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UDC: 616-006.81-06:616.89-008
https://doi.org/10.2298/VSP180414185V

Depression, anxiety and quality of life in patients with melanoma

Depresija, anksioznost i kvalitet života kod bolesnika sa melanomom

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Abstract

Background/Aim. Recent investigations have established a significant correlation between melanoma and quality of life, as well as anxiety and depression in these patients. In prognosis of melanoma, the most important is the stage in which it is diagnosed. The objective of the study was to analyze the quality of life, anxiety and depression in patients with a diagnosis of melanoma at different stages of the disease. **Methods.** In our cross-sectional study, 40 consecutive patients with melanoma, diagnosed and treated at the Department of Dermatology and Venerology, Military Medical Academy in Belgrade during the period from October to November 2015, were included. Twenty respondents were in stages I and II (localized disease) and 20 respondents in the stage IV (distant metastases). We used European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (EORTC QLQ 30), Beck anxiety inventory (BAI) and Beck depression inventory (BDI). The statistical analysis included parametric and non-parametric descriptive statistics. **Results.** In patients with stages I and II of the disease, anxiety scores were higher in comparison to those in patients with the stage IV (37.5 vs. 14.5, respectively; $p < 0.05$), but depression was more pronounced (6 vs. 2.5, respectively; $p < 0.05$) in patients with the IV stage of the disease. There were statistically significant differences in all segments of quality of life between patients with stages I and II and those with the stage IV of the disease. The global quality of life was significantly worse in patients with the IV stage (33.5 vs. 83), the symptomatology was more pronounced (78.5 vs. 0) and the functioning was significantly worse (31 vs. 85) in relation to patients with stages I and II ($p < 0.01$) for all segments of quality of life. **Conclusion.** Anxiety and quality of life decrease, while depression increases with melanoma stages. The need for adequate social and family support as well as psychological assistance in order to achieve better coping with the illness are necessary in patients with melanoma. Further studies are needed for monitoring of anxiety, depression and quality of life from the moment of diagnosis of the disease over time, as well as the impact of new treatment modalities on these parameters.

Key words:
melanoma; quality of life; depression; anxiety; surveys and questionnaires.

Apstrakt

Uvod/Cilj. Nedavna istraživanja pokazala su značajnu korelaciju između melanoma i kvaliteta života, kao i anksioznosti i depresije kod ovih bolesnika. U prognozi melanoma, najvažnija je faza u kojoj je dijagnostikovan. Cilj ove studije bila je analiza kvaliteta života, anksioznosti i depresije kod bolesnika sa dijagnozom melanoma u različitim stadijumima bolesti. **Metode.** U našoj studiji preseka su bili uključeni bolesnici dijagnostikovani i lečeni od melanoma (n = 40) na Klinici za kožne i polne bolesti Vojnomedicinske akademije u Beogradu od oktobra do decembra 2015. godine. Dvadeset bolesnika bilo je u I i II stadijumu (lokalizovana bolest), a preostalih 20 u IV fazi (udaljene metastaze). U istraživanju smo koristili Upitnik za procenu kvaliteta života obolelih od melanoma Evropskog udruženja za istraživanje i terapiju kancera (EORTC QLQ 30), Bekov upitnik o anksioznosti (BAI) i Bekov upitnik o depresiji (BDI). Statistička analiza uključila je parametarsku i neparametarsku opisnu statistiku. **Rezultati.** Kod bolesnika u I i II stadijumu bolesti anksioznost je bila veća u poređenju sa bolesnicima u IV stadijumu bolesti (37,5 naspram 14,5; $p < 0,05$), ali je depresija bila izraženija (6 naspram 2,5; $p < 0,05$) kod bolesnika u IV stadijumu. Nađene su statistički značajne razlike u svim segmentima kvaliteta života između bolesnika koji su bili u I i II stadijumu i bolesnika u IV stadijumu bolesti. Ukupan kvalitet života značajno je bio lošiji kod bolesnika u IV stadijumu (33,5 naspram 83), simptomatologija izraženija (78,5 naspram 0), a funkcionisanje značajno lošije (31 naspram 85) u odnosu na bolesnike u I i II stadijumu ($p < 0.01$) za sve segmente kvaliteta života. **Zaključak.**

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Anksioznost i kvalitet života opadaju, dok simptomi depresije rastu sa stadijumom napredovanja melanoma. Potreba za adekvatnom socijalnom i porodičnom podrškom, kao i psihološku pomoć neophodna je kod bolesnika sa melanomom, kako bi se što bolje podnela bolest. Dodatna istraživanja su potrebna za praćenje anksioznosti, depresije i kvaliteta života od trenutka dijagnoze bolesti tokom vremena, kao i uticaja novih modaliteta lečenja na sve ove parametre.

Ključne reči:
Melanoma; kvalitet života; depresija; anksioznost; ankete i upitnici.

Introduction

The incidence of melanoma is increasing worldwide, especially in fair-skinned over-exposed white population. Incidence rate of melanoma in Europe is currently 10–25 *per* 100,000 inhabitants. The incidence is continually increasing at all ages and it is predicted that this trend will further continue. The most significant increase in incidence was detected in men over the age of 60 [1, 2].

In prognosis of melanoma, the most important is the stage in which it is diagnosed. If diagnosed occurred at an early stage, at the stage I, the five-year survival rate is 97% for the Ia and 92% for the Ib stage. In the IIa stage, the five-year survival rate is 81% and in the IIc stage 53%, while in the IV stage, it is low – 15% [3].

In recent years, due to important aspect of cancer research, new forms of biological therapy were implemented which have increased survival of patients with melanoma. However, it is not just about the length of life, but also about the quality of life (QoL) of patients with melanoma. There are a few studies dealing with the evaluation of the long-term effect of melanoma on the quality of life and the psychic status of patients with melanoma. In the study carried out in the Netherlands, it was shown that the quality of life of patients with melanoma was not significantly different from the quality of life of the general population [4–6].

According to some studies, about 30% of patients with melanoma suffered from significant distress, especially women and youth. Depression is growing with stages of melanoma and it is higher (approximately about 18–44%) in later stages the disease. The highest level of anxiety is registered in the period of diagnosis and later decreases [7–10].

The aim of this study was to analyze the quality of life, anxiety and depression of patients with melanoma at different stages of the disease.

Methods

A cross-sectional study was conducted in 40 consecutive patients diagnosed with melanoma and treated at the Department of Dermatology and Venerology, Military Medical Academy in Belgrade, during the two-month period, from October to November 2015. Although about 140 patients with melanoma on the average have been hospitalized at our Department of Dermatology and Venerology every year, only patients who were diagnosed and treated during the period when the study was conducted were included. Only patients who volunteered to participate in our study were included and all of them signed an informed consent. The research was approved by the Ethics Committee of the Military Medical Academy in Belgrade and it was carried out according to all the regulations of the Helsinki Declaration. Patients were divided into two groups: the first group consisted of 20 patients in stages I and II (localized disease) melanoma and the second group consisted of 20 patients in the stage IV melanoma (with distant metastases).

Psychological instruments

Assessing of QoL has been done using the validated cancer-specific questionnaire – the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionairre C30. The EORTC QLQ-C30 is a patient self-rating questionnaire consisting of three symptom scales (fatigue, nausea/vomiting, pain), five function scales (physical, role, social, emotional, cognitive functions), and five single items assessing symptoms such as dyspnoea, insomnia, appetite loss, constipation and diarrhea. Basing on those scores we could calculate a global health status/QoL score. All scores of the QLQ-C30 were transformed linearly so that all scales vary from 0 to 100 in a row with the EORTC scoring manual. Patients gave their answers ranked on a 4-point scale (from 1 in general to "4" very much), barring the GH/QoL scale of the EORTC QLQ-C30, which has a 7-point scale (from 1 “very poor” to 7 “excellent”). A linear transformation was used to standardize the raw score, so that overall scores ranged from 0 to 100. For the EORTC QLQ-C30, a higher score in GH/QoL or a functioning scale represents a better level of quality of life and functioning; a higher score in a symptom scale represents a worse level of symptoms [11]. Previously, the licenses for the use of the questionnaire by the EORTC were set out.

The Beck Anxiety Inventory (BAI) is an inventory for self-assessment of the severity of various symptoms related to anxiety in terms of how he felt last week. The BAI contains 21 multiple-choice items [12]. The scale is intended for people over the age of 17 years. For each symptom, four options are offered, and the respondent should choose the one that best describes his condition. The response options are from not at all over mild and moderate to severe. The minimum score is 0, and the maximum score is 63. It is considered that the score above 10 at the BAI

indicates a mild anxiety, the score above 19 shows moderate anxiety and the score above 30 indicates severe anxiety.

The Beck Depression Inventory (BDI), is one of the most appropriate psychometric tests for measuring the severity of depression. The BDI consists of 21 questions for self-reported disability. It shows high levels of internal consistency (alpha coefficient) ranging from 0.73 to 0.95 in psychiatric populations, as has been confirmed so far in many studies [12–14]. The BDI measures the general depression syndrome consisting of three correlated subcars, while for each question and statement, a response of 0 (neutral) to 3 (the most difficult) can be given. Summing the items yields a total score ranging from 0 to 63 [12]. It is considered that the score above 10 indicates a mild depression, the score above 19 shows moderate depression, and the score above 30 indicates a serious depression [13, 14].

Statistical analysis

Statistical analysis included parametric and non-parametric descriptive statistics, depending on the nature of data. Data analysis was carried out using IBM SPSS (Statistical Package for the Social Sciences) software version 20.0. For the normal distribution of all numerical parameters and scores, Kolmogorov-Smirnov test was used. We got the results showing that in all monitored and calculated parameters and scores there was normal distribution (z was less than 1.96, and $p < 0.05$), so that it was possible to apply parametric methods in further analysis.

Results

The average age of the patients in the first group was 54.8 ± 13.76 years and 62.85 ± 11.47 in the second group ($p > 0.05$). Men were also dominated by both groups (60% in the first and 70% in the second group). The presence of some chronic somatic diseases such as hypertension, diabetes, hyperlipidemia and the like, reported 35% patients in the first group and 50% patients in the second group. There were no statistically significant differences between groups in age, gender and presence of chronic somatic diseases (Table 1). In patients with stages I and II melanoma, anxiety scores were higher in comparison to those in the stage IV disease patients (37.5 vs. 14.5, respectively; $p < 0.05$), but depressive symptoms were more pronounced in the IV stage patients (2.5 vs. 6, respectively; $p < 0.05$) (Table 2).

Table 1

Demographic data of the patients with melanoma

Variables	I and II stages (localized disease)	IV stage (distant metastases)	*p*
Age (years), mean ± SD	54.65 ± 13.76	62.85 ± 11.48	ns
Gender (male), %	60	70	ns
Chronic somatic diseases (presence), %	35	50	ns

SD – standard deviation; ns – non significant.

There were statistically significant differences in all segments of QoL between patients that were in stages I and II melanoma and patients in the IV stage melanoma. The global QoL was significantly worse in patients in the stage IV (33.5 vs. 83), the symptomatology was more pronounced (78.5 vs. 0) and the functioning was significantly worse (31 vs. 85) in relation to patients with stages I and II melanoma ($p < 0.01$ for all segments of QoL) (Table 2).

Discussion

Recent investigations have established a significant correlation between melanoma stages and QoL, as well as anxiety and depression symptoms in these patients. Although some researchers were studying the stages of melanoma, anxiety and depression, the QoL of melanoma patients in our country were not analyzed.

In our investigation, we found that patients with stages I and II melanoma (localized disease) had a severe level of anxiety unlike patients with the IV stage of the disease (distant metastases) who had mild anxiety. Our results are in accordance with other investigations. When a patient faces the diagnosis of melanoma, his/her knowledge of malignant disease and its unpredictable prognosis, even when the disease is detected at an early stage, has the consequence of the appearance of fear, anxiety and insecurity. Intensive regular follow-up procedures with radiological and laboratory exams during the first three years can contribute to increase in anxiety. Many studies have shown that anxiety is higher in earlier melanoma stages and that it later slowly decreases. Adaptation to the diagnosis of melanoma and coping with the diagnosis, dealing with various treatment modalities, with or without support of his/her family, friends and social environment, greatly influences the anxiety in later stages of the disease, too [15–19].

Table 2

EORTC QLQ C30, BDI and BAI in the melanoma patients

Questionnaire	Stages I and II (localized disease)	Stage IV (distant metastases)	*p*
BAI score, mean	37.5	14.5	0.05
BDI score, mean	2.5	6	0.05
EORTC-QLQ C30 (Global QoL) score, mean	83	33.5	0.01
symptomatology	0	78.5	0.01
functioning	85	31	0.01

EORTC-QLQ C30 – European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionary C30; BAI – Beck Anxiety Inventory; BDI – Beck Depression Inventory; QoL – Quality of Life.

Depressive symptoms occur very rarely in earlier stages of melanoma, but, as the time passes. the patients become aware of the inevitability of the outcome of the disease, regardless to the exhaustion of various modalities of treatment, exhaustion of the disease itself, progression of the disease and depressive symptoms slowly appear. Depression symptoms are in a certain extent present in most melanoma patients at stage IV of the disease, but in minimal level, and the level of depression symptoms is significantly higher than in respondents in stages I and II melanoma. Our results are in accordance with other studies, which also found that depression symptoms occur in later stages of the disease [19–21].

The global QoL, measured by the EORTC C30 questionnaire, showed a very low level in the IV stage melanoma patients. In the IV stage melanoma (distant metastases), the global QoL depends on the type of applied therapy, its side effects and the prevalence and localization of metastases. Our results are in accordance with other studies where the global QoL is low in the IV stagemelanoma patients, too [22–24]. The low level of global QoL in the IV stage melanoma patients was more than twice lower than in stages I and II of the disease. We could explain our results with the fact that the overall global QoL is decreasing during the time, because of the progression of the malignant disease that affects the complication of everyday functioning, including some financial difficulties and symptomatology, considered primarily fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhea, etc. [24–29]. The data obtained in our study are in accordance with the data obtained in other surveys that support the declining functioning of melanoma patients as well as their global QoL as the symptomology grows [30–32].

In our investigation, we found that in stages I and II of the disease, severe level of anxiety was result of uncertainty and fear of the disease expansion which patients were faced for the first time. In these stages of melanoma, there was not influence on the QoL which stayed uncompromised and high, including low level of depressive symptoms. With progression of melanoma, situation was drastically changed. When metastasis already occurred, anxiety fell down because patients have been yet accepted the disease itself and the current condition. Depressive symptoms slowly increased from the stage I and II to stage IV because patients slowly became aware of the progression and inevitability of the outcome of the disease. In addition, in the stage IV melanoma, functioning in all segments including physical, emotional, cognitive and social functioning was compromised, which also affected the increase of depressive symptoms.

Our findings are very important in clinical practice, because they could help in planning the psychological and psychiatric support in every melanoma stage.

Limitation of the study

The group of 40 patients included in our cross-sectional study was small, and requires further investigations. Further investigation should be focused on determining gender differences in the quality of life, depression and anxiety in patients with different melanoma stages.

Conclusion

The results of our research show that anxiety is highest in the period of melanoma diagnosing and subsequently decreases, while depressive symptoms are more pronounced in later stages. Also, the quality of life of patients with melanoma is significantly worse in the stage IV stage than in the first two stages. Because of that, the need for adequate social and family support as well as psychological help in order to achieve better coping with illness are necessary. Learning techniques to overcome fear and stress would help in better functioning of all affected, regardless of the stage of the disease. The most severe cases of anxiety and depression, in addition to psychotherapeutic interventions, should also be considered for pharmacotherapy. The need for a multidisciplinary team that would be involved in monitoring patients from the moment of the establishing the diagnosis of melanoma is of exceptional importance and includes a dermatologist, surgeon, radiotherapist, neurologist, as well as psychotherapist.

R E F E R E N C E S

1. *Tran AD, Fogarty G, Nowak AK, Espinoza D, Rowbotham N, Stockler MR*, et al. A systematic review and meta-analysis of utility estimates in melanoma. Br J Dermatol 2018; 178(2): 384–93.
2. *Malkhasyan KA, Zakharia Y, Milhem M.* Quality of life outcomes in patients with advanced melanoma: a review of the literature. Pigment Cell Melanoma Res 2017; 30(6): 511–20.
3. *Garbe C, Peris K, Hauschild A, Saiag P, Middleton M, Bastholt L,* et al. European Dermatology Forum (EDF); European Association of Dermato-Oncology (EADO); European Organisation for Research and Treatment of Cancer (EORTC). Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline - Update 2016. Eur J Cancer 2016; 63: 201–17.
4. *Arnold M, Holterhues C, Hollestein LM, Coebergh JW, Nijsten T, Pukkala E,* et al. Trends in incidence and prediction of cutaneous melanoma across Europe up to 2015. J Eur Acad Dermatol Venereol 2014; 28(9): 1170–8.
5. *Rodríguez-Cerdeira C, Molares-Vila A, Carnero-Gregorio M, Corbalán-Rivas A.* Recent advances in melanoma research via "omics" platforms. J Proteomics 2018; 188: 152–66.
6. *Rat C, Hild S, Gaultier A, Khammari A, Bonnaud-Antignac A, Quereux G*, et al. Anxiety, locus of control and sociodemographic factors associated with adherence to an annual clinical skin monitoring: a cross sectional survey among 1000

high- risk French patients involvedin a pilot-targeted screening programme for melanoma. BMJ Open 2017; 7(10): e016071.
7. *Hamama-Raz Y.* Does psychological adjustment of melanoma survivors differs between genders? Psychooncology 2012; 21(3): 255–63.
8. *Schuermeyer I, Maican A, Sharp R, Bena J, Triozzi PL, Singh AD.* Depression, anxiety, and regret before and after testing to estimate uveal melanoma prognosis. JAMA Ophthalmol 2016; 134(1): 51–6.
9. *Fischbeck S, Imruck BH, Blettner M, Weyer V, Binder H, Zeissig SR,* et al. Psychosocial care needs of melanoma survivors: are they being met? PLoS One 2015; 10(8): e0132754.
10. *Beutel ME, Fischbeck S, Binder H, Blettner M, Brähler E, Emrich K,* et al. Depression, anxiety and quality of life in long-term survivors of malignant melanoma: a register-based cohort study. PLoS One 2015; 10(1): e0116440.
11. *Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A.* The EORTC QLQ-C30 scoring manual. 3rd ed. Belgium, Brussels: European Organization for Research and Treatment of Cancer; 2001.
12. *Beck AT, Epstein N, Brown G, Steer RA.* An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988; 56(6): 893–7.
13. *Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J.* An inventory for measuring depression. Arch. Gen. Psychiatry 1961; 4: 561–7.
14. *Beck AT, Steer RA, Garbin MG.* Psychometric properties of the Beck Depression Inventory Twenty-five years of evaluation. Clin Psychol Rev 1988; 8(1): 77–100.
15. *Pflugfelder A, Kochs C, Blum A, Capellaro M, Czeschik C, Dettenborn T,* et al. German Dermatological Society; Dermatologic Cooperative Oncology Group. Malignant melanoma S3-guideline "diagnosis, therapy and follow-up of melanoma". J Dtsch Dermatol Ges 2013; 11(Suppl 6): 1–116, 1–126. (English, German)
16. *Mayer S, Teufel M, Schaeffeler N, Keim U, Garbe C, Eigentler TK,* et al. The need for psycho-oncological support for melanoma patients: Central role of patients' self-evaluation. Medicine (Baltimore) 2017; 96(37): e7987.
17. *Bonnaud-Antignac A, Bourdon M, Dréno B, Quéreux G.* Coping strategies at the time of diagnosis and quality of life 2 years later: a study in primary cutaneous melanoma patients. Cancer Nurs 2017; 40(1): E45–E53.
18. *Holterhues C, Cornish D, van de Poll-Franse LV, Krekels G, Koedijk F, Kuijpers D,* et al. Impact of melanoma on patients' lives among 562 survivors: a Dutch population-based study. Arch Dermatol 2011; 147(2): 177–85.
19. *Hamama-Raz Y, Solomon Z, Schachter J, Azizi E.* Objective and subjective stressors and the psychological adjustment of melanoma survivors. Psychooncology 2007; 16(4): 287–94.
20. *Mendis S, Davis S, Norrving B.* Organizational update: the world health organization global status report on noncommunicable diseases 2014; one more landmark step in the combat against stroke and vascular disease. Stroke 2015; 46(5): e121–2.
21. *Albrecht K, Droll H, Giesler JM, Nashan D, Meiss F, Reuter K.* Self-efficacy for coping with cancer in melanoma patients: its association with physical fatigue and depression. Psychooncology 2013; 22(9): 1972–8.
22. *Vogel RI, Strayer LG, Ahmed RL, Blaes A, Lazovich D.* A Qualitative Study of Quality of Life Concerns following a Melanoma Diagnosis. J Skin Cancer 2017; 2017: 2041872.
23. *Dubravčić ID, Brozić JM, Aljinović A, Sindik J.* Quality of life in Croatian metastatic melanoma patients. Coll Antropol 2014; 38(1): 69–74.
24. *Nowe E, Stöbel-Richter Y, Sender A, Leuteritz K, Friedrich M, Geue K.* Review article: cancer-related fatigue in adolescents and young adults: a systematic review of the literature. Crit Rev Oncol Hematol 2017; 118: 63–9.
25. *Hinz A, Singer S, Brähler E.* European reference values for the quality of life questionnaire EORTC QLQ-C30: Results of a German investigation and a summarizing analysis of six European general population normative studies. Acta Oncol 2014; 53(7): 958–65.
26. *Hamel JF, Pe M, Coens C, Martinelli F, Eggermont AM, Brandberg Y, Bottomley A.* A systematic review examining factors influencing health related quality of life among melanomacancer survivors. Eur J Cancer 2016; 69: 189–98.
27. *Fischbeck S, Imruck BH, Blettner M, Weyer V, Binder H, Zeissig SR,* at al. Psychosocial care needs of melanoma survivors: are they being met? PLoS One 2015; 10(8): e0132754.
28. *Palesh O, Aldridge-Gerry A, Bugos K, Pickham D, Chen JJ, Greco R,* et al. Health behaviors and needs of melanoma survivors. Support Care Cancer 2014; 22(11): 2973–80.
29. *Mehnert A, Koch U.* Psychological comorbidity and health-related quality of life and its association with awareness, utilization, and need for psychosocial support in a cancer register-based sample of long-term breast cancer survivors. J Psychosom Res 2008; 64(4): 383–91.
30. *Tas F, Karabulut S, Guveli H, Kurul S, Erturk K, Guveli M*, et al. Assessment of anxiety and depression status in Turkish cutaneous melanoma patients. Asian Pac J Cancer Prev 2017; 18(2): 369–73.
31. *Tesio V, Ribero S, Castelli L, Bassino S, Leombruni P, Caliendo V,* et al. Psychological characteristics of early-stage melanoma patients: a cross-sectional study on 204 patients. Melanoma Res 2017; 27(3): 277–80.
32. *Pereira MG, Ponte M, Ferreira G, Machado JC.* Quality of life in patients with skin tumors: the mediator role of body image and social support. Psychooncology 2017; 26(6): 815–21.

Received on April 14, 2018.
Revised on October 29, 2018.
Accepted on November 6, 2018.
Online First November, 2018.