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RESEARCH

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Relationship between BMI and chemotherapy-induced peripheral neuropathy in cancer patients: a dose-response meta-analysis

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Abstract

Objective This meta-analysis aimed to evaluate the dose-response relationship between body mass index (BMI) and the risk of chemotherapy-induced peripheral neuropathy (CIPN) in cancer patients.

Methods We conducted a dose-response meta-analysis of 10 studies involving 6,841 cancer patients. Studies reporting BMI and CIPN outcomes were selected. The relationship between BMI and CIPN was assessed using random-effects models and restricted cubic splines to model the dose-response association.

Results Pooled analysis revealed a significant association between higher BMI and increased risk of CIPN, with an odds ratio (OR) of 1.55 (95% CI, 1.20–1.99). A dose-response analysis demonstrated a clear linear relationship between BMI and the risk of CIPN. For every 5 kg/m^2 increase in BMI, the relative risk of CIPN increased by approximately 15%. Subgroup analyses showed stronger associations in breast cancer patients and those treated with taxane or platinum-based regimens. Sensitivity analyses confirmed the robustness of the results, and mild publication bias was observed.

Conclusions Higher BMI is significantly associated with an increased risk of CIPN, with a dose-dependent effect. Weight management interventions, such as dietary modifications and physical activity, may reduce CIPN risk, particularly in patients with elevated BMI undergoing chemotherapy with neurotoxic regimens.

Keywords BMI, Chemotherapy-Induced Peripheral Neuropathy, Dose-Response Relationship, Meta-analysis

Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a common and debilitating side effect of chemotherapy, affecting up to 60% of patients undergoing certain chemotherapy regimens, including those involving neurotoxic agents such as taxanes and platinum-based compounds [1, 2]. Symptoms of CIPN—such as pain, numbness, tingling, and motor dysfunction—can significantly impair patients' quality of life and interfere with their ability to carry out daily activities [3, 4]. Furthermore, CIPN can lead to dose reductions, delays, or discontinuations of chemotherapy, potentially compromising cancer treatment outcomes [5]. Given the high incidence and the substantial burden of CIPN, understanding the factors that predispose patients to this condition is crucial for optimizing chemotherapy regimens and improving clinical outcomes.

Body mass index (BMI), a widely used measure to assess adiposity, is recognized as an important determinant of various health outcomes, including cancer

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prognosis, chemotherapy-related toxicity, and overall survival [6–9]. Elevated BMI, particularly in the form of overweight and obesity, is associated with a higher risk of comorbid conditions such as diabetes, hypertension, and cardiovascular disease, all of which may exacerbate the adverse effects of chemotherapy [9, 10]. In recent years, BMI has been implicated in the development of chemotherapy-induced toxicities, with some studies suggesting that higher BMI could increase the risk of developing CIPN [11, 12]. However, the relationship between BMI and CIPN remains inconclusive. While certain studies indicate that overweight and obese individuals are more susceptible to developing CIPN [12], other research has found no significant association between BMI and the risk of neuropathy [13, 14]. Another important limitation of the existing literature is the reliance on categorical comparisons of BMI, such as normal weight versus overweight or obese categories. Although these studies provide valuable insights, they do not offer a comprehensive understanding of how incremental changes in BMI affect the risk of CIPN.

To address this gap, we conducted a dose-response meta-analysis to systematically evaluate the relationship between BMI and CIPN risk. This approach allows for a more granular assessment of the impact of BMI on CIPN, offering insights into whether small increases in BMI lead to measurable changes in risk. We aim to provide robust, evidence-based conclusions that can inform clinical practice and suggest potential interventions to mitigate the risk of CIPN, particularly in patients who are overweight or obese. Considering that BMI is a modifiable factor, our findings may have important implications for weight management strategies in cancer care, potentially reducing the incidence and severity of CIPN in high-risk populations.

Methods

Study design

This study is a dose-response meta-analysis designed to assess the relationship between BMI and the risk of CIPN. We systematically reviewed and synthesized data from studies that reported on the association between BMI and the risk of CIPN in cancer patients undergoing chemotherapy. The meta-analysis was conducted following the Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (Table S1) to ensure methodological rigor and transparency [15, 16]. The analysis was independently performed by two researchers (LZJ and ZHB), with a third reviewer (WZ) consulted to resolve any discrepancies.

Data sources

A comprehensive literature search was conducted to identify relevant studies published up until October 2024. Databases including PubMed, Embase, and Web of Science were searched using a combination of the following terms: "chemotherapy-induced peripheral neuropathy", "CIPN", "body mass index", "BMI", "obesity", "risk", and their variants. Full research strategies used in every single database were showed in Table S2. Only studies involving chemotherapy regimens associated with CIPN, such as taxanes (including paclitaxel) and platinum agents, were included in this meta-analysis. Studies where anthracyclines were used alone, without concomitant neurotoxic agents, were excluded. The search was supplemented by a manual review of reference lists from relevant articles and previous reviews to ensure any potential inclusion. No language restrictions were applied, and only studies published in peer-reviewed journals were considered.

Eligibility criteria

Studies were included if they met the following criteria:

1. Study Design: Clinical trials and observational studies including cohort studies, cross-sectional study, and case-control studies.
2. Population: Adults with cancer undergoing chemotherapy who were evaluated for CIPN risk.
3. Exposure: Studies that reported BMI as a continuous variable or categorized it into groups (e.g., underweight, normal weight, overweight, obese).
4. Outcome: Studies that assessed the occurrence of CIPN.
5. Statistical Data: This meta-analysis exclusively included studies that reported adjusted odds ratios (ORs) with 95% confidence intervals (CIs) or conducted multivariable analyses. These studies accounted for key confounders such as age, sex, and comorbidities within their individual analyses.

Studies were excluded if:

- They involved pediatric populations or non-human subjects.
- They did not report sufficient data on the relationship between BMI and CIPN (e.g., lacked effect size and adjusted data or required information for calculation).
- Studies focused on diabetic polyneuropathy or other unrelated neuropathies to maintain the specificity of the findings for CIPN.

Data extraction and quality assessment

Two authors independently extracted data from the included studies, using a standardized data extraction form. The following information was extracted:

- Study Characteristics: First author, year of publication, study design, cancer type, chemotherapy regimen, sample size, follow-up duration.
- BMI Measurement: Categories of BMI (e.g., underweight, normal weight, overweight, obese) or continuous BMI data.
- Outcome Measures: The assessment method for CIPN and the statistical measures (RR, OR, HR, etc.).
- Confounders: Relevant variables adjusted for in the analysis (e.g., age, sex, chemotherapy type, diabetes status).

To assess the quality of the included studies, we used the Newcastle-Ottawa Scale (NOS) for observational studies, which evaluates studies based on selection, comparability, and outcome assessment [17]. Studies with a NOS score ≥ 7 were considered to be of high quality. Discrepancies between reviewers were resolved by consensus or consultation with a third reviewer.

Dose-response analysis

We conducted a dose-response meta-analysis following the methods described by Greenland and Longnecker [18]. When median or mean values were not reported but data were presented in ranges, we estimated category midpoints by averaging the lower and upper boundaries. For open-ended categories, we set the midpoint of the highest category at 1.5 times its lower boundary, while the midpoint of the lowest category was set at 0.5 times its upper boundary. The analysis employed a restricted cubic spline model with at least three knots to capture potential non-linear relationships between BMI and CIPN risk. All statistical analyses were performed using Stata 18.0 (StataCorp, College Station, TX).

Statistical analysis

Pooled ORs with 95% CIs were calculated using a random-effects model, which accounts for both within-study and between-study heterogeneity. We chose the random-effects model due to the expected heterogeneity across studies in terms of patient populations, chemotherapy regimens, and methods of assessing CIPN. Heterogeneity across studies was assessed using the I^2 statistic, where I^2 values of 25%, 50%, and 75% were considered low, moderate, and high heterogeneity, respectively [19, 20]. To explore potential sources of heterogeneity, we conducted subgroup analyses based on study design, study center, region, chemotherapy regimen, BMI grouping, sample size, and NOS score. We also performed the 'leave-one-out' sensitivity analyses to assess the robustness of our findings, which involved excluding individual studies to determine whether any single study disproportionately influenced the pooled results. Publication bias was assessed using funnel plots and Egger's test [21]. A visual inspection of the funnel plots allowed us to assess asymmetry, while Egger's test was used to statistically evaluate the presence of bias. A p-value < 0.05 was considered indicative of significant publication bias. All statistical analyses were performed using Stata 18.0 (StataCorp, College Station, TX).

Results

Study selection

A comprehensive search identified 278 records from PubMed, Embase, and Web of Science. After removing duplicates, 112 unique records remained and were screened based on titles and abstracts. Of these, 97 studies were excluded for not meeting the inclusion criteria. Subsequently, 15 full-text articles were assessed for eligibility. Among them, five studies were excluded for the following reasons: absence of BMI data ($n=2$), lack of adjusted or multivariate data ($n=2$), and irrelevance to the study objective ($n=1$). Ultimately, a total of 10 studies fulfilled the inclusion criteria and were incorporated into the final meta-analysis [13, 14, 22–29] (Fig. 1).

Study characteristics

The included studies encompassed a total of 6,841 patients and were conducted across diverse regions, including the USA, Iran, Kenya, Korea, Japan, Indonesia, and China (Table 1). The studies primarily investigated breast cancer patients, with chemotherapy regimens dominated by taxane-based treatments, followed by paclitaxel, cisplatin, and anthracycline. The sample sizes ranged from 38 to 3,387 participants, with the largest study conducted in the USA. Most studies adjusted for confounding factors, including age, comorbidities, tumor characteristics, treatment regimens, and socioeconomic variables, ensuring robust statistical analyses. Methodological quality, assessed using the NOS, ranged from moderate to high, with scores between 5 and 8. Seven studies were classified as high-quality (NOS ≥ 7), the remaining ones moderate quality (Table 2).

Association between BMI and CIPN

Pooled analysis revealed a significant association between higher BMI and increased risk of CIPN, with an odds ratio (OR) of 1.55 (95% CI, 1.20–1.99) (Table 3, Fig. 2). Moderate heterogeneity was observed across the studies ($I^2=61.6\%$; $P=0.005$), justifying the use of a random-effects model. This finding highlights that patients

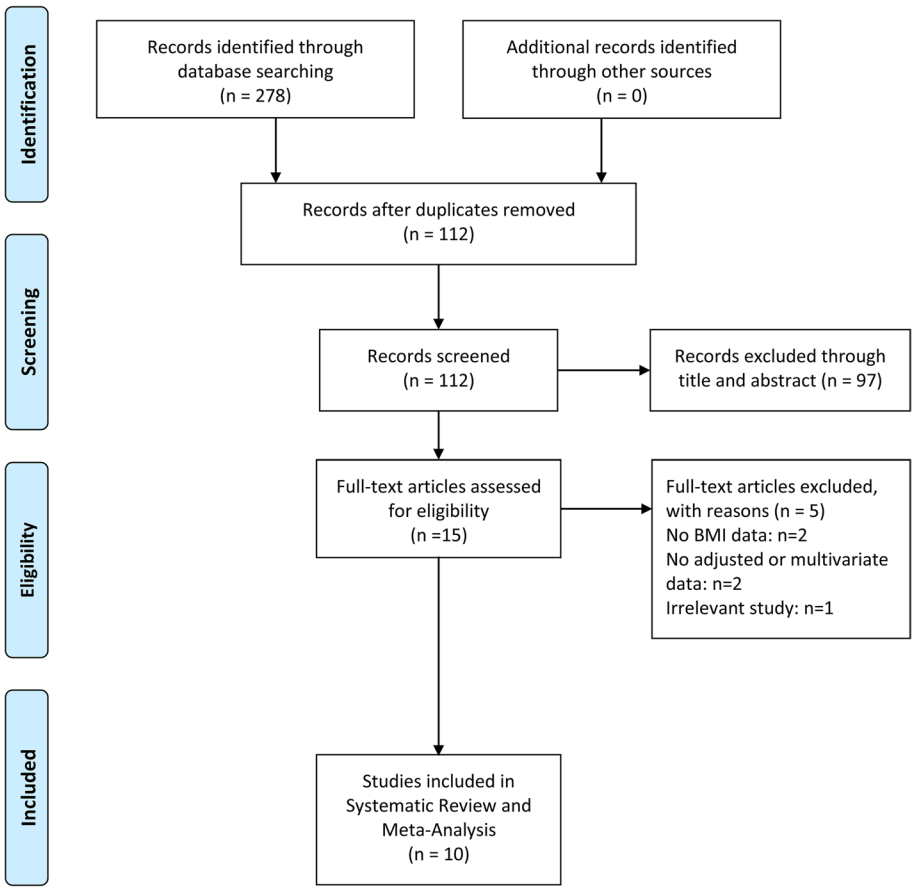

Fig. 1 The PRISMA flow chart of literature search strategies

with higher BMI have a substantially elevated risk of developing CIPN compared to those with lower BMI. To explore the potential source of heterogeneity across studies, we carried out several subgroup analyses (Table 3). Retrospective studies demonstrated a stronger association (OR, 1.61; 95% CI, 1.33–1.95; P < 0.0001) compared to prospective studies (OR, 1.38; 95% CI, 0.92–2.06; P = 0.118). Geographical differences were noted, with studies from Europe and America reporting a higher association (OR, 1.82; 95% CI, 1.36–2.44; P < 0.0001) compared to those from Asia (OR, 1.23; 95% CI, 0.88–1.72; P = 0.217). Taxane-based chemotherapy regimens showed a significant association with CIPN (OR, 1.55; 95% CI, 1.20–2.01; P = 0.001), whereas cisplatin-based chemotherapy did not exhibit statistically significant associations with CIPN (OR, 1.60; 95% CI, 0.19–13.76; P = 0.669). Studies stratified by tertiles of BMI exhibited a stronger effect size (OR, 1.80; 95% CI, 1.04–3.12; P = 0.035) compared to quartiles. To further confirm the robustness of the results, we conducted the 'leave-one-out' sensitivity analysis. We found that exclusion of individual studies did not meaningfully alter the pooled effect size, with the overall OR consistently remaining within the 95% CI (Fig. 3). This demonstrates the stability of the association between BMI and CIPN across the included studies, underscoring the robustness and reliability of the overall pooled estimate.

Dose-response relationship

A dose-response analysis demonstrated a clear linear relationship between BMI and the relative risk of CIPN (Fig. 4). For every 5 kg/m^2 increase in BMI, the relative risk of CIPN increased by approximately 15%. This linear trend suggests that the risk of CIPN rises proportionally with increasing BMI, with no evidence of nonlinearity (P for nonlinearity = 0.5058).

Publication bias

Publication bias was assessed through visual inspection of the funnel plot and Egger's regression test. The funnel plot appeared symmetrical (Fig. 5), indicating minimal evidence of publication bias. Additionally, Egger's test yielded a P-value > 0.05, further supporting the absence of significant publication bias. Regardless of these, the small

Table 1 Baseline characteristics of included studies

Author (Year)	Study type	Study center	Country	No. of patients	Cancer types	Chemotherapy regimens	Adjuvant or neoadjuvant chemotherapy	BMI groups (sample size)	OR (95% CI) in multivariate regression	Adjustment for confounders
Heather Greenlee 2016 [23]	Retrospective Cohort	Single-center	The USA	1,237	Breast cancer	Taxane(Docetaxel or Paclitaxel)	NA	<25; 25-29.9; >30	1(reference); 2.37 (1.19-4.88); 3.21 (1.52-7.02)	Age, race, education, income, BMI, fruit/vegetable intake, moderate-to-vigorous physical activity, antioxidant use, tumor stage, number of positive nodes, taxane drug, taxane schedule, prior taxane treatment, comorbidities, and baseline FACT-NTX score
Ting Bao 2016 [22]	Cross-sectional	Multi-center	The USA	296	Breast cancer	Taxane(Docetaxel or Paclitaxel)	Adjuvant and neoadjuvant chemotherapy	<25; 25-30; >30	1(reference); 1.42 (0.79-2.55); 1.94 (1.03-3.65) 1.44 (0.77 to 1.98)	Age, race, education level, employment status, and tobacco use
Zohreh Ghoreishi 2018 [23]	Randomized controlled trial	Single-center	Iran	57	Breast cancer	Taxane(Paclitaxel)	NA	NA	NA	Age and progesterone receptor
Mohammed S Ezzi 2019 [13]	Cross-sectional	Single-center	Kenya	67	Primary cancers[a]	Cisplatin	NA	<18.5; 18.5 to <25; 25 to <30; >30	0.5 (0.1 to 2.1); 1(reference); -; 1.6 (0.2 to 14.8)	NA
Kyung-Lak Son 2022 [14]	Retrospective Cohort	Single-center	Korea	48	Breast cancer	Taxane(Docetaxel)	Adjuvant chemotherapy	<23; >23	1.80 (0.36-8.97)	Age, BMI, education, type of operation, alcohol use, smoking, sleep quality, depression, and anxiety
Yuko Kanbayashi 2022 [25]	Prospective self-controlled	Single-center	Japan	38	Breast cancer	Taxane(Paclitaxel)	Adjuvant and neoadjuvant chemotherapy	NA	1.13(1.01-1.26)	NA
Ciao-Sin Chen 2023 [26]	Prospective cohort	Multi-center	The USA	1,191	Breast cancer	Taxane(Paclitaxel)	Adjuvant chemotherapy	8-25; 26-31; 32-89	1.55(0.8-2.89); 1.04 (0.58-1.81); 2.02 (1.21-3.4)	Age and paclitaxel schedule
R Dixon Dorand 2023 [27]	Retrospective Cohort	Single-center	The USA	3387	Primary cancers[b]	Taxane(Paclitaxel or Docetaxel)	NA	<18.5; 18.5 to <25; 25 to <30; >30	1.04 (0.61 to 1.77); 1(reference); 1.31 (1.06 to 1.61); 1.49 (1.21 to 1.83)	Prior chemotherapy, prior radiotherapy, cancer type, and cancer stage

Table 1 (continued)

Author (Year)	Study type	Study center	Country	No. of patients	Cancer types	Chemotherapy regimens	Adjuvant or neoadjuvant chemotherapy	BMI groups (sample size)	OR (95% CI) in multivariate regression	Adjustment for confounders
Juan Adrian Wiranata 2024 [29]	Prospective cohort	Single-center	Indonesia	170	Breast cancer	Anthracycline, taxane, and capecitabine	Neoadjuvant, adjuvant and palliative chemotherapy	<19.01; 19.01-21.85; >21.85	1(reference); 0.36 (0.11 to 1.23); 0.52 (0.17 to 1.59)	NA
Sun Lixian 2024 [28]	Prospective cohort	Single-center	China	350	Breast cancer	Taxane(Paclitaxel)	Adjuvant chemotherapy	<24(111); >24(166)	8.139(1.157-57.24)	NA

[a] Musculoskeletal, lung, head and neck, genitourinary, gastrointestinal, and breast cancers

[b] Breast cancer, head and neck cancers, lung and other respiratory cancers, gynecological cancers, Gastrointestinal cancers, and unknown cancers

Table 2 Methodological quality assessment of included studies by Newcastle-Ottawa scales

Study	Selection				Comparability	Outcome			Total Score
	Exposed Cohort	Nonexposed Cohort	Ascertainment of Exposure	Outcome of Interest		Assessment of Outcome	Length of Follow-up	Adequacy of Follow-up	
Heather Greenlee 2016 [23]	*	*	*	*	*	*	*	——	7
Ting Bao 2016 [22]	*	——	*	*	——	*	*	——	5
Zohreh Ghoreishi 2018 [23]	*	——	*	*	——	*	*	——	5
Mohammed S Ezzi 2019 [13]	*	*	*	*	**	*	*	——	8
Kyung-Lak Son 2022 [14]	*	*	*	*	**	*	*	——	8
Yuko Kanbayashi 2022 [25]	*	*	*	*	**	*	*	——	8
Ciao-Sin Chen 2023 [26]	*	*	*	*	*	*	*	——	7
R Dixon Dorand 2023 [27]	*	*	*	*	**	*	*	——	8
Juan Adrian Wiranata 2024 [29]	*	——	*	*	——	*	*	——	5
Sun Lixian 2024 [28]	*	*	*	*	*	*	*	——	7

Single asterisk indicates 1 score, double asterisk indicates 2 scores, and dash indicates 0 scores

number of included studies ($n=10$) may limit the statistical power of these analyses. Accordingly, it was hardly to rule out the potential publication bias.

Discussion

The main findings

This dose-response meta-analysis demonstrates a significant association between elevated BMI and an increased risk of CIPN in cancer patients. The pooled OR of 1.55 (95% CI, 1.20–1.99) indicates that individuals with higher BMI face a substantially increased risk of developing CIPN. This finding emphasizes BMI as a clinically relevant, potentially modifiable risk factor that should be considered in oncological treatment planning.

Potential mechanisms

The observed association between elevated BMI and CIPN showed that obesity exacerbated chemotherapy-related neurotoxicity. Several underlying mechanisms may explain this relationship. Firstly, BMI can influence the pharmacokinetics of chemotherapeutic agents and adipose tissue may serve as a reservoir, which may lead to prolonged drug exposure and increased neurotoxic effects on peripheral nerves [30]. Secondly, obesity is characterized by chronic inflammation mediated by elevated levels of pro-inflammatory cytokines, which may amplify neuronal sensitivity and increase the risk of peripheral nerve damage [31, 32]. Thirdly, metabolic dysregulation associated with obesity, including insulin resistance and impaired glucose metabolism, may further impair nerve repair mechanisms and exacerbate chemotherapy-induced nerve injury [33, 34]. Additionally, obesity-related changes in peripheral nerve structure, such as reduced nerve fiber density, have been documented in diabetic neuropathy and may also apply to CIPN [35]. Finally, a recent study demonstrates that metabolomic profiling can predict CIPN in breast cancer patients, with amino acid metabolism playing a key role in its pathogenesis [36]. Among 249 identified metabolites associated with neurologic toxicity, pathways such as D-glutamine and D-glutamate metabolism, valine/leucine/isoleucine biosynthesis, and arginine and proline metabolism were significantly implicated. The findings suggest that chemotherapy may induce neuropathy by disrupting amino acid metabolism, oxidative stress balance, and neuronal energy homeostasis. Anyway, the exact mechanism is not fully understood and further research is needed to clarify the association between elevated BMI and increased risk of CIPN.

Subgroup analyses revealed notable variations based on study design, geographic location, and chemotherapy regimen. Retrospective studies reported a stronger association than prospective studies, possibly due to biases inherent in retrospective designs, including incomplete data collection and recall bias. Geographic differences were also observed, with studies conducted in Europe

Table 3 Subgroup analyses of relationship between BMI and chemotherapy-induced peripheral neuropathy

Subgroup	No. Studies	Test of Relationship		Test of Heterogeneity	
		OR (95% CI)	*P* Value	I^2, %	*P* Value
Total	10	1.55(1.20-1.99)	0.001	61.6	0.005
Study design					
Prospective study	5	1.38(0.92-2.06)	0.118	64.4	0.024
Retrospective study	5	1.61(1.33-1.95)	< 0.0001	0.4	0.404
Study center					
Single center	8	1.43(1.08-1.90)	0.012	61.5	0.011
Multi center	2	1.99(1.33-2.97)	0.001	0	0.923
Region					
Asia	6	1.23(0.88-1.72)	0.217	30.1	0.209
Europe and America	4	1.82(1.36-2.44)	< 0.0001	35.9	0.197
Chemotherapy regimens					
Taxane based chemotherapy	9	1.55(1.20-2.01)	0.001	65.8	0.003
Cisplatin based chemotherapy	1	1.60(0.19-13.76)	0.669	NA	NA
BMI grouping					
Tertiles	4	1.80(1.04-3.12)	0.035	57.2	0.071
Quartiles	2	1.49(1.21-1.83)	< 0.0001	0	0.949
Others	4	1.34(0.92-1.94)	0.128	41.5	0.163
Sample size					
<100	4	1.15(1.03-1.28)	0.012	0	0.716
>100	6	1.81(1.23-2.67)	0.003	55.8	0.046
NOS score					
Moderate	3	1.33(0.76-2.33)	0.319	50.5	0.133
High	7	1.64(1.20-2.24)	0.002	68.3	0.004

and the United States reporting a stronger association compared to those from Asia. This variability may reflect differences in BMI definitions, genetic susceptibility, dietary habits, and access to healthcare services, all of which could influence the observed outcomes. The type of chemotherapy regimen played a critical role in modulating the BMI-CIPN relationship. Taxane-based therapies, such as docetaxel and paclitaxel, showed the strongest association with CIPN among patients with elevated BMI. Taxanes are known for causing sensory neuropathy due to their disruption of microtubule dynamics in peripheral nerves. Interestingly, studies involving cisplatin and anthracyclines showed weaker or nonsignificant associations, suggesting that the effect of BMI on CIPN risk may be chemotherapy-specific. These findings suggest that personalized dosing regimens based on BMI could be particularly beneficial for patients receiving taxane-based treatments.

The linear dose-response analysis further strengthened the validity of the findings. The risk of CIPN increased incrementally with higher BMI values, with no evidence of a plateau or threshold effect. This suggests that even modest reductions in BMI could meaningfully reduce CIPN risk, providing a strong rationale for incorporating weight management strategies into cancer treatment protocols.

Clinical implications

The findings of this meta-analysis have significant implications for clinical practice, particularly in the management of CIPN. The clear association between elevated BMI and an increased risk of CIPN suggests that BMI is a modifiable risk factor that clinicians can target to potentially reduce the incidence and severity of this condition. With obesity and overweight being prevalent among cancer patients, especially those undergoing chemotherapy, incorporating weight management strategies into cancer care could serve as a practical intervention to prevent or mitigate CIPN. Interventions aimed at reducing BMI, such as structured weight-loss programs combining dietary modifications, exercise, and behavioral therapies, may not only improve overall health outcomes but could directly influence the risk of CIPN. BMI, although a widely used surrogate for obesity, does not account for fat distribution, particularly central adiposity, which may have a stronger influence on CIPN development. BMI reduction may reduce overall obesity, but different weight management strategies including reducing central

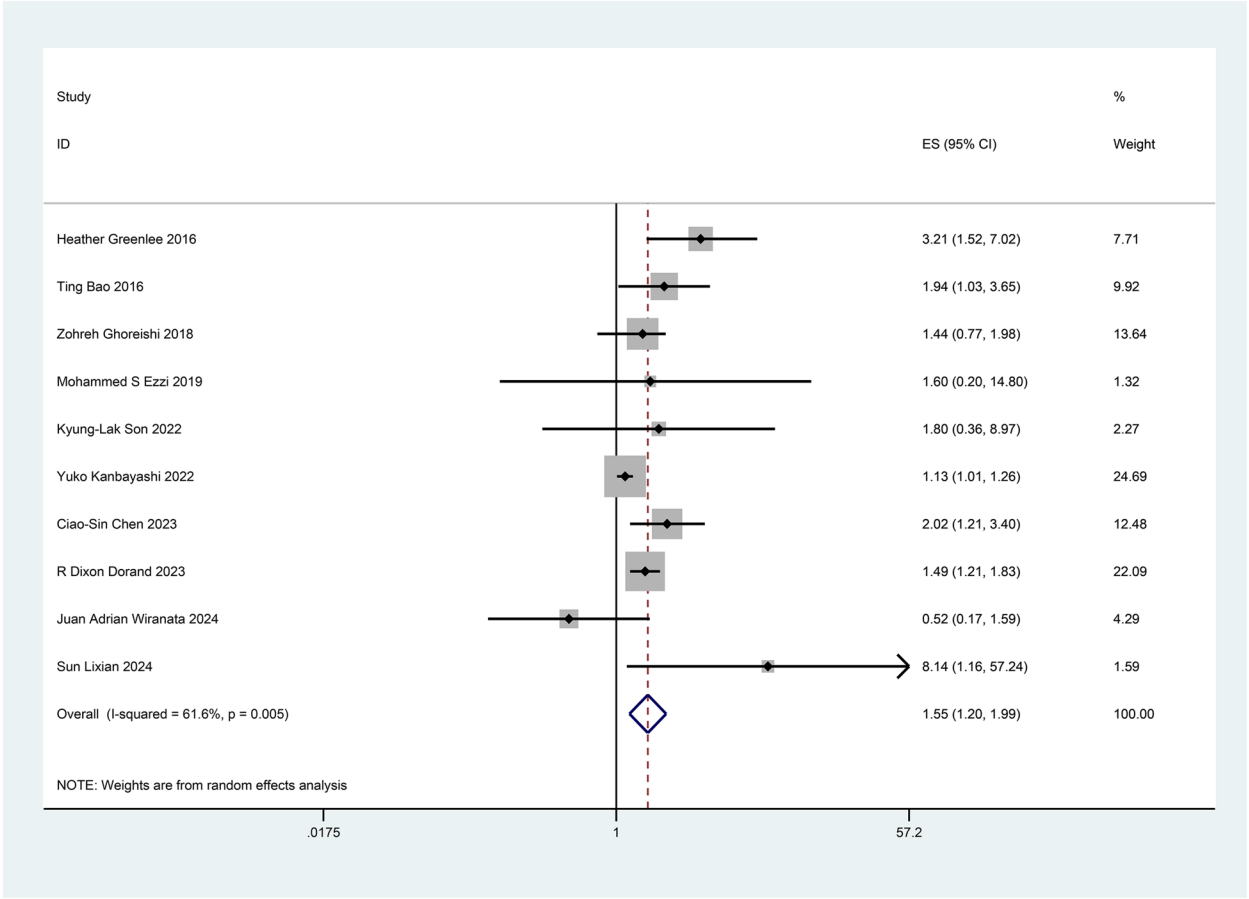

Fig. 2 Forest plot of correlation between BMI and the risk of CIPN in patients with cancers. BMI: Body mass index; CIPN: Chemotherapy-induced peripheral neuropathy

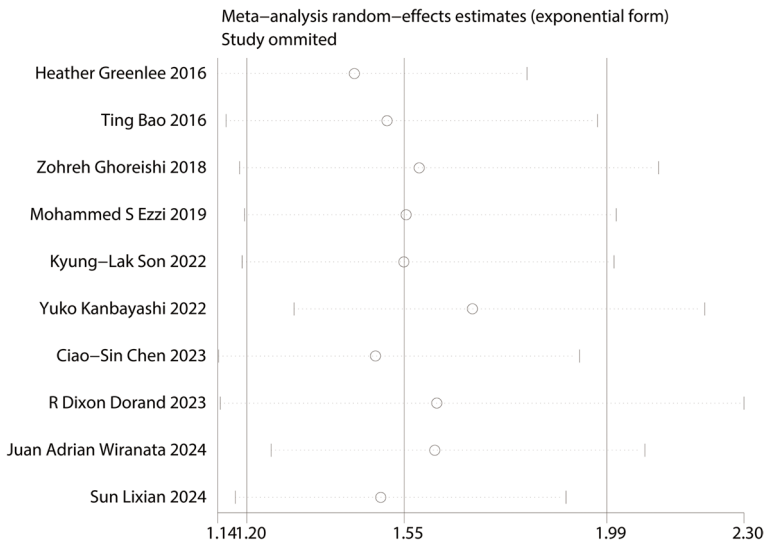

Fig. 3 The "leave-one-out" sensitive analysis

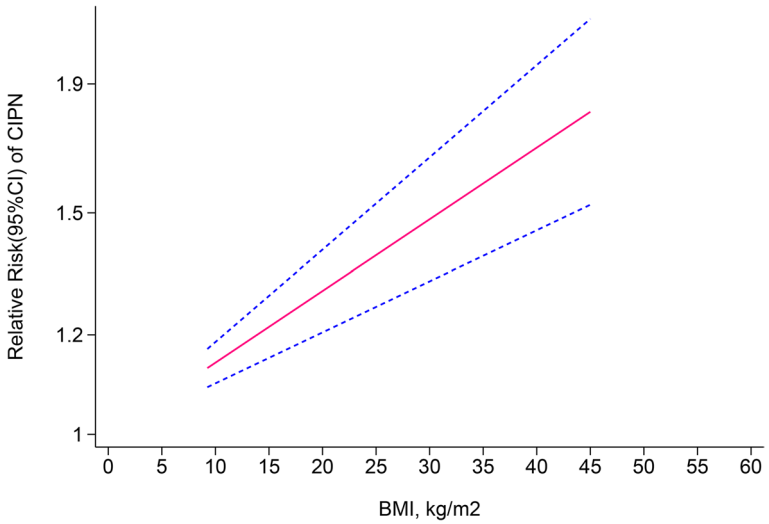

Fig. 4 Funnel plot for examining the potential publication bias. Begg's test, $p = 0.474$

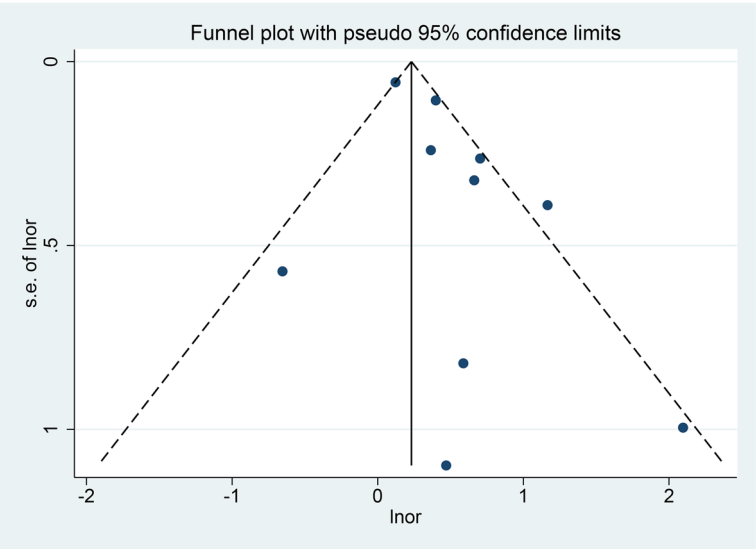

Fig. 5 Dose–response relationships between BMI and the risk of CIPN in patients with cancers. BMI: Body mass index; CIPN: Chemotherapy-induced peripheral neuropathy

adiposity, may have differential effects on CIPN risk. Given the metabolic and inflammatory implications of central adiposity, it is plausible that reducing visceral fat could have distinct effects on CIPN risk and progression. Visceral fat accumulation is linked to systemic inflammation and insulin resistance, both of which may exacerbate CIPN by increasing oxidative stress and neuroinflammation. Future research should investigate whether targeted fat reduction strategies, particularly those focusing on visceral fat, can attenuate CIPN symptoms more effectively than overall weight loss. This would help refine post-treatment lifestyle recommendations for CRC survivors to optimize both neurological and metabolic health. Furthermore, considering that CIPN is strongly associated with chemotherapy agents like taxanes and platinum compounds, patients receiving these regimens might benefit particularly from such interventions. Since CIPN can lead to treatment interruptions, dose reductions, and diminished quality of life, reducing BMI could serve as an effective approach to enhancing chemotherapy tolerability, treatment adherence, and ultimately, cancer outcomes. Moreover, healthcare providers should consider

routine screening for overweight and obesity in cancer patients before initiating chemotherapy, followed by tailored recommendations for weight management as part of a comprehensive cancer care plan. Interestingly, increasing evidence indicated that exercise during chemotherapy significantly reduce the risk of CIPN [37, 38]. Accordingly, nutrition counseling, exercise programs, and even pharmacological treatments for obesity should be integrated into the treatment protocol, particularly for patients at high risk of developing CIPN. In doing so, clinicians can optimize treatment plans and reduce the long-term burden of chemotherapy-induced toxicities.

Strengths and limitations

One of the strengths of this meta-analysis is the inclusion of studies with diverse cancer types, chemotherapy regimens, and CIPN assessment methods. This broadens the applicability of our findings across various patient populations. Additionally, our use of a dose-response approach, which takes into account the continuous nature of BMI, allows for a more detailed understanding of the relationship between BMI and CIPN risk compared to previous studies that relied on BMI categories. The restricted cubic spline model used in this analysis provides a more precise estimate of the association. Furthermore, the robustness of our findings was supported by sensitivity analyses, which confirmed the consistency of the results despite variations in study design and potential sources of bias.

While this meta-analysis provides valuable insights, several important limitations should be considered when interpreting the results.

Firstly, the vast majority of studies included in this analysis were observational in nature. Although we found a significant association between BMI and CIPN, observational studies are susceptible to confounding, which may distort the true relationship. For example, patients with high BMI often have other comorbidities, such as diabetes, hypertension, and metabolic syndrome, which are themselves associated with neuropathy and may exacerbate CIPN independently of BMI. While the included studies provided adjusted ORs and conducted multivariable analyses to account for confounders, the lack of individual-level data in our meta-analysis precluded additional covariate adjustments. Consequently, residual confounding cannot be entirely ruled out. For example, unmeasured variables, such as the duration and dose of chemotherapy, may influence the observed associations. Moreover, the dose-response analysis was performed using estimated midpoints for categorical BMI data, a standard approach in dose-response meta-analysis. However, this methodology introduces certain assumptions about the data, which may be inconsistent with real results. Similarly, regardless of the possible dose-response relationship between BMI and CIPN risk, the biological plausibility of this association should be interpreted with caution given the limitations of the study design. Future studies using individual-level data may provide more precise and accurate dose-response estimates.

Secondly, while the dose-response model used in this study is a strength, the methods for BMI assessment varied across studies. Some studies used self-reported BMI, which could introduce bias due to underreporting or misclassification, particularly in obese individuals. Others employed clinical or measured BMI, which tends to be more accurate. The variability in CIPN assessment methods also presents a limitation, as different studies used a range of tools, from clinical evaluations to neurophysiological tests. This heterogeneity in assessment methods may lead to discrepancies in the reported prevalence and severity of CIPN, affecting the consistency of the results across studies.

Thirdly, while our study included a broad range of cancer types and chemotherapy regimens, the findings may not be fully generalizable to all patient populations. For instance, patients with different cancers were included in the current study, and these patients may experience different chemotherapy-related toxicities. Additionally, the specific chemotherapy regimens and dosing schedules can influence the severity of CIPN, yet not all regimens were equally represented in the included studies.

Finally, the potential for publication bias exists. Although we employed statistical methods to assess and adjust for this bias, it is possible that studies with negative or null results were not published or included in the analysis, potentially overestimating the true effect size. Additionally, the relatively small number of included studies means that the effect size may still be overestimated. Therefore, larger studies and future meta-analyses with more robust data are necessary to confirm these findings.

Conclusions

In conclusion, this meta-analysis provides compelling evidence that elevated BMI is a significant risk factor for CIPN, particularly in patients undergoing taxane-based chemotherapy. The linear dose-response relationship highlights the potential benefits of BMI reduction in mitigating CIPN risk. Incorporating weight management strategies, individualized chemotherapy dosing, and routine neurological monitoring into cancer care protocols reduce the risk of CIPN and improve patient outcomes. Future research should explore the mechanistic pathways linking obesity to CIPN and evaluate the effectiveness of

multidisciplinary interventions targeting this modifiable risk factor.

Abbreviations

BMI	Body mass index
CIPN	Chemotherapy-induced peripheral neuropathy
RR	Relative risk
OR	Odds ratio
HR	Hazard ratio
CI	Confidence interval
NOS	Newcastle-Ottawa Scale

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-025-03716-2.

Supplementary Material 1: Table S1. PRISMA checklist.

Supplementary Material 2: Table S2. The detailed search strategy in three databases.

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None.

Authors' contributions
LYB and WZ conceptualized, designed, and revised the manuscript; LZJ and ZHB searched the literature, collected the data, organized the data, and drafted the manuscript; LYB, LZJ, and ZHB collected the data; LZJ and ZHB performed the statistical analyses. All authors contributed to the article and approved the submitted version.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
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Competing interests
The authors declare no competing interests.

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