Long-term course of psychiatric disorders in cancer patients: a pilot study

Langzeitverlauf psychischer Erkrankungen bei Krebspatienten: eine Pilotstudie

Abstract

Background: About one third of cancer patients suffer from a psychiatric disorder. However, only few studies feature long-term assessment of psychiatric disease in cancer patients, covering a broad range of diagnoses, and employing high-quality instruments.

Patients and methods: A total of 62 patients underwent assessments during a 3-year follow-up period after initial cancer diagnosis. The Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders was administered to measure psychiatric morbidity at baseline (t_1) and two follow-ups (t_2 and t_3). Follow-up assessments took place from 6 to 18 months (t_2) and from 24 to 36 months (t_3) after baseline. Biomedical and psychosocial factors were evaluated to identify predictors of psychiatric disorders using univariate and multivariate analyses.

Results: At t_1, at least one DSM-IV diagnosis was found in 29% of the cases. At follow-ups, the frequency of psychiatric morbidity increased to 36% at t_2 and 44% at t_3, respectively. New occurrence of psychiatric disease at follow-ups was 18% at t_2, and 38%, at t_3. Predictors of psychiatric disorders were low social support, low physical functioning, metastases, complications of disease, and loss of sportive activity.

Conclusion: Persistence and amount of newly diagnosed psychiatric disorders during three years after cancer treatment should be considered in the treatment of cancer patients, especially in individuals with accordant predictive factors.

Keywords: psychiatric morbidity, DSM-IV, cancer, clinical course, predictors

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Zusammenfassung

Hintergrund: Etwa ein Drittel aller Krebspatienten leidet unter einer psychischen Erkrankung. Dennoch gibt es bisher nur wenige Studien, die unter Einschluss eines breiten Diagnosespektrums die psychische Komorbität von Krebspatienten im Langzeitverlauf mit elaborierten Instrumenten erfassen.

Patienten und Methoden: Insgesamt 62 Patienten nahmen nach Krebsdiagnose am gesamten Verlauf der 3-jährigen Studie teil. Das Strukturierte Klinische Interview für DSM-IV wurde zur Erhebung psychischer Erkrankungen bei Aufnahme (t_1) sowie zu zwei Nachfolgeuntersuchungen (t_2 and t_3) eingesetzt. Die Nachfolgeuntersuchungen fanden im Zeitraum von 6 bis 18 Monaten (t_2) und 24 bis 36 Monaten (t_3) nach der Aufnahmeuntersuchung statt. Biomedizinische und psychosoziale Einflussgrößen wurden ausgewertet, um Prädiktoren psychischer Erkrankungen mittels uni- und multivariater Analyse zu bestimmen.

Ergebnisse: Bei Aufnahme erhielten 29% der Patienten eine DSM-IV-Diagnose. Zu beiden Nachfolgeuntersuchungen zeigte sich ein Anstieg der Häufigkeit psychischer Erkrankungen mit 36% zu t_2 und 44% zu t_3. Ein Neuauftreten psychischer Erkrankungen zeigte sich bei beiden Nachfolgeuntersuchungen mit 18% zu t_2 und 38% zu t_3. Prädiktoren

psychischer Erkrankung waren geringe soziale Unterstützung nach Krebstherapie, ein niedriges körperliches Funktionsniveau, Metastasen oder andere ernste Komplikationen sowie der Verlust sportlicher Aktivität.

Schlussfolgerung: Persistenz und Neuauftreten psychischer Krankheiten auch im späten zeitlichen Verlauf nach Krebsdiagnose sollten bei der Behandlung von Krebspatienten beachtet werden – insbesondere bei Vorhandensein von Risikofaktoren.

Schlüsselwörter: psychiatrische Erkrankung, DSM-IV, Krebs, Verlauf, Prädiktoren

Introduction

Various reviews on psychological adjustment to a cancer diagnosis have demonstrated that about one third of cancer patients suffer from a psychiatric disorder [1], [2], [3], [4]. It has also been shown in particular studies that psychiatric morbidity in cancer patients may be negatively associated with the patients' quality of life [5], [6], the duration of hospitalization [7], [8], the compliance with anti-cancer treatment [9], [10], mortality [11], and the risk of suicide [12].

Prevalences however, vary significantly depending on patient characteristics (e.g. type of cancer, stage of disease, age and sex) and methods of investigation (e.g. interview versus questionnaire). Structured interviews, based on current nosographic classifications as DSM-IV or ICD-10 are considered to be the 'gold standard' to register the criteria of a formal psychiatric diagnosis. Table 1 summarizes the results of recent studies that comply with this requirement. All of these studies are cross-sectional in design, displaying rates of mental disorders at a certain point of time since diagnosis or treatment. However, little is known about a longitudinal perspective on psychiatric symptoms. Available studies on clinical course commonly feature only short follow-up intervals (up to one year) [13], [14], [15], [16], [17] or findings were raised without using a structured interview for diagnosis [18], [19], [20], [21], [22], [23].

Yet the long-term course of psychiatric disorders in cancer patients could be vitally important for planning and reviewing psychosocial interventions: knowledge about course characteristics as progression, regression or frequent transitions between different disorders could influence the choice of interventions to be applied for addressing these problems.

To the best of our knowledge, there are only three studies that describe the course of psychiatric disorders in a prospective way during the period of at least one year, employing diagnostics based on structured interviews as mentioned above:

- Uchitomi et al. assessed 212 non-small cell lung cancer (NSCLC) patients 1, 3, and 12 months after curative resection [24]. The prevalence of depression did not change significantly in the year after surgery (8%, 5% and 5% respectively). However, major depression decreased while minor depression stayed constant. Other disorders had not been taken into account in this report.

- Akechi et al. investigated prevalence, predictors and change of adjustment disorders (AD), major depression (MD) and post-traumatic stress disorder (PTSD) in 85 terminally ill cancer patients [25]. At baseline, 16% of the patients showed symptoms of AD and 7% had symptoms of MD. PTSD had not been diagnosed. At follow-up, 11% were diagnosed with AD and 12% with MD. About 30% of all patients had changed in their initial diagnosis (including "none"), showing all possible transitions with an emphasis on changes from MD to AD. It may be criticized however, that time to follow-up had a wide range from 7 to 633 days and a median of only 58 days. Anxiety disorders (other than PTSD) have not been taken into account.

- Burgess et al. evaluated prevalence and predictive factors of anxiety and depression in 170 patients with breast-cancer [26]. During a five-year period, these women were interviewed four times to cover the complete interval. Point prevalence of depression was 33% at diagnosis, 24% at three months and around 15% after 12 months and beyond. The one-year-prevalences dropped continuously from 48% in the first year to 15% in the fifth year. Unfortunately, the course of anxiety and depression had not been displayed separately in this study, as the course of anxiety levels is discussed controversially in literature with references to constant levels of anxiety even more than 12 months after cancer diagnosis [19], [21].

Associated or predictive factors of psychiatric disease include demographic [24], [26], psychosocial [18], [26] and biomedical variables [20], [27]. Psychosocial factors like social support, own children or psychiatric distress in patient's history were generally reported to have a higher impact on prediction of mental disorders in cancer patients than biomedical factors like cancer state, age or sex [18], [26]. Naturally, most of these factors have been found in relation to short term investigations and may not necessarily predict psychiatric disease several years after cancer treatment.

Summarizing, there is a lack of studies featuring long-term assessment of psychiatric disease in cancer patients, covering a broad range of diagnoses, and employing high-quality instruments.

Table 1: Cross-sectional studies investigating psychiatric disorders in cancer patients using DSM or ICD based interviews

Population	n	Time of investigation	Results	Reference
Patients with different types of cancer	146	Within 18 months after diagnosis	44.5% psychiatric disorders 28% adjustment disorders 10% affective disorders 4% anxiety disorders	[34]
Laryngectomees	189	0-26 years after surgery	23% psychiatric disorders 12% affective disorders 2% anxiety disorders 8% alcohol abuse	[36]
Patients with different types of cancer	117	During inpatient treatment	30% psychiatric disorders	[37]
Patients with breast cancer	207	3-6 weeks post breast cancer diagnosis	18% psychiatric disorders 14% anxiety disorders 4% affective disorders	[38]
Patients with different types of cancer	78	First days after admission before surgery	28% psychiatric disorders 22% adjustment disorders	[9]
Patients with different types of cancer	150	During inpatient treatment	29% psychiatric disorders 14% adjustment disorder 11% major depressive episode	[27]
Patients with unresectable NSCLC	129	Between time of diagnosis and initial treatment	79% psychiatric disorders 13% adjustment disorder 5% major depression 8% alcohol abuse 46% nicotine abuse 2% panic disorder 1% social phobia 1% specific phobia	[16]
Patients with otolaryngological cancer	50	Post surgery	9% major depression 14% adjustment disorders	[39]

Therefore, in our study, newly diagnosed cancer patients were followed for three years, assessing psychiatric morbidity with a structured interview based on a comprehensive range of DSM-IV diagnoses. Furthermore, factors predictive of psychiatric disease during three years after cancer diagnosis have been identified using reliable and valid instruments.

Patients and methods

Sample and design

The primary sample (n=689) was formed consecutively from individuals with a cancer diagnosis who had undergone inpatient treatment between June 2002 and July 2004 in a hospital affiliated to the University of Leipzig (visceral surgery, urology, radiotherapy and gynaecology) or the maternity clinic of the community hospital St. Georg (Leipzig). The eligibility criteria for patient recruitment in the study were: 1) age 18 years or older, 2) newly diagnosed cancer with curative therapy approach, 3) knowledge of cancer diagnosis, 4) being in acceptable physical and mental condition to complete the questionnaires and participate in an interview taking at least 45 minutes, and 5) having sufficient verbal communication skills in

German language. Concerning criterion (4), eligibility was discussed by physicians and investigators on a case-by-case basis to avoid biased judgement and selection bias. The study was approved by the local Ethics committee of the University of Leipzig and funded by The German Federal Ministry for Education and Research. Each patient was informed both verbally and in written form about the goals of the study, the voluntary nature of their participation and the confidentiality of information shared.

General demographic and clinical characteristics, including age, sex, tumour site, UICC state (Union Internationale Contre le Cancer) and type of therapy were obtained from patients' medical charts, whereas socio-demographic attributes as income, educational level, having a partner or family and religious and national affiliations were retrieved using an additional questionnaire. Then, psychological measurement using a semi-structured interview was arranged during the first three days after admission (baseline, t_1).

As a result of economic limitations of the study, only n=100 patients living near the city centre of Leipzig could be included for follow-up examinations. They were selected by random, minimizing the distance of their domicile to the city centre. Thus, first follow-up examination (t_2) was conducted 6 to 18 months after t_1 on n=100 local residents of Leipzig and second follow-up (t_3) was ar-

ranged 24 to 36 months after t_1 with n=62 patients who participated both at t_1 and t_2. At both follow-ups a comprehensive evaluation of the patient's mental disorders had been carried out using a semi-structured interview. This interview was also used at t_3 to investigate patients' history of psychiatric disorders, i.e. whether a mental disorder was present before diagnosis of cancer (lifetime). Additionally, certain aspects of quality of life (including physical functioning, pain and social well-being) were assessed using two questionnaires to gather information on potential correlations of psychiatric morbidity.

Information concerning death dates and current postal address was provided by the local census bureau. Participants were interviewed by a psychologist, interviews took place in hospital at baseline and at home during follow-up examinations.

Assessment instruments

Psychiatric morbidity

To cover a broad range of information about patients' psychiatric disorders in a standardized way, the Structured Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) was administered to assess psychiatric morbidity. The variant used in the present investigation was the Structured Clinical Interview for DSM-IV, German Version [28], a translation and adaptation of the 'Structured Clinical Interview for DSM-IV – Research Version (SCID-1, Version 2.0)'. The interview provides the diagnosis of affective disorders (including major depression and dysthymia), anxiety disorders (including panic disorder, social phobia, specific phobia, posttraumatic stress disorder and generalized anxiety disorder), stress disorders (including acute stress disorder and adjustment disorder), and screens for substance abuse (including pharmaceuticals, drugs, nicotine and alcohol). To constitute a diagnosis, certain criteria have to be met, including severity and duration of symptoms and their impact on everyday activities - taking into account that symptoms should not be direct physiological result of intoxication or general medical factors. The reliability of SCID has been reported to be satisfactory [29] and is commonly used for validation for other psychiatric diagnostic instruments [30], [31]. Cohen's kappa was used to assess interrater reliability for 45 randomly selected interviews in this study. Interrater agreement for all current diagnoses was $\kappa=0.95$ (SD=0.12).

Demographic, biomedical and psychosocial attributes

To find potential factors associated with mental disorders, demographic (sex, age, social affiliation, marital status, number of children, nationality, membership of religious group), psychosocial and biomedical data (UICC stage, tumour localization, type of treatment, cancer recurrence, history of psychiatric treatment) were recorded in this study. While most of the biomedical and demographic data were registered during inpatient admission as described above, selected psychosocial characteristics were asked for at second follow-up, employing certain scales of two questionnaires: 1) The European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30), which is a questionnaire developed to assess the quality of life in cancer patients [32]. Its scales "physical functioning" and "pain" used in this investigation, take into account the physical ability to master daily-life activities and subjects' impairment caused by pain, respectively. 2) The Functional Assessment of Cancer Therapy-General, which is the core module of the Functional Assessment of Chronic Illness Therapy-measurement system, a collection of Quality-of-Life questionnaires targeted to the management of chronic illness [33]. Its scale "Social/Family Well-Being" applied in this study, informs about the degree of social support and intimacy of relationships to other persons. Additionally, single item questions concerning patients' satisfaction with their job, their habitation, their financial situation, the extent of sportive activities and the importance of spirituality were asked.

Statistical analysis

Intergroup differences in categorical, nonparametric, and continuous variables were tested with the chi-square statistics (or Fisher's exact test if applicable), the Wilcoxon two-sample test, and the unpaired t test, respectively. Binary logistic regression analysis with forward and backward selection method was used to find the potential predictors of psychiatric morbidity after diagnosis of cancer. The model for logistic regression was tested for goodness of fit with the Hosmer and Lemeshow test. SPSS® 13.0 (SPSS Inc. Chicago, IL, USA) and G*Power® 2.0 (Faul, F. & Erdländer, E.) were used for data storage and analysis.

Results

Sample characteristics

Of 689 patients who were interviewed during the first three days after admission (baseline), n=100 local residents of the City of Leipzig were selected (see sample and design for details) at first follow-up, which was conducted 5 to 18 months (mean 13 months) after baseline. At second follow-up (between 23 and 38 months after baseline, mean 28 months), 20 patients were excluded due to death (n=10) or insufficient physical or mental conditions (n=10). An additional 16 patients could not be contacted by mail or by telephone using updated address information from local census bureaus and 2 patients refused further participation for other reasons. Thus, the final study group consisted of 62 individuals with a complete data set of three assessments.

The mean age of participants was 59.5 years (SD=11.7, range = 34-84 years) and 66% were female. Table 2 shows the demographics for the sample. The participants were primarily German (92%), married or living with a partner (63%), having own children (79%), middle class (66%) and most were not members of a religious group (73%).

Table 2: Demographic characteristics of participants

Variables	Categories	n	%
Age	<50	12	19
	50-65	26	42
	≥65	24	39
Socio-economic status	Upper class	6	10
	Middle class	41	66
	Lower class	10	16
	Unknown	5	8
Marital status	Married / live with partner	39	63
	Divorced or widowed	14	23
	Single	9	14
Children	Yes	49	79
	No	8	13
	Unknown	5	8
Nationality	German	57	92
	Other nationality	1	2
	Unknown	4	6
Member of religious group	Yes	11	18
	No	45	73
	Unknown	6	9

The medical characteristics are described in Table 3. Individuals predominantly had stage II or III disease (61% of classified tumours) and were suffering from breast or urogenital cancer (66%). Most patients had undergone surgery (66%). In all mentioned biomedical and socio-demographic variables, the final sample did not differ significantly from the sample at first follow-up.

Table 3: Medical characteristics of participants

Variables	Categories	n	%
Cancer stage (UICC)	0	4	6
	I	11	8
	II	19	31
	III	10	16
	IV	4	6
	unknown	14	23
Localisation	Breast	16	26
	Lung	3	5
	Urogenital	25	40
	Gastrointestinal	12	19
	Nervous system	0	0
	Other	6	10
Therapy	Surgery	41	66
	Chemotherapy	3	5
	Radiotherapy	3	5
	Radio-chemotherapy	8	13
	Other	7	11

Prevalence of mental disorders

At baseline, at least one DSM-IV diagnosis was given in 29% of the cases. At both follow-ups, the frequency of psychiatric morbidity did increase (t_2: 36%; t_3: 44%). A detailed report of diagnoses is illustrated in Table 4. Affective disorders remained constant over time (t_1: 13%, t_2: 13% and t_3: 16%) but the prevalence of dysthymia increased (t_1: 0%, t_2: 6% and t_3: 13%), whereas major depressive episodes occurred less frequently. Anxiety disorders advanced from initially 8% to 27% at both follow-ups. At t_2, this class of disorders is predominated by posttraumatic stress disorder (8%), generalized anxiety disorder (10%) and panic disorder (10%). At t_3, in contrast, social phobia (7%), specific phobia (10%) and generalized anxiety disorder (11%) played the major role. Stress disorders occurred only at baseline (12%) and second follow-up (8%). Considerable substance abuse was found throughout all points in time of investigation (t_1: 15%, t_2: 11% and t_3: 13%).

Clinical course of psychiatric morbidity

In 18% of the cases, individuals not suffering from psychiatric morbidity at baseline, had a DSM-IV diagnosis at first follow-up. At second follow-up, 38% of the patients were newly diagnosed with mental illness. The rates of psychiatric disorders did not decrease during the three years after initial treatment of cancer (x^2=1.49, df=1, p=0.223, power=0.8 at an effect size=0.36. According to conventions for x^2-tests an effect size of 0.3 is regarded as medium). A history of psychiatric morbidity before the diagnosis of cancer was found in 26 (42%) individuals. During the whole period of investigation (up to 38 months after clinical assessment), a total of 39 persons (63%) were given a psychiatric diagnosis on at least one occasion. For 20 of these individuals (51%) this was the first occurrence of a psychiatric disease in lifetime. Individual changes of the patients' DSM-IV diagnoses are shown in Figure 1. Affective disorders were found predominantly in patients with former affective disorder (5 of 8 subjects at t_2), anxiety disorder (4 of 10 subjects at t_3) or were newly diagnosed (4 of 10 subjects at t_3). Of 17 individuals with an anxiety disorder at t_2 (t_3), 7 patients were suffering from a stress disorder (anxiety disorder). At both follow-ups another 7 patients with an anxiety disorder had no DSM-IV diagnosis at baseline or t_1, respectively. All three patients with an acute stress disorder at second follow-up were suffering from newly diagnosed metastases (data not shown). Substance abuse was found predominantly in individuals with former substance abuse (5 of 7 subjects at t_2) or former anxiety disorder (6 of 8 subjects at t_3).

Table 4: Rates of DSM-IV diagnoses in cancer patients at time of diagnosis (t_1), 5 to 18 months after (t_2) and 23 to 38 months after (t_3). Multiple diagnoses were possible.

	t_1			t_2			t_3		
	n	r	95% CI	n	r	95% CI	n	r	95% CI
Affective disorders	8	0.13	0.07-0.24	8	0.13	0.07-0.24	10	0.16	0.09-0.27
Dysthymic disorder	0	0.00	0.00-0.06	5	0.08	0.04-0.18	8	0.13	0.07-0.24
Major depressive episode	8	0.13	0.07-0.24	3	0.05	0.02-0.14	2	0.03	0.01-0.12
Anxiety disorders	5	0.08	0.04-0.18	17	0.27	0.18-0.40	17	0.27	0.18-0.40
Generalized anxiety disorder	3	0.05	0.02-0.14	6	0.10	0.05-0.20	7	**0.11**	**0.06-0.21**
Panic disorder	1	0.02	0.00-0.08	6	0.10	0.05-0.20	2	0.03	0.01-0.12
Posttraumatic stress disorder	1	0.02	0.00-0.08	5	0.08	0.04-0.18	2	0.03	0.01-0.12
Social phobia	0	0.00	0.00-0.06	2	0.03	0.01-0.12	4	0.07	0.03-0.15
Specific phobia	2	0.03	0.01-0.12	3	0.05	0.02-0.14	6	0.10	0.05-0.20
Stress disorders	8	0.13	0.07-0.24	0	0.00	0.00-0.06	5	0.08	0.04-0.18
Acute stress disorder	6	0.10	0.05-0.20	0	0.00	0.00-0.06	3	0.05	0.02-0.14
Adjustment disorder	2	0.03	0.01-0.12	0	0.00	0.00-0.06	3	0.05	0.02-0.14
Substance abuse	9	0.15	0.08-0.26	7	0.11	0.06-0.21	8	0.13	0.07-0.24
Alcohol abuse	2	0.03	0.01-0.12	3	0.05	0.02-0.14	4	0.07	0.03-0.15
Pharmaceuticals abuse	3	0.05	0.02-0.14	1	0.02	0.00-0.08	3	0.05	0.02-0.14
Drugs abuse	0	0.00	0.00-0.06	0	0.00	0.00-0.06	0	0.00	0.00-0.06
Nicotine abuse*	5	0.08	0.04-0.18	4	0.07	0.03-0.15	7	0.11	0.06-0.21
Any DSM-IV diagnosis (without nicotine abuse)	18	0.29	0.19-0.42	22	0.36	0.25-0.48	27	0.44	0.32-0.56

n: number of patients, r: estimated rate, CI: confidence interval
*Consumption of at least 10 cigarettes daily

Predictive factors for psychiatric morbidity

During the period from baseline investigation to second follow-up, 39 patients (63%) were diagnosed with at least one DSM-IV diagnosis. In respect of demographic, biomedical and psychosocial attributes, there were several differences between patients with and without psychiatric morbidity. Variables at t_3 which showed a p<0.1 in univariate analysis were used as covariates in a binary logistic regression analysis model to find the predictors of mental disorders during up to 38 months after diagnosis of cancer. By binary logistic regression analysis, the following four predictive variables could be found in both forward and backward selection (power of 0.8 at an effect size of 0.21): social support after cancer therapy (p=0.045) and good physical functioning regarding daily activities (p=0.067) were negatively correlated with psychiatric morbidity, whereas metastases or other severe complications of treatment (p=0.004) and loss of sportive activity (p=0.065) were positively correlated (Table 5). This configuration had a Nagelkerke R^2 of 0.526 in forward selection and a non-significant Hosmer-Lemeshow

chi square indicating reasonable model fit (χ^2=11.52, df=8, p=0.989).

Table 5: Predictors of psychiatric morbidity at second follow-up in cancer patients

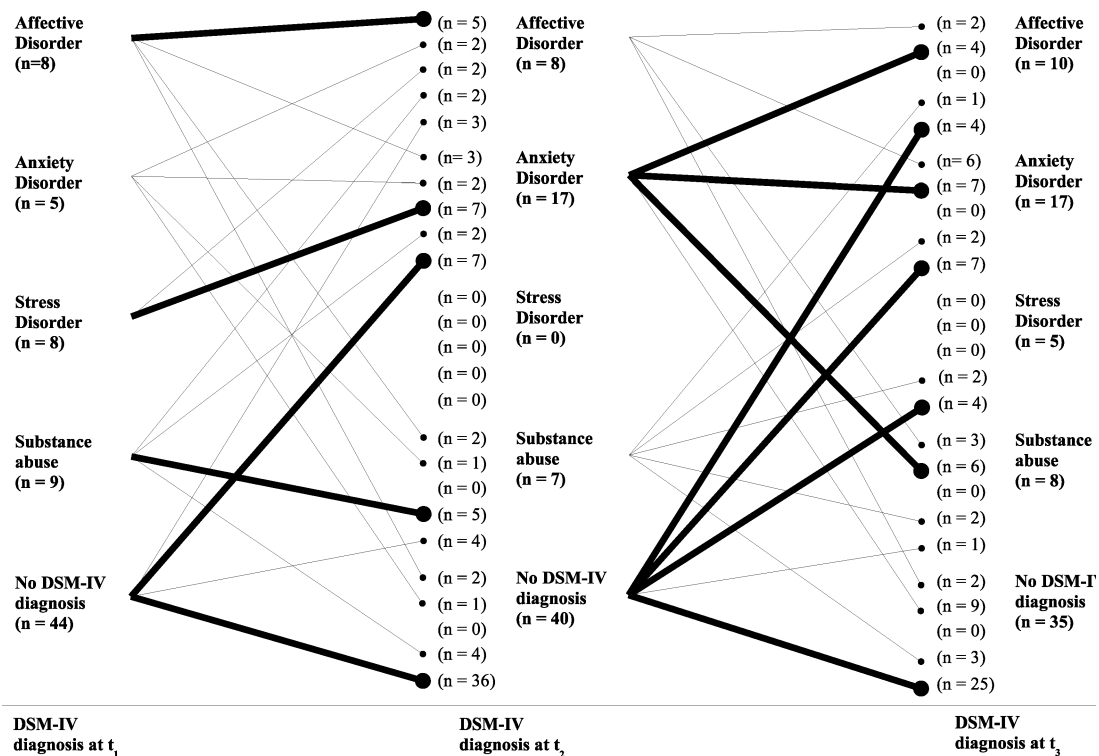| Predictors	Adjusted OR	95% CI	p
Social support after cancer therapy	0.82	0.67-1.00	0.045
Good physical functioning in daily activities after cancer therapy	0.79	0.61-1.02	0.067
Metastases or severe complications of treatment	28.08	2.89-272.60	0.004
Loss of sportive activity after cancer therapy	9.46	0.87-102.68	0.065

Figure 1: Course of psychiatric morbidity in cancer patients (n=62) during three years of investigation (time of diagnosis (t_1), 5 to 18 months after (t_2) and 23 to 38 months after (t_3)). Lines stand for individual changes of diagnosis over time, with the number of patients at the dotted end of each line, respectively. Thick lines indicate main influences from a certain class of disorder found at the previous assessment point. Multiple diagnoses were possible (therefore, numbers do not add up necessarily).

Discussion

The present investigation has the character of a pilot study which prospectively assesses a broad range of psychiatric diagnoses in a population of patients with cancer during a 3-year period after initial treatment and analyses predictive factors of psychiatric morbidity during this period. It was designed to retrieve data concerning a long-term clinical course using standardized diagnostic criteria with reliable and valid instruments that might be useful for future research.

Our finding showed that the rates of psychiatric disorders did not decrease during the three years after initial treatment of cancer. While the rate of psychiatric morbidity at t_1 is in line with results of other studies, our findings of the follow-ups have to be discussed in more detail. In our study, prevalence of anxiety disorders increased from 8% at baseline to 27% at first follow-up and stayed constant in second follow-up. In contrast, Burgess et al. [26] found a significant decrease of depression and anxiety during the second and third year after diagnosis of breast cancer. However, a shortened version of SCID, focusing on symptoms of depression and anxiety, had been used in Burgess' investigation and it remains unclear if dysthymia and different kinds of anxiety disorders were taken into account. Other studies reported a constant level of anxiety over time [19], [20], [21], but did not use semi-structured clinical interviews for investigation.

Another important point concerning anxiety disorders is that they were likely to arise later than one year after diagnosis of cancer: 41% of patients with an anxiety disorder at t_2 or t_3 had no DSM-IV diagnosis at baseline or t_2, respectively (7 out of 17 in each case). A considerable part of late onsets has also been found for affective disorders and stress disorders at second follow-up, the latter being associated with the occurrence of metastases or severe complications of treatment. The *de novo* manifestation of psychiatric disorders at t_2 and t_3 shows the importance of observing psychological distress in cancer patients over years, even if they did not receive a DSM-IV diagnosis at the time of cancer occurrence.

Affective disorders remained constant over time. However, the prevalence of dysthymia increased, whereas major depressive episodes occurred less frequently. This finding is compatible with other studies [19], [24]: the severity of depressive symptoms decreases and gives way for milder, but chronic dysthymia. Noticeable, however, are rates of adjustment disorders below 5% found in this study, compared to reported rates of up to 28% [34]. This might have one of the following reasons: 1) in investigations using a limited range of diagnoses, adjustment disorders could have been used as a container diagnosis, e.g. cases that could have been diagnosed as acute stress reaction or minor depression were diagnosed as adjustment disorder with anxiety or depressed mood, respectively. 2) Adjustment disorders are clinically significant as evidenced by either "distress that is in excess of what would be expected from exposure to the stressor" or "significant impairment in social, occupational or educa-

tional functioning", two assertions that leave a considerable range of interpretation [17].

Predictors of psychiatric morbidity during a 3-year period after cancer diagnosis were a lack of social support, occurrence of metastases or other severe complications, insufficient physical function in daily life activities and loss of sportive activity after cancer treatment. Except for the occurrence of metastases, these predictors are in line with the assertion made in the introduction, that psychosocial factors have a higher impact on prediction of mental disorders in cancer patients than biomedical factors. However, patients with recurrence have been described in the literature as experiencing a sharp increase in levels of anxiety and depression [26].

Our study has several limitations. First of all, since the sample size of individuals participating in the first follow-up had to be reduced seriously due to economic limitations of the study (n=100, 15 % of initial sample size n=689) and a drop-out of 38% was recorded at t_3 (n=62, 9% of initial sample size), generalizing the results in detail may not be possible. On the other hand, our sample differed only in sex (more females) and cancer localisation (more breast cancer) from the sample of all cancer patients assessed during the period of investigation (n=689). Although the role of sex differences is discussed controversially, a review article [35] and our own findings found no sex differences in prevalence of psychiatric morbidity in cancer patients. Second, the selection of urban inhabitants at first follow-up (which was also due to economic limitations) might have led to a bias against rural populations. Third, the time span of each follow-up assessment is large (12 months), which impairs the comparability within the sample. At a given time gap of at least 6 months between follow-ups, grouping of the patients still seemed justifiable, though. Furthermore, the need of treatment of specific phobia and social phobia is discussed controversially and may put into perspective the considerable increase of these disorders at both follow-ups. However, at least social phobia in the context of impaired function and altered appearance after treatment (e.g. head and neck surgery) is a well-known indication for psychological intervention. Even specific phobia, such as agoraphobia, may have essential consequences for tomography and other techniques where the patient has to lay quietly in a narrow tube for quite a long period of time. Finally, conducting a regression analysis with a sample size of 62 may be of low significance. In our example, the analysis had a power of 0.8 at an effect size of 0.21 (according to conventions for regression analyses an effect size of 0.15 is regarded as medium).

Notwithstanding these limitations, it may be summarized that both, noticeable persistence and amount of newly diagnosed psychiatric disorders during three years after cancer treatment should be considered in the treatment of cancer patients, especially in individuals with positive predictive factors. As a matter of course, small sample size and high drop-out rate constitute the preliminary character of this study. Yet it could be shown, that psychiatric disorders may prevail or arise even years after cancer diagnosis. To learn more about the temporal patterns of psychiatric disorders in cancer patients, and to efficiently provide professional psychological support, more well-designed long-term studies with larger numbers of participants are desirable.

Notes

Conflicts of interest

None declared.

Acknowledgments

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