일차 진료에서 만성신질환의 관리

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1) CKD & eGFR

2) Hypertension

3) Anemia

4) Others

Definition and classification of CKD

1.1: DEFINITION OF CKD

1.1.1: CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. (*Not Graded*)

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.

GFR categories in CKD

GFR category	GFR (ml/min/1.73 m^2)
G1	≥90
G2	60-89
G3a	45-59
G3b	30-44
G4	15-29
G5	<15

MDRD equation

16 March 1999 Volume 130 Number 6

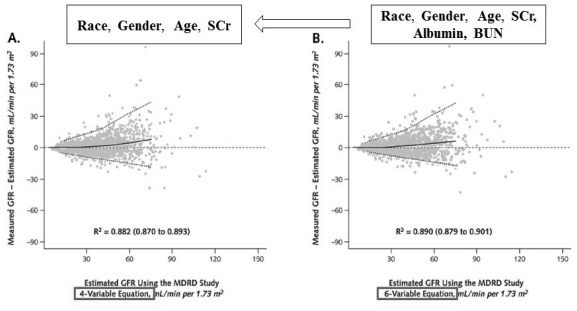
Annals of Internal Medicine

A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation

Andrew S. Levey, MD; Juan P. Bosch, MD; Julia Breyer Lewis, MD; Tom Greene, PhD; Nancy Rogers, MS; and David Roth, MD, for the Modification of Diet in Renal Disease Study Group*

- The **M**odification of **D**iet in **R**enal **D**isease (MDRD) Study
  : Multicenter, controlled trial
  To evaluate the effect of dietary protein restriction and strict blood pressure control
- Enrolled patient number ; **1628**
- Glomerular filtration rate (GFR) : measured as the renal clearance of **^{125}I-iothalamate**
- Creatinine Clearance (Ccr)
  : 24hr urine collection, single measurement of serum creatinine
- GFR, Ccr : expressed per 1.73 m^2 of body surface area

MDRD equation



MDRD equation (4-variables)
= 175 x standardized **SCr** $^{-1.154}$ x **Age** $^{-0.203}$ x 1.212 [if **black**] x 0.742 [if **female**]

Using standardized serum creatinine values in the Modification of Diet in Renal Disease Study Equation for estimating glomerular filtration rate
Ann Intern Med 2006

CKD-EPI equation

ARTICLE | Annals of Internal Medicine

A New Equation to Estimate Glomerular Filtration Rate

Andrew S. Levey, MD; Lesley A. Stevens, MD, MS; Christopher H. Schmid, PhD; Yaping (Lucy) Zhang, MS; Alejandro F. Castro III, MPH; Harold I. Feldman, MD, MSCE; John W. Kusek, PhD; Paul Eggers, PhD; Frederick Van Lente, PhD; Tom Greene, PhD; and Josef Coresh, MD, PhD, MHS, for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration)*

Ann Intern Med 2009;150:604-612.

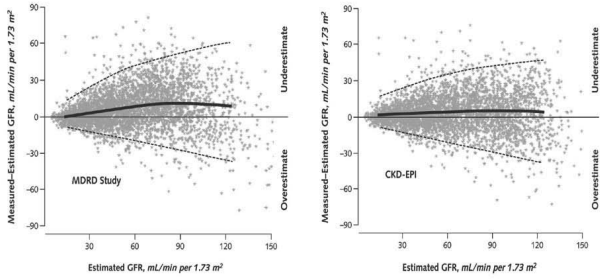
CKD-EPI equation

Table 2. The CKD-EPI Equation for Estimating GFR on the Natural Scale*

Race and Sex	Serum Creatinine Level, μmol/L (mg/dL)	Equation
Black		
Female	≤62 (≤0.7)	$GFR = 166 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$
	>62 (>0.7)	$GFR = 166 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$
Male	≤80 (≤0.9)	$GFR = 163 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$
	>80 (>0.9)	$GFR = 163 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$
White or other		
Female	≤62 (≤0.7)	$GFR = 144 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$
	>62 (>0.7)	$GFR = 144 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$
Male	≤80 (≤0.9)	$GFR = 141 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$
	>80 (>0.9)	$GFR = 141 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$

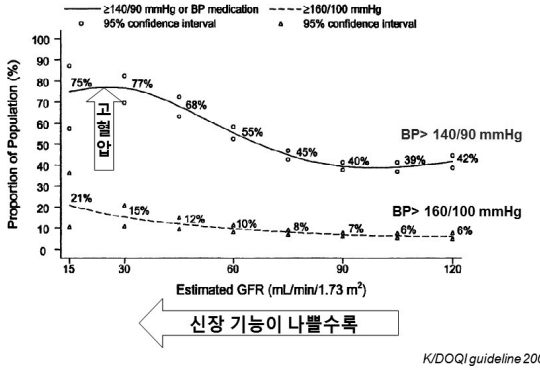
Used parameters : **Race**, **Gender**, **Age**, **Serum creatinine**
(the same variables of MDRD 4-variable equation)

Comparison between two equations



GFR and hypertension

NHANES III (National Health and Nutrition Examination Survey, n=15,600)



K/DOQI guideline 2004

Increased BP and ESRD risk

Blood-Pressure Category*	No. of Men	No. with End-Stage Renal Disease	Age-Adjusted Rate per 100,000 Person-Years†	Adjusted Relative Risk (95% CI)‡
Optimal	61,089	51	5.3	1.0
Normal but not optimal	81,621	86	6.6	1.2 (0.8–1.7)
High normal	73,798	134	11.1	1.9 (1.4–2.7)§
Hypertension				
Stage 1 (140~159/90~99)	85,684	275	21.0	3.1 (2.3–4.3)§
Stage 2 (160~179/100~109)	23,459	158	43.6	6.0 (4.3–8.4)§
Stage 3 (180~209/110~119)	5,464	73	96.1	11.2 (7.7–16.2)§
Stage 4 (>210/>120)	1,429	37	187.1	22.1 (14.2–34.3)§
Total	332,544	814	15.6	—

Klag MJ et al., *NEJM 1996*

Epidemoiology of hypertension in CKD patients

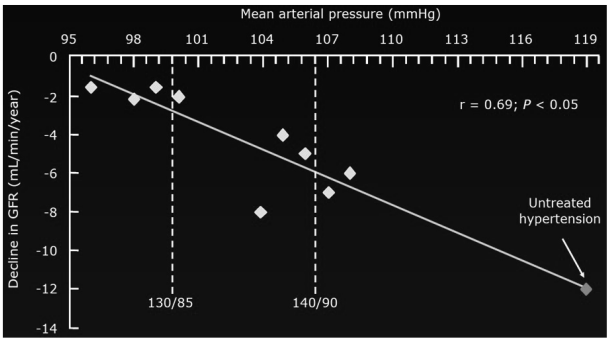
- Most (60~100%) patients with CKD have hypertension
- Cardiovascular disease (CVD)
  : leading cause of death on dialysis patients
- Left ventricular hypertrophy (LVH)
  : common and almost universal with ESRD
- Benefit of lower BP target
  → renal & cardioprotective effect
- Goal of HTN treatment in CKD
  - reduce cardiovascular morbidity and mortality
  - preserve renal function: reduce proteinuria

Causes of hypertension in CKD patients

- Preexisting essential hypertension
- Extracellular volume expansion
- Renin-angiotensin aldosterone stimulation
- Increased sympathetic activity
- Increased body weight
- Erythropoietin administration
- Renovascular disease
- Divalent ions and parathyroid hormone
- Miscellaneous: AV fistula etc.

Reducing target-organ damage

Reduced blood pressure slows the rate of GFR decline



Bakris et al., *Am J Kidney Dis. 2000*

KDIGO ('12): Target Blood Pressure

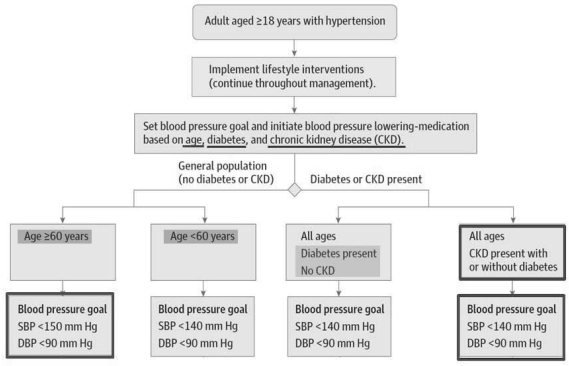
Management of blood pressure in adult CKD patients

Albuminuria (mg/day)[a]	BP Target mm Hg	Preferred agent
<30	⩽140/90 mm Hg	None
30-300	⩽130/80 mm Hg	ACE-I or ARB
>300	⩽130/80 mm Hg	ACE-I or ARB

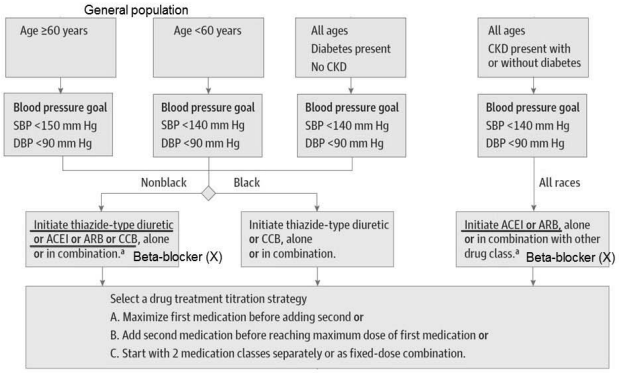
Does the presence of DM change the recommendations?

→ 'No'

JNC 8: Target Blood Pressure



Target Blood Pressure & Management



Anemia

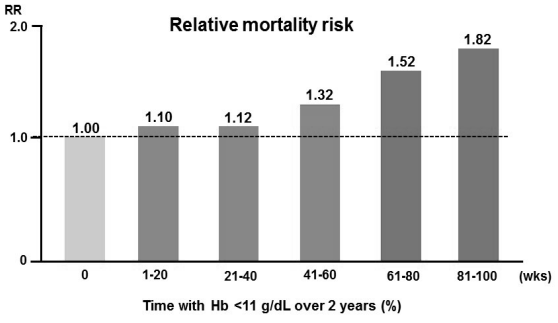
- Definition of **anemia** in CKD adults
  - Hb **< 13.0** g/dL in **males**
  - Hb **< 12.0** g/dL in **females**
- Frequency of testing for anemia

  Anemia(-) CKD, stage 3 → at least annually
  CKD, stage 4~5 → at least twice per year

  Anemia(+) CKD, stage 3~5 → at least **every 3 months**
- Investigation of anemia
  - Complete blood count (CBC), absolute reticulocyte count
  - ferritin, transferrin saturation (TSAT), vitamin B12, and folate

Anemia and outcomes

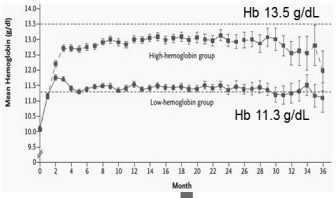
Duration of Hb <11 g/dL increases Mortality Risk in Dialysis patients



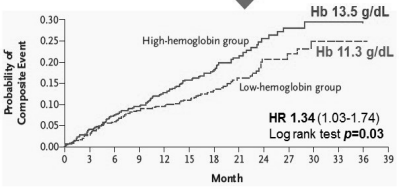
Ofsthun et al. *NDT 2005*

CHOIR study

1432 CKD patients
(eGFR 27.2: stage 4)
→ Hb 13.5 vs Hb 11.3

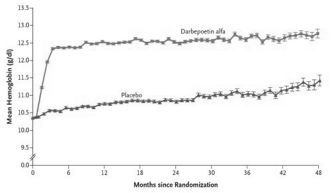


Death
Acute MI
Hospitalization d/t CHF
Stroke

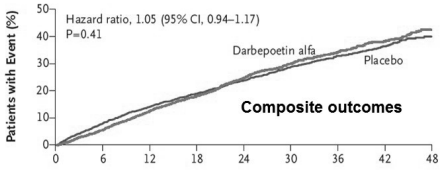


Singh et al. NEJM *2006*

TREAT study



- DM CKD (stage 3~4)
- Hb <11.0 g/dL
- Primary outcome: composite outcomes
  (Death + CV event + ESRD)
- Hb target: Group 1: 13.0 g/dL
  Group 2: rescue if Hb <9.0



Pfeffer et al. NEJM *2009*

Target Hb

KDIGO guideline (2012)

3.4.1: For adult CKD ND patients with Hb concentration **≥10.0 g/dl**, we suggest that ESA therapy **not** be **initiated**. (2D)

3.4.2: For adult CKD ND patients with Hb concentration **<10.0** g/dl, we suggest that **the decision whether to initiate ESA therapy be individualized** based on the rate of fall of Hb concentration, prior response to iron therapy, the risk of needing a transfusion, the risks related to ESA therapy and the presence of symptoms attributable to anemia. (2C)

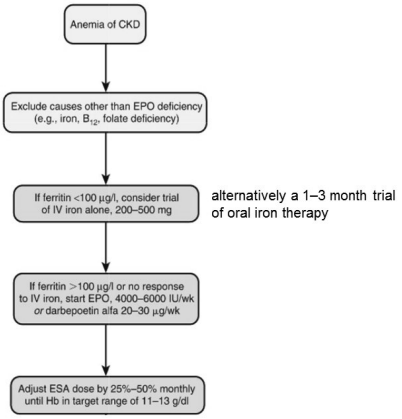
3.5.1: In general, we suggest that ESAs **not** be used to maintain Hb concentration **above 11.5 g/dl** in adult patients with CKD. (2C)

3.6: In all adult patients, we recommend that ESAs **not** be used to **intentionally** increase the Hb concentration **above 13 g/dl**. (1A)

Harrison's Internal Medicine (19th ed)

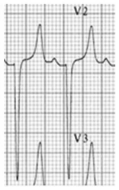
Target: Hb 10.0~11.5 g/dL

Management of Anemia in CKD



Hyperkalemia

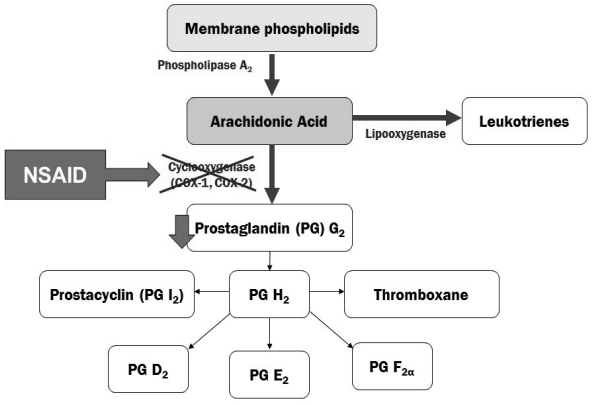
- Clinical manifestation
  1) Cell membrane depolarization
     : weakness, paralysis, hypoventilation
  2) Decreased renal ammoniagenesis
     : metabolic acidosis
  3) Cardiac toxicity
     : Serum K^+ 농도와 반드시 비례하지는 않음
     가장 초기 EKG 소견 : peaked T wave
     prolonged PR interval and QRS duration,
     atrioventricular conduction delay,
     loss of P waves, ventricular fibrillation or asystole



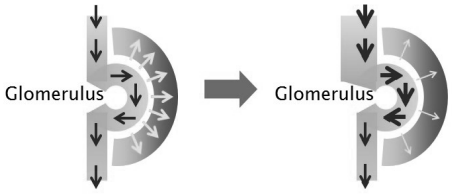
Current treatment of Hyperkalemia

치료제	용량	작용시작	효과지속시간
1. Calcium gluconate (10%) (↓membrane excitability)	10~20ml IV over 2~3'	1~3분	30~60분
2. Sodium bicarbonate (8%)	50~100mEq IV	5~10분	~2hr
3. Insulin + glucose (세포내로 이동)	RI 20U + D50W 100cc (15~30min)	15분	4~6hr
4. Albuterol (salbutamol)	nebulized inhaler로 10분에 10 mg 투여		
5. 양이온 교환수지 (kalimate 또는 kayexelate)	25~50g (경구/직장)	1~2hr	4~6hr
6. 혈액/복막 투석		(수분 내)	

NSAID

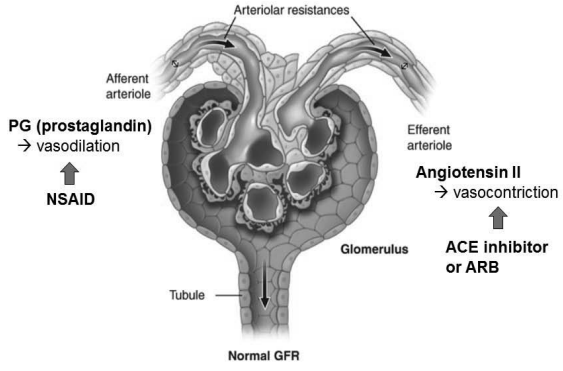


NSAID



- **GFR이 감소될 상황이 되면 → prostaglandin 생성 증가**
  → afferent arteriole을 확장
  → renal blood flow와 사구체 여과율 유지
- **Prostaglandin** : GFR 유지에 중요한 역할
  → 만약, 생성이 저하되면 → AKI 가능성↑

Mechanism of AKI d/t NSAID



Harrison's Principles of Internal Medicine, 18th ed.

Renal complications d/t NSAID

1) Acute kidney injury

2) Edema / Hypertension (d/t sodium retention)

3) Hyponatremia (d/t water retention)

4) Hyperkalemia

Common conditions of NSAID induced AKI

Conditions associated with NSAID-induced acute kidney injury

Volume depletion: emesis, diarrhea, sepsis, hemorrhage
Medications: diuretics, ACE-I, ARB, calcineurin inhibitors
Cirrhosis
Congestive heart failure
Nephrotic syndrome
Hypercalcemia (severe)
Chronic kidney disease
Renal artery stenosis
Older age
Angiotensin converting enzyme (ACE) inhibitor and angiotensin receptor blocker (ARB)

UptoDate

Chronic metabolic acidosis

3.4: ACIDOSIS

3.4.1: We suggest that in people with CKD and serum bicarbonate concentrations <22 mmol/l treatment with oral bicarbonate supplementation be given to maintain serum bicarbonate within the normal range, unless contraindicated. (*2B*)

2012 KDIGO guideline

with oral sodium bicarbonate supplementation. Animal and human studies have suggested that even modest degrees of metabolic acidosis may be associated with the development of protein catabolism. Alkali supplementation may attenuate the catabolic state and possibly slow CKD progression and accordingly is recommended when the serum bicarbonate concentration falls below 20–23 mmol/L. The concomitant sodium load mandates careful attention to volume status and the need for diuretic agents.

Harrison's Internal Medicine, 19th Edition. Chapter 335, Page 1814