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Development of Distress During a Radiotherapy Course in Patients Irradiated for Breast Cancer

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Abstract. *Background/Aim: Breast cancer patients receiving radiation therapy (RT) may experience considerable distress. We investigated the course of distress during an RT-course for breast cancer. Patients and Methods: Three-hundred-and-thirty breast cancer patients completed Distress Thermometers before and directly after RT. Distress was evaluated in the entire cohort and different groups of age, sex, Karnofsky performance score (KPS), intent of RT, and previous RT. Results: Mean change of distress scores was –0.4 points, which was significantly associated with KPS. Decrease of distress was more pronounced in patients with KPS ≤80 or age <64 years. Deterioration (yes vs. no) was non-significantly associated with no previous RT. In patients with pre-RT distress scores ≤5 points, mean score increased by +0.5 points; no significant associations between characteristics and investigated endpoints were found. Conclusion: Psychological assistance should be offered to all patients irradiated for breast cancer, particularly to those with risk factors, regardless of the pre-RT distress score.*

Breast cancer is the most common primary tumor type among women in Western countries (1). Many of these patients receive radiation therapy (RT), either as loco-regional treatment following breast surgery or for metastatic disease. Anticipated treatment may induce considerable distress for the corresponding patients. In a previous study of breast cancer patients assigned to adjuvant RT following breast-conserving surgery or mastectomy, 46% of patients reported fears prior to the start of RT, 38% worry, 29% sadness, and 29% nervousness (2). These emotional problems are part of the National Comprehensive Cancer Network Distress Thermometer (NCCN-DT) (3). In the study of Mose *et al*., 48% of patients assigned to adjuvant RT of early-stage breast cancer reported distress related to the upcoming RT (4). In addition, Goldschmidt Mertz *et al*. found that 43% of patients with newly diagnosed breast cancer felt distressed, when a cut-off value of 7 points on the NCCN-DT (points range between 0 and 10, with 10 points indicating maximum distress) was used (5). When using a cut-off value of 3 points, even 77% of the patients were considered distressed. The highest rates were observed for worry and nervousness (5). Luutonen *et al*. found depressive symptoms and distress in 32% and 28% of breast cancer patients treated with adjuvant RT (6). Moreover, Browall *et al*. have shown that emotional functioning is positively correlated with the quality of life of patients receiving adjuvant RT for breast cancer (7).

Current literature demonstrates that emotional and psychological distress are common in breast cancer patients assigned to RT. However, little is known regarding the course of distress scores during an RT-series. In a previous study including different types of malignancy, the change of distress during the RT-course was significantly associated with the primary tumor type (8). Therefore, it was considered reasonable to perform separate studies for the most common tumor entities. The present study focuses specifically on patients irradiated for breast cancer.

Patients and Methods

In a cohort of 330 breast cancer patients who received RT at the University Medical Center Schleswig-Holstein (UKSH) in Lübeck or the Medical Practice for Radiotherapy and Radiation Oncology, Hannover, between 11/2021 and 11/2022, the course of distress during RT was assessed. This retrospective study was approved by the ethics committee in Lübeck and Hannover. The course of distress was evaluated with the NCCN-DT, which was completed

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Table I. *Entire cohort (n=330): Distribution of patient characteristics.*

Characteristic	Subgroup	Number of patients (n)	Proportion (%)
Age at radiotherapy	≤64 Years	144	44
	65-79 Years	146	44
	≥80 Years	40	12
Sex	Female	325	98
	Male	5	2
Karnofsky performance score	≤80	87	26
	90-100	243	74
Intent of treatment	Curative	282	85
	Palliative	48	15
Previous radiotherapy	No	275	83
	Yes	55	17
All patients		330	100

Table II. *Entire cohort (n=330): Mean changes of distress scores during the radiotherapy course. p-Values were calculated with the Wilcoxon two-sample test (2 subgroups) or Kruskal-Wallis test (≥3 subgroups).*

Characteristic	Subgroup	Mean change (points)	Standard deviation	*p*-Value
Age at radiotherapy	≤64 Years	±0.0	2.8	
	65-79 Years	–0.6	2.8	
	≥80 Years	–1.0	2.4	0.098
Sex	Female	–0.4	2.8	0.65
	Male	–0.4	4.0	
Karnofsky performance score	≤80	–1.1	2.9	**0.006**
	90-100	–0.1	2.7	
Intent of treatment	Curative	–0.4	2.9	0.82
	Palliative	–0.4	2.4	
Previous radiotherapy	No	–0.3	2.8	0.13
	Yes	–1.0	2.6	
All patients		–0.4	2.8	

Significant *p*-values are shown in bold.

by the patients prior to RT (pre-RT) and directly after the last fraction of RT (post-RT). Patients were asked to rate their level of distress on the NCCN-DT by giving points between 0 (no distress) and 10 (maximum imaginable distress) (3).

In addition to calculation of mean changes (plus standard deviations) of the distress scores during RT and change of distress in general (improvement, no change, or deterioration), five characteristics were analyzed for associations with changes of distress. These were age (≤64 *vs.* 65-79 *vs.* ≥80 years), sex (female *vs.* male), Karnofsky performance score (KPS ≤80 *vs.* 90-100), intent of RT (curative *vs.* palliative), and experience of previous RT (no *vs.* yes). Characteristics are summarized in Table I.

The mean values and standard deviations of changes of distress scores (post-RT *minus* pre-RT scores) were calculated. The Wilcoxon signed rank test was used to assess whether there was a significant change from pre-RT to post-RT distress scores in the entire cohort. Associations between characteristics and mean changes of distress scores were evaluated using the Wilcoxon two-sample (2 subgroups) and the Kruskal-Wallis (≥2 subgroups) tests.

In addition, course of distress represented by improvement (decreased score by ≥2 points), no change (difference between –1 and +1 point), or deterioration (increased score by ≥2 points) of distress was assessed. For the corresponding statistical analyses, the Wilcoxon two-sample and the Kruskal-Wallis tests were applied. Furthermore, we analyzed the characteristics regarding the binary variable "deterioration *vs.* no deterioration" (increase *vs.* no increase by ≥2 points) of distress, using the Chi-square test and a logistic regression for univariable and multivariable analyses, respectively. Additional subgroup analyses were performed in the 208 patients with lower pre-RT distress scores of ≤5 points since physicians may be less inclined to offer these patients psychological assistance when compared to patients with higher pre-RT distress scores. For all statistical analyses, *p*-values <0.05 were considered indicating significance and *p*-values <0.11 indicating a trend.

Results

In the entire cohort, the mean change of distress scores was –0.4 (±2.8) points (p=0.008), with mean pre-RT scores of 4.8 (±2.6) and post-RT scores of 4.4 (±2.6). The mean change was significantly associated with KPS (p=0.006), and age showed a trend (p=0.098). Decrease of distress scores was more pronounced in patients with a KPS ≤80, and in elderly (–0.6 points) and very elderly (–1.0 point) patients (Table II). Regarding changes of distress scores (improvement, no change, or deterioration), a significant association was also found for KPS 90-100 (p=0.001) and a trend for age (p=0.108) (Table III). When using the binary variable "deterioration *vs.* no deterioration", deterioration was non-significantly (trend) more frequent in patients who had not previously received RT (23% *vs.* 13%, p=0.092) (Table III). On multivariable analysis, age (p=0.65), KPS (p=0.70), intent of RT (p=0.91), and previous RT (p=0.25) were not significantly associated with deterioration of distress.

In the subgroup analyses in the 208 patients with pre-RT distress scores of ≤5 points, the mean change of distress scores was +0.5 (±2.6) points (p=0.006), with mean pre-RT scores of 3.1 (±1.7) and post-RT scores of 3.7 (±2.4). No significant associations were found between investigated characteristics and mean change of distress scores (Table IV), between characteristics and change of distress given as improvement, no change, or deterioration (Table V), and between characteristics and deterioration of distress (binary variable) (Table V).

Discussion

The quality of life of breast cancer patients scheduled for RT can be significantly impaired by emotional and psychological distress (7). Mose *et al.* found in their study of 111 patients irradiated for early-stage breast cancer that

Table III. *Entire cohort (n=330): Improvement (minus ≥2 points), no change, and deterioration (plus ≥2 points) of distress scores during radiotherapy. p-values were calculated with the Wilcoxon two-sample test (2 subgroups) or Kruskal-Wallis test (≥3 subgroups). Additional p-values were calculated for comparisons of subgroups regarding the binary variable "deterioration yes vs. no" using the Chi-square test.*

Characteristic	Subgroup	Change of distress scores			*p*-Value	*p*-Value*
		Improvement n, (%)	No change n, (%)	Deterioration n, (%)		
Age at radiotherapy	≤64 Years	41 (28)	68 (47)	35 (24)	0.108	0.39
	65-79 Years	51 (35)	66 (45)	29 (20)		
	≥80 Years	18 (45)	16 (40)	6 (15)		
Sex	Female	109 (34)	147 (45)	69 (21)	0.70	1.00
	Male	1 (20)	3 (60)	1 (20)		
Karnofsky performance score	≤80	40 (46)	32 (37)	15 (17)	**0.001**	0.29
	90-100	70 (29)	118 (49)	55 (23)		
Intent of treatment	Curative	98 (35)	121 (43)	63 (22)	0.77	0.22
	Palliative	12 (25)	29 (60)	7 (15)		
Previous radiotherapy	No	89 (32)	123 (45)	63 (23)	0.16	0.092
	Yes	21 (38)	27 (49)	7 (13)		
All patients		110 (33)	150 (45)	70 (21)		

**p*-Values for comparisons of subgroups with respect to the binary variable "deterioration yes *vs*. no". Significant *p*-values are shown in bold.

53% of the patients felt distressed due to the diagnosis of breast cancer and 48% of the patients due to the upcoming RT (4). In another study of 276 breast cancer patients receiving adjuvant RT, 28.4% of patients reported distress (6). In the study of Goldschmidt Mertz *et al*., the mean distress score after the diagnosis of breast cancer, likely prior to the start of any treatment, was 5.4 (±3.1) points when using the NCCN-DT (5). Rates of distress depended on the cut-off value of the distress score and were reported to be 43% (cut-off=7 points) and 77% (cut-off=3 points), respectively. In our previous study of breast cancer patients assigned to adjuvant RT, the specific rates of the six emotional problems assessed in the NCCN-DT ranged between 12% and 46% (2).

When compared to other tumor entities, the prevalence of pre-RT emotional problems rates in breast cancer patients was similar to the prevalence found in patients with rectal or anal cancer (11-47%) and patients with head-and-neck cancers (10-44%), lower than in patients with gynecological cancers (16-57%) and malignant gliomas (23-63%), and higher than patients with lung cancer (15-38%) and prostate cancer (5-27%) (9-14). These data show that pre-RT emotional distress is comparably common in breast cancer patients and requires more attention to identify patients needing psychological assistance. This holds true also for distress during the course of RT, which has been investigated only in very few studies. Luutonen *et al*. concluded that the medical staff should be more aware of depression and distress during RT of breast cancer (6). In the study of Mose *et al*., 36% of the patients who experienced pre-treatment anxiety did not improve during the course of RT. Moreover, in our previous pilot study that investigated the course of distress during RT, the mean distress score slightly increased (+0.1 points) in the subgroup of 55 patients irradiated for breast cancer (8).

Table IV. *Patients with a baseline distress score of ≤5 points (n=208): Mean changes of distress scores during the radiotherapy course. p-values were calculated with the Wilcoxon two-sample test (2 subgroups) or Kruskal-Wallis test (≥3 subgroups).*

Characteristic	Subgroup	Mean change (points)	Standard deviation	*p*-Value
Age at radiotherapy	≤64 Years	+0.9	2.7	0.27
	65-79 Years	+0.3	2.5	
	≥80 Years	±0.0	2.2	
Sex	Female	+0.5	2.6	0.77
	Male	±0.0	0.0	
Karnofsky performance score	≤80	+0.1	2.7	0.23
	90-100	+0.6	2.5	
Intent of treatment	Curative	+0.5	2.6	0.30
	Palliative	+0.9	1.9	
Previous radiotherapy	No	+0.6	2.6	0.70
	Yes	+0.2	2.3	
All patients		+0.5	2.6	

The present study investigated the course of distress in a larger cohort of 330 patients and additionally evaluated potential risk factors for increased distress. In contrast to our previous study, it was now shown that the mean distress score decreased during the course of RT (8). This difference can be mainly explained by the six times larger sample size

Table V. *Patients with a baseline distress score of ≤5 points (n=208): Improvement (minus ≥2 points), no change, and deterioration (plus ≥2 points) of distress scores during radiotherapy. p-values were calculated with the Wilcoxon two-sample test (2 subgroups) or Kruskal-Wallis test (≥3 subgroups). Additional p-values were calculated for comparisons of subgroups regarding the binary variable "deterioration yes vs. no" using the Chi-square test.*

Characteristic	Subgroup	Change of distress scores			*p*-Value	*p*-Value*
		Improvement n, (%)	No change n, (%)	Deterioration n, (%)		
Age at radiotherapy	≤64 Years	15 (17)	40 (46)	32 (37)	0.22	0.34
	65-79 Years	25 (26)	46 (47)	27 (28)		
	≥80 Years	6 (26)	11 (48)	6 (26)		
Sex	Female	46 (22)	95 (46)	65 (32)	0.86	1.00
	Male	0 (0)	2 (100)	0 (0)		
Karnofsky performance score	≤80	15 (34)	16 (36)	13 (30)	0.20	0.78
	90-100	31 (19)	81 (49)	52 (32)		
Intent of treatment	Curative	44 (24)	85 (45)	59 (32)	0.58	0.78
	Palliative	2 (10)	13 (62)	6 (29)		
Previous radiotherapy	No	40 (22)	83 (46)	59 (32)	0.49	0.34
	Yes	6 (23)	14 (54)	6 (23)		
All patients		46 (22)	97 (47)	65 (31)		

**p*-Values for comparisons of subgroups with respect to the binary variable "deterioration yes *vs*. no".

in the present study, leading to greater validity of the results. Moreover, the current study identified risk factors for increase of distress, namely a KPS of 90-100, younger age, and no previous RT. An inverse correlation between distress and age was previously described for cancer patients in general (15-19) and for breast cancer patients in different situations including RT (2, 4-6, 20-22). An association between no previous RT and increased distress has not been described before. However, one may speculate that patients irradiated for the second or third time are more used to the procedure of RT and less scared than patients receiving their first course of RT. According to intuition, one would have expected an association between lower KPS and increase of distress. The fact that patients with a higher KPS of 90-100 were more likely to experience increased distress during their RT-course may be explained by the fact that they had lower pre-RT distress scores than patients with a KPS ≤80 (mean 4.5 *vs*. 5.6). Moreover, in our pilot study including different tumor types, mean decrease of distress was non-significantly less pronounced in patients with a KPS of 90-100 (+0.3 to –0.6) than in patients with a KPS of 60-80 (–0.2 to –2.0) (8). Despite the consistency with results of previous studies, the retrospective nature of the present study including the risk of a hidden bias needs to be kept in mind.

In conclusion, psychological assistance should be offered to all patients irradiated for breast cancer, regardless of the pre-RT distress score. This applies particularly to those patients with risk factors for increased distress during their RT-course. The results of this study should be confirmed in a prospective cohort of patients.

Conflicts of Interest

The Authors indicate that there are no conflicts of interest related to this study.

Authors' Contributions

C.D., S.J., N.Y.Y. and D.R. participated in the design of the study. C.D. provided the data, which were analyzed by a professional statistician supported by D.R. The article was drafted by D.R. and N.Y.Y., and subsequently reviewed and approved by all Authors.

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