

Low Mid-Upper Arm Circumference, Calf Circumference, and Body Mass Index and Mortality in Older Persons

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Background. Low body mass index is a general measure of thinness. However, its measurement can be cumbersome in older persons and other simple anthropometric measures may be more strongly associated with mortality. Therefore, associations of low mid-upper arm circumference, calf circumference, and body mass index with mortality were examined in older persons.

Methods. Data of the Longitudinal Aging Study Amsterdam, a population-based cohort study in the Netherlands, were used. The present study included community-dwelling persons 65 years and older in 1992–1993 ($n = 1,667$), who were followed until 2007 for their vital status. Associations between anthropometric measures and 15-year mortality were examined by spline regression models and, below the nadir, Cox regression models, transforming all measures to sex-specific Z scores.

Results. Mortality rates were 599 of 826 (73%) in men and 479 of 841 (57%) in women. Below the nadir, the hazard ratio of mortality per 1 standard deviation lower mid-upper arm circumference was 1.79 (95% confidence interval, 1.48–2.16) in men and 2.26 (1.71–3.00) in women. For calf circumference, the hazard ratio was 1.45 (1.22–1.71) in men and 1.30 (1.15–1.48) in women and for body mass index 1.38 (1.17–1.61) in men and 1.56 (1.10–2.21) in women. Excluding deaths within the first 3 years after baseline did not change these associations. Excluding those with a smoking history, obstructive lung disease, or cancer attenuated the associations of calf circumference (men) and body mass index (women).

Conclusions. Based on the stronger association with mortality and given a more easy assessment in older persons, mid-upper arm circumference seems a more feasible and valid anthropometric measure of thinness than body mass index in older men and women.

Key Words: Aged—Anthropometry—Body mass index—Mortality—Thinness.

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THE increased mortality risk at low body mass index (BMI; $\text{weight}/[\text{height}^2]$) values in old age is well established (1–5). BMI is therefore commonly incorporated in the assessment of undernutrition (6,7) or frailty (8) in older persons. The causality of this association is still debated and is recently suggested to be largely explained by chronic obstructive pulmonary disease and lung cancer (9).

Unfortunately, BMI is acknowledged to be of limited use in an older population for practical reasons (7). Measurement of height and weight can be a cumbersome procedure in older persons due to spinal deformities and difficulties with standing. Moreover, spinal deformities and fluctuations in body weight due to fluid retention might diminish the validity and reproducibility of this measure and thus influence the association with mortality. Alternative, easy-

to-assess anthropometric measures of thinness are therefore needed for this specific population group.

Low mid-upper arm circumference (MUAC) (6,10–11) and low calf circumference (12,13) have been proposed as alternative measures for determining thinness in older persons. Given the lack of a golden standard for assessing thinness, examining their association with mortality is considered a valid approach and was previously used for determining a clinical relevant cutoff point for low BMI in adults (14). A systematic comparison of the associations of these three anthropometric measures with mortality is however lacking.

Another deliberation when trying to maximize the association between an anthropometric measure and mortality is the hypothesis that low muscle mass is more strongly related to mortality than low fat mass in adults (15–17). In line with

this hypothesis, a previous study in community-dwelling older persons showed that a low corrected arm muscle area (MUAC—factor \times triceps skinfold thickness) was more strongly associated with mortality than a low BMI (18). Unfortunately, this measure requires triceps skinfold thickness measurement and additional calculation, which hampers its practical implementation. Moreover, studies based on accurate imaging techniques to validly assess muscle mass in older persons show inconsistent results as to whether a low muscle mass and/or low fat mass is associated with an increased mortality risk (19,20).

The aim of the present study was to examine and compare the associations of simple anthropometric measures, that is, low MUAC, low calf circumference, and low BMI, with 15-year all-cause mortality in a population-based sample of community-dwelling older men and women. By studying these associations, we aim to examine whether or not BMI can be substituted by MUAC or calf circumference to assess thinness in older persons, based on their equally strong or preferably stronger association with mortality.

METHODS

Study Sample

This study used prospective data of the Longitudinal Aging Study Amsterdam (LASA). LASA is an ongoing study on predictors and consequences of changes in physical, emotional, cognitive, and social functioning in older people in the Netherlands. A random sample stratified by age and sex according to expected mortality after 5 years was drawn from the population registries of 11 municipalities in three geographical areas of the Netherlands. A total of 3,107 men and women aged 55–85 years were enrolled at the baseline examination in 1992–1993. The total sample is representative of the Dutch general older population. Examinations are repeated approximately every 3 years and consist of a general face-to-face interview and a medical interview in the respondent's home. The details of the LASA study have been described elsewhere (21). For the present study, community-dwelling respondents aged 65 years and older in 1992–1993 ($n = 2,001$) with valid anthropometric measurements ($n = 1,667$) were included. The study was approved by the Ethics Review Board of the VU University Medical Center, and informed consent was obtained from all respondents.

Measures

Vital status and date of death was traced until June 1, 2007 through the registers of municipalities in which the respondents were living. Survival time was calculated in days from the baseline measurement in 1992–1993 to June 1, 2007. For six respondents, survival time was censored at April 1, 2003 due to incomplete follow-up after this date.

Anthropometric data were collected during the medical interview by trained research nurses using a standardized

protocol. Particularities during the measurements were reported using standard forms. Height was measured to the nearest 0.001 m using a stadiometer. When no valid height measurement could be obtained due to the recorded particularities, such as “not able to stand,” “shoes,” “kyphosis,” or “scoliosis,” or height missing, one of the following imputation methods were applied: (a) a valid follow-up measurement of height was used; (b) height was calculated for those with scoliosis or kyphosis using gender-specific prediction rules based on age and knee height (22) developed within the LASA sample with a valid height and knee height measurement; and (c) self-reported height was used. This imputation was performed in 112 of 1604 (7%) respondents. Knee height of the left leg was measured using a Mediform sliding caliper (Medical Express, Beaverton, OR) with the knee and ankle joints fixed at 90° angles. Weight was measured to the nearest 0.1 kg using a calibrated bathroom scale (Seca, model 100; Lameris, Utrecht, the Netherlands). Recorded weight particularities that lead to exclusion of respondents were “amputation,” “brace,” and “prothesis.” In addition, weight was adjusted for, respectively, “clothing” (–1 kg), “corset” (–1 kg), and shoes (–1 kg) (23). Self-reported weight was used when no measured weight was available (1%). BMI ($n = 1,604$) was calculated as body weight (kg) divided by height (m) squared. MUAC ($n = 1,626$) was measured at the left arm in duplicate to the nearest 0.001 m at a point midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna. The mean of two MUAC measurements was used for the analyses. Calf circumference was measured in half the study sample ($n = 877$) to the nearest 0.001 m on the left leg with the respondent standing straight, feet 20 cm apart, body weight equally distributed on both feet, and at the level of the widest circumference of the calf. The intraclass correlation coefficients for two duplicate anthropometric measures were >0.99 for MUAC and calf circumference (duplicate measurements of calf circumference were performed during one of the follow-up cycles of LASA).

The presence (yes or no) of obstructive lung disease (OLD; asthma, chronic bronchitis, or pulmonary emphysema) and cancer (malignant neoplasms) was determined by explicitly asking the participants whether they had these diseases. The accuracy of self-report data for these diseases as compared with general practitioners' information was shown to be adequate (24). Smoking status and history was assessed and categorized into current, former, and never-smokers. Former smokers who stopped smoking more than 15 years ago were classified as never-smokers because mortality in former smokers approaches the level of never-smokers after a smoking cessation time of 10–20 years (25,26).

Statistical Analyses

Separate analyses were performed for men and women because sex differences in the association between

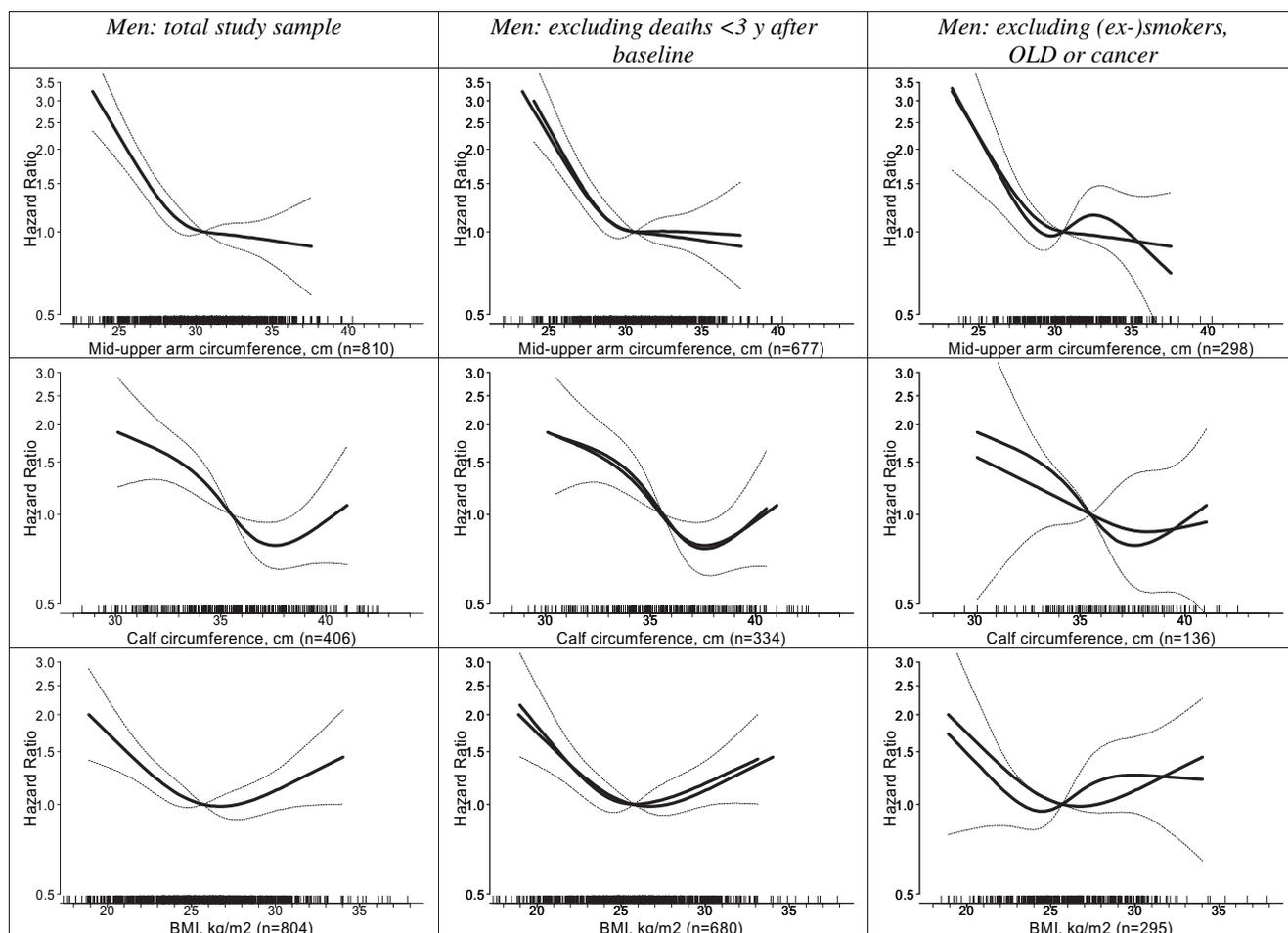


Figure 1. Dose–response associations between anthropometric measures and 15-year mortality among men, the Longitudinal Aging Study Amsterdam, 1992–1993. The left column shows the hazard ratios plotted on a logarithmic scale in the total study sample, the middle after excluding all deaths occurring within first 3 years after baseline, and the right column after excluding current and former smokers, obstructive lung disease (25), or cancer. The associations found in the total study sample (left) are superimposed in black on the other figures. Dotted lines represent the 95% confidence intervals, which converge to the median reference value (hazard ratio = 1) because standard errors become infinitely small when approaching the reference point. Rug plots are shown along the x-axes of the graphs to depict the distribution of the anthropometric measures.

anthropometric measures and mortality have been observed (14,16,27). Pearson correlation coefficients were calculated for determining associations between anthropometric measures at baseline.

The dose–response association between baseline anthropometric measures and 15-year mortality was examined by use of a Cox regression model with restricted cubic spline functions with four knots at quartiles of the independent variable. Most articles that describe the BMI mortality association in older persons convert the continuous independent variable BMI into categories (1–3). However, this method assumes homogenous risks within categories so that large sample sizes are needed to create very narrow groups (28). Spline regression models can fit complex distributions without assuming linear associations within categories, thus providing better insight into the true shape of the association (29). The hazard ratios (HR) and 95% confidence intervals (CI) were plotted using sex-specific medians of each anthropometric measure as the reference point

(HR = 1). Rug plots were calculated to depict the distribution of each anthropometric measure.

To examine the influence of preexisting illness and smoking on the association between anthropometric measures and mortality, two known methods (1–4) were used: (a) excluding those with a smoking history (current or former <15 years) or OLD or cancer, two important chronic diseases related to thinness (30); and (b) excluding all deaths occurring within the first 3 years after baseline.

Finally, the association between lower values of anthropometric measures and 15-year mortality was examined by a Cox regression model. First, all measures were transformed to sex-specific Z scores to standardize across different units of the anthropometric measures. The Z score was defined as a deviation from the sample mean value in standard deviation (SD) units. The Z scores were multiplied by -1 so that an HR > 1 indicated an increased mortality risk per 1 SD lower value of the anthropometric measure. Based on the dose–response associations depicted in Figures 1 and 2,

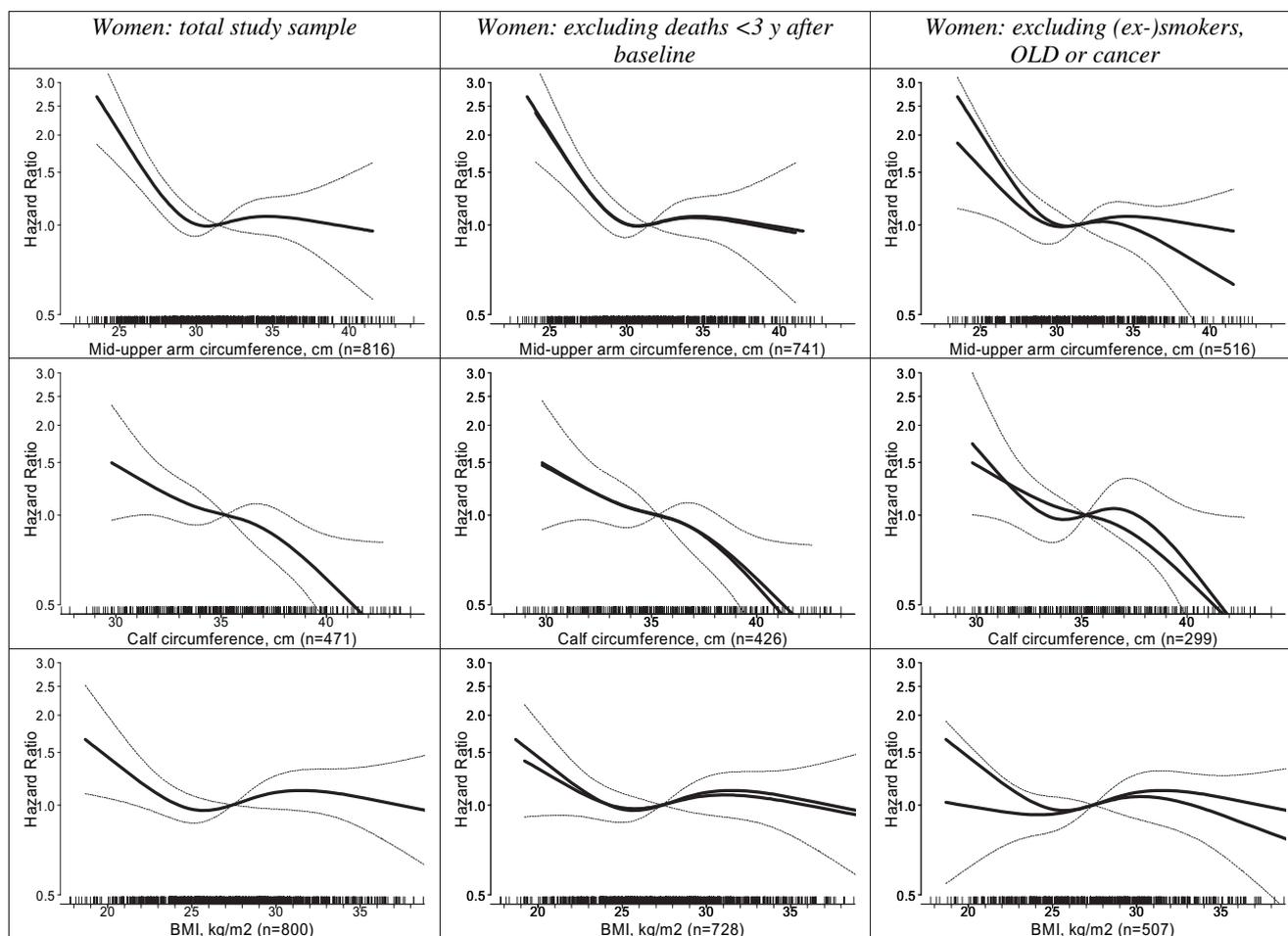


Figure 2. Dose–response associations between anthropometric measures and 15-year mortality among women, the Longitudinal Aging Study Amsterdam, 1992–1993. The left column shows the hazard ratios plotted on a logarithmic scale in the total study sample, the middle after excluding all deaths occurring within first 3 years after baseline, and the right column after excluding current and former smokers, obstructive lung disease (25), or cancer. The associations found in the total study sample (left) are superimposed in black on the other figures. Dotted lines represent the 95% confidence intervals, which converge to the median reference value (hazard ratio = 1) because standard errors become infinitely small when approaching the reference point. Rug plots are shown along the x-axes of the graphs to depict the distribution of the anthropometric measures.

these analyses were performed below the nadir of the dose–response curve. The linearity of the association in this range was furthermore confirmed by adding a quadratic term of the anthropometric measure to the model (all were nonstatistically significant). Because for calf circumference in women the association with mortality was linear across all values of calf circumference, all respondents were included. The assumption of proportional HR was checked by a time interaction test. As there is no accepted statistical method for testing the difference between two HRs using partially paired measures, we evaluated whether the HR of a measure overlapped with the 95% CI around the HR of another measure. No overlap was considered as a statistical significant difference.

We used two-sided tests at a .05 significance level. All statistical analyses were performed with SPSS 14.0 and R statistical software (R development Core Team, R Foundation for Statistical Computing, Vienna, Austria, version 2.6.2).

RESULTS

Overall, 17% (334 of 2,001) of eligible respondents were excluded due to missing data on all anthropometric measures mainly because they refused to participate in the medical interview. Compared with included respondents, those excluded were on average older and had a higher 15-year mortality rate (Table 1). Characteristics of the included study sample are shown in Table 2. Those who died within 15 years had on average a lower MUAC and calf circumference ($p < .01$), but not a lower BMI. The Pearson correlation coefficients between MUAC and BMI were .83 in both men and women. The coefficients between MUAC and calf circumference were .69 (women) and .70 (men), and between BMI and calf circumference .70 (women) and .74 (men).

Of the 826 men included at baseline, 599 (73%) died during the 15 years of follow-up. Of the 841 women, 479 (57%) died (Table 1). Figures 1 and 2 show the dose–response

Table 1. Description of the Study Sample by Inclusion and Exclusion* and Sex, The Longitudinal Aging Study Amsterdam, 1992–1993

	Men			Women		
	Included	Excluded	<i>p</i> Value [†]	Included	Excluded	<i>p</i> Value [†]
Respondents, <i>n</i> (%)	826 (85)	147 (15)		841 (82)	187 (18)	
Age, mean (<i>SD</i>), y	74.7 (5.7)	76.2 (5.4)	.003	74.1 (5.9)	75.8 (6.0)	.001
Died within 15 y, <i>n</i> /total (%)	599/826 (73)	127/147 (86)	<.001	479/841 (57)	129/187 [‡] (70)	.001

Notes: *SD* = standard deviation.

*Missing data on all anthropometric assessments because of refusal to participate in the medical interview (*n* = 324) or missing data on cancer, obstructive lung disease/smoking status (*n* = 10).

[†]Differences between included and excluded respondents are tested by means of a Student's *t* test (age) and a log rank test with adjustment for survival time (died within 15 years).

[‡]For three respondents, vital status in 2003 (all alive) was used instead of 2007.

association of each anthropometric measure with 15-year mortality. In the total study sample (Figures 1 and 2, left column), MUAC showed an inversely J-shaped association with mortality in both men and women. Calf circumference showed a U-shaped or inversely J-shaped association with mortality in men and a linearly decreasing association in women. BMI showed a U-shaped association with mortality in men and an inversely J-shaped association in women. Excluding all deaths occurring within the first 3 years after baseline (16% of men, 10% of women) hardly changed these associations (Figures 1 and 2, middle column). Excluding (former) smokers and persons with cancer or OLD (63% of men and 37% of women) resulted in a shift of the BMI nadir (point of lowest mortality risk) to the left and, in women, the association with BMI disappeared. The association with low MUAC remained (Figures 1 and 2, right column; Table 3).

Low MUAC was more strongly associated with mortality than BMI and low calf circumference (Figures 1 and 2; Table 3). In the total study sample, the HR of mortality per 1 *SD* lower MUAC was 1.79 (95% CI, 1.48–2.16) in men and 2.26 (95% CI, 1.71–3.00) in women. In both men and women, the point estimate of MUAC was higher and did not overlap with the CI of the HR of mortality per 1 *SD* lower BMI or 1 *SD* lower calf circumference (Table 3).

DISCUSSION

In this longitudinal study representative of Dutch community-dwelling persons 65 years and older, low MUAC was statistically significantly associated with an increased 15-year mortality risk in men and women, even after excluding all deaths occurring within the first 3 years after baseline or those with a smoking history, OLD, or cancer. Low MUAC was found to be more strongly associated with 15-year mortality than low BMI and low calf circumference in both men and women.

To our knowledge, this is the first study that compares mortality associations of these simple anthropometric measures of thinness in older persons from the general population. In other study populations, like in acutely hospitalized patients, low MUAC was also found to be more strongly associated with hospital mortality than low BMI (10). In community-dwelling adults, low MUAC was more strongly associated with mortality from causes other than cardiovascular disease, diabetes, or obesity-related cancers than low BMI, low hip circumference, or low waist circumference, although these differences were statistically significant for waist circumference only (31).

The association between thinness and mortality may be explained by the hypothesized adverse effects of a low muscle mass and/or low fat mass in older persons. Studies

Table 2. Characteristics of the Included Study Sample by 15-year Mortality and Sex, The Longitudinal Aging Study Amsterdam, 1992–1993

	Men					Women				
	Survived	<i>n</i> *	Died	<i>n</i> *	<i>p</i> [†]	Survived	<i>n</i> *	Died	<i>n</i> *	<i>p</i> [†]
Mid-upper arm circumference, mean (<i>SD</i>), cm	31.1 (2.6)	225	30.2 (3.2)	585	<.001	31.9 (3.6)	356	31.2 (4.0)	460	.007
Calf circumference [‡] , mean (<i>SD</i>), cm	36.3 (2.4)	117	35.3 (2.8)	289	<.001	36.1 (3.2)	214	34.9 (3.0)	257	<.001
Body mass index, mean (<i>SD</i>), kg/m ²	25.9 (2.8)	225	25.7 (3.4)	579	.434	27.8 (4.6)	349	27.6 (4.7)	451	.448
Obstructive lung disease, <i>n</i> /total (%)	22/227 (9.7)		93/599 (15.5)		.040	31/363 (8.5)		60/484 (12.4)		.093
Cancer, <i>n</i> /total (%)	9/227 (4.0)		58/599 (9.7)		.011	31/362 (8.6)		67/483 (13.9)		.023
Current/former smoker, <i>n</i> /total (%)	104/227 (45.8)		344/599 (57.4)		.004	71/363 (19.6)		119/480 (24.8)		.086

Notes: *SD* = standard deviation.

*Number of respondents with valid data for that anthropometric measure.

[†]Differences between those who died and stayed alive are tested—not adjusting for survival time—by a Student's *t* test (anthropometric measures) and a Yates' corrected chi-square test (dichotomous variables).

[‡]Measurement performed in 50% of respondents.

Table 3. The HR of 15-Year Mortality Per 1 *SD* Lower Value of Each Anthropometric Measure, The Longitudinal Aging Study Amsterdam, 1992–1993

	Men			Women		
	Included*	<i>n</i> *	HR (95% CI) [†]	Included*	<i>n</i> *	HR (95% CI) [†]
Total study sample						
Mid-upper arm circumference, cm	<30.0	344	1.79 (1.48–2.16)	<30.0	281	2.26 (1.71–3.00)
Calf circumference, cm	<37.6	311	1.45 (1.22–1.71)	All	471	1.30 (1.15–1.48)
Body mass index, kg/m ²	<26.7	516	1.38 (1.17–1.61)	<25.7	289	1.56 (1.10–2.21) [‡]
Excluding deaths within the first 3 y after baseline						
Mid-upper arm circumference, cm	<30.0	274	1.85 (1.48–2.32)	<30.0	254	2.12 (1.55–2.91)
Calf circumference, cm	<37.6	256	1.41 (1.16–1.71)	All	426	1.32 (1.15–1.52)
Body mass index, kg/m ²	<25.8	343	1.44 (1.16–1.80)	<25.7	263	1.39 (0.94–2.05)
Excluding (ex-)smokers, OLD or cancer						
Mid-upper arm circumference, cm	<30.0	106	2.17 (1.49–3.16)	<30.0	181	1.75 (1.20–2.53)
Calf circumference, cm	<38.2	103	1.25 (0.90–1.75)	All	299	1.27 (1.07–1.49)
Body mass index, kg/m ²	<24.5	88	1.44 (0.82–2.52)	<24.2	124	0.93 (0.43–1.98)

Notes: CI= confidence interval; HR= hazard ratio; OLD = obstructive lung disease; *SD* = standard deviation.

* Analyses are performed below the nadir of the dose–response curve (Figures 1 and 2).

[†] An HR > 1 indicates an increased mortality risk per 1 *SD* lower value of the anthropometric measure.

[‡] The proportional hazard assumption was violated in women, that is, there was a positive interaction between time and a decrease in BMI ($p = .02$). Stratified by time, 1 *SD* lower BMI was associated with 7-year mortality (HR = 2.13; 95% CI, 1.32–3.56), but not with 7- to 15-year mortality (HR = 1.14; 95% CI, 0.68–1.90).

favoring that low muscle mass is associated with increased mortality and not low fat mass used imprecise estimates of muscle mass like anthropometric measures (16) and bio-electrical impedance (17), but also the more accurate method total body potassium counting (15). However, these studies were not performed in older persons specifically. In older persons, based on accurate imaging methods—that is, computed tomography scanning and/or dual energy x-ray absorptiometry—the results are conflicting. One study found no clear association between low muscle mass and mortality (19), whereas another study found that both low muscle mass and low fat mass were associated with mortality in community-dwelling older persons (20). Other studies indicate that leg fat mass is associated with more unfavorable glucose and lipid levels in older persons after taking into account the association with trunk fat mass, which is in the opposite direction (32,33). In sum, both low muscle mass and low leg fat mass may be associated with increased mortality risk in older persons, but further studies using accurate imaging methods are needed.

The stronger mortality association of low MUAC compared with low BMI may thus be explained by the assumption that MUAC is a better measure of muscle mass than BMI but further research on this topic is clearly needed. Another explanation may be that spinal deformities and body fluid changes associated with old age diminish the validity and reproducibility of BMI and thus attenuate the association with mortality. Fluid retention may also explain why low calf circumference is more weakly associated with mortality than low MUAC.

To examine the effect of severe underlying disease on the association between thinness and mortality, two approaches also applied in previous studies were used (1–4). First, excluding all deaths occurring within the first 3 years after

baseline did not alter the associations, which is in line with results from a meta-analysis of 29 studies investigating the effect of excluding early deaths from the BMI mortality association (34). Excluding (former) smokers and persons with cancer or OLD resulted in a shift of the BMI nadir to the left, whereas in women the association with BMI disappeared. This suggests that underlying disease may explain (part of) the association with low BMI, especially in women. These results give rise to reasonable doubt about a causal link between low BMI and mortality, which is in line with a recent large collaborative study that showed that the association between low BMI and mortality was largely explained by chronic obstructive pulmonary disease and lung cancer (9). In contrast, the mortality association of low MUAC remained after exclusion of these diseases, which supports a potential causal link between low MUAC and mortality.

An important advantage of using MUAC compared with BMI is that it can be easily obtained in older persons using a simple measure tape. As an illustration, for the 112 respondents of our study with no a valid height measurement (height was imputed), 100 had a valid MUAC measurement. There are no constraints of standing problems or spinal deformities and a negligible influence of fluid retention. As indicated by our study as well as by others (35), the reproducibility of MUAC measurements has been shown to be exceptionally good with intraclass correlation coefficients of .98 for between-observer (35) and 0.99 for within-observer variations, with the patient in either sitting or standing position (35).

A second advantage of using MUAC compared with BMI is that the dose–response association with mortality seems to follow a similar pattern in both men and women. This also holds for the distribution of MUAC; the 5th percentile of

MUAC was 25 cm in both men and women (data not shown). This suggests that a potential MUAC cutoff point used to define thinness could be similar for men and women.

Our study has some limitations. Although the LASA sample is a representative sample of the general Dutch older population, in this study, 17% was excluded due to missing data on anthropometric measures, resulting in a younger and healthier sample. This could have led to an underestimation of the strengths of the observed associations. Furthermore, we could not directly test the differences in strength of the association with mortality between the three anthropometric measures because different subjects are inevitably included in each analysis. For example, those with a low BMI may not have a low MUAC, and calf circumference was measured in only 50% of subjects. However, visual inspection of the figures and comparison of the HRs consistently showed that low MUAC was most strongly associated with mortality. Another limitation is that although we applied commonly used methods to eliminate confounding by underlying (severe) diseases and smoking, it is generally known that causality cannot be determined using observational cohort studies.

The strengths of this study are the long (15 years) follow-up and the fact that commonly used and easy-to-assess anthropometric measures were studied, which enhances the potential applicability of the results to clinical practice. Another strength was the use of sophisticated spline regression techniques that allowed a detailed study of the exact dose-response associations, which turned out to be nonlinear. Future research is needed to assess whether these results can be replicated in other study populations and with other relevant outcome measures.

In conclusion, low MUAC was statistically significantly associated with an increased 15-year all-cause mortality risk in community-dwelling older persons. It was more strongly associated with mortality than low BMI and low calf circumference. Given the reliable and easy assessment of MUAC in older persons, MUAC seems a more feasible and valid measure of thinness than BMI in older men and women.

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