Management of Atherosclerotic Renal Artery Stenosis

Nicolaos E. Madias, MD
Chairman, Department of Medicine
St. Elizabeth's Medical Center
Maurice S. Segal, MD Professor of Medicine
Tufts University School of Medicine

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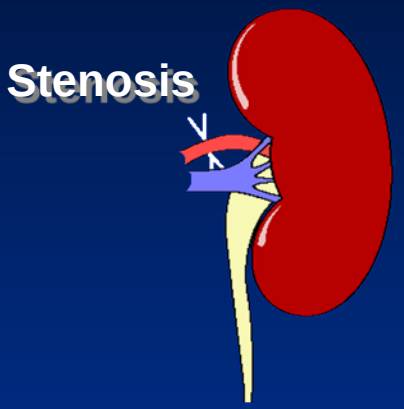
Magnitude of the Problem

- General hypertensive population: ~1-5%
- Unselected elderly subjects: ~7%
- ESRD: ~5-15%
- Patients undergoing coronary arteriography: ~20%
- Older patients with congestive heart failure: ~30%
- Older patients with resistant hypertension: ~45%
- Patients undergoing aortic or LE arteriography: ~50%



Growth of PTRA/Stenting in the US

Year	1996	2006
# of Procedures	~7,500	~40,000

Indications for Revascularization

- Resistant hypertension
- Progressive renal insufficiency
- Recurrent exacerbations of CHF

Does PTRA/Stenting Reduce Blood Pressure?

Medical Therapy vs PTRA

Trial	RAS	Patients, n	F/U, mo	BP Outcome
Webster, 1998	U	14 vs 13	6	161/88 vs 173 /95 (NS)
	B	16 vs 12		171/91 vs 152/83 (<0.005)
Plouin, 1998	U	26 vs 23	6	141/84 vs 140/81 (NS)
van Jaarsveld, 2000	U/B	50 vs 56	12	162/88 vs 152/84 (NS)

BP, blood pressure; U, unilateral; B, bilateral

Does PTRA/Stenting Improve/Preserve Renal Function?

Medical Therapy vs PTRA

Trial	RAS	Patients, n	F/U, mo	Scr or Ccr
Webster, 1998	U	14 vs 13	6	1.8 vs 1.7 (NS)
	B	16 vs 12		1.7 vs 2.2 (NS)
Plouin, 1998	U	26 vs 23	6	74 vs 77 (NS)
van Jaarsveld, 2000	U/B	50 vs 56	12	62 vs 70 (NS)

Scr, serum creatinine; Ccr, creatinine clearance; U, unilateral; B, bilateral

A Meta-Analysis of the Three Randomized Controlled Trials

- "Balloon angioplasty has a modest but significant effect on blood pressure and should be considered for patients with atherosclerotic renal artery stenosis and poorly controlled hypertension."

- "There is no evidence supporting its use in improving or preserving renal function, although none of the trials were designed to address this issue."

Nordmann AJ et al, *Am J Med* 2003;114:44-50

Does PTRA/Stenting Prevent Recurrent Exacerbations of CHF?

- No randomized controlled trials available

- Gray et al, *Vasc Med* 2002;7:275-279

  39 patients underwent PTRA/Stenting

  Following the procedure, hospitalizations for CHF declined markedly and NYHA functional class improved

  The number of patients receiving ACEI also increased (15% vs 49%)

Does PTRA/Stenting Reduce the Incidence of Cardiovascular Events?

- *No randomized controlled trials available*

Annals of Internal Medicine

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

Tufts-New England Medical Center, Boston, Massachusetts

Ann Intern Med. 2006;145:901-912

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

Growth of PTRA/Stenting in the US

Year	1996	2006
# of Procedures	~7,500	~40,000

Far too few or far too many?

Averages Conceal Variable Responses in Clinical Trials

Averages Conceal Variable Responses in Clinical Trials

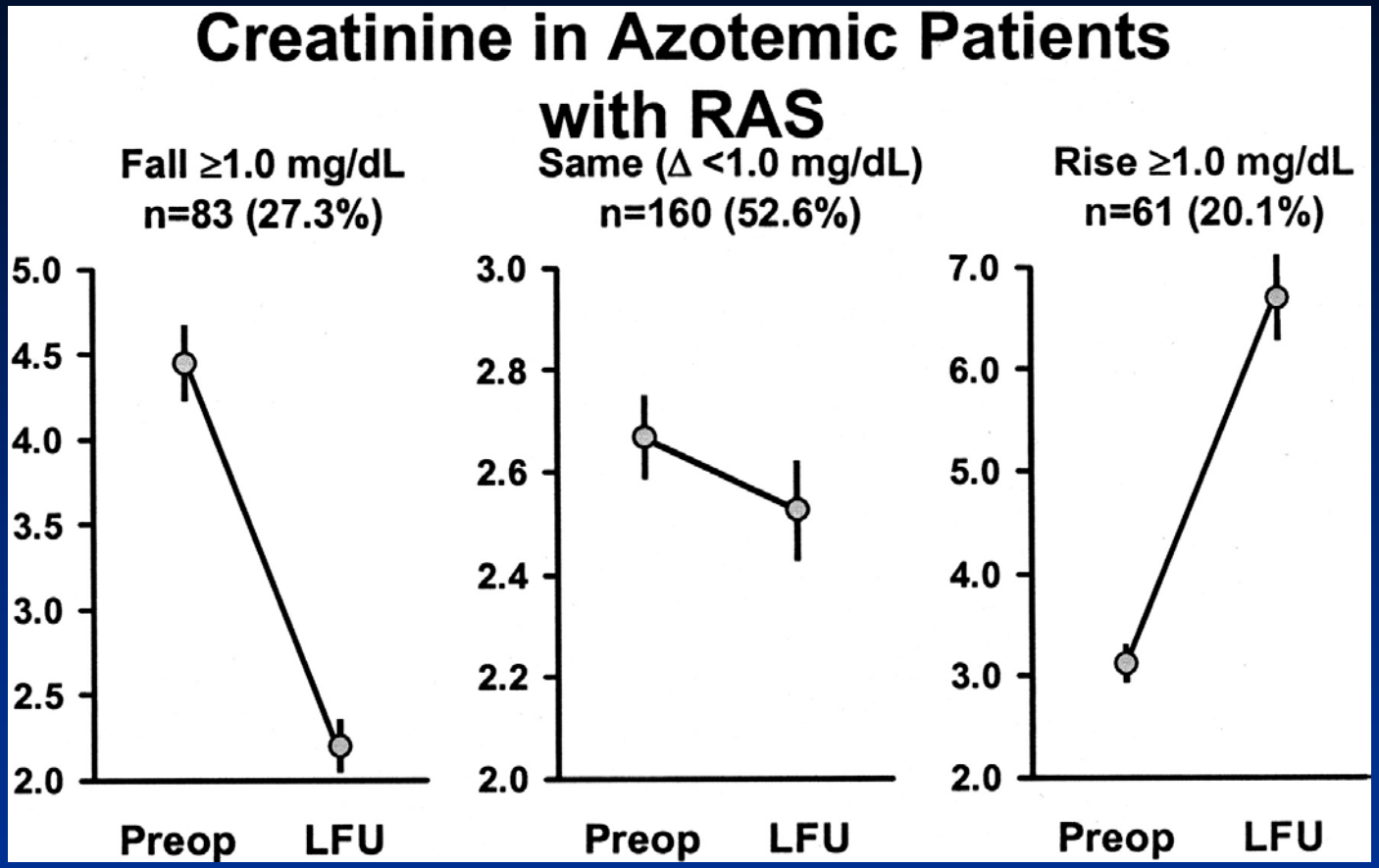
- 304 azotemic patients (Scr ≥ 2.0 mg/dl) with atherosclerotic RAS underwent successful surgical revascularization. Mean follow up was > 3 years for the group.

	Baseline	Latest Follow Up	Significance
Mean Scr	3.3	3.4	NS

Textor, SC. *J Am Soc Nephrol* 2004;15:1974-1982

Cont'd

Averages Conceal Variable Responses in Clinical Trials (Cont'd)



Textor, S. C. J Am Soc Nephrol 2004;15:1974-1982

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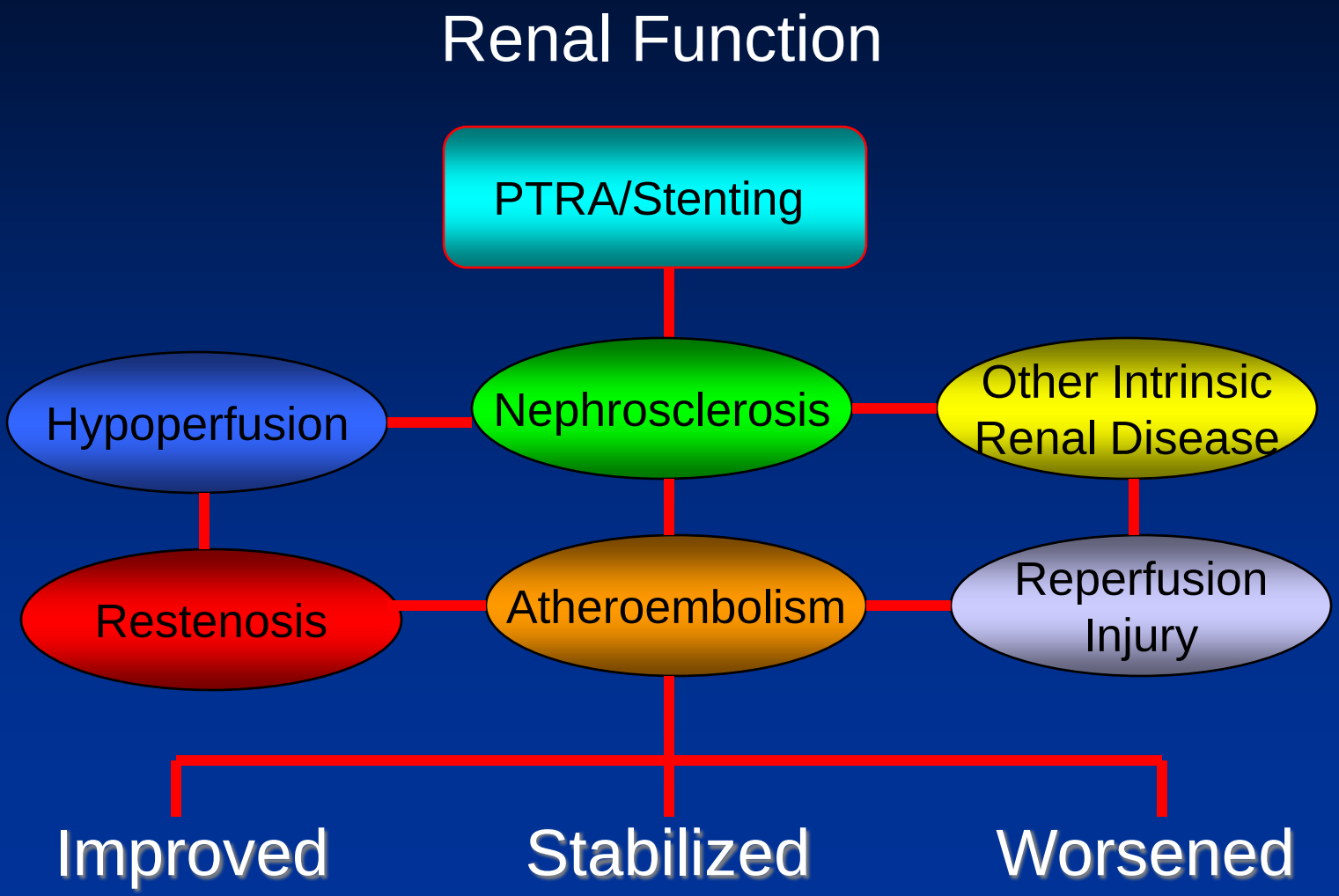
Contemporary Outcomes of PTRA/Stenting

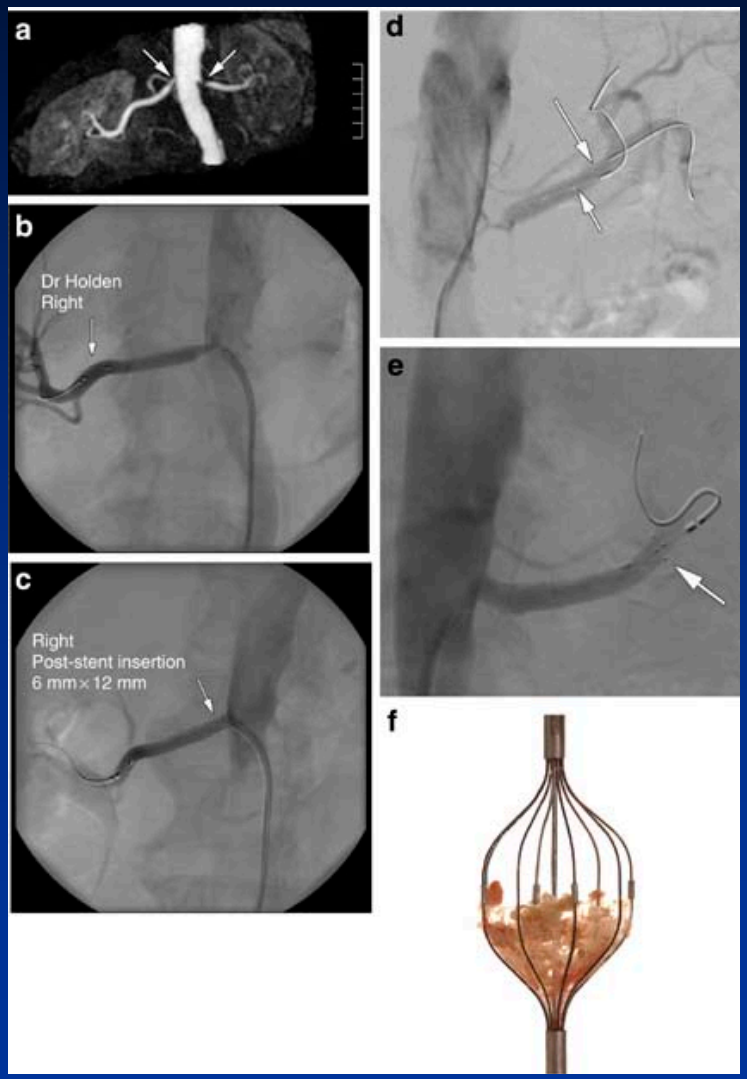
Technical Success	Improved BP	Renal Function I	S	W	Restenosis	Complications
97%	75%	30%	50%	20%	12%	13%

BP, blood pressure; I, improved; S, stabilized; W, worsened

Renal Function Following PTRA/Stenting



PTRA/Stenting with Embolic Protection



- 63 patients, median age 70.2 years, stage 3-4 GFR
- Technical success 100%
- 60% of filter baskets contained macroscopic embolic material
- At 6 months postintervention, restenosis rate 8%.
  Renal function improved in 40%, stabilized in 57%, and worsened in 3%

Holden et al. *Kidney Int* 2006;70:948-955

Four Prospective Trials

- **CORAL**

  The Cardiovascular Outcomes in Renal Atherosclerotic Lesions Trial

- **ASTRAL**

  Angioplasty and STent for Renal Artery Lesions

- **STAR**

  STent Placement and BP and Lipid-Lowering for Progression of Renal Dysfunction Caused by Atherosclerotic Ostial Stenosis of the Renal Artery

- **RAVE**

  Renal Atherosclerotic ReVascularization Evaluation

The Cardiovascular Outcomes in Renal Atherosclerotic Lesions Trial

- CORAL is a prospective, randomized, multicenter, unblinded trial comparing the effects of PTRA/Stenting/embolic protection device and optimal medical therapy to optimal medical therapy alone on a composite of adverse cardiovascular and renal events

- 1080 patients with resistant hypertension (SBP $\geq$ 155 mm Hg on $\geq$ 2 medications), angiographically defined atherosclerotic RAS $\geq$ 60%, and Scr $\leq$ 3 mg/dl, will be randomized to the two arms of the trial and followed for $\leq$ 5 years

- Sponsored by the NHLBI, NIH

Optimal Medical Therapy in the CORAL Trial

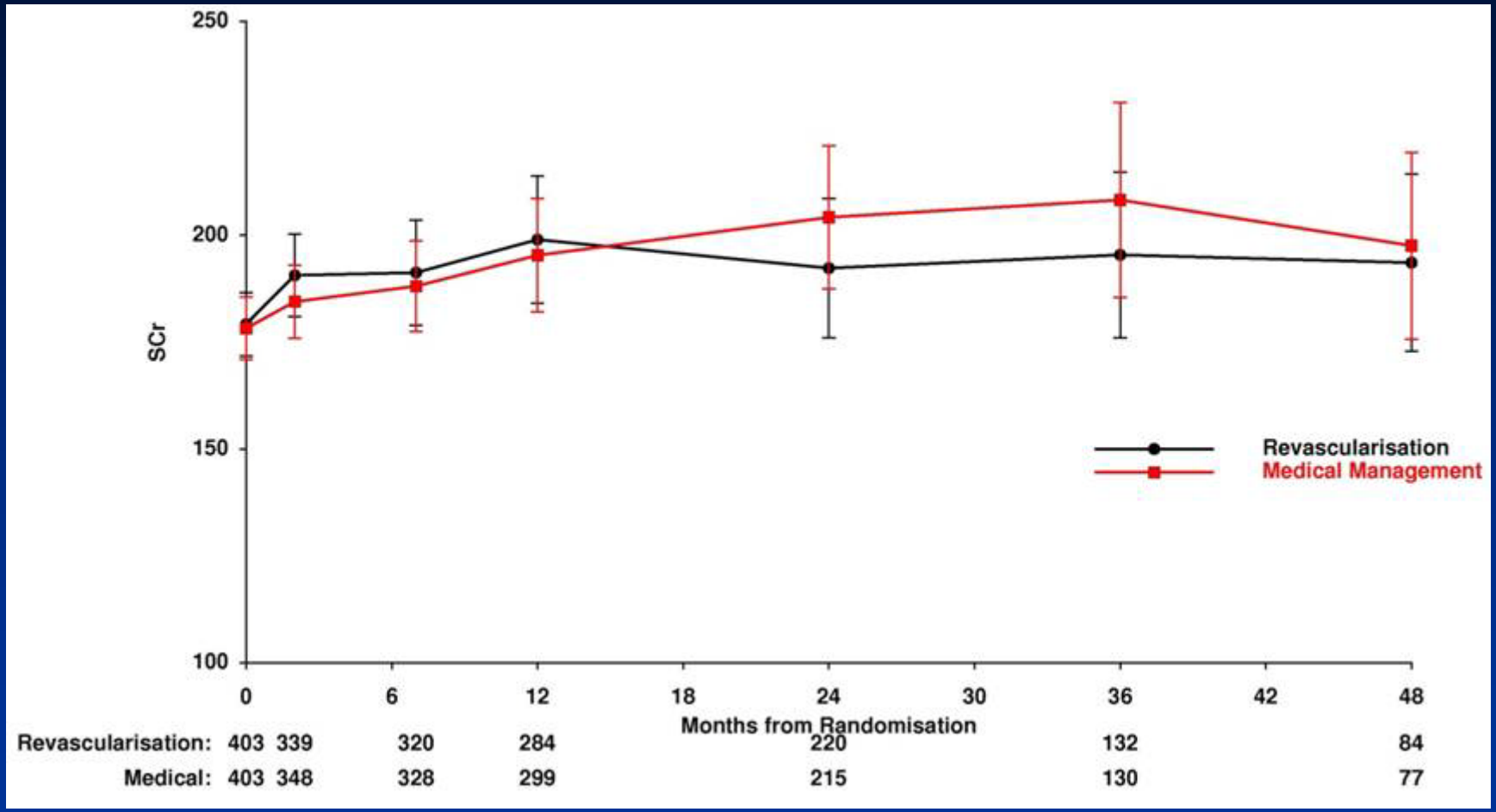
Risk Factor	Approach
Hypertension	Target BP < 140/90, < 130/80 for diabetics or proteinuric patients; ARB as first-line agent or, if not tolerated, ACEI; thiazide or loop diuretic; CCB, β-blocker, α-blocker, and vasodilator
Dyslipidemia	Target LDL < 100 mg/dl, consider < 70 mg/dl
Diabetes	Target HbA1c < 7%; foot and eye care
Antiplatelet agent	Aspirin, clopidogrel, or ticlopidine
Smoking	Cessation
Chronic kidney disease	Tight control of BP, dyslipidemia, and diabetes; management of anemia and hyperparathyroidism

The Cardiovascular Outcomes in Renal Atherosclerotic Lesions Trial

- Primary end point is event-free survival from a composite of clinical events, including cardiovascular or renal death, stroke, myocardial infarction, hospitalization for CHF, and progressive renal insufficiency (doubling of Scr or need of permanent renal replacement therapy)

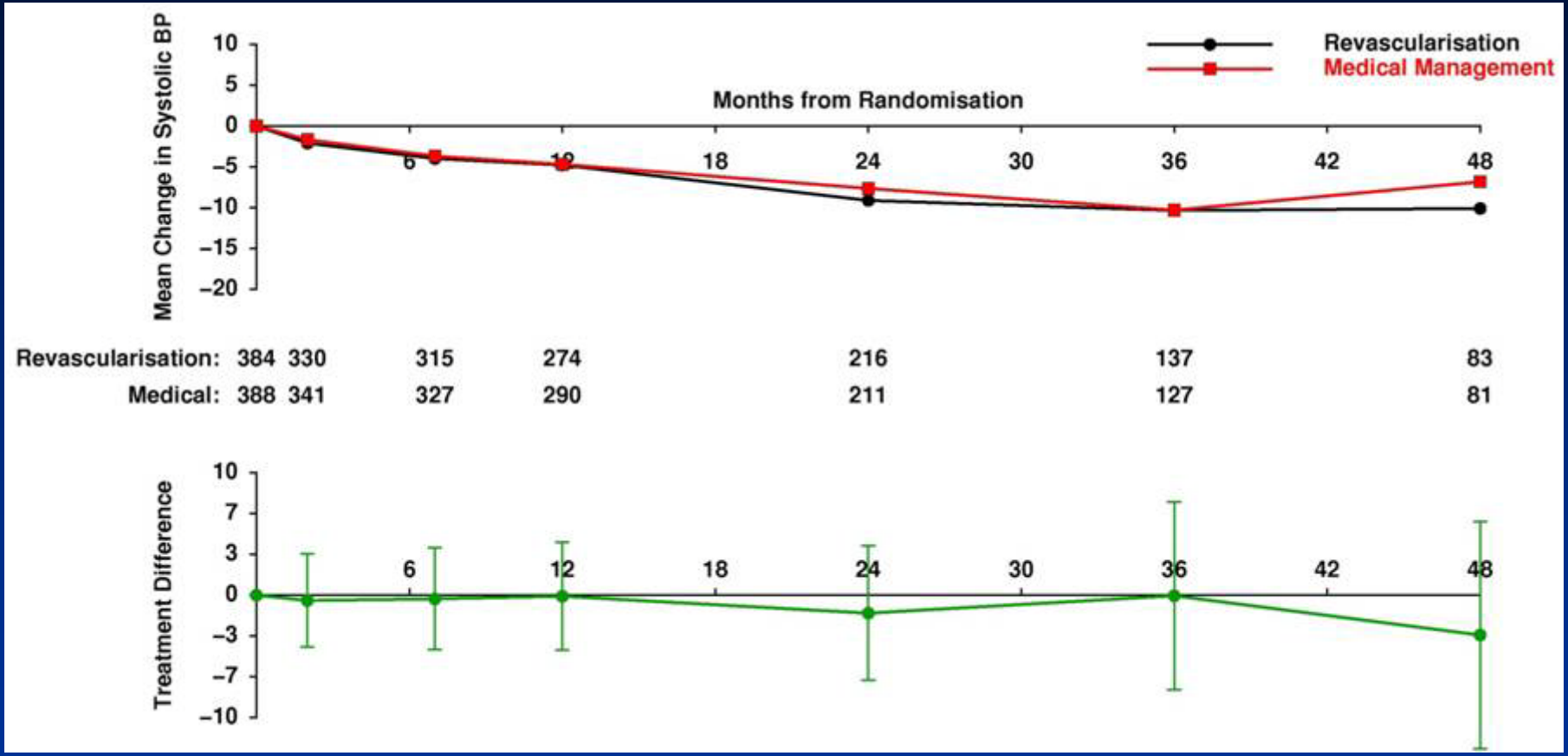
- Twelve secondary end points will be examined, including all-cause mortality, a number of group interactions, longitudinal renal function, SBP, renal artery patency, quality of life, and cost effectiveness.

ASTRAL
Course of Scr



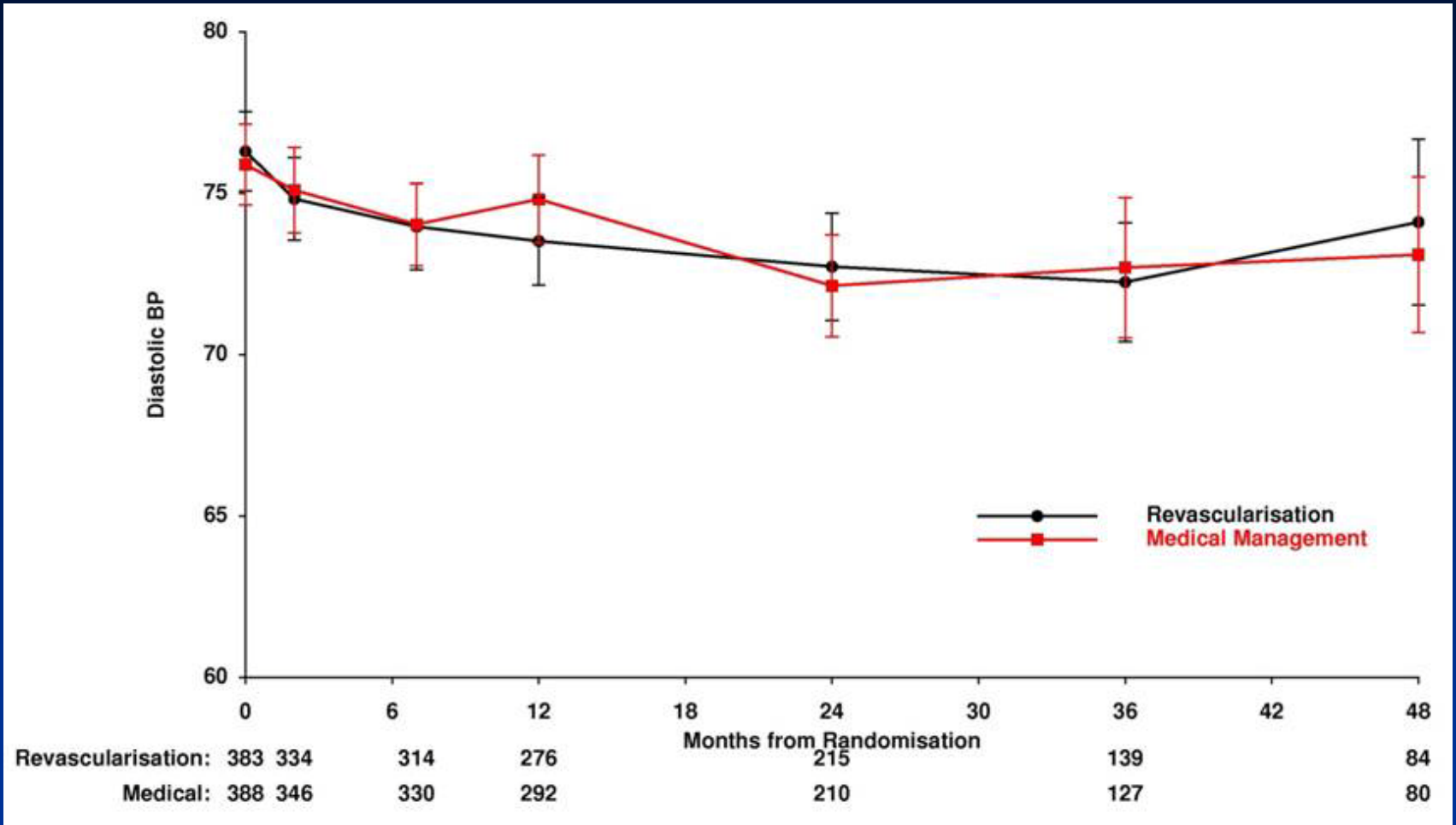
Kalra, PA. *XLV ERA-EDTA Congress*, 2008 (Abstract)

ASTRAL
Mean Change in Systolic BP



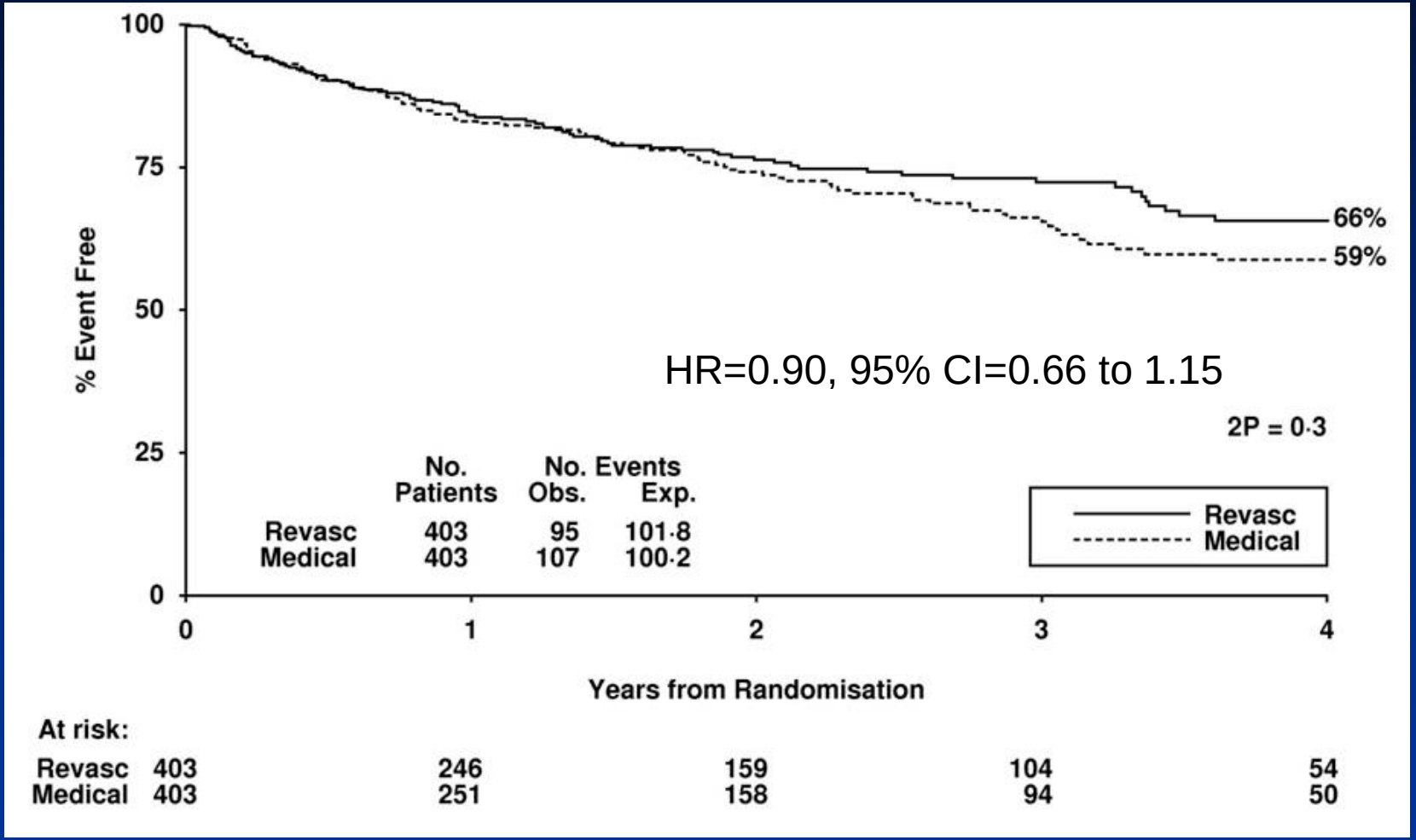
Kalra, PA. *XLV ERA-EDTA Congress*, 2008 (Abstract)

ASTRAL
Course of Diastolic BP



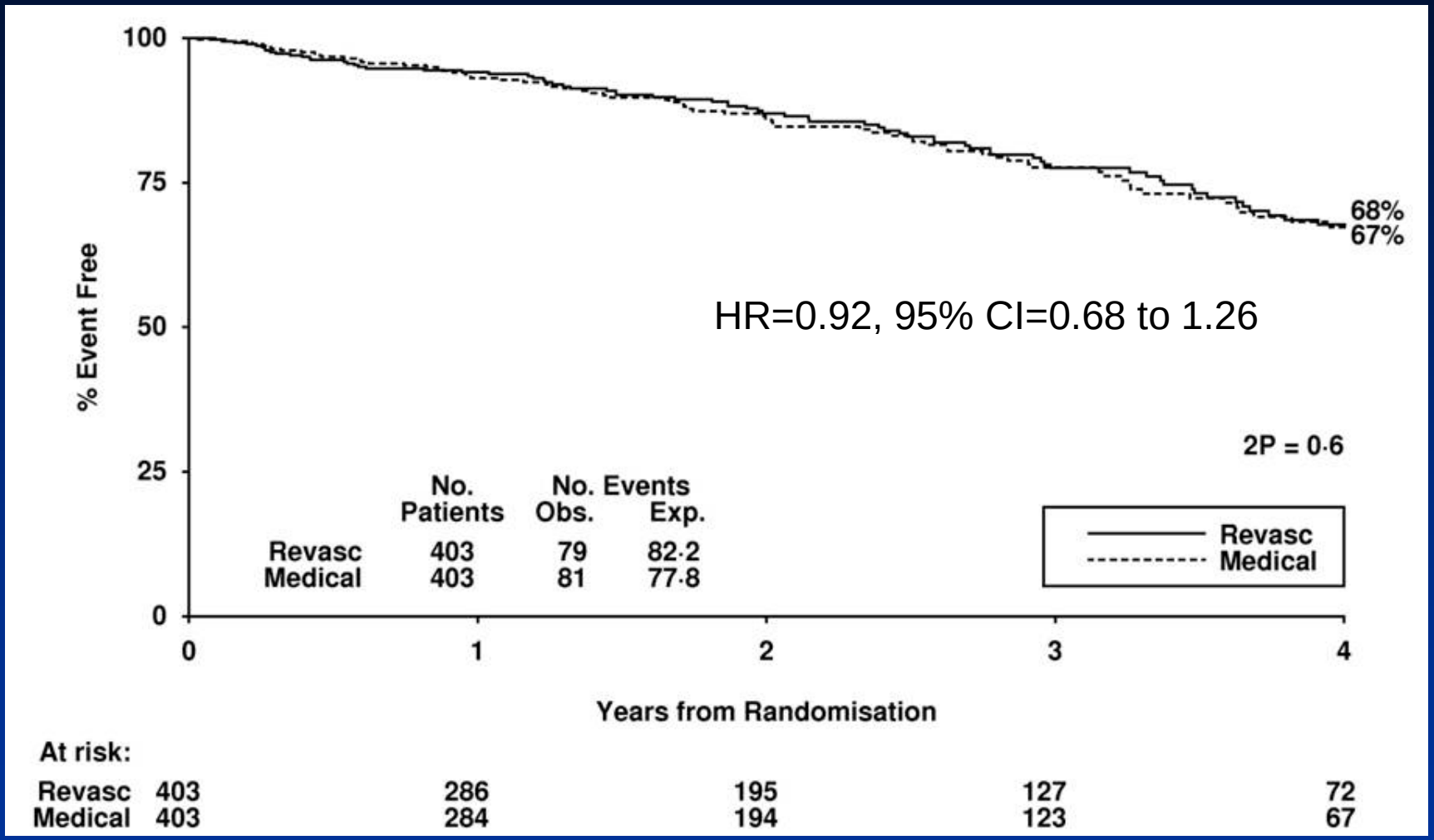
Kalra, PA. *XLV ERA-EDTA Congress*, 2008 (Abstract)

ASTRAL
Time to First MI, Stroke, Vascular Death, or Hospitalization for Angina ,Fluid Overload, or Cardiac Failure



Kalra, PA. *XLV ERA-EDTA Congress*, 2008 (Abstract)

ASTRAL
Mortality



Kalra, PA. *XLV ERA-EDTA Congress*, 2008 (Abstract)

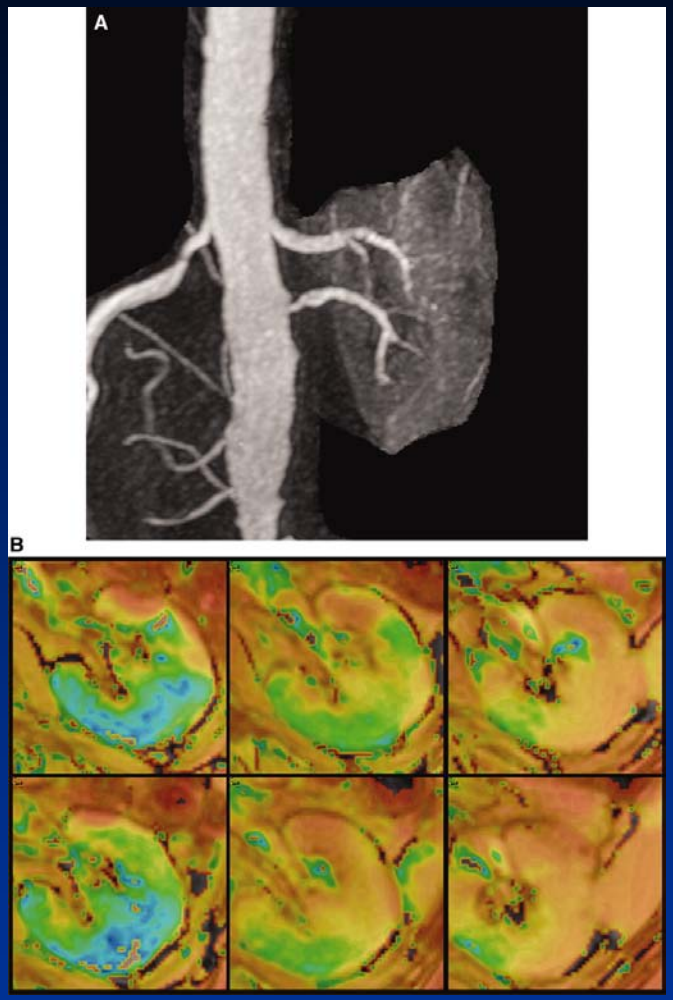
Clinical Questions Relevant to Determining Role of Revascularization

Clinical Questions	Evaluation Tools/ Considerations
• What is the severity of RAS?	Quantitative angiography, translesional gradient, intravascular ultrasound
• Is the lesion(s) treatable with reasonable risk?	Location, associated aortic disease, aneurysm, occlusion, accessory vessels
• Is the lesion(s) contributing importantly to disease?	Activation of pressor systems, historical course of blood pressure and renal function, renal size discrepancy, other intrinsic renal disease
• What is the likelihood of substantial benefit from revascularization?	Rapidity of clinical evolution, other intrinsic renal disease, salvageability of renal function (resistive index, renal size), associated comorbidities, risk of RAS progression, procedural risks, response to medical therapy

Future Directions

- Nature of hypoperfusion-related renal damage
- Interaction of hypoperfusion-related renal damage with other microvascular renal disease
- Methods for identifying and modifying pathways contributing to hypoperfusion-related renal damage
- Functional tools for defining “critical perfusion pressure” threshold
- Optimal methods for tracking progression of RAS
- Tools for determining salvageability of renal function
- Optimization of endovascular repair

BOLD MRI to Evaluate Tissue Oxygenation in RAS



Textor, S. C. et al. J Am Soc Nephrol 2008;19:780-788

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