NGAL, a new markers for acute kidney injury

- Prof. J. Delanghe, MD, PhD
- Dept. Clinical Chemistry
- Ghent University

- Lecture Feb 8, 2011

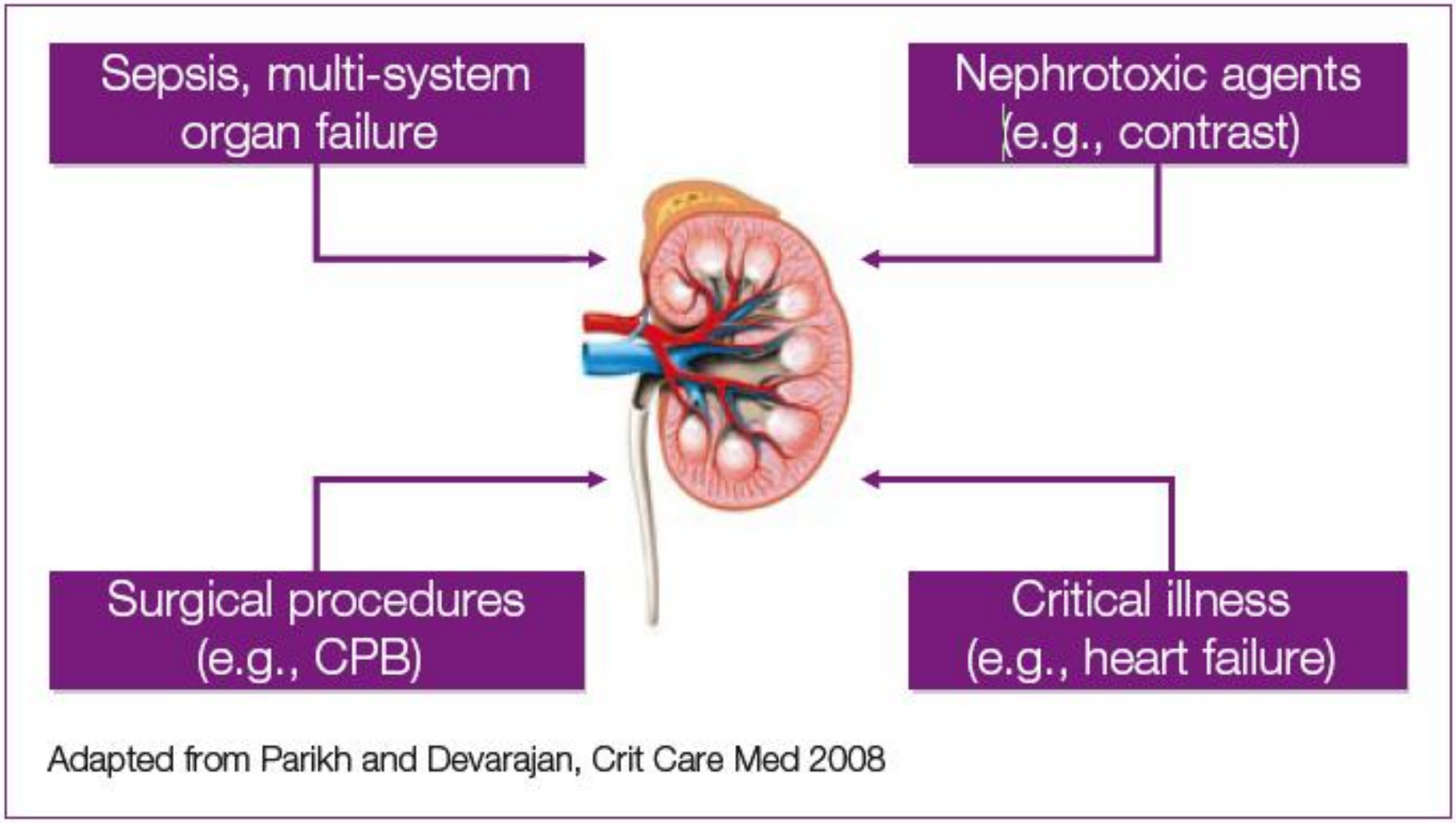
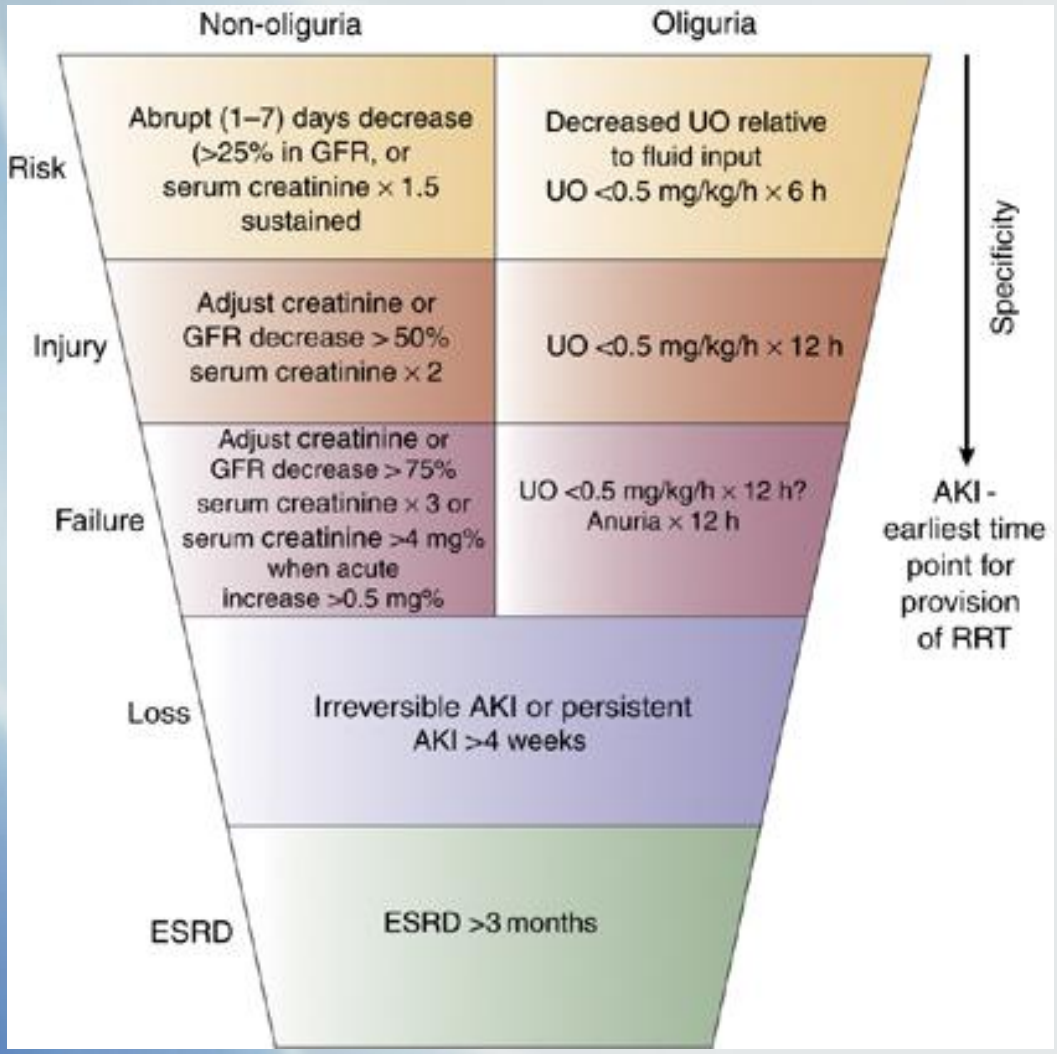


Fig. 1: Common causes of acute kidney injury


Non-oliguria
Oliguria
Risk
Abrupt (1–7) days decrease (>25% in GFR, or serum creatinine × 1.5 sustained
Decreased UO relative to fluid input UO <0.5 mg/kg/h × 6 h
Injury
Adjust creatinine or GFR decrease >50% serum creatinine × 2
UO <0.5 mg/kg/h × 12 h
Failure
Adjust creatinine or GFR decrease >75% serum creatinine × 3 or serum creatinine >4 mg% when acute increase >0.5 mg%
UO <0.5 mg/kg/h × 12 h? Anuria × 12 h
Loss
Irreversible AKI or persistent AKI >4 weeks
ESRD
ESRD >3 months
Specificity
AKI - earliest time point for provision of RRT

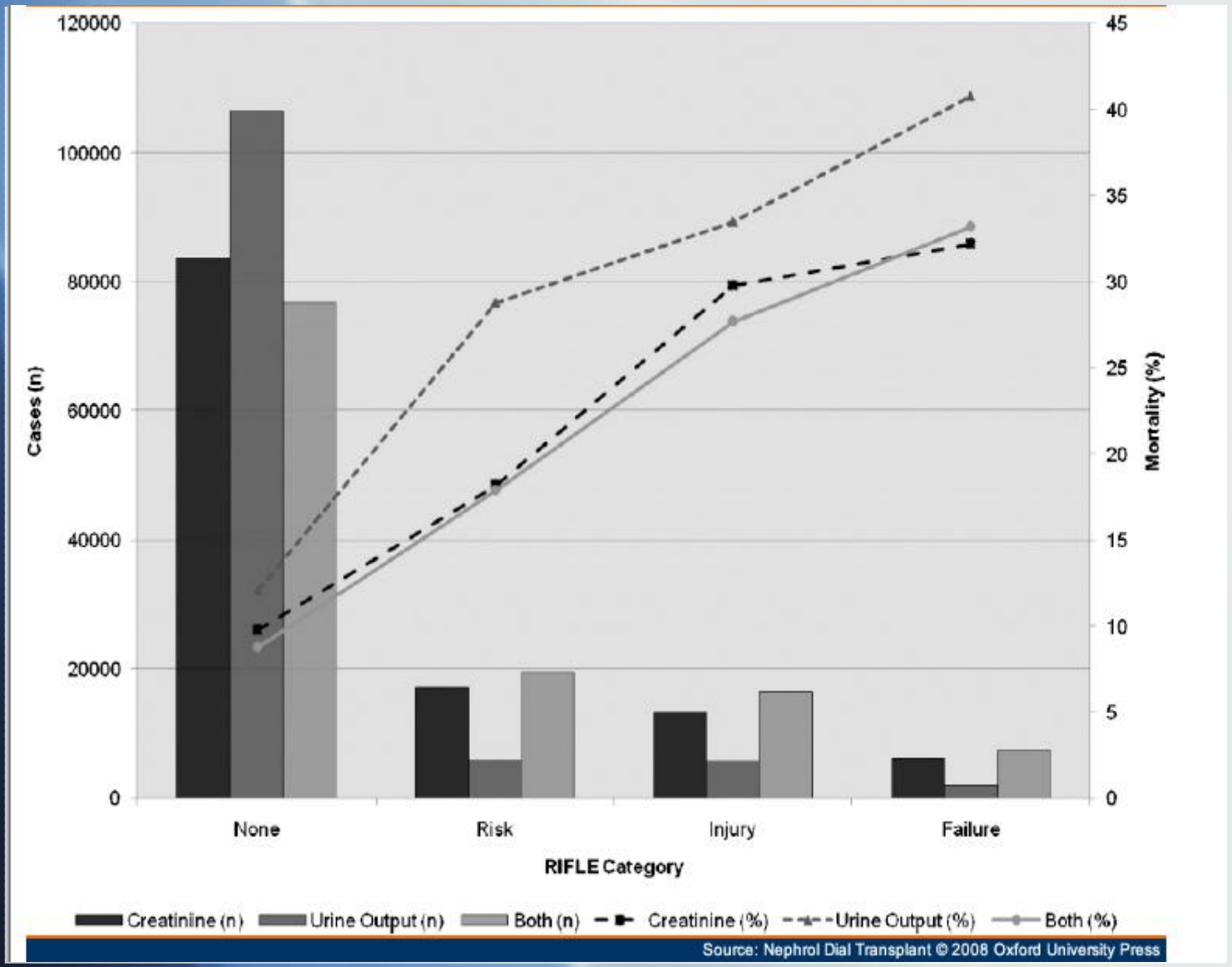

120000
100000
80000
60000
40000
20000
0
Cases (n)
45
40
35
30
25
20
15
10
5
0
Mortality (%)
None
Risk
Injury
Failure
RIFLE Category
Creatinine (n)
Urine Output (n)
Both (n)
Creatinine (%)
Urine Output (%)
Both (%)
Source: Nephrol Dial Transplant © 2008 Oxford University Press

Table 2. Predictors of mortality using time-dependent covariates

Previous table | Figure and tables index

Cox model (modified with permission from Chertow *et al.*[23])	Parameter	
	RR	95% CI
Age (per decade)	1.13	1.01–1.26
Sepsis[a]	1.87	1.33–2.63
CNS failure[a]	4.58	3.30–6.35
Liver failure[a]	1.90	1.34–2.71
Hematologic failure[a]	1.46	1.01–2.10
Dialysis[b]	1.79	1.21–2.66

CI, confidence interval; CNS, central nervous system; RR, relative risk.

[a] Sepsis status and organ system failure updated daily, last value carried forward where missing.

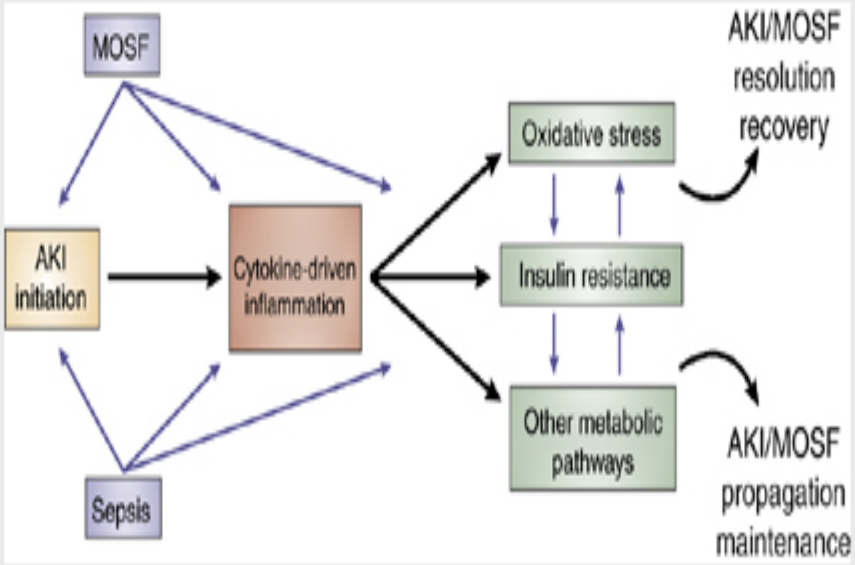
[b] Dialysis status carried forward after initiation.

Table 1. Hospital-acquired AKI: mortality and cost associated with selected changes in SCr

▲ Figure and tables index

Increase in SCr (mg/dl)	Multivariable OR (95% CI)	Area under ROC curve	Increase in total cost
0.3	4.1 (3.1–5.5)	0.84	$4,886
0.5	6.5 (5.0–8.5)	0.86	$7,499
1.0	9.7 (7.1–13.2)	0.84	$13,200
2.0	16.4 (10.3–26)	0.83	$22,023

AKI, acute kidney injury; CI, confidence interval; OR, odds ratio; ROC, receiving operating characteristic; SCr, serum creatinine.



A proposed mechanistic approach to dysmetabolism of AKI. The dysmetabolism of accompanying critical illness is exacerbated in AKI owing to loss of kidney homeostatic function. Once established, these metabolic derangements, along with other potential pathways including, but not limited to endothelial dysfunction, interact with each other to the extent that they may be the decisive factor leading to recovery or death. On the other hand, they also represent intriguing targets for future interventions in patients with AKI.

Serum creatinine is an inadequate marker for AKI.

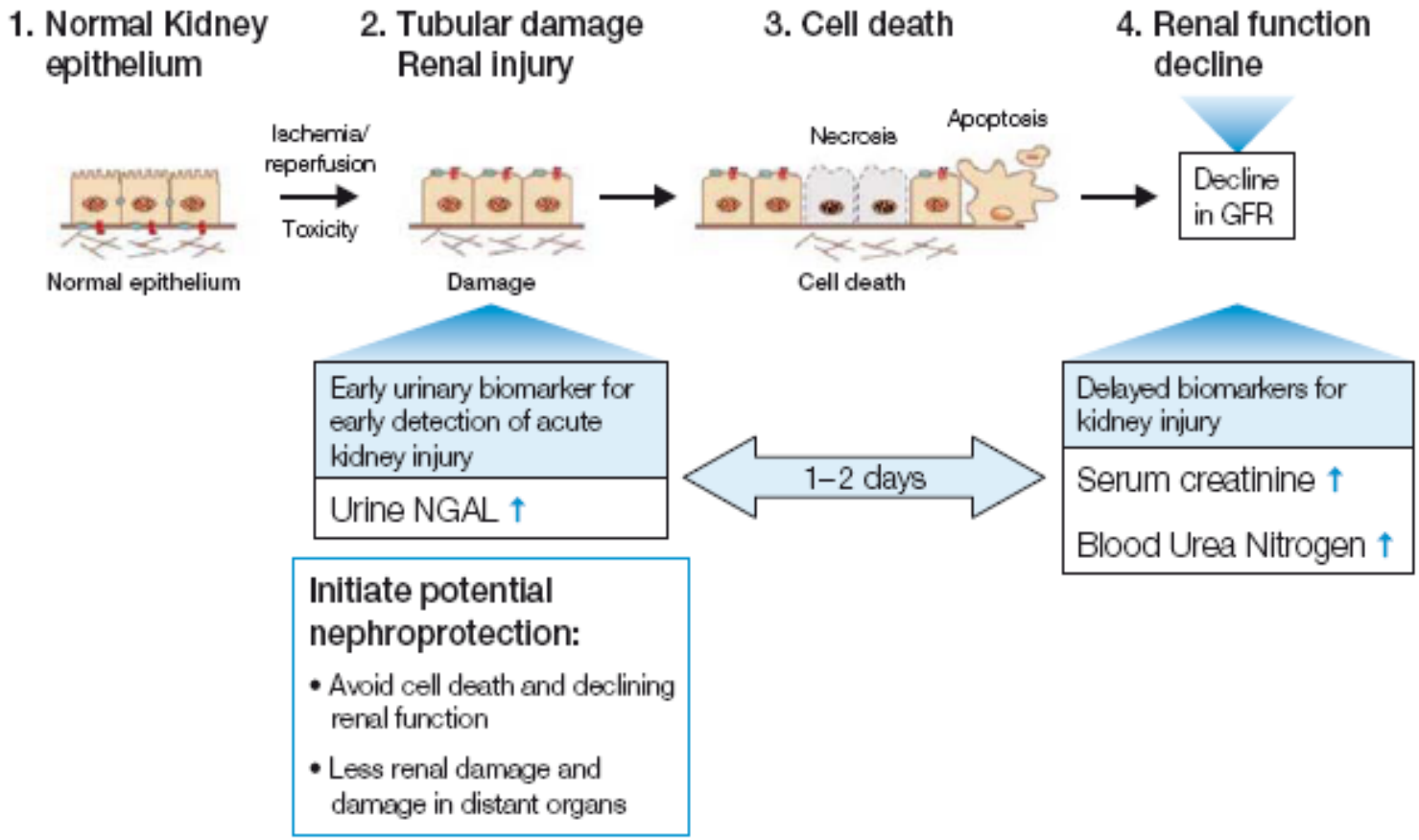
> 50% of renal function must be lost before an elevation in serum creatinine is detected.

Serum creatinine does not accurately depict kidney function until a steady state has been reached, which may require several days.

Although animal studies have shown that AKI can be prevented and/or treated using several maneuvers, these must be instituted very early after the insult, well before the rise in serum creatinine becomes apparent.

Monitoring of NGAL levels can potentially provide a very early warning to providers of critical care.
NGAL levels: a excellent biomarker for the subsequent development of AKI and its complications. Results are available within ± 15 min, and require only µl quantities of sample.

Fig. 1: Early diganostic of Acute Kidney Injury with urine NGAL



Modified from: Vaidya et al. Annu Rev Pharmacol Toxicol 2008 (20)

Requirements for an AKI marker

- Allows early detection

- A clinically acceptable assay for diagnosing AKI should be a robust system that can measure the appropriate analyte rapidly day or night.

ACUTE KIDNEY DISEASE MARKERS

Table 1 Current status of promising acute kidney injury (AKI) biomarkers in various clinical situations

Biomarker Name	Sample Source	Cardiac Surgery	Contrast Nephropathy	Sepsis or ICU	Kidney Transplant	Commercial Test?
NGAL	Plasma	Early	Early	Early	Early	Biosite[a]
Cystatin C	Plasma	Intermediate	Intermediate	Intermediate	Intermediate	Dade-Behring
NGAL	Urine	Early	Early	Early	Early	Abbott[a]
IL-18	Urine	Intermediate	Absent	Intermediate	Intermediate	None
KIM-1	Urine	Intermediate	Not tested	Not tested	Not Tested	None

NGAL neutrophil gelatinase-associated lipocalin, *IL-18* interleukin 18, *KIM-1* kidney injury molecule 1

[a] In development

Pediatr Nephrol 2008;23:2151

NGAL	Urine	<2 h post-CPB	2 h post-contrast	48 h pre-AKI	12-24 h post-tx	ELISA ARCHITE
IL-18	Urine	6 h post CPB	Not increased	48 h pre-AKI	12-24 h post-tx	ELISA
KIM-1	Urine	12 h post CPB	Not tested	Not tested	Not tested	ELISA
L-FABP	Urine	4 h post-CPB	24 h post-contrast	Not tested	Not tested	ELISA
NL	Plasma	<2 h post-CPB	2 h post-contrast	48 h pre-AKI	Not tested	ELISA, Tri

le 1. Novel biomarkers for the early prediction of AKI in humans. AKI: acute kidney injury, defined as a 50% ease in serum creatinine from baseline; NGAL: neutrophil gelatinase-associated lipocalin; IL-18: interleukin -1: kidney injury molecule 1; L-FABP: liver-type fatty acid binding protein. The times indicated (in hours) refe earliest time points at which the biomarker is increased significantly from baseline. #The ARCHITECT Assay i nufactured by Abbott Diagnostics. * The Triage NGAL Test is manufactured by Biosite Inc.

Lipocalins: Ligand Binding Proteins

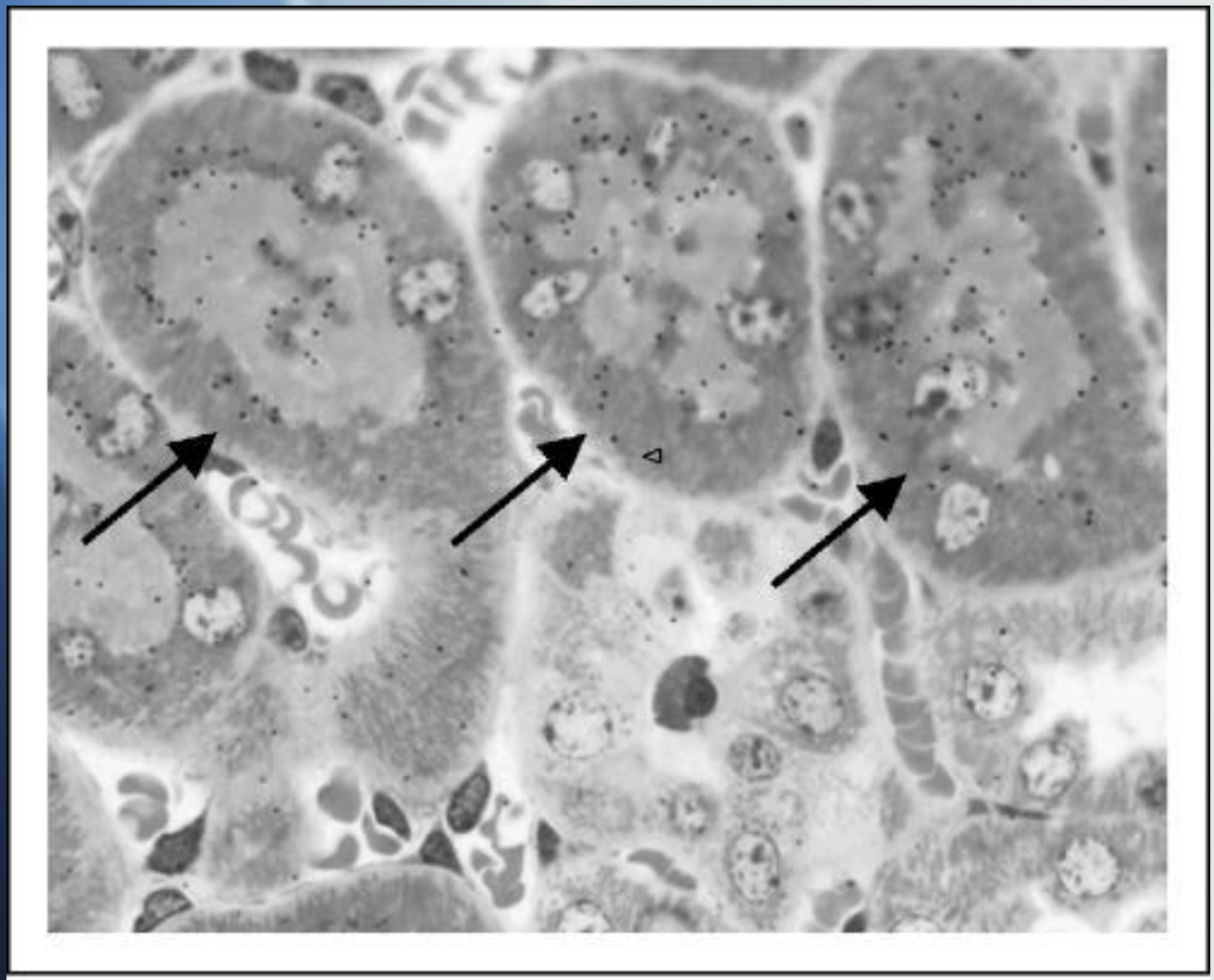
- Bilin Binding Protein.....Heme derivative
- Insecti- and Crustacyanin....astaxanthin
- Alpha2Uglobin..... pheromone, petrol
- Aphrodisin.....pheromone
- Nitrophorins.....Heme
- Alpha1microglobulin.....Hemoglobin
- MUP.....Pheromones
- RBP.....Retinoids
- Purpurin.....Retinoids
- Rat epididymal retinoic acid.Retinoids
- NGAL.....?
- Lipocalin 12.....?
- Lipocalin 13.....?

NGAL, a new marker…

(a) NGAL : enterochelin complex (colorless) and (b) NGAL : enterochelin:iron complex (red). These complexes are stable for days in solution.

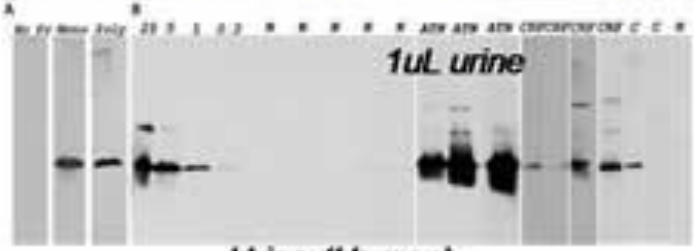
NGAL

- lipocalin-2 (LCN2): 25 kDa protein
- Binds neutrophilic metalloproteinase-9 (MMP-9)
- major NGAL ligand: siderophores -> bacteriostatic
- Expression in various tissues: kidney, lung, stomach, colon
- ↑ damaged epithelial cells
- biomarker for AKI,
- limitations: plasma NGAL affected by CKD, hypertension, syst. infections, inflamm. conditions, anemia, hypoxia, maligninacies



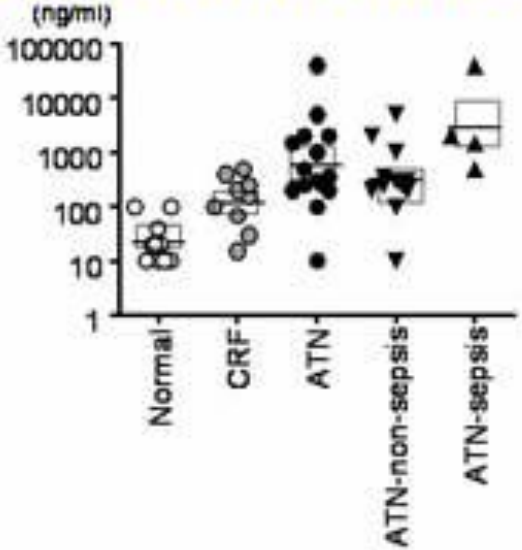
NGAL : enterochelin : ^{55}Fe was introduced into the peritoneum of the mouse and 1 h later the kidneys were inspected for ^{55}Fe by autoradiography. ^{55}Fe was found in proximal tubules (arrows) along the apical membrane and in apical endosomes, suggesting that NGAL : enterochelin : ^{55}Fe was trafficked to this site by glomerular filtration.

Urinary Ngal in Acute Renal Failure



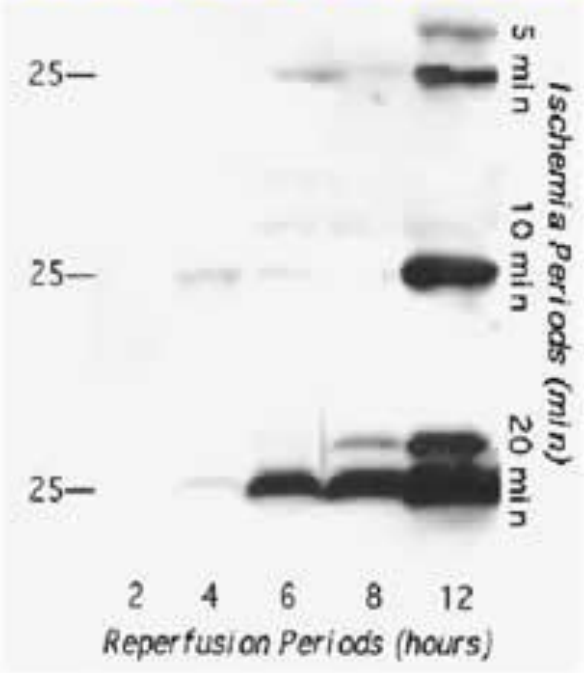
Urine (Human)

Urine (Mouse)



Mori Devarajan Barasch, JCI,2005

Urinary Ngal is Disease Dose-Dependent

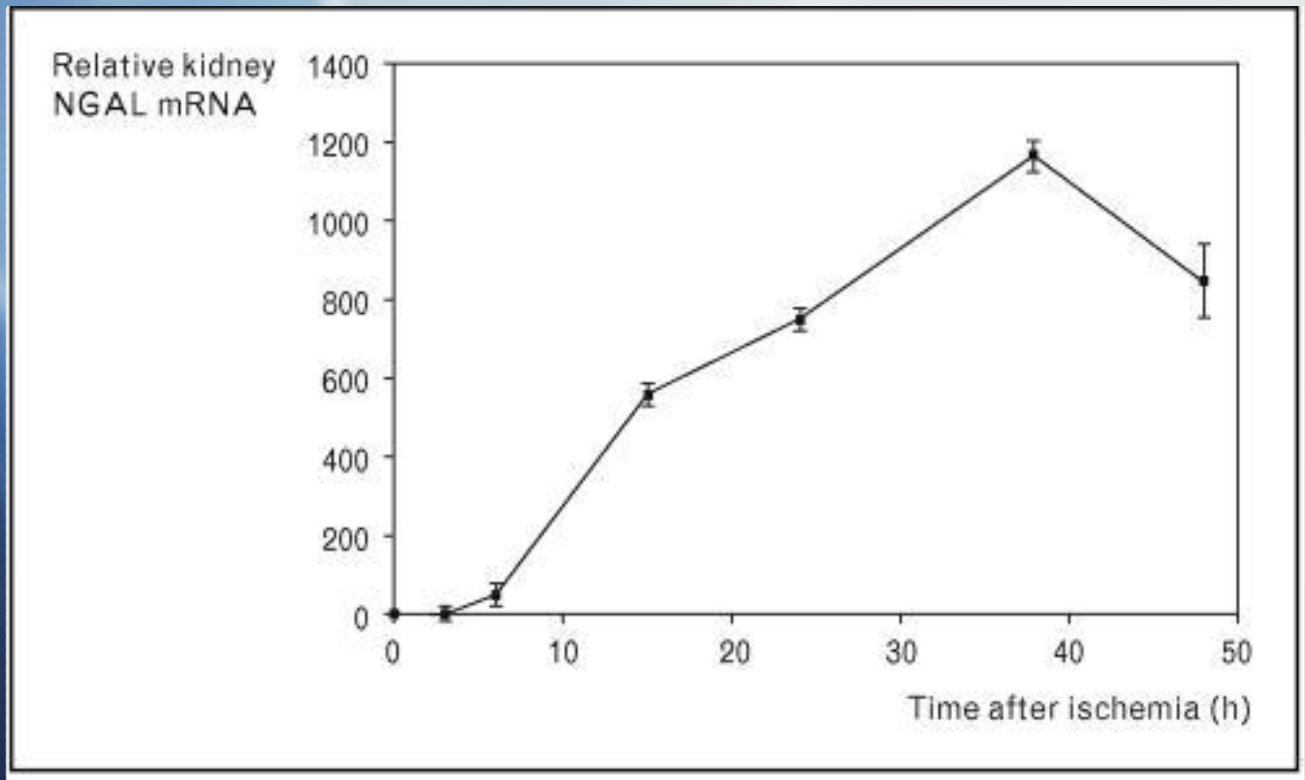


Barasch, Devarajan

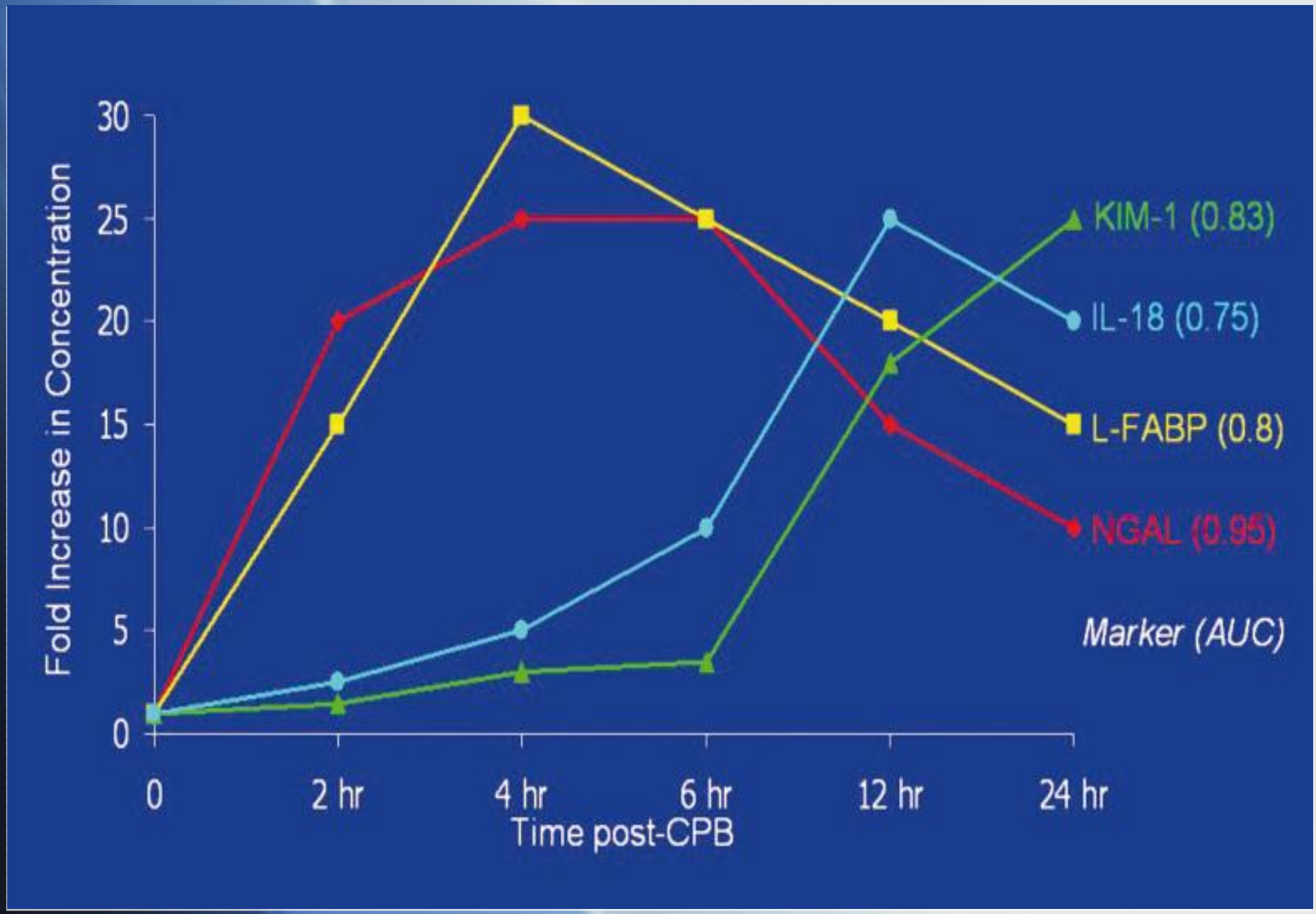
NGAL heterogeneity

- Neutrophils: dimeric NGAL (Cai 2010)

NGAL: Kinetics



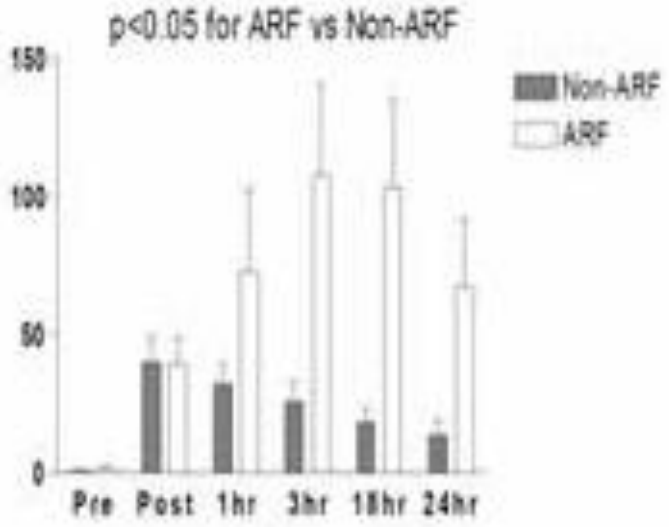
Mice were subjected to unilateral ischemia by renal artery cross clamp, followed by reperfusion for 3–48 h. NGAL mRNA was quantified in the kidney by real-time polymerase chain reaction. In our model, NGAL message rose 10-fold by 6 h and 1000-fold over 1–2 days.

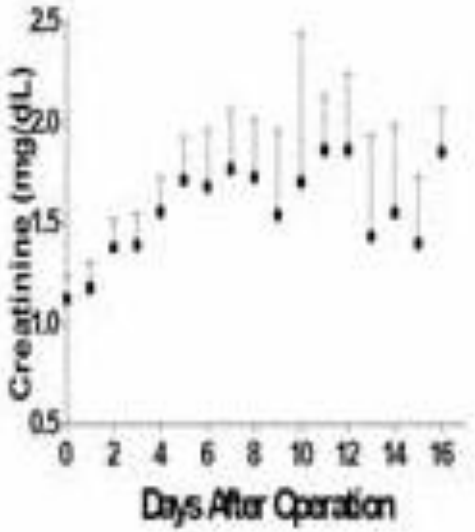

Fold Increase in Concentration
30
25
20
15
10
5
0
0
2 hr
4 hr
6 hr
12 hr
24 hr
Time post-CPB
KIM-1 (0.83)
IL-18 (0.75)
L-FABP (0.8)
NGAL (0.95)
Marker (AUC)

Kinetics of Urine Ngal

Postoperative Urinary Neutrophil Gelatinase-Associated Lipocalin is a sensitive and early marker of renal dysfunction

Gebhard Wagener, MD[1], Michael Jan[1], Mihwa Kim[1], Kiyoshi Mori, MD, PhD[4], Jonathan M. Barasch, MD, PhD[5], Robert N. Sladen, MD[6], H.T. Lee, MD, PhD[1,4]





Triage® point-of-care device for NGAL :
a POC fluorescence-based immunoassay used in conjunction with the Triage Meter (Biosite) for assaying NGAL in **EDTA-blood or plasma**. The device is a single-use cartridge that contains a monoclonal ab conjugated to a fluorescent nanoparticle, NGAL antigen immobilized on a solid phase. The specimen moves through a filter to separate cells from plasma. The plasma reconstitutes the fluorescent ab conjugate detection nanoparticles. NGAL present in the specimen prevents binding of the fluorescent detection particles to the immobilized solid phase: analyte conc ~ 1/ fluorescence.
Measurements of NGAL concentration are displayed in ± 15 min.

Clin Chem Lab Med 2011;49(2):xxx-xxx © 2011 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2011.044

Letter to the Editor

Neutrophil gelatinase-associated lipocalin (NGAL) determined in urine with the Abbott Architect or in plasma with the Biosite Triage? The laboratory's point of view

Etienne Cavalier[1], Anne-Catherine Bekaert[1], Agnès Carlisi[1], Delphine Legrand[2], Jean-Marie Krzesinski[2] and Pierre Delanaye[2,*]

Random fresh urine and EDTA samples were collected from healthy individuals and volunteers with chronic kidney disease who gave their informed consent. EDTA samples

Table 1 Precision and measurement uncertainty observed in six urine pools (Abbott Architect NGAL) and seven EDTA plasma pools (Biosite Triage NGAL).

Pool	n	Mean, µg/L	SD, µg/L	CV, %	Uncertainty, µg/L	Uncertainty, %	β-Expectation tolerance limit, µg/L	β-Expectation tolerance limit, %
Abbott Architect NGAL								
1	15	22.47	0.72	3.2	0.73	6.5	[21.0, 25.0]	[−6.7, 7.3]
2	15	81.07	2.80	3.5	3.0	7.3	[74.4, 87.8]	[−8.3, 8.3]
3	15	141.4	5.80	4.1	6.3	8.2	[124.9, 157.9]	[−11.7, 11.7]
4	15	460.0	26.3	5.7	28.7	12.5	[385.3, 534.7]	[−16.2, 16.2]
5	15	927.5	15.3	1.7	16.0	3.5	[892.6, 962.4]	[−3.8, 3.8]
6	15	1315	24.0	1.9	25.5	3.9	[1257, 1373]	[−4.4, 4.4]
Biosite Triage NGAL								
1	15	117	18.2	15.6	19.4	33.3	[72.22, 161.1]	[−38.1, 38.0]
2	15	163	25.3	15.5	26.1	32.0	[108.9, 221.3]	[−33.1, 35.7]
3	15	174	17.1	9.9	18.2	22.0	[132.6, 214.5]	[−23.6, 23.6]
4	15	199	29.0	14.6	30.0	30.2	[134.3, 263.2]	[−32.4, 32.4]
5	15	298	39.3	13.2	40.5	27.2	[210.6, 385.0]	[−29.2, 29.2]
6	15	427	67.6	15.8	69.8	32.7	[276.5, 576.6]	[−35.1, 35.1]
7	15	722	35.0	4.9	37.4	10.4	[636.0, 807.3]	[−11.8, 11.8]

The standard deviation (SD) and coefficient of variation (CV) correspond to the total variability observed during the 5 days of the experiment. Uncertainty characterizes the dispersion of the values around the (unknown) true value. The β-expectation tolerance limits show, for each level tested, where 95% of future results generated by the methods could be situated.

Clin Chem Lab Med 2011;49(2):xxx-xxx © 2011 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2011.044

Letter to the Editor

Neutrophil gelatinase-associated lipocalin (NGAL) determined in urine with the Abbott Architect or in plasma with the Biosite Triage? The laboratory's point of view

Etienne Cavalier[1], Anne-Catherine Bekaert[1], Agnès Carlisi[1], Delphine Legrand[2], Jean-Marie Krzesinski[2] and Pierre Delanaye[2,*]

Random fresh urine and EDTA samples were collected from healthy individuals and volunteers with chronic kidney disease who gave their informed consent. EDTA samples

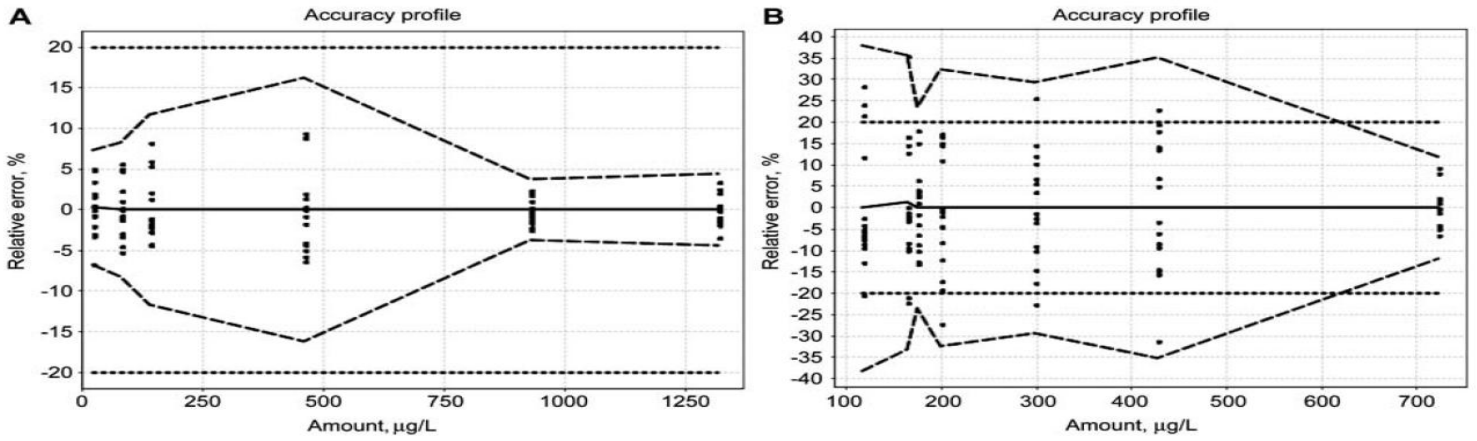


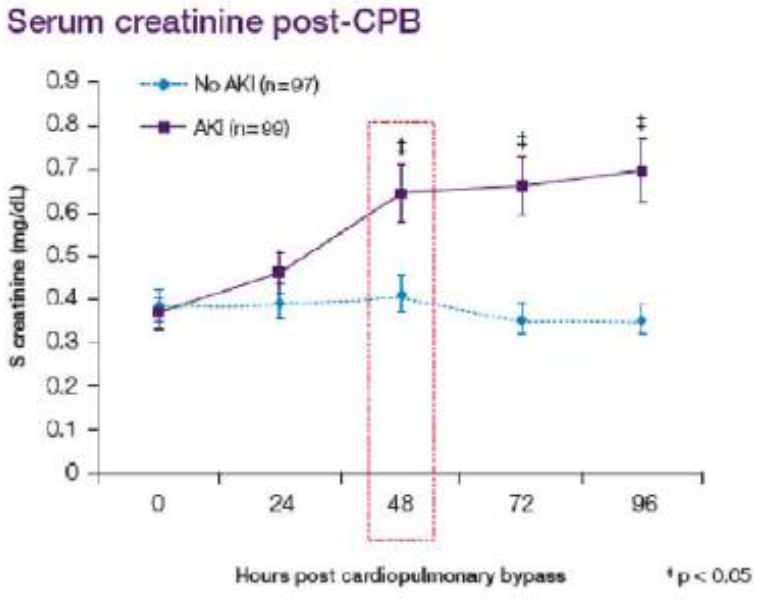
Figure 1 Error profile of the Abbott Architect NGAL (A) and Biosite Triage NGAL (B). When the β-expectation limits (––) are comprised between the maximum total allowable error (...) (shown here at ±20%), the method is considered to be valid.
Each dot represents the result of one assay. As shown here, the Biosite Triage method is valid between 619 µg/L and 722 µg/L only, whereas the Abbott Architect method is valid through the whole measurement range studied.

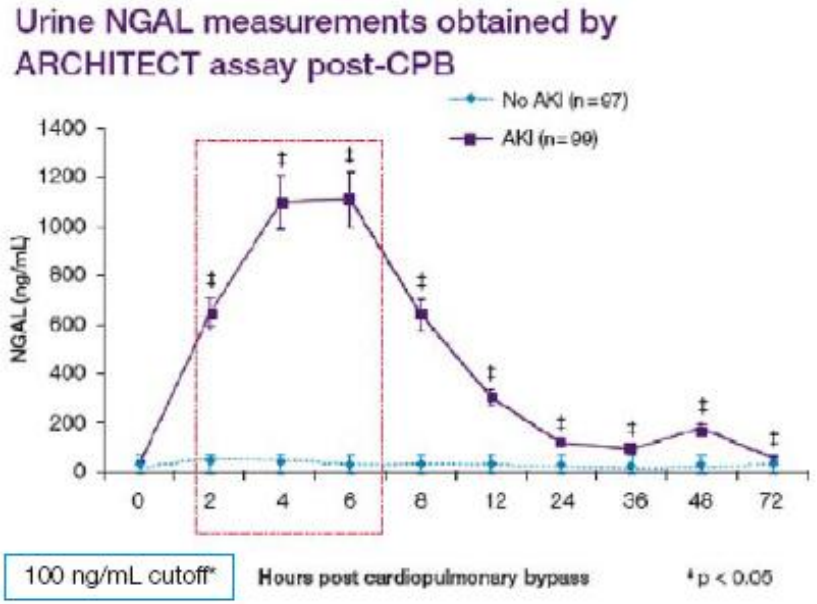
Urine vs. serum

	+	-
Serum 	*No dilution issues	*Analytical sensitivity *Interference from other organs Poor analytical performance Accumulation in renal insufficiency
Urine 	*sensitivity	*UTI interference No sample in case of oliguria

Clinical studies

Fig. 2: NGAL in Diagnosis of AKI after Cardiopulmonary Bypass Surgery



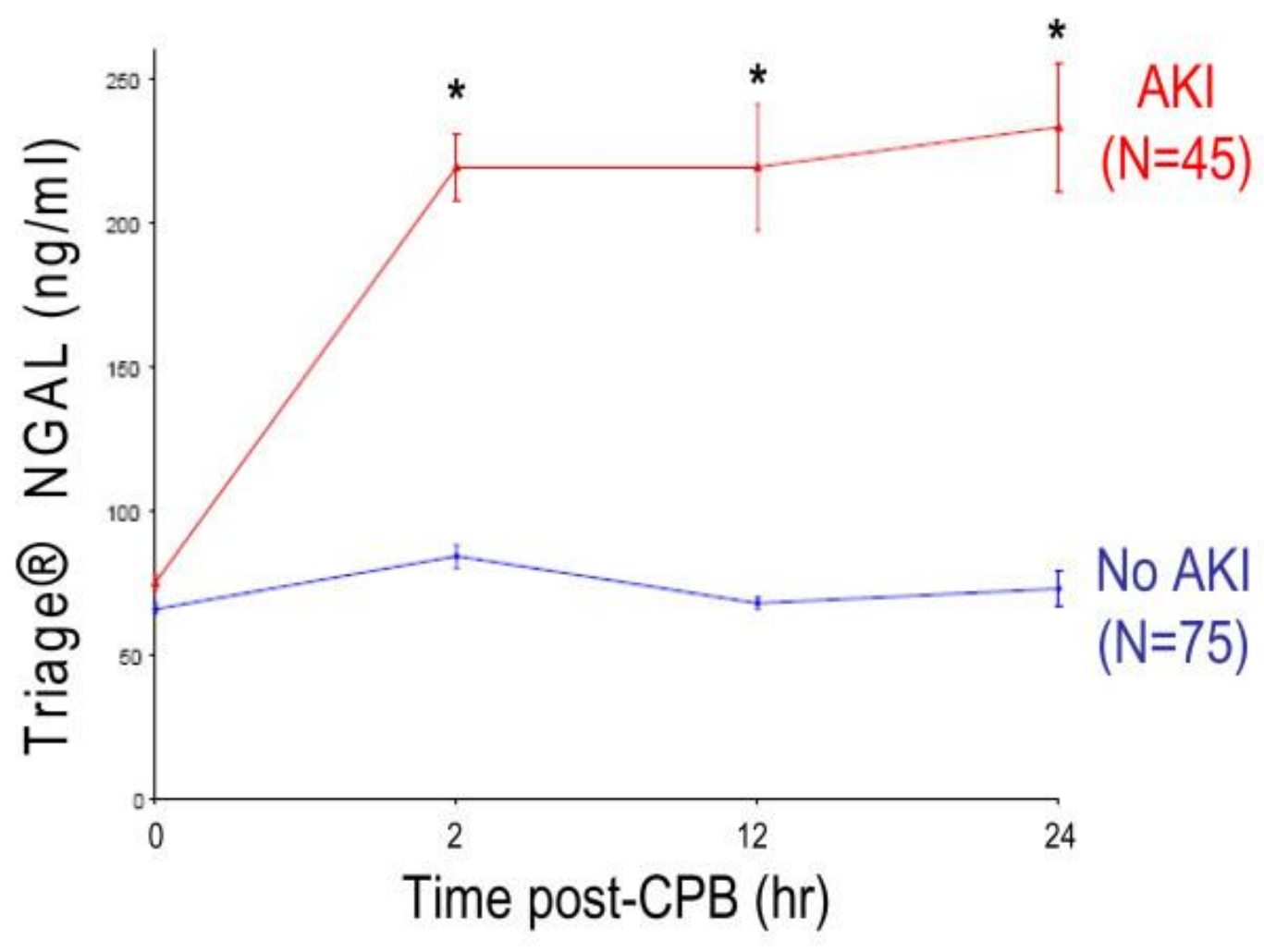


* This represents the value at which AKI can be diagnosed

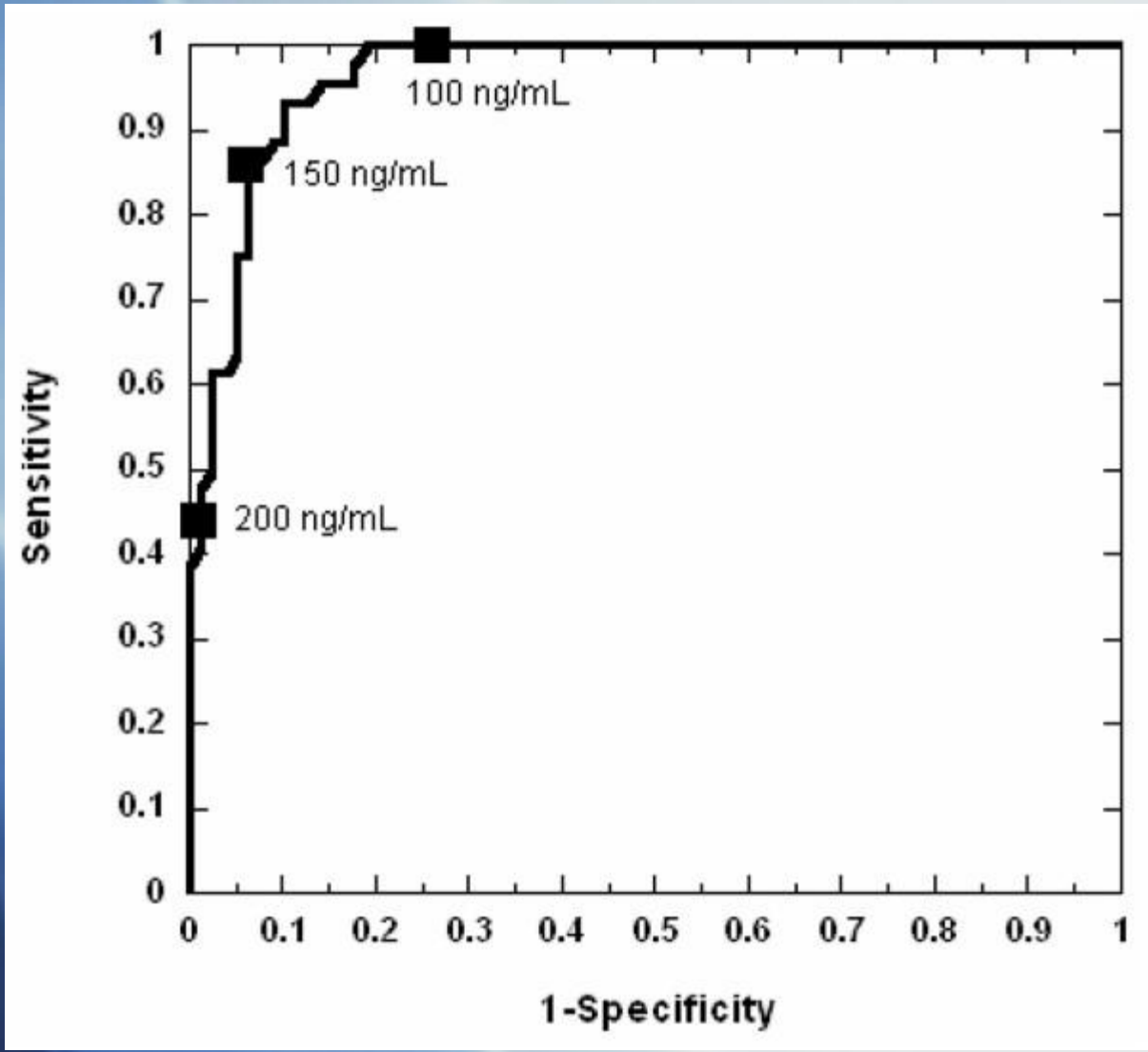
With the ARCHITECT Urine NGAL* acute kidney injury after cardiopulmonary bypass (CPB) operation could be identified 1–2 days earlier compared to creatinine.

Modified from: Bennett et al., Clin J Am Soc Nephrol 2008 (10)

* in development

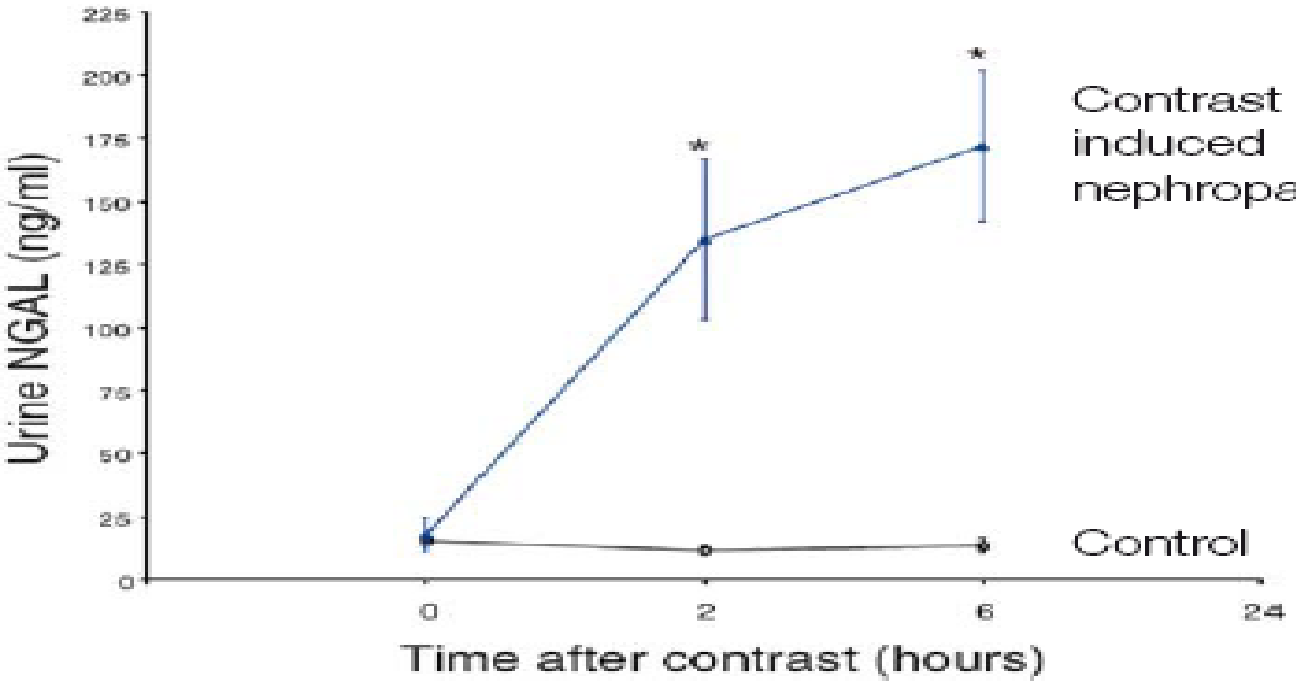


Plasma NGAL measurements obtained at various time points after CPB. AKI was defined as a 50% increase in serum creatinine from baseline. Values expressed as mean ± sd. *$P < 0.0001$ comparing AKI versus no AKI groups.



ROC analysis of the 2-hr plasma NGAL measurements with 3 cut-off levels indicated as filled squares annotated with the corresponding NGAL concentration. The AUC was 0.96 (95% CI 0.94 - 0.99). Dent *et al. Critical Care* 2007 11:R127

Fig. 3: NGAL in Diagnosis of AKI after Contrast Nephropathy



Rapid and strong elevation of Urine NGAL

Hirsch et al. Pediatr Nephrol 2007

NGAL : some studies

Urinary NGAL for the early prediction of acute kidney injury

Reference	Setting	Subjects (*n*)	Sensitivity	Specificity	AUC-ROC (CI)
AUC-ROC, area under the receiver-operating characteristic curve; CI, 95% confidence interval; NR, not reported.					
Mishra J et al.	Cardiac surgery	71	1.0	0.98	0.99 (NR)
Wagener G et al.	Cardiac surgery	81	0.73	0.78	0.80 (0.57–1.03)
Koyner J et al.	Cardiac surgery	72	0.49	0.79	0.69 (0.57–0.82)
Wagener G et al.	Cardiac surgery	426	NR	NR	0.61 (0.54–0.68)
Xin C et al.	Cardiac surgery	33	0.71	0.73	0.88 (NR)
Bennett M et al.	Cardiac surgery	196	0.82	0.9	0.93 (NR)
Portilla D et al.	Cardiac surgery	40	1.0	1.0	1.00 (NR)
Tuladhar SM et al.	Cardiac surgery	50	0.93	0.78	0.96 (0.9–1.0)
Bachorzewska-Gajewska H et al.	Contrast	100	NR	NR	NR
Ling W et al.	Contrast	40	0.77	0.71	0.73 (0.54–0.93)
Hirsch R et al.	Contrast	91	0.73	1.0	0.92 (NR)
Nickolas TL et al.	Emergency room	635	0.9	0.99	0.95 (0.88–1.0)
Zappitellii M et al.	Critical care	150	0.77	0.72	0.78 (0.62–0.95)
Makris K et al.	Critical care	31	0.91	0.95	0.98 (0.82–0.98)
Siew ED et al.	Critical care	451	NR	NR	0.71 (0.63–0.78)
Parikh CR et al.	Kidney transplant	63	0.9	0.83	0.90 (0.71–1.0)
Hall IE et al.	Kidney transplant	91	0.77	0.74	0.81 (0.70–0.92)

NGAL : some studies

Plasma NGAL for the early prediction of acute kidney injury

Reference	Setting	Subjects (*n*)	Sensitivity	Specificity	AUC-ROC (CI)
1.AUC-ROC, area under the receiver-operating characteristic curve; CI, 95% confidence interval; NR, not reported.					
Mishra J et al.	Cardiac surgery	71	0.7	0.94	0.91 (NR)
Koyner J et al.	Cardiac surgery	72	NR	NR	0.54 (0.4–0.67)
Dent CL et al.	Cardiac surgery	120	0.84	0.94	0.96 (0.94–0.99)
Tuladhar SM et al.	Cardiac surgery	50	0.8	0.67	0.85 (0.73–0.97)
Haase-Fielitz et al.	Cardiac surgery	100	0.79	0.78	0.8 (0.63–0.96)
Malyszko J et al.	Contrast	91	0.73	1.0	0.91 (NR)
Wheeler DS et al.	Critical care	143	0.86	0.39	0.68 (0.56–0.79)
Cruz DN et al.	Critical care	301	0.73	0.81	0.78 (0.65–0.90)
Constantin JM et al.	Critical care	88	0.82	0.97	0.92 (0.85–0.97)
Niemann CU et al.	Liver transplant	59	0.68	0.8	0.79 (NR)

urinary NGAL as a biomarker for AKI.

"**the development of urinary biomarkers for kidney disease is the search for our renal troponin**"

biomarkers will not necessarily replace creatinine and urine output as a means of assessing AKI--but rather it will supplement these more traditional tests, much like troponin is now used in conjunction with older methods (e.g. ECG) is diagnosing myocardial injury.

A marker such as urinary NGAL may be a better marker for injury, as serum creatinine is a marker of kidney function, and becomes elevated far after the kidney insult.

Siew et al: > 400 ICU pts underwent urinary NGAL measurement within 24 hrs of admission to an ICU; the pts were followed prospectively and assessed for AKI (increase in serum creatinine of > 0.3mg/dL or > 50% increase in baseline creatinine).

Elevated urinary NGAL levels was moderately successful in predicting AKI.

Sensitivity and Specificity of a Single Emergency Department Measurement of Urinary Neutrophil Gelatinase–Associated Lipocalin for Diagnosing Acute Kidney Injury. T Nickolas et al, Ann Int Med 2008

- A single serum creatinine measurement cannot distinguish AKI from CKD or prerenal azotemia.
- To test the sensitivity and specificity of a single measurement of urinary NGAL and other urinary proteins to detect AKI
- 635 pts admitted to the hospital with AKI, prerenal azotemia, CKD, or normal kidney function.
- AKI: a significantly elevated mean urinary NGAL level compared with the other kidney function groups; $P = 0.001$). sensitivity and specificity of NGAL for detecting acute injury were 0.900 and 0.995), resp. values were superior to those for NAG, α_1-microglobulin, α_1-acid glycoprotein, fractional excretion of Na, and serum creatinine. Urinary NGAL was highly predictive of clinical outcomes,
- A single measurement of urinary NGAL helps to distinguish acute injury from normal function, prerenal azotemia, and CKD and predicts poor outcomes.

Urinary NGAL is a better predictor of a poor clinical course than serum creatinine (defined by admission to the intensive care setting, nephrology consultation, dialysis initiation, or mortality) *(Multivariate regression analysis, Nickolas et al., Ann. Intern. Med. 2008; 148:810).*

Marker	Odds ratio (95% CI)
Urinary NGAL > 130 µg/g	24.70 (7.69 – 79.42)
Serum creatinine > 221 µmol/l	6.03 (2.25 – 16.14)

NGAL

- Neutrophil gelatinase-associated lipocalin (NGAL) is a marker of AKI.
- In CKD, NGAL is a marker of kidney disease and severity. In pts with CKD secondary to renal dysplasia, obstructive uropathy and glomerular and cystic diseases, plasma NGAL levels were inversely associated with GFR. As GFR declined to <30 ml/min, NGAL outperformed cystatin C as a marker of kidney failure. A study conducted in CKD vs controls demonstrated that NGAL levels were higher in CKD (378.3 ± 111.1 ng/ml versus 7.4 ± 3.3 ng/ml; p=0.01). NGAL was correlated with s-creatinine (p=0.02), GFR (p=0.04), and proteinuria (p=0.01).
- In pts with CKD of various etiologies, urine NGAL levels at baseline significantly correlated with future changes in serum creatinine (P = 0.0002) and GFR (P = 0.02). Alternatively, when baseline urine NGAL levels were low, serum creatinine remained stable over a mean follow-up time of 200 days.

- Paragas et al looked at the ability of urinary NGAL to distinguish between HIV pts with a collapsing FSGS pathology (e.g. "HIVAN") compared to HIV pts that had either normal kidney function or CKD from another cause.

- Pts with HIVAN had 11-x higher urinary NGAL levels compared to HIV+ controls without a reduced GFR, and still 5.5-fold higher urinary NGAL levels compared to HIV+ controls with CKD due to causes other than HIVAN. The findings may prove useful in terms of diagnosing pts with HIV and rapidly declining renal function with HIVAN in a non-invasive manner (e.g. no biopsy).

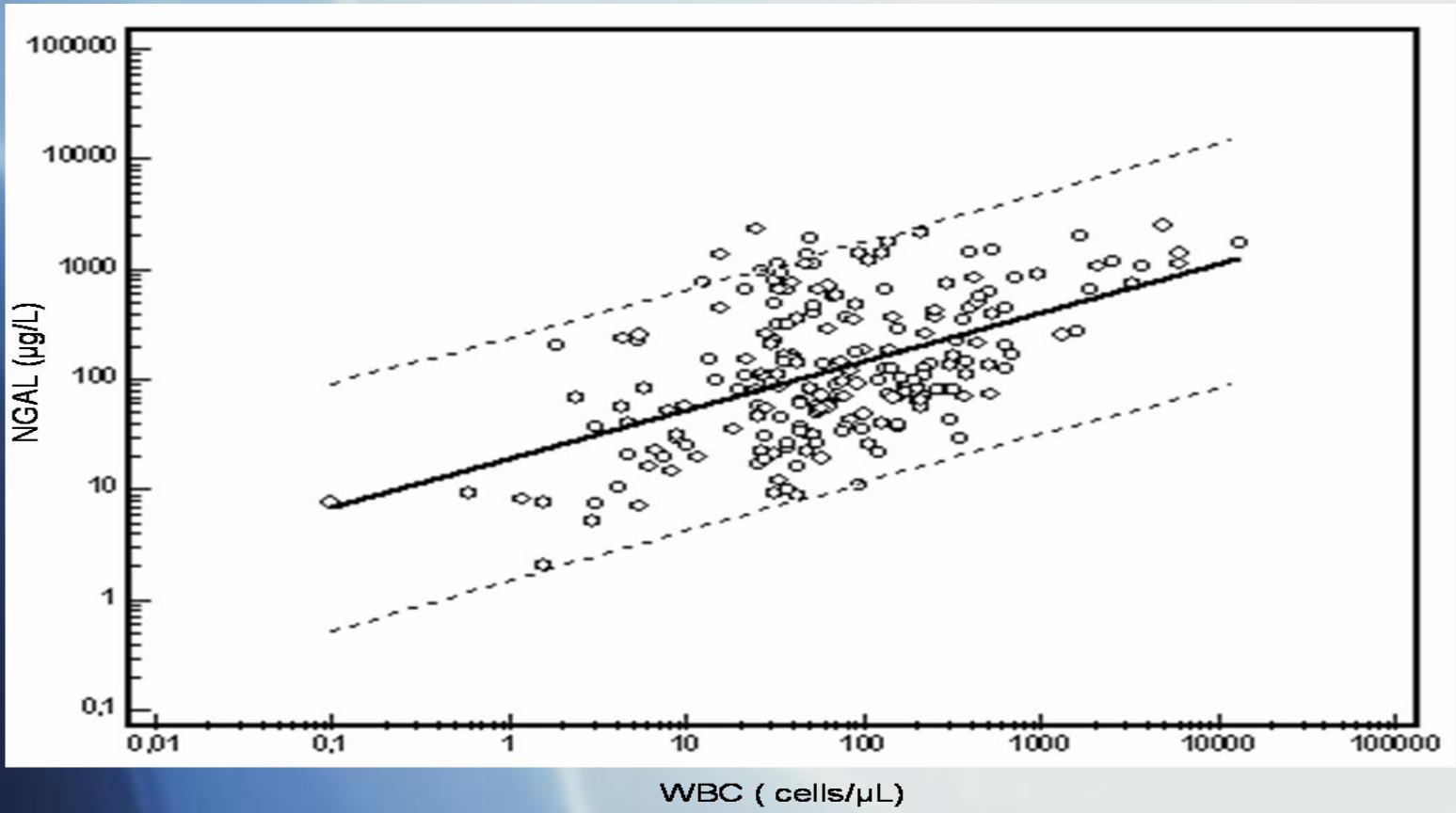
- While biopsy should still likely remain the gold standard until these findings can be confirmed, it could potentially be useful information in pts where biopsy is deemed too risky to proceed--a common situation in HIVAN pts.

- Because creatinine is an unreliable variable describing kidney function, the search for a new and sensitive marker of kidney function is underway.
- NGAL has been proven useful in the quantitation of CKD.
- Elderly heart recipients had sign higher cys C and serum NGAL and lower eGFR than their younger counterparts, despite not having a statistically different serum creatinine.
- **Serum NGAL could be a sensitive marker of kidney function, particularly in elderly patients.**

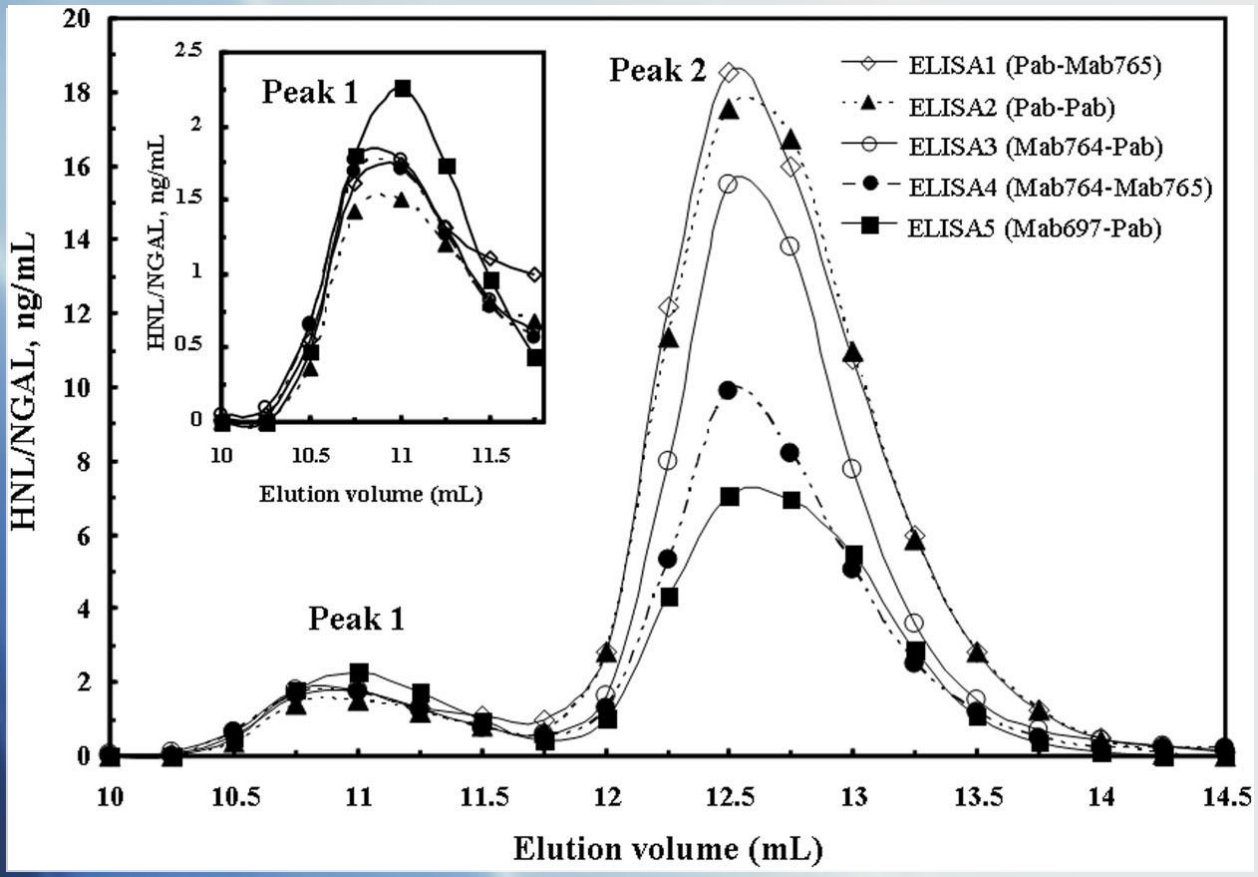
- Przybylowski P, Malyszko J, Malyszko J.
- Med Sci Monit 2010;16:CR440-4.

Neutrophil gelatinase associated lipocalin

(De Cavele AS et al, CCLM 2011, in press)

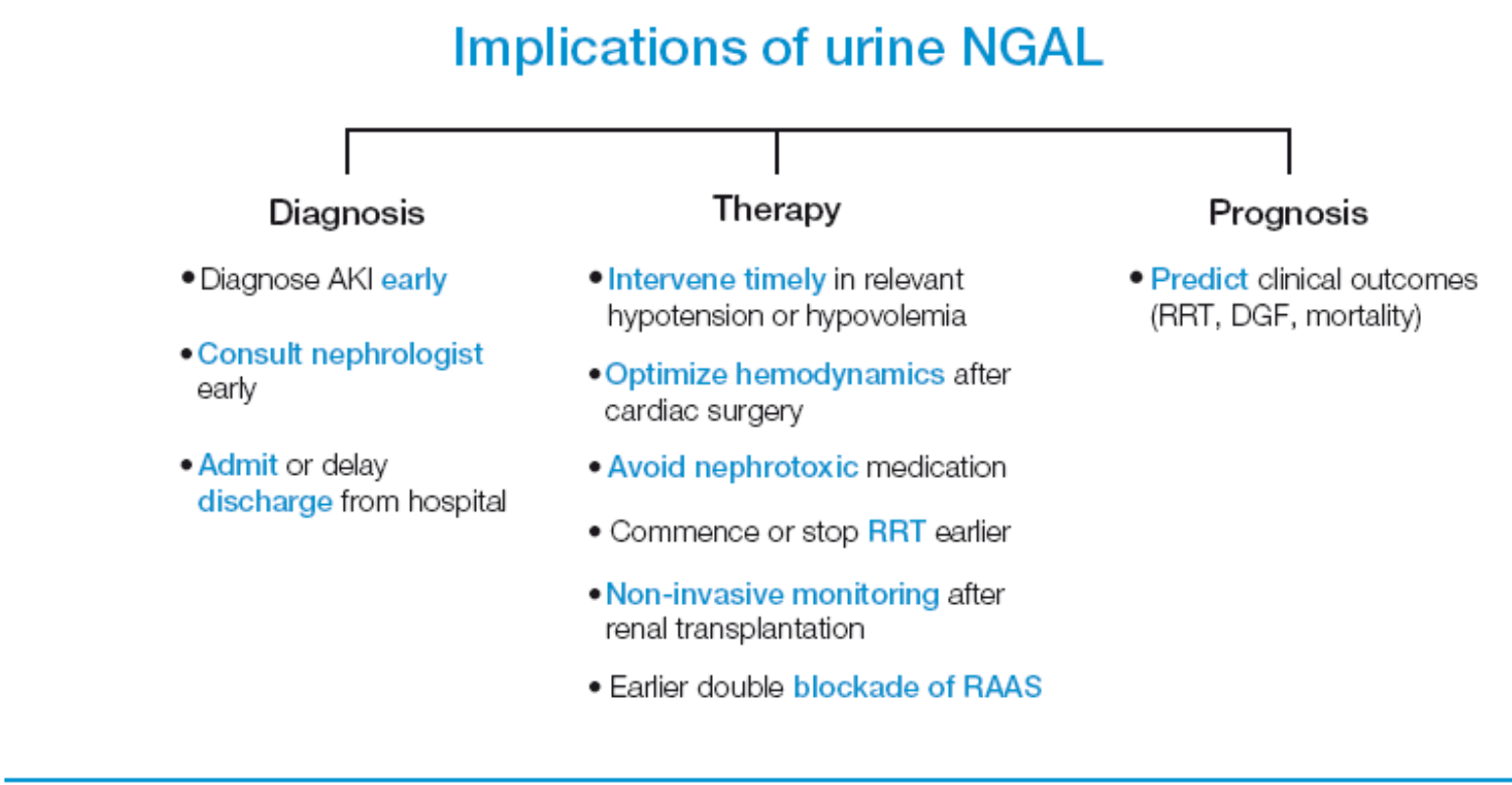


Molecular heterogeneity



- NGAL test results in urine may depend on MoAb used (Cai, CJASN, 2010, Dec)

Fig. 4: Implications of urine NGAL



AKI: acute kidney injury
RRT: renal replacement therapy
RAAS: renin angiotensin aldosterone system
DGF: delayed graft function

KIM-1

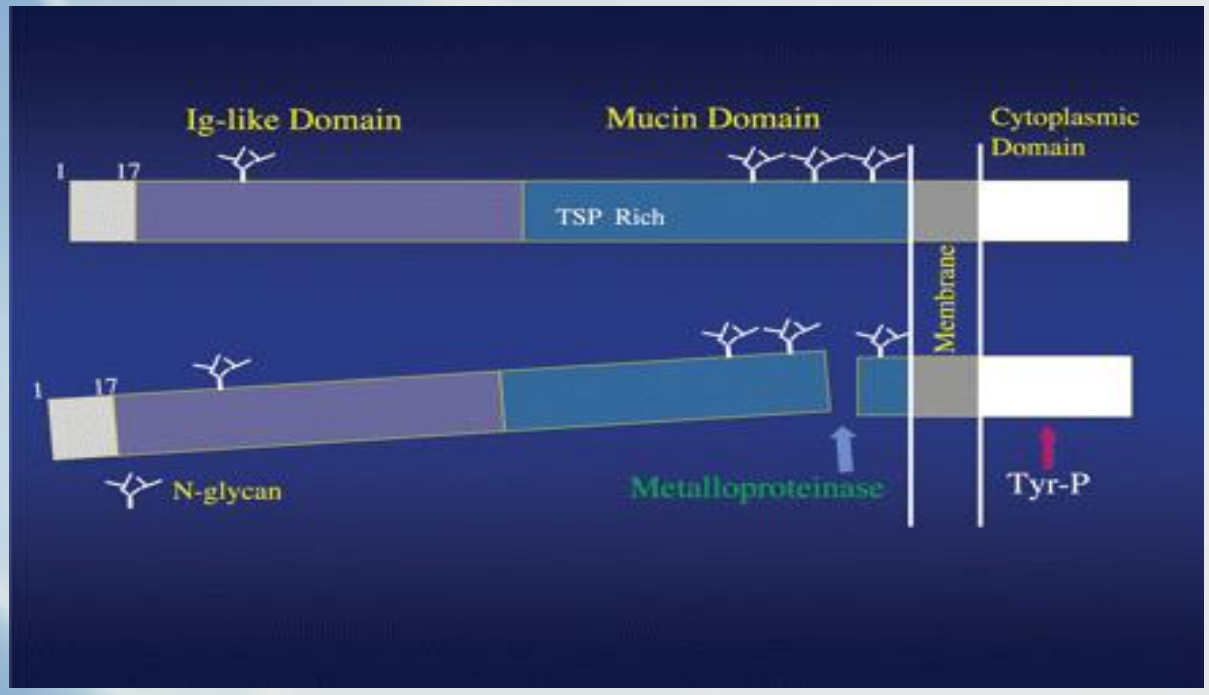
- Kidney injury molecule (KIM)-1 is a transmembrane protein, not expressed in normal kidney but upregulated in de-differentiated proximal tubule cells. After ischemic or nephrotoxic AKI, a proteolytically processed domain is found in urine. KIM-1 is induced in proximal tubules in kidney biopsies from pts with AKI (primarily ischemic). Urinary KIM-1 distinguishes ischemic AKI from prerenal azotemia and chronic renal disease.

- In pts undergoing bypass surgery, AKI (0.3 mg/dl increase in s-creatinine) developed in 31%, in whom urinary KIM-1 levels increased by ± 40% at 2 h after surgery and by >100% at the 24 h time point. In a case–control study of 40 children undergoing cardiac surgery, with AKI (a 50% increase in s-creatinine) and without AKI, urinary KIM-1 levels were markedly enhanced (AUC: 0.83 at the 12 h time point)

- Elevated urinary KIM-1 is associated with adverse outcomes in pts who develop AKI. KIM-1 is a promising candidate for inclusion in the urinary 'AKI panel'.

- KIM-1 is more specific to ischemic kidney injury and is not significantly affected by chronic kidney disease or urinary tract infections. It may be an important biomarker for differentiating between subtypes of AKI.

KIM-1



KIM-1 is a membrane glycoprotein that contains, in its extracellular portion, a 6-cysteine Ig-like domain, 2 *N*-glycosylation sites and a T/SP rich domain characteristic of mucin-like *O*-glycosylated proteins. There is 1 transmembrane domain and a short intracellular domain with a tyrosine phosphorylation signalling motif present in the renal form (KIM-1b).

Conclusions (I)

- Acute kidney insufficiency: new markers are emerging
- 2011: N-GAL available

Conclusions (II)

- NGAL provides unique diagnostic information
- Knowledge of pitfalls important
- Final positioning of NGAL testing still needs to be established