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Is fat mass a better predictor of 6-month survival than muscle mass among African children aged 6–59 months with severe pneumonia?

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Abstract

Background Pneumonia remains the leading cause of mortality among children under 5 years. Poor nutritional status increases pneumonia mortality. Nutritional status assessed by anthropometry alone does not provide information on which body composition element predicts survival. Body composition proxy measures including arm-fat-area (AFA), arm-muscle-area (AMA), and arm-muscle-circumference (AMC) could be useful predictors.

Objective To compare the ability of fat and muscle mass indices to predict 6-month survival among children with severe pneumonia.

Methods This prospective cohort study was nested in the COAST-Nutrition trial (ISRCTN10829073, 06/06/2018) conducted between June 2020 and October 2022 in Uganda and Kenya. We included children aged 6–59 months hospitalized for severe pneumonia with hypoxemia. Children with severe malnutrition, known chronic lung or cardiac diseases were excluded. Anthropometry and clinical status were assessed at enrolment and at follow-up to day 180. We examined Receiver Operator Characteristic (ROC) curves of fat and muscle mass indices with 6-month survival as the outcome, and compared the areas under the curve (AUCs) using chi-square tests. Cox survival analysis models assessed time-to-mortality.

Results We included 369 participants. The median age was 15-months (IQR 9, 26), and 59.4% (219/369) of participants were male. The baseline measurements were: median MUAC 15.0 cm (IQR 14.0,16.0); arm-fat-area 5.6cm^2 (IQR 4.7, 6.8); arm-muscle-area 11.4cm^2 (IQR 10.0, 12.7); and arm-muscle-circumference 12.2 cm (IQR 11.5, 12.9). Sixteen (4.3%) participants died and 4 (1.1%) were lost-to-follow-up. The AUC for Arm-Fat-Area was not significantly higher than that for Arm-Muscle-Area and Arm-Muscle-Circumference [AUC 0.77 (95%CI 0.64–0.90) vs. 0.61 (95%CI 0.48–0.74), $p=0.09$ and 0.63 (95%CI 0.51–0.75), $p=0.16$ respectively], but was not statistically different from MUAC (AUC 0.73 (95%CI 0.62–0.85), $p=0.47$). Increase in Arm-Fat-Area and Arm-Muscle-Circumference significantly improved

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survival [aHR 0.40 (95%CI 0.24–0.64), p = < 0.01 and 0.59 (95%CI 0.36–1.06), $p = 0.03$ respectively]. Survival prediction using Arm-Fat-Area was not statistically different from that of MUAC ($p = 0.54$).

Conclusions Muscle mass did not predict 6-month survival better than fat mass in children with severe pneumonia. Fat mass appears to be a better predictor. Effects of fat and muscle could be considered for prognosis and targeted interventions.

Keywords Pneumonia, Fat mass, Muscle mass, Children, Mortality

Introduction

Pneumonia is the leading cause of morbidity and mortality in children accounting for 14% deaths of children under 5 years and up to 22% of children between 1 and 5 years [1]. Despite effective inpatient treatment of severe pneumonia, many children are reported to die in hospital, or following hospital discharge [1–3]. While in-hospital mortality may be associated with many individual and environmental factors, the key risk factor for post-discharge mortality is poor nutritional status [2, 4–6]. Pneumonia, as are many severe infections, is associated with a catabolic state, resulting from release of stress hormones (cortisol and catecholamines) that lead to a 'hypermetabolic' response in order to rapidly mobilize energy [7]. It is largely associated with breakdown of protein to generate glucose through liver gluconeogenesis and utilization of amino acids by immune cells to produce acute phase proteins [8]. Consequently, there is rapid skeletal muscle breakdown leading to muscle cachexia or 'wasting' [9]. During fasting states, the body transitions from utilization of carbohydrates as the main source of energy to fat [7, 10]. In severely malnourished children, fat is the main source of energy [10]. An acute process like pneumonia predisposes children to poor nutritional status and may lead to severe malnutrition through loss of fat and muscle mass, which in turn increases their risk of recurrent infections and death. A cohort study among adult men with stable chronic obstructive airways disease (COPD) showed that mid-arm muscle area (MAMA) ≤ 25% was associated with an increased mortality [11]. Respiratory muscles are highly specialized and consume a large amount of energy, especially during an episode of pneumonia when the rate and effort of breathing are substantially increased. Adequate ventilatory function during hypoxic illnesses requires good muscle function, so one would expect muscle mass to be more important for survival than fat mass.

Assessment of nutritional status in hospital and field-based studies is largely based on simple practical measurements such as weight, height, mid-upper arm circumference (MUAC) and derived indices such as weight-for-height z-score (WHZ) and weight-for-age z-score (WAZ). These however do not fully describe the proportions of body tissue compartments relative to each other (body composition) which may isolate the component that might be responsible for and could be used to predict survival [12]. Furthermore, they offer no guidance on what component could be repleted to improve survival. Arm muscle area or circumference can be considered as a proxy estimate of muscle mass in the arm region. Thus, MUAC is related to muscle mass, which during catabolism serves as the principal reservoir of amino acids in vital organs [13] and may be a good predictor of survival [14]. Arm fat and muscle mass could be useful predictors of mortality in children [15, 16], such as children with pneumonia. Use of arm anthropometry including arm muscle area and arm fat area, as proxies for arm fat and muscle mass respectively in children with pneumonia could be useful for risk prediction and monitoring because it is cheap and non-invasive [17].

We hypothesized that muscle mass indices predict survival among children with severe pneumonia better than fat mass indices. The aim of the study was to compare the ability of fat and muscle mass to predict 6-month survival among children with severe pneumonia.

Methods

Description of the study

This study was a hospital-based prospective cohort study nested under the COAST-Nutrition trial (ISRCTN10829073, 06/06/2018 and PACTR202106635355751, Protocol Ref Makerere: #REC REF 2020−155). It was conducted between June 2020 and October 2022 in Uganda (Mbale Regional Referral Hospital, Soroti Regional Referral Hospital, Jinja Regional Referral Hospital, Masaka Regional Referral Hospital) and in Kenya (Kilifi County Hospital). Children were enrolled in the COAST-Nutrition trial if: aged 6 months to 12 years and hospitalized for severe pneumonia as defined by WHO (cough and or difficulty in breathing with chest indrawing and general danger signs) [18] ; had hypoxemia (pulse oximetry reading of $SPO_2 < 92\%$ recorded in room air over 5 min; and parents or guardians consented to participate in the study. Children with severe malnutrition (MUAC < 11.5 cm, and/or the presence of bilateral oedema), known chronic lung disease, or congenital cardiac disease were excluded from the clinical trial. Children were randomized to nutritional supplementation with Ready-to-Use Therapeutic Foods (RUTF) in addition to usual diet for 56 days compared to usual

diet al.one (control). Details of the main clinical trial under which this study was nested are published in the trial protocol [19].

Study and trial specific assessments

Participant recruitment and follow up

At the point of hospital admission, eligible children with suspected severe pneumonia and hypoxaemia (oxygen saturations on pulse oximetry of <92%) were screened and consecutively enrolled. Parental consent was obtained for inclusion in the trial and additional anthropometric measurements. All study participants were followed up until death or study completion (Day 180), whichever occurred first. Full details of the trial protocol including the anthropometric sub-studies have been published [19]. In this sub-study we only included children enrolled into the control arm (received only their usual diet, without supplemental feeding with ready to use therapeutic food, in addition to their pneumonia treatment) and were aged 6–59 months.

Assessment of independent variables

Participants' history (symptoms at presentation to hospital and associated factors) was obtained from caregivers and entered into a questionnaire. Clinical examination was done by medical officers and the findings as well as the results of the laboratory investigations at admission to hospital were entered in a questionnaire.

Anthropometric measures All children enrolled into the study had baseline measurements of mid-upper arm circumference (MUAC) measured with a recommended non-stretchable tape to the nearest millimeter. Triceps skinfold thickness (TST) was measured with a special caliper (Harpenden ®) by trained research staff to the nearest 0.2 mm. Two measurements were taken and the average was recorded [19]. If there were significant differences between the two measurements taken, another research assistant independently took his/her own measurements and the average was recorded. Research assistants at all sites were trained on taking anthropometric measurements prior to starting data collection and periodically for the duration of the study.

Estimation of body composition Body composition is most accurately assessed by invasive and clinically impractical procedures such as densitometry and isotope dilution for total body water [20]. Some less invasive methods use the two-compartment model to describe overall body composition by dividing the body into two compartments: fat mass (FM) and fat free mass (FFM) or lean mass which includes muscle, bone and body organs, without giving information on distribution [20]. One of the relatively simple techniques utilizes anthropometric indices incorporating MUAC and triceps skinfold thickness (TST) to measure adipose tissue distribution and estimate overall body composition using indices like arm fat area (AFA), arm muscle area (AMA) and arm muscle circumference (AMC) [21]. Arm fat area and arm muscle area calculations are based on assumptions that: (i) the arm is cylindrical; (ii) subcutaneous fat is evenly distributed around a circular core of muscle; and (iii) Triceps skinfold thickness (TST) reflects the fat components of the arm and represents twice the thickness of subcutaneous fat in the arm [21].

When the anthropometric indices were evaluated for validity among healthy and sick children (with cystic fibrosis) using dual x-ray absorptiometry and four-component model to provide reference values for arm and whole-body fat mass (FM) and fat-free mass (FFM), Chomtho et al. found that arm fat area (AFA), MUAC, and TST correlated strongly with arm FM (r=0.84–0.92) and total FM (r=0.78–0.92). However, AMA and MUAC are weakly correlated with fat free mass indices [17]. Rolland-Cachera et al. validated the arm muscle area, arm fat area, and arm circumference against magnetic resonance imaging (MRI) and found that these were indeed accurate for assessment of body composition [22]. We retrospectively calculated Arm muscle circumference (AMC), arm muscle area (AMA) and arm fat area (AFA) by the equations proposed by Rolland-Cachera. AMC, AFA and AMA were estimated from MUAC and TST. The AMC was calculated with the formula AMC=MUAC − π TST where π=22/7. The AFA is calculated from the formula MUAC × TST/2. The AMA was calculated with the formula; AMA = $(MUAC)^2/4\pi$ − MUAC × TST/2 [22]. This is illustrated in Fig. 1.

Sample size estimation

This was a sub-analysis of participants aged 6–59 months who were randomized to the control (usual diet) arm of the COAST-Nutrition trial (Fig. 2). We used a convenient sample for this study which was based on the available participants from the main trial in Uganda and Kenya. With an Area Under the Curve (AUC) of 0.8, mortality of 14% [1], a sample size of 369 children gave a confidence interval width of 0.15 for a confidence level of 0.95 [23].

Data analysis

The primary outcome was survival at day 180 of follow up (expressed as a proportion). The independent variables included MUAC, arm muscle circumference (AMC), arm muscle area (AMA), arm fat area (AFA) as well as age, gender and history (symptoms at presentation), clinical examination findings and laboratory results at admission to hospital (baseline). Receiver operator characteristic (ROC) curves for MUAC, AMC, AMA, and AFA on admission were generated using STATA version MP16

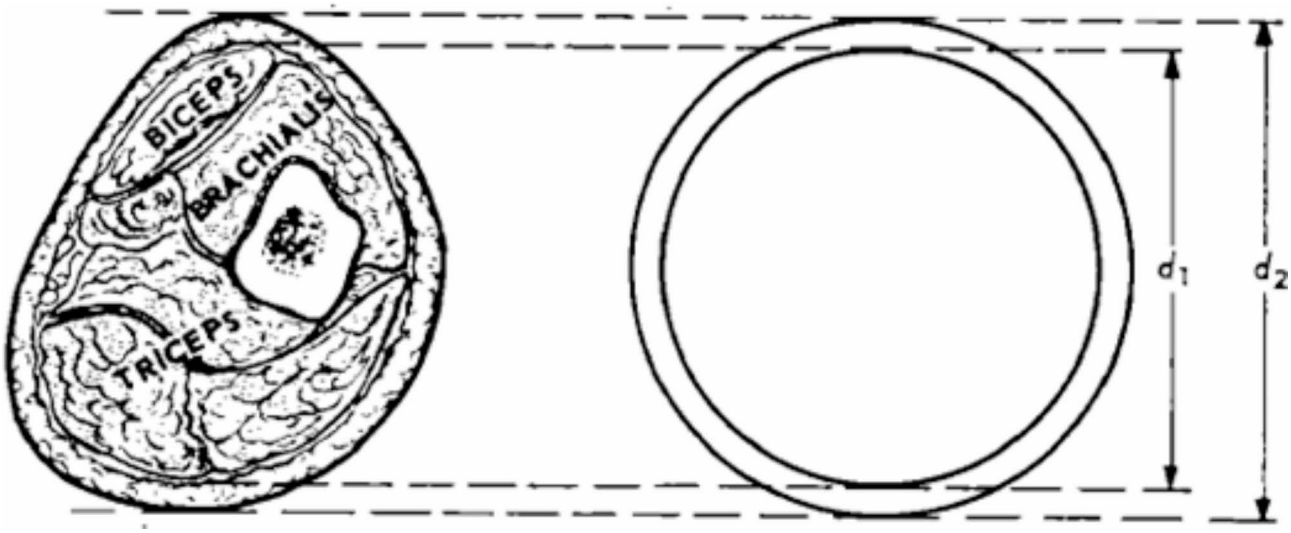

Fig. 1 Transverse section of the arm showing assumptions of fat and muscle area. *$d_1$represents arm muscle area estimate (fat free mass), while $d_{2\ represents}$the total arm area estimate. AFA = MUAC × TST/2, while AMA = (MUAC)²/4π – MUAC × TST/2*

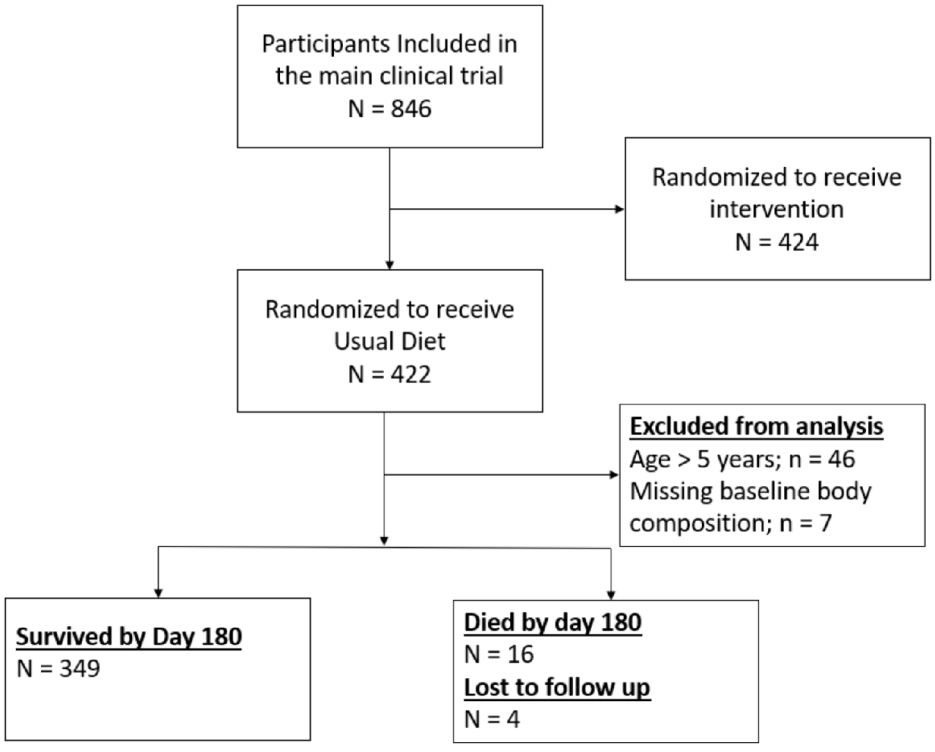

Fig. 2 Study flow reflecting participants included in this sub-study of the main trial. *A total of 369 participants were included in this study*

(StataCorp LLC, College Station, Texas, USA), and examined with survival at day 180 of follow-up as the outcome. The fat and muscle mass indices most predictive of the outcome were expected to have a greater AUC than other indices. The AUC for AFA was compared to that of AMA and AMC using the Chi-square test.

The AUC for AMC, AMA, and AFA were also compared to that of MUAC, currently the best predictor of mortality [24], using the Chi-square test. We used the Cox survival analysis model to generate hazard ratios for AMC, AMA, and AFA to that of MUAC, while controlling for baseline risk factors.

All analyses were adjusted for age in months, gender, breastfeeding status and respiratory rate at baseline (admission to hospital). These were selected based on

Table 1 Participants' baseline clinical characteristics

Characteristic	Overall *N* = 369
Age in months (Overall): median (IQR)	15 (9,26)
Age group in months; *n* (%)	
< 12 months	126 (34.2)
12–23 months	127 (34.4)
24–59 months	116 (31.4)
Male Gender; *n* (%)	219 (59.4)
History of Breast feeding; *n* (%)	334 (90.5)
Respiratory Distress (in-drawing, grunting, nasal flaring); *n* (%)	359 (97.3)
Baseline Oxygen saturation (%) Median (IQR)	89 (87, 90)
General WHO danger sign[2]; *n* (%)	94 (25.5)
Signs of shock[3]; *n* (%)	12 (3.3)
Severe Pallor; *n* (%)	32 (8.7)
Reported HIV Status; *n* (%)	
Positive	4 (1.1)
Negative	355 (96.2)
Severe Malaria; *n* (%)	72 (19.5%)
Hemoglobin concentration (g/dL)[1]; (mean, SD)	10 (2.4)
MUAC (cm); Median (IQR)	15.0 (14.0, 16.0)
TST (cm); Median (IQR)	0.8 (0.7, 0.9)
AMC (cm); Median (IQR)	12.2 (11.5, 12.9)
AMA (cm^2); Median (IQR)	11.4 (10.0, 12.7)
AFA (cm^2); Median (IQR)	5.6 (4.7, 6.8)
Weight for Height Z score (WHZ); Median (IQR)	-0.3 (-1.2, 0.6)
Weight for Age Z score (WAZ); Median (IQR)	-0.5 (-1.4, 0.2)
BMI for Age Z score (BAZ)[1]; Median (IQR)	-0.5 (-1.3, 0.4)
Height for Age score (HAZ); Median (IQR)	-0.5 (-1.4, 0.3)

[1]missing data; Hemoglobin concentration N = 367, BAZ; N = 240 [2]WHO danger signs: persistent vomiting, convulsions, lethargic or unconscious [30], *[3]Signs of shock were assessed clinically using capillary refill, pulse, and temperature gradient. MUAC; Mid upper arm circumference, TST; Triceps skinfold thickness, AMC; Arm muscle circumference, AMA; Arm muscle area, AFA; Arm fat area, BMI; Body mass index*

biological plausibility using available literature, as well as having sufficient numbers of outcomes for comparison.

Results

A total of 369 participants were included in the study. The median age was 15 months (IQR 9, 26), with 68.6% (n=253) of the participants aged 6–23 months. 59% (n=219) of the participants were male, and most were reported to have breastfed beyond 3 months (90.5%, n=334). Nearly all (97.3%, n=359) participants had signs of respiratory distress and hypoxia at presentation, with a median oxygen saturation of 89% (IQR 87, 90) on room air. Additionally, a quarter (n=94) of the participants had at least one more WHO danger sign. About one fifth (72, 19.5%) had a diagnosis of severe pneumonia at admission, 4 (1%) were known to be HIV infected, and 32 (8.7%) had severe pallor. The majority of the participants were healthy with a median MUAC of 15.0 cm (IQR 14.0, 16.0). The median AFA was 5.6 cm^2 (IQR 4.7, 6.8), median AMA 11.4 cm^2 (IQR 10.0, 12.7) and AMC 12.2 cm (IQR 11.5, 12.9). The baseline clinical and anthropometric characteristics of the study participants are summarized in Table 1. Of the 369 participants enrolled in this study, 16 (4.3%) died before Day 180 and 4 (1.1%) were lost to follow up.

Table 2 Survival prediction by anthropometric measurements using area under the curve (AUC)

Measurement	Unadjusted AUC (95% CI), (*N* = 364)	Adjusted AUC (95% CI), *N* = 360)	Chi^2*p* value*	Chi^2*p* value#
MUAC (cm)	0.70 (0.58–0.82)	0.73 (0.62–0.85)	0.47	**Ref**
AMA (cm^2)	0.61 (0.48–0.74)	0.63 (0.51–0.75)	0.09	0.01
AFA (cm^2)	0.75 (0.62–0.88)	0.77 (0.64–0.90)	**Ref**	0.47
AMC (cm)	0.64 (0.51–0.77)	0.66 (0.54–0.78)	0.16	0.04
WHZ	0.64 (0.51–0.77)	0.64 (0.50–0.78)	0.19	0.23
WAZ	0.71 (0.57–0.85)	0.73 (0.60–0.87)	0.69	0.99
BAZ*	0.50 (0.32–0.67)	0.57 (0.40–0.74)	0.13	0.20
HAZ	0.68 (0.52–0.83)	0.69 (0.53–0.84)	0.39	0.58

**N = 236 (Unadjusted), N = 233 (Adjusted), CI; Confidence interval, AUC; Area under the curve, MUAC; Mid upper arm circumference, AMC; Arm muscle circumference, AMA; Arm muscle area, AFA; Arm fat area, WHZ; Weight for Height Z score, WAZ; Weight for Age Z score, BAZ; Body mass index for Age Z score, HAZ; Height for Age score. Each ROC curve was adjusted for age in months, gender, breastfeeding status and respiratory rate.*
** Chi^2p value comparing adjusted AUC for AFA to AUC for MUAC, AMA, AFA and AMC,*
 # Chi^2p value comparing adjusted AUC for AMA, AFA and AMC to AUC for MUAC to test for statistical difference

Arm Fat Area (AFA) had higher adjusted AUC (0.75, CI 0.62–0.88) than AMA (0.61, 95%CI 0.48–0.74) and AMC) (0.63, 95%CI 0.51–0.75), but the differences were not statistically significant (p=0.09 and p=0.16 respectively).

There was no difference between the adjusted AUC for MUAC (0.73, 95%CI 0.62–0.85) and the adjusted AUC for AFA (0.75, 95%CI 0.62–0.88) (p=0.47). However, the adjusted AUC for MUAC (0.73, 95%CI 0.62–0.85) was significantly different from the adjusted AUC for AMA (0.61, 95%CI 0.48–0.74) and AMC (0.63, 95%CI 0.51–0.75) (p=0.01 and p=0.04 respectively). The AUC for WAZ was not statistically different from that of MUAC and AFA (0.73, 95%CI 0.60–0.87) (p=0.69 and p=0.99 respectively). Weight for Height z score (WHZ), HAZ and BAZ had lower AUC than that of AFA and MUAC (0.64 (95%CI 0.50–0.78), 0.69 (95%CI 0.53–0.84) and 0.57 (95%CI 0.40–0.74) respectively) but this did not reach statistical significance (p=0.19, 0.39, and 0.13 respectively for comparison with AFA and p=0.23, 0.58 and 0.20 respectively for comparison with MUAC). The unadjusted and adjusted AUC of AFA, AMA, AMC, AFA, MUAC, WHZ, WAZ, BAZ and HAZ are summarized in Table 2. The adjusted ROC curves are presented in Fig. 3.

Using the Cox survival analysis model, we estimated the hazard ratios (HR) for Day 180 mortality for the anthropometric measurements (unadjusted HR) and adjusted HR after controlling for age, gender, and signs of respiratory distress. The adjusted hazard ratios show that a 1 unit increase in MUAC, AFA, AMC, WAZ and HAZ significantly improves the chances of survival by 55%, 60%, 41%, 47%, and 30% respectively (p=0.01, <0.01,

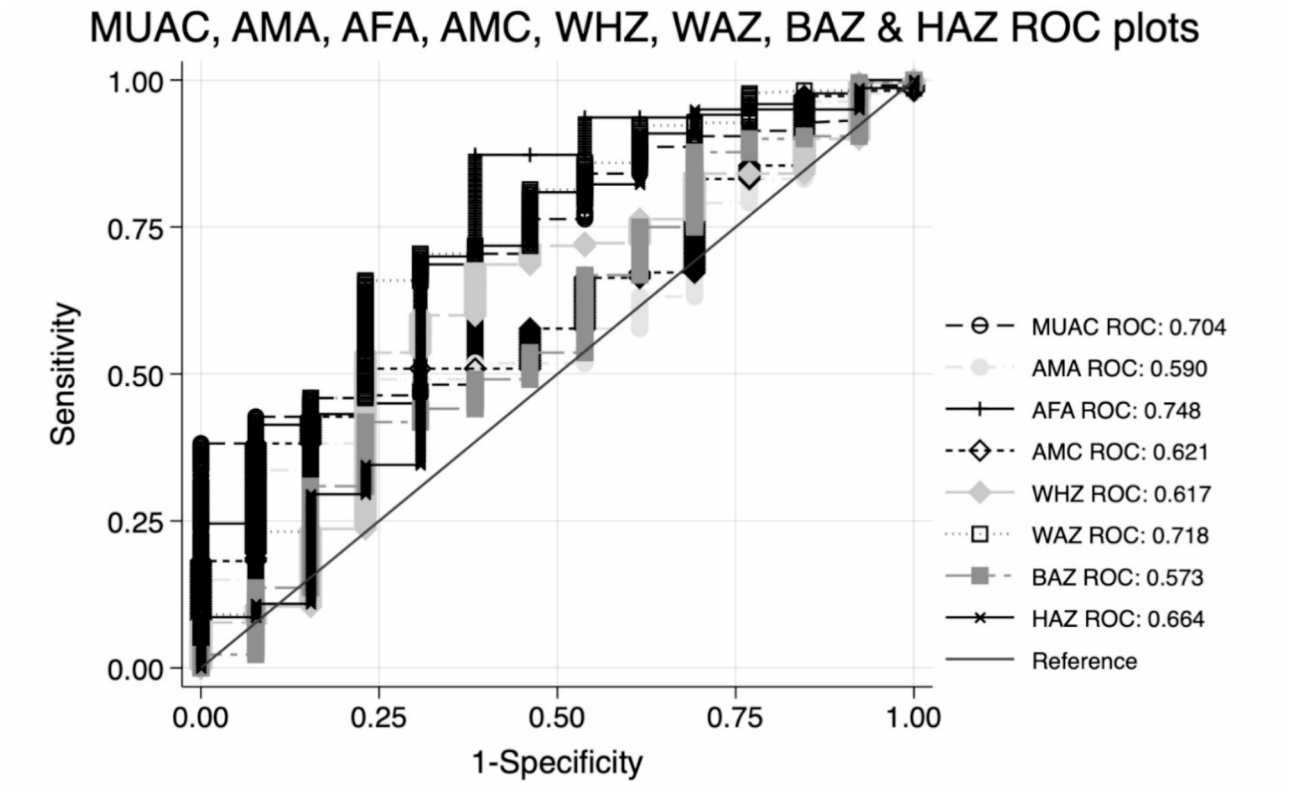

Fig. 3 Receiver Operating Curves showing ability of AUC for MUAC, AMC, AMA, AFA, WHZ, WAZ, BAZ, and HAZ to predict survival at 180 days. *Adjusted for age in months, gender, breastfeeding status and respiratory rate, MUAC; Mid upper arm circumference, AMC; Arm muscle circumference, AMA; Arm muscle area, AFA; Arm fat area, WHZ; Weight for Height Z score, WAZ; Weight for Age Z score, BAZ; Body mass index for Age Z score, HAZ; Height for Age score*

Table 3 Cox survival analysis model for mortality prediction of fat and muscle mass indices

Measure	Unadjusted (*N* = 368)		Adjusted[1] (*N* = 367)		Chi^2*p* value*
Units	HR (95%CI)	*p* value	HR (95%CI)	*p* value	
MUAC (cm)	0.48 (0.30–0.75)	0.01	0.46 (0.29–0.71)	0.01	**Ref**
AMC (cm)	0.63 (0.40–1.01)	0.06	0.59 (0.37–0.95)	0.03	0.02
AMA (cm^2)	0.82 (0.64–1.05)	0.12	0.79 (0.61–1.01)	0.07	< 0.01
AFA (cm^2)	0.44 (0.28–0.68)	< 0.01	0.40 (0.25–0.65)	< 0.01	0.54
WHZ	0.80 (0.55–1.15)	0.22	0.78 (0.54–1.13)	0.19	0.01
WAZ	0.55 (0.37–0.82)	< 0.01	0.52 (0.35–0.79)	< 0.01	0.49
BAZ	0.96 (0.68–1.33)	0.79	0.95 (0.68–1.32)	0.75	0.01
HAZ	0.71 (0.55–0.91)	0.01	0.70 (0.54–0.90)	0.01	0.07

[1]Adjusted for age in months, gender, breastfeeding status and respiratory rate, HR; Hazard ratio, MUAC; Mid upper arm circumference, AMC; Arm muscle circumference, AMA; Arm muscle area, AFA; Arm fat area, WHZ; Weight for Height Z score, WAZ; Weight for Age Z score, BAZ; Body mass index for Age Z score, HAZ; Height for Age score. **Chi^{2}p value** *comparing the hazard ratios of AMC, AMA and AFA to that of MUAC*

0.03, 0.01, and 0.01 respectively (Table 3). The hazard ratio for AFA, 0.40 (95%CI0.25–0.65) was not statistically different from that of MUAC (0.46, 95%CI 0.29–0.71, $p=0.54$), while that of AMC (0.59, 95%CI 0.37–0.95) ($p=0.03$) was significantly lower than that of MUAC, p=<0.01, (Table 3).

The hazard ratios for WHZ, and that of BAZ were significantly different from that of MUAC Table 3.

Discussion

Summary of results

We compared the ability of fat and muscle mass indices to predict survival among children hospitalized for severe pneumonia. Our findings show that in our setting, although baseline arm fat area (AFA) among children 6–59 months hospitalized with severe pneumonia had a higher AUC than arm muscle indices (arm muscle circumference and arm muscle area), the difference did not reach statistical significance. However, survival prediction using AFA in this population is not significantly

different from the current gold standard (MUAC) using AUC or hazard ratio. This suggests that AFA might predict 6-month survival better than arm muscle indices.

Body composition and survival

Muscle mass is expected to be most critical for survival of a severe pneumonia episode given the role of respiratory muscles in maintaining breathing. However, our findings suggest that fat mass may be more important in the long term for survival than muscle mass. Even though the area under the curve for arm fat area is not significantly higher than the area under the curve for arm muscle circumference and arm muscle area, it is not statistically different from that of mid upper arm circumference (the current best predictor for mortality in children under 5 years).

Relationship between body composition and survival

This is consistent with findings from Van den Broeck *et al.*'s study among children without current comorbidities in rural Congo where low-fat mass predicted mortality better than muscle mass in the long term (beyond 3 months) [15]. Van den Broeck et al. also reported that both fat and muscle mass were better survival predictors in the short term than weight for age. During starvation states, as is the case of acute illnesses like severe pneumonia, the body initially utilizes carbohydrate stores before resorting to fat and partial protein metabolism upon their depletion. The body then fully utilizes fat stores until they are depleted and an alternative source of energy is derived from protein stores for survival [25]. High fat mass during these periods delays fatal depletion of the body's protein thus improving survival. Higher fat mass has also been associated with improved survival even in other illnesses including cancer in adults [26]. This may explain the association between arm fat and survival in the long term as some protein is reserved which is important for maintenance of many cellular functions [7].

Severely malnourished children typically have depleted fat reserves which as described above, increases their risk of mortality [27]. However, our study participants were not severely malnourished, and most had relatively good nutritional status, since the median MUAC was 15 cm (IQR 14, 16) with only 1% children having HIV. Thus, other factors more likely account for the association between fat mass and survival in this population such as: (i) Fat is useful in the composition and function of immune cells which are critical in fighting and prevention of infection [28], (ii) Fat cells produce leptin which is important in the regulation of both the innate and adaptive immunity via activation of immune cells including neutrophils and macrophages as well as naïve T and B cells [29]. This means that prevention and control of fatal acute and chronic infections is probably more effective among children with higher fat mass thus improving their chances of survival.

Practical implications

These findings need to be confirmed in other settings, particularly among children with common childhood conditions leading to hospitalization and poor long-term outcomes, such as diarrheal illnesses. If confirmed, these findings are potentially relevant at clinical and public health level for: (i) identification of normal weight patients at higher risk of death following admission for common childhood conditions and (ii) designing nutritional supplementation targeting increasing fat mass such as lipid based nutritional supplements in order to improve survival after hospital discharge in this population.

Limitations

While this study assessed body composition which is a better survival predictor than weight among children hospitalized for severe pneumonia, it had some limitations. First, the equations used for estimation of fat and muscle mass indices are based on assumptions which may not be entirely correct and may introduce information bias. These equations were validated against magnetic resonance imaging (MRI) [22] in an older age group (9–15 years) and might not hold true in younger children. We were not able to perform bio-impedance analysis for the participants, which would have provided more accurate measurements for fat free mass, as arm anthropometry is known to correlate better with fat mass than fat free mass [17]. Although the results have a relatively good precision, they were constrained by the limited sample size from the main trial. Consequently, we were not able to show a statistical difference between the fat and muscle mass indices for prediction of survival in this population. We were also not able to assess separately how fat and muscle mass indices predicted survival at the time of discharge from hospital and in the immediate post discharge period (days 28 and 90 of follow up). Children with severe malnutrition, known chronic lung diseases, and congenital heart disease were excluded from the study and this may have introduced selection bias. Finally, this secondary analysis did not assess the impact of unmeasured variables (confounders) such as the food intake in individual patients during and after discharge from hospital and leptin levels among others. All these factors may have affected the findings of our study.

Conclusion

We were unable to demonstrate that muscle mass indices predict survival among children with severe pneumonia better than fat mass indices. Fat mass assessed by AFA appears to predict 6-month survival better than muscle

mass indices based on its performance against MUAC, the current "gold standard". Separate effects of fat and muscle could be considered when assessing the prognosis and targeted interventions in future.

Abbreviations

AFA	Arm Fat Area
AMA	Arm Muscle Area
AMC	Arm Muscle Circumference
AUC	Area Under the Curve
CI	Confidence Interval
COPD	Chronic Obstructive Airways Disease
FM	Fat Mass
FFM	Fat Free Mass
KCH	Kilifi County Hospital
MAMA	Mid Arm Muscle Area
MM	Muscle Mass
MRI	Magnetic Resonance Imaging
MUAC	Mid upper arm circumference
IQR	Interquartile Range
ROC	Receiver Operating Characteristic
SD	Standard Deviation
TST	Triceps Skinfold Thickness
WFA	Weight for Age z-score
WFH	Weight for Height z-score
WHO	World Health Organization

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Author contributions
DN, VM, AB, KM, CK, SK, and PO designed research; DN, FA, RO, AT, HM, CM, EN conducted research; DN and EG analyzed data; and DN, EG, AB, KM wrote the paper. DN had primary responsibility for final content. All authors read and approved the final manuscript.

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Data availability
Data described in the manuscript, code book, and analytic code will be made available upon request addressed to Prof Kathryn Maitland (kathryn.maitland@gmail.com) pending application review and approval.

Declarations

Ethics approval and consent to participate
The study was approved by the School of Medicine Ethics and Research Committee (SOMREC): Protocol Ref: #REC REF 2020 – 155), and children's parents and guardians provided written informed consent prior to participation. The study was carried out in accordance with the ICH-GCP guidelines and the ethical principles that have their origin in the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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