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Alexithymia and cancer-related fatigue: a controlled cross-sectional study

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ABSTRACT

Aims and background. The study aims to investigate the alexithymia construct in patients with a recent or longtime diagnosis of cancer as well as in healthy people, and whether alexithymia and fatigue are linked in the mentioned groups.

Methods. A first group, diagnosed less than 3 months previously (n = 63), and a second group whose cancer diagnosis dated back more than 30 months (n = 53), matched for sex, age, educational level and cancer site were assessed. Matched healthy controls (n = 50) were also evaluated. Alexithymia was assessed with the Toronto Alexithymia Scale-20, while fatigue was assessed with the Brief Fatigue Inventory.

Results. Alexithymia scores were higher in the recently diagnosed group than in the group with a longtime cancer diagnosis (t = 2.18, P <0.05). Both groups had higher scores than controls (t = 4.3, P <0.001; t = 2.01, P <0.05). Alexithymic subjects were 45.6% in the recently diagnosed and 21.4% in the longtime diagnosed group (χ^2 = 6.3, P <0.05) and 18% in controls. Fatigue was more severe in patients with a longtime diagnosis compared with recently diagnosed patients (t = 7.079, P = 0.000). A weak but significant association between fatigue and alexithymia was found in recently diagnosed patients (r = 0.27.2; P <0.05).

Conclusions. Our study confirms that alexithymia scores are higher in cancer patients than in controls. The study suggests that alexithymia could be considered a dynamic reaction to illness in recently diagnosed patients, declining during subsequent phases. High fatigue rates in patients with a longtime diagnosis of cancer underline the role of the long course of illness in the perception of fatigue. The association between fatigue and alexithymia was weak in the recently diagnosed group and not significant in patients with a longtime diagnosis, in whom fatigue was an important complaint. **Free full text available at www.tumorionline.it**

Introduction

Alexithymia, which literally means "no words for mood,"[1] is a multidimensional construct characterized by a difficulty to identify feelings, to distinguish between feelings and bodily sensations, and to describe one's own feelings to others. It is also exemplified by restricted imaginative processes and a cognitive operational style that is utilitarian and externally oriented.

Alexithymia is conceptualized as either a stable personality trait or a defensive reaction and a coping strategy to stressful events. In these hypotheses alexithymia could, alternatively, be considered as a health risk factor or a predictor of treatment outcome[2,3]. According to the first hypothesis, alexithymia has been regarded as a developmental deficit[4,5] and several studies have indicated alexitymia as a stable personality trait over time[6-8]. By contrast, some studies liken alexithymia to a coping strategy for stressful events, therefore categorizing alexithymia as a state-dependent

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phenomenon[9-13]. These controversial findings have led to debate over whether the alexithymia construct is a specific consequence of illness or a personality-related factor.

Freyberger[14] supports the hypothesis of acute and chronic "secondary alexithymia" as a reaction to stressful situations. Acute secondary alexithymia is described as a transitory state, decreasing after an acute disease episode, while chronic secondary alexithymia is described as a permanent condition associated with adjustment to chronic disease.

Alexithymia is also hypothesized to be an important factor in the development of medically unexplained physical symptoms. Indeed, a growing number of studies have assessed alexithymia in somatic diseases[15,16] and in somatoform disorders[17]. One study investigated the prevalence of alexithymia in adolescents with chronic fatigue syndrome compared to healthy adolescents[18]. A recent study investigated the role of alexithymia in the perception of pain in cancer patients, and concluded that pain was not associated with global alexithymia scores[19].

The association between alexithymia and cancer is still unclear and controversial. The investigation of alexithymia in chronic illnesses such as cancer highlights intriguing issues regarding the nature and the modulating role of this construct. Some studies have detected high alexithymia rates in cancer patients compared to healthy controls[20-22], while others failed to confirm this[23-26]. Remarkably, several studies where breast cancer patients were compared with healthy controls have specifically indicated that there is an association between breast cancer and alexithymia[21,22]. Moreover, alexithymia is associated with high levels of anxiety both in women with breast cancer and their husbands, thus underlining the role of alexithymia in favoring psychological distress[27].

However, the role of alexitymia in cancer patients seems to be more complex and requires further investigation. As a matter of fact, a recent study has shown an improvement of quality of life in highly alexithymic patients soon after surgery for colorectal cancer and speculates that alexithymia might be advantageous in evaluating post-surgery adaptation in the short term[28].

Nevertheless, in spite of the questions raised by the aforementioned studies, some important issues that would contribute to understanding the complex relationship between alexithymia and cancer have not been examined. Indeed, there is a lack of studies investigating whether alexithymia changes during the course of cancer and its relationship with the recency of diagnosis.

Like alexithymia, fatigue is considered a multidimensional construct, and can be defined as a subjective sensation of lack of energy, loss of strength, and fatigability[29]. Recently, cancer-related fatigue has been defined by the National Comprehensive Cancer Network and the American Cancer Society as "a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning"[30]. Fatigue is one of the most common symptoms in cancer patients. The prevalence in reported studies varies from 33%[31] to 100%[32], or from 25% to 99%[33], depending on the assessment measures used and the type of population included in the study.

The etiopathogenetic determinants of fatigue remain unclear: biological and psychological factors related to cancer site, phase of illness, and type of treatment contribute to its clinical manifestation. Dyspnea, insomnia, depression, and symptom burden seem to be the most commonly associated factors[29,34]. When considering psychological variables, fatigue has been frequently associated with anxiety, depression, and ineffective coping styles[29,35-37].

Some studies have investigated the prevalence of fatigue in cancer patients compared with healthy controls. The results of these studies add a number of relevant issues to the understanding of cancer fatigue. In fact, they have produced controversial results, with several reporting no differences between cancer patients and healthy controls in fatigue scores[38,39]. Some of these studies, although finding no differences between cancer patients and controls at baseline, reported a worsening in fatigue scores after chemotherapy and radiotherapy[40,41]. Other researchers have reported higher fatigue scores in cancer patients than controls[42-44]. A recent review[34] concludes that cancer-related fatigue usually worsens during cancer treatments and appears to be more severe than off-therapy fatigue.

Although fatigue has been linked to coping strategies and psychological disorders, only a few studies[45,46] have evaluated the relationship between personality and fatigue, underlining the role of the former in the perception of fatigue. Specifically, the relationship between alexithymia and cancer-related fatigue has never been examined.

The present study aims to investigate the alexithymia construct, exploring the presence of this trait at different times following diagnosis, in order to better understand the relationship between alexithymia and cancer during different phases of the illness. Furthermore, the study aims to examine possible associations between alexithymia and fatigue.

Material and methods

Population

Three different samples were assessed. The first sample was composed of patients undergoing chemotherapy treatment for a first instance of cancer who had received surgical treatment at least a month before starting chemotherapy. The inclusion criteria for this sample were a diagnosis of cancer within the previous 3 months

Table 1 - Demographic characteristics of study groups

	Cancer diagnosis <3 months	Cancer diagnosis >30 months	Controls
Gender (%)			
Male	44.4	45.2	46
Female	55.6	54.8	54
Age (years)			
Mean	59.952	65.871	60.5
SD	11.06	10.01	5.99
Level of education (years)			
Mean	9.33	8.74	9.52
SD	3.2	4.3	5.1

SD, standard deviation.

(Table 1) before starting the first chemotherapy treatment; no previous history of malignancy; a score on the Karnofsky Performance status scale ≥60, indicating a minimum ability to care for most of the individual's personal needs; no symptoms suggesting major psychopathology such as psychosis; no cognitive disorders; no neurodegenerative diseases, and no other major diseases associated with cancer. Cancer sites included breast, colon-rectum, lung and others (Table 2). Subjects were recruited among patients admitted for chemotherapy treatment at the Department of Internal Medicine of the Second University of Naples after the first general visit. Subjects who met the inclusion criteria for the study and agreed to participate were enrolled from June 2006 to December 2006. Eight patients refused to participate, leaving 63 patients who were included in the study.

The second sample consisted of patients undergoing palliative care. The criteria for inclusion of the patients in this sample were a diagnosis of cancer at least 30 months prior to selection for the study; no previous history of malignancy; a Karnofsky score ≥60; no symptoms suggesting major psychopathology such as psychosis; no cognitive disorders; no neurodegenerative diseases, and no other major diseases associated with cancer. This group had received surgical treatment as well as chemotherapy and/or radiotherapy but not in the previous month, and the group was evaluated before the first cycle of palliative treatment. This sample was recruited from January 2007 to June 2007 at the first appointment for the general medical examination at the Unit of Pain Therapy and Palliative Care of Cardarelli General Hospital in Naples. Seven patients refused to participate, leaving 53 patients to be enrolled.

Table 2 - Cancer sites

	Cancer diagnosis <3 months	Cancer diagnosis >30 months
Breast	23 (36.5%)	18 (34%)
Lung	13 (20.6%)	11 (20.7%)
Colorectal	18 (28.6%)	16 (30.2%)
Others	9 (14.3%)	8 (15.1%)

The 2 clinical groups were compared with a control group composed of 52 matched healthy people who replied to community advertisements including classified ads in local newspapers and notices put up at various recreation centers. Two persons refused to participate, leaving 50 subjects to be enrolled in the study.

The 3 groups were matched for sex, age, and education level. The 2 patient groups were also matched for cancer site. The protocol was approved by the local ethics committee.

Materials

Two different questionnaires were administered. The Toronto Alexithymia Scale (TAS-20) was used to assess alexithymia. This is a self-reporting scale comprising 20 items rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). The scale gives a total score, with a score above 60 being indicative of the presence of alexithymia[47,48]. In addition to the total score, the scale yields subscores for 3 different factors: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally oriented thinking (EOT). The scale has been translated into Italian and validated in an Italian population[49].

Fatigue was measured with the Brief Fatigue Inventory (BFI), a 9-item scale widely used to assess the presence of fatigue with a low burden for the patient. It consists of an 11-point scale (0 to 10) to measure the specific symptom of cancer-related fatigue in a single dimension. Nine items ask patients to describe the severity of their fatigue "at its worst", "usual" and "now" during the past 24 hours, with 0 indicating "no fatigue" and 10 indicating "fatigue as bad as you can imagine." Cutoff points for fatigue were defined in 2 categories: a "worst fatigue" rating of 7 or more indicates "severe," and a rating of 0 to 6 indicates "non-severe." Six additional items describe the degree to which fatigue has interfered with different aspects of the patient's life during the past 24 hours. Interference is measured on a scale of 0 to 10, with 0 meaning "does not interfere" and 10 meaning "completely interferes"[50]. This instrument has been translated and validated in Italian[51].

Statistical analysis

Means and standard deviations were used to describe the samples. Correlations between variables were assessed with Pearson's product-moment correlation test. The samples were compared using the t-test, chi-square test, and Fisher's exact test. All analyses were performed using SPSS 13.0 for Windows. The level of significance was set at 95%.

Results

Patient characteristics

The sample within 3 months of diagnosis comprised 63 patients. Eight were excluded because of their refusal to participate in the study (response rate 89%). The mean age of the patients who did not agree with the study was slightly higher than the mean age of those who participated (61.6 *vs* 59.9 years, $P = 0.610$). Five of the patients who refused to participate were women (62.5%) and 3 were men (37.5%). The mean educational level was slightly lower than that of patients who agreed to participate (7.8 *vs* 9.3 years, $P = 0.106$).

The sample with a diagnosis dating back >30 months was composed of 53 patients who participated in the study (response rate 88.3%). The mean interval since diagnosis was 37.24 months (standard deviation 5.69 months). The mean age of the patients who did not participate was slightly lower than that of the final sample (65.9 *vs* 63 years; $P = 0.386$). Four of the patients who refused to participate were women (57%) and 3 were men (43%). The educational level was lower for subjects who did not agree to participate (8.6 *vs* 7.9 years, $P = 0.057$).

No significant differences were observed between the 2 groups (within 3 months and >30 months from diagnosis) who refused to participate regarding sex ($P = 0.590$), age (61.6 *vs* 63 years, $P = 0.79$) and education (7.8 *vs* 7.9 years, $P = 0.79$).

The control group was composed of 50 subjects because 2 individuals (1 male and 1 female) did not agree to participate in the study (response rate 96%).

Alexithymia

Table 3 shows the comparisons between the mean scores on the TAS-20 in the 3 groups. Between the clinical groups the mean alexithymia scores were higher in patients with a recent diagnosis than those with a longtime diagnosis of cancer (t = 2.25, $P = 0.027$). Patients with a longtime diagnosis had higher mean alexithymia scores than controls ($P = 2.01$, $P = 0.047$) (Table 4).

Table 3 - Score comparison between recently diagnosed and longtime diagnosed patients

	Cancer diagnosis <3 months	Cancer diagnosis >30 months	T	*P*
TAS-20 mean score	57.07 (SD 9.5)	52.74 (SD 9.7)	2.25	0.027
DIF mean score	19.06 (SD 4.7)	17.71 (SD 5.3)	1.35	0.178
DDF mean score	14.96 (SD 4.2)	14.27 (SD 4.8)	0.758	0.450
EOT mean score	23.22 (SD 4.7)	21.07 (SD 4.9)	2.25	0.027
BFI mean score	3.62 (SD 2.02)	6.77 (SD 2.2)	7.079	0.000

TAS-20, 20-item Toronto Alexithymia Scale; DIF, difficulty identifying feelings; DDF, difficulty describing feelings; EOT, externally thinking; BFI, Brief Fatigue Inventory; SD, standard deviation.

Table 4 - Score comparison between clinical samples and controls

TAS-20 mean score	Over 30 months group 52.74 (SD 9.5)	Controls 48.02 (SD 12.3)	T 2.01	*P* 0.047
BFI mean score	Within 3 months group 3.62 (SD 2.2)	Controls 2.84 (SD 1.8)	T 2.04	*P* 0.044

TAS-20, 20-item Toronto Alexithymia Scale; BFI, Brief Fatigue Inventory; SD, standard deviation.

With regard to the subscales of TAS-20 (DIF, DDF, and EOT), the mean scores highlighted significant differences between recently diagnosed patients and those with a longtime diagnosis only in EOT (t = 2.25, $P = 0.027$).

Alexithymic subjects (TAS-20 ≥61) made up 45.6% of the within-3 months group, 21.4% of the >30 months group, and 18% of controls (Figure 1).

The chi-square test revealed that recently diagnosed patients were more often classified as "alexithymics" than patients diagnosed more than 30 months previously ($x^2 = 6.3$, $P = 0.02$). No differences in the presence of alexithymia were found between patients with a longtime cancer diagnosis and healthy controls ($x^2 = 0.21$, $P = 0.900$).

Fatigue

The mean fatigue scores were significantly higher in patients with a longtime diagnosis than in those with a recent diagnosis of cancer (t = 7.079, $P = 0.000$) (Table 3). Healthy people reported lower mean scores than patients with a recent cancer diagnosis (t = 2.04, $P = 0.044$) (Table 4).

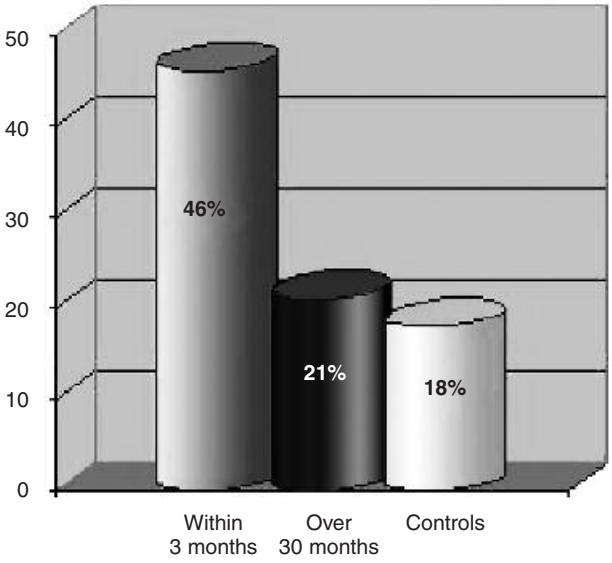

Figure 1 - Alexithymia cases.

Fatigue and alexithymia

A weak but significant association between fatigue and alexithymia was found in patients with a recent cancer diagnosis (r = 0.27 P = 0.037). This association was not seen in patients diagnosed more than 30 months previously (r = 0.027, P = .915).

In recently diagnosed subjects, the correlation between BFI and the 3 subscales of the alexithymia scale revealed that fatigue was associated with the DIF scale of TAS-20 (r = 0.34, P = 0.008), but not with the DDF scale (r = 0.014, P = 0.91) or EOT scale (r = 0.17, P = 0.863). In patients with a longtime diagnosis, fatigue was not associated with the 3 subscales mentioned (r = -0.071, P = 0.652 for DIF; r = 0.091, P = 0.570 for DDF; r = 0.036, P = 0.823 for EOT).

Alexithymia was associated with fatigue scores in the control group (r = 0.31, P = 0.036). In this group, with regard to the subscales of TAS-20, fatigue was associated with DIF (r = 0.42, P = 0.001) but not with DDF (r = 0.26, P = 0.052) or EOT (r = 0.038, P = 0.803).

Discussion

Our study confirms that mean alexithymia scores are higher in cancer patients than in healthy controls, as reported by previous studies[20-22]. However, to our knowledge these studies did not consider the time elapsed since diagnosis and largely confirm a prevalence of alexithymia in people with cancer. In the present study, patients with a recent cancer diagnosis differed from patients with a longtime diagnosis and controls both in terms of alexithymia mean scores and in the number of "cases" according to the established cut-off score.

In our opinion, this finding firstly suggests that in cancer patients the time elapsed since diagnosis should be considered an important variable influencing the association between alexithymia and cancer. Second, our data allow us to hypothesize that alexithymia could be considered as an early reaction to a life-threatening stressful event such as cancer. We are aware that this hypothesis should be investigated in depth. To our knowledge only few and heterogeneous studies have addressed this issue. Mikolajczak and Luminet[52] examined alexithymia stability in the context of increasing psychological distress (i.e., psychology students examined at the beginning of the academic year and 12 weeks later during the exam period), and found a high degree of stability despite the acute increase in psychological distress. The normative event chosen for this study, however, should not be considered an exhaustive example of the putative correlation between alexithymia and levels of distress because this experience is quite different from that caused by a life-threatening event such as a physical illness.

Kojima *et al.*[16] investigated patients after myocardial infarction and found that patients with a first myocardial infarction tended to show a remarkable decrease in alexithymia scores between the initial and 1-year interviews. The authors concluded that in post-myocardial patients, alexithymia may be considered a dynamic state influenced by prior experience of a myocardial infarction. Mantani *et al.*[27] support this hypothesis in cancer subjects, stating that alexithymia may, at least in part, have reactive characteristics attributable to the many stressful events caused by cancer.

Another recent study conducted by Luminet *et al.*[53] assessing alexithymia in women with breast cancer before and 6 months after surgery found a relative stability of alexithymia over a period of 6 months, but significantly higher alexithymia mean scores over this period. This last finding supports our hypothesis of increasing mean scores after a distressing, life-threatening event. According to the same authors, the short follow-up duration limits the view of alexithymia as a stable trait.

Moreover, our study found a significant difference between the cancer groups not only in terms of mean scores, but also in the number of cases; this result seems to confirm Freyberger's concept of secondary acute alexithymia as a reaction to stressful situations[14], suggesting that this reaction could be considered specific to physical illness rather than a generic stressful experience.

The difference between our 2 clinical samples in the EOT subscale reveals that this state reaction is mainly based on an externally oriented cognitive style. The hypothesis, supported by our study, of alexithymia as a state reaction to cancer should be further confirmed by longitudinal studies with 2 outstanding considerations: first, we do not know how many of our subjects were alexithymic prior to cancer; second, long-term longitudinal studies on cancer patients would best clarify the differences between recently diagnosed and longtime diagnosed patients found in our cross-sectional study.

Fatigue differed in the 3 groups, with the highest scores being recorded in patients with a longtime diagnosis. This finding emphasizes that the worsening of the psychophysical condition due to the long course of illness leads to a more intense experience of fatigue. Stone *et al.*[29,54] support our conclusions, pointing out that patients undergoing palliative care perceived a stronger sense of fatigue than recently diagnosed patients and healthy people, and that fatigue is one of the most severe complaints in patients with advanced cancer.

Remarkably, the mean fatigue score in our recently diagnosed sample is rather low, indicating that in the early phase of the illness, fatigue does not have a great impact on patients' functional level and quality of life. One of the 2 studies available in the literature[37] evaluating fatigue prior to cancer treatments shows that women with uterine cancer experienced a low level of fatigue despite earlier surgical treatments, thus confirming our results.

Our hypothesis of an association between alexithymia and fatigue, to our knowledge never before investigated, was not fully confirmed. In the recently diagnosed group and in controls, there was a significant but weak correlation between alexithymia and fatigue. However, this result was not confirmed in the patient group with a longtime diagnosis, where fatigue was an important complaint affecting functional levels. A possible explanation for this difference could be that in recently diagnosed patients and in controls, the score is related to a focus upon bodily sensations. A recent study of patients with panic disorders showed that alexithymic patients are more prone to amplify somatic sensations[55]. Likewise, another study underlines the role of somatosensory amplification in the presentation of somatic symptoms and its close association with other factors, such as anxiety, depression, and alexithymia[56].

In patients diagnosed over 30 months prior to the experiment, fatigue can be best explained as a consequence of psychophysical impairment due to the long course of illness. Aistars[57] has argued that prolonged stress is the major cause of fatigue in cancer patients, identifying physiological, psychological and situational factors that may result in fatigue by causing constant physical and psychological stress.

Of note, in both the recently diagnosed group and in healthy controls, fatigue is associated with the DIF subscale of TAS-20, indicating that a cognitive difficulty in processing and identifying feelings may play a role in amplifying somatic sensations. This putative explanation needs more accurate research to be performed in subjects with cancer, whereas in psychiatric patients, a previous study showed that difficulties in identifying feelings are highly predictive of somatization[58].

It is important to note that our study has some limitations: the small size of the sample and its heterogeneity (breast, lung, colon and other cancers) prevent us from generalizing our findings. The sample size also prevented us from running more sophisticated statistical analyses that could have revealed more details. The restrictive inclusion criteria strongly limited enrolment in the study and made our clinical samples rather small.

In conclusion, our study underlines a possible role of the alexithymic response as a transient coping reaction to cancer in recently diagnosed patients, although longitudinal studies are required to confirm this empirical finding and to analyze the impact of this dynamic state on quality of life. Furthermore, we found a difference in the perception of fatigue between the 2 clinical samples, pointing to the role that the long course of cancer plays in the perception of fatigue. Finally, the association between alexithymia and fatigue was not confirmed in our clinical samples: fatigue and alexithymia were only weakly correlated in recently diagnosed cancer patients, in whom the fatigue scores were rather low, and they were not at all correlated in patients with a longtime diagnosis, in whom fatigue was an important complaint.

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