Chronic kidney disease and Renal replacement therapy

Objectives:

1. Recall the epidemiology of chronic kidney disease.
2. Understand the definition of chronic kidney disease.
3. To be able to recall the classification of chronic kidney disease.
4. To be able to identify symptoms and signs of Uremia and its complications.
5. To be able to list key points in the management of chronic kidney disease.

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Recall the epidemiology of chronic kidney disease.
Understand the definition of chronic kidney disease.

Epidemiology of chronic kidney disease

Prevalence of CKD: data from USRDS in United States.	
Population	**Prevalence of CKD**
US adults	13.6%
60-69 yrs	25%
> 70 yrs	50%
HTN patients	20%
DM patients	30%

> 70% of patients with ESRD have either DM or HTN

Definition of chronic kidney disease

CKD is a syndrome not a diagnosis.
It is persistent kidney damage for 3 months.

CKD (CRF): chronic progressive irreversible loss of renal function. It is defined as the presence of clinical and/or pathologic evidence of kidney disease for at least 3 months, irrespective to the cause.
ESRD: advanced CKD (Stage-5) requiring dialysis or kidney transplantation. It is defined as the loss of renal function leading to a collection of symptoms and laboratory abnormalities also known as uremia. Not defined as a particular BUN or creatinine.

Kidney damage[1] description Important, Q from exam

1	Decreased function	eGFR < 60 ml/min (MDRD, CKD-EPI)
2	Albuminuria	ACR 30 mg/g (3.4 mg/mmol) Earliest sign, ex. DM
3	Urine sediments	RBC, casts
4	Pathology	Glomerulosclerosis, IFTA
5	Imaging[2]	Polycycstic, hydronephrosis, echogenicity, small
6	Kidney transplant	Even in the absence of other markers

1. One or more.
2. Even if labs are normal.

To be able to recall the classification of chronic kidney disease.

Classification of chronic kidney disease (CKD)

Using glomerular filtration rate (GFR) and albumin:creatinine (ACR) categories:

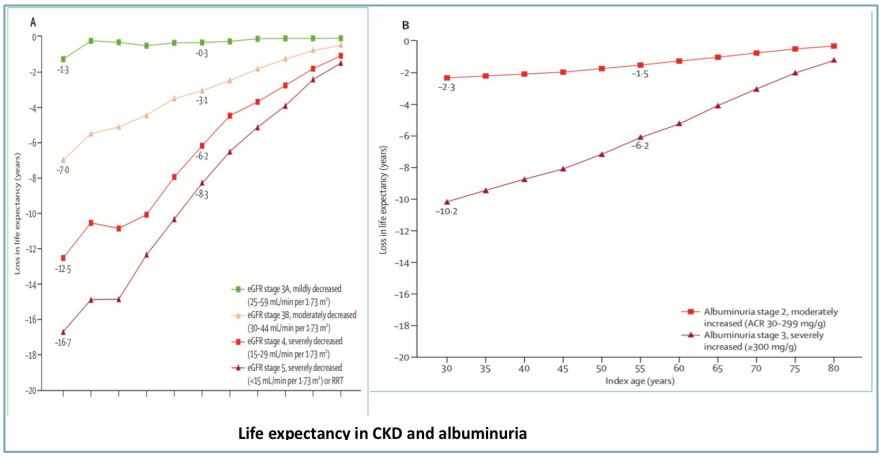
Prognosis of CKD and by eGFR and Albuminuria Categories: KDIGO 2012

eGFR categories (mL/min/1.73m²) Description and range			Persistent albuminuria categories Urine ACR (mg/mmol) Description and range		
			A1	A2	A3
			Normal	Microalbuminuria	Macroalbuminuria
			male < 2.5 female < 3.5	male 2.5 – 25 female 3.5 – 35	male > 25 female > 35
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			Worst

low risk if no other markers of kidney disease, no CKD) | Moderately increased risk | high risk | very high risk

- Albuminuria have a strong association with CVS mortality.
- Albuminuria is marker for vascular endothelial disease, if vascular endothelium of kidney is abnormal then the coronary vascular endothelium is abnormal.
- G1A3 is considered high risk even though GFR is normal, because protein large for renal tubule and can lead to fibrosis.
- Stages G1A1 and G2A1 (eGFR is >60 and no albuminuria) do not indicate CKD in the absence of other markers of kidney damage.

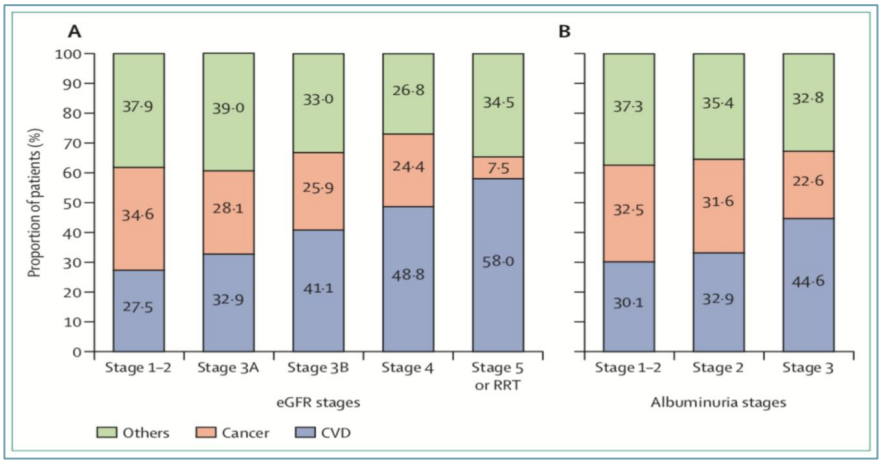
Life expectancy in CKD and albuminuria:



Life expectancy in CKD and albuminuria

- Increase in albuminuria => decrease in life expectancy.
- It's important to try to decrease albuminuria in management.

Cause of death per CKD stage:



- **CVS is the number one cause of mortality, Q from exam**
- CVS mortality risk increases with progression of CKD in both eGFR and albuminuria stages.[1]

In addition to CKD mortality risk, there is high risk of:

- ◄ Adverse surgical outcome.
- ◄ Adverse drug related adverse events.
- ◄ Increased infection rate. (Pt with CKD is considered immunocompromised)
- ◄ Increased AKI risk.
- ◄ Risk of cognitive and physical decline.

To be able to identify symptoms and signs of Uremia and its complications.

How does CKD present?

- Asymptomatic disease.
- CKD III < 10% are aware of their diagnosis.
- CKD IV 50% unaware[1] of their diagnosis.
- **Picked up during routine lab tests.**
- Hypertension
- Gout (high uric acid)
- Uremia (means end stage)

Clinical features:

Manifestations of Na+/H2O retention	• Hypertension and heart failure. • Pulmonary and peripheral edema.		
Manifestations of uremia[2]	Constitutional symptoms	• Fatigue. • Weakness. • Headaches.	
	Gastrointestinal symptoms	• Nausea and vomiting. • Loss of appetite.	• Uremic fetor: characteristic ammonia- or urine-like breath odor.
	Dermatological manifestations	• Pruritus. • Skin color changes. (e.g., hyperpigmentation, pallor due to anemia)	• Uremic frost.
	Serositis	• Uremic pericarditis. • Pleuritis.	
	Neurological symptoms	• Asterixis. • Signs of encephalopathy. • Seizures.	• Somnolence. • Coma. • Peripheral neuropathy → paresthesias.
	Hematologic symptoms	• Anemia. • Leukocyte dysfunction → ↑ risk of infection.	• ↑ Bleeding tendency caused by abnormal platelet adhesion and aggregation.

Suspect[3] and screen:

- #1 Diabetes
- #2 HTN
- CV disease
- Obesity
- Renal stone disease
- Uremia
- Recurrent UTI
- Previous AKI
- Elderly
- Family history
- Gout
- Smoking

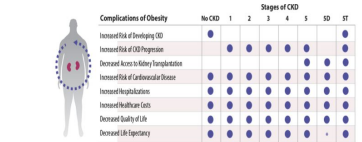


Figure 2. Obesity-related complications by stage of CKD.*Signifies the unresolved controversy over the impact of obesity on mortality in patients on dialysis related to the "obesity paradox" phenomenon. Abbreviation: CKD, chronic kidney disease.

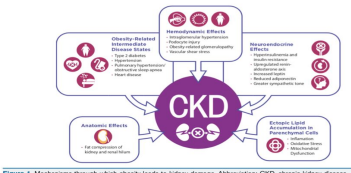


Figure 1. Mechanisms through which obesity leads to kidney damage. Abbreviation: CKD, chronic kidney disease.

1. Have no symptoms.
2. **Uremia is defined as the accumulation of toxic substances due to decreased renal excretion. These toxic substances are mostly metabolites of proteins such as urea, creatinine, β2 microglobulin, and parathyroid hormone.**
3. In order. But **diabetes and HTN are the most common** diseases we must suspect and screen for them.

Making the diagnosis[1]:

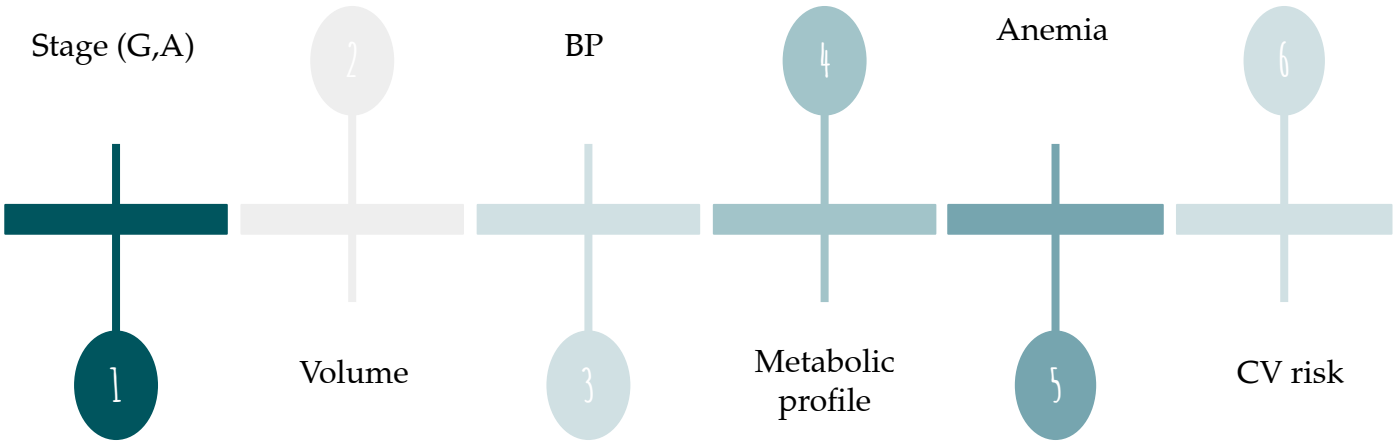
Diabetes	Hypertension
Glomerulonephritis	Tubulointerstitial disease
Obstructive uropathy	Polycystic kidney disease
Drug induced renal disease	Cardio/ hepato renal
MM	Amyloid

Table 2
Laboratory evaluation of CKD[2]

Test	Indication	Frequency
Basic metabolic panel	Prognosis, hyperkalemia	At diagnosis and periodically
Calcium, phosphate	Prognosis, metabolic bone disease	At diagnosis and again when GFR<45 mL/min/1.73 m^2
Serum albumin	Prognosis	At diagnosis
PTH, alkaline phosphatase, vitamin D	Metabolic bone disease	When GFR<45 mL/min/1.73 m^2
Hemoglobin/hematocrit	Prognosis, anemia	At diagnosis and then annually if eGFR≥30 mL/min/1.73 m^2; q 6 mo if eGFR<30 mL/min/1.73 m^2
Lipids	CV risk stratification	At diagnosis and periodically
UACR, serum creatinine	Prognosis, progression	At least yearly, more frequently in more advanced CKD or when it will affect management
HIV, HBV, HCV, RPR, SPEP	If unclear cause	At diagnosis
Complement, ANA, ANCA, anti-GBM	Only if specific syndrome suspected	At diagnosis

Renal ultrasound

Clinical assessment[3] of CKD:



- Clinical assessment aims at categorizing the patient, establishing a treatment and follow up plan.
- Intervention plan should **prevent or reverse complications** and **slow down progression** & **reduce CV disease burden.**

1. Anyone with CKD always have at least one of these, Any CKD PT must have a diagnosis.
2. If non of Lab results didn't explain CKD, biopsy might be done. For example: pt with hx of 2 years diabetes, and abnormal creatinine and proteinuria, 2 years of diabetes is less likely to affect the kidney, and we are not sure if it's diabetes or something else, we might go with kidney biopsy.
3. These are the clinical parameters that need some intervention.

EXTRA

1. Assessment of renal function (GFR) and proteinuria:

GFR

- Creatinine based.
- eGFR Vs mGFR.
- MDRD more accurate for lower GFR. (Scr + age + gender + race)
- CKD-EPI for higher GFR. (Scr + age + gender + race)

Limitations: **Normal Scr for one patient might be abnormal for another !**
Pts who are extreme thin or have advance liver disease or advance malignancy, have no muscle mass so their serum Cr might fall within normal range but they actually have some kidney disease.

albuminuria

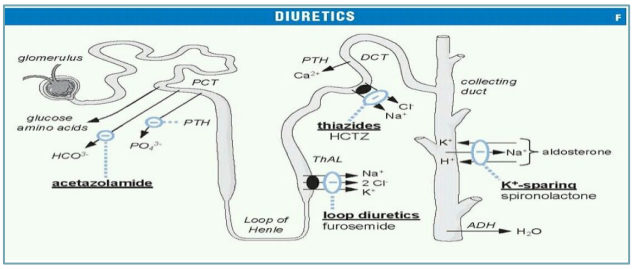
- **UACR** > 30 mg/mmol (or 300 mg/g)
- UPCR > 50 mg/mmol (or 500 mg/ g)

Table 1
Measurement of proteinuria

Test	Comments
Urine dipstick	Measures albumin; typically only detects moderately or severely increased proteinuria; prone to false-positive results
UACR	Spot test; estimates daily albumin excretion; standardized across laboratories
UPCR	Also detects nonalbumin proteins; not standardized
24-h urine protein testing	Not routinely indicated in primary care of patents with CKD

2. Assessment of volume:

- Volume expansion is common due to reduce fluid clearance.
- Salt restriction < 1.5 g/day.
- Proper doses of **diuretics**.
- Combined diuretic therapy for diuretic resistance.



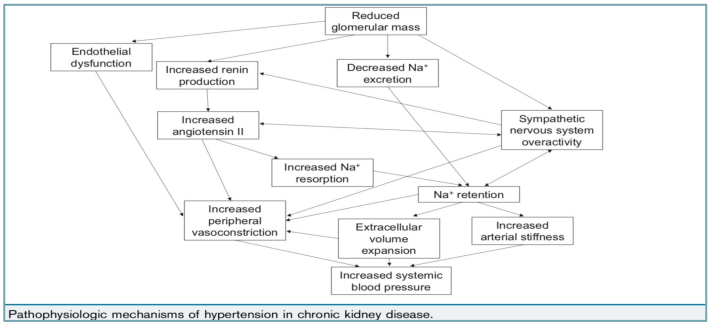
3. Assessment of blood pressure:

Difficult-to-Control BP	Definition
Resistant hypertension	Receiving ≥3 antihypertensive agents, 1 of which is a diuretic, without adequate BP control
Refractory hypertension	Receiving ≥3 antihypertensive agents, 1 of which is a thiazide-type diuretic and another of which is spironolactone, without adequate BP control

- Control the volume.
- Multiple therapeutic targets.
- Sustained HTN → worse renal function → worse HTN.
- Intensive BP control reduces the risk of CV outcomes and mortality in the CKD.
- BP and CKD is vicious cycle. ↓ filtration → hypoperfusion(tubular ischemia) → ↑ renin, ↑ angiotensin II and ↑ aldosterone → HTN.

Table 1. Definitions of Normal and Abnormal BP Based on the 2017 AHA/ACC Guideline in Patients With CKD

BP Classification[a]	Office BP	Daytime ABPM or Home BP
Normal or elevated BP	<130/80 mm Hg	<130/80 mm Hg
Sustained hypertension	≥130/80 mm Hg	≥130/80 mm Hg
White coat hypertension	≥130/80 mm Hg	<130/80 mm Hg
Masked hypertension	<130/80 mm Hg	≥130/80 mm Hg

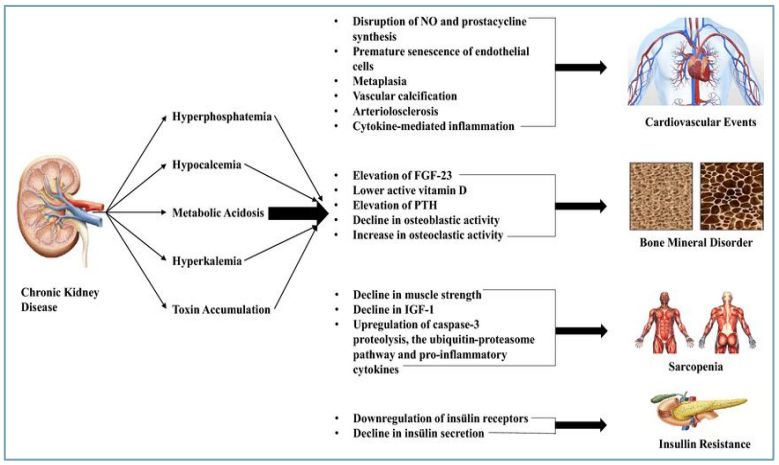


Pathophysiologic mechanisms of hypertension in chronic kidney disease.

4. Assessment of metabolic changes[1]:

- Hyperphosphatemia.
- "↓ vit D" Hypocalcemia.
- Metabolic acidosis.
- Hyperkalemia.
- Uremic toxin accumulation.

EXTRA



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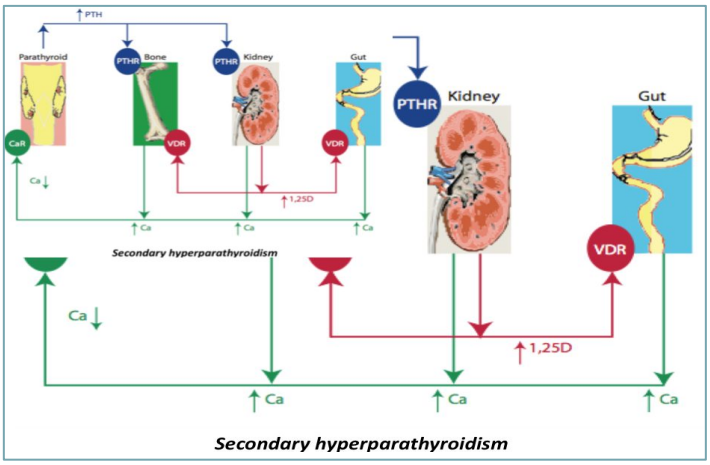
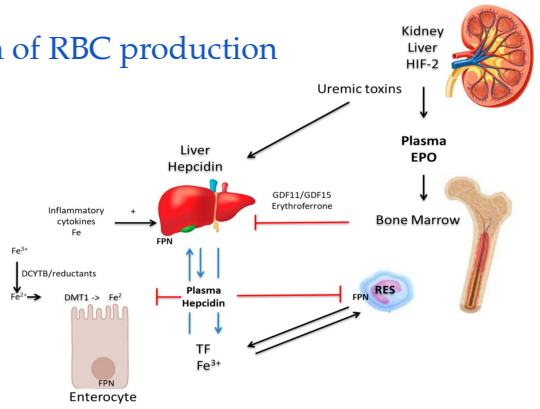


EXTRA

5. Assessment of anemia:

- Pathophysiology: ↓ synthesis of erythropoietin → ↓ stimulation of RBC production → normocytic, normochromic anemia.
- Laboratory findings:
  - ↓ Hemoglobin (Hb).
  - MCV is usually normal.
- **GFR < 30 ml/min. So stage 4 or 5.**
- Iron deficiency is common.
- Low retic count.
- What leads to anemia? 1. Advanced CKD → ↓ absorption of iron from gu = nutritional deficiency. 2. EPO.



EXTRA

6. Assessment of CV disease:

- Any CV risk factor that we look for in CV pt, we look for them too for renal pt.
- CV disease is more frequent and severe, is often not recognized, and is often undertreated!
- Strong causal association between chronic kidney disease and CV risk.
- to prevent progression of CKD = to prevent CV disease.

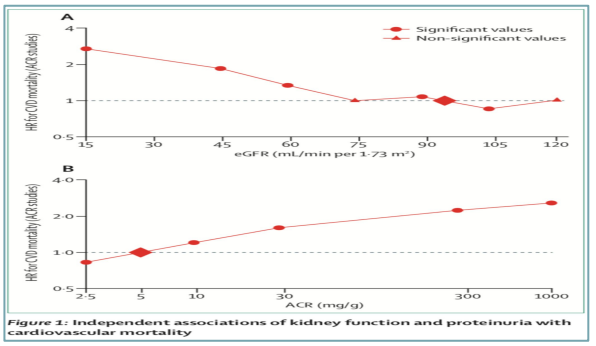


Figure 1: Independent associations of kidney function and proteinuria with cardiovascular mortality

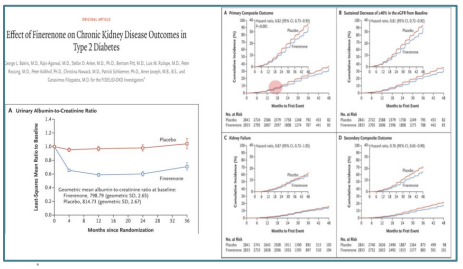
1. You don't need to know all details just focus on these 4.

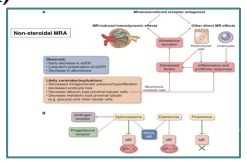
To be able to list key points in the management of chronic kidney disease.

Management of chronic kidney disease Very Important

Slow progression[1]

- **BP control** in patients with hypertension, Most important single risk for progression.
- **Glycemic control** in diabetic patients, Especially in early stage, might not help much in late stages.
- **Angiotensin blockade** in those with proteinuric CKD , **ACEI, ARB** => ↓ proteinuria, ↓ filtration stress on kidney and ↓ fibrosis pathways.
- **Avoiding nephrotoxins** and AKI, abx and contrast.
- **Bicarbonate** therapy if serum HCO3 level is less than 22 mmol/L, To reverse metabolic acidosis[2,3].
- **SGLT-2 Inhibitors**, for diabetic and non diabetic.
- **Mineralocorticoid receptor antagonists (MRA)**

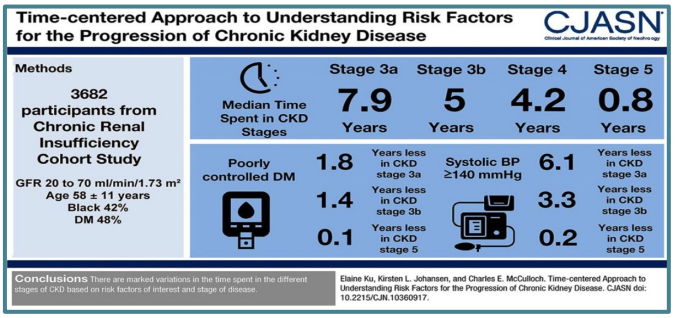




Both images are Extra

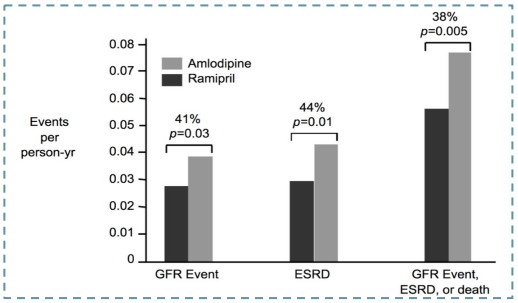
Treat complications[4]

- Secondary hyperparathyroidism
- Anemia
- Metabolic acidosis
- Hyperkalemia
- HTN

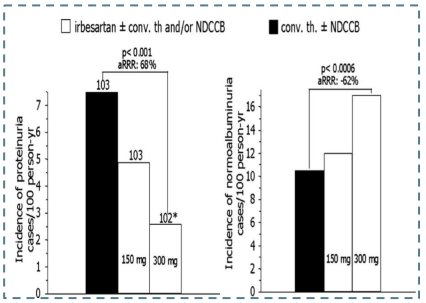


EXTRA

- **Slow progression management (Proteinuria reduction):**



AASK trial



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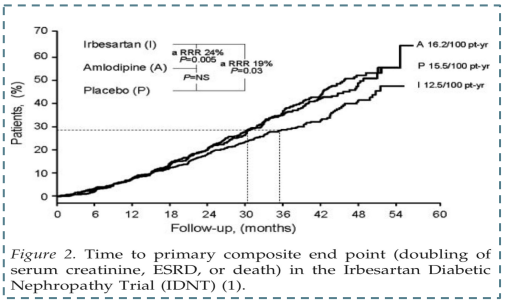
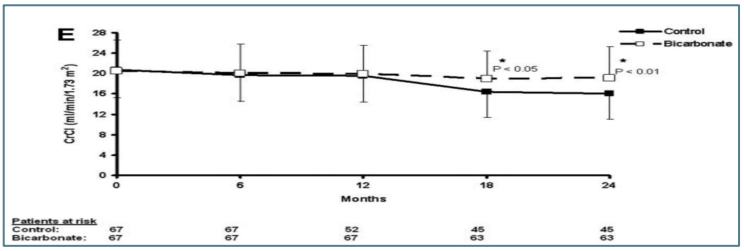


Figure 2. Time to primary composite end point (doubling of serum creatinine, ESRD, or death) in the Irbesartan Diabetic Nephropathy Trial (IDNT) (1).

IDNT

- **Slow progression management (Metabolic acidosis):**

Rx with NaHCO3 reduces the progression to ESRD



1. Evidence based.
2. Metabolic acidosis due to toxin "organic acids" accumulation and reduce bicarbonate generation by kidney.
3. Metabolic acidosis can stimulate fibrosis pathway in kidney and affect muscle strength and bone health.
4. For bone health and quality of life. "And it will be discussed in the next slide"

Cont..

EXTRA

- **Slow progression management**

Potential Target Patients for SGLT-2

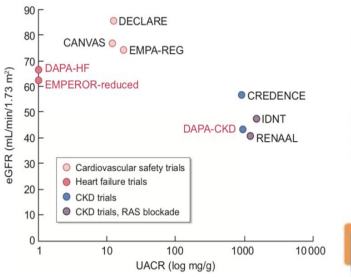
Diabetic kidney disease	• Type 2 diabetes mellitus	• eGFR ≥25 ml/min per 1.73 m^2 • UACR 200–5000 mg/g[b]
Nondiabetic kidney disease	• Etiology of kidney disease: ischemic ne phropathy, IgA nephropathy, FSGS, chronic pyelonephritis, chronic interstitial nephritis • No immunosuppression in prior 6 mo	• eGFR ≥ 25 ml/min per 1.73 m^2 • UACR 200–5000 mg/g[b]

Practical provider guide to initiating SGLT-2 inhibitors in patients with type 2 diabetes and CKD

	Assessment	Intervention	Follow-up
Patient selection	**Eligible patients:** • eGFR ≥ 30 mL/min/1.73 m^2 **High priority features:** • uACR ≥ 200 mg/g • Heart failure **Potential contraindications:** • Genital infection risk • Diabetic ketoacidosis • Foot ulcers • Immunosuppression	**Low-dose SGLT-2 inhibitor with proven benefits:** • Canagliflozin 100 mg • Dapagliflozin 10 mg • Empagliflozin 10 mg **Education:** • Sick day protocol* • Perioperative care* • Foot care	• Assess adverse effects • Review knowledge • Anticipate an acute drop in eGFR, which is generally not a reason to stop the SGLT-2 inhibitor
Glycemia	**Hypoglycemia risk?** • Insulin or sulfonylurea • History of severe hypoglycemia • HbA1c at or below goal	If high **Education:** • Hypoglycemia symptoms • Glycemia monitoring Consider insulin/sulfonylurea dose reduction	• Ask about hypoglycemia • Reduce sulfonylurea or insulin if needed
Volume	**Volume depletion risk?** • Concurrent diuretic use • Tenuous volume status • History of AKI	If high **Education:** • Volume depletion symptoms Consider diuretic dose reduction	• Re-assess volume • Reduce concomitant diuretic if needed

Table 1. Handout for the Patients when initiating Sodium Glucose Cotransporter-2 Inhibitor Therapy

- **Increase in Urine Output**
  - You may notice an increase in your urine output after starting this medication
  - Monitor your weight at home
- **Blood Pressure**
  - Monitor your blood pressure at home as this medicine may lower blood pressure
  - Inform your doctor if your blood pressure is too low, or if you experience light-headedness or dizziness
- **Blood Glucose**
  - Monitor your blood glucose level at home as this medicine may lower blood glucose
  - Inform your doctor if your blood glucose is low
- **Follow the 'Sick Day Rule'**
  - On days that you are unable to eat because you are feeling sick due to fever, infection, poor appetite, nausea, vomiting or diarrhea then hold this medicine.
  - You can resume the medicine once you are able to eat and drink.
  - If you continue to feel sick, then call your doctor as you may need to have blood tests to rule out Diabetic ketoacidosis
- **Stop the medication 3 to 4 days before a scheduled surgery that requires you to be NPO (meaning you are instructed to not eat or drink anything for several hours before your surgery)**
- **Avoid very low Carbohydrate diet and Keto diet as it may increase the risk of Diabetic Ketoacidosis**
- **Wound on your feet or legs**
  - If you notice a wound, ulcer or skin breakdown on your feet or legs, then hold this medicine and inform your doctor
- **Burning or pain during urination**
  - If you experience pain or burning on urination, then inform your doctor as you may need further evaluation
- **Redness or itching in the genital area, or foul smelling vaginal or penile discharge**
  - Keep the genital area clean
  - If you notice redness or itching in the genital area, or foul-smelling vaginal or penile discharge, then inform your doctor. You may need a cream or oral medication to treat an underlying infection



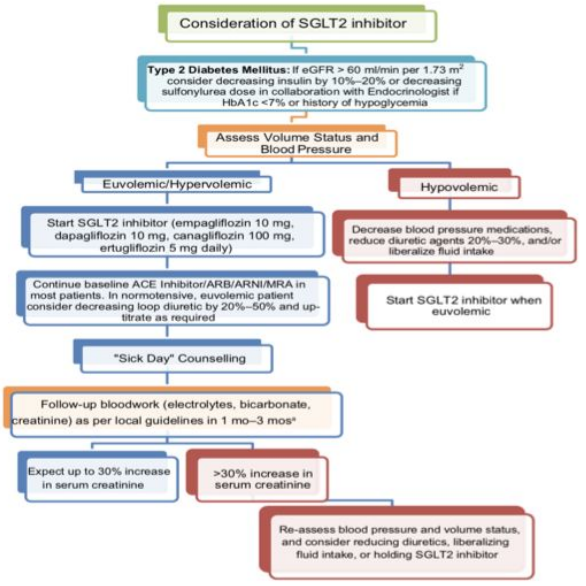
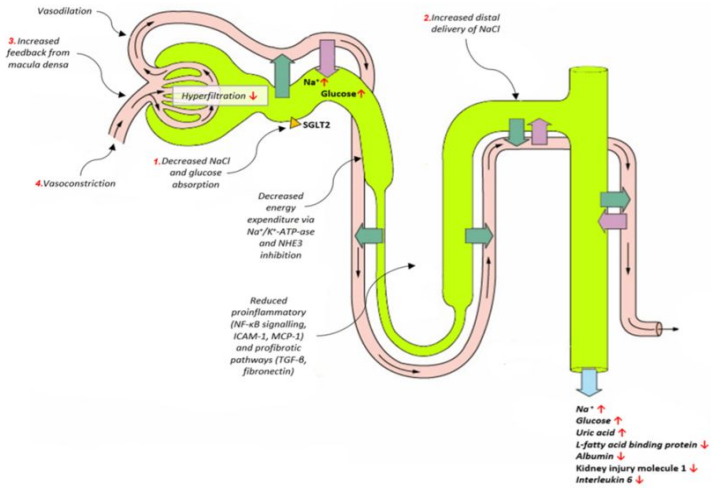
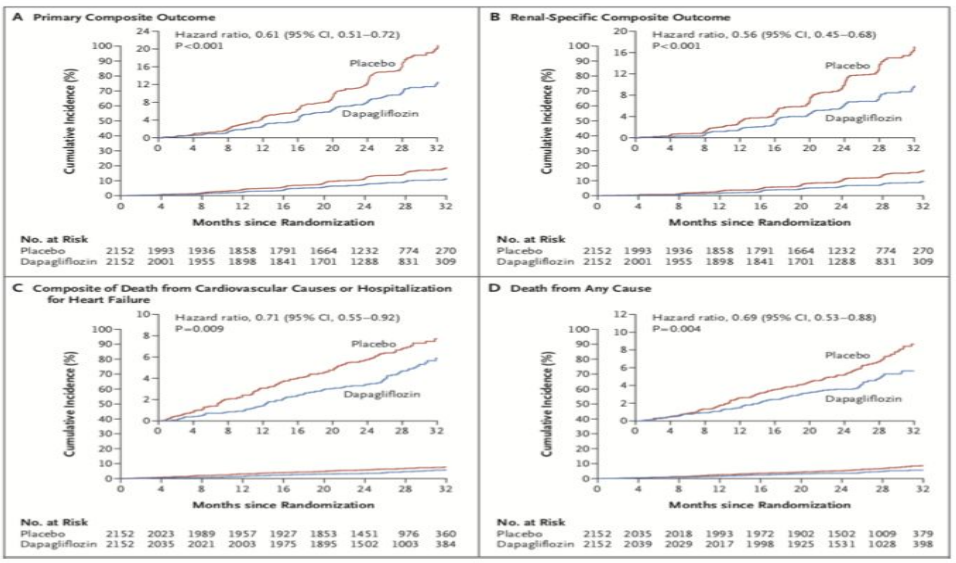


Table 1. Summary of clinical evidence concerning the role of SGLT2i in CKD.

	Study	Study Design	Study Population	SGLTi Used	Main Outcomes
CKD with DM	EMPA-REG OUTCOME trial [105]	Randomized, double-blind placebo-controlled trial	6185 patients eGFR > 30 mL/min/1.73 m^2	Empagliflozin 10/25 mg daily	Slower progression of kidney disease and lower rates of clinically relevant renal events
	Petrykiv et al. [99]	Double-blind, placebo-controlled crossover trial	33 patients UACR > 100 mg/g RAAS blockade therapy	Dapagliflozin 10 mg daily for 6 weeks	Reduced UACR by 36.2%, SBP by 5.2 mm Hg and eGFR by 5.3 mL/min/1.73 m^2 All effects reversible with discontinuation
	DECLARE TIMI-58 trial [35]	Randomized, double-blind placebo-controlled trial	17,160 patients eGFR ≥ 60 mL/min/1.73 m^2 atherosclerotic CV disease or multiple risk factors	Dapagliflozin 10 mg daily	Lower risk of ESRD or renal death in dapagliflozin group Mean decrease in eGFR was larger after 6 months, equalized by 2 years, and smaller after 3 years
	EMPEROR-Reduced trial [106]	Randomized, double-blind placebo-controlled trial	3730 patients HFrEF ≤ 40%	Empagliflozin 10 mg daily	Lower annual decline in eGFR More frequent genital tract infections
	CREDENCE trial [108]	Randomized, double-blind, trial	4401 patients eGFR 30–90 mL/min/1.73 m^2 UACR 300–5000 mg/g	Canagliflozin 100 mg daily	Lower risk of ESRD, doubling of the creatinine level or death of renal causes
CKD without DM	DIAMOND trial [112]	Randomized, double-blind, placebo-controlled crossover trial	53 adults proteinuria 500–3500 mg/24 h eGFR > 25 mL/min/1.73 m^2 RAAS blockade therapy	Dapagliflozin 10 mg daily for 6 weeks	1.5 kg reduction in body weight No significant change in proteinuria 6.6 mL/min/1.73 m^2 fall in eGFR, reversed after another 6 weeks No significant change in ABP
	DAPA-HF trial [114]	Double-blind, placebo-controlled, event-driven trial	4742 adults HFrEF ≤ 40% eGFR ≥ 30 mL/min/1.73 m^2 SBP ≥ 95 mm Hg	Dapagliflozin 10 mg daily	Lower rate of decline in eGFR per year Outcomes did not differ by baseline eGFR category
	DAPA-CKD trial [115]	Randomized, double-blind placebo-controlled multicentre trial	4304 adults eGFR 25–75 mL/min/1.73 m^2 UACR 200–5000	Dapagliflozin 10 mg daily	Lower risk of a sustained decline in eGFR Lower risk of ESRD Lower risk of death from renal or cardiovascular causes Outcomes did not differ depending on the presence of T2DM

Abbreviations: CKD: chronic kidney disease; DM: diabetes mellitus; EMPA-REG OUTCOME: Efficacy and Safety of Empagliflozin in Patients With Type 2 diabetes and Renal Impairment; UACR: urinary albumin to creatinine ratio; eGFR: estimated glomerular filtration rate; CV: cardiovascular; RAAS: renin-angiotensine-aldosterone system; CREDENCE: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation; SBP: systolic blood pressure; DECLARE-TIMI: Dapagliflozin Effect on CardiovascuLAR Events; ERSD: end-stage renal disease; AKI: acute kidney injury; HFrEF: heart failure with reduced ejection fraction; DIAMOND: Dapagliflozin in Non-diabetic Patients With Proteinuria; DAPA-HF: Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure; SBP: systolic blood pressure; T2DM: type 2 diabetes mellitus.





- *sustained decline in the estimated GFR of at least 50%*
- *end-stage kidney disease*
- *death from renal causes*

	CREDENCE	DAPA-CKD	EMPA-KIDNEY
	Double-blind, Placebo-controlled, Multicentric RCT (N=4401)	Double-blind, Placebo-controlled, Multicentric RCT (N=4304)	Double-blind, Placebo-controlled, Multicentric parallel group RCT (N=5000)
Inclusion	Type 2 DM eGFR: ≥30- 90 and UACR: >300-≤5000 mg/g Median follow up -2.62 yrs	With or without DM eGFR: ≥25-75 and UACR: ≥200-≤5000 mg/g Median follow up -2.4 yrs	With or without DM eGFR: ≥20-45 or eGFR ≥45 to <90 with UACR ≥200 mg/g
Intervention	Canagliflozin VS placebo	Dapagliflozin VS placebo	Empagliflozin VS placebo
			Results awaited
2019	Composite of ESKD, 2 X S.cr , or kidney related or CV death HR 0.70; (0.59 to 0.82) CV death, MI, or stroke- HR 0.80, (0.67 -0.95) Hospitalization for heart failure HR 0.61; (0.47 to 0.80)		
2020		Composite of sustained decline in eGFR of at least 50%, ESKD, or death from renal or CV causes-HR 0.56; (0.45 to 0.68) Composite of death from CV causes or hospitalization for heart failure HR 0.71; (0.55 to 0.92)	
2022			Primary outcomes: Kidney disease progression (defined as ESKD, a sustained decline in eGFR to <10 ml./min/1.73m², renal death, or a sustained decline of ≥40% in eGFR or CV death

Infographic by- Priti Meena, M.D @Priti899

Cont..

EXTRA

Treat complications:

1. Management of mineral bone disease (secondary hyperparathyroidism):

- ◄ High PO4: give **PO4 blinders**.
- ◄ Low Ca: Oral **calcium**.
- ◄ Low active vit D: 1 **alpha calcidol** or **calcitriol**.
- ◄ High PTH: **Cinacalcet**.

Goals of therapy: normal PO4, Normal Ca, PTH 2-3 times the normal range.

Benefit of therapy: prevent bone loss, less vascular calcification, Less CV risk.

2. Management of anemia:

Problem:

- Low EPO.
- High Hepcidin.
- Poor GI absorption of Fe.
- Low Iron stores.

Intervention

- **IV iron.**
- **Erythropoietin stimulating agents (ESA).**

Goals of therapy: Tsat >20%, Ferritin > 100, Hb 10-12.

Benefit of therapy: better quality of life, less transfusion, less LV mass, less CV disease, less death.

3. Management of hyperkalemia:

Problem:

- Low K secretion.
- Acidosis.
- Insulin deficiency.
- High K intake.
- Medications.

Intervention

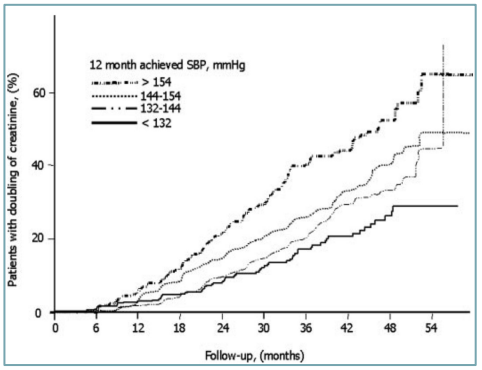
- **Loop diuretics.** - **K keylation.**
- **Bicarbonate Rx.**
- **Glycemic control.**
- **Diet restriction/chelation.**
- **Adjust meds.**

Goals of therapy: K <5.3, allow room for RAAS blockade.

4. Management of blood pressure:

Medications	CKD-Related Indications	Other Potential Indications
Diuretics		
Thiazide (eg, hydrochlorothiazide, chlorthalidone, metolazone)	Fluid overload; may improve proteinuria if used in combination with RAS inhibitors	Kidney stone prevention (hypercalciuria); Gordon syndrome; NDI
Loop (eg, furosemide, bumetanide, torsemide)	Fluid overload	Heart failure; hypercalcemia
Potassium-sparing (triamterene, amiloride)	Fluid overload; hypokalemia	Refractory hypomagnesemia; lithium toxicity/NDI

RAS Blockade		
ACEi (first-line agents if proteinuria)	Proteinuria reduction; delays progression of CKD	Heart failure with reduced ejection fraction; post–myocardial infarction
ARBs (first-line agents if proteinuria)	Proteinuria reduction; delays progression of CKD	Uric acid lowering (losartan) or gout; similar to ACEi
β-Blockers		
Selective (metoprolol, nebivolol)		Heart failure; atrial fibrillation; migraines; essential tremors; anxiety disorders; angina
Combined α-β (carvedilol, labetalol)		Heart failure; atrial fibrillation
Calcium Channel Blockers		
Dihydropyridine (amlodipine, nifedipine)		Raynaud, esophageal spasms
Nondihydropyridine (diltiazem, verapamil)	Proteinuria reduction	Atrial fibrillation



Take home messages

- Patients with CKD are more likely to die of CV disease than progressing to end-stage renal disease (ESRD).
- Prevention, early detection, and proper treatment of CKD helps reduce the risk of CKD complications and progression to ESRD.
- Albuminuria or proteinuria should always be evaluated and is an independent marker for disease progression and mortality.
- RAAS blockade is a cornerstone of therapy for CKD.

Chronic Kidney Disease (CKD)

When the creatinine remains elevated and won't come back down, it's a case of CKD. It's usually **>3 months** of **reduced GFR** (<60mL/hr, or a Creatinine~2). The stage of renal disease is based on the GFR. We use the **creatinine** as a **surrogate** for GFR. There are a number of equations that can be used to estimate the GFR by the creatinine, but to use any of them the creatinine must be stable. That is, only in chronic kidney disease can you use the Creatinine to estimate the GFR.

Stage	*Description*	*GFR*	*Tx Goals*
I	Ø GFR effect	>90	Comorbidities
II	Mild	60-89	Comorbidities
III	Moderate	30-59	Comorbidities / Complications
IV	Severe	15-29	Prepare Dialysis / Transplant
V	Kidney Failure	<15	Dialysis required for survival

The overall management of chronic kidney disease is to **prevent progression** and **manage complications**.

Intervention	*Goal*	*Progression*
ACE-inhibitor	BP <130 / <80	HTN
Insulin	bG 80-110	DM

Prevent progression

Hypertension and **Proteinuria** are managed with **Ace-inhibitors** and **Angiotensin Receptor Blockers**. Use either an ACE-I or an ARB – don't combine them. The blood pressure goal in CKD remains more aggressive than traditional hypertension management; it's **<130 / <80**.

Diabetes is managed similarly. All diabetics require annual urinalysis to assess for microalbuminuria. The A1c goal remains < 7.0. Caution must be used in CKD as insulin is renally excreted.

Complication	*Goal*	*Example*
Anemia	Hgb > 10	EPO, Iron
Secondary Hyperparathyroidism	PTH	Calcimimetics Phos Binders
Osteoporosis	Dexa > -2.5	Ca, 1,25VitD
Volume Overload	None	Loops Hemodialysis
Metabolic Acidosis	Bicarb > 20	NaBicarb

Manage Complications

Anemia results from decreased erythropoietin. The goal hemoglobin is 11-12. Anemia in CKD is usually normocytic and seen in late stage disease. Use **Erythropoietin** and **Iron supplementation** to sustain blood counts. Transfusions with dialysis can also be done.

Secondary hyperparathyroidism is a product of **phosphate retention** (elevated phosphorous stimulates PTH) and **Vitamin-D Deficiency** that leads to low calcium (low calcium stimulates PTH). Thus, **phosphate binders** such as sevelamer and **calcimimetics** such as cinacalcet are used to decrease this risk.

Chronic Kidney Disease Mineral Bone Disorders from secondary hyperparathyroidism can be protected against by giving **Calcium** and **1,25-Vitamin D** supplementation.

Volume Overload is caused by the loss of urinary output. Initially, stimulation of the nephron can be sustained using **loop diuretics** such as furosemide. Combination therapy with metolazone and furosemide is a last ditch effort to maintain adequate urinary output. Ultimately, dialysis manages volume overload.

Acidosis results in a bicarb between 12-20. **Bicarbonate** supplementation is used to reverse this.

Lecture Quiz

1:C / 2:A / 3:C / 4:A

Q1: At a routine checkup, a 42-year-old male with diabetes is found to have an eGFR of 32 ml/min/1.73 m2. When repeated 3 months later, it is 35 ml/ min/1.73 m2. His albumin:creatinine ratio (ACR) is 35 mg/mmol (310 mg/g). Macroalbuminuria is defined as ACR >30 mg/mmol (>300 mg/g). What stage of CKD does he have?

A. Stage 1
B. Stage 2
C. Stage 3
D. Stage 4

Q2:A 49-year-old woman attends your clinic suffering from chronic renal failure due to progressive glomerular disease. She appears well and her blood pressure is 141/92 mmHg. Blood tests reveal elevated phosphate, serum creatinine and urea, while calcium levels are low. Her estimated glomerular filtration rate is 35 mL/min/1.73m2. You also notice the patients cholesterol levels are moderately raised. The most appropriate management is:

A. Sevelamer
B. Parathyroidectomy
C. Oral vitamin D
D. Cinacalcet

Q3: Typical biochemical features of chronic kidney failure include:

A. Hypophosphatemia
B. Hypercalcemia
C. Metabolic acidosis
D. Polyuri

Q4: A 50-year-old man comes to the physician for a routine follow-up visit. He has hypertension, diabetes mellitus, secondary hyperparathyroidism, and end-stage renal disease. He has been on hemodialysis for the past three years. He was admitted three months ago for line sepsis, which was treated with antibiotics. He had a right below-the-knee amputation two years ago following a non-healing foot ulcer. Physical examination shows a right carotid bruit. If this patient dies within the next five years, what would be the most likely cause of his death?

A. Cardiovascular disease
B. Stroke
C. Infection
D. Cancer