Réunion du 16/11/23
FHU Sepsis

Facteurs pronostiques à long terme après un épisode d'IRA septique: résultats de l'étude SALTO

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MÉDECINE INTENSIVE RÉANIMATION CHU AMIENS PICARDIE

Consensus statement

Sepsis-associated acute kidney injury: consensus report of the 28th Acute Disease Quality Initiative workgroup

Nature Reviews Nephrology | Volume 19 | June 2023 | 401–417

Population	Age	Incidence (range)	RRT requirement (%)	Mortality (%)
Non-ICU hospitalized patients	Adult	<1 in 5 patients	<10	10–20
Critically ill patients	Adult	1 in 3 to 2 in 3 patients	5–11	NR
	Paediatric	1 in 4 patients (10–82%)	1–2	11
Patients undergoing cardiac surgery	Adult	1 in 5 patients (2–50%)	<5	10
	Paediatric	1 in 3 to 1 in 2 patients	NR	6
Patients with sepsis	Adult	1 in 20 to 1 in 2 patients	15	30–60

ICU, intensive care unit; NR, not reported; RRT, renal replacement therapy.

Hoste Nat Rev Nephrol 2018

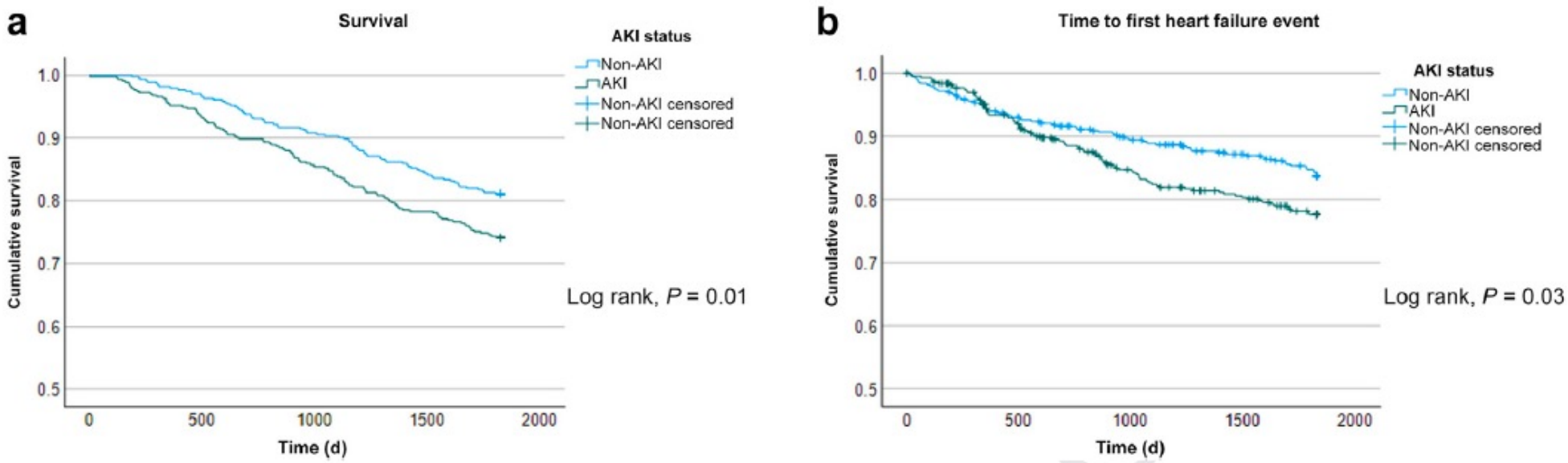


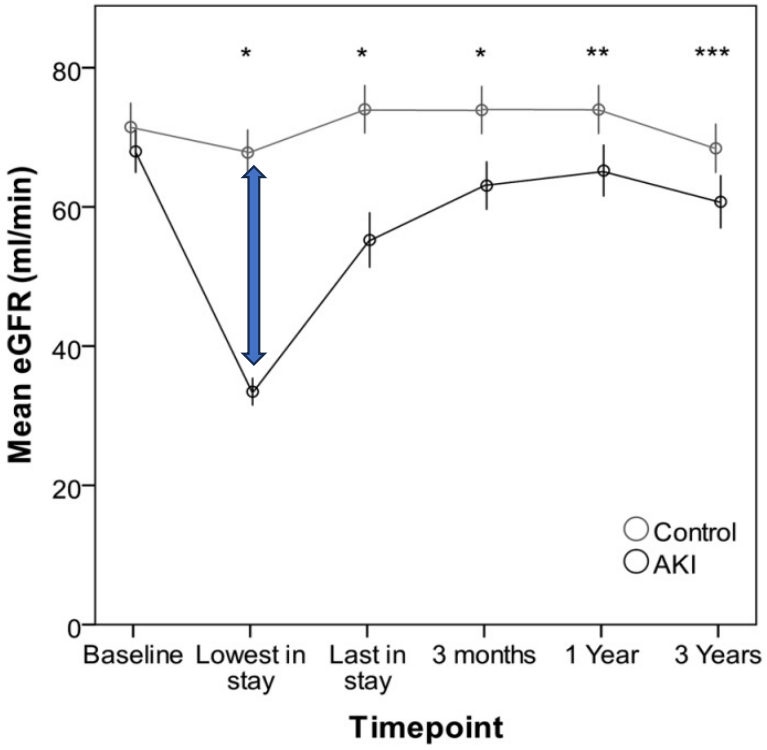
Figure 5 | Kaplan-Meier curves for outcomes of (a) mortality and (b) episodes of heart failure, comparing exposed and non-exposed groups. AKI, acute kidney injury.

Table 2 | Details of index hospital admission in the exposed (AKI) and non-exposed (non-AKI) groups

Variable	Exposed group (n = 433)	Non-exposed group (n = 433)	P[a]
ICU admission	25 (6)	4 (1)	<0.001
Details of AKI			
Severity			
Stage 1	255 (59)		
Stage 2	106 (24)		
Stage 3	72 (17)		

Horne et al, Kid Int 2023

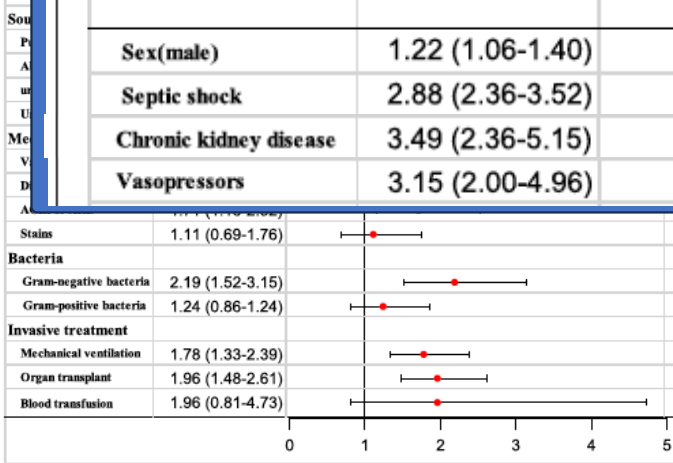
Three-year outcomes after acute kidney injury: results of a prospective parallel group cohort study



Horne et al, Kid Int 2023

- **Facteurs de risque de développer une IRA ?**

Risk factor	Pooled OR (95% CI)	Forest map	No.Studies	Univariable			Prevalence	Measure of Heterogeneity			egger'test
				Negative	Null	Positive		c^2	P -Value	I^2	
Sex(male)	1.22 (1.06-1.40)		43		33	10	60.40%	138.92	0	69.80%	0.521
Septic shock	2.88 (2.36-3.52)		7		0	7	66.37%	6.53	0.366	8.20%	0.167
Positive blood culture	1.60 (1.35-1.89)		9		5	4	41.19%	16.08	0.041	50.20%	0.847
Smoke history	1.60 (1.09-2.36)		5		3	2	43.09%	18.42	0.001	78.30%	-
Bloodstream infection	0.99 (0.80-1.24)		4		4	0	6.61%	2.78	0.427	0.00%	-
Comorbidities											
Hypertension	1.43 (1.20-1.70)		32		10	22	38.39%	119.09	0	74.00%	0.374
Diabetes mellitus	1.59 (1.47-1.71)		32		11	21	27.57%	50.93	0.013	37.10%	0.736
Stroke	1.16 (0.81-1.66)		4		3	1	22.79%	5.98	0.112	49.90%	-
Cancer	0.94 (0.80-1.09)		6		3	3	18.23%	7.87	0.163	36.50%	-
Chronic kidney disease	3.49 (2.36-5.15)		14		4	10	18.10%	46.01	0	71.70%	0.105
Cardiovascula CVD	1.31 (1.24-1.40)		11		10	1	16.30%	7.2	0.707	0.00%	0.015
Congestive heart failure	1.43 (0.85-2.41)		7		3	4	12.69%	28.15	0	78.70%	0.679
Stains	1.11 (0.69-1.76)		5	1	3	1	21.77%	21.19	0	81.10%	-
Bacteria											
Gram-negative bacteria	2.19 (1.52-3.15)		3		1	2	17.26%	0.99	0.61	0.00%	-
Gram-positive bacteria	1.24 (0.86-1.24)		4		4	0	10.43%	4.71	0.194	36.30%	-
Invasive treatment											
Mechanical ventilation	1.78 (1.33-2.39)		23	2	11	10	68.00%	185.92	0	90.05%	0.082
Organ transplant	1.96 (1.48-2.61)		3		1	2	3.76%	0.77	0.681	0.00%	-
Blood transfusion	1.96 (0.81-4.73)		3		2	1	19.46%	5.41	0.067	63.10%	-



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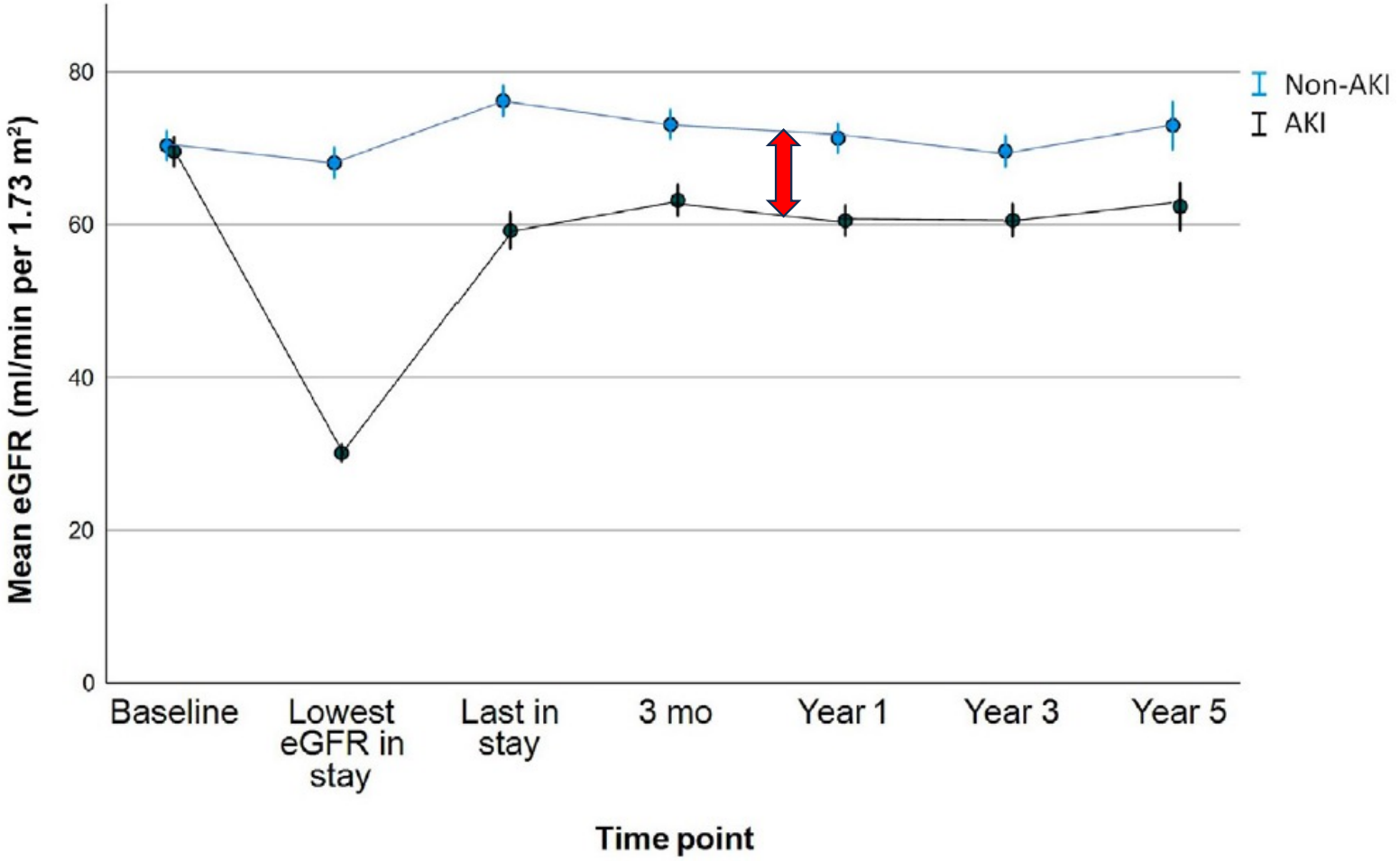
Chronic kidney disease	3.49 (2.36-5.15)		14		4	10	18.10%	46.01	0	71.70%	0.105
Vasopressors	3.15 (2.00-4.96)		7		1	6	64.61%	69.93	0	80.60%	0.144

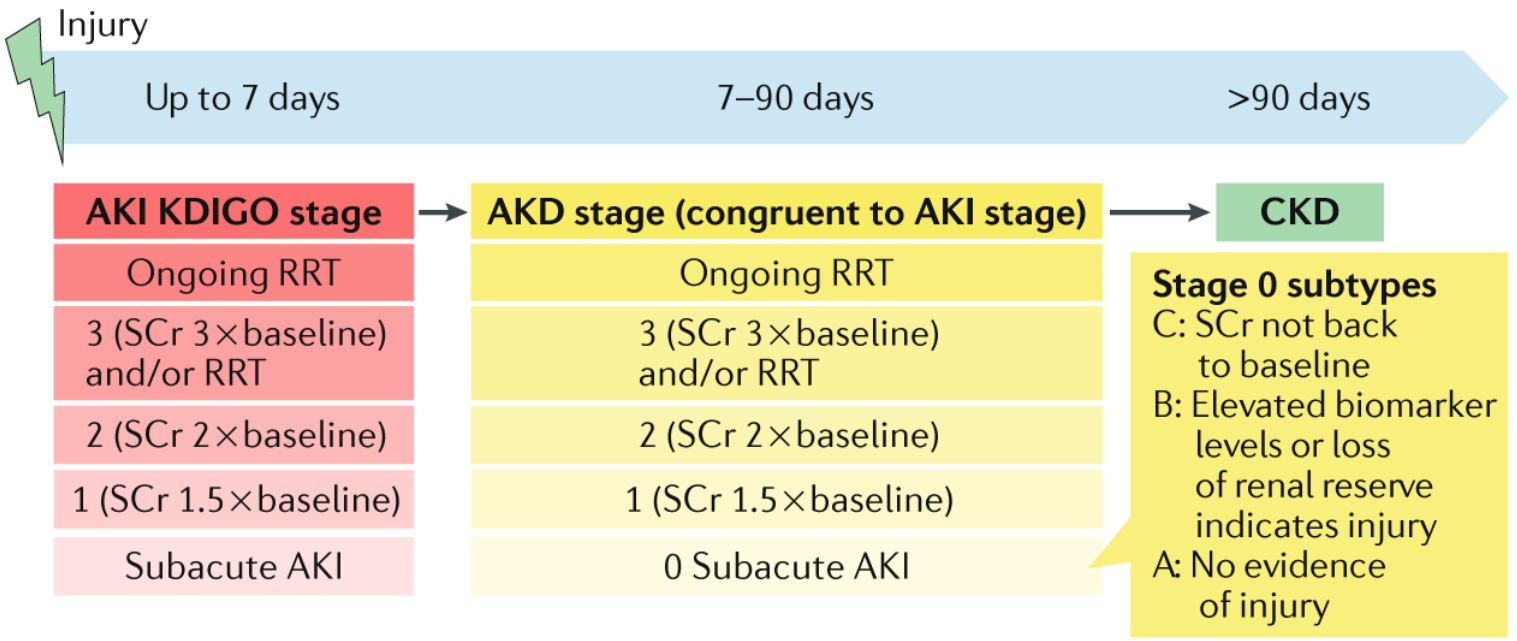
Negative, statistically significant negative association; Positive, statistically significant positive association; Null, no association; only cells with at least 1 study showing the result include number of studies—all other empty cells indicate not studies with that parameter.

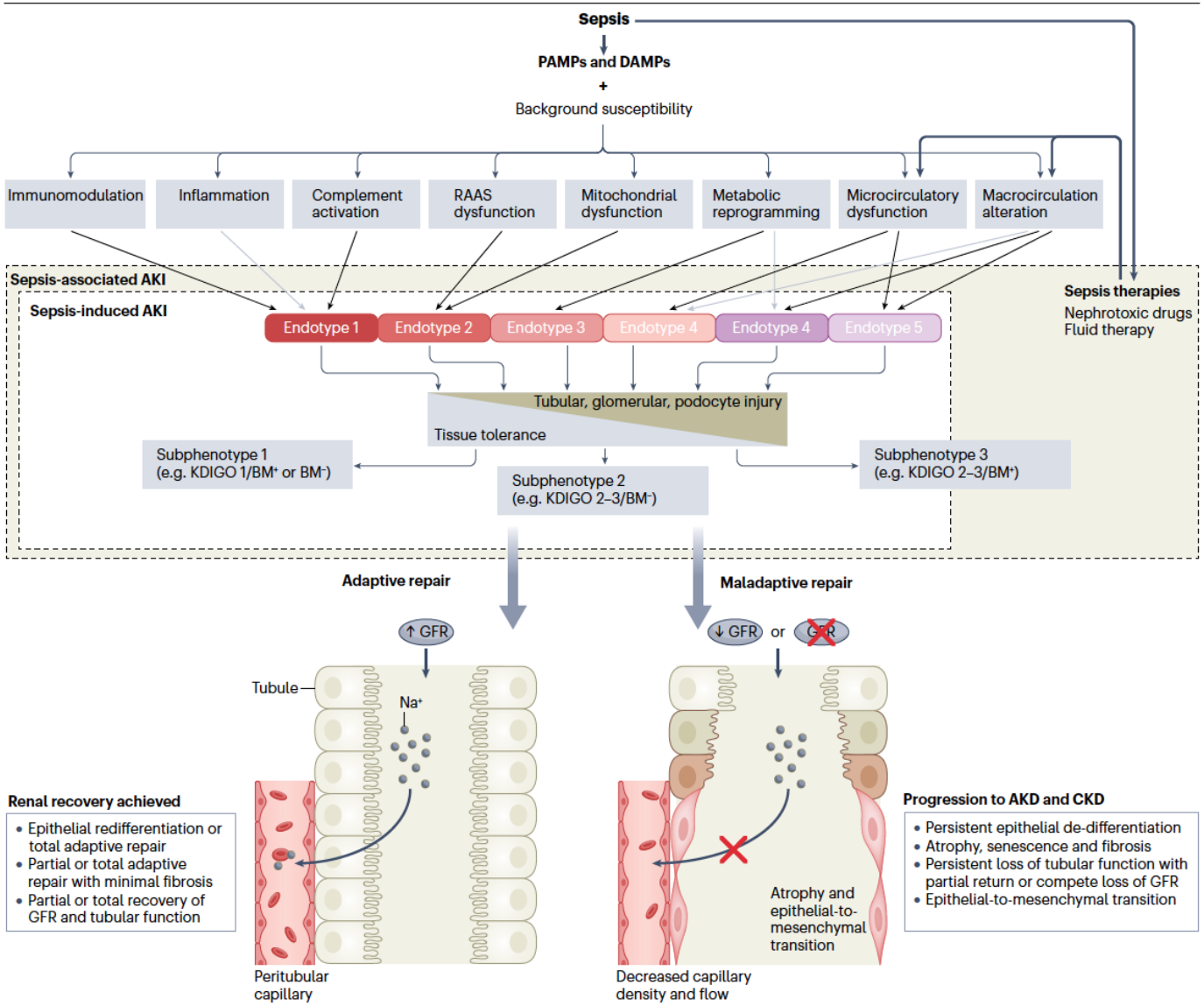
COPD:chronic obstructive pulmonary disease; ACEI OR ARB:Angiotensin converting enzyme inhibitor OR Arbitration

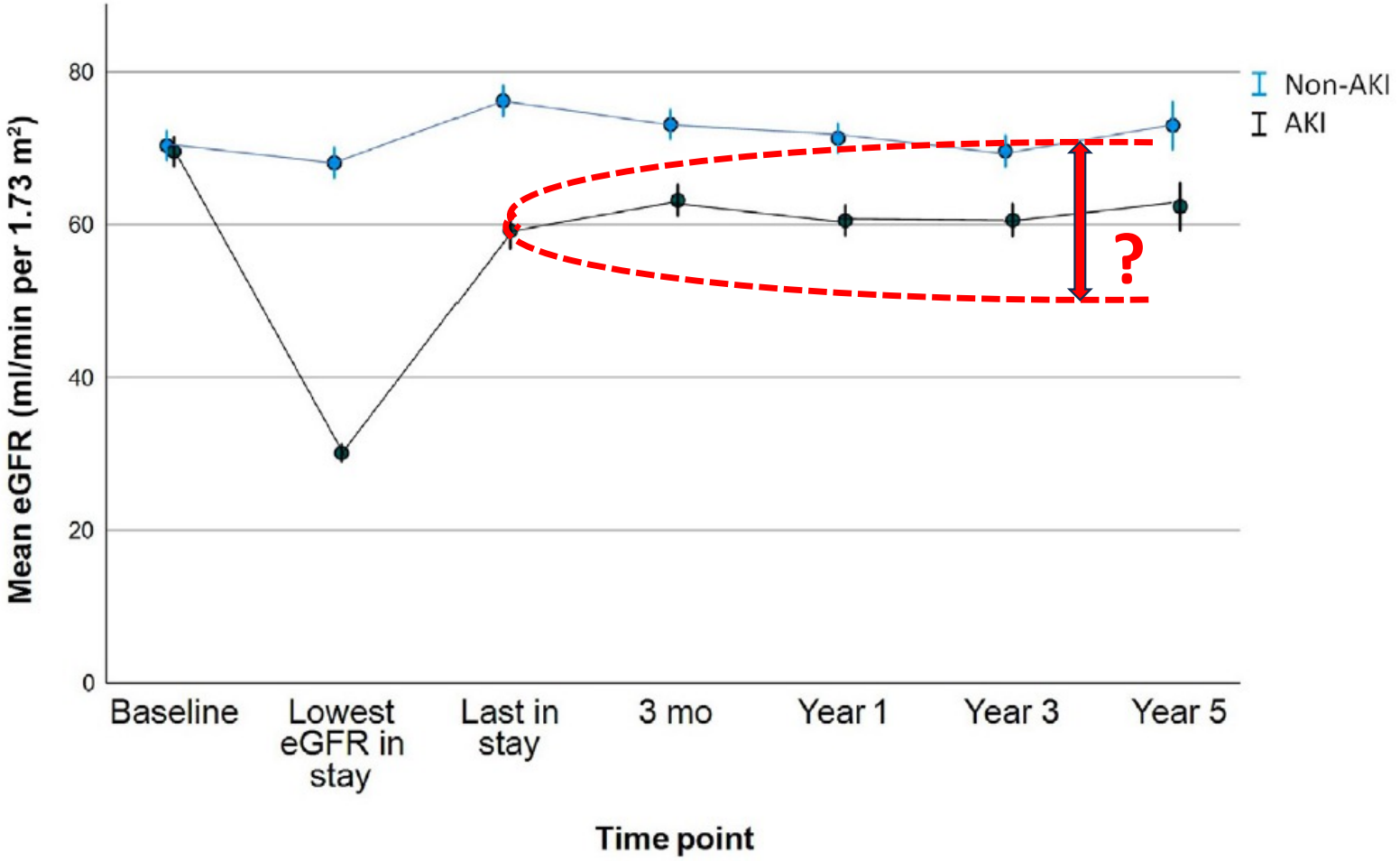
Fig. 2 Meta-analysis of risk factors of AKI

Liu *et al. BMC Nephrology* (2020) 21:318
https://doi.org/10.1186/s12882-020-01974-8


Mean eGFR (ml/min per 1.73 m²)
80
60
40
20
0
Baseline
Lowest eGFR in stay
Last in stay
3 mo
Year 1
Year 3
Year 5
Time point
Non-AKI
AKI


Injury
Up to 7 days
7–90 days
>90 days
AKI KDIGO stage
AKD stage (congruent to AKI stage)
CKD
Ongoing RRT
Ongoing RRT
3 (SCr 3×baseline) and/or RRT
3 (SCr 3×baseline) and/or RRT
2 (SCr 2×baseline)
2 (SCr 2×baseline)
1 (SCr 1.5×baseline)
1 (SCr 1.5×baseline)
Subacute AKI
0 Subacute AKI
Stage 0 subtypes
C: SCr not back to baseline
B: Elevated biomarker levels or loss of renal reserve indicates injury
A: No evidence of injury


Sepsis
PAMPs and DAMPs
+
Background susceptibility
Immunomodulation
Inflammation
Complement activation
RAAS dysfunction
Mitochondrial dysfunction
Metabolic reprogramming
Microcirculatory dysfunction
Macrocirculation alteration
Sepsis-associated AKI
Sepsis-induced AKI
Endotype 1
Endotype 2
Endotype 3
Endotype 4
Endotype 4
Endotype 5
Sepsis therapies
Nephrotoxic drugs
Fluid therapy
Tubular, glomerular, podocyte injury
Tissue tolerance
Subphenotype 1
(e.g. KDIGO 1/BM+ or BM-)
Subphenotype 2
(e.g. KDIGO 2–3/BM-)
Subphenotype 3
(e.g. KDIGO 2–3/BM+)
Adaptive repair
Maladaptive repair
↑ GFR
↓ GFR
or
Tubule
Na+
Renal recovery achieved
• Epithelial redifferentiation or total adaptive repair
• Partial or total adaptive repair with minimal fibrosis
• Partial or total recovery of GFR and tubular function
Peritubular capillary
Atrophy and epithelial-to-mesenchymal transition
Decreased capillary density and flow
Progression to AKD and CKD
• Persistent epithelial de-differentiation
• Atrophy, senescence and fibrosis
• Persistent loss of tubular function with partial return or compete loss of GFR
• Epithelial-to-mesenchymal transition


Mean eGFR (ml/min per 1.73 m²)
80
60
40
20
0
Baseline
Lowest eGFR in stay
Last in stay
3 mo
Year 1
Year 3
Year 5
Time point
Non-AKI
AKI
?

RESEARCH Open Access

Long-term outcomes after severe acute kidney injury in critically ill patients: the SALTO study

Khalil Chaïbi[1,2], Franck Ehooman[2,3], Bertrand Pons[4], Laurent Martin-Lefevre[5], Eric Boulet[6], Alexandre Boyer[7], Guillaume Chevrel[8], Nicolas Lerolle[9], Dorothée Carpentier[10], Nicolas de Prost[11,12], Alexandre Lautrette[13], Anne Bretagnol[14], Julien Mayaux[15], Saad Nseir[16], Bruno Megarbane[17], Marina Thirion[18], Jean-Marie Forel[19] Julien Maizel[20], Hodane Yonis[21], Philippe Markowicz[22], Guillaume Thiery[23], Frédérique Schortgen[24], Cécile Couchoud[25], Didier Dreyfuss[2,26,27†] and Stephane Gaudry[1,2*†]

Chaïbi *et al. Annals of Intensive Care* (2023) 13:18
https://doi.org/10.1186/s13613-023-01108-x

- Survie à long terme
- Pronostic rénal
- Qualité de vie

} A long terme + Effet de la stratégie d'initiation de l'EER

The AKIKI TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

620

Severe AKI

KDIGO 3

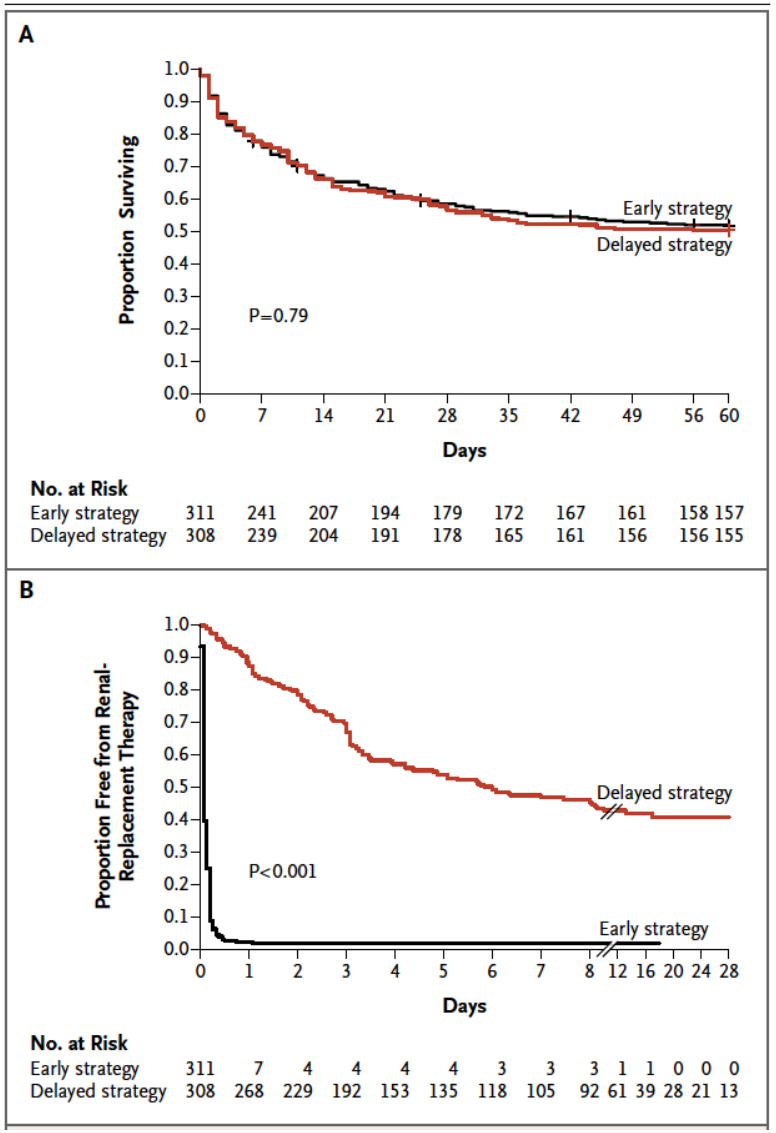
Without life threatning condition at inclusion

Start RRT immediately

Start RRT only if:

- Severe hyperkaliemia (>6.5)
- Severe acidosis (pH <7.15)
- Serum urea (> 40 mmol/l)
- Oligoanuria >72h
- Severe pulmonary edema

Gaudry NEJM 2016



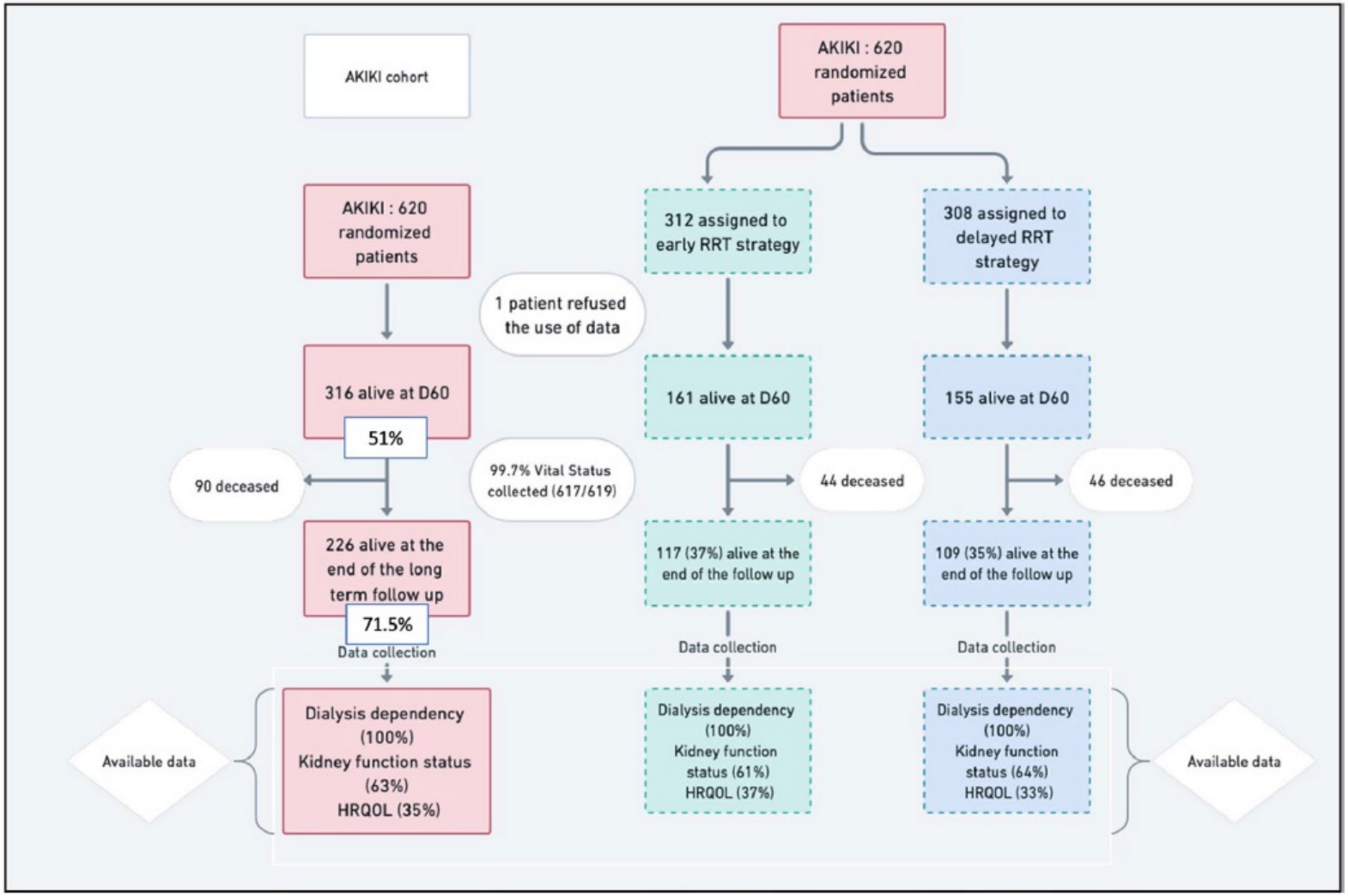
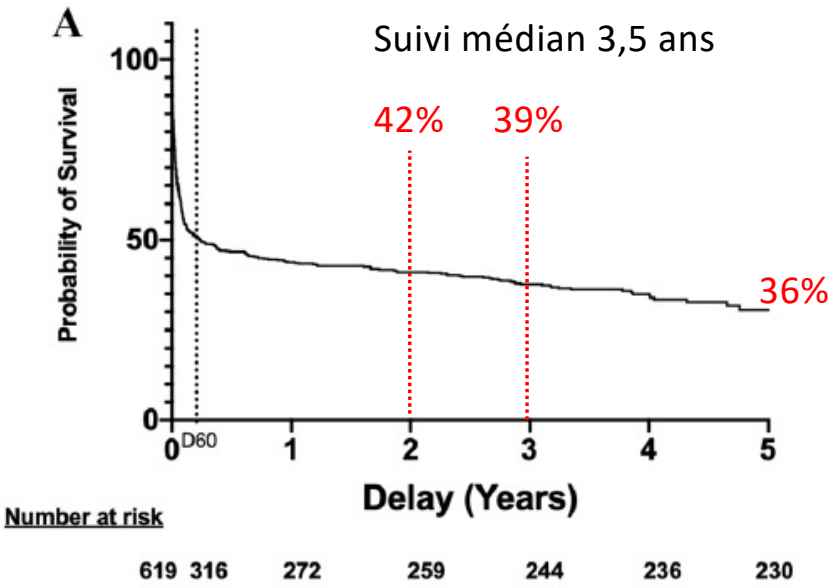
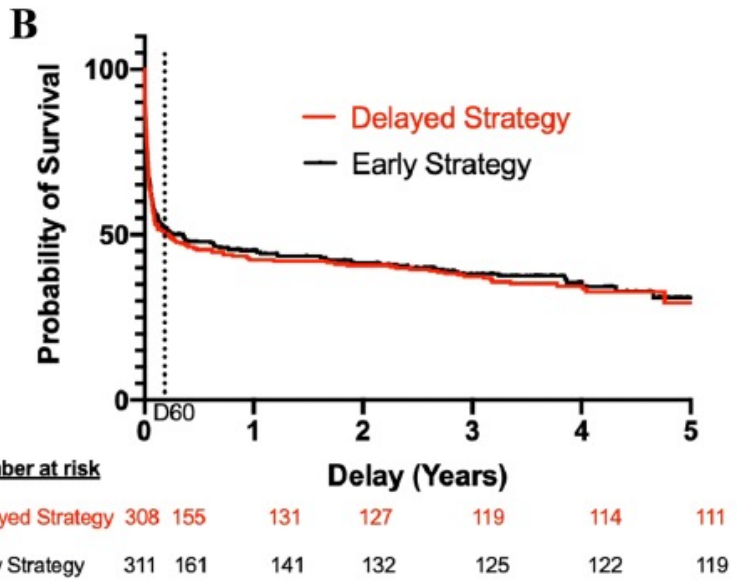


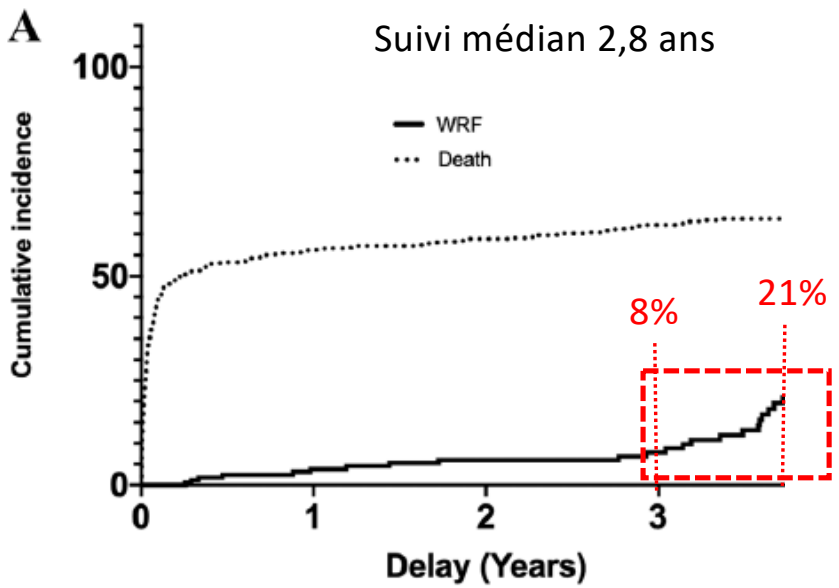
Fig. 1 Study flowchart

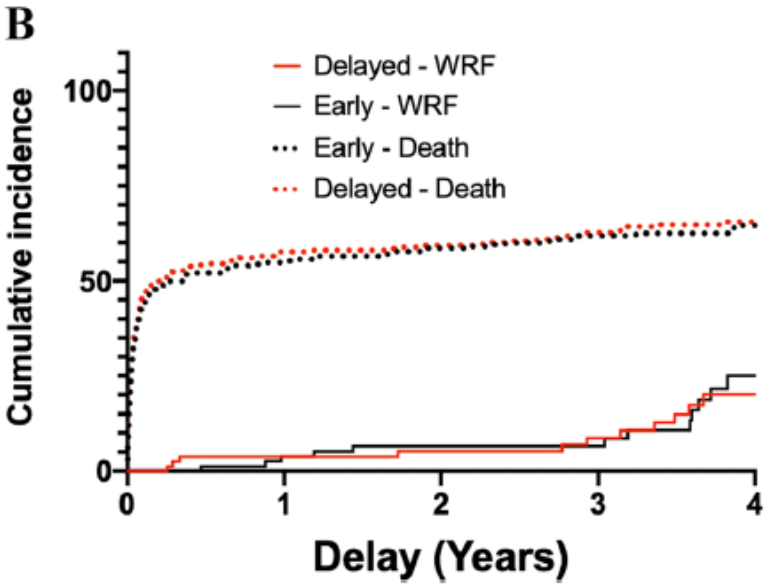
Table 1 Characteristics of the patients at baseline[a]

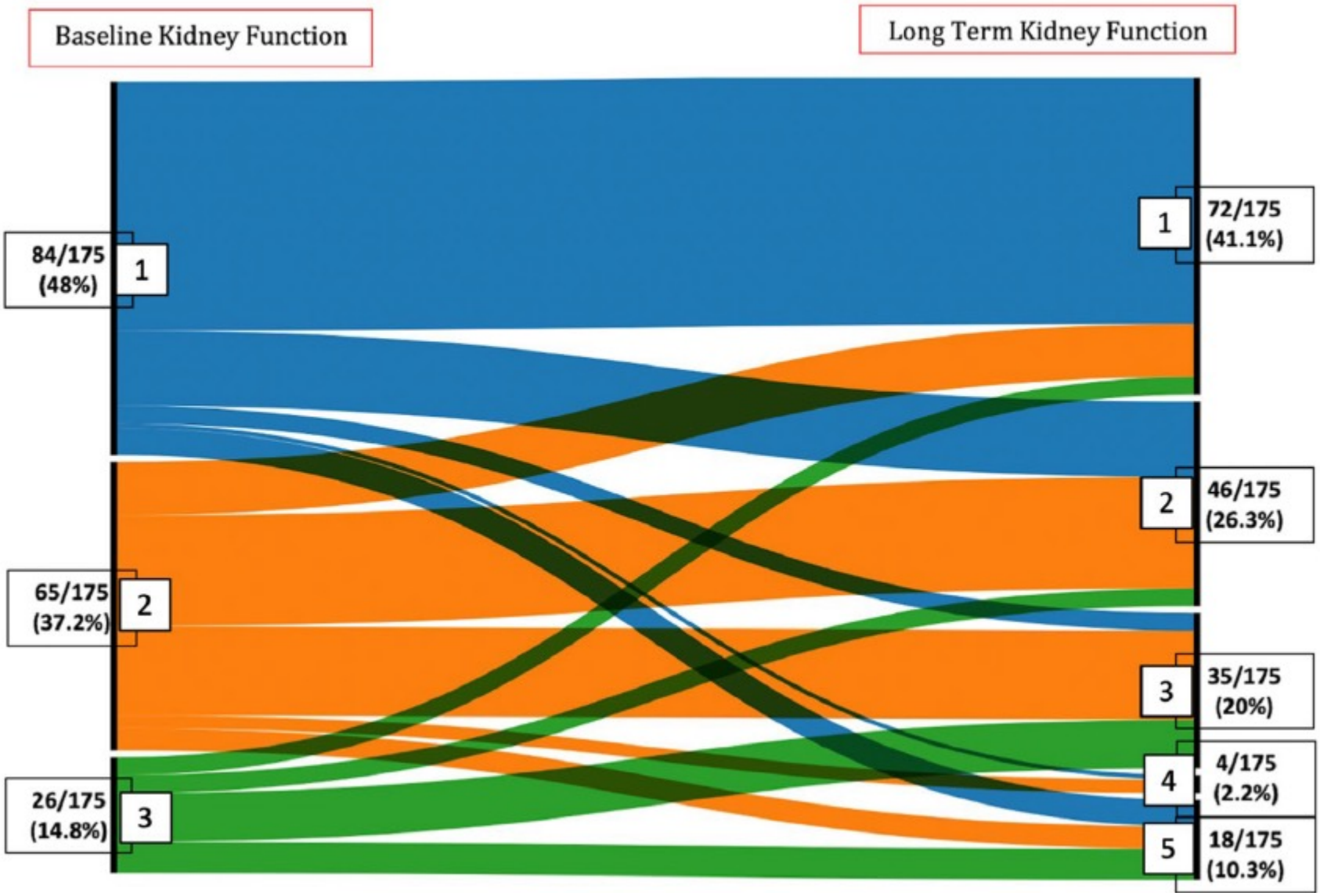
	AKIKI trial	Surviving patients 60 days after randomization			Surviving patients with Scr available beyond D90 after randomization
No of patients	*N* = 619	All *N* = 316	Early RRT strategy *N* = 161	Delayed RRT strategy *N* = 155	*N* = 175
Age—yr	66 ± 13.8	62.3 ± 14.7	60.8 ± 14.7	64 ± 14.7	62 ± 13
Sex—no. (%)					
Female	212(34)	110 (35)	55 (34)	55 (35)	60(34)
Male	407(66)	206 (65)	106(66)	100 (65)	115 (66)
Serum creatinine before ICU admission—mg/dl[b]	0.96 ± 0.28	0.95 ± 0.27	0.94 ± 0.25	0.96 ± 0.29	0.92 ± 0.23
Coexisting conditions—no. (%)					
Chronic kidney disease[c]	118 (19)	50 (16)	23(14)	27(17)	7(4)
Hypertension	328 (53)	153(48)	71(44)	82(53)	70 (40)
Diabetes mellitus	163 (26)	77 (24)	42(26)	35(23)	35(20)
Congestive heart failure	56 (9)	17 (5)	8 (5)	9(6)	3(2)
SAPS III at Enrollment[d]	73.1 ± 14.3	70.4 ± 14.8	70.8 ± 15.12	70 ± 14.05	66 ± 11
SOFA score at enrollment[e]	10.9 ± 3.2	10.3 ± 3	10.5 ± 3.11	10.16 ± 2.85	9.8 ± 2.6
Exposure to at least one nephrotoxic agent within two days before ICU—no./total no. (%)[g]					
All	389 (63)	178 (56)	93 (58)	85 (55)	92(53)
Intravenous contrast	137 (22)	70 (22)	34/93 (37)	36/85 (42)	35/92 (38)
Aminoglycoside	212(34)	95 (30)	52/93 (56)	43/85 (51)	30/92 (33)
Vancomycin	55 (9)	27 (8)	12/93 (13)	15/85 (18)	5/92 (5)
Septic shock[g]	413 (67)	167 (53)	80 (50)	87 (56)	43/92 (47)


A
Suivi médian 3,5 ans
42%
39%
36%
Probability of Survival
100
50
0
D60
0
1
2
3
4
5
Delay (Years)
Number at risk
619 316 272 259 244 236 230


B
Probability of Survival
100
50
0
D60
Delayed Strategy
Early Strategy
0
1
2
3
4
5
Delay (Years)
Number at risk
Delayed Strategy 308 155 131 127 119 114 111
Early Strategy 311 161 141 132 125 122 119


A
Suivi médian 2,8 ans
Cumulative incidence
100
50
0
WRF
Death
8%
21%
0
1
2
3
Delay (Years)


B
Cumulative incidence
100
50
0
Delayed - WRF
Early - WRF
Early - Death
Delayed - Death
0
1
2
3
4
Delay (Years)



25% des patients survivants présentent une aggravation de leur fonction rénale à long terme

Tous les patients CKD 3 évoluent vers 4 ou 5 à long terme

Table 2 Cox multivariate model for long-term mortality from randomization

Variable	Comparator	Hazard ratio (95% CI)	*P* value
Strategy	Early	1.01 (0.82–1.23)	0.9
SAPS III	One unit increase	1 (0.99–1.014)	0.12
CCF		1.28 (0.91–1.8)	0.15
CKD		1.04 (0.80–1.36)	0.74
Diabetes		0.93 (0.74–1.18)	0.56
Age	One unit increase	1.02 (1.01–1.03)	$p < 0.01$
Sex	Male	1.08 (0.86–1.34)	0.51
Hypertension		0.92 (0.73–1.15)	0.45

SAPSIII Simplified Acute Physiology *Score 3 CCF* chronic cardiac failure *CKD* chronic kidney disease

Table 3 Univariable analysis of subdistribution hazard ratios for factors associated with WRF

Variable	Comparator	Sub-hazard ratio (95% CI)	*P* value
Strategy	Early vs delayed	1.34 (0.74–2.43)	0.33
SAPS III	One unit increase	1 (0.97–1.04)	0.93
CCF		1.34 (0.47–5.27)	0.47
CKD		1.34 (0.62–2.89)	0.46
Diabetes		1.17(0.61–2.26)	0.64
Age	One unit increase	1.02 (0.99–1.04)	0.14
Sex		0.73 (0.40–1.33)	0.31

Analysis led on the 175 patients with available eGFR after D90

SAPSIII Simplified Acute Physiology *Score 3 CCF* chronic cardiac failure *CKD* chronic kidney disease

Table 4 Quality of life

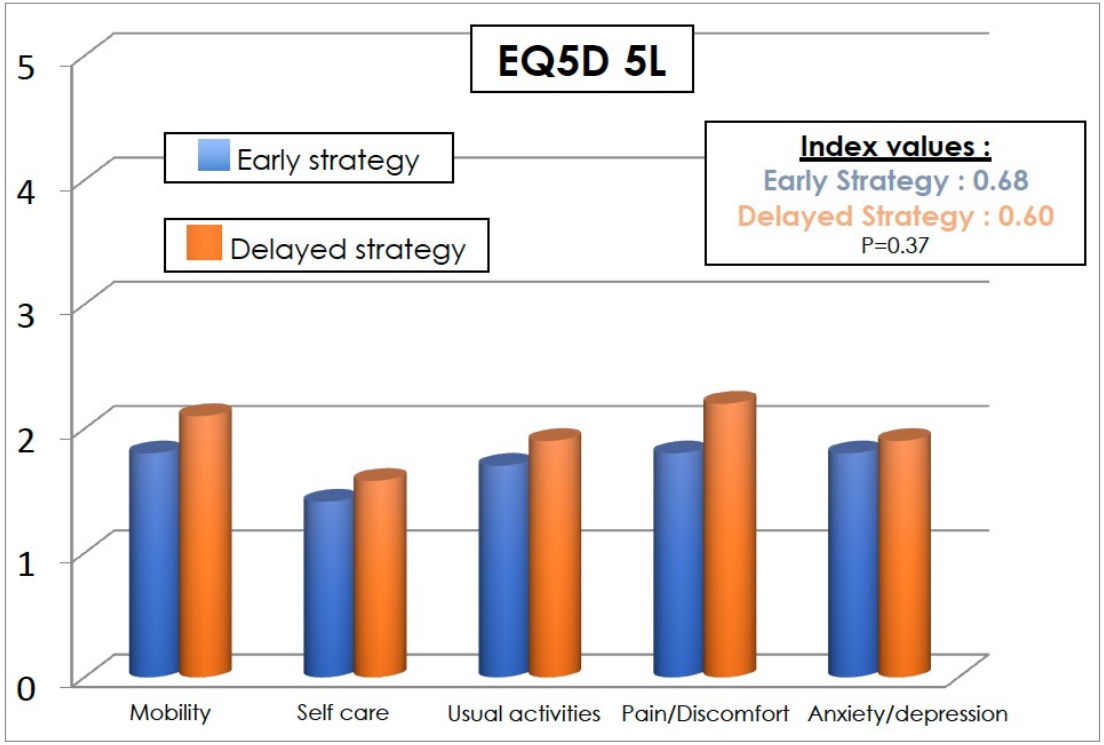
Variable	All patients	Early RRT strategy (95% CI)	Delayed RRT strategy (95% CI)	*P* value
EQ5D-5L (survivors at end of follow-up)a	0.67 (0.40–1.00)	0.71 (0.51–1.00)	0.64 (0.50–1.00)	0.32
EQ5D-5L (patients since D60)[b]	0.39(0.20–0.81)	0.35 (0.22–0.82)	0.41 (0.20–0.80)	0.70

Analysis of the survivors was led on the 80 patients who responded to the questionnaire. Analysis of patients since D60 was led on 170 patients (90 patients who died after D60 and 80 patients who responded the questionnaire). Index values are a summary of the 5 dimensions described in the manuscript

[a] All Index Values represented are medians. Interquartile ranges are in ()

[b] Including deceased patients. Death was also treated as an event because the EQ-5D index value of deceased patients is normally considered to be 0

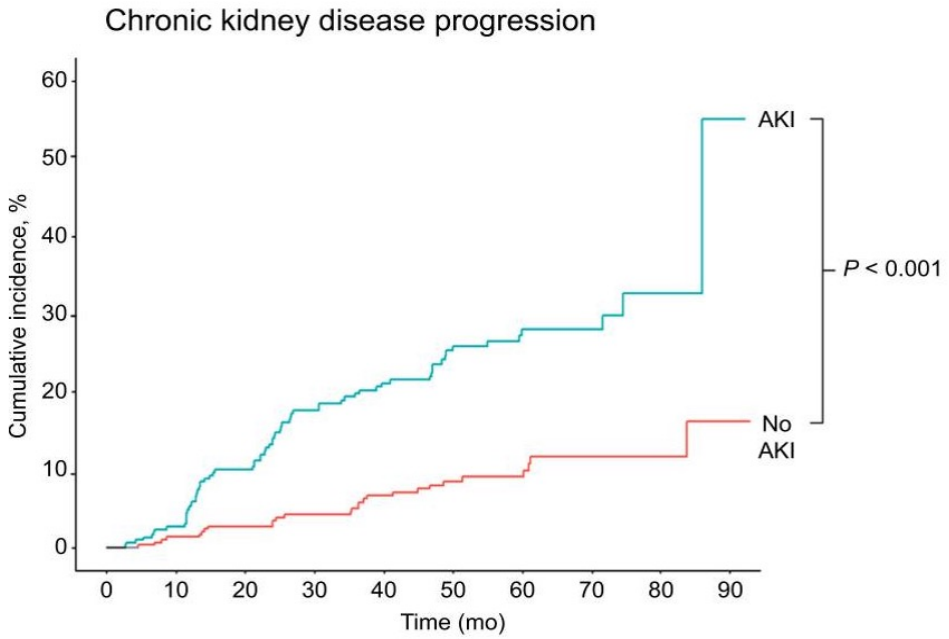
Figure S 2 EQ5D five dimensions of health in SALTO according to RRT strategy group



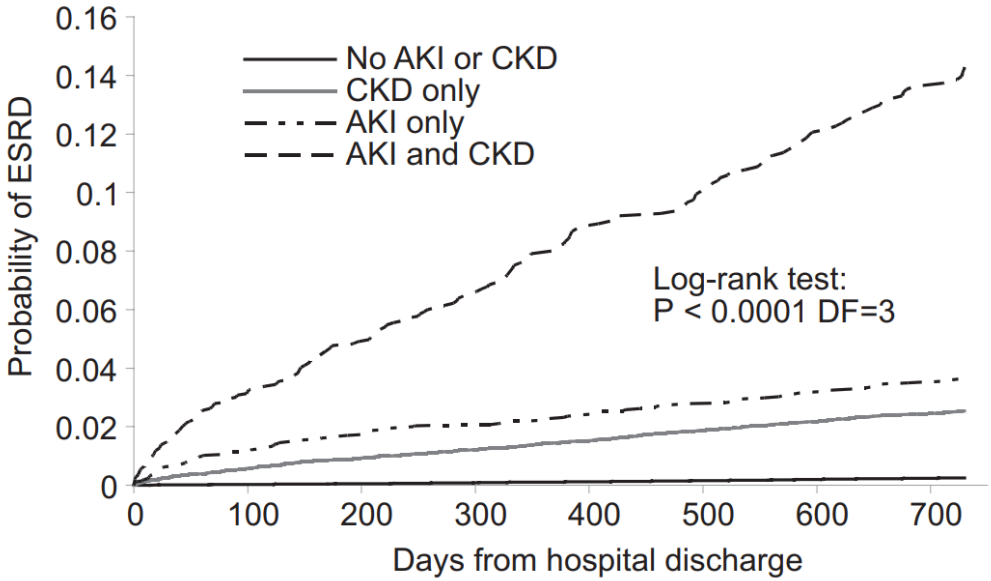
Pronostic à long terme IRA KDIGO3: SALTO

- 60% de mortalité à 3 ans
- L'âge, seul facteur de risque indépendant de mortalité identifié
- 25% des patients présenteront une aggravation de la fonction rénale à long terme
- Pas de facteur de risque indépendant d'aggravation de la fonction rénale identifié
- Une qualité de vie altérée.
- Aucune différence entre les stratégies d'EER immédiate ou retardée.

Progression de l'IRC



Ikizler et al, Kidney Int 2021



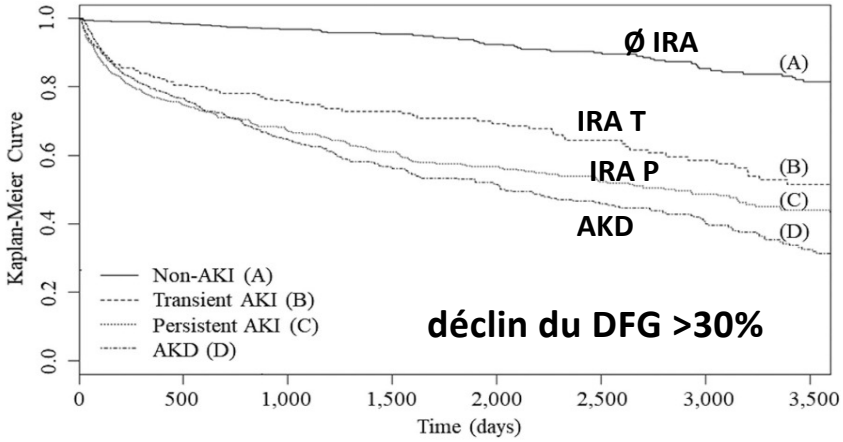
Ishani et al , JASN 2009

Risque d'IRCT (par rapport à no AKI no CKD)

« AKI and CKD HR 41 vs 8.3 CKD only »

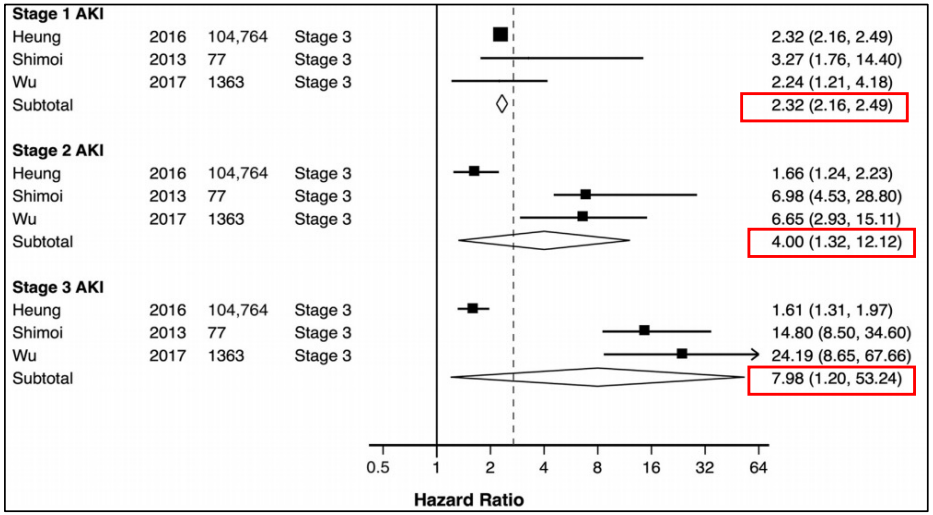
Impact de l'agression initiale

Durée de l'IRA



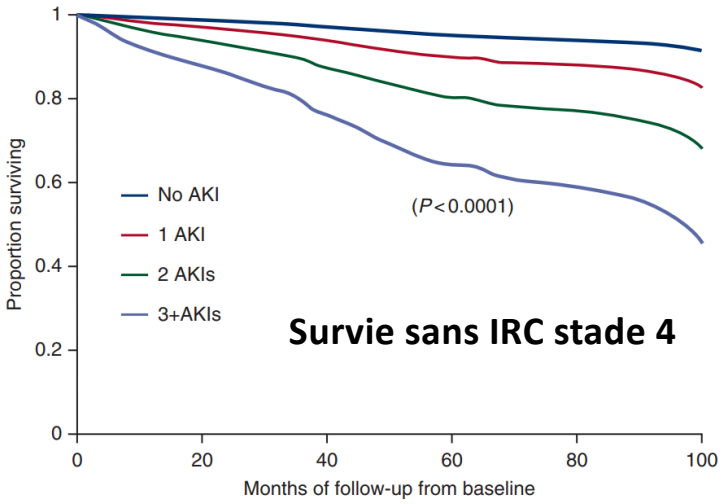
Nagata et al, Nephrology 2021

Sévérité de l'IRA



EJ See et al, Kidney Int 2019

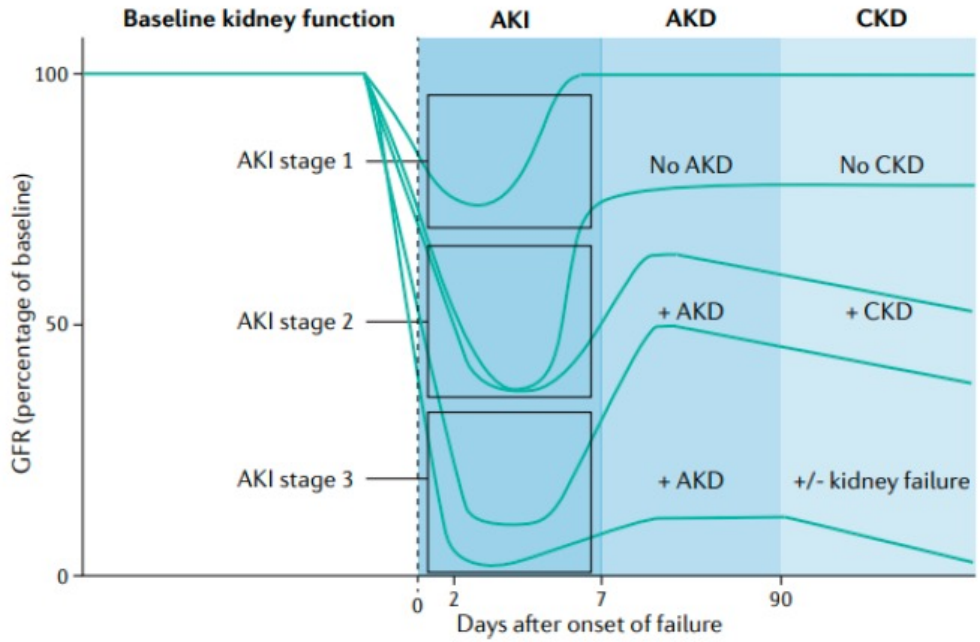
Récurrence l'IRA



Thakar et al, CJASN 2011

Terrain : âge, IRC, diabète, HTA, Ins cardiaque, cirrhose…

Horne et al, BMJ open 2017
James et al, JAMA 2017



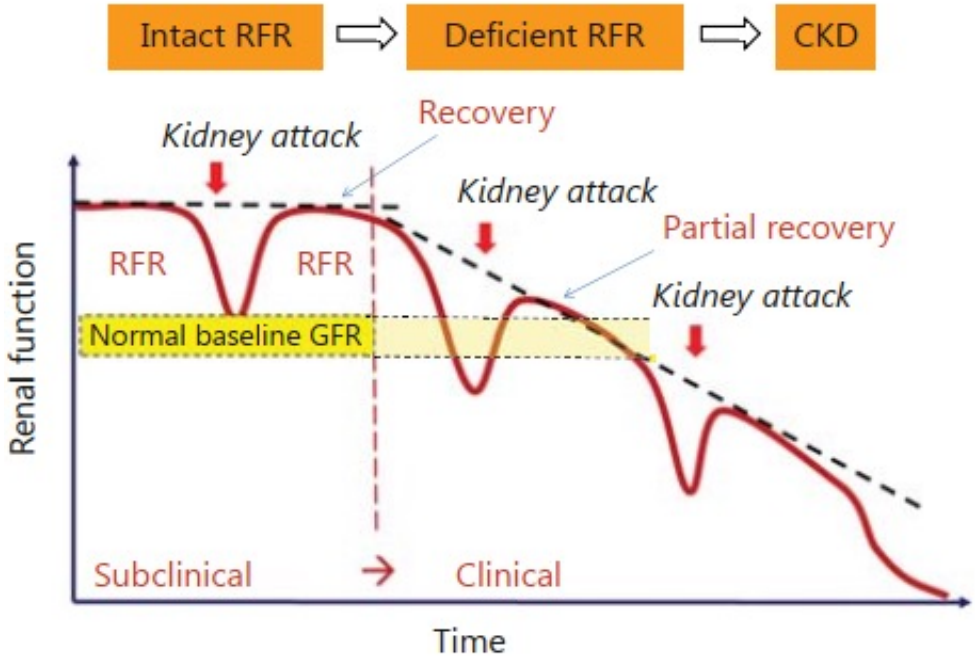
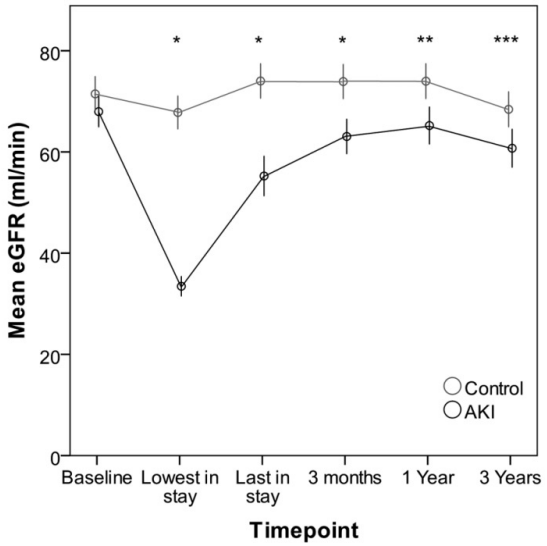


Figure 5 : Evolution de la fonction rénale après un épisode d'insuffisance rénale aiguë en fonction de sa sévérité et de sa durée. Modifié d'après Kellum et al., 2021 (12). Abréviations: AKI, acute kidney injury; AKD, acute kidney disease; CKD, chronic kidney disease; GFR, glomerular function rate.

Albuminurie-protéinurie post IRA

Three-year outcomes after acute kidney injury: results of a prospective parallel group cohort study



Albuminurie >3mg/mmol à 3 ans

IRA 46 **(40.7%)** vs control 26 (21.1%)

Protéinurie >15mg/mmol

IRA 53 (46.5%) vs control 36 (29.8%)

Horne et al, BMJ open 2017

Acute kidney injury is a risk factor for subsequent proteinuria

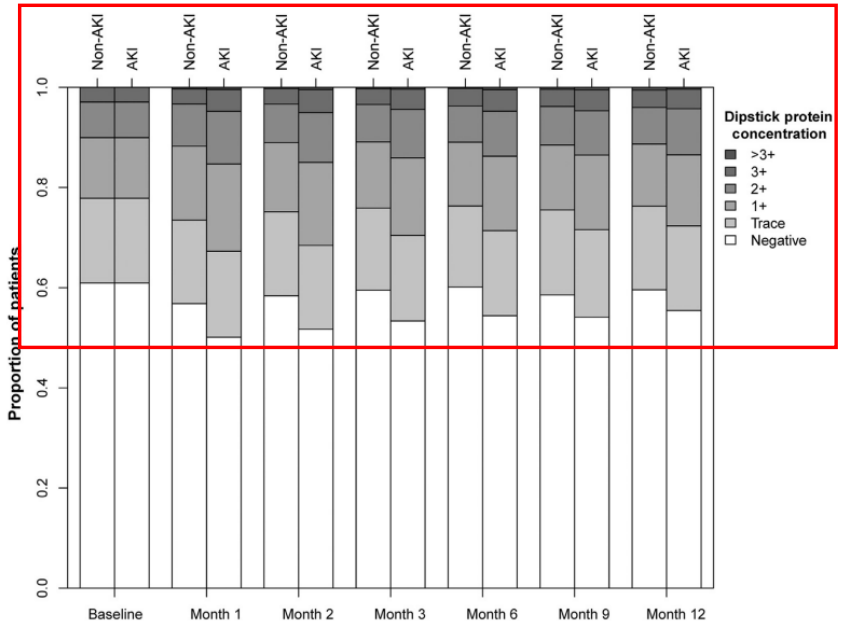
181 228 US vétérans H

2004-2012

♂ 98%, caucasien 75%

Diabète 48% HTA 78%

Matching 1:1 IRA vs Ø IRA



Parr et al, Kidney Int 2018

Précoce (pic à M1-2) maintenu à M12

Risque dépendant de la sévérité de l'IRA

Indépendant du diabète ou des Inhibiteurs SRAA

Signe d'alerte ? Facteur de risque modifiable ?

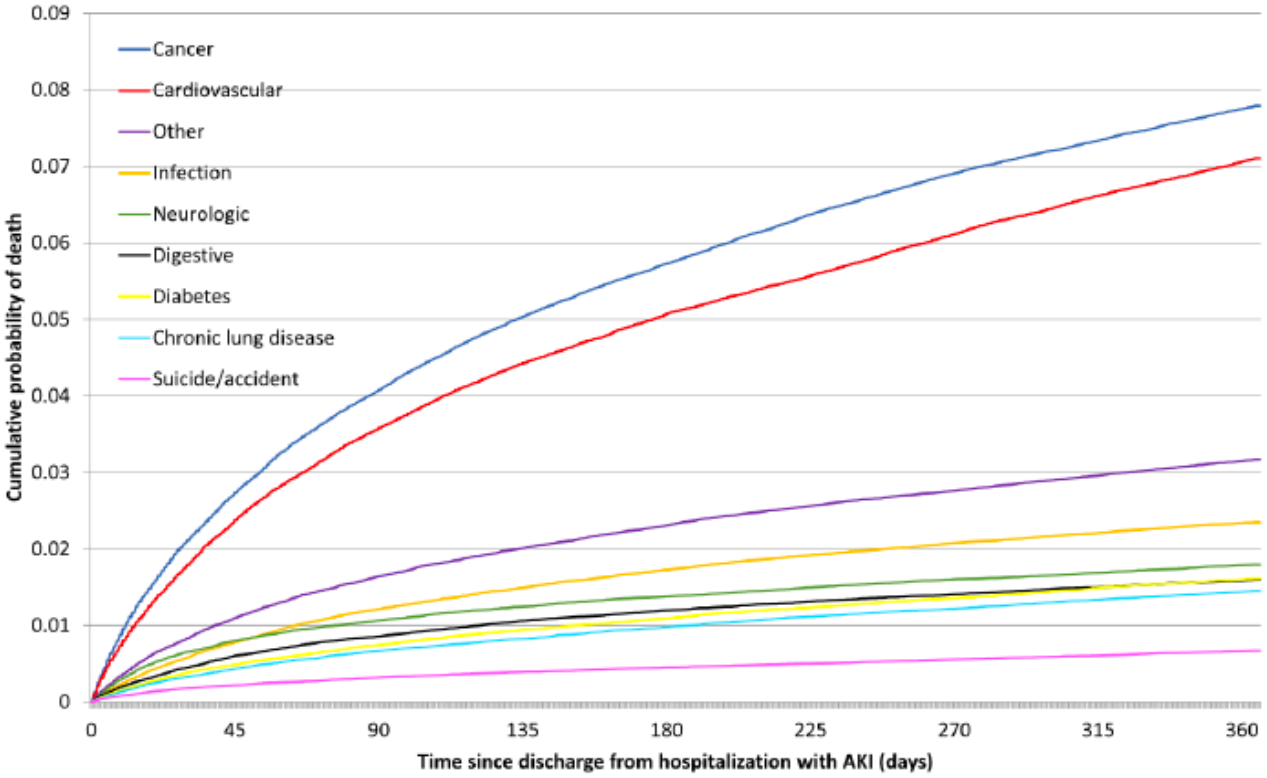


Figure 9A : Répartition des grandes causes de décès dans la première année suivant un épisode d'insuffisance rénale aiguë (Hazards ratios avec leurs intervalles de confiance 95%). D'après Silver et al. 2018 (21).

1. Cancers
2. Cardiovasculaire

Table 1 | Characteristics of biomarkers associated with AKI

Biomarkers	Sample type or application	Clinical utility
AKI stress marker[a]		
(TIMP-2)•(IGFBP7)	Urine	FDA-approved and CE-marked for clinical use (≥21 and ≥18 years of age, respectively); test designed to predict the risk of developing stage 2–3 AKI within 12 h of assessment
AKI damage markers[a]		
CCL14	Urine	CE-marked for clinical use (≥18 years of age); test designed to predict persistent stage 2–3 AKI
Dipstick albuminuria	Urine	Widely used as an initial screening tool for the evaluation of kidney disease because of its low cost, wide availability and ability to provide rapid point-of-care information
KIM-1	Urine	KIM-1 levels increase 12–24 h after tubular injury, peaking at 2–3 days[174]; FDA-approved and CE-marked for preclinical drug development
Low-molecular-weight proteins	Urine	Widely used to assess proximal tubule cell dysfunction[175]; α_1-microglobulin has been studied for the prediction of AKI-KRT[176], but validation is pending
L-type fatty acid-binding protein	Urine	Japanese MHLW-approved for clinical use (early diagnostic of kidney disease or predicting kidney prognosis)[177]
NGAL	Urine or serum	Levels peak 4–6 h after tubular injury; elevated in sepsis and inflammation[112,178] (thus, clinical use is limited in the ICU setting); commercially available NGAL assays can measure different molecular forms depending on their antibody combination; CE-marked (but not FDA-approved) for clinical use
Urine microscopy	Urine	Oldest and one of the most commonly used tests to differentiate kidney disease aetiology; prone to inter-observer variability[179]; a urine microscopy score based on the number of granular casts and/or kidney tubular epithelial cells per high-powered field[180] has been proposed for sepsis-associated AKI[180] but validation is pending
AKI functional markers[a]		
SCr	Serum	AKI is currently defined and staged according to the changes in SCr and UO; SCr is the most commonly used biomarker of kidney function and assay available in all clinical laboratories; a point-of-care SCr has been proposed to allow more frequent (for, every 3–4 h) and rapid assessment of SCr[181]
Cystatin C	Serum or urine	FDA-approved and CE-marked for clinical use for GFR estimation
penKID	Serum	CE-marked (but not FDA-approved) for clinical use (≥18 years of age)
Real-time GFR measurement	Injection	Clinical utility is currently unknown; FDA clearance to advance to human clinical studies since 2018
Furosemide stress test 2-h UO	Injection	Furosemide is the most frequently used diuretic in critically ill patients; clinical utility in AKI was recently validated in a heterogeneous cohort of critically ill adults admitted to the ICU[182]
Other AKI markers		
Intrarenal venous flow	Doppler ultrasound	Emerging non-invasive marker to assess renal congestion due to increased right-sided cardiac filling pressures, volume overload, and/or elevated intra-abdominal pressure[183]; prone to inter-observer variability
FeNa	Urine	Widely used to differentiate prerenal azotaemia from acute tubular necrosis; most utility in oliguric patients without CKD and not on diuretic therapy[184]
PERSEVERE-II	Clinical risk score	Model recently proposed to estimate the baseline risk of developing stage 2 or 3 AKI (SCr, KDIGO) on day 3 in patients with paediatric septic shock, when measured within 24 h of a septic shock diagnosis; might have limited applicability to the neonatal population, as the number of neonates in the study was small (2.4% of the total cohort); PERSEVERE-II biomarker assay might not be universally available; prospective validation is pending
Renal angina index	Clinical risk score	Score for the risk prediction of AKI or its persistence 3 days after admission validated in a heterogeneous cohort of critically ill children[114]; calculated 12 h after admission to the ICU[185]; clinical variables used in risk score universally available
RRI	Doppler ultrasound	Routinely used to estimate and monitor vascular and renal parenchymal disease; prone to inter-observer variability

Consensus statement SA AKI, Nature Reviews Nephrology 2023

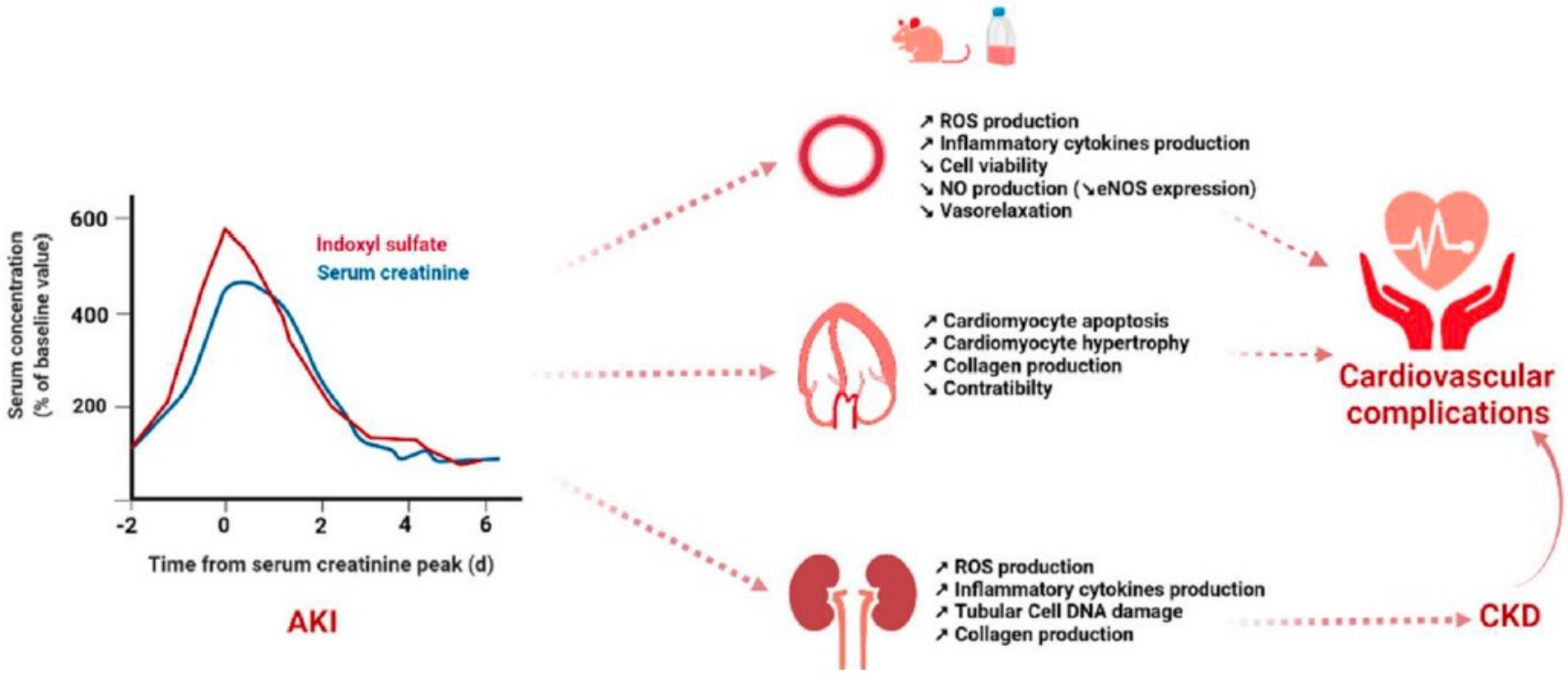
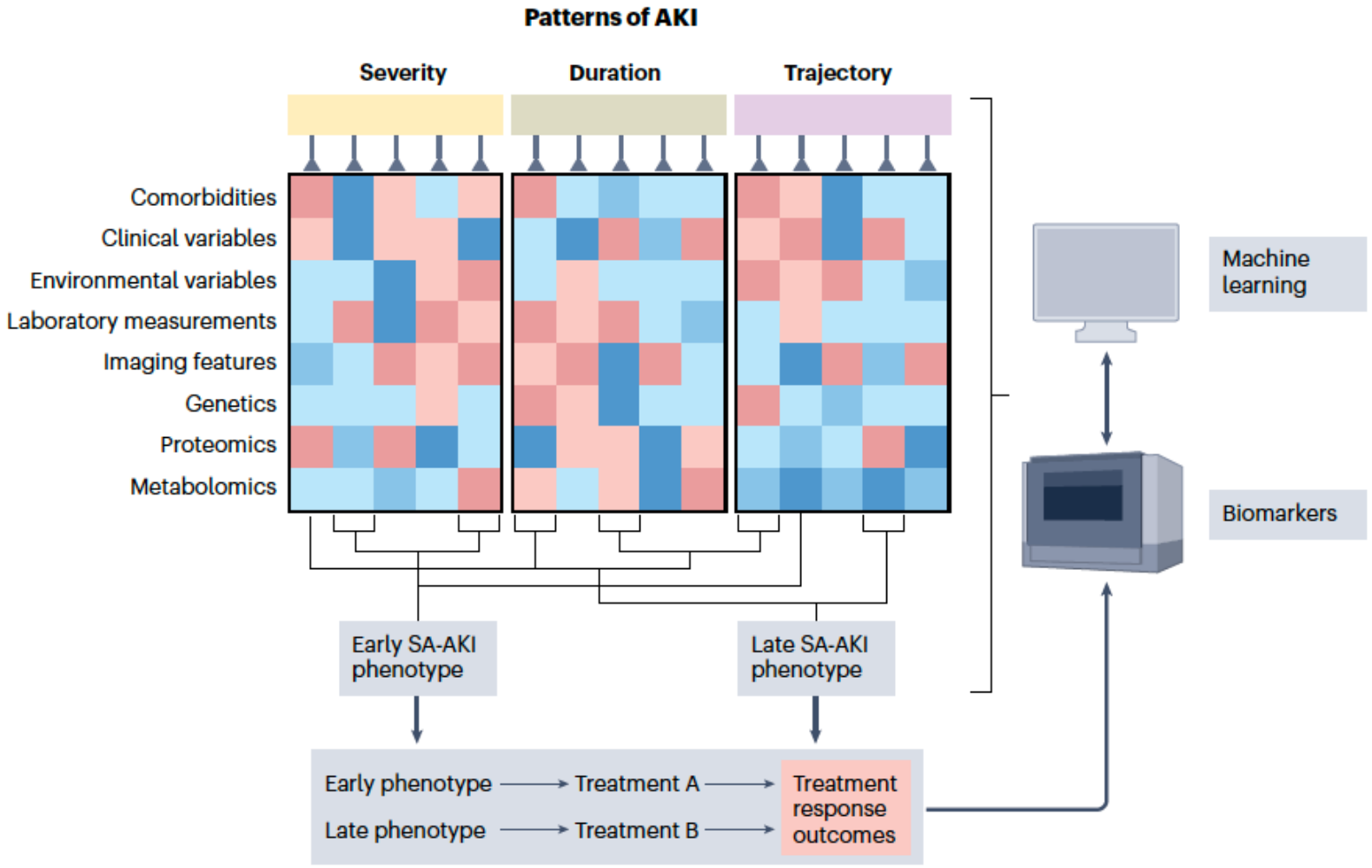


Figure 34 : Résumé des actions potentielles de l'indoxyl-sulfate sur le tissu vasculaire et cardiaque au cours de l'insuffisance rénale aiguë. D'après Caillard et al. 2022 (189). Abréviations: AKI, acute kidney injury; CKD, chronic kidney injury; DNA, deoxyribonucleic acid; NO, nitric oxide; ROS, reactive oxygen species.

Thèse PhD, P Caillard, UPJV



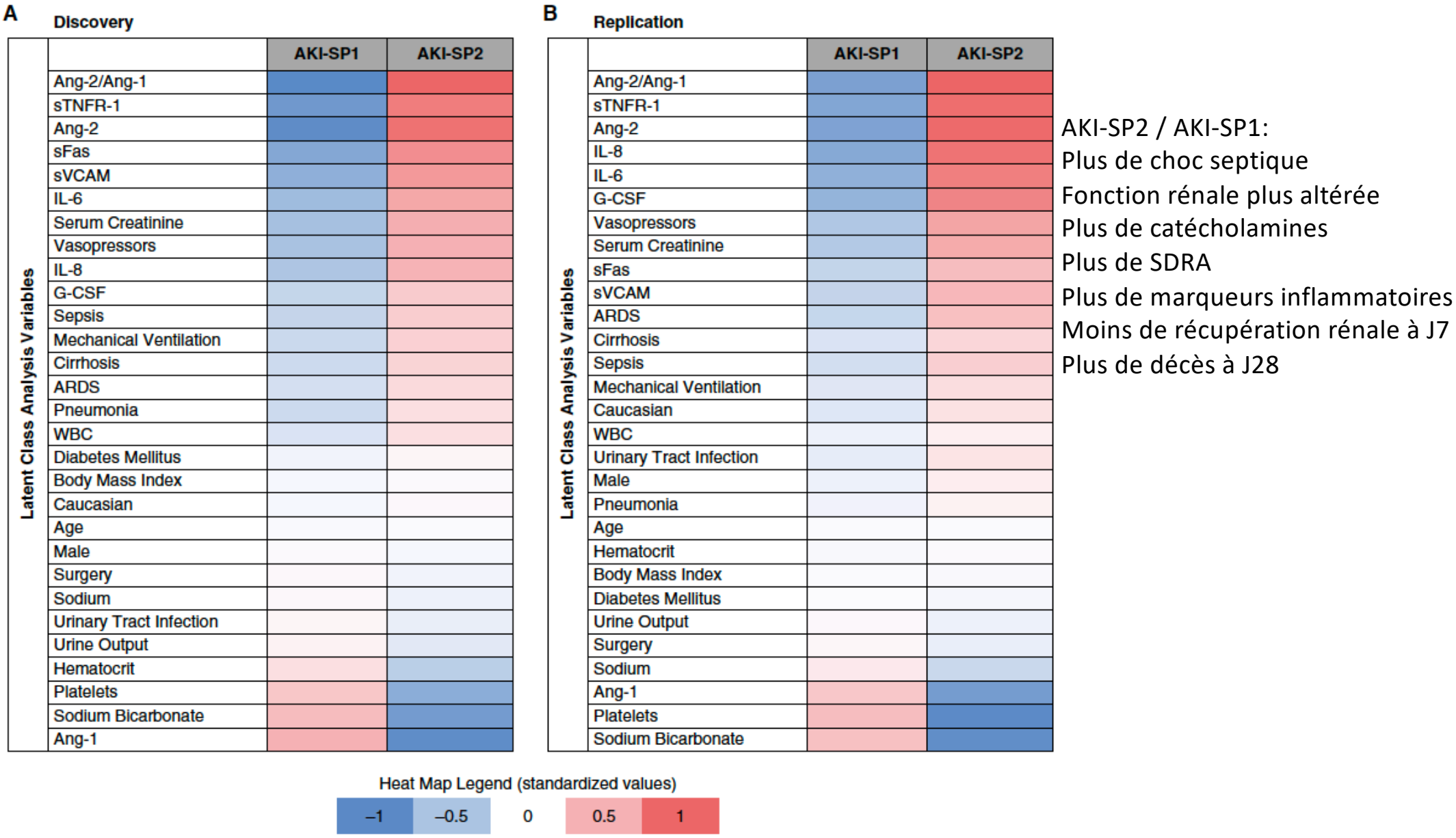
Consensus statement SA AKI,
Nature Reviews Nephrology 2023

Identification of Acute Kidney Injury Subphenotypes with Differing Molecular Signatures and Responses to Vasopressin Therapy

Pavan K. Bhatraju[1,2], Leila R. Zelnick[2], Jerald Herting[3], Ronit Katz[2], Carmen Mikacenic[1], Susanna Kosamo[1], Eric D. Morrell[1], Cassianne Robinson-Cohen[2], Carolyn S. Calfee[4,5,6], Jason D. Christie[7,8*], Kathleen D. Liu[9,10], Michael A. Matthay[4,5,6], William O. Hahn[11], Victoria Dmyterko[1], Natalie S. J. Slivinski[12], Jim A. Russell[13,14], Keith R. Walley[13,14], David C. Christiani[15,16,17], W. Conrad Liles[18], Jonathan Himmelfarb[2], and Mark M. Wurfel[1,2]

American Journal of Respiratory and Critical Care Medicine Volume 199 Number 7 | April 1 2019

	Discovery (*n* = 794)	Replication (*n* = 425)	VASST (*n* = 256)
Baseline demographics			
Age, yr	55 ± 16	57 ± 18	60 ± 16
Male	520 (65)	249 (59)	152 (59)
Race			
White	575 (77)	425 (100)	232 (91)
Comorbidities			
Diabetes mellitus	238 (30)	112 (27)	62 (26)
Cirrhosis	75 (9)	20 (5)	18 (7)
ICU events			
Sepsis-3	561 (71)	310 (73)	256 (100)
Vasopressors	232 (29)	237 (56)	256 (100)
Laboratory values			
Lowest sodium bicarbonate, mEq/L	20 ± 6	20 ± 5	18 ± 8
Lowest platelets, 10^9/L	176 ± 106	158 ± 102	65 ± 106
Maximum serum creatinine, mg/dl	2.1 ± 2.2	2.4 ± 1.6	2.9 ± 1.7
Biomarker concentrations			
Ang-2/Ang-1	4 (1–15)	21 (6–77)	6 (2–11)
sTNFR-1, pg/ml	10,151 (5,926–17,079)	14,368 (8,504–23,731)	—
IL-8, pg/ml	14 (6–34)	23 (12–54)	48 (20–148)
Primary outcome			
28-d mortality	111 (14)	93 (22)	87 (34)



AKI-SP2 / AKI-SP1:
Plus de choc septique
Fonction rénale plus altérée
Plus de catécholamines
Plus de SDRA
Plus de marqueurs inflammatoires
Moins de récupération rénale à J7
Plus de décès à J28

Application des phénotypes identifiés sur les études Discovery et Replication à la population de l'étude VASST

	AKI-SP1				AKI-SP2			
	Norepinephrine	Vasopressin	RR (95% CI)†	*P* Value	Norepinephrine	Vasopressin	RR (95% CI)†	*P* Value
Clinical outcomes								
7-d renal nonrecovery	24 (46)	23 (38)	0.80 (0.51–1.25)	0.32	44 (63)	44 (56)	0.99 (0.76–1.30)	0.96
28-d mortality	16 (31)	11 (18)	0.53 (0.30– 0.94)	0.03	30 (43)	31 (40)	1.03 (0.68–1.55)	0.88
90-d mortality	24 (46)	16 (27)	0.54 (0.32–0.92)	0.02	34 (49)	35 (45)	0.99 (0.70–1.42)	0.99

Effet favorable de la vasopressine sur le pronostic de AKI SP1

The combination of kidney function variables with cell cycle arrest biomarkers identifies distinct subphenotypes of sepsis-associated acute kidney injury: a post-hoc analysis (the PHENAKI study)

Dimitri Titeca-Beauport [1], Momar Diouf, Delphine Daubin, Ly Van Vong, Guillaume Belliard, Cédric Bruel, Yoann Zerbib, Christophe Vinsonneau, Kada Klouche, Julien Maizel

1.Medical Intensive Care Unit and EA7517, Boreal Study Group, Amiens University Hospital, Amiens, France.

MÉDECINE INTENSIVE RÉANIMATION CHU AMIENS PICARDIE

INTRODUCTION

The severity and course of sepsis-associated acute kidney injury (SA-AKI) are correlated with the mortality rate. Early detection of SA-AKI subphenotypes might facilitate the rapid provision of individualized care.

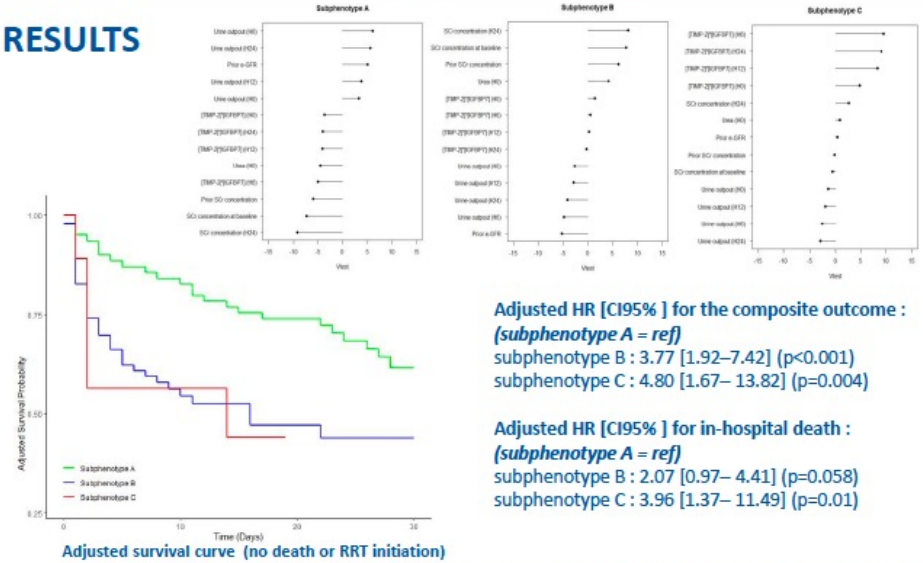
OBJECTIVES

- Determine whether the combination of serial measurements of urine levels of cell cycle arrest biomarkers and standard kidney function variables over the first 24 h could distinguish between **SA-AKI subphenotypes.**
- Compare the subphenotypes with regard to a **composite outcome of in-hospital death or the initiation of renal replacement therapy (RRT).**

METHODS

- Post-hoc analysis of data from the multicentre, prospective AKI-CHECK study [1]
- **184 patients presented with septic shock and AKI** within 6 h of the initiation of vasopressors.
- **Unsupervised hierarchical clustering of principal components approach.**
- **Candidate variables :** pre-admission SCr and eGFR, BUN at 0h, SCr at 0h and 24h, UO (ml/kg) at 0h, 6h, 12h, 24h, urine [TIMP-2]*[IGFBP7] value at 0 h, 6 h, 12 h and 24 h.
- **Adjusted survival rate (G-computation)**

RESULTS



Adjusted survival curve (no death or RRT initiation)

Adjusted HR [CI95%] for the composite outcome :
(subphenotype A = ref)
subphenotype B : 3.77 [1.92–7.42] (p<0.001)
subphenotype C : 4.80 [1.67– 13.82] (p=0.004)

Adjusted HR [CI95%] for in-hospital death :
(subphenotype A = ref)
subphenotype B : 2.07 [0.97– 4.41] (p=0.058)
subphenotype C : 3.96 [1.37– 11.49] (p=0.01)

Characteristics	Total cohort (n = 184)	Subphenotype A (*n*=99)	Subphenotype B (*n*=74)	Subphenotype C (*n*=11)	[1]*p*–value
Age (years)	69 [58–79]	67 [55– 77]	72 [62– 82]	63 [53– 71]	0.024
Stage 3 CKD	27 (15)	3 (3)	23 (31)	1(9)	<0.001
RAS inhibitor	67 (37)	29 (30)	37 (50)	1 (9.1)	0.003
SCr level (µmol/l) at 0h	150 [112– 216]	118 [93– 150]	216 [170– 281]	127 [108– 189]	<0.001
Urine output (ml/kg) at 0h	0.86 [0.39– 1.90]	1.21 [0.58– 2.92]	0.56 [0.24– 1.20]	0.30 [0.16– 0.49]	<0.001
[TIMP–2]*[IGFBP7] at 0 h	1.26 [0.26– 4.00]	0.75 [0.18– 1.87]	2.11 [0.41– 5.89]	6.37 [4.19– 14.80]	<0.001
Nonrenal SOFA score	8 [7– 10]	8 [6– 10]	8 [7– 10]	11 [9– 12]	0.014
SAPS II	55 [42– 69]	48 [39– 61]	60 [50– 75]	64 [48– 79]	<0.001
RRT at day-7	34 (18)	4 (4)	27 (36)	3(27)	<0.001
In-hospital death	68 (37)	24 (24)	35 (47)	9 (82)	<0.001

CONCLUSIONS

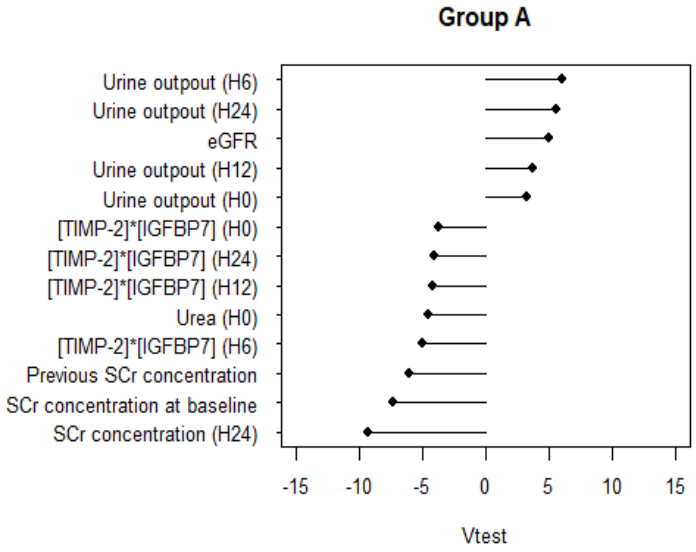
We identified three distinct SA-AKI subphenotypes (with different short-term trajectory and survival rates) by combining conventional kidney function indicators with urine measurements of a cell-cycle arrest biomarker.

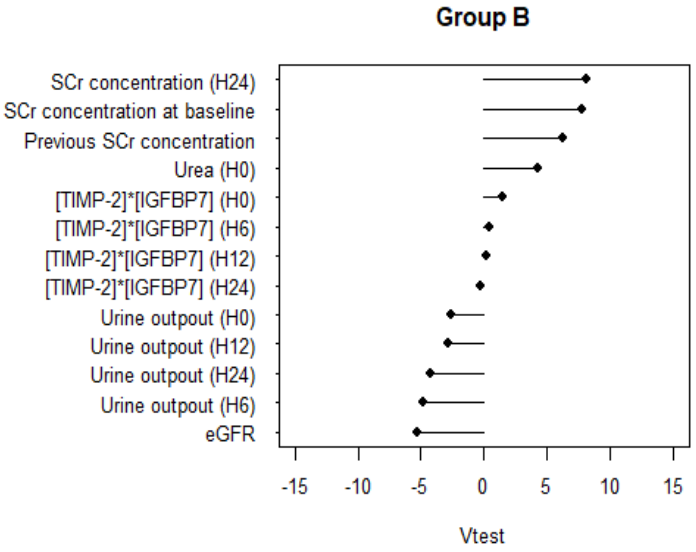
ACKNOWLEDGEMENTS

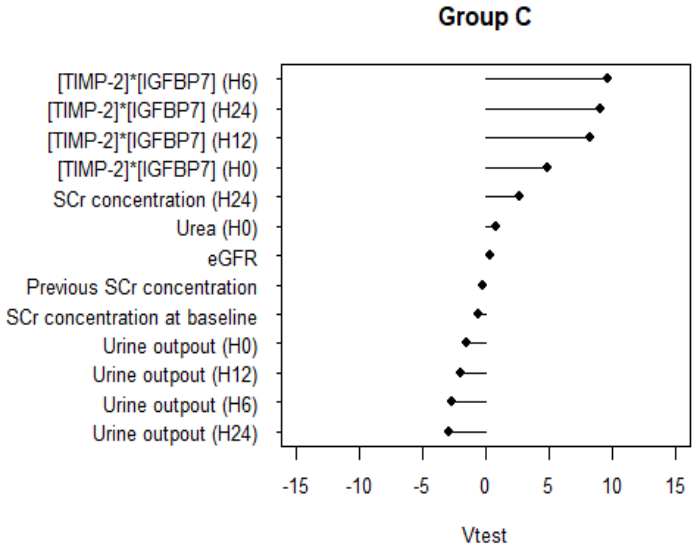
Not applicable

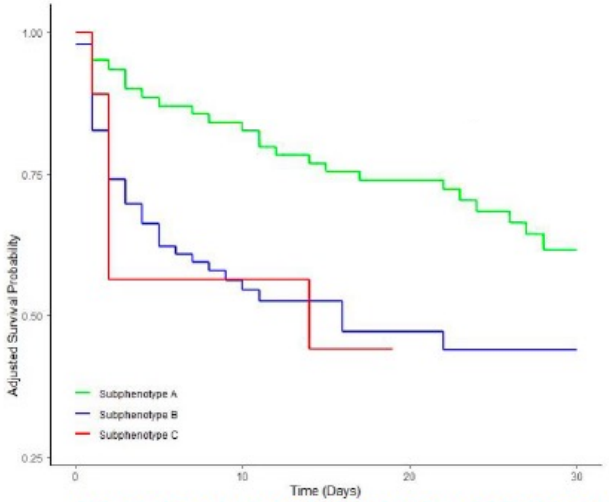
REFERENCES

1. Titeca-Beauport D, Daubin D, Van Vong L, Belliard G, Bruel C, Alaya S, et al. Urine cell cycle arrest biomarkers distinguish poorly between transient and persistent AKI in early septic shock: a prospective, multicenter study. Crit Care. 2020;24:280









Adjusted survival curve (no death or RRT initiation)

McNicholas *et al. Annals of Intensive Care* (2023) 13:43
https://doi.org/10.1186/s13613-023-01140-x

LETTER TO THE EDITOR **Open Access**

Survive or thrive after ICU: what's the score?

Bairbre A. McNicholas[1*], Ryan Haines[2,3] and Marlies Ostermann[4]

Table 4 Quality of life

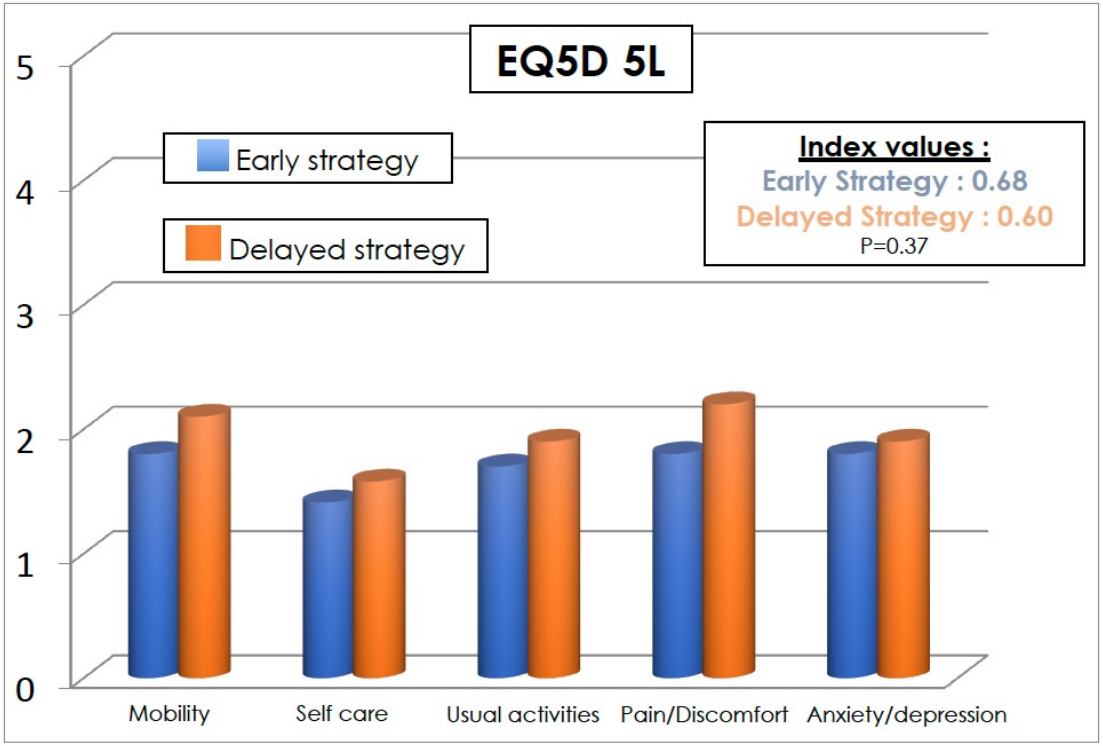
Variable	All patients	Early RRT strategy (95% CI)	Delayed RRT strategy (95% CI)	*P* value
EQ5D-5L (survivors at end of follow-up)a	0.67 (0.40–1.00)	0.71 (0.51–1.00)	0.64 (0.50–1.00)	0.32
EQ5D-5L (patients since D60)[b]	0.39(0.20–0.81)	0.35 (0.22–0.82)	0.41 (0.20–0.80)	0.70

Analysis of the survivors was led on the 80 patients who responded to the questionnaire. Analysis of patients since D60 was led on 170 patients (90 patients who died after D60 and 80 patients who responded the questionnaire). Index values are a summary of the 5 dimensions described in the manuscript

[a] All Index Values represented are medians. Interquartile ranges are in ()

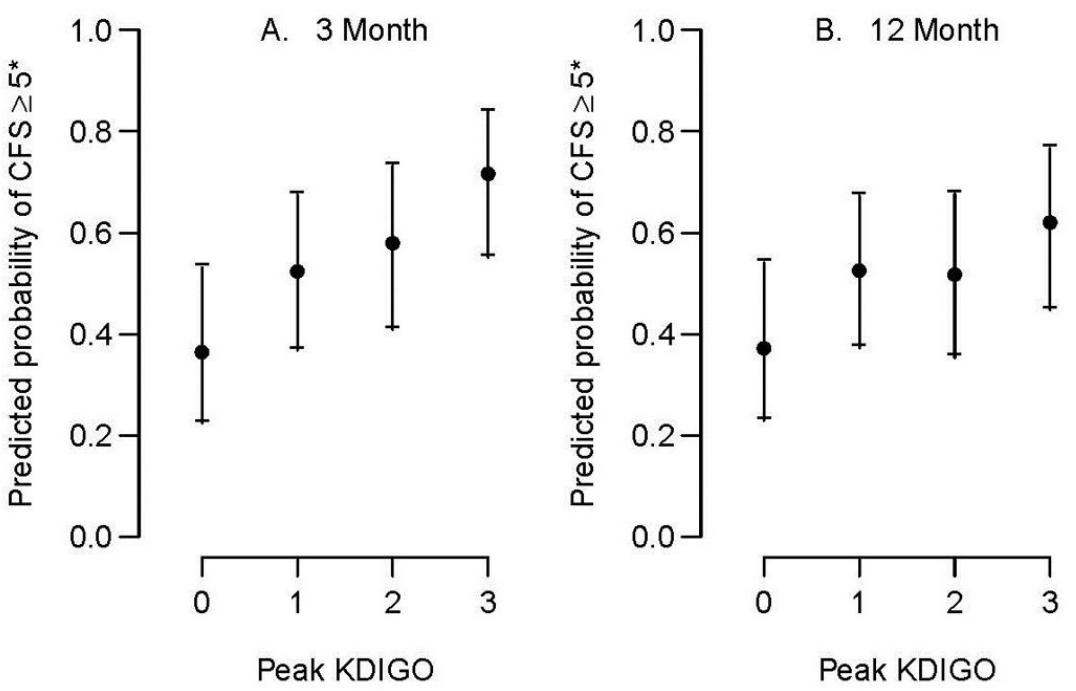
[b] Including deceased patients. Death was also treated as an event because the EQ-5D index value of deceased patients is normally considered to be 0

Figure S 2 EQ5D five dimensions of health in SALTO according to RRT strategy group



Relative risk for low HRQoL in one-year survivors (n = 1549)[b]		
Unadjusted	No eAKI	Reference
	Risk	1.03 (0.74, 1.45; 0.849)
	Injury	1.24 (0.81, 1.90; 0.318)
	Failure	1.52 (0.49, 4.72; 0.465)
Adjusted	No eAKI	Reference
	Risk	0.96 (0.68, 1.35; 0.82)
	Injury	1.14 (0.74, 1.74; 0.549)
	Failure	1.34 (0.42, 4.26; 0.612)

Soliman CCM 2016



Abdel Kader CCM 2018

Conclusion

- SALTO
  - 60% de mortalité à 3 ans
  - L'âge, seul facteur de risque indépendant de mortalité identifié
  - 25% des patients présenteront une aggravation de la fonction rénale à long terme
  - Pas de facteur de risque indépendant d'aggravation de la fonction rénale identifié
  - Une qualité de vie altérée.
  - Aucune différence entre les stratégies d'EER immédiate ou retardée.