Prospective Evaluation of Quality of Life and Nutrition Before and After Treatment for Nasopharyngeal Carcinoma

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Objective: To prospectively assess quality of life in patients undergoing chemoradiation therapy for nasopharyngeal cancer. Concurrent chemoradiotherapy is standard for advanced nasopharyngeal cancer; however, the toxic effects of this treatment are substantial.

Design: Prospective evaluation of quality of life and nutritional status before and after treatment for nasopharyngeal carcinoma.

Patients and Intervention: A cohort of 14 patients, treated with concurrent chemoradiotherapy for 7 weeks, completed the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire and Head and Neck Module before and 3, 6, 12, and 24 months after treatment. Changes in score were analyzed and correlated with the toxic effect grade.

Results: Quality of life issues during the 24 months of follow-up included poorer global health ($P=0.01$), fatigue ($P=0.01$), appetite loss ($P<0.001$), swallowing difficulties ($P=0.001$), sense problems ($P=0.001$), difficulty with social eating ($P=0.005$), dental problems ($P=0.045$), trismus ($P=0.001$), xerostomia ($P<0.001$), sticky saliva ($P=0.001$), cough ($P=0.02$), and feeling ill ($P=0.03$). Pain ($P=0.004$) and emotional functioning ($P<0.001$) significantly improved from the pretreatment rating. The median weight loss was 7 kg, with most weight loss occurring during treatment, despite nutritional support with gastrostomy feeding tubes. One patient still required percutaneous endoscopic gastrostomy feeding at 2 years after treatment. Physician-scored toxic effects correlated poorly with quality-of-life scores.

Conclusions: Quality of life and functional assessment should be important end points in the follow-up of patients with nasopharyngeal cancer who receive chemoradiotherapy. This study supports the need for ongoing support and rehabilitation in a multidisciplinary setting.

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NASOPHARYNGEAL CARCINOMA (NPC) is a relatively uncommon malignancy in Australia with an incidence of about one thirtieth of that reported in China and Southeast Asia. Concurrent chemoradiotherapy is now accepted as standard treatment for stages III and IV NPC, and many patients will achieve long-term cure despite advanced locoregional disease. Although the addition of platinum-based chemotherapy improves disease control, it is associated with considerable early and late toxic effects. Hence, subjective measures such as health-related quality of life and functional status are important end points and should be incorporated into the evaluation of therapies with substantial adverse effects.

Quality of life may be defined as a patient’s appraisal of and satisfaction with his or her current level of functioning compared with what is perceived to be possible. Evidence regarding quality of life provides patients with a comprehensible measure of the functional consequences that result from the complex interaction between disease and treatment. In addition, it gives the clinician an unbiased measure that can be used to balance the gain in disease control against the effects of treatment. The aim of this study was to evaluate prospectively the changes in quality of life during a 2-year period in patients undergoing chemoradiotherapy for NPC at a single tertiary care institution.

METHODS

POPULATION AND TREATMENT

After institutional ethics approval and patient consent were obtained, data were prospectively collected for all patients with NPC who presented to the Sydney Head and Neck Cancer Institute.
Chemotherapy was planned as 3 cycles of intravenous cisplatin (1000 mg/m² daily for 4 days) after completion of radiotherapy. No patient received the full 6 (3×2) cycles of concurrent chemotherapy, and only 3 patients tolerated 5 (3×1) cycles. Nine patients received 3 (3×1) cycles of concurrent chemotherapy, and 2 patients tolerated only 2 (2×1) cycles. In 1 patient, cisplatin was substituted with carboplatin, at a target area under the curve of 5.

**QUALITY-OF-LIFE QUESTIONNAIRE AND DATA COLLECTION**

The questionnaire consisted of the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality-of-Life Questionnaire (QLQ-C30) and the EORTC Head and Neck Cancer Quality-of-Life Questionnaire (QLQ-H&N35). The EORTC QLQ-C30 is a validated cancer-specific self-report questionnaire.4 5,6 It consists of a global quality-of-life scale, 5 functional scales (physical, role, emotional, cognitive, and social), and 9 symptom scales (fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). The EORTC QLQ-H&N35 is designed to be used together with the QLQ-C30 and is a tumor-specific, self-report questionnaire with good reliability and validity among patients with head and neck cancer and in particular, those with NPC.7 It consists of 6 symptom scales (pain, swallowing, senses [taste/smell], speech, social eating, and social contacts) and 7 single items (sexual ity, teeth problems, problems opening mouth, dry mouth, sticky saliva, cough, and feeling ill).

Patients were asked to complete questionnaires before treatment and at 3, 6, 12, and 24 months thereafter. A follow-up quality-of-life and nutrition clinic was introduced by our head and neck care coordinator (J.E.O.), dietitian (J.R.), and speech pathologist (N.R.) to assess patients, complete the questionnaires, and record nutritional variables. The time frame of the core and module questionnaires was “during the past week,” and items were scored on a Likert-type categorical scale (“not at all,” “a little,” “quite a bit,” and “very much”). The scores were linearly transformed into scales ranging from 0 to 100. A high score for global health and for a functional scale represents a better level of functioning, whereas a high score for a symptom or a single-item scale represents a high level of symptom problems.9 10 An absolute change of 10 or more corresponds to a clinically important effect on a scale of 0 to 100.11 12

**STATISTICAL ANALYSIS**

Statistical analysis was performed using SPSS statistical software, version 11 for Windows (SPSS Institute, Chicago, Ill). To avoid problems associated with multiple significance tests and repeated measures, we analyzed changes in median scores of the QLQ-C30 and QLQ-H&N35 using the Friedman analysis of variance and used the Kendall W to indicate the agreement between patients. Statistically significant differences were assumed when P<.05 was achieved. We performed post hoc analyses using the Wilcoxon signed rank test to compare differences in baseline scores and at 3, 6, 12, and 24 months, applying the Bonferroni correction; hence, significant differences were assumed when P<.0125, although P values less than .05 were recorded as trends toward significance. Correlation between toxic effects and quality-of-life scores was performed using the Spearman ρ.

**RESULTS**

**TREATMENT**

Posttreatment positron emission tomography performed 3 months after treatment showed that 12 patients had a complete response to treatment, 1 had local persistent disease, and 1 had distant metastases. Clinical and radiological surveillance during the 2-year period did not detect any other disease recurrence. Overall survival at 2 years after treatment was 86% (12 patients), with 2 patients dying of their disease.

**QUALITY-OF-LIFE QUESTIONNAIRES**

All 14 patients completed the quality-of-life questionnaires before and 3, 6, and 12 months after treatment. At 24 months, the 12 patients who remained alive and disease-free completed the questionnaires. Table 2 and Table 3 summarize the results of the EORTC QLQ-C30 and QLQ-H&N35 questionnaires, respectively. The median, mean, standard deviation, P values, and correlation coefficient (Kendall W) at diagnosis and subsequent evaluation are provided.
TOXIC EFFECTS

Toxic effects are summarized in Table 4. A cumulative toxic effect score was created by combining all recorded toxic effects and taking the median value. This had a positive correlation with fatigue (\(r = 0.89; P = .04\)) but did not correlate with global health status or any functional score. When the median grade for toxic effects for individual variables was analyzed, the only relevant significant correlations were between dysphagia and social eating (\(r = 0.88; P = .047\)) and between dysphagia and sticky saliva (\(r = 0.91; P = .03\)). Dysphagia did not correlate with swallowing problems (\(r = 0.47; P = .42\)), and xerostomia did not significantly correlate with dry mouth (\(r = 0.79; P = .11\)) or sticky saliva (\(r = 0.41; P = .50\)).

At the initial visit, the median weight was 64.3 kg (range, 45.5-90.3 kg) and the median body mass index (calculated as weight in kilograms divided by height in meters squared) was 25 (range, 20-25). During chemoradiotherapy, the median weight loss was 8.2 (range, 2.3-13.9) kg, representing a proportional weight loss of 4% to 17%. The median weight loss during the full 2 years was
7 (range, 2.2-17.3) kg or 7.9% (range, 3%-22%). Weight loss occurred principally during radiotherapy, despite support with enteral tube feeding. Thirteen patients required a gastrostomy tube for nutritional support during treatment. All feeding tubes except 1 (n=12) were removed by 6 months after treatment; the remaining patient continued tube feeding at 2 years after treatment.

There is an increasing trend toward incorporating quality-of-life assessment tools into the routine analysis of treatment outcomes for cancer patients. This is owing to the recognition that the subjective well-being of patients is almost as important as traditional measures of disease control and survival. Quality-of-life assessment improves multidisciplinary care and rehabilitation by identifying specific problems following treatment, providing better patient information, and helping to accurately define poor outcome groups.18 Prospective quality-of-life information can be used to inform patients at the time of diagnosis about the effects of treatment and their subsequent recovery. This study represents a prospective series of 14 patients undergoing quality-of-life evaluation during a 2-year period and identifies significant health and functional changes during that period.

**COMMENT**

EORTC QLQ-C30 GLOBAL HEALTH AND FUNCTIONAL SCALES

In contrast to other studies specifically looking at patients with NPC,19-21 we identified a modest but significant (P=.01) deterioration in global health status. This occurred within the initial 3 months, with a drop in the
Differences were detected in fatigue (P = .01), pain (P = .004), appetite loss (P < .001), and financial difficulties (P = .02) as shown in Figure 1. As expected, fatigue and appetite loss increased in the initial 3 months and then gradually declined. Appetite loss has a high level of interpatient correlation (W = 0.41). Financial difficulties declined over time and did not increase from the time of diagnosis. This is surprising because many patients would require leave from work during therapy; this suggests that most patients were able to return to employment in the medium term.

**EORTC QLQ-C30 SYMPTOM SCALES**

The differences exhibited in the QLQ-H&N35 questionnaire, when compared with the QLQ-C30 questionnaire, demonstrate the importance of site-specific evaluation and correspond more closely to global health status in this sample of patients with NPC. In particular, oropharyngeal function substantially deteriorated from the time of diagnosis. Specifically, patients had progressive problems with teeth (P = .045), trismus (P = .001), dry mouth (P < .001), swallowing (P = .002), and social eating (P = .005), as shown in Figure 2. Dry mouth had the highest interpatient correlation (W = 0.42) and demonstrated the greatest increase (deterioration) in the mean score (70) at 2 years. Dental problems correlated the least (W = 0.17), suggesting that caries were not inevitable in the medium term given appropriate pretreatment and posttreatment care.

In contrast to the other oropharyngeal symptom scales, sticky saliva was a major problem in the initial 6 months (P = .007), but it returned to near baseline levels at 2 years, with a high interpatient correlation (W = 0.35). The sensory problems associated with cisplatin and radiation treatments, although increased at 3 months (P = .049), tended to resolve by 1 year. Unfortunately, this was poorly correlated (W = 0.19), and some patients had major persistent problems. Other symptoms such as pain (P = .01) and feeling ill (P = .03) improved gradually over time following completion of therapy.

**DO TOXIC EFFECTS CORRELATE WITH QUALITY OF LIFE?**

Toxic effects are measured by the clinician and, although they provide important objective outcome measures, do not allow for self-reporting of symptoms. What a clinician believes to be of minor importance may demonstrate the importance of site-specific evaluation and correspond more closely to global health status in this sample of patients with NPC. In particular, oropharyngeal function substantially deteriorated from the time of diagnosis. Specifically, patients had progressive problems with teeth (P = .045), trismus (P = .001), dry mouth (P < .001), swallowing (P = .002), and social eating (P = .005), as shown in Figure 2. Dry mouth had the highest interpatient correlation (W = 0.42) and demonstrated the greatest increase (deterioration) in the mean score (70) at 2 years. Dental problems correlated the least (W = 0.17), suggesting that caries were not inevitable in the medium term given appropriate pretreatment and posttreatment care.

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**ENTERAL FEEDING**

Following the completion of therapy, fatigue and appetite loss improved and the patients gradually gained weight, allowing for the removal of all but 1 gastrostomy tube at 6 months. All patients lost weight, although they had feeding tubes for nutritional support. During treatment, patients experience nausea associated with chemotherapy and are often unable to meet their nutritional requirements. Oral feeding during treatment is a major problem, and gastrostomy tubes are essential in many patients to prevent excessive weight loss and nutritional depletion. There was a similar degree of weight loss from the time of diagnosis to the start of treatment and during therapy. These results emphasize the need for early nutritional intervention by a dietitian before commencing chemoradiotherapy.

**COMPARISON WITH LITERATURE**

It is difficult to determine whether the present series is representative, given the small sample size, skewed distribution of posttreatment care. Sticky saliva was a major problem in the initial 6 months (P = .007), but it returned to near baseline levels at 2 years, with a high interpatient correlation (W = 0.35). The sensory problems associated with cisplatin and radiation treatments, although increased at 3 months (P = .049), tended to resolve by 1 year. Unfortunately, this was poorly correlated (W = 0.19), and some patients had major persistent problems. Other symptoms such as pain (P = .01) and feeling ill (P = .03) improved gradually over time following completion of therapy.

**TABLE 4.** Severity Grading of Toxic Effects

<table>
<thead>
<tr>
<th>Toxic Effects by Time of Posttreatment</th>
<th>Grade, No. of Patients*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement</td>
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<tr>
<td>3 Months (n = 14)</td>
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<tr>
<td>Dysphagia</td>
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<tr>
<td>Mucositis</td>
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<tr>
<td>Xerostomia</td>
<td>0</td>
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<tr>
<td>Hearing loss</td>
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</tr>
<tr>
<td>Paresthesia</td>
<td>8</td>
</tr>
<tr>
<td>6 Months (n = 14)</td>
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<td>Dysphagia</td>
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<td>Mucositis</td>
<td>14</td>
</tr>
<tr>
<td>Xerostomia</td>
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<tr>
<td>Hearing loss</td>
<td>8</td>
</tr>
<tr>
<td>Paresthesia</td>
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<tr>
<td>12 Months (n = 14)</td>
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<td>Dysphagia</td>
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<td>Hearing loss</td>
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</tr>
<tr>
<td>Paresthesia</td>
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</tr>
<tr>
<td>24 Months (n = 12)</td>
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<td>Hearing loss</td>
<td>7</td>
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<tr>
<td>Paresthesia</td>
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</tbody>
</table>

*Described in Cancer Therapy Evaluation Program’s QCTD/NCI/NIH Common Terminology Criteria for Adverse Events (CTCAE), Version 3.0."
distribution, and high level of variance. However, results from previous studies are remarkably consistent, with the exception of global health status. Hammerlid et al. described quality-of-life results for 11 patients with NPC who recorded a high pain score and concerns with trouble enjoying meals, feeling ill, and dry mouth, but no change in global health. Huguenin et al. found quality-of-life issues for 12 patients with NPC to consist of dry mouth, sticky saliva, trismus, and problems with teeth and eating, with no effect on global health. Talmi et al. showed difficulties with swallowing, xerostomia, dysphagia, and hearing, again with no deterioration in global health.

**Figure 1.** Mean functional and symptom scores with significant change over time from the European Organisation for Research and Treatment of Cancer Core Quality-of-Life Questionnaire.
scores. It is difficult to explain the difference in global health status noted in the present study, but this may represent methodological or population differences. Furthermore, we cannot predict the effect on quality of life from highly conformal radiation techniques such as intensity-modulated radiotherapy, and we plan to prospectively compare this group with more recent patients treated with intensity-modulated radiotherapy.

**CONCLUSIONS**

This study gives an insight into the various issues experienced by patients who received treatment for NPC and helps identify concerns to assist with future rehabilitation needs. There is substantial deterioration on oropharyngeal function following chemoradiotherapy, and this
has a significant effect on global health status. This information gives a clearer understanding about the slow progression toward recovery following therapy that is poorly represented by physician grading of toxic effects alone. Quality of life and functional outcomes should become standard outcome measures in the comprehensive assessment of cancer therapy.

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Author Contributions: Ms Oates and Read and Drs Clark and Boyer had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Oates, Read, Reeves, and O’Brien. Acquisition of data: Oates, Read, Reeves, and Gao. Analysis and interpretation of data: Oates, Clark, Read, Gao, Jackson, Boyer, and O’Brien. Drafting of the manuscript: Oates, Clark, Read, and O’Brien. Critical revision of the manuscript for important intellectual content: Oates, Clark, Read, Reeves, Gao, Jackson, Boyer, and O’Brien. Statistical analysis: Clark and Gao. Administrative, technical, and material support: Oates, Read, Reeves, and Gao. Study supervision: Clark, Jackson, Boyer, and O’Brien.

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REFERENCES


