



## Verkalkungen bei Niereninsuffizienz: Nierenarterienstenting

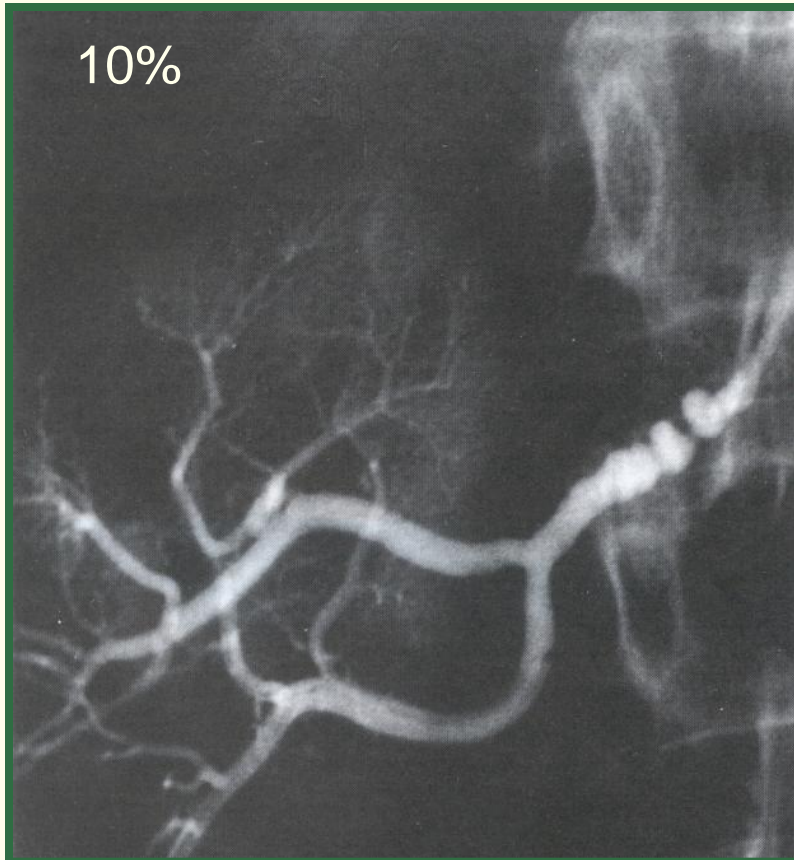
Prof. Dr. J. Radermacher Minden

23. Berliner DialyseSeminar  
Berlin, 04.12.2010



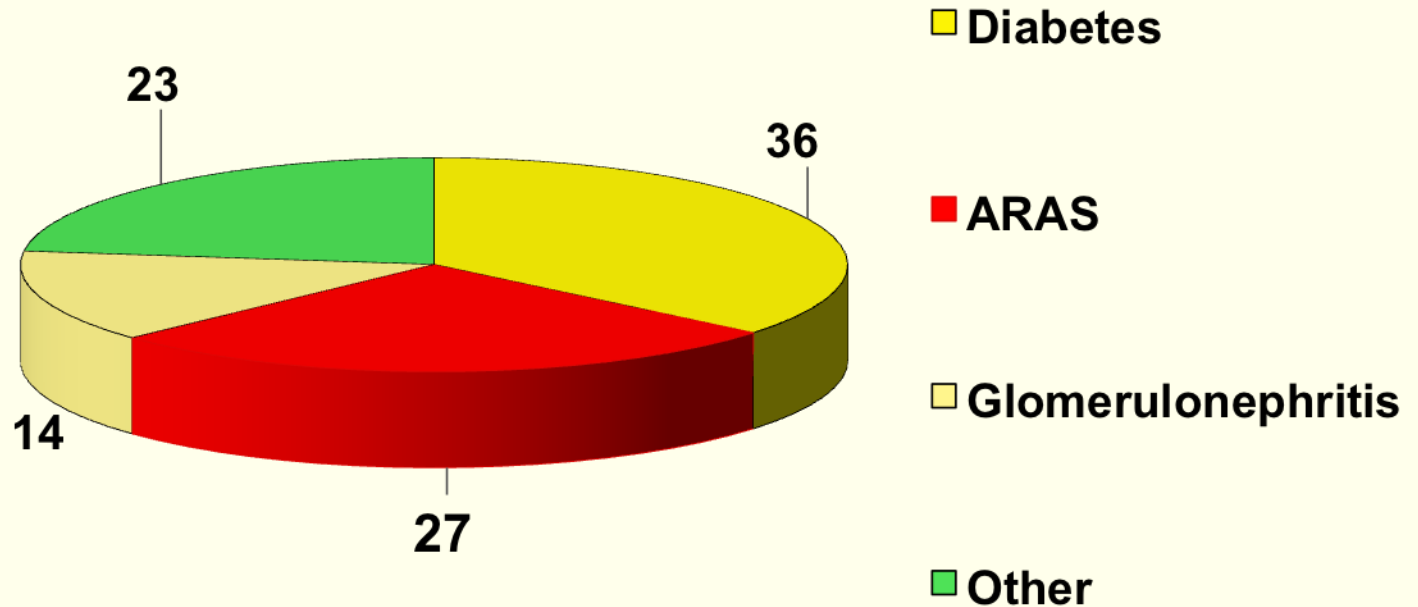
JWK  
Minden

# Nierenarterienstenose: FMD vs. Atherosklerose



# Diagnostik der Nierenarterienstenose

TNI: Prävalenz der atherosklerotischen NAS (ARAS)  
bei Dialysepatienten > 45 Jahre



*Van Ampting 2003 NDT 18:1147-51*

# NAS: Randomisierte kontrollierte Studien

## R-PTA und randomisierte kontrollierte Studien: Vergleich RPTA mit medikamentöser Therapie

DRASTIC: van Jaarsveld NEJM 2000 342: 1007-14

- 106 patients, **no significant effect**

EMMA: Plouin Hypertension 1998 31: 823-9

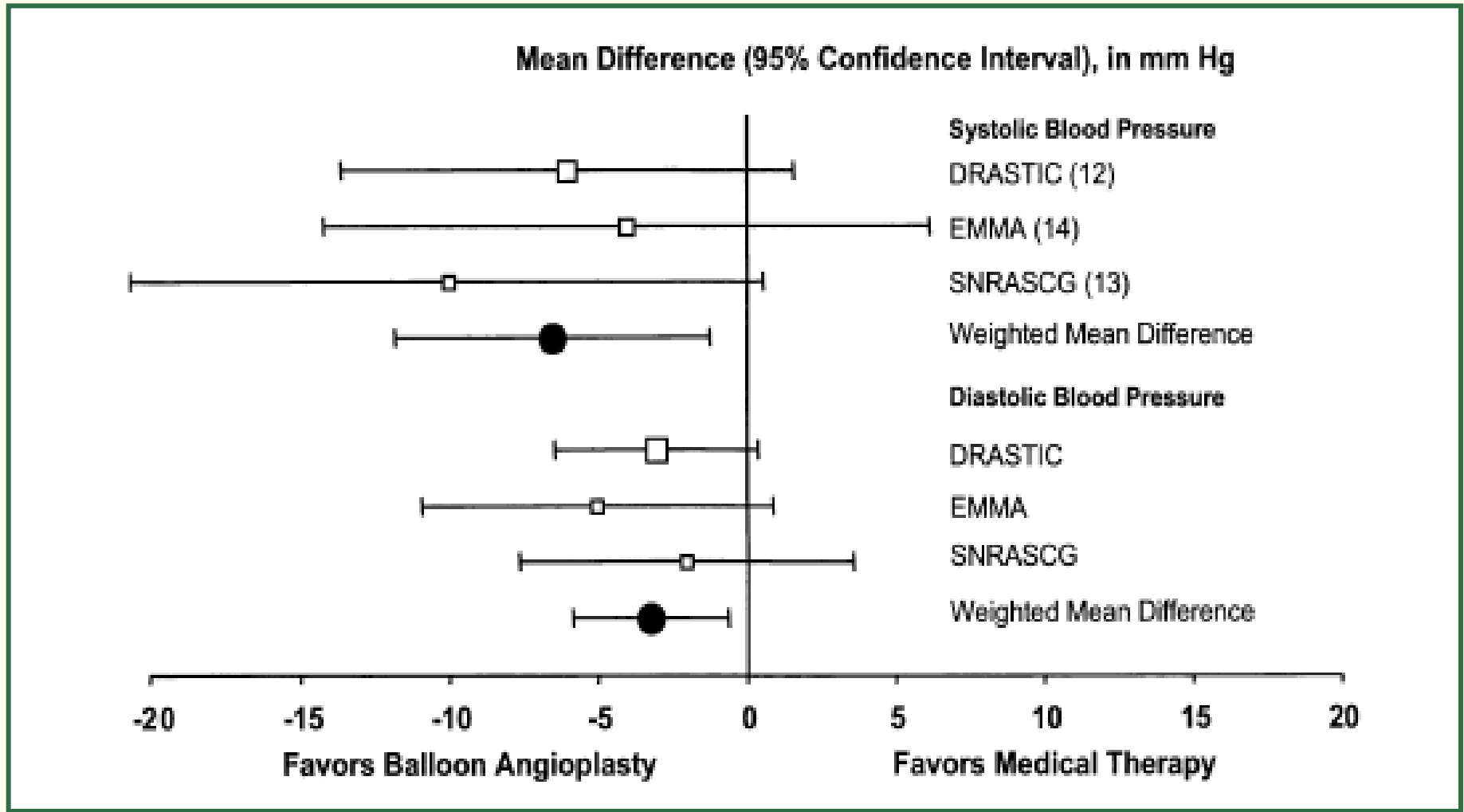
- 49 patients, **no significant effect**

Webster et al. J Hum Hypertens. 1998 12: 329-35

- 55 patients, **no significant effect**



# Metaanalyse der antihypertensiven Wirkungen von Angioplastie und medikamentöser Therapie bei arteriosklerotischer Nierenarterienstenose



# RAS: Randomised controlled trials

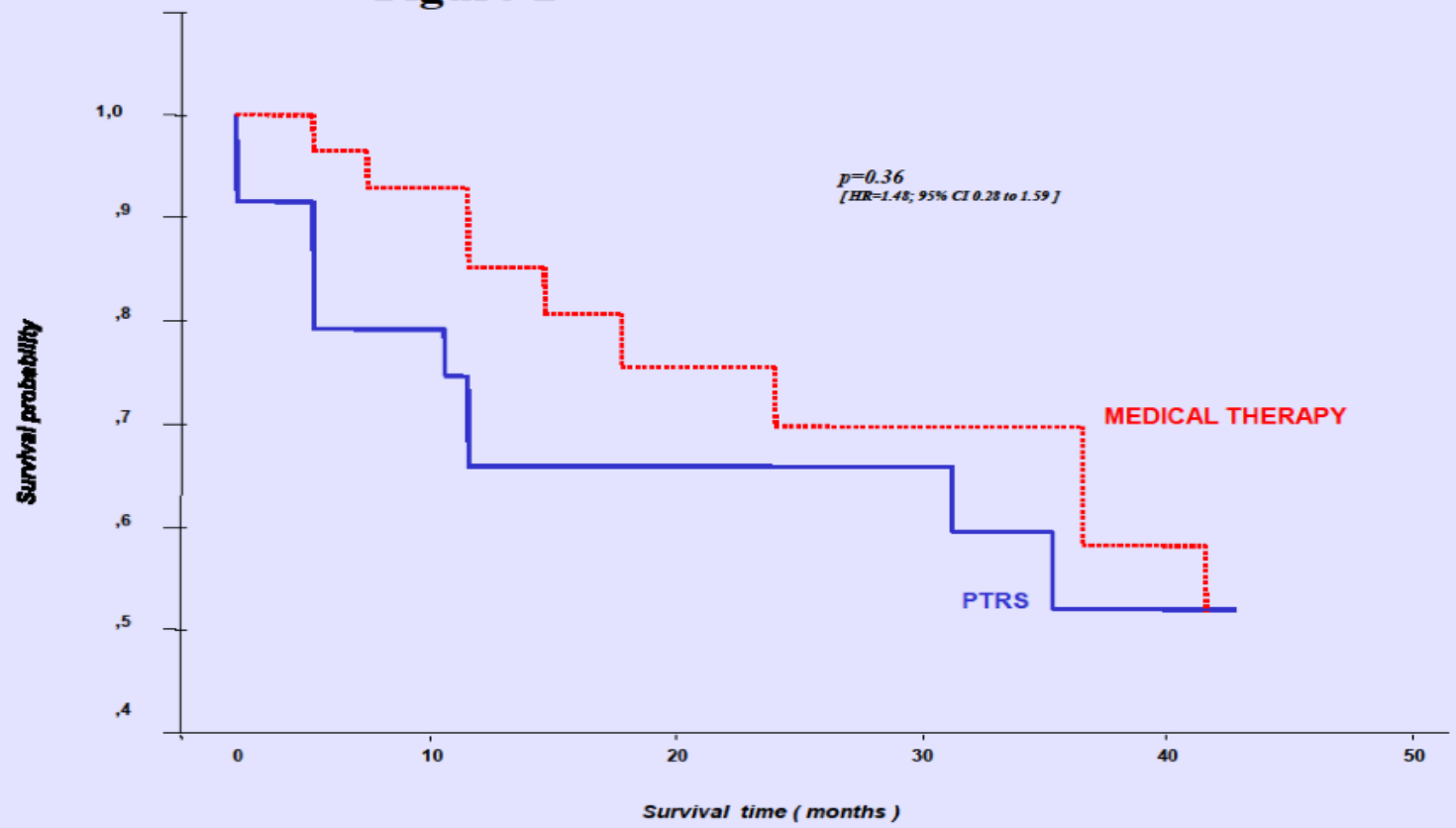
## Weitere Studien

- NITER trial (Italy):
  - **100** patients with clearance  $>30$  ml/min and RAS  $> 70\%$
  - Randomized to medical Tx (AHT, Statin, ASS) or medical treatment plus PTA
  - Outcome: Death, HD, GFR drop 20% within 2-4 years
- Star trial (Netherlands):
  - **140** patients with clearance  $< 80$  ml/min and RAS  $> 50\%$
  - Randomized to medical treatment (statin+AHT+ASA) or MT plus PTA
  - Outcome: Fall in clearance  $>20\%$  in 2-5 years
- Astral Trial (UK)
  - $> 200$  patients where their doctor is uncertain whether they are going to benefit from PTA randomized to PTA or drug treatment



- NITER trial (Italy):
  - 100 patients with clearance >30 ml/min and RAS > 70%
  - Randomized to medical Tx (AHT, Statin, ASS) or medical treatment plus PTA
  - Outcome: Death, HD, GFR drop 20% within 2-4 years
  - As of Dec. 9th 2009: Started in 2003, enrolled 80, still no final results
  - Abstract WCN Mailand 2009

**Figure 1**



<i>N of patients</i>					
PTRS	24	18	12	10	6
Medical therapy	28	24	14	12	9

# NAS: Prognose

## Weitere Studien

- NITER trial (Italy):
  - **100** patients with clearance  $>30$  ml/min and RAS  $> 70\%$
  - Randomized to medical Tx (AHT, Statin, ASS) or medical treatment plus PTA
  - Outcome: Death, HD, GFR drop 20% within 2-4 years
- Star trial (Netherlands):
  - **140** patients with clearance  $< 80$  ml/min and RAS  $> 50\%$
  - Randomized to medical treatment (MT=statin+AHT+ASA) or MT plus PTA
  - Outcome: Fall in clearance  $>20\%$  in 2-5 years
- Astral Trial (UK)
  - $> 200$  patients where their doctor is uncertain whether they are going to benefit from PTA randomized to PTA or drug treatment





# NAS: Prognose

## Weitere Studien

- NITER trial (Italy):
  - **100** patients with clearance  $>30$  ml/min and RAS  $> 70\%$
  - Randomized to medical Tx (AHT, Statin, ASS) or medical treatment plus PTA
  - Outcome: Death, HD, GFR drop 20% within 2-4 years

- Star trial (Netherlands):

- **140** patients with clearance  $< 80$  ml/min and RAS  $> 50\%$
- Randomized to medical treatment (sMT=statin+AHT+ASA) or MT plus PTA
- Outcome: Fall in clearance  $>20\%$  in 2-5 years

Annals Int Med 2009 150:840-48

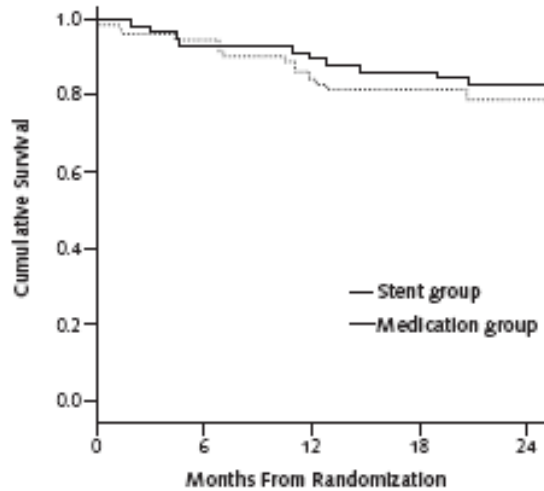
- Nur Interventionalisten mit  $> 10$  Jahren Berufserfahrung
- Screening mit MRT und CT: n=64 mit Stenose  $> 50\%$  aber nach DSA 12 Patienten mit Stenose  $< 50\%$  (20% falsch positiv)
- **Einschlußkriterium: Eingeschränkte Nierenfunktion bei gut eingestelltem Blutdruck – wenn möglich ohne ACEI**



JWK

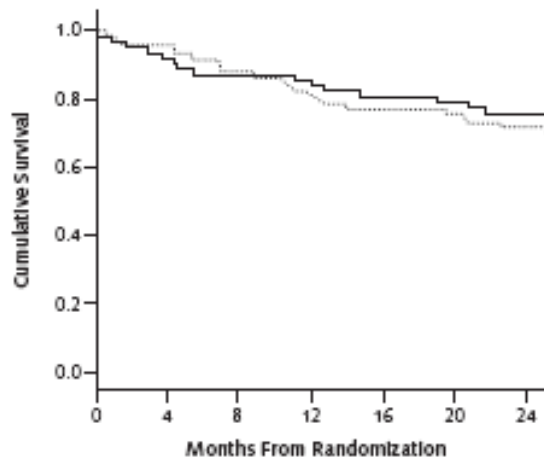
Minden

Figure 2. Survival curves for the primary end point (top) and the primary end point plus death (bottom) during 2 years of follow-up.



Patients remaining, *n*

Medication group	76	68	60	57	53
Stent group	64	54	52	50	46



Patients remaining, *n*

Medication group	76	68	60	57	53
Stent group	64	54	52	50	46

- 140 patients, **no significant effect on renal function at 1 year**
- 3 Todesfälle und 1 TNI durch Angioplastie
- No difference
  - ITT analysis (64 Stent+BMT vs 76 BMT) vs.
  - Per protocol (50 Stent+BMT vs. 90 BMT) HR 0.9 (0.4-2.0)

*Annals Int Med 2009 150:840-48*



JWK  
Minden

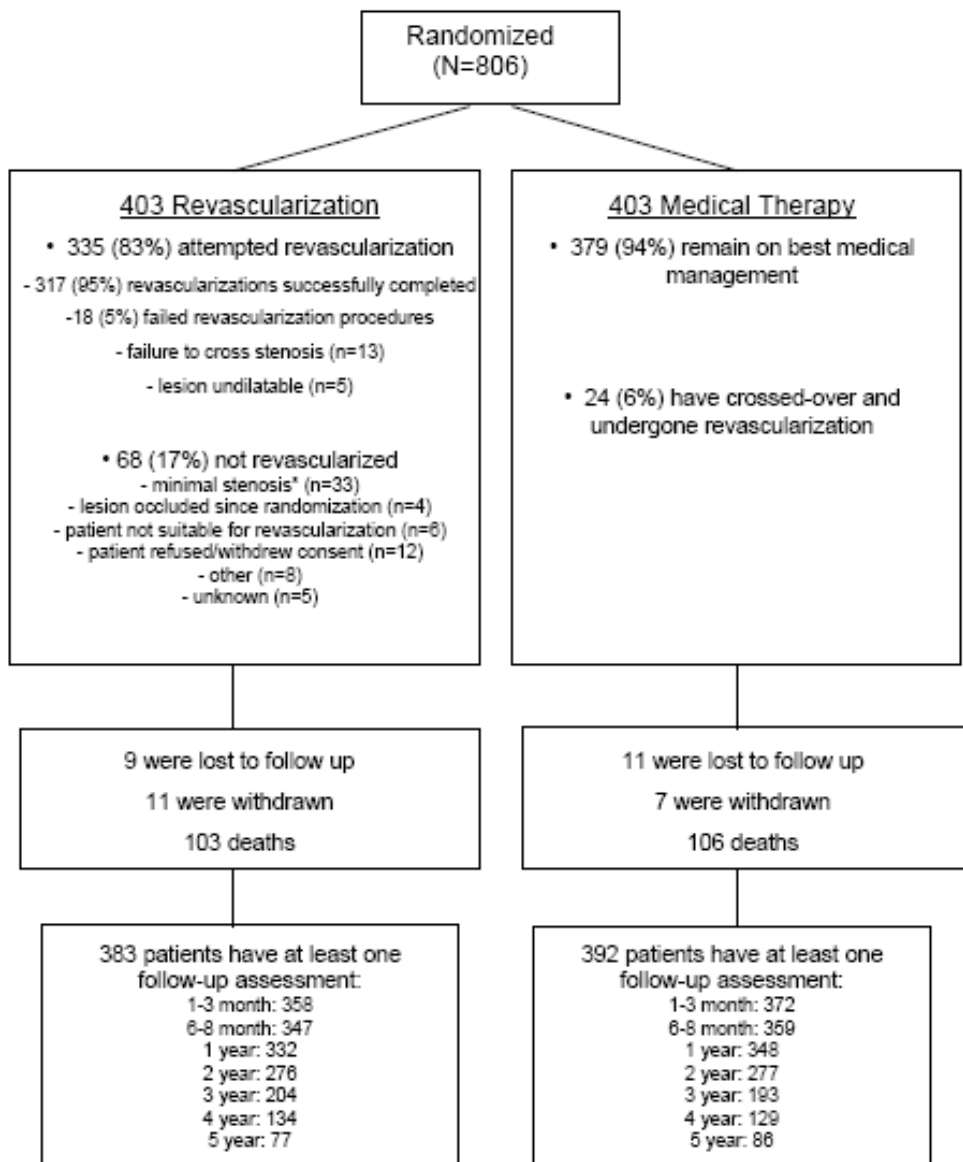
# NAS: Prognose

## Weitere Studien

- NITER trial (Italy):
  - **100** patients with clearance  $>30$  ml/min and RAS  $> 70\%$
  - Randomized to medical Tx (AHT, Statin, ASS) or medical treatment plus PTA
  - Outcome: Death, HD, GFR drop 20% within 2-4 years
- Star trial (Netherlands):
  - **140** patients with clearance  $< 80$  ml/min and RAS  $> 50\%$
  - Randomized to medical treatment (sMT=statin+AHT+ASA) or MT plus PTA
  - Outcome: Fall in clearance  $>20\%$  in 2-5 years
- Astral Trial (UK)
  - $> 200$  patients where their doctor is uncertain whether they are going to benefit from PTA randomized to PTA or drug treatment



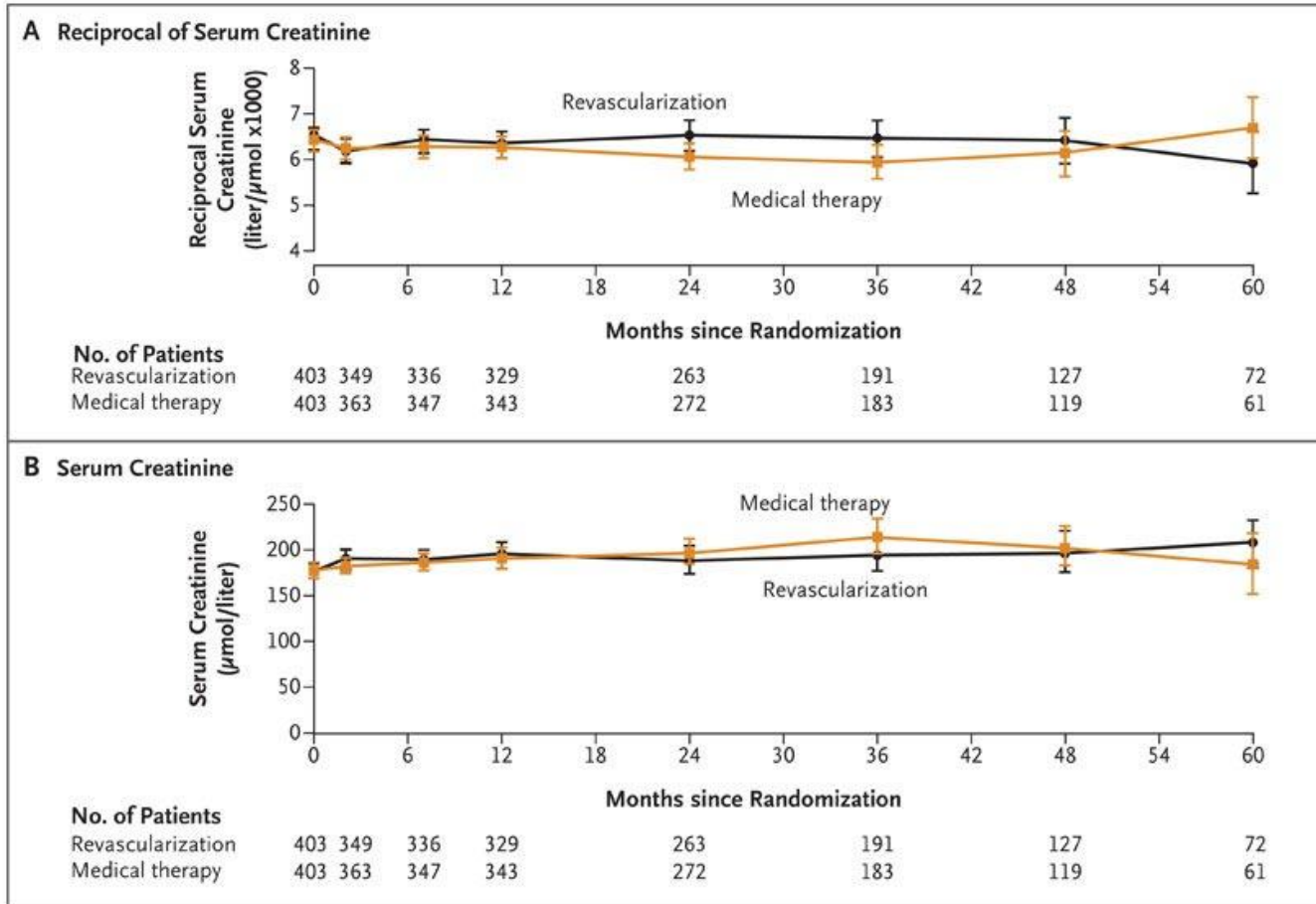
## Supplementary Appendix Figure 1: CONSORT Diagram for ASTRAL – Patient Recruitment and Follow-up



\* These patients were identified as having minimal stenosis post-randomization, as patients entered into ASTRAL based on computed tomographic (CTA) or magnetic resonance angiography (MRA) (which can over-estimate renal artery stenosis), who were randomized to revascularization, were required to have 'on the table' intraarterial angiography to check the accuracy of the CTA and MRA estimates of the renal artery stenosis.

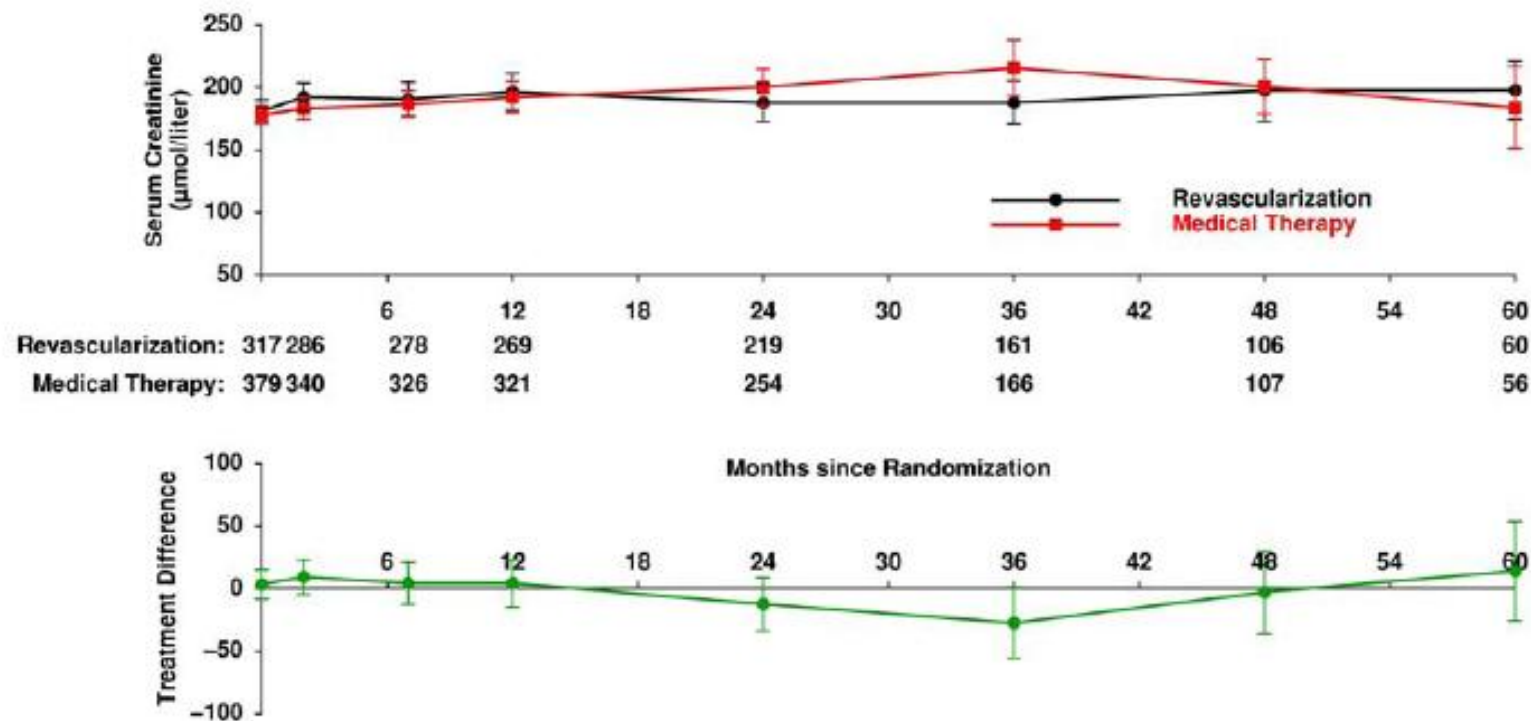


# Renal Function in Patients with Renal-Artery Stenosis Treated with Revascularization or Medical Therapy Alone



The ASTRAL Investigators. N Engl J Med 2009;361:1953-1962

## Supplementary Appendix Figure 3: Per-Protocol Analysis of Serum Creatinine ( $\mu\text{mol/liter}$ )

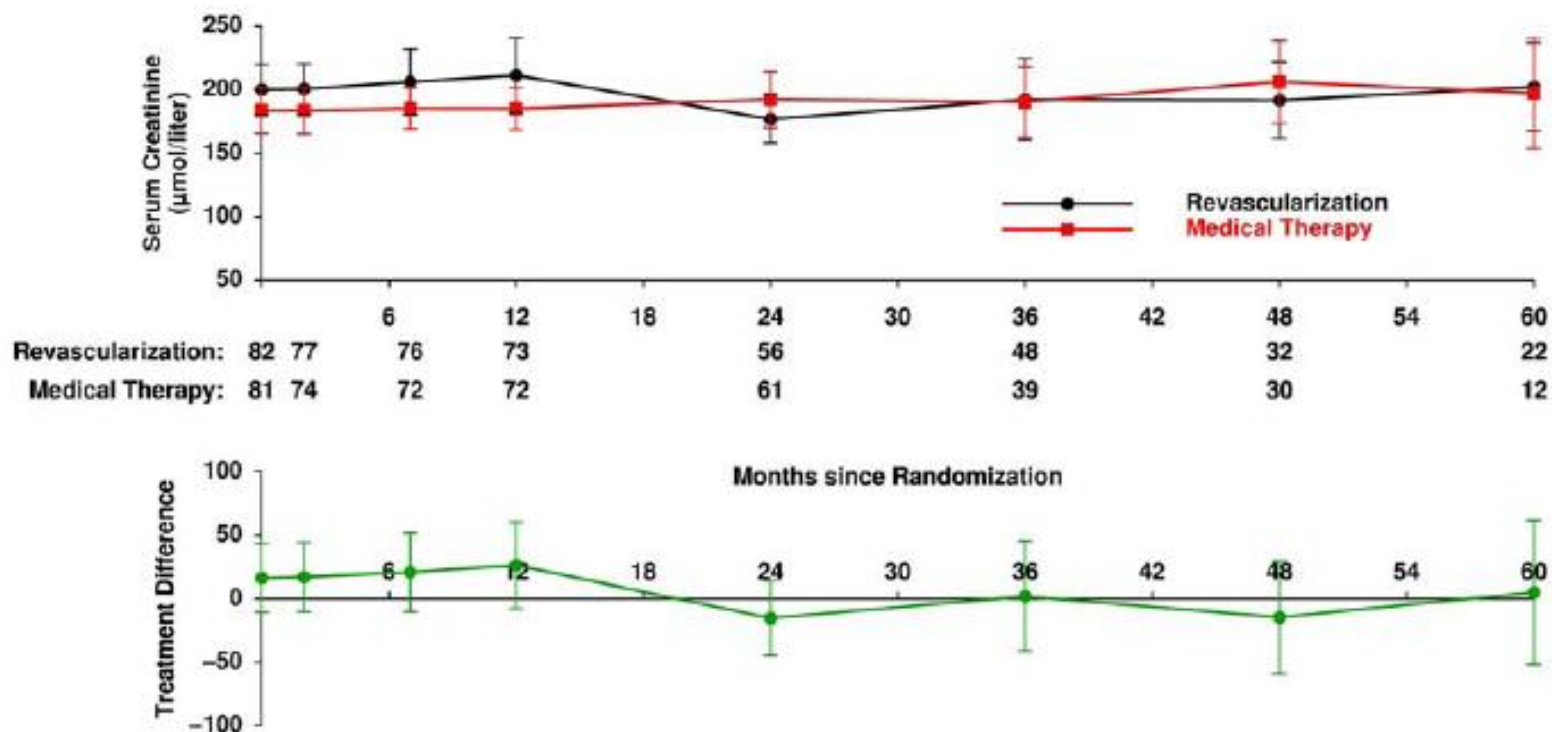


Footnote:

Per-protocol analysis based on the 317 patients' allocated revascularization which was successfully completed versus the 379 patients who remained on medical management.

A negative treatment difference is in favor of revascularization.

## Supplementary Appendix Figure 4a: Serum Creatinine ( $\mu\text{mol/liter}$ ) in the 163 Patients with Very Severe Anatomical Disease

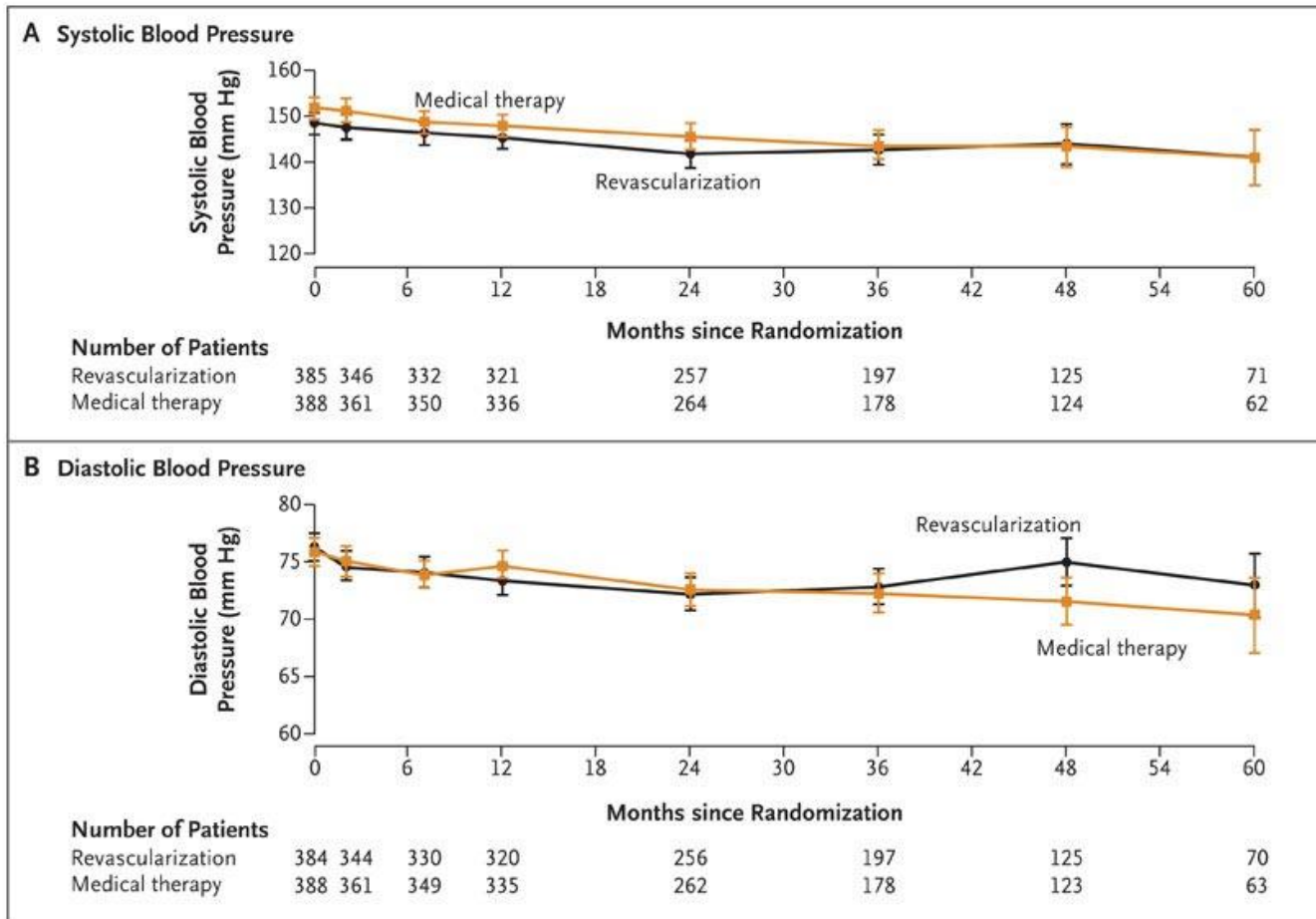


Footnote:

Severe anatomical disease defined as those patients with bilateral renal-artery stenosis  $>70\%$  ( $n=103$ ) or renal-artery stenosis  $>70\%$  in a solitary functioning kidney ( $n=60$ ).

A negative treatment difference is in favor of revascularization.

# Systolic and Diastolic Blood Pressure



The ASTRAL Investigators. N Engl J Med 2009;361:1953-1962



## Supplementary Appendix Table 1: Medication at 1 Year Follow-up Assessment

	Revascularization (N=332)	Medical Therapy (N=348)	P value
Antihypertensive drug – no./total no. (%)			
Any	321/330 (97%)	343/345 (99%)	0.03
Diuretic	206/321 (64%)	238/343 (69%)	0.15
Calcium-channel blocker	202/321 (63%)	242/343 (71%)	0.04
Beta-blocker	148/321 (46%)	189/343 (55%)	0.02
ACE inhibitor or ARB	161/321 (50%)	146/343 (43%)	0.05
Alpha blocker	124/321 (39%)	130/343 (38%)	0.85
No. of antihypertensive drugs in class – mean (range)	2.77 (1 - 6)	2.97 (1 - 6)	0.03
Antiplatelet drug – no./total no. (%)			
Any	270/327 (83%)	268/342 (78%)	0.17
Aspirin	239/270 (89%)	245/268 (91%)	0.26
Cholesterol-lowering drug – no./total no. (%)			
Any	281/328 (86%)	299/343 (87%)	0.57
Statin	273/281 (97%)	286/299 (96%)	0.33
Warfarin – no./total no. (%)	30/324 (9%)	36/327 (11%)	0.46

\* ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.



JWK  
Minden

### Supplementary Appendix Table 3: Overall Incidence of Renal and Cardiovascular Events and Mortality

	Revascularization	Medical Therapy	P value
<b>Renal Events</b>	<b>(N=383)</b>	<b>(N=392)</b>	
Acute kidney injury	25 (7%)	23 (6%)	0.70
Dialysis	36 (9%)	40 (10%)	0.71
<i>For end-stage renal disease</i>	30	31	
<i>For acute kidney injury</i>	6	9	
Transplantation	0 (-)	0 (-)	-
Nephrectomy	2 (0.5%)	1* (0.3%)	0.62
Renal arterial occlusion	5 <sup>Ω</sup> (1%)	4 <sup>Ω</sup> (1%)	0.75
Death due to renal failure	10 (3%)	17 (4%)	0.19
Number of renal events / Number of patients†	73 / 57 (15%)	80 / 58 (15%)	0.97
<b>Deaths<sup>£</sup></b>	<b>(N=403)</b>	<b>(N=403)</b>	
Cardiovascular	42 (10%)	45 (11%)	0.73
Renal	10 (2%)	17 (4%)	0.17

## 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].



- 65% der Zentren schlossen nur 1 Patienten/Jahr ein
- Nur Einschluß von Patienten bei welchen der Behandler bezüglich des Behandlungserfolgs unsicher war
  - Keine Info zu diesen Patienten



# NAS aus nephrologischer Sicht: Zusammenfassung

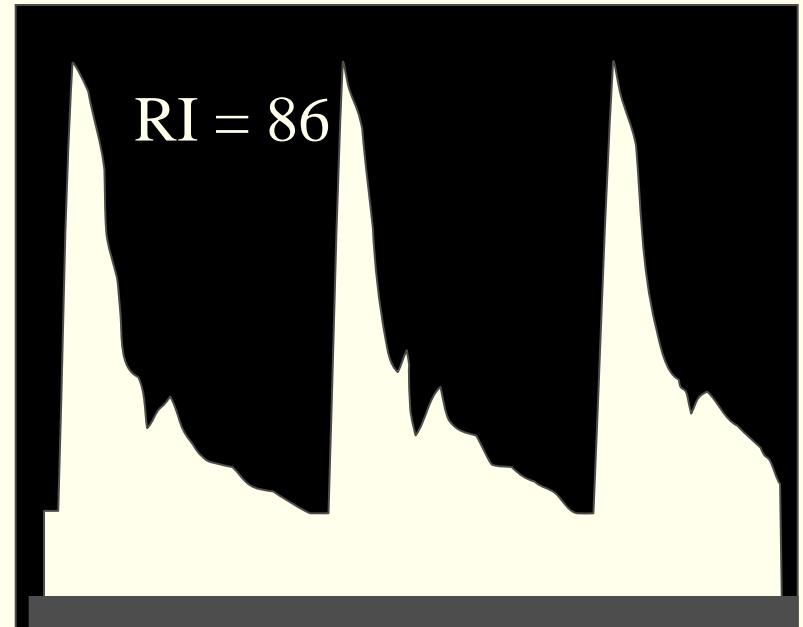
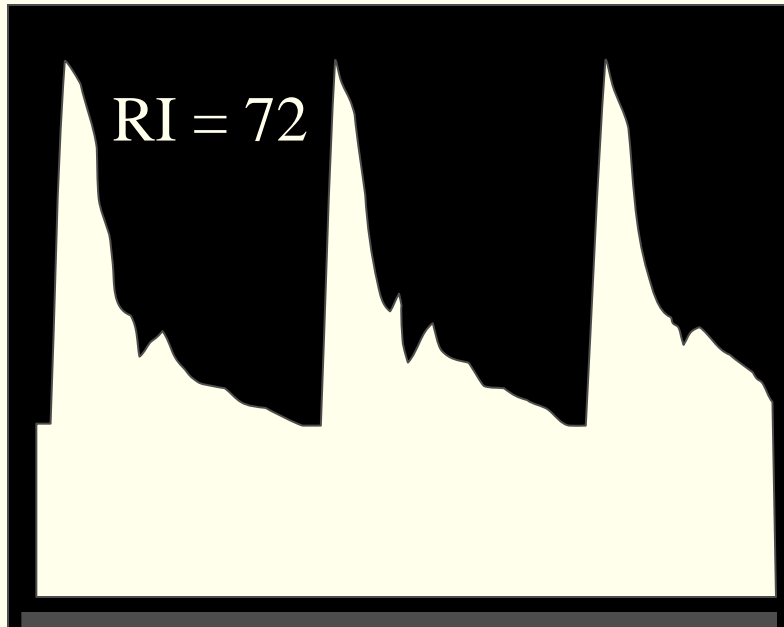
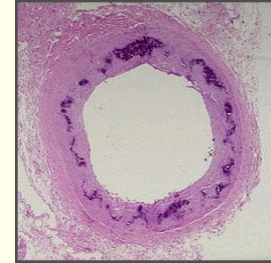
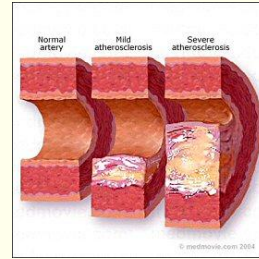
- FMD → Behandeln
- ANAS
  - Jeden Patienten in randomisierte Studien einschliessen
  - Es gibt keine ranomisierte Studie die eine Überlegenheit der PTA gegenüber der medikamentösen Therapie zeigt
    - Bezüglich Nierenfunktionsverbesserung
    - Bezüglich Blutdruckverbesserung
  - ASS + Statin + AHT incl. ACEI



# Methods to search for RVHT and RVA

Measuring the renal resistance index (RRI)

- Kidney: segmental arteries
- $RI = (1 - (V_{min} / V_{max})) * 100$



# Methods to search for RVHT and RVA

## FKDS : RRI

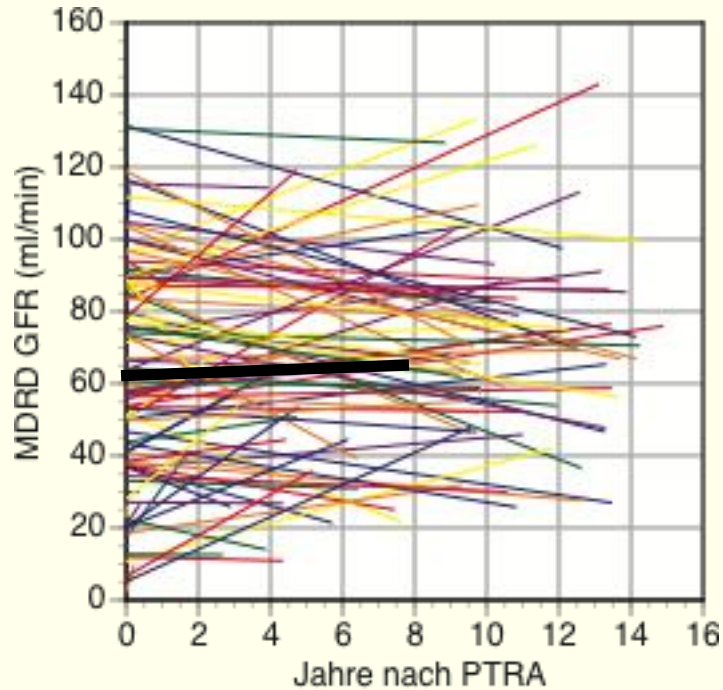
	Patient-number	Comment /n Parameter	RVHT Sensitivity / Specificity (%)	RVA Sensitivity / Specificity (%)
<b>Color coded Duplex Ultrasonography</b>				
Radermacher 2001 <sup>[38]</sup>	131	All patients RI < 0.80	99 / 85	96 / 53
Radermacher 2001 <sup>[38]</sup>	78	Impaired renal function RI < 0.80	98 /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

*Radermacher et al. 2001 NEJM 344: 410-417*

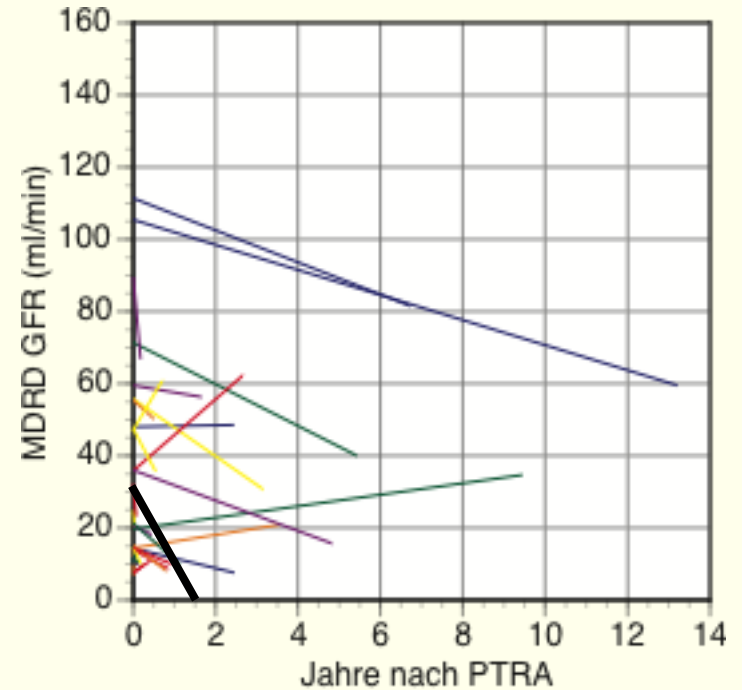


# 10 Jahres Daten

**RI < 0.80**



**RI ≥ 0.80**



# Laufende Studien zum Vergleich von Angioplastie und Antihypertensiva bei arteriosklerotischer Nierenarterienstenose

- Cooper CJ et al. Stent revascularisation for the prevention of cardiovascular and renal events among patients with renal artery stenosis and systolic hypertension: rationale and design of the CORAL trial. American Heart Journal 2006; 152: 59-66.
  - NIH/USA)
  - **1080** patients planned – 1/10 950 enrollment closed
  - Randomized to optimal medical treatment or optimal medical treatment plus PTA/Stent
  - Follow up 3.5 years, results 2014
- Schwarzwälder U, Hauk M, Zeller T. RADAR - A randomized, multi-centre, prospective study comparing best medical treatment versus best medical treatment plus renal artery stenting in patients with hemodunamically relevant atherosclerotic renal artery stenosis. Trials 2009,10:60.





# Vorschlag zur stentgestützten Angioplastie bei arteriosklerotischer NAS in Abhängigkeit von Stenosegrad und Nierenfunktion

Stenosegrad:	
$\geq 90$ %:	Niereninsuffizienz mit Lebenserwartung (LE) mindestens 2 Jahre oder akute Verschlechterung der Nierenfunktion und unbekannte LE
70-90 %:	<ul style="list-style-type: none"><li>- Progressive Verschlechterung der Nierenfunktion bei unilateraler NAS</li><li>- Jeder Patient mit bilateraler NAS<ul style="list-style-type: none"><li>- GFR <math>&lt; 60</math> und <math>&gt; 10</math> ml/min</li></ul></li><li>- NAS einer funktionellen Einzelniere</li><li>- Flash pulmonary oedema</li></ul>
$< 70$ %:	<ul style="list-style-type: none"><li>- Duplexkontrolle alle 6 Monate, Angioplastie nur bei Progression (RI!) und ausreichender Lebenserwartung</li></ul>

