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ORIGINAL ARTICLE

Distress in soft-tissue sarcoma and gastrointestinal stromal tumours patients—Results of a German multicentre observational study (PROSa)

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Abstract

Objective: Soft tissue sarcomas (STS) and gastrointestinal stromal tumours (GIST) are a group of rare malignant tumours with a high and heterogenous disease burden. As evidence is scarce, we analysed the prevalence of increased emotional distress and identified distress-associated factors in these patients.

Methods: The PROSa-study (Burden and medical care of sarcoma) was conducted between 2017 and 2020 in 39 study centres. Cross-sectional data from adult STS and GIST patients were analysed. Distress was measured with the Patient Health Questionnaire (PHQ-4). The relation of socioeconomic and clinical factors with distress was explored in adjusted logistic regression models.

Results: Among 897 patients, 17% reported elevated anxiety and 19% reported depression. Unemployed patients (odds ratio [OR] 6.6; 95% CI 2.9–15.0), and those with a disability pension (OR 3.1; 95% CI 1.9–5.0) were more likely to experience distress compared to employed patients. Also, patients with a disability pass had higher

odds of increased distress than those without (OR 1.8; 95% CI 1.2–2.7). Lowest distress was observed in patients 2 to <5 years and ≥5 years after diagnosis (comparison: <6 months) (OR 0.4; 95% CI 0.2–0.6) and (0.3; 95% CI 0.2–0.6). Patients with thoracic STS (vs. lower limbs) had twice the odds to experience distress (OR 2.0; 95% CI 1.1–3.6). Distress was seen almost twice as often in patients with progressive disease (vs. complete remission) (OR 1.7; 95% CI 1.1–2.8).

Conclusion: The prevalence of elevated distress in STS and GIST patients is high. In unemployed patients, in those with a disability pension and in newly diagnosed patients a noticeable increase was observed. Clinicians should be aware of these factors and consider the social aspects of the disease.

KEYWORDS
anxiety, cancer, depression, emotional distress, GIST, oncology, PHQ-4, psycho-oncology, soft tissue sarcoma

1 | BACKGROUND

Sarcomas are rare cancers, with about 7000 new cases per year in Germany[1] and an incidence of around five per 100,000 in Europe.[2] Five-year relative survival in 2000–2002 was 58% for soft tissue sarcomas (STS) and 68% for gastrointestinal stromal tumours (GIST).[2] Sarcomas form a heterogeneous group of tumours that includes a large variety of over 100 histological subtypes,[3] can occur anywhere in the body, and whose therapy is based on complex and divergent treatment algorithms.[4]

Sarcomas are often diagnosed late due to unspecific symptoms and rare occurrence.[5] Unplanned resections, result of misdiagnosing the tumour as a more common benign lesion, with a negative influence on the course of treatment are common.[6,7] Treatment at specialized centres is recommended by international guidelines and prolongs survival.[8–11]

The psychosocial situation of patients with STS and bone sarcomas was recently systematically reviewed. The review by McDonough et al. includes publications on health-related quality of life, psychosocial function, and unmet health-related needs,[12] and that by Storey et al. addresses the impact of sarcoma disease on psychosocial well-being.[13] McDonough et al. summarize that anxiety was most prevalent in the diagnosis phase, whereas depressive symptoms were most prevalent in the treatment phase. Female gender, older age, and marriage were among risk factors for depressive symptoms, whereas the presence of emotional support and the experience of positive social interactions were protective factors. In contrast, Storey et al. emphasized the heterogeneity of the results they found. They argue that the published literature does not provide yet a clear picture of the impact of sarcoma diagnosis and treatment on psychosocial well-being as well-designed studies in this area are lacking. Indeed, the reported prevalence of increased psychological distress in sarcoma patients ranges from 13% to 63%.[14] A different review reported frequencies of 23%–30% for depression and 13%–19% for anxiety disorders.[15]

The heterogeneity of sarcomas also raises the question to which extent certain subgroups (in terms of treatment, location of sarcoma, or entity) vary in their vulnerability to emotional distress. Here we wanted to investigate whether there are certain phases of disease development in which patients are particularly vulnerable to emotional distress and may require increased attention from care-takers. In addition, previous evaluations of our study population have shown that sarcoma patients are particularly limited in their role and social functioning compared with the general population.[16] Our study thus draws attention to the social aspects of the disease and possible socioeconomic factors of emotional distress.

In sum, we aimed to answer the following research questions:

1. What is the prevalence of increased emotional distress (depression/anxiety) in soft-tissue sarcoma and GIST patients in Germany?
2. How are disease heterogeneity, the disease course, and socioeconomic factors associated with increased emotional distress?

2 | METHODS

For the present analysis, we evaluated the data from adult patients and survivors with histologically proven STS and GIST of any entity and disease status. We excluded individuals who were mentally or linguistically unable to complete questionnaires in German. Patients were recruited within the PROSa-cohort study (Burden and Medical Care of Sarcoma in Germany: Nationwide Cohort Study Focussing on Modifiable Determinants of Patient-Reported Outcome Measures in Sarcoma Patients),[16–18] that was conducted in 39 study sites between 2017 and 2020 (NCT03521531; ClinicalTrials.gov).

Eligible patients were asked to participate during visits (treatment, diagnosis, follow-up) to the participating study centres, and in individual cases by telephone or letter. Informed consent was required for participation. The study was advised by the ethics committees of the Technical University of Dresden (EK1790422017) and the participating centres.[19]

Data collection was performed by the study coordination centre at Dresden University Hospital. Patient-reported outcome and socio-demographic data were submitted by participants to the study coordination centre by mail or online. Clinical data were submitted online to the study coordination centre by the participating study centres using documentation forms. Data were collected using the REDCap electronic data collection system (Vanderbilt University, Nashville, USA).[20]

2.1 | Study measures

The short form of the Patients Health Questionnaire (PHQ-4[21]) was used to assess emotional distress. This validated[22,23] screening instrument consists of the core diagnostic criteria for depressive disorders (PHQ-2) and generalized anxiety disorder (GAD-2) according to the Diagnostic Statistical Manual for the Diagnosis of Mental Disorders (DSM). The PHQ-4 score can take values from 0 to 12. A depressive disorder or anxiety disorder may be present if the depression or anxiety questions reach or exceed the threshold of 3.[24,25] In this case we speak of increased emotional distress.

As possible factors associated with the presence of increased distress, we examined sex, age at study entry, and the following socioeconomic variables: education, occupation, equivalent income, employment status, sick leave, disability status, household with children, smoking. As clinical factors, we analysed time since diagnosis, sarcoma type, tumour location, T-Stage, recurrence, metastasis until baseline, disease status, treatment status, received treatments, before first treatment, and comorbidities. Variable values are displayed in Table 1.

2.2 | Statistical analysis

When normally distributed, continuous variables were presented with mean and standard deviation (SD), with median and interquartile range if this was not the case. Categorical variables were reported with absolute and relative frequencies.

First, variables were analysed in relation to distress using chi-square tests (univariate approach). Next, two multivariable models using logistic regressions were fitted. The first model included the socioeconomic variables (SES-model), and the second additionally included the clinical variables (full model). Backward selection procedures with $p > 0.15$ as exclusion criteria were used, with age and sex being forced to stay in the model. Confidence intervals with 95% were calculated. Statistical analyses were performed using SPSS V.26 (IBM Corporation).

3 | RESULTS

3.1 | Description of study population

Data from 1069 STS and GIST patients were initially collected and for 897 of them information on distress was available. Of these 86% were diagnosed with STS and 14% with GIST. The gender was balanced, with half of the patients (49%) being female. The average age of all participants was 59 years (SD 14 years). For further population metrics see Table 1.

3.2 | Prevalence of elevated distress

On average, the patients achieved a PHQ-4 score of 3.0 points (SD 2.6). Depressive disorder was suspected in 174 (19%) and anxiety disorder in 151 (17%). In total 236 (26%) experienced elevated emotional distress (Table 2).

3.3 | Factors associated with elevated distress

The univariate analysis revealed significant differences according to distress level in a variety of analysed factors which are shown in Table 1.

For the multivariable logistic regression, two models were calculated. One comprised the socioeconomic (SES-model), the other all model variables (full model). In both models, unemployed patients (SES model: odds ratio [OR] 5.5; 95% CI 2.5–12.2), full model: OR 6.6; 95% CI 2.9–15.0) and those receiving a disability pension (SES: OR 3.3; 95% CI 2.0–5.3, full: OR 3.1; 95% CI 1.9–5.0) experienced more often elevated distress than patients in employment. In the SES-model, patients on sick leave were distressed more often than those not on sick leave (OR 1.7; 95% CI 1.1–2.5), in the full model those with a disability pass (OR 1.8; 95% CI 1.2–2.7) compared to those without such a status.

Patients in their first six months since diagnosis had higher odds to be highly distressed than patients beyond six months since diagnosis: The OR comparing patients in the first six months with those at 24–60 months after diagnosis were 0.4 (95% CI 0.2–0.6) and with those five or more years after diagnosis 0.3 (95% CI 0.2–0.6). Compared to patients with a sarcoma at the lower limbs, patients with thoracic sarcomas had twice the odds to experience distress (OR 2.0; 95% CI 1.1–3.6). Patients with a progressive disease course were more often distressed than patients in complete remission (OR 1.7; 95% CI 1.1–2.8). Patients who had not received any treatment yet were more likely to suffer from distress than those who had received treatment (OR 2.5; 95% CI 0.96–6.6) not significant) (Table 3).

4 | DISCUSSION

Our analysis showed an increased emotional distress in more than 25% of respondents. This observation points to a high need for psychosocial support in STS and GIST patients and if not already available, resources should be devoted to cover this need. 17% of the respondents show a possible anxiety disorder and almost 20% signs of a depressive disorder; the later value is roughly 2.5 times higher than the prevalence of depressive disorders in the German general

TABLE 1 Description study population, stratified by psychological distress

Variable	Value	No depression or anxiety *N* (row %) *N* = 661 (73.7)	Depression and/or anxiety *N* (row %) *N* = 236 (26.3)	All patients *N* (column %) *N* = 897
Socioeconomic factors				
Sex[a]	Female	311 (71.2)	126 (28.8)	437 (48.7)
	Male	350 (76.1)	110 (23.9)	460 (51.3)
Age at study entry	Mean (SD)	60.0 (14.0)	57.6 (13.8)	59.3 (14.0)
Age at study entry—group[a,b]	18 ≤ 40 years	65 (71.4)	26 (28.6)	91 (10.1)
	40 ≤ 55 years	154 (71.6)	61 (28.4)	215 (24.0)
	55 ≤ 65 years	181 (67.8)	86 (32.2)	267 (29.8)
	65 ≤ 75 years	172 (83.9)	33 (16.1)	205 (22.9)
	≥75 years	89 (74.8)	30 (25.2)	119 (13.3)
School leaving certificate[a]	None to secondary school (8/9 years)	165 (71.1)	67 (28.9)	232 (25.9)
	Secondary school (10 years)	226 (74.1)	79 (25.9)	305 (34.0)
	Vocational baccalaureate	62 (68.9)	28 (31.1)	90 (10.0)
	High school/baccalaureate	197 (78.8)	53 (21.2)	250 (27.9)
	Something else/unknown	11 (55.0)	9 (45.0)	20 (2.2)
Occupational status[a]	Blue collar worker	125 (71.8)	49 (28.2)	174 (19.4)
	Civil servant	53 (77.9)	15 (22.1)	68 (7.6)
	White collar worker	363 (72.5)	138 (27.5)	501 (55.9)
	Self employed	75 (83.3)	15 (16.7)	90 (10.0)
	Unknown/not applicable	45 (70.3)	19 (29.7)	64 (7.1)
Equivalized income	Mean (SD)	2100€ (1093€)	1967€ (1020€)	2066€ (1076€)
Equivalized income[a]	≤1250€	116 (67.1)	57 (32.9)	173 (19.3)
	1250.1€–1750€	134 (74.4)	46 (25.6)	180 (20.1)
	1750.1€–2250€	158 (75.6)	51 (24.4)	209 (23.3)
	2250.1€–2750€	61 (81.3)	14 (18.7)	75 (8.4)
	≥2750.1€	112 (75.2)	37 (24.8)	149 (16.6)
	Unknown	80 (72.1)	31 (27.9)	111 (12.4)
Employment status[a,b]	Employed/self employed	285 (77.0)	85 (23.0)	370 (41.2)
	Unemployed	11 (35.5)	20 (64.5)	31 (3.5)
	Disability pension	66 (54.5)	55 (45.5)	121 (13.5)
	Early retirement/retirement pension/ partial retirement	273 (80.1)	68 (19.9)	341 (38.0)
	Other	26 (76.5)	8 (23.5)	34 (3.8)
Sick leave[a,b]	No	510 (75.9)	162 (24.1)	672 (74.9)
	Yes	138 (67.3)	67 (32.7)	205 (22.9)
	Unknown	13 (65.0)	7 (35.0)	20 (2.2)
Disabled person pass[a,b]	No	269 (78.9)	72 (21.1)	341 (38.0)
	Yes	387 (70.5)	162 (29.5)	549 (61.2)
	Unknown	5 (71.4)	2 (28.6)	7 (0.7)
Children in household[a]	No	542 (75.3)	178 (24.7)	720 (80.3)
	Yes	79 (66.9)	39 (33.1)	118 (13.2)
	Unknown	40 (67.8)	19 (32.2)	59 (6.6)

(Continues)

TABLE 1 (Continued)

Variable	Value	No depression or anxiety *N* (row %) *N* = 661 (73.7)	Depression and/or anxiety *N* (row %) *N* = 236 (26.3)	All patients *N* (column %) *N* = 897
Smoking[a]	Never	356 (76.1)	112 (23.9)	468 (52.2)
	Former	228 (71.3)	92 (28.7)	320 (35.7)
	Actual	71 (68.6)	31 (30.4)	102 (11.4)
	Unknown	6 (85.7)	1 (14.3)	7 (0.7)
Clinical factors				
Time since diagnosis[a]	0 ≤ 0.5 years	118 (65.9)	61 (34.1)	179 (20.0)
	0.5 ≤ 1 year	78 (73.6)	28 (26.4)	106 (11.8)
	1 ≤ 2 years	92 (71.3)	37 (28.7)	129 (14.4)
	2 ≤ 5 years	175 (76.1)	55 (23.9)	230 (25.6)
	≥5 years	198 (78.3)	55 (21.7)	253 (28.2)
Sarcoma type[a]	Soft tissue sarcoma	563 (73.0)	208 (27.0)	771 (86.0)
	GIST	98 (77.8)	28 (22.2)	126 (14.0)
Tumour site[a]	Abdomen/retroperitoneum	220 (74.6)	75 (25.4)	295 (32.9)
	Thorax	46 (60.5)	30 (39.5)	76 (8.5)
	Pelvis	92 (74.2)	32 (25.8)	124 (13.8)
	Lower limbs	216 (74.7)	73 (25.3)	289 (32.2)
	Upper limbs	48 (77.4)	14 (22.6)	62 (6.9)
	Head & neck	22 (84.6)	4 (15.4)	26 (2.9)
	Unknown/other	17 (68.0)	8 (32.0)	25 (2.8)
T-stage[a]	T1	94 (77.7)	27 (22.3)	121 (13.5)
	T2–4	326 (73.6)	117 (26.4)	443 (49.4)
	Other/unknown	241 (72.4)	92 (27.6)	333 (37.1)
Metastasis until baseline[a]	No metastasis	359 (75.3)	118 (24.7)	477 (53.2)
	Metastasis	214 (72.3)	82 (27.7)	296 (33.0)
	Unknown/suspicion	88 (71.0)	36 (29.0)	124 (13.8)
Tumor recurrence[a]	No recurrence	473 (74.8)	159 (25.2)	632 (70.5)
	Recurrence	174 (71.0)	71 (29.0)	245 (27.3)
	Unknown/suspicion	14 (70.0)	6 (30.0)	20 (2.2)
Disease status[a,b]	Complete remission	278 (77.9)	79 (22.1)	357 (39.8)
	Partial remission/stable disease	222 (75.3)	73 (24.7)	295 (32.9)
	Progressive	93 (66.0)	48 (34.0)	141 (15.7)
	Unknown/not accessible	68 (65.4)	36 (34.6)	104 (11.6)
Aftercare status[a,b]	Not in aftercare	271 (67.7)	130 (32.4)	401 (44.7)
	In aftercare	379 (78.6)	103 (21.4)	482 (53.7)
	Unknown	11 (78.6)	3 (21.4)	14 (1.6)
Combined treatments[a,b]	Surgery only	177 (78.7)	48 (21.3)	225 (25.1)
	Surgery + systemic therapy	142 (73.2)	52 (26.8)	194 (21.6)
	Surgery + radiotherapy	122 (79.2)	32 (20.8)	154 (17.2)
	Surgery + radiotherapy + systemic therapy	148 (71.2)	60 (28.8)	208 (23.2)

TABLE 1 (Continued)

Variable	Value	No depression or anxiety *N* (row %) *N* = 661 (73.7)	Depression and/or anxiety *N* (row %) *N* = 236 (26.3)	All patients *N* (column %) *N* = 897
	Systemic therapy only	38 (64.4)	21 (35.6)	59 (6.6)
	Radiotherapy + systemic therapy	15 (68.2)	7 (31.8)	22 (2.5)
	Other	19 (54.4)	16 (45.7)	35 (3.9)
Before first treatment	No	650 (74.3)	225 (25.7)	875 (97.5)
	Yes	11 (50.0)	11 (50.0)	22 (2.5)
Comorbidities[a]	0	306 (74.1)	107 (25.9)	413 (46.0)
	1	228 (74.3)	79 (25.7)	307 (34.2)
	2	100 (75.2)	33 (24.8)	133 (14.8)
	3 or more	27 (61.4)	17 (38.6)	44 (4.9)

Abbreviation: SD, standard deviation.

[a]Modell variables.

[b]Significant differences (Chi Square).

TABLE 2 Prevalence of psychological distress of soft tissue sarcoma and GIST patients

Variable	Value	*N* (%)	German population
PHQ-4 (*N* = 897), mean (SD)	Sum score	3.0 (2.6)	1.8 (2.1)[a]
Anxiety	No	746 (83.2)	
	Above threshold	151 (16.8)	
	Missing data	172	
Depression	No	725 (80.8)	
	Above threshold	172 (19.2)	8.1%[b]
	Missing data	172	
Anxiety and/or depression	No	661 (73.7)	
	Yes	236 (26.3)	
	Missing data	172	

Abbreviations: GIST, gastrointestinal stromal tumours; PHQ, Patients Health Questionnaire; SD, standard deviation.

[a]Löwe 2011.

[b]Busch 2013.

population.[26] With an average of 3.0 points, the sum score of the PHQ-4 was 60% higher than the score of the German general population.[27]

A comparison to other studies on prevalence of distress in sarcoma patients is difficult as different measures were used, different populations were observed and sample sizes were small. With these limitations, it can be concluded that our results confirm the findings of previous studies in a larger and more general sample. A Portuguese study found clinically relevant symptoms of anxiety and depression in 22% resp. 14% of sarcoma patients over disease course, an Italian study in patients undergoing chemotherapy found similar frequencies of 23% resp. 13%[28] A German study in STS and bone sarcoma patients reported a high psychosocial distress in 36% of patients.[29] A Japanese study in STS patient found a prevalence of psychological distress in 20%.[14] Bone sarcoma patients, who were not included in the analysis in this paper seems to have slightly higher prevalence rates that STS patients.[14,29,30]

Heterogeneity of disease with regard to treatment, entity or tumour location, did not generally manifest in divergent odds for emotional distress. However, one exception was observed: The higher prevalence of elevated distress in thoracic sarcoma patients compared to other groups has not been previously reported. The reasons for the high burden in the aforementioned group are to be investigated but probably related to respiratory problems.[31–33] A previous qualitative analysis of quality of life issues experienced by thoracic sarcoma patients documented a range of mental health issues. Patients reported fear and anxiety about disease progression or recurrence, were living with uncertainty, experienced

TABLE 3 Psychological distress of soft tissue sarcoma and GIST patients, associated factors, results of a logistic regression

		Anxiety and/or depression					
		SES[a]			SES + clinical variables[b]		
		OR	CI	*p*	OR	CI	*p*
Sex	Female versus male	0.80	0.578; 1.1	0.17	0.72	0.51; 1.01	0.06
Age at study entry—group				0.22			0.21
	55 to <65 years (ref)						
	18 to <40 years	0.88	0.50; 1.57	0.67	0.79	0.44; 1.44	0.44
	40 to <55 years	0.84	0.55; 1.28	0.42	0.92	0.60; 1.42	0.71
	65 to <75 years	0.52	0.26; 1.04	0.06	**0.47**	0.24; 0.99	0.047
	≥75 years	0.91	0.44; 1.88	0.79	0.85	0.40; 1.80	0.67
School leaving certificate				0.06			0.03
	High school/baccalaureate (ref)						
	None to secondary school (8/9 years)	1.40	0.90; 2.18	0.14	1.46	0.92; 2.31	0.11
	Secondary school (10 years)	1.08	0.71; 1.65	0.71	1.12	0.73; 1.72	0.62
	Vocational baccalaureate	1.72	0.98; 3.02	0.06	**2.02**	1.13; 3.61	0.02
	Something else/unknown	**3.16**	1.18; 8.42	0.02	**3.32**	1.18; 9.35	0.02
Employment status				<0.001			<0.001
	Employed/self-employed (ref.)						
	Unemployed	**5.48**	2.47; 12.17	<0.001	**6.64**	2.93; 15.05	<0.001
	Disability pension	**3.25**	2.00; 5.28	<0.001	**3.05**	1.85; 5.03	<0.001
	Early retirement/retirement pension/partial retirement	1.29	0.65; 2.56	0.46	1.24	0.62; 2.47	0.55
	Other	1.12	0.46; 2.72	0.80	1.17	0.47; 2.93	0.73
Sick leave				0.04	e	e	e
	No (ref.)				e	e	e
	Yes	**1.66**	1.08; 2.54	0.02	e	e	e
	Unknown	1.76	0.64; 4.84	0.27	e	e	e
Disabled person pass		e	e	e			0.01
	No (ref)	e	e	e			
	Yes	e	e	e	**1.81**	1.22; 2.70	<0.01
	Unknown	e	e	e	1.36	0.21; 8.80	0.75
Time since diagnosis							<0.001
	0 to <0.5 years (ref)						
	0.5 to <1 year				0.60	0.35; 1.11	0.11
	1 to <2 years				0.57	0.31; 1.02	0.58
	2 to <5 years				**0.37**	0.21; 0.64	<0.001
	≥5 years				**0.32**	0.19; 0.55	<0.001
Tumour site							0.045
	Lower limbs (ref)						
	Abdomen/retroperitoneum				0.83	0.55; 1.26	0.39
	Thorax				**2.04**	1.14; 3.64	0.02

TABLE 3 (Continued)

		Anxiety and/or depression					
		SES[a]			SES + clinical variables[b]		
		OR	CI	p	OR	CI	p
	Pelvis				0.81	0.47; 1.39	0.44
	Upper limbs				0.81	0.40; 1.63	0.56
	Head & neck				0.38	0.12; 1.21	0.10
	Unknown/other				1.08	0.41; 2.82	0.88
Disease status							0.12
	Complete remission (ref)						
	Partial remission/stable disease				1.12	0.75; 1.67	0.59
	Progressive				**1.74**	1.07; 2.82	0.03
	Unknown/not accessible				1.41	0.81; 2.45	0.23
Before treatment	No versus yes				2.50	0.96; 6.56	0.06

Abbreviations: e, excluded through backwards selection, significant results bold; GIST, gastrointestinal stromal tumours; OR, Odds Ratio; *p*, *p*-value; SES, socioeconomic model.

[a]Variables in the model: age, sex, education, occupation, income, employment status, sick leave, disability status, children in household, smoking.

[b]Variables in the model: SES + time since diagnosis, sarcoma type, tumour location, T-Stage, recurrence, metastasis, disease status, treatment status, treatments, comorbidities.

changes in mood and negative emotions due to their disease and treatment, and felt angry, sad, tense, down, worried, and depressed. In addition, changes in personality such as being aggressive and grumpy, more emotionally sensitive and less self-confident were described.[34]

Disease course and disease development are playing an important role on emotional distress in sarcoma patients. We observed that distress appears to be particularly high in the first months of the disease. Here our results are consistent with that of a previous study.[35] It is possible however, that our results are influenced by survival bias and even in those who received their diagnosis more than 5 years ago, 22% of all individuals were still above threshold. Due to the recruitment strategy of the PROSa study we were not able to include a sufficient number of patients in the pre-treatment phase to produce statistically significant results. With this important limitation, the increased burden in this group is nevertheless important to note. The association between progressive disease status and increased change for emotional distress in sarcoma patients was reported previously.[35] Disease status is correlated with other potentially associated factors like treatment status or being on sick leave, which were removed from the multivariate analysis after backward selection.

Socio-economic factors are well established risk factors for emotional distress and we observed these associations as well: unemployed persons and persons on disability pensions were up to seven times more likely to have elevated emotional distress than patients in employment. The high burden of unemployed cancer patients or those with disability pension was also shown in other studies.[36] Studies in the general population are showing the relationship between unemployment and distress as well.[37] Future research should investigate possible interaction effects between cancer and unemployment. The higher burden on individuals with a vocational baccalaureate degree compared to those with a high school diploma is a finding that is difficult to explain. We found no evidence in the literature. The extent to which the observed higher burden among patients with a disabled persons pass is due to social or medical reasons, or both, cannot be further elucidated with the available data material. Female gender was not significantly associated with elevated distress in our study, but the observed confidence interval does not rule out such an association. In general, there is a well-known gender difference in distress in cancer patients[38] which was previously observed in sarcoma patient as well.[12] With regard to cancer patients in general, the same holds true for differences between age groups. Younger people are more affected,[39] which would be in line with our results. Contrarily to our results one study found increasing depression scores with increasing age in sarcoma patients in aftercare.[35]

4.1 | Study limitations

We can present data on distress from one of the largest studies on patient reported outcomes in STS and GIST patients and survivors worldwide. The 39 participating centres comprehensively represent the aspects of sarcoma treatment in Germany and have a large network of referring institutions. Previously published studies were often limited to subgroups specified by type, localisation, or treatment, or were conducted in single centres. Our analysis can provide

an overview of the sarcoma patient population as it is presented at our study centres. The possible exception are sarcomas of the skin.

The present study had a cross-sectional design. Causal conclusions are therefore not possible and there is the possibility of reverse causation. It could be the case that elevated distress leads to unemployment or inability to work and so to the necessity to receive a disability pension. Due to the study design, we could not perform an analysis of non-participants, which would have provided information on possible selection bias at the level of study participants. A non-participants analysis for all participants of the PROSa study is available elsewhere.[16] The study is probably subject to selection bias. We see this possibility mainly on the level of the study centres. The majority of our patients were recruited in university hospitals and/or specialized centres and might therefore be not representative for all sarcoma patients. Selection bias is also possible at the patient level. Here we suspect a sick survivor bias, as healthy survivors have less frequent contact with our recruiting study centres. Especially patients who are no longer in follow-up care could be reached less easily. There is also the possibility of response shift, especially when comparing newly diagnosed patients with those who received their diagnosis some time ago.

4.2 | Clinical implications

Clinicians, psycho-oncologists, and health care politicians should be aware of the high prevalence of emotional distress in STS and GIST patients as well as of the identified risk factors. They should specifically consider the social aspects of the disease.

4.3 | Conclusion

The prevalence of distress in soft tissue sarcoma and gastrointestinal stromal tumour patients is high. We identified a variety of potential risk factors for increased distress. Disabled persons, patients in precarious employment, newly diagnosed patients and those with progressive disease should be considered as particularly vulnerable groups within soft tissue sarcoma and GIST patients.

AUTHOR CONTRIBUTION

Martin Eichler wrote the article and analysed the data. Martin Eichler, Markus K. Schuler and Leopold Hentschel developed questionnaires and study design. Jochen Schmitt and Markus K. Schuler developed the conception of the study and supervised with Martin Bornhäuser the work throughout the whole study. Karin Arndt supervised the study from a patient's perspective. Martin Eichler, Leopold Hentschel, Beate Hornemann, and Susanne Singer developed the statistical analysis plan for this paper. Stephan Richter, Peter Hohenberger, Bernd Kasper, Dimosthenis Andreou, Daniel Pink, Jens Jakob, and Markus K. Schuler were responsible for the recruitment of patients or recruited patients directly. All authors have revised the manuscript critically and approved the published version.

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CONFLICT OF INTEREST

Leopold Hentschel received fees from SERVIER, outside of this work. Susanne Singer received lecture fees from Lilly, BMS, Boehringer-Ingelheim and Pfizer and fees for consulting services from Content Ed Net, all outside of this work. Dimosthenis Andreou received lecture fees from Lilly and Implantcast, all outside of this work. Daniel Pink received fees for consulting services from Lilly, PharmaMar, Roche and fees for lectures from Lilly, PharmaMar, all outside of this work. Jens Jakob received fees from Lilly and Boehringer Ingelheim, all outside of this work. Jochen Schmitt received consulting fees from Novartis, Sanofi, ALK, and Lilly, all outside of this work. Markus K. Schuler received research funding from PharmaMar and Novartis, all outside of this work. Martin Eichler, Beate Hornemann, Peter Hohenberger, Bernd Kasper, Karin Arndt, and Martin Bornhäuser declare that no conflicts of interest exist.

DATA AVAILABILITY STATEMENT

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

This study was approved by the ethics committee of the Technical University of Dresden (AZ: EK 1790422017) and the ethics committees of the participating centres, and it was conducted in accordance with the Declaration of Helsinki. The study participants gave written informed consent. This study is registered under NCT03521531 on ClinicalTrials.gov.

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