Atherosclerotic Renal Artery Stenosis: an update on treatment recommendations

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Disclosures

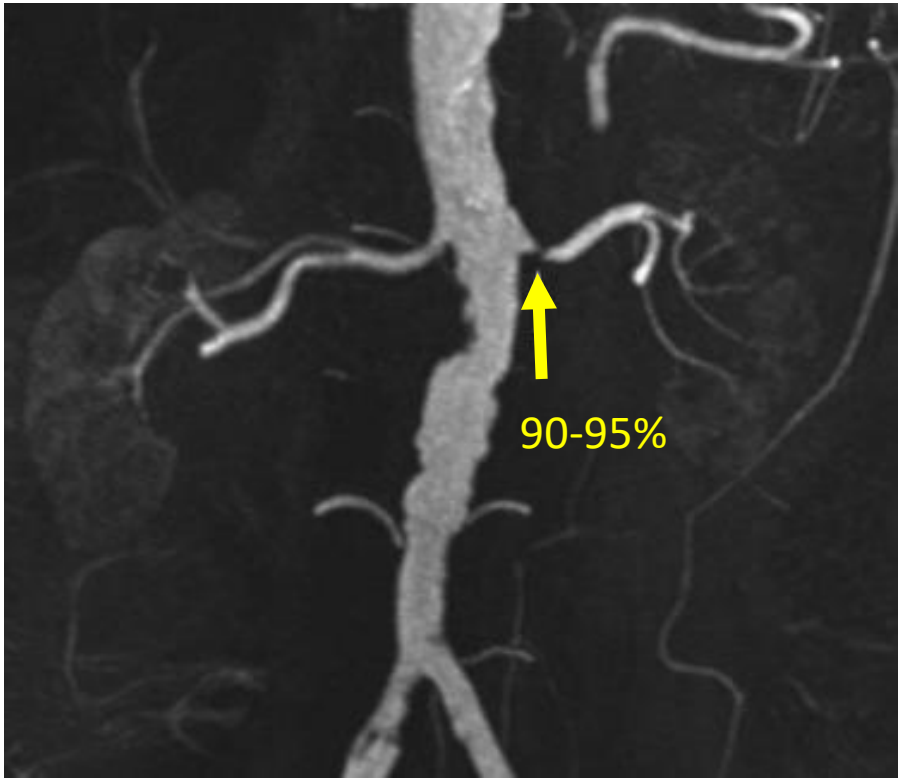
Nothing to disclose

Atherosclerotic Renal Artery Stenosis

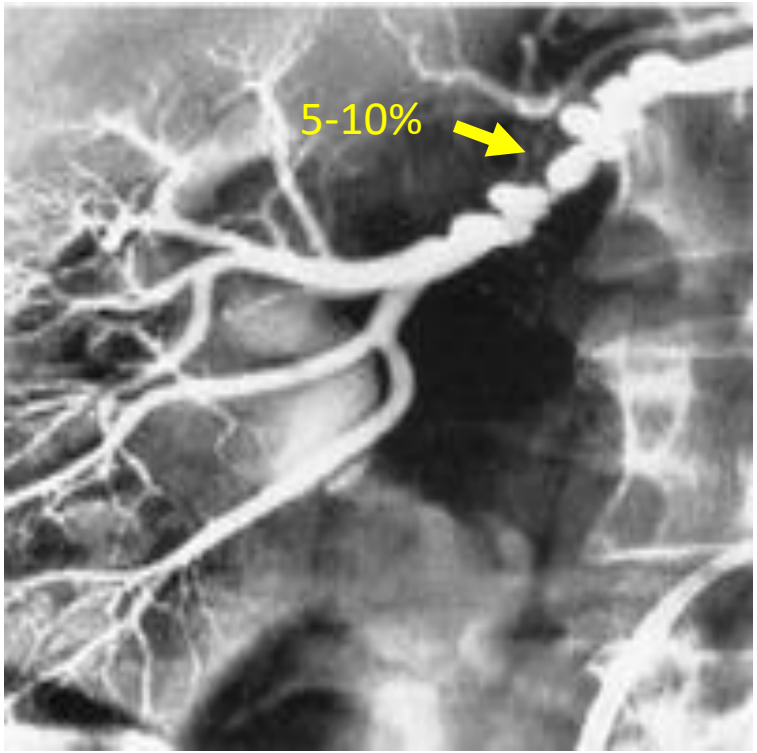
Epidemiology

Renal artery stenosis

Atherosclerotic RAS



Fibromuscular dysplasia



Prevalence of ARVD

Table 3. Prevalence and Severity of Renal Artery Stenosis According to Individual Selection Criteria

Selection Criteria	Total (N = 837)	Renal Artery Angiography			
		Normal (n = 528)	<50% (n = 189)	50%–<70% (n = 59)	≥70% (n = 61)
Severe atherosclerosis	651 (78%)	408 (63%)	146 (22%)	49 (8%)	48 (7%)
Resistant/severe HTN	264 (32%)	144 (54%)	74 (28%)	21 (8%)	25 (9%)
Renal impairment	232 (28%)	122 (53%)	53 (23%)	19 (8%)	38 (16%)
Pulmonary edema	9 (1%)	1 (11%)	4 (44%)	2 (22%)	2 (22%)
HTN components					
Resistant hypertension	245 (29%)	136 (55%)	69 (28%)	20 (8%)	20 (8%)
Severe hypertension	19 (2.3%)	8 (42%)	5 (26%)	1 (5%)	5 (26%)
Severe atherosclerosis components					
Abdominal aortic/lower extremity disease	101 (12%)	48 (48%)	22 (22%)	16 (16%)	15 (15%)
Carotid disease	97 (12%)	42 (43%)	29 (30%)	9 (9%)	17 (18%)
Severe CAD	572 (68%)	372 (64%)	124 (22%)	43 (8%)	33 (6%)
LMCA disease	89 (11%)	53 (60%)	19 (21%)	11 (12%)	6 (7%)

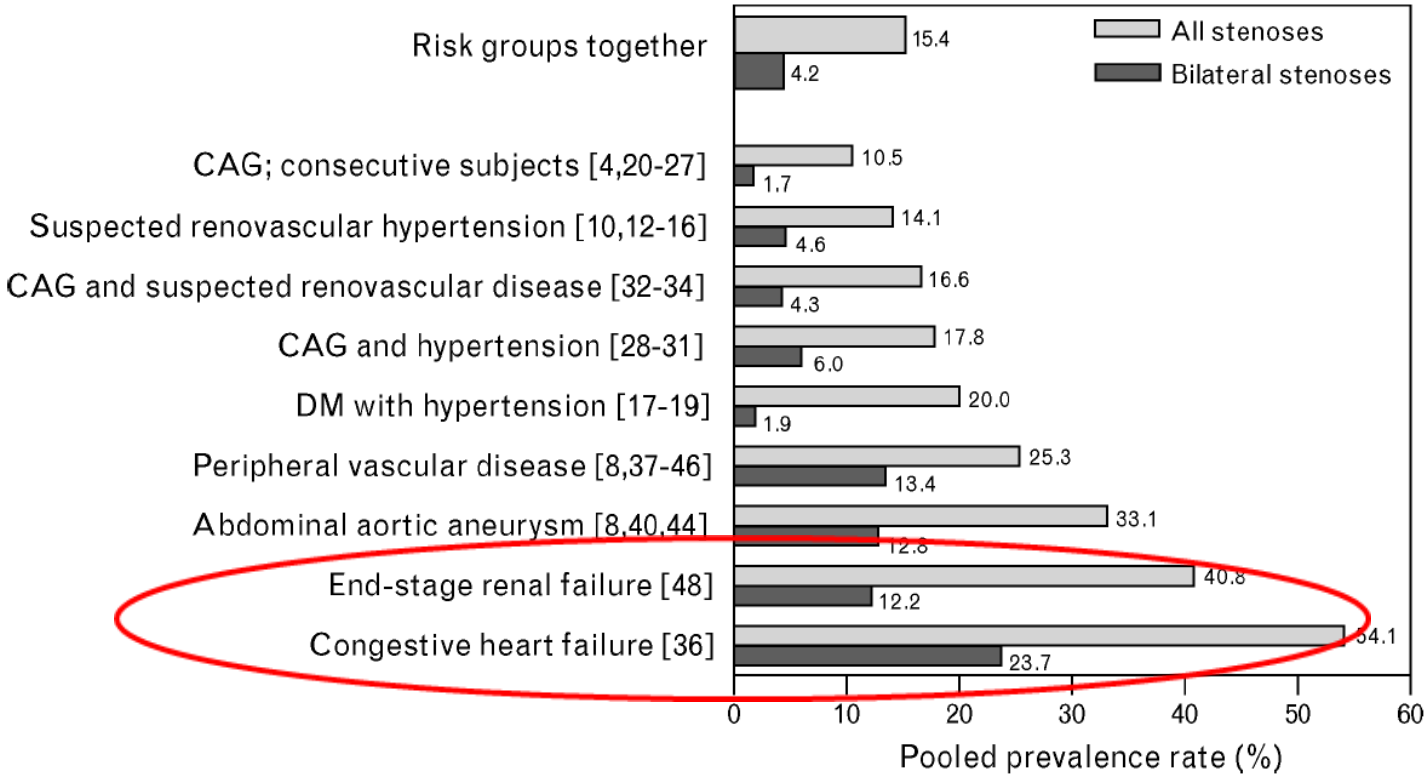
Percentages under "total" column refer to denominator of N = 837 and do not sum to 100% because patients may satisfy multiple criteria. Percentages under columns from "normal" to ≥70% are calculated based on the number in the corresponding "total" column.

CAD = coronary artery disease; HTN = hypertension; LMCA = left main coronary artery.

*Age at time of renal duplex sonography.

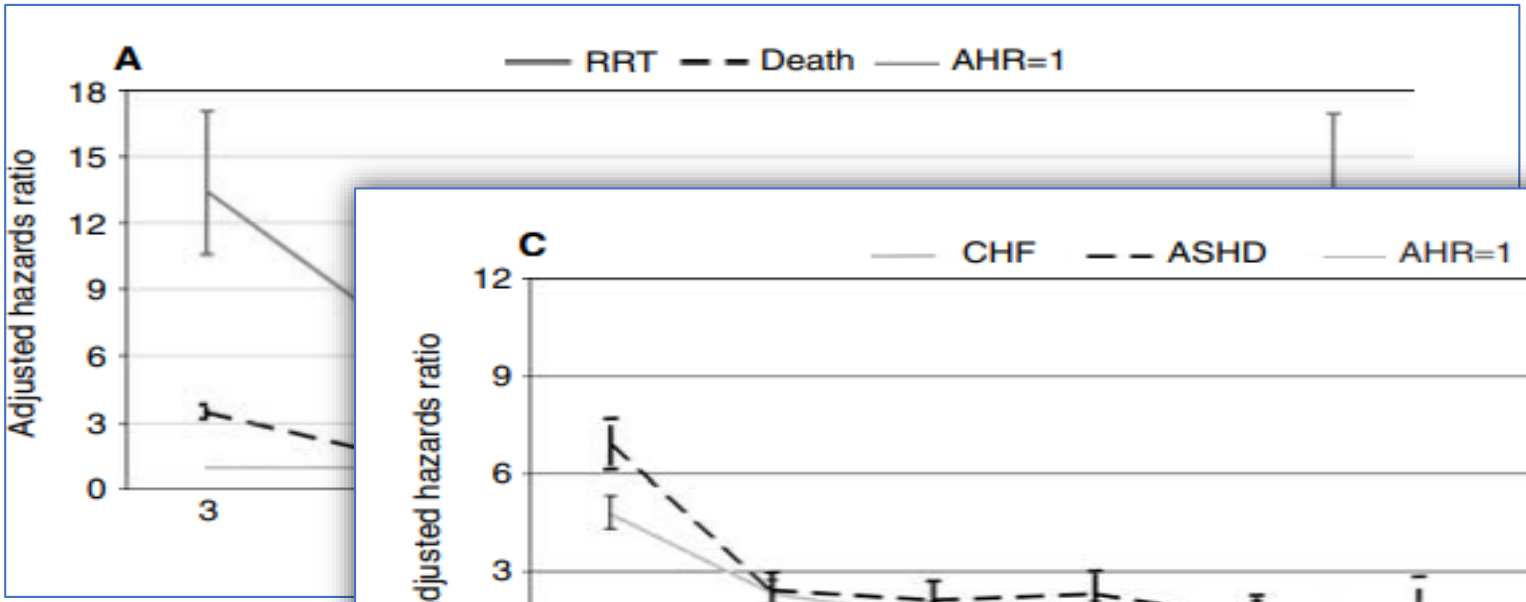
Hansen et al, J Vasc Surg 2002
Buller et al, J Am Coll Cardiol 2004

Prevalence of ARVD in high risk groups



de Mast & Beutler. *J Hypertens* 2009

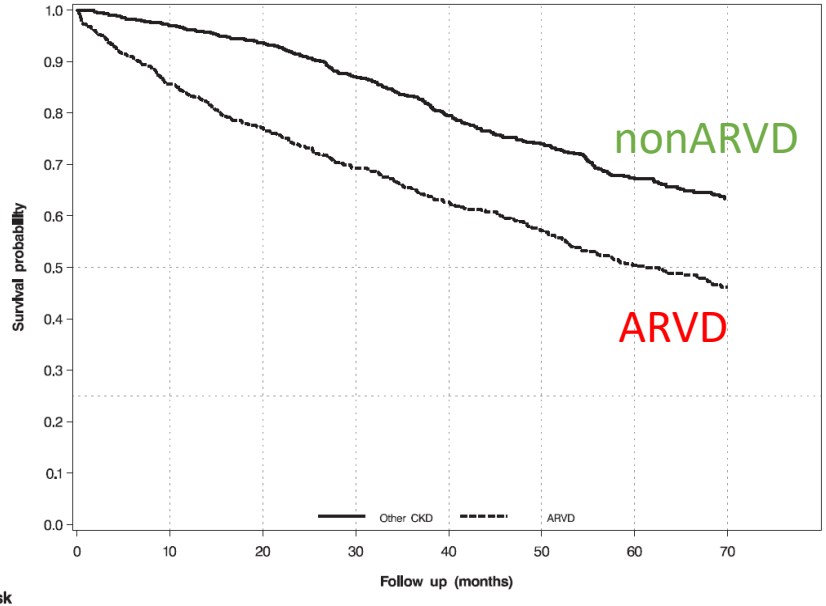
Overall prognosis of ARVD



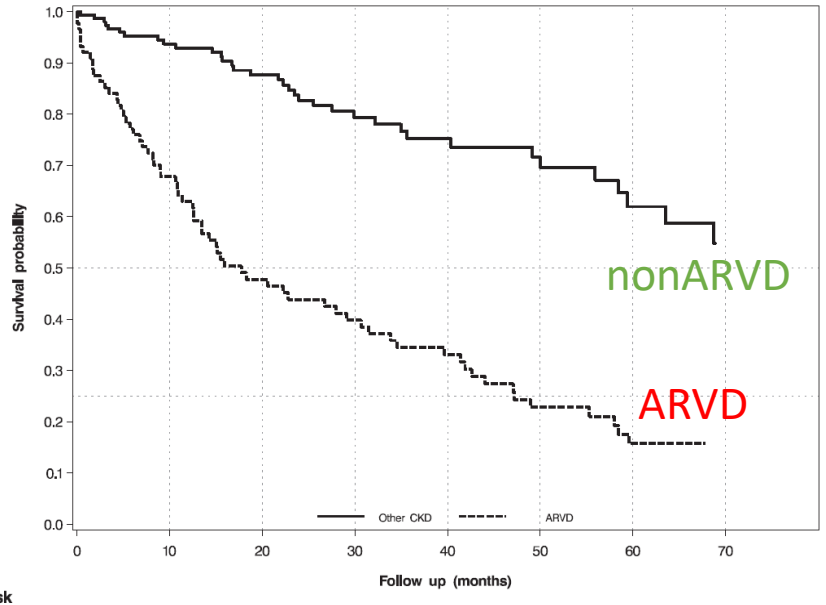
5% random sample of the US Medicare population

Kalra et. al, Kidney Int 2005

Prognosis of ARVD in CKD



Number at Risk						
Other CKD	906	843	782	682	504	321
ARVD	562	469	394	335	265	187



Number at Risk						
Other CKD	151	113	81	52	38	22
ARVD	88	50	33	25	16	9

Before dialysis ARVD vs non-ARVD had:
- increased risk for death **(HR 1.5 (1.2–1.8), *P* < 0.001**)

After dialysis ARVD vs non-ARVD had:
- increased risk for death (**HR 3.3 (2.2-5.0), P < 0.001**)

Richie et al. Nephrology (Carlton) 2017

Prognosis of ARVD by clinical presentation

n= 467 patients with ARAS ≥50%,

Table 3. Associations Between High-Risk Presentations and Risk for End Point in Medically Managed Patients

	Flash Pulmonary Edema		Rapidly Declining Kidney Function		Refractory HTN	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Death	2.19 (1.39-3.47)	<0.001	0.69 (0.42-1.12)	0.1	0.82 (0.59-1.14)	0.2
CV event[a]	3.07 (1.71-5.51)	<0.001	0.77 (0.41-1.48)	0.4	1.10 (0.67-1.62)	0.9
ESKD[b]	1.89 (0.81-4.43)	0.1	0.72 (0.381-1.69)	0.5	0.82 (0.45-1.51)	0.5

Abbreviations: CI, confidence interval; CV, cardiovascular; ESKD, end-stage kidney disease; HR, hazard ratio; HTN, hypertension.

[a]CV event defined as myocardial infarction/acute coronary syndrome, hospitalization for pulmonary edema or arrhythmia, stroke or transient ischemic attack, new onset of symptomatic angina, or deterioration of existing angina requiring interventional procedure.

[b]ESKD defined as initiation of long-term renal replacement therapy, kidney transplantation, or estimated glomerular filtration rate $< 10\,mL/min/1.73\,m^2$.

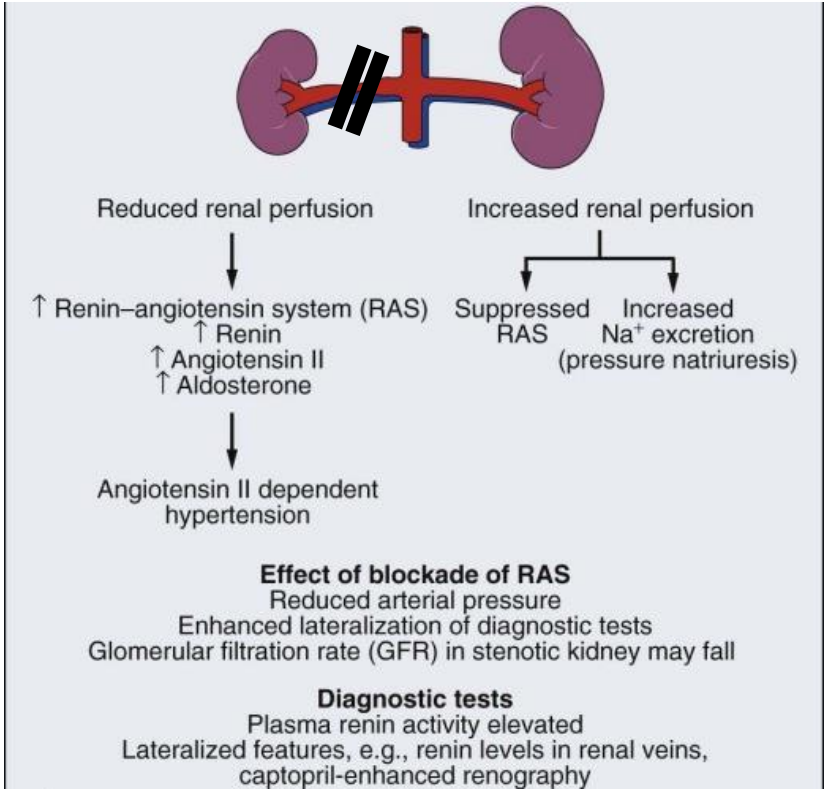
Richie et al. *Am J Kidney Dis* 2014

Atherosclerotic Renal Artery Stenosis

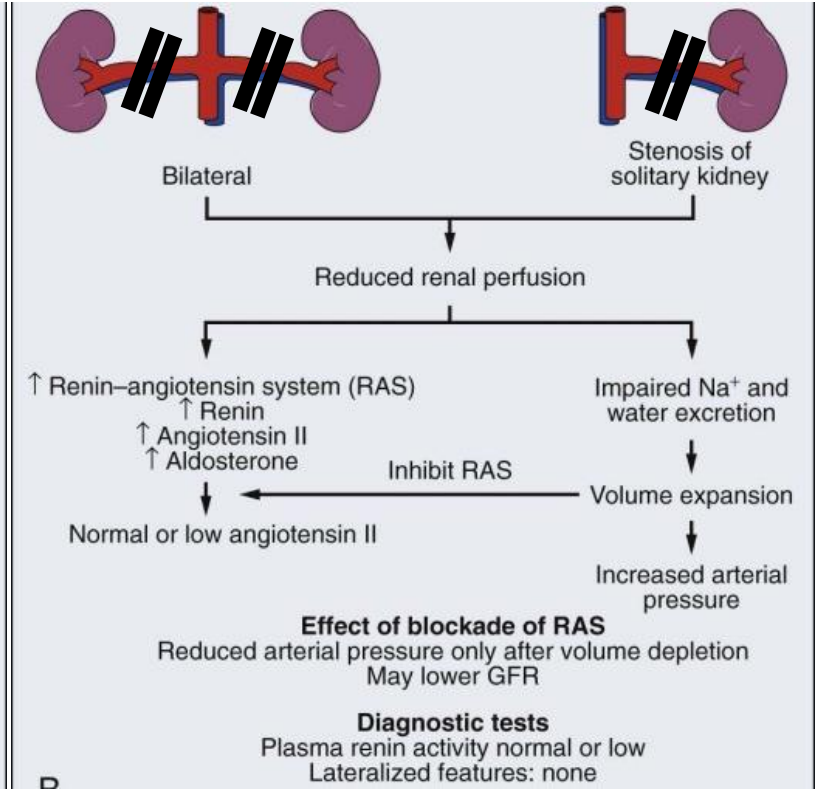
Pathophysiology

Pathophysiology

"1 clip – 2 kidney hypertension"

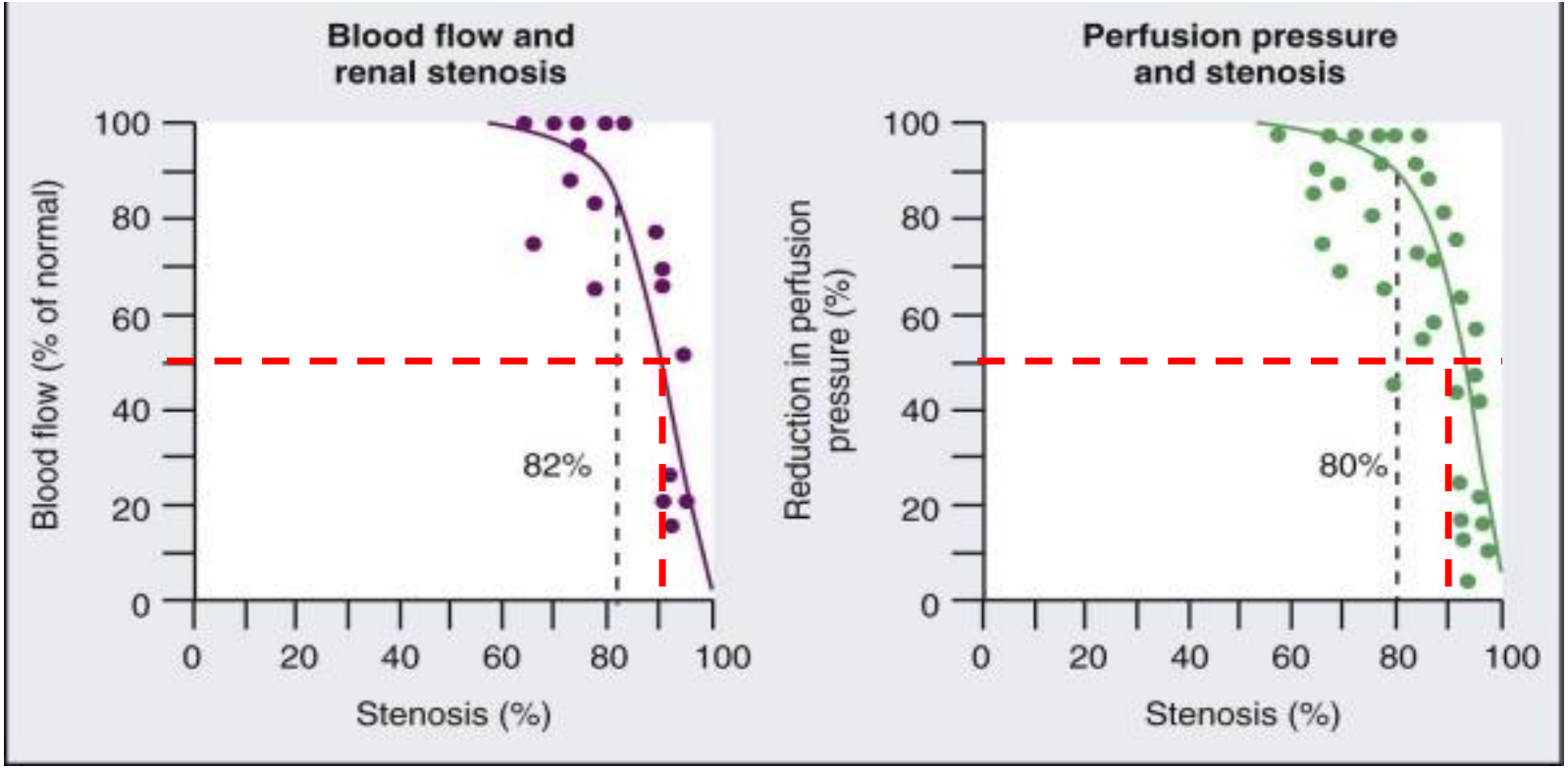


"1 clip – 1 kidney hypertension"



Textor S, Greco B. Renovascular Hypertension and Ischaemic Renal Disease. In: Floege J, Johnson RJ, Feehally J (eds). Comprehensive Clinical Nephrology, 4th Edn. Mosby Elsevier, Philadelphia, PA, 2010

Pathophysiology: importance of stenosis grade

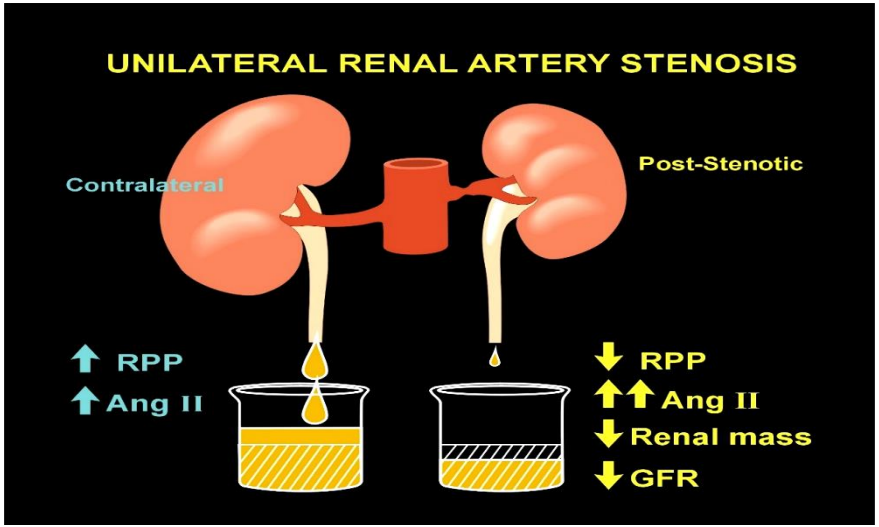


Textor S, Greco B. Renovascular Hypertension and Ischaemic Renal Disease. In: Floege J, Johnson RJ, Feehally J (eds). Comprehensive Clinical Nephrology, 4th Edn. Mosby Elsevier, Philadelphia, PA, 2010

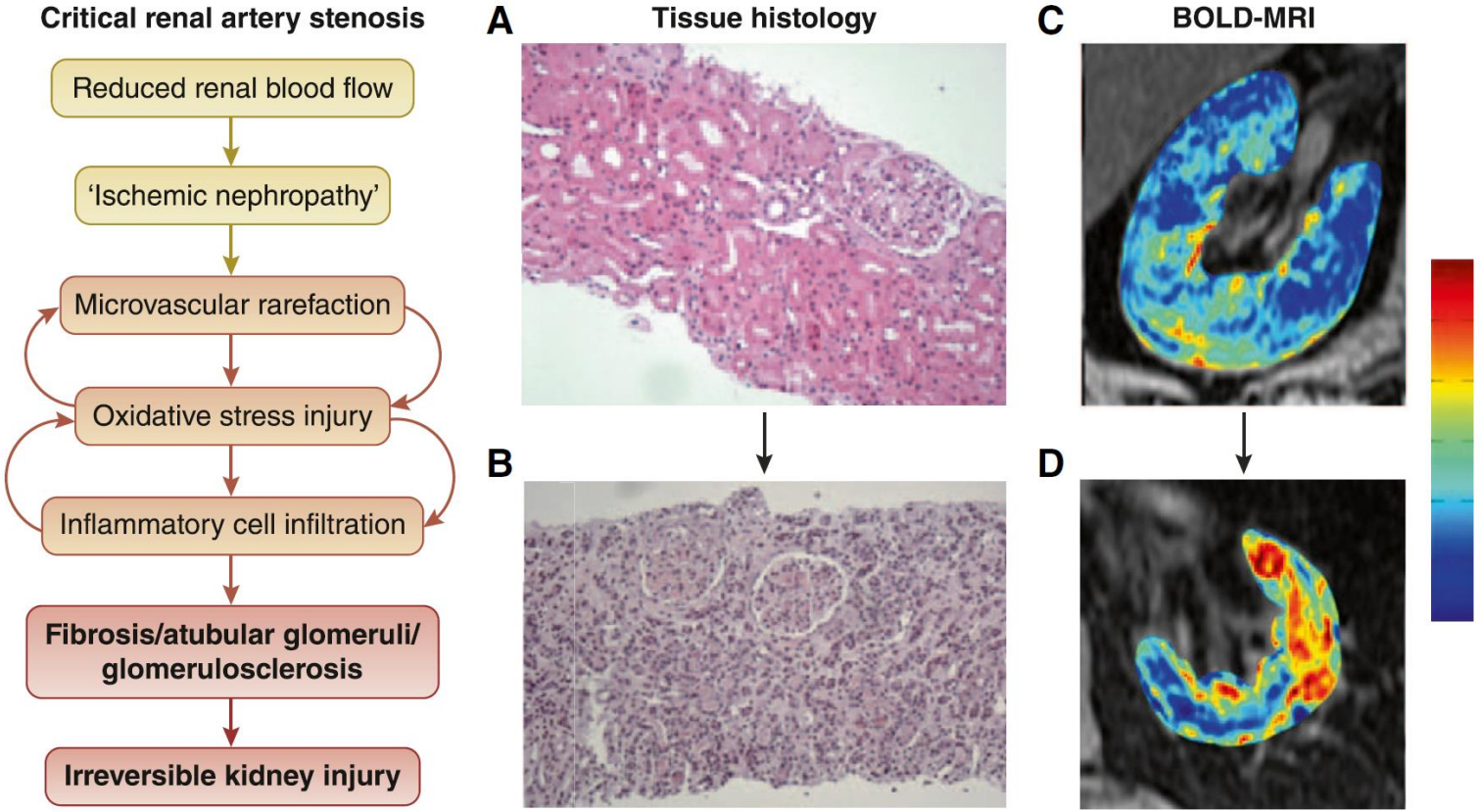
Pathophysiology of ARVD: importance of time

Irreversible parenchymal HTN:

- Prolonged exposure to high BP and high levels of ATII causes widespread arteriolar damage and glomerulosclerosis in the contralateral kidney.
- Corrective surgery for unilateral RVH was successful in 78% of those with HTN of less than 5 years duration but in only 25% of those with HTN of a longer duration.



Pathways leading to kidney injury beyond “critical” levels of RAS



Hicks et al. Am J Kidney Dis 2022

Atherosclerotic Renal Artery Stenosis

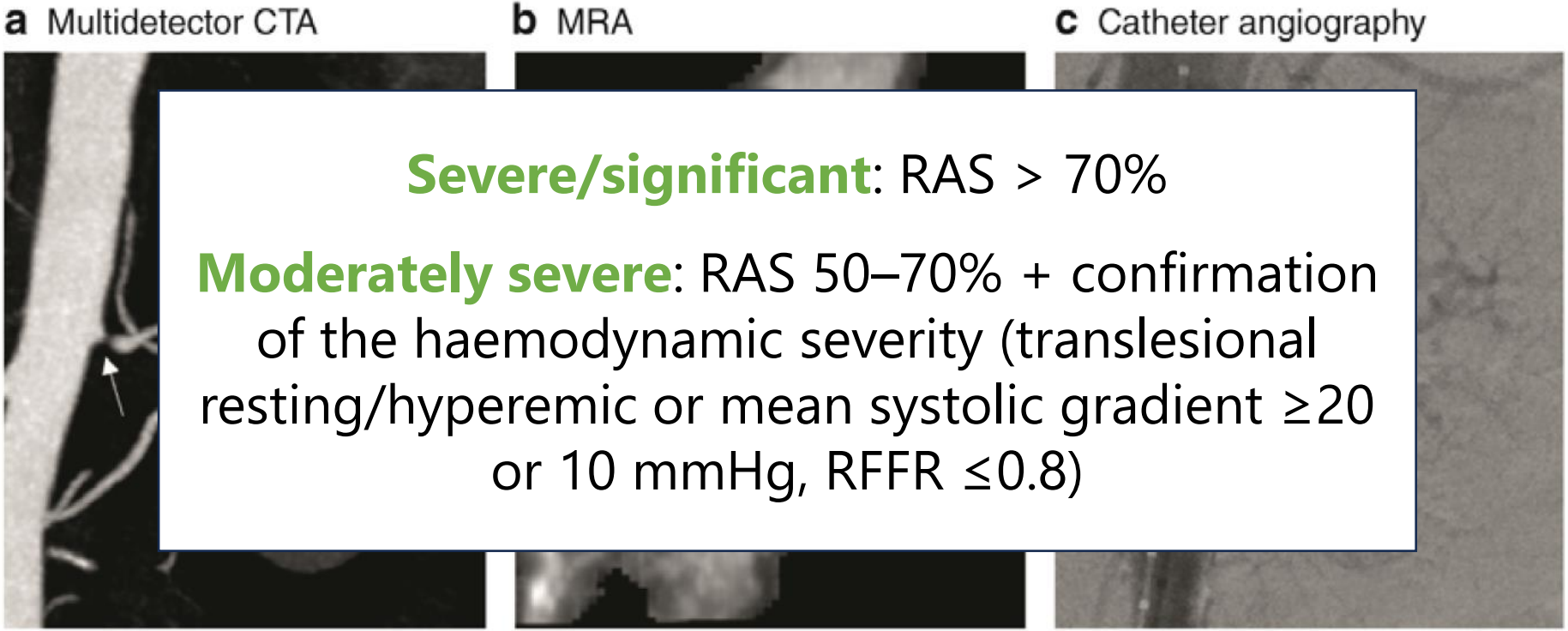
Diagnosis

Clinical presentations

Hypertension	• Sudden onset or worsening of existing hypertension • Grade III hypertension (especially in the presence of other cardiovascular risk factors or atherosclerotic disease in other circulatory beds) • Resistant hypertension
Kidney Disease	• Atrophic kidney or size difference > 1.5 cm between kidneys • Rapid, unexplained kidney function decline • Decline in kidney function (eGFR) >30% after starting treatment with ACEi/ARBs • Increased albuminuria/proteinuria due to hypertensive damage in the non-stenotic kidney in unilateral RAS
Heart failure	• Repeated hospital admissions for decompensated heart failure with preserved left ventricular function on echocardiography • Sudden unexplained (“flash”) pulmonary edema

Sarafidis, Theodorakopoulou et al, Nephrol Dial Transplant 2023

ARVD: imaging modalities



Severe/significant: RAS > 70%

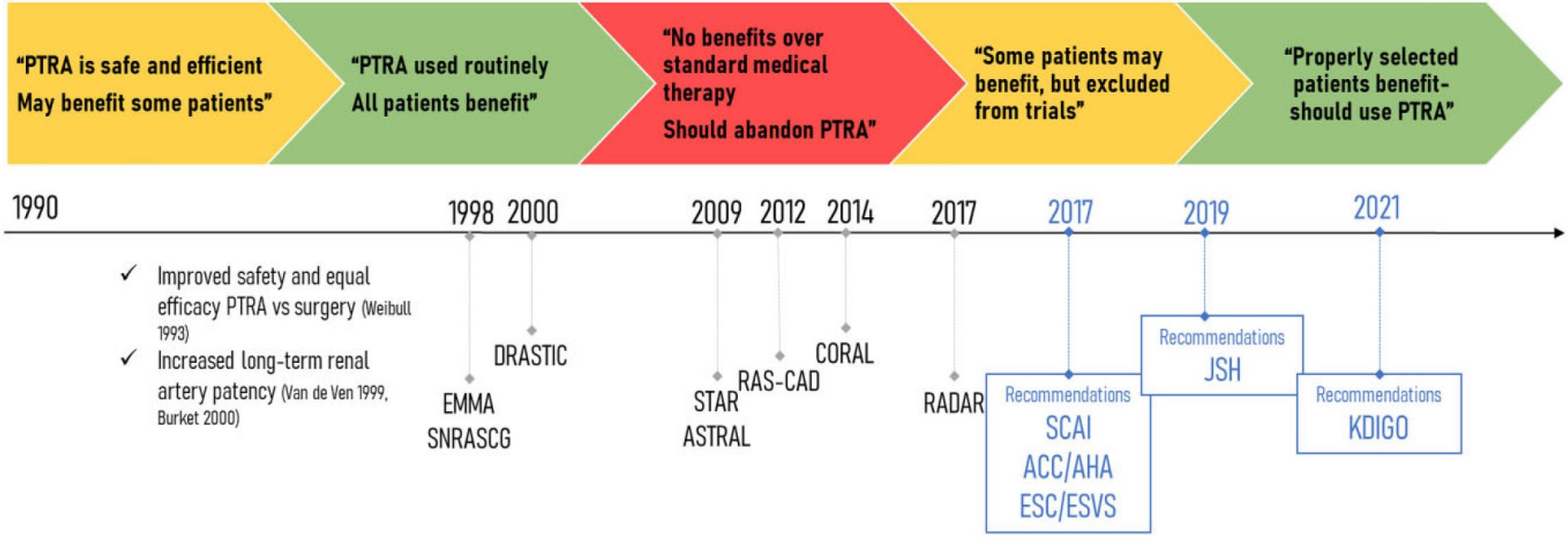
Moderately severe: RAS 50–70% + confirmation of the haemodynamic severity (translesional resting/hyperemic or mean systolic gradient ≥20 or 10 mmHg, RFFR ≤0.8)

Sarafidis, Theodorakopoulou et al. Nephrol Dial Transplant 2023
Hicks et al. Am J Kidney Dis 2022

Atherosclerotic Renal Artery Stenosis

Management

Revascularization vs Medical Therapy in ARVD



Theodorakopoulou et al. *Clin Kidney J* 2022

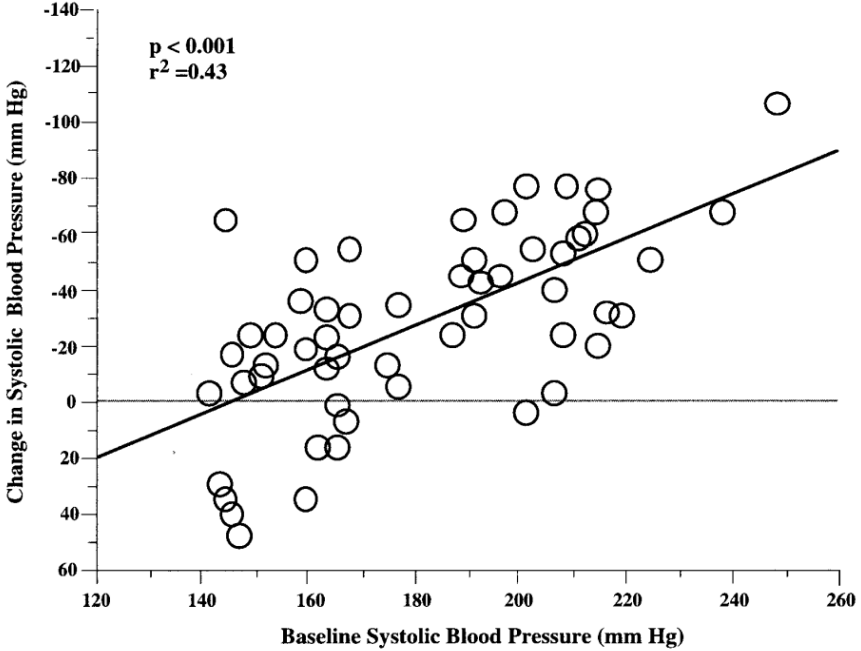
Standard Medical Therapy

- BP control
  - Multiple drug regimens
  - ACEi / ARBs :
    - First choice– Reduction in mortality
    - Generally well tolerated
    - Stability of GFR (>30% increase = ? critical stenosis)
  - Calcium Channel Blockade / Diuretic
- ↓ CV risk: statins, antiplatelets, smoking cessation, exercise, weight loss

Van der Niepen et al. Curr Hypertens Rep 2017;Hicks et al. Am J Kidney Dis 2022; Sarafidis et al. Nephrol Dial Transplant 2023

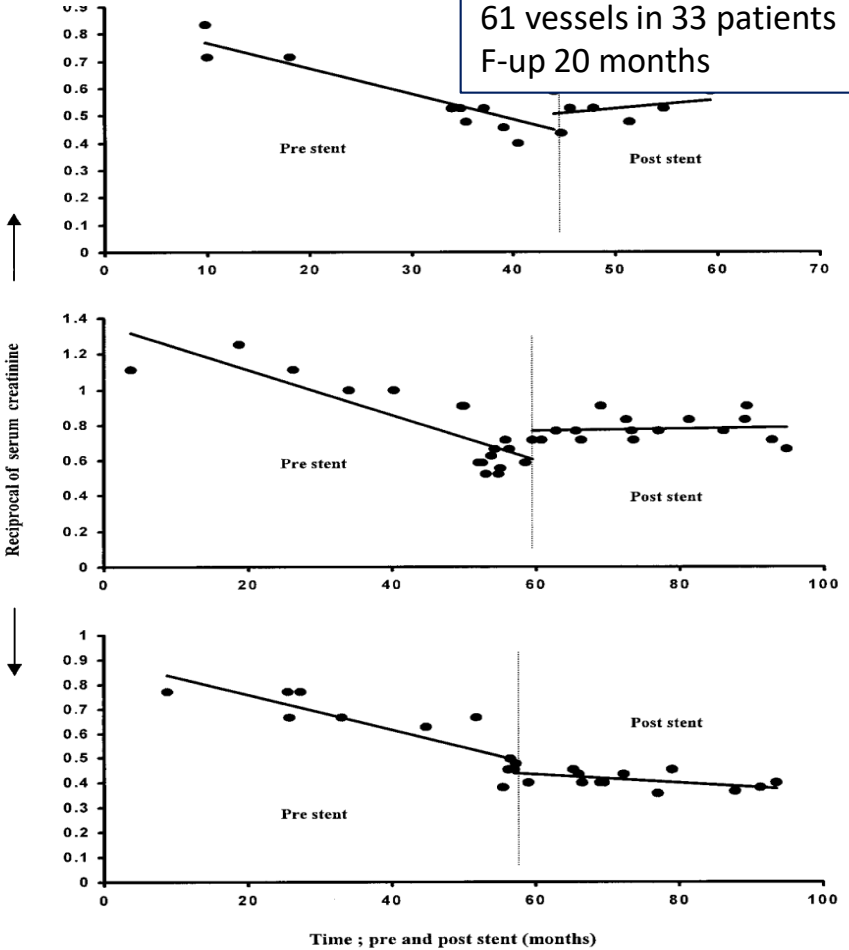
Preliminary observational studies

N=127 pts
F-up 15 months



Burket MW et al. Am Heart J. 2000

61 vessels in 33 patients
F-up 20 months



Watson PS et al. Circulation. 2000

PTRA effects on BP: Evidence from RCTs

Table 2: Major RCTs of PTRA with and without stenting versus medical therapy in ARVD.

Study ID	Design	N	Endpoints	Results
EMMA Plouin *et al.*, 1998	Multicentre RCT No blinding of intervention Standardized medical treatment FU: 6 months	49	Primary: mean 24-h BP Secondary: number and DDD of antihypertensive drugs, creatinine clearance, rate of occluded arteries, complications	No significant difference in ambulatory BP PTRA: fewer antihypertensive drugs (1.0 versus 1.78; $P < .01$), higher complication rate
SNRASCG Webster *et al.*, 1998	Multicentre RCT No blinding of intervention Standardized medical treatment FU: 6 months	55	Primary: office BP, serum creatinine Secondary: number antihypertensive drugs, complications	PTRA: significant BP reduction only if bilateral RAS; no significant difference in CV events or renal function 20% participants assigned to PTRA had a surgery
DRASTIC Van Jaarsveld *et al.*, 2000	Multicentre RCT No blinding of intervention FU: 12 months	106	Primary: mean office BP Secondary: number and DDD of antihypertensive drugs, serum creatinine, restenosis, complications	No significant difference in SBP and DBP PTRA: fewer antihypertensive drugs (1.9 versus 2.4; $P < .01$) 44% of participants assigned to medical therapy underwent revascularization at 3 months if DBP >95 mmHg despite three or more antihypertensive drugs Only 3.6% stenting

PTRA effects on renal and CV outcomes: Evidence from RCTs

Table 2: Major RCTs of PTRA with and without stenting versus medical therapy in ARVD.

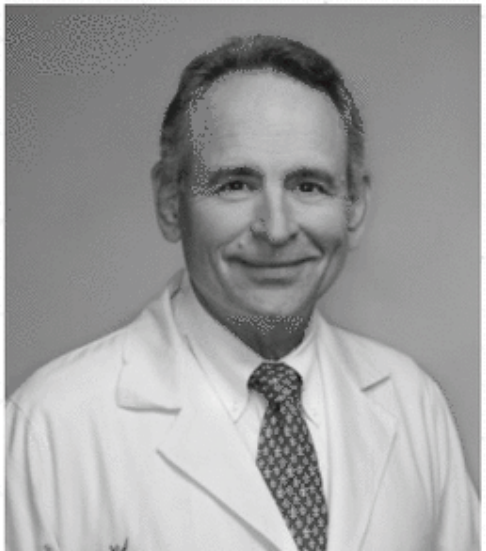
Study ID	Design	N	Endpoints	Results
STAR Bax *et al.*, 2009	Multicentre RCT No blinding of intervention FU: 24 months	140	Primary: worsening of renal function (>20% decline in eGFR with Cockcroft–Gault formula) Secondary: office BP, incidence of refractory or malignant hypertension, pulmonary oedema, CV morbidity, CV mortality, total mortality	No significant difference in renal function, BP, CV mortality and morbidity 28% of participants allocated to PTRA did not undergo revascularization, mainly due to minimal stenosis 1.3% crossover
ASTRAL *Wheatley et al.*, 2009	Multicentre RCT No blinding of intervention Medical treatment was not standardized Median FU: 34 months	806	Primary: renal outcome (reciprocal of serum creatinine) Secondary: office BP, time to renal and major CV events and mortality, complications	No significant difference in renal function, BP, CV events and mortality 17% of participants allocated to PTRA, did not undergo revascularization 6% crossover
RASCAD Marcantoni *et al.*, 2012	Single-centre RCT Single-blinded Standardized medical treatment FU: 12 months	84	Primary: change in echocardiographic LVMI Secondary: LV function, CV events and mortality, BP control, kidney function	No significant difference in change in LVMI, BP, eGFR, CV events and mortality
CORAL Cooper *et al.*, 2014	Multicentre RCT No blinding of intervention Standardized medical treatment Median FU: 43 months	947	Primary: composite of adverse fatal and non-fatal CV and renal events Secondary: all-cause mortality, SBP, restenosis, renal resistance index, QOL, cost-effectiveness	No significant difference in primary composite endpoint, any of individual components of primary endpoint or all-cause mortality Almost 17% of participants either withdrew or were lost to follow-up 5.4% of participants allocated to PTRA did not undergo revascularization 4% of participants allocated to medical therapy crossed over

Catheterization and Cardiovascular Interventions 75:305–307 (2010)

Editor's Page

Kiss My Astral: One Seriously Flawed Study of Renal Stenting After Another

Christopher J. White,* MD
Editor-in-Chief, Catheterization and Cardiovascular Interventions

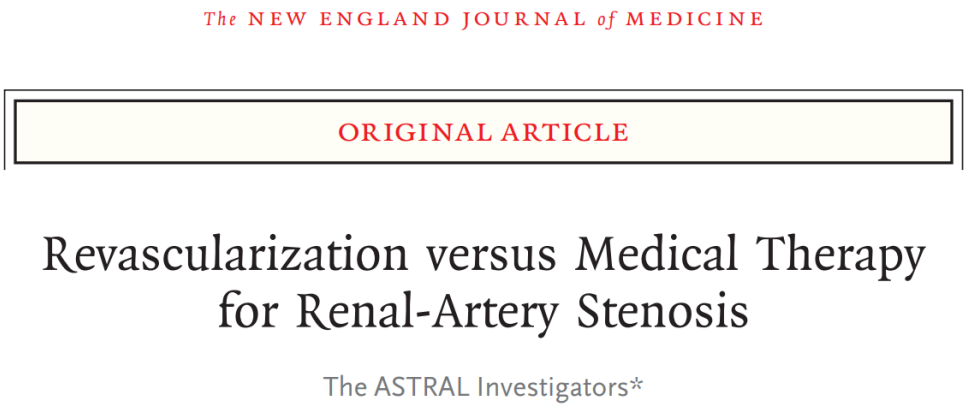


This week, the Angioplasty and STenting for Renal Artery Lesions (ASTRAL) trial was published [1]. This study offers students of clinical trials a remarkable opportunity to learn from the mistakes made by the ASTRAL group. The authors are to be congratulated on completing and publishing this study, as it takes a certain amount of courage to publish a trial this poorly conceived. I am sure they took comfort in knowing that they are not alone in reporting data that underestimate the benefits of renal artery stenting [2–4].

If the investigators' goal was to get the most of out of their concluding remarks, sort of the perfect sound bite for the 6 o'clock medical news, they did a really good job. Their findings of ''substantial risks but no evidence of a worthwhile clinical benefit from revascularization'' so grossly distorted the findings of the study that I had an ''Emperor has no clothes'' moment. You know, you read something, you think it

Criticism of RCTs in ARVD field

- Non-standardized inclusion criteria



- N=806 patients
- 1) they had "**substantial" anatomical ARAS** in at least one renal artery that was considered potentially suitable for endovascular revascularization and
- 2) **if the patient's doctor was "uncertain**" the patient would definitely have a worthwhile clinical benefit from revascularization
- median follow-up period 34 months
- primary endpoint: change in mean slope of reciprocal of Scr

Van der Niepen et al. Curr Hypertens Rep 2017; Pappacoggli et al. Hypertension 2023; Sarafidis et al. Nephrol Dial Transplant 2023

Criticism of RCTs in ARVD field

- Non-standardized inclusion criteria
- Low event rates of major outcomes
- No criterion relevant to time
- High crossover rates between treatment arms

DRASTIC
N=106 pts, 12 months f-up

Group A: 56 patients assigned to angioplasty
54 underwent angioplasty
2 received a stent

Group B: 50 patients assigned to drug therapy
22 underwent angioplasty (after 3 months)

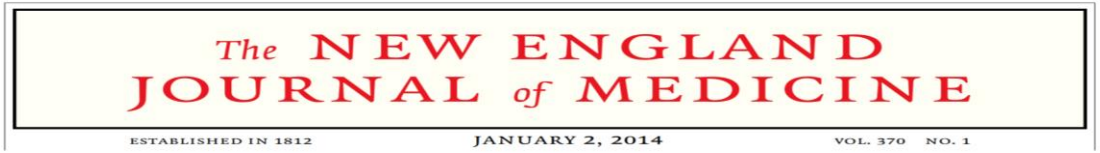
Van der Niepen et al. Curr Hypertens Rep 2017; Pappacoggli et al. Hypertension 2023; Sarafidis et al. Nephrol Dial Transplant 2023

Criticism of RCTs in ARVD field

- Non-standardized inclusion criteria
- Low event rates of major outcomes
- No criterion relevant to time
- High crossover rates between treatment arms
- Enrolment delays
- Protocol revisions during the trial

Van der Niepen et al. Curr Hypertens Rep 2017; Pappacoggli et al. Hypertension 2023; Sarafidis et al. Nephrol Dial Transplant 2023

CORAL Study


The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 2, 2014 VOL. 370 NO. 1

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*

Inclusion Criteria:

Severe RAS if they had **SBP >155 mmHg while receiving two or more** antihypertensive medications. Severe RAS was defined **angiographically** as stenosis **of at least 80%** but less than 100% of the diameter or stenosis of at least 60% but less than 80% of the diameter of an artery, with **a systolic pressure gradient of at least 20 mm Hg.**

BUT !!

A number of **subsequent changes** were made in the enrollment criteria during the course of the trial. The **threshold of 155 mmHg** for defining systolic hypertension **was no longer specified**. Patients who did not have systolic hypertension but who had renal-artery stenosis **could be enrolled if they had CKD**, which was defined as an estimated glomerular filtration rate (GFR) of less than 60 ml/ min/1.73 m^2. Severe RAS could be identified with the use of **duplex ultrasonography, MRA, or CTA**.

Cooper et al., N Engl J Med, 2014

- Non-stanc
- Low event
- No criteric
- High cross
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ARTICLE | Annals of Internal Medicine

Stent Placement in Patients With Atherosclerotic Renal Artery Stenosis and Impaired Renal Function

A Randomized Trial

Liesbeth Bax, MD, PhD; Arend-Jan J. Woittiez, MD, PhD; Hans J. Kouwenberg, MD; Willem P.T.M. Mali, MD, PhD; Erik Buskens, MD, PhD; Frederik J.A. Beek, MD, PhD; Branko Braam, MD, PhD; Frans T.M. Huysmans, MD, PhD; Leo J. Schultze Kool, MD, PhD; Matthieu J.C.M. Rutten, MD; Cornelius J. Doorenbos, MD, PhD; Johannes C.N.M. Aarts, MD; Ton J. Rabelink, MD, PhD; Pierre-François Plouin, MD; Alain Raynaud, MD; Gert A. van Montfrans, MD, PhD; Jim A. Reekers, MD, PhD; Anton H. van den Meiracker, MD, PhD; Peter M.T. Pattynama, MD, PhD; Peter J.G. van de Ven, MD, PhD; Dammis Vroegindeweij, MD, PhD; Abraham A. Kroon, MD, PhD; Michiel W.

From patients randomized to revascularization:

- 12/64 patients were falsely identified as having RAS >50% by noninvasive imaging and did not ultimately had stenting
- 6/64 patients stenting was not performed for various reasons
- 22/64 patients had 50-70% stenoses (unlikely to benefit)

Van der Niepen et al. Curr Hypertens Rep 2017; Pappacoggli et al. Hypertension 2023; Sarafidis et al. Nephrol Dial Transplant 2023

Criticism of RCTs in ARVD field

- Non-standardized inclusion criteria
- Low event rates of major outcomes
- No criterion relevant to time
- High crossover rates between treatment arms
- Enrolment delays
- Protocol revisions during the trial
- Great variability between and within study protocols in imaging techniques of RAS diagnosis and evaluation, often resulting in overestimation of the degree of stenosis
- **Inclusion of patients with mild/asymptomatic RAS, mild hypertension or advanced CKD**
- **Exclusion of patients with clinical presentation suggestive of critical RAS (recurrent flash pulmonary oedema, resistant hypertension, progressive renal function decline)**

Van der Niepen et al. Curr Hypertens Rep 2017; Pappacoggli et al. Hypertension 2023; Sarafidis et al. Nephrol Dial Transplant 2023

Ongoing (?) RCTs

Study ID	Design-Intervention	N	Status	Dates	Outcome Measures
Comparison of stenting versus best medical therapy for treatment of ostial renal artery stenosis: a trial in patient with advanced atherosclerosis [NCT00711984]	RCT, Open Label Endovascular therapy with Herkulink renal stent vs Best medical therapy	120	Unknown	Study Start 2004 (No results available)	Change in BP Change in renal function Incidence of major CV events Progression of RAS degree in the control group Incidence of renal restenosis in the stent group
Renal Stenting With Distal Atheroembolic Protection [NCT00868972]	Double masked RCT Endovascular therapy with/without distal embolic protection	150	Unknown	Study Start 2009 Study Completion 2011 (No results available)	Change in renal function Incidence of acute complication Evaluation of covariates associated with a better outcome in the atheroembolic device group Change in BP
RAVE study [NCT00127738]	Single center RCT (pilot) Endovascular therapy vs Best medical therapy	20	Unknown	Started 2007 (No results available)	Composite endpoint, death or dialysis or doubling of Scr, CV disease, Change in BP Change in antihypertensive drugs
METRAS study [NCT01208714]	Multicenter RCT Endovascular therapy vs Best medical therapy	60	Unknown	Study Start 2010	Change in eGFR as assessed by 99TcDTPA sequential renal scintiscan Change in BP Evaluation of overall renal function (including Ca2+ and PO43- metabolism) Regression of TOD
ANDORRA study [NCT02539810]	Multicenter RCT Endovascular therapy vs Best medical therapy	140	Terminated	Started 2015- stopped prematurely due to a lack of recruitment (No results available)	Change in diurnal 24-h BP Change in mean 24-h BP, home BP and office BP Change in antihypertensive medication CV events Renal events

Pappaccogli et al. Hypertension 2023; Sarafidis et al, Nephrol Dial Transplant 2023

Atherosclerotic Renal Artery Stenosis

Observational real-world evidence

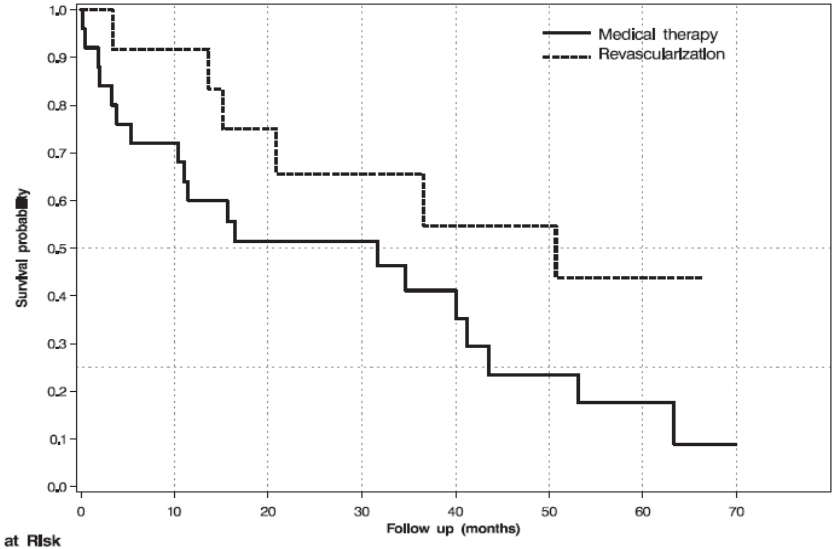
High-risk phenotypes: PTRA vs medical therapy

Assessed for eligibility (n=819)

n=467 pts with RAS>50%

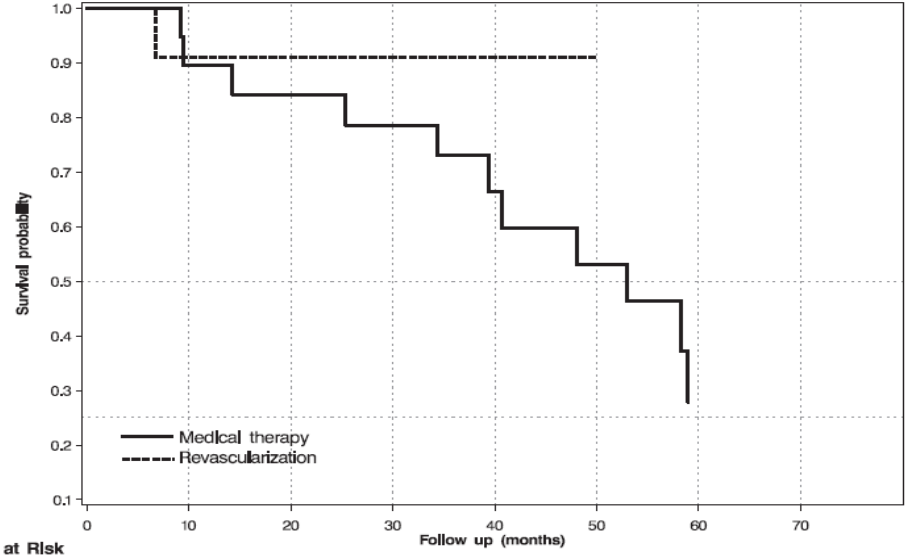
Excluded (n=352)

Missing baseline data (n=109)



Number at Risk

Medical therapy	25	15	12	8	4	2
Revascularization	12	11	6	6	5	4



Number at Risk

Medical therapy	19	17	15	12	9	3
Revascularization	11	10	9	6	5	3

High risk presentation in isolation

n=16	n=7	n=33	n=13	n=83	n=33

Flash Pulmonary Oedema

RH or rapid GFR decline

Richie et al. Am J Kidney Dis 2014

High-risk clinical phenotypes: Resistant hypertension

n= 72 with resistant HYP (dABP >135/85 mm Hg on 3 drugs)

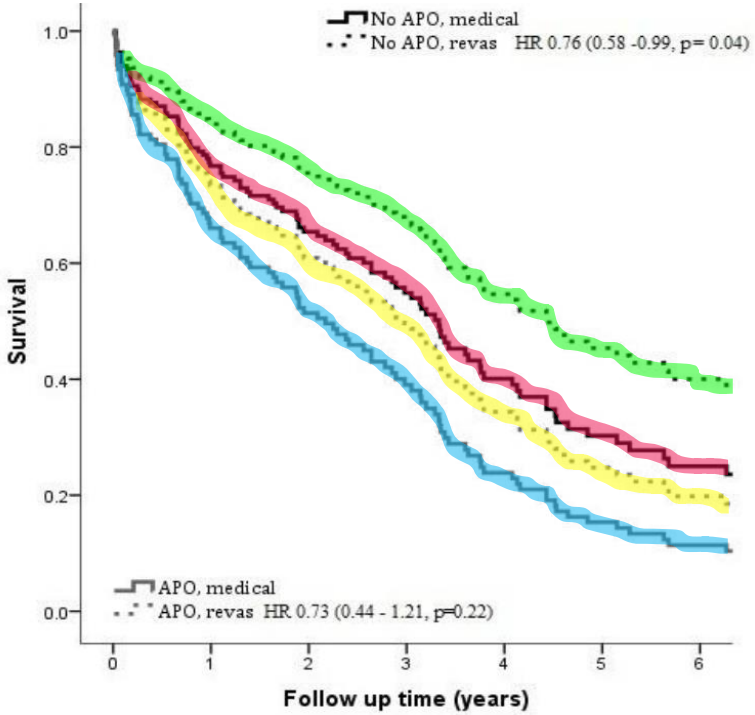
Table 2. Comparison Between Baseline Characteristics and at the First Follow-Up Visit After Renal Angioplasty (Table view)

Characteristics	Baseline (N=72)	First Visit (N=72)	*P* Value
Systolic uOBP, mm Hg	162±25	147±22	<0.001
Diastolic uOBP, mm Hg	80±14	72±14	<0.001
Systolic dABP, mm Hg	157±16	143±17	<0.001
Diastolic dABP, mm Hg	82±10	75±10	<0.001
Controlled hypertension (%)	0	34.7	<0.001
eGFR, mL/min	52 [41–63]	53 [42–67]	0.630
Antihypertensive treatment, n	4.0±1.0	3.6±1.4	0.002
DDD antihypertensive treatment, n	5.2±1.9	4.6±2.0	0.002

Courand et al., Hypertension 2019

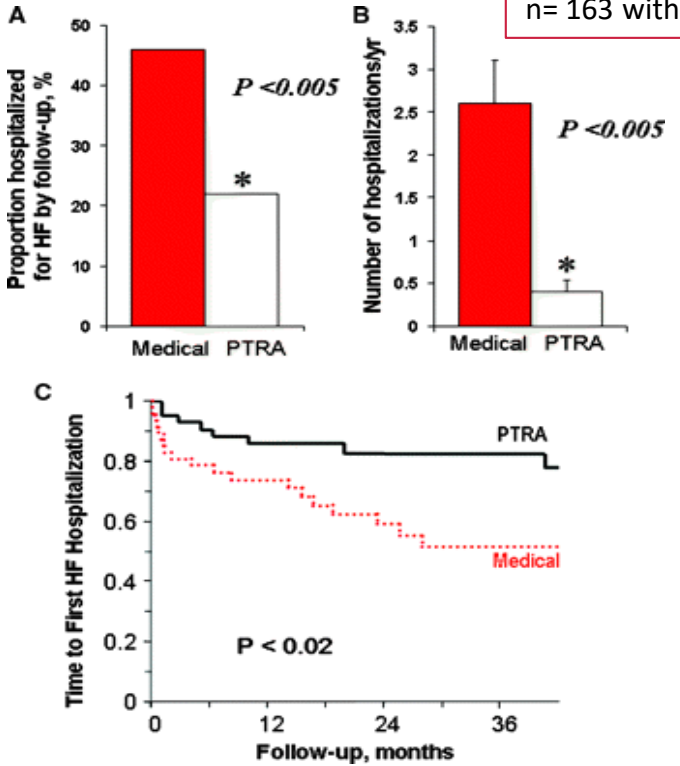
High-risk clinical phenotypes: Heart failure

n= 152 (52 with previous APO) with RAS



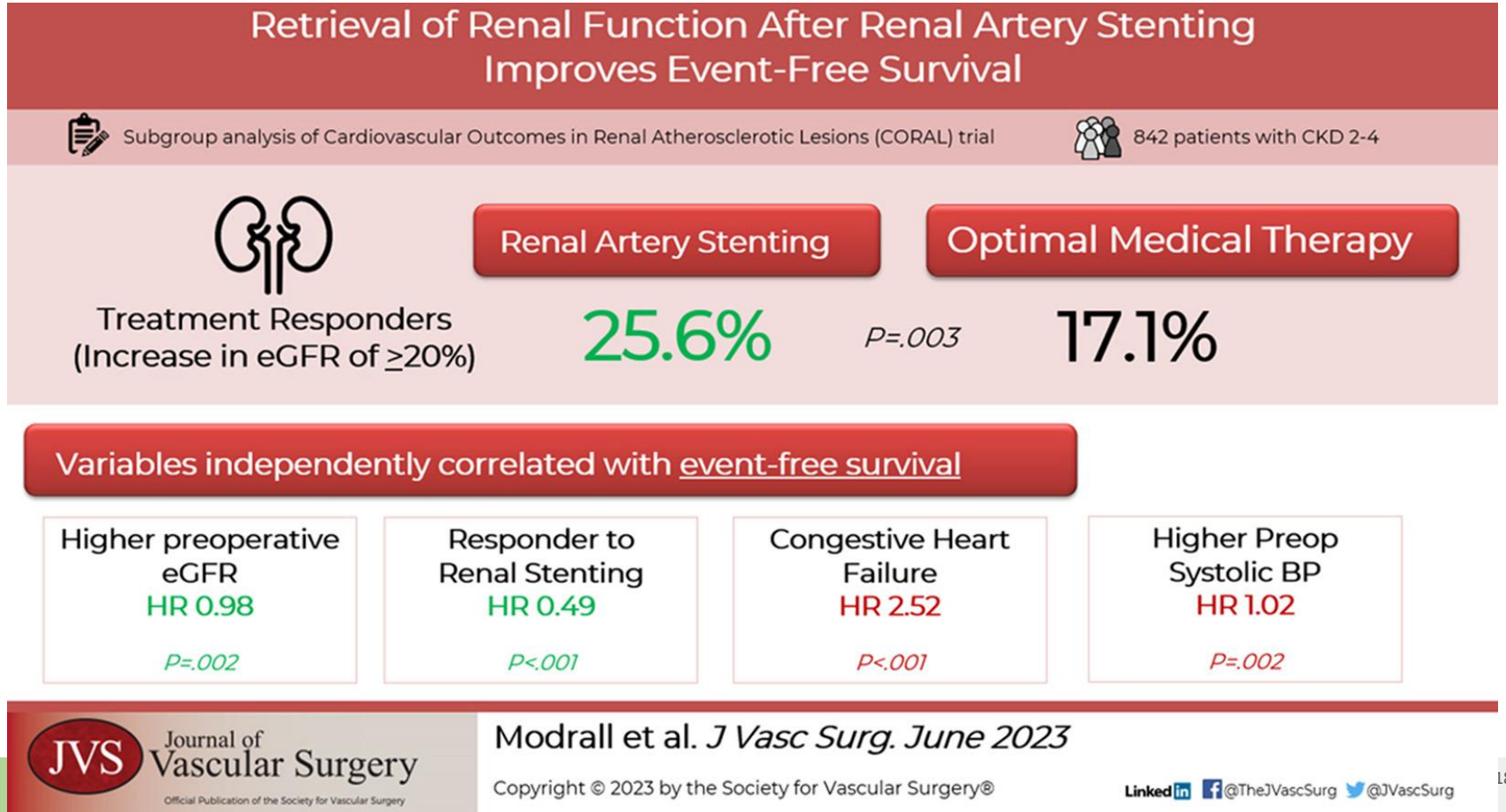
Green et al., Nephrology 2018

n= 163 with PTRA



Kane et al. Nephrol Dial Transplant 2010

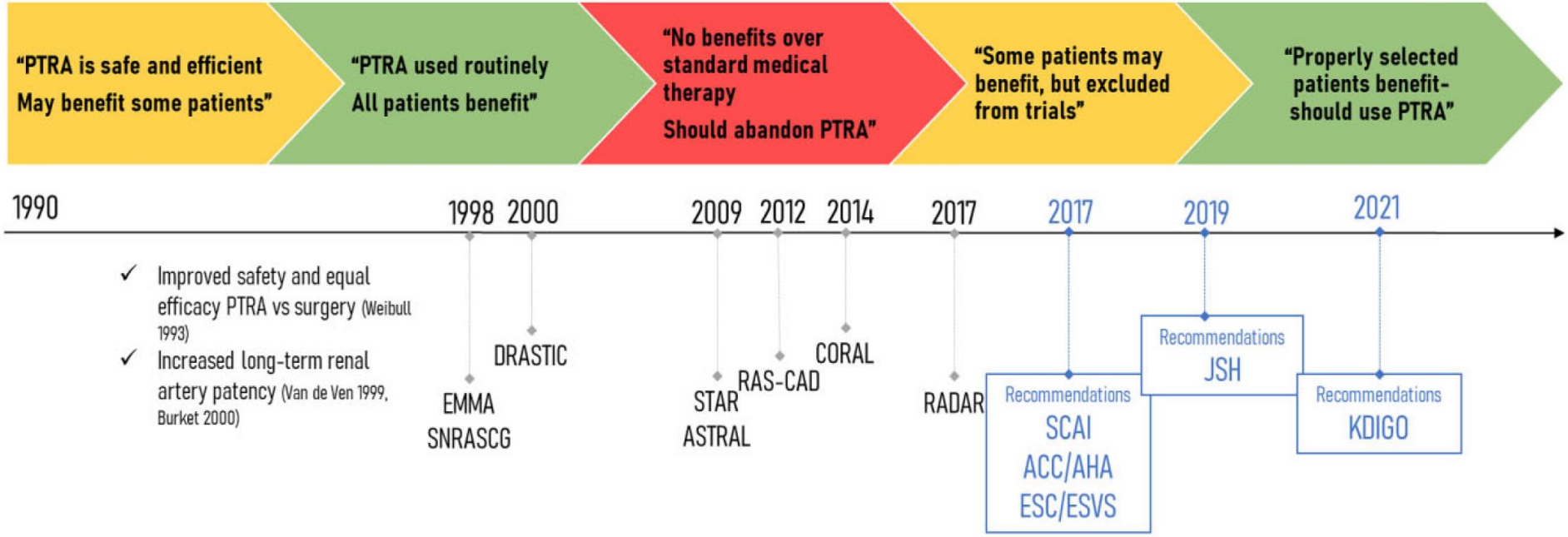
High-risk clinical phenotypes: rapid kidney function decline



Atherosclerotic Renal Artery Stenosis

Changes in recommendations

Revascularization vs Medical Therapy in ARVD



Theodorakopoulou et al. *Clin Kidney J* 2022

Special Report

AJKD

Atherosclerotic Renovascular Disease: A KDIGO (Kidney Disease: Improving Global Outcomes) Controversies Conference

Caitlin W. Hicks, Timothy W.I. Clark, Christopher J. Cooper, Áine M. de Bhailís, Marco De Carlo, Darren Green, Jolanta Małyszko, Marius Miglinas, Stephen C. Textor, Charles A. Herzog, Kirsten L. Johansen, Holger Reinecke, and Philip A. Kalra

Hypertension
Volume 79, Issue 8, August 2022; Pages e128-e143
https://doi.org/10.1161/HYP.0000000000000217

AHA SCIENTIFIC STATEMENT

Revascularization for Renovascular Disease: A Scientific Statement From the American Heart Association

Vivek Bhalla, MD, Vice Chair, Stephen C. Textor, MD, Chair, Joshua A. Beckman, MD, Ana I. Casanegra, MD, MS, Christopher J. Cooper, MD, Esther S.H. Kim, MD, MPH, James M. Luther, MD, MSCI, Sanjay Misra, MD, FAHA, Gustavo S. Oderich, MD, and on behalf of the American Heart Association Council on the Kidney in Cardiovascular Disease; Council on Hypertension; Council on Peripheral Vascular Disease; and Council on Cardiovascular Radiology and Intervention

Nephrol Dial Transplant, 2023, **0**, 1–16
https://doi.org/10.1093/ndt/gfad095
Advance access publication date: 18 May 2023

Atherosclerotic renovascular disease: a clinical practice document by the European Renal Best Practice (ERBP) board of the European Renal Association (ERA) and the Working Group Hypertension and the Kidney of the European Society of Hypertension (ESH)

Pantelis A. Sarafidis[1], Marieta Theodorakopoulou[1], Alberto Ortiz[2], Beatriz Fernandez-Fernández[2], Ionut Nistor[3,4], Roland Schmieder[5], Mustafa Arici[6], Athanasios Saratzis[7], Patricia Van der Niepen[8], Jean-Michel Halimi[9], Reinhold Kreutz[10], Andrzej Januszewicz[11], Alexandre Persu[12,†] and Mario Cozzolino[13,†]

Revascularization indications

Strong indications

- **High-grade (>70%)** renal artery stenosis in association with one of the following criteria:
  - Resistant hypertension
  - New-onset or recently uncontrolled hypertension
  - Acute pulmonary oedema or acute decompensated HF
  - Rapid decline of eGFR (bilateral stenosis or solitary kidney)
  - ACEi or ARB intolerance (≥30% eGFR reduction)
  - replacement treatment (with possibly viable renal parenchyma) if stenosis detected <3 months of renal replacement treatment or if uncontrolled hypertension with multiple (≥5) antihypertensive agents is present
- **AKI** due to acute renal artery occlusion or high-grade stenosis
- **Kidney transplant** with renal artery stenosis

Moderately strong indications

- **High-grade (>70%)** renal artery stenosis in association with one of the following criteria:
  - Chronic HF
  - Asymptomatic but either bilateral or supplying a solitary kidney with viable renal parenchyma (non-atrophic kidney, distinct renal cortex)

Sarafidis, Theodorakopoulou et al, Nephrol Dial Transplant 2023

European Society of Hypertension

2023 ESH Guidelines

- ….. Thus, the current consensus is to offer **revascularization on top of medical therapy** in patients with documented secondary hypertension because of atherosclerotic renal vascular disease or high-risk clinical profiles **and** documented high-grade stenosis (> 70%) [1418,1422,1423].
- Medical therapy **alone** could be used for individuals with asymptomatic atherosclerotic renal vascular disease with **<70% stenosis**, patients with mild or moderate hypertension that is easily controlled with antihypertensive drugs **and** low-grade stenosis, or patients with nonviable kidney parenchyma, where revascularization has little to offer. In the medically treated patients, if treatment initiation with an ACEi or an ARB results in eGFR reduction of 30%, careful reevaluation of the patient is warranted.

Mancia, Kreutz et al, J Hypertens. 2023

Evaluation of possible kidney viability

Variable	Likely to benefit	Unlikely to benefit
RAS degree	>70%	<50%
Kidney length (cm)	>8 cm[a]	<7 cm
Renal resistive index	<0.8	>0.8
Cortical thickness	Cortex distinct, e.g. >0.5 cm	Loss of corticomedullary differentiation, no cortex

[a]The suggested kidney length thresholds are relevant to individuals with average body habitus (i.e. body surface area ≈1.73 m^2). For patients with very high or very low body mass, possibly consider the ratio of kidney length to the patient's body mass index or body surface area to approximate kidney size in relation to patient's body habitus.

Sarafidis, Theodorakopoulou et al, Nephrol Dial Transplant 2023

Conclusions

- ARVD is a common clinical problem with presentations relevant to many medical specialties and important prognostic associations
- Major RCTs included patients with ARVD of various degrees and not patients with high-risk clinical presentations and/or critical stenoses
- Several pieces of observational data show that PTRA is associated with future renal and cardiovascular benefits in patients presenting high-risk ARVD phenotypes
- Such evidence resulted in a progressive shift in relevant recommendations, with most recent not-graded suggestions supporting that revascularization should be offered in selected patients with these phenotypes, after careful evaluation

Areas for further clinical research in the field of ARVD

- RCTs enrolling patients with hemodynamically significant ARVD and high-risk clinical presentations, with true renovascular hypertension rather than patients with primary hypertension and incidental RAS through a wider and more systematic use of the translesional pressure gradient
- studies testing the impact of functional non-invasive imaging, such as BOLD-MRI, to identify patients more likely to benefit from revascularization
- studies examining the efficacy of PTRA on moderate vs advanced CKD
- studies establishing the optimal timeline of revascularization to avoid delay-related ineffectiveness
- studies identifying predictors of PTRA benefit
- studies evaluating the efficacy of PTRA in combination with novel therapeutic strategies (e.g., targeting inflammation-related pathways, mesenchymal stem cells or angiogenic/growth factors)

Sarafidis et al, Nephrol Dial Transplant 2023

(A) Atherosclerotic renovascular disease

Prevalence: 6–14%[a]

Suggestive symptoms, signs and findings

Resistant hypertension
Flash pulmonary edema
Rapidly declining kidney function
Acute renal function degradation on ACEi or ARB
Generalized atherosclerosis[b]

1st choice screening test

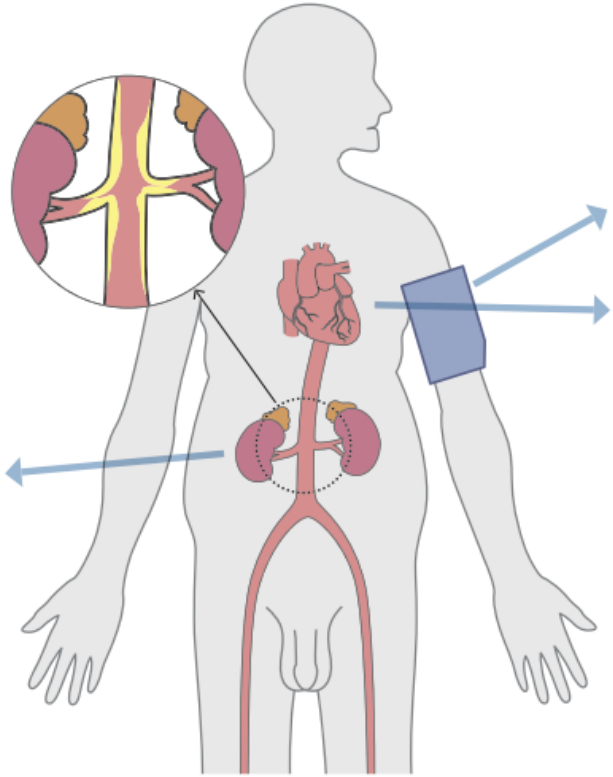
Renal artery duplex ultrasound; otherwise angio-CT or angio-MR

Further work-up

Angio-CT or angio-MR
Invasive catheter angiography

Treatment[c,d]

Antihypertensive treatment
Strict control of CV risk factors
Revascularization (selected cases)



Cardiovascular phenotype

24h ABPM – resistant hypertension, frequent non-dipping

- LVH
- Decreased diastolic function
- Decreased systolic function

Increased CV Risk and mortality

Thank you!