Syndrome cardiorénal

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Syndrome cardiorénal

Entité physiopathologique complexe touchant le cœur et les reins dans laquelle la dysfonction aigue ou chronique d'un des organes peut induire une dysfonction aigue ou chronique de l'autre organe

Table 3 Mechanisms involved in the cardio-renal interactions

Mechanisms	Causing renal injury in HF	Causing cardiac damage in CKD
Haemodynamic abnormalities: low renal blood flow and increased renal venous pressure	+++	+
Neurohormonal activation: SNS and RAA	+++	+++
Inflammatory activation and oxidative stress	+++	+++
Abnormalities of the coagulation/ fibrinolytic system	0	+++
Vascular calcification	0	+++
Anaemia	+	+++
Diuretic treatment of HF	+++/+	0

Syndrome cardiorénal (CRS)

- Type I:
  - Décompensation cardiaque aigue menant à une insuffisance rénale aigue
- Type II:
  - Anomalie chronique de la fonction cardiaque causant une insuffisance rénale chronique
- Type III:
  - Insuffisance rénale aigue entrainant une dysfonction cardiaque aigue
- Type IV:
  - Insuffisance rénale chronique causant une atteinte cardiaque
- Type V:
  - Condition systémique causant une atteinte des 2 organes

Ronco C et al. Eur Heart J 2010;31:703-711

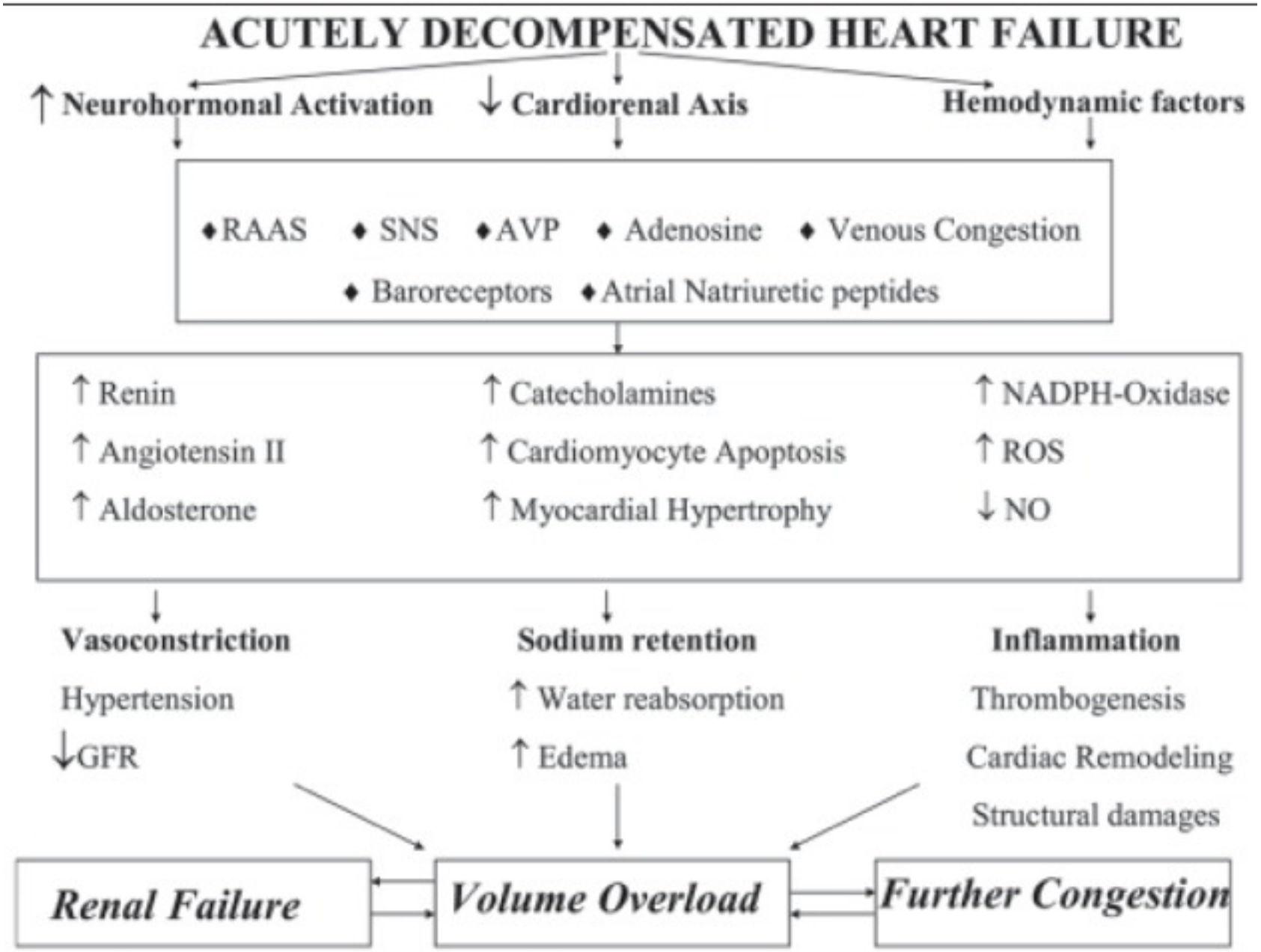
CRS 1

Table 2. Summary of studies fulfilling criteria for Type 1 CRS with a presenting diagnosis of ADHF

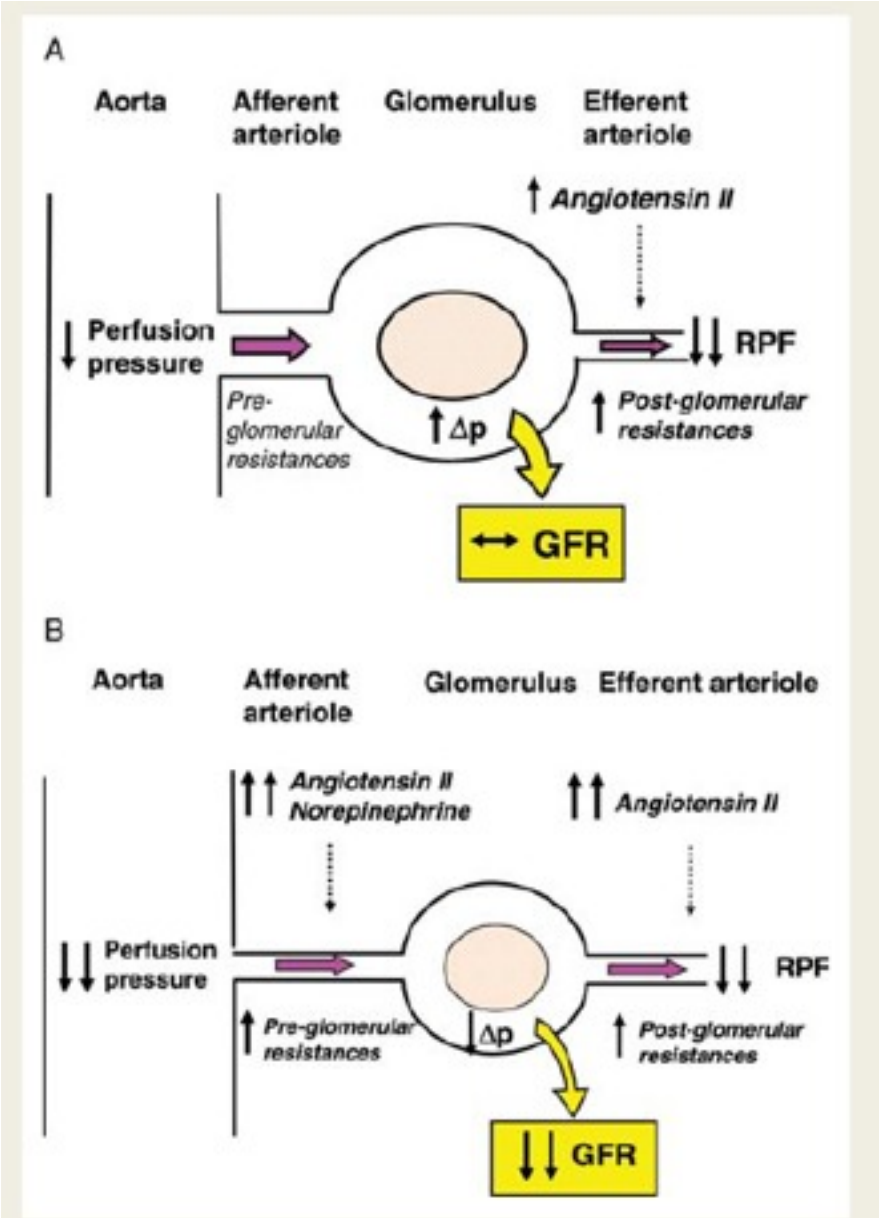
Study	Population (*n*)	Study type (data source)	AKI (WRF) definition	Incidence AKI (%)	Outcome
Krumholz *et al.* [5]	1681	Retrospective (Medicare)	SCr >26.5 μmol/L	28	In-hospital death (OR), 2.72 Increased hospital LOS, 2.3 d Increased costs, $1758 No association with readmission at 30 and 60 d
Gottlieb *et al.* [4]	1002	Retrospective	SCr >26.5 and >44.2 μmol/L	39 and 20	Increased in-hospital death Increased hospital LOS, >10 d
Smith *et al.* [15]	412	Prospective	SCr >8.8, >26.5 and >44.2 μmol/L	75, 45 and 24	All-cause death at 6 m modified by severity of AKI (HR: SCr > 0.8:0.88, SCr > 26.5:1.61, SCr > 44.2:2.86) No association with readmissions Trend in functional decline
Cowie *et al.* [11]	299	Prospective (POSH)	SCr >26.5 μmol/L	29	Increased LOS by 2 d Death/readmission rates similar
Nohria *et al.* [10]	433	Retrospective (ESCAPE Trial)	SCr >26.5 μmol/L	29.5	All-cause death (6 m) (HR) increased for SCr > 106.1 AKI (>26.5 μmol/L) not associated with death/readmission
Logeart *et al.* [13]	416	Prospective	SCr >26.5 μmol/L	37	All-cause death (6 m) or readmission (adj-HR) 1.74 Increased LOS, 3 d Risk persisted whether AKI transient or not
Metra *et al.* [14]	318	Prospective	SCr >26.5 μmol/L and ≥25%	34	CV death or readmission (adj-HR) 1.47 Increased LOS, 7 d

SCr, serum creatinine; m, months; d, days; CV, cardiovascular; LOS, length of stay.

Bagshaw ndt 2010



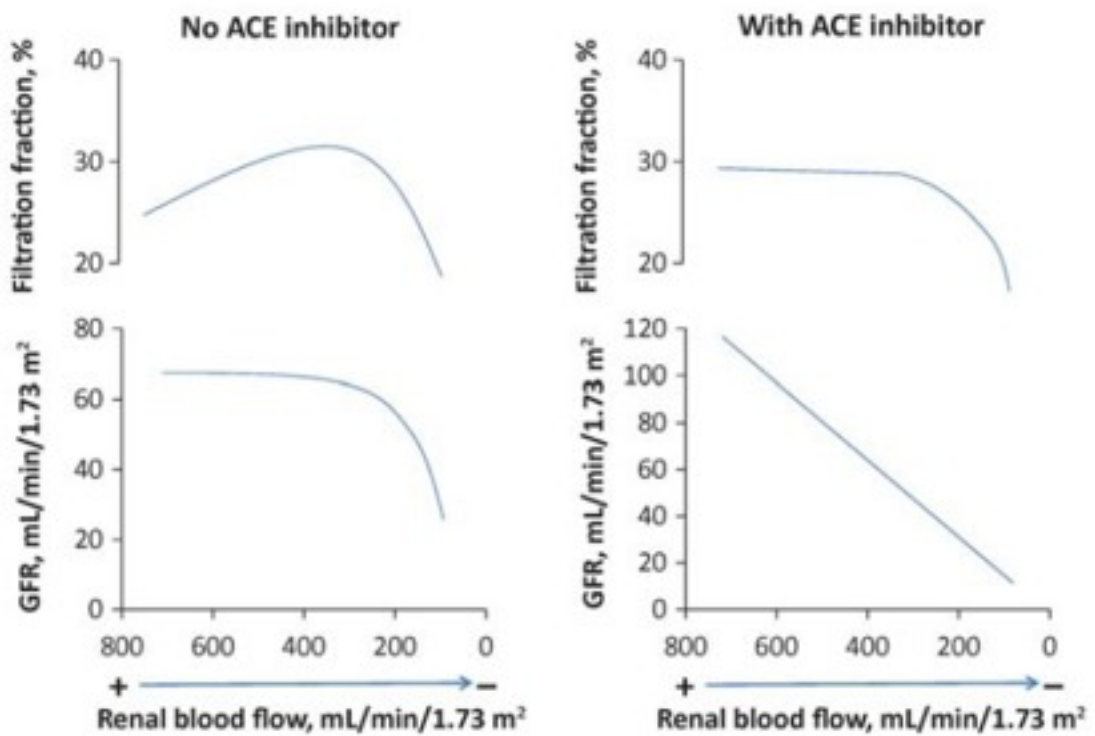
Koniari K et al European J Cardiology 2012



Hémodynamique rénale dans IC

- Dissociation entre baisse du débit cardiaque et débit rénal en défaveur du rein
- Adaptation rénale qui permet de modérer baisse de GFR (A)
- Décompensation cardiaque sévère dépasse les mécanismes adaptatifs (B)

IEC diminuent la capacité de maintenir un GFR constant en cas de baisse du débit rénal



Biais dans l'interprétation des variations de la fonction rénale

Metra M et al European Heart Journal 2012

L'élévation de la créatinine arrive rapidement et est de mauvais pronostic

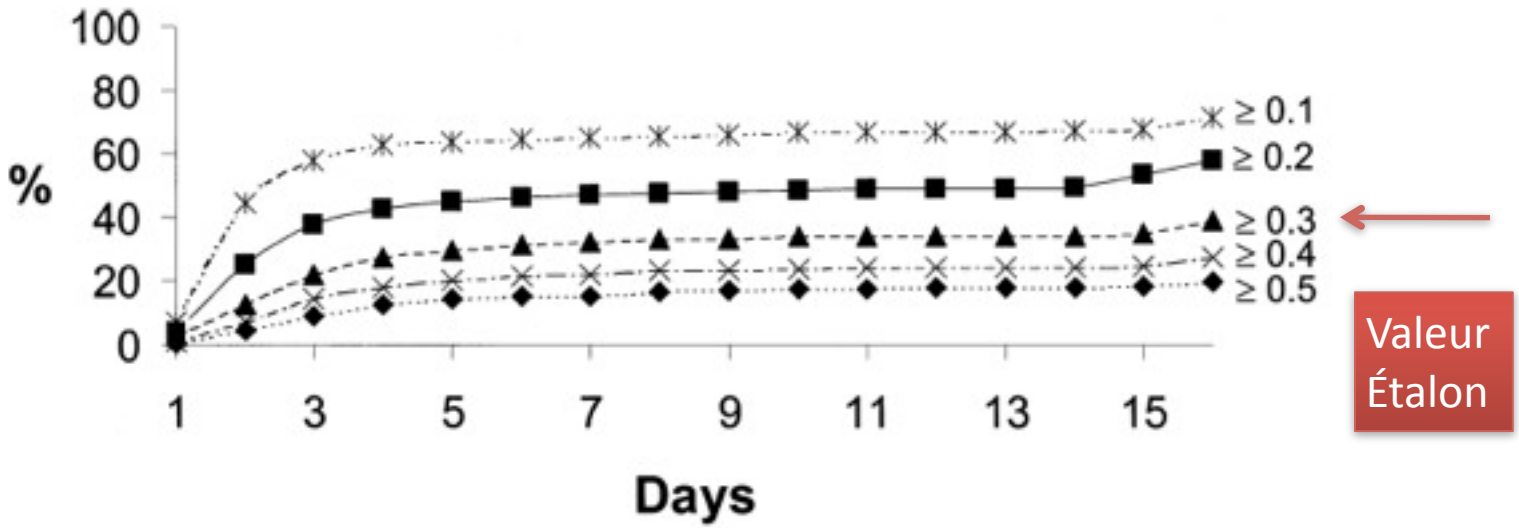
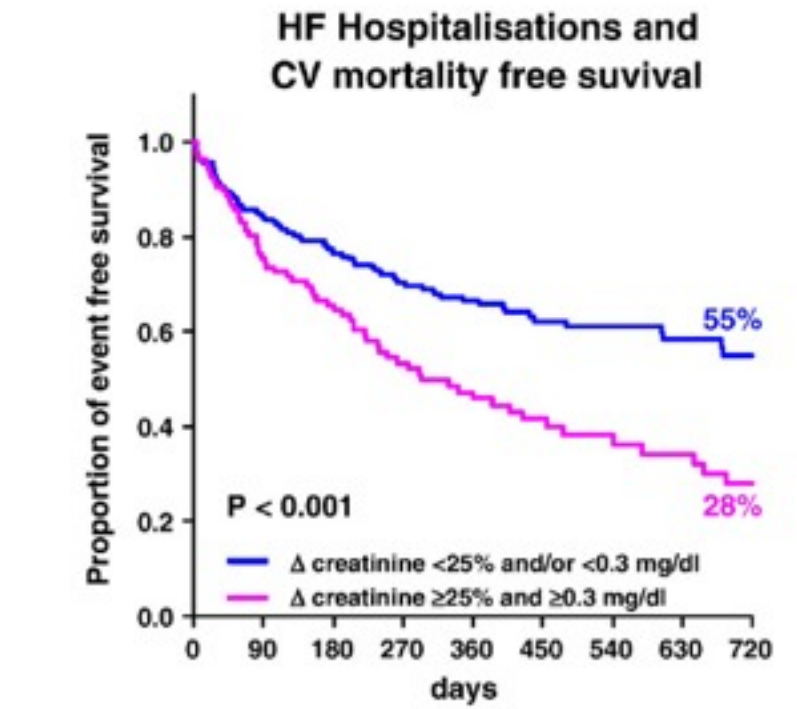


Fig. 1. The time course of development of increasing serum creatinine of various extents. When the creatinine increased, it occurred soon after hospital admission.

Gottlieb SS et al J Cardiac Fail 2002

La mortalité et le risque d'hospitalisation à deux ans est moins bon chez les patients avec IC qui montent leur créatinine.



Pts. at risk
Absolute and percent s-Cr change:

<0.3 or 25%	211	143	92	55	36
≥0.3 & 25%	107	64	36	19	14

Metra M et al Eur J Heart failure 2008

Monitoring hémodynamique ne change pas l'évolution rénale

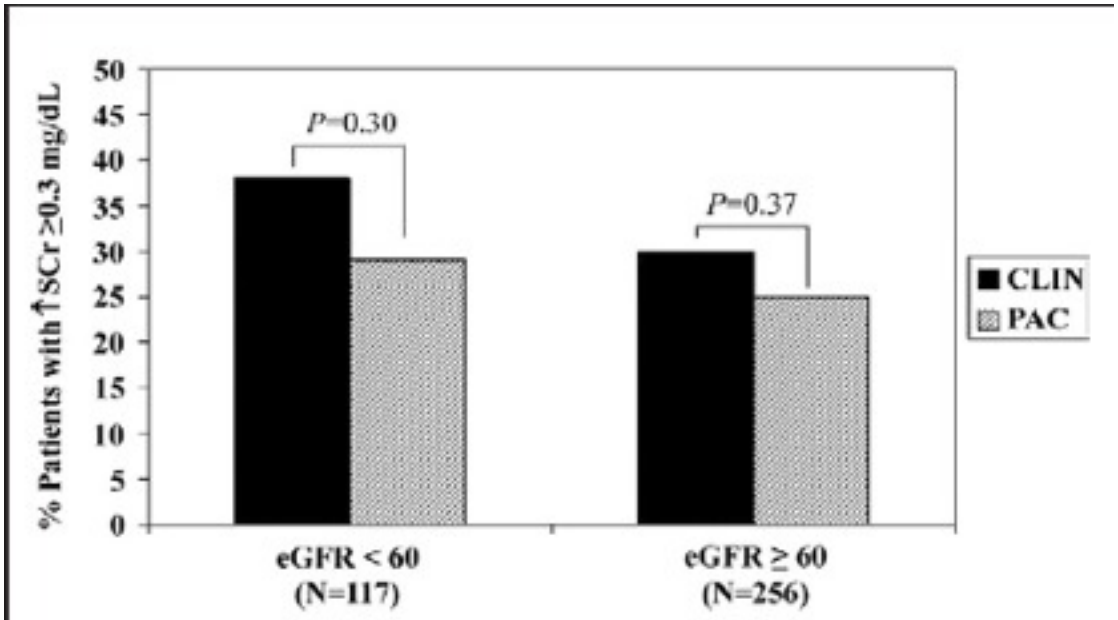


Figure 1 Impact of PAC on Worsening Renal Function in Patients Stratified by Baseline Renal Function

Optimalisation du débit cardiaque n'a pas un effet déterminant sur la fonction rénale

Nohria A JACC 2008

Une augmentation de la PVC est associée à une baisse de la fonction rénale et à une

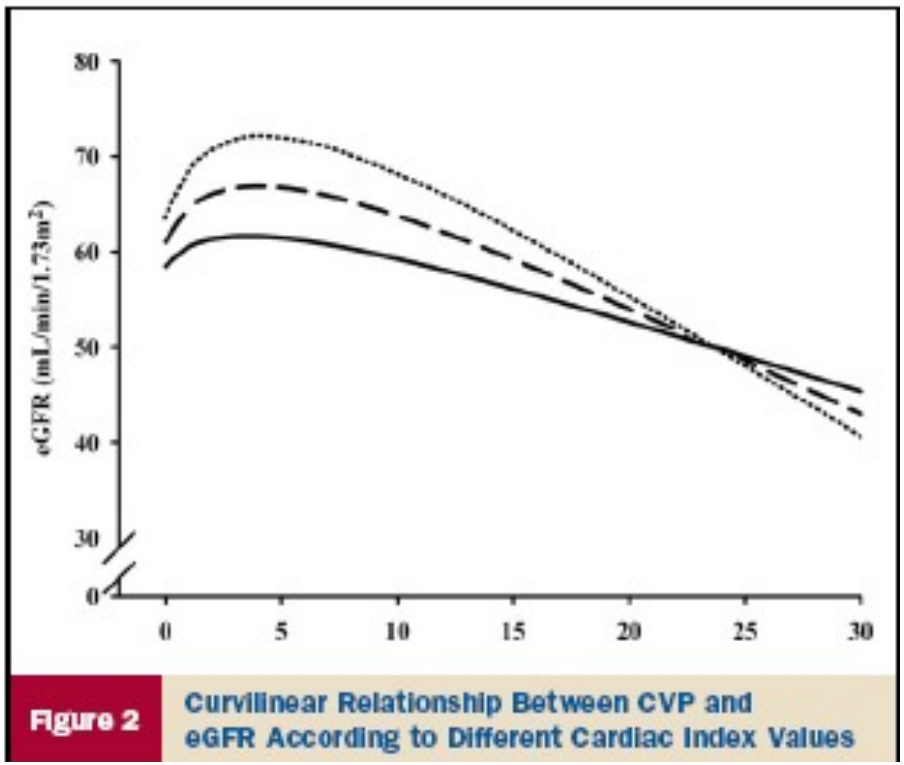


Figure 2 Curvilinear Relationship Between CVP and eGFR According to Different Cardiac Index Values

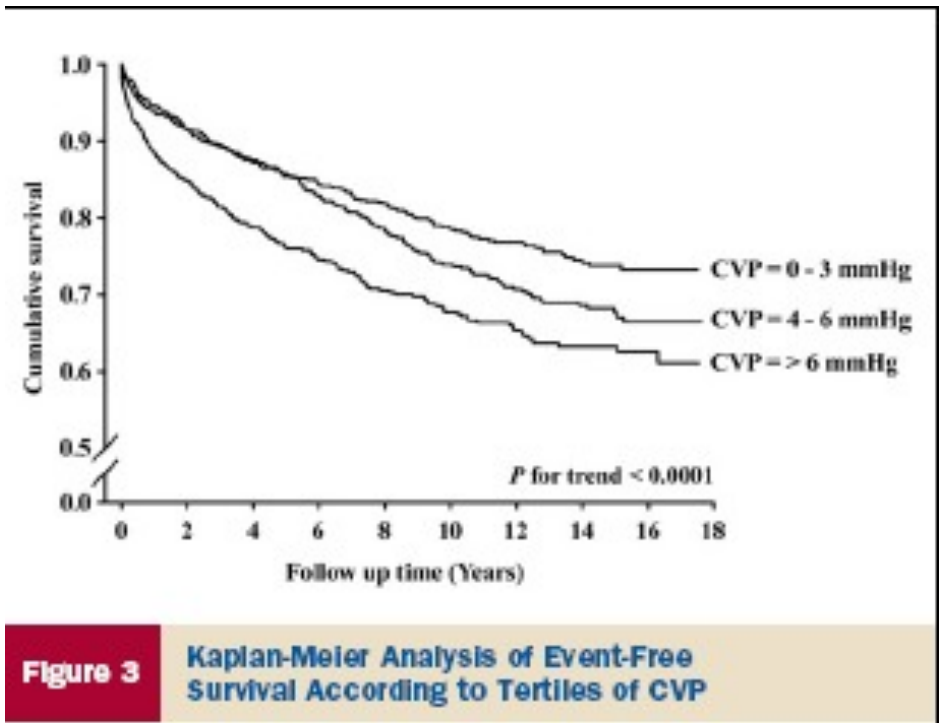
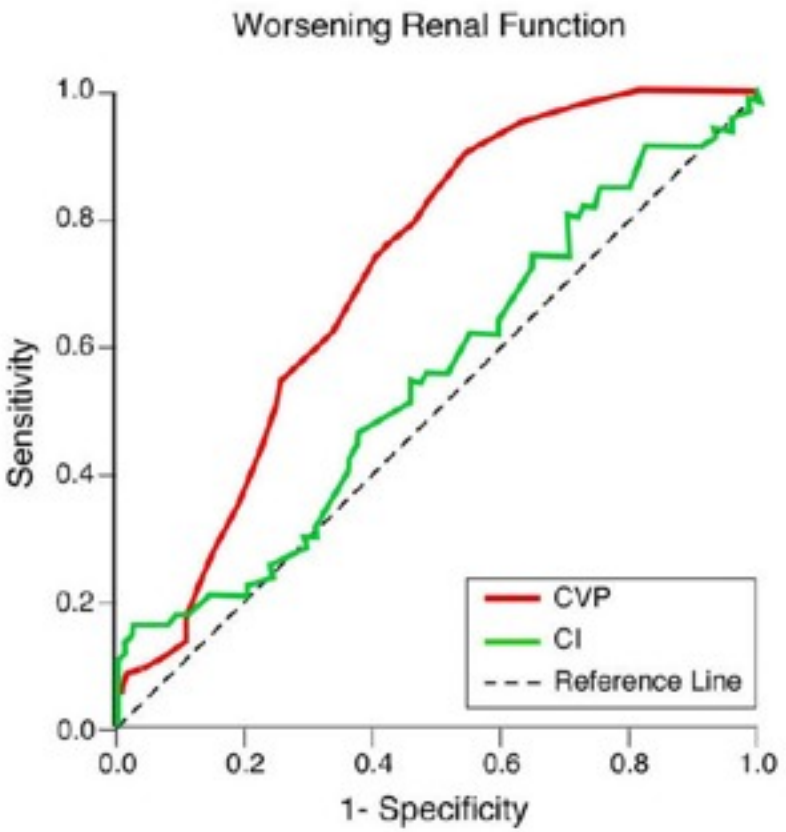


Figure 3 Kaplan-Meier Analysis of Event-Free Survival According to Tertiles of CVP

Damman K et al JACC 2009

La congestion veineuse est le facteur hémodynamique le plus important pour une aggravation de la fonction rénale



Mullens W JACC 2009

Influence de la pression intrabdominale

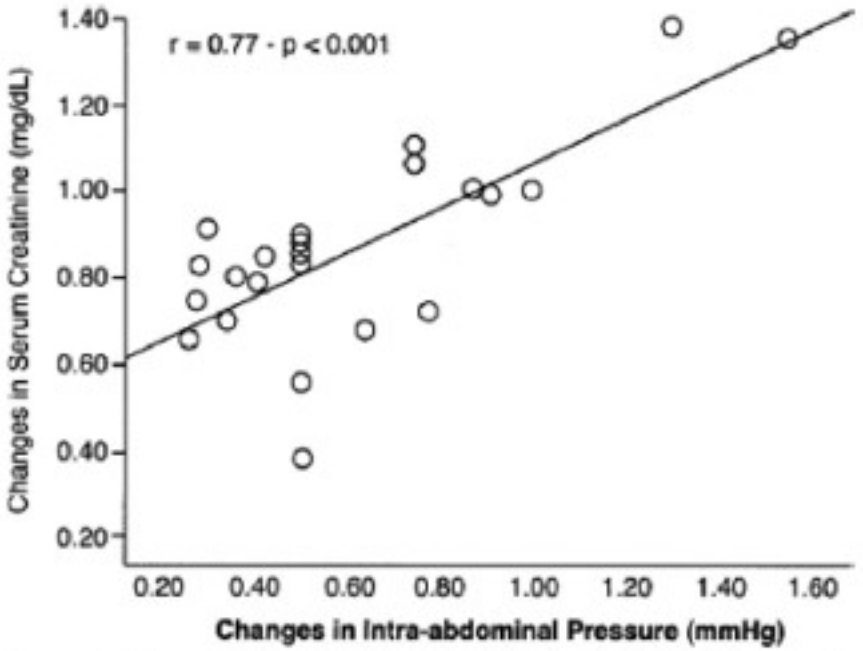
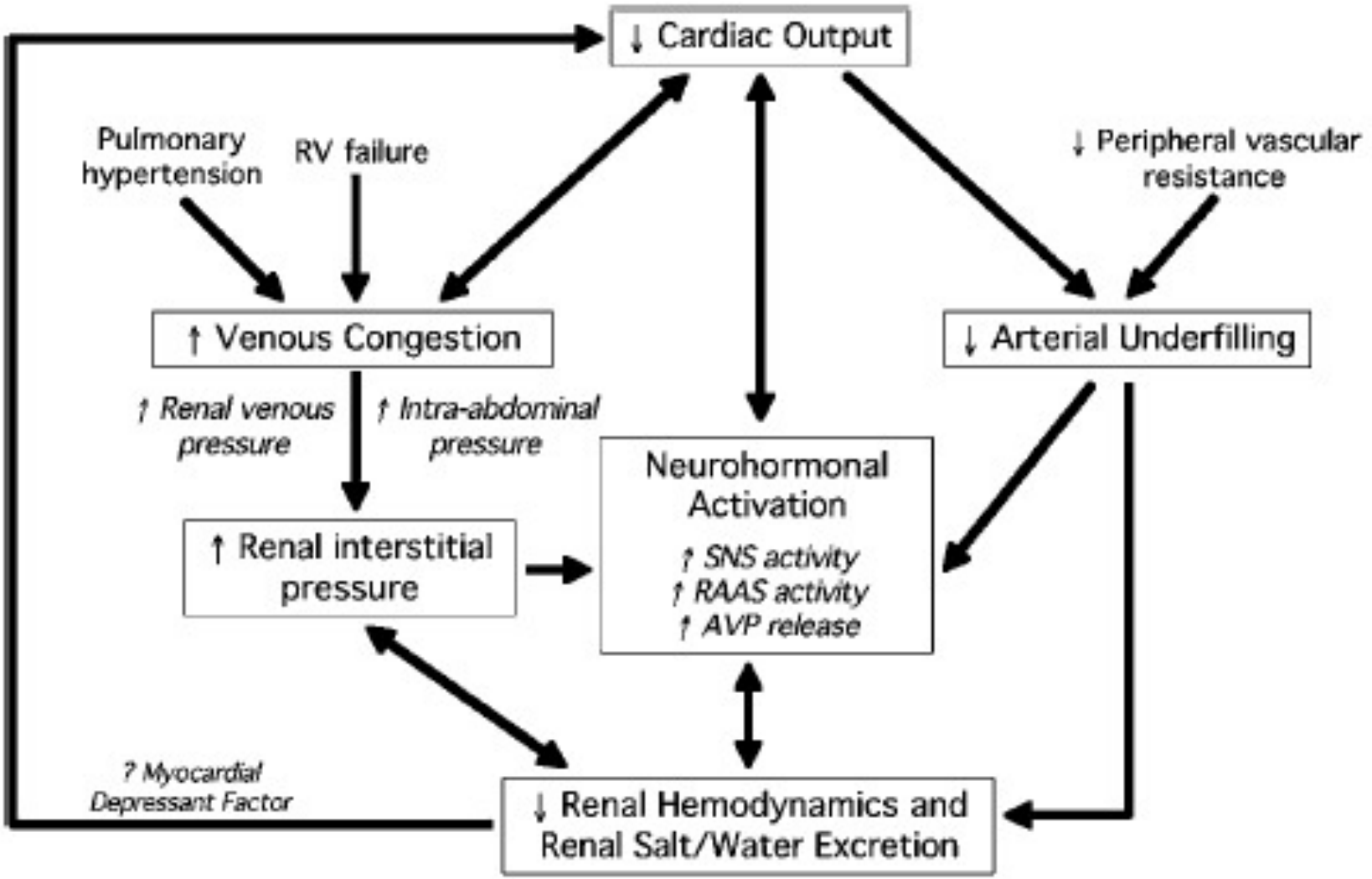


Figure 2. The relationship between changes in IAP with diuresis and the change in serum creatinine. The close relationship suggests that increased IAP may cause renal dysfunction. Reprinted with permission from Mullens et al.[17]

Mullens W et al JACC 2008



DIURETIQUES

Effets secondaires des diurétiques

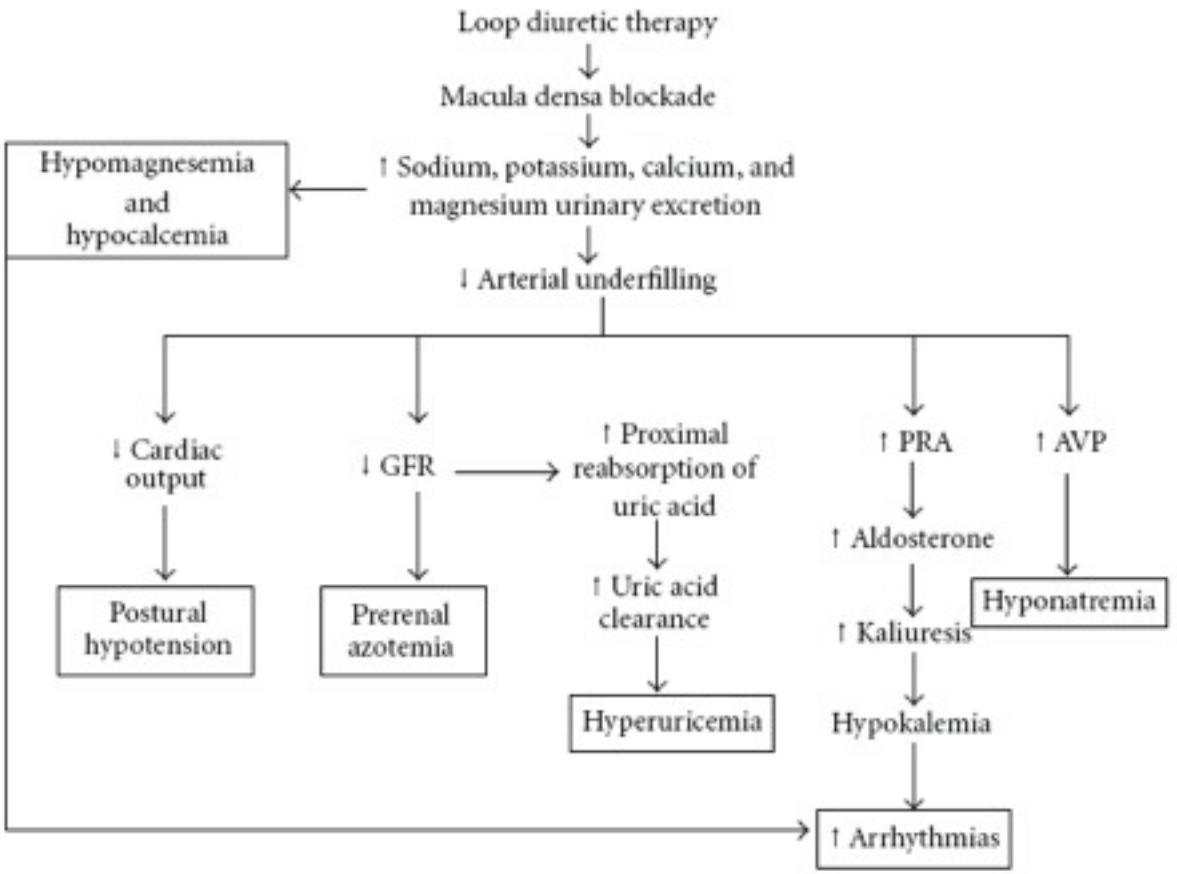


FIGURE 4: The mechanisms of adverse effects of loop diuretics (with permission from [11]).

Schrier RW NEJM 1988

Dosage of diuretics does not influence 30 days-survival

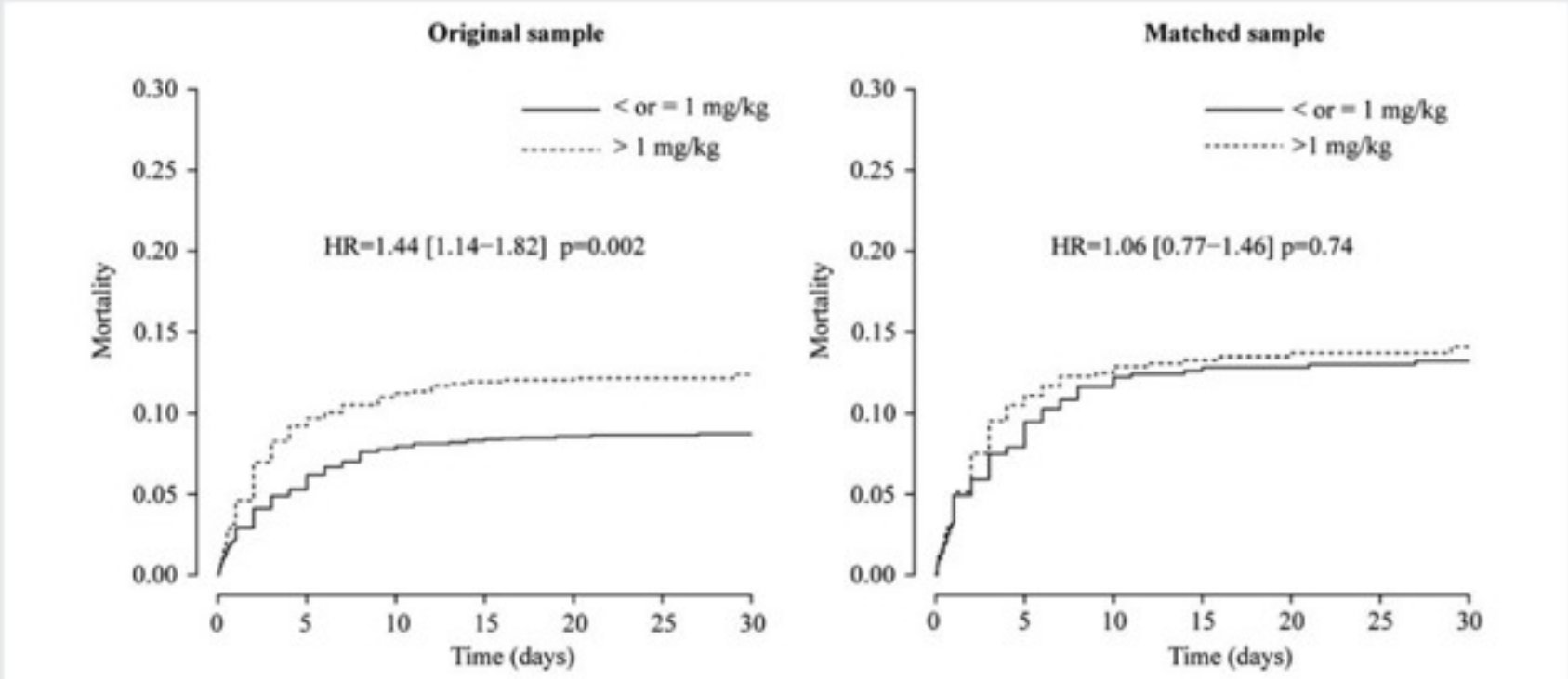
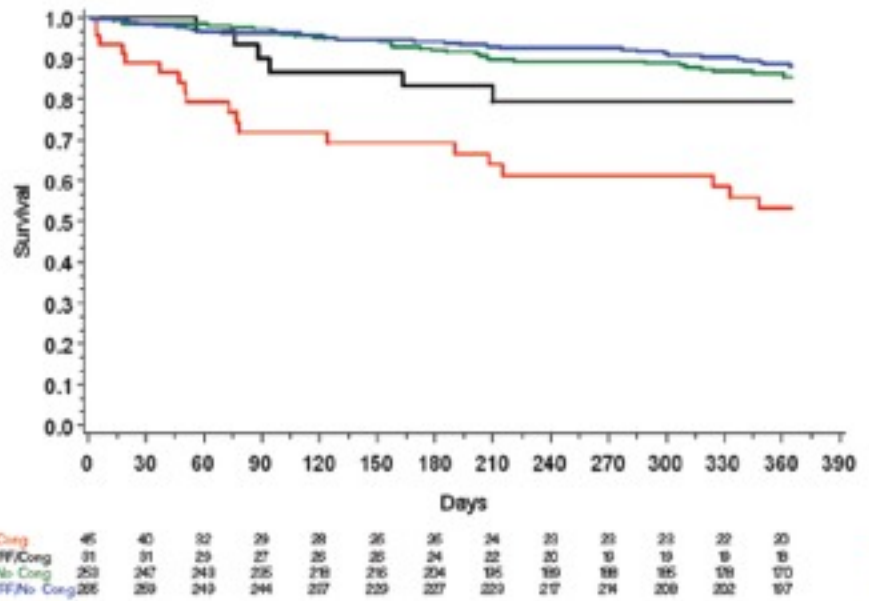
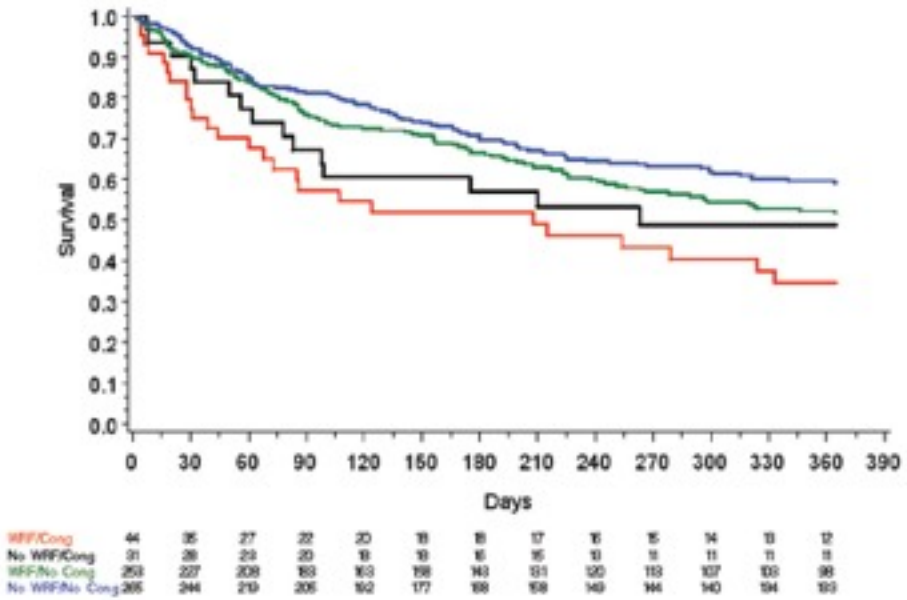


Figure 3 Mortality curves for the high-dose diuretic and low-dose diuretic groups before (left) and after (right) matching.

Yilmaz MB et al European J Heart Failure 2011

Worsening renal function on the presence of signs of venous congestion is the most important predictor of death at 1 year





Metra M et al Circulation: Heart failure 2012

Worsening kidney function in decompensated heart failure: treat the heart, don't mind the kidney

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European Heart Journal 20121

Ultrafiltration serait-elle la solution?

Table 2. The potential benefits and risks of peripheral ultrafiltration application in ADHF patients

Benefits	Risks
Predictable reduction of fluid overload	Local complications (e.g. anticoagulation, vein access)
Protection from electrolyte disturbances	Local and systematic infections
Correction of hyponatraemia	No long-term mortality data
No neurohormonal activation	Close patient supervision
Improvement of exercise capacity	Cost
Less hospitalizations	

Koniari K et al European J Cardiology 2012

Cardiorenal rescue study in acute decompensated heart failure (CARRESS_HF)

- Patients avec décompensation cardiaque aigue et augmentation creatinine 26.5 umol/L et persistance d'une congestion veineuse
- Randomisation 1:1 ultrafiltration versus prise en charge pharmacologique en étapes
- Objectif principal: changement de créatinine et poids ensemble (estimation bivariée) à 96 heures.
- 200 patients

Aquadex

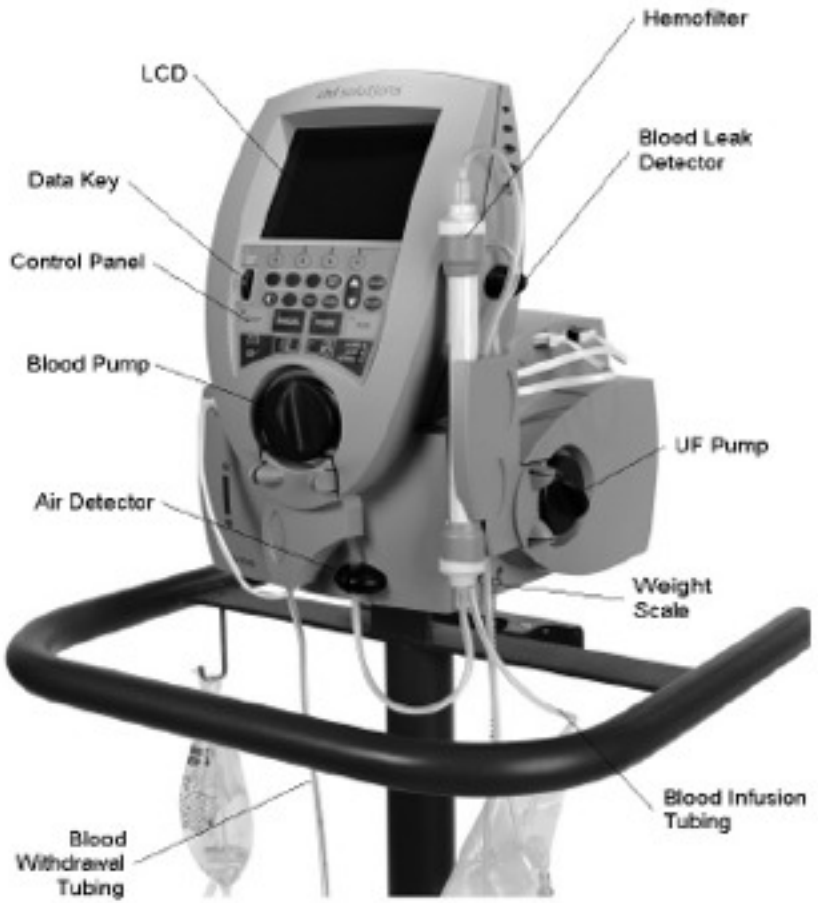


Figure 1 Aquadex Fluid Removal System

Protocole

- Restriction hydrique à 2 L/24h
- Régime à 2 g de Na
- Poids et créatinine tous les jours
- IEC, Bbloquants, digoxine selon médecins en charge
- Groupe Ultrafiltration:
  - Ultrafiltration 200ml/h
  - Vasodilatateurs ou vasotoniques interdits

Protocole

Table 3. Stepped Pharmacologic Care Treatment Algorithm

Urine output (UO) goals to be assessed daily from randomization to 96 hours
- UO >5 L/d → Reduce current diuretic regimen *if desired*
- UO 3–5 L/d → Continue current diuretic regimen
- UO <3 L/d → See diuretic grid

24-hour assessment
- UO recommendations as above
- Advance to next step on grid if UO <3 L/d

48-hour assessment
- UO recommendations as above
- Advance to next step on grid if UO <3 L/d
- Consider dopamine or dobutamine at 2 μg/kg/h if SBP <110 mm Hg and EF <40% or RV systolic dysfunction.
- Consider nitroglycerin or nesiritide if SBP >120 mm Hg (any EF) and severe symptoms

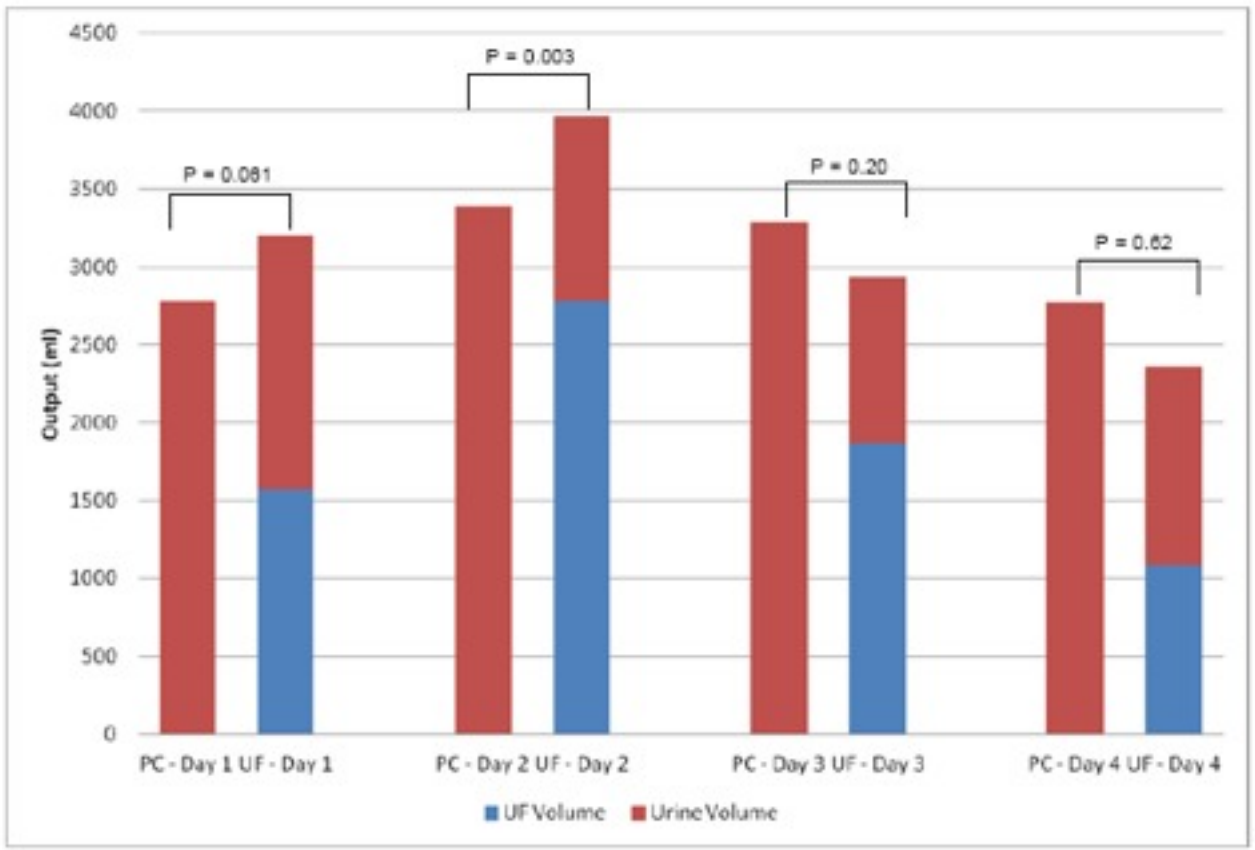
72- and 96-hour assessments
- UO recommendations as above
- Advance to next step on grid if UO <3 L/d
- Consider dopamine or dobutamine at 2 μg/kg/hr if SBP <110 mm Hg and EF <40% or RV systolic dysfunction.
- Consider nitroglycerin or nesiritide if SBP >120 mm Hg (any EF) and severe symptoms
- Consider hemodynamic guided IV therapy, LVAD, dialysis, or ultrafiltration crossover

Diuretic Grid

	Current Dose	Suggested Dose	
		Daily Loop Dose	Thiazide
A	<80 mg	40 mg IV bolus + 5 mg/h	None
B	81–160 mg	80 mg IV bolus + 10 mg/h	5 mg metolazone once daily
C	161–240 mg	80 mg IV bolus + 20 mg/h	5 mg metolazone twice daily
D	>240 mg	80 mg IV bolus + 30 mg/h	5 mg metolazone twice daily

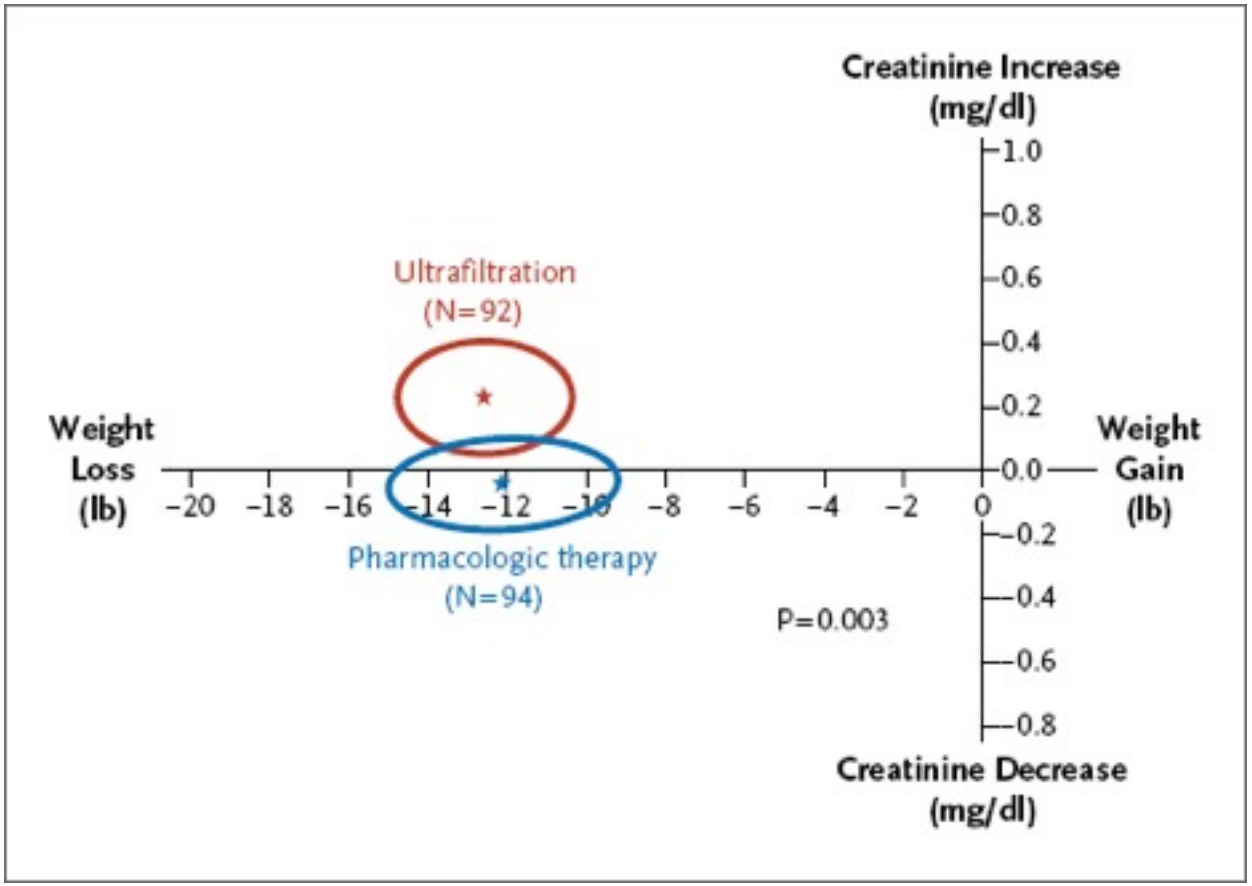
SBP, systolic blood pressure; EF, ejection fraction; RV, right ventricle; LVAD, left ventricular assist device; Loop, loop diuretic dose in furosemide equivalents.

FIGURE S3: TOTAL FLUID OUTPUT BY DAY



PC=Pharmacologic care; UF=Ultrafiltration

Ultrafiltration dans la décompensation cardiaque aigue



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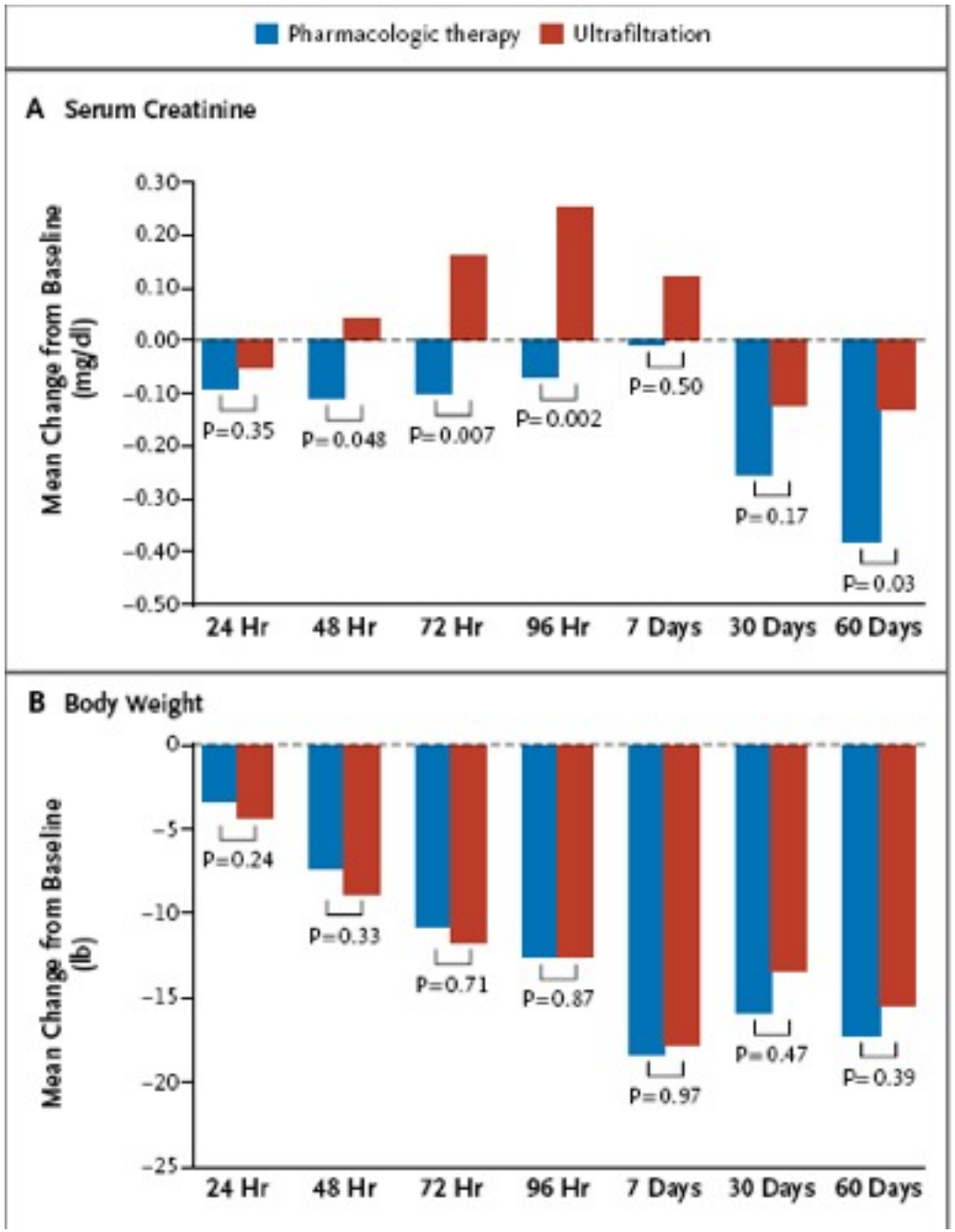


Evolution créatinine et poids

Bart BA NEJM 2012

Effets secondaires plus nombreux

Table 3. Serious Adverse Events.

Event	Pharmacologic Therapy (N=94)	Ultrafiltration (N=94)
	no. of patients (%)	
Any	54 (57)	68 (72)
Heart failure	28 (30)	31 (33)
Other cardiovascular disorder	5 (5)	6 (6)
Renal failure	14 (15)	17 (18)
Anemia or thrombocytopenia	5 (5)	8 (9)
Catheter-site hemorrhage	0	2 (2)
Electrolyte disorder*	3 (3)	0
Gastrointestinal hemorrhage	3 (3)	7 (7)
Pneumonia or other respiratory disorder	6 (6)	10 (11)
Sepsis, bacteremia, or cellulitis	4 (4)	8 (9)
Other	19 (20)	17 (18)

Bart BA NEJM 2012

Conclusion de l'étude

- Pas d'avantage de l'ultrafiltration sur diurétiques
- Plus d'effets secondaires avec UF
- Avantages d'une approche standardisée sur les objectifs de la diurèse et le dosages des diurétiques et autres traitements

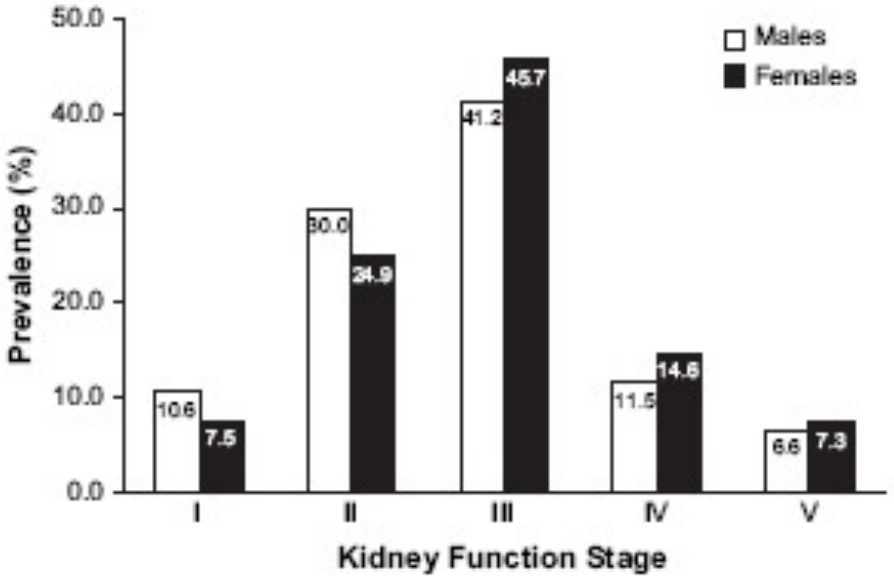
CRS 2

Table 4. Summary of studies fulfilling the criteria for Type 2 CRS

Study	Population (*n*)	Study type (data source)	Cardiac disease	CKD	Outcomes (%)
Heywood *et al.* [19]	118 465	ADHERE registry	ADHF	eGFR 60–89, 27.4%; eGFR 30–59, 43.5%; eGFR 15–29, 13.1%; eGFR <15, 7%	OR for in-hospital mortality: eGFR ≥90, 1.0; eGFR 60–89, 2.3; eGFR 30–59, 3.9; eGFR 15–29, 7.6; eGFR <15, 6.5
Elsayed *et al.* [21]	13 826	Prospective (ARIC and CHS)	Baseline CVD in 12.9%	eGFR decrease of at least 15 mL/min/1.73 m^2 to a final level <60 mL/min/1.73 m^2 was seen in 34% of patients with baseline CVD	OR for development of kidney disease, 1.54 (CVD *versus* non-CVD)
Ahmed *et al.* [71]	7788	Retrospective (DIG trial); propensity-matched study	Ambulatory patients with CHF	eGFR <60 in 45%	Matched HR: (CKD *versus* non-CKD) all-cause death, 1.71
Campbell *et al.* [20]	7788	Retrospective (DIG trial); propensity-matched study	Ambulatory patients with CHF	eGFR <60 in 45%	Matched HR: (CKD *versus* non-CKD) all-cause hospitalization, 1.18
Dimopoulos *et al.* [24]	1102	Retrospective (single centre)	Adult congenital heart disease	eGFR 60–89, 41%; eGFR <60, 9%	All-cause death (HR): eGFR ≥90, 1.0; eGFR <60, 3.25
Hillege *et al.* [72]	298	Retrospective (CATS trial)	First anterior wall MI	Change in GFRc: placebo, −5.5 mL/min/year; captopril, −0.5 mL/min/year	All-cause death: 1-year, 8%

ARIC, Atherosclerosis Risk in Communities Study; ADHF, acute decompensated heart failure; GFRc, GFR estimated by Cockroft–Gault; CATS, Captopril and Thrombolysis Study; CVD, cardiovascular disease; CHS, Cardiovascular Health Study; DIG, Digoxin Investigator Group.

ADHERE database: prévalence et impact de l'IRC chez 118'465 patients avec



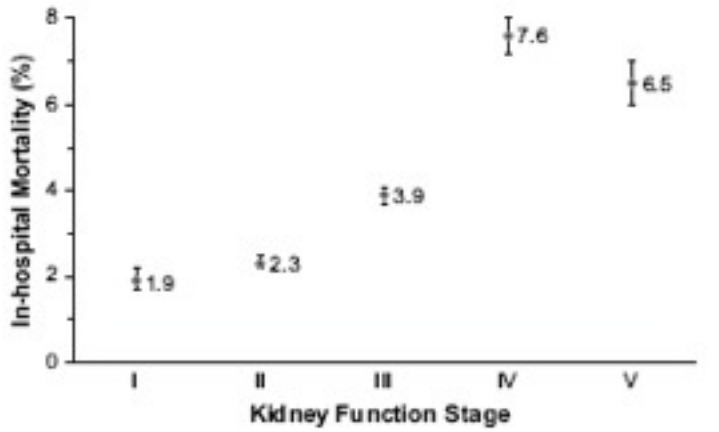


Fig. 2. In-hospital mortality by kidney function stage for patients admitted with ADHF. Error bars depict the 95% CIs for the point estimates.

Heywood JT et al J Card Vasc 2007

CHARM: independent effect of baseline GFR on 4-year survival

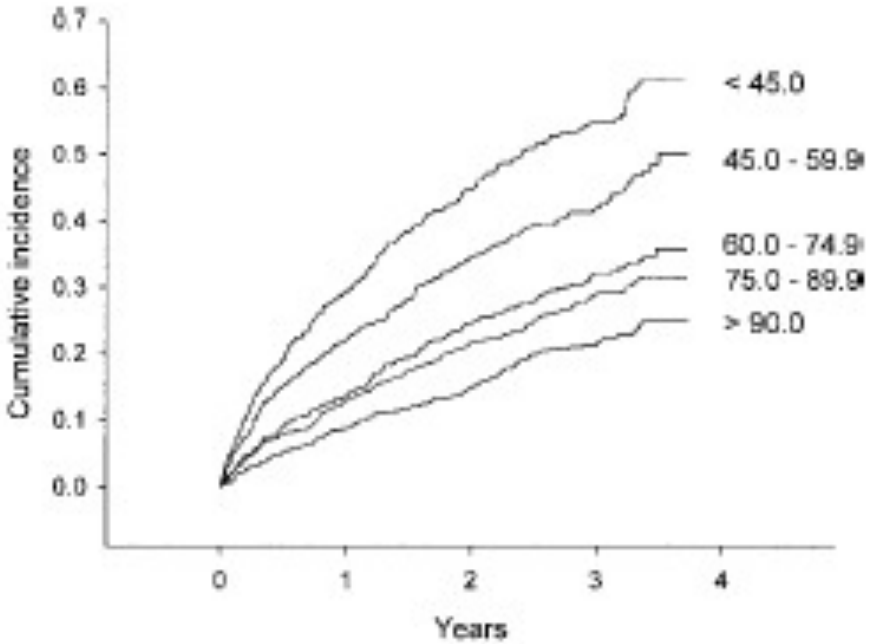


Figure 2. Kaplan-Meier plot of cumulative incidence of cardiovascular death or unplanned admission to hospital for the management of worsening CHF stratified by approximate quintiles of eGFR in mL/min per 1.73 m^2 (time in years).

Hillige et al Circulation 2006

Baseline GFR influences mortality at 24 months

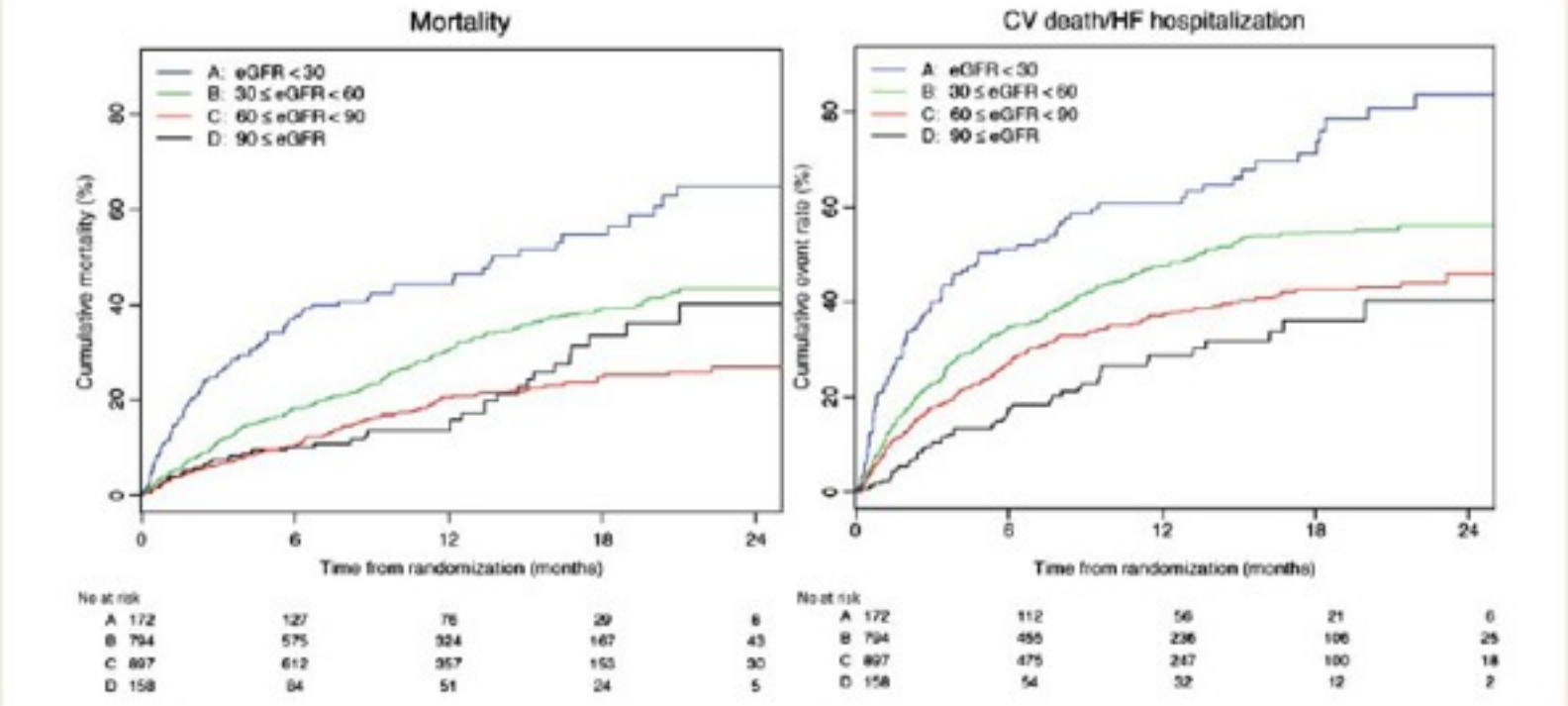
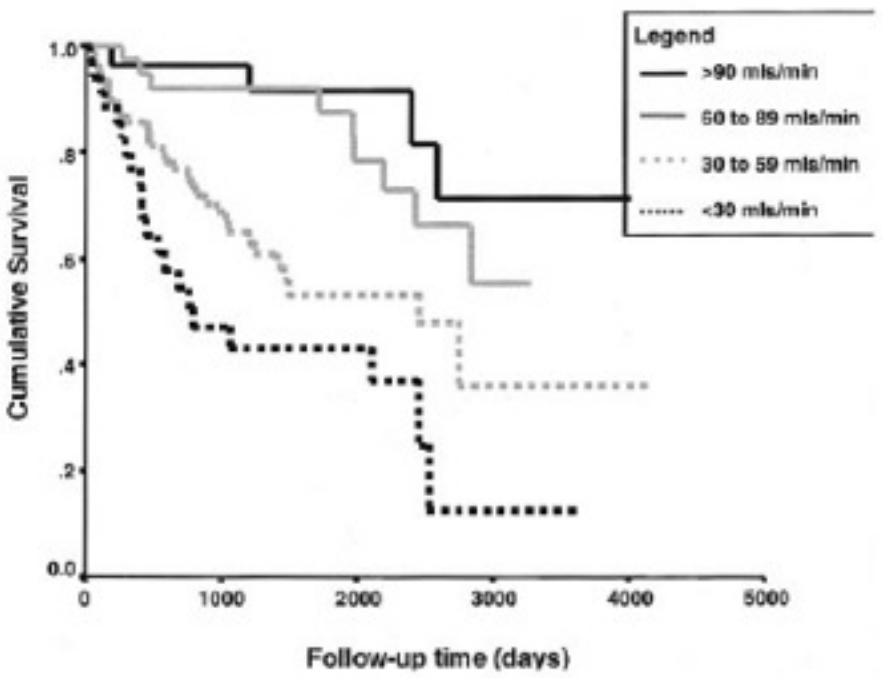


Figure 2 Kaplan–Meier analysis of outcomes according to baseline estimated glomerular filtration rate.

Blair JEA et all European Heart J 2011

Baseline GFR determines 1-year survival in CHF patients



Survival stratified by baseline creatinine clearance. Log-rank statistic=27.98 ($P<0.0001$).

McAllister FA et al Circulation 2004

ACEI and BB are associated with similar reductions in mortality in patients with and without renal insufficiency

TABLE 2. Multivariate Predictors of All-Cause Mortality During Median 2.5-Year Follow-Up, by Cox Proportional Hazards Model

Variable	*P*	Hazard Ratio	95% CI
Serum creatinine (per 1-μmol/L increase)	0.002	1.002	1.001–1.003
Age (per 1-year increase)	<0.001	1.03	1.02–1.04
Female	<0.001	0.63	0.49–0.80
NYHA class III/IV	<0.001	1.92	1.52–2.43
β-Blockers	<0.001	0.57	0.45–0.72
Spironolactone	0.001	0.13	0.04–0.42
Other vasodilators	0.001	0.41	0.24–0.69
Systolic dysfunction	0.002	1.54	1.18–2.02
ACE inhibitor	0.001	0.60	0.45–0.81

McAllister FA et al Circulation 2004

Baseline GFR influences CV treatment et pénalise les patients CKD

Table 2 Medications at randomization and at discharge

eGFR (mL/min/1.73 m²)	Group 1 ≥90.0	Group 2 60.0–89.9	Group 3 30.0–59.9	Group 4 <30	P-value
At randomization					
ACE-I/ARBs	136 (79.1)	707 (89.0)	743 (82.8)	113 (71.5)	<0.001
Beta-blocking agents	114 (66.3)	558 (70.3)	627 (69.9)	112 (70.9)	0.8
Spironolactone	103 (59.9)	446 (56.2)	483 (53.9)	59 (37.3)	<0.001
Digoxin	100 (58.1)	399 (50.3)	420 (46.8)	58 (36.7)	0.001
Diuretics	168 (97.7)	764 (96.2)	872 (97.2)	152 (96.2)	0.6
Lipid-lowering agents	52 (30.2)	259 (32.6)	346 (38.6)	62 (39.2)	0.02
Nitroglycerin	26 (15.1)	133 (16.8)	158 (17.6)	24 (15.2)	0.8
Amiodarone	14 (8.1)	87 (11.0)	200 (22.3)	47 (29.8)	<0.001
Inotropic agents	5 (2.9)	23 (2.9)	46 (5.1)	13 (8.2)	0.007
IV nitroglycerin	11 (6.4)	53 (6.7)	41 (4.6)	4 (2.5)	0.09
Nesiritide	6 (3.5)	26 (3.3)	53 (5.9)	18 (11.4)	<0.001
At discharge					
ACE-Is/ARBs	146 (86.4)	700 (89.9)	724 (83.1)	95 (64.2)	<0.001
Beta-blocking agents	130 (76.9)	598 (76.8)	629 (72.2)	101 (68.2)	0.05
Spironolactone	106 (62.7)	501 (64.3)	516 (59.2)	57 (38.5)	<0.001
Digoxin	100 (59.2)	381 (48.9)	403 (46.3)	53 (35.8)	<0.001
Diuretics	157 (92.9)	739 (94.9)	834 (95.8)	136 (91.9)	0.1
Lipid-lowering agents	55 (32.5)	272 (34.9)	351 (40.3)	60 (40.5)	0.06
Nitroglycerin	11 (6.5)	74 (9.5)	96 (11.0)	19 (12.8)	0.2
Amiodarone	12 (7.1)	90 (11.6)	198 (22.7)	45 (30.4)	<0.001
Inotropic agents	2 (1.2)	11 (1.4)	16 (1.8)	4 (2.7)	0.6
IV nitroglycerin	0 (0.0)	2 (0.3)	1 (0.1)	0 (0.0)	0.8
Nesiritide	5 (3.0)	10 (1.3)	24 (2.8)	3 (2.0)	0.2

Blair JEA et all European Heart J 2011

CRS 4

Table 5. Summary of studies fulfilling criteria for Type 4 CRS

Study	Population (n)	Study type (data source)	CKD stage	Cardiac outcomes (%)	Outcomes (%)
Herzog *et al.* [37]	34 189	Retrospective (USRDS)	ESKD	Cardiac death: 1-year, 43%; 2-year, 52%; 5-year, 70.2%; 10-year, 85%	All-cause: 1-year, 59%; 2-year, 75%; 5-year 90%; 10-year, 97%
Culleton *et al.* [32]	6233	Retrospective (FHS)	'Mild' CKD	CV events (M/F), 21.3/25.6 per 1000 p.-y.	All-cause (M/F), 33.3/39.5 per 1000 p/y
Dries *et al.* [33]	6797	Retrospective (SOLVD)	'Moderate' CKD: eGFR, 30–51	HF death, 7.5–24%; death/hospitalization, 31–62%; arrhythmic death, 6–9%	CKD predicted: all-cause death (RR 1.41); HF death (RR 1.68); death/hospitalization (RR 1.33)
Henry *et al.* [36]	631	Prospective (HOORN)	eGFR, 72.5	CV death (RR): 1.11 per 5 μmol/L ΔSCr; 1.26 per 5 mL/min ΔGFR	All-cause (RR): 1.08 per 5μmol/L ΔSCr; 1.15 per 5 mL/min ΔGFR
Mahon *et al.* [39]	585	Retrospective (DIG Substudy)	By eGFR quartiles: Q1 (<47.1), Q2 (47–64), Q3 (64–86), Q4 (≥86)	Recent ADHF hospitalization: Q1, 39%; Q2, 36%; Q3, 23%; Q4, 27%	All-cause mortality: Q1, 37% (HR 2.1); Q2, 29% (HR 1.6); Q3, 18% (HR 0.9); Q4, 21%
Muntner *et al.* [40]	6534	Retrospective (NHANES II)	eGFR <70, 75.9%	CV death (rate per 1000 p.-y.): eGFR ≥90, 4.1; eGFR 70–89, 8.6; eGFR <70, 20.5	All-cause death (HR): eGFR ≥90, 1.00; eGFR 70–89, 1.64; eGFR <70, 2.00
Cheung *et al.* [31]	1846	Retrospective (HEMO)	ESKD	First and total cardiac hospitalizations: 19.4/34.7 per 100 p.-y.; 42% for CHD	Cardiac death: 6.6 per 100 p/y; 39% of all deaths, CHD accounted for 61.5%
Go *et al.* [35]	1.1 million	Retrospective (Kaiser Permanente)	≥CKD stage III or eGFR <60	CV event (rate per 100 p.-y./HR): eGFR 45–59, 3.65/1.4; eGFR 30–44, 11.3/2.0; eGFR 15–29, 21.8/2.8; eGFR <15, 36.6/3.4	All-cause mortality (per 100 p.-y./HR): eGFR 45–59, 1.1/1.2; eGFR 30–44, 4.8/1.8; eGFR 15–29, 11.4/3.2; eGFR <15, 14.1/5.9
Foley *et al.* [34]	1 091 208	Retrospective (Medicare/ USRDS)	CKD 3.8% (diagnostic coding)	CV event incidence: AMI, 4–7 per 100 p.-y.; CHF, 31–52 per 100 p.-y. (HR, 1.28–1.79)	All-cause death: HR, 1.38–1.56
Hillege *et al.* [38]	2680	Retrospective (CHARM)	eGFR <60, 36%	CV death/hospitalization (HR): eGFR ≥90, 1.0; eGFR 75–89, 1.17; eGFR 60–74, 1.24; eGFR 45–59, 1.54; eGFR <45, 1.86	All-cause death (HR): eGFR ≥90, 1.0; eGFR 75–89, 1.13; eGFR 60–74, 1.14; eGFR 45–59, 1.50; eGFR <45, 1.91
McCullough *et al.* [40]	37 153	Retrospective (KEEP)	eGFR <60, 14.8%	Prevalence CVD (OR): eGFR ≥90, 1.0; eGFR 60–89, 1.1; eGFR 30–59, 1.4; eGFR <30, 1.3	All-cause death (HR): CKD only, 1.98; CVD only, 3.02; CKD + CVD, 3.80
McCullough *et al.* [41]	(KEEP/NHANES) 69 296/17 061	Retrospective (KEEP/ NHANES)	(KEEP/NHANES) CKD 26.8/15.8	(KEEP/NHANES) prevalence CVD (OR): CKD, 1.34/1.37; no CKD, 1.0/1.0	KEEP all-cause death, 1.52 per 1000 p/y (RR ~ 4.6)
McCullough *et al.* [42]	31 417	Retrospective (KEEP)	eGFR <60 or ACR ≥30, 20.6%	Risk CVD/death (OR): CKD, 1.44; no CKD, 1.0	Worst survival for combined CKD and CVD at time of screening

ESKD, end-stage kidney disease; CKD, chronic kidney disease; DM, diabetes mellitus; HTN, hypertension; CHF, congestive heart failure; CVD, cerebrovascular disease; MA, microalbuminuria; CHD, coronary heart disease; LVH, left ventricular hypertrophy; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ADHF, acute decompensated heart failure.

Classification IRC

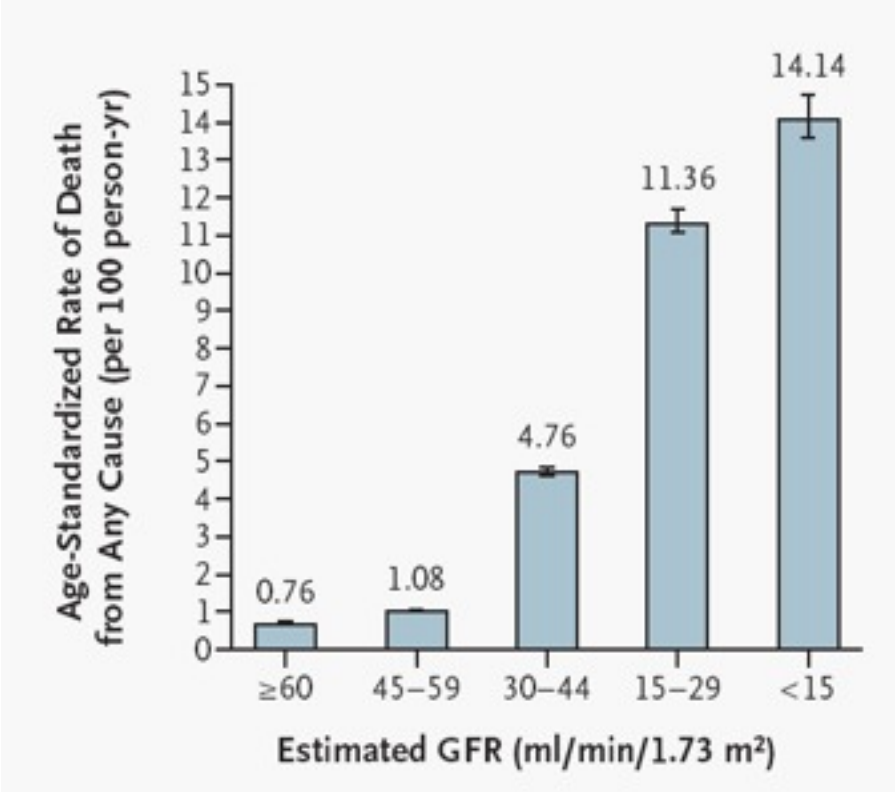
Table I Stages of chronic kidney disease

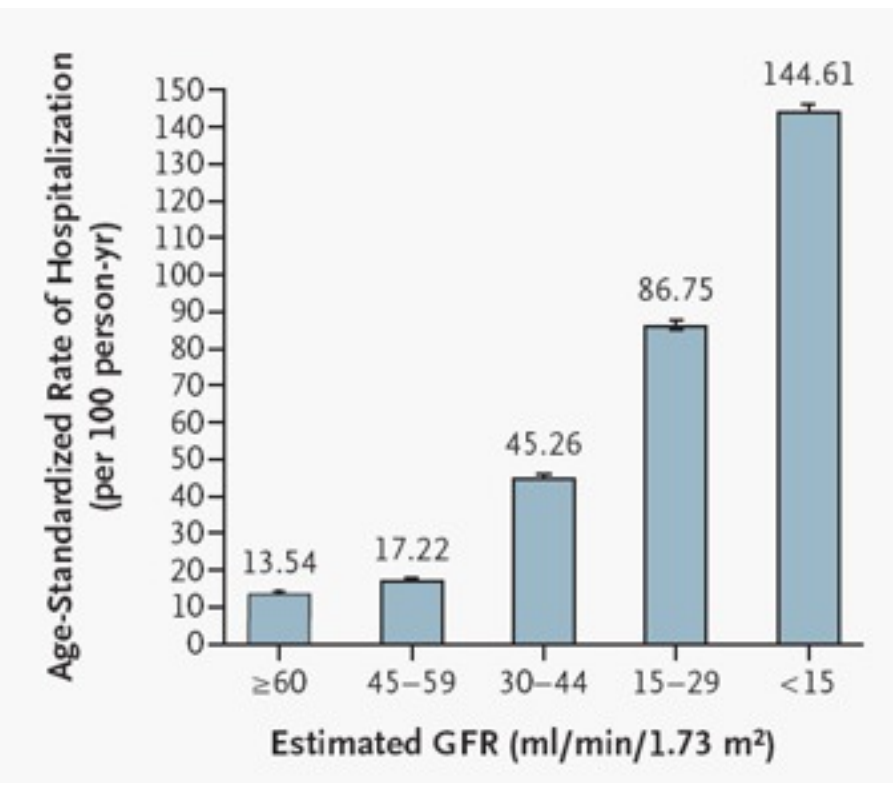
Stage[1,2]	Description	GFR (mL/min/1.73 m^2)	Albuminuria stages (ACR, mg/g)		
			A1 normal <30	A2 high 30–299	A3 very high, nephrotic ≥300
1	Kidney damage with normal or high GFR	≥90		✓	✓
2	Kidney damage with mild reduction in GFR	60–89		✓	✓
3a	Mild-, moderate reduction in GFR	45–59	✓	✓	✓
3b	Moderate-, severe reduction in GFR	30–44	✓	✓	✓
4	Severe reduction in GFR	15–29	✓	✓	✓
5	Kidney failure	<15 or dialysis	✓	✓	✓

ACR, albumin to creatinine ratio.

KDIGO 2011

L'IRC augmente le risque de mortalité et d'hospitalisations





Go A et al, NEJM, 2004

Suivi longitudinal et évolution d'une population avec CKD

- Besoin de dialyse sur 5 ans:
  - 1.1% CKD 2: 60-89 ml/min
  - 1.3% CKD 3: 30-59 ml/min
  - 19.9% CKD 4: 15-29 ml/min

Keith et al Arch Intern Med 2004

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  - 19.9% CKD 4: 15-29 ml/min

Mortalités:

19.5%
24.3 %
45.7 %

Keith et al Arch Intern Med 2004

Diminution de la fonction rénale: mort or IRC terminale?

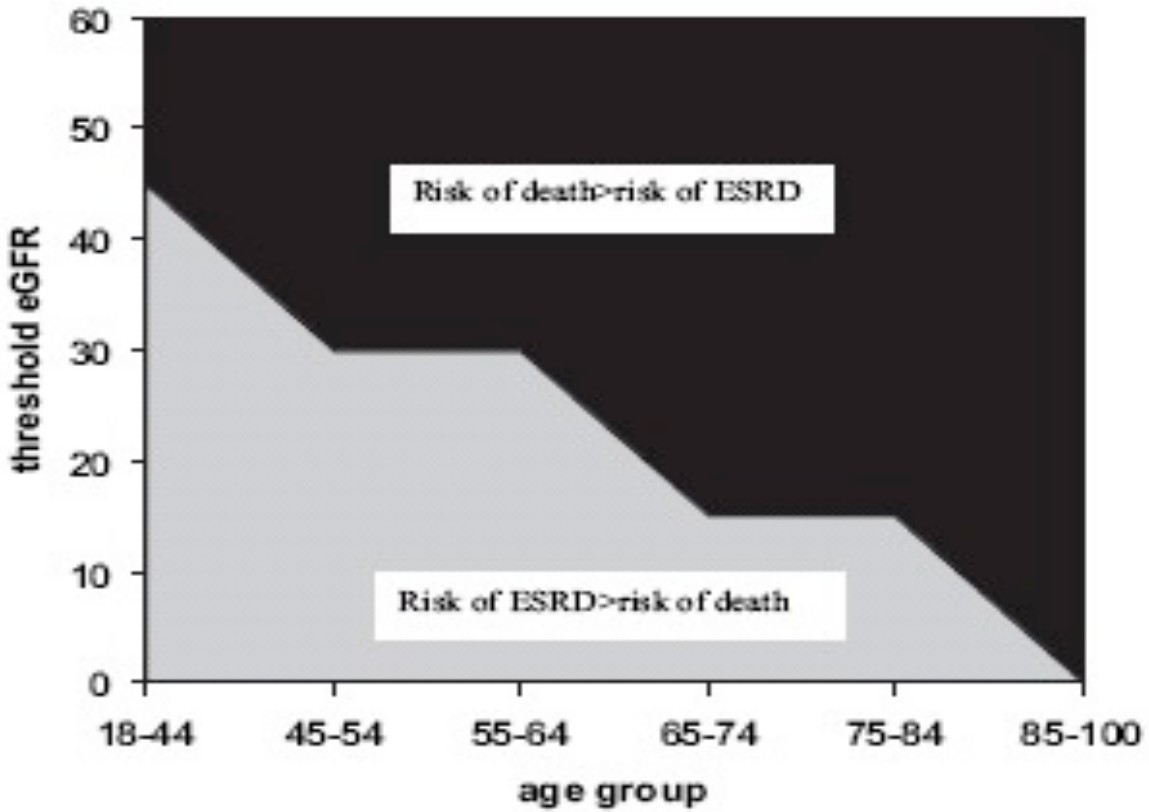


Figure 2. Baseline eGFR threshold below which risk for ESRD exceeded risk for death for each age group.

Ohare et al J Am Soc Nephrol 17:846-53, 2006

Diminution de la fonction rénale: mort or IRC terminale?

L'insuffisance rénale est un facteur de risque cardiovasculaire

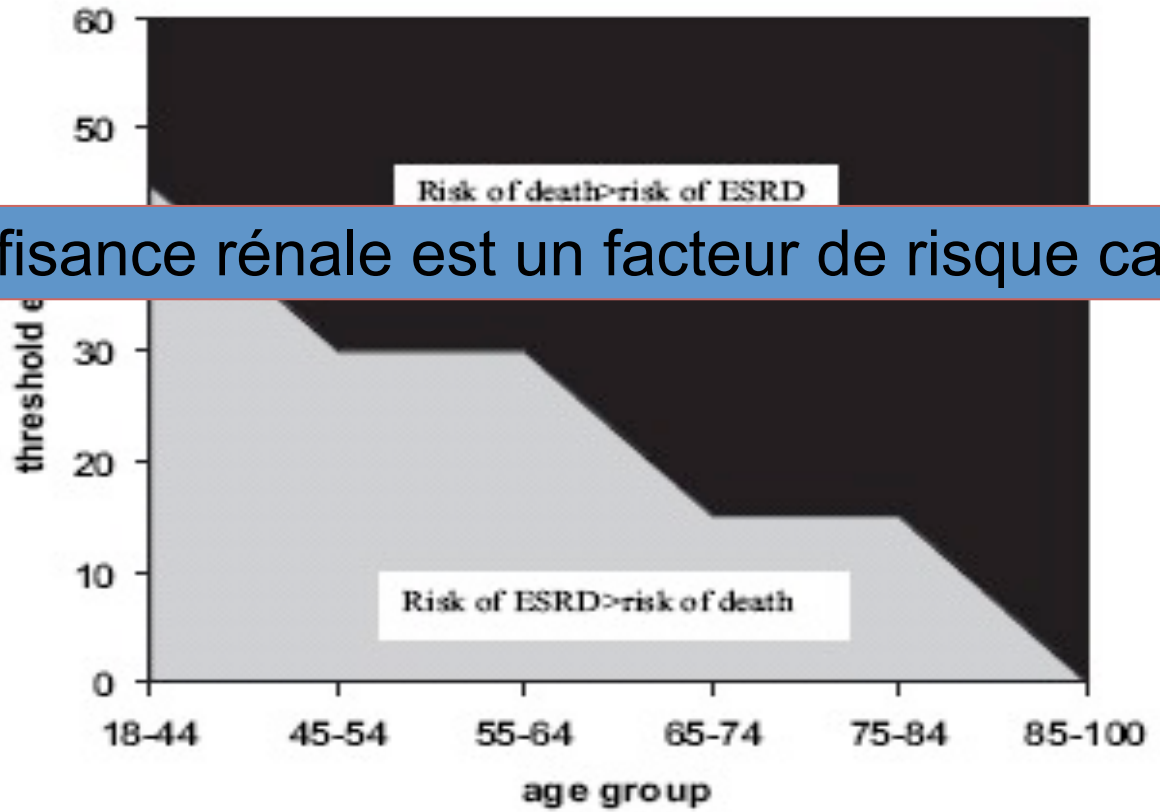


Figure 2. Baseline eGFR threshold below which risk for ESRD exceeded risk for death for each age group.

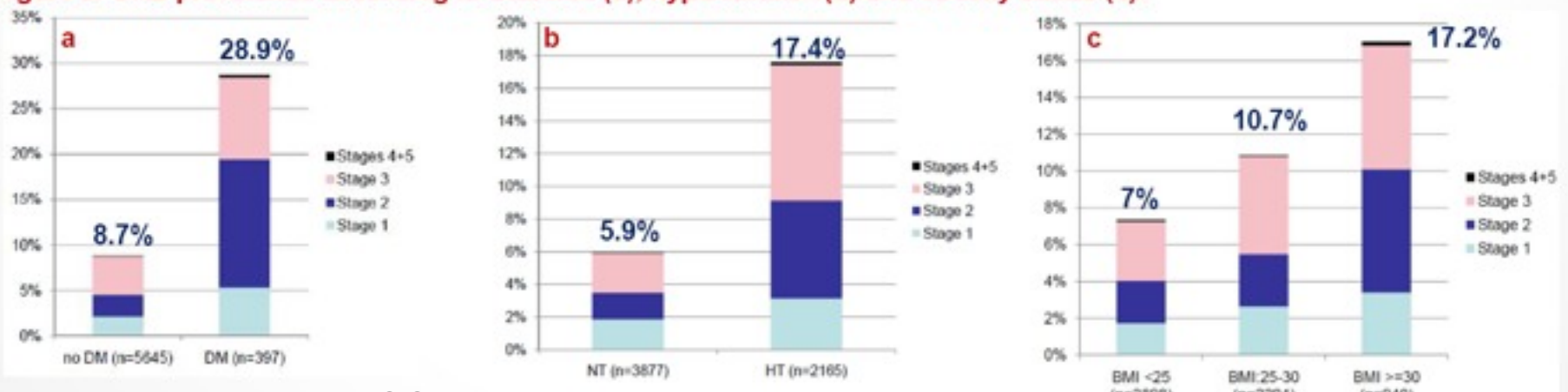
Ohare et al J Am Soc Nephrol 17:846-53, 2006

Répartition CKD en Suisse

Table 1: CKD stages distribution

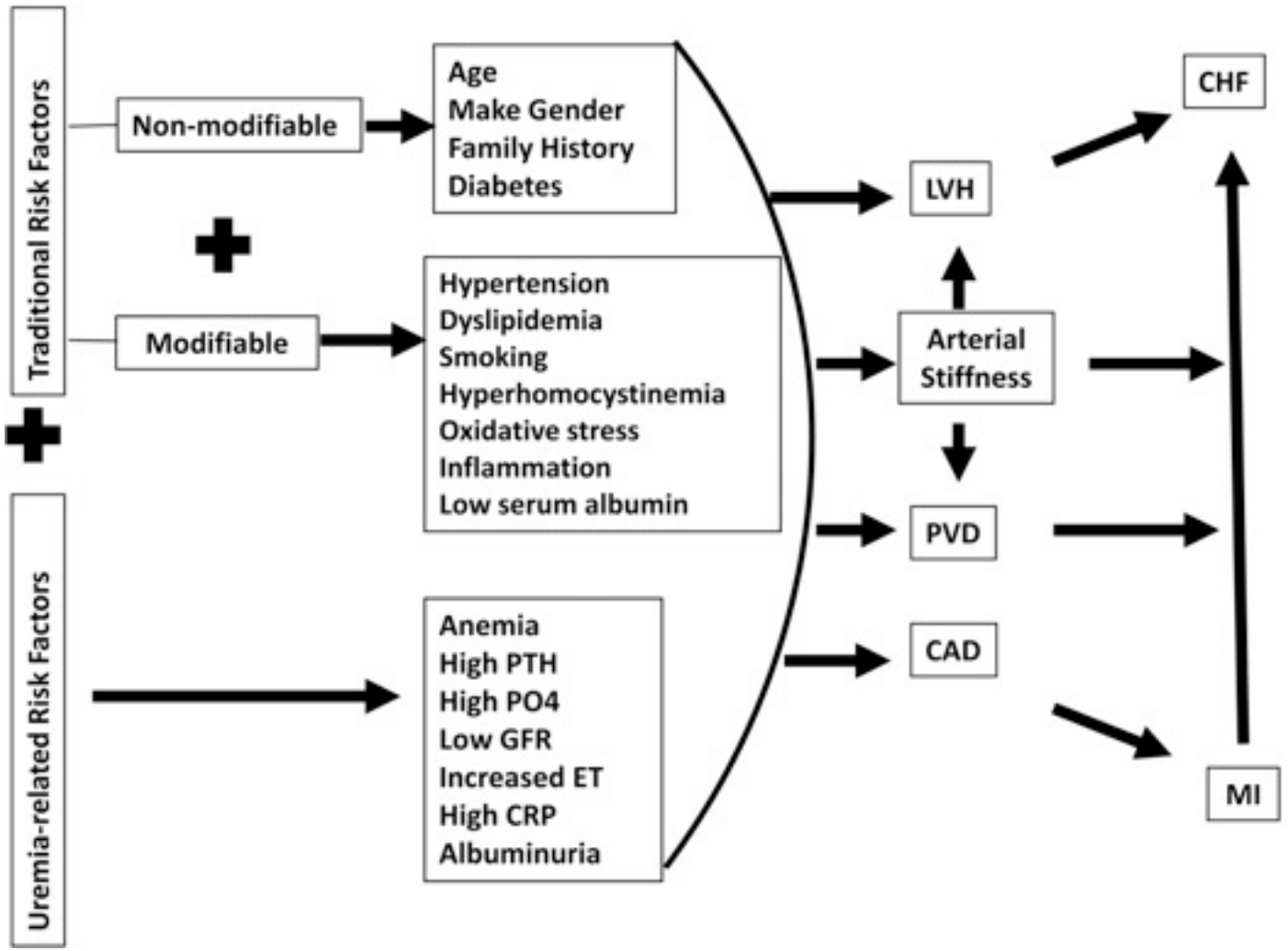
Stages	MDRD	CKD-Epi
1	2.1%	2.3%
2	3.5%	3.2%
3	4.7%	4.5%
4-5	0.17%	0.17%
TOTAL	**10.4%**	**10.2%**
3-5	**4.87%**	**4.67%**

Figure 2: CKD prevalence according to diabetes (a), hypertension (b) and obesity status (c).



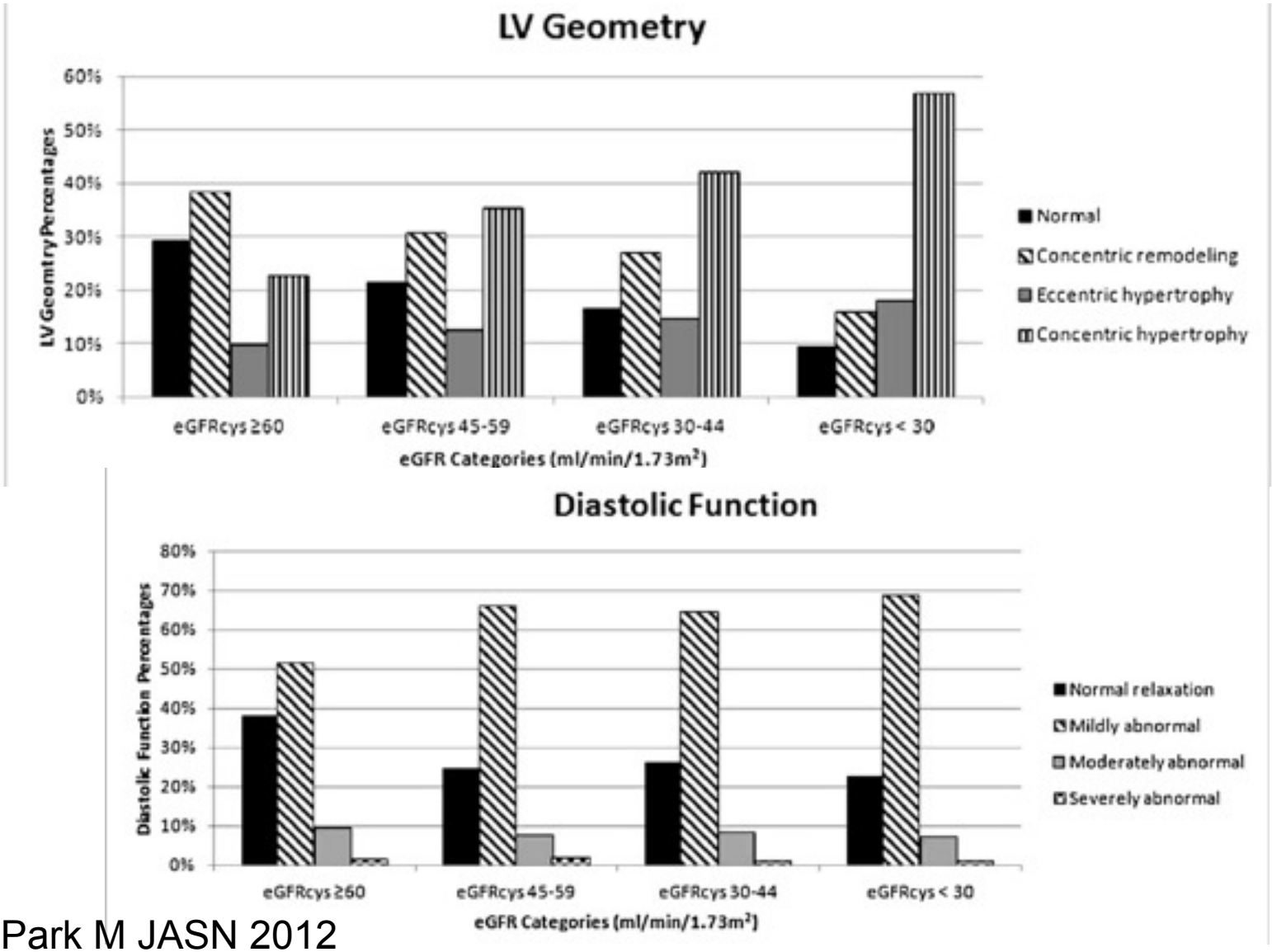
Ponte B et al SSN 2011

Factors in cardiovascular disease for ESRD patients.



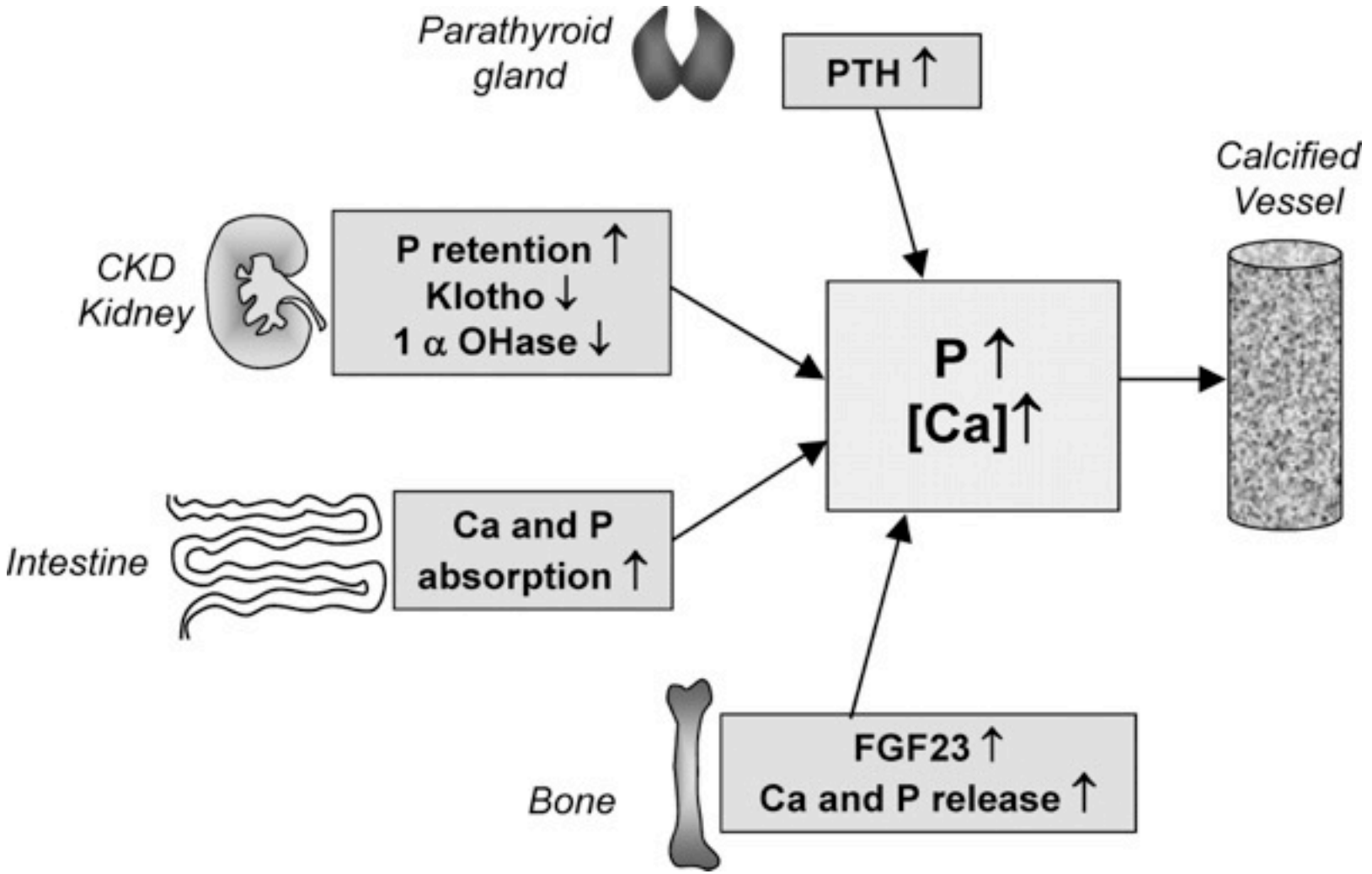
Henrich W L CJASN 2009;4:S106-S109

Subclinical cardiac abnormailties in CKD



Park M JASN 2012

Overview of the factors involved in dysregulated calcium (Ca) and phosphate (P) homeostasis in chronic kidney disease (CKD).



Shanahan C M et al. Circulation Research 2011;109:697-711

Anomalies lipidiques

Box 1 | Mechanisms of atherosclerosis in patients with CKD and ESRD

Oxidative stress and inflammation[94,98,99]

- Oxidation of lipoproteins
- Endothelial injury and dysfunction
- Leukocyte activation, adhesion and infiltration of the artery wall
- Myocardial dysfunction and fibrosis

Impaired cholesterol metabolism[100]*

- Accumulation of oxidation-prone VLDL remnants (also known as intermediate density lipoprotein)
- Formation of abnormal LDL

HDL deficiency and dysfunction[101,102]

- Impaired antioxidant, anti-inflammatory, and reverse cholesterol transport capacities

Impaired chylomicron metabolism[40,68]

- Accumulation of highly oxidation-prone chylomicron remnants

*Cholesterol biosynthetic capacity remains unchanged in the liver but is markedly suppressed in the remnant kidney and vascular tissues in CKD.[101,102] Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease.

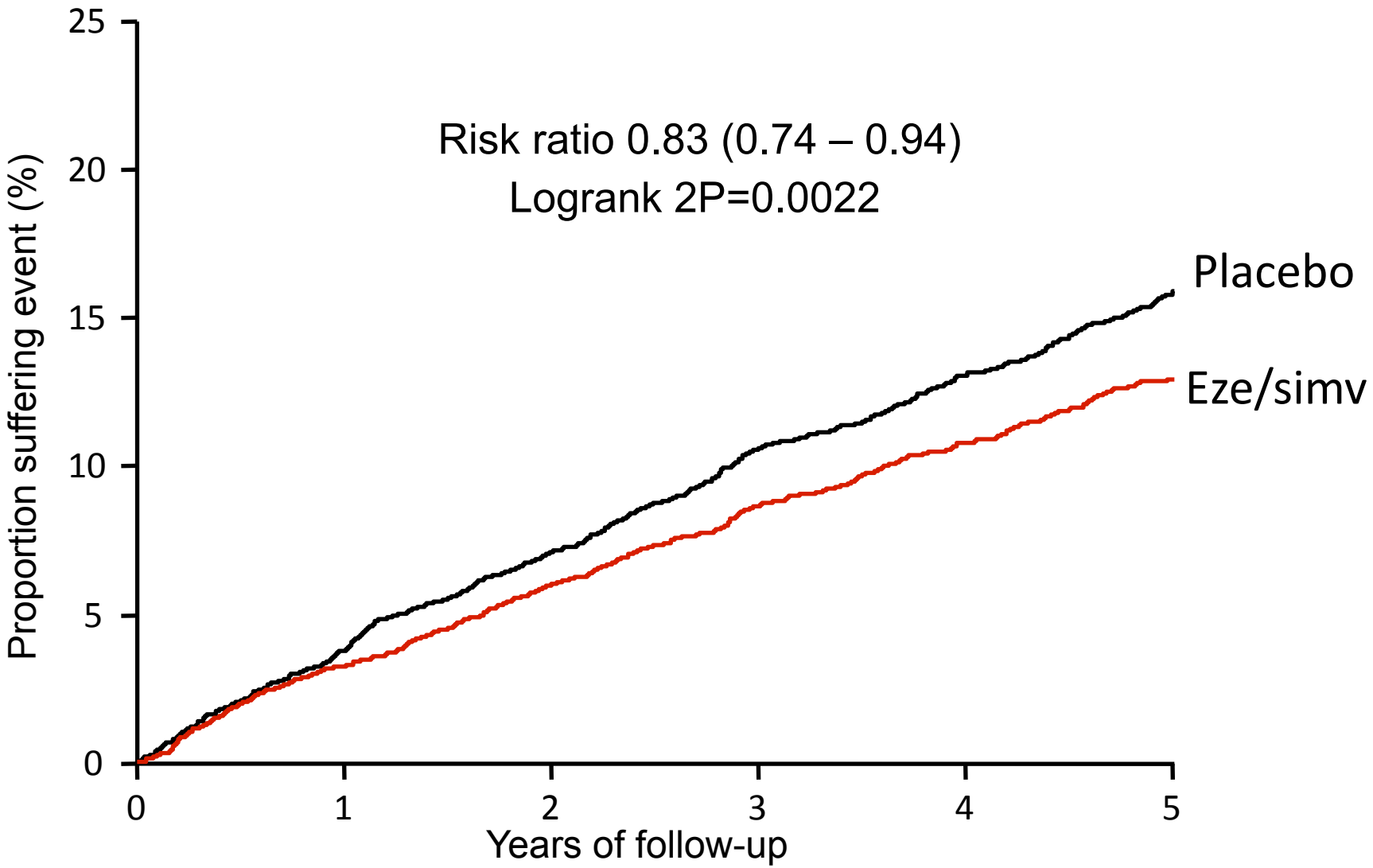
Résumé des études interventionnelles sur les dyslipidémies

Table 1 | Comparison of the 4D, AURORA and SHARP studies

Study	Study name and design	Population and treatment	Outcomes
Wanner *et al.* (2005)[24]	4D: multicenter, randomized, double-blind, prospective study	1,255 patients (aged 18–80 years) with type 2 diabetes mellitus, on maintenance hemodialysis for <2 years; treatment with atorvastatin 20 mg daily (619 patients) vs placebo (636 patients); median follow-up 4 years	No significant difference between groups in rates of the composite primary end point; 1 year: 12.6% (treatment) vs 11.2% (placebo); 3 years: 31.9% (treatment) vs 30.5% (placebo); incidence of fatal stroke significantly higher in the atorvastatin group (relative risk 2.03, 95% CI 1.05–3.93, P=0.04)
März *et al.* (2011)[27]	*Post hoc* analysis of the 4D study data	Not applicable	Significantly reduced rates of adverse outcomes with atorvastatin in patients with LDL cholesterol levels in the highest quartile: composite primary end point (HR 0.69, 95% CI 0.48–1.00); cardiac death (HR 0.58, 95% CI 0.34–0.99); sudden cardiac death (HR 0.48, 95% CI 0.25–0.94); nonfatal myocardial infarction (HR 0.62, 95% CI 0.33–1.17); all cardiac events combined (HR 0.68, 95% CI 0.47–0.98); death from all causes (HR 0.72, 95% CI 0.52–0.99)
Fellström *et al.* (2009)[25]	AURORA: multicenter randomized, double-blind, placebo-controlled study	2,773 patients (aged 50–80 years) on maintenance hemodialysis for >3 months; treatment with rosuvastatin (1,389 patients) vs placebo (1,384 patients); median follow-up 3.8 years	No significant differences between groups in mortality or primary and secondary end points: primary end point (events per 100 patient-years); 9.2 (treatment) vs 9.5 (placebo), HR 0.96, 95% CI 0.84–1.11; all-cause mortality (events per 100 patient-years); 13.5 (treatment) vs 14.0 (placebo), HR 0.96, 95% CI 0.86–1.07
Baigent *et al.* (2011)[26]	SHARP: randomized, double-blind study	9,270 patients (3,023 on dialysis and 6,247 not on dialysis); treatment with simvastatin plus ezetimibe vs placebo; median follow-up 4.9 years	17% proportional reduction in major atherosclerotic events (rate ratio 0.83, 95% CI 0.74–0.94, logrank P=0.002)

Abbreviation: HR, hazard ratio.

SHARP: major atherosclerotic events

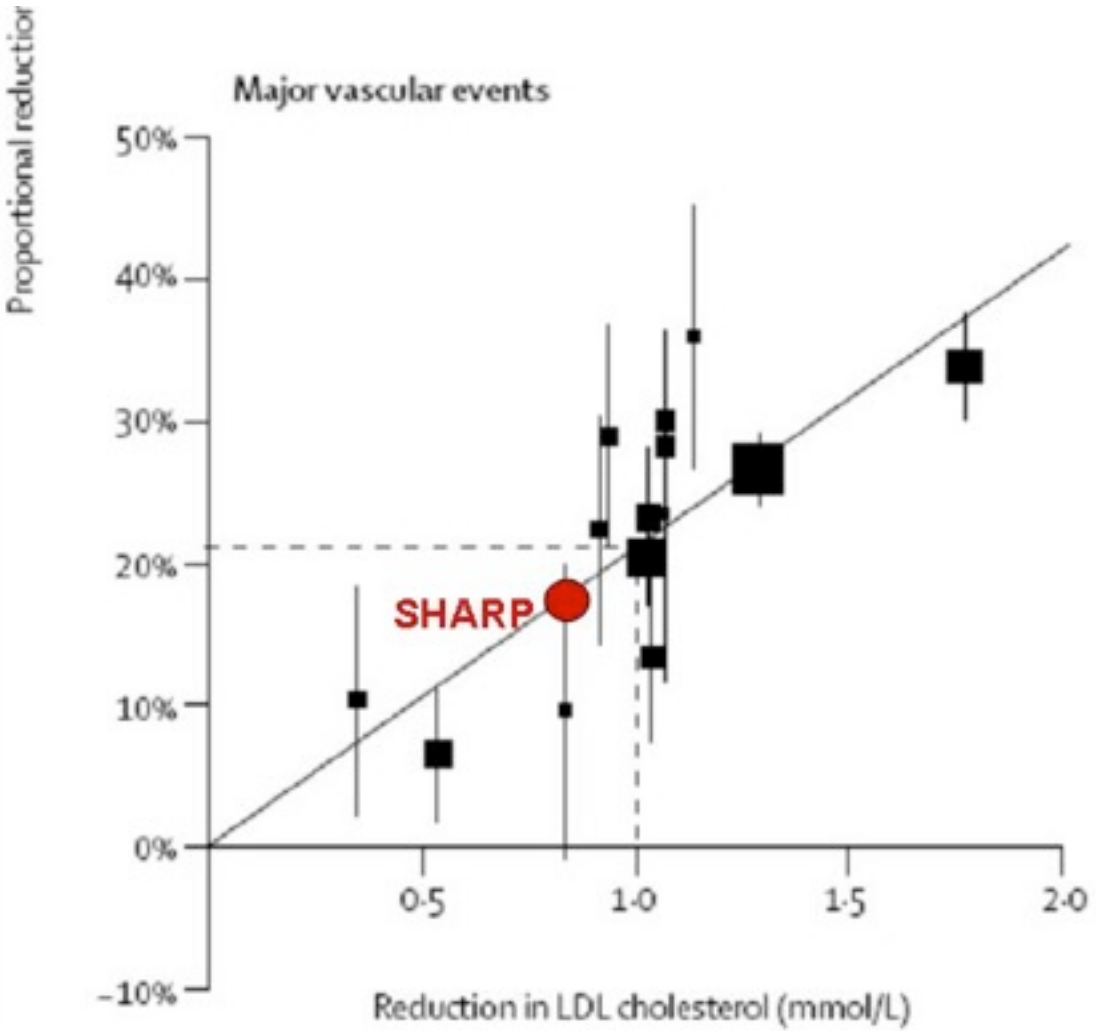


Baigent C, et al. *The Lancet* 2011;377(9784):2181 - 2192

SHARP: effect on major atherosclerotic events

- significant **17% reduction in major atherosclerotic events with 0.85 mmol/L LDL-C reduction**

  -> **similar to the effects seen in the CTT with statin regimens of equivalent LDL lowering efficacy**

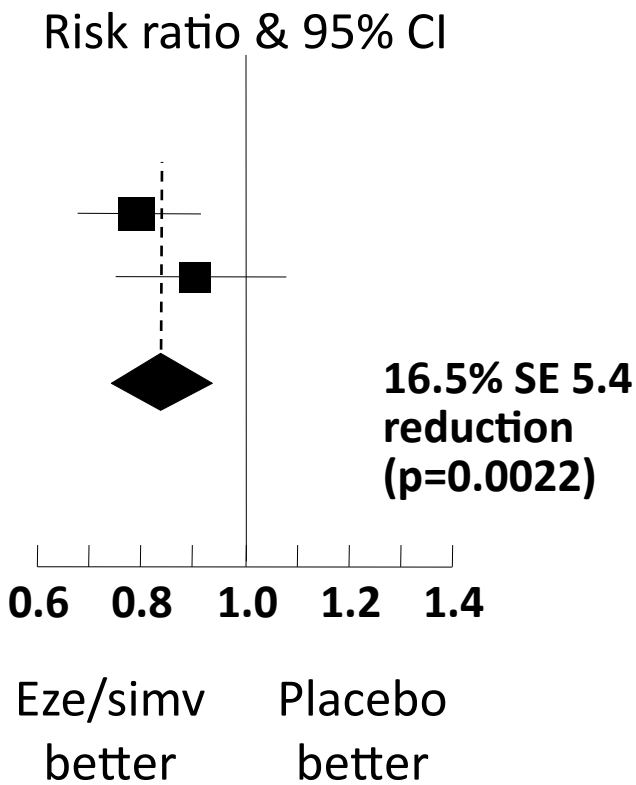


Baigent C, et al. *The Lancet* 2011;377(9784):2181 - 2192

SHARP: major atherosclerotic events by renal status at randomization

	Eze/simv (n=4650)	Placebo (n=4620)
Non-dialysis (n=6247)	296 (9.5%)	373 (11.9%)
Dialysis (n=3023)	230 (15.0%)	246 (16.5%)
Major atherosclerotic event	**526 (11.3%)**	**619 (13.4%)**

No significant heterogeneity between non-dialysis and dialysis patients (p=0.25)



Baigent C, et al. *The Lancet* 2011;377(9784):2181 - 2192

Conclusions

- Le rein et le cœur sont liés pour le meilleur et pour le pire
- Une bonne fonction rénale est gage de meilleur survie dans l'insuffisance cardiaque aigue et chronique
- La valeur pronostic négative d'une élévation de la créatinine doit être interprétée en tenant compte des traitements associés et de la réponse aux traitements
- Les diurétiques bien utilisés restent la base du traitement de la décompensation cardiaque aigue

Conclusions

- CKD est un facteur de risque CV et entraine des modifications cardiaques.
- IEC, Bbloquants, MC inhibiteurs sont sous-utilisés chez les patients avec CKD.
- CKD ne modifie pas le bénéfice cardiaque de ces traitements
- Parmi les facteurs de risques CV dans CKD, un traitement intensif de la dyslipidémie est indiqué.
- L'efficacité du traitement des autres facteurs de risque lié à CKD reste à prouver.