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Original Article

Epidemiology and outcomes of early *versus* late septic acute kidney injury in critically ill patients: A retrospective cohort study

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ABSTRACT

Background: It was recently proposed to distinguish early from late sepsis-associated acute kidney injury (SA-AKI). We aimed to determine the relative frequency of these entities in critically ill patients and to describe their characteristics and outcomes.
Methods: We included in this retrospective cohort study all adult patients admitted for sepsis in a tertiary ICU between 2010 and 2020. We excluded those on chronic dialysis or without consent. We extracted serum creatinine, hourly urinary output, and clinical and socio-demographic data from medical records until day 7 or ICU discharge. AKI presence and characteristics were assessed daily using KDIGO criteria. We compared patients with early (occurring within 2 days of admission) or late (occurring between day 2 and day 7) SA-AKI. We conducted sensitivity analyses using different definitions for early/late SA-AKI.
Results: Among 1835 patients, 1660 (90%) fulfilled SA-AKI criteria. Of those, 1610 (97%) had early SA-AKI, and 50 (3%) had late SA-AKI. Similar proportions were observed when only considering AKI with elevated sCr (71% *vs.* 3%), severe AKI (67% *vs.* 6%), or different time windows for early SA-AKI. Compared with early SA-AKI patients, those with late SA-AKI were younger (median age [IQR] 59 [49–70] *vs.* 69 [58–76] years, $p < 0.001$), had lower Charlson comorbidity index (3 [1–5] *vs.* 5 [3–7], $p < 0.001$) and lower SAPSII scores (41 [34–50] *vs.* 53 [43–64], $p < 0.001$). They had similar (24% *vs.* 26%, $p = 0.75$) in-hospital mortality.
Conclusions: AKI is almost ubiquitous in septic critically ill patients and present within two days of admission. The timing from ICU admission might not be relevant to distinguish different phenotypes of SA-AKI.
Ethics approval: Ethics Committee Vaud, Lausanne, Switzerland (n°2017-00008).

Introduction

Sepsis and acute kidney injury (AKI) represent very common and intertwined syndromes in critically ill patients. Indeed, sepsis is the leading cause of AKI in intensive care units (ICU) while AKI is complicating up to 50% of sepsis episodes [1]. Their combination, sepsis-associated AKI (SA-AKI), independently increases mortality and hospital stay duration [2,3]. To date, most interventions targeting SA-AKI have failed to improve clinical outcomes, probably due to the heterogeneity of underlying pathophysiological alterations [4]. Indeed, the long-assumed ischemic etiology for AKI (“acute tubular necrosis”) is now increasingly challenged [5,6]. SA-AKI is most probably the result of a complex, time-evolving, interplay between background susceptibility (comorbidities), specific injury mechanisms (inflammation, complement activation, endothelial dysfunction, coagulation activation, mitochondrial dysregulation, oxidative stress, micro, and microcirculatory dysfunctions), and therapy associated factors (use of vasopressors, nephrotoxic drugs or mechanical ventilation) [7,8].

The Acute Disease Quality Initiative (ADQI) workgroup has recently proposed to distinguish early (AKI occurring within 48 h of sepsis diagnosis) from late (AKI occurring between 48 h and 7 days) SA-AKI [8]. The hypothesis was that early and late SA-AKI

Abbreviations: AKI, acute kidney injury; KDIGO, Kidney Disease Improving Global Outcomes; ICU, intensive care unit; IQR, interquartile range; RRT, renal replacement therapy; SA-AKI, sepsis associated AKI.

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might correspond to two separate phenotypes with different distributions of underlying mechanisms, prognosis, and perhaps therapeutic response to interventions. A similar temporal distinction was observed in critically ill patients with acute respiratory distress syndrome (ARDS) and septic shock, where those with late-onset diseases appeared to have a worse prognosis [9,10], perhaps due to lower injury tolerance in patients with previously established organ failure. Previous studies have suggested that early AKI could be associated with a lower mortality rate and may be associated with pathophysiological mechanisms distinct from those involved in late-onset forms [11,12]. However, these studies used outdated definitions for AKI, and heterogeneous cutoffs for early *versus* late onset.

Accordingly, we aimed to determine the relative distribution of early *versus* late onset SA-AKI in sepsis patients requiring ICU admission, using the current KDIGO definition for AKI and the cutoff for early SA-AKI proposed by ADQI, and to report on patients' characteristics and outcomes.

Methods

Design, population, data collection

This observational retrospective study was conducted in the Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland. We used the previously described LAUS'AKI cohort in which all adult (>18 years old) patients admitted to a medico-surgical ICU between January 1st, 2010, and June 15th, 2020 could be included [13]. Patients with documented or expressed wishes of non-participation in clinical research, those with end-stage renal disease, those who stayed less than 6 h in ICU, and those with missing KDIGO defining data (*i.e.*, less than 6 h of UO measurements, or absence of sCr measurement) were excluded. In the present study, we included only patients admitted to ICU with sepsis as the main diagnosis. In the case of multiple eligible admissions during the study period, only the first one was considered. Data in the LAUS'AKI cohort were previously extracted from electronic medical records [Metavision® (IMD Soft, Tel Aviv, Israel) and Soarian® (Cerner, North Kansas City, USA)]. In particular, demographic characteristics, underlying medical conditions, admission status, and medical interventions were collected. Charlson comorbidity index and illness severity score at admission (SAPS II score corrected for creatinine) were computed. Daily serum creatinine (sCr) and hourly urinary output (UO) measurements were extracted until day 7 or ICU discharge, whichever occurred first. Patients' vital status at day-90 was assessed by cross-referencing the dataset with the Swiss national death registry.

Definitions

Sepsis and sepsis onset

Sepsis was defined by the documentation of a main diagnostic code of "sepsis" or "septic shock" fulfilled by a senior intensivist. In addition, patients with one of the following main admission codes "infection", "endocarditis", "peritonitis" or "pneumonia" and the need for either noradrenaline infusion or mechanical ventilation (increase in SOFA score ≥2 at admission) were also deemed to have sepsis, according to the Sepsis 3 definition [14]. Since international guidelines recommend admitting patients with sepsis who require ICU admission within 6 h; we assumed that ICU admission was a reasonable surrogate for the onset day of sepsis [15]. This was supported by a recent study demonstrating that the delay between sepsis onset and ICU admission was <24 h [16].

Acute kidney injury

Definition and imputation methods for baseline serum creatinine and body weight have been described in detail elsewhere [13]. AKI was defined, as per KDIGO definition, as a >50% elevation of sCr relative to baseline and/or an increase in sCr by 26.5 μmol/L within 48 h and/or a urinary output of less than 0.5 mL/kg/h for a minimum duration of 6 h. Similarly, AKI severity was defined based on KDIGO staging, using sCr and UO criteria [17]. We attributed to each ICU day from admission day (day 0) to day 7, the highest AKI stage reached on that day, based on (1) sCr criteria (sCr stage), (2) UO criteria (UO stage), and (3) the highest among sCr and UO criteria (overall stage). If one of the two criteria was missing (sCr or UO), the presence and staging of AKI were determined based on the available criterion alone. UO stage was defined each hour by the averaged urine output (UO) measured over the 6, 12, or 24 preceding hours and adjusted to the patient's body weight (units in mL/kg/h).

Early versus *late AKI*

Patients with AKI on ICU day 0 and/or day 1 were included in the "early SA-AKI" group. Those with new AKI episodes on ICU days 2–7 were included in the "late SA-AKI" group.

We also explored alternative definitions of early and late AKI. Alternative definition 1 considered day 0, day 1, and day 2 to define early-AKI. Alternative definition 2 applied to patients admitted to the hospital within 24 h of ICU admission, and considered hospital admission as day 0, instead of ICU admission.

Renal recovery

Renal recovery was defined in ICU survivors by the absence of AKI based on KDIGO criteria at ICU discharge.

Statistical analyses

Continuous data are reported as median (interquartile range—IQR) and compared using the Wilcoxon rank sum test. Categorical variables are expressed as number (percentage) and compared using chi-square or Fisher's exact test.

In the main analysis, we considered the onset day of the first AKI episode, regardless of stage and diagnostic criterion (sCr, UO, or both). We compared the incidence, characteristics, and outcomes of patients in the early and the late SA-AKI groups. We performed sensitivity analyses, using alternative definitions for early and late SA-AKI (see above) or considering only severe (stage 2 and 3) AKI or only AKI based on sCr criteria. In addition, to account for the uncertainty associated with sepsis onset, we repeated our analyses after exclusion of patients transferred from another ICU or an intermediate care unit or exclusion of those admitted to the hospital for more than 48 h prior to ICU admission. Finally, since the modern sepsis definition was proposed in 2016, we have repeated our analyses after splitting our cohort into two periods (ICU admissions between <2016 and >2016).

All statistical analyses were performed with STATA version 17.0 (StataCorp LP, College Station, Texas). A two-tailed p-value < 0.05 was considered statistically significant.

Ethics

This study received approval from the Ethics Committee Vaud, Lausanne, Switzerland (n°2017-00008). According to the Swiss Federal Act on Research involving Human Beings (article 34), retrospective utilization of non-genetic health-related personal data was authorized if the patient (or its legal representative) had not expressed wishes of non-participating to clinical research.

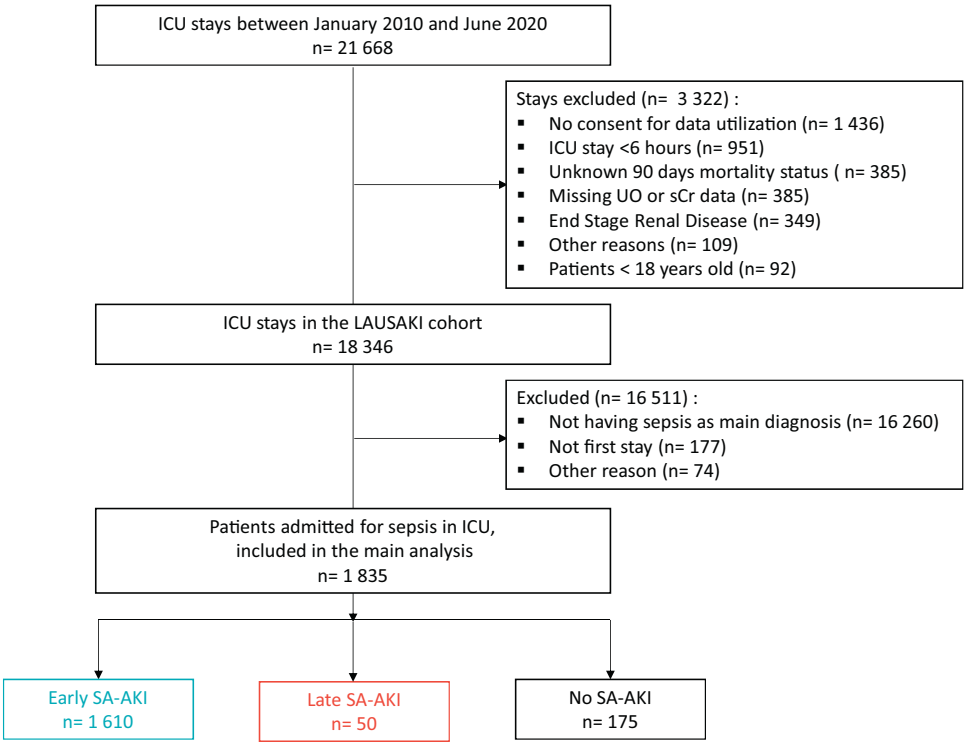

Fig. 1. Flow diagram for patients' selection.
Early SA-AKI is defined by the presence of AKI within 2 days of admission in patients with a main diagnosis of sepsis. Late SA-AKI is defined by the diagnosis of an AKI between day 2 after ICU admission and day 7 or ICU discharge, whichever occurred first (see main body for precisions).
AKI: acute kidney injury, ICU: intensive care unit, SA-AKI: sepsis-associated AKI.

Results

Population

Among the 15,620 patients (18,345 admissions) included in the original cohort, 1835 (12%) were admitted for sepsis and could be included in the present study (Fig. 1). Patients were mostly males (n = 1213, 66%), with a median (IQR) age of 68 (57–76) years. Most of them were admitted from the operating room (n = 498, 27%), emergency room (n = 490, 27%), or intermediate care (n = 406, 22%). Median (IQR) SAPS II at ICU admission was 51 (41–63). 1114 (60%) patients had septic shock and 503 (27%) had sepsis as their main diagnosis code for ICU admission. The remaining 218 (12%) patients had a diagnosis of pneumonia, peritonitis, endocarditis, or other infections and required either noradrenaline or mechanical ventilation on ICU admission.

AKI incidence and timing

Among study patients, 1660 (90%) fulfilled AKI criteria. As shown in Fig. 2, AKI was present on ICU admission day in 1383 (75%) patients and developed on day 1 in 227 (13%). Altogether, 1610 (97%) of SA-AKI patients fulfilled the criteria for early SA-AKI and 50 (3%) for late SA-AKI. When considering only the patients who were still alive and AKI-free in the late-period (n = 144), late SA-AKI occurred in 50 (35%) of these at-risk patients (81patients were discharged alive and without AKI before day 2).

Compared with patients with early SA-AKI, those with late SA-AKI were younger (median [IQR] 59 [49–70] *vs.* 69 [58–76] years old, $p < 0.001$), had less comorbidities (median [IQR] Charlson comorbidities index: 3 [1–5] *vs.* 5 [3–7], $p < 0.001$] and lower SAPS II scores (median [IQR] 41 [34–50] *vs.* 53 [43–64], $p < 0.001$) (Table 1). Daily prevalence and severity profile of AKI remained stable among patients still alive and hospitalized in ICU during the seven days following admission (Fig. 3).

Initial AKI severity and diagnosis criteria

Initial SA-AKI severity was higher in the early compared with the late group (Table 2). AKI was severe (stage 2 or 3) on diagnosis day in 977 (60%) in the early group *versus* 11 (22%) in the late group, $p < 0.001$. Among patients diagnosed with stage 1 AKI, 348 (55%) patients with early SA-AKI further progressed to stage 2 or 3 *versus* 5 (13%) in the late group, $p < 0.001$.

AKI diagnosis was based on the sole UO criteria (no sCr rise) in 379 (24%) of early SA-AKI and in 36 (72%) of late SA-AKI, $p < 0.001$.

Outcomes

Among study patients, 224 (12%) died within 7 days of ICU admission (218 in the early-AKI group, 3 in the late AKI group, and 3 without AKI (after day 2)). A further 83 (5%) patients died during the rest of their ICU stay (overall ICU mortality rate 17%).

Compared with early SA-AKI patients, those with late SA-AKI had a similar in-hospital (24% *vs.* 26%, $p = 0.75$) and 90-day mortality (30% *vs.* 33%, $p = 0.67$). In addition, patients with late SA-AKI had more renal recovery at ICU discharge compared with those with early SA-AKI (86% *vs.* 66%, $p = 0.0042$) and required less RRT during their ICU stay (4% *vs.* 23%, $p < 0.001$) (Table 2).

Compared with patients *without* AKI, those with late SA-AKI had higher in-hospital mortality (24% *vs.* 5%, $p < 0.001$) and 90-day mortality rate (30% *vs.* 8%, $p < 0.001$) and a longer ICU stay (6 [4–9] *vs.* 2 [1–4] days, $p < 0.001$), despite similar characteristics at baseline (except for more chronic heart failure among late SA-AKI patients 28% *vs.* 14%, $p = 0.018$). Patients with early SA-AKI had more comorbidities and were more severe at ICU admission as

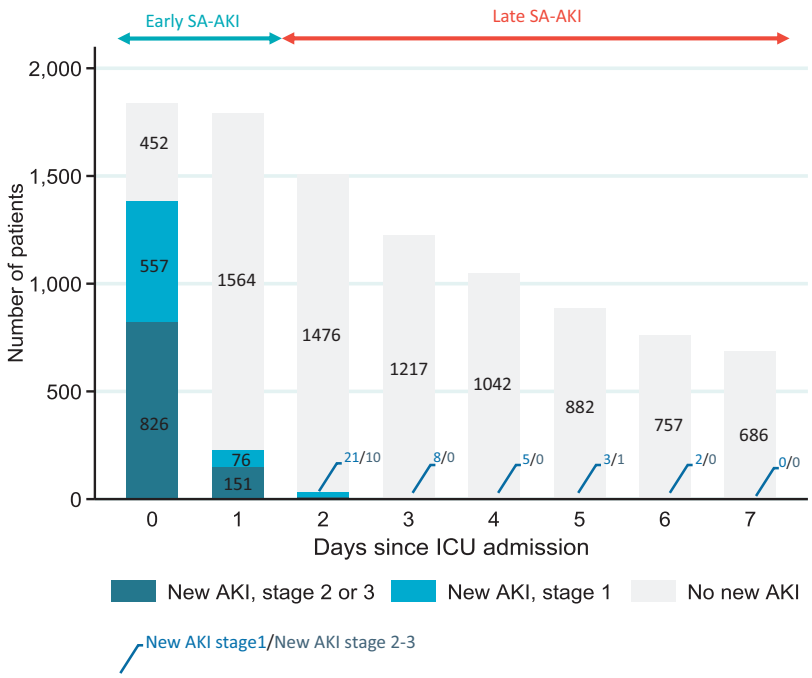

Fig. 2. Incidence of SA-AKI within the first seven days of ICU admission.
AKI diagnosis and stage at diagnosis according to KDIGO criteria.
SA-AKI: sepsis-associated acute kidney injury, ICU: intensive care unit.

Table 1
Characteristics of patients with SA-AKI.

	Early SA-AKI (n = 1610)	Late SA-AKI (n = 50)	*p*-value
Patients' characteristics			
Age, years	69 [58–76]	59 [49–70]	<0.001
Sex, male	1078 (67%)	29 (58%)	0.19
Body mass index, kg/m^2	25 [22–29]	22 [19–25]	<0.001
Charlson score	5 [3–7]	3 [1–5]	<0.001
Chronic kidney disease (GFR<30 mL/min)	315 (20%)	3 (6%)	0.016
Baseline sCr (µmol/L)	71 [52–102]	58 [48–73]	0.002
Chronic heart failure	483 (30%)	14 (28%)	0.76
Diabetes	432 (27%)	7 (14%)	0.043
Hypertension	835 (52%)	14 (28%)	<0.001
COPD	276 (17%)	6 (12%)	0.34
Onco-hematological diseases	534 (33%)	19 (38%)	0.48
Stay characteristics			
Surgical admission	783 (49%)	22 (44%)	0.51
Origin of admission			0.33
Operating room	437 (27%)	9 (18%)	
Emergency room	431 (27%)	11 (22%)	
Intermediate care	357 (22%)	12 (24%)	
Other ICU	225 (14%)	12 (24%)	
Other	157 (10%)	6 (12%)	
Hours since hospital admission	12 [2–141]	30 [3–215]	0.25
Time from hospital admission to ICU admission			0.21
<24 h	919 (57%)	22 (44%)	
24–48 h	110 (7%)	6 (12%)	
48 h–7 d	220 (14%)	7 (14%)	
>7 days	361 (22%)	15 (30%)	
Characteristics at ICU admission			
Noradrenalin, yes	1424 (88%)	35 (70%)	<0.001
Mechanical ventilation, yes	960 (60%)	21 (42%)	0.013
SAPS II score	53 [43–64]	41 [34–50]	<0.001
Leucocytes, G/L	13 [7–20]	12 [6–20]	0.58
Arterial lactate (mmol/L)	2.3 [1.35–4]	1.4 [1–2.68]	<0.001
CRP (mmol/L)	173 [85–289]	140 [90–231]	0.13

Data are presented as median [interquartile range — IQR] for continuous measures, and n (%) for categorical measures. Continuous measures are compared with a Wilcoxon rank-sum test, categorical measures are compared with a Pearson's chi-square test. COPD: chronic obstructive pulmonary disease, GFR: glomerular filtration rate, ICU: intensive care unit.

compared to those without AKI. They also had worse outcomes (see Supplementary file, Table 1 and Table 2).

Sensitivity analyses

As shown in Fig. 4, similar results were obtained when using alternative definitions and time windows for early SA-AKI. Indeed, when only considering sCr to diagnose AKI, irrespective of its severity, 1303 (71%) had early SA-AKI, and 62 (3%) had late SA-AKI. Similarly, when restricting the analyses to patients with severe (Stage ≥2) AKI, 1229 (67%) had early AKI, and 112 (6%) had late AKI.

When considering admission day, day one, and day two to define early SA-AKI (alternative definition 1), early SA-AKI was present in 1641 (89%). Similarly, when considering timing relative to *hospital* admission (alternative definition 2) in patients with ≤24 h between hospital and ICU admission (n = 1016), early SA-AKI was present in 914 (89%). Similarly, as shown in Supplementary Fig. 1, results remained unchanged after the exclusion of patients admitted from another hospital or from an intermediate care unit or those with a hospital stay >48 h before ICU admission. They were also similar in the two periods (<2016 and >2016).

Discussion

Key findings

We conducted a large observational study including patients with sepsis requiring ICU admission, to assess the respective incidence of early *versus* late SA-AKI and to report on patients' characteristics and outcomes. We found that AKI was present on ICU admission or diagnosed within 2 days in almost *all* patients admitted for sepsis. Findings were similar when considering only AKI with sCr rise, severe AKI, or when using slightly different time windows to define early AKI. Compared with early SA-AKI, late SA-AKI was more frequently identified by oliguria and tended to be of lower initial severity. Patients with late SA-AKI had fewer comorbidities and lower severity scores on ICU admission

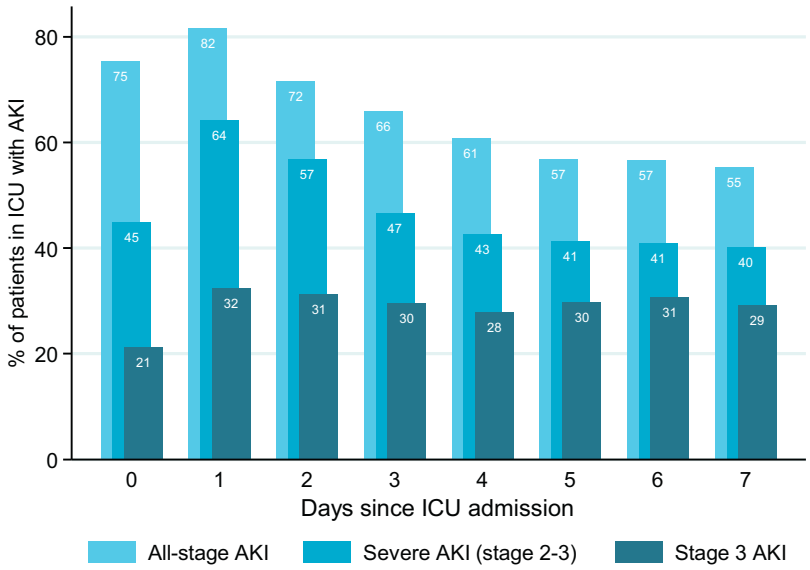

Fig. 3. Prevalence of SA-AKI within the first seven days of ICU admission.
AKI presence and staging according to KDIGO criteria.
SA-AKI: sepsis-associated acute kidney injury, ICU: intensive care unit.

Table 2
Outcomes of patients with SA-AKI and characteristics of AKI episodes.

	Early SA-AKI (n = 1610)	Late SA-AKI (n = 50)	*p*-value
Outcomes			
90-day mortality	529 (33%)	15 (30%)	0.67
In-hospital mortality	419 (26%)	12 (24%)	0.75
ICU mortality	294 (18%)	8 (16%)	0.68
ICU length-of-stay	5 [2–10]	6 [4–9]	0.092
Hospital length-of-stay	22 [9–40]	20 [9–39]	0.83
RRT during ICU stay	376 (23%)	2 (4%)	0.001
Renal recovery at ICU discharge[a]	872 (66%)	36 (86%)	<0.0084
Characteristics of AKI episodes			
Initial AKI stage			<0.001
Stage 1	633 (39%)	39 (78%)	
Stage 2	554 (34%)	10 (20%)	
Stage 3	423 (26%)	1 (2%)	
Criterion diagnosis			<0.001
Serum creatinine	611 (38%)	10 (20%)	
Urine output	379 (24%)	36 (72%)	
Both	620 (39%)	4 (8%)	

Data are presented as median [interquartile range — IQR] for continuous measures, and n (%) for categorical measures. Continuous measures are compared with a Wilcoxon rank-sum test, categorical measures are compared with a Pearson's chi-square test.
ICU: intensive care unit, RRT: renal replacement therapy.
[a] Renal recovery is defined by the absence of AKI based on KDIGO criteria at discharge, in ICU survivors (n = 1358).

compared with those with early SA-AKI. However, the two groups of patients had similar lengths of stay and mortality rates.

Comparison with other studies

Our results are largely comparable to those obtained in a recent multicenter study conducted in Australia which also aimed to compare early and late SA-AKI [18]. In this cohort, compared to ours, patients had lower illness severity and AKI was more frequently diagnosed at stage 1 and based on UO alone. Hence, patients in this cohort might have been included earlier in the course of the disease. However, similar to the present study, the authors observed a very short median (IQR) delay from sepsis to AKI diagnosis, of 0 [0-1] days. Several other studies have reported a high incidence and an early onset of SA-AKI. In a cohort of 33,300 critically ill patients with sepsis, Bagshaw et al. observed that 42% of patients had AKI within 24 h of admission according to the RIFLE definition and averaging UO over 24 h [2]. Similarly, using the KDIGO definition, Poukkanen et al. reported an incidence of SA-AKI of 53.2%, with a median AKI onset of 9 h [19]. The even higher incidence of AKI among sepsis patients observed in our study may be explained by our strict application of the KDIGO criteria and the method used to identify oliguria, which consisted of computing averaged urinary output values over sliding time windows. Previous studies have shown that these two factors may lead to a more frequent diagnosis of AKI as compared with other AKI classifications (such as AKIN or RIFLE) or oliguria definition (using consecutive hours of urine output under the threshold) [20–22]. However, even when only considering sCr for AKI diagnosis, the incidence of SA-AKI in our cohort remained very high.

Compared to late SA-AKI, early SA-AKI was associated with higher disease severity, higher RRT requirement, and lower renal recovery at discharge, but no difference in mortality. Other studies report conflicting results. Some have suggested that late-onset AKI could be associated with mortality while others did not [11,12,23]. In particular, the question of whether early and late SA-AKI are associated with different pathophysiological mechanisms remains unanswered. Data obtained from animal models of SA-AKI suggest that early SA-AKI is not associated with major tissular changes [6]. The timing and determinants of cellular damage remain unclear to this day.

Implications for clinicians and policymakers

The fact that AKI appears almost ubiquitous in the early phase of sepsis requiring ICU admission is consistent with the presence of a common pathophysiological pathway leading to both sepsis and AKI, which might respond to similar therapeutics [24]. However, it also makes AKI-preventive strategies unlikely to be useful, at least if initiated *after* ICU admission. Such strategies should rather be targeting patients in the emergency department, on the ward, or in the operating room if at all [25,26]. In the ICU, future research should rather focus on interventions aiming to improve *recovery* or limit progression from SA-AKI. This is further reinforced by the higher percentage of recovery and the lowest progression rate

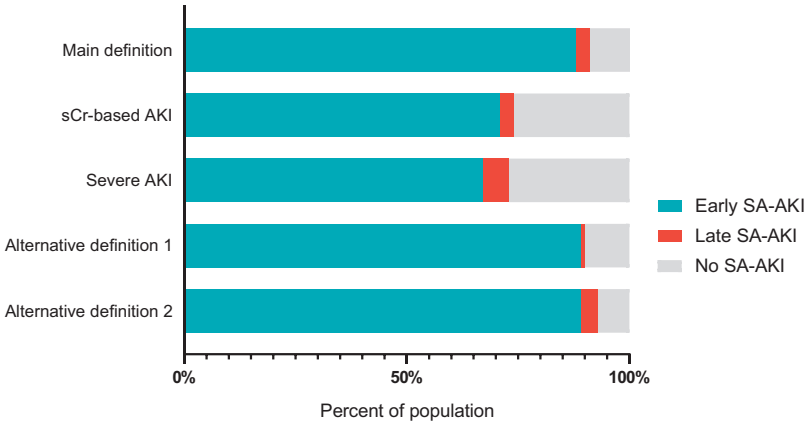

Fig. 4. Incidence of SA-AKI across different definitions and time windows for early SA-AKI.
Main definition for early SA-AKI: any AKI diagnosed on D0 (admission day) or D1.
SCr-based-AKI definition: only AKI with elevated sCr (based on KDIGO definition), and time windows of the main definition apply.
Severe AKI definition: only AKI stage 2 or stage 3 (based on KDIGO definition), time-windows of the main definition apply.
Alternative definition 1 for early SA-AKI: any AKI diagnosed on D0, D1 or D2.
Alternative definition 2 (restricted to patients admitted in the hospital ≤24 h before ICU admission [n = 1016]): The main definition applies with hospital admission instead of ICU admission as T0 (beginning of early time-windows).
AKI: acute kidney injury, SA-AKI: sepsis-associated acute kidney injury, sCr: serum creatinine.

observed in the late group. In addition, as previously suggested, our results highlight the importance of accurate urine output measurement which enabled the identification of AKI earlier in a high percentage of patients, particularly in the late group [13,27]. If the timing of AKI onset does not seem relevant to differentiate phenotypes of AKI associated with outcomes, AKI diagnosis criteria and trajectory could represent alternatives, that should be further investigated.

Strengths and limitations

Our study has several strengths. We used high quality and high granularity data [13]. Indeed, urine output was documented on an hourly basis with a low rate of missing values. This allowed for precise and accurate documentation of oliguria and ultimately the use of unmodified KDIGO criteria to assess the presence of AKI and its severity. Also, we could include more than 1800 patients admitted to a tertiary ICU for sepsis over 10 years, making this study one of the largest cohorts to report on SA-AKI epidemiology.

However, as a monocentric retrospective study, some limitations must be considered. First, the very small number of patients with late SA-AKI limited the relevance of a comparison with those with early SA-AKI; in particular, it did not seem appropriate to perform multivariate models. Second, patients in this cohort had very high severity scores at ICU admission with most having septic shock. Different results might be observed in cohorts with less severe presentation. Third, the ADQI group proposed to consider 48 h from sepsis *onset* (and not ICU admission) to separate early from late SA-AKI. However, sepsis onset is difficult to appreciate with precision. According to international recommendations, we have considered that the onset of sepsis requiring ICU admission occurs usually within hours before ICU admission [15,16]. In our study, the vast majority of patients received vasopressors at ICU admission, suggesting an acute increase in SOFA score ≥2, warranting ICU admission. ICU admission day may therefore correspond to an acceptable surrogate for sepsis onset day. Exclusion of patients admitted from another intensive care unit or hospitalized for more than 48 h did not change our results in sensitivity analyses. Overall, we found that the origin of admission, duration of hospital stay before ICU admission, and admission year had virtually no impact on our main result, further reinforcing our result. Fourth, our definition of early-AKI was based on calendar days and not on 48-h time periods. However, our results were consistent when using slightly modified time windows in sensitivity analyses. Fifth, patients who died or were discharged alive without AKI within 48 h, could not develop late SA-AKI. However, they account for a very small number of patients (4% of all patients). Finally, we have not considered sepsis acquired *while* in ICU. Those patients might be more easily amenable to AKI preventive strategies and should be studied in further studies.

Conclusions

AKI occurs in 90% of critically ill patients admitted with sepsis and almost always within two days of ICU admission. The timing from ICU admission might not be a relevant criterion to distinguish different phenotypes and injury mechanisms of SA-AKI.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Vaud, Switzerland (n°2017-00008,). According to the Swiss Federal Act on Research involving Human Beings (article 34), retrospective utilization of non-genetic health-related personal data was authorized if the patient (or its legal representative) had not expressed wishes of non-participating to clinical research). Due to the retrospective, non-interventional nature of the study, necessity of written informed consent was waived.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Disclosure of interest

The authors have no conflicts of interest to declare in relation to this work.
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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.accpm.2023.101332.

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