Malnutrition-Inflammation Score Independently Determined Cardiovascular and Infection Risk in Peritoneal Dialysis Patients

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Key Words

Peritoneal dialysis • Malnutrition-inflammation complex syndrome • Malnutrition-inflammation score • Charlson comorbidity index • Chronic kidney disease

Abstract

Background: The malnutrition-inflammation score (MIS) is an indicator of malnutrition-inflammation complex syndrome and an outcome-predictor in maintenance hemodialysis (MHD) patients. However, its utility in peritoneal dialysis (PD) patients and its association with the Charlson comorbidity index (CCI) have not yet been examined. **Methods:** All chronic stable PD outpatients in the PD center of National Taiwan University Hospital in January 2006 were studied and followed for up to 18 months. The baseline MIS and CCI at the beginning of the study and the dates and causes of mortality or hospitalization during the study period were obtained. **Results:** A total of 141 PD patients were enrolled. During the study period, 8 patients died and 40 patients had major cardiovascular or infection events. The CCI correlated positively and significantly with the MIS ($r = +0.344$, $p < 0.001$). The MIS and CCI were both independent predictors of cardiovascular and infection events in the multivariate Cox proportional

hazard model. For every one unit increase in the MIS, the adjusted hazard ratio for mortality was 1.177 (95% CI 1.050–1.320, $p = 0.005$). For every one unit increase in the CCI, the adjusted hazard ratio for mortality was 1.180 (95% CI 1.046–1.330, $p = 0.007$). **Conclusions:** MIS can predict fatal and non-fatal cardiovascular and infection events in chronic stable PD patients. The CCI, which is closely associated with the MIS, is an independent determinant of cardiovascular and infection events as well. Interventional studies are indicated to confirm the utility of the MIS in PD populations who undergo nutritional or anti-inflammatory treatments.

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Introduction

Malnutrition-inflammation complex syndrome (MICS) is a term coined to denote the close relationship between protein-energy malnutrition, inflammation, and clinical outcomes in dialysis patients [1]. The clinical importance of this syndrome had been demonstrated in both maintenance hemodialysis (MHD) and peritoneal dialysis (PD) patients [2, 3]. To identify the presence and severity of MICS in PD patients, many studies use C-re-

active protein, pro-inflammatory cytokines, albumin, prealbumin, body composition, and anthropometrics as indices of inflammation or nutrition status [3, 4]. Although these simple parameters can easily be assessed, they are affected by many factors other than malnutrition or inflammation. In addition, the identification of a 'complex' syndrome using only 1 or 2 parameters is clearly incomprehensive and can easily lead to biased results. A comprehensive and quantitative measure called the malnutrition-inflammation score (MIS) was developed by Kalantar-Zadeh et al. [6]; it is determined on the basis of the medical history, physical examination, body mass index (BMI), and laboratory parameters of the patient. In MHD patients, the MIS is associated with 1- and 5-year prospective mortality [5, 6], and it is superior to the subjective global assessment (SGA) and other inflammatory markers in predicting 5-year mortality [5]. Our previous study also found the MIS to be a useful tool in the risk stratification of Asian hemodialysis patients [7]. However, the utility of the MIS in PD patients had rarely been examined, although some authors have found a reasonable correlation between the MIS and SGA in this population [11, 14, 15].

The Charlson comorbidity index (CCI) is a comorbidity scale that has been developed for general medical patients [8], but its application in dialysis patient populations to predict clinical outcomes, including length of hospital stay, inpatient costs, and mortality, has also been confirmed [9, 10]. Although the CCI has been accepted as a valid predictor of outcomes in incident PD patients, its utility in prevalent PD patients has not yet been established.

Several comorbidities, including hepatitis C, diabetes mellitus (DM), and cardiovascular disease, have been associated with more severe malnutrition or inflammation conditions in end-stage renal disease (ESRD) [1, 12, 13]. From this point of view, the MIS may have a strong correlation with the CCI. The primary aim of our study is to validate the use of the MIS and the CCI in prevalent PD patients. The secondary aim is to clarify the association between malnutrition, inflammation, and comorbidities in a PD population.

Subjects and Methods

Patients

All patients who received chronic PD treatment in the PD center of the National Taiwan University Hospital in January 2006 were recruited into the study. The study protocol conformed to the ethical guidelines of our institution, and informed consent

was obtained from each participant. The following patients were excluded from the study: patients who had received PD for less than 3 months, those who had received MHD for more than 3 months before initiation of PD, those who received PD due to renal graft failure, and those who had been hospitalized or had a documented acute infection in the recent 3 months. These exclusion criteria ensured that all the enrolled subjects were chronic stable PD patients. Age, gender, BMI, duration of PD, and comorbid conditions were recorded for all enrolled patients. The duration of PD was defined as the duration of time from the first day of PD treatment to January 1, 2006. The MIS and CCI of each patient was also recorded in January 2006.

Data Collection

All enrolled patients received standard clinical care and were followed up for 18 months until June 30, 2007. The date and cause of mortality, hospitalization, and dropout during the study period were documented for all patients. Patients were classified as having a major cardiovascular event if the major cause of death or hospitalization was acute coronary syndrome, ischemic heart disease, congestive heart failure, cardiac arrhythmia, or peripheral arterial disease. They were classified as having a major infection event if the major cause of death or hospitalization was PD-related infection, including peritonitis and exit site infection, sepsis, pneumonia, urinary tract infection, cellulitis, or any systemic or localized infection. Patients with an emergency room (ER) stay over 24 h were also classified as being hospitalized, and the causes of the ER stay were documented after chart review.

All laboratory measurements were performed in the laboratories of National Taiwan University Hospital using standardized and automated methods. All blood samples were obtained in January 2006. The glomerular filtration rate (GFR) of residual renal function was calculated as the mean of 24-hour renal urea clearance and 24-hour renal creatinine clearance. The GFR within 2 months of the beginning of this study was defined as the baseline residual renal function. The weekly fractional urea clearance (Kt/V) was the sum of peritoneal Kt/V and the residual renal Kt/V, which was calculated using the urea kinetic model formula. The results of the peritoneal equilibration test (PET), which were expressed as D/D₀ glucose ratio and D/P creatinine ratio at the 4th hour, were all obtained within 6 months before or after the initiation of the study.

Malnutrition-Inflammation Score and Charlson Comorbidity Index

The MIS consisted of 4 main parts, the medical history, physical examination, BMI, and laboratory parameters of the patient [6] (table 1). The medical history included weight changes, dietary intake, gastrointestinal symptoms, functional capacity, and presence of comorbidities. The number of years the patient was on dialysis treatment was also defined as a type of morbidity. The physical examination involved detection of loss of subcutaneous fat and signs of muscle wasting. Laboratory parameters were defined as the serum albumin and serum total iron-binding capacity (TIBC) levels. Each of the above-mentioned 10 components had 4 levels of severity ranging from 0 (normal) to 3 (severely abnormal). One of the investigators (H.-H.W.) interviewed all the patients in January 2006 to obtain information on physical morbidity and self-care ability and assessed their subcutaneous muscle tissue and muscle mass. The MIS of the patients was recorded

Table 1. Components of the MIS

MIS components	Score			
	0	1	2	3
<i>Medical history</i>				
1 Change in body weight (overall change in the past 3–6 months)	<0.5 kg	0.5–1.0 kg	≥1 kg but <5%	≤5%
2 Dietary intake	good appetite, no deterioration in dietary intake	suboptimal solid dietary intake	moderate overall decrease to full liquid diet	hypocaloric liquid to starvation
3 Gastrointestinal symptoms	no symptoms with good appetite	mild symptoms, poor appetite, or nauseated occasionally	occasional vomiting or moderate GI symptoms	frequent diarrhea or vomiting or severe anorexia
4 Functional capacity (nutritionally related functional impairment)	normal to improved functional capacity, feeling fine	occasional difficulty with baseline ambulation or feeling tired frequently	difficulty with otherwise independent activities (e.g., going to bathroom)	bed/chair-ridden or little to no physical activity
5 Comorbidity	on dialysis <1 year and no comorbidity	dialyzed for 1–4 years, or mild comorbidity (excluding MCC*)	dialyzed >4 years or moderate comorbidity (including 1 MCC*)	any severe multiple comorbidity (≥2 MCCs*)
<i>Physical examination</i>				
6 Decrease fat stores or loss of subcutaneous fat (below eyes, triceps, biceps, chest)	no change	mild	moderate	severe
7 Signs of muscle wasting (temple, clavicle, scapula, ribs, quadriceps, knee, interosseous)	no change	mild	moderate	severe
<i>Body size</i>				
8 BMI	≥20	18–19.9	16–17.99	<16
<i>Laboratory parameters</i>				
9 Serum albumin, g/dl	≥4	3.5–3.9	3.0–3.4	<3.0
10 Serum TIBC, mg/dl	≥250	200–249	150–199	<150

* MCC includes congestive heart failure class III or IV, full-blown AIDS, severe coronary artery disease, moderate to severe chronic obstructive pulmonary disease, major neurological sequelae, metastatic malignancy, or recent chemotherapy.

accordingly. The CCI was also scored in January 2006 using the method of Charlson et al. [8] (table 2). Because all patients were on dialysis, the minimum Charlson score was 2. The Framingham criteria was used in the diagnosis of congestive heart failure [25].

Statistical Analysis

The data were analyzed using SPSS for Windows version 15.0 (SPSS software, Chicago, Ill., USA). The results of descriptive analysis were expressed as mean $\pm$ standard deviation unless otherwise specified. Comparisons between patients were performed using the two-tailed Student t test for normally distributed data, Mann-Whitney U test for median data, and χ^2 test for categorical data. The association between the MIS and other variables was estimated using Spearman's rank correlation.

Multivariate Cox proportional hazards models were fitted to the collected data to model the probability of major cardiovascular or infection events. The variable selection approach was a step-

wise procedure. For each variable that stayed in the Cox model, the hazard ratio and its 95% CI were calculated. For all statistical testing, the type I error (α) was taken as 0.05 and, thus, $p < 0.05$ indicated a statistically significant result.

Results

Among the 170 patients who received chronic PD in our institution in January 2006, 29 were excluded as they met the exclusion criteria. Thus, a total of 141 subjects were enrolled in this study. They were all dialyzed using bicarbonate-buffered PD solution. The characteristics of these patients and comparisons between patients who had and did not have major cardiovascular and infection

Table 2. Charlson comorbidity index scoring system

Score	Condition
1	Myocardial infarction (history, not ECG changes only) Congestive heart failure Peripheral vascular disease (includes aortic aneurysm ≥ 6 cm) Cerebrovascular disease: CVA with mild or no residua or TIA Dementia Chronic pulmonary disease Connective tissue disease Peptic ulcer disease Mild liver disease (without portal hypertension, includes chronic hepatitis) Diabetes without end-organ damage (excludes diet-control alone)
2	Hemiplegia Moderate or severe renal disease Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes) Tumor without metastases (exclude if >5 year from diagnosis) Leukemia (acute or chronic) Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor AIDS (not just HIV positive)
For each decade >40 years of age, a score of 1 is added to the above score. ECG = Electrocardiogram; CVA = cerebrovascular accident; TIA = transient ischemic attack.	

events are shown in table 3. The average age of the patients was 52.8 ± 14.1 years. Eighty patients were female. The duration of PD ranged from 0.3 to 19.34 years with a median of 2.58 years. Sixteen (11.3%) patients had underlying diabetes, 9 (6.4%) had a history of myocardial infarction, 15 (10.6%) had congestive heart failure, and 8 (5.7%) had malignancy. The median baseline residual renal function GFR was 0.57 ml/min, with a range from 0 to 5.85 ml/min. Fifty-five patients had no residual urine. The average GFR of participants who had residual urine was 2.79 ml/min. The median MIS was 3, with a range from 0 to 13. The median CCI was 3.

A total of 8 patients died during the 18-month study period. Four patients died of cardiovascular disease, three of infections, and one from gastrointestinal bleeding. Forty patients had major cardiovascular or infection

events during the study period. The MIS was higher in patients who died or had major events (fig. 1, 2). As shown in table 3, the patients with major cardiovascular or infection events were older, had a lower serum albumin, and a higher MIS and CCI than patients without major events. The comorbidities among patients with and without major events were also different. Overall, 23 patients dropped out during the study period. Of these, 9 patients received renal transplantation, 13 changed their dialysis modality to hemodialysis, and 1 was transferred to another hospital for personal reasons.

The correlation coefficient for the MIS and relevant variables are listed in table 4. In our study populations, women tended to have a higher MIS. The MIS had a positive correlation with PD duration and serum ferritin levels. It was negatively and significantly correlated with the residual renal function, hemoglobin, blood urea nitrogen (BUN), creatinine, and phosphate. The D/P creatinine and D/D₀ glucose had no significant correlation with MIS. Congestive heart failure was the only underlying disease which had significant correlation with the MIS. However, the CCI correlated positively and significantly with the MIS. The time to first hospitalization was shorter in patients with a higher MIS and these patients tended to have more hospitalization days. The frequency of exit site infection and PD peritonitis was unrelated to the MIS. The correlation coefficients for the MIS and albumin, BMI, and TIBC are not listed in the table because they are components of the MIS system.

In the univariate Cox proportional hazard model for all-cause mortality, both the MIS and CCI showed strong associations with prospective mortality (table 5). The relative risk of death for each unit increase in the MIS was 1.804 (95% CI 1.424–2.285, $p < 0.001$). The relative risk for all-cause mortality for each unit increase in the CCI was 1.930 (95% CI 1.474–2.527, $p < 0.001$). In the univariate Cox proportional hazard model for major cardiovascular or infection events (table 6), an increased risk of cardiovascular and infection events was observed in patients with high MIS, high CCI, old age, and low plasma albumin. The associations between major events and gender, residual renal function, dialysis efficiency, and peritoneal transporter status were insignificant. The results of the multivariate Cox proportional hazard model for major cardiovascular and infection events are listed in table 6. Both the MIS and CCI had significant predictive power for major events after incorporating the effects of age, gender, residual renal function, and plasma albumin concentration. For every unit increase in the MIS, the hazard ratio for major events was 1.177 (95% CI 1.050–1.320, $p =$

Fig. 1. Comparison for MIS between survived and deceased patients. The deceased patients had a significantly higher MIS than the survived patients.

Fig. 2. Comparison for MIS between patients with and without major cardiovascular or infection events. Patients with major events had a significantly higher MIS than those without.

Table 3. Patients characteristics according to the presence of cardiovascular or infection events in PD population

	All participants (n = 141)	Patients with major events* (n = 40)	Patients without major events* (n = 101)	p value
Age, years	52.8 ± 14.1	57.2 ± 15.2	51.1 ± 13.3	0.019
Gender, male/female	61/80	13/27	48/53	0.132
PD durations, years	2.58 (1.56, 4.87)	3.02 (1.37, 4.62)	2.51 (1.71, 4.88)	0.889
Comorbidity				
DM	16 (11.3%)	8 (20.0%)	8 (7.9%)	0.073
CAD	9 (6.4%)	5 (12.5%)	4 (3.9%)	0.118
CHF	15 (10.6%)	10 (25.0%)	5 (4.9%)	0.001
Viral hepatitis [†]	7 (4.9%)	1 (2.5%)	6 (5.9%)	0.673
Malignancy	8 (5.7%)	2 (5.0%)	6 (5.9%)	1.000
BMI	22.65 ± 3.17	22.33 ± 3.16	22.78 ± 3.18	0.455
Residual renal function, ml/min	0.57 (0, 1.63)	0.43 (0, 1.27)	0.63 (0, 1.71)	0.302
Weekly Kt/V _{urea}	2.26 ± 0.32	2.256 ± 0.344	2.256 ± 0.305	0.994
D/D ₀ glucose	0.400 ± 0.080	0.406 ± 0.073	0.398 ± 0.082	0.566
D/P creatinine	0.620 ± 0.089	0.623 ± 0.100	0.618 ± 0.085	0.701
Low	14 (9.9%)	4 (10.0%)	10 (9.9%)	1.000
Low average	84 (59.6%)	22 (55.0%)	62 (61.9%)	0.569
High average	40 (28.4%)	12 (30.0%)	28 (27.9%)	0.837
High	3 (2.1%)	2 (5.0%)	1 (0.9%)	0.194
Albumin, g/dl	3.97 ± 0.35	3.84 ± 0.39	4.02 ± 0.33	0.006
Total cholesterol, mg/dl	201.2 ± 44.7	204.2 ± 49.9	200.0 ± 42.6	0.616
Triglyceride, mg/dl	168.4 ± 118.7	177.6 ± 125.6	164.7 ± 116.3	0.562
MIS	3 (2, 4)	4 (2, 6)	3 (2, 4)	0.001
CCI	3 (2, 5)	5 (4, 8)	4 (3, 5)	0.003

Data presented as mean ± SD, median (25th, 75th percentile) or number of patients (percentage).

* Major events: fatal or nonfatal major cardiovascular or infection events.

[†] Five patients had chronic hepatitis B or C without portal hypertension, 2 patients had moderate-to-severe liver disease.

PD = Peritoneal dialysis; DM = diabetes mellitus; CAD = coronary artery disease; CHF = congestive heart failure; Kt/V_{urea} = dialysis urea clearance; D/D₀ glucose = ratio of dialysate glucose at 4 h to dialysate glucose at time zero in peritoneal equilibration test; D/P creatinine = equilibration ratio between dialysate creatinine and plasma creatinine at 4 h in peritoneal equilibration test.

Table 4. Spearman correlation coefficient of MIS and demographic, anthropometric, comorbidity, laboratory, and hospitalization data

	Correlation coefficient	p value
Gender, male	-0.276	0.001
Age	0.086	0.311
PD duration	0.245	0.003
Residual renal function	-0.367	<0.001
Weekly Kt/V _{urea}	0.036	0.671
D/D ₀ glucose	-0.020	0.813
D/P creatinine	0.086	0.313
Comorbidity		
DM	0.091	0.281
CAD	0.092	0.279
CHF	0.243	0.004
Viral hepatitis	-0.040	0.641
Malignancy	0.073	0.391
CCI	0.344	<0.001
Hemoglobin	-0.212	0.012
Total cholesterol	0.003	0.973
Fasting glucose level	0.030	0.728
BUN	-0.312	<0.001
Creatinine	-0.262	0.002
Calcium	0.165	0.051
Phosphate	-0.210	0.013
i-PTH	0.036	0.669
Fe	-0.117	0.167
Ferritin	0.180	0.032
Time to first hospitalization, all-cause	-0.164	0.052
Time to first hospitalization, cardiovascular disease or infection	-0.181	0.032
Total days of hospitalization	0.172	0.042
Frequency of exit site infection	-0.048	0.569
Frequency of PD peritonitis	0.110	0.196

Kt/V_{urea} = Dialysis urea clearance; D/D₀ glucose = the ratio of dialysate glucose at 4 h to dialysate glucose at time zero in peritoneal equilibration test; D/P creatinine = the equilibration ratio between dialysate creatinine and plasma creatinine at 4 h in peritoneal equilibration test.

Table 5. Hazard ratio for all-cause mortality according to univariate Cox proportional hazard model

Variable	HR (95% CI)	p value
MIS (per one score increase)	1.804 (1.424–2.285)	<0.001
CCI (per one score increase)	1.930 (1.474–2.527)	<0.001

0.005), and for every unit increase in the CCI, the hazard ratio for major events was 1.180 (95% CI 1.046–1.330, $p = 0.007$). This established model did not change even after incorporating the parameters that were significantly correlated with the MIS in table 2, including PD duration, underlying disease with congestive heart failure, hemoglobin, urea nitrogen, creatinine, calcium, phosphate, and ferritin.

Discussion

In this prospective cohort study, we confirmed that the MIS is an independent predictor of fatal and nonfatal cardiovascular and infection events in chronic stable PD patients. We also showed that the MIS is correlated significantly with early hospital admission and prolonged hospital stay. Although the MIS system was originally developed for MHD patients, some researchers found that it can be applied in PD populations. In Chinese PD patients, the MIS and SGA score have a reasonable correlation in a cross-sectional study and the longitudinal changes in these two scores have moderate agreement with each other [11, 14]. In another prospective study with 50 PD patients who were followed up for 6 months, Afsar et al. [15] showed that the MIS was independently associated with a higher risk for future hospitalization. The weakness in previous investigations in PD patients is the lack of direct association between the MIS and prospective mortality. Our study elucidated that a higher MIS in prevalent PD patients is associated with a higher risk of cardiovascular disease- or infection-related mortality and hospital admission, even after considering the influence of age, gender, and other parameters correlated with the MIS. This finding suggests that the MIS is a practical evaluating system in PD populations and it deserves more use in clinical practice.

Only 8 patients (5.5%) died during the study period. It is well known that Asian PD patients have a survival advantage, with the 1-year survival rate at around 90% and the 2-year survival rate at around 80% [19, 23]. However, our PD populations had even better survival than incident Asian PD patients in other reports [19, 23]. One reasonable explanation is that the median MIS and CCI were low, which means that our study population was relatively well nourished and had fewer comorbidities. Although multivariate analysis could not be established based on such a small number of outcomes, the strong association between the MIS and prospective all-cause mortality in the univariate Cox proportional hazard model implies

Table 6. Hazard ratio for major cardiovascular or infection events according to univariate and multivariate Cox proportional hazard model

Variable	Univariate Cox proportional hazard model		Multivariate Cox proportional hazard model*	
	HR (95% CI)	p value	HR (95% CI)	p value
MIS (per one score increase)	1.226 (1.102–1.324)	<0.001	1.177 (1.050–1.320)	0.005
CCI (per one score increase)	1.247 (1.109–1.403)	<0.001	1.180 (1.046–1.330)	0.007
Age (per one year increase)	1.031 (1.007–1.057)	0.012		
Gender (male to female)	1.616 (0.834–3.132)	0.145		
Residual renal function (per 1 ml/min increase)	0.865 (0.667–1.121)	0.246		
Albumin (per 1 g/dl increase)	0.322 (0.135–0.767)	0.010		
Weekly Kt/V _{urea} (per 1 unit increase)	0.991 (0.350–2.812)	0.987		
D/P creatinine (per 1 unit increase)	1.116 (0.032–39.28)	0.952		

* Variable selection by stepwise procedure. Age, gender, residual renal function, plasma albumin concentration, weekly Kt/V_{urea}, and D/P creatinine were adjusted and these parameters had an insufficient significance level to remain in the model.

that the MIS may be an independent predictor of death in prevalent PD patients. A larger scale study is necessary to prove this assumption.

The correlation between the MIS and other parameters may explain why it had a good predictive power for hospitalization and mortality. Our patients with a high MIS tended to have reduced residual renal function, low hemoglobin levels, and a high CCI, all of which are correlated with higher morbidity and mortality in PD populations [10, 16, 17]. The negative correlation between the MIS and parameters such as BUN, creatinine, and phosphate may indicate an effect of reverse epidemiology [18]. Thus, an individual with low BUN, creatinine, or phosphate levels may have a poor state of nutrition rather than good small solute clearance or mineral metabolism. For the same reason, the positive correlation between the MIS and serum ferritin may imply a more aggravated inflammatory status rather than better iron storage, given that ferritin is also a marker for acute inflammation. Unlike the study of Sezer et al. [24], which found a positive correlation between MIS and D/P creatinine ratio, our study did not reveal any significant correlation between these 2 parameters. Although further studies are necessary to analyze such discrepancies, one possible explanation is the different composition of patient populations: 88% of our patients were average transporters, while approximately 35% of the patients in Sezer's study were low transporters.

The CCI was another independent predictor of prospective mortality and hospitalization in our PD patients.

High scores on the CCI, which represent the severity of comorbidities, indicate adverse clinical outcomes in incident PD patients [10, 20]; however, the utility of the CCI in prevalent PD patients is ill defined. Since type 2 malnutrition is a consequence of comorbidities [21], it could very well be inferred that malnourishment in a prevalent PD patient may be associated with a high CCI. Our study verified this by demonstrating a significant positive correlation between the MIS and CCI. A close association between malnutrition and the CCI was also observed in another study, which defined malnourishment on the basis of the SGA [22]. It could be speculated that comorbidities can influence outcomes because of their ability to induce malnutrition and inflammation. This is partially but not entirely true since the influence of CCI reduces but the CCI remains an independent determinant of prospective event risk in the Cox proportional hazard model after incorporating the effects of the MIS. Given that the CCI is valid in both incident and prevalent PD populations, incorporating regular assessment with the CCI may be worthwhile as a part of routine clinical practice.

The influence of residual renal function was found to be insignificant in our multivariate Cox proportional hazard models for cardiovascular and infection risk. This result was unexpected because substantial evidence links residual renal function to inflammation, malnutrition, and cardiovascular death [16]. One rational reason for this odd finding is that our participants were prevalent PD patients; 42% of them had received PD for more than 3 years, and 63% had a GFR of less than 1 ml/min at the

beginning of the study. As most of the patients lose their residual urine, the residual renal function no longer plays a significant role in determining clinical outcomes, and the effects of malnutrition, inflammation, and comorbidity thus become dominant.

Our study has several drawbacks. All of our patients were Asian and this may limit the potency to extrapolate our conclusions to other ethnic groups. Because of the policy of strict patient selection in our PD center, the proportion of our participants with DM was relatively small (11.3%). The particular composition of our study population may also have influenced the clinical outcomes. Only the laboratory parameters at the start of the cohort were included for statistical analysis, and time-varying confounders were not adjusted. To offset this deficiency, the rate of decline of residual renal function was calculated, because we thought it is the most important time-varying laboratory parameter related to morbidity and mortality. However, the associations between the rate of decline of residual renal function and clinical outcomes in our PD population were insignificant (data not shown). Finally, inflammatory markers such as C-reactive protein and interleukin-6 were not checked in our study population. In MHD patients, the MIS has been proven to have good correlation with inflammatory markers and have

better predictability of mortality than any single marker [5]. Although the prognostic value of the MIS and inflammatory markers were not compared in our PD population, there is high probability the results would be similar to those in MHD patients. This is because as a comprehensive scoring system, the MIS is theoretically more accurate than any single parameter in evaluating a 'complex' syndrome such as MICS.

In conclusion, our study confirmed that the MIS can predict cardiovascular and infection risks in chronic stable PD patients. The CCI, which is closely associated with the MIS, is an independent determinant of major cardiovascular and infection events as well. Interventional studies are indicated to confirm the utility of the MIS in PD populations undergoing nutritional or anti-inflammatory treatment.

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