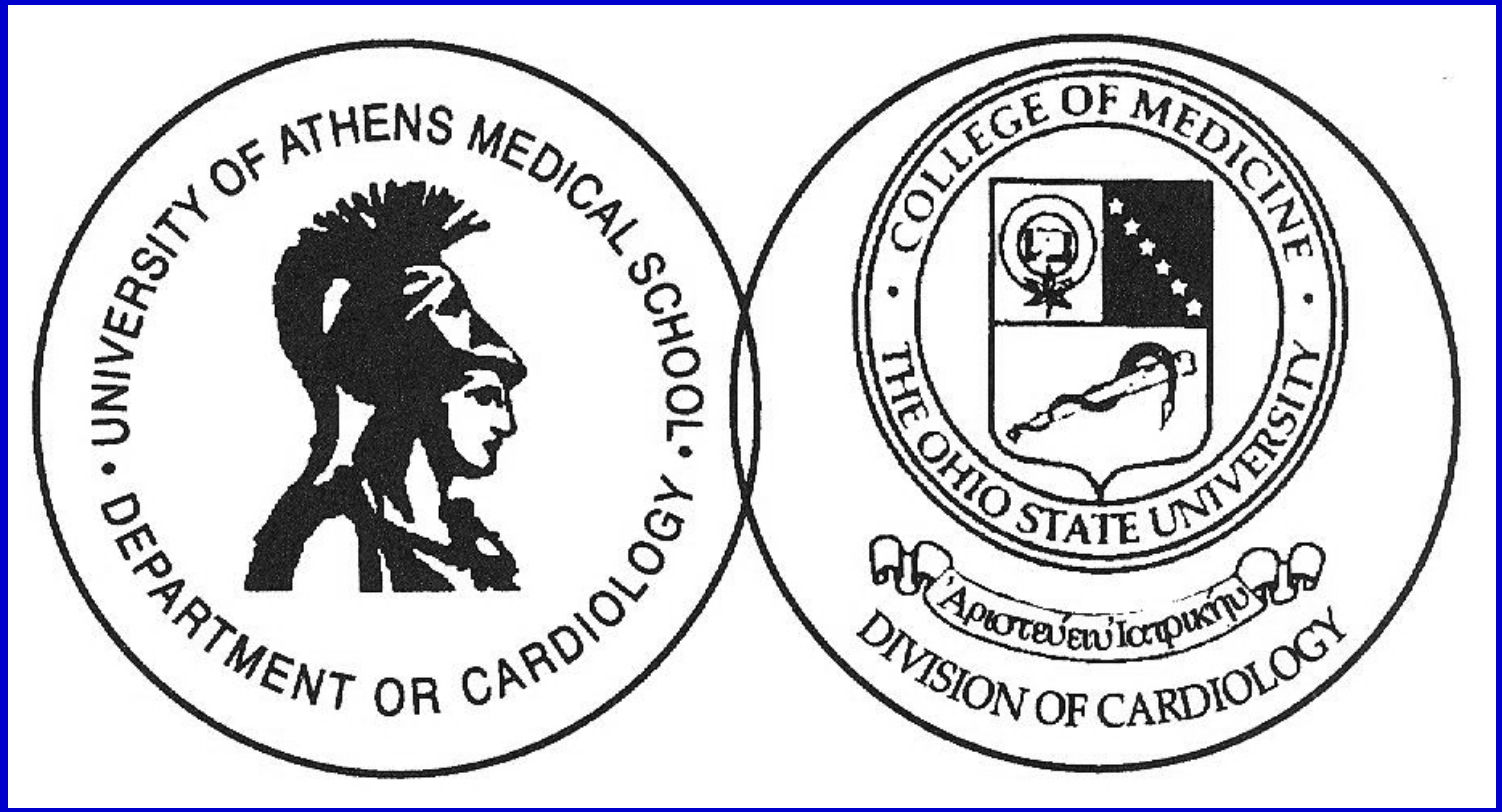

UNIVERSITY OF ATHENS MEDICAL SCHOOL
DEPARTMENT OR CARDIOLOGY
COLLEGE OF MEDICINE
THE OHIO STATE UNIVERSITY
Ἀριστεύειν ἰατρικήν
DIVISION OF CARDIOLOGY

CardioRenal Interrelationship

Harisios Boudoulas, Dr, Dr Hon
Professor, Academician (an. mem.)
The Ohio State University, Columbus, Ohio, USA
Biomedical Research Foundation, Academy of Athens, Greece

Επί της πρώτης επιτυχούς μεταμοσχεύσεως νεφρού επί ανθρώπου παρ' ημίν.

Κ. Τούντας, Δ. Βαλτής, Α. Μαρσέλος, Γ. Μπλάτζας, Χ. Μπουντούλας, Φ. Χαρσούλης, Δ. Τούσης, Χ. Πισιώτης

Ελληνική Ιατρική, 1968

CARDIORENAL

DISORDERS AND DISEASES

CARL V. LEIER, M.D.
HARISIOS BOUDOULAS, M.D.

CardioRenal
Disorders and Diseases

Carl V. Leier, M.D. & Harisios Boudoulas, M.D.

Second Edition, revised and expanded

Chapter 72

Renal DISORDERS AND Cardiovascular Disease

HARISIOS BOUDOULAS ▪ CARL V. LEIER

HEART DISEASE
A textbook of Cardiovascular Medicine
EDITED BY EUGENE BRAUNWALD

CardioRenal Interrelationship

- Health
- Certain conditions and diseases

CardioRenal Interrelationship in Health

CardioRenal Interrelationship: Cardiac Output Homeostasis

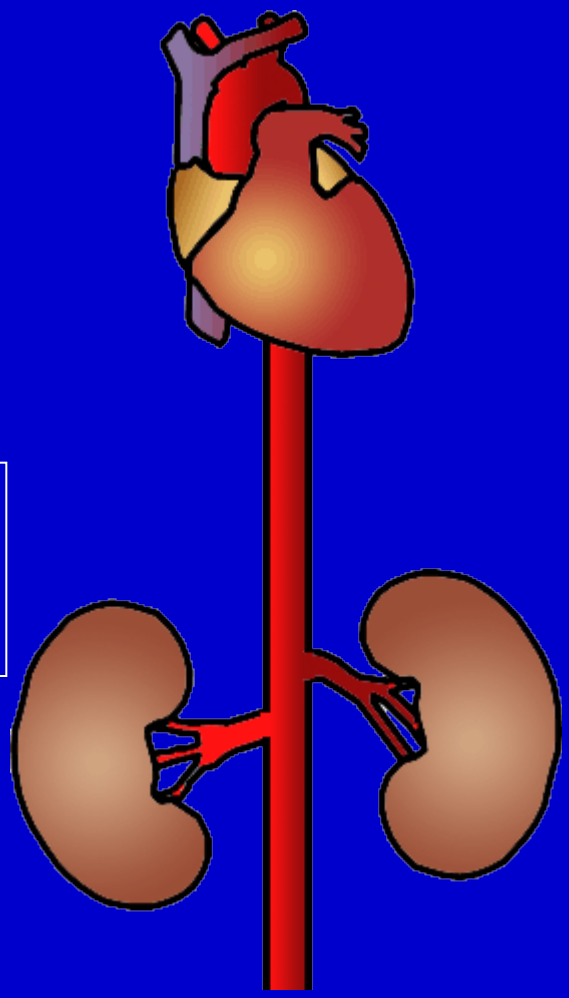
↑ Cardiac output

↑ Cardiac Filling Pressure

↑ Vascular volume

Electrolytes H_2O Retention

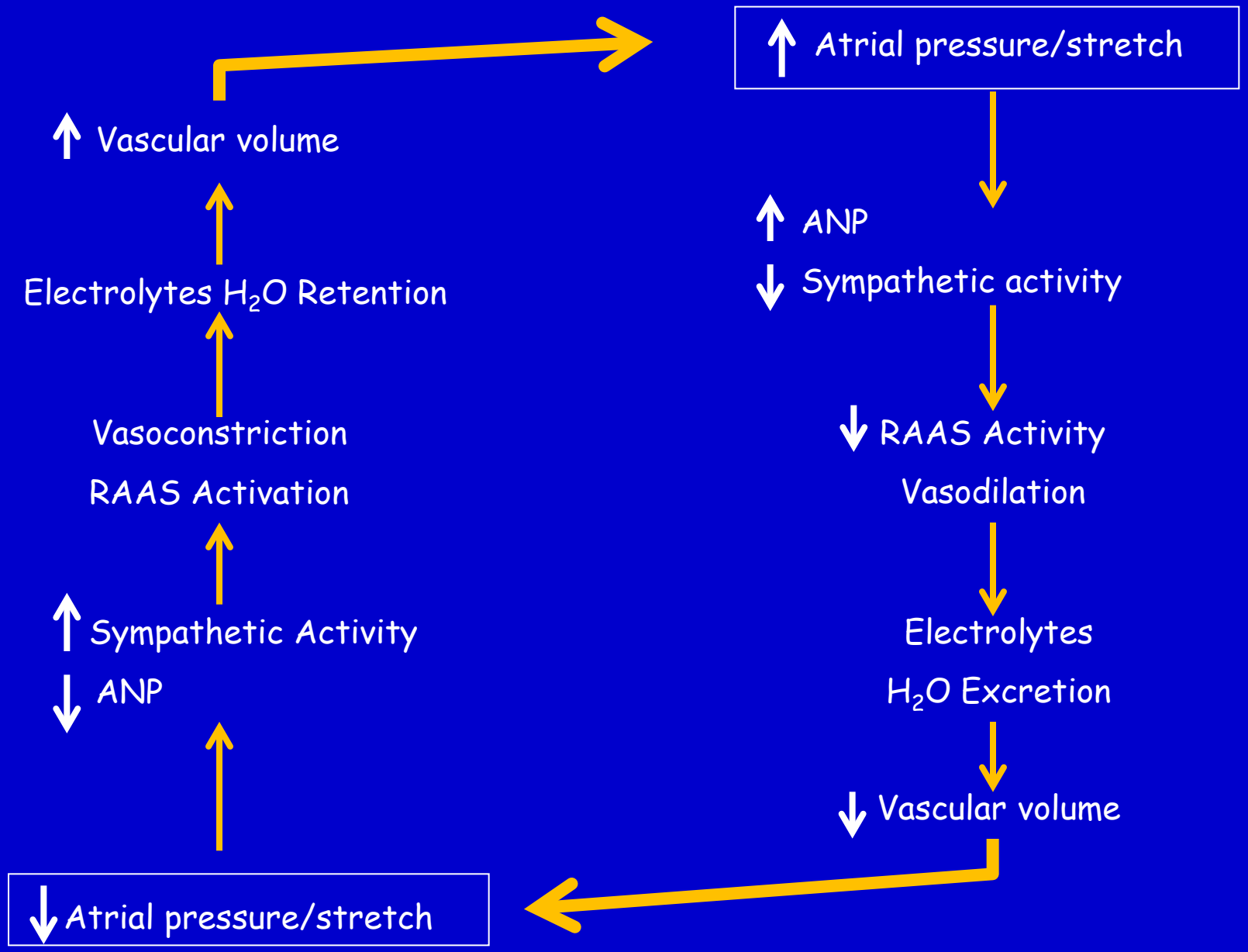
↑ Renal perfusion/ function



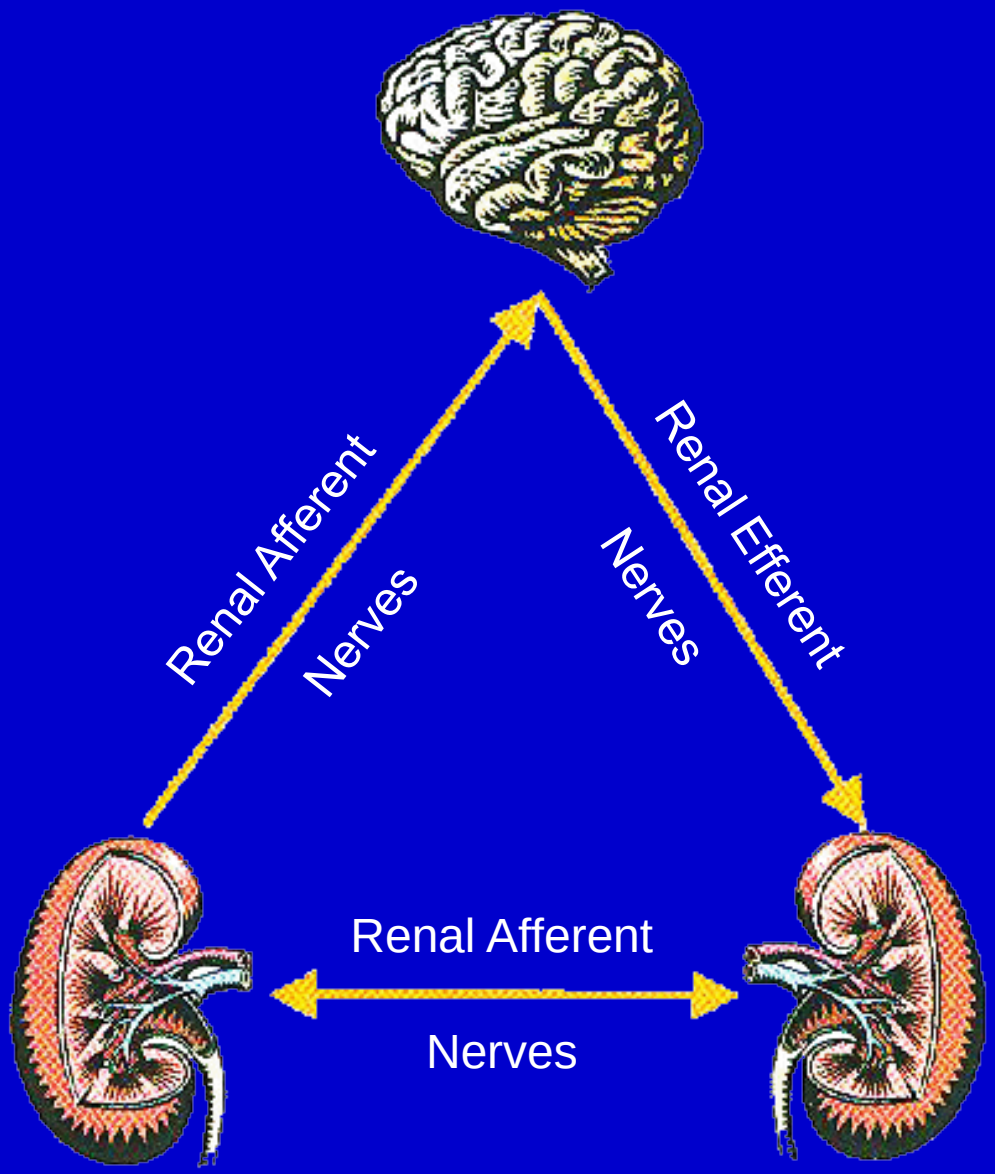
↓ Cardiac output

↓ Renal perfusion/function

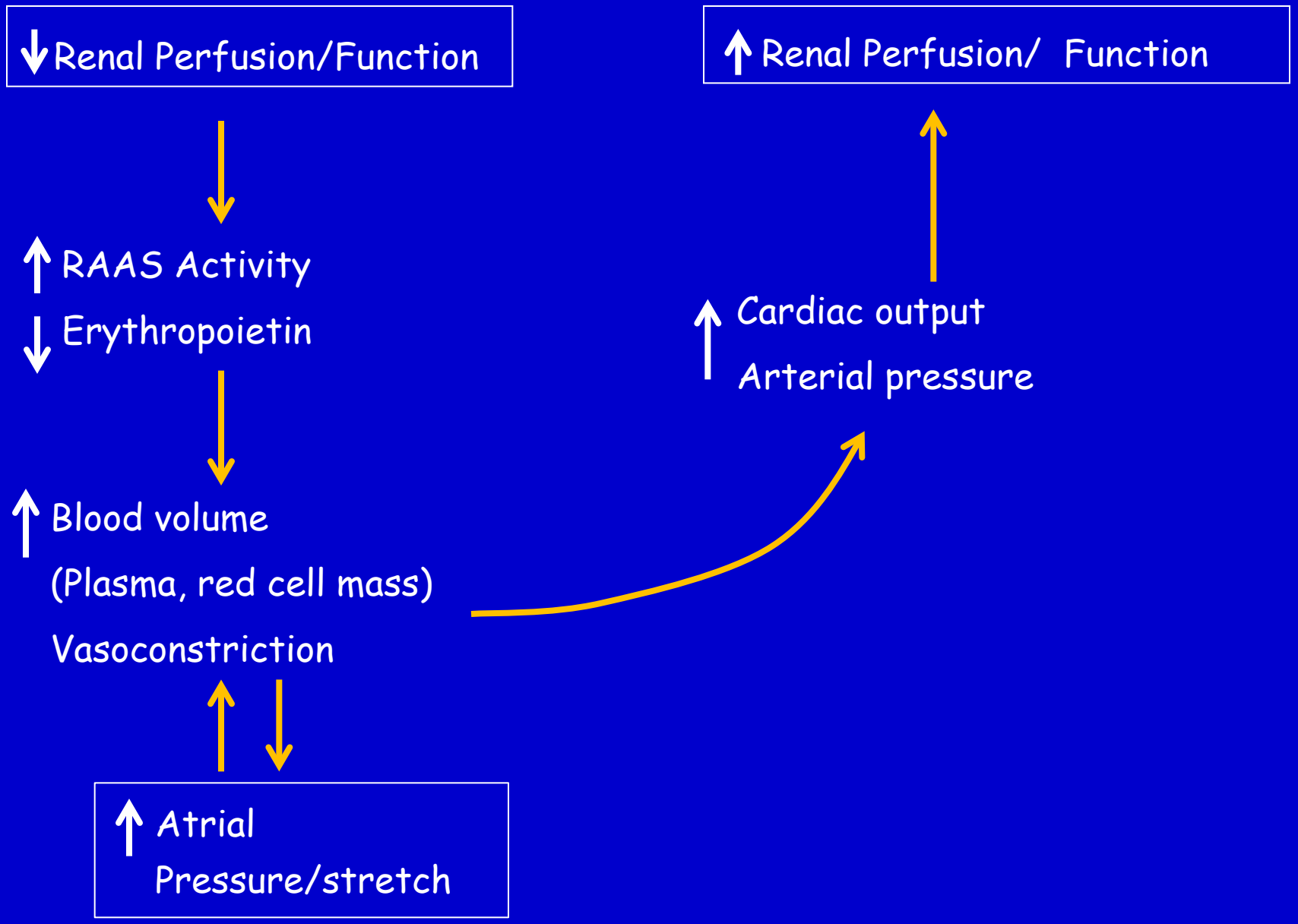
CardioRenal Interrelationship: Cardiovascular Pressure/Volume Homeostasis



CardioRenal Interrelationship: Blood Pressure Homeostasis

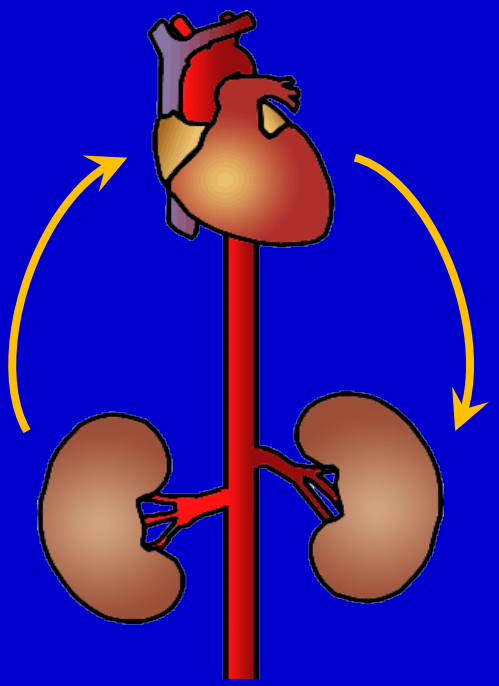


CardioRenal Interrelationship: Renal Perfussion/Function Hemostasis



CardioRenal Interrelationship in Health

The heart and the kidney constitute one interactive unit important for homeostases:



- Cardiovascular volume/pressure
- Cardiac output
- Renal perfusion/function
- Neurohumoral

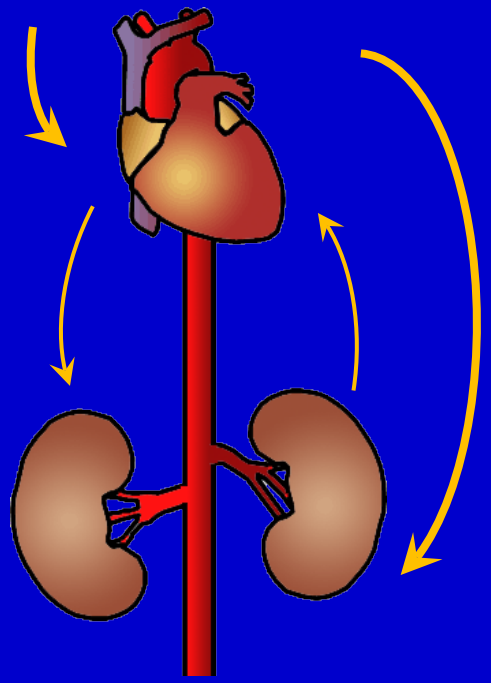
"The whole is greater than the sum of the parts."

-Aristotelis

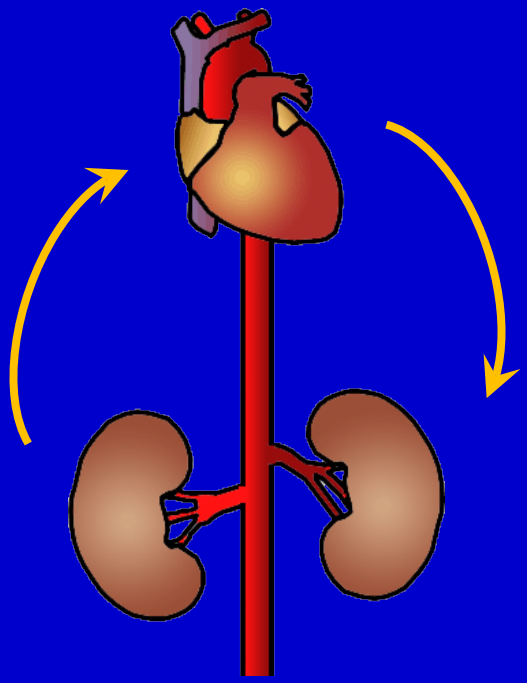
CardioRenal Interrelationship in Certain Conditions and Diseases

CardioRenal Interrelationship

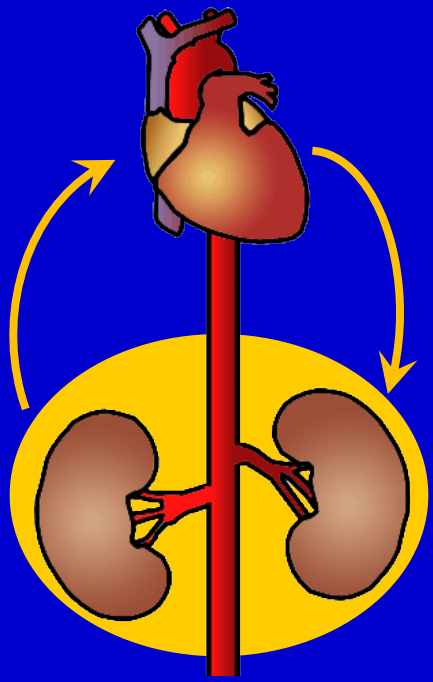
Systemic Conditions and Diseases



Cardiovascular Disorders and Diseases



Renal Disorders and Diseases

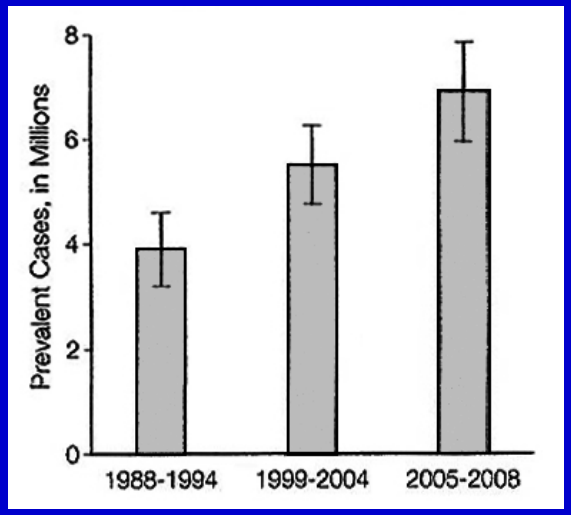


Boudoulas K, Boudoulas H
Cardiology, 2011; 120: 135-138

Chronic Kidney Disease (CKD) in the United State

- More than 20 million Americans with CKD (1 of 10 adults)
- Leading causes are diabetes (36% of all cases) and poorly controlled hypertension (23% of all cases)

Diabetic Kidney Disease in the United States



National Kidney Foundation 2007

de Boer IH et al. *JAMA* 2011; 305: 2532

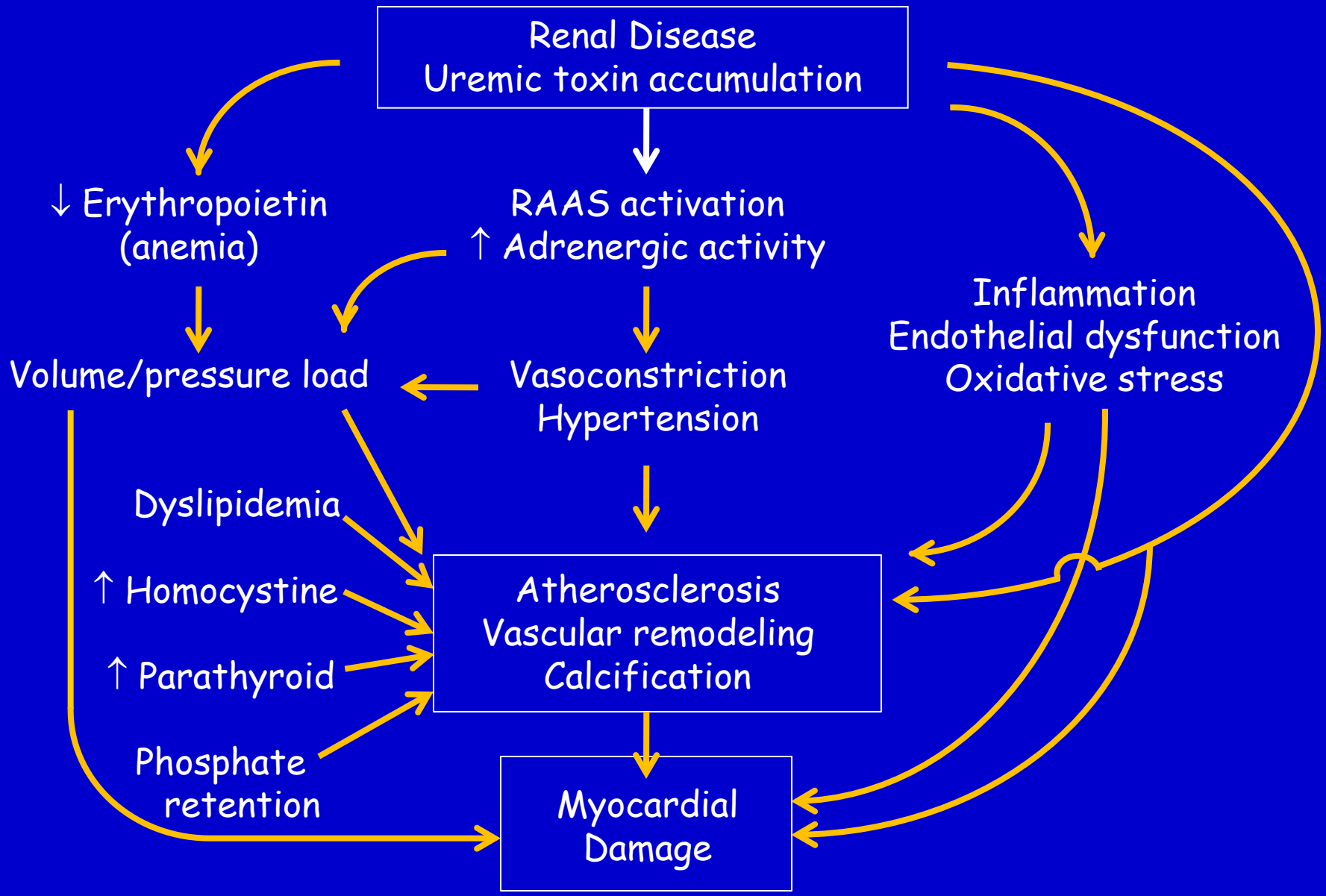
Chronic Kidney Disease and CV Risk

GFR (ml/min)	CV Risk (OR)
> 90	? (Proteinuria - degree)
60-89	1.5
30-59	2-4
15-29	4-10
< 15	20-1000

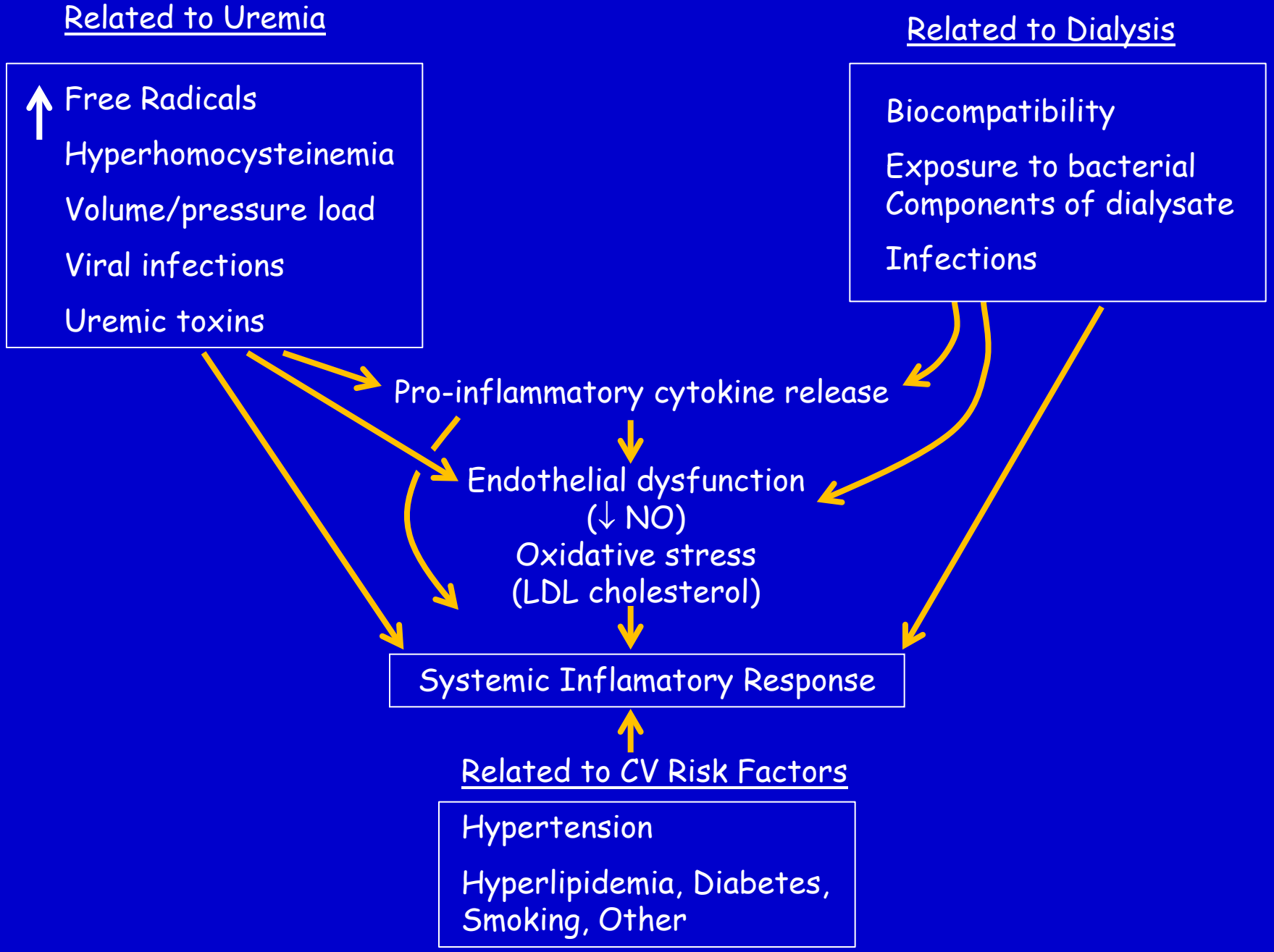
-Almost all patients with CKD have stiff aorta
-In hemodialysis patients the incidence of CAD is 40%, CHF 40%,and LVH 70%

Schiffrin et al. *Circulation* 2007; 116: 85
Zocani C et al. *Kidney Int* 2011; Suppl I: 2-5

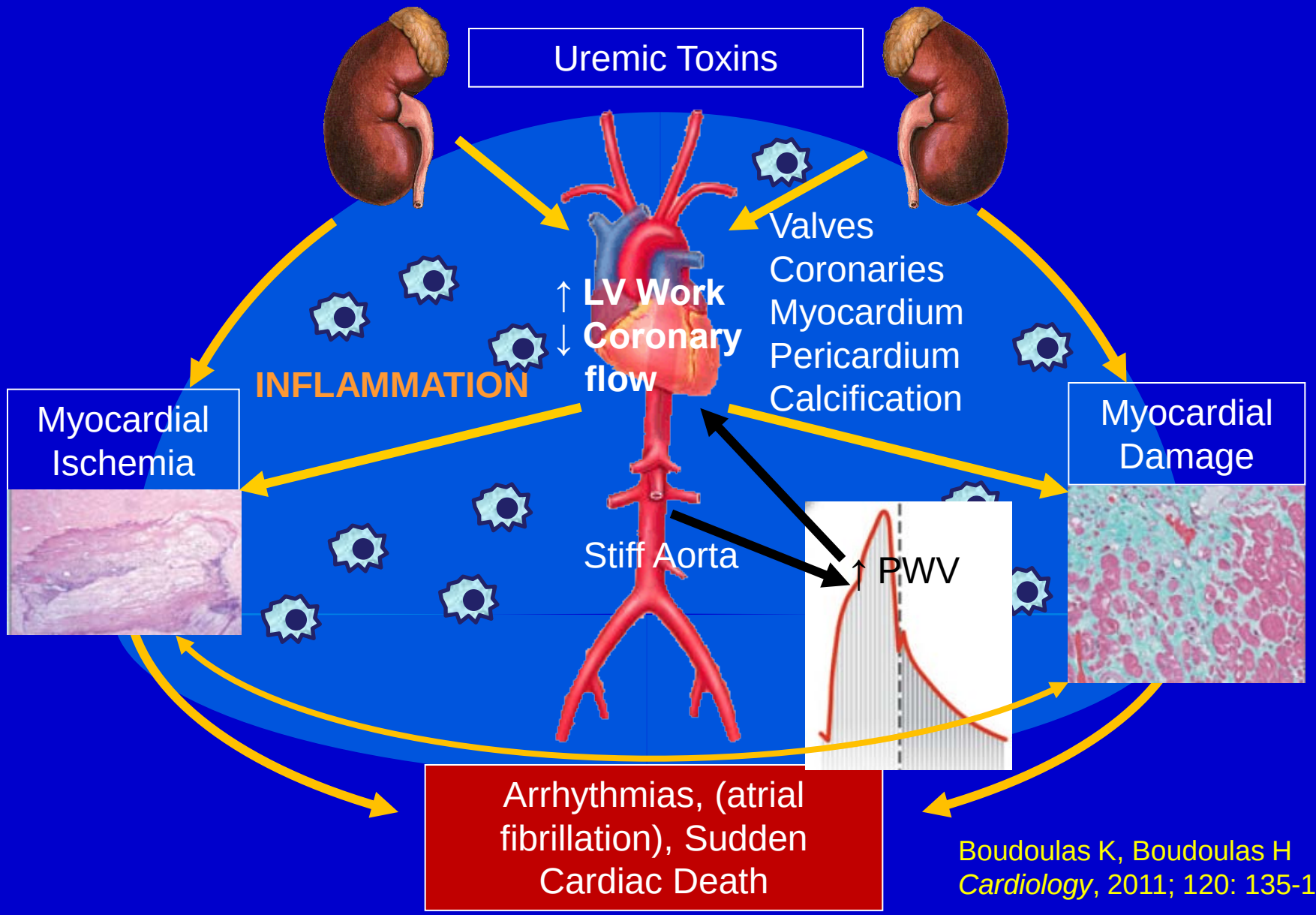
CardioRenal Interrelationship in Cronic Renal Disease



Inflammatory Process in Renal Disease

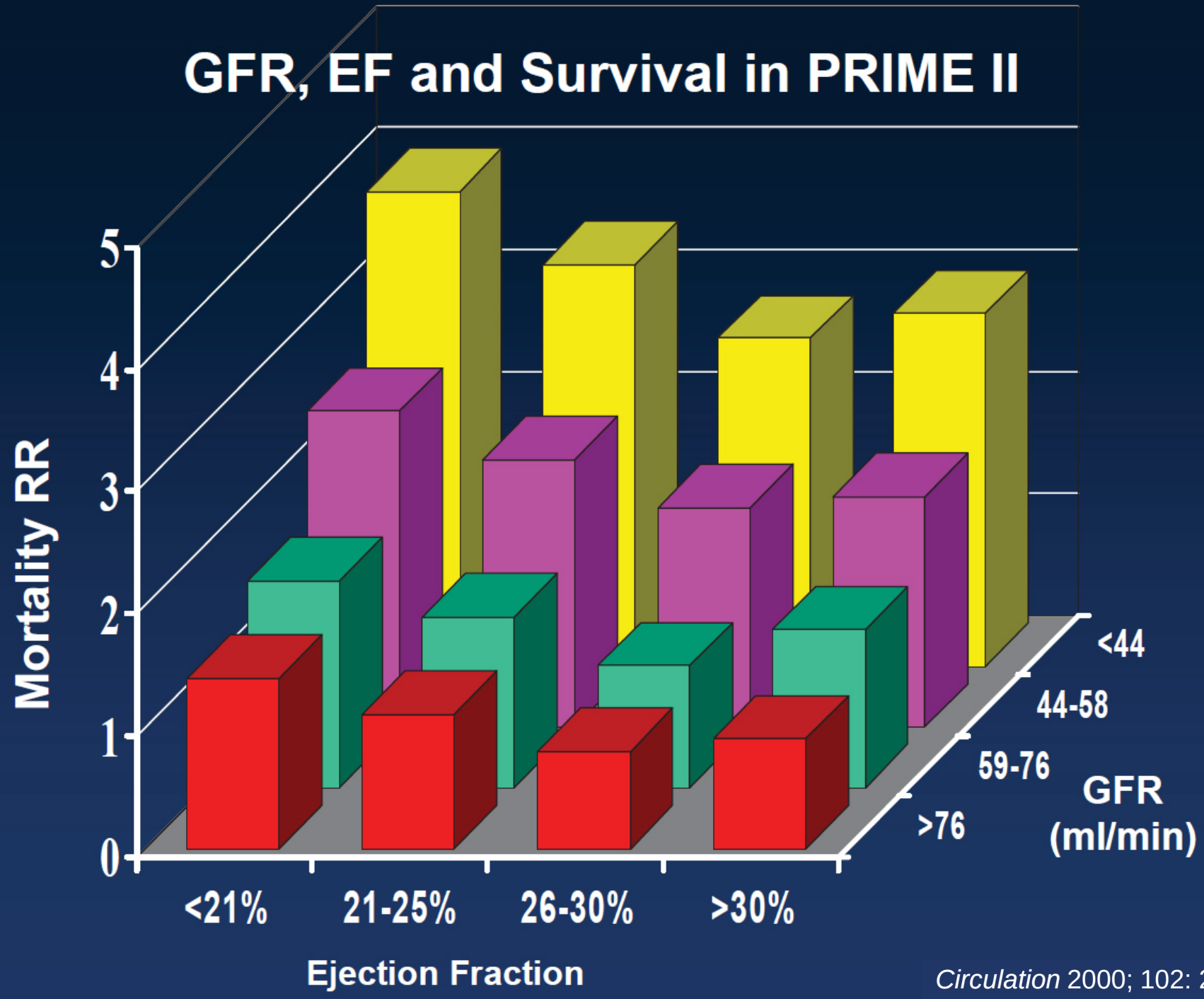


CardioRenal Interrelationship in Renal Disease



Boudoulas K, Boudoulas H
Cardiology, 2011; 120: 135-138

GFR, EF and Survival in PRIME II



Circulation 2000; 102: 203

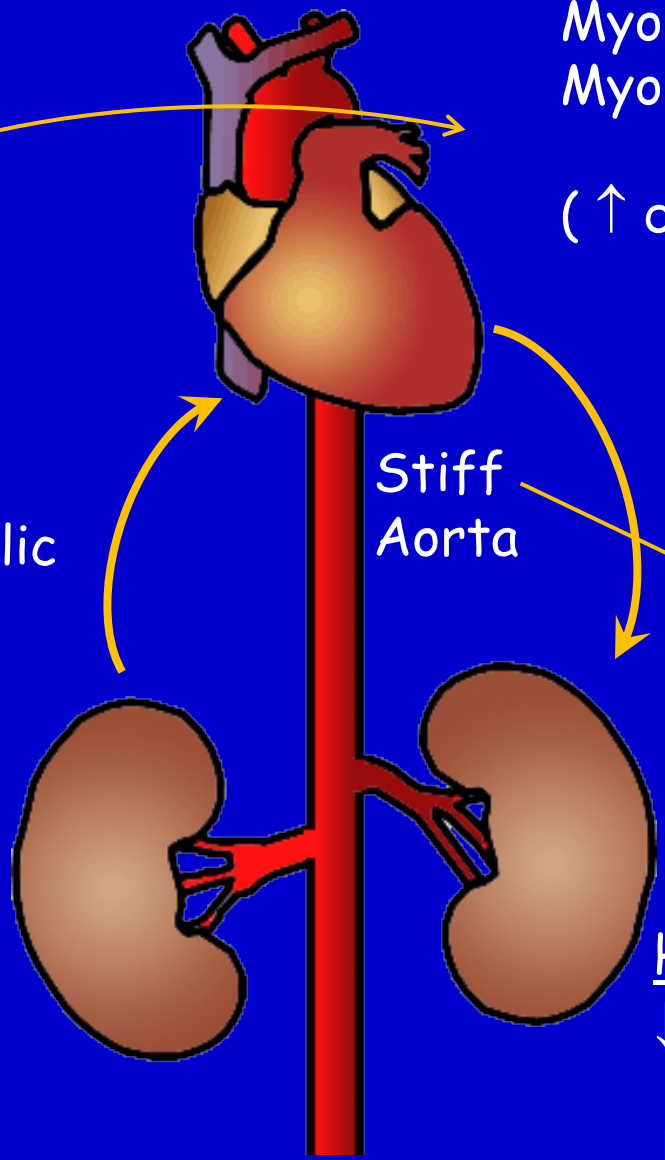
CardioRenal Interrelationship: Diagnostic and Therapeutic Considerations

Myocardial Hypertrophy/Damage
Myocardial Ischemia

↓

(↑ diastolic pressure, other)

Dialysis
A-V fistula
Hypoxemia
Electrolyte/metabolic
Abnormalities



Stiff
Aorta

Pressure / Volume Load

Homeostasis is lost
↓ Excretion: H_2O, Na, dye, other
↓ Erythropoietin

Brain Natriuretic Peptides in Renal Disease

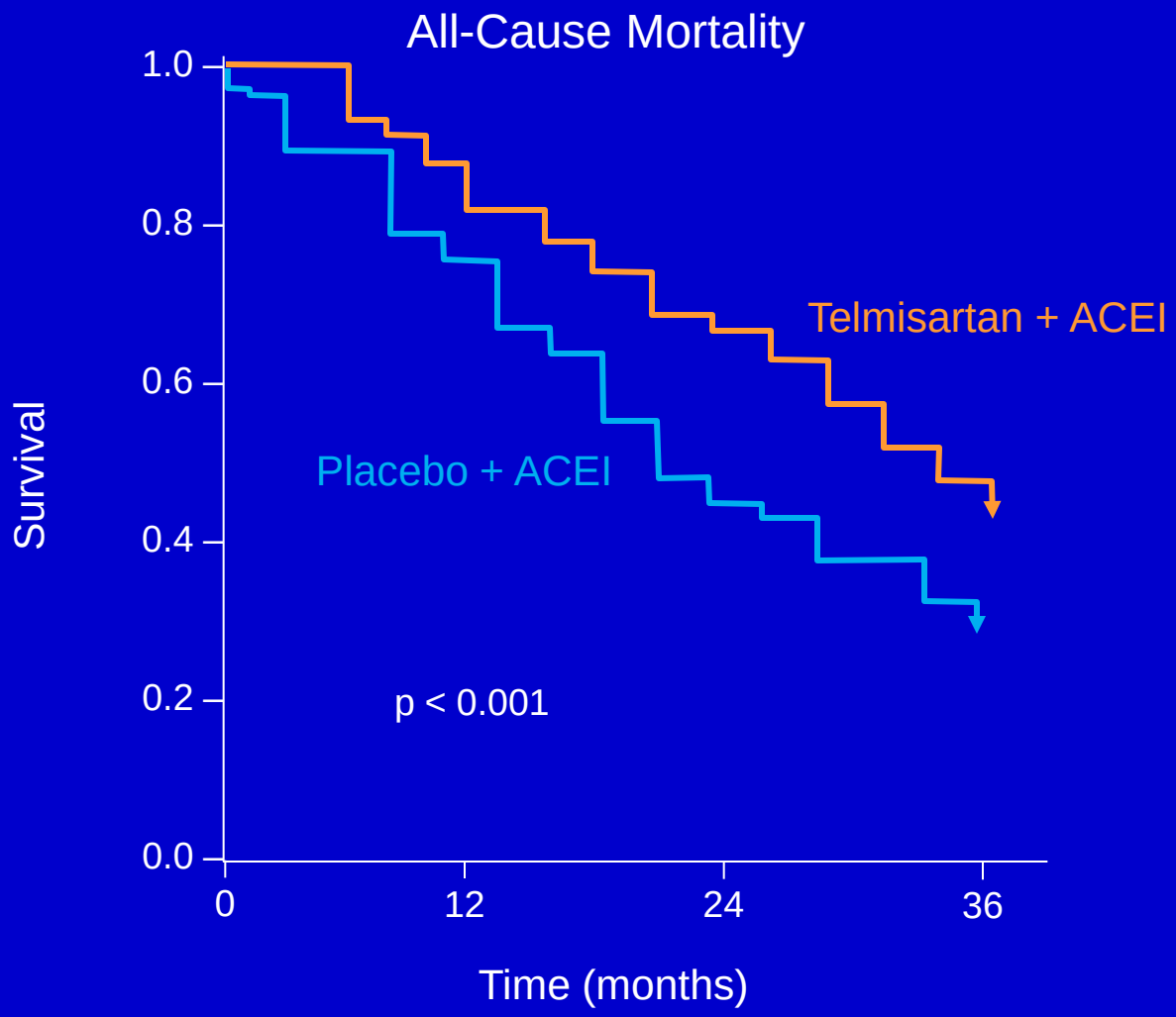
- Brain natriuretic peptides (BNP) are high in almost all patients with renal disease

- High BNP in renal disease constitutes a risk prognostic indicator

Heart Failure in Patients with Chronic Renal Disease

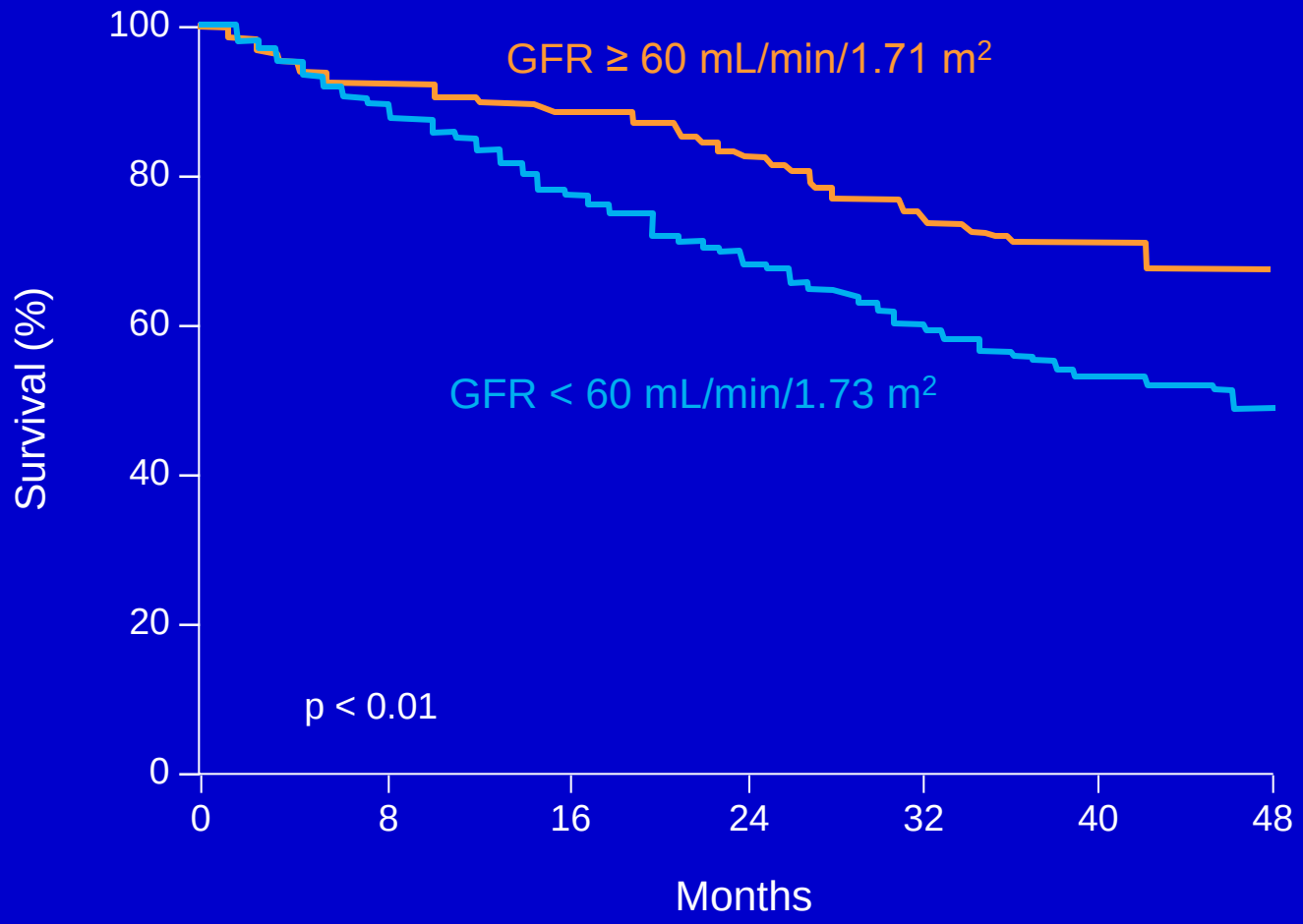
- β-Blockers
- ACE inhibitors, angiotensin blockers ?
- Diuretics ?; ultrafiltration
- Electrolyte/metabolic problems
- Dialysis (daily ?), peritoneal
- Effect of right ventricular function and venous congestion
- Hemodynamic monitoring ?
- Portable artificial kidney (nanotechnology) ?

Effects of Telmisartan Added to ACEI on Mortality in Hemodialysis Patients with Heart Failure



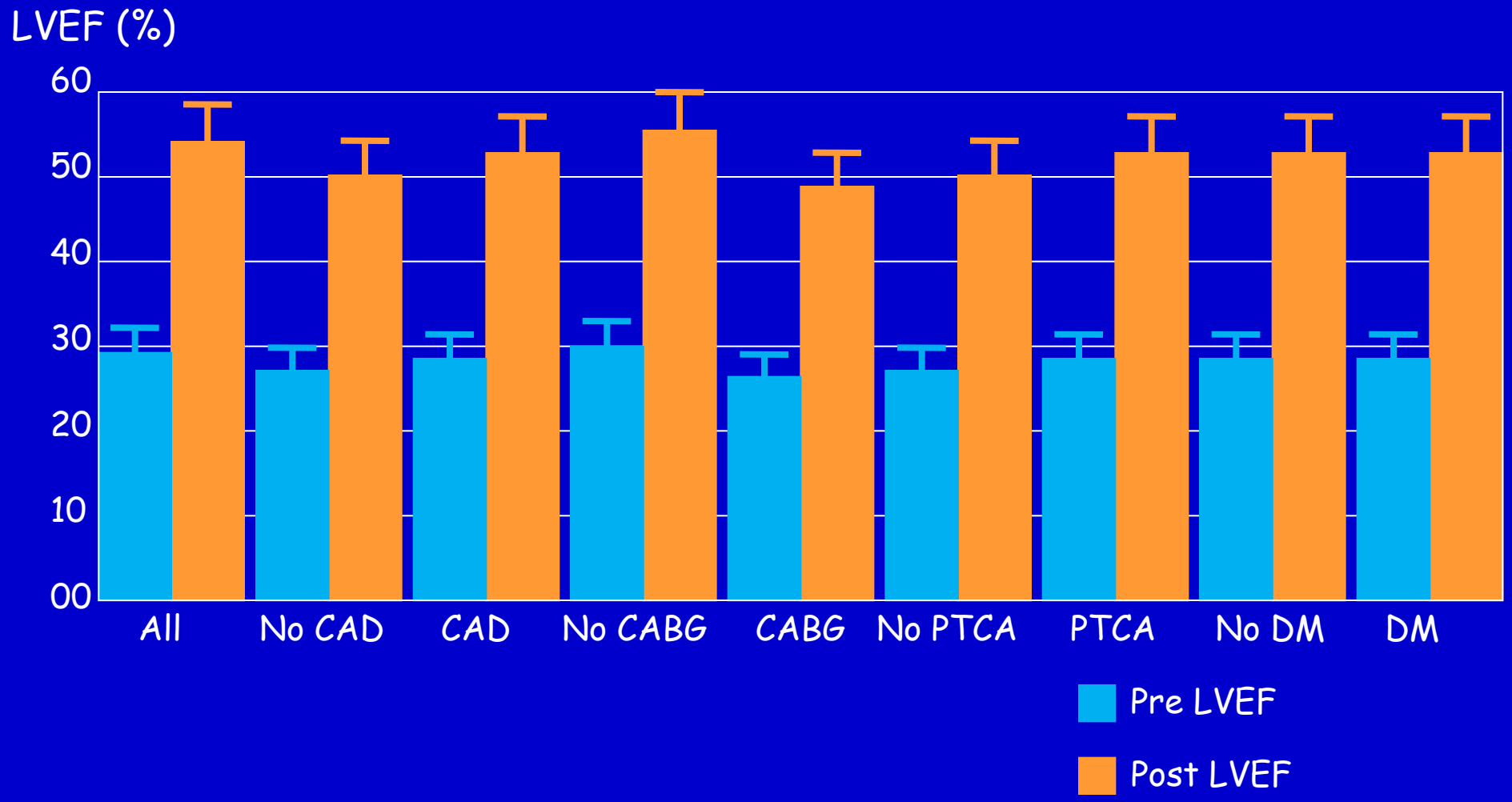
Cice J et al. *JACC* 2010; 56: 1701

Survival Following Cardiac Resynchronization Therapy



Lin G et al. *Eur Heart J* 2011; 32: 184

LVEF before (on dialysis) and After Kidney Transplantation



Wal RK, et al. JACC 2005; 45: 1051-1060

Declining Glomerular Filtration Rate (GFR) Linked to Mortality Risk After Myocardial Infarction (MI)

- 103,233 patients with AMI (England and Wales)
    - 41,931 – ST elevation – CKD 32.8%
    - 61,302 – non ST elevation – CKD 50.6%
- Patients with chronic kidney disease (CKD) had a significantly increased risk of death, and the risk increased as GFR declined

American Society of Nephrology – November 2011

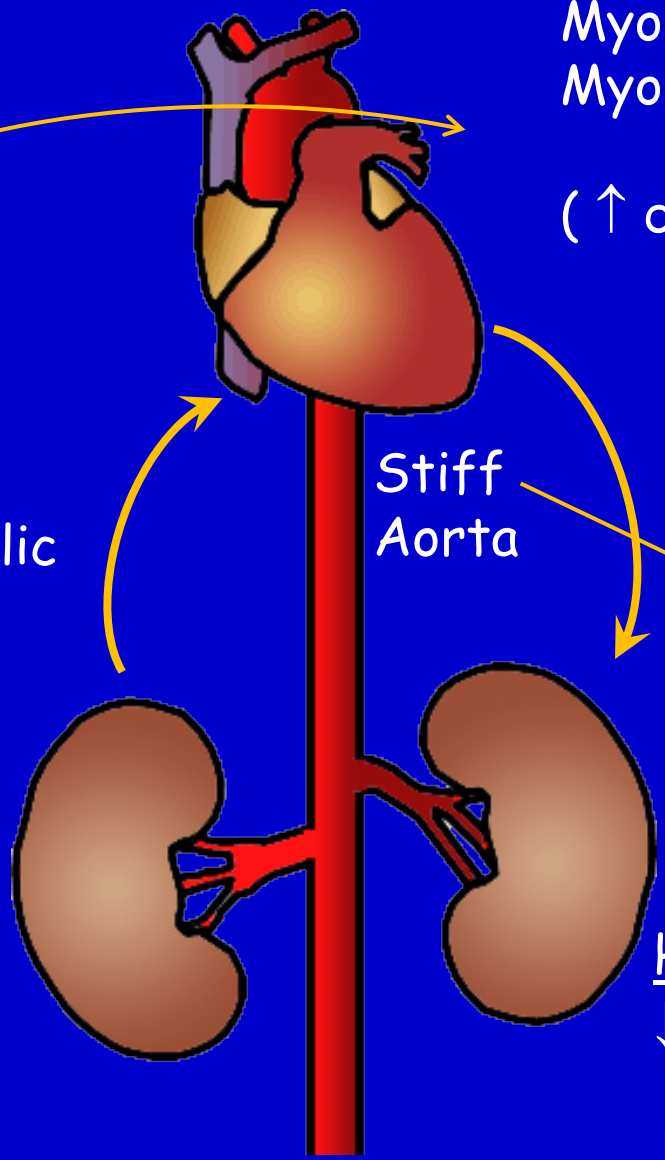
CardioRenal Interrelationship: Diagnostic and Therapeutic Considerations

Myocardial Hypertrophy/Damage
Myocardial Ischemia

↓

(↑ diastolic pressure, other)

Dialysis
A-V fistula
Hypoxemia
Electrolyte/metabolic
Abnormalities



Stiff
Aorta

Pressure / Volume Load

Homeostasis is lost
↓ Excretion: H_2O, Na, dye, other
↓ Erythropoietin

Contrast Induced Nephropathy (CIN)

GFR < 60 ml/min/1.72 m^2

↓

Stop non steroid antiinflammatory, diuretic, metformin

↓

Hydration (normal saline, Lasix ?)

↓

N acetylcysteine (optional)

↓

Limit contrast dye amount

↓

Serum creatinine at 24 hrs

↓

Repeat creatinine until peak if CIN occurs

Marcutzi et al. *JACC Cardiac Interv* 2012; 5: 90-97

Troponin (Tn) Elevation in Patients with Renal Disease

- Troponin levels are elevated in patients with renal disease with and without acute myocardial infarction

- A dynamic change of Tn concentration > 20% is consistent with myocardial infarction

- Elevation of Tn in renal failure constitutes a risk prognostic indicator

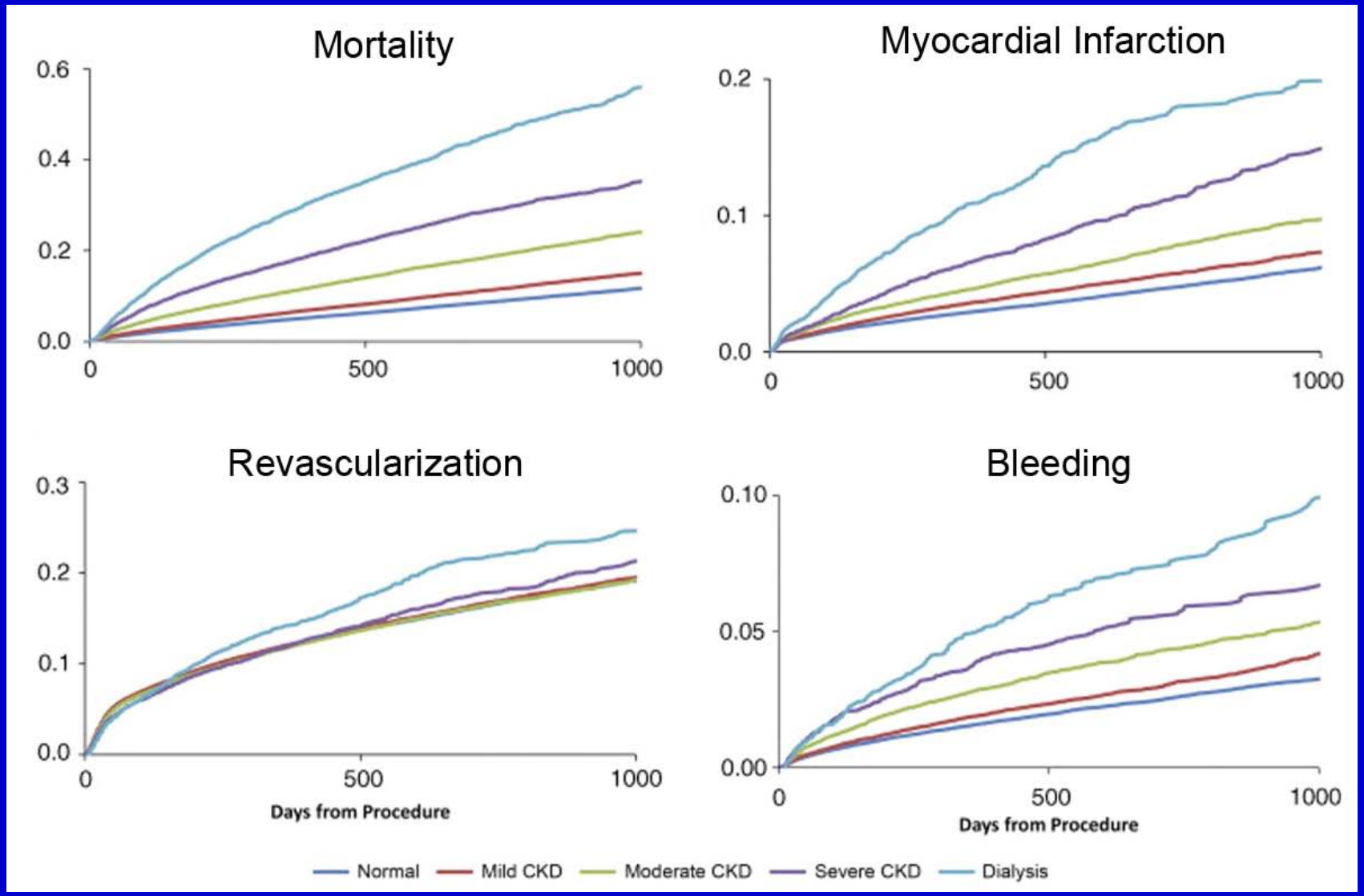
Mahajan VS, Jarolin P. *Circulation* 2011; 124: 2350-54
Agewall S et al. *Eur Heart J* 2011; 32: 404-411
White HD. *JACC* 2011; 57: 2406

Coronary Artery Disease in Chronic Renal Disease

- β-Blockers
- ACE inhibitors
- Statins
- The role of vitamin D
- Hemocystein reduction (?)
- Procoralan
- Ranolazine
- Antiplatelet therapy (platelet functional studies post PCI ?)

Drug-Eluting Stents (DES) in Chronic Kidney Disease (CKD): Cumulative Incidence of Events Stratified by Severity of CKD

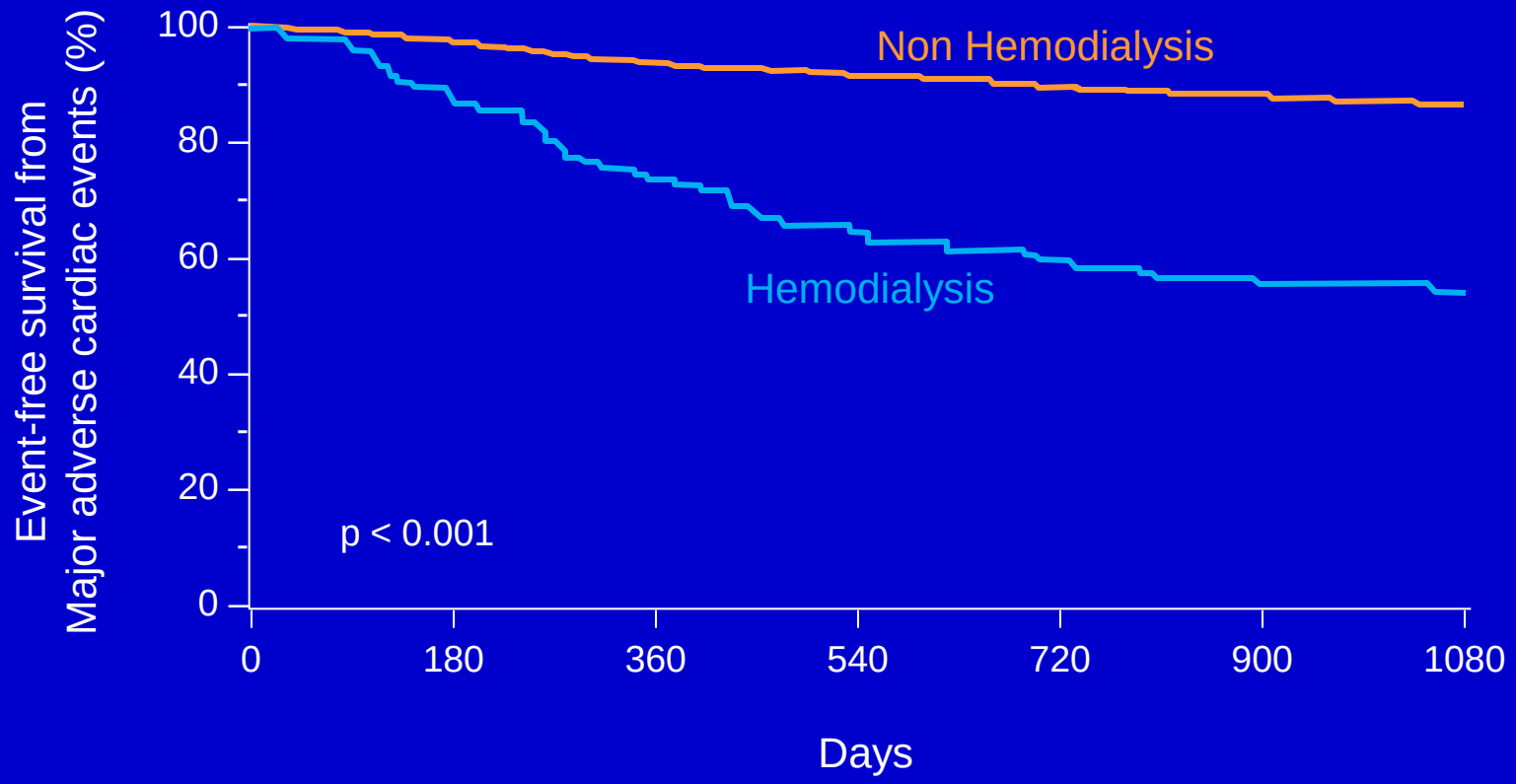
283,593 pts, 65 years or older; 42.8% had CKD



Lower Mortality and MI Rates with DES Compared to BMS

Tsai TT et al. *JACC* 2011; 58: 1859

Three Year Clinical Outcomes After Sirolimus-Eluting Stent Implantation



Otsuka Y et al. *Eur Heart J* 2011; 32: 829

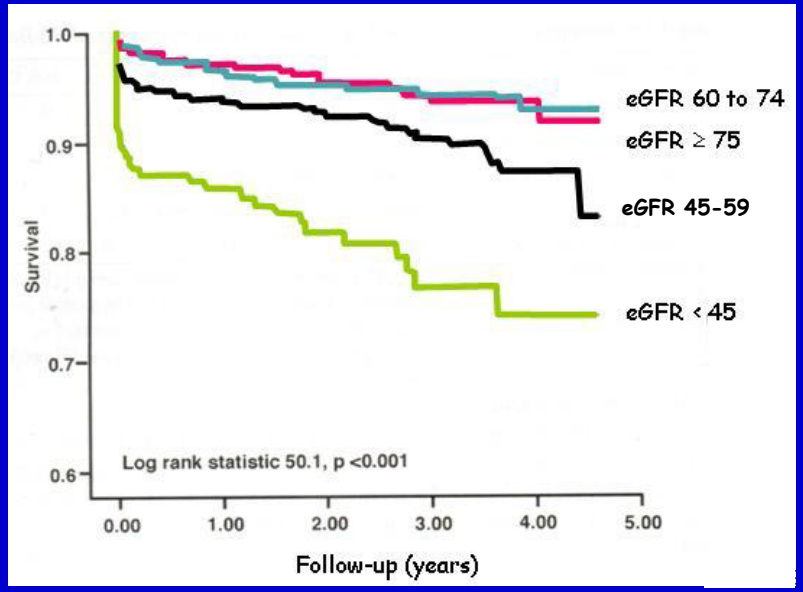
Antiplatelet Therapy in Patients with Chronic Kidney Disease (CKD)

GFR	>90 (proteinuria)	60-89	30-59	15-29	<15
Aspirin	SE	SE	SE	SE	SE
Ticagrelor (studies needed)	SE	SE	SE	SE	SE
Prasugrel	SE	SE	Unknown	Unknown	Unknown
Clopidogrel	SE	SE	↑ Bleeding	? Effect	

Safe, S; Effective, E

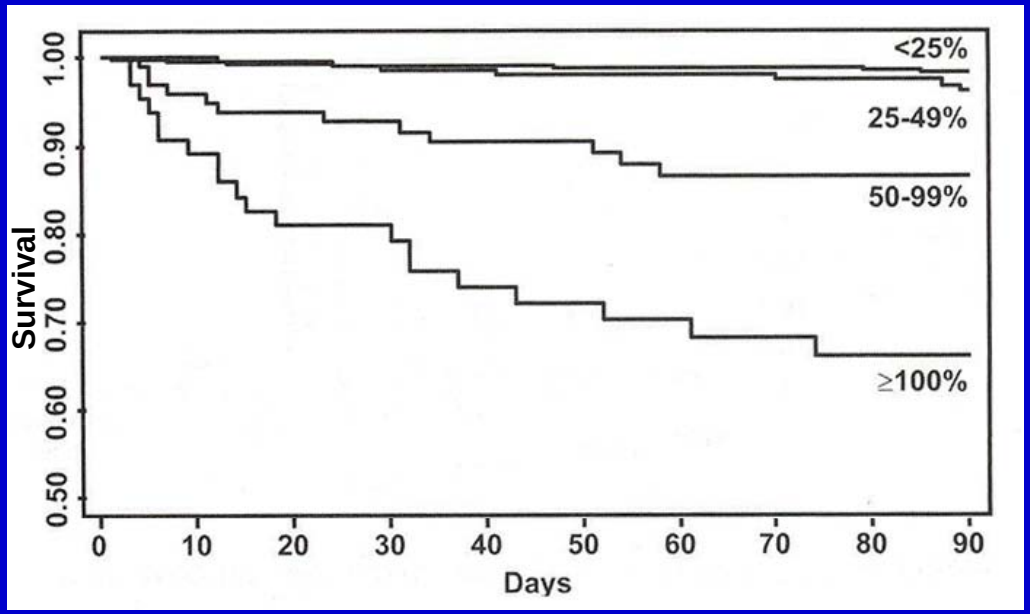
Barsa SS, et al. *JACC* 2011; 58: 2263-69
State of the Art paper

Survival After CABG in Relationship to eGFR



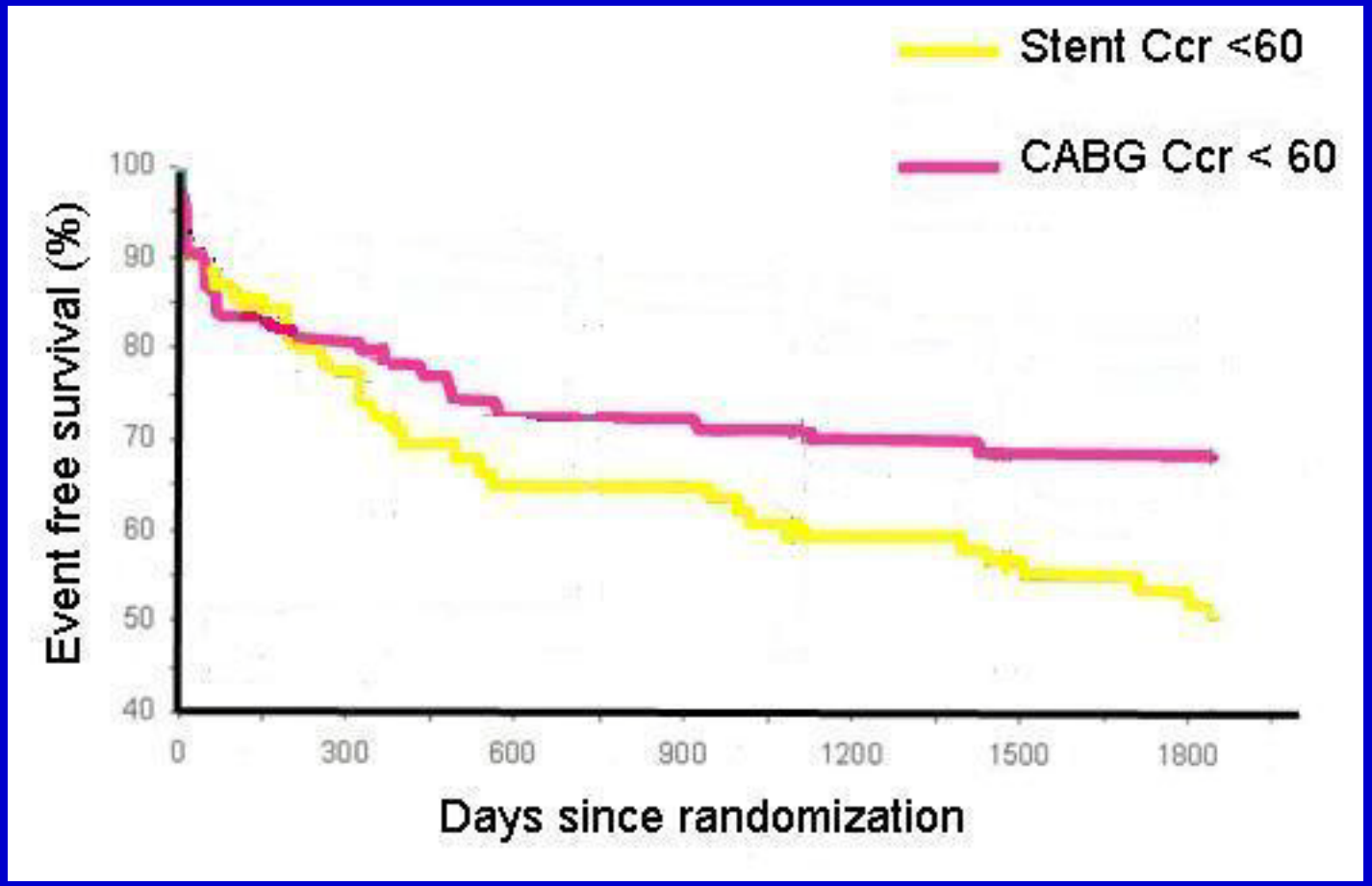
Hillis GS et al. *Circulation* 2006; 113: 1156

90-Day Survival After Coronary Bypass Surgery in Relationship to Creatinine Increase



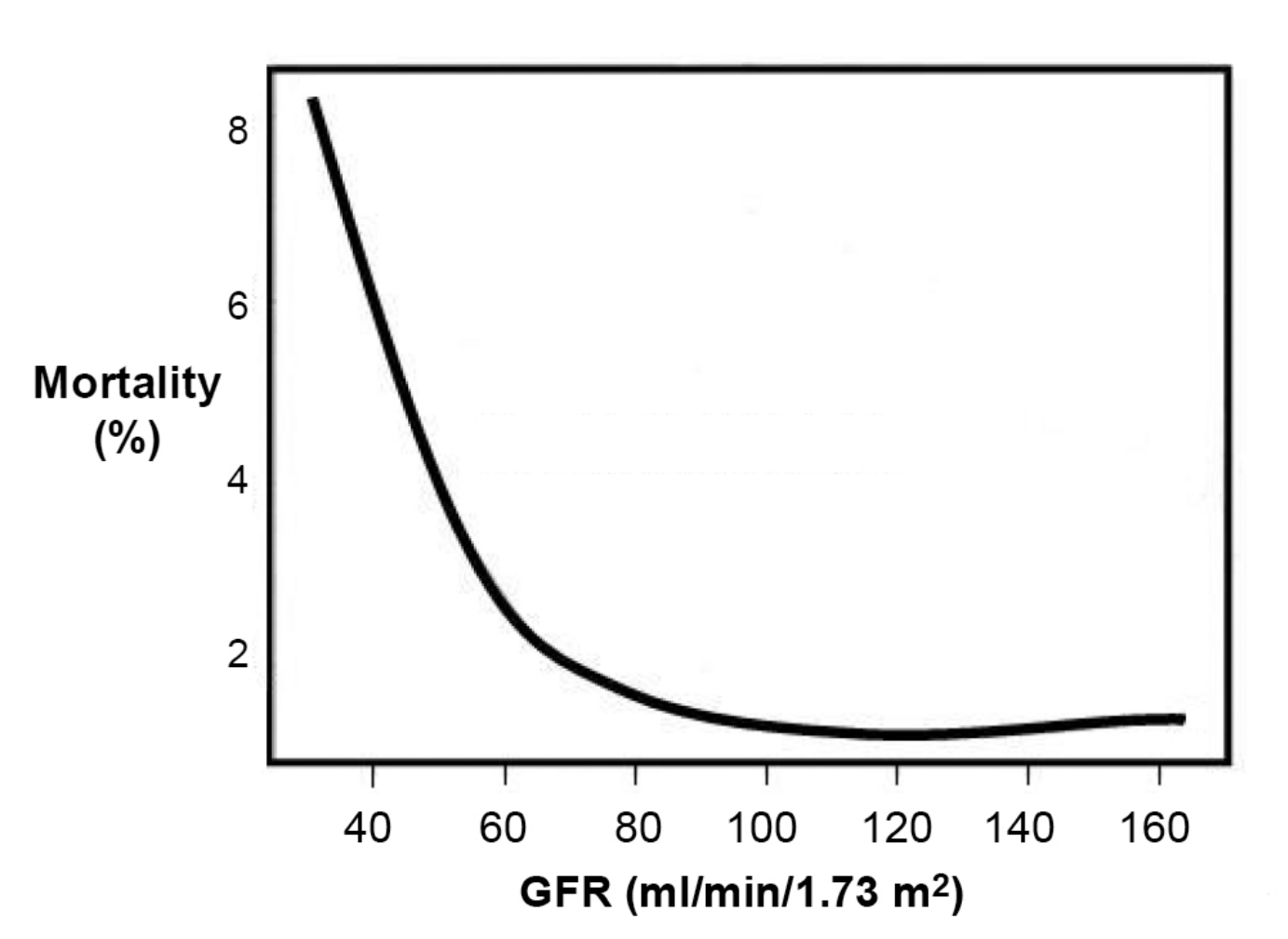
Brown JR. *Circulation* 2006; 114 (suppl I): I-409

Bypass vs Stent: Event Free Survival in Relationship to Renal Function



Modified from Aoki J, et al. Eur Heart J 2005; 26: 1488

Estimated Probability of Operative Mortality (CABG) in Relation to GFR Among Nondialysis Patients



Cooper WA et al. *Circulation* 2006; 113: 1063

Cardiac Surgery and Renal Function

- Renal dysfunction is a risk factor for adverse cardiac events after coronary bypass surgery

- Acute renal failure in patients undergoing cardiac surgery is a strong prognostic indicator

- Even minimal increases in serum creatinine after cardiac surgery is associated with increased mortality

- Hybrid approach ?

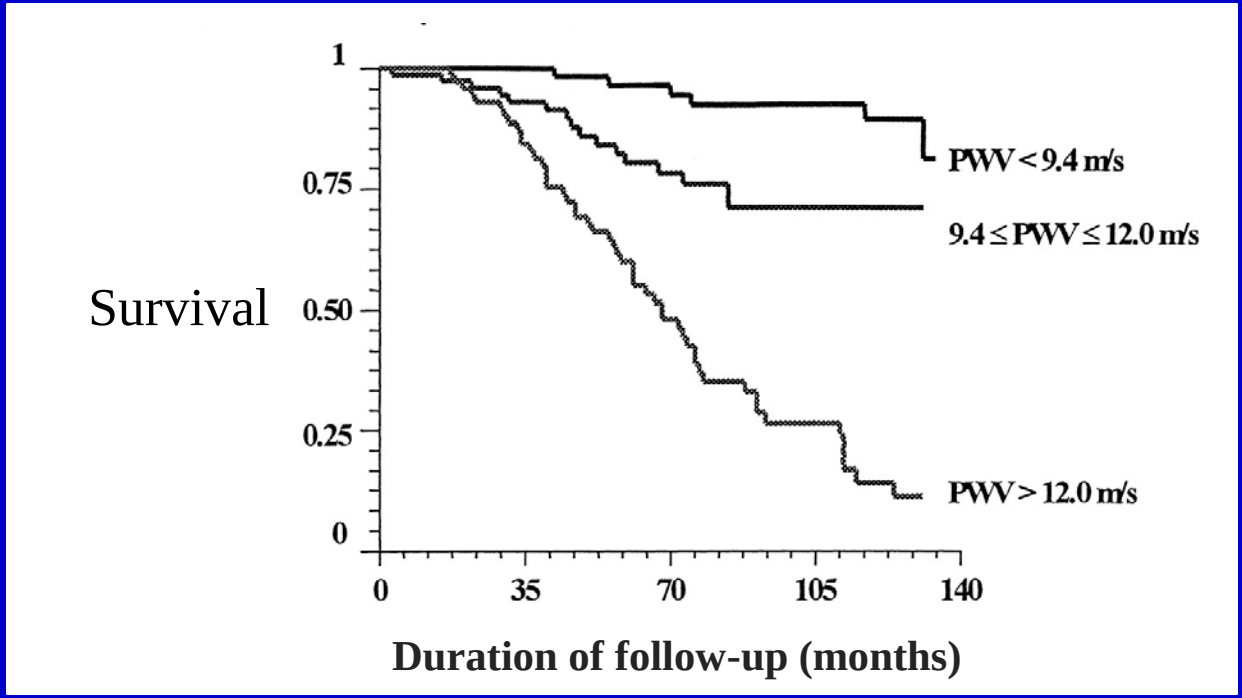
Hybrid Cardiovascular Operating Room

Operating Room

Catheterization Lab

Vanderbilt University Hybrid OR/Lab First in USA

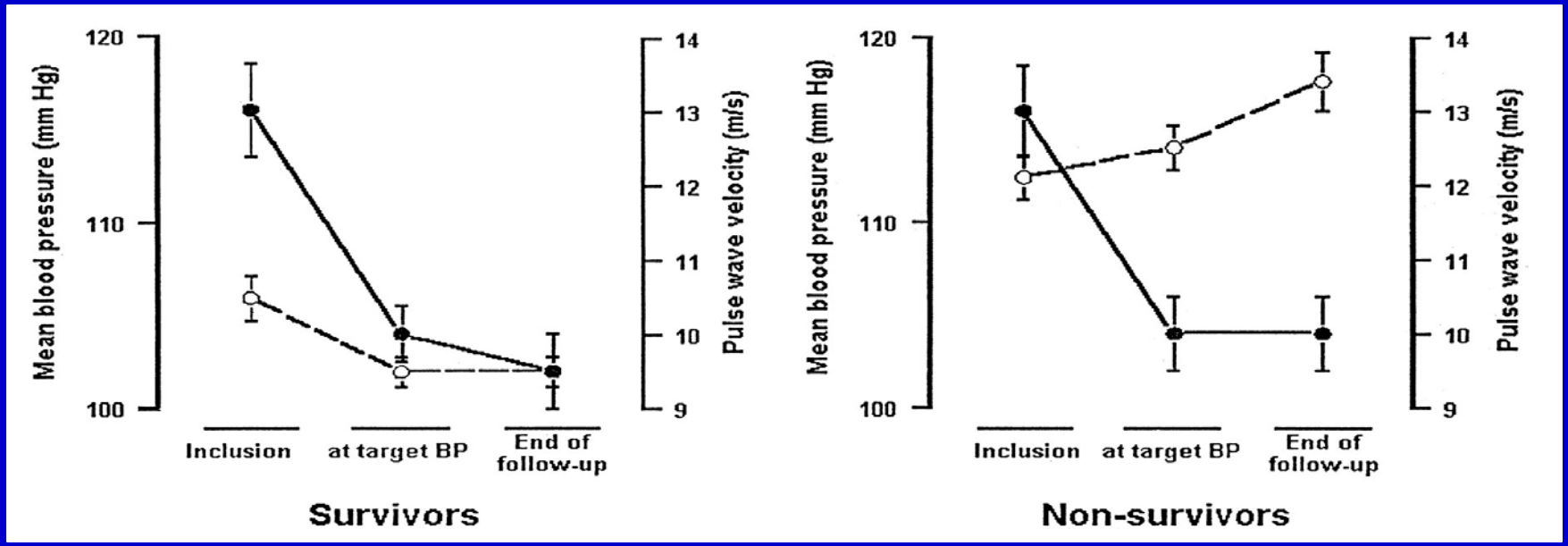
Deleterious Effects of Aortic Stiffness in Renal Disease



Blacher J et al. *Circulation* 1999;99:2434

Association of aortic PWV with vascular calcification in hemodialysis patients. Raggs P et al. *Kidney Int* 2007; 71: 802-87

Improvement of Aortic Function in Renal Disease Increases Survival



Guerin AP et al. *Circulation* 2001;103:987

Severamer vs calcium based phosphate binders

- Block GA et al. *Kidney Int* 2007; 71: 438-41
- Suki WN et al. *Kidney Int* 2007; 72: 1130-37
- Portable artificial kidney (?)

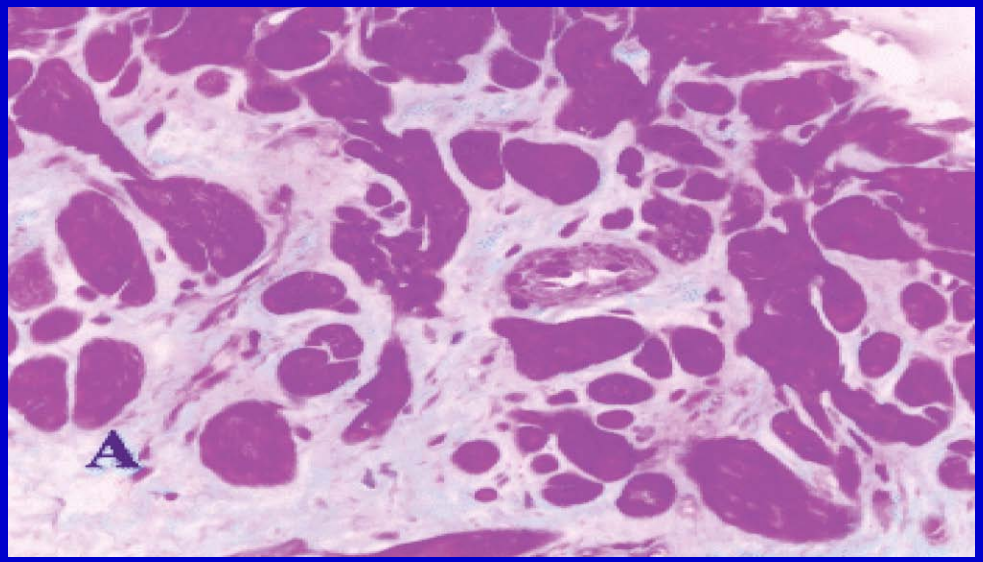
Sudden Cardiac Death in Dialysis Patients

- Estimated rate of sudden cardiac death in dialysis patients is approximately 7% per year (27% of all deaths).

- Possible explanations:
  - CAD
  - LVH – fibrosis
  - Rapid electrolyte shifts
  - Autonomic nervous system dysfunction

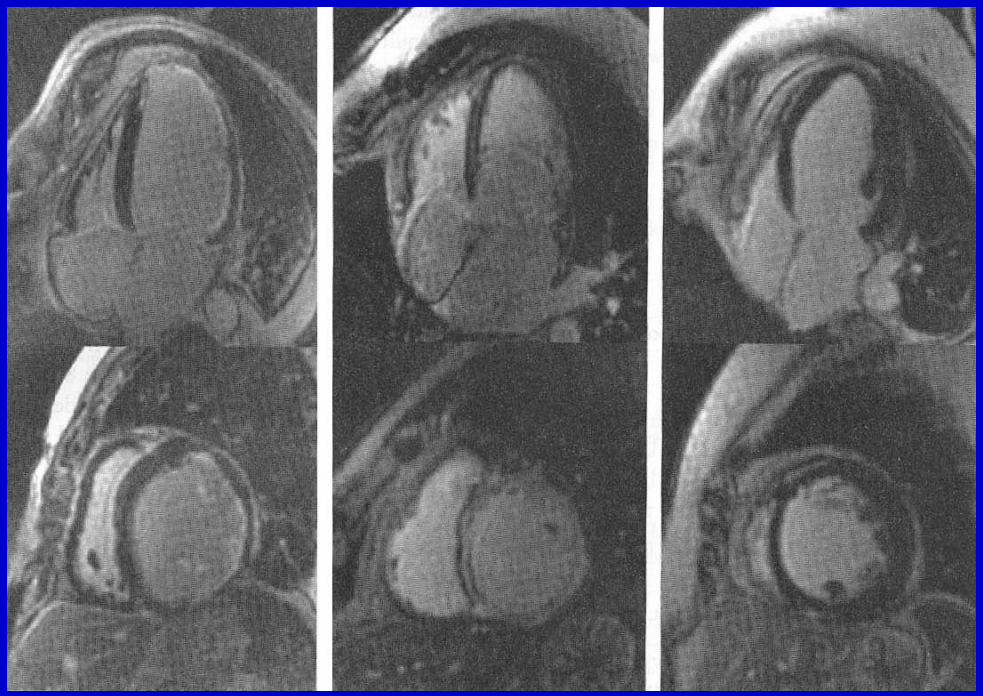
Semin Dial 2008; 21: 300-307
Eur Heart J 2009; 30: 1559-1564

Myocardial Fibrosis in a Patient with Sudden Death Who Was on Dialysis



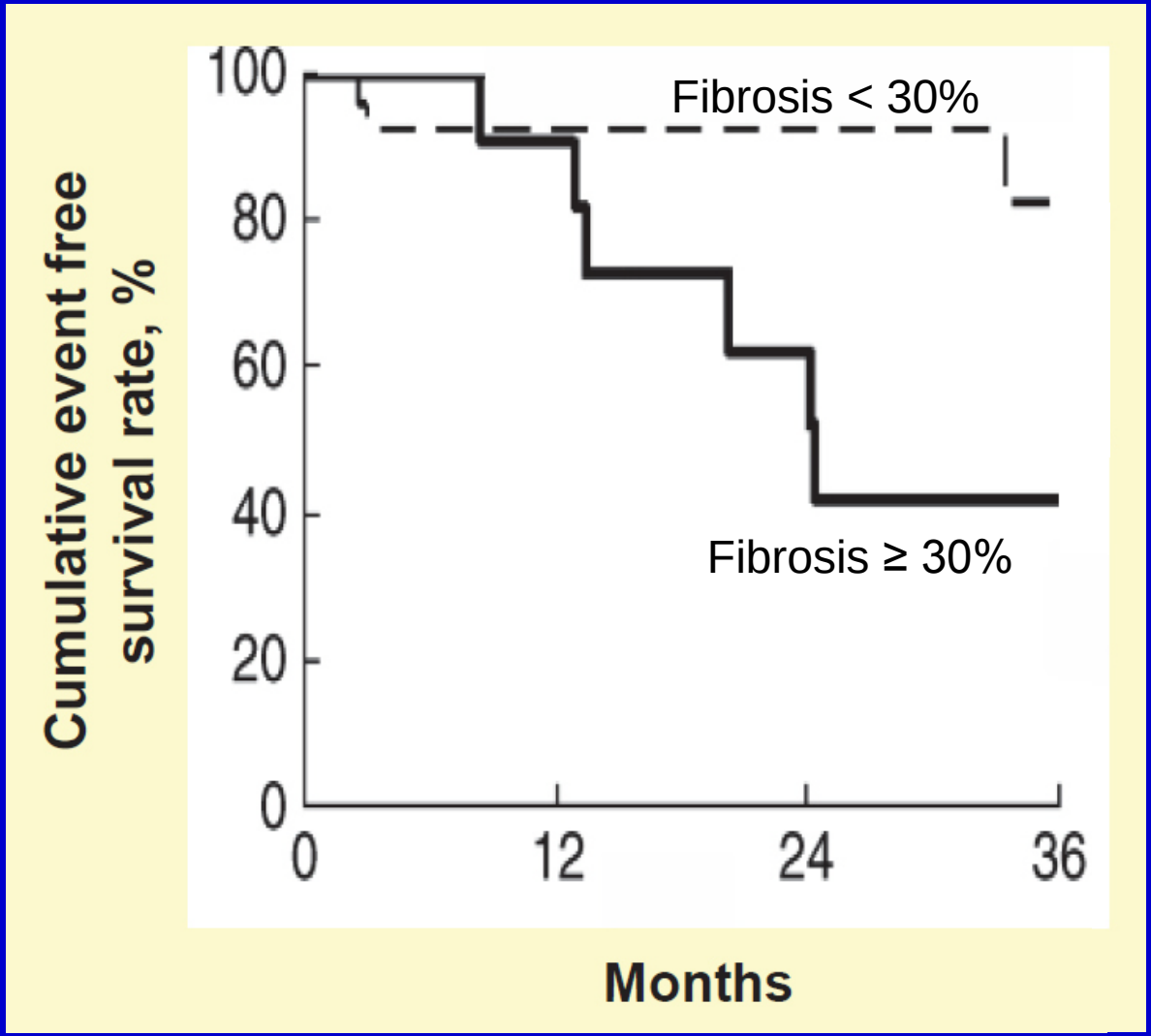
Modified from *Kidney Int* 2005; 67: 333

Detection of Myocardial Fibrosis with MRI



Iles et al.
JACC 2011; 57: 821-8

Cumulative Survival for Cardiac Death in Dialysis Patients Stratified by Extent of Fibrosis



Modified from *Kidney Int.* 2005; 67: 333

Sudden Cardiac Death in Renal Disease Approach to the Problem

- Implementation of multiple strategies will require:
    - MRI to follow fibrosis
    - β-Blockers
    - Dialysis modality
    - Revascularization
    - ICD

CardioRenal Interrelationship: Concluding Remarks

- The heart and the kidney constitute one interactive unit important for cardiovascular function, renal function and neurohumoral homeostasis in health.

- Systemic conditions and diseases often affect both cardiac and renal structure and function.

- Cardiovascular disorders and diseases often affect renal structure and function.

- Renal disorders and diseases often affect cardiovascular structure and function.

CardioRenal Interrelationship: Concluding Remarks

- A normal heart in chronic renal disease is the exception rather than the rule

- Cardiovascular disease is a major cause of death (often sudden) in renal disease, even after kidney transplantation.

- Abnormalities associated with chronic renal disease (eg. volume/pressure overload) may initiate or precipitate cardiac symptoms

- Management of patients with cardiovascular and renal disease requires understanding of the basic mechanisms of renal and cardiovascular physiology/pathophysiology, their interrelationship and the pharmacokinetics/pharmacodynamics of cardiovascular drugs.

Indices of Renal Function: Present and Future

- Estimated creatinine clearance (eCcr) (mL/min) = [(140 – age) x weight (kg)]/[serum creatinine (mg/dL x 72]

- Cystatin C

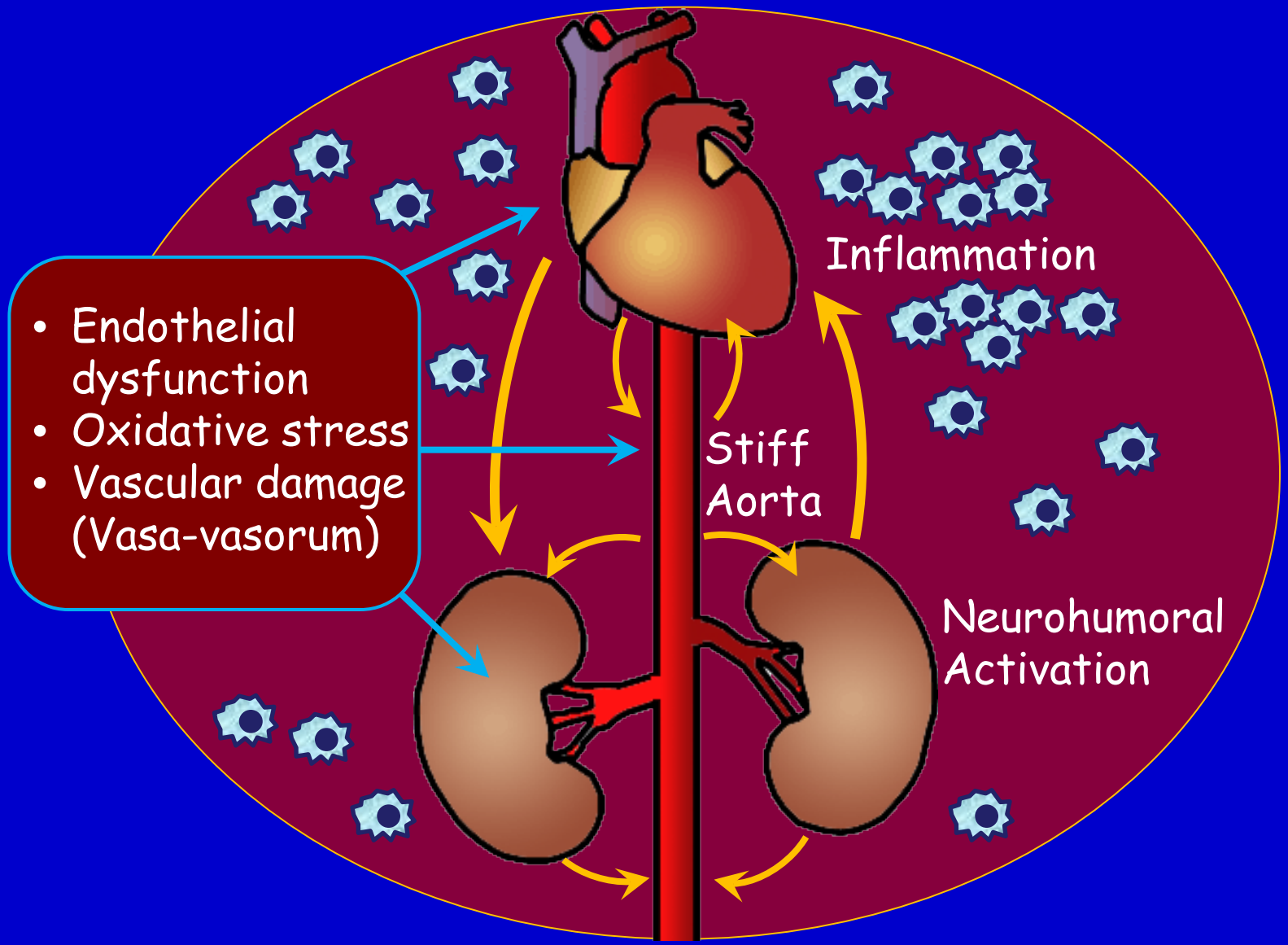
- Neutophil gelatinase associated Lipolacin (NGAL)

- Fibroblast growth factor 23 (FGF-23)

- Other

Nickolas TL et al. *JACC* 2012; 59: 246-55

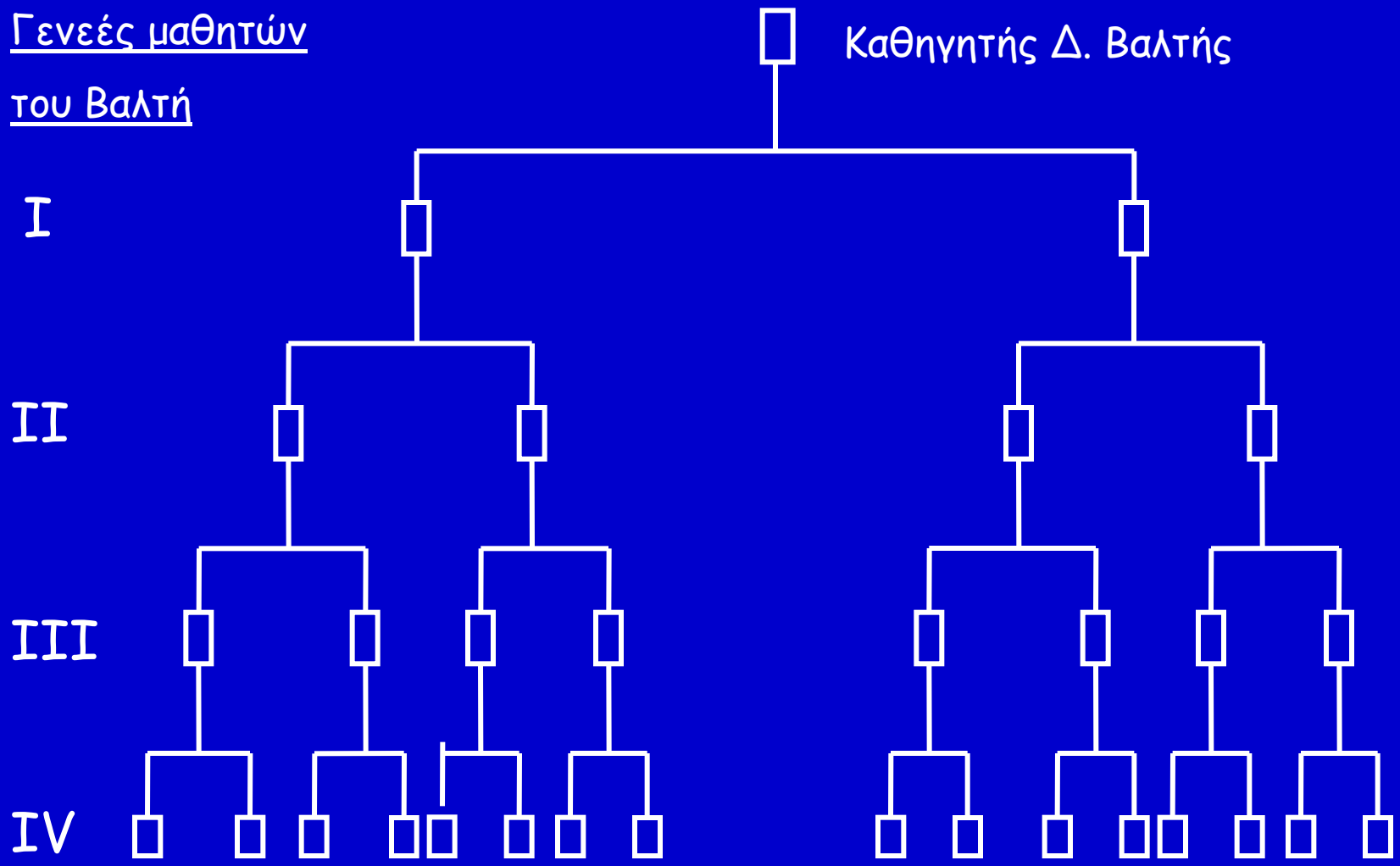
CardioRenal Interrelationship in Renal Disease



Better understanding of CardioRenal interactions, prevention, early detection and aggressive management of Cardiac/Renal disorders will improve outcomes in patients with Renal, Cardiac and CardioRenal diseases.

René Magritte. *La Clairvoyance*, 1936

Το πνεύμα της Κλινικής Βαλτή
"Γενεαλογικό Δένδρο"

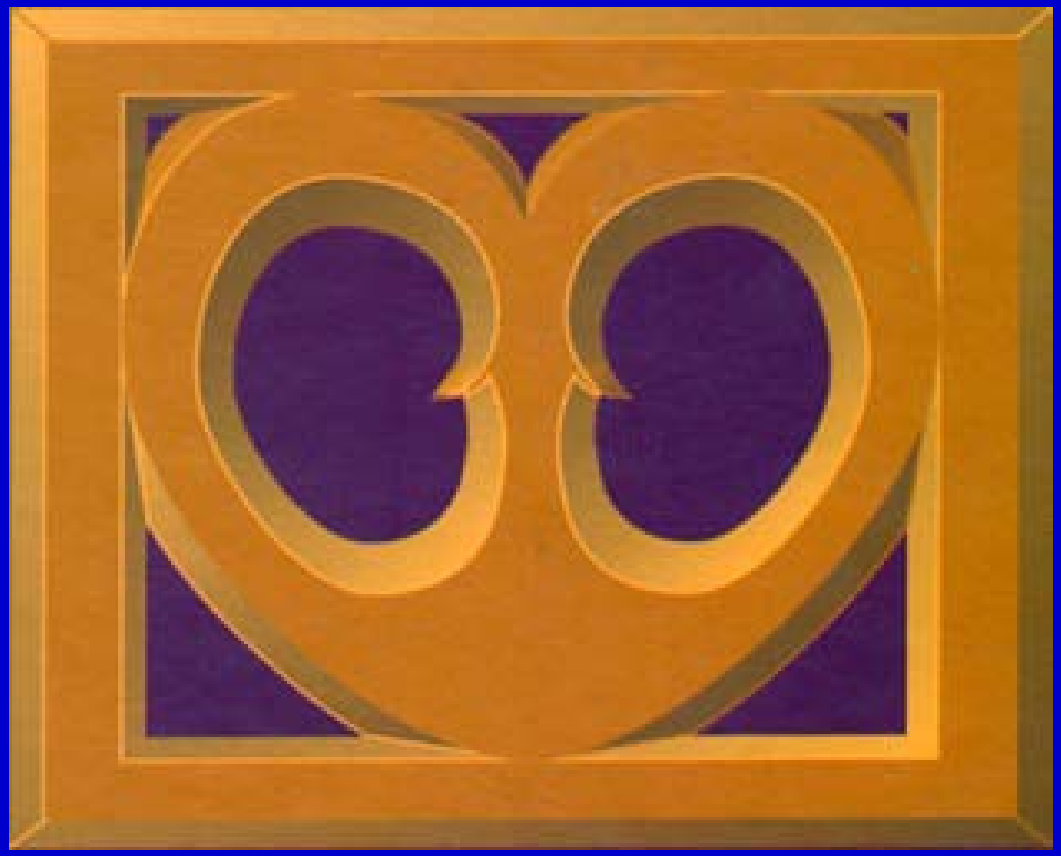


"A teacher affects eternity; he can never tell where his influence stops"

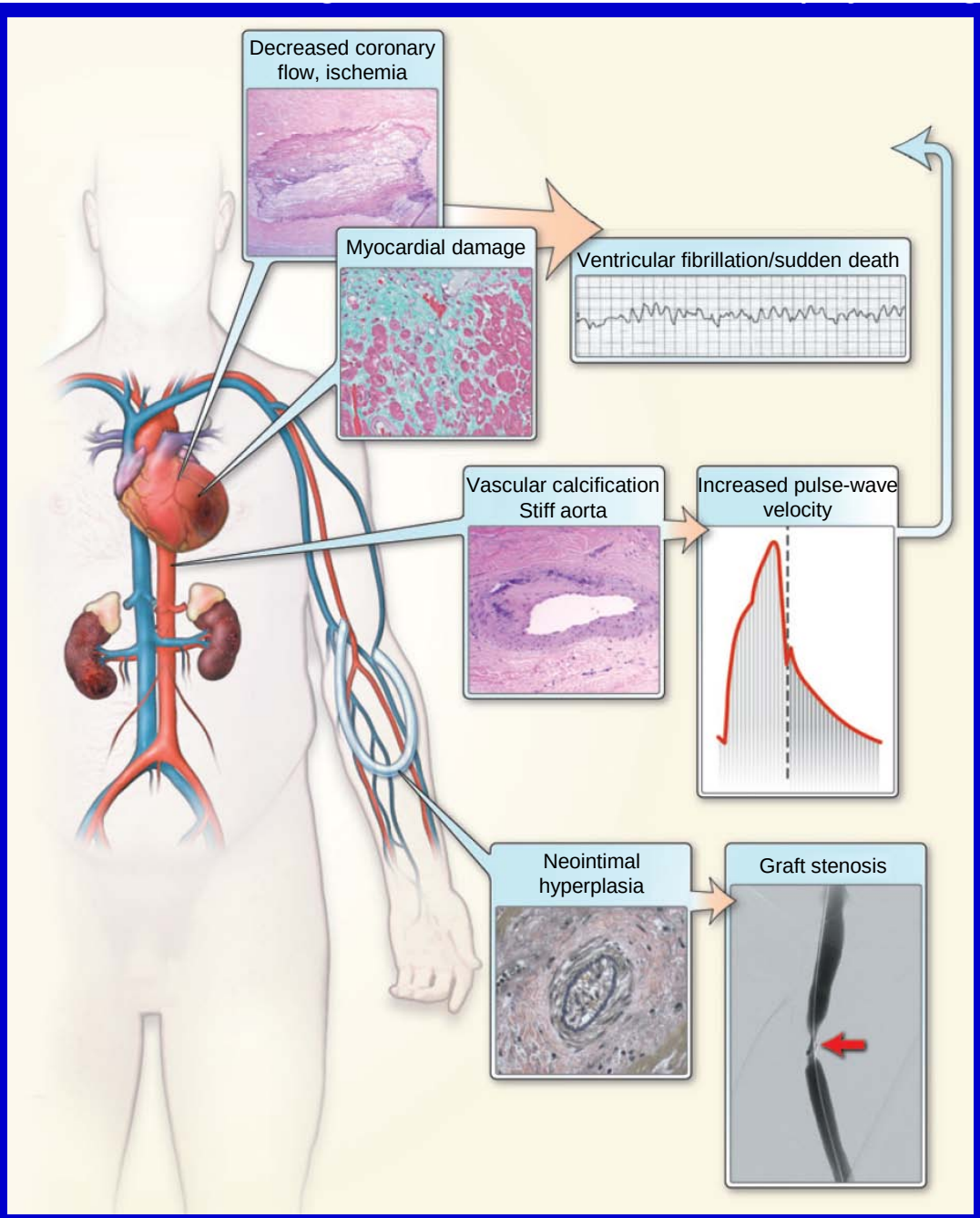
Henry B. Adams

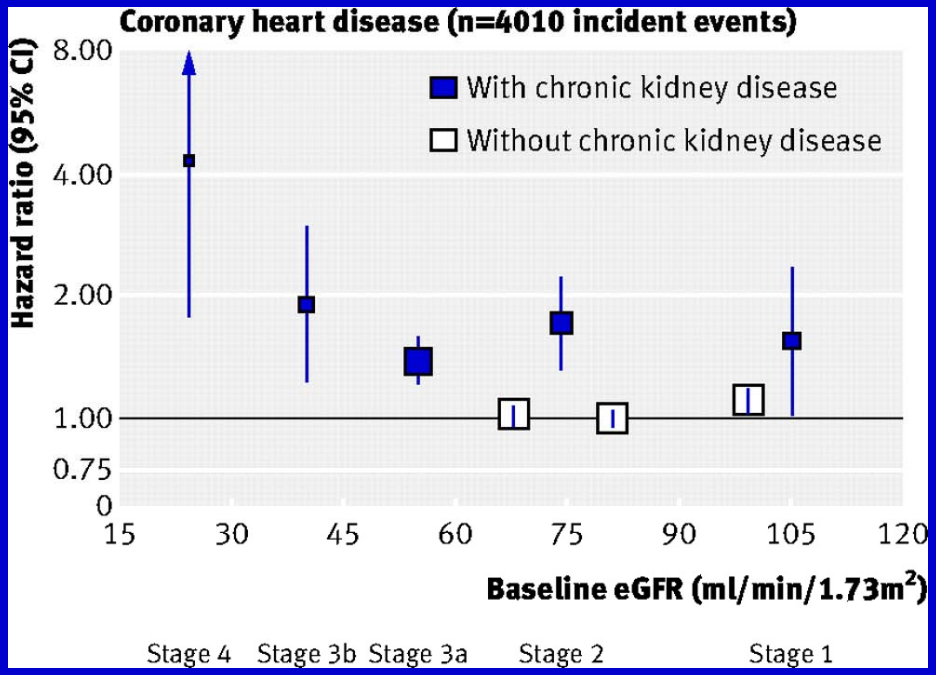
CardioRenal Interrelationship

The Heart and the Kidney Constitute One Interactive Unit



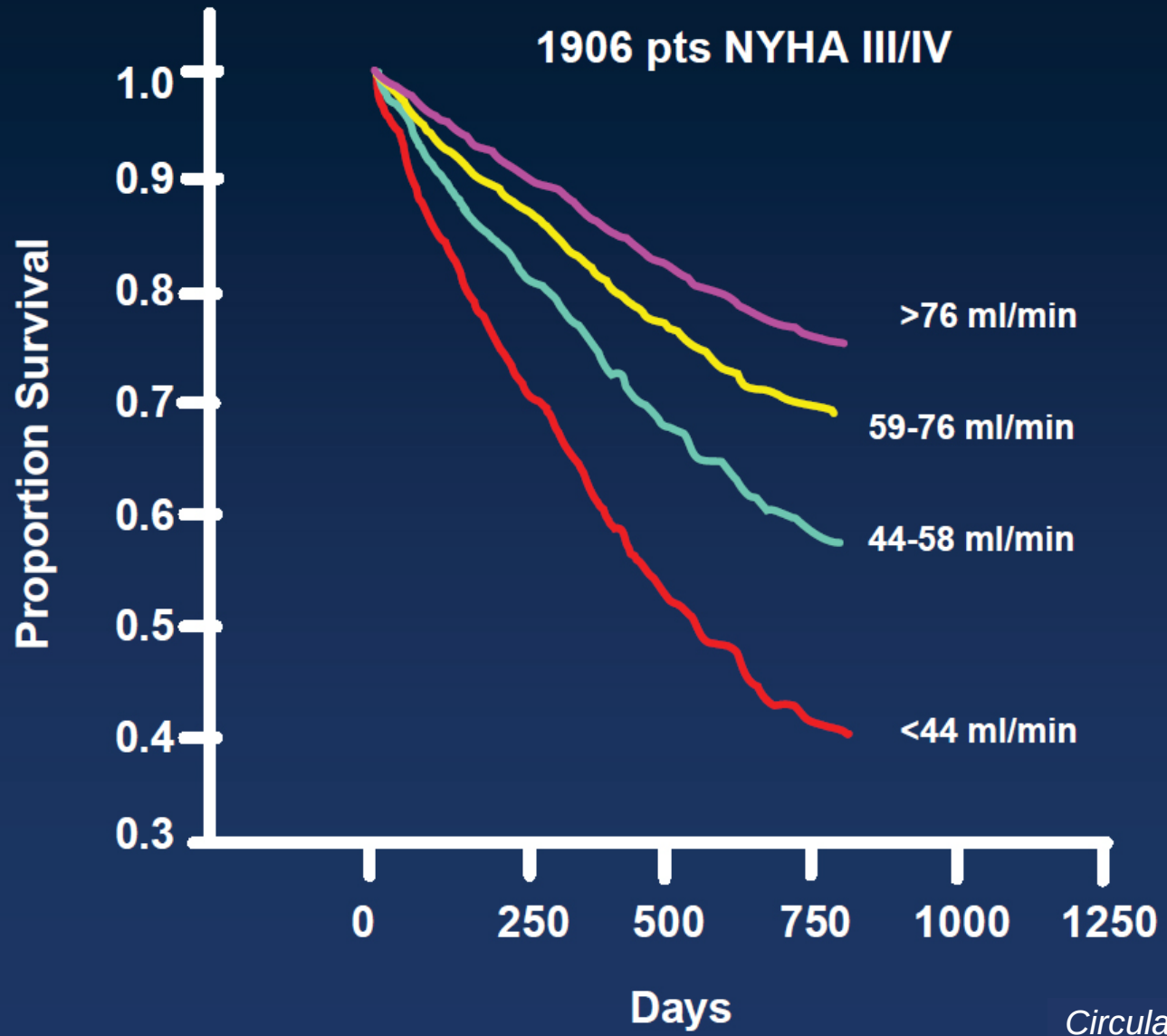
Cardiovascular Risk in End-Stage Renal Disease: Pathophysiologic Mechanisms





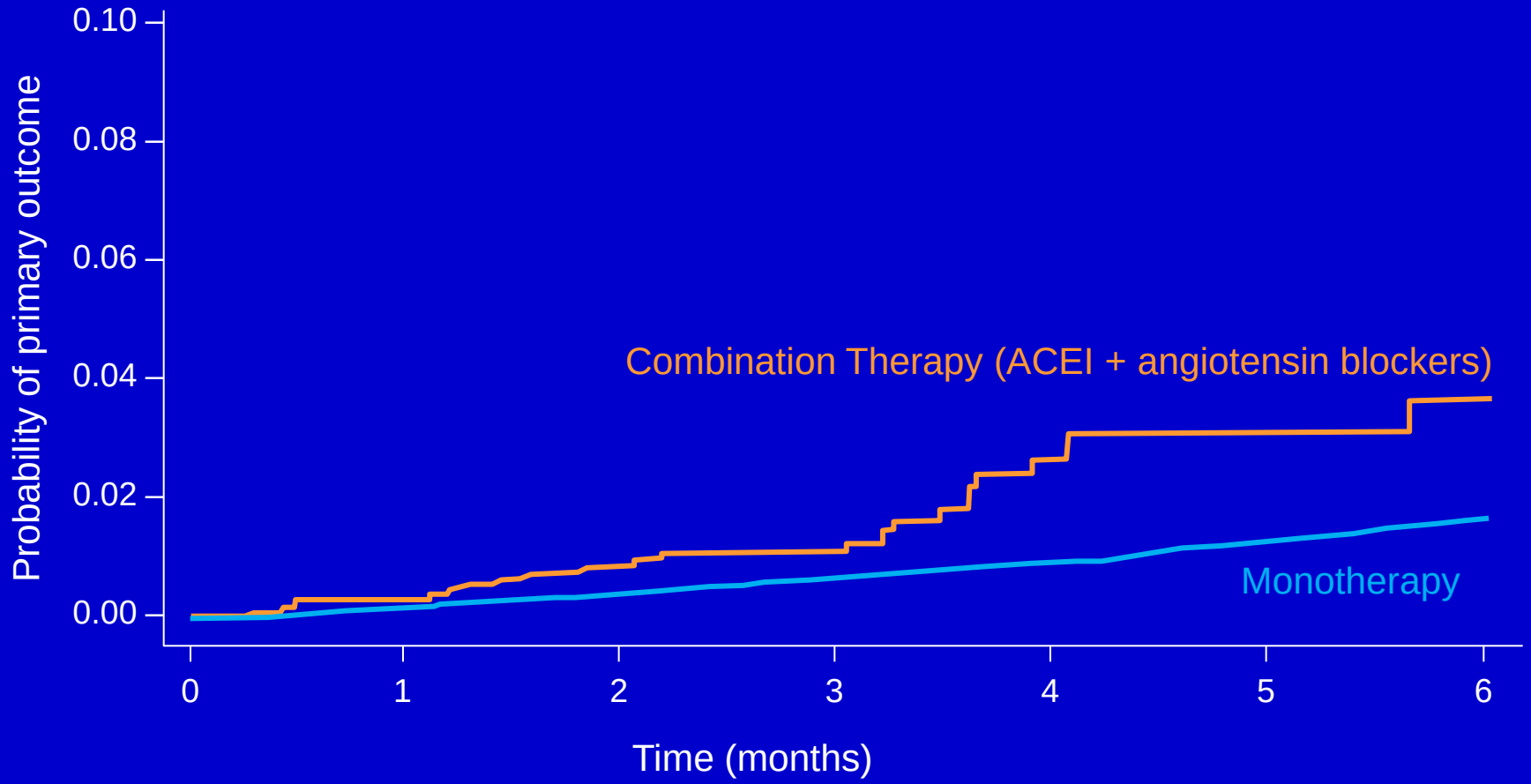
BMJ 2010; 341: 4986

GFR and Survival in PRIME II:
Cox-adjusted Survival analysis



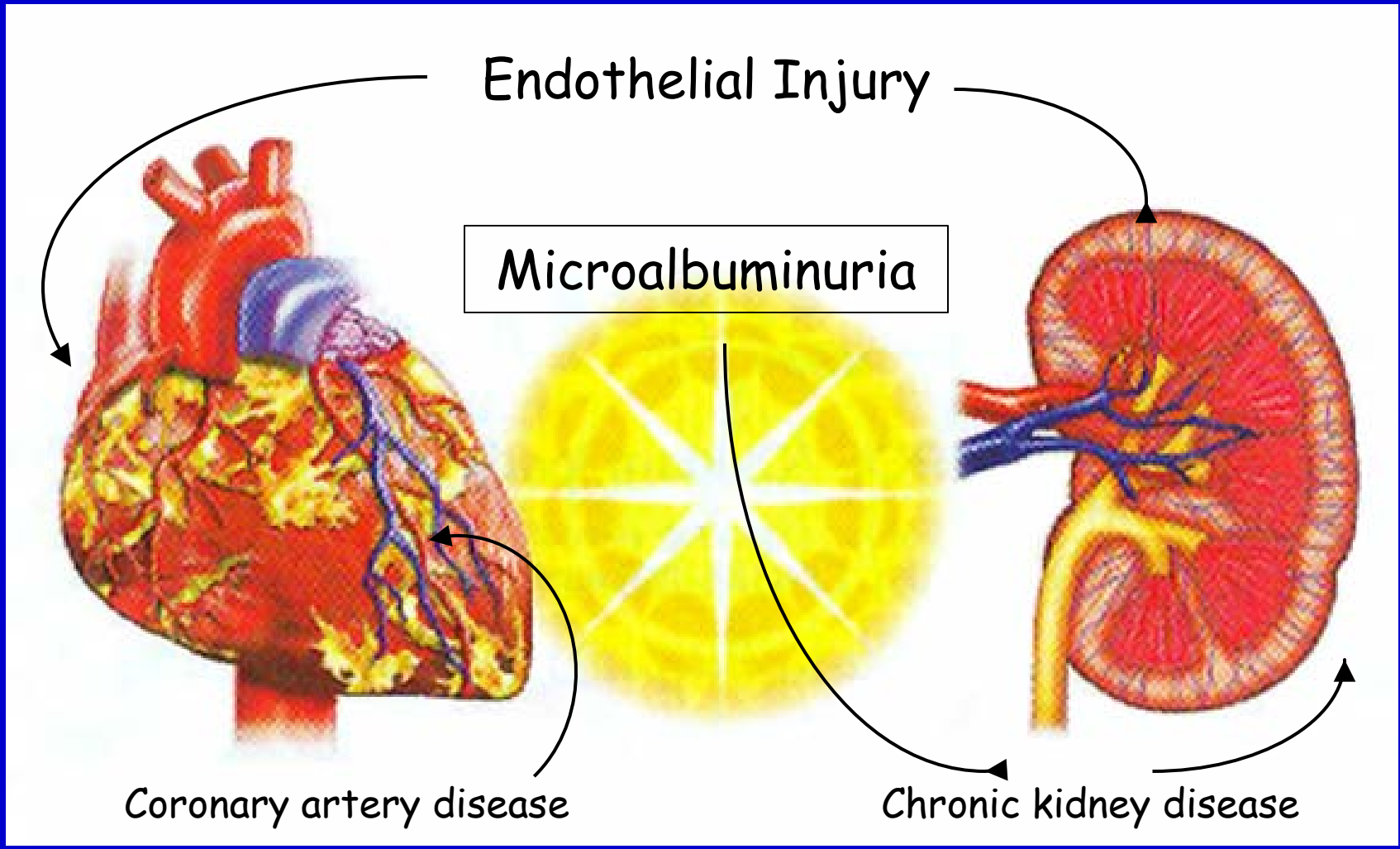
Circulation 2000; 102: 203

Angiotensin Converting Enzyme Inhibitors (ACEI) with Angiotensin Receptor Blockers in Elderly

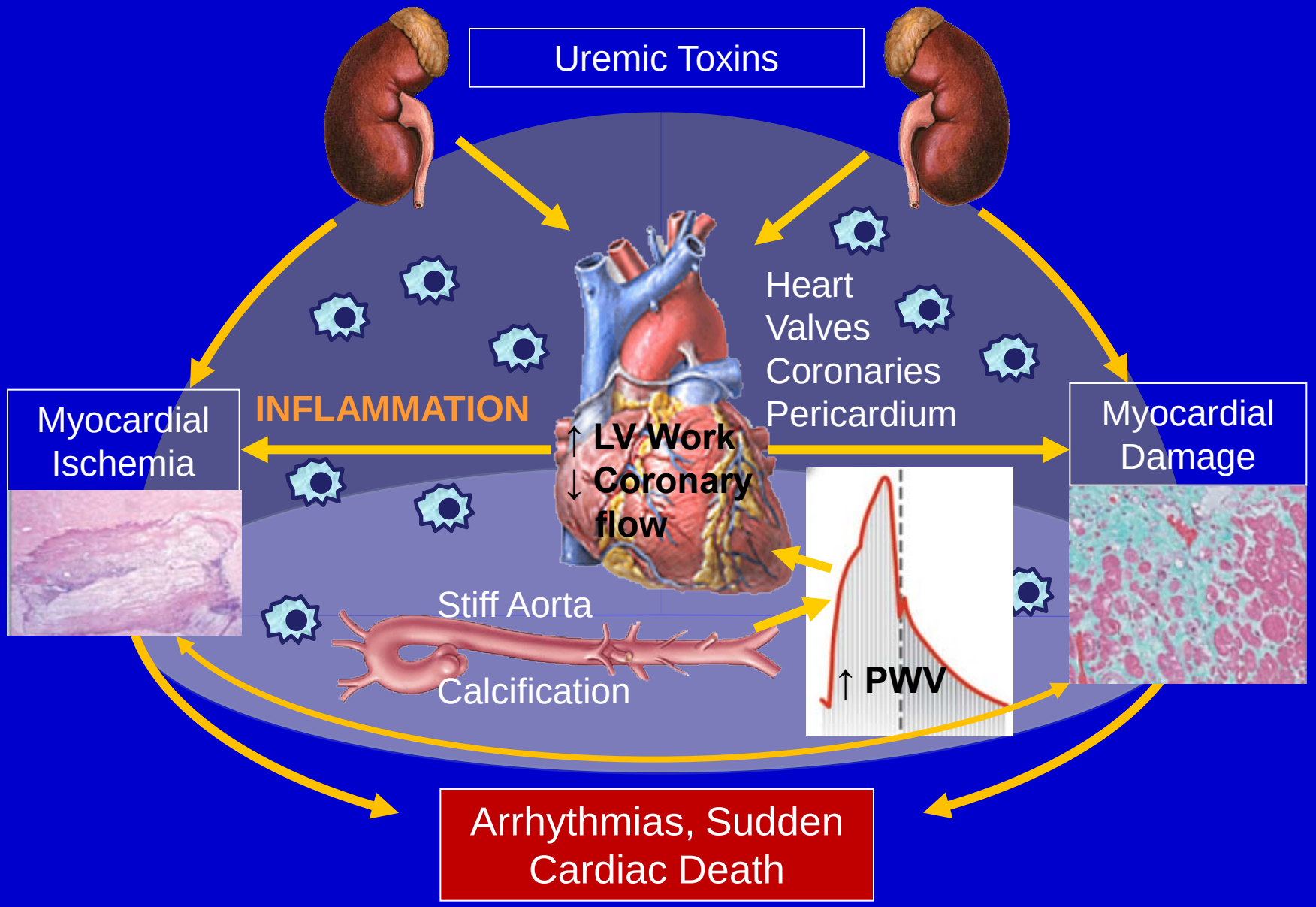


McAlister, et al. *CMAJ* March 2011

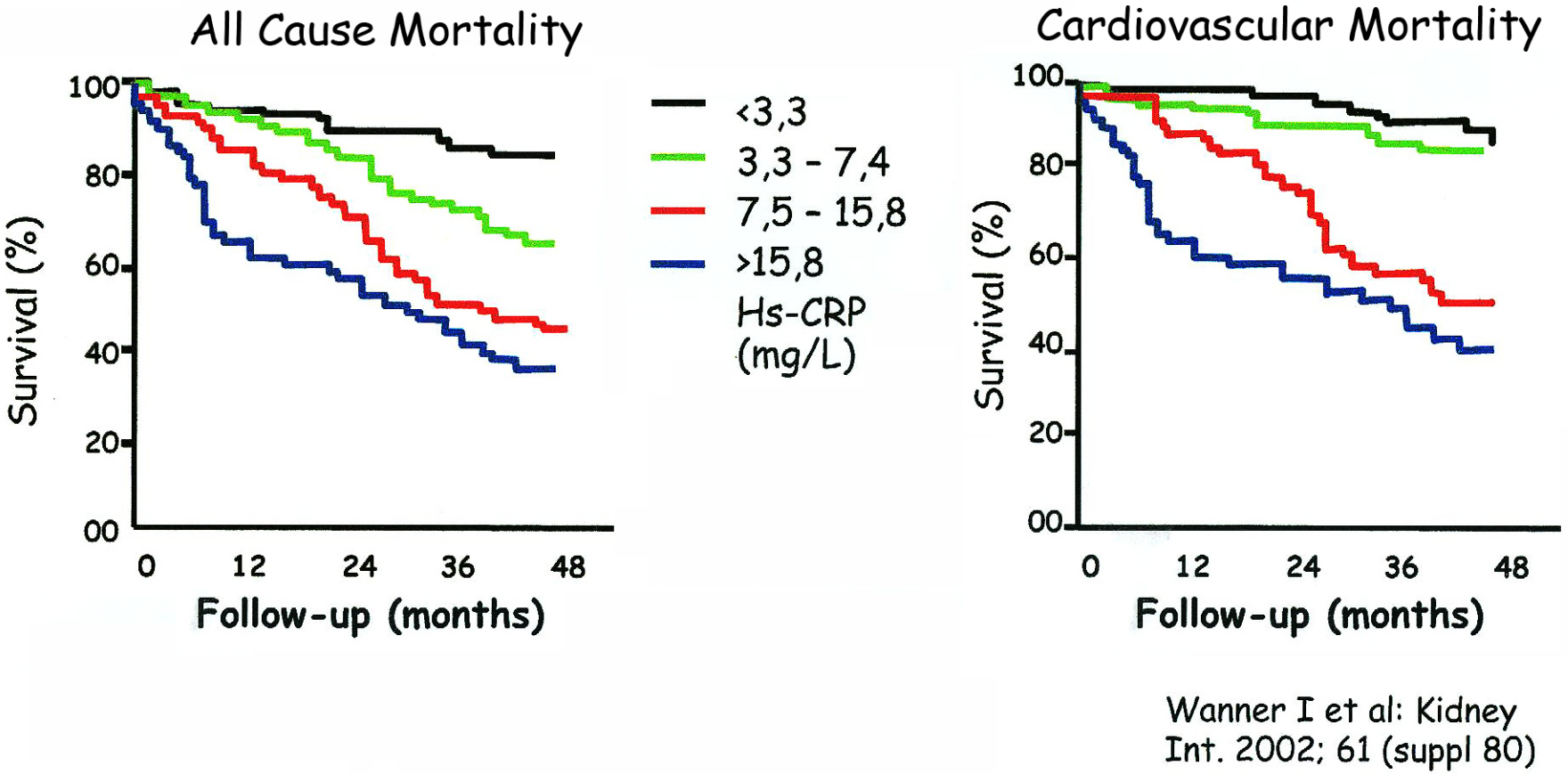
Interrelationship Between Proteinuria and CAD



CardioRenal Interrelationship:
Renal Insufficiency/Failure



Mortality in Hemodialysis Patients in Relation to Inflammation



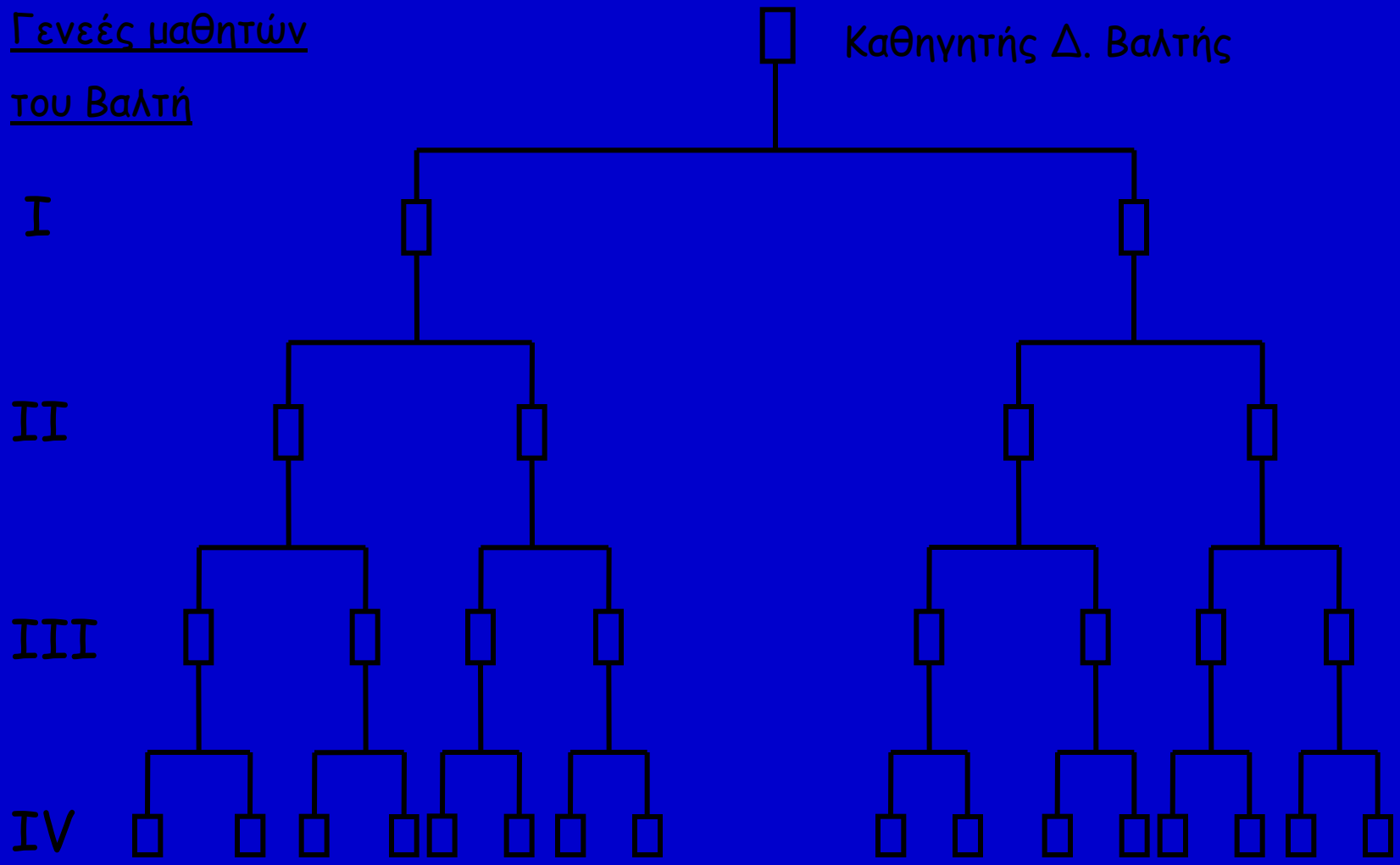
Wanner I et al: Kidney Int. 2002; 61 (suppl 80)

Long-Term (10 year) Risk Stratification After Myocardial Infarction

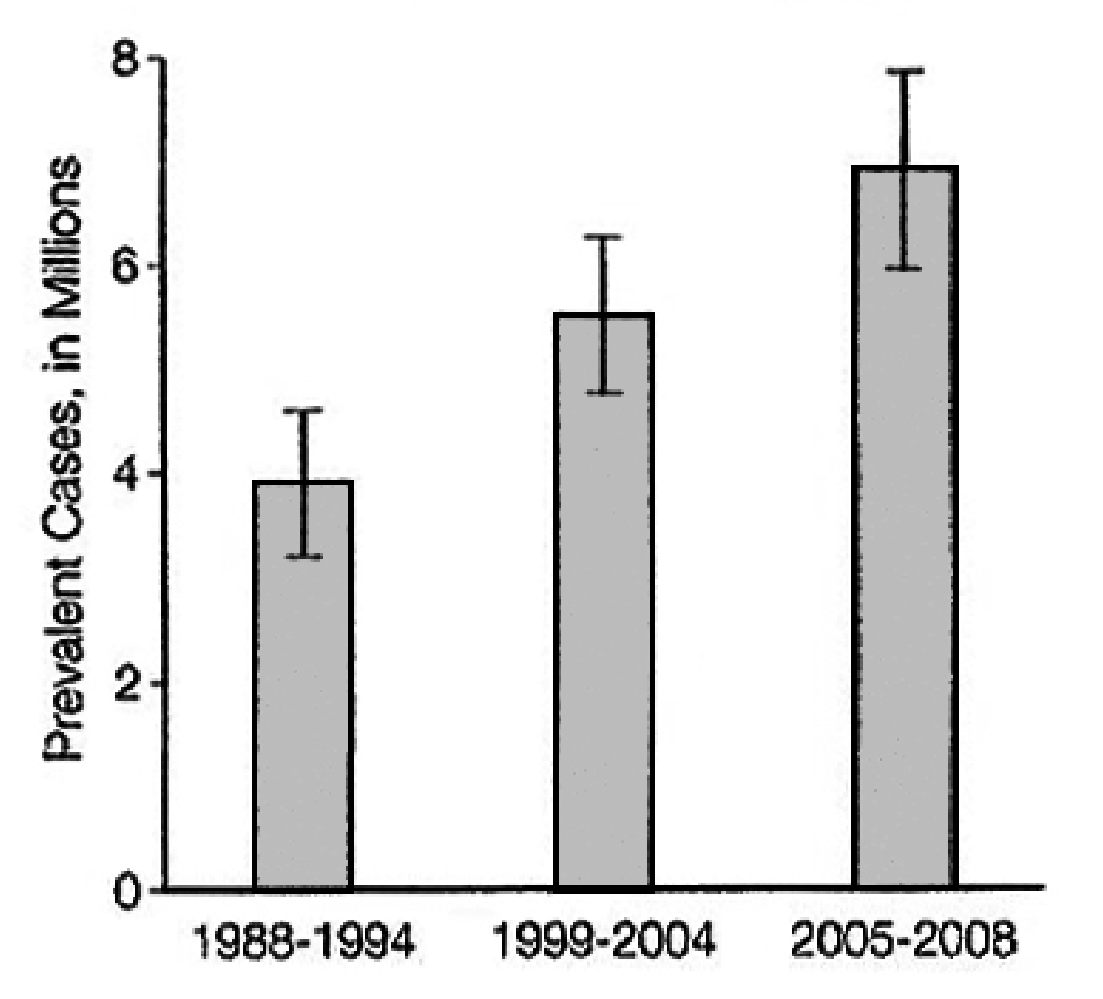
Ten year rates of mortality and heart failure was 5-10 times higher when lower GFR was present together with isolated NT-pro BNP or depressed LVEF.

Palmer SC et al. *Eur Heart J* 2010; 30: 1486

Το πνεύμα της Κλινικής Βαλτή
"Γενεαλογικό Δένδρο"



Diabetic Kidney Disease in the United States



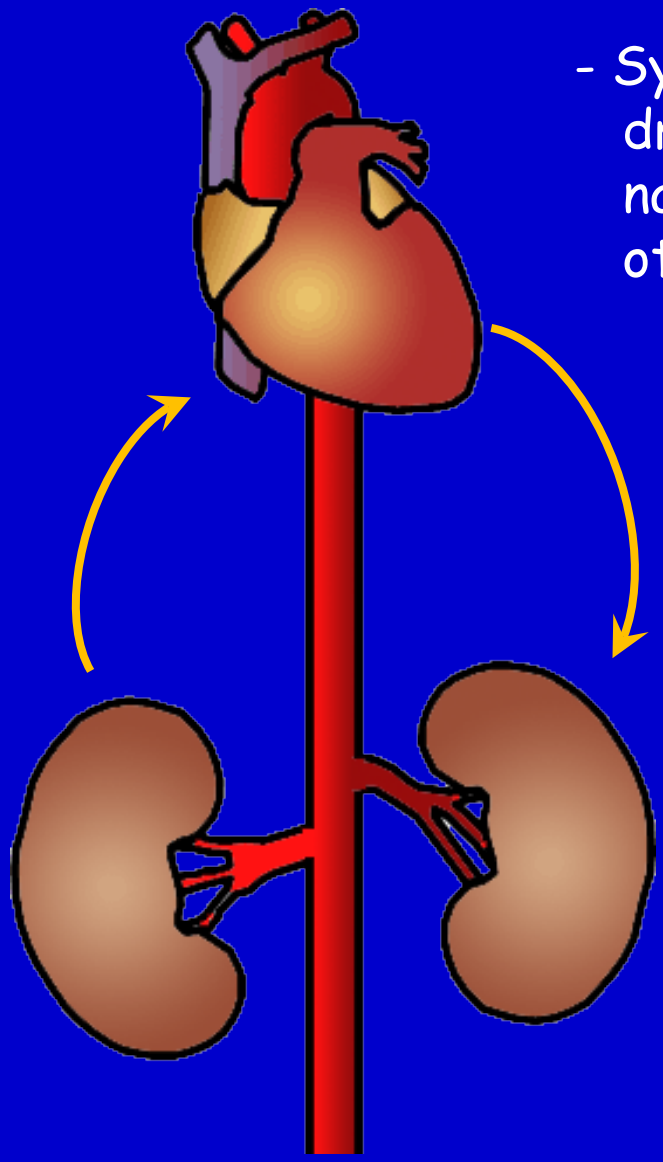
de Boer IH et al. *JAMA* 2011; 305: 2532

CardioRenal Interrelationship: Therapeutic Considerations

- Volume/pressure overload (anemia, A-V fistula, arterial pressure, aortic stiffness) should be optimized.

- Erythropoiesis stimulating agents should be used to treat or prevent symptomatic anemia and to avoid the need for transfusions (not to treat a number)

- Dose of pharmacologic agents should be modified.



- Symptoms may mimic drug side effects (e.g. nausea, vomiting, other).

Homeostasis is lost

↓ Excretion: H_2O, Na, drugs, other

↓ Erythropoietin

Neurohumoral activation