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Risk factors for in-hospital mortality in patients starting hemodialysis

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Abstract

Background: Incident hemodialysis patients have the highest mortality in the first several months after starting dialysis. This study evaluated the in-hospital mortality rate after hemodialysis initiation, as well as related risk factors.
Methods: We examined in-hospital mortality and related factors in 2,692 patients starting incident hemodialysis. The study population included patients with acute kidney injury, acute exacerbation of chronic kidney disease, and chronic kidney disease. To determine the parameters associated with in-hospital mortality, patients who died in hospital (nonsurvivors) were compared with those who survived (survivors). Risk factors for in-hospital mortality were determined using logistic regression analysis.
Results: Among all patients, 451 (16.8%) died during hospitalization. The highest risk factor for in-hospital mortality was cardiopulmonary resuscitation, followed by pneumonia, arrhythmia, hematologic malignancy, and acute kidney injury after bleeding. Albumin was not a risk factor for in-hospital mortality, whereas C-reactive protein was a risk factor. The use of vancomycin, inotropes, and a ventilator was associated with mortality, whereas elective hemodialysis with chronic kidney disease and statin use were associated with survival. The use of continuous renal replacement therapy was not associated with in-hospital mortality.
Conclusion: Incident hemodialysis patients had high in-hospital mortality. Cardiopulmonary resuscitation, infections such as pneumonia, and the use of inotropes and a ventilator was strong risk factors for in-hospital mortality. However, elective hemodialysis for chronic kidney disease was associated with survival.

Introduction

The annual mortality rate of hemodialysis (HD) patients exceeds 20% [1]. The mortality rate is even higher during the 1st year of dialysis therapy, especially in the 1st few months [1]. However, the risk factors for in-hospital mortality are largely unknown. Early mortality occurring in the 1st 90 days after starting renal replacement therapy (RRT) is responsible for a large proportion of the 1st year mortality rate, which ranges 12.6–32.0% [2]. Short-term prognosis studies report varying results because of different methodologies [3]. For example, Canadian studies considered the early period as the 1st 6 months after starting RRT [4,5], whereas others excluded mortality that occurred in the 1st month [6]. Meanwhile, the United States Renal Data System registry excludes all patients who did not survive beyond 90 days and only analyzes mortality that occurred in patients aged more than 65 years [7].

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The most common cause of death in dialysis patients is cardiovascular disease followed by infectious disease. A recent study examining early mortality among incident HD patients during the 1st 120 days versus the subsequent 121–365 days shows cardiovascular diseases were still the most common cause of death during the entire 1st year [8].

Although previous studies have identified several important factors associated with increased mortality in incident HD patients, few have addressed the risk factor patterns and their temporal changes during their 1st few months of dialysis therapy. It is crucial to determine if these risk patterns remain constant or change over time, so that targeted interventions can be used at different periods of time. Therefore, the present study examined the risk factors for in-hospital mortality after the start of HD therapy in incident HD patients who had started treatment.

Methods

Study population and design

We reviewed the records of 2,692 new patients who started HD at the Chonnam National University Hospital from January 1, 2007 through December 31, 2011. Patients with acute kidney injury (AKI), acute exacerbation of chronic kidney disease (CKD), or CKD with programmed RRT were included.

Data collection and definitions

The following clinical data were collected: age, sex, body mass index, cause of admission, presence of cardiopulmonary resuscitation (CPR), comorbidity, first mode of HD (i.e., emergency or programmed dialysis), in-hospital medication, vascular access, dialysis frequency (times per week), and mortality during hospitalization.

The following laboratory parameters were recorded at admission and when starting HD: blood gas analysis parameters such as PaO_2 and HCO_3^-; blood parameters such as white blood cell count, hemoglobin, blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, total bilirubin, direct bilirubin, sodium, potassium, calcium, phosphorus, albumin, C-reactive protein (CRP), and low-density lipoprotein cholesterol; and urinalysis parameters such as proteinuria ($>$30 mg/g creatinine) and hematuria (red blood cells $>$3/high power field).

Statistical analyses

To determine the parameters associated with in-hospital mortality, patients who died in hospital (nonsurvivors) were compared with those who survived (survivors). All continuous variables are presented as mean $\pm$ standard deviation. For univariate analysis, categorical and continuous variables were analyzed with the χ^2 test and Student t test, respectively. Variables associated with in-hospital mortality showing $P < 0.25$ in univariate analysis were entered into multivariate stepwise logistic regression analysis. Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) were calculated. All analyses were two tailed, and the level of significance was set at $P < 0.05$. All analyses were performed using SPSS, version 18.0, for Windows (SPSS Inc., Chicago, IL, USA).

Results

The clinical parameters of the study patients are summarized in Table 1. Of 2,692 patients, 451 (16.8%) died during hospitalization after starting incident HD. Survivors were younger than nonsurvivors (60.2 ± 14.6 years vs. 64.7 ± 14.9 years, $P < 0.001$). Sex and body mass index did not differ between nonsurvivors and survivors. The prevalence of diabetes mellitus was higher in survivors, whereas the prevalence of solid tumors, hematologic malignancy, and smoking was

Table 1. Comparison for clinical risk factors at starting hemodialysis

Variables	Nonsurvivor (n=451)	Survivor (n=2,241)	P
Age (y)	64.7 ± 14.9	60.2 ± 14.6	<0.001
Sex (male)	283 (62.7)	1,367 (61.0)	0.492
Body mass index (kg/m^2)	22.9 ± 3.9	23.2 ± 6.4	0.412
On admission			
Via emergency room	360 (79.8)	1,644 (73.4)	0.004
After cardiac pulmonary resuscitation	94 (20.8)	16 (0.7)	<0.001
Comorbidities			
Hypertension	237 (52.5)	1,630 (72.7)	0.246
Diabetes mellitus	176 (39.7)	1,116 (49.8)	<0.001
Cardiovascular disease	63 (14.0)	335 (14.9)	0.663
Hyperlipidemia	10 (2.2)	56 (2.5)	0.868
Solid tumor	87 (19.3)	237 (10.6)	<0.001
Heart failure	17 (3.8)	79 (3.5)	0.876
Hematologic malignancy	38 (8.4)	34 (1.5)	<0.001
Smoking	161 (35.7)	665 (29.7)	0.035
Cause of admission			
Chronic kidney disease	149 (33.0)	1,565 (69.8)	<0.001
Urinary tract infection	9 (2.0)	27 (1.2)	0.180
Pneumonia	78 (17.3)	112 (5.0)	<0.001
Acute myocardial infarction	31 (6.9)	83 (3.7)	0.004
Postchemotherapy	27 (6.0)	31 (1.7)	<0.001
Postbleeding	107 (23.7)	218 (9.7)	<0.001
Stone	10 (2.2)	35 (1.6)	0.315
Postoperation	17 (3.8)	58 (2.6)	0.160
Others	23 (5.1)	112 (5.0)	0.612

Data are presented as mean ± SD or n (%).

Table 2. Laboratory findings at admission

Variables	Nonsurvivor (n=451)	Survivor (n=2,241)	P
PaO_2 (mmHg)	96.7 ± 59.2	86.5 ± 49.2	<0.001
HCO_3 (mmol/L)	18.3 ± 6.8	18.3 ± 6.8	0.930
White blood cell ($10^3/mm^3$)	14.0 ± 17.2	9.9 ± 7.5	<0.001
Hemoglobin (g/dL)	10.6 ± 2.6	9.9 ± 3.2	<0.001
AST (U/L)	240.4 ± 1,760.7	106.9 ± 914.0	0.118
ALT (U/L)	97.3 ± 371.7	59.1 ± 326.2	0.043
Total bilirubin (mg/dL)	1.6 ± 3.6	0.9 ± 1.5	<0.001
Direct bilirubin (mg/dL)	1.2 ± 1.8	0.8 ± 2.2	0.017
Albumin (g/dL)	3.1 ± 1.2	3.4 ± 1.1	<0.001
Blood urea nitrogen (mg/dL)	47.1 ± 35.5	71.4 ± 48.5	<0.001
Creatinine (mg/dL)	3.4 ± 3.0	7.8 ± 6.0	<0.001
Sodium (mEq/L)	135.2 ± 7.9	134.8 ± 8.4	0.333
Potasssium (mEq/L)	4.5 ± 1.1	5.5 ± 4.7	0.087
PT (INR)	1.4 ± 0.8	1.3 ± 0.5	0.338
Lactate dehydrogenase (U/L)	1,311.2 ± 3,036.7	704.7 ± 1,430.0	<0.001
C-reactive protein (mg/dL)	9.5 ± 9.5	5.6 ± 17.6	<0.001
Inorganic phosphate (mg/dL)	4.7 ± 2.3	5.6 ± 15.5	0.214
Total calcium (mg/dL)	7.2 ± 2.0	7.1 ± 2.6	0.258
Low-density lipoprotein (mg/dL)	84.6 ± 45.7	97.4 ± 40.9	0.003
Proteinuria	295 (65.4)	1,615 (72.1)	<0.001
Hematuria	383 (84.9)	1,734 (77.3)	0.263

Data are presented as mean ± SD or n (%).
AST, aspartate transaminase; ALT, alanine transaminase; INR, international normalized ratio; PT, prothrombin time.

Table 3. Laboratory findings at initial hemodialysis

Variables	Nonsurvivor (n=451)	Survivor (n=2,241)	P
PaO_2 (mmHg)	95.3 ± 42.1	86.9 ± 55.3	<0.001
HCO_3 (mmol/L)	17.4 ± 6.9	18.3 ± 7.0	0.006
White blood cell ($10^3/mm^3$)	13.9 ± 10.8	9.7 ± 6.2	<0.001
Hemoglobin (g/dL)	10.0 ± 2.1	9.7 ± 3.0	0.015
AST (U/L)	485.7 ± 2,268.1	130.0 ± 997.0	0.001
ALT (U/L)	205.0 ± 736.0	69.5 ± 388.2	<0.001
Total bilirubin (mg/dL)	2.4 ± 4.3	1.0 ± 3.0	<0.001
Direct bilirubin (mg/dL)	1.9 ± 2.7	1.8 ± 25.9	0.933
Albumin (g/dL)	2.9 ± 1.1	3.3 ± 1.0	<0.001
Blood urea nitrogen (mg/dL)	71.2 ± 45.9	81.1 ± 198.1	0.289
Creatinine (mg/dL)	4.5 ± 2.8	8.2 ± 6.2	<0.001
Sodium (mEq/L)	138.0 ± 7.7	135.4 ± 7.7	<0.001
Potassium (mEq/L)	4.7 ± 1.1	5.3 ± 1.7	0.255

Data are presented as mean ± SD or n (%).
ALT, alanine transaminase; AST, aspartate transaminase.

higher in nonsurvivors. Regarding the cause of admission, CKD was more common among survivors, whereas pneumonia, acute myocardial infarction, chemotherapy, and bleeding were more common among nonsurvivors.

The laboratory findings at admission are shown in Table 2. Compared with survivors, nonsurvivors had a significantly higher white blood cell count and CRP level, as well as lower albumin and serum creatinine levels. The laboratory findings at the start of HD are shown in Table 3. Metabolic acidosis, hypoxia, leukocytosis, and liver function test results were worse in nonsurvivors, whereas hemoglobin, serum albumin, and creatinine levels were lower in nonsurvivors.

Details on in-hospital medications, clinical assistive devices, and vascular access are shown in Table 4. The use of loop diuretics, inotropes, vancomycin, and steroids was more common in nonsurvivors. Meanwhile, the use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, statins, calcium channel blockers, and anticoagulants was more common in survivors. The rate and duration of intensive care unit (ICU) care, use of continuous RRT, and ventilator treatment were more common in nonsurvivors. Vascular access via the femoral vein was more common in nonsurvivors, whereas access via a tunneled cuffed catheter and arteriovenous access, including arteriovenous fistula and arteriovenous graft, were more common in survivors.

The results of the multivariate analysis of risk factors for in-hospital mortality in incident HD patients are shown in Table 5. The presence of CPR was the strongest risk factor for in-hospital mortality, with an aHR of 31.47 (95% CI: 5.766–171.814), followed by pneumonia (aHR: 6.408; 95% CI: 2.007–20.454), solid tumor (aHR: 4.171; 95% CI: 1.333–13.023), inotrope use (aHR: 11.846; 95% CI: 3.650–38.440), ventilator use (aHR: 7.561; 95% CI: 2.142–26.686), ICU care (aHR: 6.021; 95% CI: 2.093–17.316), and vancomycin administration (aHR: 2.563; 95% CI: 1.140–5.762). Meanwhile, statin administration decreased the risk of in-hospital mortality after adjusting for clinical and biochemical parameters (aHR: 0.199; 95% CI: 0.065–0.610).

The risk factors for in-hospital mortality after excluding CPR, inotrope administration, ventilator use, ICU care, and vancomycin are shown in Table 6. Arrhythmia (aHR: 3.253; 95% CI: 2.179–4.856), hematologic malignancy (aHR: 2.088;

Table 4. Comparison for risk factors associated with medication and dialysis modality

Variables	Nonsurvivor (*n* = 451)	Survivor (*n* = 2,241)	*P*
Hemodialysis (h/wk)	8.4 ± 5.4	9.4 ± 3.7	<0.001
In-hospital medication			
Loop diuretics	381 (84.5)	1,374 (61.3)	<0.001
Inotropics	394 (87.4)	860 (38.4)	<0.001
ACEI	62 (13.7)	456 (20.3)	<0.001
ARB	97 (21.5)	1,040 (46.4)	<0.001
Statin	31 (6.9)	449 (20.0)	<0.001
CCB	166 (36.8)	1,328 (59.3)	<0.001
Vancomycin	176 (39)	296 (13.2)	<0.001
Steroid	123 (27.3)	290 (12.9)	<0.001
Anticoagulation	145 (32.2)	1,142 (51.0)	<0.001
ICU care	354 (78.5)	433 (19.3)	<0.001
ICU duration (d)	18.1 ± 26.0	13.4 ± 16.2	0.003
CRRT	110 (24.4)	75 (3.3)	<0.001
CRRT duration (d)	10 (2.2)	56 (2.5)	0.541
Ventilator	310 (68.7)	216 (9.6)	<0.001
Access			
Femoral venous	289 (64.1)	644 (28.8)	<0.001
Temporary jugular venous	43 (9.5)	243 (10.8)	0.451
Jugular venous, tunneled cuffed jugular catheter	77 (17.1)	576 (25.7)	<0.001
Arteriovenous fistula or graft	42 (9.3)	778 (34.7)	<0.001

Data are presented as mean ± SD or *n* (%).
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CRRT, continuous renal replacement therapy; ICU, intensive care unit.

Table 5. Multivariate analysis for risk factors for in-hospital mortality

Variables	Adjusted hazard ratio	CI	*P*
Age (y)	1.031	0.264–4.025	0.966
Sex (male)	0.812	0.311–2.121	0.671
Body mass index (kg/m^2)	0.589	0.148–2.348	0.453
Via emergency room	2.157	0.868–5.357	0.098
After cardiac pulmonary resuscitation	31.474	5.766–171.814	<0.001
Hypertension	0.835	0.326–2.141	0.708
Diabetes mellitus	1.727	0.696–4.288	0.239
Solid tumor	4.171	1.333–13.023	0.014
Pneumonia	6.408	2.007–20.454	0.002
Albumin on HD	0.545	0.279–1.065	0.074
Inotropics	11.846	3.650–38.440	<0.001
Statin	0.199	0.065–0.610	0.005
Vancomycin	2.563	1.140–5.762	0.023
Intensive care unit	6.021	2.093–17.316	0.001
Ventilator	7.561	2.142–26.686	0.002
CRRT	0.597	0.168–2.1138	0.423

Data are presented as mean ± SD or *n* (%).
CI, confidence interval; CRRT, continuous renal replacement therapy; HD, hemodialysis.

95% CI: 1.041–4.189), pneumonia (aHR: 3.302; 95% CI: 2.033–5.364), postbleeding (aHR: 2.569; 95% CI: 1.680–3.928), other infections (aHR: 1.525; 95% CI: 1.068–2.176), and CRP (aHR: 1.011; 95% CI: 1.001–1.021) were significant risk factors for in-hospital mortality, whereas programmed HD for CKD significantly decreased the risk of in-hospital mortality (aHR: 0.424; 95% CI: 0.279–0.643).

Discussion

In the present study, the in-hospital mortality rate of patients starting incident HD was 16.8%, which is similar to that in previous studies, ranging 11–26% [3,5,9–11]; this variation is likely due to different methodologies used in data collection and analysis. Several studies report that both all-cause and cardiovascular-related mortality rates are highest during the 1st 2 months of dialysis therapy [11,12]. However, CPR was the strongest risk factor in the present study; the reason might be study population, which included patients with AKI of various causes. Previous studies have focused on evaluating the risk factors for CKD [8,13]. However, this population-based study focused on patients receiving incident HD, including not only those with CKD but also those with AKI.

A study of the UK Renal National Registry cohort, including patients receiving HD and peritoneal dialysis, that used several models to predict the 3-year survival of incident dialysis patients reports older age, Caucasian ethnicity, diabetes mellitus and other primary causes of end-stage renal disease, history of cardiovascular disease, and smoking as risk factors for increased mortality [13].

In the present study, early mortality did not differ significantly between sexes. Some studies report a lower risk of mortality in women in 1-year survival analyses [12]. Older age, solid tumor,

Table 6. Multivariate analysis for risk factors of in-hospital mortality

Variables	Adjusted hazard ratio	CI	P
Age (y)	1.004	0.992–1.015	0.548
Sex (male)	0.949	0.680–1.325	0.760
Body mass index (kg/m^2)	0.990	0.948–1.033	0.635
Hypertension	0.809	0.560–1.168	0.258
Diabetes mellitus	1.057	0.738–1.513	0.764
Solitary tumor	1.340	0.834–2.155	0.227
Arrhythmia	3.253	2.179–4.8568	<0.001
Hematologic malignancy	2.088	1.041–4.189	0.038
Chronic kidney disease	0.424	0.279–0.643	<0.001
Pneumonia	3.302	2.033–5.364	<0.001
Other infections	1.525	1.068–2.176	0.020
Postbleeding	2.569	1.680–3.928	<0.001
Acute myocardial infarction	1.337	0.645–2.772	0.435
Creatinine	7.561	2.142–26.686	0.002
Albumin	0.993	0.860–1.146	0.922
C-reactive protein	1.011	1.001–1.021	0.027

CI, confidence interval.

and hematologic malignancy were significantly more common in nonsurvivors in the present study. Among the causes of admission, programmed HD for CKD was more common in survivors, whereas pneumonia, acute myocardial infarction, prior chemotherapy, and prior bleeding were more common among nonsurvivors. The frequencies of urinary tract infection and postoperative AKI did not differ between survivors and nonsurvivors. The higher in-hospital mortality rate in pneumonia patients may be associated with ventilator use and ICU care.

A low serum albumin level is reported to be a predictor of mortality in dialysis patients [8,14,15]. Hypoalbuminemia, an indicator of malnutrition, is a powerful independent predictor of mortality in patients on RRT [12,16,17]. Furthermore, serum albumin is reported to be a predictor of hospitalization and mortality [18,19]. Although serum albumin levels were lower among nonsurvivors in the present study, this was not a significant risk factor for in-hospital mortality after adjusting for other confounders. In-hospital mortality might be associated with the acute stage; albumin's half-life is approximately 20 days, which may be too long present in the acute stage, such as during CPR or acute myocardial infarction. Meanwhile, CRP and leukocytosis were higher in nonsurvivors, suggesting in-hospital mortality may be associated with infection.

An interesting finding of the present study is the seemingly paradoxical association between diabetes and lower in-hospital mortality, which has also been reported by Bradbury et al [8]. A possible explanation for this finding is that patients with diabetes mellitus are more likely to see a physician on a regular basis than nondiabetic patients; therefore, they might be better prepared for the transitional period of early dialysis therapy and programmed HD, resulting in lower mortality. A second reason might be that diabetic patients accounted for a small proportion of AKI patients and a large proportion of CKD patients, who received programmed HD.

Among clinical variables, the type of the vascular access was strongly associated with mortality. Central venous catheter insertion is strongly associated with mortality compared with arteriovenous fistula or arteriovenous graft in HD patients [20–23]. In the present study, jugular catheter insertion did not show different in-hospital mortality between survivors and nonsurvivors. However, femoral catheter insertion was more common in nonsurvivors, whereas tunneled cuffed jugular catheters, arteriovenous fistula, and arteriovenous graft were significantly more common in survivors. These findings are concordant with a previous report indicating uncuffed catheters are associated with adverse outcomes and are independent risk factors for hospitalization compared with tunneled cuffed catheters [24].

The present study has several limitations. First, the study population included not only CKD but also AKI patients. Thus, the study population might be heterogeneous in terms of the underlying diseases and related risk factors for kidney injury. Second, the possibility of residual confounding factors due to unmeasured confounders or measurement errors in the included factors could not be excluded. Finally, as this was a retrospective, single-center, observational study, it was not possible to demonstrate a causal relationship between dialysis initiation and in-hospital mortality.

In summary, incident HD patients had a high in-hospital mortality rate. CPR, infections such as pneumonia, and the use of inotropes and ventilators were strong risk factors for in-hospital mortality in patients starting incident HD. Meanwhile, elective HD for CKD reduced the risk of in-hospital mortality.

Conflicts of interest

All authors have no conflicts of interest to declare.

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