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Original Article

Hospital Mortality of Septic Acute Kidney Injury Requiring Renal Replacement Therapy in the Postoperative Elderly[☆]Wei-Lun Liu¹, Jen-Yu Wang², Tao-Min Huang³, Chih-Cheng Lai¹, Cheng-Yi Wang², Yu-Chang Yeh⁴, Anne Chou⁴, Ton-Shin Chu³, Yu-Fung Lin³, Jaiinn-Shiun Chiu³, Pi-Ru Tsai⁵, Vin-Cent Wu³, Wen-Je Ko⁶, Kwan-Dun Wu³, Wei-Jie Wang^{7*}, on behalf of the NSARF Study Group⁸

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SUMMARY

Background: Septic acute kidney injury (AKI) is a common complication in intensive care units (ICU), it and portends a higher risk of morbidity and death than nonseptic AKI. However, its outcome and prognostic factors among elderly postoperative patients remain unknown. We aimed to determine the risk factors and predictors of mortality among postoperative elderly patients (≥ 65 years) with septic AKI requiring acute dialysis.

Methods: The study protocol was based on that of a clinical cohort study of renal failure patients in the database of the National Taiwan University Surgical ICU Acute Renal Failure (NSARF) Study Group. From January 2002 to July 2009, patients (aged > 18 years) with postoperative AKI requiring renal replacement therapy (RRT) were recruited for this study. Each case of septic AKI before operation was identified and patients with end-stage renal disease were excluded.

Results: A total of 292 postoperative patients with septic AKI requiring dialysis were identified during the study period. The mean (SD) age was 65.9 (11.9) years and 68.2% were men. Abdominal surgery was the most common type of surgery (42.8%), followed by cardiovascular (28.8%) and chest surgery (15.4%). The most common indications for RRT in this study cohort were azotemia in 223 patients (76.4%) and fluid overload in 62 patients (21.2%); 92 (31.5%) patients had one indication, 170 (58.2%) had two indications, and 30 (10.3%) had more than three indications. The elderly patients (those ≥ 65 years) had anemia, underwent abdominal surgery, and received dialysis for fluid overload more frequently than the young adults. By contrast, the young adults were more likely to present with shock requiring vasopressor use and have abnormal liver functions. In the elderly subgroup, the outcome was found to be associated with mechanical ventilator use, but not with disease severity, comorbidities, types of surgery and the indication for dialysis.

Conclusions: The hospital mortality of postoperative elderly patients with septic AKI was more than 60% and was not affected by age. Mechanical ventilator use was the major risk factor and prognostic factor for elderly patients in this clinical setting.

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1. Introduction

Acute kidney injury (AKI) is defined as an abrupt decline in renal function resulting in the inability to excrete metabolic wastes and

maintain a proper fluid and electrolyte balance. AKI is a common complication of critical illness and occurs in 5% of all in-hospital patients and in 6%–23% of intensive care unit (ICU) patients^{1–3}. Furthermore, the occurrence of AKI in critically ill patients increased morbidity and mortality^{4–6}. Patients with severe AKI after a major operation were associated with a high risk of having a poor outcome and an increased costs for care^{2,7}; the negative impact might extend beyond the discharge of such patients from the hospital.

[☆] All contributing authors declare no conflict of interest.

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The common etiologies of in-hospital AKI included sepsis, hypotension, and the use of nephrotoxic agents or radio-contrast media⁸. Sepsis was the leading cause of AKI in critically ill patients and was associated with about 70% of all AKI cases^{9–11}. The increasing prevalence and extended clinical consequences of AKI in the elderly are of great concern from a clinical and public health perspective. However, studies on clinical characteristics, outcomes, and prognostic factors of elderly septic AKI in postoperative patients remain scarce. Therefore, this study aimed to clarify the clinical manifestations and risk factors of postoperative elderly patients with septic AKI. Because the elderly subgroup is of great interest in the era of aging, we also try to elucidate the difference of clinical presentations between the young and the elderly and further analysis prognostic factors of elderly patient outcomes.

2. Materials and methods

2.1. Setting and patients

The study protocol was based on that of a clinical cohort study of renal failure patients in the database of the National Taiwan University Surgical ICU Acute Renal Failure (NSARF) Study Group^{12–14}, which was carried out in one medical center (National Taiwan University Hospital, Taipei, Taiwan) and its three branch hospitals (National Taiwan University Hospital, Yun-Lin branch, Yun-Lin, Taiwan; Far Eastern Memorial Hospital, New Taipei city, Taiwan, and Tao-Yuan General Hospital, Tao-Yuan, Taiwan), after obtaining the approval of the Institutional Review Board of National Taiwan University Hospital. From January 2002 to July 2009, patients (aged >18 years) with postoperative AKI requiring renal replacement therapy (RRT) were recruited for this study. Each case of septic AKI was identified based on the consensus criteria¹; those patients with end-stage renal disease requiring dialysis before operation and patients who had undergone renal transplantation were excluded.

2.2. Definitions

Disease severity was assessed by using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score¹⁵, the Sequential Organ Failure Assessment (SOFA) score¹⁶, the Multiple Organ Dysfunction Score (MODS)¹⁷, and the Simplified Acute Physiology Score II (SAPS II)¹⁸. The criteria for organ failure have been proposed previously^{19,20}. Sepsis was defined as the persistence or progression of the signs and symptoms of systemic inflammatory response syndrome with a documented or presumed persistence of infection¹. The intra-aortic balloon pump and/or extracorporeal membrane oxygenation were considered for refractory circulatory shock¹⁸. The choice of renal replacement therapy modality was made according to the evaluation of the attending physician after considering the clinical characteristics of the patients. The indication for hemodialysis was as previously reported^{15,21,22} in brief: (1) azotemia (Blood urea nitrogen (BUN) > 80 mg/dL and serum creatinine (sCr) > 2 mg/dL with uremic symptoms (165 patients), (2) fluid overload with a central venous pressure > 12 mm Hg or pulmonary edema with a PaO₂/FiO₂ < 300 (90 patients), (3) hyperkalemia (serum K⁺ > 5.5 mmol/L) despite medical treatment (43 patients), (4) oliguria (urine amount < 100 mL/8 hours) with or without use of diuretics (295 patients), and (5) acidosis [pH < 7.2 in arterial blood gas (21 patients)].

The dialysis modality was chosen according to the hemodynamics of patients as previous report^{11,21,22}. Continuous veno-venous hemofiltration (CVVH) was used if the dose of inotropic equivalent of more than 15 points was required to maintain systolic blood pressure up to 120 mm Hg, APACHE II score > 28 at

initializing renal replacement therapy, or SBP < 120 mm Hg despite inotropic agents. CVVH was performed with high-flux filters (Hemofilter, PAN-10, Asahi Kasei Medical Company, Japan) using HF 400 (Infomed, Geneva, Switzerland) and a hemofiltration flow of 35 mL/kg/hour with a blood flow of 200 mL/minute. Replacement fluid was bicarbonate-buffered and was administered predilutionally at a dynamically adjusted volume to achieve the desired fluid therapy goals. All RRT was performed via a double-lumen catheter with coagulation free.

2.3. Statistical analysis

Variables measured in this study were expressed as mean ± SD. Comparisons of continuous variables between two groups were performed using independent-sample *t* tests (Student's *t* test). Categorical variables were presented as counts and percentages and compared using the chi-square test. All statistical analyses were performed with SPSS 12.0 software (SPSS Inc., Chicago, IL), and a *p* value <0.05 was considered statistically significant.

3. Results

3.1. Study population and patient characteristics

Two hundred ninety-two postoperative patients with septic AKI requiring dialysis were identified during the study period. The demographic and clinical characteristics of these patients are summarized in Table 1. The mean (SD) age was 65.9 (11.9) years and 68.2% of the patients were men. Hypertension was the most common underlying disease (49%), followed by diabetes mellitus (29.8%). Abdominal surgery was the most common type of surgery (42.8%), followed by cardiovascular (28.8%) and chest surgery (15.4%). The most common indications for RRT in this study cohort were azotemia in 223 patients (76.4%) and fluid overload in 62 (21.2%): 92 (31.5%) patients had one indication, 170 (58.2%) had two indications, and 30 (10.3%) had more than three indications.

3.2. Comparison of clinical features between the adults and the elderly patients

A comparison of the baseline characteristics between the adult patients (< 65 years) and the elderly patients (≥ 65 years) are presented in Table 2. The elderly patients had anemia, underwent abdominal surgery and received dialysis for fluid overload more frequently than the adult patients. In contrast, the adult patients were more likely to present with shock requiring vasopressor use, and have abnormal liver functions, including aspartate aminotransferase (GOT) and total bilirubin.

3.3. Comparison of clinical features between the patients who survived and those who did not

To evaluate the risk factors of in-hospital mortality of postoperative elderly patients with septic AKI, we compared the clinical features of those who survived and those who did not (Table 3). Among this elderly subgroup, the outcome was found to be associated with mechanical ventilator use, but not with disease severity, comorbidities, the types of surgery, and the indication for dialysis.

4. Discussion

AKI is not uncommonly seen in the perioperative period and in the ICU, and the incidence of postoperative AKI among patients with normal preoperative renal function was about 7.5%²³. In

Table 1
Demographic and clinical characteristics of 292 postsurgical patients with septic acute kidney injury requiring dialysis.

Variable	No (%) or mean ± SD of patients
Sex, male	199 (68.2)
Age, yr	65.9 ± 11.9
Age ≥ 65 yr	178 (60.1)
BMI, kg/m ²	23.2 ± 4.0
Disease severity at ICU admission	
APACHE II	10.6 ± 6.2
SOFA	7.7 ± 3.7
SAPS	46.9 ± 12.7
SAPS III	62.8 ± 7.5
MODS	6.3 ± 3.4
Comorbidities	
Hypertension	143 (49.0)
Diabetes mellitus	87 (29.8)
Coronary artery disease	29 (9.9)
Liver cirrhosis	20 (6.8)
Malignancy	13 (4.5)
Pulmonary disease	7 (2.4)
Stroke	7 (2.4)
Pre-episode renal function	
BUN, mg/dL	30.1 ± 28.1
Serum creatinine level, mg/dL	1.8 ± 1.3
Estimated creatinine clearance rate (Ccr), ml/min	53.9 ± 37.5
Estimated Ccr < 60 ml/min	133 (45.5)
Surgical category	
Abdominal	125 (42.8)
Cardiovascular	84 (28.8)
Thoracic	45 (15.4)
Plastic	24 (8.2)
Orthopedic	8 (2.7)
Neurology	6 (2.1)
Indications for dialysis	
Azotemia	223 (76.4)
Fluid overload	62 (21.2)
Oliguria	37 (12.7)
Severe acidosis	13 (4.5)
Hyperkalemia	7 (2.4)
ICU mortality	175 (59.9)
Hospital death	121 (67.1)

APACHE II = Acute Physiology and Chronic Health Evaluation II; BUN = blood urea nitrogen; ICU = intensive care unit; MODS = Multiple Organ Dysfunction Score; SAPS = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment.

a prospective, multinational, and multicenter observational study of 1753 critically ill patients with AKI, sepsis was considered the leading etiology of AKI, causing 833 (47.5%) episodes of AKI²⁴. Although septic AKI frequently occurs and leads to higher mortality in critically ill patients^{9–11}, this report is the first to study the clinical characteristics of septic AKI among postoperative elderly patients in a surgical ICU. The results showed that both in-ICU and in-hospital mortality were greater than 50% in this clinical setting, which is consistent with a previous study in which the 90-day mortality of 342 postsurgical patients with AKI irrespective of etiologies was 60%²⁵. This would suggest that the development of septic AKI requiring RRT leads to a substantial risk of mortality.

Since clinicians face a clinical entity with such high mortality, a better understanding of the risk factors of septic AKI in postoperative care is urgently needed to help physicians identify the precipitating factors and prevent the further occurrence of septic AKI among postsurgical patients. The elderly consume twice as many medications overall, including nephrotoxic agents, compared with younger patients. The vasodilatory increase in the renal plasma flow and glomerular filtration rate that constitutes renal functional reserve is reduced markedly in healthy elderly individuals, compromising renal adaptation after acute ischemia, and

Table 2
Comparison of clinical features of postsurgical septic acute kidney injury patients requiring dialysis based on age.

Variable	No (%) or mean ± SD of adult (18–65 yr) (n = 114)	No (%) or mean ± SD of elderly (> 65 yr) (n = 178)	p value
Sex, male	84 (73.7)	115 (64.6)	0.123
Age, year	49.7 ± 12.6	76.2 ± 6.1	< 0.001
Body mass index, kg/m ²	23.4 ± 4.1	23.1 ± 4.0	0.942
Disease severity			
SAPS	47.6 ± 14.0	46.4 ± 11.7	0.077
APACHE II	10.8 ± 6.0	10.5 ± 6.4	0.573
MODS	6.9 ± 3.5	6.0 ± 3.2	0.071
SOFA	8.3 ± 3.9	7.3 ± 3.4	0.05
SAPSIII	64.7 ± 7.8	61.5 ± 7.0	0.344
Comorbidities			
Hypertension	44 (38.6)	99 (55.6)	0.006
Diabetes mellitus	30 (26.3)	57 (32.0)	0.359
Congestive heart failure	23 (20.2)	24 (13.5)	0.143
Liver cirrhosis	9 (7.9)	11 (6.2)	0.637
Malignancy	4 (3.5)	9 (5.1)	0.772
Estimated Ccr < 60 ml/min	44 (38.6)	89 (50.0)	0.0738
Stroke	2 (1.8)	11 (6.2)	0.087
Indications for dialysis			
Azotemia	84 (73.7)	140 (78.7)	0.395
Oliguria	82 (71.9)	124 (69.7)	0.695
Fluid overload	34 (29.8)	28 (15.7)	0.005
Severe acidosis	7 (6.1)	13 (7.3)	0.815
Hyperkalemia	4 (3.5)	10 (5.6)	0.577
Intervention			
Mechanical ventilator	106 (93.0)	157 (88.2)	0.23
Vasopressor	39 (34.2)	40 (22.5)	0.031
Acute Kidney Injury			0.461
Network criteria			
Stage 1	38 (33.3)	72 (40.4)	
Stage 2	36 (31.5)	52 (29.2)	
Stage 3	40 (35.1)	54 (30.3)	
Laboratory findings			
Hemoglobin level, g/dL	11.35 ± 2.7	10.29 ± 1.95	0.016
Albumin, g/dL, mean ± SD	2.87 ± 0.69	2.94 ± 0.65	0.804
AST, U/L	229.15 ± 588.38	107.3 ± 419.34	0.005
Total bilirubin, mg/dL	4.85 ± 10.71	2.03 ± 4.38	< 0.001
Outcome			
Hospital death	75 (65.8)	121 (68.0)	0.648

APACHE II = Acute Physiology and Chronic Health Evaluation II; AST = aspartate aminotransferase; Ccr = creatinine clearance rate; MODS = Multiple Organ Dysfunction Score; SAPS = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment.

heightening susceptibility to AKI. Age-related alterations in renal tubular function also may heighten susceptibility to AKI because renal sodium conservation in response to dietary sodium restriction is attenuated in the elderly. It is the age-related renal and systemic changes as well as frequent comorbidities that render older individuals greatly susceptible to acute renal impairment. Abelha and colleagues²³ reported that high-risk surgery and congestive heart disease were identified as preoperative determinants of AKI in the postoperative periods. Previous studies found that septic AKI was associated with greater aberrations in hemodynamics and laboratory parameters, greater severity of illness, and a greater need for mechanical ventilator and vasoactive therapy²⁶. Similarly, Neveu and colleagues²² reported that patients with septic AKI were older and had greater disease severity than patients with nonseptic AKI. The present study showed the consistent findings that most patients with septic AKI during the postoperative period had various comorbidities and needed mechanical ventilator use.

Since aging populations are rapidly becoming a global phenomenon, an awareness of the clinical features of elderly

Table 3
Comparison of clinical features of elderly postsurgical septic acute kidney injury patients (≥ 65 yr) requiring dialysis who survived or died in the hospital.

Variable	No (%) or mean \pm SD of patients who survived ($n = 57$)	No (%) or mean \pm SD of in-hospital patients who died ($n = 121$)	<i>p</i> value
Sex, male	38 (66.7)	77 (63.6)	0.739
Age, yr	75.18 \pm 5.4	76.73 \pm 6.4	0.122
Body mass index, kg/m ²	23.55 \pm 4	22.89 \pm 3.97	0.389
Disease severity			
SAPS	45.44 \pm 10.52	46.84 \pm 12.28	0.088
APACHE II	9 \pm 7.52	11.21 \pm 5.73	0.839
MODS	5.44 \pm 3.03	6.19 \pm 3.27	0.181
SOFA	7.47 \pm 3.32	7.23 \pm 3.48	0.836
SAPSI	61.42 \pm 6.47	61.6 \pm 7.25	0.236
Comorbidities			
Diabetes mellitus	17 (29.8)	40 (33.1)	0.732
Congestive heart failure	8 (14.0)	16 (13.2)	1
Stroke	6 (10.5)	5 (4.1)	0.178
Liver cirrhosis	3 (5.3)	8 (6.6)	1
Malignancy	2 (3.5)	7 (5.8)	0.721
Surgical category			
Abdominal	28 (49.1)	57 (47.1)	0.873
Cardiovascular	18 (31.6)	27 (22.3)	0.199
Thoracic	5 (8.8)	21 (17.4)	0.173
Plastic	3 (5.3)	10 (8.3)	0.554
Orthopedic	3 (5.3)	3 (2.5)	0.386
Neurology	0 (0.0)	3 (2.5)	0.552
Indications for dialysis			
Azotemia	50 (87.7)	90 (74.4)	0.05
Severe acidosis	34 (59.6)	90 (74.4)	0.055
Fluid overload	6 (10.5)	22 (18.2)	0.27
Hyperkalemia	3 (5.3)	7 (5.8)	1
Oliguria	2 (3.5)	11 (9.1)	0.23
Intervention			
Ventilator	46 (80.7)	111 (91.7)	0.046
Vasopressor	14 (24.6)	26 (21.5)	0.702

APACHE II = Acute Physiology and Chronic Health Evaluation II; AST = aspartate aminotransferase; MODS = Multiple Organ Dysfunction Score; SAPS = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment.

patients in this clinical setting is important. In this study, 178 (61%) of 292 patients were older than 65 years, and the elderly patients were more likely to have hypertension. In addition, most of the elderly patients developed septic AKI after receiving abdominal surgery, and the levels of hemoglobin of this group were significantly lower than that of the adults. By contrast, the adult patients were more likely to receive dialysis due to fluid overload and need vasopressor use for hypotension than the elderly patients, and the liver enzyme levels of the adults were significantly higher than those of the elderly patients. Although there was a trend toward more stage I acute kidney injury in the elderly group, there was no significant difference in disease severity between the adult and elderly patients, and the associated hospital mortality was similar among these two subgroups. Therefore, despite the cases number is limited in the present work, this finding suggests that age itself may not influence the outcome of septic AKI in postoperative patients in the same severity of critical illness.

The overall in-hospital mortality of the 178 postsurgical elderly patients with septic AKI was as high as 68%. To determine the prognostic factors for a poor outcome, we evaluated the possible risk factors on patient outcome, and only mechanical ventilator use was found to be associated with mortality among these patients. This was consistent with the results of a previous study in which mechanical ventilator use was one of the significant risk factors for hospital mortality²⁶. This may imply that the presence of acute

respiratory failure in elderly patients with septic AKI portends a worse prognosis.

This study had several limitations. First, it was performed in four hospitals and the characteristics of the mixed surgical intensive care unit (SICU) patients were heterogeneous. Second, the facility of the each hospital was different and may have influence on the analysis of outcome. Third, we only enrolled the patients requiring renal replacement therapy, and the information about the numbers of all patients received surgery is lacking. Therefore, the knowledge about the percentage of septic acute kidney injury requiring renal replacement therapy in every surgical category remains unknown.

In conclusion, the mortality of postoperative patients with septic AKI, irrespective of age, remains high. Mechanical ventilator use is the major risk factor and prognostic factor for elderly patients in this clinical setting.

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