CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY
JANUARY 23-25 2014
MARRIOTT RIVE GAUCHE & CONFERENCE CENTER PARIS, FRANCE

Can we Predict Success of Renal Artery Stenting? Angioplastie stenting rénal : peut-on prédire la réussite ?

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Disclosure

Speaker name:

Monika L. Gloviczki.....

- ☐ I have the following potential conflicts of interest to report:
- ☐ Consulting
- ☐ Employment in industry
- ☐ Shareholder in a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)
- ☒ **I do not have any potential conflict of interest**

Atherosclerotic renal artery stenosis (ARAS)

Prevalence of ARAS increases with

- age
- other risk factors of atherosclerosis
- end-stage renal failure
- heart failure

In 14% of patients with newly initiated dialyses ARAS was the cause of end-stage renal disease

Potential Indications for Revascularization of ARAS

- Uncontrolled renovascular hypertension
- Ischemic nephropathy
- Flash pulmonary edema
- Bilateral high grade renal artery stenosis
- Solitary functioning kidney

Indications for Revascularization of ARAS

American Heart Association Recommendations for Revascularization of Atherosclerotic Renal Artery Stenosis (ARAS)

Asymptomatic stenosis

- Percutaneous revascularization can be considered for treatment of an asymptomatic bilateral or solitary viable kidney with hemodynamically significant ARAS (class IIb, level of evidence [LOE] C)
- Usefulness of percutaneous revascularization of asymptomatic unilateral hemodynamically significant ARAS in a viable kidney is not well established and is currently clinically unproved (class IIb, LOE C)

Hypertension

- Percutaneous revascularization is reasonable for patients with hemodynamically significant ARAS and accelerated hypertension, resistant hypertension, malignant hypertension, hypertension with unexplained unilateral small kidney, and hypertension with intolerance to drug treatment (class IIa, LOE B)

Preservation of renal function

- Percutaneous revascularization is reasonable for patients with ARAS and progressive chronic kidney disease with bilateral ARAS or ARAS of a solitary functioning kidney (class IIa, LOE B)
- Percutaneous revascularization can be considered for patients with ARAS and chronic renal insufficiency with unilateral ARAS (class IIb, LOE C)

Effect of ARAS on congestive heart failure and unstable angina

- Percutaneous revascularization is indicated for patients with hemodynamically significant ARAS and recurrent, unexplained congestive heart failure or sudden, unexplained pulmonary edema (class I, LOE B)
- Percutaneous revascularization is reasonable for patients with hemodynamically significant ARAS and unstable angina (class IIa, LOE B)

Hirsch AT et al, J Am Coll Cardiol, 2006; Lao D et al, Mayo Clin Proc 2011

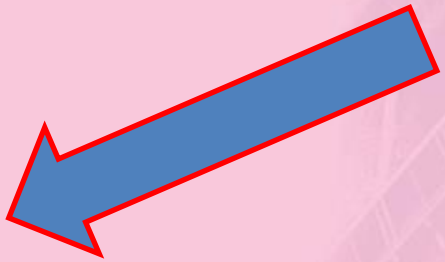
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Revascularization versus Medical Therapy for Renal-Artery Stenosis

The ASTRAL Investigators*

Patients were eligible to participate if they had 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 availa
were not eligible if they re
cularization or were cons
likelihood of requiring re
6 months, if they had nor



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.)

Wheatley et al, N Engl J Med 2009;361:1953-1962

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 [illegible] Katherine R. Tuttle, M.D., Joseph [illegible] Joseph M. Massaro, P[illegible] and Lance D. Dworkin[illegible]

Table 1. Baseline Characteristics of the Study Population, According to Treatment Group.*

Characteristic	Stenting plus Medical Therapy (N=459)	Medical Therapy Only (N=472)
Angiographic findings	Means ± SD	
% Stenosis, as assessed by core laboratory	67.3±11.4	66.9±11.9
% Stenosis, as assessed by investigator	72.5±14.6	74.3±13.1

CONCLUSIONS

Renal-artery stenting did not confer a significant benefit with respect to the prevention of clinical events when added to comprehensive, multifactorial medical therapy in people with atherosclerotic renal-artery stenosis and hypertension or chronic kidney disease. (Funded by the National Heart, Lung and Blood Institute and others; ClinicalTrials.gov number, NCT00081731.)

Positive outcomes of RAS: improved BP control

Factor	Author, year	Study	N of patients
Improved BP and mean number of antihypertensive meds	Dervisoglu, 2010	Retrospective	36
Improved BP and mean number of antihypertensive meds	Kobo, 2010	Open, prospective	166
Improved BP and decreased number of antihypertensive meds	Yildiz, 2013	Open, prospective (bilateral ARAS)	5
Improved BP and QoL	Laird, 2010	Prospective registry	188
Improved BP	Guo, 2010	Open, prospective	68
Improved BP	Wolak, 2011	Retrospective	32
Improved BP	Mazza, 2011	RCT	18
Improved BP	Ginzburg, 2013	Retrospective	41
Reduction in SBP	Jaff, 2012	Open, prospective, multicenter	202
Reduction in the number of antihypertensive meds	Kumbhani, 2011	Metaanalysis of 6 RCT	1208

Other positive outcomes of RAS

Factor	Author, year	Study	N of patients
Improvement in serum cratinine in patients with higher baseline levels, improved BP	Sapoval, 2010	Registry	251
Improved eGFR and mortality in patients with renal impairment	Kalra, 2010	Twin-center open study	530 (stent/meds)
Echocardiographic parameters reflecting LV diastolic function and cardiac symptoms	Kawarada, 2010	Open, prospective	61
LV mass reduction	Rzeznik, 2011	Open, prospective	84
Improved heart failure (HF) control and reduction in HF hospitalizations	Kane, 2010	Retrospective	100 (stent/meds)
Clinical benefit in 63%	Eklof, 2009	Retrospective	152
Improved fractional hypoxia (BOLD), cortical perfusion and blood flow	Saad, 2013	Open, prospective, controlled	50
Increased ipsilateral kidney volume	Modral, 2012	Retrospective	38

Can we predict the success of renal stenting?

Clinical factors predicting success of renal artery stenting (RAS)

Factor	Author, year	Study	Number of patients
High baseline DBP and pulse pressure	Ronden, 2010	Meta-analysis of 11 prospective studies	1552
Elevated baseline SBP > 150 mmHg	Weinberg, 2013	Meta-analysis of 5 prospective, multicenter studies	901
Lower pulse pressures reflecting less advanced vascular stiffness	Dieter, 2009	Open, prospective	243
Requirement for ≥ 4 meds, preoperative DBP > 90 mmHg	Modrall, 2011	Retrospective	149
HTN emergency, number of antihypertensive meds, lack of Angina/CHF	Modrall, 2012	Retrospective (RAS in patients with HTN emergencies, urgencies, and angina/CHF)	52

- Failure to achieve adequate blood pressure with optimal medical therapy
- HTN emergency

Factors predicting success of RAS: Hemodynamically significant lesion

Factor	Author, year	Study	N of patients
Duplex resistive index (RI)	Eklof, 2009	Retrospective	152
RI	Santos, 2010	Retrospective	106
RI	Yuksel, 2012	Retrospective	73
RI	Cianci, 2010	Open, prospective	40
RI	Cianci, 2013	Open, prospective	55
Hyperemic systolic gradient ≥ 21 mmHg corresponding to the average IVUS area stenosis of 78%	Leesar, 2009	Open, prospective	62
Dopamine-induced mean transstenotic pressure gradient ≥ 20 mmHg	Mangiacapra, 2010	Open, prospective	53
Grade of renal stenosis	Rzeznik, 2011	Open, prospective	84

- Grade of renal artery stenosis (>70%)
- Duplex resistive index (peak systolic velocity - end-diastolic velocity/ peak systolic velocity) < 0.8 indicate no microvascular disease
- Transstenotic pressure gradient ≥ 20 mmHg

Hemodynamically significant lesion

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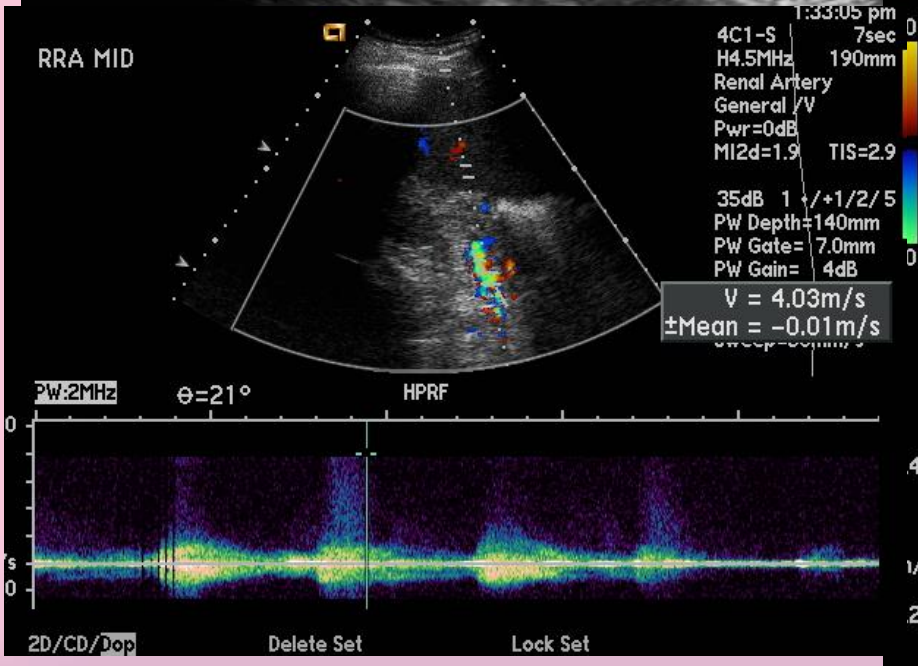
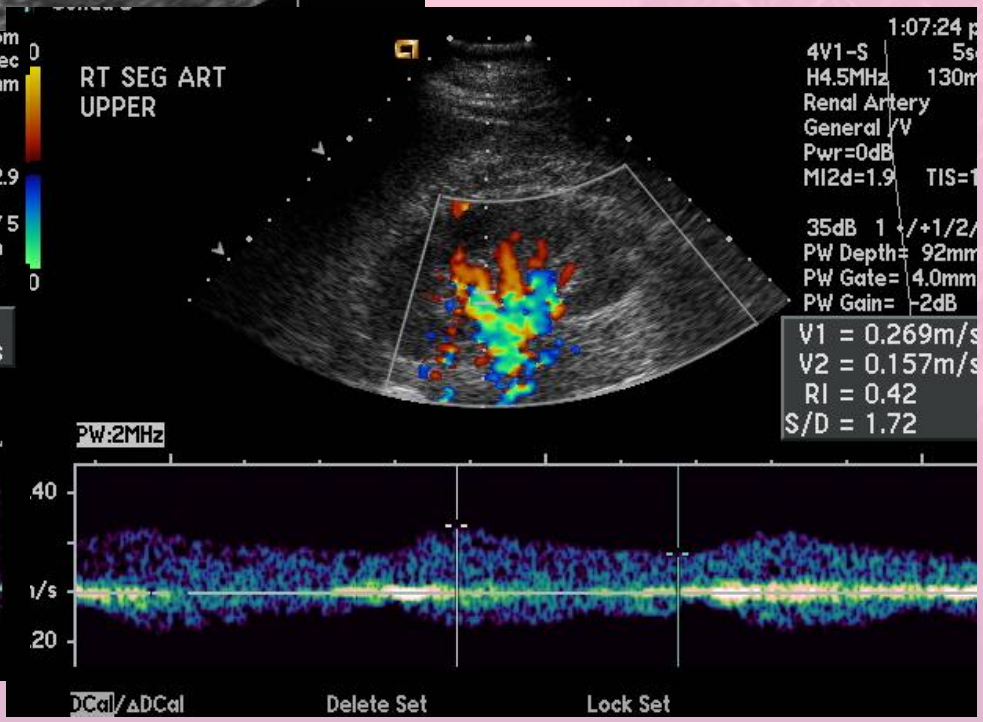
Renal artery duplex

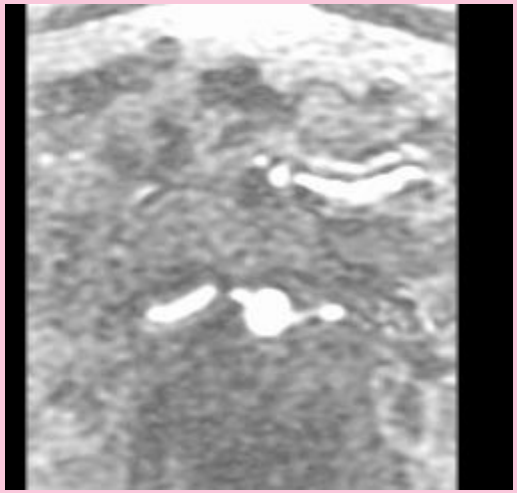
Right kidney

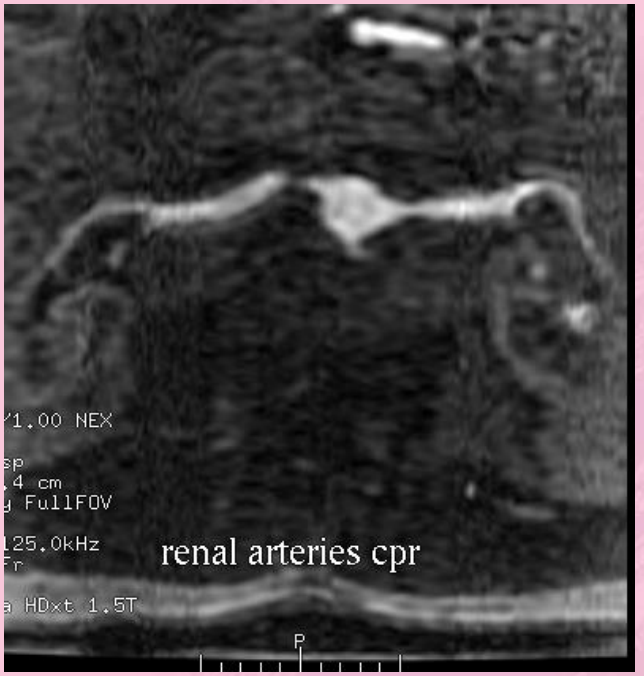




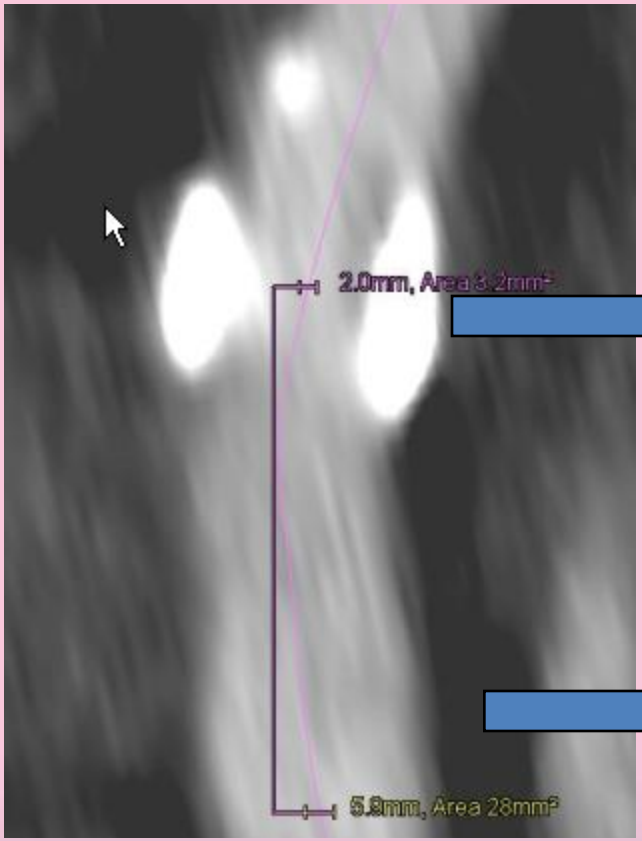
Hemodynamically significant lesion

Magnetic Resonance Angiogram

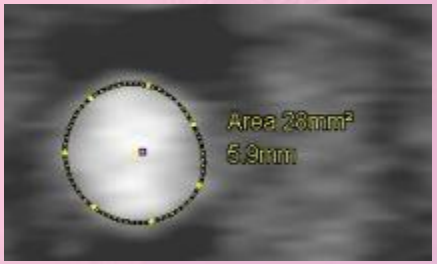




Assessment of the stenosis: Residual luminal areas provide degree (%) of renal artery obstruction



@ Stenosis



Baseline

But 5% of normotensive healthy kidney donors have some renal artery lesions visible on the computed tomography (CT) angiograms !

Poor correlation between Trans-stenotic Gradients and Angiographic diameter stenosis

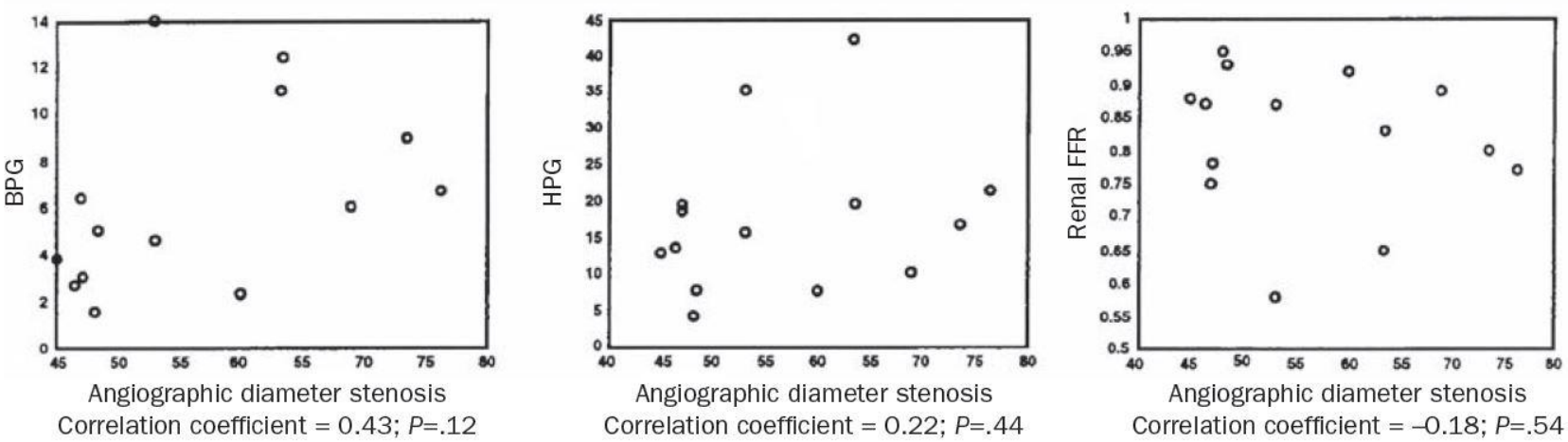


FIGURE. There is a poor correlation of quantitative angiographic diameter stenosis with baseline mean translesional pressure gradient (BPG) (left), hyperemic mean translesional pressure gradient (HPG) (middle), and renal fractional flow reserve (FFR) (right).
From *Catheter Cardiovasc Interv*,[17] with permission.

White, Mayo Clin Proc 2011

Trans-stenotic Gradients and Renin Release

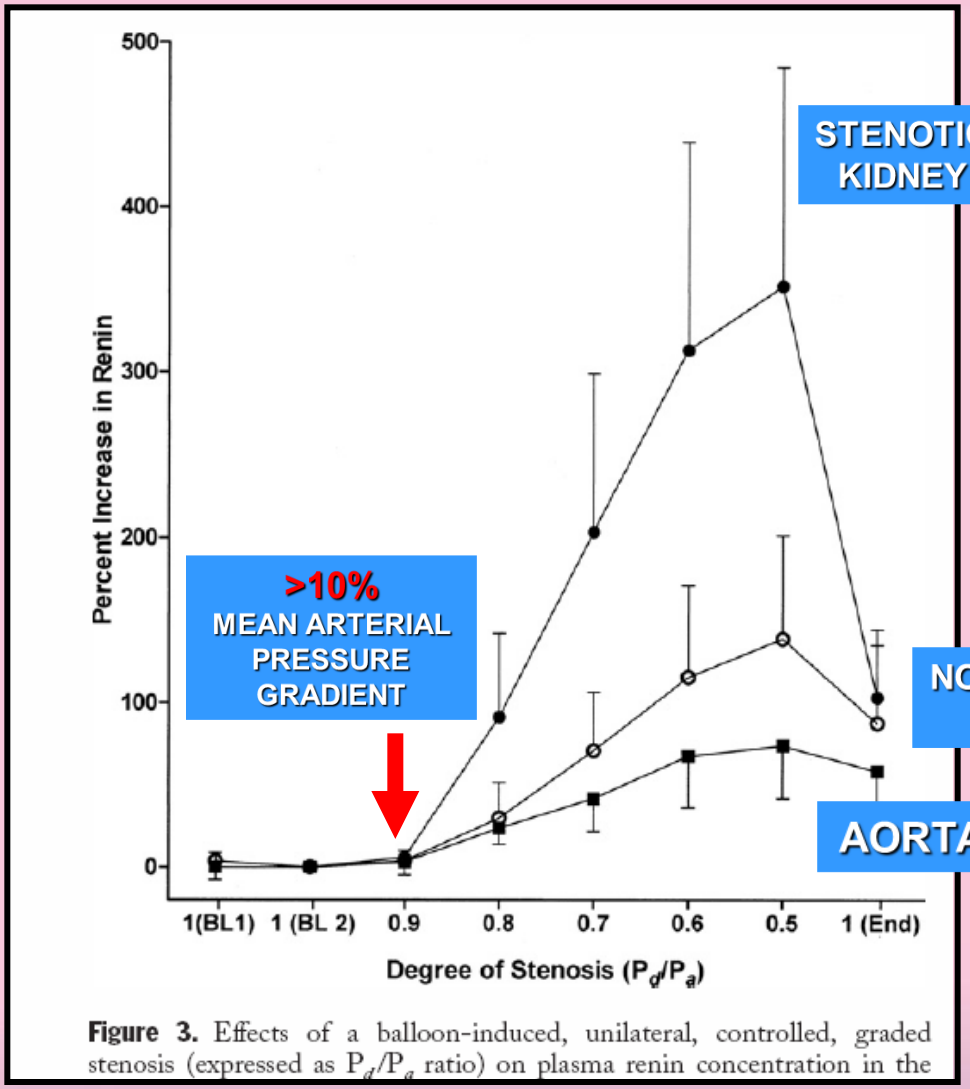
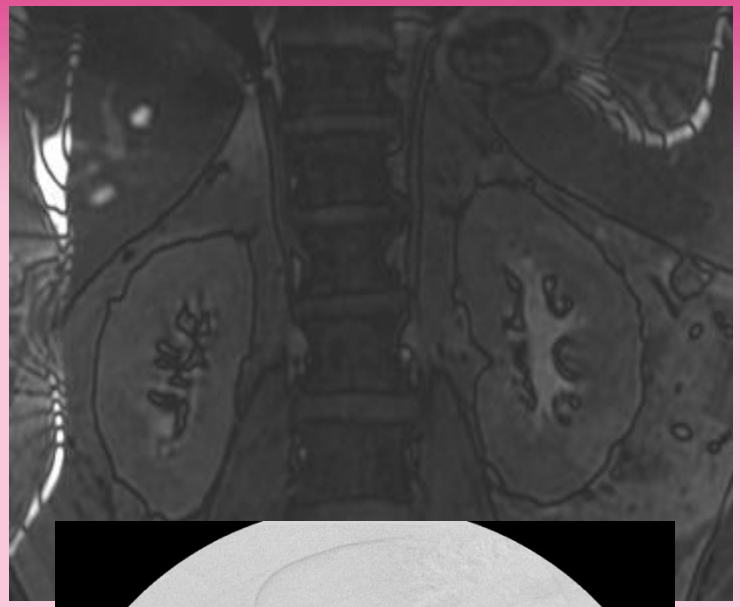
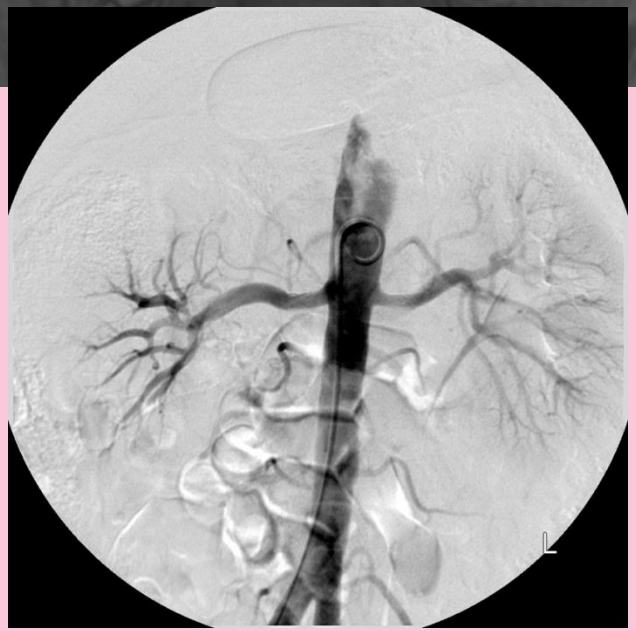


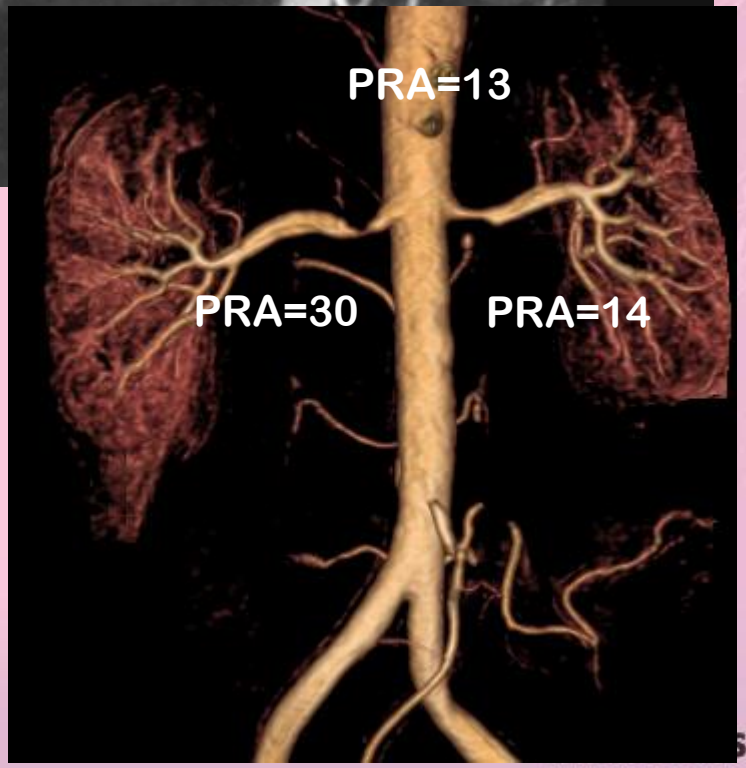
Figure 3. Effects of a balloon-induced, unilateral, controlled, graded stenosis (expressed as P_d/P_a ratio) on plasma renin concentration in the

No effect until pressure reduction >10% corresponding to average 25 mm SBP or 12 mm Hg MAP

De Bruyne et.al., JACC 2006







6 months later: 122/ 70, No Meds.

Factors predicting success of RAS: kidney size and cortical thickness

Factor	Author (year)	Study	Number of patients
Larger ipsilateral kidney (volume>150 cm^3)	Modrall, 2011	Retrospective	149
Abnormal renal cortical thickness	Padigala, 2009	Retrospective	31
Parenchymal preservation after RAS	Davies, 2010	Retrospective	592
Contralateral kidney size > 9 cm	Davies, 2009	Retrospective	447

Multidetector CT results

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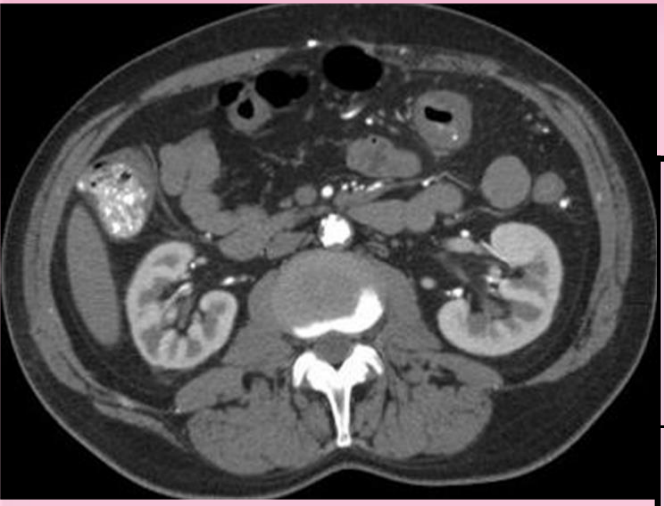

	Moderate ARAS 13 stenotic kidneys	Severe ARAS 17 stenotic kidneys
K volume (cc/m2 of BSA)	58.5* ± 7.1	20.1**& ± 6.9
Renal blood flow (mL/min)	292.6* ± 51.2	186.4**& ± 42.7
% of RBF on the affected side	43.5* ± 2.7	28.5**& ± 4.5

*p <.05 and ** p ≤.001 vs vs Contralateral kidney/ Essential hypertensive patients,
& p<.001 vs Moderate ARAS

Factors predicting success of RAS: baseline renal function

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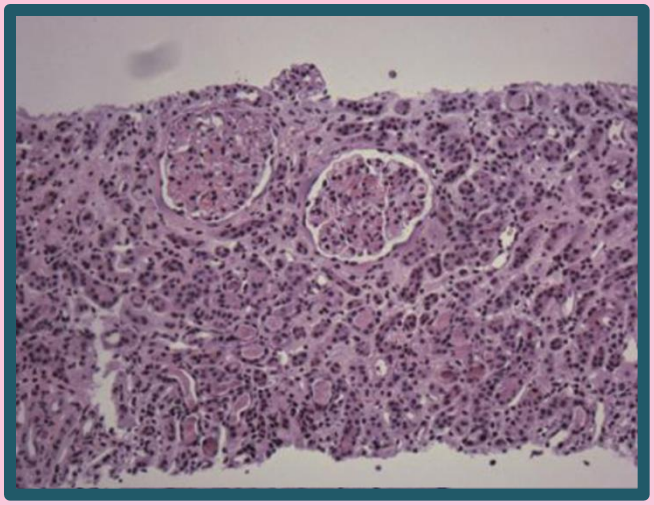
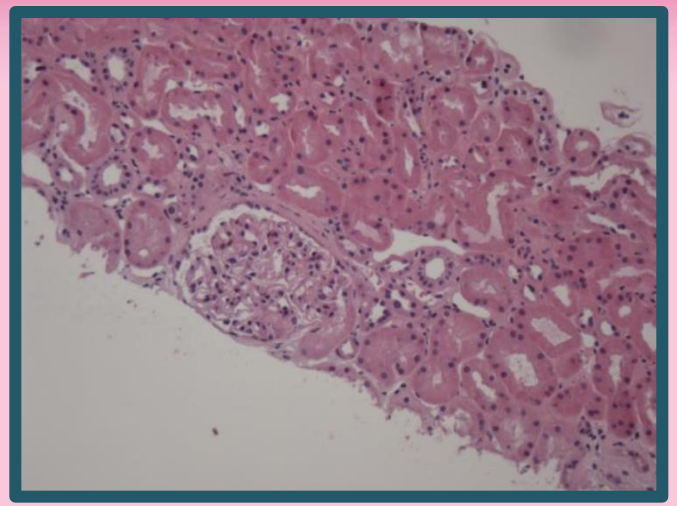
Factor	Author, year	Study	N of patients
Impaired renal function (eGFR <60 mL/min/1.73 m^2)	Singer, 2009	Open, prospective	67
Poor baseline renal function	Albertal, 2010	Open, prospective	100
Baseline eGFR ≥ 40 mL/min/1.73m^2	Beck, 2010	Retrospective	129
Baseline eGFR ≥ 60 mL/min/1.73m^2	Chang, 2010	Open, prospective	110
Rapid kidney function deterioration	Valluri, 2012	Retrospective (cohort "outside of the ASTRAL")	127
Steep decline in preoperative renal function	Modrall, 2011	Retrospective (RAS for kidney salvage)	61
Rapid decline of GFR in patients with bilateral ARAS or single kidney	Mannarino, 2012	Open, prospective	30
GFR > 60 mL/min	Prajapati, 2013	Open, prospective	86
Higher baseline serum creatinine	Trani, 2013	Open, prospective (patients with CKD)	62
Lower uricemia and proteinuria	Cianci, 2013	Open, prospective	55

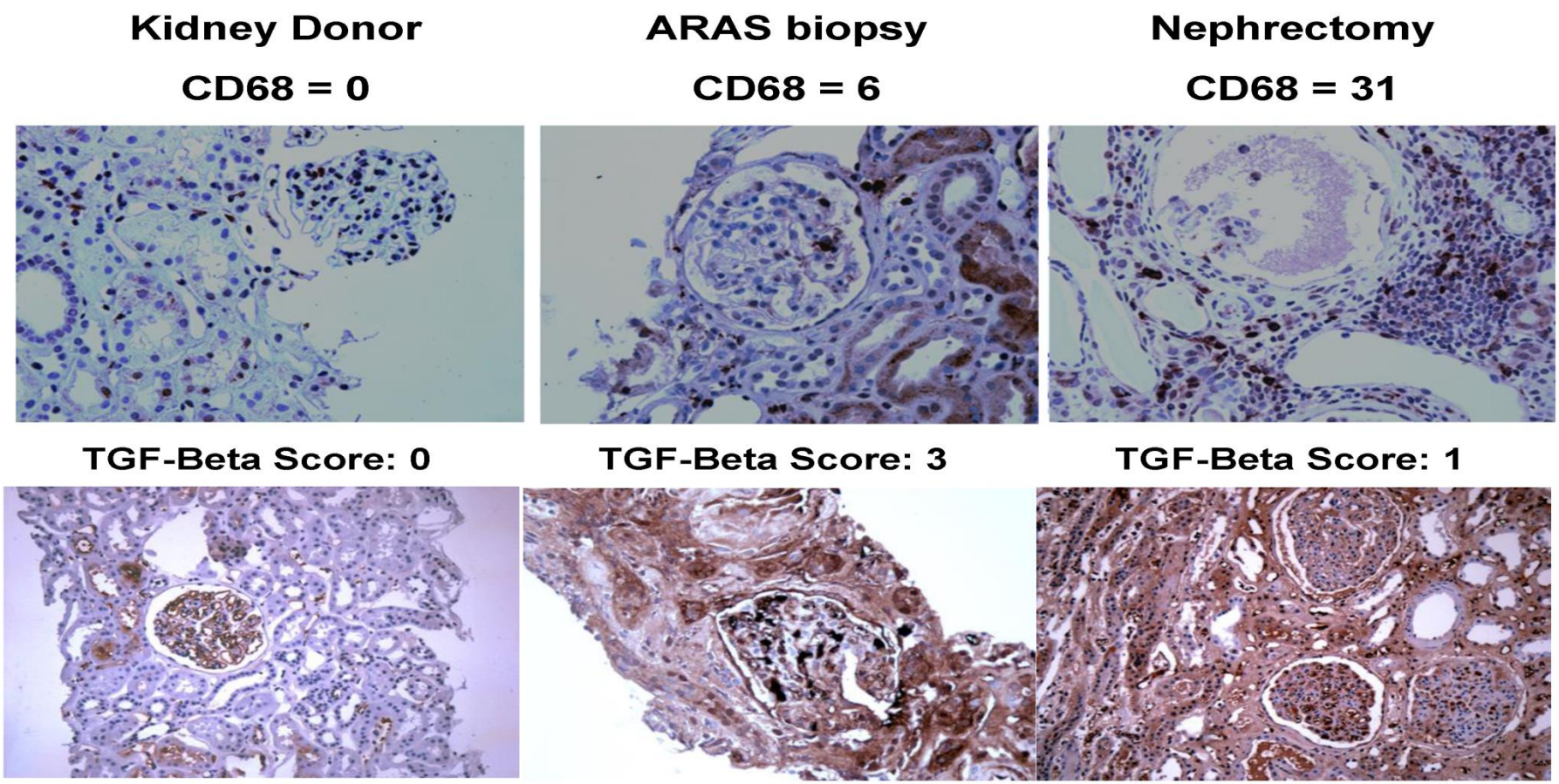
- Rapid decline in preoperative renal function





Histologic evidence of intact viable glomeruli was used in the past as predictive determinant of salvageable renal parenchyma.

Novick AC et al, Renal Vascular Disease, 1996

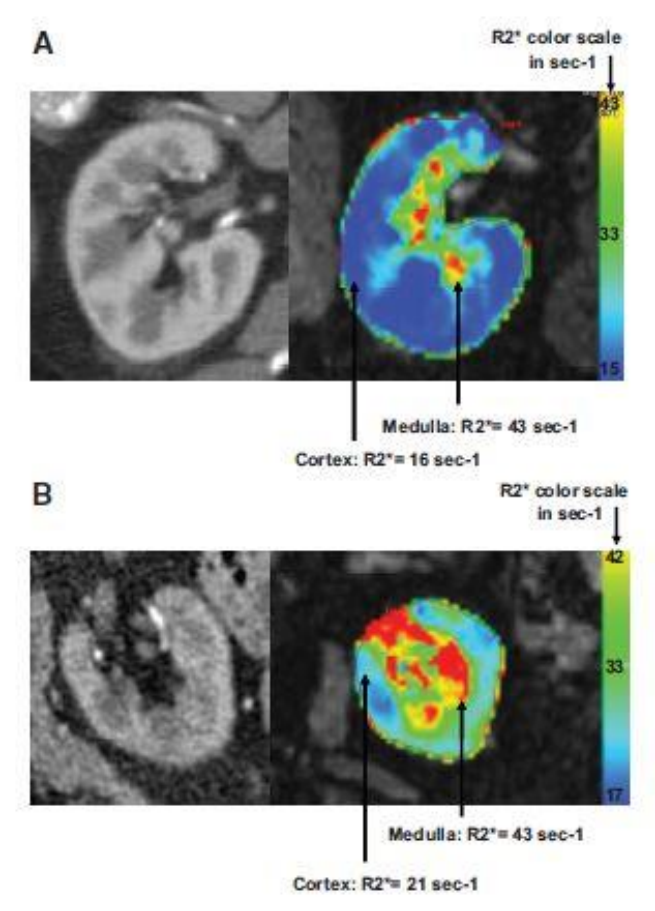


Activation of Transforming Growth Factor β and accumulation of tissue macrophages in addition to progressive interstitial fibrosis, even in ARAS kidneys with preserved structure and function.

Gloviczki ML et al, CJASN 2013

Other factors predicting success of RAS

Factor	Author, year	Study	N of patients
Clonidine use	Modrall, 2011	Retrospective	149
Male gender	Albertal, 2010	Open, prospective	100
Male gender	Beck, 2010	Retrospective	129
Female gender	Prajapati, 2013	Open, prospective	86
Lower C-Reactive Protein	Trani, 2013	Open, prospective (patients with CKD)	62
Smaller necrotic core in the plaque on intravascular ultrasound virtual histology	Prasad, 2011	Open, prospective	17
B-type natriuretic peptide >50pg/mL	Staub, 2010	Open, prospective	120
High ratio R2*(BOLD MR) / isotopic single kidney GFR	Chrysochou, 2012	Open, prospective	28
Antiplatelet reducing distal embolization during protected RAS	Kanjwal, 2010	RCT	42
Statins administration	Davies, 2009	Retrospective	447
Use of distal protection device	Miyashita, 2013	Retrospective (RAS for kidney salvage)	23



Blood Oxygen Level Dependent Magnetic Resonance (BOLD MR)

Cortical hypoxia and expansion of medullary hypoxic zones in severe ARAS

Gloviczki ML et al, Hypertension 2011

Examples of :
A: Moderate ARAS
B: Severe ARAS (ultrasound velocities >384 cm/s)

CONCLUSIONS

- Factors predicting success of RAS include:
  - Failure to achieve adequate blood pressure with optimal medical therapy
  - Severity of hypertensive disease (HTN emergency…)
  - Hemodynamically significant lesion
    - Grade of renal artery stenosis >70%
    - Duplex resistive index <0.8
    - Transstenotic pressure gradient ≥20 mmHg
  - Rapid decline in renal function during antihypertensive treatment, in particular with ACE inhibitors or angiotensin receptors blockers
  - Viability of renal parenchyma (kidney size > 7 cm, BOLD MR, biopsies)

CONCLUSIONS

- New evaluations like BOLD MR will further improve selection of candidates for renal artery stenting.

Thank you / Merci