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Eisen und Kalium – Alles ganz einfach?

Rolle von Eisen und Kalium bei der Therapie der Herzinsuffizienz

Ralph Wendt
Abteilung Nephrologie
Klinik für Infektiologie/Tropenmedizin, Nephrologie und Rheumatologie

13.06.2019

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COI

lecture fees / advisory board honaria / traval grants:

Fresenius Medical Care, Vifor Fresenius Pharma, Amgen, Shire, Novartis, Alexion, Otsuka, Cellpharm, Ablynx**,** Daiichi Sankyo

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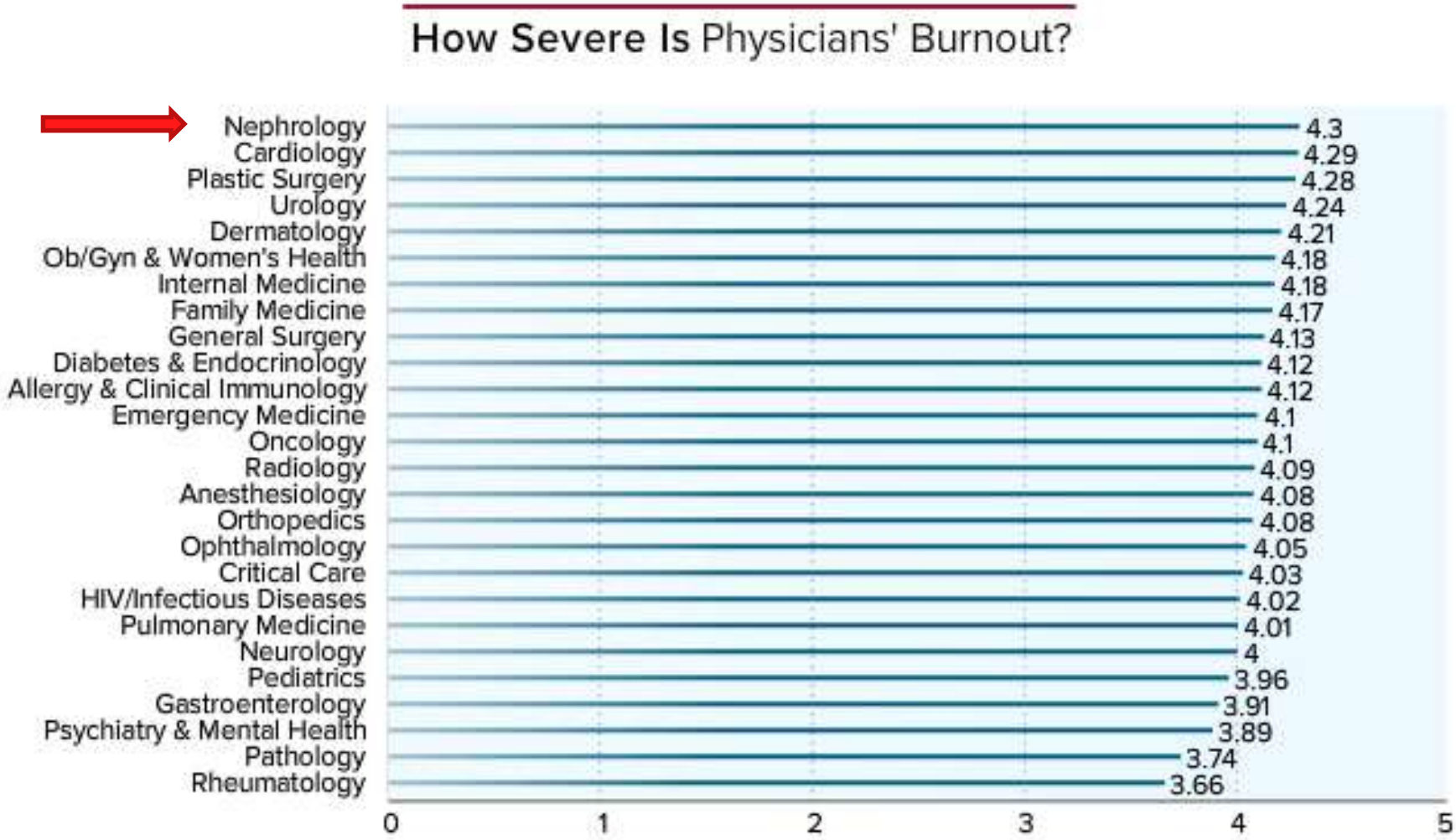
Gemeinsames Leid ist…



Medscape nephrologist lifestyle report 2015, Carol Peckham, Jan 26, 2015

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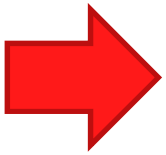
JAMA Network Open

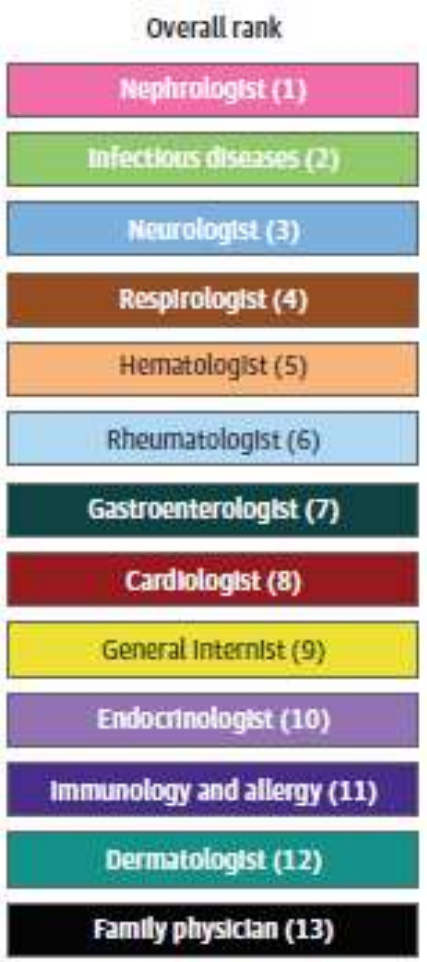
Original Investigation | Health Policy

Comparison of the Complexity of Patients Seen by Different Medical Subspecialists in a Universal Health Care System

Marcello Tonelli, MD, SM, MSc; Natasha Wiebe, MMath, PStat; Braden J. Manns, MD, MSc; Scott W. Klarenbach, MD, MSc; Matthew T. James, MD, PhD; Pietro Ravani, MD, PhD; Neesh Pannu, MD, SM; Jonathan Himmelfarb, MD; Brenda R. Hemmelgarn, MD, PhD

Complexity Rankings by Physician Type





Tonelli et al., JAMA Netw Open. 2018;1(7):e184852

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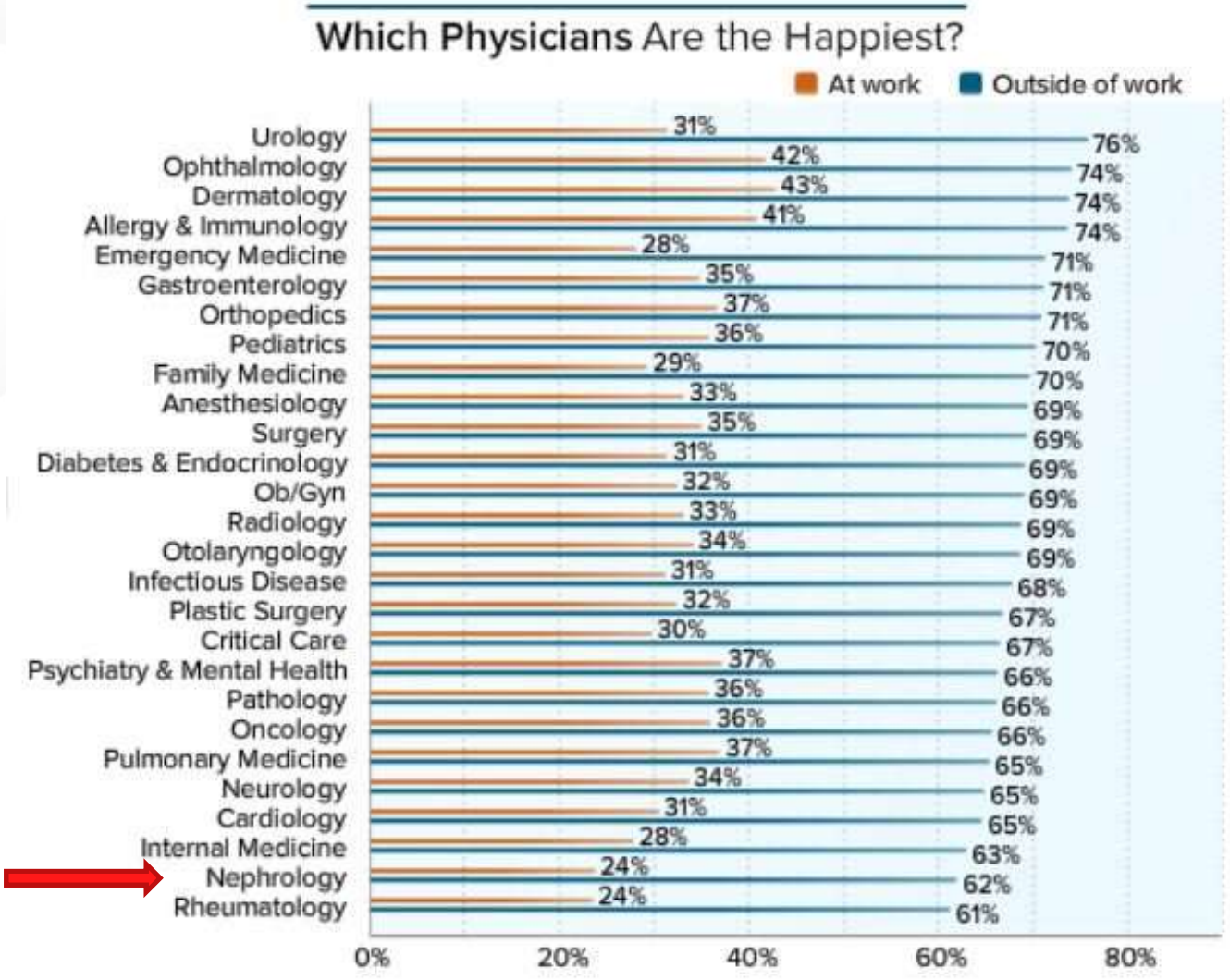

Medscape nephrologist lifestyle report 2015, Carol Peckham, Jan 26, 2015

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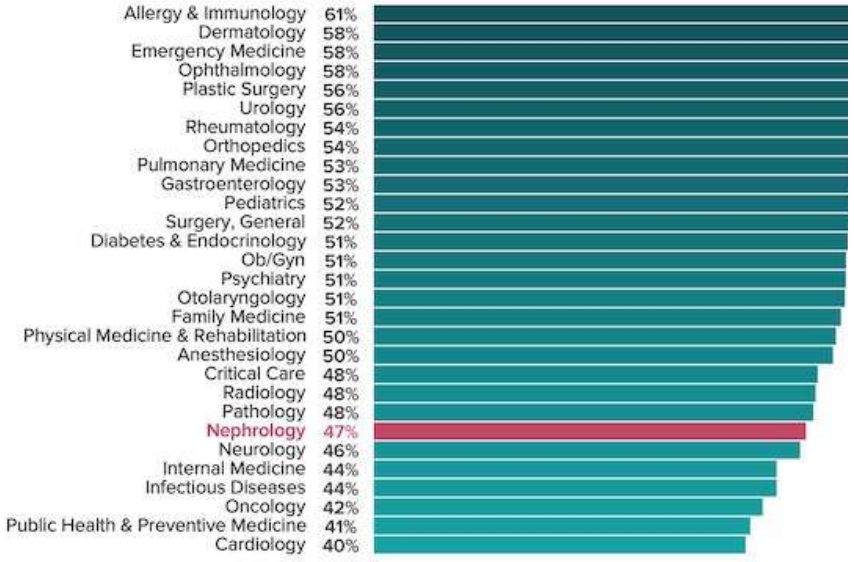
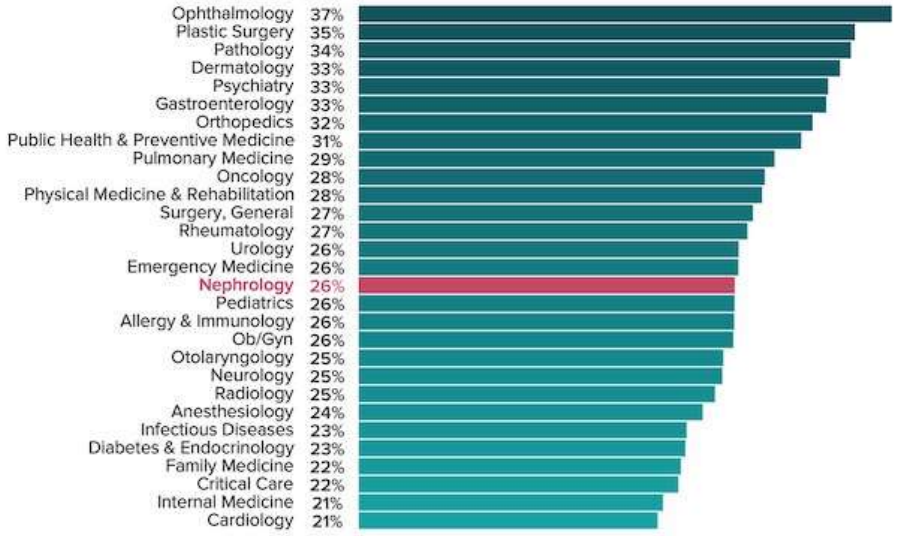
Und 2018 ????

Which Physicians Are Happiest Outside of Work?



Which Physicians Are Happiest at Work?



Medscape nephrologist lifestyle report 2018

Exsikkose ???

„…weil…der Patient hat eine trockene Zunge und eine trockene Haut…“

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JACC: HEART FAILURE
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http://dx.doi.org/10.1016/j.jchf.2014.09.007

Intravenous Fluids in Acute Decompensated Heart Failure

Behnood Bikdeli, MD,*† Kelly M. Strait, MS,* Kumar Dharmarajan, MD, MBA,*‡ Shu-Xia Li, PHD,* Purav Mody, MBBS,*§ Chohreh Partovian, MD, PHD,¶ Steven G. Coca, DO, MS,‖ Nancy Kim, MD, PHD,*¶ Leora I. Horwitz, MD, MHS,*¶ Jeffrey M. Testani, MD, MTR,† Harlan M. Krumholz, MD, SM*†#**

TABLE 3 Risk-Adjusted Hospitalization Outcomes by Therapy

	Critical Care Admission*	Late Intubation	Renal Replacement Therapy	In-Hospital Death
No treatment with intravenous fluids†	—	—	—	—
Treatment with intravenous fluids†	1.57 (1.45–1.71)	1.46 (1.25–1.71)	2.04 (1.62–2.55)	2.02 (1.82–2.24)

Many patients who are hospitalized with HF *and receive diuretics also receive intravenous fluids* during their early inpatient care, and the proportion varies among hospitals.

Such practice is associated with worse outcomes.

Bikdeli et al., J Am Coll Cardiol HF 2015;3:127–33

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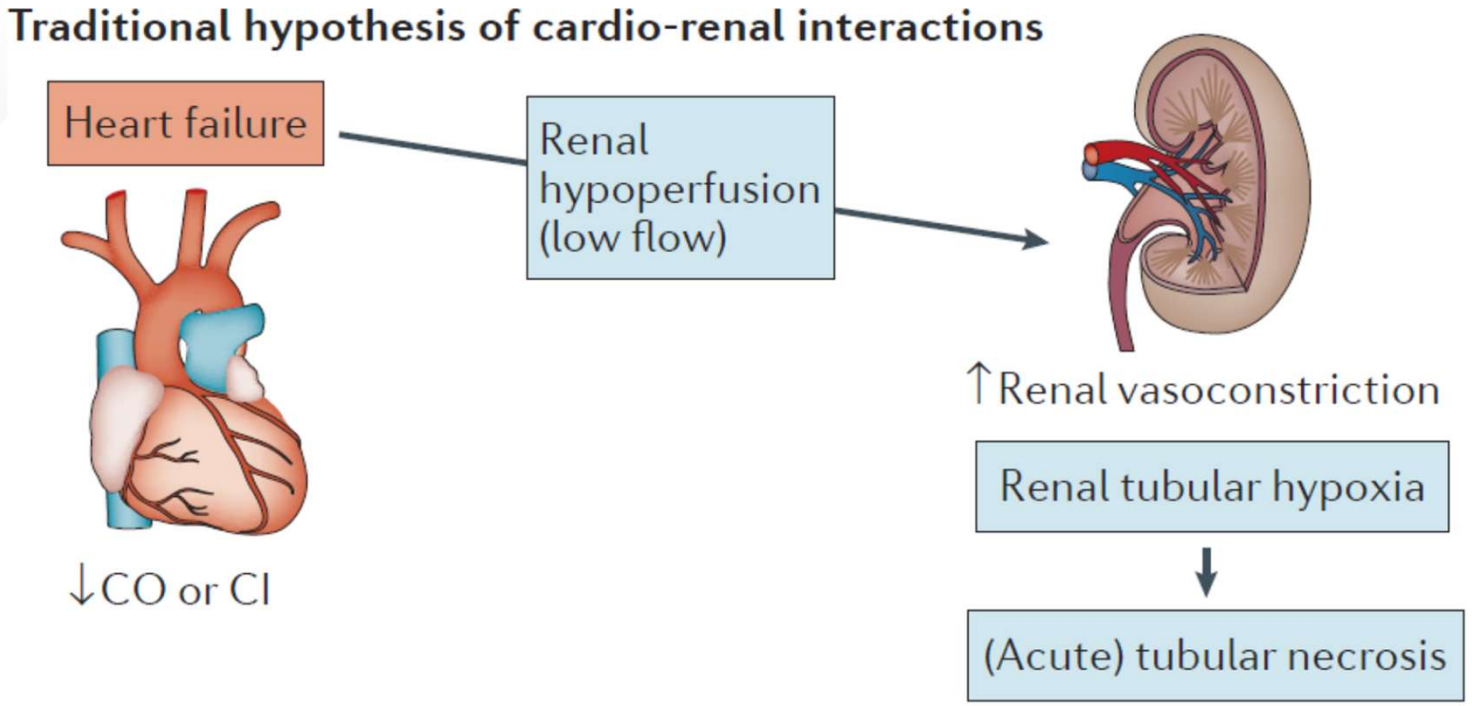
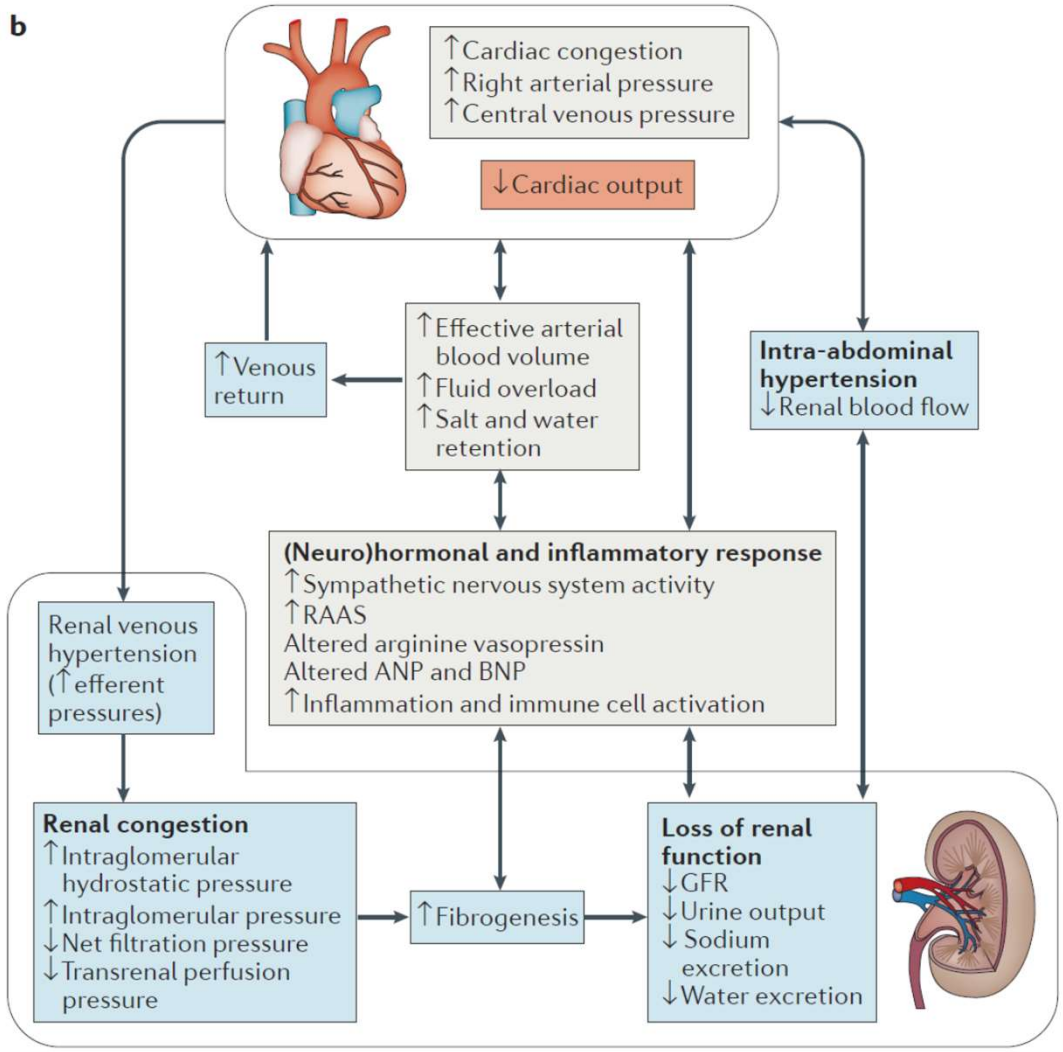
Traditional hypothesis of cardio-renal interactions



Schefold et al., Nature Reviews Nephrology volume12, pages610–623 (2016)

Haemodynamic mechanisms in cardio-renal interactions



Schefold et al., Nature Reviews Nephrology volume12, 610–623 (2016)

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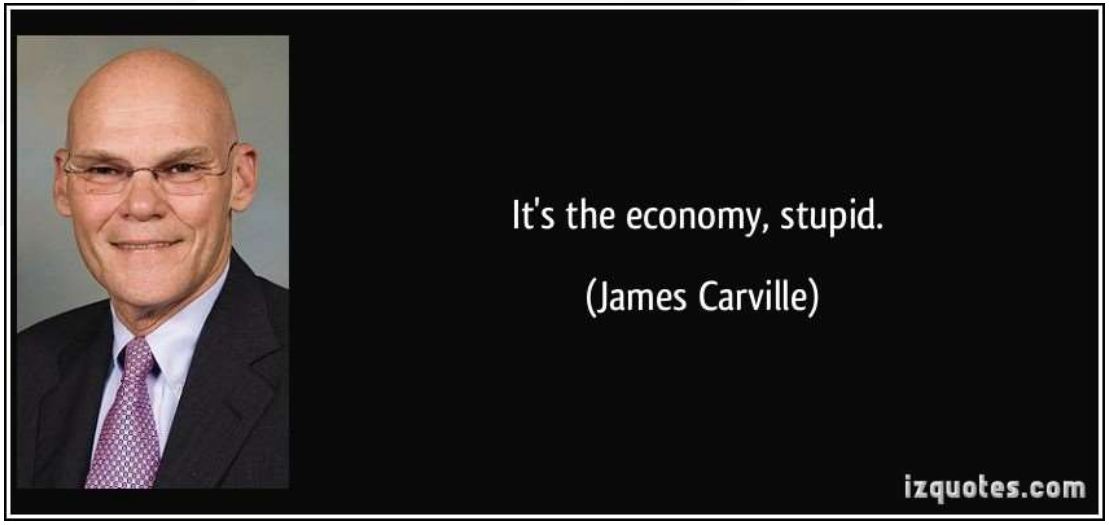

Cardiorenal syndrom

„It‘s venous congestion, stupid!“

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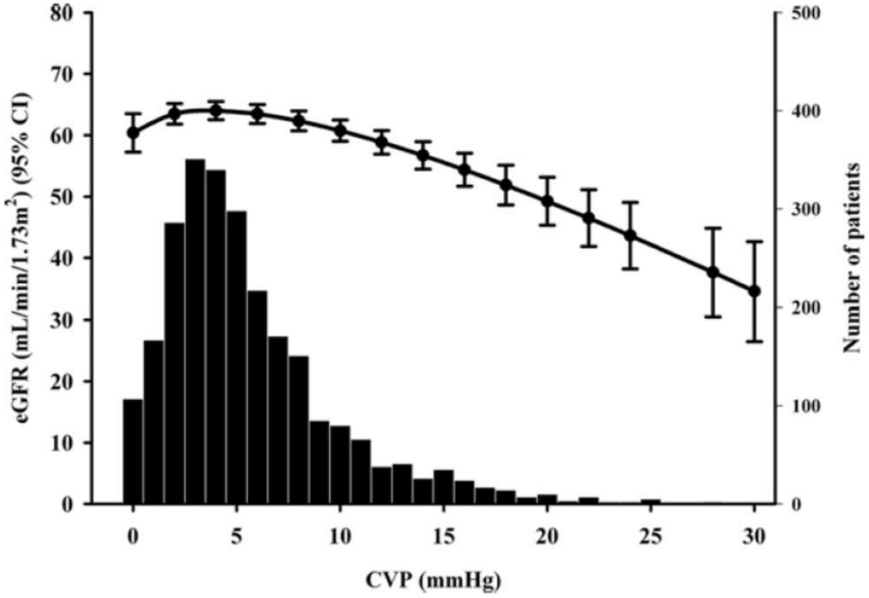
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2008.08.080

Heart Failure

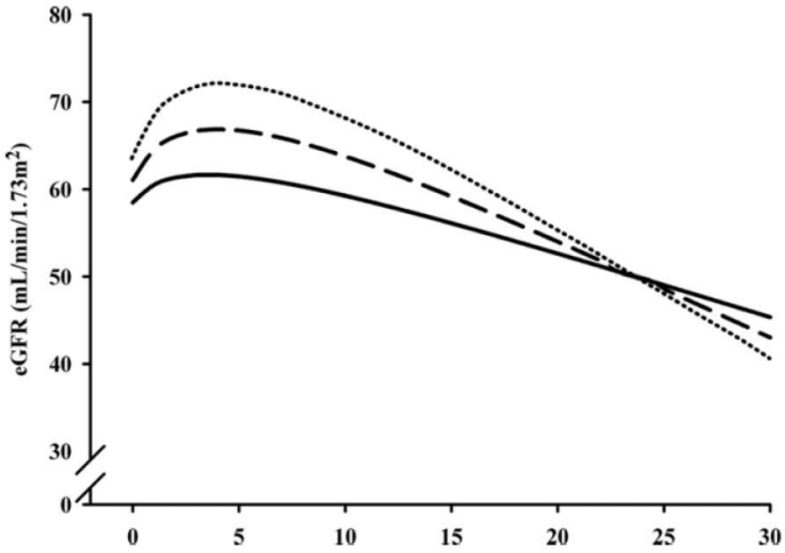
Increased Central Venous Pressure Is Associated With Impaired Renal Function and Mortality in a Broad Spectrum of Patients With Cardiovascular Disease

Kevin Damman, MD,* Vincent M. van Deursen,* Gerjan Navis, MD, PHD,†
Adriaan A. Voors, MD, PHD,* Dirk J. van Veldhuisen, MD, PHD, FACC,*
Hans L. Hillege, MD, PHD*‡
Groningen, the Netherlands

Distribution of CVP and Relationship Between CVP and eGFR



Relationship Between CVP and eGFR According to Different Cardiac Index Values



Solid line cardiac index 2.5 l/min/m2;
dashed line cardiac index 2.5 to 3.2 l/min/m2;
dotted line cardiac index 3.2 l/min/m2

Damman et al., J Am Coll Cardiol 2009;53:582–8

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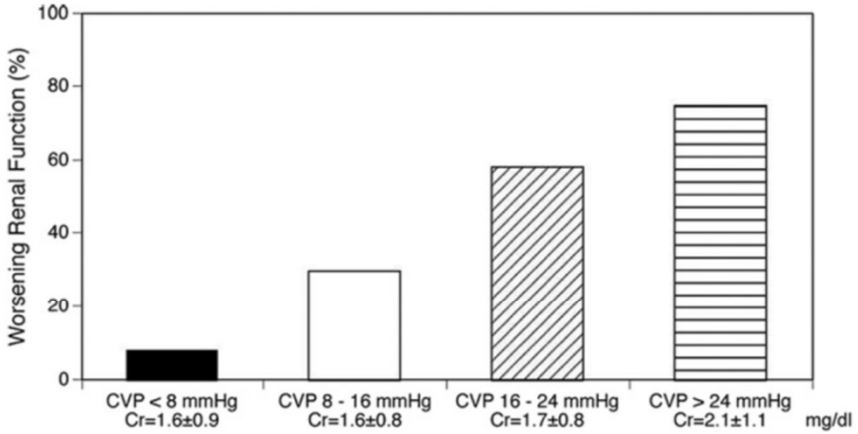
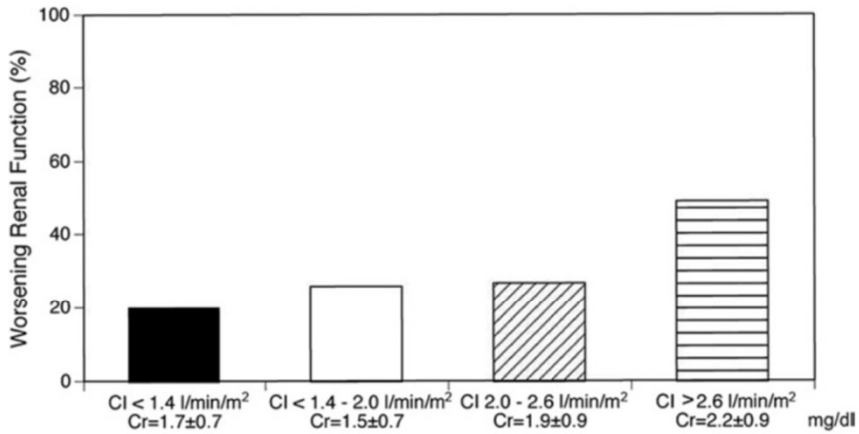
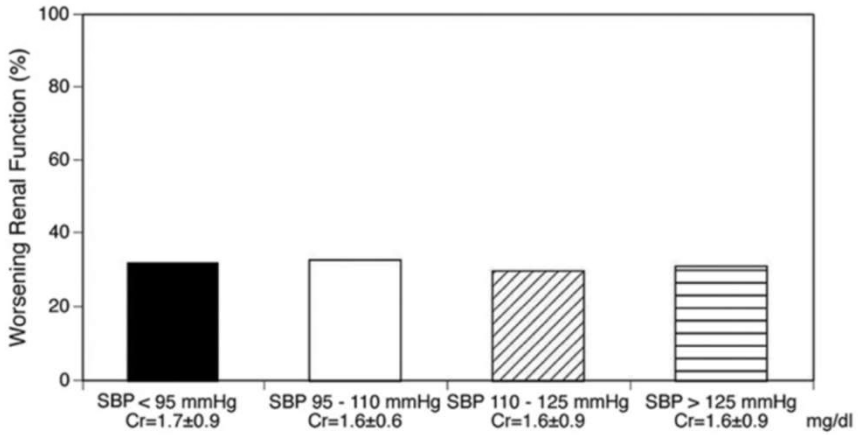
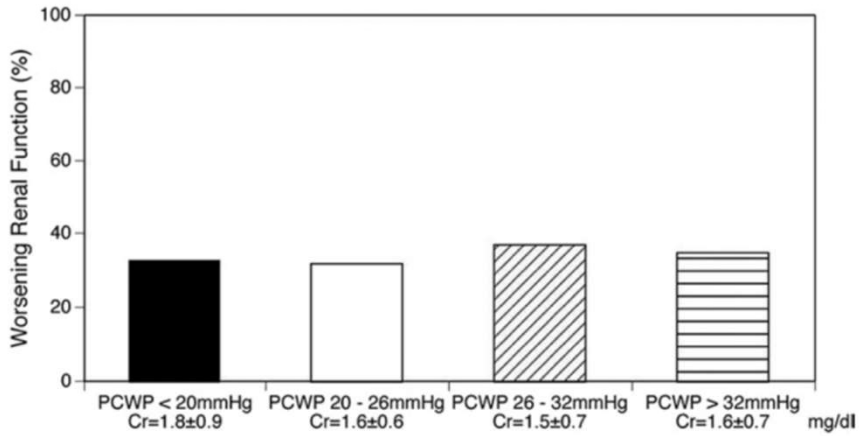
Importance of Venous Congestion for Worsening of Renal Function in Decompensated Heart Failure

Prevalence of Worsening Renal Function During Hospitalization accord. to Categories of Admission CVP, CI, SBP, and PCWP









Mullens et al., J Am Coll Cardiol 2009;53:589–96

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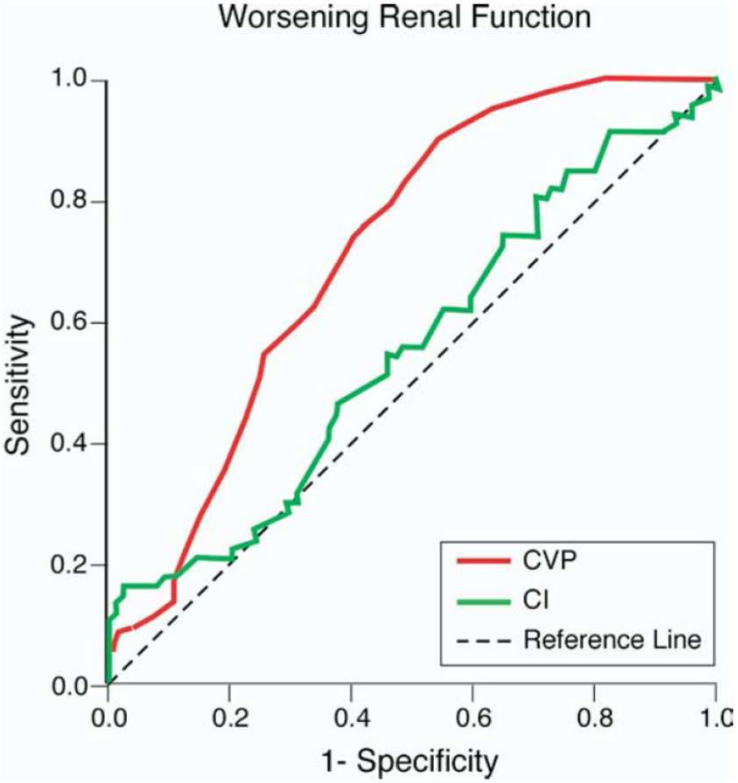
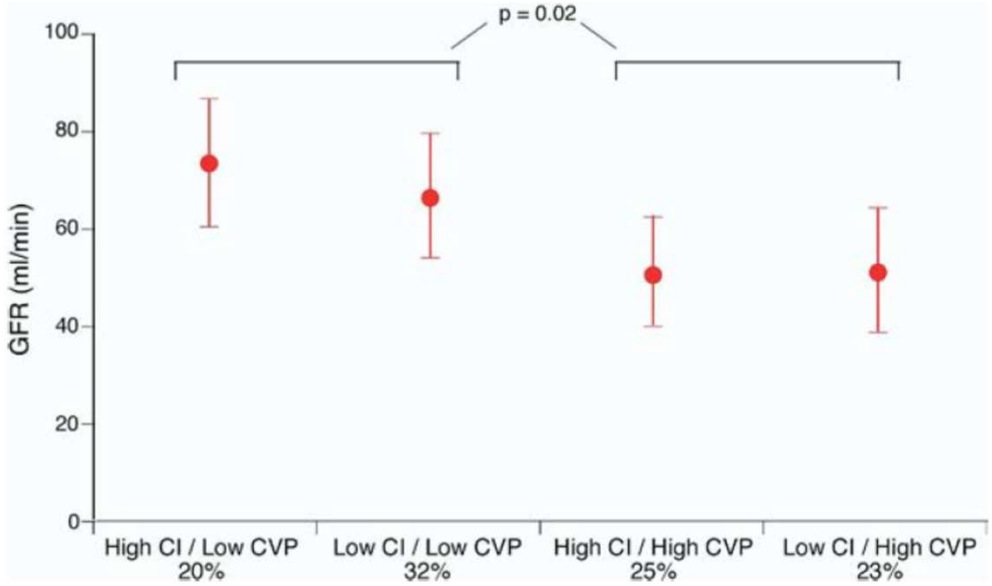
Importance of Venous Congestion for Worsening of Renal Function in Decompensated Heart Failure



Relative Contributions of CVP and CI to GFR at Time of PAC Removal



Mullens et al., J Am Coll Cardiol 2009;53:589–96

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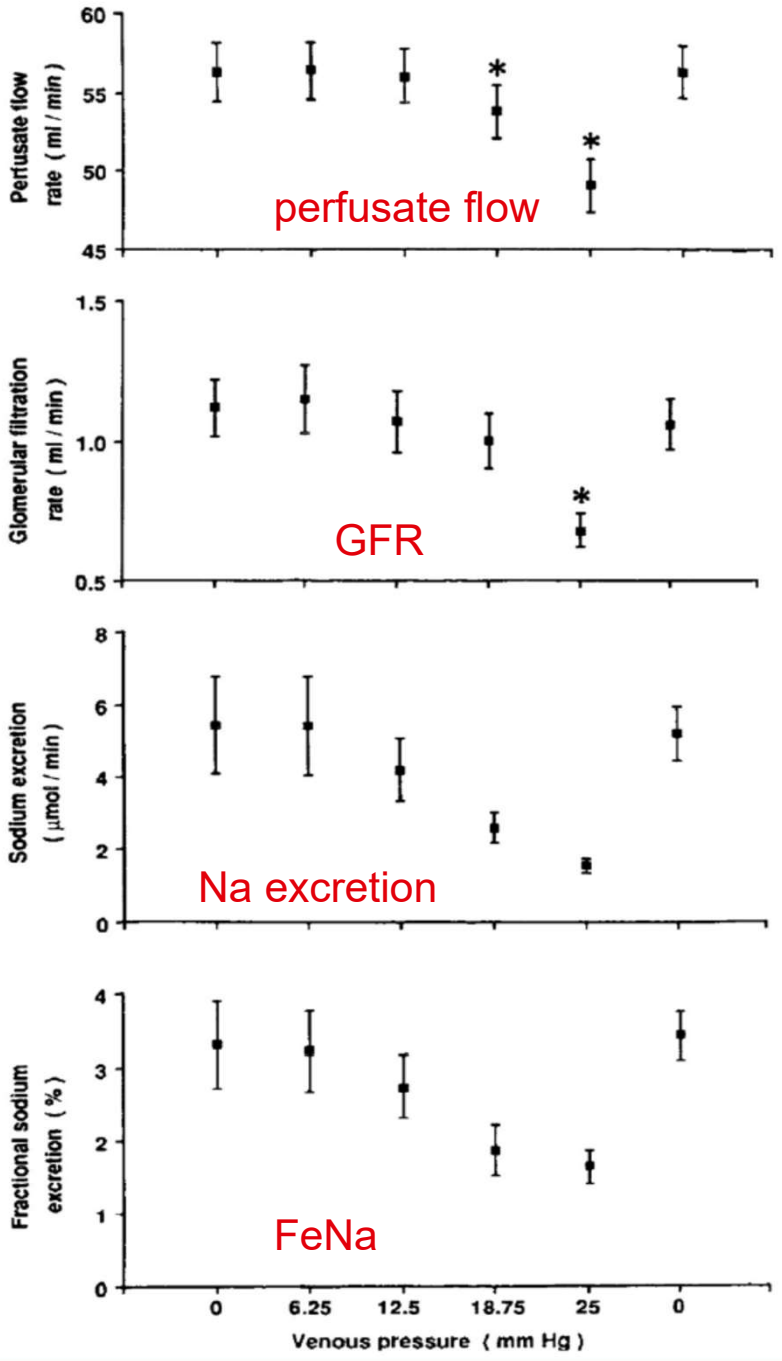
stepwise increase in
venous pressure
in kidneys perfused at
constant arterial pressure



Venous pressure

Bellomo et al. Ann. Intensive Care (2017) 7:49

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Was nun tun, wenn bei korrekter Therapie
der (dekompensierten) Herzinsuffizienz
das Kreatinin steigt ?

Antwort: (meistens) nichts! So weitermachen!

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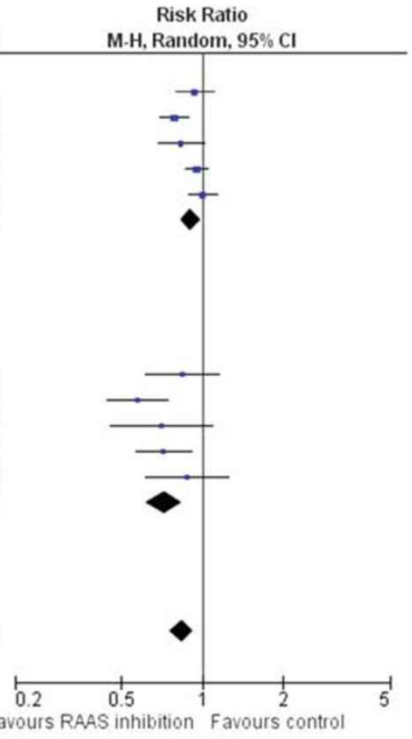
Reduction in all-cause mortality associated with the use of RAASi was significantly greater in the presence of WRF than in the no WRF

European Journal of Heart Failure (2014) 16, 41–48
doi:10.1002/ejhf.13

Worsening renal function during renin–angiotensin–aldosterone system inhibitor initiation and long-term outcomes in patients with left ventricular systolic dysfunction

Hannah Clark[1], Henry Krum[1,2], and Ingrid Hopper[1,2]*

Study or Subgroup	RAAS inhibition Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 no WRF intervention vs control						
EPHESUS (Rossignol 2011)	255	2425	274	2453	12.4%	0.94 [0.80, 1.11]
RALES (Vardeny 2012)	256	683	371	781	14.3%	0.79 [0.70, 0.89]
SAVE (Jose 2006)	137	781	171	812	10.5%	0.83 [0.68, 1.02]
SOLVD (Testani 2011)	599	2854	642	2917	15.4%	0.95 [0.86, 1.05]
VaL-HeFT (Lesogor 2013)	404	2162	436	2341	14.3%	1.00 [0.89, 1.13]
Subtotal (95% CI)		**8905**		**9304**	**66.8%**	**0.91 [0.83, 0.99]**
Total events	1651		1894			
Heterogeneity: Tau² = 0.01; Chi² = 9.59, df = 4 (P = 0.05); I² = 58%						
Test for overall effect: Z = 2.07 (P = 0.04)						
2.1.2 WRF intervention vs control						
EPHESUS (Rossignol 2011)	66	493	67	421	6.6%	0.84 [0.61, 1.15]
RALES (Vardeny 2012)	56	139	42	60	8.1%	0.58 [0.44, 0.75]
SAVE (Jose 2006)	26	116	33	104	4.1%	0.71 [0.45, 1.10]
SOLVD (Testani 2011)	84	324	102	282	8.9%	0.72 [0.56, 0.91]
VaL-HeFT (Lesogor 2013)	71	302	33	123	5.5%	0.88 [0.61, 1.25]
Subtotal (95% CI)		**1374**		**990**	**33.2%**	**0.72 [0.62, 0.84]**
Total events	303		277			
Heterogeneity: Tau² = 0.01; Chi² = 5.19, df = 4 (P = 0.27); I² = 23%						
Test for overall effect: Z = 4.10 (P < 0.0001)						
Total (95% CI)		**10279**		**10294**	**100.0%**	**0.84 [0.76, 0.93]**
Total events	1954		2171			
Heterogeneity: Tau² = 0.01; Chi² = 25.39, df = 9 (P = 0.003); I² = 65%						
Test for overall effect: Z = 3.40 (P = 0.0007)						
Test for subgroup differences: Chi² = 6.09, df = 1 (P = 0.01), I² = 83.6%						



Clinicians should not be deterred from using RAAS inhibitors in the setting of WRF

Clark et al., European Journal of Heart Failure (2014) 16, 41–48

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Heart Failure

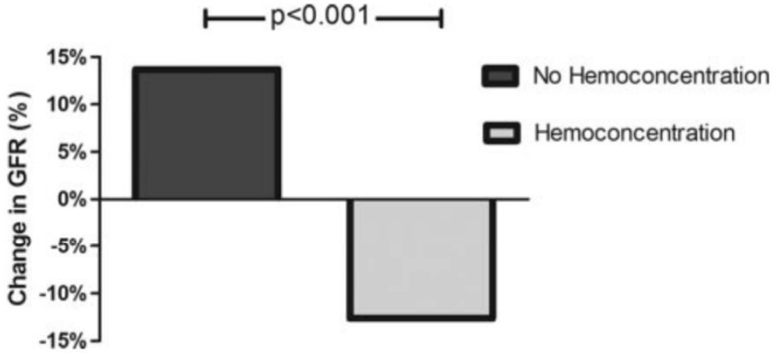
Potential Effects of Aggressive Decongestion During the Treatment of Decompensated Heart Failure on Renal Function and Survival

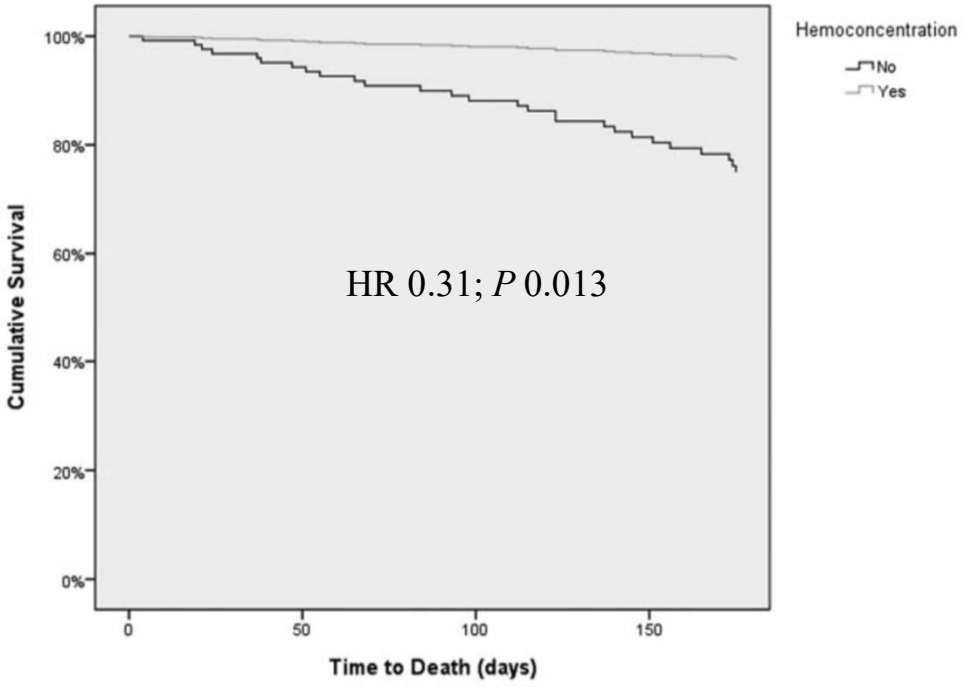
Jeffrey M. Testani, MD; Jennifer Chen, BS; Brian D. McCauley, BS;
Stephen E. Kimmel, MD, MSCE; Richard P. Shannon, MD

Relationship between aggressive decongestion and outcomes

Hemoconcentration was strongly associated with worsening renal function (odds ratio, 5.3; *P*0.001)

Patients with hemoconcentration had significantly lower 180-day mortality (hazard ratio, 0.31; *P*0.013).





Testani et al., Circulation. 2010;122:265-272

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Circulation

ORIGINAL RESEARCH ARTICLE

Worsening Renal Function in Patients With Acute Heart Failure Undergoing Aggressive Diuresis Is Not Associated With Tubular Injury

There is pervasive concern that decreases in GFR (as measured by serum creatinine or cystatin C) in the setting of aggressive diuresis of heart failure patients reflects renal tubular injury.

Ahmad et al., Circulation. 2018 May 8;137(19):2016-2028

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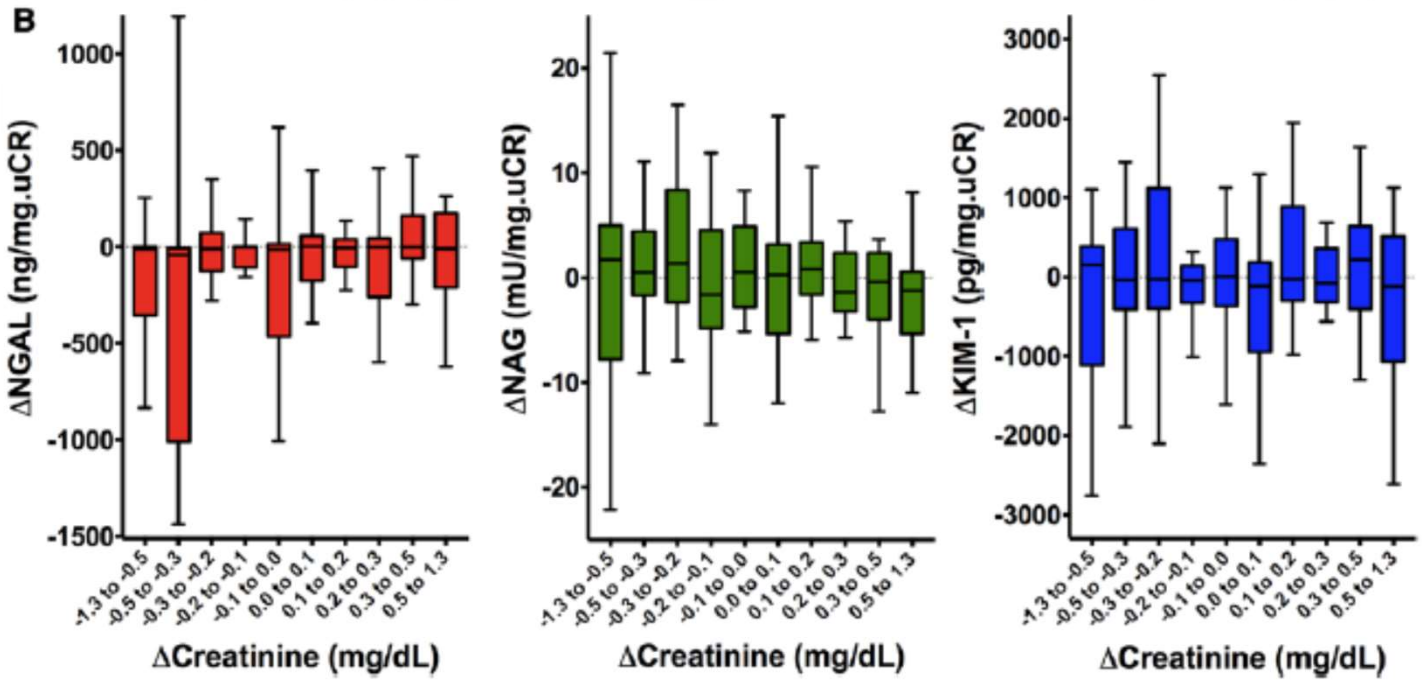
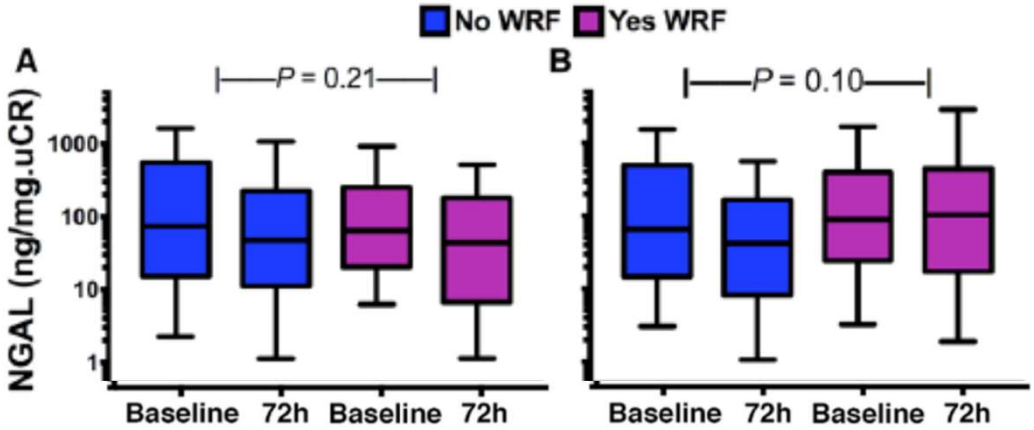
Worsening Renal Function in Patients With Acute Heart Failure Undergoing Aggressive Diuresis Is Not Associated With Tubular Injury





Ahmad et al., Circulation. 2018;137(19):2016-2028

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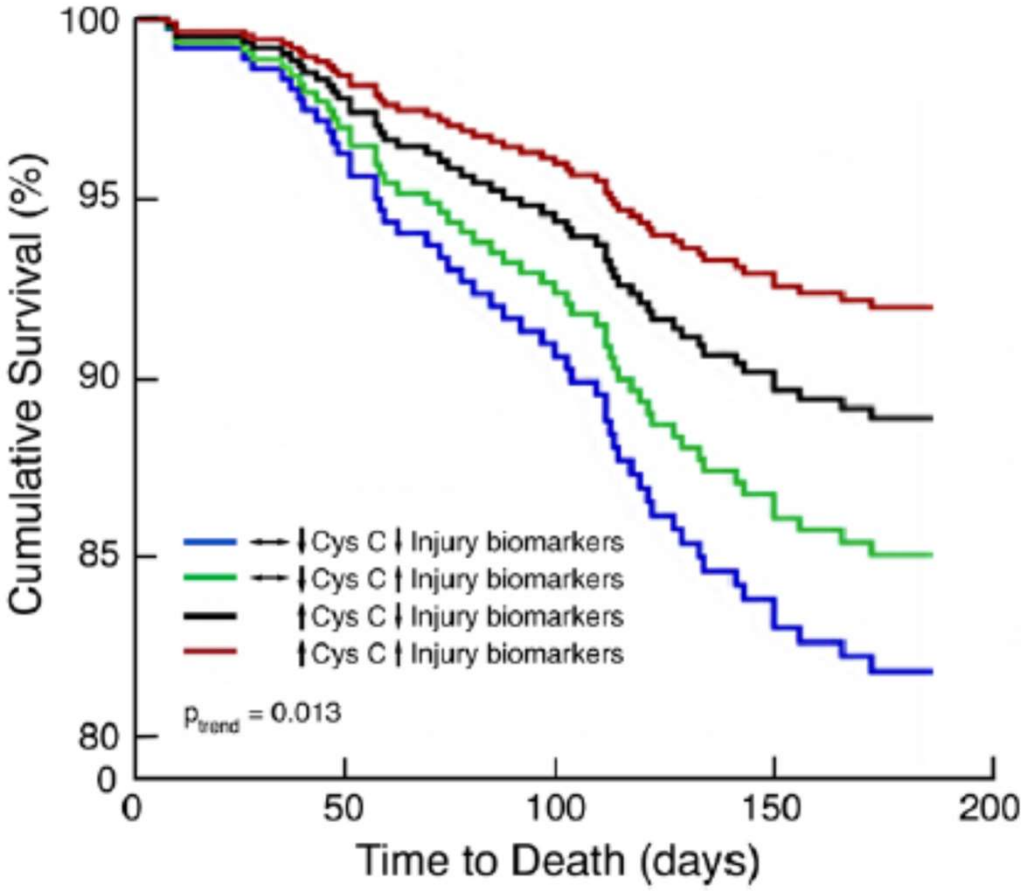
Associations between kidney tubular injury biomarkers and renal dysfunction with survival



Ahmad et al., Circulation. 2018 May 8;137(19):2016-2028

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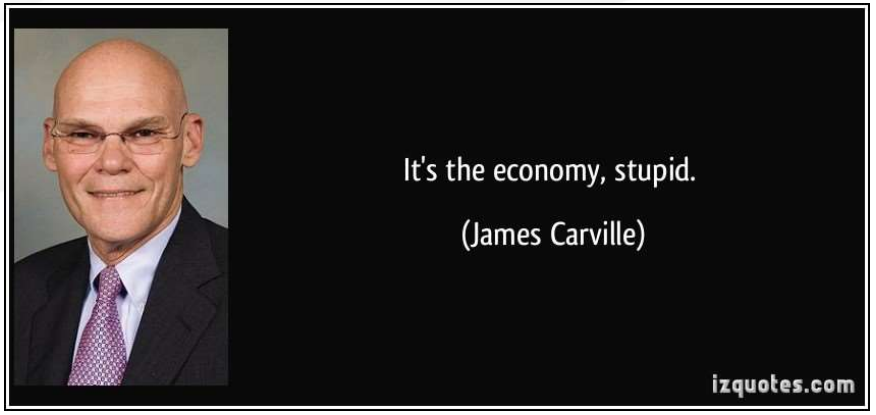


Cardiorenal syndrom

„It‘s venous congestion, stupid!“

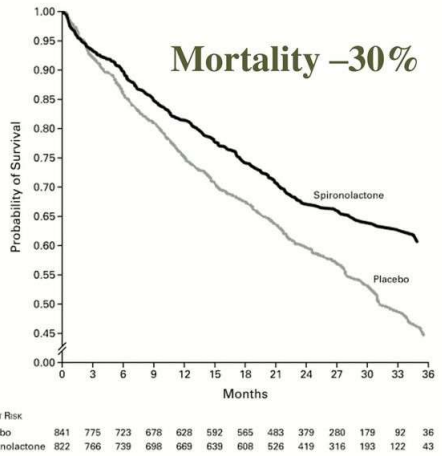
„Try to Dry“

Benefit der RAAS-Blockade bei systolischer Herzinsuffizienz

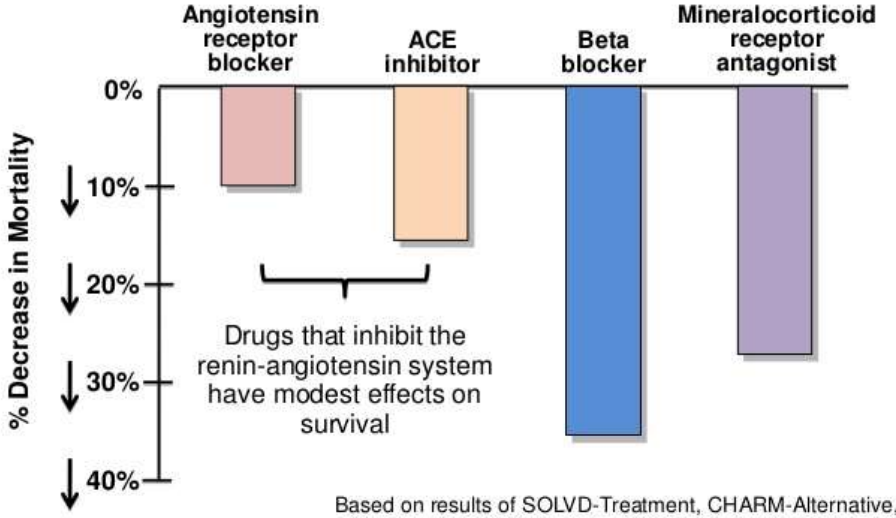
RALES-Trial: Spironolactone

Chronic heart failure
NYHA III, IV
ACE-I + loop diuretic
LVEF <35%

Pitt, B. et al. N Engl J Med 1999;341:709-717

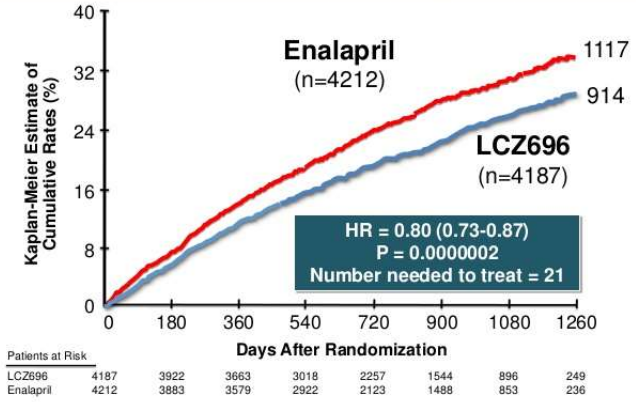


Drugs That Reduce Mortality in Heart Failure With Reduced Ejection Fraction



Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF

PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)



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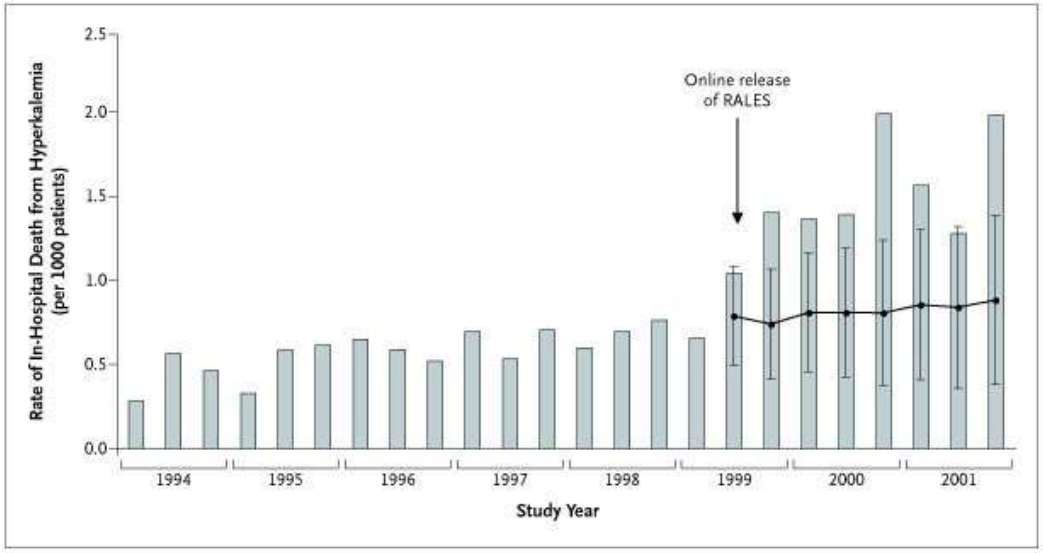
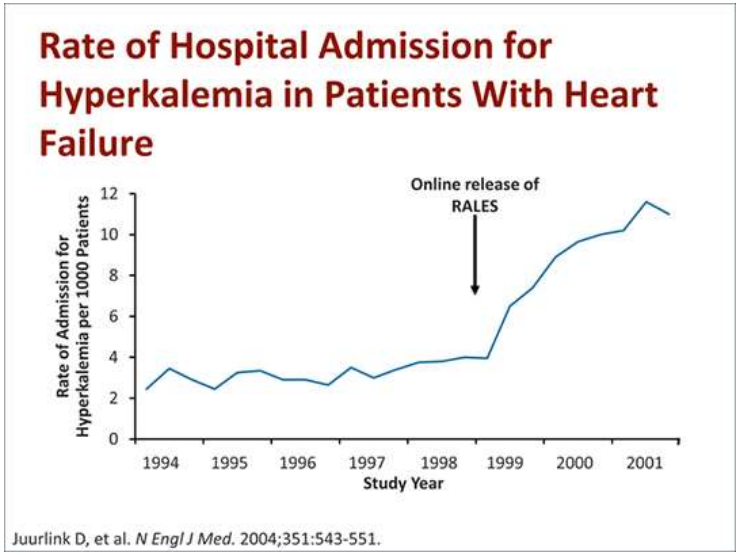
Rates of Hyperkalemia after publication of RALES





Juurlink et al., N Engl J Med 2004; 351:543-551

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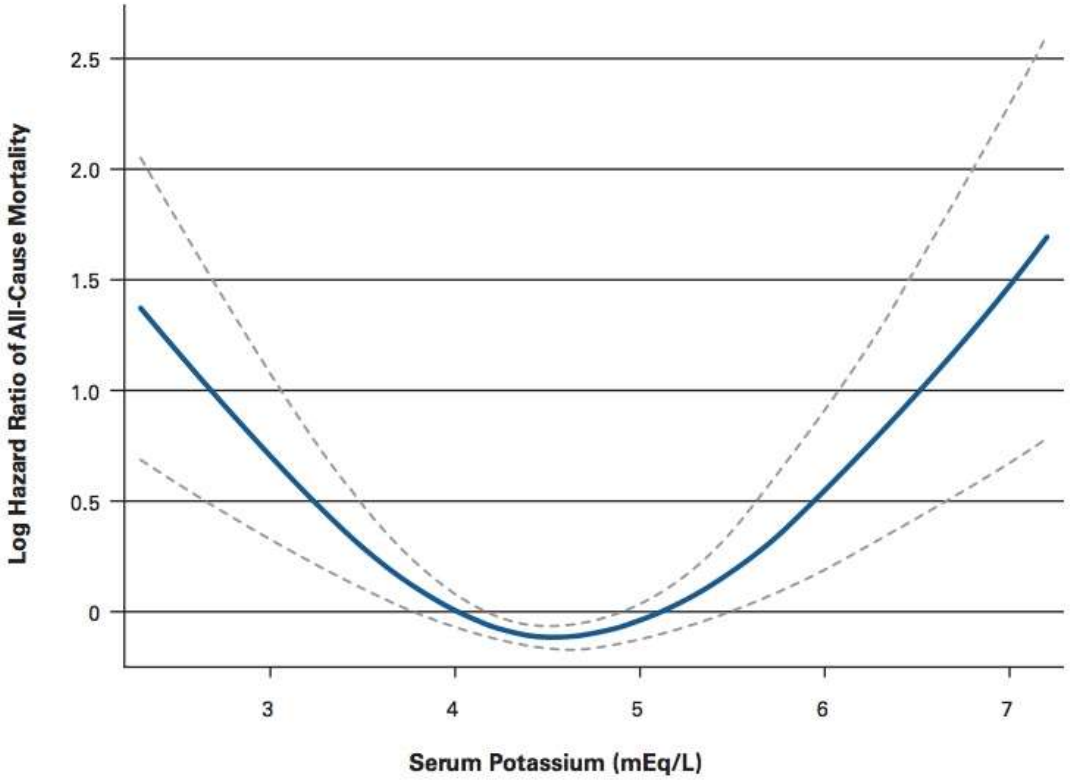
The Relation of Serum Potassium Concentration with Mortality in patients with CKD



Dunn et al. Am J Manag Care. 2015;21:S307-S315

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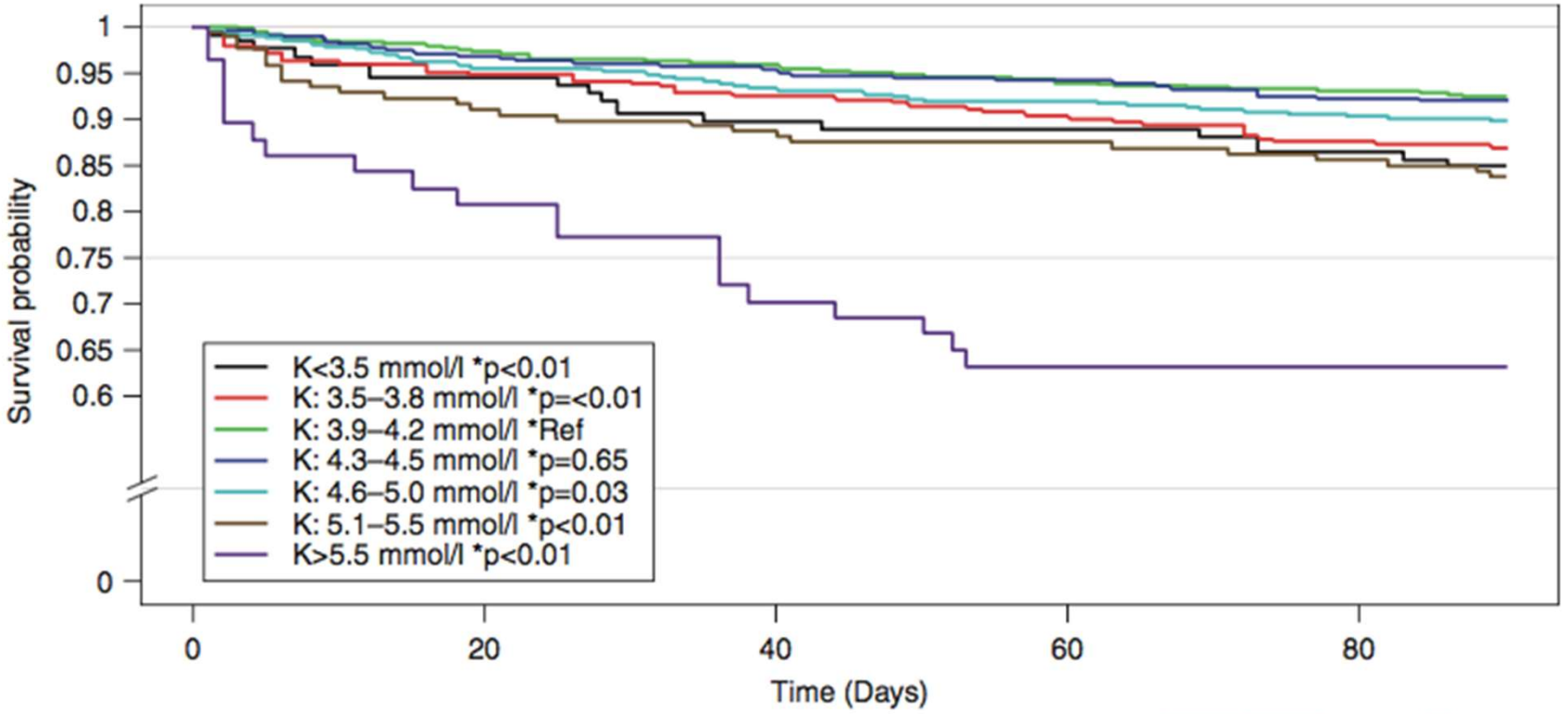
Mortality risk and serum potassium in heart failure after myocardial infarction



Krogager et al. European Heart Journal (2015) 1, 245–251

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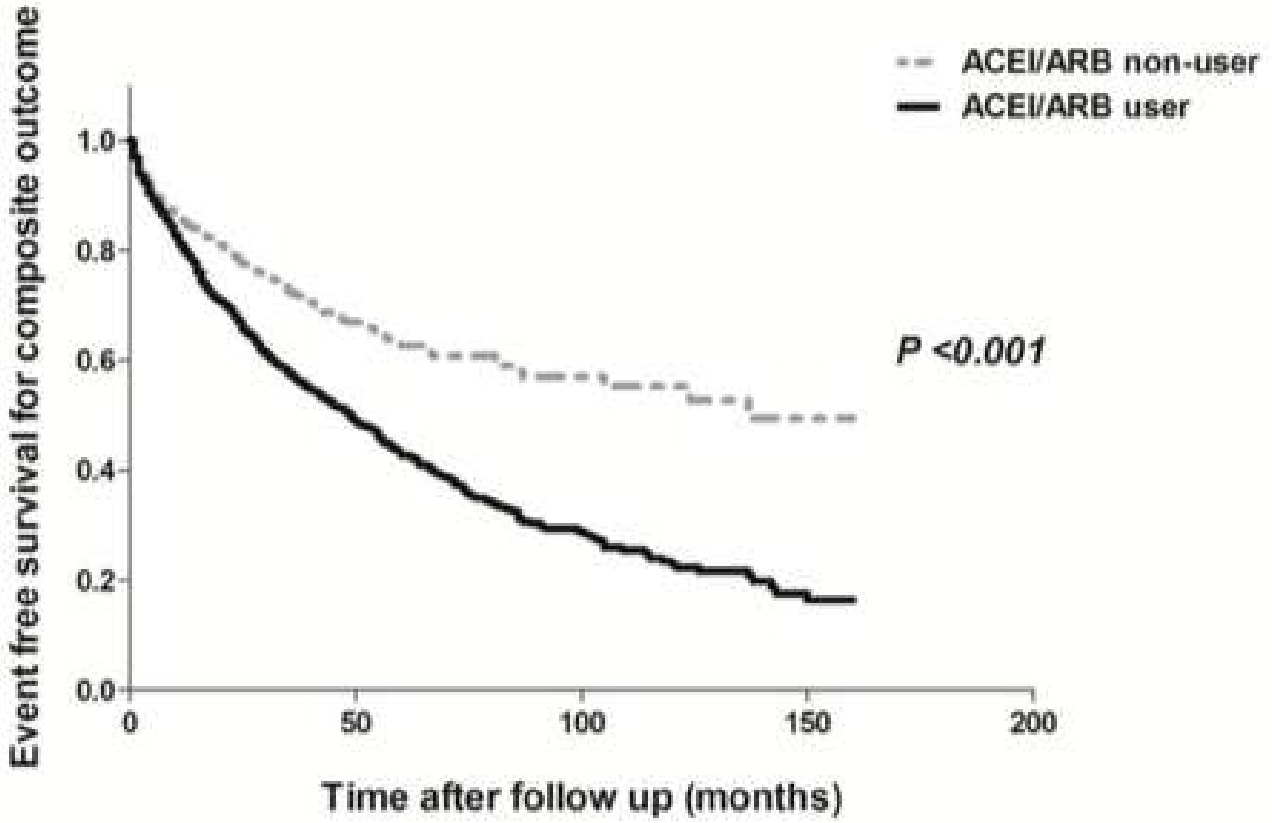
RAAS Blockade on Renal Outcomes and Mortality in Patients with Advanced CKD



Yun Jung Oh et al. PLOS One (2017) 12, e0170874

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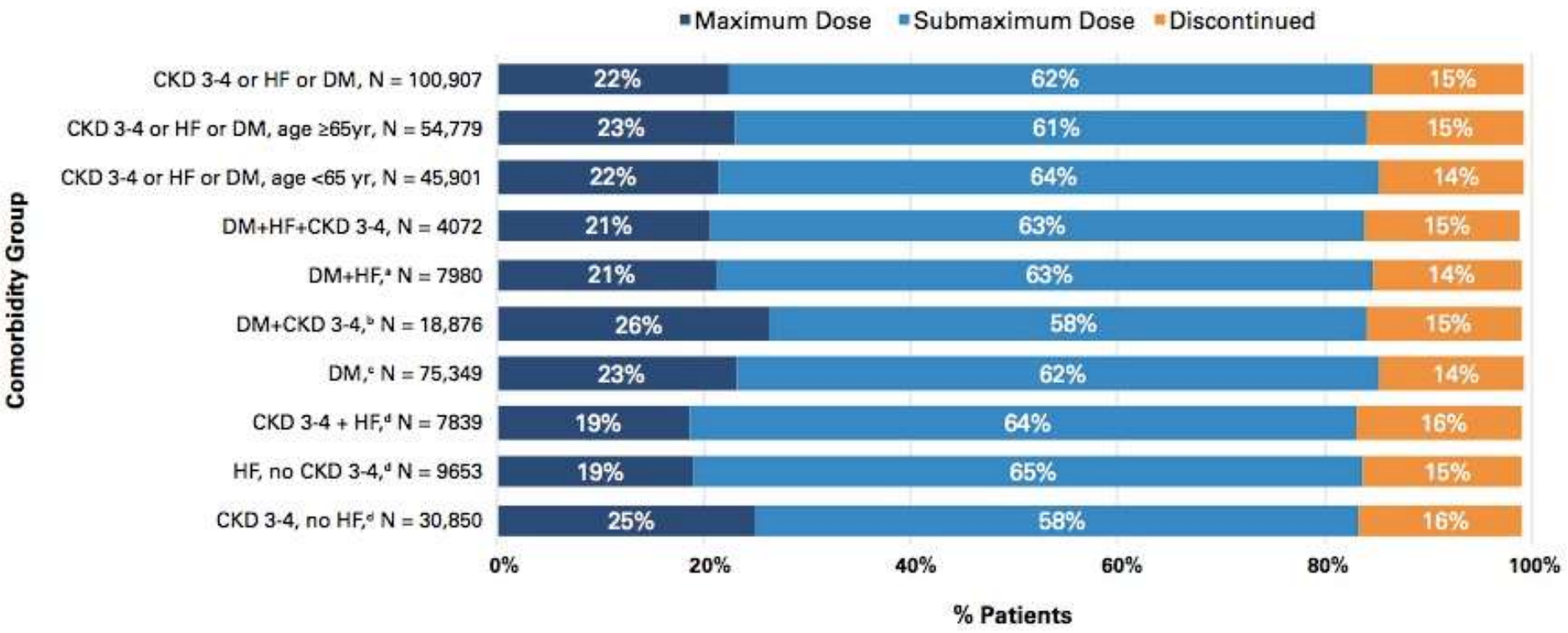
RAAS Blockade und Therapie-Erfolg



Epstein et al. Am J Manag Care. 2015;21:S212-S220

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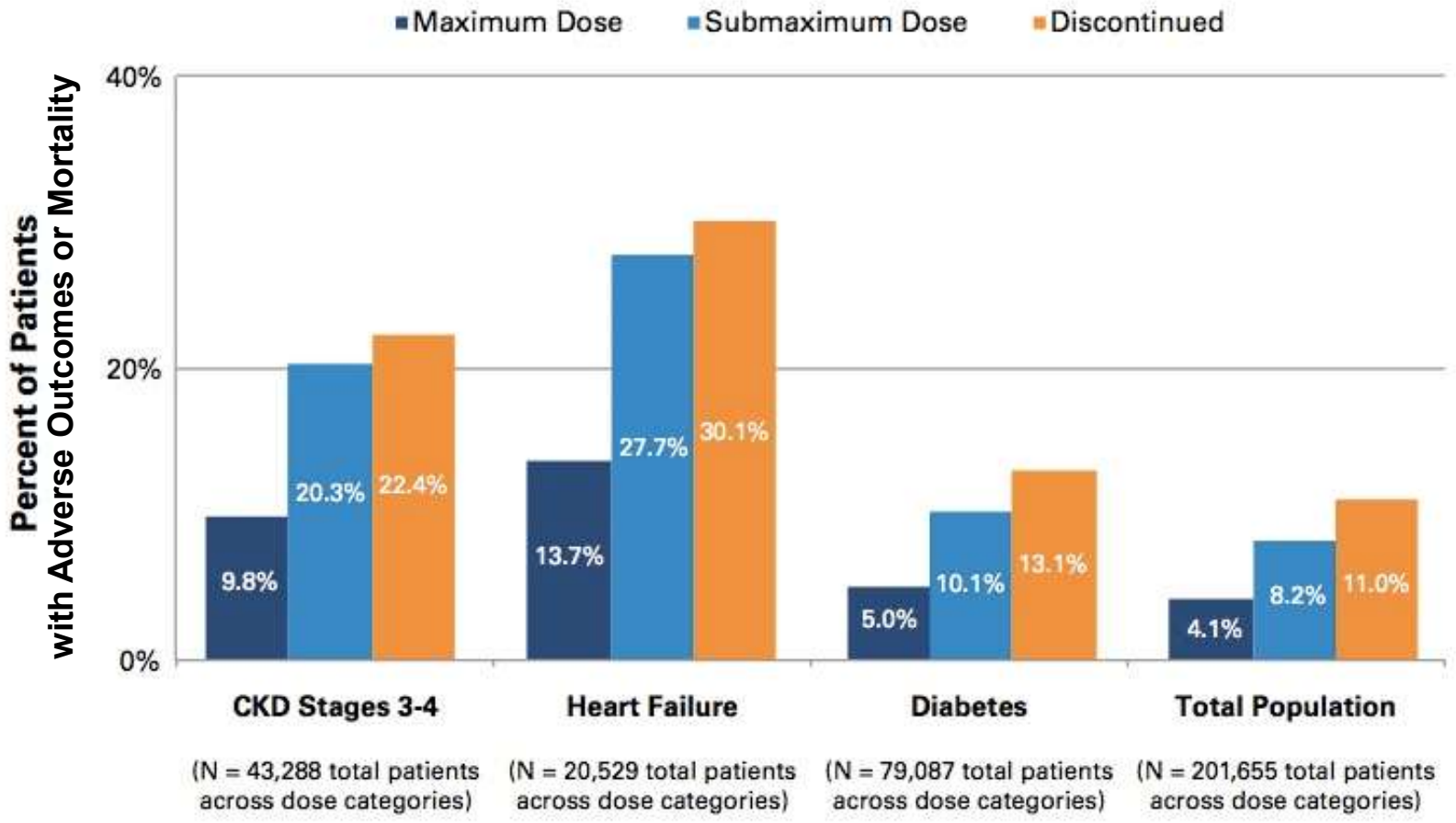
RAAS Blockade und Therapie-Erfolg



Maximale RAAS Blockade schützt

Epstein et al. Am J Manag Care. 2015;21:S212-S220

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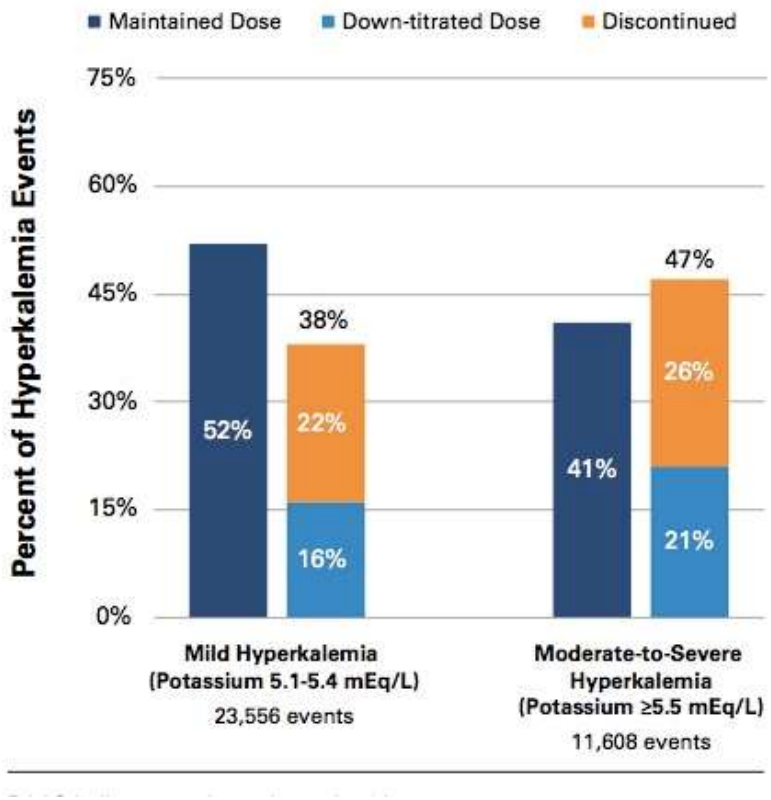
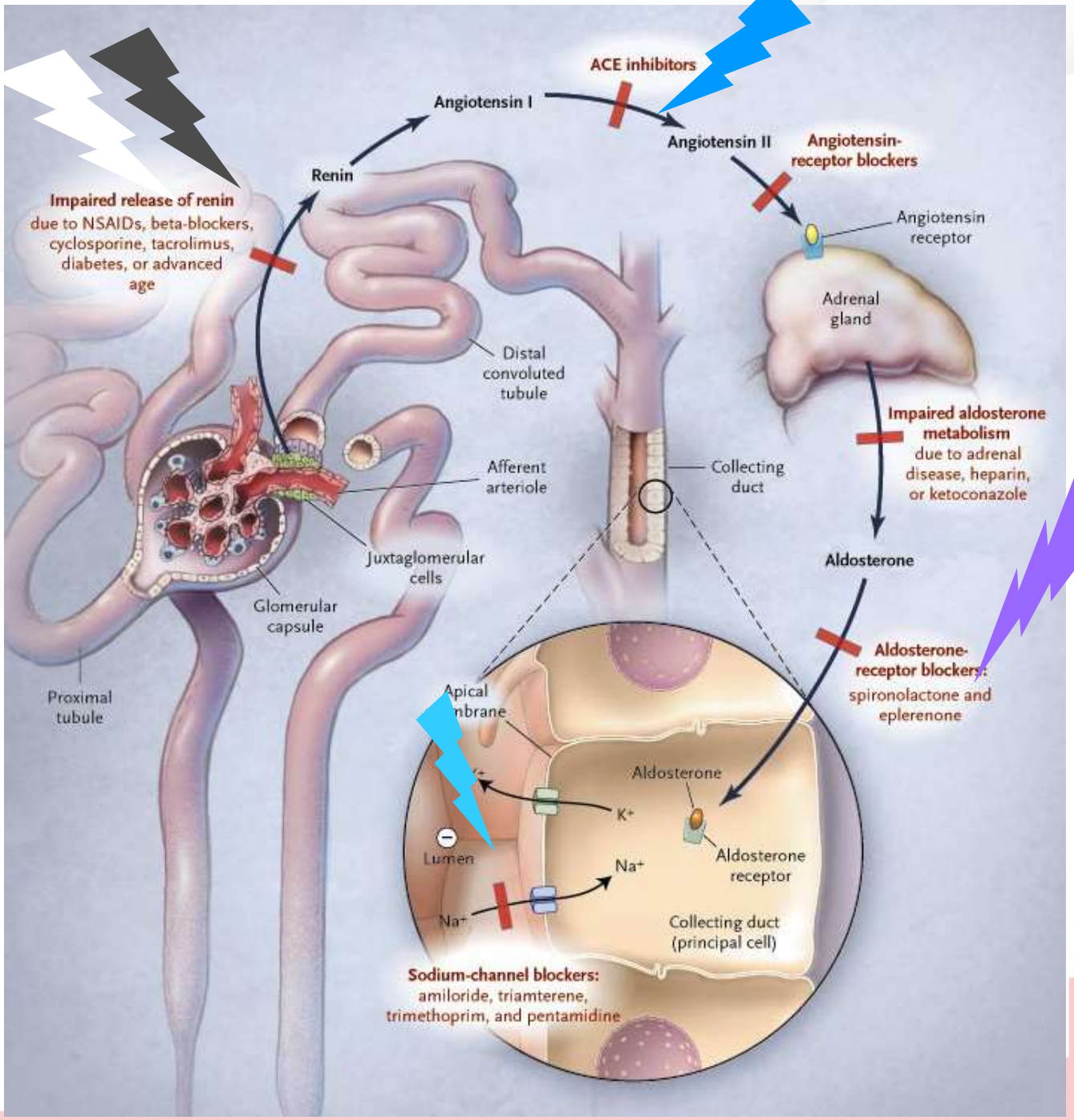
RAAS Blockade und Hyperkaliämie



Epstein et al. Am J Manag Care. 2015;21:S212-S220



NSAR

ACE-Hemmer

ß-Blocker

Spironolakton

Amilorid

Niereninsuffizienz
Diabetes

Palmer, NEJM 2004

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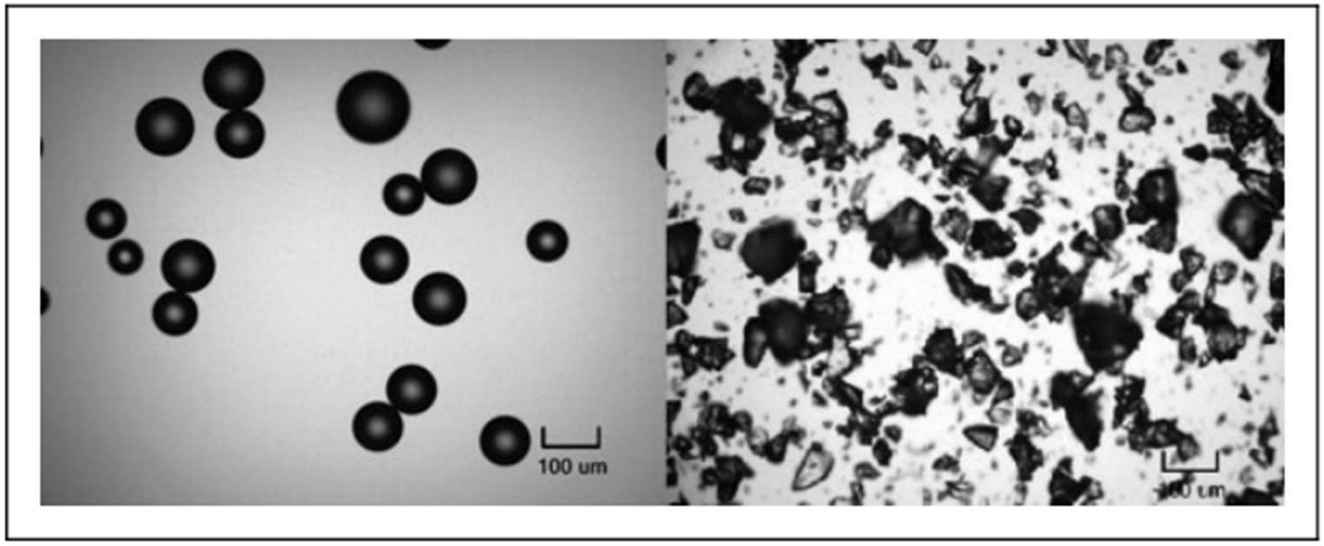
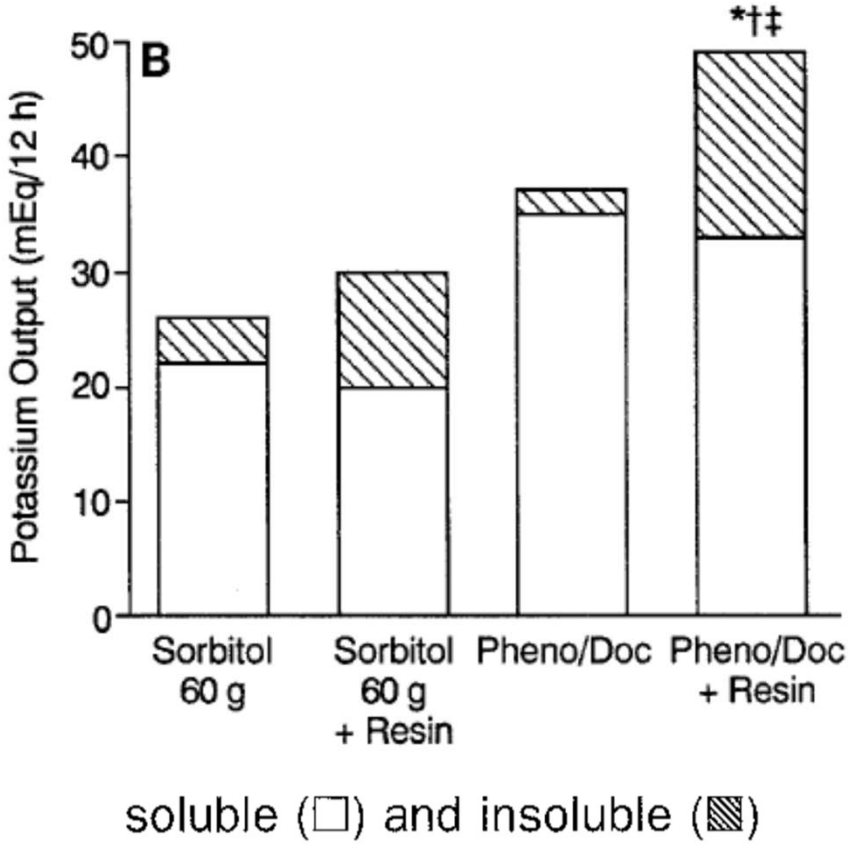
Patiromer vs Resonium (SPS)



- Sphärisches Polymer
- Austauschion Calcium
- Bindung von 8.5 mmol Kalium pro Gramm Patiromer

Li L. et al. J Cardiovasc Pharmacol Ther. 2016

Are cation exchange resins effective for the treatment of hyperkalemia?



Emmett et al., GASTROENTEROLOGY 1995;108:752-760

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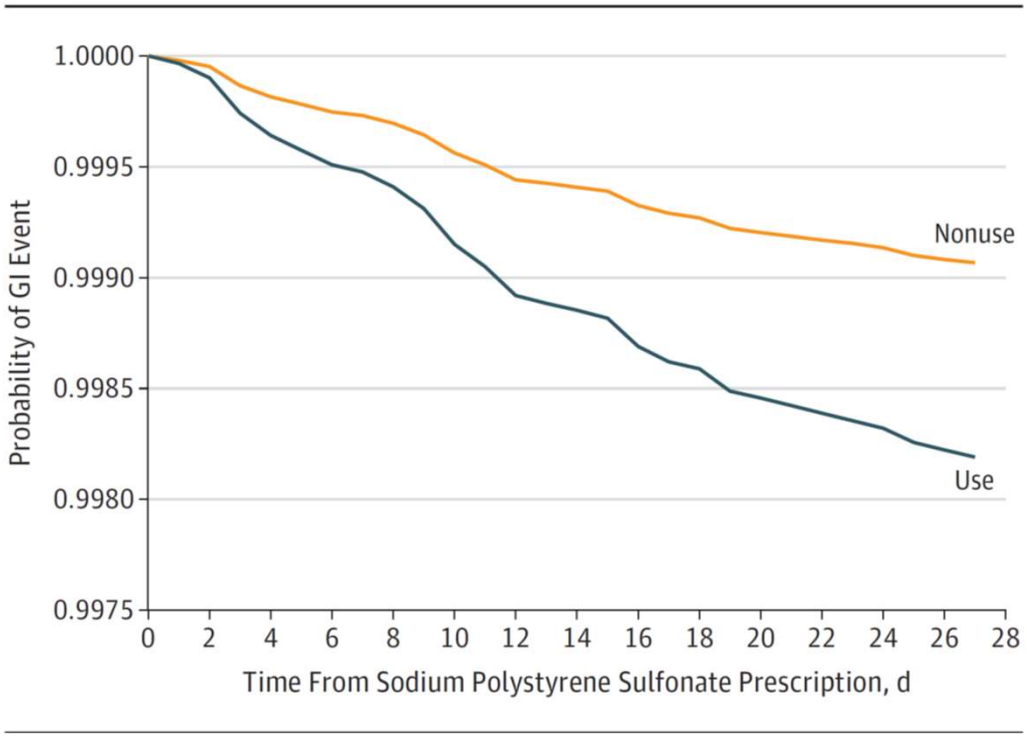
JAMA Internal Medicine | Original Investigation

Risk of Hospitalization for Serious Adverse Gastrointestinal Events Associated With Sodium Polystyrene Sulfonate Use in Patients of Advanced Age

J. Ariana Noel, MD; Sarah E. Bota, BSc; William Petrcich, MSc; Amit X. Garg, MD; Juan Jesus Carrero, PhD; Ziv Harel, MD; Navdeep Tangri, MD; Edward G. Clark, MD; Paul Komenda, MD; Manish M. Sood, MD

Population-based, retrospective matched cohort study, 1 853 866 patients



higher risk of an adverse GI event over the following 30 days
37 events [0.2%]; incidence rate, vs 18 events [0.1%]; incidence rate,

Noel et al., JAMA Intern Med., 2019

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Studienprogramm Patiromer

Research

Original Investigation

Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease
The AMETHYST-DN Randomized Clinical Trial

George L. Bakris, MD; Bertram Pitt, MD; Matthew R. Weir, MD; Mason W. Freeman, MD; Martha R. Mayo, PharmD; Dahlia Garza, MD; Yuri Stasiv, PhD; Rezi Zawadzki, DrPH; Lance Berman, MD; David A. Bushinsky, MD; for the AMETHYST-DN Investigators

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 15, 2015 VOL. 372 NO. 3

Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors

Matthew R. Weir, M.D., George L. Bakris, M.D., David A. Bushinsky, M.D., Martha R. Mayo, Pharm.D., Dahlia Garza, M.D., Yuri Stasiv, Ph.D., Janet Wittes, Ph.D., Heidi Christ-Schmidt, M.S.E., Lance Berman, M.D., and Bertram Pitt, M.D., for the OPAL-HK Investigators*

European Heart Journal (2011) 32, 820–828
doi:10.1093/eurheartj/ehq502

FASTTRACK CLINICAL

Evaluation of the efficacy and safety of RLY5016, a polymeric potassium binder, in a double-blind, placebo-controlled study in patients with chronic heart failure (the PEARL-HF) trial

Bertram Pitt[1]*, Stefan D. Anker[2,3], David A. Bushinsky[4], Dalane W. Kitzman[5], Faiez Zannad[6], and I-Zu Huang[7], on behalf of the PEARL-HF Investigators

[1]University of Michigan, Ann Arbor, MI, USA; [2]Department of Cardiology, Charité Medical School, Applied Cachexia Research, Campus Virchow-Klinikum, Berlin, Germany; [3]Centre for Clinical and Basic Research, IRCCS San Raffaele, Rome, Italy; [4]University of Rochester School of Medicine, Rochester, NY, USA; [5]Wake Forest University School of Medicine, Winston-Salem, NC, USA; [6]Department of Cardiology, Inserm, Centre d'Investigation Clinique 9501 and U 961, CHU Nancy, Nancy, France; and [7]Relypsa, Santa Clara, CA, USA

Received 10 September 2010; revised 3 December 2010; accepted 14 December 2010; online publish-ahead-of-print 5 January 2011

Research

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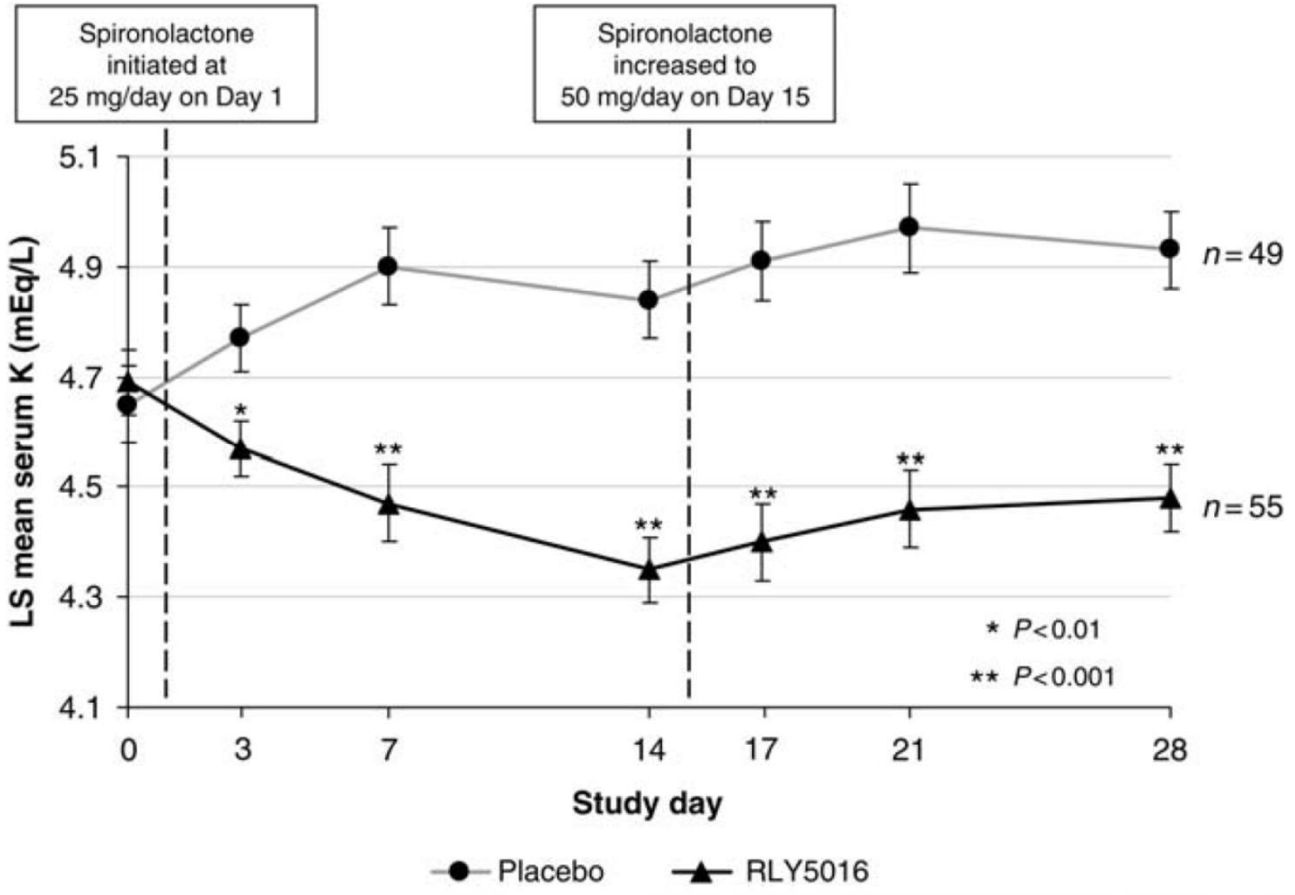
Primärer Endpunkt: Serumkalium



Pitt B. et al. Eur Heart J. 2011

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Nebenwirkungen

	Placebo (n = 49)	Patiromer (n = 56)
Unerwünschte Ereignisse (UE)	15 (31 %)	30 (54 %)
Zahl der Patienten mit mindestens 1 GI UE	3 (6 %)	12 (21 %)
• Flatulenz	0	4 (7 %)
• Diarrhoe	1 (2 %)	3 (5 %)
• Obstipation	0	3 (5 %)
• Erbrechen	0	2 (4 %)
Schwerwiegende UE	2 (4 %)	2 (4 %)
• Insgesamt	0	0
• In Zusammenhang mit Studienmedikation		
Todesfälle	1 (2 %)	0 (0 %)
UE bedingter Studienabbruch	3 (6 %)	4 (7 %)

Pitt B, et al. Eur Heart J. 2011;32:820-828

Klinikum St.GEORG

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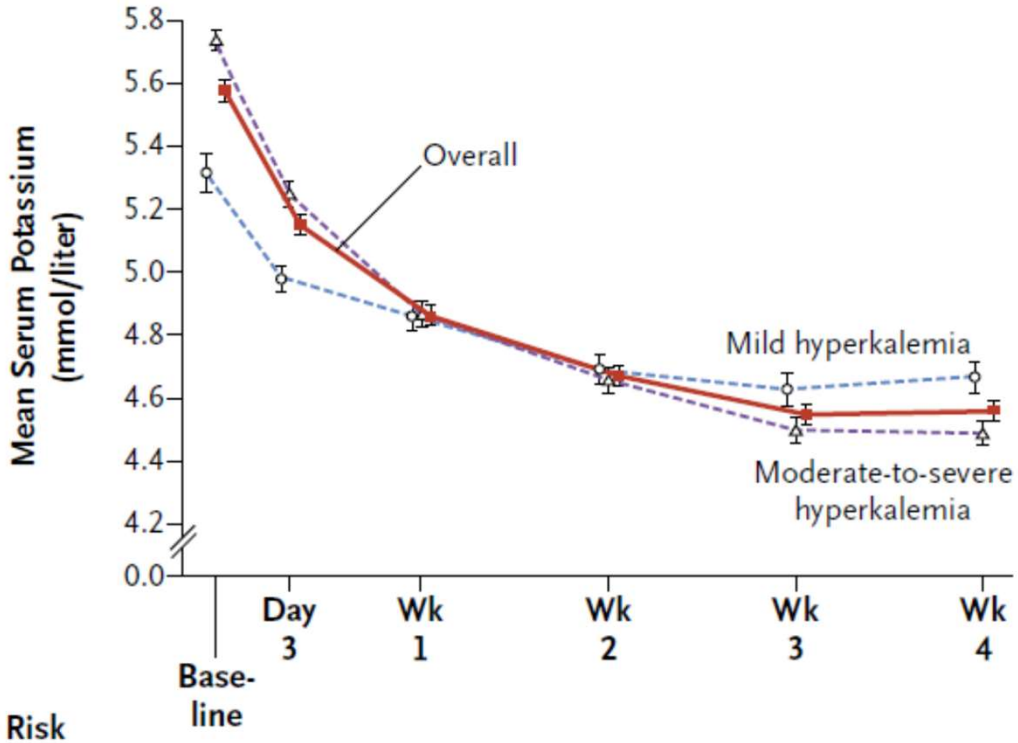
Verlauf der Serumkaliumspiegel



No. at Risk	Base-line	Day 3	Wk 1	Wk 2	Wk 3	Wk 4
Overall	243	217	237	228	221	219
Mild hyperkalemia	92	80	90	87	85	85
Moderate-to-severe hyperkalemia	151	137	147	141	136	134

Weir et al., N Engl J Med 2015;372:211-21

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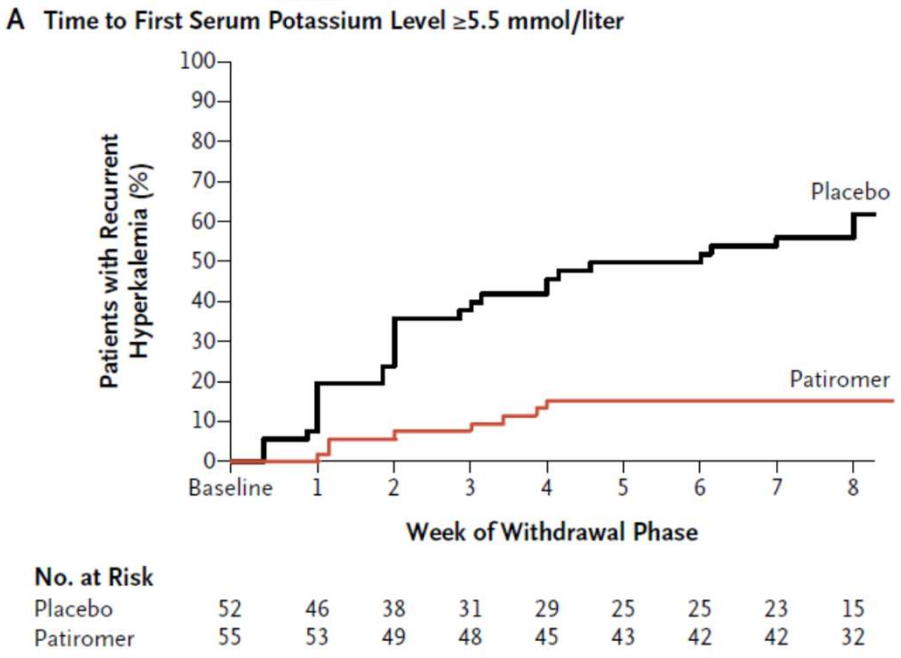
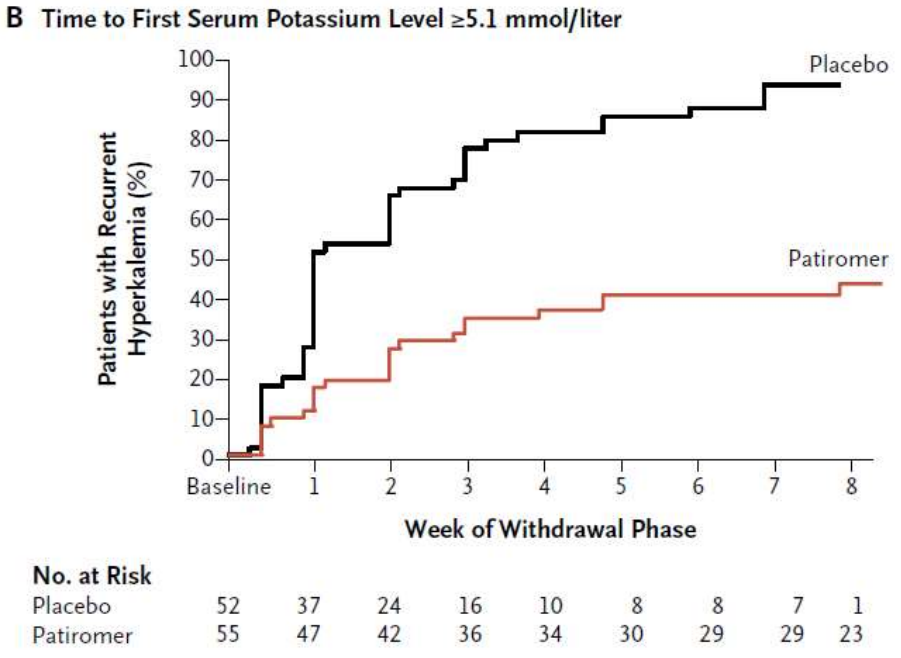
Wiederauftreten von Hyperkaliämie





Weir et al., N Engl J Med 2015;372:211-21

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Research

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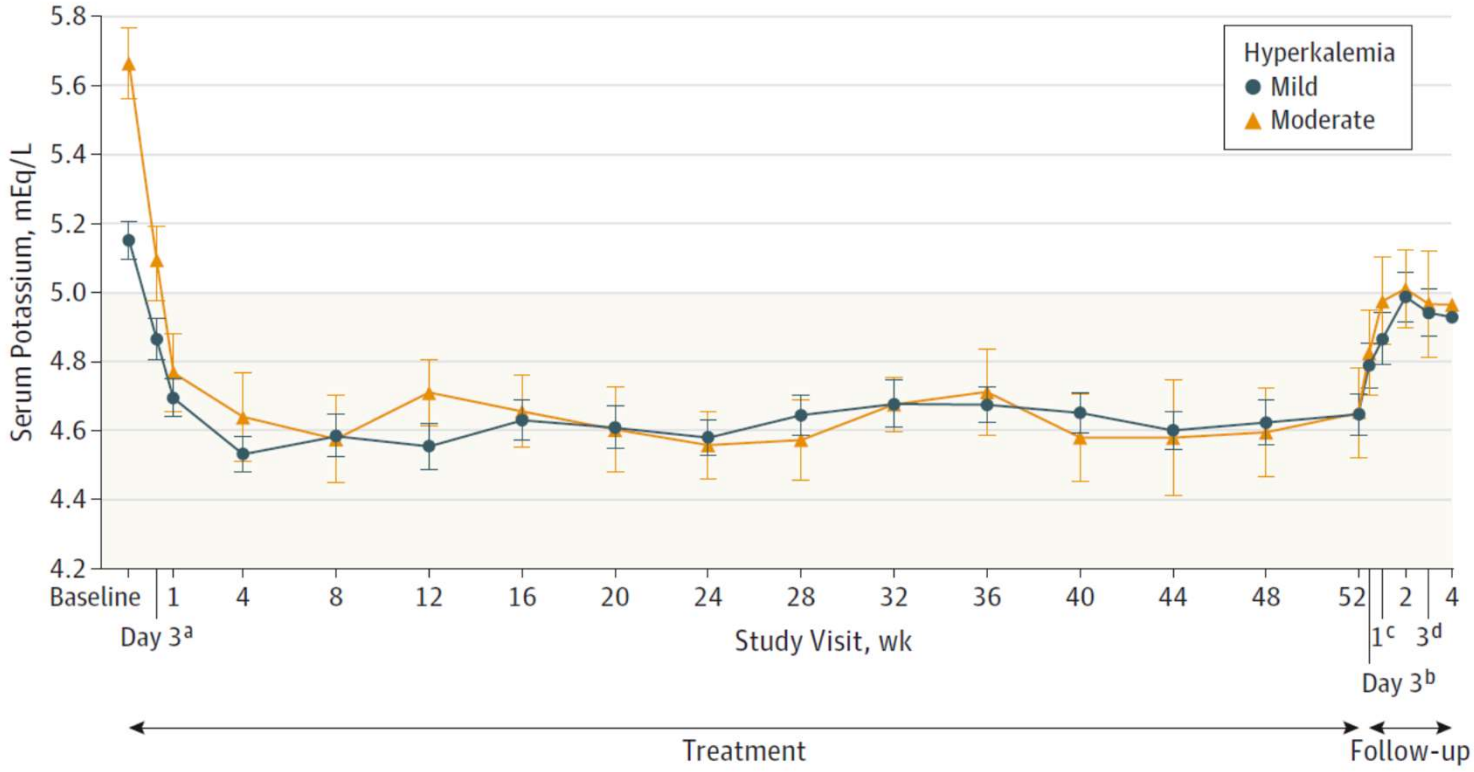
Serum Potassium Levels Over 52 Weeks



No. of patients

Hyperkalemia																	
Mild	218	204	199	192	175	168	161	161	163	158	156	151	148	149	145	131	126
Moderate	83	83	73	70	65	62	62	62	61	53	53	53	52	49	49	48	47

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Patiromer for hyperkalemia under RAASi

Enables ongoing RAASi therapy!

hard to resist

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DIAMOND trial

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site

Home > Search Results > Study Record Detail

Save this study

Patiromer for the Management of Hyperkalemia in Subjects Receiving RAASi Medications for the Treatment of Heart Failure (DIAMOND) (DIAMOND)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03888066

Recruitment Status : Recruiting
First Posted : March 25, 2019
Last Update Posted : May 27, 2019

See Contacts and Locations

Sponsor:
Relypsa, Inc.

Collaborator:
Vifor Pharma

Information provided by (Responsible Party):
Relypsa, Inc.

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description Go to

Brief Summary:
The purpose of this study is to determine if patiromer treatment of subjects who developed hyperkalemia while receiving RAASi medications will result in continued use of RAASi medications in accordance with heart failure (HF) treatment guidelines and thereby decrease the occurrence of the combined endpoint of cardiovascular (CV) death and CV hospitalization events compared with placebo treatment.

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What about „Eisen“ ?

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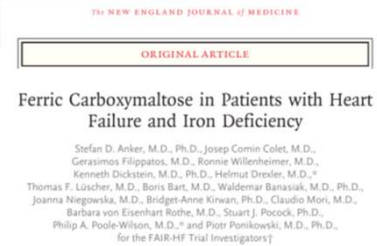

THE NEW ENGLAND JOURNAL of MEDICINE

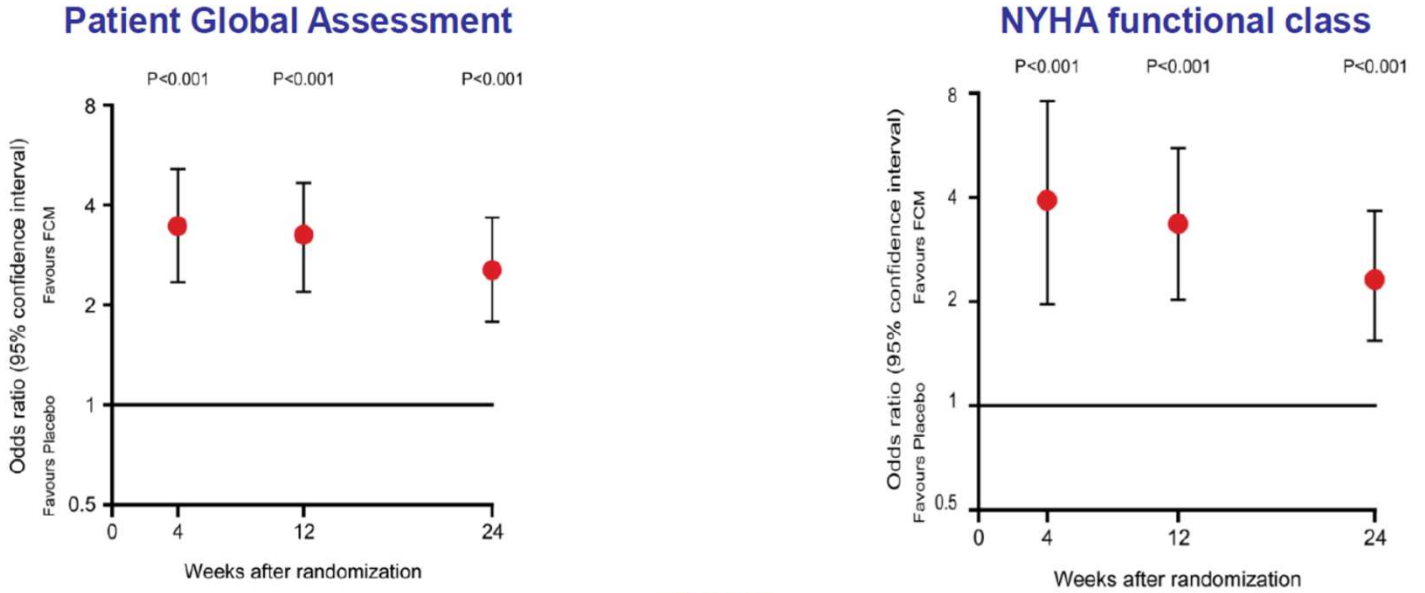
ORIGINAL ARTICLE

Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency

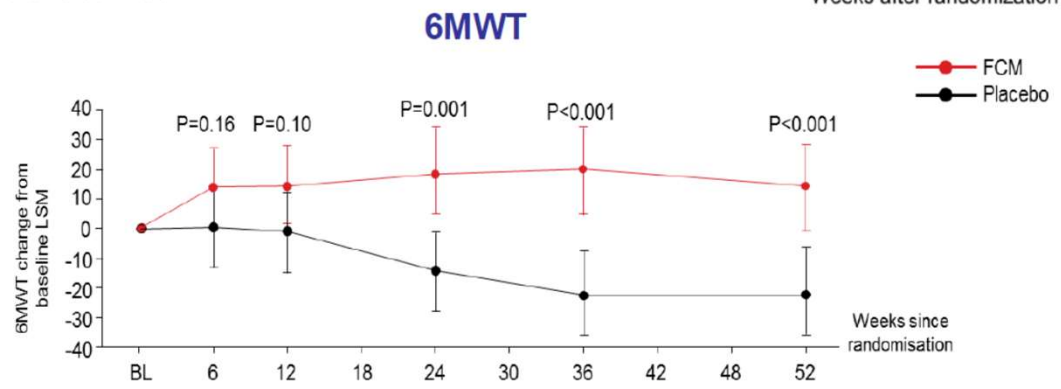
Stefan D. Anker, M.D., Ph.D., Josep Comin Colet, M.D., Gerasimos Filippatos, M.D., Ronnie Willenheimer, M.D., Kenneth Dickstein, M.D., Ph.D., Helmut Drexler, M.D., Thomas F. Lüscher, M.D., Boris Bart, M.D., Waldemar Banasiak, M.D., Ph.D., Joanna Niegowska, M.D., Bridget-Anne Kirwan, Ph.D., Claudio Mori, M.D., Barbara von Eisenhart Rothe, M.D., Stuart J. Pocock, Ph.D., Philip A. Poole-Wilson, M.D., and Piotr Ponikowski, M.D., Ph.D., for the FAIR-HF Trial Investigators

Effekte von Ferrocarboxymaltose in HFrEF:
FAIR-HF and CONFIRM-HF

FAIR-HF[1]



CONFIRM-HF[2]



improves symptoms, functional capacity, and quality of life

1. Anker SD, et al. *N Engl J Med* 2009;361:2436-48
2. Ponikowski P, et al. *Eur Heart J* 2015;36:657-68.

Klinikum St.GEORG

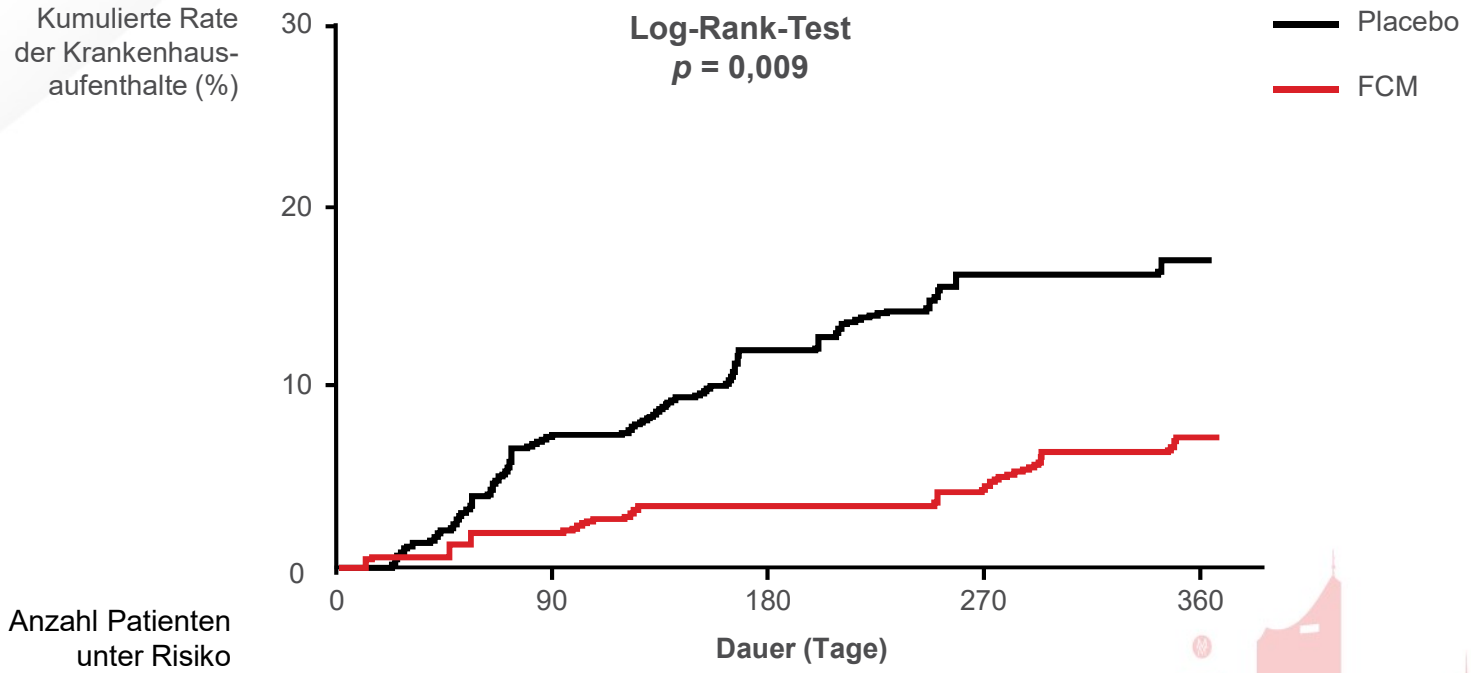
European Heart Journal (2015) 36, 657–668
doi:10.1093/eurheartj/ehu385

FASTTRACK ESC HOT LINE
Heart failure/cardiomyopathy

Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency[‡]

Piotr Ponikowski[1,2*], Dirk J. van Veldhuisen[3], Josep Comin-Colet[4], Georg Ertl[5,6], Michel Komajda[7], Viacheslav Mareev[8], Theresa McDonagh[9], Alexander Parkhomenko[10], Luigi Tavazzi[11], Victoria Levesque[12], Claudio Mori[12], Bernard Roubert[12], Gerasimos Filippatos[13], Frank Ruschitzka[14], and Stefan D. Anker[15], for the CONFIRM-HF Investigators

Erster Krankenhausaufenthalt aufgrund sich verschlechternder Herzinsuffizienz



Anzahl Patienten unter Risiko					
Placebo	151	138	127	117	78
FCM	150	140	131	126	77

Ponikowski et al. Eur Heart J 2015;36:657–668.

Klinikum St.GEORG

RED-HF Studie – Keine Effekte auf die Hospitalisierungsrate unter Darboetin alfa im Vergleich zum Placebo

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Anemia with Darbepoetin Alfa in Systolic Heart Failure

Karl Swedberg, M.D., Ph.D., James B. Young, M.D., Inder S. Anand, M.D., Sunfa Cheng, M.D., Akshay S. Desai, M.D., Rafael Diaz, M.D., Aldo P. Maggioni, M.D., John J.V. McMurray, M.D., Christopher O'Connor, M.D., Marc A. Pfeffer, M.D., Ph.D., Scott D. Solomon, M.D., Yan Sun, M.S., Michal Tendera, M.D., and Dirk J. van Veldhuisen, M.D., Ph.D., for the RED-HF Committees and Investigators*

Death from Cardiovascular Causes or First Hospitalization for Worsening Heart Failure

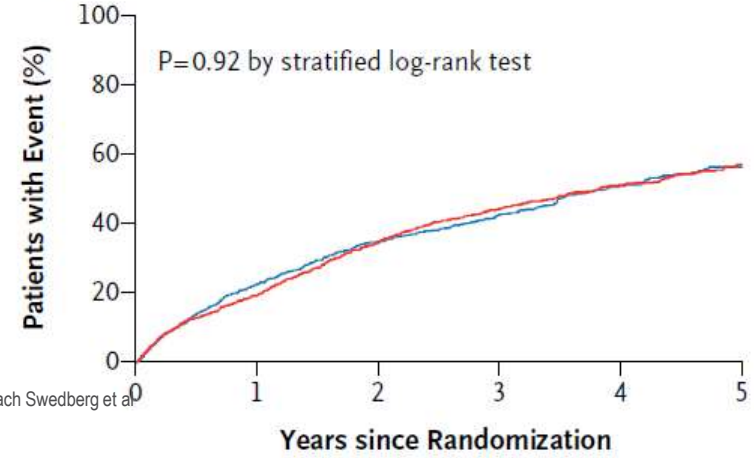


Abbildung nach Swedberg et al

No. at Risk

Placebo	1142	956	818	695	591	497	395	290	211	154	92
Darbepoetin alfa	1136	975	855	712	581	473	385	281	212	161	101

Swedberg K et al. N Engl J Med 2013; 368:1210-1219

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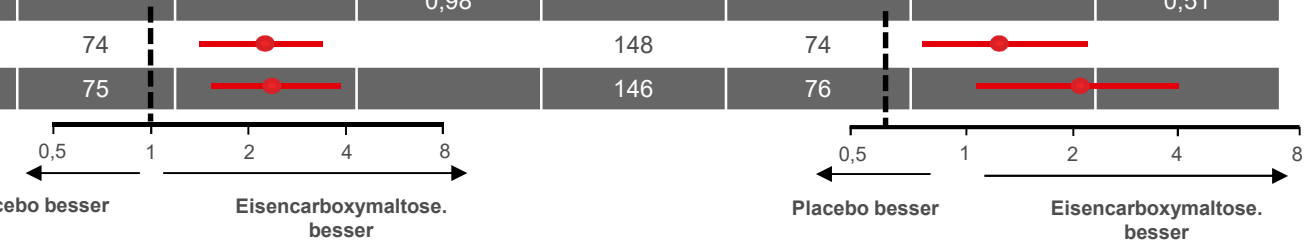
Eisencarboxymaltose (i.v.) verbessert PGA und NYHA-Klasse bei Herzinsuffizienzpatienten **mit und ohne** Anämie

	Selbst berichtete globale Patientenbeurteilung				Funktionsklassen nach NYHA			
Teilgruppe	Eisen-carboxy-maltose, n	Placebo, n	Odds Ratio (95%-KI)	*p*-Wert für Interaktion	Eisen-carboxy-maltose, n	Placebo, n	Odds Ratio (95%-KI)	*p*-Wert für Interaktion
Hämoglobin				0,98				0,51
≤12,0 g/dl	146	74			148	74		
>12,0 g/dl	146	75			146	76		



Filippatos et al., European Journal of Heart Failure (2013) 15, 1267–1276

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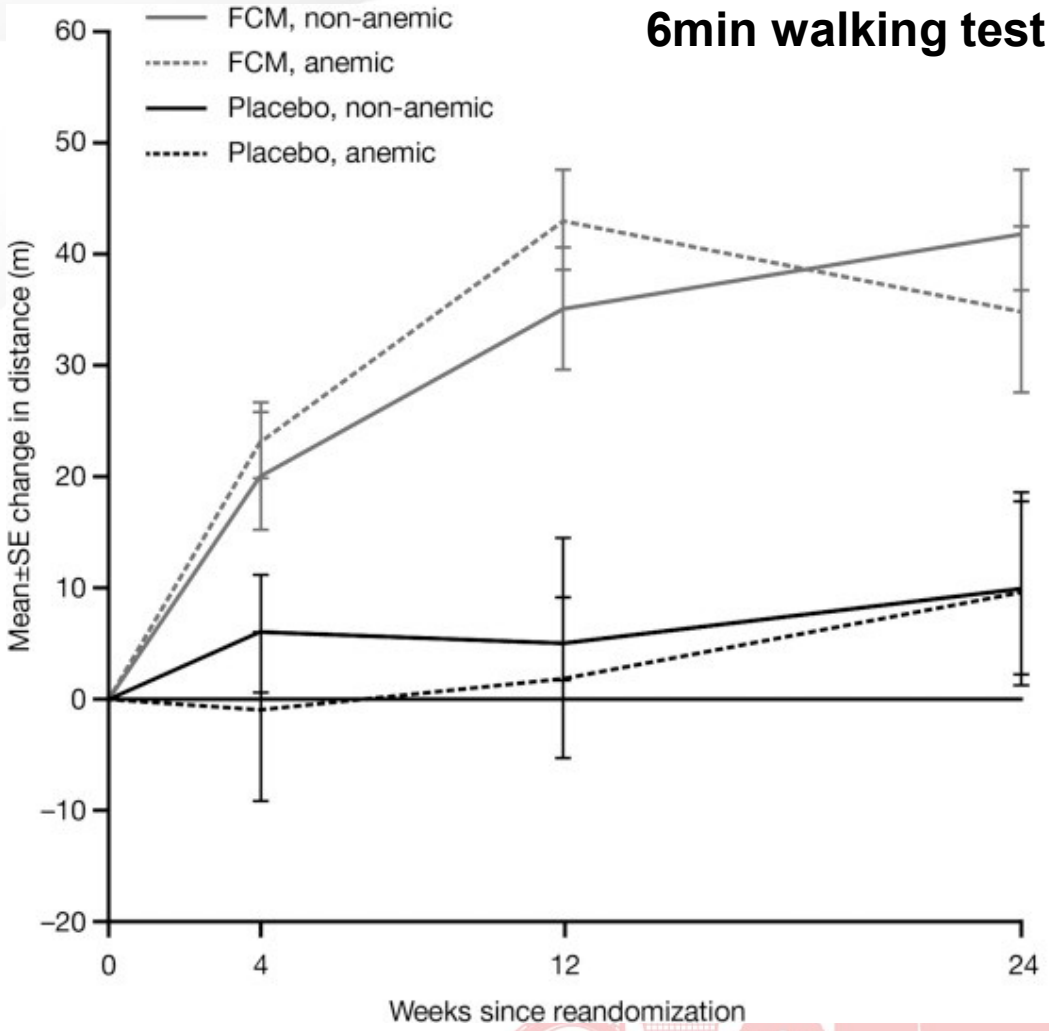
i.v. ferric carboxymaltose in CHF patients with and w/o anaemia

6min walking test



P treatment effect		P
Anemic	Week 4	<0.001
	Week 12	<0.001
	Week 24	0.01
Non-anemic	Week 4	0.04
	Week 12	0.002
	Week 24	<0.001

Filippatos et al., European Journal of Heart Failure (2013) 15, 1267–1276

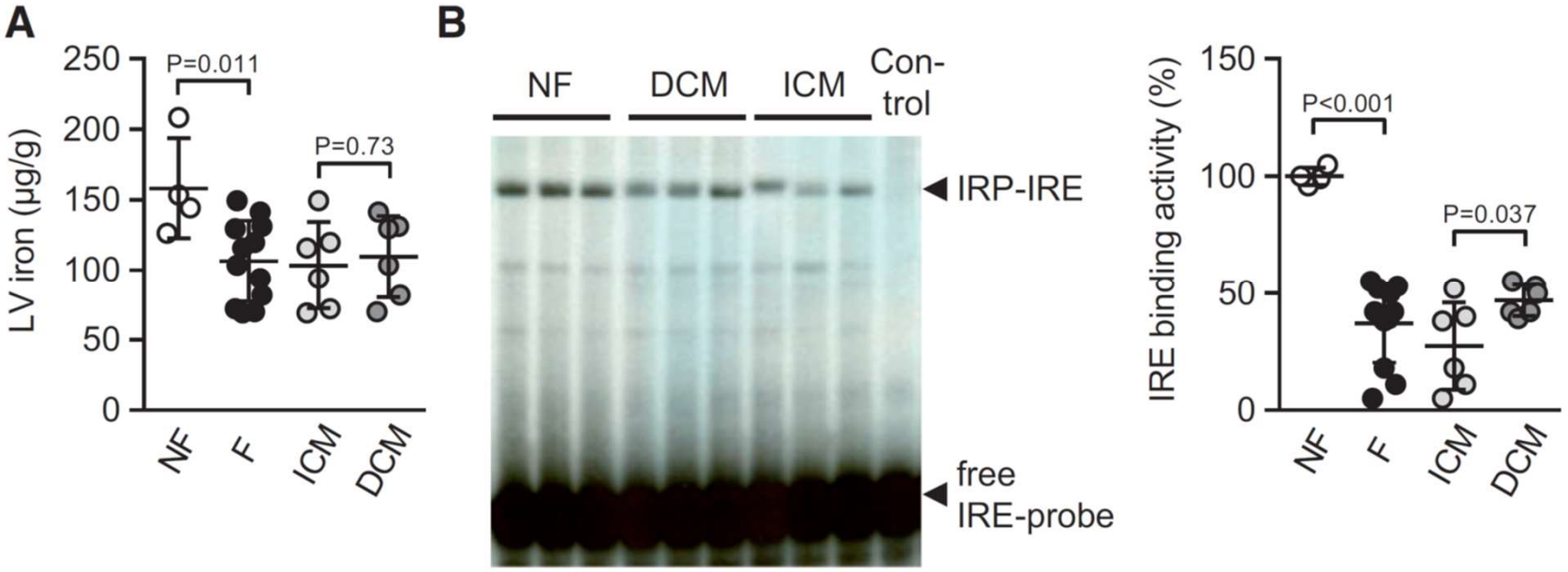
Klinikum St.GEORG

European Heart Journal (2017) 38, 362–372
doi:10.1093/eurheartj/ehw333

BASIC SCIENCE

Iron-regulatory proteins secure iron availability in cardiomyocytes to prevent heart failure

Saba Haddad[1,2], Yong Wang[1,2], Bruno Galy[3,4], Mortimer Korf-Klingebiel[1,2], Valentin Hirsch[1,2], Abdul M. Baru[1,2], Fatemeh Rostami[1,2], Marc R. Reboll[1,2], Jörg Heineke[2], Ulrich Flögel[5], Stephanie Groos[6], André Renner[7], Karl Toischer[8], Fabian Zimmermann[9], Stefan Engeli[10], Jens Jordan[10], Johann Bauersachs[2], Matthias W. Hentze[3]. Kai C. Wollert[1,2]. and Tibor Kempf[1,2]*



Haddad et al., European Heart Journal (2017) 38, 362–372

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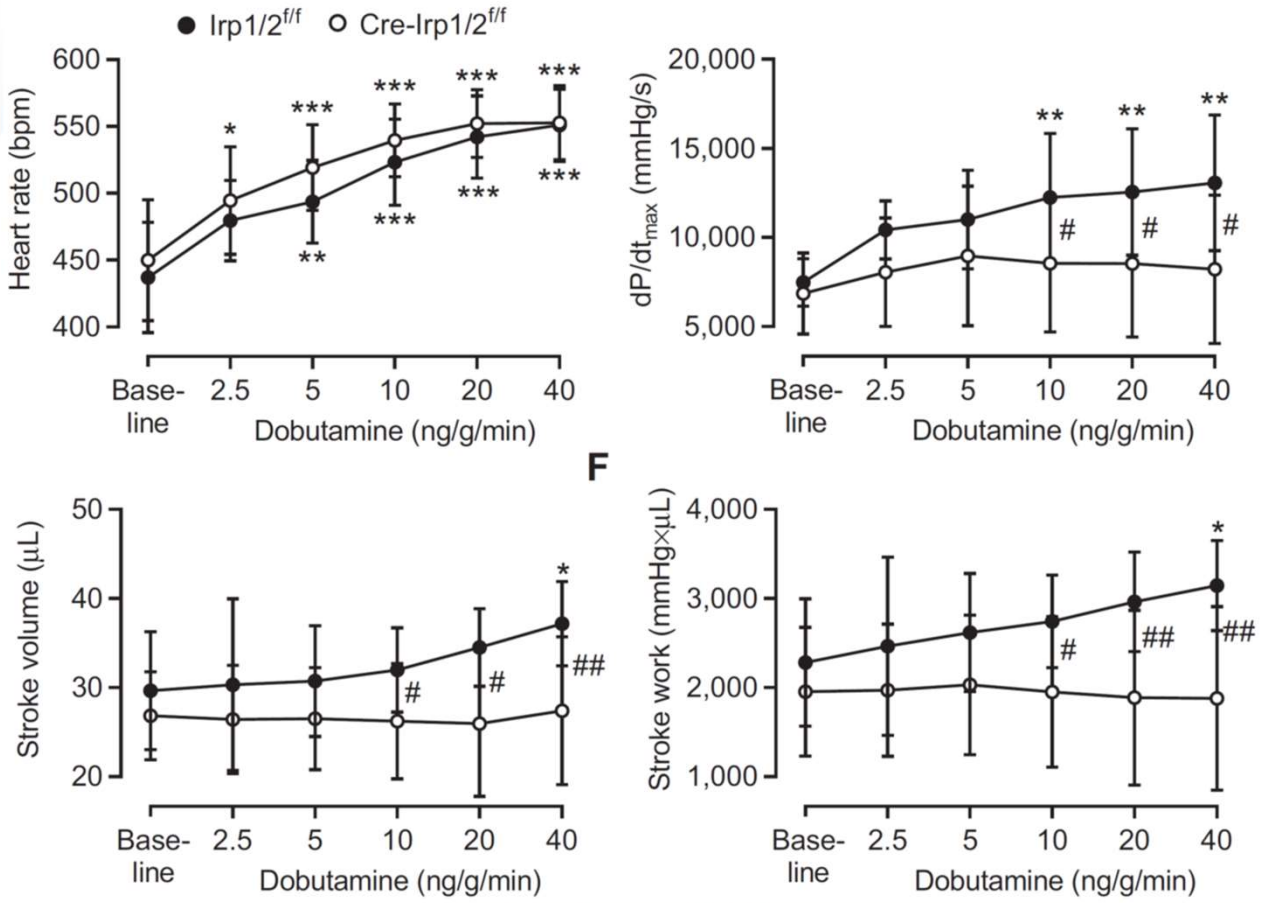
Eisenmangel und myokardiale Dysfunktion



Haddad et al., European Heart Journal (2017) 38, 362–372

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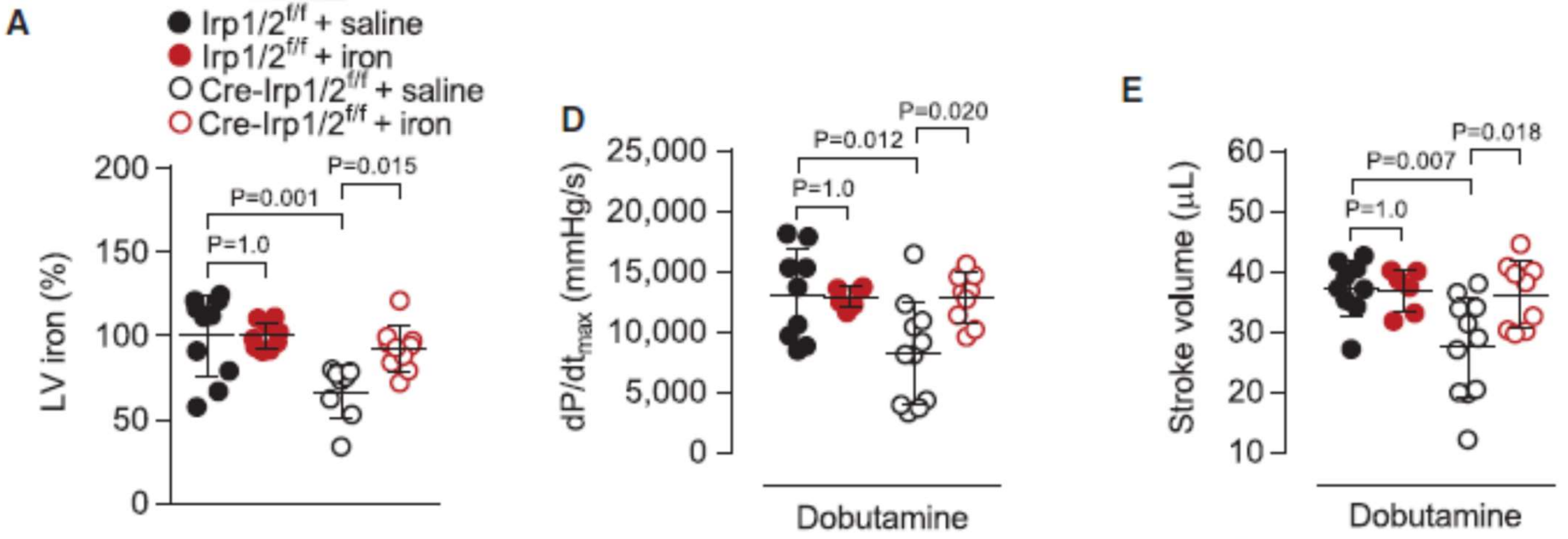
Iron supplementation rescues mitochondrial respiration and inotropic reserve in Irp-targeted mice.



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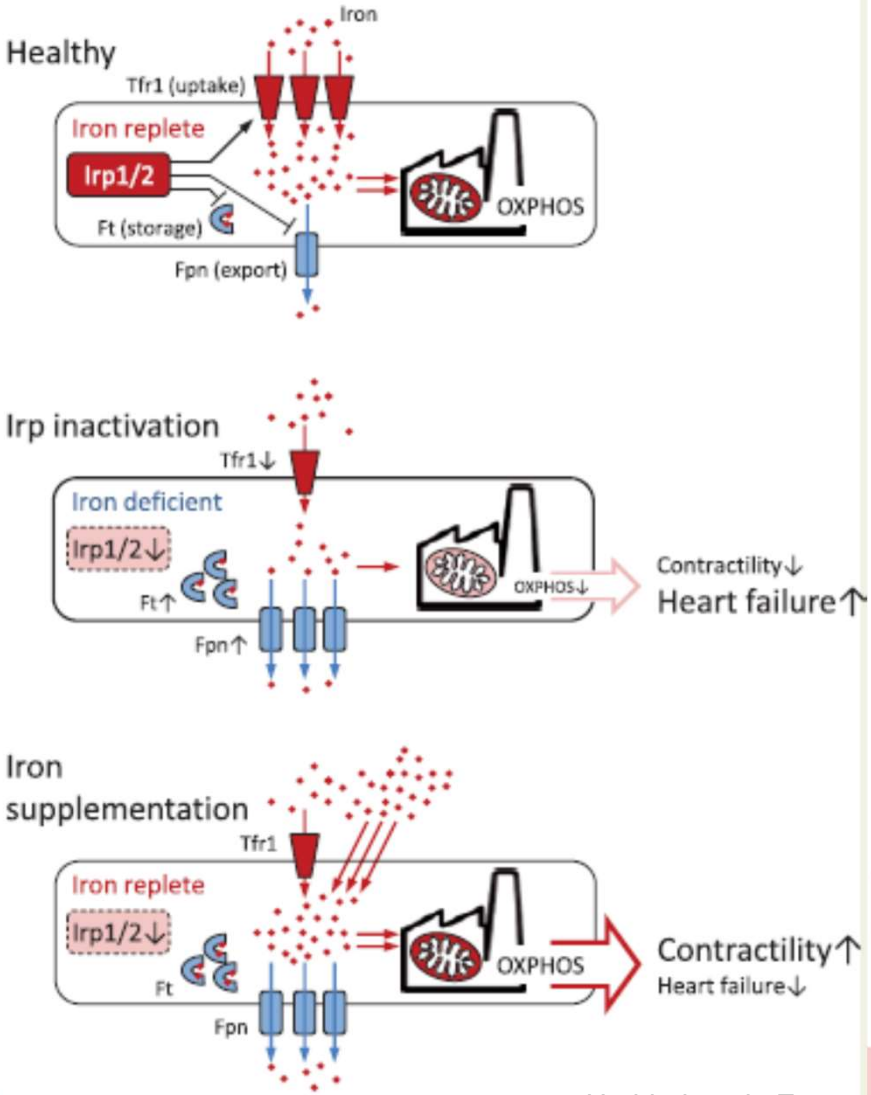
Eisenmangel und myokardiale Dysfunktion

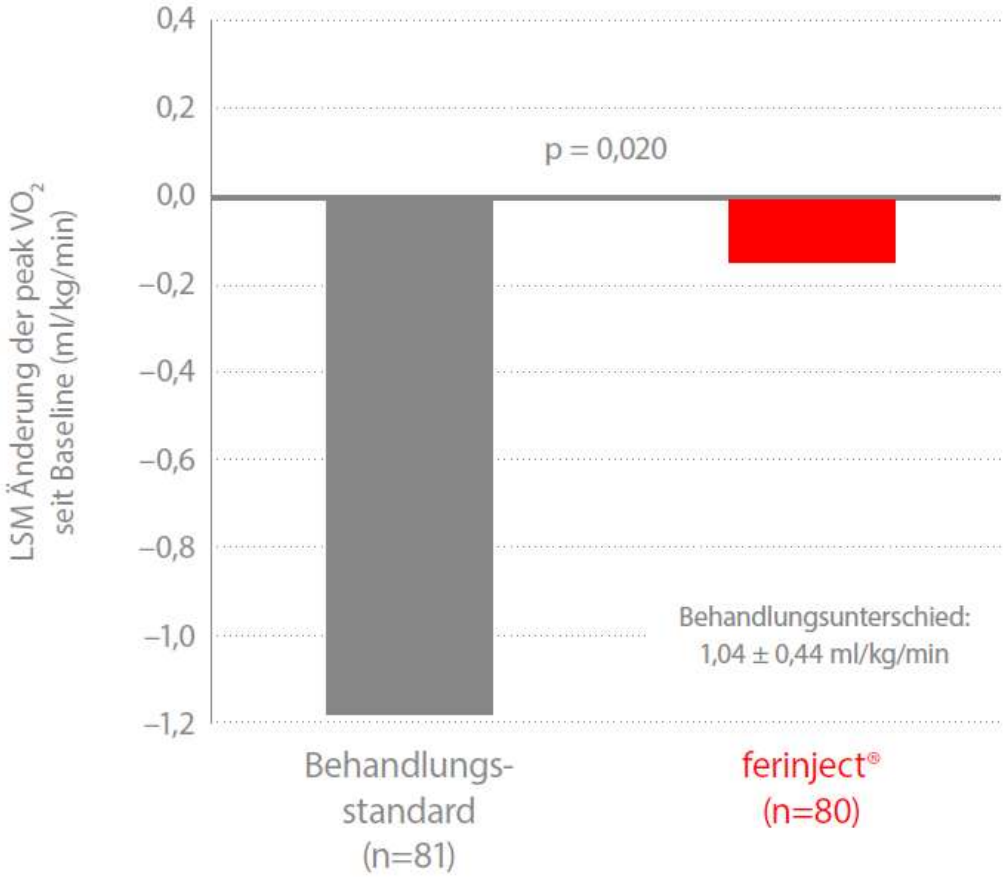


Haddad et al., European Heart Journal (2017) 38, 362–372

Klinikum St.GEORG

EFFECT-HF: iv ferric carboxymatose

Signifikant bessere maximale VO_2 vs. Standardbehandlung in Woche 24*



Van Veldhuisen et al. Circulation 2017

Zusammenfassung

- Kardiorenales Syndrom: venöse Kongestion! Try to dry! Euvolämie herstellen ist das Ziel! Kein Kreatinin-Fetischismus betreiben!
- Patiromer ermöglicht Patienten mit wichtiger Indikation für RAASi-Therapie (Survival Benefit) und Hyperkaliämie die Weiterführung der RAASi-Therapie, relativ wenige NW
- Herzinsuffizienz mit Eisenmangel profitiert signifikant und klinisch relevant von einer intravenösen Eisenrepletion, unabhängig vom Hb
- Orales Eisen hat KEINEN Nutzen bei systolischer Herzinsuffizienz

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Vielen Dank!

Fragen ?

Kontakt: ralph.wendt@sanktgeorg.de

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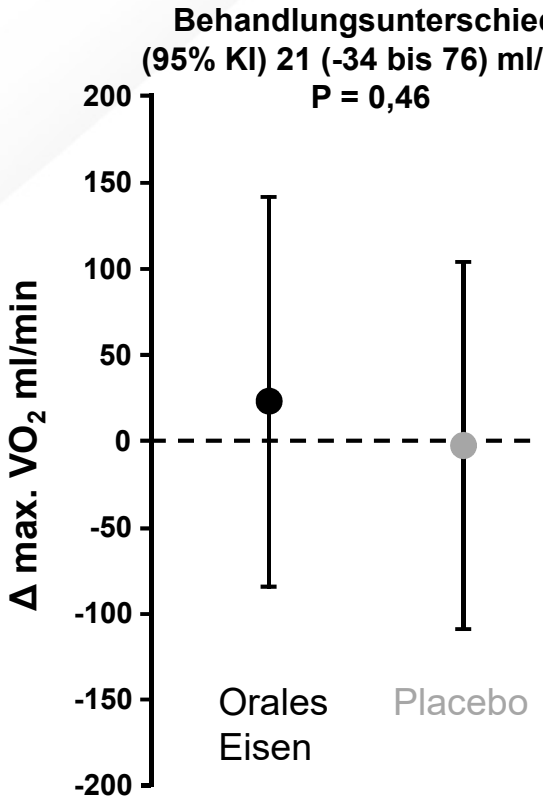
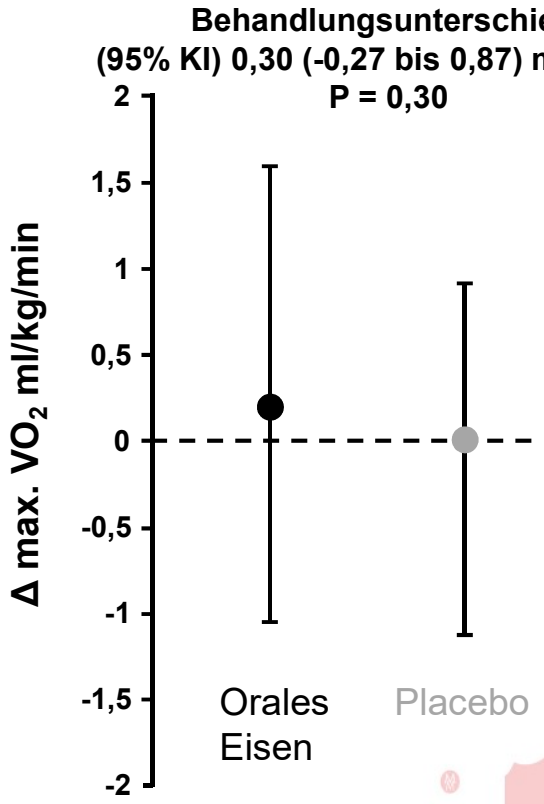
IRONOUT HF: orales Eisen bei HFrEF





Lewis et al., JAMA. 2017;317(19):1958-1966

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IRONOUT HF: Ergebisse Eisenparameter

Iron Indexes	Median (95% CI)				Difference in Change From Baseline (95% CI)	*P* Value
	Week-16 Values		Change From Baseline to Week 16			
	Oral Iron	Placebo	Oral Iron	Placebo		
Iron, µg/dL	80 (59 to 99)	72 (58 to 90)	6 (−12 to 29)	1 (−23 to 18)	11.0 (2.8 to 19.1)	.009
TIBC, µg/dL	371 (336 to 405)	374 (339 to 428)	−12 (−43 to 5)	−0.5 (−22 to 17)	−13.4 (−22.2 to −4.6)	.003
Tsat, %	22 (16 to 28)	20 (15 to 25)	2 (−3 to 7)	0 (−5 to 5)	3.3 (1.1 to 5.4)	.003
Ferritin, ng/ml	95 (58 to 134)	75 (42 to 123)	18 (−8 to 38)	1 (−15 to 17)	11.3 (−0.3 to 22.9)	.06
Hepcidin, ng/ml	8.9 (5.0 to 14.3)	7.8 (4.2 to 12.7)	1.7 (−1.0 to 5.6)	−0.3 (−3.2 to 3.1)	1.5 (−0.6 to 3.7)	.17
sTfR, mg/L	3.7 (2.9 to 4.4)	3.9 (3.1 to 4.8)	−0.3 (−0.8 to 0.1)	0.0 (−0.5 to 0.4)	−0.3 (−0.6 to −0.1)	.01

Lewis et al., JAMA. 2017;317(19):1958-1966

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FIND CKD trial

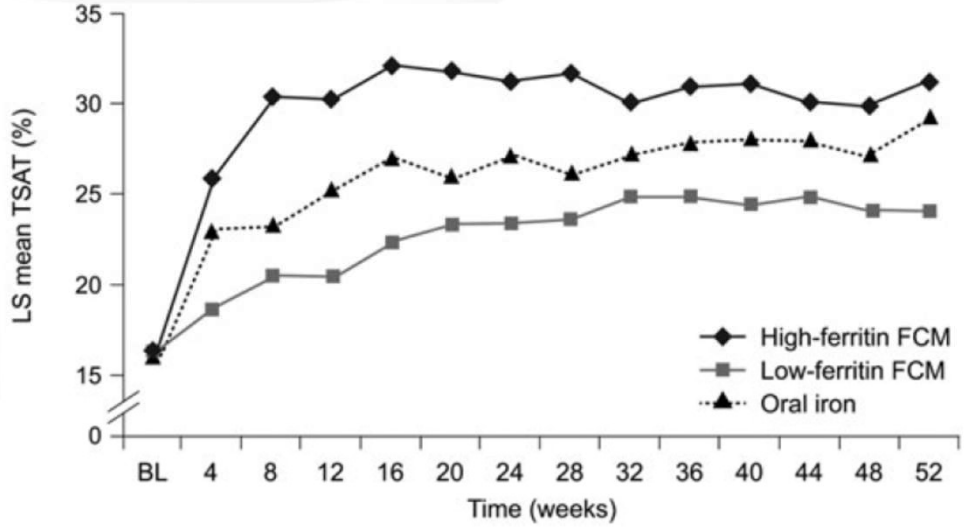
Nephrol Dial Transplant (2014) 0: 1–10
doi: 10.1093/ndt/gfu201

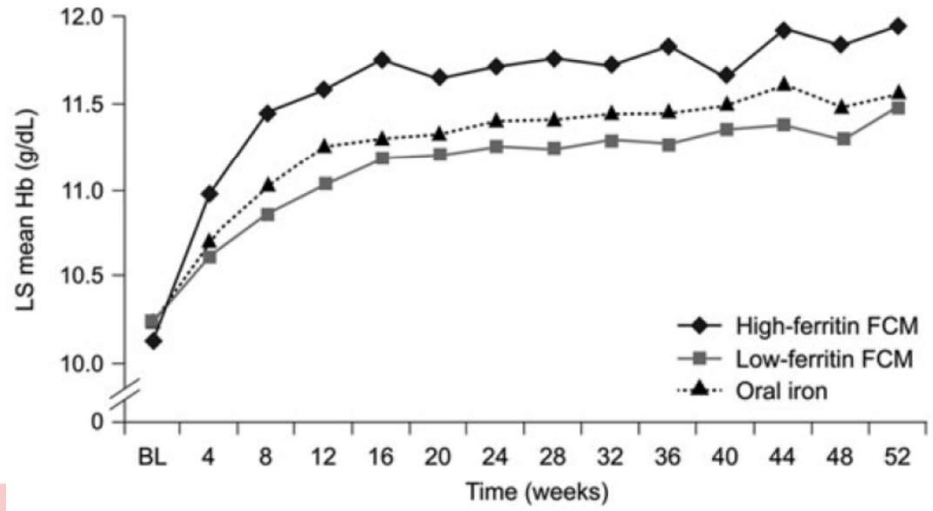
ndt Nephrology Dialysis Transplantation

Original Article

FIND-CKD: a randomized trial of intravenous ferric carboxymaltose versus oral iron in patients with chronic kidney disease and iron deficiency anaemia

Iain C. Macdougall[1], Andreas H. Bock[2], Fernando Carrera[3], Kai-Uwe Eckardt[4], Carlo Gaillard[5], David Van Wyck[6], Bernard Roubert[7], Jacqueline G. Nolen[7] and Simon D. Roger[8] on behalf of the FIND-CKD Study Investigators†





IRONOUT HF vs FIND-CKD:

- Höhere Dosis 2x150mg vs 2x100
- Fe-polysaccharid vs Fe-sulfat
- 16 Wo vs 52 Wo
- TSAT 19/20 vs 16
- Ferritin 70/75 vs. 57
- Hepcidin level vergleichbar

Macdougall et al., Nephrol Dial Transplant (2014) 0: 1–10

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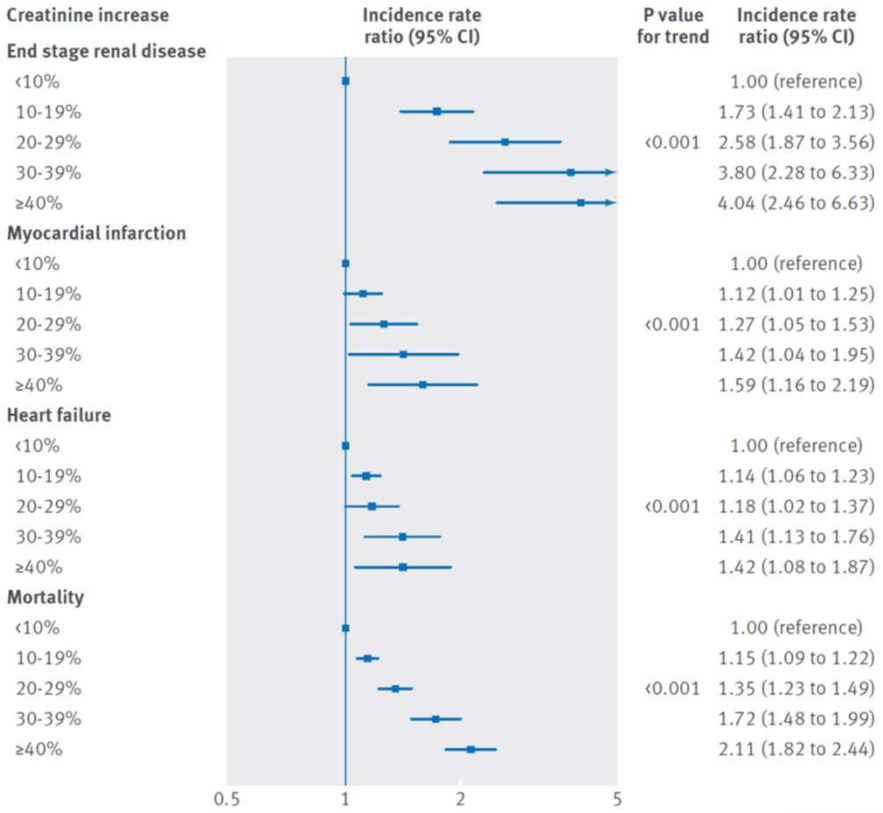
RESEARCH

OPEN ACCESS

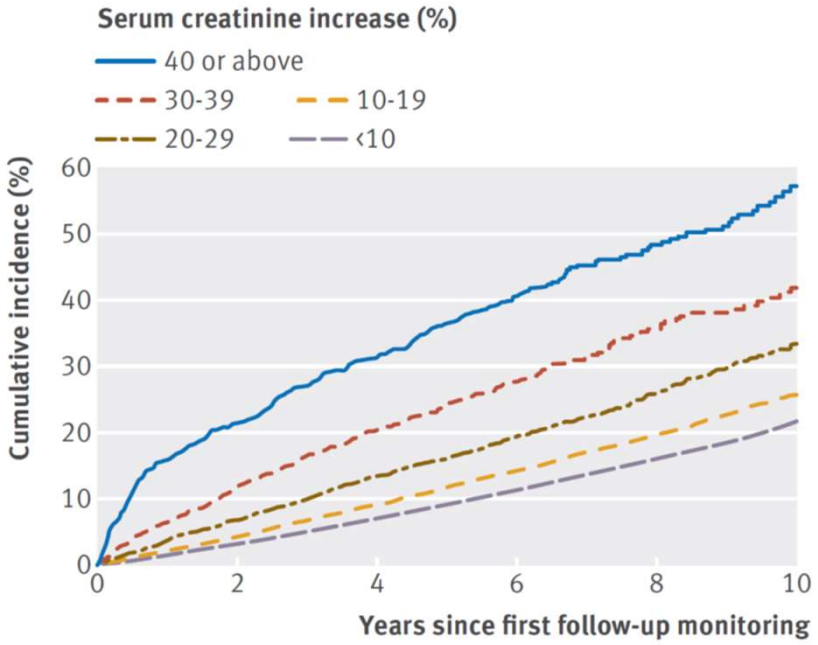
Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study

Morten Schmidt,[1,2,3] Kathryn E Mansfield,[1] Krishnan Bhaskaran,[1] Dorothea Nitsch,[1] Henrik Toft Sørensen,[2] Liam Smeeth,[1] Laurie A Tomlinson[1]

Cardiorenal risks associated with levels of creatinine increase after renin-angiotensin system blockade



Cumulative mortality according to levels of creatinine increase after renin-angiotensin system blockade



Schmidt et al., BMJ 2017;356:j791

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Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study

Morten Schmidt,[1,2,3] Kathryn E Mansfield,[1] Krishnan Bhaskaran,[1] Dorothea Nitsch,[1] Henrik Toft Sørensen,[2] Liam Smeeth,[1] Laurie A Tomlinson[1]

Characteristic	Serum creatinine elevation after starting ACEI/ARB	
	≥30% (n=2078)	<30% (n=120 285)
Female sex	1166 (56.1)	55 482 (46.1)
Age, years:		
<50	292 (14.1)	21 959 (18.3)
50-59	322 (15.5)	27 955 (23.2)
60-69	452 (21.8)	31 820 (26.5)
70-79	540 (26.0)	25 908 (21.5)
≥80	472 (22.7)	12 643 (10.5)
Comorbidities*		
Diabetes mellitus	494 (23.8)	26 433 (22.0)
Myocardial infarction	219 (10.5)	5468 (4.5)
Heart failure	395 (19.0)	5756 (4.8)
Hypertension	1333 (64.1)	91 042 (75.7)
Arrhythmia	358 (17.2)	8122 (6.8)
Peripheral arterial disease	124 (6.0)	3044 (2.5)
Chronic kidney disease (eGFR)†:		
Stage ≤2 (≥60)	1612 (77.6)	98 702 (82.1)
Stage 3a (45-59)	281 (13.5)	16 387 (13.6)
Stage 3b (30-44)	143 (6.9)	4502 (3.7)
Stage 4 (15-29)	42 (2.0)	694 (0.6)
Co-medications		
β blockers	493 (23.7)	20 474 (17.0)
Calcium channel blockers	352 (16.9)	22 700 (18.9)
Thiazides	435 (20.9)	25 281 (21.0)
Loop diuretics	594 (28.6)	8693 (7.2)
Potassium sparing diuretics	183 (8.8)	2354 (2.0)
NSAIDs	706 (34.0)	28 306 (23.5)

Schmidt et al., BMJ 2017;356:j791

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Cardiorenal Syndrome Type 1

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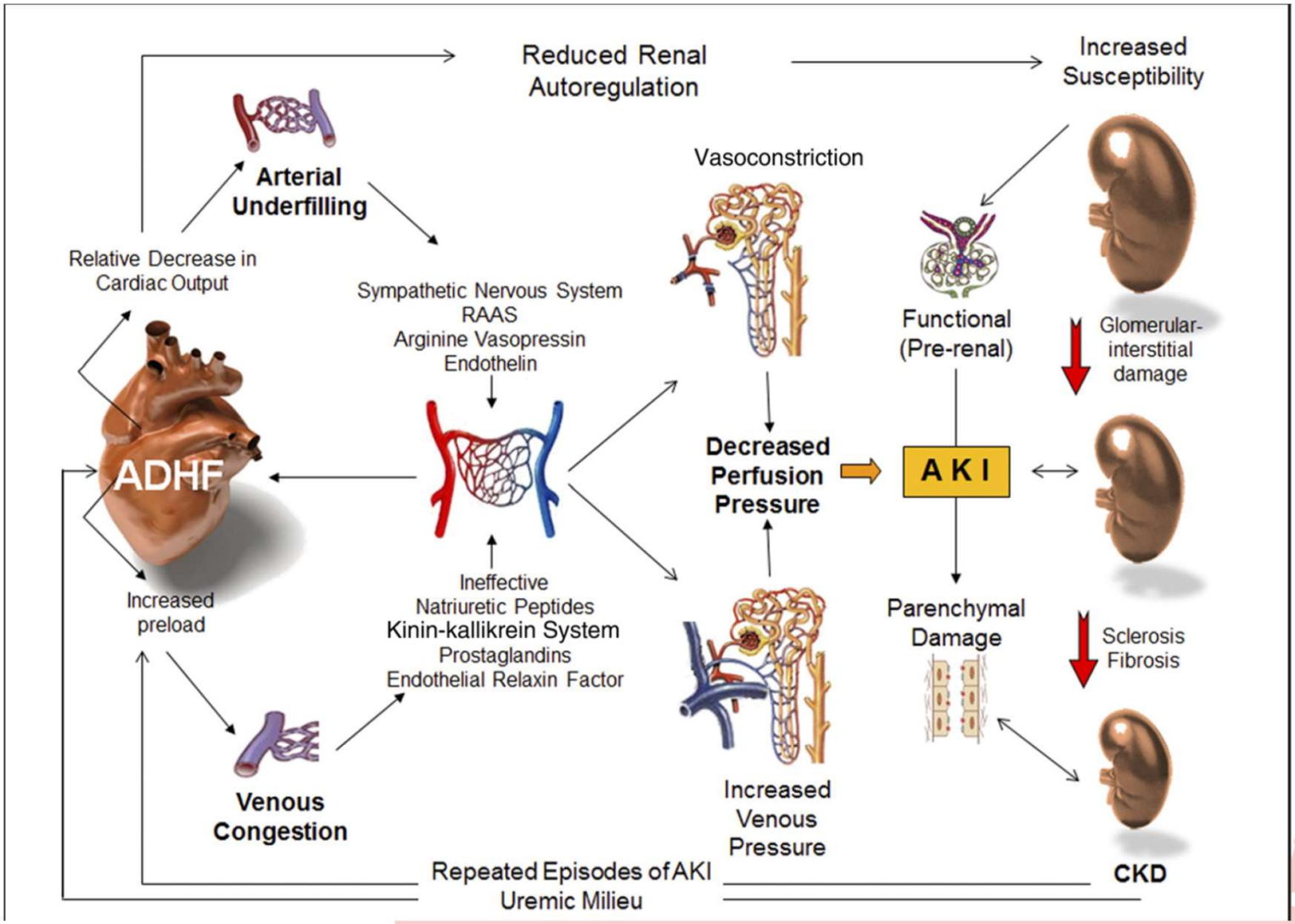
http://dx.doi.org/10.1016/j.jacc.2012.01.077

STATE-OF-THE-ART PAPER

Cardiorenal Syndrome Type 1

Pathophysiological Crosstalk Leading to Combined Heart and Kidney Dysfunction in the Setting of Acutely Decompensated Heart Failure

Claudio Ronco, MD,*† Mariantonietta Cicoira, MD,‡ Peter A. McCullough, MD, MPH§‖¶#
Vicenza and Verona, Italy; and Warren, Southfield, Detroit, and Novi, Michigan



Ronco et al., J Am Coll Cardiol 2012;60:1031–42

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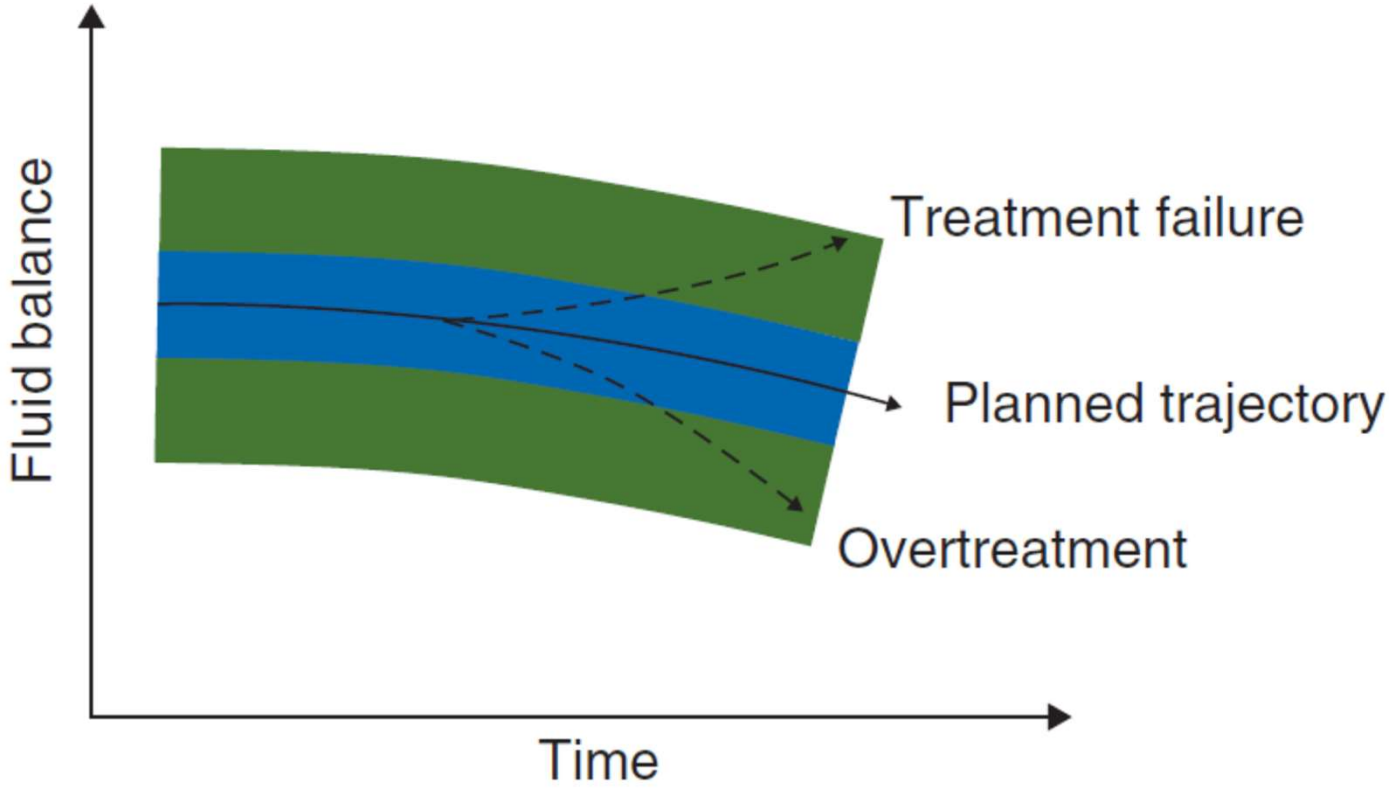
	Ca iv	Insulin - Glukose	Beta2 Mimetika	$NaHCO_3$	Resonium
Mechanismus:	antagonisiert die kardialen Effekte der Hyperkaliämie	Kaliumshift nach intrazellulär (aktiviert Na/K-ATPase)	Kaliumshift nach intrazellulär (aktivieren Na/K-ATPase)	Kaliumshift nach intrazellulär	15g Resonium können theoretisch 60mmol Kalium eliminieren, Austausch von Na bzw. Ca gegen K im Darm
Wirkeintritt:	ca. 2 min	15-30min	5-30min	30 min	?
Wirkdauer:	30-60min	2-4-6h? senkt K um ca. 1mmol/l	2-4h? senkt K um ca. 0,5mmol/l	Effekt ist umstritten, nur bei Azidose geben	> 4h
Dosis:	2 Amp. 10% Ca-Glukonat 10ml	20 iE Insulin + 40-50g Glucose z.B. 200ml G20% + 20iE Insulin	12 Hübe Salbutamol über 2min (1,2 mg) Fertiginhalat enthält 1,25mg	> 100-150ml=mmol NaBi 8,4% Gabe in G5%	15g bis zu 4 x/d mit Laxantien!,
NW:	Cave: Digitalistoxizität stark erhöht!	Überwachung von Blutglukose erforderlich	kardiovaskulär?Tachykardie/ APS	Volumen-belastung	Ischämie, Kolitis, Nekrosen, Koprostase, Erbrechen

Oder Dialyse


Fluid balance
Time
Treatment failure
Planned trajectory
Overtreatment

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Peripheral Edema, Central Venous Pressure, and Risk of AKI in Critical Illness

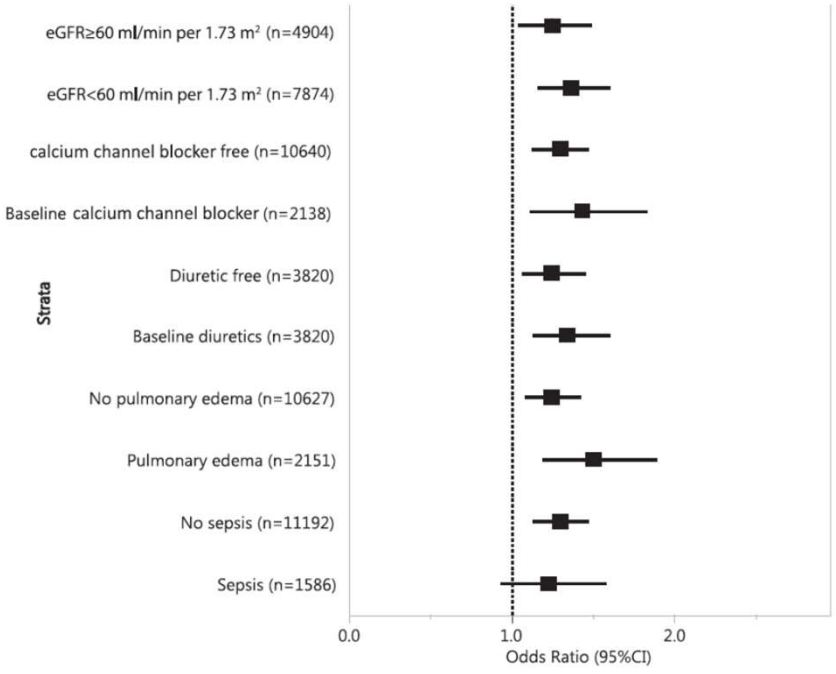
Kenneth P. Chen, Susan Cavender,† Joon Lee,†‡ Mengling Feng,†§ Roger G. Mark,† Leo Anthony Celi,*† Kenneth J. Mukamal,* and John Danziger**

Periphere Ödeme und Risiko für AKI

Table 3. Peripheral edema severity and subsequent risk of AKI

Risk	No Edema	Trace Edema	1+ Edema	2+ Edema	3+ Edema
Odds ratio	Ref	1.34	1.17	1.47	1.57
95% CI		1.10 to 1.65	0.96 to 1.14	1.18 to 1.8)	1.07 to 2.31
P value		<0.01	0.13	<0.001	0.02

Association of Peripheral Edema and AKI per subgroup



Chen et al., Clin J Am Soc Nephrol 11: 602–608, 2016

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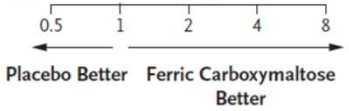
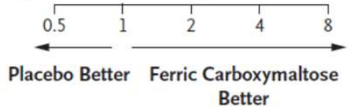
Results by subgroups

Subgroup	Self-Reported Patient Global Assessment: Ferric Carboxymaltose (no. of patients)	Self-Reported Patient Global Assessment: Placebo (no. of patients)	Self-Reported Patient Global Assessment: Odds Ratio (95% CI)	Self-Reported Patient Global Assessment: P Value for Interaction	NYHA Functional Class: Ferric Carboxymaltose (no. of patients)	NYHA Functional Class: Placebo (no. of patients)	NYHA Functional Class: Odds Ratio (95% CI)	NYHA Functional Class: P Value for Interaction
Hemoglobin				0.98				0.51
≤120 (g/liter)	146	74			148	74		
>120 (g/liter)	146	75			146	76		
Median ferritin				0.45				0.78
≤39 (μg/liter)	153	72			154	72		
>39 (μg/liter)	139	77			140	78		
Estimated GFR								
<60 (ml/min/1.73 m^2 of body-surface area)	119	67		0.22	121	68		0.27
≥60 (ml/min/1.73 m^2 of body-surface area)	173	82			173	82		
Median age				0.10				0.89
≤69.7 yr	149	75			149	76		
>69.7 yr	143	74			145	74		
Sex				0.99				0.29
Male	140	68			142	68		
Female	152	81			152	82		
NYHA class				0.66				0.17
Class II	52	27			52	27		
Class III	240	122			242	123		
Median LV ejection fraction				0.86				0.76
≤33%	169	70			171	70		
>33%	123	79			123	80		
Heart failure				0.60				0.55
Nonischemic	56	30			56	30		
Ischemic	236	119			238	120		
Diabetes				0.87				0.53
No	202	113			204	113		
Yes	90	36			90	37		
Median BMI				0.94				0.73
≤27.37	150	71			152	72		
>27.37	142	78			142	78		





Anker et al., NEJM 2009;361:2436-48

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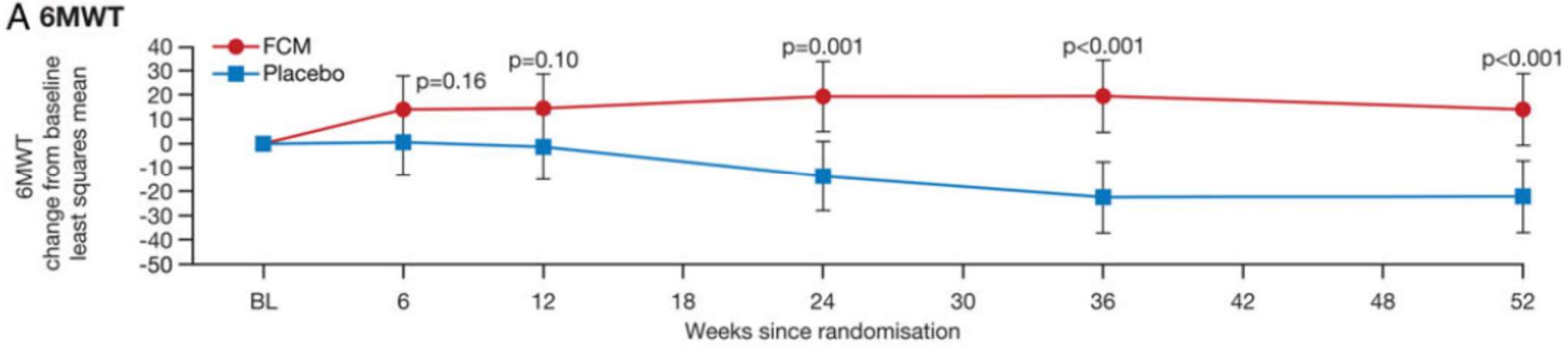
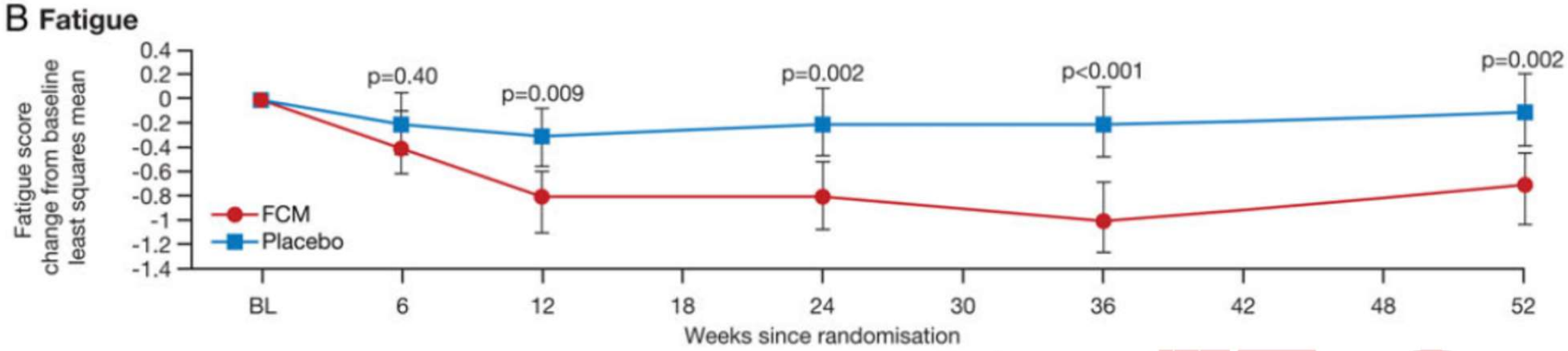
Confirm-HF-Trial

6min walking test and Fatigue





Ponikowski et al., European Heart Journal (2015) 36, 657–668

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Patiromer Nebenwirkungen

Obstipation*†	6,2 %
Hypomagnesiämie‡	5,3 %
Diarrhoe	3 %
Übelkeit	2,3 %
Abdominalschmerz	2,9 %
Flatulenz	1,8 %

- Hypokaliämie bei 2,3 %

1. Weir MR et al. N Engl J Med 2015;372:211-21; 2. Bakris GL et al. JAMA 2015;314:151-61; 3. Veltassa® Fachinformation

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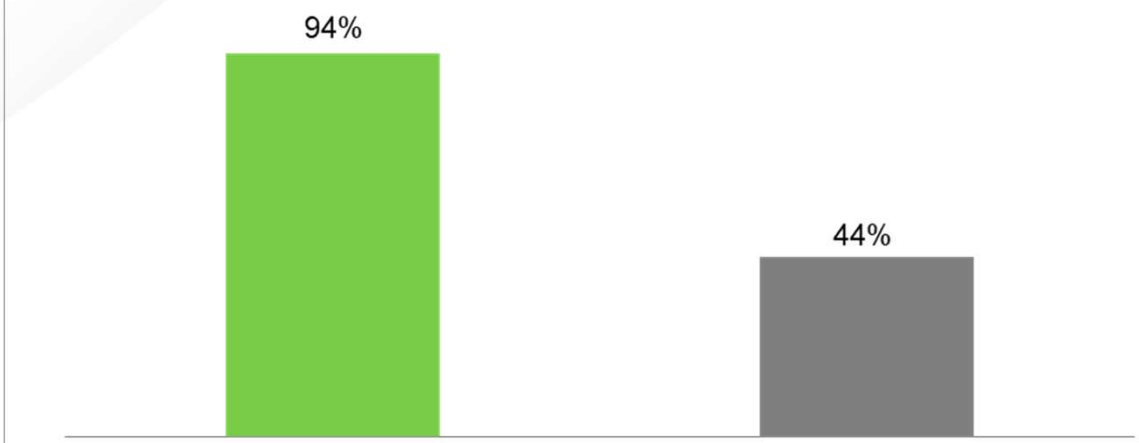
Patiromer ermöglicht Fortsetzung der RAASi-Therapie

Anteil der Patienten unter RAAS-Inhibitor-Therapie am Ende der randomisierten 8-wöchigen Absetzphase (in %)



Patiromer (n = 55) Placebo (n = 52)

Modifiziert nach Weir MR et al. 2015

Weir MR, et al. N Engl J Med 2015;372;211–221.

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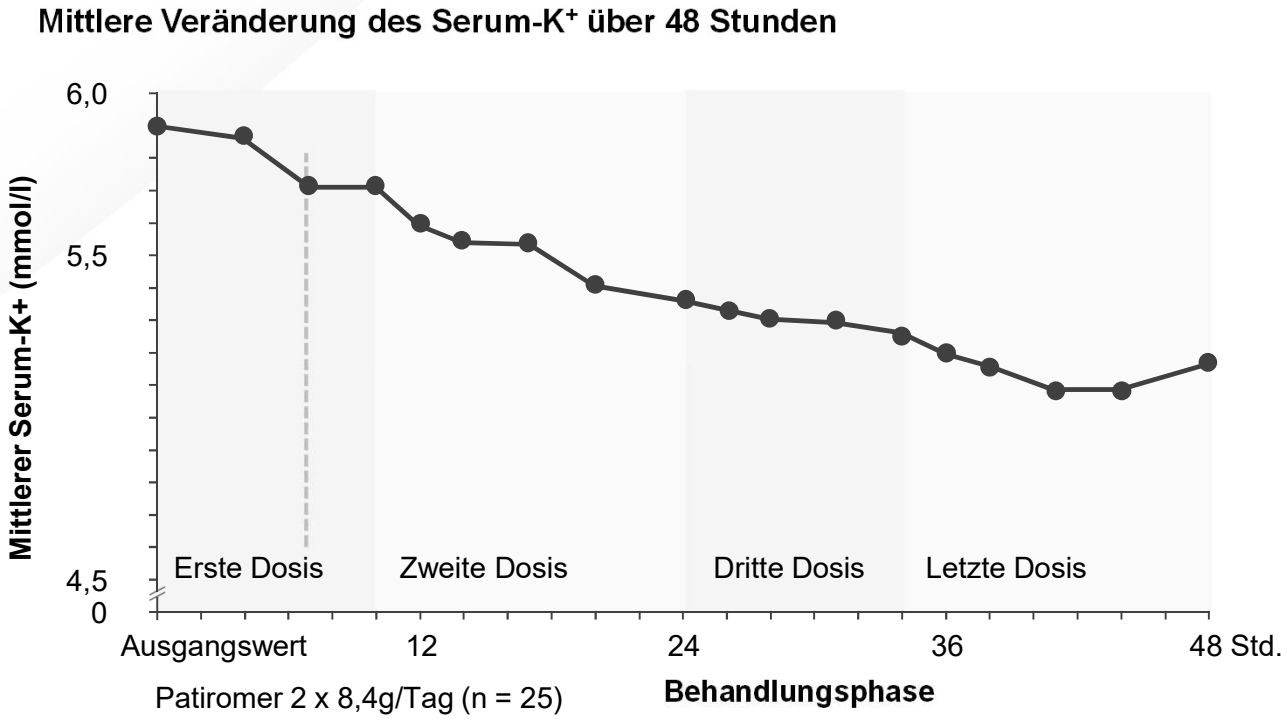
Wirkeintritt der Kaliumsenkung



Modifiziert nach Bushinsky et al. 2015 [1]

Bushinsky DA, et al. Kidney Int. 2015; 88: 1427–1433

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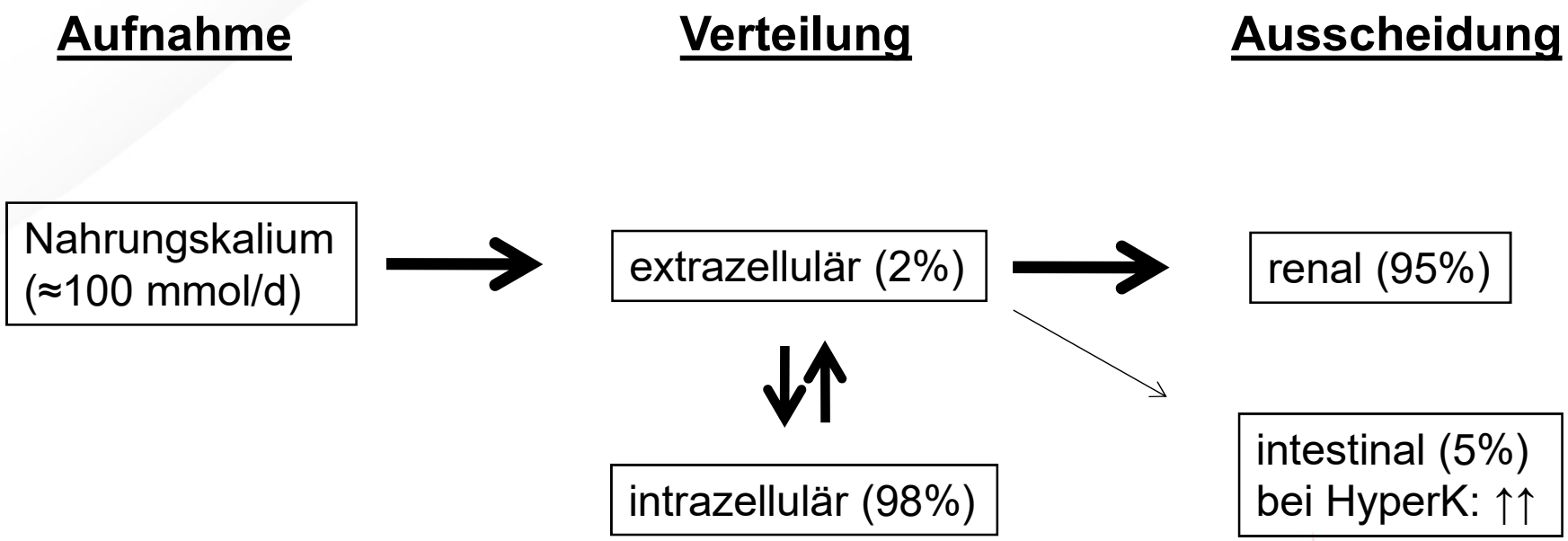
Grundlagen Kalium-Homöostase



Palmer, Clin J Am Soc Nephrol, 2015
Battle,Boobes, EBioMedicine, 2015