The Association Between Stress Level and Laboratory Parameters, Sex, Age and Stage Disease in Patients with Digestive and Bronchopulmonary Neoplasms

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We conducted a prospective study to determine whether there is a possible correlation between stress level and age, sex, cancer site, disease stage and to explore whether stress level changed during each visit. Patients diagnosed with digestive or bronchopulmonary neoplasms over a period of 6 months were included in our study. The level of stress for each patient was investigated using a questionnaire developed by an authorized psychiatrist. The questionnaire comprised 10 items and the score for each component ranged from 0 to 3, a higher score indicating a higher level of stress. For the purpose of this study, a score > 20 indicated a high level of stress. Each patient included in our study completed the questionnaire during three consecutive visits in our department. Our study revealed a statistically significant association between age and stress level, whereas no correlation was found between stress level and laboratory parameters, tumor site and disease stage.

Keywords: stress level, digestive neoplasm, bronchopulmonary neoplasm

Cancer is considered one of the major causes of death and its incidence is expected to increase in the future, despite the reduction in cancer mortality worldwide [1]. Along with the improvement of outcomes and survival rates following diagnosis, patients must face the effects of the cancer treatment which may vary from short-term adverse reactions to serious complications that greatly influence the patients' quality of life (QoL) [2]. A diagnosis of cancer is often associated with anxiety, pessimism and depression, as patients have to confront the illness[3, 4]. The quality of life represents a major factor of evaluation in chronic disease, particularly in cancer. Quality of life is broadly defined as an individual's perception and is influenced, among other, by the person's physical health, psychological state and level of independence[5]. In addition to the symptoms of the illness, patients experience complex issues that can harm their mental state [6]. The most significant predictors for stress are considered to be fatigue, worse role functioning, social functioning, financial problems [7], worry, nervousness, and sleep difficulties [6]. Such factors can potentially influence treatment adherence and survival rates. Alarmingly, it is estimated that one in four patients is depressed, with odds of depression among cancer patients more than five times higher than in the general population [8]. Furthermore, the risk of psychiatric distress is approximately twice higher among cancer patients, older age groups being less susceptiblethan young ages. No definitive correlation was found between anxiety, depression and tumor stage[9]. Furthermore,changes in biological parameters are usually related to poor prognosis in certain diseases[10, 11], these leading to high level of stress in those patients. Cancer-related fatigue is a frequent aspect in cancer, interfering with patients' life activities. Anemia is present in a large number of fatigued patients.Anaemia is one of the most important causes of fatigue in cancer patients. It is usually diagnosed based on various clinical signs and low haemoglobin levels. Anaemia is caused by aggressive therapy or it can be related to the advanced stages of the disease [12].

Nowadays, innovative treatment regimens offer patients superior outcomes and grant the opportunity to focus on ensuring a better quality of life[13]. In this study we aim to correlate the level of stress in cancer patients with age, gender, tumor stage, and laboratory parameters(creatinine level and complete blood cells count) for a better understanding of the physical and psychological aspects of this pathology.

Experimental part

Participants and methods

Patients diagnosed with digestive or broncho-pulmonary neoplasms, and consecutively referred to the Department of Medical Oncology at Oncolab Craiova over a period of 6 months (between January 1 and June 30 2017), were

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included in our study. Inclusion criteria were age >18 years, a confirmed diagnosis of digestive or lung cancer, and performance status (Eastern Cooperative Oncology Group) score 0–2. Patients with mental disorders or chronic fatigue syndrome were excluded.

The level of stress for each patient was investigated using a questionnairedeveloped by an authorized psychiatrist. The questionnaire comprised 10 items and the score for each component ranged from 0 to 3, a higher score indicating a higher level of stress. For the purpose of this study, a score > 20 indicated a high level of stress.

Each patient included in our study completed the questionnaire during three consecutive visits in our department. Informed consent was obtained prior to the initial assessment.

For each patient the following information was recorded: baseline characteristics such as age and sex, diagnosis, cancer site and disease stage. Laboratory parameters (complete blood cells count and creatinine level) and score of stress questionnaire were recorded during each of the three visits.

The aim of our study was to investigate possible correlations between stress level and age, sex, cancer site, disease stage and to explore whether stress level changed during each visit.

Statistical analysis

The analysis was performed with descriptive statistics – mean, relative frequency, std. deviation – Repeated-measures designs (GLM), Mixed design ANOVA (GLM), and Generalized Estimating Equations (GEE) model. Stress level according to visits was analysed with Repeated-measures designs (GLM). Stress level according to visits was analysed regarding sex, and tumor types with Mixed design ANOVA (GLM). Association between the stress level and different kind of factors-age, tumor stage, haemoglobin, leukocyte, platelet, creatinine laboratory parameters, sex, and tumor type-was examined with Generalized Estimating Equations model (GEE). A two-sided p value of < 0.05 was regarded as statistically significant. The available-case analysis was applied for handling missing data. Statistical analyses were performed with IBM SPSS Statistics software version 24.0 (SPSS Inc., Chicago, IL, USA).

Results and discussions

Participants

Sixty-seven patients who fulfilled the inclusion criteria and did not meet any exclusion criteria were included in the study after signing the informed consent.The majority of the participants were men (53 men vs 14 women). The mean age of the study population was 63.88 ± 9.88 SD years (range: 42-88). Among the included patients 10 different tumor types were diagnosed, the most frequent diagnosis was bronhopulmonary neoplasm (34.3 %). Most of the participants had stage IV disease (44.8 %) at the time of the inclusion. The baseline characteristics of the study population are summarized in table 1.

The stress level related to each visit

Surprisingly, in our study we found that the mean stress level was the highest during the second visit and the lowest during the third visit (20.358, 95% CI 18.820 – 21.896 vs 21.045, 95% CI 19.391 – 22.699 vs 19.970, 95% CI 18.291 – 21.649). However, there was no statistically significant difference between the stress scoresregistered during each visit (p = 0.354). Summarizing all of the values, the mean score for stress level was 20.458 ± 6.643 (range: 5 – 30).

Table 1

THE BASELINE CHARACTERISTICS OF THE STUDY POPULATION. IN CASE OF 3 PATIENTS WE DID NOT HAVE DATA TO ASSESS THE STAGE. N = NUMBER OF PATIENTS, SD = STANDARD DEVIATION.

Variables	n (%) or years
Sex (man/woman), n (%)	53 (79.1) / 14 (20.9)
Age (mean ± SD), years	63.88 ± 9.88
Tumort type, n (%)	
bile duct cancer	1 (1.5)
colon cancer	13 (19.4)
esophagus cancer	2 (3)
gastric cancer	8 (11.9)
hepatocarcinoma	2 (3)
larynx cancer	1 (1.5)
lung cancer	23 (34.3)
pancreatic cancer	5 (7.5)
rectal cancer	11 (16.4)
small intestinal cancer	1 (1.5)
Stage, n (%)	
II	1 (1.5)
II/A	7 (10.5)
II/B	3 (4.5)
III	5 (7.5)
III/A	4 (6)
III/B	9 (13.4)
III/C	5 (7.5)
IV	30 (44.8)
no data	3 (4.5)
Total, n (%)	67 (100)

The dot plot on figure 1 shows the correlation between stress level and time (visits).

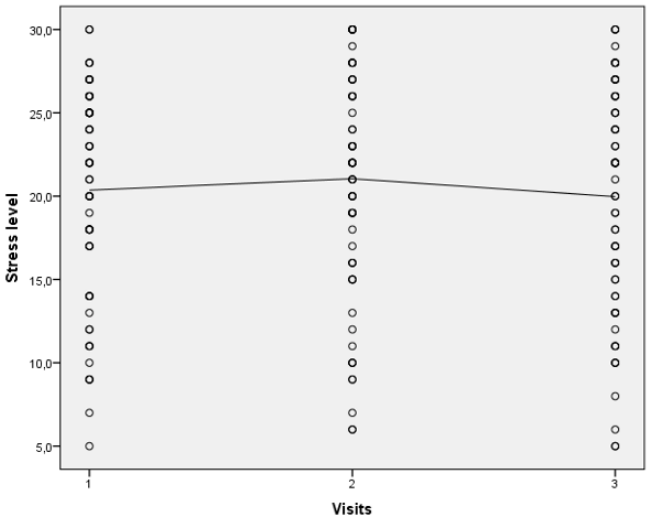

Fig. 1. The change of stress level with time. The horizontal axis represents the time (number of visits), the vertical axis represents the stress level, according to the questionnaire. Each circle shows a measure of a single patient in a given timepoint (visit). Thicker circles mean that there are more patients with the same value at the same visit. There is no statistically significant difference in stress level between the visits (p = 0.354)

Correlation between stress level and age or sex

There was a statistically significant association between stress level and age (p = 0.046). If the age increases by 1 unit (one year) the score for stress decreases by 0.119. The dot plot on figure 2shows the correlation between stress level and age.

There was no significant difference between men and women regarding stress level (p = 0.625). Table 2shows the mean scores of stress level of men and women

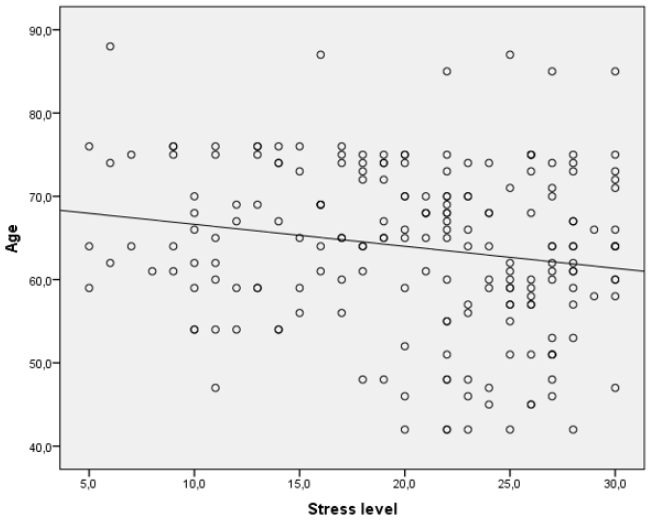

Fig. 2. The correlation between age and stress. The horizontal axis represents the stress score according to the questionnaire, the vertical axis represents the age in years. Each circle shows a measure of a single patient. Thicker circles mean that there are more measures with the same value. The stress level decreases significantly with age (p = 0.046)

Table 2

THE STRESS SCORES OF BOTH MEN AND WOMEN DURING EACH VISIT. THERE IS NO STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN THE VISITS REGARDING SEX OF THE PATIENTS (p = 0.632). SD = STANDARD DEVIATION

Number of visit	Sex	Stress level (mean)	SD	Number of patients
1	Men	20.40	6.47	53
	Women	20.21	5.84	14
	Total	20.36	6.30	67
2	Men	20.74	6.91	53
	Women	22.21	6.36	14
	Total	21.04	6.78	67
3	Men	19.72	6.94	53
	Women	20.93	6.83	14
	Total	19.97	6.88	67

measured on each visit. Figure 3 shows the association between sex and stress level.

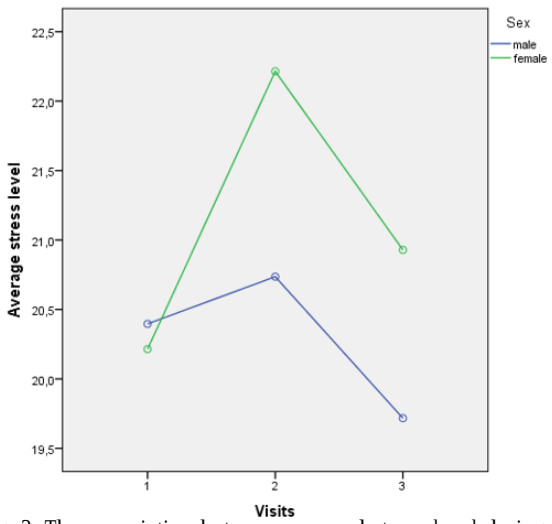

Fig. 3. The association between sex and stress level during the three visits. The horizontal axis represents the timepoint of the visits, the vertical axis represents the average stress level of men and women. There is no statistically significant difference between the visits regarding sex (p = 0.632) and there is no significant correlation between sex and stress level (p = 0.625)

The effect of tumor site and stage on the stress level

Because of the small number of cases we could not evaluate the effect of tumor site in patients with bile duct cancer (1 patient), esophagus cancer (2 patients), hepatocarcinoma (2 patients), larynx cancer (1 patient), pancreatic cancer (5 patients) and small intestinal cancer (1 patient). Regarding the remaining tumor sites we found that patients with colon cancer have lower stress level (average 3.463) than patients with other cancer sites (p = 0.046). Other analyses did not show significant correlations between tumor site and stress. Table 3 and figure 4 summarize our results regarding stress level and tumor site.

Table 3

THE DIFFERENCE IN STRESS LEVEL BETWEEN DIFFERENT TUMOR TYPES AND BETWEEN VISITS REGARDING EACH CANCER. ONLY PATIENTS WITH COLON CANCER HAVE SIGNIFICANTLY LOWER STRESS LEVEL IN COMPARISON WITH PATIENTS WITH OTHER TUMOR TYPES (p = 0.046).

Tumor type	Comparison	p-value
Colon cancer	Between visits	0.989
	Colon cancer vs other cancers	0.046
Gastric cancer	Between visits	0.163
	Gastric cancer vs other cancers	0.278
Lung cancer	Between visits	0.459
	Lung cancer vs other cancers	0.090
Rectal cancer	Between visits	0.833
	Rectal cancer vs other cancers	0.922

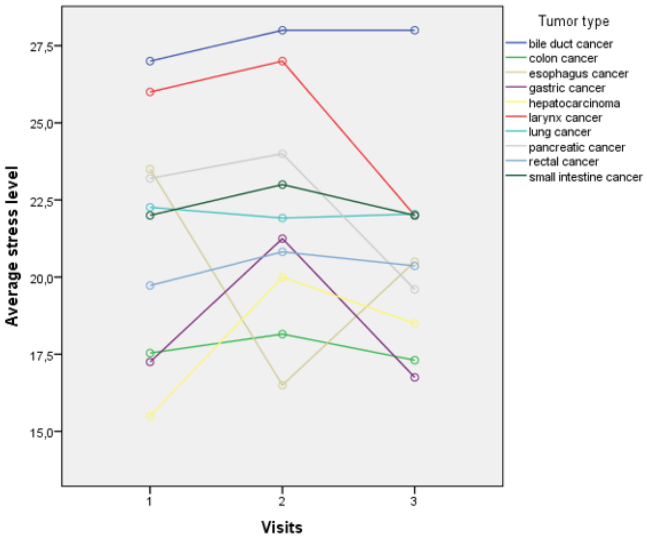

Fig. 4. The relationship between stress level and cancer types during the visits. The horizontal axis represents the timepoint of the 3 visits, the vertical one represents the average stress level

There was no significant correlation between tumor stage and stress level (p = 0.643), (fig. 5).

The association between laboratory parametres and stress level

We examined the effect of different laboratory parametres (hemoglobin, leucocyte number, platelet count, creatinine) on the stress level. The statistical analysis did not find any significant correlation between stress level and these parameters. We excluded one patient from the leucocyte analysis because the

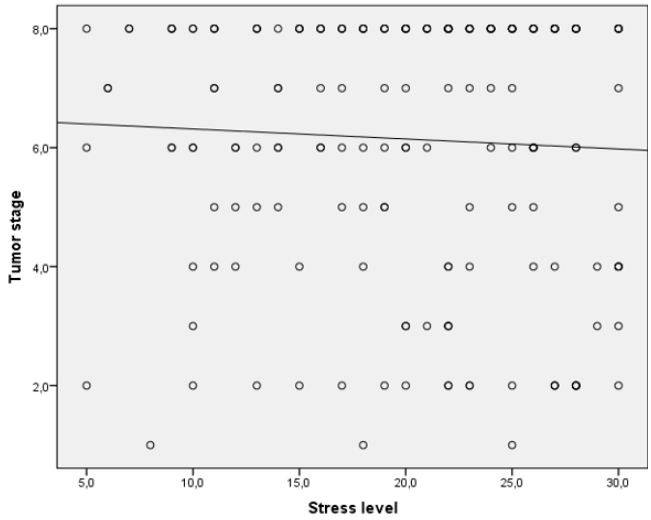

Fig. 5. The relationship between tumor stage and stress level. The horizontal axis represents the stress score according to the questionnaire, the vertical axis represents the tumor stage (1: St. II; 2: St. II/A; 3: St. II/B; 4: St. III; 5: St. III/A; 6: St.III/B; 7: St. III/C; 8: St. IV). Each circle shows a measure of a single patient. Thicker circles mean that there are more measures with the same value. There is no statistically significant correlation between tumor stage and stress level (p = 0.643)

parameter was extreme outlier. The results of the statistical analyses are summarized in table 4 and in figure 6.

In the context of the growth and aging of the population, combined with high risk factors, cancer becomes a pathology with ever increasing prevalence[14, 27-31]. As new studies emerge, the psychological component is taken into account in addition to the physical effects of the illness, as cancer does great harm to the patients' mental state, often leading to pessimism, anxiety and depression [3] As a result, psychological distress is regarded as the *sixth vital sign* for cancer patients, as well as an important predictor of QoL[15].

In this study we aim cu correlate psychological distress in cancer patients with age, gender, tumor stage, and laboratory tests. First of all, age is one of the predictors or correlations explored when evaluating both psychological and physical aspects of a certain pathology. Furthermore, age is widely regarded as a potential risk factor for distress, depression, and anxiety (DDA), especially in adolescents and young adults (AYA) [16]. National Cancer Institute defines the term as age 15-39 years. A recent study aims to identify a pattern for such results, stating that AYA experience difficulties with identity development, emotional relationships, making independent decisions, and body image [17]. In addition, younger patients report higher levels of pain, fatigue, drowsiness, depression, and anxiety than older patients [18]. On the other hand, the QoL in elder people is strongly influenced by their resilience[19], which is defined as a common response to losses and conditions of severe stress during the lifecycle as well as declining health [20]. Similar research showed that younger patients are more likely to be distressed and in need for additional care as compared to patients over 65 years of age [21]. Our study supports these findings, revealing a significant relationship between age and stress level (p=0.046), as age increases by 1 unit (one year) the stress level decreases by 0.119.

Patients' concerns, both physical and psychosocial, provide a better understanding of the patterns of distress, especially when evaluated over a period of time. After examining these aspects over the year following diagnosis, a recent study shows that levels of DDA generally decreased, although approximately a third of the patients maintained clinical levels of distress. This suggests that certain patients experience anxiety, distress, and depression in a transient manner, while others experience them continuously [22]. Our data, retained over 3

Table 4

THE EFFECT OF LABORATORY FINDINGS ON THE STRESS LEVEL. NONE OF THE ABOVE MENTIONED PARAMETERS HAS A SIGNIFICANT EFFECT ON STRESS LEVEL OF THE PATIENTS. n = NUMBER OF AVAILABLE DATA.

Laboratory parameters	Data available (n / all measures)	p-value
Hemoglobin	200 / 201	0.196
Leucocyte number	199 / 201	0.112
Platelet count	200 / 201	0.058
Creatinine	176 /201	0.597

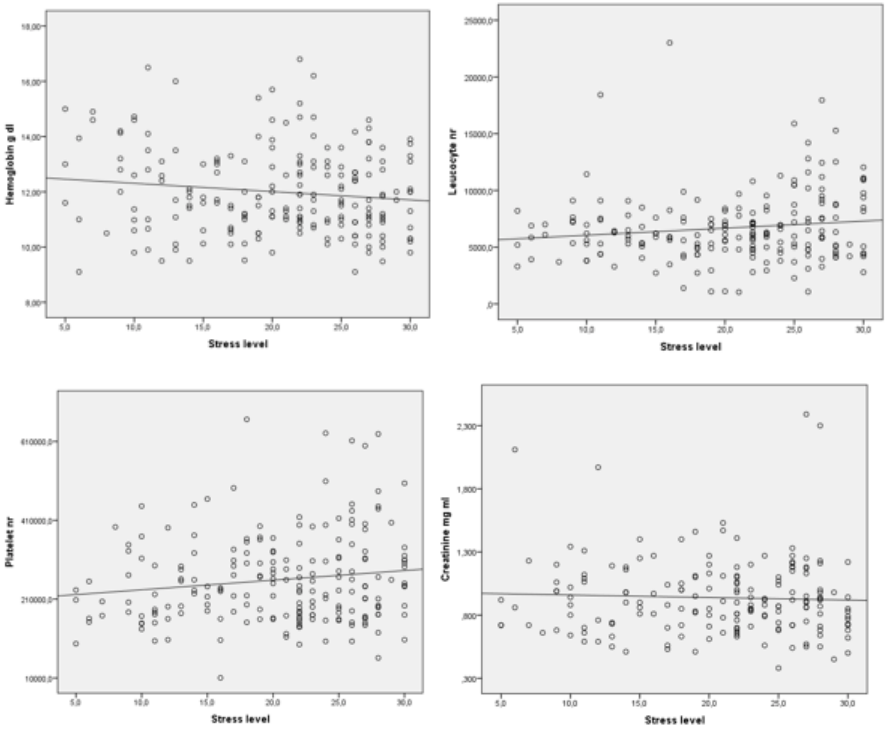

Fig.6. The relationship between laboratory findings and stress level. There is no significant correlation between the above mentioned parameters and stress level.

consecutive hospital admissions, showed no significant difference between scores regarding stress levels ($p=0.354$).

Similarly, no correlation was observed between tumor stage and stress levels ($p=0.643$), or between other laboratory testsand patients' psychological distress. Research shows significant association between hemoglobin levels and fatigue, the latter being linked to depression and anxiety [12] and treatment of cancer-related anemia can lead to higher energy levels, which in turn suggests an improvement of QoL[23]. While the likelihood to score higher distress levels is greater among patients with advanced cancer, phenomena partially explained by the fact that they suffer from more severe physical symptoms [24], other studies conclude that demoralization and depressive symptoms are unrelated to tumor stage (UICC stages 0–II vs III/IV) [25], and performance status [26].

Conclusions

Our study revealed a statistically significant association between age and stress level, whereas no correlation was found between stress level and laboratory parameters, tumor site and disease stage. Although the values of laboratory parameters can offer valuable information regarding the prognosis and management for each patient, our results showed that they have no impact on the psychological stress related to the disease.

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