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University of Zurich[UZH]

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

BOSTON UNIVERSITY

HIRSLANDEN

ADPKD SYMPOSIUM

Klinik Hirslanden, 4. Oktober 2016

SICHERE UND ERFOLGREICHE BLUTDRUCKTHERAPIE BEI ADPKD

Prof. Dr. med. Stefan Russmann

Aktuelle Evidenz zu intensiver Blutdrucksenkung

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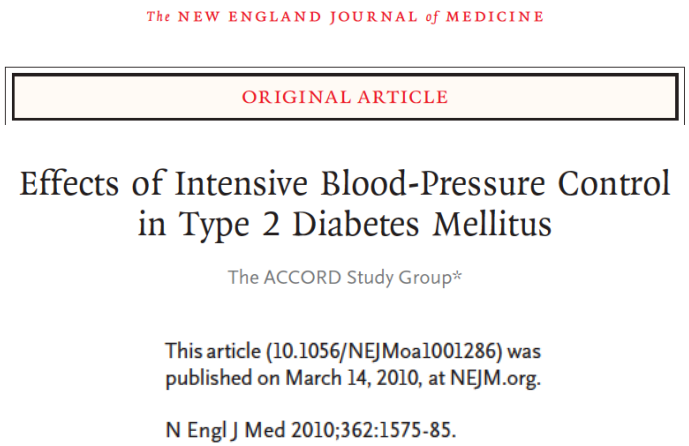
ACCORD STUDIE

N=4‘733
HR=0.88 (95%CI 0.73-1.06)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

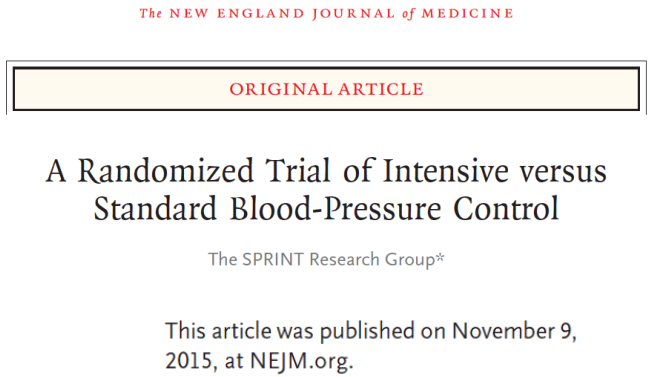
The ACCORD Study Group*

This article (10.1056/NEJMoa1001286) was published on March 14, 2010, at NEJM.org.

N Engl J Med 2010;362:1575-85.

SPRINT STUDIE

N=9‘361
HR=0.73 (95%CI 0.60-0.90)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

This article was published on November 9, 2015, at NEJM.org.

→ Ziel: RR systolisch <120 mmHg, wenn toleriert

Ergebnisse SPRINT Studie

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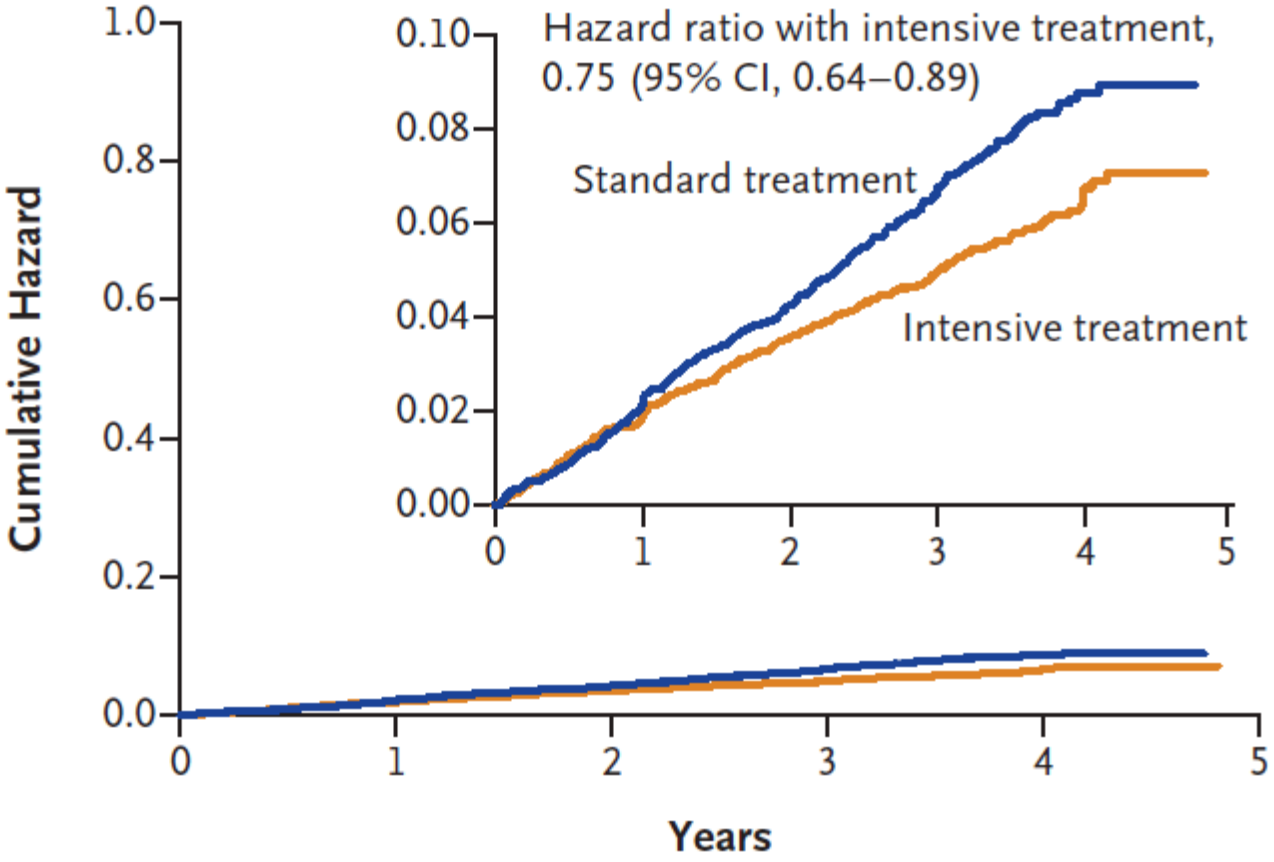
A Primary Outcome



No. at Risk

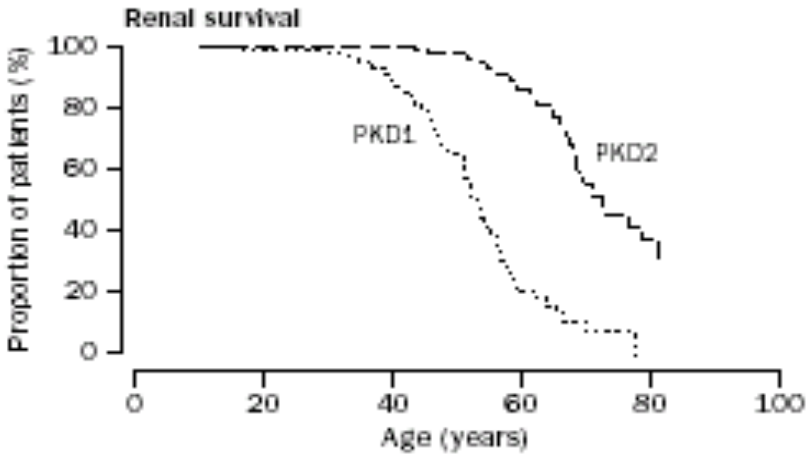
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

Table 3. Serious Adverse Events, Conditions of Interest, and Monitored Clinical Events.

Variable	Intensive Treatment (N=4678)	Standard Treatment (N=4683)	Hazard Ratio	P Value
	no. of patients (%)			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001
Monitored clinical events				
Adverse laboratory measure§				
Serum sodium <130 mmol/liter	180 (3.8)	100 (2.1)	1.76	<0.001
Serum sodium >150 mmol/liter	6 (0.1)	0		0.02
Serum potassium <3.0 mmol/liter	114 (2.4)	74 (1.6)	1.50	0.006
Serum potassium >5.5 mmol/liter	176 (3.8)	171 (3.7)	1.00	0.97
Orthostatic hypotension¶				
Alone	777 (16.6)	857 (18.3)	0.88	0.01
With dizziness	62 (1.3)	71 (1.5)	0.85	0.35

Hypertonie und PKD

- Fortschreitende PKD ist mit Nierenfunktionsverlust assoziiert
- Fortschreitende PKD ist mit Hypertonie assoziiert
- Fortschreitende PKD ist mit zunehmender Aktivierung des Renin-Angiotensin-Aldosteron-Systems (RAAS) assoziiert



Hateboer et al, THE LANCET 353:103, 1999

Nierenerkrankungen und RAAS-Hemmung

- Bei Glomerulonephritis und diabetischer Nierenerkrankung führt medikamentöse RAAS-Blockade zu verlangsamtem Fortschreiten der Nierenerkrankung

PKD und RAAS-Hemmung?

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- Kleine Studie (n=24) von 2001:
  ACE-Hemmer aber nicht Diuretika verlangsamen Nierenfunktionsverlust (GFR)

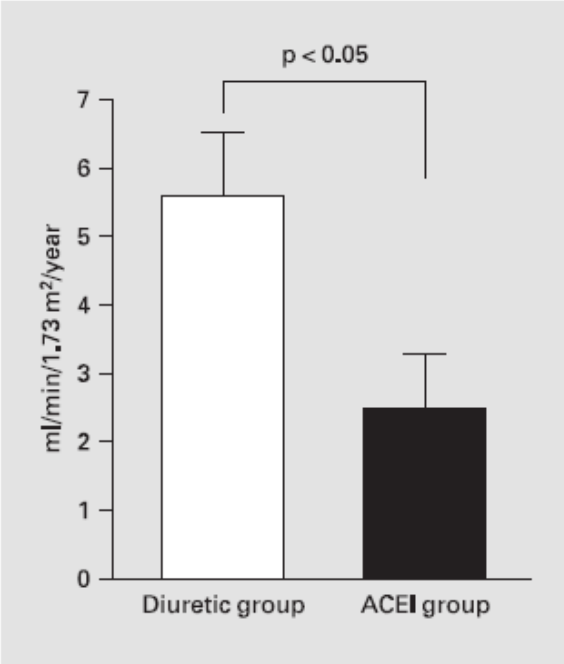

Fig. 1. The annual loss of creatinine clearance adjusted for initial creatinine clearances was significantly larger in the diuretic group than the ACEI group (5.6 vs. 2.5 ml/min/1.73 m^2, $p < 0.05$).

American Journal of Nephrology

Clinical Study

Am J Nephrol 2001;21:98–103

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Diuretics versus Angiotensin-Converting Enzyme Inhibitors in Autosomal Dominant Polycystic Kidney Disease

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Ann M. Johnson[a] Arlene B. Chapman[b] Patricia A. Gabow[a]
Robert W. Schrier[a]

Hypertonie, RAAS-Hemmung und PKD

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HALT STUDY A

The NEW ENGLAND JOURNAL of MEDICINE

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Blood Pressure in Early Autosomal Dominant Polycystic Kidney Disease

Robert W. Schrier, M.D., Kaleab Z. Abebe, Ph.D., Ronald D. Perrone, M.D., Vicente E. Torres, M.D., Ph.D., William E. Braun, M.D., Theodore I. Steinman, M.D., Franz T. Winklhofer, M.D., Godela Brosnahan, M.D., Peter G. Czarnecki, M.D., Marie C. Hogan, M.D., Ph.D., Dana C. Miskulin, M.D., Frederic F. Rahbari-Oskoui, M.D., Jared J. Grantham, M.D., Peter C. Harris, Ph.D., Michael F. Flessner, M.D., Ph.D., Kyongtae T. Bae, M.D., Charity G. Moore, Ph.D., M.S.P.H., and Arlene B. Chapman, M.D., for the HALT-PKD Trial Investigators*

N=558 (15-49 Jahre)
Baseline GFR > 60 ml/min
BP sys. 95-110 vs. 120-130
ACE-Hemmer *plus* AT2-Antagonist vs. nur ACE-Hemmer

Hypertonie, RAAS-Hemmung und PKD

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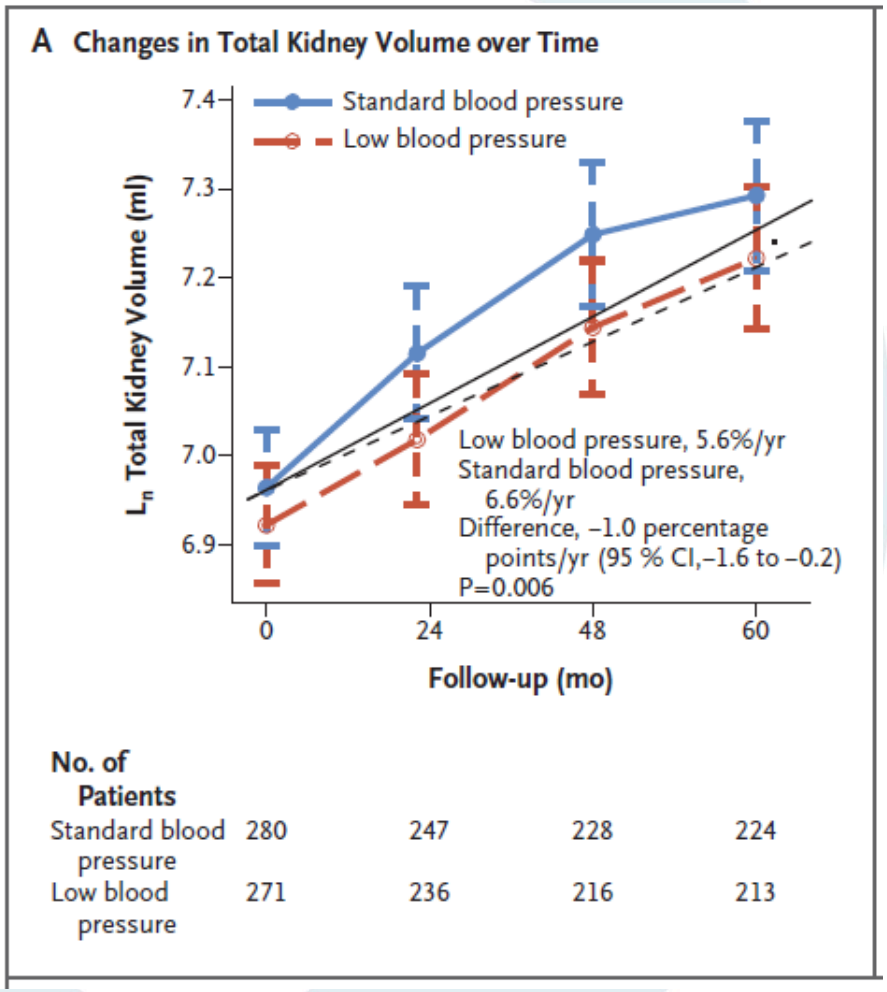
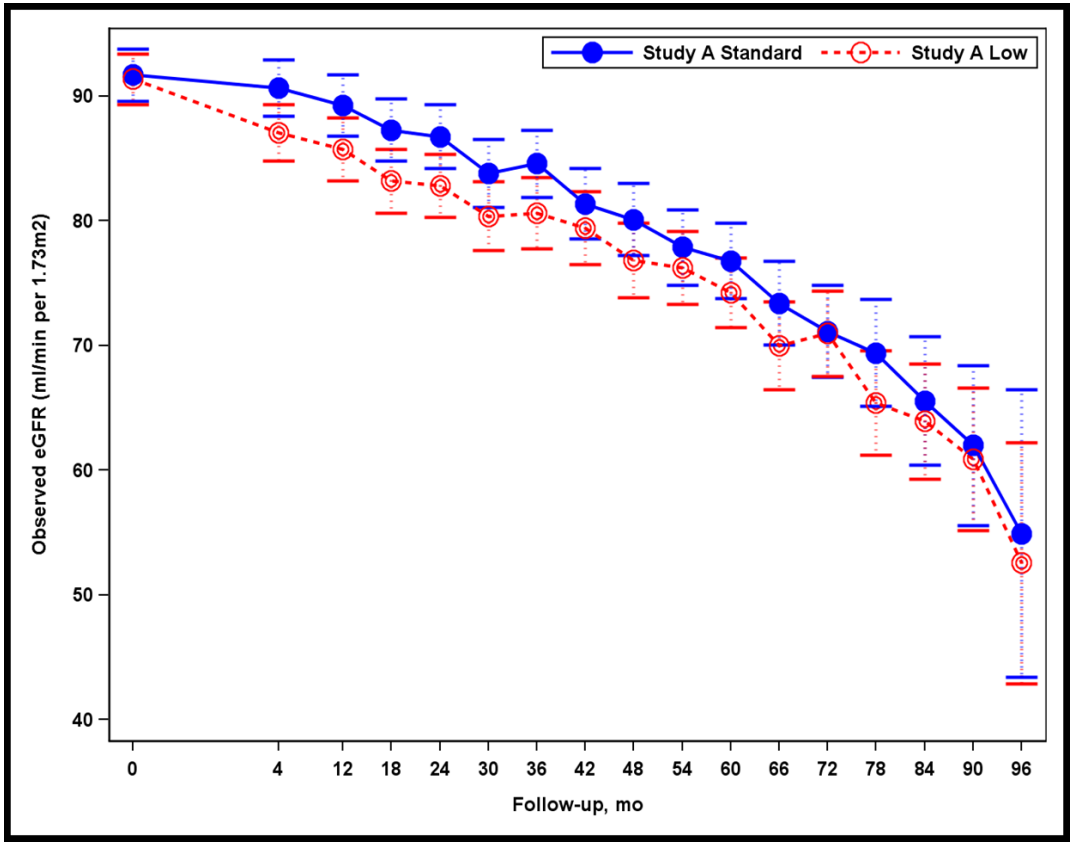
Nierenvolumen (TKV)



Nierenfunktion (eGFR)



Hypertonie, RAAS-Hemmung und PKD

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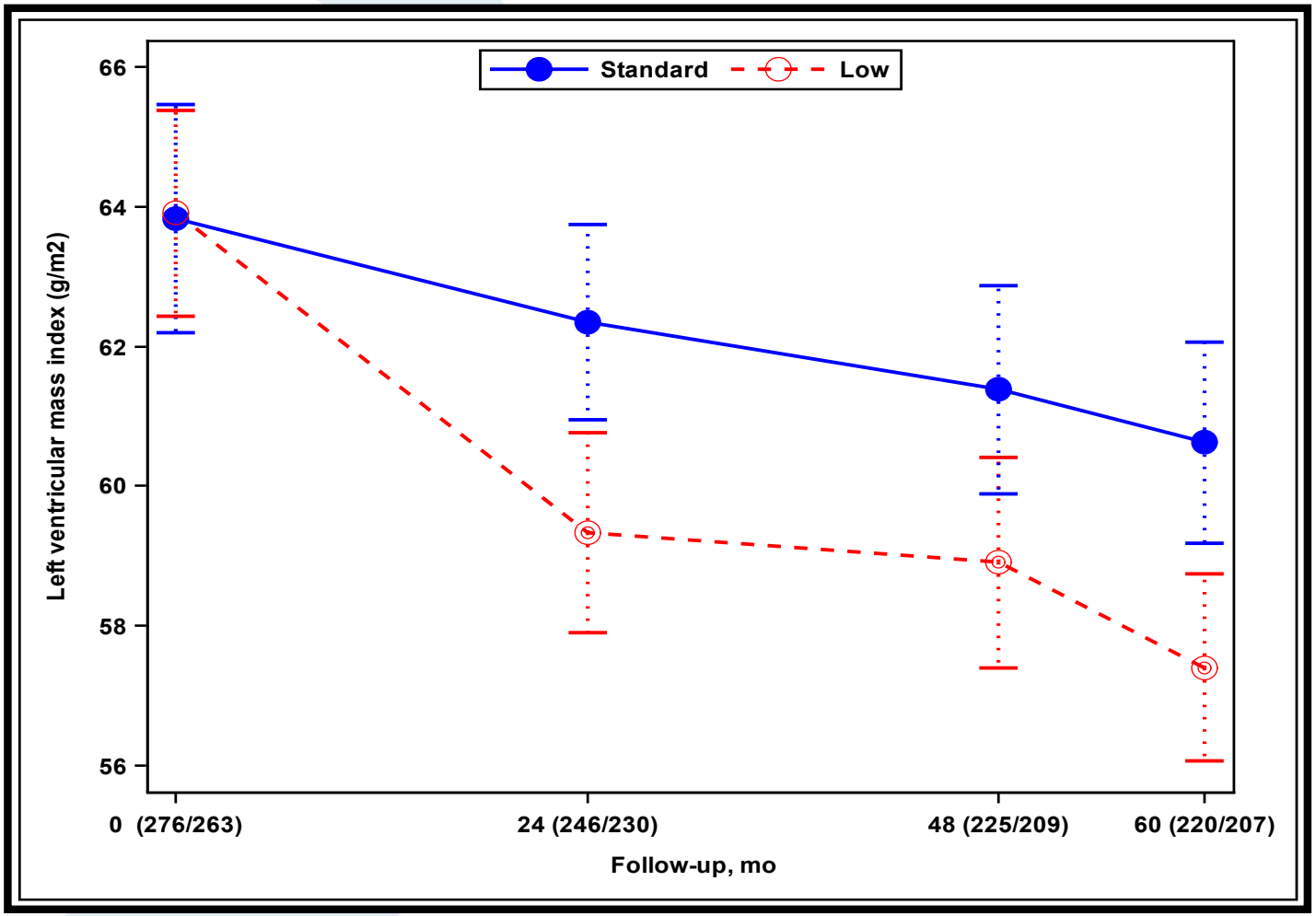
HALT STUDY A

LV Herzhypertrophie



Hypertonie, RAAS-Hemmung und PKD

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HALT STUDY A

Unerwünschte Ereignisse

	Standard BP (n=284)	Low BP (n=274)
Mean Follow-up duration (years)	5.7	5.6
Acute kidney injury events, participants (%)	4.6%	5.8%
Hyperkalemia – Any events, participants (%)	3.2%	2.6%
Hospitalizations, incidence per 100 py	7.43	6.07
Cardiac-related hospitalizations, incidence per 100 py	0.80	0.59
Death, total events, participants (%)	0.7%	0.0%

Hypertonie, RAAS-Hemmung und PKD

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HALT STUDY B

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Angiotensin Blockade in Late Autosomal Dominant Polycystic Kidney Disease

Vicente E. Torres, M.D., Ph.D., Kaleab Z. Abebe, Ph.D., Arlene B. Chapman, M.D., Robert W. Schrier, M.D., William E. Braun, M.D., Theodore I. Steinman, M.D., Franz T. Winklhofer, M.D., Godela Brosnahan, M.D., Peter G. Czarnecki, M.D., Marie C. Hogan, M.D., Ph.D., Dana C. Miskulin, M.D., Frederic F. Rahbari-Oskoui, M.D., Jared J. Grantham, M.D., Peter C. Harris, Ph.D., Michael F. Flessner, M.D., Ph.D., Charity G. Moore, Ph.D., M.S.P.H., and Ronald D. Perrone, M.D., for the HALT-PKD Trial Investigators*

This article was published on November 15, 2014, at NEJM.org.

N=486 (18-65 Jahre)
Baseline GFR 25 bis 60 ml/min
ACE-Hemmer *plus* AT2-Antagonist vs. nur ACE-Hemmer

Hypertonie, RAAS-Hemmung und PKD

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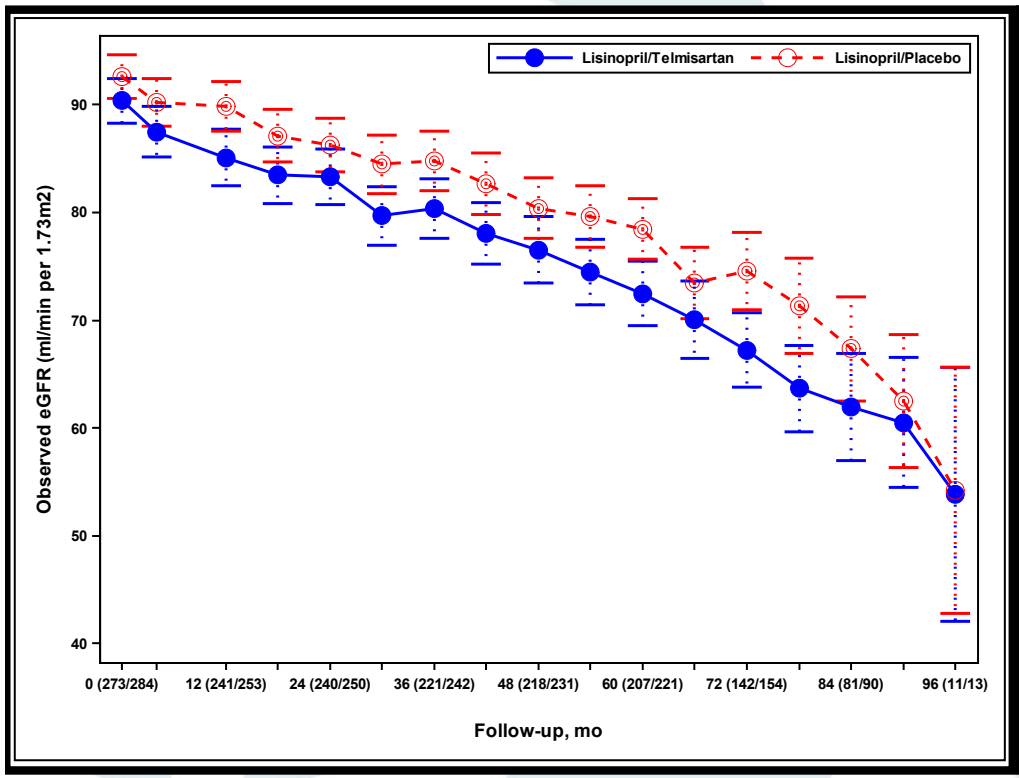
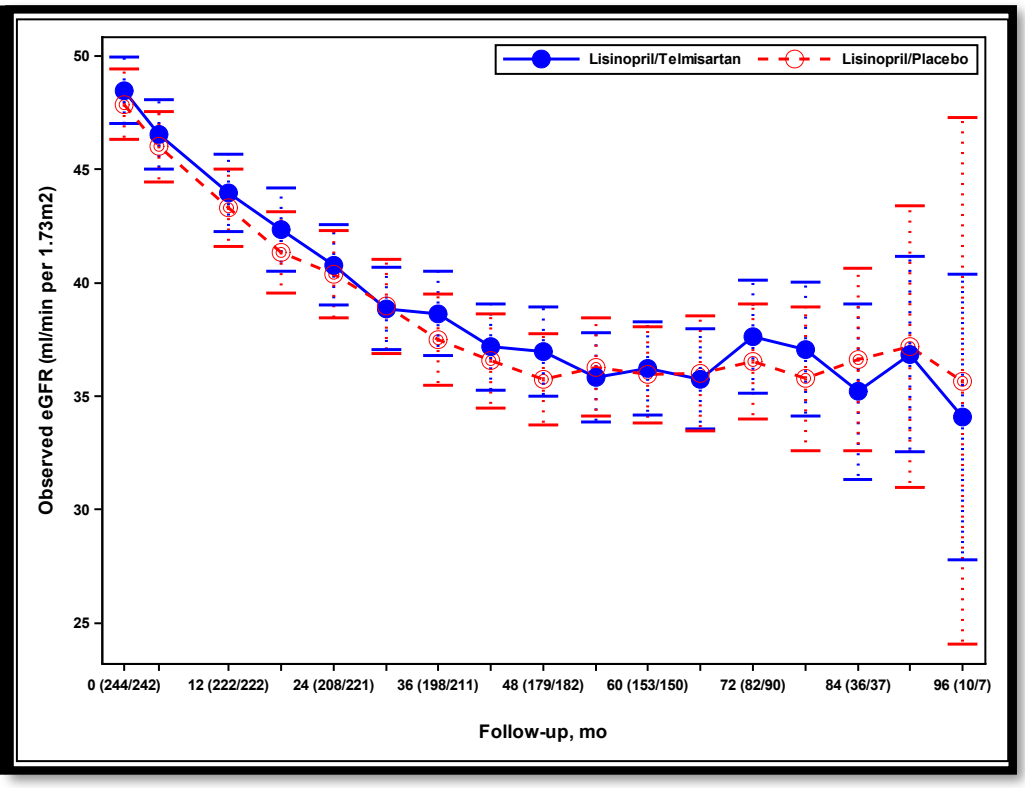
HALT STUDY A/B

eGFR





Schlussfolgerungen Hypertonie und PKD

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- Kein Hinweis auf zusätzlichen Nutzen durch doppelte (ACE-Hemmer plus AT2-Antagonist) vs. einfache RAAS-Blockade
(HALT A und B Studie)
- Intensive Blutdrucksenkung <110 mmHg hat nachgewiesenen positiven Effekt auf **Nierenvolumen, LV Herzhypertrophie und Proteinausscheidung**
(HALT A Studie)
- Positiver Effekt durch RR <110 mmHg auf GFR nicht nachgewiesen, aber über langen Zeitraum möglich
- Intensive RR-Senkung ist generell sicher, aber mögliche unerwünschte Wirkungen müssen antizipiert und monitorisiert werden

Risk factor	Management recommendation
Symptomatic heart failure or LVEF <35%	No evidence for target < 120 mm Hg
Autosomal Dominant Polycystic Kidney Disease (ADPKD) at CKD stage 1 to 3	Target 110/75 mm Hg and lower
Glomerulonephritis, proteinuria, secondary cause of hypertension	Blood pressure target unknown, reduction of proteinuria to 1 g per day and lower is recommended
eGFR <20 ml/min	No evidence for target < 120 mm Hg Avoid RAAS-inhibitors and thiazide-like diuretics
Renal artery stenosis	Avoid RAAS-inhibitors
History of stroke	Involve vascular neurologist, lower blood pressure only slowly and monitor closely for orthostatic hypotension, dizziness/syncope
History of electrolyte imbalances (Na+, K+)	Close monitoring Select diuretics, RAAS-inhibitors and aldosterone antagonists to counterbalance electrolyte imbalances
Concomitant use of NSAIDs	Avoid in chronic renal disease Avoid combination with RAAS-inhibitors
Diabetes	Monitor for orthostatic hypertension
Aortic and mitral valve stenosis, obstructive cardiomyopathy	Avoid RAAS-inhibitors
Concomitant use of lithium	Monitor lithium plasma levels as hyponatremia may induce lithium toxicity

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Clinical Pharmacologist and Toxicologist

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