



Body Composition of Chronic Kidney Disease Patients: A Multi-Stage Analysis

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Abstract

With accelerated muscle proteolysis, a decrease in muscle mass is evident in chronic kidney disease (CKD) patients. This eventually leads to nutritional disturbance that for a long has been mostly attributed to malnutrition. This predisposes patients to premature morbidity and mortality. Assessing body composition, thus, becomes vital. In this cross-sectional study, CKD patients (n = 47) of stages 2, 3a, 3b and 4 were assessed for their lean tissue mass, adipose tissue mass and overhydration by body composition monitor. Lean tissue index and fat tissue index were calculated as lean tissue mass and adipose tissue mass in kilogram divided by patients' height in square meters. Patients were assessed for their handgrip strength (HGS) by Jamar hydraulic hand dynamometer, and also for their 7-day diet history. Mean lean tissue index of CKD patients was $11.73 \pm 2.49 \text{ kg/m}^2$. About 34 (72.3%) out of 47 patients were below the reference value of lean tissue index. A significant difference in lean tissue index ($P = 0.03$) was observed at various stages. Patients at stage 4 had the lowest lean tissue index. Lean tissue was significantly ($P = 0.03$) low in patients consuming protein $<0.6 \text{ gm/kg/day}$. All 47 patients had less than normal HGS values. Patients' mean fat tissue index was $14.86 \pm 6.18 \text{ kg/m}^2$ and had water retention with a mean overhydration of $1.47 \pm 2.12 \text{ L}$. CKD patients were malnourished with a significant low lean tissue index. Dietary protein intake and HGS of these patients were positively associated with lean tissue index.

Keywords: body composition; chronic kidney disease; lean tissue index; malnutrition; muscle strength

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Introduction

Chronic kidney disease (CKD) is defined as abnormalities in structure and functioning of the kidney present for >3 months, with health implications (1). CKD has characteristic uremic symptoms such as disturbances in protein and energy metabolism, hormonal derangement, presence of inflammatory cytokines and inadequate dietary intake because of anorexia and nausea (2). Stimulation of ubiquitin–proteasome pathway (UPP) in kidney disease patients cleaves muscle protein (3–6). This affects patients' overall body composition, and

thus nutritional status. Poor nutritional status predisposes CKD patients to premature morbidity and mortality.

Body composition refers to body's elements, molecules and tissues. It is a measure of density, tissue thickness, weight of a compartment and percentage of body weight (7). Assessment of body composition in clinical practice is essential as it can directly predict changes in nutritional status, especially in case of severe nutritional involvement (8), such as in CKD.

With decrease in muscle mass, strength of the body is also compromised. Handgrip strength (HGS) is found to be an

important determinant of bone mineral content and is positively correlated with lean tissue (9). HGS thus has immense importance as a functional indicator of CKD.

In patients, body composition is assessed by various methods, such as neutron activation, computed tomography, magnetic resonance spectroscopy, dual energy X-ray absorptiometry (DEXA), total body water, today body scanning, bio-impedance analysis (BIA) and anthropometry. Amongst all, DEXA, BIA and anthropometry have the highest precision, reliability and utility (7). However, because of impaired body water regulation in CKD patients, identifying body composition correctly with these measures becomes difficult. For higher accuracy and objectivity, body composition monitor (BCM) has a great importance in measuring body composition of CKD patients (10). BCM determines adipose tissue mass (ATM), lean tissue mass (LTM) and overhydration (OH) correctly (2). It assesses undernutrition at an early stage of illness (8). Assessment of body composition not only identifies undernutrition in CKD but also may predict dual metabolic burden by identifying high or normal fat mass with low lean mass (11).

Hence, the present study is aimed to analyse the body composition of CKD patients at multi-stages (2, 3a, 3b and 4) of illness, and to find an association of lean tissue with patient's dietary protein intake and their HGS.

Materials and Methods

Locale

A private hospital in New Delhi, India, with a well-established renal outpatient department and willing to participate in the research formed the locale.

Ethical Approval

Approval to conduct the study was taken from the Institutional Review Board (IRB) and the Ethics Committee of the institute (Ref. No.: TS/MSSH/SKT-2/NEPHRO/IEC/14-35).

Subjects

Chronic kidney disease patients (at stage 2, 3a, 3b and 4) aged ≥ 18 years were selected for the study. Sample number was calculated by using malnutrition prevalence (19.6%) in CKD patients (12), which gave a sample size of approximately 120 patients, considering 25% sample loss. However, out of 120, 47 (32 males and 15 females) patients consented to undergo body composition analysis.

Body Composition

Body composition of the patients was measured by BCM to assess three major compartments: ATM, LTM and OH.

It works on the principle of bio-impedance spectroscopy. It is based on 3-Compartment (3-C) model, that is, LTM, ATM and OH. The 3-C model uses a correction factor for body mass index (BMI) and is validated against gold standard dilution methods to determine total body water (TBW), extracellular water (ECW) and intracellular water (ICW). BCM, in addition, is adjusted and corrected for the hydration factor (13), which usually varies due to impaired body salt and water regulation in CKD patients. Body composition was measured by applying electrical frequency (5 kHz–1000 kHz) to the patient (14). Complete body composition analysis was done through a software, Fluid Management Tool (FMT) (8). Lean tissue index (LTI) and fat tissue index (FTI) were calculated as LTM or ATM in kilogram divided by patients' height in square meters. In order to compare the patients' obtained values of LTI, FTI and OH, BCM-derived (Fresenius Medical Care) reference range values of more than 1000 healthy subjects aged 18–75 years were used (8). Reference ranges were calculated by a percentile-based analysis of LTI, FTI, and ECW:ICW ratio (absolute and relative fluid overload). Normal range values varied with gender and age (10).

Handgrip Strength and Diet History

Handgrip strength was measured by Jamar hydraulic hand dynamometer (USA), model: 5030J1, S/N: 30809187. It has key features such as dual-scale readout, displayed isometric grip force from 0 to 200 lbs (90 kg), peak hold needle to automatically retain the highest reading until reset, and dye-cast aluminium handle, which easily adjusted to five grip positions, from 1.3/8" to 3.3/8" in half-inch increments. Patients' diet history for last 7 days was taken to estimate the mean protein intake of a day. All foods consumed in 7 days were observed to identify various sources of protein.

Statistical analysis

Statistical testing was conducted with SPSS 20. Statistical tests such as Student's t-test, analysis of variance (ANOVA) were used to assess differences between mean values; Pearson's correlation (r) was used for association within selected variables. Regression analysis was used to find the strength of relationship between dependent and independent variables.

Results

Study population

In the selected sample of 47 CKD patients, 32 were males and 15 females. The mean age of the patients was 53 ± 13.5 years, and the majority were literate and sedentary in their activity. Diabetic nephropathy was the most common ($n = 23$) causative factor of CKD. Mean BMI of the patients

was 27.6 ± 5.6 kg/m² with a mean weight of 75 ± 15.7 kg and a height of 164.9 ± 8.1 cm. According to the World Health Organisation's (WHO, 2004) BMI cut-off points (15), about 31 patients were pre-obese, 15 had normal BMI, and one patient was underweight.

Body composition

Mean values of LTM of the patients was 33.08 ± 8.36 kg and that of ATM was 41.26 ± 16.79 kg (Table 1). Mean LTI calculated was 11.73 ± 2.49 kg/m². Out of 47 CKD patients, 34 (72.3 %) were below the reference value of LTI. Stage-wise comparison showed a significant difference in LTI ($P = 0.03$) across all stages. Multiple regression showed association of stages with LTI; at stage 4, the value of LTI decreased by 1.916 unit with $P = 0.03$, keeping other confounding variables (age, gender, BMI, albumin, total cholesterol, and FTI) constant. Mean FTI calculated was 14.86 ± 6.18 kg/m². Up to 19 CKD patients (40.4%) had high FTI. Mean OH of patients was 1.47 ± 2.12 L (range: -1.7 – 11.1 L), while ECW% was $7.73 \pm 10.86\%$ (range: -16.9 – 48.8%).

Mean LTI was high in males (12.29 ± 2.44 kg/m²) compared to females (10.52 ± 2.21 kg/m²). However, keeping age and BMI constant, compared to males, females had no association with LTI. Both males and females at higher age had lower LTI.

Fat tissue index was high in females (16.04 ± 6.85 kg/m²) than males (14.85 ± 6.18 kg/m²). With the progression of age, there was an increase in FTI in both genders.

There was a significant correlation between LTI and FTI ($\rho = -0.425$, p value = 0.003, respectively. ρ , Pearson's correlation). Regression analysis between both the variables showed that for 1 unit increase in FTI, LTI decreased by 0.171 unit ($P = 0.003$).

Association of body composition with dietary protein intake and handgrip strength

Patients consuming <0.6 gm/kg/day of protein had significantly ($P = 0.03$) less LTI (10.43 ± 0.90 kg/m²) compared to patients who had a protein intake of >0.6 gm/kg/day with LTI = 12.18 ± 0.36 kg/m² (t-test). HGS was significantly correlated with LTI ($r = 0.52$, $P < 0.001$) (Table 2).

Table 1: Body composition of CKD patients (n = 47).

Body composition	CKD stages					P-value
	Total (n = 47) Mean (SD)	2 (n = 9) Mean (SD)	3a (n = 10) Mean (SD)	3b (n = 14) Mean (SD)	4 (n = 14) Mean (SD)	
LTM (kg)	33.08 (8.36)	33.31 (4.25)	37.02 (6.03)	35.10 (11.16)	28.10 (6.57)	0.04*
LTI (kg/m ²)	11.73 (2.49)	11.90 (1.08)	13.15 (2.19)	12.11 (3.16)	10.23 (1.94)	0.03*
LTI reference values (BCM)						
Lower LTI (kg/m ²)	13.49 (1.97)	14.34 (2.03)	13.48 (1.85)	13.50 (2.03)	12.92 (1.96)	
Higher LTI (kg/m ²)	18.72 (2.43)	19.84 (2.42)	18.74 (2.39)	18.72 (2.5)	17.98 (2.39)	
ATM (kg)	41.26 (16.79)	47.97 (18.92)	33.99 (10.75)	39.80 (17.68)	43.59 (17.45)	0.30
FTI (kg/m ²)	14.86 (6.18)	11.98 (3.58)	17.17 (6.38)	14.17 (7.02)	16.11 (6.3)	0.25
FTI reference values (BCM)						
Lower FTI (kg/m ²)	5.52 (1.86)	4.42 (1.84)	5.44 (2.15)	5.57 (2.03)	6.24 (1.21)	
Higher FTI (kg/m ²)	16.19 (3.25)	14.71 (2.13)	15.66 (3.19)	16.49 (4.45)	17.21 (2.17)	
OH (Litres)	1.47 (2.12)	1.60 (2.14)	1.70 (2.21)	1.50 (2.13)	1.47 (2.12)	0.45
ECW%	7.73 (10.86)	8.76 (11.12)	9.09 (11.11)	7.87 (10.94)	7.73 (10.86)	0.30

*P significant at 0.05 level (statistical test: ANOVA).

CKD: Chronic kidney disease; LTM: Lean tissue mass; LTI: Lean tissue index; BCM: Body composition monitor;

ATM: Adipose tissue mass; FTI: Fat tissue index; OH: Overhydration; ECW: Extra cellular water.

CKD stages as defined by Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) Equation, 2009 (1).

LTI or FTI = LTM or ATM (kg) divided by height (m²).

LTI or FTI reference values (BCM; Fresenius Medical Care) were previously derived from 1000 healthy subjects aged 18–75 years (10).

Table 2: Correlation of body composition of CKD patients with handgrip strength (HGS).

Body composition (n = 47)	Overall	
	r	P-value
LTI (kg/m ²)	0.52	<0.001**
FTI (kg/m ²)	-0.15	0.31

**P-value significant < 0.01 (statistical test: Pearson correlation coefficient).

r: Correlation coefficient; LTI: Lean tissue index; FTI: Fat tissue index.

LTI or FTI = LTM or ATM (kg) divided by height (m²).

After correlating age and gender, CKD patients with low LTI had less than average HGS (mean HGS in patients: males, 28.55 ± 5.24 kg; females, 14 ± 0.14 kg) compared to Asians as well as age- and gender-stratified normative data of a population-based study (16, 17).

Discussion

Lean tissue index is an essential indicator of malnutrition, which predisposes patients to premature morbidity and mortality (18, 19). This study shows low LTI in CKD patients, which further decreases with progression of the disease. Patients at stage 4 had higher prevalence of malnutrition as compared to patients of initial stages. Hence, assessing body composition at the earliest is advantageous.

Low dietary protein intake (<0.6 gm/kg/day) is associated with low LTI. Similarly, a study has reported a low protein diet intake as a possible risk factor of malnutrition in CKD (20). In contrast, a study on low protein diet has demonstrated muscle protein metabolism adapted to restricted protein intake (21). However, present study clearly indicates significant relation of lean tissue index with dietary protein intake.

Handgrip strength is a key determinant of bone mineral content and was found to be positively correlated with lean tissue index. A strong association between low muscle mass and low physical strength is evident in a study (9).

In the present study, regression analysis showed an increase in adiposity with a decrease in lean mass. According to the WHO expert consultation, Asians generally have a higher percentage of body fat than Caucasians of the same age, sex and BMI (15).

In a normal hydrated state, OH remains within ±1 SD, with maximum ECW being 5.8%. For the present study group, mean values of OH and ECW% were higher, indicating water retention but with no significant difference across stages of the disease. Higher the water retention, higher the mortality among kidney disease patients (22).

Following are the strengths of the study: BCM is based on physiological tissue model which precisely distinguishes OH from LTM and ATM. Thus, change in osmotic pressure influences OH without affecting body composition. BCM used in the study is a validated tool (22) and has previously defined reference range values (8).

Conclusion

This study concludes that CKD patients are malnourished with low LTI, particularly at the later stages of the disease. In addition, low LTI is positively associated with poor HGS and low protein intake (<0.6 gm/kg/day). Body composition assessment, thus, emerges as a significantly clinical objective measure. It add a great value in the early diagnosis of malnutrition as well as facilitates early intervention in CKD patients. The study also shows a possibility of improvement in body composition with increased intake of protein.

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