Charlson Comorbidity Index for Prediction of Outcome of Acute Kidney Injury in Critically Ill Patients

Sumaira Talib,[1] Fatima Sharif,[1] Sidra Manzoor,[1] Sonia Yaqub,[2] Waqar Kashif[2]

[1]Aga Khan University, Karachi, Pakistan
[2]Section of Nephrology, Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan

Keywords. acute kidney injury, comorbidity, Charlson Comorbidity Index, intensive care unit, mortality

Introduction. This study aimed to determine predictors of outcomes in critically ill patients with acute kidney injury (AKI), and to study the impact of the Charlson Comorbidity Index (CCI) as a prognostic indicator.
Materials and Methods. This retrospective study included critically ill patients who were admitted with AKI or developed AKI during their hospital stay. The impact of comorbidity was evaluated by the CCI, while severity of AKI was assessed by the RIFLE criteria.
Results. The mean age of 786 patients with AKI was 59.0 ± 17.0 years (59% men). The most common cause was sepsis in 51% of the patients. In-hospital mortality rate was 42%. The need for mechanical ventilation (odds ratio [OR], 1.93; 95% confidence interval [CI], 1.23 to 3.04), vasoactive drugs (OR, 9.67; 95% CI, 6.35 to 14.73), dialysis (OR, 1.78; 95% CI, 1.14 to 2.78), failure class of RIFLE criteria (OR, 2.02; 95% CI, 1.00 to 4.08), and a CCI greater than 6 (OR, 2.20; 95% CI, 1.38 to 3.52) were independently associated with mortality. At 90 days of follow-up, 6% of the patients were dialysis dependent, while 32% and 62% had partial and complete recovery, respectively. In multivariable analysis, a CCI greater than 6 (OR, 0.47; 95% CI, 0.26 to 0.83), need for dialysis in hospital (OR, 0.31; 95% CI, 0.17 to 0.54), and failure class (OR, 0.19; 95% CI, 0.07 to 0.55) were independent predictors of poor renal outcomes.
Conclusions. The CCI independently predicts in-patient mortality and poor renal outcomes in patients with AKI.

IJKD 2017;11:115-23
www.ijkd.org

Original Paper

INTRODUCTION

Acute kidney injury (AKI) is one of the most feared complications in hospitalized patients owing to its potential for causing serious impact on outcomes. Acute kidney injury is not a just single condition, but rather encompasses a spectrum of disease with minimal to severe dysfunction.[1] Affecting millions of patients worldwide, AKI is responsible for prolonging length of hospital stay, need for intensive care unit (ICU) admission, increasing cost of care, and a high progression rate to chronic kidney disease (CKD), which in turn leads to tremendous utilization of resources and poor quality of life.[2,3] Despite recent advances in treatment modalities, incidence of AKI is on the rise, with 0.25% in the general population, 18% in the hospitalized patients and as high as 60% in critically ill patients.[2] Moreover, AKI is independently associated with death, with rates increasing as the disease severity increases from 'risk (R)' to 'injury (I)' to 'failure (F)', as per the RIFLE criteria.[4] Early recognition of patients at risk of developing even milder degrees of AKI is of utmost importance, since not only the severe

but even the milder forms of injury can potentially have grave consequences.

Comorbidity plays a vital role in the health status of a person and few would disagree that it is an important consideration in the overall management of the critically ill patients. The Charlson Comorbidity Index (CCI) is a commonly used clinical scoring system, which assess prognosis based on the patient's comorbid conditions. It was first introduced by Charlson and colleagues in 1987, based on a longitudinal survey conducted in a cohort of 559 patients admitted to the medical units.[5] The goal was to formulate a method to categorize comorbidities that had the potential to significantly influence the risk of mortality. The results of the study revealed 19 conditions that were significant prognostic indicators of survival, and each condition was assigned a weighted score based on the relative mortality risk. The weighted index was then validated in a cohort of 685 patients with breast cancer. Since then, CCI has proven to be an effective prognostic indicator of mortality in not only the medical conditions but also those requiring surgical interventions.[6-11]

Data on impact of comorbid conditions on outcomes of AKI remains scarce. The aim of this study was to determine predictors of mortality and renal recovery in critically ill patients with acute kidney injury, and to test whether CCI is a valid prognostic indicator in these patients.

MATERIALS AND METHODS

Study Setting

This descriptive study was conducted by the Section of Nephrology at the Aga Khan University Hospital, Karachi, Pakistan. Aga Khan University Hospital is a major tertiary care hospital catering to more than 20 million people of Karachi and the surrounding region. With an operational strength of 577 beds, the facility serves over 50 000 inpatients and 600 000 outpatients annually. Established since 1985, it is one of the few teaching hospitals in South Asia accredited by the Joint Commission for International Accreditation.[12]

The study was done in compliance to the International Helsinki Declaration and a formal approval was taken from the Ethical Review Committee of the Aga Khan University Hospital prior to commencement. Identification of the study participants was kept strictly confidential throughout the duration of the study.

Study Population

All patients of age 15 years and above requiring high dependency unit, special care unit or ICU admitted with or who developed AKI during their hospital stay were included in the study. Those patients were admitted to high dependency unit or special care unit who required an intermediate level of care between that offered in the general ward and that offered in the ICU, such as provision of noninvasive ventilation.

Acute kidney injury was defined as either a 50% percent rise in serum creatinine if baseline creatinine was known or a serum creatinine equal to or greater than 2 mg/dL (clinician's judgment was relied upon after reviewing the records to exclude patients with stable CKD). Patients with known stage 5 CKD (estimated glomerular filtration rate, using Cockroft-Gault equation, less than 15 mL/min), posttransplant patients, and patients on regular dialysis were excluded from the study.

RIFLE Criteria

An increase in the serum creatinine concentration was used to assign a category in the RIFLE classification; urine output criterion was not used since obtaining reliable data from the records was not possible. The criteria used to stratify patients into different classes according to the RIFLE classification are summarized in Table 1.

Data Collection

The medical record numbers of patients admitted

Table 1. RIFLE Criteria for Assessing Severity of Acute Kidney Injury

RIFLE Category	Serum Creatinine Criteria
Risk	Increase by 1.5 times baseline but < 4 mg/dL
Injury	Increase by 2 times baseline but < 4 mg/dL
Failure	Increase by 3 times baseline or ≥ 4 mg/dL
Loss	Persistent acute kidney failure = complete loss of kidney function > 4 weeks
End-stage renal disease	End-stage renal disease = complete loss of kidney function > 3 months

to the high dependency unit, special care unit and ICU were initially extracted from the medical record database of our institution. File records with a diagnosis of AKI were then manually reviewed. The recorded data included demographics of the patients including age, sex, body weight (measured or estimated at admission); laboratory investigations including baseline serum creatinine level, creatinine and blood urea nitrogen levels on admission, and peak creatinine and creatinine levels at discharge; and other clinical parameters including comorbid conditions, length of hospital stay, need for mechanical ventilation, need for vasopressors, diuretic use, and dialysis.

Comorbidity was defined as preexisting medical conditions present at the time of admission. Medical conditions including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, peptic ulcer disease, chronic liver disease, dementia, chronic pulmonary disease, connective tissue disorders or autoimmune disease, diabetes mellitus, hypertension, preexisting kidney disease, malignancies (solid and hematologic) with or without metastases and acquired immunodeficiency syndrome were recorded. Comorbidity was then objectively evaluated using the CCI.[5]

Outcomes

The following 2 clinical outcomes were assessed: (1) in-hospital mortality and (2) kidney function status at 90 days. Renal function status was further categorized according to the Acute Dialysis Quality Initiative criteria into no recovery (remained dialysis dependent), partial recovery (off renal replacement therapy and serum creatinine concentration improved but did not reach the baseline), and complete recovery (serum creatinine concentration improved to baseline). 'Poor renal outcomes' were classified as no recovery or partial recovery according to the aforementioned criteria following an episode of AKI.

Statistical Analysis

The statistical analysis was conducted by using the Statistical package for social science SPSS (Release 16.0 standard version, copyright © SPSS). A descriptive analysis was performed for the demographic and clinical characteristics and results are presented as mean ± standard deviation for quantitative variables and numbers (percentages) for qualitative variables. The difference in characteristics between the survivors and nonsurvivors was performed using either the chi-square test for nominal variables or the Student *t* test for numerical variables. For the analysis of outcomes, groups were compared using the chi-square test while the analysis of variance test was used for comparison of quantitative variables.

A logistic regression analysis was performed to estimate the odds of mortality with AKI, adjusting for associations with sex, length of hospital stay, CCI, diuretic use, need for vasopressors, dialysis, mechanical ventilation, prior kidney dysfunction, kidney failure on admission, and the RIFLE criteria. A similar model was utilized using the same variables to estimate the odds of renal recovery amongst survivors. *P* values less than .05 were considered significant.

RESULTS

Patients

Over 11 000 medical records of patients were searched, out of which a list of 1600 patients with AKI was generated. Seven hundred and eighty-six patients eventually fulfilled the inclusion criteria. The mean age was 59.0 ± 17.0 years and 461 (59%) patients were men. The majority of the patients (n = 666; 84%) were admitted under the medicine service, while the remaining 126 admissions (16%) occurred in the surgical units. The most common etiologies of AKI were sepsis in 403 (51%), hypovolemia in 186 (23%), and acute myocardial infarction or cardiogenic shock in 143 (18%) patients. Other causes included acute glomerulonephritis in 6 (0.8%), acute tubulointerstitial nephritis in 8 (1.0%), and obstructive uropathy in 27 (3.4%) patients.

Table 2 shows the list of comorbid conditions included in the CCI and the prevalence of these conditions in our study population.

Characteristics of Survivors and Nonsurvivors

A total of 331 patients (42%) died during the hospital stay. Table 3 and Figure 1 summarize the differences in characteristics between the survivors and nonsurvivors. Out of 470 patients who had normal baseline kidney function, 219 (47%) died as compared to 112 patients (35%) with impaired baseline kidney function (*P* = .002). Patients who

Table 2. Score of Comorbid Conditions Included in the Charlson Comorbidity Index and Their Prevalence in the Study Population

Clinical Condition	Score	Patients (%)
Myocardial infarction	1	272 (34.6)
Congestive heart failure	1	67 (8.5)
Peripheral vascular disease	1	7 (0.9)
Cerebrovascular disease	1	71 (9.0)
Dementia	1	5 (0.6)
Chronic pulmonary disease	1	49 (6.2)
Connective tissue disease	1	30 (3.8)
Peptic ulcer	1	3 (0.4)
Mild liver disease and cirrhosis	1	32 (4.1)
Diabetes without complications	1	0
Renal disease	2	229 (29.1)
Diabetes with complications	2	330 (42.0)
Paraplegia or hemiplegia	2	0
Any malignancy	2	120 (15.3)
Moderate to severe liver disease	3	31 (3.9)
Malignancy with metastasis	6	5 (0.6)
Acquired immunodeficiency syndrome	6	0

had developed kidney failure during their hospital stay had a higher mortality rate as compared to patients who had kidney failure on admission (60% versus 33%, respectively; $P < .001$). A total of 216 patients (27%) required dialysis during their hospital stay. A higher rate of mortality was observed in the patients who required dialysis (49% versus 40%, respectively; $P = .02$). Need for mechanical ventilation ($P < .001$), vasoactive drugs ($P < .001$), and prior diuretic use ($P = .01$) were significantly associated with mortality.

In multivariable analysis (Table 4), the need for mechanical ventilation ($P = .004$; odds ratio [OR], 1.93; 95% confidence interval [CI], 1.23 to 3.04), vasoactive drugs ($P < .001$; OR, 9.67; 95% CI, 6.35 to 14.73), dialysis ($P = .01$; OR, 1.78; 95% CI, 1.14 to 2.78), failure class of RIFLE criteria ($P = .05$; OR, 2.02; 95% CI, 1.00 to 4.08), and a CCI greater than 6 ($P = .001$; OR, 2.20; 95% CI, 1.38 to 3.52) were found to be independently associated with mortality.

Renal Outcomes Amongst Survivors

Table 5 summarizes the differences in characteristics between different renal outcomes amongst the survivors. A total of 455 patients (58%) got better and were discharged. At 90 days, 25 (6%) were dialysis dependent, while 146 (32%) and 284 (62%) had partial and complete recovery to baseline, respectively. The CCI successfully predicted the renal outcomes with the index being higher in patients who remained dialysis dependent (mean score, 5.44) as compared to those who either had

Table 3. Comparison of Acute Kidney Injury Survivors and Nonsurvivors

Characteristic	All (n = 786)	Survivors (n = 455)	Non Survivors (n = 331)	*P*
Mean age, y	59.0 ± 17.0	58.6 ± 16.6	59.1 ± 17.6	.68
Age group				
< 60 years	353 (45)	206 (58)	147 (42)	
≥ 60 years	433 (55)	249 (58)	184 (42)	.81
Male sex	461 (59)	262 (57)	199 (43)	.47
Baseline kidney dysfunction	316 (40)	204 (65)	112 (35)	.002
Kidney failure on admission	509 (65)	343 (67)	166 (33)	< .001
Diuretic use	387 (49)	207 (53)	180 (47)	.01
Mechanical ventilation	275 (35)	95 (35)	180 (65)	< .001
Vasoactive drugs	379 (48)	116 (31)	263 (69)	< .001
RIFLE criteria				
Risk	79 (10)	45 (57)	34 (43)	
Injury	166 (21)	106 (64)	60 (36)	
Failure	541 (69)	304 (56)	237 (44)	.21
Dialysis	216 (27)	111 (51)	105 (49)	.02
Mean dialysis duration, d	6.3 ± 7.7	7.5 ± 8.5	5.1 ± 6.7	.02
Mean baseline creatinine	1.18 ± 0.55	1.24 ± 0.57	1.09 ± 0.48	.01
Mean creatinine				
On admission	3.53 ± 2.94	3.99 ± 2.93	2.88 ± 2.82	< .001
At discharge	3.13 ± 2.23	2.60 ± 2.14	3.87 ± 2.12	< .001
Peak value	4.81 ± 2.83	4.93 ± 2.95	4.64 ± 2.63	.15
Mean length of hospital stay, d	10.5 ± 10.9	11.6 ± 12.2	8.9 ± 8.6	< .001

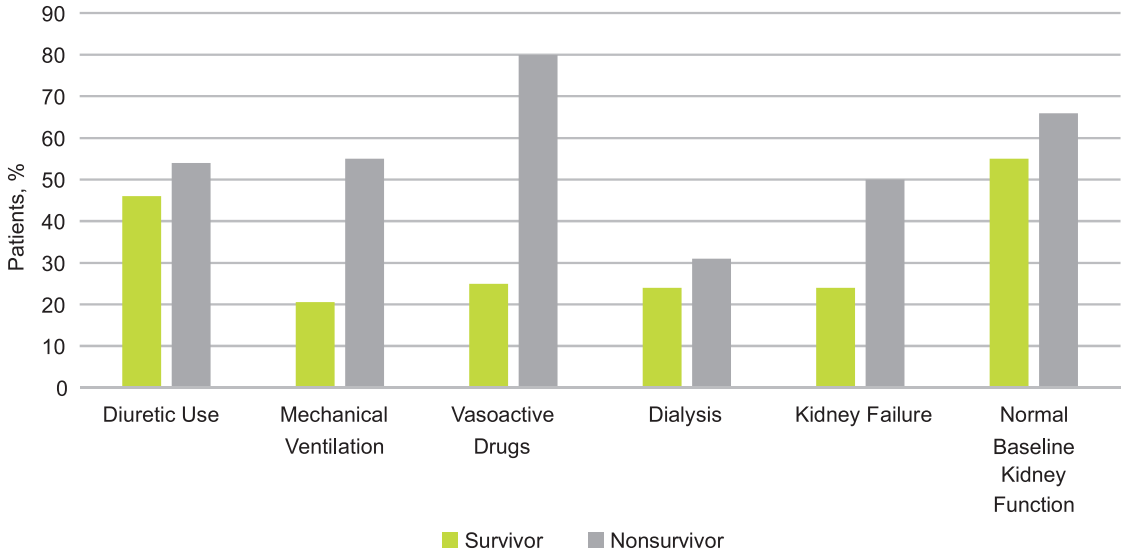

Figure 1. Comparison of survivors and nonsurvivors of acute kidney injury.

Table 4. Multivariable Analysis of Characteristics on Overall Mortality

Parameter	Odds Ratio	95% Confidence Interval	*P*
Male sex	1.24	0.86 to 1.81	.26
Diuretic use	0.69	0.45 to 1.04	.07
Mechanical ventilation	1.93	1.23 to 3.04	.004
Vasoactive drugs use	9.67	6.35 to 14.73	< .001
Dialysis	1.78	1.14 to 2.78	.01
Kidney failure on admission	0.23	0.14 to 0.36	< .001
Impaired baseline kidney function	0.58	0.38 to 0.89	.01
Charlson index > 6	2.20	1.38 to 3.52	.001
Length of stay > 10 days	0.31	0.20 to 0.48	< .001
RIF Criteria			
Risk	1	…	…
Injury	0.90	0.44 to 1.87	.78
Failure	2.02	1.00 to 4.08	.05

partial recovery (mean score, 5.13) or complete recovery (mean score, 4.42; *P* =.008). Around 80% of the patients who had complete recovery, had a CCI of 6 and greater as compared to the other two groups (*P* < .001). In multivariable analysis (Table 6), the need for dialysis (*P* < .001; OR, 0.31; 95% CI, 0.17 - 0.54), failure class (*P* = .002; OR, 0.19; 95% CI, 0.07 to 0.55), and a CCI greater than 6 (*P* = .01; OR, 0.47; 95% CI, 0.26 to 0.83) were found to be independently associated with poor renal outcomes. Figure 2 shows the median and interquartile range of CCI with regards to the renal outcomes of our study population.

DISCUSSION

This study describes the utility of the CCI as a predictor of in hospital mortality and its impact as a prognostic indicator in a large sample of critically ill patients with AKI. The CCI has been one of the most commonly used clinical scores to assess the impact of comorbid conditions. Not only has it been used as a successful predictor of mortality in medical conditions such as systemic lupus erythematosus, myocardial infarction, and sepsis, but also in conditions requiring surgical interventions such as intra-cerebral hemorrhage, hip fracture surgery, and tumor nephrectomy for renal cell carcinoma.[6,7,9-12,13] Furthermore, it has been adapted to predict resource utilization in the management of patients with chronic diseases and may help to reduce costs incurred by prospectively identifying patients at high risk of complications.[14]

While CCI has been used in patients with end-stage renal disease,[15] the use of an overall

Table 5. Renal Outcomes Amongst Survivors

Characteristic	Survivors of Acute Kidney Injury (n = 455)			*P*
	Dialysis Dependence (n = 25)	Partial Recovery (n = 146)	Recovery to Baseline (n = 284)	
Mean age, y	57.8 ± 13.8	58.7 ± 16.5	58.7 ± 16.9	.96
Age group				
< 60 years	14 (56)	68 (47)	124 (44)	
≥ 60 years	11 (44)	78 (53)	160 (56)	.45
Male sex	13 (52)	82 (56)	167 (59)	.73
Patient service				
Medicine	25 (100)	135 (93)	232 (82)	
Surgery	0	11 (7)	52 (18)	.001
Mean Charlson index	5.4 ± 2.2	5.1 ± 2.6	4.4 ± 2.5	.008
Charlson index group				
≤ 6	17 (68)	89 (61)	227 (80)	
> 6	8 (32)	57 (39)	57 (20)	< .001
Baseline kidney function				
Normal	6 (24)	68 (47)	177 (62)	
Impaired	19 (76)	78 (53)	107 (38)	< .001
Kidney failure on admission	24 (96)	124 (85)	195 (69)	< .001
Nephrology input	25 (100)	134 (92)	202 (71)	< .001
Mechanical ventilation	9 (36)	24 (16)	62 (22)	.06
Vasoactive drugs use	10 (40)	36 (25)	70 (25)	.23
Diuretic use	14 (56)	72 (49)	121 (43)	.23
Dialysis	22 (88)	53 (36)	36 (13)	< .001
Mean length of hospital stay, d	14.9 ± 12.8	8.9 ± 7.1	12.6 ± 13.9	.005
RIF criteria				
Risk	0	5 (3)	40 (14)	
Injury	0	10 (7)	96 (34)	
Failure	25 (100)	131 (90)	148 (52)	< .001

Table 6. Multivariable Analysis of Characteristics on Renal Recovery Amongst Survivors

Parameter	Odds Ratio	95% Confidence Interval	*P*
Male sex	1.14	0.71 to 1.84	.58
Diuretic use	0.74	0.44 to 1.26	.27
Mechanical ventilation	0.89	0.43 to 1.84	.76
Vasoactive drugs use	1.02	0.56 to 1.86	.95
Dialysis	0.31	0.17 to 0.54	< .001
Nephrology input	0.286	0.136 to 0.599	.001
Kidney failure on admission	0.72	0.38 to 1.37	.32
Impaired baseline kidney function	0.75	0.44 to 1.27	.28
Charlson index > 6	0.47	0.26 to 0.83	.01
Length of stay > 10 days	3.25	1.82 to 5.82	< .001
RIF Criteria			
Risk	1	…	…
Injury	1.31	0.39 to 4.34	.66
Failure	0.19	0.07 to 0.55	.002

comorbidity index has rarely been reported in AKI. In our study, a higher CCI was an independent predictor of both in-hospital mortality and poor renal recovery. Bagshaw and colleagues first reported its significance in patients with severe acute kidney failure and found it to be an independent predictor of one year mortality (P = .002, odds ratio, 1.2; 95% confidence interval, 1.1 to 1.3),[16] while 2 other studies also describe similar associations.[17,18] Our study reports these associations in a much larger sample as compared to the previous studies. Additionally, the criteria that we used to define AKI according to creatinine levels enabled us to accurately identify patients

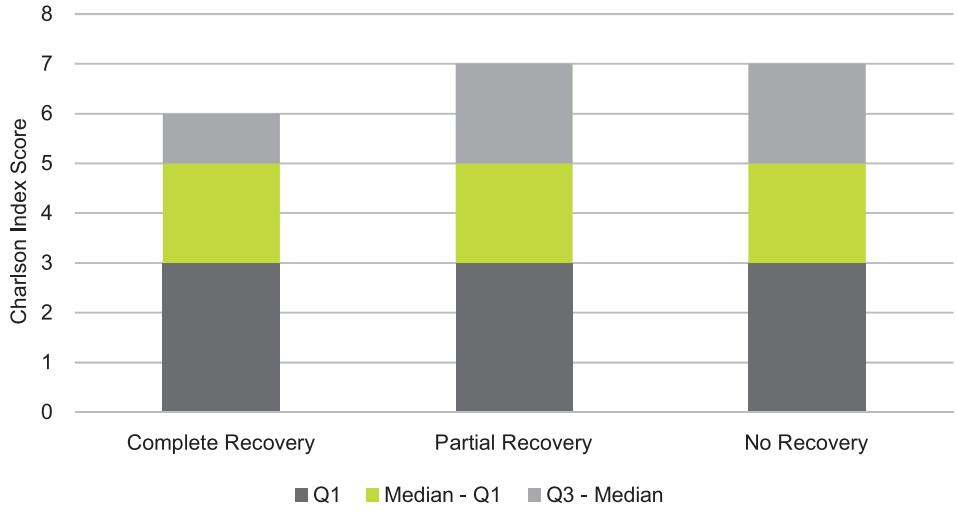

Figure 2. Median and interquartile range of Charlson Index according to renal outcomes

with AKI, whereas the criteria used previously by Bagshaw and colleagues might have led to an underestimation of acute kidney failure, resulting in an erroneous exclusion of patients from the study.[16] The use of this index in AKI can better aid physicians to estimate the overall outcome of the patient, counsel the families and provide well informed management decisions.

Epidemiological studies have shown that the incidence of AKI is much higher than previously thought and is associated with high rates of mortality,[19,20] which were also seen in our study. However, those who survived showed good prognosis for renal recovery, highlighting the importance of risk stratification in these patients. The RIFLE criteria has been shown to be a good outcome predictor in patients with AKI,[3] and the failure class of RIFLE was associated with mortality and poor renal outcomes in our study as well. However, recent studies have demonstrated that the RIFLE classification is only useful when predicting short term outcomes, is unable to predict mortality at and beyond 90 days.[19,21] Moreover, it does not take into account the effect of comorbidities, even though it has been well documented that comorbid conditions such as heart, lung and liver disease, and cancers may adversely affect the outcomes in patients with AKI.[19,22]

Other predictors of in-hospital mortality seen in our study included the need for mechanical ventilation and vasoactive drugs which is consistent with the literature.[22,23] Kuiper and colleagues in their review discuss 3 mechanisms by which mechanical ventilation may induce renal injury. Firstly, renal blood flow may be compromised due to strategies such as permissive hypercapnia and hypoxemia. Secondly, it may affect renal hemodynamics by its effect on cardiac output and lastly, mechanical ventilation may result in pulmonary bio-trauma leading to release of systemic inflammatory mediators directly damaging the kidneys.[24] Although the use of diuretics was associated with mortality in the univariate analysis, this effect was negated in the multivariate model. The use of diuretics may convert an oliguric form to a non-oliguric form and delay the recognition of AKI or underestimate its severity. This in turn may delay the time for obtaining consultation of the nephrologists or initiation of dialysis. Moreover, diuretics may be directly nephrotoxic to the kidneys. However, there are conflicting reports in the literature on the effect of diuretics on mortality. Mehta and coworkers reported the use of diuretics to be significantly associated with an increased risk of death, whereas Uchino and colleagues in a multicenter, multinational study did not find any link between the two parameters.[25,26]

Survivors had higher admission creatinine levels as compared to patients who died. This obvious paradox has been previously reported in the literature.[27-29] Cerda and coworkers reported in a cohort of 134 critically ill patients that a higher serum creatinine at the time of initiation of continuous renal replacement therapy was independently associated with a better survival (odds ratio, 1.438; 95% confidence interval, 1.034 to

1.999).[27] In our study, this finding can be explained by the similar peak creatinine levels in both the survivors and nonsurvivors, which suggests that the nonsurvivors had a greater proportionate increase in their creatinine level, and therefore, a greater degree of kidney dysfunction leading to a higher mortality rate. Moreover, a lower serum creatinine may indicate fluid overload and decreased muscle mass or malnutrition resulting in poor outcomes. Secondly, patients who developed kidney failure later in the course of hospitalization were found to have a higher mortality rate while kidney failure on admission was independently associated with a better chance of survival. Another plausible explanation for these associations is that dialysis may be initiated earlier in patients with impaired baseline kidney function, thus improving their chances of survival as compared to those with normal baseline kidney function. This is because patients with preexisting CKD may require a lesser burden of disease in terms of number of organ failures to reach a point where they would need renal replacement therapy.[27]

There are certain limitations to our study which need to be addressed. The first limitation is the lack of a control group of patients without AKI. Second, due to the retrospective nature of the study, there might be a possibility of selection bias. We could not evaluate the urine output criteria of the RIFLE classification, either, due to the study design. Furthermore, clinical judgement was used to exclude those patients who had stable CKD, thus there is a possibility of human error. Lastly, this is a single center study and hence the results could not be generalized to the entire population.

CONCLUSIONS

The CCI is a predictor of outcomes including mortality and recovery of kidney function in critically ill patients with acute kidney injury. Kidney injury occurring during hospital stay, lower serum creatinine on presentation, and need for dialysis are predictors of poor outcomes. Although a high proportion of critically ill patients with AKI die during hospitalization, our data shows that in those who survive, there is a good prognosis for renal recovery.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative workgroup. Acute kidney failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8:R204–12.
2. Singbartl K, Kellum JA. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. Kidney Int. 2012;81:819-25.
3. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: A systematic review. Kidney Int. 2008;73:538-46.
4. Bagshaw SM, George C, Bellomo R, et al. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. Nephrol Dial Transplant. 2008;23:1569-74.
5. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373-83.
6. Jönsen A, Clarke AE, Joseph L, et al. Association of the Charlson comorbidity index with mortality in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2011;63:1233-7.
7. Núñez JE, Núñez E, Fácila L, Bertomeu V, Llàcer A, Bodí V, Sanchis J, Sanjuán R, Blasco ML, Consuegra L, Martínez A, Chorro FJ. [Prognostic value of Charlson comorbidity index at 30 days and 1 year after acute myocardial infarction]. Rev Esp Cardiol. 2004;57:842-9. Spanish.
8. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, Januel JM, Sundararajan V. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011;173:676-82.
9. Bar B, Hemphill JC 3rd. Charlson comorbidity index adjustment in intracerebral hemorrhage. Stroke. 2011;42:2944-6.
10. Kirkland LL, Kashiwagi DT, Burton MC, Cha S, Varkey P. The Charlson Comorbidity Index Score as a predictor of 30-day mortality after hip fracture surgery. Am J Med Qual. 2011;26:461-7.
11. Ather MH, Nazim SM. Impact of Charlson's comorbidity index on overall survival following tumor nephrectomy for renal cell carcinoma. Int Urol Nephrol. 2010;42:299-303.
12. Khawaja A, Zubairi AB, Durrani FK, Zafar A. Etiology and outcome of severe community acquired pneumonia in immunocompetent adults. BMC Infect Dis. 2013;13:94.
13. Çıldır E, Bulut M, Akalın H, Kocabaş E, Ocakoğlu G, Aydın ŞA. Evaluation of the modified MEDS, MEWS score and Charlson comorbidity index in patients with community acquired sepsis in the emergency department. Intern Emerg Med. 2013;8:255-60.
14. Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. J Clin Epidemiol. 2008;61:1234-40.
15. Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting

the Charlson Comorbidity Index for use in patients with ESRD. Am J Kidney Dis. 2003;42:125-32.

16. Bagshaw SM, Laupland KB, Doig CJ, et al. Prognosis for long-term survival and renal recovery in critically ill patients with severe acute kidney failure: a population-based study. Crit Care. 2005;9:R700-9.
17. Ortiz Librero M, Mon Mon C, Herrero Berrón JC, et al. [The importance of comorbidity in nephrologists' assessment of acute kidney failure]. Nefrologia. 2009;29:430-8. Spanish.
18. Bagshaw SM, Mortis G, Godinez-Luna T, Doig CJ, Laupland KB. Renal recovery after severe acute kidney failure. Int J Artif Organs. 2006;29:1023-30.
19. Ali T, Khan I, Simpson W, et al. Incidence and outcomes in acute kidney injury: a comprehensive population-based study. J Am Soc Nephrol. 2007;18:1292-8.
20. Uchino S, Kellum JA, Bellomo R, et al. Acute kidney failure in critically ill patients: a multinational, multicenter study. JAMA. 2005;294:813-8.
21. Maccariello E, Soares M, Valente C, et al. RIFLE classification in patients with acute kidney injury in need of renal replacement therapy. Intensive Care Med. 2007;33:597-605.
22. Bagshaw SM, Laupland KB, Doig CJ, et al. Prognosis for long-term survival and renal recovery in critically ill patients with severe acute kidney failure: a population-based study. Crit Care. 2005;9:R700-9.
23. Bagshaw SM, George C, Dinu I, Bellomo R. A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant. 2008;23:1203-10.
24. Kuiper JW, Groeneveld AB, Slutsky AS, Plötz FB. Mechanical ventilation and acute kidney failure. Crit Care Med. 2005;33:1408-15.
25. Mehta RL, Pascual MT, Soroko S, Chertow GM; PICARD Study Group. Diuretics, mortality, and nonrecovery of kidney function in acute kidney failure. JAMA. 2002;288:2547-53.
26. Uchino S, Doig GS, Bellomo R, et al. Diuretics and mortality in acute kidney failure. Crit Care Med. 2004;32:1669-77.
27. Cerdá J, Cerdá M, Kilcullen P, Prendergast J. In severe acute kidney injury, a higher serum creatinine is paradoxically associated with better patient survival. Nephrol Dial Transplant. 2007;22:2781-4
28. Uchino S, Bellomo R, Morimatsu H, et al. External validation of severity scoring systems for acute kidney failure using a multinational database. Crit Care Med. 2005;33:1961-7.
29. Mehta RL, Pascual MT, Gruta CG, Zhuang S, Chertow GM. Refining predictive models in critically ill patients with acute kidney failure. J Am Soc Nephrol. 2002;13:1350-7.

Correspondence to:
Waqar Kashif, MD
Department of Medicine, Section of Nephrology,
The Aga Khan University Hospital, PO Box 78400, Karachi, Pakistan
Tel: +300 202 0194
E-mail: drwaqarkashif@gmail.com

Received May 2016
Revised September 2016
Accepted October 2016