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The effect of neck dissection on quality of life after chemoradiation

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Abstract

Objective—To determine differences in QOL between head and neck cancer patients receiving chemoradiation versus chemoradiation and neck dissection.

Methods—A prospective cohort study was conducted at 2 tertiary otolaryngology clinics and a VA. Sample: 103 oropharyngeal Stage IV SCCA patients treated via chemoradiation +/− neck dissection. Intervention: self-administered health survey collecting health, demographic, and QOL information pretreatment and 1 year later. Main outcome measures: QOL via SF-36 and HNQoL. Descriptive statistics were calculated for health / clinical characteristics, demographics, and QOL scores. T-tests evaluated changes in QOL over time.

Results—65 patients received chemoradiation and 38 chemoradiation + neck dissection. Only the pain index of the SF-36 showed a significant difference between groups ($p<.05$) with the neck dissection group reporting greater pain.

Conclusions—After post-treatment neck dissection, patients experience statistically significant decrement in bodily pain domain scores, but other QOL scores are similar to those of patients undergoing chemoradiation alone.

Introduction

Head and neck cancer is a devastating disease with 40,000 new cases affecting Americans each year. Despite advances in understanding of the disease and changes in treatment, death rates from squamous cell carcinoma (SCCA) have fallen little over past decades. Beyond the morbidity and mortality of the disease, the treatment is itself associated with side effects. This

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is especially the case because of the complex integration of form and function within the head and neck. Recently the effect of treatment of these cancers on patient function and outcomes has been strongly considered. This push began with a move toward organ preservation treatment initially put forth via such studies as the VA Larynx Trial,[1] and has been advanced by a growing literature on QOL outcomes in head and neck cancer.[2-5]

At our treatment sites, concurrent chemoradiation has become the treatment of choice for most patients with advanced oropharyngeal SCCA. In this group, the decision of whether to perform a post-treatment neck dissection has become somewhat difficult. For patients with discrete evidence of nodal disease post-treatment, the necessity of a neck dissection is obvious. For patients without clear evidence of continued regional disease, particularly those with bulky pre-treatment lymphadenopathy, there is no consensus on performing neck dissection. Our management in this setting continues to evolve, especially because of the increasing use of positron emission tomography (PET) for post-treatment surveillance.

The study of the functional and QOL implications of post-treatment neck dissection has thus become paramount. Outcomes literature indicates there are QOL implications from chemoradiation and from neck dissection, such as pain and shoulder dysfunction. The functional implications of adding a post-treatment neck dissection to chemoradiation therapy, however, have yet to be specifically considered. Hence the objective of this study is to evaluate the effect that such a neck dissection has on QOL in patients with primary oropharyngeal SCCA treated with organ preservation therapy. It is our hope that this will assist clinicians as they weigh the potential oncologic merit of neck dissection against any potential resultant changes in QOL.

Methods

A prospective cohort study was conducted at two tertiary care centers, the University of Michigan Health System and Henry Ford Hospital, and the Ann Arbor Veterans Affairs (VA) Hospital. Patients enrolled from 2003 to the present as part of the University of Michigan Head and Neck Cancer Specialized Programs of Research Excellence (SPORE). IRB approval was obtained at all institutions. Patients with newly diagnosed oropharynx cancer were identified by treating physicians and recruited in person in a clinical setting. Only stage IV patients treated with chemoradiation were included, in order to limit the sample to a more homogeneous group with advanced disease. Subjects were excluded if they did not speak English, were pregnant, were under 18, were psychologically unstable, had previous major head and neck surgery, had previous chemotherapy or radiation therapy to the head and neck (other than for lymphoma), had evidence of distant metastatic disease, did not agree to participate, or did not survive to one year. Patients who were treated with surgical resection at the primary site (11 patients), had bilateral neck dissections (2 patients), or had a radical neck dissection with resection of CN XI (4 patients) were also excluded. These subjects were excluded as the known increased surgical morbidity of these procedures would likely result in an altered quality of life from the remainder of the patients who received neck dissections (either selective neck dissection or modified radical neck dissection sparing Cranial Nerve XI). All patients in the study were treated with chemoradiation therapy under several protocols for cure.

At our treating institutions, the indications for post chemoradiation neck dissection continue to evolve. During the study period, surgeons performed post-treatment neck dissections for evidence of nodal disease on clinical exam and post-treatment CT, as well as for new regional disease during follow-up. In addition, during the first two years of the study, surgeons performed post-treatment neck dissection for patients with evidence of 3cm or larger pretreatment nodes. During the last year of the study, some surgeons utilized PET / CT at 3-4 months post-treatment in the setting of “complete response” to detect residual neck disease

and determine if neck dissection was indicated, while others continued to dissect for pretreatment nodes 3cm or greater. Selective neck dissection was the procedure of choice and was extended by surgeons to modified radical neck dissection if necessary for complete resection. Neck dissections were performed by 7 head and neck oncology surgeon sub-specialists, with nearly 60% of these being performed by 2 surgeons. Modified radical neck dissections were performed in the standard fashion, and selective neck dissections included nodal groups described by Medina.[6] All selective neck dissections included at least levels II and III, but not level V. Although the surgeons taking part in the study all maintain a similar approach to neck dissection, there remains inherent heterogeneity within the surgical group. More information on levels and structures dissected as well as surgeons performing dissection can be seen in Table 2.

Participating subjects completed a self-administered health questionnaire. Research assistants helped facilitate recruitment and data collection. Subjects signed a consent document prior to participation and required approximately 20 minutes to complete the survey. Participants were compensated with $10.

The self-administered survey collected data on clinical and outcomes measures. The primary measures of QOL were the SF-36 and the HNQoL (Head and Neck Quality of Life Instrument) (Table 1). The SF-36 is a validated general measure used to assess social, physical, role, and emotional functioning.[7] Disease specific QOL outcomes were measured with the HNQoL instrument. This tool uses 20 items to investigate the four domains of communication, emotional well-being, head and neck pain, and eating and swallowing.[8] These instruments are well described in the literature.

The survey also collected data on health behaviors, depressive symptoms, and demographics, including age, gender, race, education, and marital status. A medical record review was conducted to collect clinical information including cancer subsite, cancer stage, comorbidities, and treatment received. As the large majority of the subjects in the study are considered white, race was designated as white (non-Hispanic) and non-white. Other clinical characteristics collected included tracheostomy status, disabled status, and mean BMI. Disabled status was determined by evaluating if patients were actively working prior to being diagnosed with cancer, and in this case were then told by their physicians that they were not able to work secondary to their cancer. Depression was evaluated via the Geriatric Depression Scale – Short Form (GDS-SF) in which probable depression is indicated by a score of four or above. Alcohol abuse was investigated via the Alcohol Use Disorder Identification Test (AUDIT). This tool uses ten items to delineate alcohol related difficulties with a score of eight or above. Answering yes to smoking within the last month designated a patient as a smoker.

Data points were recorded at baseline and one year. For continuous variables analysis was conducted on the change in score from baseline to 1-year. Descriptive statistics (means or frequency distributions) were computed for all variables. Bivariate analyses using t-tests, $\chi 2$ and Fisher's exact tests compared the 2 treatment groups on age, gender, race, marital status, education level, comorbidities, hospital site, and specific tumor site within the oropharynx. Paired t-tests and the sign test were used to detect changes within groups from baseline to 1-Year. T-tests were used to compare the change in scores for differences between treatment groups. Since this is a pilot study, no multiple test corrections were used. The data were analyzed with SAS (SAS Institute, Inc., Cary, NC). Values for $p < 0.05$ were considered statistically significant. The funding source had no role in study design.

Results

Of 103 study patients, 65 received chemoradiation alone, and 38 required chemoradiation and neck dissection. Demographic and clinical information can be seen in Table 2. The majority of patients were treated at the University of Michigan. Both treatment groups were largely comprised of white males in their fifties, and were relatively well-balanced with respect to age, gender, race, education level, comorbidity, and marital status.

There were no statistically significant differences in the baseline characteristics of the treatment groups other than N3 status. There were 8 (12%) N3 patients in the chemoradiation alone group and 12 (32%) in the neck dissection group, and this difference was statistically significant by Fisher's exact test (p=.03). Other T and N designations were equally represented in both groups. Most patients had primary cancers of the tonsil (largest group) and base of tongue. Subsites were almost equally represented between those that required neck dissection and those that did not (Table 2).

The chemoradiation/post-treatment neck dissection group included 38 patients of which the neck dissections were split nearly evenly between selective (n=22, 58%) and modified radical (n=16, 42%).

Differences in QOL measures were calculated within each individual treatment group over the one-year time interval (Table 3). Mean baseline QOL scores were very similar between the testing groups with all mean domain scores on the SF-36 and the HNQOL falling within 0.2 to 6.9 points of each other. When compared with US population norms,[7] all mean scores recorded for the SF-36 at baseline and one year later, fall below the national average. This is true for both treatment groups with the exception of the mental health score for the chemoradiation alone group at one year follow-up, which is equal to the population norm at 74.7.

For the QOL measures within each treatment group, some had changes from baseline to one year that were significant. Those treated with chemoradiation alone experienced a significant improvement in the pain ($p<.01$) and mental health ($p<.05$) domains of the SF-36 as well as the emotional distress domain of the HNQoL ($p < .01$). For patients with added neck dissection, they also experienced a statistically significant improvement in the mental health domain of the SF-36 and emotional distress domain of the HNQoL (both $p < .05$) This group, however, had a decrease in the pain domain of the SF-36 which was not statistically significant. Both treatment groups experienced a significant decline in the physical function domain of the SF-36 ($p <.05$) and in the eating domain on the HNQoL ($p < .01$).

Changes in clinical characteristics were also evident from baseline to one year. No patients required tracheostomy. Both treatment groups had a significant improvement in depression scores from baseline to one year ($p < .01$). Also, both groups had significant improvement in rates of smoking ($p < .01$) and alcohol use ($p <.05$) from baseline to one year. BMI decreased in a significant manner from baseline to one year for both groups ($p < .01$).

Table 4a compares how much change in QOL each treatment group experienced from baseline to one year. Only the bodily pain index of the SF-36 showed a significant difference between groups, with the post-chemoradiation neck dissection group experiencing more pain ($p = .041$) however this did not manifest on the HNQoL pain domain. No other domains within the SF-36 or HNQoL showed a significant difference between the two groups. Table 4b compares changes in QOL from baseline to one year within the neck dissection group (selective neck dissection versus modified radical neck dissection). Only in the mental health domain of the SF-36 did these groups have a significant difference, with the selective neck dissection experiencing an improvement in mental health scores while the modified radical group had a small decline.

Although the HNQoL pain domain as a whole did not show a significant difference between treatment groups, the pain domain scores of the HNQoL were then evaluated individually to determine if any of the individual items of this domain were different between groups. This post-hoc analysis evaluated changes within each group from baseline to year one as well as for differences between the two treatment groups (Table 5). As seen in Table 5a, both groups experienced a statistically significant improvement in the amount of pain medication taken from baseline year one. When the change from baseline to year one was compared between treatment groups, one aspect of the HNQoL pain domain – the shoulder / neck pain score -- showed the neck dissection group having a greater decline in shoulder and neck pain scores from baseline to year one, however this was not significant ($p = .06$).

Discussion

As the debate continues regarding the oncologic merits of post-treatment neck dissection, the consideration of the effects of neck dissection on QOL is essential. This study is the first to show that other than pain, there were no differences in QOL scores between Stage IV oropharyngeal cancer patients treated with chemoradiation versus chemoradiation and neck dissection. The evidence of greater pain in the neck dissection group is consistent with the literature on the effects of neck dissection on QOL. In the early years of this surgery, a shoulder syndrome was recognized,[9,10] and the handicaps associated with radical neck dissection and resection of CN XI were documented.[11] More recently new measures have been developed to evaluate QOL and function after neck dissection, and the evidence has grown documenting the effects of this surgery. Terrell et al found neck dissection was associated with decrement in QOL in physical functioning domains.[12] More limited (selective) neck dissections cause less pain and decrement in QOL, while sparing CN XI and avoiding dissection of level V likewise have positive effects.[13-17] Chepeha et al found that functional results after neck dissection were influenced positively by increased patient weight and negatively by radiation.[15]

As no study to date has specifically evaluated patients undergoing neck dissection *after* chemoradiation, the finding of greater pain in the neck dissection group is important. This study was completed within a single stage and site of the head and neck to remove the possibility of deficit variation secondary to site of primary and treatment required (i.e.-radiation field). It is interesting however, that the difference between the treatment groups did not manifest in all portions of the evaluation relating to pain. Importantly there was no difference in the HNQoL pain domain. As this measure is more specific to head and neck related pain, this suggests that the difference in pain between groups is likely small. Likewise, it is important that no other differences of significance were appreciated in the other quality of life domains evaluated. Further follow-up in this patient population will determine if differences in pain scores will remain in the long term or scores will become more similar over time.

At baseline both study groups were quite similar in clinical characteristics and QOL scores. After undergoing treatment both treatment groups experienced changes in their QOL. Notably, within each treatment group, patients experienced a significant improvement in the mental health and emotional distress domains, and depression decreased in both groups. This is consistent with previous literature with similar follow-up, with improvement of mental health scores over time after treatment, but not during initial treatment for cure.[18-20] Most likely this results from improved patient outlook after survival to one year. Both treatment groups also showed a significant decline in physical function and eating domains from baseline to one year which is consistent both with clinical experience and previous literature. Not surprisingly on nearly all domains of the SF-36, our patients' QOL scores at baseline and one year were below the national average, reinforcing the significant impact of oropharyngeal SCCA.

Both patient groups experienced significant change in some clinical characteristics from baseline to one year. Alcohol and tobacco use decreased in both groups as has been shown in previous literature. These behaviors are interrelated; Duffy et al have shown that smokers are more likely to be problem drinkers and problem drinkers are more likely to be smokers.[21] One must consider, however, the exclusion of those patients who did not survive past one year who potentially continued to use alcohol and tobacco.

Finally, one must consider limitations of the study. The sample size was small, and there were more subjects in the chemoradiation alone group. In addition, the neck dissection group has inherent heterogeneities. All pretreatment characteristics were similar at baseline with the exception of N3 status which was significant. Inherent to the question being asked by the study, there were a larger percentage of neck dissection patients that were N3, as patients with bulky nodal disease are more likely to require post-treatment neck dissection. As such, more aggressive nodal disease could potentially be the etiology of greater pain in this group. Finally, patients who died before completing one year follow-up, did not agree to participate, or were lost to follow-up were excluded from the study, and such patients may have had different QOL experiences.

Thus, in our study, patients who underwent post-chemoradiation neck dissection did not experience vastly different QOL than their counterparts who did not undergo neck dissection. Significant differences in the SF-36 pain domain are not surprising given the literature on the effects of neck dissection on pain, shoulder function, and QOL. It is notable, however, that there were no other significant differences in change of QOL between the two groups.

Conclusion

Concurrent chemoradiation has become the standard of care at many institutions for treating several sites of head and neck cancer. The decision as to when to perform a post-treatment neck dissection for oncologic reasons is complex. Large pretreatment cervical nodal disease has shown increasing rates of “complete response” to therapy, and the optimum use of PET for surveillance of the post-treatment neck is yet to be definitively determined. The addition of QOL information to this clinical decision making process is helpful. In this case, post-treatment neck dissection after chemoradiation significantly affected patient QOL only in the Bodily Pain domain of the SF-36, and thus was not consistent across all pain domains tested. As no other differences emerged, our impression is that in patients treated for cure with chemoradiation, post-treatment neck dissection adds some decrement in patient QOL but should be performed when oncologically indicated.

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Table 1

SF-36 and HNQoL Domains and Items

SF-36 Subscale	Meaning of Measure
Physical Functioning	Limitations in performing concrete physical activities because of health
Role-physical	Problems with work or other daily activities because of physical health
Bodily pain	Extent of pain or limitations because of pain
General health	Perception of health / health outlook
Vitality	Level of energy
Role-emotional	Problems with work or other daily activities because of emotional problems
Social functioning	Extent and frequency of interference with social activities because of physical and emotional problems
Mental health	Feeling of nervousness and depression

HNQoL Subscale	Meaning of Measure
Eating	Problems chewing Dryness while eating Problems with taste Problems swallowing soft foods / solids Problems swallowing liquids Problems opening your mouth
Communication	Talk to others Talk on the phone Problems with clarity of voice Problems with volume of voice
Emotional distress	Embarrassment about condition Concerns about appearance Emotional problems Financial worries Worry that condition will get worse Frustration about condition
Pain	Shoulder or neck pain General physical problems Pain / burning in mouth Frequency of pain medication use

Table 2

Demographic and Clinical Characteristics[a]

Measure	Chemoradiation N=65	+ Neck dissection N=38
Mean Age (years)	58.8 (SD 9.9) **N (%)**	55.4 (SD 8.4) **N (%)**
Gender		
Male	56 (86%)	36 (95%)
Female	9 (14%)	2 (5%)
Race		
White	62 (95%)	37 (97%)
Non-White (all others)	3 (5%)	1 (3%)
Marital Status		
Married	41 (63%)	29 (76%)
Not married	24 (37%)	9 (24%)
Educational level		
High school or less	21 (32%)	14 (37%)
Some college or more	44 (68%)	24 (63%)
Hospital Site		
University of Michigan	53 (81%)	34 (89%)
Ann Arbor VA	7 (11%)	4 (11%)
Henry Ford Hospital	5 (8%)	0
Comorbidity status		
None or Mild	46 (71%)	29 (76%)
Moderate or Severe	19 (29%)	9 (24%)
Cancer Site		
Base of Tongue	29 (45%)	18 (47.5%)
Tonsil	32 (49%)	18 (47.5%)
Other Oropharynx[b]	4 (6%)	2 (5%)
Type of Neck Dissection		
Selective Neck Dissection		22 (58%)
Levels I-III		1 (3%)
Levels I-IV		17 (45%)
Not Otherwise Specified		4 (10%)
Modified Radical Neck Dissection		16 (42%)
Sparing CN XI only		5 (13%)
Sparing CN XI and IJ vein		1 (3%)
Sparing CN XI, SCM, IJ vein		2 (5%)
Not Otherwise Specified		8 (21%)
Surgeon Performing Neck Dissection		
Surgeon 1		12 (32%)
Surgeon 2		10 (26%)

Measure	Chemoradiation N=65	+ Neck dissection N=38
Surgeon 3		5 (13%)
Surgeon 4		4 (10.5%)
Surgeon 5		4 (10.5%)
Surgeon 6		2 (5%)
Surgeon 7		1 (3%)

[a] There are no significant differences between treatment groups, except N3 status

[b] Includes Soft Palate, Vallecula, Lateral Wall, and Unspecified Oropharynx.

Table 3

Differences in QOL and clinical characteristics between baseline and 1-year for patients treated with chemoradiation alone and those requiring neck dissection.[a]

Measure	Chemoradiation alone N=65			+ Neck dissection N=38		
	Baseline	1-Year	Change	Baseline	1-Year	Change
SF36						
Physical Functioning	76.5 (26.6)	68.2 (25.8)	−8.3*	79.4 (22.2)	71.1 (23.1)	−8.2*
Role Physical	57.7 (42.6)	46.5 (44.3)	−10.9	53.3 (41.6)	44.7 (43.6)	−8.6
Body Pain	64.2 (26.5)	72.2 (21.6)	8.0**	62.4 (23.3)	60.2 (25.1)	−2.2
General Health Perceptions	63.4 (19.8)	63.4 (20.8)	−0.4	61.1 (19.4)	62.6 (20.9)	1.6
Vitality	51.5 (24.2)	53.3 (20.4)	1.8	51.7 (21.7)	52.9 (22.2)	1.2
Social Functioning	70.0 (26.2)	72.5 (25.3)	2.5	66.4 (29.7)	74.7 (25.1)	8.2
Role Emotional	63.6 (44.0)	70.3 (39.0)	6.3	58.8 (43.5)	66.7 (40.3)	7.9
Mental Heath	68.5 (19.1)	74.7 (18.5)	6.2*	62.7 (20.0)	70.5 (20.6)	7.8*
HNQOL						
Eating	76.6 (25.7)	55.7 (22.2)	−20.9**	81.8 (21.3)	57.0 (24.1)	−24.8**
Communication	76.0 (24.1)	70.8 (27.3)	−5.2	75.8 (22.6)	69.2 (24.7)	−6.6
Emotional Distress	68.2 (19.1)	79.2 (18.5)	11.0**	61.8 (22.5)	72.9 (23.2)	11.1**
Pain	66.6 (26.2)	71.3 (21.7)	4.7	59.7 (21.2)	63.0 (27.1)	3.3
Clinical Characteristics						
Mean BMI	27.2 (5.3)	23.5 (3.7)	−3.7**	29.4 (6.7)	24.9 (5.1)	−5.5**
Disabled	19 (46%)	14 (37%)		6 (23%)	12 (44%)	
Depressive Symptoms	30 (46%)	20 (32%)	**	21 (55%)	15 (41%)	**
Smoker, past month	22 (34%)	11 (17%)	**	13 (34%)	4 (11%)	**
Alcohol Problem	10 (16%)	2 (3%)	*	9 (24%)	2 (5%)	

[a]Tested for differences in the same group from baseline to 1-Year using paired t-tests for continuous variables and the Sign test for dichotomous variables. Differences between groups are presented in Table 4.

*p<.05

** $p < .01$

Table 4a

Comparing change in QOL scores between baseline and 1-year for patients treated with chemoradiation alone versus those requiring neck dissection.[a]

Measure	Chemoradiation N=65	+ Neck dissection N=38	p-value
SF36			
Physical Functioning	−8.3	−8.2	.993
Role Physical	−10.9	−8.6	.829
Body Pain	8.0	−2.2	.041*
General Health Perceptions	−0.4	1.6	.661
Vitality	1.8	1.2	.901
Social Functioning	2.5	8.2	.338
Role Emotional	6.3	7.9	.877
Mental Heath	6.2	7.8	.700
HNQOL			
Eating	−20.9	−24.8	.511
Communication	−5.2	−6.6	.834
Emotional Distress	11.0	11.1	.977
Pain	4.7	3.3	.801

[a] Tested for differences between treatment groups in the change in QOL scores (mean difference in change from baseline to 1-Year) using t-test.

* p<.05

Table 4b

Comparing change in QOL scores between baseline and 1-year for patients treated with modified radical neck dissection versus those treated with selective neck dissection.[a]

Measure	Modified Radical Neck Dissection N=16	Selective Neck Dissection N=22	p-value
SF36			
Physical Functioning	−12.0	−5.5	.440
Role Physical	−3.1	−12.5	.620
Body Pain	−1.9	−2.4	.955
General Health Perceptions	−1.8	4.0	.461
Vitality	0.9	1.4	.952
Social Functioning	10.9	6.3	.632
Role Emotional	−2.1	15.1	.322
Mental Heath	−0.3	13.6	.029*
HNQOL			
Eating	−25.0	−24.6	.967
Communication	−8.6	−5.1	.778
Emotional Distress	8.9	12.7	.575
Pain	3.9	2.8	.903

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Table 5

a. Differences in HNQOL Pain Individual Questions in patients treated by chemoradiation alone versus chemoradiation + neck dissection. N=103
b. Average changes in HNQOL Pain by group from baseline to 1 year

	Chemoradiation N=65			+ Neck dissection N=44		
	Baseline	**1 year**	**Change**	**Baseline**	**1 year**	**Change**
HNQOL Pain						
General Bothered by Physical HN Problems	3.8 (1.2)	3.8 (1.2)	0.08	3.4 (1.2)	3.7 (1.1)	0.24
Pain Burning Discomfort	3.5 (1.5)	3.6 (1.2)	0.02	3.6 (1.1)	3.7 (1.2)	0.08
Shoulder Neck Pain	4.1 (1.2)	4.2 (1.2)	0.11	3.7 (1.2)	3.2 (1.3)	−0.47
Pain Meds	3.2 (1.4)	3.8 (1.4)	0.56*	2.8 (1.2)	3.5 (1.6)	0.68**

	Chemoradiation N=65	**+Neck dissection N=38**	**P-Value**
HNQOL Pain			
General Bothered by Physical HN Problems	0.08	0.24	.582
Pain Burning Discomfort	0.02	0.08	.847
Shoulder Neck Pain	0.11	−0.47	.060
Pain Meds	0.56	0.68	.725

Tested for differences in same group from baseline to 1-Year.

*P<.05

**P < .01

HNQoL Pain Scores were reversed and scored on a scale of 1-5. The higher the score, the better the QoL.

Testing for Differences in change score between groups