Original Article

Assessment of muscle mass and its association with protein intake in a multi-ethnic Asian population: relevance in chronic kidney disease

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Background: Clinical practice guidelines recommend objective nutritional assessments in managing chronic kidney disease (CKD) patients but were developed while referencing to a North-American population. Specific recommendations for assessing muscle mass were suggested (mid-arm circumference, MAC; corrected mid-arm muscle area, cAMA; mid-arm muscle circumference, MAMC). This study aimed to assess correlation and association of these assessments with dietary protein intake in a multi-ethnic Asian population of healthy and CKD patients. **Methods**: We analyzed 24-hour urine collections of selected participants to estimate total protein intake (TPI; g/day). Ideal body weight (IDW; kg) was calculated and muscle assessments conducted. Analyses involved correlation and linear regression, taking significance at $p<0.05$. **Results**: There were 232 stable CKD patients and 103 healthy participants comprising of 51.0% male, 38.5% Chinese, 29.6% Malay, 23.6% Indian, and 8.4% others. The mean TPI was 58.9±18.4 g/day in healthy participants and 53.6±19.4 g/day in CKD patients. When normalized to ideal body weight, TPI-IDW (g/kg/day) was similar in healthy and CKD participants. Overall, TPI was associated with MAC (r=0.372, $p<0.001$), cAMA (r=0.337, $p<0.001$), and MAMC (r=0.351, $p<0.001$). TPI-IDW was also associated with MAC (r=0.304, $p<0.001$), cAMA (r=0.202, $p<0.001$), and MAMC (r=0.200, $p<0.001$) but not for TPI normalized to actual body weight. When examined separately, TPI was associated with MAC, cAMA, and MAMC in both CKD and healthy participants, but was associated with TPI-IDW only in CKD patients. **Conclusion**: Total protein intake was associated with muscle assessments in all participants. TPI normalized to IDW should only be used in CKD patients.

Key Words: Asian Continental Ancestry Group, protein, kidney failure, chronic diet, nutrition assessment

INTRODUCTION

Guidelines on the nutritional assessment of chronic kidney disease (CKD) patients have been promulgated by several organizations.[1-3] The objective nutritional assessments may include body mass index (BMI), percentage of standard body weight, mid-arm circumference (MAC), triceps skin-fold (TSF), mid-arm muscle area (AMA), corrected AMA (cAMA), and mid-arm muscle circumference (MAMC).[1,4-6] These measures however, referred to a North-American general population (U.S. NHANES-National Health and Nutrition Examination Survey-II data).[4-6] The measures in a CKD patient population are compared to a "normal" reference population (the US NHANES) data; suggesting that patients with values lower than the reference population may be at risk of protein-energy malnutrition and therefore, have a lower muscle mass. There are several assumptions which need to be satisfied before we can adopt these recommendations for assessing populations outside of the United States. First, the assessments of the "general" or "standard" population will be similar to the NHANES II reference population, especially for healthy people without kidney disease. Second, the measures have a strong correlation and association with daily protein intake. Third, if the "general" or "standard" population is not similar to the NHANES II reference population, then a reference standard population data needs to be established for the external population in question. It is therefore unclear how these measures compare in an Asian population as no reference tables for these assessments have been published. Correlation of dietary protein intake with these assessments of muscle mass is unknown.[7,8] In this cross-sectional study, (1) we assessed several of these anthropometry-based muscle mass assessments and their association with dietary protein intake, and (2) provided comparison tables of these

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Manuscript received 17 October 2013. Initial review completed 09 December 2013. Revision accepted 19 April 2014.
doi: 10.6133/apjcn.2014.23.4.01

assessments in a multi-ethnic Asian population of healthy and stable chronic kidney disease participants.

METHODS

This is a sub-study of data from the Singapore Kidney Function Study Phase 1 (SKFS1; D/2007/524) and the Asian Kidney Disease Study (AKDS; D/2007/00225), approved by the institution review board.[9]

Participants

In SKFS1, we recruited 103 healthy volunteers presenting to the National University Hospital, Singapore. The inclusion criterion was non-pregnant adults (>21 years). Volunteers were excluded if they had any of the following: inability to consent, physical conditions that render phlebotomy for blood samples difficult, inability to collect urine samples successfully, use of regular medications, hypertension, diabetes, possible kidney dysfunction (by urinalysis, or on renal imaging), and any condition that potentially interferes with the accuracy of the measurement of GFR. Volunteers were screened with urine dipsticks for hematuria, leukocyturia, proteinuria, and microalbuminuria. The target sample size was 3 male and 3 female volunteers per decade from age 21 years per ethnic group (Chinese, Malay, Indian and others).

In AKDS, we recruited 232 patients with CKD presenting to the outpatient nephrology clinics in the National University Hospital, Singapore. The inclusion criteria were non-pregnant adult (>21 years), serum creatinine with an estimated or measured GFR (MDRD, Cockroft-Gault 10 or creatinine clearance) of 10 mL/min to 90 mL/min, "stable CKD" defined as two sets of serum creatinine measured >60 days apart of less than 20% difference, and the definition of CKD that followed the clinical practice guidelines.[11] Patients were excluded if they had any of the following: inability to consent, physical conditions that render phlebotomy for blood samples difficult, inability to collect urine samples successfully, acute kidney function deterioration, or any condition that potentially interferes with the accuracy of the measurement of GFR.

Laboratory tests

All participants performed a 24-urine collection and presented the following day for GFR measurement, anthropometric measurements (height, weight, waist-hip circumference, blood pressure, triceps skin-fold) and provision of blood and urine samples. GFR was determined by 3-sample plasma clearance of an intravenous bolus of 99mTc-DTPA.[12] Body surface area was calculated using the du Bois equation.[13] Urine urea nitrogen (g/day) was measured in the 24-hour urine collections to estimate dietary protein intake using the following formulae: total protein intake (g/day) = 6.25 × urine urea nitrogen + 30 × weight (in kg).

Nutritional assessments

Using the measured parameters, dietary protein intake, ideal body weight, and measures of muscle mass were estimated using the following formulae:

Total protein intake (TPI, g/day) = 6.25 × urine urea nitrogen + 30 × weight (in kg)

Ideal body weight: weight (kg) = 22.99 × height^2 (m).[14]

Measures of muscle mass 1:

MAMC (cm) = MAC (cm) - (π × TSF)

cAMA (cm²) in men = $[(MAC - \pi \times TSF)^2/4\pi] - 10$

cAMA (cm²) in women = $[(MAC - \pi \times TSF)^2/4\pi] - 6.5$

Statistics

We expressed total protein intake per actual body weight and per ideal body weight for comparisons. Data were presented as mean±SD, or median and inter-quartile range depending on distribution. Standard statistical tests including t-test, ANOVA, chi-square test, Pearson correlation, and linear regression were used where appropriate. We tested the measures of muscle assessment MAC, cAMA, and MAMC against TPI, TPI per ideal body weight (TPI-IDW), and TPI per actual body weight (TPI-ABW) by considering all data as a whole, and separate datasets of healthy and CKD participants. Pearson's r denotes the strength of the correlation and linear regression quantifies this relationship. Significance was taken at the 5% level. Non-significant *p*-values are reported as NS. Analyses were performed on JMP 10 (Cary, NC, USA).

RESULTS

There were 335 participants (Table 1). Using a body mass index (BMI) of 23.0 as the normal upper limit in Asians, healthy participants were on average 5.0±10.4 kg overweight, and CKD patients were 11.8±13.6 kg overweight. CKD patients were older (58.4±12.8 vs 42.5±14.3 years; $p<0.001$), shorter (1.59±0.09 vs 1.62±0.10 m; $p=0.008$), weighed more (70.3±15.9 vs 65.7±12.8 kg; $p=0.010$), and had higher BMI (27.6±5.45 vs 24.9±4.03 kg/m^2; $p<0.001$); but average BSA was similar to healthy participants. In CKD, the average GFR was about half that of healthy participants (52±27 vs 101±16 mL/min/1.73 m^2; $p<0.001$). They also had a lower TPI (53.6±19.4 vs 58.9±18.4 g/day; $p=0.021$) which is associated with a lower serum albumin (41.8±3.2 vs 43.5±2.6 g/L; $p<0.001$). However, TPI normalized to ideal body weight (TPI-IDW) was similar between CKD patients and controls (0.91±0.30 vs 0.97±0.28 g/kg/day; $p=0.102$).

Muscle mass

The distribution of mid-arm circumference (MAC), triceps skin-fold (TSF), corrected AMA (cAMA), and mid-arm muscle circumference (MAMC) is shown in Table 2. Overall, in all participants, the TPI (g/day) was correlated with muscle mass assessments (Figure 1), MAC (r=0.372, $p<0.001$), cAMA (r=0.337, $p<0.001$), and MAMC (r=0.351, $p<0.001$). Using linear regression, TPI was associated with MAC (25.7+0.078×TPI; $p<0.001$), cAMA (19.1+0.207×TPI; $p<0.001$), and MAMC (18.1+0.067× TPI; $p<0.001$).

The TPI-IDW (g/kg/day) for all participants also correlated with muscle mass assessments: MAC (r=0.304, $p<0.001$), MAMC (r=0.200, $p<0.001$), and cAMA (r=0.202, $p<0.001$). By linear regression, TPI-IDW was associated with MAC (26.1+4.15×TPI; $p<0.001$), cAMA (23.03+8.13×TPI; $p<0.001$), and MAMC (19.5+2.48× TPI; $p<0.001$). No significant associations were seen when TPI was normalized using actual body weight.

When healthy and CKD participants were examined

Table 1. Characteristics of participants

	All (n=335)	SKFS1[†] (n=103)	AKDS[‡] (n=232)	*p*-value[*]
Age (years)	53.5±15.1	42.5±14.3	58.4±12.8	<0.001
Men (n, %)	171 (51.0)	51 (49.5)	120 (51.0)	NS
Ethnicity (n, %)				<0.001
Chinese	129 (38.5)	35 (34.0)	94 (40.5)	
Malay	99 (29.6)	25 (24.3)	74 (31.9)	
Indian	79 (23.6)	23 (22.3)	56 (24.1)	
Others	28 (8.4)	20 (19.4)	8 (3.5)	
Smokers (n, %)	68 (20.4)	22 (21.4)	46 (20.0)	NS
Diabetes (n, %)	119 (35.5)	0	119 (51.3)	<0.001
Hypertension (n, %)	192 (57.3)	0	192 (82.8)	<0.001
Height (m)	1.60±0.09	1.62±0.10	1.59±0.09	0.008
Weight (kg)	68.9±15.1	65.7±12.8	70.3±15.9	0.010
Body mass index (kg/m^2)	26.8±5.21	24.9±4.03	27.6±5.45	<0.001
Body surface area (m^2)	1.72±0.21	1.70±0.20	1.73±0.01	NS
Ideal body weight (kg)	59.2±7.0	60.7±7.2	58.5±6.7	0.008
Measured glomerular filtration rate (mL/min/1.73 m^2)	67±33	101±16	52±27	<0.001
Serum creatinine (μmol/L)	127±86	70±16	153±92	<0.001
Serum albumin (g/L)	42.3±3.1	43.5±2.6	41.8±3.2	<0.001
24-hr urine urea nitrogen (g/day)	6.77±2.91	7.45±2.80	6.47±2.92	0.004
Total protein intake (g/day)	55.3±19.2	58.9±18.4	53.6±19.4	0.021
Protein intake/ideal body weight (g/kg/day)	0.93±0.29	0.97±0.28	0.91±0.30	0.102
Mid-arm circumference (cm)	30.0±4.03	29.5±3.74	30.2±4.15	NS
Triceps skinfold thickness (cm)	2.61±1.04	2.60±1.05	2.62±1.04	NS
Mid-arm muscle circumference (cm)	21.8±3.67	21.4±3.64	22.0±3.68	NS
Corrected arm muscle area (cm^2)	30.6±11.8	29.1±11.3	31.2±12.1	NS

[†]SKFS1: Singapore Kidney Function Study; [‡]AKDS: Asian Kidney Disease Study; [*]NS: non-significant.

Table 2. Nutritional assessments by age

Measures[†]	Age (years)								*p*-value[*]
	Study[‡]	20-30	30-40	40-50	50-60	60-70	70-80	80-90	
MAC	SKFS1	28.5±3.2	30.3±4.5	29.8±3.2	30.5±4.1	28.9±2.4	27.1±4.8	-	NS
(cm)	AKDS	29.1±6.4	29.5±4.3	31.9±4.7	30.9±3.3	30.4±4.2	28.6±4.1	25.8±2.5	0.005
TSF	SKFS1	2.5±1.1	2.6±1.2	2.4±0.7	3.0±1.3	2.8±0.9	1.6±0.4	-	NS
(cm)	AKDS	2.6±0.8	3.0±0.9	2.7±0.9	2.8±1.1	2.6±1.1	2.3±1.0	1.6±0.4	NS
cAMA	SKFS1	26.9±10.8	32.5±14.6	32.0±10.7	28.5±9.4	24.7±5.8	21.7±9.6	-	NS
(cm^2)	AKDS	28.4±12.8	25.6±7.9	37.5±16.9	31.9±11.2	31.5±11.5	28.8±10.8	24.9±6.7	0.031
MAMC	SKFS1	20.7±3.8	22.2±4.4	22.3±3.4	21.3±3.3	20.2±2.0	19.3±3.4	-	NS
(cm)	AKDS	20.9±4.3	20.2±2.7	23.5±4.8	22.2±3.6	22.2±3.4	21.3±3.5	20.9±2.0	NS

[†]MAC: mid-arm circumference; TSF: triceps skinfold; cAMA: corrected mid-arm muscle area; MAMC: mid-arm muscle circumference.
[‡]SKFS: Singapore Kidney Function Study; AKDS: Asian Kidney Disease Study. [*] NS: non-significant.

separately, TPI was associated with MAC, cAMA, and MAMC in both groups. However, TPI-IDW was significantly associated with these measures only in CKD patients. (Table 3)

DISCUSSION

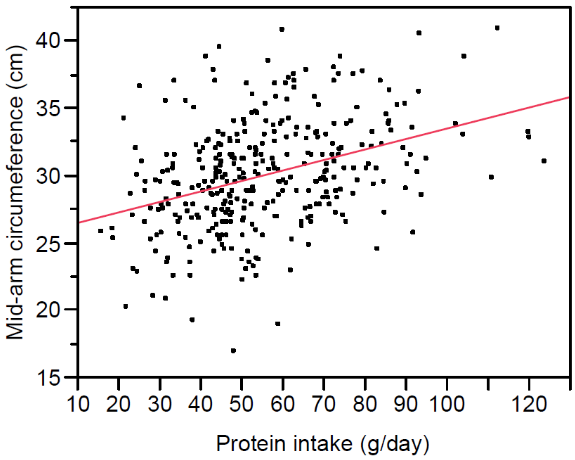
The estimation of daily protein intake from urine collections is a cumbersome process and not feasible in daily clinical practice. Simpler, validated methods should be considered to assess protein intake and malnutrition. Periodic monitoring and assessments for muscle mass in comparison to a reference population is recommended by the KDOQI guidelines.[1] However, it has never been shown if protein intake is associated with these measures of muscle mass in an Asian population. Moreover, the clinical outcomes are referred to the NHANES population, and it is unclear how accurately these measures relate to our multi-ethnic population.[1] Our study shows that MAC, cAMA and MAMC were associated with daily total protein intake in both healthy and CKD Asian patients. But total protein intake normalized to ideal body weight applied only to CKD patients. The correlation was stronger with absolute daily total protein intake rather than intake values normalized to ideal body weight. This may be a result of the fact that body weight is part of the formula for calculating protein intake from 24-hr urine urea nitrogen.

Adequate dietary protein intake in healthy and stable chronic kidney disease participants should maintain muscle mass, i.e. taking adequate protein per kg body weight of muscle. To reduce potential confounding in clinical practice from fat mass (in overweight and obese partici-

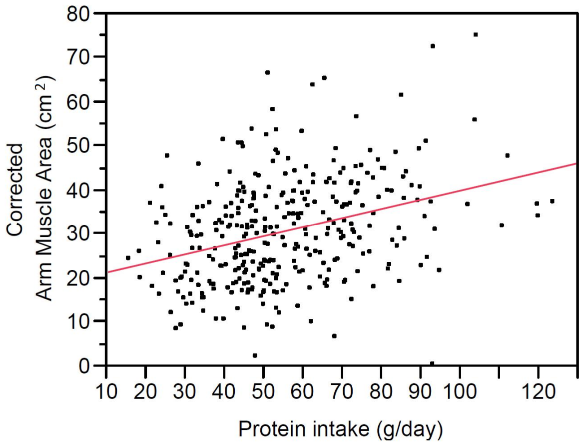
Table 3. Correlation of muscle assessments with protein intake

Measures†	Correlation/linear association with:					
	Total protein intake (g/day)			Total protein intake/ideal body weight (g/kg/day)		
	All‡	SKFS1‡	AKDS‡	All‡	SKFS1‡	AKDS‡
MAC (cm)	r=0.372, *p*<0.001 25.7+0.078×TPI; *p*<0.001	r=0.263, *p*<0.001 26.4+0.053×TPI; *p*=0.0072	r=0.433, *p*<0.001 25.2+0.09×TPI; *p*<0.001	r=0.304, *p*<0.001 26.1+4.15×TPI-IDW; *p*<0.001	r=0.139, *p*<0.001 27.8+1.82×TPI-IDW; *p*=NS	r=0.379, *p*<0.001 25.4+5.26×TPI-IDW; *p*<0.001
cAMA (cm^2)	r=0.337, *p*<0.001 19.1+0.207×TPI; *p*<0.001	r=0.242, *p*<0.001 20.4+0.15×TPI; *p*=0.0138	r=0.393, *p*<0.001 18.1+0.24×TPI; *p*<0.001	r=0.202, *p*<0.001 23.03+8.13×TPI-IDW; *p*<0.001	r=-0.0096, *p*<0.001 29.5-0.38×TPI-IDW; *p*=NS	r=0.298, *p*<0.001 20.2+12.03×TPI-IDW; *p*<0.001
MAMC (cm)	r=0.351, *p*<0.001 18.1+0.067×TPI; *p*<0.001	r=0.273, *p*<0.001 18.2+0.05×TPI; *p*=0.0052	r=0.402, *p*<0.001 17.9+0.08×TPI; *p*<0.001	r=0.200, *p*<0.001 19.5+2.48×TPI-IDW; *p*<0.001	r=0.154, *p*<0.001 21.2+0.20×TPI-IDW; *p*=NS	r = 0.287, *p*<0.001 18.8 + 3.54×TPI-IDW; *p*<0.001

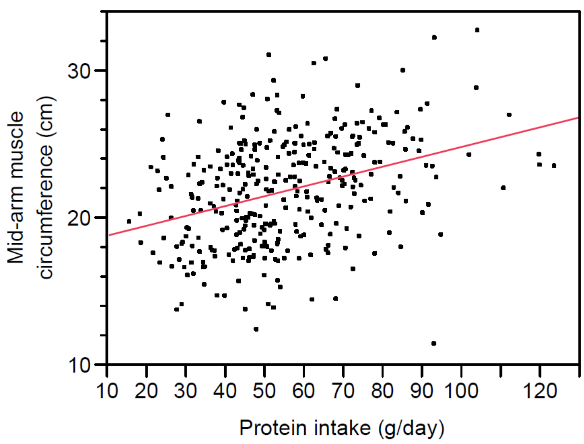
†MAC: mid-arm circumference; TSF: triceps skinfold; cAMA: corrected mid-arm muscle area; MAMC: mid-arm muscle circumference. ‡All: all participants (n=335); SKFS1: Singapore Kidney Function Study (n=103); AKDS: Asian Kidney Disease Study (n=232). NS: non-significant.



(a) Mid-arm circumference: r=0.372, p<0.001; 25.7+0.078× TPI; p<0.001.



(b) Corrected arm muscle area: r=0.337, p<0.001; 19.1+0.207× TPI; p<0.001.



(c) Mid-arm muscle circumference: r=0.351, p<0.001; 18.1+ 0.0670×TPI; p<0.001.

Figure 1. Relationship between muscle assessments and daily total protein intake in all participants (n=335)†. †TPI: total protein intake (g/day).

pants), and edema in CKD patients, protein intake is usually normalized to "edema-free" "standard" body weight. Our data shows that daily total protein intake has a better correlation and linear association with muscle mass assessments than normalizing its value to ideal body weight. Nonetheless, normalization appears to be valid in CKD patients. Therefore, our study suggests that these anthropometry-derived estimates of muscle mass may be used for assessment of nutrition in Asian CKD patients, and guide dietary counseling, even though they were originally derived from non-Asian populations.

The strengths of our prospective study include the fairly large study size for patients with anthropometry, reference GFR measurements, and systematic urine collections for objective urea nitrogen assay, which were consistently performed by the same research personnel. Recruitment was strategized to ensure a spread of healthy and CKD patients over the GFR range with adequate numbers of participants' representative of ethnicity and gender. We are limited by the lack of a reference standard method of assessment (dual-energy X-ray absorptiometry, computed tomography or magnetic resonance imaging) for muscle mass. The use of 24-hr urine urea nitrogen to estimate dietary protein intake assumes steady state protein intake and stable metabolic and clinical status. Participants with inter-current illness, randomly reduced or increased dietary protein intake, and catabolic conditions may result in erroneous conclusions. There are no current data tables of these nutritional assessments for the general population of Singapore in both healthy people and CKD patients. Skinfold thickness which is a reflection of body fat stores may also be affected by ethnicity.[15] Our study population and size would be inadequate to provide definitive data tables for the nutritional assessments as establishing reference tables normally requires about 120 subjects for each parameter-category assessed (e.g. age groups, sex, ethnicity, etc.) but these data provide an opportunity for future comparisons and further study.

In summary, current nutrition assessment (muscle) methods proposed by clinical practice guidelines may be validly applied to a multi-ethnic Asian population of CKD and healthy individuals.

ACKNOWLEDGEMENT

We acknowledge members of the Asian Kidney Disease Study and Singapore Kidney Function Study which include Prof Sunil Sethi, Dr Arvind Kumar Sinha, and Dr Borys Shuter.

This study was funded primarily by the National Kidney Foundation of Singapore (NKFRC2007/08). Dr Teo was also supported by the National Medical Research Council (block vote), and the National University of Singapore Yong Loo Lin School of Medicine Faculty Research Committee (Ministry of Education Academic Research Fund).

AUTHOR DISCLOSURES

The authors have no conflict of interest to declare.

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多民族亚裔人群中肌肉质量评估及与蛋白质摄入量之间的关系：与慢性肾病的相关性

背景：在慢性肾脏病患者的管理中，临床实践指南推荐的客观营养评估是参考北美人群开发的。具体的肌肉质量评估建议如下：中臂围（MAC）、校正的中臂肌肉面积（cAMA）和中臂肌围（MAMC）。本研究的目的是在多民族亚裔人群中评估健康人和慢性肾脏病患者肌肉质量与膳食蛋白质摄入量之间的关系。**方法**：我们分析了所收集的参与者 24 小时尿来估算总蛋白质摄入量（TPI，克/天）。计算理想体重（IDW，千克）并评估肌肉。应用相关性和线性回归分析，显著性定义为 $p<0.05$。**结果**：共有 232 名稳定的慢性肾脏病患者和 103 名健康志愿者参加，其平均年龄为 53.5±15.1 岁， 51.0%为男性，其中华人占 38.5%、马来人占 29.6%、印度人占 23.6%、其他民族的人占 8.4%。健康志愿者和慢性肾脏病患者的 TPI 分别为 58.9±18.4 克/天和 53.6±19.4 克/天。当标准化为理想体重，健康志愿者和慢性肾脏病患者的 TPI-IDW（克/千克/日）相似。总体来看，TPI 与 MAC、cAMA 和 MAMC 相关，相关系数分别为：0.372、0.337 和 0.351（$p<0.001$)。TPI-IDW 也与 MAC、cAMA 和 MAMC 相关，相关系数分别为：0.304、0.202 和 0.200（$p<0.001$），但是 TPI 标准化为实际体重与这些肌肉质量评估参数没有相关性。当单独分析时，MAC、cAMA 和 MAMC 与健康志愿者和慢性肾脏病患者的 TPI 都有关，但只与慢性肾脏病患者的 TPI-IDW 有关。**结论**：总蛋白质摄入量与所有参与者的肌肉评估有关，TPI 标准化为理想体重只适用于慢性肾脏病患者。

关键词：亚洲大陆世系人群、蛋白质、肾功能衰竭、慢性饮食、营养评估