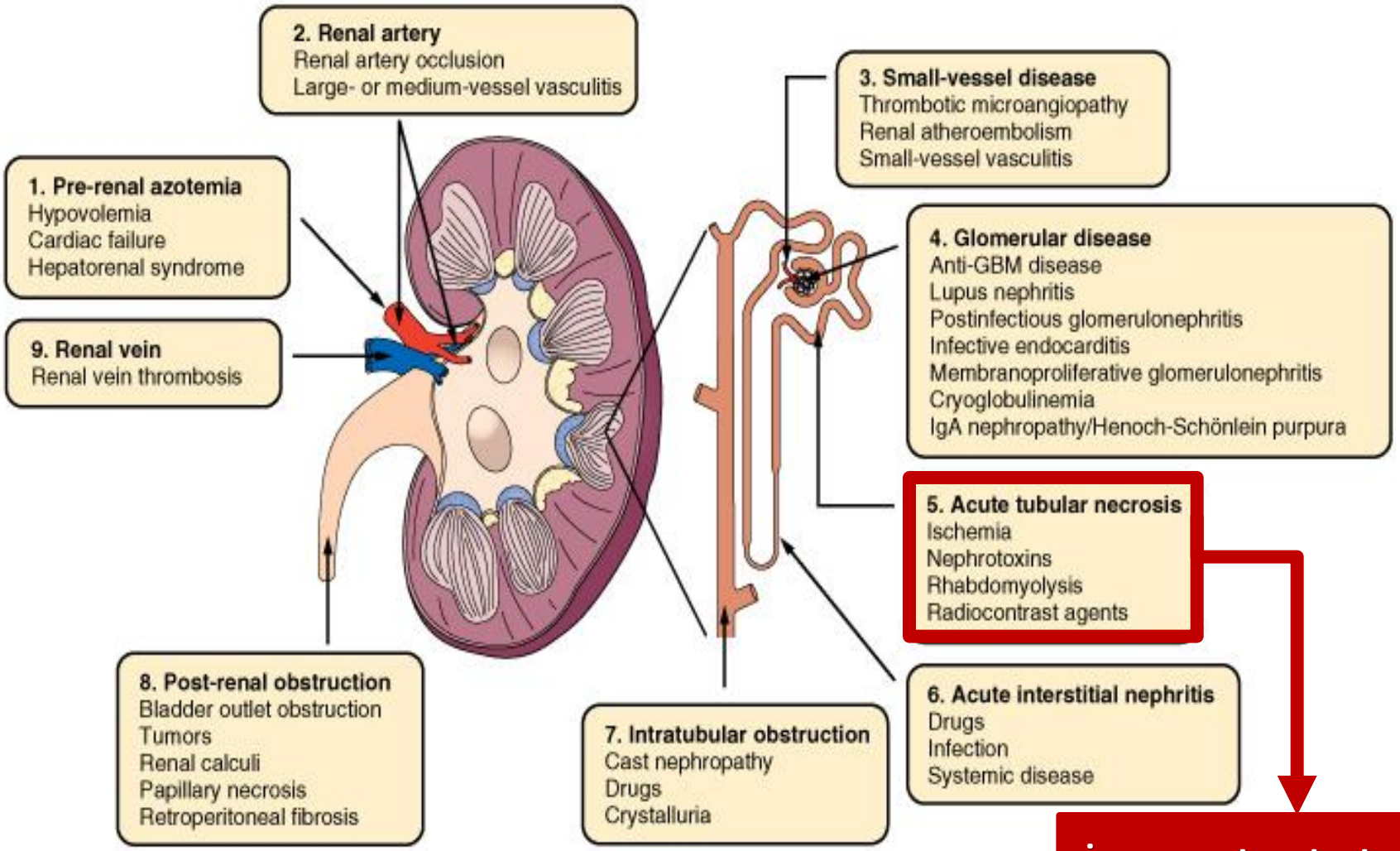
- Son 7 gün içinde bazal serum kreatinin konsantrasyonunun ≥1.5 kat artışı

  veya

- İdrar hacminin 6 saat boyunca <0.5 ml/kg/saat olması

KDIGO (Kidney Disease Improving Global Outcomes) 2012 Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Vol 2, Issue 1, March 2012

Akut Böbrek Hasarının Nedenleri



İntrarenal nedenlerin %85'inden sorumlu

Johnson, Feehally, Floege: Comprehensive Clinical Nephrology, 2015

Kronik Böbrek Hastalığının Tanımı

Böbrek yapısında veya işlevlerinde 3 aydan daha uzun süren bozukluklar

Criteria for CKD (either of the following present for >3 months)

Markers of kidney damage (one or more)	Albuminuria (AER ≥30 mg/24 hours; ACR ≥30 mg/g [≥3 mg/mmol]) Urine sediment abnormalities Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by histology Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR <60 ml/min/1.73 m^2 (GFR categories G3a-G5)

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

KDIGO (Kidney Disease Improving Global Outcomes) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Vol 3, Issue 1, January 2013

Kronik Böbrek Hastalığının Evrelemesi

GFR categories in CKD

GFR category	GFR (ml/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Albuminuria categories in CKD

Category	AER (mg/24 hours)	ACR (approximate equivalent) (mg/mmol)	ACR (approximate equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol]).

KDIGO (Kidney Disease Improving Global Outcomes) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Vol 3, Issue 1, January 2013

Kronik Böbrek Hastalığının Evrelemesi

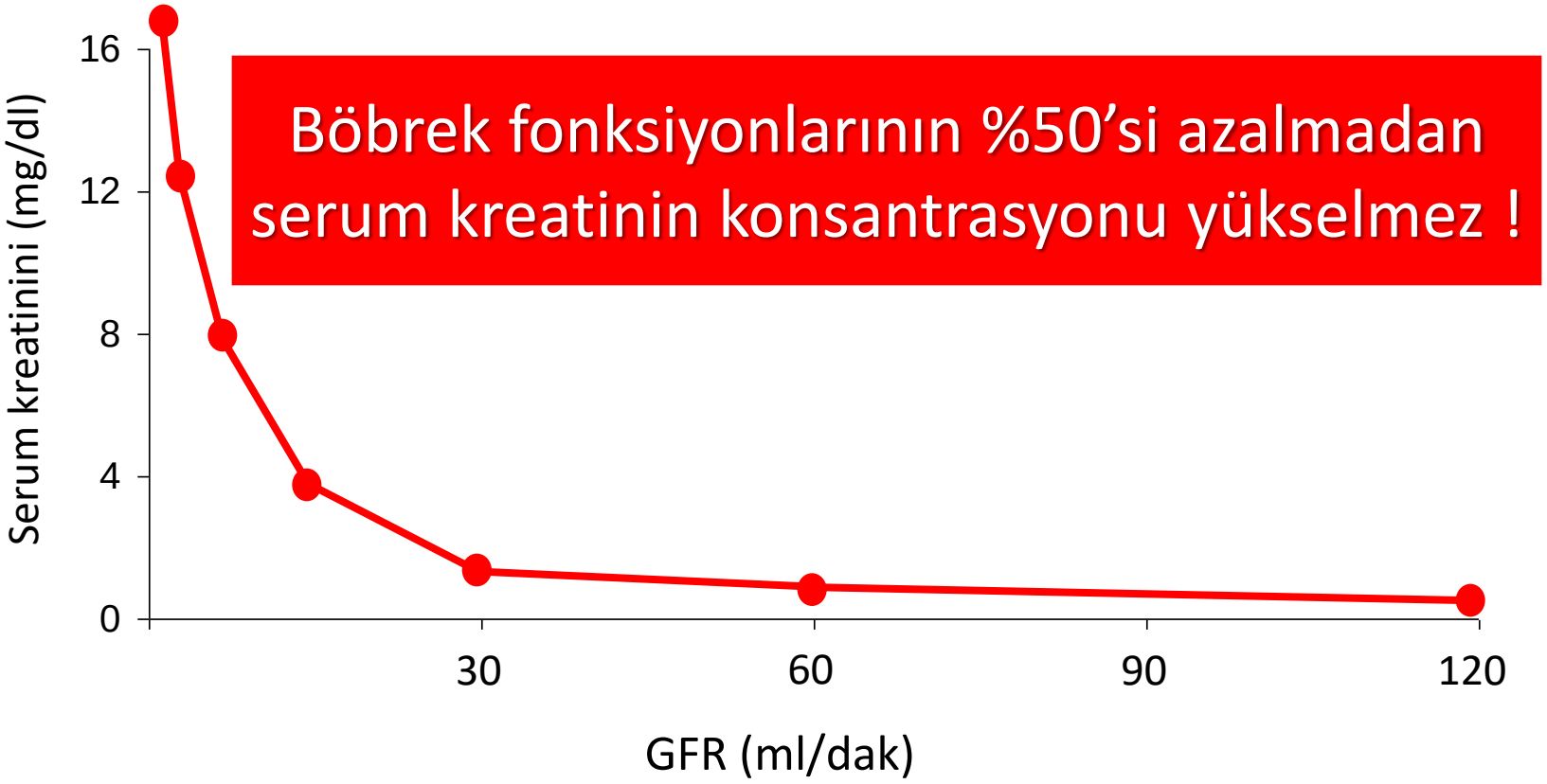
Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

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			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

KDIGO (Kidney Disease Improving Global Outcomes) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Vol 3, Issue 1, January 2013

Serum Kreatinini – GFR İlişkisi



Böbrek fonksiyonlarının %50'si azalmadan serum kreatinin konsantrasyonu yükselmez !

Kreatinin klirensi hesaplanmalı

GFR'nin Hesaplanması için Kullanılan Formüller

Cockroft-Gault formula[5]

Male $C_{cr}\ (ml/min) = \dfrac{(140 - age) \times weight}{72 \times S_{cr}(mg/dl)}$ or $C_{cr}\ (ml/min) = \dfrac{(140 - age) \times weight}{0.814 \times S_{cr}(mmol/l)}$

Female $C_{cr}\ (ml/min) = \dfrac{(140 - age) \times weight \times 0.85}{72 \times S_{cr}(mg/dl)}$ or $C_{cr}\ (ml/min) = \dfrac{(140 - age) \times weight \times 0.85}{0.814 \times S_{cr}(mmol/l)}$

MDRD study equation (four-variable equation)[7]

$$GFR\ (ml/min/1.73\ m^2) = 186 \times S_{cr}\ (mg/dl)^{-1.154} \times Age^{-0.203} \times 0.742\ (\text{if female}) \times 1.210\ (\text{if black})$$

or

$$GFR\ (ml/min/1.73\ m^2) = 32{,}788 \times S_{cr}\ (mmol/l)^{-1.154} \times Age^{-0.203} \times 0.742\ (\text{if female}) \times 1.210\ (\text{if black})$$

MDRD Study Equation for Use with Standardized Serum Creatinine (Four-variable equation) [7]

$$GFR\ (ml/min/1.73\ m^2) = 175 \times \text{Standardized } S_{cr}(mg/dl)^{-1.154} \times age^{-0.203} \times 0.742\ (\text{if female}) \times 1.210\ (\text{if black})$$

or

$$GFR\ (ml/min/1.73\ m^2) = 30{,}849 \times \text{Standardized } S_{cr}(mmol/l)^{-1.154} \times age^{-0.203} \times 0.742\ (\text{if female}) \times 1.210\ (\text{if black})$$

CKD-EPI Equation for Use with Standardized Serum Creatinine [12]

$$GFR\ (ml/min/1.73\ m^2) = 141 \times \min(S_{cr}/k, 1)^{a} \times \max(S_{cr}/k, 1)^{1.209} \times 0.993^{Age} \times 1.018\ (\text{if female}) \times 1.157\ (\text{if black})$$

where k is 0.7 for females and 0.9 for males, a is –0.329 for females and –0.411 for males, min indicates the minimum of S_{cr}/k or 1, and max indicates the maximum of S_{cr}/k or 1.

Female
- ≤ 0.7 ⊠ $GFR = 144 \times (S_{cr}/0.7)^{-0.329}$
- > 0.7 ⊠ $GFR = 144 \times (S_{cr}/0.7)^{-1.209}$

Male
- ≤ 0.9 ⊠ $GFR = 141 \times (S_{cr}/0.9)^{-0.411}$
- > 0.9 ⊠ $GFR = 141 \times (S_{cr}/0.9)^{-1.209}$

$\times (0.993)^{Age}$ $\times 1.157$ (if black)

*Age in years, weight in kg, S_{cr}, serum creatinine

HİV İnfeksiyonuna veya Tedavisine Bağlı Böbrek Hastalıkları

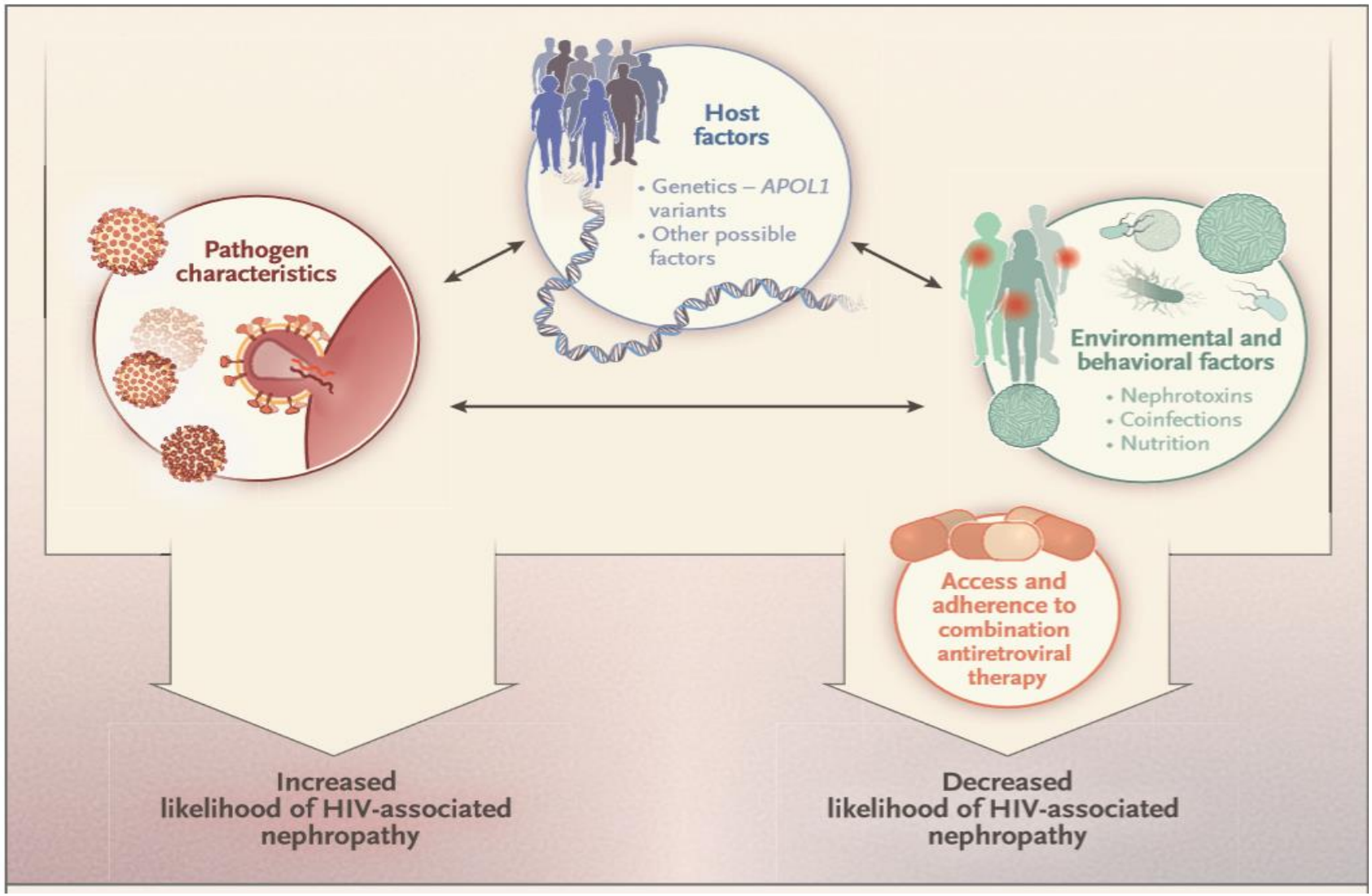
	Entity	Frequency	Associations
Glomerular	HIV-associated nephropathy (HIVAN)	Common	African descent; often advanced HIV disease
	HIV-associated immune complex kidney disease (HIVICK)	Common	All ethnic backgrounds
	Thrombotic microangiopathy	Uncommon	
	Membranoproliferative glomerulonephritis, with or without cryoglobulin-associated vasculitis	Rare	Hepatitis C; enfuvirtide
	Membranous nephropathy	Rare	Hepatitis B
	Fibrillary and immunotactoid glomerulopathies	Rare	
	Amyloid nephropathy (AA type)	Rare	
	Minimal change nephropathy	Rare	Nonsteroidal antiinflammatory medication
Tubular	Acute kidney injury	Moderately common	Aminoglycosides, cidofovir, foscarnet
	Proximal tubule injury (Fanconi syndrome)	Moderately common	Tenofovir disoproxil fumarate, adefovir, cidofovir, didanosine
	Diabetes insipidus	Uncommon	Amphotericin, tenofovir disoproxil fumarate, didanosine, abacavir
	Chronic tubular injury	Moderately common	Amphotericin, cidofovir, adefovir, tenofovir disoproxil fumarate
	Crystal nephropathy	Uncommon	Indinavir, atazanavir; sulfadiazine, ciprofloxacin, intravenous acyclovir
Interstitial	Interstitial nephritis	Uncommon	Allergy to β-lactam, sulfa, ciprofloxacin, rifampin, proton pump inhibitor, allopurinol, phenytoin; also causes of crystal nephropathy listed earlier, BK virus; generally advanced disease Immune reconstitution inflammatory syndrome; generally advanced disease; after initiation of antiretroviral therapy

Kopp, Naicker: Comprehensive Clinical Nephrology, 2019

HİVAN
(HIV-Associated Nephropathy)

- İlk olarak 1984 yılında tanımlanmıştır.
- Afrika kökenlilerde beyazlara göre daha sıktır.
- İlerleyici böbrek yetersizliği ve proteinüri görülür.
- HİV ile böbrek epitel hücrelerinin infeksiyonudur.
- Genetik duyarlılığı APOL1 geni olanlarda daha sıktır.
- İnsidansı antiretroviral tedavisi sonrası giderek azalmıştır.

HİVAN'ın Patogenezi

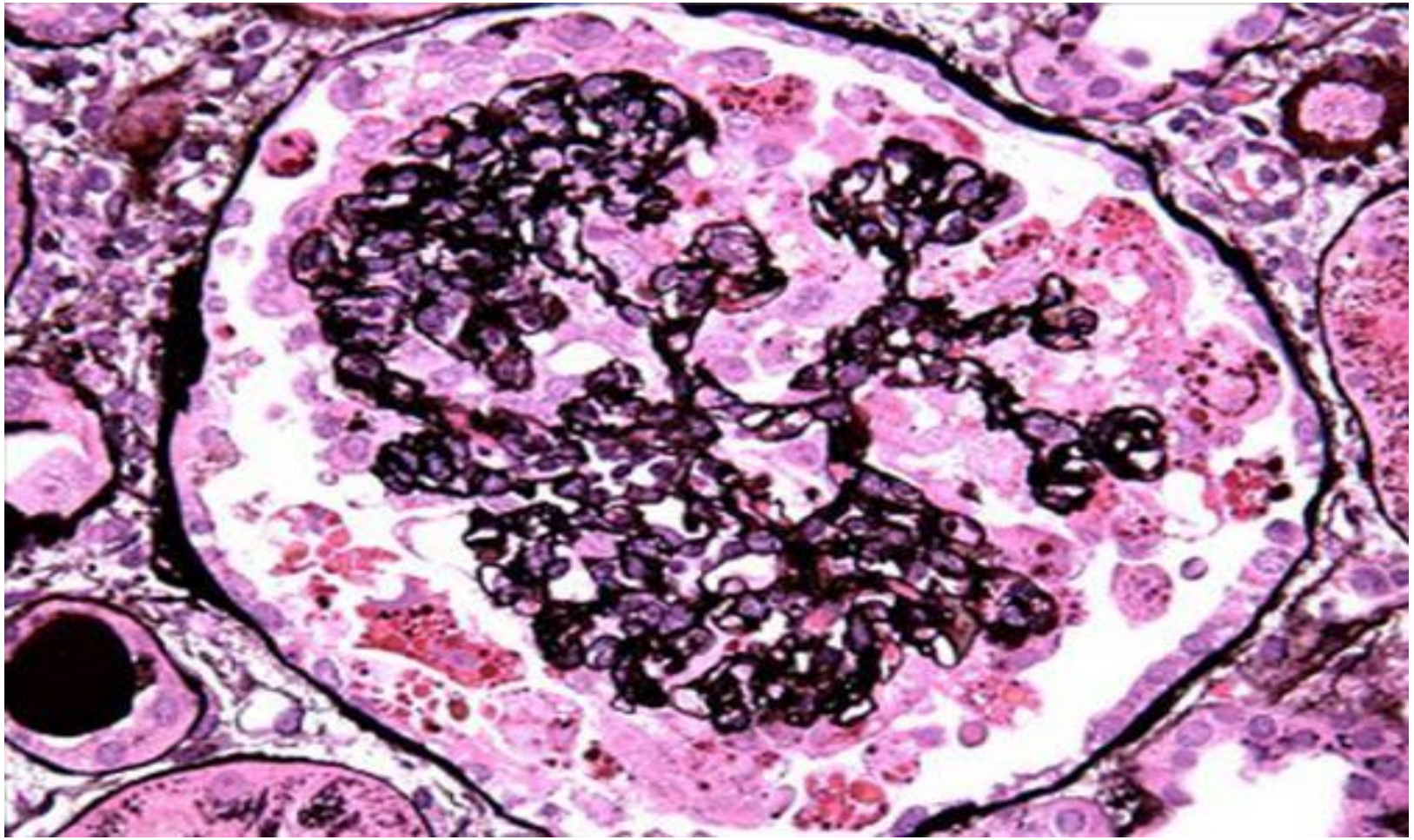


Cohen et al: N Engl J Med 2017:377: 2363-2374

HİVAN'ın Klinik Bulguları

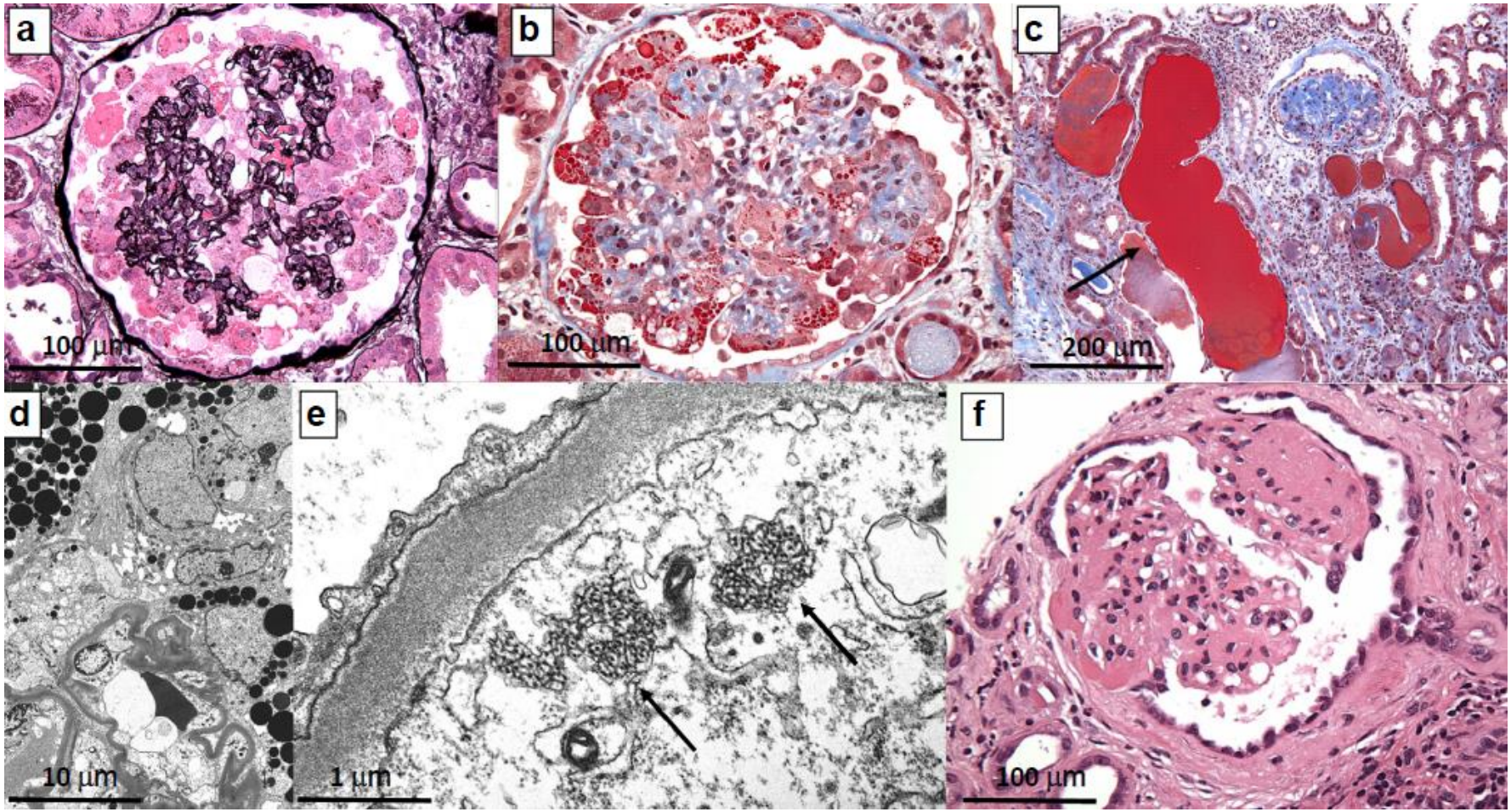
- Afrika kökenliler
- İlerlemiş HİV hastalığı
- Hipertansiyon
- Ödem
- Hematüri
- Nefrotik düzeyde proteinüri
- Böbrek fonksiyonlarında hızlı bozulma

HİVAN



Glomerüler kapiller lümen bazal membran hücrelerinin kollapsı ile tıkanması ve glomerüler epitelin hipertrofi ve hiperplazisi

HİVAN



- Kollapsing fokal segment glomeruloskleroz; tubuluslarda dilatasyon; yoğun interstisyel inflamasyon; tubuloretiküler inklüzyonlar

HİVAN'ın Tedavisi

- ART almıyorsa hemen başlanır.
- ART alan hasta toksisite açısından gözden geçirilir/değiştirilir.
- ACE inhibitörleri ve ARB (proteinürik ve/veya hipertansif hastalarda)
- Glukokortikoidler, renal fonksiyonlar ve proteinüri üzerine etki?
- Takipte nefrotoksik ilaçlardan sakınmak gerekir.

Nephrol Dial Transplant (2006) 21: 2809–2813
doi:10.1093/ndt/gfl337
Advance Access publication 24 July 2006

Original Article

NDT
Nephrology Dialysis Transplantation

Antiretroviral therapy in the treatment of HIV-associated nephropathy

Mohamed G. Atta[1], Joel E. Gallant[2], M. Hafizur Rahman[1], Nagapradeep Nagajothi[3], Lorraine C. Racusen[4], Paul J. Scheel[1] and Derek M. Fine[1]

Table 1. Baseline characteristics of the study patients[a]

	Group I (ART- treated) $n=26$	Group II (ART-untreated) $n=10$	Excluded, $n=16$	P-value[a]
Age (years)	42.8 (±8.3)	37.2 (±4.5)	39.6 (±8.9)	0.05
Race (% black)	96	90	100	0.47
Sex (% females)	42	20	50	0.21
Hypertension (%)	65	40	50	0.17
Diabetes (%)	7.7	–	12.5	0.37
IDU (%)	65	50	50	0.40
Hepatitis-B (%)	4.2	22.2	0	0.11
Hepatitis-C (%)	64	55.6	50	0.65
Serum creatinine (mg/dl)	4.7 (±1.9)	7.8 (±2.9)	10.4 (±3.7)	<0.001
GFR (ml/minute/1.73 m^2)	20 (±13)	14 (±14)	7 (+4)	0.18
CD4+ (cells/mm^3)	160 (±170)	161 (±130)	155 (±136)	0.99
Proteinuria (g/day)	7.2 (±6.1)	6 (±4.2)	9.4 (±10)	0.57
Albumin (g/dl)	2.8 (±1.1)	2.4 (±0.7)	2.1 (±0.8)	0.28
ACE-I therapy (%)	4.4	29	6.25	0.06
Steroid therapy (%)	65	60	31	0.76

[a]Indicates the difference between group I and II.
All units are mean ± SD unless otherwise indicated.
IDU, injection drug use; GFR, glomerular filtration rate; ACE-I, angiotensin-converting enzyme inhibitor.

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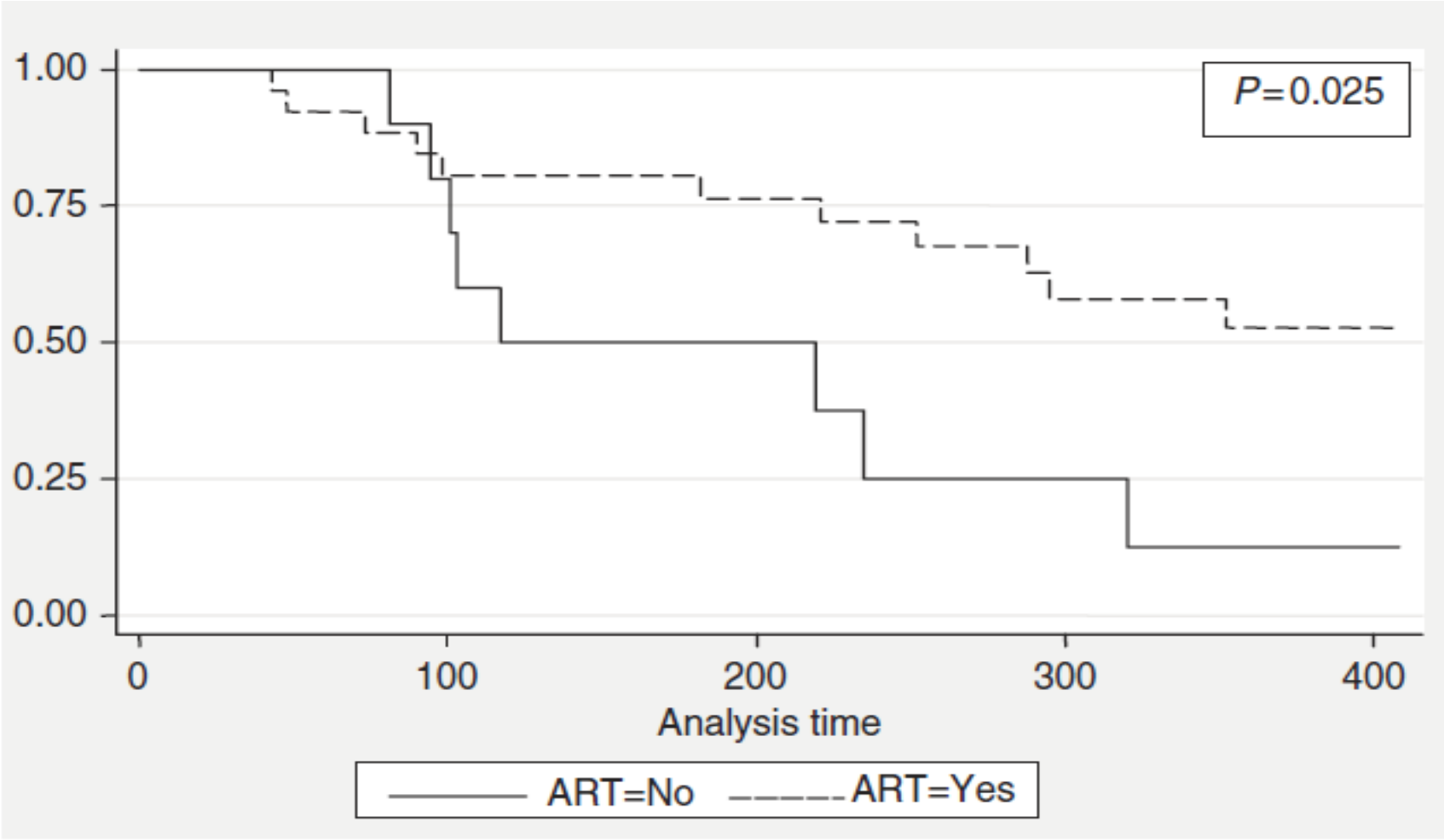

Atta et al: Nephrol Dial Transplant 21: 2809-2813, 2006

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Kopp, Naicker: Comprehensive Clinical Nephrology, 2019

HIVICK

(HIV Immune Complex Kidney Disease)

Table 1 | Pathologic classification of HIV-related kidney diseases

I. Glomerular-dominant[a]

a. Podocytopathies (all characterized by extensive foot process effacement)[b]
   i. Classic HIVAN
   ii. FSGS (NOS) in the setting of HIV
   iii. Minimal change disease in the setting of HIV
   iv. Diffuse mesangial hypercellularity in the setting of HIV
   v. Other podocytopathy in the setting of HIV

b. Immune complex-mediated glomerular disease[a]
   i. IgA nephropathy in the setting of HIV
   ii. Lupus-like glomerulonephritis in the setting of HIV
   iii. Lupus nephritis in the setting of HIV
   iv. Membranous nephropathy in the setting of HIV
      - Indicate whether HBV positive, HCV positive, PLA2R positive (should not preclude workup for other secondary causes)
   v. Membranoproliferative pattern glomerulonephritis in the setting of HIV
      - Indicate whether HCV positive (should not preclude workup for other secondary causes)
   vi. Endocapillary proliferative and exudative glomerulonephritis in the setting of HIV
      - Post-streptococcal, staphylococcal-associated, other
   vii. Fibrillary or immunotactoid glomerulonephritis in the setting of HIV
   viii. Other immune complex disease in the setting of HIV

Swanepoel et al. Kidney Int 93: 545-559, 2018

HIVICK
(HIV Immune Complex Kidney Disease)

- Mezangial, subendotelyal, intra ve epimembranöz immun kompleks depolanmaları
- İmmun kompleksler HİV antijeni ve antikor (gp 120 HİV'e karşı) içerir.
- Depolanmalar çok yoğun olabilir (lupus benzeri GN)
- İnterstisyel infiltrasyon sıktır. HİVAN'a göre daha fazla B hücreleri görülür.
- Böbrek yetersizliğinin ilerlemesi HİVAN'a göre daha yavaştır.

HIVICK
(HIV Immune Complex Kidney Disease)

- Klinikte, böbrek yetersizliği, mikroskopik hematüri, hipertansiyon ve nefrotik sendrom ile kendini gösterir.
- Hipokomplementemi ve kriyoglobulinemi görülebilir.
- MPGN veya daha seyrek olarak membranöz nefropati şeklindedir.
- Kesin tanı için böbrek biyopsisi gerekir.

HİV ile İlişkili Glomerulonefrit

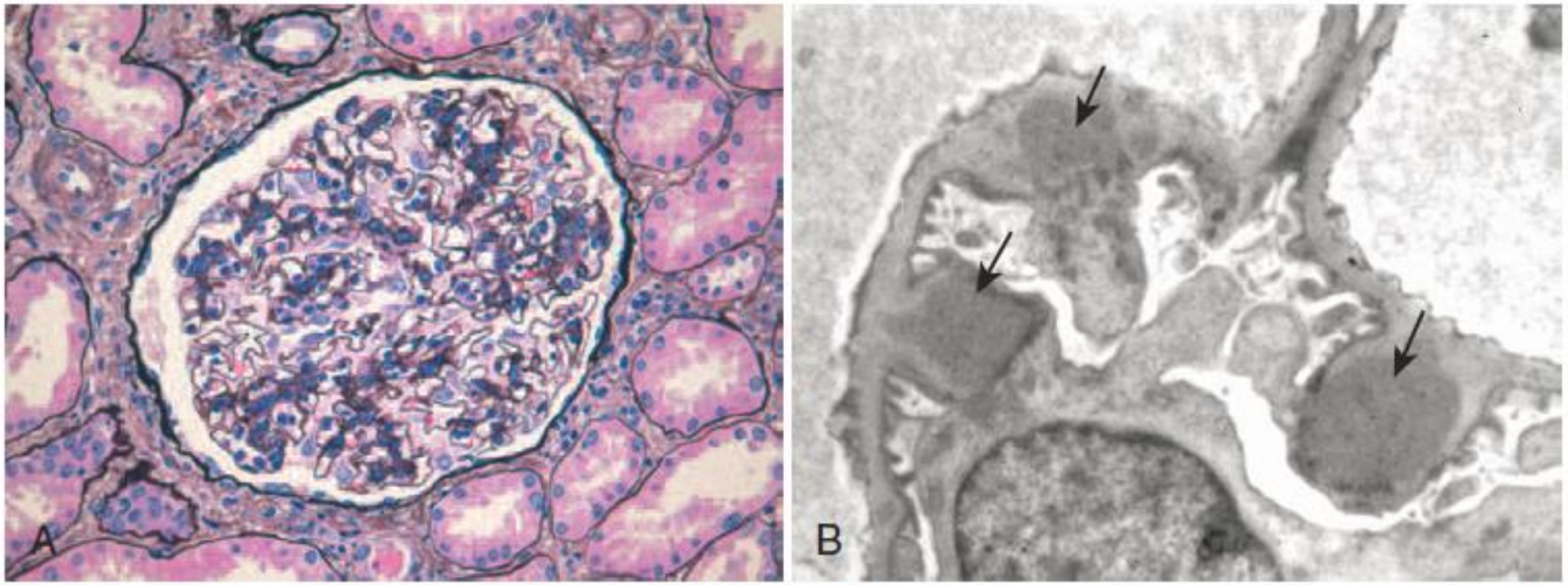

Fig. 56.2 HIV-associated glomerulonephritis. This HIV-positive patient presented with microhematuria and non-nephrotic proteinuria with normal renal function. Renal biopsy shows mild mesangial expansion (A), with mesangial and paramesangial deposits, together with varying numbers of subepithelial-based deposits *(arrows)*, resulting in the "ball-and-cup" appearance (B). (Courtesy Professor Stewart Goetsch, University of the Witwatersrand, Johannesburg, South Africa.)

Comparison of Risk Factors and Outcomes in HIV Immune Complex Kidney Disease and HIV-Associated Nephropathy

Matthew C. Foy, Michelle M. Estrella,† Gregory M. Lucas,† Faryal Tahir,§ Derek M. Fine,† Richard D. Moore,‡‖ and Mohamed G. Atta‡*

Summary

Background and objectives HIV-associated nephropathy (HIVAN) is well described, but the clinical features of a group of renal pathologies characterized by Ig or immune complex depositions referred to as HIV-associated immune complex kidney disease (HIVICK) have not been well established. The objective of this study is to assess risk factors for HIVICK compared with contemporaneous control participants.

Design, setting, participants, & measurements A nested case-control study of 751 HIV-infected patients followed from January 1996 to June 2010 was conducted. Groups were compared using the chi-squared test or rank-sum analysis. Conditional logistic regression was used to estimate odds ratios (ORs) for HIVICK. Incidences of overall ESRD and with/without combined antiretroviral therapy (cART) exposure were calculated.

Results HIVICK patients were predominantly African American (92%). Compared with matched controls, patients with HIVICK were more likely to have HIV RNA >400 copies/ml (OR, 2.5; 95% confidence interval [95% CI], 1.2 to 5.2), diabetes (OR, 2.8; 95% CI, 1.1 to 6.8), and hypertension (OR, 2.3; 95% CI, 1.2 to 4.5). Compared with HIVAN, patients with HIVICK had more antiretroviral therapy exposure, lower HIV viral loads, and higher CD4 and estimated GFR. ESRD was less common in the HIVICK versus the HIVAN group (30% versus 82%; $P<0.001$), and the use of cART was not associated with ESRD in HIVICK patients (25% versus 26; $P=0.39$).

Conclusions HIVICK was predominantly observed in African-American patients and associated with advanced HIV disease. ESRD incidence is lower in HIVICK patients compared with those with HIVAN. Unlike HIVAN, cART use was not associated with the incidence of ESRD in HIVICK.

Clin J Am Soc Nephrol 8: 1524–1532, 2013. doi: 10.2215/CJN.10991012

*Division of Internal Medicine, Louisiana State University Health Science Center, Baton Rouge, Louisiana; Divisions of ‡Nephrology, †Infectious Diseases, and ‖General Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland; and §Dow University of Health Sciences, Karachi, Pakistan

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Comparison of Risk Factors and Outcomes in HIV Immune Complex Kidney Disease and HIV-Associated Nephropathy

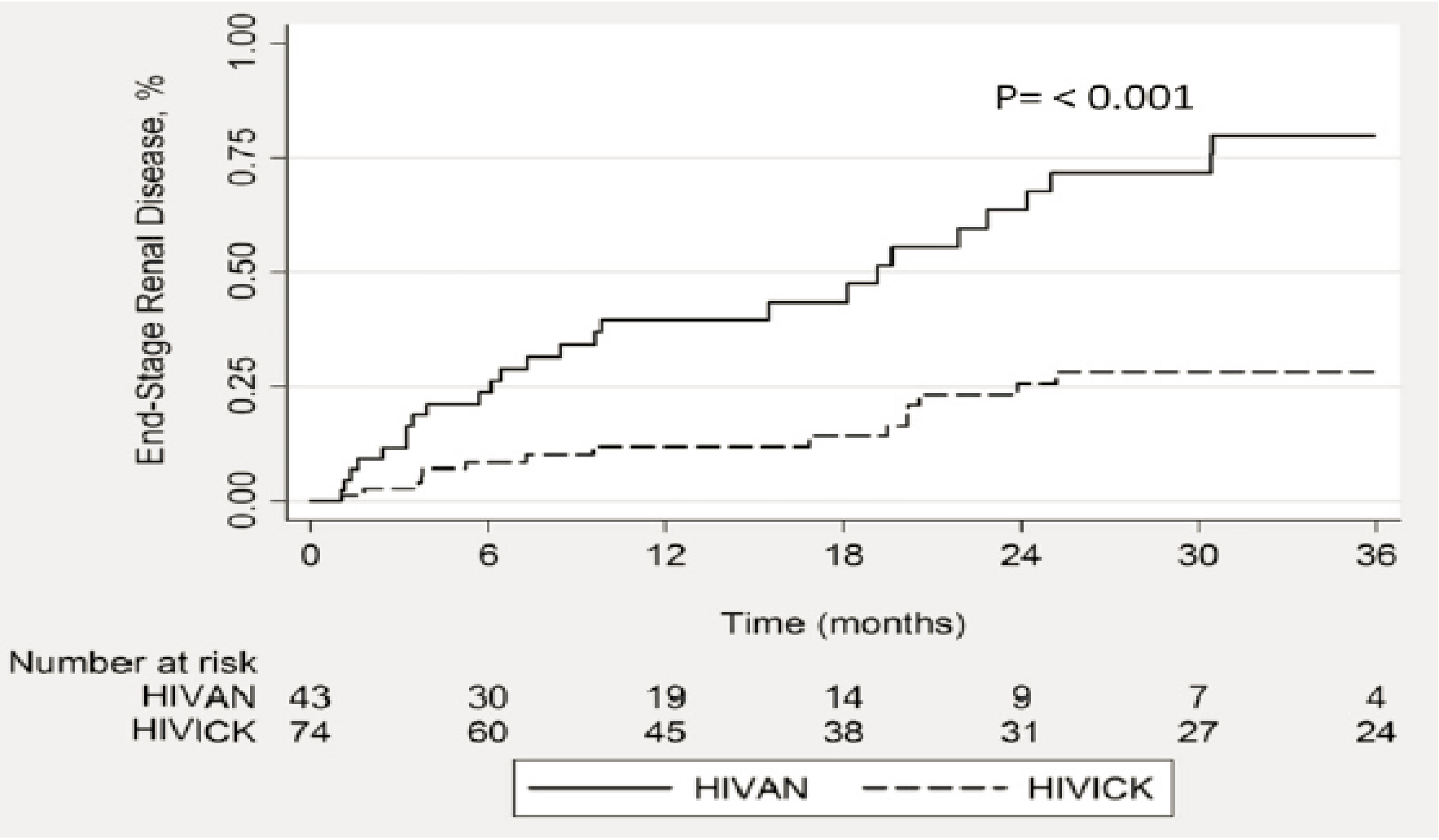
Table 2. Baseline characteristics of patients with HIVICK and HIVAN and their respective controls

Characteristic	HIVICK		HIVAN	
	Patients (n=83)	Controls (n=332)	Patients (n=56)	Controls (n=224)
Age (yr)	46 (41–51)	45 (41–51)	42 (36–46)	42 (36–47)
Men	56 (67)	224 (67)	33 (59)	132 (59)
African-American race	77 (92)	246 (74)	54 (96)	165 (77)
Injection drug use	53 (64)	156 (47)	28 (50)	103 (46)
Diabetes	13 (16)	24 (7)	6 (11)	14 (6)
Hypertension	42 (51)	95 (29)	18 (32)	42 (19)
Hepatitis C positive	52 (63)	152 (48)	30 (54)	105 (49)
Hepatitis B positive	4 (5)	22 (7)	1 (2)	12 (6)
Any prior antiretroviral therapy	40 (48)	200 (60)	21 (38)	137 (61)
Prior cART[a]	36 (43)	191 (57)	10 (18)	109 (49)
HIV1 RNA, log (IQR)	4.28 (2.06–4.89)	2.6 (1.7–4.39)	5 (3.6–5.57)	2.67 (1.87–4.38)
HIV RNA ≥400 copies/ml	48 (68)	145 (46)	35 (90)	93 (52)
CD4+cell count (cells/mm^3)	263 (156–469)	361 (222–574)	122 (24–271)	335 (137–525)
CD4+cell count <200 cells/mm^3	27 (36)	73 (22)	28 (61)	81 (36)
Nadir CD4+cell count (cells/mm^3)	122 (61–244)	163 (46–290)	46 (15–200)	160 (59–360)
Serum creatinine (mg/dl)	1.5 (1.2–2.3)	0.9 (0.8–1.0)	2.3 (1.7–3.8)	0.9 (0.7–1.1)
eGFR (ml/min per 1.73 m^2)	54 (37–74)	105 (84–122)	32 (18–53)	105 (89–125)
Proteinuria (mg/d)	920 (436–2085)	n/a	2115 (379–8781)	n/a
Time since enrollment (yr)	4.4 (1.1–9.7)	41. (1.2–7.9)	1.5 (0–4.9)	1.3 (0.4–4.2)

Data are presented as n (%) or median (interquartile range) unless otherwise specified. HIVIC, HIV-associated immune complex kidney disease; HIVAN, HIV-associated nephropathy; cART, combined antiretroviral therapy; IQR, interquartile range; eGFR, estimated GFR by the Chronic Kidney Disease Epidemiology Collaboration equation; n/a, not applicable.
[a]cART 3 months prior.

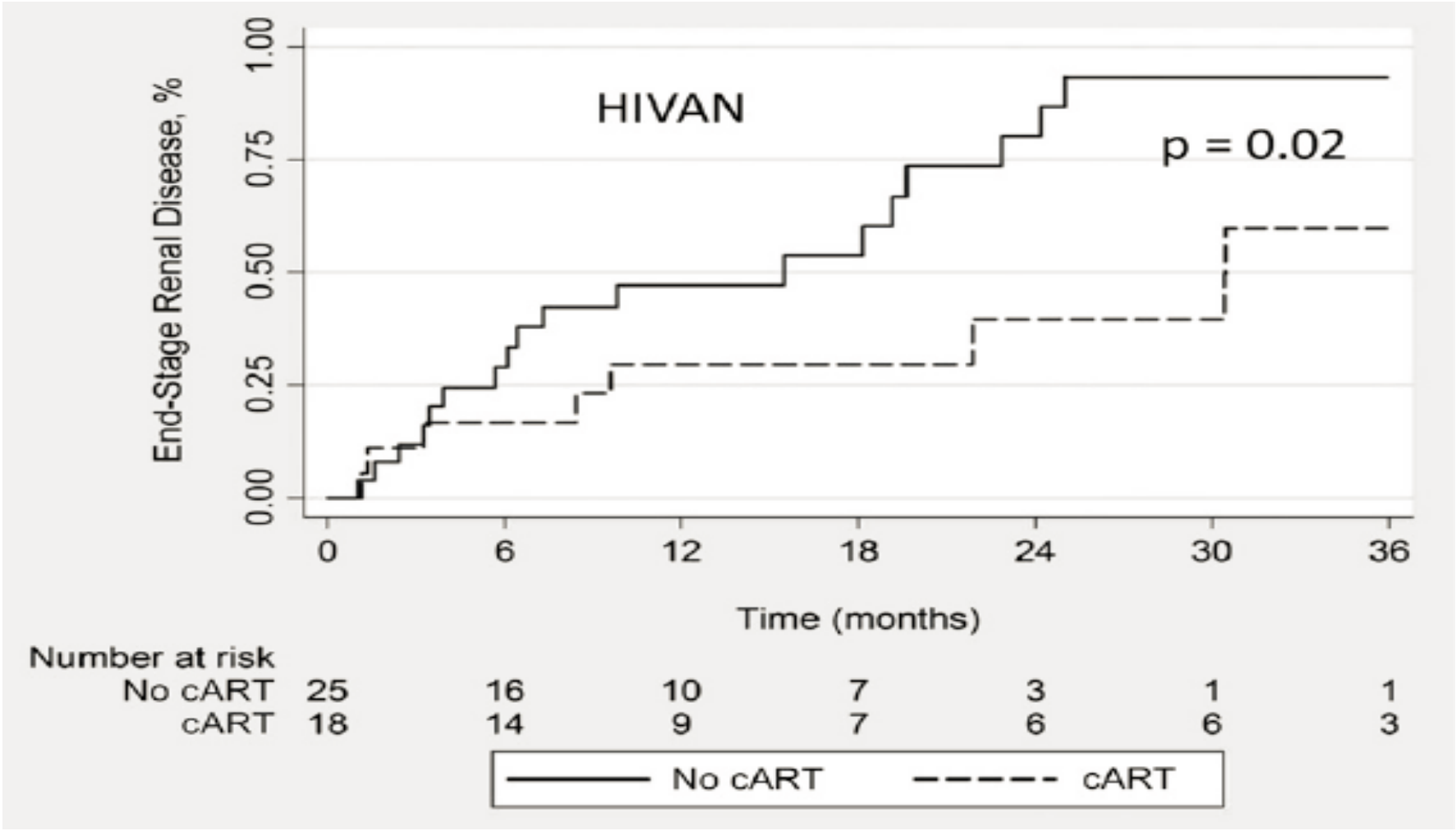
Foy ey al: Clin J Am Soc Nephrol 8: 1524-1532, 2013

Comparison of Risk Factors and Outcomes in HIV Immune Complex Kidney Disease and HIV-Associated Nephropathy



Foy ey al: Clin J Am Soc Nephrol 8: 1524-1532, 2013

Comparison of Risk Factors and Outcomes in HIV Immune Complex Kidney Disease and HIV-Associated Nephropathy



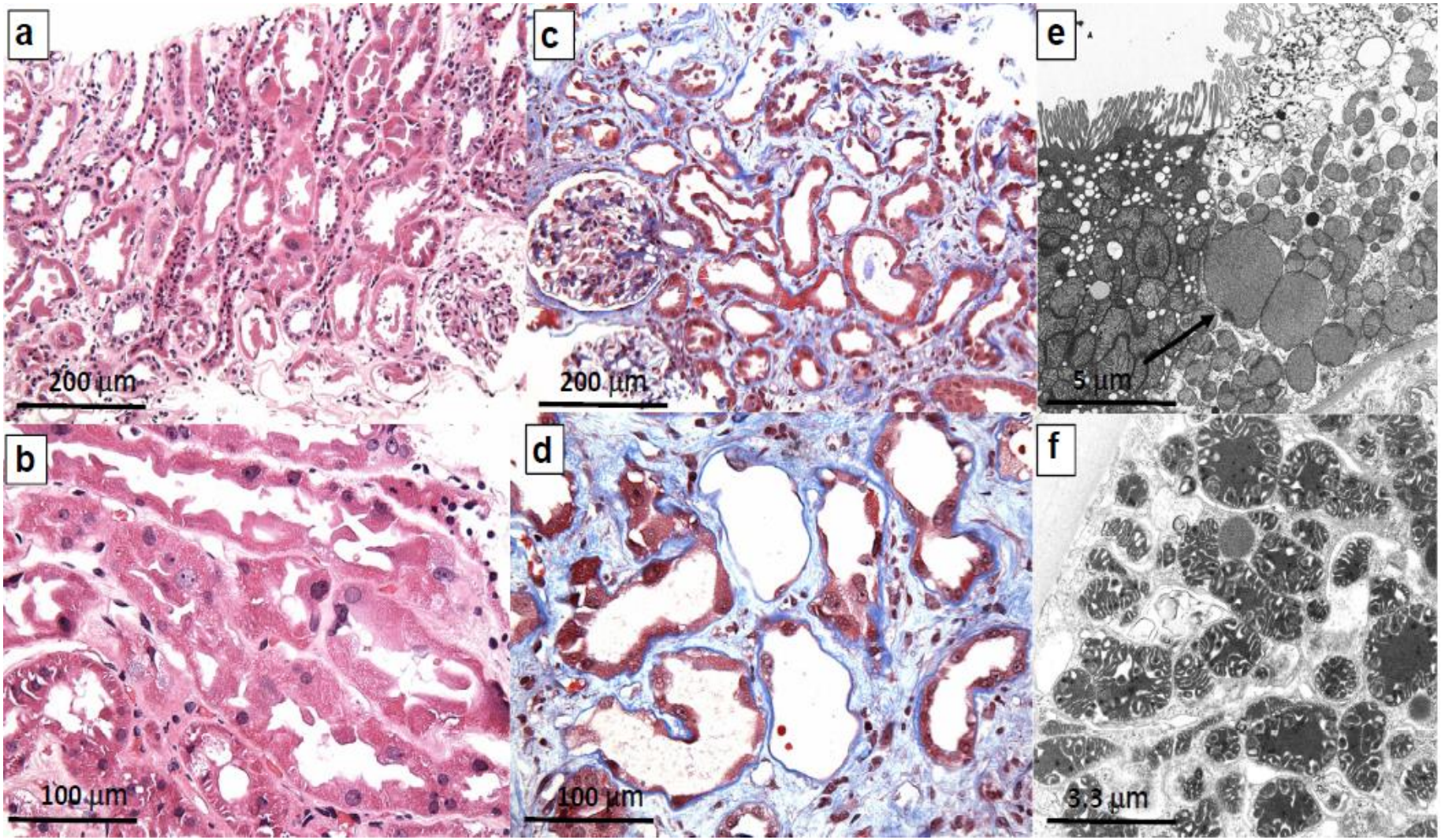
Foy ey al: Clin J Am Soc Nephrol 8: 1524-1532, 2013

Antiretroviral Tedavinin Renal Toksisitesi

Antiretroviral Class	Antiretroviral Therapy	Renal Effect	Clinical Recommendations
Protease inhibitors	Indinavir	Nephrolithiasis, crystalluria, dysuria, papillary necrosis, acute kidney injury, interstitial nephritis Ritonavir may increase toxicity of indinavir	Daily fluid intake of >2 l/day
	Atazanavir	Crystalluria, stones, interstitial nephritis	
	Ritonavir	Increases levels of TDF	
Reverse transcriptase inhibitors	Tenofovir disoproxil fumarate (TDF)	Renal tubular damage: Proximal tubular dysfunction, Fanconi syndrome, nephrogenic diabetes insipidus, acute tubular necrosis, acute kidney injury	Patients taking TDF should be monitored for signs of tubular dysfunction (elevated serum creatinine, hypophosphatemia, low serum uric acid, acidosis, glycosuria, proteinuria)

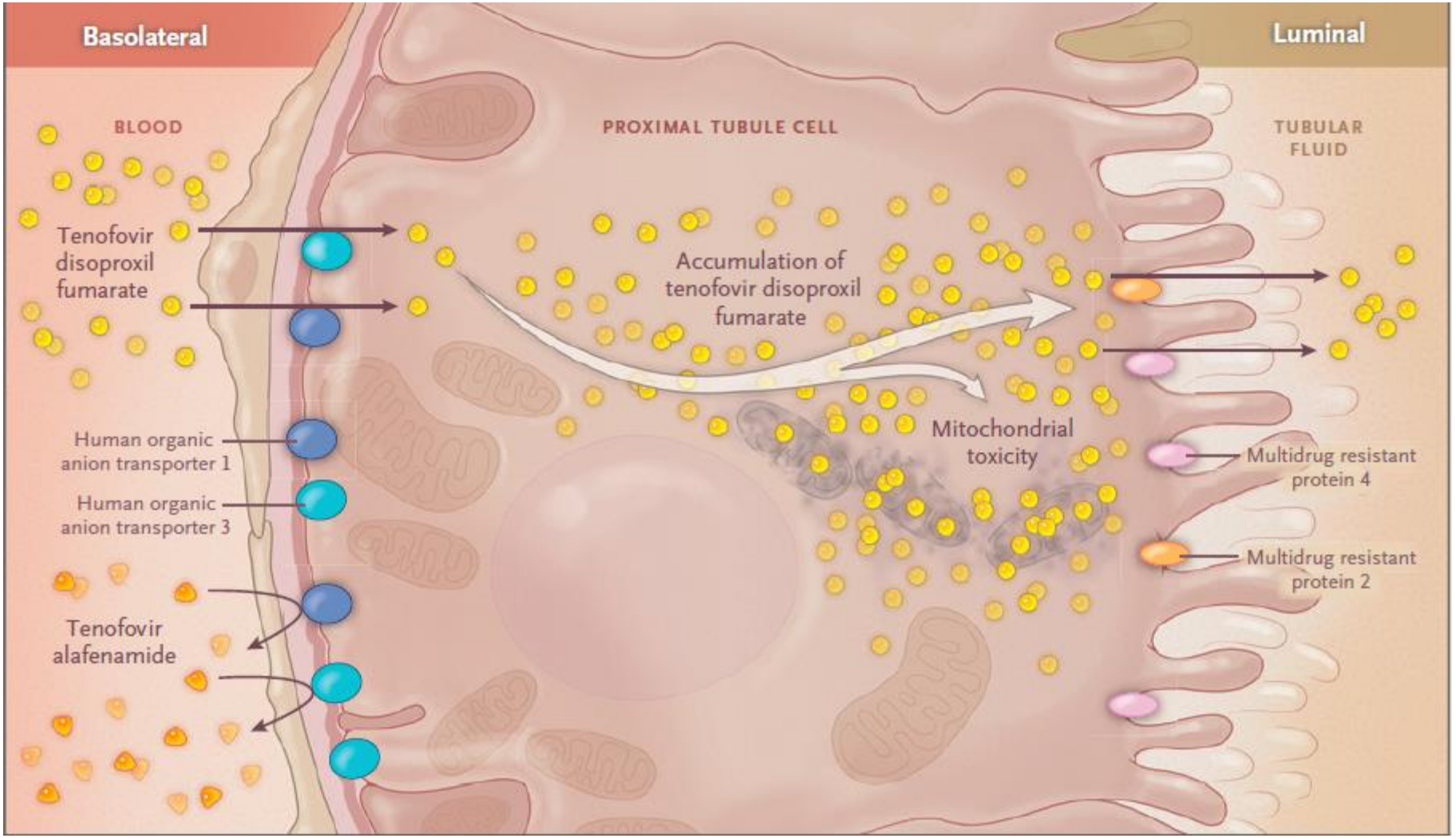
Kopp, Naicker: Comprehensive Clinical Nephrology, 2019

Tenofovir Nefrotoksisitesi



Swanepoel et al. Kidney Int 93: 545-559, 2018

Tenofovir Nefrotoksisitesi



Cohen et al: N Engl J Med 2017:377: 2363-2374

Kidney disease in the setting of HIV infection: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

Charles R. Swanepoel[1], Mohamed G. Atta[2], Vivette D. D'Agati[3], Michelle M. Estrella[4], Agnes B. Fogo[5], Saraladevi Naicker[6], Frank A. Post[7], Nicola Wearne[1], Cheryl A. Winkler[8], Michael Cheung[9], David C. Wheeler[10], Wolfgang C. Winkelmayer[11] and Christina M. Wyatt[12]; for Conference Participants[13]

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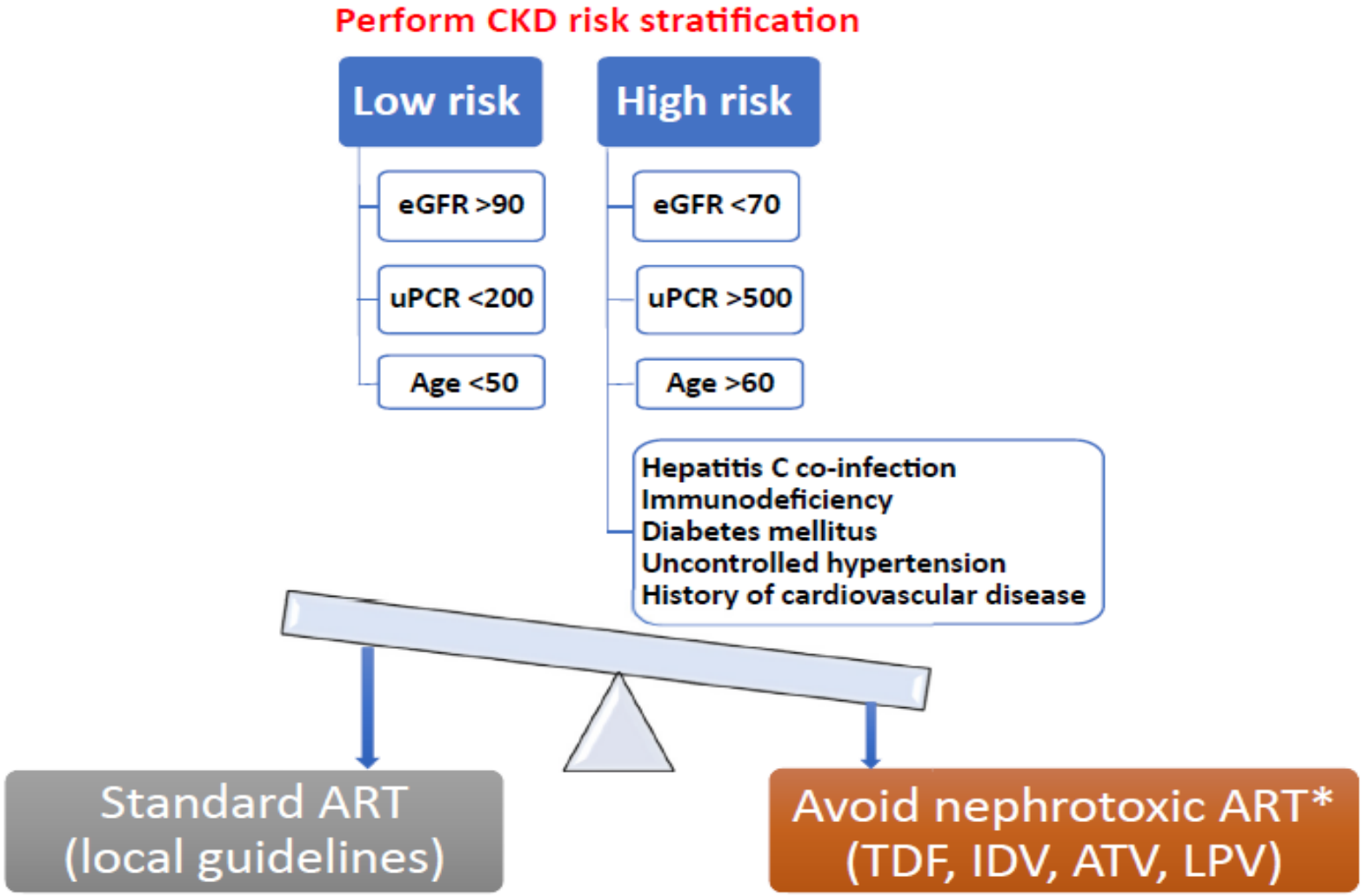
Antiretroviral Tedavi (ART) ile İlgili Öneriler



TDF: Tenofovir Disproksil Fumarat; IDV: Indinavir
ATV: Atazanavir; LPV: Lopinavir

Swanepoel et al. Kidney Int 93: 545-559, 2018

HİV (+) Hastalarda Kronik Böbrek Hastalığı Gelişimi için Risk Faktörleri

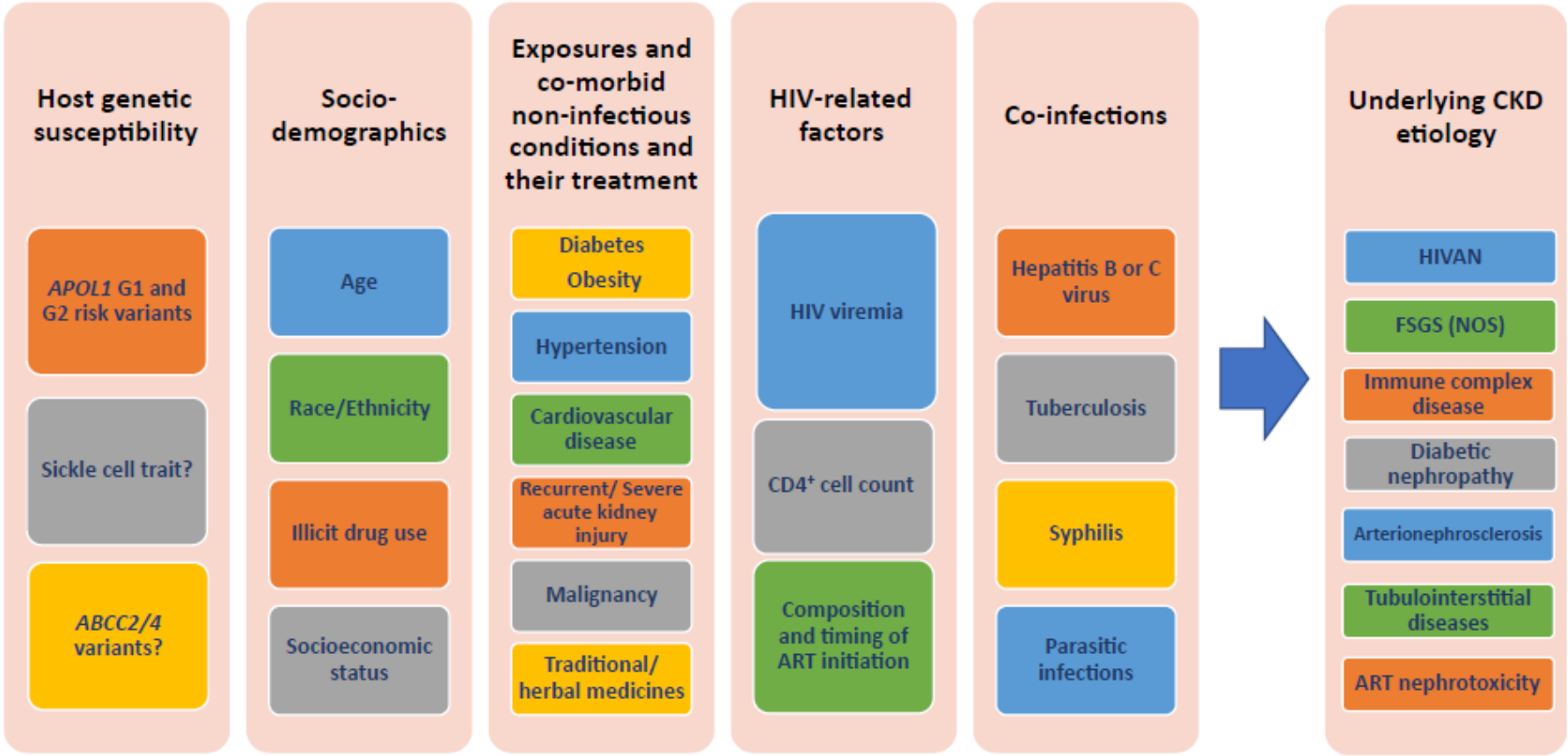
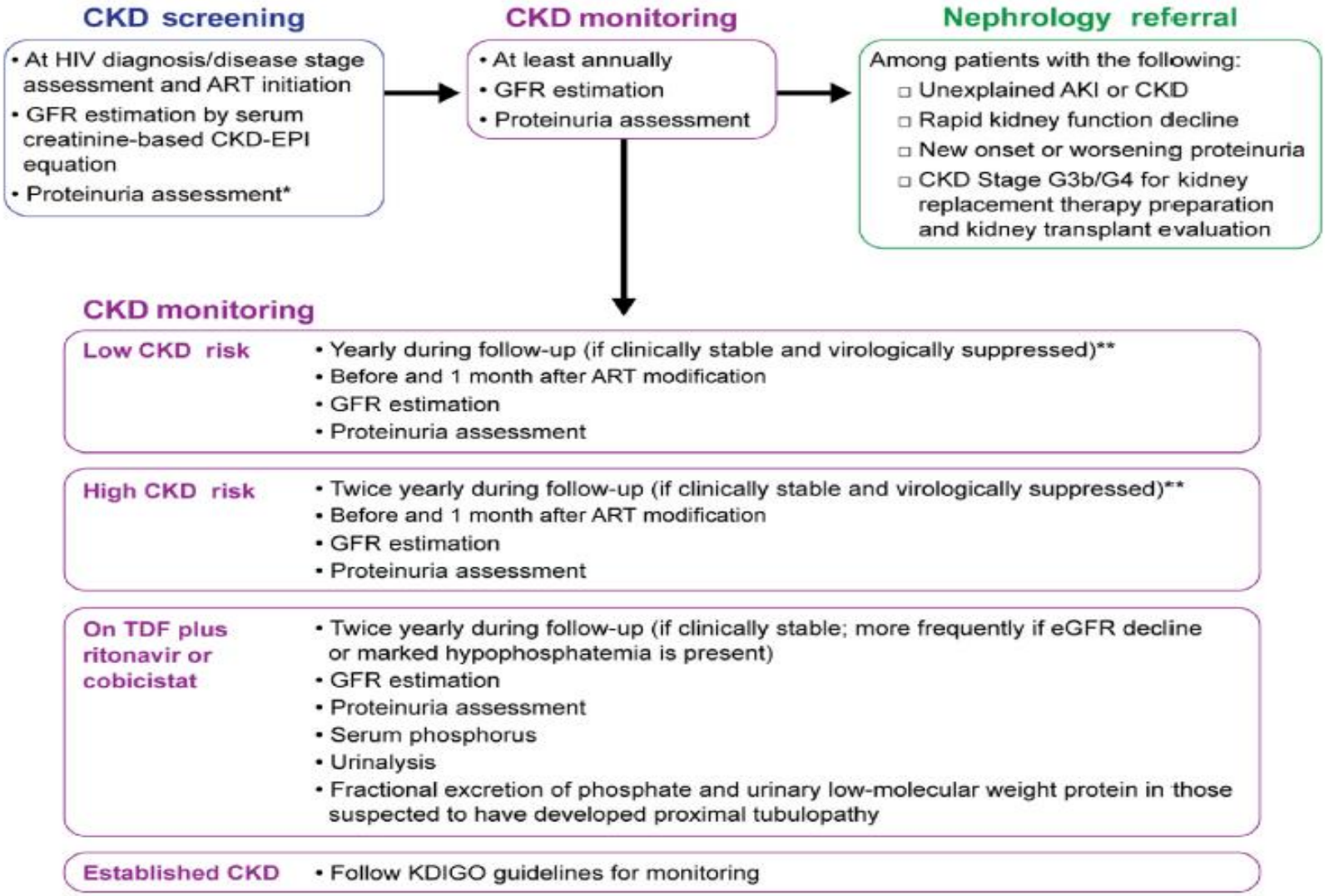


Figure 4| Risk factors and underlying etiologies of CKD in HIV-positive individuals. *APOL1*, apolipoprotein L1; *ABCC*, ATP-binding cassette transporter proteins; ART, antiretrovial therapy; CKD, chronic kidney disease; FSGS (NOS), focal segmental glomerulosclerosis, not otherwise specified; GN, glomerulonephritis; HIVAN, HIV-associated nephropathy.

Swanepoel et al. Kidney Int 93: 545-559, 2018

HİV (+) Erişkinlerde Böbrek Hastalığı Taraması ve Takip Önerileri



Swanepoel et al. Kidney Int 93: 545-559, 2018

HİV (+) Erişkinlerde Kronik Böbrek Hastalığı Risk Faktörlerinin Tedavi Önerileri

Risk factor	Recommendations
Hypertension	
Nonproteinuric	• Target systolic blood pressure ≤140 mm Hg[116]
Proteinuric	• Target systolic blood pressure ≤130 mm Hg[116] • Preferred antihypertensive: ACE inhibitors or angiotensin receptor blockers[116]
Diabetes mellitus	• Target hemoglobin A1c ~7%*[103]
Hepatitis B virus co-infection	• Treat per existing guidelines[118,121] • TAF may be used in patients with eGFR ≥ 30 ml/min per 1.73 m^2.[154] • Where TAF is unavailable or in patients with eGFR < 30 ml/min per 1.73 m^2, dose-adjusted TDF or entecavir may be considered.
Hepatitis C virus co-infection	• Treatment per existing guidelines[120,155] • In patients with HCV genotypes 1 and 4 and CKD G4-5, ribavirin-free grazoprevir/elbasvir[156–158] or glecaprevir/pibrentasvir regimens may be effective[164,165] • In patients with genotypes 2, 3, 5, and 6 and CKD G4-5, the pan-genotypic glecaprevir/pibrentasvir regimen can be used[164,165]; sofosbuvir-based regimens can be used in patients with any genotype, but should be avoided or dose adjusted in patients with eGFR < 30 ml/min per 1.73 m^2.[159–161] In addition, the combination of ledipasvir and sofosbuvir with TDF should be avoided.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; HCV, hepatitis C; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.
*Hemoglobin A1c may underestimate glycemia in HIV-positive individuals.[162,163]

Swanepoel et al. Kidney Int 93: 545-559, 2018

Antiretroviral Tedavi

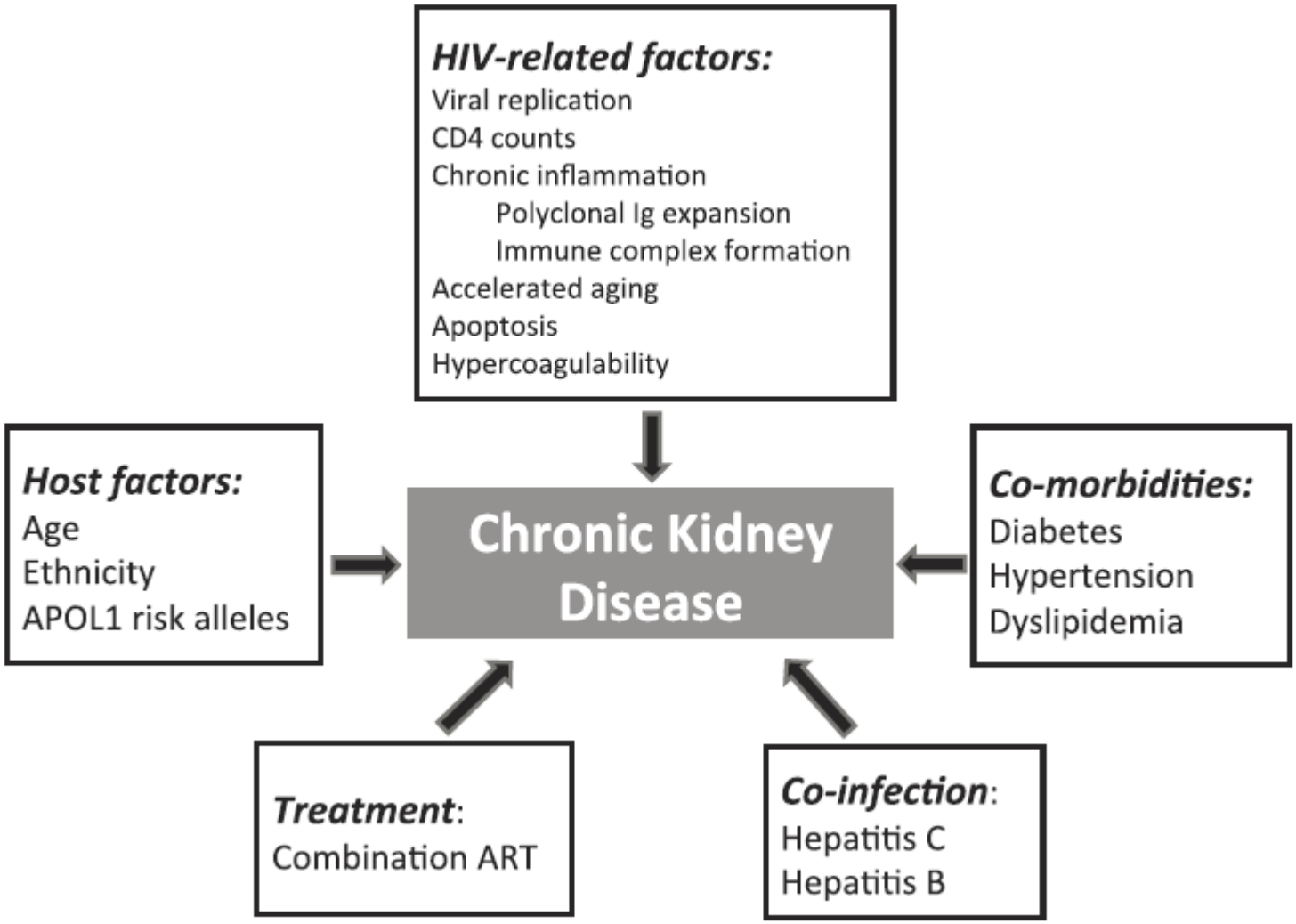
TABLE 56.3 Adjustments in Drug Dosing for Antiretroviral Medications in Current Use

Medication Class	Medication	Adjustment for GFR	Dosing in Dialysis
NRTI (8)	Abacavir	No change	No change
	Didanosine (ddi)	Reduce for eGFR <60	No dose after dialysis
	Emtricitabine (FTC)	Reduce for eGFR <50	Dose after dialysis
	Lamivudine (3TC)	Reduce for eGFR <50	No dose after dialysis
	Stavudine (d4T)	Reduce for eGFR <50	Reduce dose
	Tenofovir disoproxil fumarate (TDF)	Reduce for eGFR <50	Dose after dialysis
	Tenofovir alafenamide	Not needed	Use not recommended
	Zidovudine (AZT)	Reduce for eGFR <15	Reduce dose
NNRTI (4)	Efavirenz	No change	No change
	Etravirine	No change	No change
	Nevirapine	No change >eGFR 20, not recommended eGFR <20	Dose after dialysis
	Rilpivirine	Not recommended for severe chronic kidney disease	Dose after dialysis probably not needed
Protease inhibitor (8)	Atazanavir	No change	Depends on status
	Darunavir	No change	No data
	Fosamprenavir	No data	No data
	Indinavir	No change	No change
	Nelfinavir	No data	No data
	Ritonavir	No change	No data
	Saquinavir	Not recommended for severe chronic kidney disease	No data
	Tipranavir	Probably no change	No data
Fusion inhibitor (CCR5)	Enfuvirtide	No change	No data
Entry inhibitor (gp41)	Maraviroc	Avoid for eGFR <30	Avoid
Integrase inhibitor (3)	Dolutegravir	Complex, suggest reviewing primary data	Avoid
	Elvitegravir	No change	No data
	Raltegravir	No change	Avoid administering before dialysis
Pharmacokinetic enhancer	Cobicistat	No change. For eGFR, avoid combination with TDF	No data

Shown are 26 antiretroviral drugs approved by the U.S. food and drug administration (FDA) as of 2018. Combination drugs, of which 14 are currently approved by the FDA, are not listed here.
eGFR, Estimated glomerular filtration rate; *TDF*, tenofovir disoproxil fumarate.

Kopp, Naicker: Comprehensive Clinical Nephrology, 2019

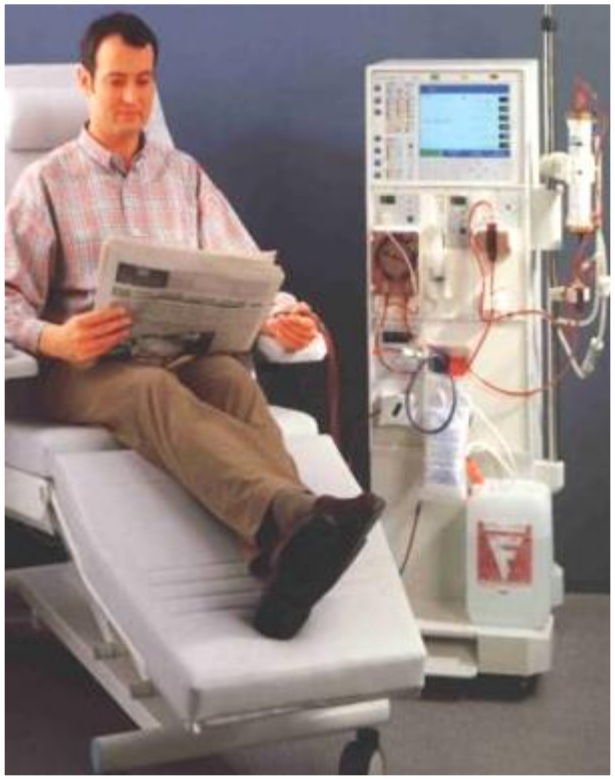
HİV ile İnfekte Hastada Kronik Böbrek Hastalığı



Hou, Nast: Curr Opin Nephrol Hypertens 27: 2018

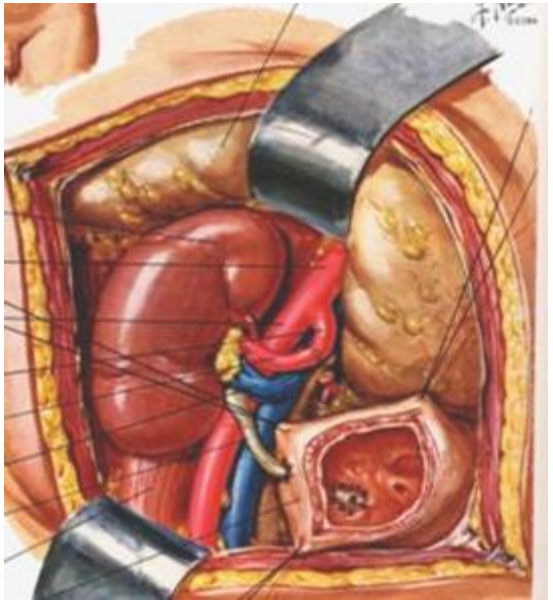
Renal Replasman Tedavileri

Kronik Hemodiyaliz



Kronik
Periton Diyalizi

Böbrek
Transplantasyonu
Kadavra verici
Canlı verici



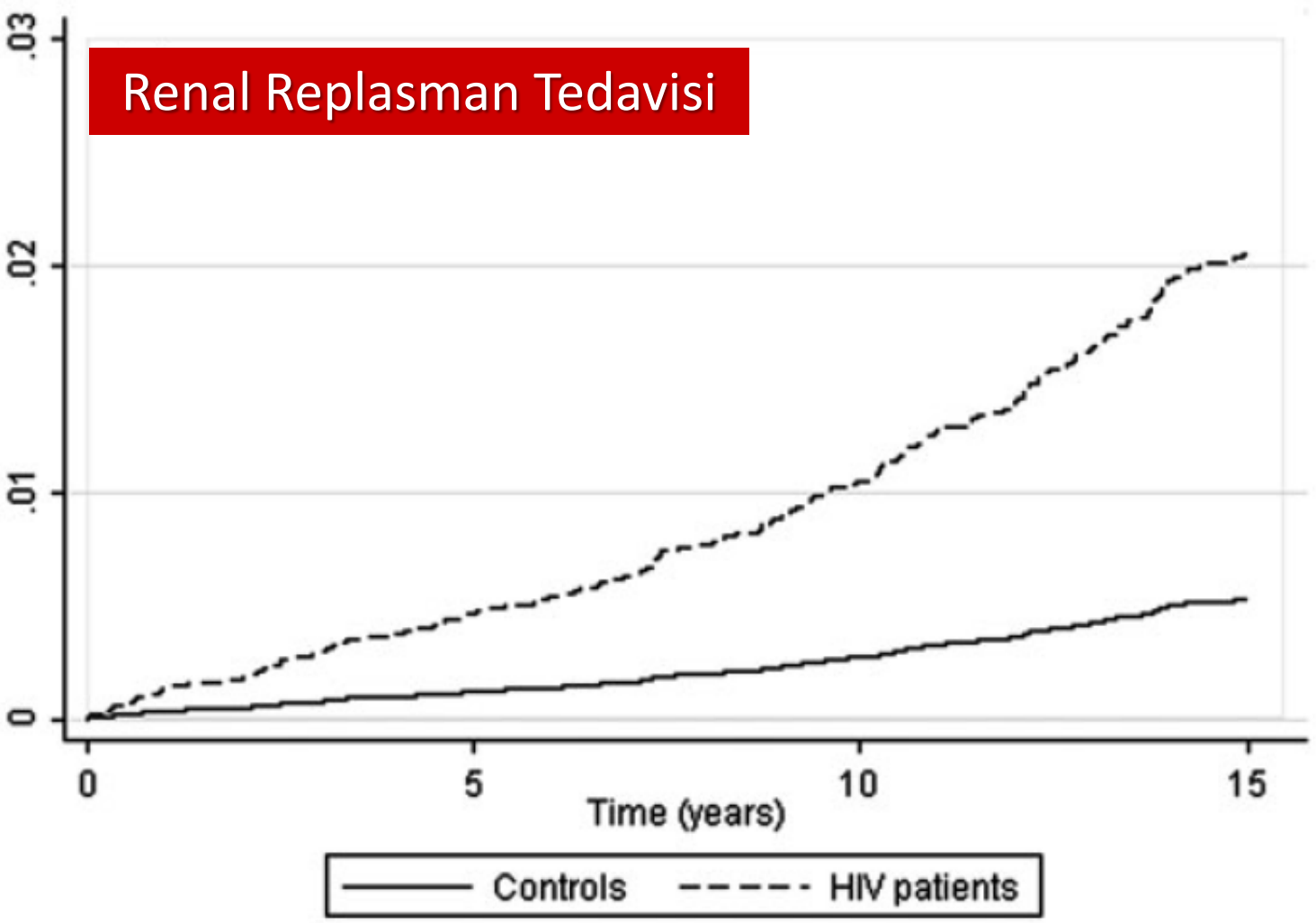
Increased risk of dialysis and end-stage renal disease among HIV patients in Denmark compared with the background population

	HIV patients (aRRT/cRRT)[a]	Controls (aRRT/cRRT)[a]
Number	5300	53 000
Number of events (%)	68 (1.3)/19 (0.4)	182 (0.3)/66 (0.1)
Follow-up, median (IQR), years	8.0 (3.1–13.7)/8.0 (3.1–13.8)	11.2 (5.8–15.0)/11.2 (5.8–15.0)
Lost to follow-up (%)	22 (0.4)	98 (0.2)
Emigrated during follow-up (%)	219 (4.1)	2037 (3.8)
Died during study period (%)	1338 (25.2)	2454 (4.7)
Age at study inclusion, median (IQR), years	37 (30–44)	37 (30–44)
Male (%)	4036 (76.2)	40 360 (76.2)
Race		
Caucasian	4167 (78.6)	–
African	683 (12.9)	–
Other/unknown	450 (6.7)	–
Route of infection		
MSM (%)	2407 (45.5)	–
IDU (%)	563 (10.6)	–
Heterosexually (%)	1928 (36.4)	–
Others (%)	402 (5.6)	–
HIV diagnosis after 1 January 1997	2486 (46.9)	–
Diabetes during study period (%)	131 (2.5)/132 (2.5)	1303 (2.5)/1309 (2.4)
Type 1 (%)	36 (0.7)	230 (0.4)/232 (0.5)
Type 2 (%)	80 (1.5)	975 (1.8)/979 (1.8)
Other (%)	15 (0.3)/16 (0.3)	117 (0.2)/117 (0.2)
Hypertension during study period (%)	219 (4.1)/220 (4.1)	2557 (4.8)/2574 (5.0)
Hepatitis C co-infection (non-IDU)	354 (6.7)	–
AIDS diagnosis during study period (%)	788 (14.8)/790 (14.9)	–
CD4 cell count at baseline (IQR)	290 (120–480)	–
eGFR baseline (mL/min pr. 1.73 m^2)		
>90 (%)	1776 (33.5)	–
60–90 (%)	1177 (22.2)	–
≤60 (%)	69 (1.3)	–
Missing (%)	2278 (43)	–

aRRT, any renal replacement therapy; cRRT, start of chronic renal replacement therapy; IQR, interquartile range; MSM, men who have sex with men; IDU, intravenous drug users; eGFR, estimated glomerular filtration rate.
[a]Presented if there is a difference between aRRT and cRRT.

Rasch et al. Nephrol Dial Transplant 29: 1232-1238, 2014

Increased risk of dialysis and end-stage renal disease among HIV patients in Denmark compared with the background population



Rasch et al. Nephrol Dial Transplant 29: 1232-1238, 2014

HİV (+) Hastalarda Böbrek Transplantasyonu

- Meets standard criteria for kidney transplant recipients, *plus* the following:
- Effective HIV suppression for ≥6 months prior to transplantation
  - Undetectable plasma HIV-1 RNA
  - CD4+ cell count > 200 cells/mm^3
- No active opportunistic infections
- No history of:
  - Progressive multifocal leukoencephalopathy
  - Primary central nervous system lymphoma
  - Pulmonary aspergillosis
  - Visceral Kaposi's sarcoma
  - Coccidiomycosis
  - Chronic intestinal cryptosporidiosis >1 month
- Hepatology evaluation for patients co-infected with hepatitis B or hepatitis C virus

Swanepoel et al. Kidney Int 93: 545-559, 2018

Outcomes of Kidney Transplantation in HIV-Infected Recipients

Table 1. Baseline Characteristics of Allograft Donors and of 150 HIV-Infected Kidney-Transplant Recipients and Post-Transplantation Characteristics.*

Characteristic	Value
Donor at baseline	
Age — yr	
Median	41
Interquartile range	27–49
Six-antigen–matched kidney — no. (%)	21 (14)
Deceased — no. (%)	102 (68)
Expanded criteria — no. (%)†	18 (18)
High infectious risk — no. (%)	31 (30)
Recipient at baseline	
Age — yr	
Median	46
Interquartile range	40–51
Male sex — no. (%)	117/150 (78)
Race or ethnic group — no. (%)‡	
White	42/150 (28)
Black	103/150 (69)
Other	5/150 (3)

Stock et al. N Engl J Med 363: 2004-2014, 2010

Outcomes of Kidney Transplantation in HIV-Infected Recipients

Table 1. Baseline Characteristics of Allograft Donors and of 150 HIV-Infected Kidney-Transplant Recipients and Post-Transplantation Characteristics.*

Cause of disease — no. (%)‖	
Hypertension	38/150 (25)
HIV-associated nephropathy	36/150 (24)
Diabetic nephropathy or glomerulosclerosis	13/150 (9)
Focal glomerulosclerosis	9/150 (6)
Unknown or other cause	54/150 (36)
Prior opportunistic complication — no. (%)¶	36/150 (24)
CD4+ count — per mm^3‖	
Median	524
Interquartile range	385–672
Viral hepatitis — no. (%)	
Hepatitis C RNA detectable	28/150 (19)
Hepatitis B surface antigen–positive	5/150 (3)
HAART regimen — no. (%)**	
Protease-inhibitor–based	63/150 (42)
NNRTI-based	59/150 (39)
Protease-inhibitor–based and NNRTI-based	15/150 (10)
Nucleoside analogues only	5/150 (3)
Raltegravir-based	6/150 (4)
None	2/150 (1)

Stock et al. N Engl J Med 363: 2004-2014, 2010

Outcomes of Kidney Transplantation in HIV-Infected Recipients

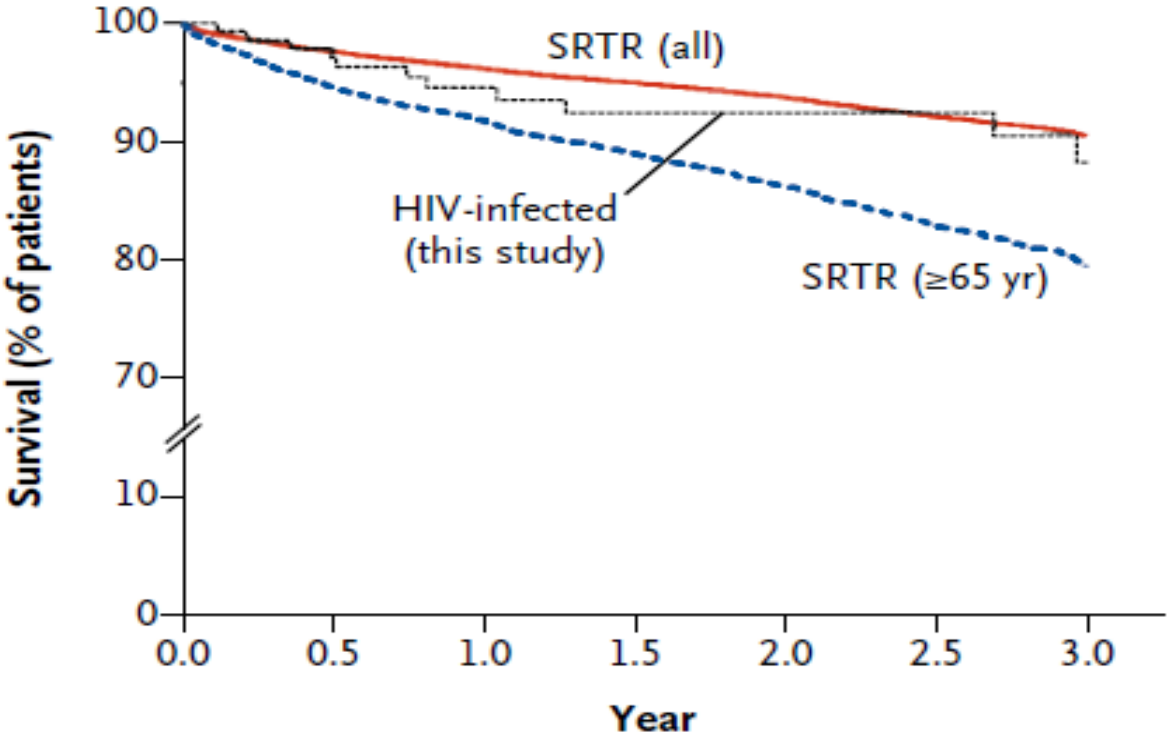
Table 1. Baseline Characteristics of Allograft Donors and of 150 HIV-Infected Kidney-Transplant Recipients and Post-Transplantation Characteristics.*

Recipient after transplantation	
Immunosuppression at 1 wk — no. (%)	
Tacrolimus	99/150 (66)
Cyclosporine	33/150 (22)
Mycophenolate mofetil	131/150 (87)
Basiliximab or daclizumab induction	76/150 (51)
Antithymocyte globulin induction	48/150 (32)
Cyclosporine trough level — ng/ml	
At 1 mo	
Median	176
Interquartile range	118–246
At 1 yr	
Median	127
Interquartile range	106–142
Tacrolimus trough level — ng/ml	
At 1 mo	
Median	9.1
Interquartile range	6.0–11.9
At 1 yr	
Median	7.2
Interquartile range	5.5–9.1

Stock et al. N Engl J Med 363: 2004-2014, 2010

Outcomes of Kidney Transplantation in HIV-Infected Recipients

A Patient Survival

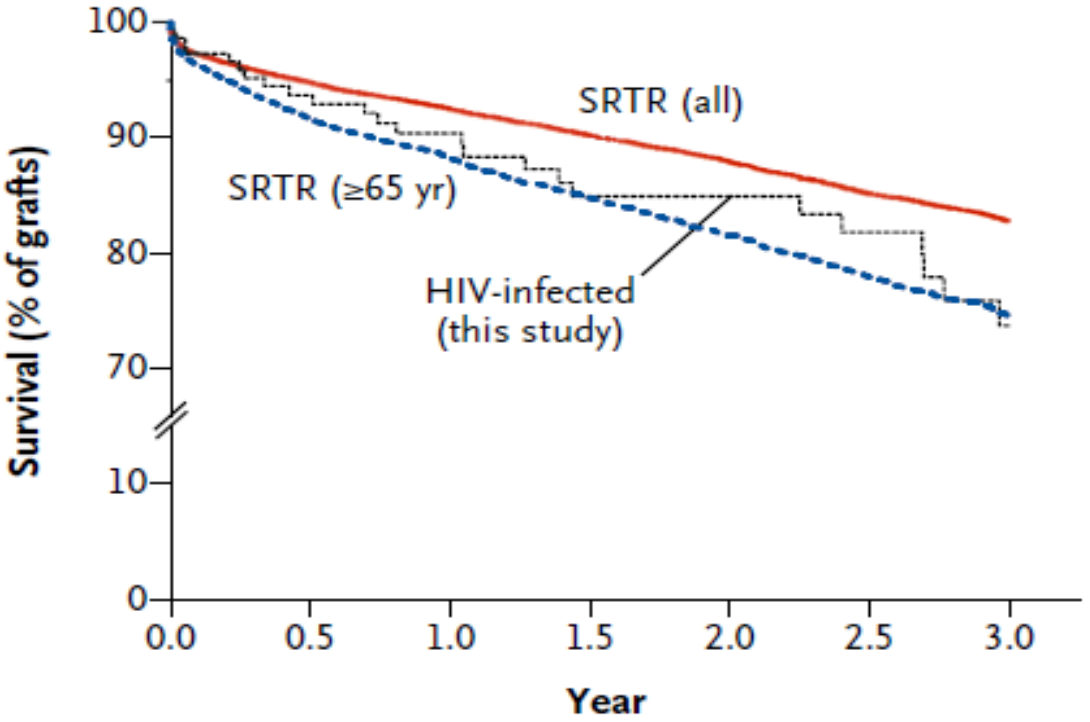


No. at Risk			
SRTR (all)	29,928	16,792	6508
HIV-infected (this study)	96	68	36
SRTR (≥65 yr)	4,226	2,215	836

Stock et al. N Engl J Med 363: 2004-2014, 2010

Outcomes of Kidney Transplantation in HIV-Infected Recipients

B Graft Survival



No. at Risk			
SRTR (all)	29,064	16,114	6215
HIV-infected (this study)	93	64	31
SRTR (≥65 yr)	4,103	2,133	807

Stock et al. N Engl J Med 363: 2004-2014, 2010

Outcomes of Kidney Transplantation in HIV-Infected Recipients

Table 2. Rates of Patient Survival and Graft Survival at 1 Year and 3 Years among HIV-Infected Kidney-Transplant Recipients (Study Patients) and Patients in the SRTR Database.*

Population	Patient Survival		Graft Survival	
	At 1 Year	At 3 Years	At 1 Year	At 3 Years
	percent (95 percent confidence interval)			
Study patients	94.6 (88.9–97.4)	88.2 (78.3–93.8)	90.4 (83.9–94.3)	73.7 (61.9–82.4)
SRTR patients				
Age ≥65 yr	91.8 (91.1–92.4)	79.5 (78.0–80.9)	88.3 (87.5–89.1)	74.4 (72.9–75.9)
Overall	96.2 (96.0–96.4)	90.6 (90.2–91.0)	92.5 (92.3–92.8)	82.8 (82.3–83.3)

* SRTR denotes Scientific Registry of Transplant Recipients.

Stock et al. N Engl J Med 363: 2004-2014, 2010

ORIGINAL ARTICLE

HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years

Elmi Muller, M.B., Ch.B., M.Med., Zunaid Barday, M.B., Ch.B.,
Marc Mendelson, M.D., Ph.D., and Delawir Kahn, M.B., Ch.B., Ch.M.

- Prospektif ve non-randomize çalışma
- 27 HIV-pozitif hasta
- CD4 T-hücre sayısı ≥ 200 /mm^3
- Plazma HIV RNA (-)
- Ortanca takip süresi: 2.4 yıl

Muller et al. N Engl J Med 372: 613-620, 2015

HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years

Characteristic	Patients (N=27)
Age — yr	
Median	41
Interquartile range	39–43
Male sex — no. (%)	15 (56)
Race — no (%)†	
Black	26 (96)
Mixed race	1 (4)
Cause of chronic kidney disease — no. (%)	
Hypertension	1 (4)
Membranous glomerulonephritis	1 (4)
Biopsy-confirmed HIV-associated nephropathy	5 (19)
Presumed HIV-associated nephropathy	20 (74)
CD4 T-cell count — cells/mm³	
Median	288
Interquartile range	236–511

Muller et al. N Engl J Med 372: 613-620, 2015

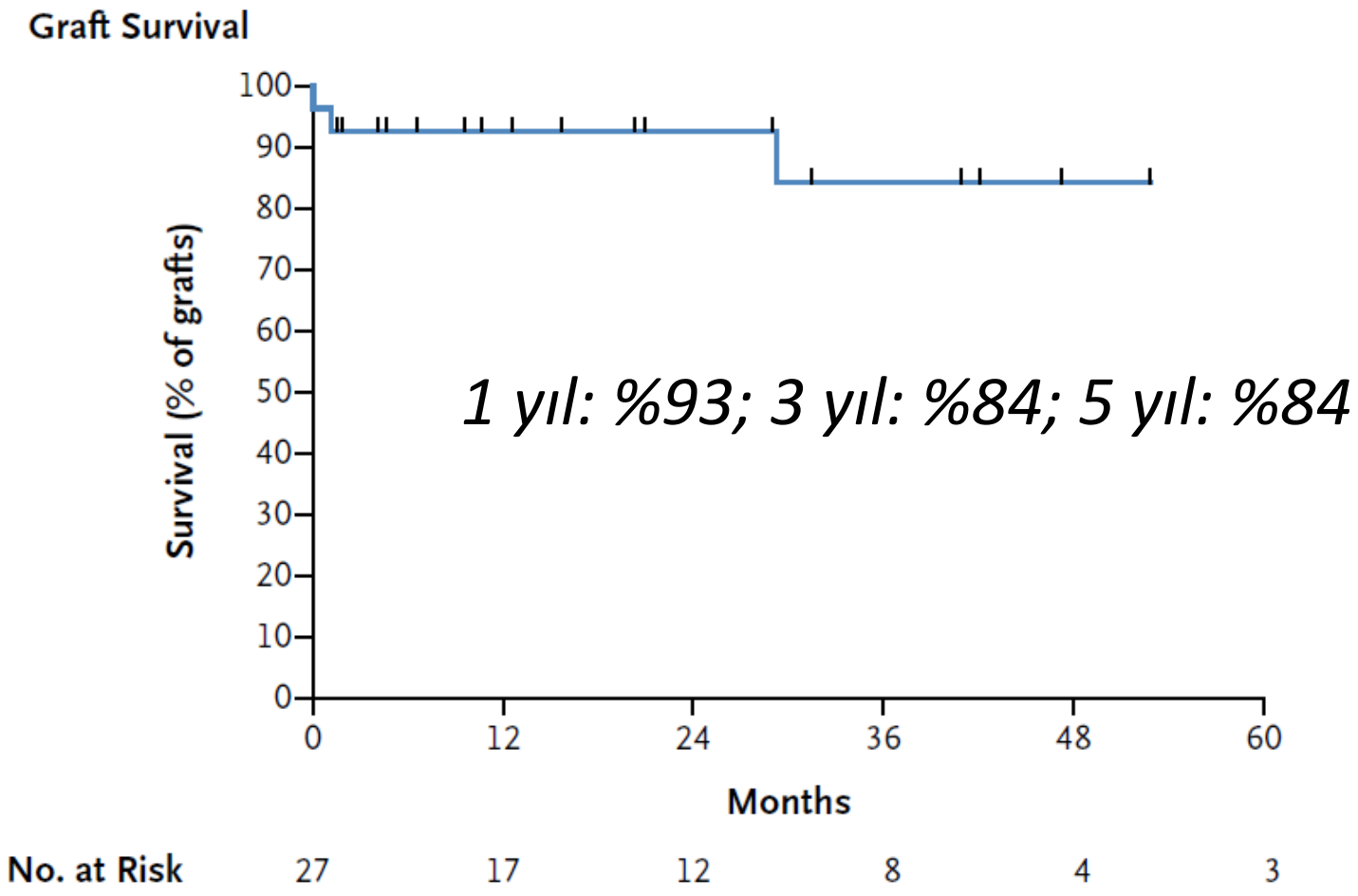
HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years

Characteristic	Patients (N=27)
Positive for hepatitis B surface antigen — no. (%)	3 (11)
ART regimen — no. (%)	
Protease inhibitor–based therapy	11 (41)
NNRTI-based therapy	16 (59)
Antibody induction therapy‡	
ATG	
No. of patients (%)	10 (37)
Cumulative dose — mg	
Median	475
Interquartile range	400–750
Thymoglobuline	
No. of patients (%)	17 (63)
Cumulative dose — mg	
Median	600
Interquartile range	450–1000

Muller et al. N Engl J Med 372: 613-620, 2015

NNRTI: Nonnucleoside reverse-transcriptase inhibitor

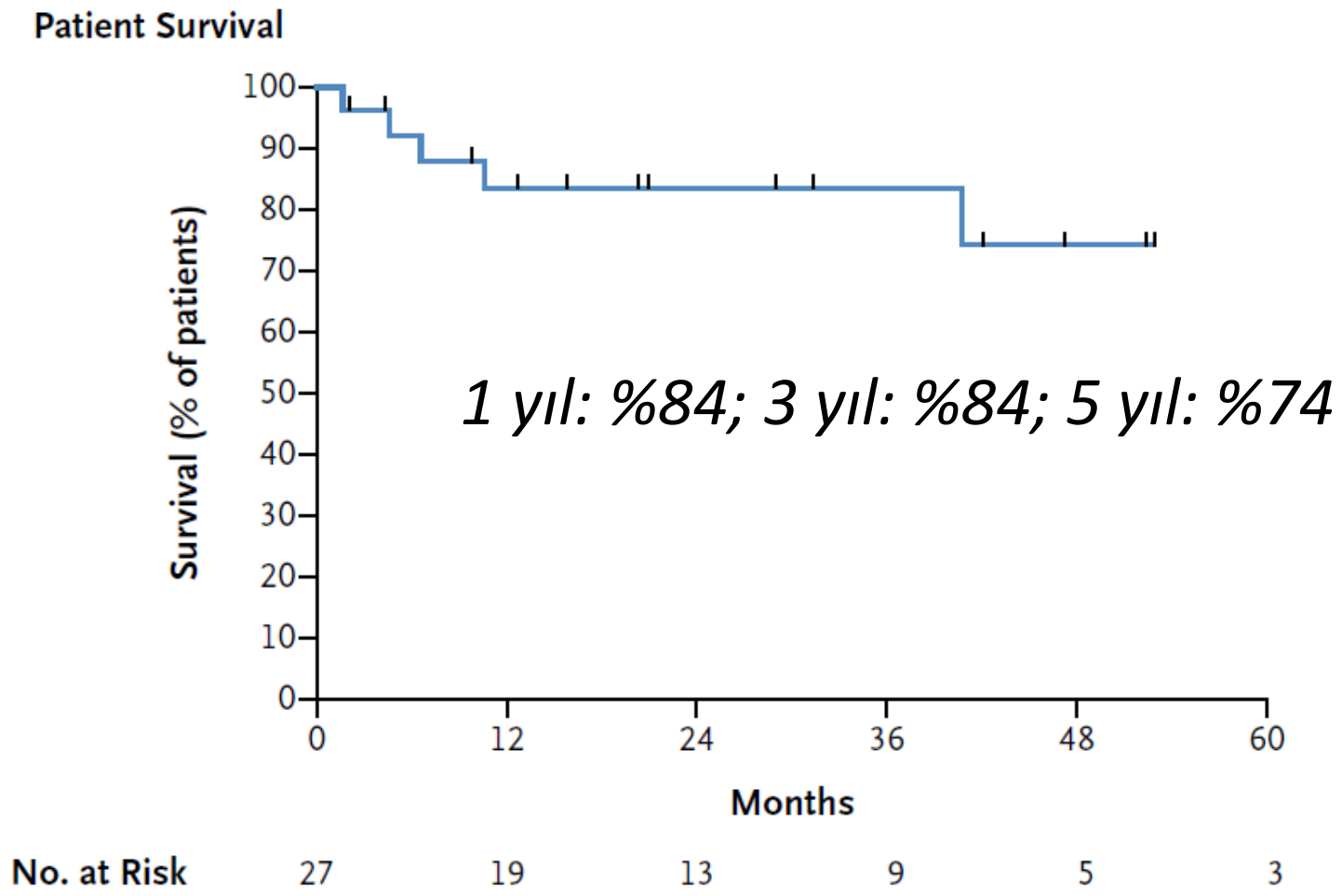
HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years



1 yıl: %93; 3 yıl: %84; 5 yıl: %84

Muller et al. N Engl J Med 372: 613-620, 2015

HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years



1 yıl: %84; 3 yıl: %84; 5 yıl: %74

Muller et al. N Engl J Med 372: 613-620, 2015

HİV ve Böbrek Transplantasyonu

- HİV infeksiyonu olan kronik böbrek hastalarında tedavi yöntemlerinden biri böbrek transplantasyonudur.
- İdeal immunosupressif tedavi bilinmemektedir.
- Klinik çalışmalarda yüksek sıklıkta rejeksiyon bildirilmiştir.
- İmmünsupressif tedavinin HİV infeksiyonunun seyrine olumsuz bir etkisi yoktur.
- Bazı immünsupressif ilaçlar, antiretroviral etkiler gösterebilir.
- Antiretroviral tedavi ile immunsupressif ilaçlar arasında etkileşim olmadığından emin olunmalıdır.

Nashar, Sureshkumar. World J Nephrol 5 (4): 300- 307, 2016

Sabrınız için teşekkür ederim…