When is Revascularization Considered in Renal Artery Stenosis?

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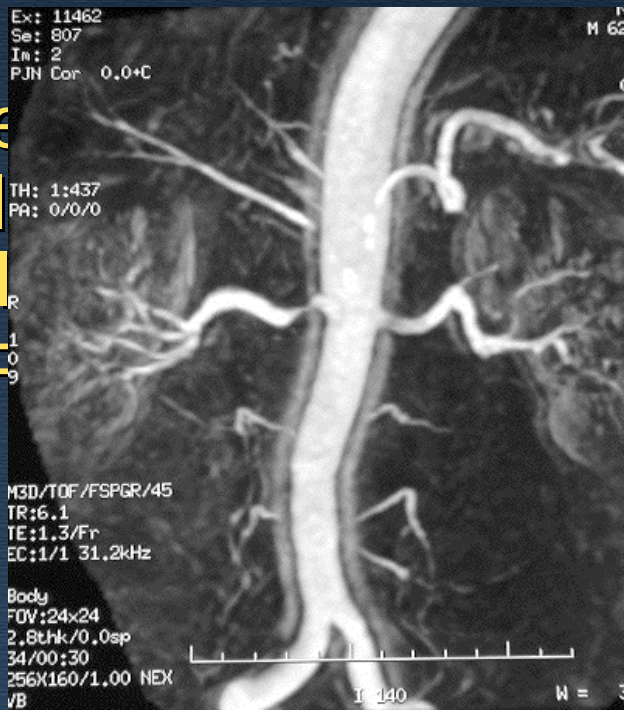

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Renovascular disease: incidence

- <1% in general, but more in selected populations:
  - Iliofemoral arterial disease: 30%-40%
  - Carotid disease: 20%-30%
  - Coronary artery disease: 20%-30%
  - Congestive heart failure: 30%
  - ESRD: 20%
- 80% atherosclerotic/20% fibromuscular dysplasia
- In general, the severity of associated atherosclerotic disease correlates with renal artery stenosis severity

Renovascular disease: pathophysiology

Hypertension

- Renal parenchymal hypoperfusion with activation of the renin-angiotensin-aldosterone system
  - Vasoconstriction
  - Aldosterone-mediated volume expansion
  - Endothelial dysfunction (chronic changes)
- Modulated by contralateral kidney naturesis and ipsilateral capsular collaterals

Renal insufficiency

- Ipsilateral chronic hypoperfusion and progressive “ischemic nephropathy”
- Contralateral hypertensive arteriolar nephrosclerosis
- Continuous cholesterol/atheromatous embolization?

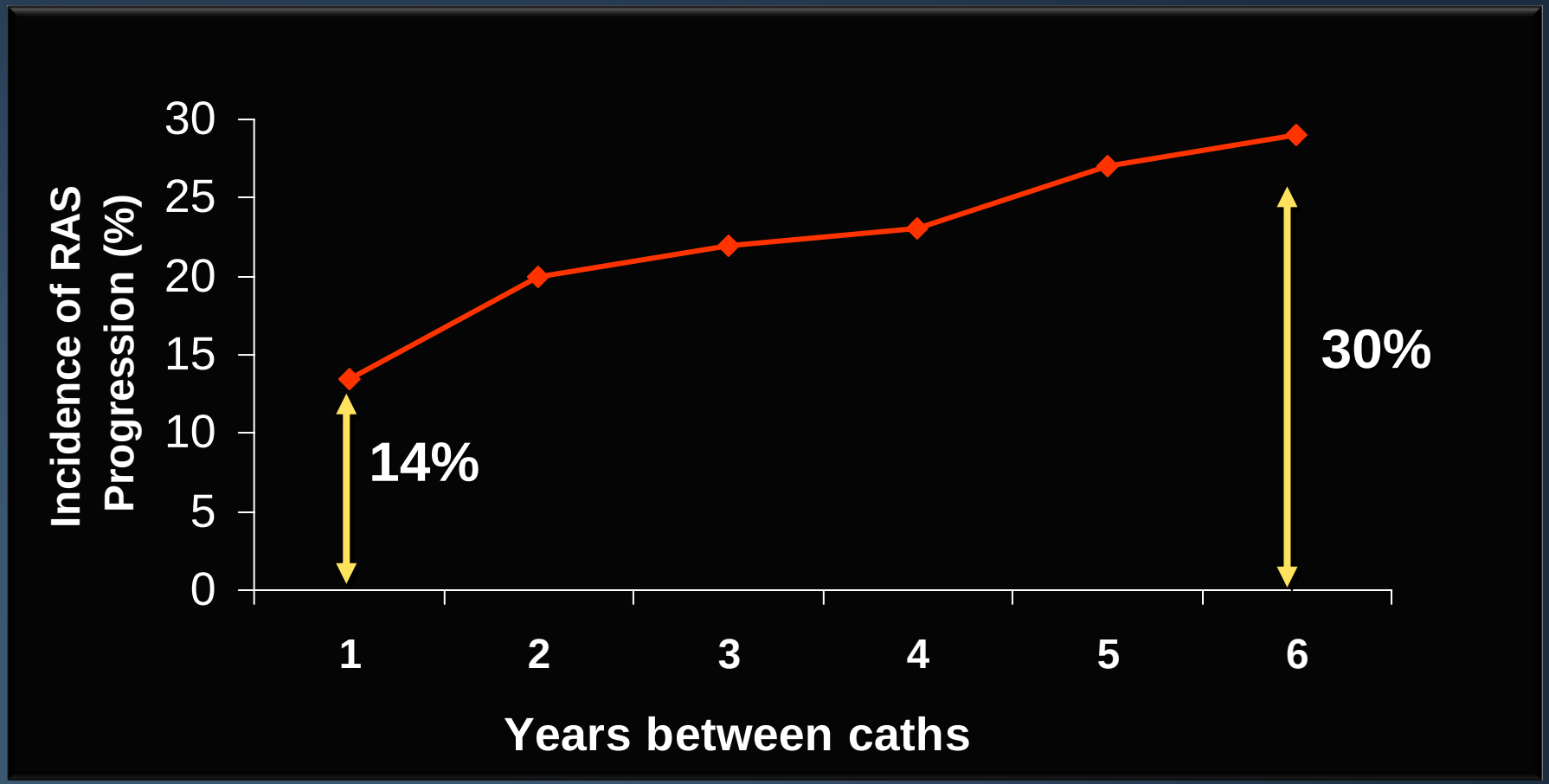
Renal Artery Stenosis is a Progressive Problem

- Review of 5 angiographic trials
- Progression in 49%
- Progression to occlusion in 14%

Greco BA and Breyer JA. Semin Neph 1996;16:2-11.

RAS Progression

RAS progression according to time between studies (N = 1189)



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Crowley JJ, et al: Am Heart J 1998;136:913-8.

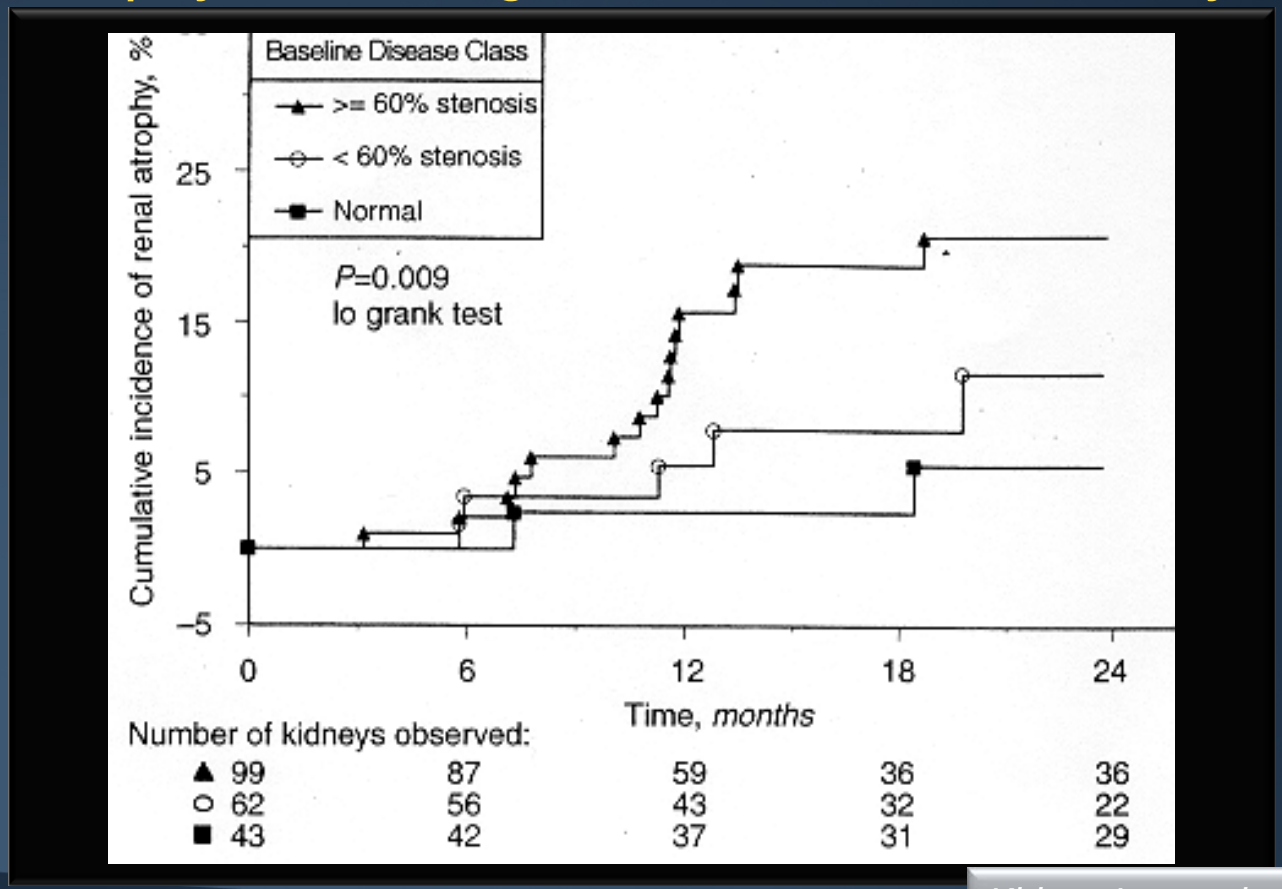
Risk of atrophy in kidneys with atherosclerotic renal artery stenosis

- 122 patients with at least one renal artery stenosis/204 kidneys followed for a mean of 33 months
- Patients followed with Renal Artery Duplex Ultrasonography performed every six months

Kidney International 1998;53:735-42

Risk of atrophy in kidneys with atherosclerotic renal artery stenosis

Renal Atrophy According to Baseline Renal Artery Disease



Kidney International 1998;53:735-42

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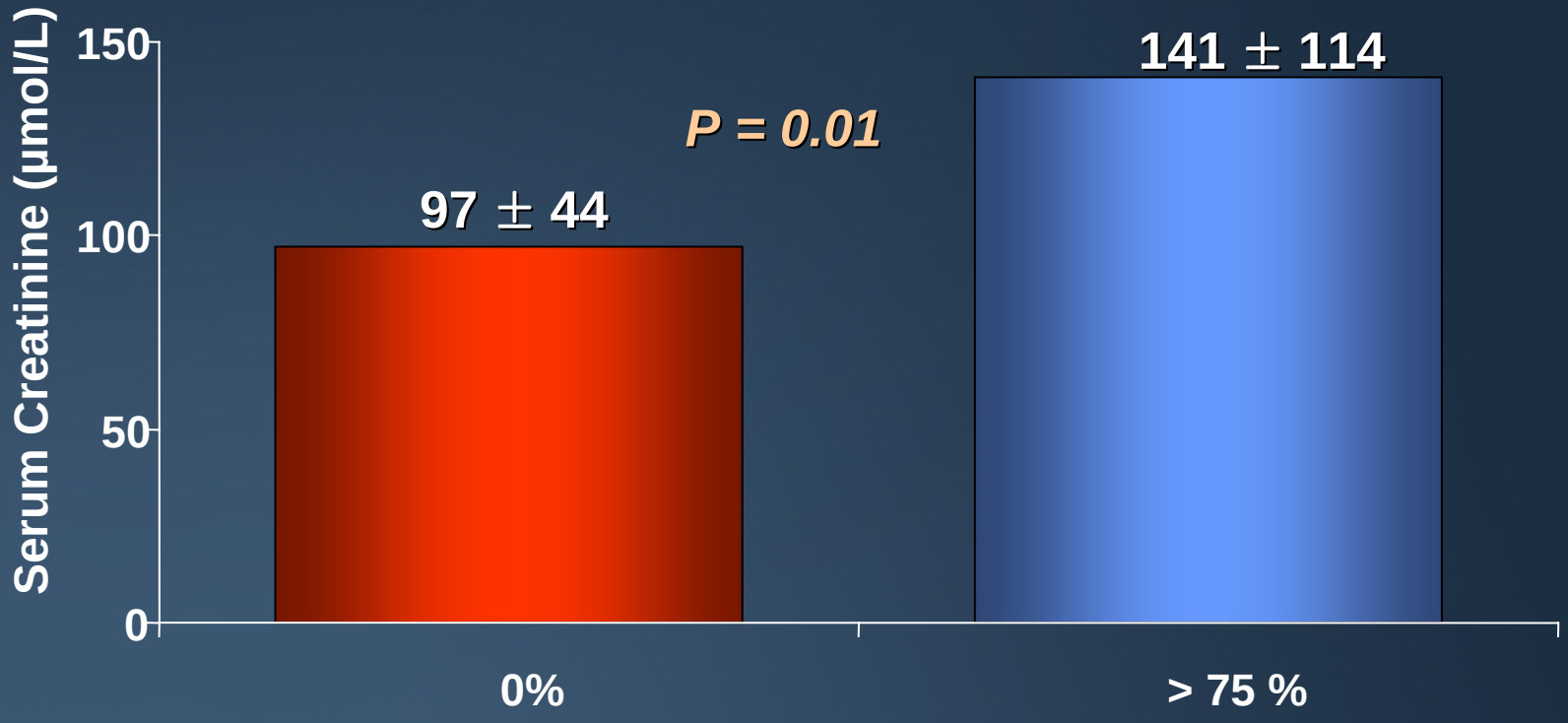
Loss Of Renal Function

Disease progression is associated with a decline in renal function.



Patients with normal renal arteries at baseline.

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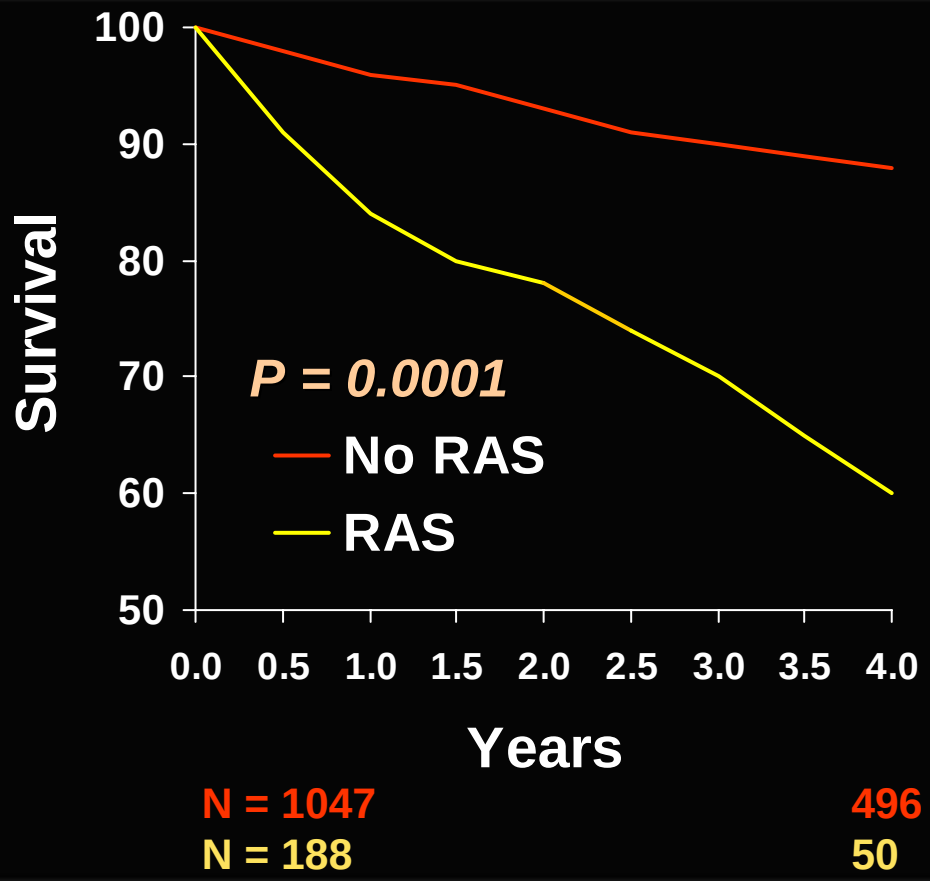
Crowley JJ, et al: Am Heart J 1998;136:913-8.

Renal artery stenosis is an independent predictor of mortality

Mulivariate Analysis



Variable	Risk Ratio	P value
RAS	2.9 (1.7 - 7.0)	0.0001
LVEF	1.7 (1.2 - 2.2)	0.0002
CRI	1.3 (1.1 - 1.5)	0.02
CHF	2.4 (1.3 - 4.1)	0.0021

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Conlon PJ, et al: J Am Soc Nephrol 1998;9:252-56.

Renovascular disease: medical therapy

- In unilateral disease, ACEI and ARB's are safe and effective
- Beta-blockers are also effective
- Medications usually effective in controlling hypertension associated with RAS
- However, renal size and GFR continue to decrease even with good hypertensive control
- Compared with surgery, long-term mortality with medical therapy is worse

Renovascular disease: percutaneous Rx

Angioplasty

- Limited by suboptimal acute (<80%) and long-term success rates (restenosis 20%-25%)

- New England Journal of Medicine 2001
  - ~100 patients randomized to either medical therapy or renal angioplasty
  - Results: ½ medical patients crossed-over to angioplasty, and an overall reduction in antihypertensive medication in angioplasty group was obsereved
  - Intention-to-treat analysis: no difference in Rx

Conclusions not supported by the data generated

Intervene in the Appropriate Scenario

- Dialysis-Dependent Renal Failure
- Chronic Renal Insufficiency
- Refractory/Resistant Hypertension
- Cardiac Disturbance Syndrome
- Need for Use of ACEI/ARB
- Unilateral Renal Artery Stenosis

Does renal stenting preserve renal function?

- Observational study of stenting in patients with:
  - Chronic renal insufficiency (Cr $\geq$ 1.5 $\leq$ 4.0 mg/dL)
  - Global renal ischemia ($\geq$ 70% stenosis)
    - Bilateral RAS
    - Unilateral RAS with solitary kidney
- Renal function
  - regression lines of 1/SCreat over time

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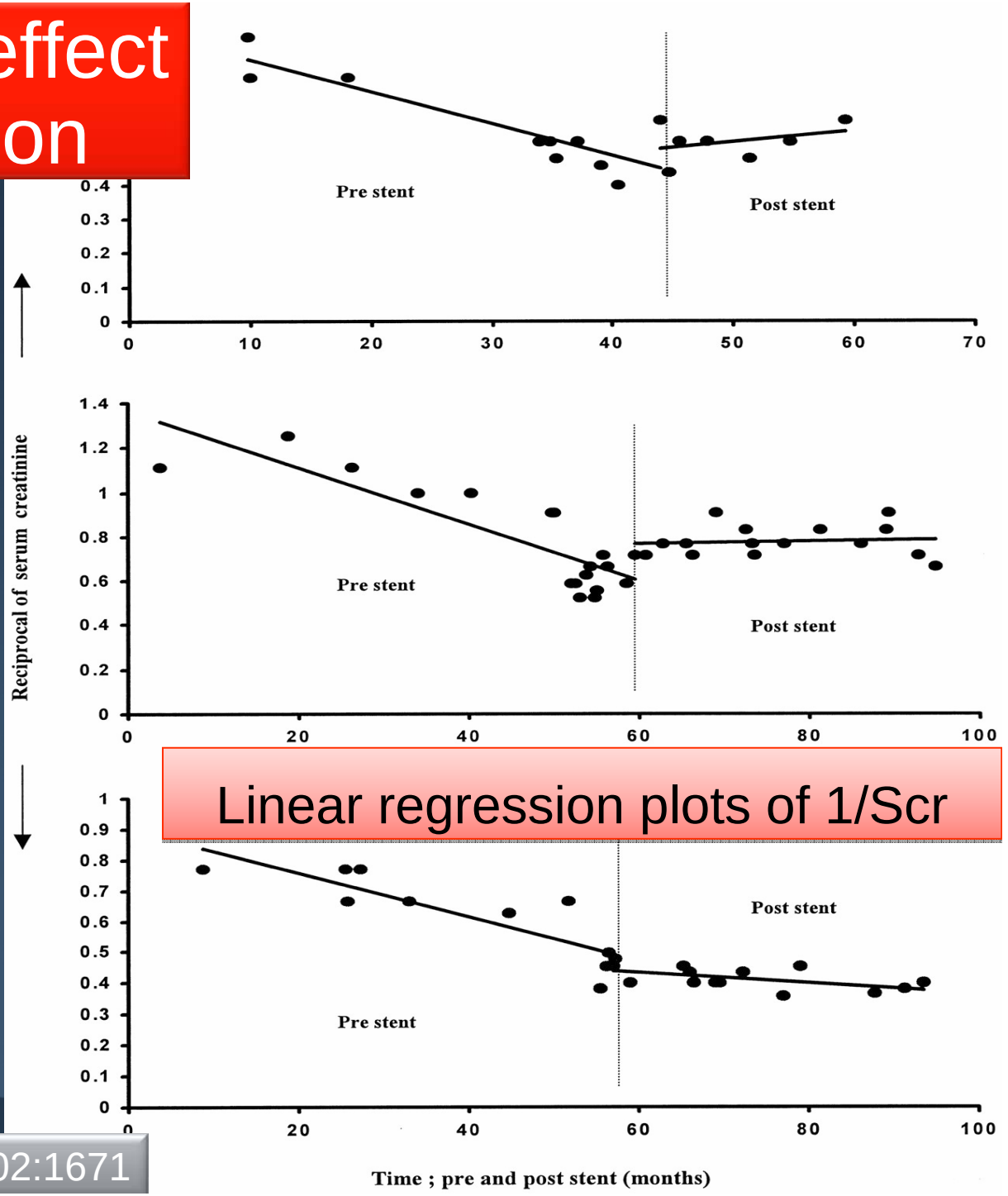
Watson et al: Circulation 2000;102:1671

Renal stenting: effect on renal function

"improvement"

"stabilization"

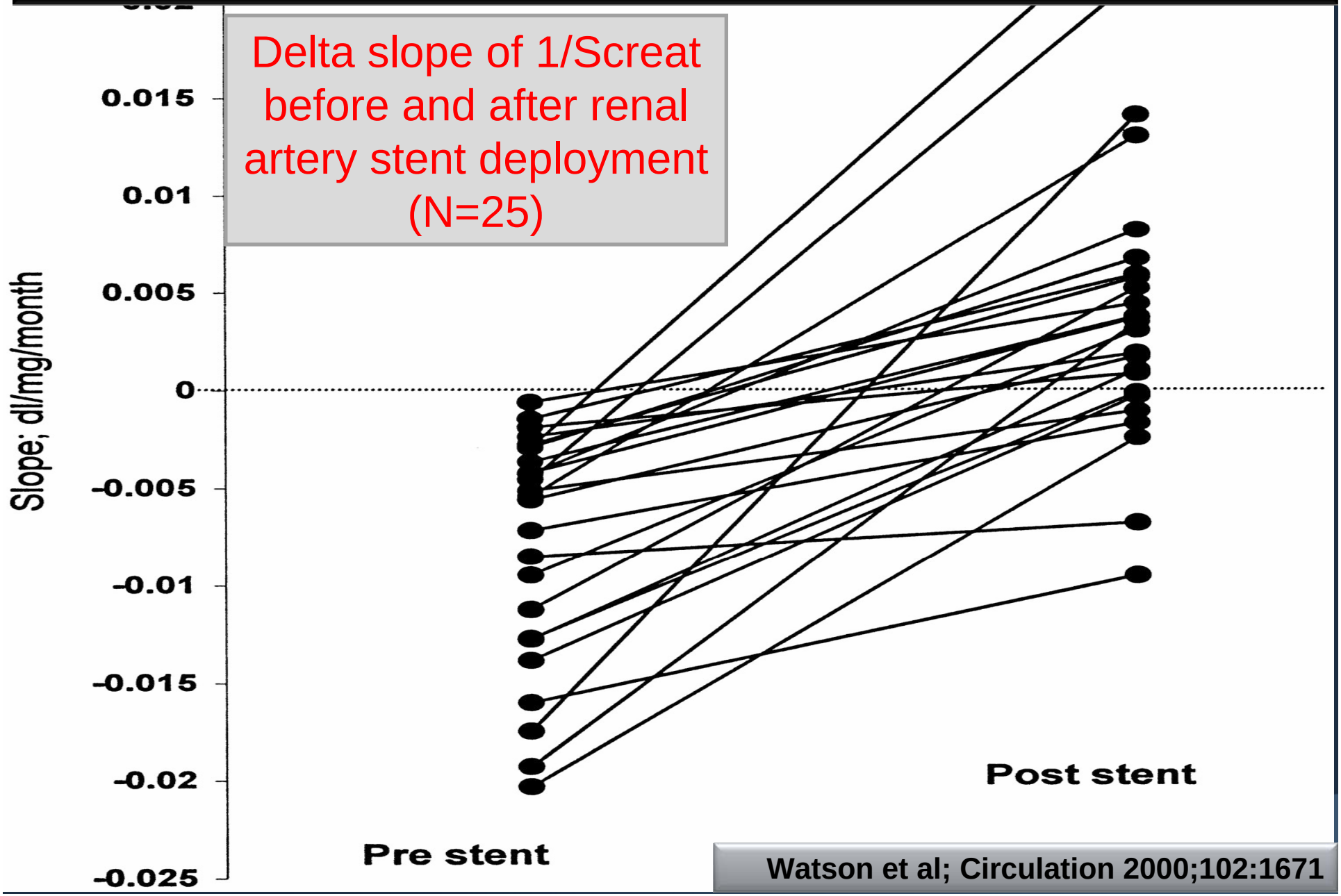
"slowing of deterioration"



Linear regression plots of 1/Scr

Watson et al; Circulation 2000;102:1671

Renal stenting: effect on renal function



Watson et al; Circulation 2000;102:1671

Meta-Analysis: PTRA vs Medicine in Hypertension and RAS

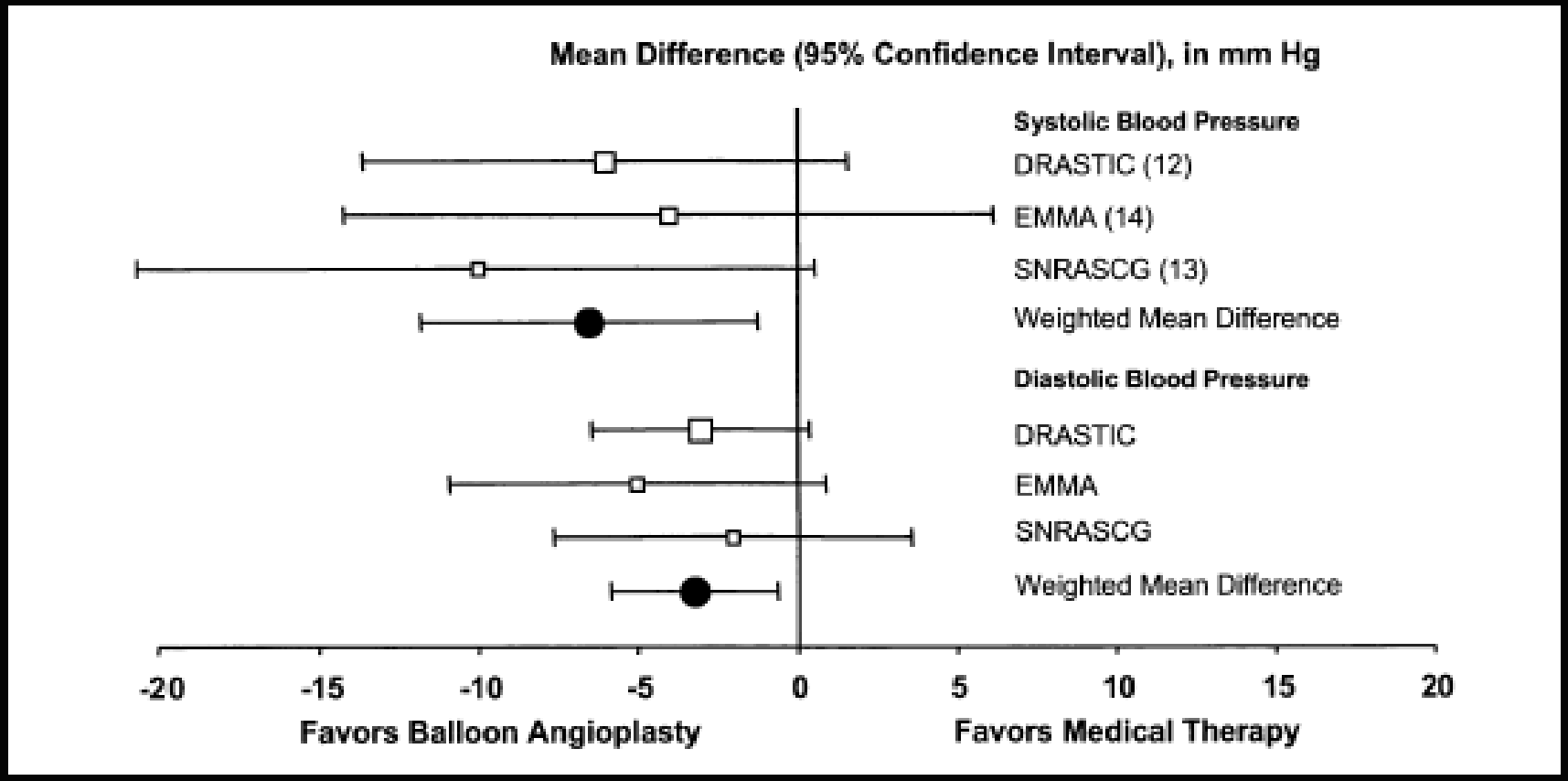
Table 1. Characteristics of Included Studies Comparing the Effects of Medical Therapy with Balloon Angioplasty for the Treatment of Hypertension with Renal Artery Stenosis

Study (Reference)	Number of Patients: Angioplasty	Number of Patients: Medical Therapy	Bilateral Stenosis Number (%)	Follow-up (months)	Run-In Period	Primary Outcome	Crossover from Medical Therapy to Angioplasty Number (%)	Comment
DRASTIC (12)	56	50	24 (23)	12	—	Office blood pressure	22 (44)	3-month analysis before, 12-month analysis after crossover
EMMA (14)	23	26	0	6	2 to 6 weeks	24-hour ambulatory blood pressure	7 (27)	Endpoints documented before crossover in medical therapy group
SNRASCG (13)	25	30	28 (51)	6	4 weeks	Office blood pressure	0	Results of patients with unilateral and bilateral renal artery stenosis were reported separately

DRASTIC = Dutch Renal Artery Stenosis Intervention Cooperative trial; EMMA = Essai Multicentrique Medicaments vs Angioplastie trial; SNRASCG = Scottish and Newcastle Renal Artery Stenosis Collaborative Group trial.

Am J Med 2003;114:44-50

Meta-Analysis: PTRA vs Medicine in Hypertension and RAS



Am J Med 2003;114:44-50

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Data-supported facts about renal therapy

- Is superior to balloon-angioplasty
- Is safer than surgery
- Can achieve clinical goals in *certain* individual patients
  - Improve control of HTN
  - Preserve renal function
  - Control of cardiac disturbance syndromes (CHF/Angina)

Renovascular disease: percutaneous Rx

Predictors of effectiveness of renal stenting for hypertension

- MAP>110 and/or the presence of bilateral renal artery stenosis (1)
- Low renal vascular resistance (2)

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1. Rocha-Singh KJ et al. Catheter Cardiovasc Interv 1999Jun;47(2):173-4
2. Mukherjeea D et al. Am Heart J 2001 Nov 1;88(9): 1064-6

Renovascular disease: percutaneous Rx

Renal artery stenting vs. angioplasty

Study has shown stenting (n=40) superior to angioplasty (n=15) due to late deterioration of the angioplasty results, especially in patients with baseline azotemia

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Rundback JH et al. Heart Dis 1999 Jul-Aug; 1(3): 121-5

Renovascular disease: percutaneous Rx

Age and its relationship to renal artery stenting

Compared to patients <75 (n=80), patients >75 years (n=19) still have a significant antihypertensive effect after stenting, and no significant difference in renal deterioration or progression to dialysis.

Bloch et al. Am J Hypertens Oct; 14(10): 983-8

Renovascular disease: percutaneous Rx

Patients with solitary kidney and renal stenting

- A recent small (n=26) in this patient subset demonstrated improvement in renal function, as assessed by stabilized creatinine levels in 62% of patients stented, but continued renal deterioration in 38% of those treated.
- Best predictor of improvement was baseline creatinine levels---conclusion: intervene early in these patients

1. Chatziioanou A et al. Eur J Vasc Endovasc Surg 2002 Jan;23(1):49-54

Renovascular disease: percutaneous Rx

Renal artery stenting and embolic protection

- A small study using Percusurge as the embolic protection device in 32 procedures demonstrated feasibility and safety. Total occlusion time averaged 6.55 minutes.
- At ~6 month follow-up no deterioration in renal function was noted, and improvement in hypertension was noted.
- “Debris was returned in all cases”

1. Henry M et al. J Endovasc Ther 2001 Jun;8(3):227-37.

Renovascular disease: percutaneous Rx

Large series

- 363 renal stenting procedures analyzed
- 100% procedural success, no deaths or surgery
- Median 16 month follow-up:
  - 70% had reductions in BP regardless of baseline renal function
    - SBP decreased 164 mmHg to 142 mmHg $p<0.001$
  - In patients with baseline renal insufficiency, 73% improved or stabilized and 27% continued deterioration
    - Post-procedural azotemia 12%, persistent in only 2%
  - 10% mortality, predicted by CAD and azotemia
  - Restenosis low and predicted by vessel size <4.5mm

Lederman RJ et al. Am Heart J 2001 Aug; 142 (2): 314-23

Renovascular disease: percutaneous Rx

Renal artery stenting: Conclusions

- Good acute and long-term success rates
- Complication rates improved and low
  - Hemorrhage, embolism, renal failure
  - Mortality <1%
- Efficacy
  - Improved hypertension in 2/3 (cure 10%)
  - Stabilized or improved renal function in 2/3
  - Improved CHF and coronary ischemia control

UK MULTI-CENTRE TRIAL IN
ATHEROSCLEROTIC RENOVASCULAR DISEASE

ASTRAL

Angioplasty and STent for Renal Artery Lesions

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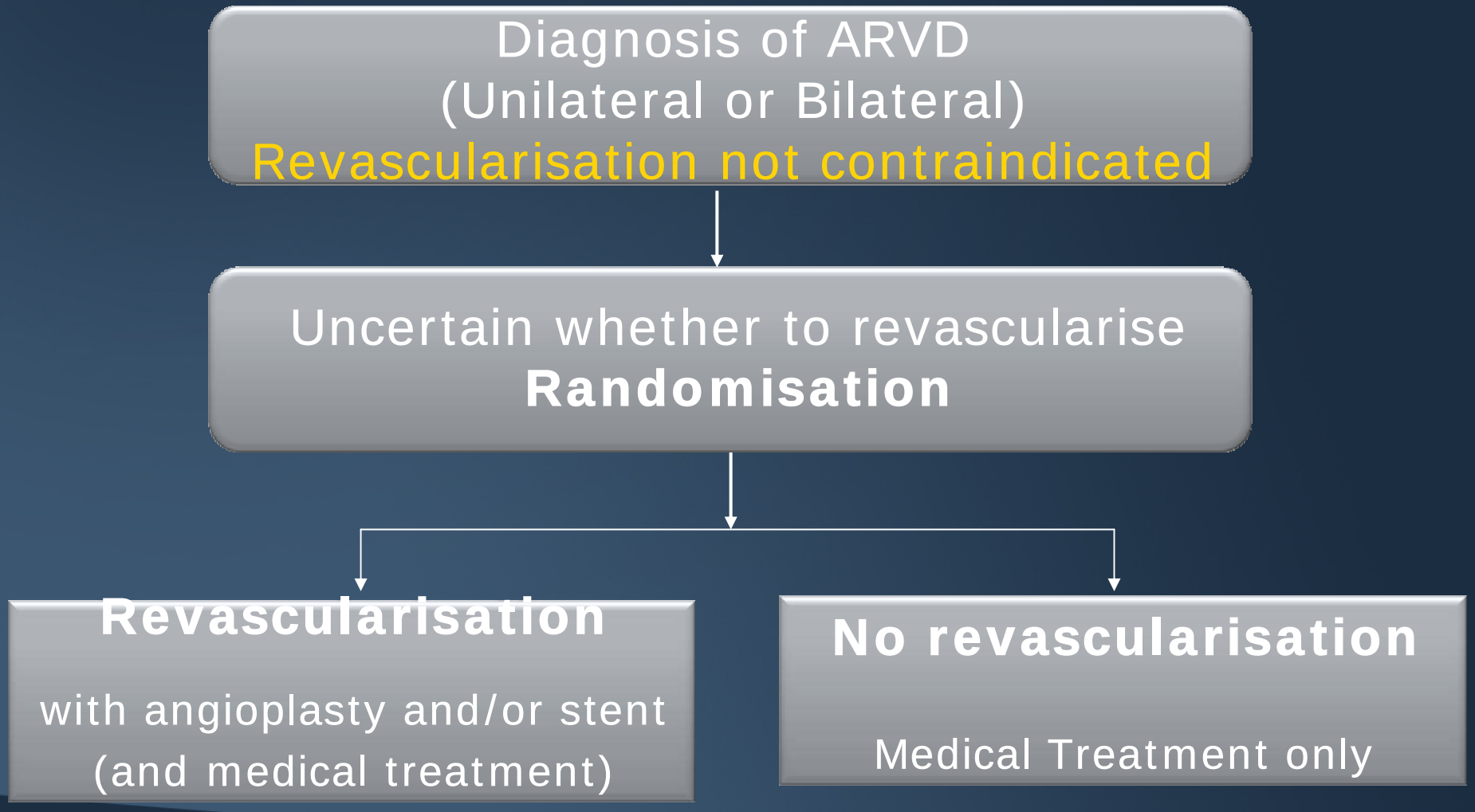
ASTRAL Trial Schema



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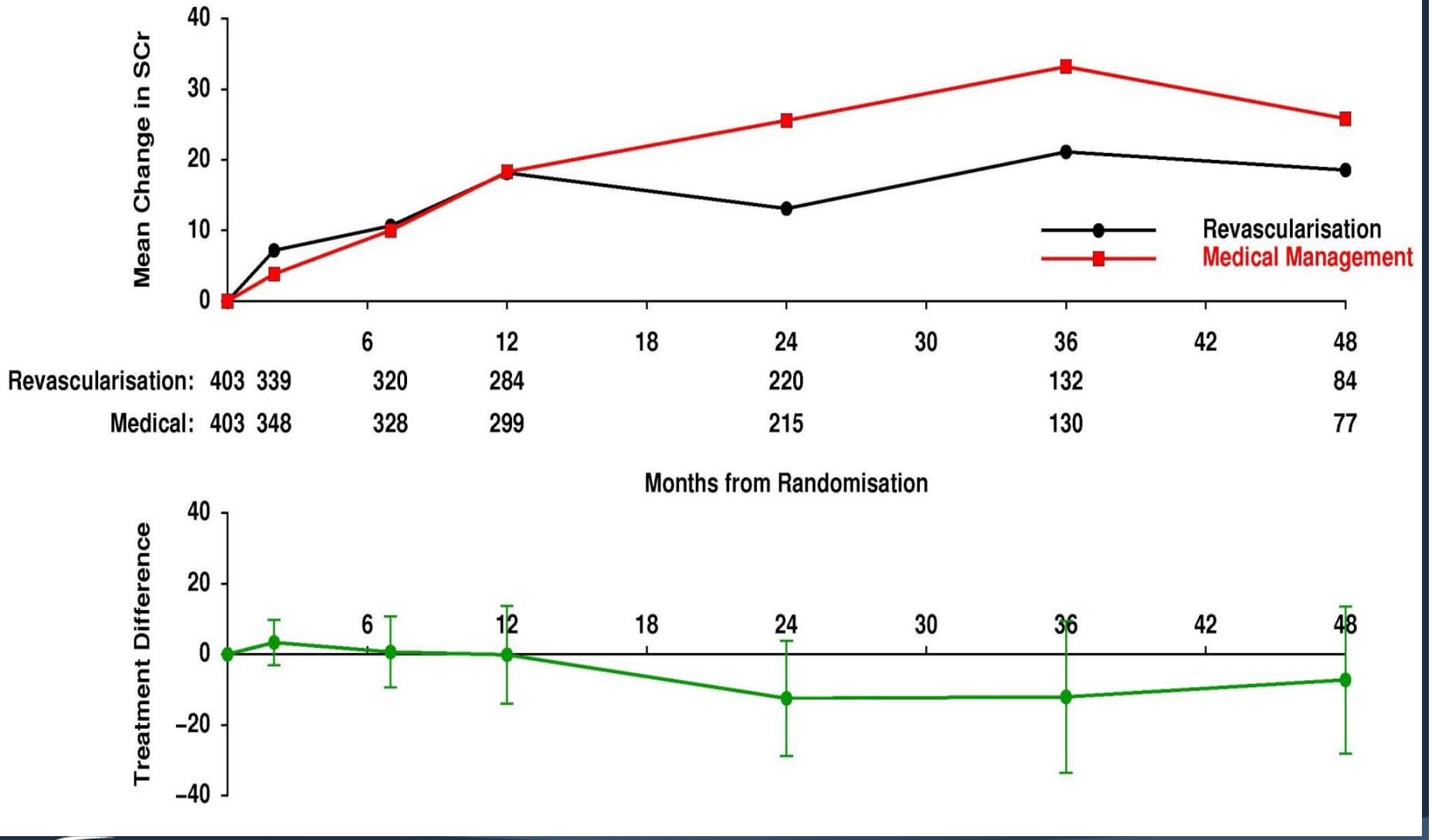
ASTRAL Trial

- No baseline differences between groups in:
  - Blood pressure
  - Renal function
  - Angiography
  - Medical treatment

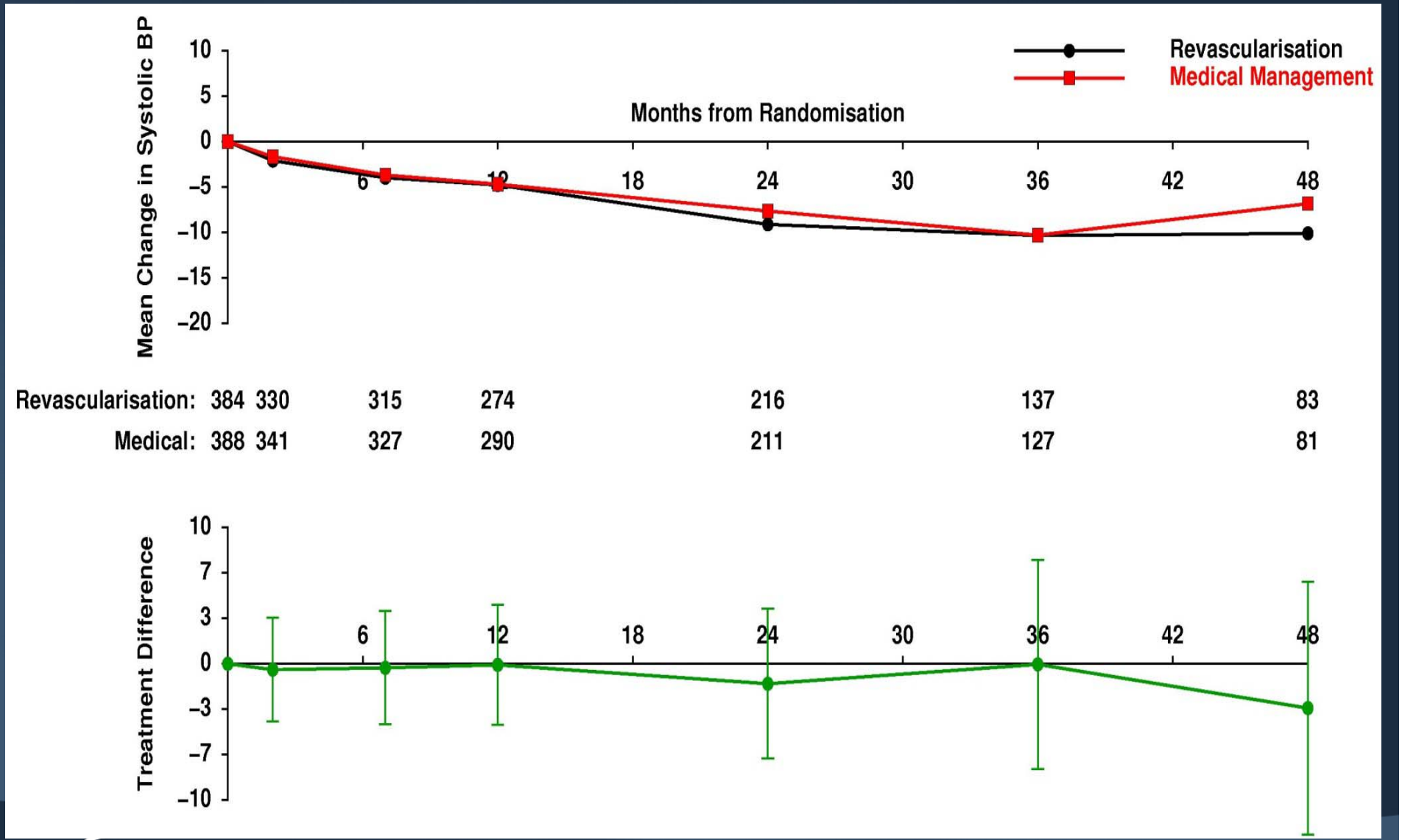
Procedural safety

- 24 patients experienced an immediate post-op complication
  - Revascularisation = 23 / 308 (7%)
  - Medical = 1 / 18 (6%)

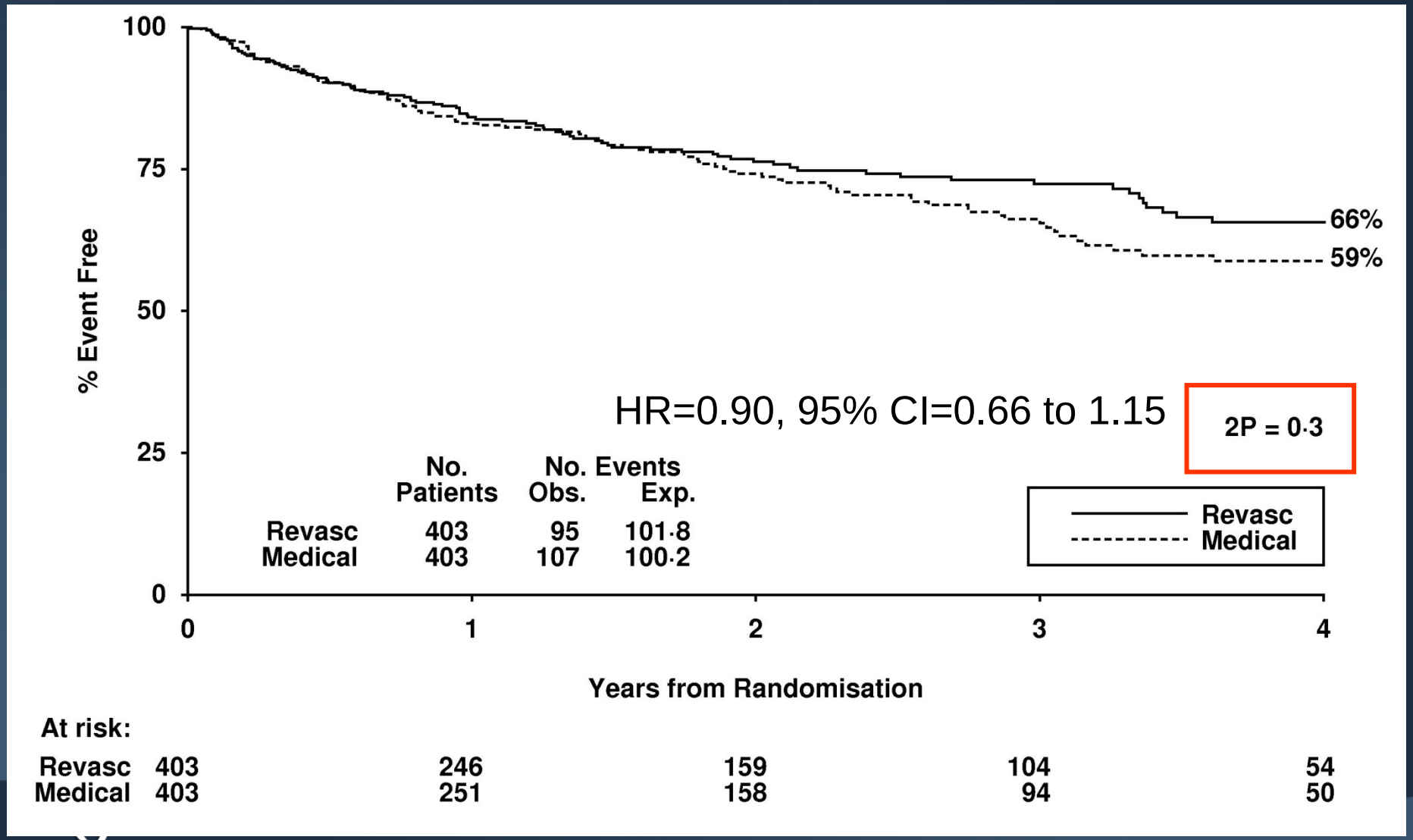
Mean change in SCr



Mean change in systolic BP



Time to first MI, stroke, vascular death or hospitalization for angina, fluid overload or heart failure



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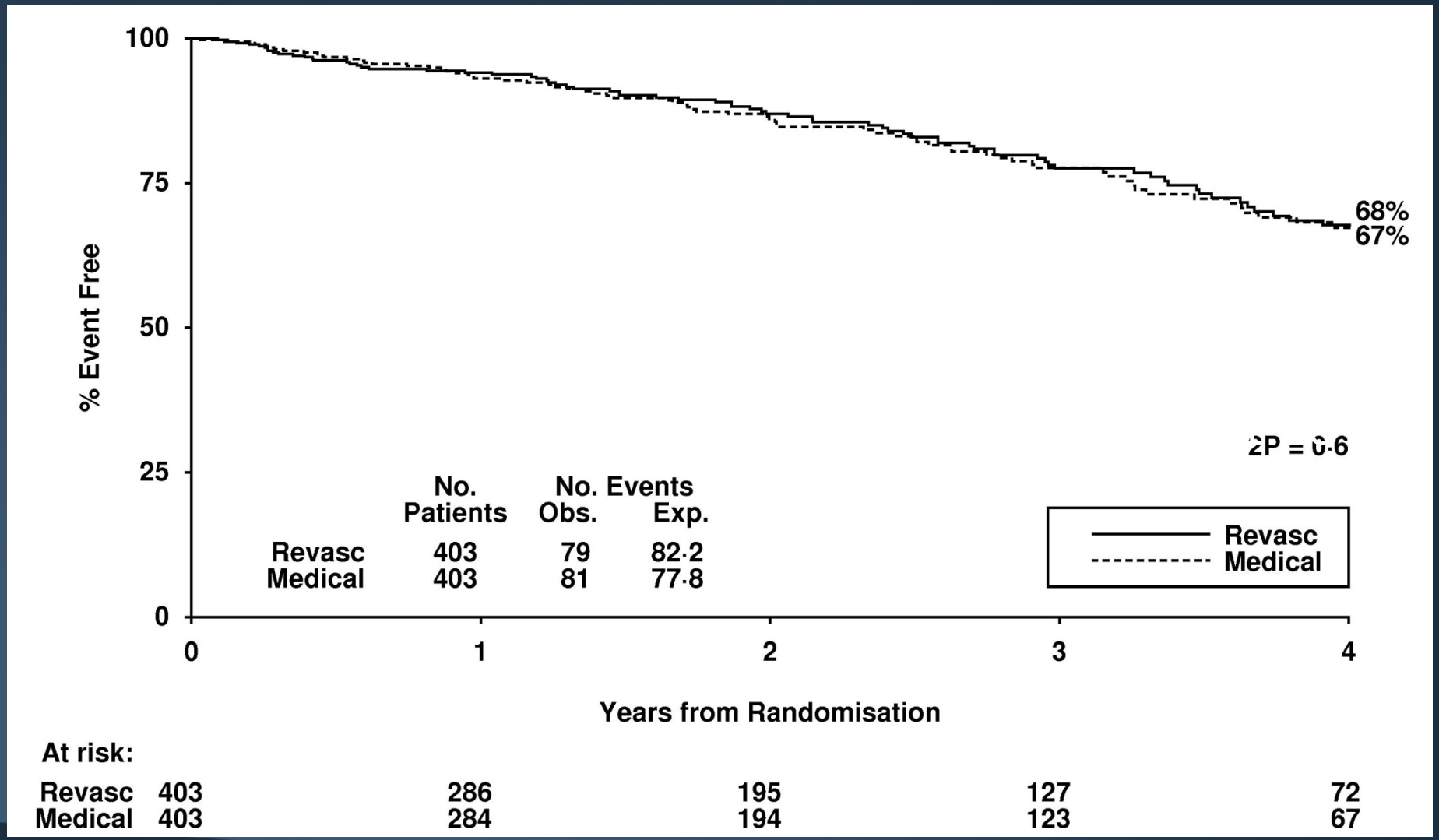
Mortality


100
75
50
25
0
% Event Free
68%
67%
2P = 0·6
No. Patients
No. Events Obs.
Exp.
Revasc 403 79 82·2
Medical 403 81 77·8
Revasc
Medical
0
1
2
3
4
Years from Randomisation
At risk:
Revasc 403 286 195 127 72
Medical 403 284 194 123 67

Summary

- Currently no evidence of a benefit for revascularisation on renal function in the ARVD patients entered into ASTRAL: ***those in whom clinicians 'uncertain' of whether to revascularize***
- Also no evidence of differences between the arms for any of the secondary endpoints (i.e. blood pressure, major events)
- No evidence of differences in treatment effect across the various subgroups
- Longer follow-up is needed
- Plan to update meta-analysis published in NDT in 2003 to include ASTRAL and other trials

Critique

- The indications for the patients entered into this study are unclear:
  - ? Hypertension
    - If so, was it resistant?
  - Renal insufficiency
  - The presence of a renal stenosis without clinical indication?
- Severity of stenosis
  - Method of measurement?
  - Physiologic testing?
- Complication rate excessive

Renovascular disease: therapeutic paradigm

- Evaluate probability of RAS based on risk factors
- Recommend therapy based on:
  - Age
  - Adequacy of blood pressure control
  - Renal function/size
  - Bilateral disease or solitary kidney
  - Associated conditions (CHF, CAD)
  - Atherosclerotic vs. fibromuscular origin
  - Decreasing procedural morbidity
  - ?drug-eluting stents change paradigm?

Atherosclerotic Renal Artery Stenosis

- Incidence
  - General Population ---------- 0.1%
  - Hypertension ---------- 4.0%
- Prevalence in an autopsy series
  - 27%
  - In patients > 70 years, 62

Am J Med 1964;37:14-22

Atherosclerotic Renal Artery Stenosis

Incidence of RAS in Patients with Peripheral Vascular Disease

Reference	% (Total No. of Patients)
Dustan (1964)	37 (149)
Olin (1990)	39 (189)
Wilms (1990)	22 (100)
Choudri (1990)	59 (100)
Swartbol (1992)	49 (100)
Missouris (1994)	45 (127)

Scoble JE. *In Renal Vascular Disease* 1996:143-9

Prevalence of bilateral renal artery stenosis

Reference	Stenotic Arteries, N	Bilateral, N (%)	Method
Holley, 1964	159	105 (66)	Autopsy
Wollenweiber, 1968	109	67 (61)	Angio
Dean, 1981	41	14 (34)	Angio
Tollefson, 1991	48	14 (29)	Angio
Harding, 1992	192	52 (27)	Angio
Total	549	252 (46)	

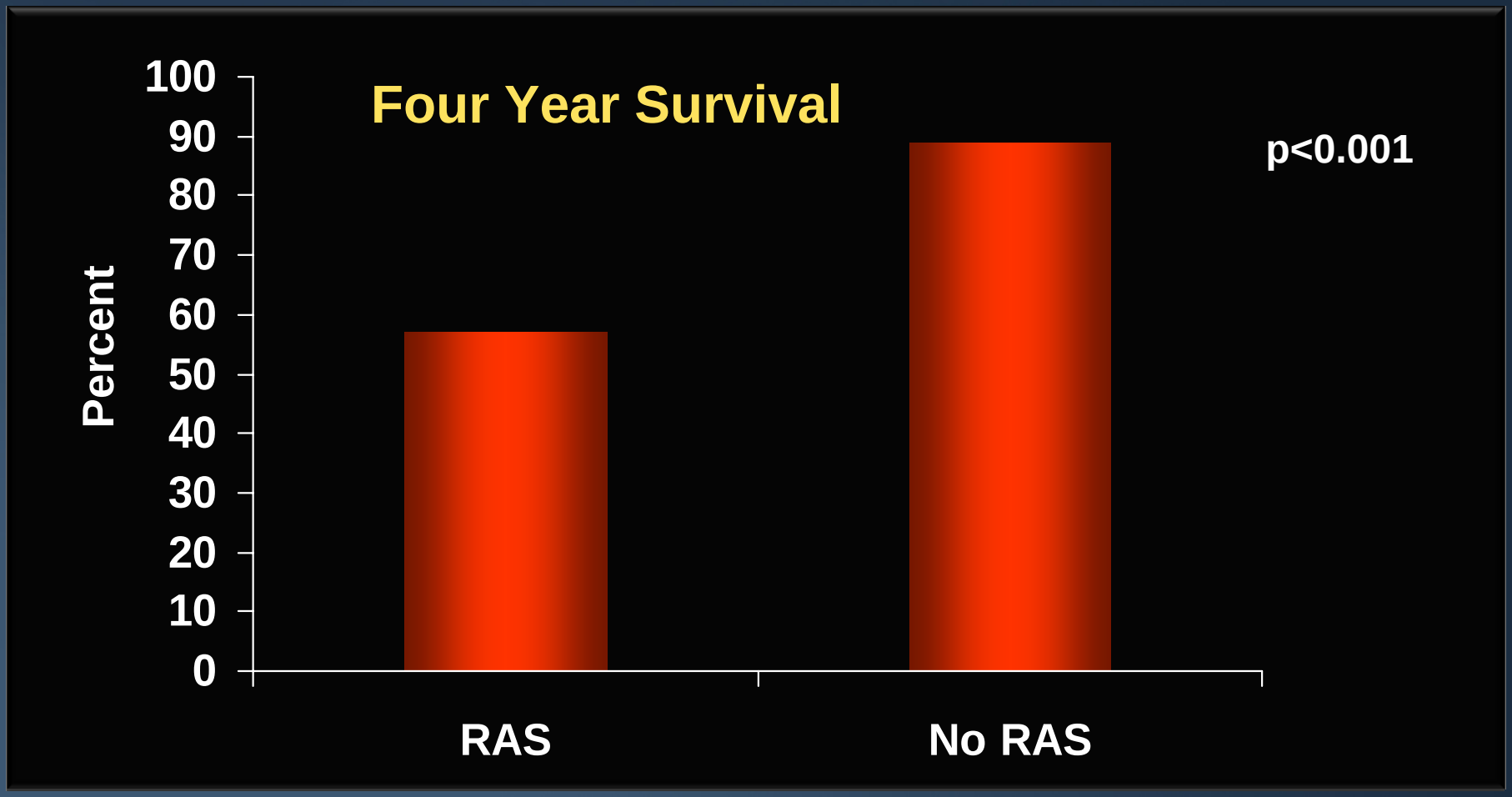
Ann Intern Med 1993;118:712-9

Renal artery stenosis: coronary artery disease and mortality

- 3987 patients underwent coronary arteriography followed by abdominal aortography
- Significant RAS defined as >75%
- Patients followed for 4 years prospectively
- 4.8% of patients with RAS
  - 0.8% with bilateral RAS

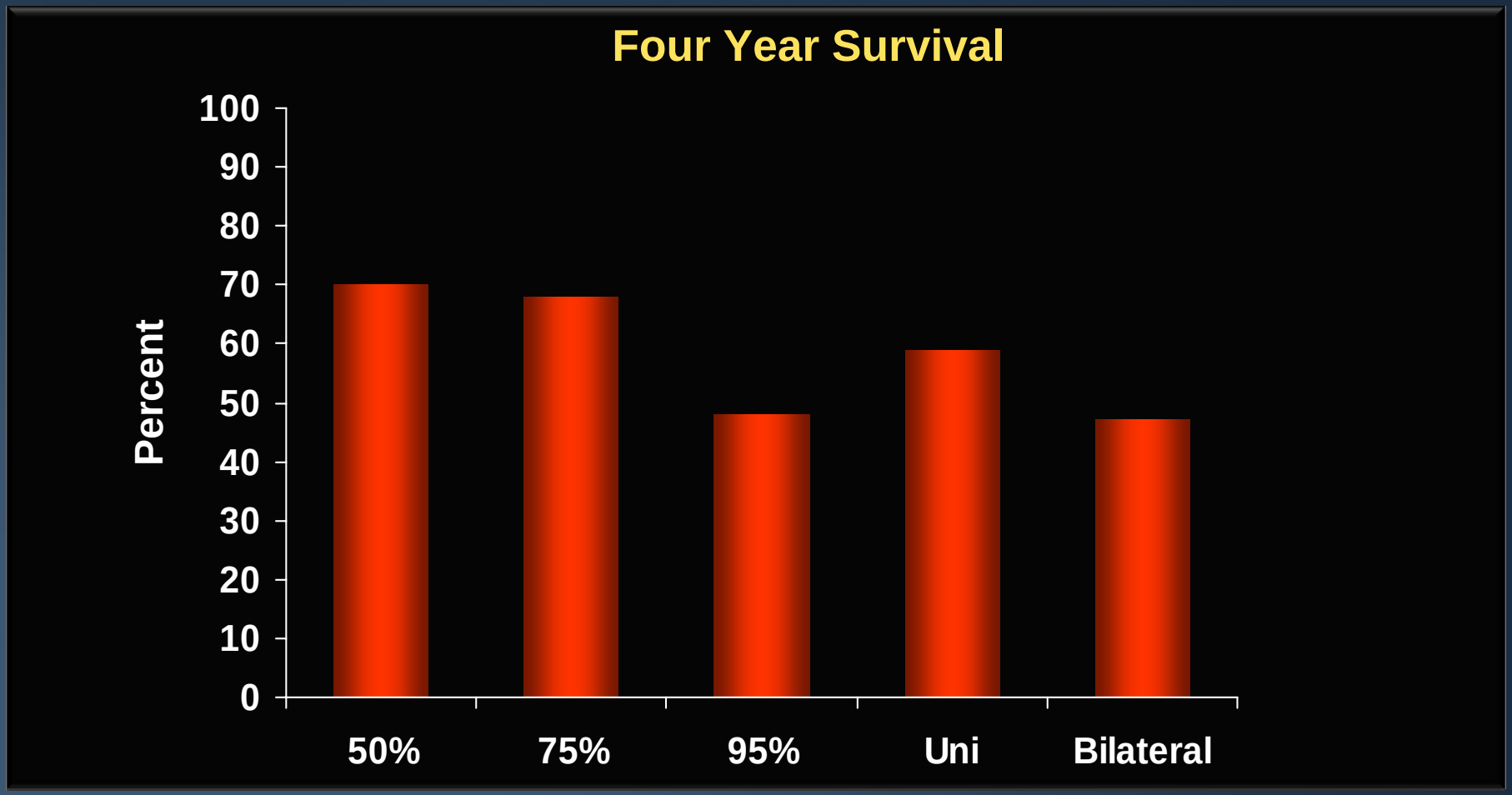
Conlon PJ, et al. *Kidney International* 2001;60:1490-7

Renal Artery Stenosis, Coronary Artery Disease, and Mortality



Conlon PJ, et al. *Kidney International* 2001;60:1490-7

Renal Artery Stenosis, Coronary Artery Disease, and Mortality



Conlon PJ, et al. *Kidney International* 2001;60:1490-7

What Does The Future Hold?

- Trial to (finally) demonstrate impact of renal artery intervention on survival, major cardiovascular events, hypertension, and (potentially)
  renal function
- Role of Embolic Protection Devices in renal artery intervention
- Benefit of Drug-Eluting Stents in renal artery intervention

The CORAL Trial
Cardiovascular Outcomes of Renal Artery Lesions

Prospective, Randomized Trial of Patients with RAS and HTN: Stent and Med Rx vs Med Rx Alone

Primary Endpoint Events

- Cardiovascular death
  - Any within 30 days of randomization
  - CV death ≥ 31 days
- Myocardial infarction
- Hospitalization for congestive heart failure
  - ≥30 days post randomization
- Stroke

- Uncontrollable hypertension
  - > 200 systolic and or >120 diastolic mm Hg
  - all tolerable medications
- Progressive renal insufficiency
  - decrease in iohexol-determined GFR of ≥ 33%
  - Persists 14 days
- Need for renal replacement therapy
  - ≥ 31 days post randomization

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Renal artery stenting: therapeutic targets

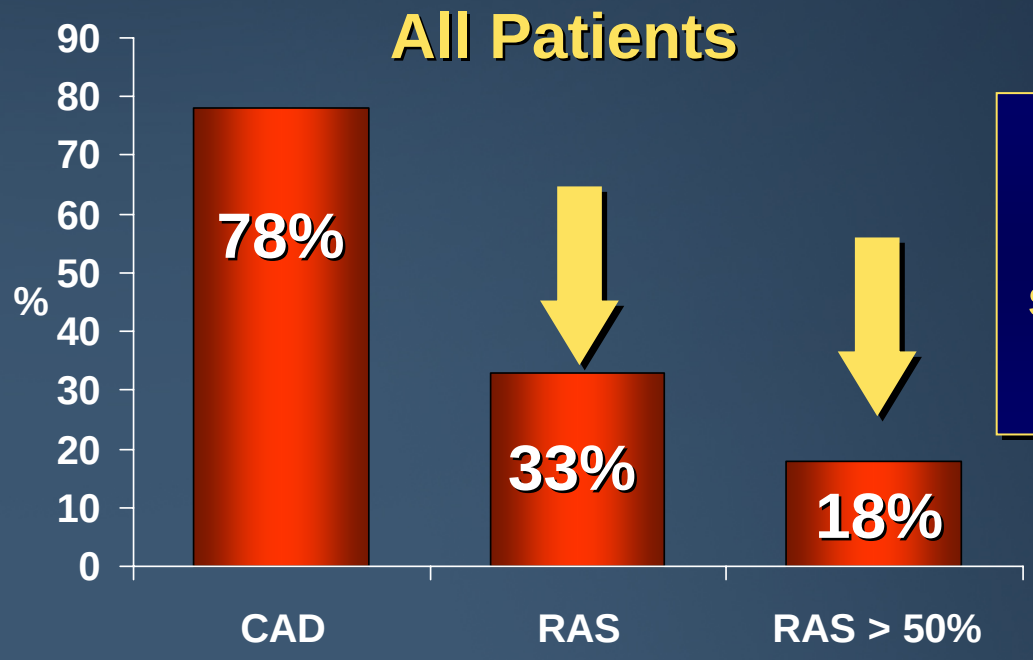
- Effective therapy for stenting in the appropriate clinical scenario
  - Truly refractory/resistant HTN with RAS
  - Renal insufficiency with ischemia to functioning renal mass
  - Cardiac disturbance syndromes with ischemia to functioning renal mass

Renal Artery Stenosis

	INCIDENCE
General population	0.1%
Hypertensive population	4.0%
HTN & suspected CAD	10 - 20%
Malignant HTN	20 - 30%
Malignant HTN & renal insufficiency	30 - 40%
HTN and PAD	44%

Incidence of Unsuspected RAS

- 196 consecutive patients referred for coronary angiography for suspected CAD underwent (drive-by) renal angiography.



22% (1 in 5) of the patients with CAD had significant (> 50%) renal artery stenosis.

Jean WJ, et al: Cathet Cardiovasc Diagn 1994;32:8-10.

The Consequences: Renovascular Hypertension

- Cardiovascular
- Renal

Natural History of Renal Artery Disease

- Trend in untreated or medically treated renal artery stenoses for progression of stenosis (to occlusion) and loss of renal function.

Natural history of renal artery stenosis

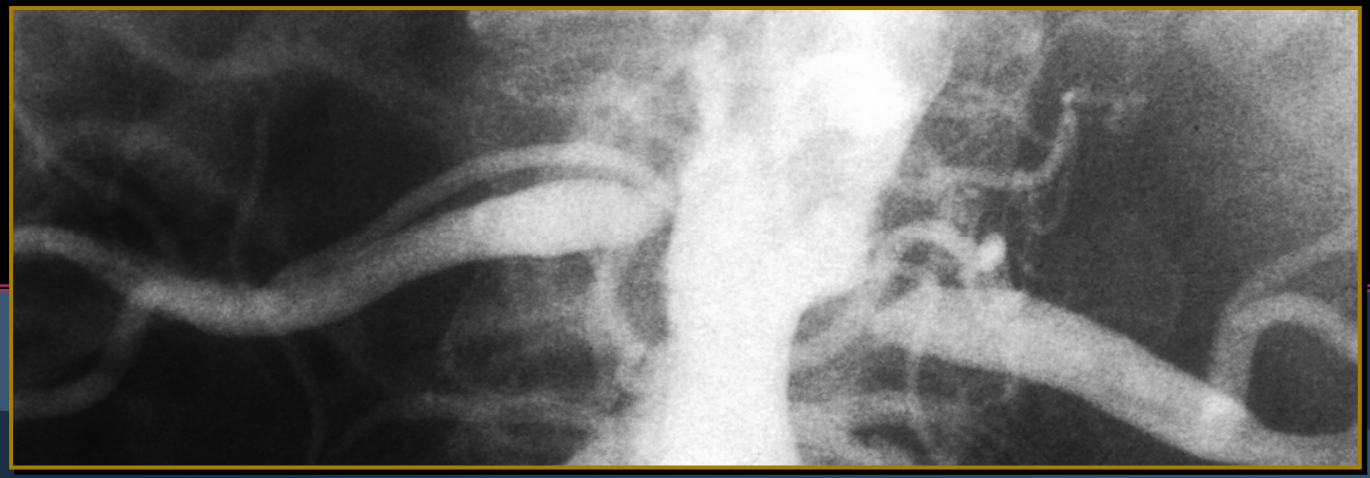
- 84 pts & 139 renal arteries not treated with revascularization followed for 13 months
- Progression at two years in 42%
- Progression to occlusion in 11%

Zierler RE, et al: J Vasc Surg 1994;19:250.

Criteria For Renal Stenting

asymptomatic

- Which lesions, if any, should be treated ?
  - Solitary ≥ 70% stenosis.
  - Bilateral ≥ 70% stenoses.
  - Unilateral ≥ 70% stenosis.



Can stenting renal artery stenosis improve or stabilize renal function?

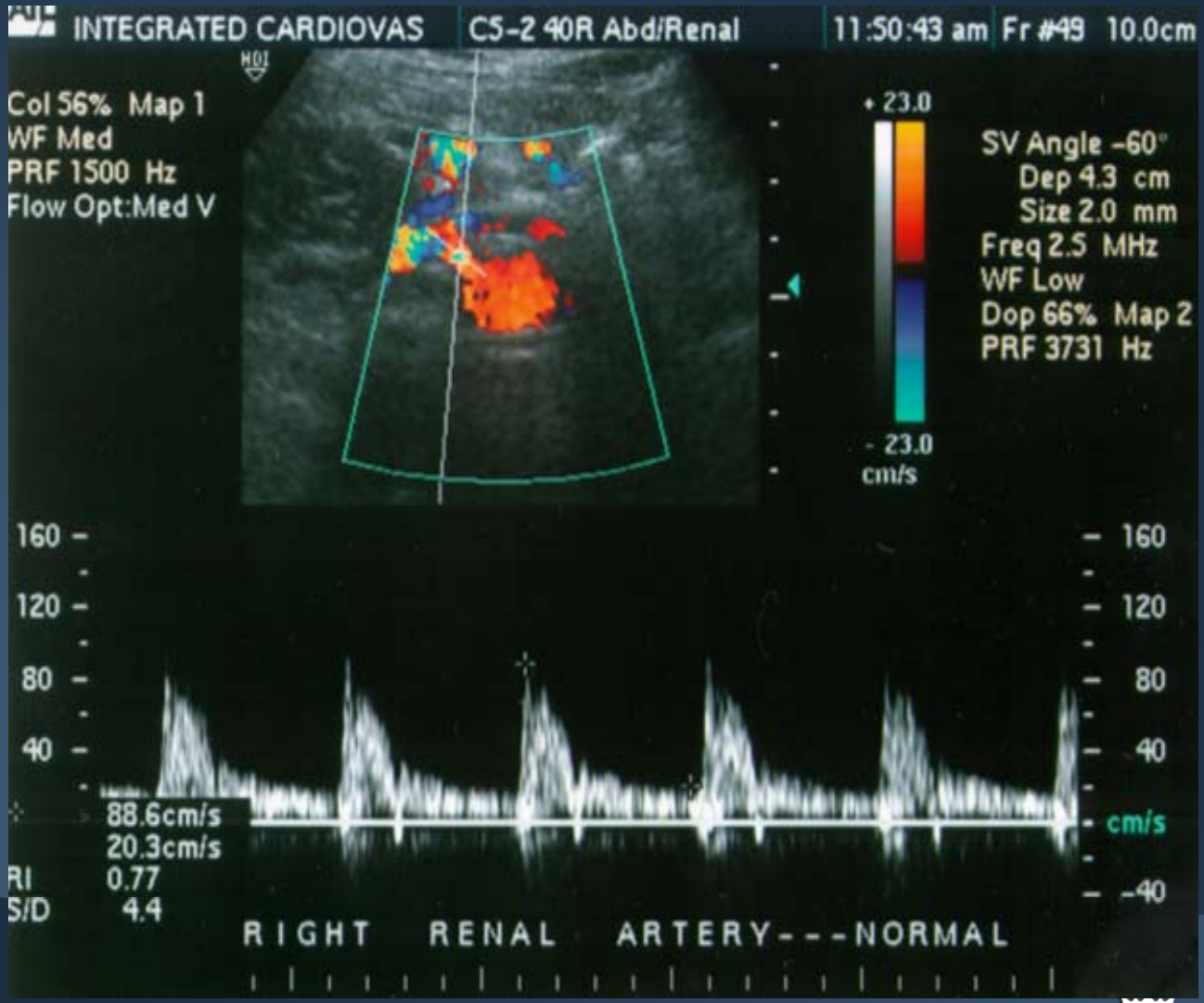
- Renal stent deployment in patients with
  - Chronic renal insufficiency (Cr ≥ 1.5 mg/dL).
  - Global renal ischemia (≥ 70% stenosis).
    - Bilateral RAS.
    - Unilateral RAS with solitary kidney.
- Renal function assessed with slopes or regression lines for the reciprocal of serum creatinine over time.

Watson PS, et al: Circulation 2000;102:1671.

Stent Complications

Renal Stents	Number	Death	Dialysis	Major Comp
Blum	74	0	0	0
Harjai	88	0	0	0
Tuttle	148	0	0	4.10
Rocha-Singh	180	0.6	0	2.60
Burket	171	0	0.7	0.70
White	133	0	0	0.75
Dorros	163	0.6	0	1.80
TOTAL	957	< 1%	< 1%	1.4%

Renal Artery Duplex Ultrasonography



Courtesy of M.Jaff

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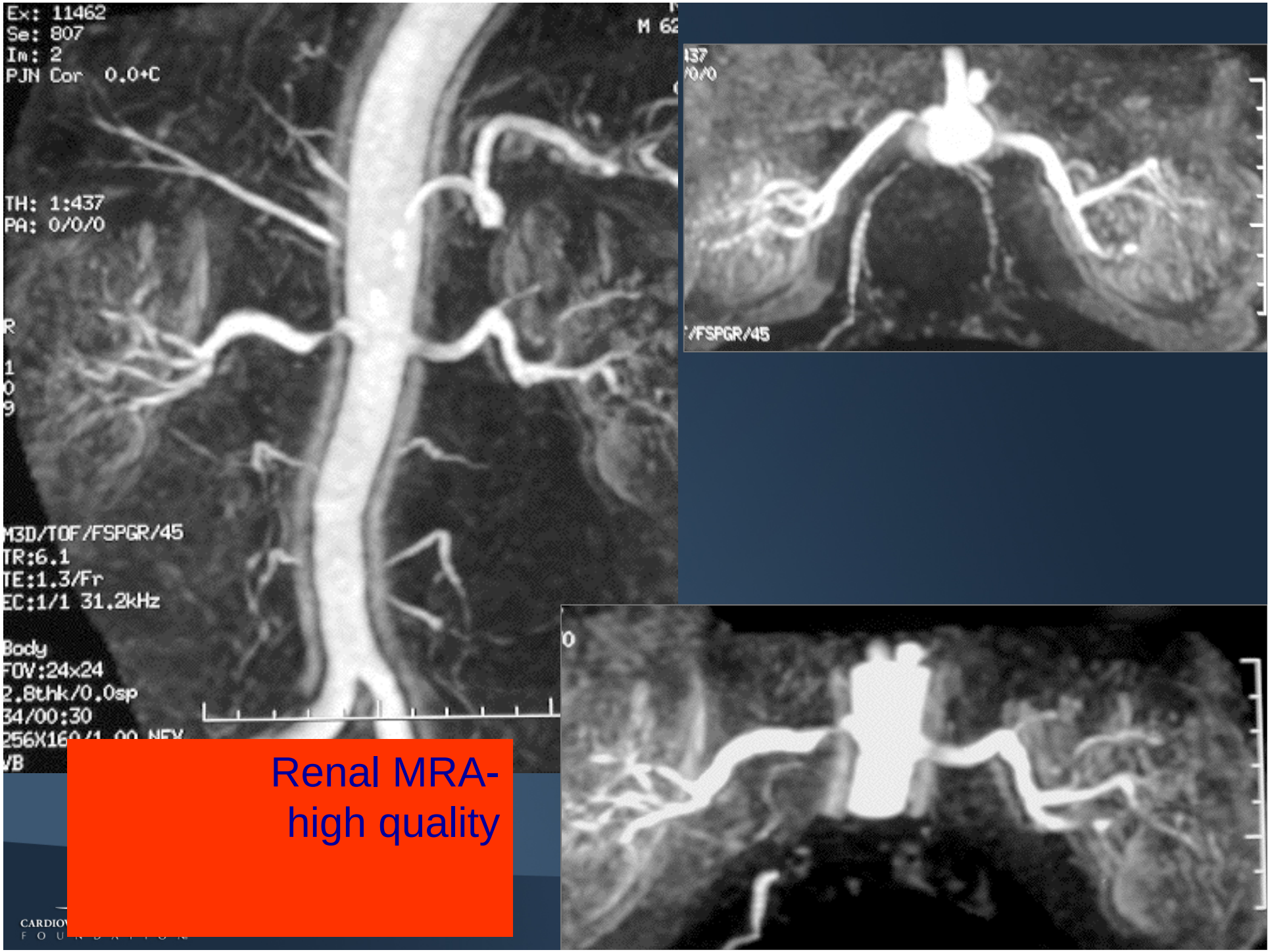
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Body
FOV:24x24
2.8thk/0.0sp
34/00:30
/FSPGR/45
Renal MRA-
high quality

Renal Artery Stenosis and Intervention *Shifting Trends*

- Increasing prevalence
- Heightened awareness
- Increasing detection
  MRA, Duplex, CTA

- Explosive growth in procedure volume

Renal Stenting Trends
*Charges submitted to Medicare**

Procedure	1996	1998	2001
PTA only	3780	3840	4380
Stent only	1220	2400	5740
Both	2660	5160	8400
Renal Bypass	4040		2260

Changes over 5 years:

Renal Intervention	+242%	
Renal Stenting	+364%	4X
Renal Bypass Surg	- 45%	

IS THIS CHANGE JUSTIFIED???

* Extrapolated from 5% file data

Renal Artery Stenosis
Truth and Consequences

- Progressive disease
- Tremendous cost to society of ESRD
  - US hemodialysis program - >$25 billion/year by 2010
- lost wages
- effect on quality of life

Screening and Management of RAS
Confounding Issues

- Absence of disease-specific symptoms
  - progression is silent
- Pathophysiologic effect on kidney poorly understood
- Cause & effect relationship between lesion and clinical syndromes (e.g. HTN, CHF, azotemia) is unclear
  - Difficult to predict which patients will derive benefit, or to what degree
- Literature reflects variable results from RAR
- Conflicting opinions about who should be screened/treated

Renal Artery Stenosis
What we don't know…

Whether individual patients will benefit

What are the predictors of response to revascularization

Pathophysiology to explain decline in renal function

Mechanism and relative contribution of RAS to deterioration in renal function

Knowledge base in RAS lags far behind that for CAD

What have we learned from trials and experience?

Renal anioplasty (with bail-out stent) vs. primary stenting

	POBA(n=42)	STENT(n=43)	
1° success (<50% residual)	24 (57%)	37 (88%)	p<0.05
6 mo patency	12 (29%)	30 (75%)	
Restenosis	48%	14%	p<0.05
Crossover	12 (29%) (5 acute)		

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van de Ven et al, Lancet 1999 Jan 23;353:282-6

Renal Stenting: Technical Success

Study series	Year of publication	Study period	No. of Arteries	Stent type	Ostial lesion (%)	Success definition	Technical success (%)
Rodriguez-Lopez [20]	1999	93 - 96	125	Palmaz	66	No RS / dissection	98
van de Ven [9]	1999	93 - 97	52	Palmaz	100	RS* < 50%	90
Henry [21]	1999	NA	104	AVE	77	RS < 20%	99
Rocha-Singh [12]	1999	93 - 95	180	Palmaz	43	#PG < 5mmHg	98
Tuttle [22]	1998	91 - 96	148	Palmaz	100	RS < 30%	98
Dorros [23]	1998	90 - 95	202	Palmaz	NA	RS < 50%	99
Rundback [24]	1998	NA	54	Palmaz	NA	RS < 30%	94
White [25]	1997	92 - 94	133	Palmaz	81	RS < 30%	99
Harden [17]	1997	92 - 95	32	Palmaz	75	RS < 10%	100
Blum [8]	1997	89 - 96	74	Palmaz	100	RS < 50%	100
Henry [26]	1996	90 - 94	64	Palmaz	53	RS < 20%	100
Iannone [27]	1996	92 - 93	83	Palmaz	78	RS < 30%	99
Hennequin [28]	1994	87 - 91	21	Wallstent	33	NA	100
Rees [29]	1994	88 - 92	296	Palmaz	100	RS < 30%	98

* RS=residual stenosis # PG=pressure gradient

~98%

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Lim and Rosenfield, Curr Int Cardiol 2000,2:130-139.

Renal Stenting: Incidence of restenosis

Table 2. Restenosis Rate of Renal Stents

Study series	No. of Arteries	Arteries evaluated (%original total arteries)	Ostial lesion (%)	Stent type	Method of evaluation	Average time to evaluation(month)	Restenosis
van de Ven, 1999	52	50 (95%)	100	Palmaz	angio*	6	21%
Rocha-Singh, 1999	180	158 (88%)	43	Palmaz	duplex + angio	13	12%
Tuttle, 1998	148	49 (33%)	100	Palmaz	angio	8	14%
Rundback, 1998	54	28 (52%)	NA	Palmaz	angio* + spiral CT	12	26%
White, 1997	133	80 (60%)	81	Palmaz	angio*	9	19%
Harden, 1997	32	24 (75%)	75	Palmaz	angio*	6	12%
Blum, 1997	74	74 (100%)	100	Palmaz	angio*	24	11%
Henry, 1996	64	54 (84%)	53	Palmaz	angio*	14	9%
Iannone,1996	83	69 (85%)	78	Palmaz	duplex	11	14%
Dorros, 1995 [30]	92	56 (61%)	100	Palmaz	angio*	7	25%
Hennequin, 1994	21	20 (95%)	33	Wallstent	angio*	29	20%
Rees, 1994	296	150 (51%)	100	Palmaz	angio*	7	33%
					weighted average	***10***	

~20%

Lim and Rosenfield, Curr Int Cardiol 2000;2:130-139

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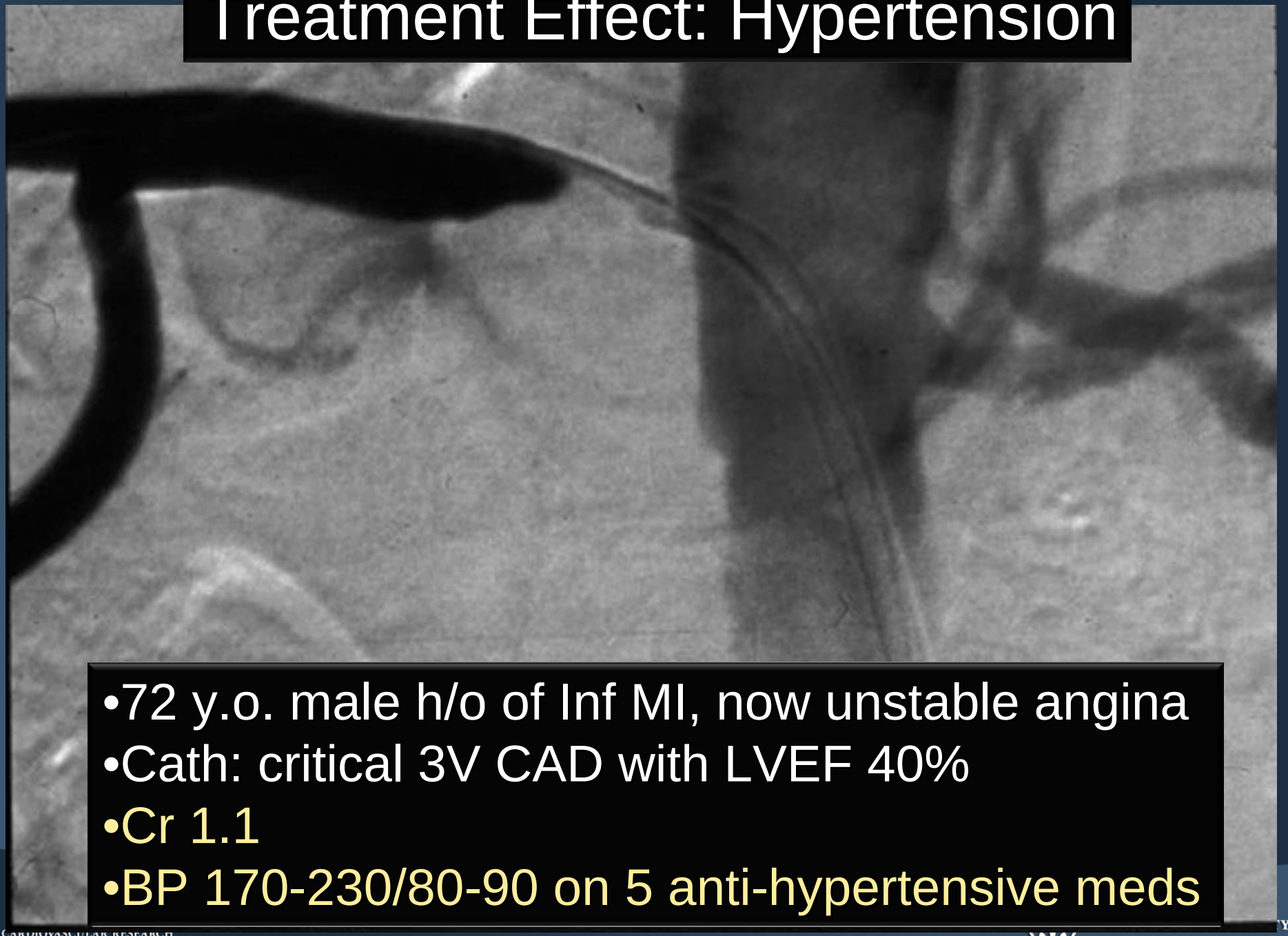
Renal artery stenosis in 2008
Possible targets of stenting

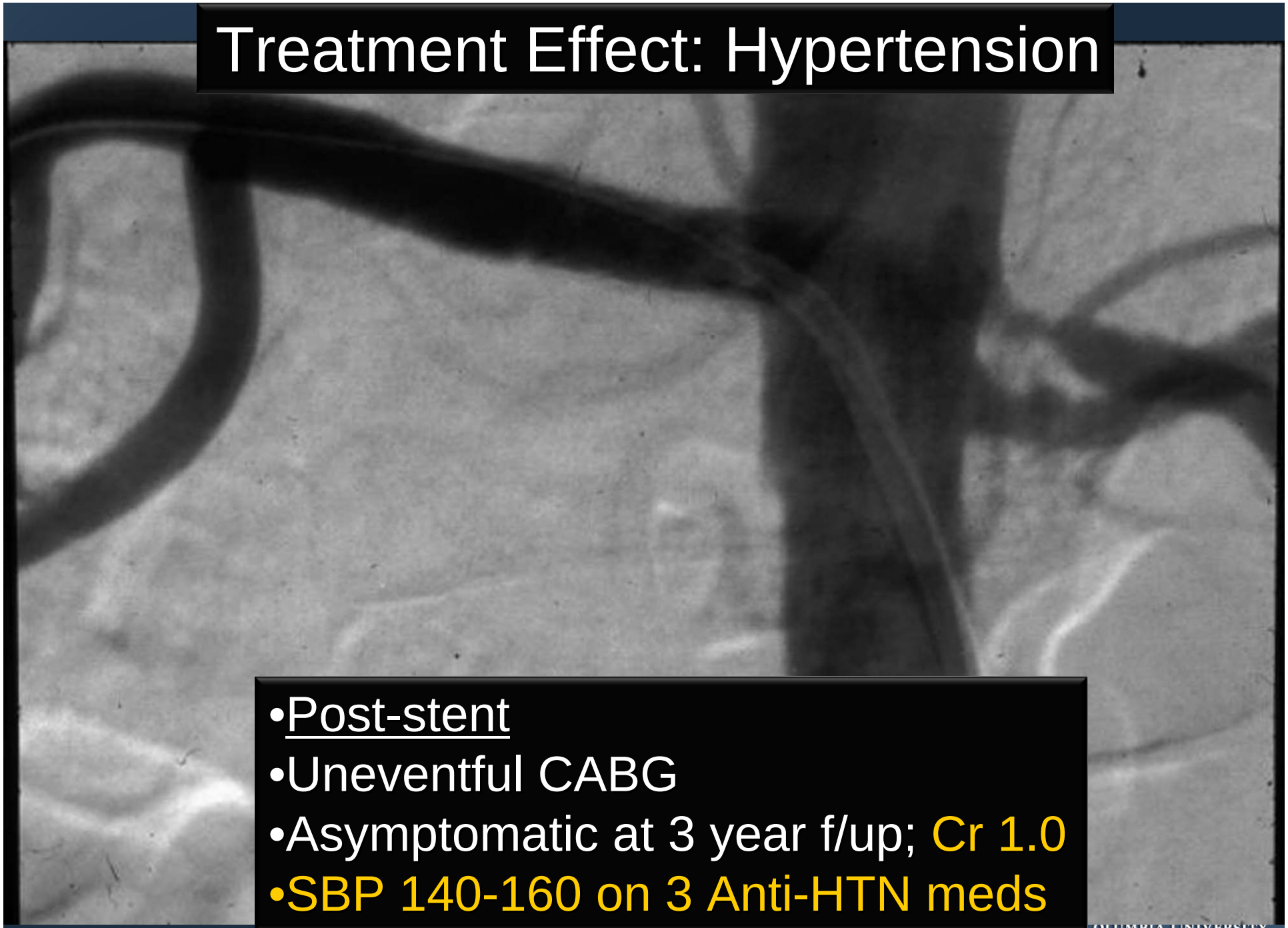
- HTN
- Renal Preservation
- Cardiac Disturbance Syndromes
- Mortality (?)

Treatment Effect: Hypertension



- 72 y.o. male h/o of Inf MI, now unstable angina
- Cath: critical 3V CAD with LVEF 40%
- Cr 1.1
- BP 170-230/80-90 on 5 anti-hypertensive meds

Treatment Effect: Hypertension

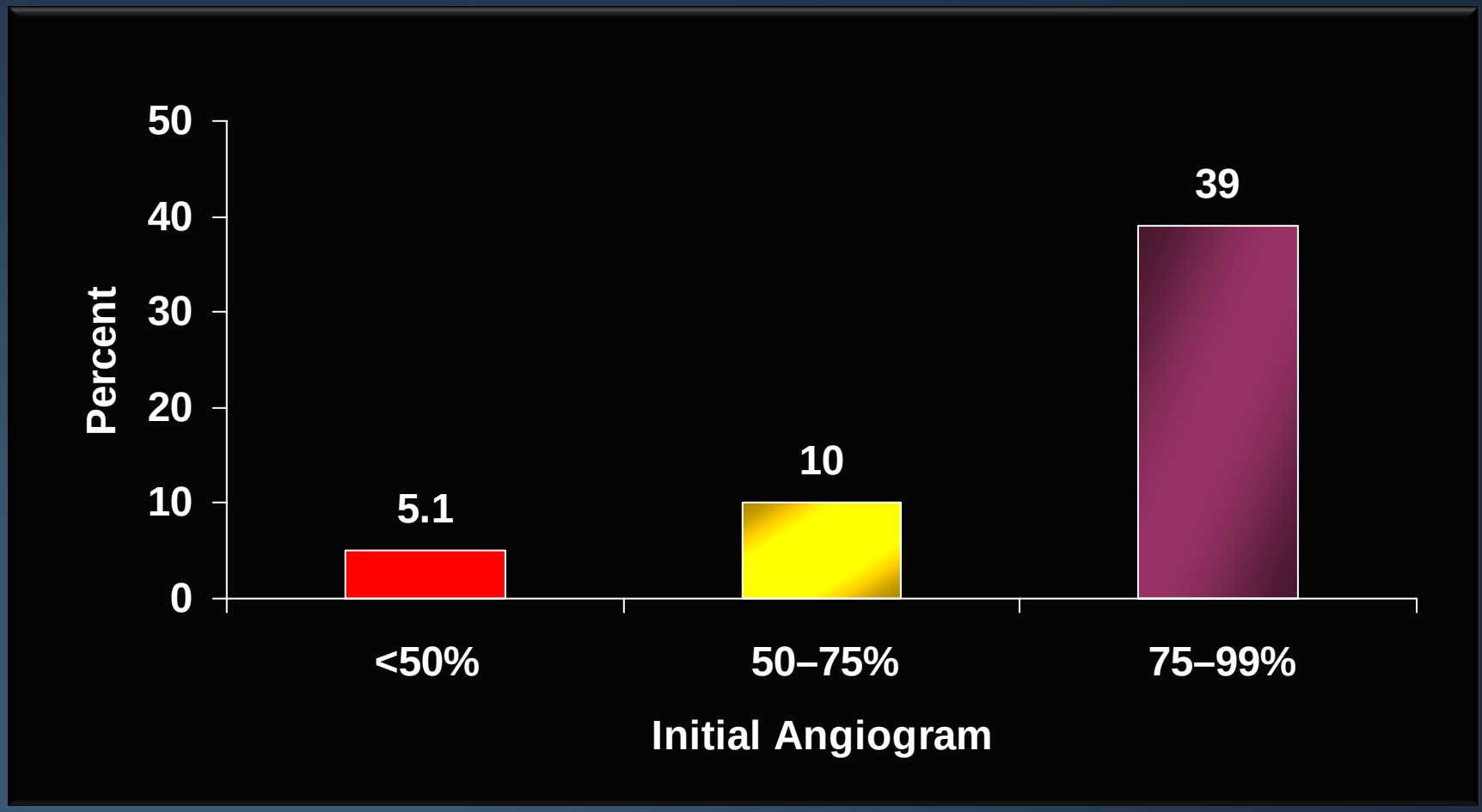


- Post-stent
- Uneventful CABG
- Asymptomatic at 3 year f/up; Cr 1.0
- SBP 140-160 on 3 Anti-HTN meds

Stenting effect on hypertension: *ASPIRE 2 Trial*

		Systolic pressure	
Visit	N	Mean±SD	P-value
Baseline	208	167.6±25.2	
Discharge	202	147.6±22.3	<0.001
1 month	196	151.5±24.4	<0.001
6 month	182	149.2±22.9	<0.001
9 month	178	149.5±23.8	<0.001
24 month	158	149.3±25.3	<0.001

Progression to occlusion increases with severity of stenosis



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Schrieber MJ, et al. *Urol Clin North Am* 1984;11:383

Implications of renal stenosis
Progressive loss of renal mass

- Duplex q6 months on 122 pts, 204 kidneys
- Renal atrophy (loss of 1cm length)
- mean f/up 33 months

Duplex finding	Renal Atrophy
normal	5.5%
<60%	11.7%
≥60%	20.8%

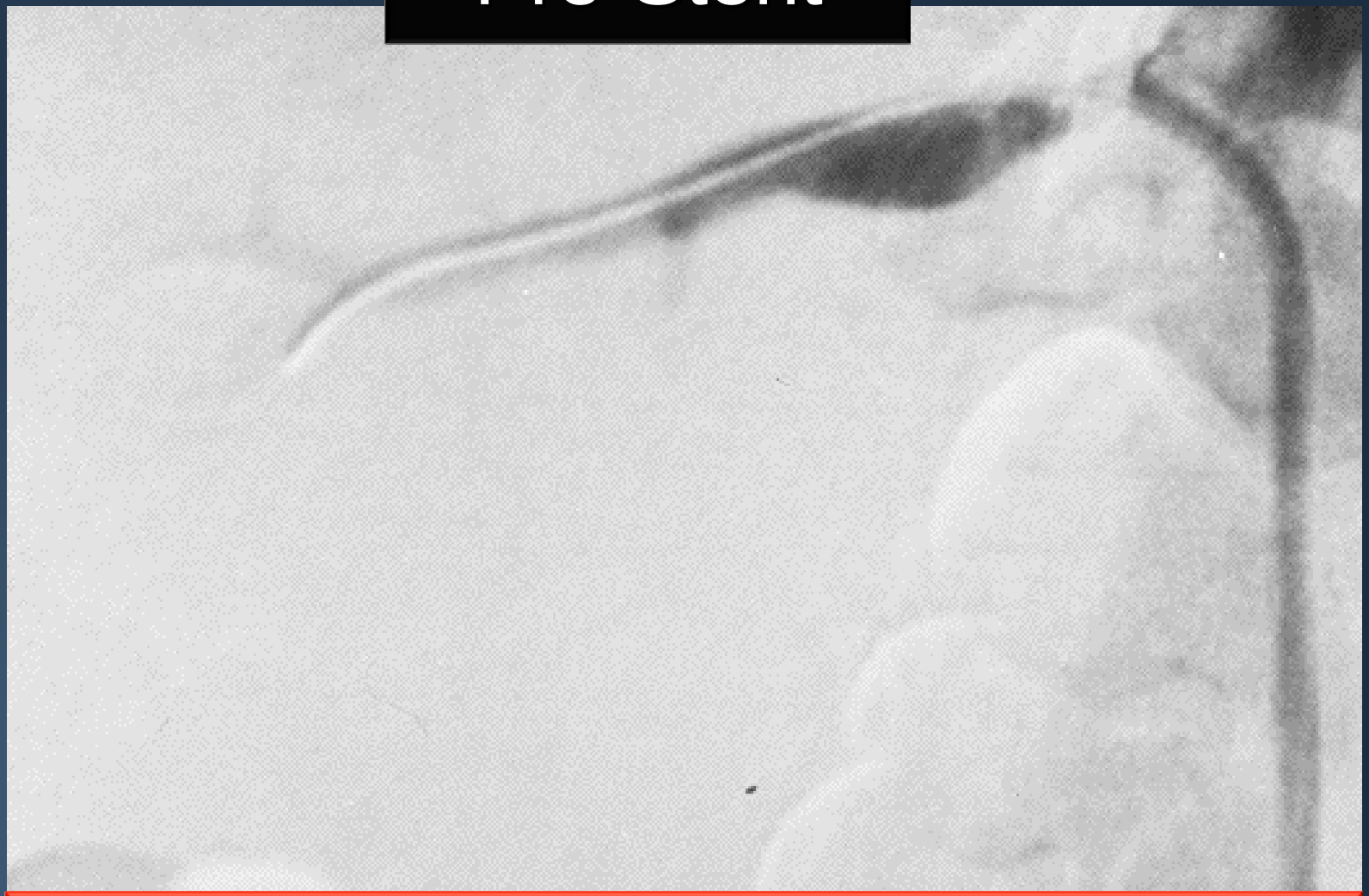
- Other factors correlated with renal atrophy:
  - elevated Creatinine
  - SBP>180
  - PSV>400cm/sec, EDV≤5cm/sec

Caps et al, Kidney Int'l, 1998,735-42

Renal artery stenosis
Progression and timing of intervention

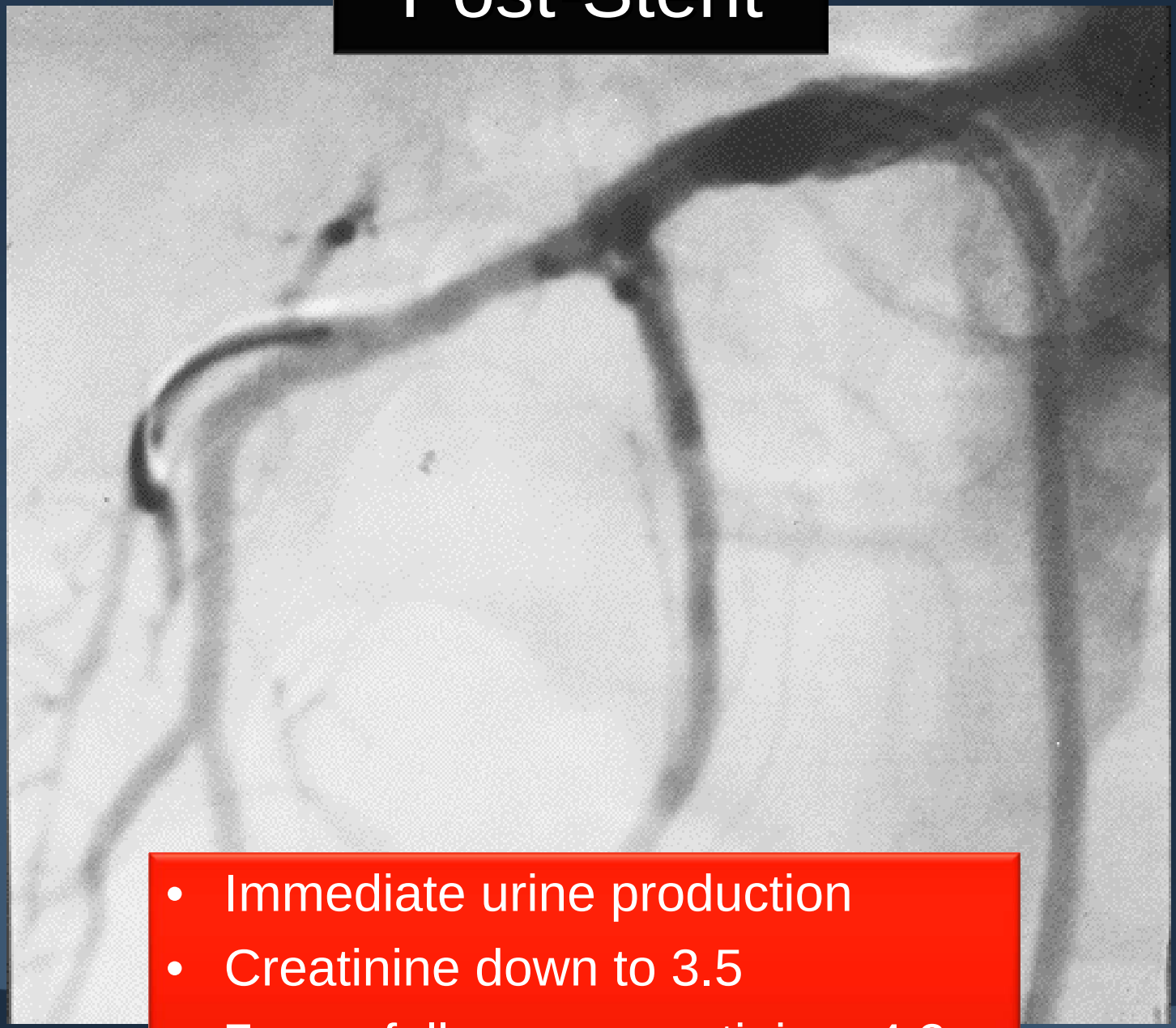
- Progression is unpredictable in the individual patient
  - Occurs in significant percentage of patients, who stand to suffer consequences
- Waiting until progression is measurable by atrophy or notable decline in renal function may be too late for RAR to have desired impact

Pre-Stent



- 72 year old male
- Acute anuric renal failure immediately post CABG
- Failure to thrive

Post-Stent



- Immediate urine production
- Creatinine down to 3.5
- 7 year follow-up: creatinine=4.2

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Effect On Renal Function: *ASPIRE 2 Trial*

Creatinine

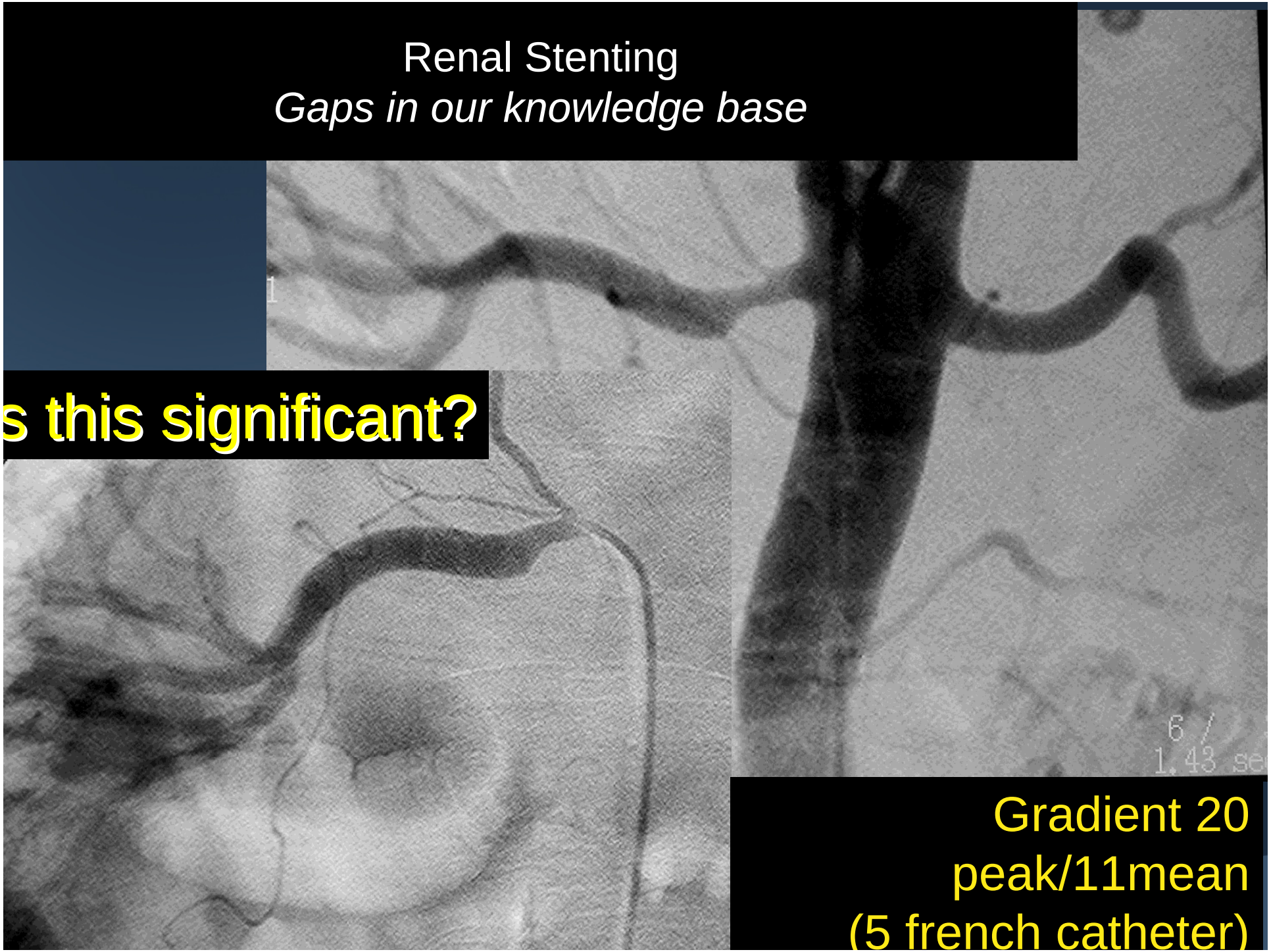
Visit	N	Mean±SD	P-value
Baseline	207	1.36±0.52	
1 month	187	1.35±0.62	0.74
6 month	174	1.41±0.61	0.03
9 month	173	1.40±0.61	0.31
24 month	153	1.46±0.81	0.04

Uncertainties in renal disease therapy

- How to **predict** the effect of RAR on control of HTN, renal function, and mortality in a given patient with RAS?
- What represents a “significant” percent stenosis or gradient?
- How does acute and long-term success vary based on factors like vessel diameter, resistive index in distal vascular bed, DM?
- What is the true rate of complications from PTRA and stenting, and what is the causality (atheroemboli, contrast, other)?
- Will distal embolic protection improve outcomes?

Renal Stenting

Gaps in our knowledge base



Renal Artery Stenting vs Medical Therapy

Randomized Trials:

Columbia University Medical Center
The Cardiovascular Research Foundation

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PTRA vs. Medical Rx for HTN

van Jaarsveld et. al, NEJM, April 2000, 342:1007

- 106 patients, randomized to PTRA vs. meds
- % diam stenosis >50
- Creatinine <2.4
- Outcomes: BP, meds, renal function, patency at 3 and 12 months

PTRA vs. Medical Rx for HTN

van Jaarsveld et. al, NEJM, 4/2000, 342:1007

106 patients, randomized to PTRA vs. meds

	PTRA	Medical	
• SBP	179 ---> 169	180 ---> 176	
• Mean	104 ---> 99	103 ---> 101	
• Meds	2.5	3.1	(p<.001)
• Creatinine	1.2	1.2	

Conclusion: "For treatment of HTN and RAS, angioplasty has little advantage over drug therapy."

PTRA vs. Medical Rx for HTN

van Jaarsveld et. al, NEJM, April 2000, 342:1007

PTRA group

- only 2/56 received stent (54/56 had POBA)

Medical group

– 22/50 (44%) crossed to PTRA

– 8/50 (16%) developed renal artery occlusion

– 6/50 (12%) had >50% increase in creat (vs. 4% in PTRA group)

van Jaarsveld et. al, NEJM, April 2000, 342:1007
ISSUES

- grossly underpowered
- average 2 interventions/site
- Optimal revasc. strategy (ie.stenting) not employed
- Many occlusions and crossovers in medical group

JACC, Vol 43, 5/04, 1614-16.

EDITORIAL COMMENT

"Renal Artery Stenosis: 'Fortuitous Diagnosis', Problematic Therapy"

-Weinrauch and D'Elia

"…studies (to date do) not address the consequences of RAS in a population."

Renal Artery Stenting
Need for Large-scale Randomized Trial

Weinrauch and D'Elia
JACC, Vol 43, 5/04, 1614-16.

"Experience has demonstrated that less than half of patients undergoing (renal revascularization) benefit with respect to HTN control or rescue of an ischemic organ"

"Review of the literature found a high incidence of CV death with no evidence for prolongation of life after RAR"

Renal Artery Stenting
Need for Large-scale Randomized Trial

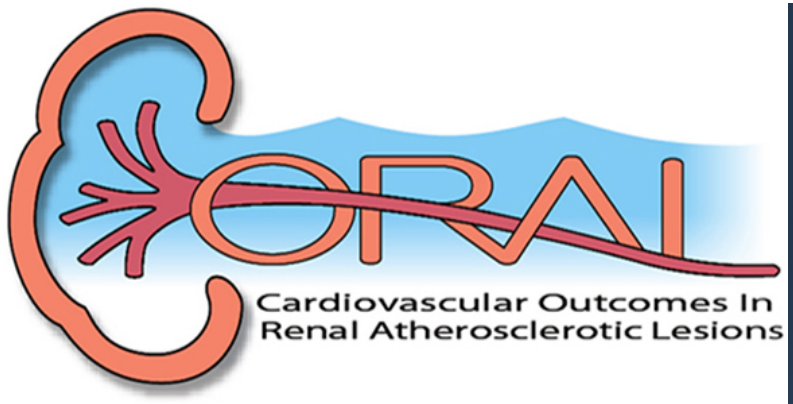
Weinrauch and D'Elia
JACC, Vol 43, 5/04, 1614-16.

"The only benefit that should be accepted as a reason for revascularization…is one that can be measured."

"In the absence of randomized controlled studies, clinicians would do well to…pursue long-term follow-up of this cohort to determine the significance of RAS with respect to specific heart and kidney disease outcomes…"

Renal Artery Stenosis
Defining the Future

- Trial to demonstrate impact of renal artery intervention on survival, major cardiovascular events, hypertension, and renal function
- Improve case selection - multivariate models to establish predictors of success or failure
- Role of Embolic Protection Devices
- Anti-restenosis therapies
  - DES



National Heart, Lung, and Blood Institute

- ***Hypothesis***: Medical therapy with stenting of hemodynamically significant, angiographically documented, renal artery stenoses in subjects with systolic hypertension reduces the incidence of adverse cardiovascular and renal events compared with medical therapy alone.

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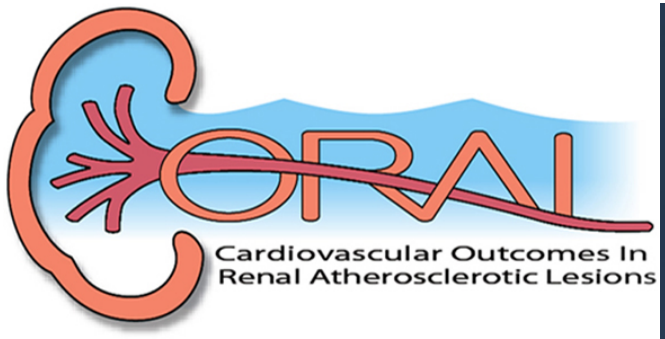

National Heart, Lung, and Blood Institute

Population:

- 1080 patients with atherosclerotic RAS
- Up to 85 US sites

Inclusion Criteria

- Systolic hypertension
  - ≥155 mm Hg
  - on ≥2 antihypertensive medication
- ≥1 renal artery stenosis
  - ≥60% with a 20 mm Hg systolic pressure gradient
  - ≥80% no pressure gradient required.

National Heart, Lung, and Blood Institute

- Optimal Medical Therapy (OMT)
  - All receive ARB (Candesartan)
  - LDL, BP and HbA1c to guideline
- OMT plus Stent Revascularization
  - Angioguard embolic protection
  - Genesis balloon expandable stent

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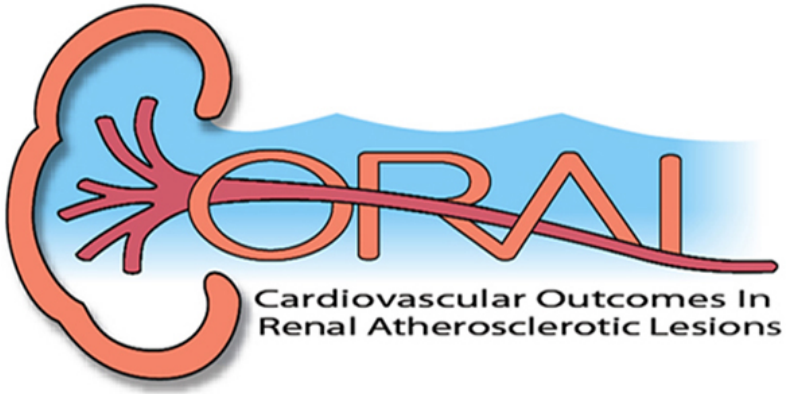

National Heart, Lung, and Blood Institute

- Survival free from Cardiovascular and Renal Adverse Events
  - Cardiovascular or Renal Death
  - Stroke
  - Myocardial Infarction
  - Hospitalization from CHF
  - Progressive Renal Insufficiency
  - Renal Replacement Therapy

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RAR- Effect on Renal Function

Study series	No. of patients	Renal function		
		Improved (%)	Stable (%)	Deteriorated (%)
van de Ven, 1999	42	12%	62%	26%
Rocha-Singh, 1999	150	22%	70%	8%
Tuttle, 1998	129	15%	81%	4%
Dorros, 1998	163	18%	48%	34%
Rundback, 1998	45	20%	47%	33%
Harden, 1997	32	34%	38%	28%
Weighted Averag		**19%**	**62%**	**19%**

Lim and Rosenfield, Curr Int Cardiol 2000,2:130-139.