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Critical Care Medicine

EPIDEMIOLOGY OF CARDIO-RENAL SYNDROMES

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Critical Care Medicine

DISCLOSURES/CONFLICTS

- Inverness Medical Innovations Inc.
- Baxter Inc.

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OUTLINE

- Definition of Cardio-Renal Syndrome
- Epidemiology of Subtypes
- Summary

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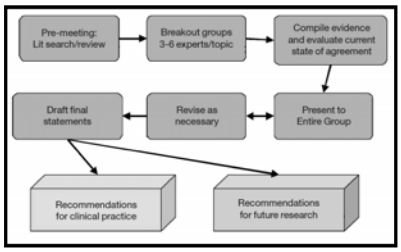
ACUTE DIALYSIS QUALITY INITIATIVE (ADQI)

ADQI

A process towards developing Consensus and Guidelines for Dialysis in the Critically ill Patient



Critical Care Medicine

ADQI VII: VENICE, ITALY THE CARDIO-RENAL SYNDROME

Critical Care Medicine

ADQI VII: THE CARDIO-RENAL SYNDROME

European Heart Journal
doi:10.1093/eurheartj/ehp507

CLINICAL RESEARCH

Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative

Claudio Ronco[1,2*], Peter McCullough[3], Stefan D. Anker[4,5], Inder Anand[6], Nadia Aspromonte[7], Sean M. Bagshaw[8], Rinaldo Bellomo[9], Tomas Berl[10], Ilona Bobek[1], Dinna N. Cruz[1,2], Luciano Daliento[11], Andrew Davenport[12], Mikko Haapio[13], Hans Hillege[14], Andrew A. House[15], Nevin Katz[16], Alan Maisel[17], Sunil Mankad[18], Pierluigi Zanco[19], Alexandre Mebazaa[20], Alberto Palazzuoli[21], Federico Ronco[11], Andrew Shaw[22], Geoff Sheinfeld[23], Sachin Soni[1,24], Giorgio Vescovo[25], Nereo Zamperetti[26], and Piotr Ponikowski[27] for the Acute Dialysis Quality Initiative (ADQI) consensus group

ADQI VII: THE CARDIO-RENAL SYNDROME

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General Definition:

We defined the broad term "Cardio-Renal Syndromes" as "disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other".

THE CARDIO-RENAL SYNDROME

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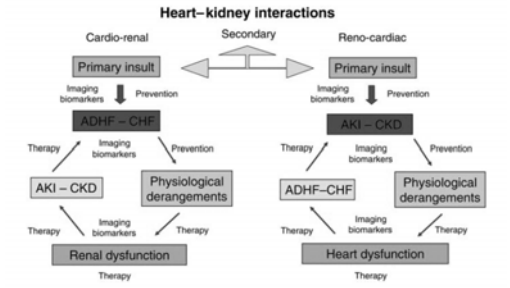

CARDIO-RENAL SYNDROME: TYPE 1

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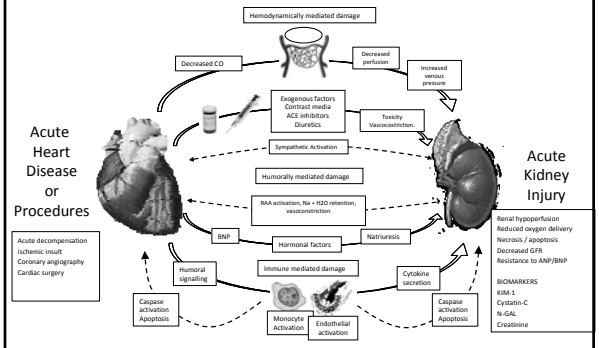
Definition:

Acute worsening of heart function leading to kidney injury and/or dysfunction.

CARDIO-RENAL SYNDROME: TYPE 1



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CARDIO-RENAL SYNDROME: TYPE 1

- Epidemiology is challenging:
  - Retrospective/secondary analyses
  - Definition of worsening renal function (WRF)
  - Variable observed time-at-risk

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ACUTE DECOMPENSATED HEART FAILURE (ADHF)

Study	n	Type	AKI	Incidence
Krumholz (2000)	1681	Retrospective	SCr >26.5	**28**
Gottlieb (2002)	1002	Retrospective	SCr >26.5	**39**
Smith (2003)	412	Prospective	SCr >26.5	**45**
Cowie (2006)	299	Retrospective	SCr >26.5	**29**
Nohria (2008)	433	Retrospective	SCr >26.5	**30**
Logeart (2008)	416	Prospective	SCr >26.5	**37**
Metra (2008)	318	Prospective	SCr >26.5	**34**

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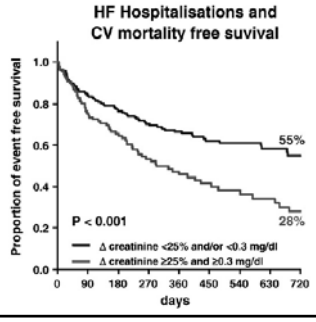
AKI IN ADHF

- AKI associated with increased:
  - ICU admission
  - Lengths of ICU/hospital stay
  - In-hospital mortality
  - 30-day re-hospitalization
  - Health costs/resource use

Worsening renal function in patients hospitalised for acute heart failure: Clinical implications and prognostic significance

Marco Metra [a,*], Savina Nodari [a], Giovanni Parrinello [b], Tania Bordonali [a], Silvia Bugatti [a], Rossella Danesi [a], Benedetta Fontanella [a], Carlo Lombardi [a], Patrizia Milani [a], Giulia Verzura [a], Gadi Cotter [c], Howard Dittrich [d], Barry M. Massie [e], Livio Dei Cas [a]



Metra et al Eur J Heart Fail 2008

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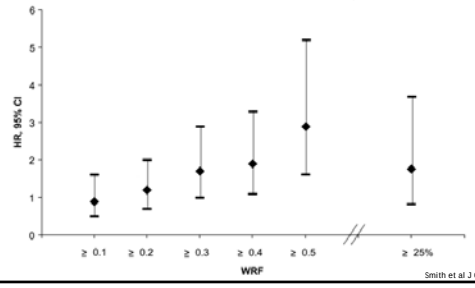
Worsening Renal Function: What Is a Clinically Meaningful Change in Creatinine During Hospitalization With Heart Failure?

GRACE L. SMITH, MPH,* VIOLA VACCARINO, MD, PhD,† MIKHAIL KOSIBOROD, MD,‡ JUDITH H. LICHTMAN, PhD,§ SUSAN CHENG, BA,‖ SUZANNE G. WATNICK, MD,* HARLAN M. KRUMHOLZ, MD‖¶



Smith et al J Card Fail 2003

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ACUTE CORONARY SYNDROME (ACS)

Study	n	Type	AKI	Incidence
Goldberg (2003)	1038	Retrospective	SCr >44.2	**10**
Jose (2006)	1854	Retrospective	SCr >26.4	**12**
Latchamsetty (2007)	1417	Prospective	SCr >44.2	**10**
Newsome (2008)	87094	Retrospective	Variable	**43**
Parikh (2008)	147007	Retrospective	SCr >26.5	**20**

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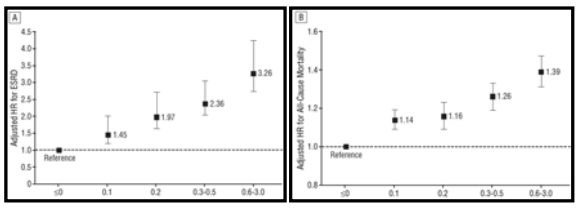
AKI IN ACS

- AKI associated with increased:
  - In-hospital mortality
  - Cardiovascular events
  - Re-hospitalization
  - Progression to ESKD
  - Health costs/resource use

Long-term Risk of Mortality and End-Stage Renal Disease Among the Elderly After Small Increases in Serum Creatinine Level During Hospitalization for Acute Myocardial Infarction

Britt B. Newsome, MD, MPH, MSPH; David G. Warnock, MD; William M. McClellan, MD, MPH; Charles A. Herzog, MD; Catarina I. Kiefe, PhD, MD; Paul W. Eggers, PhD; Jeroan J. Allison, MD, MS



Newsome et al Arch IM 2008

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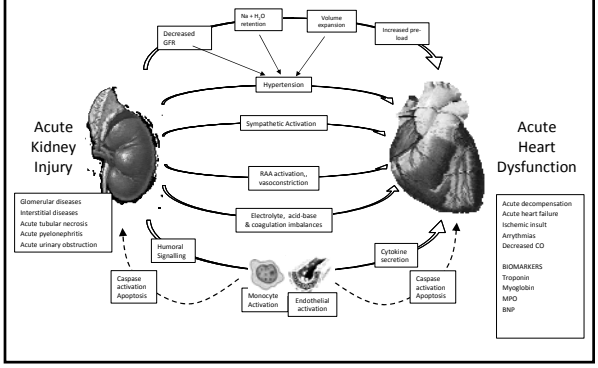
Cardio-Renal Syndrome: Type 3

Definition:

Acute worsening of kidney function leading to heart injury and/or dysfunction.

CARDIO-RENAL SYNDROME: TYPE 3



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CARDIO-RENAL SYNDROME: TYPE 3

Prototypical Conditions
Contrast-induced nephropathy
Drug-induced nephropathy
Major non-cardiac surgery-associated AKI
Cardiac surgery-associated AKI
Post-infectious GN
Rhabdomyolysis
Acute pyelonephritis
Post-obstructive uropathy

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CARDIO-RENAL SYNDROME: TYPE 3

- Epidemiology is challenging:
  - Heterogeneity in predisposing conditions
  - Different methods for defining AKI
  - Variable baseline risk in individuals for development of acute cardiac dysfunction
  - Failure of many clinical studies of AKI to report the occurrence of acute cardiac dysfunction as outcomes

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CARDIO-RENAL SYNDROME: TYPE 3

- Incidence estimates/outcomes:
  - Disease-specific
  - Context-specific

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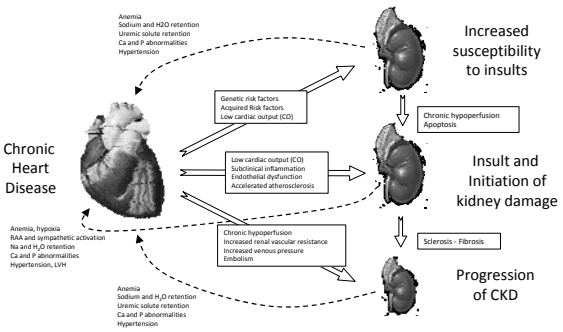
CARDIO-RENAL SYNDROME: TYPE 2

Definition:

Chronic abnormalities in heart function leading to kidney injury or dysfunction.

CARDIO-RENAL SYNDROME: TYPE 2



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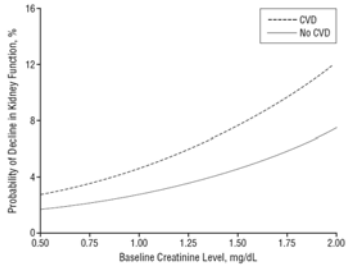
CARDIO-RENAL SYNDROME: TYPE 2

Study	n	Type	CVD	eGFR<60
Heywood (2007)	118465	ADHERE	ADHF	72
Elsayed (2007)	13826	ARIC/CHS	CVD	34
Ahmed (2007)	7788	DIG	CHF	45
Campbell (2009)	1102	Retrospective	CHD	9

Cardiovascular Disease and Subsequent Kidney Disease

Essam F. Elsayed, MD; Hocine Tighiouart, MS; John Griffith, PhD; Tobias Kurth, MD, ScD; Andrew S. Levey, MD; Deeb Salem, MD; Mark J. Sarnak, MD, MS; Daniel E. Weiner, MD, MS



Elsayed et al Arch IM 2007

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CARDIO-RENAL SYNDROME: TYPE 2

- Future Investigations to evaluate:
  - Rate of progression of CKD in patients with established CVD
  - Whether synergistic interaction
  - Effect of cardio-protective therapies on progression/exacerbation of CKD
  - Mechanistic link of heart-kidney interaction (i.e. biomarkers)

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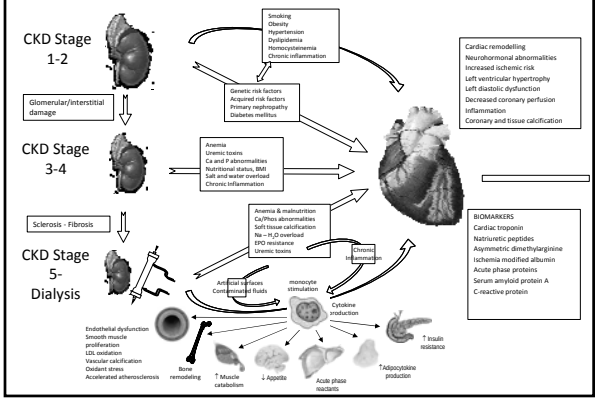
CRS: TYPE 4

Definition:

Chronic kidney disease (CKD) leading to heart injury, disease and/or dysfunction.

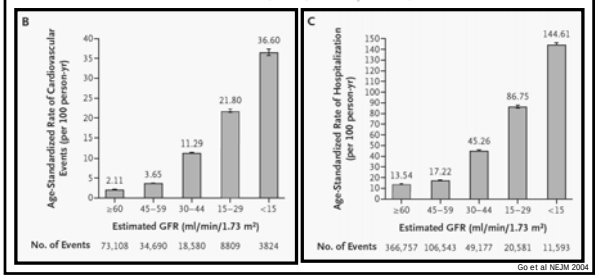
CARDIO-RENAL SYNDROME: TYPE 4



ORIGINAL ARTICLE

Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization

Alan S. Go, M.D., Glenn M. Chertow, M.D., M.P.H., Dongjie Fan, M.S.P.H., Charles E. McCulloch, Ph.D., and Chi-yuan Hsu, M.D.



Go et al NEJM 2004

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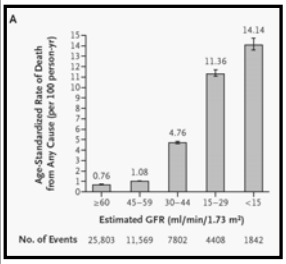

eGFR	Death	CV Event	Hospital
≥60	1.0	1.0	1.0
45-60	1.2	1.4	1.1
30-44	1.8	2.0	1.5
15-29	3.2	2.8	2.1
<15	5.9	3.4	3.1

Go et al NEJM 2004

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CARDIO-RENAL SYNDROME: TYPE 2/4

- Heart/kidney disease:
  - Commonly co-exist
  - Uncertain primary vs. secondary
  - Unable to discriminate CRS Type 2/4

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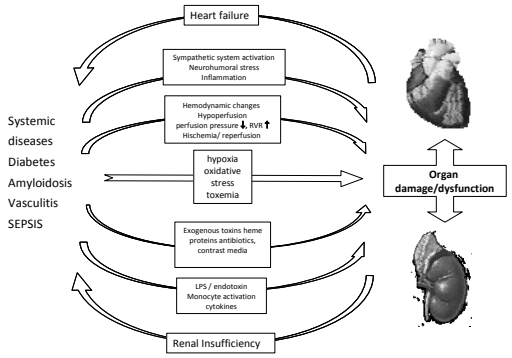
CARDIO-RENAL SYNDROME: TYPE 5

Definition:

Systemic condition leading to simultaneous injury and/or dysfunction of heart and kidney.

CARDIO-RENAL SYNDROME: TYPE 5



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CARDIO-RENAL SYNDROME: TYPE 5

Acute Systemic Illness	Chronic Systemic Illness
Severe sepsis/septic shock	Hypertension
Infections (i.e. HIV, HCV)	Diabetes Mellitus
Drug toxicity (i.e. cocaine)	Amyloidosis
CTD (i.e. SLE, APLA, PSS)	Multiple myeloma
Microangiopathy (i.e. TTP)	Sarcoidosis
Vasculitis	Cirrhosis
Malignancy (i.e. lymphoma)	Pulmonary hypertension

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CARDIO-RENAL SYNDROME: TYPE 5

- Epidemiology:
  - Disease-specific
  - Context-specific
  - Time-varying

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CARDIO-RENAL SYNDROME: TYPE 5

- Pathophysiology:
  - Mechanisms of secondary heart-kidney interaction?
  - Co-existent vs. genuine bidirectional interaction?

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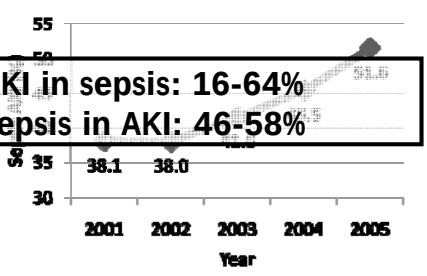
CRS TYPE 5: SEPSIS

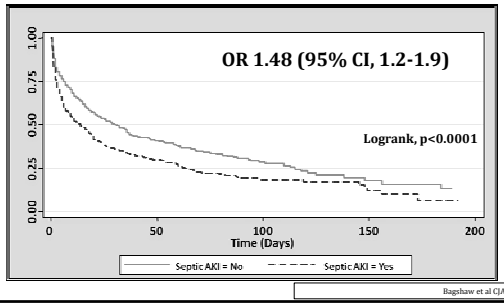


AKI in sepsis: 16-64%
Sepsis in AKI: 46-58%

Bagshaw et al Crit Care 2008

Septic Acute Kidney Injury in Critically Ill Patients: Clinical Characteristics and Outcomes

Sean M. Bagshaw,*† Shigehiko Uchino,*†¶ Rinaldo Bellomo,* Hiroshi Morimatsu,‡ Stanislao Morgera,§ Miet Schetz,‖ Ian Tan,¶ Catherine Bouman,** Ettiene Macedo,†† Noel Gibney,† Ashita Tolwani,‡‡ Heleen M. Oudemans-van Straaten,§§ Claudio Ronco,‖‖ and John A. Kellum;*** for the Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators

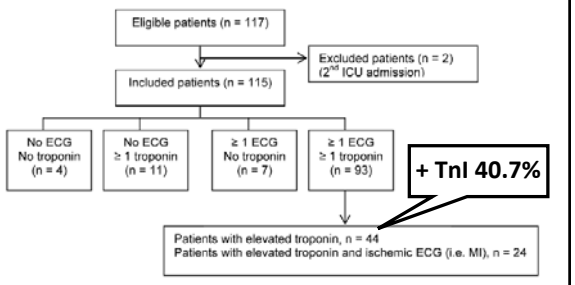


Bagshaw et al CJASN 2007

Research **Open Access**

Elevated troponin and myocardial infarction in the intensive care unit: a prospective study

Wendy Lim[1], Ismael Qushmaq[1], Deborah J Cook[2], Mark A Crowther[3], Diane Heels-Ansdell[4], PJ Devereaux[5] and the Troponin T Trials Group



Lim et al Crit Care 2003

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SEPTIC MYOCARDIAL DYSFUNCTION

- Incidence estimates variable due to:
  - Timing of assessment of cardiac dysfunction (i.e. TnI, BNP, ECHO, ECG?)
  - Severity of illness/organ failure
  - Duration of illness prior to evaluation

…however, elevated cardiac-specific TnI in 30-85%

Cardiac Troponins I and T Are Biological Markers of Left Ventricular Dysfunction in Septic Shock

Kristien M. ver Elst,[1] Herbert D. Spapen,[2] Duc Nam Nguyen,[2] Christian Garbar,[3] Luc P. Huyghens,[2] and Frans K. Gorus[1,*]

Characteristics	TnI/TnT + (n=23)	TnI/TnT – (n=23)
Age (med)	71	56
APACHE II Score (med)	27	20
Prior AMI (%)	39	4
ECG signs ischemia (%)	0	0
LV dysfunction (TEE) (%)	**78**	**9**
Peak CRP (med)	245	284
Survival (%)	39	69

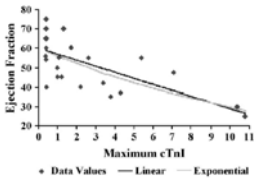
Ver Elst et al Clin Chem 2000

ELSEVIER
International Journal of Cardiology 95 (2004) 13–17
International Journal of Cardiology
www.elsevier.com/locate/ijcard

Cardiac troponin I predicts myocardial dysfunction and adverse outcome in septic shock

Nirav J. Mehta[a], Ijaz A. Khan[a,*], Vipin Gupta[b], Ketan Jani[b], Ramesh M. Gowda[b], Peter R. Smith[b]

	TnI + (n=16)	TnI- (n=21)
APACHE II score	**28**	**20**
Vasoactives (%)	**94**	**53**
Regional WMA (%)	**56**	**6**
EF (%)	**46**	**62**
Mortality (%)	**56**	**24**



Mehta et al Int J Cardiol 2004

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CARDIO-RENAL SYNDROME: TYPE 5

- Pathophysiology:
  - Mechanisms of secondary heart-kidney interaction?
  - Co-existent vs. genuine bidirectional interaction?
- Needed:
  - Studies to evaluate concomitant acute kidney/myocardial injury in sepsis

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SUMMARY

- **Heart-kidney interaction:**
  - Exceedingly common/increasing
  - Presence can induce/exacerbate or acceleration dysfunction/injury of other
  - May be classified into several syndromes
  - Several knowledge gaps exist

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THANK YOU FOR YOUR ATTENTION!