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Meta-Analysis of the Effect of Nutritional Support on Treatment Tolerance and Complications during Chemotherapy for Bone Tumors

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Abstract

Objective: To evaluate the effects of nutritional support on treatment tolerance and complications in patients with bone tumors undergoing chemotherapy via a meta-analysis. **Methods**: The China National Knowledge Infrastructure (CNKI), Wanfang, VIP, PubMed, and Web of Science databases were searched from inception to February 2025 for clinical controlled trials on nutritional support for patients with bone tumors during chemotherapy. Review Manager 5.3 software was used to conduct a meta-analysis of the included studies. **Results**: A total of 11 studies involving 935 patients were included. The meta-analysis indicated that nutritional support significantly improved hemoglobin (MD = 5.70, 95% CI: 4.30 - 7.10, $P < 0.00001$), prealbumin (MD = 26.76, 95% CI: 23.43 - 30.10, $P < 0.00001$), and BMI (MD = 0.80, 95% CI: 0.05 - 1.55, $P = 0.04$). It also reduced the incidence of complications (OR = 0.33, 95% CI: 0.20 - 0.55, $P < 0.0001$) and malnutrition (OR = 0.45, 95% CI: 0.29 - 0.72, $P = 0.0007$), shortened the length of hospital stay (MD = −0.72, 95% CI: −1.10 - −0.34, $P = 0.0002$), alleviated negative emotions (MD = 11.60, 95% CI: 10.16 - 13.04, $P < 0.00001$), and enhanced quality of life (MD = 18.05, 95% CI: 14.10 - 21.99, $P < 0.00001$) and self-management ability (MD = 1.59, 95% CI: 1.28 - 1.90, $P < 0.00001$). **Conclusion**: Nutritional support can significantly improve treatment tolerance and reduce the risk of complications in patients with bone tumors undergoing chemotherapy. However, these findings require further validation through additional high-quality studies.

Keywords

Bone Tumor, Chemotherapy, Nutritional Support, Treatment Tolerance,

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Complications, Meta-Analysis

1. Introduction

Chemotherapy is a key modality for the treatment of bone tumors. However, patients undergoing chemotherapy frequently experience adverse reactions, such as nausea, vomiting, and mucositis, leading to inadequate nutritional intake and consequent malnutrition. Malnutrition not only compromises chemotherapy tolerance, necessitating dose adjustments or treatment interruptions, but also increases the risk of complications, including infection and myelosuppression. Research indicates that nutritional support can mitigate chemotherapy-induced toxicity by improving metabolic status and enhancing immune function [1]. Nevertheless, the comparative efficacy of different nutritional support modes (enteral, parenteral, or combined) has not been definitively established. This meta-analysis was therefore conducted to systematically evaluate the effects of nutritional support on treatment tolerance and complications in patients with bone tumors undergoing chemotherapy.

2. Subjects and Methods

2.1. Literature Search Strategy

2.1.1. Databases and Search Terms

A literature search was conducted in the China National Knowledge Infrastructure (CNKI), Wanfang, VIP, PubMed, and Web of Science databases. The Chinese search terms included: (bone tumor OR osteosarcoma OR chondrosarcoma OR fibrosarcoma OR myeloma) AND (chemotherapy) AND (nutrition support OR dietary intervention OR enteral nutrition OR parenteral nutrition). The English search terms were: ("bone tumour" OR "osteosarcoma" OR "chondrosarcoma" OR "fibrosarcoma" OR "myeloma") AND ("chemotherapy") AND ("nutrition support" OR "dietary intervention" OR "enteral nutrition" OR "parenteral nutrition").

2.1.2. Outcome Measures

① Primary outcomes: chemotherapy tolerability (hemoglobin) and complications. ② Secondary outcomes: prealbumin, incidence of malnutrition, length of hospital stay, body mass index (BMI), psychological state, quality of life, and self-management.

2.2. Literature Inclusion and Exclusion Criteria

The inclusion criteria were as follows: studies had to be randomized controlled trials; participants were patients with pathologically confirmed bone tumors undergoing chemotherapy; and the intervention group received nutritional support (including enteral nutrition, parenteral nutrition, dietary guidance, or mixed nutritional support) during chemotherapy, while the control group received routine interventions.

Exclusion criteria: case reports and cohort studies; duplicate publications; studies with a sample size of less than 30; studies in which the observation group did not receive specified nutritional support; studies with incomplete or unextractable data; publications in languages other than Chinese or English; Literature that is inconsistent with the research topic and review articles.

2.3. Data Extraction

In accordance with the established inclusion criteria, retrieved literature was first de-duplicated using Endnote literature management software. Subsequently, two researchers independently screened the titles and abstracts to exclude clearly ineligible articles. The full texts of potentially eligible articles were then reviewed to determine final inclusion. Data extraction was conducted using software such as Excel, covering basic information, intervention measures, outcome indicators, and corresponding data.

2.4. Risk of Bias Assessment

The quality of the included studies was systematically evaluated using the Cochrane risk-of-bias tool, encompassing the following domains: ① Random sequence generation: assessment of whether scientific randomization methods, such as random number tables or computer-generated sequences, were employed; ② Allocation concealment: analysis of whether group assignments were concealed using methods such as sealed envelopes or a centralized system; ③ Blinding: determination of the blinding status for participants, intervention providers, and outcome assessors; ④ Incomplete outcome data: verification of whether participant dropout or loss to follow-up compromised the integrity of the data analysis; ⑤ Selective reporting: examination of the consistency between the study protocol and the final reported outcome measures.

The risk level for each item was classified into three categories: low risk, indicated by a clear description of a standard procedure (e.g., use of a random number table); high risk, indicated by significant methodological flaws (e.g., pseudo-random allocation based on admission order); and unclear risk, where the publication provided insufficient information to permit a judgment.

2.5. Statistical Analysis

Data analysis was performed using Review Manager 5.3. Dichotomous variables were evaluated using the risk ratio (RR) with its 95% confidence interval (CI), while continuous variables were evaluated using the standardized mean difference (SMD) with its 95% CI. A random-effects model was applied in cases of significant heterogeneity ($P \leq 0.10$ or $I^2 \geq 50\%$); otherwise, a fixed-effect model was used. A P-value of <0.05 was considered to indicate statistical significance. Funnel plots were constructed to assess for publication bias. Supplementary note: Among the literature included in this study, the validated scales and scoring characteristics used to assess psychological status, quality of life, and self-management are as follows: Psychological status: Anxiety and depression-related scales are mainly used (such as Hamilton Anxiety Scale [HAMA], Hamilton Depression Scale [HAMD]). The scoring range is usually 0 - 56 points (for HAMA) or 0 - 53 points (for HAMD). A higher score indicates a more severe level of anxiety/depression (negative scoring) [2] [3]. Quality of life: The Quality of Life Score for Cancer Patients (QOL) is adopted, with a scoring range of 0 - 100 points. A higher score indicates a better quality of life (positive scoring) [4] [5]. Self-management ability: The Self-Management Ability Scale is used, with a scoring range of usually 0 - 40 points. A higher score indicates a stronger ability of patients to self-manage disease treatment, diet, and lifestyle (positive scoring) [3] [5]. All the above scales are mature tools with verified reliability and validity. Their scoring directions and ranges remain consistent across the included studies, ensuring the comparability of outcome indicators.

3. Results

3.1. Literature Search Results and Literature Quality

The literature search yielded 142 potentially eligible studies. After the removal of duplicates and exclusion of 131 articles upon full-text review, a final total of 11 studies were included in the analysis (**Figure 1**). Of these 11 studies, 3 were assessed as having a high risk of bias because group allocation was not based on randomization principles. The remaining 8 were classified as having a low risk of bias for reporting explicit randomization methods (**Figure 2**). These 8 low-risk studies complied with standardized operations in terms of random allocation methods, data integrity, and other dimensions. Their data results constitute the

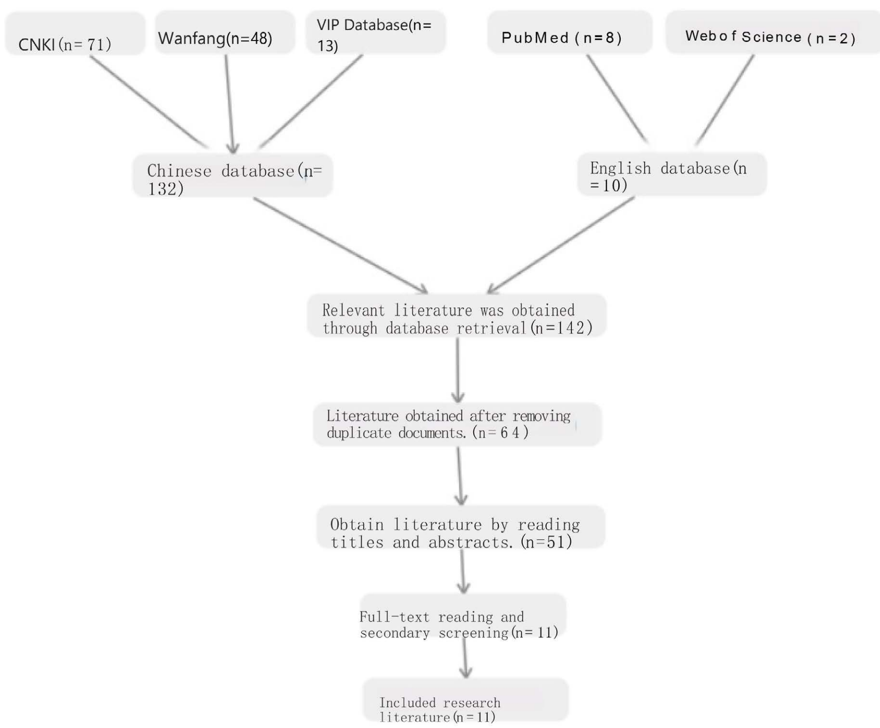

Figure 1. Literature screening flowchart.

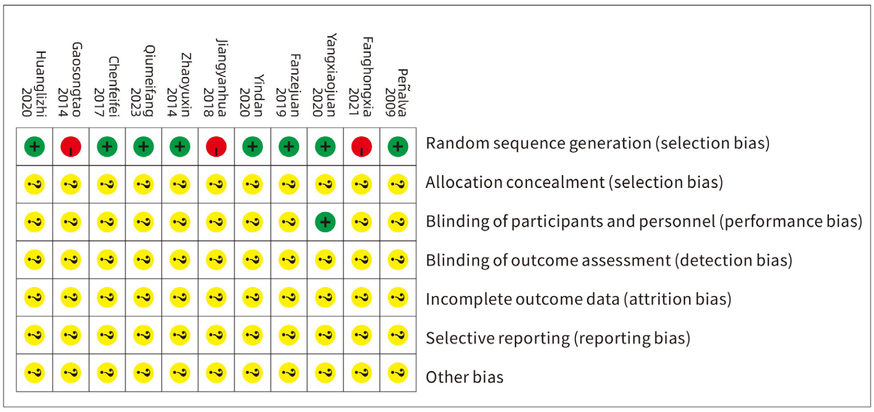

Figure 2. Literature quality assessment.

main basis for the study's conclusion that "nutritional support can significantly improve the treatment tolerance of bone tumor patients undergoing chemotherapy and reduce the risk of complications," thus ensuring the reliability and scientificity of the analysis results.

3.2. General Characteristics of Included Literature

Among the 11 included studies, one was published in English and ten in Chinese, comprising a total of 935 patients. The intervention for the observation group consisted primarily of nutritional support in six studies, while nutritional support was mentioned as part of the intervention in the remaining five. See Table 1.

Table 1. General characteristics of included literature.

First author	Year of publication	Grouping method	Number of cases	Interventions		Intervention time	Observation indicators
				Control group	Observation group		
Peñalva A [6]	2009	random	125	Flavored supplements/non-flavored (neutral) supplements	"Kitchen" food as a supplement	-	④
Gao Songtao [7]	2014	Different years	68	Nutritional risk screening score ≥ 3 points indicates the need for parenteral nutrition support.	Nutritional risk screening score ≥ 3 points Joint nutritional support	During chemotherapy	②③⑤⑥
Zhao Yuxin [8]	2014	random	30	enteral nutrition	Enteral + parenteral nutrition	7d	①②⑤
Chen Feifei [4]	2017	random number method	50	Routine nursing interventions	Intensive nursing intervention	-	②⑧
Jiang Yanhua [9]	2018	Admission time	82	Nutritional intervention should be provided when the appetite score in the quality of life (QOL) assessment for cancer patients is ≤3 points.	Patients with a Nutritional Risk Screening (NRS 2002) score of ≥3 points should receive nutritional intervention.	6 cycles of chemotherapy	④

Continued

Fan Zejuan [10]	2019	Random allocation principle	60	routine care	Dietary care	-	①⑥
Yang Xiaojuan [11]	2020	randomized single-blind method	200	Conventional enteral nutrition therapy	Supplemental parenteral nutrition therapy	15d	②④⑤
Huang Lizhi [2]	2020	Random number table method	90	routine care	Traditional Chinese Medicine Nursing	1 cycle of chemotherapy	⑦
Yi Dan [5]	2020	Odd or even numbers at the end of the hospital admission number	80	personalized care	Personalized care combined with self-efficacy care	-	⑧⑨
Fang Hongxia [12]	2021	Admission time	70	routine care	Implement nutritional support therapy on top of regular care	7d	①②③
Qiu Meifang [3]	2023	random	80	routine care	Conventional + Roy Adaptation Model Nursing	-	⑦⑨

Note: ① Tolerability; ② Complications; ③ Prealbumin; ④ Incidence of malnutrition; ⑤ Length of hospital stay; ⑥ Body mass/BMI; ⑦ Psychological state; ⑧ Quality of life; ⑨ Self-management.

3.3. Primary and Secondary Endpoints

3.3.1. Hemoglobin

Three studies [8] [10] [12] reported on hemoglobin levels, encompassing a total of 160 patients (n = 80 in the observation group and n = 80 in the control group). Subgroups were divided by nutritional types, which are "routine care + nutritional support", "dietary nursing", and "enteral + parenteral nutrition vs enteral nutrition". The meta-analysis revealed significant heterogeneity among these studies ($I^2 = 81\%$, $P = 0.005$); therefore, a random-effects model was employed. The forest plot indicates that nutritional support improved hemoglobin levels in bone tumor patients during chemotherapy (MD = 5.70, 95% CI: 4.30 - 7.10, $P < 0.00001$), as shown in Figure 3.

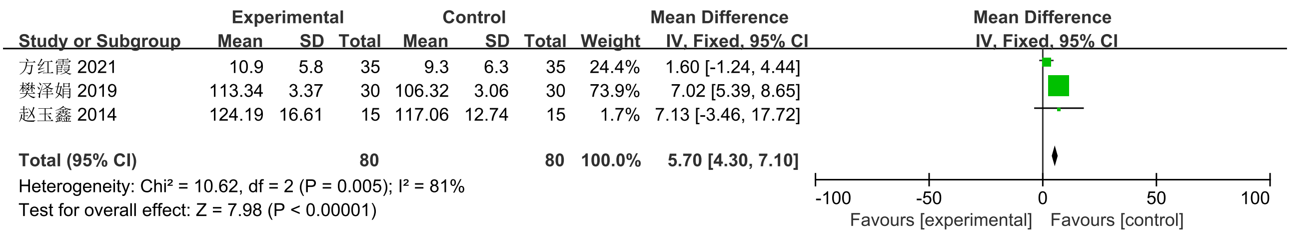

Figure 3. Hemoglobin forest plot.

3.3.2. Complications

Five studies [4] [7] [8] [11] [12] reported on complications, involving a total of 418 patients (211 in the observation group and 207 in the control group). The meta-analysis revealed low heterogeneity among the five studies (I^2 = 0%, P = 0.85); therefore, a fixed-effects model was employed. The forest plot indicated that nutritional support significantly reduced the incidence of complications in bone tumor patients during chemotherapy (OR = 0.33, 95% CI: 0.20 - 0.55, P < 0.0001), as shown in Figure 4.

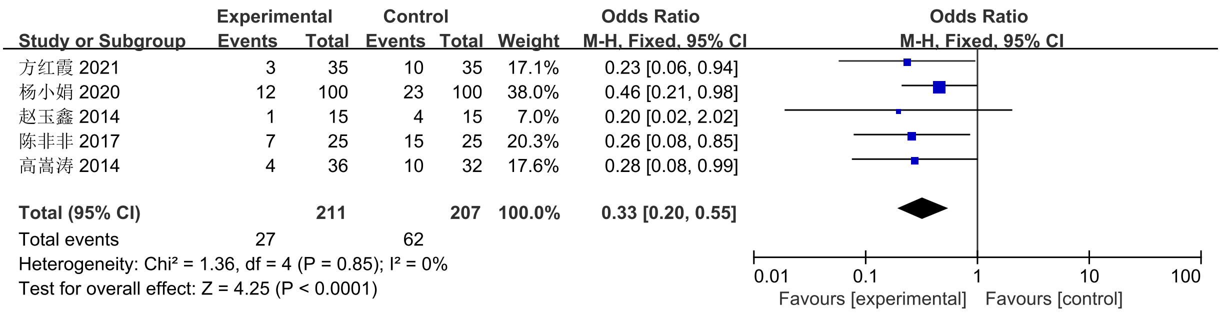

Figure 4. Complications forest plot.

3.3.3. Prealbumin

Two studies [7] [12] reported on prealbumin levels, encompassing a total of 138 patients (71 in the observation group and 68 in the control group). The nutritional types are "combined nutrition vs. simple parenteral nutrition" and "routine care + nutritional support". The meta-analysis revealed significant heterogeneity between the two studies (I^2 = 96%, P < 0.00001); therefore, a random-effects model was employed. The forest plot indicated that nutritional support improved prealbumin levels in bone tumor patients undergoing chemotherapy (MD = 26.76, 95% CI: 23.43 - 30.10, P < 0.00001) (Figure 5).

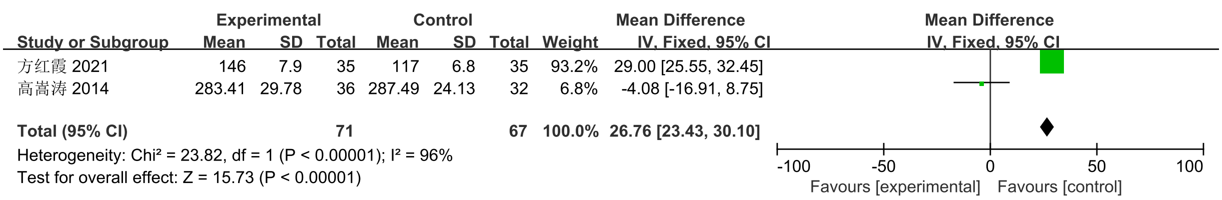

Figure 5. Prealbumin forest plot.

3.3.4. Incidence of Malnutrition

Three studies [6] [9] [11] reported the incidence of malnutrition, encompassing a total of 407 patients (186 in the observation group and 221 in the control group). A meta-analysis revealed low heterogeneity among these studies (I^2 = 0%, P = 0.65); therefore, a fixed-effects model was employed. The forest plot (Figure 6) indicated that nutritional support significantly reduced the incidence of malnutrition in bone tumor patients during chemotherapy (OR = 0.45, 95% CI: 0.29 - 0.72, P = 0.0007).

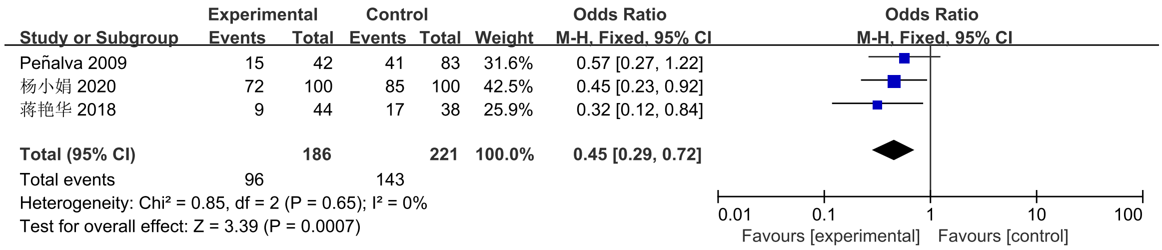

Figure 6. Malnutrition incidence forest plot.

3.3.5. Length of Hospital Stay

Three studies [7] [8] [11] reported data on the length of hospital stay for a total of 298 patients (151 in the observation group and 147 in the control group). Subgroups were divided by tumor types, which are "multiple myeloma", "sacral tumor" and "osteosarcoma". A meta-analysis revealed significant heterogeneity among the three studies ($I^2 = 96\%$, $P < 0.00001$); therefore, a random-effects model was employed. The forest plot indicates that nutritional support was associated with a shorter length of hospital stay for patients with bone tumors (MD = −0.72, 95% CI: −1.10 - −0.34, $P = 0.0002$) (Figure 7).

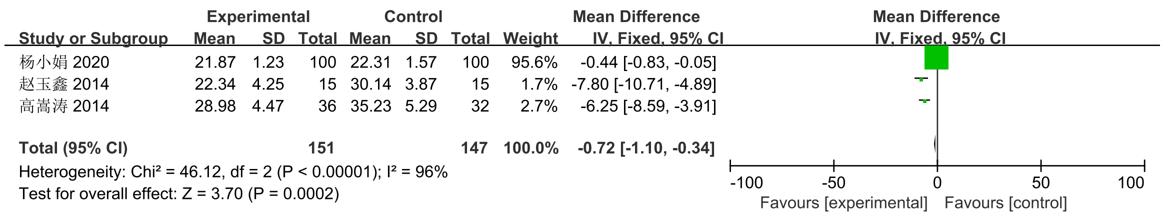

Figure 7. Forest plot of length of stay.

3.3.6. BMI

Two studies [6] [10] reported on BMI, encompassing a total of 128 patients (66 in the observation group and 62 in the control group). The nutritional types are "dietary nursing" and "kitchen food supplements vs. flavoring supplements". The meta-analysis revealed significant heterogeneity between the two studies ($I^2 = 95\%$, $P < 0.0001$); therefore, a random-effects model was employed. The forest plot indicated that nutritional support improved the BMI of patients with bone tumors (MD = 0.80, 95% CI: 0.05 - 1.55, $P = 0.04$), as shown in Figure 8.

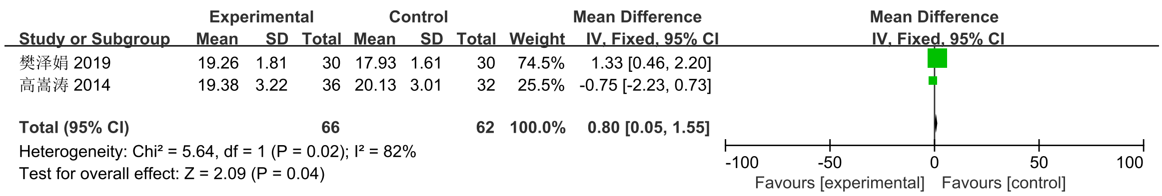

Figure 8. BMI forest plot.

3.3.7. Psychological State

Two studies [2] [3] reported on psychological state scores, involving a total of 170 patients (85 in the observation group and 85 in the control group). All are aimed at patients with multiple myeloma, with consistent tumor types. The meta-analysis revealed significant heterogeneity between the two studies ($I^2 = 95\%$, $P < 0.0001$); therefore, a random-effects model was employed. The forest plot indicated that nutritional support alleviated negative emotions in bone tumor patients undergoing chemotherapy (MD = 11.60, 95% CI: 10.16 - 13.04, $P < 0.00001$), as shown in Figure 9.

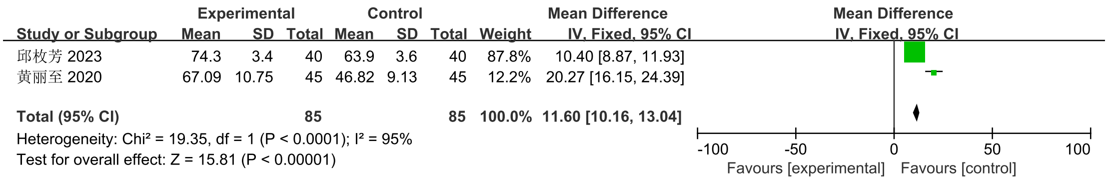

Figure 9. Mental state forest plot.

3.3.8. Quality of Life

Two studies [4] [5] reported quality of life scores, comprising a total of 130 patients (65 in the observation group and 65 in the control group). Subgroups divided by research quality. The meta-analysis revealed significant heterogeneity between the two studies ($I^2 = 95\%$, $P < 0.0001$); therefore, a random-effects model was employed. The forest plot indicated that nutritional support improved the quality of life for bone tumor patients during chemotherapy (MD = 18.05, 95% CI: 14.10 - 21.99, $P < 0.00001$), as shown in Figure 10.

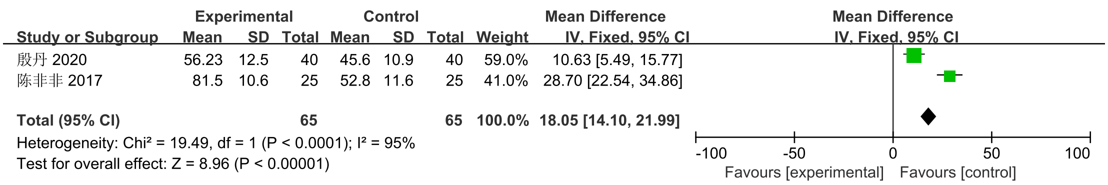

Figure 10. Quality of life forest plot.

3.3.9. Self-Management

Two studies [3] [5] reported quality of life scores, including a total of 160 patients (n = 80 in the observation group, n = 80 in the control group). Meta-analysis revealed significant heterogeneity between the two studies ($I^2 = 83\%$, $P = 0.02$); therefore, a random-effects model was employed. The forest plot indicated that nutritional support improves the self-management ability of patients with bone tumors during chemotherapy (MD = 1.59, 95% CI: 1.28 - 1.90, $P < 0.00001$) (see Figure 11).

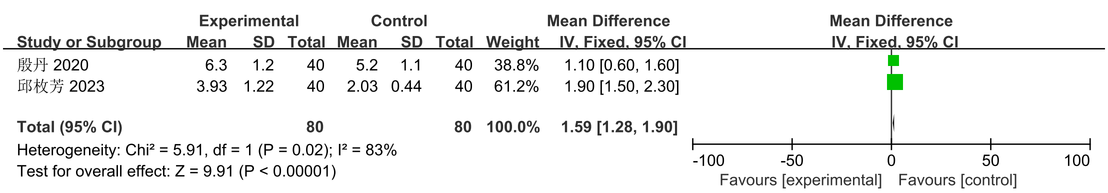

Figure 11. Self-management forest plot.

3.4. Assessment of Publication Bias

Funnel plot (**Figure 12**) shows that, the comparison of complications between the two groups revealed an asymmetrical distribution of effect sizes. The effect size points were relatively dispersed, suggesting potential publication bias in the research results.

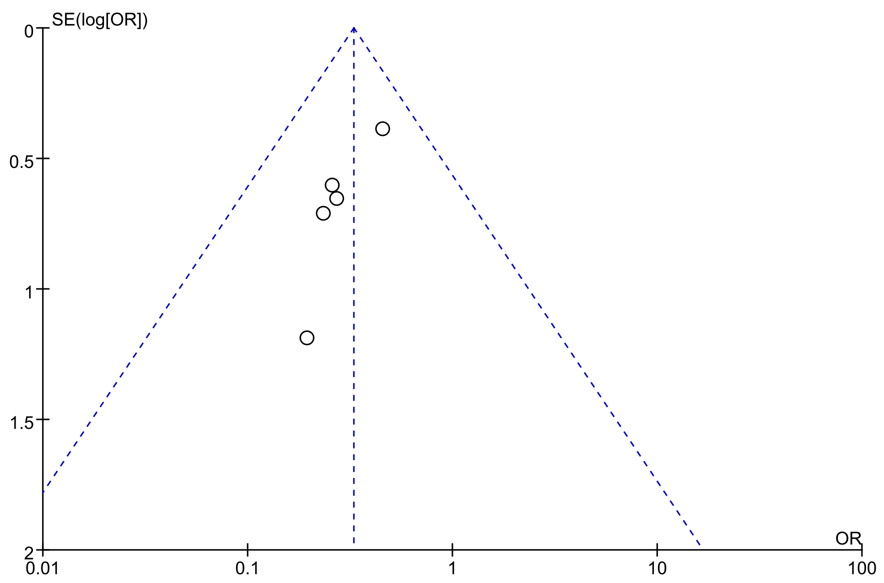

Figure 12. Complication funnel plot.

4. Discussions

Patients with bone tumors exhibit a significantly higher incidence of malnutrition, attributable to the combined effects of the disease and its treatment, such as chemotherapy. Chemotherapeutic agents not only inhibit tumor growth but also damage healthy cells, causing adverse effects including loss of appetite, digestive dysfunction, and metabolic disorders. These issues, in turn, exacerbate weight loss, muscle wasting, and decreased immunity, thereby directly compromising treatment tolerance. Common chemotherapy-induced toxicities include gastrointestinal issues (e.g., nausea, vomiting, diarrhea), myelosuppression (manifesting as leukopenia and thrombocytopenia), and hepatorenal dysfunction. These side effects not only restrict nutritional intake but also elevate the risk of complications like infection and anemia, often necessitating treatment interruptions or dose adjustments. While numerous clinical studies have endorsed the benefits of nutritional intervention [13] [14], research focused on the specific cohort of bone tumor patients remains fragmented and lacks a systematic synthesis of evidence. A meta-analysis that integrates data from high-quality studies can elucidate the precise impact of nutritional support on treatment tolerance and complications in this patient population, thereby providing an evidence-based foundation to guide clinical practice.

In this study, the meta-analysis indicated that nutritional support significantly improved hemoglobin, prealbumin, and BMI in bone tumor patients undergoing chemotherapy; reduced the incidence of complications and malnutrition; shortened hospital stays; alleviated negative emotions; and enhanced quality of life and self-management capabilities. These findings demonstrate the positive role of nutritional support for bone tumor patients during chemotherapy. Cancer patients with malnutrition as defined by GLIM have poorer overall survival and disease-free survival, and are more likely to develop postoperative complications [15]. This indicates that malnutrition significantly affects the clinical outcomes of cancer patients, emphasizing the importance of paying attention to patients' nutritional status in cancer treatment.

Wu Ligui *et al.* [16] reported that the postoperative application of enteral immune nutritional support for patients with gastrointestinal tumors might not reduce the incidence of common postoperative complications. This finding is inconsistent with the results of the present study, possibly because their research subdivided nutritional support methods, which suggests that the efficacy of different nutritional therapies varies. Furthermore, due to insufficient understanding of the registration process at the initiation of the study, the importance of PROSPERO registration in reducing selective reporting bias and improving research transparency was not fully recognized, and the registration process was not completed in accordance with the specifications during the study initiation phase.as this analysis included only two studies for each of the outcomes of prealbumin, BMI, psychological state, quality of life, and self-management, these findings require further validation in larger-scale studies. The funnel plot indicated that the effect size points were scattered, possibly due to large random errors from small sample sizes leading to result instability; moreover, blinding was not implemented in some studies, nutritional support protocols (e.g., calorie calculation, formula differences) were not standardized, and long-term follow-up data were lacking. Future research is required to increase the sample size, to conduct multi-center RCTs, and to further determine the optimal nutritional intervention model.

5. Conclusion

In conclusion, nutritional support improves treatment tolerance and reduces the risk of complications in patients with bone tumors undergoing chemotherapy. Further research comparing the efficacy of different nutritional intervention models is warranted to facilitate the development of individualized nutritional therapy plans through evidence integration.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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