RESEARCH ARTICLE

Assessment of Anxiety and Depression Status in Turkish Cutaneous Melanoma Patients

Faruk Tas*, Senem Karabulut, Hulya Guceli, Sidika Kurul, Kayhan Erturk, Murat Guceli, Hasibe Kinik

Abstract

Background: Even though anxiety and depression are two mood disorders encountered commonly in cancer patients only few trials have been carried out so far in melanoma patients. The aim of the study was to determine the clinical prevalence of these disorders in Turkish cutaneous melanoma patients and to clarify possible clinicopathological factors influencing them. Material and methods: A total of 100 consecutive outpatient melanoma patients were enrolled and asked to complete the Hospital Anxiety and Depression Scale (HADS) questionnaire immediately after scheduled visits. Results: A total of 24 participants had clinical anxiety and 8 were diagnosed with borderline anxiety. Fifteen were diagnosed with clinical depression and 20 with borderline depression. Prior to melanoma diagnosis the majority of the patients, 93 and 86, were assessed as normal in terms of their anxiety and depression status, respectively (p<0.001). A statistically significant correlation was found between anxiety and depression scores (p<0.001). The patients with advanced disease were significantly more anxious and depressive than those with early stage disease. None of the other socio-demographic parameters was found to be correlated with anxiety and depression status. Conclusions: Because a large group of Turkish melanoma patients, nearly one third of the cohort, was found to be suffering from relevant anxiety and depression, it is of uttermost importance that psychological support and pharmacological intervention for these patients be commenced as soon as possible.

Keywords: Anxiety- depression- melanoma- prevalence- Turkish

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Introduction

Anxiety and depression are the most commonly reported mood disorders in general population. The prevalence of depression is 5-9% in western world and anxiety disorders are encountered about twice as commonly as depression; with a prevalence of 18% (Waraich, 2004; Kessler, 2005). Anxiety and depression are also common in cancer patients (Mitchell, 2013; Mitchell, 2011). In a meta-analysis conducted on cancer patients, the prevalences of major depression and anxiety were found 16% and 10%, respectively (Mitchell, 2011). Since in most of the studies patients were interviewed early in the course of the disease the prevalence of mood disorders in cancer survivors still remained to be elucidated (Mitchell, 2013; Pirl, 2009). In an important meta-analysis including the pooled sample of 51 381 cancer survivors, the prevalence of depression was 11.6% and the prevalence of anxiety was 17.9% in 48 964 cancer survivors (Mitchell, 2013). These findings revealed that among long-term cancer survivors anxiety was more common than depression. In another cross-sectional observational study on 178 patients diagnosed with miscellaneous cancers, 48% of cases were reported having anxiety disorder (Stark, 2002). A novel study on 1 385 Brazilian cancer patients showed that the prevalence of anxiety was between 21.5 and 27.4% and the prevalence of depression was 21.1% (Lima, 2014). Females had significant higher rates of both anxiety and depression than men did.

Since, so far, only a few number of studies have examined the psychological stress among melanoma patients, it has not been yet fully understood whether or not the psychological factors have dramatic influences on melanoma patients (Kasparian, 2009; Kasparian 2013a, Kasparian 2013b). It has been shown that approximately 30% of melanoma patients reported psychological distress that needed for clinical intervention (Kasparian, 2009; Kasparian 2013a, Kasparian 2013b; Molassiotis, 2014). Anxiety and depression are the most commonly reported psychological disorders whose the symptoms typically arise immediately after the diagnosis and continue the length of the treatment of melanoma. The symptoms of anxiety appear to predominate those of depression during the disease phases. In terms of anxiety level, a wide variability was found among studies with different sample sizes and nationalities (23%, ranging from 7 to 44%) and depression (11%, ranging from 6 to 28%) (Kasparian, 2009; Kasparian 2013a, Kasparian 2013b; Molassiotis, 2014; Erim, 2013; Albrecht, 2013; Bergenmar, 2004; Blum, 2003).
There are controversial data assessing the factors that may have predictive values on mood disorders in melanoma patients. We therefore aimed to perform a survey among Turkish melanoma patients to determine the extent of the mood disorders and analyze various biological and socio-demographical factors that might have possible effects on them.

Materials and Methods

Study population and procedures

This study was conducted on adult patients diagnosed with cutaneous melanoma at the Department of Medical Oncology, Institute of Oncology, Istanbul University. Patients who were in a pre-terminal state and too sick to complete the interview were excluded. Patients were asked to complete the questionnaire immediately after their scheduled visits. All potentially eligible patients attending the clinics were chosen and assessed consecutively. Interviews were completed between July 2013 and September 2014.

The questionnaires were handed out to the patients by their physician on arrival as outpatients. The majority of the interviews were self-administered but occasionally they were conducted face to face. The patients were explained that all of the shared information was and would be treated in confidence and that refusal to participate in the study would not in any way jeopardize the care they received. Informed consent was obtained from all of the patients and the study was reviewed and approved by the regional ethical committee.

Instrument

Hospital Anxiety and Depression Scale (HADS), an internationally widely used reliable and valid instrument for the assessment of anxiety and depression among medically ill patients, was used in this study (Zigmond, 1983). Each of the two scales is made up of 7 items, which are summed to give a score ranging from 0 to 21. Scores lower than 7 are considered to be normal; borderline scores range from 8 to 10 points, and clinically relevant anxiety and depression is indicated above 10 points. Socio-demographic information was provided by the patients. Relevant medical data such as stage of the disease, were collected by interviewing oncologist.

Statistical analysis

SPSS for Windows version 21.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. All categorical variables were summarized using frequencies and percentages. Relationship and comparisons of several clinical categorical variables were evaluated by Pearson chi-square was used. Fisher’s exact test was used where Pearson chi-square test was inapplicable. Mc-Nemar’s test was used to describe change anxiety and depression status of patients in before and after diagnosis of disease. Spearman’s rank order correlation was used for correlation analysis. All statistical analyses were two-sided, and comparisons made in which probability values equal or less than 0.05 were considered statistically significant.

Results

Patients

The study population comprised 64 men and 36 women, in total 100 cases. The median age was 51 years; ranging from 16 to 81. Socio-demographic and clinical characteristics of patients are given in Table 1. Most of the patients were married (n=79), had children (n=77), were high school and university educated (n=59), did not work (n=59), lived in urban areas (n=85), and had advanced disease (n=68). Only 36 patients were first admissions.

Anxiety and depression status

After the diagnosis 24 participants had clinical anxiety and 8 were diagnosed with borderline anxiety (Table 2) and the remaining patients showed no symptom of anxiety (n=68), whereas before the diagnosis majority of them (i.e. 93 patients) were within the normal limits in terms of anxiety, 3 patients and 4 patients of whom had borderline anxiety and clinically apparent anxiety, respectively.

Fifteen patients were classified as clinically depressive and 20 were classified as having borderline depression after melanoma diagnosis was made (Table 2) and the remaining 65 patients had no symptoms of depression, whereas prior to the diagnosis most of the patients were not in depression (n=86), e.g. only 10 patients and 4 patients of whom were diagnosed with borderline depression and clinical depressive disorder, respectively.

Table 1. Patient Characteristics

| Variables                              | n   |
|----------------------------------------|-----|
| No. of patients                        | 100 |
| Age, years                             |     |
| <50 / ≥50                              | 47/53|
| Gender                                 |     |
| Male / Female                          | 64/36|
| Marital status                         |     |
| Single/Married/Divorce or separated    | 17/79/4|
| Children                               |     |
| 0/1/2/3/4/more                         | 23/17/38/14/3/5|
| Education status                       |     |
| Illiterate/Basic/High school/University| 5/36/28/31|
| Occupation                             |     |
| Working/Not working-retired            | 41/29/30|
| Income                                 |     |
| Low/Moderate/High                      | 7/65/28|
| Born place                             |     |
| Rural/Urban                            | 48/52|
| Living place                           |     |
| Rural/Urban                            | 15/85|
| Stage of disease                       |     |
| 0/1/2/3/4                              | 2/9/21/41/27|
| Type of patient                        |     |
| New admission/ on follow-up            | 36/64|
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was significantly negatively correlated with the anxiety scores ($p=0.016$). Contrarily, the correlations of the levels of anxiety with tumor characteristics, such as localization, tumor thickness and tumor stage, were not significant.

Furthermore, 175 melanoma patients with stage IB (42%), II (31%) and III (27%) completed surveys exclusively on depression in another trial (Albrecht, 2013). The study showed rather low levels of depression, 6.3% of them had subclinical and 7.4% had clinical levels of depressive symptoms. None of the studied variables including medical and socio-demographic showed a significant relationship with depression status. Additionally, it revealed also no significant effect of low-dose IFN-alpha treatment on depression.

However, trials with large numbers of patients also studied these two mood disorders together. Bergenmar et al. studied 437 early stage (stage I-II) Swedish melanoma patients who had completed the HADS in three months after the diagnosis (Bergenmar, 2004). Six percent of patients had borderline depression. Mostly, young patients, women, patients without ulcerated tumors, patients with tumors with low mitotic index and Clark level II tumors had borderline and clinically apparent levels of anxiety. Furthermore, the young melanoma patients showed clinical level of depression. However, no relationships were found between anxiety or depression and outcome in terms of relapse. In other trial, Blum et al. investigated these mood disorders in 615 German melanoma patients by using HADS (Blum, 2003). A few number of patients (5%) had moderate depressive symptoms. The significant relationships were found between various clinical/socio-demographic parameters, such as gender, age, marital status, the presence of cutaneous or regional lymph node metastasis, and depression. Furthermore, a total of 472 English melanoma patients with mostly early stages (stages I-II (67%) were studied (Molassiotis, 2014). Twenty-nine percent of the patients had signs of anxiety (15.6% borderline and 13.4% definitive) and 11% showed depression symptoms (7.5% borderline and 3.4% definitive). Moreover, patients with nodal disease had significantly higher levels of anxiety and depression.

This study population comprised 64 men and 36 women, in total 100 cases. Interestingly, most of them

### Table 2. Anxiety and Depression Status of Patients in Before and After Diagnosis

|                          | Anxiety n | Depression n |
|--------------------------|-----------|--------------|
| Current (after diagnosis) |           |              |
| Clinically               | 24        | 15           |
| Borderline               | 8         | 20           |
| Normal                   | 68        | 65           |
| Former (before diagnosis)|           |              |
| Clinically               | 4         | 4            |
| Borderline               | 3         | 10           |
| Normal                   | 93        | 86           |

|                          | p value   | p value   |
|--------------------------|-----------|-----------|
| Normal v Clinically manifest+Borderline | <0.001    | <0.001    |
| Normal+Borderline v Clinically manifest | <0.001    | 0.01      |

**Correlation of anxiety and depression status in before and after diagnosis**

Both anxiety and depression ratios were found statistically significantly higher after the diagnosis than before the diagnosis ($p<0.001$) (Table 2).

**Relationship between anxiety and depression status of patients after diagnosis**

Both clinically and clinically/borderline statuses of patients were found statistically significantly correlated with each other ($rs=0.485$, $p<0.001$ and $rs=0.530$, $p<0.001$, respectively).

**Variables affecting on anxiety and depression status**

The relationships between potential socio-demographic/disease related variables and anxiety/depression status in melanoma patients were shown in Table 3. The patients with advanced disease were significantly more anxious and depressive than early-disease patients. The disease duration and other socio-demographic parameters were not found to be correlated with either anxiety or depression status.

**Discussion**

Current literature shows that mood disorders, anxiety and depression, in melanoma patients are generally moderate. Over the last years, a small number of studies regarding mood disorders have been studied in melanoma patients (Kasparian, 2009; Molassiotis, 2014; Erim, 2013; Albrecht, 2013; Bergenmar, 2004; Blum, 2003). In a small novel study, Erim et al assessed exclusively the anxiety levels in 70 German melanoma patients, mostly (79%) stage I-II, by using the HADS questionnaires (Erim, 2013). They found that a small group of patients suffered from anxiety; 10% of the patients had borderline levels, and 7% showed a clinically apparent increase in anxiety score. Age was significantly negatively correlated with the anxiety score ($p=0.04$). Moreover, significant relationships were found only between the anxiety levels and involved lymph nodes and illness duration. While involvement of the lymph nodes demonstrated a positive correlation with the anxiety score ($p=0.017$), however, illness duration was significantly negatively correlated with the anxiety scores ($p=0.016$). Contrarily, the correlations of the levels of anxiety with tumor characteristics, such as localization, tumor thickness and tumor stage, were not significant. Furthermore, 175 melanoma patients with stage IB (42%), II (31%) and III (27%) completed surveys exclusively on depression in another trial (Albrecht, 2013). The study showed rather low levels of depression, 6.3% of them had subclinical and 7.4% had clinical levels of depressive symptoms. None of the studied variables including medical and socio-demographic showed a significant relationship with depression status. Additionally, it revealed also no significant effect of low-dose IFN-alpha treatment on depression.
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had advanced disease (n=68). We found dramatically increased levels of anxiety and depression in patients after the diagnosis compared to before the diagnosis. This finding was expected and well correlated with literature data. After the diagnosis, 24 participants were clinically anxious and 8 were diagnosed with borderline anxiety. Similarly, after the melanoma diagnosis 15 patients were classified as clinically depressive and 20 patients had borderline depression. Both these scores regarding anxiety and depression were significantly higher than those brought up in other trials. We believe that this is the result of the fact that the majority of the patients had advanced diseases. As expectedly, both statuses of the mood disorders in melanoma patients were significantly correlated with each other. When we studied the relationships between potential socio-demographic/disease related variables and anxiety/depression status in melanoma patients, exclusively patients with advanced disease were significantly more anxious and depressive than early-disease patients. No effect of disease duration (new diagnosis versus on follow-up) on psychological scores was found. Likewise, none of the other socio-demographic parameters was found to be correlated with anxiety and depression status.

Table 3. Comparisons of Anxiety and Depression Status of the Patients after Diagnosis

| Variables               | n   | Anxiety Borderline and Clinically manifest | Depression Borderline and Clinically manifest |
|-------------------------|-----|--------------------------------------------|---------------------------------------------|
| Age, years (p)          |     | 0.20                                       | 0.14                                        |
| <50                     | 47  | 18                                         | 20                                          |
| ≥50                     | 53  | 14                                         | 15                                          |
| Gender (p)              |     | 0.12                                       | 0.86                                        |
| Male                    | 64  | 17                                         | 22                                          |
| Female                  | 36  | 15                                         | 13                                          |
| Marital status (p)      |     | 0.23                                       | 0.74                                        |
| Married                 | 79  | 23                                         | 27                                          |
| Single                  | 21  | 9                                          | 8                                           |
| Children (p)            |     | 0.60                                       | 0.67                                        |
| 0-1                     | 40  | 14                                         | 13                                          |
| ≥2                      | 60  | 18                                         | 22                                          |
| Education status (p)    |     | 0.41                                       | 0.57                                        |
| Low                     | 41  | 15                                         | 13                                          |
| High*                   | 59  | 17                                         | 22                                          |
| Occupation (p)          |     | 0.63                                       | 0.48                                        |
| Working                 | 41  | 12                                         | 16                                          |
| Not working             | 59  | 20                                         | 19                                          |
| Income (p)              |     | 0.99                                       | 0.19                                        |
| Low+Normal              | 72  | 23                                         | 28                                          |
| High                    | 28  | 9                                          | 7                                           |
| Born place (p)          |     | 0.88                                       | 0.93                                        |
| Rural                   | 48  | 15                                         | 17                                          |
| Urban                   | 52  | 17                                         | 18                                          |
| Living place (p)        |     | 0.19                                       | 0.11                                        |
| Rural                   | 15  | 7                                          | 8                                           |
| Urban                   | 85  | 25                                         | 27                                          |
| Stage of disease        |     | 0.73                                       | 0.02                                        |
| Early                   | 32  | 11                                         | 8                                           |
| Advanced**              | 68  | 21                                         | 29                                          |
| Stage of disease (p)    |     | 0.04                                       | 0.05                                        |
| Nonmetastatic           | 73  | 19                                         | 14                                          |
| Metastatic              | 27  | 13                                         | 10                                          |
| Type of patient (p)     |     | 0.12                                       | 0.42                                        |
| On new admission        | 36  | 8                                          | 7                                           |
| On follow-up            | 64  | 24                                         | 17                                          |

*, includes high school and university; **, includes stages III and IV

* had advanced disease (n=68). We found dramatically increased levels of anxiety and depression in patients after the diagnosis compared to before the diagnosis. This finding was expected and well correlated with literature data. After the diagnosis, 24 participants were clinically anxious and 8 were diagnosed with borderline anxiety. Similarly, after the melanoma diagnosis 15 patients were classified as clinically depressive and 20 patients had borderline depression. Both these scores regarding anxiety and depression were significantly higher than those brought up in other trials. We believe that this is the result of the fact that the majority of the patients had advanced diseases. As expectedly, both statuses of the mood disorders in melanoma patients were significantly correlated with each other. When we studied the relationships between potential socio-demographic/disease related variables and anxiety/depression status in melanoma patients, exclusively patients with advanced disease were significantly more anxious and depressive than early-disease patients. No effect of disease duration (new diagnosis versus on follow-up) on psychological scores was found. Likewise, none of the other socio-demographic parameters was found to be correlated with anxiety and depression status.
In conclusion, a large group of Turkish melanoma patients, nearly one third of the cohort, suffered from relevant anxiety and depression. Since the anxiety and depression scores were found significantly high, we suggest that the melanoma patients be provided with the psychological support and pharmacological intervention immediately once the diagnosis is made. The small sample size and using only one psychometric instrument could be considered as major limitations and might have influenced the results. We believe that our study will be a contribution to the literature, because to the best of our knowledge this is one of the preliminary articles in which a group of melanoma patients with all stages, especially advanced stage, was analyzed in terms of their anxiety and depression statuses. Further studies with larger patient populations are necessary to determine the extent of mood disorders in melanoma and their potential clinical significances for the disease.

Conflict of Interest Statement
None

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