

Surgery and Financial Toxicity are Risk Factors for Distress in Cancer Survivors: A Cross-sectional Study

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Abstract

Background: Patients with cancer often face some level of distress, regardless of disease stage. Distress in cancer survivors has a negative impact on their quality of life. The goal of this study was to identify risk factors for distress, understand how treatment associated with distress and reveal the relationship between the psychological and financial distress.

Methods: This was a multi-center cross-sectional study of patients with cancer requiring surgery or chemotherapy. Patients completed questionnaires regarding their demographics, disease characteristics, psychological distress, and financial toxicity. A multivariable logistic regression model was used to examine factors associated with distress in surgical versus chemotherapy treatment groups.

Results: A total of 409 patients participated in the study. Patients treated with surgery ($n = 172$) were more likely to be female, unemployed, early stage compared with patients undergoing chemotherapy ($n = 237$). Multivariable analysis revealed that surgical patients tended to have a higher risk of distress compared with patients receiving chemotherapy (OR, 95% CI: 3.086, 1.854–5.137) due to higher rates of nervousness, pain, and difficulty with bathing/dressing, and patients with high financial toxicity had a higher risk of distress compared with those with low financial toxicity (OR, 95% CI: 2.000, 1.278–3.130). The relationship between financial toxicity and psychological distress was stronger in the chemotherapy group, with the correction coefficient -0.294 and slope -1.196.

Conclusion: Patients who underwent surgery and reported higher financial toxicity were more likely to experience distress. Multidimensional distress screening and psychosocial interventions should be provided pre- and post-operatively for patients.

Introduction

Cancer diagnosis and treatment often lead patients to face some level of distress, regardless of disease stage. [1, 2] Distress is conceptualized as a multifactorial, unpleasant experience of a psychological, social, spiritual, and/or physical nature that may interfere with the ability to cope effectively with the physical symptoms and treatment of cancer,[3] and has been considered the sixth vital sign, after pain, in cancer care. [4] Distress in patients with cancer may reduce adherence to treatment, decrease quality of life, and increase cancer-specific mortality. [5–7] Early screening for distress leads to timely multicomponent intervention, which in turn improves quality of life.

Many studies of distress have focused on the emotional problems (e.g., anxiety, depression) and physical problems (e.g., fatigue) of distress, with little attention to treatment-related and financial factors. [8–10] Financial toxicity has been defined as objective financial burden and subjective financial distress experienced by cancer patients as a result of their treatment. [11] Assessment of financial toxicity may help to build a framework for financial counseling interventions on par with symptom management (e.g., for fatigue or pain). [12] The present study was conducted to identify demographic, clinical, and

socioeconomic predictors of distress, understand how treatment associated with distress and reveal the relationship between the financial toxicity and distress.

Methods

Study Design and Procedure

A cross-sectional observational study was conducted at three public cancer treatment centers: Cancer Hospital of China Medical University (Liaoning Cancer Hospital & Institute), Anshan Tumor Hospital, and the Fourth Hospital of Fushun City from March 2017 to October 2018. Patient inclusion criteria included being of age 18 years or older; participating in Social Health Insurance (SHI) of China; receiving a new diagnosis of stomach, lung, colorectal, or breast cancer within two months; and undergoing treatment with surgery, chemotherapy, or both. Patients who were illiterate, unable to understand and respond to the study survey, and/or receiving treatments through a clinical trial were excluded from study. This study was approved by the Ethics Committee of Liaoning Cancer Hospital & Institute (No.20170302).

Prior to the survey, the trained researchers, the oncology nurses, explained to the patients the study purpose and that participation was voluntary. All participating patients provided informed consent. The patients completed the entire questionnaire except for the clinical information section, which was pre-populated from the electronic health record.

Measures

Sociodemographic and Clinical Characteristics

Demographic information and clinical characteristics were solicited in the first part of the questionnaire, including age, sex, marital status, educational background, employment status, medical insurance status, cancer type, the time of diagnosis, clinical stage of cancer, and type of treatment.

Psychological Distress Assessments

Several instruments are available to identify the distress of patients with cancer [13]. The Distress Thermometer and Problem List (DT&PL) is widely used as a self-reporting tool for the screening of distress in patients with cancer. [14, 15] The DT is a single-item, self-reporting instrument measuring the amount of distress experienced by patients within the last week, with a score ranging from 0 (no distress) to 10 (extreme distress). The PL groups various problems patients with cancer encounter after diagnosis into five problem categories: practical, family, emotional, physical, and spiritual. Problems are selected by checking a corresponding “yes” or “no” on the survey. The Chinese version has been validated in various types of cancer patients. [16] A score of 4 or higher on the DT indicates significant distress. The prevalence of distress and specific problems were analyzed in the current study.

Financial Toxicity Assessments

All patients also completed the COmprehensive Score for financial Toxicity (COST) survey to assess for financial toxicity. The COST measure was previously developed and validated by de Souza et al. to assess financial toxicity in patients with cancer. [17, 18] Briefly, the COST is an 11-item measure of financial toxicity examining one financial item, two resource items, and eight affect items. The patients were asked to respond on a five-point Likert scale, from 0 (not at all) to 4 (very much). The total score ranges from 0 to 44 points. Lower COST values indicate severe financial toxicity. Our team translated and adapted the Chinese version with high reliability ($\alpha = 0.89$) among patients with cancer. [19] The COST scores were stratified by high and low financial toxicity, and we defined high financial toxicity as lower or equal to the median.[20]

Statistical Analysis

All sociodemographic and clinical characteristics of patients were summarized using descriptive statistics. Categorical variables were presented as frequencies and percentages. The chi-square test was used for comparing the group differences in categorical variables. Associations between factors were derived by multiple logistic regression models after adjusting for factors including occupation and insurance. Factors examined were age, sex, marital status, educational background, annual household income, type of cancer, type of treatment, and degree of financial toxicity. Pearson correlation coefficient was used to test associations among the COST and DT scores. Statistical analyses were performed with SAS 9.2 software. All tests were two-sided and P values of 0.05 or less were considered statistically significant.

Results

Characteristics of the study population

A total of 409 patients participated in the study. The demographic and clinical characteristics of patients are presented in Table 1. The median age was 59 years and more patients identified as female (55.3%) than male. Approximately 90.0% of patients identified as married, 24.4% as employed, and 17.6% as having high school education or more. In addition, 40.6% of patients were diagnosed with stage III cancer, and the most frequently reported type of cancer was lung (31.1%) followed by breast (27.4%). The patients were grouped into two categories for analysis based on treatment methods: chemotherapy alone ($n = 237$, 57.9%), and surgery ($n = 172$, 40.1%), which included surgery alone or combined with chemotherapy. The two groups were similar in age ($P = 0.092$), marital status ($P = 0.936$), educational background ($P = 0.218$), and household income ($P = 0.671$); the significant variations included sex ($P < 0.001$), employment status ($P = 0.005$), cancer type ($P < 0.001$), and clinical stage ($P < 0.001$).

Table 1
Characteristics of Patients

		Chemotherapy (<i>n</i> = 237)	Surgery (<i>n</i> = 172)	<i>P</i> value	Total (<i>n</i> = 409)
Median age (range)		58 (34–79)	60 (28–80)	0.092	59 (28–80)
Sex	Male	129 (54.4)	54 (31.4)	< 0.001	183 (44.7)
	Female	108 (45.6)	118 (68.6)		226 (55.3)
Marital status	Married	213 (89.9)	155 (90.1)	0.936	368 (90.0)
	Unmarried	24 (10.1)	17 (9.9)		41 (10.0)
Employment status	Employed	70 (29.5)	30 (17.4)	0.005	100 (24.4)
	Unemployed	167 (70.5)	142 (82.6)		309 (75.6)
Educational background	Primary school	134 (56.5)	109 (63.4)	0.218	243 (59.4)
	Middle school	55 (23.2)	39 (22.7)		94 (23.0)
	High school or above	48 (20.3)	24 (14.0)		72 (17.6)
Household income	< 50 000	168 (70.9)	126 (73.3)	0.671	294 (71.9)
	≥ 50 000	55 (23.2)	34 (19.8)		89 (21.8)
Cancer type	Stomach	51 (21.5)	20 (11.6)	< 0.001	71 (17.4)
	Lung	60 (25.3)	67 (39.0)		127 (31.1)
	Colorectal	79 (33.3)	20 (11.6)		99 (24.2)
	Breast	47 (19.8)	65 (37.8)		112 (27.4)
Clinical stage	I	19 (8.0)	46 (26.7)	< 0.001	65 (15.9)
	II	54 (22.8)	84 (48.8)		138 (33.7)

		Chemotherapy (<i>n</i> = 237)	Surgery (<i>n</i> = 172)	<i>P</i> value	Total (<i>n</i> = 409)
	III	127 (53.6)	39 (22.7)		166 (40.6)
	IV	37 (15.6)	3 (1.7)		40 (9.8)

Prevalence of the distress and financial toxicity

Distress was present in 56.5% of the patients, and a total of 231 patients scored ≥ 4 on the DT. Physical, emotional, and practical problems were reported as the major sources of distress. Regarding practical problems, financial factors (*n* = 162, 70.1%) were reported the most. Worry (*n* = 145, 62.8%) and fatigue (*n* = 115, 49.8%) were most prevalent among emotional and physical problems. Patients who reported financial toxicity (*n* = 217, 53.1%) had COST scores below or equal to the median of 18. Surgical intervention was associated with a higher degree of patient distress than chemotherapy alone ($P < 0.001$). There was no significant difference regarding financial toxicity. The prevalence of the distress and financial toxicity is presented in Fig. 1.

Factors Associated With Distress

In the unadjusted analyses, higher income and lower financial toxicity were associated with lower prevalence of distress. A lung cancer diagnosis, early stage of disease, and surgical intervention were associated with higher prevalence of distress. In the final multivariable model, treatment type and financial toxicity were found to be significantly associated with distress when controlling for age, marital status, employment status, and educational background. These findings are demonstrated in Table 2. Patients in the surgery group reported more distress than the chemotherapy group (OR, 95% CI: 3.086, 1.854–5.137). Similarly, patients with a higher degree of financial toxicity, reflected by lower COST scores, had a greater risk of distress than those with a lower degree of financial toxicity (OR, 95% CI: 2.000, 1.278–3.130).

Table 2
Factors associated with distress on univariate and multivariate analyses

		Univariate analysis		Multivariate analysis	
		OR (95% CI)	<i>P</i>	OR* (95% CI)	<i>P</i>
Age (years)	< 45	Reference			
	45–59	1.293 (0.633 to 2.642)	0.480		
	≥ 60	0.979 (0.484 to 1.981)	0.954		
Sex	Male	Reference			
	Female	1.344 (0.907 to 1.993)	0.140		
Marital status	Married	Reference			
	Unmarried	1.098 (0.571 to 2.113)	0.779		
Employment status	Employed	Reference			
	Unemployed	1.142 (0.726 to 1.797)	0.565		
Educational background	Primary school	Reference			
	Middle school	1.034 (0.640 to 1.671)	0.891		
	High school or above	1.186 (0.695 to 2.025)	0.531		
Household income	< 50 000	Reference			
	≥ 50 000	0.645 (0.418 to 0.996)	0.048	0.691 (0.371 to 1.032)	0.066
Cancer type	Stomach	Reference			
	Lung	2.196 (1.216 to 3.967)	0.009	1.562 (0.794 to 3.074)	0.196
	Colorectal	1.680 (0.909 to 3.107)	0.098	1.670 (0.840 to 3.318)	0.144
	Breast	1.720 (0.944 to 3.135)	0.076	0.800 (0.351 to 1.825)	0.800
Clinical stage	I	Reference			

*ORs were adjusted for factors including age, sex, marital status, employment status and educational background in the multivariate regression model.

		Univariate analysis		Multivariate analysis	
	II	0.544 (0.287 to 1.032)	0.063	0.545 (0.270 to 1.099)	0.090
	III	0.374 (0.201 to 0.697)	0.002	0.483 (0.237 to 0.986)	0.046
	IV	0.423 (0.186 to 0.966)	0.041	0.627 (0.245 to 1.603)	0.330
Treatment	Chemotherapy	Reference			
	Surgery	2.865 (1.889 to 4.346)	< 0.001	3.086 (1.854 to 5.137)	< 0.001
Financial toxicity	Low	Reference		Reference	
	High	1.937 (1.303 to 2.879)	0.001	2.000 (1.278 to 3.130)	0.002
*ORs were adjusted for factors including age, sex, marital status, employment status and educational background in the multivariate regression model.					

Further analysis was to understand how surgery increased distress. The results showed that patients in the surgery group reported higher rates of nervousness ($P = 0.001$), pain ($P < 0.001$), and difficult with bathing/dressing ($P = 0.008$) compared with the chemotherapy group. Figure 2 outlines the top 10 factors causing distress in the treatment groups.

Financial Toxicity and Distress in Treatment Groups

The association between overall distress and financial toxicity, respectively measured by the DT and COST, based on treatment is presented in Fig. 3. The correction coefficient between financial toxicity and distress was -0.188 , and the COST score decreased by 0.572 points for every 1-point increase in the DT score ($P = 0.014$). This suggests that a higher degree of financial toxicity is associated with greater distress in the surgery group. For patients in the chemotherapy group, the correction coefficient was -0.294 , and every 1-point increase in the DT score decreased the COST score by 1.196 points.

Discussion

In the literature, the prevalence of distress among patients with cancer varies by country, cancer type, sex, age, and other sample characteristics. [21–25] Prior studies identified worry on the DT&PL as the most distressing, possibly as a surrogate for the intensity of distress. [26] McFarland et al. reported that 40% of patients with breast cancer had fatigue, the most common physical problem associated with distress. [27]

Unlike previous studies, [28, 29] in this study financial difficulty was the highest-ranking single item associated with distress. The prevalence of psychological distress and financial toxicity was 56.5% and 53.1%, respectively. Most patients experienced at least one practical, physical, or emotional problem, primarily financial difficulty (70.1%), worry (62.8%), and fatigue (49.8%). In this study, worry was a leading item in the emotional problem domain, but inferior to financial difficulty among all items attributed to distress. The prevalence of financial concerns among patients with cancer may be due to the need to make financially-based decisions throughout cancer treatment. [30] Cancer-related financial problems have been associated with increased risk for depressed mood, a higher frequency of worry, and a significant and frequent source of distress among patients with cancer. [31, 32]

Several studies have examined distress among surgical inpatients. Basak et al. found that approximately half of surgery inpatients had depression and approximately one-quarter had anxiety. [33] Pastore et al. found that patients undergoing surgery for urological cancer had clinical levels of anxiety (9.8%) and depression (3.6%). [34] Furthermore, a significant correlation was observed between distress and esophagectomy among patients with esophageal cancer. [35] In the current study, 70.9% surgical treatment group reported a significantly psychological distress. One potential explanation was that patients underwent surgery were worried about preoperative preparation and postoperative pain. [36]

The results of studies examined the effects of different treatment options on distress among cancer patients are inconsistent. Female patients who underwent chemotherapy were more likely to report fatigue and nausea, whereas surgical patients did not report these physical problems. [27] Patients with breast cancer who underwent mastectomy with reconstruction reported higher levels of distress compared with patients undergoing lumpectomy and mastectomy only.[10] Our data showed that statistically significant differences were noted between the surgery and chemotherapy group for nervousness, pain, and problems with bathing/dressing. Surgical treatment was a significant predictor of psychological distress with 3.09 times risk for psychological distress versus chemotherapy treatment. Further studies are needed regarding preoperative intervention and postoperative management for distress among cancer patients undergoing highly invasive procedures.

The literatures support the relationship between poor socioeconomic status (e.g., a low household income, financial problems) and psychological distress. [37, 38] Approximately 22% of patients with cancer were worried about paying medical bills. [39] Lung and colorectal cancer patients with limited financial reserves reported increased pain.[40] One possible explanation was that cancer patients with poor financial status encountered more barriers to timely diagnosis, optimal treatment, and survivorship care [41, 42]. Carrera et al. suggested that financial toxicity could be coupled with the use of DT&PL in screening for distress.[11]

To our knowledge, this is the first study identifying the relationship between COST and DT in hospitalized patients with cancer. In the current study, COST scores were negatively related to DT scores in two groups, suggesting a higher degree of financial toxicity correlates with a greater severity of distress. Financial toxicity was significantly associated with distress, even after controlling for age, sex, and cancer type.

This study has some limitations. First, the cross-sectional observational design could not evaluate dynamic changes of DT and COST with treatment, and did not provide interventions to patients with significant distress. Second, patients undergoing radiotherapy treatment were not included in this study, mainly because very few patients receive radiotherapy as first-line or primary treatment. Finally, participations were solicited from three tertiary-level cancer centers from different cities, but all in Northeast China. Therefore, the application of the study findings is limited to patients with cancer in China.

Patients with cancer experience distress caused by physical, emotional and financial problems. Frequently, these problems overlap and exacerbate one another. This study demonstrates that a significant proportion of cancer survivors above the threshold for psychological and financial distress, provides preliminary evidence for an association between treatment and financial toxicity and distress, and evaluates predictors of distress in adults with cancer. The findings confirm that surgical treatment and severe financial toxicity are significant predictors of distress.

Declarations

Authors' contributions

Huihui Yu participated in study conducting, data analysis and interpretation, drafting the manuscript and approval of final manuscript. **Tingting Zuo** participated in data interpretation and approval of final manuscript. **Xue Bi, Hui Li, Haiyang Xing, Li Cao, Lijuan Cai, Zhen Zhang** participated in collection and assembly of data and approval of final manuscript. **Yunyong Liu** participated in study designing, critically revising the manuscript, approval of final manuscript and is the guarantor of the study.

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Compliance with ethical standards

Conflict of interest

The authors declare no conflicts of interest.

Ethics approval

This study was approved by the Ethics Committee of the Liaoning Cancer Hospital and Institute (No.20170302).

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Figures

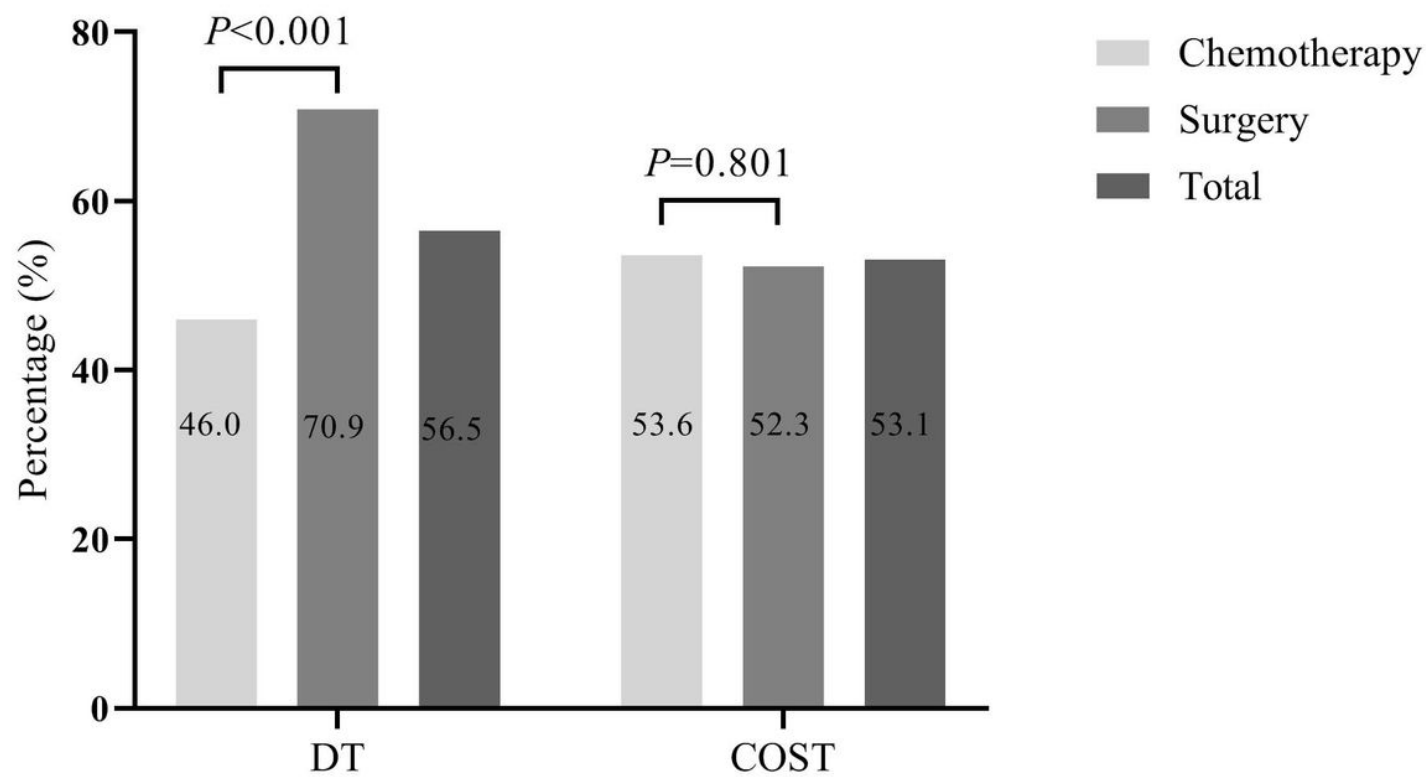


Figure 1

The prevalence of the distress and financial toxicity

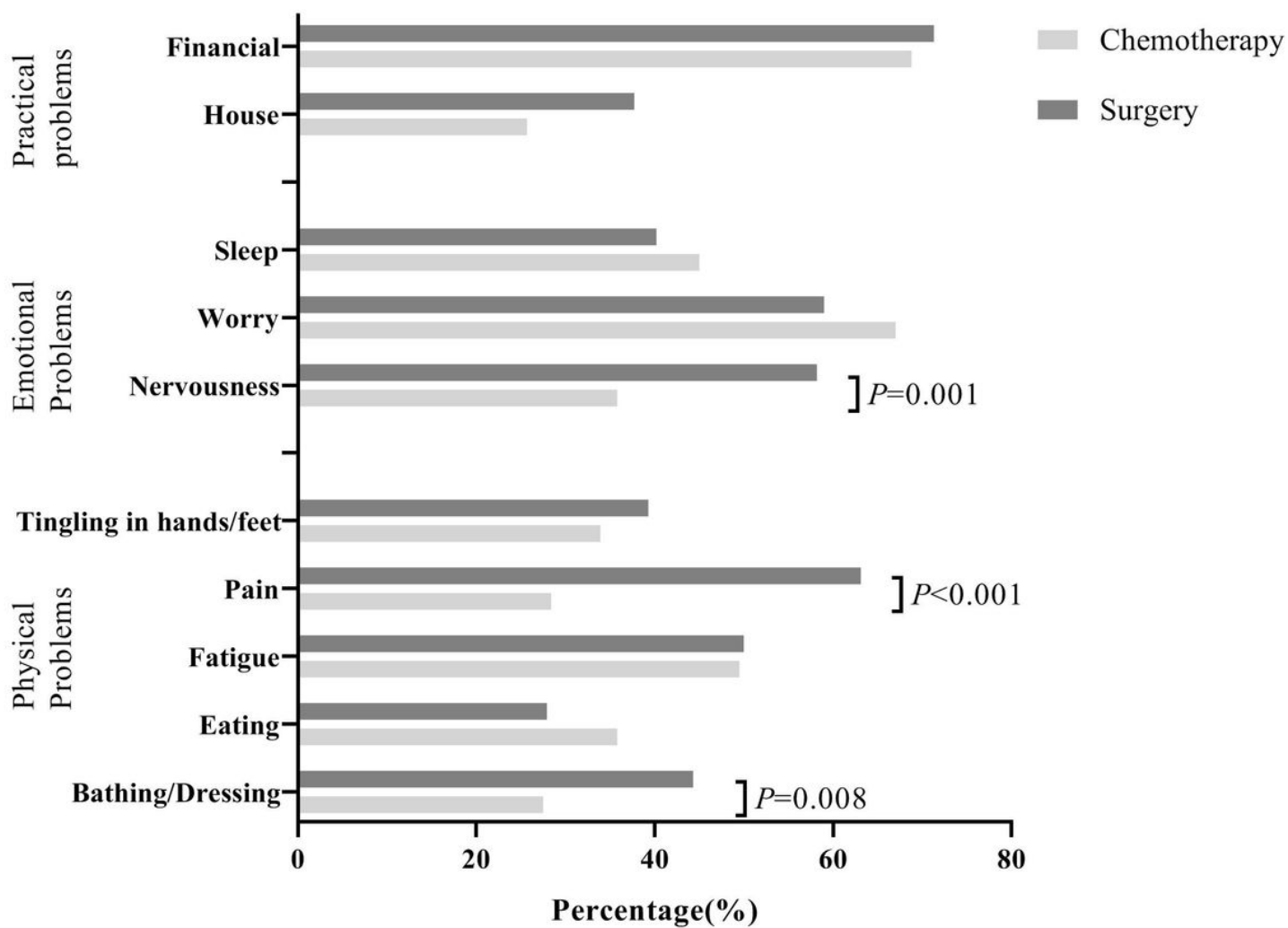


Figure 2

Outlines the top 10 factors causing distress in the treatment groups.

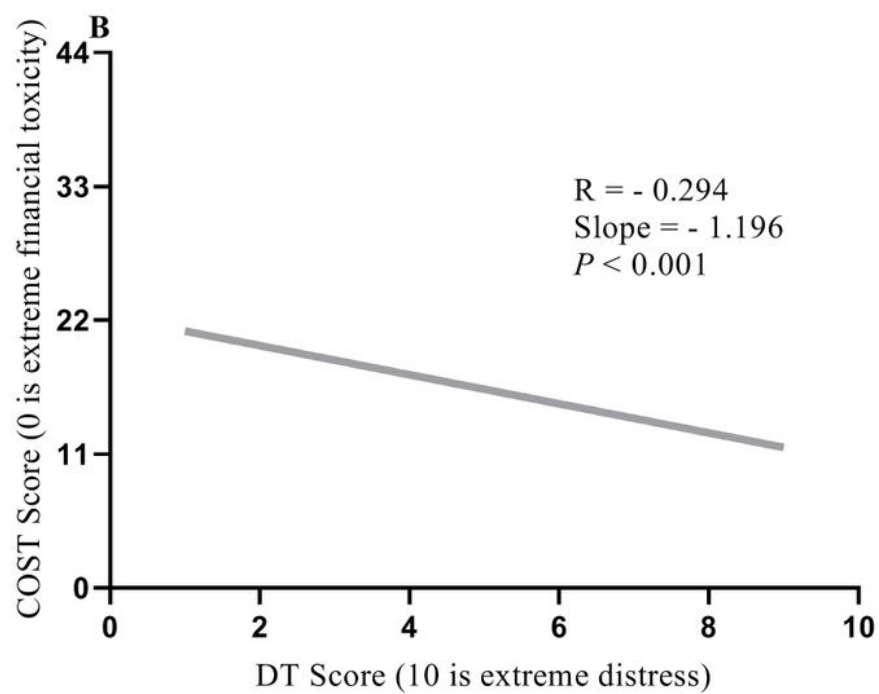
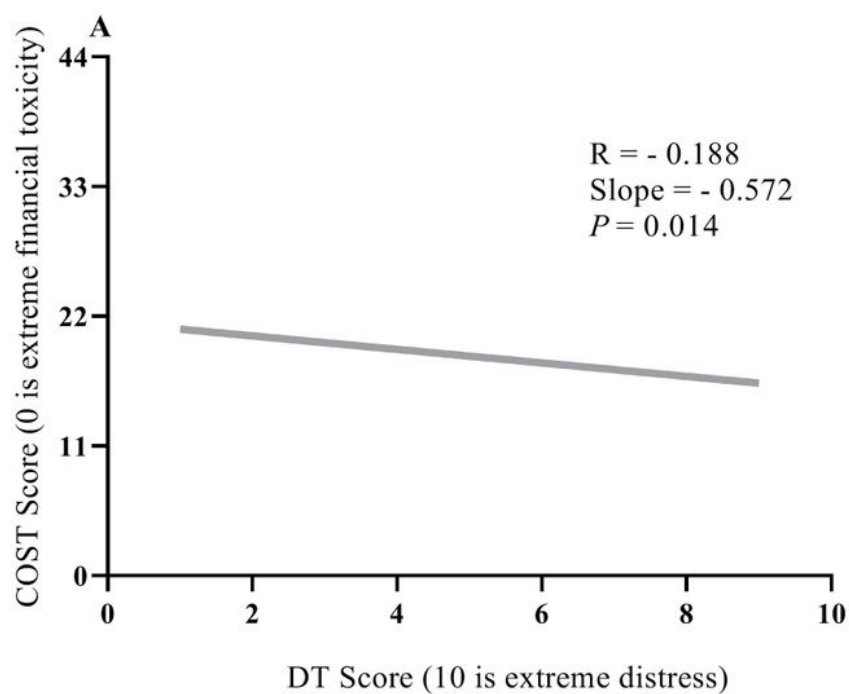


Figure 3

The association between overall distress and financial toxicity, respectively measured by the DT and COST, based on treatment