

Relation Between Malnutrition and the Presence of Symptoms of Anxiety and Depression in Hospitalized Cancer Patients

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Abstract

Background

Anxiety and depression are a common issue in patients with cancer, yet understudied among hospitalized patients. The aim of this study was to estimate the prevalence of anxiety and depression symptomatology in cancer inpatients and its relationship with malnutrition.

Methods

Cross-sectional study in hospitalized cancer patients. A nutritional assessment was done using GLIM criteria to diagnose malnutrition. Data regarding anxiety and depression symptomatology was obtained with the Hospital Anxiety and Depression Scale (HADS).

Results

A total of 282 inpatients were assessed. GLIM criteria found 20% (66) of well-nourished and 80% (216) with malnutrition. HADS presented an average score of 8.3 ± 4.4 with respect to anxiety and an average score of 7.7 ± 4.6 with respect to depression. 54 % showed a possible presence of anxiety and 45.3% showed a possible presence of depression.

In malnourished patients, HADS score tended to be higher with respect to anxiety (8.5 ± 4.3 in malnourished vs 7.1 ± 4.6 in well-nourished; $p=0.06$) and was significantly higher with respect to depression (8.2 ± 4.6 in malnourished vs 5.3 ± 4.0 in well-nourished; $p<0.001$).

After controlling for potential confounders, malnourished patients were 1.98 times more likely to present anxious symptomatology (95% CI 1.01-3.98; $p=0.049$) and 6.29 times more likely to present depressive symptomatology (95% CI 1.73-20.47; $p=0.005$).

Conclusions

The presence of anxiety and depression symptomatology in oncological inpatients is high. There is an association between malnutrition and presenting anxious and depressive symptomatology in hospitalized cancer patients.

1. Introduction

Cancer disease and nutritional status are closely linked. Malnutrition is a common issue among these patients, being present in up to 80% of them and increasing morbidity and mortality [1]. The prevalence of malnutrition increases in advanced-stage cancer patients who require hospital admission [2].

It is believed that depression is a frequent condition in cancer patients, mainly for issues related to the severity of the disease and the side effects of treatments [3]. Depression and anxiety occur up to 20% and

10% of patients with cancer respectively [4], although some authors estimate a higher prevalence, especially in patients with advanced cancer or palliative therapy [5, 6].

Depression is associated with poor adherence to cancer treatment and poor cancer survival [7]. Depression and anxiety disorder are associated with an increased risk of mortality and their co-occurrence further increased the risk [8]. Cancer patients with anxiety and depression were at greater risk for emergency department visits and hospitalizations, experienced longer hospital stays, and accrued higher healthcare costs [9].

The relationship between malnutrition and psychological factors has been described in cancer patients. Studies indicate the association between depression and less food consumption, weight loss and malnutrition [10, 11]. Patients experiencing weight loss and other symptoms of malnutrition often report higher levels of psychological distress, which manifest as more severe fatigue, insomnia, anxiety, and depression, further contributing to disease progression [12]. Whether malnutrition is an important risk factor of distress is still not clear. The symptoms of malnutrition and psychological distress overlap, but few studies have focused on the relationship between them [10].

To our knowledge, there are few published data on the prevalence of symptoms of anxiety and depression at its relationship with malnutrition in hospitalized cancer patients. These patients also tend to have more advanced stages, which could condition this possible association.

Our hypothesis is that the prevalence of anxiety and depression symptoms is high in hospitalized cancer patients and is related to the high rate of malnutrition in these patients [2].

The aim of the study was to assess the relationship between nutritional status and the level of anxiety and depression in hospitalized patients with cancer.

2. Methods

We designed an observational, prospective study of clinical practice performed at Hospital Regional Universitario de Málaga. 351 patients were assessed for eligibility after admission to the Oncology ward. Inclusion criteria were patients with solid or hematological neoplasm, length of stay above 48 hours who signed informed consent. Exclusion criteria were patients with length of stay below 48 hours, readmission before one month and terminally ill. After the application of inclusion and exclusion criteria, 282 were evaluated, being 69 excluded (Fig. 1).

2.1. Assessment of the nutritional status

We performed a nutritional assessment according to GLIM criteria within the first 24 hours after admission. To diagnose malnutrition, at least one phenotypic criterion and one etiologic criterion should be present [13].

2.1.1. Phenotypic criteria:

We assessed unintentional weight loss (> 5% in 6 months), low BMI (for age < 70 years normal values were considered as BMI ≥ 20 kg/m², and for age ≥ 70 normal values were established as BMI ≥ 22 kg/m²), and/or reduction of muscle mass basing hand grip strength (HGS). Weight was assessed with a weighing scale adjusted to 0.1 kg (SECA 665, Germany) and height was obtained by a stadiometer (Holtain limited, Crymch, UK). With these two values, body mass index (BMI) was calculated.

Handgrip strength was used to estimate fat-free mass and was measured in the dominant hand with a Jamar dynamometer (*Asimow Engineering Co., Los Angeles, CA*). The patients performed the test while sitting with shoulder adducted and forearm neutrally rotated, elbow flexed to 90°, and forearm and wrist in neutral position. Patients were told to perform three consecutive contractions one minute apart from each other, and mean value was calculated. Results were expressed in absolute figures and compared with the reference population [14]. Values under the fifth percentile were considered as low strength.

2.1.2. Etiologic criteria:

Etiologic criteria were assessed by reduced intake (estimated as per quartiles) or assimilation (as per clinical record), and/or inflammatory response of the disease (patients were considered as presenting chronic disease-related inflammation using Glasgow Prognostic Score) [15, 16].

2.2. The questionnaire

The presence of symptoms of anxiety and depression was measured with Hospital Anxiety and Depression Scale (HADS) questionnaire. The HADS is a brief patient self-report measure of anxiety and depression requiring patients to report their symptoms during the previous week [17]. The HADS has demonstrated reliability and validity in cancer patient populations [18] and has been found to be an effective screening tool for cancer patients currently undergoing treatment [19].

The HADS consists of 14 items and two subscales, one measuring anxiety (HADS Anxiety subscale), with seven items, and another measuring depression (HADS Depression subscale), with seven items, which score separately.

HADS Anxiety subscale focus mainly on symptoms of generalized anxiety disorder and HADS Depression subscale is focused on anhedonia, the main symptom of depression. Each item is scored on a response-scale with four alternatives ranging between 0 and 3. The possible scores range from 0 to 21 for each of the two subscales, taking 2–5 minutes to complete [17]. Subscale scores from 0 to 7 are classified as normal. Subscale scores ranging from 8 to 11 are typically used for identifying the possible presence of anxiety and depression (“doubtful cases”) and subscale scores over 11 indicates the probable presence (“caseness”) of a mood disorder [20].

2.3. Data analysis

Quantitative variables were expressed as the mean \pm standard deviation. Quantitative variables distribution was assessed using Kolmogorof-Smirnof test. Differences between quantitative variables were analyzed using Student's t test and, for variables not following a normal distribution, using non-parametric tests (Mann-Whitney or Kruskall-Wallis). We designed multivariate logistic regression models in which the dependent variable was the cut-off points of the HADS subscales according to the nutritional status determined by GLIM criteria, controlling also for sex, age and tumor stage. For calculations, significance was set at $p < 0.05$ for two tails. The data analysis was performed with the SPSS 22.0 program (SPSS Inc., Chicago, IL, 2013).

3. Results

282 patients admitted to Inpatient Oncology Unit were evaluated. Their mean age was of 60.4 ± 12.6 years, and 55.7% of them were male. Their general features are displayed in Table 1. Most patients (92.9%) had an advanced-stage tumor (17.7% stage III, 75.2% stage IV). The most frequent types of neoplasm were lung (25.2%), colon (13.0%), breast (13%), and esophagogastric (11.8%). At the moment of admission, a nutritional assessment according to GLIM criteria was performed, detecting 80% (216) of patients with malnutrition (Table 1). 20.6% (58) of the patients had a low BMI and 37.9% (107) had low HGS.

HADS presented an average score of 8.3 ± 4.4 points with respect to anxiety (8.0 ± 4.5 points in male vs 8.7 ± 4.3 points in female) and an average score of 7.7 ± 4.6 with respect to depression (7.5 ± 4.8 points in male vs 7.8 ± 4.3 points in female). With these data, 54% of our patients showed a possible presence of anxiety and 45.3% showed a possible presence of depression.

Table 1
General features. Prevalence of anxiety and depression symptomatology.

		n = 282
Age (years)	mean ± SD	60.4 ± 12.6
Sex	n (%)	
Men		157 (55.7)
Women		125 (44.3)
Tumor stage	n (%)	
I		7 (2.5)
II		13 (4.6)
III		50 (17.7)
IV		212 (75.2)
BMI (kg/m²)	mean ± SD	
Men		24.7 ± 4.9
Women		24.5 ± 5.1
Hand-grip strenght (kg)	mean ± SD	
Men		26.21 ± 8.58
Women		16.51 ± 6.70
Malnutrition according to GLIM criteria	n (%)	216 (80%)
HADSA score	mean ± SD	8.30 ± 4.40
HADSD score	mean ± SD	7.68 ± 4.61
Possible presence of anxiety (HADSA ≥ 8)	n (%)	127 (54%)
Possible presence of depression (HADSD ≥ 8)	n (%)	106 (45.3%)
Probable presence of anxiety (HADSA ≥ 11)	n (%)	62 (26.4%)
Probable presence of depression (HADSD ≥ 11)	n (%)	63 (26.9%)
BMI: body mass index; GLIM: Global Leadership Initiative on Malnutrition; HADSA: Hospital Anxiety and Depression Scale anxiety subscale; HADSD: Hospital Anxiety and Depression Scale depression subscale; SD: standard deviation;		

In malnourished patients according to GLIM criteria, average score tended to be higher with respect to anxiety (8.5 ± 4.3 points in malnourished vs 7.1 ± 4.6 in well-nourished; $p = 0.06$) and was significantly

higher with respect to depression (8.2 ± 4.6 points in malnourished vs 5.3 ± 4.0 points in well-nourished; $p < 0.001$) (Fig. 2).

Table 2 shows the logistic regression data (crude and adjusted) for the risk of presenting anxious or depression symptomatology in malnourished patients. After controlling for potential confounders, in malnourished patients according to GLIM criteria the odds ratio of presenting anxious symptomatology was 1.98 times greater than in well-nourished [95% CI 0.99–3.98; $p = 0.05$] and the odds ratio of presenting depression symptomatology in these patients was 6.29 times greater than in well-nourished [95% CI 1.73–20.47; $p = 0.005$].

Table 2

Risk of presenting anxious or depression symptomatology in malnourished patients. Adjusted for age, sex and cancer stage.

Odds ratio	Crude			Adjusted				
	95% CI		P value	Odds ratio	95% CI		P value	
	Lower	Upper			Lower	Upper		
Possible presence of anxiety (HADS _A ≥ 8)	2.06	1.04	4.06	0.037	1.98	1.01	3.98	0.049
Probable presence of anxiety (HADS _A ≥ 11)	1.03	0.48	2.21	0.93	1.05	0.48	2.32	0.89
Possible presence of depression (HADS _D ≥ 8)	6.73	2.71	16.73	< 0.001	6.29	2.51	15.75	< 0.001
Probable presence of depression (HADS _D ≥ 11)	6.08	1.81	20.48	0.004	5.95	1.73	20.47	0.005
Bold: statistically significant								

4. Discussion

The presence of anxiety and depression symptomatology in oncological inpatients is high and there is an association between this symptomatology and malnutrition in our series.

We used HADS questionnaire to identify anxious and depressive symptoms. Cancer research has extensively applied subscale thresholds of 11 to indicate the likely presence of anxiety and/or depression, reported as achieving 70–95% sensitivity and 83% specificity with respect to clinical interview [21] although some authors suggest that the recommended cut-off scores for the HADS may result in under-reporting of psychiatric morbidity among patients with cancer [22]. An optimal balance between sensitivity and specificity was found using a cut-off score of 8 or above for both HADS Anxiety and HADS Depression [21].

Previous studies in cancer patients found a prevalence of 12–15% of anxiety symptomatology and a prevalence of 5.7-7% of depression symptomatology using HADS threshold of ≥ 11 [23]. In the present study, using a HADS threshold of ≥ 11 , 26.9% of patients were identified with a likely presence of depression and 24.4% of them were identified with a probable presence of anxiety. Using a HADS threshold of ≥ 8 , highlights that close to half of respondents were identified with a likely presence of depression and 54% of them were identified with a probable presence of anxiety.

Even using a HADS threshold of ≥ 11 , the rate of anxiety and depression symptomatology in our series is higher than in the series previously described.

Most of the patients of our study (92.9%) had an advanced-stage tumor (17.7% stage III, 75.2% stage IV), many of them under palliative therapy. Prevalence of anxiety and depression increases with the cancer stage. A study found that the baseline prevalence of anxiety and depression symptomatology in 126 patients treated with palliative systemic therapy for advanced cancer was 35.9 and 56.5%, respectively [6].

Figures also vary by cancer type, with major depression affecting an estimated 13% of patients with lung cancer, 11% of those with gynecological cancers, 9% in breast cancer, 7% in colorectal cancer, and 6% in genitourinary cancers [24]. The highest levels of anxiety are reported in lung, gynecological, and hematological cancers [19]. The most frequent types of neoplasm in our series were lung (25.2%), colon (13.0%), breast (13%), which could explain higher rates of anxious and depressive symptoms.

A review and meta-analysis showed the prevalence of major depression (15%), minor depression (20%), and anxiety (10%) in patients treated for cancer [4].

Linden et al performed a study with 10153 cancer outpatients using the Psychosocial Screen for Cancer questionnaire. Across cancer types, 19.0% of patients showed clinical levels of anxiety and another 22.6% had subclinical symptoms. Further, 12.9% of patients reported clinical symptoms of depression and an additional 16.5% described subclinical symptoms [24].

In a study performed in a 8235 adult outpatients using the Brief Symptom Inventory questionnaire (BSI-18) [25], mixed anxiety/depression symptoms were seen in 12.4% of patients; depression symptoms in 18.3%, and anxiety symptoms in 24.0% [26]. A former study conducted in Spain [5], that included outpatients who had undergone cancer surgery in the previous month and who initiated adjuvant chemotherapy, showed a prevalence of malnutrition of 36.4%, depression symptoms in 35.5%, and anxiety symptoms in 35.2% of the patients using also the BSI-18.

We found an association between presenting anxious and depression symptomatology and malnutrition in hospitalized oncologic patients. Previous studies also point towards this association [27–32]. Chabowski et al. found that the deterioration in nutritional status is associated with a significant worsening in terms of depression, anxiety, and pain. [28]. Gosak et al. found a significant correlation between nutritional status and HADS scores, with more distressed patients found in the

malnourished/cachectic subgroups [29]. Santos et al. found the presence of depression in 52.9% elderly malnourished patients undergoing treatment for cancer [33]. The utility of a short depression screening in predicting malnutrition has been demonstrated [31].

The link between malnutrition and major depression is both complicated and correlative. It remains unclear whether depression in cancer patients is the cause or consequence of impaired nutritional status [34]. Van Liew et al. demonstrated that there is a dynamic reciprocal association between depressive symptoms and weight loss: changes in either variable were associated with concurrent changes in the other variable [32]. Therefore, depression might lead to a lack of appetite, loss of interest in self-care, apathy, and physical weakness. These conditions appear to be linked in a cycle whereby major depression might cause anorexia and result in malnutrition, whereas malnutrition related with cancer directly impair appetite [30]. Biological mechanisms linking distress and malnutrition have been identified, suggesting a link between cancer-related anorexia and depression caused by an impairment of serotonin [10].

The presence of malnutrition and poor recognition of depression and anxiety is strongly associated with reduced quality of life and survival in cancer patients [5, 7, 8]. However, given that some risk factors for nutritional decline in cancer patients are non-modifiable (e.g., stage, site, treatment), it is noteworthy that psychological symptoms are treatable, which may lead to an improvement in nutritional status [35]. However, 73% of these depressed cancer patients do not receive effective psychiatric treatment, and only 5% see a mental health professional [36]. These observations underline the importance of the assessment and treatment of both psychological symptoms and nutritional assessment.

Our study has several strengths; it is a cross-sectional study with a substantial number of subjects. Furthermore, it applies simple techniques to measure and define malnutrition, as well as the presence of anxiety and depression symptoms.

All the same, there are potential limitations in our study. It was a single-center cross-sectional study; thus, results should be interpreted with caution. It could only provide clues for a causality relationship between these two factors and no causal links can be drawn.

The high rates of anxiety and depression symptomatology found in our study, and the strong relationship found between malnutrition and psychological distress are a robust argument for implementation of systematic screening for psychological distress, and for comprehensive psychosocial support for all patients with advanced cancer throughout the disease trajectory. The HADS questionnaire is a suitable tool for this type of screening [6].

In conclusion, the presence of anxiety and depression symptomatology in oncological inpatients is high. There is an association between malnutrition and presenting anxious and depression symptomatology in hospitalized oncologic patients. The significant levels of depression and anxiety in these patients indicate the need for early supportive psychotherapy or pharmacological interventions. Further studies are needed for better understand the causality of this association.

Declarations

Compliance with Ethical Standards.

The study was approved by the Provincial Research Ethics Committee of Málaga (reference number #01052016). The ethical principles stated in the latest revision of the Declaration of Helsinki and good clinical practice standards were applied.

Consent to participate.

Informed consent was obtained from all individual participants included in the study.

Consent for publication.

Not applicable.

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Conflicts of interest.

All authors declare independence from the sponsoring body in the design, execution, and analysis of results and the compiling of the conclusions, and deny any conflicts of interest with the organizations mentioned above.

Authors' contributions.

Conceptualization, F.J.S.-T., M.R.-V., and G.O.; data curation, V.C.-B., F.J.S.-T., and I.G.-A.; formal analysis, F.J.S.-T. and G.O.; funding acquisition, G.O.; investigation, V.C.-B., F.J.S.-T., M.B., and I.G.-A.; methodology, V.C.-B., F.J.S.-T., M.R.-V., and M.B.; project administration, V.C.-B., M.R.-V., and G.O.; supervision, G.O.; writing—original draft, F.J.S.-T.

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Data availability.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Figures

Study Flow Diagram

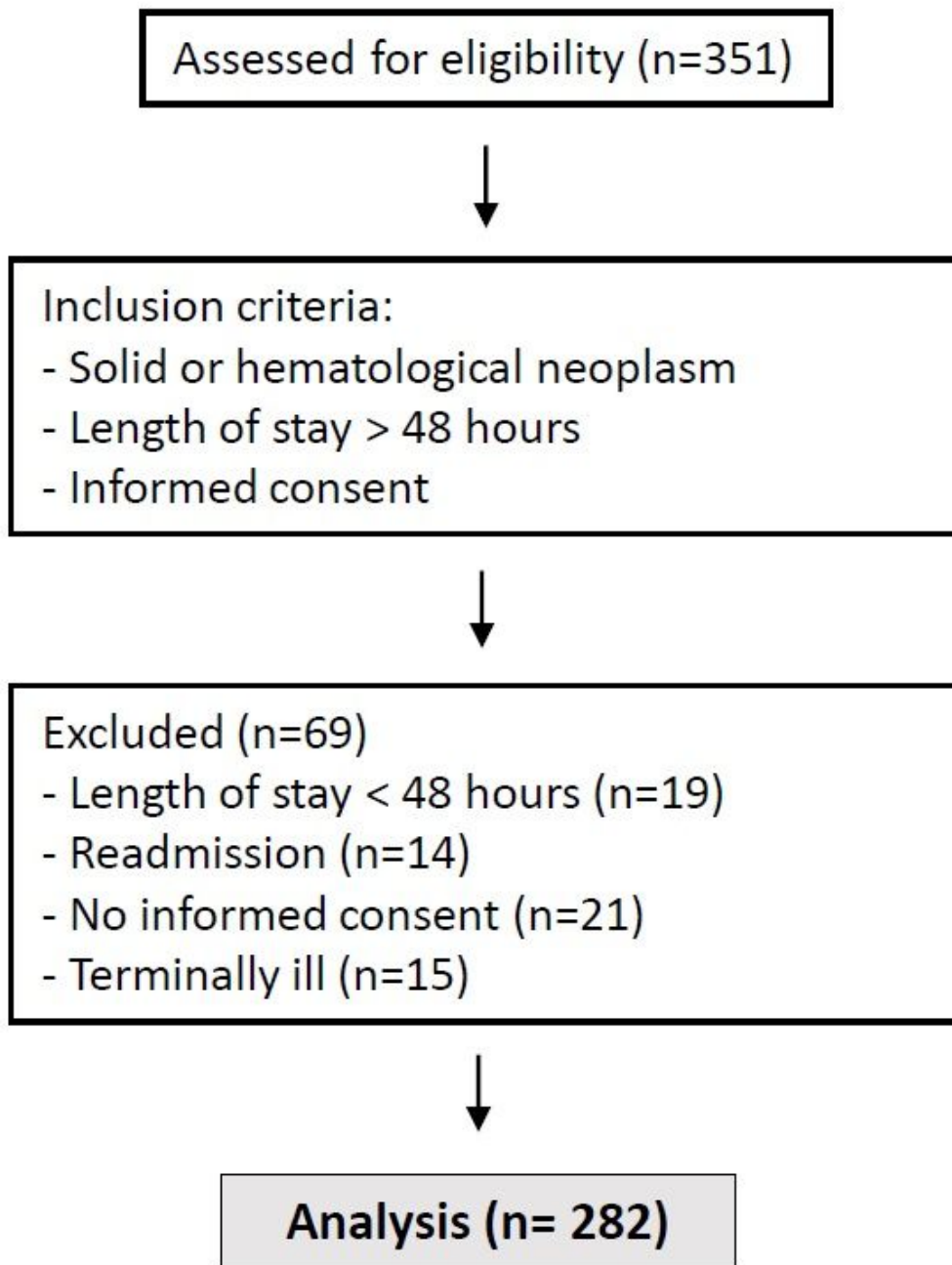


Figure 1

Study Flow Diagram.

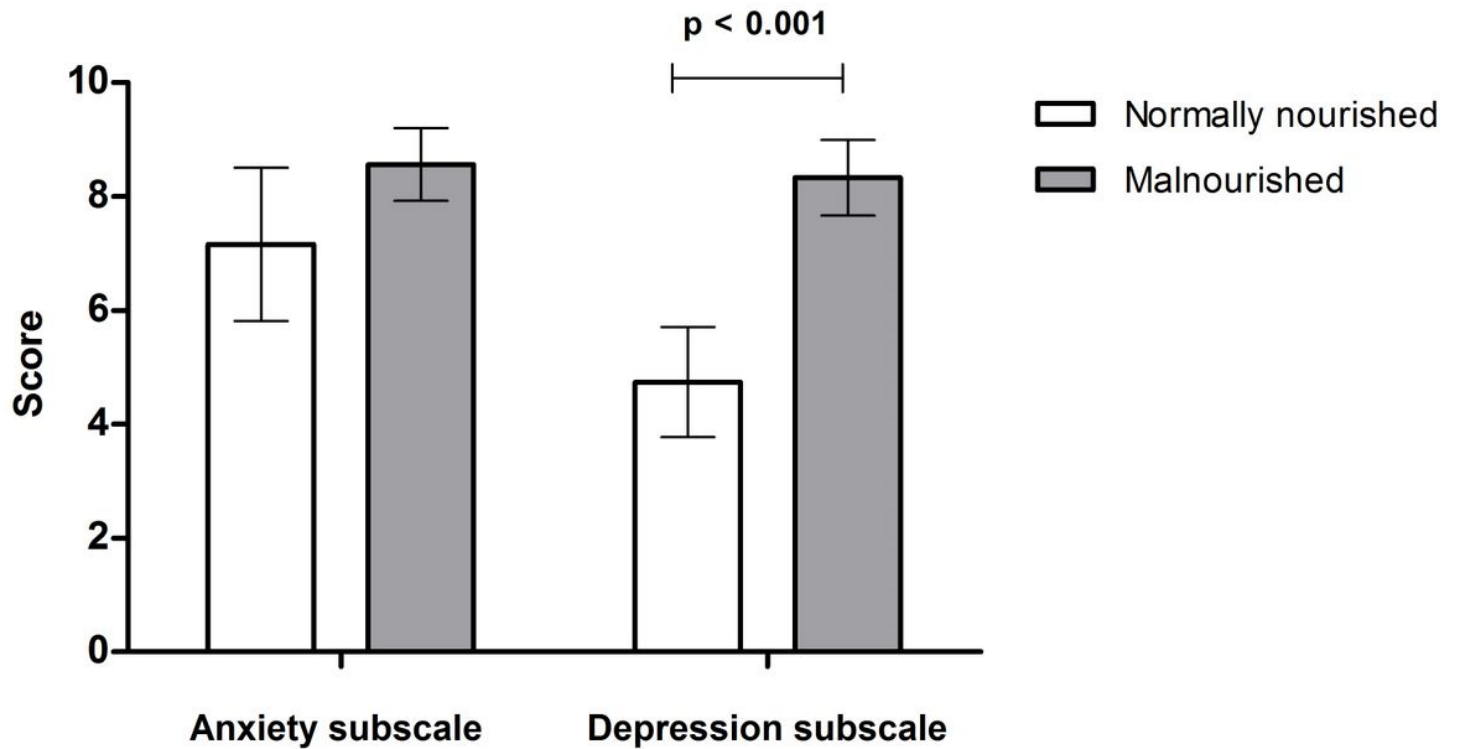


Figure 2

Association between malnutrition and HADS anxiety and depression subscales.

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