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Integrated Management with Oral Nutritional Supplements and Resistance Exercise for Non-Peroperative Gastric Cancer Patients with Coexisting Malnutrition and Sarcopenia: An Evidence Summary

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Abstract

Objective

This study aims to systematically synthesize the evidence on the combined use of oral nutritional supplements (ONS) and resistance exercise (RE) for the management of coexisting malnutrition and sarcopenia in non-perioperative gastric cancer (GC) patients, with the goal of developing a standardized clinical protocol.

Background

GC patients exhibit a high prevalence of coexisting malnutrition and sarcopenia, exacerbating complications and healthcare burdens. Despite ONS and RE being recommended interventions, evidence-based protocols integrating both modalities are lacking, particularly for Asian populations where GC accounts for 52.6% of global cases.

Methods

Guided by the PIPOST framework, this study defined: Population—adult GC patients with malnutrition, sarcopenia, or the co-occurrence of both conditions (coexisting malnutrition and sarcopenia); Intervention—ONS + RE; Practitioners—multidisciplinary teams; Outcomes—nutritional/muscle metrics, clinical endpoints, cost-effectiveness; Settings—hospitals, communities, homes; Evidence types—guidelines, systematic reviews, RCTs, and expert consensus, etc. Using the "6S" model, 3,587 articles (2015–2025) from 16 databases were screened. AGREE II, AMSTAR 2, and JBI tools assessed quality. Evidence was graded using JBI pre-ranking (Levels 1–5) and FAME recommendations (A/B).

Results

A total of 49 articles were analyzed, consisting of 10 guidelines, 12 systematic reviews, 4 RCTs, 5 cross-sectional studies, 2 cohort studies, 16 expert consensuses. 83 evidence statements were synthesized across five domains: Screening, Assessment, and Diagnosis; Multidisciplinary Collaboration; Advantages of Combined ONS and RE; ONS-Specific Protocols; RE Protocols. Based on a comprehensive analysis of 83 evidence statements, this study developed a standardized clinical protocol flowchart that integrates ONS and RE for managing coexisting malnutrition and sarcopenia in patients with GC.

Conclusion

This study systematically synthesizes the best available evidence on ONS combined with RE for managing coexisting malnutrition and sarcopenia in GC patients, providing scientific guidance for clinical practitioners—including gastrointestinal surgeons, clinical dietitians, rehabilitation specialists, nursing staff, and primary care providers—in developing and implementing personalized nutrition-exercise intervention protocols. Concurrently, resource-optimized strategies (e.g., non-device-dependent screening tools, low-equipment exercise regimens) reduce healthcare costs and improve regional healthcare accessibility, particularly in resource-constrained settings.

Introduction

In 2022, gastric cancer (GC) accounted for 968,000 new cases globally, ranking fifth among all malignancies, with 659,900 related deaths (1). As a high-incidence region for GC, China bears a particularly severe disease burden, reporting 509,000 new cases (52.6% global incidence) and 400,400 deaths (60.7% of global mortality) in the same year (2). GC patients are at high risk for malnutrition and sarcopenia, two pathophysiologically interrelated conditions that frequently coexist and synergistically drive a debilitating clinical cycle, leading to significantly worsened outcomes (3). Some scholars have

conceptualized this as "Malnutrition-Sarcopenia Syndrome (MSS)"(3). More importantly, regardless of its nomenclature, the clinical co-existence of malnutrition and sarcopenia is widely recognized to be closely associated with worse prognoses. Long et al. (4) analyzed 242 GC patients undergoing surgery and found a postoperative incidence of coexisting malnutrition and sarcopenia of 54.55%, a state which significantly increased frailty risk. Chen et al. (5) demonstrated in a study of 742 elderly GC patients that those with both conditions had higher complication rates, longer postoperative hospital stays, and elevated medical costs compared to patients with either condition alone.

While oral nutritional supplements (ONS) serve as a foundational intervention, their efficacy in this complex scenario is optimized as part of a multimodal strategy. High-protein ONS can mitigate weight loss and preserve muscle mass (6), especially when enriched with essential amino acids to enhance anabolism (7). Critically, combined strategies exhibit synergy: integrating ONS with resistance exercise (RE) not only improves nutritional and physical function metrics (e.g., grip strength) in elderly patients (8–9) but can also attenuate postoperative muscle loss and improve treatment tolerance. International guidelines endorse "nutrition support + exercise" for GC patients (10); however, a critical gap exists in evidence-based, integrated protocols for the specific management of co-existing malnutrition and sarcopenia in non-perioperative GC patients. Current research often focuses on sarcopenia in aging (10) or other cancers (11), leaving a lack of tailored, systematic guidance for this high-risk GC subgroup, which limits clinicians' ability to implement effective, timely interventions.

This study, therefore, aims to systematically review global evidence and synthesize findings to develop an integrated ONS-RE management protocol for non-perioperative GC patients with coexisting malnutrition and sarcopenia, aligning with the pathophysiological and clinical context of this population. The goal is to provide a structured, evidence-informed approach to disrupt the "malnutrition-sarcopenia-poor prognosis" cycle, establish standardized care pathways, and ultimately improve patient nutritional status, muscle function, and clinical outcomes.

Materials and Methods

1.1 Identify Research Questions (Based on PIPOST Framework)

This study was prospectively registered at the Evidence-Based Nursing Centre of Fudan University (a Joanna Briggs Institute [JBI] Centre of Excellence; Registration ID: ES20257568), adhering to standardized evidence-based practice protocols to ensure methodological transparency and traceability. Guided by the PIPOST framework developed by the JBI Collaborating Centre for Evidence-Based Nursing, this study systematically structures evidence-based research questions through the following analytical dimensions: The target population (P) comprises adult patients (≥ 18 years) diagnosed with GC and coexisting malnutrition and sarcopenia (i.e., the clinical co-occurrence of both conditions). Studies focusing on patients with either condition alone were also considered for inclusion to ensure a comprehensive evidence base for the respective nutritional and exercise components of the intervention, given the shared pathophysiology and management principles.The intervention (I) focuses on implementing tailored ONS protocols combined with structured RE programs. These interventions are delivered by practitioners (P) from multidisciplinary teams, including oncologists for treatment coordination, clinical dietitians for personalized ONS prescriptions, rehabilitation specialists for RE protocol design, and nurses for patient education and adherence monitoring. Outcomes (O) are evaluated across three interrelated dimensions: patient-level outcomes—including nutritional parameters (e.g., serum albumin, NRS-2002 score), muscle metrics (e.g., skeletal muscle index [SMI], handgrip strength), and clinical endpoints (e.g., 30-day complication rate, chemotherapy completion rate, 1-year survival); practitioner-level outcomes—such as awareness of, acceptance of, and fidelity to evidence-based practices; and system-level outcomes—including cost-effectiveness analyses and institutional adoption rates of standardized ONS-RE management protocols. The settings (S) span tertiary hospital oncology wards (not in the early postoperative phase), outpatient chemotherapy centers, community-based rehabilitation facilities, and home care environments (long-term follow-up). The types of evidence (T) prioritized encompass clinical practice guidelines, systematic reviews, expert consensus statements, randomized controlled trials (RCTs), cohort studies, and diagnostic studies to ensure methodological rigor and translational applicability.

1.2 Retrieval Strategies

Guided by the "6S" evidence-based pyramid model, this study systematically retrieved evidence from January 2015 to April 2025, prioritizing the highest levels of clinical guidance and descending to implementation-focused research. Databases included the JBI Evidence-Based Nursing Collaborating Centre, UpToDate, BMJ Best Practice, American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), Chinese Society for Parenteral and Enteral Nutrition (CSPEN), National Guideline Clearinghouse(NGC), Cochrane Library, PubMed, Web of Science, Embase, Guidelines International Network (GIN), China National Knowledge Infrastructure (CNKI), Wanfang Database, MedLive, and China Biology Medicine disc (CBMdisc). The evidence retrieval strategy for this study incorporated both Medical Subject Headings (MeSH) and free-text keywords to comprehensively capture literature pertaining to oral nutrition and resistance exercise in GC patients with malnutrition, sarcopenia, or the co-occurrence of both conditions. The strategy was designed to capture evidence on the management of the individual conditions as well as their combination, to ensure a robust foundation for developing an integrated protocol. MeSH terms included: "Stomach Neoplasms", "Malnutrition", "Sarcopenia", "Muscular Atrophy", "Enteral Nutrition", "Dietary Supplements", "Resistance Training", and "Exercise Therapy". Free-text keywords included: "gastric cancer", "coexisting malnutrition and sarcopenia", "concurrent malnutrition and sarcopenia", "malnutrition-sarcopenia syndrome", "cancer-related muscle wasting", "oral nutritional supplementation", "high-protein oral nutrition", "progressive resistance training", "skeletal muscle index" and "chemotherapy tolerance". Detailed search strategies for both Chinese and English sources are provided in the Supporting Information.

1.3 Criteria for Inclusion and Exclusion

(1) Patient population: Adults (≥ 18 years) with GC and comorbid with malnutrition, sarcopenia, or specifically, the co-occurrence of both conditions (coexisting malnutrition and sarcopenia). Studies focusing on patients with either malnutrition or sarcopenia alone were also eligible for inclusion. This approach ensured a comprehensive evidence base for the nutritional and exercise components relevant to managing the complex, co-existing state. (2) Treatment phase: Patients undergoing chemotherapy, patients not in the early postoperative rehabilitation period, and palliative care patients (with an expected survival of > 3 months). (3) Intervention focus: Studies involving ONS and RE, particularly combined interventions that integrate both modalities.

(4) Evidence types: Included clinical practice guidelines, systematic reviews, expert consensus statements, randomized controlled trials (RCTs), cohort studies, and cross-sectional investigations to ensure methodological rigor and translational applicability. (5) Outcome measures: Studies that reported on nutritional parameters (e.g., serum albumin, NRS-2002 score), muscle metrics (e.g., skeletal muscle index [SMI], handgrip strength), clinical endpoints (e.g., 30-day complication rate, chemotherapy completion rate), and implementation outcomes (e.g., adherence rates, cost-effectiveness). (6) Language and publication: Publications in Chinese or English, with a focus on studies from January 2015 to April 2025, to ensure up-to-date evidence.

Exclusion criteria included: (1) Animal studies, case reports, or non-peer-reviewed commentaries;

(2) Low-quality literature, defined as guidelines rated as Grade C, systematic reviews with a methodological quality score ≤ 4 points, or expert consensus with 50% of entries rated “No” or 80% rated “Unclear”; (3) Outdated guidelines/systematic reviews superseded by updated versions; (4) Literature lacking full-text accessibility or essential outcome data. Grey literature was excluded unless supplemented by peer-reviewed follow-ups. (5) Duplicate publications. (6) Traditional reviews, or systematic review protocols. (7) Excluded patients in the early postoperative period (< 4 weeks) to ensure the intervention was administered in non-surgical or long-term post-operative clinical settings and to focus on non-operational/chronic care-related management.

1.4 Literature Quality Evaluation

1.4.1 Guidelines

The methodological rigor of included guidelines was independently appraised by four evaluators utilizing the 2017 Appraisal of Guidelines for Research and Evaluation II (AGREE II) framework (12). Inter-rater reliability was quantified via the Intraclass Correlation Coefficient (ICC), with the following interpretative thresholds: ICC < 0.40 (poor reliability), 0.45–0.75 (good reliability), and > 0.75 (excellent reliability).

AGREE II operationalizes quality assessment through 23 discrete items structured within six core domains (Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, Editorial Independence). Each item employs a 7-point Likert scale (1 = strongest disagreement, 7 = strongest agreement). Domain-specific scores are derived by summing item responses and converting the raw sum into a standardized percentage (i.e., the ratio of the observed score to the maximum attainable score per domain). Guideline inclusion and recommendation strength were determined by standardized domain percentages: Grade A (Strongly Recommended): All six domains ≥ 60%; Grade B (Recommended): ≥3 domains ≥ 60% and <3 domains ≤ 30%; Grade C (Not Recommended): ≥3 domains < 30%.

1.4.2 Other type

Methodological quality was independently appraised by two evidence-trained reviewers using AMSTAR 2 for systematic reviews and JBI Critical Appraisal Tools (2016) for expert consensus, RCTs, cohort studies, and cross-sectional studies. In case of disagreements, arbitration will be conducted by the hospital's Evidence-Based Nursing team. When there is a conflict of evidence, priority will be given to evidence-based evidence, high-quality evidence, and the most recent evidence published in authoritative journals. The AMSTAR 2 tool comprises 16 items, each rated as "Yes", "Partial Yes", or "No", with its four-level confidence rating defined as: High confidence (no critical flaws and ≤ 1 non-critical flaw, enabling directly applicable evidence synthesis); Moderate confidence (> 1 non-critical flaw without critical flaws, providing accurate synthesis but requiring limitations acknowledgment); Low confidence (1 critical flaw regardless of non-critical flaws, resulting in unreliable synthesis and necessitating cautious interpretation); and Critically low confidence (≥ 2 critical flaws, invalidating conclusions and precluding evidentiary use). Notably, AMSTAR 2 excludes "Not Applicable" ratings and prioritizes critical domain flaws (items 2/4/7/9/11/13/15) as primary downgrade criteria. For JBI tools: expert consensus employs 6 domains rated "Yes" (1 point), "No" (0 points), or "Unclear" (0 points); RCTs utilize 13 items assessing randomization, blinding, follow-up, and outcome analysis, each rated "Yes", "No", "Unclear", or "Not Applicable" (13); cohort studies apply 9 items rated "Yes", "No", or "Unclear" based on selection/comparability/outcome validity; Diagnostic studies employ a 10-item tool to evaluate the quality, focusing on four key domains: participant selection, inclusion/exclusion criteria, definition of the reference standard, and data analysis procedures. Each item is assessed against the following criteria: yes, no, unclear, or not applicable.

If there was a disagreement on the quality of the literature, a consensus was reached after consultation with the third researcher with higher qualifications. In case of conflicts between different sources of evidence, the principle of evidence-based, high-quality, and the latest published evidence should be given priority.

1.5 Evidence Grading and Recommendation Levels

The evidence was summarized by two nursing postgraduate students trained in evidence-based nursing, adhering to the following principles: (I) for consistent content, prioritize concise and comprehensible evidence; (II) for complementary content, integrate evidence based on linguistic logic; (III) for conflicting content, prioritize evidence by quality, source credibility, and recency of authoritative publications. Using the JBI evidence pre-ranking system (2014) (14), evidence was classified into grades 1 (highest) to 5 (lowest). Two researchers independently graded extracted evidence, with disagreements resolved through third-researcher arbitration to achieve consensus. The recommendation levels were divided into Level A (strong recommendation) and Level B (weak recommendation) based on the JBI FAME framework.

Results

2.1 Literature retrieval process and general characteristics of the included literature

The process of literature screening is detailed in Fig. 1. An initial search yielded 3,587 articles from both Chinese and English databases, with an additional six articles identified through other sources. After removing 750 duplicate documents using E-study software, 2,843 articles remained for title and abstract screening. During this phase, 2,561 articles were excluded based on predetermined criteria. The remaining 282 articles underwent full-text assessment, and 233 were excluded for the following reasons: updated guidelines (n = 4), ineligible study subjects (n = 86), improper research type (n = 112), inadequate outcome measures (n = 22), full text unavailable (n = 4), and duplicate publications (n = 3). Ultimately, 49 studies met inclusion criteria and were assessed for eligibility, comprising: Guidelines (n = 10), Expert Consensus (n = 16), Systematic Reviews (n = 12), Randomized Controlled Trials (n = 4), Cross-sectional Studies (n = 5), and Cohort Study (n = 2). The essential characteristics of the included literature are presented in Supporting Information.

2.2 Evaluation of publication quality

2.2.1 Quality evaluation of guidelines

This review included 10 guidelines (15–24). The average percentage and recommended grade for each domain are listed in Table 1. 6 guidelines (15–19, 22) had a recommendation grade of A. The remaining guidelines (20–21, 23–24) had a recommendation grade of B. Seven guidelines were of good overall quality and approved for inclusion in the review.

Table 1
Guide quality evaluation results.

Guideline	Percentage standardization by area (%)						≥ 60%	30—60%	<30%	Recommended level
	□	□	□	□	□	□				
Li. (15)	95.83	90.28	88.02	95.83	63.54	100	6	0	0	A
Volkert et al. (16)	83.33	88.89	94.79	93.06	78.13	98.08	6	0	0	A
Arends et al. (17)	98.61	87.5	96.88	91.67	85.42	96.15	6	0	0	A
Muscaritoli et al. (18)	97.22	86.11	87.5	93.06	44.79	98.08	5	1	0	A
McClave et al. (19)	97.22	88.89	95.31	97.22	85.42	98.08	6	0	0	A
Lim et al. (20)	95.83	91.67	72.92	95.83	58.33	100	5	1	0	B
Chinese Society of Nutritional Oncology. (21)	94.44	91.67	71.88	97.22	59.38	100	5	1	0	B
Clinical Nutrition and Health Branch et al. (22)	94.44	84.72	72.92	94.44	61.46	98.08	6	0	0	A
Li et al. (23)	95.83	66.67	51.04	94.44	3.13	53.85	3	1	2	B
Chinese Society of Nutritional Oncology. (24)	98.61	68.06	62.50	91.67	15.63	55.77	4	1	1	B

Note: □Scope and purpose; □stakeholder involvement; □rigour of development; □clarity and presentation; □applicability; □Editorial independence.

2.2.2 Quality evaluation of expert consensus

A total of 16 expert consensuses (25–40) and were included in this review. All expert consensus were of high quality and, hence, were deemed eligible for inclusion. The evaluation results are provided in Table 2.

Table 2
Expert Consensus Quality Assessment Results

Expert consensus	Source of opinion	Standing in field	Population	Analytical process	Extant literature	Incongruence with literature
Chen et al. (25)	Yes	Yes	Yes	Yes	Yes	Unclear
Zanker et al. (26)	Yes	Yes	Yes	Yes	Yes	No
Cruz-Jentoft et al. (27)	Yes	Yes	Yes	Yes	Yes	Yes
Shanghai Anticancer Association Oncology Nutrition and Supportive Therapy Professional Committee (28)	Yes	Yes	Yes	Yes	Yes	Unclear
Chinese Nutrition Society Geriatric Nutrition Branch et al. (29)	Yes	Yes	Yes	Yes	Yes	No
Arends et al. (30)	Yes	Yes	Yes	Yes	Yes	No
Kang et al. (31)	Yes	Yes	Yes	Yes	Yes	Unclear
Laparoscopic & Endoscopic Surgery Group et al. (32)	Yes	Yes	Yes	Yes	Yes	No
Cui et al.(33)	Yes	Yes	Yes	Yes	Yes	Unclear
Geriatrics Branch Chinese Medical Association et al. (34)	Yes	Yes	Yes	Yes	Yes	No
Wu et al.(35)	Yes	Yes	Yes	Yes	Yes	No
Chinese Society of Nutritional Oncology et al.(36)	Yes	Yes	Yes	Yes	Yes	Unclear
Liu et al. (37)	Yes	Yes	Yes	Yes	Yes	No
Kang et al. (38)	Yes	Yes	Yes	Yes	Yes	No
Kiss et al. (39)	Yes	Yes	Yes	Yes	Yes	Yes
Cederholm et al. (40)	Yes	Yes	Yes	Yes	Yes	Unclear

2.2.3 Quality evaluation of systematic reviews

A total of 12 systematic reviews (41–52) were evaluated using the AMSTAR 2 scale.

The evaluation results can be found in Table 3.

2.2.4 Quality evaluation of randomized controlled trials

4 randomized controlled trials (53–56) were incorporated into the study. The evaluation results are provided in Table 4.

Table 4
Results of quality evaluation of randomized controlled trials.

Inclusion of literature	1	2	3	4	5	6	7	8	9	10	11	12	13
Kokubo et al.(53)	Yes	Unclear	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No
Morato Martínez et al. (54)	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Omori et al. (55)	Yes	Unclear	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Wei et al. (56)	Yes	Unclear	Yes	Unclear	Unclear	Unclear	No	Unclear	Yes	Yes	Yes	Yes	Yes

Note:1: Was the random allocation sequence truly generated? 2Was blinding of participants implemented? 3Was allocation concealment applied? 4Were dropouts/losses to follow-up described and included in analysis? 5Was blinding of outcome assessors performed? 6Were baseline characteristics comparable? 7Were co-interventions identical? 8Were outcome measurement methods consistent? 9Was the outcome assessor's reliability established? 10Was the data analysis appropriate?

2.2.5 Quality evaluation of Diagnostic Study

5 Diagnostic Studies (57–61) were incorporated into the study. The evaluation results are provided in Table 5.

Table 5
Diagnostic Study Literature Quality Assessment Results

Inclusion of literature	1	2	3	4	5	6	7	8	9	10
Fu et al. (57)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chen et al. (58)	No	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes
Huang et al. (59)	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	
Chen et al. (60)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not Applicable	Yes	Yes
Zuo et al. (61)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Note:1.Was the sample selected randomly or consecutively?2.Was a case-control design avoided?3.Were exclusion criteria clearly defined and appropriate?4.Were assessors of the diagnostic test blinded to the gold standard results? 5.Was a diagnostic threshold pre-specified?6.Was the gold standard accurately defined and valid?7.Were assessors of the gold standard blinded to the diagnostic test results?8.Was the time interval between tests clinically appropriate? 9.Was the same gold standard applied to all participants?10.Were all participants included in the final analysis?

2.2.6 Quality evaluation of Diagnostic Study

5 Diagnostic Studies (62–63) were incorporated into the study. The evaluation results are provided in Table 6.

Table 6
Quality assessment results of cohort study literature

Inclusion of literature	1	2	3	4	5	6	7	8	9
Ferreira et al. (62)	No	No	No	yes	yes	No	No	yes	yes
Lu et al. (63)	Unclear	yes	yes	yes	yes	yes	No	yes	yes

Note:1.Was the sample representative of the target population?2.Were cohorts comparable at baseline regarding exposure/outcome determinants?3.Were efforts made to minimize selection bias in cohort allocation?4.Were confounders identified and controlled for in design/analysis?5.Were outcomes measured using objective/standardized criteria?6.Was follow-up duration sufficient for outcomes to occur?7.Were loss-to-follow-up described and accounted for in analysis?8.Were outcome assessment methods reliable? 9.Were statistical methods appropriate for study design?

2.3 Summary and Analysis of Best Evidence

Based on a systematic compilation of evidence regarding ONS and RE interventions for the management of coexisting malnutrition and sarcopenia in GC patients, this study summarized 83 best practice recommendations across five domains: screening, assessment, and diagnosis; multidisciplinary collaboration; the synergistic rationale for combined ONS and RE; ONS-specific protocols; and RE protocols. These recommendations are detailed in Table 7.

Table 7
Summary of the best evidence

Level 1 entries	Secondary entries	Tertiary entries	Level	Recommendation Grade
Screening, Assessment, and Diagnosis of Coexisting Malnutrition and Sarcopenia in GC	Screening Targets and Timing	1. High-risk populations: Patients with comorbidities (gastrointestinal tumors, diabetes, chronic kidney disease), frailty, undergoing radiotherapy/chemotherapy/surgery, age ≥ 55 years, advanced stage (III/IV), low BMI (< 18.5 kg/m²), or weight loss ≥ 5% during treatment (20, 36, 39, 47).	5	A
		2. Malnutrition and sarcopenia screening should be performed at diagnosis and throughout treatment for GC patients (32, 38–39).	5	A
		3. Screening is highly recommended prior to the initiation of chemotherapy and should be conducted regularly throughout the treatment course (e.g., every 4–8 weeks) (47).	5	B
	Nutritional Risk Screening	4. Non-surgical patients: NRS2002 for ages < 65 (score ≥ 3 indicates risk); MNA-SF for ages ≥ 65 (score ≤ 11 indicates risk) (32, 38, 40, 47, 59).	1	A
		5. Post-gastrectomy patients: SNRSGC recommended (score ≥ 7 indicates risk) (60).	4	B
		6. All patients identified at nutritional risk or with treatment-induced malnutrition risk require comprehensive assessment using oncology-validated tools (39).	5	A
	Malnutrition Assessment and Diagnosis	7. PG-SGA is the gold standard for comprehensive nutritional assessment (15, 32, 35, 46).	1	A
		8. GLIM criteria combined with calf circumference (CC) are recommended for malnutrition diagnosis in GC (39, 57).	5	A
		9. Combined PG-SGA and GLIM (using CC or ASMI) improves diagnostic accuracy (57).	4	B
		10. Extended assessment parameters: Anorexia screening, body composition (CT/BIA), inflammatory markers (CRP/albumin), resting energy expenditure (indirect calorimetry), physical activity (30).	1	A
	Sarcopenia Risk Screening	11. Primary recommendation: Left calf circumference (Asian thresholds: male < 34 cm, female < 33 cm) (25, 33, 57, 58).	3	A
		12. Secondary tools: SARC-CalF score ≥ 11 (25, 63) or a positive Finger-Ring Test (22).	2	A
		13. SARC-F is not recommended due to low sensitivity (29).	5	B
		14. Patients at risk require comprehensive assessment of muscle mass, strength, and function (39).	5	A

Level 1 entries	Secondary entries	Tertiary entries	Level	Recommendation Grade
	Sarcopenia Diagnosis and Staging	15. Muscle mass: BIA-measured appendicular skeletal muscle index (ASMI) preferred (male ≤ 7.0 kg/m², female ≤ 5.7 kg/m²) (25, 27, 33, 37).	2	A
		16. CT remains gold standard for research due to cost/access limitations (27).	4	B
		17. Alternative calculation: Skeletal Muscle Content Score = 0.536618×Age(y) − 3.846154×BMI (kg/m²) − 0.091536×Hb(g/L) − 8.694426×6m gait speed(m/s) + 179.23506; score < 109.5 indicates low muscle mass (28).	3	A
		18. Muscle strength: Electronic dynamometer-measured grip strength (max of ≥ 2 trials per hand). Thresholds: male < 28 kg, female < 18 kg. Alternative: 5-time sit-to-stand test ≥ 12 s (25).	5	A
		19. Physical Function: Six-meter gait speed is recommended, with a cut-off value of < 1 m/s. In cases of walking difficulty, the 5-times sit-to-stand time is substituted, using a cut-off value of ≥ 12 seconds. For other Short Physical Performance Battery (SPPB) components, a score ≤ 9 is specified. (20, 22, 24–25, 37).	1	A
		20. Diagnostic criteria:□Low muscle strength; □Low muscle mass/quality; □Low physical performance. Meeting□alone= presarcopenia; □+□ = sarcopenia; □+□+□ = severe sarcopenia (28).	5	A
		21. Low gait speed may substitute for device-dependent measures when unavailable (26).	3	A
	MSS Diagnosis	22. Phase angle (PhA) is recommended for MSS diagnosis when CT unavailable. Malnutrition thresholds: male PhA < 5.70°, female PhA < 5.07°; Sarcopenia thresholds: male PhA < 5.28°, female PhA < 4.81° (61).	3	B
Multidisciplinary Collaboration	Multidisciplinary Collaboration	23. Integrated management by dietitians, rehabilitation specialists, oncologists, and nurses (30, 39).	5	B
Synergistic Effects of RE Combined with ONS	Advantages and Implementation Strategies	24. RE combined with nutrition supplementation significantly improves muscle strength and function (29, 31, 33). ONS containing 15–20 g of protein rich in essential amino acids or leucine, along with approximately 200 kcal (836.8 kJ) of energy, are recommended for administration during the post-exercise period (29).	1	A
		25. High-protein diet + resistance training yields superior outcomes (27, 30).	1	A
		26. RE preferentially improves lean mass and lower-limb function (48, 56).	1	A
		27. RE takes priority over pharmacological interventions (26).	1	A
ONS-Specific Protocols	ONS Indications and Duration	28. Indication parameters: Food intake < 75% (past 2 weeks) for adults < 60y or < 60% for > 5 days in adults ≥ 60y; nutrition-impact symptoms	5	B

Level 1 entries	Secondary entries	Tertiary entries	Level	Recommendation Grade
		(nausea/vomiting/diarrhea) > 3 days; weight loss ≥ 5% in 1 month or ≥ 10% in 6 months; PG-SGA score ≥ 2; high-nutrition-impact diseases (esophageal/gastric/pancreatic cancer); major surgery; advanced cancer (stage III-IV) (62).		
		29. ONS is first-line for weight loss due to reduced intake (e.g., post-gastrectomy) if GI function preserved (34, 36, 38).	1	A
		30. Consider ONS throughout adjuvant chemotherapy for malnourished/high-risk GC patients (45, 59).	1	B
		31. ONS supplementation recommended during chemotherapy cycles, especially in initial phases (Cycles 1–2) (45).	3	A
		32. Postoperative ONS ≥ 3 months; long-term use may stabilize weight (50, 59).	1	A
		33. Contraindications: Complete bowel obstruction, severe dysmotility, malabsorption syndromes (e.g., short bowel), metabolic disorders (e.g., celiac disease), dysphagia (Water Swallow Test ≥Grade 3) (34, 42–43).	1	B
	Nutritional Requirements	34. Total energy intake: 105–126 kJ/kg/d(25-30kcal/ kg/d) (17, 23, 30, 38).	5	B
		35. In critical illness: Start with hypocaloric support (< 70% target) for 3–7d, then escalate (19, 38).	5	B
		36. For normal renal/hepatic function: Protein 1.2–1.5 g/kg/d (≥ 50% high-quality), distributed across meals (23, 25–26, 29, 31, 33, 38, 55, 62).	2	A
		37. Critical illness/severe malnutrition-sarcopenia: Protein 1.5–2.0 g/kg/d, with escalation to 2.5 g/kg/d permitted in hypermetabolic states or patients receiving frequent hemodialysis or continuous renal replacement therapy (CRRT) (19, 22, 38).	5	A
		38. Whey protein > casein; dairy protein > soy protein (28, 41).	1	A
		39. Whey protein dosing: 15–20 g per dose, twice daily (33, 41).	2	B
		40. Total ONS: 400–600 kcal/d, protein 30–40 g/d (34, 38, 50).	1	A
	Formula and Nutrient Selection	41. Non-tumor-bearing patients: Standard formulas; tumor-bearing patients: Tumor-specific formulations (21).	5	B
		42. β-hydroxy-β-methylbutyrate (HMB)-enriched ONS (3 g/d) improves muscle mass and strength, especially postoperatively or during chemo/radiotherapy (24, 31, 33, 37, 44).	1	B
		43. High-energy density formulas (≥ 1.5 kcal/ml) for fluid-restricted patients (38), contraindicated in total gastrectomy patients (21).	3	B

Level 1 entries	Secondary entries	Tertiary entries	Level	Recommendation Grade
		44. Pre-major surgery: Immunonutrition formulas (glutamine/arginine/ω-3) (36, 38).	1	A
		45. Intact protein formulas are preferred, except in cases of pancreatitis or severe malabsorption (34, 38). For individuals with severely impaired intestinal function, ONS based on elemental formulas may be considered (38).	5	B
		46. Whey protein and mixed-amino-acid ONS improve weight, BMI, and skeletal muscle mass (28).	1	A
		47. Select high-fat (> 50% energy), low-carbohydrate (< 30%), ω-3 PUFA-rich, antioxidant-rich, whey-based formulas (18, 24, 28, 34, 49).	1	A
		48. Routine ω-3 PUFA supplementation not recommended (31, 38).	1	A
		49. Arginine/glutamine-fortified ONS not routinely recommended (38).	3	B
		50. Probiotic-supplemented ONS not routinely recommended (38).	3	B
		51. Leucine/glutamine/mixed-amino-acid ONS reduce chemotherapy toxicity (oral mucositis) and improve nutritional markers (49).	2	B
		52. Select vitamin D-fortified formulas if serum 25(OH)D < 70 nmol/L (31, 33).	1	A
		53. For serum 25(OH)D < 50 nmol/L: Supplement 600–800 IU/d to maintain > 50 nmol/L (24, 28–29, 34).	3	B
		54. Chronic kidney disease: Low-potassium/low-phosphorus formulas (38).	3	B
		55. Adequate calcium intake to improve muscle contraction (31).	1	A
		56. Diabetes: Low-carbohydrate formulas with slow-release carbs (53).	1	B
		57. Diarrhea: Fiber-containing formulas (38)	2	B
	ONS Administration and Adherence	58. Considering the patient's preference for sweet or fruity liquid formulations, and in accordance with their taste habits and preferences, the use of safe flavorings is permitted. To enhance adherence, formulations that are viscous, salty, tomato-flavored, or have an off-taste should be avoided (54).	1	-
		59. "3 + 3 Model": Three main meals plus three ONS doses (between meals/post-dinner). Each dose: 15–20 g protein (rich in EAA/leucine) + ~ 200 kcal (21, 28).	5	B
		60. In accordance with the principle of gradual progression, which advocates initiating with low doses and low concentrations, various methods can be employed to facilitate the intake of ONS.	5	B

Level 1 entries	Secondary entries	Tertiary entries	Level	Recommendation Grade
		These methods include sipping (50–100 ml), taking small amounts orally multiple times, and incorporating ONS into daily meals. The intake of ONS should be incrementally increased in a stepwise manner until the target intake volume is ultimately achieved. (16, 34–35).		
		61. ONS adherence ≥ 80% maintains weight and grip strength (62).	1	A
		62. Antiemetics for nausea/vomiting; appetite stimulants for anorexia (35).	5	B
		63. Implementation of the ONS treatment plan and achievement of energy targets, as well as gastrointestinal function assessment: Evaluate daily until the target volume is reached, and then evaluate twice weekly after the target volume is achieved; Frequency of assessment for body weight, muscle mass, muscle strength, and dietary intake: Once a week to once every two weeks. (35).	5	B
		64.Individuals consuming ONS are encouraged to document their daily ONS intake through a diary or tabular format. The recorded information should encompass the timing and volume of ONS consumption, any adverse reactions along with their potential causes, and details regarding their dietary intake (35).		
		65.Consumers of ONS and their caregivers are encouraged to actively participate in the formulation and implementation of the ONS treatment plan. Additionally, caregivers are encouraged to enhance their supervision and management of the implementation of the ONS treatment plan for the consumers (35).		
RE Protocols	Initiation Timing and Risk Assessment	66. Start RE in high-risk malnutrition-sarcopenia populations (20, 26, 39, 47); initiate early in chemotherapy (52).	1	A
		67.Pre-exercise assessment for fall/frailty risks (31).	3	A
		68.Contraindications: Active bleeding, uncontrolled pain/infection, recent DVT/PE, bone metastases, thrombocytopenia (< 50×10^9/L) (25).	2	B
	Exercise Modality	69. Upper limb/core: Dumbbell press, elastic band training, seated row, wall push-up (6).	1	A
		70. Lower limb focus: Leg press, knee extension, hip flexion, squat (48, 51).	1	A
	Exercise Intensity	71. Weeks 1–2 (beginner): Low intensity (40–60% 1RM), Borg RPE 12–14; progress by 5–10% 1RM weekly to moderate-high intensity (60–80% 1RM) (26, 30, 33).	1	A
		72.Repetitions/Sets: Beginner: 8–10 repetitions/set, 1–2 sets with 1–2 min rest; increase repetitions before load (20, 33).	1	B

Level 1 entries	Secondary entries	Tertiary entries	Level	Recommendation Grade
	Duration and Frequency	73. Session duration: 30–60 min (incl. 5–10 min warm-up/cool-down with walking/joint mobility) (29, 33, 48, 51).	1	A
		74. Frequency: ≥3 sessions/week, 48h apart (20, 33, 48, 51).	1	A
	Intervention Period	75. Minimum 8 weeks to improve muscle mass/function (48, 51); 12–16 weeks for significant gains (51–52).	1	B
	Precautions	76. Maintain exercise logs with dedicated oversight (33).	5	B
		77. Supervised group exercise + social support enhances efficacy (51).	1	A
		78. Post-exercise: 2-min walk + major muscle group stretching (33).	5	A
		79. Pre-session: Vital signs + Borg scale for baseline fatigue/respiration (33).	5	B
		80. Intra-session: Monitor BP, HR, SpO_2, fatigue (33).	5	B
		81. Post-session: Assess fatigue (Borg scale), vital signs; individualize prescription (33).	5	A
		82. Reassessment: Inpatients every 1–2 weeks; community patients every 4 weeks (34).	5	B
	Exercise Termination Criteria	83. □Severe dyspnea, diaphoresis, pallor; □ Chest pain; □Dizziness/syncope; □Limb cramps or severe fatigue/pain; □Gait imbalance; □SBP ≥ 180 mmHg; □SBP drop ≥ 20 mmHg with tachycardia; □SpO_2 <85%;□ Intolerance (33)		

2.4 Standardized ONS and RE Protocol for GC Patients with Coexisting Malnutrition and Sarcopenia

Based on a comprehensive analysis of 83 evidence statements (Table 7), this study developed a standardized clinical protocol flowchart that integrates ONS and RE for managing coexisting malnutrition and sarcopenia in patients with GC. Figure 2 details the core operational parameters of this protocol.

Discussion

This evidence summary synthesizes 83 best-practice recommendations across five domains (screening, multidisciplinary collaboration, ONS protocols, RE, and monitoring) for managing the co-occurrence of malnutrition and sarcopenia in non-perioperative GC patients. The integration of ONS with structured RE demonstrates synergistic benefits, addressing both nutritional deficits and muscle loss—a critical vicious cycle that defines this co-existing condition and significantly impacts clinical outcomes.

3.1 Synergistic Efficacy of Combined Intervention

High-protein ONS (providing 1.2–2.5 g/kg/d protein) delivers essential amino acids (e.g., leucine) and HMB to activate the mTORC1 signaling pathway, thereby stimulating muscle protein synthesis (MPS) while suppressing catabolism (64–65). During chemotherapy, patients with gastrointestinal tumors frequently experience muscle atrophy due to aberrant protein metabolism, whereas high-protein ONS stabilizes skeletal muscle mass index (SMMI) and reduces cachexia risk (66–67). For instance, one study demonstrated that nutritional intervention attenuated L3SMI (third lumbar skeletal muscle index) loss during chemotherapy and decreased sarcopenia incidence (68)RE (≥ 3 sessions/week at 40–80% 1RM intensity) induces mechanical loading to activate the IGF-1/PI3K/Akt pathway, enhancing muscle hypertrophy and mitochondrial function (69). In cancer patients, low-to-moderate load resistance training increases lean body mass and grip strength (8, 51). Integrated nutrition-exercise interventions (e.g., home-based exercise + nutritional care) synergistically improve nutritional status, sarcopenia, and quality of life (QoL), particularly in elderly GC patients (70–71). Although international guidelines endorse the "nutrition + exercise" model, optimal protocols for GC (e.g., protein dosage, exercise modality) require further evidence.

3.2 Key Implementation Elements

3.2.1 Screening Strategy: High-Risk Population Identification and Tool Optimization

Early identification of the co-occurrence of malnutrition and sarcopenia is critical, with the high-risk population encompassing individuals aged ≥ 55 years, advanced GC (stage III/IV), BMI < 18.5 kg/m², weight loss ≥ 5% during treatment, comorbidities (e.g., diabetes, renal disease), frailty status, or those undergoing chemotherapy/radiotherapy/surgery (Evidence 1). Screening timing mandates initiating dynamic monitoring of nutritional risk and sarcopenia at diagnosis (Evidence 2), followed by regular reassessment pre-chemotherapy and every 4–8 weeks (Evidence 3). Tool selection requires stratification: for nutritional risk screening, non-surgical patients aged < 65 years should utilize the Nutritional Risk Screening 2002 (NRS2002, score ≥ 3 indicating risk), while those ≥ 65 years adopt the Mini-Nutritional Assessment Short Form (MNA-SF, score ≤ 11 indicating risk) (Evidence 4); patients with gastric surgery history are recommended the Specialized Nutritional Risk Screening for GC (SNRSGC, score ≥ 7 indicating risk) (Evidence 5). For sarcopenia risk screening, priority is given to left calf circumference (Asian thresholds: male < 34 cm, female < 33 cm) (Evidence 11), supplemented by SARC-CalF or the Finger-Ring Test (Evidence 12), whereas SARC-F is not recommended due to insufficient sensitivity (Evidence 13).

3.2.2 Assessment and Diagnosis Require Stratified Integration and Precise Quantification

Nutritional assessment prioritizes the Patient-Generated Subjective Global Assessment (PG-SGA) as the gold standard (Evidence 7), while GLIM criteria combined with calf circumference (CC) measurement are recommended for malnutrition diagnosis (Evidence 8), with extended indicators including inflammatory markers (CRP/albumin), body composition (CT/BIA), and resting energy expenditure (Evidence 10). Crucially, single-tool efficacy is limited; thus, combining Patient-Generated Subjective Global Assessment (PG-SGA) with GLIM criteria (incorporating calf circumference or skeletal muscle index) significantly enhances diagnostic comprehensiveness (Evidence 9). Sarcopenia diagnosis requires a three-dimensional evaluation: (1) Muscle mass: Clinically, bioelectrical impedance analysis (BIA)-measured appendicular skeletal mass index (ASMI) is the preferred method (male ≤ 7.0 kg/m², female ≤ 5.7 kg/m²) (Evidence 15), or alternatively, the skeletal muscle mass calculation formula (score < 109.5) (Evidence 17); (2) Muscle strength: Handgrip strength (male < 28kg, female < 18kg) or the 5-time sit-to-stand test (≥ 12 seconds) (Evidence 18); (3) Physical function: 6m gait speed <1m/s or Short Physical Performance Battery (SPPB) score ≤ 9 (Evidence 19). Diagnostic criteria are explicitly defined: isolated low muscle strength indicates presarcopenia; low muscle strength plus low muscle mass confirms sarcopenia; superimposed low physical activity denotes severe sarcopenia (Evidence 20). In resource-limited settings, phase angle (PhA) serves as a surrogate marker (male < 5.28°, female < 4.81° suggests sarcopenia) (Evidence 22).

3.2.3 Dynamic Monitoring and Resource Allocation Are Required During Implementation

The cascade screening-assessment linkage necessitates that high-risk populations initially screened by universal tools (NRS2002 for ages < 65, MNA-SF for ages ≥ 65) undergo further in-depth evaluation using oncology-specific instruments, primarily the Patient-Generated Subjective Global Assessment (PG-SGA) (Evidence 7). Furthermore, dynamic monitoring cycles mandate reassessment of gait speed, grip strength, and nutritional indicators every 4–8 weeks for chemotherapy patients (Evidence 3). This includes implementing the ONS treatment plan and assessing achievement of energy targets, alongside gastrointestinal function evaluation—conducted daily until the target volume is reached, then twice weekly thereafter—with assessments for body weight, muscle mass, muscle strength, and dietary intake performed weekly to biweekly (Evidence 63). For resource-optimized protocols in settings lacking CT/BIA equipment, the combination of calf circumference (Asian thresholds: male < 34 cm, female < 33 cm) and phase angle (PhA; sarcopenia thresholds: male < 5.28°, female < 4.81°) serves as a feasible alternative (Evidence 22); while BIA remains prioritized for muscle mass quantification in clinical practice, CT is reserved for research contexts due to accessibility constraints (Evidence 17). Clinically, this stratified approach significantly enhances the detection of co-existing malnutrition and sarcopenia, with calf circumference emerging as a cost-effective metric particularly suitable for primary care (Evidence 11). Critical caveats include: the SARC-F tool should not be used alone due to high false-negative risks (Evidence 13), whereas low gait speed (< 1 m/s) provides a reliable sarcopenia indicator when advanced devices are unavailable (Evidence 21).

The intervention strategy for GC patients with coexisting malnutrition and sarcopenia should be dynamically adjusted based on the patient's pathological status, treatment phase, and resource accessibility. Formula differentiation is critical: for *active tumor-bearing status*, prioritize tumor-specific formulations with high-fat (> 50% energy), low-carbohydrate (< 30%), and whey-protein enrichment (Evidence 47); for *non-tumor-bearing patients*, standard intact-protein formulas are applicable (Evidence 41); for *diabetes comorbidity*, adopt slow-release carbohydrate formulations to reduce glycemic fluctuations (Evidence 56); and for *patients with diarrhea*, supplement soluble dietary fiber to improve gut barrier function (Evidence 57). In hypermetabolic states or in patients undergoing frequent hemodialysis or CRRT, protein intake may be increased to 2.5 g/kg/d (Evidence 37). RE) requires precise progression: during the *initial phase (1–2 weeks)*, implement low-intensity training (40–60% 1RM), monitoring exertion via the Borg Scale (RPE 12–14) (Evidence 71), with gradual advancement to moderate-high intensity (60–80% 1RM) based on tolerance and functional assessments.

3.3 Inclusion and Exclusion Criteria on Generalizability

The inclusion criteria for this study were carefully designed to ensure the relevance and quality of the evidence, particularly focusing on non-perioperative GC patients with comorbid malnutrition, sarcopenia, or specifically, the co-occurrence of both conditions (coexisting malnutrition and sarcopenia). By including geriatric patients with malnutrition or sarcopenia, the study aims to capture a broader patient demographic, acknowledging the high prevalence of these conditions in older adults and their potential overlap with GC populations. However, this inclusion may also have certain limitations in terms of generalizability. For instance, while the definition of geriatric inclusion is broad, it does not fully specify the proportion of patients with GC among the elderly cohort, which might lead to a risk of including studies that focus primarily on elderly populations without a clear link to GC.

The exclusion of early postoperative patients (< 4 weeks) serves to ensure that the interventions studied are relevant to long-term non-surgical management, thereby focusing on chronic care and palliative settings. This decision is justified by the need to distinguish between acute postoperative recovery and non-perioperative management, but it may limit the applicability of the findings to patients in the immediate postoperative phase who may also experience significant nutritional and muscular declines. Similarly, the exclusion of animal studies, case reports, and non-peer-reviewed literature was necessary to ensure the reliability and validity of the evidence. However, this may reduce the scope of available studies, especially those from low-resource settings or those that are less rigorously reported. Moreover, by restricting the evidence types to clinical practice guidelines (excluding Grade C), systematic reviews with high methodological scores, and peer-

reviewed RCTs, the study emphasizes high-quality, evidence-based interventions. While this enhances the clinical credibility and translational potential of the results, it may also exclude certain studies that, although of lower methodological quality, could provide real-world insights into the effectiveness of ONS and RE combined in diverse clinical contexts. Lastly, the limitation to Chinese and English publications from 2015 to 2025 ensures the use of recent, locally relevant literature, but could potentially exclude important studies in other languages, especially from non-English-speaking regions that may have unique patient care settings or different management practices.

In summary, while these criteria enhance the scientific rigor and clinical applicability of the evidence, they may also limit the generalizability of the findings to broader populations, global settings, or more acute postoperative phases. Future studies should consider expanding the scope to include more diverse populations and methodological types to further validate the efficacy of ONS and RE in managing coexisting malnutrition and sarcopenia across different healthcare environments and patient subgroups.

3.4 The Long-term Benefits and Potential Value of ONS Combined with RE for GC Patients with Coexisting Malnutrition and Sarcopenia

The combined intervention of ONS and RE represents a potential long-term therapeutic strategy for managing coexisting malnutrition and sarcopenia in GC patients. Although current RCTs are predominantly limited to 3–6 months of follow-up, emerging evidence suggests promising potential for sustained efficacy, functional muscle preservation, and mitigation of delayed complications. Primarily, ONS delivers high-quality protein (typically whey protein or branched-chain amino acid-enriched formulations) to supply essential amino acids during the post-resistance exercise anabolic window, significantly enhancing muscle mass and strength. This synergy improves muscle quantity, physical performance, and quality of life in cancer-related sarcopenia, particularly with leucine- and vitamin D-fortified formulations (72). Additionally, multimodal perioperative interventions (nutrition + exercise) are emphasized in GC surgical guidelines. Ida et al. identify perioperative malnutrition and sarcopenia as critical determinants of postoperative complications and long-term prognosis, advocating for "synergistic nutrition-exercise interventions" as a future research priority (73). While extant studies focus on short-term changes in weight or lean body mass, RE-activated muscle protein synthesis persists > 48 hours; coupling this with fractionated daily ONS intake may sustain long-term nitrogen equilibrium and attenuate muscle atrophy postoperatively (74). Notably, indirect evidence from long-term weight management studies post-gastrectomy demonstrates that short-term (6–8 weeks) elemental diet interventions—primarily targeting weight restoration—significantly reduce weight loss magnitude at 1-year follow-up, indicating early nutritional support confers durable body composition benefits (75). Integrating RE could further suppress annual muscle mass decline, thereby reducing functional deterioration, fall risk, and chemotherapy/radiotherapy delays attributable to sarcopenia. Consequently, despite limited RCT follow-up durations, four dimensions substantiate the long-term benefit potential of ONS + RE in managing coexisting malnutrition and sarcopenia in GC: (1) Sustained anabolic stimulation: Elevated muscle synthesis rates (> 48h post-RE) combined with fractionated high-protein ONS enable prolonged nitrogen equilibrium; (2) Functional preservation: High-protein, leucine-fortified ONS + RE improves physical performance in elderly cohorts, suggesting applicability for maintaining daily activity in GC patients; (3) Delayed complication reduction: Long-term muscle mass preservation mediates risk reduction for postoperative infections, pulmonary complications, and treatment interruptions; (4) Survival and quality of life: Sarcopenia improvement correlates with enhanced overall survival, positioning combined interventions as pivotal in long-term GC rehabilitation. Future research should therefore design ≥ 12-month RCTs to systematically evaluate ONS + RE impacts on muscle mass, functional capacity, complication incidence, and overall survival, thereby establishing an evidence base for precision nutrition-exercise protocols.

3.5 Limitations

Despite systematically synthesizing the best available evidence on combined ONS and RE interventions for GC patients with co-existing malnutrition and sarcopenia, this study exhibits several limitations: (1) limited generalizability due to the underrepresentation of high-risk populations (e.g., advanced GC with ECOG performance status ≥ 3, frail elderly ≥ 80 years, or multi-comorbidities) and predominant focus on Asian cohorts, lacking cross-ethnic/regional validation; (2) inadequate standardization of interventions, exemplified by broad ONS protein dosage ranges (1.2–2.5 g/kg/d) without precision

stratification based on tumor stage or metabolic status, ambiguous RE progression criteria (e.g., "gradual increase to moderate-high intensity"), and insufficient refinement of home-based equipment alternatives; (3) incomplete control for confounders, such as chemotherapy regimen variations (e.g., neurotoxicity from platinum agents impairing RE adherence) and socioeconomic support levels, potentially overestimating the independent treatment effects; (4) deficiencies in evaluation systems, including overreliance on physiological metrics (serum albumin, grip strength, skeletal muscle index) with insufficient integration of patient-reported outcomes (PROs) like quality of life (EORTC QLQ-C30), fatigue (MFI-20), or psychological status (HADS), alongside narrow muscle function assessment (limited to grip strength/gait speed) omitting activities of daily living (ADL scales) or muscle metabolic markers (e.g., serum creatine kinase), compounded by short follow-up durations (mostly ≤ 6 months) lacking ≥ 1-year survival rates, muscle function sustainability, or delayed complication data (e.g., osteoporosis); (5) evidence heterogeneity and quality concerns, with 4/10 guidelines rated AGREE II Grade B (editorial independence ≤ 60%) and 3/7 cross-sectional studies scoring ≤ 17/20, indicating methodological limitations, while some recommendations relied on low-grade evidence (e.g., "finger-ring test for sarcopenia screening") without GC-specific validation; (6) unverified clinical translatability, particularly regarding home-based execution details (e.g., ONS palatability adjustments, RE safety monitoring tools); (7) inadequate guidance for special scenarios, such as protein adjustment thresholds in renal/hepatic impairment (e.g., eGFR < 30 mL/min), contraindicated RE motions for spinal bone metastases, or evidence-based ONS formulation selection for dysphagia (Water Swallow Test ≥grade 3). These limitations necessitate resolution through multicenter large-sample trials, intelligent tool development, and long-term follow-up studies.

Conclusion

Based on the current clinical practice status of managing coexisting malnutrition and sarcopenia in patients with GC, ONS combined with RE has been validated as a safe, cost-effective core intervention. However, its real-world application remains suboptimal, with significant adherence challenges. This paper systematically identified high-level evidence from domestic and international sources, summarized the best evidence for managing this co-existing condition through integrated ONS-RE interventions, and provided practice recommendations across key domains, including screening and diagnosis, the rationale for combined therapy, and precise protocols for both ONS and RE.

Through this evidence synthesis, we aim to encourage clinicians and healthcare professionals to adopt these best practices to guide standardized care. The evidence demonstrates that this combined strategy can safely and effectively disrupt the "malnutrition-muscle loss-adverse prognosis" cycle. Resource-optimized approaches (e.g., using phase angle as an alternative to CT for assessing muscle mass) enhance feasibility in diverse settings, while the "3 + 3" nutritional model combined with progressive RE can improve functional outcomes like grip strength and treatment tolerance. Nonetheless, successful translation requires strategies tailored to patient preferences (e.g., palatable ONS formulations) and clinical status (e.g., protein adjustment in renal impairment). Future efforts should focus on validating the long-term efficacy of home-based protocols in multicenter trials, refining implementation guides for special populations (e.g., patients with bone metastases), and promoting sustained adherence through dynamic monitoring, ultimately establishing a patient-centered, precision management pathway for GC patients with coexisting malnutrition and sarcopenia.

Declarations

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Author contributions

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Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Disclosure statement

The authors declare that they have no conflicts of interest to disclose.

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Table 3

Table 3 is available in the Supplementary Files section.

Figures

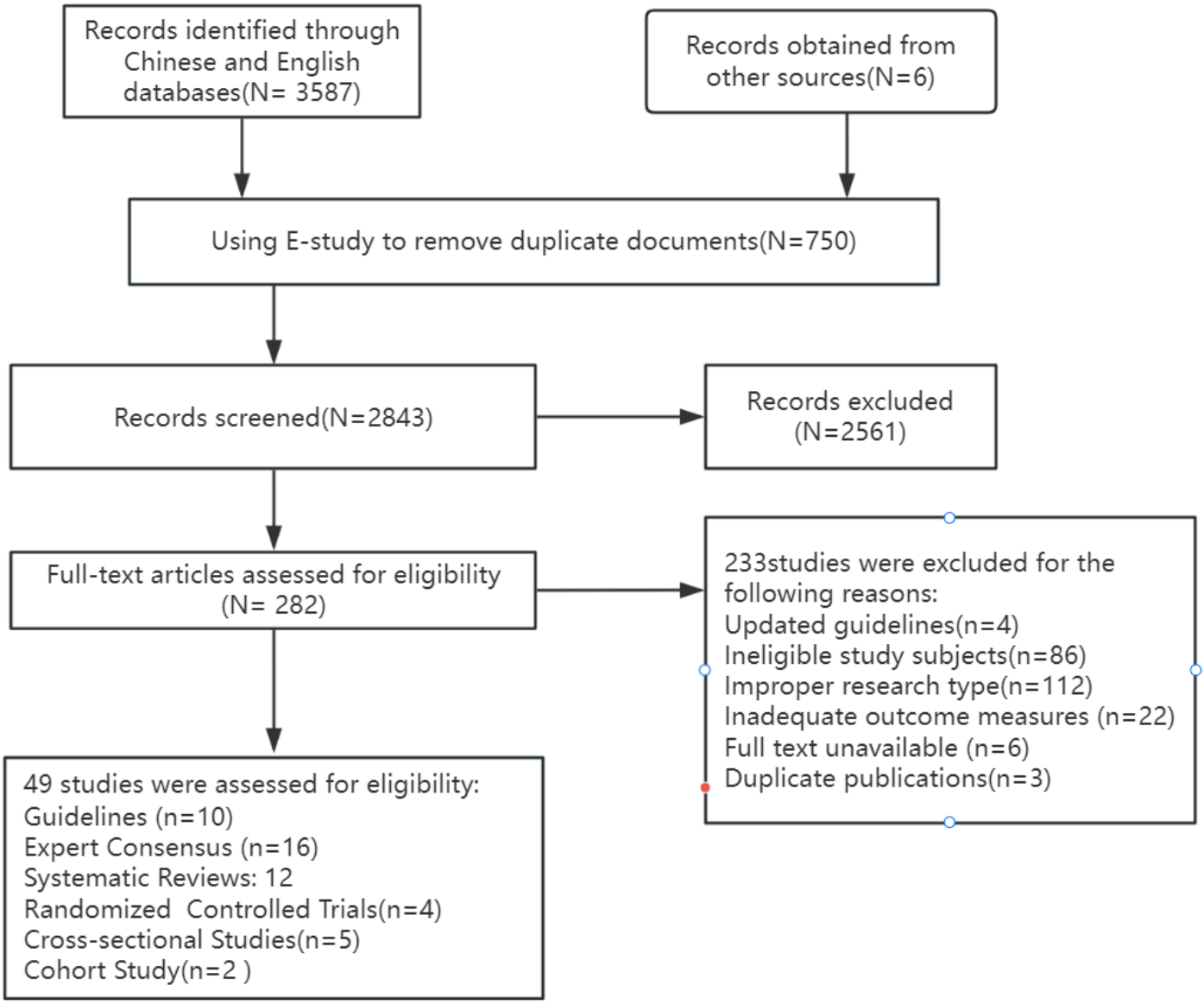


Figure 1

PRISMA flowchart of paper selection

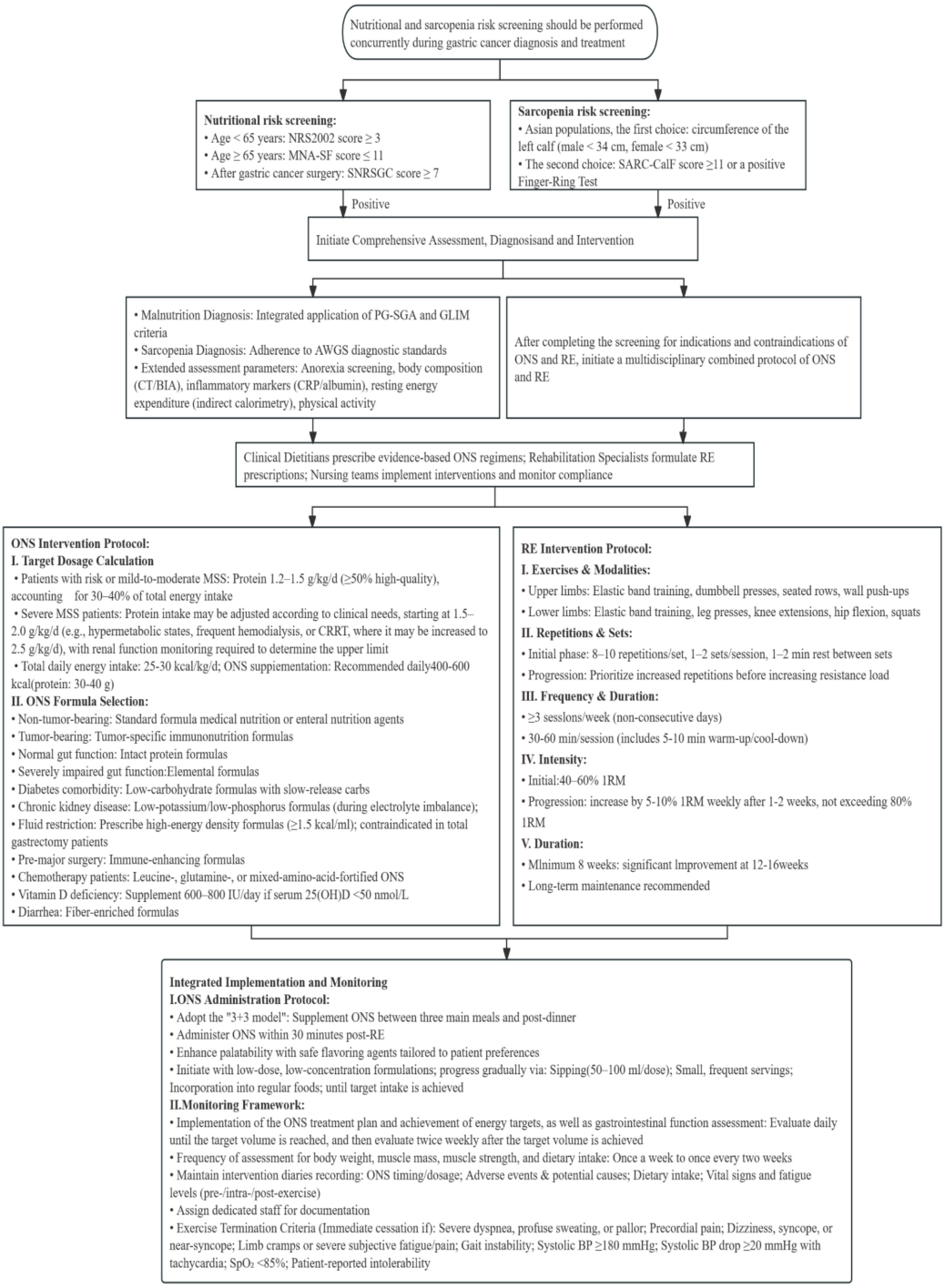


Figure 2

Standardized Intervention Algorithm Combining ONS and RE for Gastric Cancer Patients with Coexisting Malnutrition and Sarcopenia

Supplementary Files

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- Table3Systematicevaluationormeta.docx
- Table1PubMedsearchstrategy.docx