Καρδιονεφρικό Σύνδρομο στο Σακχαρώδη Διαβήτη

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Νεφρολόγος
Επιμελητής Α΄
Α΄ Παθολογική Κλινική ΠΓΝ ΑΧΕΠΑ

ΚΑΡΔΙΟΝΕΦΡΙΚΟ ΣΥΝΔΡΟΜΟ

- Γενικά δυσλειτουργία καρδιάς και νεφρών
- Οξεία ή Χρόνια Δυσλειτουργία ενός οργάνου μπορεί να επιφέρει Οξεία ή Χρόνια δυσπραγία του άλλου οργάνου
- Απόλυτη συσχέτιση στη λειτουργία των δύο οργάνων

Cardiorenal syndrome classification

CRS Type I (Acute Cardiorenal Syndrome)
Abrupt worsening of cardiac function (e.g. acute cardiogenic shock or acutely decompensated congestive heart failure) leading to acute kidney injury
CRS Type II (Chronic Cardiorenal Syndrome)
Chronic abnormalities in cardiac function (e.g. chronic congestive heart failure) causing progressive and potentially permanent chronic kidney disease
CRS Type III (Acute Renocardiac Syndrome)
Abrupt worsening of renal function (e.g. acute kidney ischaemia or glomerulonephritis) causing acute cardiac disorder (e.g. heart failure, arrhythmia, ischemia)
CRS 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
CRS Type V (Secondary Cardiorenal Syndrome)
Systemic condition (e.g. diabetes mellitus, sepsis) causing both cardiac and renal dysfunction

Cl Ronco & colleagues

Journ of the Amer Coll of Cardiology: Vol 52, No 19, 2008

Ταξινόμηση Καρδιονεφρικού Συνδρόμου

- Τύπου Ι: Οξύ Καρδιονεφρικό Σύνδρομο
- Τύπου ΙΙ: Χρόνιο Καρδιονεφρικό Σύνδρομο
- Τύπου ΙΙΙ: Οξύ Νεφροκαρδιακό Σύνδρομο
- Τύπου IV: Χρόνιο Νεφροκαρδιακό Σύνδρομο
- Τύπου V: Δευτεροπαθές Καρδιονεφρικό Σύνδρομο

Τύπου I
Οξύ Καρδιονεφρικό Σύνδρομο

Αιφνίδια επιδείνωση της καρδιακής λειτουργίας
έχει ως αποτέλεσμα την Οξεία Νεφρική βλάβη

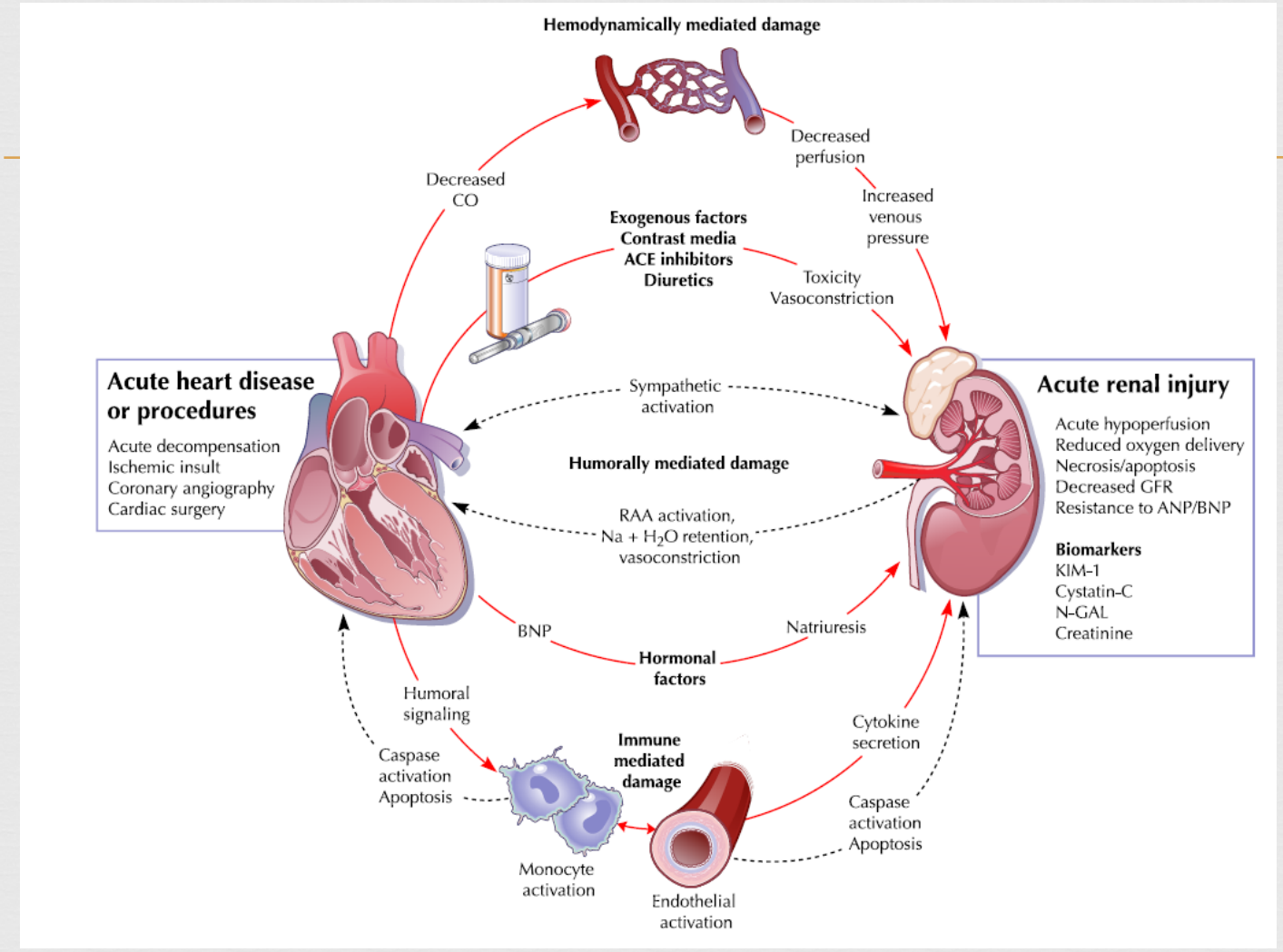
Αίτια:

α) Οξύ πνευμονικό οίδημα με διατήρηση της συστολικής λειτουργίας της αριστερής κοιλίας (LV)

β) Οξεία μη αντιρροπούμενη καρδιακή ανεπάρκεια

γ) Καρδιογενής καταπληξία (καρδιογενές shock)

δ) Δεξιά καρδιακή ανεπάρκεια

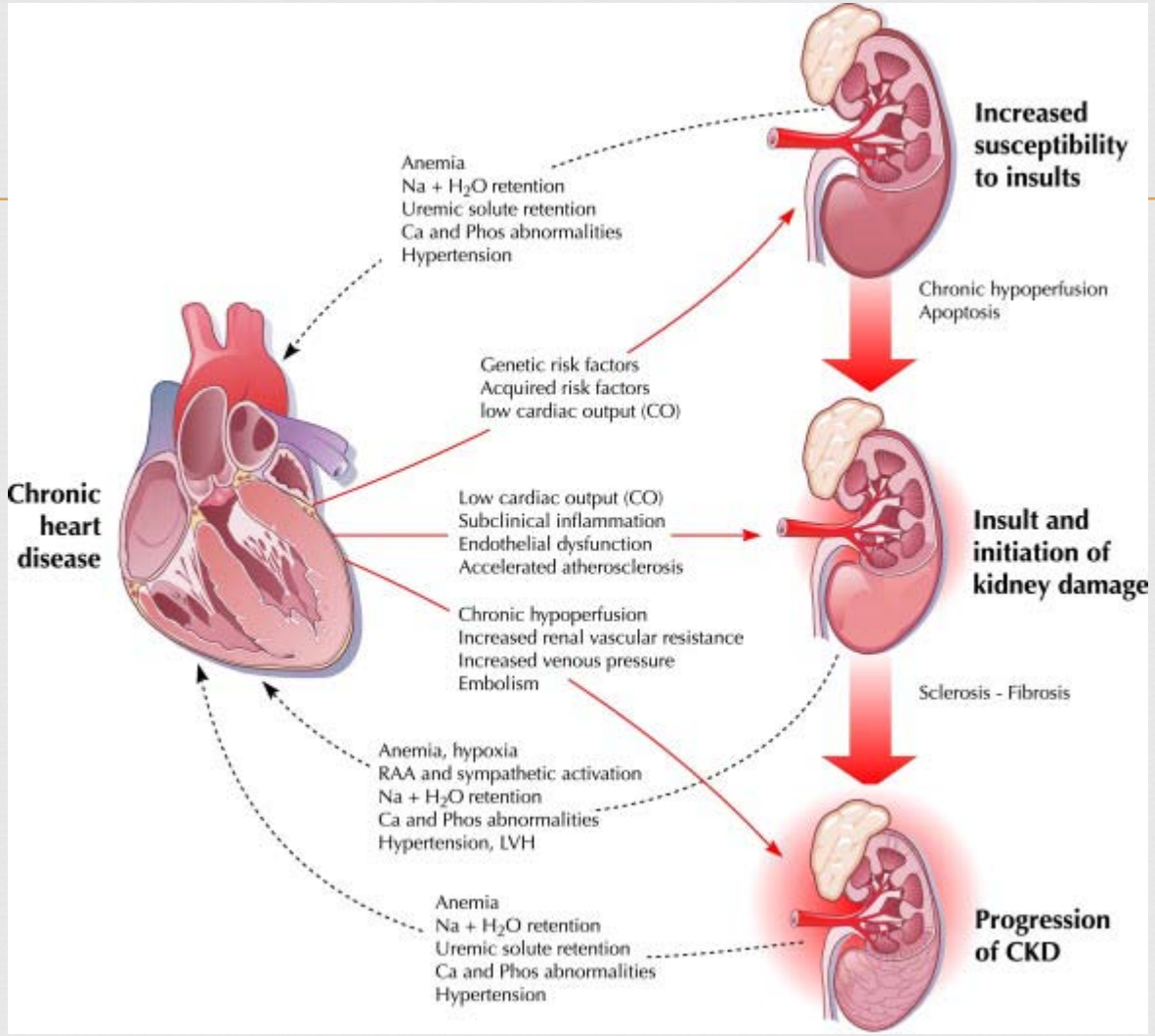

Hemodynamically mediated damage
Decreased perfusion
Increased venous pressure
Toxicity Vasoconstriction
Exogenous factors
Contrast media
ACE inhibitors
Diuretics
Decreased CO
Acute heart disease or procedures
Acute decompensation
Ischemic insult
Coronary angiography
Cardiac surgery
Sympathetic activation
Humorally mediated damage
RAA activation, Na + H_2O retention, vasoconstriction
Acute renal injury
Acute hypoperfusion
Reduced oxygen delivery
Necrosis/apoptosis
Decreased GFR
Resistance to ANP/BNP
Biomarkers
KIM-1
Cystatin-C
N-GAL
Creatinine
BNP
Natriuresis
Hormonal factors
Humoral signaling
Caspase activation Apoptosis
Immune mediated damage
Cytokine secretion
Caspase activation Apoptosis
Monocyte activation
Endothelial activation

Τύπου ΙΙ
Χρόνιο Καρδιονεφρικό Σύνδρομο

Προϋπάρχουσα χρόνια καρδιακή δυσλειτουργία ευθύνεται για προοδευτική επιδείνωση ή/και μόνιμη νεφρική βλάβη

Αιτία:

Χρόνια συμφορητική καρδιακή ανεπάρκεια

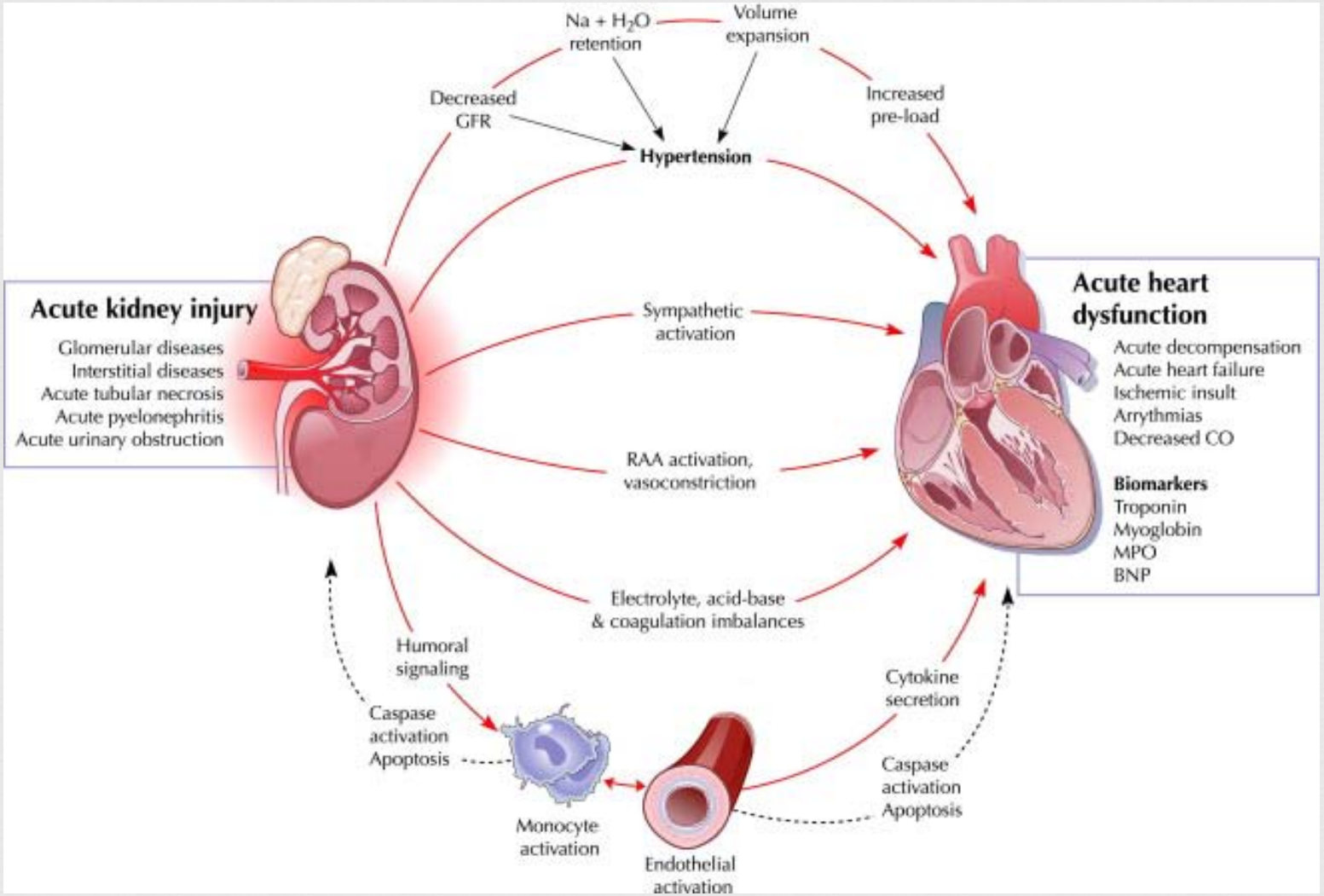

Increased susceptibility to insults
Anemia
Na + H2O retention
Uremic solute retention
Ca and Phos abnormalities
Hypertension
Chronic hypoperfusion
Apoptosis
Genetic risk factors
Acquired risk factors
low cardiac output (CO)
Chronic heart disease
Low cardiac output (CO)
Subclinical inflammation
Endothelial dysfunction
Accelerated atherosclerosis
Insult and initiation of kidney damage
Chronic hypoperfusion
Increased renal vascular resistance
Increased venous pressure
Embolism
Sclerosis - Fibrosis
Anemia, hypoxia
RAA and sympathetic activation
Na + H2O retention
Ca and Phos abnormalities
Hypertension, LVH
Anemia
Na + H2O retention
Uremic solute retention
Ca and Phos abnormalities
Hypertension
Progression of CKD

Τύπου ΙΙΙ
Οξύ Νεφροκαρδιακό Σύνδρομο

Αιτία:

Αιφνίδια επιδείνωση της νεφρικής λειτουργίας ευθύνεται για επιβάρυνση και δυσλειτουργία της καρδιάς

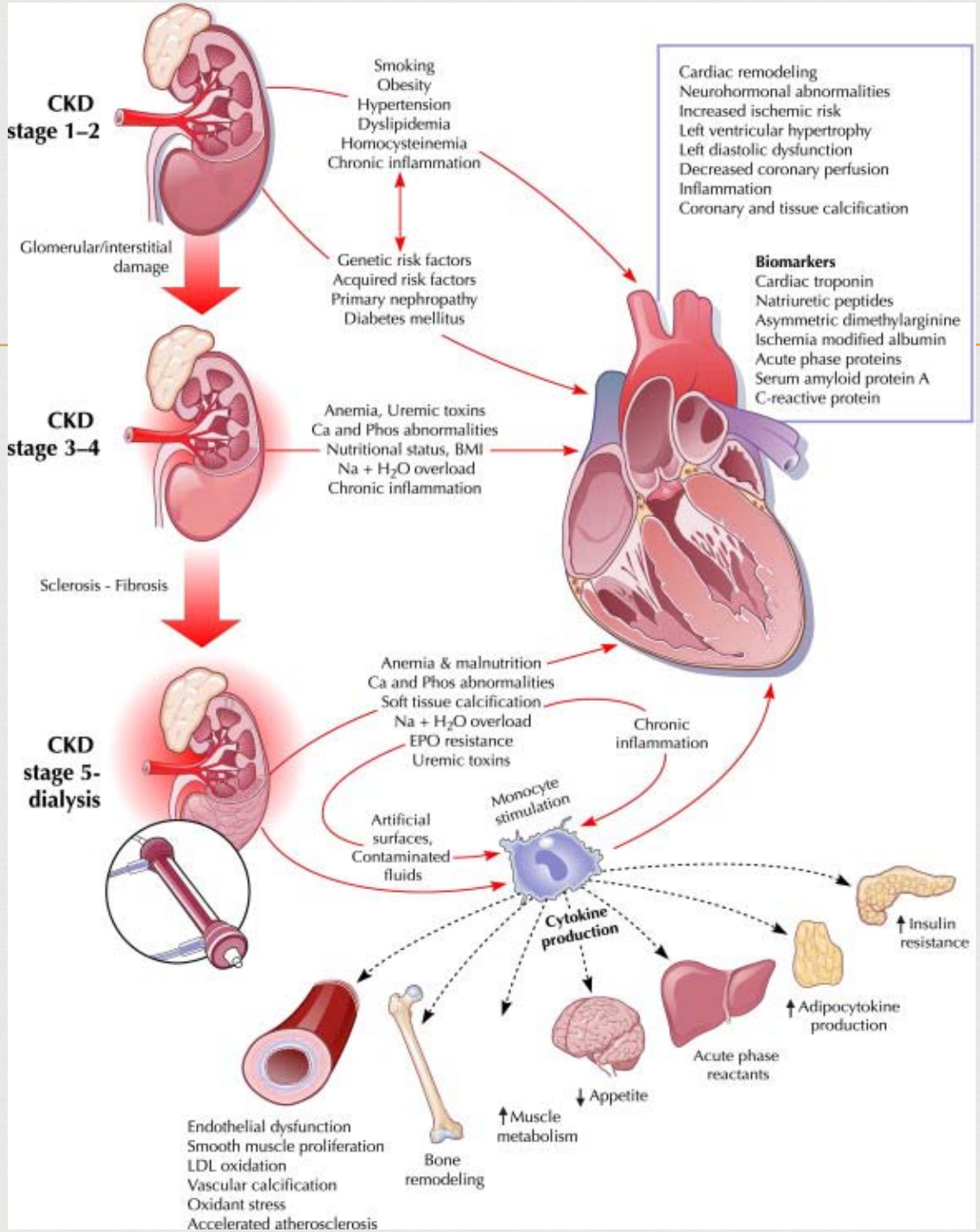
- Διαταραχή του ισοζυγίου ύδατος, λόγω ελάττωσης της απεκκριτικής ικανότητας των νεφρών
- Ηλεκτρολυτικές διαταραχές
- Διαταραχές της οξεοβασικής ισορροπίας
- Αγγειοσύσπαση


Na + H_2O retention
Volume expansion
Decreased GFR
Increased pre-load
Hypertension
Acute kidney injury
Glomerular diseases
Interstitial diseases
Acute tubular necrosis
Acute pyelonephritis
Acute urinary obstruction
Sympathetic activation
RAA activation, vasoconstriction
Electrolyte, acid-base & coagulation imbalances
Acute heart dysfunction
Acute decompensation
Acute heart failure
Ischemic insult
Arrythmias
Decreased CO
Biomarkers
Troponin
Myoglobin
MPO
BNP
Humoral signaling
Caspase activation Apoptosis
Monocyte activation
Endothelial activation
Cytokine secretion
Caspase activation Apoptosis

Τύπου IV
Χρόνιο Νεφροκαρδιακό Σύνδρομο

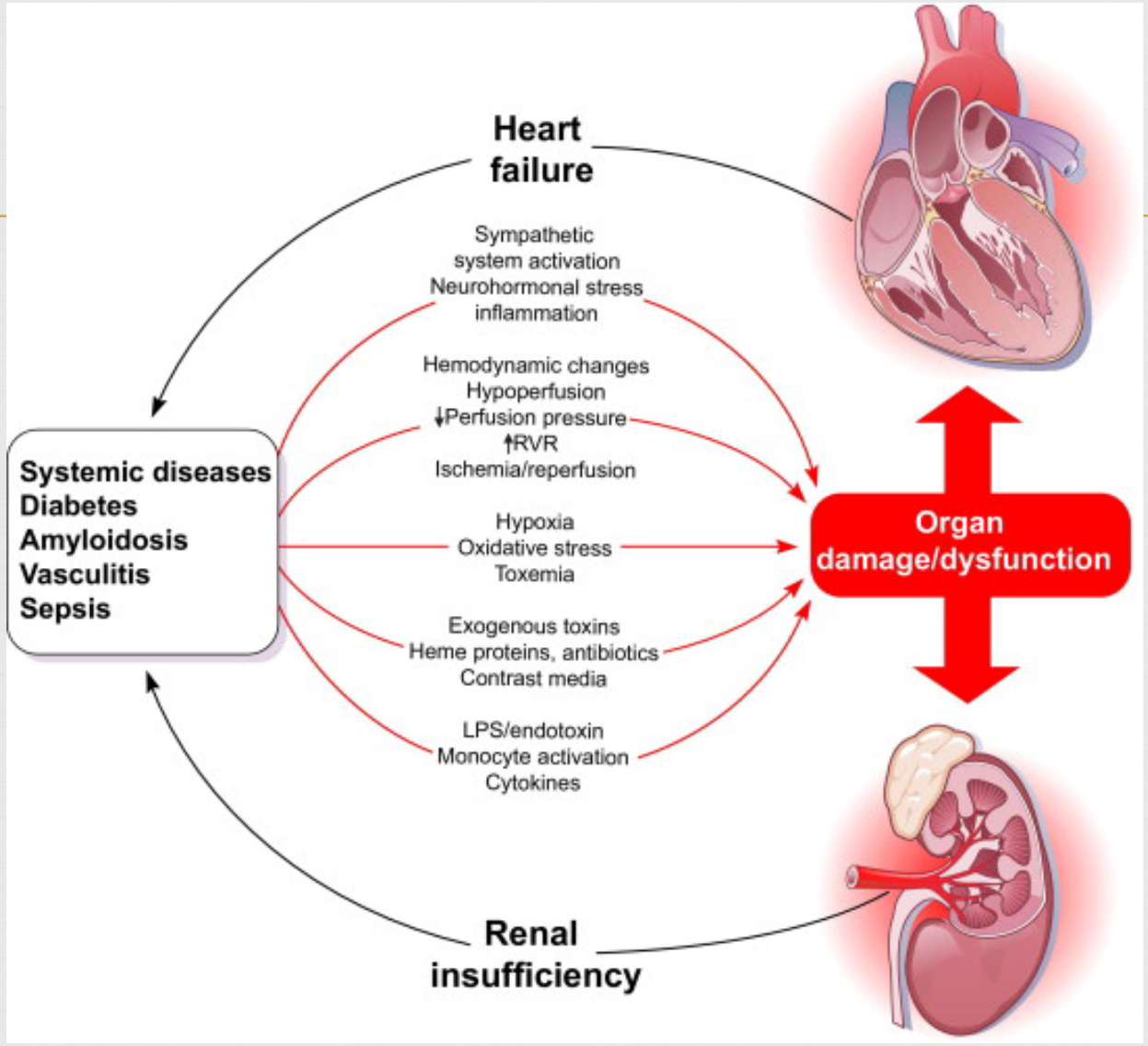
Χρόνια Νεφρική βλάβη με προοδευτική επιδείνωση νεφρικής λειτουργίας επιφέρει την καρδιακή δυσλειτουργία

- υπερτροφία αριστερής κοιλίας
- διαστολική δυσλειτουργία
- στεφανιαία νόσος


CKD stage 1–2
Smoking
Obesity
Hypertension
Dyslipidemia
Homocysteinemia
Chronic inflammation
Glomerular/interstitial damage
Genetic risk factors
Acquired risk factors
Primary nephropathy
Diabetes mellitus
Cardiac remodeling
Neurohormonal abnormalities
Increased ischemic risk
Left ventricular hypertrophy
Left diastolic dysfunction
Decreased coronary perfusion
Inflammation
Coronary and tissue calcification
Biomarkers
Cardiac troponin
Natriuretic peptides
Asymmetric dimethylarginine
Ischemia modified albumin
Acute phase proteins
Serum amyloid protein A
C-reactive protein
CKD stage 3–4
Anemia, Uremic toxins
Ca and Phos abnormalities
Nutritional status, BMI
Na + H2O overload
Chronic inflammation
Sclerosis - Fibrosis
CKD stage 5-dialysis
Anemia & malnutrition
Ca and Phos abnormalities
Soft tissue calcification
Na + H2O overload
EPO resistance
Uremic toxins
Chronic inflammation
Monocyte stimulation
Artificial surfaces, Contaminated fluids
Cytokine production
Insulin resistance
Adipocytokine production
Acute phase reactants
Appetite
Muscle metabolism
Bone remodeling
Endothelial dysfunction
Smooth muscle proliferation
LDL oxidation
Vascular calcification
Oxidant stress
Accelerated atherosclerosis

Τύπου V Δευτεροπαθές Καρδιονεφρικό Σύνδρομο

- Συνδυασμός καρδιακής και νεφρικής δυσλειτουργίας
- Αποτέλεσμα οξείας ή χρόνιας νόσου
  - σήψη
  - σακχαρώδης διαβήτης
  - αμυλοείδωση
  - αγγειίτιδες
  - συστηματικός ερυθηματώδης λύκος
  - υπέρταση


Heart failure
Sympathetic system activation
Neurohormonal stress
inflammation
Hemodynamic changes
Hypoperfusion
↓Perfusion pressure
↑RVR
Ischemia/reperfusion
Hypoxia
Oxidative stress
Toxemia
Exogenous toxins
Heme proteins, antibiotics
Contrast media
LPS/endotoxin
Monocyte activation
Cytokines
Systemic diseases
Diabetes
Amyloidosis
Vasculitis
Sepsis
Organ damage/dysfunction
Renal insufficiency

Himanshu Sekhar Mahapatra,[1] Robert Lalmalsawma,[1]
Narendra Pal Singh,[1] Mahender Kumar,[1] Suresh Chandra Tiwari[2]

Classification of Cardiorenal Syndrome Proposed By Ronco and Colleagues[16]*

Type	Name	Mechanism	Clinical Conditions	Markers	References
Type I	Acute cardiorenal syndrome	Abrupt worsening of kidney function leading to acute kidney injury	Acute cardiogenic shock and acutely decompensated congestive heart failure	ET-1, Troponin, CPK-MB	17
Type II	Chronic cardiorenal syndrome	Chronic abnormalities in kidney function causing progressive and potentially permanent kidney disease	Chronic congestive heart failure	ET-1, BNP	17, 18
Type III	Acute renocardiac syndrome	Abrupt worsening of kidney function causing acute cardiac disorder	Acute kidney ischemia and glomerulonephritis	TNF-α, IL-1, IL-6, IL-8	3, 19
Type IV	Chronic renocardiac syndrome	Chronic kidney disease contributing to decline in cardiac function	Chronic glomerular and Interstitial disease	PTH, CPP product, Cystatin C	16, 20, 21,22
Type V	Secondary cardiorenal syndrome	Systemic condition causing both cardiac and kidney dysfunction	Diabetes mellitus, Sepsis	…	…

*ET-1 indicates endothelin-1; CPK-MB, creatine phosphokinase-MB; BNP, B-type natriuretic peptide; TNF, tumor-necrosis factor; IL, interleukin; PTH, parathyroid hormone; and CPP, calcium-phosphate product. Ellipses indicate not applicable.

Protein Biomarkers for the Early Detection of Acute Kidney Injury

- Cystatin C Proximal tubule injury
- KIM-1 Ischemia and nephrotoxins
- NGAL (lipocalin) Ischemia and nephrotoxins
- NHE3 Ischemia, pre-renal, post-renal AKI
- Cytokines (IL-6, IL-8, IL-18) Toxic, delayed graft function
- Actin-actin depolymerizing F Ischemia and delayed graft function
- -GST Proximal T injury, acute rejection
- -GST Distal tubule injury, acute rejection
- L-FABP Ischemia and nephrotoxins
- Netrin-1 Ischemia and nephrotoxins, sepsis
- Keratin-derived chemokine Ischemia and delayed graft function

Heart Failure and Renal Dysfunction

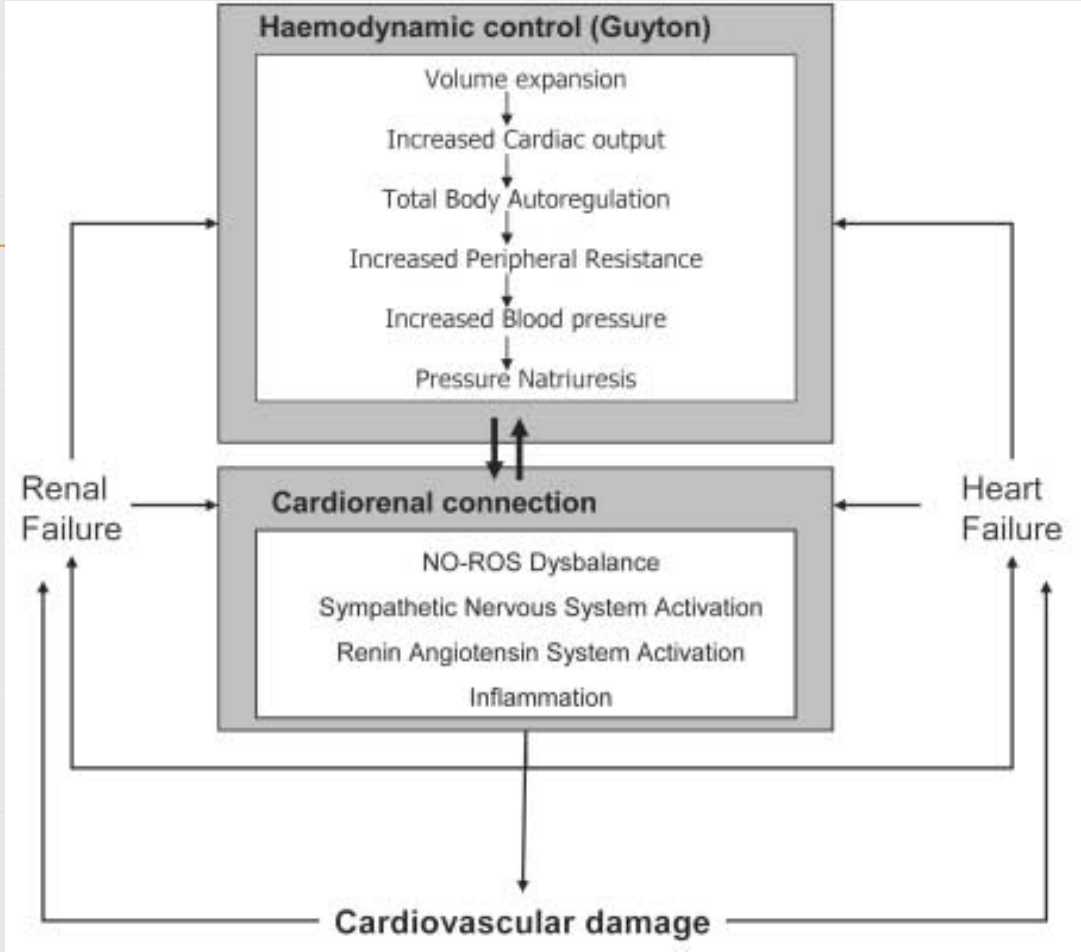
The Delicate Balance

Balance

- Close follow-up
- Personalized therapy
- Individualized fluid equilibrium
- Plasma and urine electrolytes

Imbalance

- Excessive salt and/or water ingestion
- ↑ RAAS, SNS, AVP
- Borderline ventricular function
- Borderline renal function
- Anemia



Pathophysiological basis of the severe cardiorenal syndrome. The model of Guyton explains heart–kidney interaction with respect to extracellular fluid volume, cardiac output, and mean arterial pressure. When one of these organs fails, a vicious circle develops in which the renin–angiotensin system, the NO–ROS balance, the sympathetic nervous system, and inflammation interact and synergize, here called the cardiorenal connection.

Προδιαθεσικοί Παράγοντες

PP Liu. Cardiorenal syndrome in heart failure: A cardiologist's perspective. Can J Cardiol 2008;24(Suppl B):25B-29B.

Risk factors for renal dysfunction in heart failure
Hypertension
Diabetes
Severe vascular disease
Elderly age
Past history of:
Heart failure
Renal dysfunction
Heart failure and renal dysfunction

Factors associated with HF in adult diabetic patients

- Age
- Duration of diabetes
- Insulin use
- Ischemic heart disease
- Peripheral arterial disease
- Elevated serum creatinine
- Poor glycemic control
- Microalbuminuria

Κλινική εκδήλωση

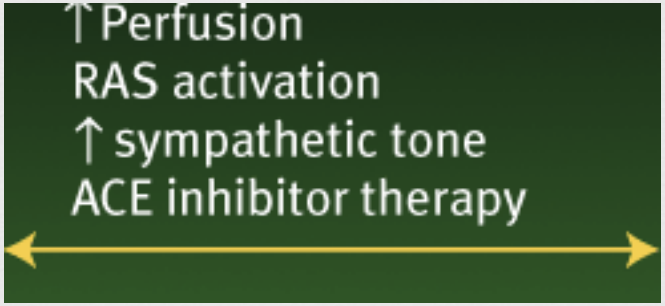
- Αιμοδυναμικές διαταραχές
- Καρδιοαναπνευστική επιβάρυνση (δύσπνοια, ορθόπνοια, ταχυκαρδία)
- Πνευμονικό οίδημα
- Ολιγοανουρία
- Μικτή οξεοβασική διαταραχή
- Επιδείνωση δεικτών νεφρικής λειτουργίας

Παθοφυσιολογία

- Διαταραχές καρδιακής λειτουργίας
- Διαταραχές όγκου
- Νευροορμονικές διαταραχές
- Αναιμία

Hypothesis

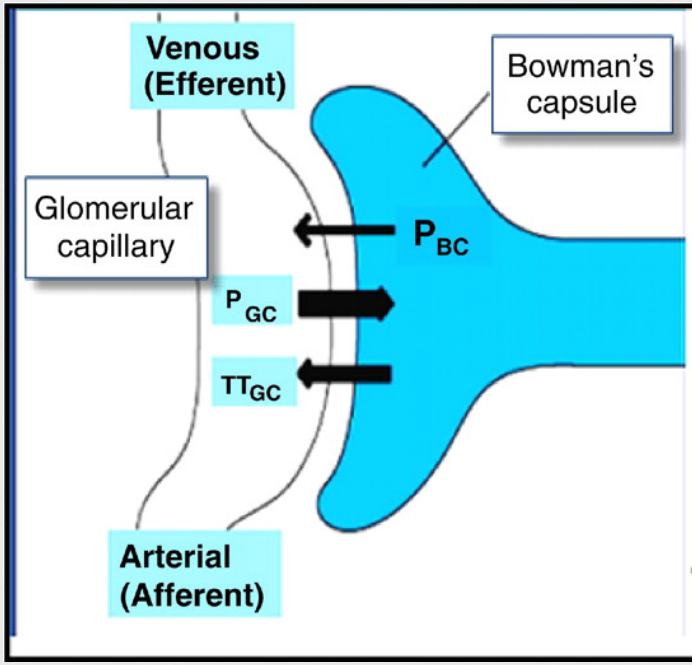
- Renal impairment could be a marker for worsening HF.
- Renal impairment could be on the causal pathway to worsening HF



- Προχωρημένου σταδίου καρδιακή ή νεφρική ανεπάρκεια (μη αντιρροπούμενη) προκαλεί:

- αύξηση αγγειοσυσπαστικών ουσιών (AVP, ET-1, NE, A-II, Αδενοσίνης)
- ανισορροπία μεταξύ αγγειο-συσπαστικών/διασταλτικών ορμονών (νατριουρητικά πεπτίδια, PG, NO, βραδυκινίνη)
- αύξηση προφορτίου
- αύξηση της φλεβικής πίεσης στους νεφρούς
- συμβολή στην πρόκληση νεφρικής βλάβης
- αύξηση του RAAS
- ελάττωση GFR
- αυξημένη κατακράτηση Na+

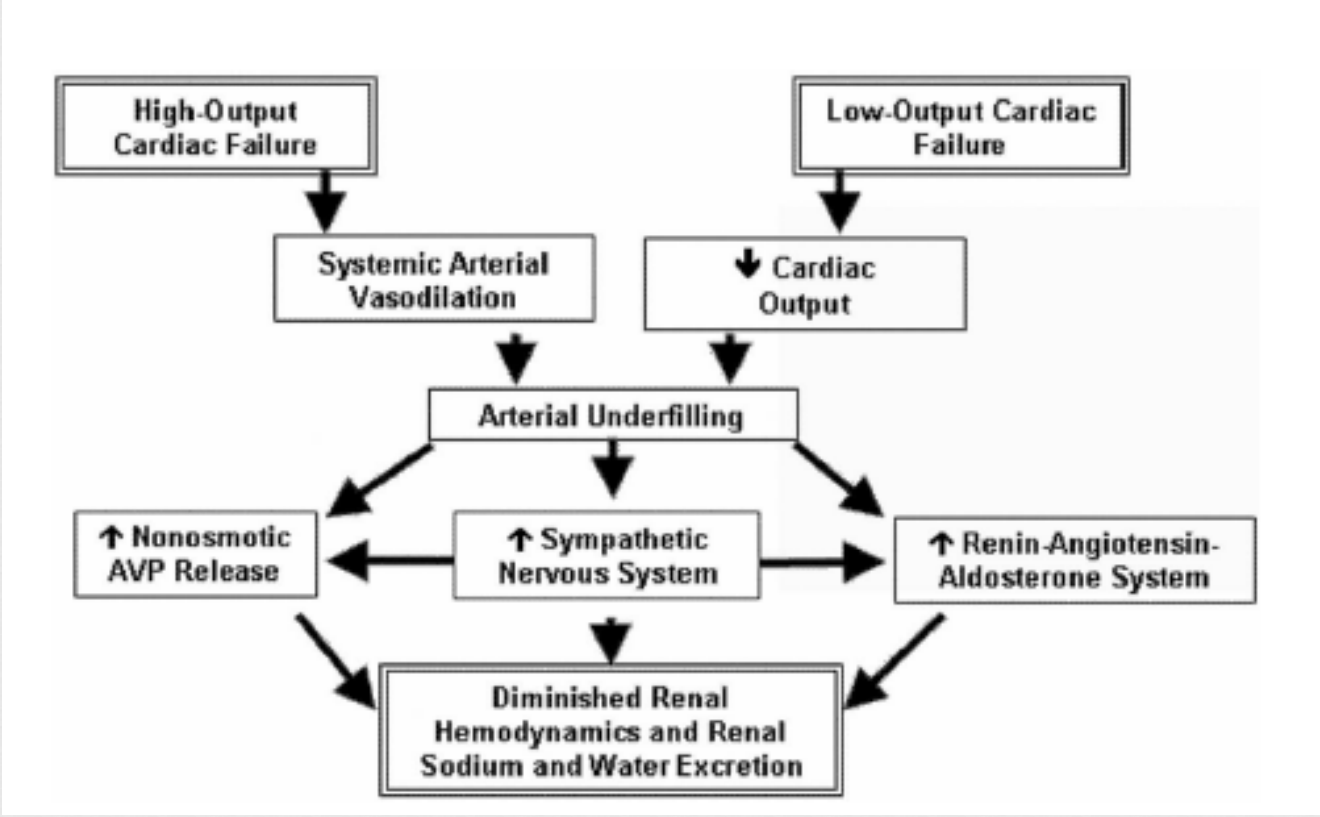
Impact of Venous Congestion on Glomerular Net Filtration Pressure



Forces	Normal: Afferent end of glomerular capillary (mmHg)	Normal: Efferent end of glomerular capillary (mmHg)	↑ RA pressure: Afferent end of glomerular capillary (mmHg)	↑ RA pressure: Efferent end of glomerular capillary (mmHg)
1. Favoring Filtration				
Glomerular-capillary hydrostatic pressure, P_{GC}	**60**	**58**	**55**	**63**
2. Opposing Filtration				
a. Hydrostatic pressure in Bowman's capsule, P_{BC}	**15**	**15**	**15**	**15**
b. Oncotic pressure in glomerular capillaries, π_{GC}	**21**	**33**	**21**	**33**
Net filtration pressure (1-2)	**24**	**10**	**19**	**15**
Filtration pressure:	*14 mmHg*		*4 mmHg*	

JACC Journal of the American College of Cardiology

Παθοφυσιολογία της οξείας μη αντιρροπούμενης καρδιακής ανεπάρκειας



Clin J Am Soc Nephrol 4: 2013–2026, 2009

Επιδείνωση της κ/α

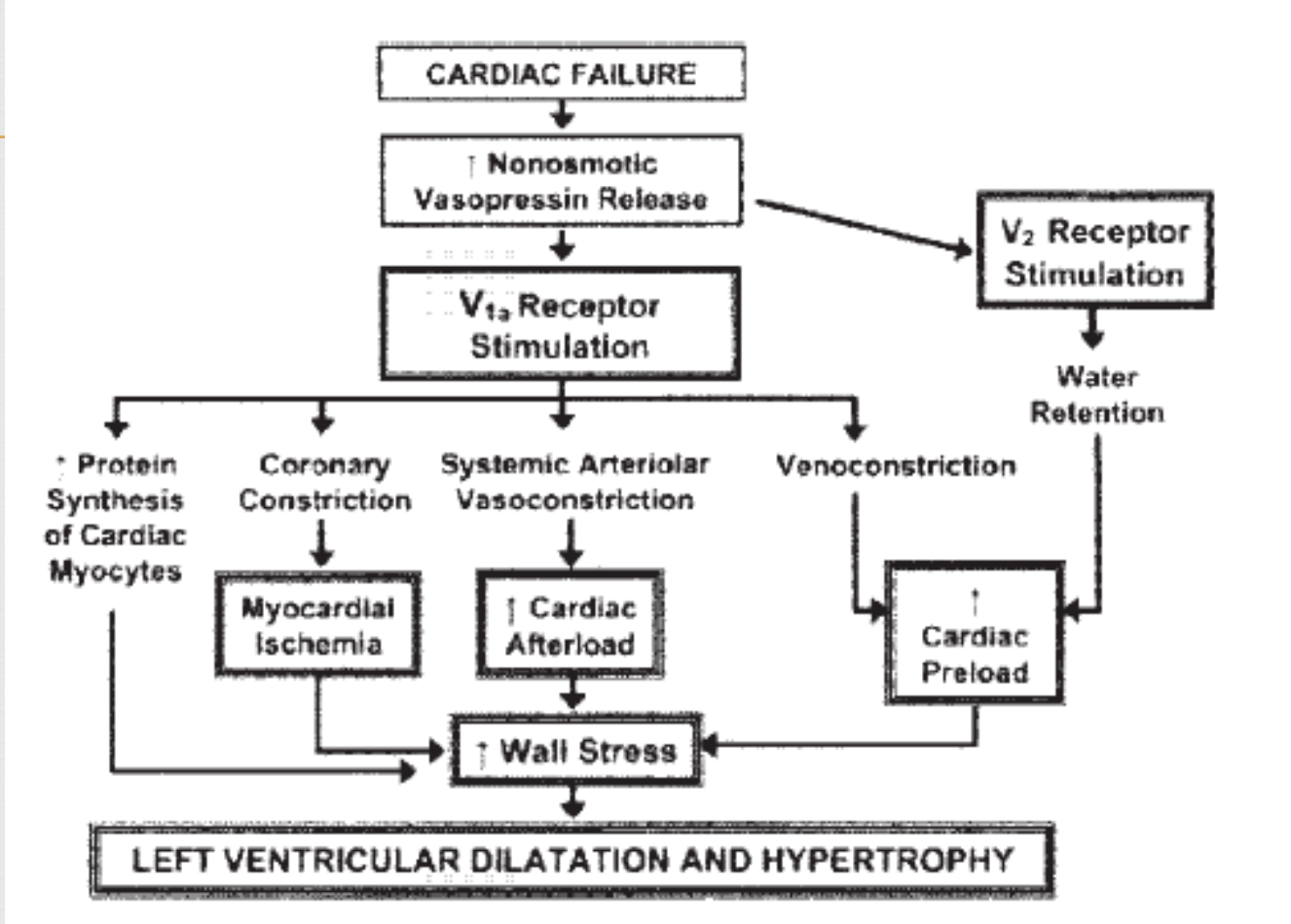
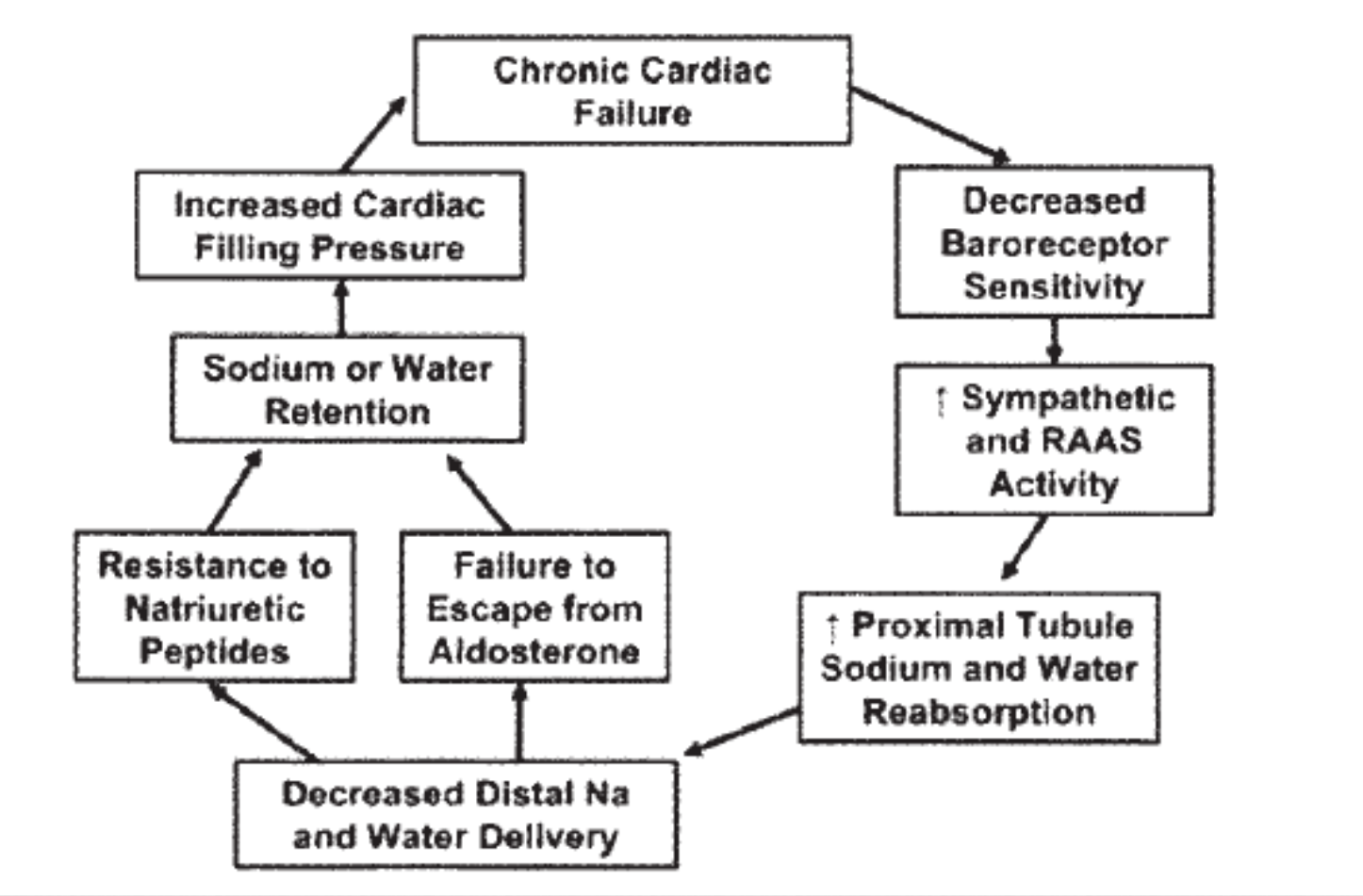


Figure 3. Vasopressin stimulation of V2 and V1a receptors can contribute to events that worsen cardiac function. [Reprinted from *J Am Coll Cardiol*, vol. 47, Schrier RW, Role of diminished renal function in cardiovascular mortality: Marker or pathogenetic factor? pp. 1–8, copyright 2006 (ref. 6), with permission from Elsevier.]

Επιδείνωση της κ/α



Clin J Am Soc Nephrol 4: 2013–2026, 2009

Μηχανισμοί βελτίωσης της κ/α

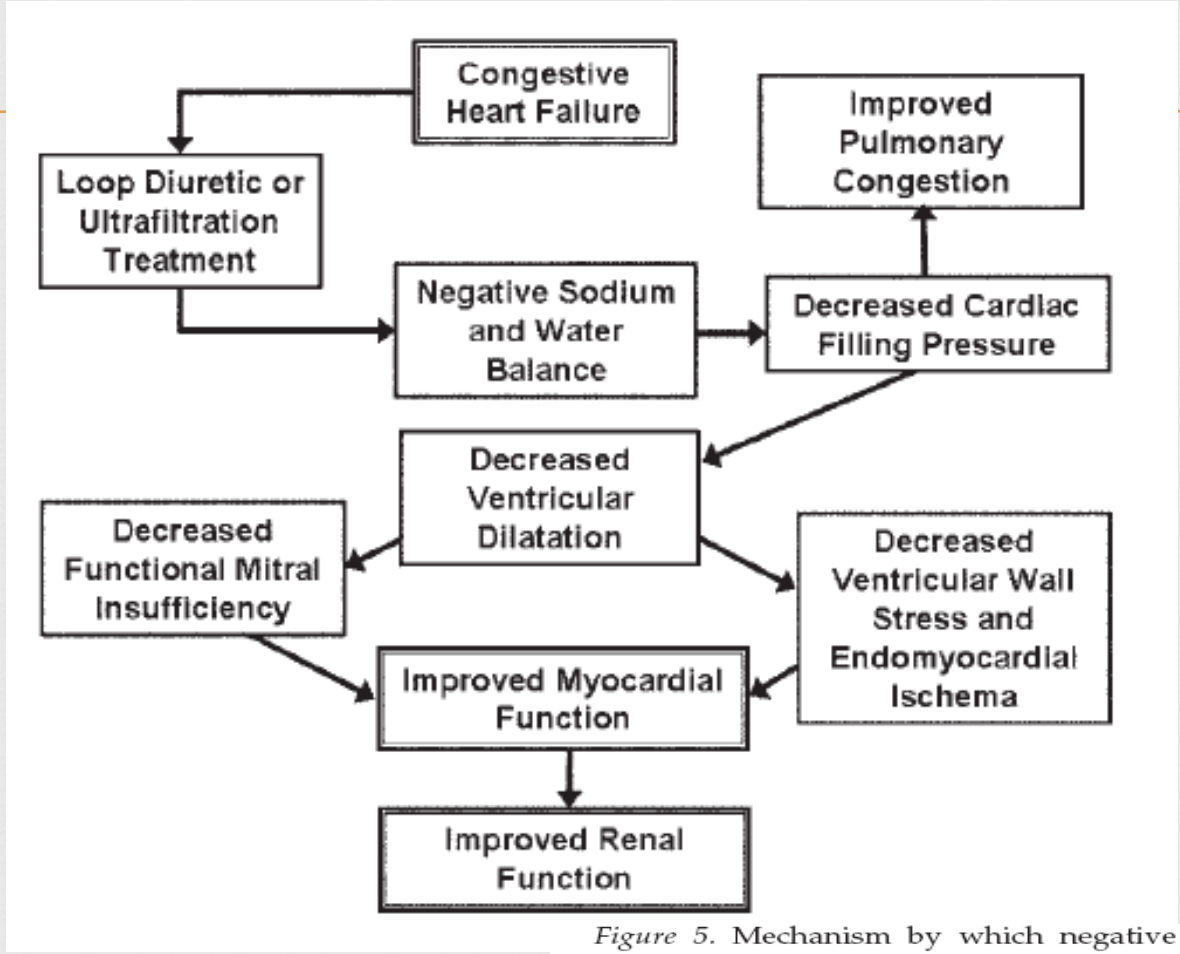
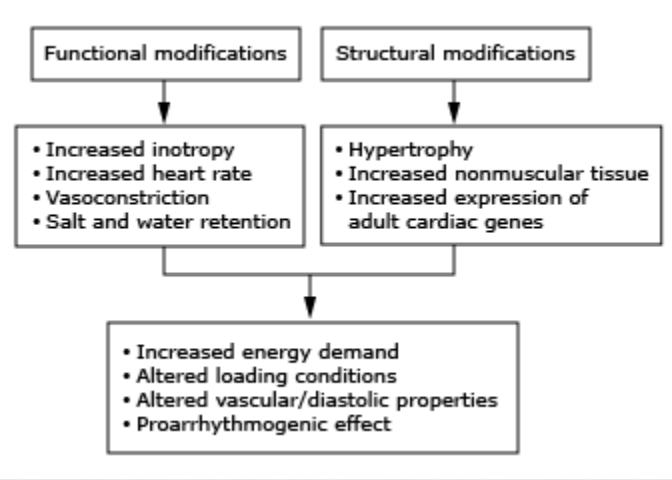
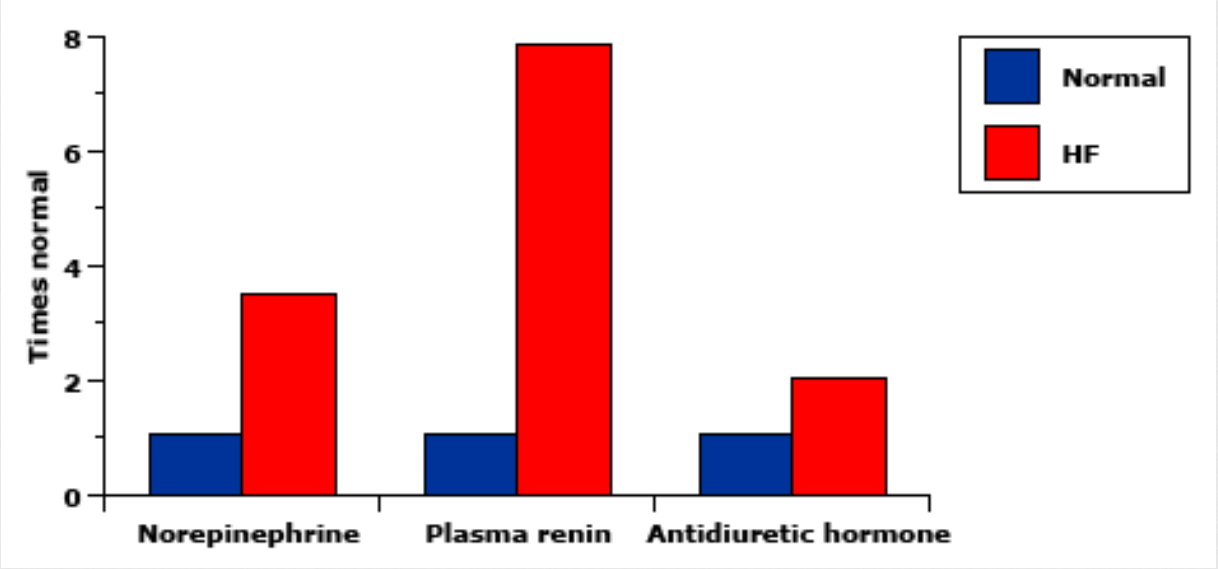


Figure 5. Mechanism by which negative sodium and water balance may improve myocardial and renal function in CHF. [Reprinted from *J Am Coll Cardiol*, vol. 47, Schrier RW, Role of diminished renal function in cardiovascular mortality: Marker or pathogenetic factor? pp. 1–8, copyright 2006 (ref. 6), with permission from Elsevier.]

Functional and structural modifications following neurohormonal stimulation in heart failure



Hormone levels in HF



Plasma levels of norepinephrine, renin activity, and antidiuretic hormone are increased two to eight fold (when compared to normal subjects) in patients with stable heart failure treated with digitalis, but not diuretics or vasodilators.

Data from: Francis, GS, Goldsmith, SR, Levine, TB, et al, Ann Intern Med 1984; 101:370.

Cardiorenal syndrome

- Cardiorenal syndrome – term used to define the interdependence of the heart and kidney.
- In heart failure – interactions present between heart and kidney that increase circulating blood volume and thereby worsen heart failure (HF).
- At worst case – therapy to treat HF may be limited by decline in renal function.

Features of the cardiorenal syndrome

- Heart failure with decreased eGFR < 60 mL/min/1.73 m2.
- Worsening of renal function (>25%) during treatment of acute decompensated HF
- Diuretic resistance
- Persistent congestion despite: oral, IV, IVI or combination of diuretic + thiazide + aldosterone antagonist.

The cardiorenal syndrome in diabetes mellitus

Hussein H. Karnib [*], *Fuad N. Ziyadeh*

The cardiorenal syndrome in patients with diabetes mellitus represents a systemic condition that affects both the cardiovascular and renal systems. Diabetes is a well established risk factor for cardiovascular disease (CVD), and a significant proportion of diabetic patients go on to develop clinically significant nephropathy. In the diabetic state the kidney is involved by progressive sclerosis/fibrosis and proteinuria, due most likely to overactivity of the transforming growth factor-beta system and, to some extent, the vascular endothelial growth factor system, respectively. The pathogenesis of CVD in diabetes is multifactorial, involving hemodynamic forces, humoral/metabolic factors, and oxidative stress. Addition-

DIABETES RESEARCH AND CLINICAL PRACTICE 89 (2010) 201–208

Επιδημιολογία

- 250 εκατομ. Διαβητικών
- Πρόβλεψη για 380 εκατομ. το 2025
- Μεγάλο φορτίο υγειονομικής περίθαλψης
- Μικρο/μακρο-αγγειοπάθεια
- Διαβητική νεφροπάθεια
- 45% των νέων-ESRD είναι Σ/Δ
- >30% με Σ/Δ και CVD
- Σημαντική αιτία πρόωρης θνητότητας

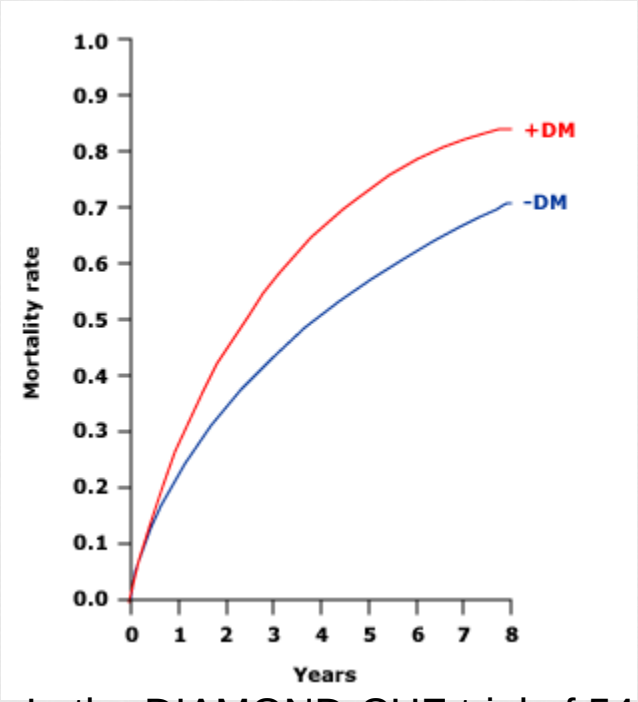
Pavkov ME et al Am J Kidney Dis 2008;51:759–66

Επιπλοκές Σ/Δ

- Παράγων για CVD
- Λευκωματουρία
- Σημαντικό ποσοστό νεφροπάθειας
- Αρτηριακή υπέρταση
- Γενικευμένη μεταβολική διαταραχή
- Προοδευτική σκλήρυνση/ίνωση
- Περιφερική αγγειοπάθεια
- Αμφιβληστροειδοπάθεια

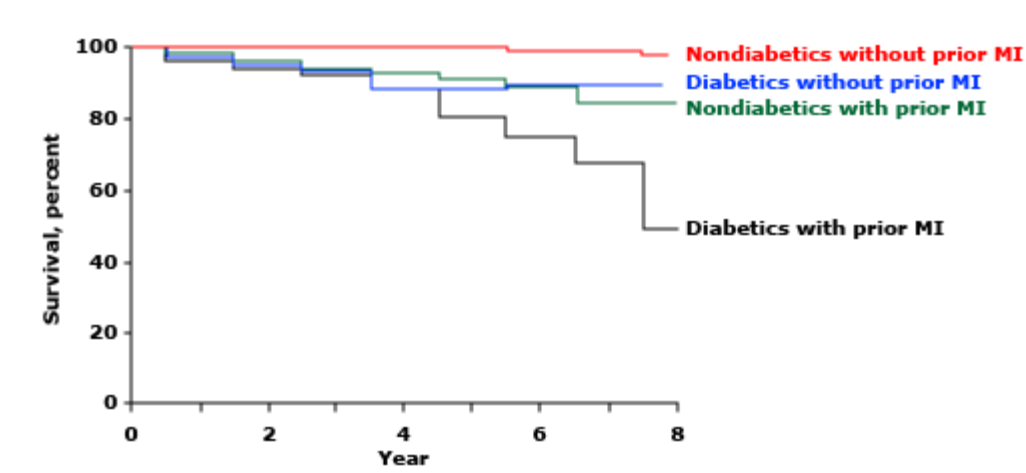
Επίδραση του Σ/Δ στη θνητότητα από κ/α

- **Cumulative mortality from all causes in patients with heart failure with and without diabetes**

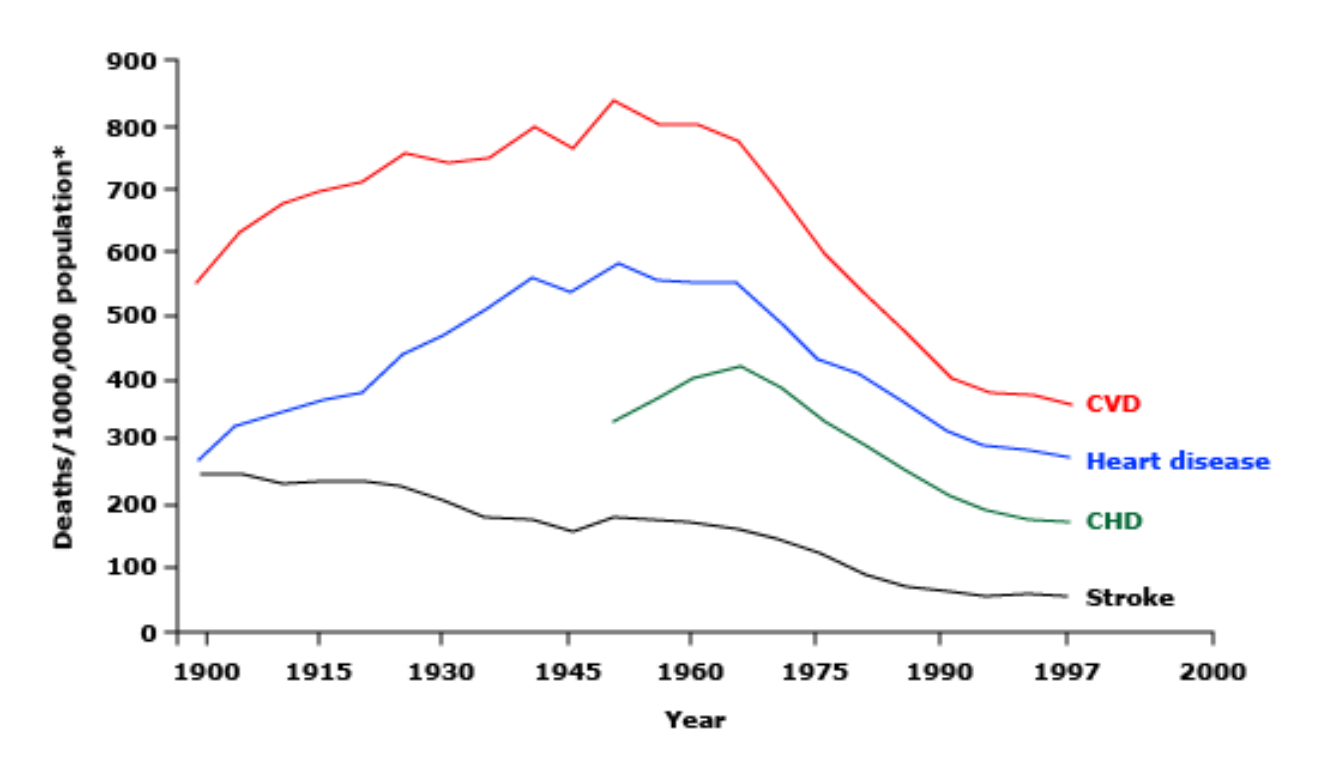


Effect of diabetes on HF mortality. In the DIAMOND-CHF trial of 5491 patients with heart failure (HF), 900 (16 percent) had diabetes mellitus. Mortality for patients with diabetes was significantly higher than for those without diabetes (31 versus 23 percent at one year, adjusted risk ratio 1.5, 95% CI 1.3 to 1.6).

Επιβίωση


Survival, percent
100
80
60
40
20
0
0
2
4
6
8
Year
Nondiabetics without prior MI
Diabetics without prior MI
Nondiabetics with prior MI
Diabetics with prior MI

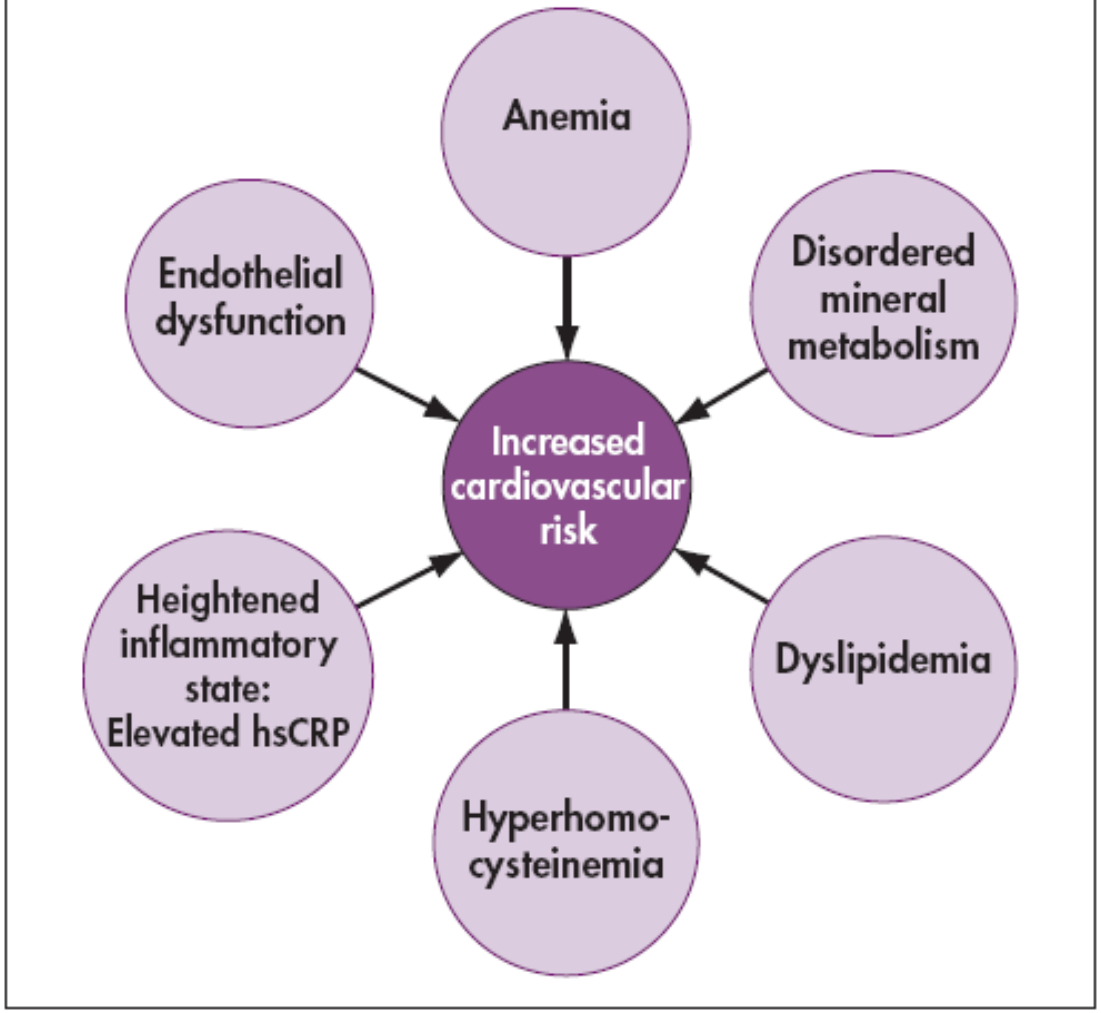
Death rates for major cardiovascular diseases have decreased in the United States



During the years 1900 to 1960 there was an increase in the death rate from all cardiovascular diseases (CVD), all heart diseases, and coronary heart disease (CHD). However, since 1960 the number of death from all CVD, heart disease, and stroke have markedly declined. Rates are age-adjusted to 2000 standard.

Data from Cooper, R, Cutler, J, Desvigne-Nickens, P, et al, Circulation 2000; 102:3137.

Figure 1: Additional risk factors for cardiovascular disease in patients with renal disease



NEPHROLOGY

The Cardiorenal Syndrome: Nontraditional Cardiovascular Risk Factors in Patients with Renal Disease

By SHONA PENDSE, MD, MMSC.

NOVEMBER 2008 | Volume 6, Issue 9

AKI

AKI in ICU: A Grave Prognosis

Prospective observational study of 29,269 ICU pts with AKI in 23 countries.
Incidence of AKI: 5% - 6%
AKI patients have high prevalence of co-existing chronic disease
- CKD: 30% -- CAD 37%
- DM 29% -- Chronic Liver Dis 21%
Mortality in hospital: 60%

Uchino, S. et al. JAMA 2005;294:813-818

AKI in ICU

1,726 AKI ICU Admissions:
Contributing Factors to AKI

1. Septic shock 820 (47.5%)
2. Major surgery 592 (34.3%)
3. Cardiogenic shock 465 (26.9%)
4. Hypovolemia 442 (25.6%)
5. Drug-induced 328 (19.0%)
6. Hepatorenal syndrome 99 (5.7%)
7. Obstructive uropathy 45 (2.6%)
8. Other 211 (12.2%)

Uchino, S. et al. JAMA 2005;294:813-818

Medications and AKI

Hemodynamic: Impaired autoregulation
ACEI/ ARB/ NSAIDs/ COX2s/ contrast
Glomerular: FSGS/ Glomerulonephritis
Pamidronate/Gold/Rifampin/captopril/ Interferon
Vascular: vasculitis/ HUS
PTU/ hydralazine/allopurinol/PCN/ Sulfa/ gemcitabine/ Plavix/Cyclosporine/allopurinol
Tubular: ATN/ RTA
Aminoglycosides/ Ampho B/ Tenofovir/ contrast/ Bactrim
Tubular/Interstitial: AIN/obstruction
PCN's, methicillin/ sulfa/ rifampin/ Bactrim/ACV/ Indinavir

AKI

- Diagnosis of AKI:

  at present there are few, specific interventions proven to prevent or treat AKI.

- Why?

  - are we making the diagnosis to late to make a difference?

  - we need to look at the renal equivalent to cardiac troponin to diagnose “Renal Angina”

AKI

Primary diagnosis of AKI at present is with change in:

1. creatinine
2. BUN
3. urine studies (microscopic for casts, urine Na)
4. urine output

- Are there any better or newer diagnostic markers?

Management of AKI

1. Identify patient risk factors
   advanced age, DM
   cirrhosis/hepatic failure
   CKD, CHF
   volume depletion, sepsis
   recent CABG
   exposure to nephrotoxins
2. On presently available evidence - 3 criteria should prompt concern of evolving AKI:
   - oliguria
   - rising creatinine
   - fluid overload

CJASN - May 2010 – Goldstein and Chawla et al

AKI

AKI - analysis of the new lab data

Best for differential diagnosis of established AKI:
- serum cystatin C
- urine IL-18
- KIM-1

Best for early diagnosis of AKI:
- serum cystatin C
- urine NGAL
- IL-18
- glutathione- S-transferase-pi and y-glutathione

Best for mortality risk prediction:
- urine for KIM-1
- IL-18
- N-acetyl-B-dglucosaminidase

Coca, KI 73;1008-1016: 2008

J Chin Med Assoc • October 2007 • Vol 70 • No 10

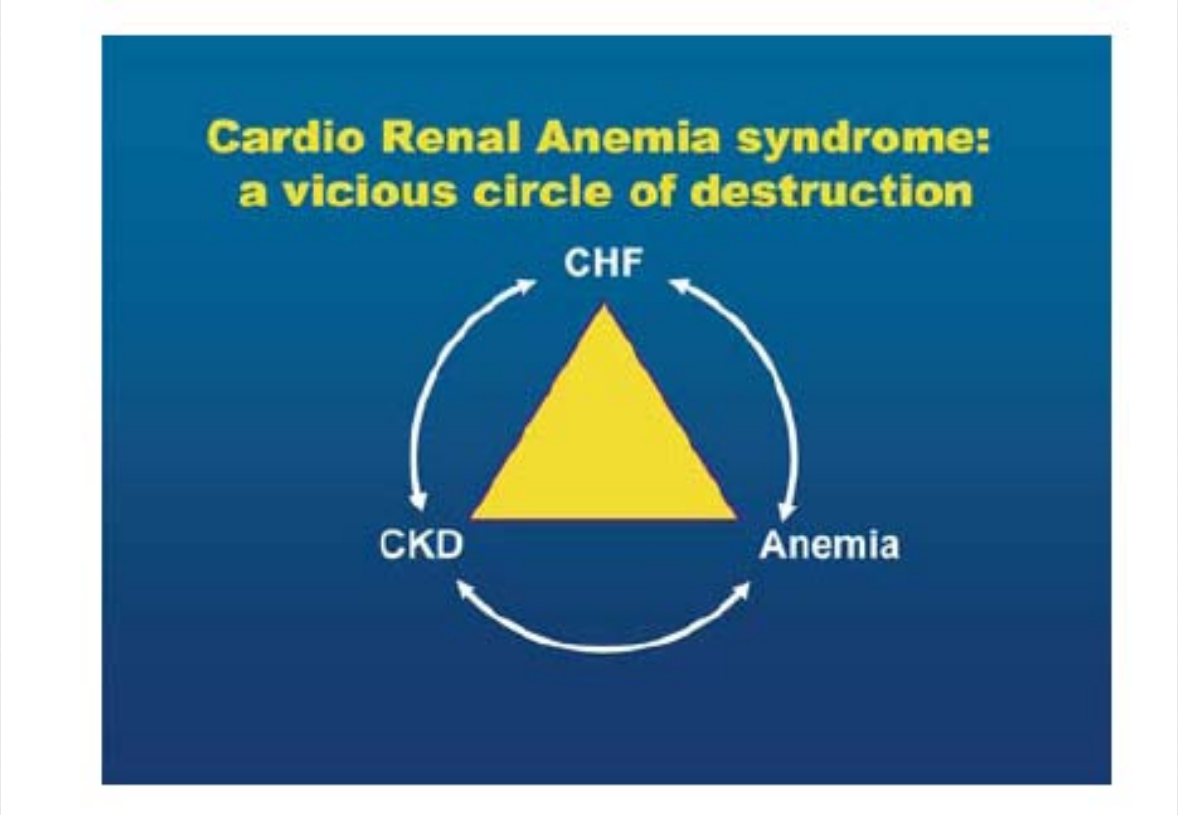
Cardiorenal Anemia Syndrome in Chronic Kidney Disease

REVIEW ARTICLE

Anemia is a frequently encountered problem of chronic kidney disease (CKD) and deteriorates as renal function declines. Anemia increases the risk of death in CKD patients with diabetes and hypertension, which are the 2 leading causes of CKD. Recent studies suggest that correction of anemia improves patient quality of life and may delay the progression to end-stage renal disease. Anemia is often only treated in the late stages of CKD or after the initiation of renal replacement therapy. Thus, anemia of CKD is often unnoticed and lacks appropriate treatment. To practically manage high-risk

This paper provides recommendations for the diagnosis and management of anemia associated ternational practice guidelines. [*J Chin Med Assoc* 2007;70(10):424–429]

Αλληπίδραση
Συμφορητικής Καρδιακής Ανεπάρκειας
Χρόνιας Νεφρικής Νόσου - Αναιμίας



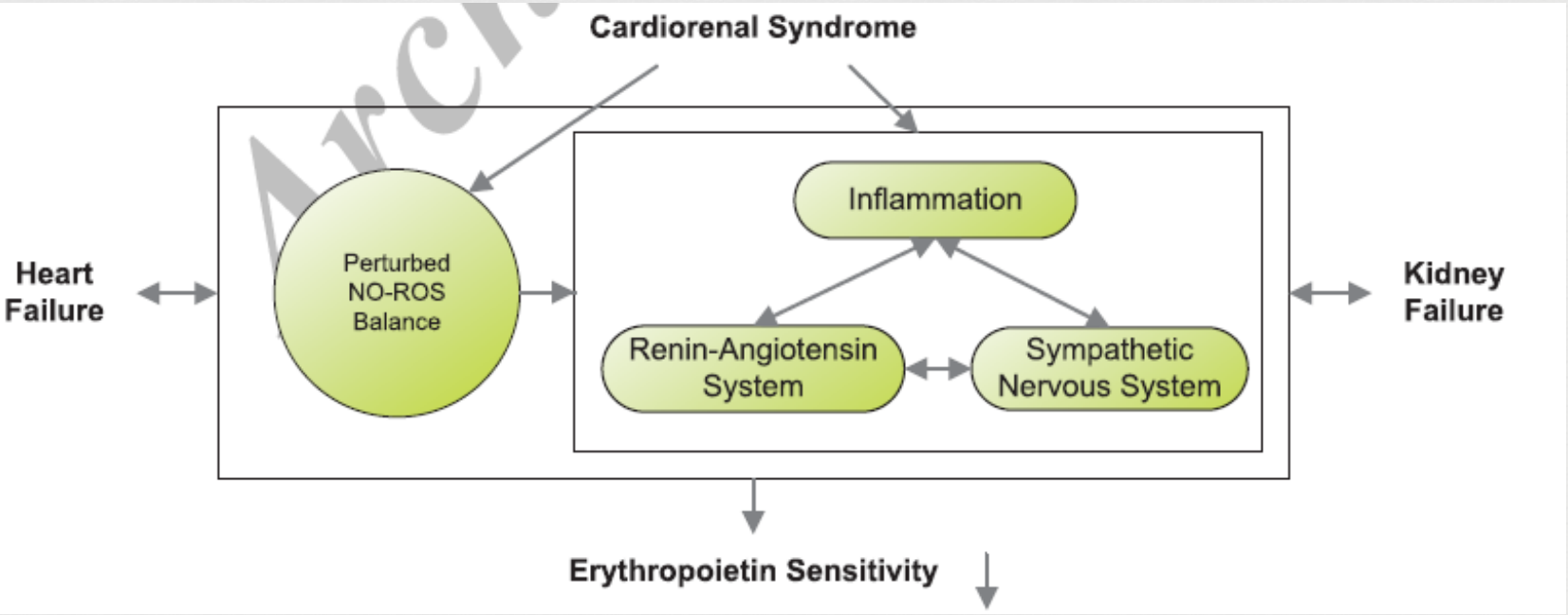
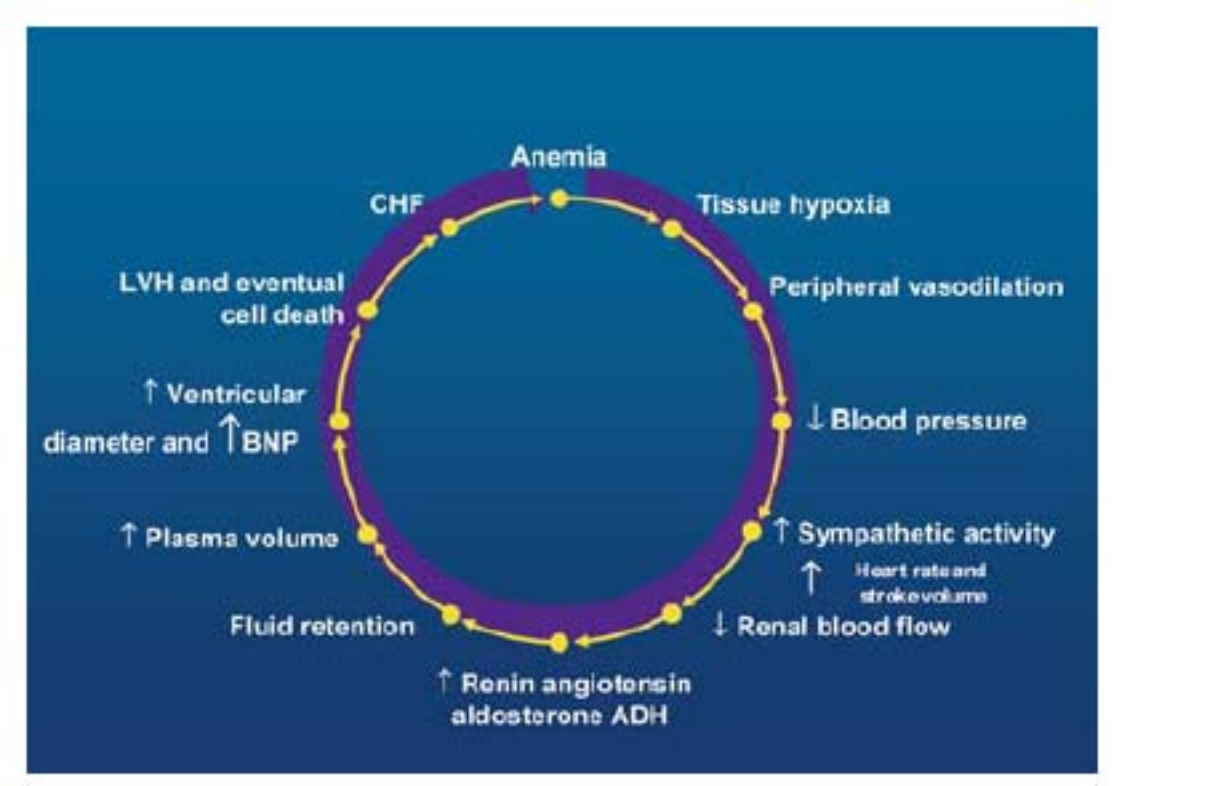


Figure 1. Cardiorenal connection and its effect on erythropoietin. Imbalance between nitric oxide and reactive oxygen species, by increased inflammation, increased activity of the rennin-angiotensin system, and increased activity of the sympathetic nervous system, causes cardiorenal syndrome. Together, these "cardiorenal connectors" decrease sensitivity to erythropoietin. NO-ROS indicates nitric oxide-reactive oxygen species.

Himanshu Sekhar Mahapatra & co
Iranian Journal of Kidney Diseases 2009;V. 3:61-70

Μηχανισμός πρόσληψης υγρών και καρδιακής ανεπάρκειας στην αναιμία



Therapeutic Strategies for Heart Failure in Cardiorenal Syndromes

Andrew A. House, MD, MSc,[1] Mikko Haapio, MD,[2] Johan Lassus, MD,[3] Rinaldo Bellomo, MD,[4] and Claudio Ronco, MD[5,6]

Cardiorenal syndromes are disorders of the heart and kidneys whereby acute or long-term dysfunction in one organ may induce acute or long-term dysfunction of the other. The management of cardiovascular diseases and risk factors may influence, in a beneficial or harmful way, kidney function and progression of kidney injury. In this review, we assess therapeutic strategies and discuss treatment options for the management of patients with heart failure with decreased kidney function and highlight the need for future high-quality studies in patients with coexisting heart and kidney disease.
Am J Kidney Dis 56:759-773.

American Journal of Kidney Diseases, Vol 56, No 4 (October), 2010: pp 759-773

Αντιμετώπιση

- Πρόληψη
  - ομάδες υψηλού κινδύνου
  - αποφυγή νεφροτοξικών (αντιβιοτικά-σκιαγραφικά-αντιφλεγμονώδη)
  - ορθή χρήση καρδιολογικών-αντιϋπερτασικών - διουρητικών
- Έγκαιρη αναγνώριση
- Γενικά μέτρα
- Εξειδικευμένη αγωγή (π.χ. Nesiritide)

Canadian Cardiovascular Society consensus recommendations on heart failure and concomitant renal dysfunction

Recommendations

- Heart failure patients with stable renal function (serum creatinine levels less than 200 µmol/L) should be monitored for serum potassium and creatinine if combination therapy is used or in the presence of potential dehydration (class I, level B).
- Patients with heart failure with increasing serum creatinine should be assessed for reversible causes such as concomitant medications (eg, nonsteroidal anti-inflammatory drugs), hypovolemia, hypotension, urinary tract obstruction or infection (class I, level C).
- In oliguric heart failure patients who are hemodynamically stable, diuretics, ACE inhibitors, ARBs, spironolactone and nonheart failure drugs that can impair renal function should be reviewed daily (class I, level C).
- In stable heart failure patients who are not oliguric but have increasing serum creatinine levels of more than 30% from a previous stable baseline, the dose of diuretics, ACE inhibitors, ARBs and spironolactone may be reduced until renal function stabilizes (class 1, level C).
- In heart failure patients not responding adequately to more than 240 mg intravenous furosemide daily, treatment options include:
  - More frequent or higher doses of intravenous boluses of diuretic (class IIb, level C);
  - Combination with thiazide diuretic, eg, hydrochlorothiazide or metolazone (class IIA, level B); or
  - Continuous intravenous furosemide infusion (class IIa, level B).

Can J Cardiol Vol 24 Suppl B July 2008

Table 1. Pharmacologic agents in the management of acute decompensated heart failure

Medication	Initial Dose	Dose Range	Comments
Diuretics			
Furosemide	20 to 80 mg IV bolus	20 to 400 mg boluses may repeat q6 to 8H	Infusion is recommended at 5 to 40 mg/h. If >240 mg/h, risk of ototoxicity increases.
Torsemide	10 to 40 mg bolus	20 to 200 mg bolus	Continuous infusion: 5 to 20 mg/h
Bumetanide	0.5 to 2 mg bolus	0.5 to 4 mg bolus	Continuous infusion: 0.1 to 0.5 mg/h
Vasodilators			
Nitroprusside	0.3 to 0.5 μg/kg/min	0.3 to 5 μg/kg/min	Infusion rates of >10 μg/kg/min may cause cyanide toxicity. Also, caution in active myocardial ischemia.
Nitroglycerine	10 to 20 μg/min	20 to 400 μg/min	severe headache, hypotension, closed-angle glaucoma
Nesiritide	No bolus	0.005 to 0.03 μg/kg/min	Titration: increased infusion rate by 0.005 μg/kg/min (no more than every 3 h, up to a maximum of 0.03 μg/kg/min).
Inotropes			
Dopamine	2 to 5 μg/kg/min	2 to 20 μg/kg/min	May increase mortality. Caution for arrhythmia.
Dobutamine	1 to 2 μg/kg/min	1 to 20 μg/kg/min	May increase mortality. Caution for arrhythmia.
Milrinone	50 μg/kg IV loading dose over 10 min; then 0.25 to 1.0 μg/kg/min infusion	0.10 to 0.75 μg/kg/min	May increase mortality. Caution for arrhythmia.
Other			
Levosimendan	0.05 to 0.2 μg/kg/min bolus over 10 min followed by infusion	0.5 to 2.0 μg/kg/min	May increase mortality. Not approved in the United States. Caution for hepatic impairment and left-ventricular outflow obstruction.

ΣΥΜΠΕΡΑΣΜΑΤΑ

1. Οξείες ή χρόνιες καταστάσεις αλληλεπιδρούν στη λειτουργία των δύο οργάνων
2. Απαιτείται βαθειά κατανόηση και γνώση των παθοφυσιολογικών μηχανισμών για την καλύτερη φροντίδα των ασθενών
3. Συνεργασία καρδιολόγων /νεφρολόγων /εντατικολόγων
4. Αποφάσεις ομοφωνίας για την ανάπτυξη θεραπευτικών μεθόδων, ανάλογα με τον τύπο του συνδρόμου
5. Απαραίτητη η διεξαγωγή μεγάλων τυχαιοποιημένων μελετών με σχεδιασμένες παρεμβάσεις στοχεύοντας στη μείωση της νοσηρότητας και της θνητότητας