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Pleural effusion negatively impacts survival of patients undergoing maintenance hemodialysis

To the Editor,

Pleural effusion (PE) is a common clinical presentation of chronic kidney disease (CKD).[1] Recently, two prospective observational studies evaluated the association of PE and mortality.[2,3] One study revealed that the presence of bilateral and transudative PE was an indicator of increased mortality.[2] The other study revealed that patients with PE caused by congestive heart failure and CKD in addition to bilateral PE had high mortality.[3] Thus, we hypothesized that PE at the time of initiating maintenance hemodialysis is closely associated with poor outcome. We examined chest X-ray (CXR) images at the time of initiating maintenance hemodialysis to evaluate the association between PE and mortality.

This was a single-center, retrospective survey study. The local ethics committee of Hikone Municipal Hospital approved this study and waived off the requirement of obtaining written informed consent for all participants.

We reviewed all medical records of the patients who were started on maintenance hemodialysis at Hikone Municipal Hospital between January 2013 and December 2017. Patients who were followed up for a minimum of 3 months post initiation of maintenance hemodialysis or until death were included. Patients who had undergone peritoneal dialysis or had values missing from their medical records were excluded. Survival data were calculated from the time of initiating maintenance hemodialysis to time of death.

PE was assessed using CXR images <1 week before the initiation of maintenance hemodialysis. PE was considered to be mild if the costophrenic angle was blunt, moderate if the effusion occupied one-third to half of the hemithorax, and severe if more than half of the hemithorax was opacified.[4]

Continuous variables were compared using Wilcoxon rank-sum test and expressed as mean ± standard deviation, whereas categorical variables were compared using chi-square test and presented as frequencies with percentage. Survival was compared using Kaplan–Meier plots and log-rank test. The multivariate Cox proportional hazards model was used for evaluating differences between survival and the following explanatory variables, age, heart disease, serum albumin level, and PE. All statistical analyses were performed using JMP® 10 statistical software package (SAS Institute; Cary, NC, USA); $p < 0.05$ was considered to be statistically significant for all analyses performed.

We screened 88 patient records, of which 6 were excluded for following reasons; 4 were followed for <3 months post initiation of maintenance hemodialysis, 1 underwent peritoneal dialysis, and another had missing CXR image before the initiation of maintenance hemodialysis. A final total of 82 patients were included in our study.

Clinical characteristics of study patients are presented in Table 1. The mean follow-up from the time of initiating maintenance hemodialysis was 765.6 ± 475.4 days. The incidence of PE at the time of initiating maintenance hemodialysis was 48.8% (40/82 patients); PE was bilateral in 21 patients (52.5%) and unilateral in 19 patients (47.5%). Patients with PE were older and had a higher frequency of heart disease than those without PE. The presence of PE, regardless of its severity, was significantly associated with lower survival probability (Fig. 1). After adjusting for age, heart disease, and serum albumin level, the presence of PE was significantly associated with lower survival probability (hazards ratio: 2.78 [95% CI, 1.047–8.23, $p = 0.040$]).

PE at the time of initiating maintenance hemodialysis was associated with poor prognosis. Studies assessing the correlation between mortality and PE caused by CKD are limited. Kwan et al. retrospectively described that PE was associated with high mortality in patients undergoing maintenance peritoneal dialysis.[5] DeBiasi et al. prospectively reported that patients with PE caused by CKD had high mortality.[3] These data are consistent with our findings. However, the underlying association between PE and mortality remains unknown. Future studies exploring the underlying association between high mortality and PE at the time initiating maintenance hemodialysis are required.

In this study, the incidence of PE at the time of initiating maintenance hemodialysis was 48.8%. Two previous studies have shown that the incidence of PE was 6.7% in patients with CKD (stage 3–5) under pre-maintenance dialysis and 20.2% in those undergoing long-term maintenance hemodialysis.[4,6] These differences could be influenced by the timing of evaluating PE.

Table 1 Clinical characteristics of study participants.

	Total	Pleural effusion	No pleural effusion	*p*-Value
Number	82	40	42	
Age, y	70.8 ± 12.3	74.7 ± 9.5	67.1 ± 13.5	0.014
Male/female, n (%)	58/24 (70.7/29.3)	30/10 (75/25)	28/14 (66.7/33.3)	0.41
Body mass index, kg/m²	23.7 ± 4.1	23.3 ± 4.1	24.0 ± 4.0	0.33
Comorbidities				
Hypertension*, *n* (%)	62 (75.6)	32 (80.0)	30 (71.4)	0.37
Diabetes mellitus*, *n* (%)	46 (56.1)	23 (57.5)	23 (54.8)	0.80
Heart disease†, *n* (%)	20 (24.4)	15 (37.5)	5 (11.9)	0.0070
Cerebrovascular disease‡, *n* (%)	8 (9.8)	5 (12.5)	3 (7.1)	0.41
Cancer, *n* (%)	14 (17.1)	5 (12.5)	9 (21.4)	0.28
Chronic obstructive pulmonary disease, *n* (%)	1 (1.2)	1 (2.5)	0 (0)	0.30
Liver disease, *n* (%)	1 (1.2)	0 (0)	1 (2.4)	0.33
Collagen disease, *n* (%)	2 (2.4)	1 (2.5)	1 (2.4)	0.97
Thyroid disease, *n* (%)	6 (7.3)	4 (10.0)	2 (4.8)	0.36
Laboratory data				
Hemoglobin, g/dL	9.2 ± 1.9	9.2 ± 1.9	9.3 ± 1.9	0.75
Total protein, g/dL	6.1 ± 0.7	6.0 ± 0.8	6.2 ± 0.7	0.36
Albumin, g/dL	3.1 ± 0.6	3.0 ± 0.7	3.3 ± 0.6	0.025
Uric acid, mg/dL	6.9 ± 2.2	6.4 ± 1.9	7.3 ± 2.4	0.14
Urea nitrogen, mg/dL	91.4 ± 33.2	80.9 ± 25.0	101.4 ± 37.4	0.0073
Estimated glomerular filtration rate§, ml/min/1.73 m²	5.62 ± 1.87	6.32 ± 1.94	4.95 ± 1.54	0.0019
Hemodialysis access				
Arteriovenous fistula or graft, *n* (%)	55 (67.1)	25 (62.5)	30 (71.4)	0.39
Catheter, *n* (%)	27 (32.9)	15 (37.5)	12 (28.6)	
Pleural effusion	40 (48.8)			
Bilateral/unilateral, *n* (%)		21/19 (52.5/47.5)		
Severity, mild/moderate/severe, *n* (%)		24/14/2 (60/35/5)		

* End-stage renal disease cause or morbidity.
† Heart disease included congestive heart failure, peripheral artery disease or amputation, angina pectoris, and atherosclerotic heart disease.
‡ Cerebrovascular disease included cerebral infarction or hemorrhage and carotid artery stenosis.
§ The renal function was evaluated by estimating glomerular filtration rate using the following equation developed for Japanese patients; estimated glomerular filtration rate (ml/min/1.73 m²) = 194 × serum creatinine$^{-1.094}$ × age$^{-0.287}$ (×0.739, if female).[7]

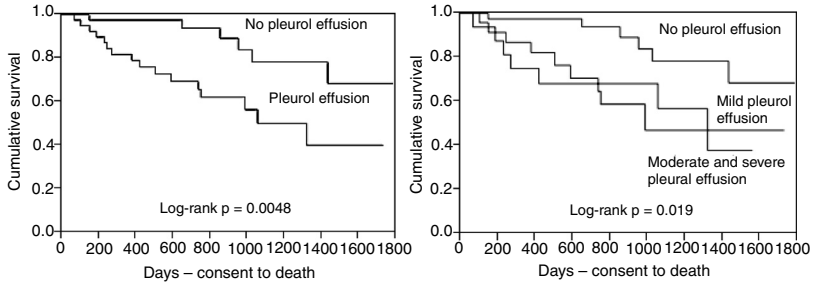

Figure 1 Kaplan–Meier survival plots for long-term mortality for pleural effusion vs. no pleural effusion (A) and for severity of pleural effusion (B).

This study has four major limitations. First, this single-centered study included only a small number of patients. Second, we did not evaluate PE by modalities other than CXR, including chest computed tomography and thoracic ultrasonography. Third, the cause of PE could not be determined because thoracentesis was not performed. Fourth, other prognostic factors, including parathyroid hormone levels and activities of daily living, were not evaluated.

We identified that PE at time of the initiation of maintenance hemodialysis was a common complication associated with poor prognosis. Future studies examining whether the initiation of maintenance hemodialysis before PE can enhance prognosis are required.

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Conflict of interest

The authors have no conflicts of interest to declare.

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Cystic fibrosis – How we reach adult life

Fibrose Quistica – Como chegamos à idade adulta

Until recently, cystic fibrosis (CF) was considered a paediatric disease, and transition of patients to adult care was rarely performed due to low life expectancy and reduced experience from adult Medicine in the follow-up of this disease. Nowadays, due to significant improvement of CF survival rates, almost all of these patients reach adulthood.[1,2] The transference of teenagers with a chronic disease like CF to adult care is a very stressful phase, sometimes faced with some anxiety by both parents and patients. Therefore, a transition period is fundamental for both, with the aim of promoting the patient's autonomy and acceptance of new roles, but also giving continuity of care. In the Specialized Centre of Cystic Fibrosis (SCCF) of the Hospital Santa Maria (Lisbon), this transition happens over three appointments, where both paediatric and adult physicians are present. Since the implementation of this programme in 2000, 54 young adults have been transferred to adult care.

The aim of this study was to characterize the clinical status of CF patients during the year of transition to adult care in a 7-year period.

We conducted a retrospective, descriptive study of all patients transferred to adult care between January 2010 and December 2016. Clinical records were reviewed and the following data were obtained: sex, age at diagnosis, genotype, treatment performed, complications, airway bacterial colonization, lung function (forced expiratory volume in 1s (FEV_1)) and nutritional status (body mass index – BMI) in the year of transition. IBM SPSS v21.0® and Microsoft Excel 2013® were used for the descriptive analysis.

From a total of 87 patients followed at the SCCF during the study period, 25 had reached adult age, of which 19 were transferred to adult Pulmonology. The main reasons for delay in transfer to adult care were either clinical instability or personal reasons (e.g. waiting for placement in University in another city). Nine (47%) patients were male, median age at diagnosis was 2.8 years [minimum 34 days; maximum 14 years] and 9 were homozygous for F508del mutation. Most patients (79%, $n = 15$) presented exocrine pancreatic insufficiency, six (32%) had liver disease, two (11%) CF-related diabetes and four (21%) had only pulmonary manifestations (Table 1). All patients were transferred to adult care up to the age of 21 years, the majority (63%, $n = 12$) at 18 years.

Regarding pulmonary function, six (32%) patients presented $FEV_1 < 70\%$, of which only 1 had severe obstruction ($FEV_1 < 40\%$) (Table 1).

Concerning nutritional status, three patients (16%) had a BMI < 18 kg/m^2.

As for airway bacterial colonization, the most common microorganisms isolated during the year of transition were *Staphylococcus aureus* ($n = 12$) and *Pseudomonas aeruginosa* ($n = 11$) (Fig. 1), which were responsible for chronic colonization in 57.9% and 31.6% of patients, respectively.

In terms of treatment, 13 (68%) patients had inhaled antibiotics, 16 (84%) dornase alfa and 16 (84%) pancreatic enzymes. No patients were on home oxygen therapy.

With improvements in healthcare in the last decades, nowadays 85% of chronic paediatric patients reach adulthood,[3] highlighting the importance of continued care and transition programmes to adult Medicine. Understand-