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Physical condition, nutritional status, fatigue, and quality of life in oncological out-patients

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Abstract

Objective: Early detection of limited physical activity and nutritional deficiencies in cancer survivors could contribute to early treatment and preservation of quality of life. The aim of this study is to describe the association of physical condition and nutritional status with fatigue and quality of life in oncological out-patients.

Methods: Data in this descriptive study was collected on bioelectrical impedance analysis, postural stability (stability index), body mass index, Karnofsky Index, quality of life (Short-Form 36-Item Health Survey) and fatigue (multidimensional fatigue inventory-20) in a consecutive sample of 203 oncological out-patients. Phase angle was calculated from bioelectrical impedance analysis. Values were intercorrelated and compared to appropriate standard values.

Results: Phase angle and stability index outcomes were far below the values of a healthy population of similar age ($p < 0.001$). Quality of life was significantly lower than in the normal population ($p < 0.001$), and the level of fatigue was significantly higher ($p < 0.001$). Phase angle correlated with Karnofsky Index ($p = 0.002$) and Short-Form 36-Item Health Survey Summary physical function ($p < 0.001$). Furthermore, multidimensional fatigue inventory-20 scales 'physical fatigue' and 'reduced activity' were significantly associated with phase angle ($p = 0.04$, $p = 0.005$). Stability indices correlated with Short-Form 36-Item Health Survey physical function.

Conclusion: The physical condition and the nutritional status are key components determining the individual quality of life of oncological out-patients. These variables also showed an association with the manifestation of fatigue. Results highlight the need for interdisciplinary cooperation to detect physical, nutritional and psychological deficiencies in oncological out-patients.

Keywords

Lifestyle medicine, cancer survival, bioelectrical impedance analysis, quality of life, fatigue, exercise, nutrition

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Background

Cancer diagnosis and the subsequent treatment are often associated with a reduced physical performance and a decrease of physical well-being. Typical characteristics are, inter alia, significant weight loss and cachexia. Data on the prevalence of malnutrition broadly vary depending on evaluation criteria, such as tumour type, site and extension, as well as cancer treatment. The prevalence of malnutrition among cancer patients is estimated between 15% and 80%.[1] Those particularly affected by malnutrition are patients with cancer in head and neck regions, the gastrointestinal tract and pancreatic cancer. Main symptoms comprise weight loss and asthenia of varying degrees. Even before starting cancer

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treatment, patients can experience profound metabolic and physiological alterations with an increased need of macro- and micronutrients.[2] Malnutrition can influence the effectiveness and success of chemotherapy, radiotherapy, and cancer-related surgery due to changes in metabolism, pharmacokinetics and healing dynamics. Moreover, malnutrition seems to be responsible for changes in absorption, protein binding, hepatic metabolism and renal elimination of drugs and their metabolites.[1,2]

However, there are also cancer patients with a high body mass index (BMI). For example, Gioulbasanis et al.[3] examined 1469 patients with metastatic cancer primaries. Of these, 594 (41.9%) were overweight or obese. Overweight and obese individuals are at a greater risk of cancer of the breast, colon, endometrium, gallbladder, oesophagus, pancreas and kidneys.[3,4]

Both conditions do impact on the health-related quality of life (QoL). The effects of malnutrition or cancer-related anorexia and cachexia can range from general fatigue to an increased risk of infection, impaired wound healing, greater risk of osteoporosis and fractures due to falls. Furthermore, it can lead to poorer performance and contribute to muscle wasting and reduced mobility.[4,5] Depending on the type, up to 40% of cancer patients die of progressive malnutrition.[5] An excess of body fat, however, can also impair health-related QoL during treatment and cancer survival. Frenzel et al.[6] assessed 70 women with breast cancer undergoing chemotherapy. Of these, 73% showed an excess of body fat. Those women with excess of body fat had a significantly lower general health-related QoL score compared to those with normal body fat.

Obese cancer patients face more side effects, a greater risk of tumour recurrence and reduced QoL than patients with the same cancer type but normal body weight.[7,8] Fatigue is a variable and frequent symptom in cancer patients. Apart from a marked exhaustion and cognitive as well as emotional constraints, typical indicators also include general weakness and low physical ability.[9] The negative impact of fatigue on the QoL of cancer patients is widely acknowledged.[10,11] Fatigue is associated with a higher BMI, higher waist circumference and less physical activity.[12]

In turn, obesity and inactivity contribute to poorer QoL among cancer survivors. Furthermore, fatigue and reduced QoL are also associated with anorexia resulting from changes in metabolism, obstructions, vomiting, diarrhoea or difficulties in swallowing.[13,14] Malnutrition may cause abnormal muscle function due to a lack or an imbalance of essential metabolites and a loss of muscle mass.

It is difficult to determine an impending malnutrition or loss of muscle mass by merely assessing the BMI. Malnutrition results in an imbalance of body fluids and a change in cell membranes.[15] Therefore, bioelectrical impedance analysis (BIA) plays an important role in measuring the nutritional status among cancer patients.[16] Phase angle (PA), as one of the parameters obtained from BIA, can be understood as a marker of the fluid distribution between the intra- and extra-cellular medium and can be considered an additional tool to detect malnutrition.[17] In their study with patients suffering from lung cancer, Toso et al.[18] were able to demonstrate that changes in BIA values occurred prior to a clinically manifest cachexia and that these changes had a greater significance in relation to mortality than any weight loss. Similar results were found in patients with pancreatic cancer or cancer of the colon. In these cases, PA proved to be a better predictor of survival time than age, the stage of the tumour, albumin levels or the nutritional status according to the Subjective Global Assessment.[19,20]

Santarpia et al.[21] demonstrated an association between survival time and PA in advanced cancer patients. In this study, patients with low PA scores had a significantly shorter survival than those with higher PA scores.

Malnutrition or cancer-related anorexia and cachexia lead to poorer performance and contribute to muscle wasting, fatigue and reduced mobility.[5] Winters-Stone et al.[22] demonstrated that breast cancer survivors revealed reduced muscle strength associated with cancer-related symptoms. Chemotherapy, hormonal therapy, as well as muscle weakness and difficulty in balance and walking have been linked to falls in cancer survivors.[23,24]

Compared to healthy individuals, breast cancer survivors demonstrated poorer postural stability, when tested within 30 days after completing chemotherapy.[25] Postural stability requires the interaction of musculoskeletal and sensory systems.[26]

The musculoskeletal component of postural stability includes the biomechanical properties of body segments, muscles and joints. The sensory component incorporates vision, vestibular function and somatosensation, which act to inform the brain of the position and movement of the body in three-dimensional space.[26] Postural stability can be defined as the ability of an individual to maintain the position of the body, or more specifically, its centre of mass, within specific boundaries of space, referred to as stability limits. Stability limits are boundaries in which the body can maintain its position without changing the base of support.[26] This definition of postural stability is useful as it highlights the need to discuss stability in the context of a particular task or activity, for example, regarding the prevention of falls. In a study among elderly cancer survivors (67.9 ± 8.8 years), more than half of participants (54%) had experienced at least one fall in the past 12 months and 30% had experienced two or more falls.[27] It was demonstrated that falls are a significant problem, and balance control is a determinant of perceived physical function and well-being.

In turn, muscular and balance training in older or chronically fatigued patients can prevent falls, reduce fatigue and contribute to a better functional state of the patient.[28]

The vicious circle of reduced physical performance, fatigue symptomatology and decreased QoL (see Figure 1) is frequently recognised in the treatment of oncological disorders.

An early recognition of both nutritional deficiencies and reduced physical ability could potentially contribute to a

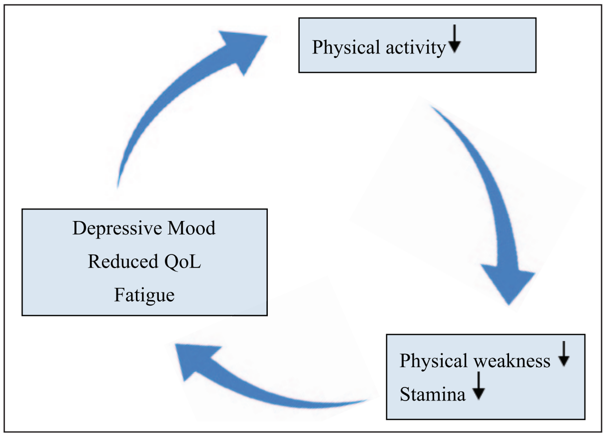

Figure 1. Vicious circle of reduced performance.

preservation of physical resources in tumour patients during all phases of therapy, thus breaking the vicious circle delineated in Figure 1.

Relatively little, however, is known about the association of fatigue and QoL with variables reflecting malnutrition and postural stability. The objective of this cross-sectional correlational study, therefore, is to identify and demonstrate the relation of physical variables (BMI, PA, and stability index) to the Karnofsky Index (KI), QoL and fatigue.

Methods

Participants

This study and its consent procedure were approved by the Ethics Committee of the Medical Council of Hamburg (PV 4620). Written informed consent was obtained from all patients before enrolment. Due to a lack of current data, a descriptive research design was used to describe characteristics of oncological out-patients with the aim to gain a better understanding of the topic.

Oncological out-patients treated at eight out-patient centres in the north of Germany were recruited in a consecutive convenience sample of oncological out-patients irrespective of tumour type, stage of illness, and kind of therapy. Prerequisite for the voluntary participation was an adequate knowledge of the German language.

Patients were excluded from participation either due to their age (only under age, but no other age limitation), due to existing disability, or due to acute strong emotional stress at the time of the study. Regardless of study participation, all oncological out-patients of the centres were offered a nutritional guidance session.

Statistical analysis

In order to detect mean differences/linear relationships between our sample and appropriate standard values from the general healthy population, a one-sample t-test and a correlation analysis using Pearson correlation coefficient (r) were applied. The considered appropriate standard values refer to age groups corresponding to the sample and were retrieved from current literature. The significance value was set at alpha 0.05. Power analysis considering one-sample t-test with a small effect size ($d \geq 0.20$), an alpha of 0.05 and a power of 0.80, revealed a minimal sample size of 199 patients. With this sample size, we are also able to detect Pearson correlations $r \geq 0.20$ (alpha 0.05 and power 0.80). The statistical analysis was performed using the statistical software SPSS 18 (PASW 18, IBM).

Anthropometric measurements

Phase angle. BIA was conducted by trained nutritional scientists. Patients were positioned in a relaxed horizontal position using the Model Data Input Nutriguard-MS, Data Input, Pöcking, Germany. Two gel electrodes were applied to the patient's right hand and right foot. Electrodes on the hand were aligned with the main surface on the soft tissue between the second and third metacarpal and above the fissure of the wrist. On the foot, they were attached to the soft tissue between the second and third metatarsal and the back of the foot in a horizontal line to the inner ankle. Data of sex, height, weight and age were added to the software. PA was calculated by the direct ratio between resistance (R) and reactance (Xc). R and Xc were directly measured in Ohms at 50 kHz, 800 µA. PA was obtained using the following formula: PA = arcTAN (Xc /R).

PA is a marker of the amount and quality of soft tissue mass as well as hydration status. PA has been described as a prognostic tool in cancer research.[29,30] The optimal value for men in the age group 18 to 29 years lies between 6.0° and 7.7°, for middle aged men (30–59 years) between 5.6° and 7.4° and for men in the elderly age group (>60 years) between 4.7° and 6.6°.[31] Considering women, the optimal value of PA lies between 5.2° and 6.8° for the age group 18–29 years, as well as for women between 30 and 59 years and 4.7° and 6.4° for elderly women over 60 years.[31]

MFT S3-Check. The MFT S3-Check is a test device for the functional assessment of balance ability and postural stability.[32] The test system consists of an unstable, uniaxial platform with an integrated sensor and corresponding software. The round platform has a diameter of 55 cm and is connected to a base plate with a horizontal axis. It can be tilted up to 12° to both sides. Movements of the test participant's centre of gravity cause the platform to tilt. This tilt is measured by a tilt sensor, which has a range of +20° to −20° and an accuracy of 0.5°. Data was collected at a sampling rate of 100 Hz and was transmitted to the software via an USB port that also served as a power source (5 V). Two different test directions could be measured by simply turning the testing system 90°. If the axis of rotation corresponded to the sagittal plane, this movement was referred to as 'left-right measurement'. If the axis of rotation corresponded to the frontal plane, the movement was referred to as 'front-back measurement'. The tests were conducted in both directions, and for each test direction the system calculated the *stability index* (SI; SI left/right and SI front-back). For the calculation of the SI, the test system incorporates the number and magnitude of movements of the platform as well as the deviation from the horizontal position of the platform (left/right or front/back).[32]

The MFT S3-Check fulfils reliability and validity criteria and is used in fitness and physiotherapy settings.[33–35] Additionally, age- and sex-related standard values were generated from the data of more than 5000 subjects (8–70 years of age).[32] As the test device was not available at all cooperating centres, only a subsample of patients (n = 44) was measured in this study.

Psychometric methods

Karnofsky Index

The Karnofsky Index (KI)[36] estimates limitations in activity, self-reliance and self-determination in patients with malign tumours. It is a general measure of patients' independence and has been widely used as a general assessment tool for cancer patients. The scale ranges from a maximum of 100 percent (no limitations) to 0 percent (death). Data was collected by trained nutritional scientists.

Short-Form 36-Item Health Survey

The Short-Form 36-Item Health Survey (SF-36)[37] includes multi-item scales which assess eight health concepts: (1) limitations in physical activities due to health problems; (2) limitations in social activities due to physical or emotional problems; (3) limitations in usual role activities due to physical health problems; (4) physical pain; (5) general mental health (psychological distress and well-being); (6) limitations in usual role activities due to emotional problems; (7) vitality (energy and fatigue) and (8) general health perceptions. Each dimension is directly transformed into a 0–100 scale. Physical component summary (PCS) and mental component summary (MCS) subscales were calculated using norm-based scoring methods.[37] The lower the score, the lower the QoL, that is, a score of 100 is equivalent to the best QoL. The SF-36 scale is a reliable and valid instrument. It is gaining increasing importance in evaluating the usefulness of medical therapies and is widely used in oncological settings.

Multidimensional fatigue inventory

The Multidimensional fatigue inventory (MFI)-20[38] is the internationally most utilised tool for the measurement of fatigue. It allows the interindividual and intraindividual comparison of the extent, type and intensity of fatigue. The MFI comprises five dimensions, that is, 'general fatigue', 'physical fatigue', 'reduced activity', 'reduced motivation', and 'mental fatigue'. Each subscale contains four items, the scores per item run from 1 to 5. Scores per scale can range from a minimum of 4 to a maximum of 20. A higher score indicates more fatigue. The MFI-20 is a reliable and valid instrument to assess fatigue in cancer patients.[39]

Results

The sample comprised 203 oncological out-patients from eight oncological out-patient centres in Northern Germany. Of the 203 participants, 54.7% were female (n = 111) and 45.3% male (n = 92). The average age was 64.1 years (standard deviation (SD) = 11.3 years).

The number of study participants in the age group 20–65 years was lower (n = 93) than those in the age group of participants from 66 to 90 years (n = 110). With 97 patients, gastrointestinal tumours were most frequent in this sample, followed by 55 patients suffering from gynaecological or breast tumours. Other types included 22 haematological tumours, 18 tumours of the respiratory tract, and 11 urological tumours. As shown in Table 1, 143 participants (70.4%) were married, 157 participants (77.7%) had at least one child and more than half of the patients were retired mostly due to their age over 65 years (n = 117, 57.6%; Tables 1 and 2).

Physical data

The average BMI among female patients was 25.3 kg/m^2 (SD = 7.3), and 24.4 kg/m^2 (SD = 4.8) among males (Table 4). In this study, only less than half of the participants (42.5%) showed normal BMI values appropriate to their age group.

The overall mean PA was 4.7° (SD = 0.8), 4.9° (SD = 0.9) for men (5th and 95th percentiles: 3.3, 6.6) and 4.6° (SD = 0.8) for women (5th and 95th percentiles: 3.3, 5.9). As displayed in Table 4, standard values for same aged men were set by a mean of 6.9° (SD = 1.1, 5th and 95th percentiles: 5.4, 8.9) and for women by a mean of 5.9° (SD = 0.8, 5th and 95th percentiles: 4.7, 7.5).

More than half (61.3%) of the participants reached PA scores below standard values, with a higher portion of females (n = 68, 65.4%) than males. Compared to a sample of men and women of the same age group without any chronic disease or cancer, the cancer patients of our study showed significant poorer results ($p < 0.001$; Table 3).

MFT S3-SI

Mean values for MFT S3-SI of both genders (n = 44) were significantly ($p < 0.001$) below standard values of the respective healthy age group (men and women of the same age but with no chronic diseases or cancer; Table 4).[32]

Table 1. Sociodemographic characteristics.

Variable	n	Percentage of cases
Gender (n = 203)		
Male	92	54.7
Female	111	45.3
Age group (n = 203)		
20–65 years	93	45.8
66–90 years	110	54.2
Civil status (n = 203)		
Single	23	11.3
Married	143	70.4
Divorced	16	7.9
Separated	2	1.0
Widowed	18	8.9
Stable partnership	1	0.5
Children (n = 203)		
Yes	157	77.3
No	46	22.7
Job situation (n = 203)		
Full-time	48	23.6
Part-time	15	7.5
Retired	117	57.7
Homemaker (female/male)	11	5.4
Unemployed	10	4.9
Self-employed	2	0.9

Table 2. Clinical characteristics.

Variable	n	Percentage of cases
Cancer type (n = 203)		
Gastrointestinal	97	47.8
Breast/gynaecological	55	27.1
Haematological	22	10.8
Respiratory	18	8.9
Urological	11	5.4
Metastases (n = 203)		
Yes	90	44.4
No	99	48.8
Not known	14	6.8
Comorbidities (n = 199)		
Yes	99	49.8
No	84	42.3
Not known	16	7.9
Therapy (n = 203)		
Ever surgical treatment	139	68.5
Ever chemotherapy	176	86.7
Ever radiotherapy	63	31.0
Ever hormone therapy	22	10.8

KI

The KI showed a mean of 79.8% (SD = 11.5%) and a median of 80%. Two patients scored 40% (40 = disabled; requires special care and assistance), 18 patients scored about 50-60% (50-60 = requires considerable/occasional assistance), 94 patients scored about 70-80% (70-80 = cares for self/normal activity), 73 patients described themselves at 90% (90 = able to carry on normal activity), and a further 9 patients scored 100% (100 = no complaints).

Table 3. PA in both sexes compared to age-specific healthy subjects.

Subjects	PA < 5°	PA = 5°–7.5°	PA > 7.5°
Cancer patients (N = 191)	117 (61.3%)	74 (38.7%)	–
Male cancer patients (n = 87)	49 (56.3%)	38 (43.7%)	–
Female cancer patients (n = 104)	68 (65.4%)	68 (65.4%)	–
Standard values (N = 111)	36 (32.4%)	72 (64.9%)	3 (2.7%)
Male healthy subjects (n = 43)	6 (14.3%)	35 (83.3%)	2 (2.4%)
Female healthy subjects (n = 68)	30 (43.5%)	37 (54.4%)	1 (2.1%)

PA: phase angle (standard values for healthy subjects from Barbosa-Silva et al.[40]).

Table 4. Mean and standard deviation of gender-specific anthropometric values and reference values for PA and SI.

Variable	n	Male	n	Female
Height (m)	91	1.77 (0.07)	108	1.66 (0.09)
Weight (kg)	91	76.9 (15.3)	108	68.3 (14.3)
BMI (kg/m²)	91	24.4 (4.8)	108	25.3 (7.3)
PA (°)				
Cancer patients	87	4.9 (0.9)	104	4.6 (0.8)
Standard values	832	6.9 (1.10)	1135	5.9 (0.83)
MFT S3 front/back				
Cancer patients	22	6.3 (0.6)	22	5.9 (0.7)
Standard values	3616	4.9 (1.2)	3737	4.8 (1.2)
MFT S3-SI left/right				
Cancer patients	22	6.3 (0.6)	22	6.1 (0.8)
Standard values	3616	4.6 (1.2)	3737	4.5 (1.2)

BMI: body mass index; PA: phase angle (standard values from Barbosa-Silva et al.[40]); SI: stability index (norms for reference values from Raschner et al.[32]).

SF-36

Sample values for the PCS (M = 37.0, SD = 9.5) as well as MCS (M = 45.9, SD = 11.3) of the SF-36 (n = 200) were all significantly below standard values of the general population ($p > 0.001$). The test handbook for the SF-36 further provides standard values of a mixed cancer sample, including 122 patients with oncological diseases diagnosed with ICD-code C00-D48.[37] Data of the mixed cancer sample was collected at the beginning of a stay in a rehabilitation clinic.[37] Our samples' standard values for PCS were significantly below ($p < 0.001$) and for MCS, significantly above ($p = 0.02$) the

Table 5. Mean and standard deviation of the SF-36 summary and subscales of the study patients compared to the general population and a mixed sample of cancer patients (ICD-10-diagnosis-code: C00-D48).

Subscale/summary scale	Study patients (N = 203)	General population (N = 421)	t, p	Mixed cancer patients (N = 122)	t, p
Physical functioning	58.6 (25.6)	96.4 (10.2)	20.9, <0.001	61.7 (25.9)	1.7, 0.83
Role limitations physical	28.9 (35.4)	96.7 (14.3)	26.8, <0.001	27.8 (39.0)	0.5, 0.65
Bodily pain	61.9 (27.8)	94.5 (14.7)	16.5, <0.001	54.4 (30.0)	3.8, <0.001
Social functioning	65.8 (25.8)	94.9 (12.0)	16.1, <0.001	63.3 (27.2)	1.4, 0.18
General mental health	65.4 (17.9)	79.2 (13.9)	10.9, <0.001	60.7 (20.8)	3.7, <0.001
Role limitations emotional	60.9 (44.3)	96.9 (13.9)	11.3, <0.001	49.3 (45.1)	3.6, <0.001
Vitality	43.9 (18.9)	72.1 (13.9)	20.9, <0.001	43.4 (21.3)	0.4, 0.71
General health perception	45.9 (16.5)	79.8 (13.4)	28.9, <0.001	53.8 (19.2)	6.7, <0.001
SF-36 PCS	37.0 (9.5)	56.1 (4.2)	27.5, <0.001	38.6 (11.4)	2.3, 0.02
SF-36 MCS	45.9 (11.3)	53.2 (5.9)	8.8, <0.001	42.5 (12.4)	4.2, <0.001

SF-36: 36-Item Short-Form Survey; PCS: physical component summary; MCS: mental component summary.
Norms for reference values (general population and mixed sample of cancer patients) from Morfeld et al.[37]

Table 6. Mean and standard deviation in MFI-20 subscales of tumour out-patients compared to the general population.

Subscale	Cancer patients (N = 203)	General population (N = 666)	t, p
General fatigue	12.9 (3.9)	10.5 (3.7)	8.6, <0.001
Physical fatigue	12.3 (3.6)	10.7 (4.3)	6.1, <0.001
Reduced activity	12.4 (4.8)	10.4 (4.0)	5.8, <0.001
Reduced motivation	9.8 (3.5)	9.5 (3.4)	1.1, <0.26
Mental fatigue	9.7 (3.8)	8.9 (3.5)	2.9, 0.003

MFI-20: multidimensional fatigue inventory.
Norms for reference values from Schwarz et al.[41]

scores of the mixed cancer sample (see Table 5). No particular significant gender- or age-specific differences were detected. Mean values and SD of the subscales, summary scales and singular item (displaying health changes during the past year) are shown in Table 5.

MFI-20

When comparing the means, oncological out-patients reached significantly higher scores ($p<0.001$ or $p=0.003$, respectively) on four of the five MFI-20 scales than the same aged population group in a study of Schwarz et al.[41] There was no significant difference between males and females (see Table 6).

Interdependence of psychometric and physical variables

BMI significantly correlated with PA ($r=0.217$, $p=0.003$); however, no significant correlation was found for the KI ($r=0.053$, $p>0.05$), nor the MFI-20- and SF-36-scales ($p>0.05$). Furthermore, BMI showed no significant correlation with either SF-36 or MFI-20 subscales (Table 7). The KI was found to be related to PA ($r=-0.302$, $p<0.001$, Table 7), but not to MFT S3-SI (see supplementary Table 2). PA significantly correlated with SF-36 PCS ($r=306$, $p<0.001$; Table 7), the SF-36 subscales (see supplementary Table 1) 'physical functioning' ($r=0.363$, $p<0.001$), 'role limitations physical' ($r=0.242$, $p=0.001$), 'general health perception' ($r=0.202$, $p=0.005$) and 'vitality' ($r=0.157$, $p=0.03$), as well as with the MFI-20 subscales (see supplementary Table 2) 'physical fatigue' ($r=-0.194$, $p=0.009$), reduced activity' ($r=-0.170$, $p=0.02$) and 'reduced motivation' ($r=-0.162$, $p=0.03$).

A significant negative correlation was found for SF-36 PCS and MFT S3-SI front/back ($r=-0.380$, $p=0.01$) and MFT S3-SI left/right ($r=-0.370$, $p=0.01$). Further significant correlations were observed between MFT S3-SI front/back as well as for MFT S3-SI left/right and SF-36 'physical functioning' (see supplementary Table 1). SF-36 MCS showed no significant correlations with MFT S3-SI. Only MFT S3-SI left/right was found to be significantly correlated with MFI-20 'physical fatigue' ($r=0.394$, $p=0.008$; see supplementary Table 2).

Discussion

The results reveal that oncological out-patients showed PA scores below standard values. Furthermore, the SI significantly differed from the norm, and patients suffered from a fatigue

Table 7. Correlations of PA, BMI, SF-36 summary scales, KI and MFI-20.

Variable	SF-36 PCS	SF-36 MCS	KI	MFI-20 General fatigue	MFI-20 Physical fatigue	MFI-20 Reduced activity	MFI-20 Reduced motivation	MFI-20 Mental fatigue
PA (n = 191)	0.306***	−0.007	−0.302***	−0.128	−0.194**	−0.170*	−0.162*	−0.070
BMI (n = 199)	−0.055	0.052	0.053	0.029	0.048	−0.069	−0.033	0.008

BMI: body mass index; SF-36: 36-Item Short-Form Survey; PCS: physical component summary; MCS: mental component summary; MFI-20: multidimensional fatigue inventory; KI: Karnofsky Index; PA: phase angle.
*$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.

level higher than in the same aged general population.[41] In addition, oncological out-patients experienced a reduced QoL. However, in comparison to a mixed cancer sample including oncological patients diagnosed with ICD-10 code C00-D48, our sample showed significantly better mental QoL (MCS) but a reduced physical QoL (PCS). The difference in scores between the sample- and the mixed cancer sample might result from the timepoint of data collection. While the mixed sample was tested at the beginning of their stay in a rehabilitation hospital, which begins after the first treatment, data of the study sample was collected during ambulatory treatment. Therefore, the study sample did not face the acute phase of the illness. Additionally, the study sample was more confronted with daily life burdens, which are not that present within a hospital setting.

Correlation analysis demonstrated an association between PA and physical QoL, PA and fatigue as well as PA and KI. Physical QoL was related to postural stability (SI).

In our study, oncological out-patients' poor PA values and limited postural stability point to nutritional and mobility deficits demonstrating the patients' bad physical condition and a need for action. Our participants' fatigue scoring was higher than values in the general population, and QoL was decreased on a physical as well as mental level.[37] This indicates that besides the need to improve the physical condition, psychological support is also required.

Besides several screening tools of varying complexity, the PA has proved to be an important parameter in evaluating the nutritional status of oncological patients in our sample. In patients with pancreatic cancer, PA was a better prognostic indicator of improved nutritional status than body weight.[42] PA, which is a direct derivative of the reactance and resistance measurements, has shown good correlations with outcome and health status in several diverse cancer populations and when compared with healthy control populations.[43,44,45] This suggests that PA can be considered as an effective marker of qualitative changes in body composition in cancer patients. Changes in BIA measures can be recorded prior to a clinical manifestation of cachexia.[18] This demonstrates that this parameter is suitable for an early assessment of the nutritional status, thus allowing an earlier nutritional intervention. Combining PA and other malnutrition screening tools may increase early detection of nutritional status among tumour patients. This, in turn, can lead to better results in treatment as malnutrition is associated with increased morbidity and mortality.[46] Moreover, there is an association between survival time and PA. Higher PA scores are related to longer survival time among cancer populations.[16,30,47]

More than half of all oncological out-patients in our study showed PA scores below standard values. It is generally agreed that a PA of less than 5° requires medical management.[30] This result shows an association between PA and general health perception. The closer PA is to the standard value, the better patients rate their state of health. The results of the latter study show that PA is positively associated with physical components of QoL. Our sample of oncological out-patients with a higher PA also showed a better QoL on the physical level.

These findings were supported by Norman et al.[46] The authors found that tumour patients with a low PA, admitted to hospital, had a significantly lower nutritional and functional status and impaired QoL compared to patients with higher PA values.

In our study, a lower PA was also associated with increased fatigue or vice versa on two of the five MFI-20 Scales as well as a lower KI. Taken into account the oncological out-patients' low PA values and the association between PA and QoL, fatigue and KI, it becomes obvious that there is a need for interventions that increase PA and reduce malnutrition in cancer patients.

Physical activity is a promising tool to improve PA and the physical condition of cancer patients. Intervention studies could determine that body composition, aerobic fitness, muscle strength, QoL and fatigue can be improved by a combined resistance and aerobic training.[48,49] Positive effects of physical activity interventions regarding upper and lower body strength were revealed during and after cancer treatment. Furthermore, moderate effects of physical activity interventions on fatigue, aerobic fitness, muscular strength and QoL were demonstrated.[50,51] Besides physical activity, nutrition is vital to improve the PA.

Among patients with advanced pancreatic cancer, the PA significantly increased in response to parenteral nutrition.[42] Cupisti et al.[52] found that level and intensity of physical activity among stable dialysis patients were positively related to PA and to dietary nutrient intake. Therefore, combined nutritional and physical activity interventions promise to be a useful tool for enhancing the PA.

In prostate cancer patients, physical activity also showed a positive effect on balance.[48] In this study, the oncological out-patients presented an impaired postural stability, putting them at a higher risk of falls.[26] Furthermore, the SI showed a positive association with the physical component of QoL, hence training of postural stability could contribute to enhance QoL.

A hint to this hypothesis was given by Huang et al.,[27] who demonstrated that balance control is a determinant of perceived physical function and well-being.

It can be summarised that oncological out-patients in our study showed limitations in postural stability and body composition represented by a lower PA, a decreased QoL and a level of fatigue higher than standard values.

We found correlations between the physical status of oncological out-patients and the physical component of SF-36. This indicates that the physical data support the psychological construct and that QoL of cancer patients depends on their physical fitness.

Several intervention studies already provided indications supporting the assumption that all of these deficits can be improved by physical activity and nutritional interventions.

The decrease in QoL in the mental composite score, which in this study is not associated with the other parameters, furthermore indicates the need for psychological support.

This study has several limitations. Participants differ in sociodemographic characteristics, tumour type and health status. The mixed study sample may restrict the generalisation on the outcome of PA values for different cancer types and stages of the disease. Further prospective studies with more homogeneous cancer entities and cancer stages are recommended. Second, the study was performed in out-patient cancer centres, and results among the participating centres may differ due to different treatment strategies or local circumstances. Furthermore, the participation in this study was voluntary. This may have resulted in selection bias. Due to the cross-sectional character of this study, correlations cannot differentiate cause and effect. A longitudinal study would help to find out whether the correlation found between PA and QoL is a false correlation or whether the QoL is improving with an increasing PA and worsens with a decreasing PA.

Finally, the validity of algorithms for the assessment of BIA is challenged as sample-specific assessments, for example, assessments of patients with different tumour types and stages are not available. In tumour patients, the water electrolyte balance is altered due to various reasons, for example, chemotherapy. This may cause interference since the hydration of body tissue might change the resistance to the electrical current.[45] Acute body mass changes or protein malnutrition may also represent a limitation to the use of BIA.[43] However, recent studies suggest that BIA-derived PA values may serve as an independent prognostic indicator for nutritional status and survival in cancer patients with different diseases.[21,30]

Despite these limitations, the results of this study suggest that anthropometric measures contribute to the assessment of the individual level of physical fitness, QoL and fatigue among out-patient cancer survivors. Considering the patients' reduced health-related QoL and low PA on one hand and the correlation between PA and reduced activity, physical fatigue, KI and the physical health–related QoL on the other hand, it becomes obvious that there is a need for interventions combining physical activity and nutrition.

Regular physical activity can be an additional and particularly important factor in oncological treatment with the objective of improving the QoL of tumour patients and reducing fatigue in any stage of the illness.[53,54]

The need for psychological support, in addition to an intervention, including nutrition and physical activity, is underlined by the low values on the mental health component summary scale, unrelated to PA.

To break the cancer-specific vicious circle of reduced physical performance, fatigue symptomatology, and limited QoL, it is recommended to employ multimodal individualised approaches incorporating components, such as physical activity, nutrition counselling and psychological support. Further research should particularly focus on trials to investigate the effectiveness of multimodally tailored interventions in the population of cancer survivors.

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Ethical approval

This study and its consent procedure were approved by the Ethics Committee of the Medical Council of Hamburg, Germany (PV 4620).

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Informed consent

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