Renal Hypertension

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RENAL HYPERTENSION

The most common causes of secondary HTN

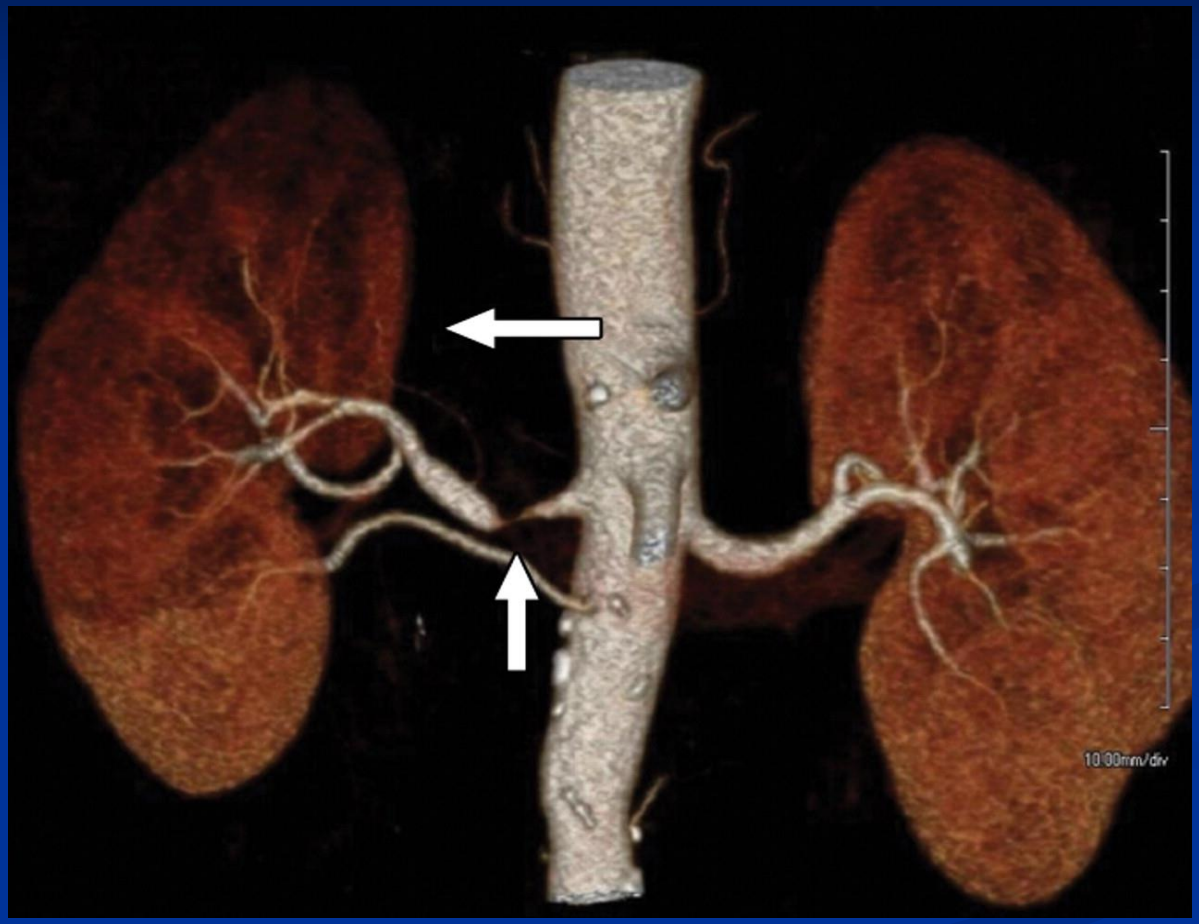
1- Renal parenchymal HTN

2- Renovascular HTN

3- Tumor induced

RENAL ARTERY STENOSIS-RENOVASCULAR HTN

Renal Artery Stenosis



Ashar Luqman, M.D

August 10, 2010

Definition

Renal artery stenosis: is the narrowing of the renal artery, **most often caused by atherosclerosis or fibromuscular dysplasia** .

This narrowing of the renal artery can impede blood flow to the target kidney.

Hypertension and atrophy of the affected kidney may result from **renal artery stenosis**, ultimately leading to renal failure if not treated

Pressure gradient of 20 mmHg across stenotic area during angiography is usually considered to be of hemodynamic significance

Epidemiology

Common Disease:	Incidence
General Population	0.1%
HTN	4.0%
HTN and suspected CAD	10-20%
Malignant HTN	20-30%
Malignant HTN and Renal Insufficiency	30-40%

Causes

- Common causes
- Atherosclerosis
- Fibromuscular dysplasia

- Less Common causes
- Vasculitis (Takayasu's arteritis)
- Dissection of the renal artery.
- Thromboembolic disease
- Renal artery aneurysm
- Renal artery coarctation
- Extrinsic compression
- Radiation injury

Fibromuscular Dysplasia

- Accounts for 10% of all cases of RAS. 90% cases involve media
- Affect females, age 15-50
- Rarely leads to renal artery occlusion
- Genetic predisposition, smoking, hormonal factors, and disorders of the vasa vasorum are possible risk factors

- Angiography:

  Site: distal renal artery

  Beaded, aneurysmal appearance

- Treatment:

  Ballon Angioplasty :

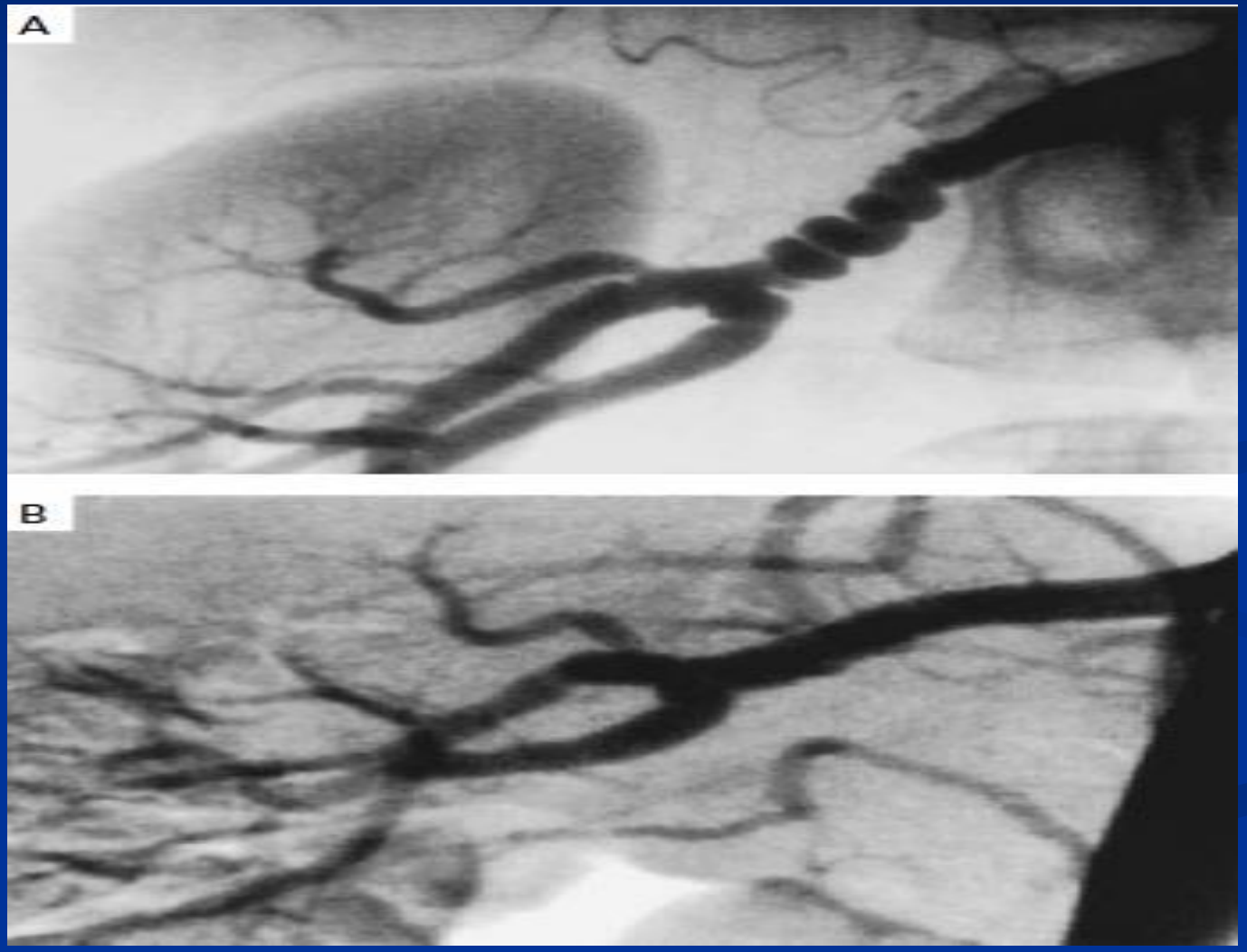
  Successful in 82-100%

  Restenosis in 10%

  Cure HTN in 60%

Safian. NEJM. 2001;344: 341-442

Fibromuscular Dysplasia



Atherosclerosis

- Accounts for >2/3rd of the cases of RAS
- Primarily affects men over the age of 45

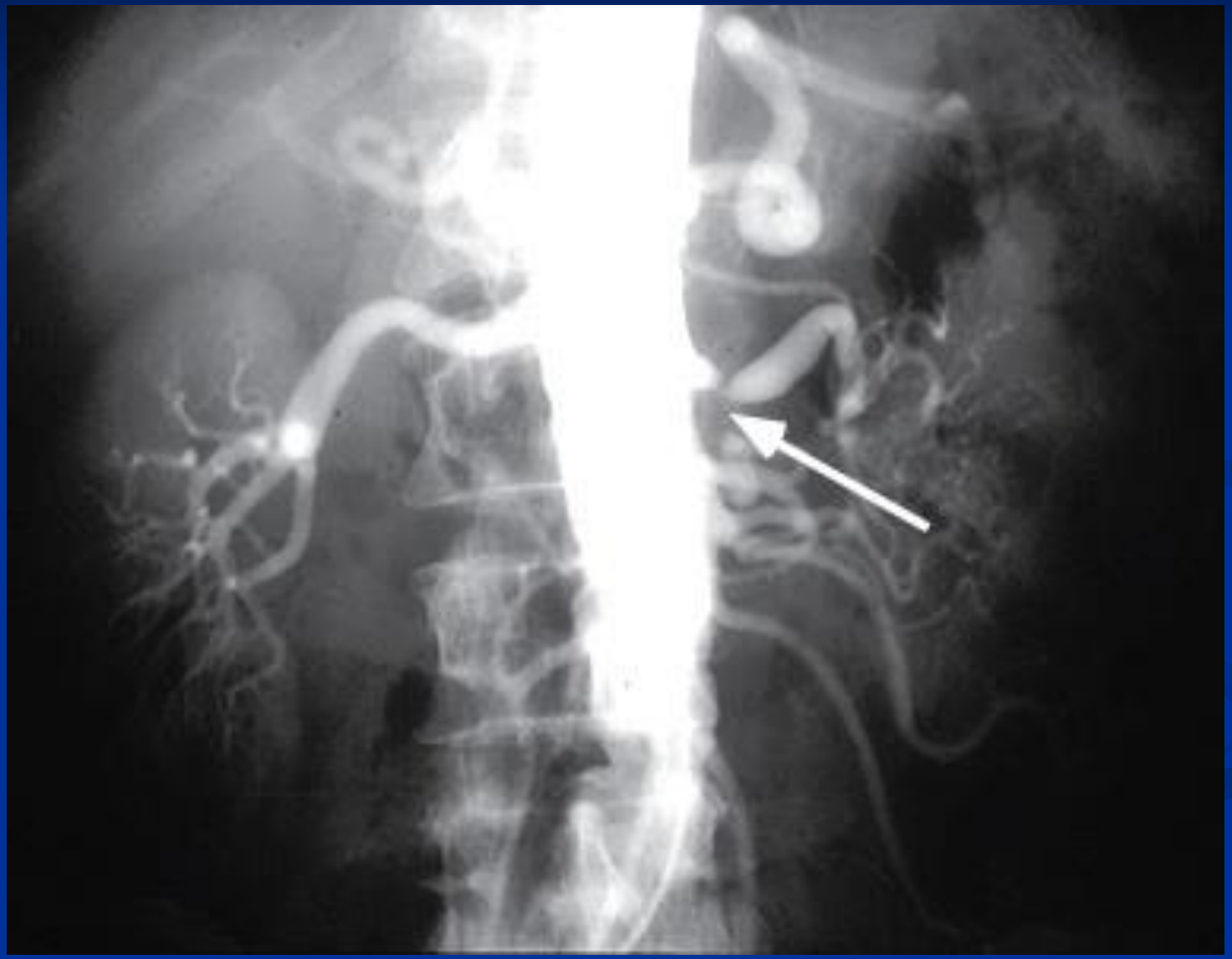
Usually involves the aortic orifice or the proximal main renal artery.

In advanced cases, segmental and diffuse intrarenal atherosclerosis may also be observed

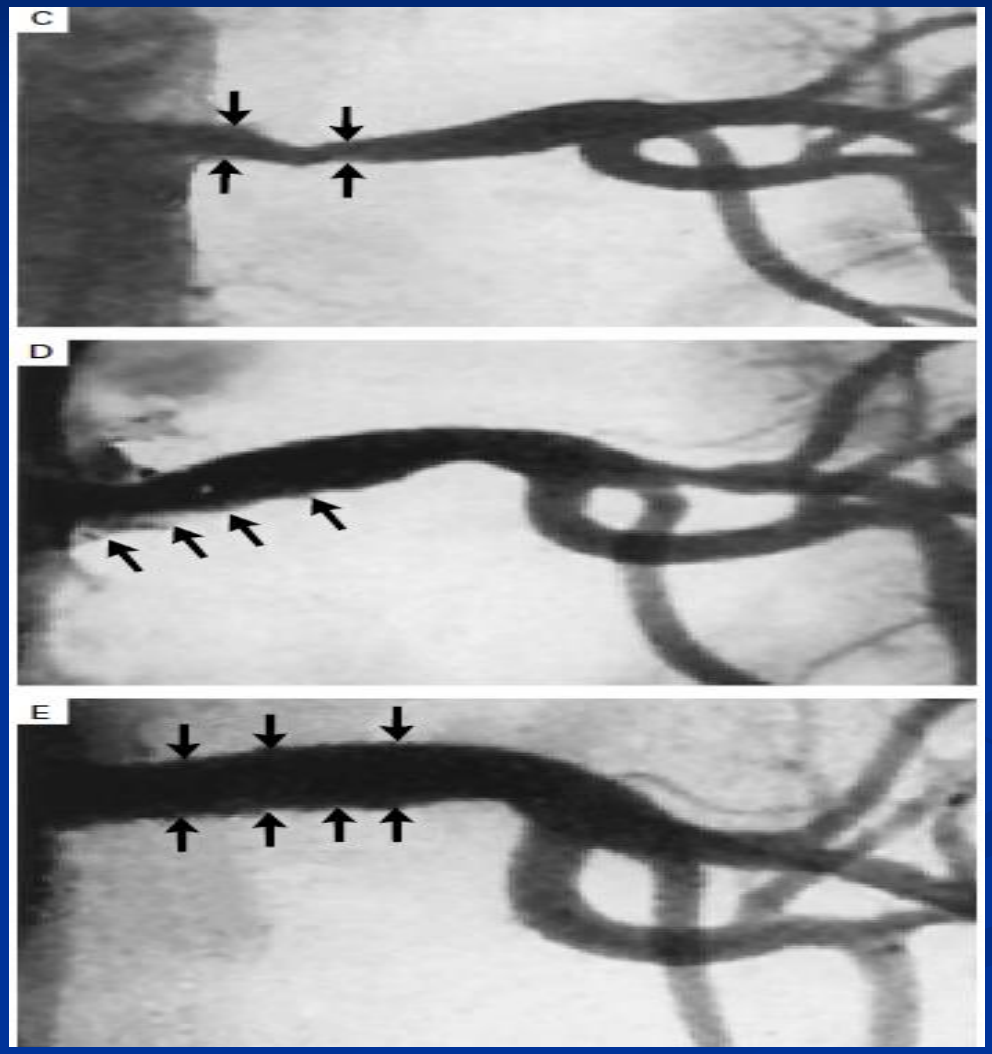
- RAS is particularly common in old patients with diffuse atherosclerosis particularly with diabetes, aortoiliac occlusive disease, CAD, or HTN but can occur as a relatively isolated renal lesion
- 51% have progressive disease, 3-16% have total occlusion and renal atrophy developed in 21% of cases with stenosis >60%

Caps MT et al Circulation 1998;98:2866

Atherosclerosis, a common cause of RAS

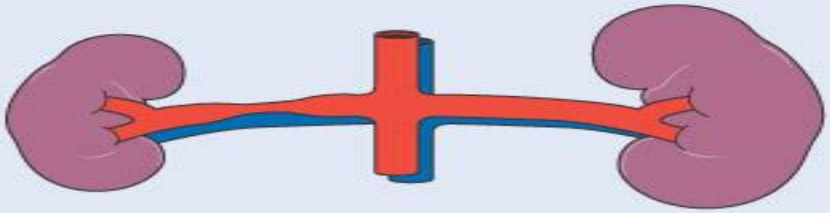


Atherosclerosis



Pathophysiology (Goldblatt model)

Unilateral renal artery stenosis



Reduced renal perfusion

↑ Renin–angiotensin system (RAS)
↑ Renin
↑ Angiotensin II
↑ Aldosterone

Angiotensin II dependent hypertension

Increased renal perfusion

Suppressed RAS

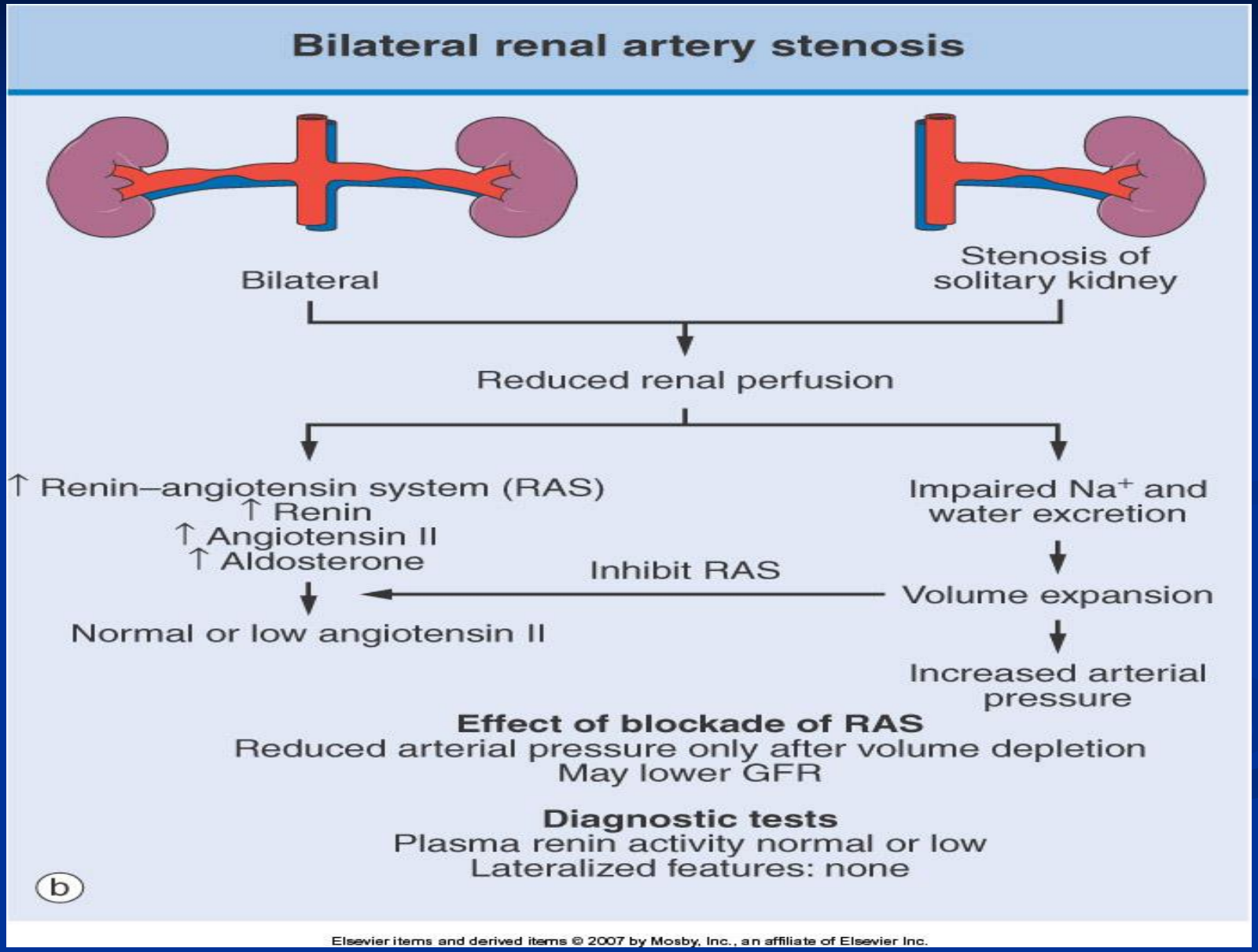
Increased Na^+ excretion (pressure natriuresis)

Effect of blockade of RAS
Reduced arterial pressure
Enhanced lateralization of diagnostic tests
Glomerular filtration rate (GFR) in stenotic kidney may fall

Diagnostic tests
Plasma renin activity elevated
Lateralized features, e.g., renin levels in renal veins, captopril-enhanced renography

(a)

Pathophysiology



Clinical Findings

- **HTN**:
- Difficult-to-control hypertension despite adequate medical treatment
- Accelerated or malignant hypertension
- Severe hypertension (diastolic blood pressure >120 mm Hg) or resistant hypertension
- Paradoxical worsening of hypertension with diuretic therapy
- Onset of hypertension occurring in patients younger than 30 years or older than 50 years
- Hypertension with an asymmetric kidney

Clinical Findings

- **Renal abnormalities**
- Unexplained azotemia (suggestive of atherosclerotic renal-artery stenosis)
- Azotemia induced by treatment with an angiotensin-converting–enzyme inhibitor
- Unilateral small kidney
- Unexplained hypokalemia

Clinical Findings

- **Other findings:**
- **Abdominal bruit, flank bruit, or both**
- **Severe retinopathy**
- **Carotid, coronary, or peripheral vascular disease**
- **Unexplained congestive heart failure or acute pulmonary edema**

Renovascular HTN and Pulmonary Edema

- **Recurrent Pumonary Edema :**
  - **HTN induced increase in after-load.**
  - **Diastolic dysfunction (LVH)**
  - **Sodium retention, with bilateral disease.**

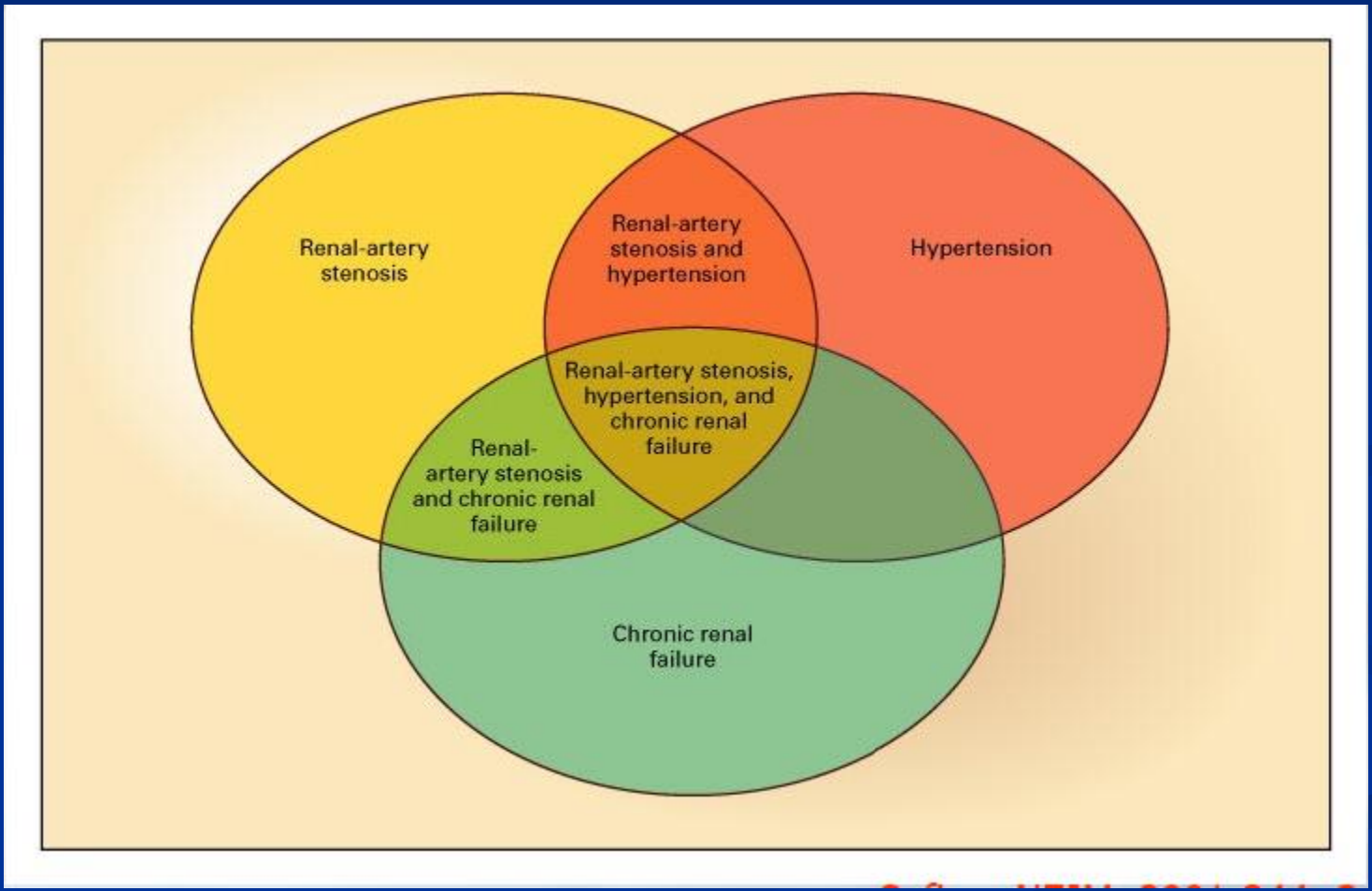
Pickering, TG, et al. Recurrent pulmonary oedema in hypertension due to bilateral renal artery stenosis: Treatment by angioplasty or surgical revascularization. Lancet 1988; 2:551.

Protienuria with RVH

- **Nephrotic range protienuria !.**
- **Regression of protienuria with correction of vascular lesion.**
- **Presence of protienuria, DOES NOT exlcude renovascular HTN.**

Chen R etal, Reversible renin mediated massive protienuria successfully treated by nephrectomy. J Urol 1995;153:133-134.

Clinical Syndromes in RAS



Renovascular HTN

- RVH: **The most common correctable cause of secondary HTN**.
- A syndrome of **elevated blood pressure, and decreased renal perfusion.**
- **Relatively Less common in blacks**.
- Incidence
  - ~ < 1% in patients with mild to moderate HTN.
  - **10-45% in patients with acute (superimposed on essential), severe, and or resistant HTN.**

Davis etal, Prevalence of renovascular hypertension in patients with grade III or IV retinopathy. N Engl J Med 1979; 301:1273

RAS and Hypertension; Possible Clinical Presentations

- **True reno-vascular HTN.**
- **Essential HTN with presence of RAS, but *not* contributing to hypertension.**
- **Essential HTN with superimposed HTN secondary to RAS.**
- **RAS with presence of renal parenchymal disease. (Ischemic CKD)**

Ischemic Renal Disease

- Critical reduction in renal blood flow to functioning renal parenchyma leading to decreased GFR, which overtime causes progressive renal injury and atrophy and thus, permanent loss of renal structural and functional integrity

- Ischemic renal disease has three anatomic variations:

1. Unilateral stenosis and occlusion in a single kidney

2. Bilateral critical renal artery stenosis or occlusion

3. Unilateral stenosis or occluison with contralateral atrophy/nonfunction

Ischemic Renal Disease

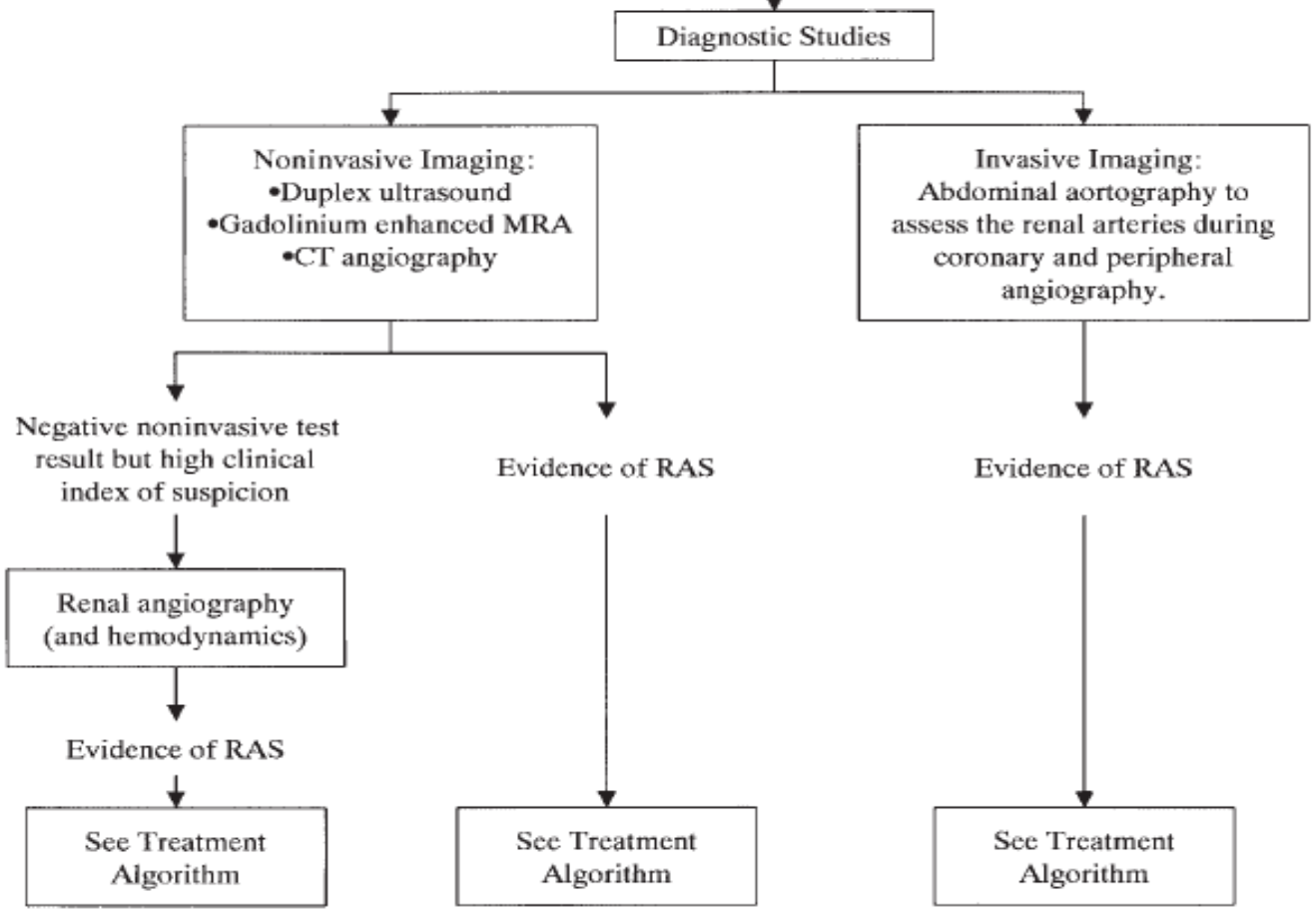
Figure 61.5 Ischemic glomerular changes. This Jones silver stain of a glomerulus demonstrates the glomerular collapse associated with wrinkling of the basement membrane characteristic of ischemia.

(Courtesy of Dr. R. Horn.)

ACA/AHA Guidelines

Clinical Clues to the Diagnosis of Renal Artery Stenosis

1. Onset of hypertension before the age of 30 years or severe hypertension after the age of 55.* (Class I; 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 ACE inhibitor or ARB agent. (Class I; LOE B)
4. Unexplained atrophic kidney or size discrepancy between kidneys of greater than 1.5 cm.† (Class I; LOE B)
5. Sudden, unexplained pulmonary edema. (Class I; LOE B)
6. Unexplained renal dysfunction, including individuals starting renal replacement therapy. (Class IIa; LOE B)
7. Multi-vessel coronary artery disease. (Class IIb; LOE B)
8. Unexplained congestive heart failure. (Class IIb; LOE C)
9. Refractory angina. (Class IIb; LOE C)



Screening And Diagnostic tests for Renal Artery Stenosis

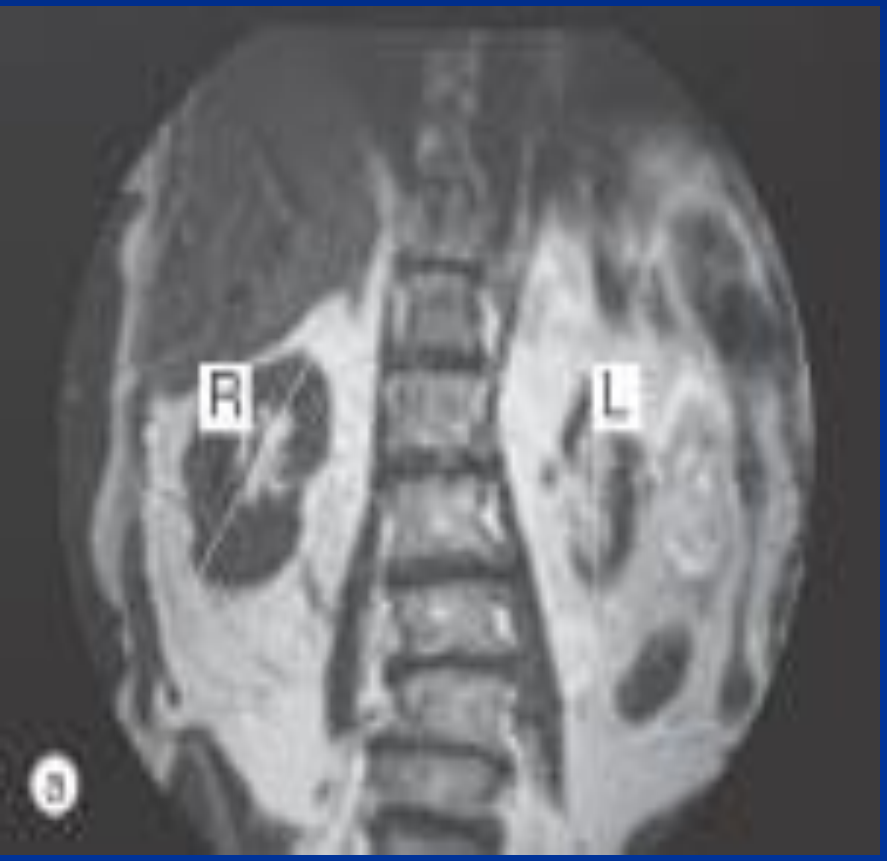
- Renal Arteriogram
  - **Gold standard.**

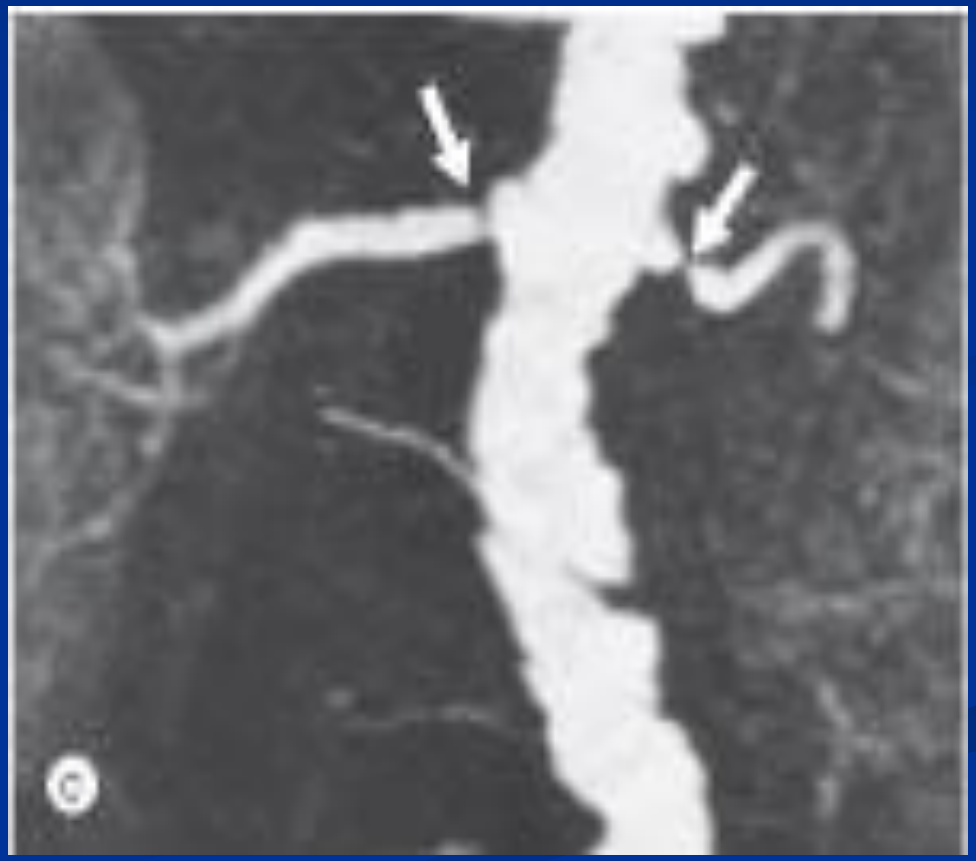
- **Non Invasive Tests of Choice:** **depends on patient factors/ availability/ expertise.**
  - **MRA**
  - **CT Angiogram**
  - **Duplex Doppler ultrasound.**

MRA in Renal Artery Stenosis

- Mainly for suspected atherosclerotic lesions.
- Non invasive, good for proximal lesions.
- Low Sensitivity for fibromuscular Disease.
- Caution with GFR <30 ml/min.
  - Nephrogenic systemic Fibrosis: potentially fatal.

MRA in Renal Artery Stenosis





MRA and Renal Artery Stenosis

Postma, CT etal *Magnetic resonance angiography has a high reliability in the detection of renal artery stenosis. Am J Hypertens 1997; 10:957.*

- Compared MR vs Digital substraction arteriography.
- N 37
- MR had 100% sensitivity, 96 % specificity .
- Missed 9/12 accessory renal arteries.

Vasbinder, et al. *Accuracy of computed tomographic angiography and magnetic resonance angiography for diagnosing renal artery stenosis. Ann Intern Med 2004; 141:674.*

- 350 patients; compared MR / CTA/ DSA
- 20% patients had RAS.
- Sensitivity of MRA was 62% and spec. 84%
- Study limitations. 36% Patients had FMD, large no. of patients without high clinical suspicion.
- MR has limited utility in FMD (22 % sensitivity. 96% specificity.)

Spiral CT with CT Angiogram:

- Non-Invasive, highly accurate, lower risk than Digital Substraction Arteriography .
- Nephrotoxic potential.
- Better for atherosclerotic lesions, lower sensitivity In FMD ~ *28%.*

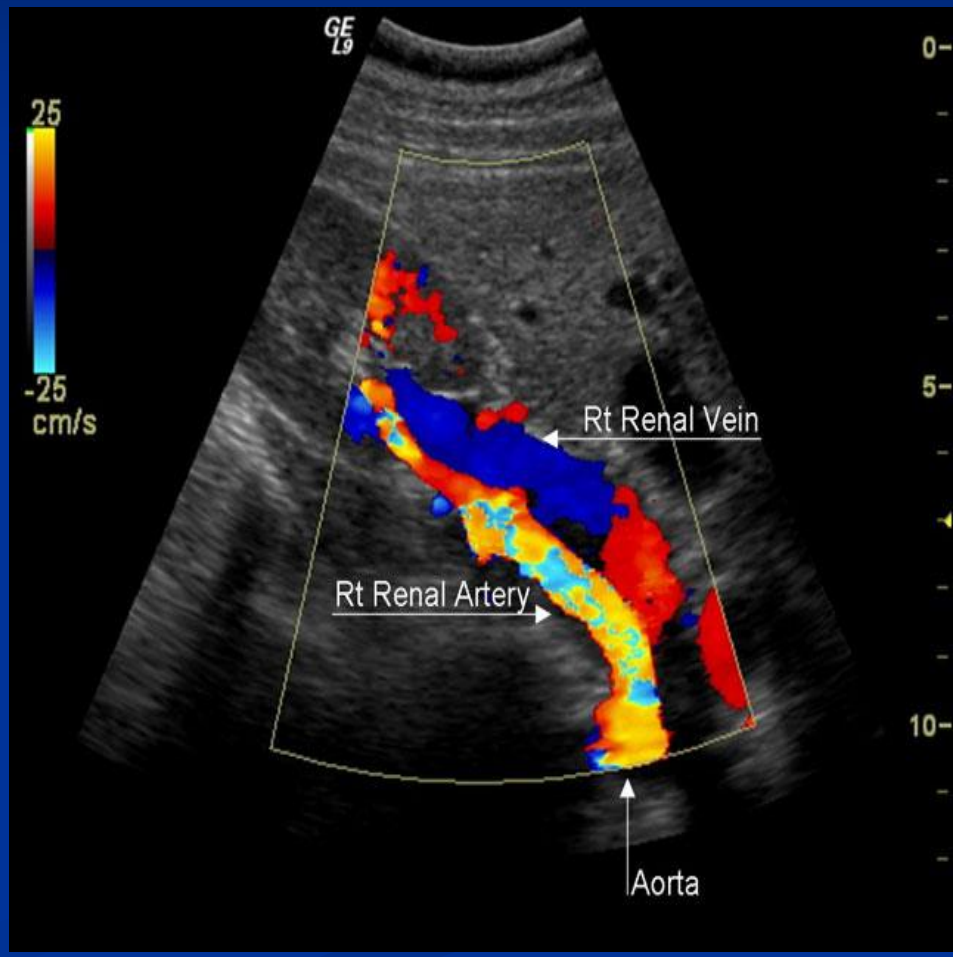
- ***Kim, et al.*** *Renal artery evaluation: comparison of spiral CT angiography to intra-arterial DSA. J Vasc Interv Radiol 1998; 9:553.*
  - N 50
- **CTA demonstrated 27 of 28 accessory renal arteries (detection rate = 96%).**
- **For the detection of stenoses greater than 50% (37 of 127 renal arteries, at 40 sites), the sensitivity and specificity of CTA were 90% and 97%, respectively.**
- **For the detection of stenoses greater than 50% in the main renal arteries (32 of 99 main renal arteries, at 32 sites), the sensitivity and specificity of CTA were 100% and 97%, respectively.**
- **Conclusion: CTA is a reliable and accurate screening modality for the evaluation of renal arteries in patients with suspected renovascular hypertension and in potential renal donors.**

- ***Olbricht, et al.*** *Minimally invasive diagnosis of renal artery stenosis by spiral computed tomography angiography. Kidney Int 1995; 48:1332*
  - N 62, spiral CT with Angiogram compared with arteriogram.
  - **98% sensitive. 94 %specific.**

Duplex Doppler Ultrasound

- Non Invasive, can detect bilateral disease/ recurrent and or re-stenosis.
- Anatomic and functional assessment of renal arteries.

  Compares systolic flow velocity of renal artery to aorta.
- Highly operator dependant/ time consuming .
- Measurement of peak systolic velocity 85% sensitive and 92% specific.



Williams, GJ, et al. *Comparative accuracy of renal duplex sonographic parameters in the diagnosis of renal artery stenosis: paired and unpaired analysis*. AJR Am J Roentgenol 2007; 188:798.

Comparing Non invasive tests

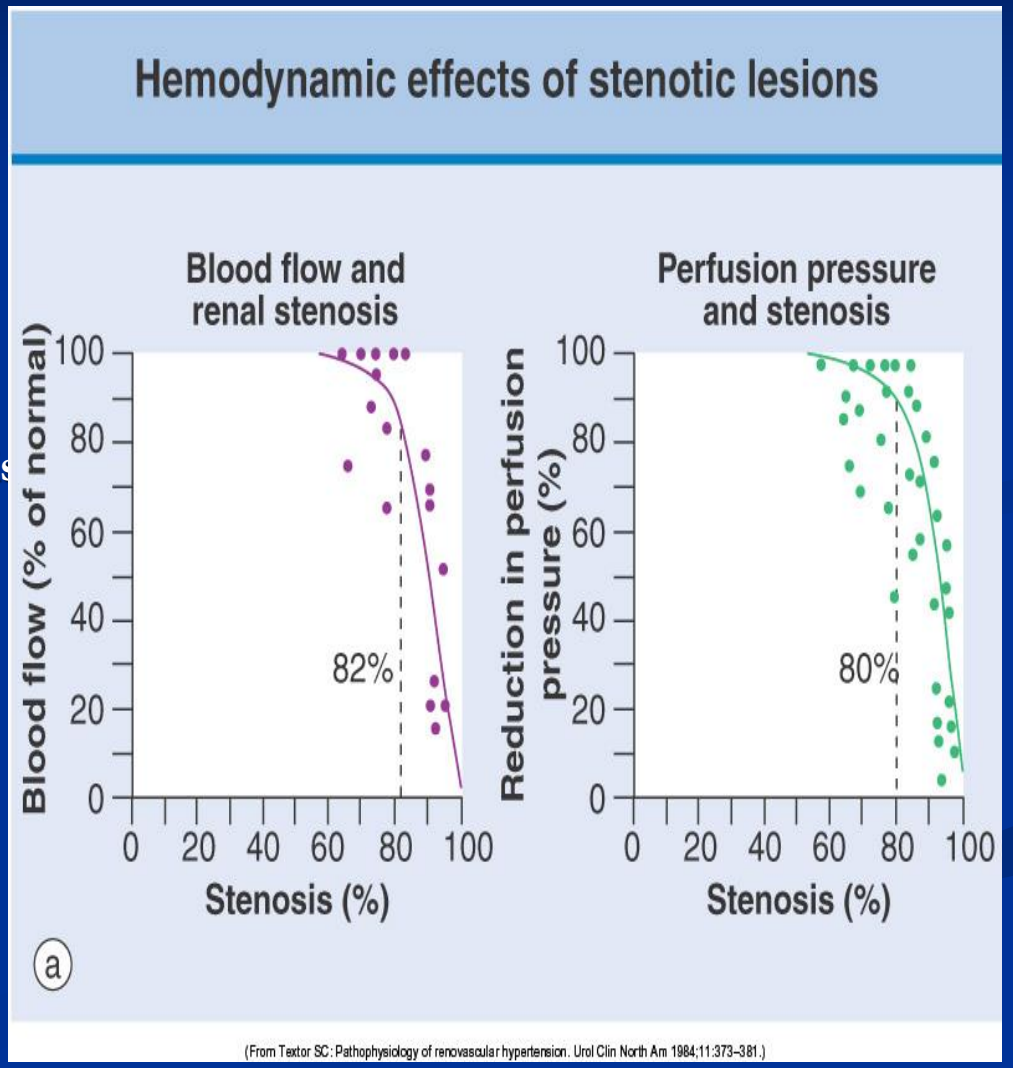
Table 1: Average of test characteristics for noninvasive diagnosis of atherosclerotic renal artery stenosis					
Test	No. of studies	Sensitivity	Specificity	Positive predictive value	False-positive rate
CTA	8	92% (64-100%)	90% (56-99%)	88% (68-98%)	10% (1-44%)
MRA	10	88% (62-100%)	80% (67-98%)	76% (49-93%)	20% (2-33%)
RDS	21	85% (50-95%)	92% (73-97%)	84% (29-94%)	8% (3-27%)

CLINICAL SIGNIFICANCE OF STENOTIC LESIONS.

Clinical history is important.

>75% Occlusion of 1 or both arteries on arteriogram is diagnostic.

50% stenosis with post-stenotic dilatation is suggestive of RVH.

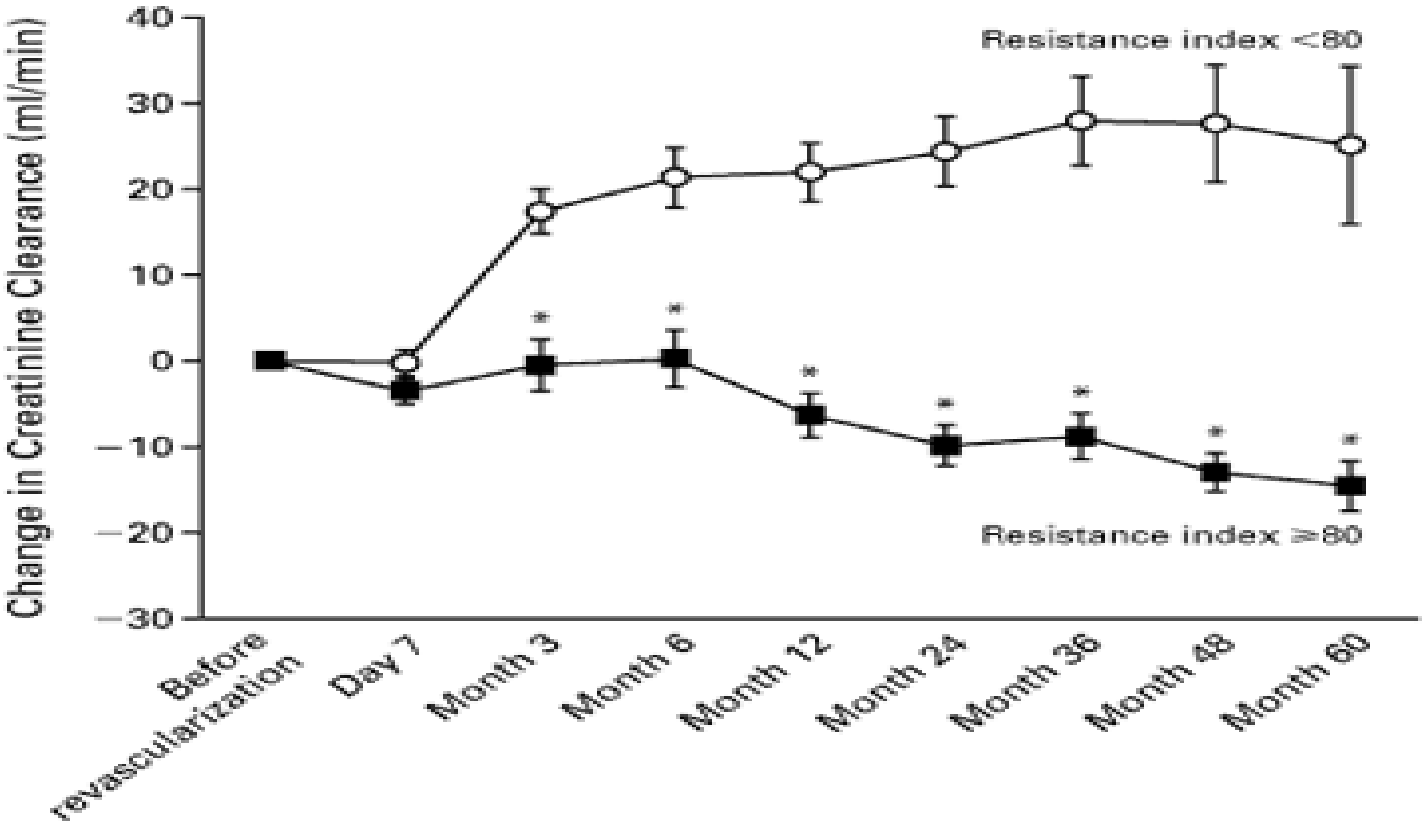


Predicting outcomes of the revascularization

- **Resistive Index:**
  - **Patients with resistive index >0.8**
    - **80% had decline in renal function**
    - **50% dialysis dependant**
    - **Only 1 patient had > 10mmhg reduction in BP.**
  - ***Patients with RI < 0.8***
    - **94 % had significant reduction in BP.**
    - **3% had decline in renal function**

Radermacher, J, et al. Use of Doppler ultrasonography to predict the outcome of therapy for renal-artery stenosis. ***N Engl J Med 2001; 344:410.***

Predicting outcomes of the revascularization

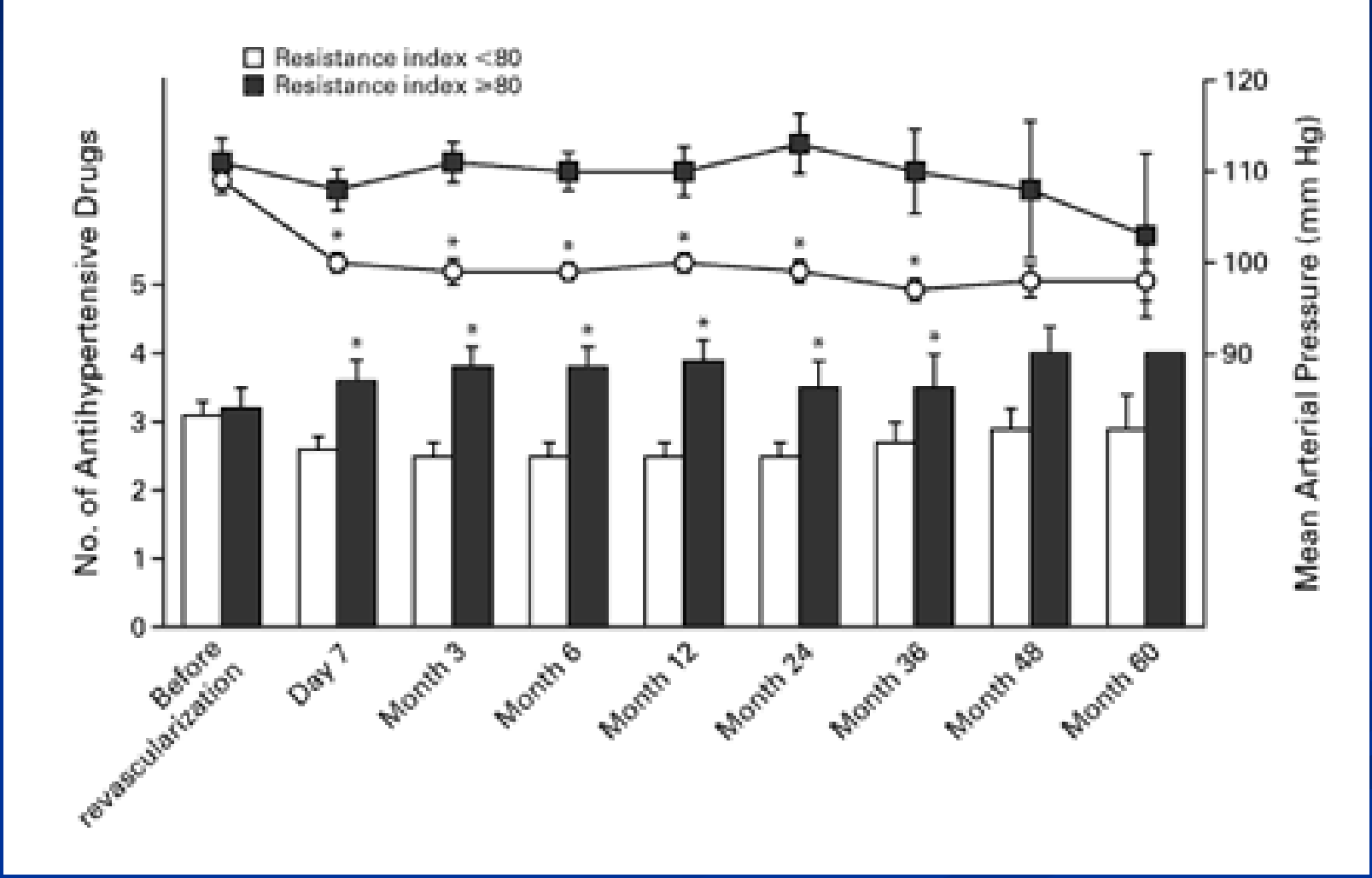


No. with Follow-up Data

Resistance index <80	96	96	95	83	73	59	43	34	21
Resistance index ≥80	35	35	33	31	26	21	16	8	5

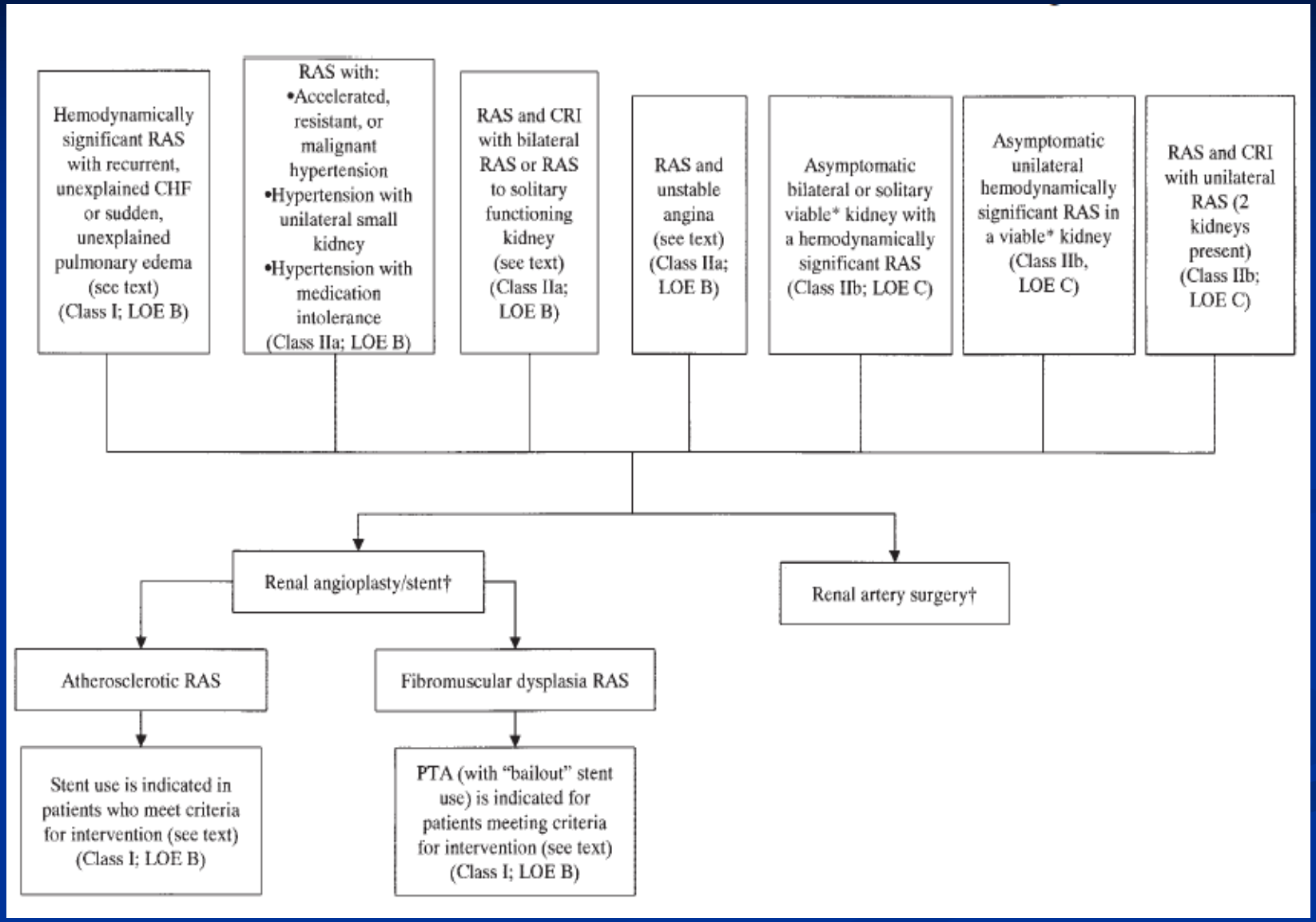
Radermacher, J, et al. Use of Doppler ultrasonography to predict the outcome of therapy for renal-artery stenosis. ***N Engl J Med 2001; 344:410.***

Predicting outcomes of the revascularization



Radermacher, J, et al. Use of Doppler ultrasonography to predict the outcome of therapy for renal-artery stenosis. ***N Engl J Med 2001; 344:410.***

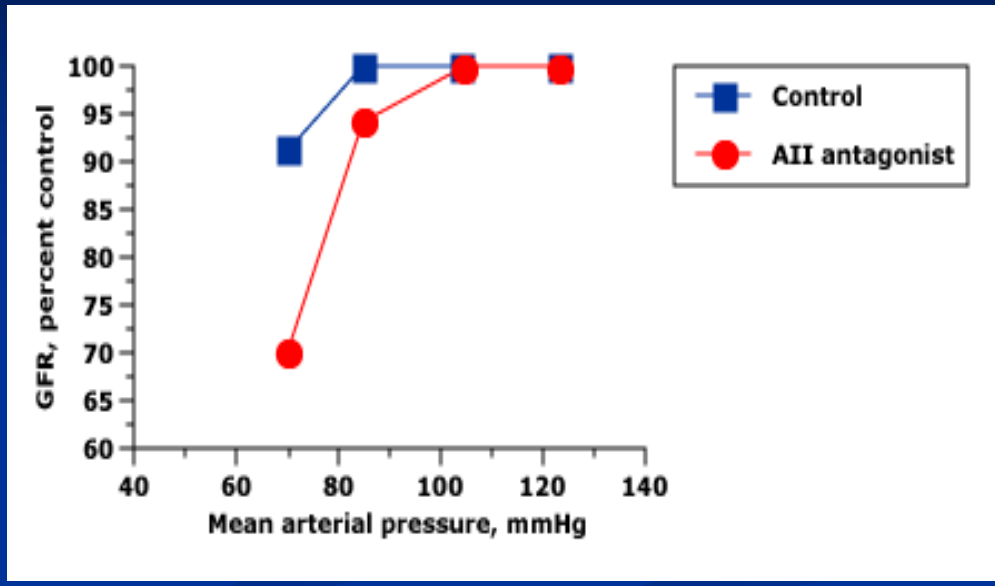
Treatment



Recommendations are based on 2005 ACC/AHA guidelines for peripheral arterial disease.

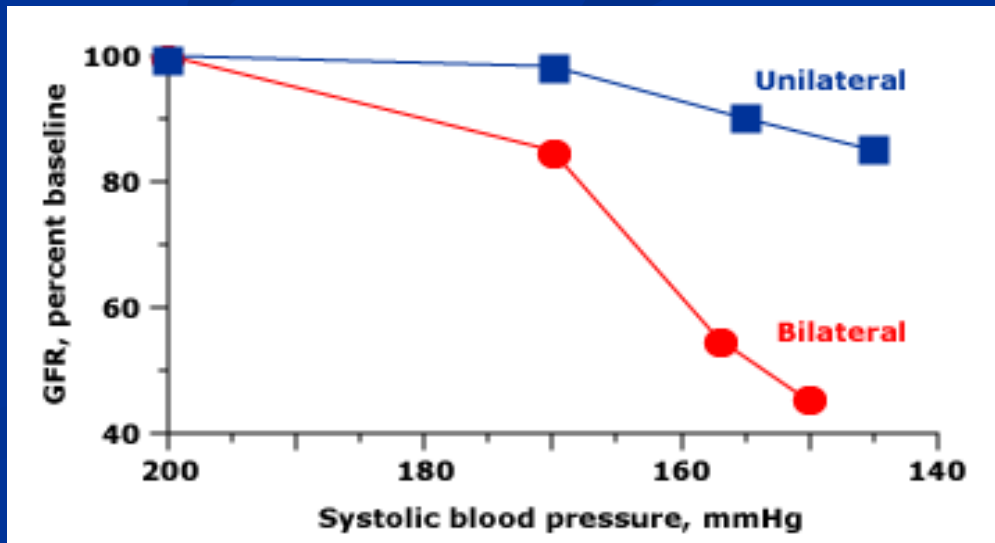
Medical Therapy

- Optimal medical therapy in recent randomized trials has included aggressive blood pressure (BP) control with multiple agents, lipid lowering therapy with a statin, antiplatelet agents and smoking cessation
- ACE-I, CCB, BB (Level of evidence A)
- ARB (Level of Evidence B)



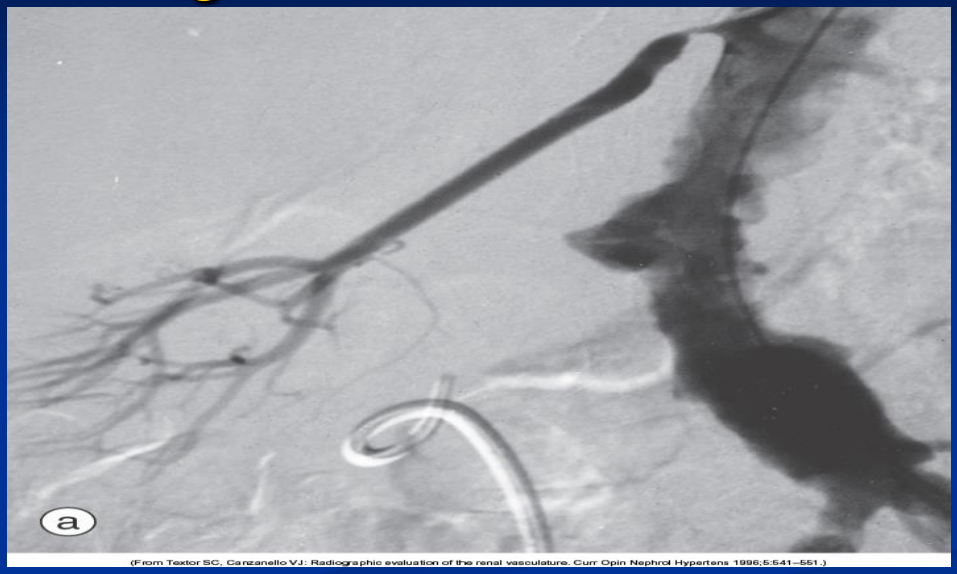
- Concern with ACE-I
  - Reduction In GFR.
  - Usually minimal elevation in SCr., only 5-10% have larger increase
- Severe bilateral disease:

  Marked reduction in GFR with ANY HTN agent. --→ intervention recommended

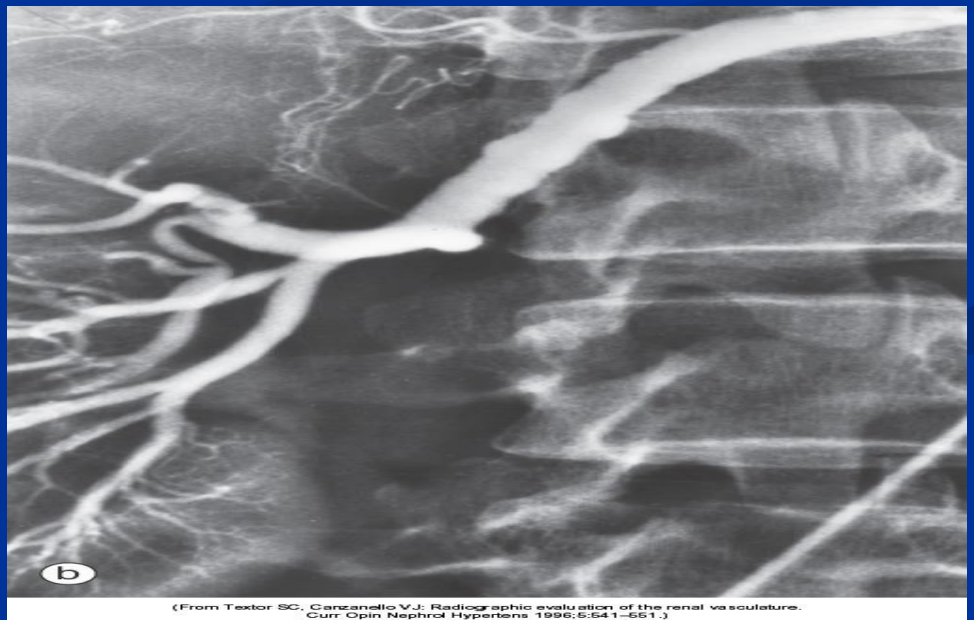


PTRA and Stenting for RAS

- *2005 ACC/AHA Guidelines:*
  - Stenting Ostial lesions.(patients meeting criteria for intervention)
  - Balloon angioplasty alone for FMD (with bailout stent , if necessary)



(From Textor SC, Canzanello VJ: Radiographic evaluation of the renal vasculature. Curr Opin Nephrol Hypertens 1996;5:541–551.)



(From Textor SC, Canzanello VJ: Radiographic evaluation of the renal vasculature. Curr Opin Nephrol Hypertens 1996;5:541–551.)

PTRA and Stenting for RAS

- Angioplasty alone is less successful.
- Meta-analysis of 24 studies comapring Angioplasty vs stent placenment at 6-29 months

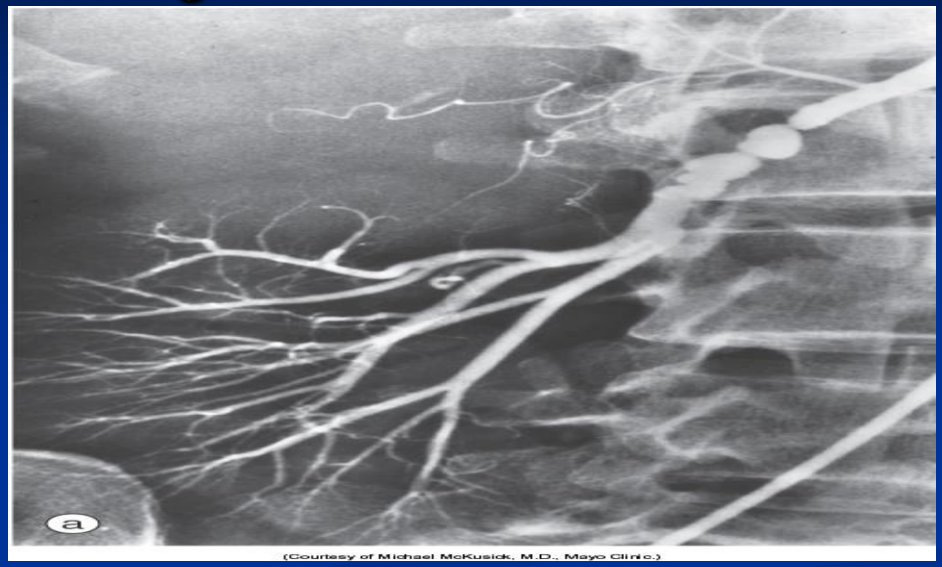
  Restenosis: 26% VS 17%

  Tech. success: 77% vs 98%

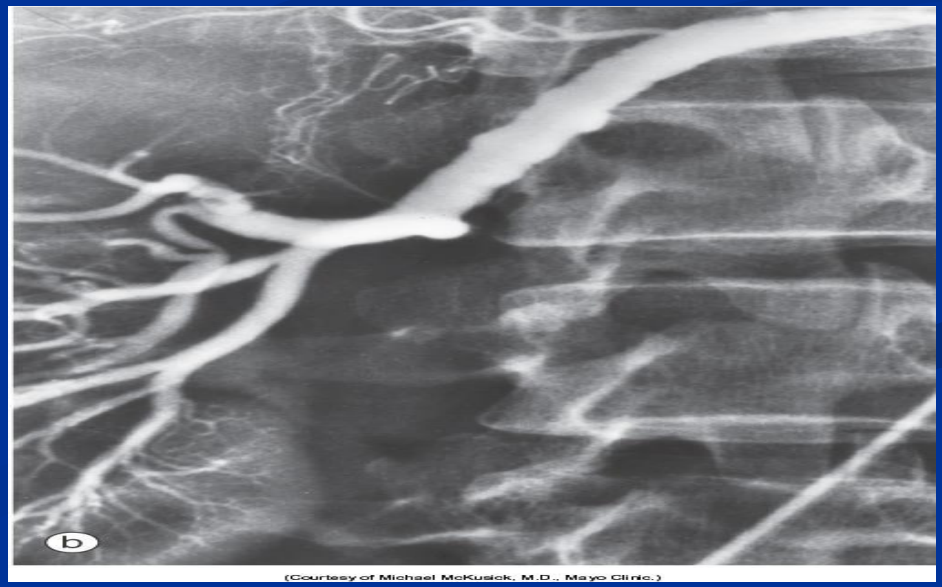
- Small non randomized studies shown benefit for
  - BP control and improvement in renal function
  - However those studies were not well powered

Highly Effective in Ostial lesions.

- 65-80% success rate. 11-17% re-stenosis.



(Courtesy of Michael McKusick, M.D., Mayo Clinic.)



(Courtesy of Michael McKusick, M.D., Mayo Clinic.)

Surgical Revascularization

- Surgical Revascularization :
  - Bilateral Repair, unilateral repair with contralateral nephrectomy of non functioning , atrophic kidney.
  - 70-90% cure rate reported.
  - 3-6% mortality.
  - Indications:
    Aortic Reconstruction
    (Aneurysm, aorto-iliac occlusive disease)
    Multiple small renal arteries.

Outcome %	FMD N 575	ASRD N 631
Cured	62	37
Improved	26	46
Cured/+ Improved	89	84
Failure	10	15

Stanley JC, Surgical Treatment of renovascular hypertension. Am J Surg 1997;174:102-110)

Renal parenchymal HTN

Renal parenchymal hypertension: is a form of **secondary hypertension** caused **by kidney disease**. It may occur in the course of **glomerulonephritis, diabetic nephropathy (diabetic kidney disease), systemic connective tissue diseases (systemic lupus erythematosus, systemic sclerosis, systemic vasculitis), tubulointerstitial nephritis, obstructive nephropathy, polycystic kidney disease, reflux nephropathy, large solitary kidney cysts (rare), postirradiation nephropathy, hypoplastic kidney, renal tuberculosis** (rare).

The main mechanisms leading to hypertension in chronic kidney disease (CKD) include

1-**impaired urinary sodium and water excretion (impaired pressure natriuresis);**

2- **excessive kidney release of vasoconstrictors** (angiotensin II and endothelin 1);

3- **vasodilator deficiency** (eg, NO);

4-**sympathetic activation;**

5- **endocrine and metabolic disturbances** (including calcium/phosphate metabolism).

The accelerated development of atherosclerosis and calcification of the vascular wall leads to an increased stiffness of the walls of large arteries.

Sodium and water retention with subsequent volume overload increase with progression of kidney disease.

An increase in venous return and cardiac output causes sympathetic activation, which results in increased vasoconstriction of the resistance vessels and an **increase in peripheral vascular resistance.**

Hypertension often develops at an early stage of kidney disease, when the glomerular filtration rate (GFR) is only slightly reduced (it may be the presenting feature). Sodium and water retention manifest as peripheral edemas only in some patients. **Untreated hypertension accelerates the progression of kidney disease and may itself be a cause of (hypertensive) nephropathy.**

Kidney diseases are the most common causes of treatment-resistant and malignant hypertension.

Diagnostic tests

Perform the same diagnostic tests as in all patients with hypertension (see Essential Hypertension) as well as studies necessary for the diagnosis of the kidney disease responsible for the hypertension. **Note that there may be other contributors to hypertension in patients with renal parenchymal disease, including renovascular disease and drug therapy (erythropoietin-stimulating agents, calcineurin inhibitors). Consider also unrecognized nonsteroidal anti-inflammatory drug (NSAID) use as a potential contributor to both hypertension and CKD.**

Kidney tumors and hypertension

Renal cell carcinoma may also be associated with a range of paraneoplastic manifestations of which hypertension may be a particularly common entity, occurring in 20%–40% of all cases; however, the prevalence of essential hypertension is such that many of these cases may be confounded by a simple association rather ...

Renin-producing tumors, such as renin-secreting RCCs and juxtaglomerular cell tumors (JXG), can autonomously secrete renin, leading to activation of the systemic renin-angiotensin-aldosterone system (RAAS) and subsequent hypertension.

Additionally, RCC may cause hypertension through a mass effect, compromising renal perfusion pressure and indirectly activating the0 RAAS.

In rare cases, tumors containing adrenal tissue may produce renin, aldosterone, or sex steroids, contributing to hypertension or adrenogenital syndromes.

Questions?