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Impact of psychological interventions on the intraoperative outcomes in transcatheter arterial chemoembolization for hepatocellular carcinoma: A meta-analysis

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Abstract: Objective: This meta-analysis aimed to evaluate the impact of psychological interventions on the intraoperative outcomes in patients undergoing transcatheter arterial chemoembolization (TACE) for liver cancer. **Methods:** A comprehensive search was conducted using computer databases including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), China Biomedical Literature Database (CBM), and Wanfang Database. Reference lists of relevant studies were also reviewed to ensure completeness. The quality of included studies was assessed using the Jadad scoring system. Meta-analysis was performed using RevMan 5.2.7, a statistical software provided by the Cochrane Collaboration. **Results:** A total of eight studies comprising 790 patients were included, comparing psychological intervention groups with control groups. The meta-analysis revealed significant differences favoring the psychological intervention group in systolic blood pressure (MD = -15.95 mmHg, 95% CI: -22.31 to -9.25, $P < 0.0001$), heart rate (MD = -10.68 bpm, 95% CI: -13.87 to -7.48, $P < 0.0001$), anxiety scores (MD = -2.39, 95% CI: -3.35 to -1.43, $P < 0.0001$), and the incidence of intraoperative anxiety (OR = 0.32, 95% CI: 0.19 to 0.52, $P < 0.0001$) compared to the control group. **Conclusion:** Psychological interventions significantly alleviated negative emotions in patients undergoing TACE for liver cancer, contributing to better intraoperative stability in the control group. These findings suggest that psychological support may facilitate the smooth conduct of the TACE and potentially enhance overall treatment outcomes.

Keywords: hepatocellular carcinoma; psychological intervention; transarterial chemoembolization (TACE); intraoperative outcomes; meta-analysis

1. Introduction

Liver cancer remains one of the leading causes of cancer-related mortality globally [1,2]. Key risk factors for hepatocellular carcinoma (HCC) include smoking, substance abuse, alcohol consumption, and a high body mass index (BMI), all of which contribute significantly to patient mortality [3]. Epidemiological data reveal that China accounts for the highest number of deaths from alcohol-related liver cancer among 204 countries and regions, with males and individuals aged 40–75 years facing a disproportionately higher disease burden compared to females and other age groups

[4]. As a result, improving the prognosis of liver cancer patients has become a critical public health challenge. Surgical interventions have been shown to substantially enhance both overall survival and cancer-specific survival in liver cancer patients [5]. With ongoing advancements in medical technology and the growing emphasis on “patient-centered” care, minimally invasive treatment options have garnered increasing attention and are progressively being integrated into clinical practice. Transcatheter arterial chemoembolization (TACE) has become a widely recognized alternative to surgical intervention for the management of liver cancer [6,7]. This minimally invasive technique involves the precise delivery of chemotherapeutic agents directly to hepatic tumors via catheterization of the hepatic artery, providing a targeted and efficacious therapeutic modality. Nevertheless, liver cancer predominantly afflicts middle-aged and elderly populations, who frequently encounter substantial economic and emotional burdens associated with the disease [8]. From an objective perspective, patients with liver cancer often develop adverse perceptions regarding the severity of their condition, which may be further compounded by financial strain and emotional distress, thereby reinforcing detrimental cognitive patterns. For instance, while therapeutic agents such as Camrelizumab and Lenvatinib have shown significant efficacy in improving quality-adjusted life years, their costs are substantially higher compared to conventional treatments like sorafenib [9]. Additionally, rehospitalization due to comorbidities can further intensify the financial burden on patients [10]. From a subjective standpoint, the clinical manifestations of liver cancer can profoundly disrupt daily functioning, detrimentally impact psychological well-being and exacerbating the overall symptom burden. Empirical studies have consistently established a robust association between heightened symptom burden and elevated levels of anxiety and depression among cancer patients [11]. Moreover, cancer patients often experience varying degrees of perioperative pain, which may persist for up to one month following surgery [12]. This persistent pain can further exacerbate negative emotional states in patients. Furthermore, TACE is typically conducted under local anesthesia, necessitating that patients remain conscious throughout the procedure. This heightened state of awareness may exacerbate stress and anxiety, resulting in elevated blood pressure and heart rate, which could not only impede the procedural workflow but also potentially undermine its therapeutic efficacy [13,14]. Consequently, addressing these psychological challenges is imperative, as heightened stress and emotional distress may adversely affect procedural outcomes and overall treatment success. In light of these considerations, there is an urgent imperative to investigate and implement effective interventions aimed at ameliorating negative emotional responses, optimizing therapeutic efficacy, and ultimately enhancing the quality of life for patients undergoing TACE.

A study investigated the potential of preoperative visits in mitigating postoperative psychological stress among liver cancer patients, demonstrating that such interventions are both feasible and beneficial [13]. These preoperative visits, which serve as a form of psychological intervention, offer patients critical information and emotional support, thereby addressing their psychological needs prior to surgery. As healthcare continues to evolve towards a more integrative model, biopsychosocially oriented practitioners, including health psychologists, psychiatrists, and nurses, will work closely with surgical and interventional specialists such as

neurosurgeons, anesthesiologists, and radiologists, playing a crucial role in patient care [15]. Psychological interventions have gained substantial recognition as valuable tools in clinical practice for alleviating negative emotions and stress in patients [16]. Commonly utilized interventions include counseling, relaxation techniques, and cognitive-behavioral therapy. Extensive research has shown that these interventions effectively reduce preoperative anxiety and stress, thereby improving patients' overall experiences and clinical outcomes [17–19]. Moreover, psychological interventions have been demonstrated to be cost-effective in the context of cancer care [20]. By alleviating negative emotional states and improving treatment adherence, these interventions indirectly reduce overall treatment costs, thereby easing the financial burden on patients.

However, these studies are often constrained by limitations such as small sample sizes, resource limitations, and variability in methodological rigor. The issue of small sample sizes is influenced not only by patients' willingness to participate but also by local healthcare resources and environmental factors. Additionally, resource constraints often restrict the scope of research projects, leading to deviations from prescribed methodologies during implementation. These limitations may introduce bias, thereby undermining the reliability and generalizability of the findings. Consequently, a comprehensive understanding and validation of the efficacy of psychological interventions in the context of TACE remain elusive. To address these gaps, this study conducts a systematic quantitative meta-analysis of existing research, aiming to rigorously evaluate the impact of psychological interventions on reducing negative emotions and improving outcomes in patients undergoing TACE. By synthesizing data from multiple studies, this meta-analysis seeks to provide robust evidence regarding the effectiveness of psychological interventions and offer evidence-based recommendations for their integration into clinical practice.

2. Materials and methods

2.1. Inclusion and exclusion criteria

The inclusion criteria for this study required that original data be derived from publicly available literature and comprise rigorously designed randomized controlled trials (RCTs). Only studies published in English or Chinese were eligible for inclusion. Eligible participants were patients with a confirmed diagnosis of hepatocellular carcinoma (HCC), all of whom underwent TACE and received standardized perioperative care.

Routine care, as operationalized in this study, comprised standardized perioperative management delivered by healthcare professionals. This included comprehensive explanations of preoperative preparations, potential intraoperative complications, and postoperative considerations associated with TACE, which were provided to both patients and their families. The psychological intervention group received supplementary structured psychological support in addition to the aforementioned routine care. Specifically, psychological interventions were delineated as follows: (1) targeted educational sessions focusing on the pathophysiology of liver cancer and the procedural details of TACE, (2) proactive resolution of patient concerns through evidence-based positive reinforcement techniques, and (3) facilitation of

effective bidirectional communication between patients and healthcare providers. These interventions were meticulously designed to alleviate anxiety and promote psychological well-being throughout the perioperative period.

Primary outcome measures included intraoperative physiological parameters (heart rate and blood pressure) and the incidence of intraoperative anxiety. Exclusion criteria were applied to studies that (1) included patients who did not undergo TACE, (2) presented irrelevant content, (3) were duplicate publications, (4) lacked sufficient data for analysis, (5) exhibited methodological deficiencies (e.g., high risk of bias), or (6) incorporated confounding therapeutic factors that could obscure the evaluation of psychological interventions' impact on negative emotional states.

2.2. Literature search

To identify relevant studies, a comprehensive search strategy was implemented using the following key terms: (liver cancer OR hepatocellular carcinoma) AND (psychological intervention) AND (transcatheter arterial chemoembolization). The search was conducted across multiple databases, including PubMed, Embase, and the Cochrane Library, covering the period from January 1991 to January 2024. Prior to the primary search, synonyms and related terms for the key concepts were identified and incorporated into the search strategy to ensure its comprehensiveness and optimize the retrieval of pertinent literature.

To further enhance the robustness of the search, a secondary search was performed by manually reviewing the reference lists of all studies identified in the initial search. This approach aimed to minimize the risk of omitting relevant studies and to maximize the likelihood of capturing all eligible publications for inclusion in the analysis.

2.3. Literature screening

Studies were systematically screened based on predefined inclusion and exclusion criteria. Two independent researchers conducted an initial review of the titles and abstracts of the retrieved studies to exclude those that clearly did not meet the inclusion criteria. For studies deemed potentially eligible, the full texts were thoroughly reviewed to confirm their suitability for inclusion. In instances where discrepancies arose between the two researchers regarding study eligibility, a senior researcher was consulted to adjudicate and make the final determination on inclusion.

2.4. Quality assessment

The methodological quality of the included studies was rigorously assessed to evaluate their design, implementation, and analytical processes, with the primary objective of minimizing or preventing bias and systematic errors. To ensure a standardized evaluation, the Jadad scale was employed to assess the methodological rigor of the selected studies.

2.5. Data extraction

Data extraction was performed using a standardized, pre-designed form, which encompassed the following categories: (1) general information, including the title,

authors, publication date, and source; (2) study characteristics, such as sample size, gender distribution, and mean age of participants; (3) outcome measures, comprising intraoperative mean systolic blood pressure, intraoperative mean heart rate, and the incidence of intraoperative anxiety; (4) definition of anxiety, which incorporated both standardized self-rating anxiety scales (SAS) and self-developed anxiety-related questionnaires, with their evaluation results included in the meta-analysis; and (5) group classifications, distinguishing between the control group (receiving standard TACE surgical care) and the intervention group (receiving psychological interventions and health education in addition to standard care). In cases of missing data, attempts were made to contact the corresponding authors directly to obtain the necessary information.

2.6. Statistical analysis

The meta-analysis was performed using RevMan 5.2.7 software, provided by the Cochrane Collaboration. Heterogeneity among the included studies was initially evaluated using the I^2 statistic and P -values. If the studies exhibited low heterogeneity ($P > 0.10$ and $I^2 < 50\%$), a fixed-effects model was applied for data synthesis. Conversely, in cases of significant heterogeneity ($P < 0.10$ and $I^2 > 50\%$), a random-effects model was utilized. For continuous outcome measures, the mean difference (MD) or standardized mean difference (SMD) was calculated to evaluate treatment efficacy, while odds ratios (ORs) were computed for dichotomous outcomes. All effect sizes were reported with 95% confidence intervals (CIs). Publication bias was assessed using Egger's test when the number of included studies was ≥ 5 . Furthermore, sensitivity analysis was conducted to examine the robustness and reliability of the meta-analysis findings.

3. Results

3.1. Literature search results

A total of 64 original studies were initially identified through comprehensive literature searches. Following a rigorous review of titles and abstracts based on the predefined inclusion and exclusion criteria, 43 studies were excluded. These exclusions comprised 2 duplicate publications, 10 non-RCTs, and 31 studies that failed to meet the inclusion criteria. The remaining 21 articles underwent full-text review, during which 7 studies were further excluded: 6 studies were inconsistent with the inclusion criteria upon detailed examination, and 1 study could not be retrieved.

Among the 14 studies that remained, 6 were excluded after full-text assessment: 2 articles lacked complete outcome measures, 1 article was of poor methodological quality, and 3 articles reported irrelevant outcomes. Ultimately, 8 studies involving a total of 790 patients were included in the final analysis, comparing psychological intervention groups with control groups (**Figure 1**). Of these, 397 patients were assigned to the psychological intervention group, while the remaining 393 patients served as the control group.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

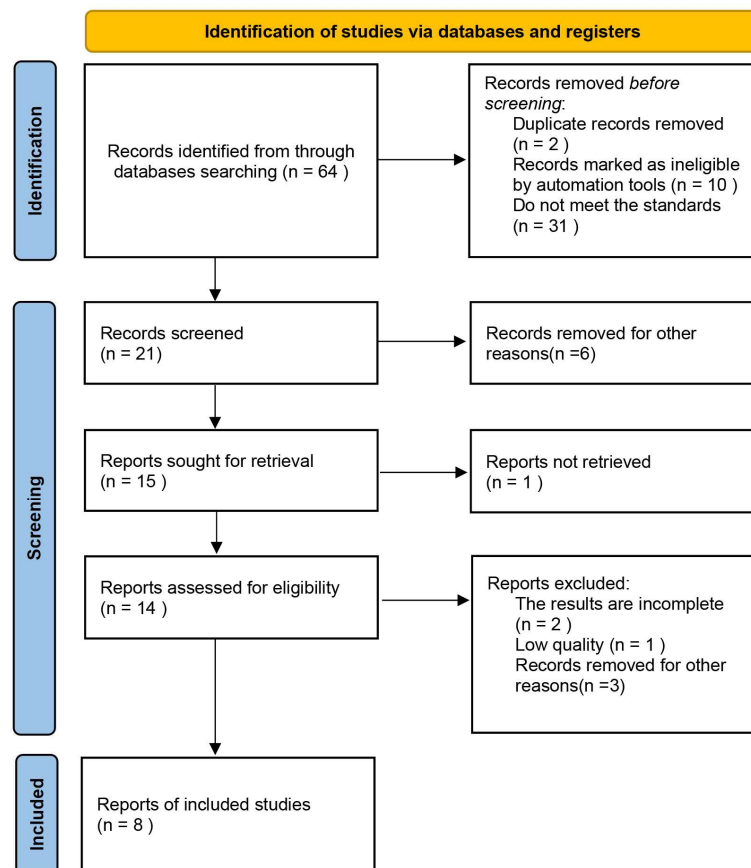


Figure 1. Flowchart of the literature searching and screening.

3.2. General characteristics and quality assessment of included studies

Among the 8 studies included in the analysis, no statistically significant differences were observed between the intervention and control groups in terms of gender distribution, age, preoperative mean systolic blood pressure, or preoperative mean heart rate (**Table 1**). All selected studies were RCTs. However, none of the studies provided details regarding randomization concealment, implementation of blinding, or reporting of participant dropouts. Based on the Jadad scale evaluation, the overall quality of the included studies was classified as low risk of bias.

Heterogeneity assessment revealed significant variability in intraoperative systolic blood pressure ($P < 0.10$, $I^2 > 50\%$) and intraoperative heart rate ($P < 0.10$, $I^2 > 50\%$), necessitating the use of a random-effects model for combined analysis. In contrast, intraoperative anxiety exhibited no significant heterogeneity, and a fixed-effects model was employed for these calculations. Funnel plots for intraoperative systolic blood pressure and intraoperative anxiety incidence demonstrated asymmetry, suggesting the potential presence of publication bias.

Table 1. General information of included studies.

Studies	Group	Ncase	M/F	Average age (years)	Preoperative average blood pressure (mmHg)	Preoperative average heart rate (times/min)
Zhang [21]	Intervention	35	58/12	46 (32–70)	122 ± 12	86 ± 8
	Control	35			115 ± 17	82 ± 14
Zhang [22]	Intervention	32	23/9	56 (42–73)	NA	NA
	Control	30	25/5	55 (40–72)	NA	NA
Zhang et al. [23]	Intervention	122	96/26	50.6 (28–72)	126.7 ± 12.5	84.3 ± 12.2
	Control	120	92/28	48.9 (32–71)	133.2 ± 14.6	97.5 ± 10.9
Qiu et al. [24]	Intervention	40	40/40	57.9 (36–72)	114.8 ± 9.9	76.1 ± 6.3
	Control	40			115.6 ± 9.2	75.8 ± 6.6
Lin et al. [25]	Intervention	50	41/9	42.1 ± 5.6	NA	NA
	Control	50	38/12	41.9 ± 6.1	NA	NA
Xia et al. [26]	Intervention	50	35/15	61.0 ± 8.1	NA	NA
	Control	50	37/13	62.0 ± 7.9	NA	NA
Wang [27]	Intervention	25	31/19	56.46 ± 11.23	NA	NA
	Control	25			NA	NA
Gao et al. [13]	Intervention	43	25/18	48.58 ± 7.23	NA	70.88 ± 7.11
	Control	43	26/17	48.66 ± 7.66	NA	71.16 ± 8.12

3.3. Comparison of intraoperative systolic blood pressure

Seven studies [13,21,23–27] reported intraoperative mean systolic blood pressure. Meta-analysis revealed significant heterogeneity among these studies ($P < 0.01$, $I^2 = 90\%$), prompting the use of a random-effects model. The results were statistically significant (MD = −15.95 mmHg, 95% CI: −22.31 to −9.25, $P < 0.0001$), indicating that psychological intervention prior to TACE effectively reduces intraoperative systolic blood pressure elevation induced by negative emotions in patients compared to the control group (Figure 2).

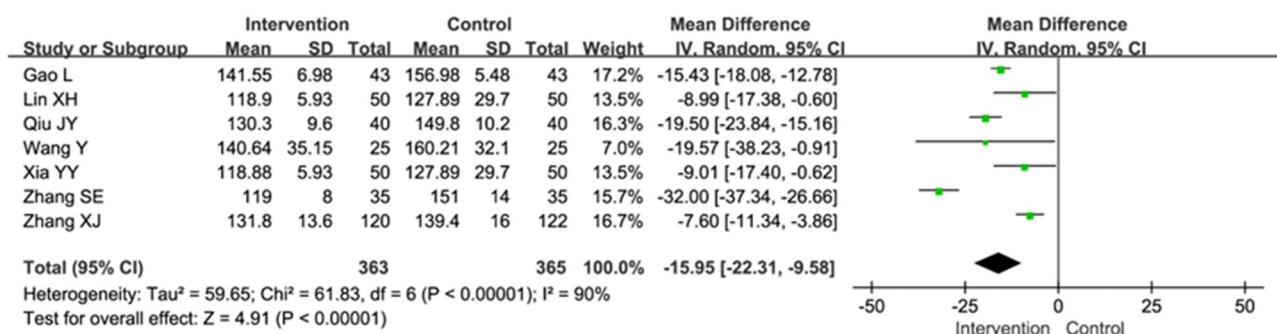


Figure 2. Comparison of intraoperative systolic blood pressure.

3.4. Comparison of intraoperative heart rate

Seven studies [13,21,23–27] reported intraoperative mean heart rate. Significant heterogeneity was observed ($P < 0.10$, $I^2 = 88\%$), leading to the application of a random-effects model. The results were statistically significant (MD = −10.68 bpm, 95% CI: −13.87 to −7.48, $P < 0.0001$), suggesting that psychological intervention prior

to TACE significantly reduces the incidence of tachycardia induced by negative emotions in patients (Figure 3).

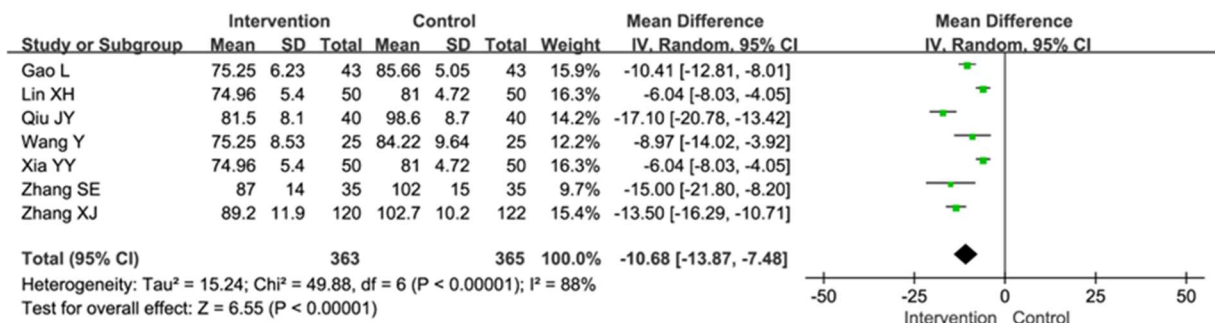


Figure 3. Comparison of intraoperative heart rate.

3.5. Incidence of intraoperative anxiety

Five studies reported data on anxiety levels following psychological interventions (Figure 4A). One study [13] analyzed differences in anxiety scores between the intervention and control groups. Due to the availability of quantitative data from only one study, a fixed-effects model was used. The results demonstrated that psychological interventions significantly reduced anxiety in TACE patients ($MD = -2.39$, 95% CI: -3.35 to -1.43 , $P < 0.0001$). Additionally, four studies [12,13,16,17] provided data on the incidence of intraoperative anxiety. Meta-analysis revealed no significant heterogeneity ($P = 0.75$, $I^2 = 0\%$), allowing for the use of a fixed-effects model. The results were statistically significant ($OR = 0.32$, 95% CI: 0.19 to 0.52 , $P < 0.0001$), indicating that psychological intervention prior to TACE effectively alleviates intraoperative anxiety in patients (Figure 4B).

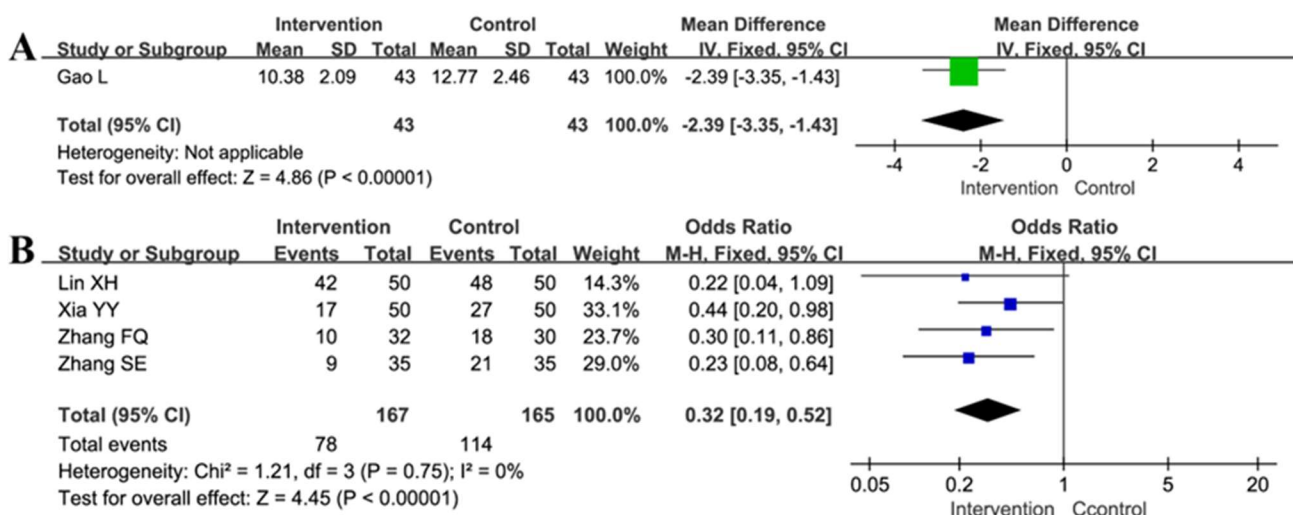


Figure 4. Incidence of intraoperative anxiety, (A) anxiety score; (B) anxiety rate.

3.6. Heterogeneity analysis

A subgroup analysis was conducted based on the type of anxiety assessment scale used: self-developed anxiety-related questionnaires and the Self-Rating Anxiety Scale (SAS). The combined results of the four studies were analyzed using a random-effects

model, revealing no significant heterogeneity ($I^2 = 0\%$). Further heterogeneity analysis showed no heterogeneity in the SAS group ($I^2 = 0\%$). However, the group using self-developed anxiety-related questionnaires exhibited moderate heterogeneity, though the difference was not statistically significant ($I^2 = 41\%$) (**Figure 5**).

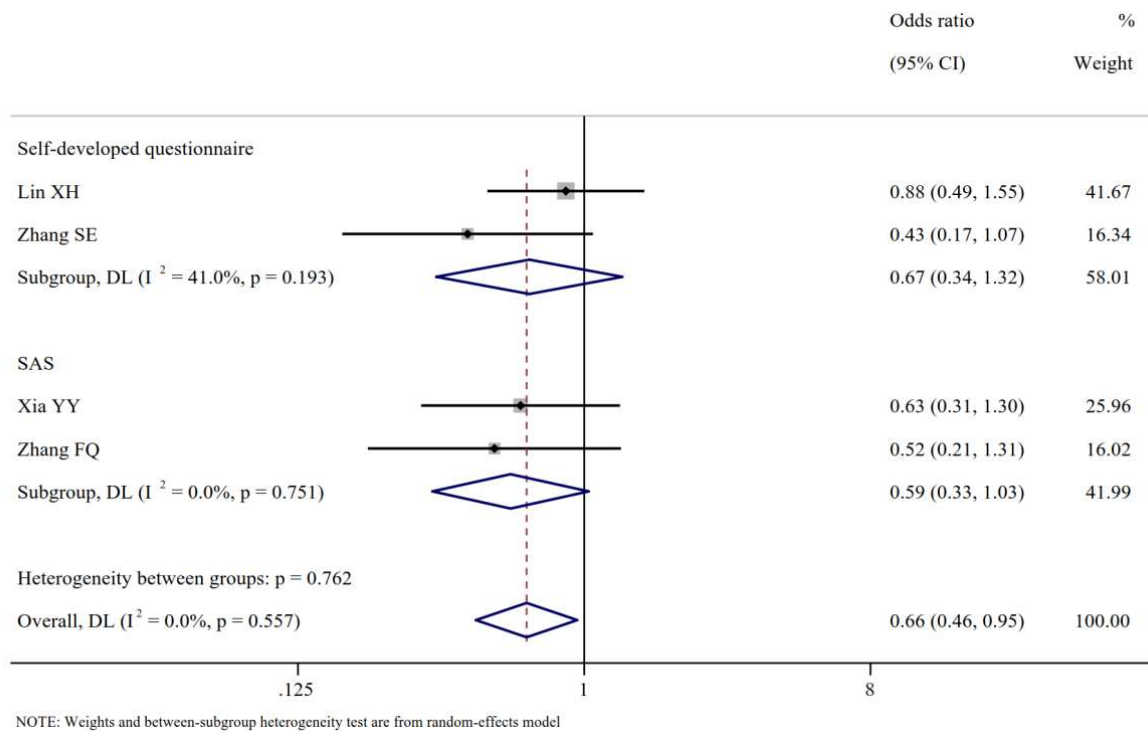


Figure 5. Heterogeneity analysis of anxiety incidence.

3.7. Bias analysis

The Egger's test results indicated that there was insufficient statistical evidence to suggest the existence of publication bias regarding intraoperative systolic blood pressure ($P = 0.9916$) and heart rate ($P = 0.1555$).

3.8. Sensitivity analysis

After excluding the study with lower quality [24] and that exhibiting high data variability [25], the sensitivity analysis showed that the outcome indicators remained stable with minimal variation. Consequently, the results of the meta-analysis are considered to be robust and reliable.

4. Discussion

Negative emotions can establish a self-reinforcing negative feedback loop, adversely affecting both mental and physical health. These emotional responses, often characterized by complex psychological stress reactions, are typically triggered by perceived threats [28,29]. In patients with liver cancer undergoing TACE, such stress responses commonly manifest as elevated blood pressure, increased heart rate, and heightened emotional tension during the procedure [30]. These physiological and psychological reactions can significantly disrupt the TACE process, compromise its efficacy, and potentially lead to adverse outcomes, including suboptimal procedural

results and diminished patient well-being [30,31]. This study found that psychological interventions effectively suppress the elevation of diastolic blood pressure and heart rate while also reducing anxiety and improving negative emotional states.

Psychological interventions have been demonstrated to mitigate the impact of negative emotions on both mental and physical health, emerging as a widely recognized and clinically effective approach for alleviating emotional distress in cancer patients [32–34]. Originally developed to address symptoms and improve the quality of life in individuals with psychiatric disorders, psychological therapy has increasingly been adopted as a cost-effective strategy for managing psychological stress and emotional challenges in non-psychiatric populations. Although not originally designed to address the emotional burdens associated with medical procedures, psychological interventions have proven effective in reducing distress and fatigue, which are prevalent and debilitating among cancer patients [35]. These symptoms, among the most prevalent and debilitating aspects of the disease, significantly affect both the physical and psychological well-being of patients [36]. Research indicates that psychological interventions, including various forms of counseling, cognitive-behavioral therapy, and stress management techniques, can substantially improve patient outcomes [37,38]. By addressing the emotional and psychological needs of patients, these interventions not only help in reducing pain and fatigue but also enhance the overall treatment experience [39–41]. Given the profound impact of negative emotions on the efficacy of treatments like TACE, incorporating psychological support into standard care protocols offers a promising strategy for improving patient outcomes.

Our meta-analysis sought to evaluate the effectiveness of psychological interventions in reducing stress responses and improving outcomes for patients undergoing TACE. The results support the hypothesis that preoperative psychological intervention can have a significant positive impact on managing negative emotions during the procedure. Specifically, the analysis revealed that psychological intervention effectively reduced intraoperative blood pressure and heart rate, which are key indicators of stress. This reduction in stress responses contributes to a smoother TACE procedure, potentially enhancing procedural success and improving patient recovery [42,43]. As mentioned earlier in the introduction, pain persists throughout the perioperative period [12]. Pain can elevate heart rate and blood pressure, exacerbating stress responses. Our psychological interventions can mitigate these stress responses, thereby indirectly reducing the adverse physiological effects of pain during treatment. Furthermore, our analysis revealed that psychological interventions are effective in reducing intraoperative anxiety, a common and debilitating emotional response during medical procedures. Effectively managing anxiety can lead to better procedural outcomes, increased patient comfort, and an overall positive treatment experience. This, in turn, can enhance patient adherence to therapy, strengthen the physician-patient relationship, and facilitate the smooth implementation of follow-up care. The statistical significance of our findings underscores the value of psychological interventions in addressing the emotional challenges faced by patients undergoing TACE.

Despite these promising results, several limitations must be acknowledged. A primary concern is the use of self-developed questionnaires for anxiety assessment in

some studies, with only three studies employing the standardized SAS [22,26]. The lack of standardized assessment tools may have limited the comprehensiveness and objectivity of the findings, potentially hindering the ability to fully capture the extent of anxiety reduction achieved through psychological interventions.

Another limitation of this meta-analysis is the quality of the included studies. Although the meta-analysis incorporated eight studies, all of which were RCTs, the overall quality of these studies was moderate. Variations in the qualifications of nursing staff, differences in available equipment, and the technical expertise of TACE practitioners across the studies may have contributed to this heterogeneity. Furthermore, all of the included studies were conducted within a single country, which may limit the generalizability of the findings to international patient populations. The specific cultural, clinical, and procedural contexts in which these studies were conducted may not fully represent the experiences of patients in other regions. To address these limitations, further high-quality clinical research is needed to validate the findings of this meta-analysis and assess the broader applicability of psychological interventions across diverse patient populations.

In conclusion, this meta-analysis demonstrates that psychological interventions effectively mitigate negative emotional responses, including elevated blood pressure, increased heart rate, and intraoperative anxiety, in patients undergoing TACE. The findings underscore the importance of integrating psychological support into standard care protocols for liver cancer patients, offering a valuable complement to conventional treatments. Healthcare professionals play a pivotal role in providing positive emotional support, which can alter patients' fearful perceptions of the disease. By addressing patients' concerns about their diagnosis and the surgical procedure, healthcare providers can help patients better understand their treatment, ultimately reducing fear and anxiety. By focusing on the emotional and psychological dimensions of patient care, psychological interventions have the potential to enhance treatment outcomes, improve procedural experiences, and contribute to overall patient well-being. Further research is required to validate these findings and explore the broader application of psychological interventions in diverse clinical settings, thereby advancing the quality of care for patients undergoing TACE and similar procedures.

Author contributions: Conceptualization, LR and WZ; methodology, LR; software, LR; validation, LW, MW and WZ; formal analysis, LR; investigation, LR; resources, WZ; data curation, LR; writing—original draft preparation, LR; writing—review and editing, LW; visualization, LR; supervision, WZ; project administration, WZ; funding acquisition, WZ. All authors have read and agreed to the published version of the manuscript.

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