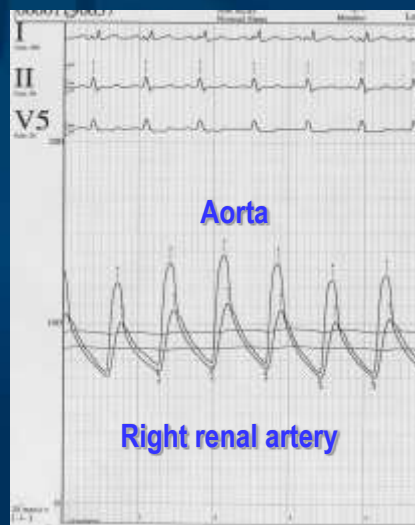


Renal Artery Stenosis, what is remaining for intervention?

Prof. Dr. Hesham Boshra
Professor of Cardiology
Beni sueif University

Renal angiography + hemodynamic assessment

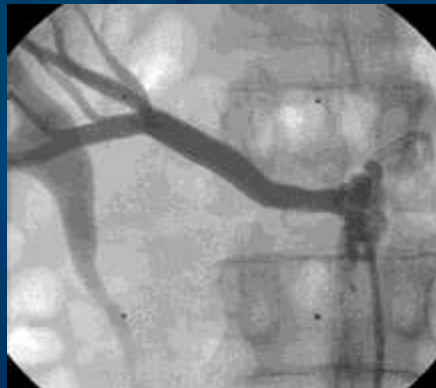


The 'classic' patient for renal artery revascularization

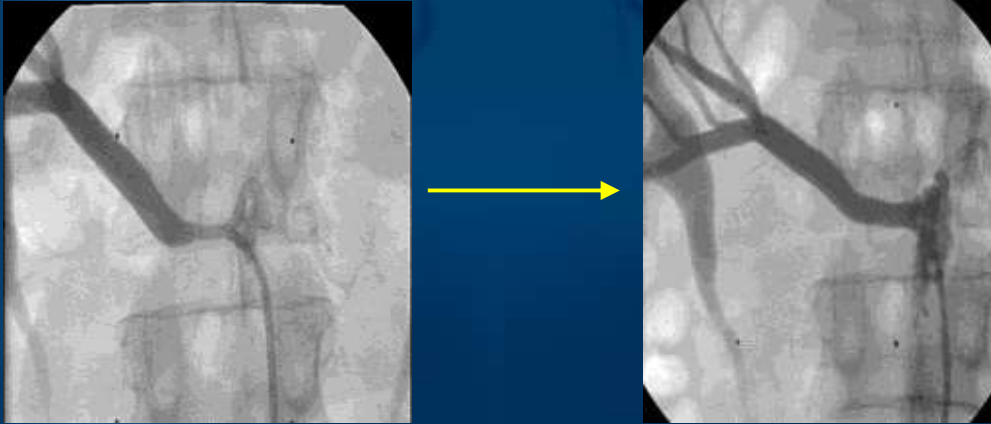
- ❑ 55 year old male
- ❑ HTN, known CAD (prior PCI)
- ❑ Admitted with CP/SOB, BP 194/124 mm Hg
- ❑ BP Rx: ACEI, beta blocker, nitrate
- ❑ Creatinine 1.6 mg/dl, HCT 41.8%
- ❑ Referred for cardiac catheterization

Renal artery revascularization

- Accelerated HTN
- Mild elevation in creatinine
- Symptoms



Did We Benefit This Patient?



Outline

- ❏ Introduction.
- ❏ Natural History.
- ❏ Management of RAS.
 - Medical vs interventional (Revascularization, Stenting).
 - Evidence Review.
- ❏ Where do we stand now? (Conclusion)

Introduction

- ❏ Technological advances in endovascular revascularization for ARAS in recent years have been spectacular,
 - With a technical success of over 98%
 - 4- fold increase in the number of these procedures done nowadays.

However, despite their widespread use, considerable controversy exists regarding the clinical benefits of these procedures.

Introduction “Hot Topics”

- ❏ The role of Stenting for ARAS is hotly debated among different specialties.
- ❏ If we may generalize a bit
 - Interventionalists (cardiology, interventional radiologists, vascular surgeons, and vascular medicine specialists) have been in favor of liberal use of stenting.
 - Nephrologists often favor medical therapy alone.
- And as with all controversial issues, each group feels rather strongly about its position!!

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Natural History



Atherosclerotic RAS

- Usually ostial
- Associated with diseased aorta
- Can be unilateral or bilateral



Natural History



RAS is common in patients with vascular disease

Prevalence of RAS

- Proven MI 12%
- Undergoing cardiac catheterization 6-19%
- Lower extremity PVD 22-59%

Predictors of RAS in patients undergoing cardiac catheterization

- CAD; Age; PVD; serum creatinine; hypertension

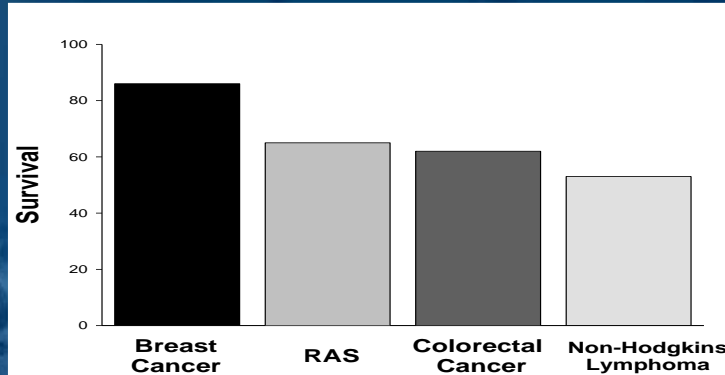
Natural history

RAS is a marker of a poor prognosis



Natural history

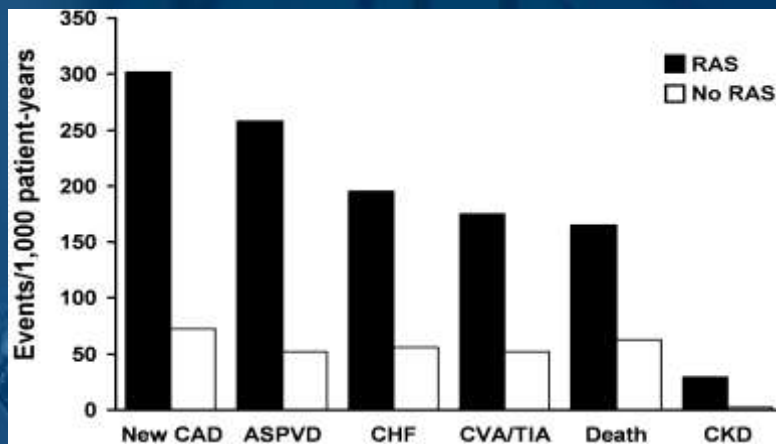
Effect of RAS on Prognosis – Relative Five year Survival



Ries LAG et al. SEER Cancer Statistics Review, 1973-1998.
National Cancer Institute, September 2000.

Natural History

Clinical Events in Patients With RAS



Claims data from a 5% random sample of the United States Medicare population were used to select patients without atherosclerotic renovascular disease in the 2 years preceding December 31, 1999 (N= 1,085,250), followed until December 31, 2001.

Outline

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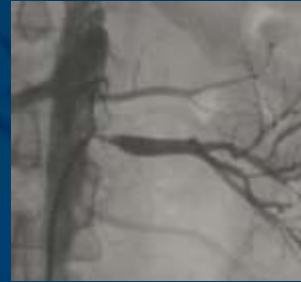
Management of RAS

Options include:

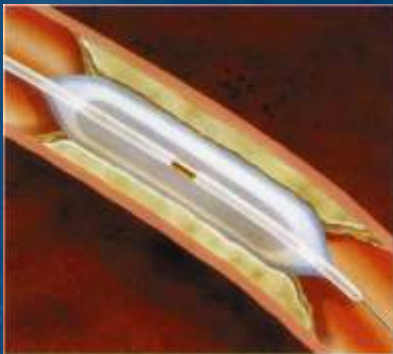
- Medical Management.
- Non Medical.
 - I. Angioplasty.
 - II. Angioplasty plus stenting.
 - III. Surgical reconstruction.

Optimal Medical Treatment

- ❑ ARB + diuretic to get BP to target
 - <140/90 mm Hg
 - <130/80 mm Hg with DM
- ❑ LDL to goal
 - Currently <100 (or 70) mg/dl
- ❑ Diabetes Management
 - HbA1c to target (<7%)
- ❑ Smoking Cessation
- ❑ Anti-platelet therapy (aspirin +/- clopidogrel/prasugrel)



What role does revascularization play?



Treatment of RAS



Evidence-based Medicine

Annals of Internal Medicine

REVIEW

Effectiveness of Management Strategies for Renal Artery Stenosis: A Systematic Review

Ethan Balk, MD, MPH; Gowri Raman, MD; Mei Chung, MPH; Stanley Ip, MD; Athina Tatsioni, MD; Alvaro Alonso, MD; Priscilla Chew, MPH; Scott J. Gilbert, MD; and Joseph Lau, MD

Background: Atherosclerotic renal artery stenosis is increasingly common in an aging population. Therapeutic options include medical treatment only or revascularization procedures.

Purpose: To compare the effects of medical treatment and revascularization on clinically important outcomes in adults with atherosclerotic renal artery stenosis.

Data Sources: The MEDLINE database (inception to 6 September 2005) and selected reference lists were searched for English-language articles.

Study Selection: The authors selected prospective studies of renal artery revascularization or medical treatment of patients with atherosclerotic renal artery stenosis that reported mortality rates, kidney function, blood pressure, cardiovascular events, or adverse events at 6 months or later after study entry.

Data Extraction: A standardized protocol with predefined criteria was used to extract details on study design, interventions, outcomes, study quality, and applicability. The overall body of evidence was then graded as robust, acceptable, or weak.

Data Synthesis: No study directly compared aggressive medical therapy with angioplasty and stent placement. Two randomized

trials compared angioplasty without stent and medical treatments. Eight other comparative studies and 46 cohort studies met criteria for analysis. Studies generally had poor methodologic quality and limited applicability to current practice. Overall, there was no robust evidence. Weak evidence suggested no large differences in mortality rates or cardiovascular events between medical and revascularization treatments. Acceptable evidence suggested similar kidney-related outcomes but better blood pressure outcomes with angioplasty, particularly in patients with bilateral disease. Improvements in kidney function and cure of hypertension were reported among some patients only in cohort studies of angioplasty. Available evidence did not adequately assess adverse events or baseline characteristics that could predict which intervention would result in better outcomes.

Limitations: The evidence from direct comparisons of interventions is sparse and inadequate to draw robust conclusions.

Conclusions: Available evidence does not clearly support one treatment approach over another for atherosclerotic renal artery stenosis.

Ann Intern Med. 2006;145:901-912.
For author affiliations, see end of text.

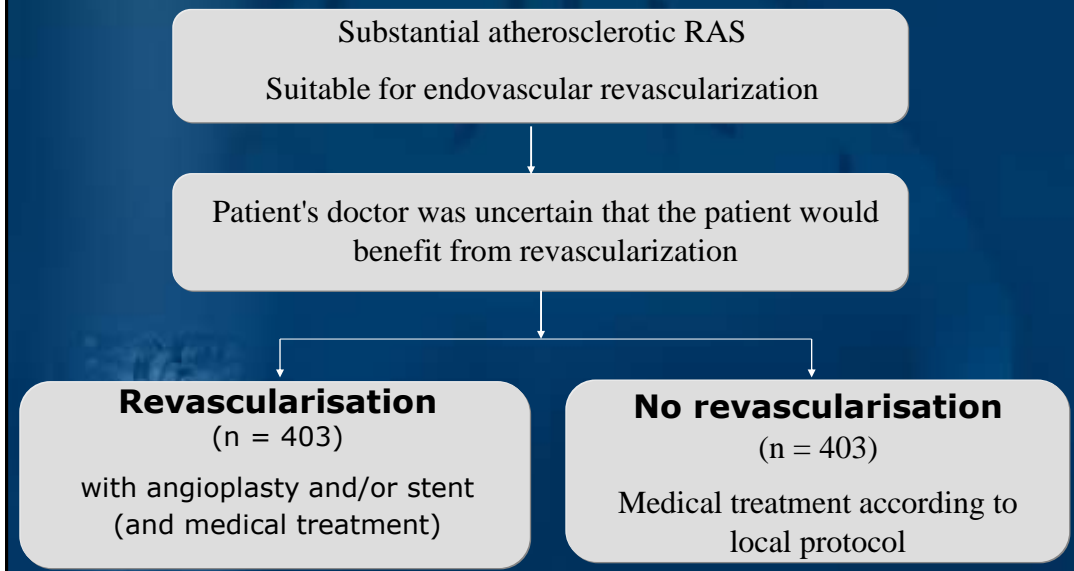
www.annals.org

Angioplasty and STent for Renal Artery Lesions



NEJM 2009;361:1953-1962

ASTRAL Trial



PATIENT CHARACTERISTICS

	Revasc.	Medical	P-value
Mean age (range)	70 (42 – 86)	71 (43 – 88)	0.7
Male	63%	63%	0.9
Current smoker	20%	22%	0.5
Diabetes	31%	29%	0.5
CHD	49%	48%	0.2
PVD	41%	40%	0.7
GFR (ml/min)	40.3 (5.4 – 124.5)	39.8 (7.1 – 121.7)	0.7

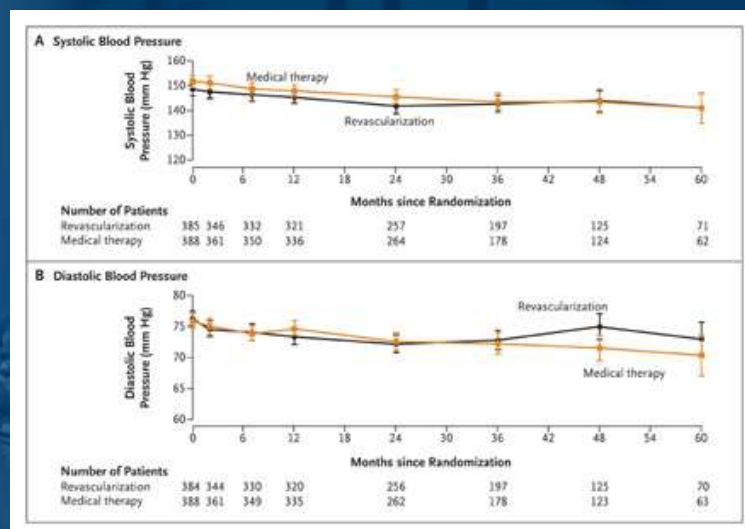
Blood Pressure, Cholesterol, Stenosis

Related laboratory measures			
Mean blood pressure (range) — mm Hg			
Systolic	149 (87–270)	152 (90–241)	0.07
Diastolic	76 (45–120)	76 (46–130)	0.63
Mean total cholesterol (range) — mmol/liter			
	4.7 (0.1–14.8)	4.7 (1.9–9.6)	0.79
Renal physiology			
Stenosis ¶			
Mean (range) — %	76 (40–100) †	75 (20–99)	0.29
Severity — no. (%)			
<50%	2 (<1)	4 (1)	0.68
50–70%	159 (39)	164 (41)	
>70%	242 (60)	235 (58)	
Mean length of kidney (range) — cm			
	9.7 (6–14)	9.8 (6–20)**	0.44

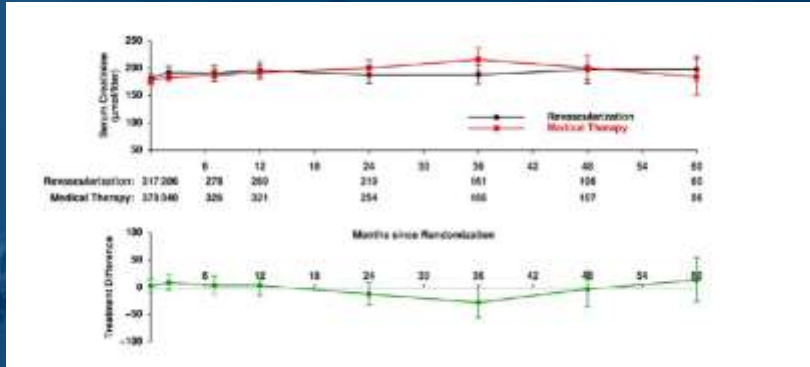
Medications at One Year

	Revasc.	Medical	P-value
Any Anti-hypertensives	97%	99%	0.03
Diuretic	64%	69%	
Ca ² antagonist	63%	71%	
Beta-blocker	46%	55%	0.02
ACE-I, A-II antagonist	50%	43%	0.05
Alpha-blocker	39%	38%	
Mean no. anti-hypertensives	2.77 (1 - 6)	2.99 (1 - 6)	0.03

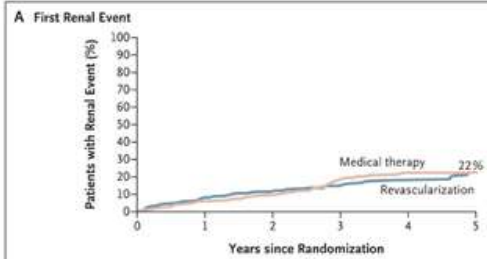
Blood Pressure



Serum Creatinine

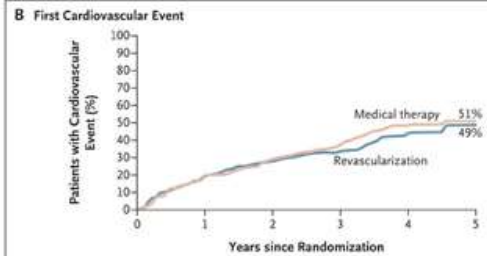


Clinical Events



No. at Risk

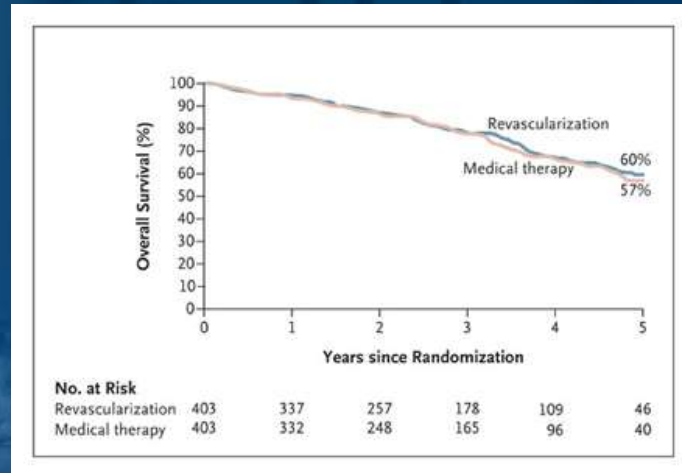
Revascularization	403	315	236	157	99	39
Medical therapy	403	319	233	145	84	37



No. at Risk

Revascularization	403	278	200	133	77	33
Medical therapy	403	286	194	118	61	27

Survival



Procedural Complications

- ❑ 38 periprocedural complications (9%) who underwent revascularization
- ❑ 19 of these events (in 17 patients) were considered to be serious complications
 - Pulmonary edema (1) and Myocardial infarction (1)
 - Renal embolizations (5), Renal arterial occlusions (4) and Renal-artery perforations (4)
 - Femoral-artery aneurysm (1)
 - Cholesterol embolism leading to peripheral gangrene and amputation of toes or limbs (3)

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.)

RAS and stenting – has the question been answered?



Criticisms of ASTRAL

1. Selection bias and inexperienced operators

- ❑ On average, 2 patients per center per year underwent randomization, which indicates serious selection bias or inexperienced staff at centers with very low intervention rates.
- ❑ This concern is supported by a low rate of technical success (317 of 403 patients [79%] in the revascularization group) as compared with reports in the literature of 98% respectively.

NEJM 2010;362:762

Criticisms of ASTRAL

2. There was a significant reduction in the number of antihypertensive drugs in stent treated patients

Against the definitive conclusion that renal-artery revascularization provides no clinical benefit.

NEJM 2010;362:762

Criticisms of ASTRAL

3. Patients with mild or moderate RAS

- ▣ patients with a mild or moderate degree of renal-artery stenosis, medical management is as effective as revascularization over a 5-year follow-up period.

NEJM 2010;362:762

Criticisms of ASTRAL

4. Were the patients on the right drugs?

Only about 40 to 50% of the patients were treated with drugs that block the pathway of the renin–angiotensin–aldosterone system; the use of such drugs is currently recommended in any patient with atherosclerotic renal-artery stenosis.

NEJM 2010;362:762

Criticisms of ASTRAL

5. Not all patients in the intervention group had stenting

Furthermore, 17% of the patients in the revascularization group did not proceed to revascularization after invasive angiography.

NEJM 2010;362:762

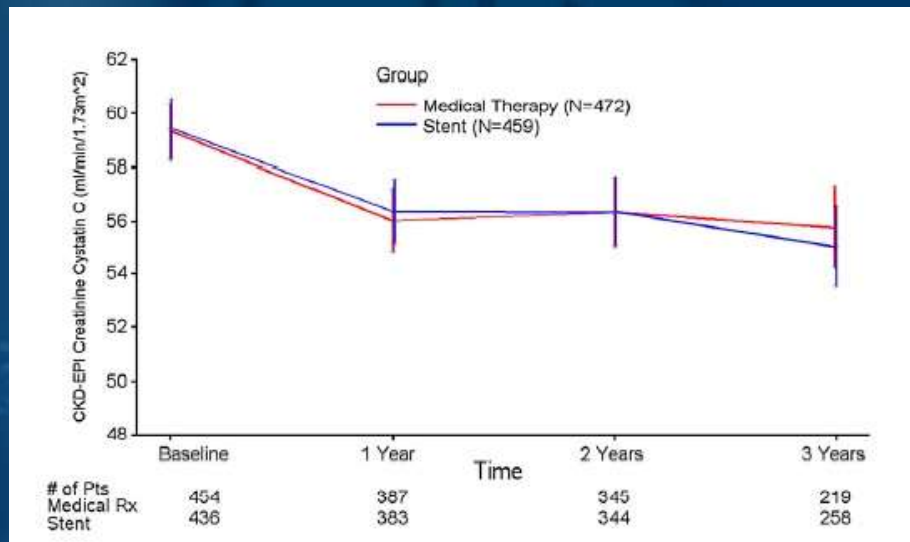


- **NIH Funded Trial**
- **Prospective, multi-center, two armed, randomized, unblinded survival (time to event) clinical trial** (from May 2005 to September 2012).
- **To test the hypothesis that optimal medical therapy + stenting reduces the incidence of cardiovascular and renal events compared to optimal medical therapy alone in patients with systolic hypertension**
- **>100 centers participating, 1080 patients**



- ☐ Documented history of systolic hypertension (>155 mm Hg) on 2 or more antihypertensive medications
- ☐ One or more renal artery stenosis (> 60% stenosis)
- ☐ All patients receive OMT - Randomization to stent vs no stent

Results



Conclusion

Stenting did not influence eGFR in participants with atherosclerotic renal artery stenosis receiving renin-angiotensin system inhibition–based therapy. Predictors of clinical events were traditional risk factors for CKD and cardiovascular disease.

Clin J Am Soc Nephrol 11: 1180–1188, 2016. doi: 10.2215/CJN.10491015

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Renal Artery Stenosis, what is remaining for intervention?



Renal Artery Stenosis, what is remaining for intervention?
Medical treatment is better

Based on an expert panel review of scientific data, the SCAI concluded that patients with the following are most **likely to benefit** from RAS :

- ❑ Cardiac disturbance syndromes (flash pulmonary edema or acute coronary syndrome)
- ❑ Hypertension that has not been controlled by three or more medications at maximal tolerated doses
- ❑ Severe stenosis in both kidneys or severe stenosis in a single functioning kidney where blood pressure or renal dysfunction cannot be managed medically

The SCAI concluded that patients with any of the following are typically **not good candidates** for renal artery stenting :

- ❑ Mild or moderate stenosis (less than 70%)
- ❑ Long-standing loss of renal blood flow
- ❑ Complete occlusion of the renal artery

Some questions need to be answered?

- ❑ Does RAS contribute to progression of vascular disease?
- ❑ Are there different phases of RAS with potentially different treatments?
- ❑ Will optimal treatment differ based on patient characteristics?
- ❑ What constitutes optimal medical therapy?
- ❑ What outcomes should we measure?
- ❑ Is the disease more than just BP and GFR control?

RAS – Still much to learn!