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Lung cancer distress: screening thermometer meta-analysis

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ABSTRACT

Objectives The distress is associated with the life quality and prognosis of patients with lung cancer. Distress thermometer (DT) has been widely recommended for distress screening. This study was conducted to summarise the positive rate of distress in patients with lung cancer using DT screenings.

Methods The PubMed, Embase, PsycINFO and Cochrane Library databases were comprehensively searched to identify all eligible studies published before 31 December 2021. Studies were eligible if they were published in peer-reviewed literature and evaluated distress levels by DT.

Results Ten eligible studies, including a total of 2111 patients, were included in this analysis, and their methodological quality was moderate. The pooled positive rate of distress in patients with lung cancer was 49.04% (95% CI 41.51% to 56.60%). The subgroup analysis revealed that the distress positive rate was significantly different ($p<0.05$) across North America, Europe and China with values of 53.33% (95% CI 45.22% to 61.37%), 43.81% (95% CI 31.57% to 56.43%) and 38.57% (95% CI 33.89% to 43.41%), respectively. Moreover, the distress positive rate was significantly different between men and women ($p<0.05$). Additionally, in terms of histological type, clinical tumour, node, metastasis stage, previous treatment and DT threshold, the distress positive rate had no significant differences. No significant publication bias was identified by Begg's funnel plot and Egger's test.

Conclusions The summarised distress positive rate was high and was significantly different according to gender and region. DT screening should be recommended for routine clinical practice and more attention should be given towards distress management.

Key messages

What was already known?
⇒ Distress thermometer (DT) has been widely used for routine screening.
⇒ The positive rate of distress by DT screening is diverse and the influential factors related to distress are complicated.

What are the new findings?
⇒ This study confirmed the summarised positive rate of distress in patients with lung cancer was as high as 49.04%.
⇒ The distress positive rate was associated with gender and region. However, the positive rate of distress was not related to histological type, clinical tumour, node, metastasis stage, previous treatment and DT threshold.

What is their significance?
⇒ Almost half of the patients with lung cancer suffered from distress.
⇒ Routine distress screening might be necessary to develop early interventions and to improve distress management. The psychological problems of female patients and region difference should be paid more clinical attention.

OBJECTIVES

According to the GLOBOCAN 2018 cancer report, lung cancer remains the leading malignancy in both morbidity (11.6%) and mortality (18.4%).[1] In China, there are 781 000 new cases of lung cancer each year.[2] Despite the dramatic development of immunotherapy and target therapy, the 5-year survival rate for advanced lung cancer remains low.[3] Furthermore, studies indicated potential relationships between poor prognosis and severe respiratory symptoms of lung cancer and the high incidence of psychological distress.[4]

Distress refers to discomfort and unpleasant experiences, and distressful patients suffer from psychological problems, such as depression, anxiety, panic disorders, social isolation and even spiritual crisis.[5] Accordingly, about 30%–40%

of patients with cancer were with moderate to severe psychological stress, which seriously lower the quality of life and even the prognosis.[6 7] Thus, distress screening should become the the first-step routine assessment, and psychological care is needed to relieve psychological distress.

There are many instruments for distress assessments, such as Brief Symptom Inventory-18 (BSI-18), Hospital Anxiety and Depression Scale (HADS), Profile of Mood Scale, Beck Depression Inventory, Symptoms Checklist-90 and distress thermometer (DT).[8–10] DT is a single-dimensional psychological measurement tool to effectively screen for distressful symptoms and to identify the source of distress. Taking advantage of simple procedure, easy interpretation, and high sensitivity and specificity,[7 10 11] we found that DT has been widely recommended by the National Comprehensive Cancer Network (NCCN) for clinical routine distress screening in all patients with cancer.[10] DT has also been internationally validated and proven to deliver reliable results in multiple languages.[11]

Numerous studies have reported the distress positive by DT screenings in malignant diseases[12 13]; however, the positive rate of distress in patients with lung cancer varies among different studies due to different research designs and enrolled populations.[7 14 15] The influential factors related to distress in patients with lung cancer also remain largely unknown. Thus, this study aimed to explore the positivity of distress in patients with lung cancer by DT screenings and to explore its related influential factors.

METHODS

Literature search strategy

We conducted this meta-analysis in accordance with the standards of Meta-analysis of Observational Studies in Epidemiology.[16] A comprehensive literature search was carried out in PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Embase (http://www.embase.com), PsyclNFO (http://www.apa.org/pubs/databases/psycinfo/index.aspx) and the Cochrane Library (http://www.cochranelibrary.com) for relevant articles published before 31 December 2021. The search terms are shown as follows: "psychological distress," "distress thermometer," "psycho-social problems," "lung cancer," and "lung neoplasms." No language restriction had been applied. The search results of different databases are shown in online supplemental tables S1–S4. In addition, the paper literature was manually searched, and references included in the relevant reviews and literature were screened for additional eligible studies. All procedures were conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[17]

Inclusion and exclusion criteria

The inclusion criteria were as follows: adult patients with lung cancer (≥18 years old) diagnosed pathologically or treated in the hospital; the references provide the outcome of positivity of distress, and the NCCN DT was used; and lastly, observational studies or randomised controlled trials. However, studies were excluded if they met the following criteria: DT score of patients with lung cancer was reported as mean±SD, yet no study for positive rate of distress was provided; studies were reviews, letters and comments; and lastly, the one with the most complete information was chosen among repeated studies or multiple studies using the same data.

Data extraction and study quality assessment

Data were extracted from eligible studies by two investigators independently based on a predesigned standardised form. The following variables were extracted: author's name, year of publication, study design, region, age, sample size, gender, histological type, clinical tumour, node, metastasis (TNM) stage and DT threshold. Any discrepancies were discussed and resolved. The Joanna Briggs Institute (JBI) critical appraisal tool was used for quality assessment in this study. The JBI checklist contains nine evaluation items, and each item can be evaluated as 'yes', 'no' and 'unclear or not applicable', corresponding to 'low risk', 'high risk' and 'unclear risk', respectively. For a single study, if one or more items are evaluated as high risk, then the risk bias of this study is high. For the studies without the high risk, if there are three or more items are evaluated as unclear risk, then the risk bias of this study is unclear. Finally, the risk bias of other studies is low. The PROSPERO ID is 167 635.

Statistical analysis

The meta-analysis was conducted by Stata V.11.0 statistical software. The effect measures were presented with positive rates with 95% CIs. The risk difference with 95% CI was used to assess differences between men and women, and between non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Cochran's Q and I^2 tests were used to performed the heterogeneity test.[18] The pooled $p<0.05$ or $I^2>50\%$ was considered significant, and a random effects model was used to pool the estimates if significant heterogeneity was presented between studies; otherwise, a fixed effects model was used for analysis. Subgroup analyses of region, previous treatment, clinical TNM stage, DT threshold and sample size were also performed. In addition, publication bias was evaluated with the funnel plot and Egger's test.

RESULTS

Study retrieval

The method used to choose studies is illustrated in figure 1. A total of 615, 929, 96 and 178 studies were screened in PubMed, Embase, PsyclNFO and the Cochrane Library database, respectively. Then, 25 studies were retained after screening for the title/

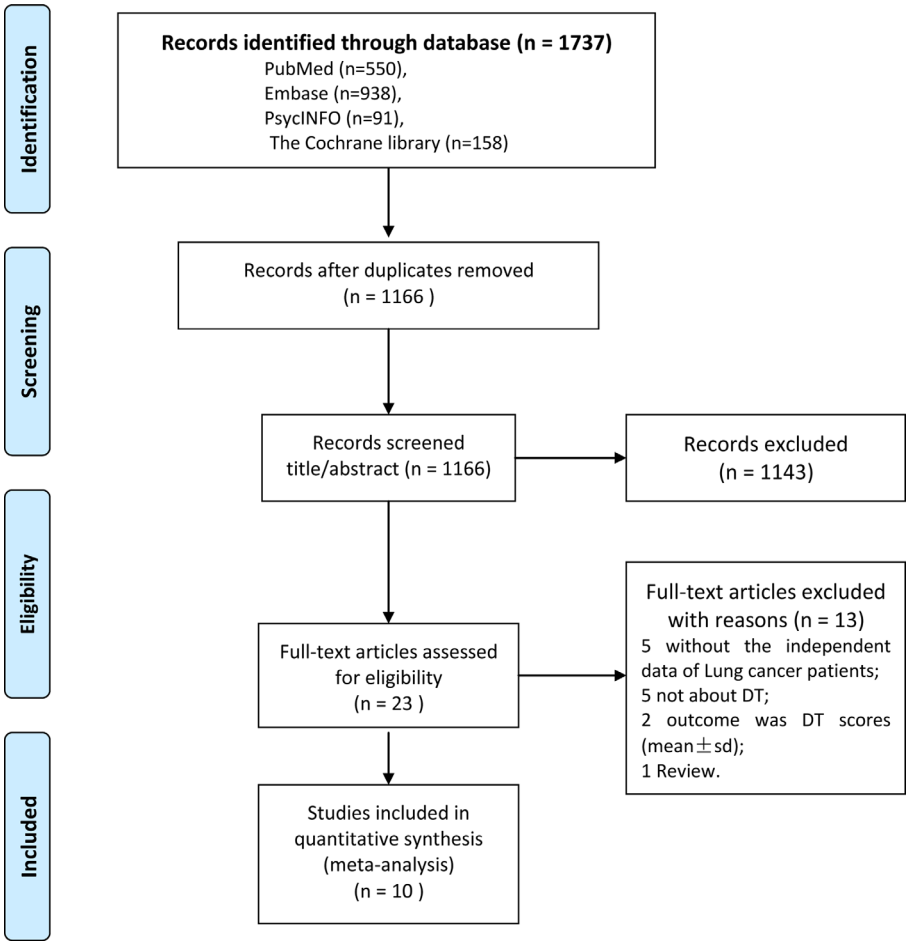

Figure 1 Flowchart of literature search and study selection. DT, distress thermometer.

abstract. Of these, 15 studies were excluded after a full-text reading, including 5 studies without independent data on patients with lung cancer, 5 studies not involving DT, 2 studies reporting outcomes via DT scores as mean±SD and 1 review. At the end, a total of 10 studies were enrolled in the analysis.[6 7 14 19–25]

Characteristics of studies

The sample size in each study varied from 33 to 549, and a total of 2111 patients with lung cancer were registered in the 10 included studies. Among them, 1082 patients were evaluated as distress with DT positive. All the studies were published before 31 December 2021. Moreover, the threshold of DT ranged from 4 to 5. Among these, only Carlson *et al*[20] simultaneously reported data for both baseline and follow-up (table 1). Therefore, cross-sectional study data were used to pool the positive rate of distress across all literature. The results of quality assessment suggested that three articles were evaluated as unclear risk and the rest seven articles were evaluated as low risk (online supplemental table S5). Overall, the risk bias of included studies was small and the methodological quality was moderate.

Summarised positive rate of distress in patients with lung cancer

A total of 10 studies reported positivity of distress in lung cancer patients based on DT screenings. It could be concluded that there is significant heterogeneity among studies (I^2=90.59%, p<0.01). The random effects model was used to estimate the effect size. As result, 1082 patients were evaluated as distressed by DT screening. The summarised positive rate was 49.04% (95% CI 41.51% to 56.60%) in all studies (figure 2).

Main related influential factors of distress in patients with lung cancer

In stratified analyses by region, the positive rate of distress in North America, Europe and China was 53.33% (95% CI 45.22% to 61.37%), 43.81% (95% CI 31.57% to 56.43%) and 38.57% (95% CI 33.89% to 43.41%), respectively. Moreover, the combined results of the three groups were significantly different (p<0.05) (figure 3).

As shown in table 2, four studies based on men and women and three studies based on NSCLC and SCLC were screened out. The combined positive rate for men and women was 42.20% (95% CI 33.76% to 50.87%)

Table 1 Characteristics of the studies included in the meta-analysis

Study, year	Country	Study design	Patients, N	M/F	Medium age (years)	Histological types	Clinical TNM stage	Previous treatment	Cut-off
Acquati and Kayser,[19] 2017	USA	Cross- sectional	93	51/42	62	NR	23 I&II, 67 III&IV	47 combined treatments, 39 single modalities and 7 patients without treatment	DT ≥4
Carlson *et al*,[6] 2019	USA	Cross- sectional	507	263/244	NR	NR	NR	Pivotal visits	DT ≥4
Carlson *et al*,[20] 2010	USA	Cross- sectional	549	NR	NR	Mixed	40 I, 66 II, 141 III, 194 IV	Newly diagnosis or treatment	DT ≥4
de Mol *et al*,[25] 2017	The Netherlands	Cross- sectional	113	64/49	63	Mixed	113 III	At the time of the first cycle of treatment (first-line carboplatin)	DT ≥5
Geerse *et al*,[7] 2019	The Netherlands	Cross- sectional	97	53/44	60	Mixed	26 I and II, 61 III and IV	Newly diagnosed or recurrent lung cancer starting systemic treatment	DT ≥5
Lynch *et al*,[21] 2010	UK	Cross- sectional	33	15/19	62	Mixed (24 SCLC, 3 SCLC and 7 others)	1 I, 15 III, 8 IV	Since initial diagnosis varied from less than 3 months to over 2 years	DT ≥4
McFarland *et al*,[22] 2019	USA	Cross- sectional	109	41/68	65	Mixed	109 IV	On active treatment for at least 1 month	DT ≥4
Sherry *et al*,[14] 2017	USA	Cross- sectional	92	NR	NR	NR	Metastatic lung cancer	Undergoing cancer treatment	DT ≥4
Steinberg *et al*,[23] 2009	Canada	Cross- sectional	98	54/44	63	87 NSCLC, 11 SCLC	NR	First visit postdiagnosis and prior to any treatment	DT ≥4
Tan *et al*,[24] 2019	China	Cross- sectional	420	313/107	57	332 NSCLC, 88 SCLC	212 I-III, 208 IV	First time to the thoracic department of Hunan Cancer Hospital	DT ≥4

DT, distress thermometer; F, female; M, male; NR, not reported; TNM, tumour, node, metastasis.

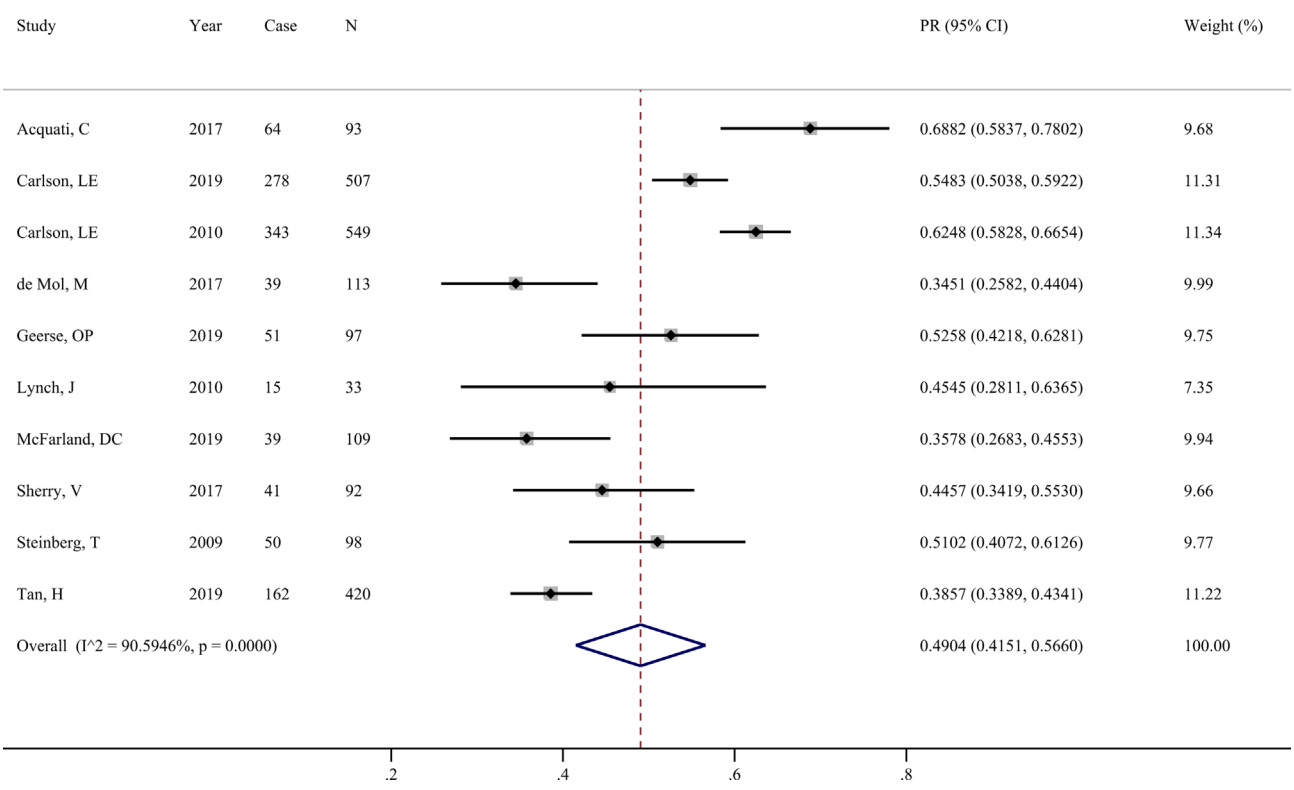

Figure 2 Forest plot for the meta-analysis of pooled PR of distress in the overall sample. PR positive rate.

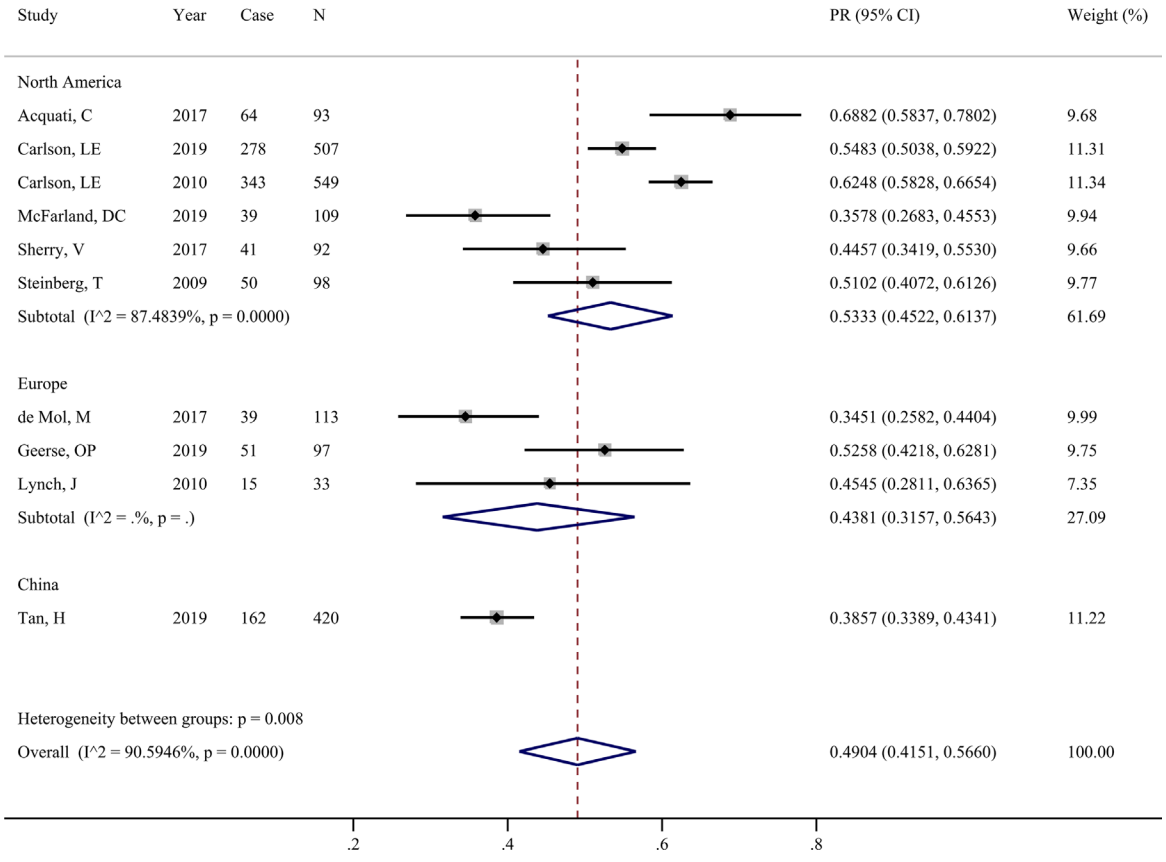

Figure 3 Forest plot for region. PR, positive rate.

Table 2 Characteristics of the studies in special group

Study	Year	Country	Distress cut-off	Case/N				
				Male	Female	NCLC	SCLC	Chemotherapy
Carlson *et al*[20]	2019	USA	DT ≥4	129/263	149/244	NR	NR	NR
de Mol *et al*[26]	2017	The Netherlands	DT ≥5	21/64	18/49	35/99	4/14	5/9
Geerse *et al*[7]	2019	The Netherlands	DT ≥5	27/53	24/44	42/77	8/18	32/54
Tan *et al*[24]	2019	China	DT ≥4	115/313	47/107	130/332	32/88	136/349

DT, distress thermometer; NR, not reported; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

and 49.71% (95% CI 37.99% to 61.45%), respectively (figure 4A). The pooled risk difference between men and women was −8.84% (95% CI −14.84% to −2.84%); the difference was significant (p<0.05) (figure 4B).

Additionally, the influence of histological type was analysed. The pooled positive rates of NSCLC and SCLC were 42.26% (95% CI 32.91% to 51.90%) and 36.35% (95% CI 27.65% to 45.49%), respectively (online supplemental figure S1A). The merged risk difference for NSCLC and SCLC was 4.39% (95% CI −05.20% to 13.99%), which was not a significant difference (p>0.05) (online supplemental figure S1B). The combined positive rates were 46.15% (95% CI 26.59% to 66.63%) in stages I and II, 33.96% (95% CI 27.62% to 40.76%) in stages I–III, 34.51% (95% CI 25.82% to 44.04%) in stage III, 41.51% (95% CI 36.62% to 46.48%) in stage IV and 55.74% (95% CI 42.45% to 68.45%) in stages III and IV, which were not significantly different (p>0.05). Meanwhile, the previous treatment was analysed. The pooled results were 49.07% (95% CI 32.34% to 65.90%) for chemotherapy, 35.71% (95% CI 12.76% to 64.86%) for surgery and adjuvant chemotherapy, 34.29% (95% CI 25.77% to 43.34%) for chemotherapy and radiotherapy, and 47.06% (95% CI 22.98% to 72.19%) for biological therapy (online supplemental figure S3), which were not significantly different (p>0.05). Thus, the positivity of distress was not related to histological type, clinical TNM stage and previous treatments.

Further, the combined distress positive rate for cut-off values of 4 and 5 were 50.46% (95% CI 42.02% to 58.88%) and 42.74% (95% CI 36.09% to 49.53%), respectively. Positive rate decreases as the threshold increases; however, the difference is not statistically significant (p>0.05) (online supplemental figure S4). Additionally, stratified analyses were conducted by sample size. The combined positive rates of the sample size of <100 vs the ≥100 groups were 53.10% (95% CI 44.08% to 62.02%) and 45.62% (95% CI 34.52% to 56.95%), respectively, which is not a significant difference (p>0.05) (online supplemental figure S5). Thus, the distress was not affected by DT threshold and clinical sample size.

Publication bias

Publication bias was acquired from Begg's funnel plot and Egger's test. The funnel plots did not expose any clear asymmetry (figure 5). No significant publication bias was identified (p>0.05). Both measures indicated that there was a lack of significant small sample effects between the included studies.

DISCUSSION

This study pooled the distress positivity of patients with lung cancer by DT screenings and found the

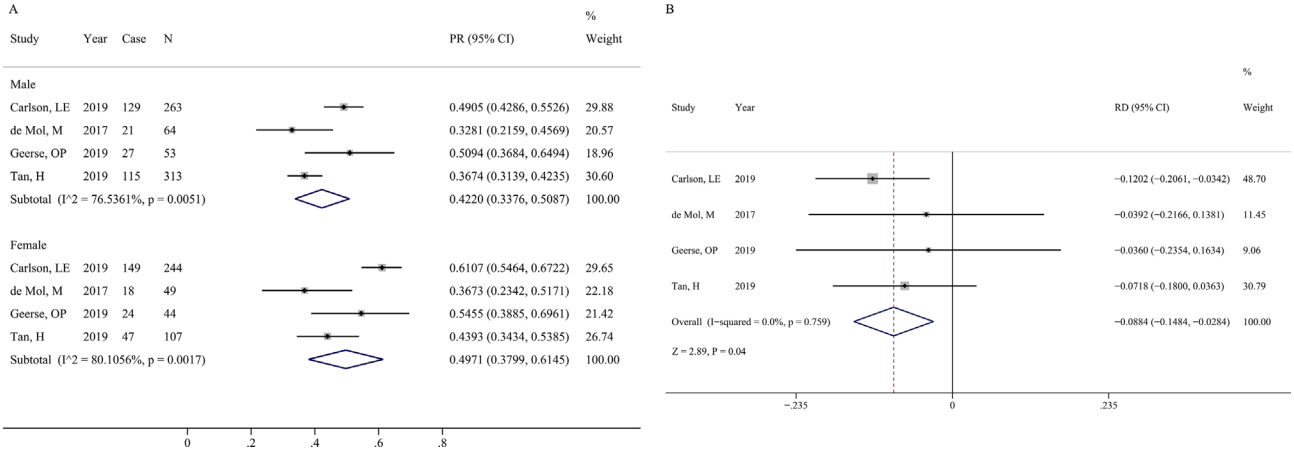

Figure 4 (A) Forest plot for male gender versus female gender. (B) Forest plot of RD for male gender versus female gender. PR, positive rate; RD risk difference.

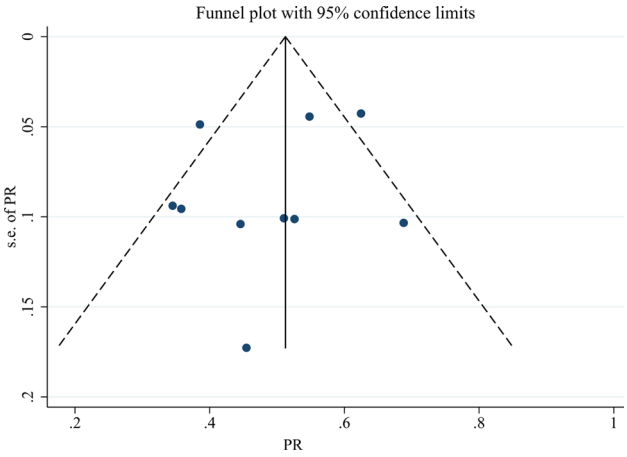

Figure 5 Funnel plot for the included studies that examined small study effects. PR, positive rate.

summarised positive rate of distress was high. Almost half of the patients with lung cancer were distressed, which was with tremendous clinical challenge. Further, the positive rate of distress was significantly differently related to region and gender. There was no significant difference with histological type, clinical TNM stage, previous treatment, DT threshold and sample size. To the best of our knowledge, this is the first study to summarise the distress positivity of patients with lung cancer using DT screening based on a meta-analysis.

This study illustrated that distress was found in about half of patients with lung cancer. Carlson *et al*[6] reported difference in distress by cancer type, such as higher rates of distress positivity among those with lung cancer (54.8%). Plank *et al*[26] reported a distress prevalence of 65% in patients with lung cancer. Moreover, among 3095 malignant patients screened by the BSI-18, the percentage of distress cases among lung cancer was 57.6%, which is the highest, followed by the percentage among patients with cancer of the pancreas (52.2%).[27] In this study, the positive rate of distress in lung cancer was 49.04%, based on previous publications, which was higher than primary brain cancer (38%),[12] prostate cancer (28%)[28] and head and neck cancer (35%–41%).[29] High psychological distress may result from fear of recurrence, uncertainty of survival, health-related stigma, weakened respiratory system, as well as financial problems.[4] Psychological distress lowers the quality of life and negatively impacts treatment compliance, which were related with poor prognosis. Thus, routine screening and evaluation of distress at the initial time of lung cancer diagnosis might provide an opportunity for early intervention and improve distress management.

We also found the positive rate of distress in different regions featured significant differences. Despite having the largest lung cancer population, China only had one eligible publication.[24] In the related study, the prevalence of distress in patients with lung cancer in China was 38.6%, and the most common causes were financial concerns and worry. Moreover, the populations in rural areas (54.7%–74.7%) have higher levels of distress than urban areas (25.3%–45.3%) due to poor education with limited access to healthcare and low income.[24] Mou *et al* reported that the proportion of the distress in patients of Cancer Centre of West China Hospital of Sichuan University in Chengdu with lung cancer was 30% using the HADS,[30] and the top five causes of distress were worry, disease treatment, breathing, pain and sleep. In addition, the prevalence in USA ranged from 43.4% using the BSI[31] to 61.6% by DT screenings.[32] Carlson *et al*[27] found a slightly lower level of distress (37.8%) in patients with lung cancer in Canada using the DT as a screening tool. However, many studies lack sensitivity and specificity data for DT screening, and define DT positivity as distress prevalence while ignoring the possibility of false positivity. The experience of distress is found worldwide, but the form it takes, including how the patient with cancer puts it into words or otherwise experiences it, varies from culture to culture. It has reported that the key expressions of spiritual well-being and distress in cancer patients are culturally dependent.[33] Besides, religious patients with cancer might live their spirituality through religiosity and other dimensions to reduce anxiety . Thus, the differences in prevalence of distress in regions may be related to the enrolled populations, cultural, religious, education and income differences.[34] More studies will be needed to evaluate prevalence rates in Asian countries, and the source of distress should be explored.

Our results also indicate that the positive rate of distress remarkably differs based on gender. This difference may reflect a gender difference in willingness to report distress but could also arise from the usage of emotional approach in coping. Using HADS evaluation, there was 41% distress in female patients with lung cancer compared with a 29% in male patients, which is a remarkable difference.[35] Among a total of 228 patients with lung cancer, the percentage of distress was 58.2% vs 33.6% in women and men, respectively.[36] Among 5335 patients with cancer assessed by DT screenings, the prevalence of distress was 36.0% vs 28.7% in women and men, respectively.[37] A recent review indicated that the prevalence of distress in pan-cancer patients was higher in female compared with male.[6] These findings were quite consistent with our results. In addition, it has been reported that across cancer types, female patients with cancer showed higher prevalence rates of anxiety and depression than male patients.[38] Also, our finding was consistent with higher rates of anxiety and depression in the general healthy female population as compared with the male population.[39] Thus, the psychological problems of female patients should be paid more clinical attention, and more support should be given by family, friends and society.

Psychological distress is common among patients with cancer; however, distress symptoms are often ignored and not given appropriate professional treatment.[40] Additional follow-ups would help in distress management. Routine screening and follow-up assessment will be needed to

establish individualised interventions. Mindfulness-based stress reduction therapy, telephone interventions and exercise interventions could be used to alleviate psychological distress symptoms.

As far as we know, this is the first meta-analysis on distress positivity among patients with lung cancer by DT screenings. Furthermore, the methodological quality of this meta-analysis is moderate, and there is no significant publication bias in this study. However, there are still some limitations regarding the present study. The included literature was mainly cross-sectional studies, without adequate follow-up data; thus, it was not possible to evaluate changes in distress following treatment or psychological counselling. Also, there is a significant heterogeneity among included studies, and the source of heterogeneity cannot be found through the subgroup analysis due to the limited sample size. In the future, more studies with follow-up data will be needed to evaluate the differences in positivity of distress across different regions and by gender.

CONCLUSIONS

In the present study, the summarised positive rate of distress in patients with lung cancer is high. Because of almost half of the patients suffered from distress, routine distress screening and evaluations might be necessary to develop early interventions and to improve distress management. Moreover, the distress positivity was associated with gender and region, which were not related to histological type, clinical TNM stage, previous treatment and DT threshold. Thus, the psychological problems of female patients and region difference should be paid more clinical attention.

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Contributors LZ, XL and FT carried out the conception and design of the research. RZ, WP and HY participated in the acquisition of data. XH, LY, MW, LJ and FL carried out the analysis and interpretation of data. LZ and XL participated in the design of the study and prepared and revised the manuscript. All authors read and approved the final manuscript. LZ and XL were guarantor of this manuscript.

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Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository.

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