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Depressive Symptoms, Social Anxiety, and Perceived Neck Function in Patients with Head and Neck Cancer

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Abstract

Background—This study examined the relationships of depressive symptoms and social anxiety with perceived neck function in patients treated for head and neck cancer.

Methods—Depressive symptoms, social anxiety, and perceived neck-related function were measured at baseline, post treatment, every six weeks thereafter for one year following end of treatment, and at 15 and 18 months post treatment. Group-based trajectory modeling was used to generate clusters of patients with similar baseline and trajectories of perceived neck-related function after head and neck cancer treatment.

Results—Participants included 83 subjects who had completed at least one follow-up assessment. Three clusters of longitudinal patterns in neck disability were identified: none/mild, moderate, and severe. Significant associations were found between membership in the neck disability index trajectories and membership in the longitudinal patterns of depressive symptoms and social anxiety.

Conclusions—Impaired physical function and psychological distress are intertwined for patients with head and neck cancer long after completing treatment.

Keywords

oncology; head and neck; depressive symptoms; anxiety; physical function

INTRODUCTION

Over half a million people worldwide are diagnosed with head and neck cancer (HNC) annually.¹ Risk factors for this disease include tobacco and alcohol use as well as human papillomavirus (HPV) for oropharyngeal carcinoma and Epstein Barr virus (EBV) for nasopharyngeal carcinoma.² Although the majority of patients are middle aged and male, more females and younger individuals are being diagnosed with HNC due to the spread of HPV.

Treatment for HNC is rigorous and may include extensive surgery and chemoradiation. This multimodality therapy often results in functional loss including difficulties with speech, eating, sight, and smell, as well as musculoskeletal impairment involving the neck, shoulders, and jaw.³ Because of the highly visible location and structures affected, the disease and its treatment are both psychologically and physically intrusive.⁴

Recovery from HNC and its treatment is an extended process. In particular, morbidity may persist for months or years after the completion of treatment, impairing survivors' ability to complete activities of daily living and decreasing their quality of life.⁵ Lymphedema and fibrosis are ubiquitous in this population and are associated with significant functional deficits.^{6,7} For example, individuals who are not able to drive a car due to limited neck mobility may become socially isolated from pre-cancer social networks. Other individuals who have difficulty eating may find it awkward to socialize with their friends and family over meals. Changes in a survivor's voice make it difficult to communicate clearly. Survivors of HNC with lymphedema are more likely to report altered sensation symptoms including numbness, heaviness, and warmth, swelling, problems breathing and swallowing, and increased pain in the head and neck area as opposed to those without lymphedema.⁸

Decline in general physical function has been associated with increased psychological distress in patients with HNC.⁹⁻¹⁰ Specifically, survivors may experience social anxiety, making every-day interactions with family, friends, and others problematic.¹⁰ However, no known studies have examined the association between perceived neck functional loss, depressive symptoms and social anxiety. It is important for clinicians to anticipate which patients may experience depressive symptoms, and social anxiety along with functional loss so early intervention can be initiated. Therefore, the objective of this study was to examine the relationship between depressive symptoms and social anxiety with perceived neck-related functional loss in patients with HNC.

METHODS

Sample

Five hundred and three patients with newly diagnosed head and neck cancer patients were screened over a 25-month period at Vanderbilt-Ingram Cancer Center (VICC) to participate in a study that had as its primary aim to examine the prevalence and nature of late-effect internal, external, and combined lymphedema and fibrosis.. Of the 149 patients who were approached by study staff to discuss participation, 100 gave informed consent. Depressive symptoms and social anxiety were captured as part of the study. Eligibility criteria included:

(1) newly diagnosed, histologically proven HNC (carcinoma of the oral cavity, larynx, pharynx, paranasal sinuses and nasal cavity, or saliva glands); (2) stage II disease or greater; (3) age 21 or older; (4) willing and able to undergo baseline and follow-up assessment at VICC; and (5) able to speak and understand English. Exclusion criteria for continuation in the study included: (1) documented cognitive impairment that would preclude the ability to provide informed consent; (2) unwilling to undergo routine follow-up at VICC; and (3) recurrent cancer. No restrictions were placed on the type of treatment participants received for inclusion in the study. Seventeen patients were lost to follow-up or withdrawn prior to the initial 3-month follow-up assessment. Eighty-four were in the study three months post-treatment, 83 of which completed the first post-treatment follow-up and therefore comprised the study sample.

Procedure

The study was approved by the Vanderbilt Institutional Review Board and the VICC Scientific Review Committee. Participants provided written informed consent prior to study entry. They were asked to complete study measures at baseline (prior to radiation and/or chemotherapy), end of HNC treatment, every 6 weeks thereafter until 48 weeks following the end of HNC treatment, and at 15- and 18 months following the end of HNC treatment for a total of 11 assessment time points.

Measures

Demographic and clinical information, disease and treatment information, head and neck-related function, depressive symptoms, and social anxiety were examined in this study. Demographic and clinical information as well as disease and treatment information were collected by a trained research assistant from the medical record. Head and neck-related function, depressive symptoms, and social anxiety data were collected via self-report measures either in person or via mail depending on what was most convenient for participants. These self-report measures took approximately 15–30 minutes to complete. Other variables measured in the study but not included in this analysis are detailed in Ridner et al. 2016.⁶

Demographic and clinical information collected included age, gender, race, highest grade of education, marital status, employment status, residence, smoking and alcohol history, insurance, and medical problems.. Disease and treatment information included date of diagnosis, type, location of tumor, stage, and treatment details.

Musculoskeletal impairment related to neck dysfunction was measured using the Neck Disability Index (NDI). The NDI is a 10-item instrument that taps components of daily life that may be affected by neck pain and dysfunction.¹¹ Items include: pain; personal care; lifting; reaching; headache; concentration; work; driving; sleeping; and recreation. A Gutman-style response format is used, with six possible responses reflecting increasing degrees of disability. Items are summed to provide a total score.¹¹ Scores of 10–28% are considered mild disability, 30–48% moderate disability, 50–68% severe disability, 72% or more complete disability.¹¹

Depressive symptoms were measured using the Center for Epidemiological Studies Depression Scale (CES-D). The CES-D is a 20-item instrument designed to measure current level of depressive symptomatology, with emphasis on the affective component, depressed mood.¹² The symptoms are among those on which a diagnosis of clinical depression is based but which may also accompany other diagnoses to some degree. Each item is scored 0 “less than one day”, 1 “some or a little of the time (1–2 days)”, 2 “occasionally or a moderate amount of time (3–4 days)”, or 3 “most or all of the time (5–7 days)”. Four items are reverse scored. A score of greater than 16 is used to identify individuals who may be at risk for clinical depression.¹³ The study participant’s medical oncologist was immediately notified each time a participant scored 16 or greater on the CES-D.

Social anxiety was measured using the Liebowitz Social Anxiety Scale (LSAS). This generic scale contains 24 items that assess social interaction and performance situations an individual may face. Each situation is rated on a 4-part scale (0=none to 3=severe) for both fear and avoidance. Some example situations include going to a party, meeting strangers, and talking with people you don’t know very well. Originally designed as a clinician administered scale, it has been tested as a self-report instrument with adequate internal consistency. Both the clinician administered and self-report versions have been found to be internally consistent ($\alpha = 0.96$).¹⁵

Data Analysis

IBM SPSS version 24 was used for data analysis. Due to the positive skewness of the data distributions, median and interquartile (IQR) values were used to describe primary study variables. Handling of missing data in the measures are described elsewhere.⁶ To maximize the number of assessments within each of the critical post-treatment time periods and use cases with randomly missing assessments within those periods, the assessment periods were collapsed into those between 1–6 weeks post-treatment (designated end-of-treatment or EOT), 12–24 weeks (3–6 months) post, 30–36 weeks (~9 months) post, 42–48 weeks (~12 months), and 60–72 weeks (> 12 months) post-treatment. If more than one score for the NDI, CES-D, or LASA was available during any of these periods, the maximum score was used for the analyses reported here.

Because the primary focus of this secondary analysis was on the longitudinal patterns of neck-related function (NDI trajectories) and the associations of specific longitudinal patterns (trajectories) of depressive symptoms and social anxiety with those NDI trajectories in patients with HNC post-treatment, group-based trajectory modeling (SAS PROC TRAJ) was determined to provide the optimal approach. This approach was used to generate ‘clusters’ of patients with similar baseline and trajectories of neck-related function (NDI) for the 12–18 months post-HNC treatment. Akaike information criteria (AIC) and Bayesian information criteria (BIC) statistical indices were used to determine the optimal shape (linear, quadratic, etc) and number of clusters in the longitudinal data. A separate group-based trajectory modeling analysis was used to generate clusters of patients with similar trajectories of depressive symptoms (CES-D) and social anxiety (LSAS). For each of the trajectory modeling analysis, baseline and at least one post-treatment assessment value were required for inclusion in the analysis (number of participants = 83). To verify the reliability of the

findings, a second analysis of each measure was conducted using only the subsample of cases who had an assessment at least 1-year post-treatment (N=62). The shape and number of clusters were replicated in each result, therefore, the larger sample findings are reported here. Descriptive statistical and graphical summaries were used to explore the relationships among the trajectories of NDI, CES-D, and LSAS scores. Likelihood Chi-Square tests were used to test the associations of the NDI trajectories with those observed for CES-D and LSAS. Linear mixed-level analysis (between NDI trajectory groups, within-subject patterns of CES-D and LSAS scores) were used to test for differences in the patterns of CES-D and LSAS scores among the NDI trajectory groups (clusters). Statistically significant main or interaction effects from this analysis would suggest an association of the NDI trajectory pattern with the longitudinal pattern of CES-D and/or LSAS scores. Consistent findings from the Likelihood Chi-Square test associations of the 'groups' formed by the trajectory modeling and the findings from the linear mixed modeling approach would provide convergent validation for the associations between the two phenomena.

To explore possible associations of demographic and treatment characteristics with the derived NDI trajectories, tests of those variables (e.g., age, gender, t, PEG tube) were conducted using Chi-Square tests of independence (nominal characteristics) or Kruskal-Wallis tests (ordinal, continuous characteristics). An alpha level of 0.05 was used for determining statistical significance. If post-hoc tests were required, a Bonferroni-corrected alpha level was used.

RESULTS

Sample Characteristics

The details of the screening, recruitment, and enrollment data for the primary study are described in Ridner et al 2016.⁶ Of the 100 participants recruited for the primary study, 83 were ultimately included in study analyses. Of the 17 patients lost to follow-up, four did not complete baseline assessments. The remaining 13 participants lost to follow-up were more likely to be single or widowed, have Stage IV disease, received induction chemotherapy, and have metastatic disease.⁶ The majority of participants were Caucasian (n=75, 90.4%), male (n=60, 72.3%), and middle-aged (mean = 57.8 years). Most participants were married or living with a partner (n=65, 78.3%) and had a history of tobacco use (n=61, 73.5%). The most common tumor location was the oropharynx (n=36, 43.4%). Although one participant was initially reported to have Stage II disease, it was later reclassified as Stage I disease after enrollment in the study. The majority of participants received concurrent chemoradiation treatment for their disease (n=81, 97.6%), and slightly less than one third of participants had surgery in addition to concurrent chemoradiation treatment (n=24, 29.3%). Approximately half of participants had a PEG tube at some point during the study (n=41, 49.4%). Of the 83 participants with baseline values for the study measures, there were values for 82 at end-of-treatment, 81 3- to 6-months post-treatment, 71 9-months, 62 12-months, and 62 between 12- and 18-months post-treatment. Additional sample characteristics are described in Ridner et al. 2016.⁶

NDI Trajectories

The optimal group-based trajectory model in terms of best fit using the BIC and AIC criteria resulted in three clusters of longitudinal patterns in NDI illustrated in Figure 1. More than a third of the participants (N=30, 36.1%) were experiencing notable levels of neck disability prior to treatment. The median level increased during treatment and generally fluctuated around the initial level throughout the study period. There was no detectable decrease in severity. The smallest cluster of participants (N=15, 18.1%) demonstrated minimal disability prior to treatment with some increasing levels at the end-of-treatment with diminishment to very few limitations by 18-weeks post-treatment and subsequently. The remaining approximate 46% of participants (N=38, 45.8%) demonstrated similar levels of disability to the prior cluster before HNC treatment however they experienced considerably higher levels of neck disability at end-of-treatment and the limitations did not diminish as much post-treatment. Summaries of the demographic and clinical characteristics of the NDI trajectory groups are shown in Table 1. Current or past medical problems and the need for a PEG tube demonstrated the strongest associations with the NDI trajectory patterns. Those with current or past medical problems and those in need of a PEG tube were more likely to demonstrate an NDI pattern consistent with one of the more severe trajectories ($p < 0.05$, see Table 1). There were also statistically significant differences among the trajectory groups in terms of education and gender ($p < 0.05$). Post-hoc pairwise tests among the three groups revealed that compared to the severe-to-moderate trajectory group, the moderate-to-mild trajectory group had a higher median education (14 vs. 12 years) and a higher percentage of males (84.2% vs. 56.7%, $p < 0.05$). (see Table 1).

Associations of NDI Trajectories with Depressive and Social Anxiety Symptoms

Illustrations of the longitudinal clusters of participants derived from the CES-D and the LSAS scores are shown in Figure 2. Notably similar to the number of clusters observed for the NDI scores, 3–4 clusters were observed for those measures with similar proportions in the severity levels (~15% minimal, 45–55% moderate-to-mild, ~35% severe-to-moderate). Statistically significant associations were found between membership in the NDI trajectories and membership in the longitudinal patterns of CES-D and LSAS (Cramer's V, CES-D: 0.55, $p < 0.001$; LSAS Total: 0.35, $p = 0.002$; LSAS Fear: 0.35, $p = 0.002$; LSAS Avoid: 0.35, $p = 0.003$). In other words, 77% (N=23 of 30) of the participants who manifested the severe-to-moderate NDI longitudinal pattern, also manifested the CES-D pattern characterized by the highest levels of depressive symptoms. Slightly more than half of those in the severe-to-moderate NDI longitudinal cluster (N=16 of 30, 53.3%) also were members of the LSAS cluster with the highest levels of social anxiety.

Consistent with those findings, statistically significant differences in the patterns of prior and post-treatment symptoms of depression and social anxiety were revealed among the three NDI trajectory groups. The CES-D and LSAS scores for each of the NDI groups are summarized in Table 2. Mixed-effects GLM revealed not only a main effect of NDI group on CES-D ($F_{(df=2)}=243.91$, $p < 0.001$) but also a statistically significant interaction effect of NDI group and time of assessment ($F_{(df=22)}=2.40$, $p = 0.001$). Post-hoc contrasts revealed that prior to and through 6 months post-treatment, the severe-to-moderate neck disability group had statistically significantly higher levels of depressive symptoms than did the other

two trajectory groups (all *Bonferroni* $p < 0.01$). Rates of CES-D scores in the clinical range (≥ 19) in that severe-to-moderate disability group were 53.3% at baseline (N=16 of 30) and more than 70% at End of Treatment and 6-months post-treatment (N=23 and 21). Respective rates for the other two trajectories were $< 25\%$ at baseline, increased to 30–35% at End of Treatment and reduced to $< 20\%$ at 6-months post-treatment. The groups defined by NDI trajectories further delineated themselves in terms of depressive symptoms a year and more post-treatment. The minimal disability trajectory group had lower CES-D-scores than did the trajectory with moderate-to-mild disability, which had lower scores than did the severe-to-moderate trajectory group (all *Bonferroni* $p < 0.01$). Rates of clinically significant depressive symptoms remained $> 50\%$ in the severe-to-moderate trajectory group while rates in the other trajectory groups diminished to $< \sim 10\%$.

While no statistically significant interaction effects were observed on the LSAS scores, statistically significant main effects of NDI trajectory were observed (Total: $F_{(df=2)}=84.93$, $p < 0.001$; Fear: $F_{(df=2)}=85.50$, $p < 0.001$; Avoidance: $F_{(df=2)}=84.28$, $p < 0.001$). Throughout the longitudinal course of the study, the participants with an NDI trajectory characterized by severe-to-moderate disability had higher levels of social anxiety than did those with the moderate-to-mild levels of disability who in turn had higher levels of social anxiety than did those with minimal disability levels (all *Bonferroni* $p < 0.001$).

Discussion

Our sample was reflective of the age, gender, and tumor pathology of individuals diagnosed with HNC.¹⁶ Although the majority of individuals in the greater population are diagnosed with oral cavity cancer, the largest number of individuals in our study were diagnosed with oropharyngeal cancer. This may be due to the increase in HPV rather than smoking and drinking as a causative factor for oropharyngeal cancer, particularly among younger individuals.

High symptom burden following treatment for HNC has been well documented.^{7,17,18} Our findings indicate that after treatment for HNC, self-reported impaired neck-related function is not only associated with depressive symptoms and social anxiety but these issues also cluster into one of three distinct symptom trajectories. Only a small number of patients in our study experienced a symptom trajectory that could be characterized as minimal. More than a third of patients experienced a severe to moderate symptom trajectory. The most common symptom trajectory experienced by patients began with minimal symptom burden that escalated to a moderate level immediately after treatment and eventually declined. Symptom burden returned to a mild level but not reach level of minimal symptom burden over the subsequent 18 months.

Impaired physical function and psychological distress are clearly intertwined for patients with HNC long after completing treatment. Our findings are supported by other studies examining diverse types of impaired physical function and psychological distress in this population. In a longitudinal study of 101 patients with HNC, a higher number of treatment-related physical symptoms predicted both depression and anxiety.¹⁹ Another study of 280 patients diagnosed with HNC found that participants with speech and eating concerns reported the highest levels of body image disturbance compared to those without such

concerns.²⁰ Of the known studies that examine post-cancer treatment symptom trajectories, 21–26 none have examined the trajectories of symptom clusters including depressive symptoms, social anxiety, and perceived neck function in individuals with HNC.

Strengths and Limitations

A key strength of our study is that participants were largely reflective of the greater population of individuals with HNC. Another strength of our study is the longitudinal design that allowed us to identify symptom cluster trajectories; we followed patients from their time of diagnosis until 18 months after the end of treatment. Additionally, we used valid and reliable data collection tools.

However, there were significant differences in participants who were lost to follow-up and those included in this analysis. Given that participants who were lost to follow-up were more likely to have a higher disease stage, induction chemotherapy, and metastatic disease, these participants likely experienced a higher symptom burden than included participants.

Another limitation of this study is the possibility of survivor bias. Symptom burden, particularly in the moderate to mild cluster trajectory, may have appeared to improve because the individuals with a greater symptom burden died at some point during the 18 months after the end of treatment. This supports the assertion that patients with HNC have a particularly high level of sustained symptom burden after treatment.

An additional limitation is the recruitment of participants at only one location in the United States. Although our recruitment was representative of individuals with HNC who seek care at our institution, African Americans, among other racial minorities were underrepresented in our sample.

Because of the small trajectory groups, we were unable to adjust for possible demographic and clinical confounding variables. A larger study of this population is needed to facilitate this analysis.

Finally, other important limitations include limited statistical power based on the small sample sizes of the trajectory groups, exploratory analysis of secondary data, the inability to draw causal inferences from our data, the use of a generic social anxiety measure rather than a disease-specific measure, and the absence of information about patients with more limited disease.

Implications

Given our findings, it is clear that patients with HNC must be holistically supported not only throughout treatment, but also during the months following the end of treatment. This type of support must include mental health referrals as well as rehabilitation for functional impairments for affected patients. As our findings most likely underestimate the severity of symptom trajectories following treatment for HNC, it may be important for clinicians to identify individuals who are more likely to experience a more severe symptom trajectory. Interventions directed at individual treatable contributing factors may be of benefit for patients.

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Figure 1.
NDI Trajectories*

*NDI = Neck Disability Index; EOT = End of Treatment

Figure 2.

Illustrations of CES-D and LSAS Trajectory Patterns*

*EOT = End of Treatment; CES-D = Center for Epidemiological Studies Depression Scale;

LSAS = Liebowitz Social Anxiety Scale

Table 1

Demographic and Clinical Characteristics of the NDI Trajectory Groups (No. of Participants=83).

Characteristic	Overall (No. of Participants=83)	Minimal (No. of Participants=15)	Moderate-Mild (No. of Participants=38)	Severe- Moderate (No. of Participants=30)	<i>p</i> - value [*]
	Mean (SD)				
Age	57.8 (11.3)	56.1 (13.3)	58.9 (11.2)	57.3 (10.6)	0.574
	Median [IQR]				
Education (years)	13.0 [12–15]	12.0 [12–16] ^{a,b}	14.0 [12–16] ^a	12.0 [11–14] ^b	0.010
Gender	No. of Participants (%)				0.042
Female	23 (27.7)	4 (26.7) ^{a,b}	6 (15.8) ^b	13 (43.3) ^a	
Male	60 (72.3)	11 (73.3) ^{a,b}	32 (84.2) ^b	17 (56.7) ^a	
Race					0.658
White	75 (90.4)	13 (86.7)	35 (92.1)	27 (90.0)	
Black/African American	6 (7.2)	1 (6.7)	2 (5.3)	3 (10.0)	
Other	2 (2.4)	1 (6.7)	1 (2.6)	0 (0.0)	
Marriage					0.363
Married/Partnered	65 (78.3)	12 (80.0)	32 (84.2)	21 (70.0)	
Single/Widowed/Other	18 (21.7)	3 (20.0)	6 (15.8)	9 (30.0)	
Employment					0.134
Employed	36 (43.4)	8 (53.3)	20 (52.6)	8 (26.7)	
Not Employed	38 (45.8)	7 (46.7)	14 (36.8)	17 (56.7)	
Other	9 (10.8)	0 (0.0)	4 (10.5)	5 (16.7)	
Residence					0.211
City	34 (41.0)	4 (26.7)	14 (36.8)	16 (53.3)	
Country	42 (50.6)	8 (53.3)	21 (55.3)	13 (43.3)	
Other	7 (8.4)	3 (20.0)	3 (7.9)	1 (3.3)	
Smoke (current or past)	61 (73.5)	8 (53.3)	27 (71.1)	26 (86.7)	0.052
Drink Alcohol (current or past)	48 (57.8)	8 (53.3)	22 (57.9)	18 (60.0)	0.913

Characteristic	Overall (No. of Participants=83)	Minimal (No. of Participants=15)	Moderate-Mild (No. of Participants=38)	Severe- Moderate (No. of Participants=30)	p- value
Medical problems (current or past)	60 (72.3)	7 (46.7) ^a	27 (71.1) ^{a,b}	26 (86.7) ^b	0.018
Median [IQR]					
Months since Diagnosis at Baseline	1.09 [0.6-2.0]	1.35 [0.5-2.4]	0.99 [0.7-1.9]	1.02 [0.6-2.0]	0.272
Cancer Type	No. of Participants (%)				
Squamous Cell Carcinoma	69 (83.1)	12 (80.0)	34 (89.5)	23 (76.7)	
Other Type Carcinoma	14 (16.9)	3 (20.0)	4 (10.5)	7 (23.3)	
Cancer Location					0.293
Oropharynx	36 (43.4)	7 (46.7)	21 (55.3)	8 (26.7)	
Known HPV of Oropharynx	23 (63.9)	6 (85.7)	13 (61.9)	4 (50.0)	0.341
Oral Cavity	16 (19.3)	3 (20.0)	6 (15.8)	7 (23.3)	
Larynx	12 (14.5)	1 (6.7)	4 (10.5)	7 (23.3)	
Nasopharynx	6 (7.2)	2 (13.3)	3 (7.9)	1 (3.3)	
Other	13 (15.7)	2 (13.3)	4 (10.5)	7 (23.3)	
Stage					0.788
Stages I/II	4 (4.8)	0 (0.0)	3 (7.9)	1 (3.3)	
Stage III	21 (25.3)	4 (26.7)	9 (23.7)	8 (26.7)	
Stage IV	58 (69.9)	11 (73.3)	26 (68.4)	21 (70.0)	
PEG Tube (any)	41 (49.4)	2 (13.3) ^a	23 (60.5) ^b	16 (53.3) ^b	0.007
Induction Chemotherapy	43 (51.8)	9 (60.0)	20 (52.6)	14 (46.7)	0.694
Concurrent Chemoradiation	81 (97.6)	14 (93.3)	37 (97.4)	30 (100.0)	0.386
Total Treatment					0.568
Induction + ChemoXRT	35 (42.2)	8 (53.3)	17 (44.7)	10 (33.3)	
ChemoXRT	14 (16.9)	1 (6.7)	5 (13.2)	10 (33.3)	
Surgery + ChemoXRT	24 (28.9)	4 (26.7)	12 (31.6)	8 (26.7)	
Surgery + XRT	2 (2.4)	1 (6.7)	1 (2.6)	0 (0.0)	
Induction + Surgery + ChemoXRT	8 (9.6)	1 (6.7)	3 (7.9)	4 (13.3)	

*Tests of differences were conducted using Chi-Square tests of independence (nominal characteristics) and Kruskal-Wallis tests (ordinal, continuous characteristics). An alpha level of 0.05 was used for overall statistical significance. Post-hoc tests used a Bonferroni-corrected alpha level of 0.017.

Superscripts within the cells indicate specifically which trajectory groups were statistically significantly different.

Table 2

Summaries of CES-D and LSAS Scores by NDI Trajectory group^{*}

	Baseline	End of Treatment	3–6 Months Post Treatment	9 Months Post Treatment	12 Months Post Treatment	Greater than 12 Months Post Treatment
CES-D	Median Score [IQR]					
None/Mild NDI	10.0 [2–14]	11.0 [6–19]	5.0 [3–12]	4.0 [1–7]	3.0 [0–4]	3.0 [0–3]
Moderate NDI	9.5 [6–18]	16.0 [10–21]	12.0 [7–16]	6.0 [3–13]	6.0 [2–12]	5.0 [2–12]
Severe NDI	19.0 [9–29]	26.0 [19–38]	25.0 [15–34]	20.0 [14–31]	22.0 [16–36]	21.5 [17–39]
Clinically Significant CES-D Score No. of Participants (%)						
None/Mild NDI						
<19	13 (86.7)	10 (66.7)	14 (93.3)	15 (100.0)	14 (93.3)	15 (100.0)
>=19	2 (13.3)	5 (33.3)	1 (6.7)	0 (0.0)	1 (6.7)	0 (0.0)
Moderate NDI						
<19	30 (78.9)	26 (70.3)	30 (81.1)	30 (90.9)	27 (93.1)	26 (89.7)
>=19	8 (21.1)	11 (29.7)	7 (18.9)	3 (9.1)	2 (6.9)	3 (10.3)
Severe NDI						
<19	14 (46.7)	7 (23.3)	8 (27.6)	11 (47.8)	6 (33.3)	4 (22.2)
>=19	16 (53.3)	23 (76.7)	21 (72.4)	12 (52.2)	12 (66.7)	4 (77.8)
LSAS Fear	Median Score [IQR]					
None/Mild NDI	11.5 [4–23]	14.0 [3–27]	12.0 [0–22]	7.0 [0–18]	10.0 [0–16]	6.0 [0–20]
Moderate NDI	18.0 [6–33]	32.7 [9–53]	20.0 [6–37]	18.0 [2–28]	14.5 [3–22]	13.5 [5–28]
Severe NDI	26.5 [11–44]	34.0 [19–57]	41.0 [18–66]	42.0 [17–59]	44.5 [19–67]	38.0 [23–67]
LSAS Avoidance						
None/Mild NDI	12.0 [4–23]	14.0 [3–28]	12.0 [0–24]	7.0 [0–18]	10.0 [0–16]	6.0 [0–20]
Moderate NDI	19.0 [6–34]	32.0 [10–55]	20.5 [6–36]	18.3 [2–31]	15.5 [3–22]	14.0 [5–30]
Severe NDI	25.5 [11–45]	34.0 [19–57]	41.0 [20–66]	42.0 [19–59]	46.0 [19–67]	36.0 [23–69]
LSAS Total						
None/Mild NDI	23.5 [8–44]	28.0 [7–55]	24.0 [0–46]	14.0 [0–36]	20.0 [0–32]	12.0 [0–40]
Moderate NDI	37.0 [12–66]	65.0 [19–107]	39.9 [13–73]	36.5 [4–59]	30.0 [6–44]	27.5 [10–59]

	Baseline	End of Treatment	3–6 Months Post Treatment	9 Months Post Treatment	12 Months Post Treatment	Greater than 12 Months Post Treatment
Severe NDI	52.0 [22–88]	68.0 [39–114]	82.0 [38–132]	84.0 [36–117]	90.5 [39–133]	74.0 [47–136]

* NDI Trajectory Groups: None/Mild: Number of Participants=14–15 all times of assessment; Moderate: Number of Participants=36–38 baseline to 6 months post-treatment, Number of Participants=28–33 9 months to 18 months post treatment; Severe: Number of Participants=29–30 baseline to 6 months post-treatment, Number of Participants=17–23 9 months to 18 months post-treatment