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Original Article

ORIGINAL ARTICLE

Modified creatinine index as a marker of skeletal muscle mass in peritoneal dialysis patients

Jack Kit-Chung Ng[1], Winston Wing-Shing Fung[1], Gordon Chun-Kau Chan[1], Phyllis Mei-Shan Cheng[1,2], Wing-Fai Pang[1], Kai-Ming Chow[1] and Cheuk-Chun Szeto[1,2]

[1]Carol & Richard Yu Peritoneal Dialysis Research Centre, Departments of Medicine & Therapeutics, Prince of Wales Hospital and [2]Li Ka Shing Institute of Health Sciences (LiHS), Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong, China

Correspondence to: Cheuk-Chun Szeto; E-mail: ccszeto@cuhk.edu.hk

ABSTRACT

Background. Sarcopenia is common in peritoneal dialysis (PD) patients. Modified creatinine index (MCrI) by the Canaud's formula and single-pool Kt/V value is an accurate surrogate marker for muscle mass in hemodialysis patients. However, the method of calculation and validity of MCrI has not been tested in PD.

Methods. In the exploratory cohort, we studied 138 consecutive patients converted from PD to hemodialysis. Their MCrI during PD, calculated by the Canaud's formula with total weekly Kt/V, and the conventional MCrI after conversion to HD, were compared by the Bland–Altman method. Their correlation with muscle mass as determined by bioimpedance spectroscopy and creatinine kinetic methods was explored. The result was then validated in a second cohort of 605 incident PD patients.

Results. In the exploratory cohort, the average bias of computing MCrI during PD and hemodialysis was 0.758 mg/kg/day (95%CI −4.356 to 5.873 mg/kg/day). The MCrI during PD significantly correlated with the muscle mass by creatinine kinetics ($r = .684$, $P < .0001$) and by bioimpedance spectroscopy ($r = .641$, $P < .0001$), but not with protein nitrogen appearance, overhydration, or adipose tissue mass, and the result was similar in the validation cohort. For incident PD patients, MCrI quartile was significantly associated with the risk of death from all cause in 12 months (Gray's test, $P = .013$) but not conversion to chronic hemodialysis ($P = .14$).

Conclusion. In PD patients, MCrI computed by the Canaud's formula and total weekly Kt/V is a simple and reliable marker of skeletal muscle mass and may serve as a short-term prognostic indicator.

Keywords: frailty, malnutrition, renal failure

INTRODUCTION

Sarcopenia is common in chronic dialysis patients [1] and it contributes to their functional impairment and morbidity [2]. Although the revised European consensus on the definition of sarcopenia focuses on low muscle strength as a key characteristic of sarcopenia [3], the original European Working Group on Sarcopenia in Older People (EWGSOP), is commonly used in patients with chronic kidney disease [1]. In the EWGSOP definition, sarcopenia could be defined by the loss of muscle mass, i.e. 2 standard deviations below the mean of young adults or by the sex-specific

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KEY LEARNING POINTS

What was known:

- Sarcopenia is common in peritoneal dialysis (PD) patients. Modified creatinine index (MCrI) by the Canaud's formula and single-pool Kt/V value is an accurate surrogate marker for muscle mass in hemodialysis patients.

This study adds:

- The MCrI during PD significantly correlated with the muscle mass by creatinine kinetics and by bioimpedance spectroscopy. For incident PD patients, MCrI quartile was significantly associated with patient survival and technique survival.

Potential impact:

- MCrI is a simple and reliable marker of skeletal muscle mass and may serve as a short-term prognostic indicator for PD patients.

cutoff points [1]. Assessment of skeletal muscle mass represents a valuable means for risk stratification of dialysis patients [1, 4], and assists in the decision of nutritional support and exercise training [4–6].

Skeletal muscle mass can be determined by several methods, but none of them is ideal [1]. Anthropometric measurements are simple but crude [7, 8], while imaging techniques (either CT scan or magnetic resonance imaging) are accurate but not suitable for routine clinical use [9, 10]. Lean tissue mass (LTM), which are often taken as an acceptable surrogate for skeletal muscle mass, can be determined by multifrequency bioimpedance spectroscopy [11, 12], typically during the assessment of fluid status. However, there is a considerable systemic difference when LTM is measured by different equipment models [1, 13, 14], which limits its use for extended longitudinal study or cross-center comparison.

Creatinine kinetic method is a reliable way to determine skeletal muscle mass [15, 16]. The traditional creatinine index was defined as the normalized creatinine production rate, which was the sum of creatinine excretion and metabolic degradation [15, 17]. Although the traditional creatinine index is an accurate marker of skeletal muscle mass and a prognostic indicator of mortality and cardiovascular disease in hemodialysis (HD) patients [18, 19], its computation requires post-dialysis serum creatinine concentration, dialysate and 24-hour urine collection to compute creatinine generation rates. To simplified the calculation and facilitate routine clinical use, Canaud *et al.* [20] constructed a user-friendly formula that is calculated from demographic parameters, pre-dialysis serum creatinine concentrations, and single-pooled Kt/V for urea. The parameter was originally called 'simplified creatinine index' [20], but was more frequently referred to as modified creatinine index (MCrI) by subsequent researchers. In HD patients, MCrI has been validated as an accurate surrogate measure for muscle mass [20, 21].

However, the application of MCrI to peritoneal dialysis (PD) patients has not been explored. Since the dialysis adequacy of PD is typically reported as total weekly Kt/V, adaptation of the original formula by Canaud *et al.* [20] may introduce a systemic bias. The objective of the present study is to compare MCrI as measured during PD and HD, and to determine the use of MCrI as a marker of skeletal muscle mass in PD patients. We first identified a cohort of patients who were converted from PD to HD, and determined their MCrI before and after the conversion. The result was further validated by a separate cohort of incident PD patients.

METHODS

This study was approved by the Joint Chinese University Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (approval numbers CRE-2015.250 and CRE-2021.367). All study procedures were compliant with the Declaration of Helsinki.

Case selection

In the first cohort, we retrospectively identified 138 consecutive patients who were converted from PD to HD in our center from 2006 to 2020. We excluded patients who had ongoing infections, weight change over 5% of the baseline body weight, were unlikely to survive for 3 months, were planned to have elective living donor transplant, or transfer to another renal center within 3 months. The modified creatinine indices were computed when they were stable after conversion to HD, as well as while they were on PD and within 3 months of conversion. The result of multifrequency bioimpedance spectroscopy performed at the same time was reviewed. In addition, we also reviewed the record of their dialysis adequacy assessment, fat-free edema-free body mass (FEBM) by creatinine kinetics, and other assessment of nutritional status performed while the patients were on PD and within 3 months of conversion.

In the second cohort, we analyzed a separate prospective cohort of 605 incident PD patients. Patients who were planned to have elective living donor transplants or transferred to other renal centers within 6 months of PD were excluded. Their MCrI was computed at 4 weeks after patients were stable on PD. The results of multifrequency bioimpedance spectroscopy, dialysis adequacy assessment, FEBM by creatinine kinetics, and other assessment of nutritional status performed at the same time were also reviewed.

Modified creatinine index

The MCrI during hemodialysis (MCrI-HD) was calculated by the formula as described by Canaud *et al.* [20]:

$$\begin{aligned}\text{MCrI-HD (mg/kg/day)} &= 16.21 + (1.12 \times [1 \text{ if 78 male; 0 if female}]) \\ &- (0.06 \times \text{age (years)}) \\ &- (0.08 \times \text{single-pooled Kt/V for urea}) \\ &+ (0.009 \times \text{serum creatinine before dialysis } (\mu\text{mol/L}))\end{aligned}$$

In this study, the modified creatinine index during peritoneal dialysis (MCrI-PD) was calculated by the same formula, with the total weekly Kt/V for urea to replace the single-pooled Kt/V, and serum creatinine was measured at the steady state:

$$\begin{aligned}\text{MCrI-PD (mg/kg/day)} = {} & 16.21 + (1.12 \times [1 \text{ if male; } 0 \text{ if female}]) \\ & - (0.06 \times \text{age (years)}) \\ & - (0.08 \times \text{weekly Kt/V for urea}) \\ & + (0.009 \times \text{serum creatinine at steady state } (\mu\text{mol/L}))\end{aligned}$$

Multifrequency bioimpedance spectroscopy

We used a validated multifrequency bioimpedance spectroscopy device (Body Composition Monitor, Fresenius Medical Care, Germany) as previously described [22, 23]. Briefly, LTM, adipose tissue mass (ATM), and volume of overhydration (OH) were determined. All measurements were performed with 2 l of indwelling PD fluid as a previous study suggested that the presence of peritoneal dialysate had an insignificant effect on BCM measurement [24].

Fat-free edema-free body mass by creatinine kinetics

FEBM was determined by the creatinine kinetic method, with 24-hour urine and dialysate collection, according to the formula described by Forbes and Brunining [25]:

$$\begin{aligned}\text{FEBM (kg)} = {} & 7.38 + [0.029 \times (\text{creatinine excretion (mg/day)} \\ & + \text{creatinine degradation (mg/day)})]\end{aligned}$$

$$\begin{aligned}\text{while} \quad & \text{creatinine excretion (mg/day)} \\ = {} & [\text{urine} + \text{dialysate creatinine output (mmol/day)}] \times 0.113\end{aligned}$$

$$\begin{aligned}& \text{creatinine degradation (mg/day)} \\ = {} & 0.38 \times (\text{plasma creatinine (mmol/l)} \times 0.0113) \\ & \times \text{body weight (kg)}\end{aligned}$$

Other measures of nutritional status and dialysis adequacy

The method of dialysis adequacy assessment in PD has been described previously [26]. In essence, 24-hour urine and dialysate collection were performed for the calculation of the total Kt/V. Residual kidney function was represented by the residual glomerular filtration rate, which was calculated as the average of 24-hour urinary urea and creatinine clearances [27]. Normalized protein nitrogen appearance (NPNA) was calculated by the modified Bergstrom's formula [28]. During HD, single-pool Kt/V (sp-Kt/V) was calculated from the pre- and post-dialysis blood urea level by the second generation Daugirdas II equation [29]. Serum albumin level was measured by the bromocresol purple method.

Clinical outcome

All patients in the second cohort were followed for 12 months. The clinical management was decided by individual clinician and not affected by the study. We analyzed their patient survival and technique survival rates, as well as the total number of hospital admission and duration of hospital stay in 12 months. For patient survival, recovery of renal function, loss to follow up, and transfer to other dialysis centers were censored, while conversion to long-term HD and kidney transplant were taken as competing events. For the analysis of technique survival, patient death and kidney transplant were taken as competing events, while recovery of renal function, loss to follow up, and transfer to other dialysis centers were censored.

Statistical analysis

Statistical analysis was performed by SPSS for Windows software version 25.0 (IBM, Armonk, NY, USA) and R version 4.4.1 (R Foundation for Statistical Computing Platform). Demographic and clinical data were compared between groups by Student's *t*-test, one-way analysis of variance (ANOVA), or chi-square test as appropriate. MCrI-HD and MCrI-PD were compared by the modified Bland–Altman method [30]. In this analysis, the difference between MCrI-HD and MCrI-PD was plotted against MCrI-HD, which was taken as the reference value. Correlations with other nutritional parameters were explored by the Spearman's rank correlation coefficient. Since male patients generally had more muscle mass and a higher MCrI-PD than females, MCrI-PD was grouped into quartiles by gender for the analysis of the second cohort. The risks of death and conversion to chronic HD were analyzed by the cumulative incidence curves and compared by Gray's test for equality of cumulative incidence functions across groups. For the number of hospital admissions and duration of hospital stay, data were compared between MCrI-PD quartiles by the Jonckheere–Terpstra test. *P* values $<.05$ were considered statistically significant. All probabilities were two-tailed.

RESULTS

Difference between MCrI in PD and HD

From 2006 to 2020, we identified 213 patients who were converted from PD to HD in our center; 75 cases were excluded because of death within 3 months of conversion (20 cases), persistent systemic inflammation (18 cases), documented drastic change in nutritional status (32 cases), or incomplete data (five cases). We analyzed the remaining 138 patients; 82 patients due to peritonitis, and 56 due to non-peritonitis (mostly mechanical) reasons. Their baseline clinical and biochemical characteristics are summarized in Table 1. There was a significant correlation between MCrI-PD and MCrI-HD ($r = .633$, $P < .0001$). When the patients were converted from PD to HD, paired MCrI results were lower in HD, using sp-KT/V and pre-dialysis serum creatinine, than the ones obtained in PD, using total weekly KT/V and steady state serum creatinine (23.0 ± 3.2 vs 22.2 ± 2.9 mg/kg/day, paired Student's *t*-test, $P = .001$).

The modified Bland–Altman plot that compared the two methods of calculating MCrI is shown in Fig. 1. The average bias of the two methods of computing MCrI was 0.758 mg/kg/day (95%CI −4.356 to 5.873 mg/kg/day). The bias was similar between patient who were converted to HD because of peritonitis (0.489 mg/kg/day, 95%CI −4.400 to 5.374) and non-peritonitis reasons (1.152 mg/kg/day, 95%CI −4.232 to 6.537) ($P = .143$). There was a modest but significant inverse correlation between the difference of the two measurements and the MCrI computed by sp-Kt/V from HD ($r = -.288$, $P = .001$). The difference of the two MCrI also had modest but significant correlations with the duration of PD ($r = .252$, $P = .003$), residual renal function ($r = -.359$, $P < .0001$), and serum albumin level ($r = .342$, $P < .0001$).

Table 1: Baseline clinical and biochemical characteristics of cohort #1.

	All cases	Peritonitis	Not peritonitis	P value
no. of patients	138	82	56	
sex (M:F)	88:50	47:35	41:15	.056
age (years)	59.2 ± 12.3	59.3 ± 13.2	59.1 ± 11.0	.907
body weight (kg)	70.0 ± 17.3	68.0 ± 17.3	72.1 ± 17.1	.111
body height (cm)	164.0 ± 8.5	163.7 ± 8.7	165.8 ± 7.9	.034
BMI (kg/m^2)	25.9 ± 5.5	25.6 ± 5.8	26.3 ± 5.2	.472
duration of PD (months)	64.2 ± 54.2	63.5 ± 48.7	65.3 ± 61.8	.853
renal diagnosis, no. of cases (%)				.277
diabetic nephropathy	47 (34.1%)	29 (35.4%)	18 (32.1%)	
glomerulonephritis	56 (40.6%)	35 (42.7%)	21 (37.5%)	
hypertension	7 (5.1%)	4 (4.9%)	3 (5.4%)	
polycystic kidney	6 (4.3%)	2 (2.4%)	4 (7.1%)	
urologic causes	4 (2.9%)	1 (1.2%)	3 (5.4%)	
others or unknown	18 (13.0%)	11 (13.4%)	7 (12.5%)	
comorbid conditions, no. of cases (%)				
diabetes	56 (40.6%)	34 (41.5%)	22 (39.3%)	.798
ischemic heart disease	29 (21.0%)	19 (23.2%)	10 (17.9%)	.452
cerebrovascular disease	18 (13.0%)	13 (15.9%)	5 (8.9%)	.236
Charlson's score	5.7 ± 2.6	5.8 ± 2.9	5.4 ± 2.2	.339
residual GFR (ml/min/1.73 m^2)	1.17 ± 1.77	1.14 ± 1.88	1.21 ± 1.62	.837
biochemical parameters				
hemoglobin (g/dl)	9.06 ± 1.52	8.97 ± 1.56	9.19 ± 1.48	.405
serum albumin (g/l)	32.2 ± 5.7	32.2 ± 5.5	32.2 ± 6.2	.984
FEBM (kg)	39.0 ± 11.9	38.0 ± 11.5	40.5 ± 12.4	.211
bioimpedence spectroscopy				
overhydration (l)	3.8 ± 3.3	3.5 ± 3.2	4.3 ± 3.6	.256
LTM (kg)	40.8 ± 10.8	38.9 ± 9.4	43.8 ± 12.2	.036
ATM (kg)	23.4 ± 14.9	24.0 ± 12.2	22.5 ± 14.6	.628
Kt/V				
total Kt/V during PD	1.70 ± 0.39	1.75 ± 0.38	1.62 ± 0.40	.059
sp-Kt/V during HD	1.32 ± 0.34	1.31 ± 0.38	1.35 ± 0.27	.434
MCrI (mg/kg/day)				
during PD, by total Kt/V	23.0 ± 3.2	22.6 ± 3.2	23.5 ± 3.3	.085
during HD, by sp-Kt/V	22.2 ± 2.9	22.1 ± 2.9	22.4 ± 2.9	.547

GFR, glomerular filtration rate. Data were compared by [a]Chi square test and [b]Student's *t*-test.

MCrI as a marker of muscle mass in PD

In the first cohort, both MCrI measured during PD and HD had modest but significant correlations with patients' age, body weight, and height. The MCrI during PD significantly correlated with the FEBM by creatinine kinetics ($r = .684$, $P < .0001$) and LTM by bioimpedance spectroscopy ($r = .641$, $P < .0001$), but not with NPNA, overhydration volume, or ATM by bioimpedance spectroscopy (Fig. 2 and Supplementary Table S1). The MCrI during HD also had similar but less robust correlation with the FEBM and LTM (Supplementary Table S1).

In the second cohort, we studied 605 incident PD patients. Their baseline clinical and biochemical characteristics were summarized and compared according to the MCrI-PD quartiles in Tables 2 and 3, respectively. In essence, patients with more advanced age, lower body weight, higher comorbidity load, and lower serum albumin level had a lower MCrI-PD. However, MCrI-PD tended to be higher in patients with worse residual renal function and lower total Kt/V. In the second cohort, the MCrI-PD also significantly correlated with the FEBM by creatinine kinetics ($r = .483$, $P < .0001$) and LTM by bioimpedance spectroscopy ($r = .521$, $P < .0001$), but not with NPNA. In this cohort, MCrI-PD also had significant but modest correlation with serum albumin level, overhydration volume, or ATM by bioimpedance spectroscopy (Fig. 2 and Supplementary Table S1).

Prognostic role of MCrI in PD

Patients in the second cohort were followed for 12 months. During the follow-up period, 26 patients died. The causes of death were cardiovascular diseases (eight cases), stroke (two cases), non-peritonitis infections (six cases), sudden cardiac arrest (seven cases), malignancy (two cases), and termination of dialysis (one case). During the same period, another 10 patients were converted to chronic HD, and 10 had kidney transplantation. The cumulative incidence curves of the second cohort, according to the MCrI quartile, is shown in Fig. 3. The 1-year cumulative incidence of dying from all causes for MCrI-PD quartiles I to IV were 3.1%, 2.0%, 4.6%, and 7.2% ($P = .013$). The cumulative incidence of conversion to chronic HD in 1 year for MCrI-PD quartiles I to IV were 1.3%, 1.3%, 0.7%, and 2.6% ($P = .14$). Given the small number of events, elaborated multivariate survival analysis was not performed.

During the first 12 months on PD, the second cohort had 1308 hospital admissions for a total of 8559 days; 92 patients (15.2%) did not require hospitalization. The average rate of hospitalization was 2.24 admission per year, or 14.7 days of hospital stay per year. The number of hospital admissions during the first year of PD for MCrI quartiles I to IV were 2 (1–3), 2 (1–3), 1 (1–3), and 2 (1–3) (Jonckheere–Terpstra test, $P = .730$); and the durations of hospital stay for MCrI quartiles I to IV

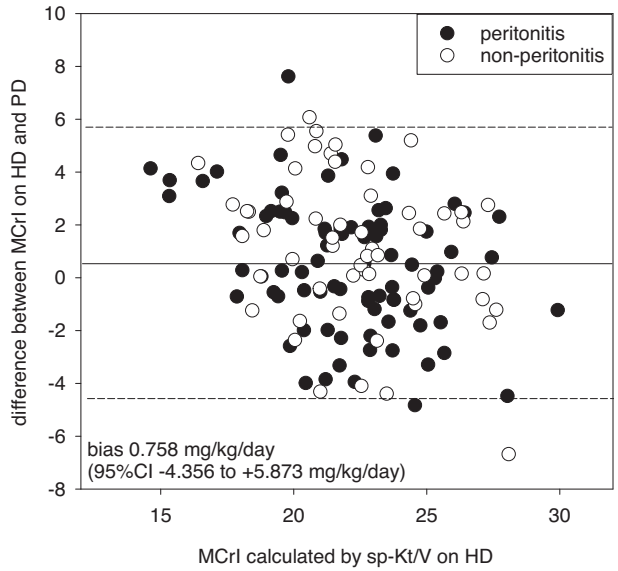

Figure 1: Bland–Altman plot of the difference in MCrI measured during HD and PD versus MCrI during HD in Cohort #1. Patients were divided into two groups according to the cause of conversion from PD to HD: closed circles represent conversions due to peritonitis; open circles represent conversions due to other reasons.

were 8 (2–18), 6 (2–14), 5 (2–19), and 8 (2–18) days per year ($P = .906$).

DISCUSSION

Our study represents the first major study that validates the use of MCrI for the estimation of skeletal muscle mass in PD patients, and the result seems robust across two separate cohort of patients. The absolute values of MCrI in our two cohorts of PD patients were like those reported in HD [18–21]. Nonetheless, it is important to note that although the systemic bias of calculating MCrI with total weekly Kt/V in PD, compared to sp-Kt/V in HD, appeared to be small, the variability (i.e. the confidence interval of the difference between them) was substantial, and we did not identify any clinical factor that could account for the variability.

Although there are other noninvasive methods for the assessment of muscle mass in PD patients [1], MCrI has the distinct advantage in that it is simply calculated by age, sex, serum creatinine, and weekly Kt/V. The computation does not require any additional test or cost, and could readily be incorporated into the protocol of routine patient monitoring. Although FEBM by the creatinine kinetic method could also be computed from the same 24-hour dialysate and urine samples used for dialysis adequacy (i.e. total Kt/V) assessment, it requires the measurement of dialysate creatinine output, which is neither a routine test in

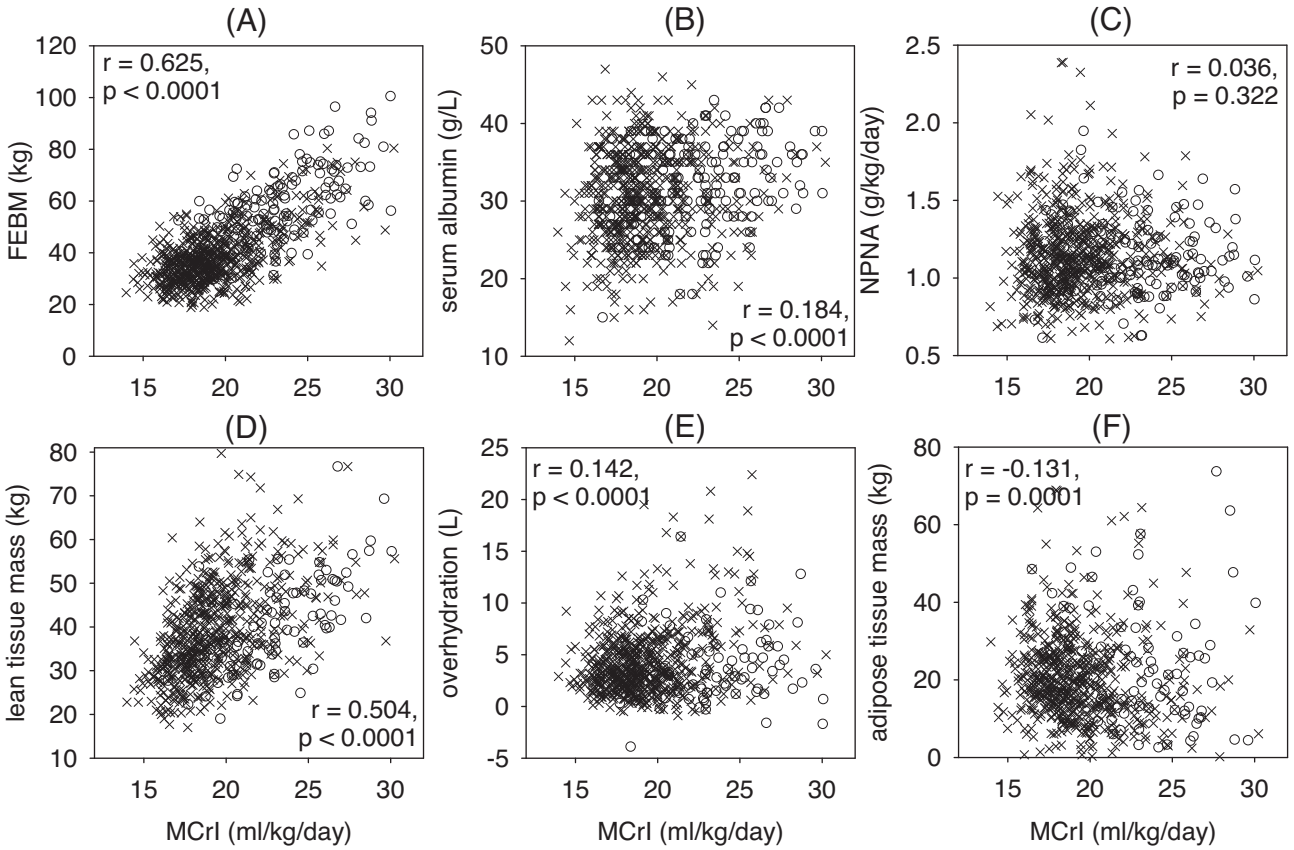

Figure 2: Correlation between MCrI and (**a**) FEBM as determined by creatinine kinetics; (**b**) serum albumin level; (**c**) NPNA; (**d**) LTM; (**e**) overhydration volume (OH); and (**f**) ATM. LTM, OH, and ATM were measured by multifrequency bioimpedance spectroscopy. Open circles represent cases of cohort #1; crosses represent cohort #2. The overall Spearman's rank correlation coefficients, with the data of the two cohorts combined, are depicted. See Supplementary Table S1 for the detailed result of subgroup analysis of individual cohorts.

Table 2: Baseline clinical characteristics of cohort #2 according to MCrI quartile.

		MCrI quartile				
	Al cases	I	II	III	IV	*P* value
no. of patients	605	151	151	151	152	
sex (M:F)	357:248	89:62	89:62	89:62	90:62	
MCrI (mg/kg/day)						
male	19.9 ± 2.6	17.4 ± 0.7	18.9 ± 0.3	20.3 ± 0.5	23.5 ± 2.0	
female	18.3 ± 2.2	16.0 ± 0.6	17.4 ± 0.3	18.5 ± 0.4	21.3 ± 1.9	
age (year)	60.0 ± 11.6	68.3 ± 7.6	63.8 ± 8.2	58.9 ± 9.3	49.0 ± 11.1	.0001
body weight (kg)	65.0 ± 14.8	62.2 ± 12.6	63.9 ± 14.0	64.6 ± 11.3	69.3 ± 19.3	.0001
body height (cm)	162.1 ± 8.6	159.9 ± 7.7	161.4 ± 8.6	162.4 ± 8.5	164.6 ± 8.8	.0001
body mass index (kg/m^2)	24.6 ± 4.5	24.2 ± 4.0	24.5 ± 4.5	24.5 ± 3.8	25.3 ± 5.3	.166
blood pressure (mmHg)						
systolic	143.5 ± 21.2	142.0 ± 19.2	145.2 ± 22.4	141.9 ± 21.3	144.9 ± 21.9	.350
diastolic	76.4 ± 12.7	72.5 ± 11.8	76.2 ± 12.1	76.3 ± 12.2	80.6 ± 13.3	.0001
underlying renal diagnosis, no. of patients (%)						.001
diabetes	317 (52.4%)	92 (60.9%)	76 (50.3%)	79 (52.3%)	70 (46.1%)	
glomerulonephritis	139 (23.0%)	23 (15.2%)	27 (17.9%)	36 (23.8%)	53 (34.9%)	
hypertension	61 (10.1%)	16 (10.6%)	20 (13.3%)	19 (12.6%)	6 (4.0%)	
polycystic kidney	12 (2.0%)	2 (1.3%)	6 (4.0%)	2 (1.3%)	2 (1.3%)	
urological	13 (2.1%)	3 (2.0%)	1 (0.7%)	4 (2.7%)	5 (3.3%)	
others	9 (1.5%)	4 (2.7%)	1 (0.7%)	3 (2.0%)	1 (0.7%)	
unknown	54 (8.9%)	11 (7.3%)	20 (13.3%)	8 (5.3%)	15 (9.9%)	
major comorbidities, no. of patients (%)						
diabetes	359 (59.3%)	104 (68.9%)	88 (58.3%)	90 (59.6%)	77 (50.7%)	.003
coronary heart disease	145 (24.0%)	45 (29.8%)	36 (23.8%)	40 (26.5%)	24 (15.8%)	.011
cerebrovascular disease	102 (16.9%)	37 (24.5%)	34 (22.5%)	19 (12.6%)	12 (7.9%)	.0001
Charlson's score	6.0 ± 2.6	7.3 ± 2.3	6.4 ± 2.3	5.9 ± 2.4	4.3 ± 2.3	.0001

Table 3: Baseline biochemical characteristics of cohort #2 according to MCrI quartile.

		MCrI quartile				
	All cases	I	II	III	IV	*P* value
no. of patients	605	151	151	151	152	
hemoglobin (g/dl)	9.7 ± 1.5	10.0 ± 1.4	9.8 ± 1.4	9.6 ± 1.4	9.4 ± 1.7	.002
albumin (g/l)	30.7 ± 2.9	29.0 ± 5.9	30.2 ± 5.7	32.0 ± 5.7	31.6 ± 6.0	.0001
total Kt/V	2.20 ± 0.67	2.56 ± 0.75	2.27 ± 0.59	2.15 ± 0.60	1.81 ± 0.50	.0001
residual GFR (ml/min/1.73 m^2)	4.34 ± 3.41	5.87 ± 3.18	4.58 ± 2.83	4.04 ± 2.47	2.90 ± 4.23	.0001
NPNA (g/kg/day)	1.15 ± 0.26	1.13 ± 0.26	1.14 ± 0.28	1.16 ± 0.24	1.15 ± 0.25	.699
FEBM (kg)	38.1 ± 10.5	31.1 ± 6.2	35.3 ± 6.9	38.1 ± 7.4	47.8 ± 12.2	.0001
bioimpedenace parameters						
overhydration (l)	4.3 ± 3.3	4.0 ± 2.4	3.9 ± 2.7	4.0 ± 3.1	5.4 ± 4.4	.0001
E:I ratio	1.03 ± 1.75	1.07 ± 0.15	1.02 ± 0.17	1.01 ± 0.17	1.00 ± 0.20	.002
LTM (kg)	39.0 ± 10.5	34.8 ± 8.3	38.0 ± 9.7	39.3 ± 10.1	44.1 ± 11.5	.0001
ATM (kg)	20.6 ± 11.3	21.8 ± 10.6	20.7 ± 10.1	20.2 ± 8.8	19.5 ± 14.7	.337

E:I ratio, extracellular to intracellular fluid volume ratio. Data were compared by one-way ANOVA.

most dialysis centers nor a necessary one in the guidelines on PD adequacy [31, 32].

Although the values of MCrI calculated for PD and HD may have considerable differences, we showed that they had excellent correlations with skeletal muscle mass as determined by both traditional creatinine kinetics and multifrequency bioimpedance spectroscopy. In fact, the MCrI calculated in PD patients had consistently better correlation with skeletal muscle mass compared to the values computed in HD (see Supplementary Table S1). Since our study consists of two cohorts (one prevalent and another incident PD patients) and two methods for the validation of skeletal muscle mass, our result seems to be robust. However, we did not measure muscle strength (for example, by muscle endurance tests or exercise capacity [33]), and it probably represents an intrinsic problem of using MCrI, which estimates muscle mass, for the identification of sarcopenia, which also encompasses functional problems of skeletal muscle [4, 34]. As a result, we also did not attempt to define a cutoff MCrI value in this study for the diagnosis of sarcopenia, which will require further studies.

In this study, we showed that baseline MCrI was associated with 1-year incidence of death by competing risk analysis, but

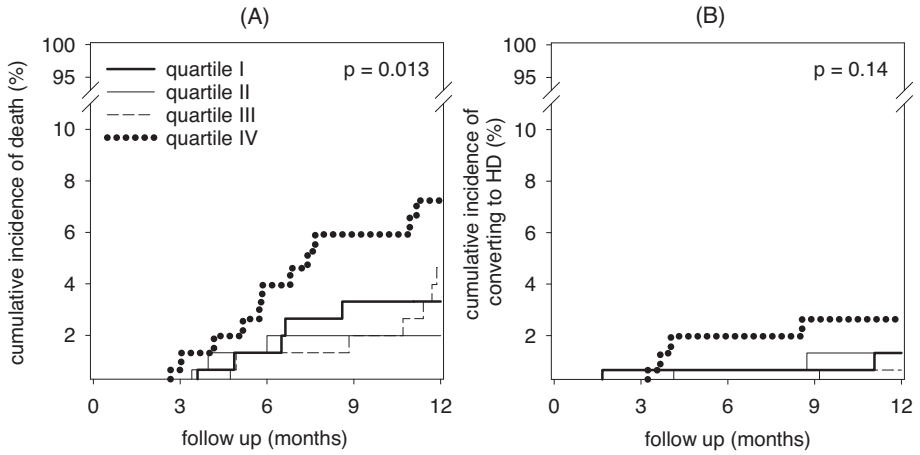

Figure 3: Cumulative incidence curves for the risk of (**a**) death from all cause; and (**b**) conversion to chronic HD of cohort #2, according to the MCrI quartile. Data were compared by Gray's test for equality of cumulative incidence functions across groups. See the Methods section for the definition of competing events.

not the risk of transfer to long-term HD or the number or duration of hospitalization, in incident PD patients. Contrary to the general expectation and previous studies in chronic HD patients [21, 35], we found that patients with the highest MCrI quartile (i.e. those with a higher muscle mass) might have a higher risk of death and conversion to HD in 1 year. The apparent harmful effect of higher MCrI seemed counter-intuitive, and the reason of this observation is not clear. It was possible that patients with very high MCrI might be in a catabolic state (increased muscle breakdown as opposed to synthesis, resulting in "falsely" increased serum creatinine level), or that a large body build or the concomitant obesity was associated with adverse clinical outcomes [36, 37]. Although it was possible that this group of patients with large body weight (i.e. a higher urea distribution volume) are more prone to underdialysis, if that was the case then a similar trend would have been observed in previous HD cohorts. Because of the limited duration of observation and small number of events, we did not perform multi-variable analysis to determine whether MCrI was an independent predictor of patient or technique survival, or to distinguish the specific causes of hospitalization (i.e. cardiovascular, infection, or other causes). Notably, further studies are necessary to determine whether MCrI is a superior short-term prognostic indicator as compared to other parameters of muscle mass (i.e. FEBM by creatinine kinetics, or LTM by bioimpedance spectroscopy).

There are other limitations of our present study. First, it is a single center study on Chinese PD patients, and the external validity of our result needs to be confirmed. Second, MCrI-PD was only measured once. Further studies are required to determine whether serial MCrI measurement can detect the change in skeletal muscle mass, and whether MCrI is suitable for serial monitoring. Moreover, patients were followed for only 12 months in the second cohort of this study, and an extended period of observation would be required to determine the long-term prognostic value of MCrI in PD, the relation between MCrI and subsequent risk of cardiovascular events and infection, as well as the prognostic role of MCrI as a time-dependent parameter (i.e. the prognostic value of serial monitoring). Intuitively, we believe one single baseline MCrI measurement would not be a long-term prognostic indicator, but further studies would be needed to define the prognostic role of serial MCrI measurement.

In summary, our present study showed that in PD patients, MCrI computed by the Canaud's formula and total weekly Kt/V is a simple and reliable marker of skeletal muscle mass, and may serve as a short-term prognostic indicator.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

Research idea and study design: J.K.C.N., C.C.S.; data acquisition: J.K.C.N., W.W.S.F., G.C.S.C., P.M.S.C., W.F.P.; data analysis/interpretation: J.K.C.N., C.C.S.; statistical analysis: J.K.C.N., C.C.S.; supervision or mentorship: K.M.C., C.C.S.; manuscript preparation: J.K.C.N., C.C.S. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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