Renal artery stenosis: Therapeutic Strategy

J Radermacher Stockholm 2005

A-RAS: Therapeutic strategy

- Whom to treat?
- Diagnosis of renovascular hypertension / Azotemia?
- Which degree of stenosis is hemodynamically relevant?
- How to treat?

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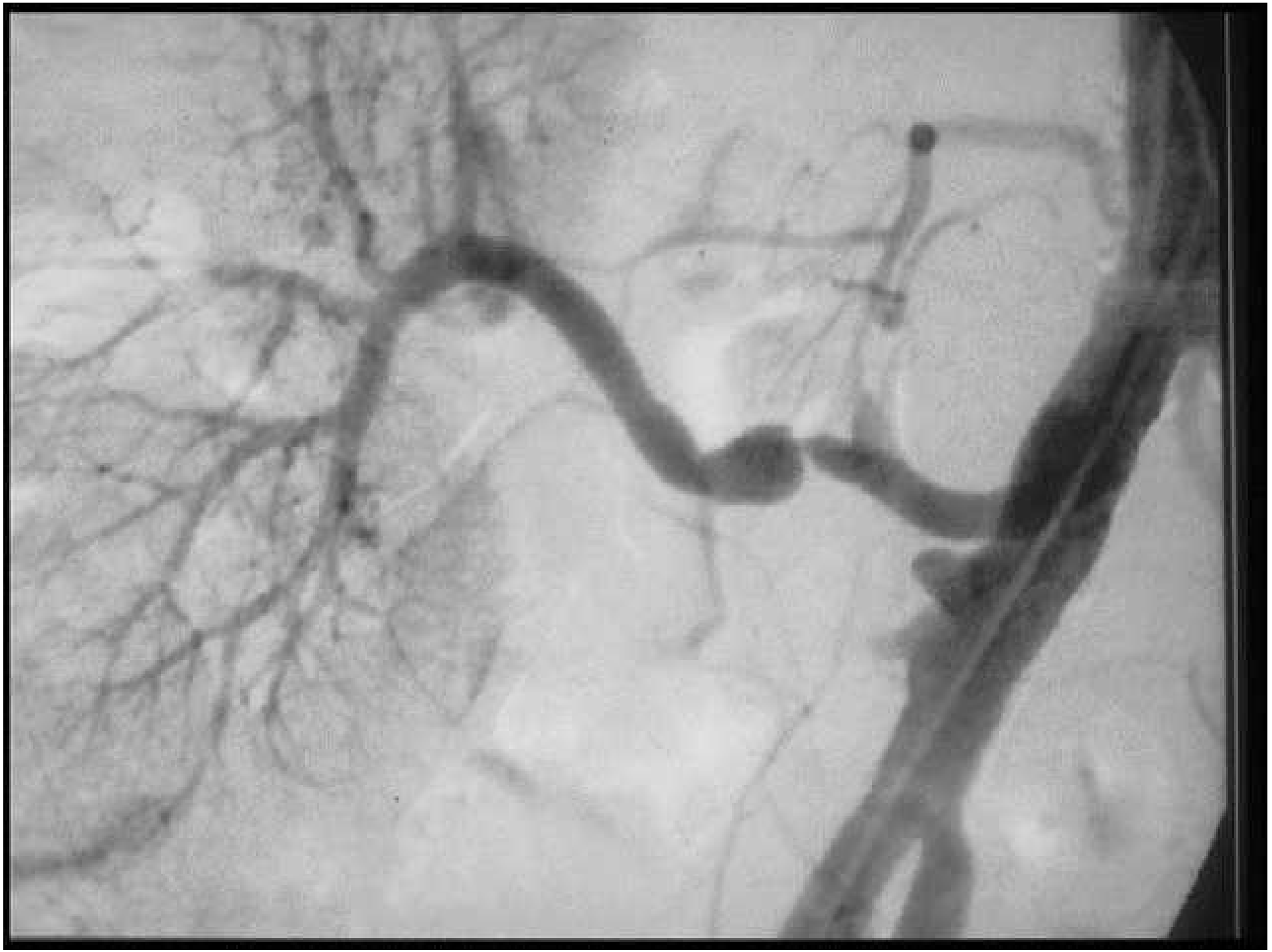

What about the patient?

Hypertension +

- **Uncontrolled with >=3 antihypertensives**
- **Acute heart failure / Flash plulmonary edema**
- **Impaired renal function**
  - **Worsening renal function after ACEI-Tx**

A-RAS: Therapeutic strategy

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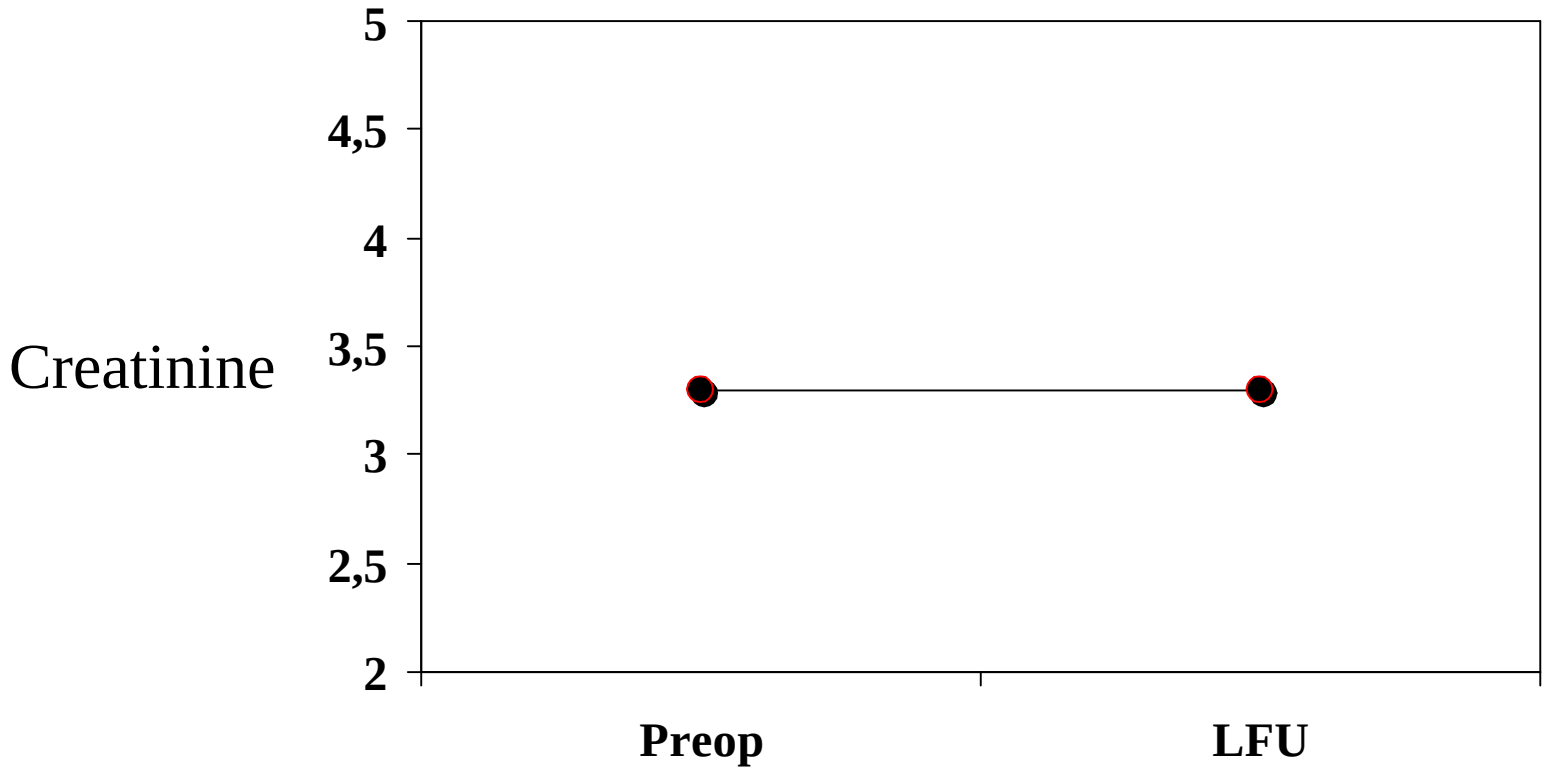
Renovascular hypertension
Renovascular azotemia

Renal artery stenosis :
RR: 170/100 mmHg
GFR: 60 ml/min

Successful PTA:
RR: 170/100 mmHg
(GFR: 60 ml/min)
20-40%

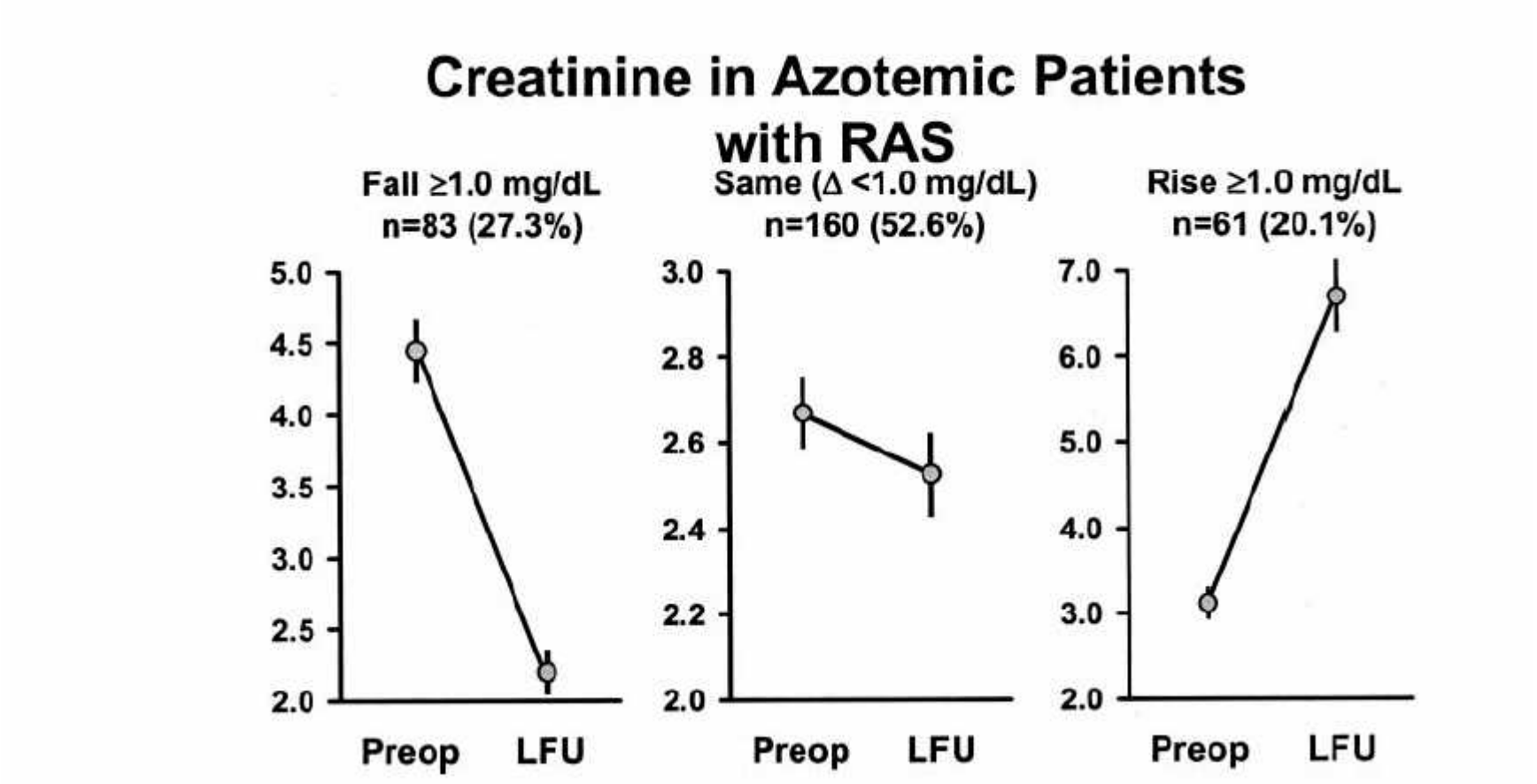
Successful PTA:
RR: 140/90 mmHg
(GFR: 85 ml/min)
60-80%

Follow up after surgical correction of RAS in 304 Patients



Textor&Wilcox 2001 Annu Rev Med 52: 421-442

Follow up after surgical correction of RAS in 304 Patients



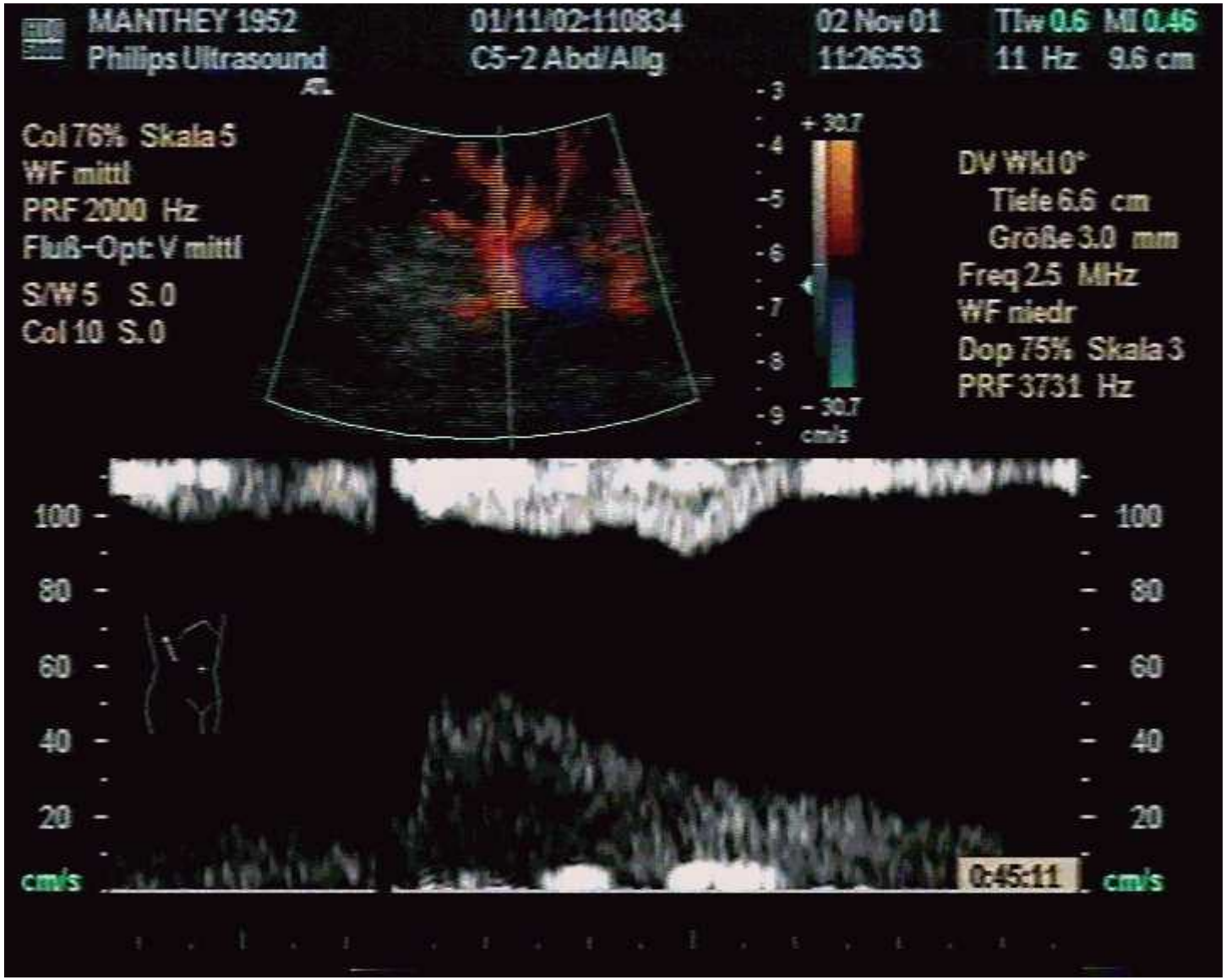
Textor&Wilcox 2001 Annu Rev Med 52: 421-442

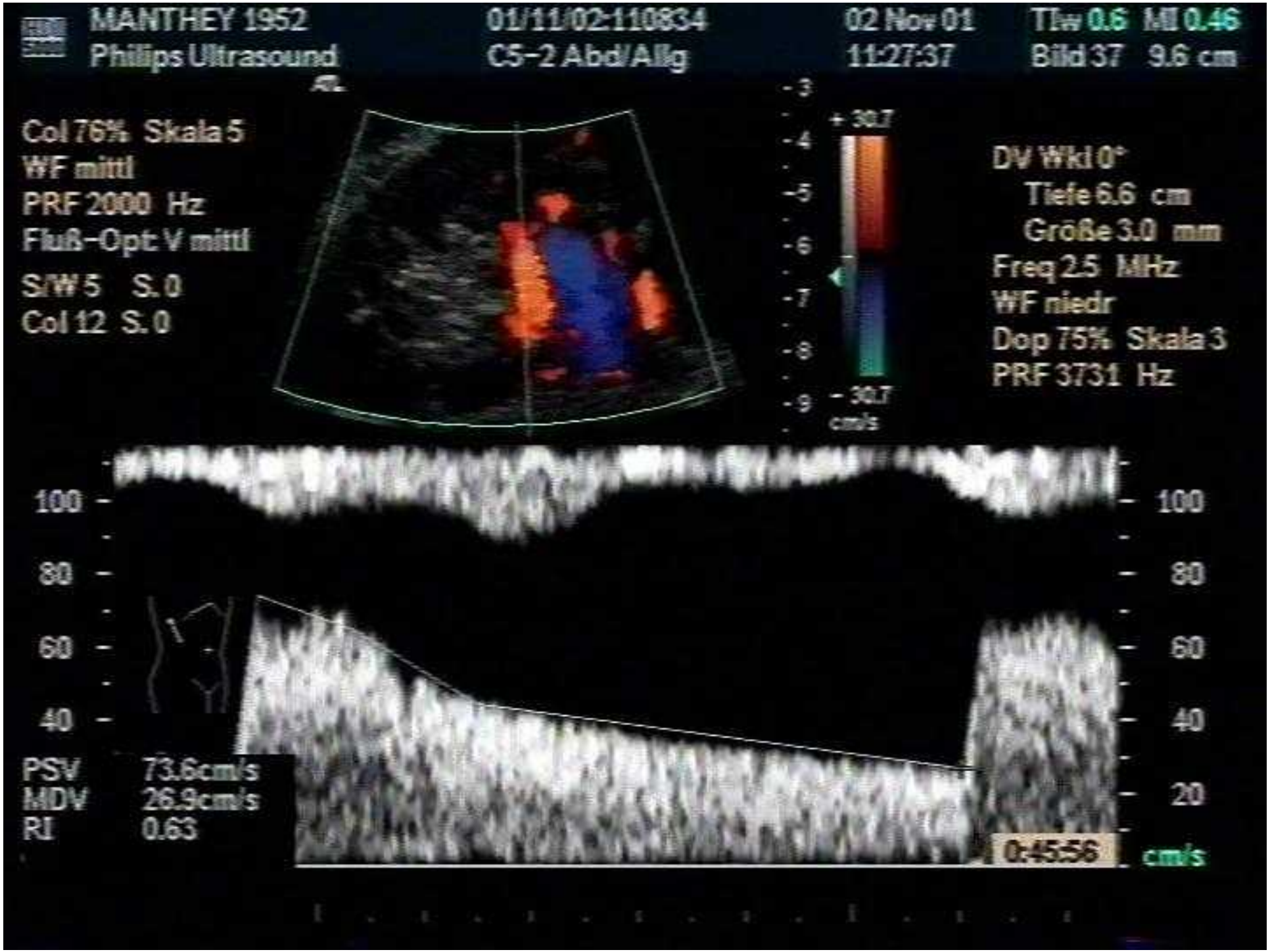
What Method to Diagnose **RVHT/RVA**?

- Selection criteria
  - > 50 patients included
  - Prospective
  - RVHT: Fall in MAP >=10mmHg with unchanged AHT
  - RVA: Improvement >= 10%
- Screening methods evaluated
  - Captopril test
  - Captopril Szintigraphy
  - Lateralised renal vein renin
  - Doppler Sonography

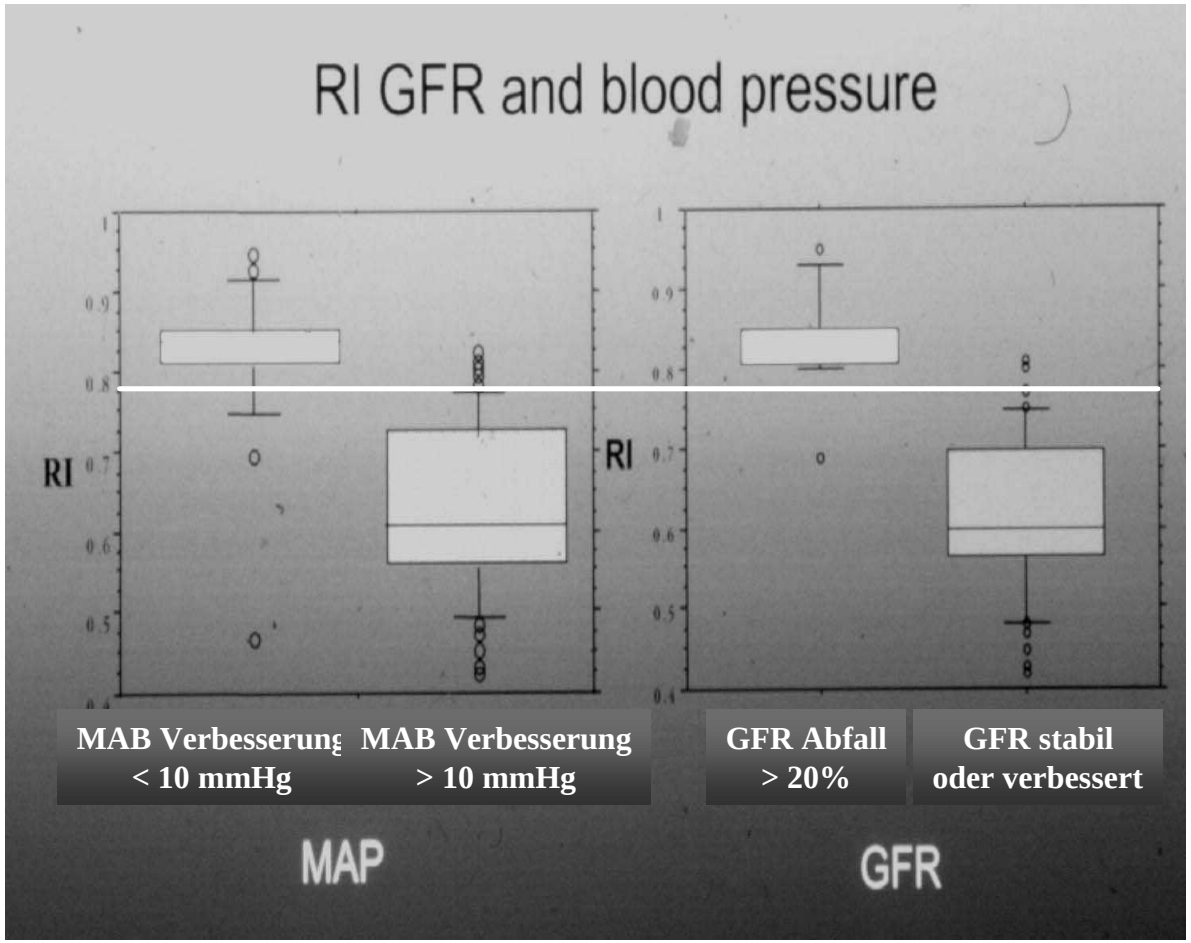
	Patienten - zahl	Kommentar / Parameter	RVHT Sensitivität / Spezifität (%)	RVA Sensitivität / Spezifität (%)
Captopril Szintigraphie				
Geyskes (1991) [12]	77	Tmax	91 / 32	k. A.
Dondi (1992) [7]	51	Renogram Muster Tmax > 5 min	87 / 93	k. A.
Elliot (1993) [8]	53	Captopril 25-50 mg Delta Tmax > 5 sec oder Delta GFR 2 min ≥10% oder Delta Exkretion> 5 min	92 / 80	k. A.
Fommei (1993) [10]	36	Normale Nierenfunktion Tracereinlagerung 2 min < 40% oder Tmax < 2 min oder > 10 min	93 / 100	k. A.
	18	Kreatinin > 123µmol/l	100 / 33	71 / 90
Harward (1995) [17]	52	n.v.	100 / k.A.	k. A.
Mittelwert:			**93 / 67**	
Captopril Test				
Elliot (1993) [8]	53	PRA > 5.7 ng/ml/h nach 25 mg Captopril	76 / 58	k. A.
Lateralisierung Nierenvenen Renin				
Martin (1993) [25]	123	Lateralisierungindex > 1.5	67 / 20	k. A.
Roubidoux (1991) [43]	133	Lateralisierungsindex > 1.5	65 / 48	k. A.

Messung des RI-Wertes mittels FKDS




MANTHEY 1952
Phillips Ultrasound
01/11/02-110834
C5-2 Abd/Allg
02 Nov 01
11:27:37
TIw 0.6 MI 0.46
Bild 37 9.6 cm
Col 76% Skala 5
WF mittl
PRF 2000 Hz
Fluß-Opt: V mittl
S/W 5 S. 0
Col 12 S. 0
+ 30.7
- 30.7
cm/s
DV Wkl 0°
Tiefe 6.6 cm
Große 3.0 mm
Freq 2.5 MHz
WF niedr
Dop 75% Skala 3
PRF 3731 Hz
100
80
60
40
20
PSV 73.6cm/s
MDV 26.9cm/s
RI 0.63
0:45:56
cm/s

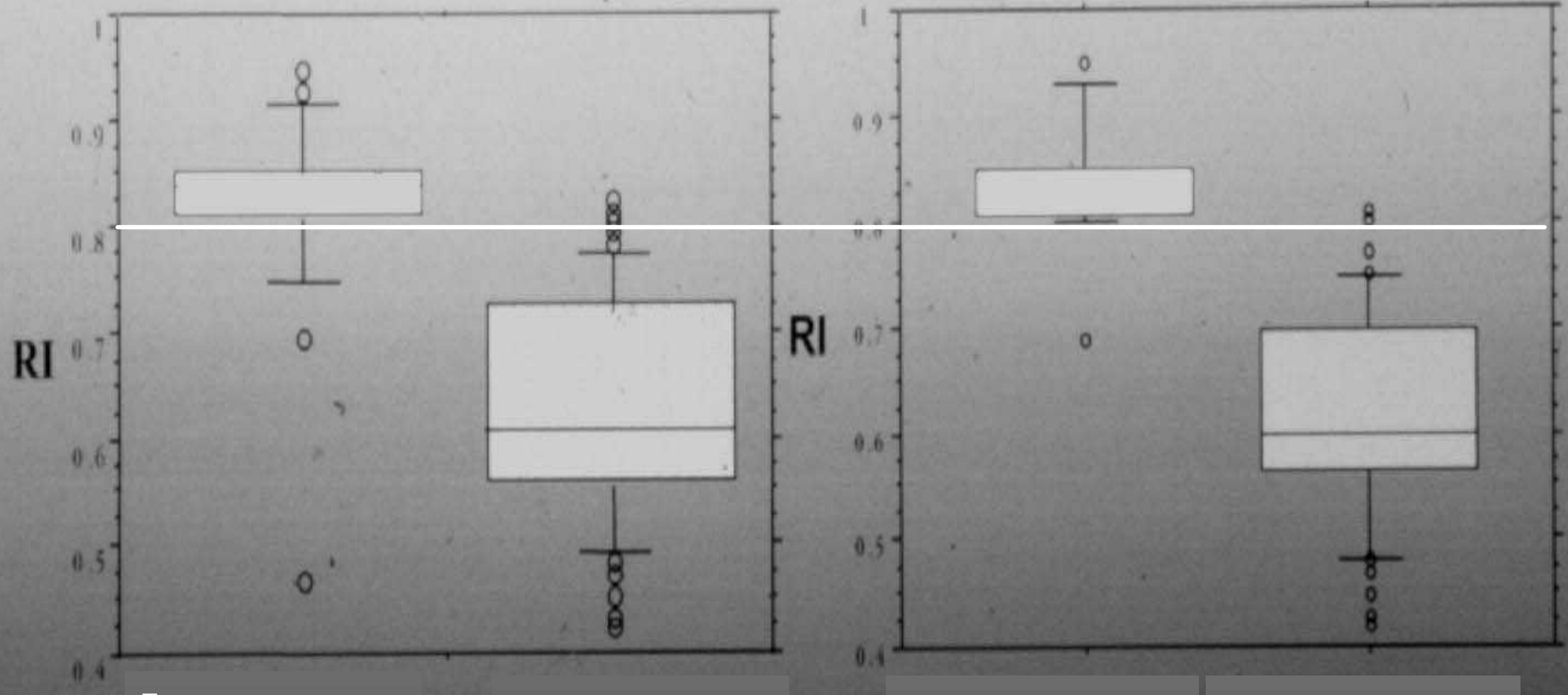
How to Diagnose renovascular hypertension / -azotemia



Retrospective analysis [1] : RI > 80 is characteristic for patients who improve neither blood pressure nor renal function

Radermacher et al. JASN 1996, 7:1554

RI GFR and blood pressure



Improvement < 10 mmHg

Improvement = 10 mmHg

GFR Decrease > 20%

GFR Stable or Improved

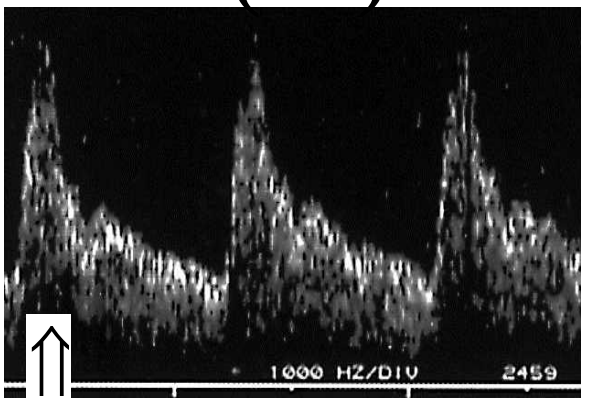
MAP

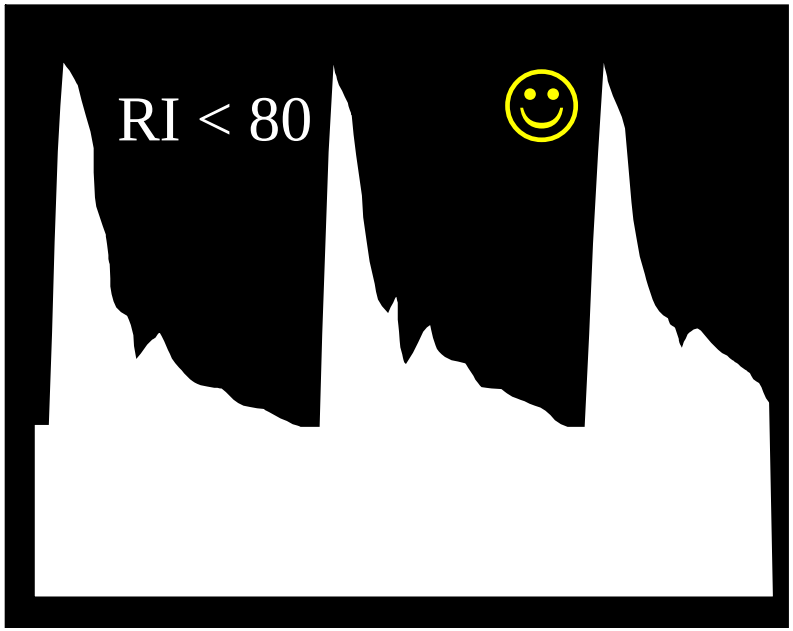
GFR

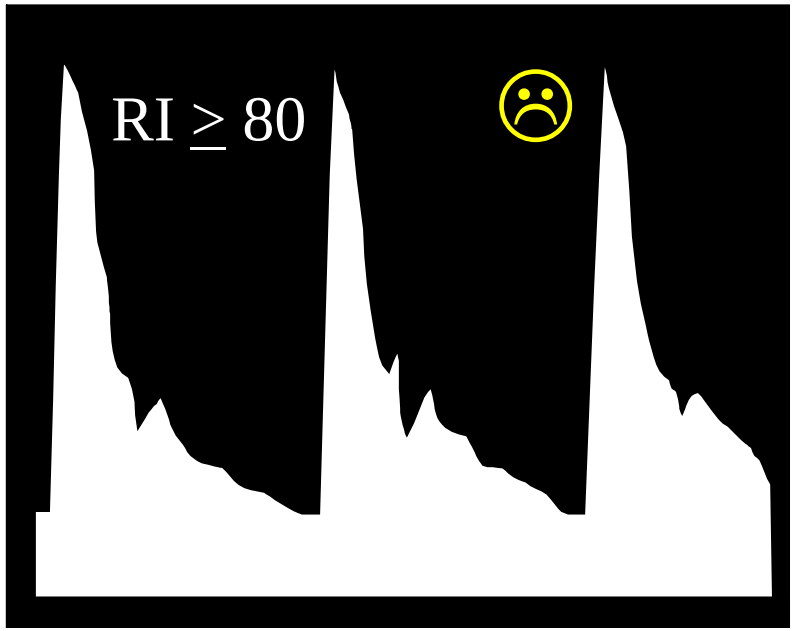
How to Diagnose RVHT / RVA :

Measuring the renal resistance index (RI)

- Proximal renal segmental artery
- RI = (1- (Vmin / V max)) * 100





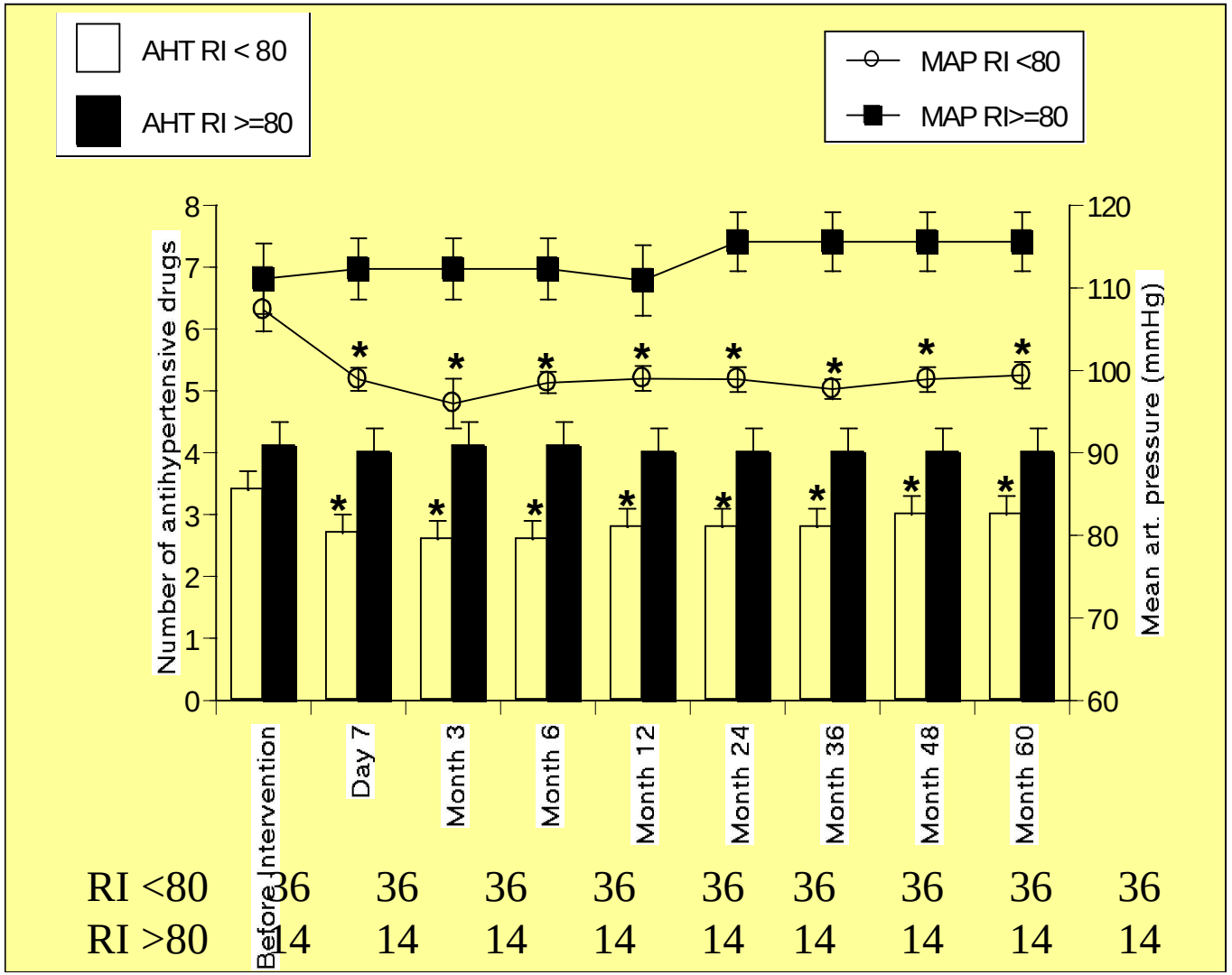


How to diagnose renovascular hypertension or azotemia

- 5950 hypertensive patients were screened for renal artery stenosis with CDS
- RI was measured in both kidneys
- RI $\geq$80 **in either** kidney was considered a poor prognostic sign
- 131 patients c. successful PTA or surgery of RAS >50%
- Measure creatinine clearance and 24h-ABP before and at month 3, 6, 12 and in yearly intervals thereafter

How to diagnose renovascular hypertension

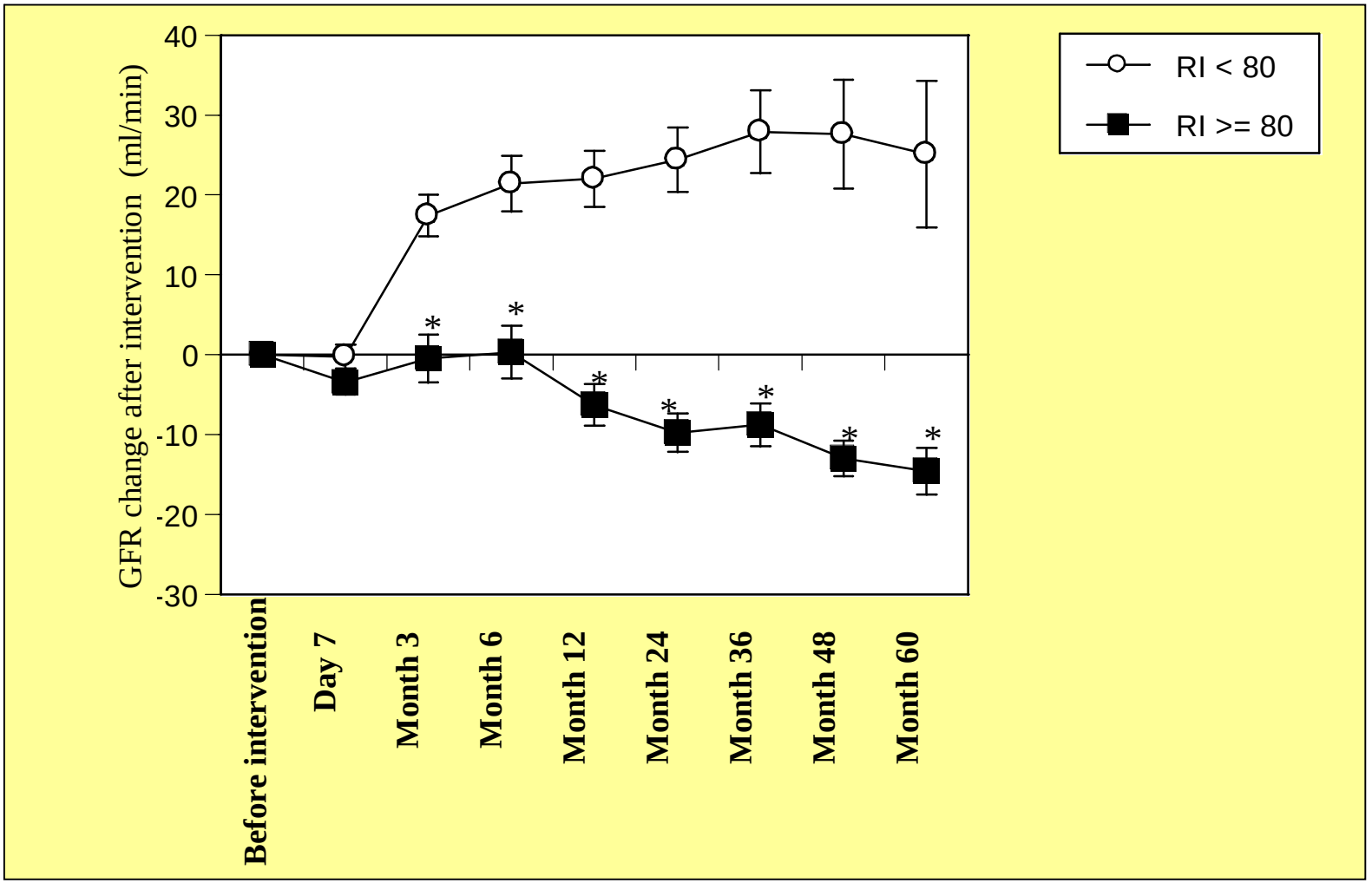
Predictive value of RI: Follow up > 5 Jahre



- RI ≥ 80 n =14
  No decrease of MAP (>10 mmHg) in 14
- RI < 80 n = 36
  No decrease of MAP (>10 mmHg) in 2

How to diagnose renovascular azotemia

Predictive value of RI

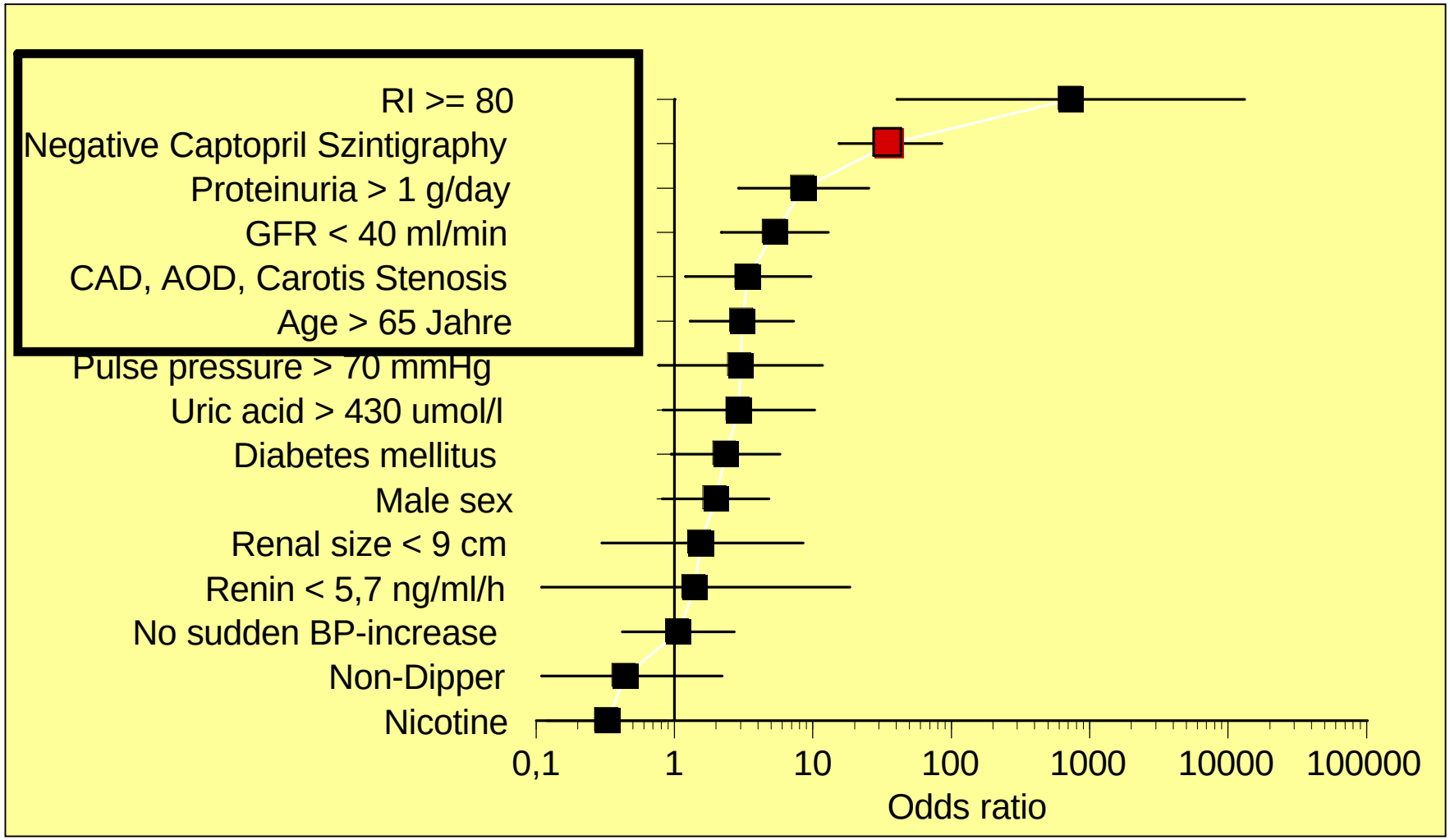


Predictive value of RI

	Patient - number	Comment / Parameter	RVHT Sensitivity / Specificity (%)	RVA Sensitivity / Specificity (%)
Color coded Duplex sonography				
Radermacher 2001 [38]	131	All Patients RI < 0.80	99 / 85	96 / 53
Radermacher 2001 [38]	78	Impaired renal function RI < 0.80	98 / 90	96 / 79

Radermacher et al. 2001 NEJM 344: 410-417

Comparison of RI with other parameters to predict declining renal function (GFR decrease >10%)



Pitfalls of RI

- Bilateral severe (>70%) stenosis
- Urodynamically relevant hydronephrosis
- Acute renal failure
- Valsalva during measurement of RI
- Extreme bradycardia (< 40)

A-RAS: Therapeutic strategy

- Whom to treat?
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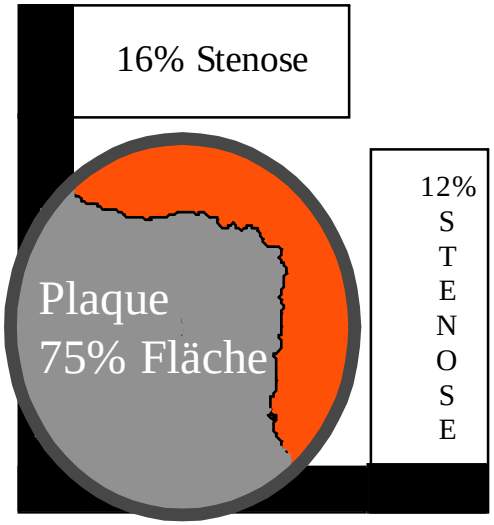
- How to treat?

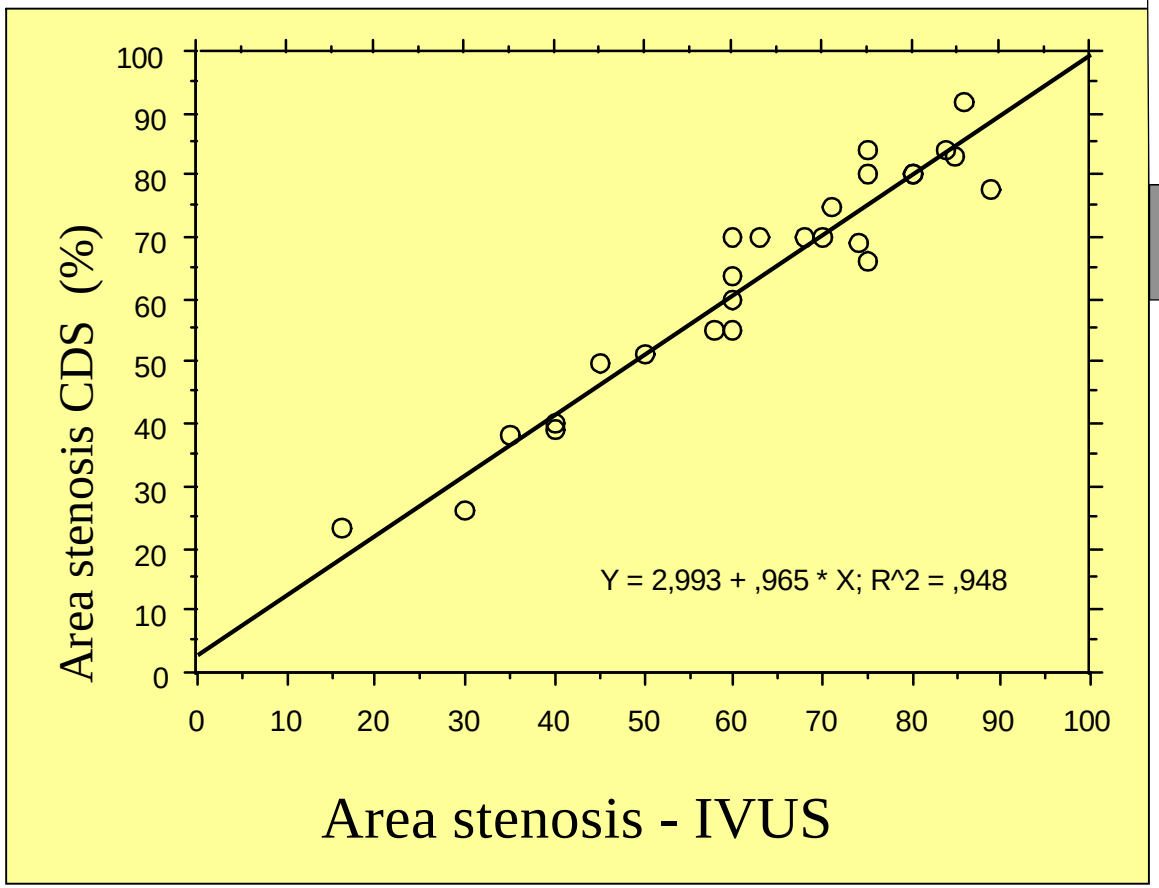
Stenosis quantification

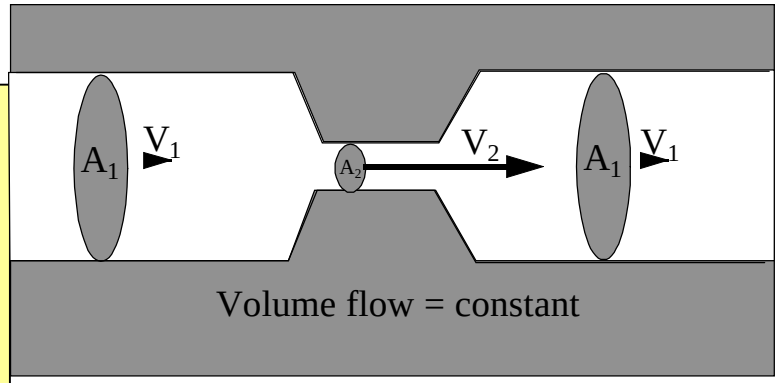
- Angiography is no really gold standard for stenosis quantification
  - 40% under- or overestimation

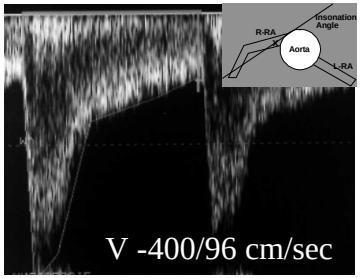


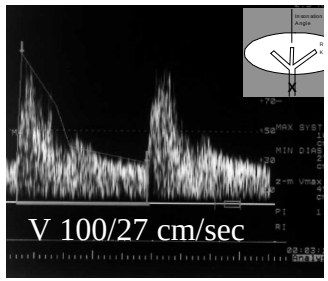
- Intravascular ultrasound is gold standard but too expensive for routine examinations
- Degree of stenosis is important for renal function improvement

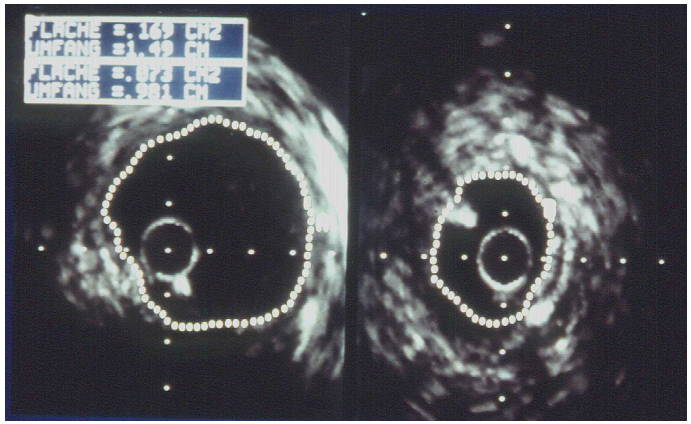
(Area)Stenosis quantification with CDS





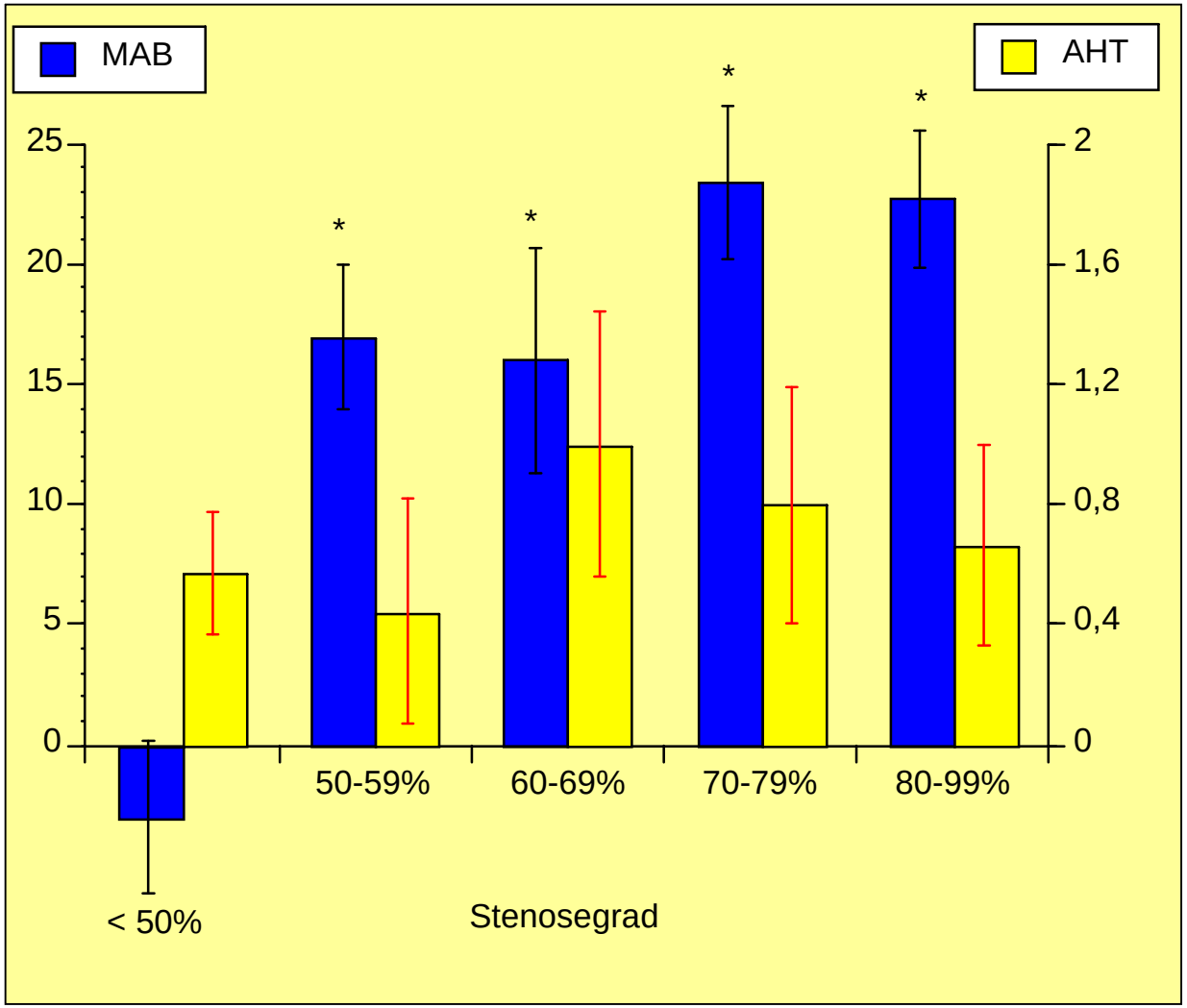






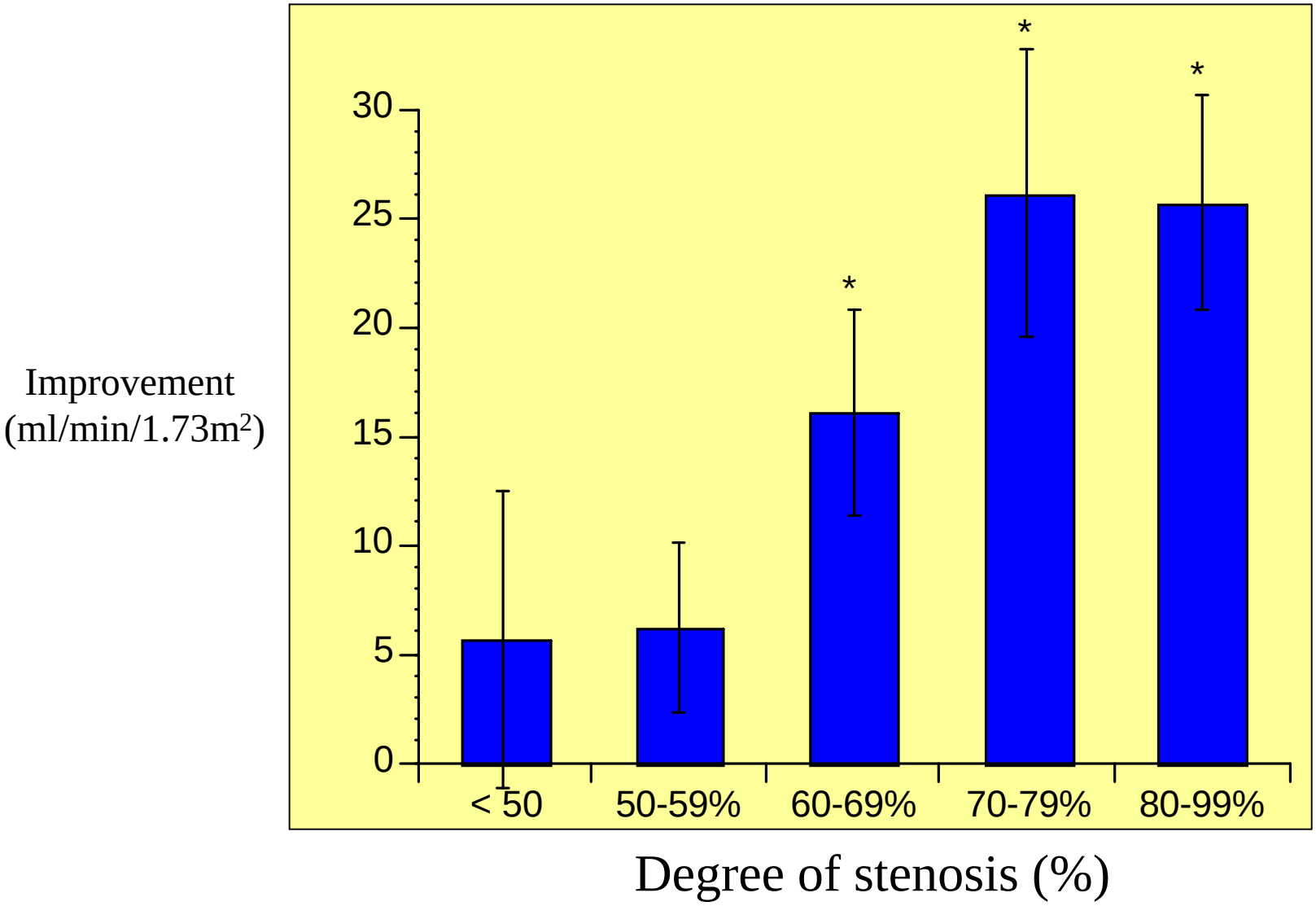
What degree of (Diameter)stenosis causes hypertension?

MAP Decrease (mmHg)



AHT drug Number decrease

What degree of stenosis causes renal impairement?



A-RAS: Therapeutic strategy

- Whom to treat?
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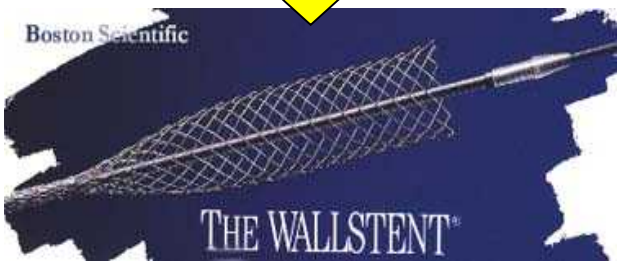
How to treat

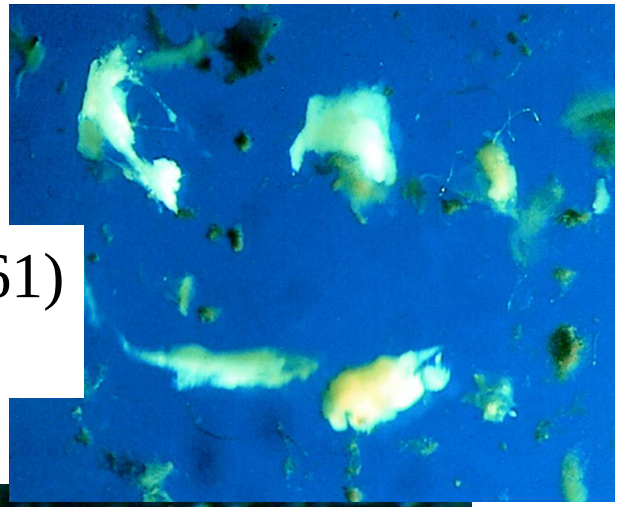
Chronic Kidney disease

Embolie

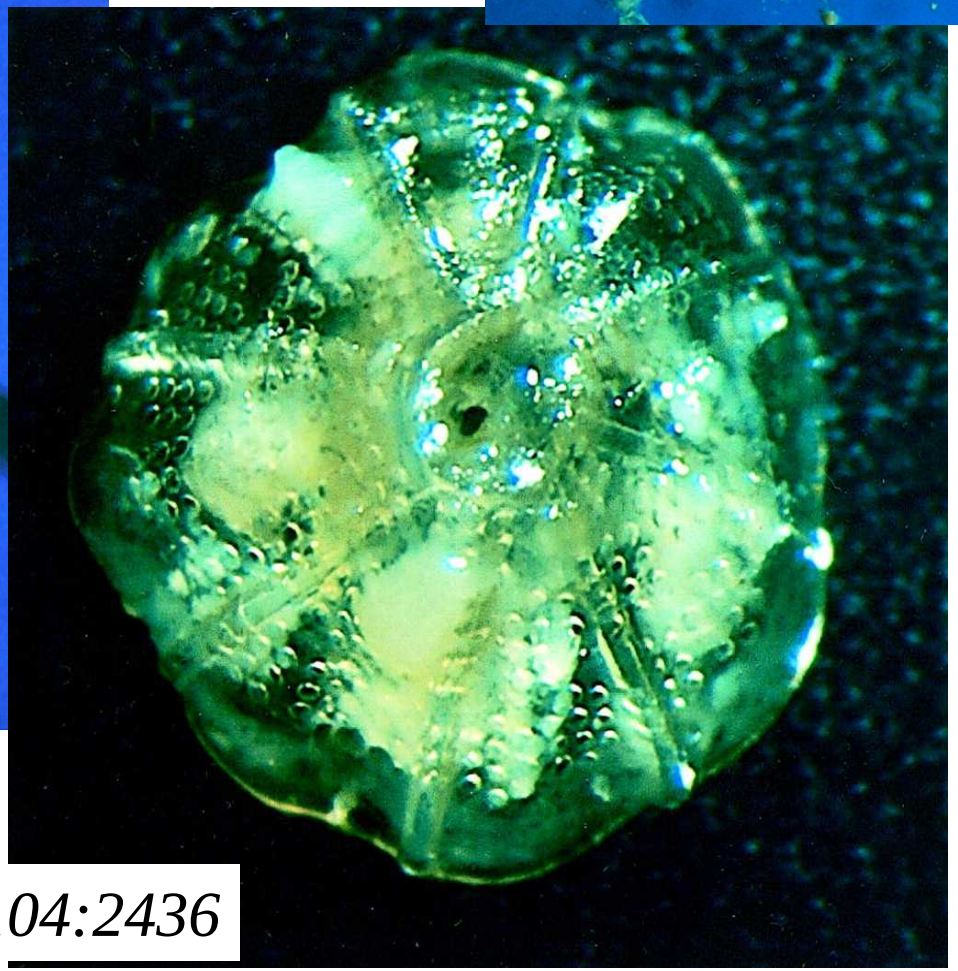
Radiocontrast-Toxicity



Coronary Angioplasty

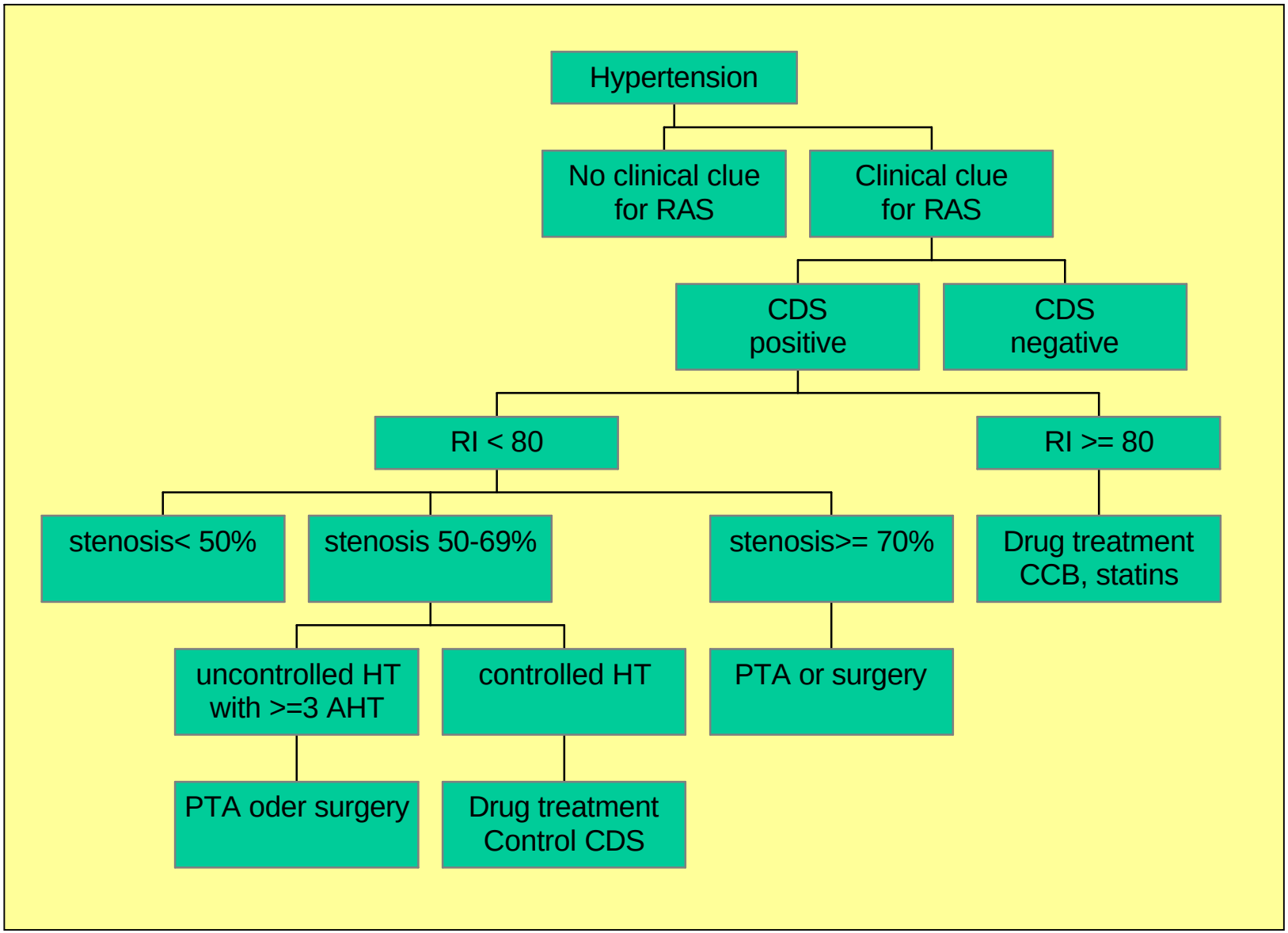


Particle: 100% (20-361)
Size: 0.015-20 mm^2



Grube et al. 2001 Circulation 104:2436

How to treat


Hypertension
No clinical clue for RAS
Clinical clue for RAS
CDS positive
CDS negative
RI < 80
RI >= 80
stenosis< 50%
stenosis 50-69%
stenosis>= 70%
Drug treatment CCB, statins
uncontrolled HT with >=3 AHT
controlled HT
PTA or surgery
PTA oder surgery
Drug treatment Control CDS

Thank you

- Collaborators
- Prof. K.M. Koch
- Prof. H. Haller
- Dr. M. Hiss
- Dr. S. Stuht
- PD. Dr Chavan

- PhD Students
- Dr. B. Stoess
- Dr. A. Vitzthum
- Dr. S. Ellis

Gibt es Möglichkeiten den RI zu senken?

Bislang keine Studien zu diesem Thema

Arterial stiffness

- Körperliches Training, Gewichtsverlust
- (Östrogene)
- (Vitamin E)
    - Chade Hypertension 2003 42:605-12 Vit C+E pigs: - Verbesserung
    - Skirme Jones J Am Coll Cardiol 2000 36:94-102 - no effect
    - Mottram Atherosclerosis 1999 145: 399-404
- AGE-Breakers
    - Kass et al. Circulation 2001 104: 1464-70
- Sildenafil
    - Jackson Am J Cardiol 1999 83: 13C-20C
- L-Arginin

Gibt es Möglichkeiten den RI zu senken? Arterial stiffness/distensibility

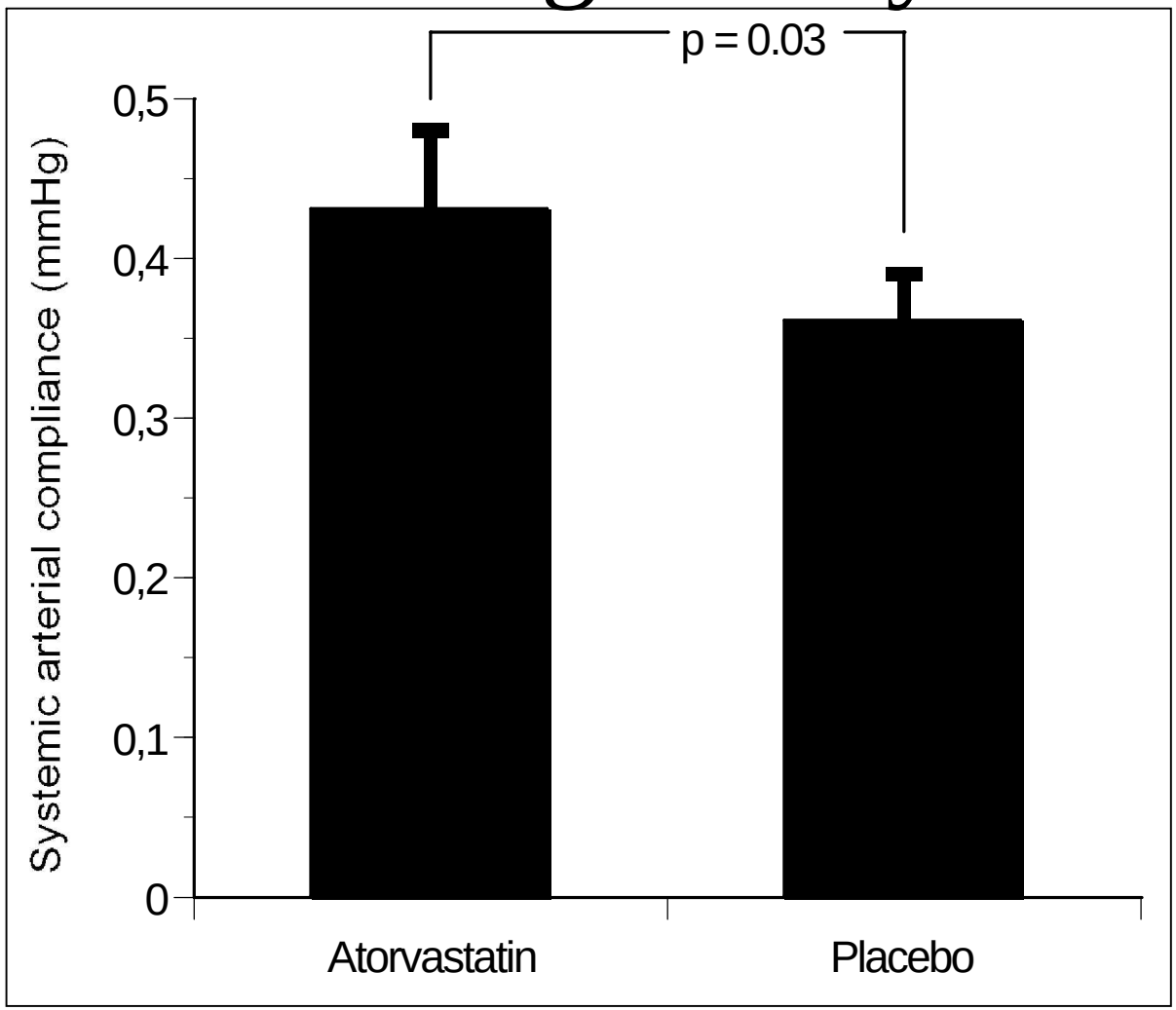
Antihypertensiva

- ACE-Hemmer / AT-1 Blocker /ß-Blocker/Diuretika/CA
  - Moexipril Soma J Cardiovasc Pharmacol 1999 33: 273-9
  - Losartan: Klemsdal Blood Pressure 1999 8: 214-9 - pos effect
  - Quinapril: J Hum Hypertens 1998 12: 18-7 - pos effect
  - Perindopril: Girerd J Am Coll Cardiol 1998 31:1964-73 - pos effect
  - HCT: „ „ „ „ - pos effect
  - Fosinopril>Propranolol: Ting Hypertension 1995 26:524-30 - pos effect
  - Amlodipin: Megnien B J Clin Pharm 1995 39: 641-9 - pos effect

Gibt es Möglichkeiten den RI zu senken? Arterial stiffness/distensibility/PWV

- Statine
  - Atorvastatin Ferrier J Am Coll Cardiol 2002 39:1020-25 - pos.effect
  - Simvastatin: Shige Atherosclerosis 2001 155: 245-50 - pos effect
  - Fluvastatin: Hausberg Kidney Int 2001 59: 1473-9 - no effect
  - Pravastatin: Kool Eur J Clin Pharm 1995 48: 217-23 - no effect

Effect of atorvastatin on large artery stiffness



- 22 Patienten
- Atorvastatin 80 mg für 3 Monate
- LDL – 48%
- Syst RR-6* mmHg

Ferrier et al J Am Coll Cardiol 2002 39: 1020-5

TABLE 5

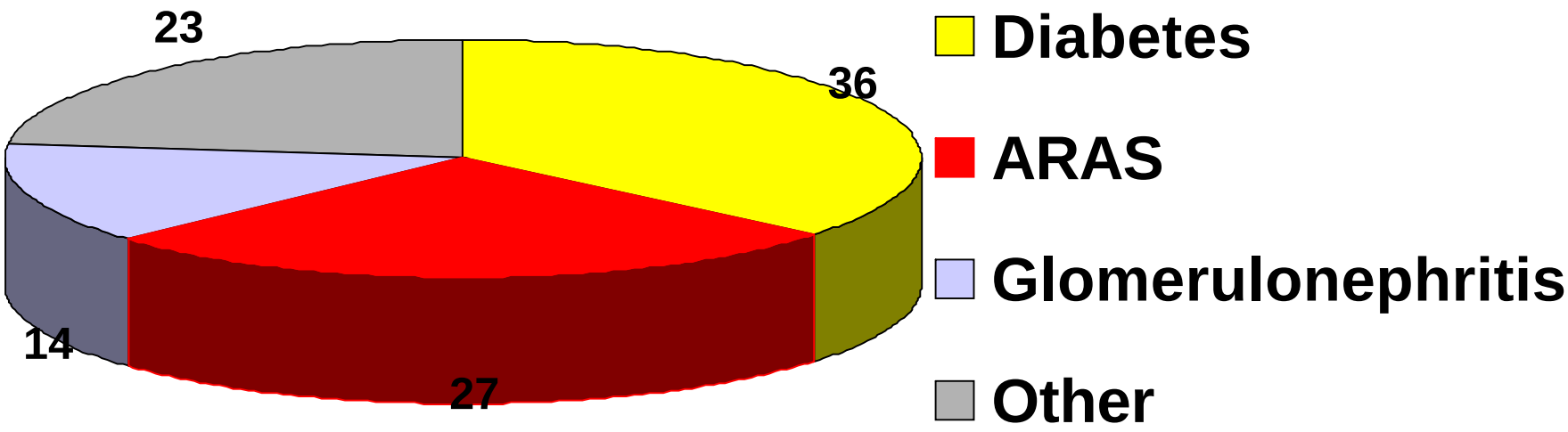
Clinical and Angiographic Follow-up in Patients Who Underwent Renal Artery Stent Placement

Study	No. Pts	Stent	Technical Success	Follow-up (months)	Hypertension		Renal Function		Restenosis	Complications
					Cure	Improved	Improved	Stable		
Wilms	11	Wallstent	83%	7	30%	40%	0%	0%	29%	3 (25%)
Kuhn	10	Strecker	80%	11	29%	43%	50%	NM	25%	4 (40%)
Ree	28	Palmaz	96%	7	11%	54%	36%	36%	39%	5 (18%)
Hennequin	21	Wallstent	100%	32	14%	86%	17%	50%	20%	4 (19%)
van de Ven	24	Palmaz	100%	6	68%	5%	36%	64%	13%	3 (11%)
Henry	59	Palmaz	100%	14	19%	57%	20%	NM	9%	2 (3%)
Iannone	63	Palmaz	99%	10	4%	35%	36%	45%	14%	11 (13%)
Blum	68	Palmaz	100%	27	16%	62%	NM	NM	11%	0 (0%)
Bosclair	33	Palmaz	100%	13	6%	61%	41%	35%	—	6 (17%)
Harden	32	Palmaz	100%	6	NM	NM	34%	34%	13%	1 (3%)
White	100	Palmaz	99%	6	NM	NM	20%	NM	19%	2 (2%)
Rundback	45	Palmaz	94%	17	NM	NM	NM	NM	25%	5 (9%)
Shannon	21	Palmaz	100%	9	NM	NM	43%	29%	0%	2 (9%)
Dorros	163	Palmaz	100%	48	3%	51%	NM	NM	—	23 (11%)
Total	678	...	98%*	16*	20%*	49%*	30%	38%	17%	11*

*Mean based on random-effects model

Reproduced with permission from Leertouwer TC, Gussenhoven EJ, Bosch JL, et al. Stent placement for renal arterial stenosis: where do we stand? A meta-analysis. Radiology 2000; 216:78–85 (57).

ESRD: Prävalenz der atherosklerotischen NAS (ARAS) bei Patienten >45 Jahre



Van Ampting 2003 NDT 18:1147-51

12-14%

Scoble et al. 1989 Clin Nephrol 31: 119-122

Mailloux et al. 1994 Am J Kid Dis 24:622-29

Überleben von Dialysepatienten in Abhängigkeit der Grunderkrankung

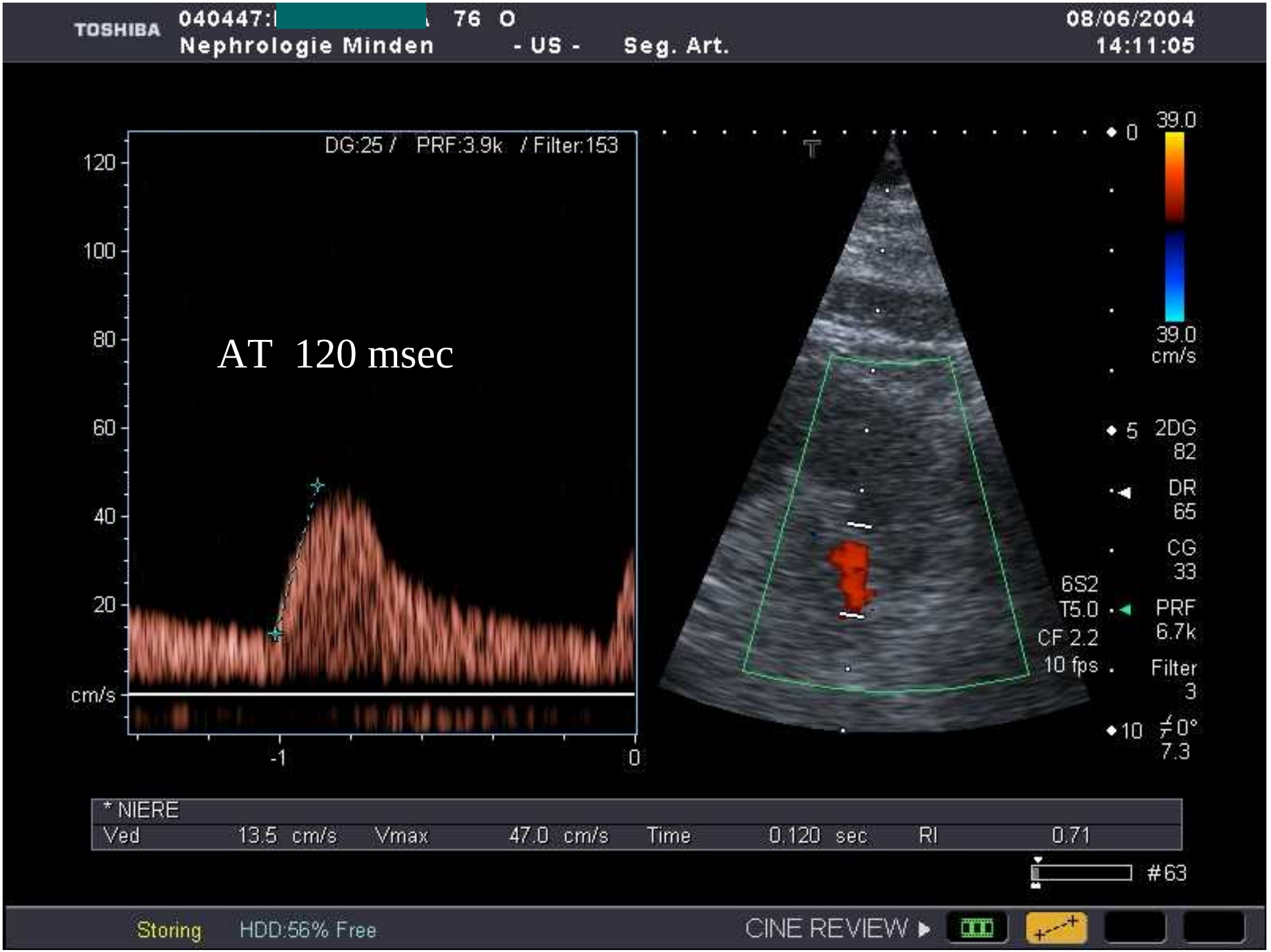
TABLE 2
Survival Estimates for Selected Renal Diagnoses on Dialysis

Diagnosis	Median Survival	Length of Survival			
		2 year	5 year	10 year	15 year
Polycystic kidney disease (n=56)	133 months	91%	77%	59%	32%
Malignant hypertension (n=23)	55 months	77%	25%	0	0
Renal vascular disease (n=83)	25 months	56%	18%	5%	0

Reproduced with permission from Mailloux LU, Napolitano B, Bellucci AG, et al. Renal vascular disease causing end-stage renal disease, incidence, clinical correlates, and outcomes: a 20-year clinical experience. Am J Kidney Dis 1994; 24:622–629 (28).

ANAS – wann behandeln?

- Patientenvorselektion
- Diagnose der renovaskulären Hypertonie / Azotämie
- Welcher Stenosegrad ist hämodynamisch relevant?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040447:
76 O
08/06/2004
Nephrologie Minden
- US -
Seg. Art.
14:11:05
DG:25 / PRF:3.9k / Filter:153
120
100
80
60
40
20
cm/s
-1
0
AT 120 msec
39.0
39.0
cm/s
2DG
82
DR
65
CG
33
PRF
6.7k
Filter
3
6S2
T5.0
CF 2.2
10 fps
0°
7.3
* NIERE
Ved 13.5 cm/s
Vmax 47.0 cm/s
Time 0.120 sec
RI 0.71
#63
Storing
HDD:56% Free
CINE REVIEW

Stenosekriterien sowie Sensitivität- und Spezifitätsangaben zur dopplersonographischen Detektion von Nierenarterienstenosen in angiographisch kontrollierten Studien

	Patienten-zahl	Stenose-kriterien	Technischer Fehler (%)	Detektierter Stenosegrad (%)	Sensitivität / Spezifität (%)
Indirekte Stenosekriterien (Paravus -Tardus)					
Stavros 1992 [51]	56	Verlust des ESP	0	≥ 60	95 / 97
Kliewer 1993 [21]	57	AT ≥ 70 ms	0	≥ 50	82 / 20
Schwerk 1994 [46]	72	Delta RI ≥ 5 %	0	≥ 50	82 / 92
			0	≥ 60	100 / 94
Speckamp 1995 [50]	123	Delta AI ≥ 80%	n.v.	≥ 70	100 / 94
Strunk 1995 [53]	50	AT ≥ 70 ms	4	≥ 50	77 / 46
Baxter 1996 [3]	73	AT > 70 ms	16	≥ 70	89 / 97
Riehl 1997 [41]	214	RI < 0.45 oder Delta RI ≥ 8 %	0	≥ 70	93 / 96
Ripolles 2001 [42]	65	AT ≥ 80 ms	0	≥ 75	89 / 99
Mittelwert	**710**		**2**		**92 / 86**

Zusammenfassung

- ANAS – wann behandeln
  - **RI unter 80**
  - **Stenosegrad über 60-70 %**
  - Therapieresistente Hypertonie (inkl. ACEI)
  - Akute Herzinsuffizienz, insbes plötzliches Lungenödem
  - Rasch verschlechternde Nierenfunktion oder Verschlechterung unter ACE Hemmer
  - Proteinurie < 1g/Tag, Kreatinin < 2 mg/dl
  - Begleittherapie immer: AHT, Plättchenaggregationshemmer und Lipidsenker

Plouin 2003 Int Angiol 22: 333-9
Safian 2003 Curr Treat Options Cardiovasc Med 5:91-101

Guidelines for the Reporting of Renal Artery Revascularization in Clinical Trials

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Although the treatment of atherosclerotic renal artery stenosis with use of percutaneous angioplasty, stent placement, and surgical revascularization has gained widespread use, there exist few prospective randomized controlled trials (RCTs) comparing these techniques to each other or against the standard of medical management alone. To facilitate this process as well as help answer many important questions regarding the appropriate application of renal revascularization, well-designed and rigorously conducted trials are needed. These trials must have clearly defined goals and must be sufficiently sized and performed so as to withstand intensive outcomes assessment. Toward this end, this document provides guidelines and definitions for the design, conduct, evaluation, and reporting of renal artery revascularization RCTs. In addition, areas of critically necessary renal artery revascularization investigation are identified. It is hoped that this information will be valuable to the investigator wishing to conduct research in this important area.

J Vasc Interv Radiol 2003; 14:S477–S492

Abbreviations: GFR = glomerular filtration rate, PTRA = percutaneous transluminal renal angioplasty, RAS = renal artery stenosis, RCT = randomized controlled trial

J. Vasc Intervent Radiol 2001 14:S477-492

Protektionssysteme bei ARAS

- Retrospektive Studie
- 37 Patienten mit renovaskuklärer Azotämie
- Angioguard guide wire system; Cordis
- 95% Nierenfunktion stabil oder gebessert, 5% unveränderte Verschlechterung der Funktion nach 12,5 Monaten (2-28)
- Embolisches Material in 65% der Körbchen

Holden & Hill 2003
J Vasc Surg 38:962-8

- Retrospektive Studie
- 56 Patienten
- Guard wire occlusion Ballon (38) oder EPI Filter (26) oder Angiogard (1)
- 8 Patienten verbessert und 45 stabil nach 23 (1-47) Monaten
- Embolisches Material bei 80% adsserviert

Henry et al. 2003
Catheter Cardiovasc Intervent
60: 299-312


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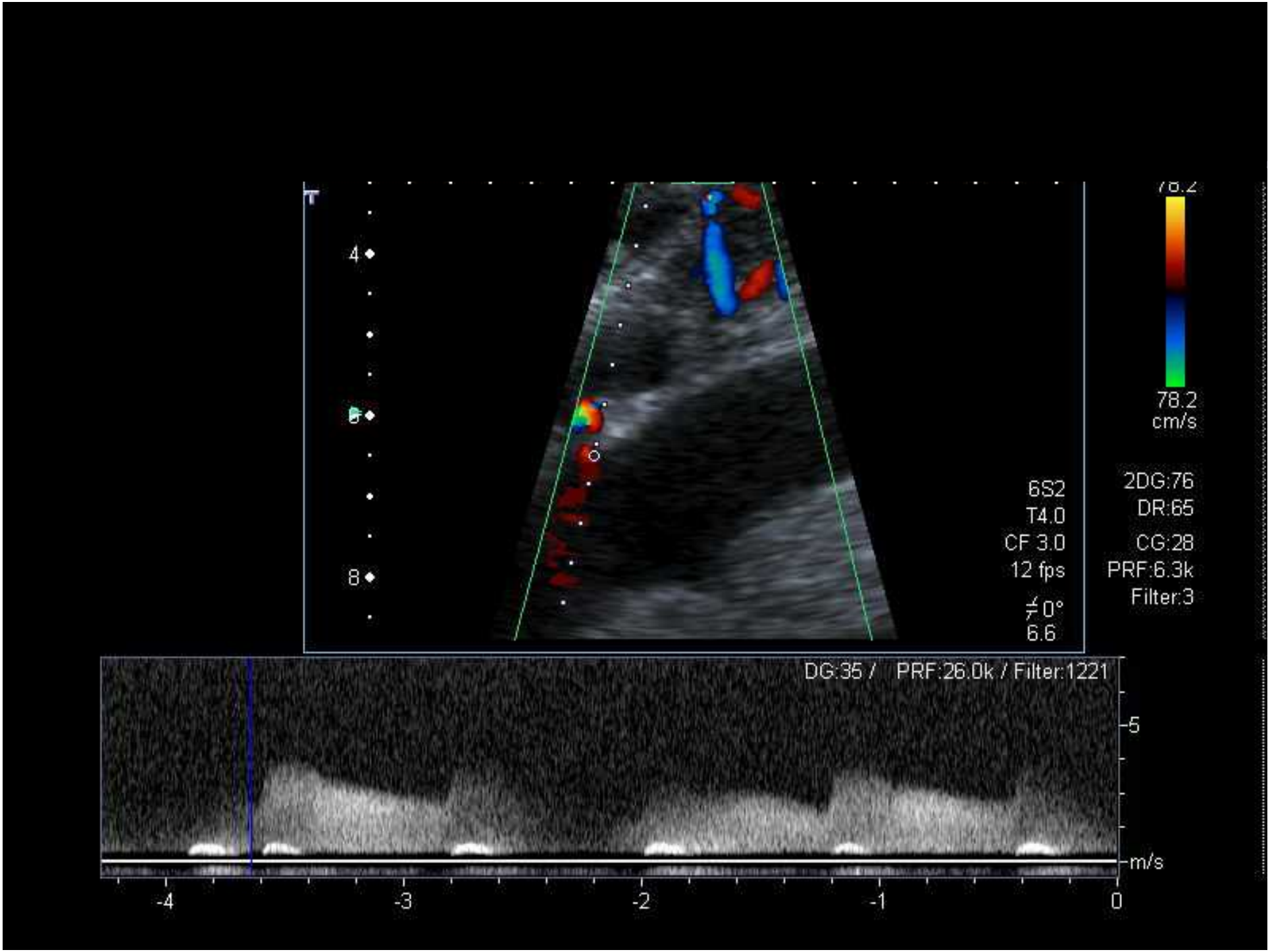
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78.2
cm/s
4
8
6S2
T4.0
CF 3.0
12 fps
0°
6.6
2DG:76
DR:65
CG:28
PRF:6.3k
Filter:3
DG:35 / PRF:26.0k / Filter:1221
-5
m/s
-4
-3
-2
-1
0