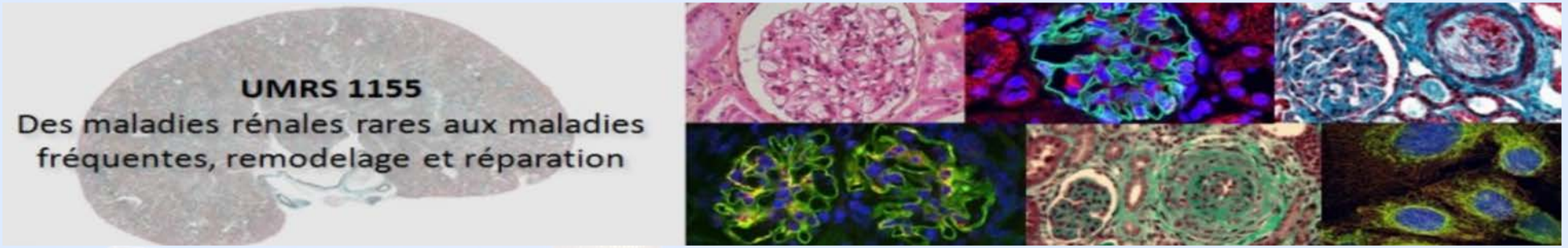


Insuffisance rénale aiguë

Actualités en réanimation 2020-2021

Stéphane Gaudry
M.D., Ph.D.
MIR
Hôpital Avicenne, Bobigny/ Hôpital Jean Verdier, Bondy
UMRS 1155, Tenon, PARIS
Groupe de Recherche en Réanimation Rénale et Métabolique (G3RM)

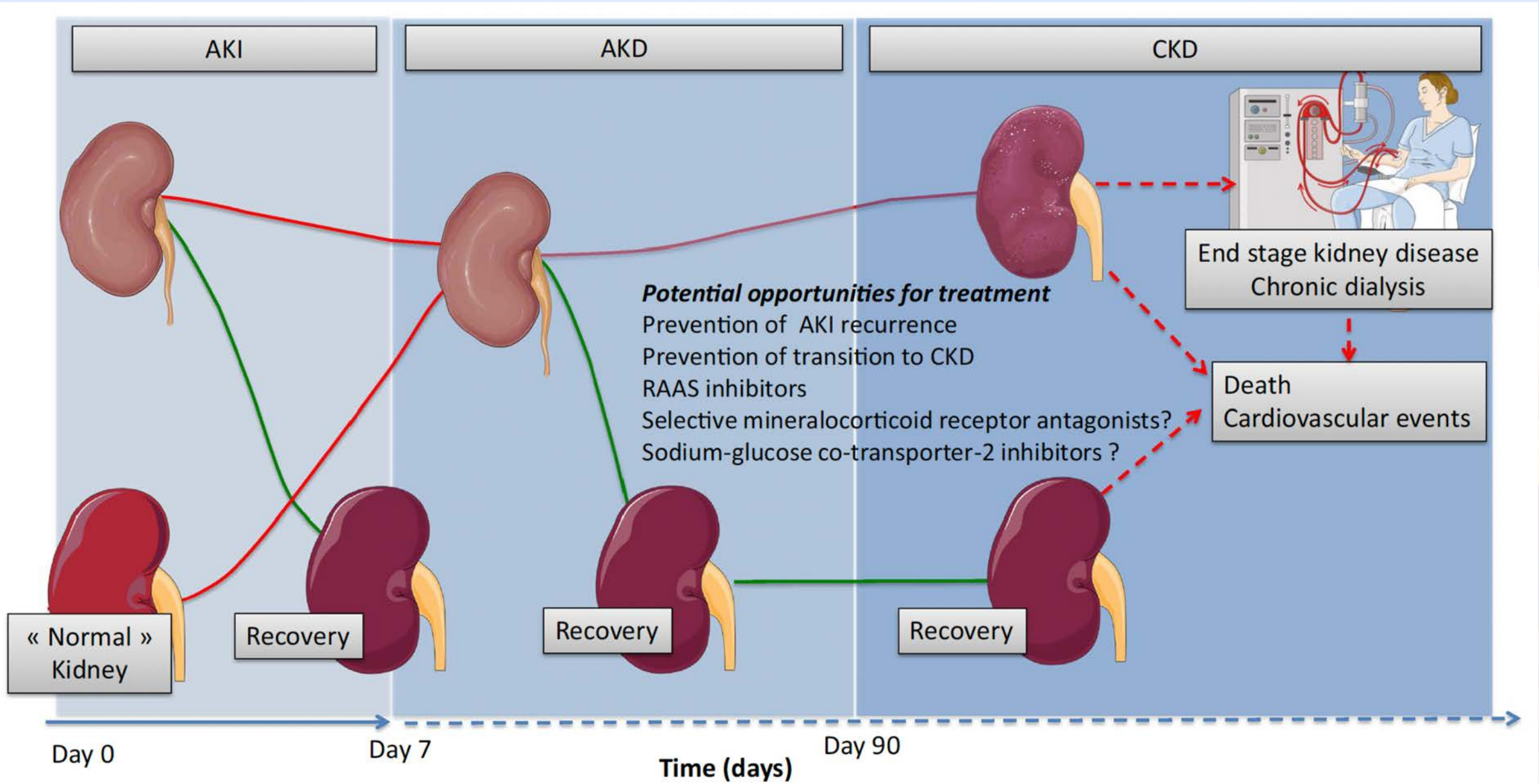
No conflict of interest regarding AKI or RRT

- *AKIKI 1 and 2 trials were funded by French ministry of health*

AKI news (2020-2021)

AKI news (2020-2021)

The definition of AKI



Pikkers et al, ICM 2021

AKI news (2020-2021)

Severe SARS-COV2 Infection

Research timeline during COVID 19 outbreak

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., Yu Hu, M.D., Wen-hua Liang, Ph.D., Chun-quan Ou, Ph.D., Jian-xing He, M.D., Lei Liu, M.D., Hong Shan, M.D., Chun-liang Lei, M.D., David S.C. Hui, M.D., Bin Du, M.D., Lan-juan Li, M.D., et al., for the China Medical Treatment Expert Group for Covid-19*

China alerts WHO

First epidemiological studies

31 DEC 19 | JAN 20 | FEB 20 | MAR 20 | APR 20

Identification of new virus COVID 19

Liver injury?

AKI?

REVIEW

Liver INTERNATIONAL WILEY

Liver injury during highly pathogenic human coronavirus infections

Ling Xu[1,2] | Jia Liu[1,2] | Mengji Lu[2,3] | Dongliang Yang[1,2] | Xin Zheng[1,2]

Nephrology

Patient-Oriented, Translational Research: Research Article

Am J Nephrol
DOI: 10.1159/000507471

Received: March 11, 2020
Accepted: March 24, 2020
Published online: March 31, 2020

Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China

Luwen Wang[a] Xun Li[a] Hui Chen[c] Shaonan Yan[a] Dong Li[b] Yan Li[b] Zuojiong Gong[a]

Online Sept, 2020

AKI and COVID19 in ICU

Severe Acute Kidney Injury in COVID-19 Patients with Acute Respiratory Distress Syndrome

Khalil Chaïbi, Myriam Dao, Tài Pham, Victor D. Gumucio-Sanguino , Fabio A. Di Paolo, Arthur Pavot, Yves Cohen, Didier Dreyfuss, Xosé Pérez-Fernandez and Stéphane Gaudry

American Journal of Respiratory and Critical Care Medicine

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American Journal of Respiratory and Critical Care Medicine

METHODS

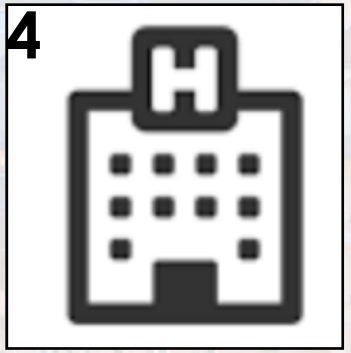
OBSERVATIONAL

COMMITTEE ON ETHICS

CLEA-2020-115

RETROSPECTIVE

MULTICENTRIC



FRANCE

SPAIN

Severe Acute Kidney Injury in COVID-19 Patients with Acute Respiratory Distress Syndrome

Khalil Chaïbi, Myriam Dao, Tài Pham, Victor D. Gumucio-Sanguino , Fabio A. Di Paolo, Arthur Pavot, Yves Cohen, Didier Dreyfuss, Xosé Pérez-Fernandez and Stéphane Gaudry

American Journal of Respiratory and Critical Care Medicine

Results

211 Patients

17% KDIGO 1

15% KDIGO 2

Within 7 days

ICU

ADMISSION

Median time

3 days

26% KDIGO 3

54%

RRT

56%

22%

22%

ICU

ALIVE HUMAN

DAY 28

Severe Acute Kidney Injury in COVID-19 Patients with Acute Respiratory Distress Syndrome

Khalil Chaïbi, Myriam Dao, Tài Pham, Victor D. Gumucio-Sanguino , Fabio A. Di Paolo, Arthur Pavot, Yves Cohen, Didier Dreyfuss, Xosé Pérez-Fernandez and Stéphane Gaudry

American Journal of Respiratory and Critical Care Medicine

26% KDIGO 3

Patients who developed **KDIGO stage 3 AKI** were more likely to have **chronic kidney disease**, **higher body mass index** and **higher SOFA** score, they received **higher PEEP** and they received **nitric oxide therapy** or **vasopressor support** more frequently;

Jiang *et al. BMC Nephrology* (2019) 20:468
https://doi.org/10.1186/s12882-019-1660-z

BMC Nephrology

RESEARCH ARTICLE Open Access

KDIGO 3 = 16%

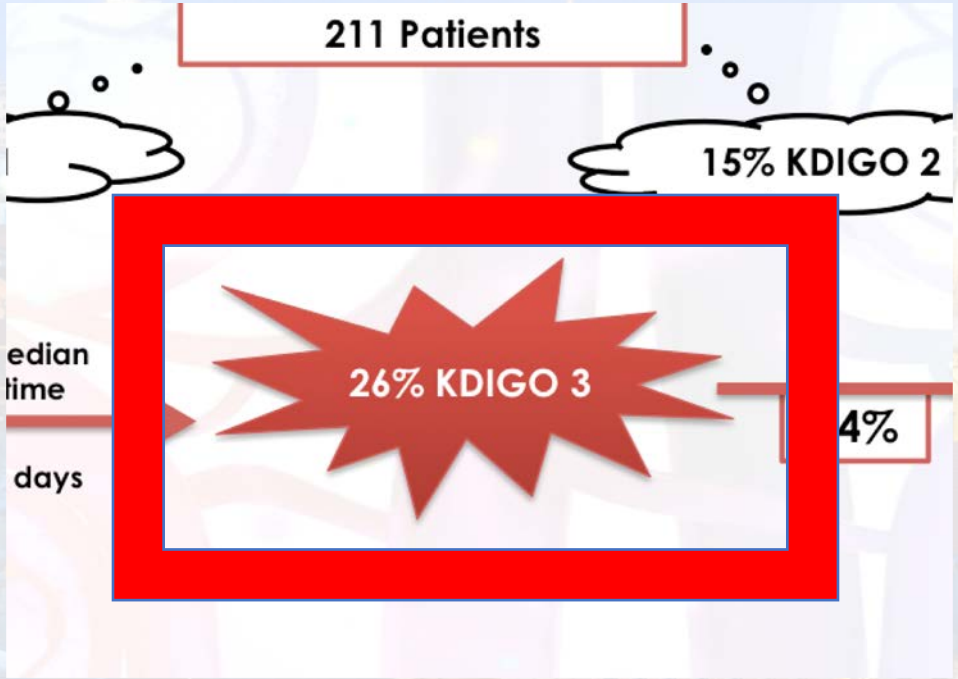
Epidemiology of acute kidney injury in intensive care units in Beijing: the multi-center BAKIT study

Li Jiang[1†], Yibing Zhu[1,2*†], Xuying Luo[1,3†], Ying Wen[1,4], Bin Du[5], Meiping Wang[1,6], Zhen Zhao[1], Yanyan Yin[1,7], Bo Zhu[1], Xiuming Xi[1*] and The Beijing Acute Kidney Injury Trial (BAKIT) workgroup

Severe Acute Kidney Injury in COVID-19 Patients with Acute Respiratory Distress Syndrome

Khalil Chaïbi, Myriam Dao, Tài Pham, Victor D. Gumucio-Sanguino , Fabio A. Di Paolo, Arthur Pavot, Yves Cohen, Didier Dreyfuss, Xosé Pérez-Fernandez and Stéphane Gaudry

American Journal of Respiratory and Critical Care Medicine



KDIGO 3 = 15%

Impact of Early Acute Kidney Injury on Management and Outcome in Patients With Acute Respiratory Distress Syndrome: A Secondary Analysis of a Multicenter Observational Study*

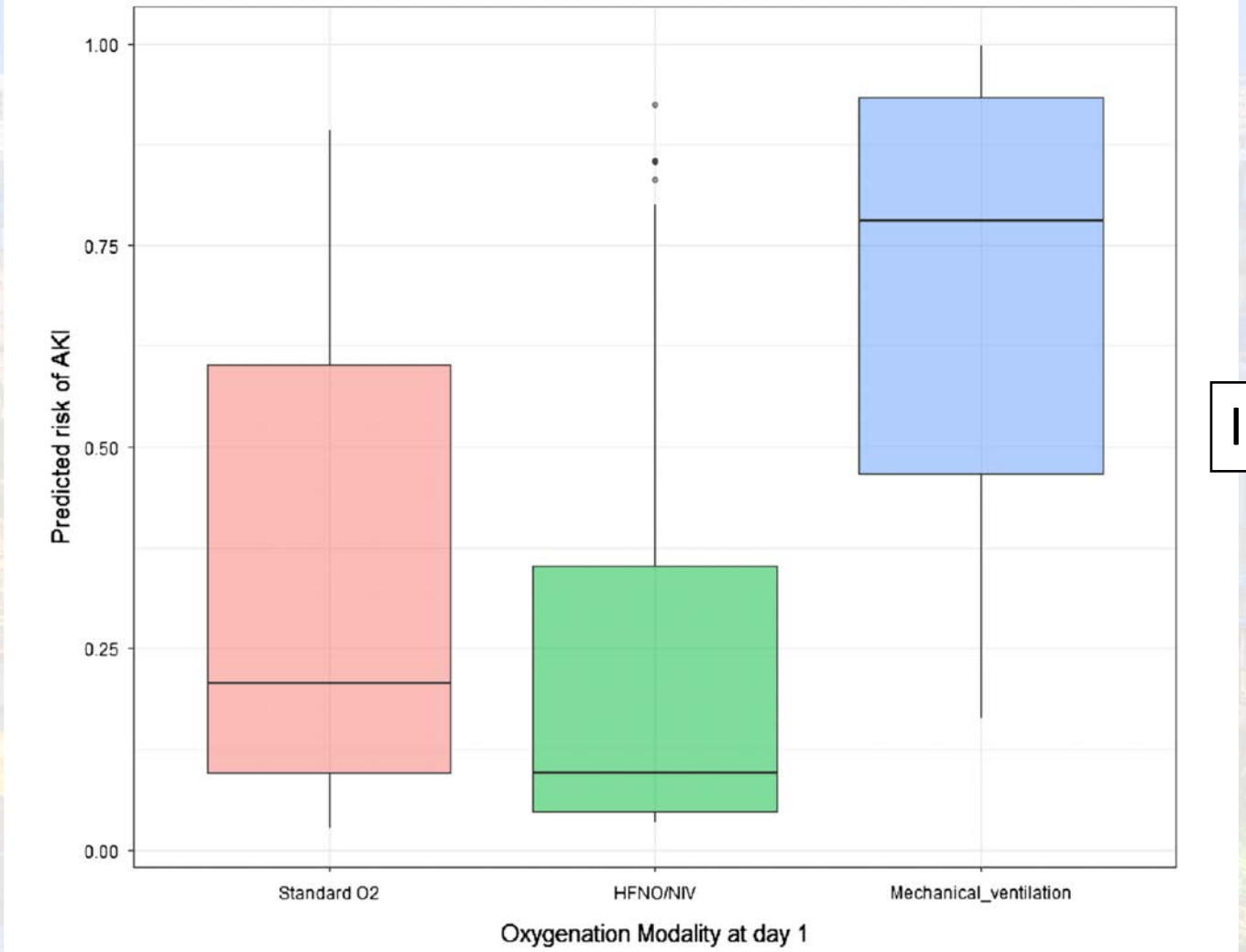
McNicholas, Bairbre A. MD, PhD[1,2,3]; Rez… …am, Tài MD, PhD[5]; Madotto, Fabiana PhD[6]; Guiard, Elsa MD, PhD[7]; Fa… …, Giacomo MD, PhD[4]; Griffin, Matthew D. MD PhD[1,2]; Ranieri, Marco M… …, MA[1,3]; on behalf of the ESICM Trials Group and the Large observational s… …the Global impact of Severe Acute respiratory FailurE (LUNG SAFE) Investigators Al… …rmation

Critical Care Medicine: September 2019 - Volume 47 - Issue 9 - p 1216-1225
doi: 10.1097/CCM.0000000000003832

RESEARCH Open Access

Acute kidney injury in SARS-CoV2-related pneumonia ICU patients: a retrospective multicenter study

Guillaume Geri[1,2,3,4*†], Michael Darmon[5,6,7†], Lara Zafrani[5,6,8], Muriel Fartoukh[9,10], Guillaume Voiriot[9,10,11], Julien Le Marec[10,12,13], Saafa Nemlaghi[10,12,13], Antoine Vieillard-Baron[1,2,3,4] and Elie Azoulay[5,6,7]

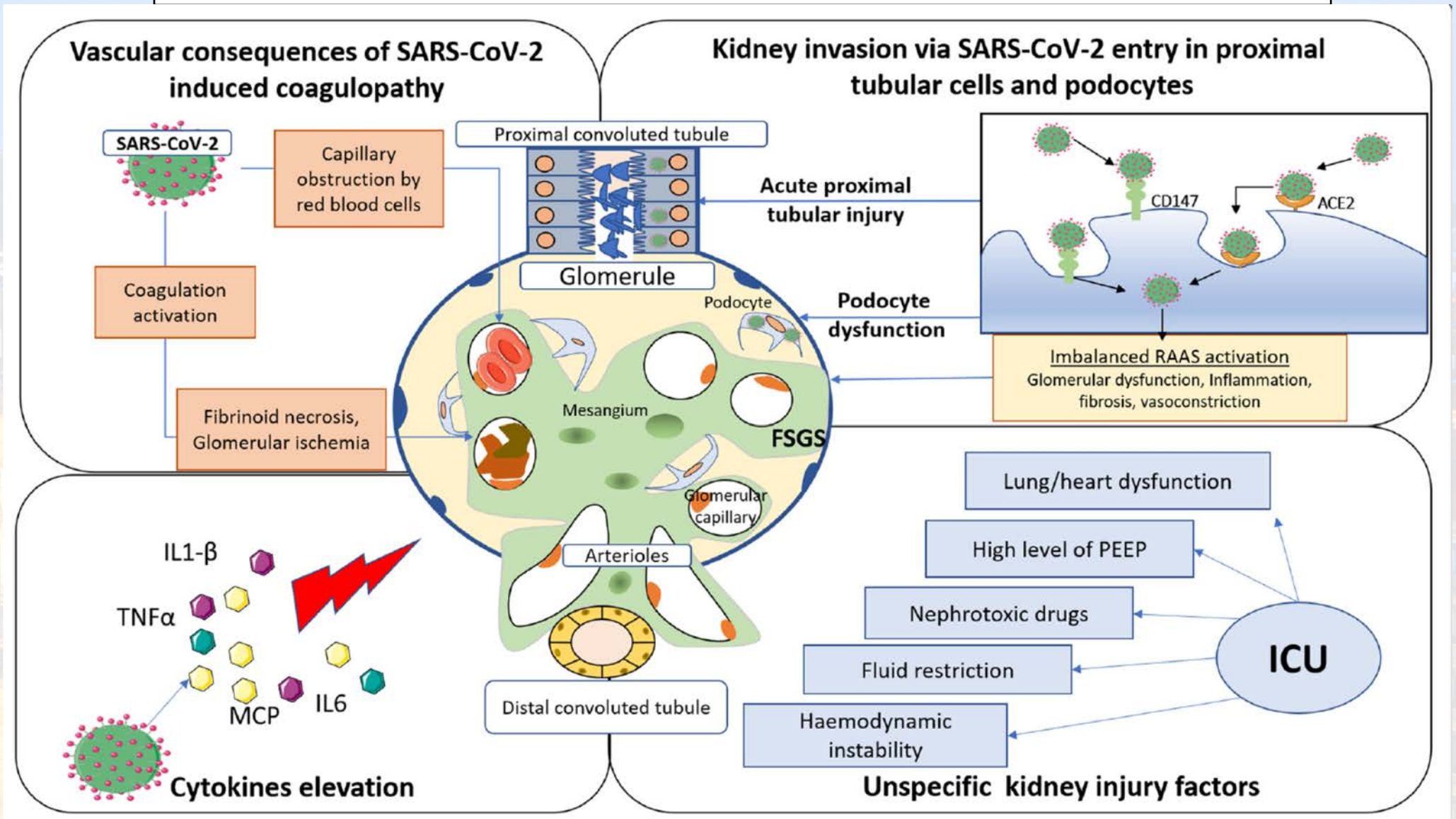


379 COVID-19 patients

25% with AKI stage 3

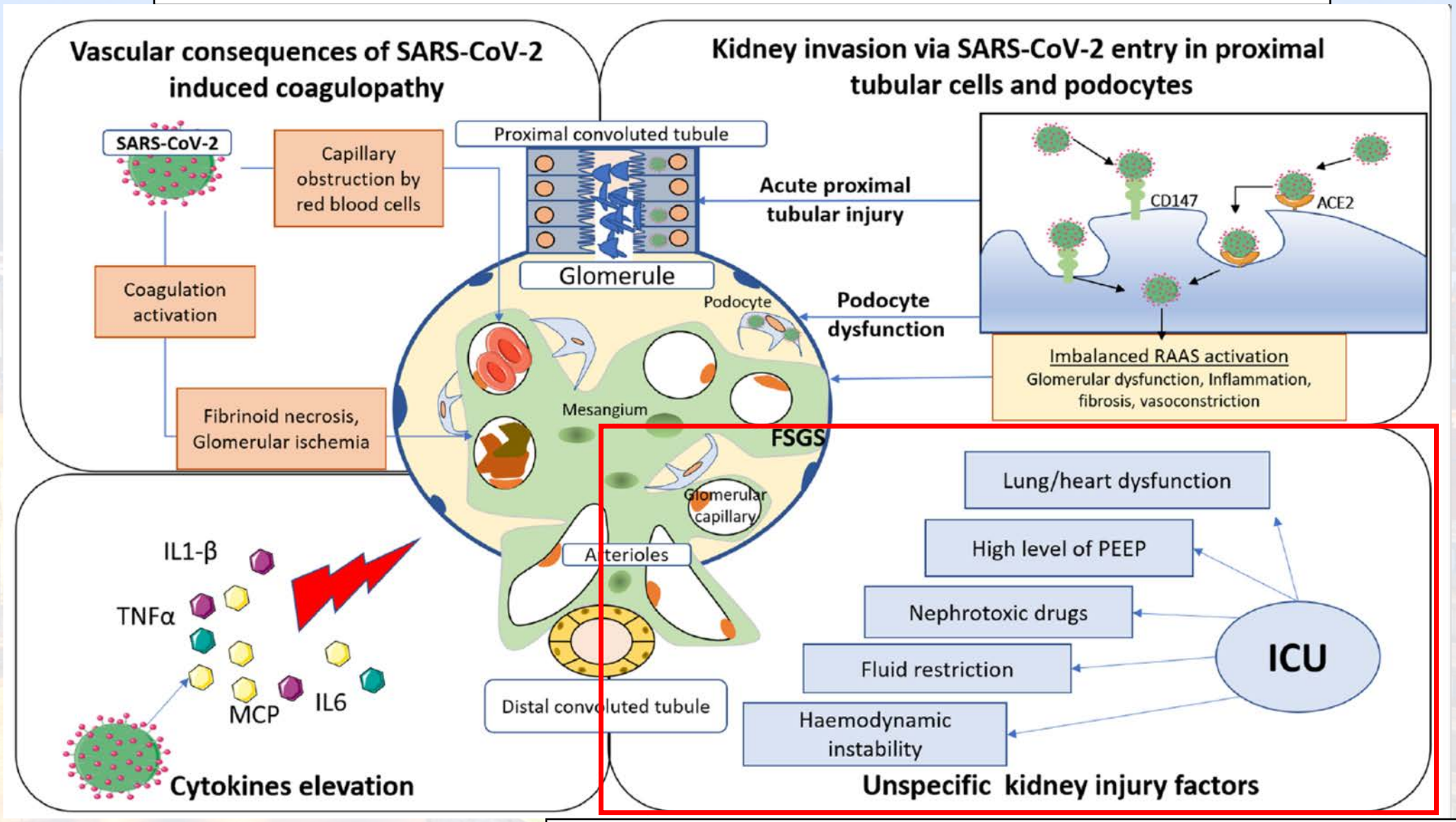
Invasive MV : OR: 4.83 [2.25–10.33]

Pathophysiology: SARS COV 2 direct effect



Acute kidney injury in critically ill patients with COVID-19, Gabarre and al, ICM, 2020

Pathophysiology: SARS COV 2 direct effect



Acute kidney injury in critically ill patients with COVID-19, Gabarre and al, ICM, 2020

Prévenir l'apparition ou l'aggravation de l'insuffisance rénale aiguë

- **limiter** les hauts niveaux de **PEEP**
- ne pas être trop restrictif sur le **remplissage vasculaire**
- **Eviter les médicaments néphrotoxiques**

Eviter les médicaments néphrotoxiques

Crise COVID: le retour aux sources (des erreurs…..)

- « *Ce traitement marche très bien ! J'ai soigné des dizaines de patients avec ce médicament dans mon service* »
- « *ça marche in-vitro ! »*
- « *C'est du bon sens ! »*
- « *Au pire ça ne pourra pas faire de mal* »
- « *Ce n'est pas éthique de faire des essais thérapeutiques randomisés en situation de crise sanitaire et d'urgence !!!* »

Back to the 80’s

La ciclosporine dans le VIH

Tous les ingrédients de la catastrophe

- **Urgence** sanitaire
- **Communication** sans contrôle
- Intervention du **politique**
- Et finalement, **Fraude**……

29 octobre 1985, conférence de presse des chercheurs (de gauche à droite) Philippe Even, Jean-Marie Andrieu et Alain Venet © Getty / Alain Noguès

Eviter les médicaments néphrotoxiques

Première vague:

Utilisation de médicaments non-éprouvés….

- Lopinavir/Ritonavir
- Remdesivir
- Hydroxychloroquine…….

Effet des traitements anti-inflammatoires

- Dexamethasone ?
- Anti-IL6 ?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 25, 2021 VOL. 384 NO. 8

Effet des traitements anti-inflammatoires

Dexamethasone in Hospitalized Patients with Covid-19

The RECOVERY Collaborative Group*

Outcome	Dexamethasone (N=2104)	Usual Care (N=4321)	Rate or Risk Ratio (95% CI)*
		no./total no. of patients (%)	
Primary outcome			
Death at 28 days	482/2104 (22.9)	1110/4321 (25.7)	0.83 (0.75–0.93)
Secondary outcomes			
Renal-replacement therapy¶	89/2034 (4.4)	314/4194 (7.5)	0.61 (0.48–0.76)

Among patients who did not require KRT at randomization, those who received dexamethasone were less likely than those in the control group to receive KRT

Effet des traitements anti-inflammatoires

Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

*RECOVERY Collaborative Group**

	Treatment allocation		RR (95% CI)	p value
	Tocilizumab group (n=2022)	Usual care group (n=2094)		
Primary outcome				
28-day mortality	621 (31%)	729 (35%)	0·85 (0·76–0·94)	0·0028
Secondary outcomes				
Use of haemodialysis or haemofiltration§	120/1994 (6%)	172/2065 (8%)	0·72 (0·58–0·90)	0·0046

AKI news (2020-2021)

Renal Replacement Therapy

The RICH trial

Oct 2020

JAMA | Original Investigation

Effect of Regional Citrate Anticoagulation vs Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy on Dialysis Filter Life Span and Mortality Among Critically Ill Patients With Acute Kidney Injury

A Randomized Clinical Trial

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Rational

JAMA | Original Investigation

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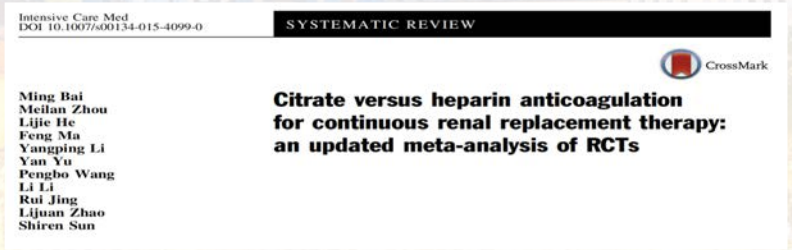

Intensive Care Med
DOI 10.1007/s00134-015-4099-0

SYSTEMATIC REVIEW

CrossMark

Ming Bai
Meilan Zhou
Lijie He
Feng Ma
Yangping Li
Yan Yu
Pengbo Wang
Li Li
Rui Jing
Lijuan Zhao
Shiren Sun

Citrate versus heparin anticoagulation for continuous renal replacement therapy: an updated meta-analysis of RCTs

2015

Circuit loss	Citrate > Heparin
Bleeding	Citrate > Heparin
Mortality	Citrate = Heparin

KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES · KDIGO

5.3.2.2: For anticoagulation in CRRT, we suggest using regional citrate anticoagulation rather than heparin in patients who do not have contraindications for citrate. *(2B)*

JAMA | Original Investigation

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Objective

"Current evidence is derived from few (underpowered) trials and the clinical benefit of regional citrate anticoagulation on **patient-centered outcomes** remains unclear"

JAMA | Original Investigation

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Objective

patient-centered outcomes

"Current evidence is derived from few (underpowered) trials and the clinical benefit of regional citrate anticoagulation on **patient-centered outcomes** remains unclear"

RICH trial was conducted to test whether regional citrate anticoagulation prolongs dialysis **filter life span** and **reduces 90-day-all-cause mortality** in critically ill patients with AKI

JAMA | Original Investigation

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Methods

patient-centered outcomes

- Randomized, multicenter (26 centers in Germany), parallel-group clinical trial
- Adults with AKI who required KRT and who had at least 1 additional condition (severe sepsis, septic shock, vasopressor, refractory fluid overload)
- **COPRIMARY OUTCOMES**: Filter life span AND 90-day mortality

JAMA | Original Investigation

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Methods

patient-centered outcomes

- Randomized, multicenter (26 centers in Germ… …ical trial
- Adults with AKI who requir… …least 1 additional condition (severe sepsis, septi… …refractory fluid overload)
- CC… …: Filter life span AND 90-day mortality

Recruitment was stopped for significant effectiveness in term of filter life span and for **futility in term of 90-day mortality**

JAMA | Original Investigation

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INTERVENTION

596 Patients analyzed

300

Regional citrate anticoagulation

Citrate added continuously to the blood before the filter of extracorporeal circuit; adjusted to ionized calcium levels

296

Systemic heparin anticoagulation

Heparin administered through IV lines at 30 mL/kg/h; adjusted to partial thromboplastin time of 45-60 seconds

JAMA | Original Investigation

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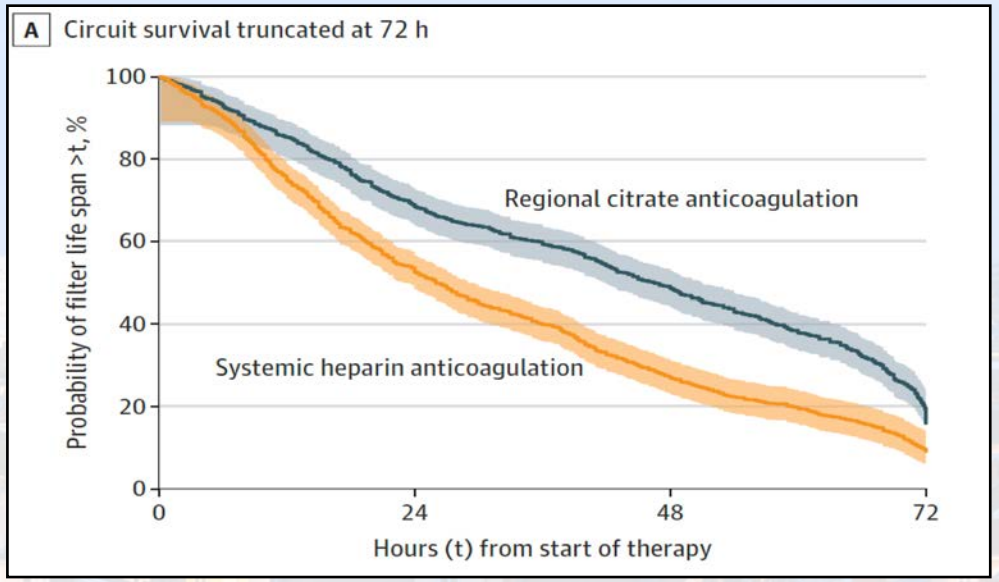
FINDINGS

Median filter life span

Regional citrate anticoagulation	Systemic heparin anticoagulation
47 hours	26 hours

The median filter life span difference was significant:

15 hours (95% CI, 11 to 20); $P < .001$



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FINDINGS

Median filter life span

Regional citrate anticoagulation
47 hours

Systemic heparin anticoagulation
26 hours

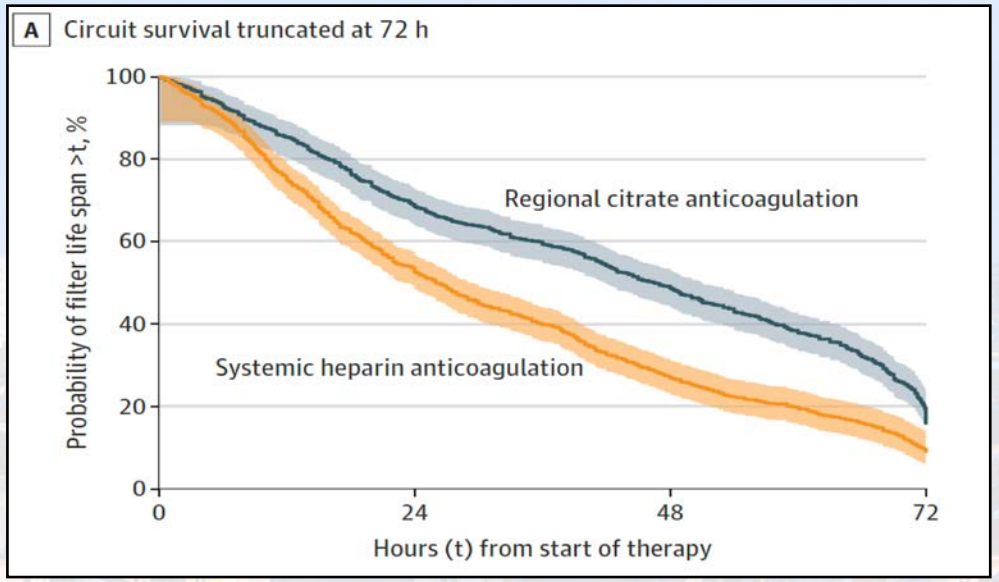
The median filter life span difference was significant:
15 hours (95% CI, 11 to 20); $P < .001$

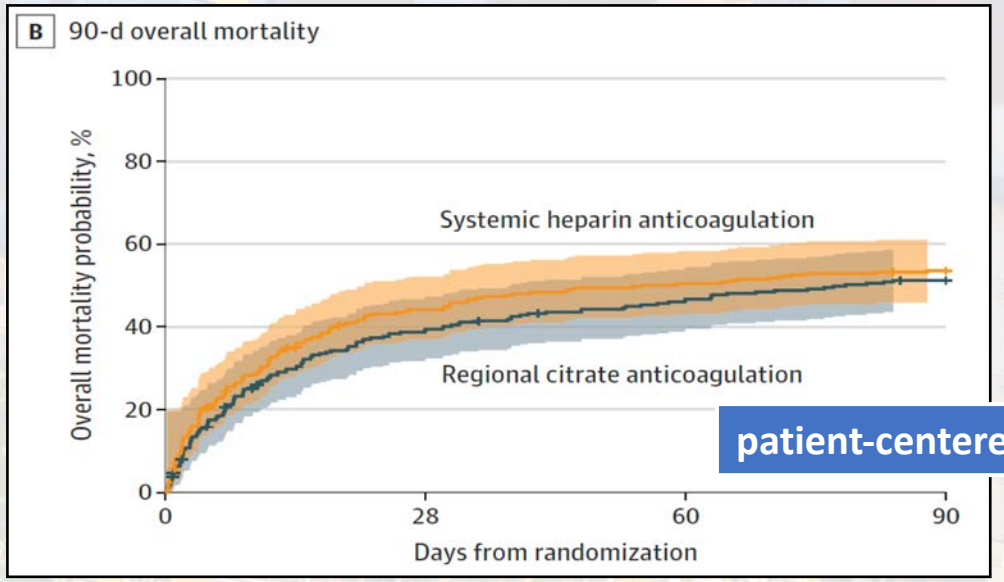
90-day mortality

Regional citrate anticoagulation
51%

Systemic heparin anticoagulation
54%

Adjusted 90-day mortality was not significant:
HR, **0.79** (95% CI, 0.63-1.004),
but the trial was underpowered for this outcome





patient-centered outcomes

JAMA | Original Investigation

Effect of Regional Citrate Anticoagulation vs Systemic Heparin Anticoagulation During Continuous Kidney Replacement Therapy on Dialysis Filter Life Span and Mortality Among Critically Ill Patients With Acute Kidney Injury

A Randomized Clinical Trial

Alexander Zarbock, MD; Mira Küllmar, MD; Detlef Kindgen-Milles, MD; Carola Wempe, PhD; Joachim Gerss, PhD; Timo Brandenburger, MD; Thomas Dimski, MD; Bartosz Tyczynski, MD; Michael Jahn, MD; Nils Mülling, MD; Martin Mehrländer, MD; Peter Rosenberger, MD; Gernot Marx, MD; Tim Philipp Simon, MD; Ulrich Jaschinski, MD; Philipp Deetjen, MD; Christian Putensen, MD; Jens-Christian Schewe, MD; Stefan Kluge, MD; Dominik Jarczak, MD; Torsten Slowinski, MD; Marc Bodenstein, MD; Patrick Meybohm, MD; Stefan Wirtz, MD; Onnen Moerer, MD; Andreas Kortgen, MD; Philipp Simon, MD; Sean M. Bagshaw, MD; John A. Kellum, MD; Melanie Meersch, MD; for the RICH Investigators and the Sepnet Trial Group

Secondary endpoints: NOT ADJUSTED FOR MULTIPLICITY

Regional citrate anticoagulation

- Higher rate of new infections (68 vs 55%)
- Persistent kidney dysfunction after 90 days (28 vs 15%)

Systemic heparin anticoagulation

- More bleeding complications (5 vs 17%)

RRT timing in ICU

2012

Absolute indications to start RRT
Life-threatening complications

- Refractory **severe hyperkalemia**
- Refractory **severe metabolic acidosis** (pH<7.15)
- **Pulmonary edema** resistant to diuretics

What is the Wait and Watch approach ?

Postpone RRT in critically ill patients with **severe AKI** who have **no life-threatening complication**

THE LANCET 2020

Delayed versus early initiation of renal replacement therapy for severe acute kidney injury: a systematic review and individual patient data meta-analysis of randomised clinical trials

Stéphane Gaudry, David Hajage*, Nicolas Benichou†, Khalil Chaïbi†, Saber Barbar, Alexander Zarbock, Nuttha Lumlertgul, Ron Wald, Sean M Bagshaw, Nattachai Srisawat, Alain Combes, Guillaume Geri, Tukaram Jamale, Agnès Dechartres, Jean-Pierre Quenot‡, Didier Dreyfuss‡*

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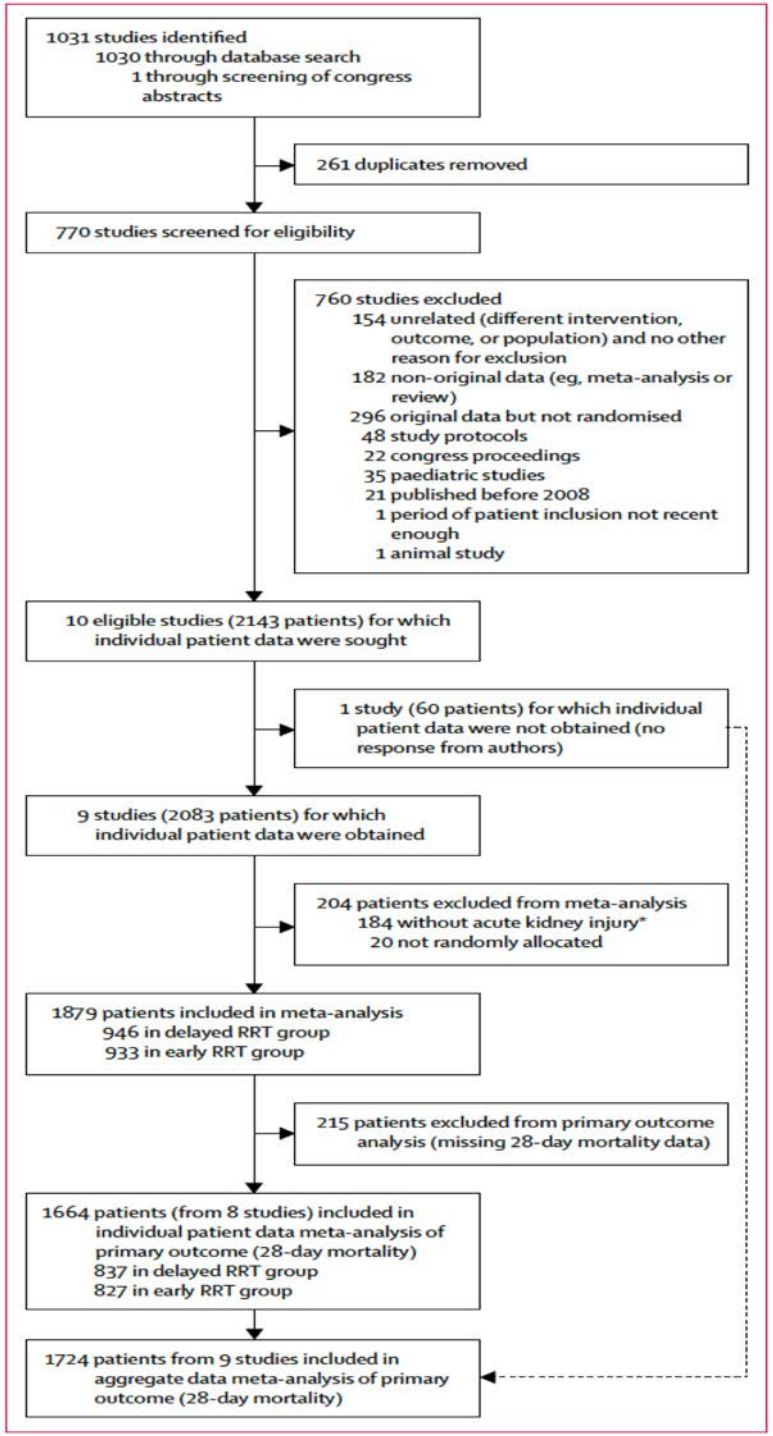
2020

- 770 studies screened for eligibility
- 10 eligible RCTs
- Individual patient data from 9 RCTs

- Jamale, AJKD 2013 ✅
- Wald, Kidney Int 2015 ✅
- Combes, AJRCCM 2015 (HEROICS) ✅
- Zarbock, JAMA 2016 (ELAIN) ✅
- Gaudry, NEJM 2016 (AKIKI) ✅
- Barbar, NEJM 2018 (IDEAL ICU) ✅
- Lumlertgul, Crit Care 2018 ✅
- Srisawat, J Crit Care 2018 ✅
- Geri, Rescuscit 2019 (HYPERDIA) ✅



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2020

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- 10 eligible RCTs
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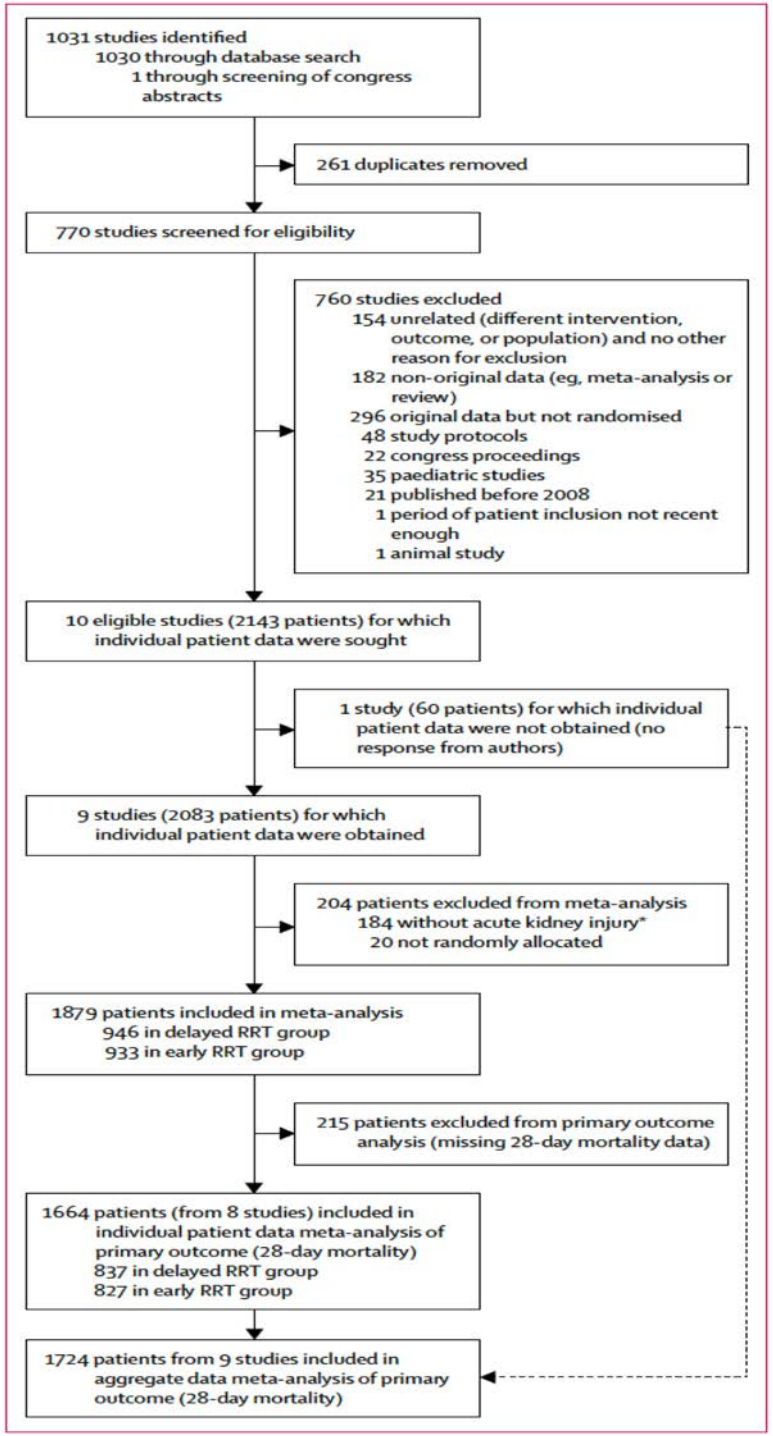
1879 Patients

933 early strategy

946 delayed strategy



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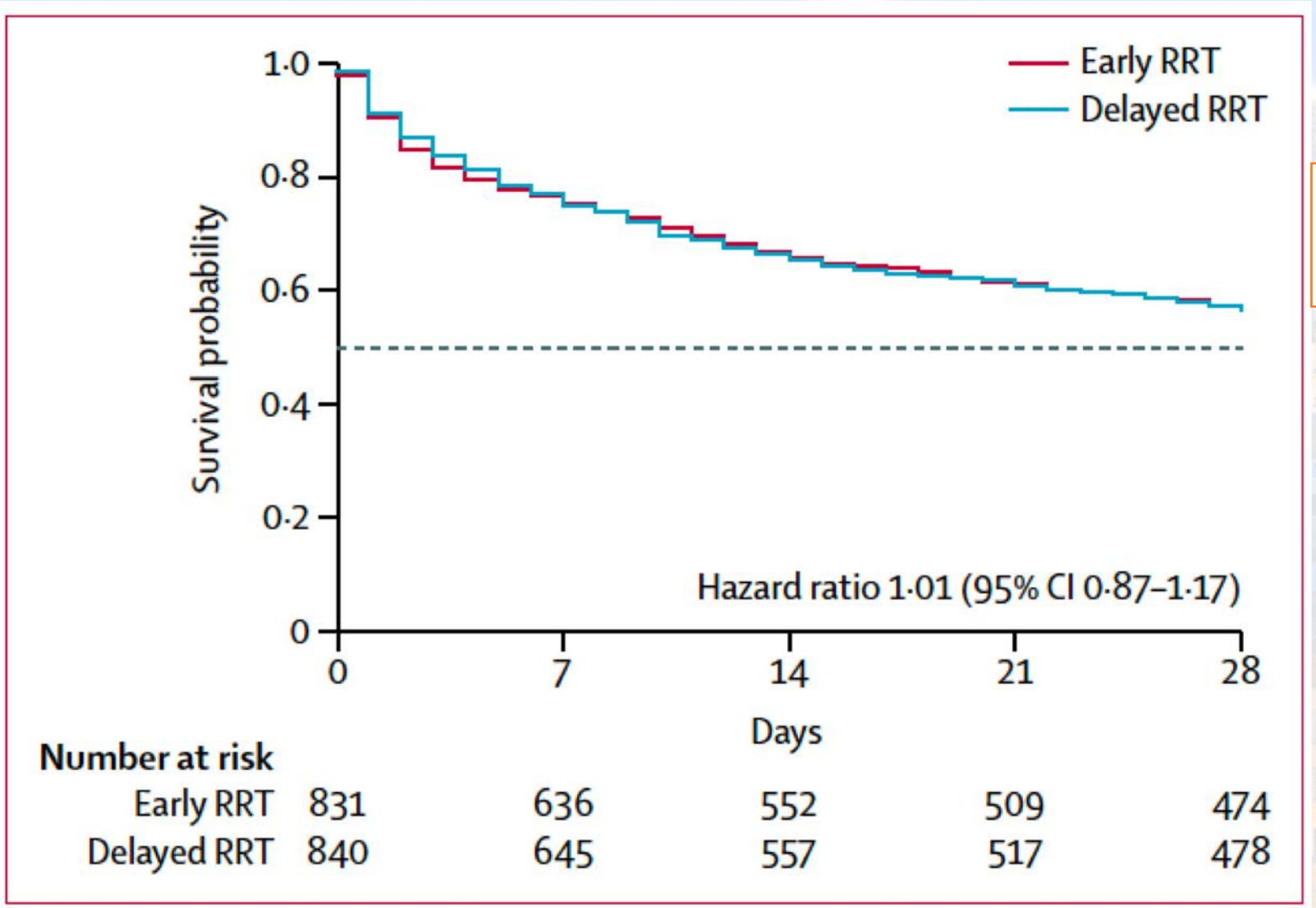
2020



42% never received RRT in the **delayed group**

Delayed versus early initiation of renal replacement therapy for severe acute kidney injury: a systematic review and individual patient data meta-analysis of randomised clinical trials

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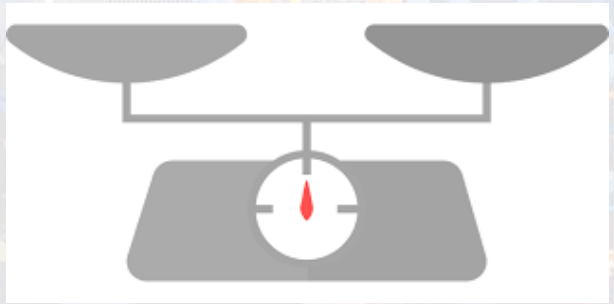
2020

Secondary outcomes

- Mortality at days 60 and 90
- Duration of hospital stay
- RRT dependence at hospital discharge
- MV-free days
- Vasopressor-free days
- Rate of adverse events



No significant difference

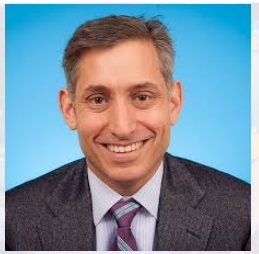
ORIGINAL ARTICLE

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

The STARRT-AKI Investigators, for the Canadian Critical Care Trials Group, the Australian and New Zealand Intensive Care Society Clinical Trials Group, the United Kingdom Critical Care Research Group, the Canadian Nephrology Trials Network, and the Irish Critical Care Trials Group*

STARRT AKI

- Multicenter, International, RCT
- 165 hospitals in 15 countries
- **2927 adults ICU** patients with **severe AKI**



Ron Wald

Sean Bagshaw

2 arms

Accelerated approach (or early) of RRT initiation

Conservative strategy of initiation of RRT as guided by standard indications and clinical judgment

ORIGINAL ARTICLE

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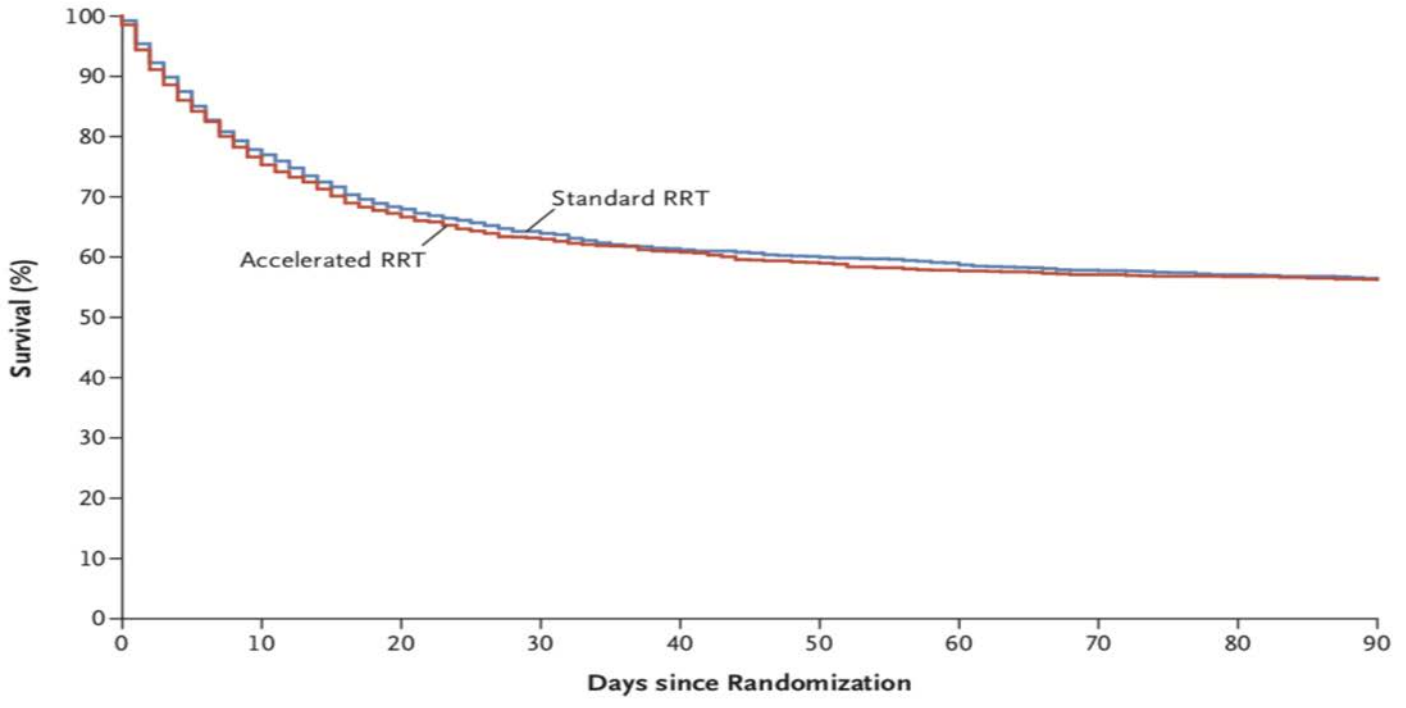
The STARRT-AKI Investigators, for the Canadian Critical Care Trials Group, the Australian and New Zealand Intensive Care Society Clinical Trials Group, the United Kingdom Critical Care Research Group, the Canadian Nephrology Trials Network, and the Irish Critical Care Trials Group*

Primary outcome

All-cause mortality Day 90



No. at Risk										
Standard RRT	1462	1138	999	939	897	878	862	844	833	823
Accelerated RRT	1465	1122	985	925	892	865	846	835	830	823

ORIGINAL ARTICLE **STARRT-AKI**

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

The STARRT-AKI Investigators, for the Canadian Critical Care Trials Group, the Australian and New Zealand Intensive Care Society Clinical Trials Group, the United Kingdom Critical Care Research Group, the Canadian Nephrology Trials Network, and the Irish Critical Care Trials Group*

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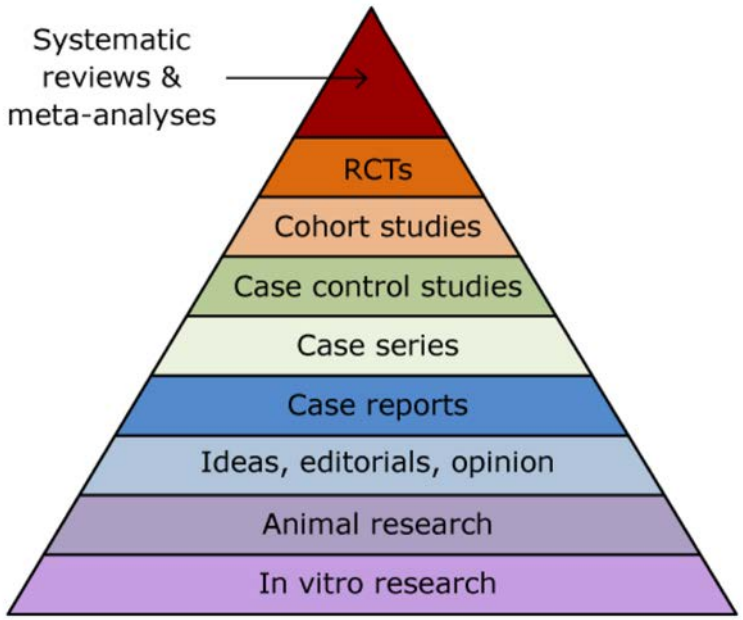
In the context of severe AKI, and in the absence of life-threatening complications (refractory severe hyperkalemia, refractory severe metabolic acidosis or pulmonary edema resistant to diuretics), delaying RRT initiation is recommended

STARRT AKI



High level of evidence

MAJOR RCTs on the timing of RRT

2016 NEJM


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

Stéphane Gaudry, M.D., David Hajage, M.D., Fréderique Schortgen, M.D., Laurent Martin-Lefevre, M.D., Bertrand Pons, M.D., Eric Boulet, M.D., Alexandre Boyer, M.D., Guillaume Chevrel, M.D., Nicolas Lerolle, M.D., Ph.D., Dorothée Carpentier, M.D., Nicolas de Prost, M.D., Ph.D., Alexandre Lautrette, M.D., Anne Bretagnol, M.D., Julien Mayaux, M.D., Saad Nseir, M.D., Ph.D., Bruno Megarbane, M.D., Ph.D., Marina Thirion, M.D., Jean-Marie Forel, M.D., Julien Maizel, M.D., Ph.D., Hodane Yonis, M.D., Philippe Markowicz, M.D., Guillaume Thiery, M.D., Florence Tubach, M.D., Ph.D., Jean-Damien Ricard, M.D., Ph.D., and Didier Dreyfuss, M.D., for the AKIKI Study Group*

2016 JAMA

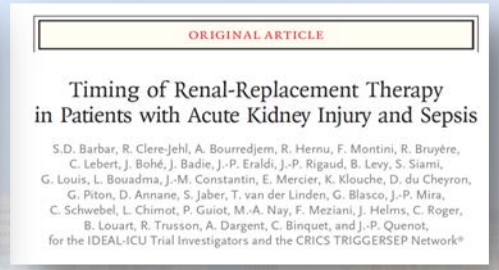

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury The ELAIN Randomized Clinical Trial

Alexander Zarbock, MD; John A. Kellum, MD; Christoph Schmidt, MD; Hugo Van Aken, MD; Carola Wempe, PhD; Hermann Pavenstädt, MD; Andreea Boanta, MD; Joachim Gerß, PhD; Melanie Meersch, MD

2018 NEJM


ORIGINAL ARTICLE

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis

S.D. Barbar, R. Clere-Jehl, A. Bourredjem, R. Hernu, F. Montini, R. Bruyère, C. Lebert, J. Bohé, J. Badie, J.-P. Eraldi, J.-P. Rigaud, B. Levy, S. Siami, G. Louis, L. Bouadma, J.-M. Constantin, E. Mercier, K. Klouche, D. du Cheyron, G. Piton, D. Annane, S. Jaber, T. van der Linden, G. Blasco, J.-P. Mira, C. Schwebel, L. Chimot, P. Guiot, M.-A. Nay, F. Meziani, J. Helms, C. Roger, B. Louart, R. Trusson, A. Dargent, C. Binquet, and J.-P. Quenot, for the IDEAL-ICU Trial Investigators and the CRICS TRIGGERSEP Network*

2020 NEJM


ORIGINAL ARTICLE

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

The STARRT-AKI Investigators, for the Canadian Critical Care Trials Group, the Australian and New Zealand Intensive Care Society Clinical Trials Group, the United Kingdom Critical Care Research Group, the Canadian Nephrology Trials Network, and the Irish Critical Care Trials Group*

	AKIKI	ELAIN	IDEAL-ICU	STARRT-AKI
Waiting time (in the delayed group)	**57 h**	**20 h**	**44 h**	**31 h**
% of patients who never received RRT in delayed group	**50%**	**9%**	**38%**	**38%**

The more you wait, the less you start RRT

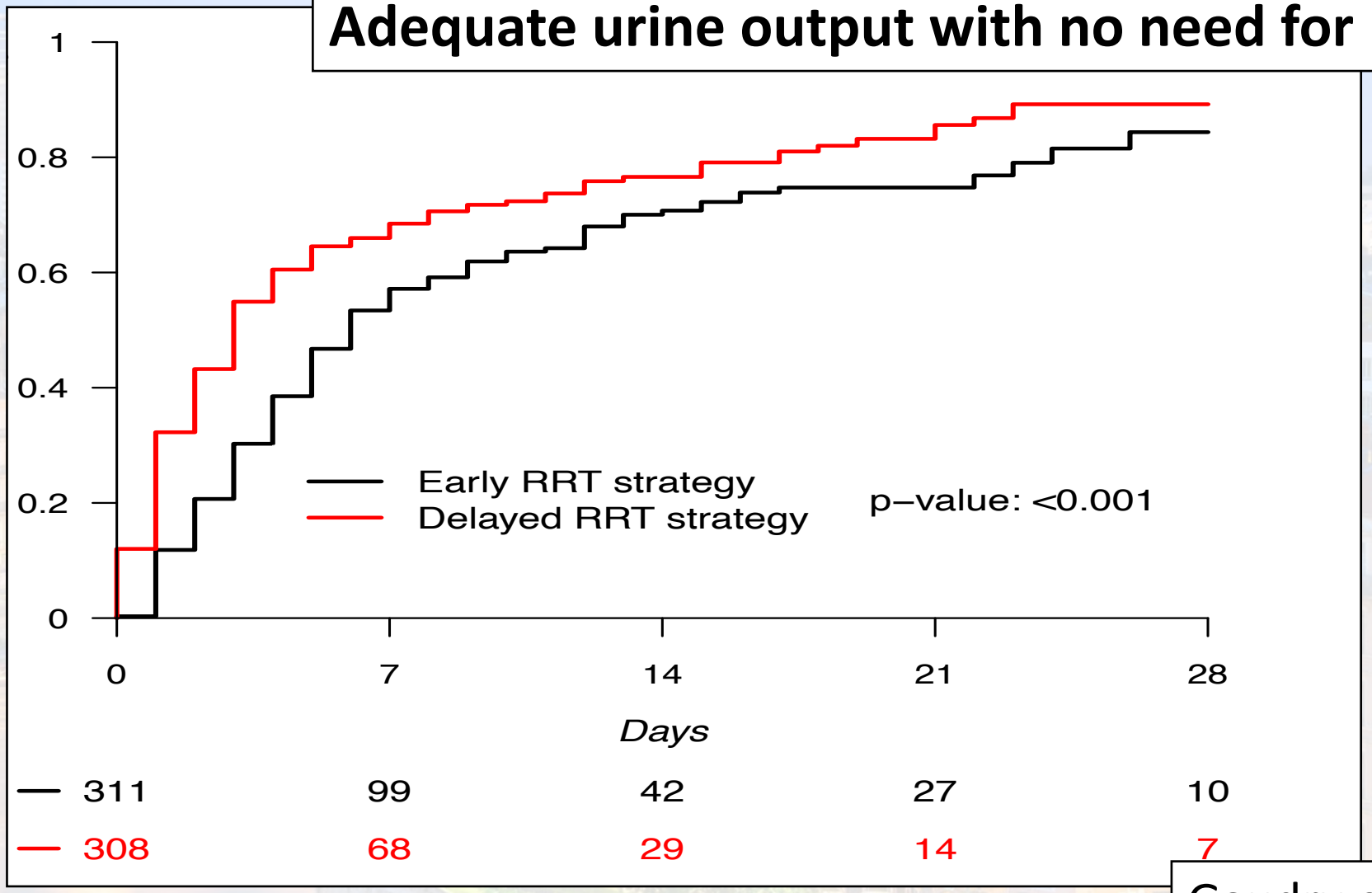
Reducing RRT *(ab)*use may be helpful for 2 reasons

- Reducing the risk of Artificial Kidney-Induced Kidney Injury
- Reducing the risk of Shortage of RRT for COVID-19 patients

Reducing the risk of Artificial Kidney-Induced Kidney Injury

AKIKI

Adequate urine output with no need for RRT



Gaudry et al NEJM 2016

Timing of Renal Support and Outcome of Septic Shock and Acute Respiratory Distress Syndrome

Stéphane Gaudry [1,2], David Hajage [3,4,5], Frédérique Schortgen [6], Laurent Martin-Lefevre [7], Charles Verney [1], Bertrand Pons [8], Eric Boulet [9], Alexandre Boyer [10], Guillaume Chevrel [11], Nicolas Lerolle [12], Dorothée Carpentier [13], Nicolas de Prost [14], Alexandre Lautrette [15], Anne Bretagnol [16], Julien Mayaux [17], Saad Nseir [18], Bruno Megarbane [19], Marina Thirion [20], Jean-Marie Forel [21], Julien Maizel [22], Hodane Yonis [23], Philippe Markowicz [24], Guillaume Thiery [6], Florence Tubach [3,5,25], Jean-Damien Ricard [1,26,27], Didier Dreyfuss[1,26,27]

URINE OUTPUT First 2 (D1-D2)

Delayed RRT

Urine output
D1-D2

1881 ml

p<0.0001

Early RRT

Urine output
D1-D2

994 ml

Timing of Renal Support and Outcome of Septic Shock and Acute Respiratory Distress Syndrome

Stéphane Gaudry [1,2], David Hajage [3,4,5], Frédérique Schortgen [6], Laurent Martin-Lefevre [7], Charles Verney [1], Bertrand Pons [8], Eric Boulet [9], Alexandre Boyer [10], Guillaume Chevrel [11], Nicolas Lerolle [12], Dorothée Carpentier [13], Nicolas de Prost [14], Alexandre Lautrette [15], Anne Bretagnol [16], Julien Mayaux [17], Saad Nseir [18], Bruno Megarbane [19], Marina Thirion [20], Jean-Marie Forel [21], Julien Maizel [22], Hodane Yonis [23], Philippe Markowicz [24], Guillaume Thiery [6], Florence Tubach [3,5,25], Jean-Damien Ricard [1,26,27], Didier Dreyfuss[1,26,27]

ULTRAFILTRATION First 2 days (D1-D2)

Delayed RRT

UF D1-D2

208 ml

Early RRT

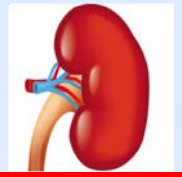
UF D1-D2

795 ml

p<0.0001

Timing of Renal Support and Outcome of Septic Shock and Acute Respiratory Distress Syndrome

Stéphane Gaudry [1,2], David Hajage [3,4,5], Frédérique Schortgen [6], Laurent Martin-Lefevre [7], Charles Verney [1], Bertrand Pons [8], Eric Boulet [9], Alexandre Boyer [10], Guillaume Chevrel [11], Nicolas Lerolle [12], Dorothée Carpentier [13], Nicolas de Prost [14], Alexandre Lautrette [15], Anne Bretagnol [16], Julien Mayaux [17], Saad Nseir [18], Bruno Megarbane [19], Marina Thirion [20], Jean-Marie Forel [21], Julien Maizel [22], Hodane Yonis [23], Philippe Markowicz [24], Guillaume Thiery [6], Florence Tubach [3,5,25], Jean-Damien Ricard [1,26,27], Didier Dreyfuss[1,26,27]



Delayed RRT	Urine output D1-D2	ns
	UF D1-D2	
Early RRT	Urine output D1-D2	
	UF D1-D2	

Reducing the risk of Artificial Kidney-Induced Kidney Injury

Intensive Care Med (2020) 46:513–515
https://doi.org/10.1007/s00134-019-05891-9

EDITORIAL

The artificial kidney induces acute kidney injury: yes

N. Benichou[1], Stéphane Gaudry[1,2,3,6*] and D. Dreyfuss[1,4,5]

Emergence of a new concept

Artificial Kidney-Induced Kidney Injury (AKIKI)
and
Permissive hyper-uremia

Reducing the risk of Artificial Kidney-Induced Kidney Injury

ORIGINAL ARTICLE

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

The STARRT-AKI Investigators, for the Canadian Critical Care Trials Group, the Australian and New Zealand Intensive Care Society Clinical Trials Group, the United Kingdom Critical Care Research Group, the Canadian Nephrology Trials Network, and the Irish Critical Care Trials Group*

STARRT-AKI

Artificial Kidney-Induced Kidney Injury

Confirmation of this concept

RRT dependence after 90 days

Early strategy: 10.4% vs **Delayed strategy: 6.0%**

RR:1.74 (95% CI: 1.24 to 2.43)

The more you wait, the less you start RRT

Reducing RRT *(ab)*use may be helpful for 2 reasons

- Reducing the risk of Artificial Kidney-Induced Kidney Injury
- Reducing the risk of Shortage of RRT for COVID-19 patients

Reducing the risk of Shortage of RRT for COVID-19 patients

Impending Shortages of Kidney Replacement Therapy for COVID-19 Patients

David S. Goldfarb,[1,2] Judith A. Benstein,[2] Olga Zhdanova,[2,3] Elizabeth Hammer,[2] Clay A. Block,[4] Nina J. Caplin,[2,3] Nathan Thompson,[2,3] and David M. Charytan[2]

CJASN 15: 880–882, 2020. doi: https://doi.org/10.2215/CJN.05180420

"An informal survey of our intensive care units (ICUs) this week demonstrates that **20%–40% of intubated ICU patients have AKI that necessitates KRT**"

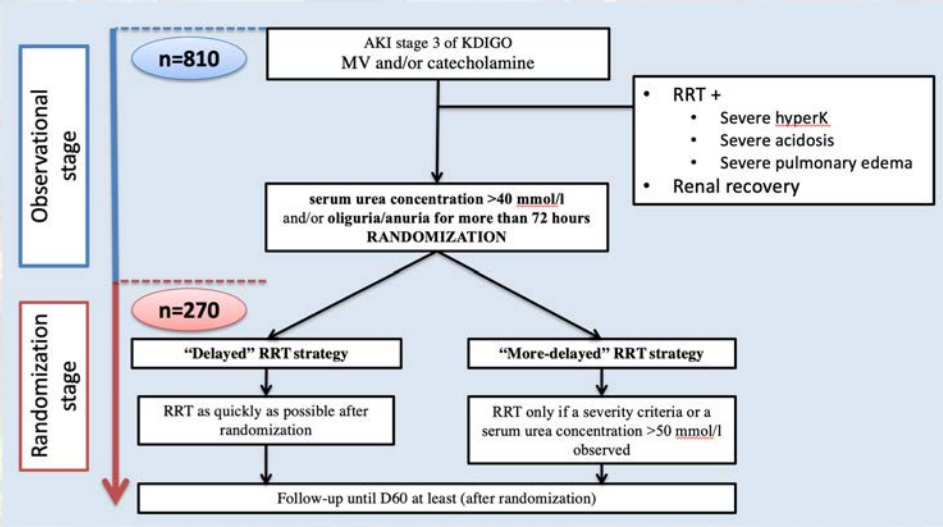
We initiated the use of **acute peritoneal dialysis**, a modality rarely used in American ICUs in recent years, to remove pressures from our CKRT supply

We must now highlight the possibility that before a deficiency of ventilators become an issue in caring for patients with COVID-19, provision of KRT may face critical shortages.

Time difference of RRT initiation between strategies (hours)

	AKIKI	ELAIN	IDEAL-ICU	STARRT-AKI
Waiting time (hours)	57	20	44	31

The Artificial Kidney Initiation in Kidney Injury 2 (AKIKI 2)
A Multi-Centre, Randomized, Controlled Trial



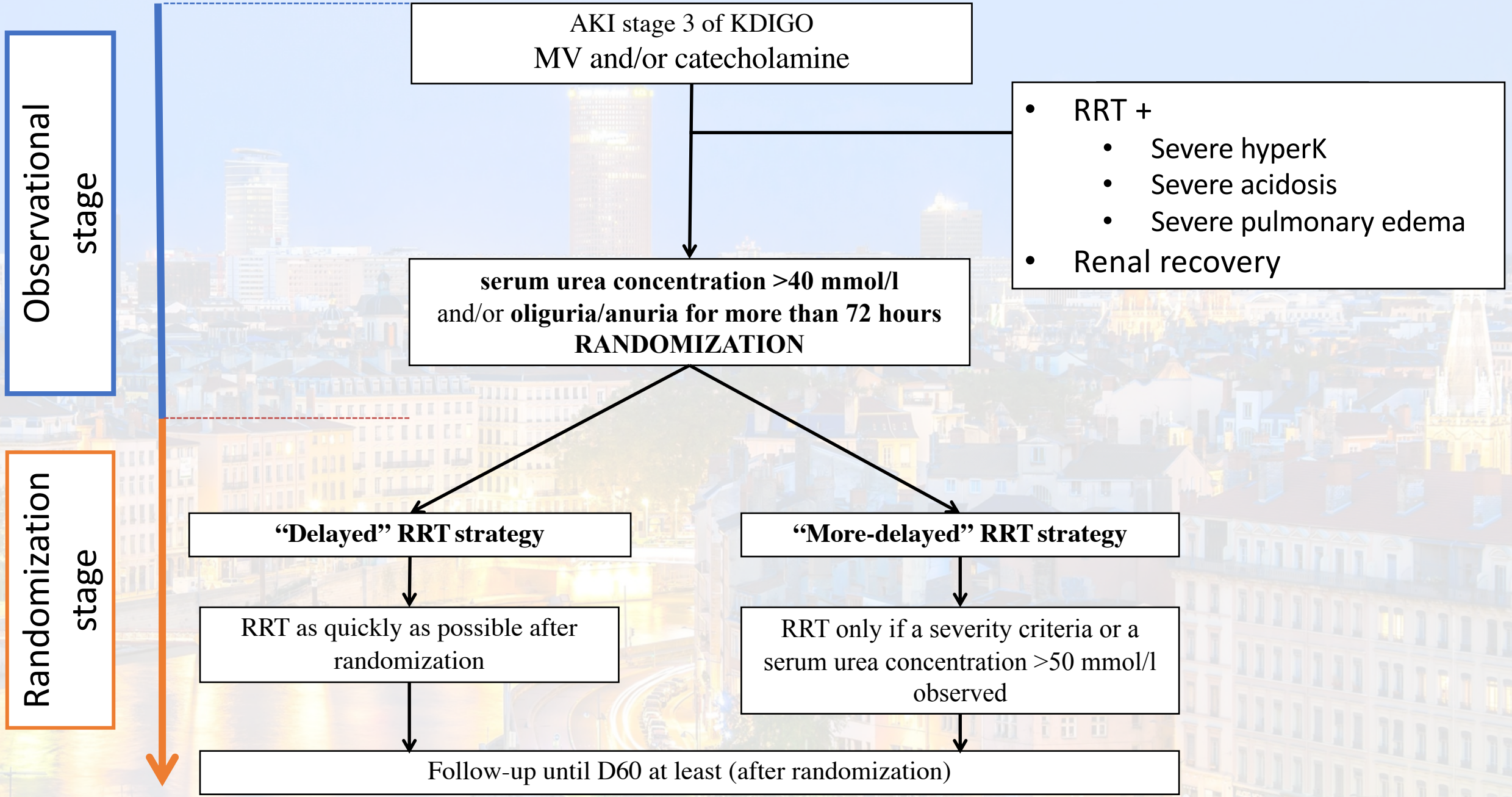
AKIKI1

Delayed Strategy Group

Pre-specified criteria

- **Severe hyperkalemia**
  potassium > 6 mmol/l, or > 5.5 mmol/l *Despite medical treatment*
- **Severe acidosis** (pH <7.15)
- **Acute pulmonary edema** due to fluid overload
  Responsible for severe hypoxemia

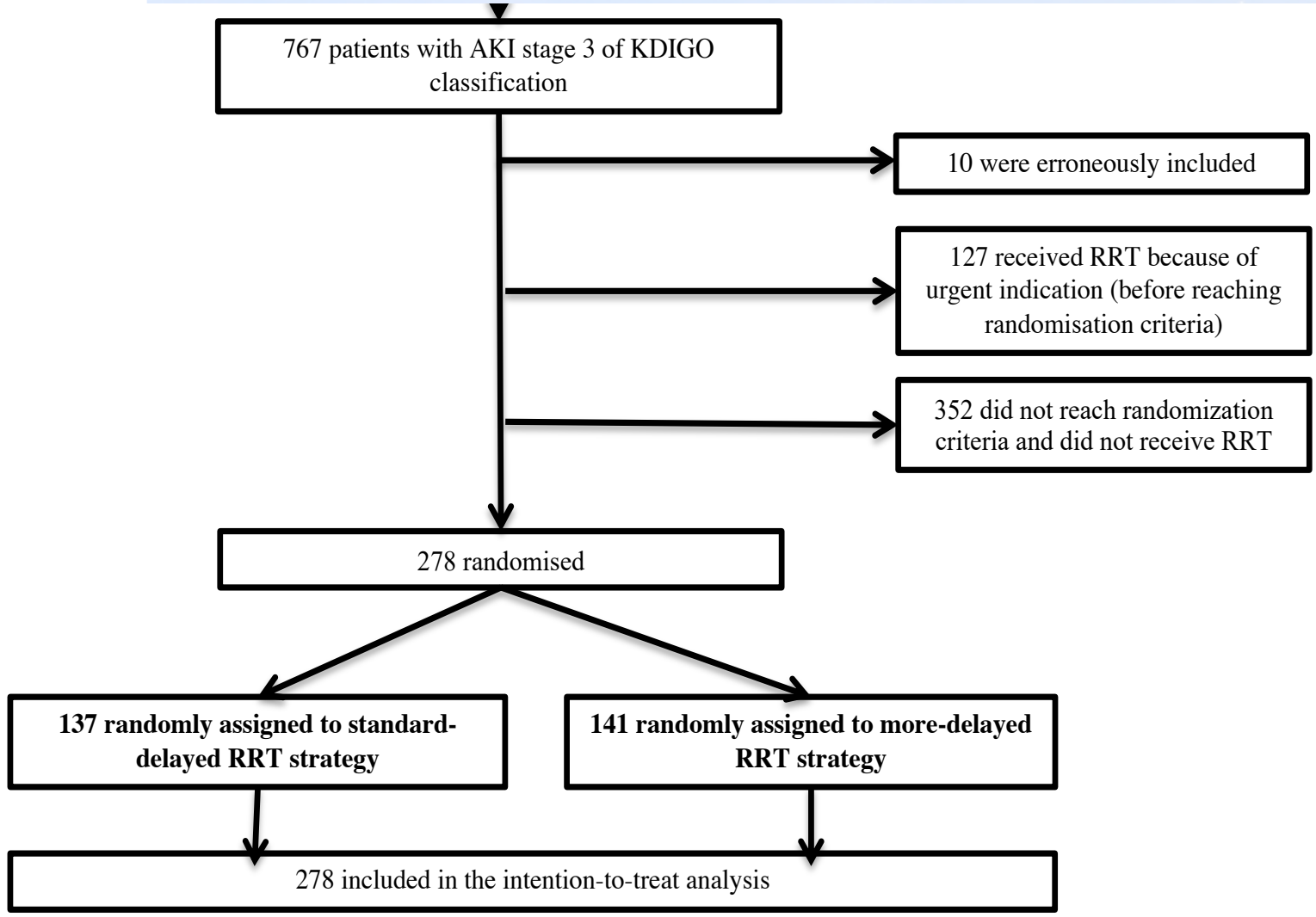
- **Oliguria/Anuria >72 hours**
- **Serum urea concentration >** 40mmol/l


Observational stage
Randomization stage
AKI stage 3 of KDIGO
MV and/or catecholamine
RRT +
Severe hyperK
Severe acidosis
Severe pulmonary edema
Renal recovery
serum urea concentration >40 mmol/l
and/or oliguria/anuria for more than 72 hours
RANDOMIZATION
"Delayed" RRT strategy
"More-delayed" RRT strategy
RRT as quickly as possible after randomization
RRT only if a severity criteria or a serum urea concentration >50 mmol/l observed
Follow-up until D60 at least (after randomization)

Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): a multicentre, open-label, randomised, controlled trial

Stéphane Gaudry, David Hajage, Laurent Martin-Lefevre, Saïd Lebbah, Guillaume Louis, Sébastien Moschietto, Dimitri Titeca-Beauport, Béatrice La Combe, Bertrand Pons, Nicolas de Prost, Sébastien Besset, Alain Combes, Adrien Robine, Marion Beuzelin, Julio Badie, Guillaume Chevrel, Julien Bohé, Elisabeth Coupez, Nicolas Chudeau, Saber Barbar, Christophe Vinsonneau, Jean-Marie Forel, Didier Thevenin, Eric Boulet, Karim Lakhal, Nadia Aissaoui, Steven Grange, Marc Leone, Guillaume Lacave, Saad Nseir, Florent Poirson, Julien Mayaux, Karim Asehnoune, Guillaume Geri, Kada Klouche, Guillaume Thiery, Laurent Argaud, Bertrand Rozec, Cyril Cadoz, Pascal Andreu, Jean Reignier*, Jean-Damien Ricard*, Jean-Pierre Quenot† , Didier Dreyfuss†

Lancet 2021



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Primary endpoint

The **median number of RRT-free days** was 12 days (IQR 0-25) in the delayed strategy and 10 days (IQR 0-24) in the more-delayed strategy (**p=0.93**)

	Delayed RRT strategy (N=137)	More-Delayed RRT strategy (N=141)	P value
RRT-free days			
All patients	12 (0-25)	10 (0-24)	0·93
Survivors	24 (15-27)	23 (14-28)	0·54
Number of patients who actually received RRT	134 (98)	111 (79)	<0·001
Time from randomisation to RRT – hours	3 (2-5)	33 (24-60)	<0·001
Mortality			
At day 28	52 (38)	63 (45)	0·26
At day 60	60 (44)	77 (55)	0·07
At ICU discharge	55 (40)	66 (47)	0·26
At hospital discharge	61 (45)	75 (53)	0·15

Prespecified multivariate analysis

Odds ratio for **death at 60 days**
2.16 (95% CI, 1·17 – 4·01, **p=0·014**)
with **more-delayed** versus delayed strategy

	Univariate analysis			Multivariate analysis		
Variable	**Odd ratio**	**CI 95%**	**P Value**	**Odd ratio**	**CI 95%**	**P Value**
More-delayed strategy	1·54	0·96-2·48	0·072	2·16	1·17-4·01	0·014
SAPS III	1·05	1·03-1·08	<0·001	1·05	1·02-1·08	<0·001
Mechanical ventilation	3·46	1·67-7·75	0·001	3·62	1·27-10·29	0·016
Catecholamine infusion	1·98	1·21-3·28	0·007	1·22	0·61-2·43	0·577
Sepsis status			0·213			0·096
Sepsis	0·66	0·34-1·27		0·48	0·20-1·13	
Septic shock	1·56	0·90-2·71		1·15	0·55-2·40	
Time between ICU admission and AKI	0·62	0·26-1·39	0·250	0·45	0·15-1·38	0·164

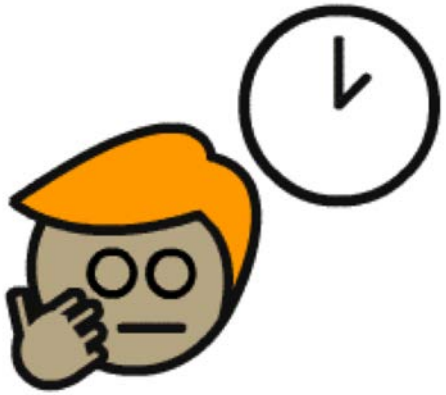
Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): a multicentre, open-label, randomised, controlled trial

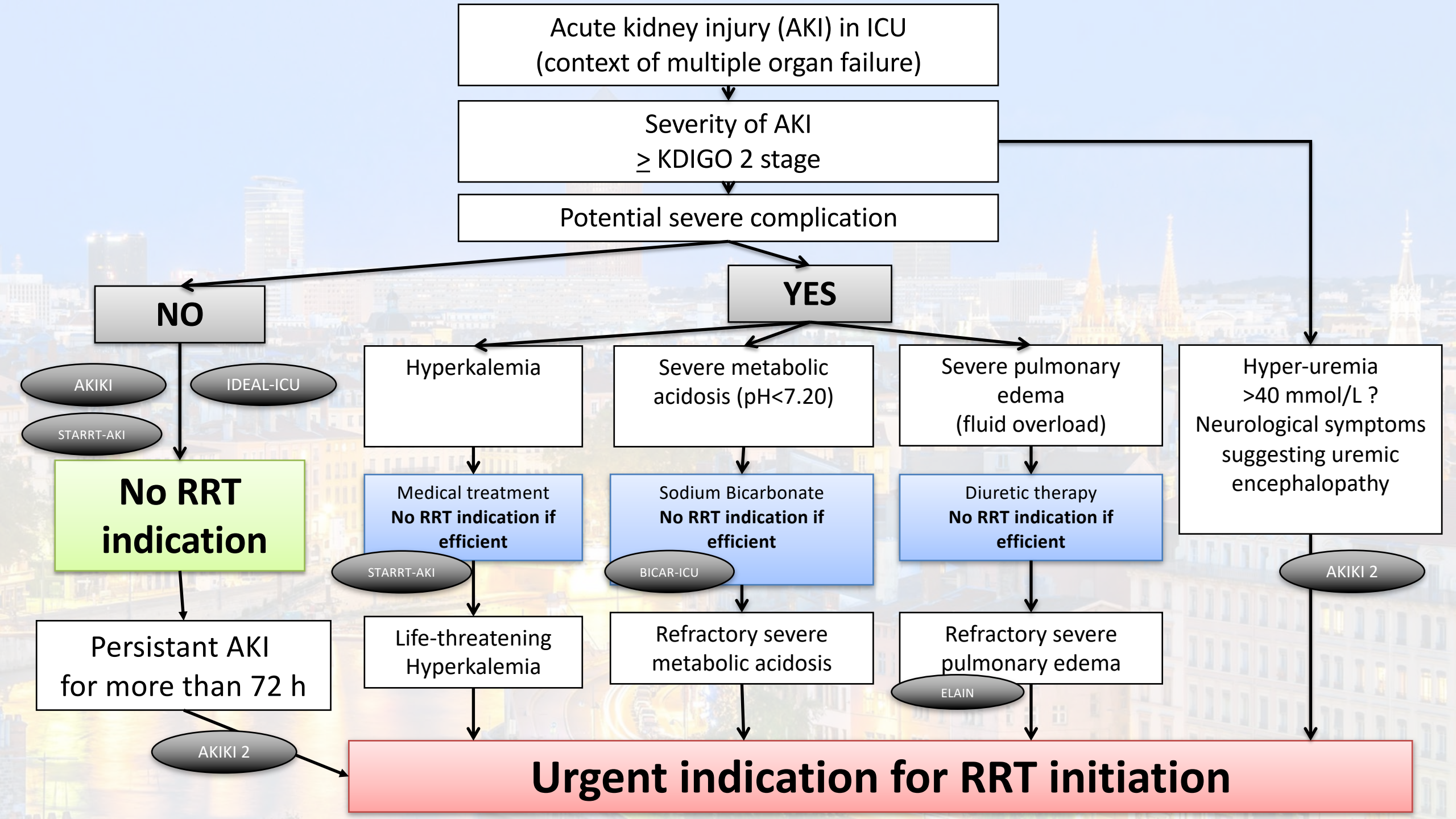
Stéphane Gaudry, David Hajage, Laurent Martin-Lefevre, Saïd Lebbah, Guillaume Louis, Sébastien Moschietto, Dimitri Titeca-Beauport, Béatrice La Combe, Bertrand Pons, Nicolas de Prost, Sébastien Besset, Alain Combes, Adrien Robine, Marion Beuzelin, Julio Badie, Guillaume Chevrel, Julien Bohé, Elisabeth Coupez, Nicolas Chudeau, Saber Barbar, Christophe Vinsonneau, Jean-Marie Forel, Didier Thevenin, Eric Boulet, Karim Lakhal, Nadia Aissaoui, Steven Grange, Marc Leone, Guillaume Lacave, Saad Nseir, Florent Poirson, Julien Mayaux, Karim Asehnoune, Guillaume Geri, Kada Klouche, Guillaume Thiery, Laurent Argaud, Bertrand Rozec, Cyril Cadoz, Pascal Andreu, Jean Reignier*, Jean-Damien Ricard*, Jean-Pierre Quenot† , Didier Dreyfuss†

To summarize the AKIKI 2 trial

Wait and see approach

Yes but not too long




Acute kidney injury (AKI) in ICU
(context of multiple organ failure)
Severity of AKI
≥ KDIGO 2 stage
Potential severe complication
NO
YES
AKIKI
IDEAL-ICU
STARRT-AKI
No RRT indication
Persistant AKI
for more than 72 h
AKIKI 2
Hyperkalemia
Medical treatment
No RRT indication if efficient
STARRT-AKI
Life-threatening Hyperkalemia
Severe metabolic acidosis (pH<7.20)
Sodium Bicarbonate
No RRT indication if efficient
BICAR-ICU
Refractory severe metabolic acidosis
Severe pulmonary edema
(fluid overload)
Diuretic therapy
No RRT indication if efficient
Refractory severe pulmonary edema
ELAIN
Hyper-uremia
>40 mmol/L ?
Neurological symptoms suggesting uremic encephalopathy
AKIKI 2
Urgent indication for RRT initiation

AKI news (2020-2021)

AKI and fluids

JAMA Internal Medicine | Original Investigation

Effect of No Prehydration vs Sodium Bicarbonate Prehydration Prior to Contrast-Enhanced Computed Tomography in the Prevention of Postcontrast Acute Kidney Injury in Adults With Chronic Kidney Disease
The Kompas Randomized Clinical Trial

Rohit J. Timal, MD; Judith Kooiman, MD, PhD; Yvo W. J. Sijpkens, MD, PhD; Jean-Paul P. M. de Vries, MD, PhD; Iris J. A. M. Verberk-Jonkers, MD, PhD; Harald F. H. Brulez, MD, PhD; Marjolijn van Buren, MD, PhD; Aart J. van der Molen, MD, PhD; Suzanne C. Cannegieter, MD, PhD; Hein Putter, PhD; Wilbert B. van den Hout, PhD; J. Wouter Jukema, MD, PhD; Ton J. Rabelink, MD, PhD; Menno V. Huisman, MD, PhD, FESC

The KOMPAS trial
February 2020

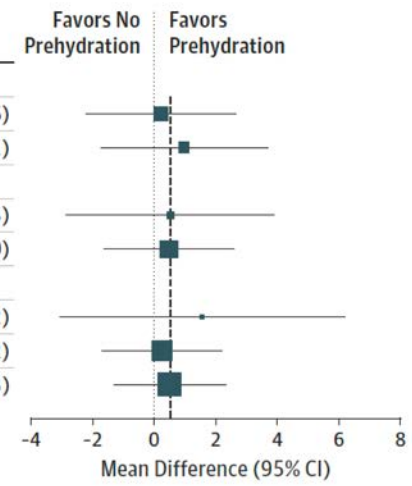
Mean relative **increase** (percentage) in **serum creatinine level 2 to 5 days**

- No prehydration: **3.0%**
- Sodium Bicarbonate prehydration: **3.5%**

Mean difference 0.5; 95% CI -1.3 to 2.3; p <0.001 for noninferiority

A Primary end point

Definition Groups	Patients, No. (%)	SD Difference	Mean Difference (95% CI)	P Value
Age, y				
≤75	301 (59.7)	1.24	0.22 (-2.23 to 2.66)	.86
>75	203 (40.3)	1.39	0.97 (-1.77 to 3.71)	.48
eGFR of 30-44 mL/min/1.73 m^2 and ≥2 RF for PC-AKI				
Yes	173 (34.3)	1.73	0.51 (-2.90 to 3.93)	.77
No	331 (65.7)	1.08	0.47 (-1.65 to 2.60)	.66
eGFR of 30-44 mL/min/1.73 m^2 and diabetes				
Yes	87 (17.3)	2.35	1.54 (-3.13 to 6.22)	.51
No	417 (82.7)	1.00	0.26 (-1.70 to 2.22)	.80
Overall estimate	504 (100)	0.93	0.51 (-1.31 to 2.33)	.58



The FLASH trial

January 2020

JAMA | Original Investigation

Effect of Hydroxyethyl Starch vs Saline for Volume Replacement Therapy on Death or Postoperative Complications Among High-Risk Patients Undergoing Major Abdominal Surgery

The FLASH Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Matthias Garot, MD; Thomas Godet, MD, PhD; Matthieu Biais, MD, PhD; Daniel Verzilli, MD; Alexandre Ouattara, MD, PhD; Olivier Huet, MD, PhD; Thomas Lescot, MD, PhD; Gilles Lebuffe, MD, PhD; Antoine Dewitte, MD, PhD; Anna Cadic, MD; Aymeric Restoux, MD, PhD; Karim Asehnoune, MD, PhD; Catherine Paugam-Burtz, MD, PhD; Philippe Cuvillon, MD, PhD; Marion Faucher, MD, PhD; Camille Vaisse, MD; Younes El Amine, MD; Hélène Beloeil, MD, PhD; Marc Leone, MD, PhD; Eric Noll, MD, PhD; Vincent Piriou, MD, PhD; Sigismond Lasocki, MD, PhD; Jean-Etienne Bazin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the FLASH Trial Group

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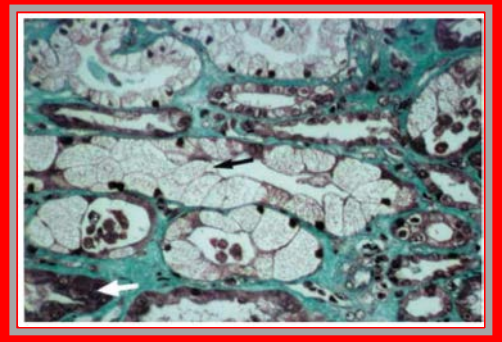
Rational

- HES have hypothetical ability to provide **faster hemodynamic stabilization** during acute hypovolemia

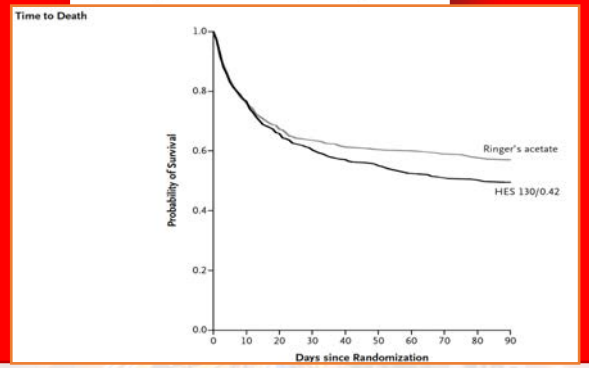
- But, HES **increase risk of death and AKI** in **critically ill patients** (US-FDA 2013)

osmotic-nephrosis-like lesions



ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis



Phillips et al. Critical Care 2013, 17:319
http://ccforum.com/content/17/3/319

CRITICAL CARE

JOURNAL CLUB CRITIQUE

Crystalloids vs. colloids: KO at the twelfth round?

Dennis P Phillips[1,2], A Murat Kaynar[1,2], John A Kellum[3] and Hernando Gomez*[1]

- However, no data from **surgical patients**

JAMA | Original Investigation

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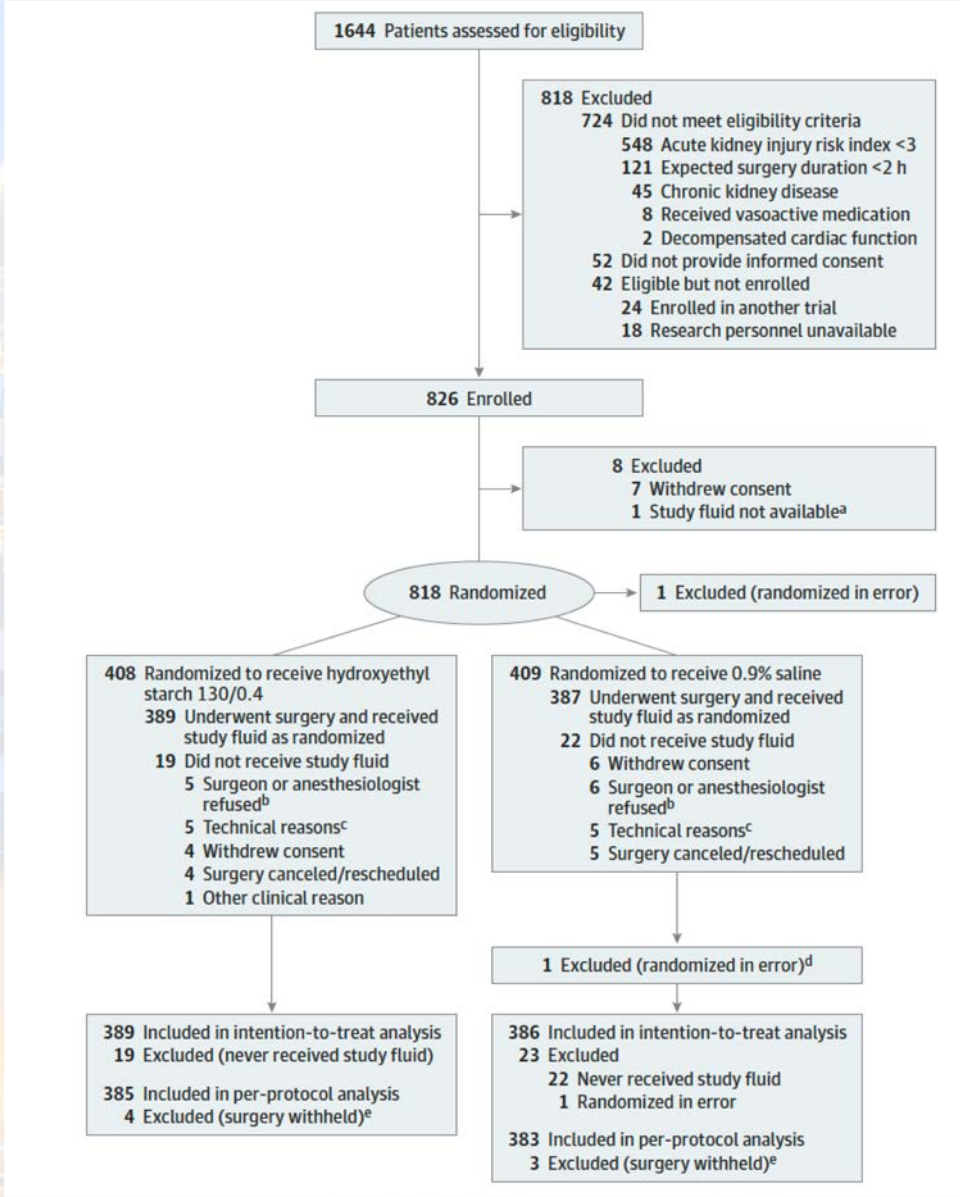
- Double-blind, RCT
- 20 French University hospital
- Inclusion criteria
  - Adults patients admitted for elective or non elective surgery
  - Anticipated duration >2 hours
  - Intermediate to high risk of developing post-op complication



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INTERVENTION

775 Patients analyzed

389

386

6% HES 130/0.4

Diluted in 0.9% saline
in 250-mL boluses
for up to 24 h

0.9% Saline

in 250-mL boluses
for up to 24 h

JAMA | Original Investigation

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Primary outcome

Composite outcome at 14 days:

- *Death*
- *Major postoperative complications*
  - *AKI stage 1*
  - *Acute respiratory failure*
  - *Acute heart failure*
  - *Major sepsis complication*
  - *Unplanned reoperation*

JAMA | Original Investigation

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Primary outcome

Death or major postoperative complications

6% HES 130/0.4
139 of 389 patients

0.9% Saline
125 of 386 patients

No significant difference:

difference, **3.3%** (95% CI, −3.3% to 10.0%)

relative risk, **1.10** (95% CI, 0.91 to 1.34); *P* = .33

JAMA | Original Investigation

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Secondary and exploratory kidney outcomes

	HES	Saline	RR (95%CI)	p
Kidney dysfunction up to day 14	**22%**	16%	1.34 (1.00-1.80)	0.05
AKI up to day 28	**23%**	17%	1.36 (1.02-1.82)	0.04

JAMA | Original Investigation

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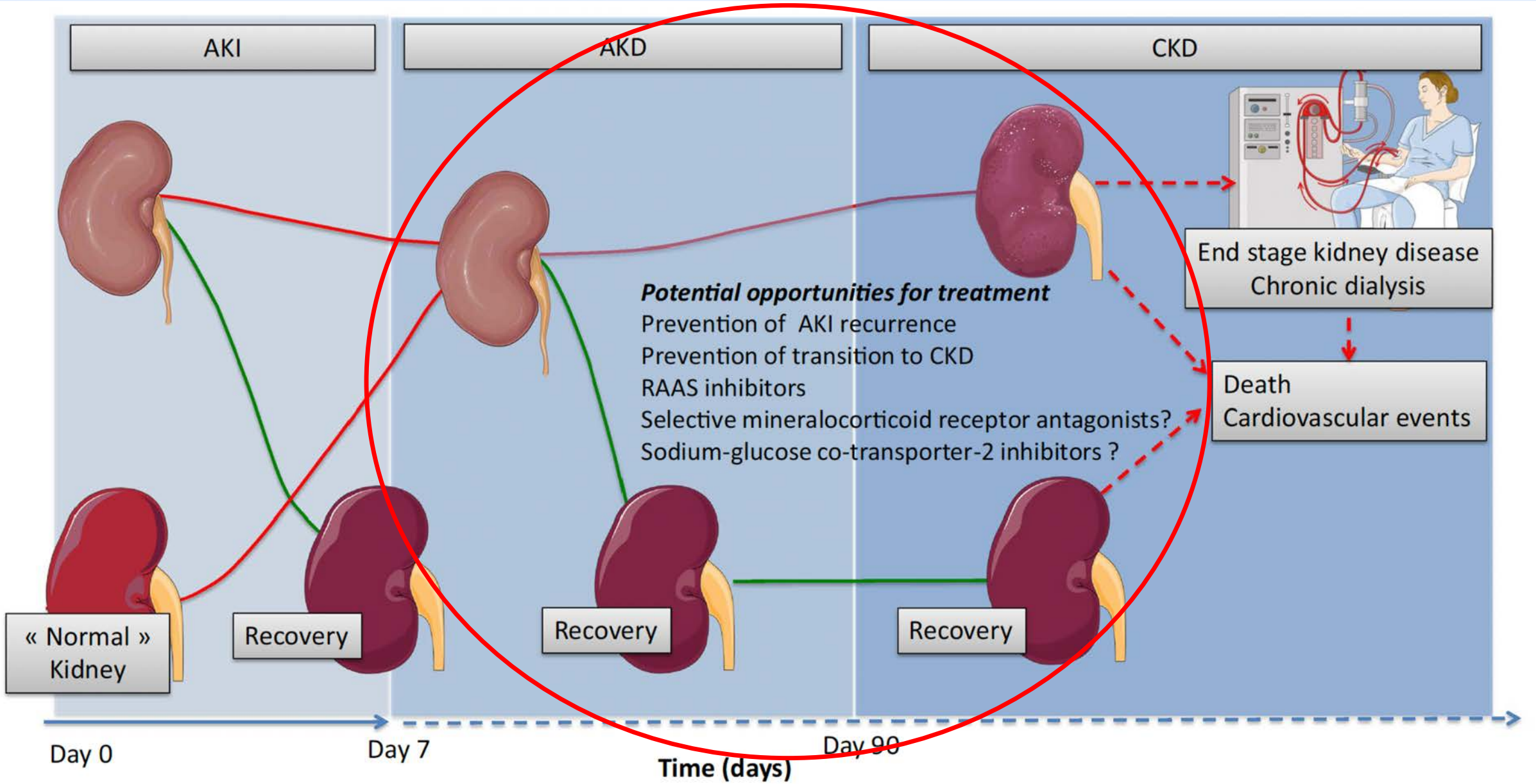
HES in the ICU or in the operative room

- Ineffective
- Nephrotoxic
- Expensive

No place for this therapeutic agent

AKI news (2020-2021)

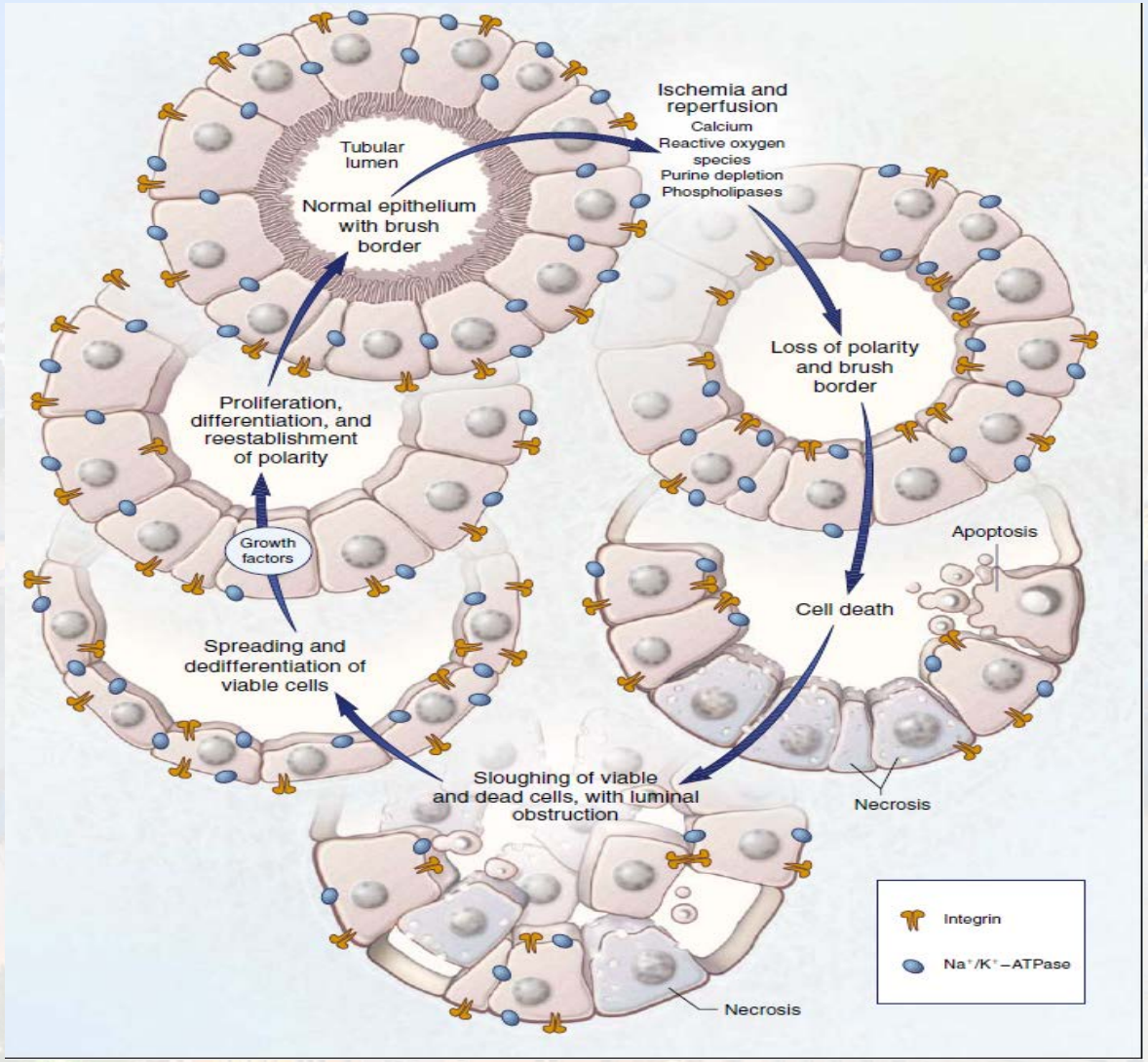
What is the future ?


AKI
AKD
CKD
End stage kidney disease
Chronic dialysis
Death
Cardiovascular events
Potential opportunities for treatment
Prevention of AKI recurrence
Prevention of transition to CKD
RAAS inhibitors
Selective mineralocorticoid receptor antagonists?
Sodium-glucose co-transporter-2 inhibitors ?
« Normal »
Kidney
Recovery
Recovery
Recovery
Day 0
Day 7
Day 90
Time (days)

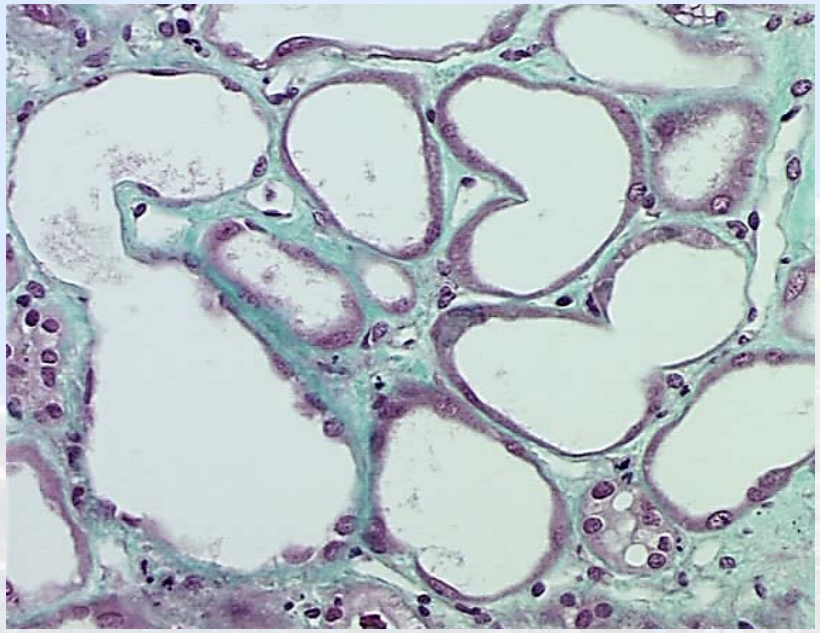
What did we think 20 years ago?

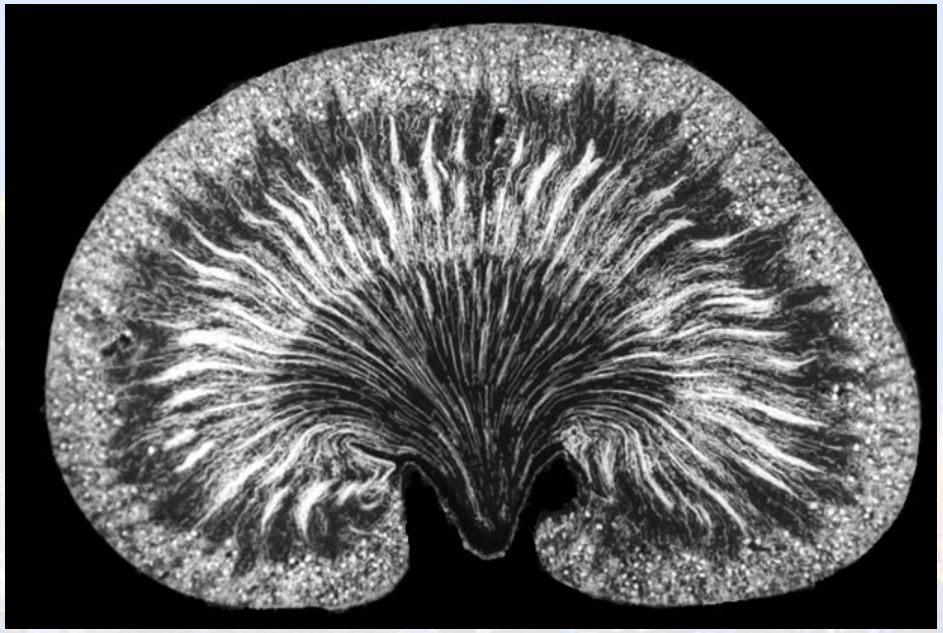
RESTITUTIO AD INTEGRUM

« The severely damaged kidney can completely restore its structure and function »



Thadhani R et al, N Engl J Med 1996

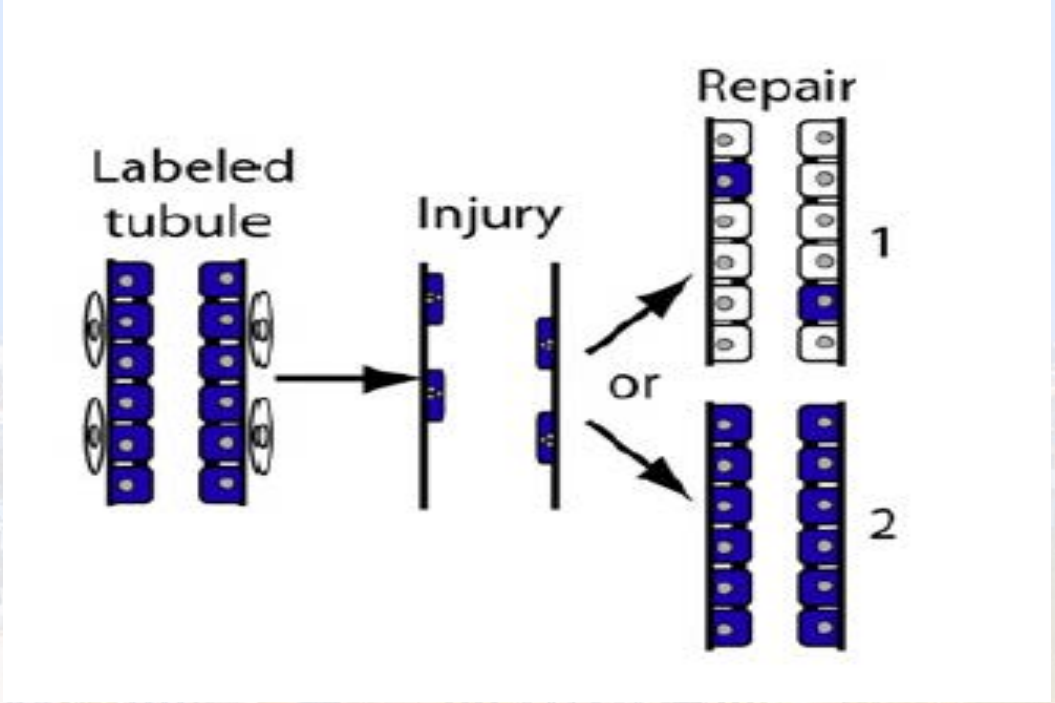


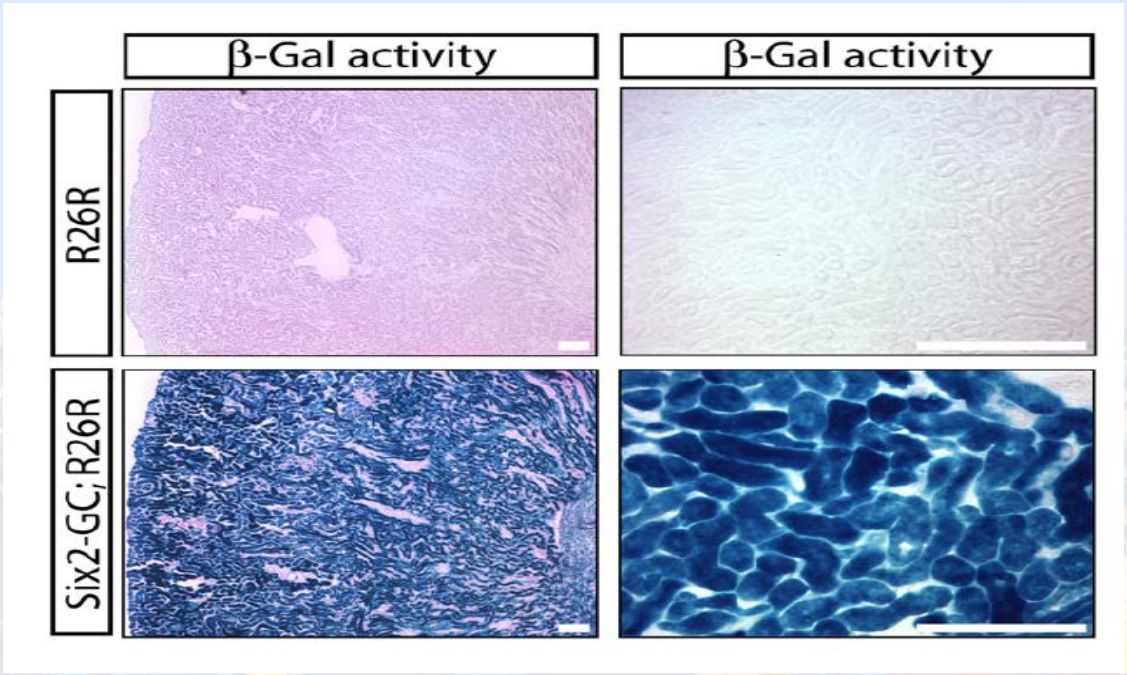


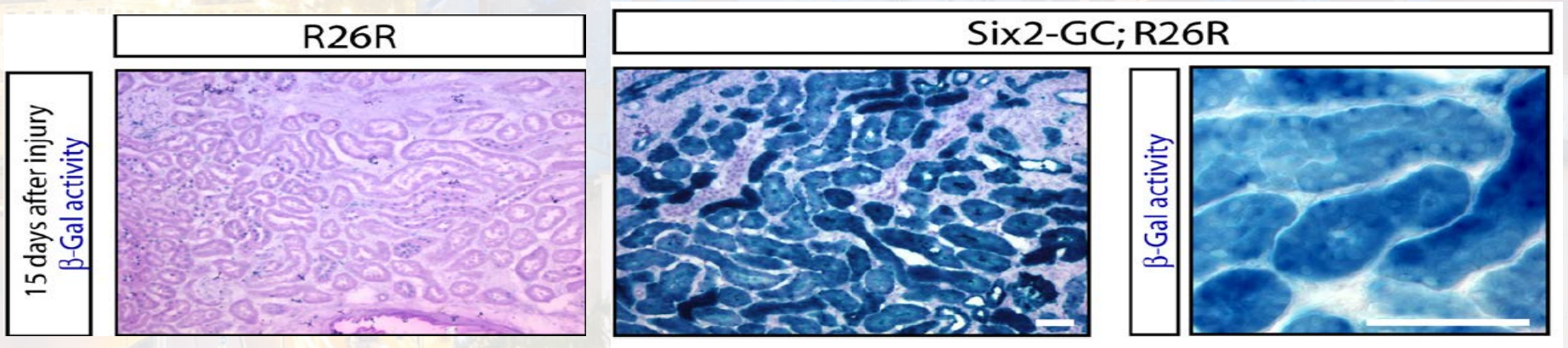
Tubular necrosis **repair** processes begin within the **first 24 hours**

There is probably a place for therapeutic intervention in ICU

The surviving tubular epithelium is in charge of the repair

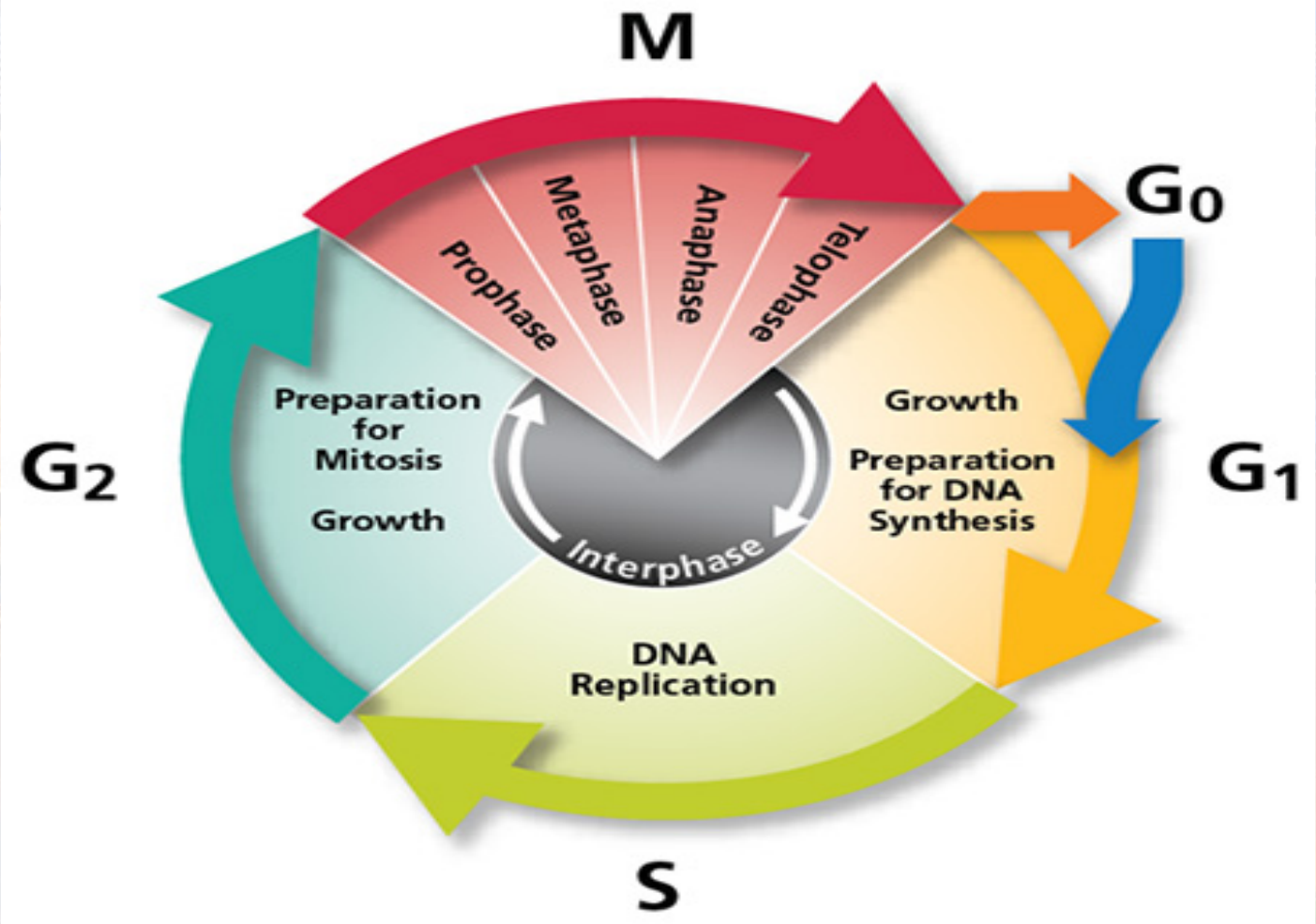






Humphreys BD, Cell Stem Cell 2008

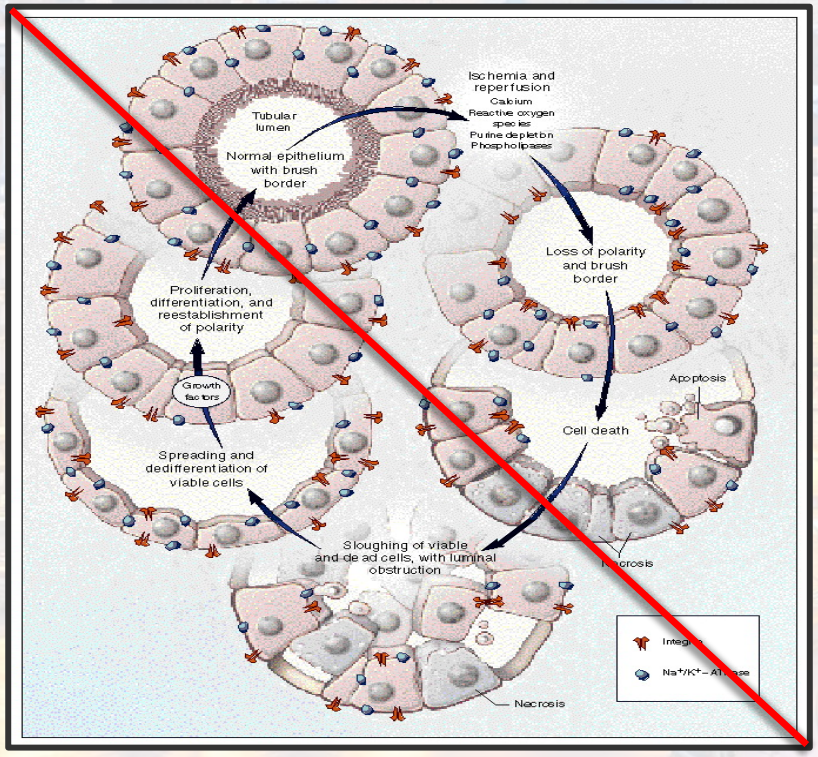
The **repair cells** were **also victims** of the first aggression and they are the sites of abnormalities of the cell cycle which have a pro-fibrotic effect



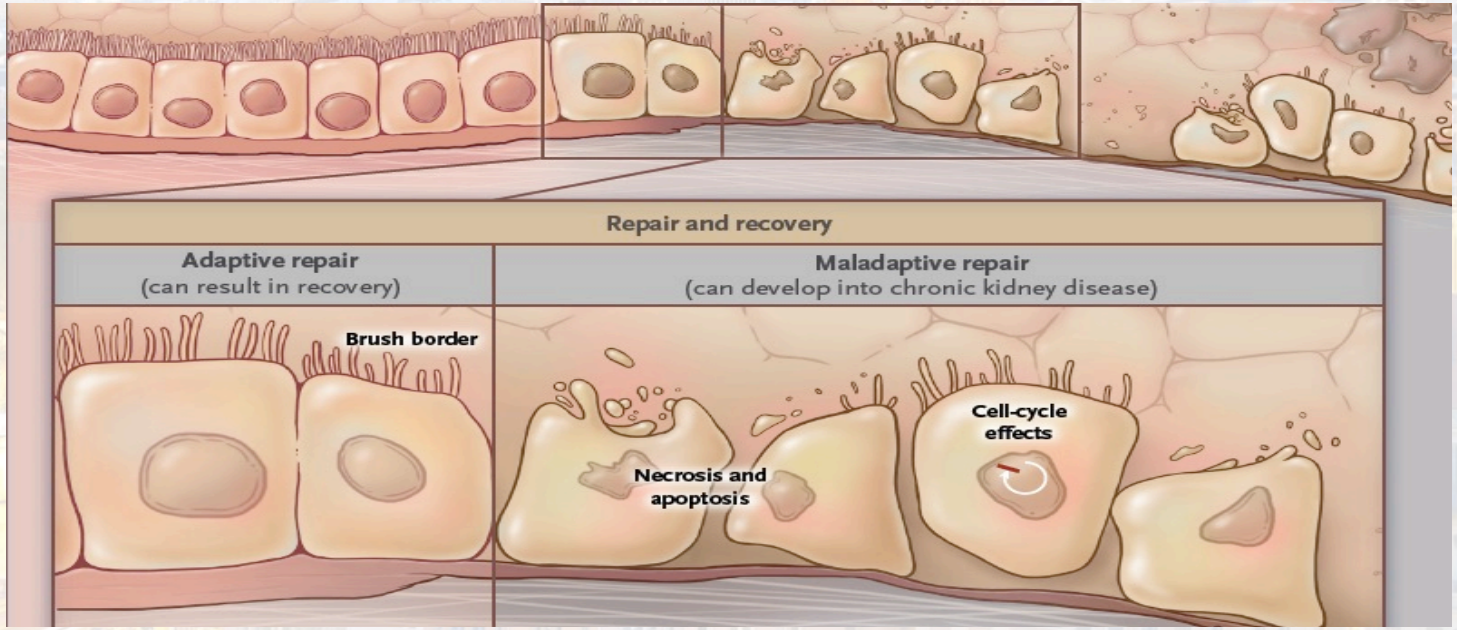
What do we think now?

*Acute Tubular Necrosis does **not** always resolve ad integrum*

« Maladaptative repair »



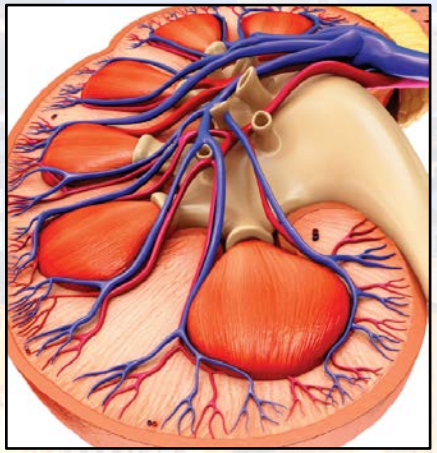
Thadhani R et al. N Engl J Med 1996



Chawla LS et al. N Engl J Med 2014

In 2016, Samir Parikh's team emphasized the importance of the metabolic pathway of **Nicotinamide Adenine Dinucleotide (NAD)** in this **renal recovery process**

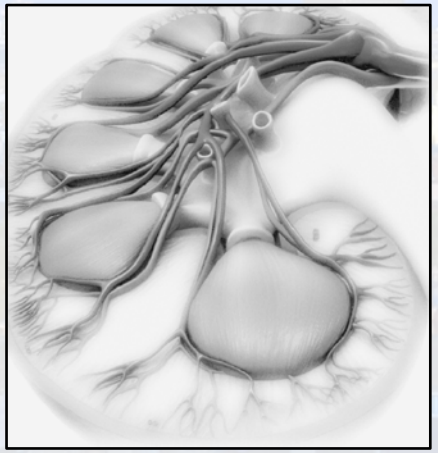
B_3 repletes pathogenic NAD+ deficiency in AKI



Inflammation
Ischemia
Renal toxins

NAD+

Vitamin B_3

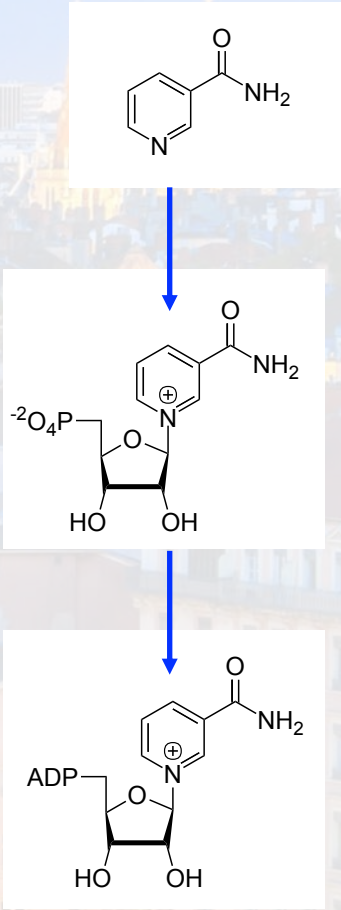


HEALTH

- HIGH NAD+ state
- Efficient fuel→ATP
- Resilient tubules

AKI

- LOW NAD+ state
- Toxic fat buildup
- Dying tubules

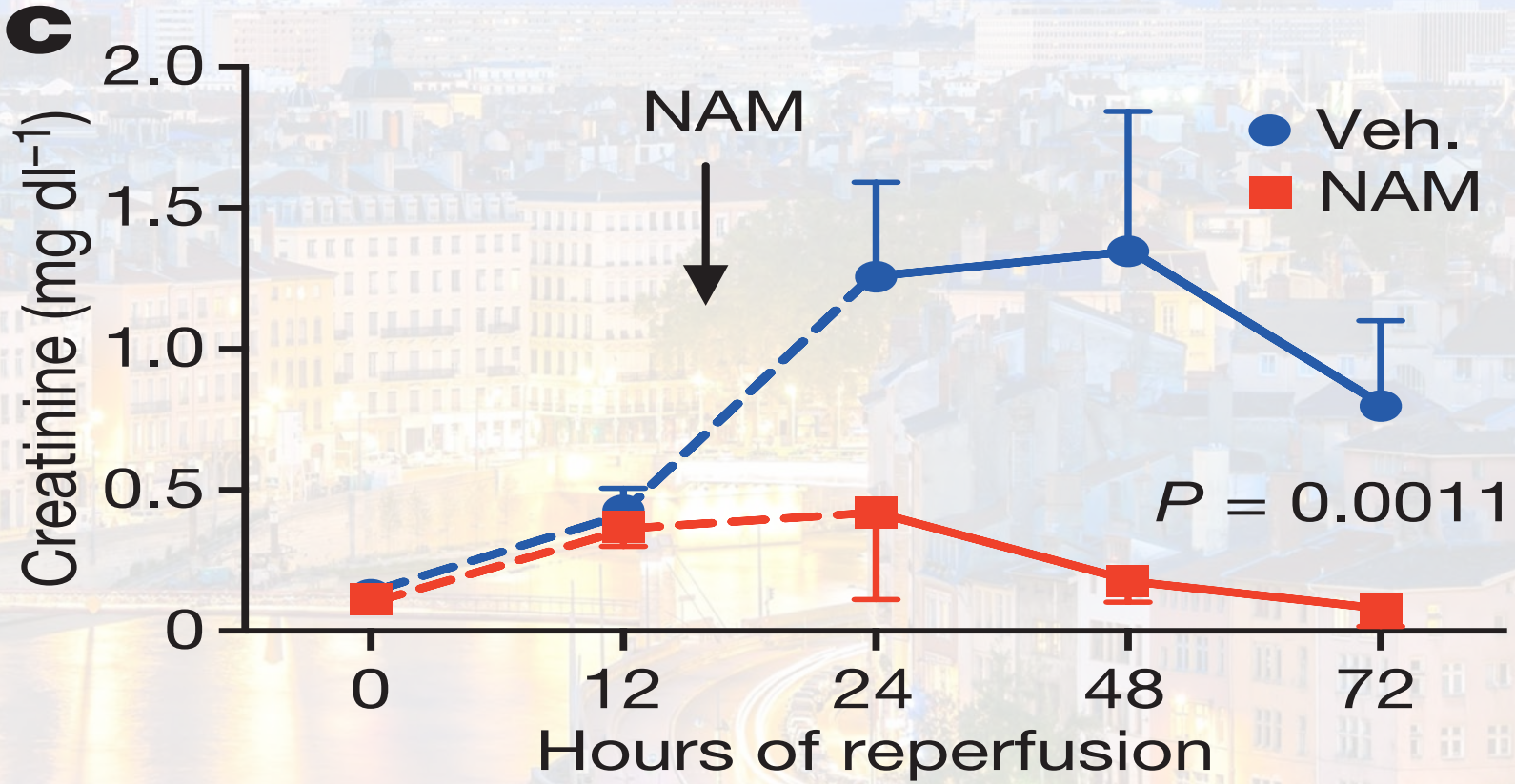


LETTER

doi:10.1038/nature17184

PGC1α drives NAD biosynthesis linking oxidative metabolism to renal protection

Mei T. Tran[1,2], Zsuzsanna K. Zsengeller[1,2,3], Anders H. Berg[3,4], Eliyahu V. Khankin[1,2], Manoj K. Bhasin[2,5], Wondong Kim[6], Clary B. Clish[7], Isaac E. Stillman[4], S. Ananth Karumanchi[1,2,8], Eugene P. Rhee[6,7] & Samir M. Parikh[1,2]

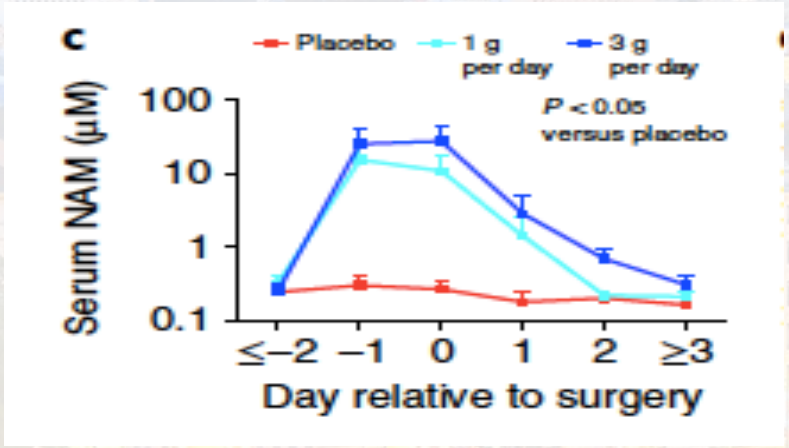


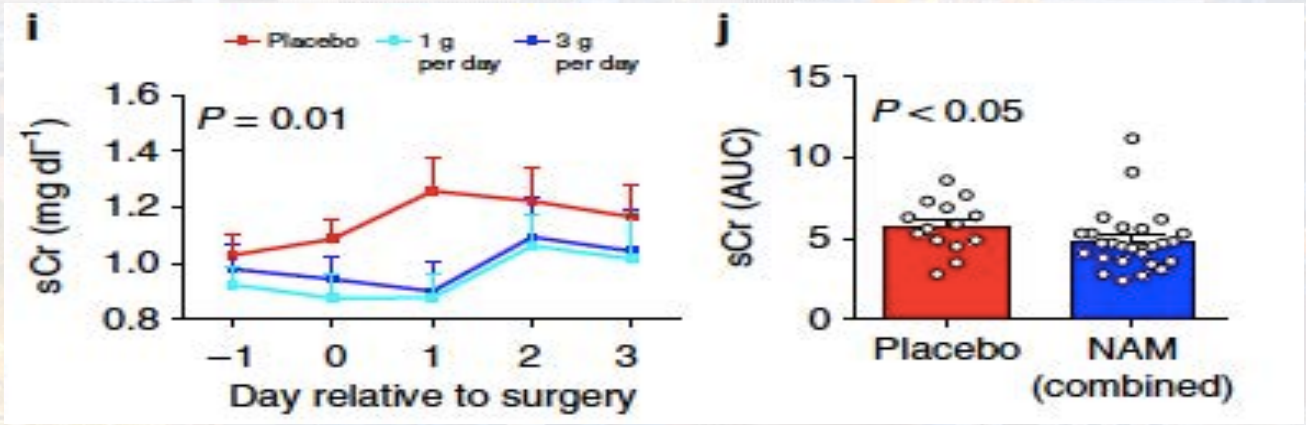
Exogenous NAM improved local NAD level and renal function in post-ischemic PG1 alpha -/- mice

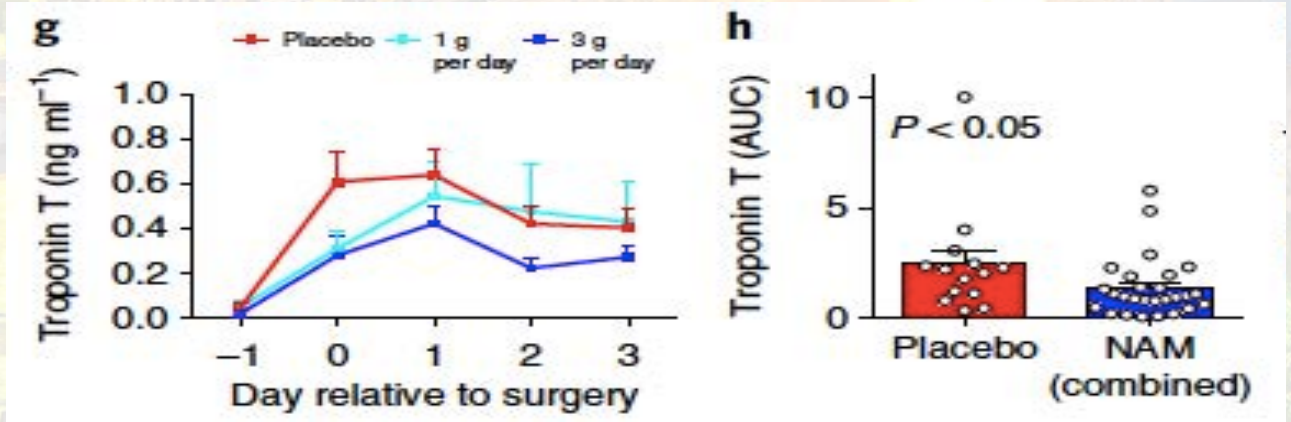
In 2018, the same team showed that during an AKI episode, tissue NAD synthesis decreases profoundly, and that nicotinamide intake protects from AKI after cardiac surgery

De novo NAD+ biosynthetic impairment in acute kidney injury in humans

Ali Poyan Mehr[1,12], Mei T. Tran[1,12], Kenneth M. Ralto[1,2,3,12], David E. Leaf[4], Vaughan Washco[1], Joseph Messmer[1], Adam Lerner[5], Ajay Kher[1], Steven H. Kim[1], Charbel C. Khoury[6], Shoshana J. Herzig[7], Mary E. Trovato[8], Noemie Simon-Tillaux[1], Matthew R. Lynch[1], Ravi I. Thadhani[6], Clary B. Clish[9], Kamal R. Khabbaz[8,13], Eugene P. Rhee[6,9,10], Sushrut S. Waikar[4], Anders H. Berg[11,13] and Samir M. Parikh[1,13]*



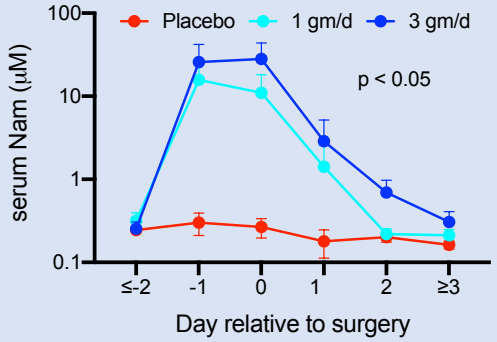




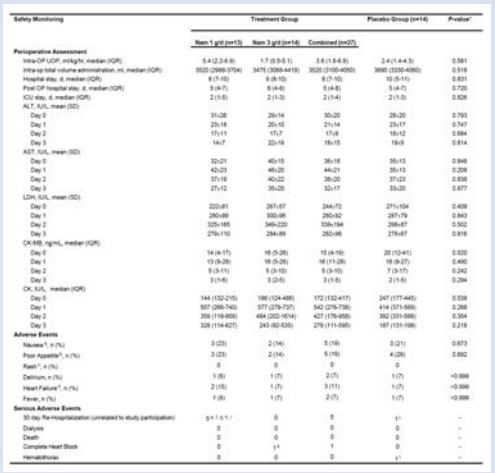
Mehr AP et al., Nat Med 2018

B_3 Pilot RCT for Cardiac Surgery AKI

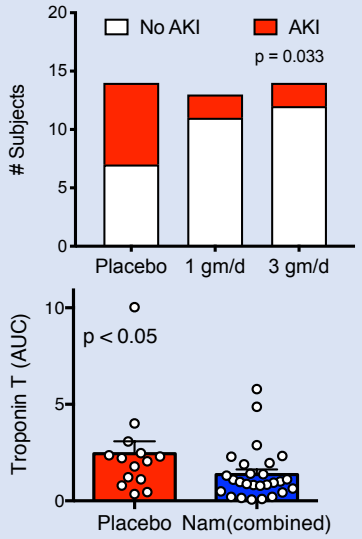
PK/PD



Safety



Efficacy



Poyan Mehr
Nat Med 2018

Is niacinamide useful in the treatment of COVID-associated AKI?

Kidney360

N=201

SARS-CoV-2 PCR positive patients with AKI (>96 hours) not on dialysis (eGFR>15).

		KRT or death	Total mortality	Change in sCr per day in KDIGO 2/3
Controls	N=111 91 from sister hospital without B3 protocol 20 pre-B3 protocol	55.9%	44.1%	0.2 mg/dl/d SE 0.08
Niacinamide B3 1 gram daily x 7 days	N=90	42.2%	24.4%	0.0 mg/dl/d SE 0.026

HR All: **0.64** [0.40-1.00]

HR KDIGO 2/3: **0.29** [0.13-0.65]

HR All: 0.59 [0.33-1.05]

HR KDIGO 2/3: **0.17** [0.05-0.52]

P-value **0.03**

Conclusion: Niacinamide was associated with lower risk of KRT/death and improved creatinine trajectory among patients with severe COVID-19-related AKI.

Nathan H. Raines, Sarju Ganatra, Pitchaphon Nissaisorakarn, ***et al***. ***Niacinamide may be Associated with Improved Outcomes in COVID-19-Related Acute Kidney Injury: An Observational Study***. ***Kidney360.*** doi: 10.34067/KID.0006452020.

Visual Abstract by Joel Topf, MD

Delayed versus early initiation of renal replacement therapy for severe acute kidney injury: a systematic review and individual patient data meta-analysis of randomised clinical trials

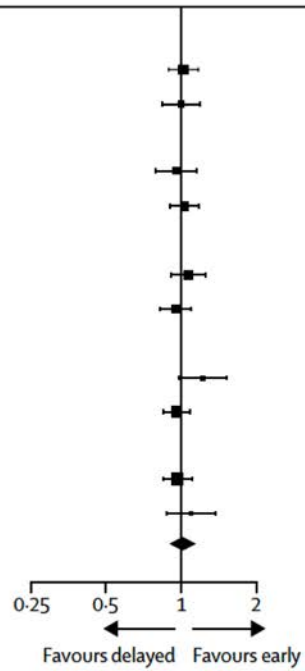
Stéphane Gaudry*, David Hajage*, Nicolas Benichou†, Khalil Chaibi†, Saber Barbar, Alexander Zarbock, Nuttha Lumlertgul, Ron Wald, Sean M Bagshaw, Nattachai Srisawat, Alain Combes, Guillaume Geri, Tukaram Jamale, Agnès Dechartres, Jean-Pierre Quenot‡, Didier Dreyfuss‡

2020

Is there any subpopulation of patients in ICU which could benefit from early or delayed RRT strategy ?

B

	28-day mortality, n/N (%)		Risk ratio (95% CI)	$P_{interaction}$
	Delayed RRT	Early RRT		
Sex				0·869
Male	228/528 (43%)	221/526 (42%)	1·02 (0·89–1·17)	
Female	138/309 (45%)	134/301 (45%)	1·00 (0·84–1·19)	
Age (years)				0·520
≤66	126/355 (35%)	143/388 (37%)	0·96 (0·79–1·16)	
>66	240/482 (50%)	212/439 (48%)	1·03 (0·91–1·17)	
SOFA score at randomisation				0·284
≤12	179/430 (42%)	165/425 (39%)	1·07 (0·91–1·26)	
>12	181/390 (46%)	185/383 (48%)	0·95 (0·82–1·09)	
Sepsis status at randomisation				0·062
No sepsis	98/209 (47%)	77/207 (37%)	1·22 (0·98–1·52)	
Sepsis	258/605 (43%)	267/600 (45%)	0·96 (0·85–1·09)	
Chronic kidney disease*				0·359
No	243/600 (41%)	271/655 (41%)	0·97 (0·85–1·11)	
Yes	92/180 (51%)	62/135 (46%)	1·09 (0·87–1·37)	
Overall			**1·01 (0·91–1·13)**	



But

The conventional subgroup analyses performed "one variable at a time" fail to convey meaningful results as they cannot fully capture all the relevant

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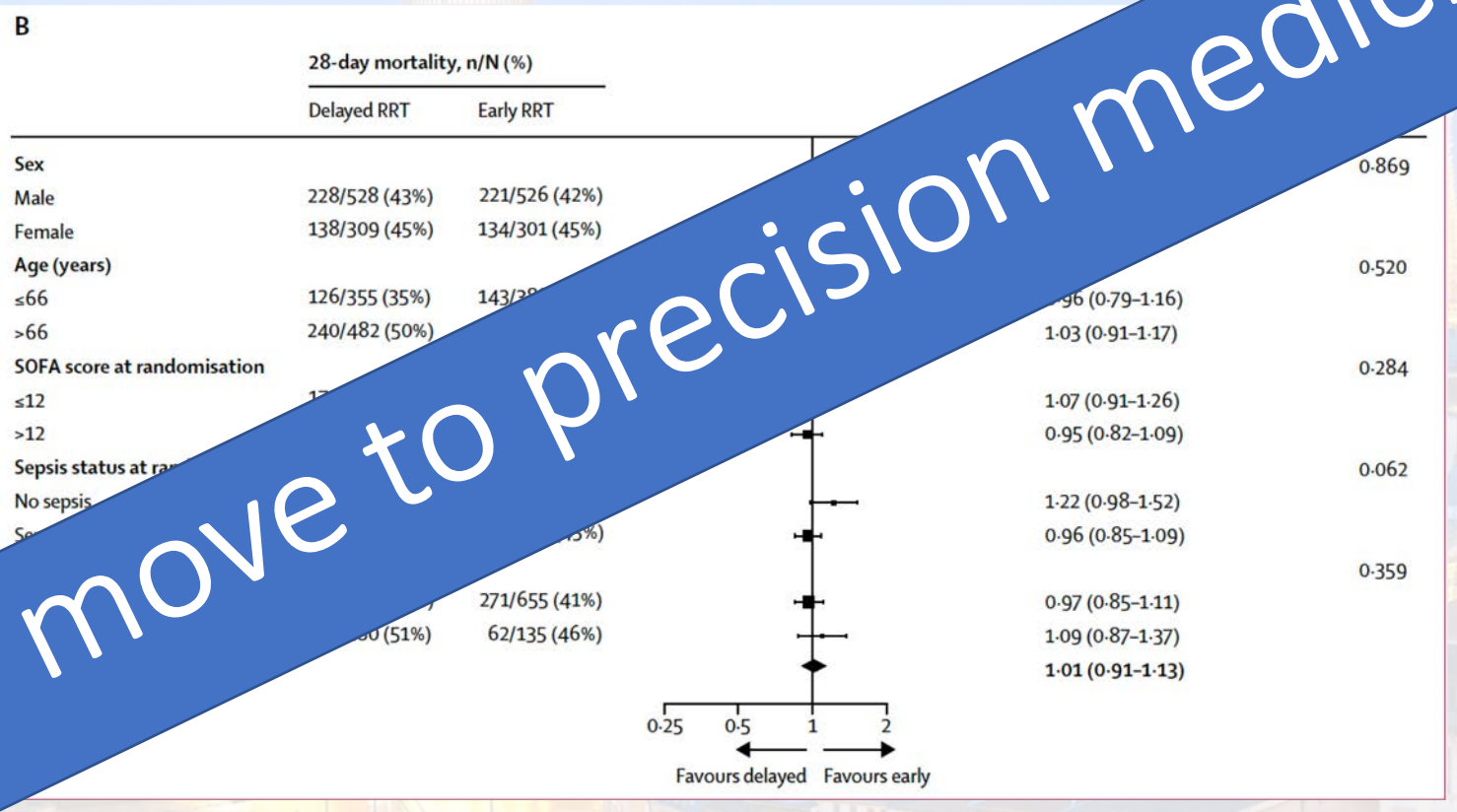


Let's move to precision medicine

But

The conventional subgroup analyses performed "one variable at a time" fail to convey meaningful results as they cannot fully capture all the relevant

An example:
Should treatment always be the same for **coronary artery disease**?

Sarah

59 yo
Diabetes mellitus
Insulin
LVEF 50%
Creatinine clearance 50ml/min
Left main coronary artery disease

Donald

69 yo
Diabetes mellitus
No insulin
LVEF 45%
Creatinine clearance 40ml/min
Three vessel artery disease

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 5, 2009 VOL. 360 NO. 10

the SYNTAX Investigators

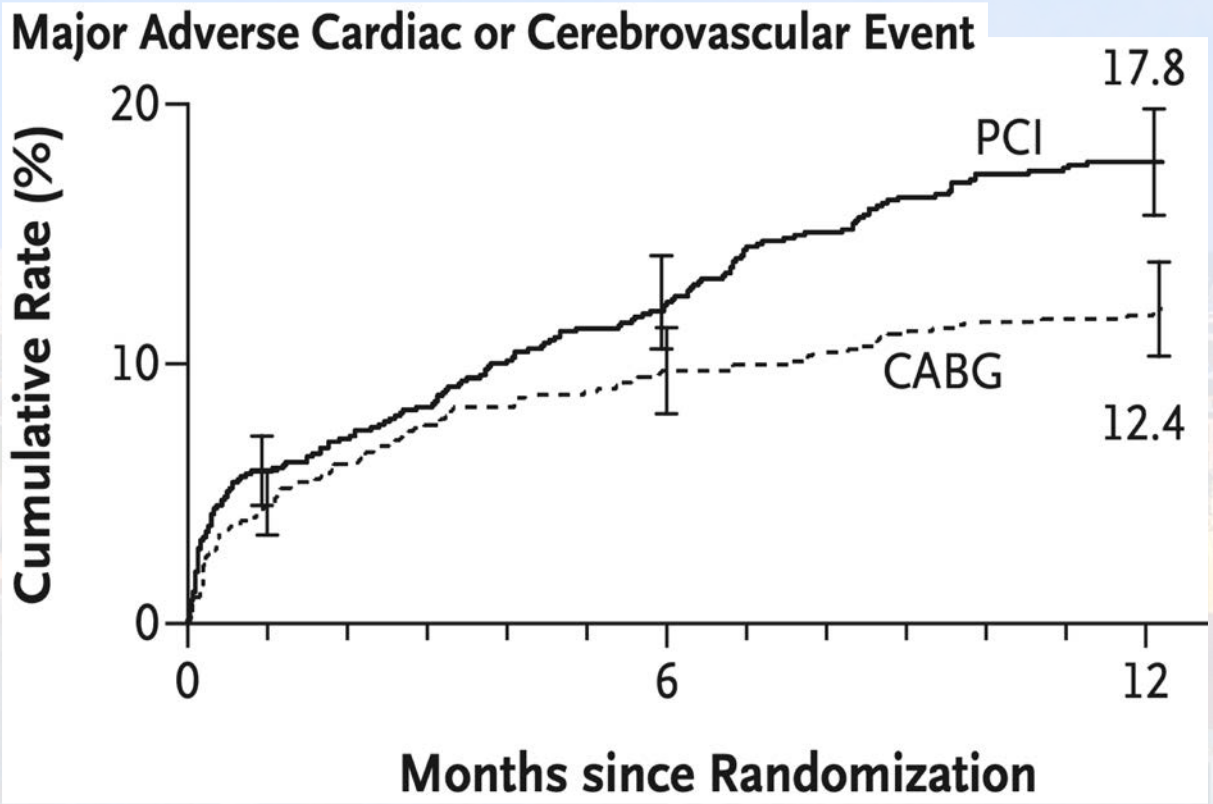
Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

Patients "previously untreated three-vessel coronary disease and those with left main coronary artery disease"

Intervention "Percutaneous Coronary Intervention (PCI)"

Control "Coronary-Artery Bypass Grafting (CABG)"

Primary Outcome major adverse cardiac or cerebrovascular event (MACCE)



Conclusion: CABG remains the standard of care for patients with three-vessel or left main coronary artery disease, since the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year

Redevelopment and validation of the SYNTAX score II to individualise decision making between percutaneous and surgical revascularisation in patients with complex coronary artery disease: secondary analysis of the multicentre randomised controlled SYNTAXES trial with external cohort validation

Kuniaki Takahashi, Patrick W Serruys, Valentin Fuster, Michael E Farkouh, John A Spertus, David J Cohen, Seung-Jung Park, Duk-Woo Park, Jung-Min Ahn, Arie Pieter Kappetein, Stuart J Head, Daniel J F M Thuijs, Yoshinobu Onuma, David M Kent, Ewout W Steyerberg, David van Klaveren, on behalf of the SYNTAXES, FREEDOM, BEST, and PRECOMBAT trial investigators

Treatment Effect Modeling: example

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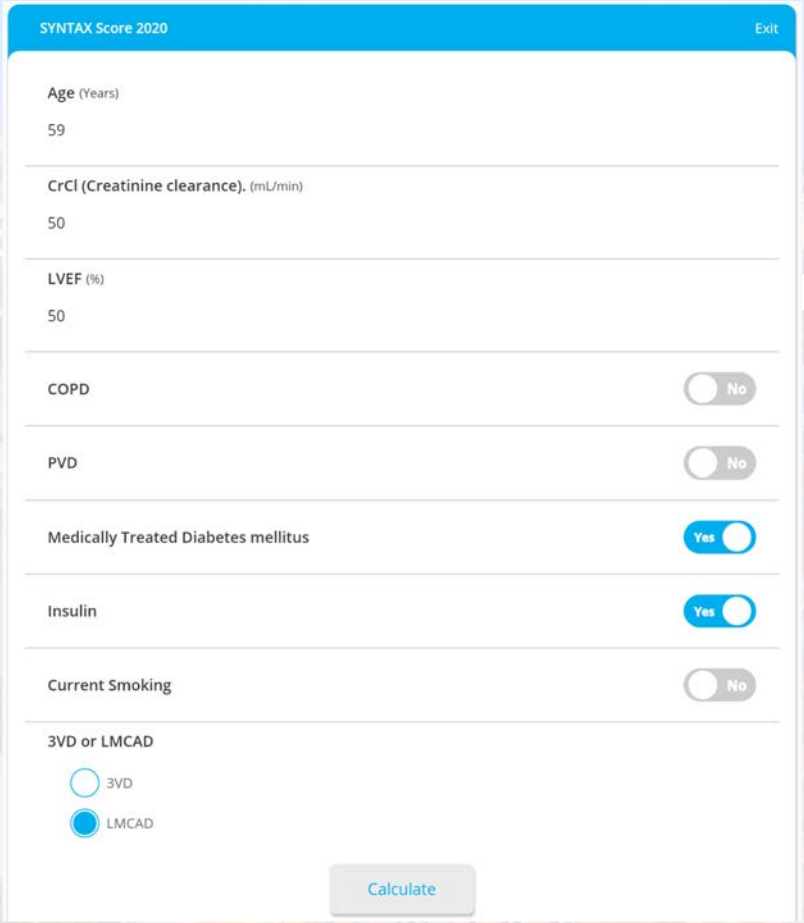

https://syntaxscore2020.com/
Takahashi et al. Lancet. 2020.

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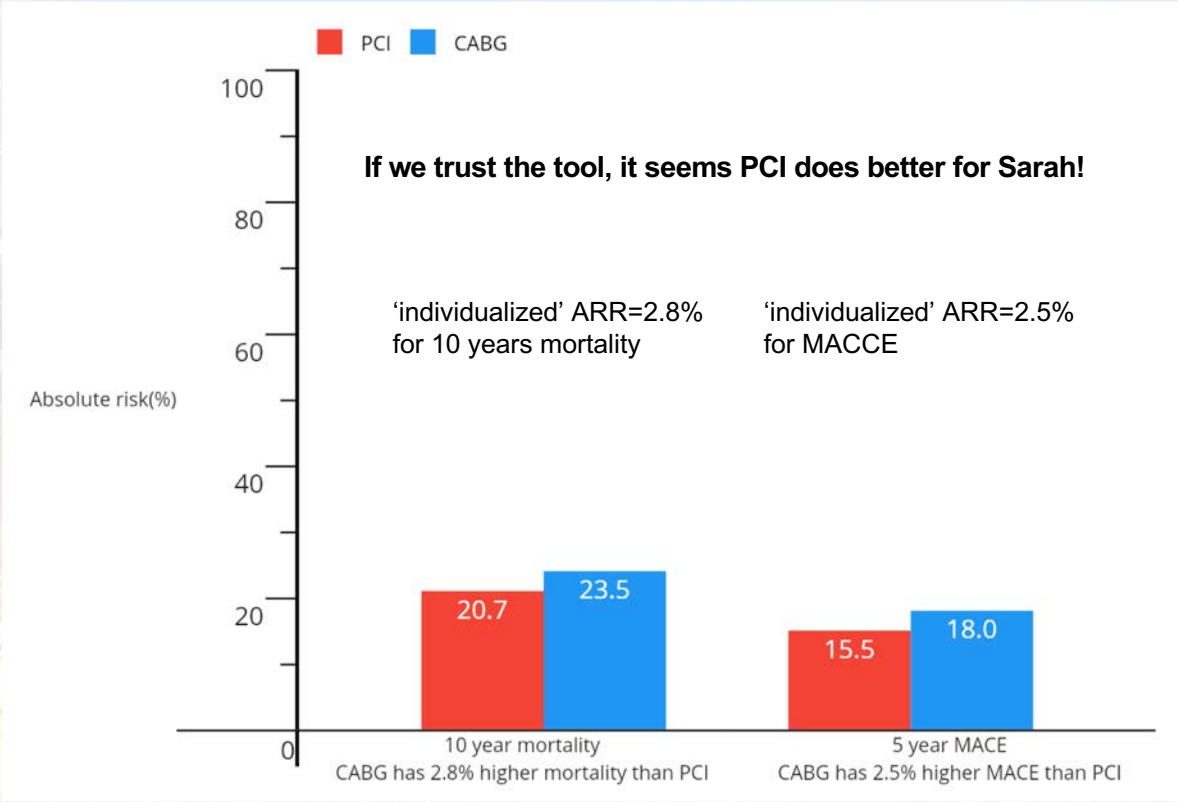

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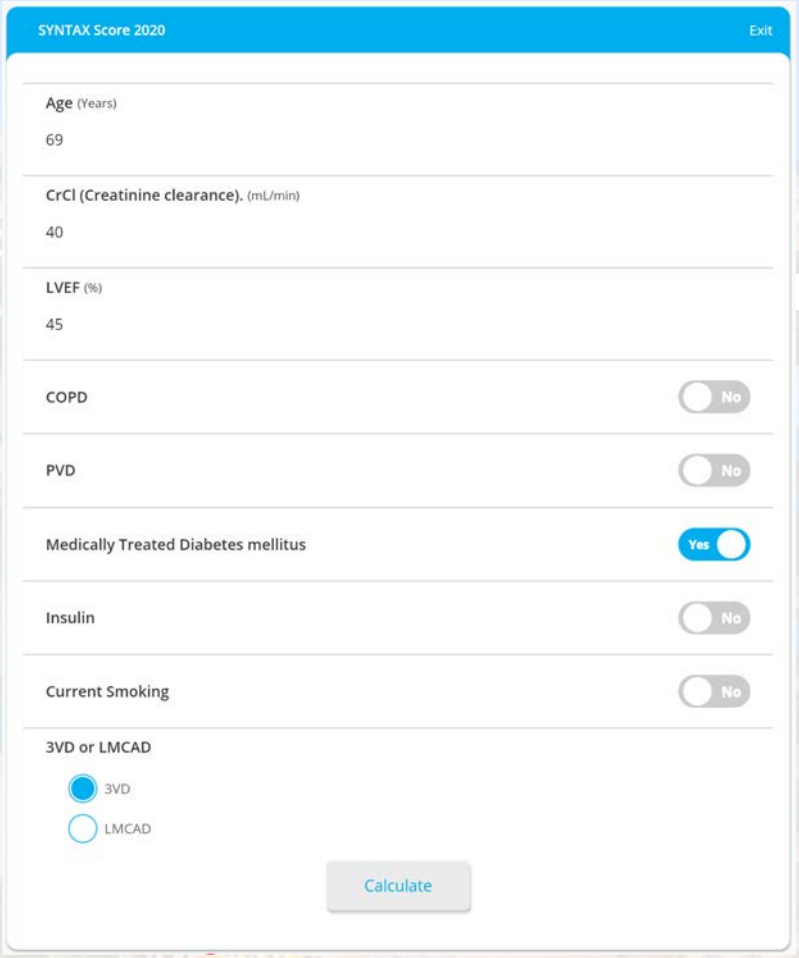

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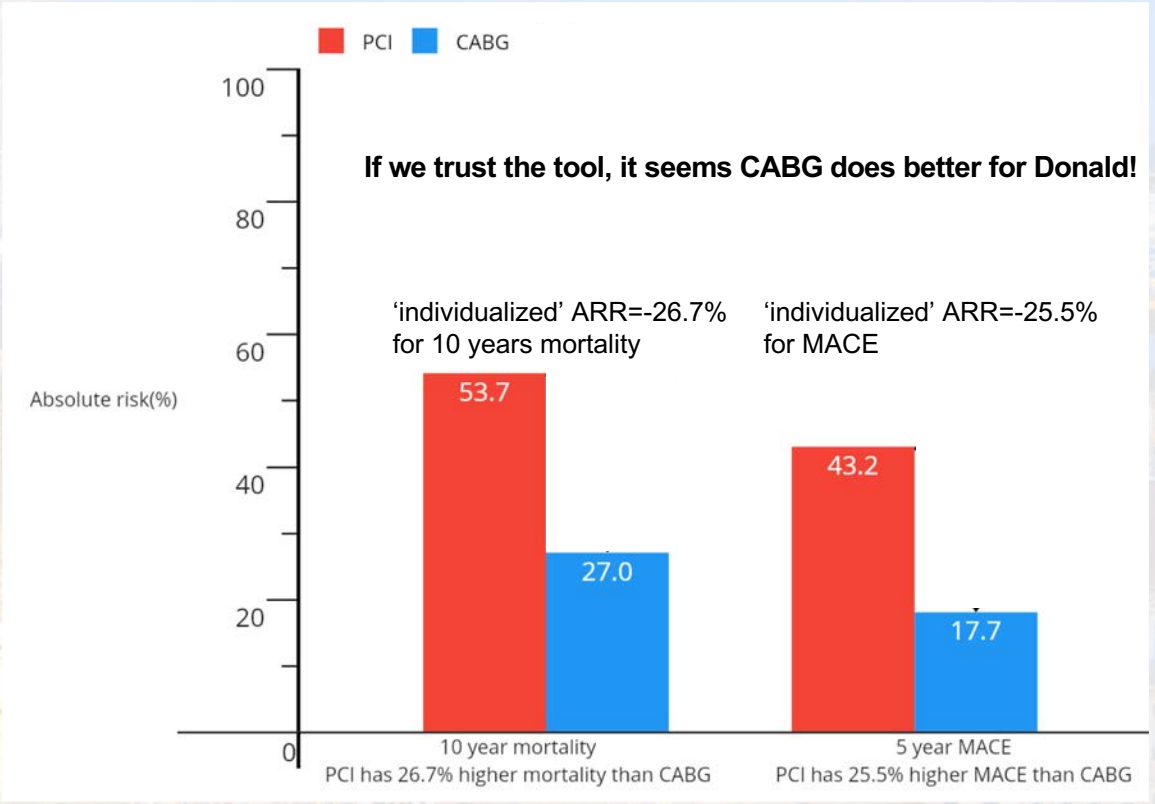

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Could we do the same with the RRT initiation strategies ?

Could we do the same with the RRT initiation strategies ?

YES !!!!

Personalization Of Renal Replacement Therapy Initiation: A Risk Modelling Approach

François GROLLEAU,[1] Raphaël PORCHER,[2] Saber BARBAR,[3] David HAJAGE,[4] Abderrahmane BOURREDJEM,[5] Didier DREYFUSS,[6] Jean-Pierre QUENOT,[7] Stéphane GAUDRY.[8]

We will use **data from AKIKI and IDEAL-ICU** to develop **a risk prediction model for RRT initiation within 48 hours** after the start of a delayed strategy and then estimate treatments effects within levels of predicted risks

Insuffisance rénale aiguë

Actualités en réanimation 2020-2021