Psychotherapy for advanced cancer patients: A meta-analysis of the quality of life and survival assessments

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Abstract

Objectives. A meta-analysis has explored the effect of psychotherapy on the quality of life (QOL) but has not explored the effect on advanced cancer patients' survival, which is highly debated. Therefore, we consider the survival days and QOL as the primary outcomes in our analysis.

Methods. Eligible studies were collected from four databases (PubMed, Embase, Cochrane Library, and Web of Science) until February 20, 2021. The pooled effect sizes were presented as weighted mean difference (WMD) or relative risk (RR) with 95% confidence intervals (CIs). Publication bias was evaluated by Egger's test, and I^2 statistics was used to assess the heterogeneity.

Results. Thirty-three studies were finally included, containing 2,159 patients in the psychotherapy group and 2,170 patients in the control group. McGill Quality of Life Questionnaire (MQOL) and European Organization for Research and Treatment of Cancer Quality of Life-C15-Palliative (EORTC-QLQ-C15-Pal) supported that QOL of the psychotherapy group was significantly higher than that of the control group, and WMD value was 0.42 (95% CI: 0.12–0.71) and 17.26 (95% CI: 11.08–23.44), respectively. No significant difference was observed between the two groups regarding to the survival time (WMD: 17.85, 95% CI: −8.79, 44.49, $P = 0.189$). Moreover, the levels of anxiety, depression, confusion, pain, and suffering were lowered in psychotherapy group (all $P < 0.05$).

Significance of results. Psychotherapy could improve the QOL of advanced cancer patients but not affect the survival time.

Introduction

Global cancer statistics report approximately 19.3 million new cancer cases and an estimated 10.0 million cancer deaths in 2020 (Sung et al., 2021). Despite advancement in cancer diagnosis and therapy, most of the patients are still definitely diagnosed at advanced stage (Zhang and Yang, 2020; Zhu et al., 2021). Advanced cancer is characterized by the poor prognosis and incurability (Luo et al., 2019), and its incidence and mortality are annually increasing (Wu et al., 2020). Studies have shown patients with advanced cancer face huge psychological burden, which affects their quality of life (QOL) (Breitbart et al., 2018; Teo et al., 2019; de Mol et al., 2020). Therefore, it is necessary to pay close attention to the psychological status of advanced cancer patients.

Psychotherapy has been increasingly applied to improve the psychological status of cancer patients at advanced stage (Breitbart et al., 2018; Rosenfeld et al., 2018; Teo et al., 2019). For advanced cancer patients, psychotherapy is effective to decrease depression, increase existential happiness, and improve QOL (Okuyama et al., 2017; Teo et al., 2019). However, the relationship between psychotherapy and survival is highly debated (Coyne et al., 2007; Kissane, 2007, 2009). Huang et al. found that advanced lung cancer patients receiving psychological intervention presented a higher survival rate than the control group (Huang et al., 2019). Hou et al. found that advanced cervical cancer patients benefited from the psychotherapy in terms of 2-year survival (Hou et al., 2021). However, some studies showed that psychotherapy was not clinically effective on the survival of patients with malignant or advanced cancers (Boesen et al., 2007; Kissane et al., 2007). An existing meta-analysis has reported the effect of psychotherapy on the depression, anxiety, distress, and QOL of advanced cancer patients (Okuyama et al., 2017), while this meta-analysis fails to consider the effect of psychotherapy on survival.

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Herein, we performed a meta-analysis based on the currently available studies to comprehensively explore the effect of psychotherapy on the QOL and survival days among advanced cancer patients, which provided evidence for the application of psychotherapy in the clinic.

Methods

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Moher et al., 2009).

Literature search strategy

The literatures were available from Pubmed, Embase, Cochrane Library, and Web of Science, and the deadline for searching literatures was February 20, 2021. Two independent researchers (Y.Q.W. and J.J.P.) searched the literatures, and search strategies included: "Psychotherapy" OR "Psychotherapies" OR "Psychosocial intervention" OR "Intervention, psychosocial" OR "Interventions, psychosocial" OR "Psychosocial interventions" OR "Psychological intervention" OR "Intervention, psychological" OR "Interventions, psychological" OR "Psychological interventions" OR "Spiritual therapies" OR "Therapies, spiritual" OR "Exorcism" OR "Exorcisms" OR "Spiritual healing" OR "Healing, spiritual" OR "Healings, spiritual" OR "Spiritual healings" OR "Psychotherapy, group" OR "Group psychotherapy" OR "Therapy, group" OR "Group therapy" OR "Supportive-expressive group" AND "Neoplasms" OR "Neoplasia" OR "Neoplasias" OR "Neoplasm" OR "Tumors" OR "Tumor" OR "Cancer" OR "Cancers" OR "Malignancy" OR "Malignancies" OR "Malignant neoplasms" OR "Malignant neoplasm" OR "Neoplasm, malignant" OR "Neoplasms, malignant."

Inclusion and exclusion criteria

Inclusion criteria: (1) patients with advanced cancer; (2) the intervention group receiving psychotherapy, while the control group receiving usual care, massage, or supportive psychotherapy; (3) randomized controlled trials (RCTs) and quasi-experimental studies; and (4) studies published in English.

Advanced cancer was defined that the study used the term "advanced cancer" or reported the patients with metastatic cancer or at III and IV stages.

The psychotherapy included group psychosocial support, cognitive-behavioral therapy, individual meaning-centered psychotherapy, positive affect skill intervention, dignity therapy, forgiveness therapy, mindfulness intervention, and focused narrative intervention.

Exclusion criteria: (1) animal experiments or *in vitro* experiments; (2) duplicated studies and studies not related to our research topic; (3) studies without full text (or only abstract available) or data not available; and (4) conference reports, case reports, meta-analyses, reviews, editorial materials, letters, protocols, errata, and notes.

Data extraction

The research data were independently screened by two researchers (Y.Q.W. and J.J.P.) in accordance with inclusion and exclusion criteria, and the third researcher (Y.L.) would participate in the data extraction when the conflict existed. The extracted data included the name of the first author, year of publication, country, study design, group, intervention type, intervention/control properties, number of participants in each group, sex, age, cancer type, and outcomes.

Outcome measurements

The primary outcomes were identified *a priori* as of interest, and the secondary outcomes were identified in the course of screening studies.

Primary outcomes

1. QOL, as measured using McGill Quality of Life Questionnaire (MQOL) (Cohen et al., 1995), Functional Assessment of Cancer Therapy (FACT-G) (Cella et al., 1993), European Organization for Research and Treatment of Cancer Quality of Life-C15-Palliative (EORTC-QLQ-C15-Pal) (Groenvold et al., 2006), EuroQol 5 Dimensions (EQ-5D) ("EuroQol Group", 1990), and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) (Aaronson et al., 1993).
2. Survival time.

Secondary outcomes

1. Mood, as measured using Hamilton Anxiety Rating Scale (HAM-A) (Hamilton, 1959), Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983), Beck Depression Inventory-II (BDI-II) (Beck et al., 1961), Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977), Patient Health Questionnaire 9 (PHQ-9) (Kroenke et al., 2001), Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being Scale (FACIT-Sp) (Peterman et al., 2002), Herth Hope Index (HHI) (Herth, 1992), Beck Hopelessness Scale (BHS) (Beck et al., 1974), Brief COPE (Carver, 1997), and Profile of Mood States (POMS) (Mcnair et al., 1971).
2. Symptom, as measured using Visual Analogue Scale (VAS) (Gift, 1989) and Brief Pain Inventory (BPI) (Cleeland and Ryan, 1994).

Methodological quality appraisal

The quality of researches relating RCTs was evaluated using the modified Jadad scale, which increased allocation concealment based on the Jadad scale (Jadad et al., 1996; Chen et al., 2020). This scale had a total score of 7, with a score of 1–3 for low quality and 4–7 for high quality. For the quality evaluation of researches relating quasi-experimental studies, Methodologic Index for Nonrandomized Studies (MINORS) scale was adopted (Slim et al., 2003). This scale was divided into 24 points, and 1–12 was considered as low quality, and 13–24 was considered as high quality.

Statistical analysis

Statistical analysis was performed using the software Stata 15.1 (Stata Corporation, College Station, TX, USA). The power of the analyses was assessed using G*Power 3.1 software (Universität Düsseldorf, Düsseldorf, Germany). The data measurement was calculated using relative risk (RR) or weighted mean difference (WMD) with 95% confidence interval (CI). Every indicator was evaluated by heterogeneity test, and measured by statistics of I-squared (I^2). The random effects model was applied with $I^2 \geq 50\%$, and the fixed effects model was used with $I^2 < 50\%$. The sensitivity analysis was performed for all

results, and publication bias was checked by Egger's test. $P < 0.05$ was considered statistical significance.

Results

Literature search and study selection

After the search procedure in database, a total of 29,934 studies were searched. After duplicates removal, 16,984 records retained. Among which, 16,837 records that subjects did not meet the requirements ($n = 9,234$), published as abstracts or protocol ($n = 3,041$), reviews or meta-analyses ($n = 2,507$), and not English articles ($n = 1,453$), included animal experiments ($n = 245$), were editorial materials, letters, correction, erratum, note ($n = 201$), case reports ($n = 138$), or unable to get full texts ($n = 18$) were excluded to obtain 147 eligible articles. After further exclusion, 33 studies were finally included, with 30 RCTs and 3 quasi-experimental studies (Supplementary File 1). In finally included studies, 17 were assessed as high-quality articles, and 16 were assessed as low-quality articles. The retrieval flowchart is seen in Figure 1. Of the total 4,329 advanced patients, 2,159 were in the psychotherapy group and 2,170 were in the control group. The baseline characteristics are shown in Supplementary Table S1.

Effect of psychotherapy on QOL and survival time

Table 1 presents the summary results of the effect of psychotherapy on QOL and survival days compared to the control group. In MQOL and EORTC-QLQ-C15-Pal, WMD values were 0.42 (95% CI: 0.12–0.71) and 17.26 (95% CI: 11.08–23.44), respectively, revealing that the QOL of the psychotherapy group was higher than that of the control group (Figure 2a,b). EORTC QLQ-C30 manifested that the global health was better (WMD: 3.86, 95% CI: 0.51–7.20, $P = 0.024$), and the constipation symptom was slighter in the psychotherapy group (WMD: −4.70, 95% CI: −7.10 to −2.29, $P < 0.001$) than the control group (Figure 2c,d). No significant heterogeneity was observed in above three scales ($I^2 = 0.0\%$). The QOL showed no difference between the two groups according to FACT-G and EQ-5D with P-value of 0.131 and 0.273, respectively. Three studies provided data on survival days, and the pooled result showed that the survival time of the two groups had no statistical significance (WMD: 17.85, 95% CI: −8.79 to 44.49, $I^2 = 10.7\%$, $P = 0.189$) (Figure 3). The power of the analysis is shown in Supplementary Table S2.

Effect of psychotherapy on mood and symptom

Table 1 shows the summary of psychotherapy effect size on mood and symptom compared to the control group. HAM-A demonstrated no significance in the anxiety between the two groups, but HADS indicated the significantly lower anxiety in the psychotherapy group (WMD: −1.62, 95% CI: −2.74 to −0.50, $P = 0.005$). HADS also displayed that the depression was lower in the psychotherapy group (WMD: −1.62, 95% CI: −2.78 to −0.46, $P = 0.010$). The similar result was found in BDI-II and CES-D, and the WMD values were −3.44 (95% CI: −6.00 to −0.87, $I^2 = 36.6\%$, $P = 0.009$)

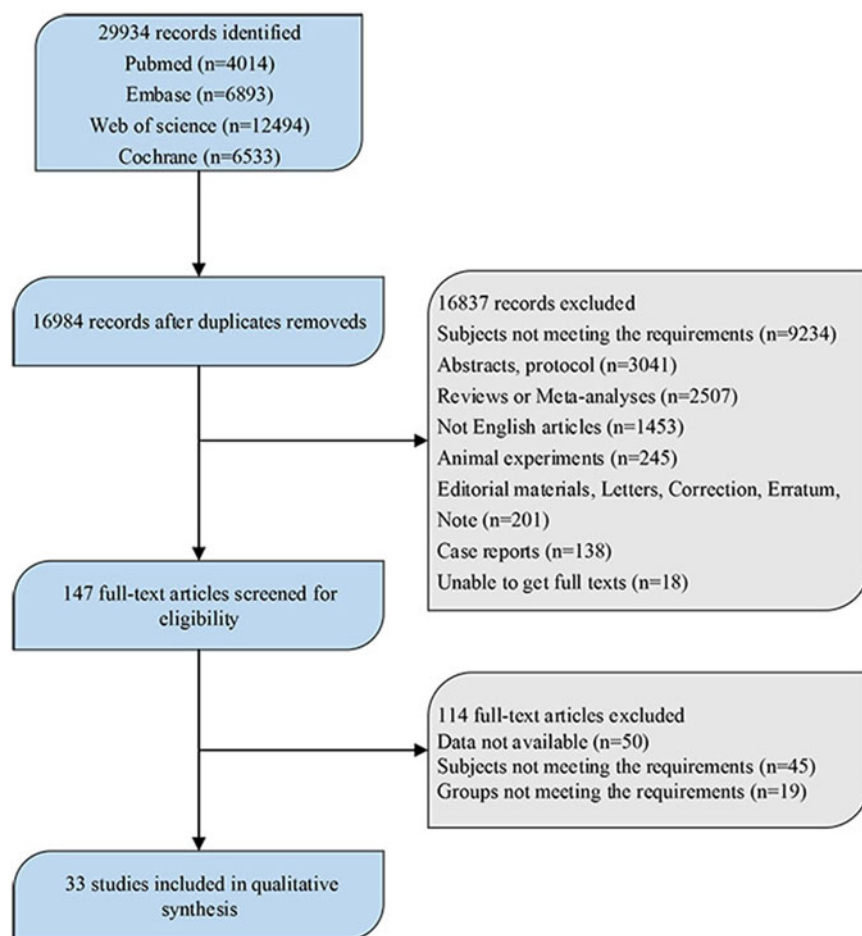Fig. 1. Flowchart of the retrieval process.

Table 1. Overall results of the meta-analysis

Outcomes	WMD/RR (95% CI)	P	I^2 (%)
QOL			
MQOL	0.42 (0.12, 0.71)	0.006	0.0
FACT-G	10.33 (−3.07, 23.74)	0.131	82.7
EORTC-QLQ-C15-Pal	17.26 (11.08, 23.44)	<0.001	0.0
EQ-5D	0.05 (−0.04, 0.13)	0.273	0.0
QoL-EORTCQLQ-C30			
Global health	3.86 (0.51, 7.20)	0.024	0.0
Constipation	−4.70 (−7.10, −2.29)	<0.001	0.0
Survival	17.85 (−8.79, 44.49)	0.189	10.7
Mood			
HAM-A	−3.16 (−6.88, 0.56)	0.096	80.3
HADS			
Anxiety	−1.62 (−2.74, −0.50)	0.005	81.4
Depression	−1.62 (−2.78, −0.46)	0.010	88.6
BDI-II	−3.44 (−6.00, −0.87)	0.009	36.6
CES-D	−7.02 (−13.29, −0.74)	0.028	0.0
PHQ-9			
Total score	−1.97 (−4.41, 0.46)	0.112	85.3
Score reduction ≥ 5	1.97 (1.31, 2.98)	0.001	0.0
FACIT-Sp			
Total score	0.03 (−1.59, 1.64)	0.975	0.0
Meaning + peace score	7.65 (−0.85, 16.16)	0.078	86.8
HHI	1.63 (−0.23, 3.49)	0.087	0.0
BHS	−0.12 (−0.86, 0.62)	0.755	0.0
Brief cope			
Active coping	−0.06 (−0.42, 0.30)	0.748	0.0
Avoidant coping	0.03 (−0.15, 0.21)	0.773	67.7
POMS			
Confusion	−1.08 (−2.13, −0.02)	0.046	13.0
Symptom			
VAS			
Pain	−0.96 (−1.30, −0.61)	<0.001	0.0
Suffering	−0.70 (−1.24, −0.16)	0.011	0.0
BPI	−0.40 (−1.20, 0.40)	0.328	0.0

WMD, weighted mean difference; RR, relative risk; CI, confidence interval; QOL, quality of life; MQOL, McGill Quality of Life Questionnaire; FACT-G, Functional Assessment of Cancer Therapy; EORTC-QLQ-C15-Pal, European Organization for Research and Treatment of Cancer Quality of Life-C15-Palliative; EQ-5D, EuroQol 5 Dimensions; QoL-EORTCQLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; HAM-A, Hamilton Anxiety Rating Scale; HADS, Hospital Anxiety and Depression Scale; BDI-II, Beck Depression Inventory-II; CES-D, Center for Epidemiologic Studies Depression Scale; PHQ-9, Patient Health Questionnaire 9; FACIT-Sp, Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being Scale; HHI, Herth Hope Index; BHS, Beck Hopelessness Scale; POMS, Profile of Mood States; VAS, Visual Analogue Scale; BPI, Brief Pain Inventory.

and −7.02 (95% CI: −13.29 to −0.74, $I^2 = 0.0\%$, $P = 0.028$), respectively. Five points or more reduced in PHQ-9 was defined as clinical significance in response to depression treatment (Lloyd-Williams et al., 2018). Although PHQ-9 revealed no

difference in depression between the two groups ($P = 0.112$), the proportion of patients with a decrease in PHQ-9 scores of five points or more in the psychotherapy group was higher than that in the control group (RR: 1.97, 95% CI: 1.31–2.98, $I^2 = 0.0\%$, $P = 0.001$). Moreover, psychotherapy greatly improved the confusion (WMD: −1.08, 95% CI: −2.13 to −0.02) according to POMS, and P-value was 0.046. In FACIT-Sp, the total score and score for meaning plus peace dimensions was not statistically significant between the two groups (both $P > 0.05$), indicating that the spiritual well-being could not be improved by psychotherapy. Moreover, HHI and BHS, respectively, showed hope and hopelessness did not have statistical significance between the two groups with P-value of 0.087 and 0.755. Displayed by Brief COPE, coping strategies were not statistically significant between the two groups with P value for active coping and avoidant coping was 0.748 and 0.773, respectively.

The symptom was measured using VAS and BPI, and no heterogeneity was observed ($I^2 = 0.0\%$). VAS revealed that the pain level was significantly lower in the psychotherapy group (WMD: −0.96, 95% CI: −1.30 to −0.61), with $P < 0.001$. Moreover, a great improvement of suffering was observed in the psychotherapy group, and WMD was −0.70 (95% CI: −1.24 to −0.16, $P = 0.011$). Nevertheless, BPI represented no significance in the pain level between the two groups ($P = 0.328$). The power of the analysis is displayed in Supplementary Table S2.

Publication bias and sensitivity analysis

Publication bias was carried out by Begg' test. No publication bias was observed in mood evaluation of anxiety (Z = 0.72, P = 0.474) and depression (Z = 0.09, P = 0.929). The sensitivity analysis was used to assess the stability of analysis results, and showed a good stability of all results, prompting that the results were reliable.

Discussion

Thirty-three studies exploring the effect of psychotherapy on the QOL or the survival days were included in this meta-analysis. Overall results manifested that psychotherapy could improve the QOL, but could not affect the survival time of advanced cancer patients. Moreover, psychotherapy lowered the levels of anxiety, depression, confusion, pain, and suffering.

The QOL of advanced cancer patients is a main concern for clinicians. In many countries, the decreased QOL of cancer patients at advanced stage is a common clinical problem (Daly et al., 2020; Hsieh et al., 2020). In addition to radiotherapy and drug treatments, psychotherapy has become an important support strategy for advanced cancer patients (Giese-Davis et al., 2002; Akechi et al., 2018). The psychological interventions were mainly centered on finding the meaning and goal at the last stages of patients' lives by strengthening the communication with families and friends to help them decrease the cancer-related distress and pain so as to improve the QOL (Teo et al., 2019). A lot of studies have reported the effective role of psychotherapy in the improvement of QOL. Breitbart et al. (2018) found that psychotherapy had a greater effect on the QOL compared with the control group. Clark et al. (2013) found that the overall QOL was higher in the psychotherapy group, and recommended psychotherapy as a supplementary strategy to improve QOL among advanced cancer patients. In this meta-analysis, the overall results
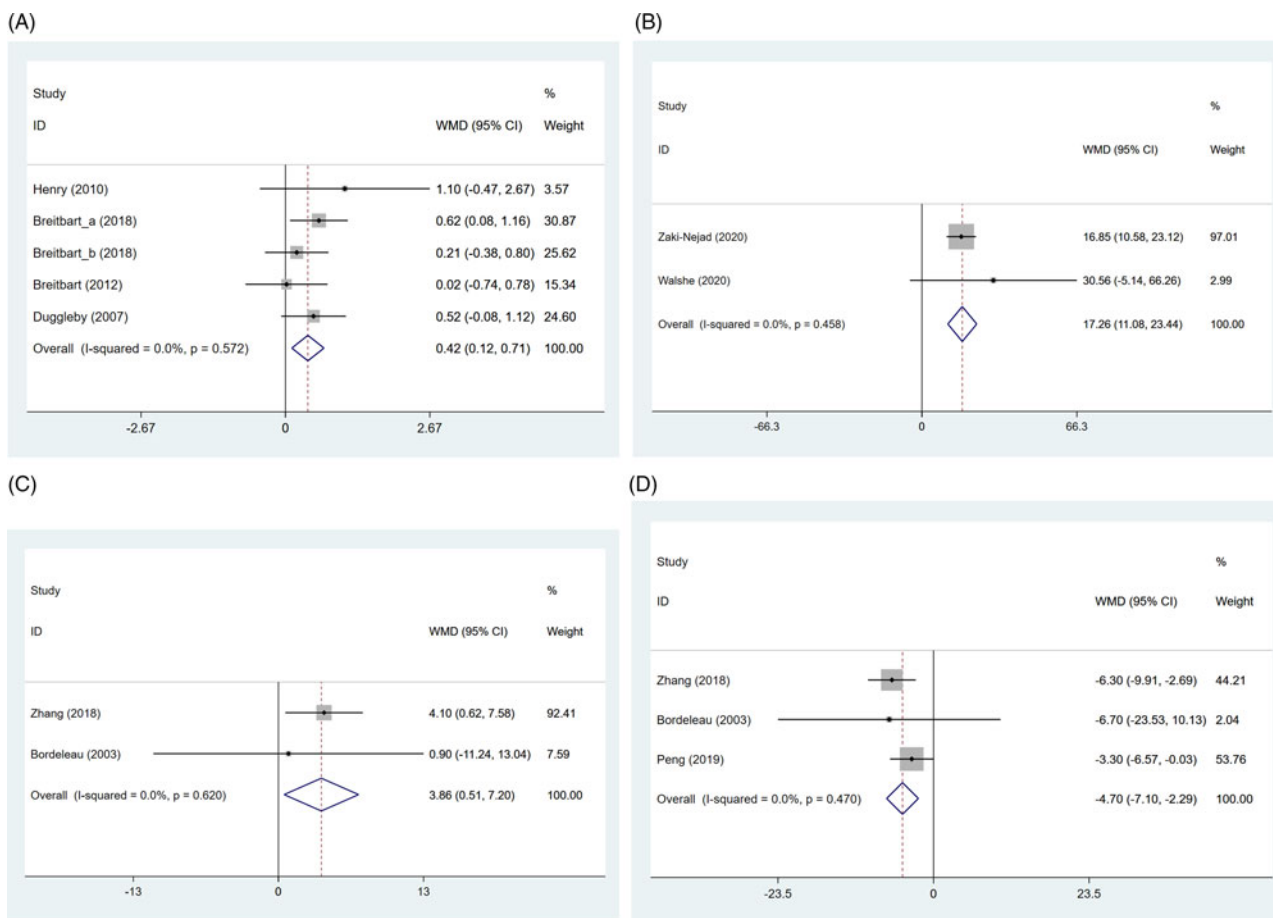
Fig. 2. Forest plots for QOL measurement: (a) MQOL, (b) EORTC-QLQ-C15-Pal, (c) global health using EORTC QLQ-C30, and (d) constipation in EORTC QLQ-C30.
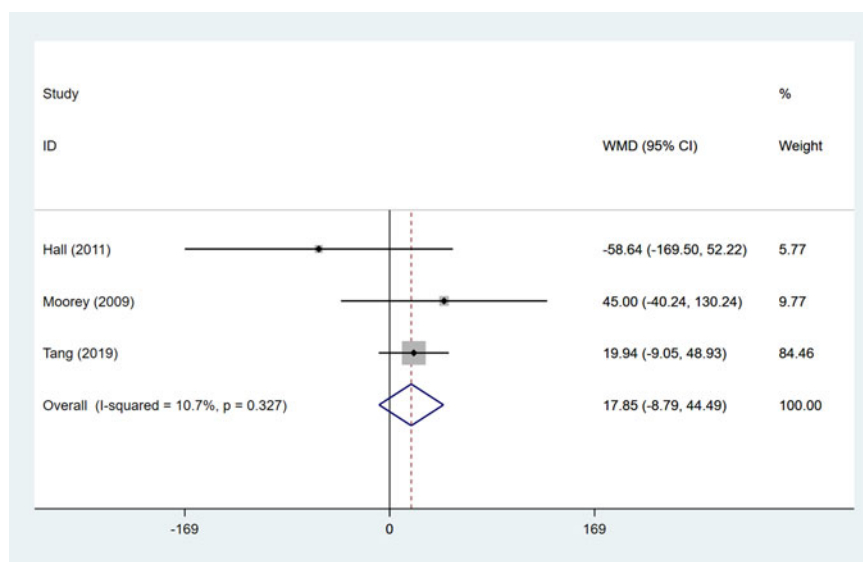
Fig. 3. Forest plots for survival days.

supported that the psychotherapy group exhibited a higher QOL than the control group.

The survival time for advanced cancer is another main concern for clinicians, patients, and their families (Peng et al., 2020). Although advanced cancer is incurable, many therapies are attempted to prolong the survival time of the patients

(O'Shaughnessy et al., 2020). Some studies have reported the impact of psychotherapy in the survival of advanced cancer patients (Coyne et al., 2007; Kissane, 2007, 2009). Our results revealed that the survival time was not affected by psychotherapy. Goodwin et al. performed a multicenter randomized controlled trial to explore the effect of psychotherapy on the survival time

of patients with advanced cancer, and the result showed psychotherapy did not prolong the survival (Goodwin et al., 2001). The similar result was found in the study of Kissane et al. (2007). However, Steel et al. (2007) reported that advanced cancer patients accepting the psychotherapy had slightly longer survival days than those not accepting the psychotherapy. Huang et al. (2019) and Hou et al. (2021) reported the similar result. Further studies were needed to make clear whether we should expect psychotherapy to impact survival time or not.

The mood and symptom managements are important to maintain the QOL of advanced cancer patients. Approximately 15% of advanced cancer patients suffer from depression, and 10–15% of them suffer from severe anxiety and other psychological symptoms (Hotopf et al., 2002). Existing studies have indicated that psychotherapy could improve the anxiety and depression of patients with advanced cancer (Teo et al., 2020). Our study also showed the lower degree of anxiety and depression in the psychotherapy group. Pain is the most common and debilitating symptoms related to cancers (Hackett et al., 2016). Among the patients with advanced cancer, about 66% of them suffer from the pain (van den Beuken-van Everdingen et al., 2016). The poorly controlled pain usually impairs patients' QOL (Marinova et al., 2021). Evidence has shown that psychological interventions can effectively improve the pain (Laely et al., 2018). In our meta-analysis, the greater improvement of pain was found in the psychotherapy group, which was consistent with studies of Kwekkeboom et al. (2018) and Warth et al. (2020).

Our meta-analysis includes a large number of studies from various databases to comprehensively evaluated the effect of psychotherapy on the QOL and survival time of advanced cancer patients. The publication bias and sensitivity analysis show the good stability of our analysis results, which make our results more reliable. However, some limitations of this study should be concerned. First, the included studies do not support us to stratify the psychotherapy interventional strategies according to the outcomes. Further studies should be performed to explore the types of psychotherapies for particular outcomes. Second, our analysis includes too many scales, and differences are existed in these scales. Therefore, it is unable to determine which scale is more suitable for the advanced cancer patients. Considering the difficulty in the implement and quality evaluation of psychological intervention in clinical experiment, innovative and practical quality evaluation systems for advanced cancer patients are needed to provide reference for the clinicians to adopt more appropriate treatment for them. Third, the power of the analyses is relatively low; thus, our analysis results require further evidence.

The implement of psychotherapy may be limited by some reasons, such as the shortage of financial supports, the shortage of practice experience in the psychotherapy among advanced cancer patients, or the shortage of professional providers. Our study still encourages the clinicians overcome such difficulties to provide evidence-based psychotherapy for the patients with advanced cancer to improve their QOL in the last period of lives.

In conclusion, psychotherapy could improve the QOL of advanced cancer patients although no effect on the survival time. The anxiety, depression, and pain were also greatly improved by psychotherapy. These findings might provide evidence-based direction for clinicians in clinical practice.

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