

Acute Kidney Injury e progressione della malattia renale cronica

Enrico Fiaccadori

Unita' di Fisiopatologia dell'Insufficienza
Renale Acuta e Cronica
Dipartimento di Medicina Clinica e Sperimentale
Universita' degli Studi di Parma

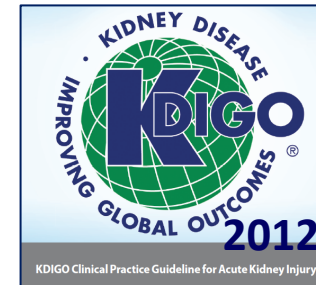
Unita' Operativa Complessa di Clinica e Immunologia Medica e
Terapia Intensiva Nefrologica
Azienda Ospedaliera-Universitaria Parma



Agenda

- Insufficienza renale acuta vs danno renale acuto (Acute Kidney Injury, AKI)
- Definizione e classificazione dell'AKI
- Epidemiologia e prognosi dell'AKI
- Progressione dall'AKI alla CKD: un continuum di malattia
- Cosa si puo' fare

AKI: diagnosi e classificazione



Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ≥0.3 mg/dl (≥26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m ²	<0.3 ml/kg/h for ≥24 hours OR Anuria for ≥12 hours

Nello stadio 3,
soprattutto nei pazienti
in terapia intensiva,
spesso si rende
necessaria la dialisi

Acute kidney injury: an increasing global concern

Norbert H Lameire, Arvind Bagga, Dinna Cruz, Jan De Maesseneer, Zoltan Endre, John A Kellum, Kathleen D Liu, Ravindra L Mehta, Neesh Pannu, Wim Van Biesen, Raymond Vanholder

Lancet 2013; 382: 170-79

Acute kidney injury: global health alert

Philip Kam Tao Li¹, Emmanuel A. Burdmann² and Ravindra L. Mehta³, for the World Kidney Day Steering Committee 2013⁴

Kidney International (2013) **83**, 372-376;

World Incidence of AKI: A Meta-Analysis

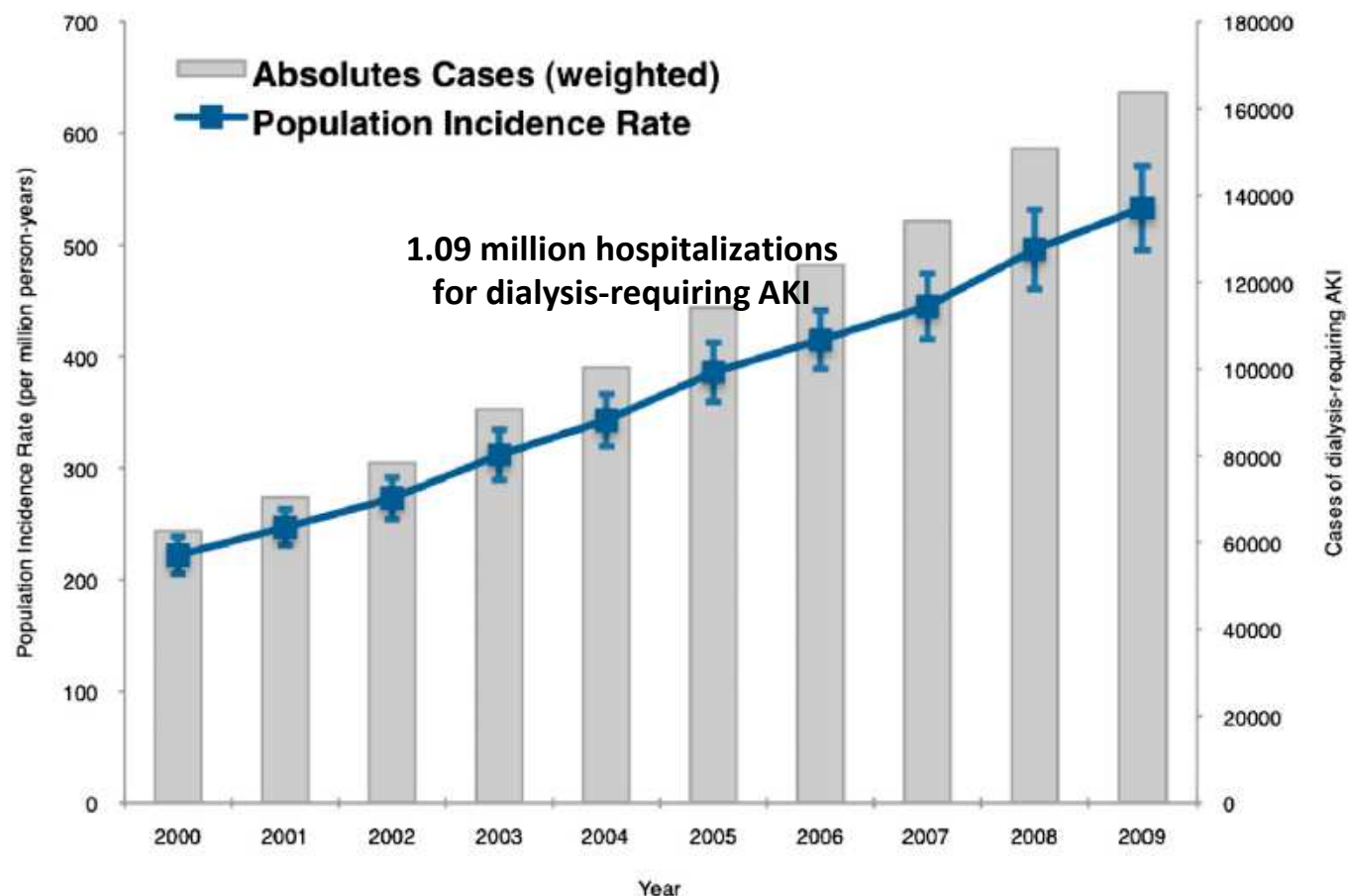
Paweena Susantitaphong,^{*,††} Dinna N. Cruz,[§] Jorge Cerda,^{||} Maher Abulfaraj,^{*} Fahad Alqahtani,^{*} Ioannis Koulouridis,^{*,†} and Bertrand L. Jaber,^{*,†} for the Acute Kidney Injury Advisory Group of the American Society of Nephrology

Table 2. Pooled incidence rate of AKI according to the KDIGO-equivalent definition

Subgroup	Studies (n)	Patients (n)	Patients with AKI (n)	AKI Incidence Rate (%)	95% Confidence Interval	Test for Heterogeneity	
						I ² Index	Q Test P Value
All	154	3,585,911	573,424	23.2	21.0 to 25.7	99.9	<0.001
Age category							
Adults	130	3,571,691	569,861	21.6	19.3 to 24.1	99.9	<0.001
Children	24	14,220	303	33.7	26.9 to 41.3	98.3	<0.001
Clinical setting							
Community acquired	7	548,398	4897	8.3	1.6 to 33.0	99.9	<0.001
Critical care	41	888,604	272,580	31.7	28.6 to 35.0	99.9	<0.001
Cardiac surgery	42	164,333	33,137	24.3	20.4 to 28.8	99.7	<0.001
Trauma	4	14,947	2557	19.9	13.6 to 28.2	98.7	<0.001
Heart failure	1	682	221	32.4	29.0 to 36.0	—	—
Hematology/oncology	3	2401	453	21.3	7.5 to 47.6	99.2	<0.001
Nephrotoxins	4	17,786	1681	12.2	6.2 to 22.7	98.7	<0.001
Hospital acquired, unspecified	52	1,948,760	257,878	20.9	17.2 to 25.2	99.9	<0.001

Temporal Changes in Incidence of Dialysis-Requiring AKI

Raymond K. Hsu,* Charles E. McCulloch,[†] R. Adams Dudley,* Lowell J. Lo,* and Chi-yuan Hsu*



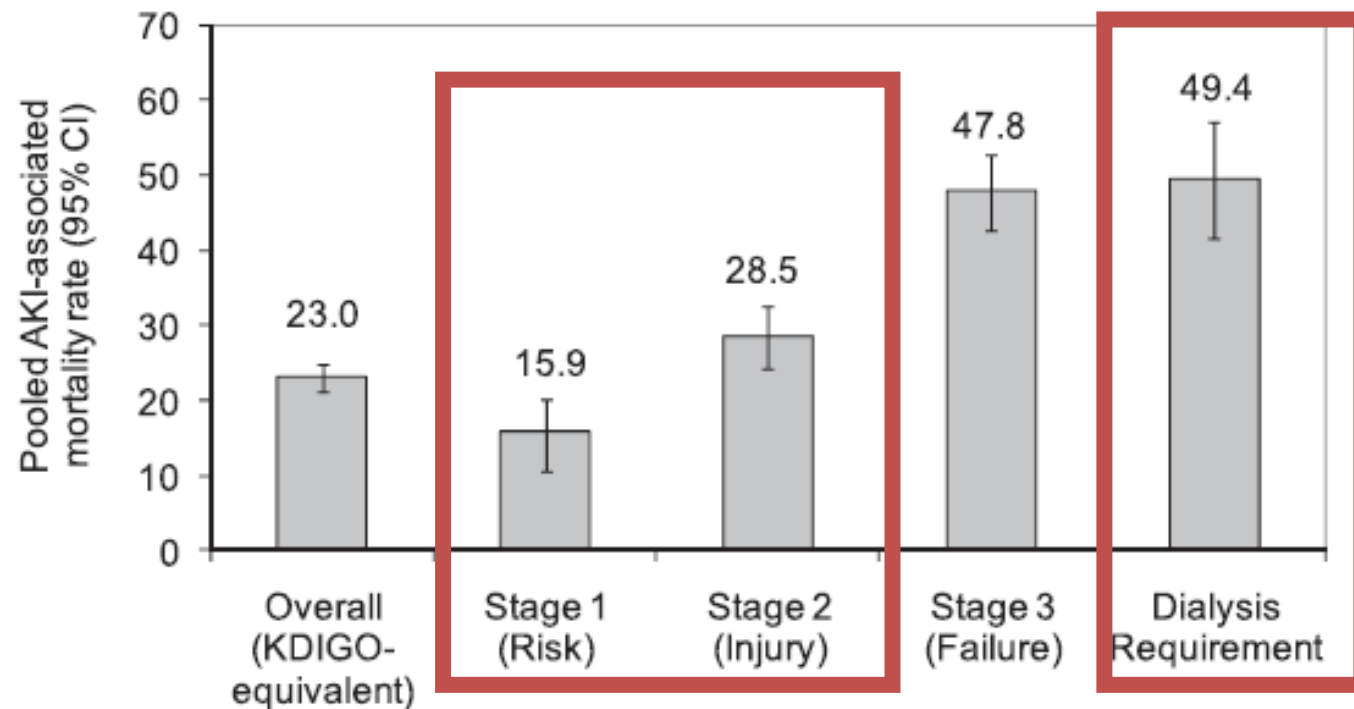
Il numero di pazienti con AKI senza necessita' di dialisi e' circa dieci volte quello dei pazienti con AKI che necessitano di dialisi

Figure 1. Population incidence of dialysis-requiring AKI in the United States from 2000 to 2009 (absolute count and incidence rate per million person-years). I bars represent 95% CIs for incidence rates. The number of cases of dialysis-requiring AKI increased from 63,000 in 2000 to almost 164,000 in 2009; the population incidence increased at 10% per year from 222 to 533 cases/million person-years.

World Incidence of AKI: A Meta-Analysis

Paweena Susantitaphong,^{*,†} Dinna N. Cruz,[§] Jorge Cerda,^{||} Maher Abulfaraj,^{*} Fahad Alqahtani,^{*} Ioannis Koulouridis,^{*,†} and Bertrand L. Jaber,^{*,†} for the Acute Kidney Injury Advisory Group of the American Society of Nephrology

**La mortalita'
dell'AKI e'
particolarmente
elevata, in tutti
gli stadi di
malattia**



No. studies	110	26	25	25	31
No. patients with AKI	429,535	8,226	42,354	42,354	6,534

L'incremento di mortalita' a breve e lungo termine dopo un episodio di AKI e' piu' spesso secondario a cause cardiovascolari

TABLE 3 In-hospital Outcome

	(+) CIN (n = 381)*	(-) CIN (n = 1,599)*
Patients with CKD		
Death	6.3%	0.8%
Cardiac death	4.0%	0.5%
Coronary artery bypass grafting	5.8%	0.5%
Major adverse cardiac event	9.3%	1.1%
Packed red cell transfusion	28%	6%
Vascular surgery of access site	5.6%	2.6%
Postprocedure length of stay, mean $\pm$ SD (d)	6.8 $\pm$ 7.1	2.3 $\pm$ 2.5
Patients without CKD		
Death	2.5%	0.1%
Cardiac death	2.0%	0%
Coronary artery bypass grafting	5.0%	0.7%
Major adverse cardiac events	6.8%	0.9%
Packed red cell transfusion	10%	2%
Vascular surgery of access site	4.6%	0.8%
Postprocedure length of stay (mean $\pm$ SD) (d)	3.6 $\pm$ 5.1	1.8 $\pm$ 2.4

*p <0.0001 for both groups.

TABLE 4 Cumulative One-year Outcome (hierarchical classification)

	(+) CIN	(-) CIN	p Value
Patients with CKD			
Death	22.6%	6.9%	<0.0001
Out-of-hospital death	16.3%	6.1%	<0.0001
Q-wave myocardial infarction	0.3%	0.8%	0.31
Target vessel revascularization	14.0%	16.9%	0.20
Major adverse cardiac events	36.9%	24.6%	<0.0001
Patients without CKD			
Death	8.0%	2.7%	<0.0001
Out-of-hospital death	6.5%	2.6%	<0.0001
Q-wave myocardial infarction	0.6%	0.5%	0.60
Target vessel revascularization	19.8%	18.7%	0.52
Major adverse cardiac events	28.4%	21.9%	<0.0001

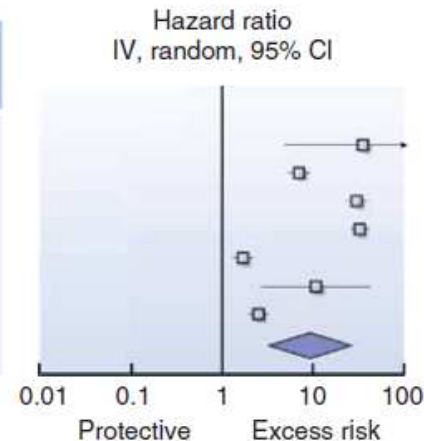
Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis

Steven G. Coca^{1,2,3}, Swathi Singanamala^{1,3} and Chirag R. Parikh^{1,2}

a

Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Weiss <i>et al.</i> (13)	10.0	32.79 (4.30–249.77)
Amdur <i>et al.</i> (22)	15.5	6.64 (5.05–8.74)
Lo <i>et al.</i> (11)	15.5	28.08 (21.01–37.53)
James <i>et al.</i> (16)	15.6	29.99 (24.32–36.99)
James <i>et al.</i> (15,23)	15.5	1.60 (1.20–2.14)
Ando <i>et al.</i> (19)	12.4	9.91 (2.48–39.63)
Ishani <i>et al.</i> (21)	15.6	2.33 (1.83–2.96)
Total (95% CI)	100.0	8.82 (3.05–25.48)

Heterogeneity: $\tau^2 = 1.87$; $\chi^2 = 446.89$, d.f. = 6 ($P < 0.00001$); $I^2 = 99\%$. Test for overall effect: $Z = 4.02$ ($P < 0.0001$)

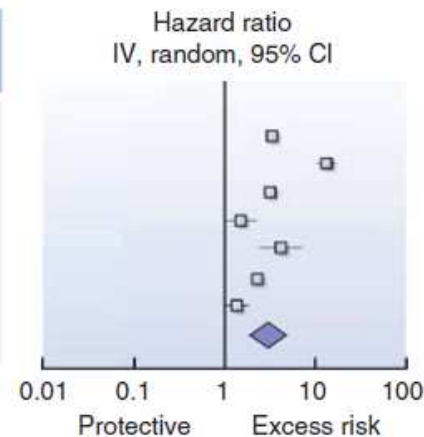


Il rischio di progredire verso una CKD e' aumentato di 10 volte

b

Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Newsome <i>et al.</i> (14)	15.0	3.26 (2.87–3.70)
Ishani <i>et al.</i> (20)	14.8	12.99 (10.57–15.96)
Wald <i>et al.</i> (17)	14.9	3.22 (2.70–3.85)
Hsu <i>et al.</i> (10)	13.5	1.47 (0.95–2.28)
James <i>et al.</i> (15,23)	12.5	4.15 (2.32–7.41)
Lafrance <i>et al.</i> (18)	15.0	2.33 (2.08–2.61)
Choi <i>et al.</i> (12)	14.4	1.37 (1.02–1.84)
Total (95% CI)	100.0	3.10 (1.91–5.03)

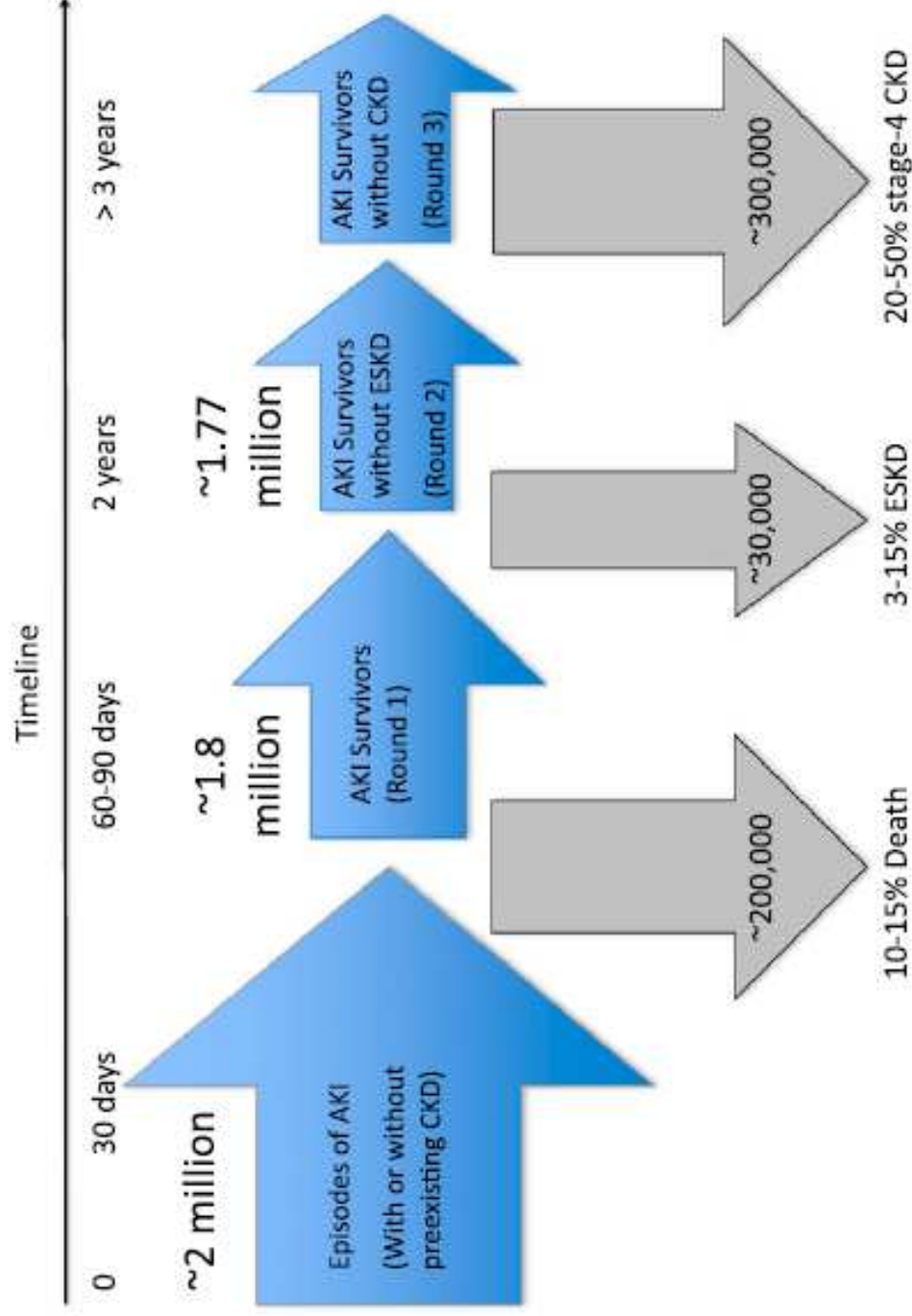
Heterogeneity: $\tau^2 = 0.40$; $\chi^2 = 252.85$, d.f. = 6 ($P < 0.00001$); $I^2 = 98\%$. Test for overall effect: $Z = 4.58$ ($P < 0.00001$)



Il rischio di dialisi cronica e' aumentato di 4 volte

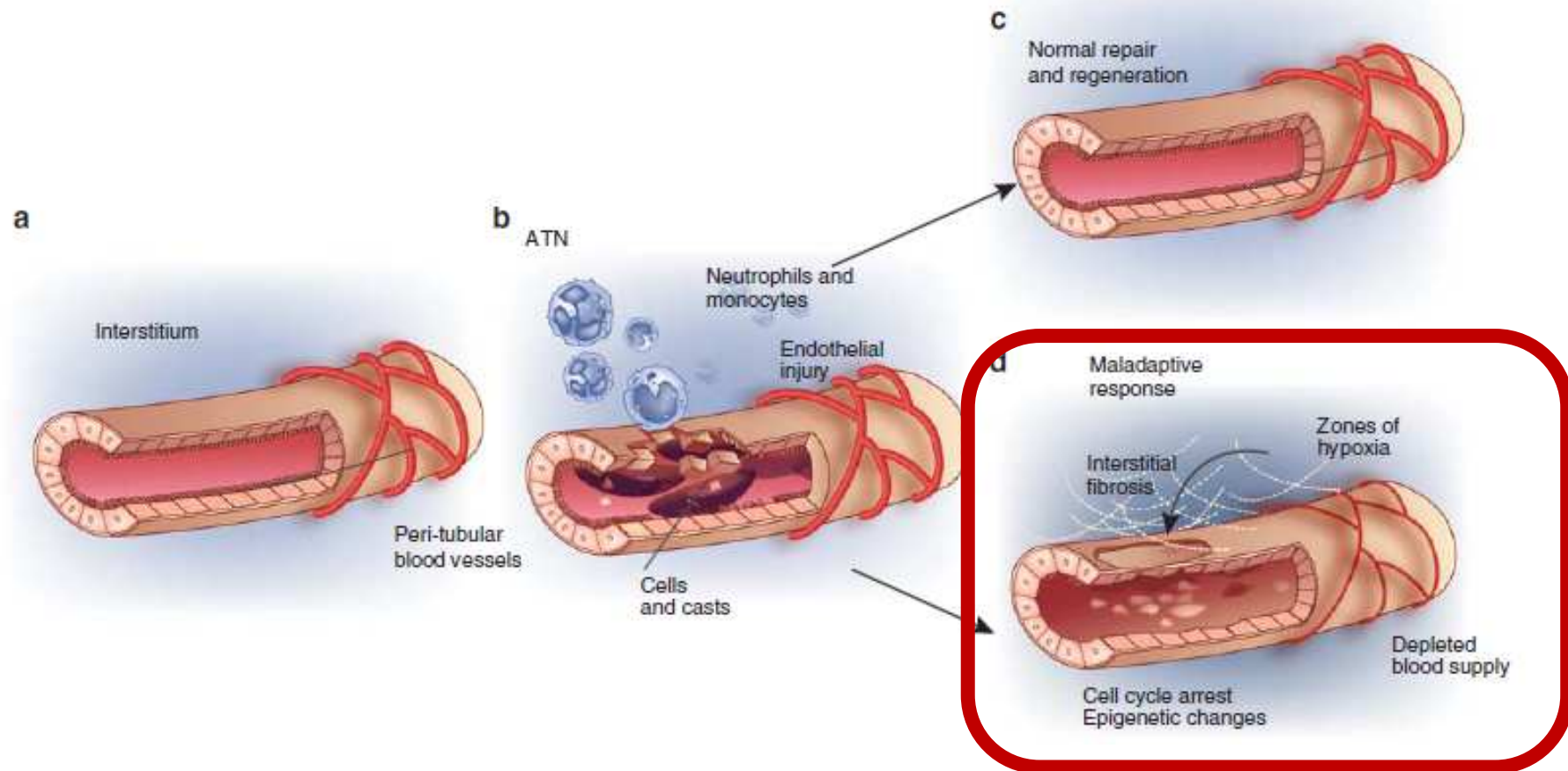
Kidney International (2012) **81**, 442–448

Estimates of AKI burden in developed countries and outcomes of survivors.

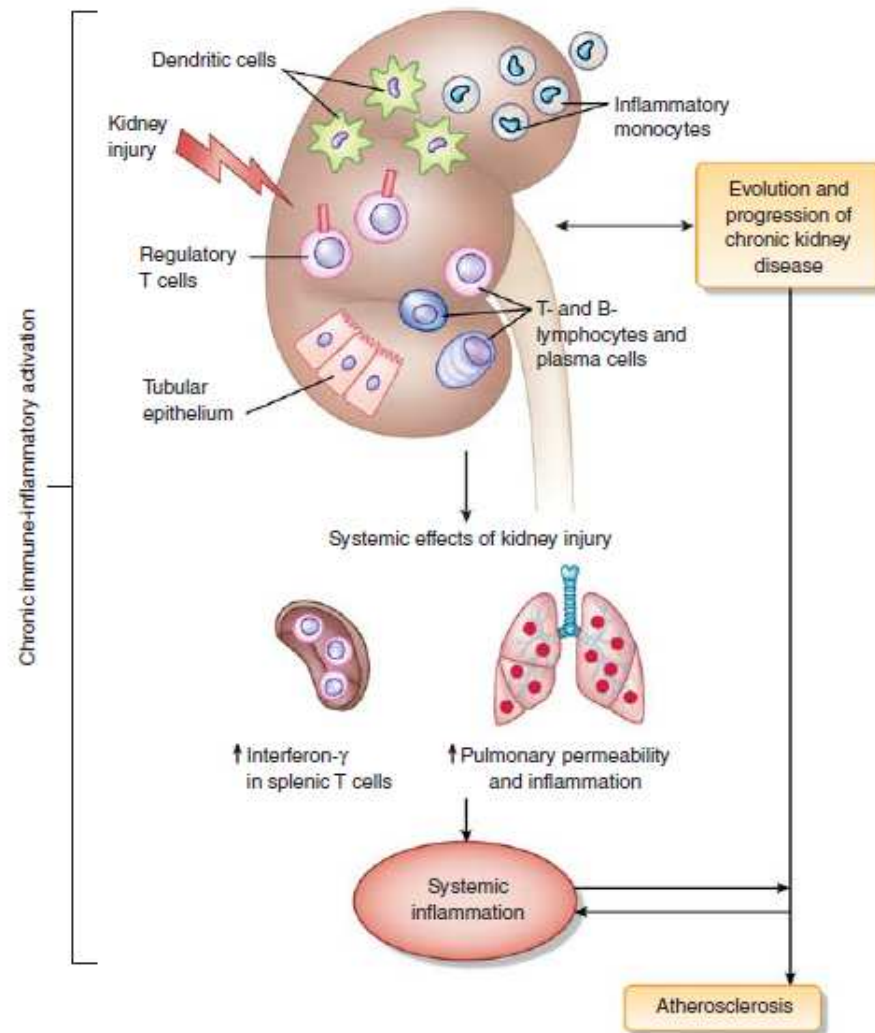


**Quali sono i meccanismi che determinano
la transizione dall'AKI alla CKD**

La fibrosi renale dopo un episodio di AKI come espressione di una risposta maladattativa all'infiammazione innescata dal danno da ischemico



Novel inflammatory mechanisms of accelerated atherosclerosis in kidney disease



**L'inflammation
secondaria
all'ischemia renale
come primum movens
di infiammazione
sistemica e
aterosclerosi
accelerata**



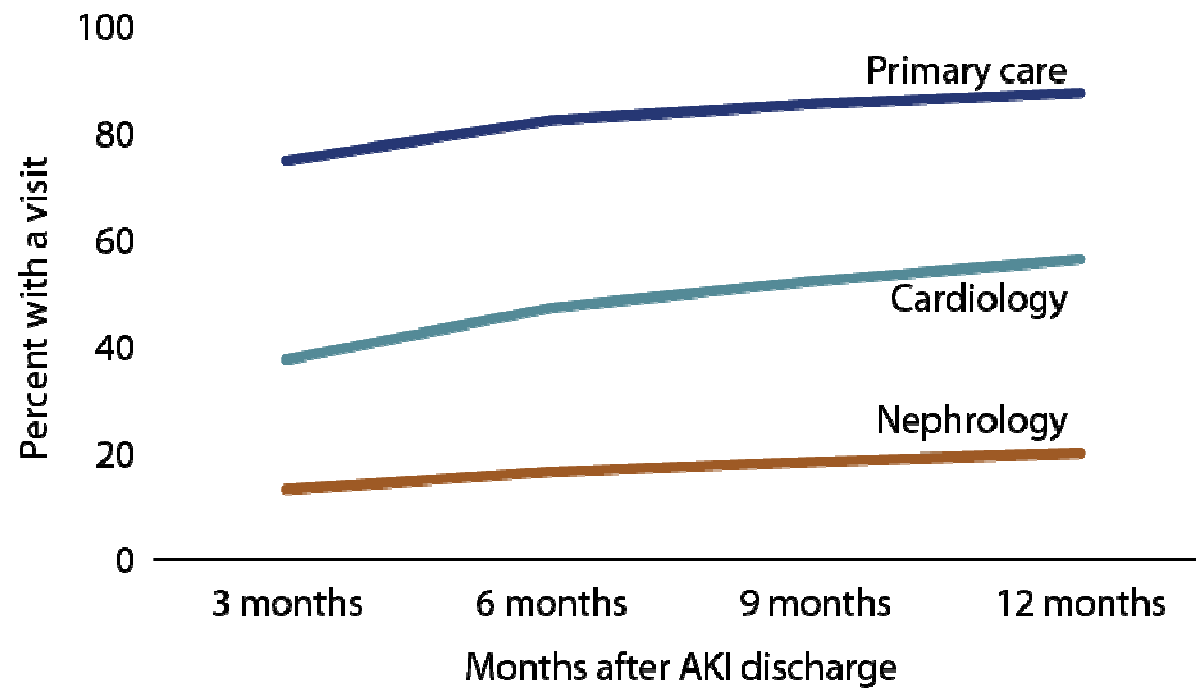
**Aumentato rischio di
eventi e decessi da
cause cardiovascolari**

Prevenzione della CKD dopo un episodio di AKI

-Il ruolo del follow-up nefrologico

-Il ruolo dell'approccio farmacologico

Visite ambulatoriali dopo un episodio di AKI



Medicare AKI patients age 66 & older, 2009–2010.

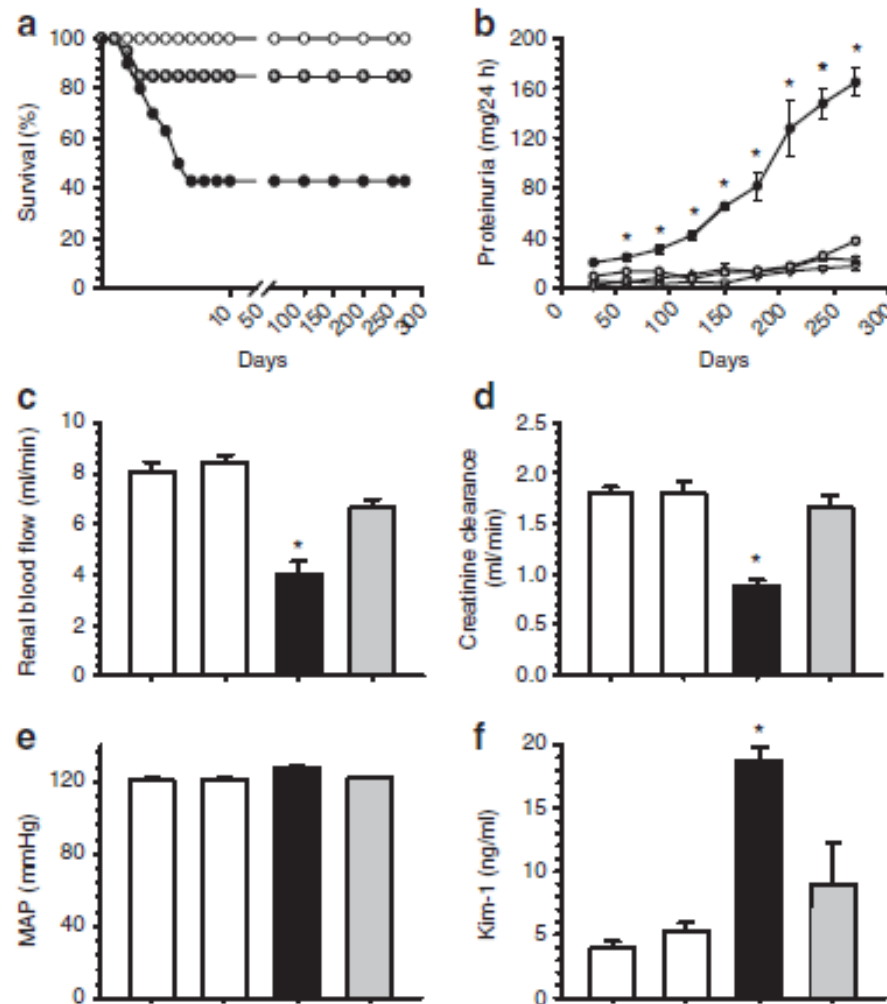
Canadian Society of Nephrology Commentary on the 2012 KDIGO Clinical Practice Guideline for Acute Kidney Injury

Le linee guida KDIGO 2013 sull'AKI suggeriscono che dopo un episodio di AKI i pazienti, dovrebbero essere valutati in termini di entità del recupero della funzione renale, CKD di nuova insorgenza o peggioramento di pre-esistente CKD a 3 mesi dall'episodio. Tale raccomandazione può avere implicazioni rilevanti sul sistema sanitario nazionale, in quanto il rapporto costo efficacia questa strategia non è noto

Tra i problemi non risolti l'appropriato trattamento dei pazienti dopo un episodio di AKI, chi debba essere sottoposto a follow-up (tutti o solo pazienti a rischio più elevato), l'identificazione dei pazienti più a rischio di progressione, e quali strategie di prevenzione debbano essere messe in atto

Spironolactone prevents chronic kidney disease caused by ischemic acute kidney injury

Jonatan Barrera-Chimal^{1,2}, Rosalba Pérez-Villalva^{1,2}, Roxana Rodríguez-Romo^{1,2}, Juan Reyna^{1,2}, Norma Uribe³, Gerardo Gamba^{1,2} and Norma A. Bobadilla^{1,2}



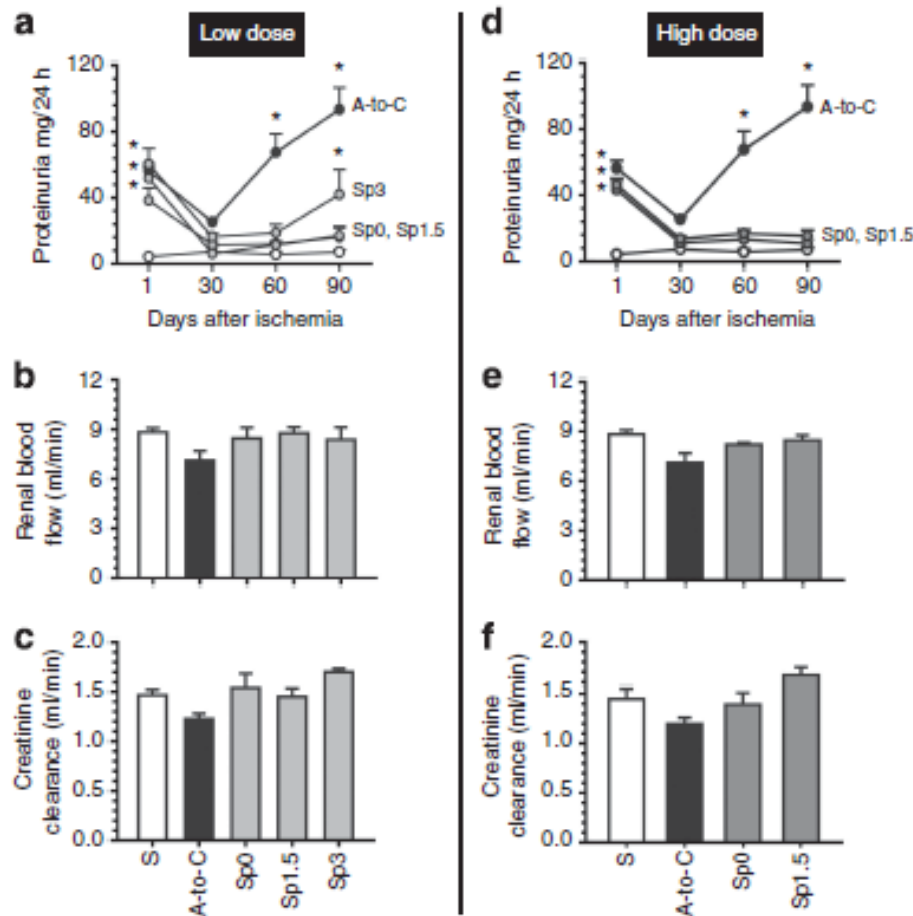
**In condizioni sperimentali
l'AKI determina sviluppo
di CKD**

**Il pre-trattamento con
spironolattone previene il
rischio di progressione**

Kidney Int 2013; 83:93-103

Spironolactone prevents chronic kidney disease caused by ischemic acute kidney injury

Jonatan Barrera-Chimal^{1,2}, Rosalba Pérez-Villalva^{1,2}, Roxana Rodríguez-Romo^{1,2}, Juan Reyna^{1,2}, Norma Uribe³, Gerardo Gamba^{1,2} and Norma A. Bobadilla^{1,2}



**Lo spironolattone
puo' prevenire lo
sviluppo di CKD
anche se
somministrato
dopo l'insulto
ischemico**

AKI Transition of Care: A Potential Opportunity to Detect and Prevent CKD

Stuart L. Goldstein, Bertrand L. Jaber,[†] Sarah Faubel,[‡] and Lakhmir S. Chawla,[§] for the Acute Kidney Injury Advisory Group of the American Society of Nephrology*

Clin J Am Soc Nephrol 8: 476–483, 2013.

Cause di CKD

- Nefropatie primitive (glomerulonefrite, nefrite interstiziale etc.)
- Nefropatie secondarie (diabete, ipertensione etc.)
- Malattie congenite (rene policistico etc.)
- Infezioni e litiasi vie urinarie
- Acute Kidney Injury**

Acute kidney injury and chronic kidney disease: an integrated clinical syndrome

Lakhmir S. Chawla^{1,2} and Paul L. Kimmel^{2,3}

La distinzione tra AKI e CKD puo' essere artificiosa nel medio e lungo termine

Il nuovo concetto di continuum di malattia nell'a CKD post AKI: una sindrome integrata caratterizzata da riduzione della funzione renale e dalla possibile progressione della riduzione della funzione renale

Kidney International (2012) **82**, 516–524