Nutritional status predicts preterm death in older people: a prospective cohort study

Lisa Söderström [a, b,*], Andreas Rosenblad [a], Eva Thors Adolfsson [a], Anja Saletti [b], Leif Bergkvist [a, c]

[a] Centre for Clinical Research, Uppsala University, County Council of Västmanland, Västmanland County Hospital, 721 89 Västerås, Sweden.

[b] Department of Public Health and Caring Sciences: Clinical Nutrition and Metabolism, Uppsala Science Park, 751 85, Uppsala, Uppsala University, Sweden.

[c] Department of Surgery, Västmanland County Hospital, 721 89 Västerås, Sweden.

[*] Corresponding author: Lisa Söderström, MSc, RD. Centre for Clinical Research, Uppsala University, County Council of Västmanland, Västmanland County Hospital, 721 89 Västerås, Sweden.

Telephone: +46 21 173969. Fax: +46 21 173733.

E-mail adress: lisa.soderstrom@ltv.se (L. Söderström)

Short titel: Nutritional status predicts preterm death in older people

Abstract

Background & aims: There is an association between malnutrition and mortality. However, it is uncertain whether this association is independent of confounders. The aim of the present study was to examine whether nutritional status, defined according to the three categories in the full Mini Nutritional Assessment (MNA) instrument, is an independent predictor of preterm death in people 65 years and older.

Methods: This prospective cohort study included individuals aged ≥ 65 years who were admitted to hospital between March 2008 and May 2009 and followed-up after 50 months (n = 1767). Nutritional status was assessed with the MNA, and factors potentially associated with malnutrition were recorded during participants hospital stay. Main outcome measure was overall survival.

Results: Based on the MNA definitions, 628 (35.5%) were well nourished, 973 (55.1%) were at risk of malnutrition, and 166 (9.4%) of the participants were malnourished at baseline. During the follow-up period 655 (37.1%) participants died. At follow-up, the survival was 75.2% for the well-nourished group, 60.0% for those at risk of malnutrition, and 33.7% for the malnourished ($p < 0.001$). After adjusting for confounders the hazard ratios (95% CI) for all-cause mortality were 1.56 (1.18–2.07) in the group at risk of malnutrition and 3.71 (2.28–6.04) in the malnourished group.

Conclusions: Nutritional status defined according to the three categories in the full MNA independently predicts preterm death in people 65 years and older. These findings are clinically important and emphasise the usefulness of the MNA for screening of nutritional status.

Keyword: nutritional status, malnutrition, Mini Nutritional Assessment, survival analysis

Introduction

Malnutrition is one of the most important medical conditions that affect the prognosis in old age.[1] In Europe about one third of older patients admitted to hospital are malnourished,[2-4] which makes it a widespread problem.[2-4] The condition is associated with several negative outcomes such as declined functional ability,[5, 6] readmissions, and a prolonged length of stay in hospital.[7] Even more critically, a systematic review from 2012 evaluating different nutrition screening tools concludes that there is some evidence that malnutrition is associated with a increased mortality.[8] However, it is still uncertain whether this association is independent of confounders. The most widely used instrument to assess nutritional status in older people is the Mini Nutritional Assessment (MNA),[2, 8] which is recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN).[9]

When examining the relationship between malnutrition and mortality, most studies analyse the total MNA scores or use varying methods of subcategorisation. Fewer studies investigate the three nutritional status groups separately.[8] The three MNA categories (well nourished, at risk of malnutrition, malnourished) are used in clinical practice. Further, as the aforementioned systematic review includes studies in different residential settings,[10 11 12] it does not specifically address the question of whether there is a relationship between nutritional status according to the MNA and mortality in older people in hospital.[8] Finally, considerable covariation may exist between nutritional status and possible confounders. Therefore, it is important to determine whether nutritional status still predicts early death after adjustment for possible confounders.

The aim of the present cohort study was to examine whether nutritional status defined according to the three categories in the full MNA instrument is an independent predictor of preterm death in people 65 years and older.

Materials and methods

Study design and participants

A baseline survey was performed to estimate the prevalence of malnutrition among people ≥65 years old admitted to a medium-sized Swedish hospital.[13] A total of 2517 individuals were assessed for eligibility to participate in the cross-sectional study. The sample at baseline consisted of 1771 participants in two internal medicine wards (*n* = 706), two surgical wards (*n* = 681), and one orthopaedic ward (*n* = 384). The final cohort for the present study consisted of 1767 participants. Figure 1 describes the reasons for exclusions and loss to follow-up.

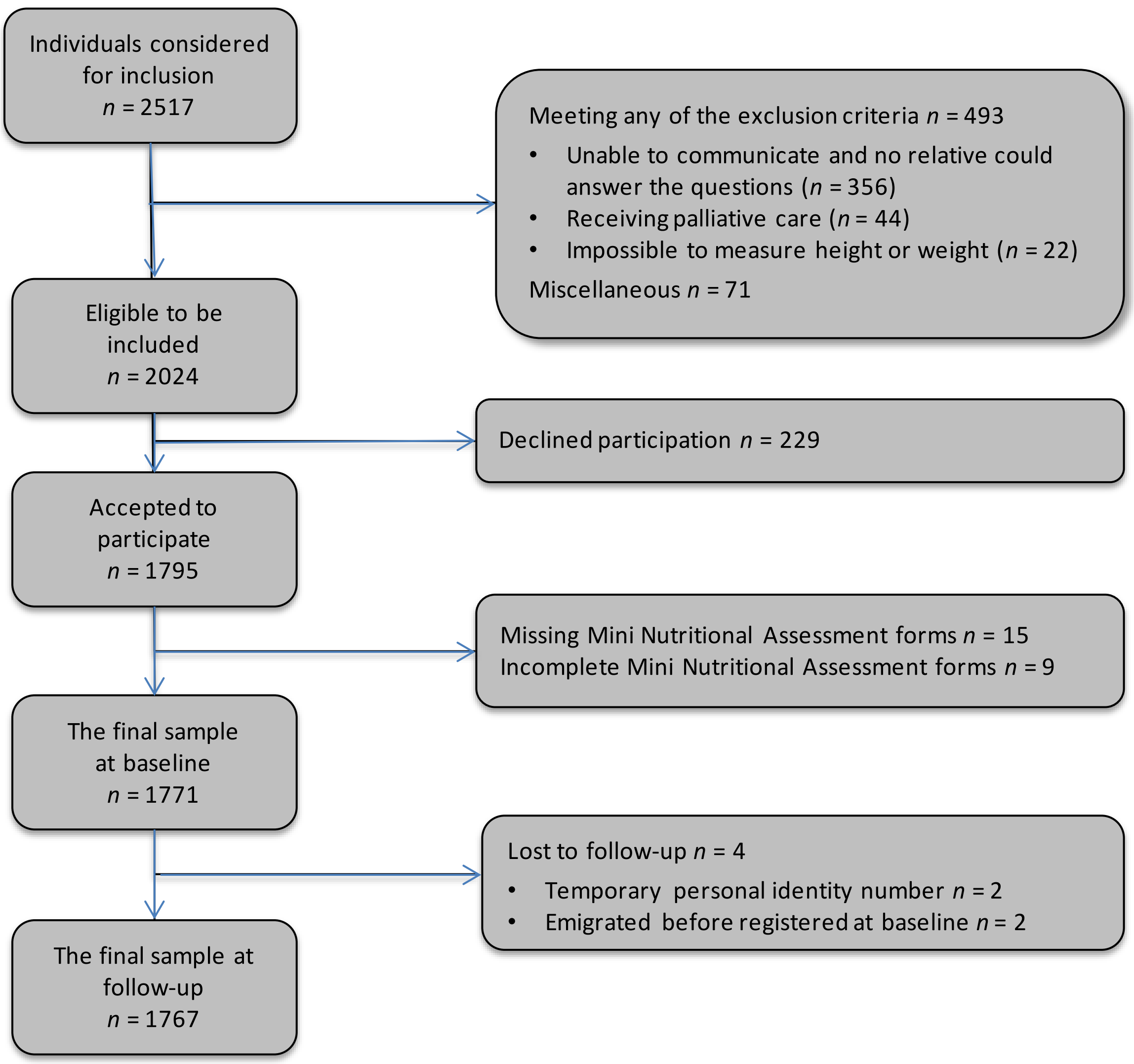

Fig. 1. Flow chart describing participant recruitment.

Data collection procedure

Baseline data were collected from 3 March 2008 to 29 May 2009. The patients were recruited consecutively during the study period, except on weekends, holidays, and when the wards were closed due to a calicivirus outbreak. The nutritional status was assessed with the MNA instrument during the participants' hospital stay, and factors potentially associated with malnutrition were recorded. Trained personnel obtained data for participant characteristics and nutritional status at baseline. A detailed description of the baseline survey has been previously published.[13]

The data collected at baseline included clinical characteristics: sex, BMI, smoking status, medication use, diagnoses, length of overnight fast, number of eating episodes, meal provision and living situation. Age was retrieved from the personal identification numbers. Smoking status was defined as current or non-smoker. Medication use before admission and the patient's diagnoses at discharge were retrieved from the patient's medical records. The diagnoses were defined according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).

Length of overnight fast was defined as the time between the last eating episode in the evening and the first eating episode the morning after. The number of eating episodes per day was recorded as how often the patients usually ate breakfast, lunch, dinner, and between-meal and evening snacks. Meal provision was recorded as: cooks independently and/or with help from spouse (cooks independently), meals on wheels, or meals in a nursing home or restaurant. Living situation was defined as living alone, cohabiting, or in a nursing home. Country of birth was obtained from the Swedish population register.

Nutritional status was assessed with the original MNA (full MNA) in all participants.
The instrument is composed of 18 items and takes about 15 minutes to complete. The threshold values of the instrument categorise individuales into three nutritional status groups:
well nourished (MNA score 24–30), at risk of malnutrition (MNA score 17–23.5), or malnourished (MNA score <17).[2] To analyse the relationship between nutritional status and mortality, the participants were followed up through the Swedish population register,[14] until 23 May 2012, i.e., between 35 and 50 months after the nutritional assessment at baseline.

Ethical considerations

The study was approved by the Regional Uppsala Ethical Review Board
(approval number: 2007-323). All participants provided their written informed consent before entering the study. If a participant was unable to communicate, a relative was asked if they objected to the patient´s participation in the study (*n* = 23).

Statistical analysis

The main focus of the present study was to examine the association between nutritional status according to MNA (well nourished, at risk of malnutrition, or malnourished) and overall survival during the follow-up period. Survival was calculated from the date of MNA assessment to the date of death. Date of emigration and end of follow-up were used as censoring dates.

For descriptive statistics, categorical data are presented as frequencies and percentages, *n* (%), while discrete and continuous data are given as means values ± standard deviations. Tests of differences among the three nutritional status groups were analysed with Pearson's χ^2-test for categorical data, Kruskal–Wallis test for discrete data, and ANOVA for continuous data.

For analysis of overall survival, Kaplan–Meier curves and associated log-rank tests were calculated, together with uni- and multivariate Cox proportional hazards regression models. In the regression analyses, nutritional status was entered as a categorical variable with three levels: well nourished, at risk of malnutrition or malnourished, with “well nourished” being the reference category. As potential confounders, the following variables were considered: age (years), female sex (yes/no), BMI and BMI × BMI, current smoking (yes/no), number of drugs, overnight fast >11 hours (yes/no), eating episodes <4 (yes/no), independent cooking (yes/no), living situation (living alone, cohabiting, or in a nursing home), country of birth (Sweden or other countries), and diagnoses.

The participant’s diagnoses were considered as potential confounders after being grouped into 15 main ICD-10 diagnostic groups and categorised as yes/no. Finally, seven specific diagnoses potentially associated with malnutrition were also considered and categorised as yes/no: diabetes mellitus, dementia and Alzheimer disease, cerebrovascular diseases, pneumonia, chronic obstructive pulmonary disease, rheumatoid arthritis, and renal failure.

The Cox regression analysis was conducted in four steps. Firstly, nutritional status and all potential confounders (except BMI, which was entered together with the quadratic term BMI × BMI) were entered separately into a Cox regression model. The number of medications was entered as a discrete variable, while age, BMI, and BMI × BMI were entered as continuous variables, and all other variables as categorical variables. Secondly, all variables that were found to be statistically significant in the first step were entered simultaneously into a multivariate Cox regression model (base model). In the third step, statistically non-significant variables were removed from the base model through a backward selection procedure, where the variables with the highest *p* values were removed one at a time and the model re-estimated, until the model included only statistically significant variables (reduced model).

In the fourth step, all confounding variables included in the reduced model were tested for interaction effects with nutritional status by separately adding each interaction effect to the reduced model. The interaction effects that were statistically significant were then added simultaneously to the reduced model. Finally, statistically non-significant variables were removed through a backward selection procedure, where the variables with the highest *p* values were removed one at a time and the model re-estimated, until the model included only statistically significant variables (final model). In all steps, all regression models were hierarchical, i.e., for all higher order terms of a variable included in the model, all lower order terms of the variable were also included. For all statistical tests, a two-sided p value < 0.05 was considered significant. All data were analysed with IBM SPSS Statistics 20.

A sample size calculation was done based on studies evaluating malnutrition and mortality in older people in hospital.[15-18] In these studies, the proportion of well-nourished patients varied between 17% and 59%, while the proportion of malnourished patients varied between 16% and 49%. Thus, the smallest proportion of well-nourished and malnourished patients one would expect, in an extreme case, would be 17% well nourished and 16% malnourished patients. Based on the aforementioned studies, the expected mortality during three years of follow-up was 24% among the well-nourished patients and 35% among the malnourished patients, i.e., a difference of 11 percentage points. To obtain a power ($1-\beta$) of 80% at a two-sided significance level of $\alpha = 0.05$ with a Z-test for difference in proportions with an expected difference in mortality of 11 percentage points, a total study population of 1682 participants would be needed. To take into account expected dropouts, non-response, and missing values, the aim was to recruit a total of 2080 participants. As the dropout rate was lower than expected, a decision was made to end recruitment when the nutritional status of 1795 participants had been assessed in the study.

Results

Participant characteristics

A total of 1767 participants were followed up in the present cohort. The mean age ± SD of the included participants was 78.1 ± 7.8 years at baseline, which was significantly lower than that of those excluded (mean age 82.0 ± 8.2 years; $p < 0.001$). Women were predominant among both the included (56.0%) and excluded (53.3%) patients. There was no significant difference in the sex distribution among the included and those excluded ($p = 0.266$). Most of the participants lived at home (95.1%) before their admission to hospital, and a minority lived in nursing homes (4.9%). Table 1 lists the characteristics of the participants at baseline in relation to their nutritional status. According to the MNA at baseline, 628 (35.5%) were well nourished, 973 (55.1%) were at risk of malnutrition, and 166 (9.4%) of the participants were malnourished. The participants from medical, surgical and orthopaedic clinics did not differ significantly regarding nutritional status ($p = 0.382$) or survival ($p = 0.112$).

Table 1 Participant characteristics at baseline, according to their nutritional assessment status (well nourished, at risk of malnutrition, or malnourished) derived from the Mini Nutritional Assessment (MNA) instrument.

	Well nourished (*n* = 628)	At risk of malnutrition (*n* = 973)	Malnourished (*n* = 166)	*p* Value [a]
Age (years), mean ± SD	76.5 ±7.2	78.6 ± 7.9	81.1 ± 7.9	<0.001
Women, *n* (%)	328 (52.2)	563 (57.9)	99 (59.6)	0.053
Body mass index (kg/m^2), mean ± SD	27.5 ± 4.0	25.7 ± 4.7	21.2 ± 4.5	<0.001
Current smoker, *n* (%)	54 (8.6)	113 (11.6)	30 (18.1)	0.002
Number of medications, mean ± SD	5.1 ± 3.6	5.5 ± 4.1	6.2 ± 4.6	0.008
Number of diagnoses, mean ± SD	2.9 ± 1.6	3.1 ± 1.7	3.5 ± 1.9	<0.001
Overnight fast, *n* (%)				<.001
≤11 h	171 (27.3)	182 (18.7)	26 (15.7)	
>11 h	456 (72.7)	790 (81.3)	140 (84.3)	
Eating episodes, *n* (%)				<0.001
≥4	392 (62.4)	458 (47.1)	59 (35.5)	
<4	236 (37.6)	515 (52.9)	107 (64.5)	
Meal provision [b], *n* (%)				
Cooks independently (yes)	582 (93.1)	824 (84.9)	109 (65.7)	<0.001
Meals on wheels (yes)	34 (5.4)	108 (11.1)	34 (20.5)	<0.001
Nursing home (yes)	12 (1.9)	44 (4.5)	23 (13.9)	<0.001
Restaurant (yes)	19 (3.0)	50 (5.1)	12 (7.2)	0.034
Living situation, *n* (%)				<0.001
Lives alone	251 (40.0)	461 (47.4)	97 (58.4)	
Cohabits	364 (58.0)	449 (46.2)	38 (22.9)	
Nursing home	13 (2.1)	62 (6.4)	31 (18.7)	
Country of birth, *n* (%)				0.026
Sweden	520 (82.8)	833 (85.6)	151 (91.0)	
Other countries	108 (7.2)	140 (14.4)	15 (9.0)	

[a] ANOVA for continuous variables, Kruskal–Wallis test for discrete variables, and χ^2 test for categorical variables.

[b] Multiple answers allowed.

Overall survival

The follow-up period was between 35 and 50 months (median 3.5 years). During this period 655 participants (37.1%) died. The Kaplan–Meier curves for the cumulative survival in the three nutritional status groups are given in Figure 2. The survival rate differed significantly among nutritional status groups. At follow-up after 50 months, survival was 75.2% ($n = 472$) for the well-nourished group, 60.0% ($n = 584$) for those at risk of malnutrition, and 33.7% ($n = 56$) for the malnourished ($p < 0.001$).

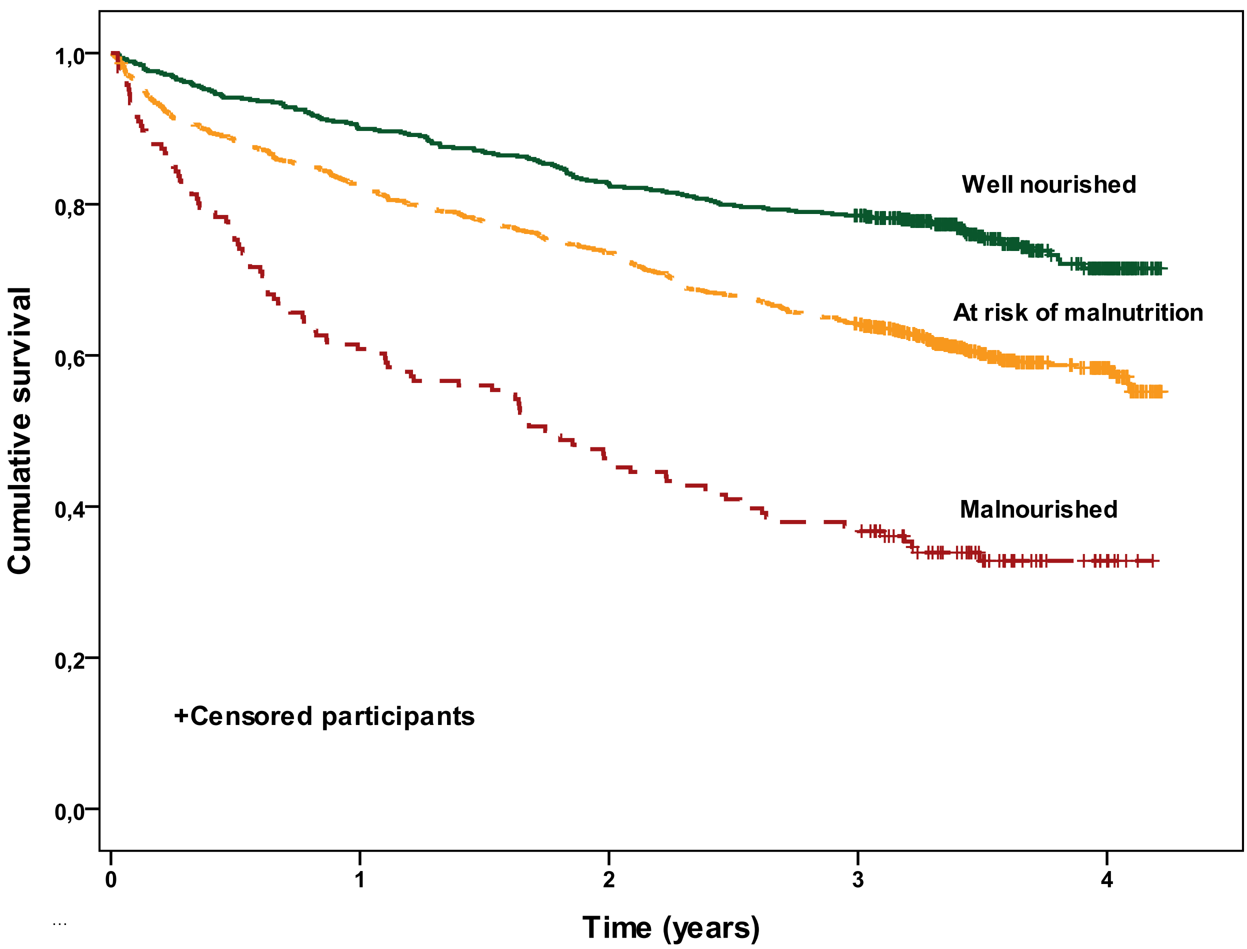

Fig. 2. Kaplan–Meier survival curves according to Mini Nutritional Assessment (MNA) categories (well nourished, at risk of malnutrition, or malnourished). There were significant differences in survival among the three nutritional status groups (log rank test $p < 0.001$).

In univariate Cox regression, the hazard ratio (HR) (95% CI) for all-cause mortality was 1.79 (1.49–2.15) for the group at risk of malnutrition ($p < 0.001$) and 4.00 (3.13–5.11) for the malnourished ($p < 0.001$), compared with the well- nourished group. After adjustments for confounding variables (Table 2) in a multivariate Cox regression model, the HR (95% CI) for all-cause mortality were still substantially higher in the group at risk of malnutrition, 1.56 (1.18–2.07), and the malnourished group, 3.71 (2.28–6.04), compared with the well-nourished. Other predictors of all-cause mortality are presented in Table 2. There was a U-shaped relationship between BMI and mortality, demonstrating that the optimal BMI for overall survival among the study population was 29.6.

Of the 1767 participants, 33 had a diagnosis of dementia registered in their medical records. Excluding these from the final Cox regression model decreased the HR to 1.54 (1.16–2.05) for the group at risk of malnutrition and increased HR to 3.86 (2.36–6.31) for the malnourished group.

Table 2 Predictors of all-cause mortality according to Cox proportional hazard regression models.

Variable	Univariate Unadjusted HR[a] (95% CI)	Base model [b] Adjusted HR (95% CI)	Multivariate Reduced model [b] Adjusted HR (95% CI)	Final model [b] Adjusted HR (95% CI)
Well nourished	Reference	Reference	Reference	Reference
At risk of malnutrition	1.79 (1.49–2.15)	1.49 (1.23–1.80)	1.49 (1.23–1.81)	1.56 (1.18–2.07)
Malnourished	4.00 (3.13–5.11)	2.02 (1.49–2.74)	2.01 (1.49–2.72)	3.71 (2.28–6.04)
Age (years)	1.06 (1.05–1.07)	1.06 (1.04–1.07)	1.06 (1.04–1.07)	1.06 (1.05–1.07)
Male sex	1.40 (1.20–1.63)	1.74 (1.47–2.06)	1.76 (1.49–2.07)	1.70 (1.44–2.00)
BMI (kg/m^2)	0.73 (0.66–0.80)	0.84 (0.75–0.93)	0.83 (0.75–0.92)	0.85 (0.76–0.94)
BMI × BMI	1.005 (1.00 –1.007)	1.003 (1.001–1.005)	1.003 (1.001–1.005)	1.003 (1.001–1.005)
Number of drugs	1.09 (1.07–1.10)	1.08 (1.06–1.10)	1.08 (1.06–1.11)	1.08 (1.06–1.11)
Overnight fast > 11 h	1.50 (1.2–1.85)	1.38 (1.11–1.70)	1.36 (1.10–1.68)	1.35 (1.10–1.67)
Does not cook independently	2.27 (1.90–2.73)	1.13 (0.90–1.41)	*	*
Living situation				
Cohabits	Reference	Reference	Reference	Reference
Living alone	1.45 (1.23–1.71)	1.20 (0.999–1.450)	1.23 (1.03–1.48)	1.32 (0.94–1.84)
Nursing home	4.12 (3.21–5.29)	1.88 (1.36–2.58)	2.09 (1.58–2.77)	4.42 (2.33–8.41)
Neoplasms (C00–D48)	2.39 (1.20–2.86)	3.06 (2.53–3.70)	3.06 (2.54–3.70)	3.06 (2.53–3.69)
Diseases of the digestive system (K00–K93)	0.72 (0.60–0.88)	0.86 (0.70–1.04)	*	*
Diseases of the musculoskeletal system and connective tissue (M00–M99)	0.76 (0.61–0.96)	0.79 (0.624–0.998)	0.79 (0.62–0.99)	0.75 (0.60–0.95)
Diabetes mellitus (E10–E14)	1.25 (1.03–1.52)	1.10 (0.88–1.37)	*	*
Dementia and Alzheimer disease (F00–F03, G30)	2.00 (1.30–3.10)	1.38 (0.89–2.15)	*	*
Pneumonia (J12–J18)	1.88 (1.34–2.64)	1.44 (1.01–2.05)	1.45 (1.02–2.06)	1.49 (1.05–2.11)
Chronic obstructive pulmonary disease (J44)	1.70 (1.26–2.31)	1.62 (1.19–2.22)	1.60 (1.17–2.19)	1.60 (1.16–2.20)
Renal failure (N17–N19)	3.22 (2.32–4.47)	2.13 (1.51–3.01)	2.14 (1.52–3.02)	2.21 (1.56–3.13)
Nutritional status × living situation	*	*	*	Reference
At risk of malnutrition × living alone	*	*	*	0.94 (0.64–1.40)
Malnutrition × living alone	*	*	*	0.59 (0.33–1.03)
At risk of malnutrition × nursing home	*	*	*	0.58 (0.28–1.18)
Malnutrition × nursing home	*	*	*	0.18 (0.08–0.42)

[a] Only univarately significant variables are presented in the table.

[b] n = 1759 in the base model, while n = 1763 in the reduced and final models.

[c] *No estimate available because the factor was not included in the model.

Discussion

In this prospective cohort study of 1767 individuals ≥65 years old, nutritional status defined according to the three categories of the full MNA was independently associated with preterm death. Malnutrition was a strong predictor for survival, as only 34% of the malnourished participants were alive at the 50-month follow-up, compared with 75% of the well-nourished group. The risk for all-cause mortality at follow-up was higher in both the group at risk of malnutrition and in the malnourished group, compared with the well-nourished group.

A secondary finding was the U-shaped relationship between BMI and mortality. The optimal BMI for overall survival in the study population was 29.6 with a decreased survival below and above this value. This indicates that overweight older people (i.e., with BMI 25–30) have a lower mortality risk than older people of normal weight (i.e., with BMI 18.5–25). This is in accordance with the results from a systematic review and meta-analysis, which reports a HR (95% CI) of 0.90 (0.86–0.95) for overweight individuals aged ≥65 years, compared with normal weight individuals.[19]

The major strengths of the present study were its sample size and the length of follow-up. This is so far the largest study examining the relationship among the three nutritional status groups defined by the MNA and mortality among older people admitted to hospital.[8 20 21] From a clinical point of view, it is more interesting to examine the three nutritional status groups rather than to examine the overall MNA score (0–30), as these categories are used to screen individuales for risk of malnutrition or malnutrition. Further, the prospective study design allowed us to control for a number of comorbidities and several other participant characteristics recorded at baseline. Other unrecognised potentially confounding factors may exist, which could affect the risk estimate. However, the magnitude and robustness of the estimates in the regression models make it unlikely that they occur purely by chance. A limitation of the study is that the results cannot be generalised to institutionalised older people.

The findings from this study relate to individuals who were living at home before admission to hospital, as only a minority of participants (4.9%) came from nursing homes. The inclusion of some participants (*n* = 33) with dementia may have led to misclassification of some individuals and hence have affected the predictive value of the MNA in the study. However, when the final model was analysed without these 33 participants, the hazard ratio for risk of malnutrition and malnutrition remained.

Previous studies that use the three nutritional status groups defined by the full MNA to predict mortality in older people admitted to hospital support the findings of the present study.[15, 20, 22-24] However, the majority of these studies do not conduct any regression analysis[15, 22-24] and only measure in-hospital mortality.[15, 23, 24] One of these studies performes both regression analyses and measures long term mortality.[20] This Australian study (*n* = 476) adjust the analyses for major disease classifications at admission and reports a hazard ratio for death in the malnourished group of 3.4 (1.07–10.87) after 18 months.[20] However, this retrospective study includes only individuals that had survived 12 months. This introduces bias and hinders a direct comparison with our cohort, where a substantial mortality was noticed the first year of follow-up. In contrast, one small Scandinavian study with prospective data analyse the three categories in the MNA to predict malnutrition in 101 individuals ≥65 years old admitted to hospital. However, after adjustment for age, sex, and Charlton comorbidity index, there is no association between malnutrition and mortality at 1-year follow-up.[21]

The prospective design of the current study, the large sample size and the adjustment for several important determinants including comorbidities, contribute to clarifying the independent relationship between nutritional status defined by MNA and mortality. The finding from the present study that 65% of older people admitted to hospital were at risk of malnutrition or malnourished, and thus had an increased risk of an early death, emphasises the importance of screening and taking appropriate actions to counteract malnutrition.

However, it is still unknown which nutritional interventions are most effective and to whom these interventions should be targeted. Large-scale prospective studies are needed to evaluate the effect of different interventions in terms of quality of life, functional status and survival.

Conclusion

In conclusion, nutritional status defined according to the three categories in the full MNA independently predicts preterm death in people 65 years and older. These findings are clinically important and emphasise the usefulness of the MNA for screening nutritional status. The results also support policymakers in continuing work to establish effective interventions against malnutrition in older people.

Statement of authorship

LS participated in the conception and design of the study, carried out the study, performed statistical analyses, interpreted the results, wrote the first draft, and edited the paper. AR participated in the conception and design of the study, performed statistical analysis, interpreted the results, wrote the statistical analysis plan, and assisted in the editing of the paper. ETA participated in the conception and design of the study, interpreted the results, and assisted in the editing of the paper. AS interpreted the results and assisted in the editing of the paper. LB participated in the conception and design of the study, interpreted the results, and assisted in the editing of the paper. All authors read and approved the final paper.

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Conflict of interest statement

The authors declare no conflicts of interest.

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