Hypertension Diagnostic Tests

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Introduction

Reasons to evaluate patients with hypertension:

1-Determine the type of hypertension

2-Assess the impact of the hypertension on target organs

3-Estimate a patient's overall risk profile of premature CVD.

Routine Laboratory Testing

- **Hematocrit**
- **urine analysis (including microscopic exam and dipstick for proteinuria)**
- **Automated blood chemistry (glucose, creatinine, electrolytes)**
- **Uric acid and calcium**
- **Lipid profile (LDL and HDL cholesterol, triglycerides)**
- **12-lead electrocardiography**

Kaplan's Clinical Hypertension
Eleventh Edition

Laboratory testing

In all patients with newly diagnosed hypertension

- **Electrolytes (including calcium) and serum creatinine (to calculate the estimated glomerular filtration rate)**
- **Fasting glucose**
- **Urinalysis**
- **Complete blood count**
- **Thyroid-stimulating hormone**
- **Lipid profile**
- **Electrocardiogram**
- **Calculate 10-year atherosclerotic cardiovascular disease risk**

Additional tests

May be indicated in certain settings:

- **Urinary albumin to creatinine ratio**

  Independent risk factor for CVD

  Necessary in all DM and CKD patients

- **Echocardiography**

  More sensitive means of identifying the presence LVH than an electrocardiogram

Additional Tests Based on History, Physical Examination, and Findings from Routine Laboratory Tests

- Hemoglobin A_{1c} (if fasting plasma glucose is >5.6 mmol/L (102 mg/dL) or previous diagnosis of diabetes)
- Quantitative proteinuria (if dipstick test is positive)
- Urinary potassium and sodium concentration and their ratio
- Home and 24-h ambulatory BP monitoring
- Echocardiogram
- Holter monitoring in case of arrhythmias
- Carotid ultrasound
- Peripheral artery/abdominal ultrasound
- Pulse wave velocity
- Ankle–brachial index
- Funduscopy

Reproduced from Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC practice guidelines for the management of arterial hypertension. *J Hypertens* 2013;31:1281–1357.

Plasma Renin Activity

- **Both PRA and plasma renin concentration (PRC) can be measured by commercial assays**
- **PRA can be measured by many commercial clinical laboratories. PRC and prorenin levels are measured mainly for research purposes.**
- **There is no clear clinical advantage of PRC over PRA**

PRA *Role in Primary Hypertension*

- **Elevated BP itself particularly volume-expanded Salt-sensitive hypertension: feedback suppression of PRA.**
- **Most patients with primary hypertension have "inappropriately" normal or even elevated PRA levels**

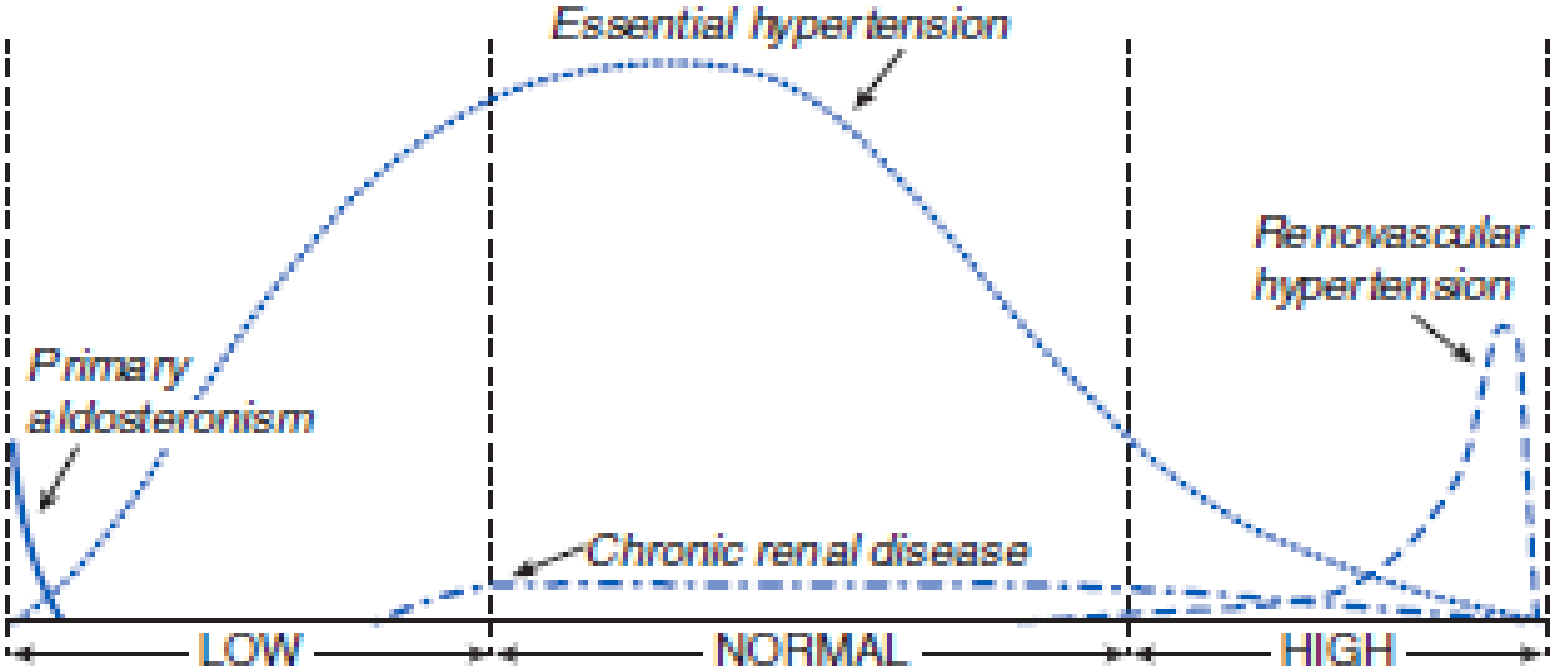


FIGURE 3-32 • Schematic representation of PRA in various hypertensive diseases. The approximate number of patients with each type of hypertension is indicated along with their proportion of low-, normal or high-renin levels. (Modified from Kaplan NM. Renin profiles. *JAMA* 1977;238:611–613.)

Clinical Conditions Affecting PRA

Decreased PRA	Increased PRA
Expanded fluid volume	Shrunken fluid volume
Salt loads, oral or intravenous	Sodium restriction
Primary salt retention	Fluid losses
Liddle syndrome	Diuretic induced
Gordon syndrome	Gastrointestinal losses
Mineralocorticoid excess	Hemorrhage
Primary aldosteronism	Decreased effective plasma volume
Cushing syndrome	Upright posture
Congenital adrenal hyperplasia	Cirrhosis with ascites
DOC, 18-hydroxy-DOC excess	Nephrotic syndrome
11β-Hydroxysteroid dehydrogenase inhibition (licorice)	Decreased renal perfusion pressure
Sympathetic inhibition	Renovascular hypertension
Autonomic dysfunction	Accelerated–malignant hypertension
Therapy with adrenergic neuronal blockers	Chronic renal disease (renin dependent)
Therapy with β-adrenergic blockers	JG hyperplasia
Hyperkalemia	Sympathetic activation
Decreased renin substrate	Therapy with direct vasodilators
Androgen therapy	Pheochromocytoma
Decrease in renal tissue	Stress: exercise, hypoglycemia
Hyporeninemic hypoaldosteronism	Hyperthyroidism
Chronic renal disease (volume dependent)	Sympathomimetic agents (caffeine)
Anephric	Hypokalemia
Increasing age	Increased renin substrate
Unknown	Pregnancy
Low-renin primary hypertension	Estrogen therapy
Black race	Autonomous renin hypersecretion
	Renin-secreting tumors
	Acute damage to JG cells
	Acute glomerulonephritis
	Decreased feedback inhibition
	Low A II levels (ACEI therapy)
	Unknown
	High-renin primary hypertension

Testing for secondary hypertension

- **It is not recommended for all patients as:**

  Secondary causes are relatively uncommon

  Testing may produce false-positive results

  It is not cost effective

- **For testing: Clinical 'clues' important**

  Age based approach essential

Secondary hypertension according to age

Age group	% with underlying cause	Most common cause
Children (<12 years)	70-85%	Renal parenchymal disease Coarctation of aorta
Adolescents (12-18 years)	10-15%	Renal parenchymal disease Coarctation of aorta
Young adults (19-39 years)	5%	Fibromuscular dysplasia Renal parenchymal disease
Middle aged adults (40-65 years)	8-12%	Primary Aldosteronism Obstructive Sleep Apnoea Cushing's syndrome Phaeochromocytoma
Older adults	17%	Atherosclerotic renovascular disease Renal failure hypothyroidism

Secondary HTN Screening Indications

- An unusual presentation of hypertension : new onset at an especially young or especially old age, presentation with stage 2 hypertension, abrupt onset of hypertension in a patient with previously normal blood pressure
- Drug-resistant hypertension
- The presence of a clinical clue for a specific cause of hypertension: an abdominal bruit (suggestive of renovascular hypertension) or low serum potassium (suggestive of primary aldosteronism)

Indications to Evaluate for Secondary Hypertension

- **Acute rise in blood pressure in a patient with previously stable readings**
- **Age of onset before puberty**
- **Age younger than 30 years in nonobese, nonblack patients with no family history of hypertension**
- **Malignant or accelerated hypertension (with signs of end-organ damage)**
- **Severe (systolic blood pressure > 180 mm Hg and/or diastolic blood pressure > 120 mm Hg) or resistant hypertension**

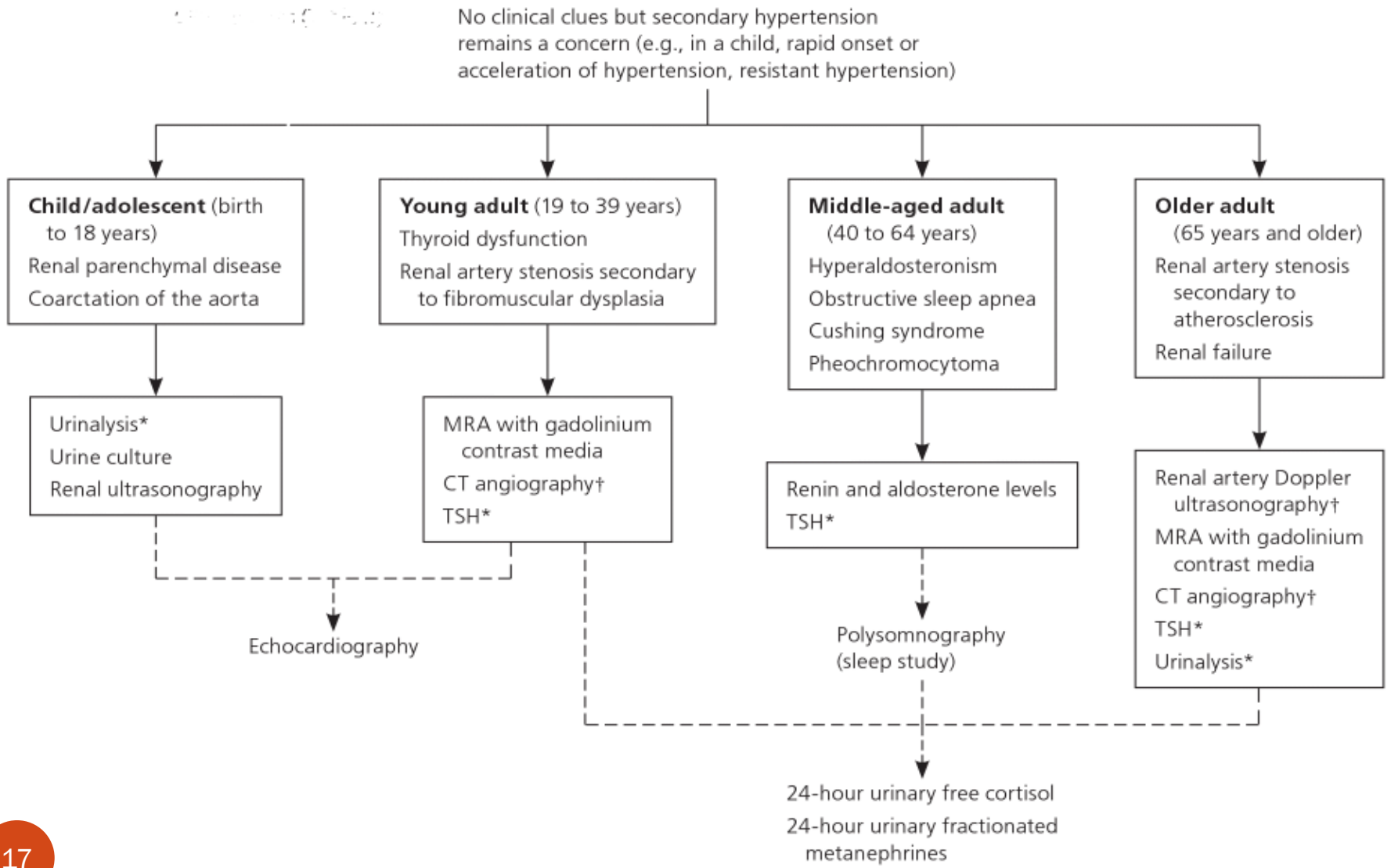
Secondary Hypertension: Discovering the Underlying Cause
LESLEY CHARLES, MD; JEAN TRISCOTT, MD; and BONNIE DOBBS, PhD University of Alberta, Edmonton, Alberta, Canada

Overall Guide to Workup for More Common Identifiable Causes of Hypertension

	Diagnostic Procedure	
Diagnosis	***Initial***	***Additional***
Chronic renal disease	Urinalysis; serum creatinine; estimated GFR	Renography
Renovascular disease	Duplex sonography	Magnetic resonance or CT angiography; angiography
Coarctation	BP in legs	Echocardiogram; aortogram
Primary aldosteronism	Plasma and urinary potassium; plasma renin and aldosterone	Plasma or urinary aldosterone after saline load; adrenal venous sampling
Cushing syndrome	Morning plasma cortisol after 1 mg dexamethasone at bedtime	Urinary cortisol after variable doses of dexamethasone; adrenal CT scans and scintiscans
Pheochromocytoma	Plasma metanephrine	Urinary catechols; plasma catechols (basal and after 0.3 mg clonidine); adrenal CT scans and scintiscans

Secondary hypertension cause	Prevalence (%)	Clinical findings
Obstructive sleep apnoea	10.0	Neck circumference; obesity; peripheral oedema.
Renal parenchymal disease	5.0	Peripheral oedema; pallor; loss of muscle mass.
Renal artery stenosis	4.5	Abdominal bruits and peripheral vascular disease.
Primary aldosteronism	7.0	Muscle weakness
Thyroid disease	1.5	Hyperthyreodism: tachycardia; accentuated heart sounds; exophthalmus; Hypothyreodism; Bradycardia; muscle weakness; myxedema.
Cushing's syndrome	0.5	Obesity; hirsutism; skin atrophy; Striae rubrae; muscle weakness; osteopenia.
Phaeochromocytoma	0.3	The paroxysmal hypertension; pounding headache; perspiration; palpitations; pallor.
Coarctation of the aorta	0.8	Different Blood Pressure (≥ 20/10 mmHg) between upper–lower extremities and/or between right–left arm; and delayed femoral pulsations; interscapular ejection murmur; rib notching on chest Rx

Thevenard G, Dal-Prá NB, Filho IDZ (2018) Major Clinical Considerations for Secondary Hypertension and Treatment Challenges:Systematic Review. J Clin Exp Cardiolog


No clinical clues but secondary hypertension remains a concern (e.g., in a child, rapid onset or acceleration of hypertension, resistant hypertension)
Child/adolescent (birth to 18 years)
Renal parenchymal disease
Coarctation of the aorta
Young adult (19 to 39 years)
Thyroid dysfunction
Renal artery stenosis secondary to fibromuscular dysplasia
Middle-aged adult (40 to 64 years)
Hyperaldosteronism
Obstructive sleep apnea
Cushing syndrome
Pheochromocytoma
Older adult (65 years and older)
Renal artery stenosis secondary to atherosclerosis
Renal failure
Urinalysis*
Urine culture
Renal ultrasonography
MRA with gadolinium contrast media
CT angiography†
TSH*
Renin and aldosterone levels
TSH*
Renal artery Doppler ultrasonography†
MRA with gadolinium contrast media
CT angiography†
TSH*
Urinalysis*
Echocardiography
Polysomnography (sleep study)
24-hour urinary free cortisol
24-hour urinary fractionated metanephrines

Specific Causes Clue

SIGNS/SYMPTOMS	POSSIBLE SECONDARY HYPERTENSION CAUSE	DIAGNOSTIC TEST OPTIONS
Increase in serum creatinine concentration of at least 50% (≥ 0.5 to 1 mg per dL [44 to 88 µmol per L]) after starting angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	Renal artery stenosis	CT angiography
Moderate to severe hypertension and unilateral small kidney/recurrent flash pulmonary edema		Doppler ultrasonography of renal arteries
Renal bruit		Magnetic resonance angiography with gadolinium contrast media

SIGNS/SYMPTOMS	POSSIBLE SECONDARY HYPERTENSION CAUSE	DIAGNOSTIC TEST OPTIONS
Elevated serum creatinine	Renal diseases	Estimated glomerular filtration rate
Proteinuria		Renal ultrasonography
Hypokalemia	Primary hyperaldosteronism	Renin and aldosterone levels to calculate aldosterone-to-renin ratio
Apneic episodes during sleep	Obstructive sleep apnea	Polysomnography (sleep study)
Daytime sleepiness		Sleep Apnea Clinical Score with nighttime pulse oximetry
Snoring		

SIGNS/SYMPTOMS	POSSIBLE SECONDARY HYPERTENSION CAUSE	DIAGNOSTIC TEST OPTIONS
Flushing	Pheochromocytoma	24-hour urinary fractionated metanephrines and normetanephrines
Headaches		Plasma free metanephrines
Labile blood pressures		
Orthostatic hypotension		
Palpitations		
Sweating		
Syncope		

SIGNS/SYMPTOMS	POSSIBLE SECONDARY HYPERTENSION CAUSE	DIAGNOSTIC TEST OPTIONS
Arm to leg systolic blood pressure difference > 20 mm Hg	Coarctation of the aorta	Magnetic resonance/CT angiography (adults)
Delayed or absent femoral pulses		Transthoracic echocardiography (children)
Murmur		

SIGNS/SYMPTOMS	POSSIBLE SECONDARY HYPERTENSION CAUSE	DIAGNOSTIC TEST OPTIONS
Buffalo hump	Cushing syndrome	24-hour urinary free cortisol
Central obesity		Late-night salivary cortisol
Moon facies		Low-dose dexamethasone suppression
Striae		
Bradycardia/tachycardia	Thyroid disorders	Thyroid-stimulating hormone
Cold/heat intolerance		
Constipation/diarrhea		
Irregular, heavy, or absent menstrual cycle		

Pheochromocytoma

One or more of the following:

- **The classic triad of headache, sweating, and tachycardia with or without HTN.**
- **Hyperadrenergic spells (self-limited episodes of nonexertional palpitations, diaphoresis, headache, tremor, or pallor). most patients with spells do not have pheochromocytoma.**
- **Onset of hypertension at a young age (eg, <20 years), resistant hypertension, or hypertension with new-onset or atypical diabetes mellitus.**
- **A familial syndrome with catecholamine-secreting tumors (MEN2,NF1).**
- **A family history of pheochromocytoma.**
- **Adrenal incidentaloma with or without hypertension.**
- **Pressor response during anesthesia, surgery, or angiography.**
- **Idiopathic dilated cardiomyopathy.**
- **A history of gastric stromal tumor or pulmonary chondromas .**

Pheochromocytoma

- **Initial biochemical testing based upon the index of suspicion:**
  - ✓ **Low index of suspicion: 24-hour urinary fractionated catecholamines and metanephrines**
  - ✓ **High index of suspicion: plasma fractionated metanephrin**
- **Biochemical confirmation of the diagnosis should be followed by radiological evaluation(CT or MRI) to locate the tumor**

Primary Aldosteronism

- Test the following patients:

- Hypertension and spontaneous or low-dose, diuretic-induced hypokalemia
- Severe hypertension (>150 mmHg systolic or >100 mmHg diastolic) or drug-resistant hypertension
- Hypertension with adrenal incidentaloma
- Hypertension with sleep apnea
- Hypertension and a family history of early-onset hypertension or cerebrovascular accident at a young age (<40 years)
- All hypertensive first-degree relatives of patients with primary aldosteronism

- not recommend screening in patients in whom the diagnosis would not change management

Primary Aldosteronism

Rare cause of hypertension

- **Serum potassium must be normal**
- **All the drugs must be stopped**
- **Making the diagnosis doesn't matter- just lower the blood pressure**

- **The initial evaluation: plasma renin activity (PRA) or plasma renin concentration (PRC) is reduced (typically undetectable) and that the plasma aldosterone concentration (PAC) is inappropriately high for the PRA (typically >10 ng/dL [>277 pmol/L])**
- **The net effect is a PAC/PRA ratio greater than 20 (depending upon the laboratory normals).**
- **Confirming the diagnosis by demonstrating inappropriate aldosterone secretion or aldosterone suppression test (use oral sodium loading and measurement of urine aldosterone excretion)**
- **Confirmatory testing exception: spontaneous hypokalemia, undetectable PRA or PRC, and a PAC ≥20 ng/dL**
- **Adrenal computed tomography (CT) : the initial test to distinguish between APA and bilateral hyperplasia. and exclude adrenocortical carcinoma**

Drug	Effect on aldosterone	Effect on renin	Effect on ARR
B-blocker	↓	↓↓	↑
Centrally acting	↓	↓↓	↑
NSAIDs	↓	↓↓	↑
K-wasting diuretics	↔↑	↑↑	↓
K-sparing diuretics	↑	↑↑	↓
ACEi/ARB	↓	↑↑	↓
Ca channel blockers (DHP)	↔↓	↑	↓

RVH suggestive features

Disorder	Suggestive clinical features
General	Severe or resistant hypertension
	An acute rise in blood pressure over a previously stable value
	Proven age of onset before puberty
	Age less than 30 years with no family history of hypertension and no obesity
Renovascular disease	An acute elevation in serum creatinine of at least 30% after administration of ACE inhibitor or ARB
	Moderate to severe hypertension in a patient with diffuse atherosclerosis, a unilateral small kidney, or asymmetry in renal size of more than 1.5 cm that cannot be explained by another reason
	Moderate to severe hypertension in patients with recurrent episodes of flash pulmonary edema
	Onset of stage II hypertension after age 55 years
	Systolic or diastolic abdominal bruit (not very sensitive)

DIAGNOSTIC TEST OPTIONS

- **Renal arteriography: gold standard**
- **Duplex Doppler ultrasonography**
- **Computed tomographic angiography (CTA)**
- **Magnetic resonance angiography (MRA)**

DIAGNOSTIC TEST

- **Without renal insufficiency: duplex Doppler, CTA, and MRA**
- **With renal insufficiency:**

  If technical expertise is available, doppler ultrasonography.

  If not: CTA

High likelihood of benefiting from the intervention

1. **A short duration (weeks or months) of blood pressure elevation prior to the diagnosis of renovascular disease: strongest clinical predictor of a fall after revascularization.**
2. **Failure of optimal medical therapy to control the blood pressure.**
3. **Intolerance to optimal medical therapy(significant rise in serum cr after initiation of a RAS inhibitor).**
4. **Progressive renal insufficiency**
5. **Suspected fibromuscular disease in a young person (to limit the need for life-long antihypertensive therapy).**
6. **Recurrent flash pulmonary edema and/or refractory heart failure.**

Home Messages

- **Majority of hypertension is primary**
- **Perform Routine Laboratory Tests for all patients**
- **Testing for secondary hypertension is not recommended for all patients**

THANKS
FOR YOUR ATTENTION