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 were strong risk factors for in-hospital mortality. However, elective hemodialysis for chronic kidney disease was associated with survival.

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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].
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 PaO2 and HCO3−; 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 ± standard deviation. For univariate analysis, categorical and continuous variables were analyzed with the χ2 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...
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.

Table 2. Laboratory findings at admission

| Variables                      | Nonsurvivor (n=451) | Survivor (n=2,241) | P     |
|--------------------------------|---------------------|--------------------|-------|
| PaO₂ (mmHg)                    | 96.7 ± 59.2         | 86.5 ± 49.2        | <0.001|
| HCO₃ (mmol/L)                  | 18.3 ± 6.8          | 18.3 ± 6.8         | 0.930 |
| White blood cell (10⁹/mm³)     | 14.0 ± 1.7.         | 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)                      | 973.3 ± 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)    | 471.2 ± 35.5        | 714.1 ± 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 |
| Potassium (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)    | 1311.2 ± 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 ± 3.0           | 7.1 ± 2.6          | 0.258 |
| Low-density lipoprotein (mg/dL)| 84.6 ± 45.7         | 97.4 ± 40.9        | 0.003 |
| Proteinuria (mg/dL)            | 295.2 (65.4)        | 1,615 (72.1)       | <0.001|
| Hematuria (mg/dL)              | 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.

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.

Table 3. Laboratory findings at initial hemodialysis

| Variables                      | Nonsurvivor (n=451) | Survivor (n=2,241) | P     |
|--------------------------------|---------------------|--------------------|-------|
| PaO₂ (mmHg)                    | 95.3 ± 42.1         | 86.9 ± 55.3        | <0.001|
| HCO₃ (mmol/L)                  | 17.4 ± 6.9          | 18.3 ± 7.0         | 0.006 |
| White blood cell (10⁹/mm³)     | 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 ± 2.9          | 0.933 |
| Albumin (g/dL)                 | 2.9 ± 1.1           | 3.3 ± 1.0          | <0.001|
| Blood urea nitrogen (mg/dL)    | 712.2 ± 45.9        | 811.1 ± 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.

The risk factors for in-hospital mortality after excluding CPR, intraoperative administration, ventilator use, ICU care, and vancomycin are shown in Table 6. Arrhythmia (aHR: 3.253; 95% CI: 2.563–9.01), ICU care (aHR: 6.021; 95% CI: 3.480–10.29), and vancomycin administration (aHR: 4.357; 95% CI: 2.635–7.05) were more common in survivors.
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: 1.764; 95% CI: 1.068–2.893), and CRP (aHR: 1.015; 95% CI: 1.001–1.030) 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,
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 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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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/m²) | 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                 | 2.179–4.858 | <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 infarct| 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.
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