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Early Mortality after the Initiation of Hemodialysis in Elderly Patients

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Summary

Background: The early mortality rate is high in elderly patients after hemodialysis initiation, and conservative kidney management (CKM) is introduced as an alternative to renal replacement therapy. Thus, we examined the prognosis of elderly dialysis patients at the Blood Purification Center of Dokkyo Medical University Hospital.

Methods: Among 378 hemodialysis-introduced patients at our hospital from November 2018 to December 2021, we examined the short-term mortality rate in 79 elderly patients of ≥ 80 years of age and analyzed the risk factors from the data at hemodialysis initiation compared to the 298 patients of < 80 years of age.

Results: For dialysis patients of ≥ 80 years of age, the mortality rate was 13% within 3 months (6% under 80), 23% (8%) within 6 months, and 28% (10%) within 12 months. Mortality after 12 months was further increased by up to 40% in patients of ≥ 90 years of age. Data at the time of the initiation of dialysis showed the risk of short-term death in elderly patients with low blood pressure, low body weight, and high hematocrit and potassium levels, and formula to predict the risk of death was proposed with a receiver operating characteristics (ROC) curve area under curve (AUC) of 0.8124.

Conclusion: The early mortality rate within 1 year after the initiation of hemodialysis was high in elderly patients. CKM could be an option in the high-risk patients with declining body weight and albumin levels, and elevated serum potassium and hematocrit.

Key Words: conservative kidney management, elderly, hemodialysis, mortality, prognosis

Introduction

In Japan, the age at the introduction of dialysis has been increasing annually, with an average age of 71.09 years (70.38 years for men, and 72.71 years for women) by the end of 2021[1)]. In addition, the mortality rate for those of ≥ 80 years of age was as high as 15.8% within 3 months and 30.2% within 1 year after the initiation of dialysis[2)]. Some patients refuse to prepare for renal replacement therapy and often say that they do not want to prepare for or start dialysis because they would rather die than receive dialysis to avoid bother-

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ing their families. However, those patients will be finally transported to the hospital by ambulance with dyspnea due to overhydration, heart failure, or loss of consciousness, and hemodialysis will be emergently introduced at the doctor's discretion. Patients who undergo emergency dialysis by catheter have a worse prognosis in comparison to those who undergo dialysis at the planned start date with an arteriovenous (AV) shunt[3]. Of note, no significant difference in life expectancy has been reported between patients who receive hemodialysis and those who receive conservative kidney management (CKM) in elderly patients of ≥ 80 years of age with a GFR < 12 mL/min[4]. Therefore, to clarify the efficacy and safety of the introduction of hemodialysis in elderly patients of ≥ 80 years of age, we investigated the short-term prognosis at 3, 6, and 12 months according to the age of patients who were introduced to dialysis at the Blood Purification Center of Dokkyo Medical University Hospital.

Methods

From November 2018 to December 2021, 378 patients were introduced to chronic maintenance hemodialysis at our hospital. Patients who were temporarily placed on hemodialysis due to AKI were excluded from this study, but one patient recovered renal function after 3 months and discontinued hemodialysis. The cumulative mortality within 3, 6, and 12 months after the introduction of hemodialysis at Dokkyo Medical University was calculated for each 10-year-old age group. We analyzed the data at the start of dialysis that contributed to death in patients of ≥ 80 years of age (n = 79) compared to patients of < 80 years of age (n = 298). In most cases (83%), patient's prognosis can be confirmed by checking electronic medical records because most hemodialysis patients who underwent hemodialysis at our hospital were checked at our hospital at least once a year to evaluate the AV shunt condition, and also because many of our patients returned to our hospital with sudden changes or severe complications.

The single-center study was approved by the Clinical Research Ethics Committee of Dokkyo Medical University (No. R-71-13J) and conducted in accordance with the Helsinki Declaration and Dokkyo Medical University Clinical Research Guidelines.

Statistics

Data are expressed as the mean ± standard error. The clinical data at the introduction of hemodialysis were statistically analyzed using a one-way analysis of variance followed by the Bonferroni post-hoc test for comparisons between groups. Gender differences and cause of death were analyzed by Chi-square analysis. A Cox proportional hazards analysis was performed to clarify the risk factors for patients of ≥ 80 years of age who died within 12 months after the initiation of dialysis, and a formula was developed to predict the risks of early mortality. We used the concordance ("c")-statistic, which corresponds to the area under the receiver operating characteristic curve. A receiver operating characteristics (ROC) curve area under curve (AUC) and Kaplan-Meier analysis were performed with SSRI software version 1.02 (Social Survey Research Information Co., Ltd., Tokyo, Japan) and SPSS software version 28.0.0.0 (IBM, Chicago, USA), and p values of < 0.05 were considered statistically significant.

Results

The clinical data at the time of the introduction of hemodialysis were compared between patients of < 80 years of age and those of ≥ 80 years of age (Table 1). Diastolic blood pressure, body weight, and serum creatinine levels were significantly lower in patients of ≥ 80 years of age.

Patients of ≥ 80 years of age at the time of the introduction of hemodialysis showed mortality rates of 13%, 23%, and 28% within 3 months, 6 months, and 12 months, respectively (Fig. 1). In patients who were ≥ 80 years of age, mortality within 12 months increased sharply in comparison to patients who were < 80 years of age (Fig. 1), whose mortality rate was similar to the previously reported average[2]. We newly found that 40% of patients of ≥ 90 years of age died within 12 months after the introduction of hemodialysis (Fig. 1).

Patients of ≥ 80 years of age who died had a significantly lower body weight, blood pressure, serum albumin, and serum creatinine at the start of dialysis in comparison to those of < 80 years of age who survived beyond 12 months after the introduction of hemodialysis (Fig. 2).

Table 1 Clinical data from patients of < 80 years of age or ≥ 80 years of age at the initiation of hemodialysis

	Under 80 years old N = 298	Over 80 years old N = 79	P value
Age	64.6 ± 0.7	84.7 ± 0.4	0.0001
Sex male:female (%)	72:28	70:30	0.858
Primary disease			
DM:HTN:CGN:UK:RPGN:TIN	46:22:14:6:3:3	35:35:15:8:3:1	0.47
SBP (mmHg)	147 ± 1	147 ± 3	0.82
DBP (mmHg)	78 ± 1	73 ± 2	0.028
Body weight (kg)	66 ± 1	58 ± 2	0.0001
BMI (kg/m^2)	26.1 ± 11.0	23.6 ± 0.6	0.21
CTR (%)	55.5 ± 0.4	56.4 ± 0.7	0.32
Serum albumin (g/dL)	3.00 ± 0.04	2.85 ± 0.08	0.09
Serum creatinine (mg/dL)	7.89 ± 0.17	6.56 ± 0.24	0.0003
Serum UN (mg/dL)	82.6 ± 1.6	88.5 ± 3.8	0.108
Serum potassium (mEq/L)	4.38 ± 0.05	4.41 ± 0.10	0.82
Serum calcium (mg/dL)	8.31 ± 0.06	8.40 ± 0.09	0.43
Serum phosphate (mg/dL)	6.03 ± 0.11	5.80 ± 0.17	0.33
Serum bicarbonate (mEq/L)	20.1 ± 0.3	20.2 ± 0.6	0.96
Hematocrit (%)	27.8 ± 0.3	28.8 ± 0.6	0.12
Uremic digestive symptoms (%)	35.9 ± 0.03	44.3 ± 0.06	0.17
Overhydration (%)	56.7 ± 0.03	64.6 ± 0.05	0.03
Bleeding tendency of uremia (%)	2.3 ± 0.9	5.1 ± 2.5	0.20
CNS symptoms of uremia (%)	1.3 ± 0.7	2.5 ± 0.8	0.45
Electrolyte disorder	30.5 ± 2.7	25.4 ± 4.7	0.37
Metabolic acidosis	43.4 ± 2.9	36.7 ± 5.5	0.28

DM: diabetes mellitus, HTN: hypertension, CGN: chronic glomerulonephritis, UK: unknown, RPGN: rapidly progressive glomerulonephritis, TIN: tubulointerstitial nephritis, SBP: systolic blood pressure, DBP: diastolic blood pressure, CNS: central nervous system, values are expressed as mean ± standard error.

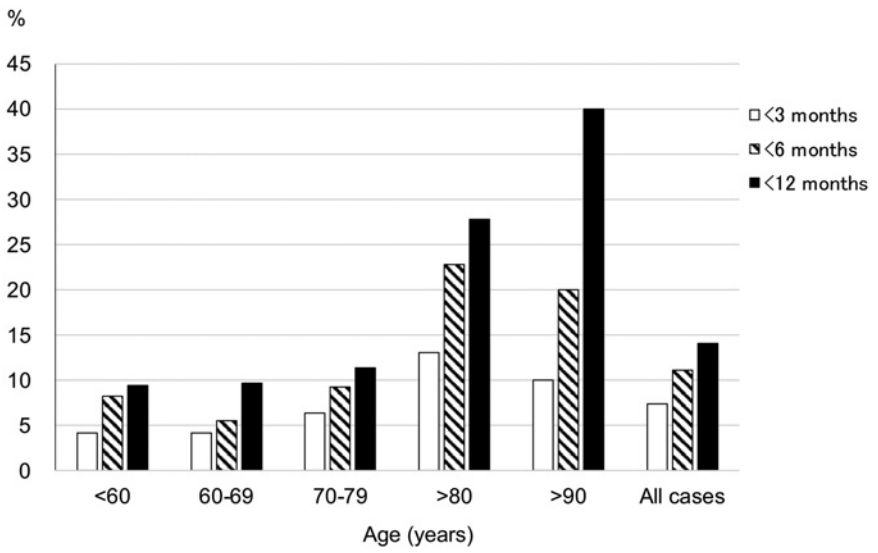

Figure 1 Comparison of 3-, 6-, and 12-month mortality by age group.

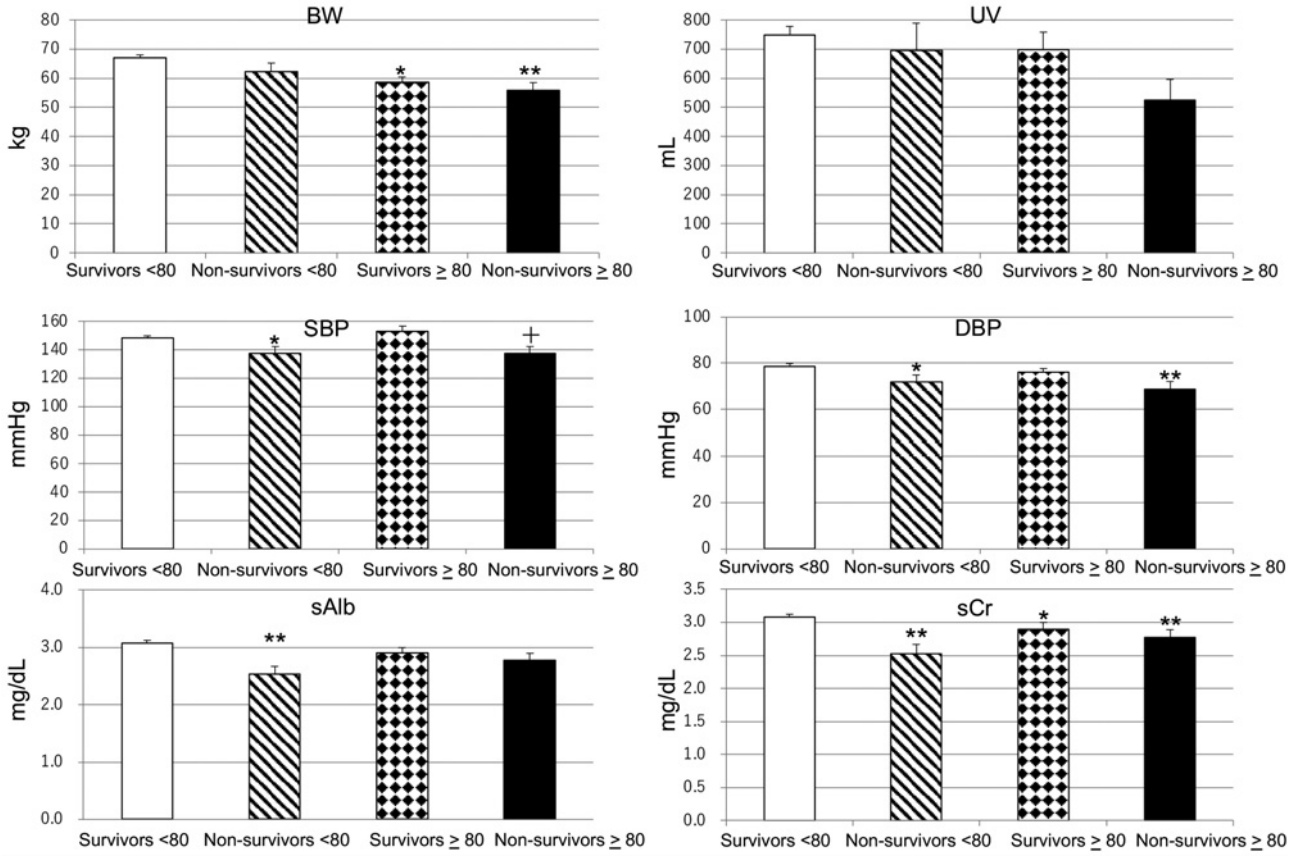

Figure 2 Comparison of body weight (BW), urine volume (UV), systolic blood pressure (SBP), diastolic blood pressure (DBP), serum albumin level (sAlb) and creatinine level (sCr) at the introduction of hemodialysis among survivors and non-survivors between patients < 80 years of age and those ≥ 80 years of age.

* $p < 0.05$, ** $p < 0.01$ vs. survival at < 80 years of age, + $p < 0.05$ vs. survival ≥ 80 years of age.

Table 2 Cox proportional hazards analysis of mortality for all patients

Covariate	Hazard ratio (HR)	95% confidence interval		P value
		minimum	maximum	
Age ≥ 80	2.17	1.26	3.73	0.005
DBP	0.98	0.96	1.00	0.038
BW	0.98	0.97	1.00	0.073
Alb	0.38	0.26	0.54	0.000
BUN	1.01	1.00	1.02	0.008
Cr	0.86	0.76	0.98	0.021
K	1.36	1.04	1.78	0.023
cCa	1.40	1.06	1.85	0.016
Ht	1.06	1.01	1.11	0.029
Over hydration	1.55	0.83	2.88	0.166

The risk factors for mortality after the initiation of hemodialysis in all patients were as follows: age ≥ 80 years, decreased DBP, serum albumin, and serum creatinine, and increased hematocrit, potassium, calcium, and BUN (Table 2). In patients ≥ 80 years of age at the time of the introduction of hemodialysis, the independent risk factors for death were decreased body weight and serum albumin and increased serum potassium and hematocrit (Table 3), suggesting that malnutrition and dehydration could be risk factors for death at the

Table 3 Cox proportional hazards analysis of mortality for patients of ≥ 80 years of age

Covariate	Hazard ratio (HR)	95% confidence interval		P value
		minimum	maximum	
SBP	0.98	0.96	1.00	0.076
DBP	0.97	0.93	1.00	0.076
BW	0.95	0.92	0.99	0.005
Alb	0.19	0.08	0.46	0.0002
K	2.62	1.49	4.58	0.0008
Ht	1.14	1.04	1.25	0.006
Digestive symptoms	0.55	0.22	1.35	0.191

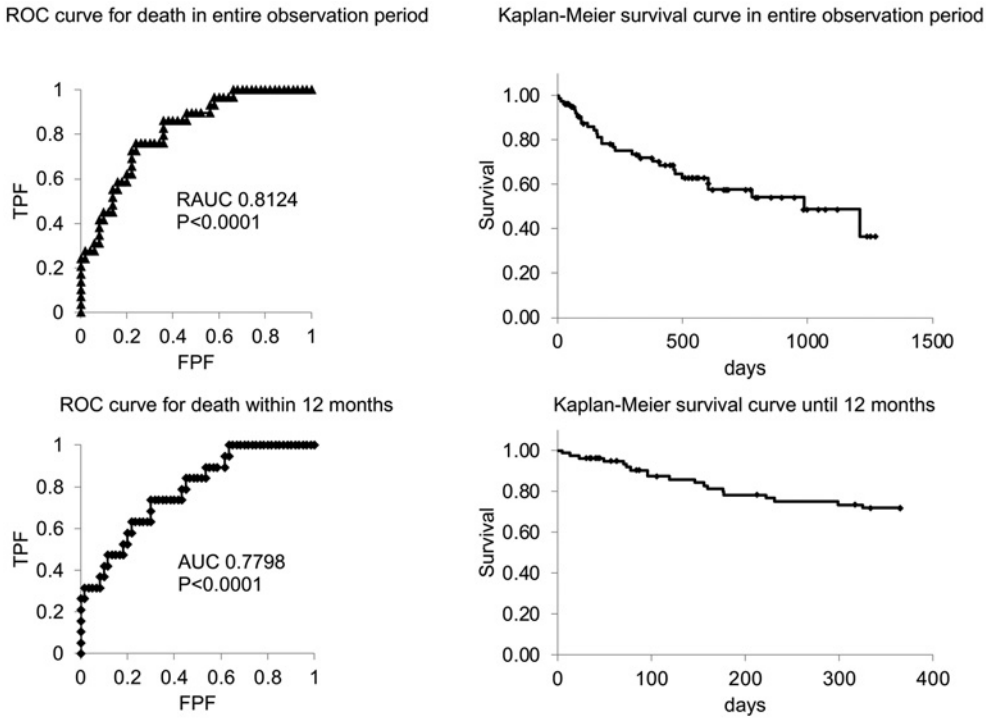

Figure 3 ROC curves for the hazard ratio for the death prediction formula and Kaplan-Meier survival curves in the entire observation period and at 12 months after the induction to hemodialysis in elderly patients of ≥ 80 years of age. FPF: False Positive Fraction, TPF: True Positive Fraction.

time of the introduction of hemodialysis.

The Cox biohazard model analysis of patients of ≥ 80 years of age at the time of the introduction of hemodialysis yielded the following hazard prediction formula.

$Hpti(t) = H0(t)\exp(-0.0215 \times SBPi - 0.0337 \times DBPi - 0.0504 \times BWi - 1.6634 \times Albi + 0.962 \times Ki + 0.131 \times Hti - 0.6021 \times GIi)$, where H0(t) was considered as 1.

Using this formula, it was possible to estimate early death after the introduction of hemodialysis with an ROC curve AUC of 0.8124 in entire observation period and of 0.7798 within 12 months. The Kaplan-Meyer survival curve is shown in Fig. 3. When all deaths were evaluated in this study, survival time after initiation of hemodialysis was estimated based on the Hpti scores in three grades: HR1, HR2 and HR3 (Table 4).

The causes of death after the introduction of dialysis in the elderly aged ≥ 80 years were infections (31%), malignancy (17%), multiple organ failure (17%), myocardial infarction (10%), and heart failure (7%). There were no statistically significant differences in comparison to patients of < 80 years of age (Table 5).

Table 4 Hpt scores and estimated survival time after the initiation of hemodialysis

	HR1	HR2	HR3
Hpt	0.000-0.010	0.010-0.0249	0.0250-0.1500
Mean	0.005	0.017	0.053
SE	0.001	0.001	0.023
Survival time (days)			
Mean	380	311	78
SE	101	75	27

Table 5 Cause of death in patients of < 80 years of age and ≥ 80 years of age

Cause of death	< 80 years N = 40	≥ 80 years N = 29	P values of Chi-square analysis
Infection	12 (30.0%)	9 (31.0%)	0.927
Malignancy	8 (20.0%)	5 (17.2%)	0.772
Multiple organ failure	3 (7.5%)	5 (17.2%)	0.212
Congestive heart failure	4 (10.0%)	2 (6.9%)	0.652
Myocardial infarction	1 (2.5%)	3 (10.3%)	0.169
Cerebrovascular diseases	4 (10.0%)	1 (3.4%)	0.300
Uremia	3 (7.5%)	2 (6.9%)	0.924
Gastrointestinal bleeding	2 (5.0%)	1 (3.4%)	0.755
Others	3 (7.5%)	1 (3.4%)	0.477

Discussion

In the present study, we demonstrated that the mortality rates within 3, 6, and 12 months after the initiation of dialysis were 13%, 23%, and 28%, respectively, in patients of ≥ 80 years of age and 40% of patients of ≥ 90 years of age died within a year. We also developed a risk formula to predict early death after the initiation of hemodialysis using data on the introduction of hemodialysis.

Prognosis of elderly patients after the introduction of hemodialysis

Early mortality after the introduction of hemodialysis elderly patients has been reported[2,3,5,6]. Otero-Lopez et al[6] reported that in 63 patients with a mean age of 80.4 ± 3.9 years, survival rates observed at 6 and 12 months were 79.4% and 73%, respectively, indicating that the mortality rates at 6 and 12 months were 20.6% and 27%, respectively. Furthermore, patients who began hemodialysis on an emergency basis or who were unable to care for themselves had higher 6-month mortality rates of 47.7% and 21%, respectively. Among 219 patients of ≥ 75 years of age in Korea, the 3- and 6-month mortality rates were 14.4% and 22.4%, respectively[7]. Using the Japanese national registry of 35,415 patients on incident dialysis, patients of ≥ 80 years of age showed high rates of early death, with a mortality rate of 15.8% within 3 months and 30.2% within 1 year after the introduction of dialysis[2]. These data are consistent with our results. Moreover, the incidence of early death within 3 months in patients of ≥ 80 years of age with a severely impaired functional status is 36.5%[2]. In patients of ≥ 80 years of age, even when CKM was selected, the prognosis after reaching GFR < 12 was similar to when selected dialysis[4]. As there are some patients who do not want or refuse to undergo hemodialysis, it is necessary to clarify the real-world data on the initiation of hemodialysis and early mortality in the elderly patients of ≥ 80 years of age.

Risk factors for early death in the elderly patients introduced to hemodialysis

In the present study, early mortality after the initiation of hemodialysis was higher in lean patients with poor nutritional indices and low blood pressure. Malnutrition with hypoalbuminemia, frailty, a poor functional

performance status and physical impairment, comorbid cognitive impairment, cancer and diabetes mellitus, and fall episodes seen in geriatric syndrome were reported as independent risk factors for mortality in elderly patients introduced to hemodialysis[6,8-11]. Although fluid overload is a well-known risk factor for death in hemodialysis patients whose hematocrit is diluted and decreased, interestingly, elevated hematocrit was a risk factor for death in elderly patients who are more prone to dehydration in this study. We could not evaluate the dose of erythropoiesis stimulating agent. The emergent initiation of hemodialysis with a venous catheter is an independent risk for early death in hemodialysis patients[6,12]. In our retrospective study, we could not evaluate the patients' frailty, functional performance status or physical impairment. The causes of death in elderly patients introduced to hemodialysis were infection (including pneumonia, catheter-associated sepsis) in 30% of patients, followed by malignancy in 17% and multiorgan failure in 17%. It is important to include the general physical and functional status, dementia and comorbidity of patients when evaluating the risk of early mortality in elderly patients undergoing hemodialysis.

Prediction of survival period after the initiation of hemodialysis and the indications for CKM

There are several reports on methods for predicting the short-term prognosis after the introduction of dialysis in the elderly. Couchoud et al.[13] scored the risk factors (including age, sex, specific comorbidities, albumin level, and mobility) using 24,348 patients of ≥ 75 years of age from the French National Renal Epidemiology and Information Network (REIN) registry, and their score system could predict 3-month expected mortality with a mean c-statistic in the 20 imputed sets of ROC curve AUC of 0.759 (95% confidence interval 0.751-0.768). Wick et al.[14] developed a 19-point risk score for 6-month mortality that included age, GFR, atrial fibrillation, lymphoma, congestive heart failure, hospitalization, and metastatic cancer, using a cohort of 2,199 older adults of ≥ 65 years of age in Alberta, Canada, with an ROC curve AUC of 0.72. These two scoring systems have external validation studies with ROC curve AUC of 0.62 and 0.72 in the former and 0.73 in the latter[7,15,16]. Santos et al.[10] reported a scoring system that included age, coronary artery disease, cerebrovascular disease with hemiplegia, duration of nephrology care before dialysis, and serum albumin in a cohort of 421 patients of ≥ 65 years of age, which showed an ROC curve AUC of 0.793.

Our formula for predicting the risk of death in elderly patients of ≥ 80 years of age showed a similar ROC curve AUC of 0.7798 for death within 12 months after the introduction to hemodialysis. Interestingly, our prediction formula only included data on blood pressure, body weight, serum albumin, serum potassium, hematocrits and gastrointestinal symptoms at the start of hemodialysis in patients of ≥ 80 years of age. As these patients mainly die from infection, CVD, and malignancy, it may be better to include these complications in the prognosis formulas[5,11,13,14]. The merit of our risk formula is that survival time after the initiation of hemodialysis was estimated with the three grades of HR1 (survive time ≥ 12 months), HR2 (survival time < 12 months), and HR3 (survival time < 3 months), as shown in Table 4. This survival estimation will help in decision-making in relation to the indications for CKM.

The present study was associated with some limitations, including the relatively small number of patients of ≥ 80 years of age (n = 79). Further studies including more patients from multiple centers should be conducted. External validation of our formula is also necessary. It was relatively easy to confirm the prognosis of patients after the initiation of hemodialysis in this local center, however, some patients may have been lost to follow-up or died without visiting our hospital. Further studies are necessary to confirm the prognosis by interviewing all patients precisely and to evaluate the prognosis formulae using external validation studies.

In conclusion, the mortality rate within one year after the initiation of hemodialysis reached 28% for patients of ≥ 80 years of age and 40% for patients of ≥ 90 years of age. Conservative kidney management could be an option for elderly patients who refuse to undergo hemodialysis and who show lean body weight, reduced blood pressure, or malnutrition associated with infection, malignancy and multiorgan failure.

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Consent for publication statement

This study was a retrospective observational study conducted only at the Dokkyo Medical University Hospital Blood Purification Center. Research projects were posted on the website of the Department of Nephrology and Hypertension, and upon request, research plans will be disclosed and explained without identifying specific individuals.

Author Contribution

Conception and design of the study, AT, MA; acquisition and analysis of data, HA, YS, AT; drafting the manuscript or figures, HA, MA; writing—review and editing, AT; visualization, AT; supervision, AT, TR; project administration, AT; funding acquisition, AT. All authors have read and agreed to the published version of the manuscript.

Disclosure Statement

The authors declare no conflicts of interest in association with the present study.

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