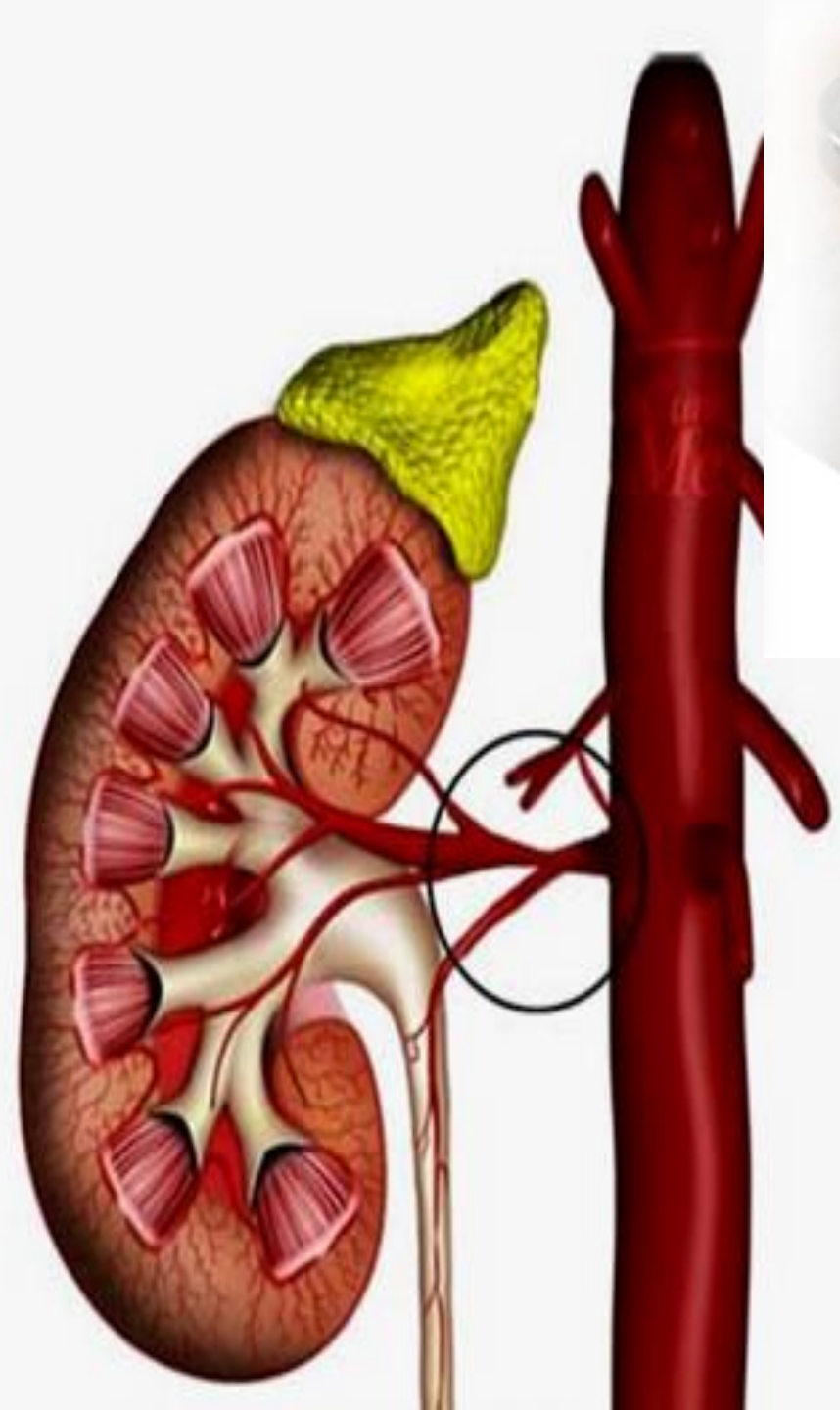


ارتفاع التوتر الشرياني كلوي المنشأ

أ.د. محمد علي النحاس

Renovascular Hypertension

Hypertension

- HTN affects 43 million adults in US
- 90-95% have "Essential HTN" without identifiable and treatable cause
- " Secondary" HTN accounts for ~5-10% of other cases and represents potentially curable disease

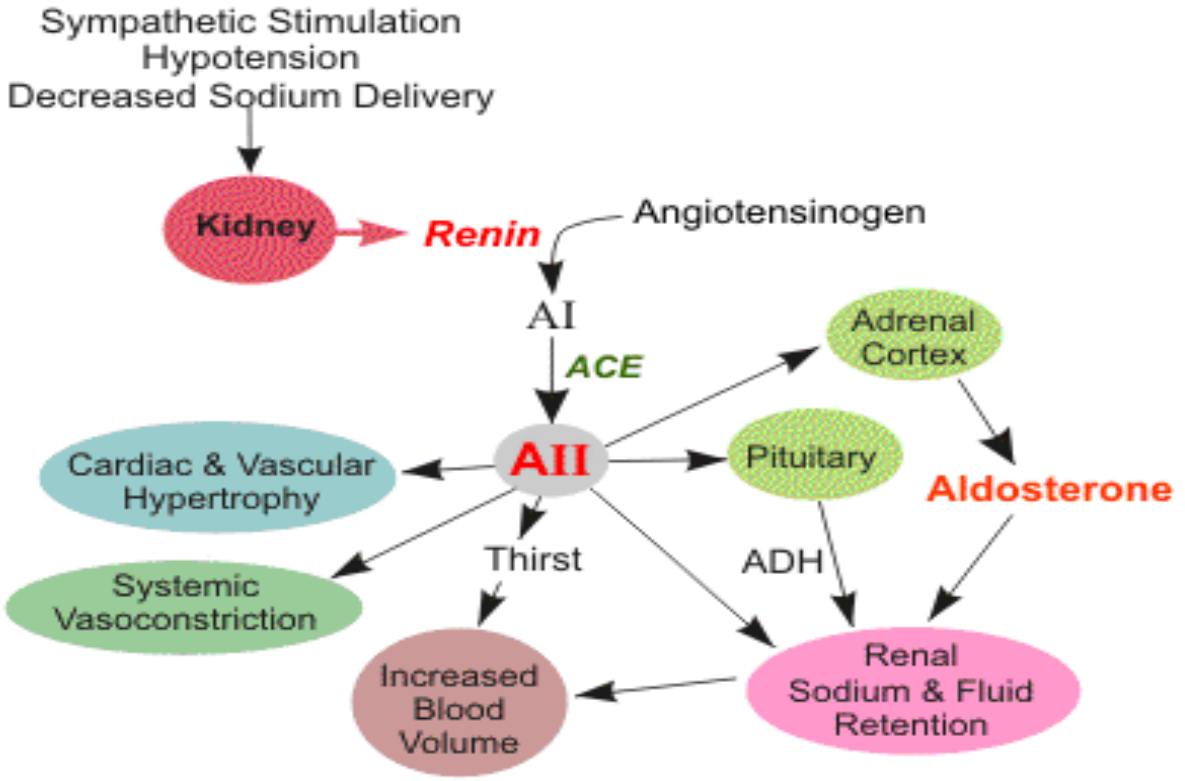
Causes of Secondary HTN

- Common
  - Intrinsic Renal Disease
  - Renovascular Dz
  - Mineralocorticoid excess/ aldosteronism
  - ? Sleep Breathing d/o
- Uncommon
  - Pheochromocytoma
  - Glucocorticoid excess/ Cushing's dz
  - Coarctation of Aorta
  - Hyper/hypothyroidism

General Considerations

Pathophysiology:

- Renovascular hypertension is initiated by progressive kidney hypoperfusion, which activates the neuroendocrine-renin-angiotensin-aldosterone system. This leads to vasoconstriction and volume expansion.
- Angiotensin II is the primary effector of renovascular hypertension.



- Renal autoregulation fails to maintain GFR when renal perfusion pressure dips below 70-85mmHg, generally correlating with a greater than 70% renal artery stenosis.

Clinical presentation

1. Onset of hypertension before age 30 y or severe hypertension after age 55 y (class I, level of evidence [LOE] B)
2. Accelerated, resistant, or malignant hypertension (class I, LOE C)
3. Development of new azotemia or worsening renal function after administration of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (class I, LOE B)
4. Unexplained atrophic kidney or size discrepancy >1.5 cm between kidneys (class I, LOE B)
5. Sudden, unexplained pulmonary edema (class I, LOE B)
6. Unexplained renal dysfunction, including patients starting renal replacement treatment (class IIa, LOE B)
7. Multivessel coronary artery disease or peripheral arterial disease (class IIb, LOE B)
8. Unexplained congestive heart failure or refractory angina (class IIb, LOE C)

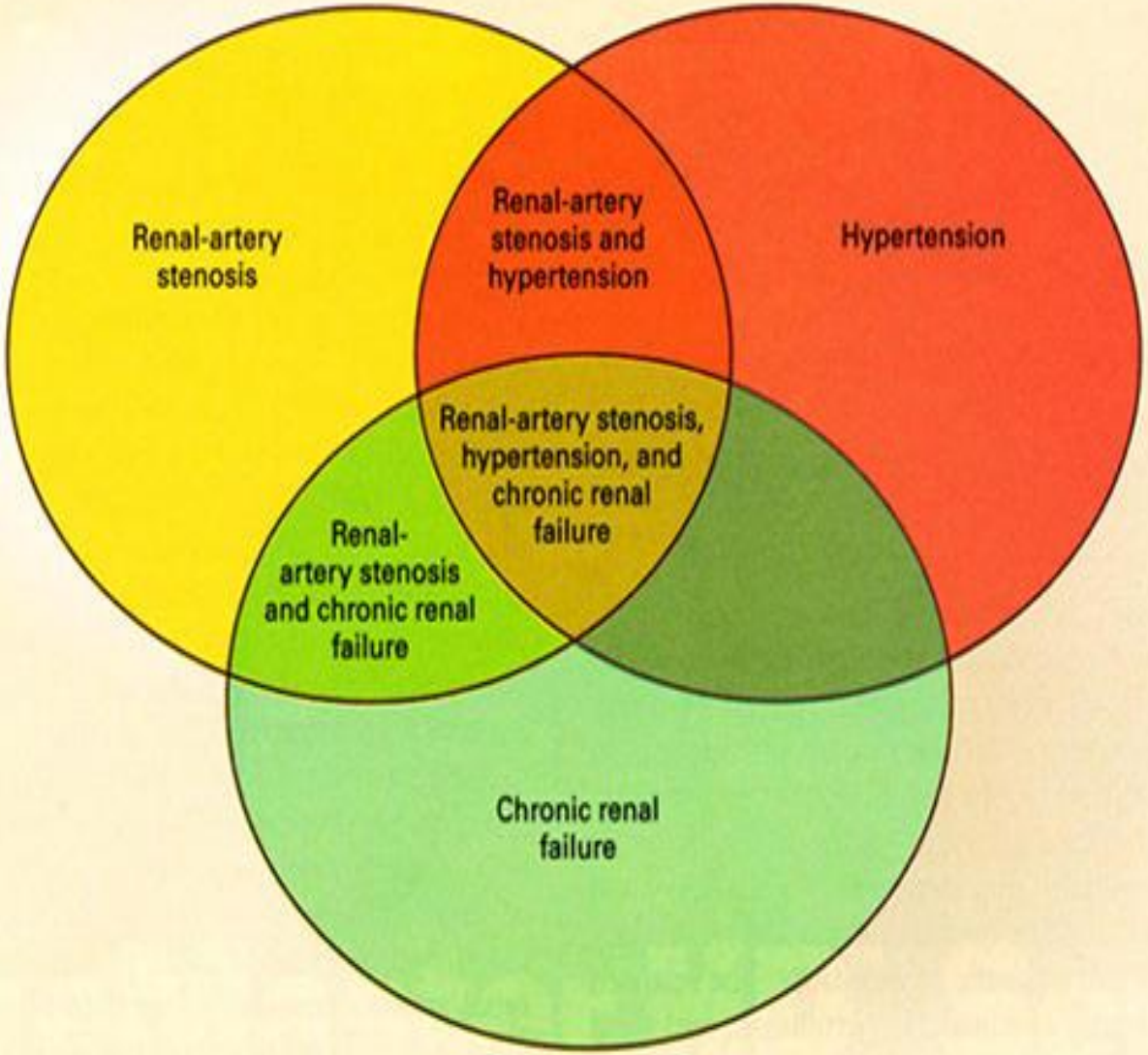
Unilateral RAS	Bilateral RAS
If a functional contralateral kidney is present, sodium retention is blunted by natriuresis from the normal kidney	Bilateral RAS or solitary kidney RAS leads to rapid volume expansion and ultimate decline in renin secretion
Renin-dependent hypertension	volume-dependent hypertension
Pressure diuresis (excess sodium and water)	No pressure diuresis
Heyperreninemia - Angiotensin II – vasoconstriction	Aldosterone induced sodium and water retention
Volume expansion avoided	HTN more dependent upon volume expansion
Renin remains high	Renin levels fall

The mechanism of elevated arterial pressure in renovascular hypertension changes over time. Though initially mediated by the effects of angiotensin II, as outlined earlier, subsequent remodeling in both the heart and resistance vessels contributes to continued pressure elevations and associated cardiovascular embarrassment.

In the end phase (Irreversible parenchymal HTN), HTN secondary to RAS does not resolve after revascularization.

Hughes et al showed that corrective surgery for unilateral RVH was successful in 78% of those with HTN of less than 5 years duration but in only 25% of those with HTN of a longer duration.

importance



- The importance of RAS is related primarily to its two major clinical manifestations: hypertension and impaired renal function
- and to their contributions to adverse cardiovascular events, dialysis dependence, and mortality

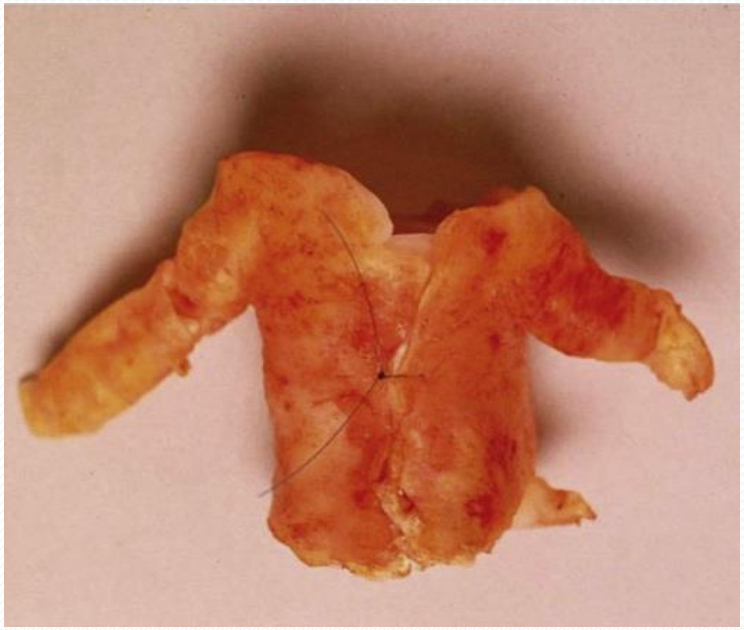
Prevalence of Anatomic Renal Artery Disease

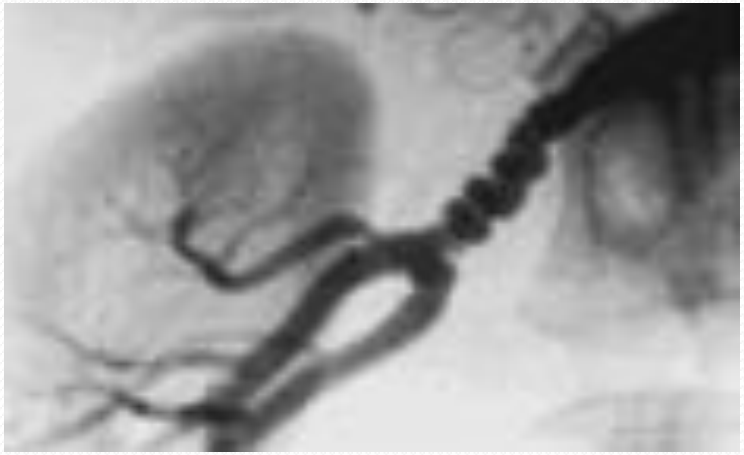
In 1964, Schwartz and White :

- The prevalence of significant stenosis was 6% in patients younger than 55 years and 40% in patients older than 75.
- Bilateral stenoses were common, found in approximately half of affected individuals.
- Atherosclerotic renal artery disease commonly involves the renal ostia, but stenoses may occur at any level within the renal arteries, including small intraparenchymal vessels

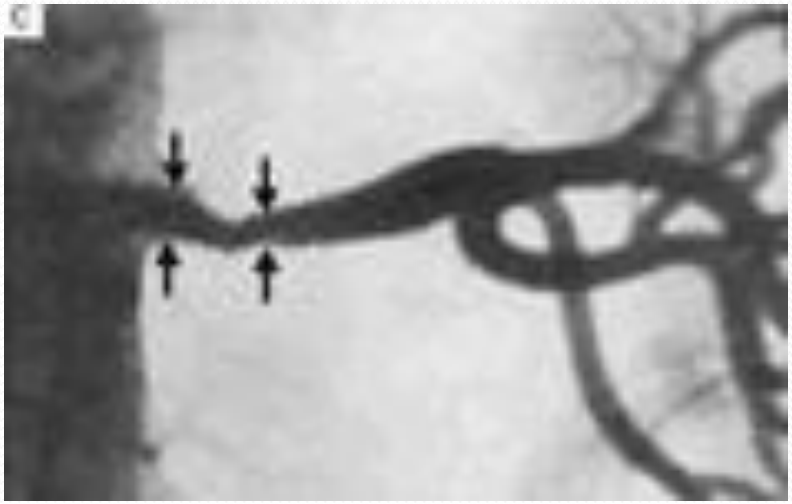
Etiology

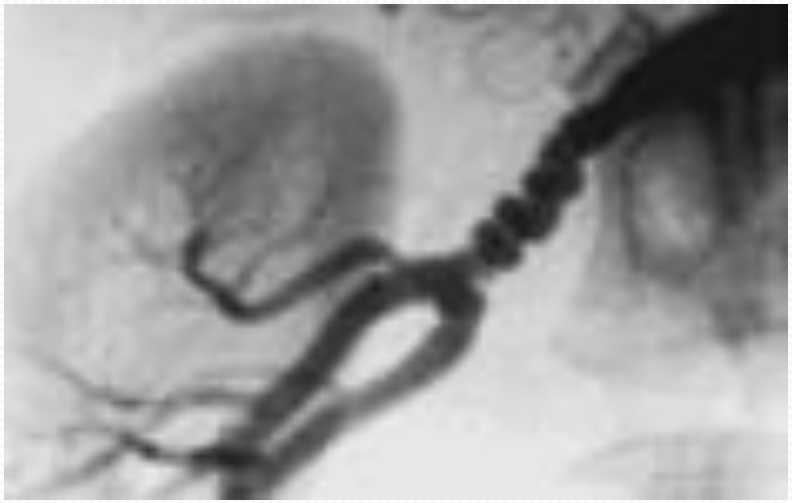
- **Atherosclerotic renal artery disease: , the most common pathology underlying renal artery disease is atherosclerosis.**
- **Other lesions affecting renal blood flow include fibromuscular dysplasia (FMD), dissection and trauma, congenital hypoplastic syndromes of the aorta and renal arteries, Takayasu's arteritis, and Post transplantation stenosis**





Atherosclerotic	Fibromuscular dysplasia
75-90% of RAS	10-25% of RAS
Usually men	Young female
age>55	age 15-40
proximal RA is the most common	often involves distal RA
PTA success 60-80% restenosis 10-47% Stent success 94-100% restenosis 11-23%	PTA success 82-100% restenosis 5-11%
"Cure" of RV HTN <30%	"Cure" of HTN in ~60%
Progression of stenosis 51%	30% progressively worsen
3-16% to occlusion	total occlusion is rare
	string of beads





History:

- In 1938, Leadbetter and Burkland, nephrectomy as a treatment for patients with hypertension and a small kidney cured only one quarter of patients with hypertension
- Freeman in 1954, transaortic bilateral renal artery thromboendarterectomy
- However, by 1960 , renal revascularization in all hypertensive patients with renal artery stenosis resulted in blood pressure benefits in less than half.

1938	Leadbetter and Burkland	nephrectomy
1954	Freeman	thromboendarterectomy
1960		renal revascularization

Risk Factors:

- The prevalence of RAS is high among patients with severe peripheral and carotid atherosclerosis (40% with peripheral arterial disease , 22% with coronary artery disease).
- Advanced age, severe hypertension refractory to multiple antihypertensive agents, and history of coexisting coronary artery or peripheral arterial disease should also raise suspicion.

Clinical Evaluation:

symptoms

- **half of individuals with anatomic renal artery disease have no associated symptoms**
- **Those with functional lesions typically present with severe hypertension, with or without reduced excretory renal function.**
- **A scenario frequently diagnostic of bilateral RAS is a patient who presents in acute renal failure upon starting treatment with an ACEI or ARB.**

Hypertension:

- Difficult-to-control hypertension despite adequate medical treatment (an optimal 3-drug regime including a diuretic in a compliant patient).
- Hypertension with renal failure or progressive renal insufficiency
- Accelerated or malignant hypertension
- Severe hypertension (diastolic blood pressure >120 mm Hg) or resistant hypertension
- Hypertension with an asymmetric kidney (>1.5 cm difference in kidney size on US).
- Paradoxical worsening of hypertension with diuretic therapy
- Onset of hypertension occurring in patients younger than 30 years or older than 50 years
- Symptoms of atherosclerotic disease elsewhere.
- Negative family history of hypertension
- Evidence of secondary hyperaldosteronism (low plasma potassium, high renin)

On examination,

- severe elevation of systolic and diastolic blood pressure,
- abdominal bruits:
  - 46% of pts with RVHT
  - 9% of pts with essential HTN
- stigmata of heart and vascular disease.
- Diminished lower extremity pulses may be present in children with coarctation or midaortic syndromes. Pulse deficits may also be found in young adults with Takayasu's arteritis or in patients presenting with aortic dissection and malperfusion.

Laboratory Findings

- elevated urea nitrogen and creatinine.
- ECG show a strain pattern with increased voltage
- Echocardiography can confirm ventricular hypertrophy with impaired diastolic relaxation.
- Plasma renin levels are rarely useful in the contemporary diagnosis of renovascular disease unless they are combined with selected invasive renal vein renin sampling.
- Measuring plasma aldosterone in patients with hypokalemia may identify those with primary hyperaldosteronism,
- Assays of urine metanephrines or serum catecholamines can identify metabolically active adrenal tumors leading to hypertension, such as Conn's disease and pheochromocytoma

DIAGNOSTIC EVALUATION

- There are two groups of diagnostic studies used to evaluate RAS:

Anatomic studies:

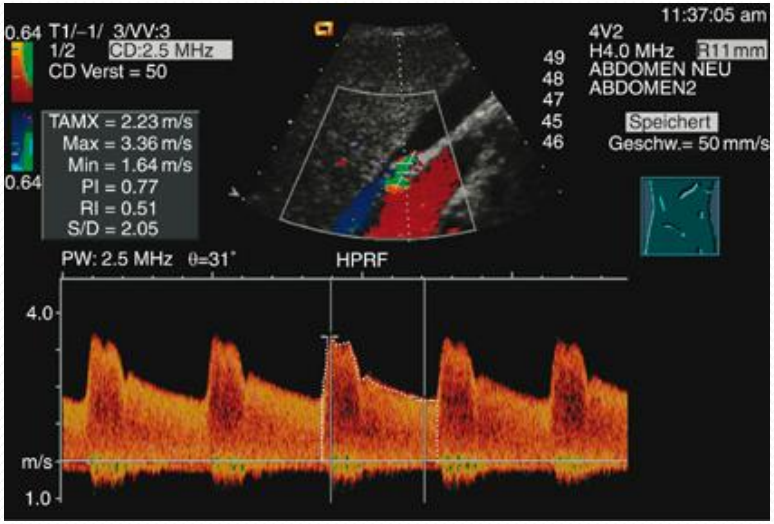
1. Duplex Ultrasonography
2. Computed Tomographic Angiography
3. MR angiography
4. Digital Subtraction Angiography(DSA)

Function studies:

1. Radionuclide Renography:
2. ACEI renography:
3. Renal Vein Renin Assays:

DIAGNOSTIC EVALUATION

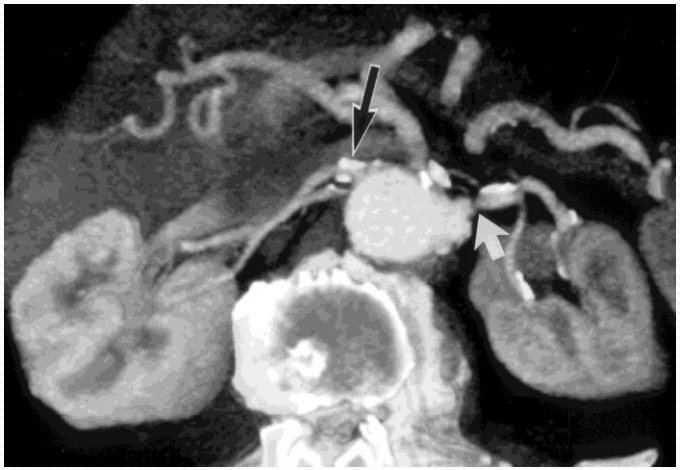
- ***Duplex Ultrasonography:***
  - the primary method of screening for renal artery disease.
  - Factors that may interfere with insonation of the renal artery include excessive bowel gas, obesity, and altered flow from advanced kidney disease.

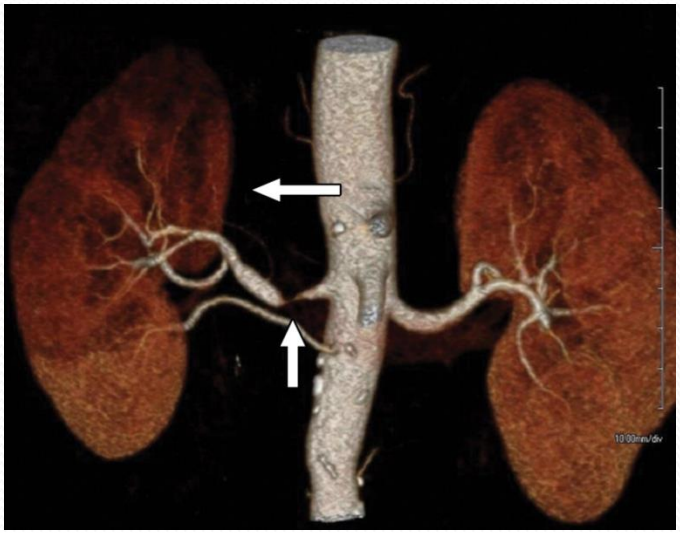


  - the accuracy of duplex ultrasonography in detecting significant RAS can exceed 90% in experienced hands. duplex ultrasonography correctly identified stenosis of greater than 60% with a sensitivity of 93%, a specificity of 98%.
  - calculate a resistive index (peak systolic velocity–end-diastolic velocity/peak systolic velocity), The resistive index has also been used to indirectly identify critical RAS. A normal value is less than 0.7. Values greater than 0.8 may indicate critical RAS

DIAGNOSTIC EVALUATION

- ***Computed Tomographic Angiography:***
- Advantages:
  - CTA is noninvasive and widely available
  - image acquisition and formatting are less technically demanding than for duplex ultrasonography or contrast-enhanced magnetic resonance angiography (MRA) of the renal arteries.
  - Sensitivity, specificity, and accuracy in defining stenosis of the main renal artery approach 100% in contemporary series.
  - The latter may help in planning surgical reconstruction of RAS by identifying locations suitable for cross-clamping and inflow sources for bypass procedures
- Disadvantages of CTA include :
  - exposure to ionizing radiation
  - iodinated contrast agents. Radiation exposure is typically greater than chest x-ray (87 to 260 fold).





DIAGNOSTIC EVALUATION

- ***Magnetic Resonance Angiography:***
- Its advantages are that
  - it is noninvasive
  - No ionizing radiation or iodinated contrast agents
  - as with CTA, data sets can be reformatted into two- or three-dimensional images.
- Magnetic resonance imaging (MRI) also has a number of limitations
  - including long scan times, which predispose to movement artifact.
  - and the tight confines of closed scanners, which may cause claustrophobia.
  - The magnetic field is disturbed by metal, so images of structures adjacent to implants (e.g., vascular stents, surgical clips, prostheses) are distorted,
  - and MRI is contraindicated in patients with implants or foreign bodies that could move in response to the magnetic force, with dire consequences (e.g., intracranial clips, cardiac pacemakers, implantable cardioverter-defibrillators, intraocular metal fragments).
  - contrast-enhanced MRA has not performed well in the setting of multiple renal arteries or in patients with FMD. motion artifact and spatial resolution limit the ability to image the middle and distal segments
  - nephrogenic systemic fibrosis. This is a scleroderma-like syndrome associated with the use of gadolinium in patients with severe renal insufficiency

DIAGNOSTIC EVALUATION

- ***Digital Subtraction Angiography(DSA)***
  - is the gold standard.
  - Its major strengths are high resolution and accuracy in defining renal artery disease
  - and its role in enabling endovascular renal reconstructions.
- Disadvantages:
  - DSA also exposes patients to ionizing radiation and nephrotoxic contrast agents;
  - it is labor intensive, requiring a team of trained specialists;
  - and it is expensive .
  - It is invasive.
  - lack the additional image information obtained with three-dimensional CTA and MRA

Diagnosis- Anatomic Studies

Diagnostic Study	***Advantages***	***Disadvantages***
Digital Subtraction Angiography: DSA	▪ Gold standard ▪ high resolution and accuracy ▪ Can visualize accessory vessels and intrarenal branches well ▪ enabling endovascular renal reconstructions	▪ ionizing radiation and nephrotoxic contrast agents ▪ Sometimes difficult to distinguish between critical and non-critical lesions ▪ Expensive & invasive ▪ lack three-dimensional images
Duplex Ultrasonography	▪ primary screening ▪ Noninvasive ▪ Inexpensive; widely available	▪ Extremely operator dependent ▪ Does not evaluate accessory vessels well ▪ Bowel gas patterns/Obesity interfere
CT angiography	▪ noninvasive &widely available ▪ less technically demanding ▪ in planning surgical reconstruction & visualization of the vessel in 3D	▪ High-contrast requirement ▪ Radiation exposure ▪ Less reliable for visualizing distal segments and small accessory arteries
MRA	▪ Noninvasive ▪ reformatted into 2d or 3d images. ▪ No ionizing radiation or iodinated contrast	▪ long scan times & claustrophobia ▪ Expensive ▪ Prior stents produce artifacts ▪ Blood flow turbulence can exaggerate measured stenosis ▪ nephrogenic systemic fibrosis

DIAGNOSTIC EVALUATION

- ***Radionuclide Renography:***
  - quantifying the uptake and excretion of specific radiolabeled molecules such as technetium 99m–labeled.
  - Abnormal uptake and excretion may localize to a kidney beyond the site of RAS, suggesting a causal relationship to loss of function
- ***ACEI renography:***
  - more commonly known as captopril renography,
  - combines renography with pharmacologic manipulation of the renin-angiotensin system.
  - in patients with documented RAS, ACEI renography is good at distinguishing between renovascular and essential hypertension and thus at identifying patients likely to benefit from revascularization
  - Captopril renal scintigraphy is no longer recommended owing to its poor sensitivity and specifcity in the presence of renal insufciency, bilateral disease, or disease in a solitary functioning kidney.
- ***Renal Vein Renin Assays:***
  - a ratio (or index) of renal vein renin to systemic renin is most useful for defining patients likely to benefit from reconstruction.
  - A ratio of 1.5 or greater is considered positive, linking ipsilateral RAS to excess renin production.
  - Of coures doesn't work in bilateral disease

Treatment:

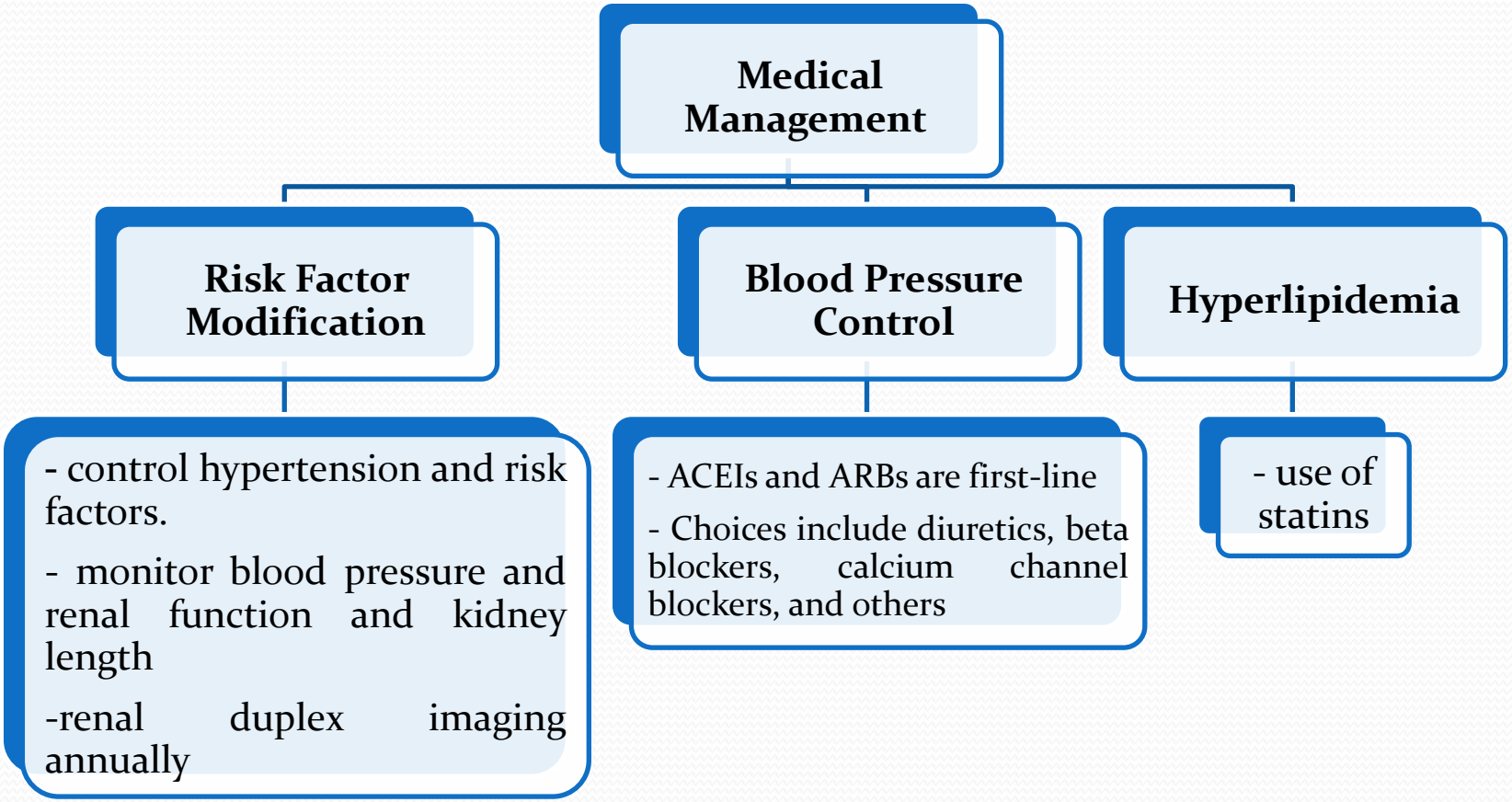
General Considerations

- In fact, no prospective randomized trial comparing renal artery reconstruction (open or endovascular) to medical management has shown improved survival, increased freedom from dialysis, or reduction in adverse cardiovascular events with intervention.

- It is important to **search for evidence of underlying irreversible parenchymal renal disease**, as this subgroup will not likely benefit from therapy.
  - **Moderate to severe protenuria**
  - **Severe renal atrophy distal to obstruction**
  - **Unilateral RAS with renal insufficiency**
  - The challenge lies in the substantial overlap between etiologic factors of aortorenal vascular disease and parenchymal kidney disease. The disease conditions that result in atherosclerotic narrowing of the renal arteries, namely diabetes mellitus, dyslipidemia, and elevated blood pressure, are also independently associated with direct kidney injury

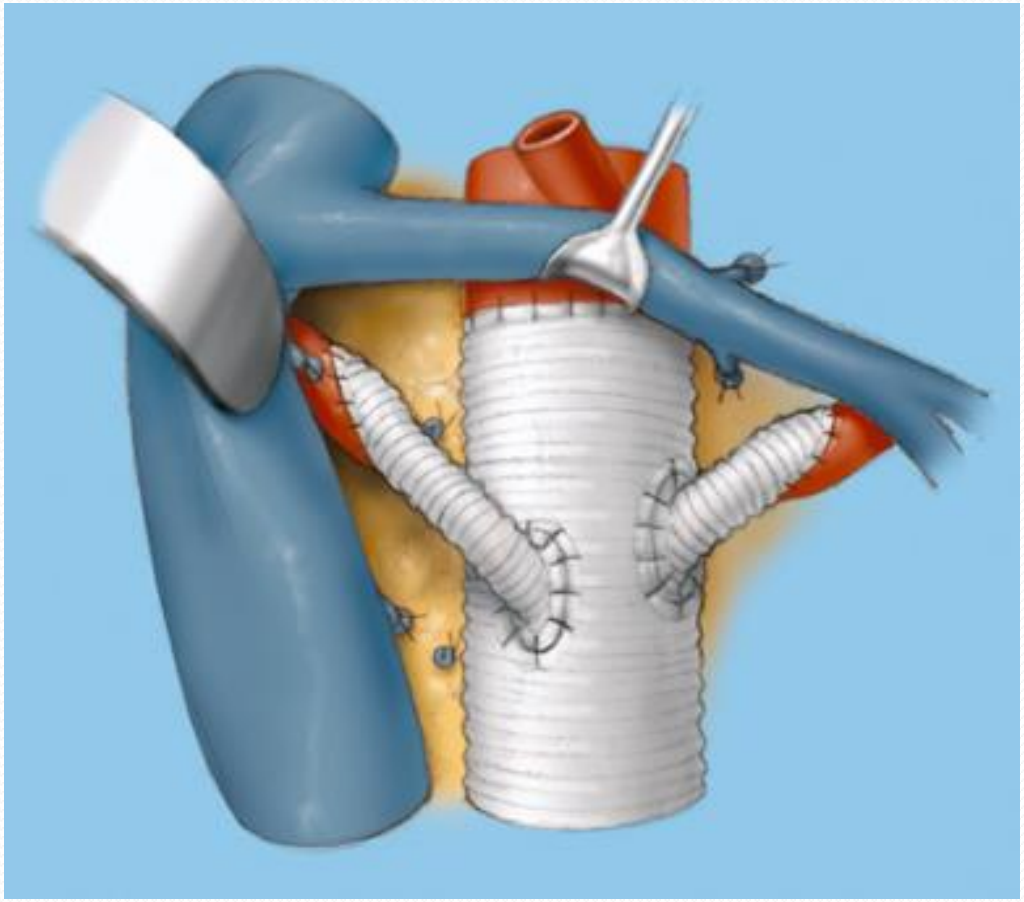
Medical Management of Renovascular Disease

- ACEI/ARB safe in unilateral RAS if careful titration and close monitoring; contraindicated in bilat RAS or solitary kidney RAS



Open Surgical Repair:

we take an aggressive approach toward the revascularization of kidneys with greater than 15% excretory function on radionuclide renography



surgery

Revasculartation

Given the relatively inferior durability of endovascular reconstructions, open surgery is advocate for:

- good-risk patients with bilateral disease

- patients undergoing concomitant aortic reconstruction for aneurysms or occlusive disease

- patients with disease in multiple ipsilateral renal arteries or branch vessels

children with congenital lesions.

- primarily in hypertensive patients with ischemic nephropathy.

Nephrectomy

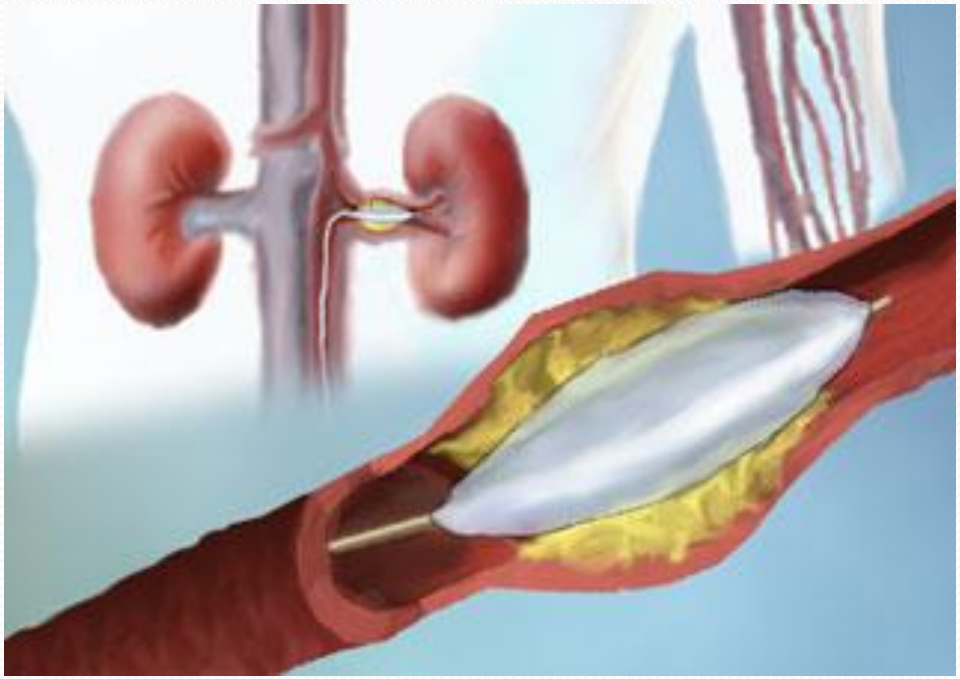
- poorly functioning kidneys

- and unreconstructable arteries

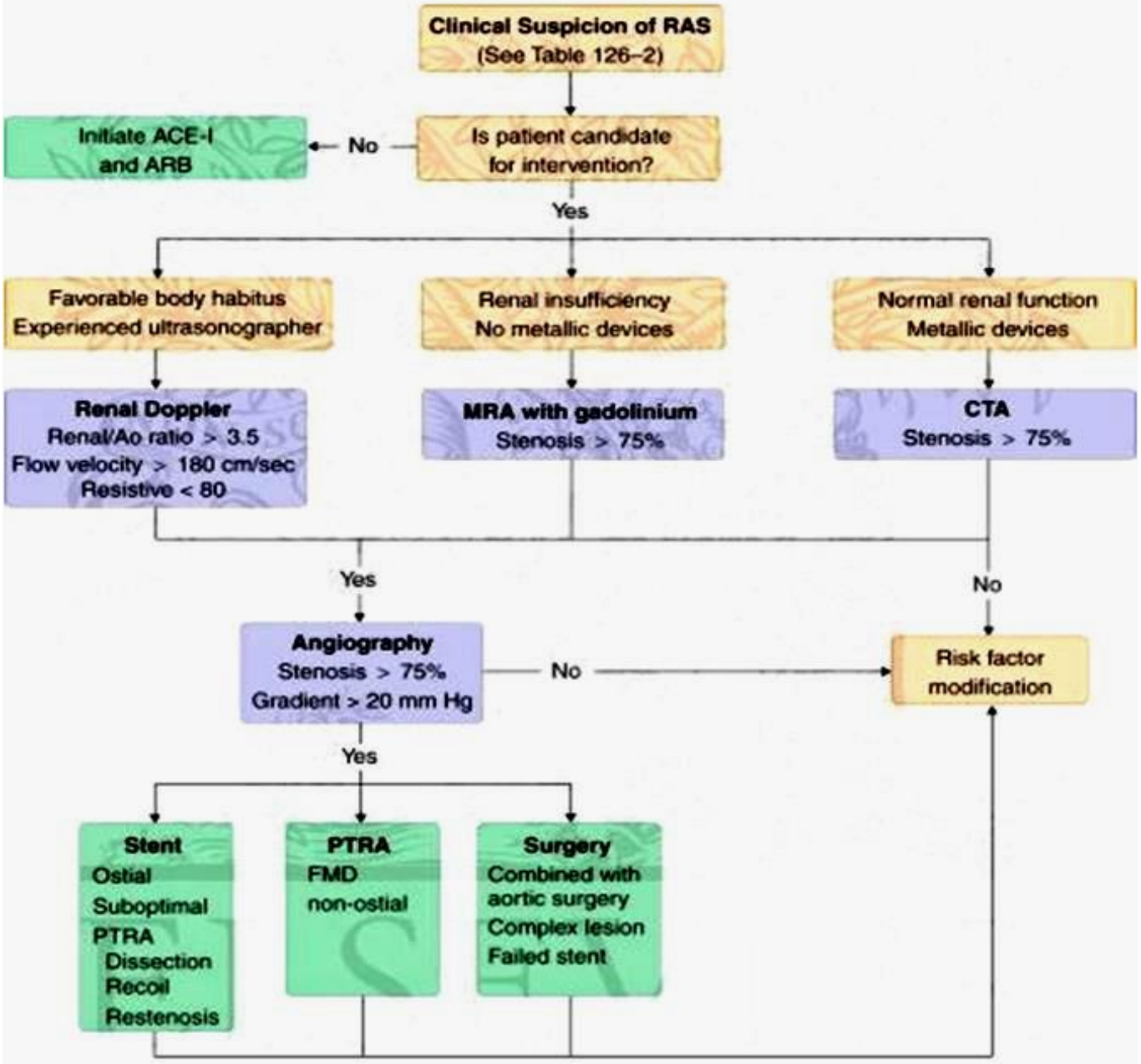
- who have failed medical management of hypertension.

Endovascular Repair

- **Given the limitations of endovascular reconstruction and the lack of a clear benefit over medical management, we generally reserve renal artery angioplasty and stenting for:**
  - **high-risk patients with severe hypertension**
  - **who have failed medical management or shown progressive loss of renal function attributable to ischemic nehropathy**



- **This plaque is typically very thick and heavily calcified, creating a rigid sheet that resists balloon dilatation. For this reason, most authorities recommend primary stenting if an endovascular repair is planned for ostial RAS.**
- **Angioplasty alone is effective at treating nonostial stenoses of the main renal artery caused by atherosclerosis or medial fibroplasia, whereas stenting has proved superior in the management of ostial lesions.**



New studies:

- Calcitriol , an active form of vitamin D, protects renovascular function in hypertension by down-regulating angiotensin II type 1 receptors and reducing oxidative stress.
- Renal nerve ablation reduces blood pressure in a patient with renovascular hypertension resistant to drug and revascularisation therapies.
- Medical therapy is best for atherosclerotic renal artery stenosis: Arguments for.
- angioplasty may result in better blood pressure control, particularly in people with bilateral disease
- Cardiovascular Outcomes with Renal Atherosclerotic Lesions (CORAL)