

Final Results of a Study Evaluating the Course of Distress Scores During Radiotherapy for Malignant Diseases

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Abstract. *Background/Aim:* Patients who receive radiotherapy (RT) may experience significant distress. This study investigated distress scores during RT for a variety of malignancies. *Patients and Methods:* Distress thermometers (scores of 0-10 points) were completed by 927 patients at baseline and end of RT. Six characteristics were evaluated for changes of distress scores including age, sex, Karnofsky performance score (KPS), tumor type, intent of treatment, and previous RT. *Results:* Mean distress scores were 4.9 (± 2.7) at baseline and 4.6 (± 2.7) at the end of RT; mean change was -0.3 (± 2.8) points. On univariable analysis, increased distress (≥ 2 points) was significantly associated with KPS 90-100 ($p < 0.001$) and curative intent ($p = 0.040$). Trends were found for age ≤ 64 years ($p = 0.062$), head-and-neck cancer ($p = 0.076$), and no prior RT ($p = 0.055$). In patients with baseline scores ≤ 5 points, deterioration rates were 30-47%. *Conclusion:* Psychological support should be offered to all patients undergoing RT. This would benefit particularly patients with risk factors for increased distress.

A considerable proportion of patients who receive radiotherapy (RT) experience distress (1-10). Very little data exists regarding the course of distress from pre-treatment baseline until the end of RT. We performed a pilot study of 200 patients in 2022 (11) demonstrating that the mean distress score decreased in the majority of patients during RT, which supports the hypothesis of habituation with daily RT. Moreover, the type of primary

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Key Words: Malignant disease, distress thermometer, distress scores, radiotherapy, risk factors.

tumor was identified as a significant risk factor for deterioration of distress, i.e., for increase of distress scores (11). In the present study, we aimed to provide additional information regarding the course of distress during RT in a larger cohort of patients and identify additional risk factors for increased distress. These high-risk patients may particularly benefit from psychological support prior to and during their treatment course.

Patients and Methods

In this study, we retrospectively investigated the distress scores of 927 patients who received RT at two German Centers: University Medical Center Schleswig-Holstein, Campus Lübeck and Medical Practice for Radiotherapy and Radiation Oncology, Hannover, between 11/2021 and 11/2022. The study received approval from the responsible Ethics Committee at the University of Lübeck (file number 2022-486). Patients completed the Distress Thermometer (DT) of National Comprehensive Cancer Network at baseline (prior to radiotherapy) and at the end (after the last fraction) of their radiotherapy course (12). The DT includes two parts. In the first part, the patients are asked to rate how much distress they have been experiencing during the past week; distress scores range between 0 points (no distress) and 10 points (maximum distress). In the second part, the patients are asked to indicate the problems they have had during the past week (yes vs. no) from a list of practical problems, family problems, emotional problems, spiritual/religious concerns, and physical problems (12).

Six characteristics were evaluated with respect to changes of distress during their radiotherapy course, calculated by subtracting the baseline score from the score at the end of radiotherapy. These characteristics included age at the start of radiotherapy [≤ 64 years vs. 65-79 years (=elderly patients) vs. ≥ 80 years (=very elderly patients)], sex (female vs. male), Karnofsky performance score (≤ 80 vs. 90-100), primary tumor type (breast cancer vs. lung cancer vs. prostate cancer vs. head-and-neck cancer vs. other tumor types), intent of treatment (curative vs. palliative), and history of previous radiotherapy (no vs. yes). Their distributions are shown in Table I.

Changes of distress scores were obtained as indicated above (post-radiotherapy score minus baseline score). The mean values and standard deviations of the changes were calculated. Moreover, the rates of improvement (decrease of distress score by at least 2 points), no change (difference of -1 , ± 0 , or $+1$ points), and



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Table I. Entire cohort (n=927): Distribution of patient characteristics.

| Characteristic | Subgroup | Number of patients (n) | Proportion (%) |
|----------------------------------|-------------------|------------------------|----------------|
| Age at radiotherapy | ≤64 Years | 308 | 33 |
| | 65-79 Years | 485 | 52 |
| | ≥80 Years | 134 | 14 |
| Sex | Female | 527 | 57 |
| | Male | 400 | 43 |
| Karnofsky performance score | ≤80 | 401 | 43 |
| | 90-100 | 526 | 57 |
| Primary tumor type | Breast cancer | 330 | 36 |
| | Lung cancer | 159 | 17 |
| | Prostate cancer | 136 | 15 |
| | H&N cancer | 56 | 6 |
| | Other tumor types | 246 | 27 |
| Intent of treatment | Curative | 598 | 65 |
| | Palliative | 329 | 35 |
| History of previous radiotherapy | No | 731 | 79 |
| | Yes | 196 | 21 |
| All patients | | 927 | 100 |

H&N, Head-and-neck.

deterioration (increase of distress score by at least 2 points) distress were provided. For statistical analyses regarding associations between investigated characteristics and mean changes of distress scores (Table II), we used the Wilcoxon two-sample test (comparison of two subgroups) and the Kruskal-Wallis test (comparison of three or more subgroups). The same tests were used for evaluation of associations between investigated characteristics and changes of distress scores considering improvement, no change, or deterioration (Table III). In addition, the characteristics were evaluated with respect to the binary variable “deterioration vs. no deterioration” of distress scores. These evaluations were performed with the Chi-square test (univariable analyses) and a logistic regression model (multivariable analyses). In all statistical analyses, *p*-values <0.05 indicated significance and *p*-values <0.10 a trend.

Physicians are more likely to offer psychological support to patients with a higher distress score at baseline than to patients with lower scores. To identify the need for such support in the latter patient group, we performed subgroup analyses in patients with a baseline distress score being less or equal when compared to the mean baseline score.

Results

Mean distress scores were 4.9 (±2.7) at baseline and 4.6 (±2.7) at the end of RT, and the mean change of distress scores was -0.3 (±2.8) points. The mean change was significantly associated with age ≤64 years (*p*=0.008), KPS 90-100 (*p*<0.001), and no history of previous RT (*p*=0.042) (Table II). Changes of distress scores considering improvement, no change, and deterioration were significantly associated with age ≤64 years (*p*=0.021) and KPS 90-100 (*p*<0.001), and a trend was found for no previous RT (*p*=0.055) (Table III).

When evaluating the six investigated characteristics with respect to deterioration of distress (no vs. yes), significant associations were identified for KPS 90-100 (*p*<0.001) and

curative intent of treatment (*p*=0.040) on univariable analyses (Table III). In addition, trends were found for age ≤64 years (*p*=0.062), head-and-neck-cancer (*p*=0.076), and no previous RT (*p*=0.055). On multivariable analyses, KPS 90-100 was significantly associated with deterioration of distress (odds ratio=0.564, 95% Wald confidence interval=0.390-0.817, *p*=0.002) (Table IV).

Since the mean distress score at baseline was 4.9 points, we performed subgroup analyses in patients with a baseline distress score of ≤5 points. In all but one groups related to the six investigated characteristics, the mean distress score increased during the course of RT (Table V). The mean change was significantly associated with KPS 90-100 (*p*=0.014), and no history of previous RT (*p*<0.001) (Table V). In these groups related to investigated characteristics, the rates of deterioration ranged between 30% and 47% (Table VI).

Discussion

A considerable proportion of cancer patients experiences distress including those treated with RT (1-10, 13-16). Distress can significantly impair the patients’ quality of life and may be associated with decreased survival (2, 17). Several studies investigated the prevalence of distress prior to RT, which varied between different tumor types (4-9). When separately considering tumor entities and the emotional problems addressed in the DT, namely worry, fear, sadness, depression, nervousness, and loss of interest in normal activities, the pre-RT prevalence ranged between 5% and 67% (4-9). However, very few studies have investigated the course of distress during RT. The study of Mose *et al.* evaluated 111 women with breast cancer receiving adjuvant RT following breast-conserving

Table II. Entire cohort (n=927): Mean changes of distress scores during the course of radiotherapy (post-treatment scores minus pre-treatment scores).

| Characteristic | Subgroup | Mean change (points) | Standard deviation | p-Value |
|-----------------------------|-----------------|----------------------|--------------------|------------------|
| Age at radiotherapy | ≤64 Years | +0.1 | 2.9 | 0.008 |
| | 65-79 Years | -0.6 | 2.7 | |
| | ≥80 Years | -0.5 | 2.7 | |
| Sex | Female | -0.3 | 2.7 | 0.83 |
| | Male | -0.3 | 2.9 | |
| Karnofsky performance score | ≤80 | -0.8 | 2.8 | <0.001 |
| | 90-100 | ±0.0 | 2.7 | |
| Primary tumor type | Breast cancer | -0.4 | 2.8 | 0.12 |
| | Lung cancer | -0.8 | 2.7 | |
| | Prostate cancer | -0.1 | 2.8 | |
| | H&N cancer | ±0.0 | 3.2 | |
| | Other types | -0.2 | 2.8 | |
| Intent of treatment | Curative | -0.2 | 2.9 | 0.20 |
| | Palliative | -0.5 | 2.6 | |
| Previous radiotherapy | No | -0.2 | 2.8 | 0.042 |
| | Yes | -0.7 | 2.6 | |
| All patients | | -0.3 | 2.8 | |

p-Values were obtained from the Wilcoxon two-sample test (two subgroups) or the Kruskal-Wallis test (three or more subgroups). H&N, Head-and-neck. Significant p-values are shown in bold.

Table III. Entire cohort (n=927): 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.

| Characteristic | Subgroup | Change of distress scores | | | p-Value | p-Value* |
|-----------------------------|-----------------|---------------------------|---------------------|-------------------------|------------------|------------------|
| | | Improvement n, (%) | No change n, (%) | Deterioration n, (%) | | |
| Age at radiotherapy | ≤64 Years | 87 (28) | 136 (44) | 85 (28) | 0.021 | 0.062 |
| | 65-79 Years | 162 (33) | 223 (46) | 100 (21) | | |
| | ≥80 Years | 54 (40) | 52 (39) | 28 (21) | | |
| Sex | Female | 164 (31) | 249 (47) | 114 (22) | 0.85 | 0.26 |
| | Male | 139 (35) | 162 (41) | 99 (25) | | |
| Karnofsky performance score | ≤80 | 161 (40) | 172 (43) | 68 (17) | <0.001 | <0.001 |
| | 90-100 | 142 (27) | 239 (45) | 145 (28) | | |
| Primary tumor type | Breast cancer | 110 (33) | 150 (45) | 70 (21) | 0.11 | 0.076 |
| | Lung cancer | 61 (38) | 70 (44) | 28 (18) | | |
| | Prostate cancer | 39 (29) | 60 (44) | 37 (27) | | |
| | H&N cancer | 17 (30) | 20 (36) | 19 (34) | | |
| | Other types | 76 (31) | 111 (45) | 59 (24) | | |
| Intent of treatment | Curative | 193 (32) | 255 (43) | 150 (25) | 0.040 | 0.10 |
| | Palliative | 110 (34) | 156 (47) | 63 (19) | | |
| Previous radiotherapy | No | 231 (32) | 322 (44) | 178 (24) | 0.055 | 0.055 |
| | Yes | 72 (37) | 89 (45) | 35 (18) | | |
| All patients | | 303 (33) | 411 (44) | 213 (23) | | |

p-Values were obtained from the Wilcoxon two-sample test (two subgroups) or the Kruskal-Wallis test (three or more subgroups). *p-Values were calculated for comparisons of subgroups with respect to the binary variable “deterioration yes vs. no” using the Chi-square test. Significant p-values are shown in bold. H&N, Head-and-neck.

surgery (18). Distress due to diagnosis of cancer was reported by 53% of the women, and 48% were afraid of the upcoming RT. During the course of RT, 36% of these women did not experience improvement of anxiety. In the study of Hess *et al.*,

a DT was completed daily during a course of RT in 71 patients with different tumor entities (1), Thirty-seven percent of these patients reported distress scores ≥4 at least once during their treatment. Mean distress scores and rates improved during the

Table IV. Entire cohort (n=927): Results of the multivariable analysis regarding the binary variable “deterioration yes vs. no”.

| Characteristic | Compared subgroups | Odds ratio (point estimate) | 95% Wald confidence interval | p-Value |
|-----------------------------|----------------------------|-----------------------------|------------------------------|--------------|
| Age | 65-79 vs. ≤64 years | 0.713 | 0.500-1.016 | 0.17 |
| | ≥80 vs. ≤64 years | 0.819 | 0.485-1.384 | |
| Sex | Female vs. male | 0.987 | 0.632-1.539 | 0.95 |
| Karnofsky performance score | ≤80 vs. 90-100 | 0.564 | 0.390-0.817 | 0.002 |
| Primary tumor type | Breast cancer vs. others | 0.675 | 0.414-1.101 | 0.17 |
| | H&N cancer vs. others | 1.486 | 0.774-2.851 | |
| | Lung cancer vs. others | 0.748 | 0.448-1.250 | |
| | Prostate cancer vs. others | 1.128 | 0.658-1.932 | |
| Intent of treatment | Curative vs. palliative | 1.097 | 0.725-1.658 | 0.66 |
| Previous radiotherapy | No vs. yes | 1.271 | 0.805-2.005 | 0.30 |

H&N, Head-and-neck. Significant p-values are shown in bold.

Table V. Patients with a baseline distress score of ≤5 points (n=548).

| Characteristic | Subgroup | Mean change (points) | Standard deviation | p-Value |
|-----------------------------|-----------------|----------------------|--------------------|------------------|
| Age at radiotherapy | ≤64 Years | +1.0 | 2.8 | 0.17 |
| | 65-79 Years | +0.5 | 2.4 | |
| | ≥80 Years | +0.6 | 2.6 | |
| Sex | Female | +0.6 | 2.6 | 0.34 |
| | Male | +0.8 | 2.6 | |
| Karnofsky performance score | ≤80 | +0.4 | 2.7 | 0.014 |
| Primary tumor type | 90-100 | +0.9 | 2.5 | 0.34 |
| | Breast cancer | +0.5 | 2.6 | |
| | Lung cancer | +0.4 | 2.6 | |
| | Prostate cancer | +0.8 | 2.6 | |
| | H&N cancer | +1.3 | 2.6 | |
| Intent of treatment | Other types | +0.8 | 2.6 | 0.94 |
| | Curative | +0.7 | 2.6 | |
| | Palliative | +0.8 | 2.6 | |
| Previous radiotherapy | No | -0.2 | 2.8 | <0.001 |
| | Yes | +0.4 | 2.4 | |
| All patients | | +0.7 | 2.6 | |

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). Significant p-values are shown in bold. H&N, Head-and-neck.

first five weeks but increased thereafter beyond baseline levels. After completion of RT, distress improved in 53% and persisted in 47% of the patients (1). More recently, we compared distress scores at the end of a RT to pre-RT baseline scores in a study of 200 patients with different primary tumor types (11). In that study, the mean change of distress scores was -0.5 (±2.6) points, which was significantly associated with primary tumor type (p=0.049). A decrease of the mean distress score was found for lung cancer, kidney cancer and prostate cancer, an increase for breast cancer, head-and-neck cancer, gastrointestinal cancers, melanoma, and cancer of unknown primary (11). That study was considered a pilot study to be followed by a larger one, which is presented now. According to its results, the mean change of distress scores was -0.3 (±2.8)

points, which is similar to the mean change found in the pilot study. In our present study, the mean change of distress scores was significantly associated with age ≤64 years, KPS 90-100, and no history of previous RT. In the pilot study, significant associations with these characteristics were not found, probably due to the much smaller sample size compared to the present study. On the other hand, primary tumor type was significantly associated with mean change of distress scores in the pilot but not in the present study. However, primary tumor type showed a least a trend (p=0.12) in the present study. Moreover, mean changes showed a difference of ≥0.4 points between both studies for several tumor types, namely +0.1 (pilot study) vs. -0.4 (present study) for breast cancer, -2.0 vs. -0.8 for lung cancer, and -0.5 vs. -0.1 for prostate cancer (11). In our present

Table VI. Patients with a baseline distress score of ≤ 5 points ($n=548$): Improvement (minus 2 or more points), no change ($\pm 0-1$ points), and deterioration (plus 2 or more points) of distress scores during the course of radiotherapy.

| 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 | 37 (19) | 78 (41) | 75 (39) | 0.39 | 0.22 |
| | 65-79 Years | 57 (21) | 132 (48) | 88 (32) | | |
| | ≥ 80 Years | 16 (20) | 38 (47) | 27 (33) | | |
| Sex | Female | 64 (20) | 149 (47) | 101 (32) | 0.27 | 0.15 |
| | Male | 46 (20) | 99 (42) | 89 (38) | | |
| Karnofsky performance score | ≤ 80 | 51 (26) | 85 (44) | 57 (30) | 0.008 | 0.062 |
| | 90-100 | 59 (17) | 163 (46) | 133 (37) | | |
| Primary tumor type | Breast cancer | 46 (22) | 97 (47) | 65 (31) | 0.19 | 0.35 |
| | Lung cancer | 20 (26) | 32 (42) | 24 (32) | | |
| | Prostate cancer | 15 (17) | 39 (44) | 35 (39) | | |
| | H&N cancer | 4 (13) | 13 (41) | 15 (47) | | |
| | Other types | 25 (17) | 67 (47) | 51 (36) | | |
| Intent of treatment | Curative | 78 (20) | 171 (45) | 135 (35) | 0.88 | 0.72 |
| | Palliative | 32 (20) | 77 (47) | 55 (34) | | |
| Previous radiotherapy | No | 88 (20) | 196 (44) | 159 (36) | 0.32 | 0.22 |
| | Yes | 22 (21) | 52 (50) | 31 (30) | | |
| All patients | | 110 (20) | 248 (45) | 190 (35) | | |

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. Significant *p*-values are shown in bold. H&N, Head-and-neck.

study, deterioration of distress occurred in 23% of the patients, which cannot be compared to previous studies, since it was not explicitly investigated before.

Significant results or trends for associations with deterioration of distress were found for KPS 90-100, curative intent of treatment, age ≤ 64 years, head-and-neck-cancer, and no previous RT. These results agree with those of previous studies performed in different situations or investigating other endpoints when compared to the present study. In a study of 148 patients from Saudi-Arabia irradiated for cancer, age and type of primary tumor were significantly associated with distress (19). In addition, several other studies revealed younger age to be associated with higher distress levels (13, 16, 18, 20). And in the study of Carlson *et al.* that evaluated the prevalence of psychological stress in cancer patients from the United States and Canada, patients with lung or pancreatic cancer were more likely to experience distress (16). The agreement of our results with findings of other studies demonstrates consistency of our data. However, when interpreting our results, the retrospective design of our study should be considered, which bears the risk of a hidden selection bias.

This also applies to the subgroup analyses performed in patients with baseline distress scores of ≤ 5 points. In these analyses, mean distress score increased during the course of radiotherapy in all groups related to investigated characteristics except no previous RT. Moreover, in these groups the rates of

deterioration were comparably high. These findings suggest that it is important to provide psychological support during a RT course not only for patients with high baseline distress scores but also for those patients with scores of ≤ 5 points.

In conclusion, the mean distress score slightly decreased during the course of RT. However, subgroups, such as patients with head-and-neck cancer, age ≤ 64 years, KPS 90-100, curative treatment, and those with no previous RT had a higher probability of deterioration of distress during their radiotherapy course. These patients likely benefit from intensive psychological support. Moreover, since many patients with lower distress scores at baseline experienced deterioration of distress during their treatment course, the offer of psychological support should not be limited to patients with higher baseline scores but provided for all patients undergoing RT.

Conflicts of Interest

On behalf of all Authors, the corresponding Author states that there are no conflicts of interest related to this study.

Authors' Contributions

C.D., S.J., S.T., 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, drafted by D.R. and N.Y.Y., was reviewed and approved by all Authors.

Acknowledgements

The study was funded by the European Regional Development Fund through the Interreg Deutschland-Danmark program as part of the project TreaT (148-1.1-21).

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Received June 14, 2023

Revised July 11, 2023

Accepted July 19, 2023