Challenges in the Diagnosis and Treatment of Renovascular Hypertension

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Definition of Renovascular Disease

- **Renal artery stenosis is defined as narrowing of the one or both of renal arteries.**
- **Atherosclerosis or fibromuscular dysplasia are the most common etiologies.**
- **Complications of renal artery stenosis are:**
  - **Side effects of severe hypertension including CKD & ESRD.**
  - **Progression of unilateral stenosis of renal artery will lead to kidney loss, but well controlled BP.**

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New Studies of Treatment

- New studies of interventions for treating RVH doesn't show benefit.
- Several prospective, randomized trials for RVH secondary to atherosclerotic disease failed to demonstrate that renal revascularization is more effective than medical therapy.
- On the basis of the clinical experience of hypertension centers, specialists have continued selective revascularization, without a summary statement by a major, multidisciplinary, national organization that identifies specific populations that may benefit.

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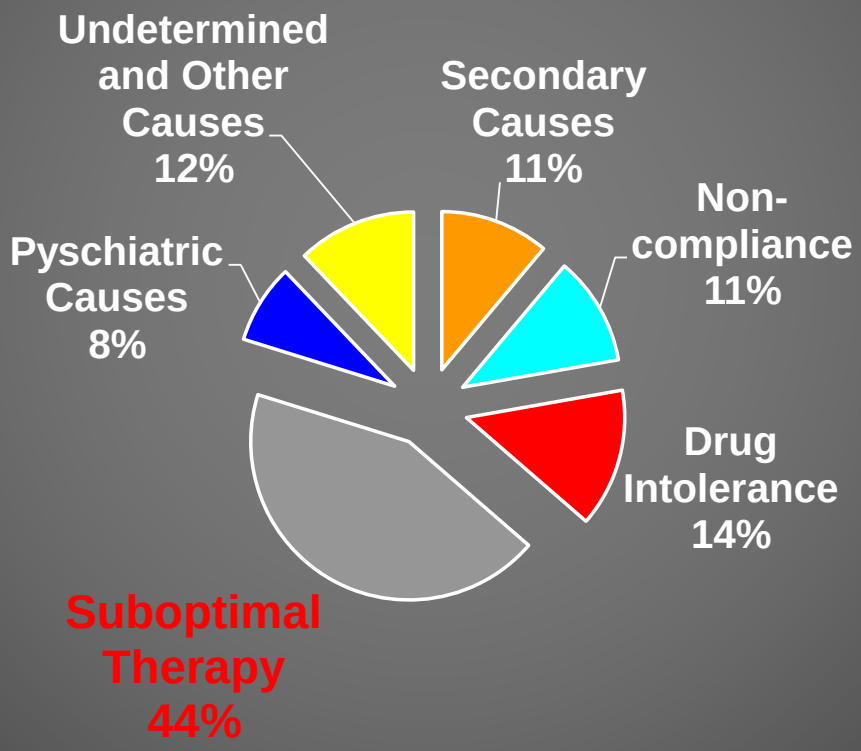
Only 11% of Classic Causes of Resistant HTN are Due to Secondary Causes



Frequency of RVH

- Prevalence of RVH accounts for less than 1 percent of cases of mild to moderate elevations in blood pressure.
- By contrast, the prevalence is much higher in patients with acute (even if superimposed upon a preexisting elevation in blood pressure), severe, or refractory hypertension

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Causes of Renal Artery Stenosis

- There are two major and two minor causes of renal artery stenosis (RAS):
- Major causes:
  - **Atherosclerosis** (in about 80% of patients) primarily affects men over the age of 45 years and usually involves the aortic orifice or the proximal 2 cm of the main renal artery.
  - **Fibromuscular dysplasia** (in about 20% of patients) is more common among younger patients (usually women) and usually affects the distal two thirds of the main renal artery and the branches of the renal arteries.
- Minor causes:
    - Embolic disorders.
    - Extrinsic compression of renal artery.

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Clinical Clues for the Diagnosis of Renovascular Hypertension (1)

- Severe and/or Resistant hypertension
- Acute rise in blood pressure over a previously stable value
- Young onset of hypertension with a negative family history
- Acute and sustained rise in serum creatinine of more than 30 percent after initiating an ACEI or ARB
- Moderate to severe hypertension in a patient with diffuse atherosclerosis, renal asymmetry that cannot be explained by another reason, or recurrent episodes of flash pulmonary edema

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Other Clinical Clues for the Diagnosis of Renovascular Hypertension (2)

- Abrupt onset hypertension after age 50
- Increasing blood pressure in previously controlled hypertension
- Malignant hypertension
- Recurrent “flash” pulmonary edema
- Epigastric murmur, or murmurs on other arteries
- Tobacco use

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There are No More Useful Tests For Diagnosis of RAS (2)

- Captopril renal radioisotopic scan that is useful to determine the relative function of each kidney
- Selective renal vein renin measurements
- Plasma renin activity (in before or after captopril administration)

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Sensitivity and Specificity of Tests for Renovascular Hypertension

Test	Sensitivity (%)	Specificity (%)
Intravenous pyelography	75	86
Routine renal scintigraphy	75-85	75-85
Plasma renin activity	50-80	84
Captopril plasma renin activity	74	89
Captopril scintigraphy	93	95
Doppler flow ultrasonography	90	90-95
Magnetic resonance angiography	90-95	95
Spiral CT scan	90-98	85-94

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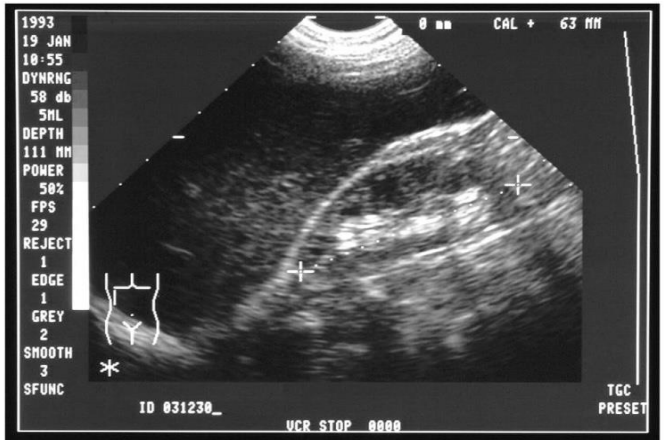
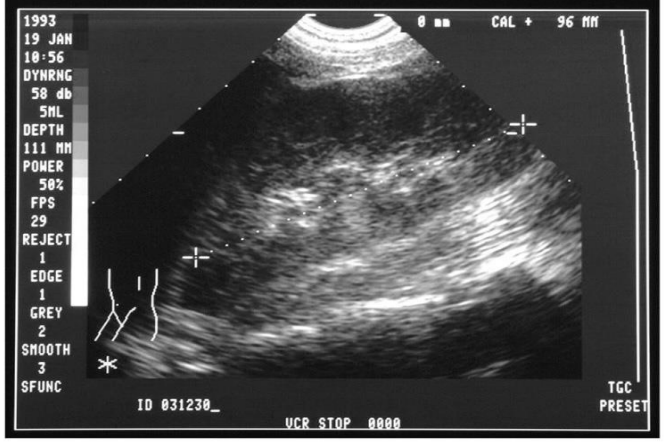
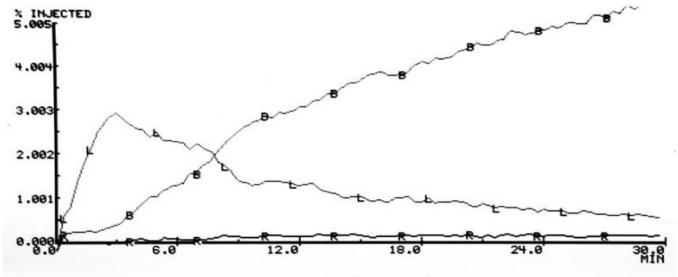
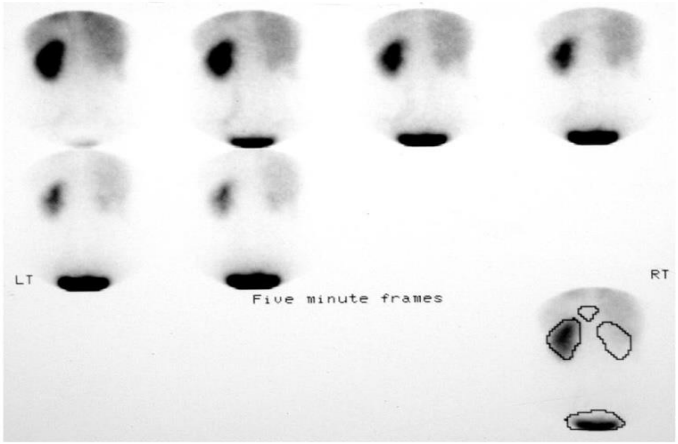
DTPA Renal Scan Showing Delayed Perfusion of Right Kidney







	Left	Right	
Relative function	100	0	%
Time to peak	3.2	23.5	Minutes
Peak uptake	2.9	0.2	% of injected activity
Uptake at 2 min	2.1	0.0	% of injected activity
Uptake at 3 min	2.8	0.0	% of injected activity
Uptake 10 min after peak	1.2		% of injected activity



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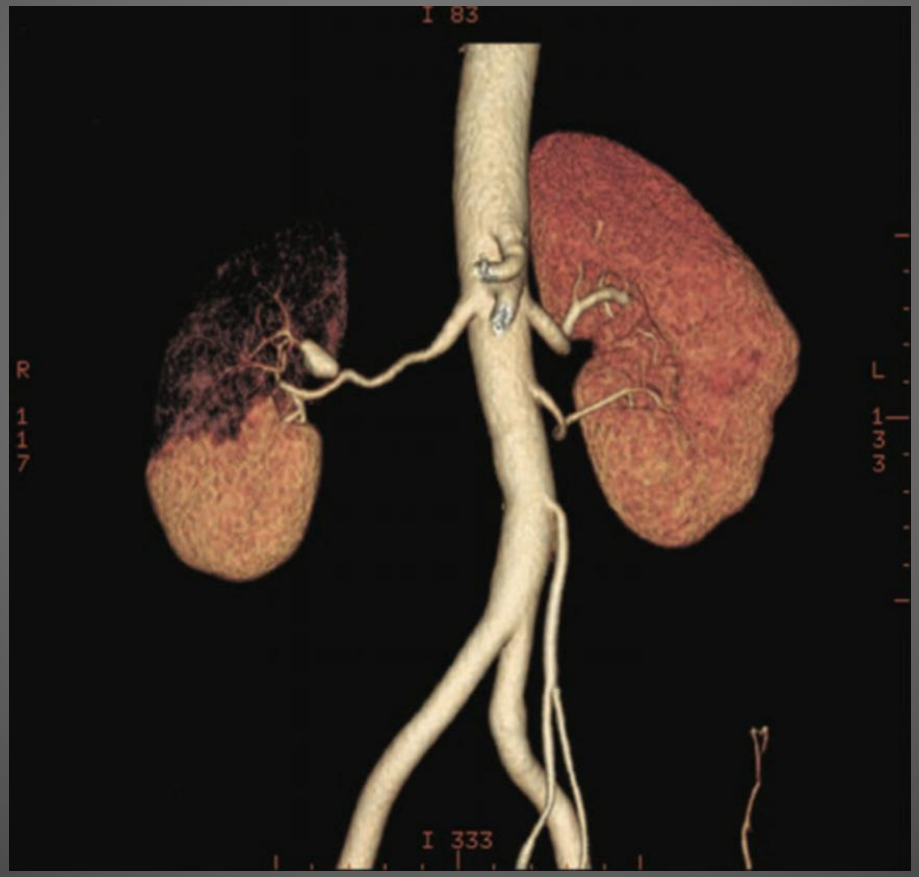
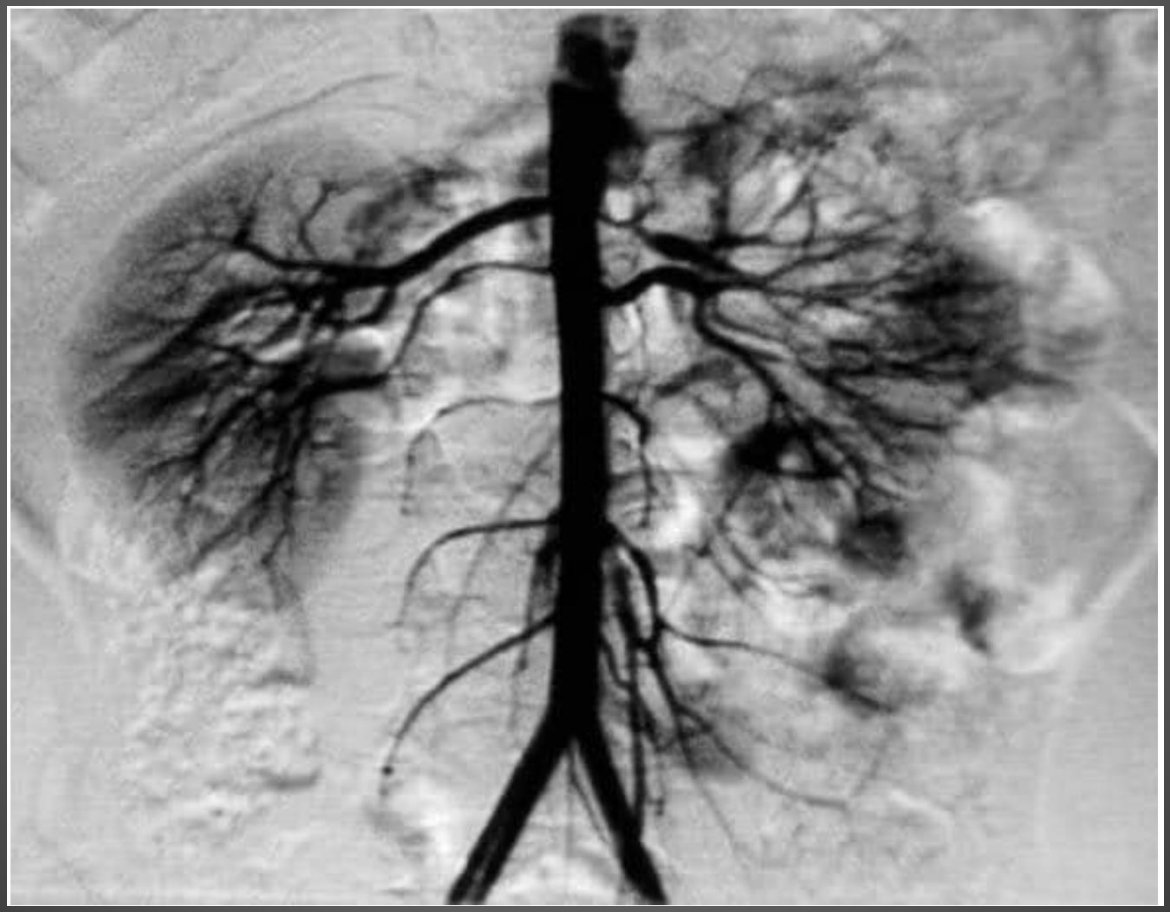
CT angiogram illustrating loss of circulation to the upper pole of the right kidney in a patient with fibromuscular disease and a renal artery aneurysm.



Another case of Fibromucular Dysplasia on Angiography



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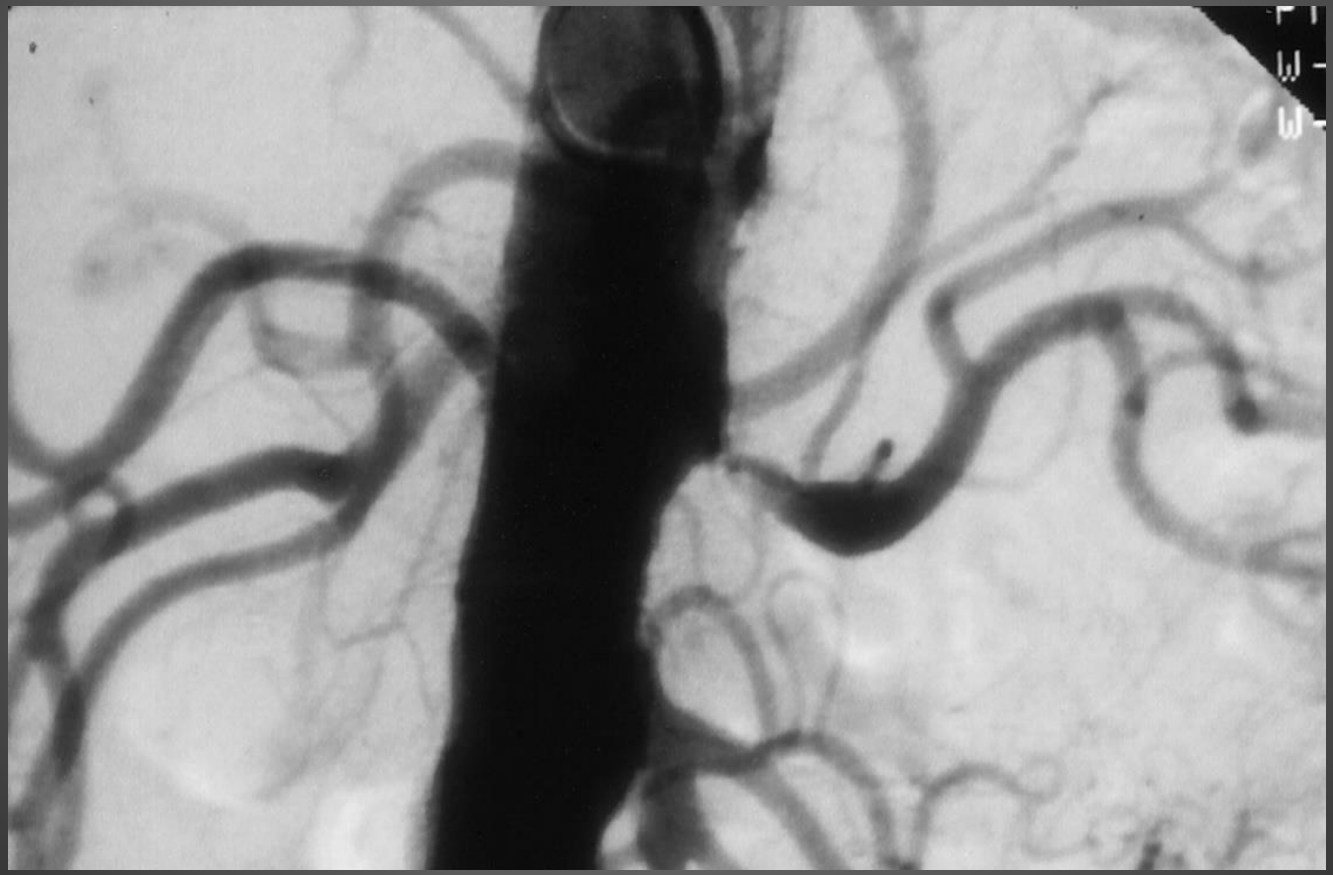
MRA Showing Renal Artery Stenosis Secondary to Atherosclerosis



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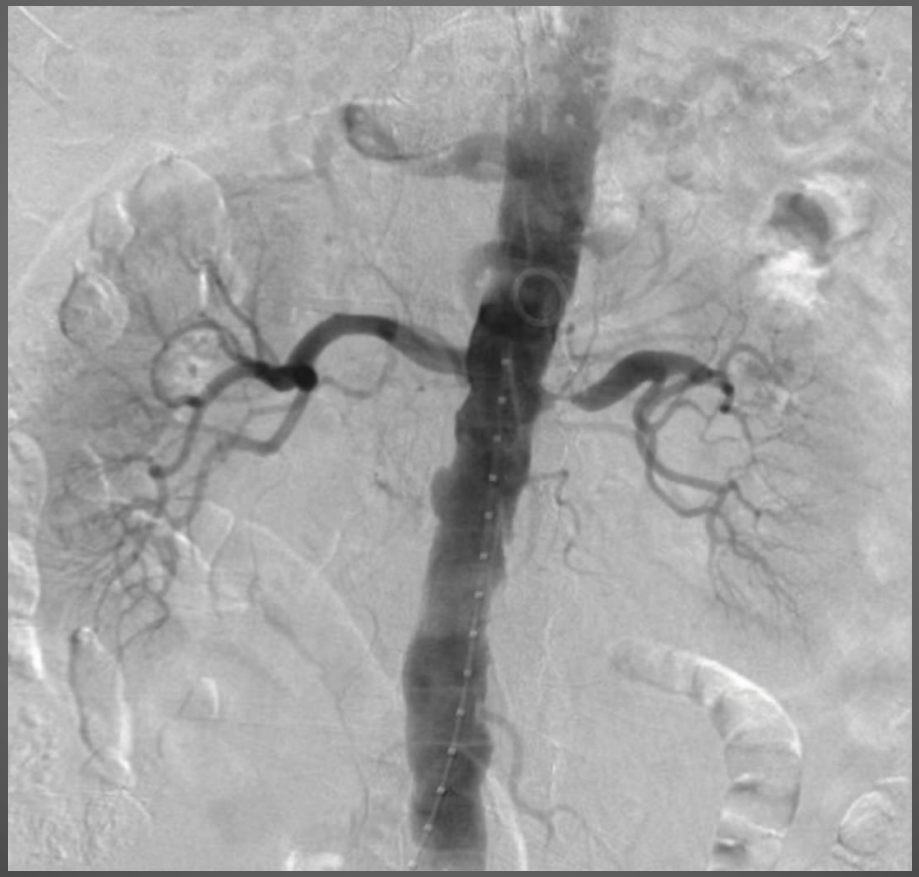
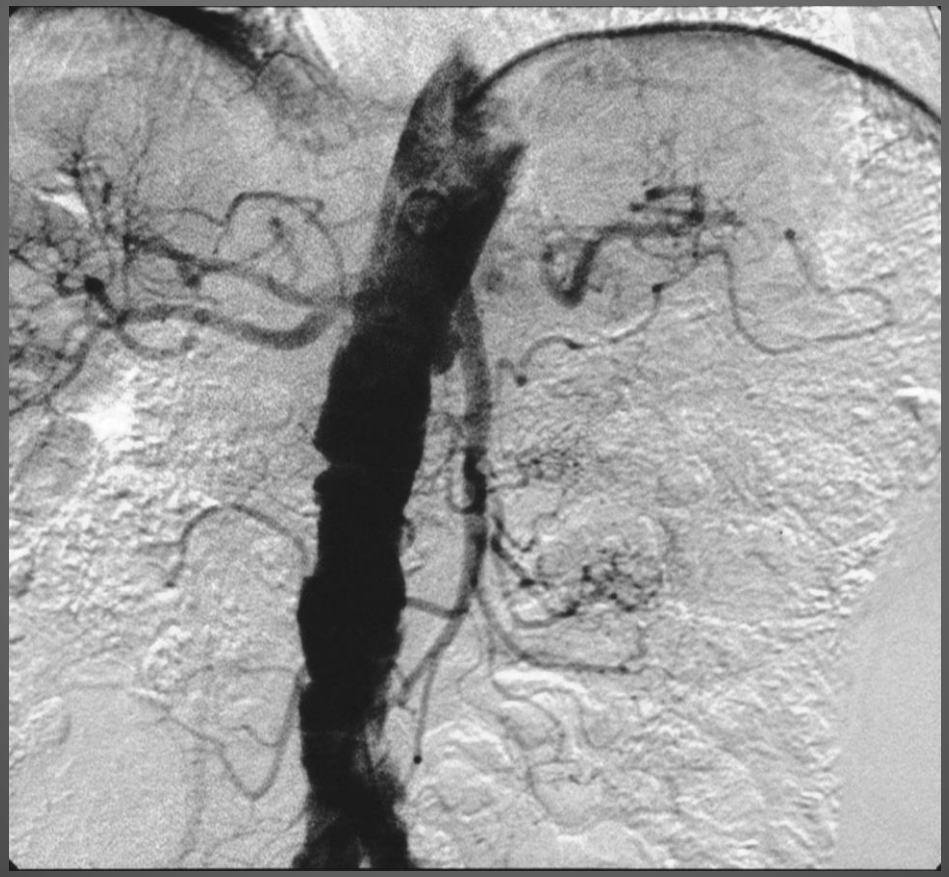
Angiography Illustrating High Grade Stenosis of the Left Kidney



Diffuse Atherosclerotic Aorta and Renal Artery Stenosis



Definition of Stenosis

- The definition of stenosis varied with the imaging study that was used:
  - The best is luminal narrowing >60 percent if diagnosed with conventional angiography
  - A peak systolic velocity >300 cm/second if diagnosed by duplex Doppler ultrasonography
  - Luminal narrowing >80 percent if diagnosed with magnetic resonance angiography or computerized tomography angiography (or >70 percent with additional evidence of kidney ischemia)
  - Systolic hypertension despite two or more antihypertensive medications and/or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 that was presumably due to the stenosis.

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Treatment of Unilateral Atherosclerotic Renal Artery Stenosis Are

- Medical therapy (essentially all patients)
- Percutaneous revascularization with angioplasty with or without stent placement
- Surgical revascularization or, in some cases, nephrectomy of a "pressor" kidney

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New Studies of Treatment

- **Several prospective, randomized trials for atherosclerotic disease failed to demonstrate that renal revascularization is more effective than medical therapy.**
- **On the basis of the clinical experience of hypertension centers, specialists have continued selective revascularization, without a summary statement by a major, multidisciplinary, national organization that identifies specific populations that may benefit.**

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Medical Treatment of Bilateral Atherosclerotic Renal Artery Stenosis

- **Calcium channel blockers:** Amlodipin, Nifedipin, Diltiazem, etc
- **Diuretics:** Hydrochlorothiazide, Spironolactone, Eplerenone,Furosemide, Etc
- **Beta blockers:** Propranolol, Atenolol, Carvedilol, Sotalol, Etc
- **Central antihypertensive:** Methyldopa, Clonidine
- **ACE inhibitors and ARBs should not be used**

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Medical Treatment of Unilateral Atherosclerotic Renal Artery Stenosis

- Ideally, antihypertensive therapy should include an agent that blocks an angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs)
- ACEIs: Captooril, Enalapril, Fosinopril, Lisinopril, Perindopril
- ARBs: Losartan, Valsartan, Telmisartan, Olmesartan, Candesartan, Irbesartan

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Revascularization Versus Medical Therapy Alone

- All patients received antiplatelet therapy plus standardized medical treatments for hypertension, hyperlipidemia, and hyperglycemia, and were then randomly assigned to revascularization by Percutaneous Translumial Renal Angioplasty (PTRA with stenting) or to no revascularization.
- Revascularisation had no additional effect on the primary outcome (a composite of cardiovascular or kidney death, stroke, myocardial infarction, hospitalization for heart failure, a reduction in eGFR by more than 30 percent, or end-stage kidney disease) as compared with medical therapy alone (35.1 versus 35.8 percent).
- Similarly, revascularization had no effect on any of the individual components of the primary outcome.

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Revascularization versus Medical Therapy Alone

- Patients assigned revascularization plus medical therapy had a mean systolic blood pressure throughout the trial that was approximately 2 mmHg lower than those assigned medical therapy alone.
- Serious adverse events associated with revascularization were uncommon.
- The most frequent serious complication of revascularisation was renal artery dissection, which occurred in 2 to 3 percent of revascularized patients.

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Revascularization Using Percutaneous Transluminal Renal Angioplasty

- **Revascularization using percutaneous transluminal renal angioplasty** (PTRA) with or without stent in combination **with medical therapy has been compared with medical therapy alone in eight randomized trials** that included patients with unilateral atherosclerotic renal artery stenosis.
- **A meta-analysis of these trials found no benefit from PTRA on mortality, end-stage kidney disease (ESKD), major cardiovascular events.**
- Only modest effects on blood pressure antihypertensive medications and/or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 that was presumably due to the stenosis.

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Treatment of Bilateral Atherosclerotic Renal Artery Stenosis or Stenosis of a Solitary Functioning Kidney

- Medical therapy alone
- Percutaneous renal angioplasty, usually with stent placement, in addition to medical therapy
- Surgical revascularization in addition to medical therapy
- Medical therapy for control of hypertension is indicated in all patients with bilateral renal artery stenosis (or unilateral stenosis in a single viable kidney)
- Revascularization, usually by percutaneous angioplasty with stenting, is reasonable in patients who have a high likelihood of benefitting from intervention

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Medical Treatment of Bilateral Renal Artery Stenosis

- Combination therapy with a diuretic plus an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) can control the hypertension in most patients with bilateral renal artery stenosis and is likely to be more effective than other antihypertensive therapy.
- In a Canadian cohort study, for example, patients with renal artery stenosis who were prescribed ACE inhibitors were significantly less likely to die or have a myocardial infarction or stroke (10 versus 13 events per 100 patient-years) as compared with similar patients prescribed other therapy.
- ACE inhibitor and ARB therapy were also associated with a lower risk of end-stage kidney disease but a higher risk of acute kidney injury (1.2 versus 0.6 events per 100 patient-years).

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