

Distress Scores During Radiotherapy for Lung Cancer: Course and Prognostic Factors

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Abstract. *Background/Aim:* Cancer treatment can lead to significant distress. We investigated the course of distress during radiotherapy (RT) for lung cancer. *Patients and Methods:* Data of 159 patients receiving RT for lung cancer were investigated for change of distress scores during RT. Five characteristics were analyzed including age, sex, Karnofsky performance score, intent of RT, and receipt of previous RT. Additional analyses were performed in patients with pre-RT scores ≤ 5 points. *Results:* Mean pre-RT and post-RT distress scores were 5.5 (± 2.6) and 4.7 (± 2.6), respectively. No characteristic was significantly associated with mean change or increase of distress. In patients with pre-RT scores ≤ 5 points, non-significantly higher rates of increased distress were found for age ≤ 64 years, female sex, and Karnofsky performance score 90-100. *Conclusion:* Distress is reduced during a course of RT for lung cancer. This may reflect a reduction in anticipatory distress after first-hand experience.

Many cancer patients scheduled for radiation therapy (RT) report psychological distress prior to the start of treatment (1-6). In our previous retrospective study of 144 patients with non-small cell lung cancer (NSCLC) or small-cell lung

cancer (SCLC), 65% of the patients indicated at least one emotional problem prior to RT (7). Moreover, in prospective studies of patients irradiated for lung cancer, rates of anxiety range between 12% and 54% and rates of depression between 20% and 65.5% (8-10). In a randomized trial, psychological distress was reported by 17-18% of the patients irradiated for unresectable NSCLC (11).

Few studies have investigated the course of distress from pre-RT baseline until the end of RT (12-14). In our pilot study including 200 patients irradiated for different types of primary tumor, distress became less pronounced during the RT course (14). This held particularly true for the subgroup of 47 lung cancer patients. However, no study has focused specifically on the course of distress during an RT series in patients irradiated for lung cancer. This study evaluated the course of distress during RT of lung cancer and aimed to identify changes in distress and corresponding prognostic factors for this specific group.

Patients and Methods

A total of 159 patients receiving RT for lung cancer between November 2021 and November 2022 were included in this retrospective study, which was approved by the responsible Ethics Committee in Lübeck (file no. 2022-486). These patients had completed the National Comprehensive Cancer Network (NCCN) Distress Thermometer before (baseline) and at the end of the RT course (15). Distress scores on the Distress Thermometer ranged from 0 (no distress) to 10 (maximum distress felt by the patients) points. Five characteristics were analyzed for changes of distress scores during the course of RT. The change of the score was calculated by subtracting the pre-RT from the post-RT score. Characteristics (Table I) were age [≤ 64 vs. 65-79 (elderly) vs. ≥ 80 (very elderly) years], sex (female vs. male), Karnofsky performance score (≤ 80 vs. 90-100), intent of RT (curative vs. palliative), and previous RT (no vs. yes).

Statistical analyses. Mean changes of distress scores during RT plus standard deviations were calculated. In addition, improvement (distress score decreased by 2 or more points), no change, and

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deterioration (distress score increased by 2 or more points) of distress were evaluated. Associations between the characteristics and mean changes of distress scores were analyzed with the Wilcoxon two-sample test (two subgroups) and the Kruskal-Wallis test (3 or more subgroups). The same tests were used for evaluating the characteristics with respect to improvement, no change or deterioration of distress scores. Furthermore, the impact of the characteristics on the course of distress was investigated using the binary variable “increase vs. no increase”. For these investigations, the Chi-square test (univariable analyses) and a logistic regression model (multivariable analyses) were applied. *p*-Values of <0.05 were considered significant and *p*-values of <0.10 indicating a trend for all statistical analyses described in this paragraph. Since physicians are less likely to offer psychological assistance to patients with lower baseline levels of distress, we performed additional analyses in patients with distress scores of ≤5 points, in order to characterize the need for assistance in this group.

Results

In the entire cohort, mean pre-RT score of distress was 5.5 (±2.6), and the post-RT score was 4.7 (±2.6). The mean change was -0.8 (±2.7) points, which was not significantly associated with any of the investigated five characteristics (Table II). When considering improvement, no change, or deterioration of distress, a trend for increased distress was found for female patients on univariable analysis (*p*=0.071, Table III). When using the binary variable “increase vs. no increase”, no significant associations were identified for any characteristics on univariable (Table III) and multivariable (Table IV) analyses.

In the additional analyses of patients with pre-RT distress scores of ≤5 points, no significant associations were also found between the investigated characteristics and mean change of distress scores (Table V). Moreover, no associations were found when considering improvement, no change, or deterioration of distress, and when using the binary variable “increase vs. no increase” (Table V and Table VI). However, rates of deterioration (increase of) distress differed by more than 10% when considering age, sex, and Karnofsky performance score (Table VI). Non-significantly higher rates of increased distress were found in patients aged ≤64 years, female patients, and patients with a Karnofsky performance score of 90-100.

Discussion

To be scheduled for a course of RT may cause considerable distress for the corresponding patients, which generally has a negative effect on the patients’ well-being (16). It may even be associated with a worse survival prognosis (1). Distress prior to a course of RT is not uncommon for many tumor entities including lung cancer. For example, pre-RT distress was reported by 65% of the patients irradiated for NSCLC or SCLC in a recent retrospective study (7). Moreover, in

Table I. Entire cohort (n=159): Distribution of patient characteristics.

Characteristic	Subgroup	Number of patients (n)	Proportion (%)
Age at radiotherapy	≤64 Years	48	30
	65-79 Years	94	59
	≥80 Years	17	11
Sex	Female	82	52
	Male	77	48
Karnofsky performance score	≤80	104	65
	90-100	55	35
Intent of treatment	Curative	70	44
	Palliative	89	56
History of previous radiotherapy	No	108	68
	Yes	51	32
All patients		159	100

prospective studies investigating RT for lung cancer, anxiety and depression were reported by 12-54% and 20-65.5% of the patients, respectively (8-10). However, very little is known about the course of distress during RT. It may increase due to acute treatment-related side effects, decrease because patients get used to RT-procedures, or remain (almost) unchanged. In our previous study of patients irradiated for different types of malignancy, the mean distress score decreased during the course of RT (14). In that study, significant differences were found for various primary tumor types. Therefore, it was considered reasonable to separately evaluate the change of distress scores during an RT course for the most common primaries. The present study focused specifically on lung cancer. It revealed that the mean distress score decreased during RT. This result agrees in principle with the change of distress found in the subgroup of lung cancer patients in our previous study (14). However, the mean change of distress scores was less pronounced in the present study (-0.8 vs. -2.0 points). This difference may be explained by the small number of lung cancer patients in the previous study compared to the present one (47 vs. 159 patients).

In addition, the present study aimed to identify risk factors of increased distress during the RT course. In the entire cohort, no significant associations were found. In the subgroup analyses of patients with a baseline distress score ≤5 points, non-significantly higher rates of increased distress (difference >10%) were associated with younger age (≤64 years), female sex, and a Karnofsky performance score of 90-100. In our previous study including different primary tumor types, change of mean distress scores during RT appeared not to be age-dependent (14). Mean scores decreased in both patients aged ≤65 years (-0.7 points) and patients aged >65 years (-0.4 points). However, decrease of mean distress score was non-significantly less pronounced in female than male patients (-0.2 vs. -1.0, *p*=0.10) in the age-group ≤65 years, and in patients with a Karnofsky

Table II. Entire cohort (n=159): Mean changes of distress scores during the course of radiotherapy (post-treatment scores minus pre-treatment scores). *p*-Values were obtained from the Wilcoxon two-sample test (two subgroups) or the Kruskal-Wallis test (three or more subgroups).

Characteristic	Subgroup	Mean change (points)	Standard deviation	<i>p</i> -Value
Age at radiotherapy	≤64 Years	-0.5	3.3	0.85
	65-79 Years	-0.9	2.3	
	≥80 Years	-0.6	2.2	
Sex	Female	-0.5	2.9	0.22
	Male	-1.1	2.4	
Karnofsky performance score	≤80	-0.7	2.5	0.81
	90-100	-0.8	2.9	
Intent of treatment	Curative	-0.6	2.6	0.40
	Palliative	-0.9	2.7	
Previous radiotherapy	No	-0.8	2.5	0.90
	Yes	-0.8	3.0	
All patients		-0.8	2.7	

Table III. Entire cohort (n=159): Improvement (minus ≥2 or more points), no change (±0-1 points), and deterioration (plus 2 or more points) of distress scores during the course of radiotherapy. *p*-Values were obtained from the Wilcoxon two-sample test (two subgroups) or the Kruskal-Wallis test (three or more subgroups). Additional *p*-values were calculated for comparisons of subgroups with respect to the binary variable “deterioration yes vs. no” using the Chi-square test.

Characteristic	Subgroup	Change of distress scores			<i>p</i> -Value	<i>p</i> -Value*
		Improvement n, (%)	No change n, (%)	Deterioration n, (%)		
Age at radiotherapy	≤64 Years	19 (40)	18 (38)	11 (23)	0.93	0.49
	65-79 Years	35 (37)	45 (48)	14 (15)		
	≥80 Years	7 (41)	7 (41)	3 (18)		
Sex	Female	26 (32)	39 (48)	17 (21)	0.071	0.29
	Male	35 (45)	31 (40)	11 (14)		
Karnofsky performance score	≤80	38 (37)	51 (49)	15 (14)	0.90	0.15
	90-100	23 (42)	19 (35)	13 (24)		
Intent of treatment	Curative	25 (36)	32 (46)	13 (19)	0.58	0.78
	Palliative	36 (40)	38 (43)	15 (17)		
Previous radiotherapy	No	42 (39)	47 (44)	19 (18)	0.89	0.99
	Yes	19 (37)	23 (45)	9 (18)		
All patients		61 (38)	70 (44)	28 (18)		

**p*-Values for comparisons of subgroups with respect to the binary variable “increase vs. no increase” of distress.

performance score of 90-100 when compared to 50-80 (-0.6 to +0.3 vs. -2.0 to -0.2, *p*=0.17). And in the study of Mose *et al.* in breast cancer patients receiving adjuvant RT, younger patients (≤58 years) experienced higher levels of distress before and during RT (12). These findings are in concordance with the results of the present study in patients with a baseline distress score ≤5 points. Moreover, in a previous study that evaluated risk factors for distress prior to the start of RT, the prevalence of emotional problems indicating psychological distress was significantly associated with younger age (≤69 years) and female sex (7). The fact that our results are mainly in line with the results of previous studies suggest consistency of our present data. However, the

retrospective nature of these data should be kept in mind during the interpretation of our results. These results illustrate the importance of psycho-oncological support for all lung cancer patients receiving RT during their course of treatment including those patients with baseline distress scores ≤5 points.

In conclusion, in many patients irradiated for lung cancer distress scores decreased during RT. Despite this finding, early psych-oncological support should be generally offered to patients irradiated for lung cancer. This accounts particularly for patients who are at risk of increased distress during their treatment course, irrespective of the pre-RT distress score.

Table IV. Entire cohort (n=159): Results of the multivariable analysis regarding the binary variable “increase vs. no increase” of distress.

Characteristic	Compared subgroups	Odds ratio (point estimate)	95% Wald confidence interval	p-Value
Age	65-79 vs. ≤64 years	0.613	0.243-1.547	0.54
	≥80 vs. ≤64 years	0.977	0.216-4.421	
Sex	Female vs. male	1.707	0.722-4.038	0.22
Karnofsky performance score	≤80 vs. 90-100	0.572	0.232-1.411	0.23
Intent of treatment	Curative vs. palliative	0.926	0.377-2.274	0.87
Previous radiotherapy	No vs. yes	1.085	0.425-2.769	0.86

Table V. Patients with a baseline distress score of ≤5 points (n=76): Mean changes of distress scores during the course of radiotherapy (post-treatment scores minus pre-treatment scores). p-Values were obtained from the Wilcoxon two-sample test (two subgroups) or the Kruskal-Wallis test (three or more subgroups).

Characteristic	Subgroup	Mean change (points)	Standard deviation	p-Value
Age at radiotherapy	≤64 Years	+1.0	3.1	0.20
	65-79 Years	+0.3	2.2	
	≥80 Years	-0.6	2.2	
Sex	Female	+0.7	2.9	0.35
	Male	+0.1	2.2	
Karnofsky performance score	≤80	+0.2	2.5	0.39
	90-100	+0.6	2.7	
Intent of treatment	Curative	+0.3	2.4	0.79
	Palliative	+0.5	2.8	
Previous radiotherapy	No	+0.2	2.4	0.54
	Yes	+0.7	2.8	
All patients		+0.4	2.6	

Table VI. Patients with a baseline distress score of ≤5 points (n=76): Improvement (minus ≥2 or more points), no change (±0-1 points), and deterioration (plus 2 or more points) of distress scores during the course of radiotherapy. p-Values were obtained from the Wilcoxon two-sample test (two subgroups) or the Kruskal-Wallis test (three or more subgroups). Additional p-values were calculated for comparisons of subgroups with respect to 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	6 (24)	10 (40)	9 (36)	0.33	0.56
	65-79 Years	9 (23)	18 (45)	13 (33)		
	≥80 Years	5 (45)	4 (36)	2 (18)		
Sex	Female	8 (21)	16 (42)	14 (37)	0.26	0.32
	Male	12 (32)	16 (42)	10 (26)		
Karnofsky performance score	≤80	13 (28)	22 (47)	12 (26)	0.28	0.15
	90-100	7 (24)	10 (34)	12 (41)		
Intent of treatment	Curative	10 (24)	20 (49)	11 (27)	0.68	0.34
	Palliative	10 (29)	12 (34)	13 (37)		
Previous radiotherapy	No	14 (29)	20 (41)	14 (31)	0.63	0.81
	Yes	6 (22)	12 (44)	9 (33)		
All patients		20 (26)	32 (42)	24 (32)		

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

Conflicts of Interest

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

Authors' Contributions

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

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