Atteintes rénales associées aux cardiopathies congénitales

Mirela Bojan, MD. PhD.
Anesthésie et Réanimation
Pôle Cardiopathies Congénitales

m.bojan@ghpsj.fr

Hôpital
Marie Lannelongue

UNIVERSITÉ
PARIS-SUD 11

Insuffisance rénale aiguë

Epidemiologie

Physiopathologie

Diagnostic

Prévention

Traitement

Insuffisance rénale chronique

A CASE OF CRUSH INJURY WITH RENAL FAILURE

BY

D. BEALL, Ph.D.

AND

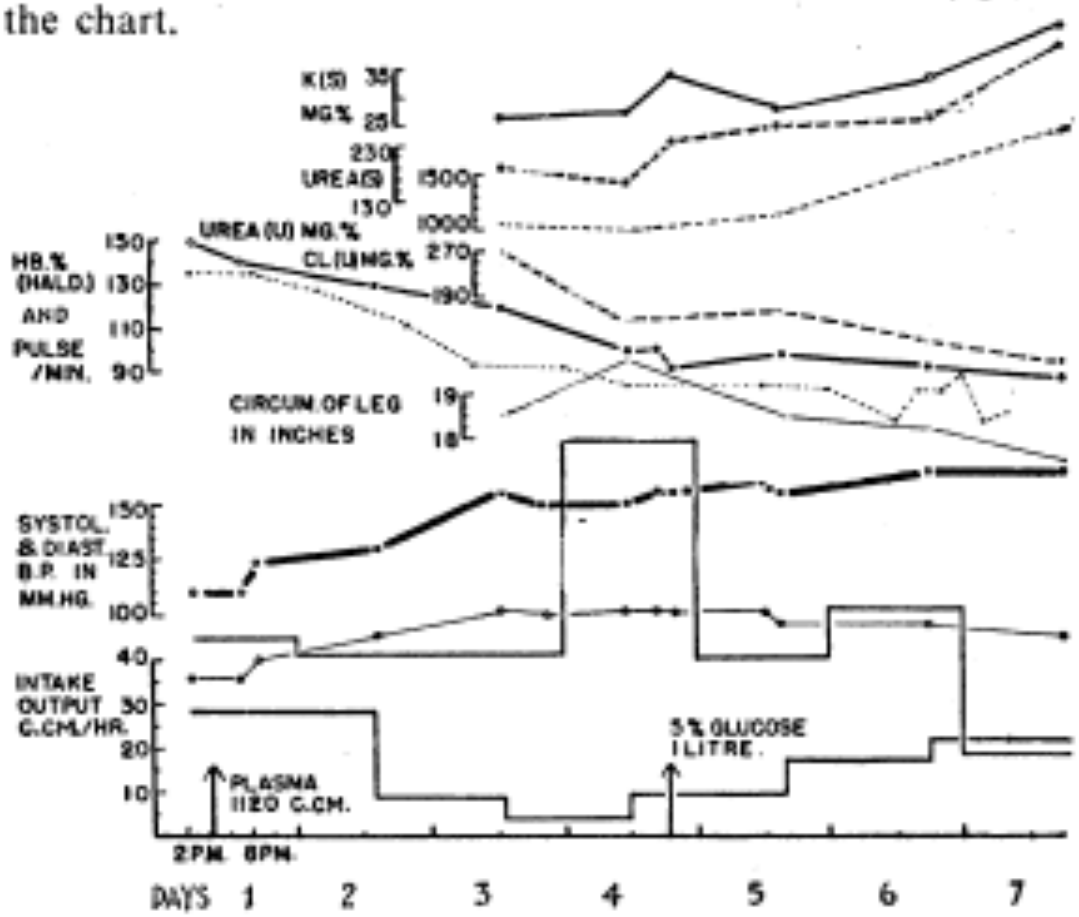
E. G. L. BYWATERS, M.B., M.R.C.P.,
British Postgraduate Medical School

R. H. R. BELSEY, F.R.C.S.

AND

J. A. R. MILES, M.A., M.B., B.Ch.
St. Thomas's Hospital

fluid balance, pulse rate, and blood-pressure readings, in the chart.



Définition IRA

	Creatinine criteria		Urine output criteria	
	RIFLE	pRIFLE and nRIFLE	RIFLE	pRIFLE
Risk	Increased creatinine x1.5 or GFR decreases >25%	Increased creatinine x1.5 or GFR decreases >25%	UO ≤0.5 mL/kg/h × 6 h	UO ≤0.5 mL/kg/h × 8 h
Injury	Increased creatinine x2 or GFR decreases >50%	Increased creatinine x2 or GFR decreases >50%	UO ≤0.5 mL/kg/h × 12 h	UO ≤0.5 mL/kg/h × 16 h
Failure	Increased creatinine x3 or GFR decreases >75% or creatinine >4 mg/dL (acute rise of >4 mg/dL)	Increased creatinine x3 or GFR decreases >75% or GFR <35 mL/min/1.73 m^2	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h

Metha RL, Crit Care 2007, Akcan-Arikan, Kidney Int 2007

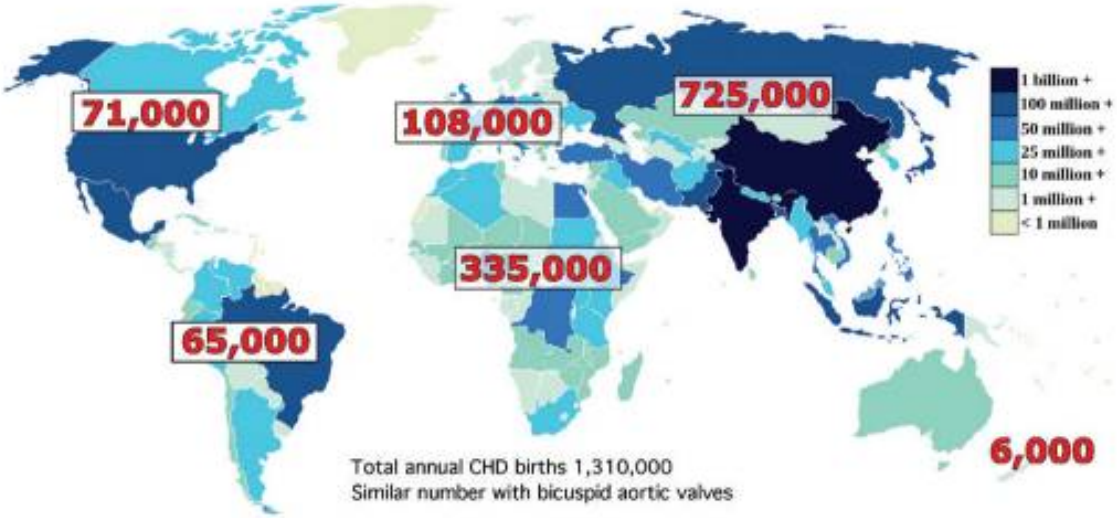


Fig. 2. Total annual births of children with congenital heart disease by continent, based on Table 1 and data on total births. The panel at the side indicates the population ranges of the different countries.

L'indidence de l'IRA postopératoire modérée/sévère est ≈ 6 par 1000
40% chez l'enfant, 50% chez le nourrisson et **60% chez le nouveau-né**

Li, Crit Care Med 2011 Blinder JTCVS 2012 Morgan, J Pediatr 2013

L'IRA, est un facteur de risque indépendant de DC postopératoire

TABLE 3. Factors independently associated with mortality in infants with acute kidney injury

Factor	Odds ratio	95% Confidence interval	*P* value
No AKI	Reference	—	—
AKI stage I	1.3	0.4–4.1	.70
AKI stage II	5.1	1.7–15.2	.004
AKI stage III	9.5	2.9–30.7	.0002
Single ventricle	2.6	1.1–6.2	.03
Circulatory support	7.0	1.8–28	.006

Blinder, J Cardiovasc Surg 2012

IRA grave nécessitant le recours à la dialyse

Studies reporting post-operative acute renal failure (ARF) treated with peritoneal dialysis in children operated on for congenital heart disease.

Reference	Location	Year	ARF (%)	Mortality in ARF patients (%)	*n*	Study design
Rigden et al. (10)	UK, London	1982	5.3	50	456	Prospective
Baxter et al. (2)	UK, London	1985	4.0	72	441	Retrospective
Gomez-Campdera et al. (7)	Spain, Madrid	1988	9.0	75	156	Retrospective
Hanson et al. (8)	USA, Colorado, Denver	1989	7.7	67	338	Retrospective
Shaw et al. (11)*	UK, Leeds	1991	2.9	68	1181	Retro-prospective
Vricella et al. (13)†	USA, California	1992	22.0	30	45	Retrospective
Giuffre et al. (6)	Canada, Toronto and Calgary	1992	1.6	58	2782	Retrospective
Picca et al. (9)	Italy, Rome	1995	2.7	79	2262	Case–control
Werner et al. (14)	Canada, Vancouver	1997	5.2	47	618	Retrospective
Sorof et al. (12)	USA, Texas, Houston	1999	5.0	20	882	Retrospective
Dittrich et al. (5)‡	Germany, Berlin	1999	14.0	27	81	Prospective
Chan et al. (4)	China, Hong Kong	2003	17.0	29	182	Retrospective
Xinjin et al. (15)	China, Beijing	2003	2.1	25	576	Retrospective
Boigner et al. (3)	Austria, Vienna	2004	5.4	40	1141	Retrospective
Baskin et al. (1)	Turkey, Ankara	2005	32.8	67	64	Retrospective
Present study	Denmark, Aarhus	2006	11.5	20	1128	Prospective

n, number of patients included in the study.
*519 were closed heart surgeries. The incidence of ARF after open heart surgery was 3.6%.
†Neonates undergoing heart transplantation.
‡Infants of <1 year using cardiopulmonary bypass during surgery.

Pedersen, Acta Anaesth Scand 2007

Necker : 2000-2008, 3014 interventions concernant 2651 nouveau-nés et nourrissons de moins d'un an, 2176 CEC,115 ARF dialysés (5,2%).

Long-term Risk of CKD in Children Surviving Episodes of Acute Kidney Injury in the Intensive Care Unit: A Prospective Cohort Study

Outcome Variables	AKIN Stage 1	AKIN Stage 2	AKIN Stage 3	Total[a]
Microalbuminuria or proteinuria[c]	2 (4.5)	5 (10.6)	5 (14.3)	12 (9.5)
GFR <60 mL/min/1.73 m^2[c]	0 (0)	0 (0)	1 (2.9)	1 (0.8)
GFR = 60-90 mL/min/1.73 m^2	24 (54.5)	14 (29.8)	10 (28.6)	48 (38.1)
Hypertension	0 (0)	3 (6.4)	1 (2.9)	4 (3.2)
Hyperfiltration	1 (2.3)	6 (12.8)	4 (11.4)	11 (8.7)

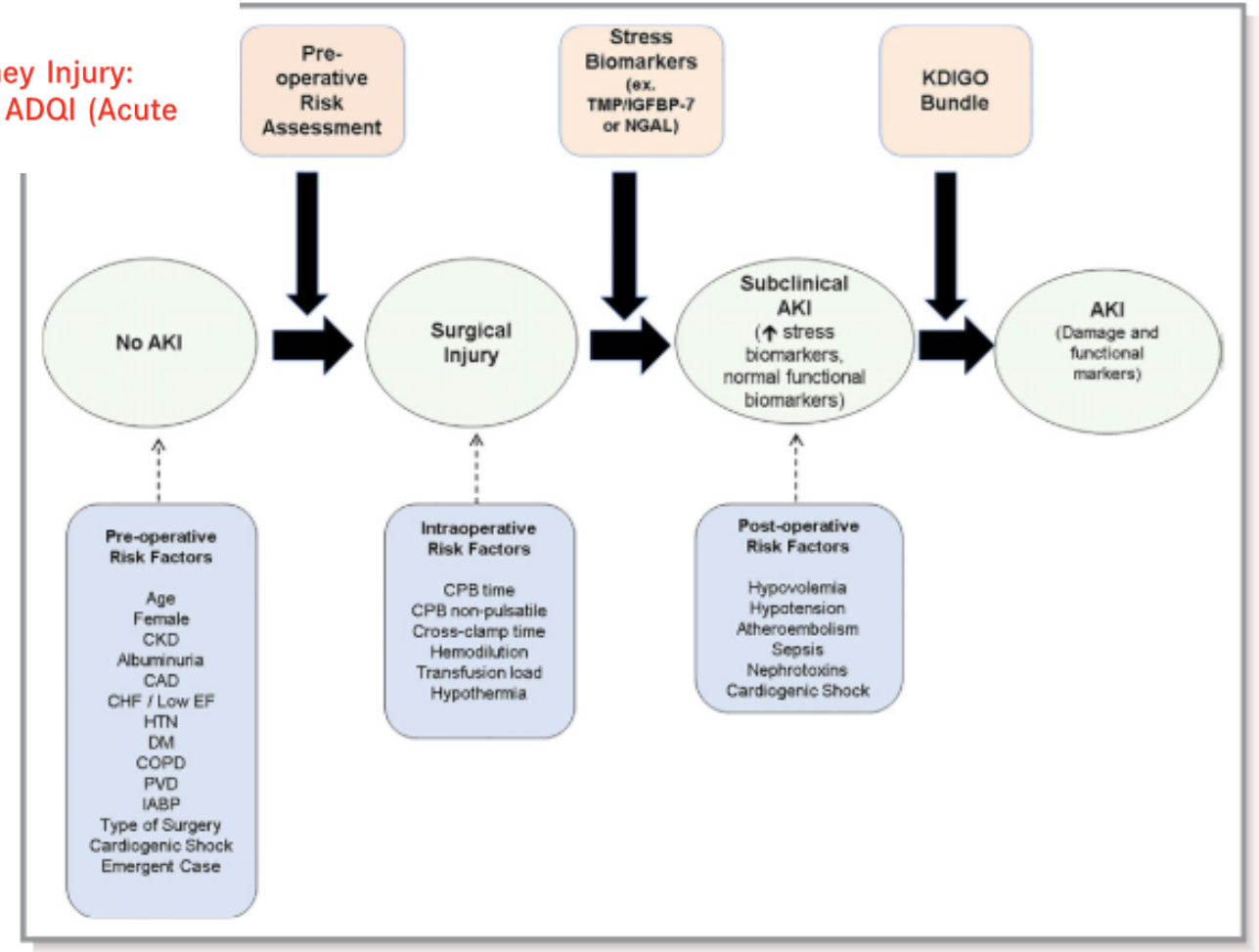
Mammen, Am J Kidney Dis 2012

SPECIAL REPORT

American Heart Association | American Stroke Association

Cardiac and Vascular Surgery–Associated Acute Kidney Injury: The 20th International Consensus Conference of the ADQI (Acute Disease Quality Initiative) Group

- Peu de facteurs prédictifs de l'IRA
- Peu de moyens de monitoring du risque d'IRA en peropératoire
- Peu de moyens thérapeutiques une fois l'IRA installée



Insuffisance rénale aiguë

Epidemiologie

Physiopathologie

Diagnostic

Prévention

Traitement

Insuffisance rénale chronique

Glomérule	Tubule rénal
DFG ≈ filtration d'un volume équivalent à la volémie / 30min	réabsorption tubulaire = 99% du DFG
Processus passif (VO2 ↓↓)	représente 90% de la VO2 rénale
Débit sanguin cortical /	médullaire ≈ 10 : 1
Ht ≈ Ht systémique	Ht ≈ 50% Ht systémique
paO2 = 20-60 mmHg	paO2 = 15-30 mmHg (<15 dans la médullaire profonde)
Métabolisme aérobie	Métabolisme anaérobie de la médullaire profonde Métabolisme aérobie de la médullaire superficielle -> susceptibilité à l'hypoxie ++++

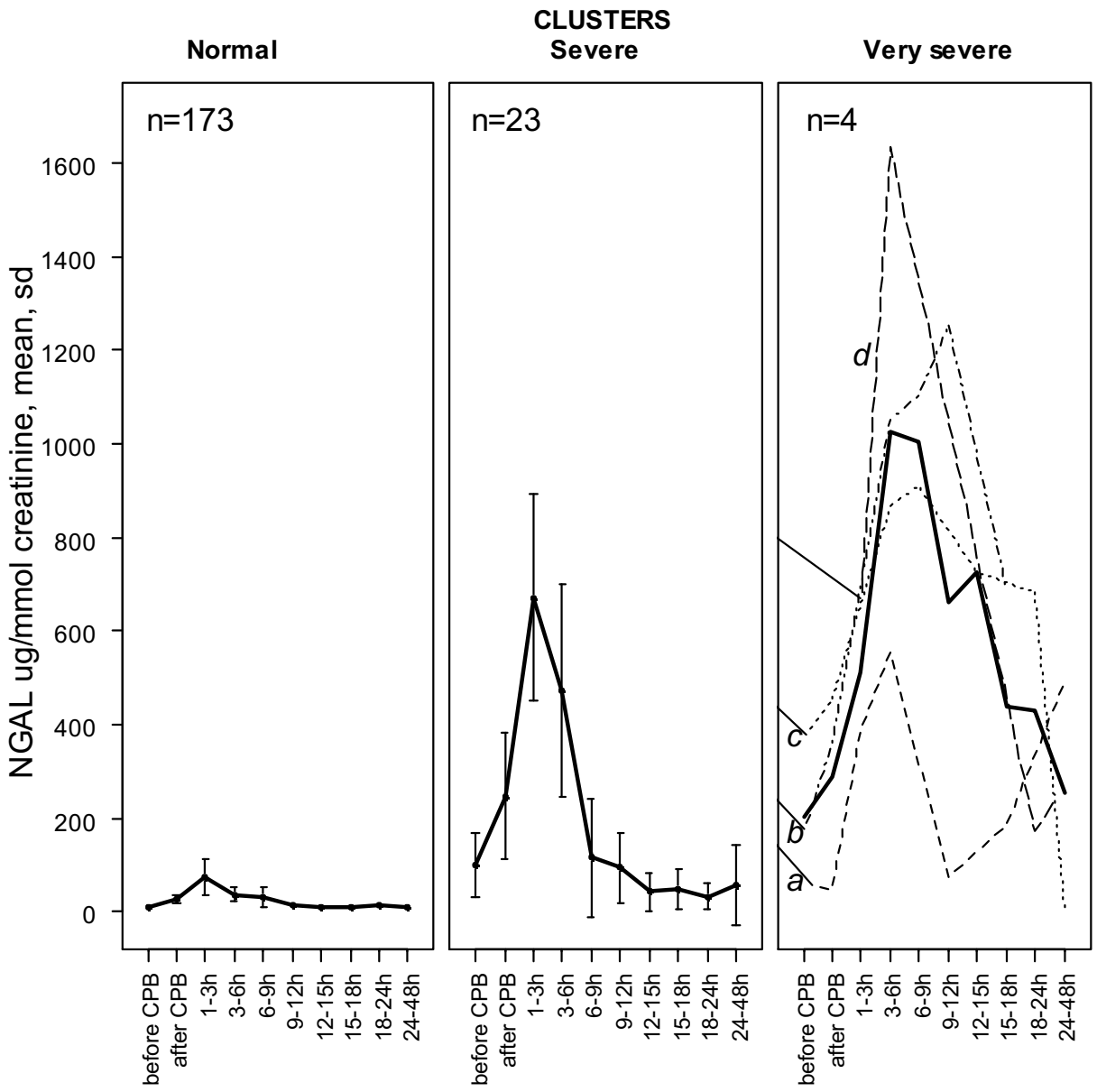
Adaptation postnatale de la fonction rénale

- DFG croît de 5 à 40 ml/min/1.73m^2 durant la première semaine
- Niveau élevé de l' Angiotensine II et de résistance vasculaire rénale

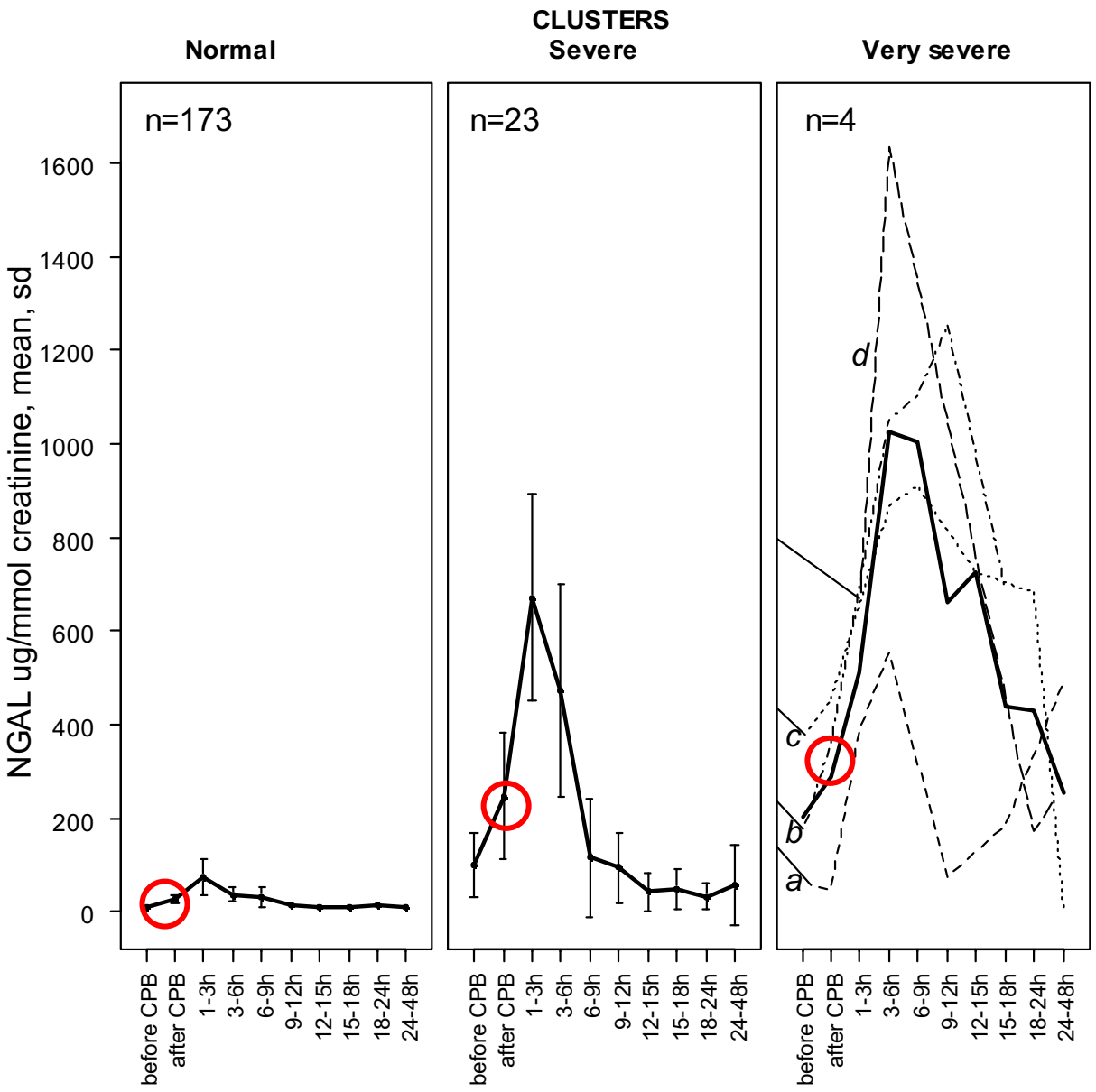
Les facteurs de risque d'IRA

Variables	% AKI cases	Adjusted OR	95% CI	P Value
Age				
> 30 days old and ≤ 2 years old	55%	1	…	…
> 2 and < 13 years old	27%	0.28	(0.16, 0.48)	< 0.0001
≥ 13 and < 18 years old	37%	0.3	(0.10, 0.88)	0.03
RACHS-1 category				
1 or 2	38%	1	…	…
3	44%	1.47	(0.83, 2.59)	0.2
4	71%	1.93	(0.50, 7.41)	0.3
Cardiopulmonary Bypass Time (minutes)				
0–60	22%	1	…	…
61–90	36%	2.14	(0.97, 4.72)	0.06
91–120	45%	2.47	(1.08, 5.65)	0.03
121–180	51%	3.2	(1.38, 7.44)	<0.01
> 180	68%	7.57	(2.6, 21.9)	<0.01

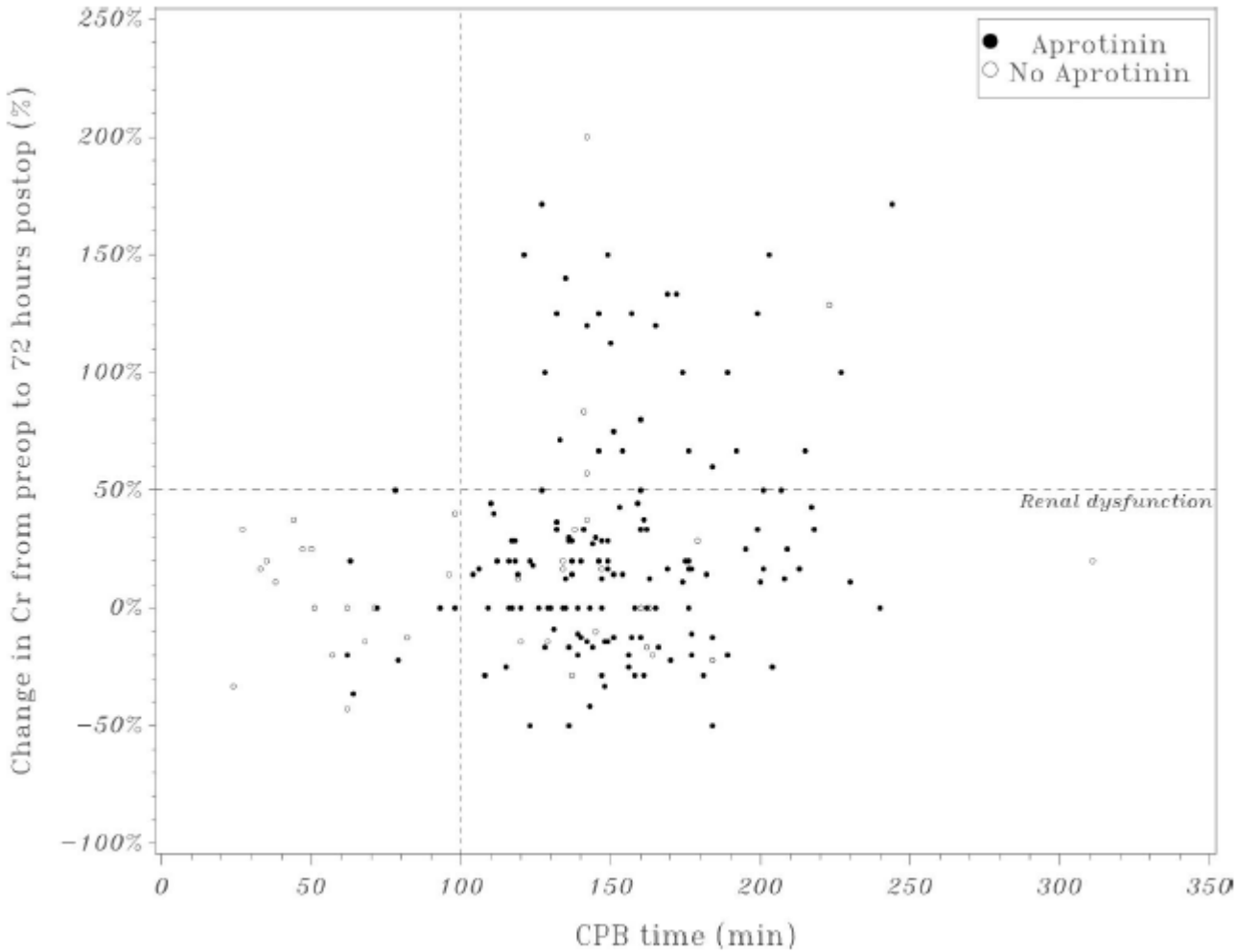
The TRIBE-AKI study, Li, Crit Care Med 2011



Bojan, Clin J Am Soc Nephrol 2014



Bojan, Clin J Am Soc Nephrol 2014



Adjusted OR of AKI for CPB time : 1.16, 95CI :[1.05-1.29]

Guzzetta, Anesth Analg 2009

Risk Factors for and Outcomes of Acute Kidney Injury in Neonates Undergoing Complex Cardiac Surgery

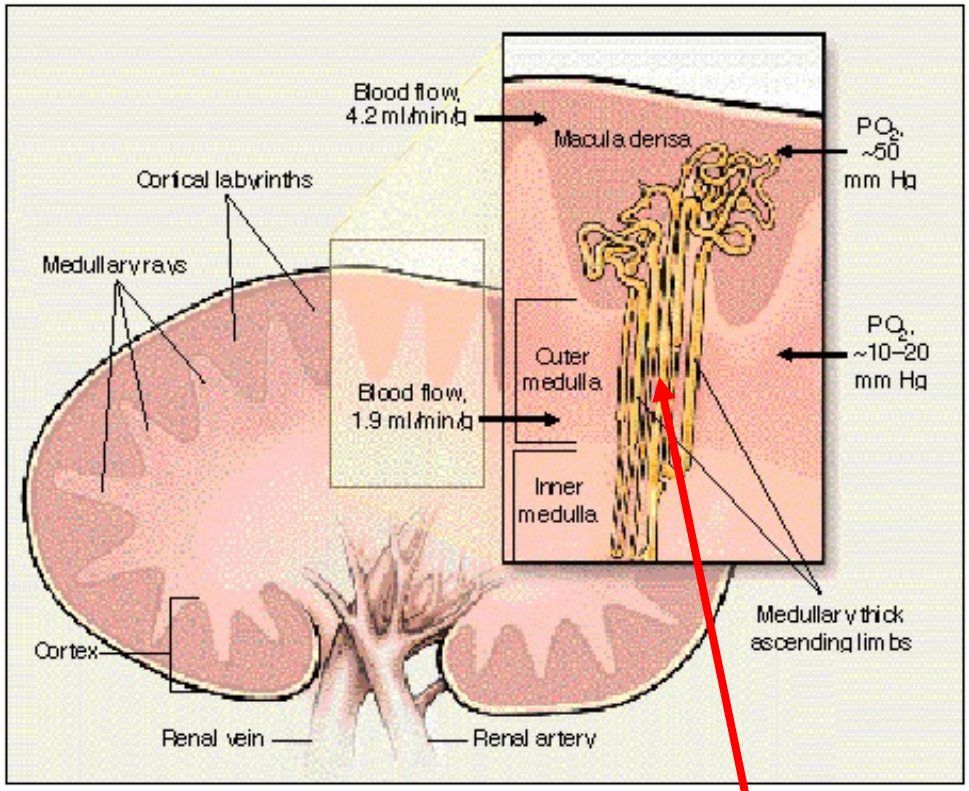
264 nouveau-nés avec chirurgie cardiaque
Incidence IRA = **64%**

Risk factor	Adjusted OR [95% CI]
Age at surgery (days)	0.97 [0.95 – 0.99]
Gestational age (weeks)	0.83 [0.69 – 0.99]

Morgan, J Pediatr 2013

L'IRA associée à la chirurgie cardiaque est due à une atteinte hypoxique de la branche ascendante de la l'anse de Henle dans la médullaire externe

Dans des conditions normales



90% de la DO_2 rénale !

IRA

1. **Vasocontriction rénale et hypoxie tubulaire**
2. **Dysfonction endothéliale par réduction de la disponibilité du NO**
3. **Atteinte des cellules tubulaires proximales**

- 40% réduction de la DO2 rénale
- 60% réduction du GFR
- 60% réduction de réabsorption du Na
- Pas de réduction de la VO_2 rénale !
- 70% augmentation de l'extraction rénale en O2

Redfors, Crit Care Med 2010

SPECIAL REPORT

American Heart Association | American Stroke Association

Cardiac and Vascular Surgery–Associated Acute Kidney Injury: The 20th International Consensus Conference of the ADQI (Acute Disease Quality Initiative) Group

Les facteurs de risque intra- et postopératoires:

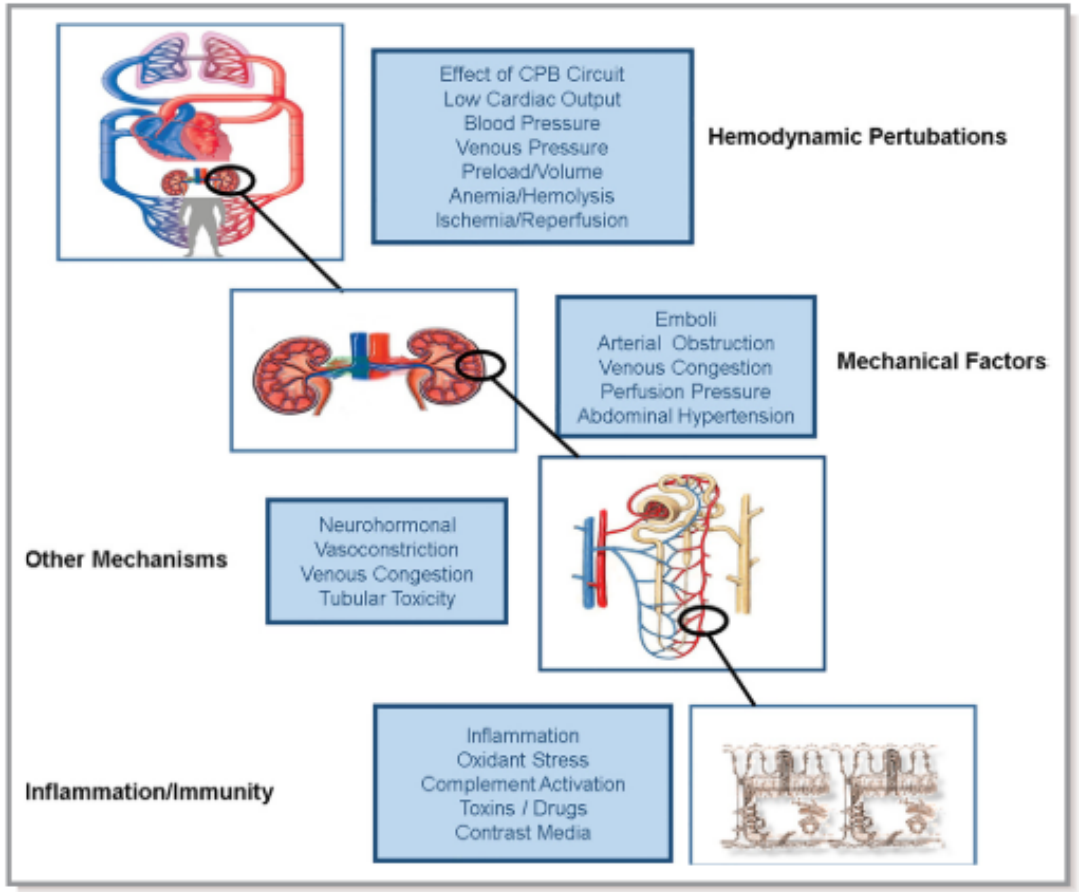
Ischémie / Reperfusion

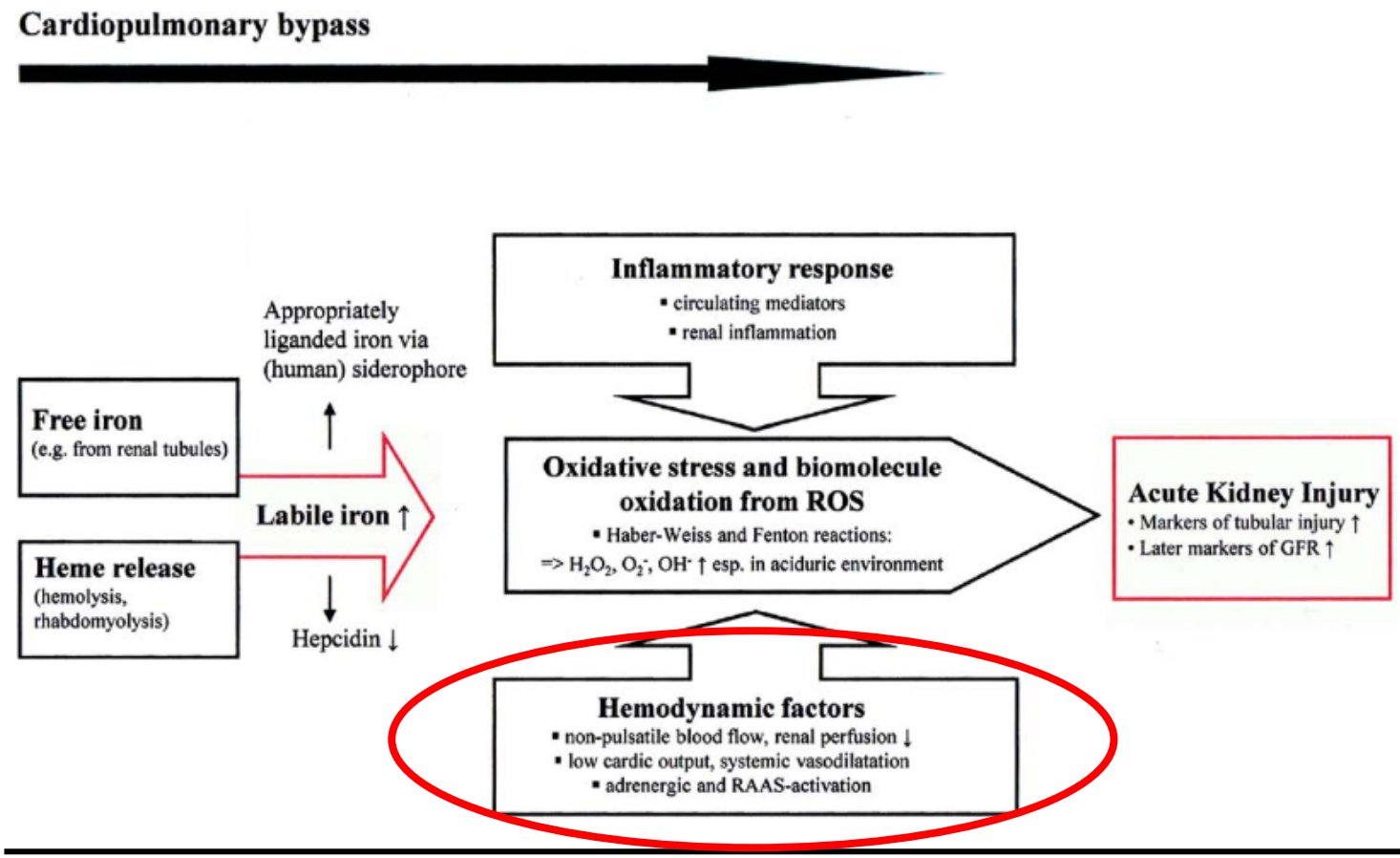
- Bas débit rénal, vasoconstriction rénale
- Anémie
- Hypotension
- Réchauffement après hypothermie

Toxicité tubulaire

- Hémolyse, transfusions
- Inflammation, stress oxydatif

Congestion veineuse





Haase, JACC 2010

Am J Physiol Regul Integr Comp Physiol 292: R1–R17, 2007.
First published September 21, 2006; doi:10.1152/ajpregu.00332.2006.

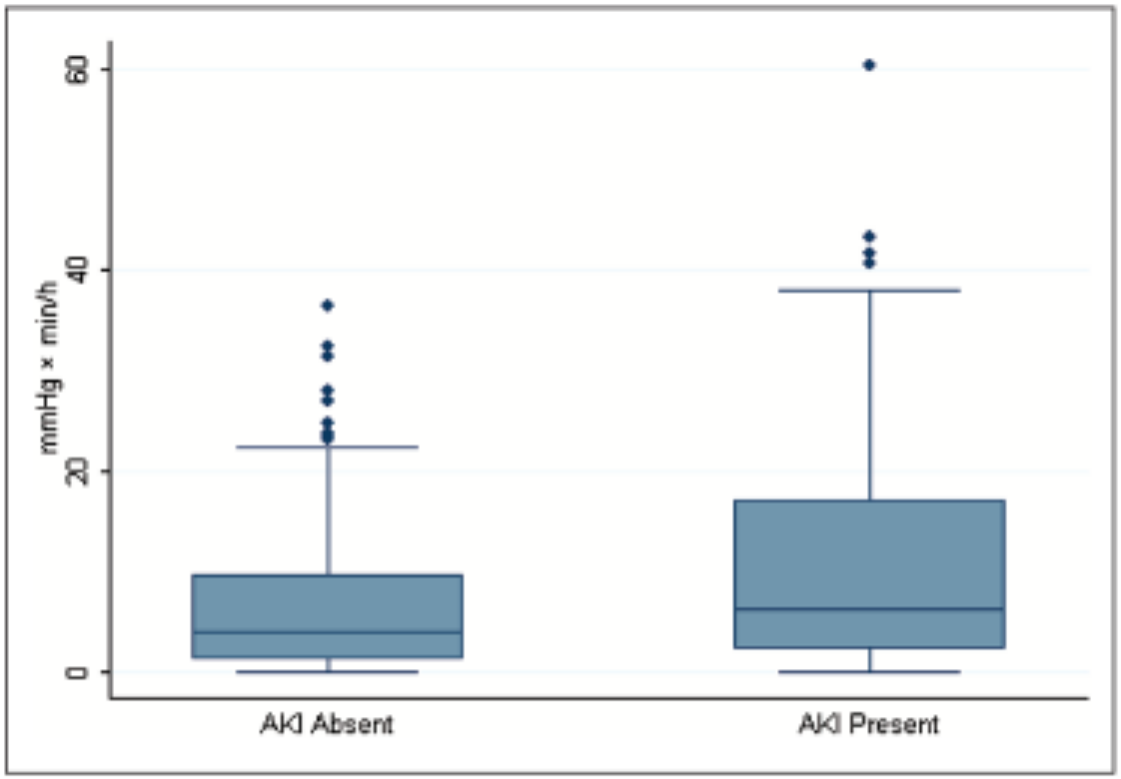
Invited Review

NEW INVESTIGATOR AWARD IN REGULATORY AND INTEGRATIVE PHYSIOLOGY OF THE WATER AND ELECTROLYTE HOMEOSTASIS SECTION, 2006

Mechanisms of renal blood flow autoregulation: dynamics and contributions

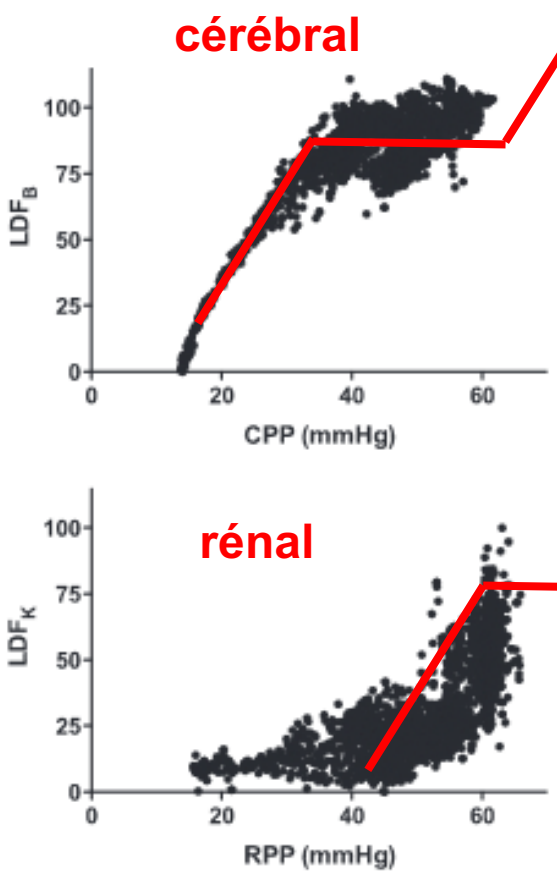
Armin Just
Department of Cell and Molecular Physiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

Réponse myogénique	Feedback tubulo-glomérulaire	3ème mécanisme
Vasoconstriction de l'artériole afférente en réponse à l'élévation de la pression intraluminale	Vasoconstriction de l'artériole afférente en réponse à l'augmentation de la concentration intraluminale de NaCl au niveau de la macula densa	?…… vasodilatation lors de chutes du DSR
<10 sec	< 1 min	< 1 min
-> régulent la balance hydro-électrolytique -> protègent l'intégrité du glomérule -> régulent la VO2 rénale		



Ono, Crit Care Med 2013

RBF pressure autoregulation is impaired in advance of CBF autoregulation



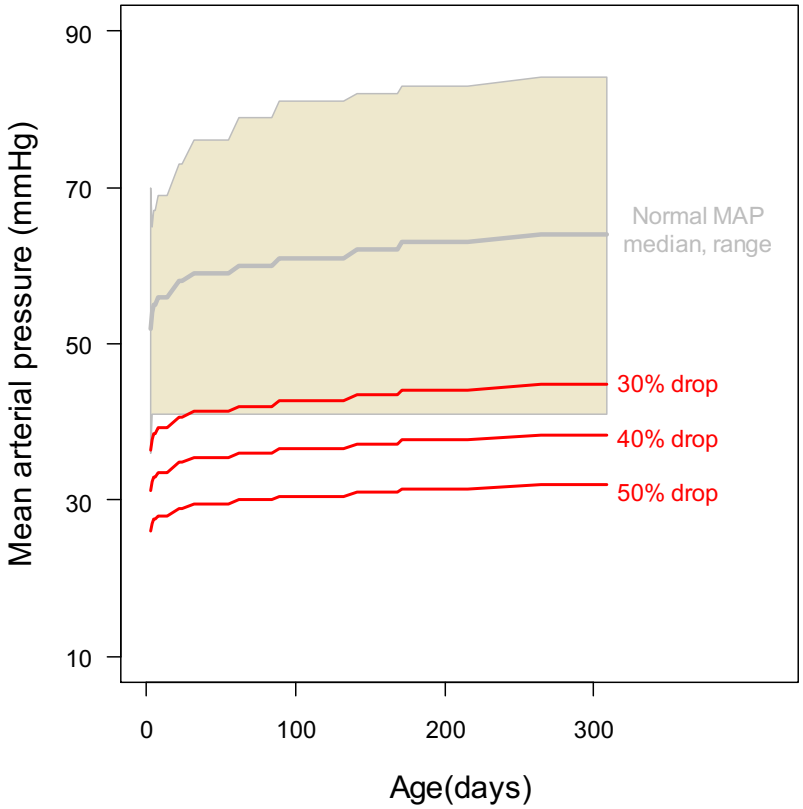
compared with cerebral laser-Doppler measurements. Renal blood flow decreased to 75%, 50%, and 25% of baseline at perfusion pressures of 60, 45, and 40 mmHg, respectively, whereas in the brain these decrements occurred at pressures of 30, 25, and 15 mmHg, respectively. The RVx compared favorably to the renal laser-Doppler

Rhee, J Appl Physiol 2012

Low perfusion pressure is associated with renal tubular injury in infants undergoing cardiac surgery with cardiopulmonary bypass

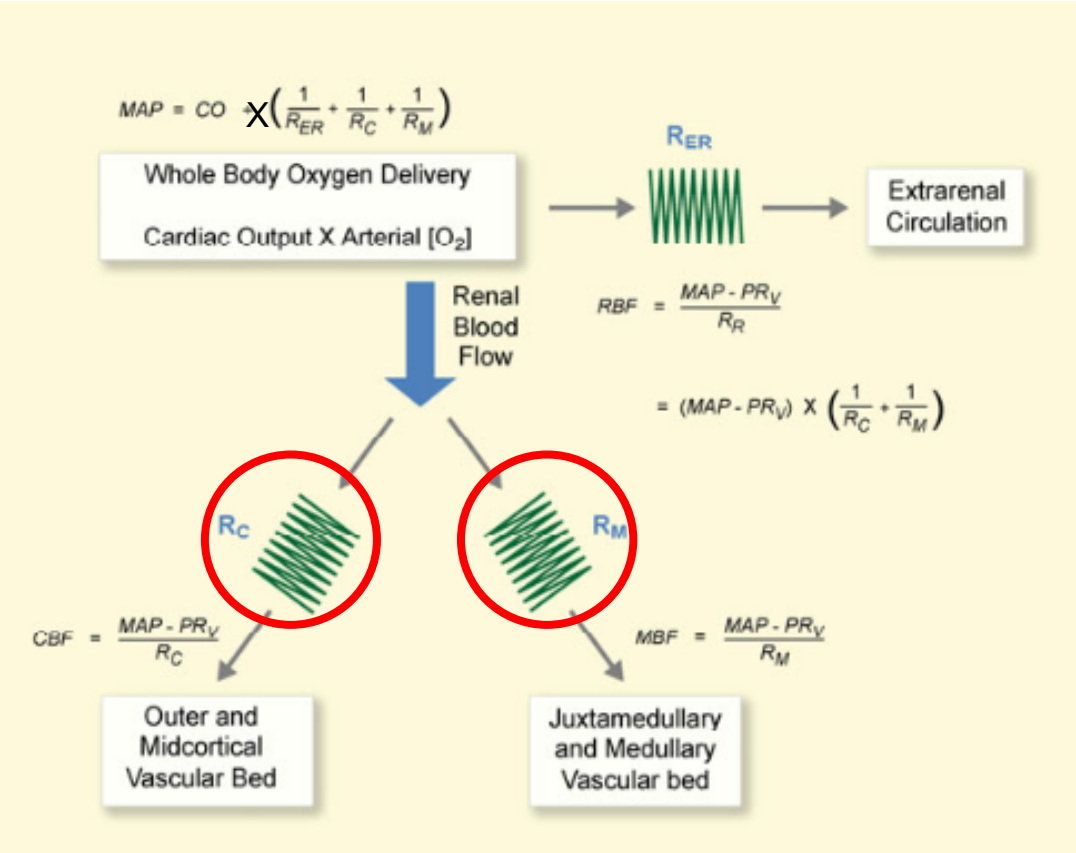
drop. A more than 40% pressure drop for 19.5 min provided a 0.65 negative predictive value for high uNGAL, and a more than 50% pressure drop for 5.4 min provided a 0.67 negative predictive value. The link between uNGAL

$DO_2 = 354.31 \pm 129.84$ ml min^{-1} m^{-2}



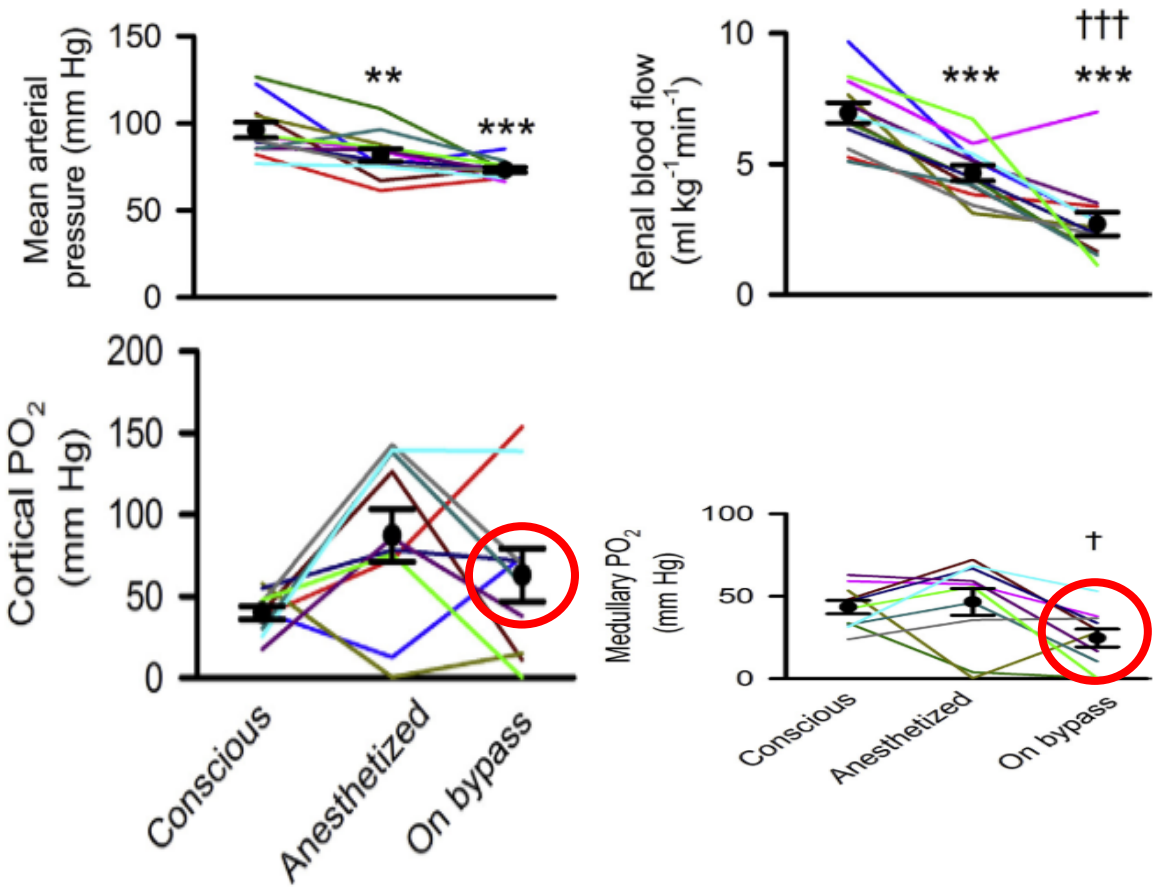
Bojan, Eur J Anesthesiol 2018

Differential control between the cortical and medullary blood flow during CPB



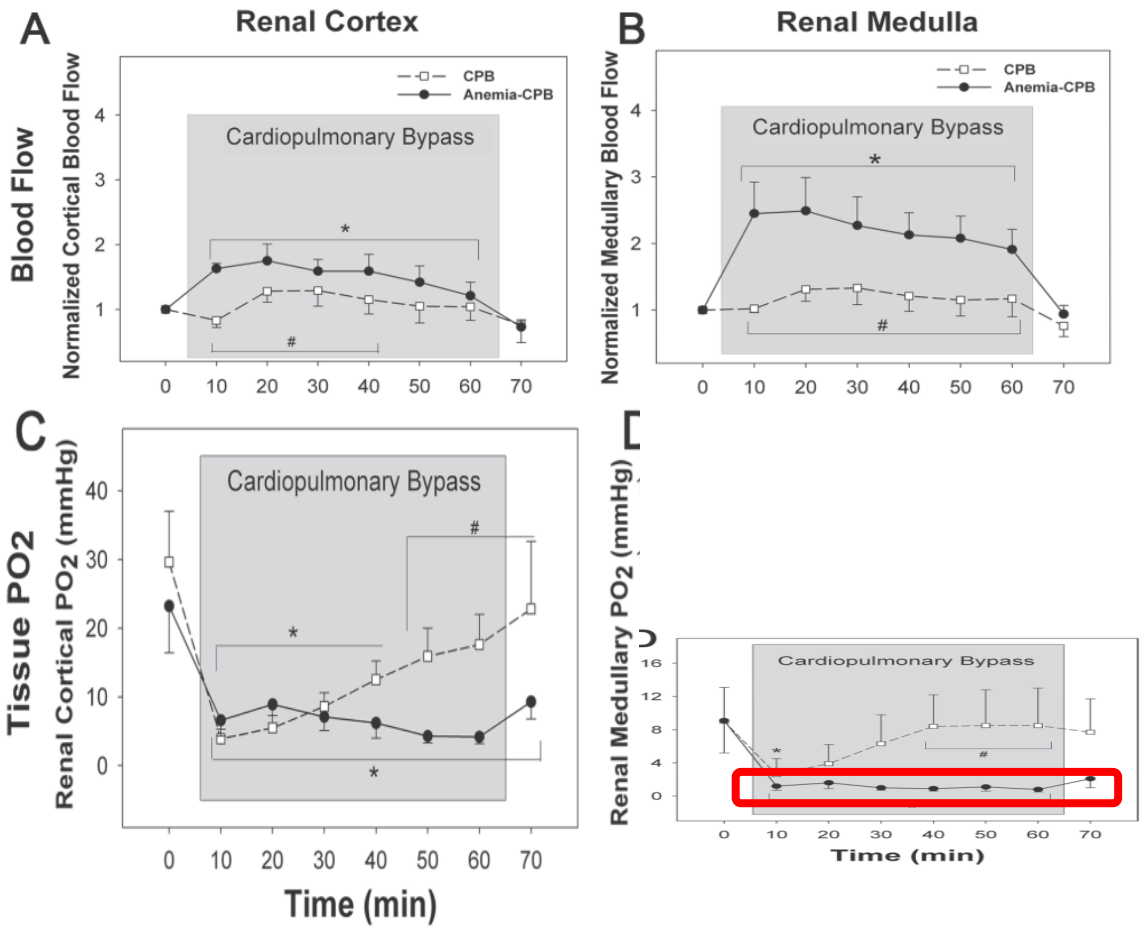
Evans, Acta Physiol (Oxf) 2018

Ischémie médulalire lors du départ en CEC



Lankadeva Kidney Int 2019

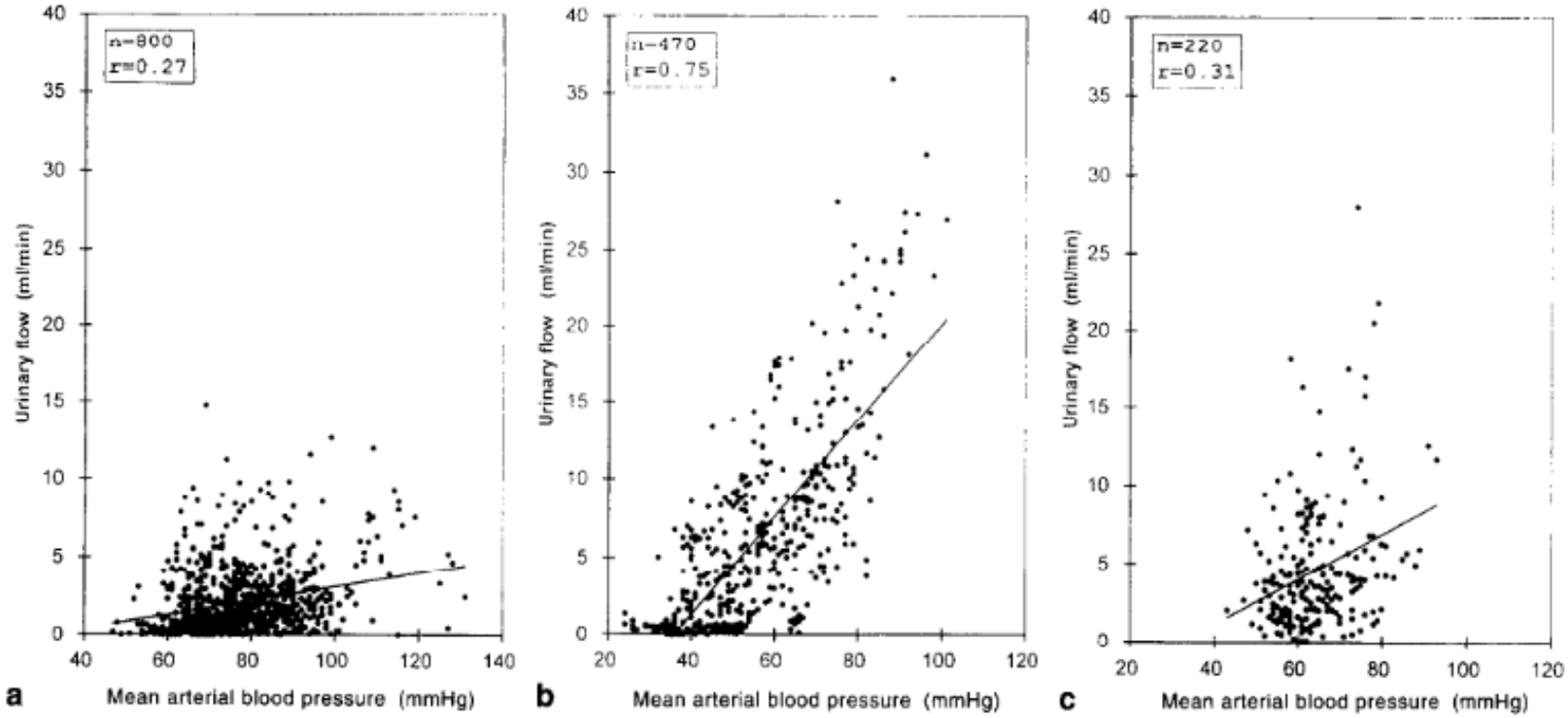
L'anémie augmente le risque d'atteinte rénale durant la CEC



Darby, Perfusion 2013

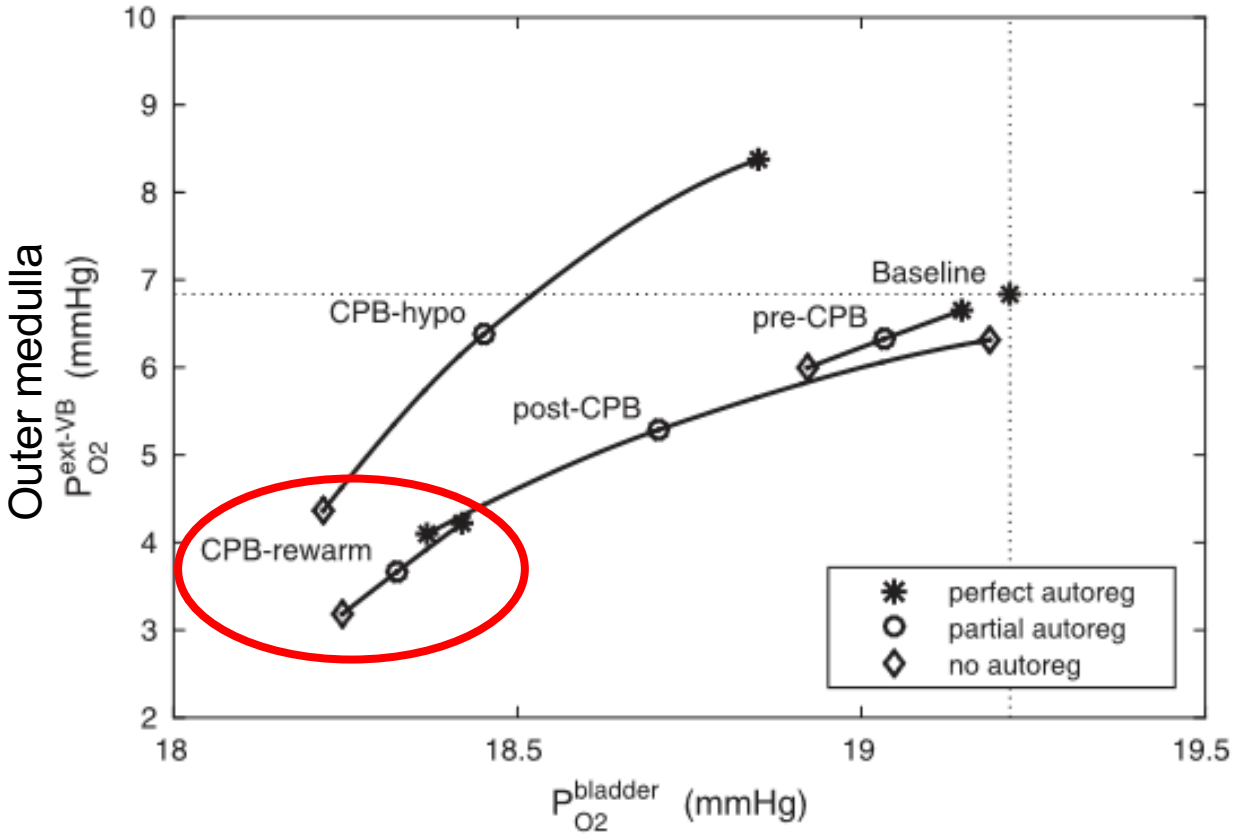
Abolition de l'autorégulation du flux sanguin rénal en CEC hypothermique

Avant CEC | CEC à 28° C | Après CEC



Andersson, Perfusion 1994

L'ischémie médullaire est aggravée durant la période de réchauffement



Le risque de développer une IRA augmente par 34% par 10 min passés avec une ligne artérielle > 37° C

Sgouralis, Mat Med Biol 2017

Newland, Perfusion 2013

Cardiac surgery-related AKI : a pigment nephropathy ?

- **Obstruction tubulaire / précipitation de l'Hb** libre dans un environnement acide
- **L'Hb libre est filtrée** passivement à travers le glomérule et entraîne la **peroxydation des membranes tubulaires**

$$O^{2-} + 2Fe^{3+} \longrightarrow 2Fe^{2+} + O_2$$

$$2O^{2-} + 2H^{+} \longrightarrow H_2O_2 + O_2$$

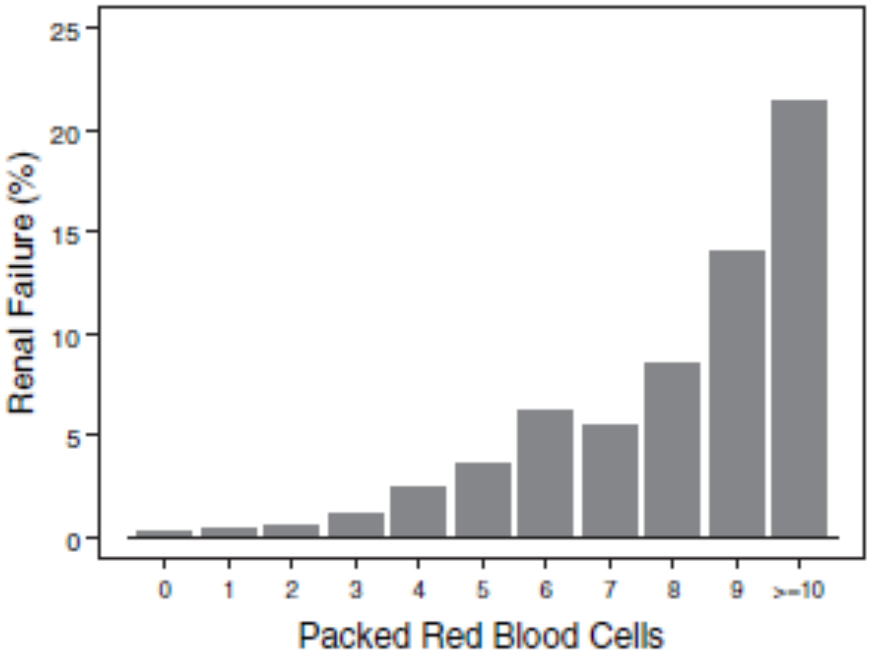
$$H_2O_2 + Fe^{2+} \longrightarrow OH^{\cdot} + OH^{-} + Fe^{3+}$$

Figure 4 Haber-Weiss and Fenton Reactions

- **L'Hb libre est un agent chélateur pour le NO libre,** ce qui entraîne une **vasoconstriction**

Haase, JACC 2010

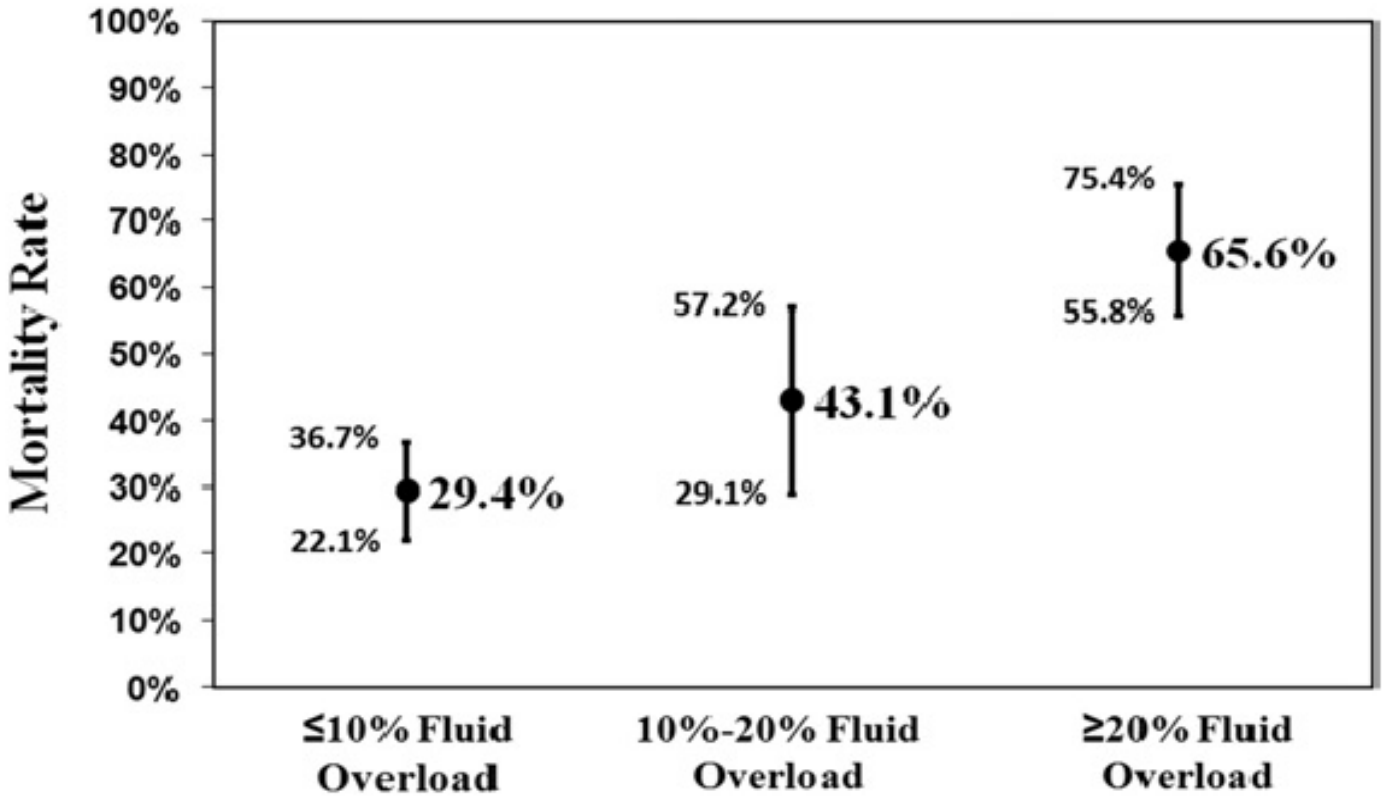
Le risque lié aux transfusions chez l'adulte



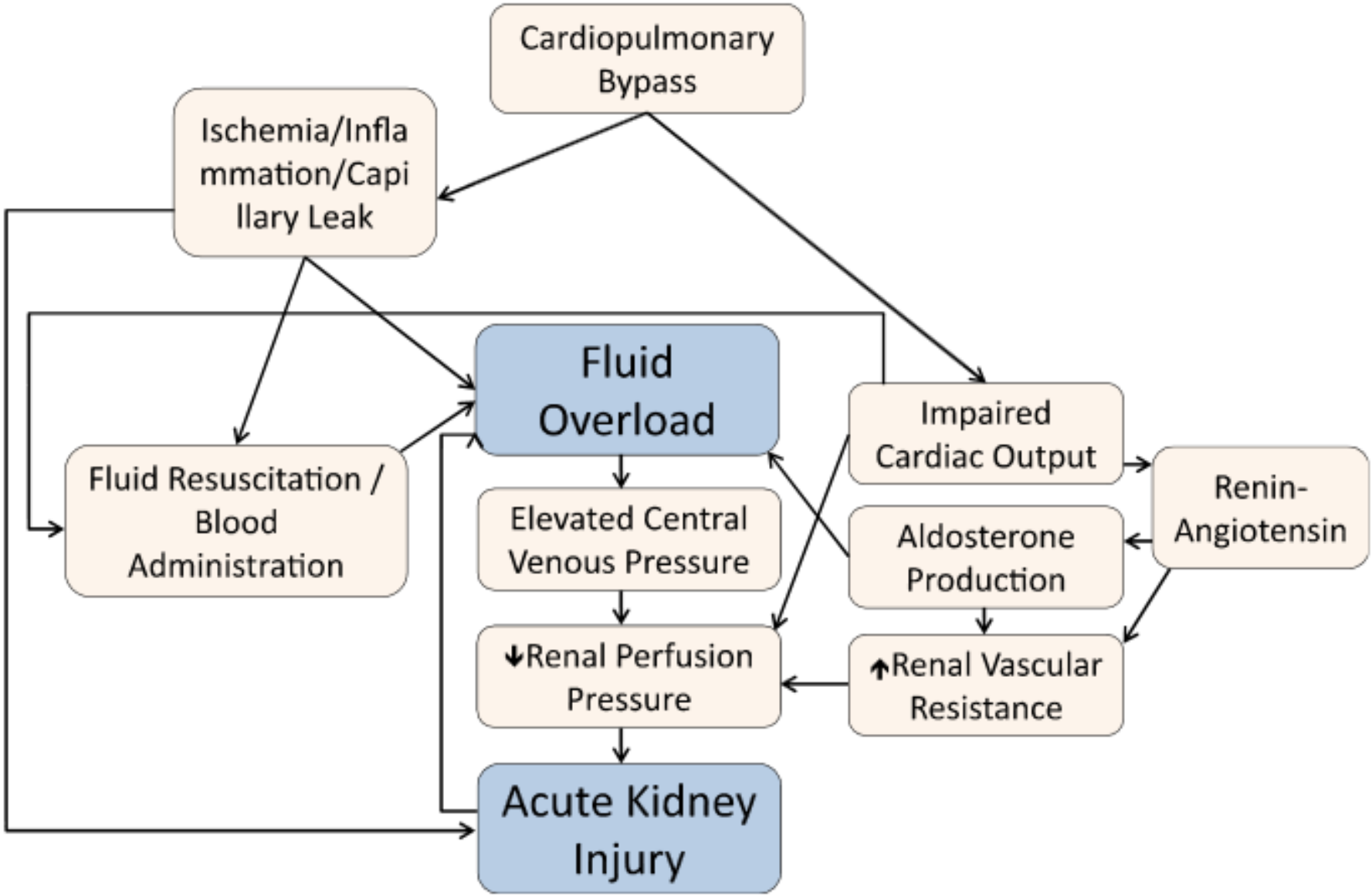
OR = 1.22 [1.19–1.26], p < 0.001 pour chaque CGR additionnel

Furnary, Circulation 2007

Fluid Overload and Mortality in Children Receiving Continuous Renal Replacement Therapy: The Prospective Pediatric Continuous Renal Replacement Therapy Registry



Sutherland, Am J Kidney Dis 2010



Kwiatowski, Pediatric Nephrol 2017

Impact of contrast exposure from computed tomography angiography on acute kidney injury after neonatal cardiopulmonary bypass surgery

Results: Fifty-six neonates were analyzed. AKI developed in 42 (75%) of patients; severe AKI (KDIGO stages 2 and 3) occurred in 18 (32%). Patient characteristics were similar at baseline and at time of CTA between those with and without severe AKI. Patients with severe AKI had longer CPB time, lower postoperative urine output, higher peak serum creatinine, and longer hospital length of stay. When considering intervals between CTA and CPB surgery $\leq$1 day (n = 19), $\leq$3 days (n = 28), and >3 days (n = 28); there was no difference in AKI incidence nor postoperative outcomes among these three interval cohorts.

Conclusion: Routine exposure to CTA and CPB surgery in close succession does not appear to increase the risk of AKI after neonatal cardiac surgery. Though other risks need to be weighed (eg, sedation, intubation, radiation exposure), this result may enable more liberal utilization of CTA for preoperative surgical planning of congenital heart operations in patients with unclear or complex anatomy.

Carlo, Congenital Heart Disease 2017

Insuffisance rénale aiguë

Epidemiologie

Physiopathologie

Diagnostic et monitoring peropératoire

Prévention

Traitement

Insuffisance rénale chronique

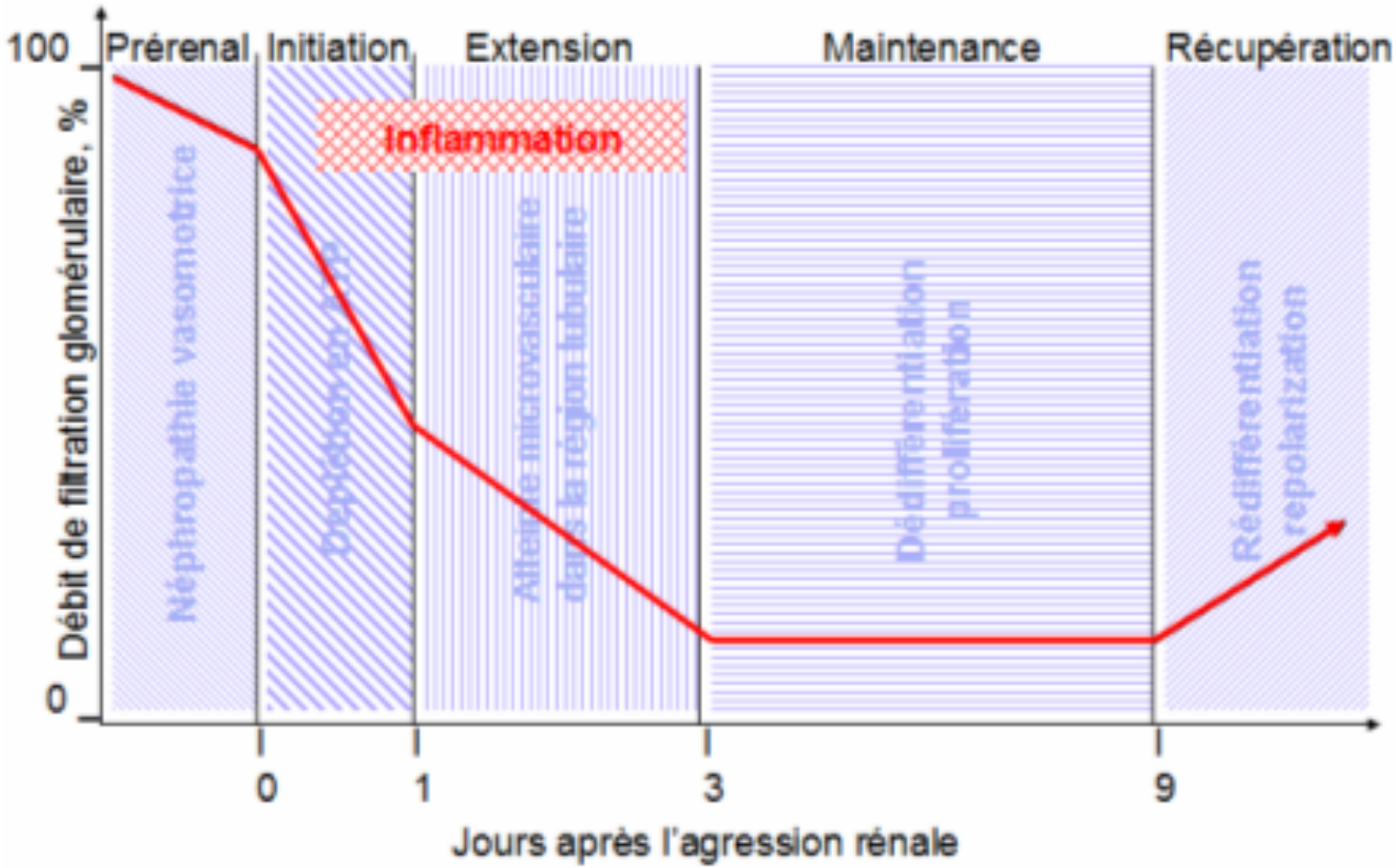
Définition IRA

	Creatinine criteria		Urine output criteria	
	RIFLE	pRIFLE and nRIFLE	RIFLE	pRIFLE
Risk	Increased creatinine x1.5 or GFR decreases >25%	Increased creatinine x1.5 or GFR decreases >25%	UO ≤0.5 mL/kg/h × 6 h	UO ≤0.5 mL/kg/h × 8 h
Injury	Increased creatinine x2 or GFR decreases >50%	Increased creatinine x2 or GFR decreases >50%	UO ≤0.5 mL/kg/h × 12 h	UO ≤0.5 mL/kg/h × 16 h
Failure	Increased creatinine x3 or GFR decreases >75% or creatinine >4 mg/dL (acute rise of >4 mg/dL)	Increased creatinine x3 or GFR decreases >75% or GFR <35 mL/min/1.73 m^2	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h

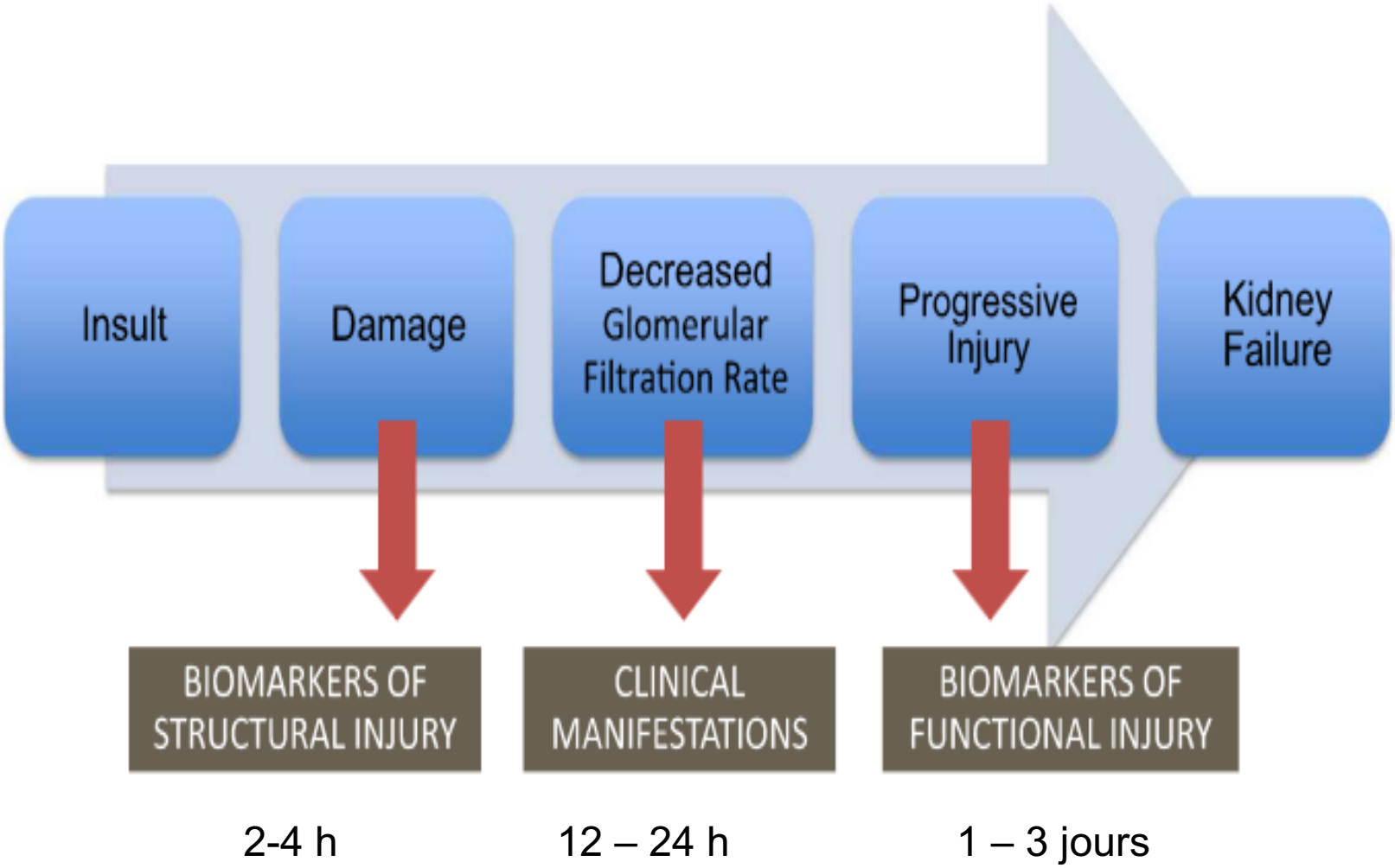
Metha RL, Crit Care 2007, Akcan-Arikan, Kidney Int 2007

Evolution de l'IRA par ischémie-reperfusion

La lésion initiale se situe au niveau tubulaire

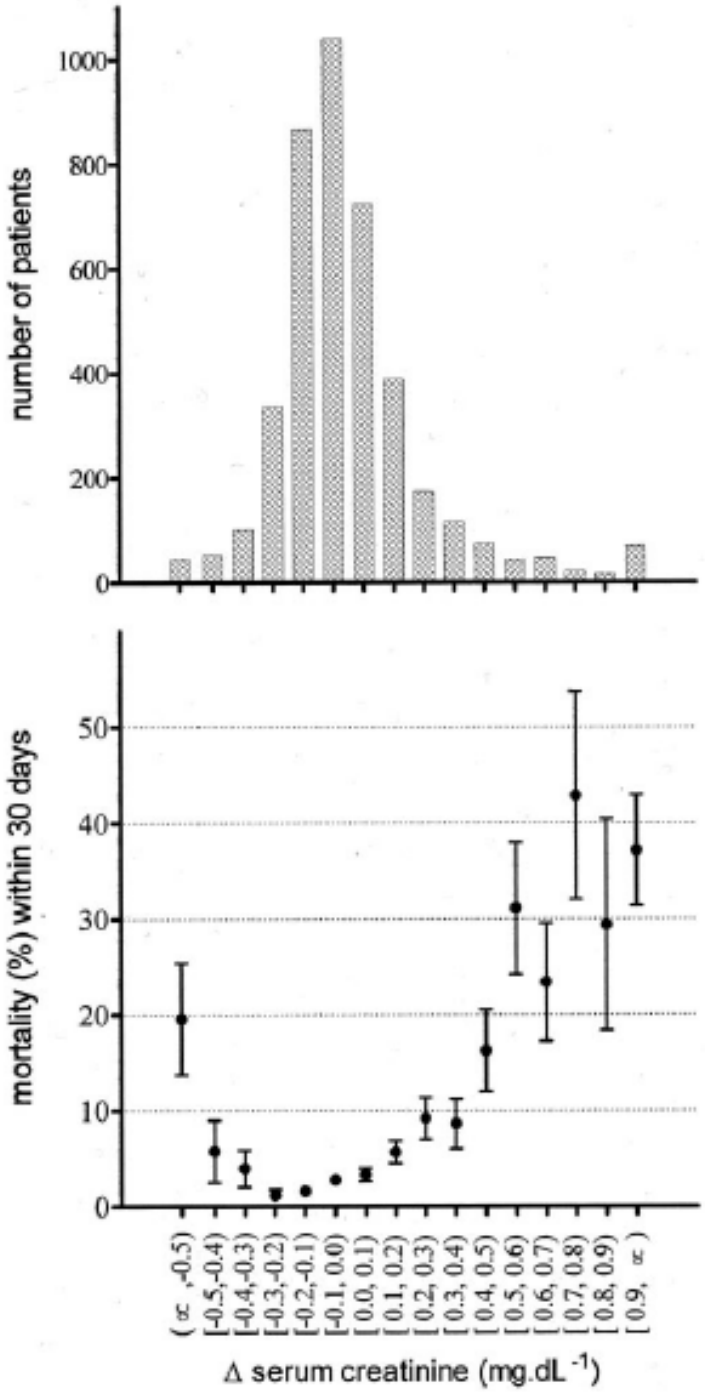


Sutton, Kidney Int 2002



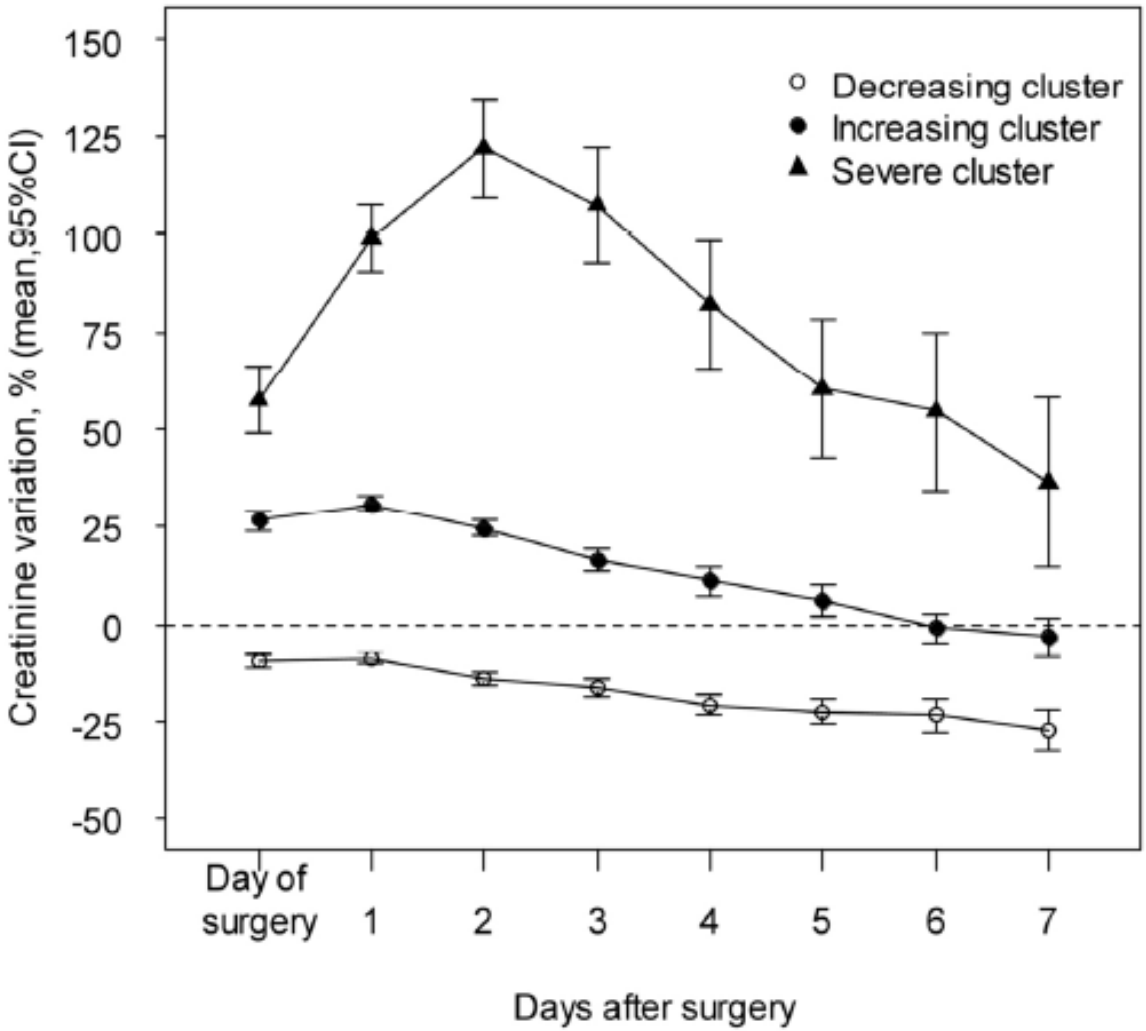
Kwiatowski, Pediatric Nephrol 2017

Problèmes posés par la créatinine plasmatique pour le diagnostic de l'IRA chez l'adulte



Lassnigg, J Am Soc Nephrol, 2004

La créatinine plasmatique pour le diagnostic de l'IRA chez le nourrisson



Necker-Enfants Malades

Variable	"Decreasing cluster" (n = 503)	"Increasing cluster" (n = 423)	P-value [a]	"Severe cluster" (n = 90)	P-value [a]
Number of blood product units on the day of surgery	3.5 ± 1.3	3.7 ± 1.5	0.017	5.4 ± 2.4	< 0.001
Required delayed sternal closure	37 (7.4)	68 (16.1)	< 0.001	54 (60)	< 0.001
Required postoperative ECMO	3 (0.6)	6 (1.4)	0.35	6 (6.7)	< 0.001
Required postoperative peritoneal dialysis	10 (2.0)	35 (8.3)	< 0.001	47 (52.2)	< 0.001

Définition IRA néonatale

	Creatinine criteria		Urine output criteria		
	RIFLE	pRIFLE and nRIFLE	RIFLE	pRIFLE	nRIFLE
Risk	Increased creatinine x1.5 or GFR decreases >25%	Increased creatinine x1.5 or GFR decreases >25%	UO ≤0.5 mL/kg/h × 6 h	UO ≤0.5 mL/kg/h × 8 h	UO <1.5 mL/kg/h for 24 h
Injury	Increased creatinine x2 or GFR decreases >50%	Increased creatinine x2 or GFR decreases >50%	UO ≤0.5 mL/kg/h × 12 h	UO ≤0.5 mL/kg/h × 16 h	UO <1.0 mL/kg/h for 24 h
Failure	Increased creatinine x3 or GFR decreases >75% or creatinine >4 mg/dL (acute rise of >4 mg/dL)	Increased creatinine x3 or GFR decreases >75% or GFR <35 mL/min/1.73 m^2	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h	UO ≤0.3 mL/kg/h × 24 h or anuria × 12 h	UO <0.7 mL/kg/h for 24 h or anuria for 12 h

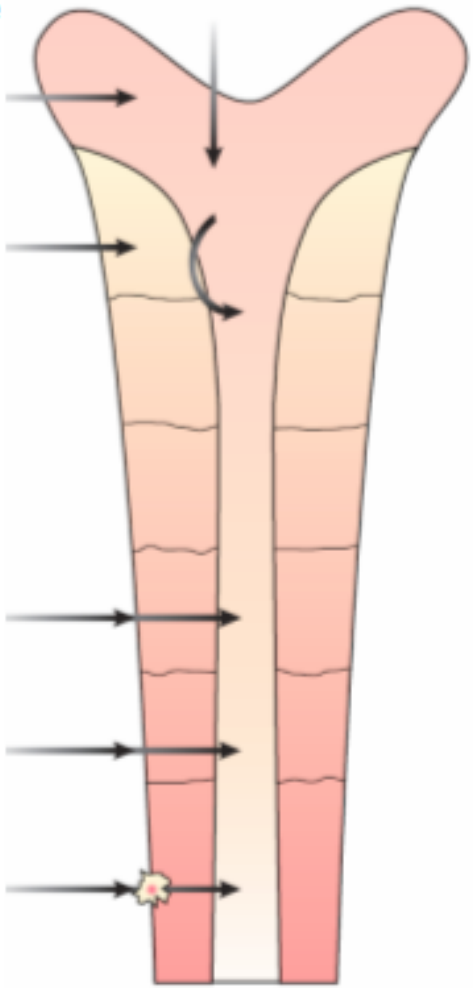
Bezerra, Nephrol Dial Transplant 2013, Ricci , Nephrol Dial Transplant 2013

Filtration des déchets azotés
créatinine

Filtration des protéines plasmatiques par altération de la barrière glomérulaire
albumine

Altération de la réabsorption tubulaire
cystatine C

Protéines tubulaires
- inductibles par l'ischémie
KIM-1
- libérées par la destruction endothéliale
L-FABP
- sécrétées par les cellules inflammatoires en réponse à l'ischémie
NGAL, IL-18



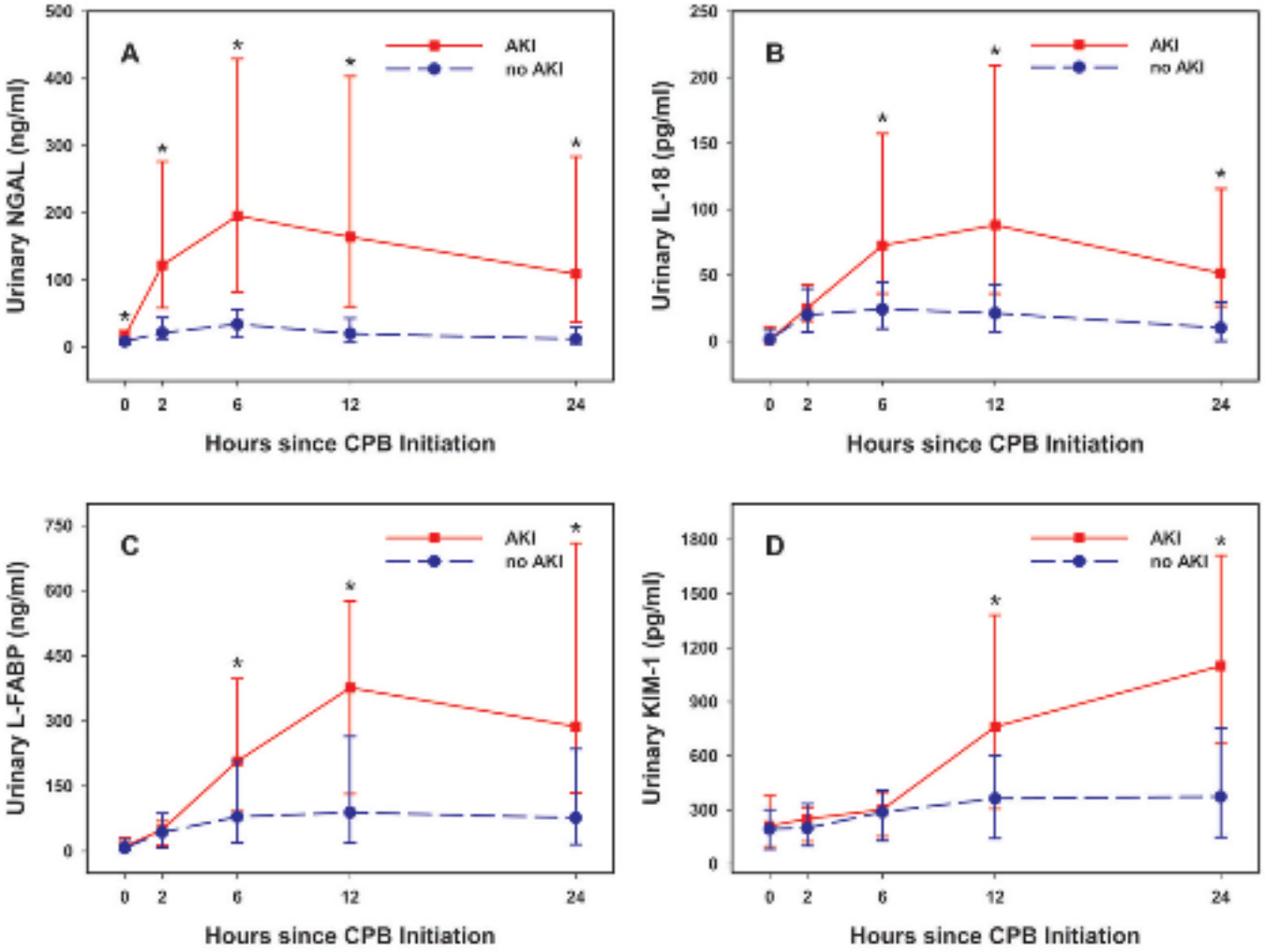
Briggs JP. Kidney Int. 2008

Biomarqueurs rénaux

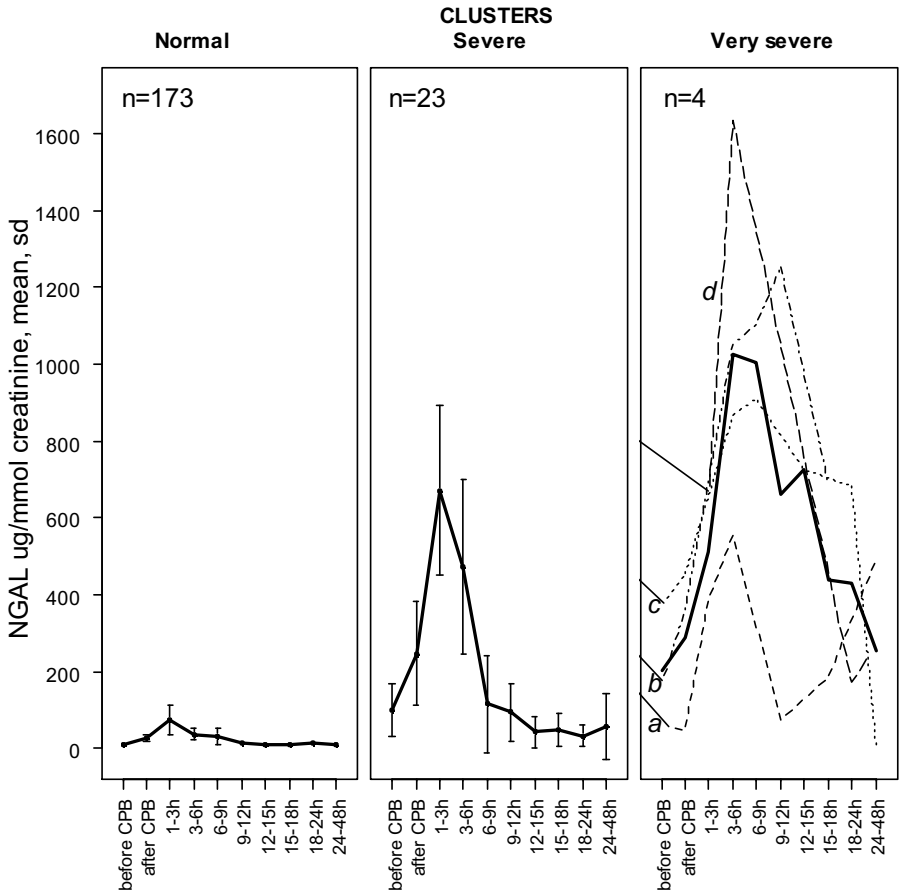
1. Marqueurs de l'atteinte tubulaire = marqueurs lésionnels (NGAL, KIM-1, LFAB, IL-18)

2. Marqueurs de la filtration glomérulaire = marqueurs fonctionnels (inuline, créatinine, cystatine C, albuminurie)

Temporal Relationship and Predictive Value of Urinary Acute Kidney Injury Biomarkers After Pediatric Cardiopulmonary Bypass



Krawczeski JACC 2011



Bojan, Clin J Am Soc Nephrol 2014

Cell-cycle arrest and acute kidney injury: the light and the dark sides

John A. Kellum[1] and Lakhmir S. Chawla[2]

Tissue inhibitor of metalloproteinases-2 (TIMP-2)
Insulin-like growth factor-binding protein 7 (IGFBP-7)

	population	[TIMP-2 * IGFBP-7] threshold
Gist Pediatr Nephrol 2016	94, average 154 days old	> 0.78 ROC area = 0.71
Meersch Plos ONE 2014	51 patients 1.5 – 3 years old	> 0.70 ROC area = 0.85

Kellum, Nephrol Dial Transplant 2016

Cell-cycle arrest and acute kidney injury: the light and the dark sides

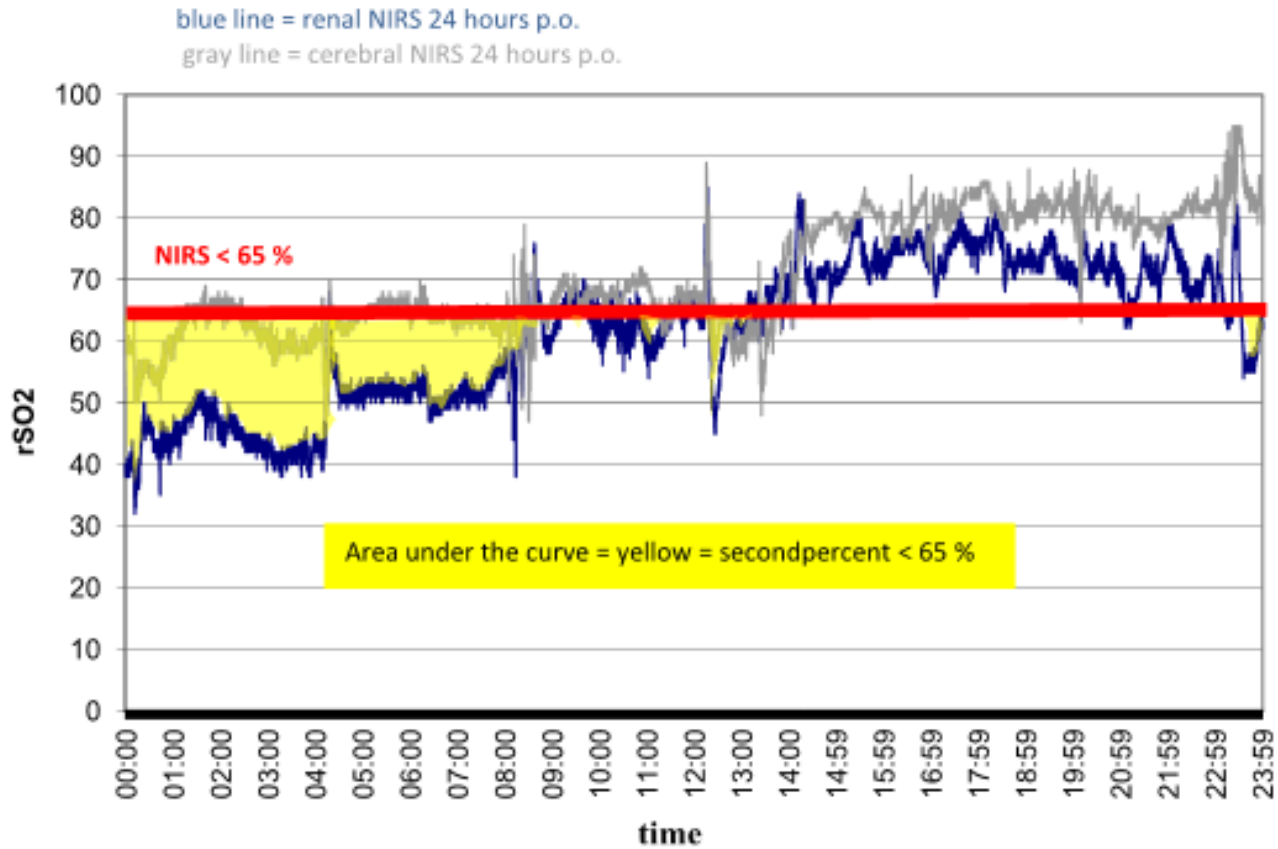
John A. Kellum[1] and Lakhmir S. Chawla[2]

Tissue inhibitor of metalloproteinases-2 (TIMP-2)
Insulin-like growth factor-binding protein 7 (IGFBP-7)

	population	[TIMP-2 * IGFBP-7] threshold
Gist Pediatr Nephrol 2016	94, average 154 days old	> 0.78 ROC area = 0.71
Meersch Plos ONE 2014	51 patients 1.5 – 3 years old	> 0.70 ROC area = 0.85

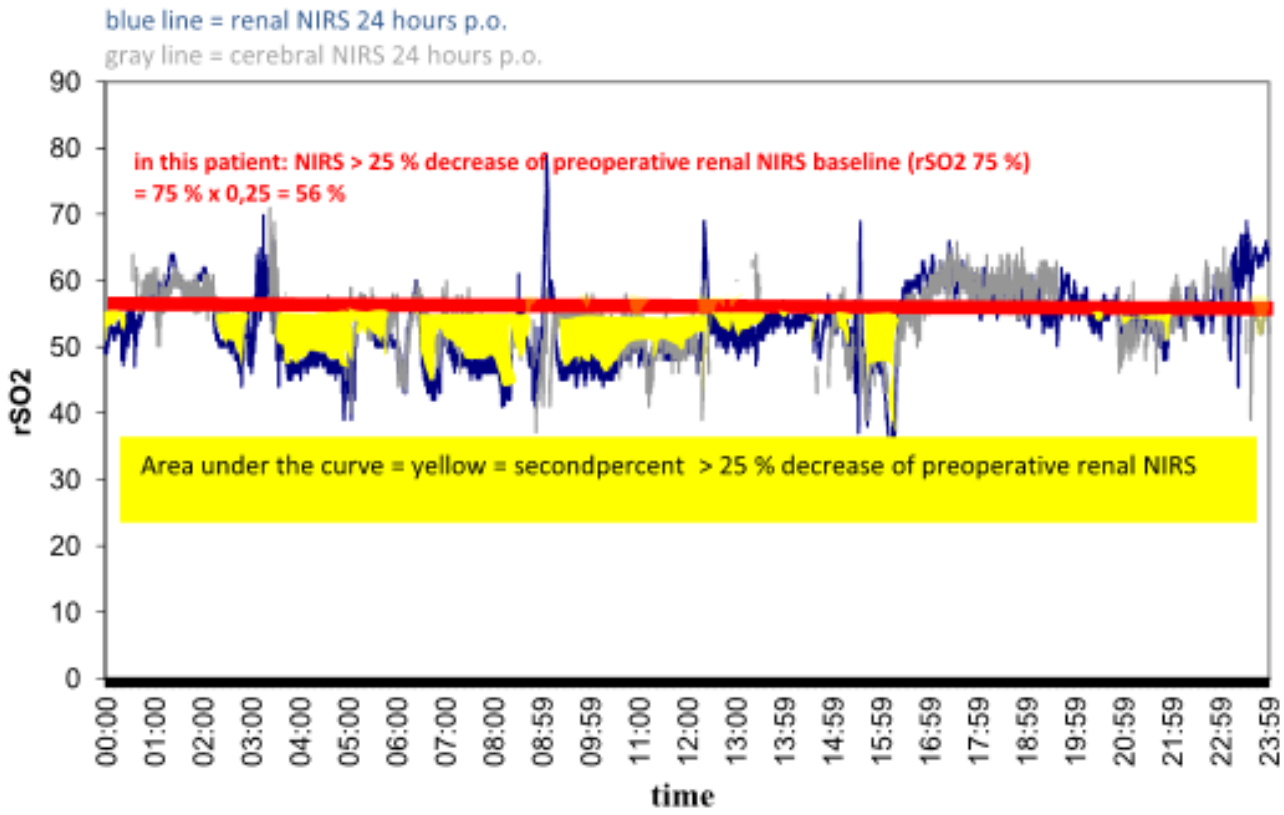
Kellum, Nephrol Dial Transplant 2016

Intraoperative renal near-infrared spectroscopy indicates developing acute kidney injury in infants undergoing cardiac surgery with cardiopulmonary bypass: a case–control study



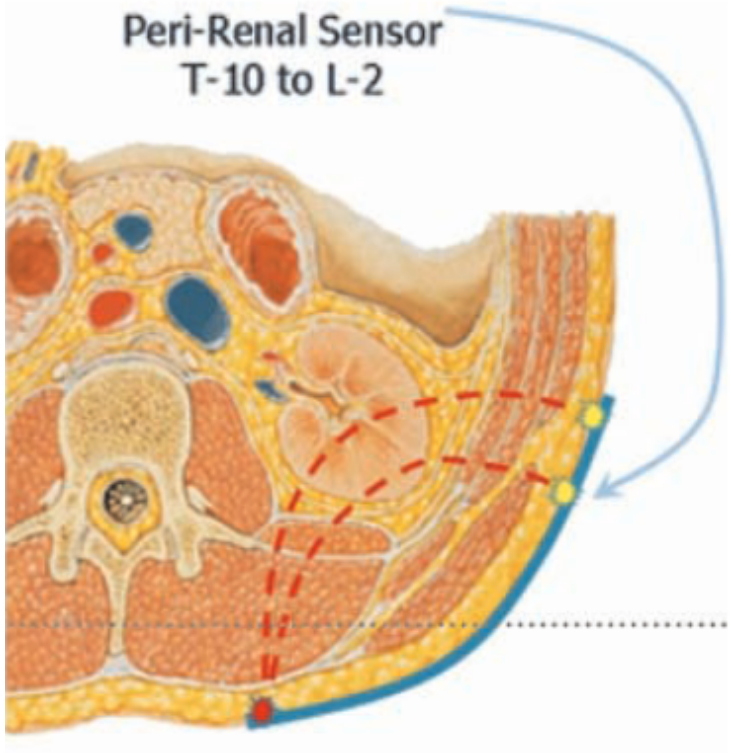
Ruf, Crit Care 2015

Intraoperative renal near-infrared spectroscopy indicates developing acute kidney injury in infants undergoing cardiac surgery with cardiopulmonary bypass: a case–control study



Ruf, Crit Care 2015

How sensitive is renal rSO_2 to detect medullary hypoxia ?



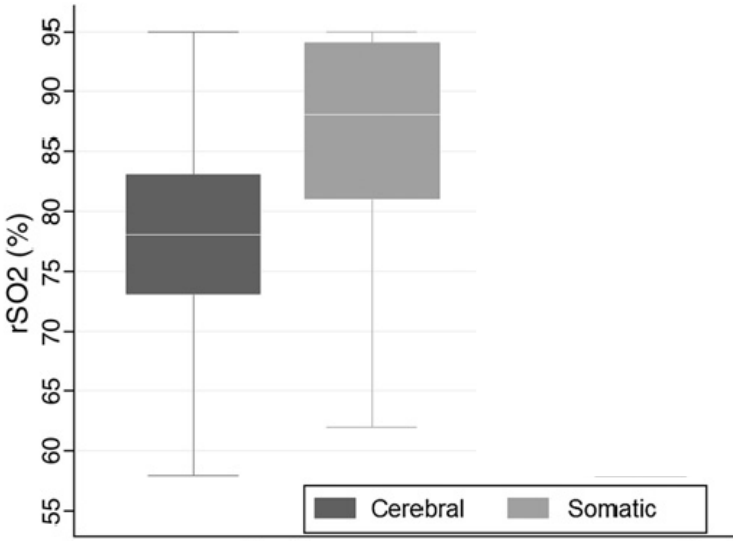
Le monitoring multisite de la rSO_2 révèle les modifications de débit régionaux per-CEC (…et peut prédire l'hypoxie médullaire… ?)

Cerebral and somatic rSO_2 in newborns at rest

Somatic circulation has sympathetically modulated resistances

At rest, the somatic-cerebral rSO_2 gradient is 10-15%

→ the somatic-cerebral rSO_2 gradient narrows with activation of the sympathetic system (low cardiac output / inadequate perfusion on CPB)



Bernal, J Pediatr Surg 2010

Insuffisance rénale aiguë

Epidemiologie

Physiopathologie

Diagnostic

Biomarqueurs

Prévention

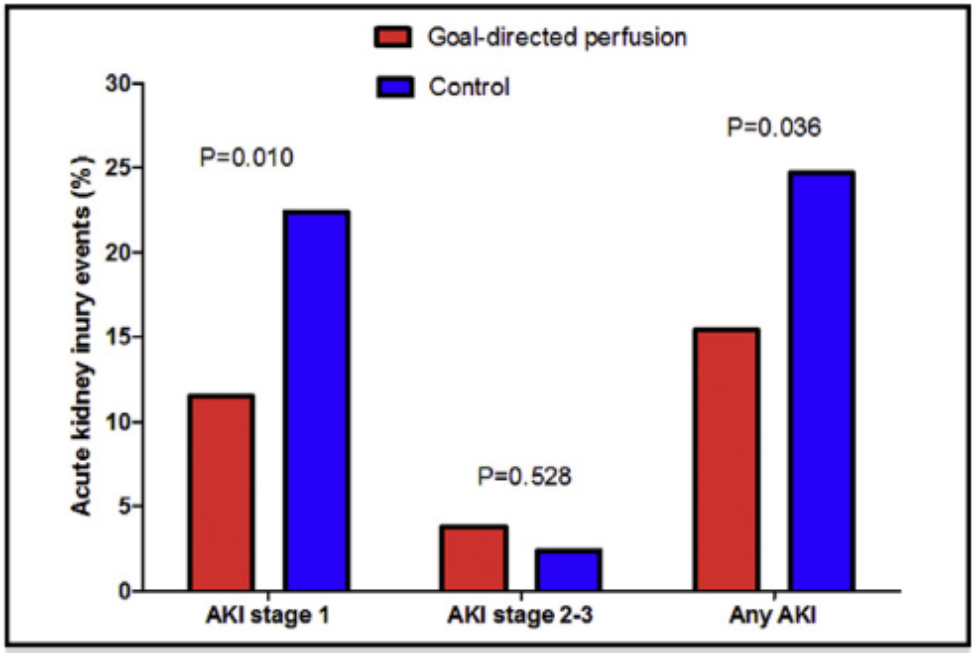
Traitement

Insuffisance rénale chronique

DO_2-directed perfusion to reduce cardiac surgery-related -AKI

Goal : maintain DO_2 > 280 ml/min/m^2 during CPB in adults

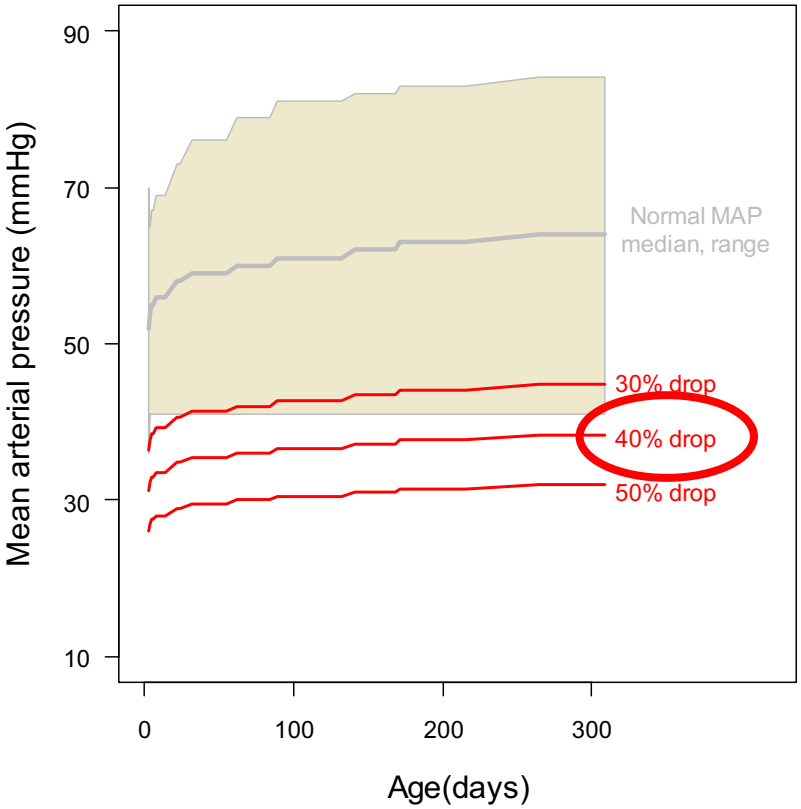
Critical DO_2 in infants ? in neonates ?



Ranucci JTCVS 2018

Mainenir la pression de perfusion en CEC > 60% de la PAM pour l'âge

drop. A more than 40% pressure drop for 19.5 min provided a 0.65 negative predictive value for high uNGAL, and a more than 50% pressure drop for 5.4 min provided a 0.67 negative predictive value. The link between uNGAL



Bojan, Eur J Anesthesiol 2018

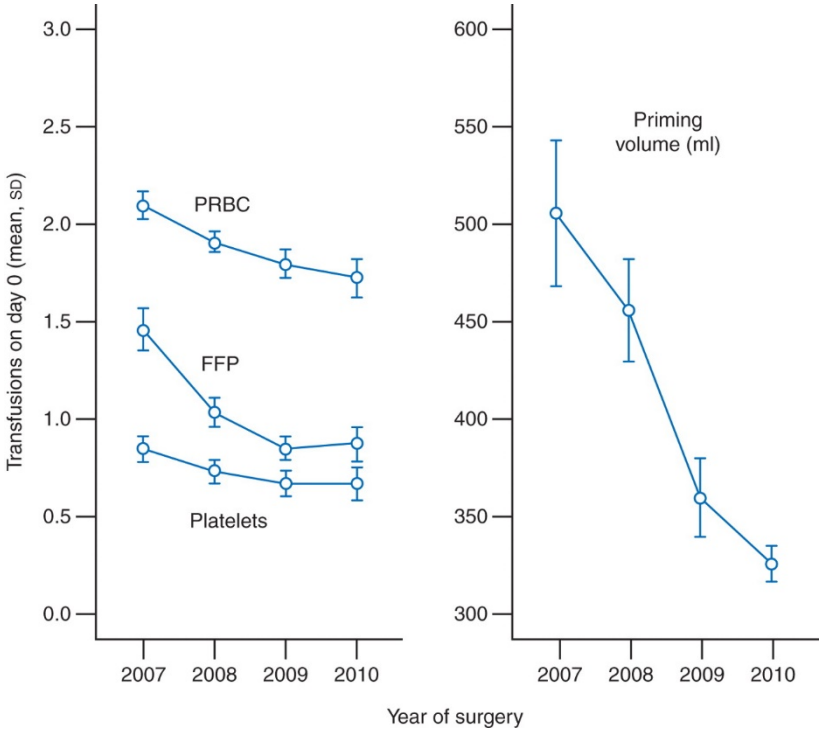
The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines for Cardiopulmonary Bypass—Temperature Management during Cardiopulmonary Bypass

3. **Surgical teams should limit arterial outlet blood temperature to <37°C to avoid cerebral hyperthermia. (Class I, Level C)**

ii. **To achieve the desired temperature for separation from bypass, it is reasonable to maintain a rewarming rate ≤ .5°C/min. (Class IIa, Level B)**

Engelman, Ann Thor Surg 2015

Éviter l'anémie et éviter les transfusions …
Miniaturization des circuits de CEC



	AKI		Severe AKI requiring dialysis	
Variable	**Adjusted OR (95% CI)**	***P*-value**	**Adjusted OR (95% CI)**	***P*-value**
Use of aprotinin	0.62 (0.35–1.08)	0.09	1.40 (0.47–4.20)	0.54
Number of PRBC transfusions on day 0	1.64 (1.12–2.41)	0.01	2.07 (1.13–3.73)	0.02
Number of FFP transfusions on day 0	2.28 (1.68–3.09)	<0.001	3.11 (1.95–4.97)	<0.001
Number of platelet transfusions on day 0	1.33 (0.93–1.92)	0.12	2.20 (1.21–4.01)	0.01

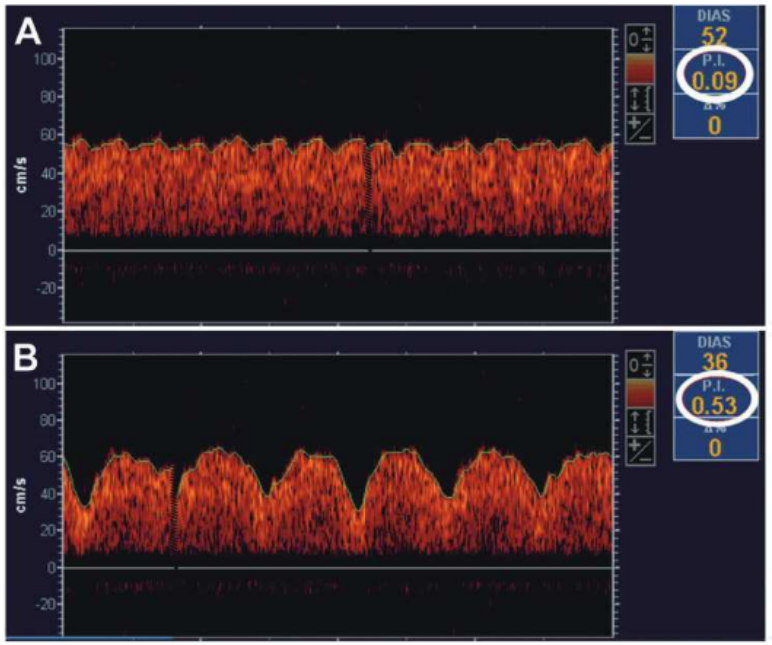
Bojan, Br J Anaesth, 2012

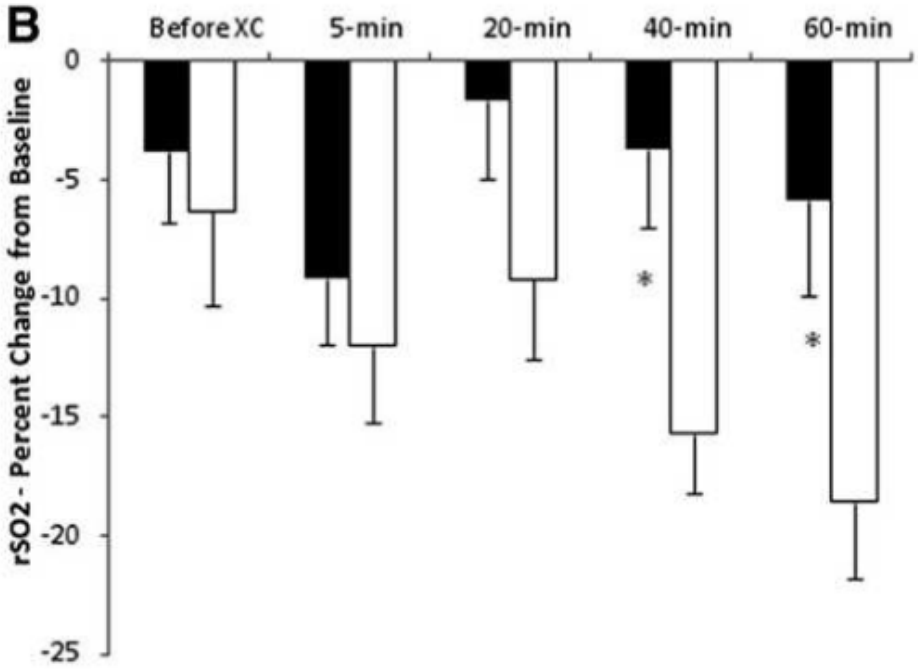
Duration of red blood cell storage and outcomes in pediatric cardiac surgery: an association found for pump prime blood

Conclusions The storage time of the red blood cells used for priming the cardiopulmonary bypass circuit in cardiac operations on newborns and young infants is an independent risk factor for major postoperative morbidity. Pulmonary complications, acute renal failure, and infections are the main complications associated with increased red blood cell storage time.

Ranucci, Critical Care 2009

Le débit pulsé améliore la rSO_2 cérébrale (… et la rSO_2 renale ?)

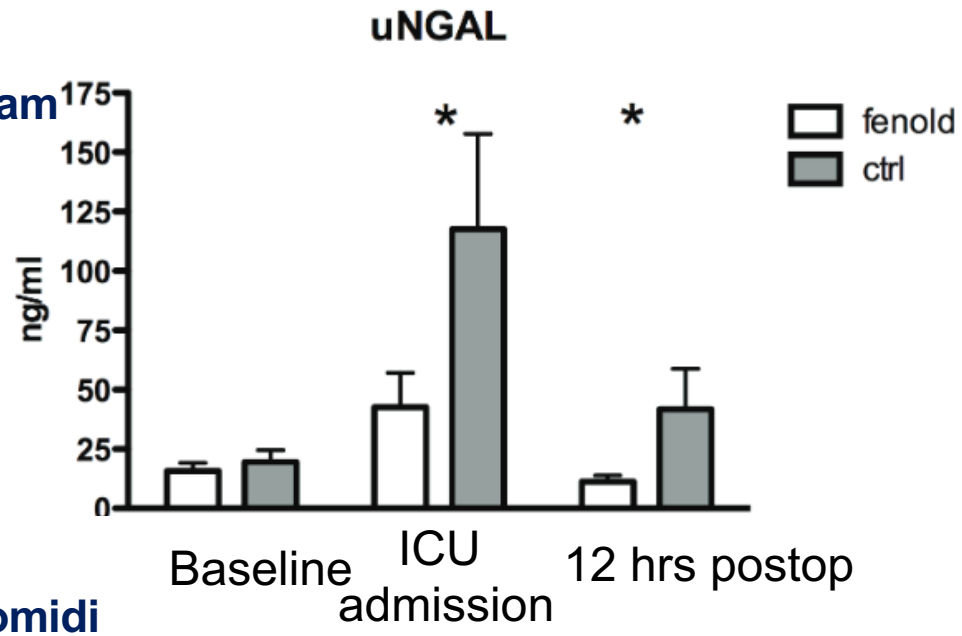




Su, Pediatric Res 2011

Renal vasodilators reduce the incidence of CS-AKI in infants

Fenoldopam



Dexmedetomidi

Kidney Injury or Creatinine Change Description	Dexmedetomidine ($n = 102$)	No Dexmedetomidine ($n = 102$)	p
AKI of any severity, %	24 (24)	36 (37)	OR, 0.54 (95% CI, 0.29–0.99; $p = 0.046$) adjusted OR, 0.43 (95% CI, 0.27–0.98; $p = 0.048$)

Ricci, Crit Care 2011

Kwiatkowski, Pediatr Crit Care Med 2016

La prophylaxie de l'IRA par le sodium bicarbonate chez l'adulte

and covariates (odds ratio [OR], 99% confidence interval [CI]: Bicarbonate *vs.* Control, 1.11 [0.77–1.60], $P = 0.45$). There was, however, a significant study-adjusted benefit in elective coronary artery bypass surgery patients in terms of renal replacement therapy (Bicarbonate *vs.* Control, OR: 0.38 [99% CI: 0.25–0.58], $P < 0.0001$) and the development of an Acute Kidney Injury Network grade = 3 (Bicarbonate *vs.* Control, OR: 0.45 [99% CI: 0.43–0.48], $P < 0.0001$).

Bailey, Anesthesiology 2015

Autres stratégies dans la prévention de l'IRA

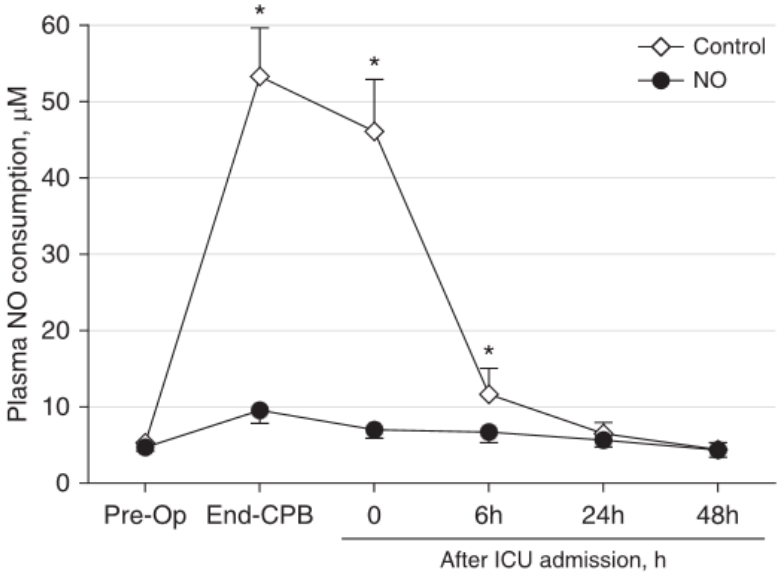
SPECIAL REPORT

American Heart Association | American Stroke Association

Cardiac and Vascular Surgery–Associated Acute Kidney Injury: The 20th International Consensus Conference of the ADQI (Acute Disease Quality Initiative) Group

Timing	Strategy	Population	Recommended	Not Recommended
Intraoperative	Volatile anesthetic agents (vs propofol)	Cardiac	2C	. . .
	Avoidance of hyperthermia	Cardiac	2C	. . .
	Pulsatile CPB	Cardiac	2D*	. . .
	Avoidance of hemodilution	Cardiac	2C	. . .
	MAP >75	Cardiac	. . .	More research needed
	Intraoperative ultrafiltration	Cardiac	. . .	More research needed

L'administration intra- et postopératoire de l'NO chez l'adulte réduit le risque d'IRA et de IRC stade 3 chez l'adulte



RR for CS-AKI within 1 week = 0.78 [0.62 – 0.97]

RR for stage 3 CKD within 1 year = 0.59 [0.36 – 0.96]

Lei, Am J Resp Crit Care Med 2018

Sodium Bicarbonate and Renal Function after Cardiac Surgery

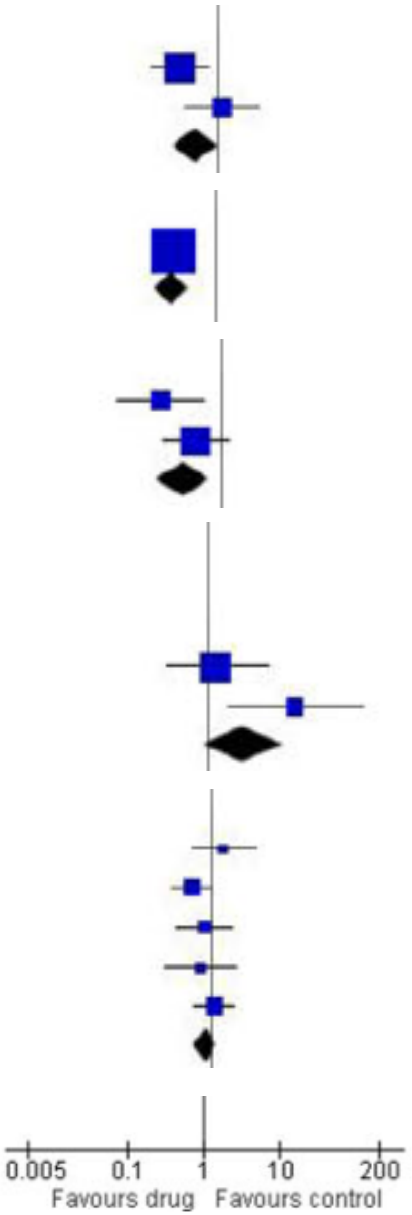
and covariates (odds ratio [OR], 99% confidence interval [CI]: Bicarbonate *vs.* Control, 1.11 [0.77–1.60], $P = 0.45$). There was, however, a significant study-adjusted benefit in elective coronary artery bypass surgery patients in terms of renal replacement therapy (Bicarbonate *vs.* Control, OR: 0.38 [99% CI: 0.25–0.58], $P < 0.0001$) and the development of an Acute Kidney Injury Network grade = 3 (Bicarbonate *vs.* Control, OR: 0.45 [99% CI: 0.43–0.48], $P < 0.0001$).

Bailey, Anesthesiology 2015

Effet estimé / risque d'IRA lors d'une utilisation à titre préventif

Patel, Heart Fail Rev 2011

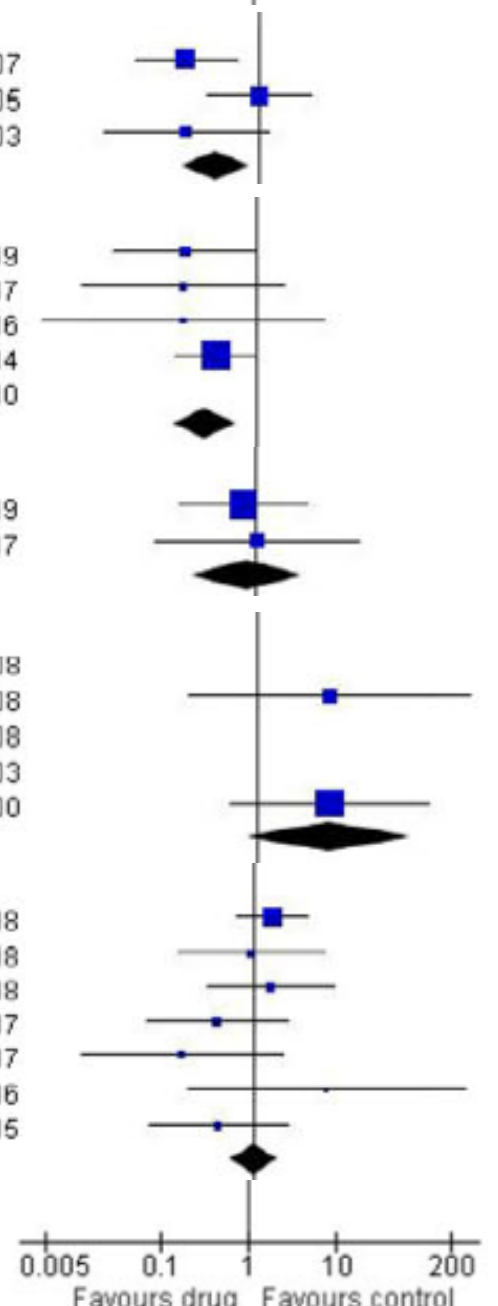
Study or Subgroup	Drug Events	Drug Total	Control Events	Control Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI	Year
1.3.2 Fenoldopam							
Cogliati 2007	12	95	27	98	61.4%	0.40 [0.20, 0.80]	2007
Bove 2005	17	40	16	40	38.6%	1.11 [0.46, 2.68]	2005
Subtotal (95% CI)		**135**		**138**	**100.0%**	**0.59 [0.34, 1.02]**	
1.3.4 Atrial Natriuretic Peptide							
Sezai 2009	40	251	92	253	100.0%	0.35 [0.23, 0.52]	2009
Subtotal (95% CI)		**251**		**253**	**100.0%**	**0.35 [0.23, 0.52]**	
1.3.5 Brain Natriuretic Peptide							
Ejaz 2009	3	45	14	49	36.5%	0.23 [0.08, 0.66]	2009
Mentzer 2007	10	141	17	138	63.5%	0.55 [0.25, 1.22]	2007
Subtotal (95% CI)		**186**		**187**	**100.0%**	**0.40 [0.21, 0.76]**	
1.3.7 Diuretics							
Smith 2008	0	23	0	24		Not estimable	2008
Yallop 2008	0	20	0	20		Not estimable	2008
Mahesh 2008	9	21	8	21	64.8%	1.21 [0.36, 4.10]	2008
Lassnigg 2000	6	41	0	40	35.2%	8.23 [1.58, 42.96]	2000
Subtotal (95% CI)		**105**		**105**	**100.0%**	**2.38 [0.89, 6.34]**	
1.3.8 N-acetylcysteine							
Adabag 2008	22	50	19	52	12.0%	1.36 [0.62, 2.99]	2008
Sisillo 2008	52	129	65	125	30.8%	0.63 [0.38, 1.02]	2008
Wijeysundera 2007	25	88	28	87	18.1%	0.84 [0.44, 1.59]	2007
Ristikankare 2006	16	38	19	39	9.4%	0.77 [0.32, 1.87]	2006
Burns 2005	44	148	42	147	29.7%	1.06 [0.64, 1.75]	2005
Subtotal (95% CI)		**453**		**450**	**100.0%**	**0.86 [0.66, 1.13]**	



Effet estimé / recours à la dialyse lors d'une utilisation à titre préventif

Patel, Heart Fail Rev 2011

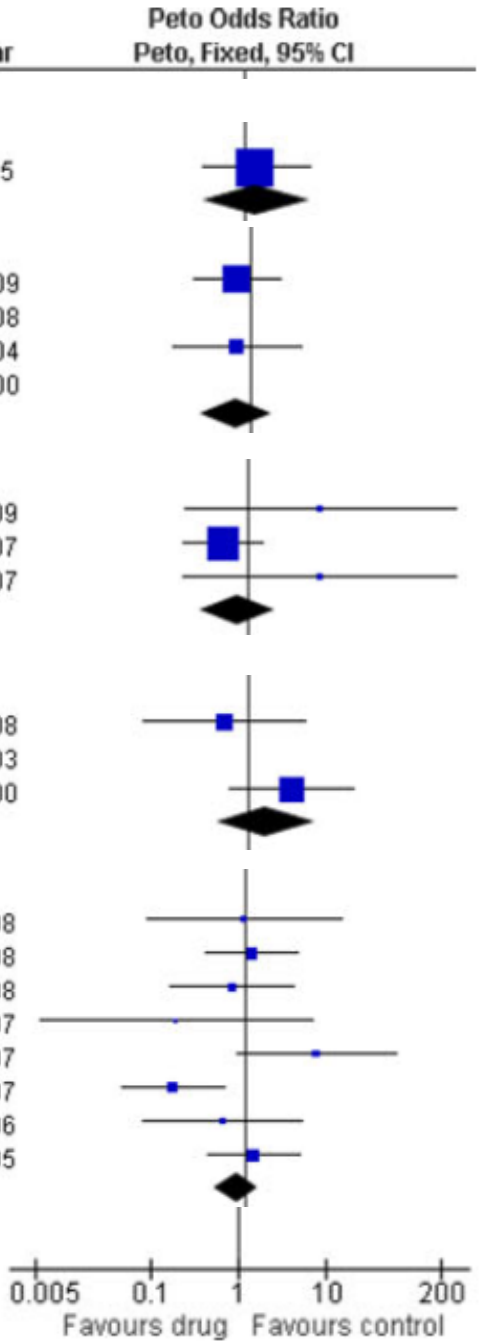
Study or Subgroup	Drug Events	Drug Total	Control Events	Control Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI	Year
1.2.2 Fenoldopam							
Cogliati 2007	0	95	8	98	42.9%	0.13 [0.03, 0.53]	2007
Bove 2005	4	40	4	40	40.6%	1.00 [0.23, 4.27]	2005
Caimmi 2003	0	80	3	80	16.5%	0.13 [0.01, 1.29]	2003
Subtotal (95% CI)		**215**		**218**	**100.0%**	**0.30 [0.12, 0.75]**	
1.2.4 Atrial Natriuretic Peptide							
Sezai 2009	0	251	4	253	19.5%	0.13 [0.02, 0.96]	2009
Sezai 2007	0	63	2	61	9.7%	0.13 [0.01, 2.08]	2007
Sezai 2006	0	75	1	73	4.9%	0.13 [0.00, 6.64]	2006
Sward 2004	6	29	14	30	65.9%	0.32 [0.11, 0.93]	2004
Hayashida 2000	0	9	0	9		Not estimable	2000
Subtotal (95% CI)		**427**		**426**	**100.0%**	**0.24 [0.10, 0.56]**	
1.2.5 Brain Natriuretic Peptide							
Ejaz 2009	2	45	3	49	71.1%	0.72 [0.12, 4.32]	2009
Chen 2007	1	19	1	20	28.9%	1.05 [0.06, 17.51]	2007
Subtotal (95% CI)		**64**		**69**	**100.0%**	**0.80 [0.18, 3.64]**	
1.2.7 Diuretics							
Yallop 2008	0	20	0	20		Not estimable	2008
Mahesh 2008	1	21	0	21	33.6%	7.39 [0.15, 372.38]	2008
Smith 2008	0	23	0	24		Not estimable	2008
Carcoana 2003	0	26	0	24		Not estimable	2003
Lassnigg 2000	2	41	0	40	66.4%	7.39 [0.45, 120.32]	2000
Subtotal (95% CI)		**131**		**129**	**100.0%**	**7.39 [0.76, 71.75]**	
1.2.8 N-acetylcysteine							
Sisillo 2008	10	129	6	125	43.8%	1.65 [0.60, 4.52]	2008
Barr 2008	2	20	2	19	10.7%	0.95 [0.12, 7.30]	2008
Adabag 2008	3	50	2	52	14.0%	1.58 [0.26, 9.46]	2008
Wijeysundera 2007	1	88	3	87	11.4%	0.36 [0.05, 2.58]	2007
Haase 2007	0	30	2	30	5.7%	0.13 [0.01, 2.14]	2007
Ristikankare 2006	1	38	0	39	2.9%	7.59 [0.15, 382.44]	2006
Burns 2005	1	148	3	147	11.5%	0.36 [0.05, 2.59]	2005
Subtotal (95% CI)		**503**		**499**	**100.0%**	**0.98 [0.50, 1.92]**	



Effet estimé / mortalité lors d'une utilisation à titre préventif

Patel, Heart Fail Rev 2011

Study or Subgroup	Drug Events	Drug Total	Control Events	Control Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI	Year
1.1.2 Fenoldopam							
Bove 2005	4	40	3	40	100.0%	1.36 [0.29, 6.36]	2005
Subtotal (95% CI)		**40**		**40**	**100.0%**	**1.36 [0.29, 6.36]**	
1.1.4 Atrial Natriuretic Peptide							
Sezai 2009	4	251	6	253	67.8%	0.67 [0.19, 2.34]	2009
Izumi 2008	0	10	0	8		Not estimable	2008
Sward 2004	2	29	3	30	32.2%	0.67 [0.11, 4.15]	2004
Hayashida 2000	0	9	0	9		Not estimable	2000
Subtotal (95% CI)		**299**		**300**	**100.0%**	**0.67 [0.24, 1.88]**	
1.1.5 Brain Natriuretic Peptide							
Ejaz 2009	1	45	0	49	7.4%	8.08 [0.16, 408.45]	2009
Mentzer 2007	4	141	8	138	85.2%	0.49 [0.15, 1.55]	2007
Chen 2007	1	19	0	20	7.4%	7.79 [0.15, 393.02]	2007
Subtotal (95% CI)		**205**		**207**	**100.0%**	**0.74 [0.25, 2.14]**	
1.1.7 Diuretics							
Mahesh 2008	1	21	2	21	37.5%	0.50 [0.05, 5.05]	2008
Carcoana 2003	0	26	0	24		Not estimable	2003
Lassnigg 2000	4	41	1	40	62.5%	3.45 [0.57, 20.82]	2000
Subtotal (95% CI)		**88**		**85**	**100.0%**	**1.67 [0.40, 6.90]**	
1.1.8 N-acetylcysteine							
Barr 2008	1	20	1	19	5.1%	0.95 [0.06, 15.76]	2008
Sisillo 2008	5	129	4	125	23.0%	1.22 [0.32, 4.60]	2008
Adabag 2008	2	50	3	52	12.7%	0.69 [0.11, 4.11]	2008
Haase 2007	0	30	1	30	2.6%	0.14 [0.00, 6.82]	2007
El-Hamamsy 2007	3	50	0	50	7.8%	7.70 [0.78, 75.76]	2007
Wijeysundera 2007	0	88	7	87	17.9%	0.12 [0.03, 0.56]	2007
Ristikankare 2006	1	38	2	39	7.7%	0.52 [0.05, 5.13]	2006
Burns 2005	5	148	4	147	23.1%	1.25 [0.33, 4.69]	2005
Subtotal (95% CI)		**553**		**549**	**100.0%**	**0.76 [0.40, 1.44]**	



Insuffisance rénale aiguë

Epidemiologie

Physiopathologie

Diagnostic

Biomarqueurs

Prévention

Traitement

Insuffisance rénale chronique

ANP
Effet estimé sur le recours à la dialyse lors d'une utilisation à titre curatif après une chirurgie lourde

Nigwekar,
Clin J Am Soc Nephrol
2009

Review: ANP in acute kidney injury (Version 08)
Comparison: 07 ANP in major surgery
Outcome: 03 Need for RRT

Study or sub-category	ANP n/N	Control n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Akamatsu 2005	2/19	7/18		9.38	0.18 [0.03, 1.06]
Brenner 1995	6/12	6/12		10.91	1.00 [0.20, 4.95]
Hayashi 2003	0/26	0/24			Not estimable
Hayashida 2000	0/9	0/9			Not estimable
Herbert 1998	6/6	6/6			Not estimable
Kute 1996	5/5	4/4			Not estimable
Langrehr 1997	4/33	6/37		13.88	0.71 [0.18, 2.78]
Meyer 1997	0/7	6/7		2.87	0.02 [0.00, 0.45]
Meyer 1999	40/114	21/58		32.65	0.95 [0.49, 1.84]
Sezai 2000	0/20	1/20		3.05	0.32 [0.01, 8.26]
Sezai 2006	0/71	1/71		3.18	0.32 [0.01, 7.99]
Sezai 2006 a	0/20	1/20		3.05	0.32 [0.01, 8.26]
Sezai 2007	0/63	2/61		3.46	0.19 [0.01, 3.93]
Swärd 2004	6/29	14/30		17.72	0.30 [0.09, 0.94]
Total (95% CI)	438	379		100.00	0.49 [0.27, 0.88]

Total events: 68 (ANP), 75 (Control)
Test for heterogeneity: Chi² = 11.13, df = 9 (P = 0.27), I² = 19.1%
Test for overall effect: Z = 2.40 (P = 0.02)

0.1 0.2 0.5 1 2 5 10

Favours ANP Favours control

Les moyens de l'épuration extra-rénale (EER)

- DP (peritoneal dialysis) : gradient osmotique et de concentration

- Méthodes d'épuration continues CRRT :
  - CVVH (continuous veno-venous hemofiltration) : gradient de pression hydrostatique
  - CVVHD (continuous veno-venous hemodialysis) : gradient de concentration
  - CVVHDF (continuous veno-venous hemodiafiltration) : les deux

- HDI (intermittent hemodialysis) : gradient de pression hydrostatique et de concentration

Liquide de dialysat en pédiatrie : iso-osmotique, tampon bicarbonate

Choix d'un mode d'EER en pédiatrie

Mode d'EER	DP	CRRT	HDI
Avantages, indications	Correction rapide d'une hyperkaliémie Surcharge hydrique modérée Facilité de la voie d'accès	Correction rapide d'une hyperkaliémie Surcharge hydrique majeure (OAP, sepsis) : hémofiltration Clearance des grosses molécules : dialyse	Correction rapide d'une hyperkaliémie Surcharge hydrique majeure (OAP, sepsis) Clearance des grosses molécules
Contre-indications	Défaut de paroi, hernie diaphragmatique Infection, tumeur, chirurgie abdominale récente ECUN Dérivation ventriculo-péritonéale Mauvaise tolérance dans les cardiopathies précharge-dépendantes	Coagulopathie	Coagulopathie Instabilité hémodynamique

La dialyse péritonéale chez le nourrisson < 1an

- Assure une ultrafiltration d'environ 4ml/kg/h chez le nouveau-né et 2,5-3,5 ml/kg/h chez le nourrisson
- Assure une clearance de la créatinine de 2 à 20ml/min/1,73m^2 chez le nouveau-né
- *Necker Enfants –Malades, 2000-2008* : une complication grave de la DP à été enregistrée pour 25.4jours de DP

Indications de L’EER à Necker

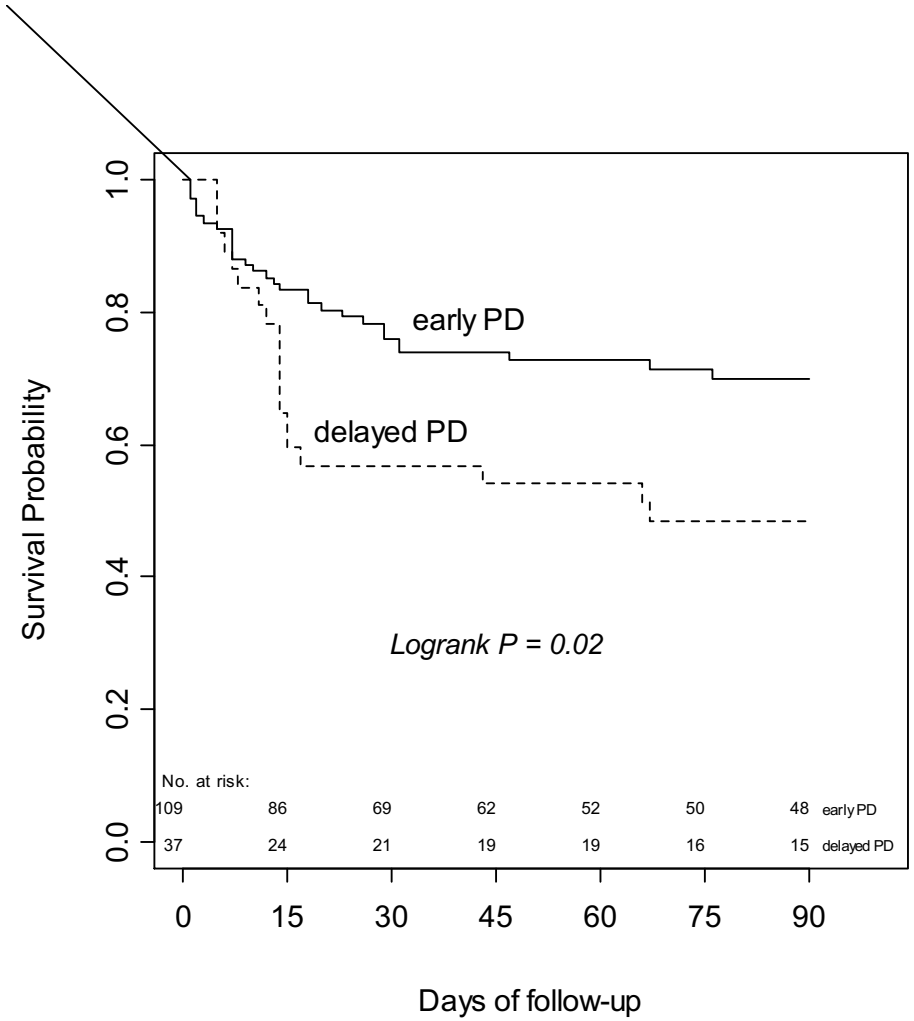
- **L'oligurie** : diurèse < 2ml/kg/h (1ml/kg/h) qui persiste au-delà de **4heures** malgré l'optimisation de la précharge, des constantes hémodynamiques
- La surcharge hydrique
- Le contexte de bas débit
- Les complications métaboliques

Time to initiation of peritoneal dialysis and short-term outcome in neonates and infants with acute kidney injury following congenital cardiac surgery

3550 patients <1 an opérés entre 2000-2009, parmi lesquels 146 ont été dialysés

Délai avant début de la dialyse: 0 – 21 jours, médiane 1 jour

Mortalité à 30 jours: 28.1%
Mortalité globale: 36.6%



HR ajusté sur l'année: 0.52 [0.29 – 0.85]

Insuffisance rénale aiguë

Epidemiologie

Physiopathologie

Diagnostic

Biomarqueurs

Prévention

Traitement

Insuffisance rénale chronique

L'atteinte rénale chronique dans les cardiopathies congénitales

Prevalence, Predictors, and Prognostic Value of Renal Dysfunction in Adults With Congenital Heart Disease

Konstantinos Dimopoulos, MSc, MD; Gerhard-Paul Diller, MD; Evdokia Koltsida, MD; Antonia Pijuan-Domenech, MD; Sofia A. Papadopoulou, MD; Sonya V. Babu-Narayan, BSc, MRCP; Tushar V. Salukhe, BSc, MRCP; Massimo F. Piepoli, MD, PhD; Philip A. Poole-Wilson, MD, FRCP; Nicky Best, BSc, MSc, PhD; Darrel P. Francis, MA, MD, MRCP; Michael A. Gatzoulis, MD, PhD

Background—Renal insufficiency in patients with ischemic heart disease and acquired heart failure is associated with higher mortality and morbidity. We studied the prevalence of renal dysfunction in adult patients with congenital heart disease (ACHD) and its relation to outcome.

Methods and Results—A total of 1102 adult patients with congenital heart disease (age 36.0±14.2 years) attending our institution between 1999 and 2006 had creatinine concentration measured. Glomerular filtration rate (GFR) was calculated with the Modification of Diet in Renal Disease equation. Patients were divided into groups of normal GFR ($\geq$90 mL · min^{-1} · 1.73 m^{-2}), mildly impaired GFR (60 to 89 mL · min^{-1} · 1.73 m^{-2}), and moderately/severely impaired GFR (<60 mL · min^{-1} · 1.73 m^{-2}). Survival was compared between GFR groups by Cox regression. Median follow-up was 4.1 years, during which 103 patients died. Renal dysfunction was mild in 41% of patients and moderate or severe in 9%. A decrease in GFR was more common among patients with Eisenmenger physiology, of whom 72% had reduced GFR (<90 mL · min^{-1} · 1.73 m^{-2}, P<0.0001 compared with the remainder), and in 18%, this was moderate or severe (P=0.007). Renal dysfunction had a substantial impact on mortality (propensity score–weighted hazard ratio 3.25, 95% CI 1.54 to 6.86, P=0.002 for moderately or severely impaired versus normal GFR).

Conclusions—Deranged physiology in adult patients with congenital heart disease is not limited to the heart but also affects the kidney. Mortality is 3-fold higher than normal in the 1 in 11 patients who have moderate or severe GFR reduction. (***Circulation*. 2008;117:2320-2328.**)

Critères KDIGO 2012

1. L'estimation du DFG doit se faire par une équation utilisant la créatinine, et si le DFG estimé est pathologique, il est conseillé de le vériofier en utilisant une équation utilisant la cystatine

bedside CKiD equation : $eGFR_{CKiD} = 0.413 * heigh/sCr$

Zappitelli equation: $eGFR_{ZAP} = (507.76 * e^{0.003 \times height})/sCysC^{0.635} * creat^{0.547}$

2. L'estimation de la fonction rénale comprend, au même titre que la mesure/estimation du DFG, la mesure de l'albuminurie

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

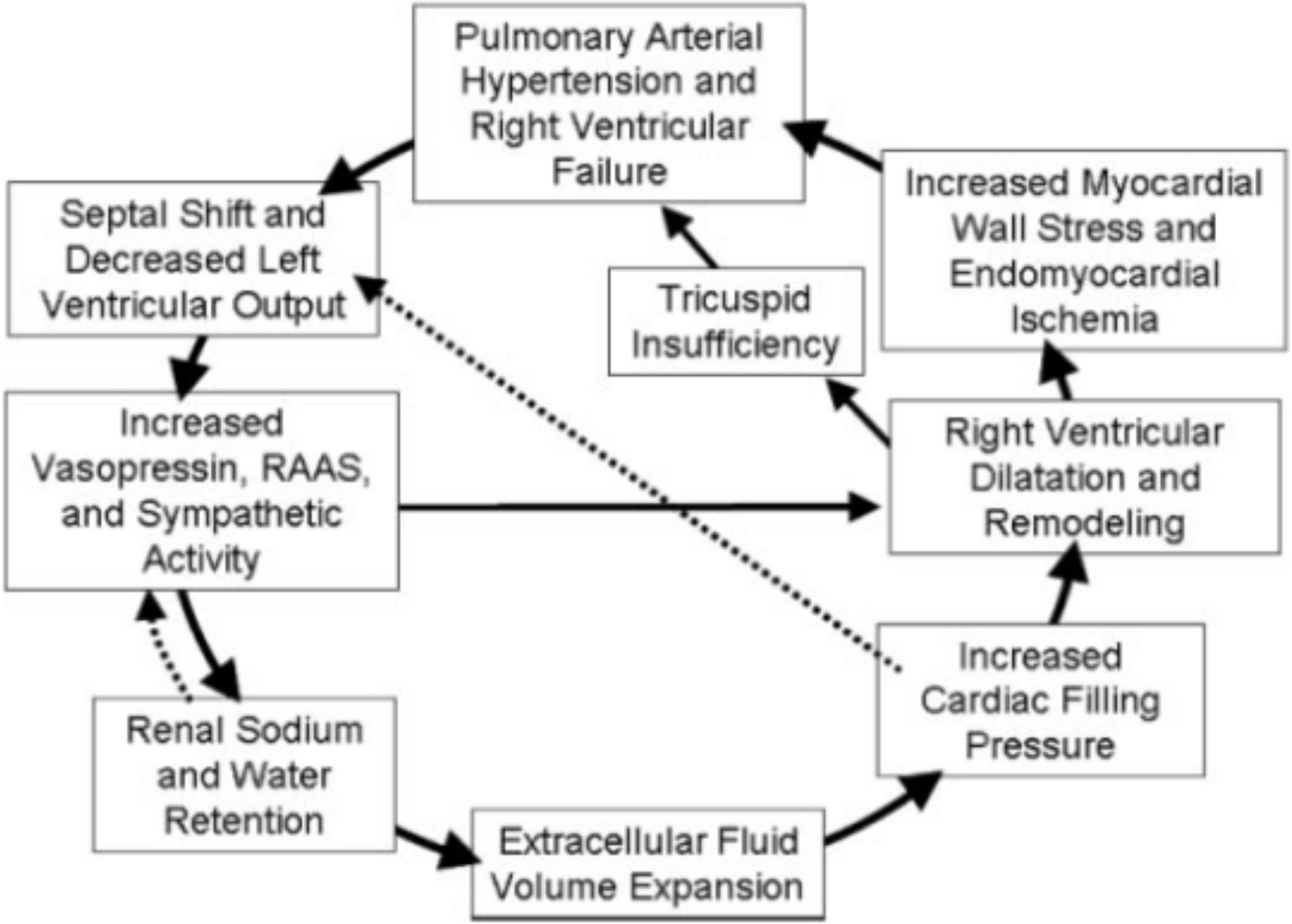
Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Facteurs de risque IRC dans les cardiopathies congénitales

1. La cyanose / viscosité
    - hyperfiltration glomérulaire -> glomérulomégalie -> protéinurie
    - augmentation des résistances vasculaires postcapillaires -> protéinurie tubulaire

2. La défaillance VG (syndrome cardio-rénal)
    - Bas débit chronique -> stimulation du système rénine – angiotensine-aldostérone -> rétention hydro-sodé

3. Défaillance du VD
    - Clearance créatinine corrélée avec la résistance vasculaire pulmonaire et la PVC (*Anne, Int J Cardiol 2009)*



Schrier, CJASN 2008

Conclusions

L'IRA est une complication sévère après chirurgie cardiaque pédiatrique

La découverte des nouveaux biomarqueurs de l'IRA représente un progrès majeur, permettant un diagnostic précoce

Il n'existe, à présent, aucune thérapie spécifique pour prévenir, atténuer ou accélérer la récupération de la fonction rénale en pédiatrie; la miniaturisation des circuits de CEC diminue son incidence

Le traitement de l'IRA reste conservateur; l'instauration précoce de la dialyse dans l'IRA grave améliore la survie

Le dépistage de l'IRC devrait faire partie du bilan de routine des patients porteurs de cardiopathie congénitale