Renal Artery Stenosis-Nothing to Do?

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Disclosures

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Abbott Vascular C, P, SB
Ablative Solutions EI
Boston Scientific AB, C, EI, SB
Cardinal Health AB, C
Cook Medical, Inc. C, P
Endologix Corp. C, P
Med Alliance SA AB, EI
Medtronic Inc., C, P
Nectero inc. EI, AB, SO
Omeros Corp, EI
Spectranetics Corp. C, SB
QT Vascular, EI
Transverse Medical AB, EI, SO
W.L. Gore C, P

AB: Advisory Board
C: Consulting Relationship
EI: Equity Interest
GS: Grant Support
P: Proctor or Training Course Sponsorships
SB: Speakers Bureau
SE: Spouse Employee
SO: Stock Options or Positions

Natural History of Renal Artery Disease

Retrospective Studies
5-yr progression 52%
5-yr occlusion 14%

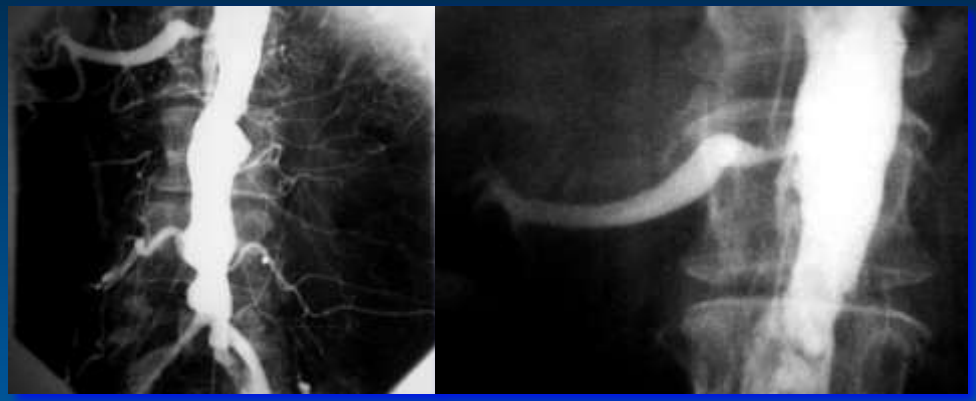
Prospective Studies
3-yr progression 24%
3-yr occlusion 9%

Retrospective	Follow-up (mos)	N	Progression %	Occlusion %
Wollenweber	3 - 88	30	21 (70%)	--
Meaney	6-120	39	14 (36%)	3 (8%)
Schreiber	12 - 60	85	37 (44%)	14 (16%)
Tollefson	15-180	48	34 (71%)	7 (15%)
Total				%)
Pros				
Dear				%)
Zierler	36	53	11 (21%)	4 (8%)
Totals	36	88	21 (24%)	8 (9%)

Average rate of progression 7% per year

Natural History of Renal Artery Disease

Renal Arteriogram January 5, 2000

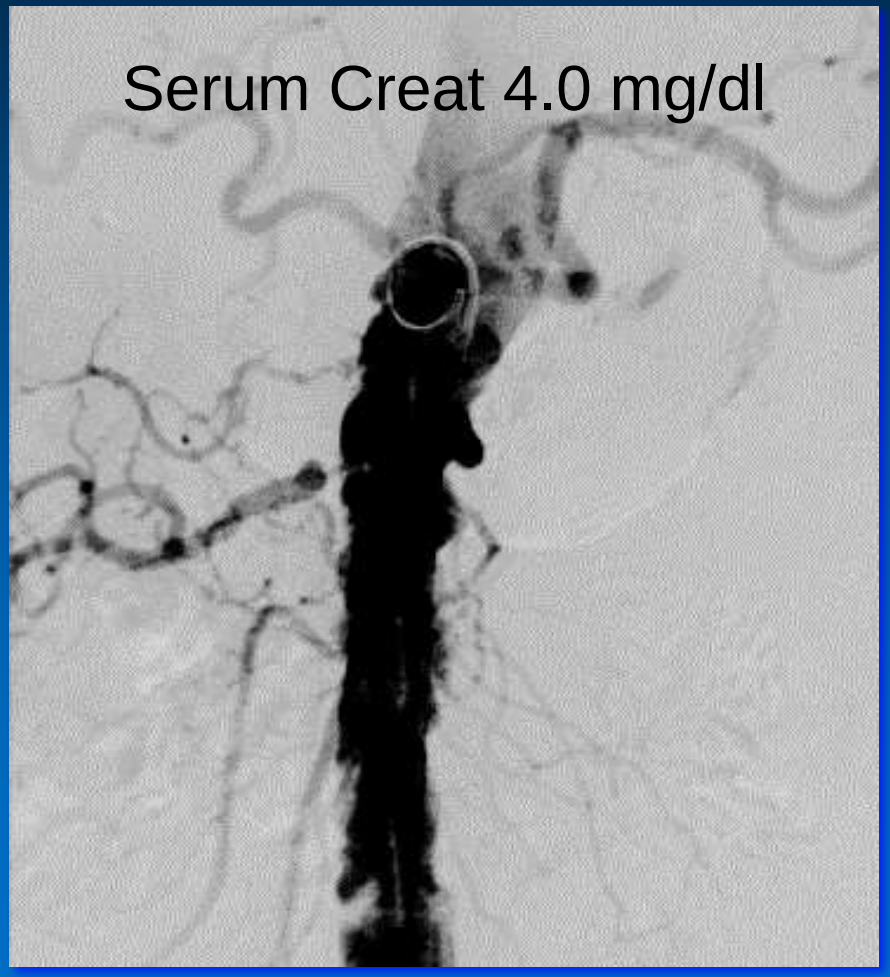


Renal artery disease - Left renal occluded
Ostal stenosis of right renal artery
Progressive loss of renal mass and function
Cortical scarring on angiography

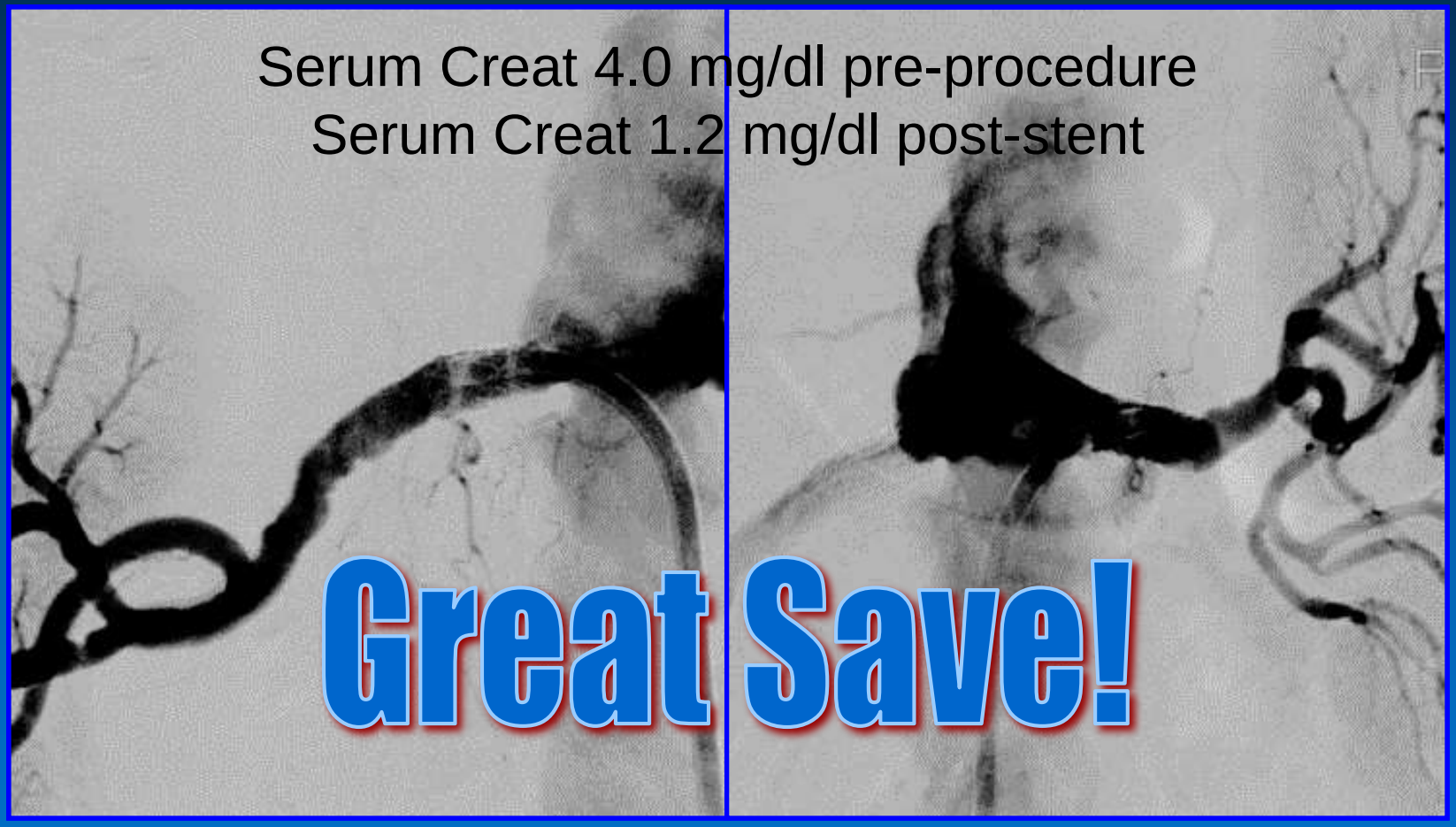
R Renal	PSV	RI	Creat	Size
4/03/02	401	0.74	0.9	11.6
3/11/03	436	0.77	1.0	11.2
9/09/04	507	0.83	1.1	10.1

Renal Arteriogram September 9, 2004

Atherosclerotic Disease - Renal Preservation

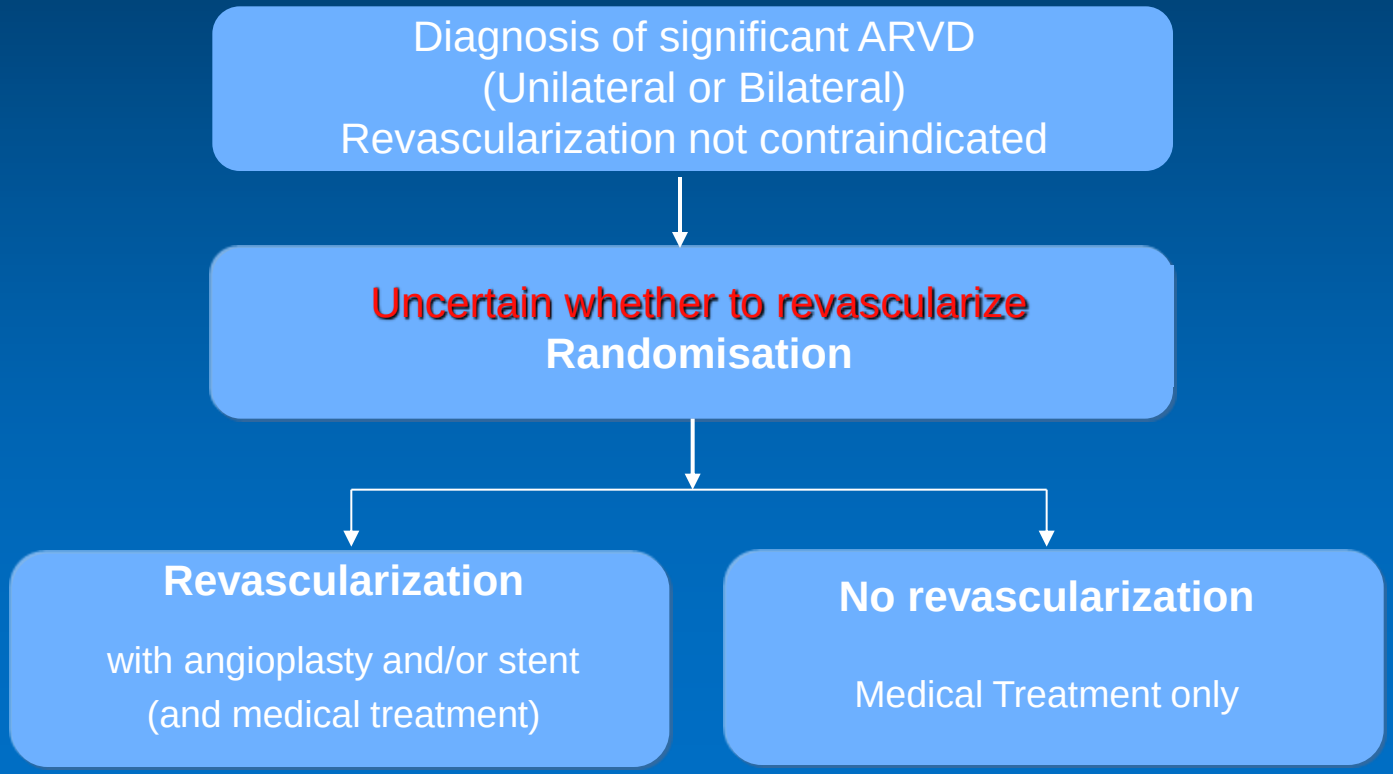


Atherosclerotic Disease - Renal Preservation



Astral Trial

Angioplasty and STent for Renal Artery Lesions



ASTRAL Investigators *N Engl J Med* 2009; 361: 1953-1962

Astral Trial

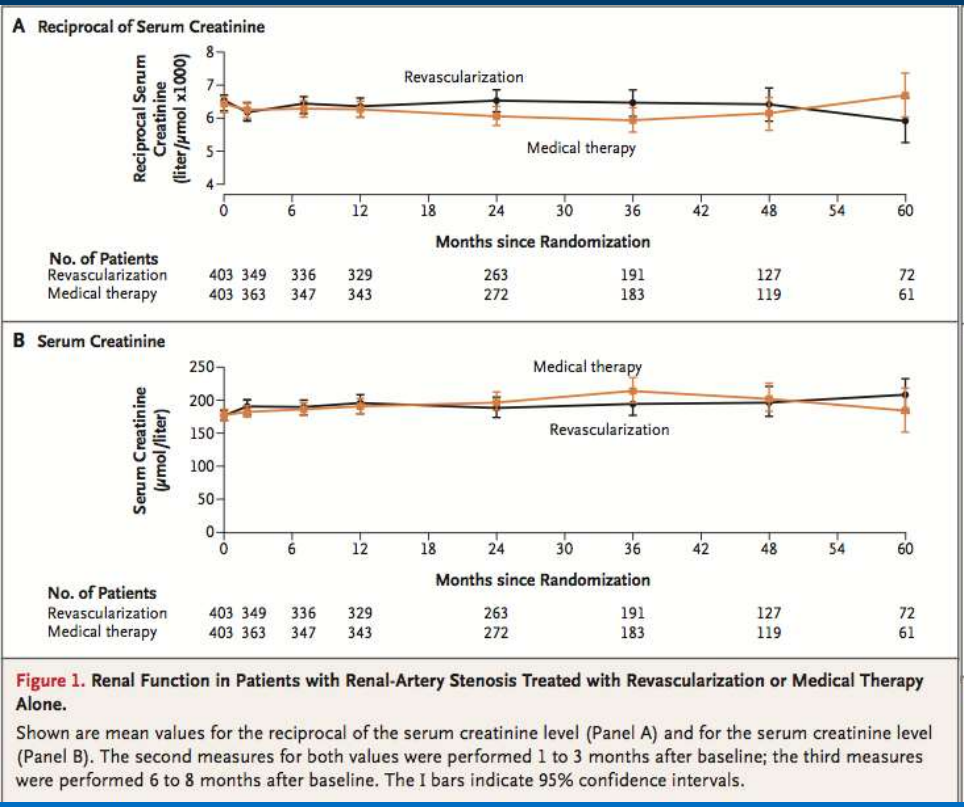


Figure 1. Renal Function in Patients with Renal-Artery Stenosis Treated with Revascularization or Medical Therapy Alone.

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.

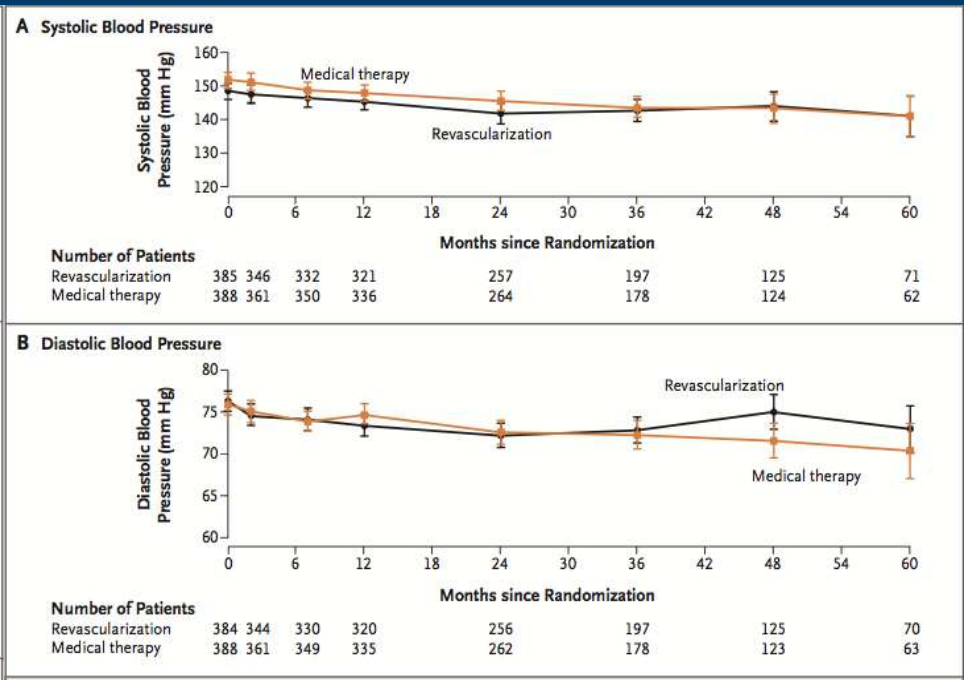
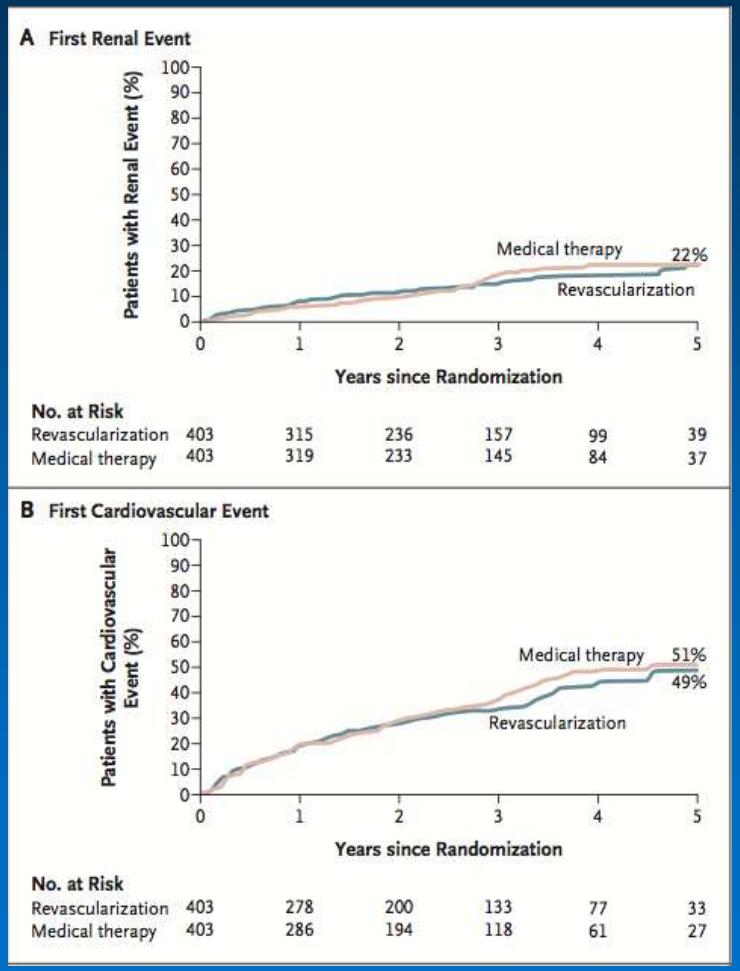


Figure 2. Systolic and Diastolic Blood Pressure.

Shown are mean values for systolic blood pressure (Panel A) and diastolic blood pressure (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.

ASTRAL Investigators *N Engl J Med* 2009; 361: 1953-1962

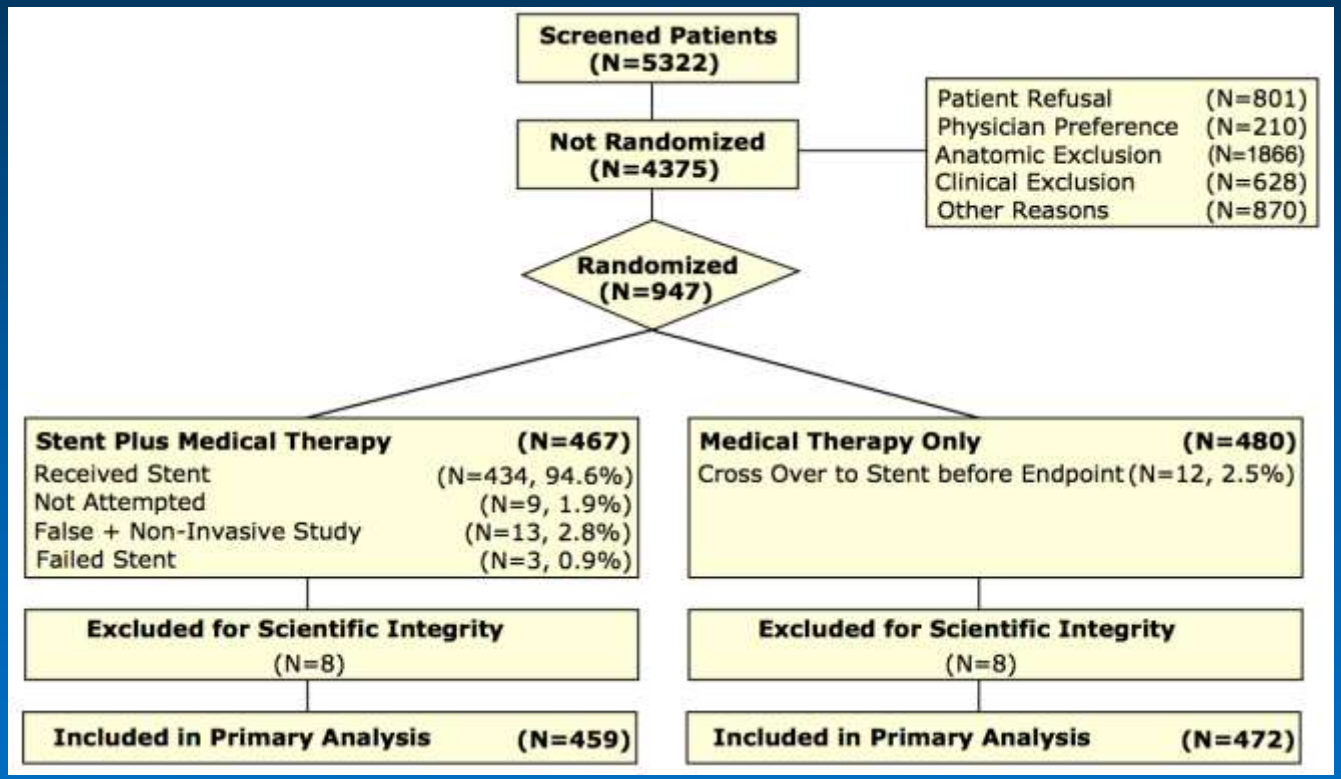
Astral Trial



- Enrolled patients with uncertain indications for revascularization
- 41% of patients had <70% stenosis
- 22% did not receive an intervention but the trial was still analyzed by intention to treat!

ASTRAL Investigators *N Engl J Med* 2009; 361: 1953-1962

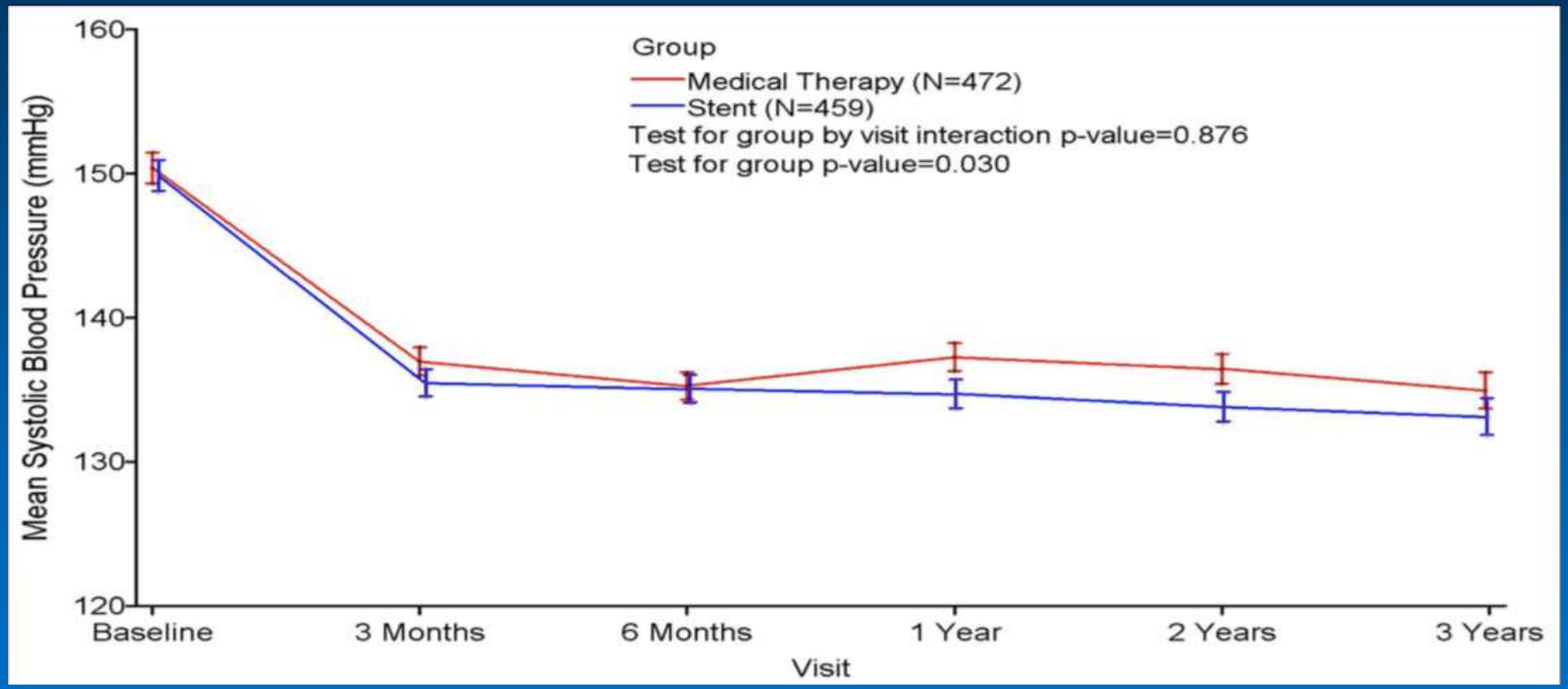
Coral Trial Design



Cooper CL *N Engl J Med* 2014; 370: 13-22

Coral Trial Outcomes

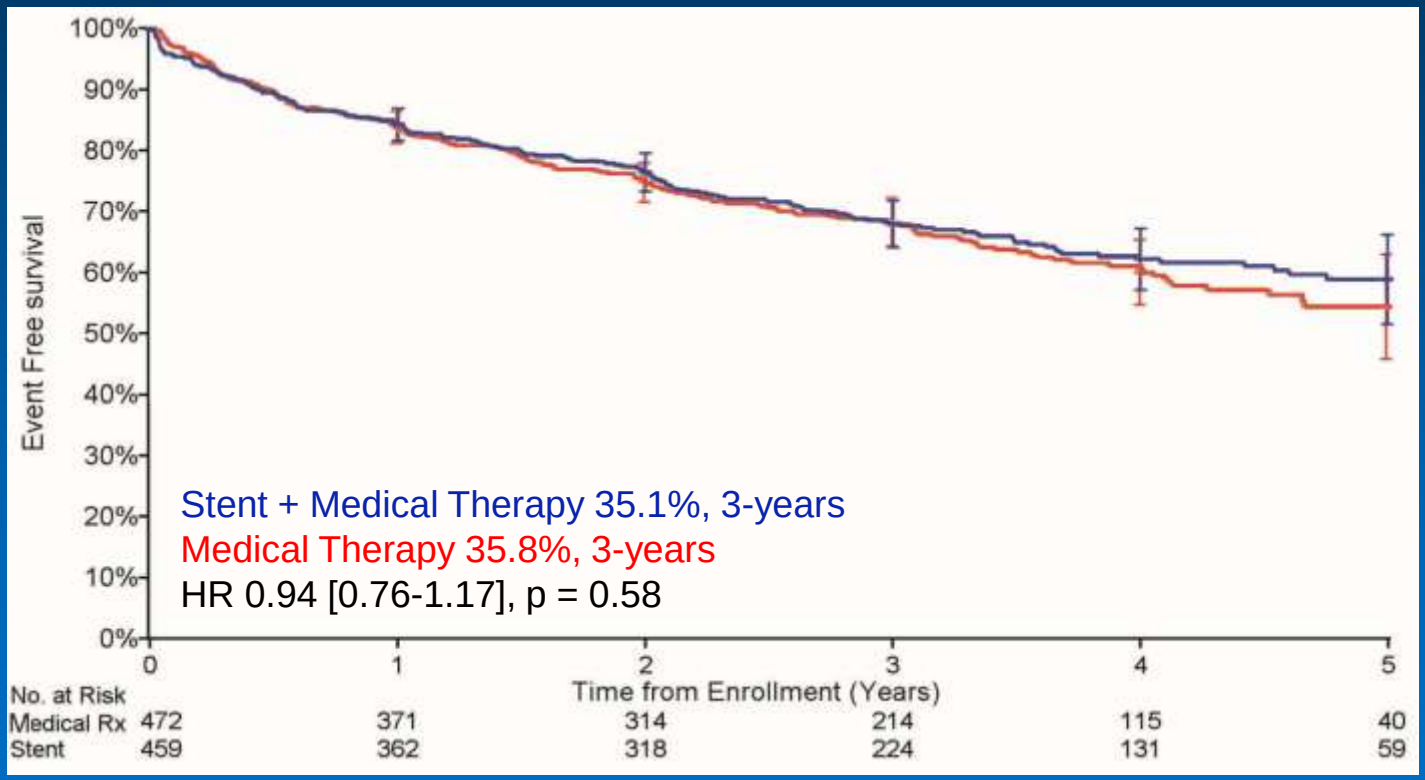
Mean Systolic Blood Pressure



Cooper CL *N Engl J Med* 2014; 370: 13-22

Coral Trial Outcomes

Primary Endpoint-Freedom from Clinical Events



Cooper CL *N Engl J Med* 2014; 370: 13-22

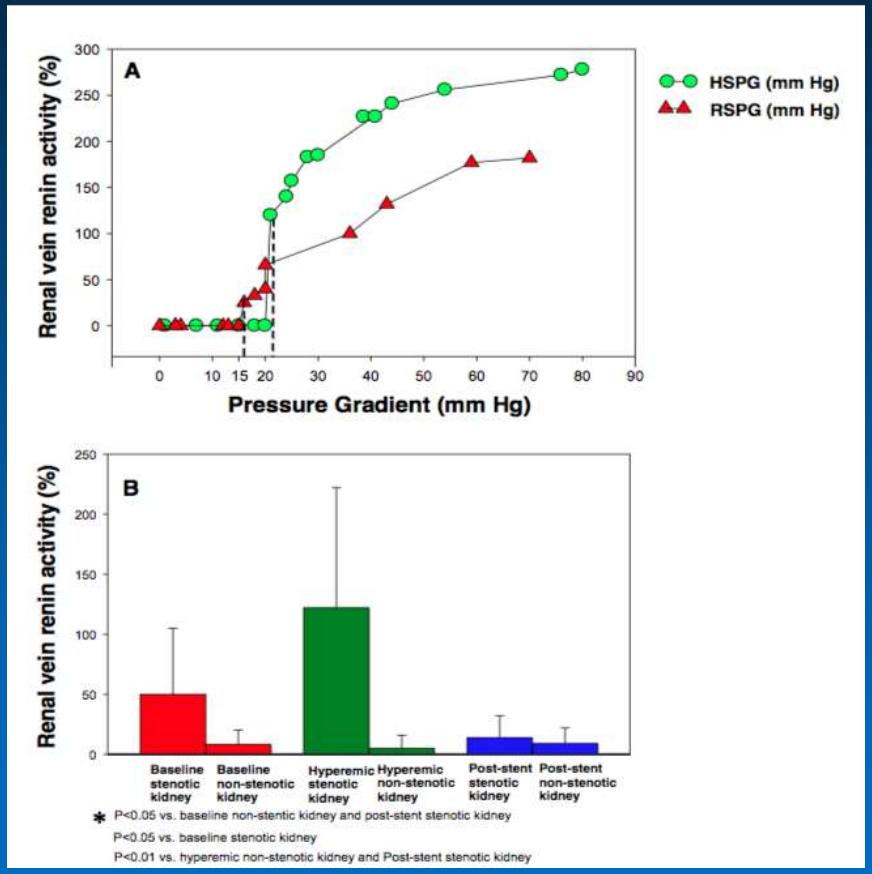
The Paradox of Renal Artery Intervention

- Technical success rates exceed 95%
- But clinical response rates lag:
  - -HTN: 70%
  - -CKD: 75%

- Are we just not picking the right patients? Lesions?
- How do we optimize efficacy?

- Is RAS the cause of hypertension?
- Is RAS the cause of renal insufficiency?
- Will treatment improve either?
- Will treatment prevent renal deterioration?

Hyperemic Pressure Gradients Better Predict Renin Production in RAS



A hyperemic pressure gradient of ≥21 mm Hg correlates with unilateral renin production

Kapoor N et al *Cather Cardiovasc Interv* 2010; 76: 726-732

Hyperemic Pressure Gradient Best Predicts BP Response Following Stenting of RAS

Table 2 Receiver-Operating Characteristic Analyses of the Optimal Cutpoints of Parameters in Predicting Hypertension Improvement After Stenting of RAS

Parameters	AUC	95% Confidence Interval	Cutpoint	Sensitivity, %	Specificity, %	Predictive Accuracy, %
Renal pressure measurements						
HSG	0.87	0.72–0.96	21 mm Hg	82	84	84
FFR	0.85	0.76–0.94	0.90	73	88	79
HMG	0.81	0.70–0.91	6.0 mm Hg	80	76	79
RSG	0.81	0.71–0.92	7.0 mm Hg	78	76	77
IVUS parameters						
MLA	0.86	0.76–0.95	7.8 mm^2	78	80	79
Area stenosis	0.82	0.71–0.92	67%	75	80	77
MLD	0.78	0.67–0.90	2.7 mm	70	76	72*
Plaque plus media area	0.73	0.60–0.85	9.0 mm^2	73	68	70*
Angiographic parameters						
Diameter stenosis	0.74	0.61–0.86	60%	68	72	69*
MLD	0.69	0.55–0.82	2.25 mm	51	80	62*†
Clinical parameters						
Systolic blood pressure	0.55	0.41–0.70	170 mm Hg	43	68	53*†
Diastolic blood pressure	0.51	0.36–0.66	95 mm Hg	41	64	50*†
Mean blood pressure	0.54	0.39–0.68	118 mm Hg	51	60	54*†

Lesser MA et al *J Am Coll Cardiol* 2009; 53: 2363–2371

The Pathophysiology of Unilateral RAS is Different Than Bilateral RAS

Does Stenting a Unilateral Lesion Impact the Contralateral Kidney?

Split Renal Function Outcome after Renal Angioplasty in Patients with Unilateral Renal Artery Stenosis

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*Hypertension Department, †Clinical Investigation Center (CIC 9201), Assistance Publique des Hôpitaux de Paris/INSERM, ‡Physiology Department and INSERM U356, and §Radiology Department, Hôpital Européen Georges Pompidou, Assistance Publique Hôpitaux de Paris, Paris, France.

Single-kidney GFR with synchronous inulin or 51 Crethylenediaminetetraacetic acid (51 Cr-EDTA) clearance and 99m Tc-diethylenetriamine pentaacetic acid (99m Tc-DTPA) scintigraphy.

The increase GFR of the stented kidney is counterbalanced by decreased hyperfiltration of the contralateral kidney.

La Batide-Alanore A et al *J Am Soc Nephrol* 2001; 12: 1235-1241

SCAI Appropriate Use Criteria for Renal Artery Intervention

Cardiac Disturbance Syndromes (Flash Pulmonary Edema or acute coronary syndrome (ACS)) with hypertension and moderate RAS with a resting translesional mean gradient of ≥ 10 mm Hg and/or severe RAS.	9	Appropriate
CKD IV bilateral moderate RAS with a resting mean translesional gradient of ≥ 10 mmHg with kidney size > 7 cm in pole-to-pole length.	8	
CKD IV and global renal ischemia (unilateral severe RAS with a solitary kidney or bilateral severe RAS) without other explanation.	7	
Resistant HTN (uncontrolled hypertension having failed maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic) and bilateral or solitary severe RAS.	7	
Resistant HTN (uncontrolled hypertension having failed maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic) and unilateral severe RAS.	6	May Be Appropriate
CKD IV and unilateral moderate RAS with a resting translesional mean gradient of ≥ 10 mm Hg without other explanation.	6	
Recurrent CHF with unilateral moderate RAS with a resting translesional mean gradient of ≥ 10 mmHg.	5	
CKD class II with bilateral severe RAS.	5	
CKD class III, stable for 1 year, with bilateral severe RAS.	5	
Resistant HTN (uncontrolled hypertension having failed maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic) with severe unilateral RAS and anatomically challenging or high risk lesion (early bifurcation, small vessel, severe concentric calcification, and severe aortic atheroma or mural thrombus).	4	
Resistant HTN (uncontrolled hypertension with failure of maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic, or intolerance to medications) and unilateral moderate (50% to 70%) RAS with a mean translesional gradient of < 10 mmHg.	3	Rarely Appropriate
CKD III progressing to CKD IV over 6 months with solitary, severe RAS, with kidney size < 7 cm in pole-to-pole length.	3	
Resistant HTN (uncontrolled hypertension having failed maximally tolerated doses of at least three antihypertensive agents, one of which is a diuretic) with unilateral chronic total occlusion of the renal artery.	2	
BP ≥ 150/100 mmHg on two medications (one a diuretic) with severe unilateral RAS.	2	
BP ≥ 150/100 mmHg on a single anti-hypertensive medicine with severe unilateral RAS.	2	
Solitary severe RAS with controlled BP and normal renal function.	2	
Bilateral severe RAS with controlled BP and normal renal function.	2	
CKD III progressing to CKD IV over 6 months with unilateral, severe RAS with kidney size < 7 cm in pole-to-pole length.	2	
CKD class II with unilateral severe RAS.	2	
Bilateral severe RAS with controlled BP and normal renal function.	2	
Bilateral severe RAS with chronic end stage renal disease on hemodialysis >3 months.	2	
Unilateral severe RAS with controlled BP and normal renal function.	1	

ACS = acute coronary syndrome; AUC = appropriate use criteria; BP = blood pressure; CHF = congestive heart failure; CKD = chronic kidney disease; RAS = renal artery stenosis. Hemodynamically significantmoderate RAS = 50% to 70% diameter stenosis with a resting or hyperemic mean translesional gradient of ≥ 10 mmHg, or a resting or hyperemic peak translesional gradient of ≥ 20 mmHg measured with a small diameter catheter or pressure wire. A severe RAS ≥ 70% diameter stenosis by visual estimation.

Klein AJ et al *Catheter Cardiovasc Interv* 2017; 1–21

Who to Treat With RAS in 2018

- Routine stenting of non-critical lesions (>60% and/or peak systolic velocity >300 cm/sec) is no longer supported by the data
- Critical atherosclerotic lesions (≥80%) causing loss of renal mass and/or function probably benefit (not well represented in the trials)
- Critical atherosclerotic lesions (≥80%) and fibromuscular lesions causing refractory HTN (SBP>160 mm Hg on 3 or more drugs) probably also benefit
- Patients failing medical therapy and having clinical events such as acute pulmonary edema, CHF, myocarial infarction or acute renal ischemia should also be treated