Research Article

Metabolic Syndrome and Mortality in Continuous Ambulatory Peritoneal Dialysis Patients: A 5-Year Prospective Cohort Study

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Keywords

Peritoneal dialysis · Metabolic syndrome · All-cause mortality · Cardiovascular mortality · Technique survival

Abstract

Background/Aims: Metabolic syndrome (MS) has been widely proved as a predictor of cardiovascular disease, all-cause, and cardiovascular mortality in general population. But its effects on mortality and technique failure have not been well illustrated in peritoneal dialysis (PD) patients. We aimed to investigate the association of MS and clinical outcomes in Chinese continuous ambulatory PD (CAPD) patients. **Methods:** A single-center, prospective, observational cohort study was conducted in CAPD patients enrolled from September 1 to December 31, 2011, and followed up until December 31, 2016. Demographic, clinical, biochemical and anthropological data were collected. The relationships between MS and mortality and technique failure were assessed using Kaplan-Meier and Cox Regression Survival Functions. **Results:** A total of 511 patients were enrolled. The baseline mean age was 48.4 ± 14.4 years, 282 patients (55.2%) were male, and 130 patients (25.4%) were diabetic. In total, 213 patients (41.7%) met the diagnostic criterion of MS. During a median of 4.4 years (interquartile range 2.3–5.3 years) follow-up period, 114 patients died, of whom, 65 patients (48%) died in MS group versus 49 patients (30%) in non-MS group. Patients who died tended to be older, higher in inflammation markers and with poorer nutritional state. Kaplan-Meier Survival Functions found patients with MS had a significant rising of all-cause mortality (log-rank test = 12.811, $p < 0.001$) and cardiovascular mortality (log-rank test = 14.529, $p < 0.001$) in all patients, and a significant rising of cardiovascular mortality (log-rank test = 4.486, $p = 0.034$) in non-diabetic patients. After adjusting for confounders, Cox Regression showed that MS was significantly associated with higher cardiovascular mortality in all patients (hazard ratio [HR] 2.21,

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95% CI 1.12–4.36, $p = 0.022$) and in non-diabetic patients (HR 2.60, 95% CI 1.07–6.35, $p = 0.036$), but it has no significant effect on technique failure. **Conclusion:** In CAPD patients, MS predicted mortality, especially cardiovascular mortality. No relationship was found between MS and technique survival.

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Introduction

Metabolic syndrome (MS) refers to a cluster of features related to increased risk of cardiovascular disease (CVD), including obesity or central obesity, dyslipidemia, diabetes mellitus or insulin resistance, together with hypertension [1–4]. The mechanism of MS has been debatable, but insulin resistance [5] and abdominal obesity [1, 6] have been demonstrated as fundamental. MS has been proved as a predictor for the development of type 2 diabetes, chronic kidney disease [7, 8], and all-cause and cardiovascular mortality in general population [9–12].

The prevalence of MS in patients on peritoneal dialysis (PD) ranges from 40 to 60%, depending on the population studied. The definition of MS in PD patients [13–15] was a little different from general population due to the glucose dialysate dwell. The impact of MS on the clinical outcome of patients such as all-cause and cardiovascular mortality in PD patients was controversial [15–20]. The association of PD technique failure with MS has not been well illustrated. So, we performed a cohort study followed the PD patients from our last cross-sectional study, which investigated the risk factors of MS, and the relationship between MS and CVD in continuous ambulatory PD (CAPD) patients in Southern China [21], to further investigate the association of MS with mortality and technique failures.

Patients and Methods

Study Population

All patients came from the PD center of the First Affiliated Hospital of Sun Yat-sen University between September 1 and December 31, 2011, who had accepted CAPD therapy longer than 1 month and visited the PD center regularly. Patients who were younger than 18 years old, or had infection during the last 3 months, or had a history of malignancy, or had incomplete clinical and laboratory data, or unwilling to sign the informed consent were excluded. All patients have used peritoneal dialysate of Baxter (Healthcare Guangzhou Co., Ltd., Guangzhou, China). The study was conducted in compliance with the ethical principles of the Helsinki Declaration (<http://www.wma.net/en/30publications/10policies/b3/index.html>) and approved by the Human Ethics Committees of Sun Yat-Sen University.

Patients' data including age, gender, primary kidney disease, presence of CVD, PD vintage, glucose load of dialysate, fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, white blood cell (WBC), red blood cell, platelet, blood urea nitrogen, serum creatinine, alkaline phosphatase, high-sensitivity C-reactive protein (HsCRP), globulin and blood uric acid were collected. Blood sample for the laboratory check was taken under the condition of fasting in the morning and measured by the automatic chemistry analyzer (Hitachi 7180 and Abbott Aeroset) in the clinical laboratory of our hospital. Residual kidney function, total weekly Kt/V, and the 4th hour dialysate to plasma ratio of creatinine were calculated and reported by PD Adequest Software (Baxter Healthcare Co., Ltd.).

Blood pressure was measured by an experienced nurse using standard sphygmomanometers on the right arm of the patients who had at least 5 min of rest and we took the mean of 3 tests as the final result. The end point of follow-up included death, transferring to other PD centers, transferring to hemodialysis (HD) center, giving up or drop out till December 31, 2016.

Diagnosis of CVD, Diabetes and MS

CVD was defined as sudden death, myocardial infarction, angina, congestive heart failure, malignant arrhythmia, stroke or peripheral vascular disease with or without amputation [3, 4]. Diabetic status was defined according to the 1999 World Health Organization (WHO) diagnostic criterion as type I or type II [5] and was registered as the primary cause of end-stage renal disease. MS diagnosis criterion was the modified version of the US National Cholesterol Education Program (NCEP), Adult Treatment Panel III (2001) [15]. It requires 3 or more of the 5 components below: (1) systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 85 mm Hg or diagnosed hypertension on treatment; (2) serum TG ≥ 1.7 mmol/L; (3) serum high-density lipoprotein-cholesterol < 1 mmol/L in male, or < 1.3 mmol/L in female; (4) fasting blood glucose ≥ 5.6 mmol/L or diagnosed diabetes on treatment; (5) body mass index (BMI) > 25 kg/m² for Asians [21, 22]. BMI, instead of waist circumference, was employed to depict the abdominal obesity. The reason for the change is that, firstly, the Tenckhoff catheter in situ and repeated distention of abdominal skin by peritoneal dialysate made abdominal skin loose; secondly, the residual peritoneal dialysate in abdominal cavity made waist circumference not readily and reliably measured in PD patients [14].

Statistical Analysis

Results were expressed as frequencies and percentages for categorical variables, mean $\pm$ SD for continuous variables, and median (interquartile range) for skewed distributions. Normality of the data was assessed with Kolmogorov-Smirnov test. For normal continuous variable, the difference between the 2 groups was assessed with Student *t* test. For data with skewed distribution, the difference was assessed with Mann-Whitney U test. The intensity of death and technique failure were calculated as the number of incident cases divided by the number of person-years of the follow-up [23]. Comparisons of the incidences were conducted with chi-square test. Two-sided $p \leq 0.05$ was considered as statistically different for comparisons between the 2 groups. Survival curves were calculated with the Kaplan-Meier method, and differences between distributions of survival were made using log-rank test. Cox proportional hazard models were used to evaluate the independent associations of MS with the risk of all-cause, cardiovascular mortality and technique failure. In the analysis of all-cause or cardiovascular survival, the end point and censored event were all-cause or cardiovascular death. The censored events for technique survival were renal transplantation, move to another PD center, and still on PD at December 31, 2016. Statistical analyses were calculated using Statistical Product and Service Solutions version 20.

Results

Patient Characteristics

A total of 511 CAPD patients were recruited for the present study, and the baseline data are compared between the MS and non-MS group in Table 1. The mean baseline age was 48.4 ± 14.4 years and 282 (55.2%) of them were male. The leading cause of end-stage renal disease was chronic glomerulonephritis ($n = 300$, 58.7%), followed by diabetic kidney disease ($n = 130$, 25.4%), hypertensive nephropathy ($n = 34$, 6.7%) and polycystic kidney disease ($n = 12$,

Table 1. Comparison of baseline data between MS and non-MS group in all patients and nondiabetic patients

Variables	All patients			Non-diabetic patients		
	MS (n = 213)	non-MS (n = 298)	p value	MS (n = 122)	non-MS (n = 259)	p value
Female, %	51.6	39.9	0.009	56.9	41.9	0.005
Smoking, %	13.6	13.8	0.927	10	12.4	0.616
Drinking, %	2.3	2.7	0.854	3.1	2.2	0.735
Age, years, mean (±SD)	53.5±0.97	44.7±0.78	<0.001	50.0±1.30	43.3±0.79	<0.001
SGA, mean (±SD)	4.7±0.9	5.0±0.9	<0.001	4.8±0.9	5.1±0.9	0.564
Height, cm, mean (±SD)	162.7±7.6	164.1±8.1	0.115	162.3±8.0	163.8±8.0	0.905
Fasting weight, kg, mean (±SD)	63.4±11.3	56.3±10.1	<0.001	63.5±12.5	56.0±10.1	0.003
BMI, kg/m ² , mean (±SD)	23.9±3.3	20.8±2.8	<0.001	24.0±3.7	20.8±2.8	<0.001
SBP, mm Hg, mean (±SD)	133.6±19.0	132.8±20.4	0.032	133.9±17.2	133.0±17.2	0.05
DBP, mmHg, mean (±SD)	80.3±11.5	85.1±12.5	<0.001	84.5±11.6	86.3±12.0	0.894
FWC, cm, mean (±SD)	90.9±9.3	81.0±7.6	<0.001	89.7±10.1	80.4±7.6	0.001
HC, cm, mean (±SD)	95.7±7.3	90.5±5.5	<0.001	95.9±7.7	80.4±7.6	<0.001
WHR, mean (±SD)	0.95±0.06	0.90±0.06	<0.001	0.93±0.07	0.89±0.06	0.026
FBG, mmol/L, median (IQR)	5.7 (4.7–7.4)	4.6 (4.2–5.2)	<0.001	5.0 (4.3–5.8)	4.6 (4.2–5.0)	<0.001
TC, mmol/L, median (IQR)	5.1 (4.3–6.2)	4.7 (4.2–5.5)	0.001	4.9 (4.1–6.3)	4.7 (4.1–5.4)	0.011
TG, mmol/L, median (IQR)	2.4 (1.9–3.6)	1.1 (0.8–1.4)	<0.001	2.4 (1.9–3.4)	1.1 (0.8–1.4)	<0.001
HDL-C, mmol/L, median (IQR)	0.92 (0.80–1.09)	1.28 (1.08–1.53)	<0.001	0.93 (0.83–1.13)	1.26 (1.06–1.51)	<0.001
LDL-C, mmol/L, median (IQR)	2.61 (1.95–3.48)	2.77 (2.37–3.44)	0.059	2.49 (1.94–3.45)	2.69 (2.32–3.37)	0.061
Albumin, g/L, median (IQR)	37.5 (35.0–40.1)	37.6 (35–40.2)	0.591	38.6 (35.7–40.8)	37.8 (35.6–340.3)	0.346
Globulin, g/L, mean (±SD)	32.0±16.8	29.4±5.5	0.001	30.6±4.72	29.5±5.2	0.181
ALP, U/L, median (IQR)	72 (58–92)	66 (50–83)	0.006	70 (58–94)	66 (51–80)	0.02
WBC, 10 ⁹ , mean (±SD)	8.3±2.6	6.4±1.8	<0.001	8.2±2.8	6.4±2.0	0.007
Hemoglobin, g/L, mean (±SD)	109.6±1.2	109.1±1.2	0.76	110.5±1.6	108.5±1.2	0.61
Platelet, 10 ⁹ , mean (±SD)	254.1±79.6	221.9±68.1	<0.001	254.3±82.3	220.9±67.5	0.461
Scr, μmol/L, mean (±SD)	963.6±321.8	1,000.3±389.1	0.075	974.7±302.2	1,010.9±378.6	0.261
hsCRP, mg/L, median (IQR)	4.5 (1.4–12.1)	1.2 (0.5–3.6)	<0.001	4.52 (1.48–11.43)	1.07 (0.51–2.99)	<0.001
BUA, μmol/L, mean (±SD)	408.6±85.8	405.7±77.3	0.712	417.0±77.9	405.8±81.9	0.77
GLD, g/day, mean (±SD)	143.5±46.7	131.3±33.0	0.001	138.0±42.6	130.3±33.3	0.034
VFA, cm ² , median (IQR)	75.4 (37.2–95.0)	24.9 (5.0–59.5)	<0.001	72.7 (33.1–99.4)	22.0 (5.0–555.8)	<0.001

The difference was considered as statistically significant when $p < 0.05$.

IQR, interquartile range; SGA, subjective global assessment of nutritional status; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FWC, fasting waist circumference; HC, hip circumference; WHR, waist to hip ratio; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein cholesterol; ALP, alkaline phosphatase; WBC, white blood cell; BUN, blood urea nitrogen; Scr, serum creatinine; hsCRP, high-sensitivity C-reactive protein; BUA, blood uric acid; GLD, glucose load of dialysate; VFA, visceral fat area.

2.3%). Of the patients enrolled, 213 of all patients (41.7%) and 125 of 381 non-diabetic patients (32.8%) met the MS diagnostic criterion. Compared to patients without MS, patients with MS tended to be older, female, and diabetic (all p value ≤ 0.05). Fasting waist circumference, waist-to-hip ratio, visceral fat area, as well as WBC, platelet, globulin, and HsCRP in peripheral blood were significantly higher in MS than in non-MS group (all p value ≤ 0.05). But diastolic blood pressure was significantly lower in patients with MS than in patients without MS.

The follow-up period was a median time of 4.4 years (interquartile range 2.3–5.3 years) for all patients. Totally, 136 patients drop out of the 213 of MS group, while 162 of 298 patients drop out of non-MS group. Main reasons of the drop out in MS group were death (65 patients, 47.8%), transfer to HD center (43 patients, 31.6%), and transplantation (22 patients, 16.2%), while in non-MS group, transplantation (58 patients, 35.8%) take the first place, followed by switching to HD center (50 patients, 30.9%) and death (49 patients, 30.2%).

Table 2. Comparison between the survivor and the dead in all patients and nondiabetic patients

Variables	All patients			Non-diabetic patients		
	the survivor (n = 397)	the dead (n = 114)	p value	the survivor (n = 325)	the dead (n = 56)	p value
MS, %	37.3	57	<0.001	30.6	43.8	0.058
Female, %	44.1	47.4	0.93	45.3	54.7	0.175
Smoking, %	13.6	14	0.878	11.7	10.9	0.859
Drinking, %	2.8	1.8	0.742	2.7	1.6	0.594
Age, years, median (IQR)	45.0 (35.0–54.0)	60.0 (50.0–70.3)	<0.001	43.0 (35.0–53.0)	57.0 (46.0–70.0)	<0.001
SGA, median (IQR)	4.0 (5.0–6.0)	4 (4.0–5.0)	<0.001	5.0 (5.0–6.0)	4 (4.0–5.0)	<0.001
WBC, 10 ⁹ /L, median (IQR)	6.7 (5.3–8.0)	7.9 (6.3–10.2)	<0.001	6.50 (5.2–7.96)	7.5 (6.05–9.92)	0.004
Hemoglobin, g/L, mean (±SD)	110.0±18.1	107.1±21.6	0.151	109.9±18.6	105.1±20.6	0.066
Platelet, 10 ⁹ /L, mean (±SD)	231.8±68.9	249.3±83.3	0.023	228.5±67.8	249.3±100.6	0.118
Ca, mmol/L, mean (±SD)	2.38±0.32	2.34±0.25	0.308	2.39±0.33	2.34±0.25	0.219
P, mmol/L, mean (±SD)	1.64±0.89	1.69±1.15	0.602	1.66±0.95	1.79±1.27	0.341
Albumin, g/L, median (IQR)	38.0 (35.6–40.5)	36.3 (33.2–38.3)	<0.001	38.6 (36.0–40.9)	36.3 (32.7–38.45)	<0.001
Globulin, g/L, median (IQR)	29.1 (26.1–32.3)	31.1 (26.9–34.8)	0.025	29.3 (26.2–32.4)	31.5 (27.15–34.7)	0.075
ALP, U/L, median (IQR)	66 (50–83)	76 (61–96)	<0.001	65 (50–81)	77 (60–101.5)	<0.001
ALT, U/L, median (IQR)	16 (11–22)	14 (11–20)	0.357	15 (11–22)	14 (10.5–19.5)	0.428
Na, mmol/L, mean (±SD)	139.2±4.12	138.7±3.94	0.278	139.2±4.09	139.1±4.07	0.965
Cl, mmol/L, mean (±SD)	99.6±5.14	98.1±3.82	0.001	99.6±5.07	98.3±3.94	0.021
Scr, μmol/L, median (±SD)	988.4±361.2	901.8±320.6	0.021	1,010.1±362.7	941.1±310.9	0.155
Urea KT/V, mean (±SD)	2.29±0.64	2.22±0.59	0.355	2.27±0.64	2.18±0.57	0.368
ReGFR, mL/min/1.73 m ² , median (IQR)	1.86 (0.40–3.55)	0.77 (0.09–3.34)	0.031	1.74 (0.41–3.38)	0.68 (0.02–5.57)	0.013
Vitamin B12, pmol/L, median (IQR)	664 (494–876)	712 (490–985)	0.119	638 (479–860)	658 (452–929)	0.717
Ferritin, μg/L, median (IQR)	154.1 (75.3–288.9)	162.3 (350.7)	0.315	152.79 (73.14–283.9)	190.52 (90.68–398.6)	0.173
Transferrin, g/L, median (IQR)	2.11 (1.84–2.45)	2.04 (1.77–2.32)	0.352	1.86 (2.14–2.46)	1.99 (1.79–2.22)	0.109
Fe, μmol/L, median (IQR)	11.7 (8.6–16.6)	9.95 (7.45–13.75)	<0.001	12.1 (8.7–17)	10.2 (7.45–15.05)	0.007
CO ₂ CP, mmol/L, mean (±SD)	26.3±3.37	26.8±2.80	0.153	26.2±3.43	26.8±2.70	0.232
HsCRP, mg/L, median (IQR)	1.47 (0.58–5.34)	5.51 (1.31–13.32)	<0.001	1.34 (0.55–4.42)	5.58 (1.77–11.73)	<0.001

The difference was considered as statistically significant when $p < 0.05$.

IQR, interquartile range; MS, metabolic syndrome; SGA, subjective global assessment of nutritional status; WBC, white blood cell; ALP, alkaline phosphatase; ALT, alanine aminotransferase; Scr, serum creatinine; ReGFR, Residual estimated glomerular filtration rate; CO₂CP, carbon dioxide combining power; HsCRP, high-sensitivity C-reactive protein.

Patient Survival

In total, 114 patients died, including 65 patients in MS groups and 49 patients in non-MS group. Patients died tended to be older, higher in inflammation markers such as WBC and HsCRP, and in poorer nutritional state (lower albumin level). The detail of the comparison was showed in Table 2. In MS group, 38 of the 65 deaths (58%) were caused by CVD versus 22 of the 49 (44%) in non-MS group. The main reasons of the death compared between MS group and non-MS group were sudden death (5.6 vs. 2.3 absolute risk [AR] per 100 person-years [pys]), myocardial infarction (2.9 vs. 1.0 AR per 100 pys), angina or congestive heart failure (3.0 vs. 0.8 AR per 100 pys), pneumonia (1.9 vs. 0.3 AR per 100 pys), and unknown reasons (1.9 vs. 0.5 AR per 100 pys), and all these comparisons were significant (p value ≤ 0.05).

Kaplan-Meier Survival Functions were made. When consider all patients ($n = 511$), a median follow-up of 4.2 years (interquartile range 2.2–5.3 years) in MS group ($n = 213$) and 4.7 years (interquartile range 2.7–5.3 years) in non-MS group ($n = 298$), all-cause mortality and cardiovascular mortality were statistically higher in MS group with both $p < 0.001$ (Fig. 1, 2). In non-diabetic patients ($n = 381$), with a median follow-up of 4.7 years (interquartile range 2.5–5.3 years) in MS group ($n = 129$) and 4.8 years (interquartile range 2.6–5.3 years)

Fig. 1. Kaplan-Meier survival functions between MS group versus non-MS group of all-cause mortality in all patients. MS, metabolic syndrome.

Fig. 2. Kaplan-Meier survival functions between MS group versus non-MS group of cardiovascular mortality in all patients. MS, metabolic syndrome.

in non-MS group ($n = 252$), cardiovascular mortality was found significantly higher in MS group than in non-MS group with $p = 0.034$ (Fig. 3). But no significance was found for all-cause mortality in non-diabetic patients. In addition, no differences of mortality were found between the 2 groups in diabetic patients ($n = 130$).

Cox Regression model was done for MS' impact on all-cause mortality and cardiovascular mortality in all, non-diabetic and diabetic patients. The indicators that may have an effect on mortality such as gender, age, WBC, PLT, HsCRP and eGFR were included. After adjusting for these confounders, MS was found significantly associated with a higher cardiovascular

Fig. 3. Kaplan-Meier survival functions between MS group versus non-MS group of cardiovascular mortality in no-diabetic patients. MS, metabolic syndrome.

Table 3. Associations between MS and CVD mortality in the COX regression models

Variables	All patients		Nondiabetic patients	
	HR	p value	HR	p value
MS	2.21 (1.12–4.36)	0.022	2.60 (1.07–6.35)	0.036
Gender	0.52 (0.28–0.96)	0.037	0.65 (0.28–1.51)	0.315
Age, years	1.07 (1.05–1.10)	0	1.06 (1.03–1.09)	<0.001
WBC	1.23 (1.05–1.43)	0.011	1.26 (1.00–1.58)	0.049
Platelet	0.99 (0.99–1.00)	0.005	0.99 (0.98–1.00)	0.004
HsCRP	1.03 (0.98–1.09)	0.277	0.97 (0.88–1.06)	0.463
eGFR	0.92 (0.81–1.04)	0.198	0.82 (0.65–1.02)	0.075

The difference was considered as statistically significant when $p < 0.05$.

MS, metabolic syndrome; WBC, white blood cell; HsCRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; CVD, cardiovascular disease; HR, hazard ratio.

mortality in all patients (hazard ratio [HR] 2.21, 95% CI 1.12–4.36, $p = 0.022$) and non-diabetic patients (HR 2.60, 95% CI 1.07–6.35, $p = 0.036$; Table 3). But no significant MS' effects on all-cause mortality were found in all, non-diabetic or diabetic patients.

Technique Survival

In the 213 patients with MS versus 298 patients without MS, 22 vs. 58 take transplantation, 5 vs. 4 transferred to other PD centers and 43 vs. 50 transferred to HD center. The technique survival rate compared between the 2 groups was not significant in all, non-diabetic or diabetic patients. Cox Regression results showed that no significant MS' effects on technique survival rate were found in all, non-diabetic or diabetic patients.

Discussion

In the present prospective cohort study with a median 4.4 years follow-up, we found that MS had an impact on higher cardiovascular mortality and all-cause mortality in PD patients. And this effect was even stronger on cardiovascular mortality, especially in non-diabetic patients.

The clinical value of MS lies in its prediction of the clinical outcome, especially all-cause and cardiovascular mortality. This value has been widely proved [10, 12, 24] in general population. Many studies including large cohorts and meta-analyses have validated this effect. A large cohort [10] with a sample of 45,542 middle-aged Taiwanese check-up population found MS may be associated with a much higher risk for all-cause mortality. A meta-analysis [25] included 87 studies ($n = 951,083$) discovered that MS was associated with an increased risk of CVD (relative risk [RR] 2.35), CVD mortality (RR 2.40), all-cause mortality (RR 1.58), myocardial infarction (RR 1.99) and stroke (RR 2.27). Another meta-analysis [11] including 21 studies showed an increased mortality for all-cause (RR 1.35) and CVD (RR 1.74). But in PD patients the results were still controversial [15–20, 26]. One study [15] ($n = 196$) compared the 4 different MS diagnostic criteria found only MS defined with WHO criterion showed an increased risk of mortality and no significant difference was found in non-diabetic population, regardless of the criteria used. Another study ($n = 139$) of non-diabetic PD patients did not found the relationship between MS and patient survival [17], But another study [18] ($n = 280$) with non-diabetic PD patients showed that patients with MS had a poorer survival rate compared to patients without MS for both all-cause and cardiovascular survival. In an Indian study, MS was found to related to a higher patient mortality in non-diabetic patients ($n = 163$) [19] and another non-diabetic cohort study ($n = 106$) [27], while a meta-analysis including PD and HD patients with or without diabetes also found a similar result [28]. Sample size variation may be an explanation for the different conclusions and large-scale studies were needed to address this issue [6].

There was still controversy about the definition of MS. Many criteria including WHO criterion, International Diabetes Federation criterion, original NCEP and modified NCEP criterion were available. We chose modified NCEP criterion because it included BMI other than waist circumference, in PD patients where Tenckhoff catheter in situ and repeated abdominal distention made waist circumference not reliable [6, 16]. Our study ($n = 511$) found a similar result in MS' prediction of mortality, especially cardiovascular mortality in CAPD patients. Kaplan-Meier Survival Functions found all-cause and cardiovascular mortality were both significantly higher in patients with MS than patients without MS in all patients and this significance was also seen in the effect of MS on cardiovascular mortality in non-diabetic patients. Cox Regression also showed solid evidence of the prediction value of MS on cardiovascular mortality in all patients (HR 2.21, 95% CI 1.12–4.36) and in non-diabetic patients (HR 2.60, 95% CI 1.07–6.35); but this significance was not seen in all or diabetic patients, whether all-cause or cardiovascular mortality. MS' impact on technique survival was not found significant in all, non-diabetic or diabetic patients. The findings of our research MS was similar with other research [6, 15, 17].

However, without a clear mechanism, no special treatment can be done in the upstream of the development of MS to prevent it from the very beginning, except measures like lifestyle change and exercises. MS' clinical value was often compared with the Framingham risk score (FRS), a simplified and common clinical tool for assessment of the risk level of coronary artery disease as well as for identifying individuals who were candidate for risk factors modification [29, 30]. Although MS has been identified to be a valid tool for predicting CVD and its predictive ability was as good as the FRS [31], Some considered that FRS [23, 32–35] was better. Therefore, the clinical importance of MS was still challenged and more studies are needed to clarify its mechanism and clinical role.

Limitations existed in this study: Firstly, the study recruited patients from only one single PD center, and the patients were mostly from the Southern China; thus, the results may not always be well applicable elsewhere. Secondly, we only included the patients that came back for regular follow-up and excluded the patients with incomplete data, which could cause bias and might influence the result. Thirdly, owing to the influence of glucose load of dialysate on hyperglycemia or the appearance of new-onset diabetes, we did not reevaluate the MS status during or at the end of the follow-up, so that the new onset MS was not diagnosed, which could affect the results of the research. Despite these, we did find a solid relationship between MS and mortality, especially its effect on cardiovascular mortality. Therefore, we assume that the results are valuable and useful, and early intervention of MS is important to prevent the clinical outcome of patients on CAPD. However, further prospective, multi-center studies with longer follow-up are needed.

In conclusion, in CAPD patients, MS predispose mortality, especially cardiovascular mortality, and no relationship was found between MS and technique survival.

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Disclosure Statement

All authors claim no conflicts of interest.

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