European Geriatric Medicine (2019) 10:619–624
https://doi.org/10.1007/s41999-019-00204-1

RESEARCH PAPER

Which laboratory malnutrition markers best predict 1-year mortality in hospitalized older adults?

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Received: 13 December 2018 / Accepted: 8 May 2019 / Published online: 24 May 2019

Key summery points

Aim To study which laboratory malnutrition markers best predict 1-year mortality in hospitalized older adults as well as among patients at risk for malnutrition.

Findings Low albumin serum levels best predict 1-year mortality in hospitalized older adults as well as among patients at risk for malnutrition, followed by low transferrin serum levels.

Message Together with low albumin serum levels, low transferrin serum levels also predict mortality in hospitalized older adults.

Abstract

Purpose To study which laboratory malnutrition markers best predict 1-year mortality in the general population of hospitalized older adults as well as among patients at risk for malnutrition.

Methods A historical prospective study. All older adults (age ≥ 65 years) hospitalized in one geriatric department during 9 months were included. Malnutrition Universal Screening Tool (MUST) was used to determine malnutrition risk. Laboratory malnutrition markers included albumin serum levels, transferrin serum levels, total cholesterol serum levels, vitamin D serum levels, and lymphocyte count. A receiver operating characteristic (ROC) curve analysis was used to study which markers best predict 1-year mortality.

Results Overall, 437 patients (63.2% women; mean age 84.7 years) were included. Overall, 126 (28.8%) patients died in the year following admission. ROC curve analysis showed that low albumin serum levels best predict 1-year mortality (AUC 0.721, $p < 0.001$), followed by low transferrin serum levels (AUC 0.661, $p < 0.001$) and low lymphocyte count (AUC 0.575, $p = 0.016$). Among 178 (40.7%) patients at risk for malnutrition, 63 (35.4%) patients died in the year following admission. ROC curve analysis showed that albumin serum levels best predict 1-year mortality in patients at risk for malnutrition (AUC 0.720, $p < 0.001$), followed by transferrin serum levels (AUC 0.659, $p = 0.001$). Regression analysis showed that low albumin serum levels were also independently associated with 1-year mortality among the whole cohort and among patients at risk for malnutrition (OR 0.2, 95% CI 0.1–0.4, $p < 0.001$, for both).

Conclusions Low albumin serum levels best predict 1-year mortality in hospitalized older adults, followed by low transferrin serum levels.

Keywords Albumin · Malnutrition · Mortality · Older adults · Transferrin

Introduction

Malnutrition is prevalent in older adults; according to Kaiser et al., 5% of community-dwelling older adults and 13% of older adults in nursing homes are malnourished, and higher incidence is recorded among hospitalized older adults [1]. Malnutrition in hospitalized older adults is a risk factor for deconditioning, moving to a nursing home, and 1-year mortality [2].

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Several markers are commonly used to detect malnutrition in the daily clinical practice; body mass index (BMI) is probably the most common anthropometric malnutrition marker; Malnutrition Universal Screening Tool (MUST) scale which includes BMI is likewise frequently used to assess malnutrition risk [3]. Laboratory malnutrition markers are also commonly used to assess malnutrition risk, including low albumin serum levels, low transferrin serum levels, low total cholesterol serum levels, low vitamin D serum levels, and low lymphocyte count [4–6].

We have sought to study which of these laboratory malnutrition markers best predict 1-year mortality in the general population of hospitalized older adults as well as among patients at risk for malnutrition.

Methods

Study design

This was a historical prospective study. All consecutive older adults (age 65 years or more) hospitalized in Sheba medical center—the largest tertiary medical center in Israel—in one geriatric department (Internal Medicine and Geriatrics D) between April 2014 and December 2014 were included. Data were obtained retrospectively, de-identified, and analyzed anonymously. Hence, informed consent was not obtained from the patients. The study was approved by the Sheba's Helsinki committee for human and animal trials.

Study population

The study group included patients who died 1 year following hospital admission, and the control group included patients who survived. Only patients admitted from the emergency room were included. Patients who were transferred to the above-mentioned geriatric department from departments other than the emergency room were excluded. In case of re-admissions, only the first admission was included in the analysis.

Study variables

The following variables were documented: age, gender, chronic co-morbidities, BMI, albumin serum levels, transferrin serum levels, total cholesterol serum levels, vitamin D serum levels, lymphocyte count, MUST scale score and all-cause mortality 1 year following hospital admission according to the national residence registration office. Laboratory malnutrition markers, BMI, and MUST scale score were evaluated routinely in every patient upon admission.

Statistical analysis

Mean and standard deviation were calculated for continuous variables. Odds ratios were calculated using univariate logistic regression analysis for the continuous variables and Chi-square test for the non-continuous variables (Tables 1, 2, 3). Receiver operating characteristic (ROC) curve analysis was used to study which laboratory malnutrition markers best predicts 1-year mortality. Multivariate logistic regression analysis (backward likelihood ratio) was used to study which laboratory malnutrition marker was associated with 1-year mortality following adjustment for age, gender, chronic co-morbidities, and BMI (Table 4). All calculations were performed using version 24 of the SPSS software (SPSS Inc., Chicago, IL, USA).

Results

Overall, 437 patients aged 65 years or more (mean age 84.7 ± 7.2 years) were included in the final analysis: 276 (63.2%) women and 161 (36.8%) men. Main diagnoses (in descending order of incidence) included: infectious diseases ($n = 126$, 28.8%), weakness and falls ($n = 95$, 21.7%), neurological diseases ($n = 68$, 15.6%), cardiovascular diseases ($n = 38$, 8.7%), musculoskeletal and soft-tissue diseases ($n = 30$, 6.9%), gastrointestinal diseases ($n = 25$, 5.7%), renal and electrolyte disorders ($n = 24$, 5.5%), anemia and bleeding ($n = 20$, 4.6%), metabolic disorders ($n = 9$, 2.1%), and others ($n = 2$, 0.5%). The most prevalent chronic co-morbidities were hypertension, dementia, cerebrovascular disease, and diabetes mellitus. According to the MUST score, 178 (40.7%) patients were at risk for malnutrition (Table 1) but only 10 (2.3%) patients had a feeding tube.

Among the whole cohort, 126 (28.8%) patients died in the year following hospital admission. Compared with survivals, deceased patients were older, and had higher prevalence of dementia, congestive heart failure, chronic renal failure, recent year venous thromboembolism, risk for malnutrition, and BMI < 18.5 kg/m^2 (Table 1). Among 178 patients at risk for malnutrition, 63 (35.4%) patients died in the year following hospital admission, and compared with survivals, they were older and had higher prevalence of dementia (Table 2).

Compared with survivals, deceased patients had lower albumin serum levels and lower transferrin serum levels—both among the whole cohort and among patients at risk for malnutrition (Table 3).

ROC curve analysis showed that among the whole cohort, low albumin serum levels best predict 1-year

Table 1 Clinical characteristics of deceased and survivors among the whole cohort

	Whole cohort ($n=437$)	Survived within 1 year ($n=311$)	Died within 1 year ($n=126$)	Odds ratio (95% confidence interval)	p value
Age, years, mean (standard deviation)	84.7 (7.2)	83.8 (6.8)	86.9 (7.4)	1.0 (1.0–1.1)	< 0.001
Female, *n* (%)	276 (63.2)	198 (63.7)	78 (61.9)	0.9 (0.6–1.4)	0.744
Hypertension, *n* (%)	349 (79.9)	251 (80.7)	98 (77.8)	0.8 (0.5–1.3)	0.511
Dementia, *n* (%)	175 (40.0)	105 (33.8)	70 (55.6)	2.4 (1.6–3.7)	< 0.001
Past stroke, *n* (%)	168 (38.4)	112 (36.0)	56 (44.4)	1.4 (0.9–2.1)	0.105
Diabetes mellitus, *n* (%)	166 (38.0)	111 (35.7)	55 (43.7)	1.3 (0.9–2.1)	0.129
Ischemic heart disease, *n* (%)	137 (31.4)	91 (29.3)	46 (36.5)	1.3 (0.8–2.1)	0.141
Atrial fibrillation, *n* (%)	115 (26.3)	75 (24.1)	40 (31.7)	1.4 (0.9–2.3)	0.119
Congestive heart failure, *n* (%)	105 (24.0)	65 (20.9)	40 (31.7)	1.7 (1.1–2.8)	0.019
Chronic renal failure, *n* (%)	84 (19.2)	51 (16.4)	33 (26.2)	1.8 (1.1–2.9)	0.023
Depression, *n* (%)	76 (17.4)	61 (19.6)	15 (11.9)	0.5 (0.3–1.0)	0.069
Chronic lung disease, *n* (%)	62 (14.2)	43 (13.8)	19 (15.1)	1.1 (0.6–1.9)	0.763
Cancer, *n* (%)	39 (8.9)	24 (7.7)	15 (11.9)	1.6 (0.8–3.1)	0.194
Parkinson's disease, *n* (%)	37 (8.5)	26 (8.4)	11 (8.7)	1.0 (0.5–2.1)	0.852
Peripheral vascular disease, *n* (%)	28 (6.4)	21 (6.8)	7 (5.6)	0.8 (0.3–1.9)	0.830
Collagen vascular disease, *n* (%)	24 (5.5)	15 (4.8)	9 (7.1)	1.5 (0.6–3.5)	0.357
Recent year venous thromboembolism, *n* (%)	7 (1.6)	2 (0.6)	5 (4.0)	6.3 (1.2–33.3)	0.023
Smoking, *n* (%)	12 (2.7)	6 (1.9)	6 (4.8)	2.5 (0.8–8.0)	0.113
MUST at risk for malnutrition, *n* (%)	178 (40.7)	115 (37.0)	63 (50.0)	1.7 (1.1–2.5)	0.014
BMI < 18.5 kg/m^2, *n* (%)	11 (2.5)	4 (1.3)	7 (5.6)	4.5 (1.3–15.9)	0.035
BMI = 18.5–20.9 kg/m^2, *n* (%)	69 (15.8)	49 (15.8)	20 (15.9)	1.0 (0.6–1.8)	
BMI > 21.0 kg/m^2, *n* (%)	357 (81.7)	258 (83.0)	99 (78.6)	1 (reference)	

MUST Malnutrition Universal Screening Tool, *BMI* body mass index

Table 2 Clinical characteristics of deceased and survivors among patients at risk for malnutrition

	Whole cohort ($n=178$)	Survived within 1 year ($n=115$)	Died within 1 year ($n=63$)	Odds ratio (95% confidence interval)	p value
Age, years, mean (standard deviation)	84.9 (7.4)	83.5 (7.1)	87.1 (7.4)	1.0 (1.0–1.1)	0.003
Female, *n* (%)	107 (60.1)	73 (63.5)	34 (54.0)	0.7 (0.3–1.2)	0.263
Hypertension, *n* (%)	113 (74.7)	86 (74.8)	47 (74.6)	0.9 (0.5–2.0)	0.999
Dementia, *n* (%)	87 (48.9)	45 (39.1)	42 (66.7)	3.1 (1.6–5.9)	0.001
Past stroke, *n* (%)	69 (38.8)	40 (34.8)	29 (46.0)	1.6 (0.9–2.9)	0.151
Diabetes mellitus, *n* (%)	76 (42.7)	47 (40.9)	29 (46.0)	1.2 (0.7–2.3)	0.529
Ischemic heart disease, *n* (%)	60 (33.7)	34 (29.6)	26 (41.3)	1.7 (0.9–3.2)	0.136
Atrial fibrillation, *n* (%)	53 (29.8)	30 (26.1)	23 (36.5)	1.6 (0.8–3.2)	0.171
Congestive heart failure, *n* (%)	34 (19.1)	20 (17.4)	14 (22.2)	1.4 (0.6–2.9)	0.433
Chronic renal failure, *n* (%)	35 (19.7)	21 (18.3)	14 (22.2)	1.3 (0.6–2.7)	0.557
Depression, *n* (%)	28 (15.7)	21 (18.3)	7 (11.1)	0.6 (0.2–1.4)	0.282
Chronic lung disease, *n* (%)	29 (16.3)	20 (17.4)	9 (14.3)	0.8 (0.3–1.9)	0.675
Cancer, *n* (%)	16 (9.0)	8 (7.0)	8 (12.7)	1.9 (0.7–5.5)	0.273
Parkinson's disease, *n* (%)	16 (9.0)	10 (8.7)	6 (9.5)	1.1 (0.4–3.2)	0.999
Peripheral vascular disease, *n* (%)	11 (6.2)	9 (7.8)	2 (3.2)	0.4 (0.1–1.9)	0.332
Collagen vascular disease, *n* (%)	12 (6.7)	5 (4.3)	7 (11.1)	2.8 (0.8–9.1)	0.117
Recent year venous thromboembolism, *n* (%)	4 (2.2)	1 (0.9)	3 (4.8)	5.7 (0.6–55.9)	0.128
Smoking, *n* (%)	6 (3.4)	4 (3.5)	2 (3.2)	0.9 (0.2–5.1)	0.999
BMI < 18.5 kg/m^2, n (%)	10 (5.6)	3 (2.6)	7 (11.1)	4.3 (1.9–17.6)	0.058
BMI = 18.5–20.9 kg/m^2, *n* (%)	66 (37.1)	46 (40.0)	20 (31.7)	0.8 (0.4–1.6)	
BMI > 21.0 kg/m^2, *n* (%)	102 (57.3)	66 (57.4)	36 (57.1)	1 (reference)	

BMI Body mass index

Table 3 Laboratory malnutrition markers among deceased and survivors

		Survived within 1 year	Died within 1 year	Odds ratio (95% confidence interval)	*p* value
Whole cohort ($n=437$)[a]					
Albumin, g/dL, mean (standard deviation)	3.5 (0.5)	3.6 (0.5)	3.2 (0.5)	0.2 (0.1–0.3)	< 0.001
Total cholesterol, mean (standard deviation)	163.4 (41.6)	164.6 (39.1)	160.5 (47.1)	1.0 (0.9–1.0)	0.385
Transferrin, mg/dL, mean (standard deviation)	199.5 (54.9)	207.2 (52.9)	180.4 (55.1)	0.3 (0.2–0.5)[b]	< 0.001
Lymphocytes, K/micL, mean (standard deviation)	1.7 (0.9)	1.8 (0.9)	1.6 (0.9)	0.7 (0.6–1.0)	0.080
Vitamin D, ng/ml, mean (standard deviation)	19.9 (9.7)	20.2 (9.5)	19.0 (10.0)	1.0 (0.9–1.0)	0.233
At risk for malnutrition ($n=178$)[a]					
Albumin, g/dL, mean (standard deviation)	3.4 (0.5)	3.5 (0.5)	3.1 (0.5)	0.2 (0.1–0.4)	< 0.001
Total cholesterol, mean (standard deviation)	156.7 (40.8)	155.8 (38.7)	158.4 (44.6)	1.0 (0.9–1.0)	0.690
Transferrin, mg/dL, mean (standard deviation)	194.1 (57.8)	203.5 (57.7)	176.9 (54.5)	0.3 (0.2–0.5)[b]	0.004
Lymphocytes, K/micL, mean (standard deviation)	1.7 (0.8)	1.7 (0.7)	1.7 (0.9)	1.0 (0.7–1.5)	0.829
Vitamin D, ng/ml, mean (standard deviation)	19.9 (10.0)	19.4 (9.9)	21.0 (10.3)	1.0 (0.9–1.0)	

[a]Missing among the whole cohort: albumin ($n=2$), total cholesterol ($n=6$), transferrin ($n=3$), lymphocytes ($n=3$), vitamin D ($n=3$); missing among patients at risk for malnutrition: albumin ($n=1$), total cholesterol ($n=2$), lymphocytes ($n=1$); [b]Per 100 units change

Table 4 Multivariate logistic regression analysis showing which variables are independently associated with 1-year mortality among the whole cohort and among patients at risk for malnutrition

	Odds ratio	95% Confidence interval	*p* value
Whole cohort ($n=437$)			
Age	1.1	1.0–1.1	< 0.001
Past stroke	1.7	1.1–2.8	0.031
Dementia	1.8	1.1–2.9	0.017
Smoking	3.9	1.1–14.1	0.032
Albumin	0.2	0.1–0.4	< 0.001
At risk for malnutrition ($n=178$)			
Age	1.1	1.0–1.1	0.030
Atrial fibrillation	2.9	1.2–7.1	0.021
Diabetes mellitus	3.2	1.5–7.7	0.008
Albumin	0.2	0.1–0.4	< 0.001

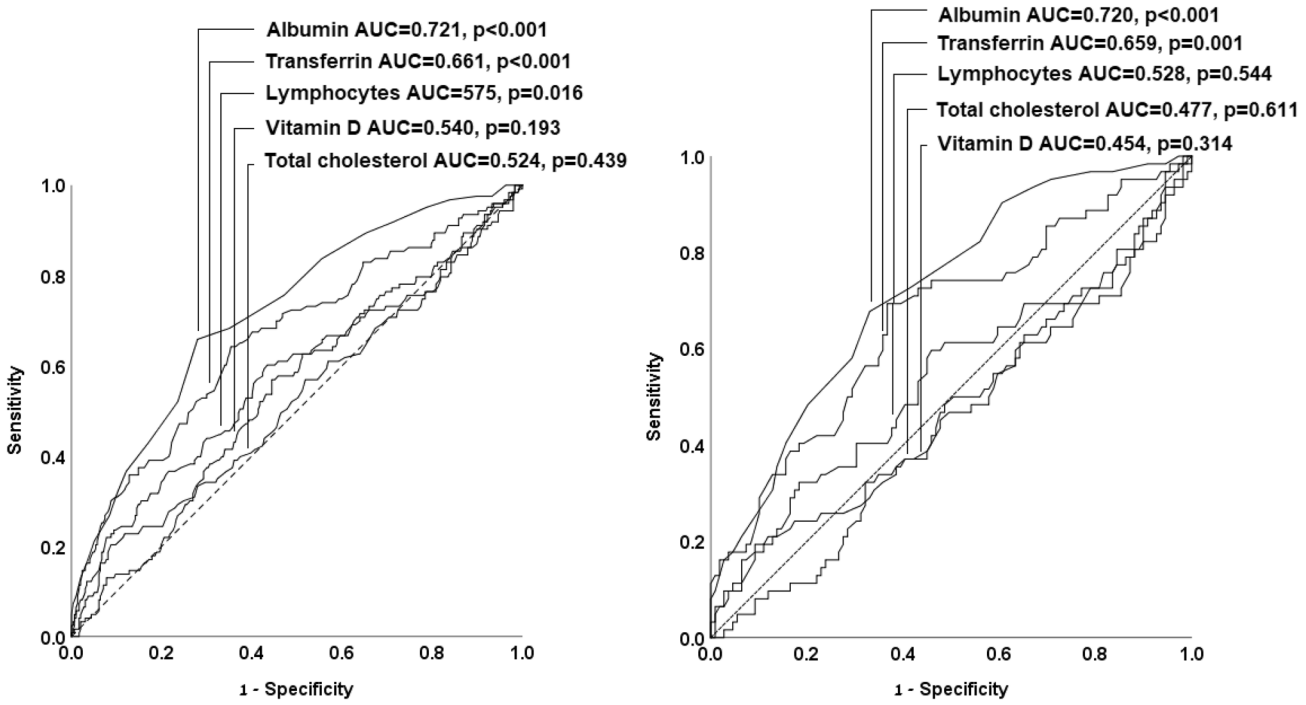
mortality, followed by low transferrin serum levels, and low lymphocyte count (Fig. 1, left). Among patients at risk for malnutrition, ROC curve analysis showed that albumin serum levels best predict 1-year mortality, followed by transferrin serum levels (Fig. 1, right).

Regression analysis showed that albumin serum levels were the only laboratory malnutrition marker negatively associated with 1-year mortality among the whole cohort and among patients at risk for malnutrition—independent of age, gender, chronic co-morbidities, and BMI (Table 4).

Discussion

The recently published GLIM criteria do not advocate the use of laboratory biomarkers in malnutrition diagnosis [7]. Nevertheless, in the daily practice laboratory malnutrition markers are commonly used to assess malnutrition risk. They include: low albumin serum levels, low transferrin serum levels, low total cholesterol serum levels, low vitamin D serum levels, and low lymphocyte count [4]. Which of these markers best predict 1-year mortality in hospitalized older adults has never been studied until now; according to the current analysis, low albumin serum levels best predict 1-year mortality in hospitalized older adults, followed by low transferrin serum levels—both among the general population of older adults and among patients at risk for malnutrition; moreover, low albumin serum levels are also associated with 1-year mortality—both among the general population of older adults and among patients at risk for malnutrition.

Previous studies and meta-analyses have assessed which laboratory malnutrition markers best predict malnutrition rather than mortality [5]; to our knowledge, this is the largest cohort of hospitalized older adults in which a head-to-head comparison between laboratory malnutrition markers has been made to assess their mortality predictive value. In 1988, Agarwal et al. have conducted a head-to-head comparison between laboratory malnutrition markers, and they have shown that low albumin serum levels best predict mortality in hospitalized older adults, but the cohort has included only



AUC = Area under the curve

Fig. 1 Receiver operating characteristic (ROC) curve analysis showing which variables predict 1-year mortality among the whole cohort (left) and among patients at risk for malnutrition (right). *AUC* Area under the curve

80 patients, and in-hospital mortality rather than long-term mortality has been studied [8]. In 1989, Woo et al. have shown that low transferrin serum levels predict mortality in older adults, but the cohort has included only institutionalized rather than hospitalized older adult, and short-term mortality of 3 months has been studied [9]. In 2004, Asensio et al. have conducted a head-to-head comparison between laboratory malnutrition markers, and they have shown that low transferrin serum levels predict mortality in hospitalized older adults, but the cohort has included only 105 patients, and in-hospital mortality rather than long-term mortality has been studied [10]. In 2011, Cereda et al. have shown that admission albumin and transferrin serum levels are lower among deceased older adults followed for 6.5 years, but the cohort has included only institutionalized rather than hospitalized older adult [11]. Furthermore, in none of these studies laboratory malnutrition markers and their role in predicting 1-year mortality in hospitalized older adults have been evaluated both among the general population of older adults and among patients at risk for malnutrition.

The predictive value and the association between low albumin serum levels and mortality are well established in the medical literature—in young and old patients, in women and men, in apparently healthy and sick patients, in community-dwelling and hospitalized patients, and in numerous diseases and conditions. It appears that albumin is a robust prognostic predictor because it is involved in various metabolic processes including muscle building, oncotic pressure adjustment, blood hormones carriage, and inflammation regulation [12–15]. The role of low transferrin serum levels in predicting mortality in hospitalized older adults is the actual novelty of the current analysis; it has been reported previously in specific diseases and conditions such as cirrhosis [16, 17], gastrointestinal cutaneous fistulas [18], Kwashiorkor [19], and following percutaneous endoscopic gastrostomy [20]; but it has never been reported in large populations like the general population of hospitalized older adults as well as among hospitalized older adults at risk for malnutrition—until now. The mechanism is not clear; both albumin and transferrin are synthesized in the liver and their production is impaired in several conditions including systemic inflammation, uremia, malignancy, and hypothyroidism [20]; these conditions are prevalent in older adults and it may partially support the current findings.

The current analysis has several limitations; first, it does not include the whole list of laboratory malnutrition markers such as creatinine serum levels, prealbumin serum levels, C-reactive protein serum levels, and hemoglobin levels [8]; second, anemia and iron status which might affect transferrin serum levels have not been studied; third, systemic inflammation which might be associated with low albumin and transferrin serum levels has not been studied [21];

finally, albumin serum levels and transferrin serum levels have not been assessed with respect to protein and iron supplementation, and total cholesterol serum levels have not been assessed with respect to statin therapy. Future studies should address these limitations, and may also include a prospective interventional branch in which hospitalized older adults with low albumin and transferrin serum levels may be treated with nutritional supplementation to reduce long-term mortality.

In conclusion, low albumin serum levels best predict 1-year mortality in hospitalized older adults, followed by low transferrin serum levels. These findings may have fundamental affect on the clinical practice by adding to albumin serum levels a laboratory mortality predictor in hospitalized older adults, namely transferrin serum levels.

Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Sheba's Helsinki committee for human and animal trials and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Data were obtained retrospectively, de-identified, and analyzed anonymously. Hence, informed consent was not obtained from the patients.

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