Patient characteristics as indicators for poor quality of life after radiotherapy in advanced nasopharyngeal cancer

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Abstract

Background
This study aimed to identify the characteristics of patients with advanced nasopharyngeal carcinoma (NPC) who experience poor quality of life (QOL) after radiotherapy.

Methods
Ninety-three Chinese NPC patients were recruited; the patients’ clinicopathological features were collected and QOL, coping mode, psychological distress and performance status were measured prior to and after radiotherapy. Patient symptoms were measured using a 13-point self-reported scale.

Results
In patients with a symptom score <14 and a medical coping confrontation score <60, the mean QOL after radiotherapy was 66.37 ± 4.56 for men with anxiety, 81.79 ± 7.55 for men without anxiety, 56.97 ± 9.16 for women with anxiety and 82.96 ± 5.05 for women without anxiety. In patients with symptom scores ≥14 and a medical coping confrontation score ≥60, females with anxiety had the lowest mean QOL (56.23 ± 7.05). In patients with anxiety before radiotherapy, those with a good performance status had a lower decline in QOL than those with poor performance status (P < 0.01), whereas the difference in the decline in QOL after radiotherapy between patients with good performance status and poor performance status was not significant (P > 0.05) in patients without anxiety. In patients with symptom scores <14, regardless of their performance status, the decline in QOL after radiotherapy was larger for patients with anxiety than for patients without anxiety. Multivariate stepwise regression showed that higher symptom score after radiotherapy, poorer performance status and anxiety before radiotherapy were associated with a decline in QOL after radiotherapy.

Conclusions
Patients who experienced poor QOL after radiotherapy tended to be females; they experienced anxiety before treatment and lacked a positive coping mode. Their QOL may be improved by timely identifying and offering them proper intervention.

Introduction
Nasopharyngeal carcinoma (NPC) is a common cancer in southern China and South-eastern Asia. Most patients are already in advanced stages of the disease when diagnosed with NPC1. Radiotherapy, which is the main treatment for advanced NPC, not only damages tumour cells but also affects normal tissue, thereby causing a series of acute adverse reactions in patients, such as hearing loss, dry or sore mouth, difficulty in chewing or swallowing, hoarseness and altered taste2. Often, the influences of these side effects on the patients’ physiological functions last far longer than the treatment3. Limited physical functions can lead to the development of psychological problems, such as fear, distress, anxiety or depression, which may seriously affect the patients’ quality of life (QOL)4,5.

A focus on QOL is paramount for patients with advanced NPC. Although the patients’ physiological functions are affected by radiotherapy, good symptomatic nursing and support can help in improving QOL of advanced NPC patients6. Studying factors related with QOL and identification of the characteristics of patients who experience poor QOL during and after radiotherapy can provide important information for clinicians and nurses.

In this study, we examined the relationships between psychological status before radiotherapy and QOL after radiotherapy, and psychological status before radiotherapy and change in QOL due to radiotherapy in advanced NPC patients. Using a stratified analysis of the effects of patient sex, performance status, coping mode and anxiety on QOL after radiotherapy and the changes in QOL during radiotherapy, we aimed to identify the patient characteristics that may indicate a high risk of experiencing poor QOL after radiotherapy. Our findings will help doctors and nurses to implement nursing and psychological interventions to improve QOL for such high-risk NPC patients.

Methods and materials
Participants
The study participants were patients with advanced NPC who were admitted to two hospitals in Fuzhou (Fujian, China) from January 2009 to December 2009. Eligible patients were (1) conscious, (2) aged 18 years or older, (3) literate, (4) patients with

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7th edition Union for International Cancer Control (UICC) stage III or IVA and (5) those who received curative concurrent chemoradiotherapy. Patients who did not undergo radiotherapy or had undergone chemotherapy before radiotherapy were excluded. Of the 116 eligible participants, 23 did not agree to participate. No patient was excluded from this study. The final sample consisted of 93 eligible participants who provided written consent. We followed these 93 patients until they completed radiotherapy. The study was approved by the Biomedical Ethics Committee of Fujian Medical University, Fujian Province, China.

An initial assessment was carried out with each patient prior to radiotherapy. Details regarding the patient’s age, sex, education level, family income and primary caregiver in the family were collected. Each patient’s performance status, haemoglobin (HB), body mass index (BMI), anxiety and depression status, coping mode, severity of head and neck symptoms and QOL were measured using questionnaires and scales (detailed below).

A second assessment was carried out after each patient’s course of radiotherapy was completed. Each patient’s HB, BMI, severity of head and neck symptoms and QOL were measured.

Measurements
The Eastern Cooperative Oncology Group (ECOG) Performance Status scale was used to measure the patients’ performance status. The Chinese version of the ECOG scale was previously found to be suitable for Chinese patients with cancer. This scale captures patient-derived functional status data on a scale of 0–4. An ECOG grade of 2–4 indicates a poor performance status, while a grade of 0–1 indicates a good performance status. In this study, the clinic nurses assessed the performance status of each patient based on their well-being and activity level over a period of 1 week.

The Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire (7 items each for the anxiety and depression subscale), was used to evaluate the level of anxiety and depression experienced by each patient. The Chinese version of the HADS was previously reported to be suitable for Chinese patients. The patients scored each item within the range 0–3, with the anxiety and depression subscale totals each ranging from 0 to 21. A total score >11 for either the anxiety or depression subscale indicated the probable presence of the respective mood disorder. In our study, the reliabilities for the Chinese version of the HADS were 0.84 for anxiety and 0.78 for depression.

The Medical Coping Modes Questionnaire (MCMQ) was used to assess the patients’ disease-coping modes. The Chinese version of the MCMQ was previously reported to be suitable for Chinese patients with cancer. The MCMQ consists of 20 items and provides scores on three subscales: confrontation, avoidance and acceptance-resignation. For each item, the patients selected the response that best represented their experience, from four possible options. The scores for the three subscales were transformed into values ranging from 0 to 100. A higher subscale score indicated a higher frequency of adopting the coping mode corresponding to the respective subscale. In this study, the reliabilities for the Chinese version of the MCMQ were 0.79 for confrontation, 0.73 for avoidance and 0.76 for acceptance-resignation.

NPC and its treatments may cause the patients to experience head and neck symptoms. In this study, we listed 13 main symptoms, including dry mouth, nasal congestion, increased nasal cavity secretions, impaired hearing, tinnitus, hoarseness, restricted tongue movement, abnormal sense of smell and taste, unpleasant cutaneous sensations, mouth ulceration, swallowing dysfunction and limited neck movement. The degree of symptom severity was measured on a scale of 0–3 (0 = no symptoms, 1 = mild, 2 = moderate and 3 = severe). Patients self-assessed the severity of their symptoms. The total symptom score was considered equal to the sum of the scores for the 13 symptoms, with a possible range of 0–39. Higher total symptom scores indicated that the patient suffered from more severe symptoms.

QOL was determined using the European Organization for Research and Treatment of Cancer Core Questionnaire (EORTC QLQ-C30 version 3.0). The Chinese version of the EORTC QLQ-C30 was previously reported to be suitable for Chinese patients with cancer. This scale is a 30-item questionnaire, including 28 items scored 1–4 and 2 items scored 1–7. After the patients completed the questionnaire, the score for each item was transformed into a value in the range of 0–100. The sum of all transformed scores for each of the 30 items was once again transformed into a value in the range of 0–100, to determine the total QOL score. A high total score indicated a good QOL. In this study, the reliability of the Chinese version of the EORTC QLQ-C30 version 3.0 was 0.83.

Statistical analysis
The paired t-test was used to compare HB, BMI, total symptom scores and QOL prior to radiotherapy and after radiotherapy. In order to identify the characteristics of the patients with poor QOL after radiotherapy, multivariate stepwise regression was applied to analyse the risk factors for poor QOL. Firstly, we analysed the risk factors for poor QOL after radiotherapy, and then stratified the risk factors to identify the characteristics of patients with poor QOL after radiotherapy. In order to examine the interaction between patient sex and anxiety on QOL after radiotherapy, the regression model included an interaction term (patient sex × anxiety). Secondly, we analysed the risk factors for a decline in QOL after radiotherapy, and...
then we stratified the risk factors to identify the characteristics of patients with a decline in QOL during radiotherapy. In order to examine the interaction between performance status and anxiety on the decline in QOL after radiotherapy, the regression model included an interaction term (performance status × anxiety). The significance level was set to 0.05, and all $P$ values were two-tailed. Data were analysed using SAS version 9.0 software (SAS Institute, Inc, Cary, NC).

### Results

Ninety-three patients with advanced NPC, including 68 (73.12%) men and 25 (26.88%) women, were enrolled in this study. The mean age (±standard deviation, SD) was 44.3 ± 12.54 for all patients, 46.13 ± 12.74 for the males and 39.25 ± 10.64 for the females. Table 1 outlines the clinicopathological features of the patients.

Before radiotherapy, the prevalence rates of anxiety and depression were 46.24% (43/93) and 43.01% (40/93), respectively, with 33.33% (31/93) of the patients experiencing both anxiety and depression. The mean scores (±SD) for the three MCMQ subscales were 60.35 ± 11.26 for confrontation, 52.69 ± 9.33 for avoidance and 50.48 ± 7.66 for acceptance-resignation. Confrontation was the most prevalent mode, with 60/93 (64.5%) patients scoring highest in this coping mode.

Table 2 shows the average (±SD) HB, BMI, symptom scores and EORTC QLC-C30 scores before and after treatment. The mean HB, BMI and QOL values were significantly lower after radiotherapy than before radiotherapy, and the mean symptom score was significantly higher after radiotherapy than before radiotherapy.

#### QOL after radiotherapy

In multivariate stepwise regression analysis, we defined 13 independent variables, including patient age, sex, educational level, family income, family caregiver, performance status prior to radiotherapy, HB after radiotherapy, symptom score (0: <14, 1: ≥14) after radiotherapy, anxiety prior to radiotherapy (1: yes, 0: no), depression prior to radiotherapy (1: yes, 0: no) and the three coping mode scores (0: <60, 1: >60). Both a low confrontation score and high symptom score were associated with a low QOL score after radiotherapy. Patient sex and anxiety had independent effects on the poor QOL score after radiotherapy, and also had an interaction with poor QOL after radiotherapy (Table 3).

In patients with symptom scores $\geq$14 and confrontation scores $\leq$60, the mean QOL after radiotherapy was 61.27 ± 10.67 for men with anxiety, 65.59 ± 12.79 for men without anxiety, 56.23 ± 7.05 for women with anxiety and 71.75 ± 2.35 for women without anxiety. The female patients with anxiety after radiotherapy exhibited a lower QOL than female patients without anxiety ($P < 0.01$); the difference in QOL after radiotherapy between male patients with or without anxiety was not statistically significant.

In patients with a symptom score $<14$ and a confrontation score $<60$, the mean QOL after radiotherapy was 66.37 ± 4.56 for men with anxiety, 81.79 ± 7.55 for men without anxiety, 56.97 ± 9.16 for women with anxiety and 82.96 ± 5.05 for women without anxiety after radiotherapy.

Table 1 Clinicopathological features of the 93 advanced NPC patients who received curative concurrent chemoradiotherapy

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>68</td>
<td>73.1</td>
</tr>
<tr>
<td>Female</td>
<td>25</td>
<td>26.9</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>84</td>
<td>90.3</td>
</tr>
<tr>
<td>Unmarried or widowed</td>
<td>9</td>
<td>9.7</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>35</td>
<td>37.6</td>
</tr>
<tr>
<td>Junior high school</td>
<td>29</td>
<td>31.2</td>
</tr>
<tr>
<td>High school</td>
<td>14</td>
<td>15.1</td>
</tr>
<tr>
<td>University</td>
<td>15</td>
<td>16.1</td>
</tr>
<tr>
<td>Family income (monthly average)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤$250</td>
<td>66</td>
<td>70.97</td>
</tr>
<tr>
<td>&gt;$250</td>
<td>27</td>
<td>29.03</td>
</tr>
<tr>
<td>Family caregivers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse or parent</td>
<td>60</td>
<td>64.5</td>
</tr>
<tr>
<td>Children or nurse</td>
<td>33</td>
<td>35.5</td>
</tr>
<tr>
<td>Clinical stage (7th UICC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>47</td>
<td>50.5</td>
</tr>
<tr>
<td>IVA</td>
<td>46</td>
<td>49.5</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensity-modulated</td>
<td>64</td>
<td>68.8</td>
</tr>
<tr>
<td>Conventional</td>
<td>29</td>
<td>31.2</td>
</tr>
</tbody>
</table>
Regardless of their symptom score, female patients with anxiety and low confrontation scores prior to radiotherapy had poor QOL after radiotherapy (both averages of QOL score <60).

Change in QOL after radiotherapy
Multivariate stepwise regression was used to identify the factors that related with the change in QOL after radiotherapy. Change in QOL, which was determined as the EORTC QLQ-C30 score after radiotherapy minus the EORTC QLQ-C30 score before radiotherapy, was a dependent variable. Fourteen independent variables were tested, including patient age, sex, educational level, family income, family caregivers, performance status before radiotherapy (good: ECOG ≤1, poor: ECOG ≥2), HB before and after radiotherapy, symptom score after radiotherapy (0: <14, 1: ≥14), anxiety before radiotherapy (1: yes, 0: no), depression before radiotherapy (1: yes, 0: no) and the three coping mode scores (0: <60, 1: >60).

The symptom score after radiotherapy, performance status and anxiety before radiotherapy were associated with changes in QOL after radiotherapy. Anxiety and performance status also had an interaction with the change in QOL (Table 4).

For patients with symptom scores ≥14, decline in QOL after radiotherapy was associated with performance status before radiotherapy if the patients suffered from anxiety prior to radiotherapy (Table 5). Table 5 shows that in patients with anxiety before radiotherapy, those with a good performance status had a lower decline in QOL than those with poor performance status (P < 0.01), whereas the difference in the decline in QOL after radiotherapy between patients with good performance status and poor performance status was not significant (P > 0.05) in patients without anxiety.

In patients with symptom scores <14, regardless of their performance status, the declines in QOL after radiotherapy were larger for patients with anxiety than patients without anxiety (Table 6).

Tables 5 and 6 show that patients with the greatest decline in QOL during radiotherapy had anxiety and a poor performance status before radiotherapy or anxiety before radiotherapy and severe treatment-induced side effects after radiotherapy.

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Discussion

This longitudinal study shows that female advanced NPC patients who experienced anxiety before treatment and lacked a positive coping mode for their disease were more likely than other patients to experience poor QOL after radiotherapy. Thus, we believe that clinicians and other caregivers should give special attention to advanced NPC patients with anxiety before radiotherapy as well as to those patients who rarely adopt a positive coping mode, especially female patients.

In this study, 95.70% of advanced NPC patients experienced a decline in QOL after radiotherapy compared with their QOL scores before radiotherapy; the relative magnitude of the decline in QOL was between 0.97% and 59.55%. The magnitude of the decline in QOL after radiotherapy was associated with patient performance status, anxiety before radiotherapy and treatment-induced side effects after radiotherapy. Patients who experienced anxiety and poor performance status before radiotherapy or those who had anxiety before radiotherapy and severe treatment-induced side effects after radiotherapy were more likely to have a large decline in QOL after radiotherapy.

Cancer is a highly stressful disease. After diagnosis, patients are subjected to intense psychological stress. Anxiety and depression are the most common psychological problems among patients with cancer14–16. Indeed, anxiety may influence a patient’s immune status, thereby influencing the course of the illness and QOL17,18. Several studies have shown that anxiety is independently associated with emotional and cognitive function, fatigue, nausea and vomiting. Furthermore, anxiety was negatively correlated with QOL in patients after radiotherapy19,20. Our results suggest that if patients with advanced NPC develop anxiety before radiotherapy, then their QOL is likely to be negatively affected after radiotherapy.

Many researchers have reported the relationship between patients’ coping modes and QOL21–23. A positive coping mode allows patients to accept the diagnosis and face their disease with an optimistic attitude, which helps to decrease the patients’ psychological stress and leads to good QOL21,22. Confrontation is recognized as a positive coping mode. In our previous study on the relationship between coping modes and the prognosis of patients with advanced stomach cancer, we found that low confrontation scores were not only an independent risk factor for poor performance status24, but also an independent risk factor for serious chemotherapy-induced side effects25. In the present study, we found that patients with poor QOL after radiotherapy had a low confrontation score. These results suggest that if nurses were able to assess the patients’ coping

Table 4 The factors that related with the change in QOL after radiotherapy in advanced NPC patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter estimate</th>
<th>Standard error</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance status*</td>
<td>0.08</td>
<td>0.02</td>
<td>3.27</td>
<td>0.0015</td>
</tr>
<tr>
<td>Symptom (after)*</td>
<td>0.01</td>
<td>0.001</td>
<td>4.05</td>
<td>0.0001</td>
</tr>
<tr>
<td>Anxiety*</td>
<td>0.07</td>
<td>0.03</td>
<td>2.50</td>
<td>0.0141</td>
</tr>
<tr>
<td>Performance status × anxiety</td>
<td>0.12</td>
<td>0.03</td>
<td>12.45</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

* Measured before radiotherapy.

Table 5 The effects of performance status and anxiety on QOL after radiotherapy in advanced NPC patients with higher symptom score (x ± s)

<table>
<thead>
<tr>
<th>Performance status</th>
<th>Anxiety</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>31.37 ± 10.81</td>
<td>21.45 ± 8.84</td>
</tr>
<tr>
<td>No</td>
<td>15.97 ± 6.83</td>
<td>14.97 ± 8.78</td>
</tr>
<tr>
<td>Mean difference</td>
<td>15.4*</td>
<td>6.48</td>
</tr>
</tbody>
</table>

* P < 0.001

Table 6 The effects of performance status and anxiety on QOL after radiotherapy in advanced NPC patients with lower symptom score (x ± s)

<table>
<thead>
<tr>
<th>Performance status</th>
<th>Anxiety</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>21.71 ± 10.08</td>
<td>11.71 ± 4.14</td>
</tr>
<tr>
<td>No</td>
<td>16.36 ± 4.55</td>
<td>8.67 ± 6.72</td>
</tr>
<tr>
<td>Mean difference</td>
<td>5.35</td>
<td>3.04</td>
</tr>
</tbody>
</table>

* P < 0.05
** P < 0.001
mode before treatment and create an appropriate intervention for patients with negative coping modes, then the patients’ QOL could possibly be improved.

Performance status is a measure of how cancer affects a patient’s daily life. It takes into account the extent of the disease symptoms, how comfortably an individual can perform their daily activities and how much help he/she requires for basic self-care. Performance status has long been recognized as a predictor of cancer outcome26; individuals with a poor performance status have a lower tolerance for cancer treatment and far worse than others with the same stage of cancer and disease extent27,28. In this study, we did not find that poor performance status affected QOL after treatment; however, we did observe that poor performance status before treatment was associated with the change in QOL after radiotherapy. In patients with mild treatment-induced side effects (symptom score <14) and poor performance status, QOL after radiotherapy remained good if the patients had a low anxiety score. Thus, we believe that attentive psychological nursing and care prior to radiotherapy may reduce the impact of poor performance status on the QOL of patients with advanced NPC.

The limitation of the current research was that the observation time point was the day after radiotherapy. A study with a longer follow-up time needs to be performed to document the ongoing changes in QOL at different time points after radiotherapy in patients with advanced NPC.

In summary, this study demonstrates that patient sex (female), a high anxiety score before treatment, and coping mode score (a low confrontation score) could potentially act as characteristic indicators for poor QOL after radiotherapy in patients with advanced NPC. Patients with the greatest decline in QOL after radiotherapy had high anxiety and poor performance status scores before radiotherapy, or poor performance status scores before radiotherapy and severe treatment-induced side effects after radiotherapy. The psychological distress and disease coping mode of advanced NPC patients should be assessed before radiotherapy. Additionally, treatment-induced side effects should be measured after radiotherapy. Thus, patients at a high risk of poor QOL could be identified and offered proper treatment, including psychological care and symptomatic treatment, in a timely manner.

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