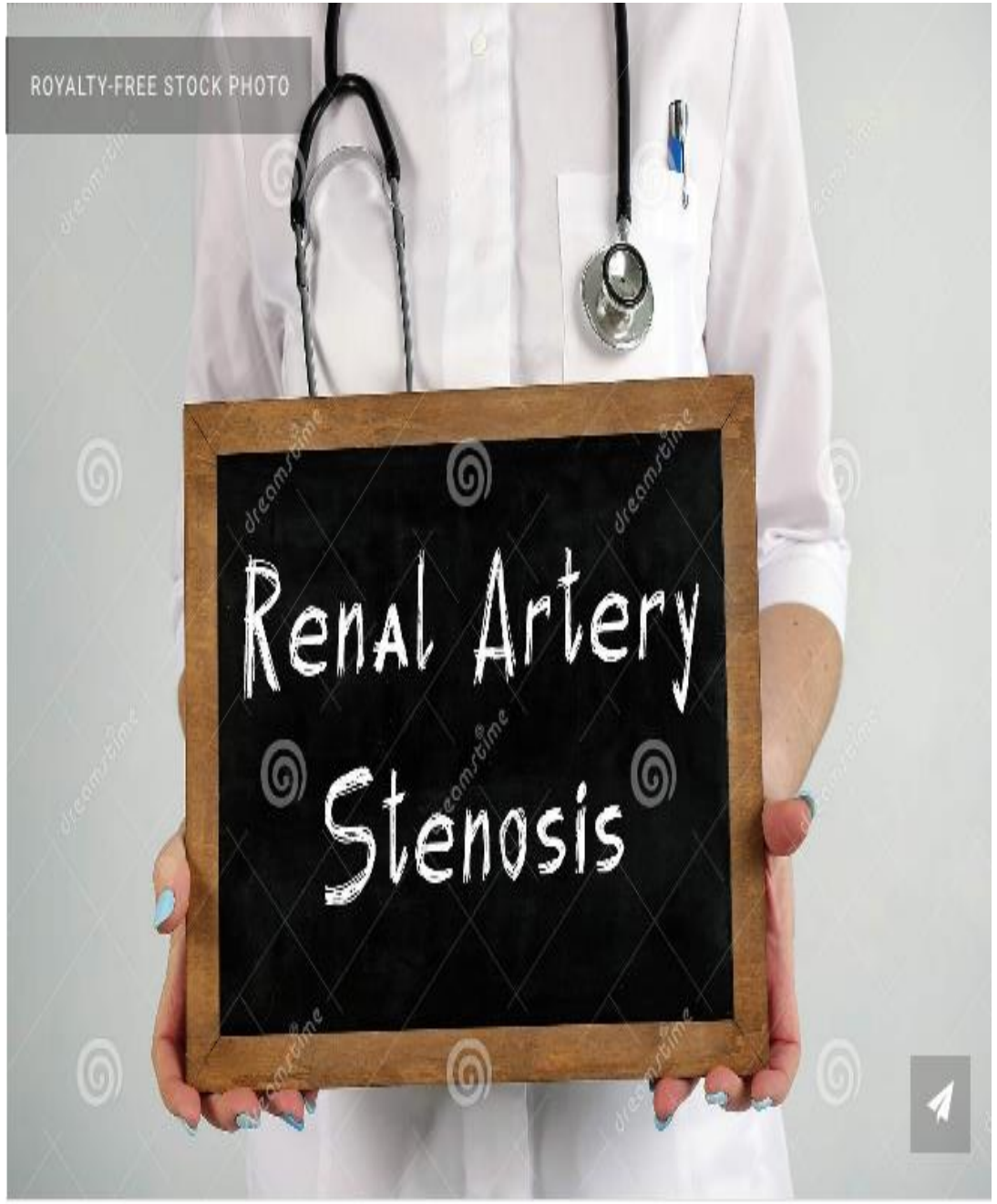


re concept about Renal Artery Stenosis with sign on the page.

IN THE NAME OF GOD

RENOVASCULAR HYPERTENTION

Dr. Farzaneh .Futuhi
Nephrologist
Assistant professor
SBMU-Loghman hospital

Issues in Renovascular Disease

Prototype of Secondary Hypertension

-Potentially treatable with revascularization

-USA: Estimated 60 million hypertensives

1-3% with RVH: >60000

Approximately:

85% Atherosclerotic disease

14% Fibromuscular diseasis

1% Other

Progressive Disorder: ?increasing prevalence?

"The prevalence of atherosclerotic renal artery stenosis in risk groups: a systematic literature review"

de Mast Q, Beutler JJ: J. Hypertens. 27:1333, 2009

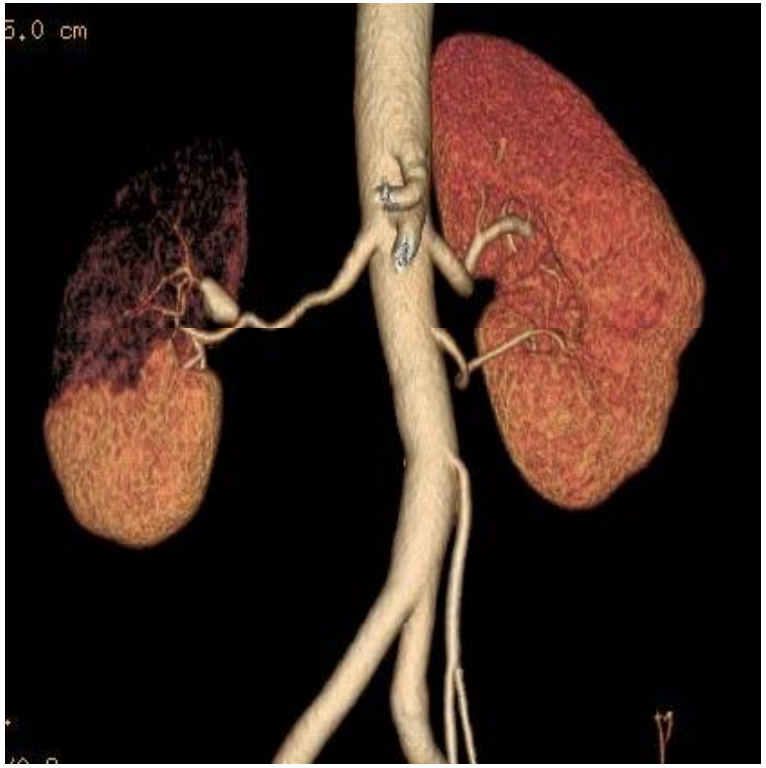
N=40 Studies: 15, 879 patients

"50% luminal" narrowing: Pooled Prevalence rates

• "Suspected Renovascular HTN"	14.1%	
• Coronary Angiography:	10.5%	
With HTN:	17.8%	
• Peripheral vascular disease:	25.3%	
• AAA:	33.1%	
• ESRD:	40.8%	?
• Congestive Heart Failure:	54.1%	?

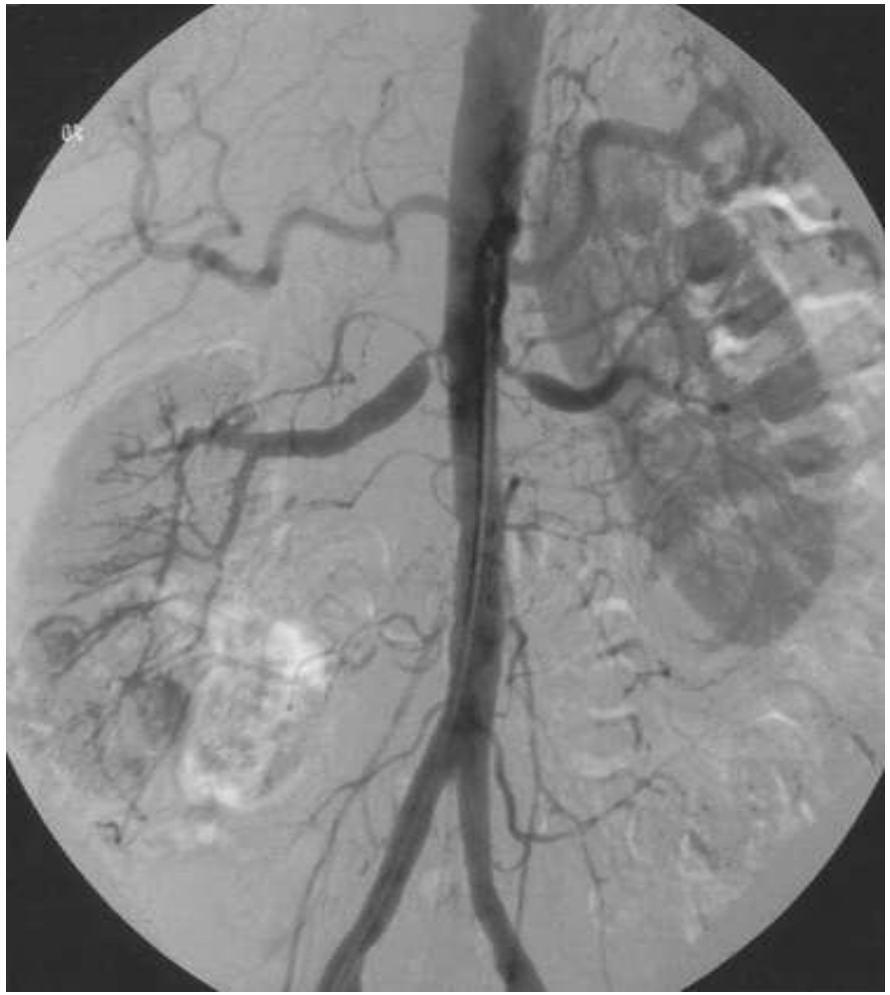
MAYO CLINIC

Renovascular Hypertension due to arterial occlusive lesions



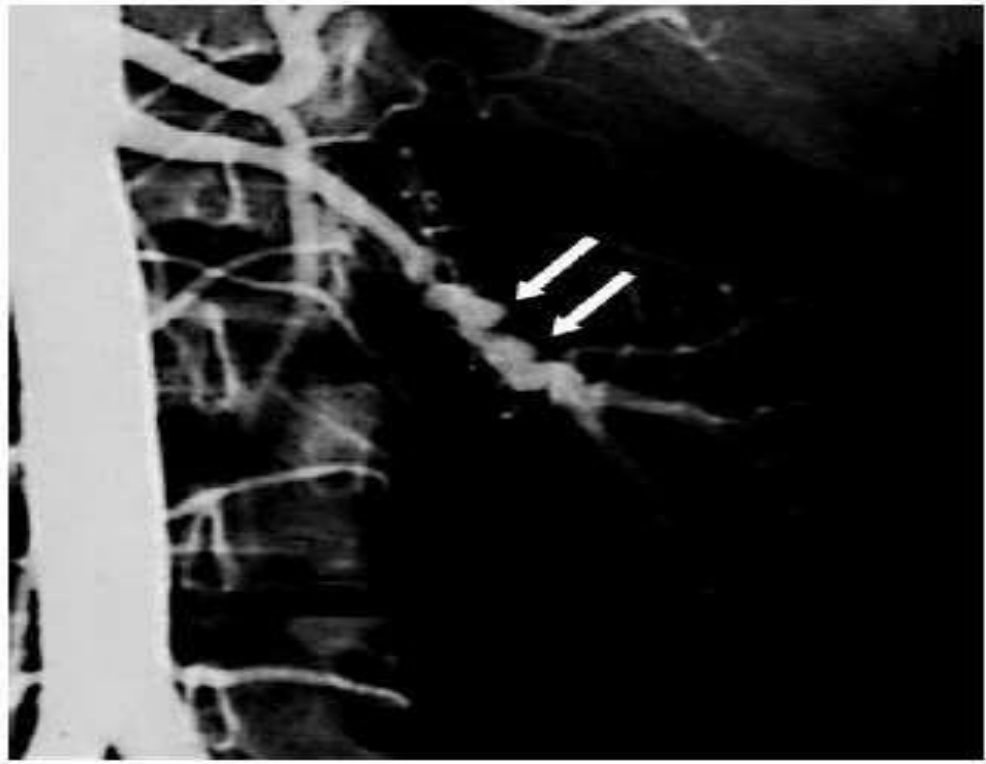
- **Fibromuscular dysplasia**
- **Atherosclerotic disease**
- **Renal artery embolism**
- **Dissection / thrombosis**
- **Post-traumatic injury**
- **Aortic stent graft occlusion**
- Vasculitis involving the renal artery (i.e. PAN)
- Neurofibromatosis
- Scleroderma

ATHEROSCLEROTIC RAS



- Patient 6th decade or older.
- More often male
- Associated with diseased aorta
- Typically involves the ostium and/or proximal one-third of the renal
- Can be unilateral or bilateral
- 70-80% have unilateral disease

FIBROMUSCULAR DYSPLASIA



- Young patients –more commonly females.
- Commonly asymptomatic
- Prevalence 2-6 %
- >60% of patients have bilateral disease.
- Medial fibroplasia (90%)>> Intimal (10%) or adventitial
- Location: **distal two-thirds of main renal artery**, in 25%, disease extends into segmental arteries
- Right renal artery is affected more frequently
- Progressive renal stenosis is seen in 37% of cases and loss of renal mass in 63%.
- Other arteries can also be involved (carotid, vertebral, iliac, and mesenteric). All patients need head imaging to r/o cerebral aneurysms
  - Angiography revels a characteristic ***string of beads a***ppearance

ABDOMINAL AORTOGRAM REVEALED A LEFT RENAL ARTERY FIBROMUSCULAR DYSPLASIA WITH THE TYPICAL "STRING OF BEADS" APPEARANCE

Unilateral Renal Artery Stenosis

Reduced renal perfusion

↑ renin-angiotensin system (RAS)
↑ renin
↑ angiotensin II
↑ aldosterone

Angiotensin II dependent hypertension

Increased renal perfusion

Supressed RAS

Increased Na^+ excretion (pressure natriuresis)

Effect of blockade of RAS

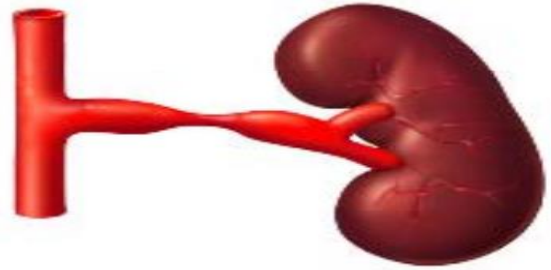
Reduced arterial pressure
Enhanced lateralization of diagnostic tests
Glomerular filtration rate (GFR) in stenotic kidney may fall

Diagnostic tests

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

Bilateral Renal Artery Stenosis

Bilateral



Stenosis of solitary kidney

Reduced renal perfusion

or impaired kidney function

↑ renin-angiotensin system (RAS)
↑ renin
↑ angiotensin II
↑ aldosterone

Impaired Na^+ and water excretion

Inhibit RAS

Volume expansion

Normal or low angiotensin II

Increased arterial pressure

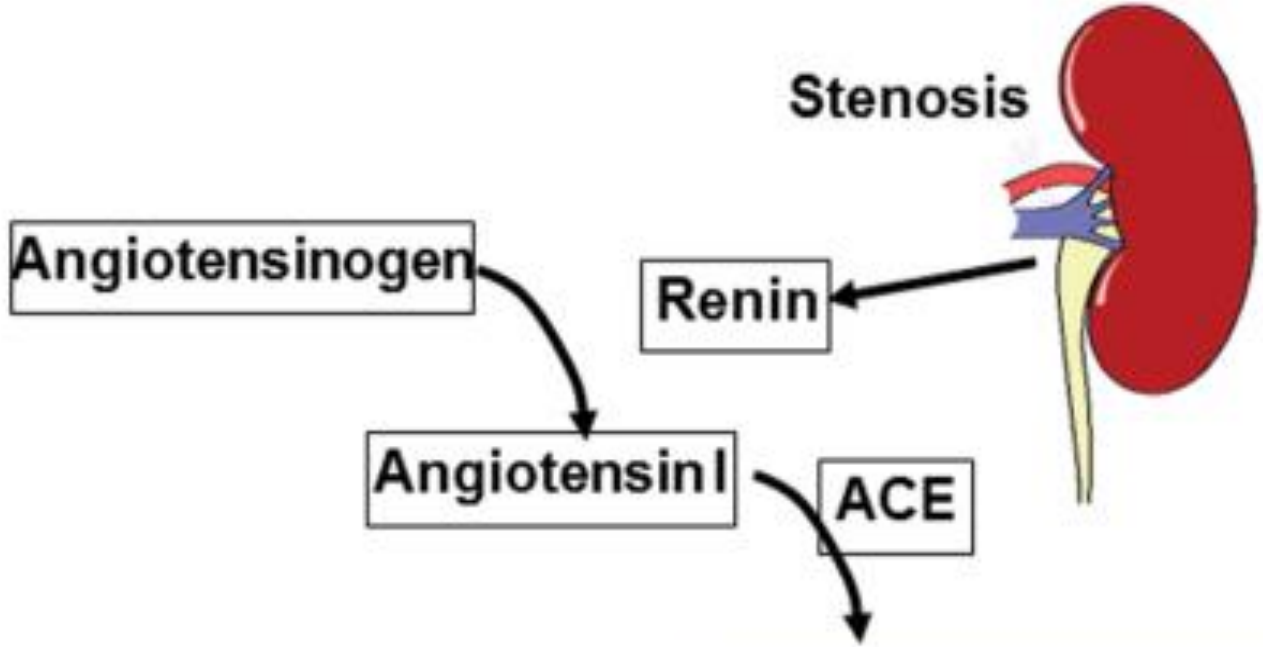
Effect of blockade of RAS

Reduced arterial pressure only after volume depletion
May lower GFR

Diagnostic tests

Plasma renin activity normal or low
Lateralized features: none

PATHOPHYSIOLOGY



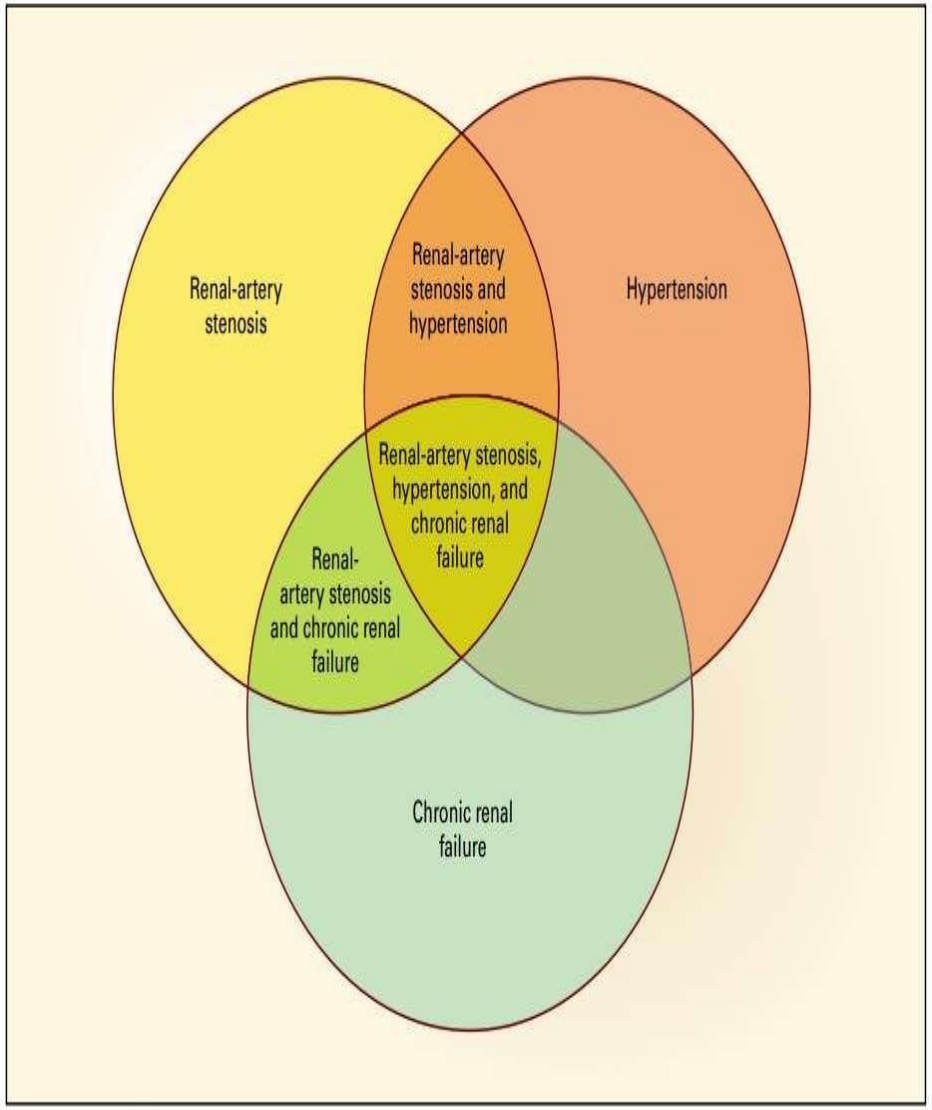
American Journal of Hypertension, 01 Jan 2018, 31(2):139-149

Angiotensin II

- Vaso-constriction
- Renal sodium retention
- Aldosterone secretion
- Vascular effects
  - Hypertrophy
  - Remodeling
  - Endothelin release
  - Prostaglandins
  - Oxidative Stress
- Sympathetic nerve system activation
- Myocardial effects
  - LV hypertrophy
  - Myoctye growth
  - LV remodeling

The morphological features

- Vascular sclerosis(contralateral kidney).
- Tubular atrophy,
- Interstitial fibrosis with inflammatory cellular infiltrate
- Atubular glomeruli,
- Cholesterol emboli,
- FSGS changes.(contralateral kidney.)



Baseline renal function is related to the extent of renal parenchymal injury rather then to the degree of stenosis.

Improvement in hypertension and renal function is related to revascularization.

RD Safian, SC Textor . *N Engl J Med* 2001; 344:431-442

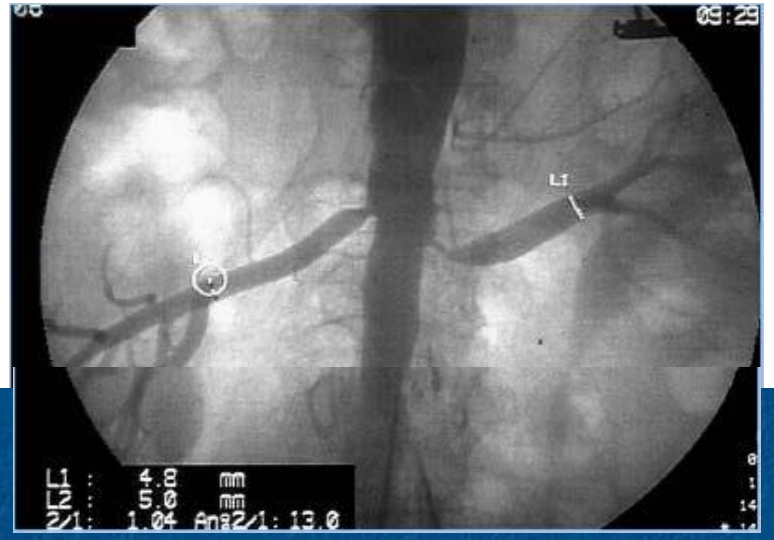
- Unilateral RAS results in vasoconstrictor-mediated HTN, Bilateral or solitary kidney RAS results in HTN with volume overload.

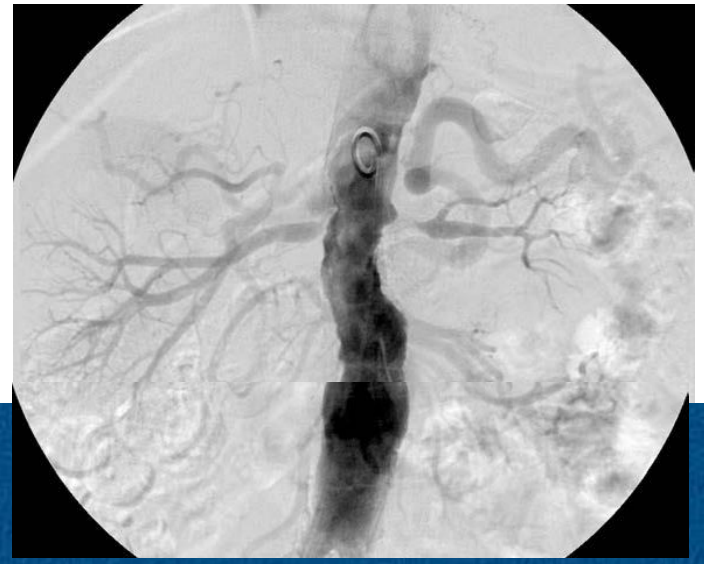
Renal artery stenosis

	Unilateral	Bilateral
RAAS activation	↑↑	↑
Na/Fluid volume state	Pressure natriuresis	Sodium retention
Cardiac output	Normal	↑
Total peripheral resistance	↑↑	↑
BP response to RAS blockade	↑↑	↑
Flash pulmonary oedema	Rare	Common
Natriuresis post angioplasty of RAS	No	Yes

BP, blood pressure; RAAS, renin–angiotensin–aldosterone system; RAS, renal artery stenosis.

Spectrum of Renovascular Disease Manifestations





Asymptomatic "Incidental RAS"

Renovascular Hypertension

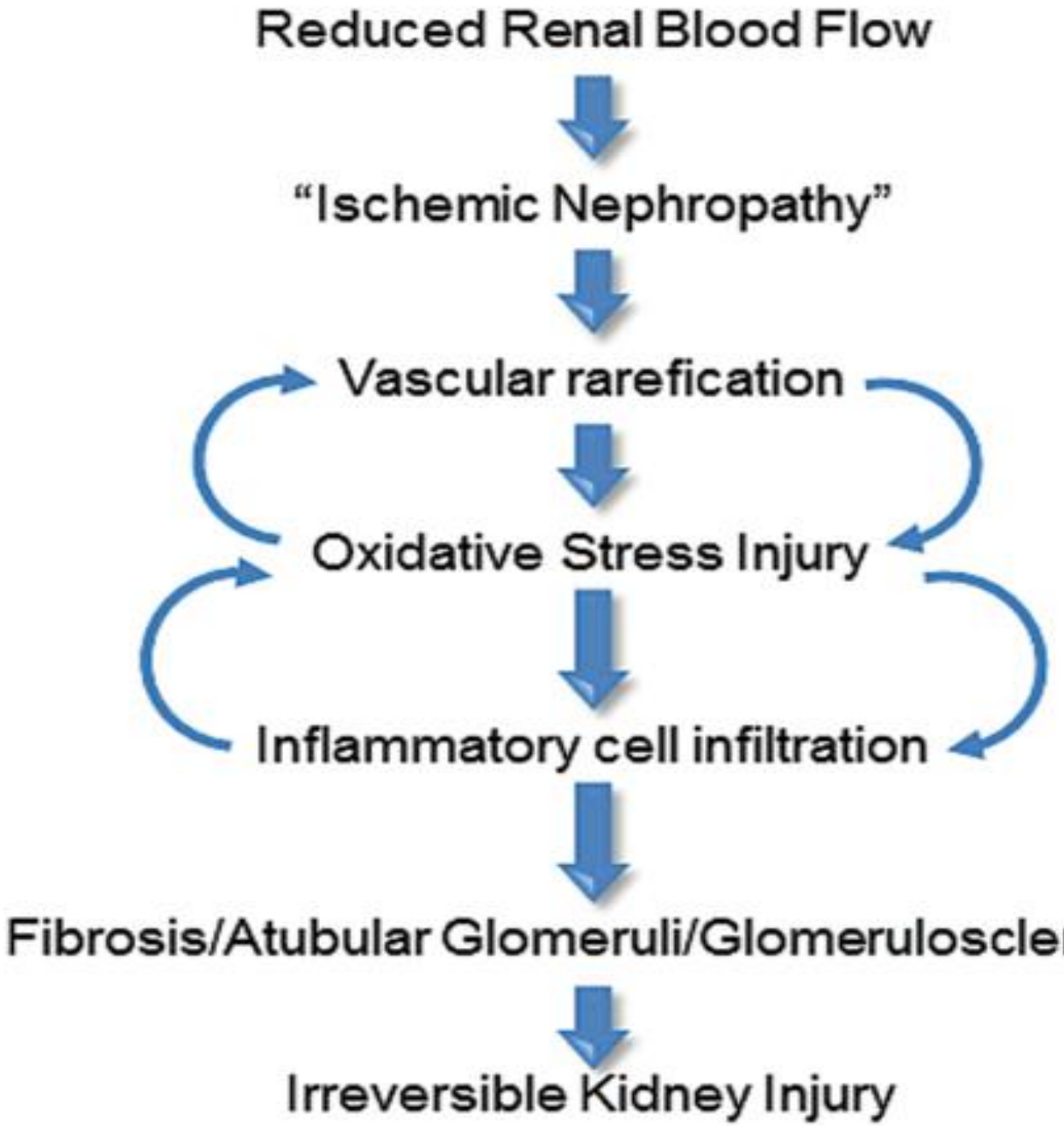
Accelerated CV Disease
Congestive Heart failure
Stroke

Ischemic Nephropathy

Textor

MAYO CLINIC

Critical Renal Artery Stenosis



- Reduced cortical perfusion
- Reduced GFR
- Activation of RAAS

- Early: Preserved cortical oxygenation
- Late: cortical hypoxia/expanded de-oxygenatic

- Loss of cortical microvessels

- Generation of toxic oxygen species
- Ischemia/reperfusion injury
- Impaired mitochondrial biogenesis
- Impaired ATP/energetics

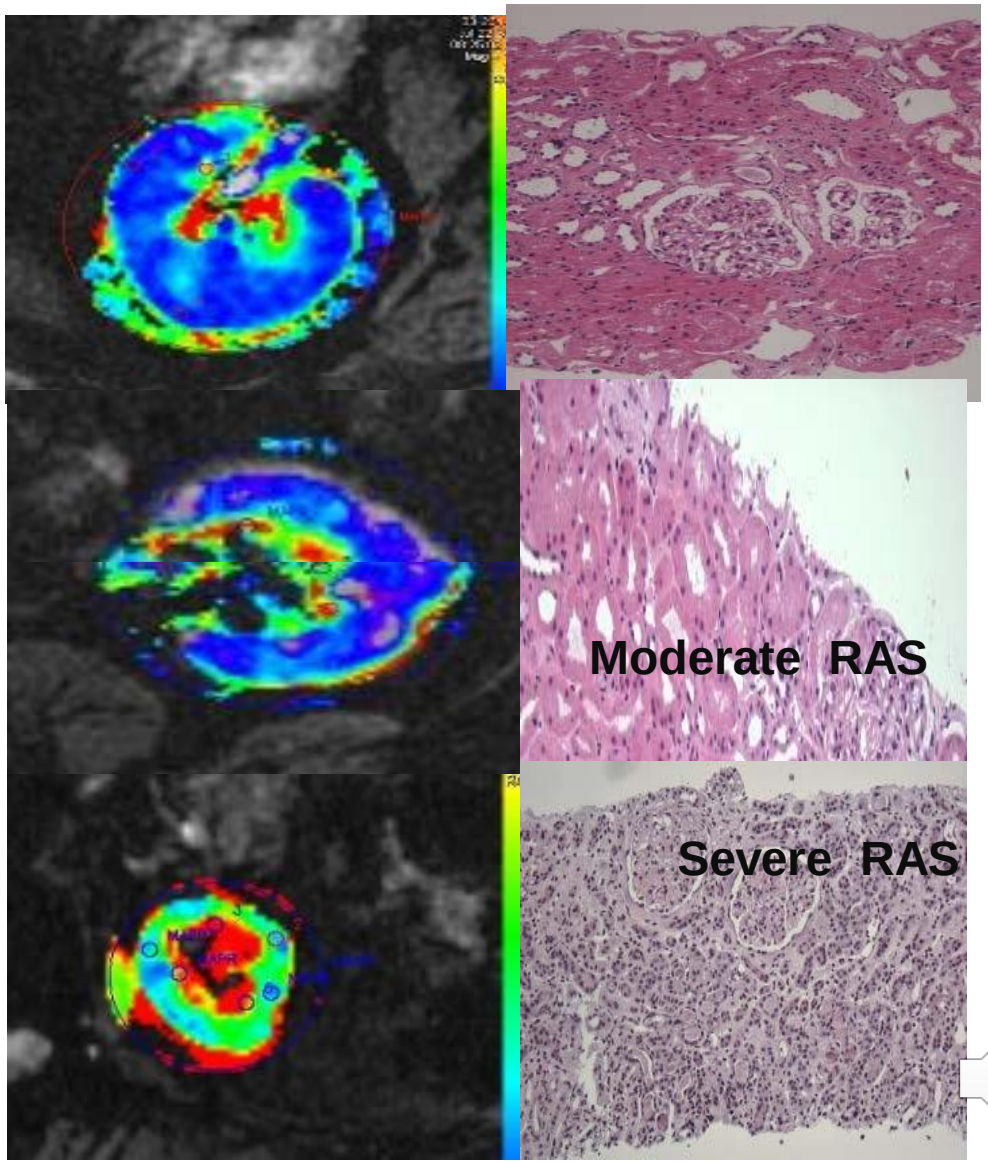
- Tissue/cellular cytokine release
- Pro-inflammatory milieu, eg, IL-6, MCP-1, TGF
- T-lymphocyte infiltration: Th1/Th2
- Macrophage infiltration: M1/M2

Human Renovascular Disease

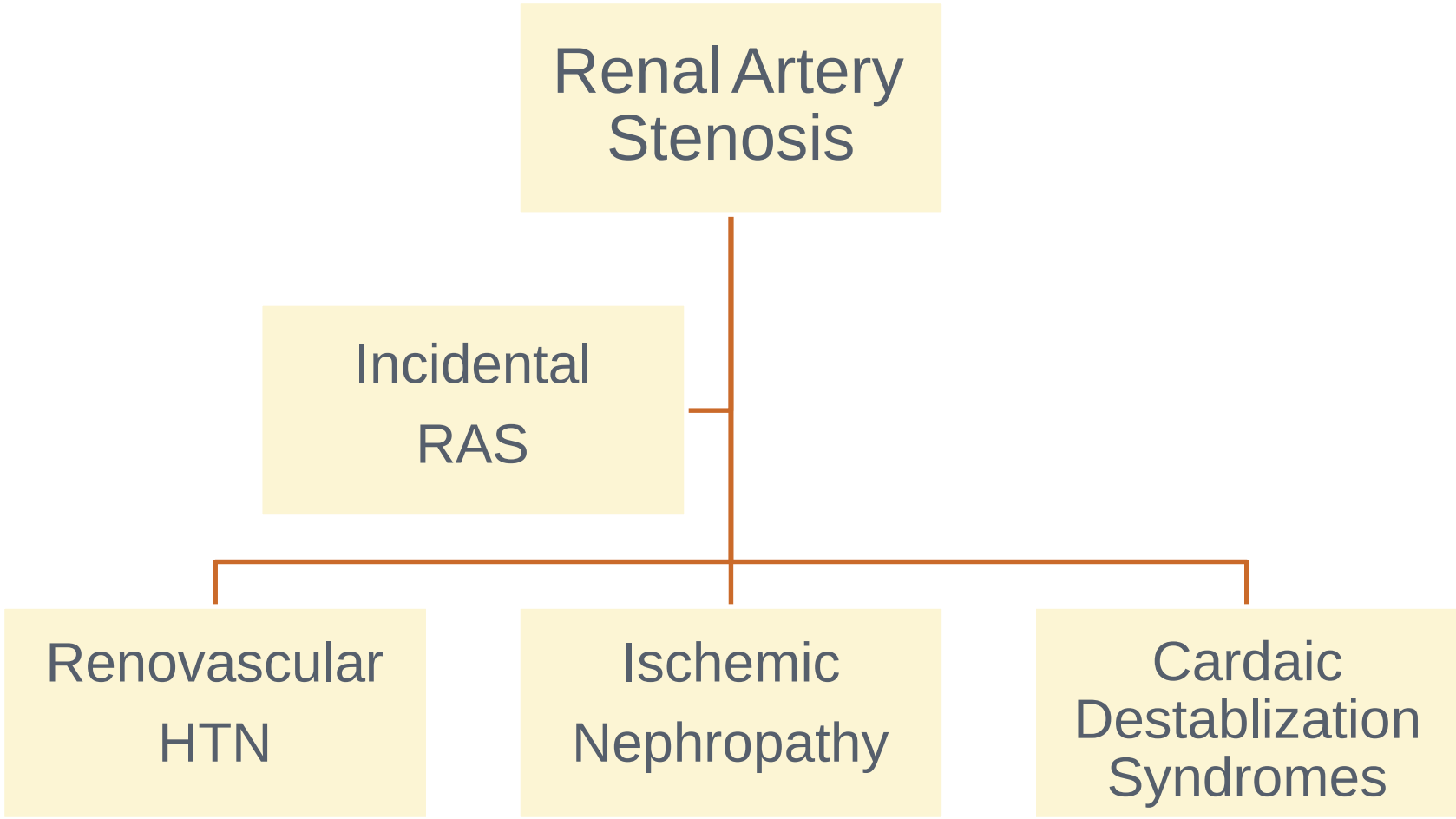
- **Renovascular Hypertension:**
  - **-Renin release**
  - **-can be managed medically**

- **“Adaptation” to reduced**
  - **-without tissue hypoxia**
  - **-minimal structural damage**

- **Advancing disease: adequate blood flow for tissue oxygenation?**
- **progressive injury -?recoverable?**

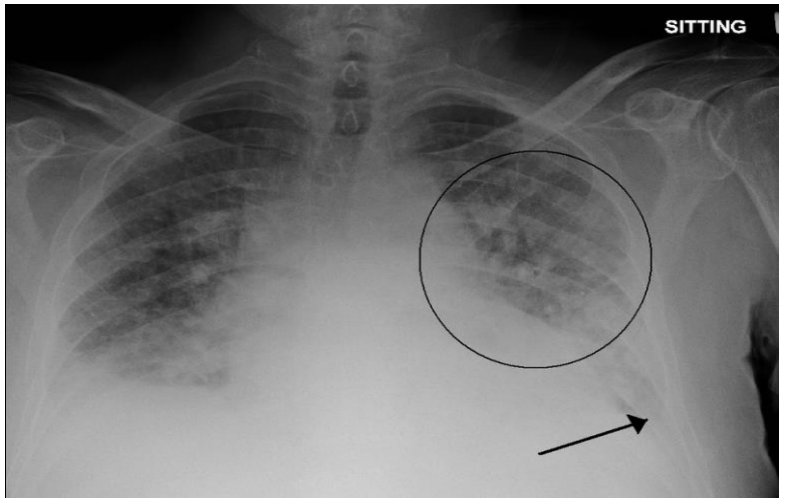


CLINICAL MANIFESTATIONS



Clinical Conditions

Renovascular hypertension,
Cardiac destabilization syndromes
Ischemic nephropathy



Cardiac destabilization syndromes include: “flash” pulmonary edema events, ADHF and ACS.

Pickering syndrome conditions that ,bilateral ARAS as they lack the compensatory mechanism of a functional kidney in regulating the body’s salt and fluid balance ,That they prone to frequent “flash pulmonary edema episodes.

Ischemic nephropathy is a condition where local ischemia to the kidney causes tubulointerstitial injury and microvascular damage due to oxidative injury that leads to interstitial fibrosis and renal atrophy.

Table 1 Functional Classification of ARAS in Association with Hypertension[26]

Grade	Description
I	Asymptomatic ARAS with normotensive blood pressure and normal renal function
II	ARAS with well controlled hypertension using medical therapy and normal renal function
III	ARAS with uncontrolled hypertension despite optimal medical therapy or clinical signs of volume overload and abnormal renal function

Note: Data from Rocha-Singh et al.[26]

Clinical risk factors for RVHT ;

•A history of hypertension with azotemia (serum creatinine level >1.5 mg/dL)

•modest proteinuria ,levels < 1.5 g/day

•Progressive renal insufficiency

•Accelerated or malignant hypertension

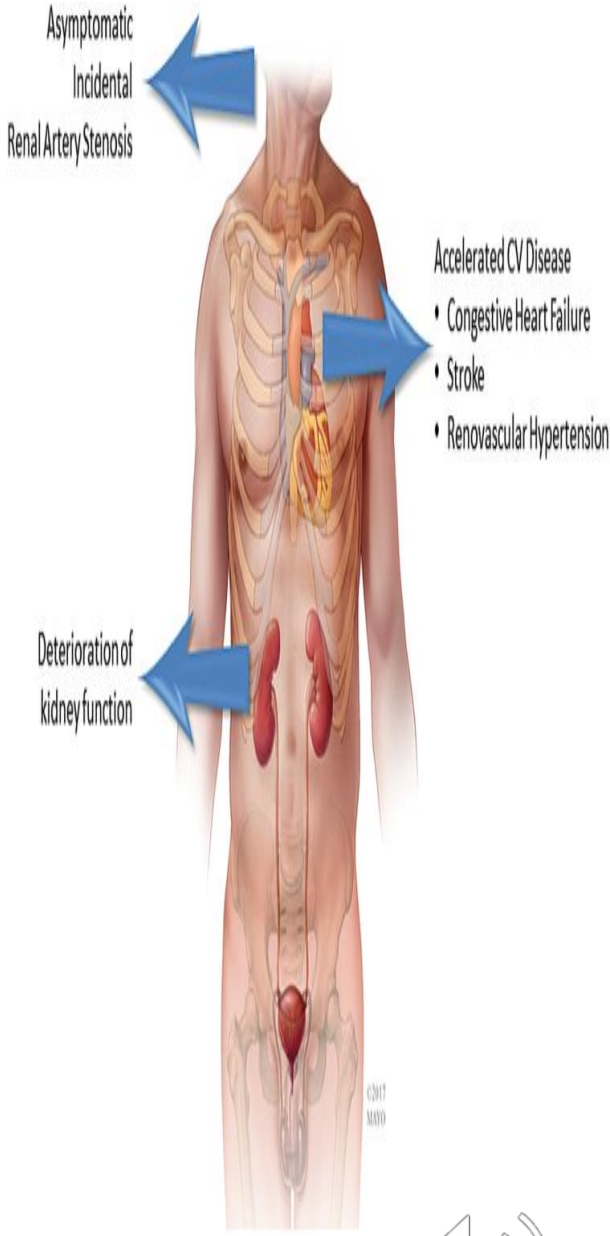
•Severe hypertension (diastolic blood pressure >120 mm Hg)

•Hypertension with an asymmetric kidney

•

•Paradoxical worsening of hypertension with diuretic therapy

•Hypertension refractory to standard therapy



DIAGNOSTIC TEST (CURRENTLY RECOMMENDED)

1. Renal artery duplex imaging is the first-line test
2. Computed tomography in patients with creatinine clearance >60 mL/min
3. Magnetic resonance angiography in patients with creatinine clearance >30 mL/min
4. BOLD MRI
5. CAPTOPRIL scintigraphy
6. Renal angiography as the gold standard for invasive assessment

ACC/AHA guidelines are in agreement that captopril renal scintigraphy, selective renal vein renin measurements, plasma renin activity, and the captopril test are not recommended as useful screening tests for RAS (class III).

Diagnostic Methods to Detect Renal Artery Stenosis (RAS)

Class I	Level of Evidence
Duplex ultrasound sonography is recommended as a screening test to establish the diagnosis of renal artery stenosis.	B
Computed tomographic angiography (in individuals with normal renal function) is recommended as a screening test to establish the diagnosis of renal artery stenosis.	B
Magnetic resonance angiography is recommended as a screening test to establish the diagnosis of renal artery stenosis.	B
When the clinical index of suspicion is high and the results of noninvasive tests are inconclusive, catheter angiography is recommended as a diagnostic test to establish the diagnosis of renal artery stenosis.	B
Class III	
Captopril renal scintigraphy is not recommended as a screening test to establish the diagnosis of renal artery stenosis.	C
Selective renal vein renin measurements are not recommended as a useful screening test to establish the diagnosis of RAS.	B
The plasma renin activity is not recommended as a useful screening test to establish the diagnosis of renal artery stenosis.	B
The captopril test (measurement of plasma renin activity following captopril administration) is not recommended as a useful screening test to establish the diagnosis of renal artery stenosis.	B

Doppler ultrasound

- Duplex ultrasonography is the initial imaging test of choice to evaluate the renal arteries
- The most important sign is peak systolic velocity (PSV).
- A PSV higher than 180 cm/s suggests the presence of stenosis of greater than 60
- The resistive index (RI), which is calculated as ((PSV-End diastolic velocity)/PSV))
- (Normal < 0.7, nephrosclerosis > 0.7)
- A positive test is more informative than
- Negative test

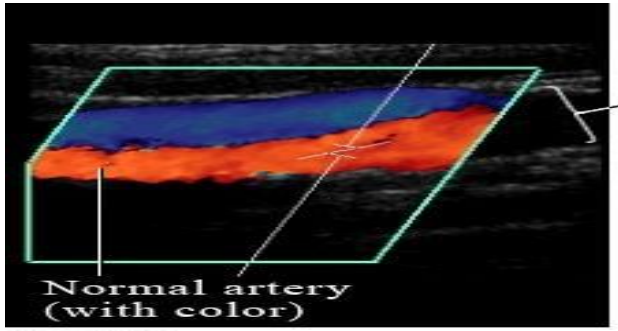


Figure 1

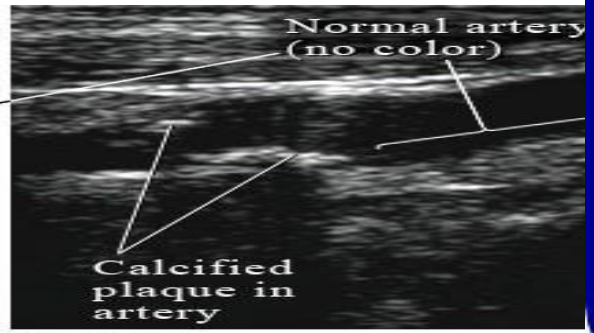


Figure 2

Renal artery stenosis

Direct signs	Indirect signs
Focal color aliasing	AT > 0.07 sec
Color bruit	AI < 3 m/s^2
Turbulence	Δ RI (right – left) > 5 %
PSV > 180 cm/sec	
Renal Aortic Ratio > 3.5	
Significant stenosis (50 – 85% diameter reduction) Sensitivity: 79 – 91% Specificity: 73 – 97%	**Severe stenosis** (> 85 % diameter reduction) Sensitivity: 95% Specificity: 97%

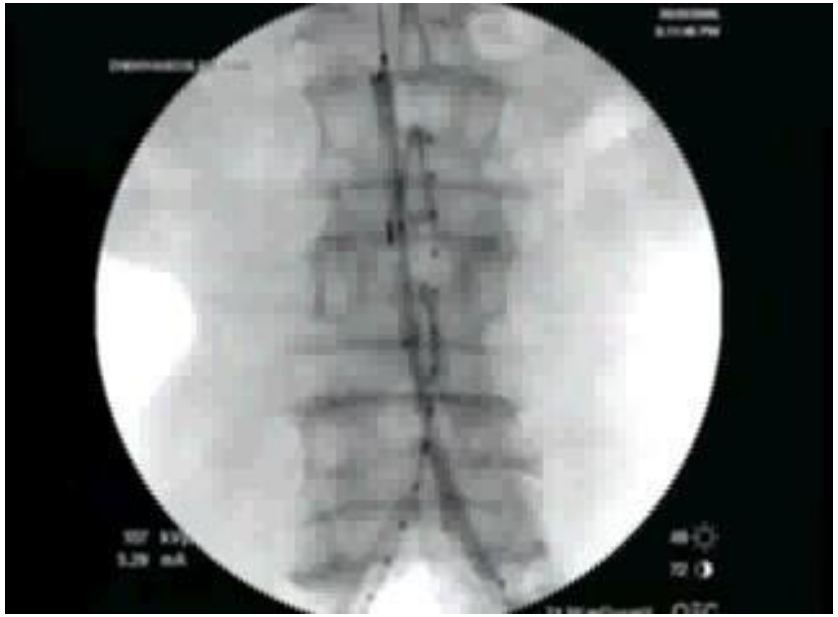
Renal Arteriography.

‘ **GOLD STANDARD**’ investigation in the diagnosis of renal arterial disease.

- Required to start treatment.

Mild: < 50%
Moderate: 50–70%
Severe: >70%

.



INDICATIONS FOR TESTING

Early or late onset of hypertension (<30 or >50 years).

Worsening control of previously well-treated hyper- tension.
“Flash” pulmonary edema.

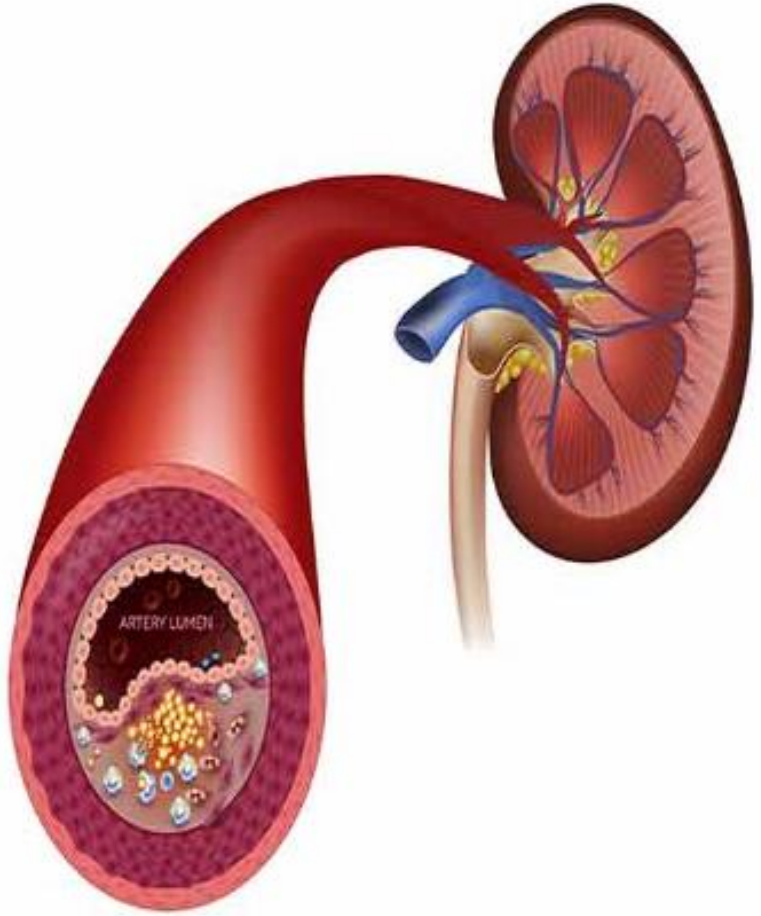
An acute elevation in serum creatinine of at least 30% after initiation of RAAS inhibitors.

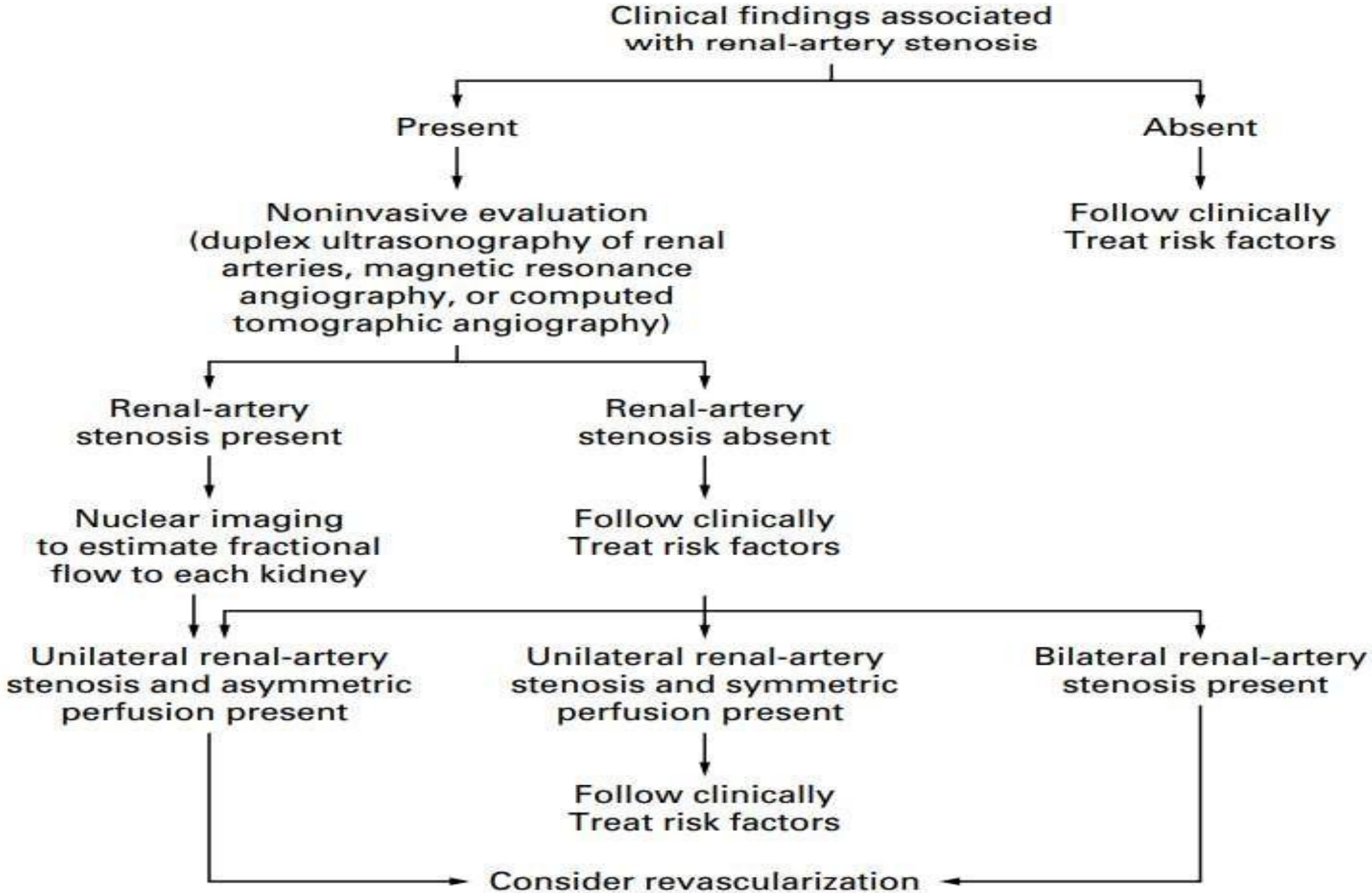
Unexplained progressive renal failure.

Unilateral atrophic kidney.

Abdominal bruit.

Unexplained hypokalemia.




Clinical findings associated with renal-artery stenosis
Present
Absent
Noninvasive evaluation (duplex ultrasonography of renal arteries, magnetic resonance angiography, or computed tomographic angiography)
Follow clinically
Treat risk factors
Renal-artery stenosis present
Renal-artery stenosis absent
Nuclear imaging to estimate fractional flow to each kidney
Follow clinically
Treat risk factors
Unilateral renal-artery stenosis and asymmetric perfusion present
Unilateral renal-artery stenosis and symmetric perfusion present
Bilateral renal-artery stenosis present
Follow clinically
Treat risk factors
Consider revascularization

LANDMARK TRIALS IN

RENAL ARTERY STENOSIS

LANDMARK NEPHROLOGY

1998

EMMA

No difference in BP after angioplasty at 6 months

SCOTTISH AND NEWCASTLE

Lower BP in those with bilateral RAS, but no difference in mortality or CV events

2000

DUTCH RAS

No difference in BP at 12 months, no difference in BP or number of HTN meds or kidney function

2009

STAR

No difference in drop in CrCl with stenting vs not stenting

ASTRAL

No difference in kidney function, BP or CV events

2014

CORAL

No difference in kidney function, BP or CV events

2017

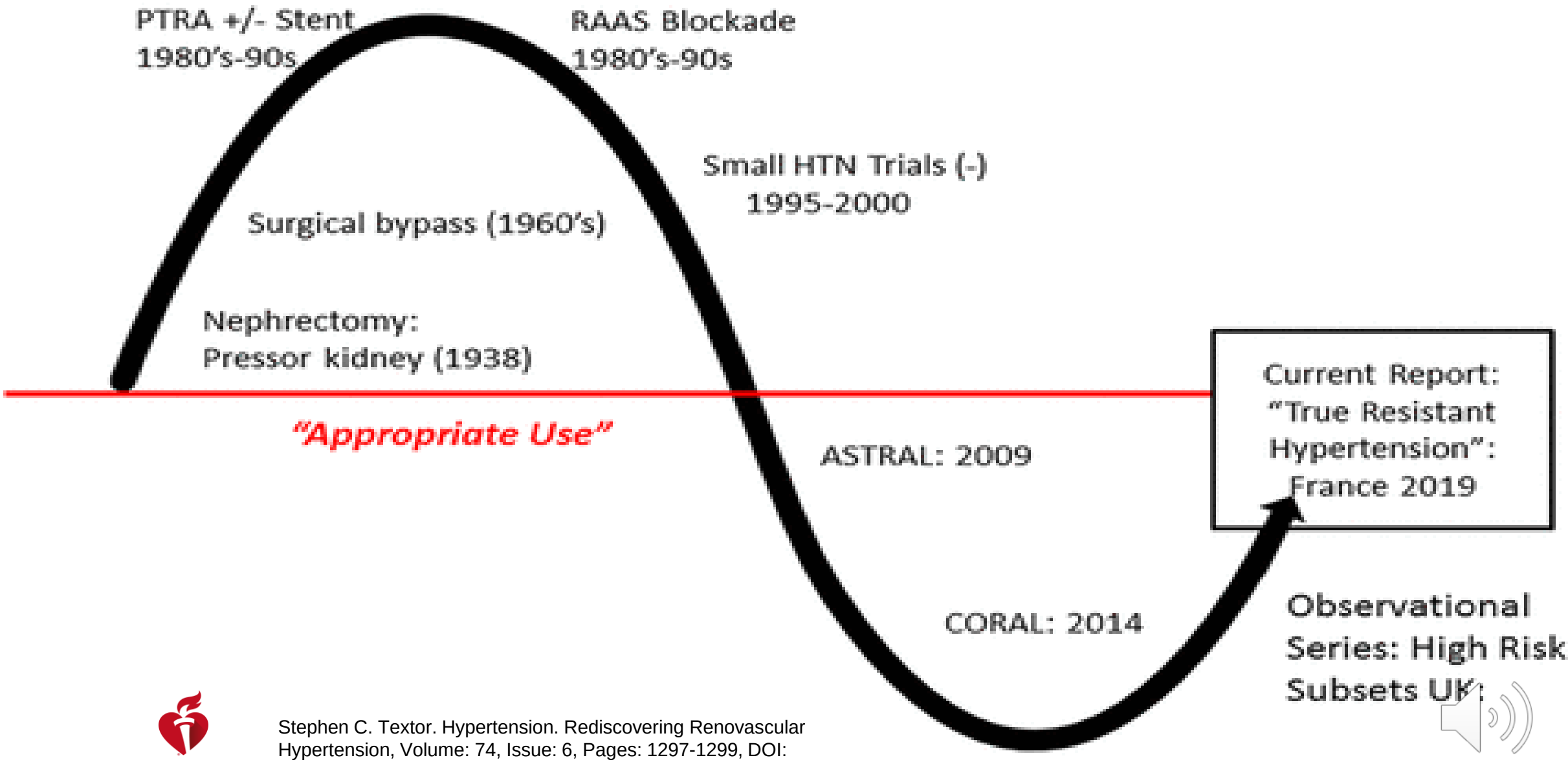
ACC/AHA RAS guidelines

Medical management recommended
If worsening clinically consider revascularization

Prospective RCTs in Renovascular Disease

- **BP Rx** *Webster, et.al: 1998*
  Plouin, et.al. 1998
  Van Jaarsveld, et.al: 2000
- **Renal Function:** *ASTRAL: 2009*
  STAR: 2009
- **Cardiovascular Outcomes:**
  Cooper, et. al. CORAL 2014

Management of Renovascular Hypertension: Enthusiasm for renal revascularization



Stephen C. Textor. Hypertension. Rediscovering Renovascular Hypertension, Volume: 74, Issue: 6, Pages: 1297-1299, DOI: (10.1161/HYPERTENSIONAHA.119.13515)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Revascularization versus Medical Therapy for Renal-Artery Stenosis

The ASTRAL Investigators*

ASTRAL: Eligibility

substantial anatomical atherosclerotic stenosis in at least one renal artery that was considered potentially suitable for endovascular revascularization and if the patient's doctor was uncertain that the patient would definitely have a worthwhile clinical benefit from revascularization, taking into account the available evidence. Patients were not eligible if they required surgical revascularization or were considered to have a high likelihood of requiring revascularization within 6 months, if they had nonatheromatous cardiovascular disease, or if they had undergone previ-

CONCLUSIONS

We found substantial risks but no evidence of a worthwhile clinical benefit from revascularization in patients with atherosclerotic renovascular disease. (Current Controlled Trials number, ISRCTN59586944.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

Christopher J. Cooper, M.D., Timothy P. Murphy, M.D., Donald E. Cutlip, M.D., Kenneth Jamerson, M.D., William Henrich, M.D., Diane M. Reid, M.D., David J. Cohen, M.D., Alan H. Matsumoto, M.D., Michael Steffes, M.D., Michael R. Jaff, D.O., Martin R. Prince, M.D., Ph.D., Eldrin F. Lewis, M.D., Katherine R. Tuttle, M.D., Joseph I. Shapiro, M.D., M.P.H., John H. Rundback, M.D., Joseph M. Massaro, Ph.D., Ralph B. D'Agostino, Sr., Ph.D., and Lance D. Dworkin, M.D., for the CORAL Investigators*

three randomized trials of STAR, ASTRAL and CORAL, there was no evidence of clinical benefit by revascularization with stenting/angioplasty above medical therapy in those with ARAS. All three trials have been criticized for not including enough high-risk patients

A meta-analysis on the these 3 major articles in addition to smaller trials. In total, it combined data from 2222 patients.

In the analysis of positive trials for changes in diastolic BP it demonstrated that this benefit is quite small (2.0 mmHg -2.00 mmHg; 95% CI -3.72 to -0.27) and there was no benefit on decreasing systolic BP.

There was also no difference in kidney function measure by Cr

The decrease in antihypertensive medications in the intervention groups was overall also quite small (MD -0.18; 95% CI -0.34 to -0.03)

There were no increase in adverse events in the intervention groups when compared to the medical management group.

Author: Gates Colbert, MD, FASN
Edited by: Bradley Denker, MD Reviewed: November 2020

LANDMARK TRIALS IN
Renal Artery Stenosis

The 2017 ACC/AHA Hypertension Guidelines have addressed ARAS and treatment guidance.
All patients with ARAS should have medical therapy citing Level 1A
If a patient has failed medical management and continues to have clinical evidence of refractory hypertension, worsening renal function or intractable heart failure, revascularization should be considered.

ACC/AHA do not fully endorse any specific procedure or evidence of outcome benefit.
There are currently several clinical trials looking at devices and other medical treatments to help determine who should benefit from intervention.

Author: Gates Colbert, MD, FASN
Edited by: Bradley Denker, MD

Observational studies have shown that after renal revascularization, ARAS individuals have improvement in their New York Heart Association(NYHA) functional class and fewer hospitalizations for ADHF.

Better controlled blood pressure.

Renal revascularization in addition to coronary intervention for individuals with cardiac destabilization syndromes results in significant improvement in their left ventricular filling pressure

American Journal of Hypertension, 01 Jan 2018, 31(2):139-149

Limitations of Clinical Trials: Atherosclerotic Renal Artery Stenosis

-excluded

most severe cases: CHF

-progressive renal dysfunction

-included

minor lesions

-wide variation in definition of BP goals / achieved levels / renal function

-circulatory congestion / volume control / drugs

-crossovers from medical to interventional arms

-short duration of follow-up

Human Renovascular Disease

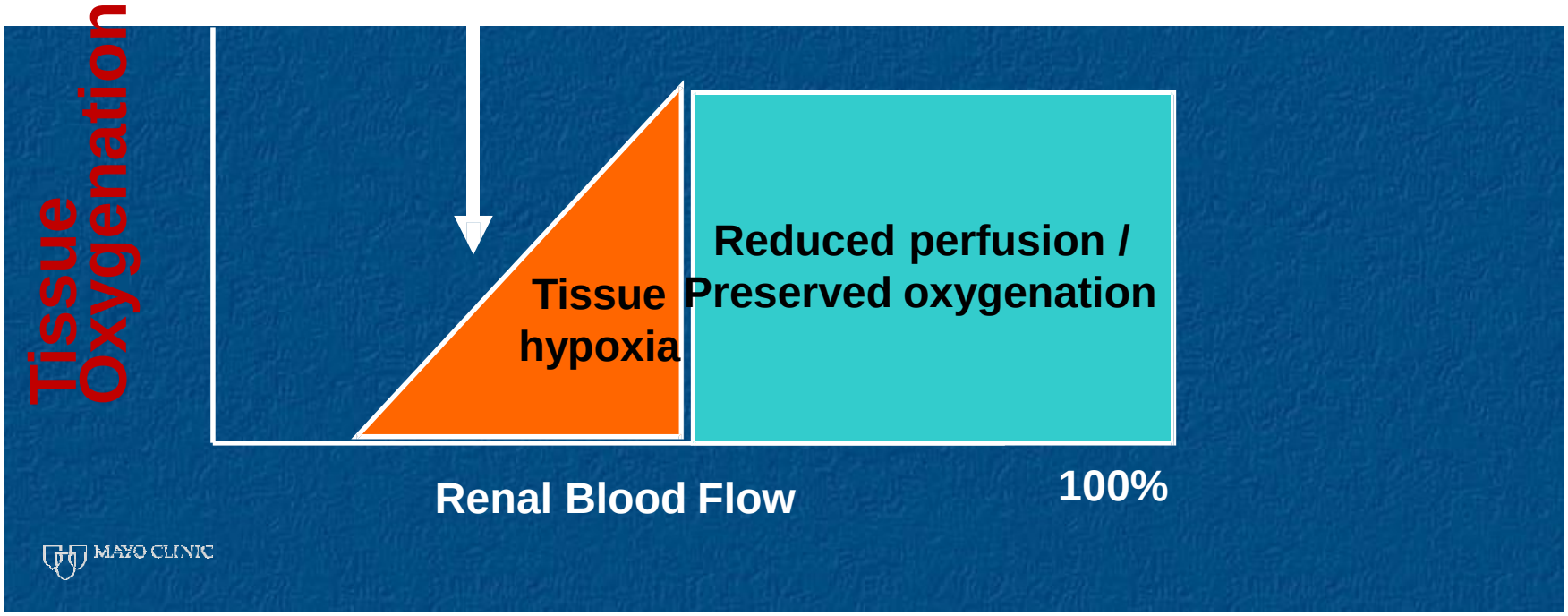
- **Renovascular Hypertension:**
  - **-Renin release**
  - **-can be managed medically**

- **“Adaptation” to reduced blood flow**
  - **-without tissue hypoxia**
  - **-minimal structural damage**

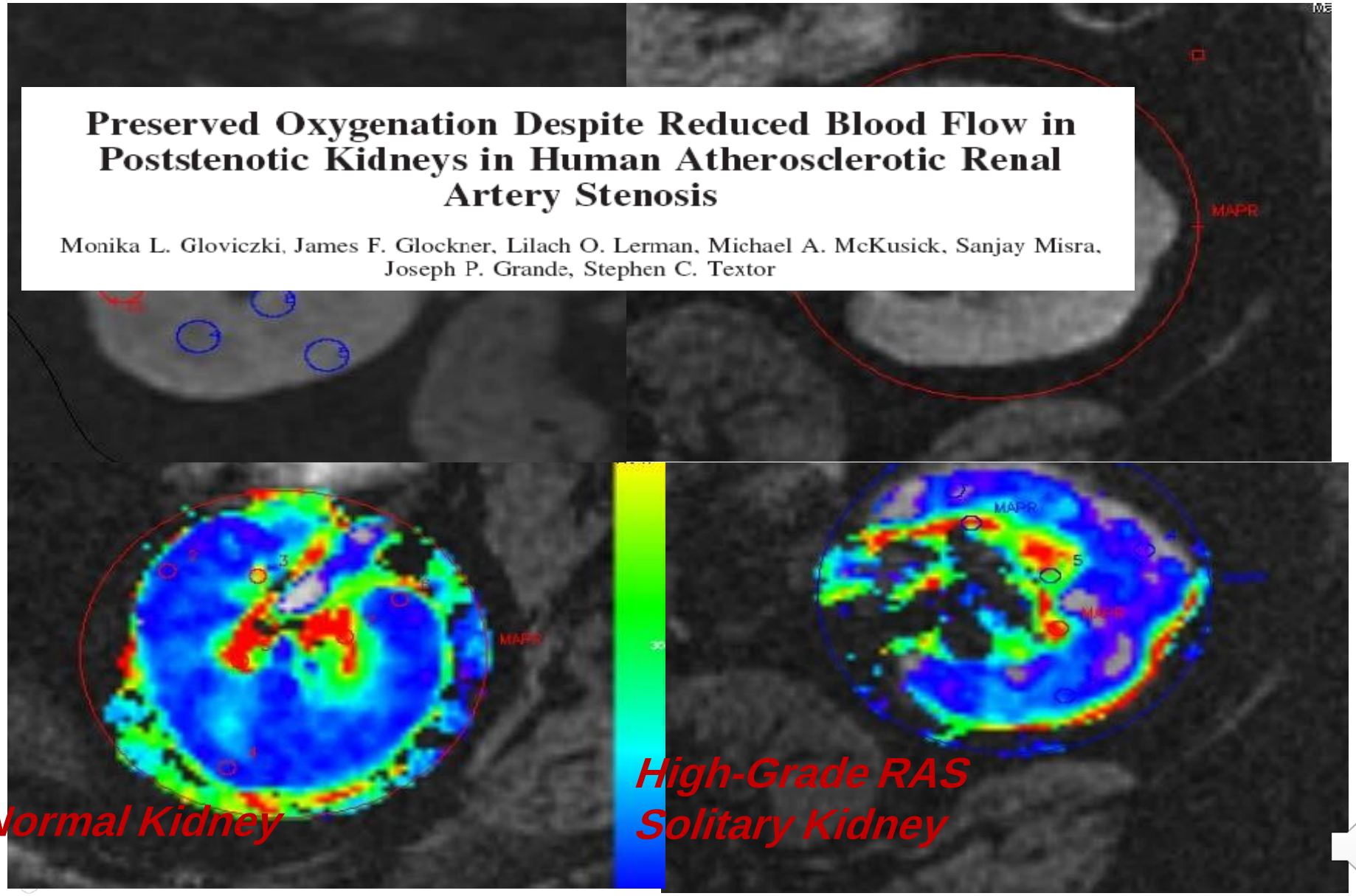
- **Advancing disease: progressive injury**
  - **-?recoverable?**

Adaptation of kidney oxygenation to reduced blood flow

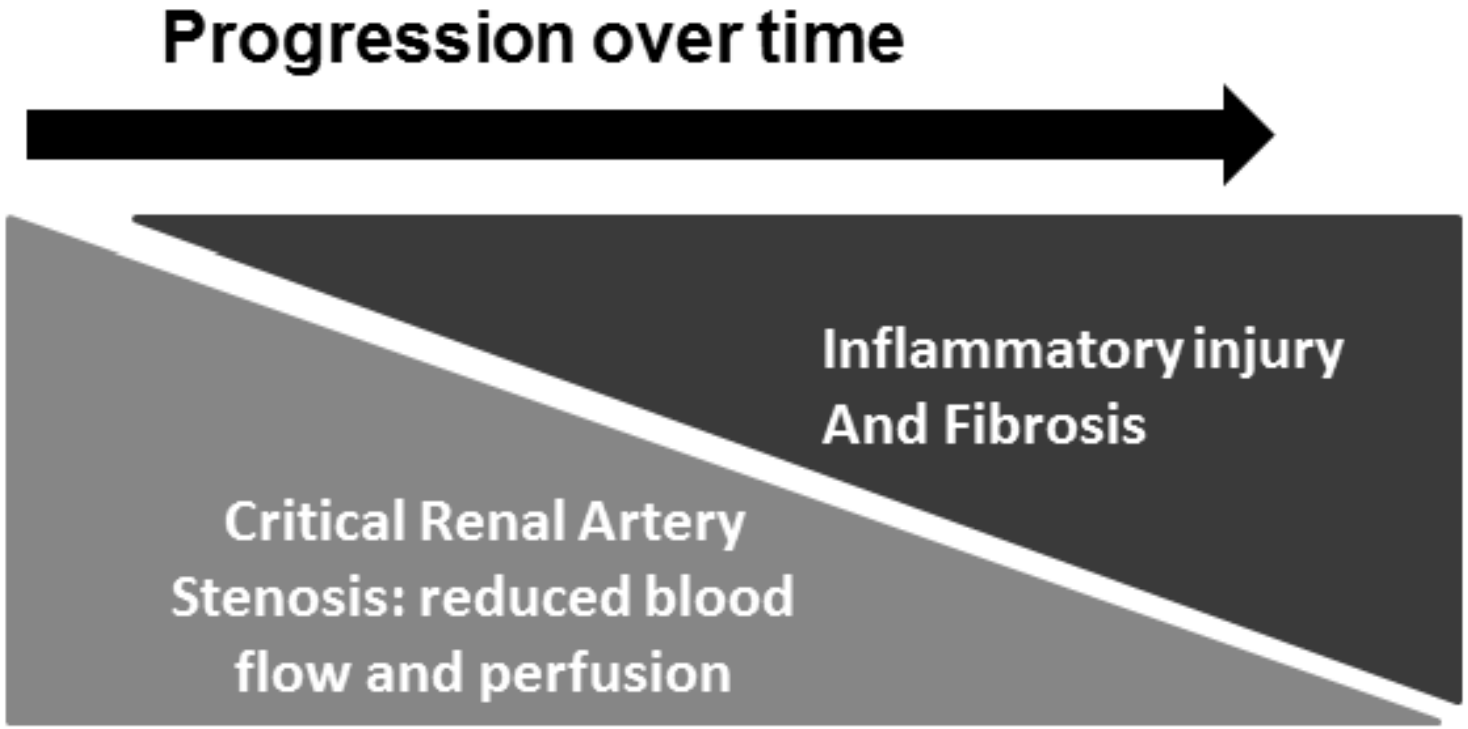
Induction of inflammatory and Fibrogenic pathways



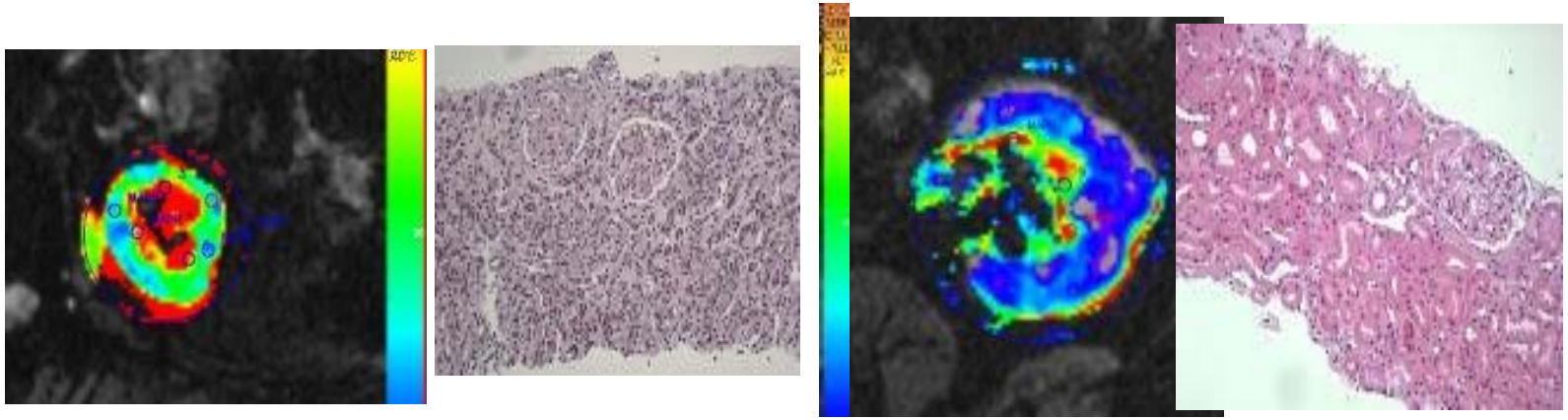
BOLD MR Imaging in Atherosclerotic RAS

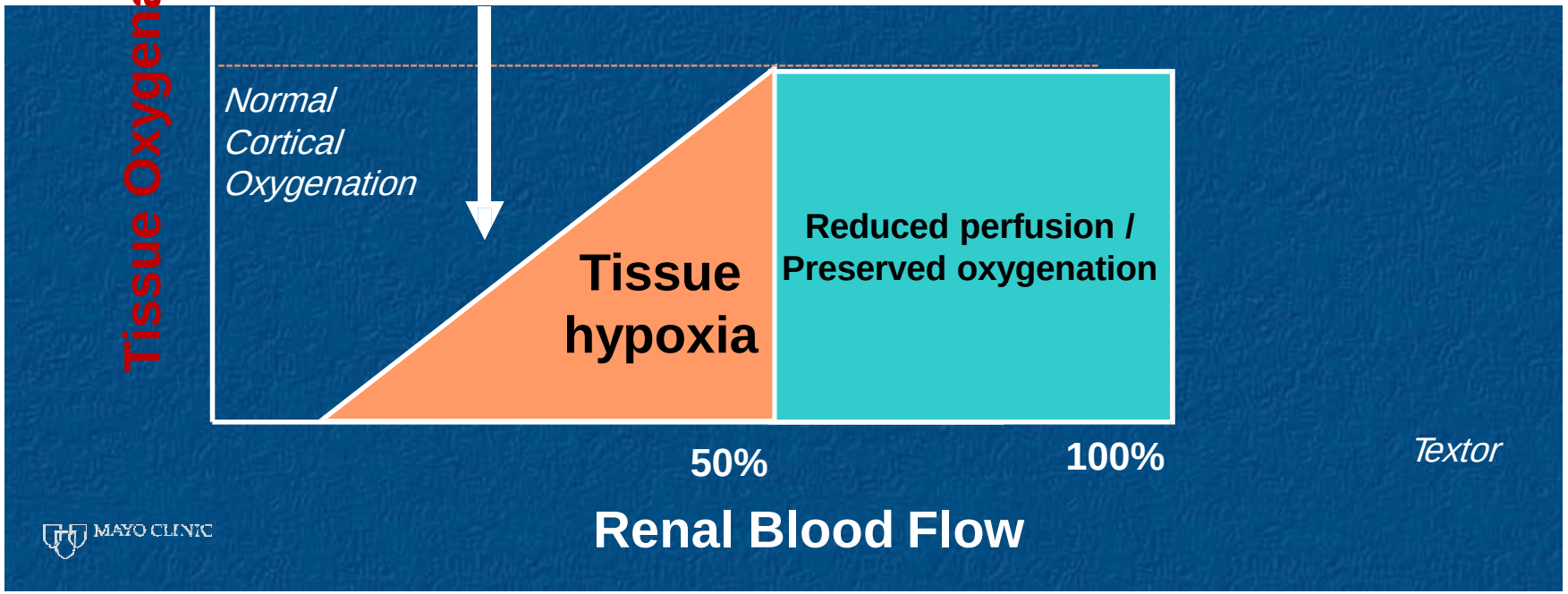


Transition from hemodynamic to inflammatory injury



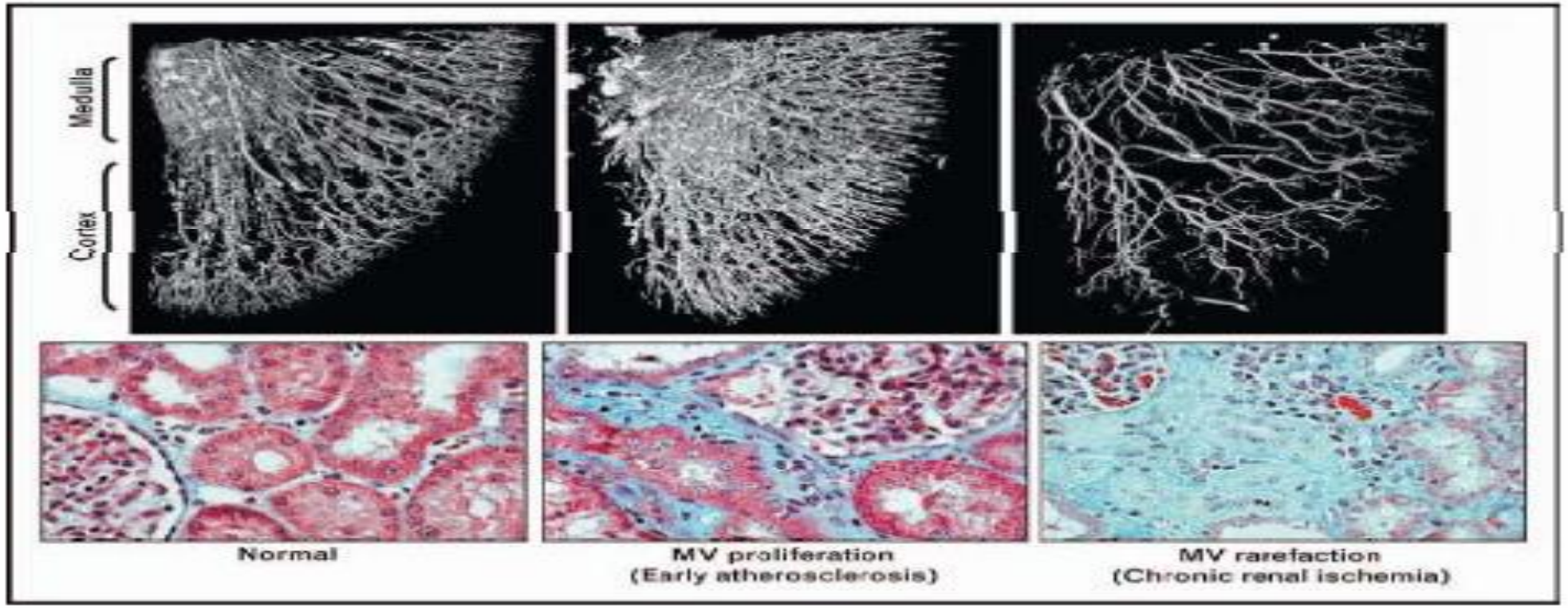
Renovascular Disease and Tissue Oxygenation





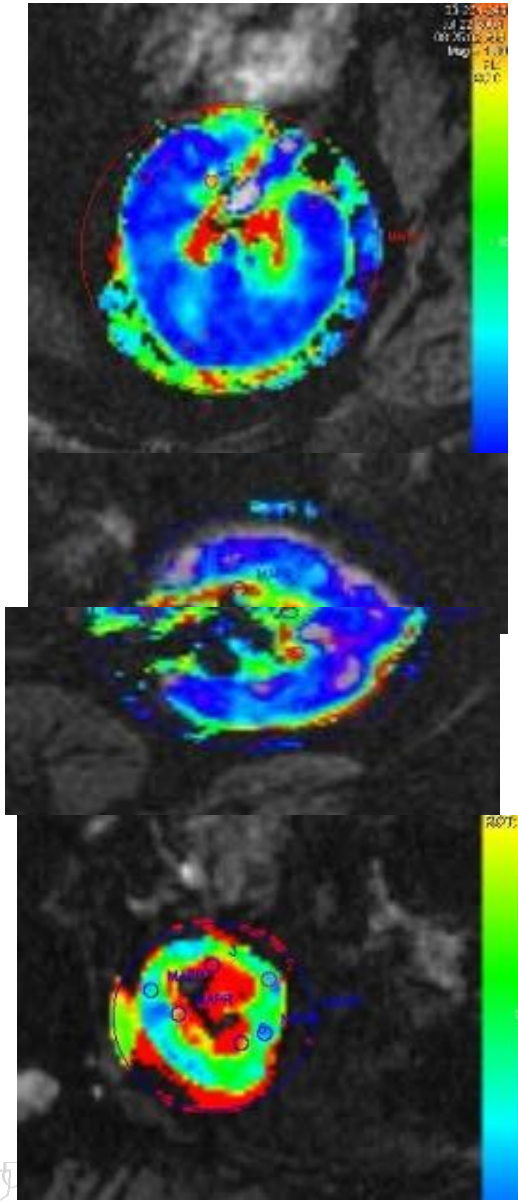
Microvascular rarefaction in Experimental Renal Artery Stenosis

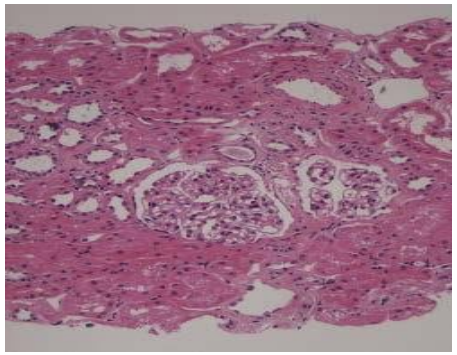
Figure 1 Representative three-dimensional reconstruction of the renal microvascular architecture (using microcomputed tomography) and renal morphology (trichrome staining) showing opposing changes in microvascular architecture in early atherosclerosis compared with chronic ischemia (top) Scale bar (trichrome): 25 µm



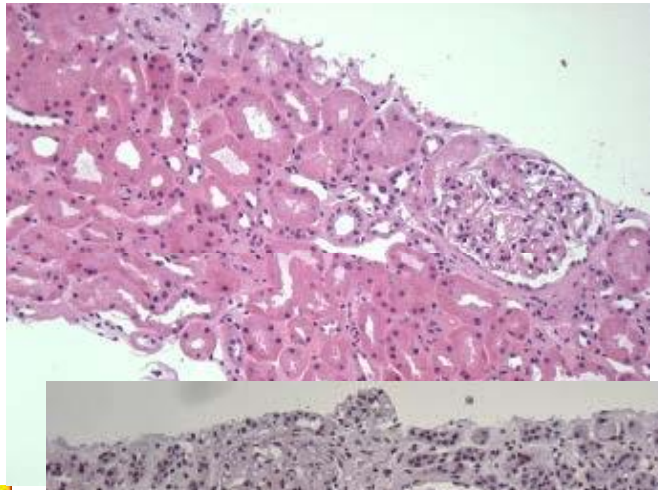
Microvascular rarefaction in particular is accompanied by severe renal fibrosis (bottom). MV, microvascular.

Lerman and Chade, 2008

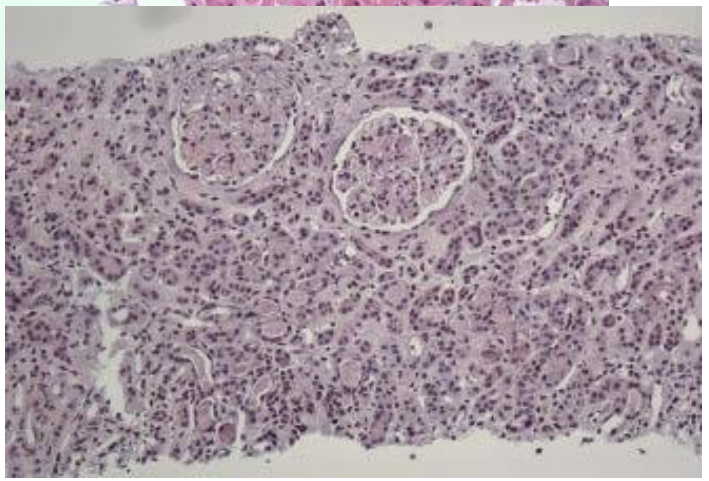




Normal



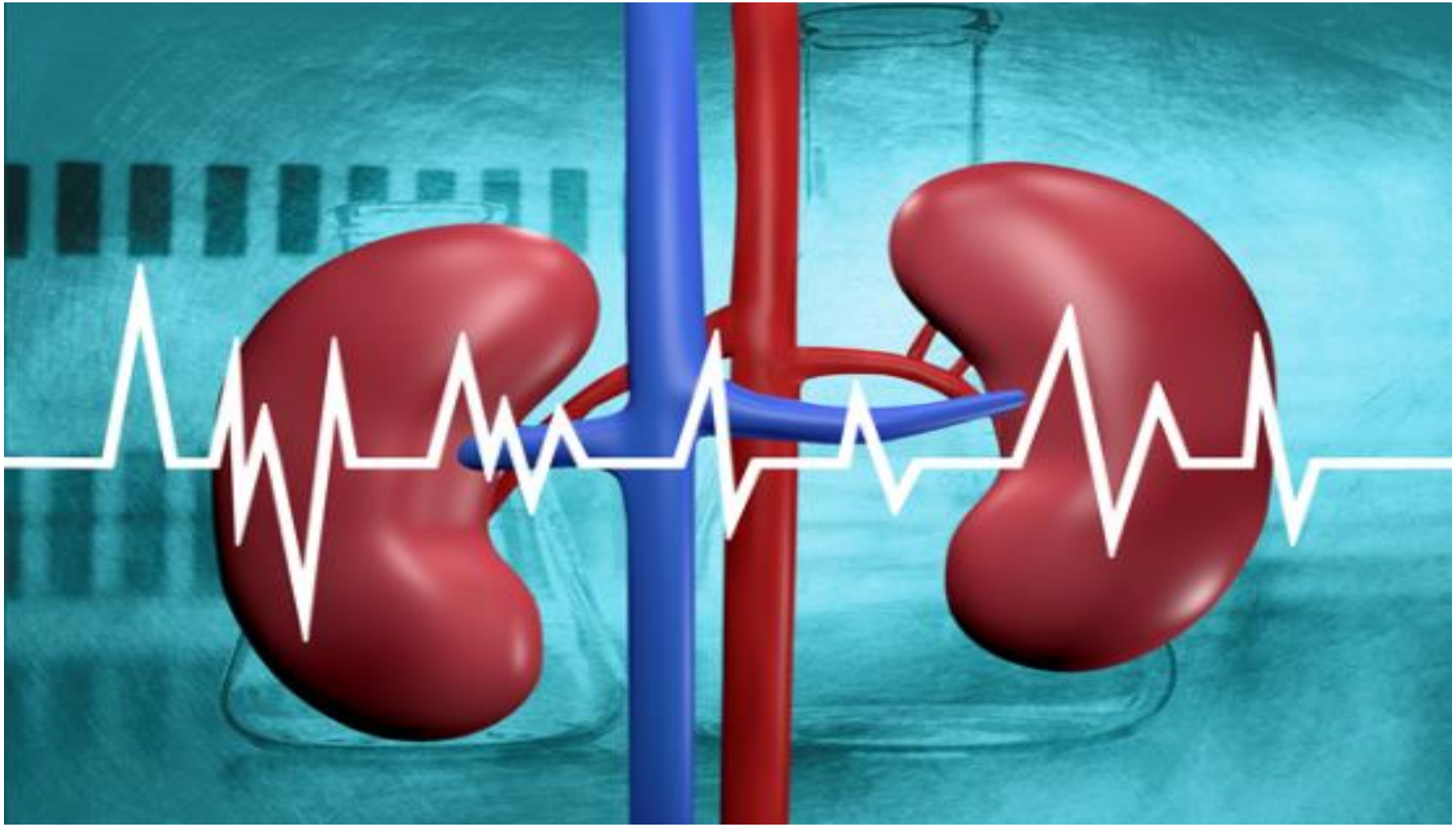
Moderate RAS



Severe RAS

Textor and Lerman, JASN 2015

Renal Artery Stenosis Treatment



Dispelling the myth: the use of renin–angiotensin blockade in atheromatous renovascular disease

Constantina Chrysochou[1], Robert N. Foley[2], James F. Young[1], Kaivan Khavandi[1], Ching M. Cheung[1] and Philip A. Kalra[1]

[1]Renal department, Salford Royal Hospital, Manchester Academic Health Science Centre, The University of Manchester, Salford, UK and [2]Chronic Disease Research Group, School of Medicine, University of Minnesota—Twin Cities, Minneapolis, MN, USA

N=621 ARVD registry patients

-Prospective: 357/378 tolerated RAB (92%)

-54/78 (78%) of Bilateral ARVD

Multivariate time-adjusted analysis:

HR for Death 0.61 (0.40-0.91) p=.02

Nephrol. Dial.Transpl. 27:1403, 2012

Many patients can be treated with medical Therapy with no loss of renal function

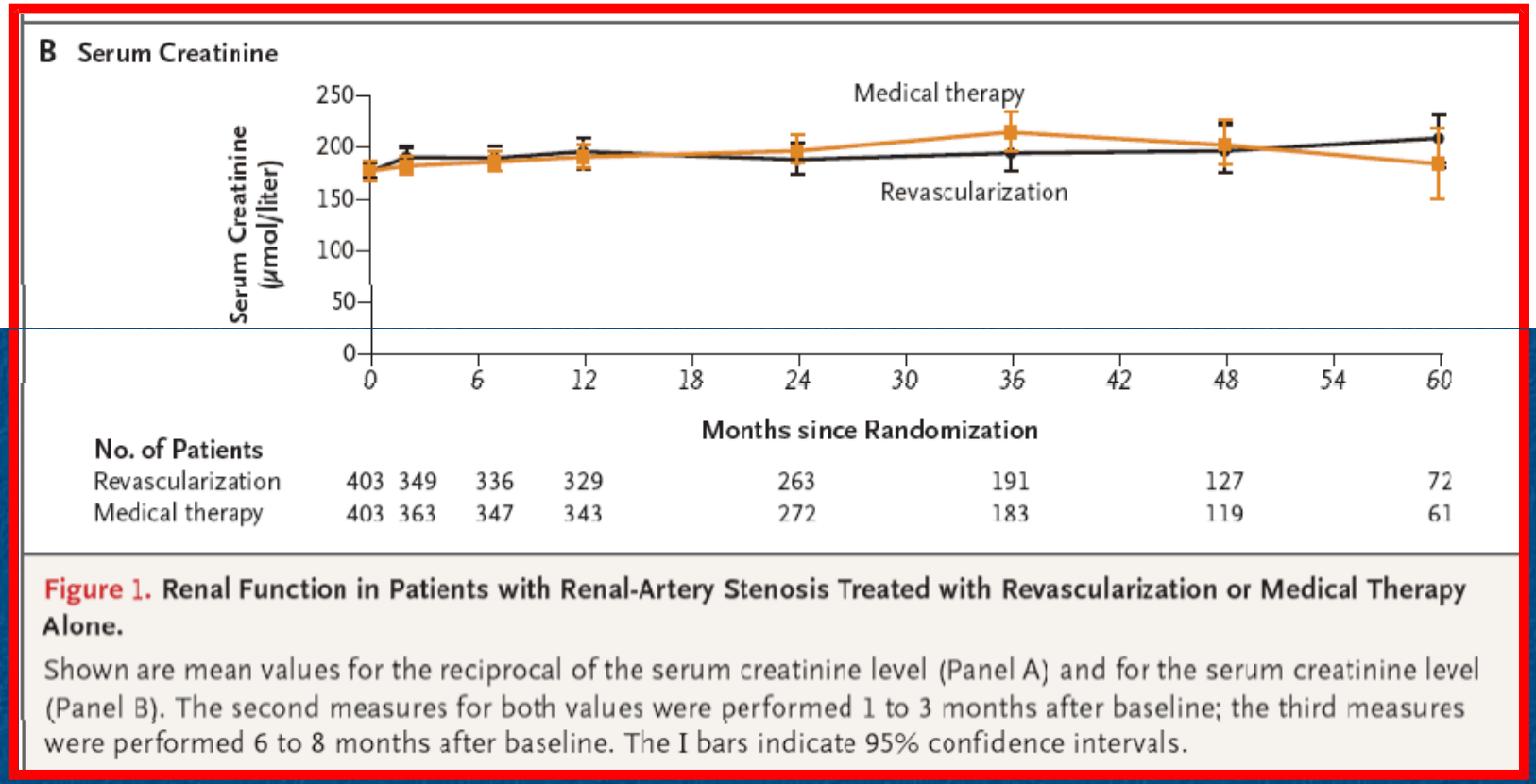


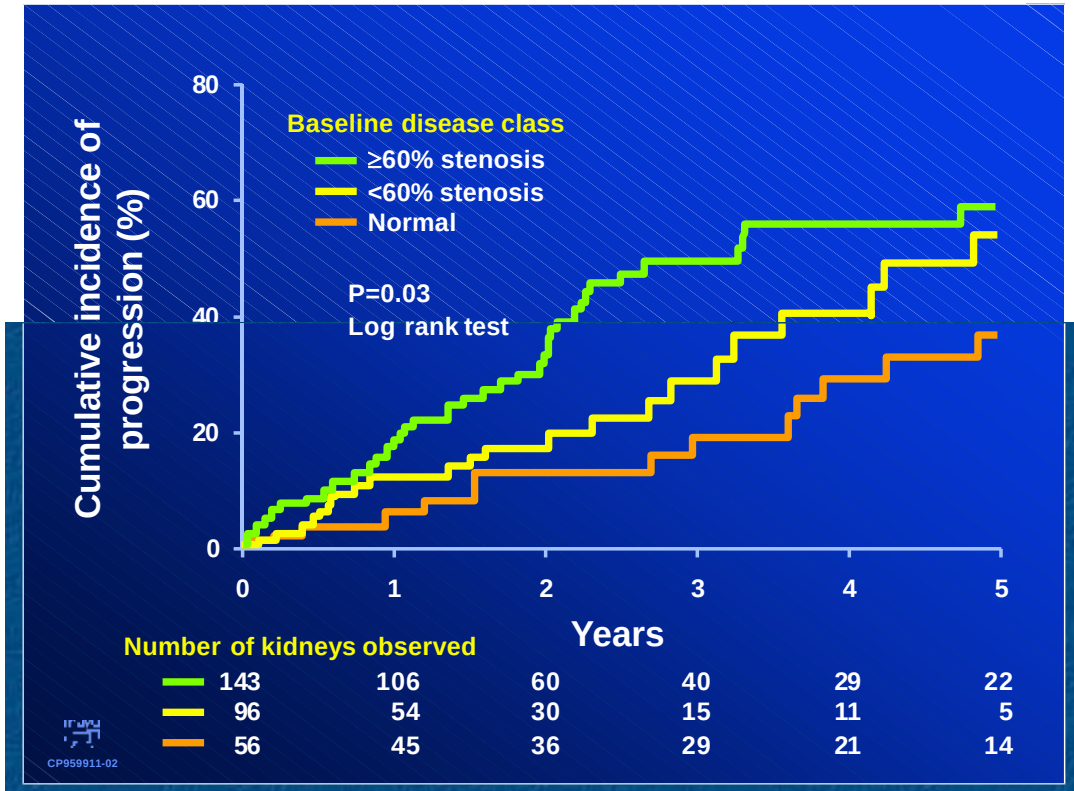
Figure 1. Renal Function in Patients with Renal-Artery Stenosis Treated with Revascularization or Medical Therapy Alone.

Shown are mean values for the reciprocal of the serum creatinine level (Panel A) and for the serum creatinine level (Panel B). The second measures for both values were performed 1 to 3 months after baseline; the third measures were performed 6 to 8 months after baseline. The I bars indicate 95% confidence intervals.

The ASTRAL Investigators: N.Engl.J.Med. 361, 2009

MAYO CLINIC

"Prospective Study of Atherosclerotic Disease Progression in the Renal Artery"



N=170 patients with study of 295 renal arteries by serial duplex scans between 1990 and 1997

Total Occlusion: 9/295 arteries (3%)

Caps, et. al. : Circulation 98: 2866-2872, 1998

MAYO CLINIC

Medical Therapy

ACC/AHA, ESC and SCAI all prefer medical therapy as the first-line treatment for RAS

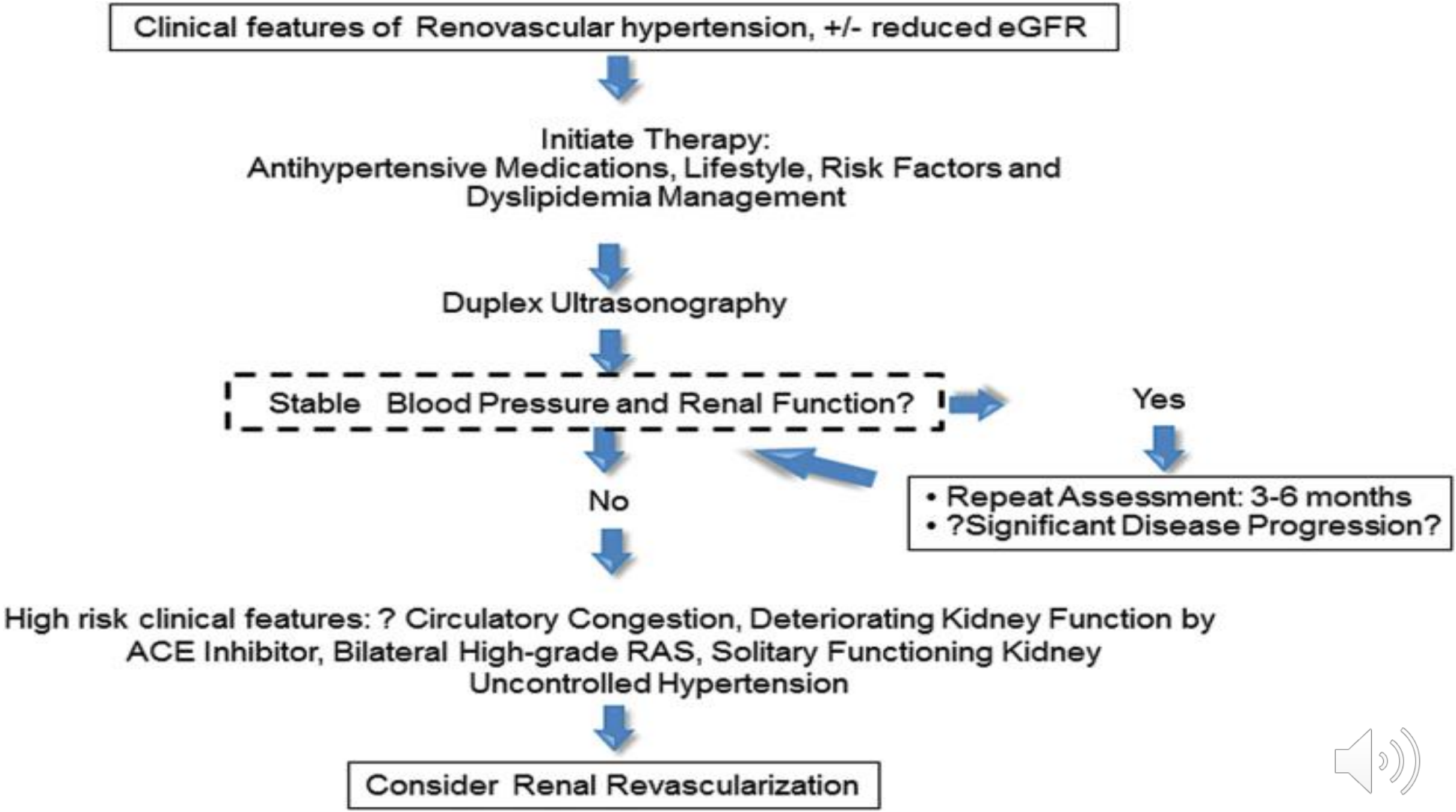
ACC/AHA and ESC recommend ACE inhibitors, ARBs, and calcium channel blockers for unilateral RAS

but ESC advises that patients with bilateral severe RAS or RAS in a single functional kidney require very careful monitoring

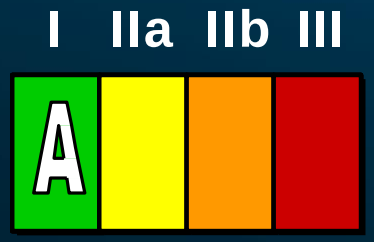
The ACC/AHA also recommends beta-blockers for treatment of hypertension associated with RAS.

The invasive and surgical options for treatment

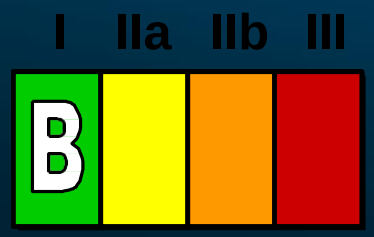
Percutaneous transluminal angioplasty (PTA)
Surgical revascularization
Nephrectomy


Clinical features of Renovascular hypertension, +/- reduced eGFR
Initiate Therapy:
Antihypertensive Medications, Lifestyle, Risk Factors and
Dyslipidemia Management
Duplex Ultrasonography
Stable Blood Pressure and Renal Function?
Yes
• Repeat Assessment: 3-6 months
• ?Significant Disease Progression?
No
High risk clinical features: ? Circulatory Congestion, Deteriorating Kidney Function by
ACE Inhibitor, Bilateral High-grade RAS, Solitary Functioning Kidney
Uncontrolled Hypertension
Consider Renal Revascularization

Pharmacological Treatment of Renal Artery Stenosis



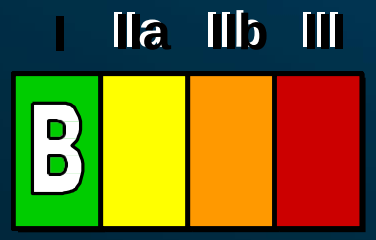
- ACE inhibitors are effective medications for treatment of hypertension associated with RAS.
- Calcium-channel blockers are effective medications for treatment of hypertension associated with unilateral RAS.
- Beta-blockers are effective medications for treatment of hypertension associated with RAS.



- Angiotensin receptor blockers are effective medications for treatment of hypertension associated with unilateral RAS.

ACC/AHA Guidelines

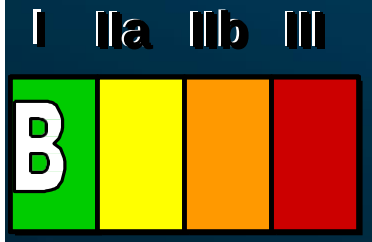
CATHETER- BASED INTERVENTIONS FOR RAS



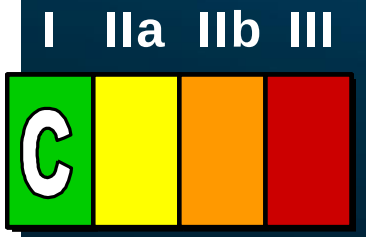
- Renal stent placement is indicated for ostial atheroesclerosic RAS lesions that meet the clinical crietria for intervention.
- Balloon angioplasty with “bail-out” stent placement if necessary is recommended for fibromuscular dysplasia lesions.

ACC/AHA Guidelines

SURGERY FOR RENAL ARTERY STENOSIS



- Fibromuscular dysplastic RAS with clinical indications, or extending
  - into the segmental arteries and those having ,macroaneurysms.
- Atheroeclerotic RAS and clinical indications for intervention, Ormultiple small renal arteries or early primary branching of the main renal artery.



- Atherosclerotic RAS in combination with pararenal aortic reconstructions (in treatment of aortic aneurysms or severe aortoiliac occlusive diseease.

ACC/AHA Guidelines

Series of PTRA in FMD:

Slovut and Olin, NEJM, 2004

Table 2. Results of Percutaneous Transluminal Angioplasty of the Renal Arteries in Patients with Fibromuscular Renovascular Disease and Hypertension.*

Study	Year	No. of Patients	Technical Success Rate	Effect on Blood Pressure			Months of Follow-up	Complication Rate
				Cured	Improved	Unimproved		
			%		%		*mean (range)*	%
Sos et al.[57]	1983	31	87	59	34	7	16 (4–40)	6
Baert et al.[58]	1990	22	83	58	21	21	26 (6–72)	NR
Tegtmeyer et al.[59]	1991	66	100	39	59	2	39 (1–121)	13
Bonelli et al.[60]	1995	105	89	22	63	15	43 (0–168)	11 (major)
Jensen et al.[61]	1995	30	97	39	47	14	12 (NR)	3 (major) 12 (minor)
Davidson et al.[62]	1996	23	100	52	22	26	NR	13
Klow et al.[63]	1998	49	98	26	44	30	9 (1–96)	0
Birrer et al.[64]	2002	27	100		74†	26	10 (NR)	7.4
Surowiec et al.[65]	2003	14	95		79†	21	NR	28.5
de Fraissinette et al.[66]	2003	70	94	14	74	12	39 (1–204)	11

* NR denotes not reported.
† The percentage shown is the total for cured and improved.

TABLE 1 Current Society for Cardiovascular Angiography and Interventions Appropriate Use Criteria and American Heart Association/American College of Cardiology Recommendations (11,35,39)

Scenario	SCAI Appropriate Use Criteria	AHA/ACC Recommendations
Cardiac disturbance syndromes (flash pulmonary edema, unstable angina, or ACS) with hypertension with moderate RAS with a resting translesional mean gradient of ≥10 mm Hg and/or severe RAS	Appropriate	Class I, Level of Evidence: B; Class IIa, Level of Evidence: B (unstable angina)
CKD stage IV with bilateral moderate RAS with a resting translesional mean gradient of ≥10 mm Hg with a kidney size >7 cm in pole-to-pole length	Appropriate	Class IIa, Level of Evidence: B
CKD stage IV and global renal ischemia (unilateral severe RAS with a solitary kidney or bilateral severe RAS) without another explanation	Appropriate	Class IIb, Level of Evidence: B
Resistant hypertension (uncontrolled hypertension having failed maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic agent) and bilateral or solitary severe RAS	Appropriate	Class IIa, Level of Evidence: B
Recurrent CHF with unilateral moderate RAS with a resting translesional mean gradient of ≥10 mm Hg	May be appropriate	Class I, Level of Evidence: B
Resistant hypertension (uncontrolled hypertension having failed maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic agent) and unilateral severe RAS	May be appropriate	Class IIa, Level of Evidence: B
Asymptomatic, unilateral, bilateral, or solitary kidney with hemodynamically significant RAS	Rarely appropriate	Class IIb, Level of Evidence: C

ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; CHF = congestive heart failure; RAS = renal artery stenosis; SCAI = Society for Cardiovascular Angiography and Interventions.

PTRA with stenting and medical therapy

Unilateral renal artery stenosis, bilateral renal artery stenosis, or stenosis of a solitary kidney and meet one or more of the following criteria

1. Recurrent congestive heart failure or sudden unexplained pulmonary edema

2. Unstable angina

3. Accelerated, resistant, or malignant hypertension

4. Hypertension with unexplained unilateral small kidney and intolerance to medication

Renal Revascularization

Severe ARAS

- luminal stenosis of >70%,
- stenosis is between 50% and 70% a trans-stenotic peak pressure gradient greater than 20 mmHg
- Mean pressure gradient greater than 10 mmHg is required.

.Revascularization in patients with severe ARAS is indicated :

- (i) cardiac destabilization syndromes :flash pulmonary edema with severe hypertension,
- (ii) resistant (refractory) hypertension
- (iii) rapidly progressive ischemic nephropathy,
- chronic kidney disease with GFR less than 45 cc/min/m2
- global renal ischemia

PTRA is most effective ;

- Mid vessel stenosis.
- The ostia of renal arteries

.

Integrated Blood Pressure Control 2020:13 71–82

Patients with nearly or completely occluded vessels, are believed to have worse outcomes after revascularization.

Ultrasound evidence of high resistance indices ≥0.8,
Marked renal atrophy (size <7 cm),
Absent function measured by split nuclear scan,
Significant albuminuria (Proteinuria >1 g/day
Hemodialysis for >3 months

Predictors of benefit regarding both improvement in BP and recovery of kidney function depend strongly on the duration of the abnormality.

Follow-Up

DUS is the recommended imaging technique to screen for in stent restenosis (ISR).

DUS is defined restenosis by greater than 70% stenosis and peak systolic velocity (PSV)greater than 395 cm/s

Patients should have routine 30-day,3-month, 6-month, 12-month and annual clinical, laboratory ,and DUS follow-up for surveillance of ISR

Complications of Renal Artery Stenting

Minor:

Groin Hematoma **N=40**

Major:

Renal Failure **N=34 (3 “fatal”)**

Segmental Infarction **N=9**

Perinephric Hematoma **N=9**

Renal artery thrombosis/occlusion **N=6**

Stent misplacement **N=5**

Other: proteinuria/ sepsis
cholesterol embolism,
iliac artery dissection

Overall:
9% Major Events

Meta-analysis: n=14 reports, n=678 patients

Outcome after PTA

Outcome better in patients FMD, than in those with atherosclerotic stenosis:

Restenosis necessitating repeat angioplasty was reported in fewer than 10% of patients with FMD and in 8-30% of those with atherosclerotic stenosis

.

Improvement in blood pressure control with fewer antihypertensive medications was achieved in 30-35% of patients with FMD and 50-60% of those with atherosclerotic lesions.

American Journal of Hypertension, 01 Jan 2018, 31(2):139-149

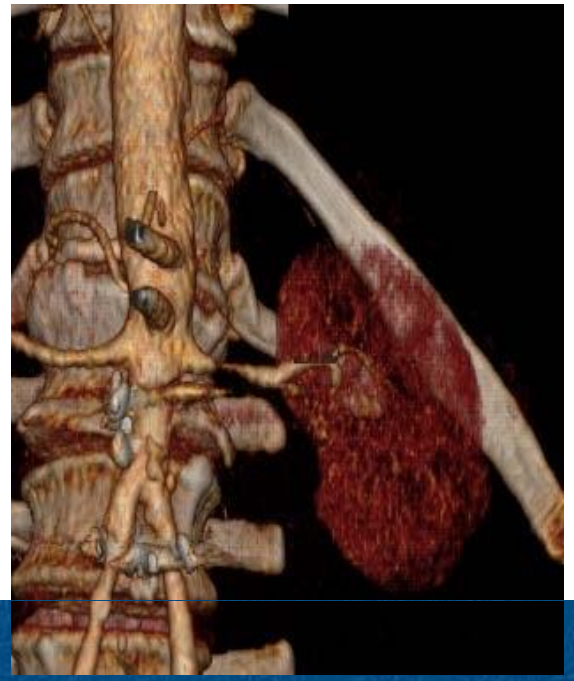
Human Renovascular Disease

- **Renovascular Hypertension:**
  - **-Renin release**
  - **-can be managed medically**

- **“Adaptation” to reduced blood flow**
  - **-without tissue hypoxia**
  - **-minimal structural damage**

- **Advancing disease: adequate blood flow for tissue oxygenation?**

- **progressive injury -?recoverable?**



“Ischemic nephropathy”? : Definition

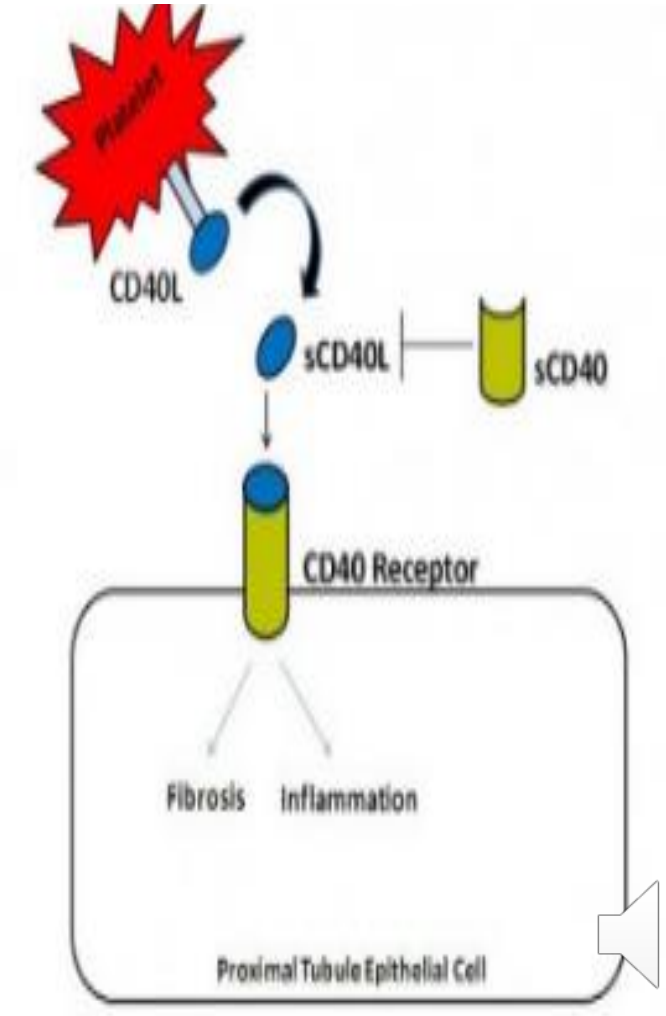
1. **“Hemodynamically significant” main renal artery disease**
2. **Loss of function (GFR) due to vascular insufficiency**
3. **?”ischemia”**

Steven T Haller

Mechanisms and Treatments for Renal Artery Stenosis

Published on December 4, 2013

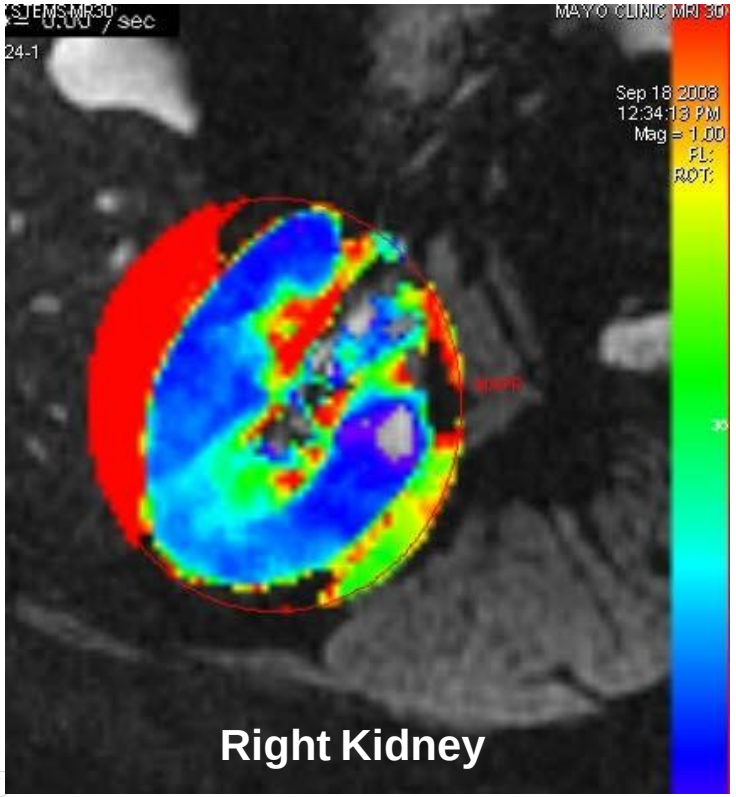
- CD40, a type-I transmembrane receptor and a member of the tumor necrosis factor (TNF) receptor superfamily, is expressed on the, cells and critically links thrombosis, inflammation, immunity, and fibrosis (Antoniades *et al.*, 2009)
- Angiotensin II, released ,during renal ischemia, increases TGF-β, which in turn increases expression of CD40 (Starke *et al.*, 2007).
- CD40 activation increases antigen-specific recognition and killing of tubular epithelial cells by cytotoxic CD8+ T cells (Starke *et al.*, 2007).
- In ARAS ,platelet-derived sCD40L travels from the atherosclerotic lesion to the kidney and activates CD40 on the proximal tubules resulting in inflammation, injury, and renal fibrosis



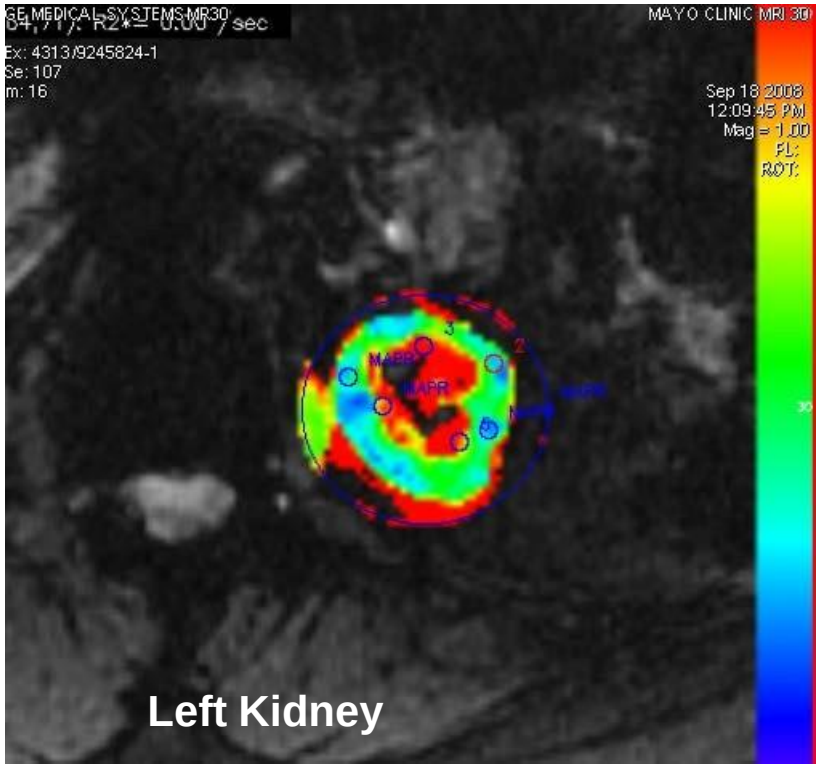
Kidney

Blood Oxygen Level–Dependent Magnetic Resonance Imaging Identifies Cortical Hypoxia in Severe Renovascular Disease

Monika L. Gloviczki, James F. Glockner, John A. Crane, Michael A. McKusick, Sanjay Misra, Joseph P. Grande, Lilach O. Lerman, Stephen C. Textor

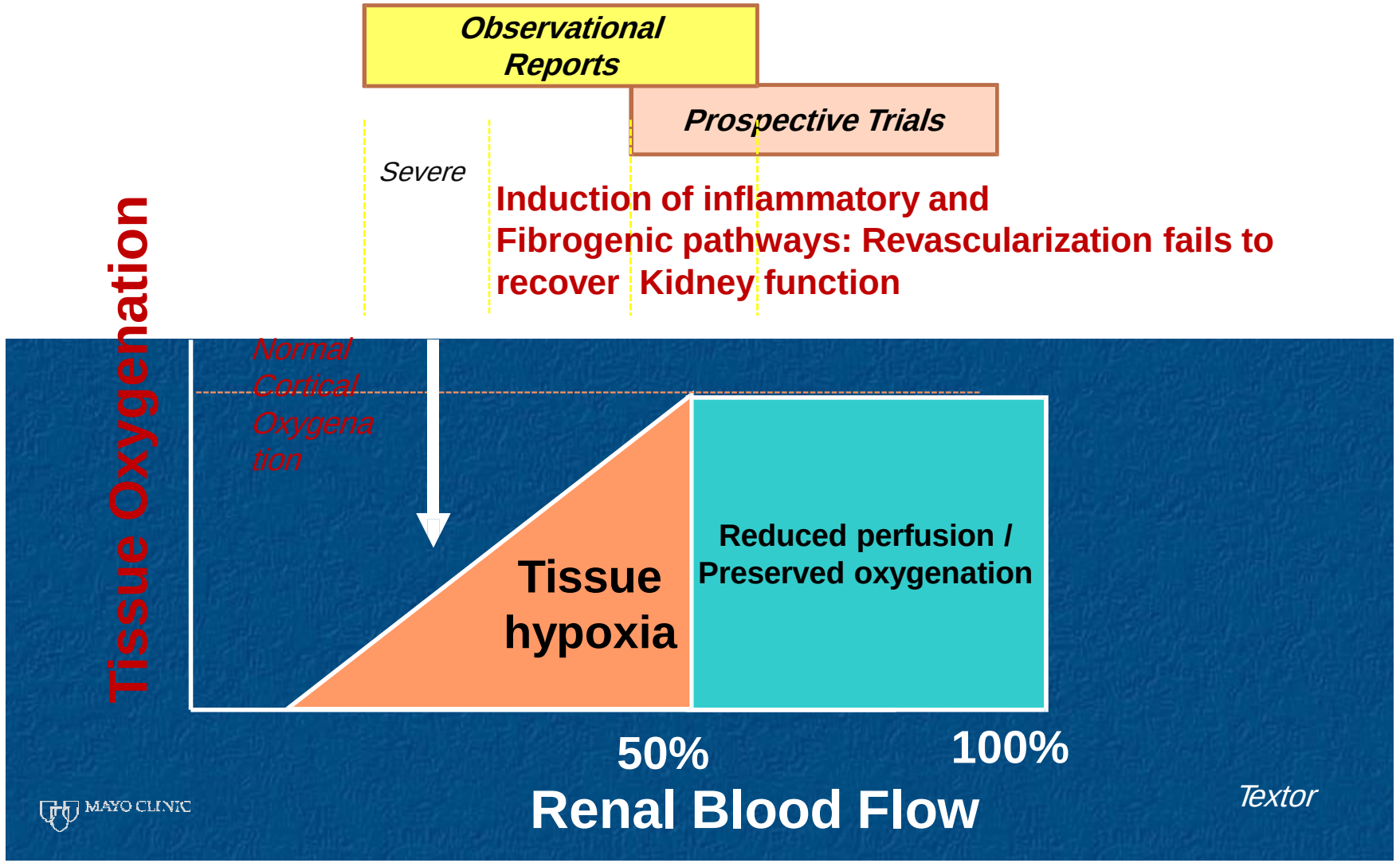


Right Kidney



Left Kidney

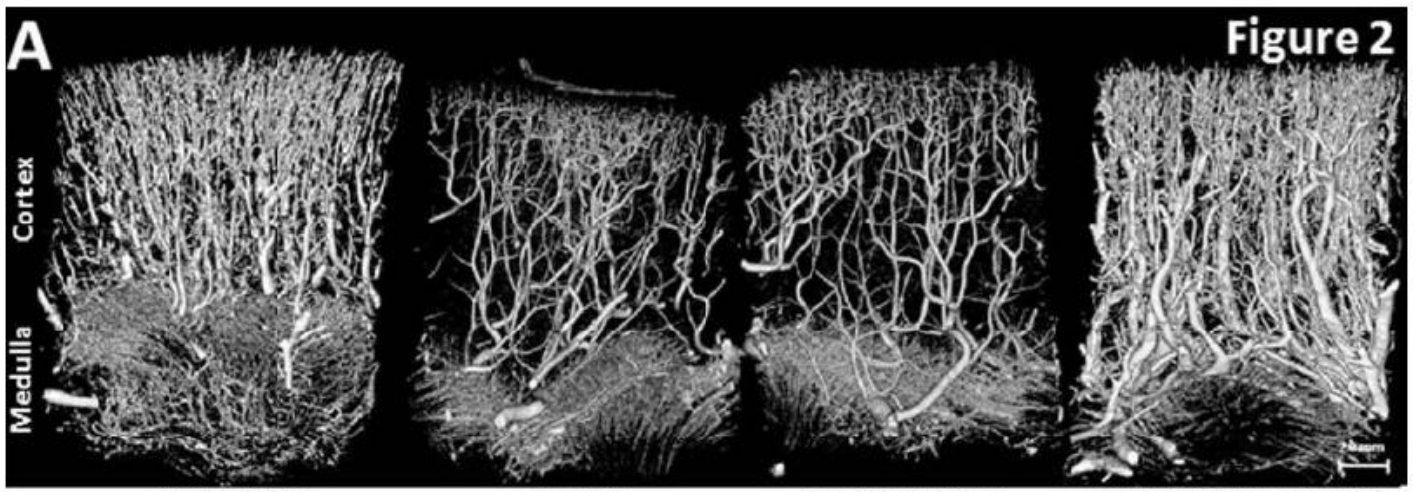
Renovascular Disease : Beyond CORAL



STEM CELLS®
30:1030-1041, 2012
TRANSLATIONAL AND CLINICAL RESEARCH

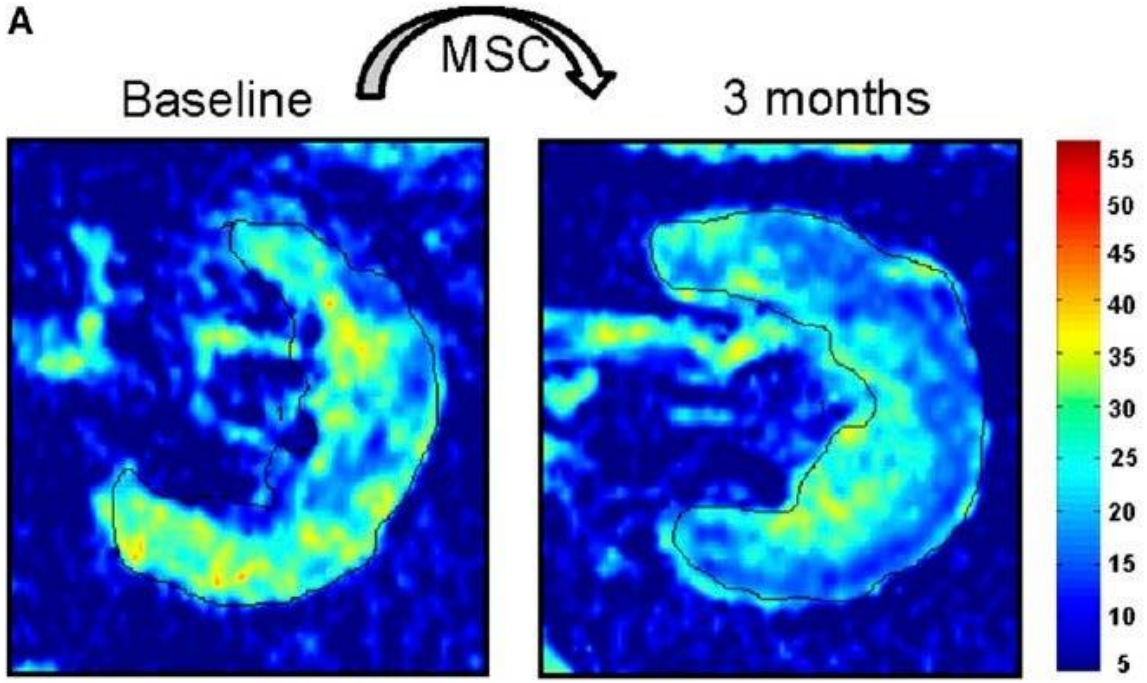
Adipose Tissue-Derived Mesenchymal Stem Cells Improve Revascularization Outcomes to Restore Renal Function in Swine Atherosclerotic Renal Artery Stenosis

Alfonso Eirin, MD[1], Xiang-Yang Zhu, MD, PhD[1], James D. Krier[1], Hui Tang, MD, PhD[1], Kyra L. Jordan[1], Joseph P. Grande, MD, PhD[1,2], Amir Lerman, MD[3]; Stephen C. Textor, MD[1], Lilach O. Lerman, MD, PhD[1,3]



Autologous Mesenchymal Stem Cells Increase Cortical Perfusion in Renovascular Disease

Ahmed Saad,* Allan B. Dietz,† Sandra M.S. Herrmann,* LaTonya J. Hickson,* James F. Glockner,‡ Michael A. McKusick,§ Sanjay Misra,§ Haraldur Bjarnason,§ Adam S. Armstrong,† Dennis A. Gastineau,† Lilach O. Lerman,* and Stephen C. Textor*



Fractional Hypoxia (>30%) fell from 12.1% to 6.8% After 3 months (p=.03)

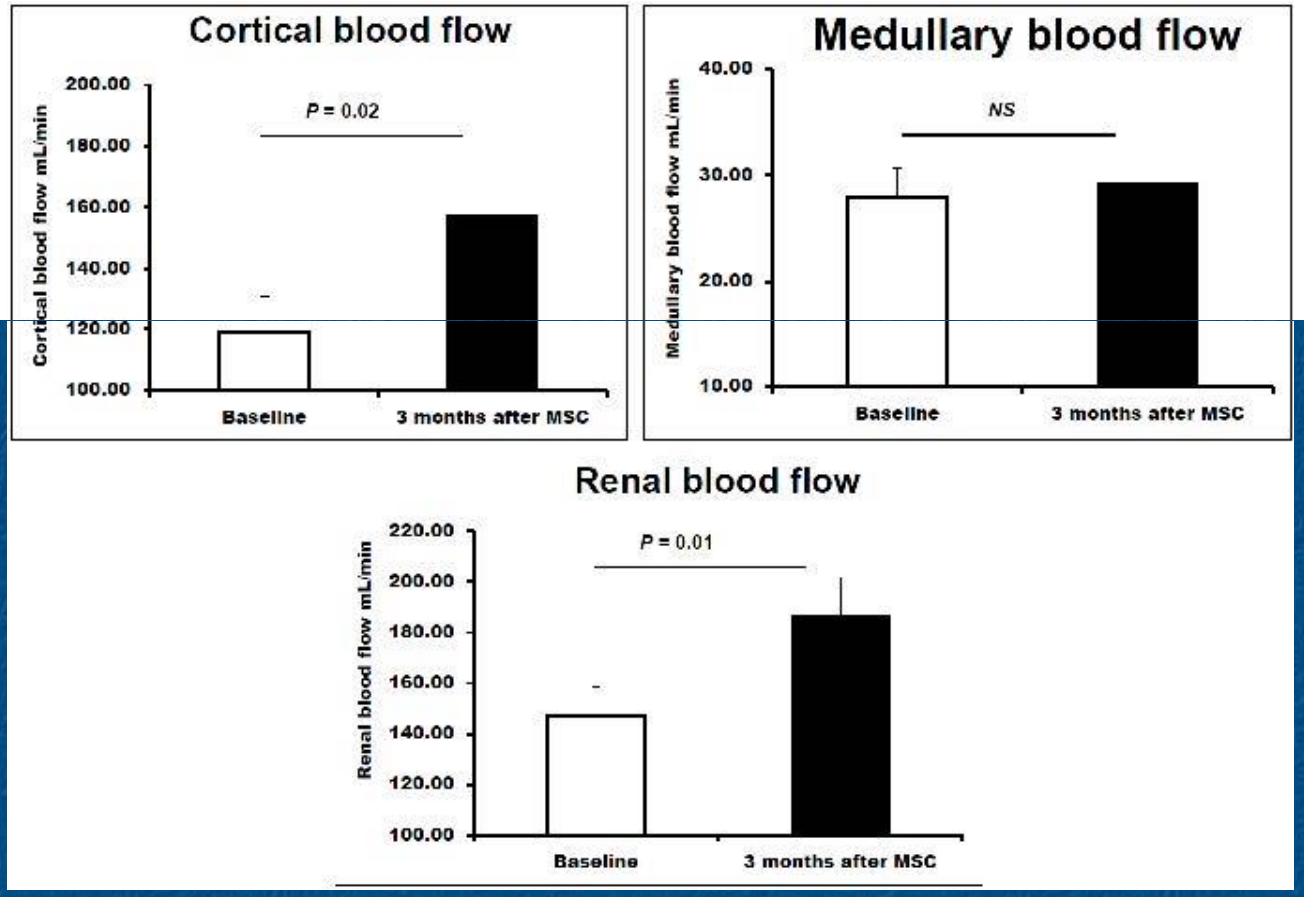
2. Repair / Regeneration after kidney injury: macrophages and mesenchymal stromal/stem cells

-angiogenesis

-immunomodulation

Am Soc Nephrol. 2017; 28(9):2777-2785.

Intra-arterial MSC increase cortical perfusion in human ARVD



MAYO CLINIC

Textor 2017

An integrated approach and future directions in the management of RVH.

Sampling of the renal vein effluents indicate cytokine profiles that are proinflammatory and may be partially protective against repetitive episodes of hypoperfusion, suggestive of “ischemic preconditioning

low baseline levels of the soluble CD40 receptor are associated with a loss of renal function in patients with renal artery stenosis at one-year follow-up (Haller *et al.*, 2013).

Mesenchymal stem cell therapy to stimulate angiogenesis and restore tissue oxygenation in experimental and human ARAS, offering the potential to boost intrinsic repair of kidneys beyond high-grade stenotic lesions..


Thank
you