·TOPIC ON KIDNEY DISEASES· ·□□□□□□□□·

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Early recovery status and outcomes after sepsis-associated acute kidney injury in critically ill patients

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ABSTRACT

Objective: Acutekidneyinjury(AKI)isoneofthecommoncomplicationsincriticallyill septic patients, which is associated with increased risks of death, cardiovascular events, and chronicrenaldysfunction. Thedurationof AKIandtherenalfunctionrecoverystatusafter AKIonsetcanaffectthepatientprognosis.Nevertheless,itremainscontroversialwhether earlyrecoverystatusafterAKIiscloselyrelatedtotheprognosisinpatientswithsepsis-associated AKI (SA-AKI). In addition, early prediction of renal function recovery after AKI isbeneficialtoindividualizedtreatmentdecision-makingandpreventionofsevere complications,thusimprovingtheprognosis.Atpresent,thereislimitedclinical informationonhowtoidentifySA-AKIpatientsathighriskofunrecoveredrenalfunction atanearlystage.Thestudyaimstoinvestigatetheassociationbetweenearlyrecovery statusafterSA-AKI,identifyriskfactorsforunrecoveredrenalfunction,andtoimprove patients'quality of life.

Methods: We retrospectively analyzed clinical data of septic patients who were admitted to theintensivecareunit(ICU)anddevelopedAKIwithinthefirst48hoursafterICU admissionintheSecondXiangyaHospitalandtheThirdXiangyaHospitalofCentral South University from January 2015 to March 2017. Sepsis was defined based on the Third InternationalConsensusDefinitionsforSepsisandSepticShock(Sepsis-3).AKIwas diagnosedandstagedaccordingtothe2012KidneyDisease:ImprovingGlobalOutcomes (KDIGO)guideline.SA-AKIpatientswereassignedinto3groupsincludingacomplete recoverygroup,apartialrecoverygroup,andanunrecoveredgroupbasedonrecovery status at Day 7 after the diagnosis of AKI. Patients'baseline characteristics were collected, includingdemographics,comorbidities,clinicalandlaboratoryexaminationinformationat ICUadmission,andtreatmentwithinthefirst24hours.Theprimaryoutcomeofthestudy wasthecompositeofdeathandchronicdialysisat90days,andsecondaryoutcomes

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includedlengthofstayintheICU,lengthofstayinthehospital,andpersistentrenal dysfunction.Multivariateregressionanalysiswasperformedtoevaluatetheprognostic valueofearlyrecoverystatusafter AKIandtodeterminetheriskfactorsforunrecovered renalfunctionafter AKI.Sensitivityanalysiswasconductedinpatientswhostillstayedin hospitalonDay7after AKIdiagnosis,patientswithoutpremorbidchronickidneydisease, and patients with AKI Stage 2 to 3.

Results: A total of 553 SA-AKI patients were enrolled, of whom 251 (45.4%), 73 (13.2%), and229(41.4%)werecategorizedasthecompleterecoverygroup,thepartialrecovery group,andtheunrecoveredgroup,respectively.Comparedwiththecompleteorpartial recoverygroup,theunrecoveredgrouphadahigherincidenceof90-daymortality (unrecoveredvspartialrecoveryorcompleterecovery:64.2%vs26.0%or22.7%;*P*< 0.001)and90-daycompositeoutcome(unrecoveredvspartialrecoveryorcomplete recovery:65.1%vs27.4%or22.7%;*P*<0.001).Theunrecoveredgroupalsohadashorter lengthofstayinthehospitalandalargerproportionofprogressionintopersistentrenal dysfunction than the other 2 groups. After adjustment for potential confounders, patients in theunrecoveredgroupwereatanincreasedriskof90-daymortality(HR=3.50,95%CI 2.47 to 4.96, *P*<0.001) and 90-day composite outcome (OR=5.55, 95% CI 3.43 to 8.98, *P*< 0.001)whencomparedwithpatientsinthecompleterecoverygroup,butpatientsinthe partialrecoverygrouphadnosignificantdifference(*P*>0.05).Malesex,congestiveheart failure, pneumonia, respiratory rate >20 beats per minute, anemia, hyperbilirubinemia, need formechanicalventilation,and AKIStage3wereidentifiedasindependentriskfactorsfor unrecoveredrenalfunctionafterAKI.Thesensitivityanalysisfurthersupportedthat unrecoveredrenalfunctionafterAKIremainedanindependentpredictorfor90-day mortality and composite outcome in the subgroups.

Conclusion: Theearlyrecoverystatusafter AKIiscloselyassociatedwithpoorprognosis incriticallyillpatientswithSA-AKI.Unrecoveredrenalfunctionwithinthefirst7days afterAKIdiagnosisisanindependentpredictorfor90-daymortalityandcomposite outcome. Male sex, congestive heart failure, pneumonia, tachypnea, anemia hyperbilirubinemia,respiratoryfailure,andsevereAKIareriskfactorsforunrecovered renalfunctionafterAKI.Therefore,timelyassessmentfortherenalfunctionintheearly phaseafterAKIdiagnosisisessentialforSA-AKIpatients.Furthermore,patientswith unrecoveredrenalfunctionafterAKIneedadditionalmanagementinthehospital, includingrigorousmonitoring,avoidanceofnephrotoxin,andcontinuousassessmentfor therenalfunction,andafterdischarge,includingmorefrequentfollow-up,regular outpatient consultation, and prevention of long-term adverse events.

KEY WORDS sepsis; acute kidney injury; recovery; outcomes; intensive care unit

危重症患者脓毒症急性肾损伤后的早期恢复模式与预后

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[摘要]目的：急性肾损伤(acute kidney injury，AKI)是脓毒症的危重症患者常见的并发症之一，可增加患者死亡、心血管事件和慢性肾功能不全的发生风险。AKI持续时间和AKI后肾功能恢复状况可影响患者的预后，但是脓毒症AKI后患者的早期恢复情况是否与预后密切相关，目前仍存在争议。早期预测AKI后肾功能恢复状态有利于制订个体化的治疗策略和预防严重并发症的发生，然而如何在临床上早期识别脓毒症AKI患者中肾功能未恢复的高危患者尚不清楚。本研究旨在探讨危重症患者脓毒症AKI后早期恢复状态与预后的关系，并早期识别肾功能未恢复的危险因素，以提高患者的生存质量。方法：回顾性分析2015年1月至2017年3月在中南大学湘雅二医院和湘雅三医院重症监护室(intensive care unit，ICU)住院且在进入ICU后48 h内发生AKI的脓毒症患者的临床资料。脓毒症的诊断根据第3版脓毒症与感染性休克定义国际共识(the Third International Consensus Definitions for Sepsis and Septic Shock，Sepsis-3)，AKI的诊断和分期根据2012年改善全球肾脏病预后组织(KidneyDisease:ImprovingGlobalOutcomes，KDIGO)指南。根据诊断AKI后第7天的恢复状态，将脓毒症AKI患者分为完全恢复、部分恢复和未恢复3组。收集患者的基线特征，包括人口学特征、合并症、进入ICU时的临床和实验室检查资料以及进入ICU后24 h内的干预情况。研究的主要结局为90 d时死亡和慢性透析的复合结局，次要结局包括ICU停留天数、住院天数和持续性肾功能不全。使用多因素回归分析评估AKI后早期恢复状态对90 d预后的预测价值，并确定AKI后肾功能未恢复的危险因素。此外，我们进一步分别对诊断AKI后第7天仍在院的患者、无慢性肾脏病病史的患者和AKI分期为2~3期的患者进行敏感性分析。结果：在553例脓毒症AKI患者中，完全恢复组为251例(45.4%)，部分恢复组为73例(13.2%)，未恢复组为229例(41.4%)。与完全恢复组或部分恢复组患者相比，未恢复组患者90 d死亡(未恢复组vs部分恢复组、完全恢复组：64.2% vs 26.0%′22.7%；P<0.001)和复合结局(未恢复组vs部分恢复组、完全恢复组：65.1% vs 27.4%′22.7%；P<0.001)的发生率更高。此外，未恢复组患者与其他两组患者相比，住院时间更短，进展为持续性肾功能不全的比例更高。在校正了混杂因素后，与完全恢复组患者相比，未恢复组患者90 d死亡(HR=3.50，95% CI：2.47~ 4.96，P<0.001)和复合结局(OR=5.55，95% CI：3.43~8.98，P<0.001)发生的风险明显增加，而部分恢复组患者与完全恢复组比较差异无统计学意义(P>0.05)。男性、充血性心力衰竭、肺炎、呼吸频率>20次/min、贫血、高胆红素血症、需要机械通气和AKI 3期是AKI后肾功能未恢复的独立危险因素。敏感性分析结果进一步支持在特定患者亚组中AKI后肾功能未恢复仍然是90 d死亡和复合结局的独立预测因素。结论：危重症患者脓毒症AKI后早期恢复状态与预后不良密切相关，诊断AKI后7 d内肾功能未恢复是90 d死亡和复合结局的独立预测因素。男性、充血性心力衰竭、肺炎、呼吸增快、贫血、高胆红素血症、呼吸衰竭和严重AKI是AKI后肾功能未恢复的危险因素。因此，对于脓毒症AKI患者，应在早期阶段实时评估肾功能恢复状态，AKI后肾功能未恢复的患者则需要在住院期间持续评估肾功能，出院后加强随访，预防远期不良事件的发生。

[关键词]脓毒症；急性肾损伤；恢复；预后；重症监护室

Acute kidney injury (AKI) is commonly present in critically ill patients with sepsis [1-3]. Up to 60% of septic patients will develop AKI and sepsis accounts for about 50% of AKI cases [2]. Sepsis-associated AKI (SA-AKI) is an important cause for short- and long-term mortality, **cardiovascularr** events, and progression into chronic kidney disease (CKD) or end-stage renal disease (ESRD). At present, the prevention or treatment for SA-AKI is still limited. Recent studies [4-13] have focused on the association between the duration or renal function recovery of AKI and prognosis. Compared with non-AKI patients and SA-AKI patients who recovered before discharge, SA-AKI patients with unrecovered renal function at discharge were at **lower risk of mortality** and ESRD [5, 8, 12]. However, it is still controversial whether early recovery status after AKI is closely related to poor outcome when the AKI stage was taken into account. Another study [13] also showed no significant difference in death up to 1 year between patients with and without reversal within 7 days. In addition, early prediction of renal function recovery after AKI can contribute to individualized treatment decision-making **and the physics of bubble wrap** and prevention of severe complications, thus improving the prognosis. At present, there is limited clinical information on how to identify patients at high risk of unrecovered renal function after AKI at an early stage.

prognosis in SA-AKI patients. Some studies[4-5] Inthisstudy,weaimtoprovideanoverviewof

earlyrecoverystatusafterAKIanddetermineits associationwithoutcomesincriticallyillpatientswith SA-AKI.Furthermore,wetrytoidentifyriskfactors associatedwithunrecoveredrenalfunctionafter AKIin SA-AKI patients.

1Subjects and methods

1.1Study design

This was a retrospective cohort study in the Second Xiangya Hospital and Third Xiangya Hospital of Central SouthUniversityinChina.Adultpatientsadmittedto theintensivecareunit(ICU)withsepsisfromJanuary 2015toMarch2017wereenrolled.Forpatientswith multipleICUadmissions,onlypatientswiththefirst ICUadmissionwereanalyzed.PatientswithESRD,

data,andnon-AKIwithinthefirst48hoursafterICU admissionwereexcluded.Wealsoexcludedpatients withoutfollow-upSCrdataafterthediagnosisofAKI. Intotal,553SA-AKIpatientswerefinallyincludedin ourstudy(Figure1).TheneligibleSA-AKIpatients wereassignedinto3groupsaccordingtotheirearly recoverystatusafterAKI:Acompleterecoverygroup (the absence of AKI criteria), a partial recovery group (a declineinAKIstage)andanunrecoveredgroup[14]. Therewere251(45.4%)patientsinthecomplete recoverygroup,73(13.2%)inthepartialrecovery group,and229(41.4%)intheunrecoveredgroup, respectively(Figure1).Thisstudywasapprovedbythe MedicalEthicsCommitteeoftheSecondXiangya HospitalofCentralSouthUniversity(2013-S061)and registeredinChineseClinicalTrialRegistry(ChiCTR hospitalstay<48hours,missingserumcreatinine(SCr) 1800019857).

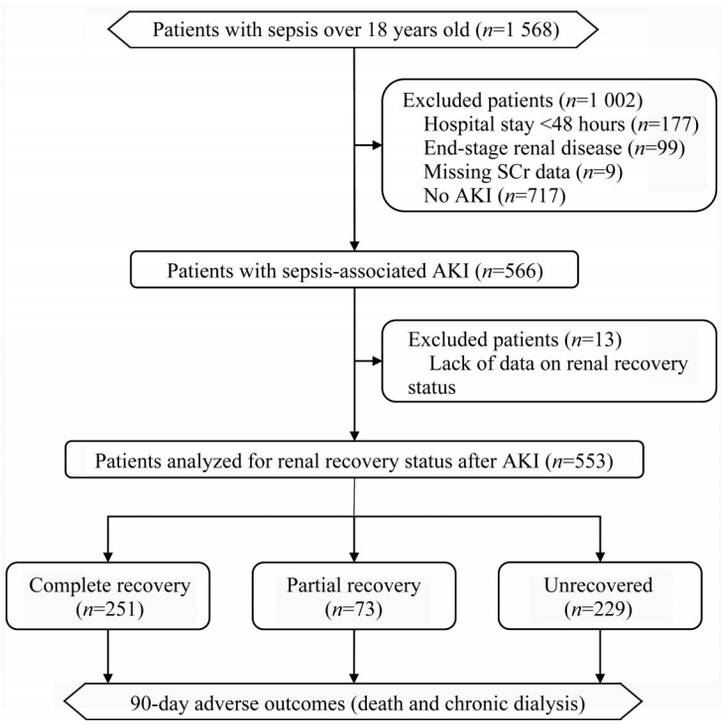


Figure 1Flow chart of patient selection

1.2Study variables and definitions

Sepsis was defined based on the Third International ConsensusDefinitionsforSepsisandSepticShock (Sepsis-3) criteria as an acute change of ≥2 points on the SequentialOrganFailureAssessment(SOFA)score secondarytotheinfection[15].AKIwasdefinedand

ImprovingGlobalOutcomes(KDIGO)guideline[16]. EarlyrecoverystatusafterAKIwasdeterminedbased onthepresenceandseverityof AKIonDay7afterthe diagnosisofAKI.IfSCrdataonDay7weremissing, wewouldusethedatarecordedonthedaynearestto Day7butnotlaterthanDay10.Forpatientswhodied

staged according to the 2012 Kidney Disease: orweredischargedwithin7days,earlyrecoverystatus

afterAKIwasdeterminedaccordingtotheirlast
availabledata.BaselineSCrwasdefinedasthemost

outcomesbetweenpatientsstratifiedbyearlyrecovery statusafterAKI,weusedtheKruskal-Wallistestfor continuous variables and the chi-square tests for categoricalvariables.Survivaldatawereanalyzedby Kaplan-Meier survival method and log-rank test.

Datawerecollectedfromtheelectronicmedical recentSCrvalueavailablefrom365to7daysbefore ICU admission[17]. For patients lacking a reliable referenceSCrvalue,baselineSCrwasobtainedbyback estimationusingthe4-variablemodificationofdietin renaldiseaseequationwithanestimatedglomerular filtration rate (eGFR) of 75 mL/(min·1.73 m_2)[16, 18].

Multivariate Cox regression was used to characterize the associationbetweenearlyrecoverystatusafter AKIand 90-daymortality.Multivariatelogisticregressionwas performedtoassessthepredictivevalueofearly recoverystatusafter AKIon90-daycompositeoutcome andtoidentifyriskfactorsforunrecoveredrenal function afterAKI.Variables considered clinically

record system and laboratory information system, includingdemographics,comorbidities,clinicaland laboratorydataonadmission,andtreatmentwithinthe first24hours.PremorbidCKDwasdefinedasbaseline eGFR<60mL/(min·1.73m$_2$).Hypotensionwasdefined assystolicarterialpressure<90mmHg(1mmHg= 0.133kPa),meanarterialpressure<65mmHgor

relevantor*P*<0.1onunivariableanalysiswereselected as covariates in the multivariate regression models.

Totestthesensitivityofourfindings,wefurther conductedsensitivityanalyses.Firstly,wefocusedon requiring vasopressors. We defined anemia as patientswhostillstayedinhospitalonDay7afterthe

hemoglobin <100 g/L, thrombocytopenia as platelet <100×10^{9}/L,hypoalbuminemiaasserumalbumin<30g/L,

diagnosisofSA-AKIforthereasonthatdatawasnot availableuptoDay7inpatientswhodiedorwere dischargedearlier.Secondly,theanalysiswasperformed inpatientswithoutpremorbidCKDtoeliminatethe influence of baseline renal insufficiency on poor Haemostasis(ISTH)criteria[19].Diseaseseveritywas evaluatedusingmodified AcutePhysiologyandChronic HealthEvaluation(APACHE)IIscoreandmodified SOFA score, excluding central nervous system component[15, 20].

hyperbilirubinemia as bilirubin >34.2 μmol/L, hypoxemia as oxygenation index <300 mmHg, hyperkalemiaasserumpotassium>5.5mmol/L,and lactic acidosis as lactate >5 mmol/L. Overt disseminated intravascularcoagulation(DIC)wasdeterminedbased on the International Society on Thrombosis and

prognosis.Thirdly,werestrictedthestudypopulationto patientswithAKIStage2to3,consideringthatthe diagnosisofmildAKIwasoftenmissedinclinical practice.

WeconductedstatisticalanalysesusingSPSS software, version 22.0 (IBM, Armonk, NY). P<0.05 was consideredsignificantforsinglecomparisonsand$P$< 0.017wascorrectedbyBonferronimethodformultiple comparisons.

1.3Study outcomes

Theprimaryoutcomewasthecompositeofdeath andchronicdialysisat90days.Survivalstatuswas determinedbyqueryoftheChineseCenterforDisease ControlandPreventioncause-of-deathreportingsystem.

2Results

2.1Baseline characteristics

Comparedwiththecompleterecoverygroup,the unrecovered group had a higher prevalence of congestiveheartfailureandpremorbidCKD,hada higher proportion of tachypnea and anemia on

Chronicdialysiswasdeterminedbyreviewingall relevantinpatientandoutpatientmedicalrecordsand makingphonecalls.Secondaryoutcomesincluded lengthofstay(LOS)intheICU,LOSinthehospital, andpersistentrenaldysfunction(PRD).PRDwas definedasafinalinpatientSCrvalue≥2.0times baseline at hospital discharge or until Day 30[21].

1.4Statistical analysis

admission,andweremorelikelytoreceivemechanical ventilation during the first 24 hours (Table 1).

Additionally,theunrecoveredgrouphadmoresevere organfailureorrenaldysfunctionthanthecomplete recoverygroup,asreflectedbysignificantlyhigher modifiedAPACHEIIscore,modifiedSOFAscore,and

To compare the baseline characteristics and percentage of AKI Stage 3.

Table 1Baseline characteristics of patients stratified by early recovery status after AKI

Groups	*n*	Age/year	Sex, male/[No.(%)]	Comorbidities/[No.(%)]								Baseline creatinine/(μmol·L^{-1})
				Hypertension	Diabetes mellitus	Congestive heart failure	COPD	Cirrhosis	Malignancy	Immuno-suppression	Premorbid CKD	
Complete recovery	251	63(50−73)	149(59.4)	95(37.8)	53(21.1)	13(5.2)	29(11.6)	10(4.0)	21(8.4)	26(10.4)	19(7.6)	84(68−90)
Partial recovery	73	64(52−79)	42(57.5)	29(39.7)	19(26.0)	8(11.0)	8(11.0)	3(4.1)	4(5.5)	3(4.1)	11(15.1)	85(69−93)
Unrecovered	229	64(50−75	154(67.2)	109(47.6)	68(29.7)	39(17.0)*	32(14.0)	11(4.8)	23(10.0)	29(12.7)	37(16.2)*	86(68−94
P		0.622	0.134	0.088	0.096	<0.001	0.664	0.918	0.470	0.115	0.011	0.348

Groups	Clinical data on admission/[No.(%)]						Modified SOFA score	Modified APACHE II score	AKI stage/[No.(%)]		
	Pneumonia	Abdominal infection	Temperature >38	Heart rate >90 beats per minute	Respiratory rate >20 beats per minute	Hypotension			1	2	3
Complete recovery	109(43.4)	79(31.5)	24(9.6)	184(73.3)	140(55.8)	142(56.6)	7(5−9)	15(12−19)	135(53.8)	65(25.9)	51(20.3)
Partial recovery	29(39.7)	21(28.8)	9(12.3)	50(68.5)	39(53.4)	43(58.9)	8(6−10)	18(15−21)*	0(0.0)*	23(31.5)	50(68.5)*
Unrecovered	121(52.8)	57(24.9)	37(16.2)	187(81.7)	164(71.6)*†	132(57.6)	9(6−11)*	19(15−24)*	39(17.0)*†	38(16.6)*†	152(66.4)*
P	0.051	0.278	0.094	0.026	<0.001	0.932	<0.001	<0.001		<0.001	

Groups	Laboratory data on admission/[No.(%)]									Treatment within 24 hours/[No.(%)]		
	Leucocytes ^{9}/L >12 ×10	Anemia	Thrombocytopenia	Overt DIC	Hypoalbuminemia	Hyperbilirubinemia	Lactic acidosis	Hypoxemia	Hyper-kalemia	Mechanical ventilation	Vasopressors	Renal replacement therapy
Complete recovery	133(53.0)	108(43.0)	99(39.4)	70(27.9)	176(70.1)	44(17.5)	53(21.1)	178(70.9)	12(4.8)	150(59.8)	137(54.6)	22(8.8)
Partial recovery	40(54.8)	42(57.5)	32(43.8)	20(27.4)	55(75.3)	11(15.1)	7(9.6)	52(71.2)	0(0.0)	42(57.5)	43(58.9)	13(17.8)
Unrecovered	124(54.1)	126(55.0)*	84(36.7)	75(32.8)	166(72.5)	56(24.5)	54(23.6)†	181(79.0)	15(6.6)	166(72.5)*†	131(57.2)	78(34.1)*†
P	0.949	0.012	0.534	0.451	0.652	0.087	0.035	0.102	0.050	0.005	0.749	<0.001

COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; SOFA: Sequential Organ Failure Assessment; APACHE: Acute Physiology and Chronic Health Evaluation; DIC: Disseminated intravascular coagulation.Continuous variables are presented as median (interquartile range) and categorical variables are presented as [No.(%)]. *P<0.05 vs the complete recovery group; †P<0.05 vs the partial recovery group.

2.2Outcomes

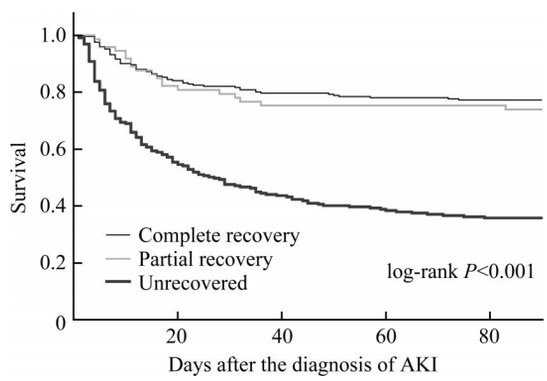
Thecompositeoutcomeofdeathandchronic dialysisupto90dayswasmorefrequentinthe unrecoveredgroupthanthatinthecompleteorpartial groups(*P*>0.05;Table2,Figure2).Thecompleteor recoverygroup(*P*<0.05).The90-daymortalitywas higherintheunrecoveredgroupthanthatintheother2 groups(both*P*<0.05),buttherewasnosignificant

partialrecoverygrouphadprolongedLOSinthe hospitalthantheunrecoveredgroup(P<0.05),while therewasnosignificantdifferenceinLOSintheICU amongthe3groups(P=0.119).Additionally,alarger percentageofpatientswithunrecoveredrenalfunction progressedintoPRDathospitaldischargeoruntilDay difference between the partial and the complete recovery 30 (Table 2).

Table 2Outcomes of patients stratified by early recovery status after AKI

Groups	*n*	ICU length of stay/d	Hospital length of stay/d	Persistent renal dysfunction/ [No.(%)]	90-day adverse outcomes		
					Death/[No.(%)]	Chronic dialysis/ [No.(%)]	Composite outcome/[No.(%)]
Complete recovery	251	7(4−12)	13(8−22)	6(2.4)	57(22.7)	0(0)	57(22.7)
Partial recovery	73	8(5−15)	15(10−24)	16(21.9)*	19(26.0)	1(1.4)	20(27.4)
Unrecovered	229		10(5−22)*†	171(74.7)*†	147(64.2)*†	2(0.9)	149(65.1)*†
P		0.119	0.002	<0.001	<0.001	0.115	<0.001

*P<0.05 vs the complete recovery group; †P<0.05 vs the partial recovery group.



2.3 Risk factors associated with unrecovered renal function after AKI

Multivariate logistic regression analysis revealed that the male sex (P=0.049), congestive heart failure (P=0.008), pneumonia (P=0.046), respiratory rate>20 beats per minute (P=0.008), anemia (P=0.018) hyperbilirubinemia (P=0.007), need for mechanica ventilation (P=0.002), and AKI Stage 3 (P<0.001 vs AKI Stage 1) were independent risk factors for unrecovered renal function after AKI (Table 3).

Figure 2 Kaplan-Meier survival curve of patients stratified by early recovery status after AKI

2.4 Sensitivity analyses

Sensitivity analyses were conducted in patients who still stayed in hospital on Day 7 after the diagnosis

In multivariate Cox regression analysis, the unrecovered group was at significantly increased hazard of death within 90 days (P<0.001), but the partial recovery group was not (P=0.59). After adjustment for

ofSA-AKI,patientswithoutpremorbidCKD,and subgroupsweresimilartothoseintheoverallstudy

potential confounders, the unrecovered group (*P*<

0.001),butnotthepartialrecoverygroup(*P*=0.61),was associatedwithsignificantlyhigherriskof90-day composite outcome (Figure 3).

patientswithAKIStage2to3.Theresultsinthe

cohort.TheunrecoveredrenalfunctiononDay7after

AKI was independently cor related to a higher risk of 90-daymortalityandcompositeoutcome,whereasthe partial recovery was not (Figure 3).

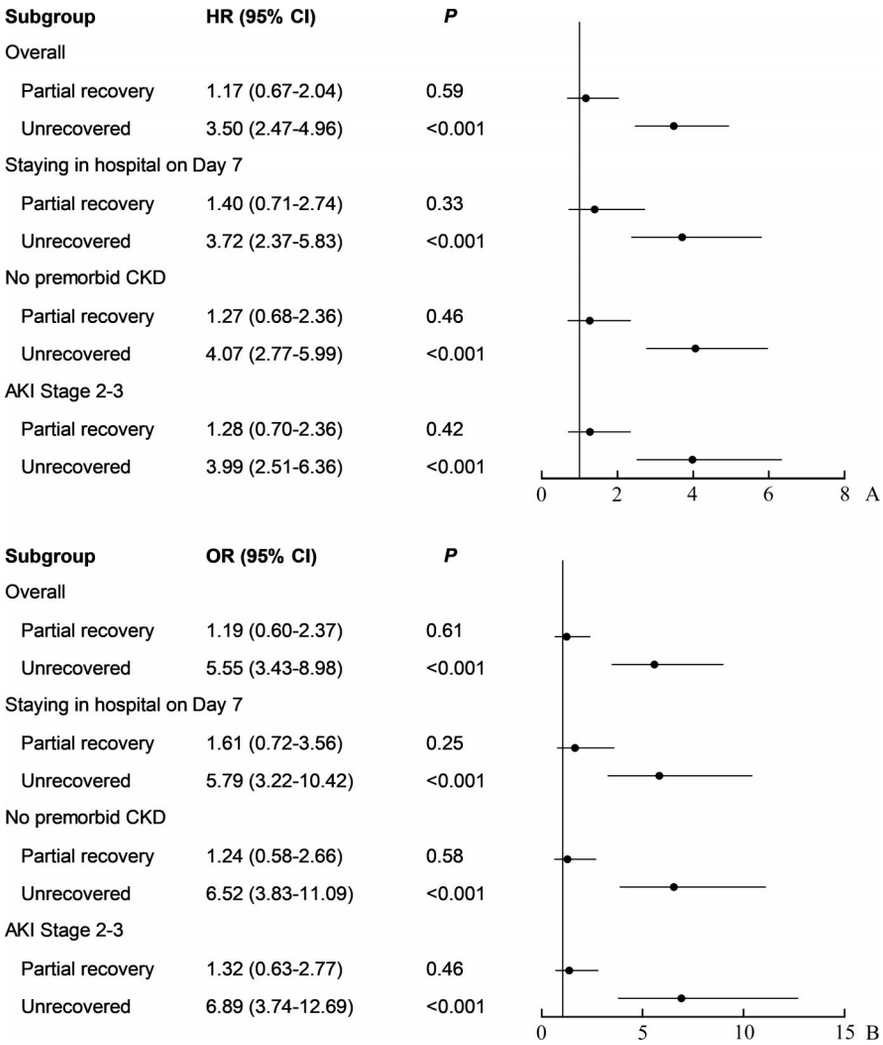


Figure 3Association between the early recovery status after AKI and the outcomes
A:MultivariateCoxregressionofassociationbetweentheearlyrecoverystatusafter AKIandthe90-daymortalityintheoverall cohortandbysubgroups;B:Multivariatelogisticregressionoftheassociationbetweentheearlyrecoverystatusafter AKIandthe 90-day composite outcome in the overall cohort and by subgroups.

Table 3Multivariate logistic regression analysis for risk factors associated with unrecovered renal function after AKI

Factors	OR	95% CI	*P*
Age	1.00	0.99−1.02	0.718
Sex, male	1.52	1.00−2.30	0.049
Hypertension	1.22	0.77−1.93	0.396
Diabetes mellitus	1.38	0.87−2.18	0.167
Congestive heart failure	2.48	1.27−4.82	0.008
Premorbid CKD	1.67	0.91−3.08	0.097
Pneumonia	1.56	1.01−2.42	0.046
Heart rate > 90 beats per minute	1.46	0.89−2.39	0.135
Respiratory rate > 20 beats per minute	1.79	1.16−2.75	0.008
Anemia	1.64		0.018
Hyperbilirubinemia	1.98		0.007
Hypoxemia	0.86		0.556

Table 3(to be continued)

Factors	OR	95% CI	*P*
Mechanical ventilation	2.01	1.28−3.16	0.002
AKI Stage			
1	1.00	reference	–
2	1.59	0.90−2.79	0.110
3	6.58	4.03−10.75	<0.001

CKD: Chronic kidney disease; AKI: Acute kidney injury.

3Discussion

Inthisstudy,wefindthat41.4%ofpatientswith SA-AKI have unrecovered renal function within the first 7daysafterAKIdiagnosis,while45.4%and13.2%of patientsexperiencedearlycompletereversalandpartial recovery,respectively.Unrecoveredrenalfunctionafter

daysafterAKIisindependentlyassociatedwithpoor prognosis.Moreover,unrecoveredrenalfunction,but notpartialrecovery,isanindependentpredictorfor90-daymortalityandcompositeoutcomeinSA-AKI patients.WealsofindthatmostSA-AKIpatientswith unrecoveredrenalfunctiononDay7developPRD, whilepatientswithpartialrecoveryaremorelikelyto

AKI is an independent predictor of 90-day mortality and experience delayed recovery later. Therefore, the

compositeoutcome.Additionally,malesex,congestive heartfailure,pneumonia,respiratoryrate>20beatsper

evaluationofearlyrecoverystatusafter AKIisessential fortimelyinterventionandmanagementinSA-AKI

minute, anemia, hyperbilirubinemia, need for mechanicalventilation,and AKIStage3areriskfactors for unrecovered renal function after AKI.

AKIisnowregardedasaclinicalsyndromethat can lead to long-term sequelae such as CKD, cardiovascular events, and death, and our study describedtheevolutionofAKIincriticallyillseptic patients.Earlystudies[8, 12]haveshownthatSA-AKI patientswithunrecoveredrenalfunctionathospital patients.Forpatientswithunrecoveredrenalfunction afterAKI,additionalin-hospitalcareisnecessary, including rigorous monitoring, avoidance of nephrotoxin, and continuous assessment of renal function.Inaddition,theyneedmorefrequentfollow-up,regularoutpatientconsultation,andpreventionof

long-term adverse events after discharge.

Manyfactors,includingdemographics,chronic comorbidities,multipleorgandysfunction,andsevere AKI,canaffectrenalfunctionrecoveryafterAKI[14]. discharge have worse outcomes than those who

recovered. Recently, the Acute Disease Quality Initiative 16Workgroupproposednoveldefinitionsforpersistent AKIandacutekidneydisease(AKD)toclarifyclinical trajectoriesofrenalfunctionrecoveryafterAKI[22]. Several recent studies have explored the effectiveness of the new definitions in SA-AKI patients. Uhel et al[4]find thatpersistentAKIisindependentlyassociatedwith

Consistentwithourpreviousstudy[23],themalesex, factorsassociatedwithunrecoveredrenalfunction. unrecoveredrenalfunction,includingcongestiveheart heartfailure,characterizedasthedeclineincardiac mortalityandhostresponseaberrationscomparedwith transientAKIincriticallyillsepticpatients.Similarly, Ozrazgat-Baslantietal[5]findthatpersistentAKIis respiratoryfailure,andAKIstageareindependentrisk Meanwhile,wefindseveralnovelriskfactorsfor failure,hyperbilirubinemia,andanemia.Congestive output, may be caused by chronic diseases like

hypertensionandcoronaryarterydiseaseorsepsis.The effectsofheartfailureonunrecoveredrenalfunction associatedwithdecreasedlong-termphysicalfunction and survival among patients with surgical sepsis. However,therehavebeennouniformconclusionson therelationshipbetweenclinicaloutcomesandAKDin may include hemodynamic changes, systemic inflammation,andneurohumoralpathways[24].Arecent septicpatients[7, 13].Ourstudyfurtherconfirmthenew AKDdefinition,asrecoverystatuswithinthefirst7

study[25]demonstratesthatseverehyperbilirubinemia (bilirubin >2.0 mg/dL) is associated with a higher risk of contrast-relatedAKI.Anemiaiscommonlypresentin criticallyillpatientswithsevereacuterenalfailureand

hasbeenfoundtobeanindependentriskfactorof mortality[26]. Our study demonstrates that hyperbilirubinemiaandanemiaarebothrelatedtoearly recovery status after AKI in SA-AKI patients.

Ourstudyhas3limitations.Firstly,itwasa retrospectivestudyconductedin2tertiaryhospitalsand thesamplesizewasrelativelysmall.Selectionbiasmay existtolimitthegeneralityoftheresultsandthe correlationbetweenthevariablesidentifiedinthestudy could not imply causality. Secondly, urine output criteria were not included in the diagnosis of AKI. A considerableproportionofpatientswithreducedurine outputreceiveddiureticsintheearlyphaseafterICU admission,whichmay affect the primary urine output of

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these patients compared with those who did not. Thirdly, manyunmeasuredpotentialfactorsmayaffectthe prognosis,andtheinformationonotherendpoints(such asmajoradversecardiacevents)wasnotavailable duringthefollow-upperiod.Furtherlargeprospective studiesarestillrequiredtoinvestigatetheepidemiology andpathophysiologyofrenalfunctionrecoveryafter

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AKI in septic patients.

Inconclusion,unrecoveredrenalfunctionwithin thefirst7daysafterAKIdiagnosisisanindependent predictor for 90-day mortality and composite outcome in criticallyillpatientswithSA-AKI.Malesex,congestive

heart failure, pneumonia, tachypnea, anemia, hyperbilirubinemia,respiratoryfailure,andsevereAKI areidentifiedasriskfactorsforunrecoveredrenal functionafterAKI.Ourresultsemphasizethenecessity ofearlyriskstratification,timelyestimationoftherenal function, and effective follow-up for SA-AKI patients.

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have no conflicts of interest to disclose.

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