Comparison of mood disorder screening scales in geriatric oncology: THYMOG study results

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Abstract

Background: Early and systematic depression screening is recommended for older patients with cancer. The objective of this study is to evaluate the performance of three different mood disorder screening scales for detection of Major Depressive Disorder (MDD) in older patients with cancer.

Methods: A prospective multicentric study was conducted in patients with cancer over 70 years of age, comparing three self-administered questionnaires: the 15-item Geriatric Depression Scale (GDS-15), the Hospital Anxiety and Depression Scale - Depression (HADS-D) and the Distress Thermometer (DT). Three weeks after initial assessment, in case of score above the standard cut-off, a reassessment of the patient’s mood was performed by the primary care physician, using the DSM-V MDD diagnostic criteria and the DT. Potential differences between an abnormal mood screening test and a confirmed MDD was assessed using variance analysis for each screening scale.

Results: 93 patients with an average age of 81 years [70 - 95 years] were included. 66 patients had at least one abnormal score on one of the screening scales. A MDD was confirmed for 10 of the 36 reassessed patients (28%). Abnormal screening by the GDS-15 (p=0.021), the HADS-D (p=0.018) and the DT (p=0.045) was significantly associated with MDD diagnosis.

Conclusions: The three screening scales enabled detection of MDD in older patients with cancer. Among the tested scales, the HADS-D could perform best in detecting MDD. However, these screening scales may not be sufficiently reliable for MDD screening in this population. Further studies are needed to confirm the results.

Background

Cancer affects people of all ages, but the risk of developing cancer increases significantly
with ageing [1]. Approximately 30% of all cancers occur in patients aged 75 years and older and nearly 7% in patients aged 85 years and older [2–4]. Considering the actual ageing of the population [5–6], estimations show that by 2050, one in two cancers will occur in people over the age of 75 [1,3,7].

Depression is the most commonly encountered psychiatric pathology in geriatric and cancer patient populations [8,11]. The estimated depression prevalence in older patients with cancer is approximately between 3% to 31% depending on the depression criteria and the cancer type [12–15]. However, depression is often under-diagnosed in older patients since the clinical presentation can differ from the younger population (more physical symptoms, fewer psychological symptoms) [16–20]. Clinicians can also attribute somatic signs of depression to usual ageing or miss nonspecific symptoms such as asthenia, weight loss, sleep disorders or sexual desire disorders [16–20]. It is estimated that 60 to 70% of depressive disorders in older patients are underdiagnosed or undertreated [9,18]. Yet, this geriatric syndrome has a significant impact on patient survival, risk of suicide, morbidity, quality of life, therapeutic management and health care costs [9,15,19,21].

Given its impact on cancer management, The Food and Drug Administration (FDA), The International Society of Geriatric Oncology (SIOG) and The French Society of Psycho-Oncology (SFPO) recommend early and systematic screening for depression disorders in older patients with cancer. The use of specific screening scales such as the Geriatric Depression Scale (GDS), the Hospital Anxiety and Depression Scale - Depression (HADS-D) or the Distress Thermometer (DT) is recommended as well [15,22,23].

However, as Nelson C et al. indicated in their 2010 systematic review, the recommendations for depression screening are less clear and many of the existing scales have not been specifically validated among older patients with cancer [15]. Despite the existing screening recommendations from health authorities and clinical practice
guidelines, there is no consensus on the choice of a specific mood disorder screening scale to use in this population. Consequently, there is a heterogeneity of practice and a risk of under diagnosis depression in this older population.

The objective of this study is to evaluate the performance of three mood disorder screening scales frequently used in geriatric oncology (GDS–15, HADS-D and DT) by comparing their level of agreement with the *Diagnostic Statistical Manual of Mental Disorders - version V* (DSM-V) [24] for major depressive disorder (MDD) diagnostic criteria in older patients with cancer or haematological malignancy. The relationships between the presence of mood disorders and various medical, psychological and socio-environmental factors were also studied.

Methods

**Study Protocol**

A prospective, multicentric, non-randomized and observational study was conducted in France between January 2016 and August 2017 in a University Hospital Center, a Regional Cancer Center and a General Hospital.

Patients who were at least 70 years of age, were fluent in French, hospitalized or outpatients, who had a confirmed diagnosis (new diagnosis, relapse or progression) of cancer or haematological malignancy which had been detected within the last month were eligible. Patients who were unable to answer questionnaires were not eligible for the study.

Before inclusion, each patient received an information note and their consent for participation was collected.

The study protocol was approved by institutional review boards and ethics committees (clinical trials: RCB 2015-A00836-43).

**Data Collection of medical, psychological and socio-**
environmental factors

After obtaining consent, the following data was collected from patient and medical record:

Socio-demographic: sex, age, living place (personal home, care institute), marital status (single, widowed, divorced, married or cohabiting),
Cancer/haematological malignancy characteristics: date of diagnosis, date of diagnosis announcement, oncological status (new diagnosis, relapse or progression), tumor location, TNM classification, oncological therapeutic plan (curative/palliative, surgery, chemotherapy, radiotherapy, hormone therapy),
Clinical assessment: general health status (according to Eastern Cooperative Oncology Group Performance Status), functional status for basic daily living activities (Katz scale) and for instrumental daily living activities (Lawton scale), assessment of actual pain and during the previous week (verbal rating scale (VRS)) as well as its impact on sleep and/or activities, and the use of analgesic treatment,
Presence of severe comorbidities according to The Cumulative Illness Rating Scale for Geriatrics (CIRS-G rate 3): number, level and type of morbidities and presence of a psychiatric history (depression, suicide attempt) and/or psychotropic treatment (benzodiazepines or derivatives, antidepressants).

Mood Disorder Screening

During the initial assessment, each patient included completed three self-administered questionnaires: the GDS-15, the HADS-D and the DT.

When patients obtained a score above the standard cut-off on one of the scales (GDS-15: score 5/15 [25,26], HADS-D: score 11/21 (cut-off indicated by Zigmond as to be used for research) [27], DT: score 4/10 [28]), a psychological consultation was suggested. Patients were also informed that they needed to consult their primary care physician within the next three weeks so their mood could be reassessed.

Diagnostic Reassessment

In the event of a score above the standard cut-off on one of the scales, the patient’s primary care physician was contacted both by telephone and mail. He was informed of the need to reassess the patient’s mood within three weeks to confirm or refute the diagnosis of a MDD (symptoms must be present for at least two weeks according to DSM-V diagnostic criteria [24]).

Mood reassessment consisted of MDD screening according to the DSM-V diagnostic criteria and completion of a DT. The DT score was chosen for the reassessment because of its fast
completion for the primary care physician unlike the other tests.
Documents sent by mail to the primary care physician included the study synopsis, a table compiling the DSM-V diagnostic criteria for MDD, a DT and a pre-stamped envelope so the reassessment could be easily sent.

Four weeks after inclusion, if no postal response was returned, the primary care physician was contacted again by the investigator. Primary care physician or patient refusal to participate or patient death was recorded.

**Statistical analysis**

The study protocol was validated by a statistical methodologist from the Biostatistics and Clinical Research Unit of a University Hospital Center. The required sample size of 93 patients was calculated based on previous studies and estimating an agreement value of at least 60% with an expected kappa value of approximately 85% according to the scales (accuracy of 25%), giving a confidence interval of 95% and a misclassified subjects rate of 25% maximum.

The data were collected into an Excel® spreadsheet (Microsoft Corporation one Microsoft Way Redmont, USA) and analyzed by a statistical methodologist using IBM®-SPSS® Statistics 22.0 software (IBM Corp. 2013. IBM SPSS Statistics for Windows, Version 22.0 Armonk).

Descriptive statistics were computed in order to characterize the sample. Potential differences between the presence of a MDD according to the DSM-V diagnostic criteria and screening for abnormal mood disorders with the GDS–15, the HADS-D and the DT were studied using an analysis of variance (ANOVAs).

ROC (Receiver Operating Characteristic) curves and analysis of areas under the curve (AUC) were used to determine the probabilities of detecting a MDD when using the tested scales. For each self-administered questionnaire, positive likelihood ratios (LR+) were
calculated to determine the probability of suffering from MDD.

The relationships between medical, psychological and socio-environmental factors and the presence of a MDD and a positive screening for mood disorders, were analyzed by a Chi-squared test or a Fischer exact test.

Pearson correlation coefficient was used to assess links between the DT scores obtained during initial assessment and during the primary care physician’s reassessment.

Patients with missing data were not included in the statistical analysis.

The results were considered statistically significant if p value was < 0.05.

Results

General Data

93 patients (37 males, 56 females, sex-ratio: 0.66) with an average age of 81 years [70 - 95 years] were included in the study.

Regarding oncological status, 74% of all cases were new diagnosis. Lymphomas (n = 22; 24%), lung cancers (n = 19; 20%) and colorectal cancers (n = 7; 8%) were the most commonly encountered cancer locations. Solid tumor cancers were metastatic in 47% of patients. Concerning oncological management, the main therapeutic plans were chemotherapy (58%), surgical treatment (17%) or exclusive palliative management (9%). 22% of patients (n = 20) had a history of depression. Among them, ongoing psychotropic treatment with benzodiazepines and/or antidepressants was found in 60% of cases (n = 12).

The general data of the study are presented in Table 1.

Mood Disorders Screening

66 patients (71%) had at least one score above the standard cut-off on one of the mood disorder screening scales. A pathological score was recorded in 48 patients according to the GDS–15 (average score: 5 [0;14], SD = 3.11), 48 patients according to the DT
(average score: 4 [0;10], SD = 2.75) and 19 patients according to the HADS-D (average score: 7 [0;18], SD = 4.48).

A pathological score in the three self-administered questionnaires was observed in 28 patients (30%).

The suggested psychological consultation was accepted in 23% of cases (n = 15) (patient self-report).

Reassessment of diagnosis

Among 66 patients who recorded at least one score above the standard cut-off of the three screening scales, 36 (55%) were reassessed within a period of three weeks by their primary care physician.

The diagnosis could not be reassessed in 30 patients due to refusal of the primary care physician to evaluate psychological status (n = 13; 43%), absence of consultation (n = 13; 43%) or patient death (n = 4; 14%).

The diagnosis of a MDD according to the DSM-V criteria was confirmed for 10 of the 36 reassessed patients (28%).

Assessing potential differences

Variance analysis showed a statistically significant relationship between the presence of a MDD according to the DSM-V diagnostic criteria and the GDS–15 (p = 0.021), the HADS-D (p = 0.018) and the DT (p = 0.045).

Analysis of ROC curves showed that the HADS-D significantly predicted a MDD according to the DSM-V diagnostic criteria (AUC = 0.760, IC<sub>95%</sub>:0.603–0.917; p = 0.017) [Figure 1-A].

No statistically significant relationship was established with the GDS–15 (AUC = 0.683, IC<sub>95%</sub>:0.453–0.912; p = 0.093) and the DT (AUC = 0.674, IC<sub>95%</sub>:0.399–0.950; p = 0.145) [Figure 1-A and Figure 1-B].

According to positive likelihood ratios (LR+), the probability of detecting a MDD was
greater for the HADS-D (LR+ = 4.28) than for the DT (LR+ = 1.55) and for the GDS-15 (LR+ = 0.11).

The data for each measurement for the different screening scales are shown in Table 2.

**Mood disorders and medical, psychological and socio-environmental factors**

Neither statistically significant relationship was found between the medical, psychological and social-environmental factors and the presence of a MDD according to the DSM-V diagnostic criteria, nor with an abnormal mood disorders screen using either the GDS-15, the HADS-D or the DT [Table 3].

**DT reassessment by the primary care physician**

Three weeks after inclusion, primary care physicians detected a pathological DT score in 16 patients (44%). The average DT score for the reassessed patients was 3 [0;10] (SD = 3.11).

Analysis of ROC curves showed that the DT test carried out during reassessment by the primary care physician was a significant predictor of MDD according to the DSM-V diagnostic criteria (AUC = 0.852, IC95%:0.659–1; p = 0.003) [Figure 1-B].

No statistically significant relationship was found between medical, psychological and socio-environmental factors and an abnormal score in the DT test carried out at three weeks [Table 3].

A strong positive correlation was found between the DT score obtained during the initial assessment and the one carried out at three weeks (R = 0.546; p = 0.001) [Figure 1-C].

**Conclusions**

Our study examined the performance of three different mood disorder screening scales for detection of major depressive disorder in older patients with cancer. To our knowledge, very few studies have examined depression and its detection in this population. The
advanced average age of our population (81 years), the presence of severe comorbidities and the heterogeneity in cancer diagnoses as well as treatment plans ensure the representativeness of our population with regards to the general geriatric cancer population. Notable similarities exist between our population and those of large-scale prospective studies carried out in geriatric oncology [29–31]. Indeed, the socio-demographic characteristics of the population in our study, such as average age, living place and marital status are comparable to those found in studies by Kenis et al [29], Soubeyran et al. [30] and in the ELCAPA study [31]. Moreover, it is worth highlighting the fact that the functional status for basic daily living activities among our population is similar to that of the ELCAPA cohort (ADL ≤ 5: 29% as against 31.5%) [31]. The general health status of the two populations was also comparable (PS ≥ 2: 52.7% as against 49.9%) [31] in contrast to that in studies by Kenis et al. (PS ≥ 2: 29.6%) [29] and by Soubeyran et al. (PS ≥ 2: 22.8%) [30]. This discrepancy may be explained by the non-inclusion of exclusive palliative care patients.

Our study shows a statistically significant association between the presence of a MDD according to the DSM-V diagnostic criteria and a pathological screening using the GDS-15, the HADS-D and the DT. These results contradict the work of Rhondali et al., who found a moderate statistical association between the DSM diagnostic criteria for MDD and the 30-item version of the GDS, but none with either the HADS or the DT [20]. This discrepancy could be explained by methodological differences in terms of sampling size and population characteristics. In addition, in their study, Rhondali et al. used a global score for HADS (combination of depression and anxiety subparts). In our study, we only used the subpart depression (HADS-D), more specific to the symptoms of depression.

GDS-15 is currently the most widely-used screening tool for detecting depression in older patients. According to a meta-analysis carried out by Wancata et al. [32] it is 80%
sensitive and 75% specific. In 2017, Saracino et al. [33] looked at the effectiveness of three scales for depression screening in patients with cancer over the age of 70. The authors found a sensitivity of 67%, a specificity of 88%, a ROC curve AUC of 0.88 (IC$_{95\%}$: 0.80–0.95) and a LR+ of 5.51 for the GDS-15 [33]. In our study, ROC curve AUC was 0.68 (IC$_{95\%}$: 0.45–0.91) and LR+ was 0.11 for this scale.

HADS is a scale designed to exclude any items relating to somatic aspects [27]. Among the general population it is reportedly 50% sensitive and 97% specific [27]. In two studies carried out among older patients with cancer, Rhondali et al. [20] and Saracino et al. [33] found for the HADS-D respectively sensitivities of 50% and 17% and specificities of 67% and 93%. In Saracino’s study [33], the ROC curve AUC of the HADS-D was 0.88 (IC$_{95\%}$: 0.81–0.97) and the LR+ was 2.26$^{32}$. In our study, we found a ROC curve AUC of 0.76 (IC$_{95\%}$: 0.60–0.92) and a LR+ of 4.28 for this scale.

These results show an important heterogeneity regarding to the properties of the two scales. The absence of consensus regarding clinical cut-off for diagnosis may partly explain these discrepancies. Furthermore, the statistical performance of these two self-administered questionnaires appears disappointing. Indeed, a sensitivity of at least 80% and a specificity of at least 70% are considered necessary for depression screening in geriatric oncology [33]. This lack of sensitivity could expose older patients with cancer to a significant risk of under-diagnosis which could lead to an increase in the risk of suicide and morbidity/mortality. On the other hand, the lack of specificity could expose patients to over-diagnosis and a consequent risk of emotional breakdown and inappropriate medication prescriptions [33]. Beyond these statistical considerations, some of the questions included in these screening scales may seem inappropriate for older patients with cancer and could be misinterpreted.
in the context of a recent cancer diagnosis. For examples “Do you feel that your situation is hopeless?” or “Do you feel full of energy?” in the GDS-15 [25–26] or the statement “I get a sort of frightened feeling as if something awful is about to happen” in the HADS-D [27]. Such statements could draw the newly diagnosed cancer patient to focus on potentially negative experiences to come, as well as exacerbate anxiety or depression. Nevertheless, Rhondali et al. highlighted the potential usefulness of these screening tools in older patients with cancer [20]. Despite wide variations in performance, the different self-administered questionnaires in this study (specifically the GDS, the HADS and the DT) identified several MDD undiagnosed during the standard clinical oncological consultation. In our study, analysis of ROC curves and positive likelihood ratios underlined that the HADS-D was the most effective screening tool for detecting a MDD. DT was designed for quick identification of individuals at risk of mood disorders (the time required for the test is less than one minute) [34]. Its use in patients with cancer is currently recommended by The National Comprehensive Cancer Network (NCCN) [35]. In our study, we experienced the original DT in a French older population and not the French Psychological Distress Scale version validated by Dolbeault et al36] whose cut-off was 3. Indeed, in elderly people, the original visual device seems to be more comprehensive than a 10 cm vertical line. In the same way, numerical scale is not appropriate for pain evaluation in this population. Our statistical analysis regarding the DT points to its potential usefulness in ambulatory medicine. From a statistical point of view, with a ROC curve AUC of 0.85 (IC95%:0.66–1) and a LR+ of 9.125, the DT carried out at 3 weeks by the primary care physician was more effective than the HADS-D. Analysis of the ROC curve and the likelihood ratio also demonstrated the significant predictive characteristics of the DT for detecting a MDD according to the DSM-V diagnostic criteria. Moreover, the strong positive correlation found between the DT score obtained during the initial assessment
and during the reassessment by the primary care physician is good evidence that this test is highly reproducible. The superior performance of the DT for ambulatory patients may be explained by the fact that these patients had greater psychological resources available when they were reassessed by their primary care physician than they had in the initial hospital environment. Further studies are needed to confirm the performance of the DT in the ambulatory setting.

Studies carried out in older patients with cancer have shown an association between depression and various factors such as feminine gender, social isolation, grief, dependency, history of depression or metastatic cancer [37–40]. In contrast to these studies, we did not find any statistically significant association between the medical, psychological, socio-environmental factors studied and the detection of a MDD or abnormal mood disorders screening. This discrepancy can be explained by the heterogeneity of our population and small sub-group sample sizes.

Patients who presented a psychiatric history and/or were undergoing a psychotropic treatment were not excluded from this screening study. This was done purposefully to evaluate if mood disorders persisted despite ongoing treatment and to better characterize the depression and/or anxiety related clinical symptoms. Among the 10 patients who presented a confirmed MDD, only three had a known history of depression and were treated using antidepressants before the study. Given the small patient sample involved, we can assume that the inclusion of these patients had only a slight impact on the results obtained. However, these results raise concerns as to the efficacy of drug treatment. For patients recently informed of their diagnosis or of relapse of a cancerous pathology, it would have been interesting to study the types of treatment prescribed, dosing regimen and length of treatment. As expected, most cases of depression were not properly recognized. The use of screening scales led to the diagnosis of seven new cases of MDD.
Furthermore, it is interesting to highlight the low acceptance rate of recommended psychological consultations (23%) as this is a critical issue for this patient population. Our study design carries several limitations, including the limited number of patients reassessed, the small sample sizes for sub-group analysis and the non-inclusion of individuals presenting neurocognitive disorders. The methodology of our study was based on reassessment of mood disorders at 3 weeks by a different, impartial physician in order to detect the persistence of these disorders (as required to diagnose a MDD). However, reassessment was carried out on a voluntary basis by the physician and this might explain the significant number of losses to follow up. This design was chosen to preserve the observational nature of the study without interfering with care and to facilitate inclusion as well.

Future research, on a larger population, is needed to confirm our results with a view of measuring the sensitivity and specificity of these three mood disorder scales in older patients with cancer and to validate their use within this specific population. As we have argued elsewhere, use of DT for ambulatory patients may be a promising measure to recognize mood disorder in older patients with cancer. Beyond the specific use of these screening tools, it seems of critical importance to call for depression in older patients with cancer to be recognized using a global, multidimensional and multidisciplinary approach, in which psychologists also play a role. Moreover, the fact that a majority of patients refuse the proposed psychological consultation should question us about our non-drug management methods in this particular population.

Declarations

Ethics approval

The study protocol was approved by institutional review boards (clinical trials: RCB 2015-A00836-43) and ethical committee CPP Nord-Ouest III (ref 2015-32 on the 2016-09-01).
Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

BB, GB, JD and JLM has planned and designed the study, BB, GB, HSL, and LG collected data, RM analyzed and interpreted the patient data, GB was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Figures

Levels of agreement between the GDS-15, the HADS-D, the Distress Thermometer and the DSM-V for detection of major depressive disorder Figure 1-A: ROC curve of the GDS-15 and the HADS-D Figure 1-B: ROC curve of the Distress Thermometer obtained during the initial assessment and during the primary care physician’s reassessment Figure 1-C: Correlation found between the Distress Thermometer obtained during the initial assessment and during the primary care physician’s reassessment Note: † Primary Care Physician (PCP)
Supplementary Files

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Table 3.pdf
Table 2.pdf