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Lean Tissue Mass Wasting is Associated With Increased Risk of Mortality Among Women With Pulmonary Tuberculosis in Urban Uganda

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OBJECTIVES: We assessed the impact of wasting on survival in patients with tuberculosis by using a precise height-normalized lean tissue mass index (LMI) estimated by bioelectrical impedance analysis and body mass index (BMI).
METHODS: In a retrospective cohort study, 747 adult pulmonary patients with tuberculosis who were screened for HIV and nutritional status were followed for survival.
RESULTS: Of 747 patients, 310 had baseline wasting by BMI (kg/m^2) and 103 by LMI (kg/m^2). Total deaths were 105. Among men with reduced BMI, risk of death was 70% greater (hazard ratio [HR] 1.7, 95% confidence interval [95% CI] 1.03–2.81) than in men with normal BMI. Survival did not differ by LMI among men (HR 1.1; 95% CI 0.5–2.9). In women, both the BMI and LMI were associated with survival. Among women with reduced BMI, risk of death was 80% greater (HR 1.8; 95% CI 0.9–3.5) than in women with normal BMI; risk of death was 5-fold greater (HR 5.0; 95% CI 1.6–15.9) for women with low LMI compared with women with normal LMI.
CONCLUSIONS: Wasting assessed by reduced BMI is associated with an increased risk for death among both men and women whereas reduced LMI is among women with tuberculosis.
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KEY WORDS: Tuberculosis, Survival, Wasting, Lean Tissue Mass Index, Body Mass Index, Bioelectrical Impedance Analysis.

INTRODUCTION

Wasting is a cardinal feature of tuberculosis, an infectious disease associated with mortality worldwide. In Africa, a significant proportion of patients with tuberculosis have a marked degree of wasting by the time they present for treatment (1–3). Wasting associated with tuberculosis is likely caused by a combination of decreased appetite and altered metabolism resulting from the inflammatory and immune responses (4, 5). Wasting is associated with impaired physical function (2), longer hospitalization days, and increased tuberculosis-related mortality (3, 6, 7).

Lean tissue mass and fat mass body composition measurements are a precise way to evaluate wasting status (8, 9). Bioelectrical impedance analysis (BIA) has been recommended as a practical and reproducible method for clinical assessment of fat and lean tissue mass (9–11). In this study, we evaluated the effects of wasting on survival by using both body mass index (BMI) and BIA measurements among patients with pulmonary tuberculosis in urban Uganda. We considered the role of sex and human immune deficiency virus (HIV) infection in evaluating the impact of body wasting on survival.

METHODS

Study Design

We performed a retrospective cohort study that comprised 747 adults ⩾18 years with pulmonary tuberculosis and known HIV serostatus. Data were extracted from the Household Contact study (12–14) and the placebo arm of the prednisolone randomized placebo-controlled clinical trial (15). All participants for the household and prednisolone

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Selected Abbreviations and Acronyms

BIA = bioelectrical impedance analysis
BMI = body mass index
CI = confidence interval
FMI = fat mass index
HIV = human immune deficiency virus
HR = hazard ratio
LMI = lean tissue mass index

studies were residents of Kampala district, and detailed selection criteria have been published elsewhere (12–15). The household contact study was conducted in two phases (1995–1999 and 2002 to the present) to describe the epidemiology of tuberculosis in urban African households. The clinical trial was conducted between 1995 to 2000 to determine whether immunoadjuvant prednisolone therapy in HIV-infected patients with tuberculosis was safe and effective at increasing $CD4^+$ T-cell counts (15).

The 747 adults in the cohort included 652 participants who were enrolled in the household contact study (312 from phase I and 340 from phase II) and 95 from the placebo arm of the clinical trial. The BIA data were collected only during the second phase of the household contact study; thus, only 311 of the 747 cohort had BIA data. The institutional review boards at Case Western Reserve University in the United States and AIDS Research Council in Uganda reviewed the study protocols and final approval was obtained from the Uganda National Council for Science and Technology. During follow-up, patients were referred to community clinics for further HIV care. Patients with tuberculosis were treated with standard four-drug chemotherapy for tuberculosis per guidelines of the Ugandan Ministry of Health.

Measurements

All participants had sociodemographic information obtained through standardized data collection forms. Active tuberculosis was confirmed by sputum smear microscopy (World Health Organization) (16) and culture at the Uganda National Tuberculosis Reference Laboratory. HIV-1 infection was diagnosed on the basis of a positive enzyme-linked immunosorbent assay for HIV-1 antibodies (Recombigen; Cambridge Biotech, Cambridge, MA). All participants had posteroanterior chest X-rays taken at baseline, and readings were performed by one experienced physician.

Nutritional status was assessed by use of baseline height and weight anthropometric measurements and BIA (Quantum II; RJL Systems, Detroit, MI) before initiation of tuberculosis therapy. Weight was determined to the nearest 0.1 kg by the use of a SECA adult balance, and standing height was determined to the nearest centimeter. BMI was computed as weight (kilograms) divided by height (meters) squared. All BIA measurements were performed by one trained observer using the same equipment and recommended standard conditions (10).

A Single-frequency BIA was performed at 50 kHz and 800 mA with standard tetrapolar lead placement (17) to measure fat and lean tissue mass. Before performing measurements on each participant, the BIA instrument was calibrated by use of the manufacturer's recalibration device. Resistance and reactance were based on measures of a series circuit (18). BIA measurements were performed in triplicate for each subject and the average was used. Lean tissue mass was calculated from BIA measurements using equations that were previously cross-validated in a sample of patients with and without HIV infection (18) and have been applied elsewhere in African studies (19–21). Fat mass was calculated as body weight minus fat-free mass.

Operational Definitions

Baseline wasting was defined by the use of BMI and height-normalized indices (adjusted for height) for lean tissue mass and fat mass as measured by BIA. BMI can be partitioned into height-normalized indices of lean tissue mass index (LMI) and fat mass index (FMI), i.e., BMI = LMI + FMI as previously reported (8, 9, 22) using BMI cutoff for malnutrition <18.5 kg/m^2 (23). The cutoffs for low LMI and FMI corresponding to a BMI <18.5 kg/m^2 (9) were as follows: LMI <16.7 (kg/m^2) for men and <14.6 (kg/m^2) for women with corresponding FMI <1.8 (kg/m^2) for men and <3.9 (kg/m^2) for women. LMI and FMI have the advantage of compensating for differences in height and age (11).

Study Outcome Variable

Observed survival was the main study outcome. It was defined as the time interval between the diagnosis of tuberculosis and death or censoring. Participants were censored at the last clinic visit when they were known to be alive or at the end of study. Mortality was assessed through a standard interview of family members or review of hospital records. When a participant failed to keep a scheduled visit, health visitors visited the participant's home to determine the vital status. Family members also provided the date of death and prominent symptoms at the time of death for those who died at home.

Statistical Analysis

For analysis using BMI, data from 747 participants was used and data from 311 participants (a subset of 747) was used for BIA body composition. The overall survival distributions for participants presenting with or without body wasting were estimated using the Kaplan-Meier method and compared using the log-rank test (24). A series of Cox proportional hazards models (25) were fit after testing for the proportional hazards assumptions using graphical methods and goodness

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of fit Schoenfeld residuals. Observed survival and baseline wasting status as measured by low BMI or LMI were used as the primary dependent and independent variables, respectively in each model. The covariables included age, sex, HIV serostatus, previous smoking history, extent of disease on chest radiography, and history of weight loss. Variables that were associated with survival in a univariate analysis or with biological plausibility were evaluated in a series of multivariable models.

Two-way interactions between baseline wasting status and the co-variables were evaluated; significant interactions were demonstrated between sex and low LMI variable for wasting and between sex and HIV serostatus on survival. Therefore, Cox regression models were fit stratified according to sex. Likelihood ratio tests were used to test the interactions. All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Baseline Characteristics of Patients With Tuberculosis

Of 747 patients who were included in the analysis for BMI, 310 (42%) had wasting whereas of the 311 participants with BIA measurements, 103 (33%) had lean tissue mass, and 135 (43%) fat mass wasting at presentation (Table 1). Overall men had a worse nutritional status at baseline compared to women. Men had significantly greater proportion of individuals with reduced BMI (63%) and reduced LMI (80%) compared with women at presentation (Table 1). Men had significantly lower BMI (18.6 $\pm$ 2.1 vs. 20.0 $\pm$ 3.3, $p < .001$) and lower FMI (2.0 $\pm$ 0.8 vs. 4.4 $\pm$ 2.8, $p < .001$) compared with women, respectively, whereas women had significantly lower LMI (15.8 $\pm$ 1.1 vs. 16.6 $\pm$ 1.4, $p < .001$) compared with men at baseline. Of note, there were no differences in body wasting at baseline between HIV-seropositive and HIV-seronegative patients with tuberculosis regardless of whether BMI, LMI, and FMI cut-off were used to assess wasting.

Datasets for BMI and the subset with BIA measurements had comparable baseline characteristics, including wasting as measured by BMI ($p = .45$), sex ($p = .56$), proportion of anemic individuals (hemoglobin $\leq$10 mg/dL; $p = .59$), current smoking status ($p = .95$), and extent of disease on chest radiography ($p = .13$).

TABLE 1. Baseline characteristics of pulmonary tuberculosis patients with normal BMI or LMI versus patients with low BMI or LMI

Characteristic	Normal BMI (n = 437)	Low BMI (n = 310)	Normal LMI (n = 208)	Low LMI (n = 103)
Sex				
Females	236 (54)	116 (37)*	126 (61)	21 (20)*
Males	201 (46)	194 (63)	82 (39)	82 (80)
Age, yrs				
≤30	257 (59)	177 (57)	135 (65)	59 (57)
>30	180 (41)	133 (43)	73 (35)	44 (43)
HIV status				
Negative	202 (46)	143 (46)	116 (56)	56 (54)
Positive	234 (54)	167 (54)	91 (44)	47 (46)
Hemoglobin, g/dL†				
>10	216 (81)	126 (64)*	151 (76)	73 (74)
≤10	51 (19)	70 (36)	48 (24)	26 (26)
Fat mass index, kg/m^2‡				
Normal	149 (79)	27 (22)*	124 (61)	52 (51)
Low	40 (21)	95 (78)	79 (39)	49 (49)
Chest x-ray disease extent§				
Normal/mild	75 (17)	36 (12)¶	39 (19)	10 (10)¶
Moderate/far advanced	357 (83)	271 (88)	164 (81)	93 (90)
Smoker‖				
No	374 (86)	219 (71)*	176 (85)	62 (60)*
Yes	61 (14)	90 (29)	31 (15)	41 (40)
Takes alcohol**				
No	266 (61)	201 (65)	151 (73)	64 (62)¶
Yes	170 (39)	109 (35)	56 (27)	39 (38)
History weight loss††				
No	111 (26)	54 (17)¶	38 (18)	13 (13)
Yes	324 (74)	255 (83)	168 (82)	90 (87)

BMI = body mass index; LMI = lean tissue mass index; LMI low = <16.7 kg/m^2 for men and <14.6 kg/m^2 for women; low BMI = <18.5 kg/m^2; and low fat mass index = <1.8 (kg/m^2) for men and <3.9 (kg/m^2) for women.
Values are n (%).
*$p < .001$.
†A total of 284 missed hemoglobin measurements because of lack of blood.
‡Fat and lean tissue mass was not measured.
§Eight missed extent variable.
¶$p < .05$.
‖Three missed history of ever smoked.
**One missed history of alcohol intake.
††Four missed history of weight loss.

Effect of Baseline Wasting on Survival

During the mean follow-up period of 31 (SD 23) months for the 747 patients with BMI measurements, 105 deaths occurred, 99 of them among HIV-seropositive patients. The overall unadjusted survival for patients with low BMI at presentation was lower than that of patients with normal BMI (Log-rank, $p = .002$; Fig. 1A). At 6 months, that is, the end of tuberculosis treatment, survival among patients with low BMI was 87% compared with patients with a normal BMI of 92%; by 12 months, survival among patients with low BMI was 85% compared with patients with a normal BMI of 91%. When we stratified the results by sex, survival proportion was significantly lower among men with low BMI compared with men with normal a BMI at diagnosis (Log-rank, $p = .033$; Fig. 1B). For women with low BMI, the survival proportion was lower than that for women with normal BMI, but this difference was not statistically significant (Log-rank, $p = .119$).

During the mean follow-up period of 26 (SD 16) months for 311 patients with BIA measurements, 30 deaths

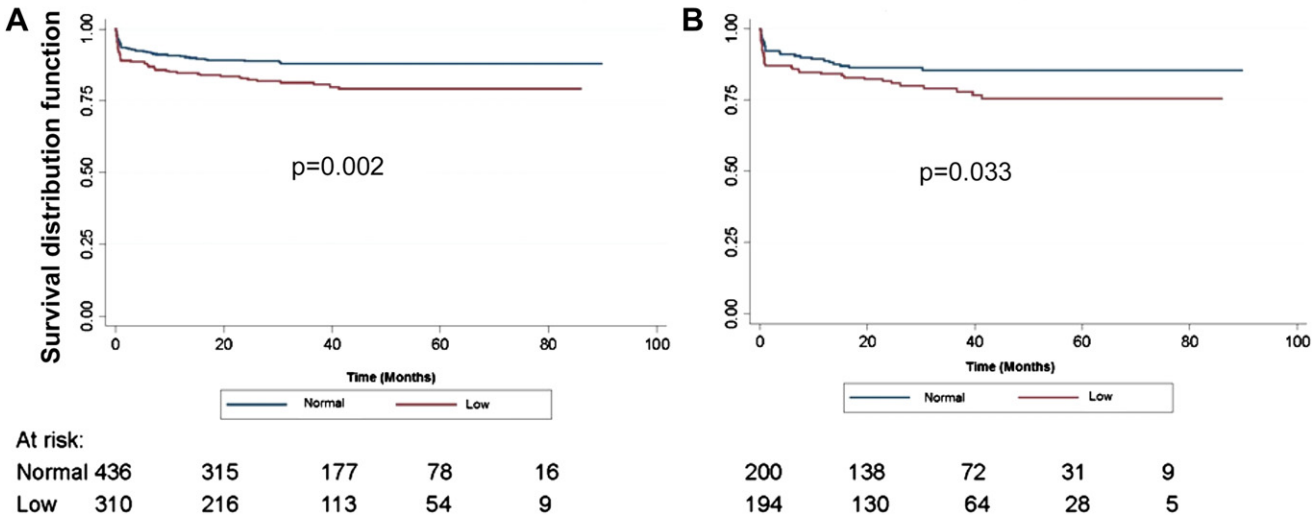

FIGURE 1. (A) Survival distribution among adult tuberculosis patients presenting with wasting (BMI <18.5 kg/m^2) compared with patients without wasting. (B) Survival distribution among adult male patients with tuberculosis presenting with wasting (BMI <18.5 kg/m^2) compared with men without wasting in urban Uganda.

occurred, 29 of them among HIV-seropositive patients. Overall unadjusted survival for 311 patients who presented with low LMI was lower compared with patients with normal LMI (Log-rank, $p = 0.016$; Fig. 2A). At 6 months, survival among patients with low LMI was 92% compared with patients with normal LMI of 97%; by 12 months, survival among patients with low LMI was 87% compared with patients with normal LMI of 96%. When we stratified by sex, survival proportion was significantly lower for women who presented with low LMI compared with women with normal LMI at presentation (Log-rank, $p < 0.001$; Fig. 2B). For men with low LMI at presentation, survival proportion was not different from those with normal LMI (Log-rank, $p = 0.65$).

Both low BMI and low LMI at tuberculosis diagnosis were associated with poor survival in univariate and multivariable Cox proportional hazards regression analyses (Tables 2, 3, and 4). The unadjusted HR for death in univariate model among patients with low BMI at diagnosis compared with patients who had a normal BMI was 1.80 (95% CI 1.23–2.64). Similarly, the unadjusted HR for death among patients with low LMI compared with patients who

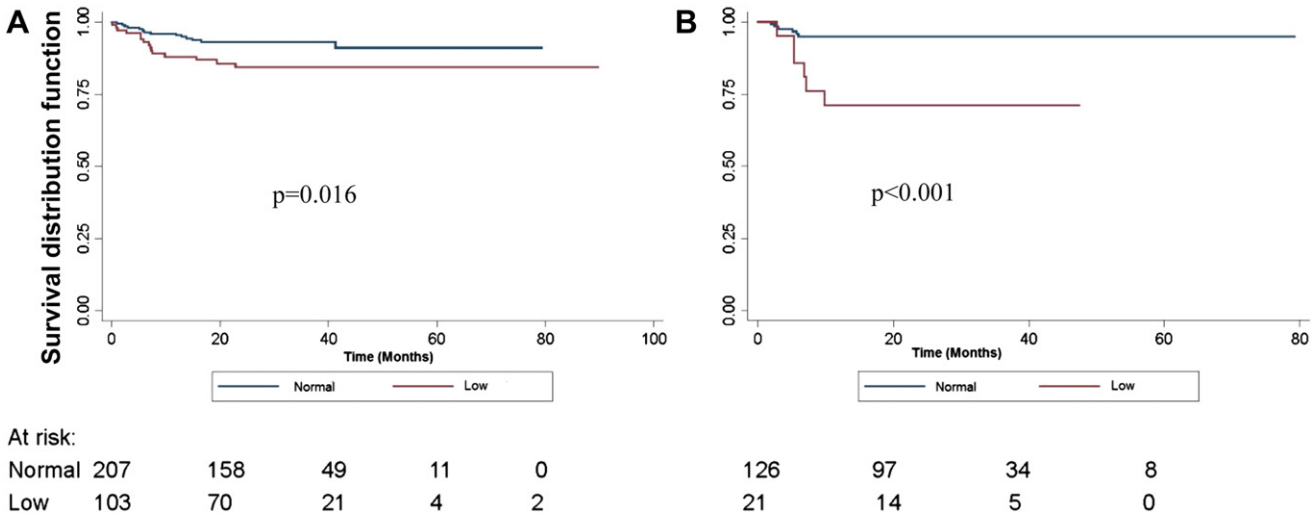

FIGURE 2. (A) Survival distribution among adult patients with tuberculosis presenting with baseline lean tissue mass wasting (LMI <14.6 kg/m^2 for women and <16.7 kg/m^2 for men) compared to patients without wasting. (B) Survival distribution among adult female tuberculosis patients presenting with lean tissue wasting (LMI <14.6 kg/m^2) compared with female patients without wasting.

TABLE 2. Univariate analysis of factors associated with mortality among adult patients with pulmonary tuberculosis in Kampala, Uganda

Characteristic	Deaths, *n* (%)	Relative hazard	95% confidence interval
BIA lean tissue mass index, kg/m^2			
Normal	14/208 (7)	1	
Low	16/103 (16)	2.34	1.14–4.80*
BIA fat mass index, kg/m^2			
Normal	16/176 (9)	1	
Low	14/135 (10)	1.15	0.56–2.36
Body mass index, kg/m^2			
Normal	47/437 (11)	1	
Low	58/310 (19)	1.80	1.23–2.64*
Sex			
Female	38/352 (11)	1	
Male	67/395 (17)	1.66	1.12–2.48*
Age, yrs			
⩽30	34/434 (8)	1	
>30	71/313 (23)	3.15	2.09–4.74*
HIV serostatus[†]			
Negative	6/345 (2)	1	
Positive	99/401 (25)	16.24	7.13–37.02*
History weight loss[‡]			
No	11/165 (7)	1	
Yes	94/579 (16)	2.59	1.39–4.84*
Previous smoking history[§]			
No	84/593 (14)	1	
Yes	20/151 (13)	0.98	0.60–1.60
Chest x-ray extent[¶]			
Normal/minimal	19/111 (17)	1	
Moderate/ far advanced	86/628 (14)	0.73	0.44–1.19

BIA = bioelectrical impedance analysis; Low lean tissue mass index = <16.7 kg/m^2 for men and <14.6 kg/m^2 for women; low fat mass index = <1.8 (kg/m^2) for men and <3.9 (kg/m^2) for women; and low body mass index<18.5 kg/m^2 regardless of sex.
*Statistically significant.
[†]One missed HIV status.
[‡]Four missed history of weight loss.
[§]Three missed history of previous smoking history.
[¶]Eight missed chest x-ray disease extent variable.

had a normal LMI was 2.34 (95% CI, 1.14–4.80; Table 2). Other univariate factors that were significantly associated with increased relative hazards of death included male sex, older than 30 years of age, HIV-seropositive status, and history of weight loss (Table 2).

The HR for death among patients with low BMI at presentation was 1.83 (95% CI 1.24–2.71) after adjusting for age, HIV, previous smoking history, extent of disease on chest x-ray, and history of weight loss (Table 3). Because our previous findings (20) showed an interaction between BMI and sex, we fitted Cox regression models stratified by sex (Table 3). Men with low BMI at presentation had a greater risk of death compared with men who had a normal BMI (HR 1.70; 95% CI 1.03–2.81). Among women, those presenting with a low compared with a normal BMI had comparable risk of death (HR 1.83; 95% CI 0.96–3.50). Other factors that were associated with the risk of death in this model included older male sex, HIV-seropositive status, and history of weight loss (Table 3).

There was significant interaction between baseline wasting as defined by low BMI and HIV serostatus on survival ($p < 0.001$). In a stratified Cox regression after adjusting for age, previous smoking history, extent of disease on chest x-ray, and history of weight loss, HIV-seropositive patients with reduced BMI had a greater risk for death compared with those with normal BMI (HR 1.63; 95% CI 1.09–2.44). Among HIV-seronegative patients, the risk of death associated with a reduced BMI was not statistically significant (HR 6.95; 95% CI 0.78–61.89).

When we used BIA as the measure of body composition, we found that patients presenting with a low LMI had a greater risk of death compared with patients with normal LMI (HR 2.36; 95% CI 1.11–5.01) after we adjusted for age, HIV, previous smoking history, extent of disease on chest x-ray, and history of weight loss (Table 4). Because of the significant interaction between LMI and sex on survival ($p = 0.003$), we fitted Cox regression models stratified by sex (Table 4), which showed that women who presented with low LMI had a greater risk of death compared with women presenting with normal LMI (HR 5.14; 95% CI 1.56–16.93), whereas men presenting with low LMI had a similar risk of death as compared with men with normal LMI (HR 1.05; 95% CI 0.40–2.77). HIV-seropositive status among men was another factor associated with risk of death (Table 4).

When we evaluated the effect of baseline fat mass wasting on survival in both unadjusted (Table 2) and adjusted Cox regression models, fat mass wasting was not associated with any risk for death regardless of sex.

DISCUSSION

In this retrospective cohort study of 747 adult patients with pulmonary tuberculosis in urban Uganda, most deaths occurred in HIV-infected persons. Wasting was associated with poor survival but the effect varied by method of body composition measurement and sex. The impact of wasting varied little between men and women when we used BMI; however, when we used LMI as defined by the BIA, we found that the effect of wasting was dramatic in women with reduced lean tissue mass but not in men. Fat mass wasting appears not to predict survival regardless of sex. This study demonstrates that loss of body mass, especially lean tissue mass, affects the survival of patients with tuberculosis, especially when they are infected with HIV.

Our findings suggest that survival is influenced by BMI in both men and women but that lean tissue mass is associated with survival only in women. For BMI, the magnitude of

TABLE 3. Relative Hazards (HR, 95% CIs) for death among tuberculosis patients with normal versus low BMI adjusted for age, HIV status, history of weight loss, previous smoking history, and extent of disease on chest X-ray and stratified according to sex in Kampala, Uganda

			Stratified models	
		Overall model	Women (n = 352)	Men (n = 395)
Characteristics	Deaths/N (%)	HR (95% CI)	HR (95% CI)	HR (95% CI)
BMI, kg/m^2				
Normal (⩾18.5)	47/437 (11)	1	1	1
Low (<18.5)	58/310 (19)	1.83 (1.24–2.71)*	1.83 (0.96–3.50)	1.70 (1.03–2.81)*
Age (years)				
⩽30	34/434 (8)	1	1	1
>30	71/313 (23)	2.32 (1.53–3.50)*	1.77 (0.93–3.36)	2.57 (1.45–4.54)*
HIV serostatus[†]				
Negative	6/345 (2)	1	1	1
Positive	99/401 (25)	15.88 (6.94–36.38)*	12.61 (3.84–41.37)*	18.48 (5.76–59.26)*
Previous smoking history[‡]				
No	84/593 (14)	1	1	1
Yes	20/151 (13)	0.69 (0.42–1.14)	0.38 (0.05–2.78)	0.61 (0.35–1.04)
History weight loss[§]				
No	11/165 (7)	1	1	1
Yes	94/579 (16)	3.40 (1.81–6.37)*	2.60 (1.00–6.76)*	4.27 (1.84–9.95)*
Chest x-ray extent[¶]				
Normal/minimal	19/111 (17)	1	1	1
Moderate/advanced	86/628 (14)	0.80 (0.49–1.32)	0.91 (0.42–2.99)	0.71 (0.37–1.37)

BMI = body mass index; CI = confidence interval; HR = hazard ratio.
*Statistically significant.
[†]One missed HIV status.
[‡]Three missed history of prior smoking status.
[§]Four missed history of weight loss.
[¶]Eight missed chest x-ray disease extent variable.

effect was similar among men and women and indicated that wasting increased the risk of death by approximately 80%. We interpret this to mean that loss of body mass in general as measured by BMI is a marker of poor survival. With BIA, we gain insight into potential mechanism that may explain the heightened risk, at least among women. In women, there is preferential loss of fat mass in order to preserve the limited lean tissue as previously described (20). When the energy reserve is spent, the body resorts to the muscle component for survival. Since we did not see any effect of lean tissue on survival in men, we surmise that they had sufficient lean tissue to meet the additional energy requirements of their illness.

Our findings also suggest that the effects of malnutrition on survival are accentuated by comorbidities (5, 26). In the face of comorbidities such as HIV, the effects of malnutrition become detectable. HIV-seropositive patients with reduced BMI at time of tuberculosis diagnosis had poor survival compared with HIV-seropositive patients with normal BMI. However, there was a minimal effect on survival among HIV-seronegative patients with reduced BMI, although the number of deaths in this group was few. In previous studies authors have also reported a similar effect that an underweight BMI is associated with increased risk of mortality whereas obese and overweight BMIs have a reduced risk of both mortality and tuberculosis (27). It is known that malnutrition can cause immune-suppression (28), and thus, tuberculosis in the presence of malnutrition might further exacerbate HIV-associated immune suppression. These interrelated effects may explain why both tuberculosis and malnutrition are associated with reduced survival among HIV-infected patients (29, 30). It may also account, in part, for the effect of tuberculosis on the natural history of HIV infection.

In this study, most deaths occurred during the first year of follow-up. There are several potential reasons for the early deaths. First, many patients presented with severe and extensive tuberculosis. More than 75% had moderate/or far advanced disease as demonstrated on chest x-ray. Second, most deaths were HIV-related, indicating that HIV-tuberculosis coinfection may be associated with additional nutritional alterations that lead to poor outcomes. The extra burdens on nutritional status include increased energy expenditure, nutrient malabsorption, reduced intake, micronutrient malnutrition, and increased production of inflammatory cytokines with lipolytic and proteolytic activity (31–33). Third, approximately one-quarter of the study population presented with anemia, which is an HIV-related complication associated with poor outcome (34). Finally, there was substantial wasting at time of

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TABLE 4. Relative hazards (HR, 95% CIs) for death among tuberculosis patients with normal versus low LMI by BIA adjusted for age, HIV status, history of weight loss, prior smoking status, and extent of disease on chest x-ray and stratified according to sex in Kampala, Uganda

			Stratified models	
		Overall model	Women (n = 165)	Men (n = 175)
Characteristics	Deaths/N (%)	HR (95% CI)	HR (95% CI)	HR (95% CI)
LMI in kg/m^2				
Normal	14/208 (7)	1	1	1
Low	16/103 (16)	2.36 (1.11–5.01)*	5.14 (1.55–16.93)*	1.05 (0.40–2.77)
Age (years)				
⩽30	10/194 (5)	1	1	1
>30	20/117 (17)	2.40 (1.10–5.21)*	3.03 (0.90–10.25)	2.82 (0.94–8.47)
HIV serostatus[†]				
Negative	1/172 (0.6)	1	1	1
Positive	29/138 (20)	31.84 (4.29–236.46)*		20.3 (2.65–155.86)*
Previous smoking history[‡]				
No	23/38	1	1	1
Yes	7/72	0.60 (0.25–1.48)		0.55 (0.20–1.54)
History of weight loss				
No	2/51 (4)	1	1	1
Yes	28/258 (11)	1.70 (0.39–7.35)	1.86 (0.21–16.25)	2.24 (0.27–18.25)
Chest x-ray extent[§]				
Normal/minimal	7/49	1	1	1
Moderate/advanced	23/257	0.91 (0.37–2.20)	0.75 (0.22–2.51)	1.93 (0.41–9.18)

BIA = bioelectrical impedance analysis; BMI = body mass index; CI = confidence interval; HR = hazard ratio; LMI = lean tissue mass index (kg/m^2); LMI low = <16.7 kg/m^2 for men and <14.6 kg/m^2 for women.
*Statistically significant.
[†]One missed HIV serostatus and fewer events among HIV-negative patients.
[‡]A total of 29 missed previous smoking history and fewer events among women.
[§]A total of 29 missed chest x-rays.

tuberculosis diagnosis in our population, yet wasting is associated with increased risk of early death.

The interpretation of findings in this study should be made with caution because the BIA method that was used in measuring body composition is not the reference standard, and the BIA prediction method used has not yet been validated in the local population. As a result, findings of body composition may be biased because of variations in hydration across ethnic groups (10). However, the prediction equations that were used in this study were previously cross-validated in individuals of different races and among men and women who were HIV-seronegative healthy controls and HIV-seropositive patients (18). Moreover, the equations have been used widely in other studies in Africa with meaningful findings (19–21, 35).

Our findings are also limited by a lack of information on dietary intake, which may contribute to some of the observed difference in body composition and survival by sex. Another limitation is that we did not have data on CD4$^+$ T-cell counts to comment on effect of HIV disease severity; however, our findings are consistent with previous studies of mortality in HIV-infected patients in Africa in which the rate of mortality was greater in men than in women (36, 37).

In conclusion, findings in this study indicate that body wasting exerts greatest effect on observed survival among HIV-infected patients with tuberculosis with body wasting and that the effect of wasting on survival varies by sex. A reduced BMI at presentation with tuberculosis is associated with increased risk for death among both men and women whereas reduced lean tissue mass is among women. These observations may need further investigations in other settings, and it may be important to consider use of LMI as part of nutritional assessment to achieve early identification of patients at risk for poor outcomes.

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