Assessment of Financial Toxicity Among Advanced Lung Cancer Patients in Western China

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Abstract

Background: Lung cancer is the primary reason of cancer-caused disability adjusted life years. Medical cost burden impacts patient's well-being through decreasing income, cutting daily expenses, leisure activities and exhausting savings. De Souza and colleagues developed and validated the COmprehensive Score for Financial Toxicity (COST). Our study aims to quantify the financial burdens of cancer therapy, to explore the relationship between financial toxicity and HRQoL in advanced lung cancer population.

Methods: Patients aged ≥ 18 years with confirmed stage III to IV lung cancer were eligible. The COST questionnaire verified by de Souza et al. was used to identify financial toxicity. Multivariable linear regression analysis with log transformation univariate analysis and Pearson correlations were used to performed the analysis.

Results: Most of the patients had an income of $< ¥50,000$ (\$7,775) annually (90.8%, $n = 138/152$). The insurance condition of the cohort was that the majority of the cohort had social insurance (64.5%), 20.4% of them had commercial insurance, 22.0% of them had both. Patients who were younger age (50 ~ 59, $P < 0.001$), employed but on sick leave, and lower income reported increased levels of financial toxicity ($P < 0.05$). The risk factors for high financial toxicity: (i) younger age (50 ~ 59), (ii) <1 month of savings, and (iii) being employed but on sick leave. Increased financial toxicity is moderately correlated with a decrease in QoL.

Conclusion: Increased financial toxicity(lower COST) is related to poorer psychological status and certain demographics. Financial toxicity is moderately correlated with a HRQoL, and it may have a demonstrable correlation with HRQoL measures.

Introduction

In most of the nations, lung cancer is the primary reason of cancer-caused disability adjusted life years (DALYs) [1, 2]. Patients diagnosed with lung cancer burdened with significant medical cost and service utilization[3, 4]. The financial burden on lung cancer patients contains direct costs and indirect costs, consisted by transportation and loss of income(out of work or on sick leave) [3, 5]. Medical cost burden impacts patient's well-being through decreasing income, cutting daily expenses, leisure activities and exhausting savings. Financial burden has been revealed as an independent risk factor for mortality as it could lead to bankruptcy of cancer patients[6].

In order to bring financial stress and its negative consequences to a more conspicuous position, the term financial toxicity was raised. It refers to an adverse effect of cancer treatment, similar to nausea and alopecia[7]. Then, De Souza and colleagues established and verified the COmprehensive Score for Financial Toxicity (COST)[8, 9]. The COST questionnaire contains 11 items and scores from 0 to 44. They validated it based on a North American population. In De Souza's study, lower COST scores indicated exceeding degree of financial toxicity. Then, studies on financial toxicity revealed a worse Health-Related Quality of Life (HRQoL) and increased psychosocial distress associated with increased financial toxicity. Meanwhile, it also impacts cancer treatment. Patients turn to take less medication than prescribed, choose over-the-counter drugs and take medicine prescribed by others to lower costs[10].

China covers approximately 20% of the world's population. As a developing country, China is confronted with the most challengeable medical funding issues. In fact, China has woven the world's largest network of basic medical insurance accessible for all and formed a healthcare service system encompassing both urban and rural areas. China's social medical insurance contains 3 types, that are basic medical insurance for urban workers, basic medical insurance for urban residents and the new rural cooperative medical system. By the end of 2016, China's social medical insurance has reached over 1.3 billion of its population nationwide, accounting for more than 95% of the total population[11]. Even so, upgrading policy level of medical insurance is still needed.

Policy level changes of the Chinese medical care insurance system should meet the maximum of the individual benefits. However, before it changes, an access to a better comprehension of the existing of financial toxicity as well as its negative effect on patient's quality of life (QoL) needed to be opened, which could improve the interventions aimed at reducing financial

distress, thus improve quality care and policy optimization. Through validated financial toxicity instrument (COST questionnaire), our study aims to assess the economic burdens of cancer care in advanced lung cancer population. We also explored the relationship between financial toxicity and HRQoL. With inferring the risk factors of financial toxicity in lung cancer patients, this study would help to improve resource allocation for early intervention[12].

Cohort And Methods

Cohort

Patients aged ≥ 18 years with stage III to IV(AJCC, 8th edition) lung cancer were eligible (non-small and small cell lung cancer), who requires ongoing multimodality care over time. Patients currently received therapy for another malignancy were excluded. Stage I or II lung cancer patients received treatment involving surgical or interventional therapies were also ineligible for this study. Ethics approval was acquired from the Human Research Ethics Committee of Xijing Hospital (KY20202077-C-1).

Variables and outcomes

Information of patients' performance, tumor stage, and histological diagnose were abstracted from electronic medical records from Xijing database. We collected patients' marital status, employment, family income and household savings data from them directly. Patient's baseline financial status were identified through past published questionnaires related to FT (**Supplementary Table 1**) and translated into Mandarin (**Supplementary Table 2**) [13]. FT was evaluated by the COST instrument[9], translated into Mandarin (**Supplementary Table 3**). Financial toxicity was considered high by greater than the cohort's median COST score[14]. Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire was used to assess Health-related quality of life (HRQoL)[15, 16]. The FACT-L instrument contains two parts, which is a common module for all cancer patients (a 27 item cancer therapy function evaluation general scale, FACT-G) and a module specifically for lung cancer patients (a 9-item lung cancer additional concern part), ranged from 0 to 136. It is ascertained that higher FACT score infers a better QoL.

Statistical analysis

We summarized the baseline and financial status by descriptive statistics. To compare the average COST scores in patients, we used multivariable linear regression analysis with log transformation. We identified significant covariates in multivariable regression analysis ($P \leq 0.10$ was considered clinical significance). The Pearson correlation was used to assess correlations between COST and FACT scores. If the coefficient was 0.20 to 0.39, the correlation was regarded as mild, 0.4-0.59 moderate, 0.60-0.79 strong and ≥ 0.80 very strong. $P < 0.05$ (two-tailed) was considered statistically significant. All statistical analyses were performed using SPSS 22.0.

Results

We accessed the cohort from September 2019 to January 2021. **Figure 1** showed the recruitment process. The baseline of the cohort included in analysis are summarized in **Table 1**. We recruited 209 potential participants, in which 152 were eligible. The median age was 62.1 years (range 32 ~ 84 years). 65.1% ($n = 99$) had metastasis and 44.9% ($n = 53$) had localized disease. The majority of patients had non-small cell carcinoma histology (63.2%, $n = 96/152$) followed by small cell carcinoma histology (27.0%, $n = 41/152$) and other lung cancer histology (9.8%, $n = 15/152$). The median value of the COST scores was 25.5 (range 4 ~ 42, mean $\pm$ SD 9.7 ± 0.8).

Financial State

Of the financial perspectives, most of the patients (90.8%, $n = 138/152$) had an household income $< ¥50,000$ (\$7,775) per year. The insurance condition of the cohort was that the majority of the cohort had social insurance (64.5%, $n = 98/152$), 20.4% of them had commercial insurance ($n = 31/152$), 22.0% of them had both ($n = 22/152$). Only one patients (0.1%) had no insurance. Housing mortgage holds the overwhelming majority of Chinese families' loan in modern China, in all probability determining the disposable income of a family. Thus, we brought residence condition to reflect patient's financial state as its close relation to individual financial pressure. Due to elderly residences, most of the patients were the owner of the house without mortgage

(62.6%, $n = 95/152$). While the occupiers with mortgage were 29.6% ($n = 45/152$). 14.5% ($n = 22/152$) patients had retirement salary to meet medical cost. Most of our cohort was retired (64.1%, $n = 84/152$). Of others, 59.6% ($n = 28/152$) changed in income when the cancer treatment started.

Variables associated with FT

Univariate analysis upon variables related to FT was described in **Table 2**. Patients at younger age (50 ~ 59, $P < 0.001$), employed but on sick leave, and lower income had increased levels of FT ($P < 0.05$). In multivariable modeling, we adjusted for potentially confounding variables and discovered patients who had < 1 months' worth of household savings turned to have higher financial toxicity ($P < 0.05$).

When compared with this value, patients who had $>1 \sim 6$ months', $7 \sim 12$ months' and >1 years' worth of savings scored 3.9 points (95% CI: 2.1 to 4.9, $P = 0.06$), 10.4 points (95% CI: 5.0 to 16.1, $P < 0.05$), and 22.6 points (95% CI: 11.6 to 26.3, $P < 0.001$) higher COST scores, respectively. As to employment condition, patients on sick leave had increased financial toxicity compared with employed patients (8.3, 95% CI: 6.3 to 11.6, $P = 0.04$) or retired (7.2, 95% CI: 4.2 to 14.6, $P = 0.02$).

In **Table 2**, we identified risk factors for higher FT scores: (i) younger age (50 ~ 59), (ii) being employed but on sick leave, and (iii) with <1 month of savings. 54.9% ($n = 52$) of our cohort had no risk factors. 32.8% ($n = 61$) had one risk factor. 8.4% ($n = 24$) had two risk factors. 3.8% ($n = 15$) had all three risk factors.

Association between FT and QoL

r value of the COST score and FACT-L was 0.44 ($P < 0.0001$), which inferred a moderate correlation of the two variables (**Figure 2**), indicating that increased FT (lower COST) is moderately associated with decreased QoL (lower FACT-L).

Discussion

Most of the cancer patients received their treatment in China's public hospitals, while private ones contributed less in treating malignancies. This study recruited patients from a public hospital in West China, among whom had all forms of health insurances (social insurances, commercial insurance, and both), similar to existing studies[9, 17]. Differed from health care systems in Australia and some European countries, China has no universal health care insurance coverage. Yet with a coverage of 95% of its population, health care system in China may not over rely on commercial insurance, unlike the United States, where approximately 33% of its population remain uninsured [18, 19].

Due to China's new policy for imported drugs and the launch of domestically-produced ones, the cost of the drug reduced. Yet, out of pocket (OOP) costs including transportation cost and accommodation for cancer therapies differs among cities. Consequently, calculating the absolute values of the patient's medical expense directly may not be sufficient to measure the financial burden on the patient's family. With the assistance of COST developed by De Souza et al., we evaluated FT among a cohort of Chinese lung cancer patients. Our study found the patient demographic factors associated with increased FT, containing younger age, employed but on sick leave and less savings. These results may help in identifying the potential patients who might have higher risk in suffer worse health effects. Previous study revealed that patients with advanced cancer demonstrated a more severe financial toxicity than physical, family, and emotional distress[20-22]. Moreover, our result supported the fact that FACT COST had a moderate correlation with HRQoL but did not accurately measure it, which may draw a similar conclusion that FT may have a negative impact on patient well-being[23]. Our result inferred the most at-risk group for financial toxicity lay in 50~59 aged population, which might be a consequence of their overall economic condition in modern China. To be specific, Chinese residents aged 50~59 may suffer the highest financial pressure in the society, due to their moral duty to support both their parents and children(to pay expenses for them), which is a common behavior among Chinese. If they were diagnosed with lung cancer, then burdened with associated financial burden, the consequence might be dramatic.

As former mentioned, health care system in China mainly relies on social insurance, which reflects the consistent effort of the Chinese government. However, including commercial health insurance, the health care system in China covers hospital related medical cost (drug and inpatient cost), but not transportation cost and accommodation for specialist appointments. Meanwhile,

residents in China must pay for medical expenses in advance, then wait for reimbursement, according to the health care policy, which may make house hold savings vital for Chinese families. On the other hand, remote residents may suffer more financial burden due to increased transportation fees and extended time of sick leave. Regretfully, our study could not validate the increased FT in patients living in remote areas.

In western countries, patients with cancer are able to get access to cancer care team, including oncologist, nurse practitioner and case manager/ financial counselor. When they have any problems in receiving cancer therapies, they can contact with one or some in the team to get professional assistance. While in China, such team merely contains oncologist and nurse practitioner, which may cause bewilderment in facing financial issues associated with medical care, due to the oncologist and nurse practitioner are unqualified in answering patients' financial questions. Oncologists in China feel the costs of medical care important, ye they are poorly prepared to discuss costs with patients in the clinic. The customer representatives of large pharmaceutical companies such as Roche, Pfizer, and Merck may play this role, yet inevitably mixed with company's interests when answering financial questions. Hence, there is an urgent need for the emergence of roles such as "financial counselor/case manager" in cancer care team of China, who should be multi-professional such as medicine and economics, qualified to offer professional help in giving or assessing financial issues during cancer therapies.

Medical data in China is hospital-independent. Unfortunately, there lies no integrated platform for researches, which made a nationwide research on financial burden upon cancer patients almost impossible. A limitation to our study was that it remained single centered. A multi-centered cohort may draw a closer conclusion to the real world. In addition, as former mentioned, our study did not contain measuring FT in patients living in remote areas, which may produce worse cancer outcomes.

This study was intended to rouse recognition of financial burden on patients with lung cancer among both policy makers and oncologists and to better identify those at the highest risks for cancer-related financial toxicity. It is undoubted that the whole society should make joint efforts in releasing such pressure. Future study should cover more areas of China, as well as more types of cancer, in order to meet the absence of nationwide platform containing medical data and to promote policy optimization.

Conclusion

The financial impact of cancer and cancer treatment has been more apparent, so does the tool of assessing it. Verified researches ensure to provide reliable conclusions in the such fields. This study revealed that FACT COST is both a valid and reliable tool in China lung cancer patients. Increased financial toxicity(lower COST) is related to poorer psychological status and certain demographics. Financial toxicity is moderately correlated with a HRQoL, and it may have a demonstrable correlation with HRQoL measures.

Declarations

DISCLOSURE STATMENT

All the authors have no conflict of interest.

AUTHOR CONTRIBUTIONS:

Jian Zhang contributed to the conception of the study and perform constructive discussions;

Tianqi Xu and Ying Zhou performed the data collection and analysis;

Tianqi Xu and Liangliang Xing wrote the manuscript;

Wenhui Yang, Hangtian Xi and Yan Zhang contributed to data analysis and manuscript preparation.

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Tables

TABLE 1. Patient demographics	
Characteristics	Values (n[%])
Age(y)	
Median	62.1
Range	32 ~ 84
Sex	
Male	81 (53.3)
Female	71 (46.7)
Marital state	
Married	144 (94.7)
Unmarried	8 (5.3)
Current smoker	
Yes	59 (38.8)
No	93 (61.2)
Insurance type	
Social insurance	98 (64.5)
Commercial insurance	31 (20.4)
Social & Commercial insurance	22 (14.5)
No insurance	1 (0.1)
Primary place of residence	
Owner/occupier – no mortgage	95 (62.6)
Owner/occupier with mortgage	45 (29.6)
Renting (>3 years)	8 (5.2)
Living with family/friends (>10 years)	2 (1.3)
Other	2 (1.3)
Current employment status	
Working full time	15 (9.9)
Working part time	8 (5.2)
Retired	101 (66.4)
Unemployed	27 (17.8)
Other (student, homemaker)	1 (0.7)
Change in employment status	
Yes	132 (86.8)
No	20 (13.2)
Household income per year (CNY)	
< 20,000	36 (23.7)

20,000 ~ 49,999	102 (67.1)
50,000 ~ 99,999	9 (5.9)
> 100,000	5 (3.3)
Current household savings (CNY)	
< 1 month (reference)	63 (41.4)
1 ~ 6 months	41 (27.0)
7 ~ 12 months	16 (10.5)
> year	32 (21.1)
Stage	
III	66 (43.4)
IV	61 (40.1)
Histology	
Small-cell carcinoma	41 (27.0)
Non-small cell carcinoma	96 (63.2)
Other	15 (9.8)
CNY, China Yuan	

TABLE 2. Patient characteristics and COST outcomes

Characteristics	Univariate analysis		Multivariable analysis	
	Coefficient(95% CI)	P value	Coefficient(95% CI)	P value
Age(y)				
<50 (reference)				
50~59	10.1 (5.7 to 19.7)	< 0.001	-5.6 (-9.8 to 8.6)	0.82
60~69	5.6 (4.2 to 8.9)	0.02	0.2 (-7.0 to 7.3)	0.56
70~79	1.3 (-2.2 to 5.1)	0.09	2.7 (-5.8 to 7.9)	0.33
>80	2.8 (-4.5 to 6.2)	0.16	1.2 (-8.9 to 10.3)	0.29
Sex				
Female (reference)				
Male	0.54 (-2.6 to 3.1)	0.49	2.7 (-0.9 to 4.3)	0.22
Marital state				
Married (reference)				
Unmarried	-5.7 (-6.4 to 2.8)	0.06	-3.3 (-4.1 to 2.2)	0.34
ECOG performance status				
0 (reference)				
1	1.0 (-5.3 to 6.6)	0.66	0.23 (-3.2 to 4.1)	0.82
≥ 2	-1.7 (-5.5 to 4.2)	0.46	-0.4 (-4.5 to 4.7)	0.76
Insurance type				
Social Insurance (reference)				
Commercial insurance	2.1 (-3.3 to 5.9)	0.52	-2.3 (-7.6 to 5.7)	0.43
Social & Commercial insurance	-8.6 (-13.8 to 4.5)	0.003	-4.6 (-6.3 to 0.2)	0.02
Current employment status				
Working full time/part time (reference)				
Employed, on sick leave	3.5 (-3.2 to 6.9)	0.05	5.6 (-6.8 to 9.9)	0.59
Retired	-6.2 (0.7 to 18.4)	0.04	1.6 (-6.8 to 9.9)	0.63
Unemployed	8.1 (-0.8 to 9.3)	0.08	1.2 (-7.8 to 10.2)	0.86
Household income per year (CNY)				
< 20,000 (reference)				
20,000 ~ 49,999	2.8 (-6.2 to 8.9)	0.33	-2.8 (-4.6 to 7.0)	0.78
50,000 ~ 99,999	6.2 (-1.3 to 7.9)	0.55	-1.3 (-2.2 to 3.4)	0.59
> 100,000	9.7 (3.8 to 13.4)	0.01	3.4 (-3.2 to 6.1)	0.42
Household savings				
< 1 month (reference)				
1 ~ 6 months	1.9 (-1.0 to 2.8)	0.18	6.2 (0.3 to 8.6)	0.06

7 ~ 12 months	8.5 (2.8 to 14.1)	<0.001	4.5 (-1.2 to 6.2)	0.34
> 1 year	11.3 (13 to 22.1)	<0.001	8.1 (6.4 to 15.4)	<0.001
ECOG, eastern cooperative oncology group; CNY, China Yuan				

Figures

Figure 1

Patient Recruitment Process. COST, the Comprehensive Score for Financial Toxicity. FACT-L, the Functional Assessment of Cancer Therapy-Lung questionnaire.

Figure 2

Correlation between financial toxicity and health-related quality of life. Increased financial toxicity (lower COST) is moderately associated with decreased quality of life (lower FACT-L). Pearson correlation coefficient: 0.44, $P < 0.0001$.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTable1FinancialStateandHealthInsuranceQuestionnaire.docx](#)
- [SupplementaryTable2ChineseVersionofFinancialStateandHealthInsuranceQuestionnaire.docx](#)
- [SupplementaryTable3ChineseVersionofFactorAnalysisoftheFinal11ItemComprehensiveScoreforFinancialToxicityCOST.docx](#)