ASSOCIATION OF BASELINE LEVELS OF PRO-INFLAMMATORY CYTOKINES WITH THE NEAR 7 -YEAR MORTALITY RATE IN INCIDENT PERITONEAL DIALYSIS PATIENTS

Yao-Lung Liu[a,b], Shih-Yi Lin[a,b], Jiung-Hsiun Liu[a,b], I-Ru Chen[a],I-Kuan Wang[a,b], Chiz-Tzung Chang[a,b], Chiu-Ching Huang [a,b]

a. Division of Nephrology and Kidney Institute, China Medical University Hospital, Taichung

b. China Medical University, Taichung

Background:

Uremic inflammation, characterized by a persistent and increased expression of proinflammatory cytokines incited by uremia milieu, is a well-recognized status among patients with chronic kidney disease(CKD) and end-stage renal disease (ESRD) . It is believed that altered activation of a network of inflammatory signaling pathways, dys -regulated cytokine production, and increased acute-phase reactants could predispose uremic patients to immunosuppressive status, cancer development, cardiovascular events, malnutrition, anemia, and eventually mortality. Recent studies have shown an association between inflammatory markers and mortality in hemodialysis patients. However, few studies have investigated the predictive role of inflammatory markers in patients just initiating peritoneal dialysis (PD).

Method:

- A total of 50 patients with end-stage renal disease and who underwent incident PD were enrolled in this study. (**Table 1**)
- We collected the clinical parameters as well as measured the titers of pro-inflammatory cytokines Interleukin-18(IL-18), Interleukin-6 (IL-6), and Interleukin-1ß(IL-1ß). Study outcomes were all-cause mortality. A Cox-regression model was used to assess the mortality risk of selected individual markers.

Results:

- The levels of IL-18, IL-16, and IL-1ß were statistically higher in the mortality group. (**Figure 1**)
- During the near-7 year prospective study, IL-18≥ 804.3pg/mL, IL-6 ≥ 3.92 pg/mL, IL-1ß ≥ 0.86pg/mL, age ≥ 50 years-old, and existence of diabetes were significantly associated with all-cause mortality.(**Table 2**)
- Patients with increasing numbers of risk markers of mortality had decreasing survival advantages (P= 0.001). (**Figure 2**)

Table 1. Clinical characteristic of the study subjects at study baseline

	Survivors (n = 26)	Death (n = 24)	P value
Age (yrs)	50.42±12.63	62.04±13.4	0.003
Men (%)	13(50%)	8(33.3%)	0.233
BMI (kg/m²)	23.64±3.59	22.92±3.23	0.462
Diabetes (%)	4(15.3%)	16(66.7%)	<0.005
Hemoglobin (g/dL)	9.96±1.46	9.96±1.59	0.998
Albumin at stating PD(gm/dl)	3.61±0.40	3.37±0.4	0.045
Calcium (mg/dL)	8.98±0.60	8.93±0.90	0.493
Phosphate (mg/dL)	5.29±1.04	4.92±1.46	0.316
Alkaline phosphatase	65.8±32.1	81.2±29.2	0.083
Intact PTH	390.8±386.9	214.7±202.1	0.052
nPCR	1.11±0.25	1.02±0.24	0.259
Transporters(H:HA:L:LA)	2:15:8:1	2:7:12:3	0.423
Total WCrCl (L/week/1.73m²)	75.14±25.96	75.82±23.41	0.922
Total Kt/V urea	2.06±0.53	2.06±0.4	0.997
Urine CCr	34.54±26.27	37.97±23.00	0.627
Urine Kt/V urea	0.7±0.51	0.7±0.37	0.977

Transporters: H: high, HA: high average, L: low, LA: low average; WCrCl= weekly creatinine clearance; K/t/V= urea clear
normalize to its volume distribution. BMI= Body mass index.

Figure 1. Differential levels of IL-18, IL-16, and IL-1ß between survival group and death group.

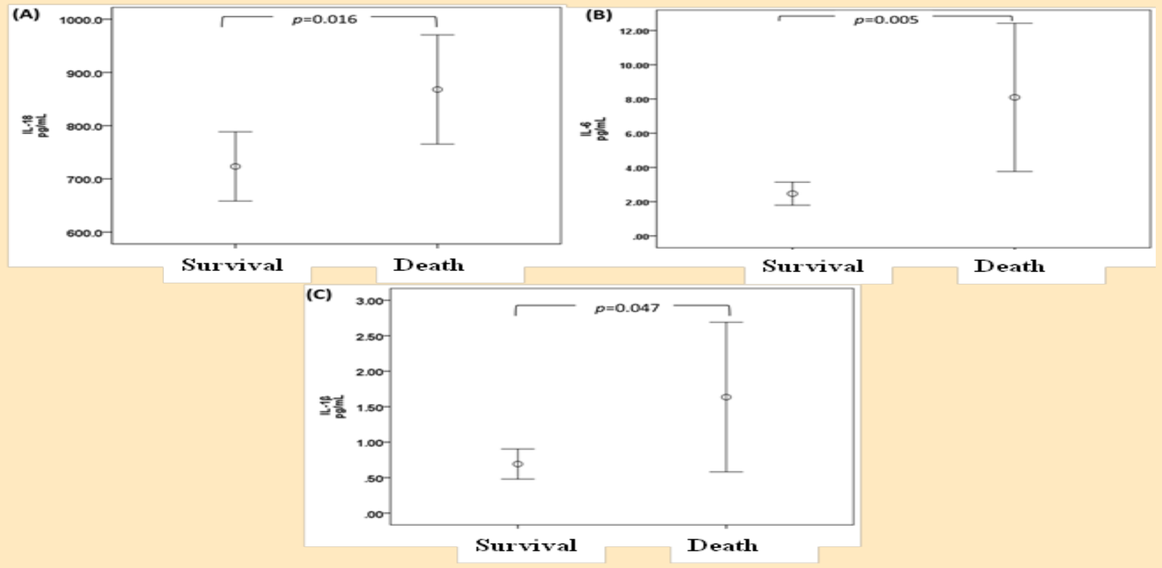

Figure 2. Survival curves of groups with 0, 1-2, 3-4, or 5-6 factors. Definition of factors: existence of diabetes mellitus, age≧50 years, IL-18≧804.3 pg/ml, IL-6≧3.92 pg/ml, IL-1ß≧0.86 pg/ml, and averages levels of albumin < 3.8 gm/dl within the first year of PD.

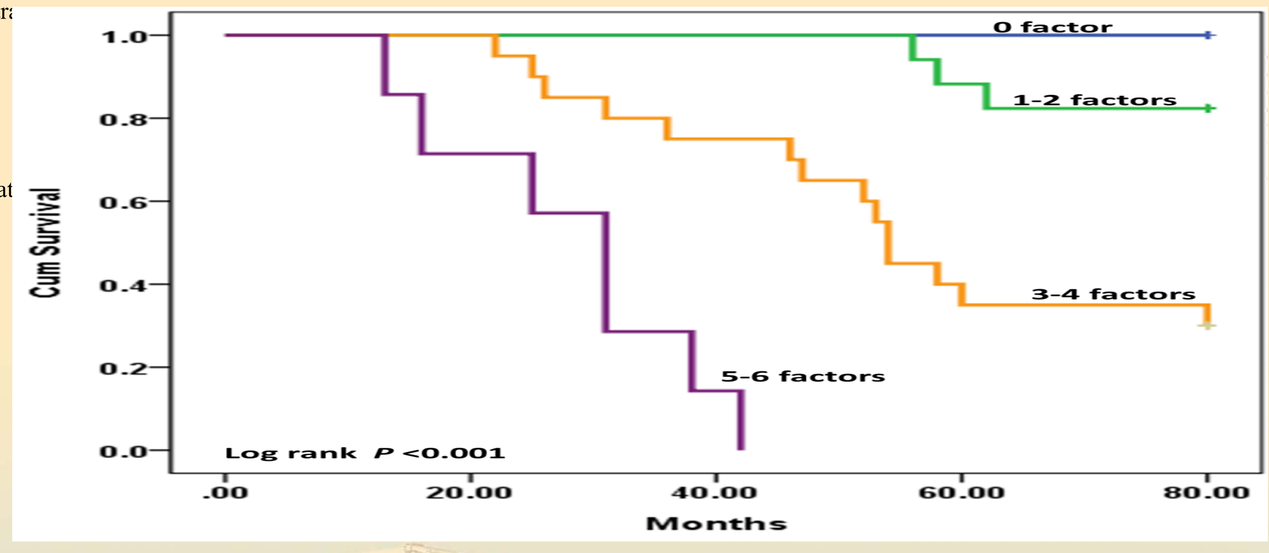

Table 2. Univariate Cox regression model of IL-18, IL-6, IL-1ß, Age>50, and Diabetes on survival function of peritoneal pat

	Odds ratio	P value
IL-18≧804.3 pg/ml	2.62	0.025
IL-6≧3.92 pg/ml	6.90	<0.001
IL-1ß≧0.86 pg/ml	5.46	0.01
Age≧50 years-old	6.83	<0.001
Diabetes Mellitus	4.73	<0.001

Conclusions:

- Clinical parameters including age ≥ 50 years-old and diabetes and inflammatory cytokines inclusive of IL-18 ≥ 804.3pg/mL, IL-6 ≥ 3.92 pg/mL, IL-1ß ≥ 0.86 pg/mL at the start of PD therapy could provide predictions for long-term mortality in the PD population. Survival advantages decreased with increasing numbers of these predictors.

中國醫藥大學附設醫院