Both low muscle mass and low fat are associated with higher all-cause mortality in hemodialysis patients

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A higher body mass index is associated with better outcomes in hemodialysis patients; however, this index does not differentiate between fat and muscle mass. In order to clarify this, we examined the relationship between measures of fat and muscle mass and mortality in 1709 patients from the Hemodialysis Study. Triceps skin-fold thickness was used to assess body fat and mid-arm muscle circumference was used to assess muscle mass. Cox regression was used to evaluate the relationship between measures of body composition with all-cause mortality after adjustments for demographic, cardiovascular, dialysis, and nutrition-related risk factors. During a median follow-up of 2.5 years, there were 802 deaths. In adjusted models with continuous covariates, higher triceps skin-fold thickness and higher body mass index were significantly associated with decreased hazards of mortality, while higher mid-arm muscle circumference showed a trend toward decreased mortality. In adjusted models, lower quartiles of triceps skin-fold thickness, mid-arm muscle circumference, and body mass index were all significantly associated with higher all-cause mortality. These studies show that body composition in end-stage renal disease bears a complex relationship to all-cause mortality.

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Although obesity is associated with higher mortality in the general population,[1] studies of dialysis patients suggest that higher body mass index (BMI) may be associated with lower all-cause and cardiovascular mortality.[2–6] The reason for this difference is unknown, but one potential explanation is that BMI does not differentiate between fat and muscle mass.

Higher fat mass is associated with inflammation and adverse outcomes in the general population,[7] although there are fewer and inconsistent data regarding this relationship in patients with end-stage renal disease.[8,9] Higher muscle mass on the other hand may be protective in dialysis patients because it is a proxy for better nutritional status. Most of the previous studies examining the importance of obesity in dialysis patients have however used BMI as a measure of obesity, therefore the interpretation remain uncertain.

The purpose of this study was to evaluate the separate associations of fat and muscle mass with all-cause mortality in hemodialysis (HD) patients. We also evaluated whether fat and muscle mass confounded or modified the association of one another and compared their associations with BMI.

RESULTS
Baseline characteristics
The demographics and other clinical characteristics of patients at baseline are shown in Table 1. The average age was 58 years, 64% were African Americans, and more than half were females. The most common cause of end-stage renal disease was diabetes (38%), followed by hypertension (34%) and glomerular disease (14%). Forty percent of patients had a history of congestive heart failure (HF) 39% had ischemic heart disease, and 44% had diabetes. Mean triceps skin-fold thickness, mid-arm muscle circumference (MAMC), and BMI were 16.3 mm, 24.8 cm, and 25.2 kg/m^2, respectively.

Participants in the highest quartile of triceps skin-fold thickness were older, predominantly women, more likely to be African American, with shorter dialysis vintage, higher prevalence of diabetes and co-morbid conditions, as well as higher BMI, higher MAMC, and lower serum creatinine levels (Table 1).

The Pearson correlation coefficients were 0.62, 0.63, and 0.17 between triceps skin-fold thickness and BMI, MAMC

Table 1 | Patient characteristics by quartile of triceps skin-fold thickness

|	Overall (n=1709)	Triceps skin-fold thickness Q1 (n=427)	Triceps skin-fold thickness Q2 (n=430)	Triceps skin-fold thickness Q3 (n=422)	Triceps skin-fold thickness Q4 (n=430)	P
Demographics						
Age (years)	57.7 (14.0)	54.4 (15.7)	59.1 (14.2)	58.2 (13.6)	59.2 (11.5)	<0.001
Women	56	26	45	71	80	<0.001
Black	64	60	60	68	69	0.002
Comorbid conditions						
Diabetes	44	22	41	53	60	<0.001
Peripheral vascular disease	16	14	16	17	18	0.36
Ischemic heart disease	39	33	43	39	41	0.01
Congestive heart failure	40	42	40	37	40	0.44
Other heart disease	63	66	65	62	59	0.12
Cerebral vascular disease	20	17	23	22	17	0.06
Smoking status						
Never	49	38	49	52	58	<0.001
Past	33	36	31	33	32	
Current	18	26	20	15	10	
Physical exam						
Height (cm)	164.8 (9.4)	167.9 (9.5)	165.5 (9.3)	163.4 (9.4)	162.4 (8.3)	<0.001
Weight (kg)	68.8 (14.4)	61.3 (11.0)	65.9 (12.4)	69.9 (13.8)	78.1 (14.4)	<0.001
Triceps skin-fold thickness (mm)	16.3 (7.9)	7.1 (1.8)	12.6 (1.5)	18.2 (1.8)	27.4 (4.2)	
MAMC (cm)	24.8 (3.8)	24.1 (3.9)	24.4 (3.6)	25.0 (3.8)	25.7 (3.9)	<0.001
BMI (kg/m^2)	25.2 (5.1)	21.5 (3.0)	23.9 (3.5)	26.0 (4.4)	29.6 (5.1)	<0.001
SBP (mm Hg)	152.1 (22.1)	150.2 (20.9)	150.1 (22.3)	152.4 (22.5)	155.5 (22.2)	0.001
Laboratory variables						
Creatinine (mg/dl)	10.3 (2.9)	10.9 (3.3)	10.3 (2.9)	10.1 (2.7)	9.9 (2.5)	<0.001
Albumin (g/dl)	3.6 (0.4)	3.7 (0.4)	3.6 (0.4)	3.6 (0.3)	3.6 (0.3)	0.86
Calcium (mg/dl)	9.3 (1.0)	9.3 (1.0)	9.3 (1.0)	9.3 (1.0)	9.2 (0.9)	0.47
Phosphorous (mg/dl)	5.8 (1.9)	5.8 (2.1)	5.6 (1.8)	5.8 (1.9)	5.9 (1.6)	0.18
Dialysis-related parameters						
Duration of HD (years)	3.7 (4.4)	4.8 (5.3)	3.8 (4.3)	3.5 (4.0)	2.8 (3.4)	<0.001

Abbreviations: BMI, body mass index; HD, hemodialysis; MAMC, mid-arm muscle circumference; SBP, systolic blood pressure.
Data are presented as mean (s.d.) for continuous variables, or as percentages for binary and categorical variables. The P-values are derived from two-sided hypothesis testing using χ^2-test for categorical variables and analysis of variance for continuous variables.

and BMI, and triceps skin-fold thickness and MAMC, respectively. MAMC was normally distributed, while triceps skin-fold thickness and BMI were slightly skewed to the right (Figure 1). During a median follow-up of 2.5 years there were 802 deaths.

Univariate analyses

In univariate analysis, higher measures of all three parameters of body composition measures were associated with lower all-cause mortality (hazards ratio (HR) 0.93 (95% confidence interval (CI) 0.86–1.00, $P = 0.04$), 0.87 (95% CI 0.81–0.94, $P < 0.001$), and 0.92 (95% CI 0.85–0.99, $P = 0.02$), respectively, for triceps skin-fold thickness, MAMC, and BMI). For triceps skin-fold thickness and BMI, the highest quartile was associated with lower risk compared with the lowest
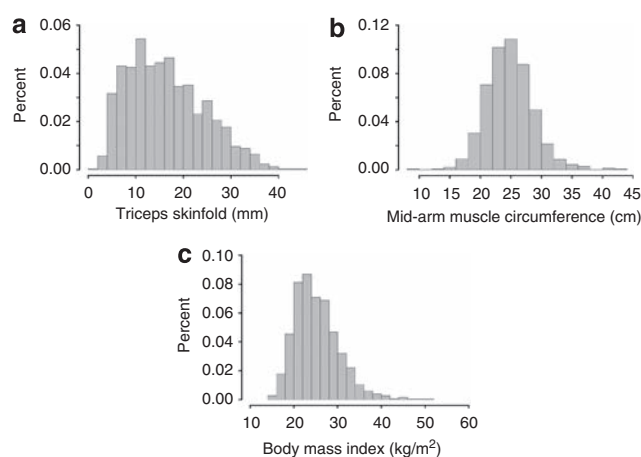
Figure 1 | Histogram of anthropometric measures.