A cross-sectional study on associations of physical symptoms, health self-efficacy and suicidal ideation among Chinese hospitalized cancer patients following diagnosis.

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Abstract
Background: To examine the association between physical symptoms and suicidal ideation among Chinese hospitalized cancer patients post-diagnosis, and test the modifying effect of health self-efficacy on this association.

Methods: A cross-sectional study was conducted among 544 cancer patients from oncology setting in two general hospitals in northeastern China. Suicidal ideation data was collected by face-to-face interview using the Yale Evaluation of Suicidality scale (YES). Patients also rated on the McGill Quality of Life Questionnaire (MQOL), the Hamilton Depression Rating scale (HAMD-17) and the Strategies Used by People to Promote Health scale (SUPPH). Multivariable logistic regression was applied to examine the impact of physical symptoms, health self-efficacy and their interactions on suicidal ideation.

Results: We found a suicidal ideation rate of 26.3% in patients following cancer diagnosis. Logistic regression showed that insomnia (aOR=1.84, 95% CI 1.13 to 3.00, p =0.015), lack of appetite (aOR=2.14, 95% CI 1.26 to 3.64, p =0.005) were significantly associated with suicidal ideation, low health self-efficacy showed a marginally significant exaggerating effect on the association between pain and suicidal ideation (aOR = 2.77, 95% CI 0.99 to 7.74, p =0.053), even after controlling socio-demographic, clinical characteristics and depression.

Conclusions: Insomnia, loss of appetite, even after adjusting depression, are associated with suicidal ideation, health self-efficacy play a moderating role on pain and suicidal ideation among Chinese cancer patients. Paying attention to these physical symptoms and promoting the sense of health self-efficacy could be useful for suicide intervention.

Background
Cancer is a major leading cause of death worldwide[1]. A cancer diagnosis and subsequent treatment can evoke psychological and physical distress in patients, complicate their life and even affect their will to live[2–4]. Cancer patients are at greater risk of suicide, with 1.3–2.6 times than the general population[5, 6]. As long-term survivorship and the number of patients living with cancer have grown significantly in the past several years in China[7], cancer can be considered as a chronic disease that
requires effective routine screening on suicide risk and ongoing management.

One of the most prominent risk factors of suicide is suicidal ideation (SI) [8-10]. Literature reported that the prevalence of SI in cancer patients ranges from 0.7% to 71.4% depending on the methodological variations in the study designs[11, 12]. For demographic and clinical correlates previous studies reported race[13], married status[14, 15], metastasis [2, 13, 16, 17], pain[18-20], physical function [3, 15, 21]were associated with SI. Psychological correlates include social support[22], coping strategies[22, 23], self-efficacy[23], anxiety[17] and depression[4, 13, 24]. However, physical symptoms due to disease itself and medical treatment are common among patients with cancer. There is still limit evidence on the associations between a wide range of physical symptoms and SI, and the role of health self-efficacy between physical symptoms and SI among hospitalized cancer patients.

Although depression is the major cause of SI[16, 17], studies indicated that the long-term effects of physical status are serious enough to result in suicidal thoughts in cancer patients[4, 18, 21, 25, 26]. A Korean study found SI was significantly associated with a set of physical symptoms, i.e. diarrhea, hair loss, usual fatigue, in stomach cancer patients[25]. However, it is unclear whether restricted a small set of specific symptoms or most symptoms increase risk of SI. For instance, numerous of studies have only focused on pain as the main risk factor for SI[17-19, 27]. Some studies have reported greater number of symptoms burden increased risk for SI[4, 21, 26]. It would be useful for health care professionals to be more aware of SI among cancer patients if they understand the association between physical symptoms and SI. Additionally, it is well known that expressions of depression maybe different across the cultures[28]. It has been reported that Asians express more physical symptoms than Westerners when experiencing depression, while the latter prone to express cognitive and psychological symptoms[28, 29]. Thus, the association between physical symptoms and SI may be different in an Asian country, e.g. China, than in western countries. However, few studies investigated the association among cancer patients in China.

On the other hand, the association between physical symptoms and SI may depend on how much a patient perceived sense of control over health[30, 31]. Health self-efficacy, refer to one's beliefs
about perceived ability to manage their health conditions[32, 33], is demonstrated plays critical role in better disease adjustments and improved quality of life among cancer patients[34, 35]. The association between self-efficacy and suicidality has been confirmed frequently[36-38]. Thus, lower level of health self-efficacy may impact on SI in cancer patients directly. Moreover, lower level of health self-efficacy may have moderating effect between physical symptoms and SI, more specific, a cancer patient may have a lower risk of reporting SI if he/she possesses a high degree of health self-efficacy. However, to our best knowledge, no research has examined the modifying effect of health self-efficacy on the relationship between physical symptoms and SI among cancer patients.

The present study aimed to investigate the association between physical symptoms and post-diagnosis SI among hospitalized cancer patients in China, and examine the potential modifying effect of health self-efficacy on this association. We hypothesized 1) physical symptoms would be associated with SI, even after adjusting for depression. 2) Among cancer patients with low level of health self-efficacy, the association between physical symptoms and SI would be greater compared to those with high levels.

Methods

Participants and procedure

Participants in this study were hospitalized patients recruited from the oncology setting in the general hospitals by cluster sampling method. Eligibility criteria included 1) diagnosed with cancer by pathology or cytology; 2) age of 18 years or older; 3) aware of their disease diagnosis; 4) provision of written informed consent. Exclusion criteria was 1) serious illness or cognitive impairment (such as dementia or delusions) or too weak to participate in the survey independently; 2) patients with language communication barriers or lack of capacity to cooperate the interview; 3) family caregivers required confidentiality of their diagnosis to the patients; This study was reviewed and approved by the Human Ethics Committee of Dalian Medical University. After a description of all procedures of the study was provided, patients signed a written informed consent before participate in the interview. This cross-sectional investigation was conducted in two general hospitals (the Second Affiliated Hospital of Dalian Medical University and the Zhongshan Affiliated Hospital of Dalian University) from
January to December 2015 in Dalian, a typical Northeast coastal city of China, the gross domestic product (GDP) ranked 26th in China in 2018, a medium level of the country. Patients were recruited consecutively in the oncology setting and we conducted our interview only if he/she had been undergoing the medical treatment for at least three days. Three interviewers received a seven-day training included general interview skills and good acknowledge of the whole instruments before the survey. All the patients were interviewed face-to-face. Interview lasts 40–50 minutes. As for cancer relevant information, such as type of cancer, stage at diagnosis, medical treatment, and metastatic status were withdrawn from the patients’ medical records.

Measures

Suicidal ideation: We used the Chinese version of the Yale Evaluation of Suicidality scale to evaluate suicidal ideation. The YES scale is a 16-item structured questionnaire assesses suicidal thoughts and actions, history of suicide attempts and feelings/attitudes on suicide[39]. Higher score indicates higher risk of suicidality. The YES has been validated among bereaved population as well as advanced cancer patients[13, 23]. The first 4 items were used as a screening measure in our study, Cronbach's $\alpha = 0.93$. Patients were asked following questions to assess SI (Since diagnosis of the disease, in light of your current circumstances, how strong would you say your wish to live has been? 1) strong, 2) moderate, 3) weak, 4) have none. How strong has your wish to die been? 1) strong, 2) moderate, 3) weak, 4) have none. Which of the following best describes your feelings about living versus dying? 1) No, 2) possibly, 3) Yes. Have you ever had thoughts of killing yourself? 1) Living outweighs dying, 2) About equal, 3) Dying outweighs living.) Those patients who endorsed the responses to questions Q1 through Q4 were 1, 4, 1, 1, identified as having no SI, If not, categorized into positive SI.

Independent variables and covariates

Physical symptoms were measured with one-item from the McGill Quality of Life Questionnaire (MQOL)[40]. Participants were asked whether have these symptoms over the previous two days with a response of yes and no. 14 items were included: pain, shortness of breath, insomnia, weakness, fatigue, nausea, lack of appetite, constipation, diarrhea, edema, cough, vomiting, fever and bloated.
Health self-efficacy: We measured health self-efficacy by using the Chinese version of the Strategies Used by People to Promote Health (SUPPH)[41]. This scale is a 29-item validated scale including three dimensions. Each item is rated on a five-point scale ranging from “little confidence” (1) to “quite a lot of confidence” (5). All the items were summed into a score. Higher score indicates a higher sense of health self-efficacy. To evaluate the relative risk of SI, the scores were categorized into high (≥50) and low groups (<50) by the median. The Cronbach's α of the current data was 0.96.

Depression: Clinician diagnosis of depression was evaluated by the 17-item version of the Hamilton Depression Rating Scale (HDRS-17)[42], which assess the severity of depression symptoms over the past week. It contains 17 items to detect depressive disorder and identify severity classification by semi-structured interview. A higher total score indicates a greater severity of depression. Severity classifications were defined as follows: 0–7 for no depression, 8–16 for mild depression, 17–23 for moderate depression, and ≥24 for severe depression. According to the proposal of Zimmerman et al[43], the cut-off value of HDRS was 8 for identifying depressive disorder. Reliability was good in the present study (Cronbach's α = 0.84; Split reliability = 0.79).

Other variables: Socio-demographic characteristics included sex, age, marital status, education, residence, employment status, household-income, smoking habit and drinking habit. Clinical related variables included site of cancer, stage at diagnosis, medical treatment, time since diagnosis and metastasis status.

Statistical analysis
Descriptive analyses, chi-square were used to compare the differences in socio-demographics and clinical associations between those who with and without suicidal ideation. Multivariate regression was used to test the regression models and the interaction effects of physical symptoms and health self-efficacy. Six different models were tested in this study. Model 1 tested the relationship between physical symptoms and SI after adjusted for socio-demographic and clinical variables. Model 2 tested physical symptoms, health self-efficacy and SI, adjusted for socio-demographic plus clinical variables. Model 3 tested physical symptoms, health self-efficacy and SI, additionally adjusted for diagnosed depression. As for the regression models of the interaction effects, Model 1 adjusted for the socio-
demographic variable and all the other physical symptoms. Model 2 additionally adjusted for clinical variables. Model 3 additionally adjusted for diagnosed depression.

All statistical analyses were performed by SPSS version 21.0 for Windows (IBM, Chicago, USA). The reported CIs were calculated at the 95% and statistical significance was set at .05 level and all tests were two-sided.

Results

Sample characteristics

A total of 700 cancer patients were invited to participate in this survey. Among them, 69 could not cooperate due to poor physical or mental health or low education level. 59 could cooperate objectively, but refused to join. 282 out of 350 hospitalized patients from Zhongshan Affiliated hospital of Dalian University (response rate 80.6%), and 290 out of 350 inpatients from Second hospital of Dalian Medical University (response rate 82.9%) agree to join our study. 28 patients failed to complete the questionnaire and exited in the halfway. Finally, a total of 544 patients were included in the analysis (valid rate 95.1%), sample characteristics are shown in Table 1. Approximately half of the sample was females 51.8%, 49.8% from Zhongshan Affiliated hospital, with a mean age of 59.9 years [standard deviation (SD)=11.6], ranging from 19 to 81 years. 78.3% primarily lived in the city. Overall, the majority sample was composed of three types of cancer: digestive system cancer (29%), lung cancer (23.7%) and breast cancer (18.9%). Approximately half of the patients were present metastasis, diagnosed with cancer more than 1 year (Table 1).

Prevalence of suicidal ideation after a cancer diagnosis

Out of the total patients (n=544), over one-forth of them reported that they have experienced SI since cancer diagnosis. The prevalence of SI was 26.3% (n=143), with 24.4% in man and 28.0% in woman.

Study factors associated with suicidal ideation

Table 2 displays a comparison of socio-demographic and clinical related characteristics between patients with and without SI. Missing data (n=4) on all variables was assumed to be in the low-risk category except for SI. Compared to patients without SI, we found that no significant difference of
most demographic variables, including sex, age, education attainment or household income between the two groups (all $p>0.05$), but significantly difference in marital status, employment status, metastasis, currently diagnosed depression. Although stage at diagnosis was not significant, $p$ value was marginal. In addition, significant differences were shown in physical symptoms (pain, short of breath, insomnia, nausea and lack of appetite) and health self-efficacy. Based on these results we entered socio-demographic factors, metastasis, stage at diagnosis and depression as control variables in the subsequent analyses.

Multivariate logistic regression analysis was conducted to examine the effect of physical symptoms on SI. In model 3 (table 3), after adjusting for socio-demographic, clinical variables and diagnosed depression, the risk of SI was significantly higher in patients with symptoms of insomnia (aOR=1.84, 95% CI 1.13 to 3.00, $p =0.015$) and lack of appetite (aOR=2.14, 95% CI 1.26 to 3.64, $p =0.005$).

In table 4, physical symptoms of insomnia and lack of appetite were significantly associated with SI in patients with low levels of health self-efficacy. According to a difference in OR between high and low health self-efficacy, Two-way interaction terms of health self-efficacy×each physical symptom were entered and tested individually. In model 3, low health self-efficacy showed a marginally significant exaggerating effect on the association between pain and suicidal ideation (aOR = 2.77, 95% CI 0.99 to 7.74, $p =0.053$), adjusted for all the confounding variables.

Discussion
Overall, our study revealed that the prevalence of post-diagnosis SI was 26.3% among Chinese hospitalized cancer patients. Patients with symptoms of insomnia or lack of appetite were at higher likelihood of reporting SI, even after adjusting for socio-demographic variables (marital status, being retired), clinical variables (stage at diagnosis, metastasis) and diagnosed depression. Furthermore, our findings suggest a marginally exaggerating effect of low health self-efficacy on pain and SI, after adjusted for all the confounding variables.

In the current study, 26.3% of the hospitalized patients reported SI following cancer diagnosis, which was higher than the previous reports (15.3–18.4%) in Chinese cancer population [17, 22, 44]. and it was also higher than that in some Western studies (7.8–17.7%) [15, 18–20, 23], but much lower than
that in Japan and Korea (34.7–71%) [16, 25, 45, 46]. Our data was comparable to those of previous researches in Spain, the United States and Taiwan (22.6–29.5%) [4, 14, 24]. The prevalence of SI varies from different studies based on different sample and measures. The majority of the sample were cancer patients of the digestive system and lung cancer, and those diagnosed with stage III and IV accounted for 70% of the total sample. Previous studies indicated cancer site and stage at diagnosis were associated factors for SI [15, 46]. Moreover, the scale utilized in our study included passive and active SI as the outcome, the passive SI referred to the death ideation as a wish to die or would be better off dead, the active SI refers to thoughts of killing oneself [47], which can elevated the prevalence.

To our best knowledge, this is the first study to examine the associations of physical symptoms, health self-efficacy and SI, and their interactions on SI among cancer patients. In line with our hypothesis, we found that patients with specific physical symptoms were more likely to report SI. Lack of appetite was about two times associated with the odds of SI after adjusted for socio-demographic and clinical characteristics. Choi et al. found physical symptoms were significantly associated with SI in stomach cancer population [25]. Prior studies demonstrated that patients with difficulties in vital function, such as eating, experience more helplessness/hopelessness and were therefore at higher risk of SI [21, 46]. The observed relationship between insomnia and SI in our study is biologically plausible. Sleeping loss can cause various endocrine and immunological changes, prior studies have proved that inhibition of the serotonin (5-hydroxytryptamine) system plays a significant role in suicide [48]. Besides, poor sleep quality can change cognitive and emotional processes, leading to behavioral changes characterized as more irritable and elevate the risk of suicidality [49].

In consistent with our second hypothesis, our study suggested that low health self-efficacy played a marginally significant exaggerating effect on the association between pain and SI, indicating that the impact of pain on SI may differ depending on the levels of health self-efficacy. An increased risk of SI was shown in those patients with low health self-efficacy and pain. Previous studies have suggested that higher level of self-efficacy could reduce the likelihood of continued pain and disability [50]. Therefore, patients with higher health self-efficacy experience their illness as less distressing, which
in turn related to a lower degree of pain and function limitation. This is in line with prior studies showing an association of higher health self-efficacy of cancer patients with lower psychological distress levels and higher quality of life [34, 35]. As health self-efficacy reflects individual’s perceived ability to cope with stress and confidence in overcoming challenges to take care of their health, may have positive emotional status with high expectation, even experiencing pain. In contrast, those with low health self-efficacy, who tend to focus on their own pain, have negative attitude and feel their life out of control, may be more likely to suffer from suicidal thoughts.

There are some limitations in our study. Foremost, our sample were recruited in cancer departments from two general hospitals in Northeast of China, thus the results may limit generalization to the cancer-specialized hospitals or the outpatients setting. Second, respondents may have not reported SI due to fear of stigma or embarrassment related to suicide related behaviors, the prevalence of SI reported in our study might be an underestimation. Third, respondents of this study were patients undergoing medical treatment, those who experiencing severe physical adverse effects and emotional distress were not included in our sample, which may product a selection bias. Fourth, the physical symptoms assessed in the past two days, which might include occasional symptoms and might not occur simultaneously with SI seems to be a serious limitation of this study. Fifth, owing to the cross-sectional study, no direct causal relationship can be made. Sixth, apart from depression disorders, we did not identify other mental disorders in analyzing the predictors. Finally, longitudinal research is needed on health self-efficacy interventions in reducing suicidal thoughts and further risks of suicide, such as future intent or prior suicide attempts.

One in four cancer patients undergoing treatment reported SI after diagnosis, indicates that the high-risk on suicidality remains an issue for this population in China. There are several clinical implications. First, medical professionals should pay more attention to those patients experiencing insomnia or lack of appetite, which may lead to SI directly. Second, Provide cognitive behavioral therapy and skills to manage physical symptoms for the patients may yield meaningful results. Third, improvement in the sense of health self-efficacy in those with low health self-efficacy patients are essential for hospital suicide prevention, especially in cancer patients with pain. We believe we can identify physical
indicators and provide long-term screening, training and psychological treatment to ameliorate the risk of suicide.

Conclusions
In summary, the current study observed significant associations between insomnia, appetite loss and SI. Furthermore, health self-efficacy showed moderating role on pain and SI among Chinese patients with cancer. Paying attention to these physical symptoms and promoting the sense of health self-efficacy could be useful for oncology professionals to detect high-risk patients early and further interventions.

Declarations
CONTRIBUTORS
Q. Xu wrote the manuscript as a first author. Professor C. Jiang conceived and designed the study as a corresponding author. Professor N. Kawakami, S. Jia and L. Lin contributed to the interpretation of the analysis results and revised the manuscript. Professor N. Kawakami and M. Fukasawa gave critical comments to this manuscript. Clinical oncology staff was involved in the collection of the data. All authors contributed significantly to the study, and have approved the final manuscript.

CONFLICT OF INTEREST
No conflict of interest declared.

FUNDING SOURCES
None

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Arial Table1.pdf
Arial Table 4 Association between physical symptoms.pdf
Arial Table2.pdf