

Heart Failure- Renal Dysfunction

Session:

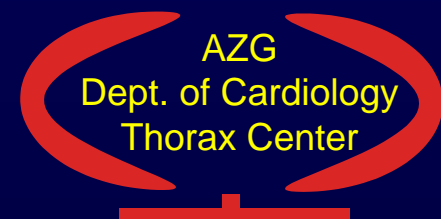
*Heart Failure – Dangerous
liaisons*

D.J. van Veldhuisen

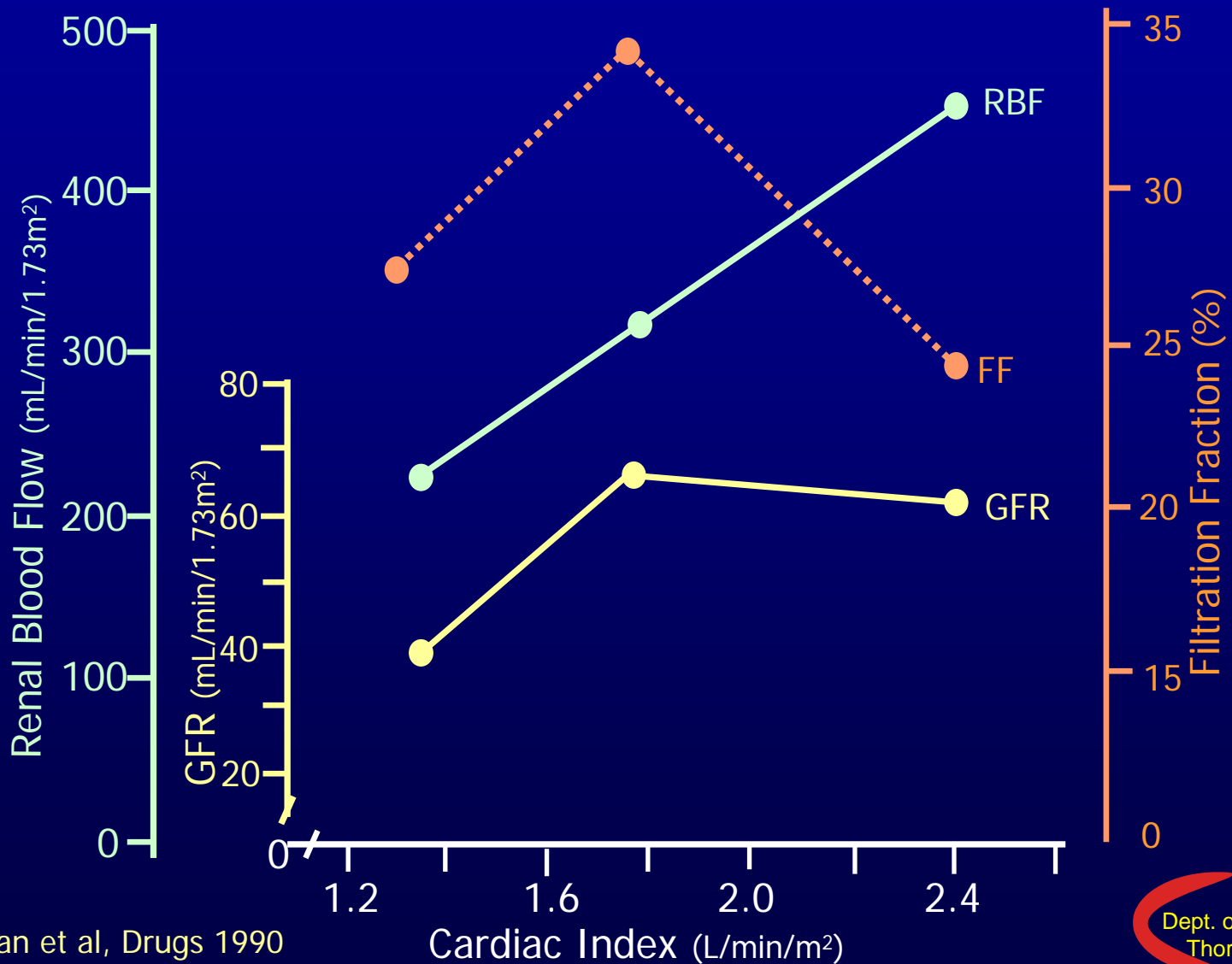
Groningen, The Netherlands,



ESC Barcelona September 5 2006

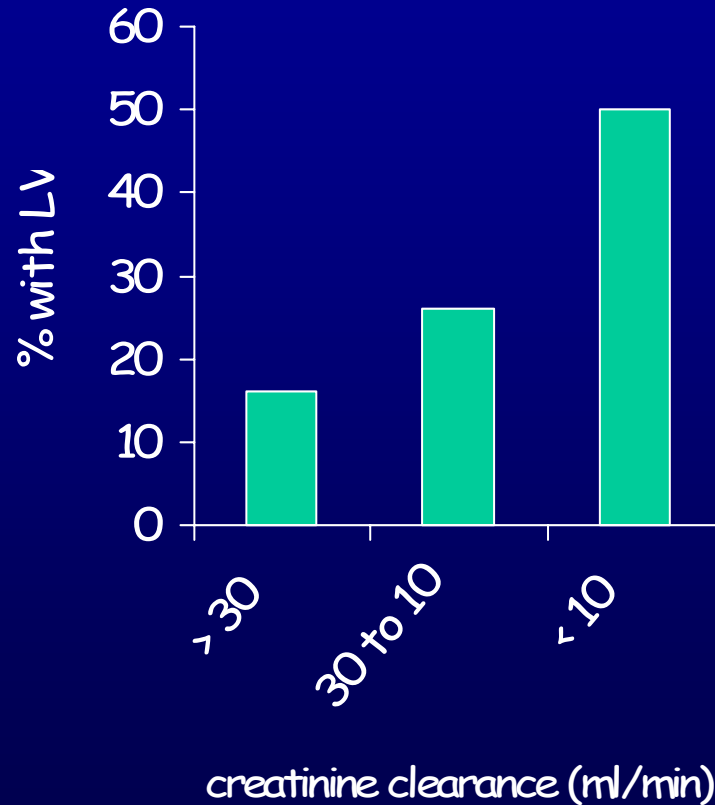


CHF leads to renal dysfunction



Ljungman et al, Drugs 1990

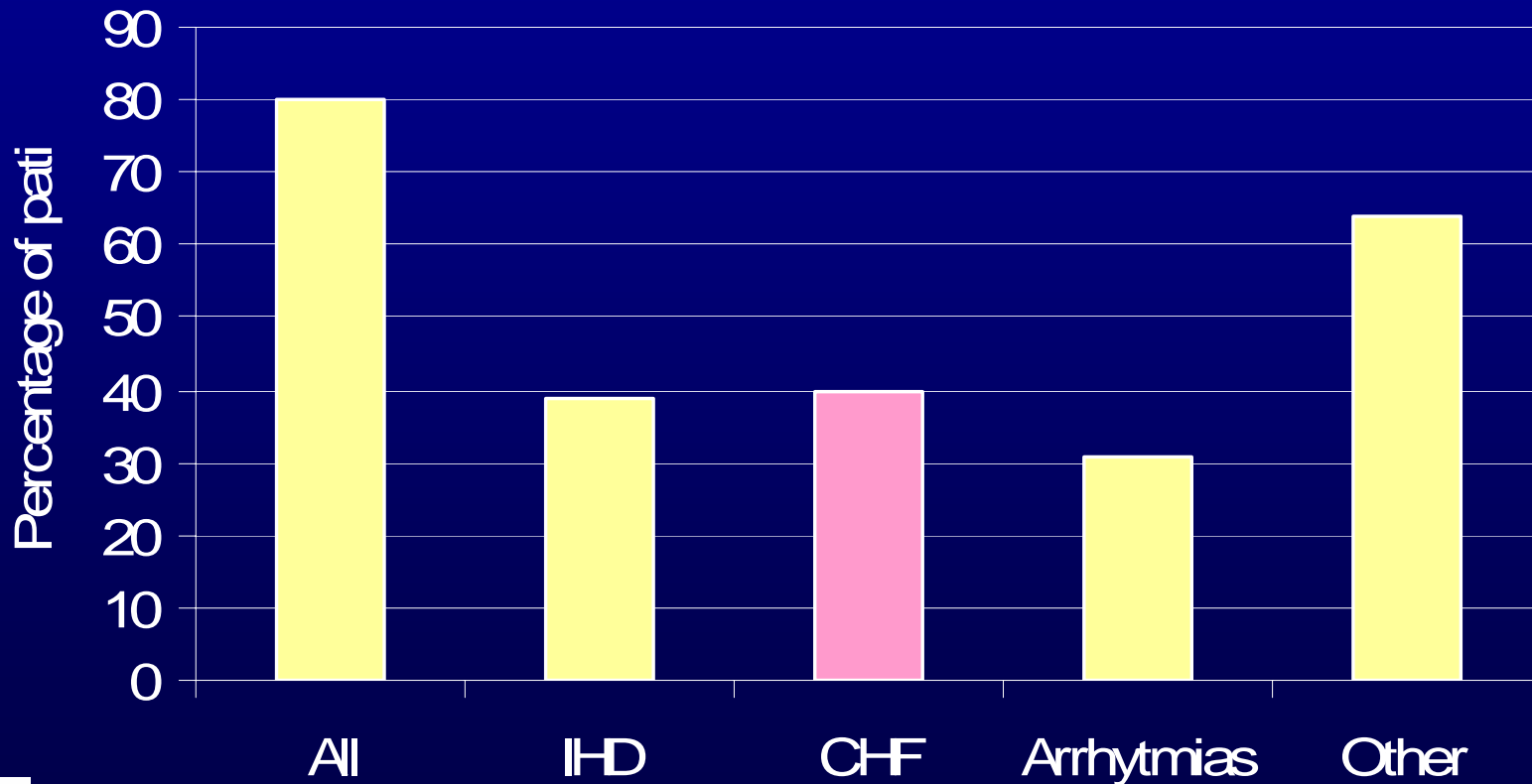
Severe renal disease also leads to end-organ damage in particular LVH



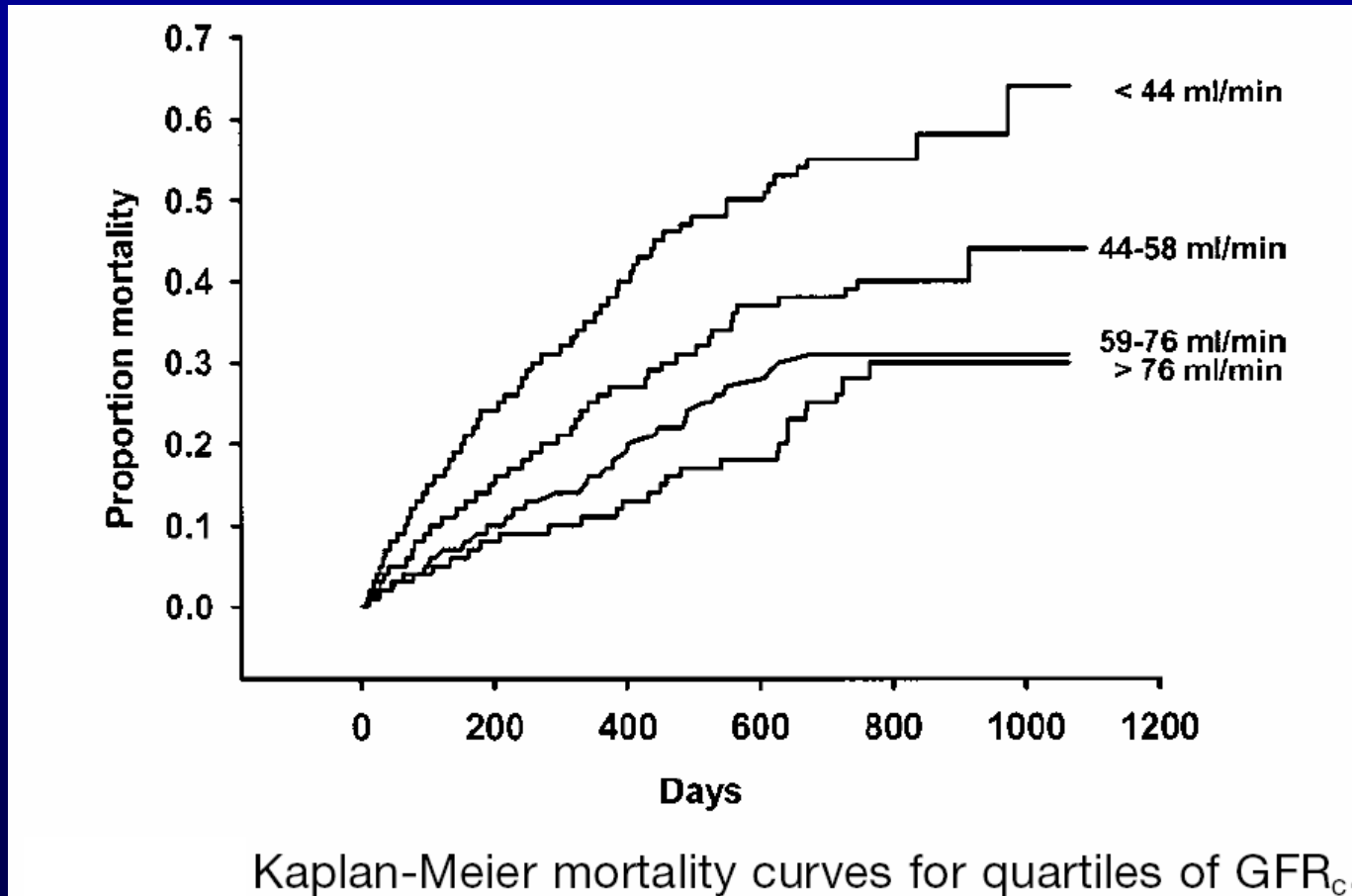
Tucker, NDT 1997; 12: 724

Presence of cardiac disease in hemodialysis patients

High incidence of CHF



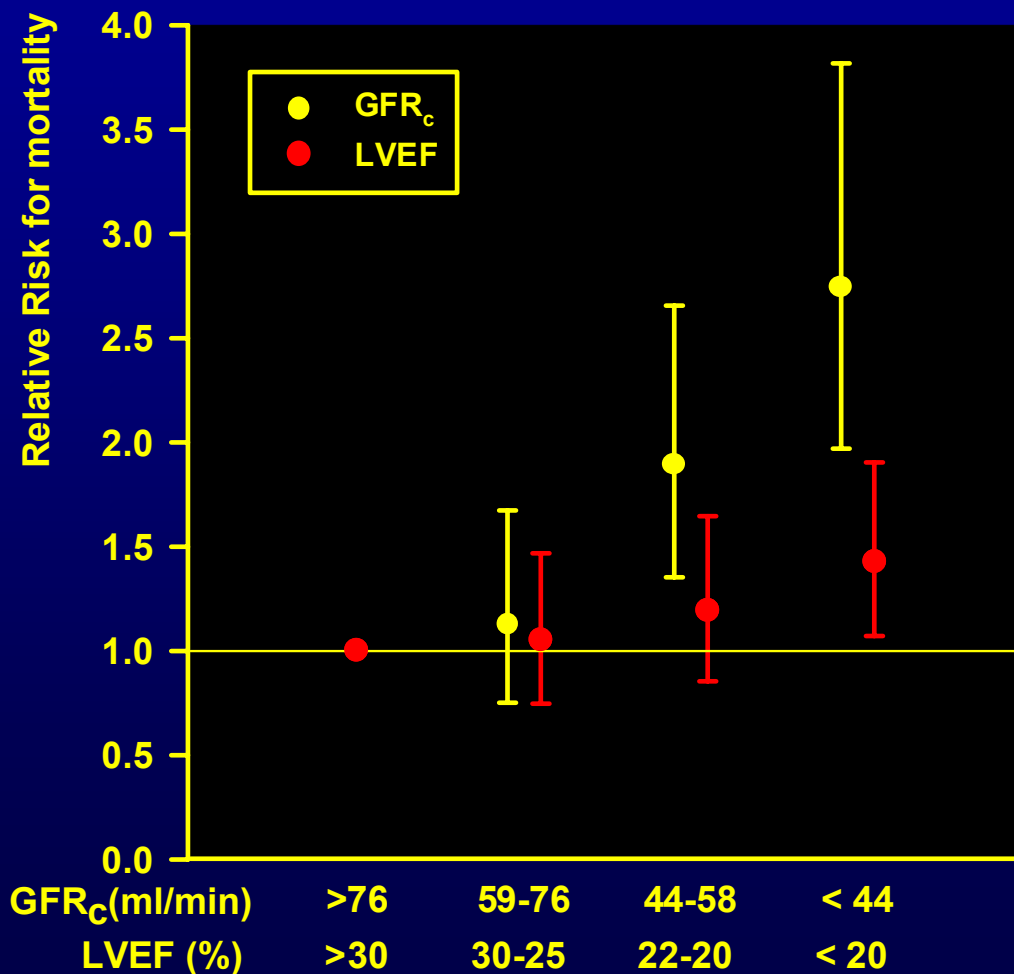
Prognostic Value of Renal function in advanced CHF



Hillege et al, Circulation 2000

GFR_c vs LVEF in advanced CHF

PRIME II



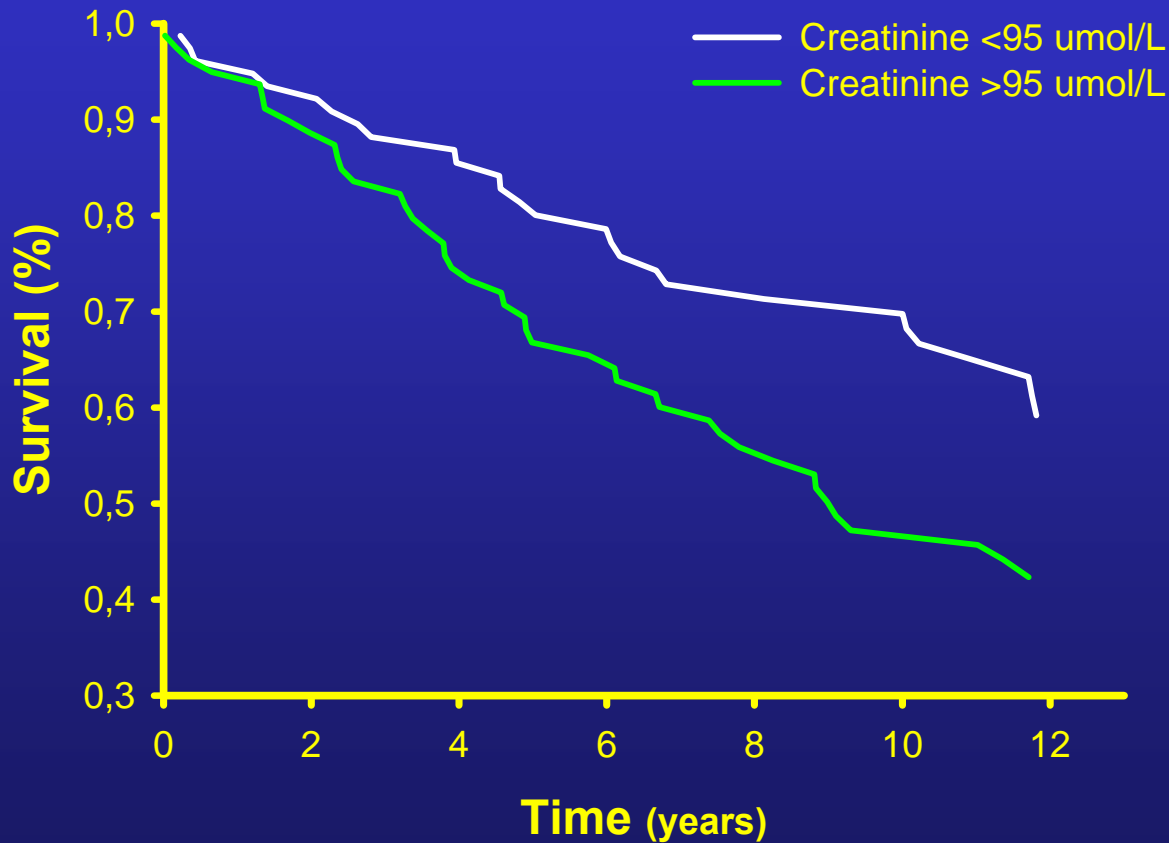
Hillege et al, Circulation 2000



Prognostic Value of Renal Dysfunction in SOLVD

	All-Cause Mortality		Pump-Failure Death	
	RR	(95% CI)	RR	(95% CI)
CrCl (<60 vs. ≥60 ml/min)	1.41	(1.15–1.74) ^{***}	1.68	(1.16–2.44) ^{**}
Age, per 5 year increase	1.09	(1.04–1.14) ^{***}	1.12	(1.02–1.22) ^{**}
EF, per 10% decrease	1.45	(1.27–1.65) ^{***}	1.58	(1.25–2.02) ^{***}
Men vs. women	1.28	(0.97–1.70) [†]	1.17	(0.71–1.90)
NYHA II vs. I	1.10	(0.93–1.31)	1.42	(1.04–1.94) [*]
Presence of:				
Prior stroke	1.78	(1.36–2.33) ^{***}	1.35	(0.79–2.31)
Prior hypertension	1.18	(0.97–1.41) [†]	1.15	(0.82–1.63)
Ischemic vs. nonischemic	0.90	(0.72–1.12)	0.77	(0.52–1.14)
Diabetes	1.29	(1.04–1.61) [*]	1.45	(0.98–2.14) [†]
Use of:				
Diuretic	1.30	(1.06–1.61) [*]	1.28	(0.87–1.89)
Antiarrhythmic drug	1.09	(0.87–1.36)	1.13	(0.76–1.69)
Antiplatelet agent	0.88	(0.74–1.05)	0.97	(0.70–1.34)
Digoxin	1.21	(0.97–1.52) [†]	1.36	(0.92–2.01)
Randomization to enalapril	0.96	(0.81–1.13)	0.81	(0.56–1.10)

Prognostic value of Renal function in patients with mild heart failure

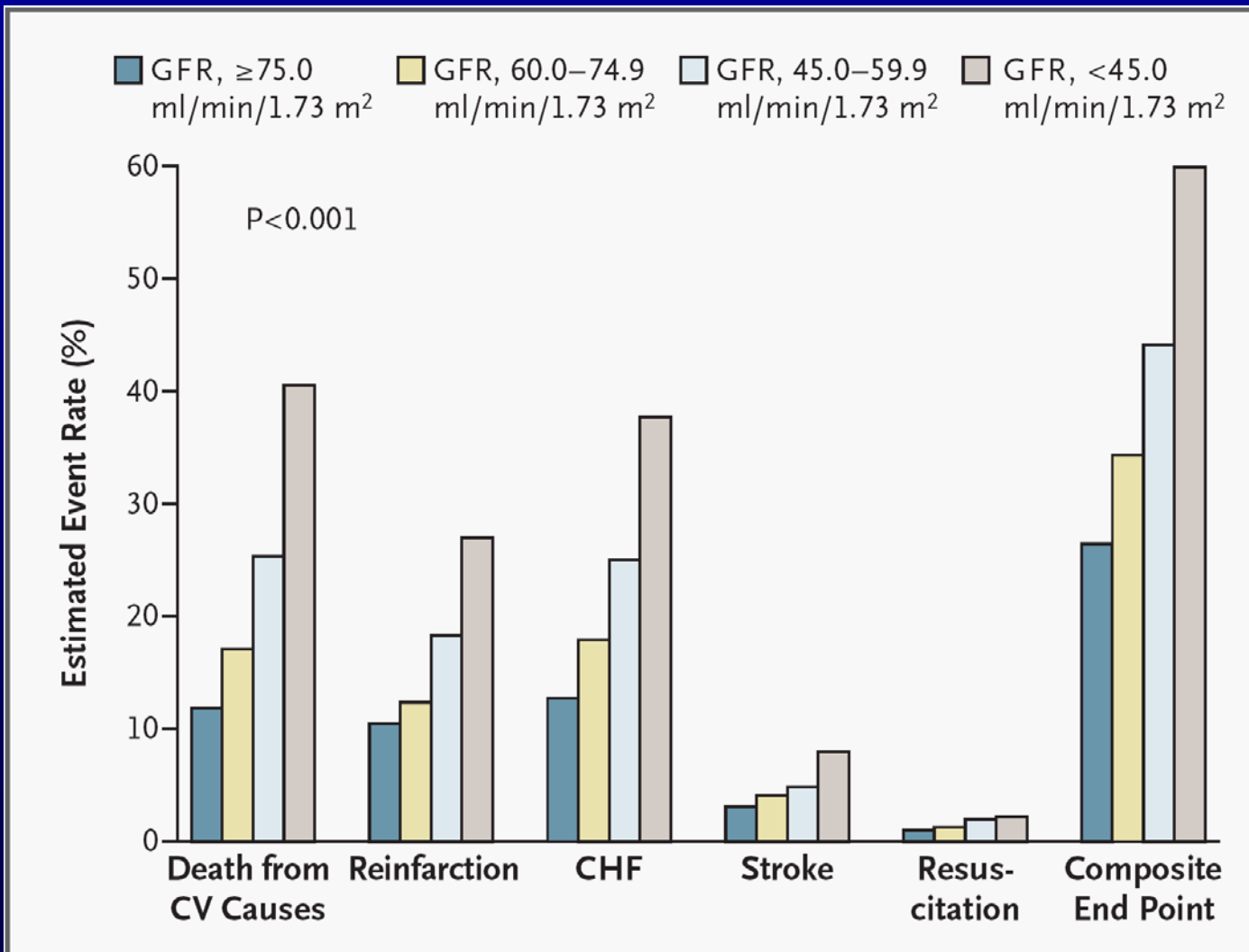


$P = 0.02$

RR: 1.77

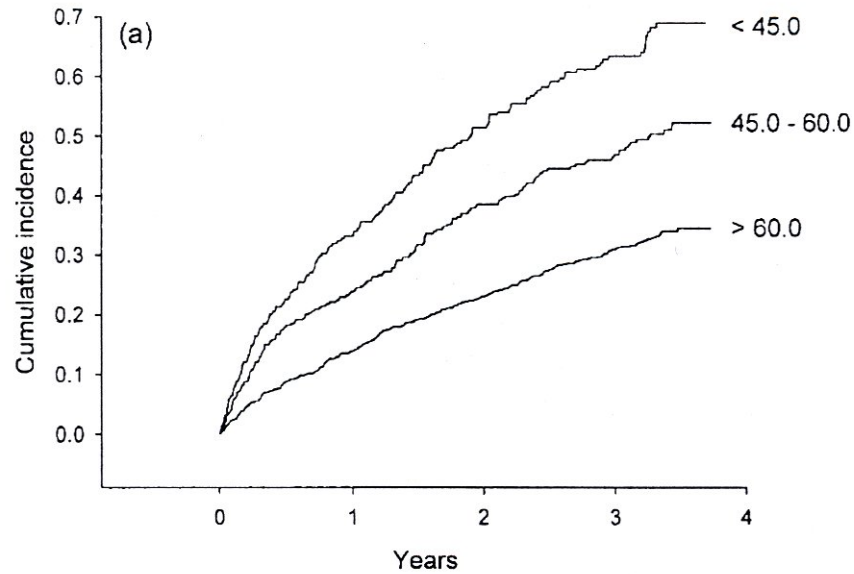


VALIANT- Renal dysfunction in pts with LV dysfunction after MI

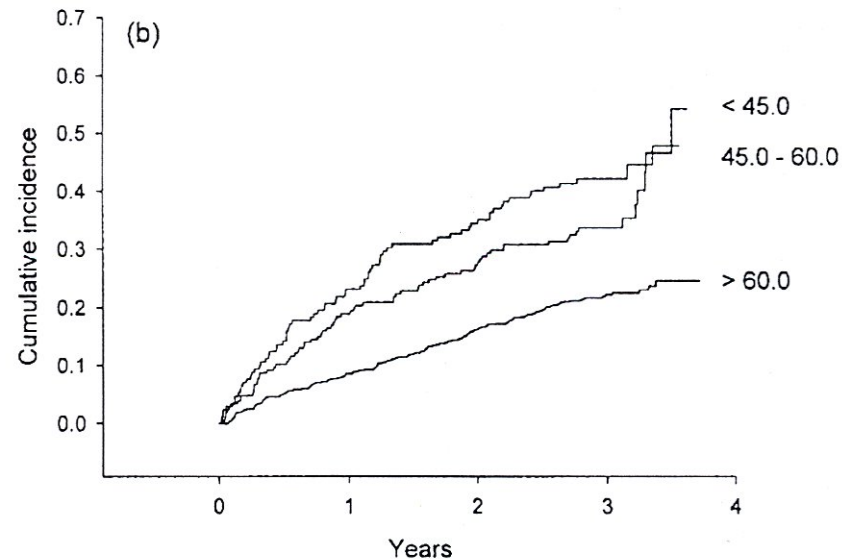


Anavekar et al. NEJM 2004

CHARM- renal function

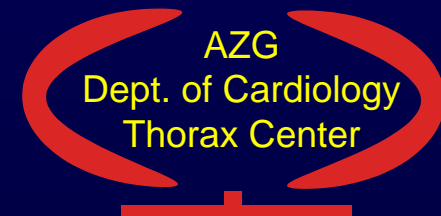


Impaired LVEF



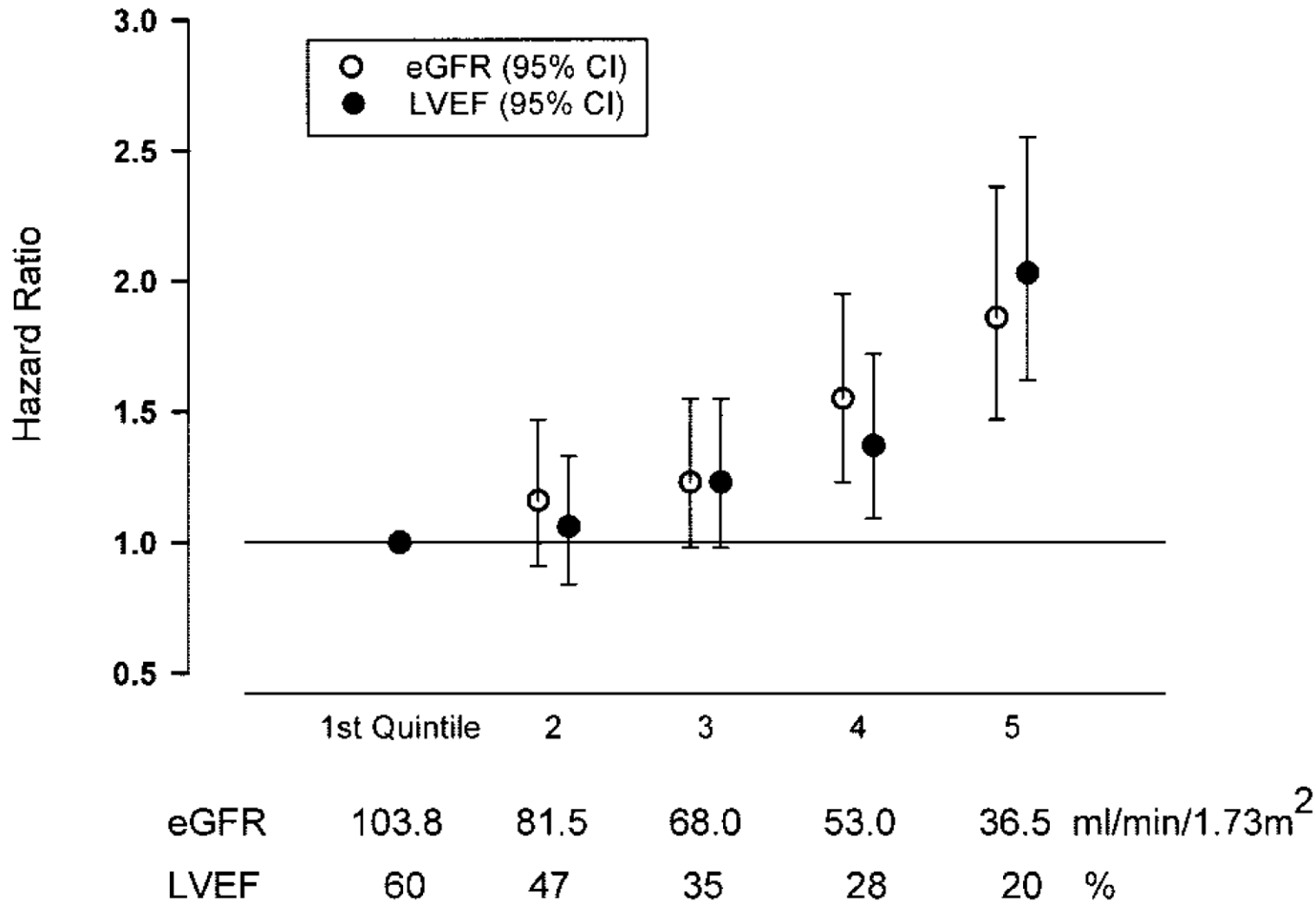
Preserved LVEF

Hillege et al
Circulation 2006



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CHARM-renal function

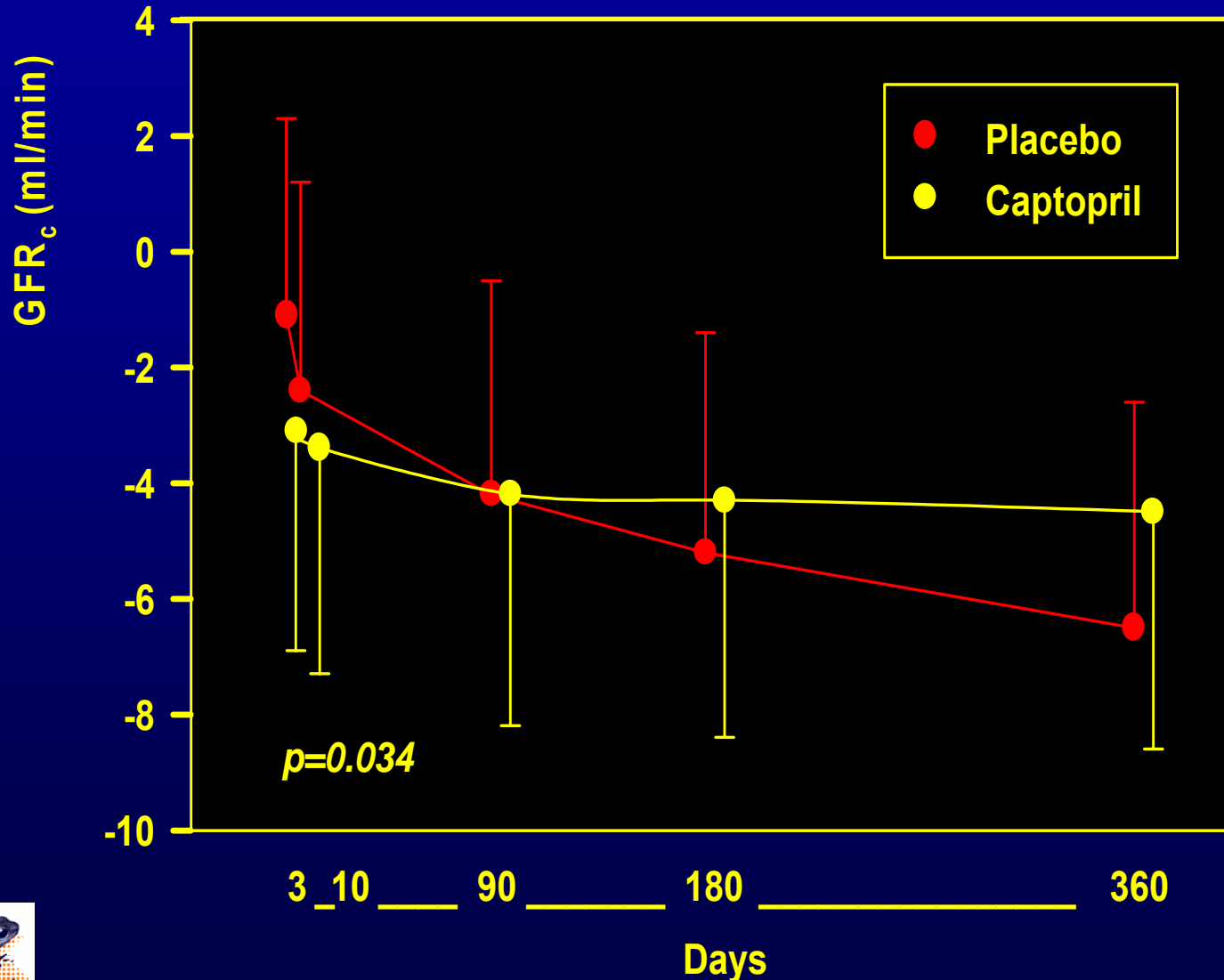


Hillege et al. Circulation 2006

Renal (dys-)function and Drug Treatment in Heart Failure



Renal function in LV dysfunction after MI is preserved by ACE-inhibition at the cost of a small initial loss

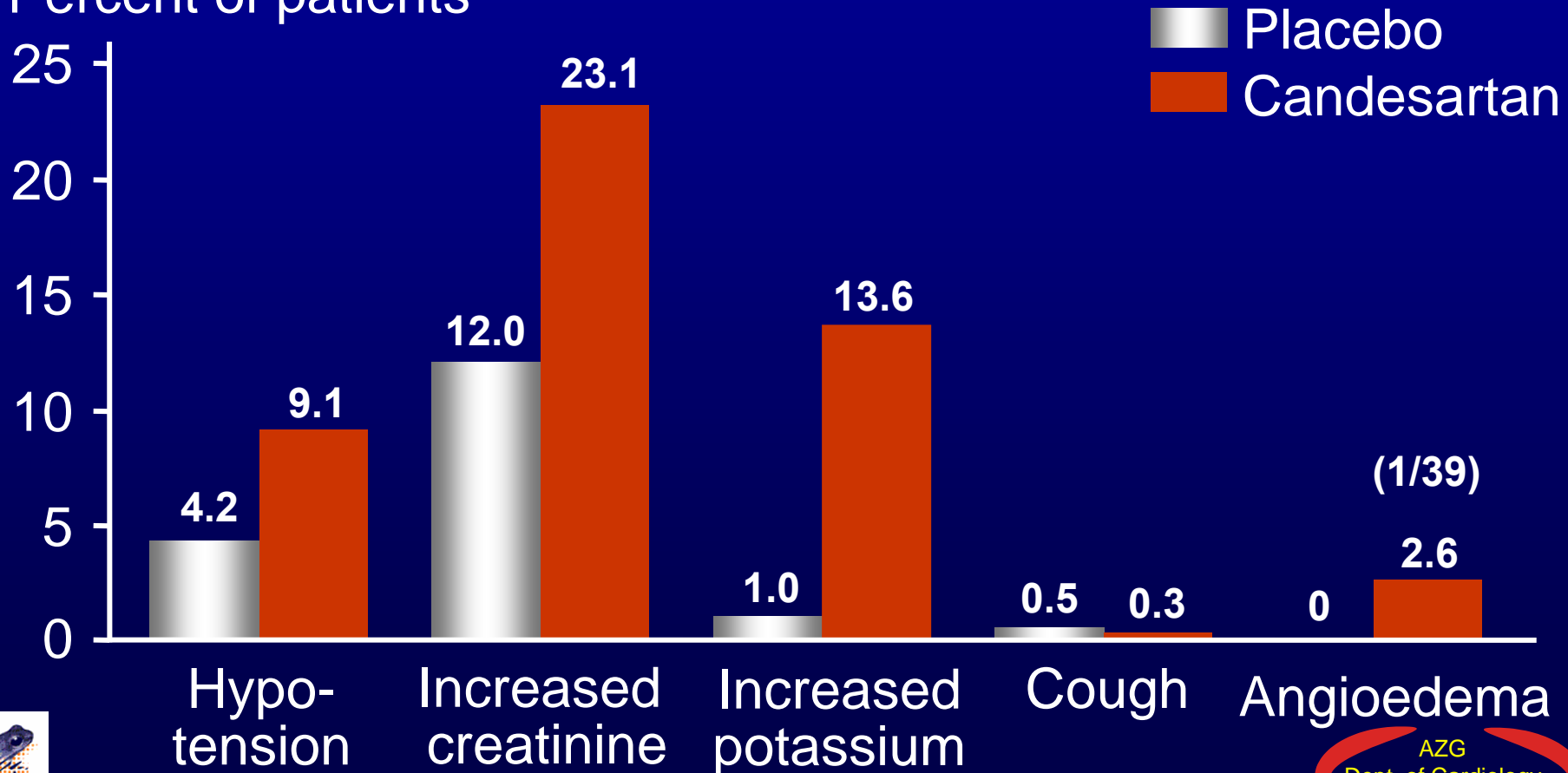


Hillege *et. al.* Eur Heart J 2003

CHARM-Alternative

Permanent study drug discontinuations

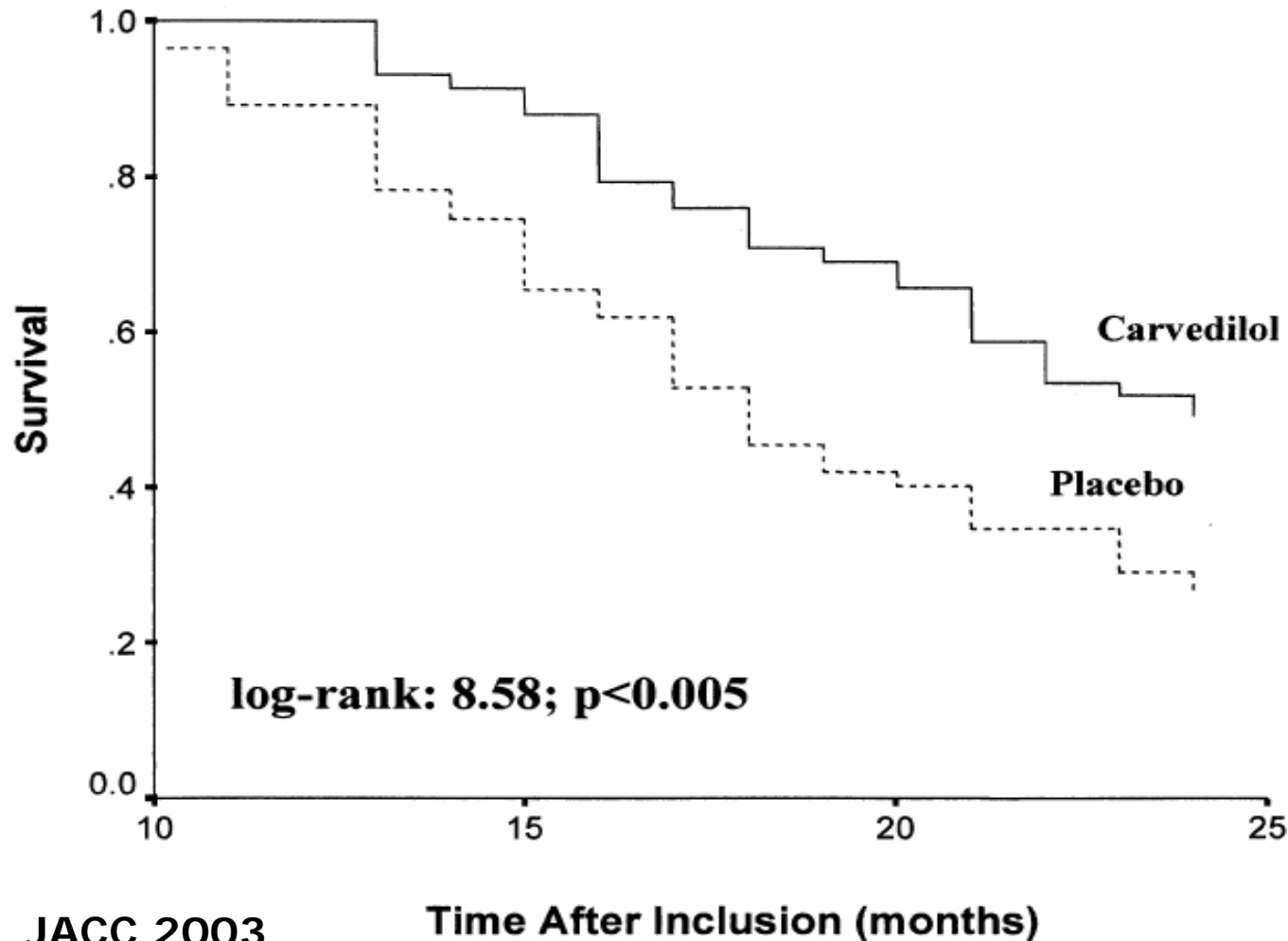
Percent of patients



Carvedilol Increases Two-Year Survival in Dialysis Patients With Dilated Cardiomyopathy

A Prospective, Placebo-Controlled Trial

Gennaro Cice, MD,* Luigi Ferrara, MD,* Antonello D'Andrea, MD,* Salvatore D'Isa, MD,*
Attilio Di Benedetto, MD,† Antonio Cittadini, MD,‡ Pina Elvira Russo, MD,* Paolo Golino, MD, PhD,*
Raffaele Calabrò, MD*



JACC 2003

Time After Inclusion (months)

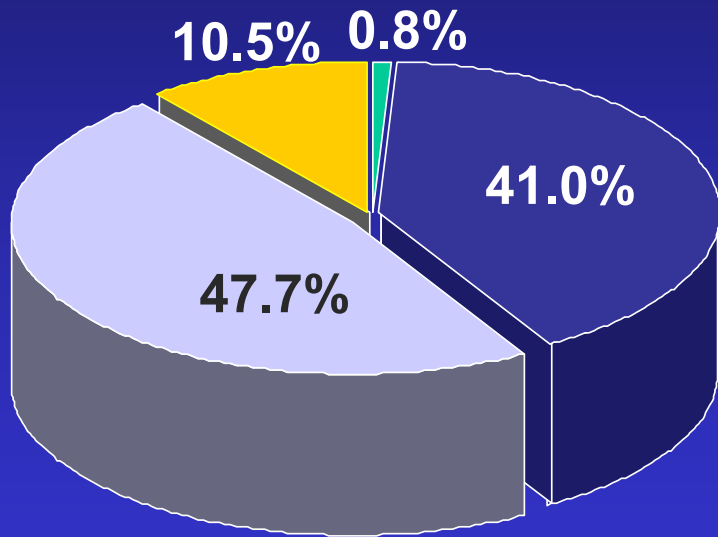
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CIBIS III population:

411 (40.7%) pts with moderate-severe ↓ eGFR (< 60 ml/min/1.73m²)

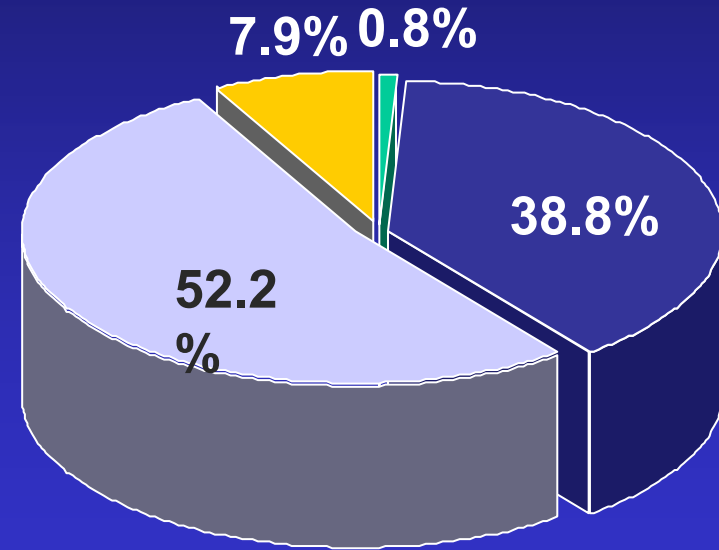
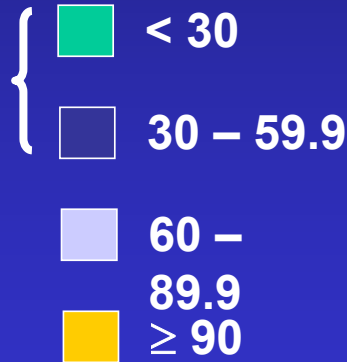
506 (50.1%) pts with mild ↓ eGFR (60 – 89.9 ml/min/1.73m²)

93 (9.2%) pts with normal eGFR (≥ 90 ml/min/1.73m²)



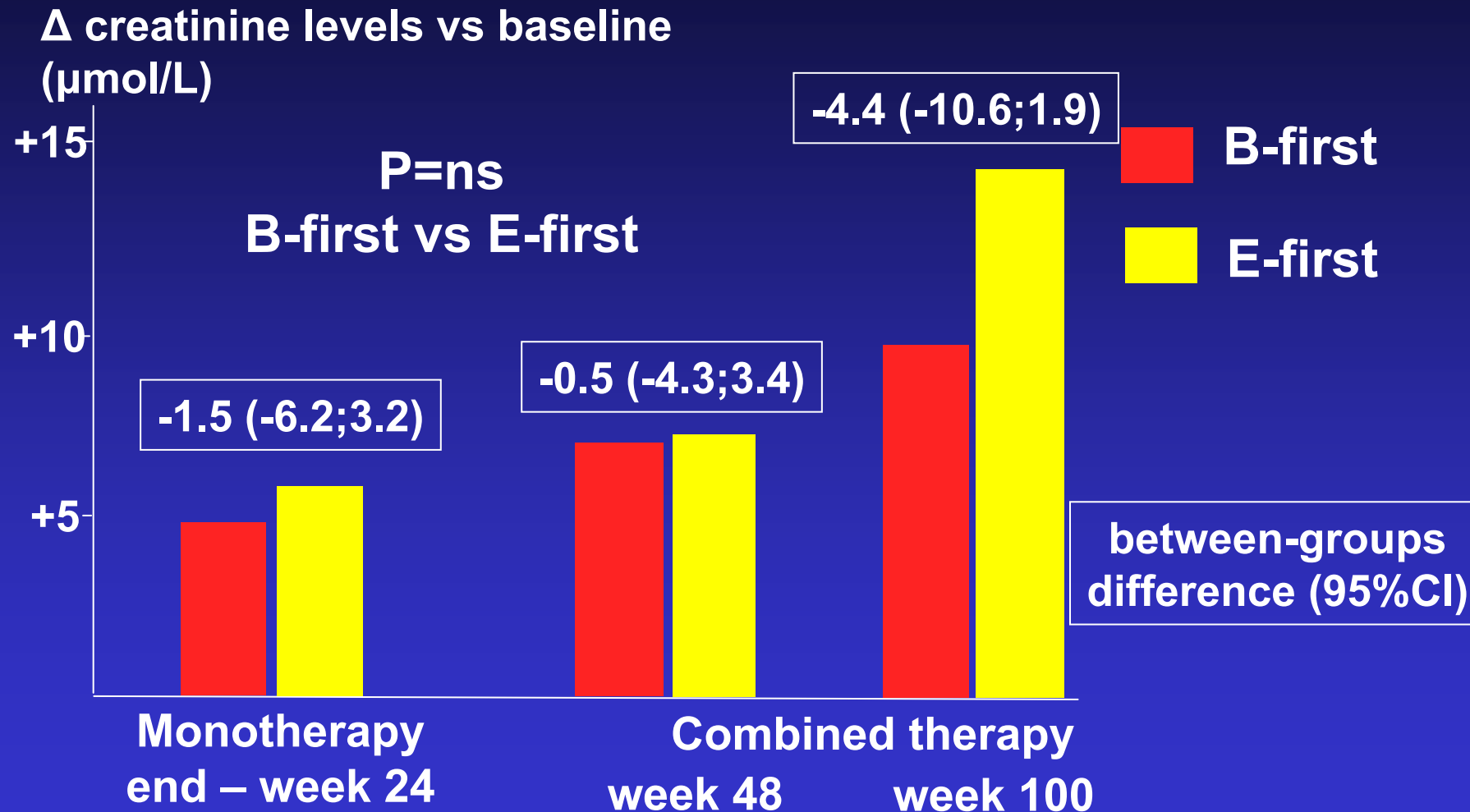
Bisoprolol-first

eGFR
(mL/min/1.73m²)



Enalapril-first

CIBIS III: changes in creatinine levels during study



Which factors are associated with renal (dys-)function in Heart Failure?



Factors associated with renal dysfunction in CHF (Smilde 2006)

Table 1. Baseline characteristics for total study population

	Total Population (n=86)
Age (years)	58 ± 12
NYHA class	2.3 ± 0.8
Sex (n, % male)	67 (78)
Diabetes (n, %)	7 (8)
Current smoking (n, %)	14 (18)
Ischemic etiology (n, %)	43 (50)
<i>Cardiorenal hemodynamic parameters</i>	
GFR (mL/min/1.73m ²)	74 ± 28
RBF (mL/min/1.73m ²)	465 ± 161
FF (%)	27 ± 5
LVEF	0.27 ± 0.09
MAP (mm Hg)	85 ± 14
NT pro BNP (pg/mL)*	786 (303-1930)
<i>Renin Angiotensin System parameters</i>	
PRA (ng/mL/h)*	24.3 (5.5-60.3)
Ang II (pmol/L)*	9.8 (4.2-14.0)
<i>Endothelial function parameters</i>	
UAE (mg/day)*	8.7 (4.5-21.4)
ADMA (umol/L)	0.68 ± 0.19
vWf (%)*	78 (48-174)
sVCAM-1 (ng/mL)*	348 (273-374)
Plasma NOx (umol/L)	31.3 ± 15.8
sES (ng/mL)*	62 (47-88)
<i>Inflammation parameter</i>	
CRP (mg/L) *	2.5 (1.2-4.3)

Table 2. Relation of GFR with conventional cardiorenal hemodynamic, RAS, endothelial and inflammation parameters.

Variables	GFR			
	r Unadjusted	P-value	r Adjusted for age and sex	P-value
<i>Cardiorenal hemodynamic parameters</i>				
RBF	0.92	<0.001	<u>0.89</u>	<0.001
UAE#	-0.24	0.027	-0.29	0.007
NT pro-BNP#	-0.61	<0.001	-0.54	<0.001
MAP	0.35	0.001	0.39	<0.001
LVEF	0.22	0.043	0.29	0.006
<i>Renin Angiotensin System parameters</i>				
PRA#	-0.35	0.001	-0.48	<0.001
Ang II#	-0.24	0.028	-0.20	0.078
<i>Endothelial function parameters</i>				
sVCAM-1*	-0.30	0.006	-0.29	0.007
vWf*	-0.29	0.007	-0.27	0.017
NOx	-0.34	0.001	-0.27	0.013
ADMA	-0.25	0.019	-0.19	0.084
sES*	-0.08	0.491	-0.06	0.604
<i>Inflammation parameter</i>				
CRP#	-0.09	0.422	0.01	0.928

Values are shown as Pearson correlation coefficients and as correlation coefficients obtained with linear regression, adjusted for age and sex. *Data logarithmically transformed.

GFR; glomerular filtration rate, RBF; renal blood flow, UAE; urinary excretion rate, NT pro_BNP; N terminal pro brain natriuretic peptide, MAP; mean arterial pressure, LVEF; left ventricular ejection fraction, PRA; plasma renine activity, Ang II; angiotensin II, sVCAM-1; soluble vascular adhesion molecule-1, vWf; von Willebrand factor, NOx; nitrate/nitrite, ADMA; asymmetric dimethyl arginine, sES; soluble E-selectin, CRP; C-reactive protein.

Factors associated with renal dysfunction in CHF: Relation with invasive hemodynamics

Table 2: Regression analysis for GFR

Variable	Univariate	Multivariate	Multivariate
	correlation coefficient	correlation coefficient	p-value
Age	-0.072		
Gender	-0.218		
RBF	0.797	0.664	<0.001
RAP	-0.616	-0.367	0.020
CI	0.404		
PVR	-0.298		
Adjusted R ²		0.609	<0.001

RBF; Renal Blood Flow, RAP; Right Atrial Pressure, CI; Cardiac Index, PVR; Pulmonary Vascular Resistance. Partial correlation coefficients adjusted for age and gender are shown in univariate analysis.

Damman et al
2006

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Conclusions

Renal dysfunction is common and has strong prognostic value in chronic heart failure.

It may be affected by drug treatment in CHF

The most important “driving force” for renal dysfunction in CHF is impaired hemodynamics.

There is a reciprocal relation between cardiac and renal failure: the cardio-renal syndrome

