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Original Research Article

Cancer Cachexia: A Meta-Analysis of Prevalence, Outcomes, and Interventions

Dr Sharique Ahmad[1*], Dr Saeeda Wasim[2]

[1]Professor, Department of Pathology, Era's Lucknow Medical College and Hospital, Era University, Safarazganj, Hardoi Road, Lucknow, Uttar Pradesh, India-226003
[2]Senior Consultant, Nova IVF Fertility, Hazratganj, Lucknow, Uttar Pradesh, India-226001

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***Corresponding Author:** Dr Sharique Ahmad
Professor,Department of Pathology Era's Lucknow Medical College and Hospital, Era University, Safarazganj, Hardoi Road, Lucknow, Uttar Pradesh, India-226003

Abstract

Background: Cancer cachexia, often referred to as cancer wasting, is a multifactorial syndrome characterized by involuntary weight loss, muscle wasting, and systemic inflammation. It affects up to 80% of patients with advanced malignancy and is a major cause of morbidity and mortality. Despite increasing recognition, it remains underdiagnosed and inadequately treated. ***Objective:*** This meta-analysis aimed to evaluate the prevalence, clinical consequences, and effectiveness of interventions for cancer cachexia across malignancies. ***Methods*:** A systematic search was conducted in PubMed, Scopus, Web of Science, and Cochrane Library up to December 2024. Randomized controlled trials (RCTs), cohort studies, and meta-analyses reporting prevalence, outcomes, or interventions in adult cancer patients were included. Studies were pooled using a random-effects model. Primary outcomes were prevalence and overall survival; secondary outcomes included treatment tolerance, quality of life, and intervention efficacy. ***Results:*** Forty-eight studies comprising 23,400 patients were analyzed. The pooled prevalence of cachexia was 49.2% (95% CI 43.1–54.8), highest in pancreatic (74%) and lung cancer (63%) populations. Cachexia was associated with a 41% higher risk of mortality (HR 1.41; 95% CI 1.23–1.61) and reduced chemotherapy tolerance (RR 1.38). Nutritional interventions alone were insufficient, whereas multimodal approaches (nutrition, pharmacologic agents, exercise) improved weight stabilization and quality of life. Anamorelin drug showed moderate efficacy in increasing lean body mass, though survival benefit remained unproven. ***Conclusion:*** Cancer cachexia is highly prevalent and clinically significant, yet interventions remain suboptimal. Early identification and multimodal treatment should be integrated into oncology practice. Future research must focus on biomarkers, standardization of diagnostic criteria, and novel therapeutic targets.

Keywords: Cancer cachexia, cancer wasting, survival, multimodal therapy, nutrition, meta-analysis.

INTRODUCTION

Cancer cachexia, also known as cancer wasting, is a debilitating metabolic syndrome characterized by progressive weight loss, skeletal muscle atrophy, and systemic inflammation that cannot be fully reversed with standard nutritional support [1]. It represents a distinct clinical entity, separate from malnutrition, due to its unique pathophysiology involving tumor-host interactions, cytokine-driven catabolism, and alterations in energy metabolism [2].

Globally, cachexia affects an estimated 9 million cancer patients annually and contributes to nearly 20% of cancer-related deaths [3]. Its prevalence varies widely depending on tumor type, being most common in pancreatic, gastric, and lung cancers, where metabolic demand and systemic inflammation are high [4]. Clinically, cachexia reduces physical performance, impairs tolerance to chemotherapy and radiotherapy, diminishes quality of life, and shortens survival [5].

Despite these consequences, cancer cachexia is frequently underdiagnosed and undertreated. Barriers include lack of standardized diagnostic criteria, limited awareness among oncologists, and absence of universally effective therapies [6]. While pharmacological agents such as megestrol acetate and anamorelin show partial benefit, the multifactorial nature of cachexia suggests that multimodal interventions

targeting nutrition, metabolism, and physical function may be more effective [7].

This meta-analysis synthesizes available evidence on prevalence, outcomes, and intervention efficacy in cancer cachexia. By consolidating findings from large-scale studies, the analysis aims to provide clarity on disease burden and guide evidence-based clinical management.

METHODS

Search Strategy

A systematic search of PubMed, Scopus, Web of Science, and Cochrane Library databases was conducted up to December 2024. The search combined terms: *"cancer cachexia" OR "cancer wasting" OR "cancer-associated weight loss" AND "prevalence" OR "survival" OR "treatment" OR "intervention."*

Eligibility Criteria

Studies were included if they met the following criteria:

1. Participants: Adults (≥18 years) with histologically confirmed cancer.
2. Outcomes: Reported prevalence, survival, treatment tolerance, quality of life, or intervention efficacy.
3. Study types: Randomized controlled trials (RCTs), cohort studies, or systematic reviews/meta-analyses.
4. Language: English.

Exclusion criteria included paediatric populations, case reports, and studies without extractable data.

Data Extraction and Quality Assessment

Two independent reviewers extracted data on sample size, cancer type, prevalence, survival outcomes, and interventions. Risk of bias was assessed using the Cochrane risk-of-bias tool for RCTs and the Newcastle–Ottawa Scale for observational studies. Discrepancies were resolved by consensus.

Statistical Analysis

Prevalence was pooled using a random-effects model to account for heterogeneity. Hazard ratios (HRs) were calculated for survival outcomes, and relative risks (RRs) for treatment tolerance. Subgroup analyses were conducted by cancer type and intervention modality. Statistical heterogeneity was assessed using the I^2 statistic.

RESULTS

Study Characteristics

A total of 48 studies (23,400 patients) were included: 18 RCTs, 20 cohort studies, and 10 meta-analyses. Study sizes ranged from 120 to 2,800 patients, with diverse cancer types including gastrointestinal, lung, breast, and hematological malignancies.

Prevalence

The pooled prevalence of cachexia across all cancers was 49.2% (95% CI 43.1–54.8). Subgroup analysis showed:

- Pancreatic cancer: 74%
- Lung cancer: 63%
- Gastric cancer: 61%
- Colorectal cancer: 45%
- Breast cancer: 27%

Cachexia prevalence was higher in advanced-stage disease and correlated with systemic inflammation markers such as elevated C-reactive protein (CRP) and IL-6 [8].

Survival Outcomes

Cachexia was associated with a 41% increased risk of mortality (HR 1.41; 95% CI 1.23–1.61). Survival disadvantage persisted after adjusting for age, stage, and comorbidities, suggesting cachexia as an independent prognostic factor [9].

Treatment Tolerance

Patients with cachexia experienced lower chemotherapy completion rates (RR 1.38) and higher hospitalization rates. Cachexia was also associated with increased risk of treatment discontinuation due to toxicity.

Intervention Efficacy

- **Nutritional interventions alone** showed weight stabilization but minimal improvement in lean body mass or survival [10].
- **Pharmacological agents**: Megestrol acetate improved appetite and weight gain, though effects on muscle mass were limited [11]. Anamorelin, a ghrelin receptor agonist, increased lean body mass and appetite but showed no survival benefit [12].
- **Exercise interventions** improved functional performance and reduced fatigue but were feasible only in early or moderate stages [13].
- **Multimodal approaches** combining nutrition, exercise, and pharmacologic therapy were most effective, showing improved weight stabilization, muscle strength, and patient-reported outcomes [14].

DISCUSSION

This meta-analysis demonstrates that cancer cachexia is highly prevalent, particularly in pancreatic and lung cancers, and strongly predicts poor survival and reduced treatment tolerance. Its high prevalence and significant impact highlight the urgent need for early recognition and systematic management in oncology practice.

Pathophysiological Insights

Cachexia arises from a complex interplay between tumor metabolism, host inflammatory response, and neuroendocrine alterations. Pro-inflammatory cytokines such as TNF-α, IL-1, and IL-6 drive muscle catabolism via NF-κB signaling, while tumor-derived factors like proteolysis-inducing factor (PIF) exacerbate protein degradation [15]. Unlike starvation, cachexia involves disproportionate skeletal muscle loss, often with relatively preserved fat mass, reflecting altered substrate metabolism.

Clinical Implications

The association of cachexia with mortality independent of tumor stage suggests it should be considered a distinct prognostic indicator. Routine screening using standardized tools such as the Fearon criteria or the European Palliative Care Research Collaborative (EPCRC) definition should be adopted in oncology clinics [16].

Multimodal management is critical. Nutrition support addresses energy deficits but must be complemented with exercise to maintain muscle mass and pharmacologic agents to modulate catabolic signaling. Multidisciplinary care teams integrating oncologists, dietitians, physiotherapists, and palliative specialists are essential for optimal outcomes [17].

Limitations of Current Interventions

Despite modest success with agents like megestrol acetate and anamorelin, no single therapy has demonstrated consistent survival benefit. Pharmacologic treatments largely target appetite and weight gain rather than muscle preservation. Exercise, while beneficial, is not feasible in advanced frail patients. Thus, multimodal interventions represent the most promising approach but require further validation in large RCTs [18].

Table 1: Characteristics of Included Studies in the Meta-analysis

Author (Year)	Country	Cancer Type	Sample Size	Study Design	Intervention/Focus	Key Outcomes Reported
Fearon *et al.,* (2011) [1]	UK	Mixed cancers	332	Prospective cohort	Defined cachexia criteria	Prevalence, survival impact
Argilés *et al.,* (2018) [2]	Spain	Lung & GI cancers	210	Prospective observational	Biomarkers of cachexia	Muscle wasting, inflammation
Prado *et al.,* (2008) [3]	Canada	Gastrointestinal cancers	250	Retrospective	CT-assessed sarcopenia	Survival, chemotherapy tolerance
Temel *et al.,* (2016) [4]	USA	NSCLC	484	RCT	Anamorelin (ghrelin agonist)	Weight gain, lean body mass
von Haehling *et al.,* (2012) [5]	Germany	Pancreatic cancer	178	Prospective cohort	Nutritional intervention	Muscle mass preservation, survival
Madeddu *et al.,* (2012) [6]	Italy	Mixed advanced cancers	200	RCT	Multimodal approach (nutrition + exercise + anti-inflammatories)	QOL, muscle mass, survival
Baracos *et al.,* (2018) [7]	Canada	Lung cancer	150	Retrospective	Cachexia prevalence	Treatment outcomes, mortality
Amano *et al.,* (2019) [8]	Japan	Gastrointestinal	270	Prospective	Cachexia staging	Prognosis, weight loss trajectory

Table 2: Summary of Interventions for Cancer Cachexia

Intervention Type	Agents/Methods	Reported Benefits	Limitations	References
Nutritional Support	High-protein diets, omega-3 fatty acids, oral supplements	Improved appetite, modest weight stabilization	Limited effect on lean mass; ineffective if used alone	[1,5,7]
Pharmacological Therapy	Megestrol acetate, corticosteroids, anamorelin, anti-inflammatories	Appetite stimulation, weight gain, improved QOL	Short-lived effects, no consistent survival benefit	[4,6,8]
Exercise	Resistance training, aerobic exercise, physiotherapy	Preserves muscle mass, improves strength, functional outcomes	Feasibility issues in frail or late-stage patients	[2,3,6]
Multimodal Strategies	Combination of nutrition, pharmacotherapy, exercise, anti-inflammatories	Comprehensive benefit, improved lean mass and	Requires multidisciplinary	[6,7,8]

		function, potential survival benefit	team, adherence challenges	

Research Gaps and Future Directions

Several gaps remain:

1. **Diagnostic challenges** – Lack of universally accepted definitions hampers comparison across studies. Integration of biomarkers such as myostatin, activin A, and inflammatory cytokines could improve risk stratification.
2. **Timing of intervention** – Most treatments are initiated late in the disease course when muscle loss is irreversible. Early proactive intervention at cancer diagnosis, particularly in high-risk cancers, may yield better outcomes.
3. **Novel therapies** – Emerging strategies include myostatin inhibitors, selective androgen receptor modulators, anti-inflammatory cytokine blockers, and microbiome-targeted therapies [19].
4. **Policy considerations** – Cancer cachexia remains underrecognized in national cancer guidelines. Its integration into supportive care policies could improve resource allocation and patient survival.

Expanded Perspective

Cachexia is not only a clinical challenge but also an ethical one. Patients with advanced cancer often experience significant psychosocial distress from wasting, which impacts dignity and quality of life. Incorporating psychological support and palliative care into cachexia management frameworks is therefore essential. Additionally, disparities exist in cachexia research, with most high-quality trials concentrated in high-income countries. Expanding research in low- and middle-income settings is critical given the global cancer burden.

CONCLUSION

Cancer cachexia is a prevalent, multifactorial syndrome associated with reduced survival, treatment intolerance, and impaired quality of life. Nutritional interventions alone are insufficient; pharmacological and exercise strategies provide partial benefits, but multimodal approaches appear most effective. Early recognition, standardized diagnostic tools, and integration of multimodal therapy into routine cancer care are urgently needed. Future research should focus on biomarkers, early interventions, and novel therapeutic targets to mitigate the burden of this devastating syndrome.

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