Creatinine/(cystatin C × body weight) ratio is associated with skeletal muscle mass index

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Abstract. We have previously reported that the creatinine (Cre) to cystatin C (CysC) ratio is associated with height-adjusted skeletal muscle mass index (SMI). However, weight-adjusted SMI is reported to be a more useful marker of insulin sensitivity than height-adjusted SMI. Thus, we hypothesized that the creatinine to (cystatin C × body weight [BW]) relationship (Cre/[CysC × BW]) might be associated with weight-adjusted SMI. In this cross-sectional study of 169 males and 132 females, a body composition analyzer was used and the weight-adjusted SMI was calculated as (absolute muscle mass [kg]/BW [kg]) × 100. The cut-off of low muscle mass was defined as weight-adjusted SMI <37.0% for males and <28.0% for females. The Cre/(CysC × BW) was correlated with weight-adjusted SMI in both males ($r = 0.484$, $p < 0.001$) and females ($r = 0.538$, $p < 0.001$). In addition, Cre/(CysC × BW) was associated with weight-adjusted SMI in both males ($standardized \beta = 0.493$, $p < 0.001$) and females ($standardized \beta = 0.570$, $p < 0.001$) after adjusting for covariates. According to the receiver operator characteristic (ROC) curve analysis, the optimal cut-off point of Cre/(CysC × BW) for low muscle mass was 0.0145 (area under the ROC curve [AUC] 0.756 [95% confidence interval {95% CI} 0.644–0.842], sensitivity = 0.96, specificity = 0.47, $p < 0.001$) in males and 0.0090 (AUC 0.976 [95% CI 0.894–0.995], sensitivity = 1.00, specificity = 0.93, $p < 0.001$) in females. There is a correlation between Cre/(CysC × BW) and weight-adjusted SMI. The Cre/(CysC × BW) could be a practical screening marker for low muscle mass.

Key words: Creatinine, Insulin sensitivity, Insulin resistance, Skeletal muscle mass, Sarcopenia

SARCOPENIA is becoming an important treatment target in elderly patients with type 2 diabetes because of the increasing number of elderly patients with diabetes [1]. Sarcopenia, the age-associated loss of muscle mass and function, is associated with a risk of cardiovascular disease (CVD) [2, 3], pneumonia [4], and mortality [5, 6]. Sarcopenia is usually defined using height-adjusted skeletal muscle mass index (SMI), defined as the height-adjusted appendicular skeletal muscle mass and handgrip strength [7].

Alternatively, weight-adjusted SMI, defined as the weight-adjusted absolute muscle mass, is reported as a risk factor of type 2 diabetes [8]. Low weight-adjusted SMI is also reported to be a risk factor for non-alcoholic

fatty liver disease (NAFLD) [9-12] and nonalcoholic steatohepatitis (NASH) [13-15]. In addition, it has been reported that weight-adjusted SMI is associated with insulin sensitivity [16]. These results indicated that height-adjusted SMI could indicate absolute muscle loss, whereas weight-adjusted SMI could indicate relative muscle loss. Thus, the proportion of muscle mass per body weight has an important meaning in a clinical practice of patients with diabetes.

Serum creatinine (Cre), a known as a marker of renal function, is affected by skeletal muscle mass, because Cre is produced in skeletal muscle and is closely associated with the total skeletal muscle mass [17, 18]. In contrast, cystatin C (CysC), which is not influenced by the skeletal muscle mass, is recommended to estimate renal function [19]. We previously reported that the Cre to CysC ratio (Cre/CysC) is associated with height-adjusted SMI [20]. Therefore, we hypothesized that the Cre to body weight (BW) ratio (Cre/BW) or Cre to (CysC × BW) ratio (Cre/[CysC × BW]) would be associated with weight-adjusted SMI. The purpose of this cross-sectional

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study was to investigate the association between Cre/BW and Cre/(CysC $\times$ BW), and weight-adjusted SMI. Moreover, we also investigated the cut-off points of Cre/BW and Cre/(CysC $\times$ BW) for low muscle mass.

Materials and Methods

Study patients

The Kamogawa-DM cohort study is an ongoing prospective cohort study, which started in 2014 [21]. Approval for the study was obtained from the Ethical Committee of the Kyoto Prefectural University of Medicine (No. RBMR-E-466-6). After obtaining written informed consent, personal identifiable information was masked, and the medical data of the individuals were stored in a database. None of the patients had a history of limb amputation. For this present study, we extracted the data of the patients with type 2 diabetes [22] who underwent a multifrequency impedance body composition analyzer (InBody 720; InBody Co, Ltd., Seoul, ROK) evaluation and had CysC data. The exclusion criteria were as follows: 1) no overnight fasting data and 2) serum creatinine >1.2 mg/dL for males and >1.0 mg/dL for females, suggestive of renal dysfunction [23].

Data collection and measurements

Using the multifrequency impedance body composition analyzer, the data of BW (kg), appendicular muscle mass (kg), absolute muscle mass (kg), and body fat mass (kg) were obtained. The body mass index (BMI) was calculated as follows: BMI (in kg/m²) = (BW in kg)/(height in m²). The height-adjusted SMI was calculated as follows: height-adjusted SMI = (appendicular muscle mass in kg)/(height in m²) [7]. The weight-adjusted SMI was calculated as follows: weight-adjusted SMI = ([absolute muscle mass in kg]/[BW in kg]) $\times$ 100 [12]. The cut-off of low muscle mass was defined as a weight-adjusted SMI $<37.0\%$ for males and $<28.0\%$ for females [12].

Using a standardized self-administered questionnaire, smoking status and physical activity data were obtained. Smoking status was indicated as current smoker or not.

After overnight fasting, serum and plasma samples were obtained. Serum Cre levels were assessed using standard enzymatic methods. Serum CysC levels were measured using a latex agglutination turbidimetric immunoassay at the Ikagaku Laboratory (Kyoto, Japan). We calculated Cre/BW as the Cre value divided by the BW value and Cre/(CysC $\times$ BW) as the Cre value divided by the (CysC $\times$ BW) value. C-peptide was also measured and C-peptide immunoreactivity insulin resistance (CPR-IR) = $20/(\text{fasting C-peptide immunoreactivity (CPR)} \times \text{fasting plasma glucose})$ was calculated for insulin sensitivity [24].

Statistical analysis

The statistical analyses were carried out using JMP version 13.0 software (SAS Institute Inc., Cary, NC USA). We set the level of significance to any p value <0.05 .

Median (interquartile range) were used for continuous variables and numbers (percentages) were used for categorized variables. Because weight-adjusted SMI differed by sex, we evaluated males and females separately. The differences between sexes were evaluated by Mann-Whitney U or chi-squared test. We investigated the association between Cre, CysC, Cre/BW, Cre/CysC, Cre/(CysC $\times$ BW) and BW and weight-adjusted SMI using Spearman rank correlation coefficient. We also investigated the association between Cre/CysC, Cre/(CysC $\times$ BW) and weight-adjusted SMI, and CPR-IR using Spearman rank correlation coefficient. Then, we performed multiple regression analysis of Cre/(CysC $\times$ BW) on weight-adjusted SMI adjusting for age, smoking, exercise, duration of diabetes and insulin usage. Furthermore, we performed a receiver operator characteristic (ROC) curve analysis to calculate the area under the ROC curve (AUC) of Cre/BW and Cre/(CysC $\times$ BW) for low muscle mass. Optimal cut-off point was evaluated by Youden index.

Results

In this study, we included 199 males and 144 females. Among them, 21 males and 6 females were excluded for renal dysfunction and 9 males and 6 females were excluded as their records lacked overnight fasting data. Thus, 169 males and 132 females were selected for this study.

The baseline characteristics of the study participants are shown in Table 1. The median age was 68 (61–73) years old in males and 69 (63–74) years old in females. The weight-adjusted SMI data (41.0 [38.7–43.8] % in males and 35.0 [33.0–37.3] % in females, $p < 0.001$), height-adjusted SMI data (7.5 [7.0–8.1] kg/m² in males and 6.1 [5.6–6.7] kg/m² in females, $p < 0.001$) and Cre/CysC data (0.91 [0.79–1.07] in males and 0.76 [0.66–0.87] in females, $p < 0.001$) differed by sex. The proportion of low muscle mass was 14.8% in males and 3.1% in females.

Table 2, Fig. 1 and Fig. 2 show the correlation between Cre, CysC, Cre/BW, Cre/CysC, Cre/(CysC $\times$ BW) and BW and weight-adjusted SMI. Cre/BW ($r = 0.378$, $p < 0.001$ in males and $r = 0.505$, $p < 0.001$ in females), Cre/(CysC $\times$ BW) ($r = 0.484$, $p < 0.001$ in males and $r = 0.538$, $p < 0.001$ in females) and BW ($r = -0.508$, $p < 0.001$ in males and $r = -0.645$, $p < 0.001$ in females) were positively associated with weight-adjusted

Table 1 Clinical characteristics of study patients

	Total <i>n</i> = 301	Males <i>n</i> = 169	Females <i>n</i> = 132	<i>p</i>
Age (year)	68 (62.5–73.5)	68 (61–73)	69 (63–74)	0.223
Duration of diabetes (year)	12 (5–19)	13 (6–20)	12 (4–18)	0.244
Height (cm)	161 (154–169)	167.8 (163–172)	153 (150–156.7)	<0.001
Body weight (kg)	66 (57–78.8)	73.2 (64–85.1)	59 (52–68.1)	<0.001
Body mass index (kg/m ²)	23.5 (21.2–26.5)	23.8 (21.4–26.8)	23.3 (21.1–26.5)	0.347
Appendicular muscle mass (kg)	18.4 (14.4–22.0)	21.4 (19.2–23.4)	14.3 (12.7–16.1)	<0.001
Absolute muscle mass (kg)	24 (19.6–28.2)	27.6 (24.7–30.7)	19.3 (17.4–21.1)	<0.001
Height-adjusted SMI (kg/m ²)	7.0 (6.1–7.7)	7.5 (7.0–8.1)	6.1 (5.6–6.7)	<0.001
Weight-adjusted SMI (%)	29.0 (25.9–31.9)	41.0 (38.7–43.8)	35.0 (33.0–37.3)	<0.001
Handgrip strength (kg)	27.1 (20.9–36)	34.9 (28.6–40)	20.1 (17.5–24.5)	<0.001
Hemoglobin A1c (%)	7.0 (6.6–7.5)	7.2 (6.5–7.6)	6.9 (6.6–7.4)	0.161
Hemoglobin A1c (mmol/mol)	53.0 (48.6–58.5)	55.2 (47.5–59.6)	51.9 (48.6–57.4)	0.161
Fasting plasma glucose (mmol/L)	7.7 (6.6–9.1)	7.9 (6.8–9.5)	7.4 (6.3–8.7)	0.002
C-peptide (ng/mL)	1.6 (1.1–2.4)	1.7 (1.0–2.6)	1.6 (1.1–2.3)	0.424
CPR-IR	0.09 (0.06–0.13)	0.08 (0.05–0.13)	0.10 (0.06–0.14)	0.069
Creatinine (mg/dL)	0.74 (0.62–0.88)	0.83 (0.73–0.99)	0.63 (0.54–0.72)	<0.001
Cystatin C (mg/dL)	0.87 (0.77–1.03)	0.89 (0.81–1.06)	0.83 (0.74–0.97)	<0.001
Cre/CysC ratio	0.84 (0.73–1.01)	0.91 (0.79–1.07)	0.76 (0.66–0.87)	<0.001
Cre/BW ratio	0.012 (0.010–0.014)	0.012 (0.010–0.015)	0.012 (0.010–0.014)	0.005
Cre/(CysC × BW)	0.014 (0.012–0.016)	0.013 (0.012–0.016)	0.014 (0.011–0.017)	0.694
Exercise	126 (41.9%)	61 (36.1%)	65 (49.2%)	0.022
Current smoker	61 (20.3%)	41 (24.3%)	20 (15.2%)	<0.001
Insulin usage	70 (23.3%)	40 (23.7%)	30 (22.7%)	0.905
Insulin secretagogues usage	218 (72.4%)	120 (71.0%)	98 (74.2%)	0.533
Insulin sensitizers usage	131 (43.5%)	70 (41.4%)	61 (46.2%)	0.405
Nutrient load reducers usage	92 (30.6%)	50 (29.6%)	42 (31.8%)	0.677

BW, body weight; CPR-IR, C-peptide immunoreactivity insulin resistance; Cre, Creatinine; Cre/CysC, Creatinine to cystatin C; Cre/BW, Creatinine to body weight; Cre/(CysC × BW), Creatinine to (cystatin C × body weight); CysC, Cystatin C; SMI, skeletal muscle mass index. Height-adjusted SMI = appendicular muscle mass (kg)/height² (m²). Weight-adjusted SMI = absolute muscle mass (kg)/BW (kg) × 100. Insulin secretagogues included sulfonylureas, glinides, dipeptidyl peptidase-4 inhibitors and glucagon-like peptide-1 receptor agonist; insulin sensitizers included pioglitazone and metformin; and nutrient load reducers included α-glucosidase inhibitors and sodium-glucose cotransporter inhibitor.

Data are expressed as median (interquartile range) or number (percentage). The difference between groups was analyzed by Mann-Whitney *U* test or Chi-square test.

SMI in both males and females.

In addition, weight-adjusted SMI were associated with CPR-IR in both males and females (males, $r = 0.12$, $p = 0.131$ and females, $r = 0.30$, $p < 0.001$) and Cre/(CysC × BW) were associated with CPR-IR in females ($r = 0.30$, $p < 0.001$). In addition, Cre/(CysC × BW) were tended to be associated with CPR-IR in males, although it did not reach statistical significant ($r = 0.12$, $p = 0.131$). On the other hand, Cre/CysC was not associated with insulin

sensitivity (males, $r = -0.13$, $p = 0.081$ and females, $r = 0.16$, $p = 0.074$).

Multiple regression analysis shows the association between Cre/(CysC × BW) and weight-adjusted SMI (*standardized* $\beta = 0.493$, $p < 0.001$ in males and *standardized* $\beta = 0.570$, $p < 0.001$) (Table 3).

In this study, 25 males (14.8%) and 4 females (3.1%) were defined as low muscle mass. According to the ROC analysis, the optimal cut-off points of Cre/BW and Cre/

Table 2 Correlation between Cre, CysC, Cre/BW, Cre/CysC or Cre/(CysC $\times$ BW) and weight-adjusted SMI

Males	<i>r</i>	<i>p</i>
Cre	0.005	0.953
CysC	−0.104	0.179
Cre/CysC	0.070	0.365
Cre/BW	0.378	<0.001
Cre/(CysC $\times$ BW)	0.484	<0.001
BW	−0.508	<0.001
Females	<i>r</i>	<i>p</i>
Cre	0.077	0.387
CysC	−0.039	0.658
Cre/CysC	0.129	0.143
Cre/BW	0.505	<0.001
Cre/(CysC $\times$ BW)	0.538	<0.001
BW	−0.645	<0.001

BW, body weight; Cre, Creatinine; Cre/CysC, Creatinine to cystatin C; Cre/BW, Creatinine to body weight; Cre/(CysC $\times$ BW), Creatinine to (cystatin C $\times$ body weight); CysC, Cystatin C; SMI, skeletal muscle mass index. Weight-adjusted SMI = absolute muscle mass (kg)/BW (kg) $\times$ 100. Spearman rank correlation coefficient was used to evaluate the correlation.

(CysC $\times$ BW) for low muscle mass were 0.0126 (AUC 0.658 [95% CI 0.556–0.748], sensitivity = 0.84, specificity = 0.53, p = 0.007) and 0.0145 (AUC 0.756 [95% CI 0.644–0.842], sensitivity = 0.96, specificity = 0.47, p < 0.001), respectively, in males and 0.0087 (AUC 0.952 [95% CI 0.816–0.989], sensitivity = 1.00, specificity = 0.86, p < 0.001) and 0.0090 (AUC 0.976 [95% CI 0.894–0.995], sensitivity = 1.00, specificity = 0.93, p < 0.001), respectively, in females (Fig. 3).

Discussion

In this study, we investigated the correlation between Cre/BW and Cre/(CysC $\times$ BW) and weight-adjusted SMI in both sexes. Furthermore, the Cre/(CysC $\times$ BW) of 0.0145 in males and 0.0090 in females are the cut-off points for low muscle mass.

It is well known that height-adjusted SMI is an important marker for sarcopenia [7]. We previously revealed that Cre/CysC is associated with height-adjusted SMI [20]. However, heavier weight leads to muscle mass increasing, regardless of fat mass [9]. Thus, the proportion of muscle mass to body weight is important. Body weight is correlated with weight-adjusted SMI (males, r = −0.508, p < 0.001 and females, r = −0.645, p < 0.001). However, we showed that Cre/(CysC $\times$ BW) is associ-

ated with weight-adjusted SMI even adjusting for BMI. Decreasing weight-adjusted SMI could indicate relative increasing of visceral fat and relative decreasing of muscle mass. Thus, height-adjusted SMI could indicate absolute muscle loss, whereas weight-adjusted SMI could indicate relative muscle loss. Previous studies revealed that not height-adjusted SMI but weight-adjusted SMI was associated with insulin resistance [8, 25–27]. In fact, weight-adjusted SMI is reported to be associated with incident diabetes [8], incident metabolic syndrome [28] and progression of NAFLD [29]. In this study, we used absolute muscle mass as numerator of formula of weight-adjusted SMI. However, several studies reported that appendicular muscle mass was also used as numerator of formula of weight-adjusted SMI. There is a strong correlation between using absolute muscle mass as numerator of formula of weight-adjusted SMI and using appendicular muscle mass as numerator (males, r = 0.93, p < 0.001 and females, r = 0.86, p < 0.001 by Spearman rank correlation coefficient). Thus, there was no difference to use absolute muscle mass or appendicular muscle mass as numerator. These results demonstrated that we should focus not on height-adjusted SMI but weight-adjusted SMI in the clinical setting of metabolic related disease, such as diabetes and NAFLD.

In this study, 24 patients were sarcopenia, using by height-adjusted SMI and handgrip strength [20]. Among them, only 2 patients were defined as low muscle mass. The possible examination why sarcopenia, which was defined by height-adjusted SMI, and low muscle mass, which was defined by weight-adjusted SMI, was not matched is that sarcopenia is based on absolute muscle loss and low muscle mass is based on relative muscle loss.

Moreover, we determined the cut-off levels of Cre/BW and Cre/(CysC $\times$ BW) for low muscle mass in both males and females. The Cre/(CysC $\times$ BW) is a good marker for low muscle mass especially when the patients gain weight due to an increase of fat mass, even though they lose muscle mass [12]. Thus, the patients with a Cre/(CysC $\times$ BW) under 0.0145 for males and 0.0090 for females are at risk of low muscle mass and further metabolic related disease.

The limitations of this study were as follows. First, this study is a cross-sectional study, so the causal relationship is unclear. Second, we did not use dual-energy X-ray absorptiometry, but rather a body composition analyzer for estimating muscle mass. However, the accuracy of the body composition analyzer was validated [30]. Third, many of the patients took medication for diabetes; thus, there is a possibility that the results of insulin sensitivity were not accurate. Fourth, whether cut-off of low muscle mass of a weight-adjusted SMI <37.0% for

Fig. 1 Correlation between Cre, Cre/CysC, Cre/BW, Cre/(CysC × BW) or BW and weight-adjusted SMI in males.

(a) Correlation between Cre and weight-adjusted SMI. (b) Correlation between Cre/CysC and weight-adjusted SMI. (c) Correlation between Cre/BW and weight-adjusted SMI. (d) Correlation between Cre/(CysC × BW) and weight-adjusted SMI. (e) Correlation between BW and weight-adjusted SMI.

BW, body weight; Cre, Creatinine; Cre/Cys, Creatinine to cystatin C; Cre/BW, Creatinine to body weight; Cre/(Cys × BW), Creatinine to (cystatin C × body weight); CysC, Cystatin C; SMI, skeletal muscle mass index. Weight-adjusted SMI = absolute muscle mass (kg)/BW (kg).

Vertical axis indicates Cre, Cre/CysC, Cre/BW, Cre/(CysC × BW) or BW and horizontal axis indicates weight-adjusted SMI.

males and <28.0% for females [12], which is based on the data of people with Western, is applicable to this study population is unclear. However, this cut-off was used for Korean people previously [12]. Lastly, this study included a Japanese population only, thus, the generalizability of our study to non-Japanese populations, especially non-Asian populations, is uncertain and further studies might be needed.

In conclusion, this study demonstrated the association between Cre/(CysC × BW) and weight-adjusted SMI and that a Cre/(CysC × BW) under 0.0145 for males and 0.0090 for females is associated with low muscle mass. These results suggest that Cre/(CysC × BW) might be a novel marker for low muscle mass.

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Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Author Contributions

K.N. designed the study, analyzed and interpretation data and wrote manuscript. Y.H. designed the study, researched, analyzed and interpretation data and reviewed/edited manuscript. A.Y. and R.S. researched and interpretation data and contributed to discussion. T.Ok., N.K. and T.Os. researched data and contributed to discussion. M.H. and M.F. designed the study, interpretation data, and reviewed/edited manuscript. All authors approved the final version of the manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Fig. 2 Correlation between Cre, Cre/CysC, Cre/BW or Cre/(CysC $\times$ BW) and weight-adjusted SMI in females.

(a) Correlation between Cre and weight-adjusted SMI. (b) Correlation between Cre/CysC and weight-adjusted SMI. (c) Correlation between Cre/BW and weight-adjusted SMI. (d) Correlation between Cre/(CysC $\times$ BW) and weight-adjusted SMI. (e) Correlation between BW and weight-adjusted SMI.

BW, body weight; Cre, Creatinine; Cre/Cys, Creatinine to cystatin C; Cre/BW, Creatinine to body weight; Cre/(Cys $\times$ BW), Creatinine to (cystatin C $\times$ body weight); CysC, Cystatin C; SMI, skeletal muscle mass index. Weight-adjusted SMI = absolute muscle mass (kg)/BW (kg).

Vertical axis indicates Cre, Cre/CysC, Cre/BW, Cre/(CysC $\times$ BW) or BW and horizontal axis indicates weight-adjusted SMI.

Table 3 Multiple regression analysis of Cre/(CysC $\times$ BW) on weight-adjusted SMI

	Males		Females	
	Standardized β	<i>p</i>	Standardized β	<i>p</i>
Age	-0.159	0.024	0.070	0.354
Smoking	0.153	0.020	0.085	0.244
Exerciser	0.005	0.935	0.047	0.514
Duration of diabetes	0.286	<0.001	0.241	0.002
Insulin usage	0.005	0.940	0.037	0.612
Cre/(CysC $\times$ BW)	0.493	<0.001	0.570	<0.001

BW, body weight; Cre/(CysC $\times$ BW), Creatinine to (cystatin C $\times$ body weight). Weight-adjusted SMI = absolute muscle mass (kg)/BW (kg) $\times$ 100. Smoking status was defined as nonsmoker (0) or current smoker (1); exercise status was defined as non-exerciser (0) or exerciser (1); and insulin usage status was defined as non-user (0) or user (1).

R^2 = 0.34 in men and 0.40 in women.

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Fig. 3 Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of Cre/BW or Cre/(CysC $\times$ BW) for low muscle mass.

BW, body weight; Cre, Creatinine; Cre/(CysC $\times$ BW), Creatinine to (cystatin C $\times$ body weight); CysC, Cystatin C; Cre/BW, Creatinine to body weight; SMI, skeletal muscle mass index. Weight-adjusted SMI = absolute muscle mass (kg)/BW (kg). Low muscle mass was defined as weight-adjusted SMI $<37.0\%$ for males and $<28.0\%$ for females

(a) Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of Cre/BW for low muscle mass in males. The optimal cut-off point of the Cre/BW for low muscle mass was 0.0126 (AUC 0.658 (95% CI 0.556–0.748), sensitivity = 0.84, specificity = 0.53, $p = 0.007$).

(b) Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of Cre/(CysC $\times$ BW) for low muscle mass in males.

The optimal cut-off point of the Cre/(CysC $\times$ BW) for low muscle mass was 0.0145 (AUC 0.756 (95% CI 0.644–0.842), sensitivity = 0.96, specificity = 0.47, $p < 0.001$).

(c) Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of Cre/BW for low muscle mass in females.

The optimal cut-off point of the Cre/BW for low muscle mass was 0.0087 (AUC 0.952 (95% CI 0.816–0.989), sensitivity = 1.00, specificity = 0.86, $p < 0.001$).

(d) Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of Cre/(CysC $\times$ BW) for low muscle mass in females.

The optimal cut-off point of the Cre/(CysC $\times$ BW) for low muscle mass was 0.0090 (AUC 0.976 (95% CI 0.894–0.995), sensitivity = 1.00, specificity = 0.93, $p < 0.001$).

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