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Review

Summary of the best evidence for prehabilitation management of patients with non-small cell lung cancer

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ABSTRACT

Objective: This study adopts an evidence-based methodology to establish a comprehensive theory foundation for preoperative prehabilitation management in non-small cell lung cancer (NSCLC) patients.
Methods: A systematic literature review linked to prehabilitation management for NSCLC patients was conducted, utilizing reputable databases such as UpToDate, BMJ Best Practice, UK NICE, SIGN, GIN, Joanna Briggs Institute Library, Cochrane Library, Web of Science, Embase, OVID evidence-based database, PubMed, Chinese Wanfang database, CNKI, CBM, ATS, BTS, AACVPR, and EACTS. The search encompassed articles, including clinical decision-making, guidelines, evidence summaries, expert consensuses, and systematic reviews, from the inception of databases up to March 31st, 2023. Two researchers performed quality assessment of the literature and subsequent evidence extraction.
Results: Nineteen articles were included, comprising five guidelines, three expert consensuses, seven systematic reviews, and four randomized controlled trials. A total of 41 pieces of evidence were summarized, addressing key aspects such as the multidisciplinary team, appropriate patient population, prehabilitation modes, timing of prehabilitation, prehabilitation assessment, prehabilitation content, quality control, and effectiveness evaluation.
Conclusions: The synthesis of the best evidence for prehabilitation management in NSCLC patients provides a solid evidence-based foundation for its implementation. It is recommended that healthcare professionals conduct thorough patient evaluations, optimize and integrate medical resources, and collaboratively engage in interdisciplinarity efforts to develop and implement personalized and multimodal prehabilitation plans.

Introduction

The widespread adoption of the enhanced recovery after surgery (ERAS) concept and pathway has significantly transformed perioperative care, emphasizing swift rehabilitation as the fundamental purpose. Traditionally, efforts to improve patient prognosis have concentrated on the intraoperative (laparoscopic surgery and epidural anesthesia) and postoperative (analgesia, early food-taking, and rehabilitation activities) phases. However, the preoperative stage has emerged as a pivotal area for intervention to expedite postoperative recovery, developing a novel strategy known as "prehabilitation" within the framework of ERAS.

Prehabilitation encompasses diverse interventions, including preoperative exercise, medication optimization, smoking and drinking cessation, cognitive enhancement, psychological support, and nutritional supplementation. The overarching aim of prehabilitation is to enhance individuals' functional and physiological capacities, enabling them to better withstand the stresses of surgery and potentially contributing to improved postoperative rehabilitation.[1] A study suggests that prehabilitation is likely to have significant positive patient health and healthcare cost implications.[2]

Lung cancer is a leading cause of global cancer-associated mortality.[3] Frequently diagnosed in advanced stages due to its asymptomatic early stage, lung cancer carries an unfavorable prognosis. Histologically divided into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC, constituting approximately 85% of cases,[4] especially in candidates for surgery, exhibits higher survival rates than SCLC. Surgical resection remains the preferred treatment for early-stage (stages I and II) NSCLC patients and selects advanced (stage IIIA) cases.[5] Minimally invasive surgical techniques such as video-assisted thoracoscopic surgery (VATS) have advanced, reducing the incision size and systemic burdens associated with lung cancer surgery.[6,7] Despite these advancements, lung cancer surgery remains highly linked to postoperative complications, such as arrhythmia, hemorrhage, pulmonary atelectasis, pleural effusion, residual cavity after surgery, persistent air leakage, and myocardial ischemia.[8] Adverse events

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contribute to extended hospital stays, intensive care units, 30-day readmissions, increased perioperative mortality, and decreased cancer survival rate.[9,10] The choice of surgical technique, lung volume reduction, and surgical approach (open or minimally invasive) all have an impact on the risk and severity of postoperative complications. Additional factors, including cancer staging, neoadjuvant therapy, patient demographics, and baseline physical condition, influence postoperative outcomes.

In this context, a systematic review has demonstrated the safety and feasibility of prehabilitation across various cancers, including lung cancer, demonstrating a strong correlation with enhanced functional exercise ability and improved patient-reported outcomes.[11] Prehabilitation plans tailored for lung cancer patients encompass elements such as exercise, smoking cessation, dietary intervention, psychological assessment, and medical optimization; however, the optimal combination of these components remains elusive.[12] Existing evidence supports the effectiveness of multimodal prehabilitation programs, integrating exercise, nutritional supplementation, and psychological support, in improving the prognosis of lung cancer patients.[13] Despite these findings, uncertainties and controversies persist regarding the mode, target population, and intensity of prehabilitation intervention. Ongoing randomized controlled trials (currently six international studies registered on ClinicalTrials.gov) seek to determine the ideal mode, optimal timing, and patient selection for prehabilitation in lung cancer, yet translational and practical research lags.[12] In the clinical context, implementing prehabilitation still lacks a robust body of evidence and reference points.

In summary, it is imperative to identify the best evidence for prehabilitation in NSCLC patients and develop evidence-based programs that consider available resources, clinical experience, and patient conditions. This study aimed to summarize the optimum evidence for preoperative prehabilitation management in NSCLC patients undergoing surgery to provide practical guidance for clinical practitioners and ultimately improve surgical outcomes in lung cancer patients.

Methods

Literature retrieval strategy

According to the "6S Evidence Resource Pyramid Model", which prioritizes higher-quality evidence towards the upper layers of the pyramid, literature retrieval for this study involved a comprehensive search across diverse databases. The selected databases included authoritative sources such as UpToDate, BMJ Best Practice, UK National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guideline Network (SIGN), International Guide Collaboration (GIN), Joanna Briggs Institute Library, Cochrane Library, Web of Science, Embase, OVID Evidence-Based Database, PubMed, Chinese Wanfang Database, Chinese Journal Full-text Database (CNKI), Chinese Biomedical Literature database (CBM), Registered Nurses Association of Ontario (RNAO), American Thoracic Society (ATS), British Thoracic Society (BTS), American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR), and the European Association for Cardiothoracic Surgery (EACTS).

The literature retrieval process involved crafting search strategies using keywords, such as "preoperative rehabilitation" and "perioperative care," "prehabilitation recommendations," "lung cancer," "thoracic surgery," and "thoracoscope." The search period extended from the inception of each database up to March 31st, 2023.

For English databases, such as PubMed, the following search strategies for systematic reviews were developed:

1. "Preoperative rehabilitation" [Title/Abstract] OR "perioperative care" [Title/Abstract] OR "prehabilitation recommendations" OR "preventive rehabilitation" [Title/Abstract];
2. "Carcinoma, Non-Small-Cell Lung" [MeSH Terms] OR "lung cancer" [Title/Abstract] OR "lung carcinoma" [Title/Abstract] OR "NSCLC" [Title/Abstract]);
3. "Thoracic surgery" [MeSH Terms] OR "thoracic operation" [Title/Abstract] OR "Lung operation" [Title/Abstract];
4. Combine #2 OR #3
5. "Systematic review" [Title/Abstract] OR "meta-analysis" [Title/Abstract]
6. Combine #1 AND #4 AND #5

Literature inclusion and exclusion criteria

The inclusion criteria were as follows: (1) the research must be directly related to prehabilitation or preoperative nursing interventions specifically designed for lung cancer. (2) The focus of the study should be on postoperative outcomes, including but not limited to postoperative complications, postoperative length of stay, and postoperative functional recovery. (3) Only publicly accessible literatures in both Chinese and English was considered.

The exclusion criteria included the following: (1) studies lacking full-text availability, (2) studies deemed to be extremely low-quality following a thorough quality evaluation, and (3) publications presenting redundant information through repeated publication.

Literature quality evaluation

Following the established literature evaluation criteria, two researchers, each equipped with expertise in lung nursing research and practical experience, and had undergone Johns Hopkings nursing evidence-based practice training program, evaluated literature quality. Any discrepancies in the evaluations were addressed through discussion or adjudication by a third researcher with expertise in the same field. For clinical decisions, recommended practices, and evidence summaries, the corresponding tools were selected for quality evaluation, determined by the literature type, after tracing back to the sources. Guidelines underwent evaluation using the Appraisal of Guidelines for Research and Evaluation (AGREEII) tool. Expert consensus was assessed using an evaluation tool from the Australian JBI Evidence-Based Health Care Center (2016). Systematic reviews were evaluated using AMSTAR2, whereas randomized controlled trials were assessed using the Cochrane risk-of-bias assessment tool. This meticulous process ensures a comprehensive and nuanced evaluation of the literature.

Evidence summary and recommendation level

In conjunction with the outcomes of the previous literature retrieval, two researchers determined a comprehensive framework detailing the evidence and content within each dimension. They meticulously classified, extracted, and summarized the relevant evidence. The original level was documented as evidence sourced from guidelines. For evidence originating from systematic reviews, expert consensuses, and initial studies lacking assigned evidence levels, the JBI Evidence Pre-Grading and Evidence Recommendation System (2014 version)[14] was employed. This system, utilizing a scale of 1–5, with level 1 denoting the highest and level 5 the lowest, was used to grade evidence. Subsequently, evidence was classified into grade A (strongly recommended) and grade B (weakly recommended) based on the JBI feasibility, appropriateness, meaningfulness, and effectiveness (FAME) structure. The general principle guiding this classification is to prioritize the inclusion of evidence-based findings, high-quality evidence, and the most recently published evidence.

Results

Baseline characteristics of the enrolled articles

A preliminary search yielded 834 articles. After a systematic literature retrieval and screening process illustrated in Fig. 1, 19 articles met the inclusion criteria. The baseline characteristics of these articles are outlined in Table 1.

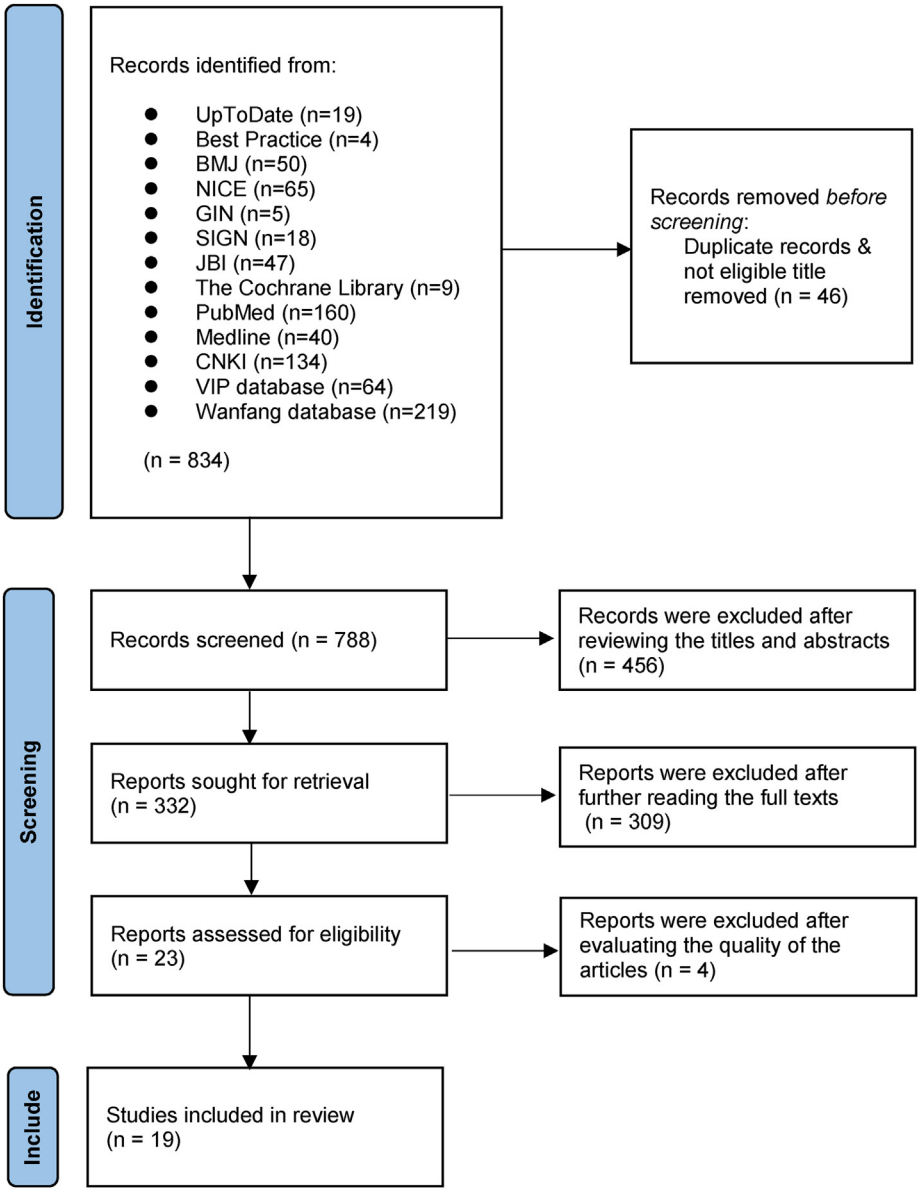

Fig. 1. Flow chart of literature retrieval and screening.

Results of literature quality evaluation

This research incorporated a total of five guidelines. Among them, the guidelines discussed by Batchelor et al.[7] achieved a standardized assessment score of 55.6% for participants and 58.3% for applicability, resulting in a grade B recommendation. The remaining four guidelines scored $\geq$ 60% across six criteria, including scope and purpose, participants, rigor, clarity, applicability, and editorial independence, leading to a grade A recommendation. All guidelines were included in the final analysis. Additionally, three consensus articles were enrolled, meeting the inclusion criteria with uniform positive evaluations, reflecting their generally high quality. Seven systematic reviews, recognized for their high-quality and comprehensive study designs, were also included for evidence extraction. Furthermore, four randomized controlled trials (RCTs) were screened, each demonstrating a low risk of bias and overall high quality, leading to their inclusion in the study, as detailed in Table 2.

Evidence description and summary

Following the extraction, analysis, comparison, and discussion of the gathered evidence, a comprehensive integration of similar content was conducted. This meticulous process culminated in the synthesis of 41 pieces of the most compelling evidence, summarized across eight aspects: multidisciplinary team, appropriate population, prehabilitation mode, prehabilitation timing, prehabilitation assessment, prehabilitation content, quality control, and effect evaluation (Table 3).

Discussion

This evidence synthesis presents a comprehensive overview of preoperative prehabilitation for NSCLC patients, encompassing three stages and eight dimensions, as illustrated in Fig. 2. Healthcare professionals are encouraged to conduct thorough patient evaluations, optimize and integrate medical resource utilization, and collaborate across disciplines to develop and implement personalized and multimodal prehabilitation programs. This approach aims to improve the standards of medical care and expedite patient recovery.

Prehabilitation multidisciplinary team: nurses can play a greater role

The involvement of multidisciplinary teams serves as the foundation for the effective prehabilitation of NSCLC patients. Emerging evidence

Table 1
Characteristics of the included articles ($N = 19$).

Author	Publication year	Article type	Article source	Research subject
Batchelor et al.[1]	2018	Guideline	PubMed	Guidelines for enhanced recovery after lung surgery
De Hert et al.[15]	2018	Guideline	PubMed	Preoperative evaluation of adults undergoing elective noncardiac surgery
Weimann et al.[16]	2017	Guideline	PubMed	ESPEN guideline: Clinical nutrition in surgery.
SIGN[17]	2014	Guideline	GIN	Management of lung cancer (2017 review)
NICE[18]	2020	Guideline	GIN	Perioperative care in adults
Wang et al.[19]	2019	Expert consensus	CNKI	Chinese expert consensus on perioperative lung protection (version 2019)
Piccioni et al.[20]	2020	Expert consensus	PubMed	Recommendations from the Italian intersociety consensus on perioperative Anesthesia Care in Thoracic Surgery (PACTS) part 1: preadmission and preoperative care
Liu et al.[21]	2022	Expert consensus	CNKI	Expert consensus on prehabilitation management for enhanced recovery in patients undergoing thoracic surgery (2022)
Cavalheri et al.[11]	2017	Systematic review	Cochrane Library	Preoperative exercise training for patients with non-small cell lung cancer
Thomsen et al.[22]	2014	Systematic review	Cochrane Library	Interventions for preoperative smoking cessation
Ferreira et al.[23]	2021	Systematic review	PubMed	Effects of preoperative nutrition and multimodal prehabilitation on functional capacity and postoperative complications in surgical lung cancer patients: a systematic review
Sebio et al.[24]	2016	Systematic review	PubMed	Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer
Mainini et al.[25]	2016	Systematic review	PubMed	Perioperative physical exercise interventions for patients undergoing lung cancer surgery: What is the evidence?
Steffens et al.[26]	2018	Systematic review	PubMed	Preoperative exercise halves the postoperative complication rate in patients with lung cancer
Rosero et al.[27]	2019	Systematic review	PubMed	Systematic review and meta-analysis of randomized, controlled trials on preoperative physical exercise interventions in patients with non-small-cell lung cancer
Ferreira et al.[28]	2021	RCT	PubMed	Multimodal prehabilitation for lung cancer surgery
Gravier et al.[29]	2022	RCT	PubMed	Prehabilitation sessions can be provided more frequently in a shortened regimen with similar or better efficacy in people with non-small cell lung cancer
Liu et al.[30]	2020	RCT	PubMed	A two-week multimodal prehabilitation program improves perioperative functional capability in patients undergoing thoracoscopic lobectomy for lung cancer
Ferreira et al.[31]	2021	RCT	PubMed	Feasibility of a novel mixed-nutrient supplement in a multimodal prehabilitation intervention for lung cancer patients awaiting surgery

RCT, randomized controlled trial.

Table 2
Bias assessment of randomized controlled trials.

Author	Item						
	Selection bias		Performance bias	Measurement bias	Follow-up bias	Publication bias	Others
	Randomization sequence	Allocation concealment					
Ferreira et al.[28]	Low	Low	Low	Low	Low	Low	Low
Gravier et al.[29]	Low	Low	Low	Low	Low	Low	Low
Liu et al.[30]	Low	Low	High	High	Low	Low	Low
Ferreira et al.[31]	Low	High	High	Low	Low	Low	Low

High, high bias; Low, low bias.

advocates for engaging specialists in the execution of multimodal prehabilitation interventions. International studies emphasize the pivotal role of various professionals within interdisciplinary teams, including anesthetists, clinical psychologists, nutritionists, exercise physiologists, fitness professionals, geriatricians, exercise specialists, nurses, occupational therapists, oncologists, physicians, physiotherapists, support workers, and surgeons. There are successful initiatives aimed toward preoperative prehabilitation optimization, including McGill's Perioperative Program and the Greater Manchester (GM) Prehab4Cancer (P4C) program.[32,33] These projects emphasize the participation and collaboration of multidisciplinary teams.

Collaborative interdisciplinarity efforts contribute to successful prehabilitation interventions,[34,35] enhancing the feasibility, effectiveness, and continuity of prehabilitation management. Gathering as many experts as possible, using a dietician, smoking cessation specialist, other well-trained and licensed professionals, and even voluntary workers can exponentially improve the health of patients. The prehabilitation team should involve four key elements to be successful: administrative support, physician support, nursing support, and patient involvement.[36] Engaging patients in it was often overlooked. Patients are the common denominator to ensure that all these supports come to fruition. The multidisciplinary members should be in close communication with each patient's prehabilitation, highly passionate about the project, and ready to invest a great deal of time and effort.

While the importance of multidisciplinary teams is underscored by current evidence, accessibility to such teams may be limited given constraints in medical resources and the large patient population. Renouf et al.[37] highlighted the crucial role of nurses in prehabilitation multidisciplinary teams. By establishing therapeutic relationships, nurses screening patients based on relevant information, providing health education, introducing patients to other team members, and dynamically monitoring patients during regular reassessment can maintain patient-centered prehabilitation interventions. This highlights the key role of nurses can play in ensuring successful prehabilitation, offering valuable insights into their contributions within the prehabilitation context.

Prehabilitation is applicable for the preoperative optimization of all NSCLC patients undergoing surgery

Evidence specific to the relevant population indicates the broad applicability of prehabilitation for all NSCLC patients undergoing surgery, with a particular emphasis on its potential benefits for elderly patients characterized by poor physical function, malnutrition, and those requiring extensive surgical resection.[38] Despite variations in the adopted prehabilitation strategies across existing studies, the effectiveness of prehabilitation has been consistently demonstrated. This efficacy is evident in studies involving lung cancer patients over 60 years old, those with locally advanced non-small cell carcinoma, and individuals diagnosed or suspected with NSCLC exhibiting a moderate to high risk of postoperative complications. Recent international multicenter clinical trials, exemplified by the CheckMate816 study, have demonstrated the effectiveness of neoadjuvant therapy.[39] Additionally, emerging evidence suggests that prehabilitation can offer benefits to this category of lung cancer patients undergoing neoadjuvant treatment.[40] However, the potential advantages of prehabilitation for younger patients or those without previous complications warrant further investigation. Considering the findings from this study, recommendations are made to prehabilitation optimize the care of all NSCLC patients undergoing surgery, acknowledging the potential benefits across diverse patient demographics and clinical scenarios.

Implementation of family-based personalized multimodal prehabilitation is recommended

The latest guidelines for postoperative recovery following lung cancer surgery, as outlined by ERAS and the European Society of Thoracic Surgery (ESTS), strongly advocate the implementation of systematic multimodal care during the preoperative stage.[1] A consensus from Italy on preoperative care suggests the superiority of multimodal prehabilitation, encompassing early assessment of respiratory function, smoking cessation, respiratory rehabilitation, nutritional status, and physical exercise, among other elements, over single-mode prehabilitation. The success of multimodal prehabilitation often hinges on the participation of a larger population, including not only healthcare professionals but also the patient's family. In particular, family members can play a crucial role in supporting the patient's smoking cessation efforts, highlighting the enhanced impact of family-based prehabilitation. Considering factors such as transportation, service accessibility, and patients' physical condition, inpatient and outpatient rehabilitation may lead to reduced patient compliance. Consequently, personalized home prehabilitation centered around family involvement is recognized as a viable solution, especially for vulnerable and elderly patients.[41] A systematic review evaluating the impact of prehabilitation and rehabilitation on the health of NSCLC patients has perceived that compared to in-hospital or out-of-hospital interventions, family-based interventions generally result in higher and more adequate compliance.[42] Given these considerations, healthcare professionals are strongly recommended to opt for a family-based personalized multimodal prehabilitation program when devising intervention plans for patients.

Much evidence highlights individualized prehabilitation interventions tailored to individuals; however, there is no consensus on how to fully conceptualize and achieve this. An individualized prehabilitation program is not only individualized to the physiology of the patient but should also consider patient-led values, needs, goals, support structures, and beliefs, which is a more complex process. Therefore, theoretical frameworks can be used to guide intervention design to help support individualized and collaborative rehabilitation programs that maximize outcomes.

The optimal timing for prehabilitation is 2–4 weeks before surgery

The timing of prehabilitation lacks a consensus in current studies, with the majority focusing on a window of 2–4 weeks before surgery. According to an expert consensus on prehabilitation, it is advised not to delay tumor surgery for more than four weeks due to the implementation

Table 3
Evidence summary of preoperative prehabilitation in NSCLC patients ($N = 41$).

Evidence item	Evidence content	Evidence level	Recommendation grade
Multidisciplinary team	1. Prehabilitation is based on multidisciplinary collaboration, and multidisciplinary evaluation contributes to the consideration of different therapeutic plans and the selection of the optimal therapeutic method[20,21]	5	B
Appropriate population	2. Patients who undergo elective or limited surgery can receive prehabilitation, especially elderly patients with poor basic physical function, malnutrition, and a large scope of surgical resection[21]	5	A
	3. Prehabilitation is recommended for patients with borderline lung function or motor ability[1]	3	B
Prehabilitation mode	4. Develop personalized and multimodal prehabilitation programs, including physical exercise, respiratory training, nutritional supplementation, and psychological optimization[21,28,30,31]	1	A
	5. Multimodal prehabilitation (early respiratory function assessment, smoking cessation, respiratory rehabilitation, nutritional status, and physical exercise) is more effective than single-mode prehabilitation[28]	5	B
	6. It is recommended to be dominated by the comprehensive outpatient rehabilitation department[29]	5	B
	7. It is recommended to make a family-based prehabilitation plan[28,30]	1	A
Timing of prehabilitation	8. 2–4 weeks before surgery[20,28,30,31]	1	A
	9. More frequent prehabilitation processes can be given in shortened therapeutic plans with similar or better therapeutic effects[29]	1	B
	10. It is not recommended to postpone surgery for more than four weeks due to the implementation of the prehabilitation plan. It is also advisable to perform prehabilitation as early as possible for cases less than two weeks from the decision of surgery to the start of surgery[21]	5	A
Prehabilitation assessment	11. A comprehensive assessment of the patient is necessary before prehabilitation[21]	5	A
	12. It is recommended to preliminarily stratify the risk through a general condition assessment of patients at the time of surgery decision in the outpatient setting, including patient age, body mass index, complications, treatment conditions, and ASA grading[21]	5	A
	13. Preoperative risk stratification aims to identify high-risk surgical patients (such as ASA $\geq$ 3, advanced cardiac disease, renal failure, VO_2max $<$ 10 mL/kg/min, ppoFEV1 or ppoDLCO $<$ 40%, systemic disease, or other risk factors)[20]	5	A
	14. It is recommended to evaluate lung function and measure ppoFEV1 and ppoDLCO before surgery. If any abnormalities are detected in pulmonary function tests, exercise tests can be subsequently performed, such as cardiopulmonary exercise test (CPET), stair-climbing test, and 6-min walking test[19–21]	5	A
	15. Cardiac function assessment is recommended with the application of electrocardiogram and TTE to quantify the possibility of cardiomyopathy[15]	2	A
	16. Assess the nutritional status and weight loss of patients[1,15,16,18,20]	1	A
	17. Assess psychological and sleep conditions of patients[21]	5	B
	18. Cognitive function assessment is based on validation tools[15]	1	B
	19. Asthenia is evaluated in a structured, multimodal manner to avoid and substitute a single measurement method[15,21]	1	A
Prehabilitation content	*Exercise training*		
	20. The main contents of exercise training include aerobic exercise training, resistance strength training, and IMT[21,24,26,27]	1	A
		1	A

(*continued on next page*)

Table 3 (*continued*)

Evidence item	Evidence content	Evidence level	Recommendation grade
	21. The optimal preoperative exercise program cannot be established yet; however, the optimal preoperative exercise training should contain at least aerobic exercise and strength training[25]		
	22. Aerobic exercise training is recommended for all prehabilitation patients. Resistance strength training is particularly crucial for the elderly population or individuals with frailty, sedentary behavior, malnutrition, chronic cardiopulmonary diseases, or other conditions[21]	5	B
	23. For patients without chronic kidney disease, it is recommended to moderately supplement high-quality protein after prehabilitation exercise training[21]	5	B
	Respiratory function exercise		
	24. It is recommended to provide preoperative respiratory function exercise guidance for patients[15,25]	1	A
	25. IMT can strengthen the fitness reserve function of inspiratory muscle and should be combined with aerobic exercise training or resistance strength training[21]	5	B
	26. In combination with breathing exercises and multiple breathing training apparatuses, deep and slow abdominal breathing can be practiced[19]	5	A
	Rectification of anemia		
	27. Anemia should be detected, examined, and rectified before surgery[1,18,21]	1	A
	28. Parenteral iron is used instead of oral iron supplements before elective surgery to treat iron deficiency anemia. Intravenous iron and erythropoietic agents are recommended[15]	1	A
	Cessation of smoking and drinking		
	29. Smoking should be ceased at least four weeks before surgery[1,15,20–22]	1	A
	30. Lung cancer surgery should not be delayed due to smoking cessation[17]	4	A
	31. Smoking cessation suggestions and effective interventions, including behavioural support and medication treatment, are provided for smokers with surgical plans[22]	1	A
	32. Preoperative drinking cessation, including medication strategies, is recommended to prevent recurrence and withdrawal symptoms, but no recommendations were suggested on the timing, duration, and intensity of drinking cessation[15]	1	B
	Nutritional supplementation		
	33. It is recommended to correct malnutrition[15,21,23]	2	A
	34. Malnourished patients should take oral nutritional supplements (preferred oral/enteral route)[1,16]	1	A
	35. The standard whole protein formula is suitable for most patients[16]	1	A
	36. Obese patients are suggested to optimize their dietary structure and reduce weight appropriately[21]	5	B
	Psychological adjustment		
	37. Patients are encouraged to adopt various forms of psychological relaxation before surgery. Interventions are necessary for patients at risk of anxiety and depression[21]	5	A
Quality control	38. Supervision and follow-up during multimodal prehabilitation are encouraged based on local conditions, including the application of wearable devices, community services, and remote healthcare[21]	5	A
	39. Treatment and management should be performed under the planning and guidance of a multidisciplinary team, which should include follow-up by clinical nurse specialists[17]	4	A
Effectiveness evaluation	40. Prehabilitation is beneficial to the improvement of cardiopulmonary parameters, such as functional ambulation performance and pulmonary function[23]	1	A
	41. 6MWT is the most used physical function measurement method[21,23]	1	A

ASA, American Society of Anesthesiologists; VO_2max, maximal oxygen consumption; ppoFEV1, predicted postoperative forced expiratory volume in the first second; ppoDLCO, predicted postoperative diffusion lung capacity for carbon monoxide; CPET, cardiopulmonary exercise testing; TTE, transthoracic echocardiography; IMT, inspiratory muscle training; 6 MWT, 6 minutes walking testing.

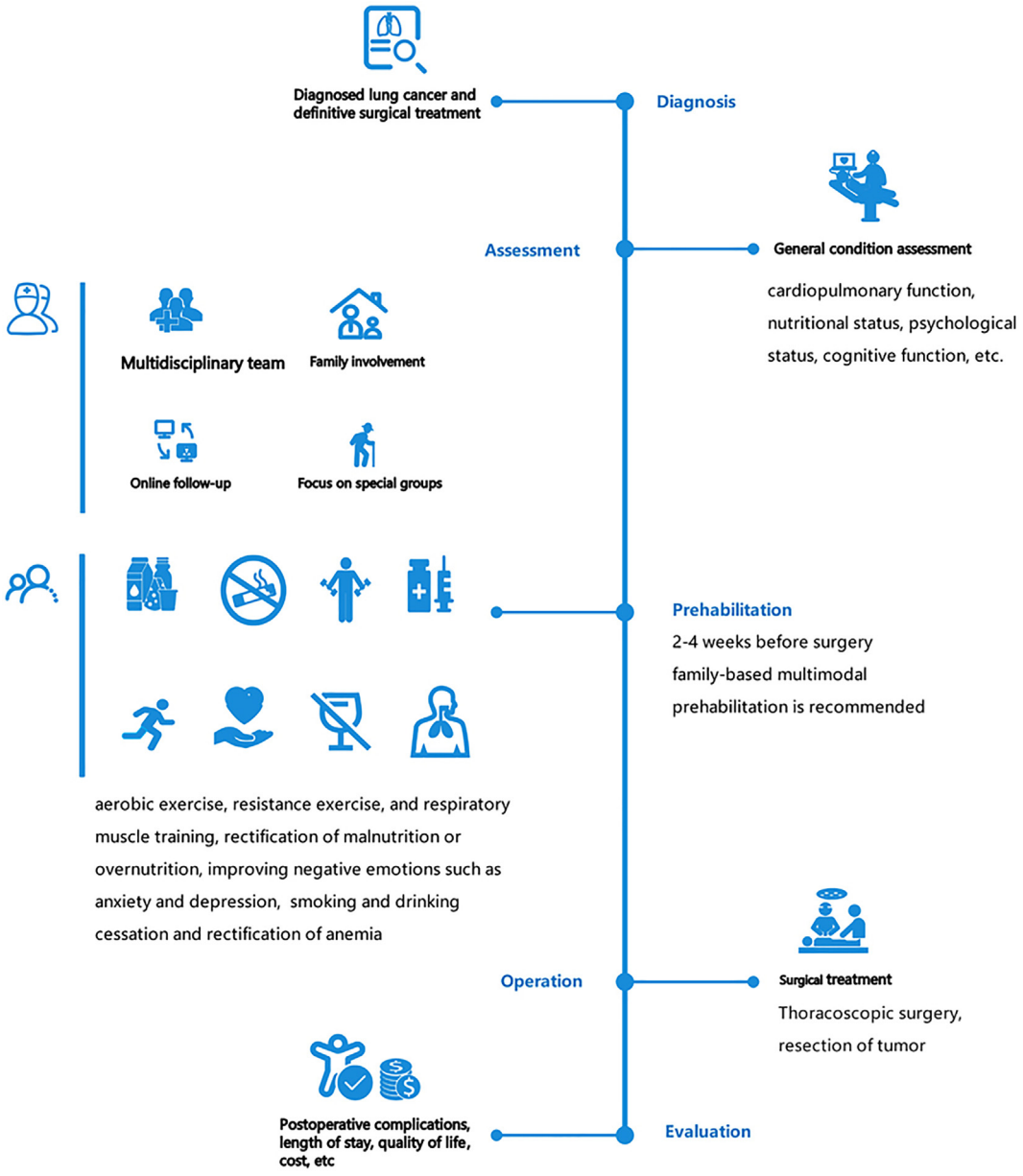

Fig. 2. Prehabilitation of NSCLC. NSCLC, non-small cell lung cancer.

of the prehabilitation plan. Additionally, for cases with less than a 2-week interval between the decision for surgery and the actual start of surgery, it is recommended to initiate prehabilitation as early as possible.[21] An insightful study comparing the efficacy of a 3-week rehabilitation program (5 times/week, 15 sessions in total) with that of a 5-week program (3 times/week, 15 sessions in total) indicated similar or improved effects with more frequent prehabilitation interventions within a short period.[29] Another study focusing on the timing of prehabilitation by Burnet et al. highlighted that newly diagnosed lung cancer patients might be inadequately prepared to embrace lifestyle changes due to the impact of disease diagnosis and treatment.[43] In the context of planned surgery for lung cancer patients, characterized by varying waiting periods from outpatient confirmation to admission due to bed shortages, this interim duration presents a suitable window for implementing prehabilitation plans in China. Despite variations across hospitals and regions, patients can utilize this waiting period to engage in effective prehabilitation strategies.

A comprehensive assessment conducted prior to prehabilitation proves beneficial for risk identification and plan formulation

Before formulating prehabilitation plans, it is imperative to conduct a comprehensive and accurate synthetic assessment of patients. This assessment serves as a crucial tool for identifying high-risk surgical patients through risk stratification, facilitating the development of safe and feasible prehabilitation plans based on the assessment results.[21] The assessment contents typically encompass general conditions, cardiopulmonary function, nutritional status, psychological well-being, and cognitive function, among other aspects. While routine preoperative assessment is a standard procedure before most surgical interventions, taking cardiac function as an example, routine assessments, including medical history, physical examination, and electrocardiogram, are performed before noncardiac surgery in adults to gauge the risk of perioperative cardiac events in patients.[44] The distinction and relationship between preoperative assessment and the assessment conducted before prehabilitation remain unclear.

Despite the ongoing need for higher-level evidence, assessment before prehabilitation plays two key roles. First, it facilitates risk stratification and identification of high-risk patients, ensuring the safety of prehabilitation interventions. Intermediate and high-risk patients need further evaluation, including the patient's physical function and psychological and cognitive status, to develop an individualized prehabilitation plan. For patients with comorbidities, the severity of comorbidities should be evaluated, and further examinations should be performed. If necessary, specialist consultation should be conducted to optimize the preoperative management of comorbidities. Second, it guides the development and adjustment of prehabilitation plans based on assessment results. For patients with severe cardiovascular and cerebrovascular diseases, severe bone and joint diseases, and high risk of falls, exercise training should be conducted with caution and should be performed under the supervision of medical staff in medical institutions (including community hospitals).[21]

Multimodal prehabilitation at least includes exercise, nutrition, and psychological contents

In current studies on prehabilitation for lung cancer patients, exercise has consistently been recognized as a fundamental component, often representing a single-mode prehabilitation known as exercise rehabilitation. As research advances, there has been a growing shift towards promoting multimodal prehabilitation interventions. Most notably, triple-mode interventions involving nutrition, exercise, and psychological health have gained prominence. Some studies have explored combinations of exercise, psychology, exercise, and nutrition, broadening the scope of prehabilitation approaches.[45] Typically, exercise within prehabilitation includes aerobic exercise, resistance training, and respiratory muscle training. Nutritional components focus on addressing malnutrition or overnutrition, while psychological aspects aim to enhance mental well-being by addressing negative emotions, such as anxiety and depression.

Moreover, preoperative smoking and drinking cessation, along with the rectification of anemia, have emerged as crucial elements in preoperative prehabilitation programs for lung cancer patients. For instance, higher-level evidence demonstrates the necessity of drinking cessation before surgery, although specific recommendations regarding optimal timing, duration, and intensity of cessation remain unclear. Despite the absence of large-scale clinical trials to definitively establish the optimal combination of prehabilitation interventions, current evidence strongly suggests that effective multimodal prehabilitation should encompass at least three aspects: exercise, nutrition, and psychology.

Various forms of supervision and follow-up can ensure the efficacy of prehabilitation

Patient compliance is an important prerequisite for the successful implementation of prehabilitation, necessitating multimodal supervision and follow-up tailored to the local conditions.[21] In many prehabilitation studies involving lung cancer patients, supervised exercise plans are prevalent, often incorporating specific strategies such as motivational interventions or supervised follow-up phone calls.[46] Throughout the prehabilitation process, various methods, including platforms such as WeChat and Wemeet, can be employed for effective follow-up and management. For instance, establishing WeChat groups facilitates communication between medical professionals and patients, enhancing information exchange and fostering peer support. Simultaneously, Wemeet can be utilized for knowledge dissemination, doctor-patient communication, and discussion. Furthermore, some studies have successfully employed wearable devices for supervision and follow-up of at-home interventions, showcasing promising results that can inform and enhance prehabilitation management strategies.

Effect evaluation and cost-benefit analysis of prehabilitation

Objective clinical outcomes following prehabilitation included measures of functional capacity (6-minute walk test, lung function, and other CPET data) as well as postoperative complications, readmission, and length of hospital stay. Most studies have highlighted the improvement in cardiopulmonary parameters in lung cancer patients with prehabilitation, with the 6-minute walk test being the most commonly used measure.

Patient-reported outcomes included patient satisfaction, quality of life, anxiety, depression scores, etc. Prehabilitation studies on other cancers also covered mood, symptoms, and daily activities. The inclusion of patient-reported outcomes indicates that fully listening to patients' expressions of prehabilitation expectations and other aspects and giving patients the right to participate in treatment decision-making and choice of treatment means is the embodiment of the “patient-centered” service concept.

Existing studies suggest that prehabilitation may bring potential cost savings in reducing complications, shortening hospital stays, and improving patient outcomes. More evidence on the cost-effectiveness of multimodal prehabilitation programs was not found, and some randomized controlled trials related to preoperative exercise interventions included health economics.[47] To gauge the effectiveness of prehabilitation programs, traditional health economics evaluations employ methodologies such as cost-benefit analysis (CBA), cost-utility analysis (CUA), and cost-consequences analysis (CCA).[48] The costs associated with quality-of-care improvement and program implementation also need to be considered when evaluating rehabilitation programs for patients with lung cancer, which include costs associated with treatment as well as costs to healthcare professionals.[49] This would provide valuable information on the economic impact of adopting prehabilitation programs for patients with lung cancer.

Evidence translation and application: strategies, ethical issues, barriers, and facilitators

The best evidence provides a reference for establishing standards and standardization of care. Healthcare professionals who need evidence can apply this evidence selectively or partly at the beginning, implying that they can choose the relatively easy-to-implement evidence to apply first. For example, they can use the JBI evidence-based medicine healthcare model or other evidence-based practice models to transform and apply evidence and formulate prehabilitation programs with stakeholder participation. Specifically, pilot projects, quality improvement programs, development of standardized protocols, and care pathways can be used. For example, McGill University in Canada designed a prehabilitation quality improvement program for lung cancer, which provided single-center data confirming that a personalized stepwise rehabilitation program is feasible, safe, and effective.[32]

The “best evidence” is only one of the most important bases for clinical decision-making, which healthcare professionals should use to inform their decisions. Healthcare providers must ethically discuss treatment options with patients; however, these options should not prevail over individual patient choices, even when strong evidence supports them. Careful, accurate, and judicious use of the best current research evidence, combined with the professional skills and clinical experience of health professionals and consideration of patient values, is essential for making clinical decisions for individual patients. Additionally, ensuring equitable access to resources and improved prehabilitation services is crucial.

Existing studies have reported barriers to implementing a robust prehabilitation program for lung cancer patients, including traditional barriers such as funding, clinician knowledge, and acceptability, as well as factors related to the healthcare system, such as access to programs

and multidisciplinary healthcare personnel.[12] There are many facilitators for establishing a viable prehabilitation program. First, health professionals should know when to refer patients to a prehabilitation program and have a clear application process for participating in the rehabilitation program. Second, patients receive referrals and advice on prehabilitation, and they are fully informed about the aims and benefits of prehabilitation (flyers, hospital websites, and improved communication between healthcare professionals and patients).[50] The current study showed that patients actively engage when recommended for rehabilitation by their physicians.

Strengths and limitations

This study has several strengths. First, the retrieval strategy was meticulously formulated by an evidence-based team through comprehensive discussions, ensuring a thorough search across various databases. The team's involvement in the evaluation, classification, and summarization of evidence enhances the reliability of the findings. Second, given the scarcity of literature on prehabilitation management in lung cancer, this study systematically integrates high-quality evidence in this field, providing valuable insights for medical professionals involved in lung cancer surgical treatment. However, this study has some limitations. The summary of evidence is confined to published studies in Chinese and English, excluding articles in other languages. Despite efforts to conduct a comprehensive literature search, there is a possibility of missing relevant evidence in non-English languages. The current body of evidence on prehabilitation primarily consists of original and secondary studies on preoperative intervention measures, with a limited availability of guidelines and systematic reviews. As the field evolves, ongoing updates and enrichments of the evidence base are anticipated.

Conclusions

By employing evidence-based methods, this study summarized 41 pieces of the best evidence for prehabilitation management in NSCLC patients from eight crucial perspectives, including multidisciplinary team, appropriate population, prehabilitation mode, timing of prehabilitation, prehabilitation assessment, prehabilitation content, quality control, and effectiveness evaluation. This comprehensive overview serves as an evidence-based foundation for medical professionals engaging in prehabilitation implementation. While existing evidence supports preoperative prehabilitation in NSCLC patients, the overall body of evidence, particularly at higher levels, remains limited. To address this gap, future research should focus on high-quality translational and practical research, which can perform multicenter and large-sample prehabilitation intervention research or use medical research council (MRC) and other theoretical frameworks to guide intervention design, help support personalized and collaborative prehabilitation plans, and provide a reference for prehabilitation management and practice of NSCLC patients.

Ethics statement

Not required.

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CRediT authorship contribution statement

Wenfang Wu: designed the study, searched, collected, and analyzed the data, provided detailed data arrangement, and wrote the manuscript. **Huayan Li**: searched, collected, and analyzed the data, revised the manuscript. **Rongrong Fan**: supervised the project and revised the manuscript. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

The data that support the findings of this study are available from the corresponding author, Rongrong Fan, upon reasonable request.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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