


Influence of Financial Toxicity on the Quality of Life in Lung Cancer Patients Undergoing Immunotherapy: The Mediating Effect of Self-Perceived Burden

Zhao-Li Zhang^{1,*}, Zhen Xu^{2,*}, Shi-Kun Yang³, Jin-Gui Huang², Feng-Mei Huang², Yu-Mei Shi²

¹Department of Nursing, Chongqing University Cancer Hospital, Chongqing, 400030, People's Republic of China; ²Department of Medical Oncology, Chongqing University Cancer Hospital, Chongqing, 400030, People's Republic of China; ³Department of Pathology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, 400072, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yu-Mei Shi, Email 515342831@qq.com

Purpose: The purpose of this study is to understand the level of quality of life (QOL) of lung cancer patients receiving immunotherapy and to clarify the potential mediating role of self-perceived burden (SPB) in the relationship between financial toxicity (FT) and QOL.

Patients and Methods: A convenience sample of 342 lung cancer patients receiving immunotherapy was recruited from a cancer hospital from October 2022 to April 2023 for this cross-sectional study. The participants were requested to complete the following structured questionnaires: a sociodemographic and clinical questionnaire, the Functional Assessment of Cancer Therapy–Lung (FACT–L), the Self-Perceived Burden Scale (SPBS) and the COMprehensive Score for Financial Toxicity (COST). The data were subjected to Pearson correlation analysis and bootstrapping analysis in structural equation modelling.

Results: The total FACT–L score was 79.90±15.84 points in 322 lung cancer patients receiving immunotherapy. FT ($\beta = 0.37$, $P < 0.01$) and SPB ($\beta = -0.27$, $P < 0.01$) had a direct effect on QOL. In addition, SPB partly mediated the association between FT and QOL, and the standardized indirect effect was 0.19, accounting for 33.9% of the total effect.

Conclusion: The present study revealed that there is still much room for improvement in the QOL of lung cancer patients during immunotherapy. A greater financial burden resulted in a greater self-perceived burden and was thus associated with inferior QOL. It is imperative for oncology nurses to routinely assess QOL, FT or risk and SPB for lung cancer patients undergoing immunotherapy as well as to assist those patients in understanding the potential financial risk of each choice and help them take more active roles in their routine clinical care.

Keywords: lung cancer, immunotherapy, quality of life, financial toxicity, self-perceived burden

Introduction

Lung cancer is one of the most prevalent types of cancer worldwide and ranks first in incidence and mortality among all malignancies worldwide according to Global Cancer Statistics 2022.¹ Notably, lung cancer, the leading cause of cancer-related death in China, accounts for 40% of global lung cancer deaths.² Worse yet, a myriad of disease- and treatment-related symptoms decrease the quality of life (QOL) of lung cancer patients, the level of which is lower in those patients than in healthy individuals and patients suffering from other malignant tumours.³ QOL is a broad-ranging concept that refers to individuals' subjective perceptions of their status and function in life and involves physical, psychological and social aspects.⁴ The level of self-appraisal QOL supplements clinical evaluation and is particularly important for health care workers to identify subgroups with poor health and improve the conditions of cancer patients by taking necessary steps.⁵

There have been a few new explorations of the therapeutic landscape of lung cancer over the past decade. Immunotherapy, such as immune checkpoint inhibitors, which are generally defined as medicinal strategies that harness the immune system to treat disease,⁶ is considered a reliable and innovative therapy for lung cancer.⁷ It can not only enhance the immune response of T cells to tumours but also act on tumour-associated macrophages, restoring the ability

of macrophages to phagocytose tumours, inhibiting tumour proliferation, and prolonging progression-free and overall survival in patients.⁸ Despite these remarkable results, immunotherapy also causes immune-related adverse events (irAEs), including fatigue, dyspnoea, cough, itch, rash, abdominal cramps, and diarrhoea.⁹ IrAEs can involve various organs and can occur at any time during or after treatment, which has the potential to impact QOL.^{10,11} Quantifying the QOL of lung cancer patients receiving immunotherapy and developing targeted interventions to increase their QOL is a primary objective in addition to prolonging survival. Recently, Wang et al¹² examined the health-related quality of life of lung cancer patients receiving immune checkpoint inhibitors in Guangdong Province. However, this study was conducted in one province of China via convenience sampling, which potentially affects representative lung cancer patients in the sample, thus limiting the generalizability of the findings. Because the possibility of QOL varies according to the sociocultural characteristics of lung cancer patients in different regions, it is necessary to conduct relevant research in other Chinese cities, providing a more comprehensive understanding of the QOL experiences of lung cancer patients undergoing immunotherapy across a broader geographical and cultural spectrum.

Exploring factors associated with QOL is conducive to formulating corresponding measures. Many studies have identified multitudinous predictors of QOL among cancer patients. Among them, financial toxicity (FT), defined as the objective financial burden and subjective financial distress of patients with cancer because of the use of innovative drugs and concomitant health services,¹³ seems to be a relatively new factor related to the QOL of cancer patients.^{14–16} The word “toxicity” is utilized because the financial cost of cancer treatment can cause clinical side effects that are comparable to physical or psychological toxicities.¹⁷ FT adversely affects patients’ preferences for decision-making, adherence to treatment and drugs, and rehabilitation during follow-up care, resulting in decreased QOL.^{18–20} A national survey study in China revealed that 77% of lung cancer patients experienced FT.²¹ Immunotherapy is among the most expensive new treatments for cancer.^{19,22} Although China’s central government has made great efforts to provide basic health care protection, public medical insurance does not cover most anticancer frontline drugs in China, and the ratio of average out-of-pocket spending is approximately 60%.²³ Xu et al²⁴ demonstrated that increased FT is related to decreased QOL in Chinese advanced lung cancer patients.

Self-perceived burden (SPB) is another fundamental factor associated with QOL.^{25–27} SPB is a multidimensional concept characterized as an individual’s empathic concern engendered from the impact of his or her disease and care needs on family members, leading to psychological distress, self-blame, and a diminished sense of self-worth,²⁸ which includes psychological burden, economic burden, treatment burden and family burden. It is believed that SPB may affect patients’ medical decision-making and treatment compliance²⁹ and even result in suicidal ideation and threaten patients’ lives.³⁰ A negative association between SPB and QOL has been identified among urologic cancer patients,³¹ chronic myeloid leukaemia patients,³² and epilepsy patients.³³ However, the same association has been poorly described among lung cancer patients treated with immunotherapy.

Additionally, the relationship between FT and SPB has been explored in previous studies. Ting et al³¹ reported a positive connection between FT and SPB among urologic cancer patients. Consistently, Yu et al³⁴ found that FT was related to patients’ perceptions of being a burden on others. Although previous studies have probed the relationships between FT and SPB with QOL individually, to date, the mediating mechanisms and internal relationships among lung cancer patients receiving immunotherapy have not been well-characterized in the literature. The process of literature review raises the possibility that SPB may act as a potential mediator between FT and QOL.

Therefore, with the purpose of providing a scientific basis and theoretical evidence to develop strategies aimed at improving QOL in such patients, the present study was designed to quantify the level of QOL in lung cancer patients treated with immunotherapy and probe the potential relationships among self-perceived burden, financial toxicity and QOL via structural equation modelling (SEM) analysis. On the basis of the above empirical background and previous findings, we hypothesized that (1) FT and SPB exert direct effects on QOL separately and (2) SPB serves as a mediator between FT and QOL.

Materials and Methods

Study Design

This was a descriptive, cross-sectional study.

Setting and Participants

Patients were recruited from the Medical Oncology Department of Chongqing University Cancer Hospital in Chongqing Municipality, China, via a convenience sampling method. Patients were recruited between October 2022 and April 2023. Chongqing is the exclusive municipality, with over 30 million registered inhabitants in southwestern China. Chongqing University Cancer Hospital is the only oncology-specific Grade 3A institution that integrates medicine, teaching, scientific research, prevention and rehabilitation in Chongqing. The proportion of hospitalized patients outside the city reached 27.16%, radiating Sichuan, Guizhou, Hubei, Yunnan and 31 other provinces (municipalities and autonomous regions). The inclusion criteria were as follows: (1) diagnosed with lung cancer pathologically; (2) aged ≥ 18 years at diagnosis with adequate education and auditory or visual ability to finish the questionnaire; (3) aware of diagnosis and treatment; and (4) Karnofsky performance status (KPS) score ≥ 60 . The exclusion criteria were as follows: (1) unable to complete the survey due to poor physical or severe mental illness; and (2) major diseases such as brain, heart, liver or kidney dysfunctions that seriously affect QOL.

The sample size was calculated on the basis of the formula: $N \geq 50 + 8m$ (where m represents the number of independent variables) to test for multifactor regression analysis.³⁵ In the present study, 14 sociodemographic and clinical factors and 6 scale-associated dimensions (COST and the SPBS) were considered independent variables. Hence, at least 210 cases ($50 + 8 * 20$) were needed in the present study. Considering the invalid survey sample, we increased the sample by 20%, which made the minimum sample size in the survey 262.

Additionally, it is believed that the minimum sample size of 200 participants is sufficient for constructing the structural equation model, and it is better not to exceed 500 cases.³⁶ Accordingly, a minimum of 262 participants were needed for the current research.

Variables and Instruments

Sociodemographic and Clinical Questionnaire

Sociodemographic variables included age, sex, education level, monthly household income, working status, medical insurance, area of residency, and marital status, and clinical data included pathology type, tumour stage, cancer duration, number of immunotherapeutic sessions, immunotherapy drugs and methods of immunotherapy.

Functional Assessment of Cancer Therapy–Lung (FACT-L 4.0, Chinese Version)

QOL was assessed with the widely used FACT-L, which consists of the 27-item FACT-G (core instrument) and the 9-item Lung Cancer Subscale (LCS).³⁷ The FACT-L covers five dimensions: social/family well-being (SFWB, 7 items), physical well-being (PWB, 7 items), functional well-being (FWB, 7 items), emotional well-being (EWB, 6 items) and lung cancer symptoms (LCS, 9 items), each of which is scored on a 5-point Likert scale from 0 (not at all) to 4 (very much). The total score is acquired by summing the five domains, and higher scores indicate a higher level of satisfaction with QOL. The Chinese version of the FACT-L has shown satisfactory internal consistency reliability, construct validity and responsiveness.³⁸ The Cronbach's α values of the five subscales ranged from 0.72 to 0.94 in the present study.

Comprehensive Score for Financial Toxicity (COST)

Financial toxicity was measured by COST, which was originally structured by de Souza et al³⁹ and considers both direct and indirect costs, such as out-of-pocket expenses for cancer treatment and disability from work. The Chinese version of the COST was translated and adapted by Yu et al³⁴ and has shown excellent testing characteristics among Chinese cancer patients (Cronbach's $\alpha = 0.85$). It has 11 items, including one financial item, two resource items, and eight affect items. The instrument was scored on a five-point Likert scale (0 as not at all, 4 as very much), and the total score ranged from 0 to 44, with higher total scores suggesting a lower FT. The Cronbach's α of the COST was 0.904 in the current study.

Self-Perceived Burden Scale (SPBS)

The abbreviated version of the SPBS was adopted to test the level of self-perceived burden. It contains 10 items focused on three dimensions: emotional burden, physical burden, and economic burden.⁴⁰ Each item was given a Likert-type scale with 5 options (1=none of the time, 5=all of the time). The total score ranges from 10 to 50, with the following stages: none (10–19), mild (20–29), moderate (30–39), and severe (40–50). Wu and Jiang translated the scale into Chinese with a satisfactory internal consistency coefficient (Cronbach's $\alpha=0.91$).⁴¹ The Cronbach's α coefficients of the scale and the three subscales "emotion burden", "physical burden" and "economic burden" were 0.819, 0.762, 0.866 and 0.815, respectively, in the current sample.

Data Collection Procedure

In the present study, two postgraduate nursing students with prior experience in data collection and extensive clinical oncology nursing experience were recruited as research assistants, and they were required to identify potentially eligible participants through medical records. Then, they collected data in the wards of the study sites; explained the purpose, content and procedure to the eligible patients; and promised that the quality of treatment and nursing would not be affected regardless of whether the patients participated in the study. After informed consent was obtained from the eligible patients, the postgraduate nursing students used a face-to-face method to hand out the paper questionnaires with the same introduction, which emphasized the anonymity and confidentiality of personal information. If the participants could not fill out the form in person, the research assistants asked their opinions one by one and ticked the answers on behalf of the participants. Each participant took approximately 20 to 25 minutes to finish all of the items. The assistants were asked to check every item for completeness and accuracy on the spot. If any missing items were found, the enrolled patients were requested to supplement them in time. In addition, the research assistants obtained information about the clinical characteristics of the participants from their electronic medical records. The research protocol was approved by the ethics review institution of Chongqing University Cancer Hospital and complied with the Helsinki Declaration.

Statistical Analysis

Epi Data v3.1 was utilized to record and check the completeness and inconsistencies of the data, which were then exported to SPSS v25 for further analyses. First, we extracted 7 eigenvalues greater than 1 with Harman's single-factor test. The variance explained by the first factor was only 34.7%, which was less than 40% of the critical standard. Clearly, no substantial CMB problem exists in the present research. In addition, the variance inflation factor (VIF<5.0) and Cook's distance (<1.0) were computed to diagnose the possibility of multicollinearity and outliers, respectively. The results also indicated that there were no outliers or serious multicollinearity in the current study (VIFs ranging from 1.004–1.569; Cook's distances ranging from 0.000–0.031). Second, sociodemographic and clinical characteristics were depicted by descriptive statistics [number, percentage, means and standard deviation (SD)]. Then, we utilized a *t* test or one-way ANOVA to compare the group differences in QOL, FT and SPB, and then performed Pearson correlation analysis to assess the correlations among each factor of FT, SPB, and QOL.

The mediation analyses were conducted via AMOS 23.0 software, which is employed to establish a mediation model. The SEM is composed of exogenous and endogenous variables, the former being FT and SPB and the latter being QOL. Maximum likelihood estimation was adopted to calculate the coefficients for all pathways and explore the best fitting model in the current study. Finally, we perform bootstrapping tests (sampling is repeated 2000 times) to calculate the 95% confidence interval (CI) for the total indirect and direct effects of the model. It is believed that the indirect effect did exist in this way if the 95% CI did not include zero. The model was considered a good fit with the following fitness indices: $\chi^2/df < 3$; root mean square error of approximation, RMSEA < 0.08; normed fit index, NFI > 0.90; goodness-of-fit index, GFI > 0.90; Tucker–Lewis index, TLI > 0.90; comparative fit index, CFI > 0.90; incremental fit index, IFI > 0.90; parsimony goodness-of-fit index, PGFI > 0.50; and parsimony normed fit index, PNFI > 0.50.⁴² A *p* value of < 0.05 was considered to indicate statistical significance for all 2-tailed tests.

Results

General Characteristics of the Participants

A total of 363 patients with lung cancer who were receiving immunotherapy met the inclusion criteria, among whom 21 patients refused to participate. Thus, 342 eligible patients participated in the investigation. After 20 respondents were excluded because of illogical (9 cases), vague (5 cases) or random answers (6 cases), the responses of 322 participants were analysed, leading to an effective response rate of 94.2%. Table 1 presents the demographic characteristics of the subjects and demographic differences in the level of QOL. A total of 322 participants were included for data analysis, the mean age of whom was 62.36 years (SD = 7.16, range 34–74). In terms of sociodemographic information, most of the participants were male (79.8%), were currently married (71.1%), were employed (69.6%), and had a monthly family income of 2000–

Table 1 Demographic and Clinical Characteristics of the Sample

Items	N (%)	FACT-L	COST	SPBS
Gender				
Male	257 (79.8)	79.83±15.87	23.47±7.44	29.87±5.76
Female	65 (20.2)	81.18±15.80	23.72±7.94	34.91±7.14
<i>t</i>		-0.160	-0.235	4.179
<i>P</i>		0.873	0.814	0.001
Age (years)				
≤ 60	104 (32.3)	83.38±16.35	22.49±7.71	30.35±5.76
>60	218 (67.7)	78.25±15.34	24.01±7.41	29.36±6.19
<i>t</i>		2.744	-1.697	1.369
<i>P</i>		0.006	0.091	0.172
Education				
Primary school or below	155 (48.1)	80.99±16.32	25.08±8.10	28.97±5.53
Junior middle school	96 (29.8)	78.74±15.79	24.36±7.34	30.22±7.21
Senior middle school or same level	44 (13.7)	78.89±15.14	22.48±6.85	29.75±5.13
College or above	27 (8.4)	79.48±14.63	21.71±7.62	31.70±5.64
<i>F</i>		0.479	3.253	1.986
<i>P</i>		0.697	0.022	0.116
Monthly family income (Yuan)				
<2000	77 (23.9)	80.53±16.07	26.48±7.14	29.68±5.70
2000~5000	184 (57.1)	79.55±15.51	24.67±7.24	29.79±5.99
>5000	61 (19.0)	80.18±16.75	22.70±7.46	29.33±6.79
<i>F</i>		0.116	2.974	0.134
<i>P</i>		0.891	0.036	0.874
Working status				
Sick leave or retired or unemployed	98 (30.4)	78.98±16.23	23.87±7.30	32.24±6.55
Full-time	75 (23.3)	80.62±15.61	22.81±7.93	26.38±5.69
Part-time	149 (46.3)	80.80±15.45	23.76±7.50	29.53±6.18
<i>F</i>		0.473	0.634	3.165
<i>P</i>		0.624	0.531	0.027
Medical insurance				
No insurance	17 (5.3)	73.41±13.59	22.71±6.12	29.76±5.17
New cooperative rural medical scheme	125 (38.8)	79.56±16.23	23.54±7.66	30.12±6.22
Urban resident basic medical insurance	90 (28.0)	77.93±16.12	23.52±6.92	30.09±5.79
Urban employee basic medical insurance	75 (23.3)	82.23±15.26	24.08±7.70	28.55±6.09
Commercial insurance	15 (4.6)	81.40±17.45	21.47±8.50	29.07±7.14
<i>F</i>		1.798	0.429	0.960
<i>P</i>		0.129	0.788	0.430

(Continued)

Table 1 (Continued).

Items	N (%)	FACT-L	COST	SPBS
Residence				
Country	124 (38.5)	80.75±15.92	23.91±7.23	29.67±6.23
Small town	78 (24.2)	78.36±16.12	24.03±7.84	30.24±6.19
City	120 (37.3)	80.06±15.64	22.82±7.42	29.33±6.23
F		0.547	0.866	0.541
P		0.579	0.422	0.583
Marital status				
Married	229 (71.1)	80.04±15.45	23.49±7.43	29.58±5.62
Others (single/ widowed/divorced)	93 (28.9)	79.85±15.47	23.58±7.82	29.91±7.08
t		-0.100	-0.094	-0.446
P		0.920	0.925	0.656
Pathology type				
Small cell	44 (13.7)	78.91±15.41	24.34±6.56	29.55±5.72
Adenocarcinoma	109 (33.9)	78.63±16.09	22.77±7.37	29.86±6.05
Squamous cell carcinoma	162 (50.3)	81.22±15.58	23.86±7.85	29.54±6.17
Big cell	7 (2.1)	75.57±20.91	22.00±7.64	30.71±7.18
F		0.836	0.740	0.134
P		0.475	0.529	0.940
Tumor stage				
Stage III	101 (31.4)	83.12±15.86	23.61±7.73	29.42±5.96
Stage IV	221 (68.6)	79.43±15.85	23.48±7.46	29.80±6.12
t		2.381	0.153	-0.522
P		0.018	0.878	0.602
Cancer duration (month)				
<12	170 (52.8)	80.30±15.29	23.61±7.30	29.26±6.24
≥12	152 (47.2)	79.46±16.47	23.41±7.80	30.14±5.85
t		0.474	0.234	-1.291
P		0.636	0.815	0.198
Number of immunotherapeutic sessions				
2~ 4 times	176 (54.7)	81.35±16.19	23.36±7.69	29.47±6.15
5th or above	146 (45.3)	78.16±15.27	23.71±7.36	29.82±5.98
t		1.801	-0.420	-0.667
P		0.073	0.675	0.506
Immunotherapy drugs				
Tislelizumab	123 (38.2)	80.47±16.69	23.89±7.28	29.33±6.04
Camrelizumab	66 (20.5)	77.18±15.67	24.06±7.58	30.42±6.10
Sintilimab	72 (22.4)	78.51±14.26	22.32±6.01	30.71±5.30
Others	61 (18.9)	83.38±15.64	21.41±6.38	28.34±6.72
F		1.878	1.377	2.163
P		0.133	0.250	0.092
Methods of immunotherapy				
Immunotherapy	47 (14.6)	85.47±16.56	24.77±7.31	28.51±6.19
Immunotherapy + chemotherapy	221 (68.6)	79.26±15.22	22.88±6.61	29.83±6.11
Immunotherapy + chemotherapy+ targeted therapy	12 (3.7)	73.00±12.87	23.00±5.54	32.17±3.83
Immunotherapy + targeted therapy	42 (13.1)	79.02±17.76	25.64±7.49	29.45±6.11
F		2.909	2.117	1.324
P		0.035	0.098	0.266

Note: Yuan (¥; ¥ 1 equivalent to 0.15 United States dollars); N: patient number.

Abbreviations: FACT-L, Functional Assessment of Cancer Therapy–Lung; COST, Comprehensive Score for Financial Toxicity; SPBS, Self-Perceived Burden Scale.

5000 (57.1%). With respect to education, 77.9% of the participants had an educational level of junior middle school or below. In terms of the clinical characteristics of the samples, squamous cell carcinoma predominated (50.3%), as did stage IV (68.6%) and immunotherapy + chemotherapy (68.6%). As shown in Table 1, statistically significant differences in age, tumour stage, methods of immunotherapy and QOL were found among the participants.

Correlation Analysis Between Variables

The descriptive statistics and correlation coefficient matrices for each variable are shown in Table 2. The mean FACT-L score was 79.90 ± 15.84 . The SPB of lung cancer patients receiving immunotherapy was significantly correlated with QOL and FT ($r = -0.438, P < 0.01$; $r = -0.595, P < 0.01$). The correlations between QOL and FT were also significant ($r = 0.466, P < 0.01$).

Relationships Between Financial Toxicity, Self-Perceived Burden, and QOL Evaluated by SEM

Figure 1 illustrates the relationships among the FT, SPB, and QOL of the participants. The model fit the empirical data very well ($\chi^2/df = 1.685$, RMSEA = 0.046, NFI = 0.957, GFI = 0.965, CFI = 0.982, TLI = 0.975, IFI = 0.982, PGFI = 0.585, PNFI = 0.696).

Figure 1 contains two figures: the upper figure shows the correlation between FT and QOL, whereas the lower figure illustrates the mediating impact of SPB on the connection between FT and QOL. FT had a positive impact on QOL (standardized effect = 0.55, $P < 0.001$); that is, higher total scores on the COST (a lower level of FT) were correlated with a greater level of QOL. In addition, as illustrated in Figure 1 (lower figure), FT had a positive effect on QOL (standardized path = 0.37, $P < 0.001$), SPB had a negative effect on QOL (standardized path = $-0.27, P < 0.01$), and FT also had a negative effect on SPB (standardized path = $-0.70, P < 0.001$).

Mediation Analysis

We applied bias-corrected bootstrap tests with 95% CI to justify the significance of the observed direct and indirect pathways. The path coefficients suggest that the total effect of FT on QOL was 0.55 (upper figure in Figure 1). After adding SPB (lower figure in Figure 1), the direct effect of FT on QOL was 0.37. The 95% CI did not include 0 (95% CI: 0.089 to 0.319, $P < 0.001$), indicating that SPB partially mediated the relationship between FT and QOL. The standardized total effect, direct effect, and the results of the mediating effect are presented in Table 3. Specifically, the indirect pathway of FT on QOL through SPB was 0.19 [$0.19 = (-0.70) \times (-0.27)$], accounting for 33.9% of the total effect [$33.9\% = 0.19/(0.19 + 0.37)$].

Table 2 Cronbach's α and Correlation Coefficient of All Variables

Variables	Range	M \pm SD	Cronbach's α	1	2	3
1. FACT-L	42–111	79.90 \pm 15.84	0.894	1	-	-
PWB	6–28	15.82 \pm 4.07	-	-	-0.330**	0.307**
SFWB	2–25	15.83 \pm 3.40	-	-	-0.261**	0.250**
EWB	5–24	13.35 \pm 3.48	-	-	-0.335**	0.374**
FEB	2–26	14.95 \pm 4.13	-	-	-0.393**	0.470**
LCS	10–32	19.95 \pm 4.76	-	-	-0.369**	0.396**
2. SPBS	13–45	29.68 \pm 6.07	0.819	-0.438**	1	
3. COST	7–40	23.47 \pm 6.98	0.904	0.466**	-0.595**	1

Note: ** $P < 0.01$.

Abbreviations: FACT-L, Functional Assessment of Cancer Therapy–Lung; SPBS, Self-Perceived Burden Scale; COST, COmprehensive Score for Financial Toxicity; SD, standard deviation; PWB, physical well-being; SFWB, social/family well-being; FFWB, functional well-being; EWB, emotional well-being; LCS, the lung cancer symptom.

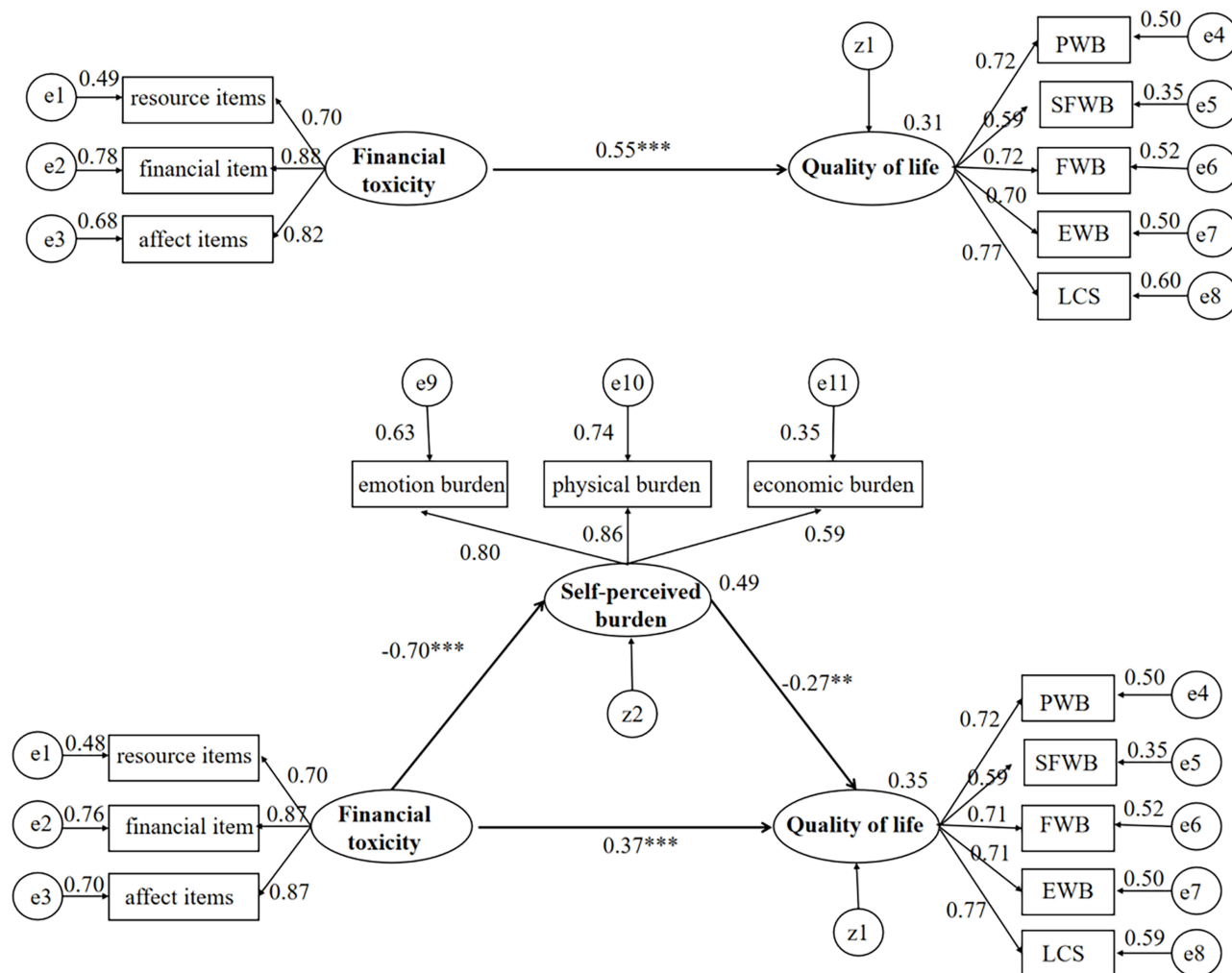


Figure 1 Model of the Mediating Role of SPB between FT and QOL.

Note: ** $p < 0.01$; *** $p < 0.001$.

Abbreviations: PWB, physical well-being; SFWB, social/family well-being; FWB, functional well-being; EWB, emotional well-being; LCS, the lung cancer symptom.

Discussion

To the best of our knowledge, this is the first study in mainland China to explore the interrelationships among financial toxicity, self-perceived burden and QOL in lung cancer patients receiving immunotherapy. The mean FACT-L score for assessing QOL was 79.90 ± 15.84 . In studies conducted in France and Germany, the mean FACT-L scores of advanced lung cancer patients receiving drug treatment were 73.1 ± 21.5 and 70.4 ± 17.2 , respectively.⁴³ Importantly, differences in demographics such as age, sex, socioeconomic status and comorbidities between study samples can affect QOL scores, so it is difficult and impracticable to compare QOL scores across countries. But one conclusion we can draw is that there is still plenty of room for improvement in the QOL levels of lung cancer patients during immunotherapy treatment. It is imperative to address and resolve the QOL issue for lung cancer patients receiving immunotherapy. In addition, this study revealed that the “emotional well-being” subscale ranked the lowest among the five functional dimensions. This can be explained by the following reasons. Immunotherapy usually involves at least 4 or 6 cycles, and patients are required to return to the hospital for each cycle. Long-term therapies and symptom burdens can cause depression, anxiety and loss of self-esteem.^{44,45}

Our results revealed that older patients have worse QOL scores. Previous studies have also demonstrated that advanced age is an independent risk factor affecting QOL in maintenance haemodialysis patients⁴⁶ and deep vein thrombosis patients.⁴⁷ This effect may be related to the decline in bodily functions, the irreversible progression of accompanying symptoms and a decline in daily activity in elderly patients. Moreover, the present data also indicated that

Table 3 Bias-Corrected Bootstrap Tests of Mediating Pathways

Paths	Standardized β	95% CI		P value	Percent (%)
		LLCL	ULCL		
Direct effect					66.1
FT-QOL	0.37	0.202	0.516	< 0.001	
SPB-QOL	-0.27	-0.443	-0.132	0.005	
FT-SPB	-0.70	-0.765	-0.623	< 0.001	
Indirect effect					33.9
FT-SPB-QOL	0.19	0.089	0.319	< 0.001	
Total effect	0.55	0.465	0.646	< 0.001	100

Abbreviations: FT, financial toxicity; SPB, Self-perceived burden; QOL, quality of life; CI, confidence interval; LLCL, lower limits confidence interval; ULCL, upper limits confidence interval.

advanced tumour stage was associated with a lower QOL. In line with this study, another study reported that patients with advanced-stage cancer had unfavourable QOL scores.⁴⁸ According to a study in Ethiopia,⁴⁹ an increased tumour stage was significantly associated with increased pain, appetite loss, and symptoms as well as decreased physical function in cancer patients. Moreover, immunotherapy combined with chemotherapy or targeted therapy is related to poor QOL, which is consistent with previous findings in China that patients receiving immune checkpoint inhibitors in combination with chemotherapy have lower QOL than patients receiving immune checkpoint inhibitors alone.¹² Studies have demonstrated that the combination of immunotherapy with chemotherapy or targeted therapies can increase treatment response rates and confer survival advantages to patients. However, the incidence of irAEs in this combined therapy context is 1.92 times greater than that in immunotherapy, and patients may experience more pronounced physical discomfort, which can negatively impact their daily living, physical capabilities, and overall functioning.⁵⁰ The present study thus provides important insights into the QOL of lung cancer patients treated with immunotherapy, as well as their ability to cope with and plan by oncology nurses. Health care providers are requested to place high value on the screening of QOL and assessment of confronting needs among those populations, which is a fundamental step towards practical and pointed countermeasures. Age, tumour stage, and immunotherapy method are important sociodemographic and clinical-related factors associated with differences in QOL among lung cancer patients. Therefore, these specific groups of patients need additional attention to their level of QOL. Clinical practitioners are advised to understand the QOL characteristics of lung cancer patients of different ages, different tumour stages and different immunotherapy methods and to develop tailored interventions.

Direct Relationships

Additionally, we found that patients' FT could predict their QOL directly, indicating that the alleviation of FT would be conducive to higher levels of QOL. This conclusion supports earlier findings in samples of testicular cancer survivors and gynaecologic cancer patients.^{15,51} Such an association could be explained in the following two ways. First, fighting cancer is a costly battle. As mentioned, the rapid emergence of effective immunotherapeutic agents has led to remarkable promise for the treatment of lung cancer patients but has increased both drug costs and costly toxicity-associated hospital stays and monitoring. Remote inhabitants may face greater financial burdens as a result of increased commuting costs and the absence of illness. As a result, patients with higher FT may reduce their spending on leisure activities, clothing or cosmetics to save expenses on cancer care and other necessities⁵² and even take less medication than advised, use over-the-counter medications and delay or forgo follow-up.^{53,54} Therefore, financial hardship has detrimental influences on QOL through reducing daily spending, reducing treatment adherence and weakening physical functioning. Second, a systematic review demonstrated relatively clear associations between FT and stress, spiritual suffering, fear of recurrence, and overall psychological symptoms.⁵⁵ Numerous studies have also reported positive associations between

increases in FT and increased levels of depression and anxiety.^{56,57} The fact that this, in turn, affects physical symptoms such as sleep disturbance and fatigue and ultimately results in inferior QOL is not controversial. Notably, another potentially interesting explanation is that anxiety or anxiety symptoms caused by FT may also contribute to elevated smoking rates in patients. Large-scale epidemiological data suggest that individuals with an anxiety disorder or elevated anxiety-related symptoms are significantly more likely to smoke cigarettes and significantly less likely to quit successfully than those without these symptoms.⁵⁸ What's more, lung cancer patients who smoke cigarettes reported more dry coughing, more shortness of breath, greater fatigue and higher mortality,⁵⁹ which are associated with greater symptom burden and reduced QOL. Saxena et al⁶⁰ showed that many patients with lung cancer who were receiving immunotherapy were experiencing financial hardship, 30% of whom reported a reduction in employment, 63% reported concerns over the financial stability of their family, and 42% reported reduced spending on vacations and basic items. While conducting financial toxicity assessments is not an indispensable task for oncology medical staff, we should be aware of the concerns of cancer patients and their families about the cost of treatment. It is also recommended that medical staff communicate with patients about finances by using prompts such as "Tell me what you know about the cost of immunotherapy", which can provide an opportunity for us to discuss the resources available to patients to ease their financial burden. A systematic scoping review has mapped previously prevalent interventions for alleviating cancer patients' FT, namely, financial navigation, financial counselling, and insurance education,⁶¹ which provides a basis for targeted measures in clinical practice.

Moreover, our findings confirmed the point that SPB was negatively associated with QOL; that is, the lower the SPB was, the better the QOL. The negative relationship between SPB and QOL in the present study was in line with earlier studies conducted among patients with chronic myeloid leukaemia in China.³² This association could be attributed to equity theory.⁶² Advanced cancer patients usually depend on families or caregivers for material and spiritual support to fight against the disease in their daily life. However, it would never be easy for them to maintain the balance between those given and those received due to life-threatening disease.⁶² The inability to reciprocate negatively impacts their mental health by means of SPB, worry, frustration, or guilt. To make matters worse, patients are more inclined to reduce the expectations and demands on caregivers or alter the inputs of others relative to their own, such as physical care, symptom management, and financial support.^{31,62,63} Accordingly, individual psychological health, the prognosis of the disease, and life satisfaction are further negatively affected. To mitigate the adverse impacts of SPB on patients, researchers have formulated targeted interventions to alleviate patients' emotional burden. Hence, health care providers should be aware of, assess and subsequently address SPB among lung cancer patients receiving immunotherapy. According to the SPB scale, the focus of interventions can be mainly divided into physical, emotional, and financial strategies. First, improving the physical burdens of patients is important, and related interventions have focused mainly on encouraging exercise,⁶⁴ mindfulness therapy (eg, mindful breathing, mindful meditation, walking meditation, and eight-session exercise),⁶⁵ and relaxation training.⁶⁶ Second, in terms of interventions in the emotional burden dimension, cognitive behavioural therapy and structured psychological interventions (including psychological support, health education for patients and their families, anticancer declaration learning) have the potential to reduce SPB.^{67,68} Finally, regarding interventions for economic burden, multidisciplinary psychosocial support, application-based guidelines on financial assistance resources and intensive symptom assessments along with supportive care have been shown to address cancer patients' financial burden effectively.^{61,69}

The Mediating Effect of Self-Perceived Burden

Another noteworthy and interesting finding of the present research is that SPB plays a mediating role in the relationship between FT and QOL in lung cancer patients receiving immunotherapy. In other words, FT may exacerbate patients' psychological burden, in turn, their poor QOL. Lung cancer patients receiving immunotherapy may be particularly susceptible to financial distress due to the increased costs of recently developed therapies and a reduction in the ability to work over time, which makes it difficult for patients to cover parenting care, domestic help, medical equipment and nutritional supplement expenses. However, influenced by the core values of collectivism and Confucianism, Chinese people consider it an obligation to take care of family members and even make self-sacrifice for the sake of the family.^{70,71} Consequently, the fear of the inability to play the role of a financial provider would cause care recipients to

develop thoughts of uselessness and feel like a burden to the entire family. These aspects further exacerbate their QOL. In this sense, as a mediating variable, SPB plays a crucial role in the relationship between FT and QOL in lung cancer patients treated with immunotherapy.

Nevertheless, several limitations should be acknowledged. The primary limitation is that we only collected data from a single hospital in Chongqing Municipality, South China, which may cause selection bias issues and reduce its ability to generalize the results to other areas due to economic and cultural differences. Further studies need to be conducted in different regions to confirm these findings. Second, given the well-established link between physical health and QOL, it is plausible that the observed QOL levels in our study may constitute a conservative estimate, as individuals with more severe physical health issues, which may negatively impact their QOL, were not included in our analysis. To address this limitation, future research should strive for more inclusive sampling strategies that minimize or clearly justify exclusion criteria. Third, although all data collection is based on verified questionnaires, the exclusive use of self-assessment QOL measures could have evoked a response bias due to social desirability, which may affect our research results to some extent. Therefore, other measurement methods need to be used in the future to further explore the correlation between QOL and financial toxicity. Finally, because a cross-sectional design was adopted in this study, the causal relationships between FT, SPB and QOL could not be considered or determined. More longitudinal studies are needed to address possible causality and fluctuations to make more convincing conclusions.

Conclusion

In summary, the results of the present study indicated that the QOL of lung cancer patients receiving immunotherapy was generally relatively low in Chongqing Municipality, China. More importantly, our findings suggest that financial toxicity has both a direct effect on QOL and an indirect effect via self-perceived burden, which is the first research project to probe the relationship between financial toxicity and quality of life in Chinese lung cancer patients. Current research strongly suggests that controlling symptoms and optimizing the QOL of patients with lung cancer continue to be vitally important objectives of immunotherapy. Considering the mediating effect of self-perceived burden, health care providers are needed to routinely screen, evaluate and manage emotional distress related to psychological burden in the future. Moreover, reducing patients' financial burden may be an effective intervention strategy to enhance QOL. The incorporation of assessments and interventions aimed at reducing financial toxicity into routine clinical care is necessary to control or address financial toxicity among lung cancer patients receiving immunotherapy.

Abbreviations

QOL, quality of life; FT, financial toxicity; SPB, self-perceived burden; irAEs, immune-related adverse events; SEM, structural equation modelling; CI, confidence interval; SD, standard deviation; VIF, variance inflation factor; CMB, common method bias; RMSEA, root mean square error of approximation; NFI, normed fit index; GFI, goodness-of-fit index; TLI, Tucker–Lewis index; CFI, comparative fit index; IFI, incremental fit index; PGFI, Parsimonious Goodness-of-Fit Index; PNFI, Parsimonious Normed Fit Index.

Data Sharing Statement

The dataset generated and analysed during the current study is not publicly available due to promises of participant anonymity and confidentiality but is available from the corresponding author upon reasonable request.

Ethics Statement

This study was performed in accordance with the principles of the Declaration of Helsinki. Approval was granted by the ethics review institution of Chongqing University Cancer Hospital. Written informed consent for the investigation was obtained from each participant.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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