بنام خداوند لطیف

Chronic kidney disease

- **INTRODUCTION** — The definition and classification of chronic kidney disease (CKD) guidelines were introduced by the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI) in 2002, and were subsequently adopted with minor modifications by the international guideline group Kidney Disease Improving Global Outcomes (KDIGO) in 2004 [1-3].
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- **Definition of CKD** — We agree with the KDOQI and KDIGO guidelines that CKD is defined by the presence of kidney damage **or** decreased kidney function **for three or more months**, irrespective of the cause

Definition: Chronic kidney disease is defined based on the presence of either kidney damage or decreased kidney function for three or more months, irrespective of cause

- The persistence of the damage or decreased function for at least three months is **necessary** to distinguish CKD from acute kidney disease.

- Kidney damage refers to pathologic abnormalities, whether established via renal biopsy or imaging studies, or inferred from markers such as urinary sediment abnormalities or increased rates of urinary albumin excretion.

- بيماري مزمن كليه از طيفي از فرايندهاي پاتوفيزيولوژيك مختلف مرتبط با عملكرد غير طبيعي كليه و يك كاهش پيشرونده در ميزان فيلتراسيون گلومرولي تشكيل ميشود

پاتوفيزيولوژي

- پاتوفيزيولوژي CKD شامل دو دسته مكانيسم است
- 1-مكانيسم آغازگر و اتيولوژي زمينه اي مثل اختلالات ژنتيكي در پيشرفت نارسايي كليه،رسوب كمپلكس هاي ايمني و التهاب در انواع خاصي از گلومرولونفريت ها يا مواجهه با سموم در انواع خاصي از بيماريهاي توبولواينترسيشيوم

- 2-گروهي از مكانيسمهاي پيشرونده شامل هيپرفيلتراسيون و هيپرتروفي نفرون هاي زنده باقي مانده كه نتيجه شايع كاهش طولاني مدت توده كليوي صرفنظر از اتيولوژي زمينه اي ميباشد

- پاسخ به کاهش تعداد نفرون ها توسط هورمون هاي وازواکتيو سيتوکين ها و فاکتورهاي رشد ميانجي گري ميشود.در حقيقت اين سازگاري کوتاه مدت هيپرتروفي و هيپرفيلتراسيون ،هنگامي که فشار و جريان نفرون افزايش يافته منجر به تخريب ساختمان گلومرول و عملکرد غير طبيعي پودوسيت ها و شکسته شدن سد فيلتراسيون ميشود که همراه با اسکلروز است

- بنظر ميرسد افزايش فعاليت درون كليوي محور رنين آنژيوتانسين نتيجه هيپرفيلتراسيون تطابقي و اسكلروز متعاقب ان ميباشد.اين روند بيان ميكند كه چرا كاهش توده كليوي ناشي ازيك insult مجزأ ميتواند سبب كاهش پيشرونده عملكرد كليوي طَي سالهاي متمادي شود

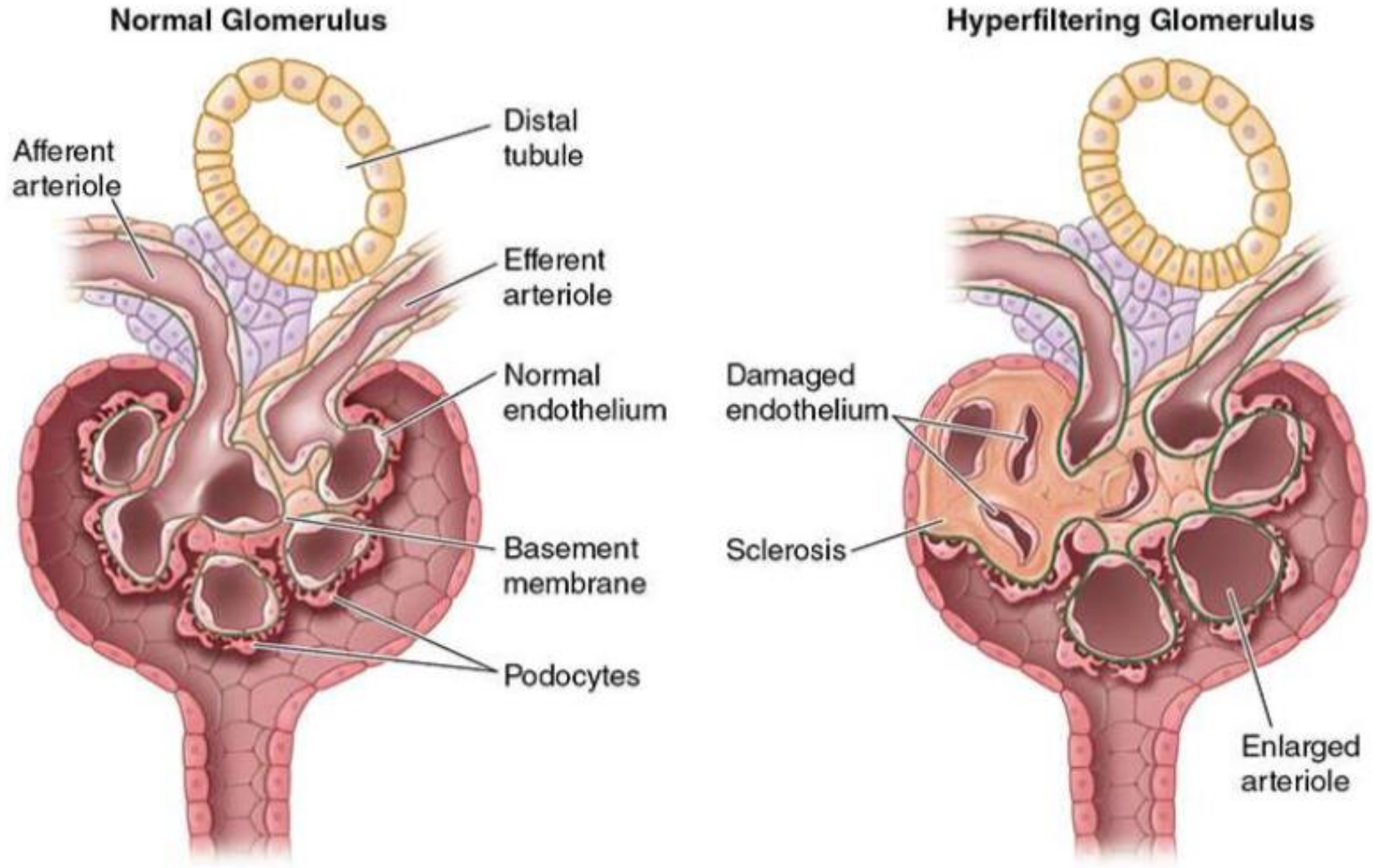


FIGURE 305-2 ***Left:*** Schema of the normal glomerular architecture. ***Right:*** Secondary glomerular changes associated with a reduction in nephron number, including enlargement of capillary lumens and focal adhesions, which are thought to occur consequent to compensatory hyperfiltration and hypertrophy in the remaining nephrons. *(Modified from JR Ingelfinger: N Engl J Med 348:99, 2003.)*

Kidney damage, as defined by structural abnormalities or functional abnormalities other than decreased GFR

Imaging abnormalities as markers of kidney damage (ultrasound, computed tomography and magnetic resonance imaging with or without contrast, isotope scans, angiography).

- Polycystic kidneys
- Hydronephrosis due to obstruction
- Cortical scarring due to infarcts, pyelonephritis or vesicoureteral reflux
- Renal masses or enlarged kidneys due to infiltrative diseases
- Renal artery stenosis
- Small and echogenic kidneys (common in later stages of CKD due to many parenchymal diseases)

- Imaging abnormalities as markers of kidney damage (ultrasound, computed tomography and magnetic resonance imaging with or without contrast, isotope scans, angiography).Polycystic kidneysHydronephrosis due to obstructionCortical scarring due to infarcts, pyelonephritis or vesicoureteral refluxRenal masses or enlarged kidneys due to infiltrative diseasesRenal artery stenosisSmall and echogenic kidneys (common in later stages of CKD due to many parenchymal diseases)

- Pathologic abnormalities (examples). Cause is based on underlying illness and pathology. Markers of kidney damage may reflect pathology.Glomerular diseases (diabetes, autoimmune diseases, systemic infections, drugs, neoplasia) Vascular diseases (atherosclerosis, hypertension, ischemia, vasculitis, thrombotic microangiopathy) Tubulointerstitial diseases (urinary tract infections, stones, obstruction, drug toxicity)Cystic disease (polycystic kidney disease)

Staging of CKD

- ●Cause of disease
- ●Six categories of GFR (G stages)
- ●Three categories of albuminuria (A stages

- ●Albuminuria − In clinical practice, albuminuria is the most frequently assessed marker of kidney damage. Albuminuria reflects increased glomerular permeability to macromolecules

- Albuminuria may reflect primary kidney disease or kidney involvement in systemic disease. In particular, albuminuria may represent widespread endothelial dysfunction, such as can be seen with hypertension, diabetes, hypercholesterolemia, smoking, obesity, and other disorders.

- Although a number of different measurement methods have been used to assess and define albuminuria (table 2), the albumin-to-creatinine ratio (ACR) in an untimed "spot" urine has many advantages (calculator 1) [25,26]. The generally accepted threshold for an abnormally elevated ACR is 30 mg/g (3.4 mg/mmol) or greater.

- Albuminuria as a marker of kidney damage (increased glomerular permeability, urine albumin-to-creatinine ratio [ACR] >30 mg/g).*The normal urine ACR in young adults is <10 mg/g. Urine ACR categories 10-29, 30-300 and >300 mg are termed "mildly increased, moderately increased, and severely increased" respectively. Urine ACR >2200 mg/g is accompanied by signs and symptoms of nephrotic syndrome (low serum albumin, edema and high serum cholesterol).Threshold value corresponds approximately to urine dipstick values of trace or 1+, depending on urine concentrationHigh urine ACR can be confirmed by urine albumin excretion in a timed urine collection

- In the KDOQI and KDIGO definition, the threshold value for abnormally elevated urine ACR (30 mg/g or higher) is applied to adults of all ages, both men and women, and all racial-ethnic groups, despite differences in creatinine excretion rate by age, sex, and race.

- Thus, sex-specific ACR thresholds that better predict a 24-hour urinary albumin excretion of 30 mg or higher (≥25 mg/g for women and ≥17 mg/g for men) have been used in some studies

- **GFR estimation** — The various GFR estimating equations use serum creatinine along with some combination of age, sex, race and body size as surrogates for the non-GFR determinants of serum creatinine, and provide more accurate estimates of measured GFR than serum creatinine alone

- براي تعيين مرحله CKD،تعيين GFR بيشتر از تكيه بر كراتينين سرم ضروري است .
- امروزه بسياري از آزمايشگاهها GFR تخميني يا eGFR را با استفاده از يكي از معادله هاي ذيل گزارش ميكنند

- GFR is the best overall index of kidney function in health and disease.The normal GFR in young adults is approximately 125 mL/min/1.73 m2; GFR <15 mL/min/1.73 m2 is defined as kidney failureDecreased GFR can be detected by current estimating equations for GFR based on serum creatinine (estimated GFR) but not by serum creatinine aloneDecreased estimated GFR can be confirmed by measured GFR, measured creatinine clearance, or estimated GFR using cystatin C

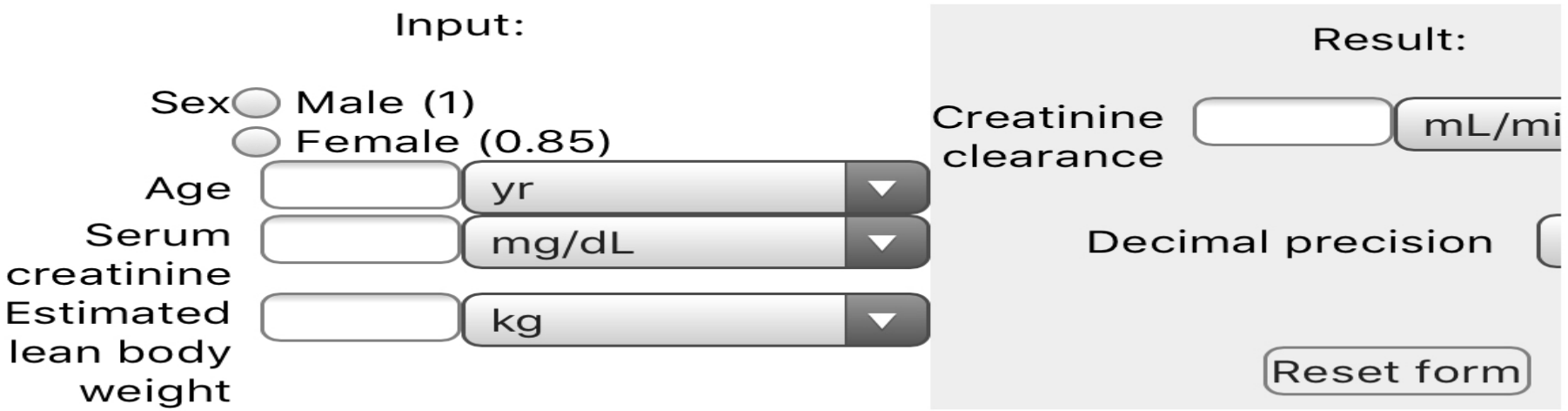
- The Modification of Diet in Renal Disease (MDRD) Study equation is the most frequently used GFR estimating equation in the US

- Cystatin C is an alternative endogenous filtration marker that may have advantages over creatinine for GFR estimation because its non-GFR determinants are less affected by race and muscle wasting, and because it is more predictive of subsequent cardiovascular disease and mortality [49-52]. Use of cystatin C and creatinine together enables more accurate GFR estimates [50,53],

TABLE 305-1 Recommended Equations for Estimation of Glomerular Filtration (S_{CR}), Age, Sex, Race, and Body Weight

1. Equation from the Modification of Diet in Renal Disease Study
Estimated GFR (mL/min per 1.73 m^2) = $1.86 \times (S_{Cr})^{-1.154} \times (age)^{-0.203}$
Multiply by 0.742 for women
Multiply by 1.21 for African ancestry
2. CKD-EPI Equation
$GFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{Age}$
Multiply by 1.018 for women
Multiply by 1.159 for African ancestry
where S_{Cr} is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is –0.329 for females and –0.411 for males, min indicates the minimum of S_{Cr}/κ or 1, and max indicates the maximum of S_{Cr}/κ or 1.

Creatinineclearance = Sex * ((140 - Age) / (Serumcreatinine)) * (Estimatedleanbodyweight / 72)



Notes

- The Cockcroft-Gault equation was developed prior to the use of standardized creatinine assays and has **not** been revised for use with creatinine values traceable to standardized reference materials. Thus, using the Cockcroft-Gault equation with creatinine values measured by most laboratories in the United States today will result in a 10 to 40 percent **overestimate** of creatinine clearance.
- You can estimate the creatinine clearance from the formula only if the serum creatinine concentration is stable.
- See UpToDate topic reviews that discuss calculation of the creatinine clearance for a review of the accuracy of the creatinine clearance as an estimate of the true glomerular filtration rate.

$$GFR = 141 * \min(Serumcreatinine/kappa, 1)^{alpha} * \max(Serumcreatinine/kappa, 1)^{-1.209} * 0.993^{Age} * Sex * Race$$

Input:

Sex ○ Female
○ Male
Race ○ White or Other (1)
○ Black (1.159)
Age [ ] years
Serum creatinine [ ] mg/dL

Results:

GFR [ ] mL/min/1.73m

Decimal precision 2

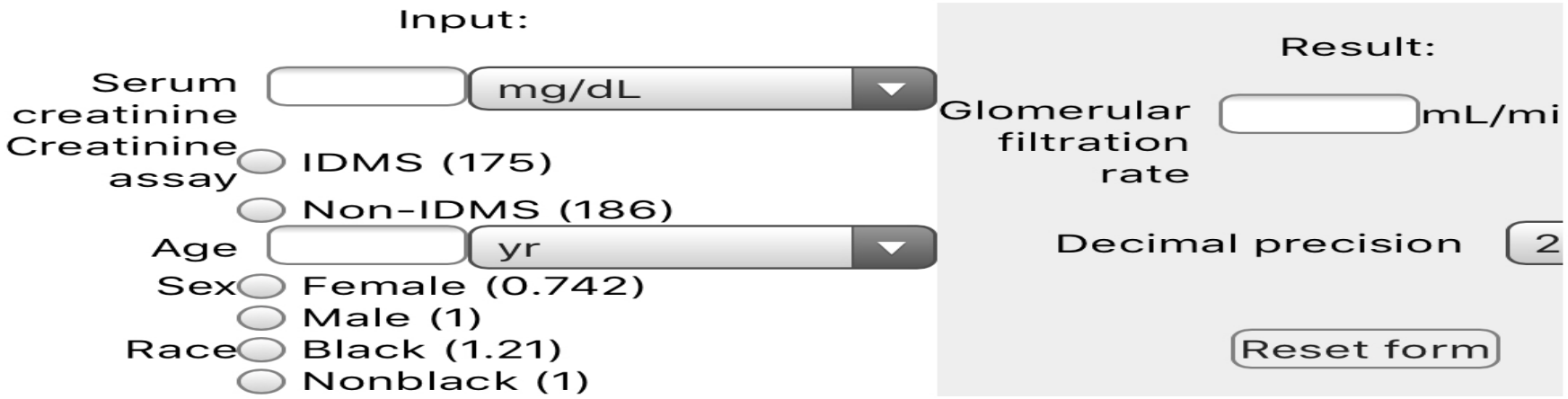
Reset form

Notes

- Glomerular filtration rate (GFR) is estimated by an equation developed by the Chronic Kidney Disease Epidemiology (CKD-EPI) Collaboration.
- For females, the following values are used: Sex = 1.018; alpha = -0.329; kappa = 0.7.
- For males, the following values are used: Sex = 1; alpha = -0.411; kappa = 0.9.

Equation parameters, such as **Race**, have two or more discrete values that may be used in the calculation. The numbers in the parentheses, eg, (1), represent the values that will be used.

Glomerularfiltrationrate = Creatinineassay * Serumcreatinine$^{-1.154}$ * Age$^{-0.203}$ * Sex * Race

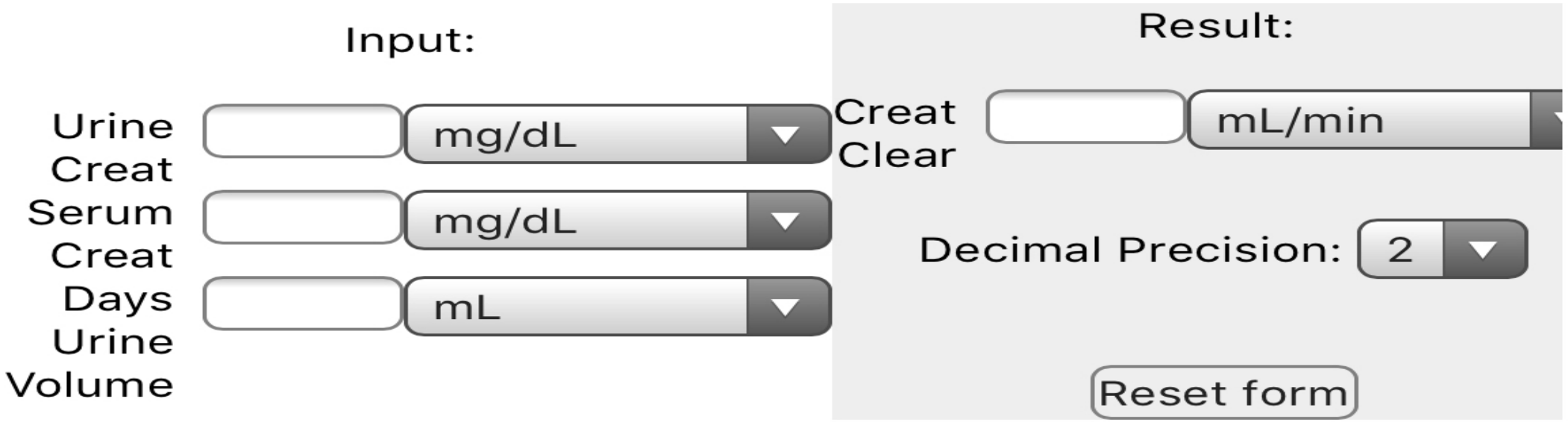


Notes

- MDRD study: Modification of Diet in Renal Disease study.
- Isotope dilution mass spectrometry (**IDMS**) indicates a method for determining creatinine concentration that has been standardized using or traceable to IDMS. Contact laboratory if uncertain as to whether or not reported values are IDMS-traceable.
- You can estimate the glomerular filtration rate from the formula if the serum creatinine concentration is stable.
- The accuracy of the abbreviated MDRD study equation as an estimate of the true glomerular filtration rate is discussed elsewhere in UpToDate.

Equation parameters, such as **Creatinine assay**, have two or more discrete values that may be used in the calculation. The numbers in the parentheses, eg, (175), represent the values that will be used.

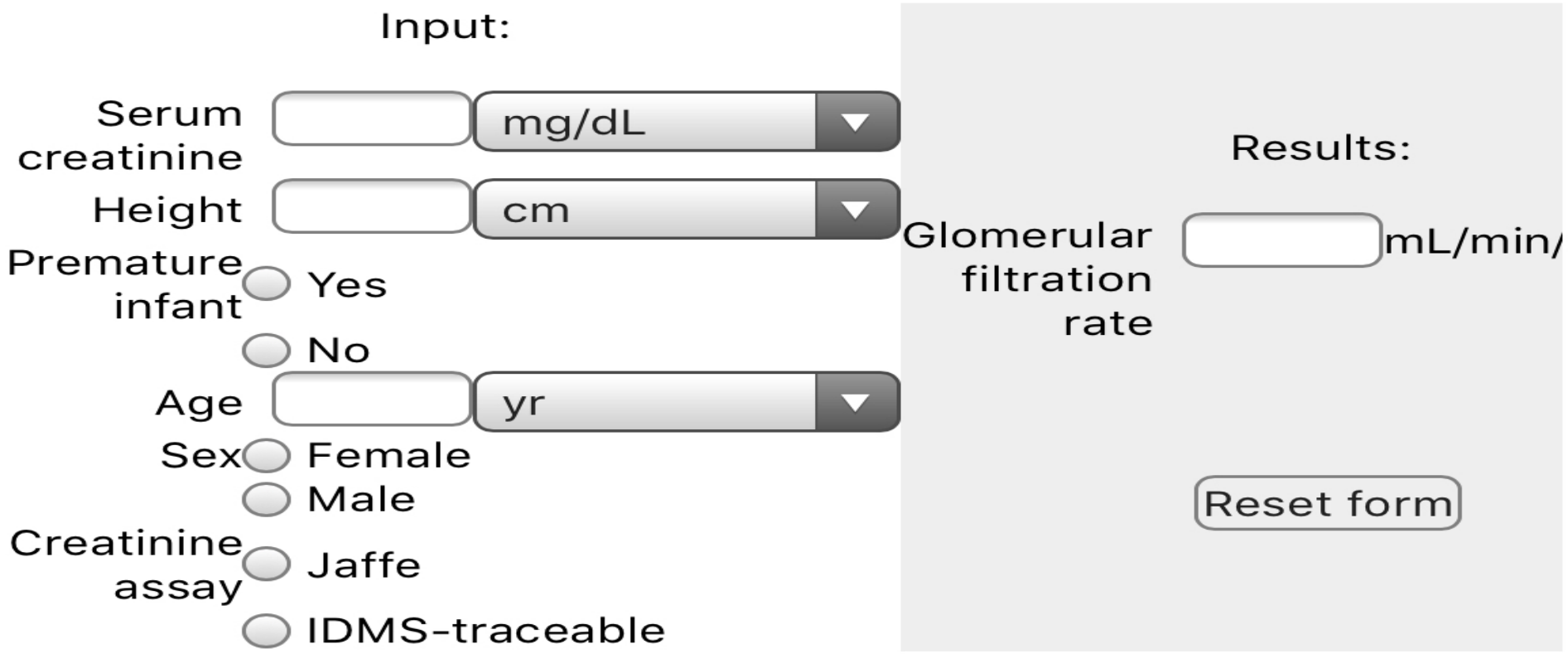
CreatClear = UrineCreat * DaysUrineVolume / SerumCreat / 1440



To calculate the creatinine clearance from a 24-hour urine collection, enter your patient's data into the appropriate data fields. The serum creatinine concentration must be stable for this formula to be valid. (See UpToDate topic reviews that discuss calculation of the creatinine clearance, for a review of the factors that limit the accuracy of this test).

Only digits 0 to 9 and a single decimal point (".") are acceptable as numeric inputs. Attempted input of other characters into a numeric field may lead to an incorrect result.

Glomerularfiltrationrate = k * Height / Serumcreatinine



Notes

- Isotope dilution mass spectrometry (**IDMS**) indicates a method for determining creatinine concentration that has been standardized using or traceable to IDMS. Contact laboratory if uncertain as to whether or not reported values are IDMS-traceable.

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	1 if CKD	1	2
	G2	Mildly decreased	60-89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45-59	1	2	3
	G3b	Moderately to severely decreased	30-44	2	3	3
	G4	Severely decreased	15-29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

GFR and albuminuria grid to reflect the risk of progression by

- ●Moderate risk (yellow) – 73 percent of patients with CKD
- ●High risk (orange) – 18 percent of patients with CKD
- ●Very high risk (red) – 9 percent of patients with CKD

Chronic kidney disease classification based upon glomerular filtration rate and albuminuria

GFR stages	GFR (mL/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)
Albuminuria stages	**AER (mg/day)**	**Terms**
A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
A2	30 to 300	Moderately increased
A3	>300	Severely increased (may be subdivided into nephrotic and non-nephrotic for differential diagnosis, management, and risk prediction)

The cause of CKD is also included in the KDIGO revised classification

- **GFR** — The GFR (G-stages) follow the original CKD classification scheme (table 3):
- ●G1 − GFR >90 mL/min per 1.73 m^2
- ●G2 − GFR 60 to 89 mL/min per 1.73 m^2
- ●G3a − GFR 45 to 59 mL/min per 1.73 m^2
- ●G3b − GFR 30 to 44 mL/min per 1.73 m^2
- ●G4 − GFR 15 to 29 mL/min per 1.73 m^2
- ●G5 − GFR <15 mL/min per 1.73 m^2 or treatment by dialysis
-

- **Albuminuria —** The three albuminuria stages follow familiar definitions of normal, moderately increased (formerly called "microalbuminuria"), and severely increased (formerly called "macroalbuminuria" and nephrotic range) albuminuria (table 3) (calculator 1):
- ●A1 − ACR <30 mg/g (<3.4 mg/mmol)
- ●A2 − ACR 30 to 299 mg/g (3.4 to 34.0 mg/mmol)
- ●A3 − ACR ≥300 mg/g (>34.0 mg/mmol)
-

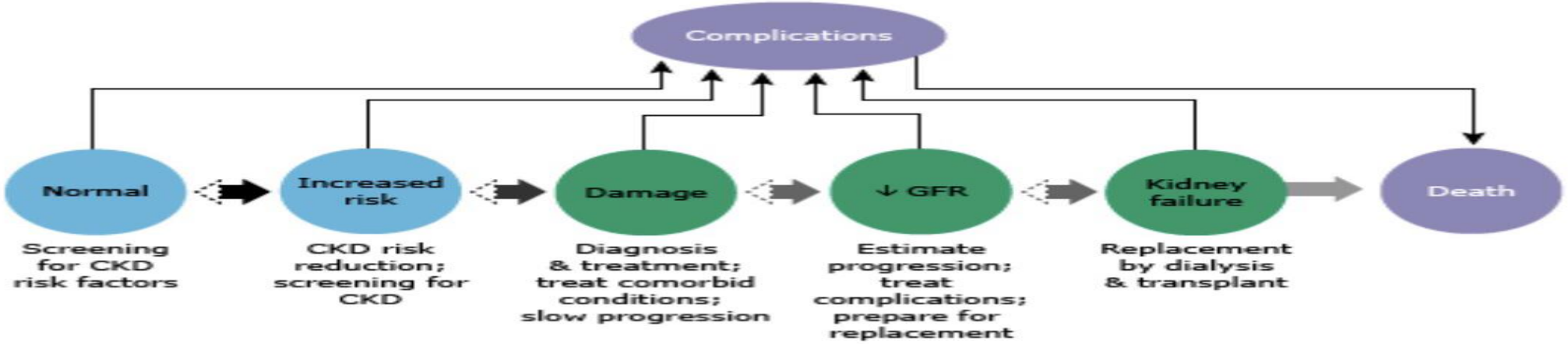
Definition and criteria for chronic kidney disease

Definition:

Chronic kidney disease is defined based on the presence of either kidney damage or decreased kidney function for three or more months, irrespective of cause.

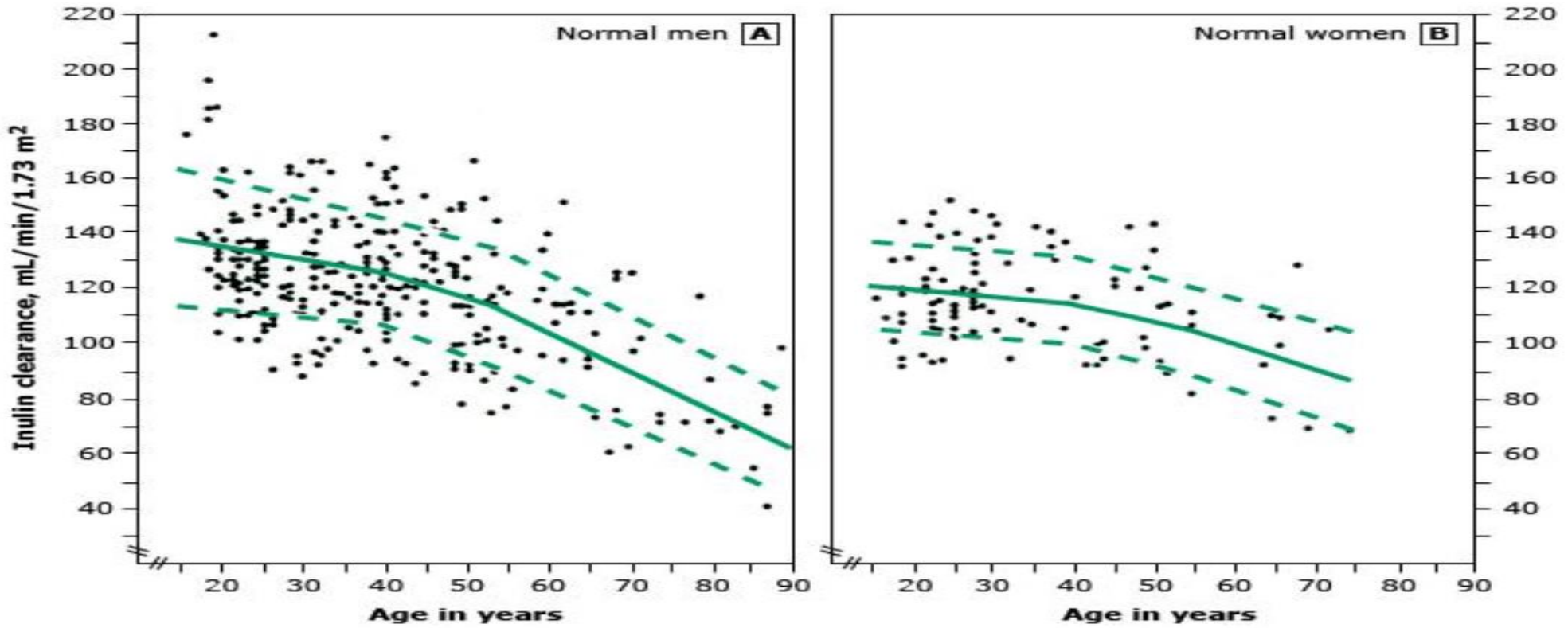
Criteria	Comment
Duration ≥3 months, based on documentation or inference	Duration is necessary to distinguish chronic from acute kidney diseases. ▪ Clinical evaluation can often suggest duration ▪ Documentation of duration is usually not available in epidemiologic studies
Glomerular filtration rate (GFR) <60 mL/min/1.73 m^2	GFR is the best overall index of kidney function in health and disease. ▪ The normal GFR in young adults is approximately 125 mL/min/1.73 m^2; GFR <15 mL/min/1.73 m^2 is defined as kidney failure ▪ Decreased GFR can be detected by current estimating equations for GFR based on serum creatinine (estimated GFR) but not by serum creatinine alone ▪ Decreased estimated GFR can be confirmed by measured GFR, measured creatinine clearance, or estimated GFR using cystatin C
Kidney damage, as defined by structural abnormalities or functional abnormalities other than decreased GFR	Pathologic abnormalities (examples). Cause is based on underlying illness and pathology. Markers of kidney damage may reflect pathology. ▪ Glomerular diseases (diabetes, autoimmune diseases, systemic infections, drugs, neoplasia) ▪ Vascular diseases (atherosclerosis, hypertension, ischemia, vasculitis, thrombotic microangiopathy) ▪ Tubulointerstitial diseases (urinary tract infections, stones, obstruction, drug toxicity) ▪ Cystic disease (polycystic kidney disease)
	History of kidney transplantation. In addition to pathologic abnormalities observed in native kidneys, common pathologic abnormalities include the following: ▪ Chronic allograft nephropathy (non-specific findings of tubular atrophy, interstitial fibrosis, vascular and glomerular sclerosis) ▪ Rejection ▪ Drug toxicity (calcineurin inhibitors) ▪ BK virus nephropathy ▪ Recurrent disease (glomerular disease, oxalosis, Fabry disease)
	Albuminuria as a marker of kidney damage (increased glomerular permeability, urine albumin-to-creatinine ratio [ACR] >30 mg/g).* ▪ The normal urine ACR in young adults is <10 mg/g. Urine ACR categories 10-29, 30-300 and >300 mg are termed "mildly increased, moderately increased, and severely increased" respectively. Urine ACR >2200 mg/g is accompanied by signs and symptoms of nephrotic syndrome (low serum albumin, edema and high serum cholesterol). ▪ Threshold value corresponds approximately to urine dipstick values of trace or 1+, depending on urine concentration ▪ High urine ACR can be confirmed by urine albumin excretion in a timed urine collection
	Urinary sediment abnormalities as markers of kidney damage, for example: ▪ RBC casts in proliferative glomerulonephritis ▪ WBC casts in pyelonephritis or interstitial nephritis ▪ Oval fat bodies or fatty casts in diseases with proteinuria ▪ Granular casts and renal tubular epithelial cells in many parenchymal diseases (non-specific)
	Imaging abnormalities as markers of kidney damage (ultrasound, computed tomography and magnetic resonance imaging with or without contrast, isotope scans, angiography). ▪ Polycystic kidneys ▪ Hydronephrosis due to obstruction ▪ Cortical scarring due to infarcts, pyelonephritis or vesicoureteral reflux ▪ Renal masses or enlarged kidneys due to infiltrative diseases ▪ Renal artery stenosis ▪ Small and echogenic kidneys (common in later stages of CKD due to many parenchymal diseases)

Conceptual model for chronic kidney disease



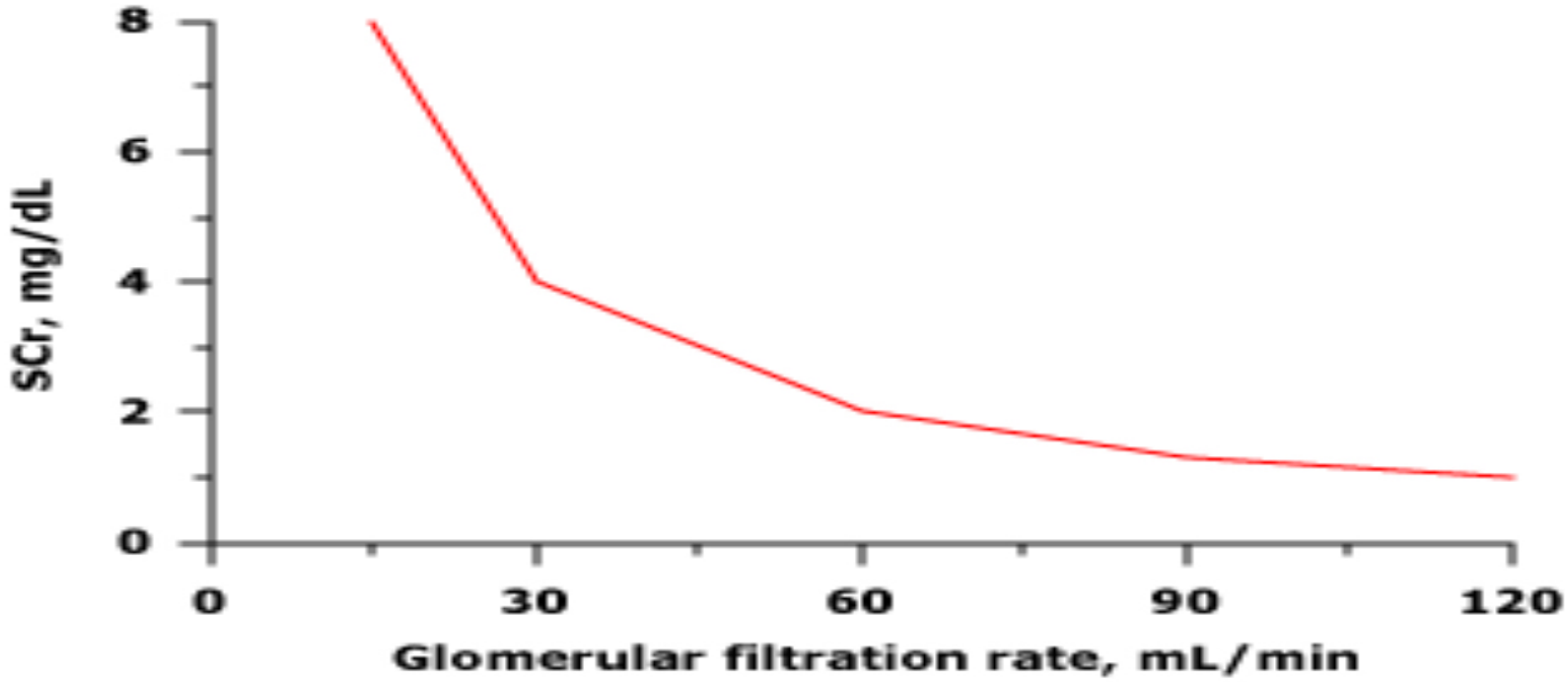
This diagram presents the continuum of development, progression and complications of chronic kidney disease (CKD) and strategies to improve outcomes. Green circles represent stages of CKD; aqua circles represent potential antecedents of CKD, lavender circles represent consequences of CKD; and thick arrows between circles represent the development, progression and remission of CKD. "CKD" is defined as the presence of either kidney damage or decreased kidney function for three or more months, irrespective of cause (underlying illness and pathology). "Complications" refers to all complications of CKD, including complications of decreased GFR, albuminuria and cardiovascular disease. Complications may also arise from adverse effects of interventions to prevent or treat the disease. The horizontal arrows pointing from left to right emphasize the progressive nature of CKD. Dashed arrowheads pointing from right to left signify that remission is less frequent than progression.

Normal values for GFR in men and women



Normal values for inulin clearance are shown for men (panel A) and women (panel B) of various ages, with the GFR measured as the urinary clearance of inulin. A GFR <60 mL/min/1.73 m^2 is the threshold for the definition of chronic kidney disease. Solid lines represent the mean value of GFR per decade of age, and dashed lines represent the value 1 SD from the mean value of GFR per decade of age.

Serum creatinine and GFR



Idealized steady-state relationship between the serum creatinine concentration (SCr) and the GFR. A fall in GFR decreases creatinine filtration and produces a proportionate rise in the serum creatinine concentration.

شناسايي ريسك فاكتورها و مرحله بندي CKD

- حتي در افراد داراي GFR نرمال مشخص كردن عواملي كه خطر CKD را افزايش ميدهد مهم است.ريسك فاكتور ها شامل:سن بالا-نژاد آفريقايي-سابقه خانوادگي بيماري كليوي،سابقه اسيب حاد كليوي در گذشته،وجود پروتئينوري ،سديمان ادراري غيرطبيعي ،يا ناهنجاري ساختاري در مجاري ادراري است

- فرمهاي إرثي نادر CKD از الگوي توارث مندلي پيروي ميكند و معمولا بخشي از يك سندرم سيستميك ميباشد.كه مثال شايع آن كليه پلي كيستيك اتوزومال غالب ميباشد.

- تحقيقات اخير در ژنتيك در رابطه با استعداد به بيماريهاي پيچيده شايع نشانگر اين بوده است كه قطعات DNA گوناگون در قسمتهاي ژنتيكي بسياري با انواع شايع CKD همراه بوده است .يك نمونه از آن يافتن نسخه آلل ژن APOI1 از نژاد جمعيتي غرب آفريقا ست كه با فراواني بسيار بالاتر در اتيولوژي هاي شايع CKD براي مثال FSGN همراه هست كه در آفريقايي ها و آمريكايي هاي اسپانيايي ديده ميشود ،همانند ساير بيماريهاي شايع إرثي عامل محيطي براي تبديل ريسك خطر ژنتيكي به بيماري نياز هست

- میانگین کاهش طبیعي سالیانه GFR در رابطه با سن به این صورت است که از حداکثر GFR تقریبا 120ml/min در دهه سوم زندگي تقریبا 1ml/min در هر سال کاهش میابد که در نهایت در هفتاد سالگي به متوسط 70ml/minمیرسد

- میانگین GFR در زنان کمتر از مردان است
- معادلات GFRتخميني فقط در صورتيكه شرايط بيمار ثابت باشد معتبر است
- اندازه گيري آلبومينوري براي تحت نظر گرفتن اسيب نفرون و پاسخ به درمان در بسياري از فرمهاي CKD كمك كننده است

- ميكروآلبومينوري اشاره به دفع مقاديري از آلبومين دارد كه توسط نوار ادراري يا روش هاي مرسوم اندازه گيري پروتئين در ادرار قابل شناسايي نباشد ،بطور ويژه اين روش يك تست غربالگري خوب براي تشخيص زود هنگام بيماري كليوي است

- CKD مرحله 1و2 معمولا علائمي ناشي از كاهش GFR ندارند.اگر كاهش GFR به مرحله 3و4 برسد عوارض باليني و آزمايشگاهي CKD برجسته تَر ميشوند .در حقيقت همه ارگانها تحت تأثير قرار ميگيرندولي شايعترين عوارض شامل :

- آنمي،خستگي پذيري زودرس ،كاهش اشتها همراه با سوءتغذيه پيشرونده ،ناهنجاري در هورمون تنظيم كننده كلسيم ،فسفر،و مواد معدني مثل كلسي تريول و هورمون PTH،و فكتور رشد فيبروبلاست FGF-23،و اختلال در هموستاز سديم پتاسيم ،آب و أسيد و باز ميباشد

اتيولوژي و اپيدميولوژي

- با توجه به اطلاعات حاصل از از پايش هاي جمعيتي تخمين زده ميشود كه حداقل 6٪ از جمعيت بالغ أمريكا داراي بيماري CKD در مرحله 1يا2 هستند .تخمين زده ميشود كه 4.5% ديگر از جمعيت أمريكا CKD مرحله 3يا4 دارند

- 5 دسته شايع علل CKD كه مسئول بيش از 90% بيماري CKD در جهان است در جدول صفحه بعد ذكر شده است

TABLE 305-2 Leading Categories of Etiologies of CKD[a]

- Diabetic nephropathy
- Glomerulonephritis
- Hypertension-associated CKD (includes vascular and ischemic kidney disease and primary glomerular disease with associated hypertension)
- Autosomal dominant polycystic kidney disease
- Other cystic and tubulointerstitial nephropathy

- CARDIOVASCULAR ABNORMALLY

CARDIO VASCULAR ABNORMALLY

- بيماري قلبي عروقي علت أصلي مورتاليتي در بيماران مبتلا به CKD در تمامي مراحل ميباشد ،ميزان افزايش خطر بيماري عروقي منتسب به CKD براساس مرحله CKD در مقايسه با جمعيت عمومي يكسان سازي شده از نظر جنس و سن از ۱۰ تا ۲۰۰ برابر است .

- بین 35 تا 40 % بیمارانیکه به مرحله پنجم CKD میرسند قبلا عوارض قلبي عروقي داشته اند.بنابراین تمرکز درمان بیمار در مراحل اولیه CKD باید به پیشگیري از عوارض قلبي عروقي معطوف شود .

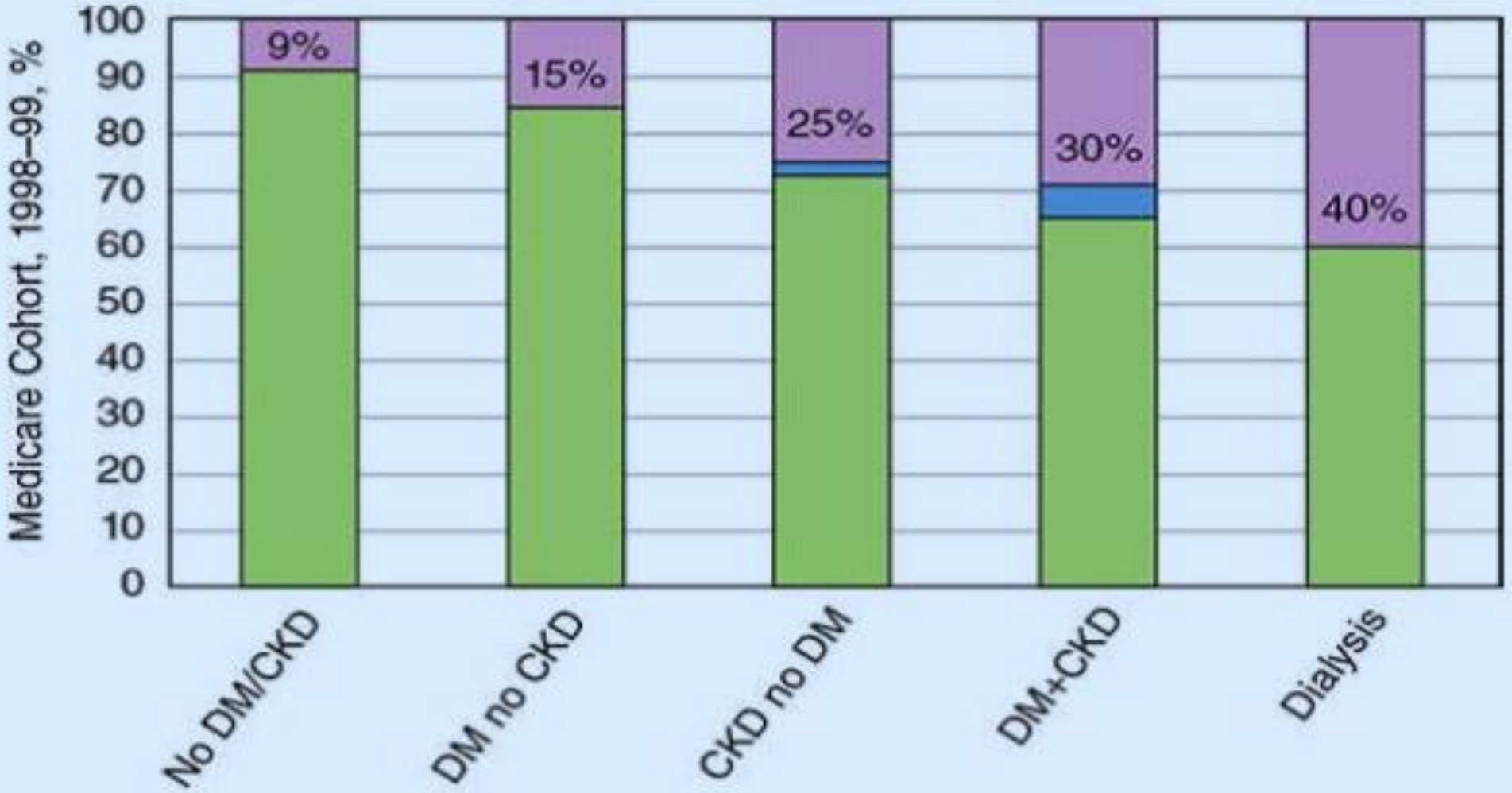


FIGURE 305-6 U.S. Renal Data System showing increased likelihood of dying rather than s
disease (CKD). 1, Death; 2, ESRD; 3, event-free. DM; diabetes mellitus. *(Data from RN Foley*

ISCHEMIC VASCULAR Disease

- CKDدر تمام مراحل ،يك عامل خطر أصلي براي بيماري كارديوواسكولار شامل بيماريهاي كرونري،سربرو واسكولار،و عروق محيطي بشمار ميرود .افزايش شيوع بيماريهاي قلبي كرونري در CKD ناشي از عوامل كلاسيك و غير كلاسيك وابسته به CKDاست.

عوامل خطر کلاسیک

- شامل :
- هیپرتانسیون
- هیپروولمي
- دیس لیپیدمي
- افزایش فعالیت سمپاتیک
- هیپر هموسیستئینمي

عوامل خطر غير كلاسيك

- شامل :
- آنمي
- هيپرفسفاتمي
- هيپرپاراتيروئيديسم
- افزايش FGF-23
- آپنه خواب
- التهاب

- بازتاب وضيعت التهابي كه با كاهش در عملكرد كليه همراه هست افزايش واكنش دهنده هاي فاز حاد مثل سايتوكين هاي التهابي و CRP و يك كاهش متناظر در واكنش دهنده هاي منفي فاز حاد مثل آلبومين و فيتوئين سرم ميباشد . وضعيت التهابي ،بيماريهاي كرونري را تسريع كرده و سطوح پايين فيتوئين ممكنست منجر به كلسيفيكاسيون عروقي سريعتر بخصوص در حضور هيپرفسفاتمي ميشود

- ديگر اختلالاتي كه در CKD ممكنست باعث ايسكمي ميوكارد شود شامل هيپرتروفي بطن چپ و بيماري ميكروواسكولار است .
- همو ديالیز با دوره هاي هايپوتانسيون و هيپوولمي همراه ممكنست ايسكمي ميوكارد را بدتر كند
- سطوح تروپونين قلبي غالبا در CKD بدون شواهد ايسكمي حاد افزايش يافته است.و در تشخيص ايسكمي ميوكارد اندازه گيري سريال مورد نياز است
- سطوح افزايش يافته پايدار ،يك فاكتور پيش بيني كننده غيروابسته براي حوادث كارديوواسكولار است

HEART Failure

- اختلال عملكرد قلب ثانويه به بيماريهاي ايسكميك ميوكارد ،هيپرتروفي بطن چپ.و كارديوميوپاتي پيشرفته،همراه با احتباس آب و نمك كه در CKD ميتوان ديد اغلب به نارسايي احتقاني قلب و يا حتي ادم ريه مي انجامد.نارسايي قلبي ميتواند نتيجه اختلال سيستوليك و يا دياستوليك و يا هر دو باشد.

- يك نوع ادم ريوي با فشار كم وجود دارد و با توزيع مايع ادم آلوئولار به شكل بال خفاش bat wing در گرافي سينه و تنگي نفس تظاهر مي يابد.اين فرايند به عنوان تظاهر وضعيت اورميك ،به افزايش نفوذپذيري آرتريول هاي آلوئولار نسبت داده ميشود كه به ديااليز پاخ دراماتيك ميدهد
- آنمي و sleep apnea هم در بيماران CKD منجر به نارسايي قلبي ميشوند

HYPERTENSION

- هيپرتانسيون يكي از شايعترين عوارض CKD است اين عارضه ممكنست در آغاز سير CKD رخ دهد و با عوارض سوء بويژه هيپرتروفي بطني و از دست رفتن سريعتر عملكرد كليوي همراه باشد.مطالعات بسياري وجود رابطه بين سطح فشارخون و ميزان پيشرفت بيماري كليه ديابتي و غير ديابتي را نشان داده اند .

- Hypertension is present in approximately 80 to 85 percent of patients with CKD [7]. The prevalence of hypertension is elevated in patients with kidney damage and a normal glomerular filtration rate (GFR) and increases further as the GFR falls.

- A variety of factors can contribute to the increased prevalence of hypertension in patients with CKD:
- ●Sodium retention is generally of primary importance, even though the degree of extracellular volume expansion may be insufficient to induce edema.

- ●Increased activity of the renin-angiotensin system is often responsible for at least part of the hypertension that persists after the restoration of normovolemia, particularly in patients with vascular disease since renal ischemia is a potent stimulus of renin secretion. Regional ischemia induced by scarring may also play a role.

- ●Hypertension can be a causative (eg, hypertensive nephrosclerosis) or contributory factor in the development of kidney disease.

- ●Hypertension may result from enhanced activity of the sympathetic nervous system [9]. The afferent signal may arise in part within the failing kidneys since it is not seen in patients who have undergone bilateral nephrectomy.

- Secondary hyperparathyroidism raises the intracellular calcium concentration, which can lead to vasoconstriction and hypertension [10]. Lowering parathyroid hormone secretion by the chronic administration of an active vitamin D analog can reduce both intracellular calcium and the systemic blood pressure

- Treatment with erythropoietin may increase blood pressure, an effect that is in part related to the degree of elevation in the hematocrit.

- Impaired nitric oxide synthesis and endothelium-mediated vasodilatation has been demonstrated in patients with uremia [11]. Although the mechanisms are unclear, potential explanations include reduced nitric oxide availability due to a state of increased oxidative stress or cofactor deficiency-induced uncoupling of nitric oxide synthase.

- ●Patients with end-stage renal disease (ESRD) are more likely to have an increase in central pulse pressure and isolated systolic hypertension [12]. Why this occurs is incompletely understood, but increased aortic stiffness probably plays an important role

- Patients with CKD may not demonstrate the normal nocturnal decline in blood pressure (such patients are called "nondippers"), a possible risk factor for hypertensive complication

TREATMENT OF HYPERTENSION IN CHRONIC KIDNEY DISEASE —

- Treatment of even mild hypertension is important in patients with CKD to protect against both progressive renal function loss and cardiovascular disease, the incidence of which is increased with mild to moderate CKD.

- **Benefits of sodium restriction** — Sodium restriction enhances the effect of many antihypertensive drugs. This is also true in patients with CKD, most of whom, as discussed below, are treated with angiotensin inhibitors to slow disease progression.

Use of diuretics and goal of therapy —

- Because of the reduction in renal function, higher doses of diuretics are typically required in patients with CKD who are usually volume expanded even in the absence of edema. Thiazide diuretics become less effective when the glomerular filtration rate (GFR) is less than 30 mL/min [18]. In such patients, loop diuretics are preferred as initial therapy. Torsemide, which has a longer duration of action than furosemide, may be preferred. (

- If edema persists, a thiazide diuretic can be added to the loop diuretic. The rationale for combined therapy is that most of the fluid leaving the loop of Henle after the administration of a loop diuretic is reabsorbed in the distal tubule, the site of action of thiazide diuretics. Thus, thiazides have an enhanced diuretic effect in patients treated with a loop diuretic.

- **Choice of antihypertensive therapy** — Attainment of goal blood pressure in patients with CKD typically requires multidrug therapy [21]. As with goal blood pressure discussed above, the choice of agent depends in part upon whether or not the patients have proteinuria.

- **Sequence of antihypertensive therapy in proteinuric CKD** — In patients with CKD who have proteinuria, defined as a protein excretion greater than or equal to 500 mg/day, we recommend angiotensin inhibitors as first-line therapy. We suggest diuretics and non-dihydropyridine calcium channel blockers (eg, diltiazem, verapamil)

- as second-line and third-line agents, although loop diuretics would be a first-line therapy with angiotensin inhibitors in patients with edema. When using angiotensin inhibitors and diuretics in combination as first-line therapy, we titrate the dose of the second drug slowly to avoid hypotension since diuretics enhance the antihypertensive effect of angiotensin inhibitors. (

First-line therapy in proteinuric CKD

- High-quality evidence favors the use of an ACE inhibitor or angiotensin II receptor blocker (ARB) as first-line therapy in patients with proteinuric CKD (ie, protein excretion greater than 500 mg/day)because, in addition to lowering the blood pressure, these drugs slow the rate of progression of CKD. The supportive data are presented elsewhere.

- Common side effects of angiotensin inhibition in patients with CKD include an acute reduction in GFR and hyperkalemia. In addition, both ACE inhibitors and ARBs are contraindicated in pregnancy. These issues are discussed in detail separately.

- If further antihypertensive therapy is required, we suggest a non-dihydropyridine calcium channel blocker (eg, diltiazem or verapamil) since these drugs also lower proteinuria. By contrast, dihydropyridines (eg, amlodipine) have little or no effect on protein excretion

- n patients with CKD who have proteinuria but **not edema**, we suggest either a diuretic or a non-dihydropyridine calcium channel blocker as second-line and then third-line therapy. Volume expansion, even in the absence of edema, often plays a major role in hypertension associated with CKD

- In patients **with edema**, we prefer initial therapy with a loop diuretic. Once the edema is controlled, an angiotensin inhibitor or a dihydropyridine calcium channel blocker (eg, amlodipine) can be added in either order if hypertension persists.

- ●In patients **without edema**, we start with an angiotensin inhibitor and then add a dihydropyridine calcium channel blocker (eg, amlodipine) as second-line therapy.

- Other antihypertensive drugs can be used as necessary in patients with CKD who have resistant hypertension. A mineralocorticoid receptor antagonist (spironolactone and eplerenone) is an effective fourth-line agent for the treatment of resistant hypertension in general and in patients with CKD. I

- The efficacy of mineralocorticoid receptor antagonists was evaluated in a study of 46 patients with a mean estimated GFR (eGFR) of 57 mL/min per 1.73 m^2 and hypertension that was not controlled with three mechanistically complementary drugs, including a diuretic and angiotensin inhibitor [26]. The mean fall in systolic pressure induced by mineralocorticoid receptor antagonists was 14.7 mmHg.

- Risk factors for hyperkalemia included a baseline eGFR ≤45 mL/min in patients with a serum potassium above 4.5 mEq/L and a fall in eGFR of more than 30 percent after therapy.

- هيپرتروفي بطن چپ و كارديوميوپاتي احتقاني از خطرناكترين عوامل خطر درافزايش مورتاليتي بيماران مبتلا به CKD ميباشد و مربوط به افزايش ECFV ميباشد علاوه براين آنمي و تعبيه فيستول وريدي شرياني براي ديالیز سبب برون ده قلبي بالا و نارسايي قلبي متعاقب آن ايجاد كند

- **Left ventricular hypertrophy** — LVH is a major risk factor for cardiovascular morbidity and mortality in ESRD patients [6,7]. Among patients with ESRD or near ESRD, the reported prevalence of LVH is nearly 75 to 80 percent, with a higher prevalence among those of greatest dialysis vintage

- فقدان هيپرتانسيون ممكنست مؤيد عملكرد ضعيف بطن چپ باشد در واقع در مطالعات اپيدميولوژيك بيماران دياليزي ،فشارخون پايين نشان دهنده بدتر بودن پيش آگهي در مقايسه با كسانيست كه داراي هيپرتانسيون ميباشند.اين فرايند در بيماران مسئول reverse causation است كه درآن عوامل خطر كلاسيك مثل هيپرتانسيون ،هيپرليپيدمي،و چاقي باعث پيش آگهي بهتري ميشوند.

- استفاده از داروهاي محرك اريتروپوئز اگزوژن ممكنست هيپرتانسيون و نياز به داروهاي آنتي هيپرتانسيو را افزايش ميدهد .پره لود مزمن ECFV هم يك عامل دخيل در هيپرتانسيون است و معمولا با استفاده از محدوديت سديم خوراكي ،ديورتيك ها و حذف مايعات از طريق دياليز هيپرتانسيون كنترل ميشود .

درمان هيپرتانسيون

- هدف كلي در درمان هيپرتانسيون در بيماران CKD ،پيشگيري از عوارض خارج كليوي هيپرتانسيون مانند بيماريهاي كارديوواسكولار و سربرووواسكولار ميباشد .در تمام بيماران CKD فشارخون بايد در سطح تعيين شده توسط برنامه راهنماي كميته ملي كنترل شود .

- در بيماران CKD با ديابت يا پروتئينوري بيش از 1g/day فشارخون بايد در حد 130/80 كنترل شود
- محدوديت نمك خط اول درمان است ،وقتي إصلاح حجم به تنهايي كافي نباشد درمان انتخابي انتي هايپرتانسيون شبيه افراد معمولي خواهد بود
- مهاركننده هاي ACEو ARB سرعت كاهش عملكرد كليه را از طريق كاهش فشار شرياني سيستميك و تصحيح هيپرفيلتراسيون و هيپرتانسيون داخل گلومرولي كه در روند پيشرفت CKD موثرند كم ميكنند

- استفاده از مهارکننده ACEو ARB ممکنست با بوجود آوردن هیپرکالمي مشکل ایجاد کنند و معمولا استفاده از مهارکننده هاي کالیورتیك مانند متولازون علاوه بر بهبود هیپرتانسیون ترشح پتاسیم را بهتر کند .دیورتیك هاي نگهدارنده پتاسیم باید با احتیاط مصرف شوند و کاربرد انها محدود شود

Treatment cardiovascular

- تعداد زيادي راهكار براي درمان عوامل خطر كلاسيك و غيركلاسيك در بيماران CKDوجود دارد
- هيپرتانسيون و سطح افزايش يافته هموسيستئين سرم و ديس ليپيدمي ،بيماري آترواسكلروزي را تسريع ميكنند و همگي از عوارض قابل درمان ميباشند
- با توجه به اينكه DMو هيپرتانسيون دو علت شايع مسبب CKDپيشرفته هستند بيماريهاي كارديوواسكولار شايعترين دليل مورتاليتي در بيماران ديالیزي ميباشد نقش التهاب بطور quantitively در بيماران كليوي مهمتر باشد.

- تغییر شیوه زندگي شامل ورزش منظم
- درمان هیپرلیپیدمي
- تغییر عوامل خطر کلاسیك

Pericardial Disease

- Chest pain كه با تنفس تشديد شود و با يك friction rub همراه هست براي پريكارديت اورميك نشانه تشخيصي مهمي محسوب ميشود
- پریکاردیت ممکن است با افیوژن پریکاردیال همراه شود و بندرت منجر به تامپوناد شود

Treatment pericardial Disease

- پريكارديت اورميك يك انديكاسيون مطلق براي شروع دياليز اورژانسي يا افزايش دفعات ان در افرادي كه قبلا ديااليز ميشده اند هست
- بدليل تمايل به خونريزي درون پريكارد ،ديااليز بدون استفاده از هپارين انديكاسيون دارد
- در بيماران با افيوژن راجعه پريكارديال بايد درناژ پريكارد را مد نظر قرار داد

Hematologic Abnormalities

- آنمي نرموكروم نرموسيتيك معمولا در مرحله ۳ CKD ديده ميشود و تقريبا هميشه در مرحله ٤ وجود دارد ،علت اوليه آنمي در بيماران CKD توليد ناكافي اريتروپوئتين توسط كليه هاست و علل ديگر شامل :

TABLE 305-3 Causes of Anemia in CKD

Relative deficiency of erythropoietin

Diminished red blood cell survival

Bleeding diathesis

Iron deficiency due to poor dietary absorption and gastrointestinal blood loss

Hyperparathyroidism/bone marrow fibrosis

Chronic inflammation

Folate or vitamin B_{12} deficiency

Hemoglobinopathy

- آنمي CKD همراه تعدادي از پيامدهاي پاتولوژيك شديد شامل كاهش تحويل و استفاده از اكسيژن بافتي،افزايش برون ده قلبي ،ديلاتاسيون بطني،و هيپرتروفي بطني است تظاهرات باليني شامل خستگي ،آنژين قلبي،نارسايي قلبي،كاهش شناخت و قدرت ذهني،و اختلال دفاع ميزبان در برابر عفونت است.

درمان آنمي

- دسترسي به ESA(Erythropoietic stimulating agent) ،يكي از مهمترين پيشرفت ها در مراقبت از بيماران كليوي ميباشد.استفاده از اين هورمونهاي نوتركيب ،نياز به انتقال منظم در بيماران شديدا آنميك CKD را از بين برده و بطور قابل توجهي بروز عفونت هاي همراه ترانسفيوژن و over load. آهن را از بين ميبرد

- ذخاير كافي آهن مغز استخوان بايد پيش از آنكه درمان با ESA آغاز شود كافي باشد.مكمل هاي آهن معمولا براي اطمينان از پاسخ مناسب به ESA در بيماران CKD نياز است.براي بيماران CKD كه هنوز ديالیز نميشوند يا بيماران تحت ديالیز صفاقي مكمل هاي خوراكي آهن بايد مورد استفاده قرار بگيرند،اگر عدم تحمل خوراكي وجود دارد ممكنست تحت انفوزيون آهن وريدي قرار بگيرند

- براي بيماران تحت همو‌ديالیز ميتوان آهن وريدي حين ديالیز تجويز كرد .بايستي در نظر داشت كه درمان با اهن ميتواند استعداد به عفونت باكتريال را افزايش دهد
- آنمي مقاوم به دوزهاي ESA با وجود ذخاير كافي آهن ممكنست به دلايل:

- التهاب مزمن یا حاد
- دیالیز ناکافي
- هیپرپاراتیروئیدیسم شدید
- از دست دادن مزمن خون یا همولیز
- عفونت مزمن
- بدخیمي

عوارض درمان آنمي

- انتقال خون خطر هپاتيت، over load آهن،و حساسيت به پيوند را افزايش ميدهد.پس بايد فقط در بيمارانيكه به آنمي به ESA پاسخ نداده اند و علامتدارند محدود شود.مطالعات انجام شده نشان داده اند كه مصرف ESAدر CKD ممكنست با افزايش خطر CVA در بيماران ديابتي و افزايش حوادث ترومبوآمبوليك و پيشرفت سريعتر به سمت نياز به دياليز همراهي دارد

- بنابراين هر منفعتي در رابطه با بهبود علائم آنميك نياز دارد كه در مقابل ريسك بالقوه كارديوواسكولار سنجيده شود
- در حال حاضر رسيدن به غلظت هموگلوبين 115-100 هدف ميباشد و نرمال شدن كامل غلظت هموگلوبين سود بيشتري را در بيماران CKD در بر ندارد

- **INTRODUCTION** — Anemia is common among patients with chronic kidney disease (CKD). Anemia underlies many of the symptoms associated with reduced kidney function and is associated with increased mortality and hospitalizations

- **Role of anemia** — Anemia has been identified as a risk factor for the development of LVH in dialysis and nondialysis CKD patients [3-5,10,11]. In an observational study including 432 hemodialysis and peritoneal dialysis patients, anemia was independently associated with an increase in left ventricular mass index [11]. In an analysis of data from the Atherosclerosis Risk in Communities Study (ARIC), among nondialysis CKD patients, anemia was predictive of left ventricular diameter after adjusting for kidney function and blood pressure [

- **Pathophysiology** — Potential mechanisms that may explain the relationship between anemia and the development of LVH among CKD patients include [12-16]:
- ●Effects of reduced oxygen delivery to the myocardium, perhaps leading to increased myocyte necrosis and apoptosis
- ●Anemia-related increased cardiac output and reduced systemic vascular resistance
- ●Increased oxidative stress
- ●Activation of the sympathetic nervous system
- A decrease in circulating endogenous erythropoietin caused by kidney disease may contribute to LVH among CKD patients. Erythropoietin receptors are present in cardiac tissue [17], and erythropoietin may have direct effects on myocardial function

DIAGNOSIS OF IRON DEFICIENCY

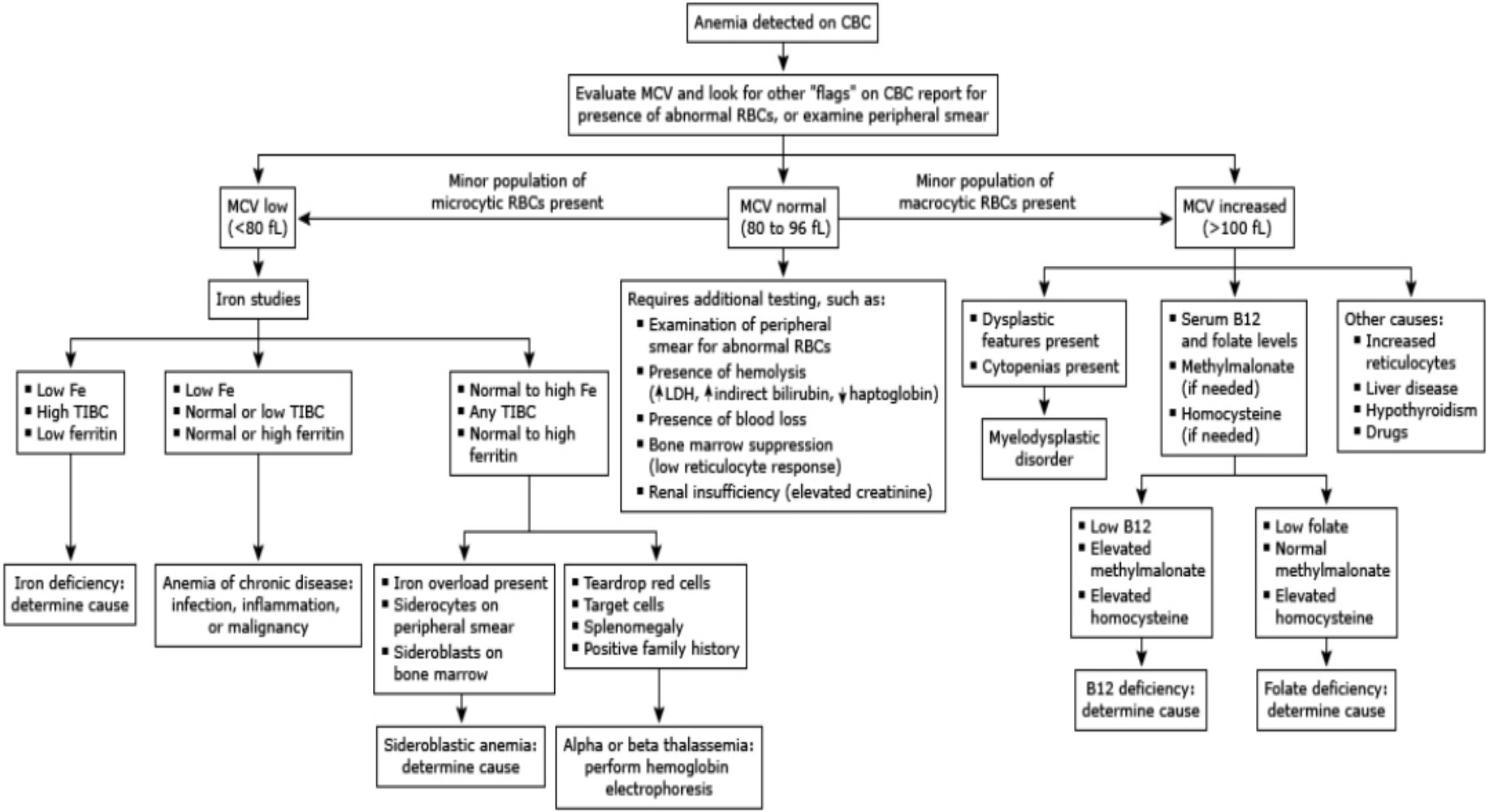
- We use the serum iron, total iron-binding capacity (TIBC), and ferritin and calculation of the percent transferrin saturation (TSAT) to estimate iron stores.

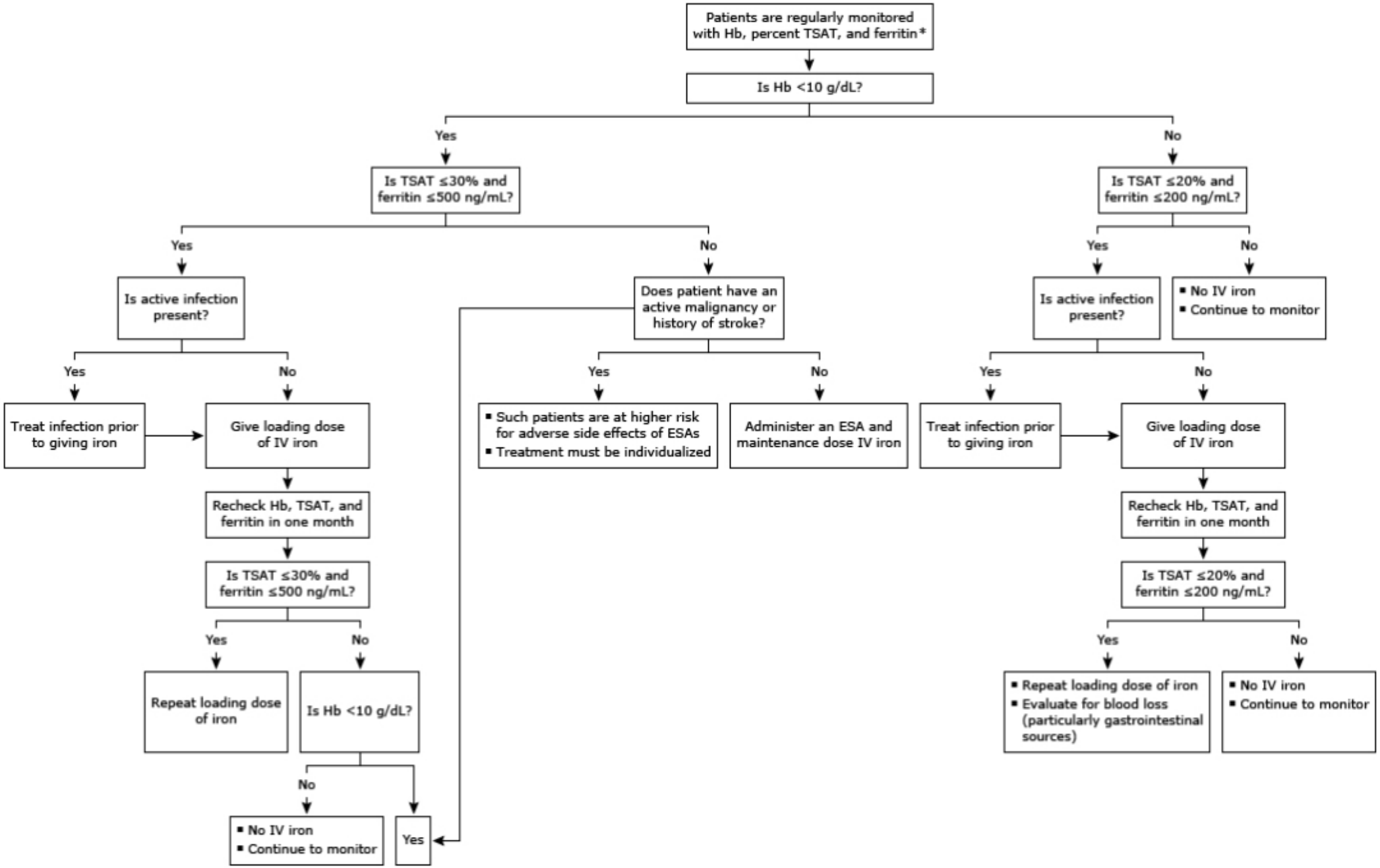
- **Initial screen** — All CKD patients, particularly those with estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2, should be screened for anemia on initial evaluation for CKD. We screen for anemia using measurement of hemoglobin (Hb) concentration.

INDICATIONS FOR TREATMENT

- ●We give iron to most **anemic** CKD patients who have a TSAT ≤30 percent and ferritin ≤500 ng/mL. Anemia is defined as an Hb concentration <13.0 g/dL for adult males and postmenopausal women and an Hb <12.0 g/dL for premenopausal women

- **DEFINITION** — Anemia is defined by the World Health Organization (WHO) as a hemoglobin (Hb) concentration <13.0 g/dL for adult males and postmenopausal women and an Hb <12.0 g/dL for premenopausal women [5]


Anemia detected on CBC
Evaluate MCV and look for other "flags" on CBC report for presence of abnormal RBCs, or examine peripheral smear
MCV low (<80 fL)
Minor population of microcytic RBCs present
MCV normal (80 to 96 fL)
Minor population of macrocytic RBCs present
MCV increased (>100 fL)
Iron studies
Low Fe
High TIBC
Low ferritin
Iron deficiency: determine cause
Low Fe
Normal or low TIBC
Normal or high ferritin
Anemia of chronic disease: infection, inflammation, or malignancy
Normal to high Fe
Any TIBC
Normal to high ferritin
Iron overload present
Siderocytes on peripheral smear
Sideroblasts on bone marrow
Sideroblastic anemia: determine cause
Teardrop red cells
Target cells
Splenomegaly
Positive family history
Alpha or beta thalassemia: perform hemoglobin electrophoresis
Requires additional testing, such as:
Examination of peripheral smear for abnormal RBCs
Presence of hemolysis (↑LDH, ↑indirect bilirubin, ↓haptoglobin)
Presence of blood loss
Bone marrow suppression (low reticulocyte response)
Renal insufficiency (elevated creatinine)
Dysplastic features present
Cytopenias present
Myelodysplastic disorder
Serum B12 and folate levels
Methylmalonate (if needed)
Homocysteine (if needed)
Low B12
Elevated methylmalonate
Elevated homocysteine
B12 deficiency: determine cause
Low folate
Normal methylmalonate
Elevated homocysteine
Folate deficiency: determine cause
Other causes:
Increased reticulocytes
Liver disease
Hypothyroidism
Drugs


Patients are regularly monitored with Hb, percent TSAT, and ferritin*
Is Hb <10 g/dL?
Yes
No
Is TSAT ≤30% and ferritin ≤500 ng/mL?
Is TSAT ≤20% and ferritin ≤200 ng/mL?
Yes
No
Yes
No
Is active infection present?
Does patient have an active malignancy or history of stroke?
Is active infection present?
No IV iron
Continue to monitor
Yes
No
Yes
No
Yes
No
Treat infection prior to giving iron
Give loading dose of IV iron
Such patients are at higher risk for adverse side effects of ESAs
Treatment must be individualized
Administer an ESA and maintenance dose IV iron
Treat infection prior to giving iron
Give loading dose of IV iron
Recheck Hb, TSAT, and ferritin in one month
Recheck Hb, TSAT, and ferritin in one month
Is TSAT ≤30% and ferritin ≤500 ng/mL?
Is TSAT ≤20% and ferritin ≤200 ng/mL?
Yes
No
Yes
No
Repeat loading dose of iron
Is Hb <10 g/dL?
Repeat loading dose of iron
Evaluate for blood loss (particularly gastrointestinal sources)
No IV iron
Continue to monitor
No
Yes
No IV iron
Continue to monitor

intravenous iron to patients with:

- ●Severe iron deficiency (ie, transferrin saturation [TSAT] <12 percent)
- ●Severe anemia (hemoglobin [Hb] <7 g/dL) in asymptomatic patients
- ●Risk of ongoing blood loss (such as a patient with chronic gastrointestinal blood loss)
- ●History of side effects to oral iron
- ●History of not responding to oral iron in the past
-

Erythropoiesis-stimulating agents

- **Indications and contraindications** — We administer ESAs to most CKD patients who have a hemoglobin (Hb) <10 g/dL,providing the transferrin saturation (TSAT) is >25 percent and ferritin >200 ng/mL. An important exception is among patients with active malignancy or a recent history of malignancy, particularly those in whom cure is anticipated, or who have had a stroke since such patients may be at higher risk for adverse effects from ESAs.

- To patients with TSAT ≤25 percent and ferritin ≤500 ng/mL, we usually administer iron before giving an ESA since they may respond to iron with an increase in Hb

- **Dosing** — The initial epoetin dose is approximately 50 to 100 units/kg/week. However, the use of lower doses would also be reasonable, particularly in patients with pretreatment Hb levels near 10 g/dL.

- we initiate therapy in most patients beginning at 4000 or 10,000 units subcutaneously once weekly or 10,000 to 20,000 units subcutaneously every other week.

- **Target hemoglobin value** — For most nondialysis CKD patients who are treated with ESAs, we maintain Hb levels between 10 and 11.5 g/dL using the lowest possible ESA dose

- To patients with TSAT ≤25 percent and ferritin ≤500 ng/mL, we usually administer iron before giving an ESA since they may respond to iron with an increase in Hb.
- We are attentive to possible symptoms of anemia in younger patients who have CKD with few comorbidities, whose symptoms of anemia may occur at higher Hb levels. For such patients, we may initiate ESAs at Hb levels of 10 g/dL or even higher after discussing potential risks and benefits with each patient.
- The administration of ESAs has substantially reduced the need for red cell transfusions (with an attendant decrease in and/or risk for transfusion-related complications). (

Abnormal Hemostasis

- بيماران در مراحل آخر CKD ممکنست دچار طولاني شدن Bleeding Time ،کاهش فعاليت فکتور 3 پلاکتي ،اختلال تجمع و چسبندگي پلاکتي ،و اختلال مصرف پروترومبين شوند .

- تظاهرات باليني شامل افزايش تمايل به خونريزي غير طبيعي bruising طولاني شدن خونريزي از زخمهاي جراحي ،منوراژي،و GIB است ،بيماران CKD استعداد بيشتري براي عوارض ترومبوآمبوليك دارند ،بويژه هنگاميكه كه پروتئينوري در محدوده سندرم نفروتيك دارند

Treatment Abnormal hemostasis

- BT طولاني و اختلالات انعقادي در بيماران CKD ممكنست بطور موقت با دسموپرسين DDAVP،كرايوسيپيتيت ،استروژن هاي كونژوگه IV،و ESA إصلاح شود .ديااليز معمولا زمان BT را إصلاح ميكند.

- با توجه به همزمان بودن مشکلات خونريزي و تمايل به ترومبوز که در بيماران CKD بطور خاص وجود دارد،تصميم در مورد استفاده از آنتي کواگولان ها بايد بر أساس هر شخص انجام گردد

- با تشکر از حسن توجه شما