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# Effect of cardiovascular risk factors and time of hospital presentation on mortality of maintenance hemodialysis patients presenting with acute pulmonary edema

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## Abstract

**Background:** Acute pulmonary edema (APE) has a poor prognosis in the general population. Mortality associated with APE in patients with end-stage renal disease (ESRD) is especially high, although specific predictors are not well understood. This study aimed to determine the potential predictive factors of outcome in patients with ESRD presenting with APE.

**Methods:** Sixty-eight patients with ESRD (mean age,  $68.9 \pm 9.9$  years; males, 66.2%; median duration of maintenance hemodialysis, 55.5 months) presenting with APE to a single tertiary medical center were retrospectively evaluated. The effects of patients' characteristics, cardiovascular risk factors, variables at hospital presentation, and clinical presentation patterns on all-cause mortality were evaluated.

**Results:** Throughout the observational period (median follow-up period, 575 days; range, 10–2546 days), 32 (47%) patients died. In univariate analysis, older age, diabetes mellitus, peripheral artery or aortic disease, hypotension, atrial fibrillation rhythm, anemia, and hypoalbuminemia were associated with higher mortality, whereas hospital presentation from midnight to 8 am was associated with lower mortality. In multivariate analysis, age (hazard ratio (HR) = 1.05, 95% confidential interval (CI) 1.01–1.09,  $p = 0.018$ ), presence of peripheral artery or aortic disease (HR = 3.36, 95% CI 1.52–7.42,  $p = 0.003$ ), time of presentation from midnight to 8 am (HR = 0.40, 95% CI 0.15–0.99,  $p = 0.047$ ), and atrial fibrillation rhythm at presentation (HR = 3.12, 95% CI 1.04–9.13,  $p = 0.044$ ) were significantly independently associated with mortality.

**Conclusions:** Our findings indicate important predictive roles of the clinical presentation pattern specific to ESRD patients, as well as their characteristics, including cardiovascular risk factors.

**Keywords:** Pulmonary edema, End-stage renal disease, Dialysis, Clinical presentation

## Background

The number of patients on maintenance hemodialysis suffering from end-stage renal disease (ESRD) is approximately 400,000 in the USA [1] and approximately 300,000 in Japan [2]. Cardiovascular disease accounts for 50% of death among these patients [3], with congestive heart failure comprising approximately 25% of death in Japan [2].

Acute pulmonary edema (APE), which is a common symptom of acute heart failure requiring hospital admission, is associated with considerable mortality [4, 5]. This condition is accompanied by severe respiratory distress, audible crackles, and orthopnea and is verified by chest X-ray [6]. In addition to respiratory support, initial treatment of APE aims to ameliorate preload and afterload [7]. In the general population, factors such as older age, hypotension, hyponatremia, and anemia at presentation are predictors of poor outcome in patients presenting with acute heart

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failure [8–11]. In patients with APE only, older age and hypotension predict mortality [5].

Despite high mortality (approximately 80% mortality at 5 years) and morbidity of APE [12, 13], evidence regarding APE in patients undergoing maintenance hemodialysis is lacking. Patients with ESRD on maintenance hemodialysis should be considered as different from the general population because they have different cardiovascular disease characteristics and responses to therapy [1, 3]. Moreover, periodic hemodialysis therapy jeopardizes their preload to fluctuate non-physiologically. Therefore, risk stratification and therapeutic guidelines according to clinical presentation described in acute heart failure in the general population, such as the clinical scenario [9, 14], may not be applicable to this cohort.

Considering the distinct patho-physiology and high mortality, specific predictors in patients with ESRD on maintenance hemodialysis presenting with APE need to be investigated. This study aimed to determine the effects of demographics, non-cardiovascular and cardiovascular factors, and clinical presentation on all-cause mortality in patients on maintenance hemodialysis presenting with APE.

## Methods

### Study design and population

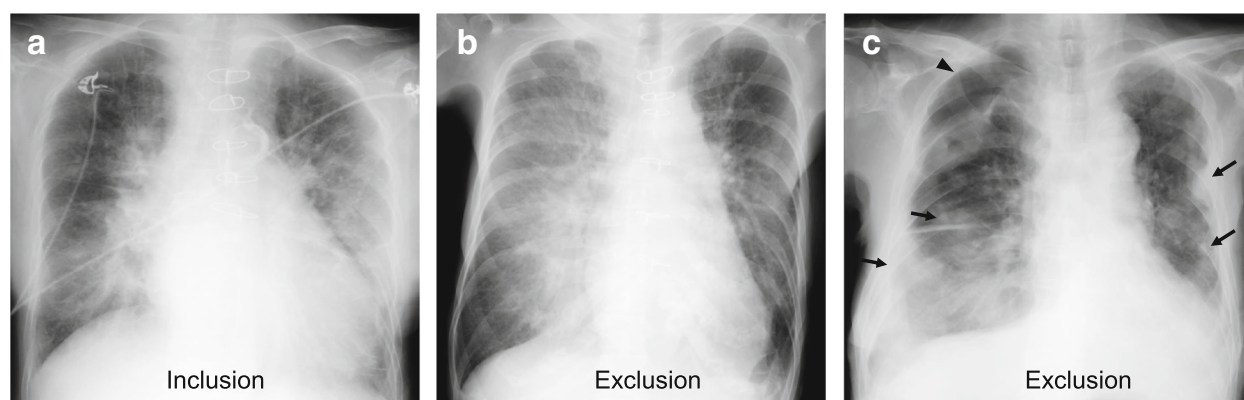
The medical records of 132 patients with ESRD on maintenance hemodialysis presenting with APE who required emergent admission were retrospectively reviewed. Patients were admitted to the Intensive Care Unit or Cardiac Care Unit in Saitama Medical University International Medical Center because of APE between April 2007 and October 2015. Maintenance hemodialysis was defined as

performance of maintenance hemodialysis for 3 months or longer before admission. Patients were included if they showed pulmonary edema on an initial chest X-ray as determined by two observers (S.N. and S.H.). Patients who showed marginal X-ray findings with their clinical course that were inconsistent with APE were excluded after discussion with a third observer using clinical information. Figure 1 shows representative X-rays of the included and excluded patients. Other exclusion criteria are shown in Fig. 2. Patients who required immediate invasive therapy for acute cardiovascular collapse (such as acute coronary syndrome) were excluded because the impact of sudden cardiac dysfunction and procedure-related outcomes may cancel the effects of the factors specifically related to maintenance hemodialysis or ESRD.

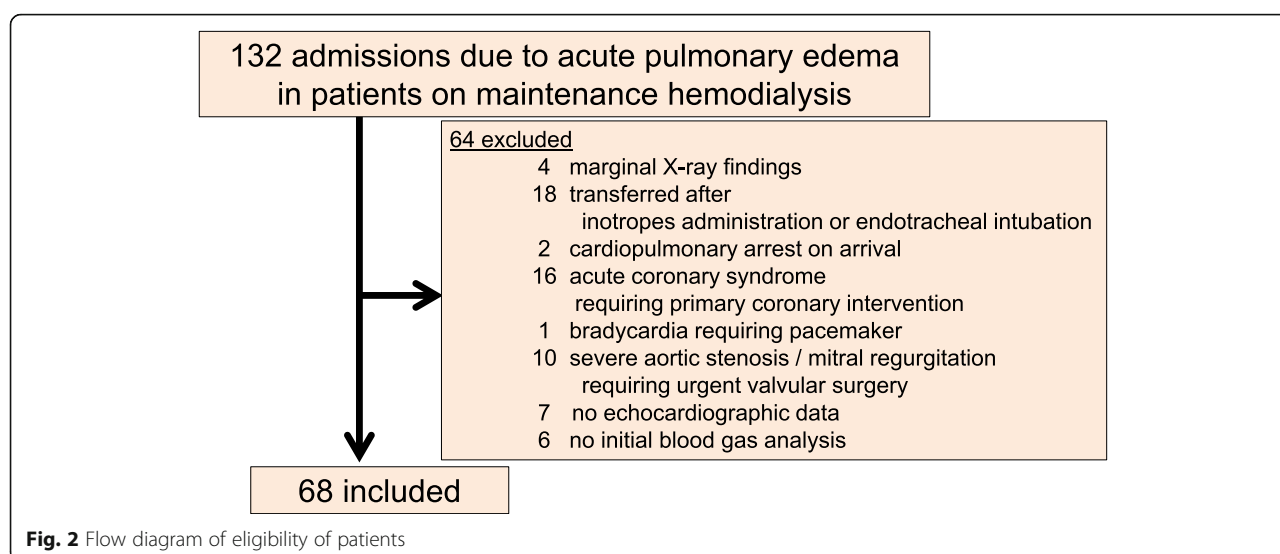
### Data collection

Baseline demographics of patients, maintenance hemodialysis data, and coexisting or previous conditions were recorded. Hypertension was defined as current or previous treatment with anti-hypertensive medication. Diabetes mellitus was defined as treatment with anti-diabetic medication or hemoglobin A1c concentration of  $\geq 6.5\%$  [15]. Dyslipidemia was defined as treatment with anti-dyslipidemic medication or fasting serum concentration of low-density lipoprotein cholesterol  $\geq 160$  mg/dl, high-density lipoprotein cholesterol  $\leq 40$  mg/dl, or total cholesterol  $\geq 240$  mg/dl [16].

Malignancy, peripheral artery and aortic disease (e.g., aortic dissection and aortic aneurysm, either treated or untreated), previous myocardial infarction, and previous cerebral infarction and hemorrhage were recorded. Previous cardiovascular interventions, such as percutaneous coronary intervention, coronary artery bypass grafting,



**Fig. 1** Chest X-rays of included and excluded patients. **a** Included patient: A 58-year-old woman with X-ray findings typical of pulmonary edema. **b** Excluded patient: A 58-year-old woman with marginal X-ray findings showing right-side-dominant infiltration and modest cardiomegaly. Upon admission, this patient had hypotension (systolic blood pressure 70 mmHg), fever ( $>38^{\circ}$ ), and elevated levels of acute inflammatory biomarkers (white blood cell count 23,140/ $\mu$ l, serum C-reactive protein 20.0 mg/dl). A systemic inflammatory response due to infection was suspected, and these abnormal parameters and X-ray findings were subsequently resolved with antibiotic therapy. **c** (excluded patient) An 81-year-old man with marginal X-ray findings showing abnormal pleural and pulmonary shadows (arrows) and pneumothorax (arrowhead). The patient had pleural and pulmonary metastases secondary to renal cancer



aortic surgery, percutaneous transluminal angioplasty or surgery for peripheral artery disease, valvular surgery, and pacemaker/cardio-defibrillator implantation, were recorded. Coronary artery anatomy collected from coronary angiography during the index or previous hospitalization was recorded. Medications that were administered prior to presentation were recorded.

For the prehospital course, the time elapsed from symptom (defined as dyspnea on exertion, paroxysmal nocturnal dyspnea, or orthopnea) onset to arrival was recorded, and the patients were divided into two groups ( $>72$  and  $\leq 72$  h); in the  $>72$ -h group, their symptoms started before the last dialysis session. Hospital presentation time was recorded and divided into the following three groups: 8 am to 4 pm, 4 pm to midnight, and midnight to 8 am [17]. The 2-day interdialytic gap, body weight gain, and body weight gain rate were recorded.

Vital signs, arterial blood gases (before initiating specific respiratory support other than oxygen supplement alone), and laboratory findings at presentation were recorded. Echocardiographic and electrocardiographic variables were recorded.

Initial therapy within 48 h was recorded, and changes in subjective dyspnea and vital signs after the initial single hemodialysis session were evaluated.

### Outcome measures

The associations between independent factors at presentation and all-cause death throughout the observation period were evaluated.

### Statistical analysis

Continuous variables are expressed as the mean  $\pm$  standard deviation or median (first to third quartile) and categorical variables as number (%). The Shapiro–Wilk test

was performed for testing normal distribution. Univariate Cox proportional regression analyses were performed to identify the association between independent variables and all-cause death. Subsequently, multivariate Cox proportional regression analyses were performed to identify potential predictors of all-cause death. Because there are no established predictors of mortality in patients on maintenance hemodialysis presenting with APE, a multivariate model was constructed with independent variables using  $p < 0.05$  in univariate analysis. Kaplan–Meier analyses were performed to test the predictive value of independent variables for mortality with the log-rank test. All statistical analyses were performed using JMP Pro.11.2.0 (SAS Institute, Inc., Cary, USA).

### Results

#### Baseline characteristics, variables of the prehospital course and at presentation, and initial therapy and response of patients

A flow diagram of the patients' eligibility is shown in Fig. 2. Sixty-eight patients were included in the final analysis. Baseline characteristics, data on maintenance hemodialysis, and coexisting or previous medical conditions are shown in Table 1. Peripheral artery disease was observed in 20 patients, including one with previous lower limb amputation. Aortic disease was observed in seven patients, including five with previous aortic surgery for their aortic dissection or aneurysm.

Coronary artery anatomy was only evaluated in 50 (73.5%) patients. Medications and previous cardiovascular interventions are shown in Additional file 1: Tables S1 and S2.

Variables of the prehospital course and at presentation are shown in Table 2. Most patients were hypertensive at presentation. Their initial therapy within 48 h after

**Table 1** Baseline characteristics of patients and univariate Cox proportional analysis for all-cause death

	Total (n = 68)	Hazard ratio	p
Demographics			
Age (years)	68.9 ± 9.9	1.06	0.003*
Male, n (%)	45 (66.2)	2.03	0.08
Body mass index (kg/m <sup>2</sup> )	21.1 (19.1–24.3)	0.95	0.30
Maintenance hemodialysis data			
Etiology of kidney disease			
Diabetic nephropathy, n (%)	44 (64.7)	1.16	0.70
Nephrosclerosis, n (%)	6 (8.8)	1.74	0.33
Others, n (%)	18 (26.5)	0.65	0.30
Duration of maintenance hemodialysis (months)	55.5 (27.3–85.5)	1.00	0.95
Frequency (times/week)	3 (3–3)	NA	NA
Each hemodialysis time (hours/day)	4.0 (4.0–4.0)	1.05	0.88
Coexisting/previous conditions, n (%)			
Previous acute pulmonary edema	24 (35.3)	1.09	0.82
Hypertension	60 (88.2)	0.64	0.44
Diabetes mellitus	52 (76.5)	2.47	0.04*
Dyslipidemia	34 (50.0)	0.97	0.94
Current smoking	10 (14.7)	0.98	0.97
Malignancy	11 (16.2)	1.12	0.82
Peripheral artery or aortic disease	21 (30.9)	2.98	0.005*
Previous myocardial infarction	21 (30.9)	1.00	0.99
Previous cerebral infarction	9 (13.2)	2.17	0.12
Previous cerebral hemorrhage	4 (5.9)	1.08	0.91
Coronary anatomy (n = 50)			
Normal coronary artery, n (%)	10 (20.0)	0.87	0.80
Left main trunk disease, n (%)	3 (6.0)	0.95	0.96
Triple vessel disease, n (%)	10 (20.0)	1.54	0.38

Continuous variables are shown as the mean ± SD or median (first to third quartile) and categorical variables as number (%)

NA not analyzed

\*p<0.05

presentation and their responses are shown in Additional file 1: Table S3; 56 (82.4%) patients required emergent hemodialysis, including continuous hemodialysis for expected hemodynamic instability. Most patients (86.4%) demonstrated relief of subjective dyspnea and hypertension after initial renal replacement therapy.

#### Univariate Cox proportional analyses for all-cause mortality

The median follow-up period was 575 days (174–966: range 10–2546 days), and the total follow-up time was 135.4 years. Throughout the observational period, 32 (47%) patients died from the following causes: myocardial infarction (n = 7), low-output circulatory failure (n = 6), acute pulmonary edema (n = 6), sudden death (n = 3), and other non-cardiovascular causes, such as malignancy (n = 3), liver failure (n = 3), pneumonia (n = 2), sepsis (n = 1), and an

unknown cause (n = 1). Index in-hospital death was observed in six (8.8%) patients. The potential cause of in-hospital death was cardiovascular events in all six patients, including low-output circulatory failure (n = 5) and acute myocardial infarction with shock (n = 1). However, most of these patients were complicated by sepsis or lower airway infection.

In univariate analysis, older age, the presence of diabetes mellitus, and peripheral artery disease or aortic disease were associated with higher all-cause mortality in the whole observational period. Lower systolic blood pressure, hematocrit, serum albumin levels, and AF rhythm at presentation were also significantly associated with higher mortality. The time of hospital presentation from midnight to 8 am was significantly associated with lower mortality (Tables 1 and 2).

**Table 2** Variables of the prehospital course and at hospital presentation, and univariate Cox proportional analysis for all-cause death

	Total (n = 68)	Hazard ratio	p
Prehospital course			
>72 h from onset to arrival, n (%)	13 (19.1)	0.90	0.83
Time of hospital presentation, n (%)			
- 8 am to 4 pm	10 (14.7)	1.88	0.17
- 4 pm to midnight	22 (32.4)	1.96	0.07
- Midnight to 8 am	36 (52.9)	0.38	0.007 <sup>†</sup>
2-day interdialytic gap, n (%)	37 (54.4)	1.09	0.81
Body weight gain (kg)	2.0 (1.0–4.0)	1.00	0.95
Body weight gain rate (%)	4.1 (1.4–6.0)	1.01	0.84
Vital signs			
Systolic blood pressure (mmHg)	182 (159–205)	0.99	0.04 <sup>†</sup>
Diastolic blood pressure (mmHg)	94 (72–115)	0.99	0.13
Heart rate (bpm)	102 (90–116)	0.98	0.15
Respiratory rate (/minute)	26 (21–30)	0.97	0.35
Saturation of peripheral oxygen (%)	97 (92–99)	0.98	0.42
Arterial blood gases			
pH	7.37 (7.26–7.44)	6.98	0.19
pCO <sub>2</sub> (mmHg)	38.8 (34.5–50.6)	0.99	0.26
pO <sub>2</sub> (mmHg)	83.4 (61.4–97.5)	1.00	0.72
HCO <sub>3</sub> <sup>-</sup> (mmol/l)	22.1 (19.6–24.6)	1.03	0.60
Echocardiographic variables (Teichholz method)			
LVEDVI (ml/m <sup>2</sup> )	77.6 (62.8–97.8)	1.00	0.53
LVESVI (ml/m <sup>2</sup> )	36.9 (25.9–50.1)	1.00	0.73
Left ventricular ejection fraction (%)	53 (41.3–61)	0.99	0.61
Left ventricular mass index (g/m <sup>2</sup> )	158 (133–190.5)	1.00	0.47
Electrocardiographic variables			
Atrial fibrillation rhythm, n (%)	10 (14.7)	3.34	0.01*
Artificially paced, n (%)	0 (0)	NA	NA
Left ventricular hypertrophy, n (%)	12 (17.6)	1.22	0.65
QRS duration (ms)	112 (101.5–120)	1.01	0.41
Laboratory findings			
White blood cell count (×10 <sup>3</sup> /μl)	10.2 (7.7–12.4)	0.97	0.56
Hematocrit (%)	34.4 ± 5.3	0.92	0.03 <sup>†</sup>
Platelet count (×10 <sup>3</sup> /μl)	213.2 ± 69.2	0.99	0.07
Blood urea nitrogen (mg/dl)	47.0 ± 16.1	1.00	0.66

**Table 2** Variables of the prehospital course and at hospital presentation, and univariate Cox proportional analysis for all-cause death (Continued)

Creatinine (mg/dl)	8.1 ± 2.3	0.88	0.08
Aspartate aminotransferase (U/l)	20 (15–30)	1.01	0.16
Alanine aminotransferase (U/l)	14 (8–17)	1.01	0.10
Albumin (g/dl)	3.7 ± 0.4	0.28	0.007 <sup>†</sup>
Blood glucose (mg/dl)	161 (120.3–217.3)	1.00	0.31
Sodium (mmol/l)	139.1 ± 3.1	0.93	0.17
Potassium (mmol/l)	4.8 (4.3–5.4)	1.04	0.84
Chloride (mmol/l)	102.0 ± 3.2	0.95	0.31
Calcium (mg/dl), n = 61	8.9 ± 0.7	0.98	0.96
Phosphate (mg/dl), n = 56	5.0 (3.6–5.8)	1.06	0.61
C-reactive protein (mg/dl)	0.53 (0.15–1.85)	1.01	0.89

Continuous variables are shown as the mean ± SD or median (first to third quartile) and categorical variables as number (%)

LVEDVI left ventricular end-diastolic volume index, LVESVI left ventricular end-systolic volume index, NA not analyzed

\*p<0.05 with a positive association, †p<0.05 with a negative association

### Potential predictors of all-cause mortality using multivariate Cox regression analysis

Variables that were significantly associated with all-cause mortality were included in the multivariate regression model. Age ( $p = 0.018$ ), presence of peripheral artery or aortic disease ( $p = 0.003$ ), time of presentation from midnight to 8 am ( $p = 0.047$ ), and AF rhythm at presentation ( $p = 0.044$ ) were significantly independently associated with mortality (Table 3).

Kaplan–Meier analyses using potential predictors (Fig. 3) showed significantly higher all-cause mortality in patients with peripheral artery or aortic disease ( $p = 0.002$ ) and with AF ( $p = 0.003$ ). Lower mortality was found in patients presenting from midnight to 8 am than in those presenting during the rest of the day ( $p = 0.007$ ).

### Discussion

The current study aimed to determine the potential predictors of mortality in patients with ESRD presenting with APE. We found that older age, the presence of peripheral or aortic disease, and AF rhythm at hospital presentation were independently associated with higher mortality, whereas the time of hospital presentation from midnight to 8 am was associated with lower mortality. These findings suggest an important role of the specific clinical presentation pattern in predicting mortality, as well as the importance of readily accessible acute data, including cardiovascular parameters.



**Table 3** Factors associated with all-cause death

	HR	95% CI	p
Age	1.05	1.01–1.09	0.018*
Diabetes mellitus	1.70	0.65–5.45	0.298
Peripheral artery or aortic disease	3.36	1.52–7.42	0.003*
Presentation from midnight to 8 am	0.40	0.15–0.99	0.047 <sup>†</sup>
Systolic blood pressure	1.00	0.99–1.01	0.956
Atrial fibrillation rhythm	3.12	1.04–9.13	0.044*
Hematocrit	0.96	0.88–1.05	0.414
Albumin	0.30	0.08–1.02	0.053

Cox proportional regression analyses were performed

HR hazard ratio, CI confidence interval

\* $p < 0.05$  with a positive association, <sup>†</sup> $p < 0.05$  with a negative association

### Cardiac or non-cardiac APE in patients on maintenance hemodialysis

Acute pulmonary edema may be caused by cardiac or non-cardiac etiology. Distinguishing cardiac from non-cardiac APE using a single parameter, such as left ventricular contractility, is often difficult [18–20], especially in patients with ESRD whose fluid status is susceptible to excessive sodium and water intake. In these patients, underlying abnormal cardiac function is common because of volume overload (e.g., anemia, arteriovenous fistulas, and dialysis therapy per se), leading to left ventricular dilatation, or pressure overload (e.g., hypertension and atherosclerosis), leading to left ventricular hypertrophy and potential relative myocardial ischemia [3]. We speculate that their potential cardiovascular pathology may directly or indirectly lead to the development of APE. Therefore, comprehensive assessment of cardiovascular information, including previous or coexisting cardiovascular disease, and echocardiographic and electrocardiographic findings as candidate contributors

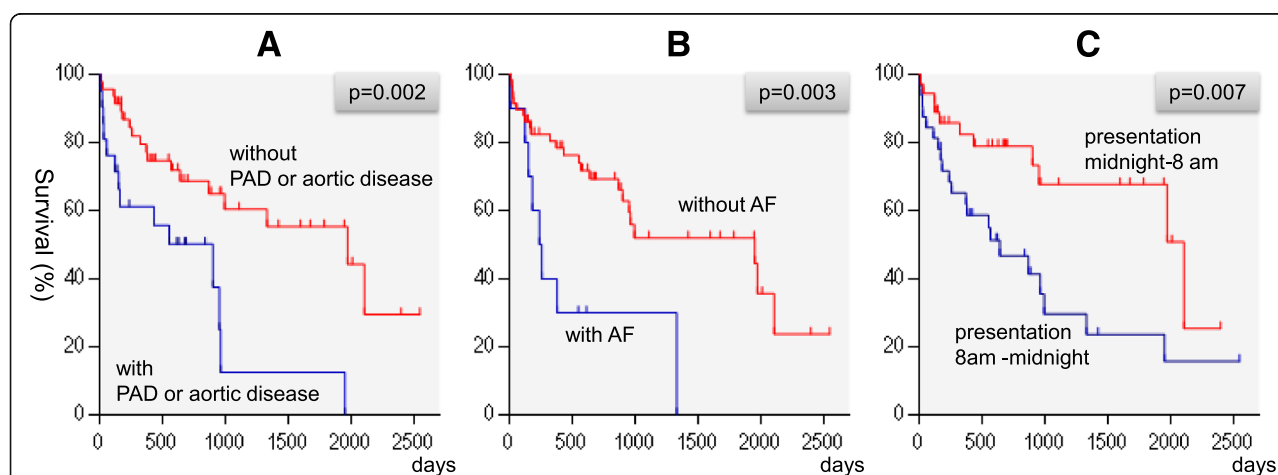
of APE may be reasonable, rather than distinguishing cardiac from non-cardiac etiology.

### Effect of comorbidities and cardiac function

Some studies focused on acute heart failure or pulmonary edema in patients with ESRD. We found that older age was significantly associated with mortality, which is consistent with previous studies [12, 21].

In our study, some conventional cardiovascular risk factors in the general population, such as coexisting dyslipidemia, hypertension, or obesity, were not associated with mortality. This finding may be partly explained by the reverse epidemiology in which these factors may play protective roles in under-nutrition [22]. In contrast, in our study, diabetes mellitus was associated with mortality in univariate analysis. Diabetes mellitus and coexisting macro- and microvascular diseases are associated with a poor prognosis in patients on maintenance hemodialysis [12, 23–25]. We also found that the presence of peripheral artery or aortic disease was a strong predictor of mortality.

We found that AF rhythm at presentation was associated with mortality. Previous studies have reported an association between AF and all-cause mortality in patients with ESRD [21, 26]. Interestingly, as demonstrated in our study, the association of AF with poor outcome was reported to be superior to that of left ventricular ejection fraction in patients with ESRD [21]. In our study, the median heart rate and duration of maintenance hemodialysis were comparable between patients with and without AF. Although the exact mechanism of a worse outcome associated with AF is unclear, potential acceleration of atrial remodeling caused by hemodialytic therapy and a high prevalence of embolic or bleeding events [21, 27] have been reported to be involved in high mortality.



**Fig. 3** Kaplan–Meier analyses. Kaplan–Meier analyses using the potential predictors showed significantly higher all-cause mortality in patients with peripheral artery disease (PAD) or aortic disease (a) and in those with atrial fibrillation (AF, b). Lower mortality was found in patients presenting from midnight to 8 am (c)

We also found that none of the acid–base parameters was associated with mortality. The acid–base imbalance observed in our cohort was mild (median pH, 7.37) and had little effect on outcome in patients with ESRD who are commonly exposed to mild acidosis [28].

### Effect of the clinical presentation pattern

In patients undergoing maintenance hemodialysis, a substantial amount of fluid is retained in interdialytic period and quickly removed at hemodialysis treatment. This leads to non-physiological fluctuation of preload. Fluid retention is the main cause of emergent hospitalization in patients undergoing maintenance hemodialysis and is associated with mortality [13, 18]. However, greater weight gain or a 2-day gap after the last hemodialysis session was not associated with mortality in our study.

We found that hospital presentation from midnight to 8 am was significantly associated with lower mortality. The association between nighttime presentation and outcomes in general populations of patients with acute heart failure has not been determined [29, 30]. The definition of nighttime presentation varies among studies; in the current study, we recognized nighttime as the time from midnight to 8 am to eliminate the evening time when many patients were still awake. The concept of circadian fluid shift may partly explain this finding. Upon lying down at night, fluid that is accumulated during the daytime redistributes rostrally by gravity, resulting in fluid shift to the lungs, as well as the upper airway [31]. We speculate that APE developing at night may simply result from a fluid shift due to volume overload, whereas APE developing during the daytime might be attributable to underlying factors other than simple volume overload, such as an altered cardiovascular condition. Additionally, the potential presence of obstructive sleep apnea, which is a prevalent condition in patients with ESRD (50–70%) [32], should be considered as a contributing factor to the better prognosis in patients who presented at night, although our study lacks polysomnographic data. In patients with concurrent ESRD and obstructive sleep apnea, rostral overnight fluid shift is associated with the severity of obstructive sleep apnea [33], possibly via an increase in the jugular vein volume and pharyngeal water content [34]. Hence, nighttime rostral fluid shift, which may lead to acute pulmonary edema, may be enhanced by obstructive sleep apnea. From a therapeutic viewpoint, rostral fluid shift resulting from fluid overload can be corrected by a single emergent hemodialysis session. Moreover, positive airway pressure, which was performed as initial respiratory management in some of our patients (Additional file 1: Table S3), might have helped to alleviate symptoms in patients with obstructive sleep apnea by unloading the inspiratory muscles and left ventricular afterload [35].

Interestingly, patients presenting at night had a higher median systolic blood pressure than did those presenting during the rest of the day. Elevated systolic blood pressure at presentation, possibly related to increased filling pressure and sympathetic hyperactivity, may favorably respond to pharmacological therapy, such as vasodilators, and is associated with lower mortality [9, 11]. In the majority of our patients who presented at night, relief of dyspnea and hypertension was observed after a single emergent hemodialysis session. We speculate that these characteristic initial therapeutic strategies and their responses may be a reflection of the hemodynamics and neurohormonal responses that are specific to patients with ESRD.

The effect of delay from symptom onset to presentation has been discussed for general heart failure [36–40]. In our study, a delay in presenting to the hospital (>72 h after initial symptoms) was not associated with mortality. We consider that because of the meticulous titration of the fluid balance at regular clinic visits, prolonged symptoms may be less common in patients with ESRD than in the general population. This situation indicates that the role of a delay in presentation is less meaningful in patients with ESRD than in the general population.

### Limitations

This study has some limitations. First, it was an observational study conducted at a single tertiary center and included relatively small number of patients. A center-specific bias involving medical transfer systems should be considered as a potential social and infrastructural factor that contributed to the better prognosis of patients who presented at night. However, we included objective variables accessible at presentation and the clinical presentation pattern and found potential predictors of mortality from our longitudinal observation. Second, coronary artery anatomy, which may be an important predictor of mortality, was evaluated in only 73.5% of patients; therefore, we might have underestimated the implication of coronary artery anatomy. Clinically accessible parameters, such as echocardiographic or electrocardiographic variables, might have partially compensated for the insufficient coronary information.

### Conclusions

In patients on maintenance hemodialysis presenting with APE, older age, the presence of peripheral artery or aortic disease, and AF rhythm at presentation were significantly associated with higher mortality, whereas the time of hospital presentation from midnight to 8 am was significantly associated with lower mortality. Our findings indicate important predictive roles of the clinical presentation pattern specific to patients with ESRD, as well as their characteristics, including cardiovascular risk factors.

## Additional file

**Additional file 1: Table S1.** Medications prior to admission. **Table S2.** Previous cardiovascular interventions. **Table S3.** Initial therapy and patients' response. (DOC 62 kb)

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None to declare

## Availability of data and materials

The datasets generated during and/or analyzed during the current study are available.

## Authors' contributions

SH and SNa designed the study and drafted the manuscript. SH, YW, and HO collected the data. SH, SNa, JT, YW, HO, TS, and SNI analyzed and interpreted the data. SI, RK, TM, and HN revised the manuscript for intellectual content. SNI approved the final manuscript. All authors read and approved the final manuscript.

## Competing interests

The authors declare that they have no competing interests.

## Consent for publication

This manuscript contains no identifiable details from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Institutional Review Board of Saitama Medical University International Medical Center (reference number: 15-280).

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