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Comparison of patient-reported need of psycho-oncologic support and the doctor's perspective: how do they relate to disease severity in melanoma patients?

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Abstract

***Objective*: Psycho-neuro-immune research suggests an association between cancer outcomes and psychosocial distress. Objective criteria to determine patients' levels of distress are important to establish potential links to disease outcomes.**

***Methods*: We compared three patient-reported with one doctor-reported measures of psycho-oncologic distress frequently used in routine cancer care and investigated associations with standard disease severity parameters in melanoma patients. We enrolled $n = 361$ patients, successively seen at two outpatient university clinics in Germany. In the naturalistic study, $n = 222$ patients had been diagnosed <180 days and were seen for the first time (Group I); $n = 139$ had been diagnosed >180 days and were in after-care (Group II).**

***Results*: Across groups, only moderate associations were seen between patient- reported and doctor-reported measures. Regarding clinical variables, disease severity and perceived need of psycho-oncologic support reported by patients or doctors showed hardly any association. After subgroup stratification, in patients of Group II, patient-reported and doctor-reported instruments showed some small associations with disease parameters commonly linked to more rapid cancer progression in patients who are in cancer after-care.**

***Conclusions*: Overall, the few and low associations suggest that need of psycho-oncologic support and clinical variables were largely independent of each other and doctors' perception may not reflect the patient's view. Therefore, the assessment of the patient perspective is indispensable to ensure that melanoma patients receive appropriate support, as such need cannot be derived from other disease parameters or proxy report. More research is needed applying psychometrically robust instruments that are ideally combined with sensitive biomarkers to disentangle psycho-neuro-immune implications in melanoma patients.**

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Background

Cancer patients frequently report high levels of stress, especially around the time of first diagnosis or when increased disease severity is revealed. Consequently, it is recommended to include the patient's perspective into clinical considerations [1–6].

While it is not unexpected that a diagnosis of cancer has an impact on psychosocial well-being, an inverse relationship seems probable as well, with various studies suggesting a range of patient-reported outcome (PRO) variables to be related to cancer incidence and progression. That is, high levels of emotional distress (e.g. high levels of depression or anxiety and overall low levels of health-related quality of life) appear as likely to be associated with deterioration as are maladaptive health behaviors and lifestyle factors (e.g. low physical activity and unhealthy diet) [3,7–11]. Other research even suggests an association between PROs and cancer recurrence in patients in after-care, such as tumor regrowth at the site of excision or occurrence of *in transit*, lymph node or distant metastasis, with consequences for survival/mortality [12–16]. A meta-analysis reported a 41% increased risk of cancer mortality after about 8 years in initially healthy study participants who had reported a low level of health-related quality of life at study enrolment [17].

In order to explore potential interactions between distress and cancer, we decided to study patients with malignant melanoma, first, because melanoma patients' needs of psycho-oncologic support are often underserved and, second, melanoma develops rapidly and its incidence is rising; hence, there is an increasing number of patients available. Also, the specific advantages of studying melanoma patients have been featured in several psycho-oncologic studies [4,6,18,19]. In addition to investigating the interaction between psychosocial variables and cancer outcomes, it is essential to reliably identify those in need of psycho-oncologic support and offer according interventions [20]. Two studies in this area, for example, investigated survival benefits for melanoma patients when engaging in psycho-oncologic support [18,19]. However, while animal experiments suggest that psychosocial strain may have causal implications in melanoma [21], this interaction remains to be established on the functional level in humans [22].

As a result, more research is needed to explore the potential impact of stress-modifying variables (e.g. sociological, societal and environmental factors, health behaviors, and psychosocial intervention) on disease pathogenesis as well as onset, severity, and progression of cancer. For this, it is essential to explore which PRO variables can reliably detect patient populations in need of psycho-oncologic support. Further, a comparison is lacking between need of support as reported by the attending physician as opposed to patients' self-report and how these relate to standard clinical outcome parameters. In this study, we set out to explore the association between patient-reported and doctor-reported perceived need of psycho-oncologic support in melanoma patients and how these variables relate to a range of clinical variables. The aim of the present study is to explore whether patients' self-reported need of psycho-oncologic support is associated with (a) the doctor's perceived need of support and/or (b) clinical variables in order to derive recommendations regarding the inclusion of patient self-report in the context of psycho-oncologic research and treatment strategies for cancer patients.

Methods

Participant recruitment

Between October 2011 and December 2013, $n = 632$ melanoma patients were seen by dermatologists at ambulatory care units of the departments of dermatology at the university hospitals of Giessen and Marburg, Germany. Recruited patients were divided into two subgroups. The first had received their melanoma diagnosis within the past 6 months and were referred to the hospital for diagnostic procedures and treatment for the first time (Group I, ≤180 days since diagnosis). The second had received their diagnosis between 6 months and 10 years prior to recruitment and were in skin cancer after-care (Group II, >180 days since diagnosis). All patients received a whole-body skin examination and were asked to fill out a range of self-report instruments described below.

Inclusion and exclusion criteria

Following pre-defined inclusion/exclusion criteria, several patients were excluded: $n = 138$ because of lack of whole-body skin examination; $n = 6$ because of missing information on tumor stage; $n = 2$ were younger than 18 years; $n = 25$ were in skin cancer after-care for longer than 10 years; and $n = 100$ had no written informed consent. Hence, a total of $n = 361$ patients (57.1%) remained for the analyses. Of these, $n = 261$ were recruited in Giessen and $n = 100$ in Marburg.

Applied instruments

Note that desire for psycho-oncologic support was not assessed in our study. Instruments employed to detect need for psycho-oncologic support were the following:

The Hornheider Screening Instrument (HSI) consists of seven items covering physical and emotional well-being, worries, social support, and perceived level of information about disease and treatment. Responses are scored from 'rather good' to 'rather bad' (scored between 0 and 2) or on a dichotomous scale (yes/no, scored 0 or 2). Items are summated (range 0 to 14). Scores ≥4 are interpreted as 'need of support' [23].

The Questionnaire on Distress in Cancer Patients-short form (QSC-R10) consists of 10 items covering pain, sleep, emotional aspects of the disease, perceived support, and information about disease and treatment. Responses are scored between 0 (does not apply), 1 (slightly agree), and 5 (strongly agree). Scores are summated (range 0 to 50). Scores of >15 are interpreted as 'need of support' [24].

The Distress Thermometer is a visual analogue scale ranging from 0 to 10, with 0 being 'not burdened at all' to 10 'extremely burdened'. Scores of ≥5 are interpreted as 'need of support' [25].

The Psycho-Oncologic Basic Documentation (PO-BaDo) consists of questions covering socio-demographic factors, details about diagnosis (location, metastases, etc.), details about treatment, and six items assessing doctors' rating of patients' psychosocial burden on a five-point scale, ranging from 0 (not at all) to 4 (very much). Scores are summated (range 0 to 24). Scores of >8 are interpreted as 'need of support' [26].

Data analyses

Demographic and clinical data were obtained from the PO-BaDo, which are presented descriptively. Differences

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between Group I versus Group II were analyzed by *t*-test statistic for independent samples or chi-square analyses. To determine correlations between patient self-report and doctor-reported need of psycho-oncologic support, the Pearson product–moment correlation coefficient was used when comparing summated scores. To determine correlations between these and clinical variables, Spearman's rank correlation coefficient was used. The following clinical variables were explored: tumor stage (categorized into three categories of severity; online only supporting information Table S1a), Breslow thickness (five categories of severity; online only supporting information Table S1a), Clark level (six categories of severity; online only supporting information Table S1a), ulceration (yes/no), positive lymph nodes (yes/no), metastases (yes/no), recurrence (yes/no), presence of further somatic symptoms (yes/no), and 'treatment during the past two months' (recoded into yes/no). Because of the categorical scaling of localization (six categories), chi-square analyses were applied to explore potential associations with psycho-oncologic need. Above variables are all part of routine patient assessment at participating clinics. All analyses were carried out in IBM SPSS Statistics 22.0®.

Results

Sample

Three hundred and sixty-one melanoma patients were included in the study. Of these, 47.1% were male; the average age was 58 years. Four in five patients were in a relationship; 83.5% had at least one child. Almost half (47.9%) of included patients were employed, while 42.7% indicated being retired. In addition, over one third (37.4%) of patients were overweight; 25.8% obese. None of above socio-demographic variables differed between recently diagnosed patients (Group I) and patients in cancer after-care (Group II; Table S1a).

In contrast to socio-demographic data, significant group differences were found regarding clinical data (Table S1b). First, significantly more patients of Group II had melanoma Stages IIc, IIIb, or IIIc (19.4% versus 7.7% of Group I) or Stage IV (7.2% versus 4.1% of Group I). Further, in Group II, Clark level and Breslow thickness were significantly worse; one in four patients (26.6% versus 2.3% in Group I) had at least one melanoma recurrence; the percentage of patients with positive lymph nodes was also significantly higher (29.3% versus 9.1% in Group I; Table S1b).

Further group differences were found regarding treatment. The majority of patients of Group I had received surgery within the past 2 months (84.5% versus 8.0% in Group II). Finally, they more frequently had at least one relevant somatic condition in addition to their melanoma (44.0% versus 25.8% in Group II; Table S1b). No group differences existed regarding psychopharmacological (7% across groups), psychotherapeutic, or psychiatric treatment (12.8% across groups; data not shown).

Self-report versus doctor-reported need of psycho-oncologic support

Mean scores of patients' self-reported need of psycho-oncologic support as measured by the HSI, the QSC-R10, and the Distress Thermometer were 3.12 (SD = 2.75), 10.04 (SD = 8.60), and 4.49 (SD = 4.36), respectively. Doctor-reported (PO-BaDo) mean need was 5.19 (SD = 4.36; Table 1). Significant group differences were found in both mean HSI and Distress Thermometer scores, with Group I reporting significantly higher mean scores – hence, higher need of support – compared with Group II (HSI: 3.47 versus 2.55, $p = 0.002$; Distress

Table 1. Need of psycho-oncologic support as measured by the HSI, QSC-R10, DT, and PO-BaDo; mean scores, standard deviations (SD); total sample and comparison of Group I versus Group II

	Total		Group I (≤180 days)		Group II (>180 days)	
	n = 361		*n* = 222		*n* = 139	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Patients' self-report						
HSI	**3.12**	2.75	**3.47***	2.74	**2.55***	2.67
QSC-R10	**10.04**	8.60	**10.16**	8.39	**9.86**	8.95
DT	**4.49**	2.70	**4.78***	2.73	**4.03***	2.60
Doctors' reports						
PO-BaDo	**5.19**	4.36	**5.68***	4.28	**4.46***	4.39

Higher levels mean higher levels of need of psycho-oncologic support across all patient and doctor self-report instruments. HSI, Hornheider Screening Instrument; QSC-R10, Questionnaire on Distress in Cancer Patients – Short Form; DT, Distress Thermometer; PO-BaDo, Psycho-oncologic Basic Documentation.
All significant values are in bold.
*Significant differences at $p < 0.05$ level (*t*-test statistic for independent samples).

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Thermometer: 4.78 versus 4.03, $p = 0.011$). Further, significant group differences were found for the PO-BaDo, with doctors rating the need of support of Group I significantly higher than that of Group II (Group I, 5.68; Group II, 4.46; $p = 0.011$; Table 1).

When applying the cut-off criteria as defined for each patient-reported and doctor-reported instrument, the number of patients considered as being 'in need of psycho-oncologic support' differed substantially between questionnaires (Table 2). That is, depending on the instrument used, a substantially different percentage of patients were found to be categorized as 'in need of support'. Largest differences were seen between the Distress Thermometer and the doctor-reported PO-BaDo. Following the Distress Thermometer, almost half of patients (48.9%) would be considered to be in this category compared with doctors' judgment (18.6%). Closely linked to above analyses, the correlational analyses indicated moderate relationships between instruments (Table 3). Largest correlations were found between respective patients' self-reported data that ranged between 0.643 (QSC-R10 correlated with HSI and Distress Thermometer) and 0.697 (HSI correlated with Distress Thermometer). Correlations between doctors' perceived need of support and patients' self-reported variables were lower, ranging between 0.536 and 0.555.

Self-report/doctor-reported assessment versus clinical variables

Hardly any statistically significant correlations were found between patient self-report instruments and tumor stage, Breslow thickness, Clark level, ulceration, positive lymph nodes, metastases, and recurrence, respectively (Table 4). The only exceptions were a small positive correlation between QSC-R10 and positive lymph nodes in Group I (0.158, $p < 0.05$) and a small negative correlation between Distress Thermometer and ulceration in Group II (0.190, $p < 0.05$). With regard to the two dichotomous variables 'further somatic symptoms' and 'treatment during the past two months', again Group I did not show statistically significant associations with self-report instruments. In contrast in Group II, the QSC-R10 showed statistically significant correlations with both 'presence of further somatic symptoms' (0.245, $p < 0.01$) and 'treatment during the past two months' (0.343, $p < 0.01$). Largest mean differences were observed for the latter variable, with patients treated during the past 2 months reporting a mean value of 16.57 (SD 9.27), while patients without treatment reported a substantially lower mean value of 8.48 (SD 8.32, data not shown). Further, the Distress Thermometer showed a statistically significant but small association with 'treatment during the past two months' (0.186, $p < 0.05$; Table 4), with means of 5.14 (SD 2.61) versus 3.82 (SD 2.56) for groups with and without treatment, respectively (data not shown).

Similar to patient self-report, hardly any statistically significant associations were found for doctors' perceived need of psycho-oncologic support. Again, the only exception were the variables 'further somatic symptoms' (0.331, $p < 0.01$; Table 4) and 'treatment during the past two months' (0.263, $p < 0.01$) in Group II. Mean values were 7.43 (SD 5.37) for patients treated during the past 2 months compared with 3.90 (SD 3.97) for patients without treatment during the past 2 months (data not shown).

Table 2. Number of questionnaires completed and number and percentage of questionnaires indicating patients' need of psycho-oncologic support

	N completed questionnaires (total)	*N* patients with need of psycho-oncologic support	% patients with need of psycho-oncologic support
Patients' self-report			
HSI	350	137	38.0
QSC-R10	323	80	24.8
DT	350	171	48.9
Doctors' reports			
PO-BaDo	333	67	18.6

For an extended legend of the names of the instruments, see Table 1.

Table 3. Correlations between HSI, QSC-R10, DT, and PO-BaDo

	HSI	QSC-R10	DT	PO-BaDo
HSI	1.000			
QSC-R10	0.697**	1.000		
DT	0.643**	0.643**	1.000	
PO-BaDo	0.540**	0.536**	0.555**	1.000

For an extended legend of the names of the instruments, see Table 1.
**Pearson product–moment correlation coefficient (correlations significant at $p < 0.01$ level).

Conclusions

The increasing incidence of melanoma diagnosed in western societies coincides with changed life conditions post-war. Since Hans Seyle developed the stress concept [27], life has changed dramatically in the modern world. This requires altered adaptive strategies for our bodies and minds. Stress is now more and more accepted as a potential pathogenic element in many non-communicable diseases [13,23,28]. To detect patients in need of psycho-oncologic support, several patient self-report instruments are routinely employed [23–26,29,30]. However, in our study three instruments commonly used in psycho-oncologic care were not congruent in melanoma patients with respect to identifying the same patient population (correlations around 0.65). Further, if doctors were asked, the association with patient self-report was even lower, which is in line with previous research in this area

Table 4. Correlations between HSI, QSC-R10, DT, PO-BaDo and clinical variables

	HSI	QSC-R10	DT	PO-BaDo
Group I (≤180 days)				
Tumor stage[1]	−0.013	0.012	0.082	−0.027
Breslow	0.061	0.074	0.028	0.109
Clark level	−0.030	0.012	0.019	−0.047
Ulceration	0.012	0.014	0.006	−0.050
Positive lymph nodes	0.037	**0.158***	0.115	0.090
Metastases	0.110	−0.001	0.097	−0.004
Recurrence	0.107	0.068	0.118	0.115
Further somatic symptoms	0.049	0.079	−0.025	0.003
Treatment, past 2 months[2]	0.083	−0.029	0.031	0.085
Group II (>180 days)				
Tumor stage[1]	−0.082	0.016	−0.086	0.111
Breslow	−0.036	−0.035	−0.138	0.087
Clark level	0.065	0.008	−0.154	0.028
Ulceration	−0.134	−0.137	**−0.190***	−0.125
Positive lymph nodes	−0.051	0.005	0.053	0.167
Metastases	0.010	0.080	−0.046	0.044
Recurrence	0.019	0.107	0.035	0.148
Further somatic symptoms	0.137	**0.245****	0.084	**0.331****
Treatment, past 2 months[2]	0.169	**0.343****	**0.186***	**0.263****

For an extended legend of the names of the instruments, see Table 1.
All significant values are in bold.
[1]Tumor stage in three categories of severity: Category 1: pTis, Ia, Ib, IIa, IIb, IIIa; Category 2: IIc, IIIb, IIIc; and Category 3: IV
[2]Treatment was dichotomized for these analyses into treatment during past 2 months (yes/no).
*Correlation coefficient based on Spearman's rho (significant at $p < 0.05$ level).
**Correlation coefficient based on Spearman's rho (significant at $p < 0.01$ level).

showing a low concordance between patient-reported and clinician-reported patient distress levels [31]. Moreover, the results of our study suggest that standard clinical disease parameters do not correlate with either of the routine instruments employed to detect need of support. Hence, depending on both the instrument used and the person asked (e.g. patient versus proxy), different conclusions may arise regarding which patients are in need of psycho-oncologic care.

The small but significantly lower need of psycho-oncologic support of patients enrolled more than 180 days after their diagnosis (Group II) – a group that presented with thicker melanomas and more progressed disease compared with Group I – can likely be explained by possible disease adaptation processes and response shifts [32]. Patients allocated to this group are past the initial diagnosis and first line surgical treatment phase and are only subjected to symptoms and further treatment if complications of surgical intervention are present or disease progresses. Of note, there was a small trend in Group II (diagnosis >180 days) toward a possible link between these indicators of likely bad prognosis ('further somatic symptoms' and 'treatment during the past two months') and higher need of psycho-oncologic care.

In this context, it is interesting to analyze aforementioned studies on the effectiveness of psychosocial interventions for melanoma treatment. Fawzy *et al.* (2003) found that such intervention reduced psychosocial strain and improved survival in addition to an anti-tumor immune response in stressed American patients based in urban areas and with a mean tumor size of 1.25 mm [18]. In contrast, a replication study published by Boesen *et al.* (2007) found improved health-related quality of life but no survival benefit in Danish patients based in rural areas with considerably lower stress levels and melanomas thinner than 1 mm [19]. Thus, it appears that patients were more stressed with thicker tumors in the former study. This raises the question of whether maladaptive health behavior and psychosocial variables are especially relevant in patients under high stress and with larger tumors.

Psycho-neuro-immune concepts provide mechanistic explanations for a potential link between physical and psychosocial aspects of cancer and its progression. Instructive examples from the literature investigate the relationship between stress and cancer drawing from well-established mouse models [21,33]. At the molecular and genomic levels, these studies were able to show that neuroendocrine stress mediators and immune imbalances are associated with cancer progression. For example, the number and size of melanoma metastases were found to depend on animals' housing environment, which involves altered stress-mediator release such as noradrenaline (NA) or brain-derived neurotrophic factor (BDNF) [21]. In humans, NA or BDNF have also been linked to higher risk of cancer

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development or increased metastatic load [3,34–36] as well as with psychosocial adjustment [37]. However, the relevance of findings from animal experimental models awaits full translation to humans.

The present study has limitations. Most importantly, the findings of moderate associations between patient self-report and doctor-reported scores as well as the overall lack of association, with only a few exceptions, between psychometric assessment and clinical variables may be due to the applied instruments. While all PRO instruments are well established and frequently applied in oncology in Germany, some may not be psychometrically robust. That is, respective items assess a range of aspects relevant to cancer patients; however, whether these items truly form a single factor 'need of psycho-oncologic support' is questionable. For example, in view of respective response scales, only the QSC-R10 and the PO-BaDo would be suitable for psychometric testing such as factor analysis. Rudimentary analyses (not shown) suggest that both scales were bi-dimensional rather than uni-dimensional and, hence, may be suboptimal for advanced statistical modeling. Moreover, psychosocial stress-modifying measures reportedly linked to tumor survival, such as repressed anger, coping style, or perceived social support [38], are not included in routine screening. For future studies, it is therefore crucial to test alternative screening instruments. In addition, it is hoped that the inclusion of biomarkers improves the predictive validity of a psycho-oncologic model regarding disease outcomes.

In summary, the assessment of 'need of psycho-oncologic support' is indispensable to ensure that melanoma patients receive appropriate care. Because of only moderate correlations between patient-reported and doctor-reported variables, we recommend that initiation of psycho-oncologic interventions be based on patients' perceptions of their own need of support. We conclude that more research is needed using psychometrically robust instruments – ideally in combination with biomarkers of stress and tumor immunosurveillance – to determine potential interactions between psychosocial strain and outcomes in melanoma patients, which shall meet the increasing need to identify key variables to form a working psycho-neuro-immune predictor model and improve the development of preventive and treatment strategies.

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Ethical approval

The main investigator responsible for the study (E. M. J. P.) ensured that the project was conducted in agreement with the Declaration of Helsinki. Ethics approval was obtained from both university hospitals.

Conflict of interest

The authors state no conflict of interest.

ABBREVIATIONS USED

brain-derived neurotrophic factor	BDNF
Hornheider Screening Instrument	HSI
natural killer cells	NK
noradrenaline	NA
Psycho-Oncologic Basic Documentation	PO-BaDo-KF
Questionnaire on Distress in Cancer Patients – Short Form	QSC-R10
T-Helper Cell	TH2

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