Effetti dello Scompenso Cardiaco sulla Funzione Renale

IL CROSS-TALK
cuore-rene
FISIOPATOLOGIA
ED ASPETTI CLINICI

Luca De Nicola

Nephrology and Dialysis Unit

Università degli Studi della Campania *Luigi Vanvitelli*

Scuola di Medicina e Chirurgia
Dipartimento di Scienze Mediche, Chirurgiche, Neurologiche, Metaboliche e dell'Invecchiamento

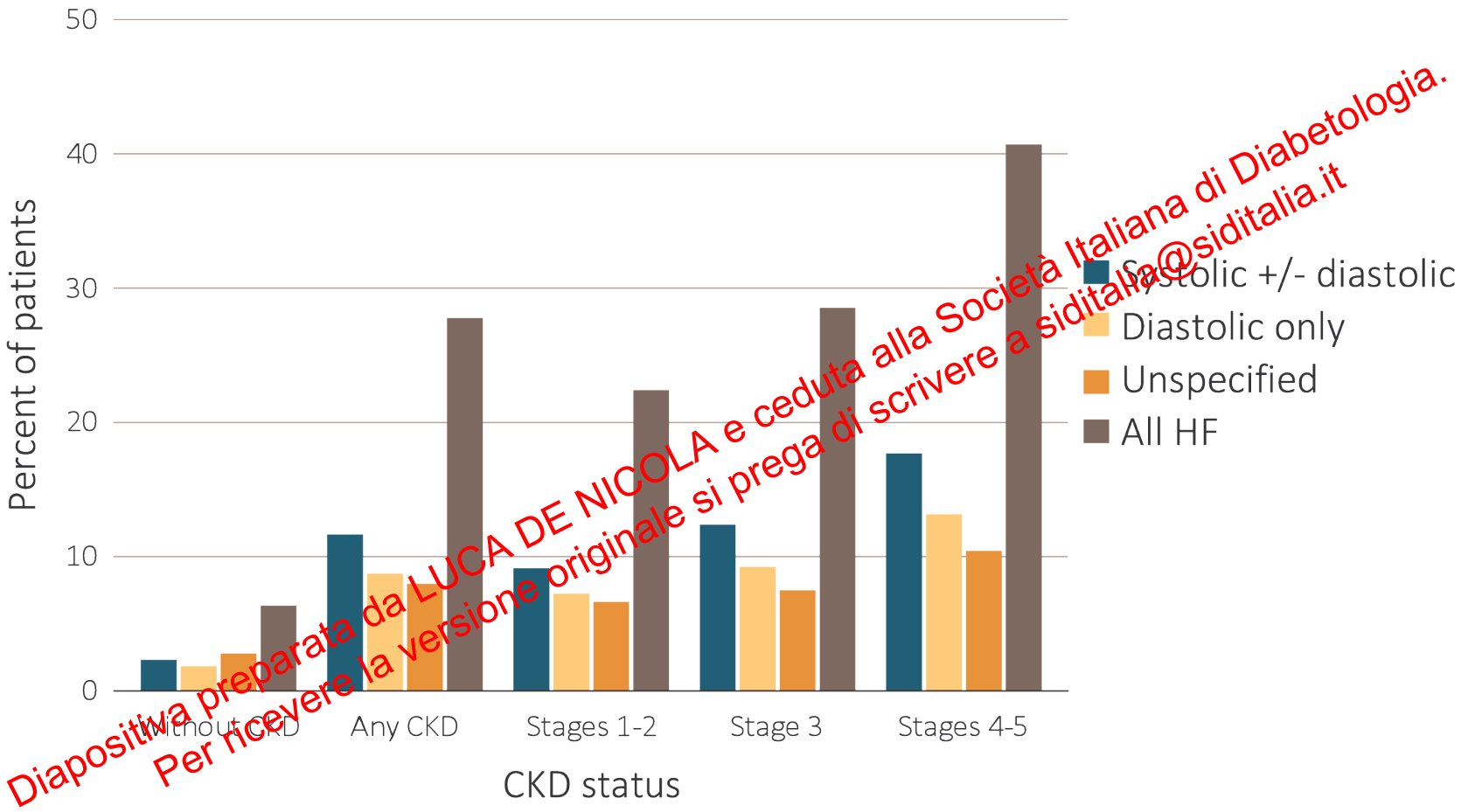
Il Prof. LUCA DE NICOLA dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- AstraZeneca
- Vifor
- Janssen

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Napoli, 30-04-2019

Heart failure in patients with or without CKD



Data Source: Special analyses, Medicare 5% sample. Patients aged 66 and older, alive, without end-stage renal disease, and residing in the United States on 12/31/2016 with fee-for-service coverage for the entire calendar year. Abbreviation: CKD, chronic kidney disease.

Mild HF in normal renal function

Intrarenal Determinants of Sodium Retention in Mild Heart Failure

Massimo Volpe, Paola Magri, Maria A. E. Rao, Sara Cangianiello, Luca DeNicola, Alessandro F. Mele, Bruno Memoli, Iolanda Enea, Speranza Rubattu, Bruna Gigante, Bruno Trimarco, Murray Epstein

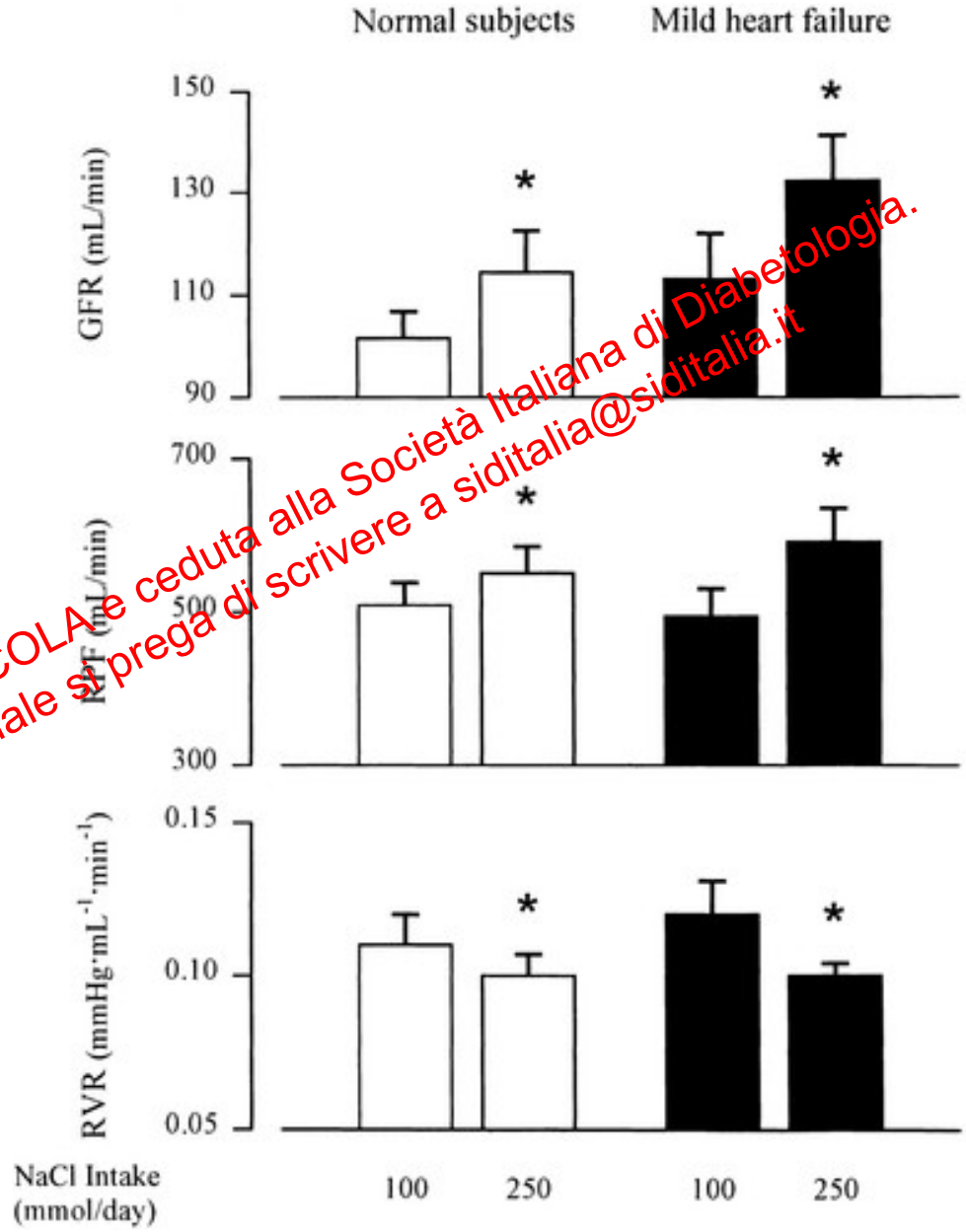
- 10 asymptomatic MHF (class I, LVEF 29.7±2.%) and normal renal function (sCreat 1.0 ± 0.06)
- 10 matched normal subjects
- Low salt intake (6 g/day) vs high salt intake (15 g/day) estimated by 24h UNaV
- Renal hemodynamics and tubular function (clearances studies)
- Effects of 6-week treatment with Enalapril 5 mg/day

Hypertension. 1997;30:168–176

Effects of increased NaCl-i on GFR, RPF and RVR in normal and MHF

Responses to high salt diet was similar in the two groups.

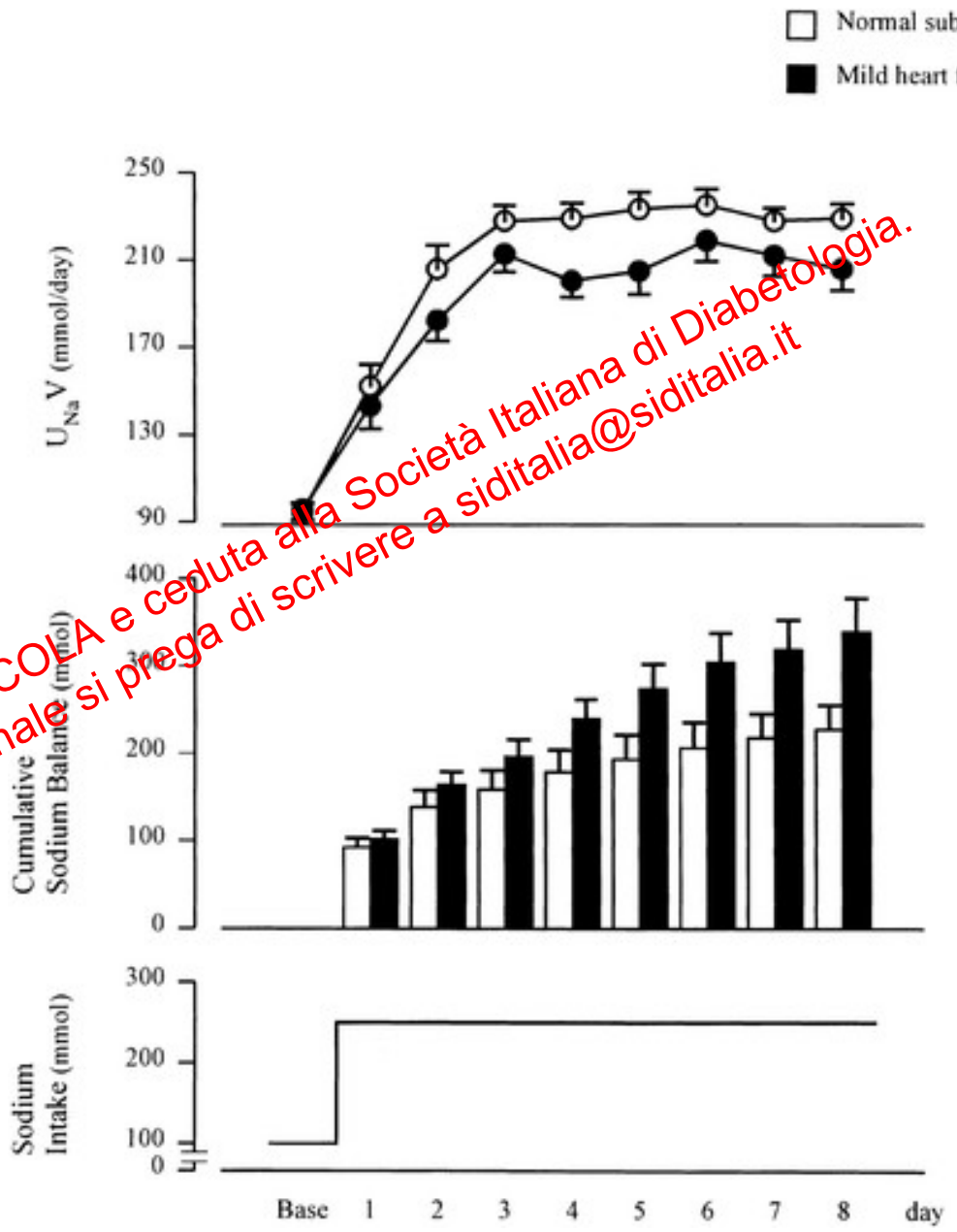
***P<.05 vs low salt**



Hypertension. 1997;30:168–176

Effects of increased NaCl-i on UNaV and Na+ balance in normal and MHF

The two groups differed in cumulative Na+ balance with increased ECV of 1.6 L in normal and 2.4 L in MHF (P<.001)



Hypertension. 1997;30:168–176

Effe… …l i… on markers of … norma…

Proximal reabsorpt… decreased in normal and i…

FL_{Na}: filtered load of Na,
FC_{H2O}: fractional clearance of free water, FE_K: fractional excretion of K,
FE_{NA}: fractional excretion of Na^+

Hypertension. 1997;30:168–176

Six weeks of Enalapril 5 mg/d restored a normal response to high salt diet

Early Impairment of Renal Hemodynamic Reserve in Patients With Asymptomatic Heart Failure Is Restored by Angiotensin II Antagonism

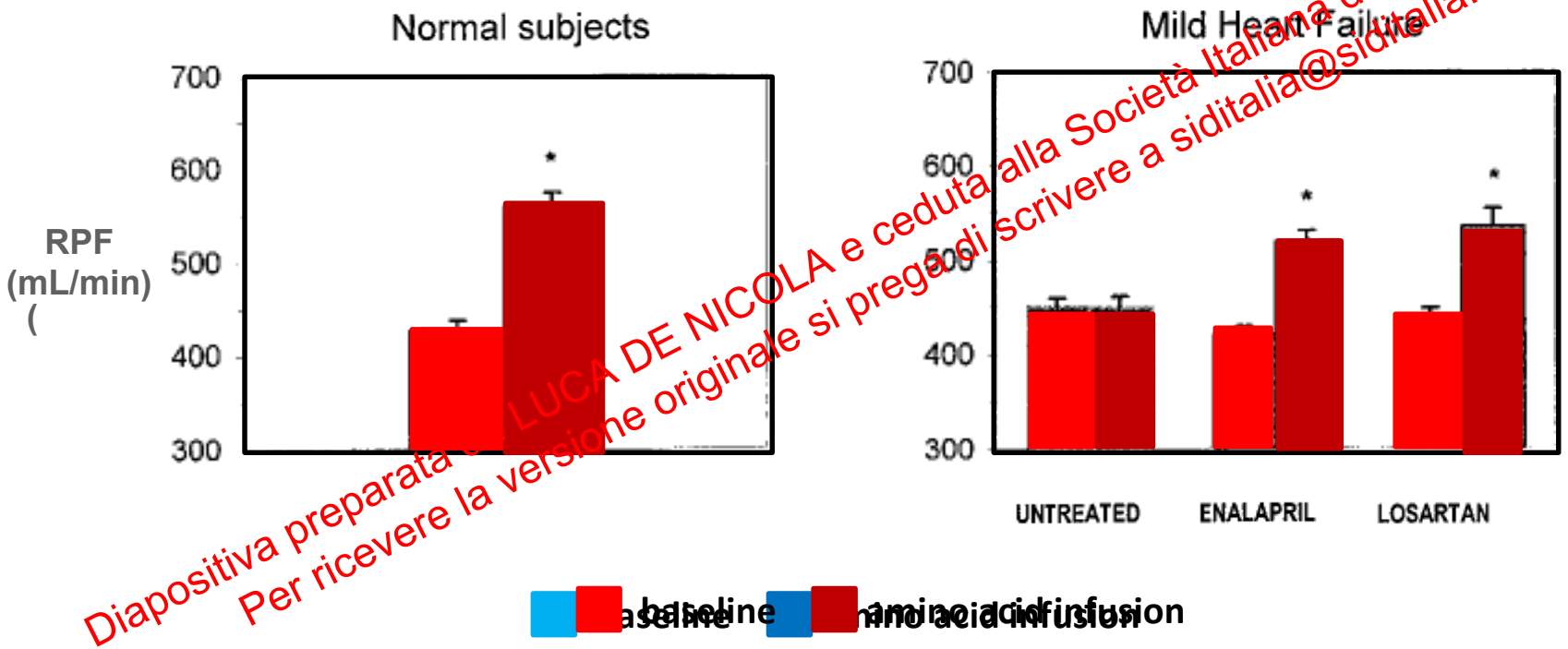
Paola Magri, MD; Maria A.E. Rao, MD; Sara Cangianiello, MD; Vincenzo Bellizzi, MD; Rosaria Russo, MD; Alessandro F. Mele, MD; Michele Andreucci, MD; Bruno Memoli, MD; Luca De Nicola, MD; Massimo Volpe, MD

	Healthy Subjects	Patients With Mild HF
Age, y	39.1±4.4	40.3±3.3
Sex, male/female	7/1	7/3
Body weight, kg	72.3±2.8	70.2±3.6
Height, cm	167.3±2.0	168.7±2.1
Blood glucose, mg/dL	92.0±4.0	90.5±3.6
Serum creatinine, mg/dL	1.04±0.03	0.90±0.06
Blood urea nitrogen, mg/dL	37.6±3.7	35.6±2.9
ANP, pg/mL	19.4±2.3	35.1±6.7*
BNP, pg/mL	10.0±4.0	30.6±7.3*
PRA, ng · mL^{-1} · h^{-1}	3.3±0.5	2.5±0.4
PA, pg/mL	47.1±9.6	51.5±10.2
SBP/DBP, mm Hg	116.3±4.5/76.9±2.7	116.5±1.8/78.0±2.0
HR, bpm	66.8±2.5	69.4±3.3
LVEDD, mm	...	59.8±1.5
LVESD, mm	...	44.2±2.2
LVEF, %	...	40.8±1.9
$U_{Na}V$, mEq/24 h	156.8±16.5	164.0±22.1
U_KV, mEq/24 h	46.6±3.5	47.3±7.1

Circulation 1998;98;2849-2854

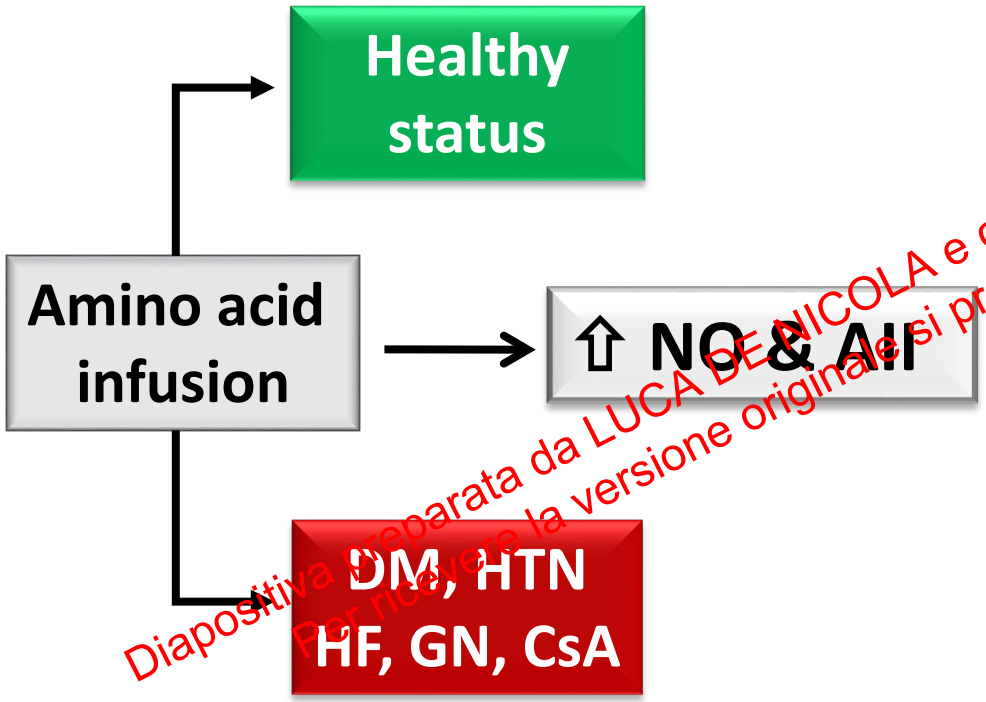
Early Impairment of Renal Hemodynamic Reserve in Patients With Asymptomatic Heart Failure Is Restored by Angiotensin II Antagonism

Paola Magri, MD; Maria A.E. Rao, MD; Sara Cangianiello, MD; Vincenzo Bellizzi, MD; Rosaria Russo, MD; Alessandro F. Mele, MD; Michele Andreucci, MD; Bruno Memoli, MD; Luca De Nicola, MD; Massimo Volpe, MD



Circulation 1998;98;2849-2854

Renal Functional Reserve is a “in vivo proxy” of Nitric Oxide/Angiotensin II balance

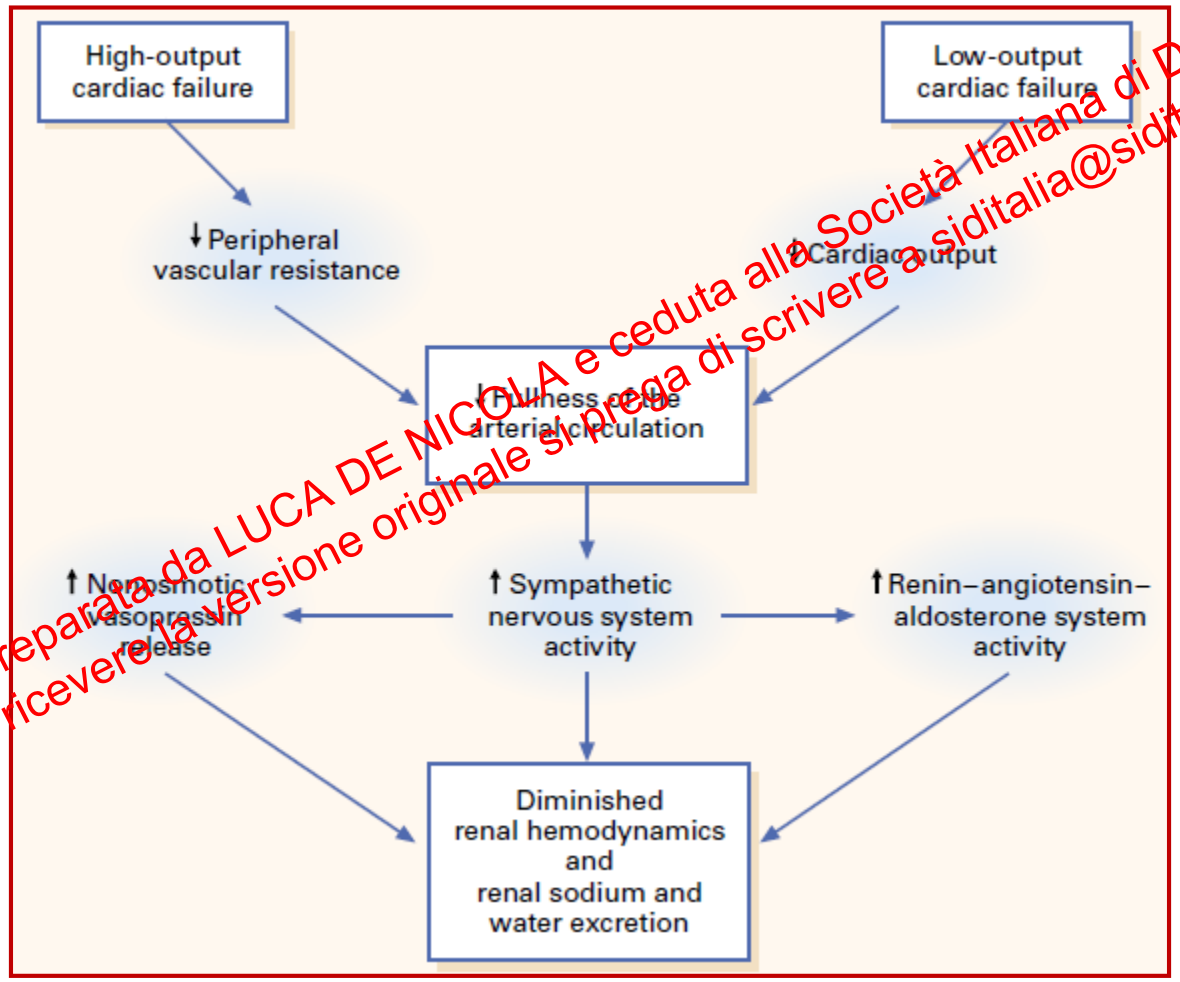


De Nicola et al: KI 1991; Diabetes 1992; JCI 1992; Hypertension 1992; JCI 1993; NDT 1994, JACC 1998

The kidney in advanced HF

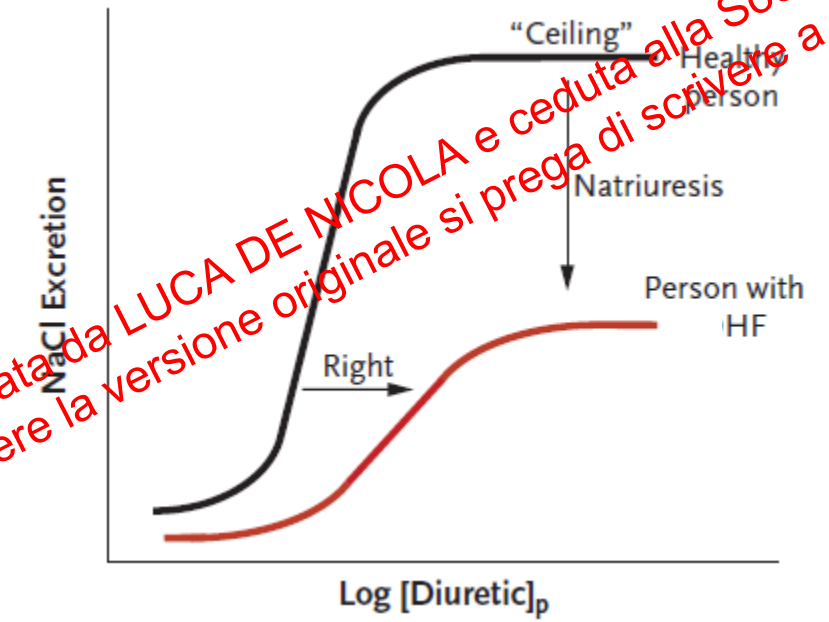
Hormones and Hemodynamics in Heart Failure

Robert W. Schrier, M.D.,
and William T. Abraham, M.D.



The New England Journal of Medicine August 19, 1999

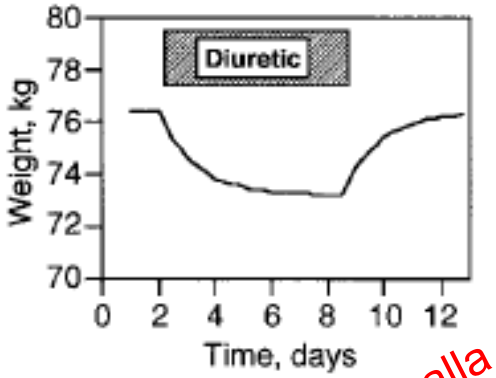
Diuretic Resistance in Human Heart Failure…

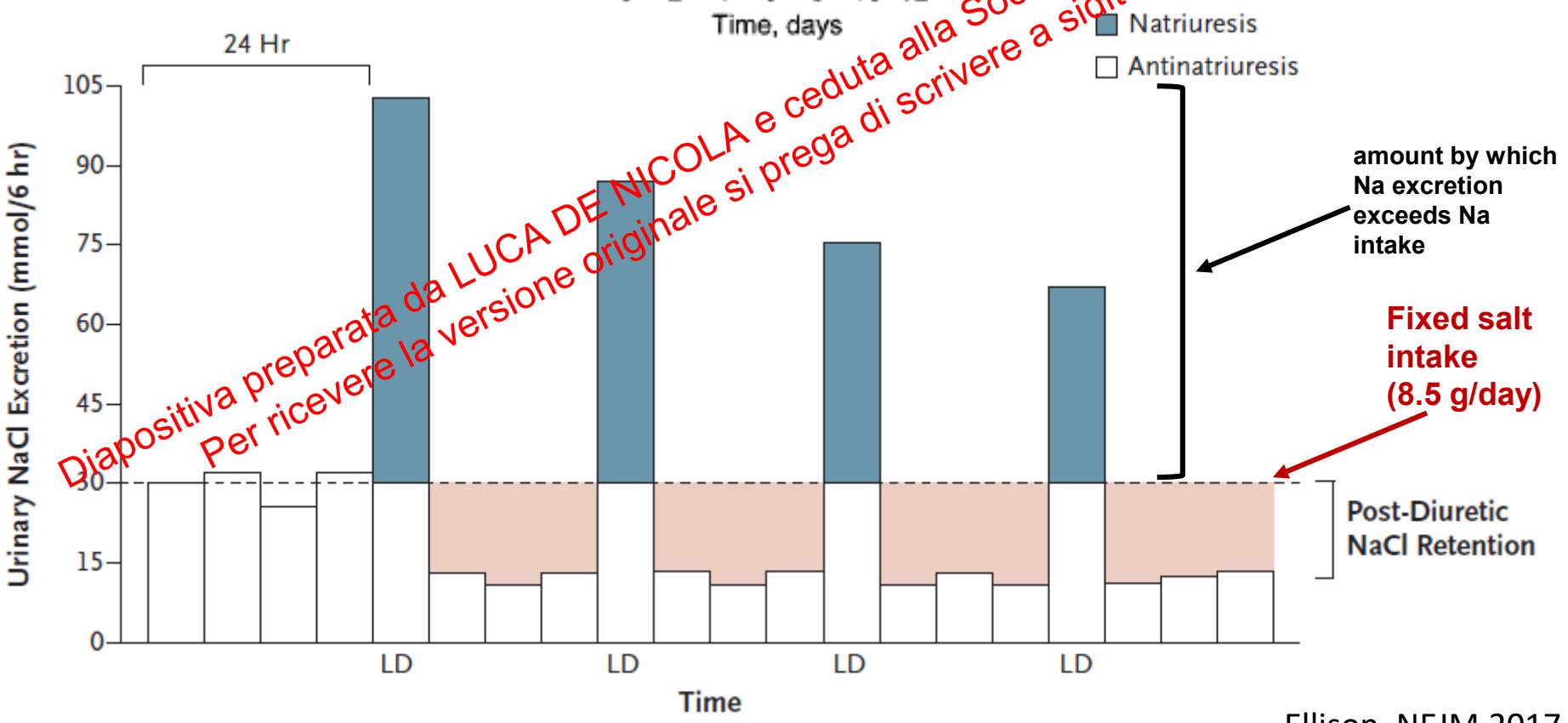


Ellison, NEJM 2017

Diuretic Resistance in Human Heart Failure…

…and role of salt intake

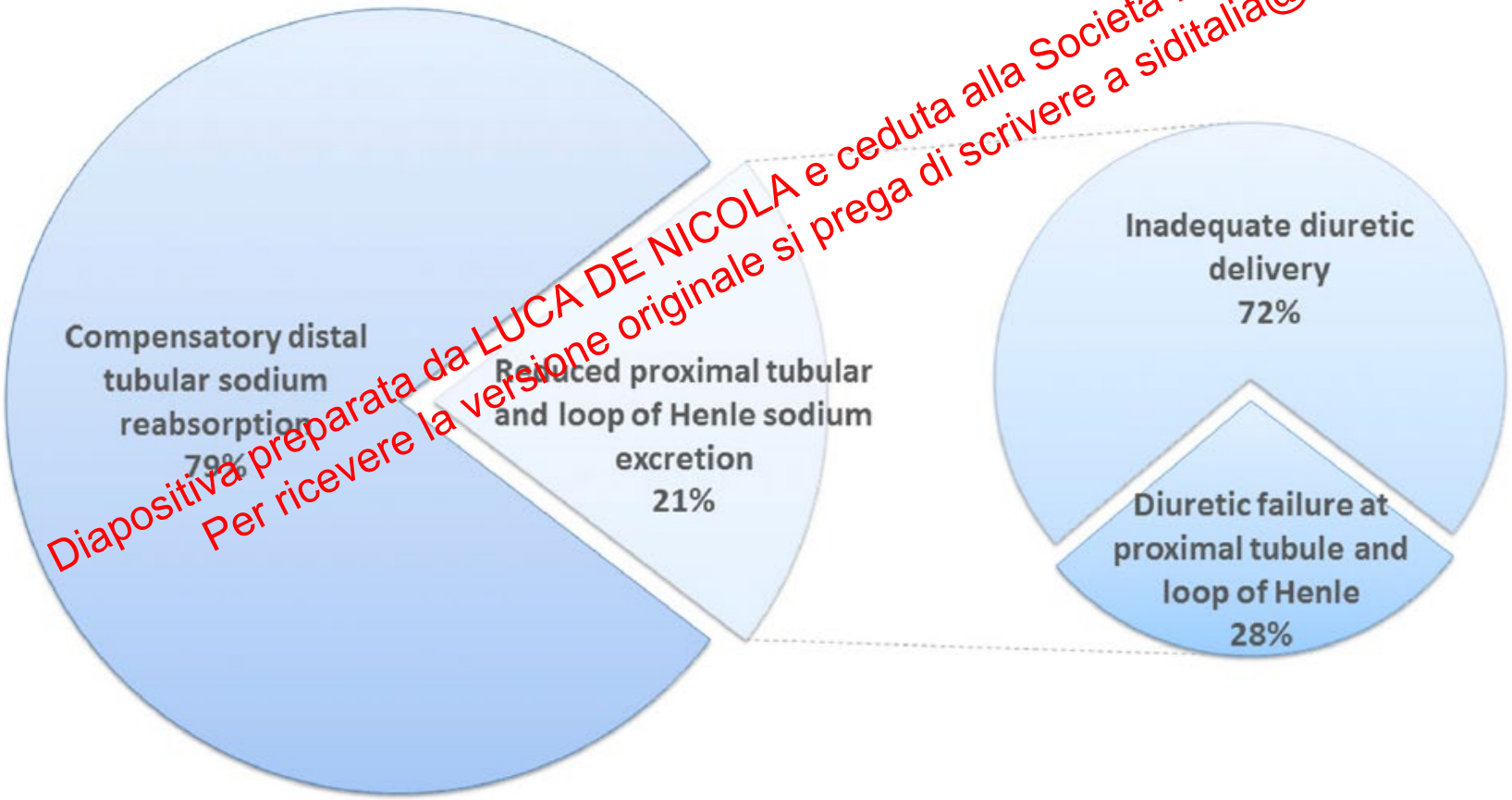




Ellison, NEJM 2017

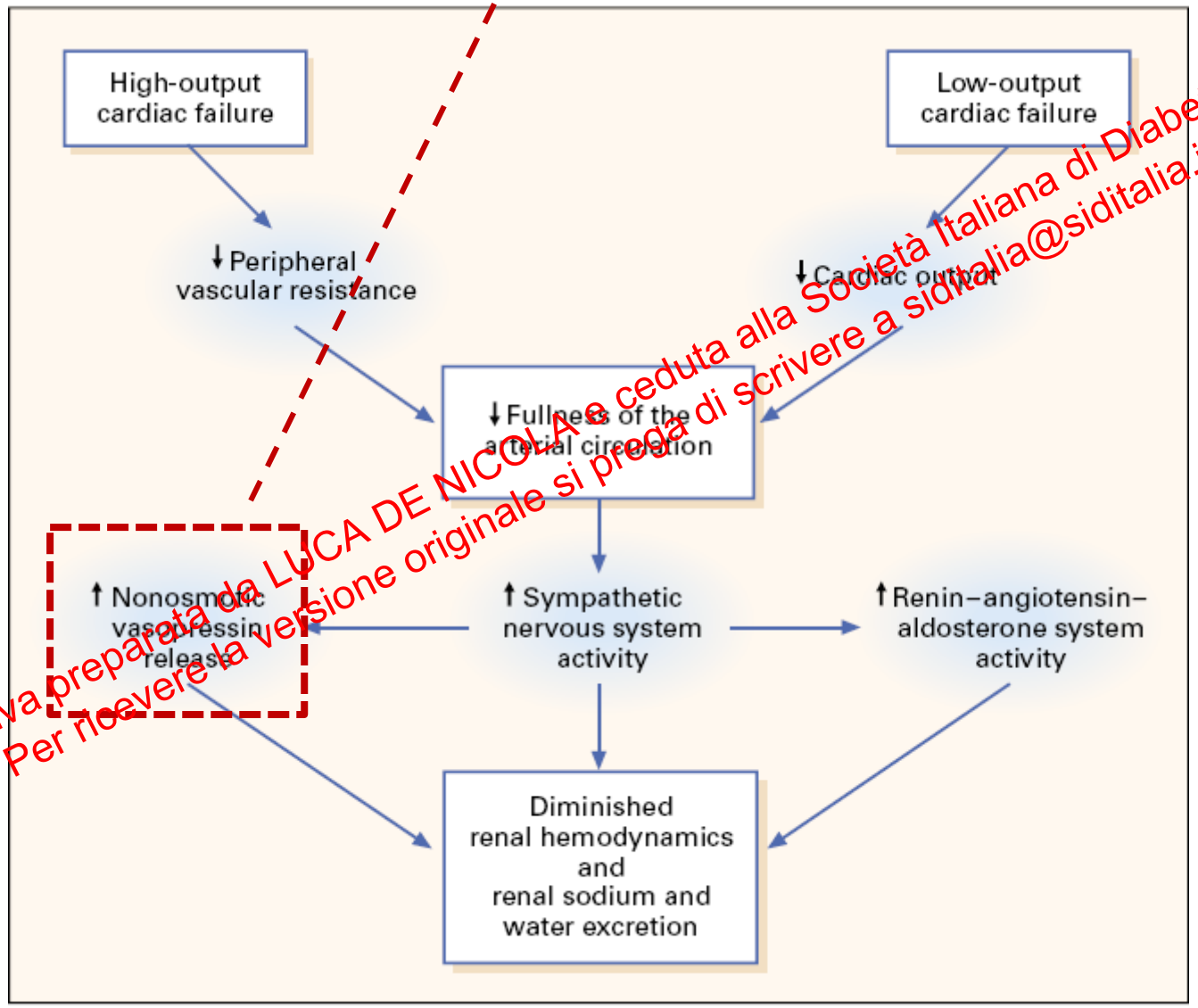
Diuretic Resistance in Human Heart Failure

- 128 patients with HF receiving treatment with loop diuretics
- Fractional excretion of lithium for in vivo assessment of proximal tubular and loop of Henle sodium handling
- FENa to assess the net sodium excreted into the urine



Rao, JASN 2017

Mechanisms of salt and water retention in HF



Schrier, NEJM 1999

The Car

Do We N
of Strategy

Journal of the American College of Cardiology
© 2008 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 51, No. 3, 2008
ISSN 0735-1097/08/$34.00
doi:10.1016/j.jacc.2007.09.043

Heart Failure

Elevated Intra-Abdominal Pressure in Acute Decompensated Heart Failure

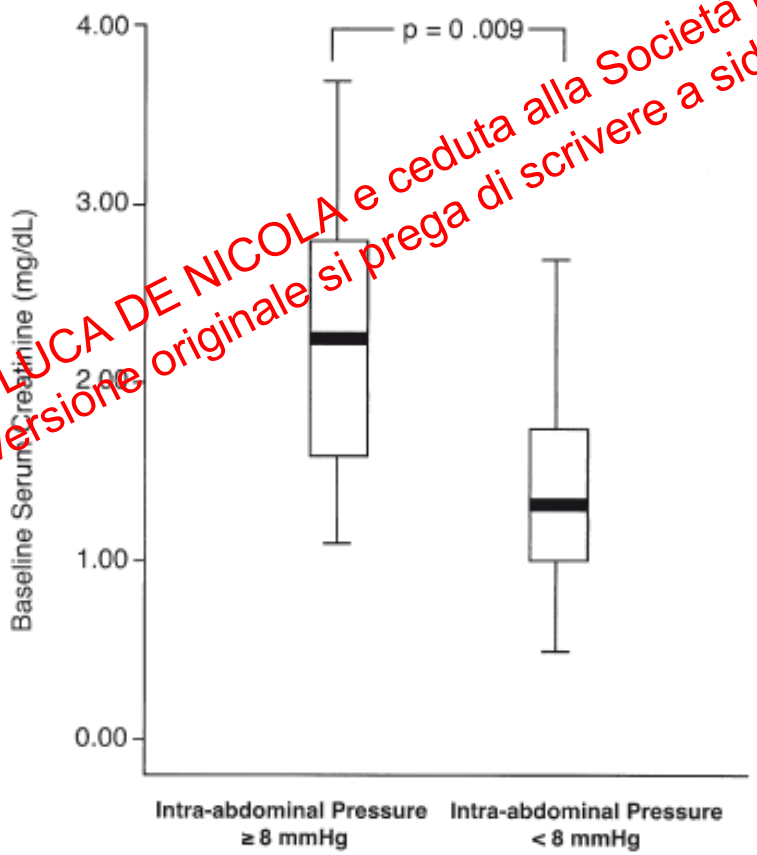
A Potential Contributor to Worsening Renal Function?

Wilfried Mullens, MD,* Zuheir Abrahams, MD, PHD,* Hadi N. Skouri, MD,*

In HF inc

to renal dysfunct

.....⇧ **intra-abdo**



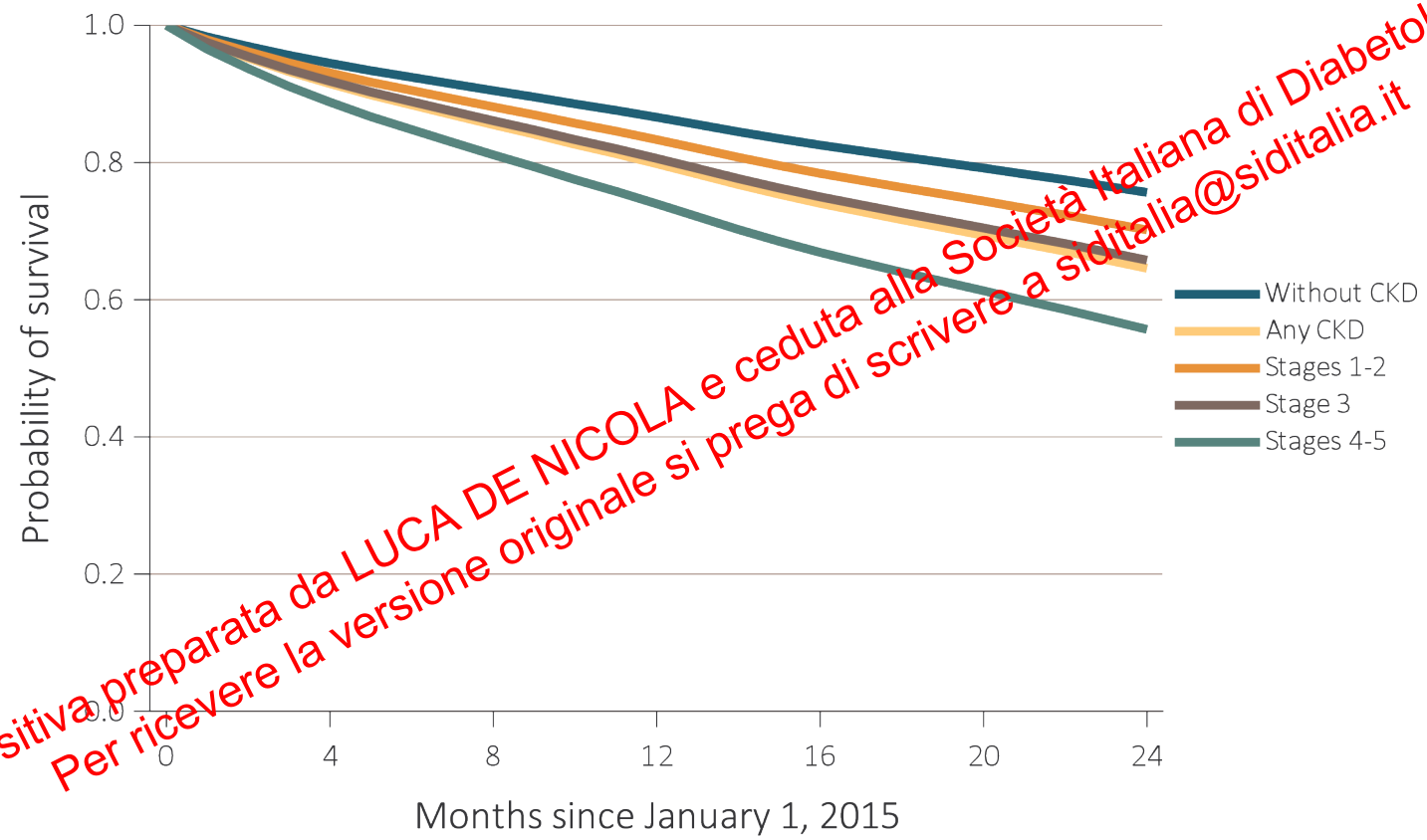
a "per se"

Jessup & Costanzo, JACC 2009

Patient outcome

Survival of patients with heart failure by CKD status

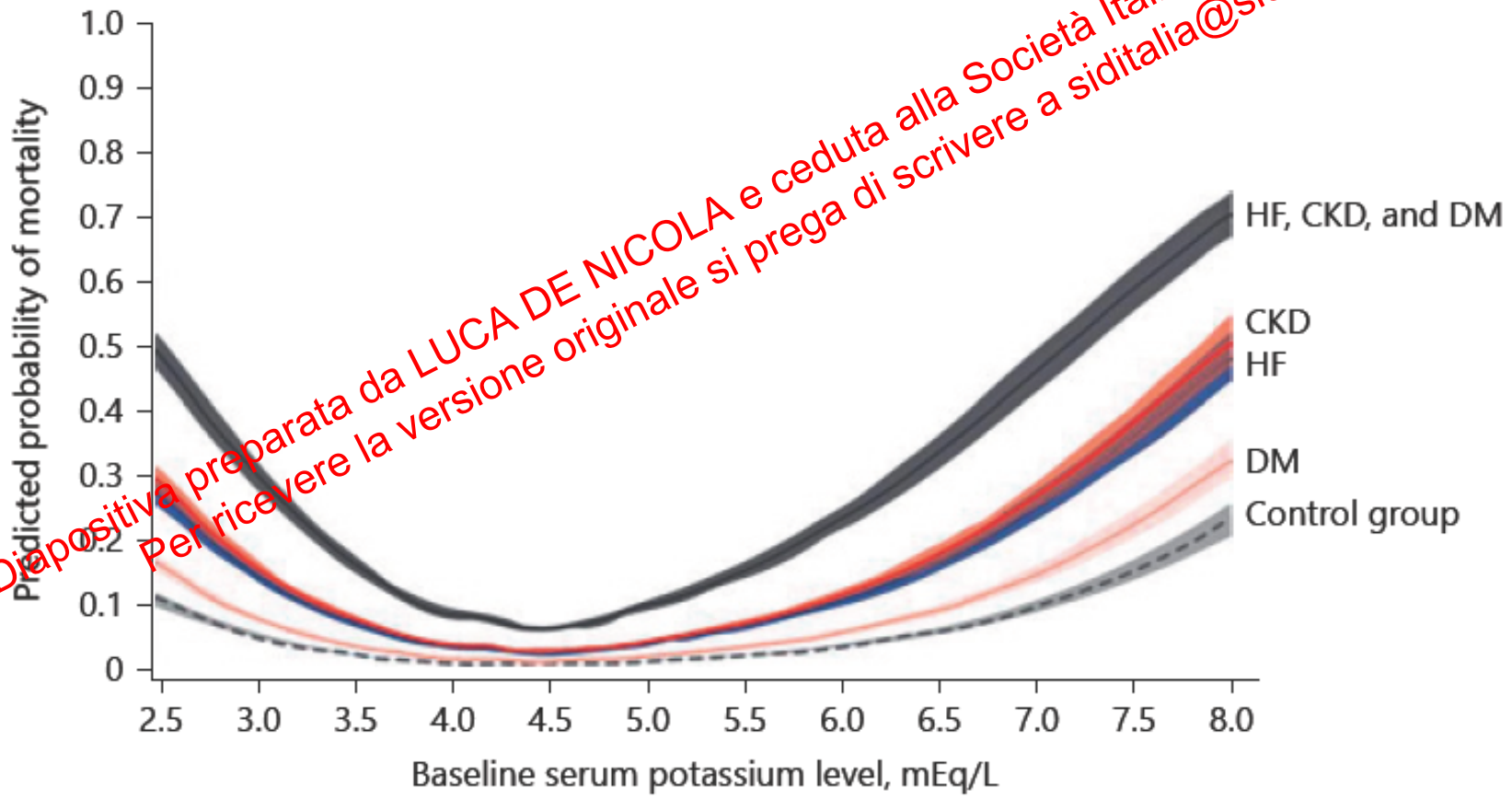
adjusted for age and sex



Data Source: Special analyses, Medicare 5% sample. Patients aged 66 and older, alive, without end-stage renal disease, and residing in the United States on 12/31/2014, with fee-for-service coverage for the entire calendar year. Abbreviation: CKD, chronic kidney disease.

Association of Serum Potassium with All-Cause Mortality in Patients with and without Heart Failure, Chronic Kidney Disease, and/or Diabetes

- 911,698 pts (US integrated health delivery networks)
- 21% DM, 11% CKD, 6% HF, 1% all 3 conditions
- Basal sK ≥5.0 mEq/L: 8.3% DM, 11.5% CKD, 9.1% in HF, 13.1% all 3 conditions



Collins, Am J Nephrol 2017

Antihypertensive Medications and the Prevalence of Hyperkalemia in a Large Health System

- **Integrated healthcare system in Pennsylvania (44 Units)**
- **Serum K measured over a three-year period (2011-13) in 194.456 outpatients**

Actions Taken After Experiencing K>5.0, K>5.5

Action Taken	Hyperkalemia, K>5.0 mEq/L (n=16834)*	Hyperkalemia, K>5.5 mEq/L (n=3582)*
Emergency room visit within 7 days	1.2% (203/16834)	3.1% (112/3582)
Repeat potassium measurement within 14 days	18.4% (3097/16834)	44.3% (1587/3582)
Prescription of kayexalate	0.7% (111/16834)	4.7% (171/3582)
Prescription or increase in kaliuretic diuretic	5.6% (946/16834)	9.2% (330/3582)
Discontinuation of ACEI/ARB in patients taking either	10.5% (793/7585)	24.3% (417/1715)
Dose reduction of ACEI/ARB in patients taking either	2.6% (196/7585)	4.8% (82/1715)
Discontinuation of K-sparing diuretic in patients taking med	23.0% (198/861)	48.5% (133/274)
Dose reduction of potassium-sparing diuretic in patients taking med	1.4% (12/861)	1.1% (3/274)

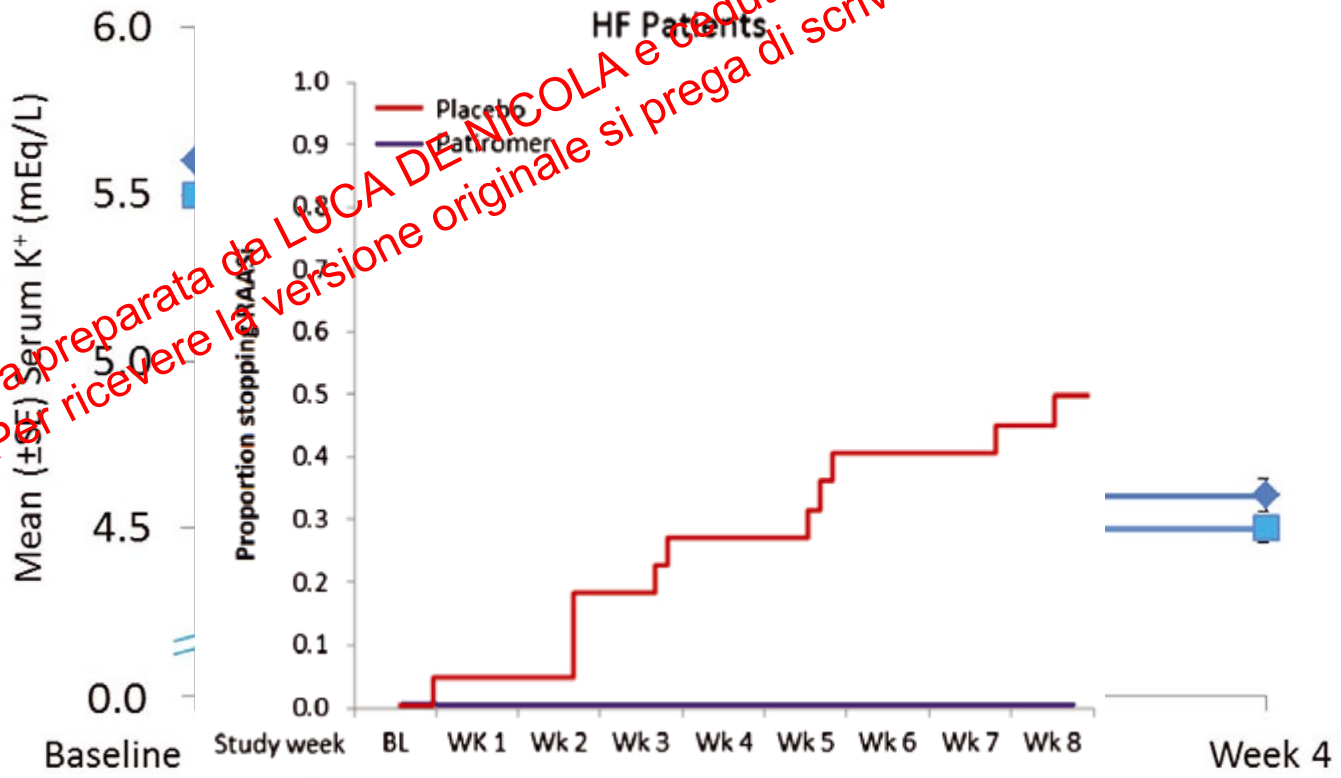
Chang, Hypertension 2016

Effect of patiromer on reducing serum potassium and preventing recurrent hyperkalaemia in patients with heart failure and chronic kidney disease on RAAS inhibitors

European Journal of Heart Failure (2015)

EUROPEAN SOCIETY OF CARDIOLOGY®

- 243 hyperkalemic patients with CKD (90% eGFR<60) under RAASi
- 42% with HF class I-III
- Patiromer vs Placebo for 4 weeks
- Primary efficacy endpoint was mean change in serum K+ from baseline to week 4



S&C: *Effects of HF on Kidney and Patient Outcome*

Ejection Fraction

⇩RFR
⇧Rprox

⇩RPF, GFR
⇩UNaV

Water retention

⇧Intra-addominal Pressure

⇩ Response to high salt

⇧ Diuretic Resistance
⇧ CKD progression
⇧ sK → RAASI Stop

⇨

ESRD
Death

Research Perspectives

The Cardio-Renal Syndrome

Type I: acute cardiorenal syndrome
Abrupt worsening of cardiac function (e.g., acute cardiogenic shock or acutely decompensated heart failure) leading to acute kidney injury.
Type II: chronic cardiorenal syndrome
Chronic abnormalities in cardiac function (e.g., chronic heart failure) causing progressive and potentially permanent chronic kidney disease.
Type III: acute renocardiac syndrome
Abrupt worsening of renal function (e.g., acute kidney ischemia or glomerulonephritis) causing acute cardiac disorder (e.g., heart failure, arrhythmia, ischemia).
Type IV: chronic renocardiac syndrome
Chronic kidney disease (e.g., chronic glomerular or interstitial disease) contributing to decreased cardiac function, cardiac hypertrophy, and/or increased risk of adverse cardiovascular events.
Type V: secondary cardiorenal syndrome
Systemic condition (e.g., diabetes mellitus, sepsis) causing both cardiac and renal dysfunction.

Ronco, JACC 2008

The Cardio-Renal Syndrome

HYPERTENSION, DIABETES, OBESITY, DYSLIPIDEMIA

Chronic inflammation

This clin

car

not *has*

pro *da*

PRECISION MEDICINE

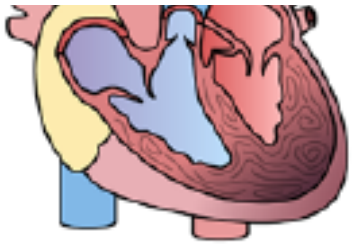
BIOPROFILING

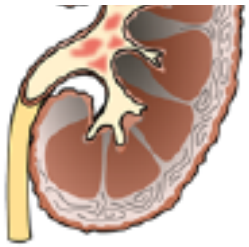
Congestion (blood pressure, volume status), potassium, eGFR, kidney injury molecules, microalbuminuria, biological fingerprint of active fibrosis

Optimization of available drugs:

RAAS inhibitors, diuretics, SGLT-2 inhibitors, potassum binders

Target antifibrotic therapy





Zannad, Circulation 2018