



Comorbid conditions and health-related quality of life in long-term cancer survivors—associations with demographic and medical characteristics

Heide Götze¹ · Sabine Taubenheim² · Andreas Dietz³ · Florian Lordick⁴ · Anja Mehnert¹

Received: 20 September 2017 / Accepted: 28 July 2018 / Published online: 10 August 2018
© Springer Science+Business Media, LLC, part of Springer Nature 2018

Abstract

Purpose Our study provides a detailed overview of comorbid conditions and health-related quality of life of long-term cancer survivors and analyses the impact of demographic, disease- and treatment-related characteristics.

Methods We present data obtained from 1000 survivors across mixed tumour entities 5 and 10 years after cancer diagnosis in a cross-sectional study. We analyse the prevalence of physical symptoms and health conditions via self-report and health-related quality of life using the EORTC QLQ-C30 in comparison to gender- and age-matched reference values of the general population.

Results Cancer survivors reported on average 5 comorbidities; 23% had 7 or more comorbid conditions. Cancer survivors reported higher physical symptom burden than the population—especially fatigue, insomnia and pain. Type and prevalence of long-term and late effects differ with disease-related factors (e.g. cancer type, treatment) and characteristics of the patient. Cancer survivors also reported lower quality of life than the population, especially in everyday activities, social life, psychological well-being and financial difficulties. There was a positive association between high quality of life and a low level of morbidity.

Conclusions The specific knowledge about physical long-term consequences for the individual types of cancer could raise awareness in health care professionals for high-risk patients and help to develop adequate prevention and survivorship programs.

Implications for Cancer survivors Limitations in the mental health area underlines the importance of psycho-oncological survivorship-care-plans, which go beyond the time of rehabilitation. Special attention should be given to the financial situation of patients in long-term follow-up care.

Keywords Cancer survivorship · Quality of life · Comorbidities · Long-term effects

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s11764-018-0708-6>) contains supplementary material, which is available to authorized users.

✉ Heide Götze
heide.goetze@medizin.uni-leipzig.de

- ¹ Department of Medical Psychology and Medical Sociology, University Medical Center Leipzig, Philipp-Rosenthal-Straße 55, 04103 Leipzig, Germany
- ² Local Clinical Cancer Registry Leipzig, University Medical Center Leipzig, Leipzig, Germany
- ³ Department of Otolaryngology, Head and Neck Surgery, University Medical Center Leipzig, Leipzig, Germany
- ⁴ University Cancer Center Leipzig (UCCL), University Medical Center Leipzig, Leipzig, Germany

Introduction

Due to the improvements in early detection, treatment and prognosis for many cancer entities, the number of cancer survivors is steadily increasing worldwide [1–3]. In the USA, over 60% of cancer patients have survived 5 years or more, and 40% have survived 10 years or more after diagnosis [4]. The growing number and diversity of cancer survivors leads to new challenges with regard to managing the long-term and late physical and psychosocial treatment consequences [5]. Those challenges include the relevance of prehabilitation and cancer rehabilitation and the need to develop and implement survivorship care programs [6, 7]. Cancer has the potential to affect every aspect of an individual's life and that impact does not end after primary cancer treatment [2, 8, 9].

Exposure to cancer and its treatments and here particularly multimodal therapy concepts may result in long-term and late health complications as well as functional limitations which might be associated with a variety of rehabilitative and supportive care needs [10–12]. Common physical symptoms and conditions experienced by cancer survivors are pain, fatigue, peripheral neuropathy, lymphoedema, gastrointestinal problems, bladder dysfunction, and early menopause [13–16]. The presence and severity of comorbid conditions is one of the strongest predictors of lower levels of physical functioning [17, 18] and poorer health-related quality of life [17, 19, 20] among cancer survivors with increasing risk for early mortality [18, 21].

There have been few studies so far investigating on comorbid conditions and quality of life in long-term cancer survivors, although in recent years a growing number of publications have emerged specifically addressing long-term survival [5, 22–24]. For example, the Dutch registry ‘Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES)’ investigated the physical and psychosocial impact of cancer and its treatment of cancer survivors [25]. Previous research focused on periods of survival up to 2 years following diagnosis and mostly on a single cancer type (e.g. breast cancer) which leads to limitations with regard to the generalizability of the findings and comparisons between different survivorship populations [21, 26].

The present study provides data from a large sample of adult long-term cancer survivors including all cancer types. We focused on periods of survival up to 10 years following diagnosis and obtained detailed medical- and treatment-related variables in a cross-sectional study. In addition, we assessed quality of life in comparison to a large representative gender- and age-matched comparison group from European general population normative studies. Our research questions are as follows:

1. Which physical symptoms, comorbid conditions and health-related quality of life do long-term cancer survivors experience 5 and 10 years after diagnosis, respectively?
2. Are there differences between long-term cancer survivors 5 and 10 years after diagnosis and the general population with regard to health-related quality of life?
3. In which way are demographic factors, disease- and cancer treatment-related characteristics associated with quality of life and the prevalence of comorbidities?

The results of our study could help health care professionals identify high-risk patients and provide the basis for the development of more specific prevention and survivorship-programs.

Patients and methods

Study design

In this cross-sectional cohort study, we recruited cancer patients who were diagnosed with cancer 5 or 10 years before via the local cancer registry in Saxony. Because in the literature the term long-term survivorship is often used at a minimum of 5 years post-cancer diagnosis [12], we choose the first measurement time at 5 years after the primary cancer diagnosis and the second measurement time at 10 years post-primary cancer diagnosis to capture late- and long-term conditions after the usual follow-up periods. Thus, we are able to show the long-term path of a cancer patient in a life stage and development perspective. In addition, gender- and age-matched European reference values of the general population were used to compare quality of life.

Study participants

Patients were eligible for study participation if they had a confirmed diagnosis of cancer 5 years (cohort 1) or 10 years (cohort 2) ago according to the local cancer registry, were aged between 18 and 85 years at the time of diagnosis and were able to speak and read German. All participants provided written, informed consent according to the Declaration of Helsinki. The study received research ethics committee approval by the University of Leipzig (Az. 070-14-10032014).

General population data

To compare health-related quality of life between long-term cancer survivors and the general population, we used European reference values for the EORTC-Quality of life questionnaire of six European general population normative studies ($n = 16,151$), matched for gender and age. A representative sample of the German adult population (2448) was randomly selected in 2012 using the Kish-selection-grid technique (participation rate 56.6% of valid addresses). The mean scores were combined with the age and gender adjusted scores of five other European normative studies from Sweden, the Netherlands, Norway and Germany (n between 1731 and 4910) for European normative values. Sample characteristics of this group were previously reported in more detail [27].

Recruitment and data collection

Access to the patients was provided by the Clinical Cancer Registry at the Cancer Center Leipzig. The Cancer Registry provided us with data on sex, age, ICD-10 diagnosis, time of diagnosis and cancer treatments received. Eligible patients were selected by the cancer registry. They received a study information letter and were asked to participate in the survey.

A prepaid reply card was enclosed. Prior to participation, all patients provided written informed consent. Patients who consented to participate received a set of questionnaires either by mail or could complete the questionnaires online using the Lime Survey software.

Study measures

Physical comorbidities

To assess the prevalence and burden of physical comorbidities, we employed a modified version of a self-report instrument developed by Bayliss et al. [28]. The original instrument comprises a list of 23 common chronic medical conditions. The specificity of the original scale was reduced by summarising similar conditions, e.g. angina/coronary artery disease and congestive heart failure was summarised as “heart disease”; rheumatoid arthritis and rheumatic disease as “rheumatism”. As we assessed cancer patients in our study, the condition “cancer” was removed. Finally, two further conditions were added: psychological diseases and polyneuropathy (sensation disorder, tingling and numbness). The following 18 medical conditions were included in the modified instrument:

Hypertension, asthma, lung disease, diabetes, thyroid disorder, back pain, rheumatism, osteoarthritis (joint related diseases), osteoporosis, colon problems (e.g. diverticulitis, irritable bowel), stomach problems (e.g. gastritis, peptic disease), kidney disease, heart disease, stroke, neurological disease (e.g. Parkinson’s disease, multiple sclerosis), eye disease, psychological diseases and polyneuropathy.

Respondents reported for each condition whether they had the condition, and if so whether it interfered with their daily activities “not at all” (1) to “a lot” (5). A comorbidity-index representing the level of morbidity can be computed. The total score ranges between 0 and 90 and represents the sum of conditions weighted by the level of interference assigned to each [29].

Health-related quality of life

The EORTC QLQ-C30 is the core questionnaire of the “European Organisation for Research and Treatment of Cancer” for evaluating health-related quality of life. It is a 30-item instrument comprised of five functioning scales, nine symptom scales and one scale measuring “Global quality of life”. All scales have a score range between 0 and 100. While high scores of the symptom scales indicate a high burden of symptoms, high scores of the functioning scales and on the Global quality of life-scale indicate better functioning resp. quality of life. The EORTC QLQ-C30 has got “satisfactory to excellent psychometric properties” [30].

Statistical analyses

We carried out quantitative data analysis using the Statistical Package for the Social Sciences (SPSS 24; IBM, Armonk, NY). We calculated descriptive statistics for both continuous (frequencies, mean, standard deviation) and categorical variables (frequencies, percentages). Comparisons between subgroups of cancer survivors in terms of demography, comorbidity and quality of life as well as comparisons between patients and population data in terms of quality of life were performed in a one-way analysis of variance (ANOVA). To counteract the problem of multiple comparisons, we used the Bonferroni correction. It is considered the simplest and most conservative method to control the familywise error rate, which tested each of the individual tests at a significance level of α/n (n = number of tested hypothesis). We evaluated multiple linear regression models to analyse in which way demographic (sex, age) and disease-related variables (time since diagnosis, cancer site, metastases/recurrence, second cancer disease, cancer treatment) (independent variables, variable level: scale or binary 0/1 coded, entered as one block) are associated with quality of life and the prevalence of comorbidities (dependent variable, variable level: scale).

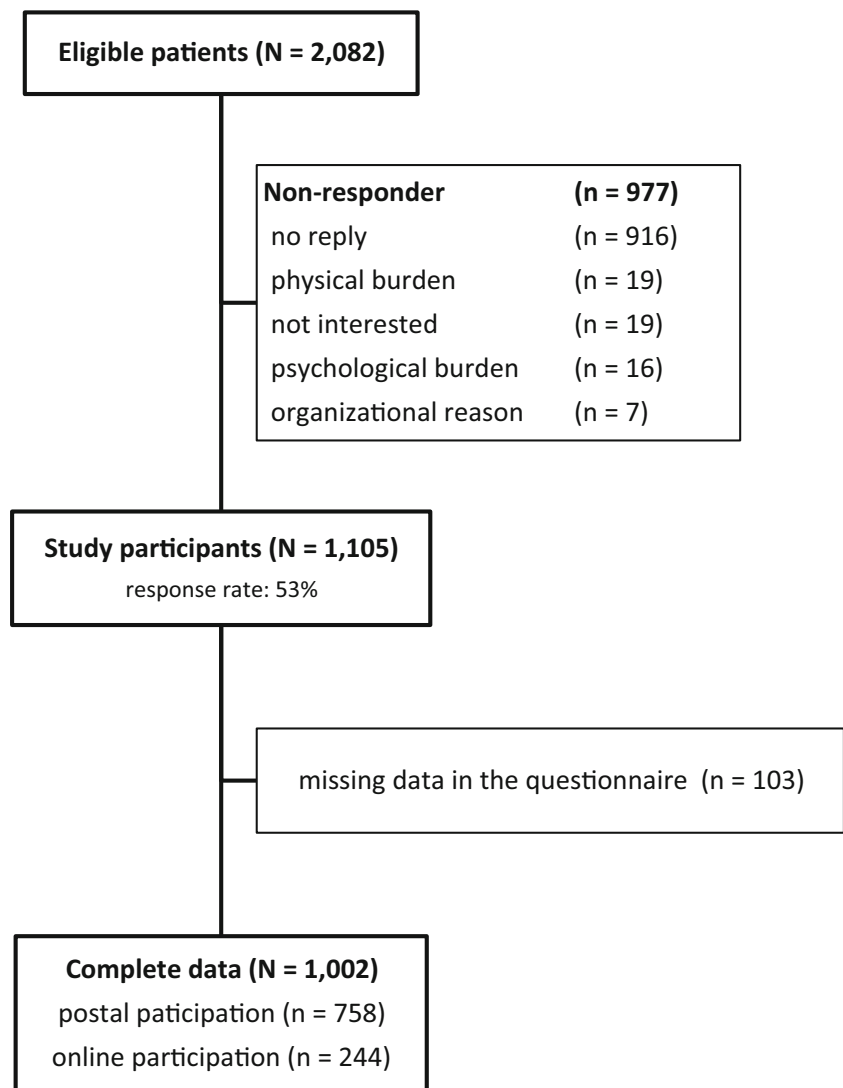
Results

Sample

Patient recruitment was carried out from 2014 October to 2015 November. Out of 2082 eligible patients, 1105 (53%) participated in the study (Fig. 1). Among those, 1002 patients returned a complete questionnaire and were included in the final analysis (postal participation: $n = 758$ /online participation: $n = 244$). Study participants were more often male (53%) than non-responders (47%) ($p = 0.013$). There were no differences in age (non-responder: $M = 65.8$ years; $p = 0.054$), time since diagnosis (non-responder 5 years: 66%/10 years: 34%; $p = 0.989$) and cancer diagnosis ($p = 0.624$) between responders and non-responders.

The patients who completed the questionnaires online were younger ($M = 62.1$ years; $p < 0.001$) and the percentage of male patients was higher (60.2% male; $p = 0.008$) than in the group of patients who participated by mail ($M = 68.2$ years; 50.5% male).

Table 1 shows social and medical characteristics for all participants separated for the two cohorts (5 and 10 years post diagnosis). In the cohort, 10 years post-diagnosis survivors had a higher household income ($p = 0.018$) and were more likely diagnosed with haematological cancer and less likely diagnosed with breast cancer ($p < 0.001$) compared to the 5-year cohort. We found no differences in sex, marital status and medical characteristics between the two cohorts ($p > 0.05$).

Fig. 1 Study profile and enrollment

Comorbid conditions

One in four long-term cancer survivors (23%) reported 7 or more comorbid conditions, on average survivors had 5 comorbid conditions (SD = 3.2) from the list of 18 conditions. Table 2 shows the number and the prevalence of comorbid conditions for both cohorts 5 and 10 years post-cancer diagnosis as well as for the frequent cancer diagnoses including breast, prostate, gynaecological, head and neck, as well as haematological cancers. We found no significant differences in the number of comorbid conditions between the two cohorts ($p = 0.219$). Across all tumour entities, hypertension, osteoarthritis, back pain and polyneuropathy were the most common comorbid conditions.

Health-related quality of life

In both cohorts, we found the highest symptom distress related to fatigue, sleep disturbances and pain (Table 3). There were no

significant differences in all quality of life dimensions between cancer survivors 5 and 10 years post-diagnosis. We compared the patients' quality of life to a representative gender- and age-matched comparison group from six European general population normative studies (male 52.9%; age group 60–69 years; $n = 16,151$) [27]. Long-term cancer survivors had lower values in all areas of quality of life than the general population, especially in everyday activities (role function), social life and psychological well-being (Table 3). Compared to the population, long-term cancer survivors reported higher physical symptom burden, especially fatigue, insomnia and pain.

Associations with demographic- and disease-related variables

To evaluate social and disease-related factors associated with quality of life and the level of morbidity of cancer survivors, we analysed the following variables: sex, age, time since diagnosis, cancer site, metastases/recurrence, second cancer disease

Table 1 Sample characteristics for both cohorts 5 and 10 years post-cancer diagnosis

		Total sample	5 years post-cancer diagnosis cohort	10 years post-cancer diagnosis cohort	<i>p</i>
		<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
Age, M (SD)		1002 (100)	660 (65.9)	342 (34.1)	
		66.7 (10.5)	66.3 (10.5)	67.6 (10.4)	0.052
	18–49 years	69 (6.9)	49 (7.4)	20 (5.8)	0.010
	50–70 years	468 (46.7)	325 (49.2)	143 (41.8)	
	71–85 years	465 (46.4)	286 (43.3)	179 (52.3)	
Sex	Male	530 (52.9)	350 (53.0)	180 (52.6)	0.947
Marital situation	Married	719 (72.0)	469 (71.4)	250 (73.3)	0.893
	Single	64 (6.4)	45 (6.8)	19 (5.6)	
	Divorced	110 (11.0)	75 (11.4)	35 (10.3)	
	Widowed	105 (10.5)	68 (10.9)	37 (10.5)	
Cohabiting	Yes	777 (79.8)	504 (78.9)	273 (81.5)	0.356
Education	Elementary school (8–9 years)	284 (28.4)	185 (28.1)	99 (29.0)	0.166
	Junior high school (10 years)	336 (33.6)	235 (35.7)	101 (29.6)	
	High school (13 years)	61 (6.1)	44 (6.7)	17 (5.0)	
	University	314 (31.4)	191 (29.0)	123 (36.1)	
	Other	5 (0.5)	4 (0.7)	1 (0.3)	
Employment status	Employed	204 (20.4)	136 (21.0)	68 (20.4)	0.847
	Retirement pension	665 (67.7)	436 (67.2)	229 (68.8)	
	Disability pension	92 (9.2)	63 (9.7)	29 (8.7)	
	Unemployed/housewife/househusband	20 (2.0)	13 (2.0)	7 (2.1)	
Household income	< 1500€	285 (28.5)	212 (32.1)	73 (21.4)	0.018
	1500–2500€	444 (44.4)	281 (42.6)	163 (47.7)	
	> 2500€	222 (22.2)	133 (20.1)	89 (26.0)	
Cancer diagnosis	Prostate	255 (25.5)	175 (26.5)	80 (23.5)	<0.001
	Breast	218 (21.8)	156 (23.6)	62 (18.2)	
	Gynaecological	95 (9.5)	59 (8.9)	36 (10.6)	
	Head and neck	78 (7.8)	53 (8.0)	25 (7.3)	
	Haematological	75 (7.5)	38 (5.8)	37 (10.9)	
	Skin	58 (5.8)	46 (7.0)	12 (3.5)	
	kidney	50 (5.0)	26 (3.9)	24 (7.0)	
	Colon	47 (4.7)	26 (3.9)	21 (6.2)	
	Other	125 (12.5)	81 (12.3)	44 (13.0)	
Medical data*	Cancer recurrence	106 (11.1)	63 (10.1)	43 (13.1)	0.193
	Metastases	104 (10.9)	75 (12.0)	29 (8.9)	0.156
	Second cancer disease	192 (19.6)	123 (19.1)	69 (20.6)	0.611
Treatment	Surgery	874 (91.9)	583 (92.7)	291 (90.4)	0.258
	Chemotherapy	363 (49.1)	241 (49.1)	122 (49.2)	0.977
	Radiotherapy	577 (68.9)	382 (68.5)	195 (69.9)	0.693
	Hormone therapy	190 (28.4)	137 (30.1)	53 (24.7)	0.168
Number of treatments	0–1	359 (36.1)	237 (36.2)	122 (36.0)	0.214
	2–3	529 (53.2)	338 (51.6)	191 (55.8)	
	≥ 4	106 (10.7)	80 (12.2)	26 (7.7)	

*Based on the self-reports of patients

and cancer treatment (ANOVA, Online Resource 1). Five years after cancer diagnosis, women had more comorbidities than men

($p < 0.001$). The prevalence of comorbid conditions increases with age in the 5- ($p < 0.001$) and 10-year cohort ($p < 0.001$).

Table 2 Comorbid conditions among the cohorts and the most frequent cancer entities

Comorbid condition	5 years post-diagnosis %	10 years post-diagnosis %	Frequent cancer entities				
			Prostate %	Breast %	Gynaecological %	Head and neck %	Haematological %
M (SD)	4.7 (3.2)	4.9 (3.2)	4.5 (3.2)	5.2 (3.0)	5.2 (3.3)	4.2 (3.5)	4.8 (3.3)
0	4.8	4.2	4.4	1.4	4.3	6.7	8.3
1–2	21.4	15.6	23.8	13.3	16.0	24.0	18.1
3–6	52.1	53.5	51.2	59.2	53.2	53.3	52.8
≥ 7	21.7	26.7	20.6	26.1	26.6	16.0	20.8
Hypertension	61.9	65.2	68.2	60.1	69.5	52.6	58.7
Osteoarthritis	61.0	62.5	65.1	67.0	63.2	44.9	54.7
Back pain	51.2	50.8	46.3	62.4	49.5	43.6	44.0
Polyneuropathy	43.1	44.7	39.2	47.2	45.3	35.9	54.7
Stomach problems	30.4	36.0	27.5	33.0	24.2	37.2	34.7
Thyroid disorder	26.8	23.4	13.7	35.3	37.9	29.5	16.0
Diabetes	24.7	27.0	25.1	19.3	29.5	21.8	26.7
Eye disease	24.5	31.8	29.4	22.5	33.7	24.4	28.0
Osteoporosis	24.2	21.6	17.3	38.1	23.2	14.1	21.3
Colon problems	21.7	26.1	16.9	23.4	30.5	15.4	22.7
Heart disease	17.4	18.9	22.0	11.9	23.2	17.9	17.3
Kidney disease	15.7	18.6	16.9	11.9	13.7	7.7	16.0
Lung disease	14.6	12.2	12.9	13.8	12.6	11.5	17.3
Psychological disease	14.3	15.3	8.2	22.9	12.6	14.1	16.0
Rheumatism	12.8	10.8	11.4	10.6	21.1	14.1	8.0
Asthma	10.0	10.1	9.8	14.2	10.5	5.1	6.7
Stroke	5.5	7.5	5.1	5.5	5.3	7.7	8.0
Neurological disease	4.3	6.9	5.5	4.1	4.2	7.7	6.7

Low disease stage without metastases or recurrence was associated with good quality of life in the 5-year cohort ($p < 0.001$). Patients with a second cancer disease showed more comorbidities ($p = 0.003$) and lower quality of life ($p < 0.001$) 5 years after diagnosis. Except surgery, all assessed cancer treatments in the past were associated with more comorbidities and lower quality of life 5 years after diagnosis ($p = 0.002 - < 0.001$). In the 10-year cohort, radio therapy in the past was associated with low quality of life ($p = 0.001$). Between quality of life and the level of morbidity, there was a significant correlation in all cancer survivors ($r = -0.489, p < 0.001$) and also in the most frequent cancer entities (prostate: $r = -0.524, p < 0.001$; breast: $r = -0.450, p < 0.001$; gynaecological: $r = -0.554, p < 0.001$; head and neck: $r = -0.432, p < 0.001$; haematological: $r = -0.433, p < 0.001$).

All variables with significant bivariate correlations with the dependent variables were included in the multiple linear regression models (Table 4). The explained variations of the regression models were in the middle range (23–25%).

Quality of life of the most frequent cancer entities decreased with higher number of comorbid conditions with

differences between the cohorts (Online Resource 2). In breast cancer survivors, health-related quality of life was most seriously impaired in all function scales ($M = 58.1 - 75.6$) and they had the highest symptom burden in fatigue ($M = 46.1$), pain ($M = 43.4$) and insomnia ($M = 48.0$) (Online Resource 3). Gynaecological cancer survivors showed low physical function (71.4), and had the highest symptom burden in dyspnea ($M = 29.8$). Head and neck cancer survivors reported highest appetite loss ($M = 16.0$) and financial difficulties ($M = 29.9$). Haematological cancer survivors showed lowest global quality of life ($M = 57.8$) and highest financial difficulties ($M = 30.6$). We found the highest quality of life in all function scales ($M = 75.4 - 83.9$) and lowest symptom burden ($M = 2.7 - 28.9$) in prostate cancer survivors.

Using linear regression models, we could show that a less invasive treatment positively affected physical health and quality of life. In the 5-year cohort, survivors who got radiotherapy (Beta = $-0.111; p = 0.003$) or chemotherapy (Beta = $-0.161; p < 0.001$) in the past showed reduced quality of life. Hormone therapy correlated with more comorbidities (Beta = $-0.167; p = 0.002$). Additional data are given in Online Resource 4.

Table 3 Quality of life (EORTC) in both cohorts 5 and 10 years post-cancer diagnosis in comparison to the European reference population (age group 60–69 years)

	5 years post-diagnosis <i>M</i> (<i>SD</i>)	10 years post-diagnosis <i>M</i> (<i>SD</i>)	Comparison 5 years–10 years <i>p</i>	Patients <i>M</i> (<i>SD</i>)	Population <i>M</i> (<i>SD</i>)	Comparison patients–population <i>p</i> *
Global quality of life	62.8 (22.3)	62.5 (21.5)	0.826	62.7 (22.0)	73.6 (19.6)	< 0.001
Functioning scales						
Physical	75.3 (21.3)	77.2 (21.0)	0.199	76.0 (21.2)	87.6 (15.1)	< 0.001
Role	67.1 (29.6)	68.8 (28.9)	0.404	67.7 (29.4)	85.7 (20.2)	< 0.001
Emotional	69.5 (25.5)	71.2 (24.5)	0.324	70.1 (25.2)	84.4 (19.7)	< 0.001
Cognitive	80.1 (21.6)	81.5 (21.5)	0.353	80.6 (21.6)	89.3 (14.5)	< 0.001
Social	70.0 (30.3)	72.0 (29.5)	0.325	70.7 (30.0)	90.3 (17.2)	< 0.001
Symptom scales						
Fatigue	38.4 (27.3)	35.8 (26.2)	0.146	37.5 (26.9)	19.6 (21.6)	< 0.001
Nausea/vomiting	5.1 (14.0)	4.9 (14.7)	0.866	5.0 (14.2)	2.5 (8.9)	< 0.001
Pain	31.8 (32.8)	29.8 (32.4)	0.369	31.1 (32.6)	21.2 (24.2)	< 0.001
Dyspnoea	23.5 (29.8)	23.0 (31.5)	0.821	23.3 (30.4)	12.9 (19.3)	< 0.001
Insomnia	37.1 (34.2)	32.6 (33.7)	0.051	35.6 (34.1)	19.4 (23.3)	< 0.001
Appetite loss	12.3 (24.1)	9.1 (20.6)	0.041	11.2 (23.0)	4.0 (13.3)	< 0.001
Constipation	10.7 (23.2)	12.0 (26.2)	0.440	11.1 (24.3)	6.0 (10.3)	< 0.001
Diarrhoea	9.9 (21.8)	9.2 (20.9)	0.642	9.7 (21.5)	4.5 (11.6)	< 0.001
Financial difficulties	19.9 (30.3)	16.6 (29.4)	0.101	18.8 (30.0)	6.5 (16.6)	< 0.001

M mean, *SD* standard deviation, *p* significance

*After Bonferroni correction $\alpha = 0.003$

Discussion

Also after the usual follow-up periods, long-term cancer survivors reported a substantial number of comorbid conditions and higher physical symptom burden than the general population. Similar to previous findings, the prevalence of comorbid conditions increases with age [10, 31]. The growing number of older survivors presents another major challenge to the healthcare system because older cancer survivors are more

likely to have multiple comorbid conditions and tend to experience poorer physical functioning than younger survivors [32].

In line with other study results, the most common symptoms were fatigue, sleep disturbances and pain [5, 11, 33, 34]. Fatigue is one of the most prevalent and most burdensome symptoms during long-term survival and persists years after treatment completion [33–36]. In a review of the literature about symptom burden and quality of life in survivorship, 21 to 35% of long-term survivors (minimum 5 years after

Table 4 Social- and disease-related predictors for comorbidities (criterion: comorbidity-index) and quality of life (criterion: EORTC–global quality of life) for both cohorts 5 and 10 years after cancer diagnosis

Social- and disease-related predictors	5 years post-diagnosis				10 years post-diagnosis			
	Comorbidity		Quality of life		Comorbidity		Quality of life	
	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>
Sex	0.115	0.001	0.067	0.172	−0.005	0.896	0.008	0.878
Cancer site	−0.048	0.165	0.043	0.374	0.017	0.621	0.081	0.100
Metastases/recurrence	0.030	0.378	0.107	0.028	0.051	0.139	0.010	0.836
Further cancer disease	0.044	0.208	0.037	0.443	−0.088	0.011	−0.002	0.970
Comorbidity	–	–	−0.477	< 0.001	–	–	−0.483	< 0.001
Quality of life	−0.471	< 0.001	–	–	−0.476	< 0.001	–	–
Adjusted R-square	24.4%		25.1%		24.4%		22.7%	

Beta standardised coefficient, *p* significance (alpha = 0.05)

diagnosis) experienced substantial fatigue [11]. Future research should especially focus on the topic fatigue to identify associations between fatigue symptomatology and cancer disease and treatment as well as other symptoms like insomnia and exhaustion. Sleep disturbance has also been presented as one of the main symptoms reported by cancer survivors [15, 33, 34]. In survivorship research, insomnia is often concurrent with fatigue; increased sleep disturbances were associated with higher symptoms of fatigue [34, 35, 37]. Prior studies showed a major impact of those common symptoms on overall quality of life in cancer survivors [11].

As reported in previous research, long-term cancer survivors of our study reported a significant lower health-related quality of life in comparison with individuals without a history of cancer—especially in everyday activities, social life and psychological well-being [38–41]. That result clearly demonstrated that a cancer disease not only increases the risk of long-term physical limitations, but can also affect the mental health. Survivorship-care-plans are also needed for psychoncological and psychosocial care, which go beyond the time of rehabilitation. The limited quality of life persisted with longer time since diagnosis [5]. Especially alarming should be the following observation: the greatest difference between long-term survivors and the population was the higher prevalence of financial difficulties in the survivors. This finding shows that cancer has a long-term negative impact on the patient's financial situation beyond treatment and aftercare. In addition to the problems of return to work after a cancer disease, there may also be long-term increased expenditure on health care, such as costs for medication or complementary treatments. This point should be explored more intensively in future studies.

Confirming previous research, we found a significant positive association between high quality of life and a low level of morbidity [20, 42]. A study about cancer survivors in the UK found that survivors who had another comorbidity in addition to their cancer were particularly at risk for reduced physical health and psychological well-being [43]. Physical health and quality of life was higher in survivors who had less invasive cancer treatments, low disease stage without metastases or recurrence and no second cancer disease. Results from the population-based PROFILES registry [25] also demonstrated a negative impact of the cancer treatment on comorbidity and quality of life in long-term cancer survivors; survivors who received chemotherapy reported more symptoms of neuropathy, and this seriously affected their quality of life [19, 44].

Limitations and strengths

Our study exclusively provides a detailed overview of the comorbid conditions and health-related quality of life in a sample of 1000 long-term cancer survivors. The sample size allows meaningful subgroup analyses (e.g. cancer type, sex, treatment). In addition to describing the prevalence of

comorbid conditions by demographic, cancer- and treatment-related variables, we assessed quality of life in comparison to a large representative gender- and age-matched comparison group from European general population normative studies.

Although our study has a number of strengths, there are also limitations. Due to the cross-sectional design of this analysis, we cannot determine whether cancer survivors are more likely to develop comorbid conditions after their diagnosis or whether they are pre-existing. Further, our study does not provide information about the severity of comorbid conditions.

Compliance with ethical standards

The research was approved by the local ethics committees. Prior to participation, all patients provided written informed consent. The study received research ethics committee approval by the University of Leipzig (Az. 070-14-10032014).

Conflict of interest The funding source was not involved in any stage of the research process. The authors declare that they have no conflict of interest.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Edwards BK, Noone A, Mariotto AB, Simard EP, Boscoe FP, Henley SJ, et al. Annual report to the nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. *Cancer*. 2014;120(9):1290–314.
2. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin*. 2016;66(4):271–89.
3. Bray F, Ren J, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *Int J Cancer*. 2013;132(5):1133–45.
4. de Moor JS, Mariotto AB, Parry C, Alfano CM, Padgett L, Kent EE, et al. Cancer survivors in the United States: prevalence across the survivorship trajectory and implications for care. *Cancer Epidemiol Biomark Prev*. 2013;22(4):561–70.
5. Arndt V, Koch-Gallenkamp L, Jansen L, Bertram H, Eberle A, Hollecsek B, et al. Quality of life in long-term and very long-term cancer survivors versus population controls in Germany. *Acta Oncol*. 2017;56(2):190–7.
6. Walsh K. Addressing psychosocial issues in cancer survivorship: past, present and future. *Future Oncol*. 2016;12(24):2823–34.
7. Salz T, Baxi S. Moving survivorship care plans forward: focus on care coordination. *Cancer Med*. 2016;5(7):1717–22.
8. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. *Int J Psychiatry Med*. 2010;40(2):163–81.
9. Hartung TJ, Brähler E, Faller H, Härter M, Hinz A, Johansen C, et al. The risk of being depressed is significantly higher in cancer patients

- than in the general population: prevalence and severity of depressive symptoms across major cancer types. *Eur J Cancer*. 2017;72:46–53.
10. Leach CR, Weaver KE, Aziz NM, Alfano CM, Bellizzi KM, Kent EE, et al. The complex health profile of long-term cancer survivors: prevalence and predictors of comorbid conditions. *J Cancer Surviv*. 2015;9(2):239–51.
 11. Wu H, Harden JK. Symptom burden and quality of life in survivorship: a review of the literature. *Cancer Nurs*. 2015;38(1):E29–54.
 12. Aziz NM. Cancer survivorship research: state of knowledge, challenges and opportunities. *Acta Oncol*. 2007;46(4):417–32.
 13. Knowles G, Haigh R, McLean C, Phillips HA, Dunlop MG, Din FVN. Long term effect of surgery and radiotherapy for colorectal cancer on defecatory function and quality of life. *Eur J Oncol Nurs*. 2013;17(5):570–7.
 14. Whitehead LC, Unahi K, Burrell B, Crowe MT. The experience of fatigue across long-term conditions: a qualitative meta-synthesis. *J Pain Symptom Manag*. 2016;52(1):131–143.e1.
 15. Brearley SG, Stamataki Z, Addington-Hall J, Foster C, Hodges L, Jarrett N, et al. The physical and practical problems experienced by cancer survivors: a rapid review and synthesis of the literature. *Eur J Oncol Nurs*. 2011;15(3):204–12.
 16. Savard J, Ivers H, Savard M, Morin CM. Cancer treatments and their side effects are associated with aggravation of insomnia: results of a longitudinal study. *Cancer*. 2015;121(10):1703–11.
 17. Vissers PAJ, Thong MSY, Pouwer F, Zanders MMJ, Coebergh JWW, van de Poll-Franse LV. The impact of comorbidity on health-related quality of life among cancer survivors: analyses of data from the PROFILES registry. *J Cancer Surviv*. 2013;7(4):602–13.
 18. Deimling GT, Arendt JA, Kypriotakis G, Bowman KF. Functioning of older, long-term cancer survivors: the role of cancer and comorbidities. *J Am Geriatr Soc*. 2009;57(Suppl 2):S289–92.
 19. Ezendam NPM, Pijlman B, Bhugwandass C, Pruijt JFM, Mols F, Vos MC, et al. Chemotherapy-induced peripheral neuropathy and its impact on health-related quality of life among ovarian cancer survivors: results from the population-based PROFILES registry. *Gynecol Oncol*. 2014;135(3):510–7.
 20. Weaver KE, Forsythe LP, Reeve BB, Alfano CM, Rodriguez JL, Sabatino SA, et al. Mental and physical health-related quality of life among U.S. cancer survivors: population estimates from the 2010 National Health Interview Survey. *Cancer Epidemiol Biomark Prev*. 2012;21(11):2108–17.
 21. Braithwaite D, Moore DH, Satariano WA, Kwan ML, Hiatt RA, Kroenke C, et al. Prognostic impact of comorbidity among long-term breast cancer survivors: results from the LACE study. *Cancer Epidemiol Biomark Prev*. 2012;21(7):1115–25.
 22. Husson O, Mols F, Ezendam NPM, Schep G, van de Poll-Franse LV. Health-related quality of life is associated with physical activity levels among colorectal cancer survivors: a longitudinal, 3-year study of the PROFILES registry. *J Cancer Surviv*. 2015;9(3):472–80.
 23. Vissers PAJ, Martucci RB, Mols F, Bours MJL, Winkels RM, Kampman E, et al. The impact of body mass index and waist circumference on health-related quality of life among colorectal cancer survivors: results from the PROFILES registry. *Nutr Cancer*. 2017;69(8):1177–84.
 24. Rowland JH, Kent EE, Forsythe LP, Loge JH, Hjorth L, Glaser A, et al. Cancer survivorship research in Europe and the United States: where have we been, where are we going, and what can we learn from each other? *Cancer*. 2013;119(Suppl 11):2094–108.
 25. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, Denollet J, Roukema JA, Aaronson NK, et al. The patient reported outcomes following initial treatment and long term evaluation of survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer*. 2011;47(14):2188–94.
 26. Danese MD, O'Malley C, Lindquist K, Gleeson M, Griffiths RI. An observational study of the prevalence and incidence of comorbid conditions in older women with breast cancer. *Ann Oncol*. 2012;23(7):1756–65.
 27. 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.
 28. Bayliss EA, Ellis JL, Steiner JF. Subjective assessments of comorbidity correlate with quality of life health outcomes: initial validation of a comorbidity assessment instrument. *Health Qual Life Outcomes*. 2005;3:51.
 29. Bayliss EA, Ellis JL, Steiner JF. Seniors' self-reported multimorbidity captured biopsychosocial factors not incorporated into two other database-based morbidity measures. *J Clin Epidemiol*. 2009;62(5):550–7.e1.
 30. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365–76.
 31. VanderWalde A, Hurria A. Early breast cancer in the older woman. *Clin Geriatr Med*. 2012;28(1):73–91.
 32. Avis NE, Deimling GT. Cancer survivorship and aging. *Cancer*. 2008;113(12 Suppl):3519–29.
 33. Ness S, Kokal J, Fee-Schroeder K, Novotny P, Satele D, Barton D. Concerns across the survivorship trajectory: results from a survey of cancer survivors. *Oncol Nurs Forum*. 2013;40(1):35–42.
 34. Romito F, Cormio C, Giotta F, Colucci G, Mattioli V. Quality of life, fatigue and depression in Italian long-term breast cancer survivors. *Support Care Cancer*. 2012;20(11):2941–8.
 35. Goldstein D, Bennett BK, Webber K, Boyle F, de Souza PL, Wilcken NRC, et al. Cancer-related fatigue in women with breast cancer: outcomes of a 5-year prospective cohort study. *J Clin Oncol*. 2012;30(15):1805–12.
 36. Bellury L, Pett MA, Ellington L, Beck SL, Clark JC, Stein KD. The effect of aging and cancer on the symptom experience and physical function of elderly breast cancer survivors. *Cancer*. 2012;118(24):6171–8.
 37. Brant JM, Beck S, Dudley WN, Cobb P, Pepper G, Miaskowski C. Symptom trajectories in posttreatment cancer survivors. *Cancer Nurs*. 2011;34(1):67–77.
 38. Husson O, Haak HR, Buffart LM, Nieuwlaat W, Oranje WA, Mols F, et al. Health-related quality of life and disease specific symptoms in long-term thyroid cancer survivors: a study from the population-based PROFILES registry. *Acta Oncol*. 2013;52(2):249–58.
 39. Schmidt ME, Chang-Claude J, Seibold P, Vrieling A, Heinz J, Flesch-Janys D, et al. Determinants of long-term fatigue in breast cancer survivors: results of a prospective patient cohort study. *Psychooncology*. 2015;24(1):40–6.
 40. Kent EE, Ambs A, Mitchell SA, Clauser SB, Smith AW, Hays RD. Health-related quality of life in older adult survivors of selected cancers: data from the SEER-MHOS linkage. *Cancer*. 2015;121(5):758–65.
 41. LeMasters T, Madhavan S, Sambamoorthi U, Kuriyan S. A population-based study comparing HRQoL among breast, prostate, and colorectal cancer survivors to propensity score matched controls, by cancer type, and gender. *Psychooncology*. 2013;22(10):2270–82.
 42. Faller H, Braehler E, Harter M, Keller M, Schulz H, Wegscheider K, et al. Performance status and depressive symptoms as predictors of quality of life in cancer patients. A structural equation modeling analysis. *Psychooncology*. 2015;24(11):1456–62.
 43. Elliott J, Fallows A, Staetsky L, Smith PWF, Foster CL, Maher EJ, et al. The health and well-being of cancer survivors in the UK: findings from a population-based survey. *Br J Cancer Suppl*. 2011;105(Suppl 1):S11–20.
 44. Mols F, Beijers T, Lemmens V, van den Hurk CJ, Vreugdenhil G, van de Poll-Franse LV. Chemotherapy-induced neuropathy and its association with quality of life among 2- to 11-year colorectal cancer survivors: results from the population-based PROFILES registry. *J Clin Oncol*. 2013;31(21):2699–707.