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Nutritional Status and Adverse Outcomes in Older Depressed Inpatients: A Prospective Study

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Abstract

OBJECTIVES: Significant weight loss and/or loss of appetite is a criterion of a depressive episode. While malnutrition is associated with many adverse health outcomes, the impact of malnutrition in late-life depression has hardly been examined. The present study aims to (1) evaluate the prevalence of malnutrition in depressed older inpatients, and (2) whether and which indices of malnutrition predict adverse health outcomes in late-life depression.

DESIGN: A prospective study at 6 months follow-up.

SETTING: A University-based psychiatric hospital.

PARTICIPANTS: 105 older adults (psychiatric inpatients suffering from unipolar MDD).

MEASUREMENTS: Participants were evaluated according the Mini Nutritional Assessment (MNA) and anthropometric measures to assess their nutritional status. Multiple regression analyses were used to evaluate the association between the MNA score as well as anthropometric measures with either falls or rehospitalization for any reason.

RESULTS: Based on the MNA score, 78 (74.3%) patients were at risk of malnutrition and 13 (12.4%) actually presented malnutrition. Malnutrition was associated with a higher age, frailty, lower body mass index, and smaller calf circumference. During follow-up, 21 (20%) patients fell, 27 (25.7%) were rehospitalized, and 3 died (2.9%). The MNA score was associated with adverse health outcomes, but a low calf circumference predicted falling (OR 4.93 [95% CI: 1.42-17.2], p=.012) and a higher calf circumference rehospitalization (OR 1.17 [95% CI: 1.01-1.35], p=.032).

CONCLUSION: Malnutrition is prevalent in older depressed inpatients. In contrast to subjective proxies for malnutrition, which are common in depression, only objective measures of malnutrition predict adverse health outcomes such as falls and rehospitalization.

Key words: Major depressive disorder, nutritional status, falls, hospitalization, older adults.

Introduction

Major depressive disorder (MDD) is an affective disorder with a 12-month and lifetime prevalence of 10.4% and 20.6%, respectively (1). Most importantly, the majority of lifetime MDD episodes are classified as moderate or severe, and 12% of adult patients are hospitalized at some point (1). Twenty percent of all costs attributable to MDD rely on hospitalization (2). Moreover, one quarter of all psychiatric hospitalizations are due to MDD (3), with an average length of stay of 6 days in a recent survey (4). The main reasons of hospital admission for MDD are severity of illness, lack of adequate therapeutic response, and functional disability compromising the activities of daily living (5). This data is relevant especially regarding older adults with MDD, who consisted in almost 10% of all hospital admissions (4), and to whom multimorbididity, geriatric syndromes and disability could result in higher hospital costs, longer periods of hospitalization and higher chance of clinical complications.

Inpatient mental health care usually follows a disease-based model, which is effective to specific conditions, but probably may not totally fit to complex older adults with higher degrees of multimorbidity and geriatric syndromes (6, 7). Several clinical (eg. nutrition; hydration; multimorbidity; polypharmacy) and prognostic (eg. frailty; disabilities) parameters may be relevant for hospitalized, depressed older patients. Nutrition has a potential role in preventive and therapeutic approaches in psychiatry, especially in affective disorders (8). Lower levels of essential nutrients (e.g. vitamin B12, folate, tryptophan) may result in lower production of neurotransmitters such as serotonin (9). Yet, data yielded from prospective cohort studies as well as clinical trials indicate that diets (e.g. Mediterranean diet) and nutrient supplementation (e.g. n-3 essential fatty acids) may potentially assist in the management of depression through adequate concentrations of n-3 essential fatty acids, folate, vitamin B12, magnesium, and zinc, essentials for normal physiological functioning (10). Recently, the gut-microbiome is even suggested as modifiable risk factor for depression (11). These data collectively illustrate the importance of an adequate nutritional state for depressed patients. Although the International Society for Nutritional Psychiatry Research recommends nutritional medicine to treat mental disorders concomitantly to usual psychiatric care, the lack of evidence from important areas in geriatric affective disorder may hinder implementation of this strategy (12).

Aging is associated with physiological as well as social changes which negatively interfere with the nutritional status, including sensory impairment, depression, poor oral health,

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and loneliness (13). Depression is generally considered as one of the main explanations for weight loss among seniors, since appetite and weight loss are common in depression (14). Weight loss is of special concern since depressed older patients are at a higher risk of malnutrition, which can initiate a cycle of nutritional inadequacy and frailty (15, 16). Most of data regarding depressive older inpatients comes from general hospitals and acute medical settings, usually involving less severe cases of depression comorbid to somatic illness (17). Moreover, the majority of these data is cross-sectional. Since malnutrition is associated with depressive disorder and at a population level increases with age, malnutrition can be expected highly common among depressed older inpatients. We hypothesize that malnutrition may be a determinant of adverse health outcomes in these patients. Therefore, the aims of the present study were to evaluate: (1) the prevalence of malnutrition in depressed older inpatients, and (2) whether and which indices of malnutrition predict adverse health outcomes (falls and rehospitalization) in late-life depression after 6 months of hospital discharge.

Methods

Study design and procedures

We conducted a 6-month prospective clinical study of 113 older adults, consecutively admitted to acute wards for geriatric psychiatry between 1 January 2017 and 31 January 2020. The study was carried out in the Institute of Psychiatry, Hospital das Clínicas da Universidade de São Paulo, a large teaching hospital in São Paulo, southwestern of Brazil. Eligible patients were those 60 years or older, admitted to the hospital due to severe (Hamilton Depression Scale >19 points) unipolar MDD. All patients were clinically diagnosed through consensus multidisciplinary meetings according to the DSM-5 classification (5). Exclusion criteria were not giving informed consent, not mastering the Portuguese language, no family member or caregiver to be interviewed, severe sensory impairment, cognitive impairment (Mini Mental State Examination <25 points), or a diagnosis of bipolar affective disorder or severe psychosis. Additionally, individuals with severe uncompensated clinical diseases or edema were excluded to avoid interference with the accuracy of the collected anthropometric data. Eight patients fulfilled at least one exclusion criteria. Two authors (ZML and ACAS) evaluated all patients every 48h and applied the study protocol and anthropometric measures within the first 24 hours of hospital admission. This study was conducted according to the ethical guidelines of research with human beings, approved by the local Ethics Committee.

Measurements

Nutritional assessment was carried out through evaluation of anthropometry and nutritional risk screening using the Mini Nutritional Assessment (MNA). The MNA is recommended by the European Society of Parenteral and Enteral Nutrition (ESPEN), the International Association of Gerontology (IAG) and the International Academy of Nutrition of Aging (IANA) for the identification of risk of undernutrition and malnutrition in older adults (18-20). Previously, a Brazilian version has been validated (21). The MNA include anthropometric measures such as the body mass index (BMI), biceps circumference, calf circumference, and self-report questions regarding lifestyle, medications, psychological problems, dietary patterns, and self-perceived health and nutritional evaluation. The sum of points for each of the variables yields the MAN final score depicting one out three possible classifications: adequate nutrition (≥24 points), at risk of malnutrition (17 to 23,5 points), and malnutrition (<17 points).

Weight in kilograms was measured with light clothing using calibrated platform-type mechanical scale with non-slip rubber mat with a capacity of up to 150 kg and sensitivity of 100 g with stainless steel slider. Height (in meters) was measured on the same scale using an attached anthropometric ruler, with a vertical and fixed bar and a square over the head forming an angle of 90°. The chromed steel ruler has 0.5 cm scales. The BMI was calculated by the formula weight/height^2 and classified according to the cutoff points recommended by the World Health Organization (WHO) (22) as underweight (BMI <18.5kg/m^2), eutrophic (18.5 <BMI <25kg/m^2), overweight (25 <BMI < 30kg/m^2) and obesity (BMI> 30kg/m^2). Regarding muscle mass, the calf circumference in centimeters has been considered the most sensitive measure in older adults, and a good indicator of malnutrition in this population (22). A flexible and inelastic measuring tape was used with 0.1 cm precision and measured with the individual seated. The WHO guidelines were considered for both technique and classification, indicating a reduction in muscle mass when its value is less than 31 cm (22).

Covariates

Age, sex, the level of education, the number of prescribed medications and frailty status were used as covariates for regression analyses. Frailty was assessed according the FRAIL questionnaire Brazilian version (FRAIL-BR) (23). The FRAIL-BR questionnaire is a self-report frailty screening scale aimed to measure frailty in clinical settings and mainly based on variables from Fried Frailty Phenotype (16). The FRAIL-BR assesses the presence of fatigue, muscle resistance, ambulation, disease burden, and loss of weight based. Each affirmative answer results in 1 point. The classification consists of 0 points: robust; 1-2: prefrail; and 3-5: frail (16).

Outcomes

Two different adverse health outcomes were the main outcome. First, the presence of any fall during follow-up. Second, a new hospital admission (rehospitalization) for any reason in the following 6 months after the hospital discharge and/or death.

Table 1. Characteristics of the study population stratified by Mini Nutritional Assessment status

Characteristic	Adequate nutrition (n=14)	At risk of malnutrition (n=78)	Protein calorie malnutrition (n=13)	Statistics
Socio-demographics:				
Age (years)	66.1 (4.8)	70.2 (6.6)	73.0 (7.6)	F=4.0, df=2, p=.022
Female sex, n (%)	5 (35.7)	43 (55.1)	5 (38.5)	Chi2=2.6, df=2, p=.266
Level of education ≥8 years, n (%)	4 (28.6)	39 (50.0)	8 (61.5)	Chi2=3.2, df=2, p=.204
Physical functioning:				
Prescribed medication (number)	8.1 (2.3)	8.4 (3.7)	8.8 (3.1)	F=0.1, df=2, p=.896
Multimorbidity, n (%)	14 (100.0)	65 (83.3)	10 (76.9)	Chi2=3.3, df=2, p=.196
Somatic diseases (number)	3.3 (1.3)	2.7 (1.4)	2.5 (1.2)	F=1.3, df=2, p=.284
Frailty, n (%)	4 (28.6)	31 (39.7)	12 (92.3)	Chi2=14.2, df=1, p=.001
Indices of malnutrition at admission:				
Any weight loss before admission	1 (7.1)	69 (88.5)	13 (100.0)	Chi2=51.3, df=2, p<.001
Body Mass Index, dimensional (kg/m^2)	28.4 (4.7)	24.1(4.5)	17.0 (2.3)	F=24.5; df=2, p<.001
Body Mass Index, categories (WHO):				
- Underweight (<18.5)	-	6 (7.7)	8 (61.5)	Chi2=45.4, df=6, p<.001
- Normal weight (≥18.5 & <25)	3 (21.4)	45 (57.7)	5 (38.5)	
- Overweight (≥25 & <30	5 (45.7)	19 (24.4)	-	
- Obesity (≥30)	6 (42.9)	8 (10.3)	-	-
Calf circumference:				
- Calf circumference >31 cm	14 (100.0)	63 (80.8)	3 (23.1)	Chi2=25.5, df=2, p<.001
- Calf circumference (cm)	35.7 (3.7)	32.7 (3.1)	29.3 (1.0)	

Table 2. Indices of malnutrition as risk factor for future falls by multiple logistic regression analyses

Indices of malnutrition	Unadjusted			Adjusted*		
	OR	[96% CI]	p	OR	[95% CI]	p
Mini Nutritional Assessment, sum score	0.94	[0.80 - 1.10]	0.450	0.90	[0.74 - 1.10]	0.299
Mini Nutritional Assessment, classification:						
- At risk	3.37	[0.41 - 27.9]	0.260	2.68	[0.29 - 24.5]	0.384
- Malnutrition	6.86	[0.63 - 74.2]	0.113	10.28	[0.67 - 15.8]	0.095
Any weight loss before admission	1.86	[0.49 - 7.05]	0.360	2.40	[0.52 - 11.2]	0.265
Body Mass Index (BMI) at admission:**						
- Underweight (<18.5)	2.28	[0.56 - 9.24]	0.249	4.75	[0.83 - 27.3]	0.081
- Overweight (≥25, <30)	1.60	[0.46 - 5.63]	0.463	2.95	[0.68 - 12.9]	0.151
- Obesity (≥30)	2.05	[0.51 - 8.19]	0.310	4.80	[0.90 - 25.5]	0.066
Calf circumference ≤31 cm	4.41	[1.55 - 12.5]	0.005	4.93	[1.42 - 17.2]	0.012
Calf circumference (cm)	0.92	[0.79 - 1.08]	0.320	0.95	[0.80 - 1.13]	0.578

* Adjusted for age, sex, level of education, number of prescribed medications, number of chronic diseases, and frailty; ** Normal weight (18.5 < BMI < 25.0) is reference category (according to the WHO categorization of BMI).

Statistical analysis

For statistical analysis, the SPSS program (Statistical Package for the Social Sciences, USA) version 21.0 was used. All categorical variables were presented in number and percentage and the continuous variables as means and standard deviations. The distribution of variables was tested using the Kolmogorov-Smirnov test to verify the hypothesis of normality, as well as to verify the distribution of data in graphs, checking skewness and kurtosis. The comparison of categorical variables was assessed using the chi-square test or the Fisher test and the ANOVA with post-hoc Tukey test for the continuous variables compared between 3 groups of nutritional status according to MNA classification. Multiple logistic regression analysis was used to assess the association of the MNA score, the BMI and the calf circumference with either falls or rehospitalization or death within 6 months of hospital discharge. In the multivariate analysis, age, sex, education, number of prescribed medications and frailty status were considered as potential covariates. P-values lower than 5% were considered statistically significant.

Table 3. Indices of malnutrition as a risk factor for rehospitalization (and/or death) by logistic regression.

Indices of malnutrition	Unadjusted			Adjusted*		
	OR	[96% CI]	p	OR	[95% CI]	p
Mini Nutritional Assessment, sum score	1.04	[0.90 - 1.21]	0.605	1.13	[0.95 - 1.33]	0.171
Mini Nutritional Assessment, classification:						
- At risk	1.35	[0.34 - 5.38]	0.674	1.18	[0.27 - 5.16]	0.824
- Malnutrition	1.25	[0.20 - 7.96]	0.813	0.71	[0.09 - 5.78]	0.749
Any weight loss before admission	0.96	[0.33 - 2.79]	0.932	0.66	[0.20 - 2.23]	0.507
Body Mass Index (BMI) at admission**						
- Underweight (<18.5)	1.54	[0.40 - 5.96]	0.535	0.90	[0.19 - 4.17]	0.888
- Overweight (≥25, <30)	1.38	[0.43 - 4.41]	0.585	1.63	[0.47 - 5.67]	0.444
- Obesity (≥30)	2.59	[0.74 - 9.07]	0.137	3.92	[0.99 - 15.6]	0.052
Calf circumference ≤31 cm	0.66	[0.22 - 1.99]	0.457	0.52	[0.15 - 1.78]	0.295
Calf circumference (cm)	1.12	[0.98 - 1.27]	0.087	1.17	[1.01 - 1.35]	0.032

* Adjusted for age, sex, level of education, number of prescribed medications, number of chronic diseases, and frailty; ** Normal weight (18.5 < BMI < 25.0) is reference category (according to the WHO categorization of BMI).

Results

Among a sample of 105 older patients hospitalized to receive inpatient care for severe MDD, only 14/105 (13.3%) had an adequate nutritional status, 78/105 (74.3%) were at risk of malnutrition, and 13/105 (12.4%) were suffering from (protein-related) malnutrition. Table 1 presents the characteristics of the study population stratified by their nutritional status. In summary, inpatients with malnutrition were older, more often frail and presented with lower BMI and calf circumference.

Mean hospital length of stay was 45.6 days. Within 6 months after discharge, 21 (20.0%) patients had at least one fall, 27 (25.7%) were rehospitalized for any reason, and 3 (2.9%) died. Seven patients were lost at the follow-up. Of these 97 patients, 21/97 (21.6%) experienced at least one fall.

Table 2 shows whether indices of nutritional status at time of admission predicts falls after discharge. The MNA score was associated with falls in the expected direction but did not achieve statistical significance. Nonetheless, malnutrition (MNA score <17) had a very high odds for falling (p=.095). A low calf circumference was significantly associated with an increased risk of falling. Moreover, having underweight or obesity had a similar odds ratio (OR) for falling, but the OR was not statistically significant, which might be due to low statistical power due to the categorization of BMI into four categories. Similarly, malnutrition itself had a high OR for falls, but it did not achieve statistical significance due to the small number of patients.

Of the 97 patients with follow-up data, 27/97 (25.7%) were rehospitalised (of which three also died).

Table 3 shows whether indices of nutritional status at time of admission predicts rehospitalization after discharge. The MNA score had no predictive value at all. A higher circumference of the calf is associated with a higher risk of rehospitalization. Having obesity had also a high OR of being rehospitalized with 6 months, albeit not statistically significant (p=.052).

Discussion

Main findings

In the present study, 12.4% of this sample of severely depressed older adults presented malnutrition. These inpatients were older, frail (92.3%) and presented lower anthropometric measures. After 6 months, 20% had at least one fall and 25.7% were hospitalized. Calf circumferences showed significant associations with these outcomes, while the MNA sum score and BMI did not. Malnutrition, underweight and obesity showed borderline non-significant associations to falls or rehospitalization.

The prevalence of malnutrition in our study was lower than expected based on previous studies in general hospitals (24-26). In these studies, malnutrition was observed in approximately 30% of admissions (24-26). Data on nutritional status in depressed older adults is scarce (27-29). Moreover, previous studies have assessed the diagnosis of depression with screening scales, which have lower diagnostic accuracy with especially increased rates of false-positive cases. Our study is unique by having assessed depressive disorder according to DSM-5 criteria. Future studies should explore the prevalence of malnutrition in late life depression in different settings, since several reviews have shown that the prevalence of malnutrition among somatically ill patients varies strongly between different health care settings (13).

Depression, both major depressive disorder as well as clinically relevant depressive symptoms, is a consistently identified risk factor for falls in older persons (30, 31). While complete understanding remains to be elucidated, the increased fall risk is definitely multifactorial. Signs and symptoms of depression, such as cognitive impairment, lower energy levels, sedentary behavior, and poor balance, appears to only partially explain this association (32). Antidepressants can also contribute to increase fall risk according to a meta-analysis of 22 studies (33). However, we did not observe differences in antidepressants, mood stabilizers, antipsychotics or

benzodiazepines according to nutritional status in our data (data available upon request), whereafter we decided to adjust for the number of medications only (as many drugs are associated with falls) (34-36). In contrast to our study, previous studies on the association between depression and falls in older adults did not adjust their analyses for the presence of frailty, which is also an important risk factor for falls (14, 37). In our study, a calf circumference lower than 31 cm predicted falls, even when adjusted for frailty. The continuous measure of calf circumference was not associated with falls, which fits with the fact that the cut-off is probably well-validated to identify sarcopenia or protein malnutrition. A lower calf circumference may point to both sarcopenia and low muscle mass. Previously, sarcopenia and low muscle strength, but not low muscle mass, have been proposed as a possible mechanism explaining the increased fall risk associated with depression in late life (38, 39). Moreover, the presence of sarcopenia and its interaction with obesity probably may also result in lower remission rates of depression as previously demonstrated (40).

A large proportion of patients are readmitted within 6 months after discharge (1,4). Reasons for readmission remain unclear and can involve medical, social and behavioral characteristics beyond suicidal attempt and recurrence of depression (4). The course of MDD among older adults is strongly connected to somatic health indicators (40-43), which may reflect a need for a more patient-centered approach.

In the present study, a higher calf circumference (dimensionally measured in centimeters) predicted rehospitalization. Also, a borderline non-significant association with obesity was observed. Obesity is also associated with depression (44) and consistently associated with a higher demand for health care utilization, including hospitalizations (45). So, our findings are in line with previous evidence of a higher health care utilization with the combination of depression and obesity (46). However, this evidence came from a younger sample of depressed individuals.

Strengths and limitations

Our study has several strengths and limitations. It is the first study to evaluate nutritional status and anthropometric parameters and its association with important adverse health outcomes such as falls and rehospitalization in older depressed inpatients in a specialized psychiatric hospital. Our analyses were adjusted for the presence of frailty, a geriatric syndrome highly associated with the targeted outcomes of this study. On the other hand, our sample size was not large enough and some of our analyses may have been underpowered, such as the potential association between MNA score and falls or the both extremes of the BMI and falls. Furthermore, our hospital has been classified as one of the best psychiatric hospitals in Brazil and all patients were given nutritional support during hospitalization. This may have reduced potentially negative effects of malnutrition on the outcomes evaluated after 6 months of hospital discharge.

Conclusion and implications

Finally, our study showed a high prevalence of malnutrition and a significant association between calf circumference and two important adverse outcomes. Additionally, borderline associations between the MNA score and BMI with the two outcomes were also observed. Nutritional status and parameters may add prognostic value in severely depressed older adults. Although most depressed patients report any weight loss before admission, self-reported weight loss was neither associated with falls, nor with rehospitalization. This may argue for implementation of objective measures (like a validated MNA score and direct measures like BMI and calf circumference) to assess nutritional status and risk stratification in psychiatric inpatients.

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