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ORIGINAL ARTICLE

The influence of distressing symptoms to levels of depression in cancer patients

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Summary

Purpose: *Our objectives were to identify the depression and the distressing symptoms in younger and elderly advanced cancer patients.*

Methods: *: The instruments that have been used were the Beck Depression Inventory (BDI) for younger patients, the Geriatric Depression Scale (GDS) for geriatric patients and the M. D. Anderson Symptom Inventory (MDASI) for the severity and impact of cancer-related symptoms.*

Results: *A trend for significant correlation was found between the GDS and MDASI symptoms for nausea (p=0.058), while a significant correlation was observed for increased sadness (p=0.011), increased constipation (p=0.021), interference of symptoms in mood (p=0.012) and in relations with people (p=0.007); interference of symptoms in mood was the most important risk factor. For younger patients, many statistically significant associations were found between distressing symptoms and depression; however, interference of symptoms in mood (p=0.045) was the only important risk factor.*

Conclusion: *Health-care professionals should take into consideration the risk factors for depressive symptoms suggesting a holistic care in advanced cancer patients.*

Key words: *advanced cancer, depression, distressing symptoms, geriatric patients, palliative care*

Introduction

Depression affects patients' physical health [1,2], quality of life [3,4] and mortality [5,6]. Depression is a frequent problem among cancer patients and is often under-diagnosed and hence, undertreated [7-15] probably because cancer patients experience neurovegetative symptoms that simulate several symptoms caused by the disease or the treatment [e.g., loss of appetite, fatigue, and sleep disturbances). Furthermore, very often, emotional well-being is significantly less likely to be documented in medical records than physical distress is [16]. Additionally, depression leads to a reduction in quality of life as well as the aggravation of physical symptoms such as pain, fatigue, and sleep disturbances [10,17]. Advanced cancer patients reporting higher physical distress such as nausea, drowsiness, worse appetite and fatigue are more likely to report higher level of depression [18,19]. Fatigue seemed to affect over 75% of patients with advanced cancer [20-25].

Moreover, elderly patients have multiple medical problems, especially those with cancer [26] as almost 71% of all cancer deaths occur in those ≥ 65 years of age [27]. Depression can be extremely distressing for the elderly cancer patients [28].

In addition, the care of elderly cancer patients is essential and very important. The oncologist should have a working knowledge of geriatric principles in order to provide comprehensive care for their symptoms [29].

A major obstacle in the study of depression in cancer patients is the difficulty for the health care professionals that they confront in separating symptoms associated with depression from those associated with cancer itself. Diagnosis is usually made using the DSM-IV criteria [30].

Our objectives were to identify the frequency of reported depression by using the MDASI among younger cancer and geriatric outpatients.

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Then, to assess the associated symptoms of cancer using the MDASI and to evaluate the screening performance of depression between MDASI and BDI for younger patients and GDI for the elderly.

Methods

Participants

The current study was performed from April 2011 to June 2012. A total of 170 advanced cancer patients (group A: patients ≤65, group B: patients >65-year-old) attending a palliative care unit, have been invited to take part in this open-label prospective trial with two parallel groups and were found eligible to participate in the study. Of these patients, 8 refused to participate in the study and thus they were excluded. The final sample consisted of 162 cancer patients (group A, N=89; group B, N=73). Criteria for inclusion were histologically confirmed malignancy, age >18 years, ability to communicate effectively with the healthcare personnel, provision of informed consent and knowledge of the disease diagnosis. Criteria for exclusion were history of drug abuse, diagnosis of a psychotic illness, or significant cognitive impairment. Research workers recorded data on disease status, treatment regimen (chemotherapy, radiotherapy), and performance status (PS) as defined by the Eastern Cooperative Oncology Group (ECOG) [31]. The study was performed in accordance to the Helsinki Declaration and according to European guidelines for good clinical practice.

Measures

Patients with a PS score of 0 or 1 were categorized as having ''good'', while those with PS 2 or 3 were categorized as having ''moderate to poor'' PS.

The severity of depression was assessed with the BDI validated in the Greek language [32]. BDI [33] is a 21-item self-report scale, measuring characteristic attitudes and symptoms of depression. Each of the inventory items corresponds to a specific category of depressive symptom or attitude consisting of a graded series of 4 self-evaluative statements. The statements are rank-ordered to reflect symptoms' severity from neutral (0) to maximum severity [2]. In 1996 Beck, Steer, and Brown recommended using a score of 10 when screening for ''mild'' depression, 16 for ''mild to moderate,'' 20 for ''moderate to severe,'' and 30 for ''severe'' depression [34].

GDS was also used as a self-report scale. A 15-item version of the GDS has been devised by Shiekh and Yesavage [35], and is probably the most common version currently used. It is suitable for screening mood disorders in outpatients in general, as well as in other non-specialized settings, as its application is shorter. The GDS-15 has been validated in Greek by Fountoulakis et al. [36].

MDASI is the third instrument, which is a brief assessment of the severity and impact of cancer-related symptoms [37] and has been validated in the Greek language [38]. It consists of 13 core symptom items that are rated based on their presence and severity. Each symptom is rated on an 11-point scale (0–10) to indicate the presence and severity of the symptom with 0 meaning "not present" and 10 meaning "as bad as you can imagine" in the last 24 h. It also includes 6 symptom interference items that are rated based on the level of symptom interference with the function of a patient's life in the last 24 h on scales 0–10 (0 = "did not interfere", 10 = "interfered completely").

Statistics

Descriptive statistics of all variables were carried out. Categorical variables were compared using the Fisher's exact test when the conditions of application of Chi-square test were not met. Quantitative variables were compared between groups using Student's t-test when data were normally distributed, and with the nonparametric test for independent series of Mann–Whitney (two-sided) when normality of distribution was not verified.

Univariate comparison of variables was assessed between MDASI symptoms and geriatric depression as binary variable (>6 cut off) was determined using a logistic regression for the first group (patients ≤65 years, N=89). Univariate analysis was then conducted and next multivariate analyses were completed to determine which of the assessed variables that were statistically significant from the univariate analysis were independent predictors of the geriatric depression in advanced cancer patients.

The same steps were followed for the second group (patients >65 years, N=73), where the univariate comparison of variables was assessed between MDASI symptoms and BDI (>16 cut off) and univariate and multivariate analyses were then conducted.

Unadjusted and adjusted odds ratios were recorded with 95% confidence interval.

A p-value of <0.05 (two-sided) was used for statistical significance, though associations reaching borderline significance ($0.05 < p < 0.1$) were also identified as being of potential interest. All analyses were carried out using the statistical package SPSS version 16.00 (SPSS, Chicago, IL, USA).

Results

MDASI symptoms and geriatric depression

Demographic and clinical characteristics for geriatric patients are summarized in Table 1. Geriatric patients' mean age was 73.23 years (±6.38). From them, 49 were male and 40 female. Twenty-nine patients had GDS score ≤6, while 60 had GDS >6.

Table 1. Demographic and clinical characteristics of cancer patients attending outpatient clinics, by GDS score

Characteristics	*All patients (N=89) N (%)*	*GDS score ≤ 6 (N=29) N (%)*	*GDS score > 6 (N=60) N (%)*	*p-value*
Age (years)				
Mean±SD	73.23±6.38	72.24±6.46	73.71±6.34	0.310[b]
Gender				
Male	49 (55.1)	16 (55.2)	33 (55.0)	1.000[a]
Female	40 (44.9)	13 (44.8)	27 (45.0)	
Diagnosis				
Breast	20 (22.5)	7 (24.1)	13 (21.7)	0.792[a]
Lung	17 (19.1)	4 (13.8)	13 (21.7)	0.566[a]
Gastrointestinal	27 (30.3)	11 (37.9)	16 (26.7)	0.329[a]
Urogenital	25 (28.1)	7 (24.1)	18 (30.0)	0.623[a]
Education				
Mean±SD	9.21±3.55	8.82±3.64	9.40±3.46	0.550[b]
Quality of life				
Mean±SD	3.53±2.81	4.07±3.10	3.26±2.64	0.209[b]
Family status				
Married	83 (93.3)	28 (96.6)	55 (91.7)	0.659[a]
Unmarried	6 (6.7)	1 (3.4)	5 (8.3)	
Metastasis				
No	29 (32.6)	12 (41.4)	17 (28.3)	0.237[a]
Yes	60 (67.4)	17 (58.6)	43 (71.7)	
Surgery				
No	36 (40.4)	11 (37.9)	25 (41.7)	0.820[a]
Yes	53 (59.6)	18 (62.1)	35 (58.3)	
Chemotherapy				
No	37 (41.6)	9 (31.0)	28 (46.7)	0.177[a]
Yes	52 (58.4)	20 (69.0)	32 (53.3)	
Radiotherapy				
No	46 (51.7)	14 (48.3)	32 (53.3)	0.821[a]
Yes	43 (48.3)	15 (51.7)	28 (46.7)	
ECOG PS				
0-1	40 (44.9)	14 (48.3)	34 (56.7)	0.820[a]
2-3	49 (55.1)	15 (51.7)	26 (43.3)	

[a]Fisher's exact test, [b]Student's t-test, GDS: geriatric depression scale, SD: standard deviation

Table 2 presents the association between patients who scored above the clinical cut-off for geriatric depression with those without depression regarding their physical and psychological symptoms according to MDASI. A higher percentage of geriatric patients reported scores above the clinical cut-off for nausea (p= 0.010), sadness (p= 0.011), vomiting (p= 0.039), constipation (p= 0.055), mood (p= 0.007), and relations with people (p= 0.012).

Table 3 shows the association between MDASI items and GDS scores. A trend for significance was found between the GDS and MDASI symptoms for nausea (p=0.058), while significant correlation was observed between the GDS and MDASI for increased sadness (p=0.011), increased constipation (p=0.021), interference of symptoms in mood (p=0.012), and interference of symptoms in relations with people (p=0.007). Multivariate analysis revealed that interference of symptoms in mood was the most important risk factor (Table 3).

MDASI symptoms and BDI

Demographic and clinical characteristics for younger patients are depicted in Table 4. Their mean age was 55.98 years (±7.06). From them, 37 were male and 36 female. Eighteen patients had

Table 2. Association between MDASI items and GDS score

MDASI items median (IQR)	*All patients (N=89) N (%)*	*GDS score ≤6 (N=29) N (%)*	*GDS score >6 (N=60) N (%)*	*p-value (Mann-Whitney)*
Pain	10 (4.0)	8 (5.0)	10 (3.7)	0.592
Fatigue	8 (5.0)	8 (7.0)	8 (4.0)	0.429
Nausea	0 (5.5)	0 (0.0)	2 (6.0)	0.010
Disturbed sleep	5 (10.0)	8 (6.0)	5 (10.0)	0.147
Distress	8 (7.5)	8 (7.5)	8 (7.7)	0.957
Shortness of breath	0 (1.5)	0 (0.0)	0 (2.0)	0.107
Loss of memory	0 (1.0)	0 (0.0)	0 (2.7)	0.167
Loss of appetite	5 (9.0)	4 (7.5)	7 (9.0)	0.309
Drowsiness (sleepy)	3 (8.0)	3 (7.5)	3 (8.0)	0.578
Dry mouth	1 (6.5)	0 (5.0)	2 (6.7)	0.117
Sadness	8 (6.0)	5 (7.5)	8.5 (4.7)	0.011
Emesis	0 (1.0)	0 (0.0)	1 (1.7)	0.039
Numbness/tingling	0 (5.0)	0 (5.0)	0 (4.7)	0.504
Diarrhoea	6 (10.0)	5 (6.5)	4 (4.7)	0.099
Constipation	7 (5.0)	6 (9.0)	8 (4.0)	0.055
General activity	7 (7.0)	5 (8.5)	7 (5.7)	0.137
Mood	0 (5.0)	0 (0.0)	0.5 (6.7)	0.007
Work	5 (8.0)	4 (9.5)	5 (7.0)	0.541
Relations with people	8 (5.0)	6 (6.0)	8 (3.0)	0.012
Walking	0 (0.0)	0 (0.0)	0 (0.0)	0.958
Enjoyment of life	3 (10.0)	5 (10.0)	2.5 (8.7)	0.239

MDASI: M.D.Anderson Symptom Inventory, GDS: geriatric depression scale, IQR: interquartile range

Table 3. Univariate and multivariate analysis for GDS > 6

MDASI items median (IQR)	*Univariate Odds ratio (95% CI)*	*p-value*	*Multivariate* Odds ratio (95% CI)*	*p-value*
Pain	1.041 (0.90-1.20)	0.587		---
Fatigue	1.090 (0.96-1.24)	0.194		---
Nausea	1.150 (0.99-1.33)	0.058	1.195 (1.00-1.43)	0.055
Disturbed sleep	0.911 (0.81-1.02)	0.109		---
Distress	1.009 (0.90-1.13)	0.872		---
Shortness of breath	1.280 (0.98-1.68)	0.074	1.195 (0.86-1.66)	0.283
Loss of memory	1.266 (0.97-1.65)	0.079	1.192 (0.88-1.56)	0.280
Loss of appetite	1.068 (0.95-1.20)	0.263		---
Drowsiness (sleepy)	0.979 (0.87-1.09)	0.706		---
Dry mouth	1.077 (0.95-1.22)	0.237		---
Sadness	1.176 (1.04-1.33)	0.011	1.134 (0.96-1.33)	0.131
Emesis	1.100 (0.89-1.35)	0.375		---
Numbness/tingling	1.027 (0.90-1.16)	0.679		---
Diarrhea	1.138 (0.98-1.31)	0.079	0.894 (0.63-1.27)	0.532
Constipation	1.175 (1.02-1.35)	0.021	1.134 (0.93-1.39)	0.220
General activity	1.114 (0.98-1.26)	0.087	0.836 (0.63-1.10)	0.137
Mood	1.254 (1.05-1.49)	0.012	1.281 (1.04-1.57)	0.018
Work	1.041 (0.93-1.17)	0.492		---
Relations with people	1.293 (1.07-1.56)	0.007	1.368 (0,94-2,00)	0.058
Walking	0.896 (0.67-1.19)	0.447		---
Enjoyment of life	0.936 (0.85-1.04)	0.211		---

*included only the significant parameters from the univariate analysis
MDASI: M.D.Anderson Symptom Inventory, GDS: geriatric depression scale, IQR: interquartile range

Table 4. Demographic and clinical characteristics of cancer patients attending outpatient clinics, by BDI score

	All patients (N=73, 100%) N(%)	*BDI score ≤16 (N=18, 25%) N(%)*	*BDI score >16 (N=55, 75%) N(%)*	*p-value*
Age				
Mean±SD	55.98±7.06	57.77±8.85	55.40±6.34	0.217[b]
Gender				
Male	37 (50.7)	8 (44.4)	29 (52.7)	0.595[a]
Female	36 (49.3)	10 (55.6)	26 (47.3)	
Diagnosis				
Breast	13 (17.8)	3 (16.7)	10 (18.3)	1.000[a]
Lung	24 (32.9)	6 (33.3)	18 (32.7)	1.000[a]
Gastrointestinal	21 (28.8)	9 (50.0)	12 (21.8)	0.035[a]
Urogenital	15 (20.5)	1 (5.6)	15 (27.3)	0.097[a]
Education				
Mean±SD	11.31±3.68	11.22±4.23	11.36±3.52	0.902[b]
Quality of life				
Mean±SD	3.24±2.39	5.11±2.70	2.63±1.95	0.002[b]
Family status				
Married	56 (78.8)	16 (88.9)	40 (74.1)	0.326[a]
Unmarried	16 (22.2)	2 (11.1)	14 (25.9)	
Metastasis				
No	23 (31.5)	6 (33.3)	17 (30.9)	1.000[a]
Yes	50 (68.5)	12 (66.7)	38 (69.1)	
Surgery				
No	37 (50.7)	8 (44.4)	29 (52.7)	0.595[a]
Yes	36 (49.3)	10 (55.6)	26 (47.3)	
Chemotherapy				
No	14 (19.2)	3 (16.7)	11 (20.0)	1.000[a]
Yes	59 (80.8)	15 (83.3)	44 (80.0)	
Radiotherapy				
No	23 (31.5)	7 (38.9)	16 (29.1)	0.560[a]
Yes	50 (68.5)	11 (61.1)	39 (70.9)	
ECOG PS				
0-1	31 (42.5)	11 (61.1)	20 (36.4)	0.099[a]
2-3	42 (57.5)	7 (38.9)	35 (63.6)	

[a]Fisher's exact test, [b]Student's t-test. BDI: Beck depression inventory

GDS score ≤6 while 60 patients had GDS >6.

Table 2 presents the association between patients who scored above the clinical cut-off for geriatric depression with those without depression regarding their physical and psychological symptoms according to MDASI. A higher percentage of geriatric patients reported scores above the clinical cut-off for nausea (p= 0.010), sadness (p= 0.011), vomiting (p= 0.039), constipation (p= 0.055), mood (p= 0.007), and relations with people (p= 0.012).

Table 5 shows the association between patients who scored the clinical cut-off of BDI with those without depression related to MDASI items. A high percentage of patients reported scores above the clinical cut-off for fatigue (p= 0.018), disturbed sleep (p= 0.027), diarrhoea (p= 0.003), interference of symptoms in patients' general activity (p<0.0005) and other symptoms. Furthermore, although univariate analysis revealed many statistically significant associations, in multivariate analysis the only important risk factor was interference of symptoms in mood (p=0.045; Table 6).

Table 5. Association between MDASI items and BDI score

MDASI items	*All patients (N=73, 100%) Median (IQR)*	*BDI score ≤16 (N=18, 25%) Median (IQR)*	*BDI score >16 (N=55 , 75%) Median (IQR)*	*p-value**
Pain	9.5 (3.0)	10 (2.7)	9 (3.0)	0.245
Fatigue	8 (5.0)	5 (6.2)	9 (4.0)	0.018
Nausea	0 (5.0)	0 (6.0)	0 (4.0)	0.690
Disturbed sleep	5 (9.0)	2 (6.2)	6 (7.0)	0.027
Distress	8 (5.0)	6.5 (10.0)	8 (4.0)	0.189
Shortness of breath	0 (3.0)	0 (4.2)	0 (5.0)	0.888
Loss of memory	0 (0.0)	0 (0.0)	2.5 (8.0)	0.248
Lack of appetite	6 (9.0)	2.5 (8.0)	7 (7.0)	0.029
Drowsiness (sleepy)	3 (7.2)	0 (3.7)	3 (7.0)	0.128
Dry mouth	0 (6.0)	0 (2.7)	0 (7.0)	0.239
Sadness	8 (5.0)	7.5 (7.0)	10 (4.0)	0.090
Emesis	0 (0.0)	0 (0.2)	0 (0.0)	0.942
Numbness/tingling	0 (5.0)	0.5 (7.5)	0 (5.0)	0.485
Diarrhoea	6 (5.0)	4.5 (3.7)	7 (5.0)	0.003
Constipation	8 (5.0)	6.5 (8.2)	10 (4.0)	0.030
General activity	7 (7.0)	3.5 (3.0)	8 (5.0)	0.0005
Mood	0 (5.2)	0 (2.7)	4.0 (7.0)	0.032
Work	4 (8.0)	2 (5.2)	5 (8.0)	0.024
Relationship with people	8 (4.0)	6 (5.5)	9 (3.0)	0.002
Walking	0 (0.0)	0 (0.0)	0 (0.0)	0.363
Enjoyment of life	3 (10.0)	1 (5.5)	4 (10.0)	0.125

*Mann-Whitney test, MDASI: M.D.Anderson Symptom Inventory, BDI: Beck Depression Inventory, IQR: interquartile range

Table 6. Univariate and multivariate analysis for BDI >16

MDASI items median (IQR)	*Univariate Odds ratio (95% CI)*	*p-value*	*Multivariate* Odds (95% CI)*	*p-value*
Pain	0.968 (0.78-1.20)	0.757		---
Fatigue	1.267 (1.05-1.52)	0.012	1.045 (0.76-1.44)	0.788
Nausea	1.009 (0.86-1.18)	0.914		---
Disturbed sleep	1.187 (1.02-1.38)	0.028	1.046 (0.82-1.34)	0.721
Distress	1.116 (0.97-1.29)	0.136		---
Shortness of breath	1.030 (0.87-1.22)	0.735		---
Loss of memory	1.75 (0.72-4.25)	0.214		---
Loss of appetite	1.170 (1.02-1.35)	0.029	1.016 (0.82-1.26)	0.881
Drowsiness (sleepy)	1.124 (0.96-1.32)	0.146		---
Dry mouth	1.093 (0.94-1.27)	0.259		---
Sadness	1.204 (1.02-1.43)	0.032	1.076 (0.80-1.44)	0.620
Emesis	1.002 (0.83-1.12)	0.855		---
Numbness/tingling	0.962 (0.84-1.10)	0.589		---
Diarrhea	1.365 (1.11-1.68)	0.003	0.703 (0.34-1.34)	0.284
Constipation	1.311 (1.08-1.58)	0.005	0.938 (0.64-1.37)	0.740
General activity	1.422 (1.16-1.74)	0.001	1.586 (0.94-2.68)	0.045
Mood	1.208 (1.01-1.44)	0.034	1.125 (0.88-1.43)	0.341
Work	1.189 (1.02-1.19)	0.031	0.892 (0.65-1.22)	0.478
Relations with people	1.577 (1.20-2.07)	0.001	1.086 (0.67-1.76)	0.738
Walking	0.824 (0.57-1.19)	0.300		---
Enjoyment of life	1.109 (0.97-1.26)	0.121		---

*included only the significant parameters from the univariate analysis and demographic and clinical characteristics (gastrointestinal, quality of life)

Discussion

Physical symptoms may vary in frequency and intensity among advanced cancer patients with depression [39]. In addition, a relationship exists between physical symptoms and the presence of depression in palliative care patients [10]. There is considerable evidence showing underassessment and undertreatment of symptoms in older people and lack of access to specialized palliative care units [40].

In the current study, the vast majority of geriatric patients (N=60) revealed depressive symptoms. Similarly, the majority of younger patients (N=55) had also depressive symptomatology. However, no patient in either group had received antidepressants or psychotherapeutic treatment. In addition, it seemed that younger patients with depression presented more physical and psychological symptoms than those without depression; however, this was not observed in the elderly population.

One would expect to find a strong association between pain and depression, however no such association was seen probably due to the low intensity of pain in our patients. Our findings, on the other hand, showed that when patients express high intensity of symptoms, such fatigue, nausea, sleep disturbances, loss of appetite, interference of symptoms in activities such as mood, work, relations with people, careful screening for depression is indicated.

Fatigue has been associated with depression in many studies [10,20,21,23]. Similarly, our findings suggest that depression is more common in younger patients than in geriatric ones who reported higher scores in fatigue, which is also one of the probable diagnostic criteria of depression. However, we can not determine the nature of this association.

The results of this study are in agreement with those of other studies [26] [4,21,26,41,42], which found that depression in younger patients was associated with poorer emotional functioning [4,41,42]. Other symptoms such as sleep disturbances, loss of appetite and fatigue [41] were also associated with depression among the cancer patients, consistent to our findings for our younger patients, while nausea was reported as distressing in patients with geriatric depression. Nausea, interference of symptoms in mood as well as in relations with people seemed to be the most common predictors of geriatric depression, consistent to other studies [29,40]. Contrary to these findings, it is interesting to note that in younger patients, although many symptoms related to depressive symptomatology in the current population, the only risk factor for depression was the interference of symptoms in general activity, similarly to other studies [10,39].

With aging, the functional status is affected and, especially in patients with cancer, the effects of the disease and its treatment may create multiple symptoms; thus, assessment and management of these symptoms are required and more research will be beneficial for the best care of geriatric patients in advanced stages of cancer.

This study has several limitations. Since depressive symptoms have been assessed by two different screening tools measuring depression, our findings can not be generalized to describe all depressive cancer patients. More research is necessary on pharmacological and non-pharmacological interventions in palliative care for cancer-related depression. Non-pharmacologic approaches consist of psychoeducational interventions, and interpersonal therapy, cognitive behavior therapy, and dynamic psychotherapy [43-45] seemed to be effective to reduce depressive symptoms in patients with cancer. The association between somatic and depressive symptoms points to a holistic approach for the health care professionals so as to provide physical and psychological support in advanced cancer patients.

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