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Assessment of psycho-emotional symptoms in cancer patients in an Oncology-Palliative Care Department from Romania

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ABSTRACT

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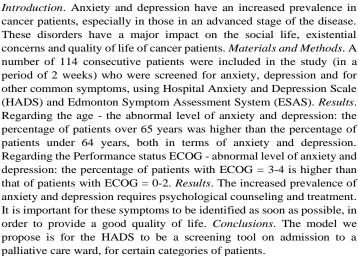
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Introduction

In palliative care, patients are vulnerable to psychological stress caused by diagnosis, treatment and the uncertainty of the future. The psychological distress starts with feelings of sadness and it can reach anxiety and depression. Not only patients are affected, but also their families [1,2].

Anxiety and depression disorders are common in palliative care, having a major impact on the patients' quality of life. It is necessary to identify patients who present these symptoms, so that they can benefit from adequate support and treatment [3,4].

In different studies, the prevalence of anxiety in patients with advanced cancer varies from 11% to 63%, while the prevalence of depression varies from 8% to 77%. At the same time, 50% of patients with advanced cancer meet the criteria for a psychiatric condition [5].

Patients recently diagnosed with cancer, who are in the period of adjustment to the disease, or those with lower functional status or with higher age are the most prone to develop symptoms of anxiety and depression [6].

Also, there is an association between anxiety and depression and physical symptoms. Anxiety is a state of unease such as worry or/ and fear resulting from the



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perception of a present or future threat. Anxiety symptoms manifest as both emotional stress and physical symptoms [7].

Depression is a pathological condition, represented by a group of signs and symptoms (sadness, hopelessness, lack of energy, loss of interest in activities, decreased concentration, inability to make decisions, suicidal thoughts). Sometimes, somatic or psychotic symptoms accompany the depression. These signs and symptoms interfere with daily activities. The etiological factors of depression are multiple: genetic, biochemical, psychological and social-environmental. Recognizing depression can be difficult in patients with somatic diseases and some symptoms such as fatigue, changes in appetite and sleep disorders are found both in depression and in somatic diseases [8].

Although controversial, screening for depression is used to identify patients who have not previously been diagnosed with depression, including patients with chronic diseases and cancer. The Hospital Anxiety and Depression Scale (HADS) was developed to be able to identify anxiety disorders and depression in patients with somatic diseases. HADS does not include symptoms such as insomnia, loss of appetite, or fatigue [7].

Symptoms encountered in patients with advanced cancer are directly related to the cancer disease, cancer treatment (surgery, radiotherapy, chemotherapy, immunotherapy), treatment of symptoms and pre-existing comorbidities. The palliative care improves symptom management (including anxiety and depression) and the patient's quality of life [9,10]. Patients have the ability to develop defense mechanisms and adapt to the diagnosis of advanced cancer and the use of coping strategies is associated with outcomes on depression and anxiety. The main physical symptoms among patients with advanced and metastatic cancer are: pain, fatigue and lack of appetite [11-13].

This research was performed to assess the prevalence of anxiety, depression and physical symptoms among palliative care patients with cancer.

Materials and Methods

We conducted a study in patients with cancer admitted to "Saint Luca" Hospital of Chronic Diseases from Bucharest, in the Oncology – Palliative Care Department. In our department, patients are hospitalized both in day hospitalization and in continuous hospitalization.

All the patients admitted in our department in a period of two weeks in September 2023 were enrolled in the study; a number of 114 consecutive patients were included. Patients were screened for anxiety, depression and for other common symptoms. The patients were evaluated by 2 questionnaires: Hospital Anxiety and Depression Scale (HADS) and Edmonton Symptom Assessment System (ESAS) [14-16].

ESAS is a screening tool for patients admitted into the Oncology – Palliative Care Department of "Saint Luca" Hospital of Chronic Diseases.

The purpose of the study was explained to the patients and they freely agreed to participate in this study by signing the informed consent. The approval from the Ethical Committee no 487/16.01.2023 has been previously obtained.

Results

The two questionnaires used are reliable and valid tools for palliative care patients, being self-administered or by trained staff. The time required to fill out the 2 questionnaire was about 10 minutes.

Table 1. Distribution according to the location of the tumors (N=114 patients).

Tumors' location	Number of patients (percentage)			
Lungs	48 (42.1%)			
Bowel and rectum	15 (13.15%)			
Breast	14 (12.28%)			
Prostate	12 (10.52%)			
Pancreas	3 (2.63%)			
Bladder	3 (2.63%)			
Kidneys	3 (2.63%)			
Malignant melanoma	3 (2.63%)			
Other cancers	13 (11.4%)			

Table 2. Patients' characteristics

Patients' characteristics	No. of patients (%)
Median age (range) (year)	68 (43-96)
Gender	
Male	64 (56.14)
Female	50 (43.86)
Life environment	
Urban	70 (61.40)
Rural	44 (38.59)
Type of hospitalization	
Day care	50 (43.86)
Continuous care	64 (56.14)
Studies	
Elementary school	76 (66.66)
High school	29 (25.43)
University	9 (7.89)
ECOG Performance status	
ECOG = 0	18 (15.78)
ECOG = 1	16 (14.03)
ECOG = 2	39 (34.21)
ECOG = 3	23 (20.17)
ECOG = 4	18 (15.78)

Table 3. Distribution of patients according to the levels of anxiety and depression (N=114 patients)							
	Normal (N/%)	Borderline (N/%)	Abnormal (N/%)				
Anxiety	69/ 60.53 %	17/ 14.91 %	28/ 24.56 %				
Depression	70/ 61.4 %	15/ 13.16 %	29/ 25.44 %				

Table 4. Distribution of patients according to the gender and the level of anxiety and depression (N=114 patients)							
	Anxiety- Normal	Anxiety- Borderline	Anxiety- Abnormal	Depression- Normal	Depression- Borderline	Depression- Abnormal	
Male: 64 patients	39 (60.94%)	13 (20.31%)	12 (18.75%)	42 (65.63%)	9 (14.06 %)	13 (20.31%)	
Female: 50 patients	30 (60%)	4 (8 %)	16 (32%)	28 (56%)	6 (12%)	16 (32%)	

Table 5. Distribution of patients according to the age and the level of anxiety and depression (N=114 patients)							
						Depression- Abnormal	
Under 64 years: 41 patients	30 (73.17%)	3 (7.31%)	8 (19.51%)	30 (73.17%)	3 (7.31%)	8 (19.51%)	
Over 65 years: 73 patients	43 (58.90%)	9 (12.32%)	21 (28.76%)	36 (49.31%)	17 (23.28%)	20 (27.39%)	

Table 6. Distribution according to the performance status ECOG and anxiety and depression levels (N=114 patients)						
	Anxiety- Anxiety- Anxiety- Depression- Depression- Normal Borderline Abnormal Normal Borderline Abnormal					
ECOG=0-2: 73 patients	58 (79.45%)	6 (8.21%)	9 (12.32%)	53 (72.60%)	12 (16.43%)	8 (10.95%)
ECOG=3-4: 41 patients	15 (36.58%)	6 (14.63%)	20 (48.78%)	13 (31.70%)	8 (19.51%)	20 (48.78%)

Table 7 . Distribution of patients according to hospitalization type and anxiety and depression levels (N=114 patients)							
	Anxiety- Anxiety- Anxiety- Depression- Dep						
Day care: 50 patients	34 (68%)	7 (14%)	9 (18%)	35 (70%)	10 (20%)	5 (10%)	
Continuous care: 64 patients	35 (54.69%)	8 (12.5%)	21 (32.81%)	35 (54.69%)	5 (7.81%)	24 (37.5%)	

Table 8. Distribution of patients according to the studies and the level of anxiety and depression (N=114 patients)							
Anxiety- Anxiety- Anxiety- Depression- Depression- Depression- Normal Borderline Abnormal Normal Borderline Abnorma							
Elementary school: 76 patients	49 (64.47%)	9 (11.84%)	18 (23.68%)	38 (50.00%)	15 (19.73%)	23 (30.26%)	
High school: 29 patients	19 (65.51%)	3 (10.34%)	7 (24.13%)	19 (65.51%)	5 (17.24%)	5 (17.24%)	
University: 9 patients	5 (55.55%)	0 (0%)	4 (44.44%)	9 (100%)	0 (0%)	0 (0%)	

Table 9. Distribution of patients according to life environment and anxiety and depression levels (N=114 patients)							
	Anxiety- Normal	Anxiety- Borderline	Anxiety- Abnormal	Depression- Normal	Depression- Borderline	Depression- Abnormal	
Urban:70 patients	47 (67.14%)	6 (8.57%)	17 (24.28%)	40 (57.14 %)	15 (21.42%)	15 (21.42%)	
Rural: 44 patients	26 (59.09%)	6 (13.63%)	12 (27.27%)	26 (59.09%)	5 (11.36%)	13 (29.54%)	

Table	Table 10. Evaluation of the main 4 symptoms according to their intensity (N=114 patients).									
No.	Symptom	Moderate (N)	Moderate (%)	Severe (N)	Severe (%)	Total (N)	Total (%)			
1	Fatigue	27	23.68	18	15.78	45	39.47			
2	Pain	27	23.68	9	7.89	36	31.57			
3	Worst feeling of well being	22	19.29	12	10.52	34	29.82			
4	Loss of appetite	12	10.52	11	9.64	23	20.17			

Statistical analysis

Statistical analysis was performed with XLSTAT program. In order to find the correlations between variables, Pearson correlation coefficient (PC) was performed; the values of p<0.05 were considered statistically significant.

We performed correlations between gender, ECOG performance status and type of hospitalization (independent variables) and pain, fatigue, loss of appetite and worst feeling of wellbeing (dependent variables). The values of Pearson correlation coefficient are indicated in Table 11.

The most powerful correlation was observed between ECOG performance status and pain, fatigue, loss of appetite and worst feeling of wellbeing respectively with $PC = 0.260 \ (p<0.001), \ 0.256 \ (p<0.001), \ 0.218 \ (p<0.01)$ and $0.268 \ (p<0.001)$, respectively. The PC values calculated for correlation between type of hospitalization and pain, fatigue, loss of appetite and worst feeling of wellbeing, respectively were $0.057, \ 0.086, \ 0.079$ and 0.112, respectively, indicating a correlation but without statistical significance (Table 11).

Table 11. Coefficients of determinat	ion (Pearson)
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Variables	Pain	Fatigue	Loss of appetite	Worst feeling of wellbeing
Gender	0.012 (p=0.06)	0.024 (p=0.17)	0.012 (p=0.08)	0.010 (p=0.09)
ECOG performance status	0.260 (p<0.001)	0.256 (p<0.001)	0.218 (p<0.01)	0.268 (p<0.001)
Type of hospitalization	0.057 (p=0.07)	0.086 (p=0.1)	0.079 (p=0.06)	0.112 (p=0.05)

Discussions

HADS is free and available online, being a self-report measurement tool designed for assessment anxiety and depression. It is using a four-point scale, ranging from 0, that means not at all, to 3, that means very often indeed. This is a 14-item self-report measurement tool designed for use in medical outpatient settings to assess depression and anxiety. Responses provided separate scores for anxiety and depression (the HADS produces two scales, one for anxiety (HADS-A) and one for depression (HADS-D), differentiating the two states). Scores are derived by summing responses for each of the two subscales or for the scale as a whole. The total score is out of 42, (21 per subscale). Anxiety or depression scale has a score range of 0-21. Higher scores indicate greater distress. The total score is: 0-7 = Normal, 8-10 = Borderline and 11-21 = Abnormal. The total HADS score may be regarded as a global measure of psychological distress [17-19].

HADS was developed by Zigmond and Snaith and evaluates the severity and causality of symptoms of anxiety and depression both in somatic and psychiatric diseases and in the general population [15,18]. HADS has been validated both for many different patient populations and for patients requiring palliative care [1]. It can be recommended for the evaluation of anxiety and depression among a general population 65-80 years old [20]. It was used to assess emotional stress in COVID-19 survivors with long COVID [21,22].

HADS is not a suitable tool for the assessment of anxiety and depression in patients with mild and moderate cognitive impairment [23]. Edmonton Symptom Assessment System (ESAS) is one of the first quantitative symptom assessment tools [2]. It is a visual analogue scale,

being a valid and reliable tool to assist in the assessment of nine common symptoms experienced by cancer patients (pain, tiredness, drowsiness, nausea, lack of appetite, depression, anxiety, shortness of breath and affected wellbeing). The patient should be instructed to rate the severity of each symptom on a 0 to 10 scale, where 0 represents the absence of the symptom and 10 represents the worst possible severity. ESAS scores 0, 1–3, 4–6 and 7–10 points on a scale of 0–10 generally correspond to none, mild, moderate and severe symptom burden. Having a professional health care present for the administration of ESAS may be helpful in certain cases [24-26].

The ESAS was initially developed by Bruera et al., as a tool for evaluating symptoms in patients hospitalized in a palliative care center, being a simple and useful method for regular evaluation of symptoms [24]. ESAS is freely available, being a validated tool and translated into multiple languages.

The ESAS evaluates symptoms efficiently and systematically, being used both in research and in clinical practice, in patients admitted for day or continuous hospitalization. It is used in oncology and in palliative care, but also in other medical specialties, to evaluate patients with chronic lung, heart, liver or kidney diseases [26].

We analyzed the results obtained from the specific questionnaire, that is HADS (Hospital Anxiety and Depression Scale).

Regarding anxiety, data are presented on:

- 1. Gender the level borderline: the percentage of men was higher than the percentage of women (20.31% compared to 8%)
- 2. Gender the abnormal level: the percentage of women was higher than the percentage of men (32% compared to 18.75%).

- 3. Age the borderline level: the percentage of patients over 65 years was higher than the percentage of patients under 64 years (12.32% compared to 7.31%).
- 4. Age the abnormal level: the percentage of patients over 65 years was higher than the percentage of patients under 64 years (28.76% compared to 19.51%).
- 5. Performance status ECOG abnormal level: the percentage of patients with ECOG = 3-4 is higher than the patients with ECOG = 0-2 (43.90% compared to 12.32%).
 6. Type of hospitalization the abnormal level: the percentage of patients from continuous care was higher
- percentage of patients from continuous care was higher than the percentage of patients from day care (32.81% compared to 18%).
- 7. Studies the abnormal level is almost similar in patients with elementary school (23.68%) compared to patients with high school (24.13%).
- 8. Life environment the borderline level is higher in rural patients (13.63%) compared with urban patients.

Regarding depression, data are presented on:

- 1. Gender the borderline level: the percentage of men was almost similar compared to the percentage of women (14.06% compared to 12%).
- 2. Gender the abnormal level: the percentage of women was higher than the percentage of men (32% compared to 20.31%).
- 3. Age the borderline level: the percentage of patients over 65 years was higher than the percentage of patients under 64 years (23.28% compared to 7.31%).
- 4. Age the abnormal level: the percentage of patients over 65 years was higher than the percentage of patients under 64 years (27.39% compared to 19.51%).
- 5. Performance status ECOG abnormal level: the percentage of patients with ECOG = 3-4 is higher than the patients with ECOG = 0-2 (48.70% compared to 10.9%).
- 6. Type of hospitalization the abnormal level: the percentage of patients from continuous care was higher than the percentage of patients from day care (37.5% compared to 10%).
- 7. Studies the abnormal level: the percentage of patients with elementary school is higher than the percentage of patients with high school (30.26% compared to 17.24%).
- 8. Life environment the borderline level is higher in urban patients (21.42%) compared with rural patients (11.36%).

Depression and anxiety have a negative impact on oncological treatment, on the quality of life as well as on survival. Recently diagnosed patients, particularly if the diagnosis has been delayed, experience significant stress, which can lead to rejection of the disease. Feelings of hopelessness, uncertainty and the loss of control have a negative impact, especially in patients with an unfavorable prognosis [27,28].

Individual factors (age, gender), psychological factors (non-adaptation to the disease, lack of hope, fear, change

in self-image, concern for others) and social factors (education level, family, social support) as well as factors related to the cancer (stage of the disease, prognosis, symptoms) and its treatment (radiotherapy, chemotherapy, treatment response, adverse reactions) contribute to the development of depression and anxiety among cancer patients [29].

Naser et al, in a study conducted on 1011 patients, which included both patients admitted to continuous hospitalization and day hospitalization, highlighted that depression and anxiety have a prevalence of 23.4%, in all patients. At the same time, the prevalence was higher in cancer patients admitted to continuous hospitalization compared to those in day hospitalization [30]. This difference is attributed to the severity of the disease or the advanced or terminal stage of the disease.

The families of elderly patients or those with ECOG performance status 3-4 must be warned about the psychoemotional vulnerability of these patients. The increased prevalence of anxiety and depression requires psychological support and treatment. It is important that these symptoms are identified as soon as possible, in order to be treated and monitored, so to provide a better life condition [31,32].

Next, we analyzed aspects, obtained from the specific tool, that is the Edmonton Symptom Assessment System (ESAS). The main symptoms with moderate and high intensity are, in descending order of frequency: fatigue, pain, the worst general condition and loss of appetite.

Tiredness was the most frequently encountered symptom in this study, in 39.46% of patients, the intensity of fatigue was moderate or high. It is a symptom, which includes sensations from exhaustion to tiredness, having a negative effect on the ability to carry out physical activities, as well as on the psycho-emotional state [33].

Fatigue needs individualized treatment approach. Fatigue occurs in over 80% of patients with advanced stage cancer, being often underestimated by health care professionals. The assessment of fatigue is done regularly in patients in whom this symptom has moderate or severe intensity. At the same time, it is necessary to know the impact that this symptom has on the quality of life [34,35].

Patients must be informed about the reversible causes that cause fatigue (unsatisfactory analgesia, in patients with severe pain, anemia), as well as about the therapeutic options. Thus, pain therapy and blood transfusion can improve fatigue [36].

Moderate physical exercises, adapted to physical capacity and energy conservation by prioritizing daily activities can also have a favorable role in the management of fatigue. Evidence is lacking to make recommendations regarding pharmacological therapy (psychostimulants, corticosteroids), nutritional supplements, sleep optimization, psychological counseling or complementary therapies [34].

Regarding the pain in the palliative care, this should not only be understood as a physical symptom but it is rather also an expression of mental stress [26].

Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage", being a personal experience influenced by psychological, social and spiritual factors. In our study, 31.57% of the patients had pain of moderate or high intensity [36].

Pain occurs in 70-90% of patients with advanced cancer, being associated with a decrease in quality of life, the concept of "total pain", referring to psychological, physical, social and spiritual symptoms. Daily activities, sleep and cognitive functions are affected in patients with pain. The loss of mobility leads to the loss of patients' independence, they become completely dependent on other people, which will increase the severity of the total pain. Suffering caused by pain is characterized by insomnia, sadness, fatigue, fear of pain. The existence of all these problems requires therapeutic interventions for anxiety, depression and cognitive disorders. The association between pain and emotional stress makes pain a difficult symptom to treat [37].

The mental health of the patient and the social pain are as important as the control of physical symptoms. At the same time, there is a close relationship between psychological pain and the spiritual coping. Patients can keep their hopes up, even if the pain progresses in intensity.

The correct identification of spiritual needs can prevent the deterioration of their physical and social condition. It is estimated that half of cancer patients have spiritual needs, this being recognized as a priority in palliative care practice and research, spiritual stress being defined as a state of suffering that was related to lack of meaning in life [37,38].

The support of family and loved ones, as well as good economic-financial status, also have a significant role in pain control [12,37]. Pain is subjective and pain management begins with its assessment, according to the characteristics of each patient. The evaluation will refer to the location, the duration, the intensity, the quality of pain and the factors associated with it [37].

The severity of the disease, the patient's discomfort, the memories of pain episodes, the reactivity to pain, the level of education contribute to the development of the pain experience [38]. A multidisciplinary approach and a multimodal treatment involving combined management of pain, symptoms and emotional distress is necessary to reduce the suffering [39,40].

Pain has different origins and the use of analgesic therapy should be individualized and adapted to the need of every patient. The active interventions are necessary for effective pain control. Pain control is a priority. Treatment of the pain as an important part of palliative care offers a better quality of life to the patients with advanced cancers [41-43].

Loss of appetite is a frequent symptom in patients with advanced cancer, aggravating anxiety and depression and having a negative impact on the quality of life. This symptom is associated in the same time with a decreased survival. This symptom will benefit from pharmacological drugs and nutritional support. Recent clinical studies have shown that some drugs such as Olanzapine or Anamorelin can reduce the loss of appetite [44-46].

In our study, loss of appetite had a moderate or high intensity in 20,16% of the patients.

The worst feeling of well-being was reported as having a moderate or high intensity by 29.82% of patients. The item well-being is not well defined, this is one of the limitations of ESAS [25].

The symptom combination of pain, fatigue, anxiety and depression has a strong impact on cancer patients, thus resulting in a decrease in the ability to adapt to daily activities [47,48].

When conducting this study, we found that the patients were satisfied with the fact that they were asked more questions about their psycho-emotional state, thus increasing their trust in the medical team, but also the hope that these symptoms will be carefully monitored, the objective being their improvement [49].

At the same time, the results of the study indicate that there is a correlation between anxiety and depression on one hand and age, ECOG performance status and physical symptoms, on the other hand [50].

Considering the high prevalence of anxiety and depression accompanying other symptoms such as fatigue, pain, loss of appetite, we consider that it is necessary to separately evaluate anxiety and depression through the HADS questionnaire, even if anxiety and depression are part of the symptoms that are also evaluated on the ESAS scale.

The results of this study recommend the screening of anxiety and depression by using the HADS questionnaire for patients admitted in continuous care, for elderly patients or with ECOG performance status=3-4, or with physical symptoms of moderate or severe intensity (fatigue, pain, the worst well-being status and loss of appetite). Regarding the physical symptoms, we consider that to be eligible for screening, the patient must have at least 1 symptom, out of the 4 listed, of moderate or high intensity.

Palliative care is a holistic approach of care, which addresses both physical symptoms and psycho-emotional, social and spiritual symptoms. Psychological distress has been associated with physical symptoms of moderate or severe intensity of suffering [51].

Depression and anxiety should not be considered normal events during the evolution of the disease, they should be screened, diagnosed, evaluated with validated tools, followed by appropriate specialized support: psychological, pharmacological treatment, social, spiritual counseling or

their combination. The patient is the one who evaluates these symptoms best.

If they are not diagnosed and treated, depression and anxiety can aggravate the evolution of the disease, thus increasing cancer-related morbidity and mortality. At the same time, patients with anxiety and depression have a lower adherence to oncological treatments, they have more readmissions and consultations at emergency departments. Mental and physical health, domains of health-related quality of life, are strongly influenced by a disease such as cancer. Depression and anxiety are associated with poor health-related quality of life and this negatively affects cancer survival rates.

Studies have shown that one-third of patients with cancer and depression do not receive any treatment for depression. Alwhaibi et al. and Findley et al. highlighted in their studies that one third of patients with cancer and depression do not receive antidepressant treatments [52,53].

Although anxiety and depression are frequently encountered among cancer patients, they are chronic conditions that can be treated. That is why early diagnosis and treatment of these symptoms alleviates the symptoms of cancer and can also reduce the adverse effects of oncological treatment. In addition, the complex care of cancer patients must be based on a multimodal treatment, therapy that should also include mental health care [54].

Following the results of this study, all patients who had a borderline or abnormal level of anxiety and depression were referred to psychological counseling.

Conclusions

Signs of anxiety (physical symptoms such as tension, tachycardia, tachypnea, tremor, heart palpitations, sleep disturbances, shortness of breath and other symptoms such as fear, obsessions or fear of dying) and depression (sadness, anger, despair, insomnia, pain and other physical symptoms) are frequently encountered in patients with advanced stage cancer. After the diagnosis, many patients lose their desire to participate in social life, they no longer find a meaning in life. Thus, anxiety and depression are frequently associated with social and spiritual distress.

The present study used the HADS, a screening tool well accepted in practice and research. The use of this tool, centered on the patient, helps the care team in the decision-making process and improve the patient centered care.

Our results are in line with the data from the specialized literature and demonstrate that patients with advanced stage cancer often suffer from anxiety or depression.

When patients are admitted to our Oncology - Palliative Care Department, the ECOG performance status is assessed for all patients and the main symptoms are screened, using the ESAS scale.

The model we propose is for HADS to be a screening tool upon admission to our palliative care ward, for the

following categories of patients: elderly patients (> 65 years old), patients with ECOG performance status=3-4, patients admitted in continuous care, and patients who have at least 1 symptom of moderate or severe intensity on the ESAS scale (from the following 4 symptoms: fatigue, pain, the worst well-being status and loss of appetite).

The purpose of screening is the complex evaluation of anxiety and depression, the identification of associated factors, the improvement of clinical support (psychological counseling) and the quality of life of patients with advanced and end-of-life cancer.

The support that the care team will give to the patient and his family is an important tool in patient care, adaptation to the disease, reduction of anxiety and depression and reduction of pain. The impact will be reflected in: better physical functioning, improvement of mood as well as of well-being.

Regarding the physical symptoms, the most powerful correlation was observed between ECOG performance status and pain, fatigue, loss of appetite and worst feeling of wellbeing respectively with PC = 0.260 (p<0.001), 0.256 (p<0.001), 0.218 (p<0.01) and 0.268 (p<0.001), respectively.

The limitations of the study are represented by the fact that it was carried out in a single center, and the design was cross-sectional.

Contributions

Conceptualization: Rahnea-Nita RA and Rahnea-Nita G; Data curation: Toma RV; Formal analysis: Dumitru M and Serbanescu GL; Investigation: Toma RV and Georgescu M; Methodology: Georgescu M and Barbu AM; Project administration: Rahnea-Nita G; Resources: Valcu EG; Supervision: Rebegea LF; Validation: Rebegea LF and Georgescu M; Visualization: Constantin GB and Barbu MA; Writing draft Rahnea-Nita RA, Rahnea-Nita G and Mihaela Dumitru; Writing revision and editing: Constantin GB.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript. Informed consent was obtained from all subjects involved in the study. This work has been conducted with the ethical approval of St. Luca Clinical Diseases Hospital from Bucharest, with the ethical approval number: 487/16.01.2023.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

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