Etat des lieux

- L’insuffisance rénale aigue (IRA) est une pathologie assez fréquente, entraînant des conséquences importantes à court et moyen terme.
- Le diagnostic d’IRA est souvent posé assez tardivement.
- Des mesures préventives et thérapeutiques sont disponibles, mais souvent prises tardivement à cause du manque de biomarqueurs prédictifs précoces.
- Ces dernières années, de nouveaux biomarqueurs sont cependant devenus disponibles.

L'IRA: un problème sérieux

- 5% de tous les patients hospitalisés et jusqu'à 30% aux soins intensifs.
- L'incidence augmente à un taux assez alarmant.
- Taux de mortalité très élevé chez les patietns dialysés aux soins intensifs.
- 25% des dialysés aux soins intensifs progresseront vers une insuffisance rénale terminale endéans les 3 ans

Devarajan, Semin Nephrol 27:637-651, 2007
Devarajan, Contrib Nephrol 160:1-16 , 2008

Biomarqueurs: Infarctus vs. IRA

Période	Infarctus du myocarde	IRA
1960s	LDH	
1970s	CPK, myoglobin	
1980s	CK-MB	
1990s	Troponin T	
2000s	Troponin I	

Amélioration de la prise en charge
Diminution drastique de la mortalité

Biomarqueurs: Infarctus vs. IRA

Période	Infarctus du myocarde	IRA
1960s	LDH	Créatinine
1970s	CPK, myoglobin	Créatinine
1980s	CK-MB	Créatinine
1990s	Troponin T	Créatinine
2000s	Troponin I	Créatinine

Amélioration de la prise en charge
Diminution drastique de la mortalité

Pas d'amélioration
Mortalité élevée

Il existe réellement un besoin de biomarqueurs d'IRA!

Limitations de la créatinine (1)

- Pas un marqueur d'atteinte rénale, mais de fonction rénale
- Limitations intrinsèques (âge, muscle, rhabdomyolyse, sexe, malnutrition,…)
- Dilution par ressuscitation fluidique
- Nécessité de perte de 50% de la fonction rénale avant que les taux ne montent
- ½ vie largement augmentée, quand GFR diminue
- Ne peut prédire la GFR que si état hémodynamiquement stable
- Peut avoir besoin de plusieurs jours pour atteindre steady state si GFR change
- Hyperglycémie et hypoprotéinémie peuvent faussement élever la créat, alors qu'hypoglycémie et hypoprotéinémie peuvent la baisse (si Jaffé)

Limitations de la créatinine (2)

- Variabilité biologique et différence critique
- Critère KDIGO: augmentation de 0.3 mg/dL ou bien 1.5 fois la baseline

- La différence critique, basée sur un CV intra-individuel de 5.95% est d'environ 18%

Table 1. Calculation of sCr RCV for different baseline values hypothesising optimal analytical variation (CV_A=0.5CV_I) and 95% significance level.*

sCr at baseline (in mg/dL)	RCV(%)	Absolute changes needed to be significant (in mg/dL)	KDIGO criterion in mg/dL	% from baseline
0.75	18.28	0.10	0.30	40.00
1.00	18.28	0.18	0.30	30.00
1.50	18.28	0.27	0.30	20.00
2.00	18.28	0.37	0.30	15.00
2.50	18.28	0.46	0.30	12.00
3.00	18.28	0.55	0.30	10.00
3.50	18.28	0.65	0.30	8.57
4.00	18.28	0.75	0.30	7.50

Si cr=2.50, une augmentation de 0.40 sera considérée comme significative par KDIGO (>0.30) alors qu'elle ne l'est pas

*CV_I is taken from current Ricos database and represents CV_I in health. Calculation of RCV shows that different absolute values are needed for a significant change according to baseline. On the other hand the fixed 0.30 mg/dL (26.5 µmol/L) of the AKI definition gives false negative results when baseline sCr is < 2.00mg/dL (176.8 µmol/L) and false positive results when baseline sCr is ≥ 2.00 mg/dL (176.8 µmol/L)

Makris, Clin Bioch 2016

Volume urinaire

- Intérêt par rapport à la créatinine:
- Cut-off prédéfini (pas besoin de valeur baseline)
- Pas affecté par certaines conditions (infections, sepsis, malnutrition)

Volume urinaire

- Désavantages:
- Erreurs transcription
- Statut hydratation, diurétiques, ressuscitation fluidique
- Perfusion rénale
- Sondes nécessaires

Résultats discordants sur la sensibilité par rapport à la créatinine, mais information importante, facile et pas chère

Mesure de la fonction rénale

- Par iohexol plasmatique, sur un ou deux time points: réalisable mais attention au troisième secteur!

- Monitoring continu: Rabito CA (JASN, 1994): souhaitable, mais pas encore réalisable en pratique.

Jeliffe and modified Jeliffe equations

((Volume of distribution × (sCr on day1 − sCr on day2))
+ creatinine production) × 100/1440/average sCr.

This simplified equation is accurate for sCr measured every 24 h. When sCr rises, sCr on Day 2 is used instead of average sCr.

The volume of distribution in deciliters is estimated to be equal to 0.4 × weight (kg) × 10. Body weight is defined as initial hospital admission weight.

Creatinine production (mg/day) is computed using the following equation: [29.305 − (0.203 × age)] × weight × [1.037 − (0.0338 × average Cr)] × correction for gender (0.85 for males and 0.765 for females).

Since this equation takes into account sCr fluctuations and creatinine production over time, but not fluid balance variations, which can also significantly influence serum creatinine measurements [15], we adjusted every sCr according to the cumulative daily fluid balance using the following equation [15]:

Adjusted creatinine = sCr × correction factor

Correction factor = [hospital admission weight (kg)
× 0.6 + Σ (daily fluid balance)]/hospital admission weight × 0.6.

The adjusted sCr was substituted for the measured sCr in the Jelliffe equation to compute the Modified Jelliffe GFR. Jelliffe and Modified Jelliffe equations were indexed to 1.73 m^2 body surface area.

Jeliffe Am J Nephrol 2002

Bouchard J NDT 2010

Validée uniquement contre la clairance urinaire de créatinine…

Différenciation IRA pré-rénale vs. IRA intrinsèque

Table 2. Traditional urinary tests used in AKI diagnosis and differentiation

Test	**Pre-renal azotaemia**	**Intrinsic AKI**
Sediment	Normal or hyaline casts	Casts, tubular epithelial cells
Sp. gravity	High >1.020	Low <1.020
uNa	Low <20 mmol/L	High>40mmol/L
FeNa	<1%	>1%
FeUr	<35%	>35%
Urine osmolality (mOsm/Kgr H_2O)	High>500	Near serum (<300)
uCr/sCr ratio	High>40	Low<10

uNa=urinary Sodium, FeNa=fractional excretion of sodium, FeUr=fractional excretion of urea, uCr=urinary creatinine, sCr=serum creatinine

Clin Biochem Rev 37 (4) 2016 161

Makris, Clin Bioch 2016

Biomarqueurs d'IRA

Caractéristique	Biomarqueur
Marqueur de filtration glomérulaire	Cystatine C
Protéines de bas PM, catabolisées au niveau tubulaire, mais libérées dans l 'urine en cas d'atteinte tubulaire	Cystatine C, β2-microglobuline, α1-microglobuline, RBP
Enzymes libérées par tubules après dommage tubulaire	N-acetyl-β-D-glucosaminidase (NAG) α- ou π-glutathione S transférase (α-GST ou π-GST)
Médiateurs inflammatoires libérés par les cellules rénales	IL-18
Protéines up-régulées en réponse à un dommage tissulaire	NGAL KIM-1 L-FABP
Biomarqueurs d'arrêt cellulaire	TIMP2 IGFBP7

Difficultés…

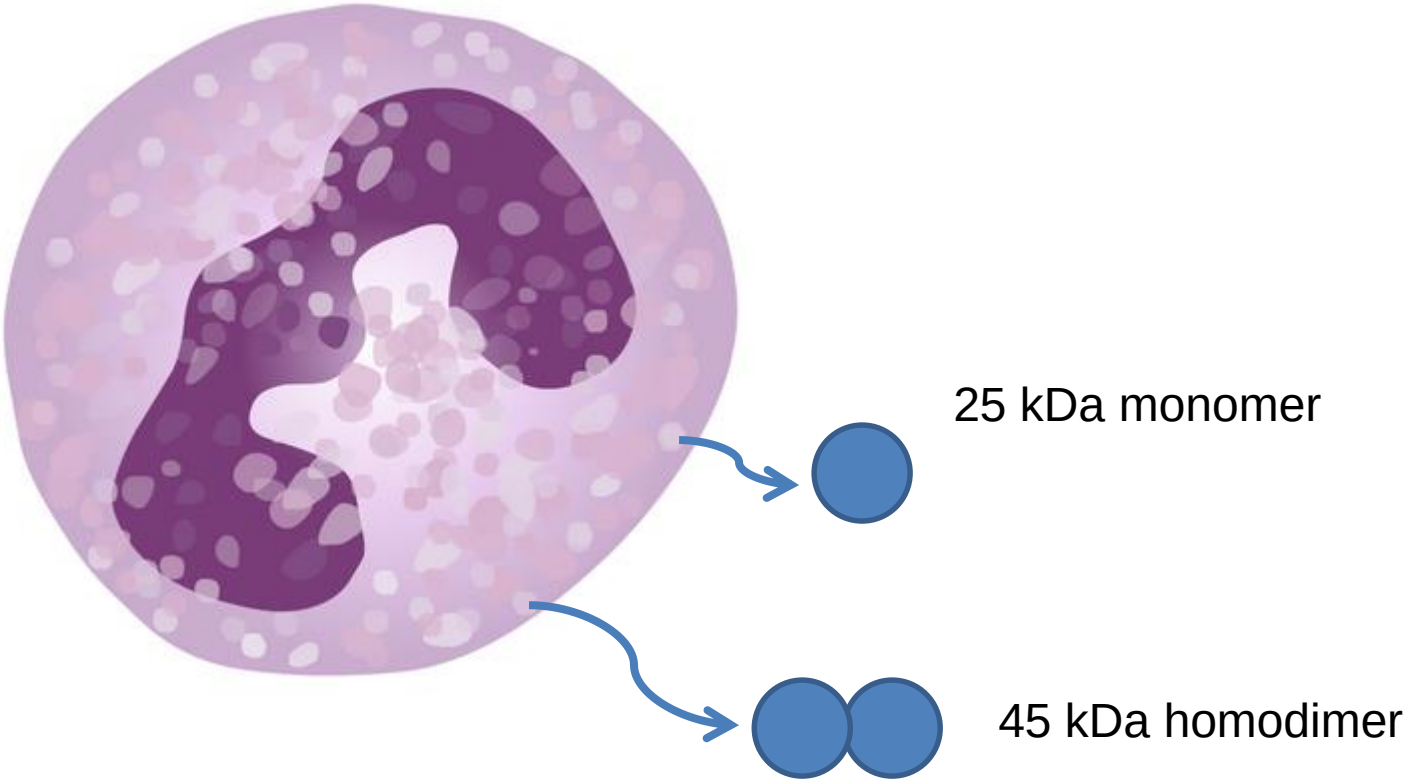
- Très bons résultats, mais dans des études avec populations ciblées
- Pas de gold standard
- Comparaison par rapport…à la créatinine!
- Résultats discordants mais: pas même atteinte étudiée, pas même cinétique, variabilité biologique, variabilité analytique etc.
- Résultats discordants plasma-urine

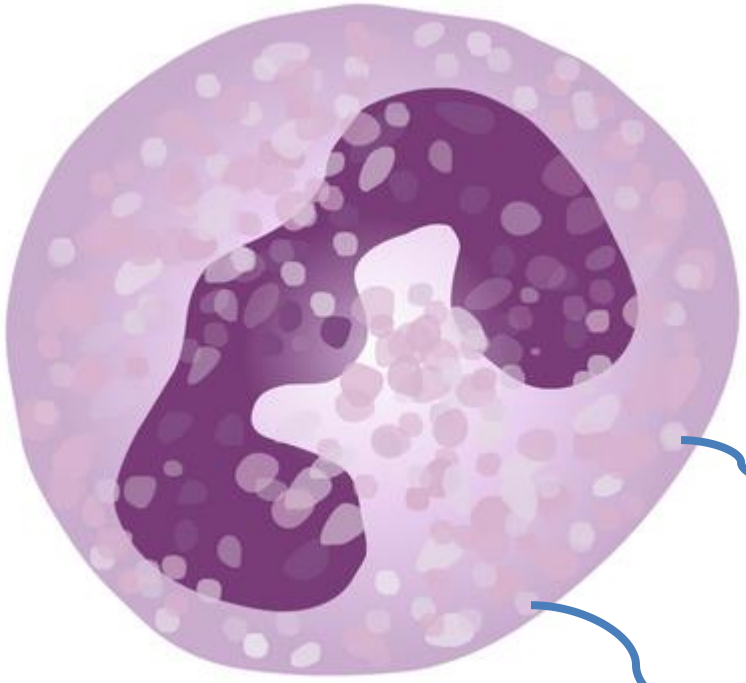
Difficultés…

Exemple du NGAL

Différentes formes plasmatiques et urinaires

- NGAL monomérique: produit par les neutros et les cellules tubulaires rénales
- NGAL homodimérique: produit seulement par les neutros
- NGAL hétérodimérique: produit par les cellules tubulaires épithéliales. Lié à la gélatinase


25 kDa monomer
45 kDa homodimer



25 kDa monomer

45 kDa homodimer

135 kDa heterodimer

Monomère urinaire principalement d’origine rénale?

Monomère urinaire et homodimère suite à un sepsis?

Monomère urinaire et homodimère suite à une infection du tractus urinaire?

NGAL monomérique et
homodimère plasmatiques

Les dosages de NGAL

- NGAL urinaire:
  - Abbott Architect
  - BioPorto sur différents automates
  - Elisas

- NGAL plasmatique
  - Triage (point of care)
  - BioPorto sur différents automates
  - Elisas

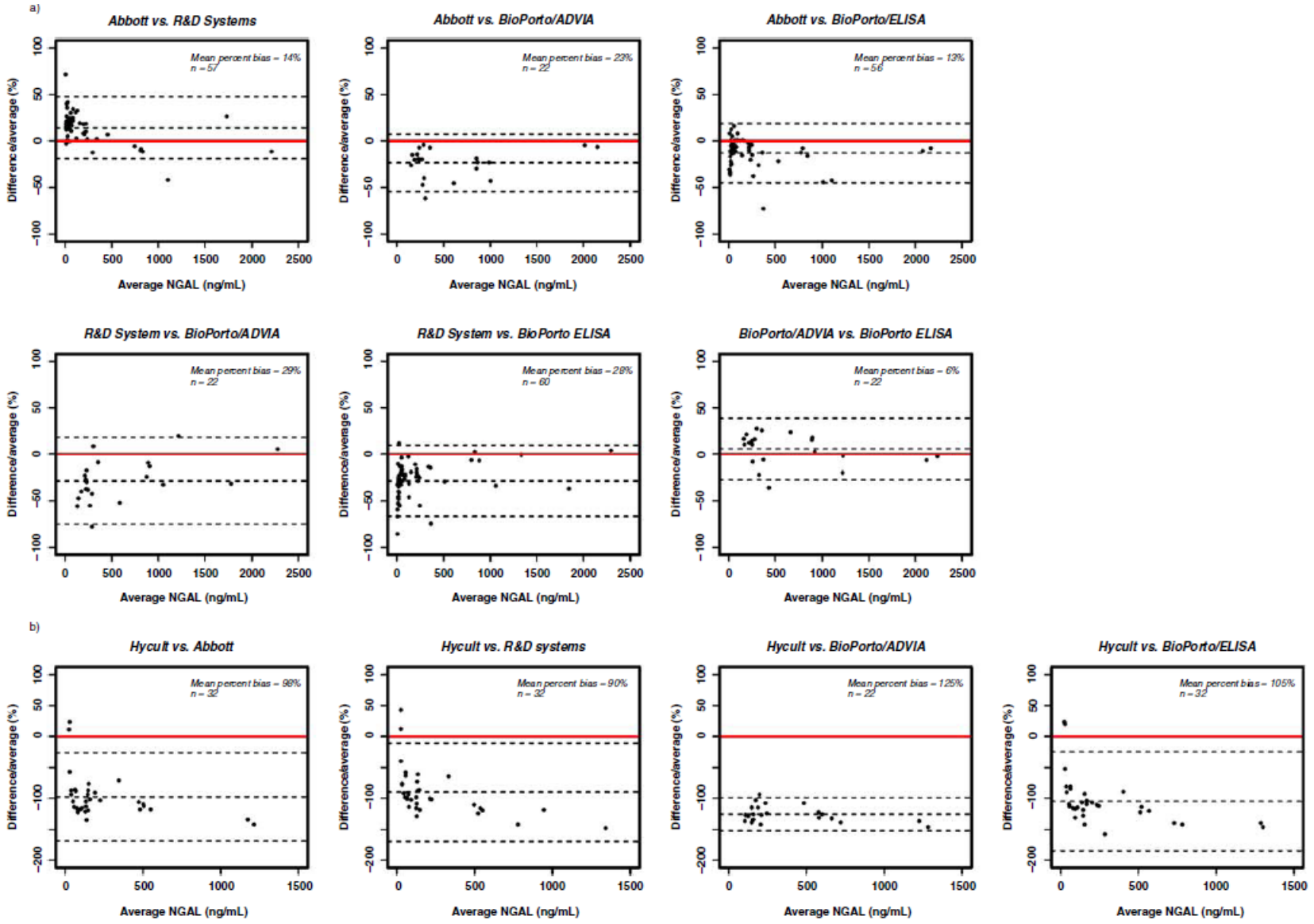
Cependant…

- Les différents anticorps utilisés reconnaissent différents épitopes
- Les différents kits ont une sensibilité et une spécificité différentes
- Le « résultat » final est la résultante des interactions des différents anticorps avec les différentes formes.
- Chaque dosage reconnaît une « mixture » différente
- Résultats d'études pas transposables (« mixtures » différentes, cross-reactivity différentes,…)
- Pas de standardisation…
- Les différentes formes de NGAL changent au cours du temps

Table 1 Summary of the performance data for the five NGAL assays evaluated in this study using urine samples

Test	BioPorto/ ADVIA®	Abbott	R&D Systems	BioPorto ELISA	Hycult
Assay standards range (ng/mL)	150–5000	10–1500	0.156–10	0.01–1	0.4–100
Dilution factor range	N/A	N/A	1/25–1/800	1/500–1/4000	1/20
Assay time (mins)	10	28	300	240	210
Imprecision %CV range (median)					
Intra-assay ($n = 5$ for each of 4 QC samples)	0.7–3.0 (2.0)	0.8–10.8 (1.4)	3.2–4.4 (3.6)	0.6–5.1 (3.4)	5.8–34.4 (8.8)
Inter-assay ($n = 10$ for each of 4 QC samples)	1.9–7.9 (3.7)	4.8–9.9 (7.6)	3.2–10.1 (7.1)	6.4–15.8 (12.6)	26.1–33.3 (30.2)
% Parallelism range (median; *n*)	1.9* (1.9; $n = 1$)	2.2–5.8 (3.0; $n = 3$)	1.9–7.9 (3.6; $n = 3$)	3.2–49.8 (44.6; $n = 3$)	17.8–30.2 (21.5; $n = 3$)
% Recovery range (median; *n*)	Not determined*	88.6–99.1 (95.6; $n = 8$)	93.5–106.7† (98.9; $n = 9$)	100.6–113.4 (104.1; $n = 8$)	73.6–95.2 (88.1; $n = 8$)
Specificity					
+ MMP-9	Not determined*	No effect	No effect	No effect	Inconclusive
+ Complex	Not determined*	No effect	No effect	No effect	Inconclusive
LOQ (including sample dilution factor)	150 ng/mL	5 ng/mL	0.078 (2.0) ng/mL	0.01 (5.0) ng/mL	1 (20) ng/mL
Haemoglobin interference					
0.75, 1.125, 2.25 μg/mL (+/++/+++)	Not determined*	No interference	No interference	No interference	Interference
5.0 mg/mL	Not determined*	Interference	Interference	Interference	Interference
Hook analysis	Hook effect	No effect	No effect	No effect	Inconclusive

Kift, ACB 2013


a)
Abbott vs. R&D Systems
Mean percent bias = 14%
n = 57
Abbott vs. BioPorto/ADVIA
Mean percent bias = 23%
n = 22
Abbott vs. BioPorto/ELISA
Mean percent bias = 13%
n = 56
R&D System vs. BioPorto/ADVIA
Mean percent bias = 29%
n = 22
R&D System vs. BioPorto ELISA
Mean percent bias = 28%
n = 60
BioPorto/ADVIA vs. BioPorto ELISA
Mean percent bias = 6%
n = 22
b)
Hycult vs. Abbott
Mean percent bias = 98%
n = 32
Hycult vs. R&D systems
Mean percent bias = 90%
n = 32
Hycult vs. BioPorto/ADVIA
Mean percent bias = 125%
n = 22
Hycult vs. BioPorto/ELISA
Mean percent bias = 105%
n = 32
Difference/average (%)
Average NGAL (ng/mL)

Etude de Glassford et al. in Intensive Care Med

- « Elisa 1 »: reconnaît une portion des 3 formes de uNGAL; résultats dépendent principalement du NGAL monomérique.
- « Elisa 2 »: reconnaît une portion de l'homodimère seulement; résultats dépendent principalement de l'homodimère
- pNGAL: triage
- uNGAL: Abbott Architect
- 102 patients admis en USI à risque d'AKI

Correlations

- Corrélation modérée entre pNGAL, uNGAL E1 et uNGAL
- Pas de corrélation entre pNGAL et uNGAL E2
- Très forte corrélation entre uNGAL et uNGAL E1
- Corrélation beaucoup plus faible entre uNGAL et uNGAL E2 et entre uNGAL E1 et uNGAL E2

AKI et mortalité

- 72/102 ont développé AKI
- Aucune mesure de NGAL n'a prédit la mortalité
- pNGAL est bien associé à la classification RIFLE-F
- Aucune mesure de NGAL urinaire n'a pu prédire une AKI

Conclusion (préliminaire…et biologique)

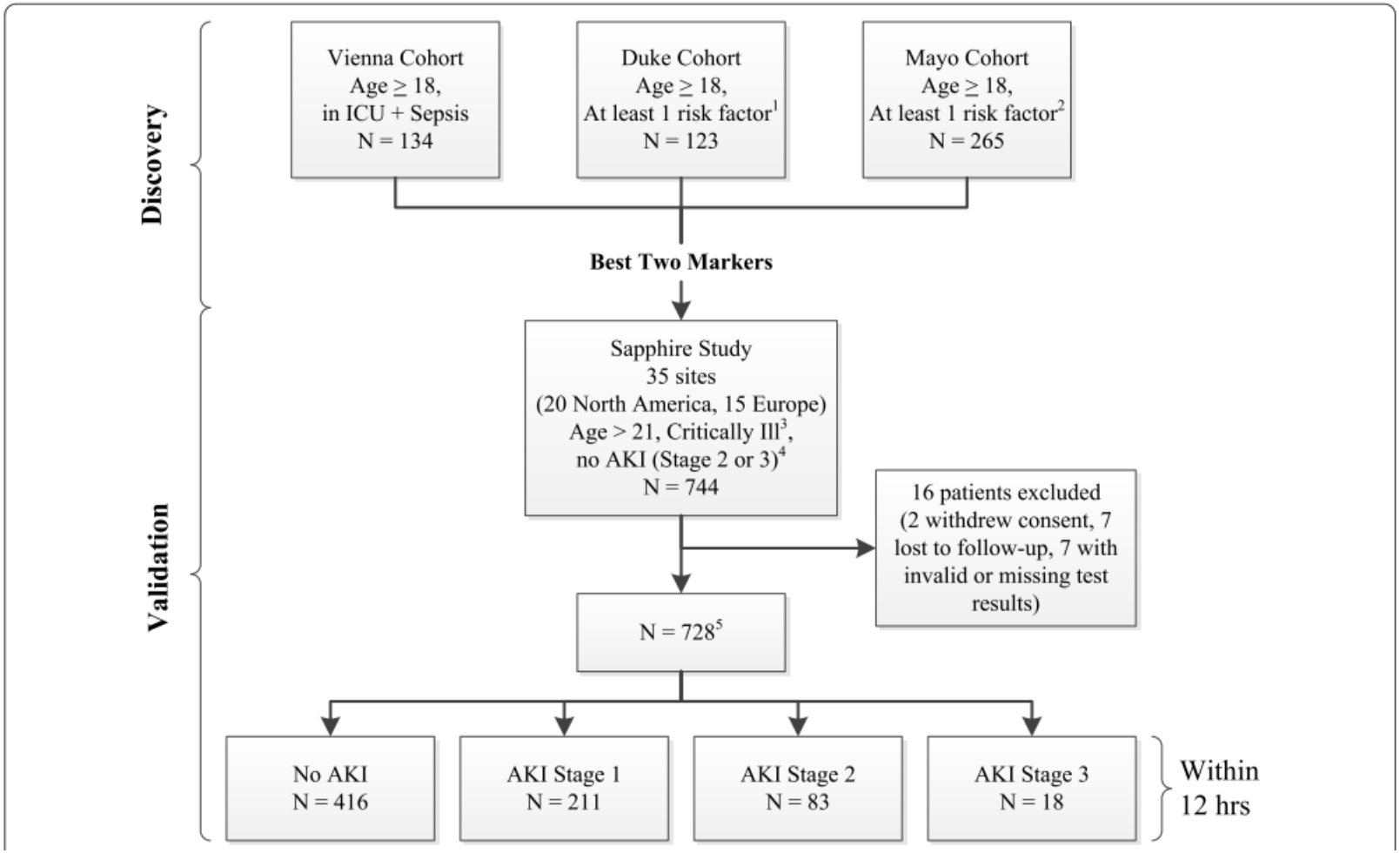
- L'interprétation d'un taux urinaire de NGAL est sujette à caution
- Le pNGAL (composé principalement d'homodimère), semble être, biologiquement (et cliniquement?) une cible beaucoup plus homogène.
- Problème: Triage est une très mauvaise méthode -> BioPorto plasmatique?
- Autre problème: concordance entre les résultats obtenus par le kit BioPorto sur différents automates.

La biologie du NGAL est plus complexe que ce que l'on ne croyait

« widespread use of NGAL in patients at potential risk of AKI is premature and should wait for a better understanding of the biology of this biomarker »

Nouvelles techniques pour doser le NGAL? Protéomique?

Nouveaux marqueurs? IGFBP-7, TIMP-2?


Discovery
Validation
Vienna Cohort
Age ≥ 18,
in ICU + Sepsis
N = 134
Duke Cohort
Age ≥ 18,
At least 1 risk factor[1]
N = 123
Mayo Cohort
Age ≥ 18,
At least 1 risk factor[2]
N = 265
Best Two Markers
Sapphire Study
35 sites
(20 North America, 15 Europe)
Age > 21, Critically Ill[3],
no AKI (Stage 2 or 3)[4]
N = 744
16 patients excluded
(2 withdrew consent, 7
lost to follow-up, 7 with
invalid or missing test
results)
N = 728[5]
No AKI
N = 416
AKI Stage 1
N = 211
AKI Stage 2
N = 83
AKI Stage 3
N = 18
Within
12 hrs

CRITICAL CARE

RESEARCH Open Access

Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury

Kianoush Kashani[1], Ali Al-Khafaji[2], Thomas Ardiles[3], Antonio Artigas[4], Sean M Bagshaw[5], Max Bell[6], Azra Bihorac[7], Robert Birkhahn[8], Cynthia M Cely[9], Lakhmir S Chawla[10], Danielle L Davison[10], Thorsten Feldkamp[11], Lui G Forni[12], Michelle Ng Gong[13], Kyle J Gunnerson[14], Michael Haase[15], James Hackett[16], Patrick M Honore[17], Eric AJ Hoste[18], Olivier Joannes-Boyau[19], Michael Joannidis[20], Patrick Kim[21], Jay L Koyner[22], Daniel T Laskowitz[23], Matthew E Lissauer[24], Gernot Marx[25], Peter A McCullough[26], Scott Mullaney[27], Marlies Ostermann[28], Thomas Rimmelé[29], Nathan I Shapiro[30], Andrew D Shaw[31], Jing Shi[32], Amy M Sprague[33], Jean-Louis Vincent[34], Christophe Vinsonneau[35], Ludwig Wagner[36], Michael G Walker[32], R Gentry Wilkerson[37], Kai Zacharowski[38] and John A Kellum[39]*

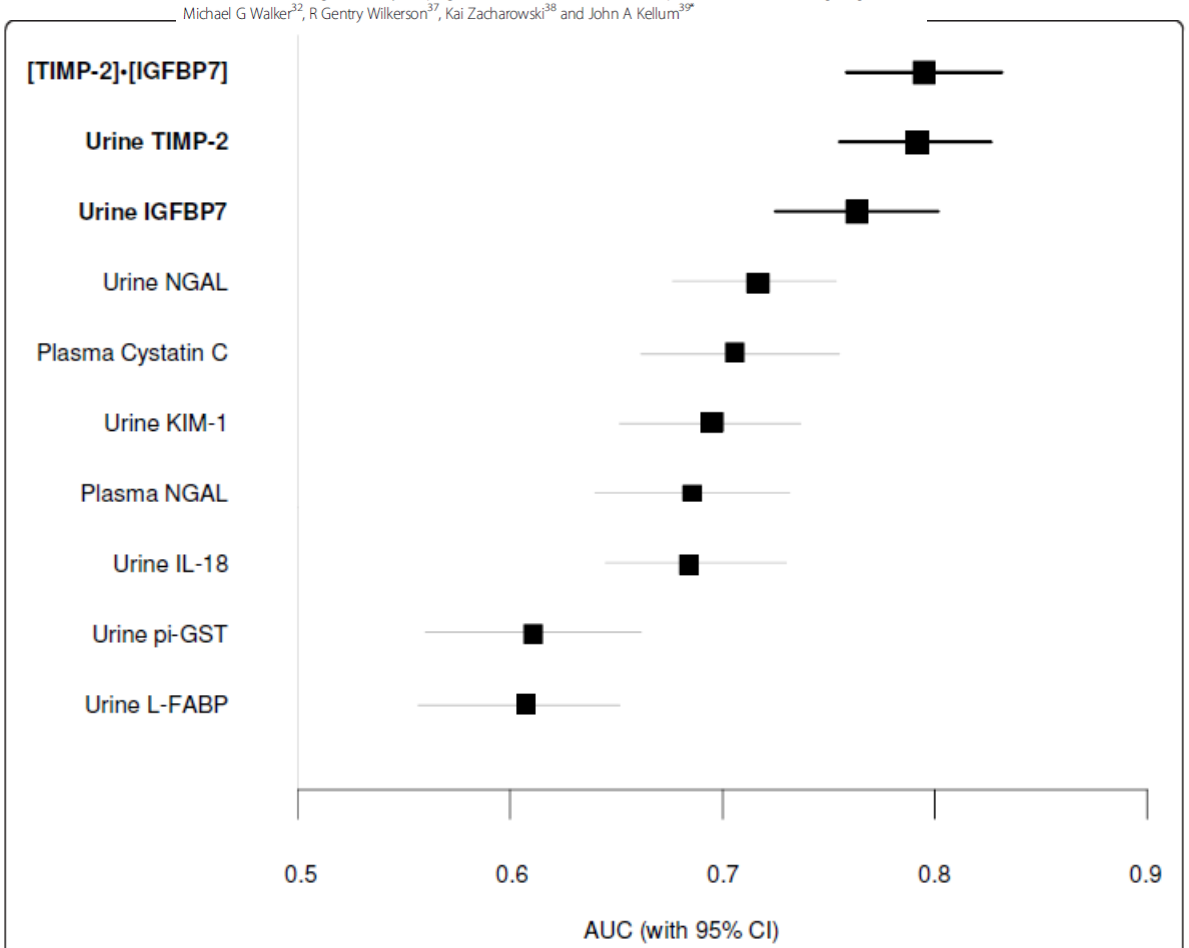


Figure 2 Area under the receiver-operating characteristics curve (AUC) for novel urinary biomarkers and existing biomarkers of acute kidney injury for the primary Sapphire study endpoint (KDIGO stage 2 or 3 within 12 hours of sample collection). Samples were collected within 18 hours of enrollment. The AUC for urinary [TIMP-2]·[IGFBP7] is larger than for the existing biomarkers (*P* value <0.002). IGFBP7, insulin-like growth factor-binding protein 7; IL-18, interleukin-18; KIM-1, kidney injury marker-1; L-FABP, liver fatty acid-binding protein; NGAL, neutrophil gelatinase-associated lipocalin; pi-GST, pi-Glutathione S-transferase; TIMP-2, tissue inhibitor of metalloproteinases-2.

Product Information

Intended Use and Indications for the NEPHROCHECK Test System

The NEPHROCHECK Test is an *in vitro* diagnostic device that quantitatively measures TIMP-2 (Tissue Inhibitor of Metalloproteinase 2) and IGFBP-7 (Insulin-like Growth Factor Binding Protein 7) proteins associated with kidney function in human urine by fluorescence immunoassay on the ASTUTE140 Meter.

The test result is intended to be used in conjunction with clinical evaluation as an **aid in the risk assessment of acute kidney injury in the critically ill.** The NEPHROCHECK Test is indicated for prescription use only.

Using the NEPHROCHECK Test Kit

The NEPHROCHECK Test System is a single-use cartridge designed to detect biomarkers of **acute kidney injury**, TIMP-2 and IGFBP-7. The test provides results in 20 minutes.

The test procedure involves the operator applying a fresh or thawed clinical urine sample (mixed with labeled fluorescent conjugate) to the NEPHROCHECK Test Cartridge, then inserting the test cartridge into the ASTUTE140 Meter for incubation, reading, result calculation and result display.

Each NEPHROCHECK Test Cartridge contains RFID cards to ensure kit expiration date and lot-specific information is downloaded. Each cartridge also includes two detection zones (one positive and one negative control) as procedural controls that are run automatically with every sample to confirm that the NEPHROCHECK Test procedure is performed correctly.

Part Number: **500003**

Order Product Code: **500003AM**

In 2013, the Sapphire study was the first investigation to find and validate the two top urinary biomarkers for the prediction of AKI risk among 340 proteins in a discovery cohort. These biomarkers, urine insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinase-2 (TIMP-2) were then validated in >700 critically ill adult patients [16]. A simple product of these biomarker levels (TIMP-2 × IGFBP7), expressed in $(ng/mL)^2/1000$, launched as a final commercial product, is known as NephroCheck (Astute Medical, San Diego, CA, USA). Following a second North American large multicenter observational trial [17], the US Food and Drug Administration approved NephroCheck in September 2014 to aid critical care physicians and nephrologists in the early prediction of AKI in the critical care setting [18]. At this time, at least three significant, reliable and reproducible multicenter studies (Sapphire, Topaz and Opal) including >1800 heterogeneous patients have validated the use of NephroCheck [16, 17, 19]. Thus a significant amount of data supports not only the test's validity but also its usefulness as a tool to predict kidney injury before AKI develops.

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POLAR VIEWS IN NEPHROLOGY

Pro: Prevention of acute kidney injury: time for teamwork and new biomarkers

Claudio Ronco; Lilia Rizo-Topete; Mara Serrano-Soto; Kianoush Kashani

Abstract ▾ View article

Opponent's comments

Wim Van Biesen

View article

Con: Cautionary tales and reservations about the adoption of new technologies and biomarkers for the management o acute kidney injury

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Abstract ▾ View article

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Claudio Ronco, MD; Lilia Rizo-Topete, MD; Mara Serrano-Soto, MD; Kianoush Kashani, MD, Msc.

View article

Moderator's view: Patient–centered approaches for optimizing AKI management: the role of kidney biomarkers

Ravindra L. Mehta

Abstract ▾ View article

Nephrol Dial Transplant (2017) 32: 408–413
doi: 10.1093/ndt/gfx016

ndt
Nephrology Dialysis Transplantation

Polar Views in Nephrology

Pro: Prevention of acute kidney injury: time for teamwork and new biomarkers

Claudio Ronco[1,2,*], Lilia Rizo-Topete[1,3], Mara Serrano-Soto[1,4] and Kianoush Kashani[5,6,7]

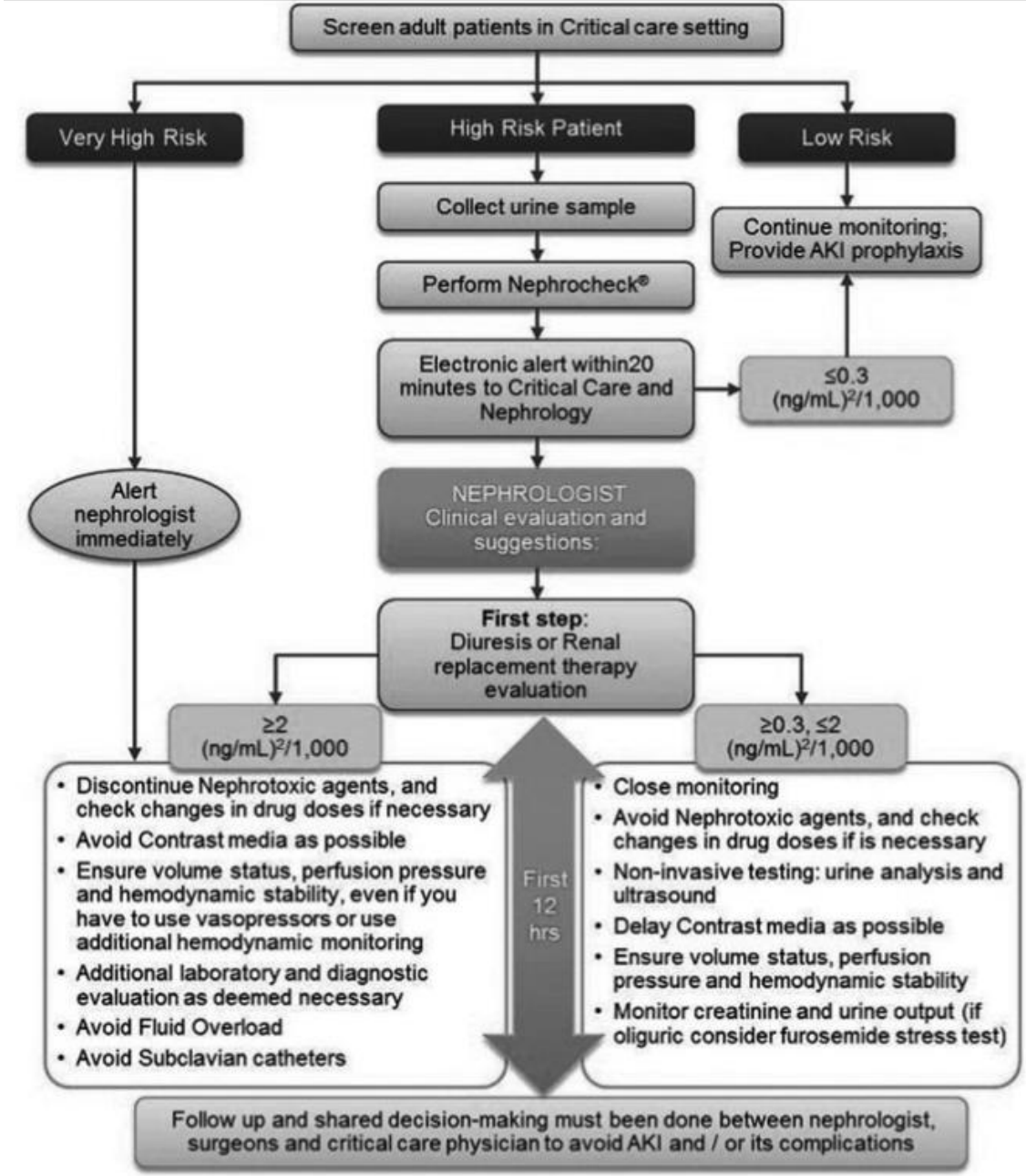

FIGURE 2: Flow chart of the NephroCheck RRT protocol implemented in Vicenza.

FIGURE 3: Example of biomarker communication to the nephrology RRT member. It is critical to know the result of the test as soon as it is available: once the result appears on the phone of the nephrologist on duty, actions may include monitoring the patient (left picture) or application of a specific checklist with actions suggested by the KDIGO guidelines (right picture) depending on the level of identified risk. If cellphone communication or a specific app linked to the electronic alert system is not available, a simple fax or telephone communication of the biomarker value can be used.

Con: Cautionary tales and reservations about the adoption of new technologies and biomarkers for the management of acute kidney injury

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The fate of the Titanic has demonstrated that overconfident trust in new technologies and neglecting established seaman skills can be deleterious. The story of Odysseus instructs us that attractive sirens along the voyage promise, with their sweet voices, a simple voyage to a safe harbour, milk and honey, but following their advice leads to shipwreck and death. The story of the Herald of Free Enterprise teaches us that neglecting tiny, simple details of well-established knowledge can result in dramatic effects. The story of the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) [1] clarifies that not applying apparently basic knowledge in the care of patients at risk for, or with, acute kidney injury (AKI) costs lives. This paper aims to defend the viewpoint that we need to invest more time, research and money to ensure that all basic interventions with established positive outcomes to prevent and manage AKI are put into practice, rather than investing in new technology with unproven additional benefit. Nephrologists should use their clinical and education skills to achieve this goal.

Limitations, limitations!!!

- Impact GFR et inflammation
- Cut-offs pas définis
- Pas de valeur ajoutée par rapport au jugement du néphrologue
- Pas de moment précis pour prélever (pas de symptômes…)
- Pas d'étude montrant une corrélation avec biopsies chez l'homme
- Bcp de faux positifs
- Ne tiennent compte que d'un seul épisode d'AKI
- Surtout pas de POCT!
- …

Well, let us be honest: although Ronco *et al.* [1] claim that NephroCheck has been 'validated', in reality the test has not succeeded in making a difference as compared with good clinical judgement [2]. In the Sapphire study [3], the area under the curve for discrimination of AKI went from 0.81 for a clinical model to 0.87 when NephroCheck was added to the clinical model. Of importance, the change in serum creatinine was deliberately left out of the model, so we have no clue what the additional value of this parameter was, and oliguria, one of the diagnostic criteria of AKI, was not even mentioned. The US Food and Drug Administration specifically warns that the test should NOT be used as a stand-alone test, and certainly not in a point-of-care set-up.

Second, the flow chart urges us to do nephroprotective actions in patients at risk, as identified by NephroCheck. I beg your pardon? Should we thus not do nephroprotection in all other patients? And if we should, what is the added value of the NephroCheck?

Third, the NephroCheck RRT model starts from the premise that AKI is a single hit, a once-in-a-hospitalisation story. We all know this is not the case, as hospitalised patients continuously face multiple threats for AKI. Accordingly, there would be a continuous need for 'NephroChecking'. Since a major part of (preventable) AKI cases are on general wards, this would pose huge problems of logistics and cost if we were to apply the proposed algorithm in all wards. If applied only to the intensive care unit, it would completely miss the target audience [4].

This brings us to the most urgent question: should we put (lots of) our health care money on a commercial test without proven additional value, or should we invest in education and awareness of AKI? The case of early electronic warning [5] has learned that prevention only works in combination with a broader program. Such programs have a proven benefit on outcome for all patients, and thus on the hard outcome of mortality.

In conclusion, there is no 'single easy solution' as promised by NephroCheck or other biomarkers [6]. The nephrology community will have to accept responsibility by educating the non-nephrology community and increase general awareness of AKI.

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IF YOU KEEP DOING THINGS THE SAME WAY OVER AND OVER YOU WILL ONLY GET THE SAME RESULTS

The Titanic tragedy occurred because of a mixture of inadequate technology and human stupidity. Many ships had sunk before just relying on seaman skills. Subsequently, the adoption of the radar proved that technology could save many lives.

The story of Odysseus teaches us that if we face the problem well prepared we can resist false promises and proceed in our journey.

The reason why the MS Herald of Free Enterprise is lying on her side in shallow waters was the negligence of the assistant boatswain, asleep in his cabin when he should have been closing the bow-door.

The comment of Van Biesen to our proposed plan to improve quality of diagnosis and care of acute kidney injury (AKI) seems to in part agree with our point of view. By suggesting that we should invest more time, research and money ensuring that all basic interventions with established positive outcome to prevent and manage AKI are put into practice, the commentary reinforces our vision of high demand for advancements in AKI care. Having taken this for granted, we respectfully disagree with the author of the commentary, who suggests we should invest only in such established actions rather than in new technology. The evidence for additional benefit provided by new technologies is emerging, although it may require time to reach a full consensus among investigators and clinicians. How many times have we seen strong resistance by laggards in the technology adoption life-cycle? We saw strong opposition to the application of bicarbonate versus acetate dialysis or of high flux biocompatible membranes versus Cuprophan. Does anybody today, even in the absence of randomized controlled trials, prefer to be treat patients with acetate dialysis and Cuprophan membranes? The truth is that progress is made by people who see beyond the obstacles and try to improve patient lives by all possible means. We should not be influenced by priorities of industrial companies, while a transparent and fruitful collaboration with industry should be welcome. We must be aware that using new technologies, although sailing in uncharted waters, may lead to new discoveries and improved clinical practice. So moving ahead with attention to patient safety, health care budgets and scientific integrity is a must for discovery and validation of new therapies and diagnostic tools. The importance of nephrology as a discipline and the perception of its role within the hospital community may also be affected by these choices. AKI is an area of fast and important development. There is no space for delays. While we should maximize the utilization of all available skills and techniques, we should also try to rapidly test and possibly implement new technologies and new approaches. If we keep doing things the same way we will get the same results over and over. And current results are not satisfactory

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Merci pour votre attention.