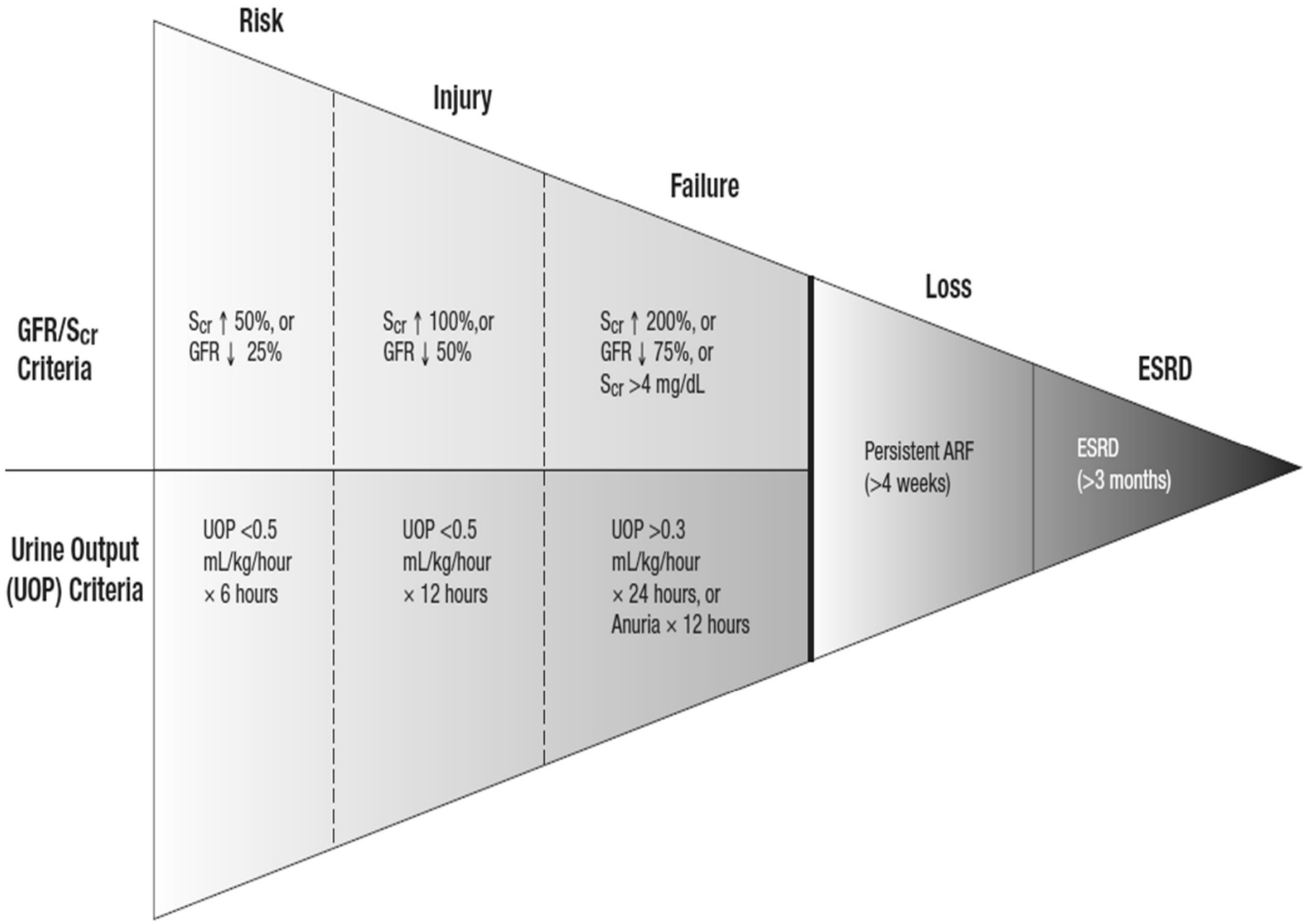
Acute Renal Failure

- Acute renal failure (ARF) is broadly defined as a decrease in glomerular filtration rate (GFR) occurring over hours to weeks that is associated with an accumulation of waste products, including urea and creatinine.


Risk
Injury
Failure
Loss
ESRD
GFR/Scr Criteria
Scr ↑ 50%, or GFR ↓ 25%
Scr ↑ 100%,or GFR ↓ 50%
Scr ↑ 200%, or GFR ↓ 75%, or Scr >4 mg/dL
Persistent ARF (>4 weeks)
ESRD (>3 months)
Urine Output (UOP) Criteria
UOP <0.5 mL/kg/hour × 6 hours
UOP <0.5 mL/kg/hour × 12 hours
UOP >0.3 mL/kg/hour × 24 hours, or Anuria × 12 hours

Category	Abnormality Causing Acute Renal Failure	Possible Causes
Prerenal	Intravascular volume depletion resulting in arterial hypotension	Dehydration Inadequate fluid intake Excessive vomiting, diarrhea, or gastric suctioning Increased insensible losses (e.g., fever, burns) Diabetes insipidus High-serum glucose (glucosuria) Overdiuresis Hemorrhage Decreased cardiac output Hypoalbuminemia Liver disease Nephrotic syndrome
	Arterial hypotension (regardless of volume status)	Anaphylaxis Sepsis Excessive antihypertensive use
	Decreased cardiac output	Heart failure Sepsis Pulmonary hypertension Aortic stenosis (and other valvular abnormalities) Anesthetics
	Isolated renal hypoperfusion	Bilateral renal artery stenosis (unilateral renal artery stenosis in solitary kidney) Emboli Cholesterol Thrombotic Medications Cyclosporine Angiotensin-converting enzyme inhibitors Nonsteroidal antiinflammatory drugs Radiocontrast media Hypercalcemia Hepatorenal syndrome
Intrinsic	Vascular damage	Vasculitis Polyarteritis nodosa Hemolytic uremic syndrome/thrombotic thrombocytopenic purpura Emboli Atherosclerotic Thrombotic Accelerated hypertension
	Glomerular damage	Systemic lupus erythematosus Poststreptococcal glomerulonephritis Antiglomerular basement membrane disease
	Acute tubular necrosis	Ischemic Hypotension Vasoconstriction Exogenous toxins Contrast dye Heavy metals Drugs (amphotericin B, aminoglycosides, etc.)

Category	Abnormality Causing Acute Renal Failure	Possible Causes
		Endogenous toxins
		Myoglobin
		Hemoglobin
	Acute interstitial nephritis	Drugs
		Penicillins
		Ciprofloxacin
		Sulfonamides
		Infection
		Viral
		Bacterial
Postrenal	Bladder outlet obstruction	Prostatic hypertrophy, infection, cancer
		Improperly placed bladder catheter
		Anticholinergic medication
	Ureteral	Cancer with abdominal mass
		Retroperitoneal fibrosis
		Nephrolithiasis
	Renal pelvis or tubules	Nephrolithiasis
		Oxalate
		Indinavir
		Sulfonamides
		Acyclovir
		Uric acid

Diagnostic Parameters for Differentiating Causes of Acute Renal Failure

Laboratory Test	Prerenal Azotemia	Acute Intrinsic Renal Failure	Postrenal Obstruction
Urine sediment	Normal	Casts, cellular debris	Cellular debris
Urinary RBC	None	2–4+	Variable
Urinary WBC	None	2–4+	1+
Urine sodium	<20	>40	>40
FE_{Na} (%)	<1	>2	Variable
Urine/serum osmolality	>1.5	<1.3	<1.5
Urine/S_{cr}	>40:1	<20:1	<20:1
BUN/S_{cr}	>20	~15	~15

Differential Diagnosis of Acute Renal Failure on the Basis of Urine Microscopic Examination Findings

Urine Sediment	Suggestive of
Cells	
Microorganisms	Pyelonephritis
Red blood cells	Glomerulonephritis, pyelonephritis, renal infarction, papillary necrosis, renal tumors, kidney stones
White blood cells	Pyelonephritis, interstitial nephritis
Eosinophils	Drug-induced allergic interstitial nephritis, renal transplant rejection
Epithelial cells	Tubular necrosis
Casts	
Granular casts	Tubular necrosis
White blood cell casts	Pyelonephritis, interstitial nephritis
Red blood cell casts	Glomerulonephritis, renal infarct, lupus nephritis, vasculitis
Crystals	
Urate	Postrenal obstruction
Phosphate	Alkaline urine, possibly secondary to *Proteus* sp. infection, postrenal obstruction

- The primary goal of therapy is to prevent ARF. If ARF develops, the goals are to avoid or minimize further renal insults that would delay recovery and to provide supportive measures until kidney function returns.

PREVENTION OF ACUTE RENAL FAILURE

- Risk factors for ARF include advanced age, acute infection, preexisting chronic respiratory or cardiovascular disease, dehydration, and chronic kidney disease (CKD).

- Decreased renal perfusion secondary to abdominal or coronary bypass surgery, acute blood loss in trauma, and uric acid nephropathy also increase risk.

- Nephrotoxin administration (e.g., radiocontrast dye) should be avoided whenever possible.

- When patients require contrast dye and are at risk of contrast dye–induced nephropathy, renal perfusion should be maximized through strategies such as assuring adequate hydration with normal saline or sodium bicarbonate solutions and administration of oral acetylcysteine 600 mg every 12 hours for four doses.

- Strict glycemic control with insulin in diabetics has also reduced the development of ARF.

MANAGEMENT OF ESTABLISHED ACUTE RENAL FAILURE:

- No drugs have been found to accelerate ARF recovery. Therefore, patients with established ARF should be supported with non pharmacologic and pharmacologic approaches through the period of ARF.

- Supportive care goals include maintenance of adequate cardiac output and blood pressure to optimize tissue perfusion while restoring renal function to pre-ARF baseline.

- Medications associated with diminished renal blood flow should be stopped. Appropriate fluid replacement should be initiated.

- Avoidance of nephrotoxins is essential in the management of patients with ARF.

- Renal replacement therapy (RRT), such as hemodialysis and peritoneal dialysis, maintains fluid and electrolyte balance while removing waste products.

Pharmacologic Approaches

- Loop diuretics have not been shown to accelerate ARF recovery or improve patient outcome; however, diuretics can facilitate management of fluid overload.

- The most effective diuretics are mannitol and loop diuretics.

- Mannitol 20% is typically started at a dose of 12.5 to 25 g IV over 3 to 5 minutes.

- Disadvantages include IV administration, hyperosmolality risk, and need for monitoring because mannitol can contribute to ARF.

- Equipotent doses of loop diuretics (furosemide, bumetanide, torsemide, ethacrynic acid) have similar efficacy. Ethacrynic acid is reserved for sulfaallergic patients.

- Continuous infusions of loop diuretics appear to be more effective and to have fewer adverse effects than intermittent boluses.

Common Causes of Diuretic Resistance in Patients with Acute Renal Failure

Causes of Diuretic Resistance	Potential Therapeutic Solutions
Excessive sodium intake (sources may be dietary, IV fluids, and drugs)	Remove sodium from nutritional sources and medications
Inadequate diuretic dose or inappropriate regimen	Increase dose, use continuous infusion or combination therapy
Reduced oral bioavailability (usually furosemide)	Use parenteral therapy; switch to oral torsemide or bumetanide
Nephrotic syndrome (loop diuretic protein binding in tubule lumen)	Increase dose, switch diuretics, use combination therapy
Reduced renal blood flow	
Drugs (NSAIDs ACEIs, vasodilators)	Discontinue these drugs if possible
Hypotension	Intravascular volume expansion and/or vasopressors
Intravascular depletion	Intravascular volume expansion
Increased sodium resorption	
Nephron adaptation to chronic diuretic therapy	Combination diuretic therapy, sodium restriction
NSAID use	Discontinue NSAID
Heart failure	Treat the heart failure, increase diuretic dose, switch to better-absorbed loop diuretic
Cirrhosis	High-volume paracentesis
Acute tubular necrosis	Higher dose of diuretic, diuretic combination therapy, add low-dose dopamine

Key Monitoring Parameters for Patients with Established Acute Renal Failure

Parameter	Frequency
Fluid ins/outs	Every shift
Patient weight	Daily
Hemodynamics (blood pressure, heart rate, mean arterial pressure, etc.)	Every shift
Blood chemistries	
Sodium, potassium, chloride, bicarbonate, calcium, phosphate, magnesium	Daily
Blood urea nitrogen/serum creatinine	Daily
Drugs and their dosing regimens	Daily
Nutritional regimen	Daily
Blood glucose	Daily (minimum)
Serum concentration data for drugs	After regimen changes and after renal replacement therapy has been instituted
Times of administered doses	Daily
Doses relative to administration of renal replacement therapy	Daily
Urinalysis	
Calculate measured creatinine clearance	Every time measured urine collection performed
Calculate fractional excretion of sodium	Every time measured urine collection performed
Plans for renal replacement	Daily

Chronic Kidney Disease:

- Chronic kidney disease (CKD) is a progressive loss of function over several months to years, characterized by gradual replacement of normal kidney architecture with interstitial fibrosis.

- CKD is categorized by the level of kidney function, based on glomerular filtration rate (GFR), into stages 1 to 5, with each increasing number indicating a more advanced stage of the disease, as defined by a declining GFR.

- CKD stage 5, previously referred to as end-stage renal disease (ESRD), occurs when the GFR falls below 15 mL/min per 1.73 m2 body surface area.

- The patient with stage 5 CKD requiring chronic dialysis or renal transplantation for relief of uremic symptoms is said to have ESRD.

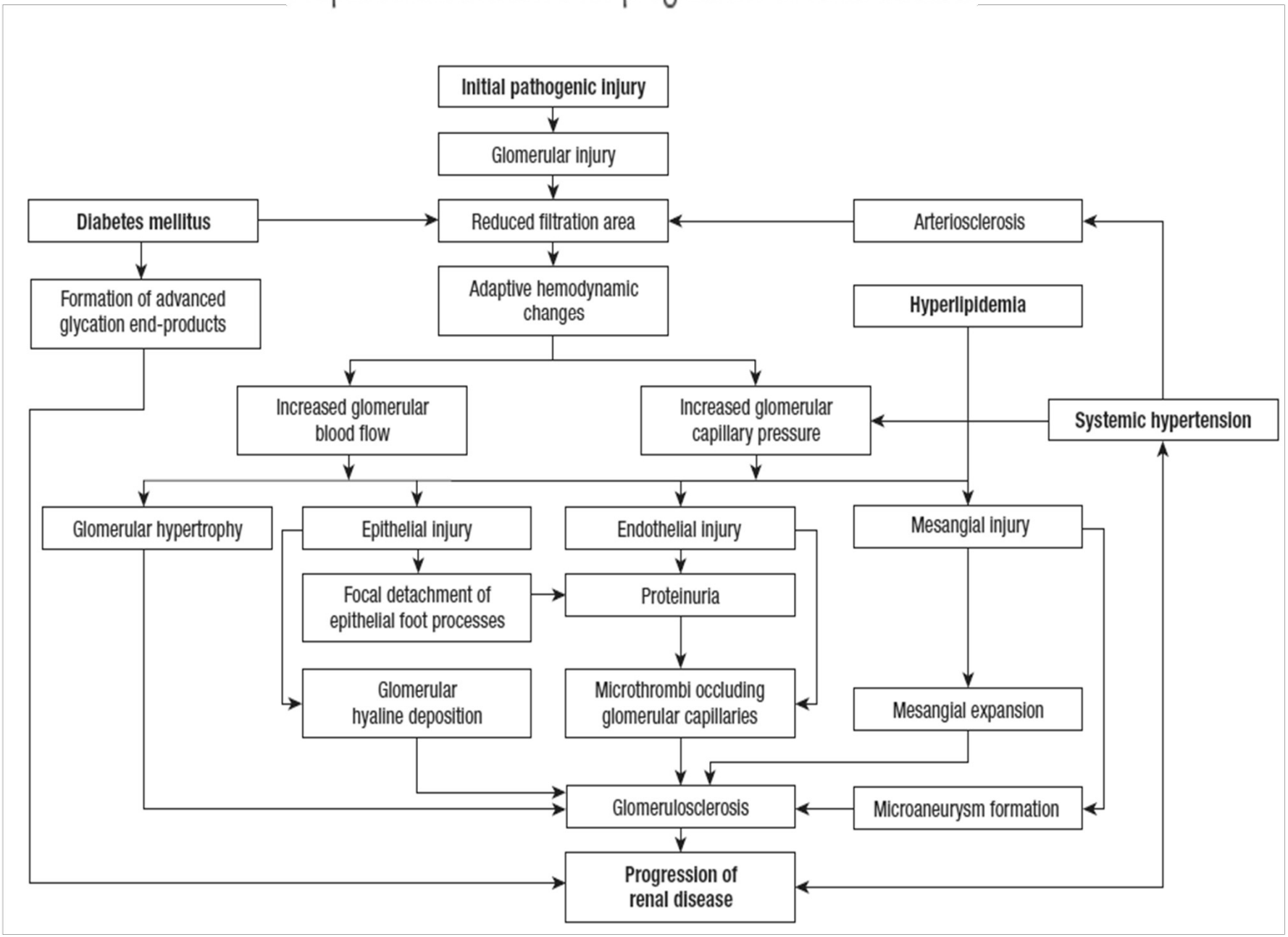
- Initiation factors initiate kidney damage and can be modified by drug therapy.

- Initiation factors include diabetes mellitus, hypertension, autoimmune disease, polycystic kidney disease, and drug toxicity.

- Progression factors hasten decline in kidney function after initiation of kidney damage.

- Progression factors include glycemia in diabetics, hypertension, proteinuria, and smoking.

Proposed mechanisms for progression of renal disease.



CLINICAL PRESENTATION:

- CKD development and progression is insidious.

- Patients with stage 1 or 2 CKD usually do not have symptoms or metabolic derangements seen with stages 3 to 5, such as anemia, secondary hyper parathyroidism, cardiovascular disease, malnutrition, and fluid and electrolyte abnormalities that are more common as kidney function deteriorates.

- Uremic symptoms (fatigue, weakness, shortness of breath, mental confusion, nausea, vomiting, bleeding, and anorexia) are generally absent in stages 1 and 2, minimal during stages 3 and 4, and common in patients with stage 5 CKD who may also experience itching, cold intolerance, weight gain, and peripheral neuropathies.

TREATMENT:

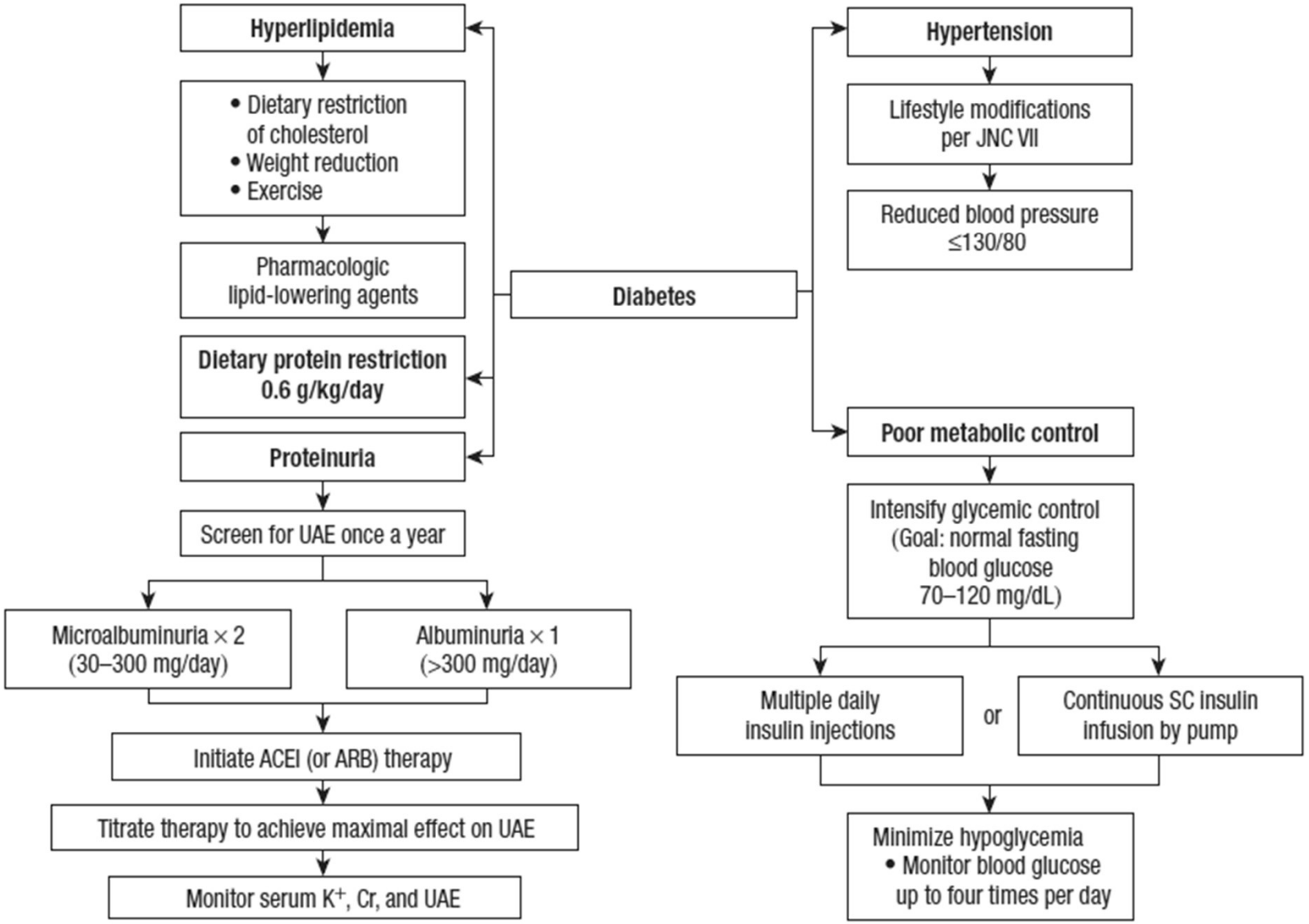
- A low-protein diet (0.6 to 0.75 g/kg/day) can delay progression of CKD in patients with or without diabetes, although the benefit is relatively small.

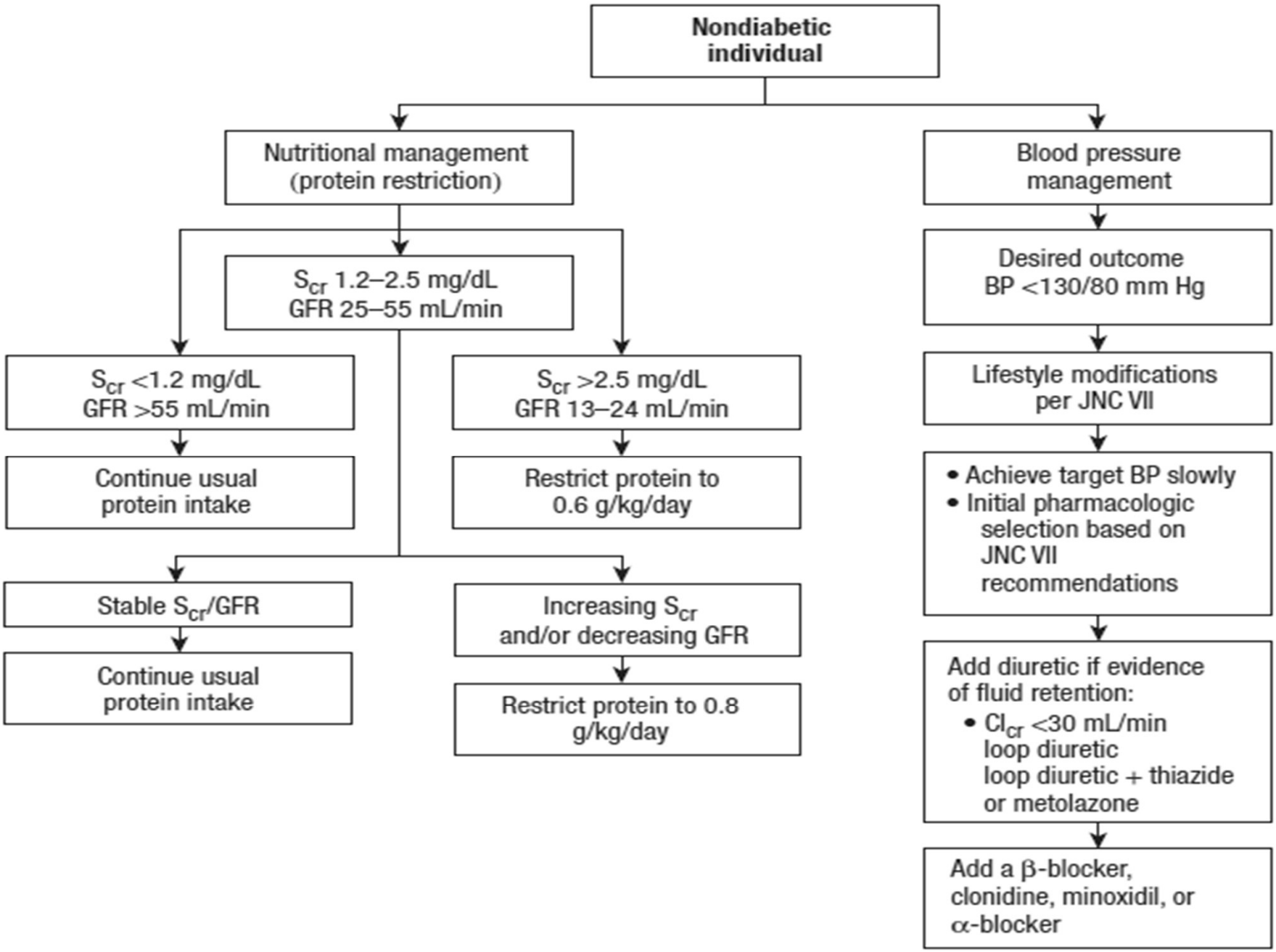
- Intensive therapy in patients with type 1 and type 2 diabetes reduces microvascular complications, including nephropathy.

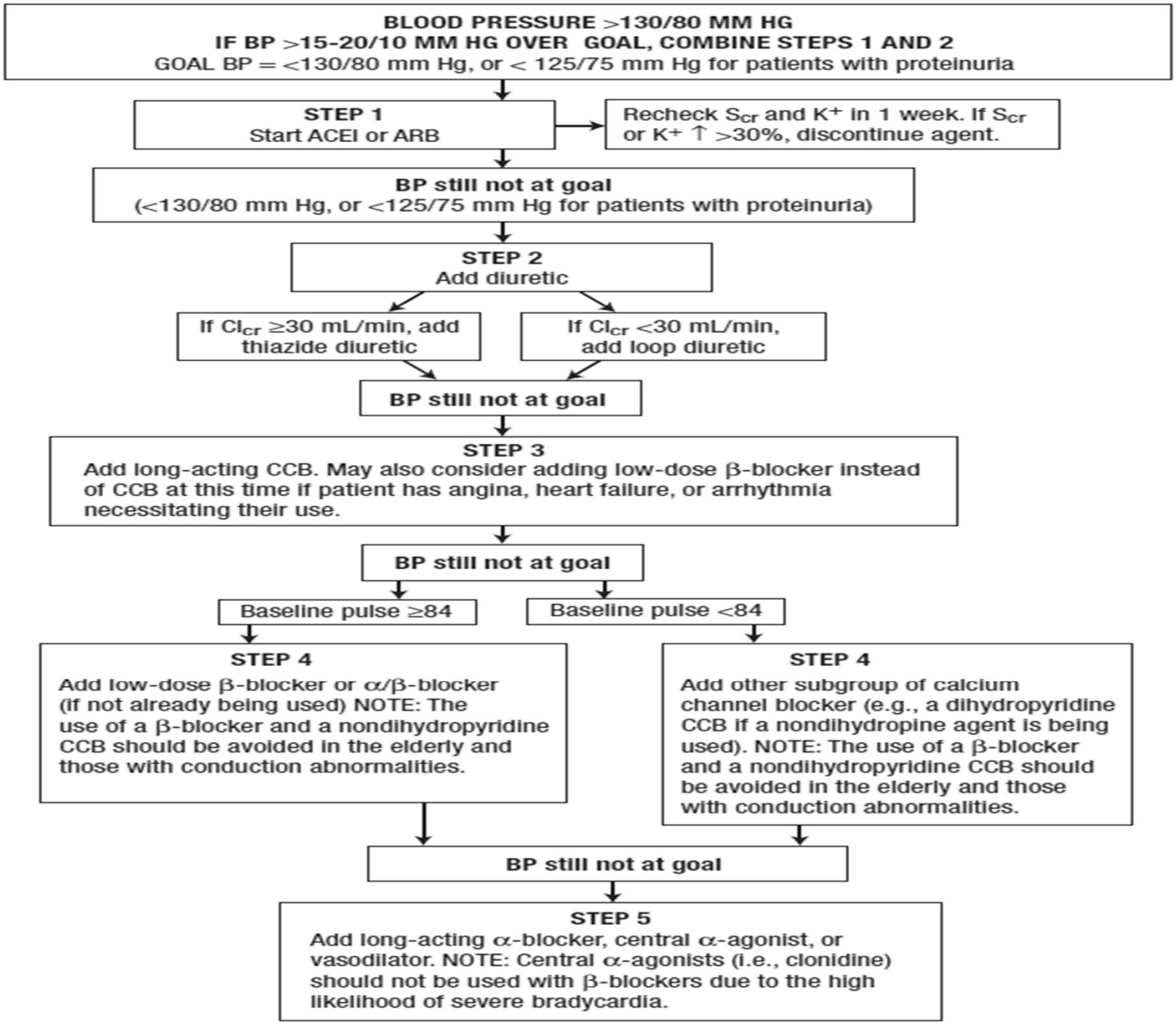
- Intensive therapy can include insulin or oral drugs and involves blood sugar testing at least three times daily.

- The progression of CKD can be limited by optimal control of hyperglycemia and hypertension.

Therapeutic strategies to prevent progression of renal disease in diabetic individuals.




Nondiabetic individual
Nutritional management (protein restriction)
Blood pressure management
S_{cr} 1.2–2.5 mg/dL
GFR 25–55 mL/min
Desired outcome
BP <130/80 mm Hg
S_{cr} <1.2 mg/dL
GFR >55 mL/min
S_{cr} >2.5 mg/dL
GFR 13–24 mL/min
Lifestyle modifications per JNC VII
Continue usual protein intake
Restrict protein to 0.6 g/kg/day
• Achieve target BP slowly
• Initial pharmacologic selection based on JNC VII recommendations
Stable S_{cr}/GFR
Increasing S_{cr} and/or decreasing GFR
Add diuretic if evidence of fluid retention:
• Cl_{cr} <30 mL/min
loop diuretic
loop diuretic + thiazide or metolazone
Continue usual protein intake
Restrict protein to 0.8 g/kg/day
Add a β-blocker, clonidine, minoxidil, or α-blocker


BLOOD PRESSURE >130/80 MM HG
IF BP >15-20/10 MM HG OVER GOAL, COMBINE STEPS 1 AND 2
GOAL BP = <130/80 mm Hg, or < 125/75 mm Hg for patients with proteinuria
STEP 1
Start ACEI or ARB
Recheck S_{cr} and K^+ in 1 week. If S_{cr} or K^+ ↑ >30%, discontinue agent.
BP still not at goal
(<130/80 mm Hg, or <125/75 mm Hg for patients with proteinuria)
STEP 2
Add diuretic
If Cl_{cr} ≥30 mL/min, add thiazide diuretic
If Cl_{cr} <30 mL/min, add loop diuretic
BP still not at goal
STEP 3
Add long-acting CCB. May also consider adding low-dose β-blocker instead of CCB at this time if patient has angina, heart failure, or arrhythmia necessitating their use.
BP still not at goal
Baseline pulse ≥84
Baseline pulse <84
STEP 4
Add low-dose β-blocker or α/β-blocker (if not already being used) NOTE: The use of a β-blocker and a nondihydropyridine CCB should be avoided in the elderly and those with conduction abnormalities.
STEP 4
Add other subgroup of calcium channel blocker (e.g., a dihydropyridine CCB if a nondihydropine agent is being used). NOTE: The use of a β-blocker and a nondihydropyridine CCB should be avoided in the elderly and those with conduction abnormalities.
BP still not at goal
STEP 5
Add long-acting α-blocker, central α-agonist, or vasodilator. NOTE: Central α-agonists (i.e., clonidine) should not be used with β-blockers due to the high likelihood of severe bradycardia.

Management of Dyslipidemia in Patients with Chronic Kidney Disease

Dyslipidemia	Goal	Initial Therapy	Modification in Therapy[a]	Alternative[a]
TG ≥500 mg/dL	TG <500 mg/dL	TLC	TLC + fibrate or niacin	Fibrate or niacin
LDL 100–129 mg/dL	LDL <100 mg/dL	TLC	TLC + low-dose statin	Bile acid sequestrant or niacin
LDL ≥130 mg/dL	LDL <100 mg/dL	TLC + low-dose statin	TLC + maximum-dose statin	Bile acid sequestrant or niacin
TG ≥200 mg/dL and non-HDL ≥130 mg/dL	Non-HDL <130 mg/dL	TLC + low-dose statin	TLC + maximum-dose statin	Fibrate or niacin