ACTA ONCOLOGICA, 2017
VOL. 56, NO. 2, 190–197
http://dx.doi.org/10.1080/0284186X.2016.1266089

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Quality of life in long-term and very long-term cancer survivors versus population controls in Germany

Volker Arndt[a,b], Lena Koch-Gallenkamp[a], Lina Jansen[a], Heike Bertram[c], Andrea Eberle[d], Bernd Holleczek[e], Sieglinde Schmid-Höpfner[f], Annika Waldmann[g], Sylke Ruth Zeissig[h] and Hermann Brenner[a,i,j]

[a]Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), Heidelberg, Germany; [b]German Cancer Research Center (DKFZ), Office of Cancer Survivorship Research, Heidelberg, Germany; [c]Cancer Registry of North Rhine-Westphalia, Münster, Germany; [d]Bremen Cancer Registry, Leibniz Institute for Prevention Research and Epidemiology – BIPS, Bremen, Germany; [e]Saarland Cancer Registry, Saarbrücken, Germany; [f]Hamburg Cancer Registry, Hamburg, Germany; [g]Institute of Social Medicine and Epidemiology, University Lübeck, Lübeck, Germany; [h]Cancer Registry Rhineland-Palatinate, Mainz, Germany; [i]Division of Preventive Oncology, German Cancer Research Center (DKFZ), Heidelberg, Germany; [j]German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany

ABSTRACT

Background: With the increasing number and diversity of cancer survivors, studies of survivors' physical, emotional, and social health are of growing importance. While there is a growing body of literature on the quality of life (QoL) of cancer patients during the early years past diagnosis, less is known regarding QoL in long-term survivors (LTS) (5 + years past diagnosis) and particularly in very long-term survivors (VLTS) (10 + years past diagnosis).
The objective of our study is to: (1) compare QoL of long-term cancer survivors and population norms; and (2) assess whether any deficits in QoL of survivors observed 5–10 years past diagnosis persist beyond the 10th year past diagnosis.
Methods: In total 6952 long-term cancer survivors (5–16 years past diagnosis of breast, colorectal, or prostate cancer) from Germany recruited in the context of the population-based CAESAR + study were compared with 1878 population-based controls without a history of cancer. QoL was assessed with the EORTC QLQ-C30. Differences in QoL between survivors and controls were assessed via multiple regression while controlling for age, gender, education, and case mix for survivors 5–9 years and 10 + years past diagnosis separately.
Results: Overall QoL in long-term cancer survivors was comparable to population norms but specific deficits in social, role, emotional, cognitive, and physical functioning and symptoms such as insomnia, fatigue, dyspnea, constipation, diarrhea, and financial difficulties were more prevalent in LTSs. Detriments in QoL persisted during the observation period and affected particularly cancer survivors at younger ages (<50 years). Non-significant aggravations in QoL with longer time since diagnosis were observed in very young and very old cancer survivors.
Conclusions: Detriments in health-related quality of life persist over more than a decade and affect predominantly younger patients. Improvements both in early and long-term follow-up care of cancer survivors seem warranted.

ARTICLE HISTORY
Received 22 August 2016
Accepted 14 November 2016

The long-term survival of most cancer patients has risen substantially during the last few decades and the majority of newly diagnosed cancer patients nowadays survive the disease. Due to improving prognosis and demographic aging, the number of cancer survivors is increasing. It is estimated that there are around 3.2 million cancer survivors in Germany, with over 60% being long-term survivors (LTSs) and a majority being older than 65 years [1]. Projections for the next 10–20 years predict 'a booming population of cancer survivors' with the biggest growth rate among the elderly (age 65 + years) [2]. However, many survivors continue to experience negative effects of cancer and its treatment on their daily lives well beyond the completion of therapy or experience detriments in physical and/or mental health which become apparent in the long run only. With the increasing number and diversity of cancer survivors, studies of survivors' physical, emotional, and social health and well-being are of growing importance [3].

Cancer is now considered a chronic disease which affects patient's life over many years [4–8]. Long-term health effects after cancer are multifaceted and comprise conditions such as osteoporosis, hypertension, heart failure, atherosclerosis, diabetes, hypothyroidism, cognitive dysfunction/dementia, or multiple cancers [4]. After adjustment for age, survivors 10–14 years past diagnosis report significantly higher total numbers of such conditions compared to those up to 10

CONTACT Volker Arndt v.arndt@dkfz.de German Cancer Research Center (dkfz), Division of Clinical Epidemiology and Aging Research (C070), Office of Cancer Survivorship Research (C071), Im Neuenheimer Feld 581, 69120 Heidelberg, Germany

Supplemental data for this article can be accessed here.

years past diagnosis. This increase in long-term effects most likely reflects treatment-related late complications [9]. Bothersome symptoms such as fatigue, depression, sleep disorders, and pain, are highly prevalent and have a major impact on overall quality of life (QoL) in short-term survivors as well as in LTSs [10]. QoL or even more specific and appropriate health-related quality of life (HRQoL) is a multidimensional concept which – although various definitions exist – usually involves physical, emotional, and social functioning.

While there is a growing body of literature on the physical, psychological, and social difficulties of cancer patients during the early years past diagnosis, less is known regarding QoL in LTSs [3,11]. Particularly in those survivors being 10+ years post-diagnosis, very little is known regarding QoL and late effects. It is evident that survivors continue to struggle with symptom burden and diminished QoL long into survivorship [10]. The literature, however, reveals some controversy when it comes to the question whether these deficits persist or even aggravate over time.

The objective of our study is to: (1) compare QoL of LTSs and population norms; and (2) assess whether any deficits in QoL of survivors observed 5–10 years past diagnosis persist beyond the 10th year past diagnosis.

Methods

Study design and study population

The study population was taken from the population-based CAESAR + study. The study was initiated in 2009 to investigate QoL in long-term (5+ years post-diagnosis) breast, colorectal, and prostate cancer survivors. Participants were identified and recruited via six German population-based cancer registries (Schleswig-Holstein, Hamburg, Bremen, Münster/North Rhine-Westphalia, Rhineland-Palatinate, and Saarland). Inclusion criteria were age 20–75 years at diagnosis and a histological confirmation of breast, colorectal, or prostate cancer during the calendar period 1994–2004. The cancer registries of Schleswig-Holstein and Rhineland-Palatinate have been established in the late 1990s. Therefore, these two registries were only able to recruit patients diagnosed from the year 2000 onwards. In addition, no colorectal cancer survivors could be recruited in Schleswig-Holstein due to logistic reasons. Of the 15 674 eligible contacted potential participants, 6952 filled in the full length questionnaire (response rate: 44%) and were included in this analysis.

Individual level QoL data from an independent sample of 2849 men and women recruited in 2013/2014 from the German general population served as external reference. Stratified by age group and sex, a total of 10 580 controls aged 18 + years were randomly selected via municipal registration offices from the general population of Germany. A questionnaire with detailed study information was mailed to potential sampled controls. The recipients were reminded by two follow-up reminder mails and a reminder phone-call (or another reminder via mail or home visit if necessary). The questionnaire included the EORTC QLQ-C30 and other internationally validated standard instruments to assess depression (Geriatric Depression Scale by Yesavage et al.), social support (Medical Outcomes Study Social Support Survey by Sherbourne and Stewart), social networks (Social Network Scale by Lubben et al.), concomitant diseases (modified version of Functional Comorbidity Index by Groll et al.), physical activity (Freiburg Questionnaire of Physical Activity by Frey et al.), and demographics. After exclusion of 425 short questionnaires respondents, 213 participants age <30 years, 39 participants age 90 years or older (to correspond to the age structure of the survivors population), and 294 participants with a self-reported history of cancer (except non-melanotic skin cancer), and 1878 participants remained as controls suitable for analysis. The sample of controls (response rate: 29%) was representative with respect to the regional distribution of the German population but persons with higher education were slightly overrepresented (data not shown).

Statistical analysis

For descriptive purposes survivors and controls were compared with respect to age, sex, nationality, education, marital status, having children, household size, and comorbidities (all items refer to time at survey). As the age and sex distribution of population controls reflects a stratified sampling scheme, direct standardization (with weights derived from the survivors' population) was employed.

Scoring of the EORTC QLQ-C30 was performed according to the EORTC scoring manual. All scores were linearly transformed to a 0–100 scale. Analysis of variance (ANOVA) and linear regression modeling were used to compare QoL of survivors and population controls adjusted for age, sex, and education. We considered education as a potential confounder as previous research indicated that low socioeconomic status (SES) is associated with poorer mental health in cancer survivors [12]. Survivors and controls also differed with respect to the distribution of occupation, household size, and comorbidities. However, as these characteristics reflect the situation at time of survey, at least some of these differences might also represent a consequence of cancer disease in case of survivors, and should therefore not be considered as confounders.

Least squares means of QoL scores were computed for survivors and controls adjusted for age, sex, education, and tumor type. Survivors were further stratified by time of diagnosis:

- 5–9 years post-diagnosis, denoted as LTS;
- 10+ years post-diagnosis, denoted as very long-term survivors (VLTS).

Finally, QoL within cancer survivors was compared by year since diagnosis with means adjusted for age, sex, education, tumor type, and extension of disease (according to the SEER staging scheme). As there were only eight participants having survived cancer for 16 years, they were included in the group of cancer survivors with 15 years since diagnosis (YSD) for this final analysis.

To reduce possible bias due to missing values (in general less than 10%), multiple imputation (Markov chain Monte Carlo method with 25 imputations) was employed before the

analyses. All analyses were performed using the SAS statistical software (Version 9.4). Differences in mean QoL scores larger than 10 points were considered clinically relevant [13]. A p value of 0.05 (two-sided) was chosen as level of statistical significance. p Values were not adjusted for multiple testing, so p values refer to the individual tests rather than a global test for differences.

Ethical approval

The study was approved by the internal review board (ethics committee) of the medical faculty of the University of Heidelberg and by all federal review boards accountable for the participating cancer registries.

All procedures involving human participants were in accordance with the Helsinki Declaration of 1975, as revised in 1983.

Results

Description of the study population

Sociodemographic characteristics of survivors and population controls are shown in Table 1. After adjustment for age and sex, survivors, and controls were comparable with respect to nationality, marital status, having children, living together with a spouse or in one-person households, history of stroke, angina pectoris, osteoporosis, and diabetes mellitus. Controls had higher proportions of subjects with 12 + years of education, and subjects reporting arthrosis and/or rheumatism. In contrast, survivors reported more often a history of depression than controls (17.3% vs. 13.5%).

Further characteristics of the population of cancer survivors are shown in Table 2. Overall, there were 3045 breast cancer survivors, 2403 prostate cancer survivors, and 1504 colorectal cancer survivors. Of the 6952 survivors, 1497 (21.5%) had survived cancer for 10+ years. These VLTS were slightly older than survivors having survived 5–9 years so far, and were characterized by a higher proportion of colorectal cancer survivors and a lower proportion of breast and prostate cancer survivors. The high proportion of VLTS with colorectal cancer represents an artifact due to disproportionate recruitment as described above. Distribution of stage was similar among VLTS and LTS whereas VLTS reported a higher proportion of disease recurrence than LTS (17.6% vs. 12.4%).

Table 1. Description of study population (after multiple imputation of missing values).

	Cancer survivors		Population controls			Difference[b]	
	n	%crude	*n*	%crude	%adj[a]	abs. %	*p*[a]
Total	6952	100.0	1878	100.0			
Age at survey							
30–49	253	3.6	502	26.7	3.6	–	–
50–59	788	11.3	365	19.4	11.3	–	–
60–69	2072	29.8	400	21.3	29.8	–	–
70–79	3165	45.5	344	18.3	45.5	–	–
80–89	674	9.7	267	14.2	9.7	–	–
Mean age (SD)	69.0	(8.9)	60.8	(14.9)			
Sex							
Male	3672	52.8	864	46.0	52.8	–	–
Female	3280	47.2	1014	54.0	47.2	–	–
German nationality	6861	98.7	1836	97.8	98.8	0.2	0.5974
Education							
≤9 years	3826	55.0	672	35.8	44.8	−10.2	<0.0001
10 years	1598	23.0	534	28.4	24.0	1.0	0.4673
12+ years	1528	22.0	672	35.8	31.2	9.2	<0.0001
Current marital status							
Single	301	4.3	226	12.0	5.6	1.3	0.0508
Married	5102	73.4	1245	66.3	70.2	−3.2	0.0268
Divorced	492	7.1	172	9.2	8.8	1.7	0.0647
Widowed	1057	15.2	235	12.5	15.3	0.1	0.8994
Living together with a spouse	5082	73.1	1392	74.1	74.2	1.1	0.4451
Having children	6037	86.8	1562	83.2	87.2	0.4	0.7372
Current household size							
1 person	1424	20.5	380	20.2	21.9	1.4	0.2816
2 persons	4730	68.0	946	50.4	64.9	−3.1	0.0358
3+ persons	798	11.5	552	29.4	13.2	1.7	0.0608
Comorbidities (self-reported history)							
Stroke	322	4.6	62	3.3	4.4	−0.2	0.7502
Myocardial infarction	384	5.5	67	3.6	4.5	−1.0	0.1879
Angina pectoris	924	13.3	159	8.5	11.3	−2.0	0.0779
Heart failure	909	13.1	161	8.6	11.4	−1.7	0.1544
Arthrosis	2274	32.7	529	28.2	36.2	3.5	0.0349
Rheumatism	523	7.5	153	8.1	10.1	2.6	0.0116
Osteoporosis	879	12.6	159	8.5	11.3	−1.3	0.2354
Diabetes mellitus	969	13.9	217	11.6	15.1	1.2	0.3449
Depression	1204	17.3	279	14.9	13.5	−3.9	0.0009
Other cancer disease	900	12.9	0	0.0	0.0	−12.9	<0.0001

[a]Adjusted to age and sex distribution of cancer survivors cohort.
[b]Difference in adjusted proportions among controls minus survivors.

Table 2. Characteristics of cancer survivors by time since diagnosis at recruitment.

	All cancer survivors		Survivors 5–9 years past diagnosis (LTS)			Survivors 10+ years past diagnosis (VLTS)			Difference VLTS-LTS	
	n	%crude	*n*	%crude	%adj[a]	*n*	%crude	%adj[a]	abs. %	*p*[a]
Total	6952	100.0	5455	100.0		1497	100.0			
Age at survey										
30–49	253	3.6	208	3.8	3.6	45	3.0	3.6	–	–
50–59	788	11.3	622	11.4	11.3	166	11.1	11.3	–	–
60–69	2072	29.8	1677	30.7	29.8	395	26.4	29.8	–	–
70–79	3165	45.5	2548	46.7	45.5	617	41.2	45.5	–	–
80–89	674	9.7	400	7.3	9.7	274	18.3	9.7	–	–
Mean age (SD)	69.0	(8.9)	68.7	(8.7)		70.5	(9.6)			
Sex										
Male	3280	47.2	2710	49.7	47.2	570	38.1	47.2	–	–
Female	3672	52.8	2745	50.3	52.8	927	61.9	52.8	–	–
Education										
≤9 years	3826	55.0	2972	54.5	54.7	854	57.0	55.1	0.4	0.7925
10 years	1598	23.0	1294	23.7	23.9	304	20.3	20.6	−3.3	0.0081
12+ years	1528	22.0	1189	21.8	21.4	339	22.6	24.3	2.9	0.0262
Tumor										
Breast	3045	43.8	2341	42.9	44.7	704	47.0	41.2	−3.6	<0.0001
Colorectal	1504	21.6	1030	18.9	18.9	474	31.7	33.6	14.7	<0.0001
Prostate	2403	34.6	2084	38.2	36.4	319	21.3	25.2	−11.2	<0.0001
Extension of disease										
Local	4652	66.9	3665	67.2	67.1	987	65.9	66.1	−1.0	0.5069
Regional	2168	31.2	1687	30.9	31.0	481	32.1	31.7	0.7	0.6165
Distant	132	1.9	103	1.9	1.9	29	1.9	2.2	0.3	0.5081
Disease recurrence (local or distant)	934	13.4	688	12.6	12.4	246	16.4	17.6	5.2	<0.0001

[a]Adjusted to age and sex distribution of total cancer survivors cohort.

Table 3. Quality of life in cancer survivors 5–16 years past diagnosis and population controls.

	Mean scores adjusted for sex and age								Mean scores adjusted for sex, age, and education							
	Survivors		Controls		Difference survivors-controls				Survivors		Controls		Difference survivors-controls			
QoL scale	Mean	SE	Mean	SE	Mean	95CL	95CU	*p*	Mean	SE	Mean	SE	Mean	95CL	95CU	*p*
Function scales																
Physical functioning	77.9	0.31	81.4	0.49	−3.5	−4.6	−2.4	<0.0001	78.9	0.32	81.9	0.49	−3.0	−4.1	−1.9	<0.0001
Emotional functioning	70.0	0.40	74.2	0.63	−4.2	−5.6	−2.8	<0.0001	70.9	0.42	74.6	0.63	−3.8	−5.2	−2.4	<0.0001
Cognitive functioning	78.0	0.37	82.2	0.58	−4.2	−5.5	−3.0	<0.0001	78.8	0.38	82.7	0.58	−3.8	−5.1	−2.6	<0.0001
Role functioning	70.4	0.47	76.5	0.73	−6.1	−7.7	−4.5	<0.0001	71.7	0.48	77.1	0.73	−5.5	−7.1	−3.9	<0.0001
Social functioning	74.7	0.46	83.3	0.71	−8.7	−10.2	−7.1	<0.0001	75.8	0.47	83.9	0.71	−8.1	−9.7	−6.5	<0.0001
Global health status/QoL	62.6	0.37	65.4	0.58	−2.8	−4.0	−1.5	<0.0001	63.9	0.38	66.0	0.57	−2.1	−3.4	−0.8	0.0011
Symptom scales																
Insomnia	36.1	0.54	30.3	0.84	5.8	4.0	7.7	<0.0001	35.1	0.55	29.8	0.84	5.3	3.4	7.1	<0.0001
Fatigue	35.4	0.42	31.1	0.66	4.3	2.8	5.7	<0.0001	34.6	0.43	30.7	0.66	3.9	2.4	5.3	<0.0001
Pain	30.6	0.49	30.1	0.77	0.4	−1.2	2.1	0.6076	29.2	0.50	29.5	0.77	−0.3	−1.9	1.4	0.7710
Dyspnea	26.0	0.48	19.7	0.74	6.3	4.6	7.9	<0.0001	24.8	0.49	19.2	0.74	5.6	4.0	7.3	<0.0001
Constipation	13.9	0.40	8.6	0.62	5.3	3.9	6.6	<0.0001	13.2	0.41	8.2	0.62	4.9	3.6	6.3	<0.0001
Diarrhea	12.8	0.36	6.0	0.57	6.8	5.5	8.0	<0.0001	12.5	0.38	5.9	0.57	6.6	5.3	7.8	<0.0001
Appetite loss	9.9	0.32	8.2	0.49	1.7	0.6	2.8	0.0019	9.4	0.33	7.9	0.50	1.4	0.4	2.5	0.0097
Nausea and vomiting	4.6	0.19	3.1	0.30	1.5	0.8	2.1	<0.0001	4.2	0.20	2.9	0.30	1.3	0.6	1.9	0.0001
Financial difficulties	16.3	0.42	9.8	0.65	6.4	5.0	7.9	<0.0001	15.0	0.43	9.3	0.65	5.8	4.3	7.2	<0.0001

95CL: 95% confidence interval (lower limit); 95CU: 95% confidence interval (upper limit); *p*: *p* Value referring to H0: QoL survivors = QoL controls; SE: standard error of mean.

Quality of life in survivors and controls

Overall, QoL in long-term cancer survivors was comparable to age-sex-matched population norms but deficits in social, role, emotional, cognitive, and physical functioning and in specific symptoms (insomnia, fatigue, dyspnea, constipation, diarrhea, and financial difficulties) were more prevalent in LTS 5–16 years past diagnosis (Table 3). All differences between survivors and controls were highly statistically significant when compared across all ages combined but not clinically relevant. Further adjustment for education decreased the difference in QoL between survivors and controls by around 10%.

Deficits in QoL among survivors were more prominent among younger age groups as indicated by age stratified analysis (Figure 1). This pattern was visible for all function scales and nearly all symptom scales (latter not shown; see Figure S1 for reviewing purposes). Clinically relevant deficits were observed in role functioning among survivors younger than age 50 and in social functioning among survivors younger than age 60 at time of follow-up. Prominent deficits in younger survivors when compared with controls were also found for cognitive functioning. These differences (Δ_{30-49}=9.9; Δ_{50-59}=7.9) did not reach the a priori defined threshold for clinical relevance.

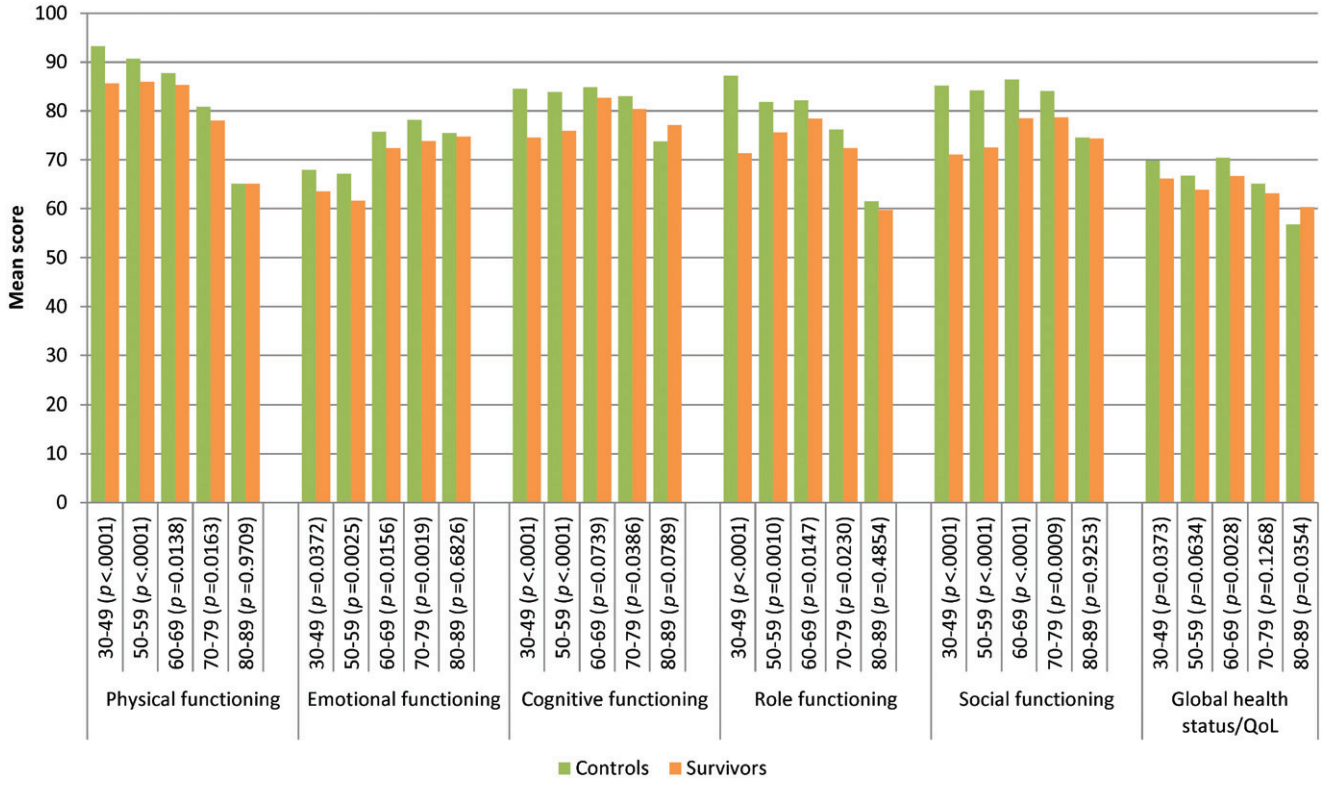

Figure 1. Age-specific quality of life in population controls and cancer survivors – EORTC QLQ-C30 function scales.
Note: Means are adjusted for age, sex, and education. *p* Values refer to H0: Mean QoL score among controls = Mean QoL among survivors.

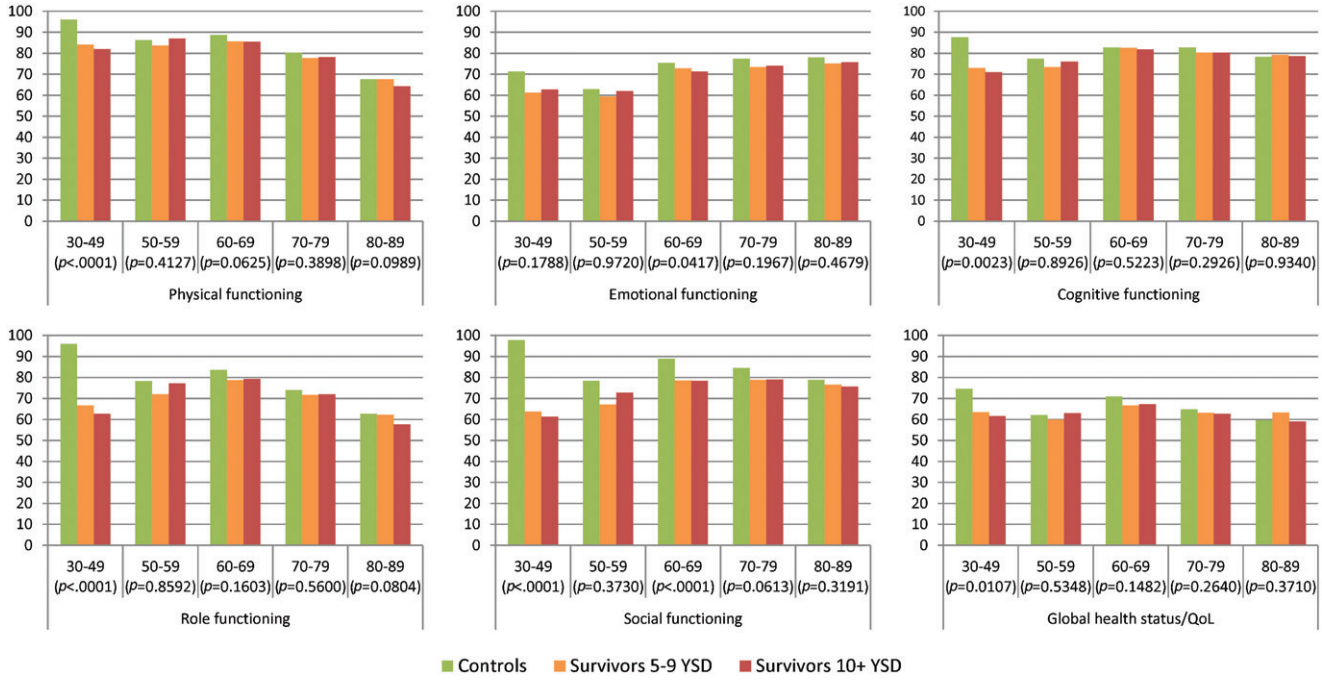

Figure 2. Age-specific quality of life in population controls and cancer survivors (mean scores) by time since diagnosis (EORTC QLQ-C30 Function scales).
Note: Y-axis: Mean QoL scores adjusted for age, sex, education, and tumor type. *p* Values refer to test of trend.

Quality of life according to time since diagnosis

Detriments in QoL persisted with longer time since diagnosis (Figure 2). Significant aggravations in QoL with longer time since diagnosis were observed in very young cancer survivors for physical, cognitive, role, and social functioning as well as overall health/QoL. Similarly, severity of certain symptoms (i.e. fatigue, pain, dyspnea, and financial difficulties) seemed to increase with longer time since diagnosis among very young cancer survivors (data not shown, see Figure S2 for reviewing purposes). No substantial change in QoL could be observed among other age groups.

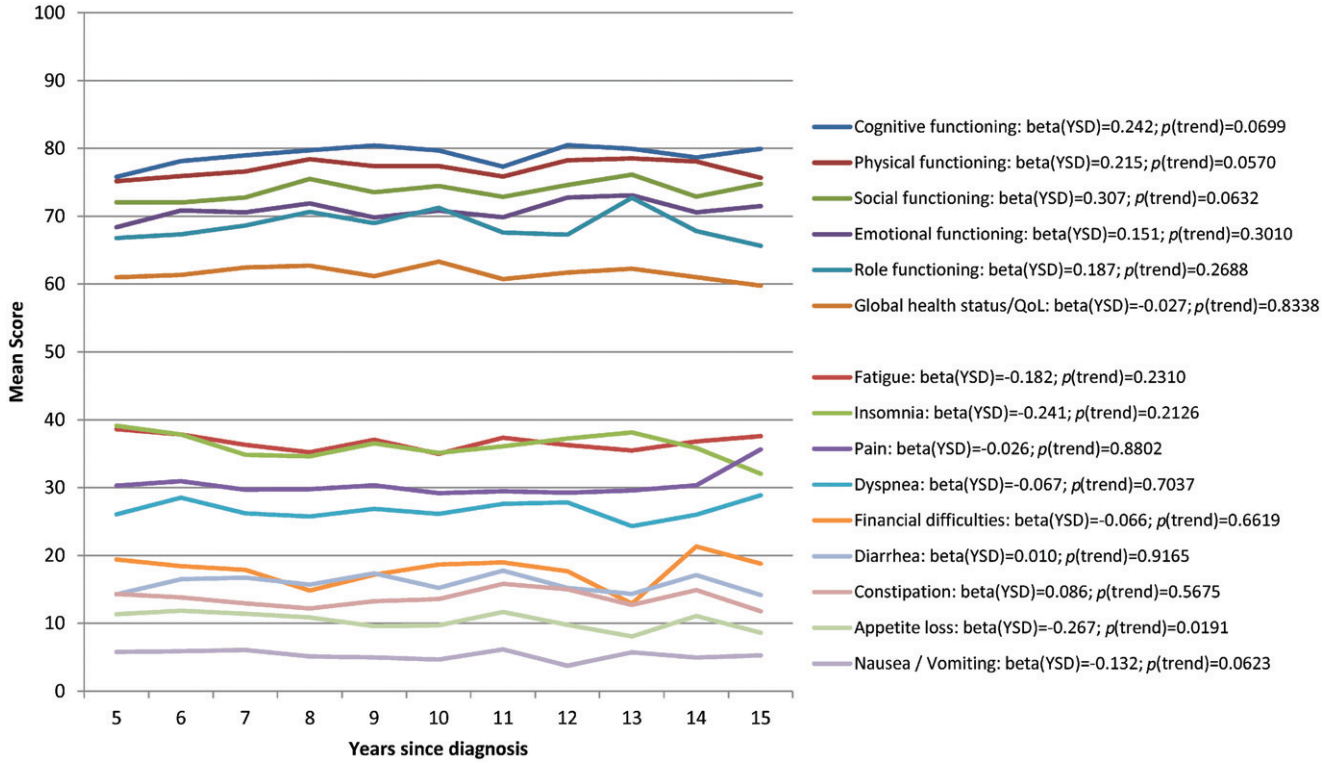

Figure 3. Quality of life in cancer survivors by years since diagnosis.
Note: Mean scores are adjusted for age, sex, education, tumor type, and extension of disease at time of diagnosis. *p* Values refer to test of trend in QoL.

Mean QoL scores in cancer survivors by year since diagnosis are displayed in Figure 3. The mean scores are adjusted for age, sex, education, tumor type, and extension of disease at time of diagnosis to account for case mix. Overall, QoL seems to be fairly constant between five and 15 years past diagnosis. Only one out of 15 scales, for instance appetite loss, exhibits a statistically significant trend (improvement) in QoL. In contrast, fatigue, insomnia, and pain seem to aggravate during the last years of the study period.

Discussion

Research on long-term sequelae of cancer survivors indicates that survivors can reach QoL levels comparable to those of the general population but that specific detriments mainly in the psychosocial domain persist [14–19]. Our large population-based study corroborates that overall QoL in long-term cancer survivors on average is comparable to population norms but that deficits in social, role, emotional, cognitive, and physical functioning as well as in specific symptoms and financial difficulties are more prevalent in LTSs. Overall, differences in QoL between survivors and controls were not clinically relevant when compared across all ages combined. However, deficits in QoL among survivors were more prominent among younger age groups. The influence of age on burden of disease is equivocal. Although overall burden of cancer may increase among the elderly, younger age groups may report higher demands of illness and view cancer as greater threat to their lives. In addition, younger patients may have fewer coping strategies and resources needed to manage a life-threatening disease like cancer whereas older persons consider their physical health in a different reference frame and tend to assess their health in terms of their age peers [20]. An alternative explanation might be that the differences between the findings in older and younger survivors result from differences in treatment as older cancer patients often receive less aggressive therapy than younger patients.

Detriments in QoL persisted or even aggravated with longer time since diagnosis, particularly in very young and very old cancer survivors. Survivors 10–14 years since cancer diagnosis are reporting significantly higher total numbers of health problems compared with those only 4–9 years past diagnosis [9]. Although younger age at diagnosis is often associated with more distress and poorer mental health, older cancer survivors represent a vulnerable population because late effects of cancer and its treatment could easily be attributed to advancing age and potentially be dismissed. In the elderly, geriatric syndromes such as hearing trouble, urinary incontinence, falls, depression, and osteoporosis are more prevalent among cancer survivors than controls [9].

Across all age groups combined, QoL seemed to be fairly constant between Year 5 and Year 15 past diagnosis. This finding is in line with a recent report from Italy based on 265 long-term cancer survivors [17]. However, our results as well as the findings from the Italian study are derived from panel comparisons which are prone to potential survival bias. The latter presumably underestimates detriments in the long run as those patients dying during the early years in the presented period will tend to have poorer QoL and more symptoms than those surviving longer. Although we tried to

minimize risk of survival bias by careful adjustment for tumor type and stage at time of diagnosis, our findings have to be interpreted with caution. Also, potential effect modification by tumor type has to be discussed. For example, previous research has indicated that QoL tends to decrease over time for prostate cancer survivors, whereas QoL improves with time for breast cancer survivors [16,21]. However, recent findings from our group based on a subsample of our study subjects with repeated measurements revealed that detriments in various QoL dimensions aggravated from Year 5 to 10 in breast [18] and in older colorectal cancer survivors [19]. Further large-scale longitudinal studies with repeated measurements of QoL and other clinically important outcomes such as recurrences of disease and late effects are warranted.

Studies comparing QoL in cancer survivors with some external population are usually limited to aggregate level data from population norms stratified by age and sex without taking account of potential confounding by SES. Ignoring differences in education between survivors and controls is very likely to result in overestimation of a potential difference in QoL as lower SES is proportionally more common among cancer patients than among controls. Adjusting for education as a robust proxy for SES attenuated the difference in QoL between survivors and controls in our study by about 10%. A history of cancer was reported by over 10% of all controls. As a history of cancer is very likely to reduce QoL, we included only controls without history of cancer. We also minimized the risk of potential bias due to different modes of administration (e.g. in-person interviews versus paper-pencil) [22] as we only included data from survivors and controls based on paper-pencil questionnaires. Also, period effects [18,19] are very unlikely in our study given the short time lag between data collection in survivors (mainly 2010/2011) and controls (2013/2014). Statistical significance was set at $p < 0.05$ and no further adjustment for multiple testing was employed. As most of our results are significant on the $p < 0.001$ level, chance findings are very unlikely to explain the pattern of our results.

A limitation of our study is the response rate of 44%, although it is comparable or even higher than the response rate of other studies examining LTS [23–25]. In general, elderly survivors and those with certain medical conditions, with a longer time period since diagnosis, or poorer health are less likely to participate in cancer survivorship studies. This non-response pattern might result in an overestimation of the observed QoL in participating survivors, which in turn corresponds to an underestimation of the true difference between survivors and controls. Likewise, non-participation among controls might also introduce bias. As described in the methods section, persons with higher education were slightly overrepresented. As all our comparisons between survivors and controls were adjusted for education, the potential bias arising from higher participation among better educated should be limited.

Overall, the CAESAR + study is one of the worldwide largest studies on LTS. By including survivors recruited via multiple population-based cancer registries a sufficient number of cases for subgroup specific analyses are available and a high level of generalizability of the results can be assumed.

Conclusions

Although overall QOL in long-term cancer survivors is comparable to population norms, deficits in role, emotional, cognitive, and social functioning as well as in specific symptoms and financial difficulties are more prevalent in LTS and persist over more than a decade after diagnosis of cancer. Although the mean difference between survivors and controls do not appear to be clinically relevant, a substantial proportion of survivors is suffering from long-lasting detriments in QoL. Improvements in long-term follow-up care seem warranted and should primarily aim to improve psychosocial needs of cancer survivors. In addition, psychosocial needs should already be addressed in early phases of follow-up care in order to prevent long-lasting manifestation of psychosocial problems.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by two grants from the German Cancer Aid [No. 108262 and 110231].

ORCID

Volker Arndt http://orcid.org/0000-0001-9320-8684
Lina Jansen http://orcid.org/0000-0001-8004-4940
Andrea Eberle http://orcid.org/0000-0003-4195-5236
Annika Waldmann http://orcid.org/0000-0002-5909-9936
SylkeRuth Zeissig http://orcid.org/0000-0002-0743-6128

References

[1] Bertz J, Dahm S, Haberland J, et al. Verbreitung von Krebserkrankungen in Deutschland. Entwicklung der Prävalenzen zwischen 1990 und 2010. Berlin: Robert Koch-Institut; 2010.
[2] Parry C, Kent EE, Mariotto AB, et al. Cancer survivors: a booming population. Cancer Epidemiol Biomarkers Prevent. 2011;20:1996–2005.
[3] Thong MS, Mols F, Stein KD, et al. Population-based cancer registries for quality-of-life research: a work-in-progress resource for survivorship studies? Cancer. 2013;119:2109–2123.
[4] Khan NF, Mant D, Carpenter L, et al. Long-term health outcomes in a British cohort of breast, colorectal and prostate cancer survivors: a database study. Br J Cancer. 2011;105:S29–S37.
[5] Harrington CB, Hansen JA, Moskowitz M, et al. It's not over when it's over: long-term symptoms in cancer survivors-a systematic review. Int J Psychiatry Med. 2010;40:163–181.
[6] Foster C, Wright D, Hill H, et al. Psychosocial implications of living 5 years or more following a cancer diagnosis: a systematic review of the research evidence. Eur J Cancer Care. 2009;18:223–247.
[7] Fossa SD, Vassilopoulou-Sellin R, Dahl AA. Long term physical sequelae after adult-onset cancer. J Cancer Surviv. 2008;2:3–11.
[8] Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. Cancer. 2008;112:2577–2592.
[9] Leach CR, Weaver KE, Aziz NM, et al. The complex health profile of long-term cancer survivors: prevalence and predictors of comorbid conditions. J Cancer Surviv. 2015;9:239–251.

[10] Wu HS, Harden JK. Symptom burden and quality of life in survivorship: a review of the literature. Cancer Nurs. 2015;38: E29–E54.
[11] Lerro CC, Stein KD, Smith T, et al. A systematic review of large-scale surveys of cancer survivors conducted in North America, 2000–2011. J Cancer Surviv. 2012;6:115–145.
[12] Aarts MJ, Mols F, Thong MS, et al. Long-term prostate cancer survivors with low socioeconomic status reported worse mental health-related quality of life in a population-based study. Urology 2010;76:1224–1230.
[13] Osoba D, Rodrigues G, Myles J, et al. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol. 1998;16:139–144.
[14] Annunziata MA, Muzzatti B, Giovannini L, et al. Is long-term cancer survivors' quality of life comparable to that of the general population? An Italian study. Support Care Cancer. 2015;23:2663–2668.
[15] Drummond FJ, Kinnear H, O'leary E, et al. Long-term health-related quality of life of prostate cancer survivors varies by primary treatment. Results from the PiCTure (Prostate Cancer Treatment, Your Experience) Study. J Cancer Surviv. 2015;9:361–372.
[16] Hsu T, Ennis M, Hood N, et al. Quality of life in long-term breast cancer survivors. J Clin Oncol. 2013;31:3540–3548.
[17] Muzzatti B, Flaiban C, Surbone A, et al. Quality of life profile in Italian long-term cancer survivors. Qual Life Res. 2015;24:959–967.
[18] Koch L, Jansen L, Herrmann A, et al. Quality of life in long-term breast cancer survivors – a 10-year longitudinal population-based study. Acta Oncol. 2013;52:1119–1128.
[19] Jansen L, Herrmann A, Stegmaier C, et al. Health-related quality of life during the 10 years after diagnosis of colorectal cancer: a population-based study. J Clin Oncol. 2011; 29:3263–3269.
[20] Wenzel LB, Fairclough DL, Brady MJ, et al. Age-related differences in the quality of life of breast carcinoma patients after treatment. Cancer. 1999;86:1768–1774.
[21] Bloom JR, Petersen DM, Kang SH. Multi-dimensional quality of life among long-term (5+ years) adult cancer survivors. Psycho-Oncology 2007;16:691–706.
[22] Gundy CM, Aaronson NK. Effects of mode of administration (MOA) on the measurement properties of the EORTC QLQ-C30: a randomized study. Health Qual Life Outcomes. 2010;8:35.
[23] Smith T, Stein KD, Mehta CC, et al. The rationale, design, and implementation of the American Cancer Society's studies of cancer survivors. Cancer. 2007;109:1–12.
[24] Geller BM, Mace J, Vacek P, et al. Are cancer survivors willing to participate in research? J Community Health. 2011;36: 772–778.
[25] Barg FK, Cronholm PF, Straton JB, et al. Unmet psychosocial needs of Pennsylvanians with cancer: 1986–2005. Cancer. 2007;110:631–639.