Health-Related Quality of Life and Utility Scores of Lung Cancer Patients Treated with Traditional Chinese Medicine in China

Liu Liu1,2, Yan Wei1,2, Yue Teng1–3, Juntao Yan1,2, Fuming Li1,2, Yingyao Chen1,2

1School of Public Health, Fudan University, Shanghai, People’s Republic of China; 2NHC Key Laboratory of Health Technology Assessment, Fudan University, Shanghai, People’s Republic of China; 3Department of Outpatient, Shanghai Research Institute of Acupuncture and Meridian, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, People’s Republic of China

Correspondence: Yan Wei, NHC Key Laboratory of Health Technology Assessment, School of Public Health, Fudan University, Shanghai, People’s Republic of China, Tel +86 18930749707, Email yanwei@fudan.edu.cn

Purpose: To assess health-related quality of life (HRQoL) and utility scores of lung cancer patients treated with traditional Chinese medicine (TCM) in China.

Methods: This cross-sectional study included lung cancer patients treated with TCM in seven tertiary hospitals in Shanghai, China. The HRQoL and utility scores of these patients were measured using the five-level EQ-5D (EQ-5D-5L). The EQ-5D-5L utility scores were derived from the Chinese EQ-5D-5L Value Set. The relationships between HRQoL and the socio-demographic and clinical characteristics of these patients were further explored by Tobit regression.

Results: This study included a total of 347 patients. Their mean ± SD and median EQ-5D-5L utility scores were 0.851 ± 0.198 and 0.893, respectively. The highest proportion of participants reporting problems was observed in the pain/discomfort dimension (57.9%) and in anxiety/depression (45.5%). Lung cancer patients treated with TCM had poor HRQoL, influenced by cancer clinical stage.

Conclusion: Lung cancer patients treated with TCM have poor HRQoL, with many patients reporting problems in the pain/discomfort and anxiety/depression dimensions. The information on health utility scores and HRQoL of lung cancer patients treated with TCM could be useful for future supportive care, economic evaluations and decision-making in China.

Keywords: lung cancer, health-related quality of life, traditional Chinese medicine, EQ-5D-5L

Introduction

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer deaths, both worldwide1 and in China.2 In 2015, 787,000 patients in China were newly diagnosed with lung cancer and 631,000 patients died of this disease, accounting for 20.03% of patients diagnosed with cancer and 26.99% who died of cancer during that year. In addition, the burden of lung cancer has increased in the past three decades. Lung cancer is one of the most aggressive malignant tumors, with a 5-year overall survival (OS) rate of about 19.7%,4 much lower than the 5-year OS rate of 40.5% among all cancer patients in China.5 In the treatment process, patients with lung cancers will suffer from the disease’s malignant degree and its therapy toxicity.5 At present, the leading treatment methods for lung cancer patients include surgery, chemotherapy, radiotherapy, and targeted therapy. Traditional Chinese Medicine (TCM), which has a long history in China, has been widely used to treat various diseases including lung cancer in China and other Asian countries or areas.6–8 In addition to their physical symptoms, lung cancer patients frequently experience depression and anxiety,9,10 having a negative impact on their health-related quality of life (HRQoL).

HRQoL, especially preference-based health-related QoL, has become an increasingly important outcome measure in the cost-utility analysis (CUA), a particular form of economic evaluation.11 HRQoL can inform patient management and policy decisions, making it important to measure HRQoL.12
Although many studies in patients with lung cancer have investigated their HRQoL after surgery, radiotherapy, and/or chemotherapy, few studies to date have evaluated their HRQoL after TCM treatment, which measured by disease-specific instruments, including the Functional Assessment of Cancer Therapy-Lung (FACT-L), the quality-of-life (QoL) instrument for lung cancer based on Traditional Chinese Medicine (QLASTCM-Lu) and European Organization for Research and the Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ-C30 and EORTC QLQ-LC13). Although these methods are valid and reliable, they are not preference-based instruments to elicit health utility scores for lung cancer patients. The present study, therefore, aimed to assess the HRQoL and utility scores in lung cancer patients who received TCM treatment and evaluate the relationships of quality of life outcomes with the socio-demographic and clinical characteristics among lung cancer patients in China.

Materials and Methods

Study Design and Setting

A cross-sectional questionnaire survey was conducted in Shanghai, China. Lung cancer patients treated with TCM were recruited successively from the seven tertiary hospitals of Shanghai in December 2020. All inpatients in the hospital ward who met the inclusion criteria were asked if they would like to participate in the survey. These seven hospitals are regional centers for TCM treatment of lung cancer; therefore, their patients are representative of lung cancer patients treated with TCM. The written informed consent was obtained from all participants prior to the interviews. The study was approved by the Ethics Review Board of the School of Public Health, Fudan University (IRB# 2020-09-0848), and it adhered to the tenets of the Declaration of Helsinki.

Participants

Patients diagnosed with lung cancer who were treated with TCM were invited to enroll in this study. Patients were excluded if they were younger than 16 years at the time of the survey, as were those unwilling to provide informed consent, unable to understand the questionnaires or with serious complications.

Data Collection

The enrolled patients completed the survey questionnaires. The questionnaire consisted of three parts: (1) socio-demographic information; (2) clinical information; and (3) HRQoL instrument. Socio-demographic information included sex, age, level of education, employment status, medical insurance and annual household income. The clinical information included type and severity of lung cancer and the duration since diagnosis. HRQoL was evaluated using the validated Chinese version of EQ-5D-5L.

EQ-5D-5L

The EQ-5D instrument is one of the most widely used generic preference-based HRQoL instruments internationally, and has been validated in patients with cancer. To reduce the ceiling effects and improve the sensitivity of the three-level version of EQ-5D (EQ-5D-3L) introduced by the EuroQol Group in the 1990s, the new five-level EQ-5D questionnaire (EQ-5D-5L) was developed in 2011. It retains the same five dimensions as the EQ-5D-3L (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with each dimension having five levels: no problems, slight problems, moderate problems, severe problems, and unable/to/extreme problems, resulting in 3125 (5^5) unique health states. The Chinese version of the EQ-5D-5L has been validated. The health utility values can be derived by the Chinese-specific scoring algorithm of the EQ-5D-5L developed by Luo et al, which yielded scores ranging from −0.391 to 1.000, with zero representing being dead, 1.000 indicating a state of full health, and negative scores indicating health status worse than death. The other component of EQ-5D-5L, the EQ Visual Analogue Scale (EQ-VAS), allowed patients to describe their current overall health on a scale ranging from 0 (the worst health state they can imagine) to 100 (the best health state they can imagine).
Statistical Analysis

Patients who supplied complete socio-demographic and clinical information and completed both the EQ-5D and EQ-VAS were included in the analysis. Continuous variables were reported as means and standard deviations (SD); due to the skewed distribution, the non-parametric Mann–Whitney U or Kruskal–Wallis test were applied to examine the differences of EQ-5D-5L health state utility scores among the various subgroups. Because the maximum health state utility score was 1, which was reported by large percentage of patients, the Tobit model was used to explore the impact of socio-demographic variables (sex, geographical region, age, educational level, employment status, medical insurance and annual household income in 2020) and clinical variables (duration since diagnosis, type and clinical stage of Lung cancer) on utility scores of lung cancer patients. All statistical analyses were performed using Stata version 16.0 (StataCorp LP, College Station, TX, USA).

Results

Characteristics of the Participants

The 347 patients with lung cancer included 187 men and 160 women, mean age 64.8 ± 8.7 years and an average duration since diagnosis of 27.3 months (Table 1). Of these patients, 82.7% lived in urban areas, 63.7% were retired, and 98.8% had health insurance. Most (58.7%) reported annual per capita household incomes ranging from 50,000 to 149,999 Chinese yuan (approximately US$ 7657 to 22,971), whereas 18.5% reported incomes below 50,000 Chinese yuan (US $7657). Of these patients, 79.5% had non-small cell lung cancer (NSCLC) and 7.5% had small cell lung cancer, with 26.4%, 14.0%, 19.2%, and 40.4% having stages I-IV lung cancer, respectively.

EQ-5D-5L Dimensions

The proportion of patients reporting problems in each dimension of the EQ-5D-5L is shown in Table 2 and Figure 1. Problems in the pain/discomfort dimension were reported by 57.9% of these patients, followed by problems in the anxiety/depression (45.5%), usual activities (34.0%), mobility (33.7%), and self-care (21.9%) dimensions. A total of 94 patients (27.1%) reported no problems in any of the five dimensions.

EQ-5D-5L Utility Scores

The mean and median of EQ-5D-5L utility scores for patients with lung cancer using the Chinese preference weights were 0.851 (SD=0.198) and 0.893 respectively (Table 3). The Shapiro–Wilk test statistics suggested that the null hypothesis of normal distribution of EQ-5D-5L utility scores was rejected (P < 0.001). Figure 2 shows the EQ-5D-5L utility scores skewed towards the right higher values.

According to the non-parametric test, the results showed EQ-5D-5L utility scores differed significant among patients living in urban, rural and other areas (P < 0.05). Those who were at III or IV stage of lung cancer had lower utility scores compared with the patients being at I stage (p < 0.05). In addition, utility scores tended to differ between employed and retired patients, as well as in patients treated according to different decision-making models and with different types of health-care insurance (P < 0.1 each) (Table 3).

Factors Associated with Health Utility Scores

The results of Tobit regression analysis are presented in Table 4. The EQ-5D utility scores were significantly lower in women than in men (P = 0.026). Lower utility scores were associated with stage III (P = 0.036) or IV (P = 0.005) cancer at diagnosis. Time since diagnosis of 13–24 months was a significant predictor of low EQ-5D-5L utility scores (P = 0.013). The residence was also significantly predicted utility scores after controlling for other factors.

Discussion

To our knowledge, this study is the first to report the EQ-5D-5L utility scores and HRQoL of lung cancer patients treated with TCM in China. These findings may be applicable to health economic evaluations of clinical and resource allocations for lung cancer within the health-care sector.
Table 1 Socio-Demographic and Clinical Characteristics of Patients with Lung Cancer

| Characteristic                                      | N (%)      |
|----------------------------------------------------|------------|
| **N (%)**                                          | 347 (100)  |
| **Sex**                                            |            |
| Male                                               | 187 (53.9) |
| Female                                             | 160 (46.1) |
| **Age (years)**                                    |            |
| <60                                                | 89 (25.7)  |
| 60–69                                              | 150 (43.2) |
| >69                                                | 108 (31.1) |
| **Residence**                                      |            |
| Rural area                                         | 53 (15.3)  |
| Urban area                                         | 287 (82.7) |
| Other                                              | 7 (2.0)    |
| **Education level**                                |            |
| Primary school or lower                            | 32 (9.3)   |
| Secondary school                                   | 122 (35.4) |
| High school or technical secondary school          | 124 (35.9) |
| University degree and above                        | 67 (19.4)  |
| **Employment status**                              |            |
| Employment                                         | 126 (36.3) |
| Retirement                                         | 221 (63.7) |
| **Annual household income per capita in 2020, Chinese yuan** |        |
| <50,000                                            | 64 (18.5)  |
| 50,000–99,999                                     | 113 (32.7) |
| 100,000–149,999                                   | 90 (26.0)  |
| ≥150,000                                           | 79 (22.8)  |
| **Decision-making model**                          |            |
| Shared decision-making                             | 315 (90.8) |
| Other                                              | 32 (9.2)   |
| **Health-care insurance**                          |            |
| No insurance                                       | 4 (1.2)    |
| Urban employee basic medical insurance             | 187 (53.9) |
| Urban and rural resident basic medical insurance   | 59 (17.0)  |
| Other insurance                                    | 97 (28.0)  |
| **Duration of disease since diagnosis (month)**    |            |
| <8                                                 | 76 (21.9)  |
| 8–12                                               | 71 (20.5)  |
| 13–24                                              | 79 (22.8)  |
| >24                                                | 121 (34.9) |
| **Clinical stage**                                 |            |
| I                                                  | 91 (26.4)  |
| II                                                 | 48 (14.0)  |
| III                                                | 66 (19.2)  |
| IV                                                 | 139 (40.4) |
| **Type of lung cancer**                            |            |
| Non-small cell lung cancer (NSCLC)                 | 276 (79.5) |
| Small cell lung cancer (SCLC)                      | 26 (7.5)   |
| Other                                              | 45 (13.0)  |

**Notes:** a Level of education missing for two patients; b per capita annual household income missing for one patient; c clinical stage missing for three patients.
The mean health state utility score, as determined by the EQ-5D-5L, in these patients was 0.851, lower than those reported in urban Chinese population (0.957), and in urban and rural residents in four cities in China (0.951), but equivalent to that of patients with non-small cell lung cancer in Taiwan of China. Before our study, a cross-sectional study of advanced non-small-cell lung cancer patients in a hospital in China found that their mean health utility score was 0.814, somewhat lower than in our patient populations. In comparison, patients with advanced lung cancer in France and Germany were found to have a mean EQ-5D-3L index score of 0.58, and patients with lung cancer in Canada also had a lower mean EQ-5D index score.

The differences among these scores may be due to differences among treatment types and clinical stage. Previous studies examined the HRQoL of patients with advanced lung cancer who received drug treatment, including targeted and chemotherapeutic agents. In contrast, the patients in the present study were recruited at tertiary hospitals, were at all stages of disease, and tended to be treated with TCM. The adverse effects of targeted drugs and chemotherapeutic agents may result in chronicity and a decrease in health utility, whereas, TCM is thought to reduce chemotherapy-related side effects and improve HRQoL. In addition, previous studies in lung cancer measured health status values using the EQ-5D-3L which has a higher ceiling effect and lower discriminatory power than the EQ-5D-5L.

In this study, pain/discomfort (57.9%) and anxiety/depression (45.5%) were the problems most frequently reported by respondents, similar to previous findings Chinese patients with advanced lung cancer. Lung cancer therefore had a significant effect on the physiological and psychological status of these patients. Pain has been reported to be an inevitable symptom in lung cancer patients and the main physical symptom causing psychological problems in elderly patients. The physiological and psychological status of these patients has been reported to be significantly affected by pain.

Table 2 Frequency of Item Response in Each EQ-5D-5L Dimension Reported by Participants

| Dimensions       | No Problem N (%) | Slight Problem N (%) | Moderate Problem N (%) | Severe Problem N (%) | Extreme Problem N (%) |
|------------------|------------------|----------------------|------------------------|----------------------|------------------------|
| Mobility         | 230 (66.3)       | 89 (25.6)            | 18 (5.2)               | 7 (2.0)              | 3 (0.9)                |
| Self-care        | 271 (78.1)       | 54 (15.6)            | 16 (4.6)               | 4 (1.2)              | 2 (0.6)                |
| Usual activities | 229 (66.0)       | 85 (24.5)            | 22 (6.3)               | 8 (2.3)              | 3 (0.9)                |
| Pain/discomfort  | 146 (42.1)       | 167 (48.1)           | 19 (5.5)               | 12 (3.5)             | 3 (0.9)                |
| Anxiety/depression | 189 (54.5)   | 136 (39.2)           | 20 (5.8)               | 2 (0.6)              | 0 (0.0)                |

Figure 1 Patients reporting problems percentage in five levels of EQ-5D.
Table 3  EQ-5D-5L Utility Scores of Participants with Lung Cancer in Different Characteristics

|                                | Range      | Mean    | SD      | Median   | P values |
|--------------------------------|------------|---------|---------|----------|----------|
| **Sex**                        |            |         |         |          | 0.216    |
| Male                           | 0.200–1.000| 0.850   | 0.214   | 0.897    |          |
| Female                         | 0.190–1.000| 0.853   | 0.178   | 0.893    |          |
| **Age (years)**                |            |         |         |          | 0.817    |
| <60                            | 0.190–1.000| 0.864   | 0.190   | 0.893    |          |
| 60–69                          | 0.160–1.000| 0.849   | 0.203   | 0.893    |          |
| >69                            | 0.200–1.000| 0.844   | 0.198   | 0.893    |          |
| **Residence**                  |            |         |         |          | 0.014    |
| Rural area                     | 0.360–1.000| 0.881   | 0.136   | 0.906    |          |
| Urban area                     | 0.200–1.000| 0.853   | 0.197   | 0.893    |          |
| Other                          | 0.160–0.940| 0.562   | 0.385   | 0.702    |          |
| **Education level**            |            |         |         |          | 0.549    |
| Primary school or lower        | 0.450–1.000| 0.848   | 0.171   | 0.918    |          |
| Secondary school               | 0.190–1.000| 0.844   | 0.196   | 0.893    |          |
| High school or technical secondary school | 0.160–1.000| 0.856   | 0.200   | 0.902    |          |
| University degree and above    | 0.200–1.000| 0.864   | 0.210   | 0.897    |          |
| **Employment status**          |            |         |         |          | 0.066    |
| Employment                     | 0.160–1.000| 0.873   | 0.183   | 0.942    |          |
| Retirement                     | 0.200–1.000| 0.839   | 0.205   | 0.893    |          |
| **Annual household income per capita in 2020, Chinese yuan** |    |         |         |          | 0.113    |
| <50,000                        | 0.260–1.000| 0.855   | 0.169   | 0.893    |          |
| 50,000–99,999                  | 0.200–1.000| 0.825   | 0.218   | 0.893    |          |
| 100,000–149,999                | 0.190–1.000| 0.868   | 0.218   | 0.942    |          |
| ≥150,000                       | 0.030–1.000| 0.868   | 0.163   | 0.893    |          |
| **Decision-making model**      |            |         |         |          | 0.080    |
| Shared decision-making         | 0.200–1.000| 0.852   | 0.204   | 0.897    |          |
| Other                          | 0.470–1.000| 0.841   | 0.130   | 0.862    |          |
| **Health-care insurance**      |            |         |         |          | 0.064    |
| No insurance                   | 0.750–0.940| 0.864   | 0.095   | 0.883    |          |
| Urban employee basic medical insurance | 0.190–1.000| 0.861   | 0.208   | 0.934    |          |
| Urban and rural resident basic medical insurance | 0.430–1.000| 0.836   | 0.146   | 0.848    |          |
| Other insurance                | 0.200–1.000| 0.841   | 0.211   | 0.893    |          |
| **Duration of disease since diagnosis (month)** |    |         |         |          | 0.738    |
| <8                             | 0.160–1.000| 0.867   | 0.181   | 0.900    |          |
| 8–12                           | 0.190–1.000| 0.857   | 0.200   | 0.888    |          |
| 13–24                          | 0.200–1.000| 0.810   | 0.258   | 0.893    |          |
| >24                            | 0.030–1.000| 0.864   | 0.157   | 0.893    |          |
| **Clinical stage**             |            |         |         |          | 0.013    |
| I                              | 0.200–1.000| 0.886   | 0.144   | 0.906    |          |
| II                             | 0.120–1.000| 0.889   | 0.181   | 0.942    |          |
| III                            | 0.160–1.000| 0.842   | 0.224   | 0.893    |          |
| IV                             | 0.200–1.000| 0.819   | 0.218   | 0.893    |          |
| **Type of lung cancer**        |            |         |         |          | 0.145    |
| Non-small cell lung cancers (NSCLC) | 0.200–1.000| 0.860   | 0.193   | 0.895    |          |
| Small cell lung cancers (SCLC) | 0.016–1.000| 0.765   | 0.282   | 0.848    |          |
| Other                          | 0.200–1.000| 0.848   | 0.154   | 0.893    |          |
| Total                          | 0.200–1.000| 0.851   | 0.198   | 0.893    |          |

**Abbreviation:** SD, standard deviation.
A more severe degree of pain is associated with the aggravation of patients’ anxiety, depression and other negative psychological emotions. Efforts are therefore needed to alleviate pain/discomfort and anxiety/depression during the treatment of lung cancer.

The present results showed three independent factors influenced the HRQoL of lung cancer patients: sex, tumor clinical stage, and residence. Women exhibited lower utility than men, in agreement with previous studies in China, Japan, and France and Germany, and in patients with other types of cancer. Patients with advanced stage cancers have more obvious physical symptoms related to the disease, and the difficulty of treatment may lead to poor prognosis or death, increasing anxiety and depression and worsening quality of life. Our results showed that residential disparities influenced the HRQoL of patients, consistent with findings previously reported in China.

This study had several limitations. First, the study population consisted of lung cancer patients from several tertiary hospitals in Shanghai, China, which may not be representative of all lung cancer patients in mainland China. However, the study population included patients at different stages of lung cancer. Second, this study was cross-sectional survey in design, and therefore could not determine the causal relationships between HRQoL and other influencing factors. These causal relationships should be examined in future longitudinal studies. In addition, we only pay attention to whether the patient has received TCM, and not whether the patient has received other treatments at the same time, which may have a certain impact on the results. Although additional studies are required, the results of this study may provide information on HRQoL on Chinese lung cancer patients receiving TCM treatment.

Conclusion
This study found that lung cancer patients treated with TCM had a low health state utility and poor HRQoL. The dimensions of reduced HRQoL most frequently reported by patients were pain/discomfort and anxiety/depression. More advanced stage tumors were associated with lower HRQoL. These results can provide basic information on health utility scores and HRQoL of lung cancer patients treated with TCM for future supportive care, economic evaluations and decision-making in China. In addition, the HRQoL of lung cancer patients may be improved by reducing pain and depression during the process of treatment.
Table 4 Factors Influencing EQ-5D-5L Utility Scores as Determined by a Tobit Regression Model

|                        | Coefficients | SE  | P values |
|------------------------|--------------|-----|----------|
| Sex                    |              |     |          |
| Male                   | Ref          |     |          |
| Female                 | −0.067       | 0.030 | 0.026    |
| Age (years)            |              |     |          |
| <60                    | Ref          |     |          |
| 60–69                  | −0.006       | 0.034 | 0.851    |
| >69                    | −0.033       | 0.038 | 0.387    |
| Residence              |              |     |          |
| Other                  | Ref          |     |          |
| Rural area             | 0.536        | 0.117 | <0.001  |
| Urban area             | 0.485        | 0.112 | <0.001  |
| Education level        |              |     |          |
| Primary school or lower| Ref          |     |          |
| Secondary school       | −0.064       | 0.053 | 0.223    |
| High school or technical secondary school | −0.045 | 0.054 | 0.405 |
| University degree and above | −0.057 | 0.060 | 0.342 |
| Employment status      |              |     |          |
| Employment             | Ref          |     |          |
| Retirement             | −0.045       | 0.030 | 0.137    |
| Annual household income per capita in 2020, Chinese yuan | | | |
| <50,000                | Ref          |     |          |
| 50,000–99,999          | −0.036       | 0.040 | 0.363    |
| 100,000–149,999        | 0.032        | 0.043 | 0.447    |
| ≥150,000               | −0.005       | 0.045 | 0.913    |
| Decision-making model  |              |     |          |
| Shared decision-making | Ref          |     |          |
| Other                  | −0.063       | 0.047 | 0.182    |
| Health-care insurance  |              |     |          |
| No insurance           | Ref          |     |          |
| Urban employee basic medical insurance | 0.124 | 0.121 | 0.307 |
| Urban and rural resident basic medical insurance | 0.047 | 0.124 | 0.702 |
| Other insurance        | 0.081        | 0.122 | 0.508    |
| Duration of disease since diagnosis (months) | | | |
| <8                     | Ref          |     |          |
| 8–12                   | −0.010       | 0.042 | 0.814    |
| 13–24                  | −0.107       | 0.043 | 0.013    |
| >24                    | −0.025       | 0.041 | 0.534    |
| Clinical stage         |              |     |          |
| I                      | Ref          |     |          |
| II                     | −0.007       | 0.046 | 0.876    |
| III                    | −0.091       | 0.043 | 0.036    |
| IV                     | −0.100       | 0.036 | 0.005    |
| Type of lung cancer    |              |     |          |
| Other                  | Ref          |     |          |
| Non-small cell lung cancers (NSCLC) | 0.050 | 0.040 | 0.210 |
| Small cell lung cancers (SCLC) | −0.033 | 0.063 | 0.604 |

Abbreviation: SE, standard error.

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