Clinical Nutrition xxx (2014) 1–5

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Bedside measures of malnutrition and association with mortality in hospitalized adults☆

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ARTICLE INFO

Article history:
Received 4 December 2013
Accepted 28 March 2014

Keywords:
Malnutrition
Africa
Acute illness
Hospitalized
Adult

SUMMARY

Background & aims: The impact of malnutrition on the outcomes of hospitalized adults in resource-limited settings such as sub-Saharan Africa (SSA) is not fully described. We aimed to determine the association between malnutrition and mortality in adults admitted to hospital in the resource-limited setting of Southwestern Uganda.

Methods: We performed a cohort study of adults admitted to the medical ward of Mbarara Regional Referral Hospital. Measures of nutritional status included: 1) body mass index (BMI), 2) the mini-nutritional assessment short form (MNA-sf), and 3) mid-upper arm circumference (MUAC). Subjects were followed until death or 30 days from admission. We used proportional hazards regression to assess associations between malnutrition and in-hospital and 30-day mortality.

Results: We enrolled 318 subjects. The prevalence of malnutrition was 25–59% depending on the measure used. In-hospital and 30-day mortality were 18% and 37% respectively. In the adjusted analysis, subjects with MNA-sf score 0–7 had a 2.7-fold higher risk of in-hospital mortality (95% CI: 1.3–5.9, $p = 0.011$) than those with a score of 8–14, and subjects with malnutrition determined by MUAC (<20 cm for males, and <19 cm for females) had a 1.8-fold higher risk of in-hospital mortality (95% CI: 0.98–3.4, $p = 0.06$) than those normally nourished. MNA-sf (HR 1.6, 95% CI: 1.02–2.6, $p = 0.039$) and MUAC (HR 1.6, 95% CI: 1.0–2.3, $p = 0.048$) were independently predictive of 30-day mortality. BMI <18.5 was not associated with in-hospital or 30-day mortality.

Conclusions: Malnutrition was common and simple measures of nutritional status predicted in-hospital and 30-day mortality. Further research is needed to understand the pathophysiology of malnutrition during acute illness and mitigate its effects.

1. Introduction

Slim disease was first described in Uganda in 1982 heralding the onset of the AIDS pandemic.[1] In 2005, 212 million people in sub-Saharan Africa (SSA) were estimated to be malnourished with the highest prevalence (37%) occurring in Southern Africa, followed by East Africa (35%).[2] Malnutrition and AIDS remain intrinsically linked, and wasted patients initiating antiretroviral therapy in SSA are at high risk of early death.[3–5] SSA is highly endemic for tuberculosis (TB) which, along with malnutrition and AIDS, also negatively affects body composition.[6]

Severe malnutrition leads to an immune suppressed state. As a consequence, malnourished patients are at higher risk for infectious complications.[7] For example, malnourished hospitalized patients are at higher risk for nosocomial bloodstream infections.[8] Despite the high prevalence of malnutrition, AIDS, and TB in SSA, little is known about the overall impact of malnutrition on the course of illness among adult inpatients in SSA.[9,10] A study from Burundi revealed that almost half of adult inpatients admitted to hospital had at least moderate malnutrition, and found that

Non-standard abbreviations: SSA, sub-Saharan Africa; TB, tuberculosis; MRRH, Mbarara Regional Referral Hospital; MUST, Mbarara University of Science and Technology; BMI, body mass index; MNA-sf, mini-nutritional assessment short form; MUAC, mid-upper arm circumference; HB, hemoglobin; MAP, mean arterial pressure; ART, antiretroviral therapy.

☆ **Conferences:** The results of this study were presented in part at the 61st Annual Meeting of the American Society of Tropical Medicine and Hygiene, November, 2012.

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http://dx.doi.org/10.1016/j.clnu.2014.03.013
0261-5614/

decreased fat free mass and triceps skinfold thickness were predictive of early mortality but actual weight and body weight loss were not associated with mortality.[11]

To better understand the association between malnutrition and outcomes in hospitalized adult patients in SSA, we conducted a prospective observational study at the Mbarara Regional Referral Hospital (MRRH) in Southwestern Uganda. We measured malnutrition using three measures of nutritional status.

2. Methods

2.1. Study design and patient population

We performed a prospective observational cohort study on the adult medical ward of MRRH, a 350 bed government teaching hospital for the Mbarara University of Science and Technology (MUST) located about 280 km southwest of the capital city, Kampala. We consecutively enrolled subjects ≥18 years who were hospitalized for an acute medical illness between April and May 2011. Subjects that were unable to participate in the weighing process or those who declined participation were excluded. We defined the primary exposure as malnutrition at admission and the primary outcome as in-hospital mortality. Secondary outcomes included length of hospital stay, 30-day mortality, or being lost to follow up at 30 days post-admission. The Institutional Review Boards at MUST and the University of Virginia approved the study.

2.2. Measures of nutritional status

We assessed malnutrition using the mini-nutritional assessment short form (MNA-sf), mid-upper arm circumference (MUAC), and the body mass index (BMI). The MNA-sf is a scoring system that incorporates anthropometric measures, questions on food intake and weight loss; and questions on psychological stress and neuropsychiatric problems.[12] To obtain the MUAC, we first determined the midpoint between the acromial and olecranon processes with a flexible tape. We then measured the MUAC from this point using a non-stretchable MUAC tape to the nearest 100th of a centimeter. To obtain the BMI, we divided the square of the subjects' height (estimated from heel to occiput to the nearest 100th of a meter) by their dry weight (estimated to the nearest 10th of a kilogram). Weights were measured with a standing scale (SECA, Chino, California, USA) for subjects who could stand, and a wheelchair scale (SECA, Chino, California, USA) for those who could not, while heights were measured with a wall tape (SECA, Chino, California, USA) for subjects who could stand, and a flexible measuring tape (SECA, Chino, California, USA), for those who could not. Given their acute illness, subjects were measured once to minimize discomfort. We standardized weighing scales at the beginning of the study and calibrated them every two weeks using a third standing weighing scale.

2.3. Demographic, clinical, and laboratory-based measurements

We collected demographic information including age, sex, and educational status, and clinical information, including suspected TB, HIV status, and vital parameters using a pretested questionnaire. For each patient, we also obtained a complete blood count (Beckman Coulter, Villepinte, France), the HIV serostatus using a three-test algorithm (screening: Determine™, Abbott Laboratories, Abbott Park, IL; confirmation: Statpak, Chembio Diagnostics, Medford, NY; tie-breaker: Unigold, Trinity Biotech, Bray, Ireland), and serum albumin using the photometric colorimetric test (Human Diagnostics, Wiesbaden, Germany). Tests were performed at the Mbarara University Research Laboratory which participates in external quality assurance programs by the National Health Laboratory Service (Johannesburg, South Africa).

2.4. Outcome determination

We followed subjects in the hospital until either death or discharge, and established the vital status of discharged subjects at 30 days post-admission through mobile telephone calls and outpatient clinic appointments.

2.5. Statistical analyses

We summarized demographic and baseline clinical variables using median and interquartile range (IQR) for continuous variables, and proportions for binary and categorical variables. MNA-sf and MUAC were transformed into 2-level categorical variables (0–7 and 8–14 for MNA-sf; <20 cm for males and <19 cm for females for MUAC). The BMI was transformed into a 3-level categorical variable: low (<18.5 kg/m^2), normal (18.5–25 kg/m^2), and high (>25 kg/m^2). Serum albumin values <3.5 g/dl were considered abnormal. We assessed the association of malnutrition with in-hospital and 30-day mortality using Kaplan–Meier techniques and proportional hazards regression. In multivariable models, we included one measure of nutritional status at a time while adjusting for age, sex, education status, HIV status, suspected TB, temperature, hemoglobin (HB) and admission mean arterial pressure (MAP). HB and MAP were transformed into restricted cubic splines for the analysis because they showed non-linear relationships with mortality. Any missing data noted during analysis were cross-checked and obtained from patient notes. We estimated that a sample size of 318 patients was needed to detect a hazard ratio ≥1.7 for 30-day mortality comparing malnourished to normally nourished subjects. Data were analyzed using Stata 13 (Stata Corp, Texas, USA).

3. Results

We assessed 355 subjects and enrolled 318. We excluded 34 subjects who were <18 years and 3 who declined to participate. The median age was 37 (IQR 27–56) years (Table 1). Nearly half the subjects were HIV infected (144 of 318, 45%) and a similar proportion were diagnosed with suspected TB (133 of 318, 42%). The prevalence of malnutrition according to MUAC, BMI, and MNA-sf was 25%, 47%, and 59% respectively (Table 1). The in-hospital mortality was 18% (57 of 318) and increased to 37% (117 of 318) at 30 days from admission. For subjects discharged alive, the median length of hospital stay was 6 days (IQR 3–9).

3.1. Prediction of in-hospital mortality

The MNA-sf and MUAC were both associated with in-hospital mortality (Table 2). In the unadjusted analysis, subjects with a low MNA-sf score had a 2.7-fold higher risk of in-hospital mortality (95% CI: 1.4–5.4, $p = 0.005$) compared to those with high scores. Subjects with a low MUAC had a 2.0-fold higher risk of in-hospital mortality (95% CI: 1.2–3.5, $p = 0.010$) compared to those with a high MUAC. A low BMI was not associated with in-hospital mortality when compared to a normal BMI (HR 1.6, 95% CI: 0.92–2.9, $p = 0.098$). In the adjusted analysis, subjects with a low MNA-sf score had a 2.7-fold higher risk of in-hospital mortality (95% CI: 1.3–5.9, $p = 0.011$) than those with a high MNA-sf score. Subjects with a low MUAC had a 1.8-fold higher risk of in-hospital mortality (95% CI: 0.98–3.4, $p = 0.060$) than those with a high MUAC (Table 2). A low BMI was not associated with in-hospital mortality

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Table 1
Summary statistics regarding demographic and clinical characteristics.

Subject characteristics	$N = 318$
Age, median (IQR)	37 (27–56)
Female sex, *n* (%)	153 (48)
Education	
Up to primary school, *n* (%)	104 (33)
Secondary education, *n* (%)	165 (52)
Tertiary education, *n* (%)	49 (15)
HIV infected, *n* (%)	144 (45)
Suspected TB, *n* (%)	133 (42)
Jaundice, *n* (%)	25 (8)
Edema, *n* (%)	66 (21)
Admission temperature	
≤36	36 (11)
36.1–37.9	180 (57)
≥38	102 (32)
Dehydrated, *n* (%)	29 (20)
Diarrhea, *n* (%)	17 (11)
Hemoglobin, median (IQR)	9 (6–12)
White cell count (K/μL), median (IQR)	5 (3–7)
Mini-nutritional assessment short form score, *n* (%)	
0–7	186 (59)
8–11	105 (33)
12–14	27 (8.5)
MUAC, *n* (%)	
<20 cm (males)/<19 cm (females)	80 (25)
>20 cm (males)/>19 cm (females)	238 (75)
BMI kg/m^2, *n* (%)	
<18.5	149 (47)
18.5–25	135 (89)
>25	34 (11)
Serum albumin g/dl, *n* (%)	
<3.5	84 (26)
≥3.5	234 (74)

when compared to a normal BMI (HR 1.4, 95% CI: 0.71–2.7, $p = 0.34$).

3.2. Prediction of 30-day mortality

Unadjusted analyses showed substantially decreased survival over 30 days among malnourished subjects (Fig. 1 and Table 3). In the adjusted analysis, subjects with a low MNA-sf score had a 1.6-fold higher risk of 30-day mortality (95% CI: 1.02–2.6, $p = 0.039$) than those with a high MNA-sf score. Subjects with a low MUAC also had a 1.6-fold higher risk of mortality (95% CI: 1.0–2.3, $p = 0.048$) than those with a high MUAC. A low BMI was not associated with 30-day mortality when compared to a normal BMI (HR 1.2, 95% CI: 0.77–1.9, $p = 0.41$).

Table 2
Unadjusted and multivariable-adjusted analysis of predictors for in-hospital mortality.

Variable	Unadjusted HR	95% CI	*p*	Adjusted HR	95% CI	*p*
MNA-sf score						
0–7	2.7	1.4–5.4	0.005	2.7	1.3–5.9	0.011
8–14	Ref	–	–	–	–	–
MUAC (cm)						
<20 (males)/<19 (females)	2.02	1.2–3.5	0.010	1.8	0.98–3.4	0.060
>20 (males)/>19 (females)	Ref	–	–	–	–	–
Serum albumin (g/dl)						
<3.5	1.5	0.86–2.5	<0.158	1.02	0.54–1.9	0.954
≥3.5	Ref	–	–	–	–	–
BMI						
<18.5	1.6	0.92–2.9	0.098	1.4	0.71–2.7	0.339
18.5–25	Ref	–	–	–	–	–
>25	0.96	0.36–2.6	0.940	0.88	0.31–2.5	0.812
Suspected TB	1.3	0.79–2.2	0.289	0.65	0.32–1.3	0.222
HIV positive status	1.6	0.93–2.7	0.093	1.3	0.66–2.7	0.418
Temperature						
≤36	2.4	1.2–4.9	0.018	2.4	1.1–5.1	0.028
36.1–37.9	Ref	–	–	–	–	–
≥38	1.8	1.0–3.2	0.054	1.5	0.78–3.0	0.219
Male sex	1.4	0.80–2.3	0.114	1.3	0.71–2.3	0.409

4. Discussion

Sub-Saharan Africa shoulders a high burden of malnutrition, infectious diseases, and critical illness, but their interactions are not well studied in adult populations in this region.[13–15] In this study, we provide a comprehensive assessment of the prevalence of malnutrition in adults admitted to a regional referral hospital in Southwestern Uganda and its association with post-admission mortality. Our findings detail an alarmingly high prevalence of malnutrition and mortality where more than half the patients were malnourished and a third died by 30 days after admission. Furthermore, malnutrition was an independent risk factor for in-hospital and 30-day mortality.

The high prevalence of malnutrition is consistent with another report of in-hospital malnutrition from nearby Burundi.[11] The etiology of malnutrition in our population is likely multifactorial including chronic illness and infection as well as issues related to poverty and food insecurity. HIV and TB, which are both associated with wasting and malnutrition, were found in almost half of our cohort.[10,16] Some studies in this region have previously reported a decline in agricultural production during the AIDS era.[17] In a recent study from Mbarara, 81% of patients initiating antiretroviral therapy (ART) were classified as food insecure and 43% were severely food insecure. In this same population, malnutrition as measured by BMI and MUAC, was 14% and 11% respectively.[18]

Adequate nutrition is an important component of supportive care for patients with critical illness. In resource-limited settings, nutritional support teams are generally not available and patients often depend on family members of friends to provide nutrition. The role of supplemental nutrition in this environment is not clear. In a study from Tanzania, the administration of multivitamin and mineral supplementation including zinc to adults receiving TB treatment reduced mortality in patients co-infected with HIV.[19] However, a meta-analysis of the benefit of oral macro-nutritional supplementation in HIV-infected adults and children was inconclusive.[20] This meta-analysis included primarily outpatients and only 4 of 14 included studies were performed in SSA. We are not aware of any studies of nutritional interventions dedicated to hospitalized adults in SSA.

One of the challenges in providing adequate support to critically ill patients is identifying which patients are at risk for poor outcomes related to malnutrition. Currently, there is no standard definition of adult malnourishment.[21] Risk assessment tools have been derived to identify patients at highest risk for adverse events from malnutrition, but they have been studied in resource rich environments, often rely on sophisticated laboratory testing, and have yet to be validated in African populations.[22] MNA-sf has been previously validated as a measure of malnutrition and predictor of mortality in elderly populations. Our results show that it may perform equally well in younger adults.[23,24] MUAC and BMI are both simple measures that are easy to perform and have been studied in HIV and TB infected populations.[3,6,25] However, MUAC was a better predictor of in-hospital mortality than BMI in our study perhaps because BMI results can be inaccurate in the presence of significant edema.

Serum albumin was an independent risk factor for 30-day but not in-hospital mortality in our cohort. In the acute setting, serum albumin can be unreliable because of inflammation from critical

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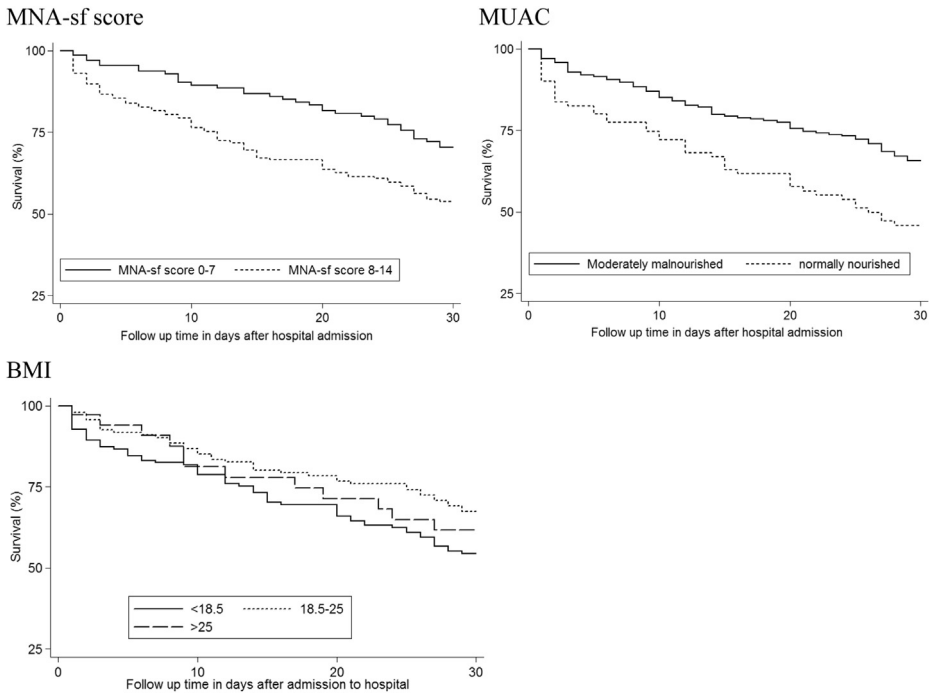

Fig. 1. Survival at 30 days after admission according to each measure of nutritional status.

illness, or dehydration.[26] Serum albumin may also remain high in the presence of protein-energy malnutrition.[27] A study comparing serum albumin to APACHE II score in predicting in-hospital mortality in critically ill patients found serum albumin to have poor sensitivity and specificity for mortality.[28] However, serum albumin has been shown to predict mortality in HIV-infected adults starting antiretroviral therapy in an outpatient setting in Tanzania.[29]

Our study has several limitations. In many cases, we were unable to confirm suspected TB cases due to resource constraints. This may have limited our ability to detect the independent role of TB in malnutrition and mortality in this population, although previous studies have shown that clinical suspicion of TB correlates well with DNA PCR proven TB diagnoses.[30] Our sample size was relatively small and this may have affected the precision of estimates of the independent association of measures of malnutrition to mortality. We took only one measurement for weight, height, and MUAC which may have reduced precision for some of the measurements. Due to the severity of illness in our patient population and because the variability of these measurements within subjects was expected to be low, we felt ethically compelled to take only one measurement in an attempt to minimize patient discomfort. However, we did standardize and calibrate instruments to minimize measurement error. Finally, the MNA-sf does include subjective criteria which may lead to false-positive results and has previously been validated in older patient populations. There are other malnutrition screening tools, including the Malnutrition Universal Screening Tool, that could have been used but they have similar inherent problems of sensitivity and specificity.

Table 3
Unadjusted and multivariable-adjusted analysis of predictors for 30-day mortality.

Variable	Unadjusted HR	95% CI	*p*	Adjusted HR	95% CI	*p*
MNA-sf						
0–7	1.9	1.3–2.8	0.002	1.6	1.02–2.6	0.039
8–14	Ref	–	–	–	–	–
MUAC (cm)						
<20 (males)/<19 (females)	1.9	1.3–2.8	0.001	1.6	1.0–2.3	0.048
>20 (males)/>19 (females)	Ref	–	–	–	–	–
Serum albumin (g/dl)						
<3.5	2.0	1.3–2.8	<0.001	1.6	1.0–2.5	0.033
≥3.5	Ref	–	–	–	–	–
BMI						
<18.5	1.6	1.1–2.3	0.029	1.2	0.77–1.9	0.406
18.5–25	Ref	–	–	–	–	–
>25	1.2	0.64–2.3	0.545	1.3	0.66–2.6	0.450
Suspected TB	1.5	1.0–2.1	0.038	1.1	0.68–1.7	0.736
HIV positive status	1.2	0.84–1.7	0.306	0.90	0.56–1.5	0.680
Temperature						
≤36	1.6	0.92–2.7	0.098	1.6	0.86–2.7	0.152
36.1–37.9	Ref	–	–	–	–	–
>38	1.1	0.77–1.7	0.507	0.92	0.58–1.4	0.709
Male sex	1.5	1.1–2.2	0.026	1.5	1.03–2.3	0.036

In conclusion, there was a high prevalence of malnutrition in adult patients admitted to a regional referral hospital in Southwestern Uganda. Measures of malnutrition were easy to perform and showed good prediction of mortality. Accordingly, our results are generalizable to resource poor settings in sub-Saharan Africa. Clinicians in such settings should have a high index of suspicion for malnutrition in adult inpatients and work within their resources to prevent malnutrition associated mortality. Future studies are needed to better understand the pathophysiology of malnutrition in this environment and to guide clinicians in providing adequate nutrition as well as appropriate supportive care to malnourished critically ill patients, while minimizing associated risks. At the same time, further assessment and amelioration of malnutrition at a community level is also needed in this setting.

Conflict of interest

No authors declare a conflict of interest.

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Acknowledgments

Statement of authorship

SBA conceived the study, collected the data, performed the analyses, and wrote the manuscript. CM conceived the study and wrote the manuscript. LAW conceived the study and wrote the manuscript. CCM conceived the study, assisted with data analyses, and wrote and edited the manuscript. All authors approved the final draft.

Sources of funding

Funding for the study was provided to SA and CCM by the Pfizer Initiative in International Health and the Center for Global Health at the University of Virginia. This initiative was conceived to fund global infectious disease research and exchange programmes between post-doctoral fellows and students from the University of Virginia and several international partners to conduct research on global health issues. The major purpose of this programme is to foster and enhance bidirectional research training. An independent board at the University of Virginia determines the research proposals that are funded. Pfizer, Inc. provided funds to promote the initiative but has no role in the planning, execution, or analysis of research protocols, including the study described in this article.

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Please cite this article in press as: Asiimwe SB, et al., Bedside measures of malnutrition and association with mortality in hospitalized adults, Clinical Nutrition (2014), http://dx.doi.org/10.1016/j.clnu.2014.03.013