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Acute Kidney Injury: Clinical Characteristics and Short-Term Outcomes in 1,519 Patients

Christina Montgomerie[a] Jonas Spaak[b] Marie Evans[c] Stefan H. Jacobson[a]

[a]Division of Nephrology, Department of Clinical Sciences, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden; [b]Division of Cardiology, Department of Clinical Sciences, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden; [c]Department of Renal Medicine, CLINTEC, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

Keywords
Acute kidney injury · Hyperkalemia · Hypokalemia · Inflammation · Malnutrition · Chronic kidney disease · Kidney recovery

Abstract
Introduction: Complex integrated information on disease mechanisms and in-hospital outcomes in mild to moderate acute kidney injury (AKI) is scarce. ***Methods:*** The Stockholm Prospective AKI Cohort Study (SAKIS) included all patients (≥18 years, $n = 1,519$) with community-acquired AKI (KDIGO criteria) admitted to the nephrology ward at Danderyd University Hospital, Stockholm, Sweden, between 2009 and 2018. Detailed laboratory measures were registered. Odds ratio for hypo- and hyperkalemia, recovery of kidney function by 30% and 50%, and in-hospital mortality were assessed by logistic regression analysis. ***Results:*** Factors independently associated with the presence of hyperkalemia at admission were high age, high serum creatinine (sCr), and low C-reactive protein (CRP). Signs of malnutrition, inflammation, and acidosis were seen in 31% of patients. Kidney recovery, defined as a reduction of sCr by 30% in-hospital (63% of all patients), was associated with higher age, female sex, lower body mass index (BMI), higher hemoglobin, and higher CRP. Factors independently associated with mortality (4.4% of patients) were high age, high BMI, and low albumin. ***Conclusion:*** This study provides a detailed description of community-acquired AKI and comprehensive analyses of integrated clinical and laboratory data associated with kidney recovery. Features related to anemia, albuminuria, malnutrition, inflammation, and acidosis associate with partial or moderate short-term recovery of kidney function, with disturbances in potassium homeostasis, and with in-hospital mortality. Future studies are warranted to analyze the long-term consequences of AKI in terms of risk of kidney failure, cardiovascular morbidity, and mortality.

Introduction

Acute kidney injury (AKI) denotes a sudden decrease in kidney function, causing a rapid increase in serum creatinine (sCr) or a decrease in urine output, or both. It was not until 2012 that a general definition of AKI was established by the Kidney Disease: Improving Global Outcomes (KDIGO) AKI Guidelines [1]. AKI is further commonly categorized into prerenal, renal, and postrenal insults depending on the underlying etiology; in addition,

Karger@karger.com
www.karger.com/kdd

Correspondence to:
Christina Montgomerie, christina.montgomerie@ki.se

there is acute on preexisting chronic kidney disease (CKD), here referred to as AKI on CKD. Prerenal and renal AKI account for 60–70% of cases [2]. Even though AKI is both common, seen in up to 16% of all hospital admissions in some series [3], and serious, accounting for an up to fourfold increase in in-hospital mortality [4], many features of its natural history remain undefined and uncertain [5, 6].

The incidence of AKI not requiring dialysis has increased in many countries during the last decades [7, 8]. In part, this may be explained by an aging, more multimorbid population. However, the increased incidence of in-hospital AKI may also reflect a greater awareness of AKI and a lower threshold for AKI diagnosis on hospital admission [9, 10]. In parallel, several studies have reported a concurrent decline in AKI-associated hospital mortality [7, 11, 12].

An association between AKI and poor long-term prognosis, with risks of the development of CKD and the start of renal replacement therapy, is supported by evidence from large systematic reviews [13–15]. However, less is known about the prognostic implications and kidney recovery rates in patients with milder forms of AKI, not being critically ill and not in need of treatment in the intensive care [16]. The duration of AKI has been demonstrated to be of significance; higher mortality rates have been reported with longer duration of mild AKI compared to shorter duration of moderate AKI [17]. Moreover, potassium disorders and their association with different stages of AKI are not well investigated. Recent studies show that higher potassium levels at admission are an independent predictor for severe AKI (stage 3) and death [18, 19]. Although KDIGO AKI guidelines advocate follow-up of AKI patients [1], only a minority see a nephrologist after hospital discharge [20]. There is a need to support clinicians in prioritizing patients with the highest risks and the most modifiable risk factors.

Some previous hospital-based studies of AKI patients may have been confounded by a lack of complete capture of laboratory data; additionally, large registry studies lack information correlating clinical features to specific and integrated data. The aim of this large, single-center study was to, in detail, characterize demographic features and laboratory findings in consecutive patients with AKI treated at a university hospital nephrology clinic, focusing on malnutrition, inflammation, acidosis, and hyperkalemia, and to report clinical and integrated laboratory factors associated with in-hospital kidney recovery and mortality.

Methods

Study Design and Cohort

This is a prospective observational study, the Stockholm Prospective Acute Kidney Injury Cohort Study (SAKIS). All patients (aged 18 or above) with AKI admitted to the Department of Nephrology at Danderyd University Hospital, Stockholm, Sweden, between 2009 and 2018 were eligible. The cohort was considered having community-acquired AKI, as most patients were admitted via the Emergency Department. Patients already dialysis-dependent were excluded, as well as patients who were admitted in the study period but were not yet discharged. Patients were followed until discharge or, when applicable, until death at the ward.

Definition of AKI and Exposures

AKI was confirmed and staged in accordance with KDIGO AKI Guidelines: stage 1: sCr 1.5–1.9 times baseline or increase of sCr ≥26.5 μmol/L; stage 2: sCr 2.0–2.9 times baseline; stage 3: sCr 3 times baseline or sCr increase to ≥353.6 mmol/L or initiation of renal replacement therapy [1], with the exception of time parameters and urine output data. Patients with sCr >130 μmol/L (1.47 mg/dL) on admission without a previously known baseline value were also included. Etiology and type of AKI (prerenal, renal, postrenal, or acute on chronic) were registered, as assessed by the attending senior consultant.

Outcomes

Patients were categorized according to potassium levels at admission: hypokalemia (<3.5 mmol/L), normokalemia (3.5–4.9 mmol/L), mild hyperkalemia (5–5.4 mmol/L), moderate (5.5–5.9 mmol/L), or severe hyperkalemia (≥6 mmol/L), as well as severity stage of AKI, adhering to the KDIGO criteria [21]. Signs of malnutrition/hypoalbuminemia, inflammation, and acidosis were defined as serum albumin <35 g/L, C-reactive protein (CRP) >20 mg/L, bicarbonate <22 mmol/L. CRP >20 mg/L was considered clinically relevant for an inflammatory process. Combinations of these three criteria in total and according to AKI type were also analyzed.

In-hospital sCr decline of at least 30% or 50% from admission was determined as a measure of partial or moderate kidney recovery, mainly in accordance with KDIGO AKI Guidelines (decrease of sCr ≥50% within 7 days) [1, 22] and a recent study by Duff and Murray [23] (decrease of sCr ≥33% within 7 days). Complete kidney recovery was not registered, as patients were generally discharged from the hospital prior to this.

Variables

Upon admission at the nephrology ward, multiple laboratory measures were registered, focusing on aspects of anemia (hemoglobin), acidosis (potassium, standard bicarbonate), electrolyte disturbances (potassium), nutritional status (body mass index (BMI), albumin), inflammation (albumin, CRP, leukocytes), and albuminuria (urine albumin/creatinine ratio [ACR]).

Statistical Analysis

Statistical analyses were performed using IBM SPSS v.27. Descriptive analysis included mean, standard deviation (SD), median values, and interquartile range (IQR) for quantitative variables. Statistical significance was considered at a p value <0.05 and a confidence interval (CI) of 95%. Data comparisons between groups

Table 1. Baseline characteristics, differences between AKI groups

	Prerenal *N* (%)	Renal *N* (%)	Postrenal *N* (%)	AKI on CKD *N* (%)	*p* value χ^{2*}	Total *N* (%)
Patients, *n*	687 (45)	166 (11)	130 (9)	536 (35)	<0.001	1,519 (100)
Female sex	342 (50)	74 (45)	30 (23)	183 (34)	<0.001	629 (41)
AKI stage 1	137 (46)	45 (15)	21 (7)	97 (32)	<0.05	300 (20)
AKI stage 2	103 (54)	21 (11)	12 (6)	56 (29)	<0.05	192 (13)
AKI stage 3	447 (44)	100 (10)	97 (9)	383 (37)	NS	1,027 (68)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	ANOVA	Mean (SD)
Age, years	73 (16)	61 (21)	76 (14)	75 (14)	<0.001[a,b,c]	73 (16)
Previous sCr, µmol/L	103 (50)	112 (58)	120 (74)	188 (107)	<0.001[d,e,c]	136 (87)
sCr admission, µmol/L	354,260)	391 (260)	561 (456)	459 (271)	<0.001[f,c,d]	413 (293)
Systolic BP, mm Hg	125 (24)	142 (25)	141 (27)	132 (25)	<0.001[d,e,f,e,c]	130 (25)
Diastolic BP, mm Hg	72 (14)	80 (14)	78 (15)	74 (14)	<0.001[f,a,e,c]	74 (14)
BMI, kg/m^2	26 (6)	27 (6)	26 (6)	27 (6)	NS	26 (6)
Hemoglobin, g/L	121 (24)	113 (21)	114 (22)	111 (21)	<0.001[d,e,f]	116 (23)
Leukocyte count, ×10^9/L	11.4 (6.2)	11.4 (11.0)	12.9 (16.2)	10.5 (9.3)	0.052[e]	11.2 (9)
Albumin, g/L	30 (7)	28 (7)	29 (6)	29 (6)	<0.01[a]	29 (7)
Potassium, mmol/L	4.4 (0.9)	4.3 (0.7)	4.7 (1.0)	4.7 (0.9)	<0.001[f,d,b,c]	4.5 (0.9)
Bicarbonate, mmol/L	21 (4)	21 (3)	20 (4)	20 (4)	<0.001[d,c]	21 (4)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	ANOVA[§]	Median (IQR)
CRP, mg/L	41 (110)	44 (102)	58 (138)	27 (94)	<0.001[d,e]	74 (110)
ACR,[g] mg/mmol	8 (22)	39 (197)	18 (55)	15 (66)	<0.001[b,c,d,e,f,c]	12 (40)
	N (%)	*N* (%)	*N* (%)	*N* (%)	χ^2	
CRP >20 mg/L	419 (65)	94 (66)	89 (72)	287 (58)	<0.01	889 (63)
Albumin <35 g/L	283 (50)	58 (48)	60 (57)	293 (65)	<0.05	694 (56)
Standard bicarbonate <22 mmol/L	479 (74)	117 (82)	102 (83)	404 (80)	<0.001	1,102 (78)

* χ^2 analysis. [§]ANOVA based on logarithmic values. Post hoc analyses using the Tukey *H* test ($p < 0.05$). [a] Pre verus renal. [b] Post versus renal. [c] Renal versus AKI on CKD. [d] Pre versus AKI on CKD. [e] Post versus AKI on CKD. [f] Pre versus postrenal. [g] Urine albumin/creatinine ratio.

were done using parametric and nonparametric methods as appropriate. χ^2 test or Fisher's exact test were used for categorical variables and the Student's *t* test or Mann-Whitney U test for continuous variables. ANOVA and the Tukey *H* test were used for comparisons between groups. Due to the non-normal distribution of CRP and ACR, logarithmic values were used. Linear correlation analyses were made using Pearson's and Spearman correlation coefficients as appropriate.

Unadjusted multiple logistic regression analysis and analyses with conditional backward selection were used to determine variables associated with the occurrence of hyperkalemia (≥5.0 mmol/L) as well as an in-hospital decrease of sCr of at least 30% or 50%, respectively. Data were expressed as odds ratio (OR) and 95% CI.

Ethical Approval

Observational data were collected, pseudonymized, and analyzed by group rather than an individual basis, without exposing individual patients. The study was approved by the Swedish Ethical Review Authority.

Results

Between January 2009 and December 2018, 1,861 eligible patients with suspected AKI were registered. Of these, 63 patients were excluded due to reassessment of their preliminary AKI diagnosis, and a further 279 since they did not fulfill the KDIGO AKI criteria of 2012. The final cohort consisted of 1,519 patients, with a mean age of 73 years (SD 16), and 41% of the patients were female. The mean sCr at admission was 413 µmol/L (SD 293). AKI stages 1–2 were seen in 33% of patients. Most patients had prerenal AKI. In the AKI on CKD group, prerenal causes likewise dominated (82%), whereas 13% had a postrenal cause. Table 1 shows baseline demographic data, clinical, and laboratory findings stratified by AKI type.

Table 2. Hypo- normo-, mild hyper-, moderate hyper-, and severe hyperkalemia in patients with AKI

	Hypokalemia <3.5 mmol/L, *N* (%)	Normokalemia 3.5–4.9 mmol/L, *N* (%)	Mild hyperkalemia 5.0–5.4 mmol/L, *N* (%)	Moderate hyperkalemia 5.5–5.9 mmol/L, *N* (%)	Severe hyperkalemia ≥6.0 mmol/L, *N* (%)	*p* value χ^{2}*
Total	150 (11)	850 (60)	215 (15)	118 (8)	95 (7)	<0.001
AKI stage 1	31 (11)	173 (63)	45 (16)	16 (6)	11 (4)	<0.001
AKI stage 2	16 (9)	105 (57)	34 (19)	16 (9)	13 (7)	<0.001
AKI stage 3	103 (11)	572 (59)	136 (14)	86 (9)	71 (7)	<0.001
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	ANOVA
Age, years	67 (17)	72 (17)	75 (13)	76 (11)	75 (13)	<0.001[a,b,c,d]
Previous sCr, µmol/L	135 (108)	129 (84)	143 (91)	150 (81)	137 (71)	NS
sCr admission, µmol/L	388 (281)	372 (258)	454 (299)	522 (335)	592 (455)	<0.001[c,d,e,f,g,h]
BMI, kg/m^2	26 (6)	26 (6)	27 (6)	26 (6)	27 (6)	NS
Hemoglobin, g/L	119 (22)	117 (23)	114 (22)	111 (24)	116 (22)	<0.05[c]
Bicarbonate, mmol/L	22 (5)	21 (4)	19 (4)	17 (4)	17 (4)	<0.001[b,c,d,e,f,g,h,i]
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	ANOVA[§]
CRP, mg/L	54 (141)	40 (111)	30 (113)	28 (84)	16 (59)	<0.001[b,c,d]
ACR, mg/mmol	14 (37)	13 (43)	15 (57)	11 (68)	8 (30)	NS

* χ^{2} analysis. [§] ANOVA based on logarithmic values. Post hoc using the Tukey H test ($p < 0.05$): [a] Hypo versus normo. [b] Hypo versus mild. [c] Hypo versus moderate. [d] Hypo versus severe. [e] Normo versus mild. [f] Normo versus moderate. [g] Normo versus severe. [h] Mild versus moderate. [i] Mild versus severe. [j] Moderate versus severe.

Table 3. Unadjusted logistic regression analysis of risk of hyperkalemia (*K* ≥5 mmol/L) and logistic regression following conditional backward selection

	Unadjusted logistic regression (hyperkalemia)			Conditional backward selection (hyperkalemia)		
	p value	OR unadjusted	95% CI	*p* value	OR adjusted	95% CI
Age (years)	<0.001	1.019	1.012–1.027	<0.01	1.024	1.013–1.035
Female sex	NS	0.921	0.743–1.140	–	–	–
BMI (kg/m^2)	NS	1.005	0.986–1.025	–	–	–
sCr admission (µmol/L)	<0.001	1.001	1.001–1.002	<0.01	1.001	1.000–1.001
Hemoglobin (g/L)	<0.01	0.993	0.988–0.998	–	–	–
Leukocyte count (×10^9/L)	NS	0.992	0.978–1.006	–	–	–
CRP (mg/L)	<0.001	0.998	0.997–0.999	–	–	–
St bicarbonate (mmol/L)	<0.001	0.816	0.789–0.842	<0.001	0.822	0.788–0.858
ACR (mg/mmol)	<0.01	1.001	1.000–1.001	<0.01	1.001	1.000–1.001
AKI stage 1	Ref					
AKI stage 2	0.061	1.475	0.983–2.214	NS	1.479	0.878–2.493
AKI stage 3	NS	1.23	0.91–1.663	NS	0.87	0.585–1.295

Table 4. Patients with hypoalbuminemia, acidosis, and inflammation alone or in combinations, characteristics, and outcomes (30% and 50% decrease in sCr in hospital)

	Criteria, *n*				*p* value[c]
	0[a], mean (SD)	1, mean (SD)	2, mean (SD)	3[b], mean (SD)	
Length of stay, days	5.3 (4.5)	6.8 (4.9)	8.7 (6.7)	9.6 (7.4)	<0.001
Age, years	64 (20)	70 (19)	73 (15)	75 (13)	<0.001
SCr previous, µmol/L	114 (64)	124 (86)	141 (94)	140 (81)	0.016
SCr admission, µmol/L	276 (142)	332 (233)	417 (316)	518 (331)	<0.001
SCr discharge, µmol/L	166 (112)	205 (159)	237 (208)	280 (248)	<0.001
Hemoglobin, g/L	133 (27)	124 (22)	114 (23)	111 (21)	<0.001
Potassium, mmol/L	4.3 (0.7)	4.6 (1.0)	4.4 (0.9)	4.7 (0.9)	<0.001
Albumin, g/L	39 (4.0)	34 (6.3)	28 (5.3)	26 (4.7)	<0.001
CRP, mg/L	7.2 (5.9)	20 (40)	85 (98)	124 (101)	<0.001
St bicarbonate, mmol/L	24 (2.2)	22 (4.0)	21 (4.2)	18 (2.8)	<0.001
	N (%)	*N* (%)	*N* (%)	*N* (%)	*p* value[d]
30% decrease in sCr in hospital	160 (53)	358 (59)	269 (61)	841 (58)	NS
50% decrease in sCr in hospital	77 (26)	201 (33)	183 (41)	492 (34)	<0.001

[a] Number of criteria fulfilled. 0 = no hypoalbuminemia, no acidosis, and no inflammation. [b] All three criteria. Patients with hypoalbuminemia, acidosis, and inflammation. [c] ANOVA. [d] χ^2 analysis.

Potassium Disturbances

At admission, 30% of patients had hyperkalemia (≥5 mmol/L) and 11% had hypokalemia (<3.5 mmol/L). The potassium levels were similarly distributed in the different AKI stages (Table 2). Mean bicarbonate levels were within the normal range in the hypokalemic group (22 mmol/L, SD 5). Patients with hyperkalemia more frequently had acidosis, higher sCr at admission, and lower albuminuria (Table 2). Linear correlation analysis showed a significant correlation between serum potassium and bicarbonate levels ($r = -0.38$, $p < 0.001$). When stratified by AKI type, sCr at admission was higher in the hyperkalemic groups of prerenal AKI, postrenal AKI, and AKI on CKD (online suppl. Table I; for all online suppl. material, see www.karger.com/doi/10.1159/000527299). Factors independently associated with hyperkalemia were higher age, higher sCr, lower CRP, and acidosis (lower standard bicarbonate) (Table 3).

Malnutrition, Inflammation, and Acidosis

At admission, 56% of patients had hypoalbuminemia and 78% had acidosis (Table 1). A linear correlation was found between albumin and CRP (Spearman correlation, $r_s = -0.46$; $p < 0.001$).

Furthermore, using the criteria for malnutrition, inflammation, and acidosis, most patients (94%) had at least one criterion, and close to one third had all three criteria fulfilled (online suppl. Table II). Patients with a higher incidence of malnutrition/inflammation/acidosis were older, had longer hospital stay, had higher sCr at admission and discharge, and had lower hemoglobin (Table 4).

In-Hospital Kidney Recovery

In our cohort, 63% of all patients had a sCr decrease of at least 30% at discharge, while 38% had a sCr decrease of at least 50%. The chance of partial or moderate kidney recovery was largest in patients with prerenal and postrenal AKI compared to renal AKI and AKI on CKD (Fig. 1). When stratifying the cohort by a sCr decrease of at least 30%, a higher CRP at admission was associated with a higher chance of kidney recovery (Table 5). Furthermore, higher hemoglobin, lower ACR, and lower BMI were similarly associated with improved kidney recovery (Table 5).

Variables independently associated with partial kidney recovery (sCr decrease by 30%) were higher age, female sex, lower BMI, higher sCr at admission, higher hemoglobin, higher CRP, and AKI stage 2 (compared to AKI stage 1) (Table 6). Variables associated with moderate kidney recovery (sCr decrease by 50%) were the same as above, with the addition of lower ACR (online suppl. Table III).

In-Hospital Mortality

In-hospital mortality was low at 4.4% (online suppl. Table IV). Mortality was slightly higher among patients

Table 5. Characteristics of AKI patients with a s-creatinine decrease ≥30% or not at discharge from hospital

	sCr decrease ≥30%, *N* (%)	sCr decrease <30%, *N* (%)	*p* value[a]
Patients, *N*	958 (63)	558 (37)	<0.001
Female sex	409 (43)	219 (39)	NS
In-hospital death	14 (1.7)	42 (9)	<0.001
AKI stage 1	173 (18)	127 (23)	<0.01
AKI stage 2	139 (15)	53 (10)	<0.01
AKI stage 3	646 (67)	378 (68)	<0.01
	Mean (SD)	Mean (SD)	
Age, years	74 (15)	71 (17)	<0.01
Length of stay, days	8 (6)	8 (7)	NS
BMI, kg/m^2	26 (6)	27 (6)	<0.01
Hemoglobin, g/L	119 (23)	111 (21)	<0.001
Leukocyte count, ×10^9/L	11.6 (9.1)	10.6 (9.2)	<0.05
Albumin, g/L	30 (6)	29 (7)	<0.05
Potassium, mmol/L	4.5 (1.0)	4.5 (0.8)	NS
St bicarbonate, mmol/L	20 (4)	21 (4)	NS
	Median (IQR)	Median (IQR)	*p* value[b]
CRP, mg/L	42 (121)	26 (88)	<0.001
ACR, mg/mmol	10 (25)	30 (127)	<0.001

[a] χ^2 analysis. [b] Student's *t* test is based on logarithmic values.

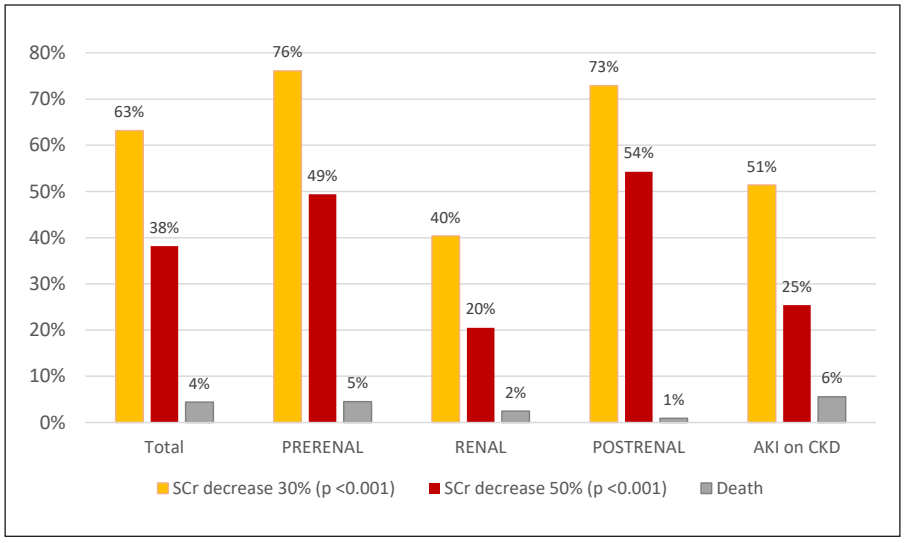

Fig. 1. Percent patients with in-hospital partial (s-creatinine decrease by ≥30%) or moderate kidney recovery (≥50% decrease)*, and in-hospital mortality¶. *The difference in sCr decrease (by 30% or 50%) between AKI groups was statistically significant. ¶Death was not registered in all patients (*N* = 1,292).

with prerenal AKI or AKI on CKD (*n* = 27 [5%] and *n* = 26 [6%]) (Fig. 1). Deceased patients were older, had lower blood pressure, lower hemoglobin, and lower albumin and bicarbonate at admission compared to survivors (online suppl. Table IV). Furthermore, patients with an increased risk of mortality more often had two or three criteria of malnutrition, inflammation, and acidosis (online suppl. Table IV). In logistic regression analysis, higher age, higher BMI, and lower plasma albumin were independently associated with the risk of in-hospital mortality, but not AKI stage (Table 7).

Table 6. Unadjusted logistic regression analysis of partial kidney recovery (≥30% sCr decrease) in AKI patients and logistic regression following conditional backward selection

	Unadjusted logistic regression (≥30% sCr decrease)			Conditional backward selection (≥30% sCr decrease)		
	p value	OR unadjusted	95% CI	*p* value	OR adjusted	95% CI
Age (years)	<0.01	1.01	1.004–1.016	<0.01	1.011	1.003–1.019
Female sex	<0.05	1.269	1.047–1.537	<0.01	1.372	1.030–1.828
BMI (kg/m^2)	<0.01	0.971	0.954–0.989	<0.01	0.968	0.947–0.991
sCr admission (μmol/L)	<0.001	1.001	1.000–1.001	<0.001	1.002	1.001–1.002
Hemoglobin (g/L)	<0.001	1.013	1.008–1.017	<0.001	1.024	1.018–1.031
Leukocyte count (×10^9/L)	<0.01	1.022	1.006–1.038	–	–	–
CRP (mg/L)	<0.001	1.003	1.001–1.004	<0.001	1.003	1.001–1.004
Potassium (mmol/L)	NS	1.063	0.954–1.185	–	–	–
Albumin (g/L)	<0.05	1.018	1.001–1.035			
St bicarbonate (mmol/L)	0.072	0.977	0.952–1.002	–	–	–
ACR (mg/mmol)	<0.001	0.999	0.998–0.999	<0.01	0.999	0.999–1.000
AKI stage 1	*Ref*					
AKI stage 2	<0.01	1.925	1.3–2.85	<0.05	1.784	1.077–2.955
AKI stage 3	NS	0.926	0.72–1.19	NS	0.842	0.603–1.176

Table 7. Unadjusted logistic regression analysis of in-hospital mortality in patients with AKI and logistic regression following conditional backward selection

	Unadjusted logistic regression in-hospital mortality			Conditional backward selection in-hospital mortality		
	p value	OR unadjusted	95% CI	*p* value	OR adjusted	95% CI
Age (years)	<0.001	1.059	1.032–1.087	<0.001	1.074	1.036–1.114
Female sex	NS	0.781	0.448–1.362	–	–	–
BMI (kg/m^2)	NS	1.018	0.97–1.07	<0.05	1.062	1.01–1.117
sCr admission (μmol/L)	NS	1.000	1.000–1.001	–	–	–
Hemoglobin (g/L)	<0.05	0.987	0.975–1.000	–	–	–
Leukocyte count (×10^9/L)	NS	1.002	0.973–1.032	–	–	–
CRP (mg/L)	NS	1.001	0.998–1.004	–	–	–
Potassium (mmol/L)	NS	1.200	0.893–1.612	–	–	–
Albumin (g/L)	<0.001	0.895	0.857–0.935	<0.01	0.915	0.869–0.963
St bicarbonate (mmol/L)	<0.01	0.899	0.841–0.962	0.066	0.925	0.851–1.005
ACR (mg/mmol)	NS	1.000	0.999–1.001	–	–	–
AKI stage 1	*Ref*					
AKI stage 2	NS	0.48	0.169–1.358	–	–	–
AKI stage 3	NS	0.807	0.441–1.476	–	–	–
Risk of in-hospital mortality in AKI patients with 0, 1, 2 criteria in comparison to patients with both hypoalbuminemia, acidosis, and inflammation						
0 criteria[a]	<0.001	0.277	0.14–0.547	–	–	–
1 criterion	0.005	0.249	0.096–0.65	–	–	–
2 criteria	0.090	0.176	0.024–1.311	–	–	–
3 criteria[b]	<0.001			–	–	–

[a] Number of criteria fulfilled. 0 = no hypoalbuminemia, no acidosis, and no inflammation. [b] All three criteria. Patients with both hypoalbuminemia (<35 g/L), acidosis (standard bicarbonate <22 mmol/L), and inflammation (CRP >20 mg/L).

Discussion

This is the first report from the SAKIS cohort. In this large, prospective observational study of AKI on hospital admission, we found that factors related to anemia, albuminuria, malnutrition, inflammation, and acidosis separately and in combination were associated with partial or moderate recovery of renal function, with disturbances in potassium homeostasis, and with in-hospital mortality.

There are abundant registry data on the short- and long-term consequences of severe acquired AKI in critically ill patients [13–16], but several gaps in our understanding of disease mechanisms and outcomes in milder AKI in patients not in need of intensive care remain. One important problem in many previous studies was the availability of clinical and laboratory data interrelating several features associated with AKI. Results obtained from large registries and consolidated health care systems often encompass information from one or few laboratory analyses, most often baseline and peak values of sCr [24], whereas data on more complex integrated information on impaired kidney function, including anemia, inflammation, malnutrition, acidosis, hypo- or hyperkalemia, and albuminuria, are missing. Also, the interpretation of results may be biased by residual confounding due to imperfect assessment of the severity of illness. Furthermore, there is scarce multifaceted information in the literature on the short-term implications of milder forms of AKI, not demanding intensive care. The SAKIS study focuses on such information.

In the present study, we demonstrate significant differences in laboratory findings between patients admitted because of clinical signs and symptoms who were judged to have prerenal, renal, postrenal, or AKI on CKD at discharge. The highest hemoglobin at admission was observed in the patients with prerenal AKI, the highest sCr, and CRP in postrenal AKI. Albuminuria and hypoalbuminemia were more often present in renal AKI patients, while patients with AKI on CKD more often were acidotic.

Potassium disturbances in AKI and CKD are serious and potentially harmful, but also modifiable by measures such as correction of acidosis, dietary restrictions, and use of potassium binders [21]. Hypokalemia has been less examined than hyperkalemia in CKD and AKI, but observational studies indicate that the mortality risk might be higher with hypokalemia than with hyperkalemia [21, 25, 26]. In our study, 30% of AKI patients had hyperkalemia on admission, of which 50% had moderate or severe hyperkalemia. Additionally, 11% had hypokalemia. Patients with moderate or severe hyperkalemia had significantly higher sCr and lower standard bicarbonate at admission, the latter in all types of AKI. Furthermore, the occurrence of hyperkalemia in AKI was independently associated with high age, high sCr, low standard bicarbonate, and low CRP at admission. Also, high potassium was associated with better kidney recovery (at least a 50% decrease in sCr) but not with in-hospital mortality.

Previous retrospective and observational studies have shown that acute hyperkalemia is associated with more severe forms of AKI and with higher mortality [19, 25, 27]. Our findings support studies indicating hyperkalemia being an early sign of AKI, as well as being an indicator of severity, especially in combination with other risk factors such as high age and acidosis. Moreover, hypokalemia is common in mild to moderate AKI and needs to be explored more in relation to the severity and outcomes of AKI.

In the present study, 82% of patients with AKI had hypoalbuminemia at admission, being most common in patients with renal AKI, and associated with signs of acute inflammation. Hypoalbuminemia in AKI and CKD may be a consequence of albuminuria, malnutrition, or inflammation and is associated with an increased mortality risk [28–31]. Albuminuria is associated with an increased risk of long-term progression of kidney failure, cardiovascular complications, and mortality in CKD [32, 33]. Metabolic acidosis is frequently observed both in patients with AKI and CKD and is linked to protein-energy malnutrition and inflammation, often designated the malnutrition inflammation complex syndrome (MICS), which relates to the risk of mortality in CKD [29, 34, 35]. These complex relationships have been less studied in patients with AKI, but some reports have shown that hypoalbuminemia, inflammation and malnutrition are risk factors for mortality also in AKI [30, 36–38]. In the present study, these modifiable parameters are associated separately and in combination with length of stay and short-term outcomes (partial kidney recovery and in-hospital mortality), indicating that early focused therapeutic measures may result in positive short-term effects. These issues warrant future prospective investigations.

In-hospital mortality was low in patients with AKI stages 1–2 in the present study. Patients who died had lower blood pressure, lower hemoglobin, and plasma albumin than those who survived, indicating cardiovascular instability at admission. This has similarly been demonstrated in other cohorts with severe AKI [38–40], but not so much in AKI patients treated at a nephrology ward. Furthermore, AKI patients with more laboratory signs of

malnutrition, inflammation, and acidosis had a higher risk of in-hospital mortality in our study, which accords with long-term outcomes in patients with CKD.

Treatment targets in AKI focus on reducing the risk of acute hemodynamic and infectious complications and to restore kidney function and reduce in-hospital mortality. In the present study, patients with a 30–50% reduction in sCr in hospital were mostly in the prerenal and postrenal AKI groups. Factors associated with improved kidney recovery in the hospital included laboratory signs of hemoconcentration and inflammation at admission in combination with a low ACR. The latter observation is a new finding and accords with the clinical interpretation of patient signs and symptoms.

The present study has several strengths. The careful design of the SAKIS study protocol enabled the identification and enrollment of all patients fulfilling the KDIGO AKI criteria in a large, regional hospital. Furthermore, clinical and laboratory data were collected according to prespecified systematic protocols, enabling the integration of complex laboratory findings in the analyses. Almost all patients underwent a kidney ultrasound. Classification of etiology, AKI type, and severity were made by senior nephrology consultants unaware of the study hypothesis. We present detailed integrated laboratory data focusing on determinants of in-hospital outcomes and features that influence recovery of kidney function, in-hospital mortality, and the occurrence of hypo- and hyperkalemia in patients with AKI in a nephrology ward. This comprehensive "real world data" provides novel, extensive information on each patient and, as such, becomes unique and representative as opposed to limited and more commonly used register data.

The study has limitations. We do not have information on whether patients have had previous AKI episodes. Also, we lack detailed information on patients' symptoms, urine volume status, and medication at admittance, as well as changes in prescriptions during hospital stay. Presently, we do not have information on long-term outcomes, but such data are currently collected and will later be described.

In conclusion, factors related to anemia, albuminuria, malnutrition, inflammation, and acidosis separately and in combination are associated with short-term recovery of kidney function, disturbances in potassium homeostasis, and in-hospital mortality in patients with AKI at a nephrology ward. Future studies are warranted to analyze the long-term consequences in terms of risk of kidney failure, cardiovascular morbidity, and mortality.

Statement of Ethics

This study protocol was reviewed and approved by the Swedish Ethical Review Authority (approval number 2020-00144). Written informed consent was not deemed necessary as the study was based on anonymized register data.

Conflict of Interest Statement

Lecture fees: Astra Zeneca (Jonas Spaak, Marie Evans, Stefan H. Jacobson). Astellas, Fresenius Medical Care (Marie Evans, Stefan H. Jacobson). Vifor Pharma (Jonas Spaak, Marie Evans). Bayer, Boehringer Ingelheim, NovoNordisk (Jonas Spaak). Baxter (Marie Evans). Advisory board: Astra Zeneca (Jonas Spaak, Marie Evans, Stefan H. Jacobson). Astellas, Vifor Pharma (Marie Evans, Stefan H. Jacobson). NovoNordisk (Jonas Spaak).

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Author Contributions

Christina Montgomerie: main contribution to data collection and preparation, statistical analyses, and manuscript writing. Jonas Spaak, Marie Evans, and Stefan H. Jacobson: contribution to statistical analyses and manuscript writing.

Data Availability Statement

All data analyzed from this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

References

1 Kidney Disease. Improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practical guideline for acute kidney. Kidney Int Suppl. 2012 Mar:1–138.
2 Rahman M, Shad F, Smith MC. Acute kidney injury: a guide to diagnosis and management. Am Fam Physician. 2012;86(7):631–9.
3 Sawhney S, Marks A, Fluck N, Levin A, Prescott G, Black C. Intermediate and long-term outcomes of survivors of acute kidney injury episodes: a large population-based cohort study. Am J Kidney Dis. 2017;69(1):18–28.
4 Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol. 2005;16(11):3365–70.

5 Rifkin DE, Coca SG, Kalantar-Zadeh K. Does AKI truly lead to CKD? J Am Soc Nephrol. 2012;23(6):979–84.
6 Hsu CY. Yes, AKI truly leads to CKD. J Am Soc Nephrol. 2012;23(6):967–9.
7 Waikar SS, Curhan GC, Wald R, McCarthy EP, Chertow GM. Declining mortality in patients with acute renal failure, 1988 to 2002. J Am Soc Nephrol. 2006;17(4):1143–50.
8 Bagshaw SM, George C, Bellomo R. Changes in the incidence and outcome for early acute kidney injury in a cohort of Australian intensive care units. Crit Care. 2007;11(3):R68.
9 Hobbs H, Bassett P, Wheeler T, Bedford M, Irving J, Stevens PE, et al. Do acute elevations of serum creatinine in primary care engender an increased mortality risk? BMC Nephrol. 2014;15(1):206.
10 Sawhney S, Fluck N, Fraser SD, Marks A, Prescott GJ, Roderick PJ, et al. KDIGO-based acute kidney injury criteria operate differently in hospitals and the community-findings from a large population cohort. Nephrol Dial Transplant. 2016;31(6):922–9.
11 Kolhe NV, Muirhead AW, Wilkes SR, Fluck RJ, Taal MW. The epidemiology of hospitalised acute kidney injury not requiring dialysis in England from 1998 to 2013: retrospective analysis of hospital episode statistics. Int J Clin Pract. 2016;70(4):330–9.
12 Xue JL, Daniels F, Star RA, Kimmel PL, Eggers PW, Molitoris BA, et al. Incidence and mortality of acute renal failure in Medicare beneficiaries, 1992 to 2001. J Am Soc Nephrol. 2006;17(4):1135–42.
13 Coca SG, Yusuf B, Shlipak MG, Garg AX, Parikh CR. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. Am J Kidney Dis. 2009;53(6):961–73.
14 Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. Kidney Int. 2012;81(5):442–8.
15 Sawhney S, Mitchell M, Marks A, Fluck N, Black C. Long-term prognosis after acute kidney injury (AKI): what is the role of baseline kidney function and recovery? A systematic review. BMJ Open. 2015;5(1):e006497.
16 Forni LG, Darmon M, Ostermann M, Oudemans-van Straaten HM, Pettilä V, Prowle JR, et al. Renal recovery after acute kidney injury. Intensive Care Med. 2017;43(6):855–66.
17 Coca SG, King JT Jr, Rosenthal RA, Perkal MF, Parikh CR. The duration of postoperative acute kidney injury is an additional parameter predicting long-term survival in diabetic veterans. Kidney Int. 2010;78(9):926–33.
18 Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, et al. AKI in hospitalized patients with COVID-19. J Am Soc Nephrol. 2021;32(1):151–60.
19 Chen DN, Du J, Xie Y, Li M, Wang RL, Tian R. Relationship between early serum sodium and potassium levels and AKI severity and prognosis in oliguric AKI patients. Int Urol Nephrol. 2021;53(6):1171–87.
20 Siew ED, Peterson JF, Eden SK, Hung AM, Speroff T, Ikizler TA, et al. Outpatient nephrology referral rates after acute kidney injury. J Am Soc Nephrol. 2012;23(2):305–12.
21 Clase CM, Carrero JJ, Ellison DH, Grams ME, Hemmelgarn BR, Jardine MJ. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2020;97(1):42–61.
22 Chawla LS, Bellomo R, Bihorac A, Goldstein SL, Siew ED, Bagshaw SM. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nat Rev Nephrol. 2017;13(4):241–57.
23 Duff S, Murray PT. Defining early recovery of acute kidney injury. Clin J Am Soc Nephrol. 2020;15(9):1358–60.
24 Huang L, Xue C, Kuai J, Ruan M, Yang B, Chen X, et al. Clinical characteristics and outcomes of community-acquired versus hospital-acquired acute kidney injury: a meta-analysis. Kidney Blood Press Res. 2019;44(5):879–96.
25 Ravioli S, Pluess E, Funk GC, Walter P, Schwarz C, Exadaktylos AK, et al. Dyskalemias in patients with acute kidney injury presenting to the emergency department are common and independent predictors of adverse outcome. Int J Clin Pract. 2021;75(1):e13653.
26 Luo J, Brunelli SM, Jensen DE, Yang A. Association between serum potassium and outcomes in patients with reduced kidney function. Clin J Am Soc Nephrol. 2016;11(1):90–100.
27 Plakht Y, Gad Saad SN, Gilutz H, Shiyovich A. Potassium levels as a marker of imminent acute kidney injury among patients admitted with acute myocardial infarction. Soroka Acute Myocardial Infarction II (SAMI-II) Project. Int J Cardiol. 2021;322:214–9.
28 Jagadeswaran D, Indhumathi E, Hemamalini AJ, Sivakumar V, Soundararajan P, Jayakumar M. Inflammation and nutritional status assessment by malnutrition inflammation score and its outcome in pre-dialysis chronic kidney disease patients. Clin Nutr. 2019;38(1):341–7.
29 Kraut JA, Madias NE. Metabolic acidosis of CKD: an update. Am J Kidney Dis. 2016;67(2):307–17.
30 Shao M, Wang S, Parameswaran PK. Hypoalbuminemia: a risk factor for acute kidney injury development and progression to chronic kidney disease in critically ill patients. Int Urol Nephrol. 2017;49(2):295–302.
31 Amdur RL, Feldman HI, Gupta J, Yang W, Kanetsky P, Shlipak M, et al. Inflammation and progression of CKD: the CRIC study. Clin J Am Soc Nephrol. 2016;11(9):1546–56.
32 Lambers Heerspink HJ, Gansevoort RT. Albuminuria is an appropriate therapeutic target in patients with CKD: the pro view. Clin J Am Soc Nephrol. 2015;10(6):1079–88.
33 Hallan SI, Matsushita K, Sang Y, Mahmoodi BK, Black C, Ishani A, et al. Age and association of kidney measures with mortality and end-stage renal disease. JAMA. 2012;308(22):2349–60.
34 Hu J, Wang Y, Geng X, Chen R, Xu X, Zhang X, et al. Metabolic acidosis as a risk factor for the development of acute kidney injury and hospital mortality. Exp Ther Med. 2017;13(5):2362–74.
35 Kalantar-Zadeh K, Mehrotra R, Fouque D, Kopple JD. Metabolic acidosis and malnutrition-inflammation complex syndrome in chronic renal failure. Semin Dial. 2004;17(6):455–65.
36 Gameiro J, Marques F, Lopes JA. Long-term consequences of acute kidney injury: a narrative review. Clin Kidney J. 2021;14(3):789–804.
37 Chawla LS, Amdur RL, Shaw AD, Faselis C, Palant CE, Kimmel PL. Association between AKI and long-term renal and cardiovascular outcomes in United States veterans. Clin J Am Soc Nephrol. 2014;9(3):448–56.
38 Li C, Xu L, Guan C, Zhao L, Luo C, Zhou B, et al. Malnutrition screening and acute kidney injury in hospitalised patients: a retrospective study over a 5-year period from China. Br J Nutr. 2020;123(3):337–46.
39 Hoste EAJ, Bagshaw SM, Bellomo R, Cely CM, Colman R, Cruz DN, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med. 2015;41(8):1411–23.
40 Singbartl K, Kellum JA. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. Kidney Int. 2012;81(9):819–25.