HEALTH-RELATED QUALITY OF LIFE IN JAPANESE LUNG CANCER PATIENTS AS DETERMINED BY TWO QUESTIONNAIRES: THE HRQOL-20 AND THE EORTC QLQ-C30


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Key Words: EORTC QLQ-C30, health-related quality of life, HRQOL-20, lung cancer patients, scale validity and reliability

Abstract

This study examines the relation between the HRQOL-20, (a Japanese 20-item generic health-related quality of life (HRQOL) questionnaire, with acceptable reproducibility, internal consistency and discriminant validity), and the European Organization for Research and Treatment of Cancer QLQ-C30 (a valid, reliable measure of generic HRQOL in lung cancer patients in multicultural clinical research settings). Lung cancer patients (n=172) completed the HRQOL-20 and QLQ-C30. The response structures to

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the questionnaires were examined by corresponding analysis and Spearman's rank correlation coefficients. The item response structure of the HRQOL-20 was equivalent to that of the QLQ-C30 and similar to the one found in a previous study of stomach cancer patients. The correlation coefficients between the HRQOL-20 (positive and negative scale scores) and QLQ-C30 (global quality of life scale score) were 0.51 and 0.64. The results provided further support for the validity and reliability of the HRQOL-20 questionnaire for lung (as well as stomach) cancer patients, in Japanese clinical research setting.

Introduction

Recently, patient-reported health-related quality of life (HRQOL) has received increased attention as an outcome measure in cancer clinical trials, beyond the traditional biomedical markers of the disease. These outcome analyses have used various instruments such as EuroQOL (The EuroQol Group, 1990), SF-36 (Ware and Sherbourne, 1992), and EORTC QLQ-C30 (Aaronson et al., 1988, 1993; Osoba et al., 1994, 1997) to assess HRQOL as evaluation criteria. The consequences of the disease for the individual patient's life have been conceptualized in the term HRQOL, which encompasses the physical, psychological and social functioning of the patient (Kaptein et al., 1993; Maille et al., 1996). In addition, patient's personality resources have been implicated in HRQOL (Fekkes et al., 2001; Schröder and Schwarzer, 2001).

In previous studies, HRQOL was examined in relation to personality in stomach cancer patients and non-cancer patients as well as healthy individuals in the context of a set of variables (physical, psychological and social) commonly thought to affect (or to be affected by) patient-reported HRQOL (Yamaoka et al., 1996, 1998a). The instruments used were a generic questionnaire (developed in a Japanese population), the HRQOL-20, which consists of 20 items related to physical, psychological and social functioning (Yamaoka, 1994; Yamaoka et al., 1996, 1998b), and the Eysenck Personality Questionnaire (EPQ) (Eysenck and Eysenck, 1975, 1991, 1993), which measures the personality traits extraversion (E), neuroticism (N) and psychoticism (P). The HRQOL-20 scores correlated positively with the Japanese version of the EPQ (Shigehisa, 1995; Shigehisa and Fukui, 1995) with regards to E and P scores, and negatively with N scores in stomach cancer patients, non-cancer patients and healthy individuals, supporting predictions arising from the hypotheses underlying the HRQOL-20 (Yamaoka et al., 1998a) as well as the EPQ (Eysenck, 1990). Such predictions can contribute to predictive
validity, in that patients with a stimulus tolerant personality (high E, low N and high P scorers) are more likely to have a better HRQOL, and high HRQOL-20 scorers are tolerant of adverse circumstances or hedonists (Vollrath and Torgersen, 2002), consistent with the theory underlying the questionnaires (Eysenck and Eysenck, 1975; Yamaoka et al., 1998a). These results of stomach cancer patients were replicated in recent studies (Shigehisa, 2000, 2001a,b).

In order to validate further the HRQOL-20 questionnaire, the present study examines HRQOL in patients with lung cancer (the current most prevalent disease in Japan) in comparison with previously examined patients with stomach cancer (which had previously been the most prevalent disease) (Yamaoka et al., 1998a). For this purpose, HRQOL is assessed by the HRQOL-20 together with the current core questionnaire, the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, a valid and reliable measure of HRQOL in Western lung cancer patients in multicultural clinical research settings (Aaronson et al., 1993; Kobayashi et al., 1998; Osoba et al., 1997). The results of the two questionnaires are analyzed in relation to each other so as to clarify the similarity (equivalence) between the questionnaires’ item response structure (the response patterns of the patients) and to verify scale reliability and concurrent validity of the HRQOL-20 on the EORTC QLQ-C30.

Methods

Subjects

The subjects were 172 lung cancer patients (131 males and 41 females) who agreed to participate in the study. Their ages ranged from 29 to 89 years old (mean 64.8, SD 11.3) for males, and 28 to 85 years old (mean 60.0, SD 14.6) for females. Informed consent was obtained from each patient in the form of mutual agreement before any part of the study commenced. The survey was conducted before treatment, while the patients were hospitalized for clinical trials, between January 1999 and March 2002. The patients responded individually to the HRQOL-20 and EORTC QLQ-C30 (version 2.0, Osoba et al., 1997). Since the survey was conducted at the beginning of the hospital stay, the total physical condition of the patients was reasonably well (about a half of the patients showing
the ECOG Performance Score less than 1) although the stage of the disease was to the contrary (about 70% of the patients were in stage 4).

**Questionnaires**

*HRQOL-20:* Examining the difference between the national character in Japan and English-speaking countries, we have made the HRQOL-20. This questionnaire consists of 20 items [see Appendix]: 14 items relate to “the state of the disease” (*State*) and six items relate to “the attitude toward the disease” (*Attitude*) (Yamaoka et al., 1994, 1996, 1998a, b). These items were selected from a series of multidimensional data analyses of over 300 items to meet the following criteria.

1) The questionnaire evaluates two factors, *Attitude* and *State*, with *Attitude* causing a change in *State*, which in turn changes the HRQOL of a patient.

2) The item response pattern of the patients (structure of the questionnaire) is similar to that of healthy individuals.

Each item (except item 19, which has two response categories, “Yes” or “No”) has three possible responses (positive, negative, and neither (or average)). The scaling is based on observation that the HRQOL-20 items have an U-shaped structure like that of scalogram analysis (Guttman, 1941), when they are classified by a multidimensional data analysis, Quantification Method III (Hayashi, 1992). In the Guttman scale, unidimensionality is guaranteed; hence scaling using category value is valid. Along with the U-shaped structure, the positive and negative response categories were clearly separated in each scatter-plot. The relationship between the items related to the physical and psychological conditions indicated that a poorer physical condition brings about a poorer psychological condition, while a better physical condition brings about a better psychological condition, as evidenced by the U-shaped structure of the item responses. Adoption of the total score (not subscale scores) of the positive or negative response category for evaluating the HRQOL is based on these observations. In the present study, two categories (positive and negative) of the total score, as the sum of the responses in each category, are used for data analysis.

The scores range from 20 (better) to 0 (poorer) for the positive response category.
and from -20 (poorer) to 0 (better) for the negative response category. A greater positive score denotes a better HRQOL. On the other hand, a greater absolute value of the negative score signifies a poorer HRQOL. Therefore, a score of 0 denotes opposite meaning between a positive and negative scores. Namely a positive score of 0 denotes a poor HRQOL and a negative score of 0 denotes a good HRQOL. Previous observations suggest that a negative score is more sensitive than a positive score in cancer patients. Test-retest correlation coefficients between the scores on this questionnaire, over a 1-week period in healthy females, were 0.64 (in the positive response category) and 0.75 (in the negative response category). Cronbach's alpha coefficients for patients with stomach cancer or other diseases were approximately 0.8. The discriminant validity and concurrent validity of the HRQOL-20 in these patients and healthy individuals have already been reported (Yamaoka et al., 1996, 1998a,b).

*EORTC QLQ-C30:* This is a current core questionnaire for patients with lung cancer in multicultural clinical research settings. Its practicability, reliability, and validity were reported in an international field study that involved 12 European, North American or English-speaking countries (Aaronson et al., 1993) and also in a Japanese clinical study of lung cancer patients (Kobayashi et al., 1998). The QLQ-C30 (version 2) (Osoba et al., 1997) incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), and a global health and quality of life scale. Six single-item symptom measures are also included.

**Statistical Analyses**

The HRQOL-20 and the QLQ-C30 item response structures were analyzed by the method of multidimensional data analysis, Quantification Method III (Hayashi, 1992) or correspondence analysis, which is similar to scalogram analysis (Guttman, 1941). These methods analyze a data structure under a simple hypothesis of linearity of the data. Internal consistency reliability was examined using Cronbach's alpha coefficient. The correlations between the two (positive and negative category) scores of the HRQOL-20 and the nine (multi-item scale) scores of the QLQ-C30 were examined using Pearson
correlation coefficient. The SAS statistical package (version 6.12) (SAS Institute, 1988) was used for these analyses.

Results

The HRQOL-20 item response structures did not differ between males and females, hence the combined results for males and females are shown in Figure 1.

![Diagram of HRQOL-20 questionnaire item responses](image)

Figure 1. Structure of the HRQOL-20 questionnaire item responses (category scores) in lung cancer patients. Males and females are combined (n=172). Result of Quantification Method III

Although the categories were moderately varied, an U-shaped structure is noted: the categories related to positive responses are shown on the left, those related to negative responses are seen on the right, and those related to intermediate (neutral) responses (neither category) in the middle. Similarly, the QLQ-C30 item response structures...
(including four functional scales, three symptom scales and a global quality of life scale items, 1-5, 6, 7, 20, 25, 21-24, 10, 12, 18, 14, 15, 9, 19, 29 and 30) did not differ between males and females, hence combined results are shown in Figure 2.

Figure 2. Structure of the EORTC QLQ-C30 questionnaire item responses (scale scores), including global quality of life scale (items 29 and 30), in lung cancer patients. Males and females combined (n=172). Result of Quantification Method III (The social functioning scale scores were excluded for integrity. The response structure of this scale (items 26, 27) deviated markedly from all other scales.)

An U-shaped structure was also noted: the global quality of life scale scores related to excellent responses (category 6 or 7) and are shown on the left, those related to poor and very poor responses (category 2 or 1) are seen on the right, and those related to intermediate (neutral) responses (neither excellent nor poor) (category 5, 4 or 3) are in the middle. These results provide evidence for the similarity (equivalence) of item response structures (response patterns of the patients except social functioning) between the two questionnaires, the HRQOL-20 and the QLQ-C30, in lung cancer patients. Therefore, the
TABLE I

Descriptive statistics and scale reliability of the HRQOL-20 and the EORTC QLQ-C30 for lung cancer patients (males and females combined) in each response category or scale (n=172).

<table>
<thead>
<tr>
<th></th>
<th>Median (Q1; Q3)</th>
<th>Range</th>
<th>Mean ± SD</th>
<th>Cronbach's alpha coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRQOL-20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>6(4,9)</td>
<td>0-16</td>
<td>6.6 ± 3.7</td>
<td>0.77</td>
</tr>
<tr>
<td>Negative</td>
<td>-3(-6,-1)</td>
<td>-16-0</td>
<td>-4.1 ± 3.5</td>
<td>0.80</td>
</tr>
<tr>
<td>EORTC QLQ-C30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global quality of life</td>
<td>50(33,67)</td>
<td>0-100</td>
<td>50 ± 25</td>
<td>0.86</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>68(60,100)</td>
<td>0-100</td>
<td>70 ± 27</td>
<td>0.67</td>
</tr>
<tr>
<td>Role functioning</td>
<td>67(50,100)</td>
<td>0-100</td>
<td>66 ± 32</td>
<td>0.85</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>75(58,83)</td>
<td>0-100</td>
<td>71 ± 21</td>
<td>0.80</td>
</tr>
<tr>
<td>Cognitive functioning</td>
<td>83(67,83)</td>
<td>0-100</td>
<td>74 ± 22</td>
<td>0.45</td>
</tr>
<tr>
<td>Social functioning</td>
<td>67(50,100)</td>
<td>0-100</td>
<td>70 ± 27</td>
<td>0.63</td>
</tr>
<tr>
<td>Fatigue</td>
<td>33(22,56)</td>
<td>0-100</td>
<td>38 ± 27</td>
<td>0.82</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>0(0,0)</td>
<td>0-100</td>
<td>5 ± 16</td>
<td>0.87</td>
</tr>
<tr>
<td>Pain</td>
<td>17(0,33)</td>
<td>0-100</td>
<td>25 ± 30</td>
<td>0.88</td>
</tr>
</tbody>
</table>
# TABLE II

Pearson correlation coefficients between the HRQOL-20 scores, for positive or negative response category, and the EORTC QLQ-C30 scores, for nine multi-item scales, in lung cancer patients, males and females combined (n=172).

<table>
<thead>
<tr>
<th>HRQOL-20</th>
<th>EORTC QLQ-C30</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTP</td>
<td>QTN</td>
</tr>
<tr>
<td>QTP</td>
<td>***</td>
</tr>
<tr>
<td>QTN</td>
<td>0.52</td>
</tr>
<tr>
<td>GL2</td>
<td>0.50</td>
</tr>
<tr>
<td>PF</td>
<td>0.40</td>
</tr>
<tr>
<td>RF</td>
<td>0.38</td>
</tr>
<tr>
<td>EF</td>
<td>0.34</td>
</tr>
<tr>
<td>CF</td>
<td>0.36</td>
</tr>
<tr>
<td>SF</td>
<td>0.17</td>
</tr>
<tr>
<td>FA</td>
<td>-0.44</td>
</tr>
<tr>
<td>NV</td>
<td>-0.26</td>
</tr>
<tr>
<td>PA</td>
<td>-0.39</td>
</tr>
</tbody>
</table>

* p<0.05 ; ** p<0.01 ; *** p<0.001.

QTP, positive response category  
QTN, negative response category  
GL2, global quality of life  
PF, physical functioning  
RF, role functioning  
EF, emotional functioning  
CF, cognitive functioning  
SF, social functioning  
FA, fatigue  
NV, nausea and vomiting  
PA, pain

Each figure signifies correlation of the HRQOL-20 scores (each score is a sum of the responses for each response category, positive or negative) and the QLQ-C30 scale scores (each score is a sum of the responses for each scale).
The following questions contain statements that people use to describe their feelings and state of health.
Please tick for each question the appropriate answer to describe your condition or feelings of the past few days.

1. How would you describe your state of health?  
   - 1. Good  
   - 2. Average  
   - 3. Bad

2. How often do you feel tired?  
   - 1. Often  
   - 2. From time to time  
   - 3. Hardly ever

3. How would you describe your mood?  
   - 1. Good  
   - 2. As usual  
   - 3. Bad

4. Are you able to do the physical activities you would like to do?  
   - 1. Always  
   - 2. Sometimes  
   - 3. Hardly ever

5. Do you have worries in everyday life?  
   - 1. A lot of worries  
   - 2. Some worries  
   - 3. No worries

6. Can you handle stress?  
   - 1. Yes  
   - 2. Fairly well  

7. How often do you have swollen legs?  
   - 1. Often  
   - 2. From time to time  
   - 3. Hardly ever

8. How often are you in physical pain?  
   - 1. Often  
   - 2. From time to time  
   - 3. Hardly ever

9. How often do you wonder if your illness might be incurable?  
   - 1. Often  
   - 2. From time to time  
   - 3. Hardly ever

10. How often do you feel irritated?  
    - 1. Often  
    - 2. From time to time  
    - 3. Hardly ever

11. How often do you feel ill?  
    - 1. Often  
    - 2. From time to time  
    - 3. Hardly ever

12. How often do you feel as if you were suffocating?  
    - 1. Often  
    - 2. From time to time  
    - 3. Hardly ever

13. How often do you feel lonely?  
    - 1. Often  
    - 2. From time to time  
    - 3. Hardly ever

14. Do you have a good appetite?  
    - 1. Yes  
    - 2. Reasonably good  
    - 3. No

15. Do you sleep well?  
    - 1. Yes  
    - 2. Reasonably well  
    - 3. No

16. Do you feel that members of your family or other people need you?  
    - 1. Yes, strongly  
    - 2. A little  
    - 3. No, I do not

17. How often are you worried about the cost of living?  
    - 1. Often  
    - 2. From time to time  
    - 3. Hardly ever

18. How would you describe your relationship with your family, friends, and neighbors?  
    - 1. Good  
    - 2. Reasonably good  
    - 3. Bad

19. Do you have pets or do you like gardening?  
    - 1. Yes  
    - 2. Reasonably well  
    - 3. No

20. Are you satisfied with your current life?  
    - 1. Very satisfied  
    - 2. Reasonably satisfied  
    - 3. Hardly ever
scores were correlated directly between the two questionnaires, and the results of the HRQOL-20 were compared with those of previous studies in stomach cancer patients.

Descriptive statistics and scale reliability for the HRQOL-20 and QLQ-C30 are shown in Table I. The median HRQOL-20 scores (for positive and negative response categories) of the present lung cancer patients were lower (6 and -3) than the scores of stomach cancer patients in the previous study (7.5 and -1). The mean QLQ-C30 scores (a global quality of life scale, five functional scales, and three symptom scales) of the present Japanese lung cancer patients (5 - 74) were generally similar to those of lung cancer patients in the original Western study (6.7 - 83.6); although the global quality of life scale score (50) and the social functioning scale score (70) were slightly lower (but the cognitive functioning scale score (74) was lower and the role functioning scale score (66) was higher) than in the Western lung cancer patients (56.7, 77.3, 83.6, 57.3).

As for the scale reliability, Cronbach's alpha coefficients are 0.77 and 0.80 for the HRQOL-20 positive and negative response categories. The alpha coefficients ranged from 0.63 to 0.88 for the QLQ-C30 global quality of life scale and seven multi-item scales, except for the cognitive functioning scale, which has a markedly lower coefficient (0.45). Hence, the reliability of the internal consistency of the HRQOL-20 and the Japanese version of the QLQ-C30 seems highly acceptable (alpha values ≥0.70 indicate adequate scale reliability).

Since there were no differences between males and females in the item response structures of the HRQOL-20 and also QLQ-C30, Pearson's rank correlation coefficients between the HRQOL-20 (for the positive and negative response categories) and QLQ-C30 (for eight multi-item scales as well as global quality of life scale) scores were obtained for the combined data on males and females. As shown in Table II, there were fairly strong correlations (0.50 and 0.57) between the QLQ-C30 (global quality of life scale score) and the HRQOL-20 (positive and negative response category scores). Fairly good correlations were also obtained between the eight multi-item scale scores of the QLQ-C30 and the positive and negative category scores of the HRQOL-20 (absolute value ranged from 0.17 to 0.44 with the positive score; and from 0.30 to 0.62 with the negative score). The coefficients were higher with the global quality of life scale (0.50, 0.57) and lowest
with the social functioning scale (0.17, 0.30) for the positive and the negative response categories. All correlation coefficients were statistically significant, indicating reasonably high concurrent validity of the HRQOL-20 questionnaire on the QLQ-C30 in Japanese lung cancer patients. In addition, correlation coefficients between the subscales (except for the social functioning scale) of the QLQ-C30 found in the present lung cancer patients (0.19 - 0.68) were comparable to those reported in the original Western study (0.12 - 0.62) (Aaronson et al., 1993).

Discussion

The HRQOL-20 questionnaire has been shown to be a satisfactory instrument for evaluating clinical trial outcomes primarily in stomach cancer patients in a Japanese population (Yamaoka, 1994; Yamaoka et al., 1994, 1996, 1998a,b; Shigehisa, 2000, 2001a, b; Shigehisa et al., 1995). The reproducibility, internal consistency, and discriminant validity of this questionnaire have been studied in these patients (Yamaoka et al., 1994, 1996, 1998a, b). Consistent with the theory behind the personality questionnaires (Eysenck, 1990), previous studies (Yamaoka et al., 1998a; Shigehisa, 2001a) have shown that stomach cancer patients who were tolerant of adverse circumstances, scoring high on the E and P scales but low on the N scale of the EPQ (one of the current core questionnaires of personality used in multicultural research settings (Lynn and Martin, 1995; Barrett and Eysenck, S.B.G 1984)), have a better HRQOL scoring high on the HRQOL-20. In the present study of lung cancer patients, the concurrent validity of the HRQOL-20 was found to be satisfactory on the current core questionnaire for lung cancer patients. The EORTC QLQ-C30 (Aaronson et al.,1993; Osoba et al.,1997; Kobayashi et al, 1998) and the response pattern of the patients, scale reliability and item response structures of these questionnaires were found to be similar (equivalent) to each other. Together with evidence from these studies, the present study provides further support for the validity of the HRQOL-20 questionnaire as an useful instrument for evaluating the consequences of cancer (diagnosis and treatment) for the individual patient’s life.

Results of the present study clearly showed that the HRQOL-20 item response scores had a U-shaped structure from the observation of the multidimensional data
analysis, the Quantification Method III. Scoring of the responses based on additivity was validated, indicating that all the item response scores contributed equally to the scoring used in the present study. The item response structure did not differ between male and female lung cancer patients. These characteristics of the data structure of the HRQOL-20 questionnaire in lung cancer patients were consistent with those in the previous studies of stomach cancer patients and also healthy individuals (Yamaoka et al., 1994, 1996, 1998a, b).

The HRQOL-20 scores for the positive and negative response categories found in the present study of lung cancer patients tended to be lower than those in the previous study of stomach cancer patients, whose HRQOL varied with personality types (Yamaoka et al., 1998a). Considering the divergent personality, this tendency or difference could be expected. On the other hand, the present (Japanese) lung cancer patients showed somewhat lower scores on the cognitive and the social functioning scales as well as the global quality of life scale, but higher scores on the role functioning scale, as compared with those reported (before treatment) by Western lung cancer patients (Aaronson et al., 1993). This difference could also be expected, given the divergent personality across cultures. The single questionnaire approach (in previous studies) did not take into account the configurations of questionnaire item responses by which patients are uniquely characterized. A patient is not either a good HRQOL-20 or QLQ-C-30 responder but is characterized by these qualities simultaneously. The present two-questionnaire approach examined unique configurations of item response structures characterized by the HRQOL-20 and QLQ-C30 simultaneously, although the HRQOL-20 has been made considering Japanese National Character.

Cronbach’s alpha coefficients (0.77 or 0.80) found in the present study of lung cancer patients for each HRQOL-20 response category were equivalent to those in the previous study (approximately 0.80) of patients with various diseases (Yamaoka et al., 1998b). Similarly, the alpha coefficients (0.45-0.88) found in the present study for the QLQ-C30 scales were comparable to those (0.54-0.86) found in the Western studies (Aaronson et al., 1993; Osoba et al., 1997). These results indicated that the reliability of
the internal consistency of the Japanese HRQOL-20 is equivalent to that of the Western QLQ-C30.

In summary, the results of the present study indicate that the HRQOL-20 score is a valid and reliable questionnaire for HRQOL for patients with lung cancer, is consistent with results of previous studies (in stomach cancer patients), and provides evidence for the concurrent validity of this questionnaire with the EORTC QLQ-C30, the current core questionnaire in multi-cultural clinical research.

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