

# The impact of lung surgery, with or without (neo-)adjuvant therapy, on physical functioning in patients with nonsmall cell lung cancer: a scoping review

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The physical functioning of patients with NSCLC tends to deteriorate after lung surgery. While the impact on ICF categories of "body function" and "activity" have been described to some depth, insights into the impact on "participation" are lacking. https://bit.ly/4hloppV

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Abstract

*Background* Patients with early stage (I–IIIA) nonsmall cell lung cancer (NSCLC) are typically treated *via* surgery, often accompanied by (neo-)adjuvant therapy. These interventions impose a significant burden on patients and potentially impact their physical functioning (PF). The impact on PF remains uncertain and existing evidence has not yet been systematically outlined.

*Objective* This scoping review aimed to synthesise evidence concerning the effects of lung surgery, with or without (neo-)adjuvant therapy, on the PF of patients with NSCLC.

*Methods* PubMed, Web of Science and Cochrane databases were systematically searched from inception until 1 July 2023. A comprehensive framework based on the International Classification of Functioning, Disability, and Health was used to define various aspects of PF. Longitudinal studies, reporting PF prior to and after NSCLC treatment, and cross-sectional studies reporting PF after treatment were included.

*Results* 85 included studies assessed the effects of surgery with (n=7) or without (n=78) (neo-) adjuvant therapy on body function (n=29), activity (n=67) and/or participation (n=15). 98% of reported outcomes within the longitudinal studies indicate a decline in PF, with 52% demonstrating significant deteriorations, with follow-up times ranging from immediately post-operative up to 1 year after treatment. Cross-sectional studies show impaired PF in 71% of reported outcomes.

*Conclusion* PF of patients with NSCLC tends to deteriorate following lung surgery, irrespective of additional (neo-)adjuvant therapy. While the negative impact of lung surgery on ICF categories of "body function" and "activity" have been described to some depth, insights into the impact on "participation" are lacking.

# Introduction

Lung cancer is the leading cause of cancer-related death worldwide, both in men and women [1–3]. According to the World Health Organization, lung cancer accounts for 2.2 million new cases annually, representing 11.7% of all cancer cases, and 1.8 million deaths, representing approximately one-fifth of all cancer-related deaths [1, 3, 4]. Nonsmall cell lung cancer (NSCLC) is the most common subtype of lung cancer, comprising approximately 85% of all cases [5]. A significant proportion of these patients (39%) are diagnosed with early-stage NSCLC (I–IIIA) [5]. Surgery is the preferred treatment option for early-stage

NSCLC in fit patients without contraindications in lung function and cardiac health, and with tumours deemed resectable in terms of pulmonary and cardiac functionality [5]. While surgery carries risks inherent to any surgical procedure, advances in surgical techniques and perioperative care have significantly improved outcomes, allowing patients to experience extended survival and improved quality of life post-surgery [6]. Often, surgical interventions are accompanied by (neo-)adjuvant therapy such as chemotherapy, radiotherapy and/or immunotherapy [7].

Surgery with or without (neo-)adjuvant therapy is likely to have a negative impact on physical functioning (PF), including exercise capacity and activities of daily living [8]. However, the precise impact of different treatment strategies on different dimensions of PF has not yet been systematically summarised. This information is crucial to design optimal nonpharmacological strategies (*e.g.*, pulmonary rehabilitation) to counteract these complications. Theoretical models such as the International Classification of Functioning, Disability, and Health (ICF) [9] offer a valuable framework to investigate and describe the impact of cancer treatment on the entire spectrum of PF. This classification comprises three categories of health condition, as follows: 1) bodily function or structure (impairment); 2) activities (limitation); and 3) participation (restriction).

Hence, this scoping review aims to systematically summarise the existing scientific literature investigating the impact of lung surgery, with or without (neo-)adjuvant therapy, on different aspects of PF in patients with NSCLC, utilising the ICF framework as a guiding structure.

#### Methods

This review followed the updated methodological framework to conduct scoping reviews proposed by PETERS *et al.* [10] and is reported according to the Preferred Reporting Items for Systematic reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR) checklist guidelines [11].

# Selection criteria

Studies were included if they met the following criteria: 1) involved patients diagnosed with NSCLC, who underwent surgery with or without (neo-)adjuvant therapy (chemo-, radio- and/or immunotherapy); 2) included at least one type of PF assessment at baseline and after NSCLC treatment or solely after treatment, with long-term follow-up periods allowed; 3) were randomised controlled trials (including a control group receiving standard care, these data were used in the current work), observational studies or case series (with a sample size greater than 10); and 4) were published in English.

## Search strategy and screening

Two researchers (S.H. and E.A.) conducted a systematic electronic literature search of the PubMed, Web of Science and Cochrane databases from inception until 1 July 2023. The comprehensive search strategy is presented in table S1. Identified references were managed using EndNote X9, an electronic library, where duplicates were identified and removed. Further screening of articles was conducted using Covidence®, an online systematic review software (Veritas Health Innovation, Melbourne, Australia; available at www. covidence.org), by four researchers (S.H., E.A., D.C. and K.Q.). The screening of titles and abstracts followed a conservative approach, excluding only studies that clearly did not meet the criteria. Full-text screening was independently conducted by two researchers (S.H. and E.A.) and any discrepancies were resolved through consensus-based discussion. Authors of studies were contacted *via* e-mail if no full text was available.

### Data extraction

A customised data collection tool in Covidence® and a data extraction table in Microsoft® Excel (Microsoft, Redmond, Washington, USA) were developed to extract the most relevant information from the included studies and facilitate their subsequent analysis and interpretation. S.H. and E.A. conducted the data extraction. A structured table in the supplementary material (table S2) includes details such as author information, publication year, country, study design, sample size, baseline characteristics (age, sex, type and stage of NSCLC, and treatment specifics), assessments of PF (tools used and timing; in cases of multiple post-treatment assessments, only the first assessment was extracted and described) and primary results. Authors of studies where no statistical analysis of the relevant data was presented in the results were contacted *via* e-mail.

# Representation of results

The results are organised according to the ICF classification, treatment type and timing of assessment. First, results are presented in accordance with the subclassification of ICF [9, 12]. Various measures pertaining to body function, activity and participation relevant for patients with NSCLC were incorporated.

Second, studies were categorised based on treatment type into "surgery" or "surgery with (neo-)adjuvant treatment". Studies where more than 30% of the included sample received both surgery and (neo-)adjuvant therapy are classified under "surgery with (neo-)adjuvant therapy". Further, results are categorised based on timing of assessment into "before *versus* after treatment" or "after treatment". After treatment, impairments or limitations are defined if outcomes are lower than 80% of their predicted values or if the study defined the outcome as impaired. A comprehensive overview of the used classifications is included in table S3. Lastly, a subgroup analysis based on treatment type was performed. Studies were categorised as either minimally invasive (video-assisted thoracic surgery (VATS) or robotic-assisted thoracoscopic surgery (RATS)), or invasive procedures (traditional thoracotomy), with studies that combine both approaches excluded from the analysis. A summary of this analysis is provided in the supplementary material (figures S1 and S2).

#### Results

#### Search results

The initial literature search yielded a total of 12 867 records, which was reduced to 12 229 after elimination of duplicates. Among these, 11 795 records were excluded during the title and abstract screening phase. Subsequently, 434 remaining articles underwent full-text screening, resulting in the inclusion of 85 articles for this scoping review. The screening process is visually depicted in the flowchart (figure 1).

# General characteristics

The 85 included studies, conducted between 1987 and 2023, assessed the effects of surgery with (n=7) or without (n=78) (neo-)adjuvant therapy on body function (n=32), activity (n=67) and/or participation (n=16) in patients with NSCLC.

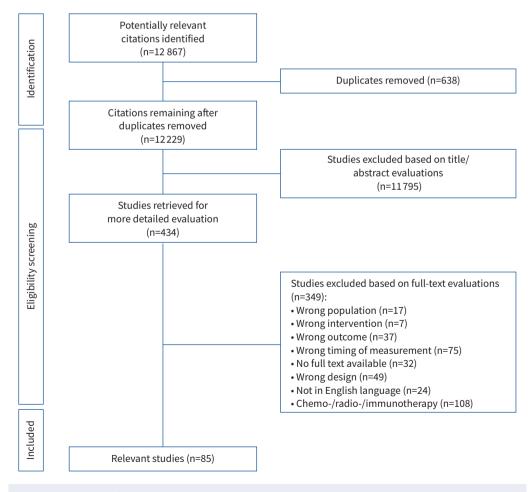


FIGURE 1 Flowchart of the search results.

# **ICF classification**

Various measures pertaining to body function, activity and participation were identified. An overview can be found in figure 2. A comprehensive summary of the measurement tools used, along with the number of studies included and their corresponding sample sizes, is provided in table S4.

An overview of the findings for different PF components can be found in figure 3 (before- *versus* after-treatment measurement) and figure 4 (only after-treatment measurement). For a detailed outline of the general characteristics of the included studies, please refer to table S2. The subgroup analysis based on treatment type can be found in figures S1 and S2.

### **Body function**

Components of PF measurements that were included in the ICF category "body function" (n=29) are body composition (n=10), peripheral muscle function (n=14) and respiratory muscle function (n=9).

#### Surgery

# Before versus after treatment

20 studies focused on body function outcomes, with follow-up ranging from post-operative day 2 up to 1 year post-surgery. Most research is available on peripheral muscle function (n=9) [13–21] and respiratory muscle function (n=8) [16, 17, 22–27]. All studies investigating quadriceps muscle function (n=8) [13–20] found a deterioration (of which five statistically significant [16–20]), ranging from -1.6% to -27.0%. Of the three studies investigating handgrip strength [18–20], two studies concluded a statistically significant deterioration overall [18, 20] and one study only demonstrated a significant deterioration in the group with a high risk of developing postoperative pulmonary complications [19]. Bicep muscle strength [21] and upper limb endurance [19] were only investigated in one study, concluding a statistically significant deterioration for both measurements. For maximal inspiratory pressure (n=8) [16, 17, 22–27], all studies showed a deterioration, ranging from -1.2% to -29.3%. Of these, two studies were statistically significant

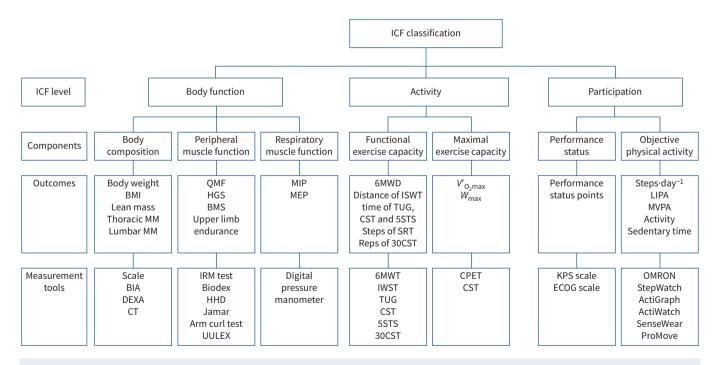


FIGURE 2 Flowchart of the International Classification of Functioning, Disability, and Health (ICF) classification and outcome measures. 5STS: 5-sit-to-stand test; 6MWD: 6-min walk distance; 6MWT: 6-min walk test; BIA: bioelectrical impedance analysis; BMI: body mass index; CPET: cardiopulmonary exercise testing; CST: chair stand test; CT: computed tomography; DEXA: dual-energy X-ray absorptiometry; ECOG: Eastern Cooperative Oncology Group performance status; HGS: hand grip strength; ISWT: incremental shuttle walk test; KPS: Karnofsky performance status; LIPA: light-intensity physical activity; MM: muscle mass; MEP: maximal expiratory pressure; MIP: maximal inspiratory pressure; MVPA: moderate-to-vigorous physical activity; QMF: quadriceps muscle force; SRT: stair run test; TUG: timed up-and-go test; UULEX: Upper-Body Ultraportable Exercise; V'<sub>O,max</sub>: maximal oxygen uptake; W<sub>max</sub>: maximal work rate.

Study outcomes	Surgery	Surgery + (neo-)adjuvant
Body function		
Body composition		
BW (kg)	0/2	
Body mass index (kg·m⁻²)		0/1
Muscle cross-sectional area (cm <sup>2</sup> )		1/1
Thoracic muscle mass (cm <sup>3</sup> ; cm <sup>2</sup> ·height <sup>-1</sup> )	1/1	
Lumbar muscle mass (cm <sup>3</sup> ; cm <sup>2</sup> ·m <sup>-2</sup> )	0/2	
Peripheral muscle function		
Quadriceps function (Nm; kg; Kgf; Kgf·kg <sup>-1</sup> ;	5/8	1/1
%BW; Nm·kg⁻¹; degrees)		
Handgrip strength (kg)	2.5/3	
Biceps curl (reps)	1/1	
Unsupported upper limb exercise (s)	1/1	
Shoulder range of motion (degrees)	1/1	
Respiratory muscle function		
Maximal inspiratory pressure (cmH <sub>2</sub> O)	3/8	
Maximal expiratory pressure (cmH <sub>2</sub> O)	2.5/8	
Activity		
Functional exercise capacity	0/20	1/2
6-min walk distance (m)	8/28	1/2
Incremental shuttle walk distance (m)	1/2	
Timed up-and-go test (s)	2/2	
Timed stair climb test (s)	2/4	
Five sit-to-stand reps (s)	1/1	
30-s chair–stand test (reps)	2/2	
Maximal exercise capacity	10 5/10	
Maximal oxygen consumption (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	12.5/19	
Maximal work rate (W)	9/11	0/1
Participation		
Performance status		
Karnofsky performance status (points)	1/1	
Eastern Cooperative Oncology Group (points)	0/1	
Objectively measured physical activity		
Daily total steps (steps ·day <sup>−1</sup> )	0/2	
Light-intensity activity (min∙day <sup>−1</sup> )	1/2	1/1
Moderate-to-vigorous intensity activity (min·day⁻¹)	1/1	1/1
Total activity (min·day⁻¹)	2/3	1/1
Time of aerobic activity (min∙day <sup>-1</sup> )	0/1	
Daily walked distance (min·day <sup>−1</sup> )	0/1	
Sedentary time (min·day <sup>-1</sup> )	0/1	1/1
Significant Nonsignificant No p-value	No p-value No	nsignificant Significant
improvement improvement improvement		

FIGURE 3 Physical functioning components before *versus* after treatment. Note: the fractions give the number of significant deteriorations divided by the total. BW: body weight; Kgf: kilogram-force; rep: repetition

[17, 27] and two studies only showed a significant deterioration in the conventional posterolateral thoracotomy group [16] and the wedge resection group [26]. For maximal expiratory pressure (n=8) [16, 17, 22–27], seven studies showed a deterioration [16, 17, 22–25, 27], ranging from –2.9 to –21.0%. Of these, two were statistically significant [17, 27] and one study only showed a significant deterioration in the conventional posterolateral thoracotomy group [16]. Within research on body composition (n=5) [28–32], thoracic muscle mass was only investigated in one study, concluding a statistically significant

Study outcomes	Surgery	Surgery + (neo-)adjuvant
Body function		
Body composition		
Body mass index (kg·m⁻²)	1/2	2
Lean mass (kg/%)		1/1
Peripheral muscle function		
Quadriceps function (% pred)	1/3	B 1/1
Handgrip strength (kg)	0/1	. 1/1
Respiratory muscle function		
Maximal inspiratory pressure (cmH <sub>2</sub> O )	1/1	L
Maximal expiratory pressure (cmH <sub>2</sub> O )	1/1	L
Activity		
Functional exercise capacity		
6-min walk distance (m)	3/5	5
Timed up-and-go test (s)	1/1	L
Stair run test (steps)		1/1
30-s chair–stand test (reps)		1/1
Gait (% BESTest)	1/1	
Balance (GAITRite)	1/1	
Maximal exercise capacity		
Maximal oxygen consumption (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	4/4	ł
Maximal work rate (W)	3/3	3
Participation		
Performance status		
Karnofsky performance status (points)	1/1	L
Eastern Cooperative Oncology Group (points)	0/1	L
Objectively measured physical activity		
Daily total steps (steps·day⁻¹)	4/5	5
Light-intensity activity (min·day <sup>−1</sup> )	3/4	ł.
Moderate-to-vigorous intensity activity (min·day <sup>-1</sup> )	4/4	ł
Total activity (min·day⁻¹)	1/1	L
Sedentary time (min·day <sup>−1</sup> )	4/4	ł
Not impaired	Impaired	

**FIGURE 4** Physical functioning components after treatment. Note: the fractions give the number of impaired outcomes divided by the total. rep: repetition.

deterioration [29]. Lumbar muscle mass was investigated in two studies, both concluding a deterioration (without specified p-value) [30, 31]. Two studies investigated body weight [28, 32], both concluding an increase of which one is statistically significant [28].

In summary, 91% (32/35 results) of the results indicate a deterioration of body function outcomes, with 49% (17/35 results) demonstrating significant deteriorations. 9% (3/35 results) found an improvement.

# After treatment

Six studies focused on body function outcomes, ranging from post-operative day 1 up to 1 year after surgery. Within body composition (n=2) [32, 33], body mass index is investigated in those two studies [32, 33], of which one study found an impairment [32]. Within peripheral muscle function (n=3) [34–36], quadriceps muscle function is investigated in three studies [34–36], of which one study found an impairment [36]. Handgrip strength is investigated in one study and found no impairment [34]. Within respiratory muscle function (n=1) [37], maximal inspiratory pressure and maximal expiratory pressure were only investigated in one study [37], concluding an impairments in both.

In summary, 50% (4/8) of the results found an impairment of body function outcomes after surgery.

# Surgery with (neo-)adjuvant therapy

# Before versus after treatment

Two studies focused on body function outcomes, ranging from post-operative day 1 up to 4-6 weeks after treatment, with research on body composition (n=2) [38, 39] and peripheral muscle function (n=1) [38]. Body mass index is only investigated in one study, concluding a deterioration (without a specified p-value) [39]. One study focused on muscle cross-sectional area and quadriceps muscle function and reported a statistically significant deterioration in both outcomes [38].

In summary, 100% (3/3 results) of the results indicate a deterioration of body function outcomes, with 67% (2/3 results) demonstrating significant deteriorations.

#### After treatment

One study focused on body function outcomes, 4-6 weeks after treatment, in body composition and peripheral muscle function (n=1) [40]. This study found no impairment in lean mass, quadriceps muscle function and handgrip strength.

## Activity

Components of PF measurements that were included in the ICF category "activity" (n=67) are functional exercise capacity (n=46) and maximal exercise capacity (n=27).

### Surgery

#### Before versus after treatment

52 studies focused on activity outcomes, ranging from post-operative day 1 up to 1 year after surgery. Most research is available on functional exercise capacity (n=35) [13–15, 17–21, 24, 25, 27, 41–64]. For the 6-min walked distance (n=28) [13, 15, 17, 18, 20, 21, 24, 25, 27, 41–59], all studies showed a deterioration when comparing post- to pre-measurements, of which eight were statistically significant [13, 15, 17, 18, 20, 21, 27, 59], ranging from -1.9% to -34.1%. The four studies investigating time of the stair-climb test [58, 62–64] all found a deterioration, of which two were statistically significant [58, 64]. Two studies investigated the repetitions of the 30-s chair–stand test, and showed both a statistically significant deterioration [21, 61]. Two studies investigated the walked distance of the incremental shuttle walk test and both showed a deterioration [14, 60], of which one is statistically significant [60]. Results of the timed up-and-go and five-repetitions sit-to-stand tests were only investigated in two [20, 61] and one [19] studies, respectively, all concluding a statistically significant deterioration.

Research on maximal exercise capacity (n=21) all found a deterioration. For maximal oxygen consumption (n=19) [20, 22, 26, 40, 62–76], 12 studies showed a statistically significant deterioration [22, 40, 64, 68–76] and one study only demonstrated a significant deterioration in the group with nonwedge resection [26] ranging from -11.9% to -30.0%. For maximal work rate (n=11) [16, 22, 26, 64, 66–70, 72, 77], nine studies showed a statistically significant deterioration [16, 22, 26, 64, 68–70, 72, 77], ranging from -12.4% to -27.0%.

In summary, 100% (69/69 results) of the results indicate a deterioration of activity outcomes, with 55% (38/69 results) demonstrating significant deteriorations.

#### After treatment

Nine studies focused on activity outcomes, ranging from post-operative day 1 up to 1 year after surgery. Within functional exercise capacity (n=8) [32, 34–36, 39, 78–80], five studies investigated 6-min walked distance [34, 35, 78–80], of which three found an impairment [34, 35, 80]. All other studies reported results that were impaired in time of timed up and go (n=1) [32], gait (n=1) [36] and balance (n=1) [36]. Within maximal exercise capacity (n=4) [34, 35, 78, 81], all studies reported impaired results in maximal oxygen consumption (n=4) [34, 35, 78, 81] and maximal work rate (n=3) [34, 35, 78]. In summary, 87% (13/15 results) of the results found an impairment in activity outcomes.

# Surgery with (neo-)adjuvant therapy

# Before versus after treatment

Four studies focused on activity outcomes, from post-operative day 1 up to 8–10 weeks after surgery. Within functional exercise capacity (n=2) [82, 83], two studies investigating 6-min walked distance found both a deterioration [82, 83], of which one was statistically significant [83]. Within maximal exercise capacity (n=2) [39, 84], maximal oxygen consumption (n=2) [39, 84] and maximal work rate (n=1) [84] all showed a deterioration (without a specified p-value).

In summary, 100% (5/5 results) of the results indicate a deterioration of body function outcomes, with 20% (1/5 results) demonstrating a significant deterioration.

#### After treatment

One study focused on activity outcomes, 4–6 weeks post-treatment, in functional exercise capacity (n=1) [39]. This study found no impairment in the number of steps in the stair run test and repetitions of the 30-s chair–stand test.

#### Participation

Components of PF measurements that were included in the ICF category "participation" (n=15) are performance status (n=4) and objectively measured physical activity (n=11).

#### Surgery

#### Before versus after treatment

Seven studies focused on participation outcomes, from post-operative day 5 up to 2 months post-surgery. Objectively measured physical activity is investigated in five studies [14, 85–88]. Light-intensity physical activity is investigated in two studies, both showing a deterioration [87, 88], of which one is statistically significant [87]. Moderate-to-vigorous-intensity physical activity is only investigated in one study, concluding a statistically significant deterioration [87]. For total activity (n=3) [14, 87, 88], all studies found a deterioration, of which two were statistically significant [87, 88]. Sedentary time is only investigated in one study, showing a statistically nonsignificant deterioration [88]. Research on daily total steps (n=2) [85, 86], time of aerobic activity (n=1) [85] and daily walked distance (n=1) [85] all concluded a deterioration, without a specified p-value.

Within research on performance status (n=2) [27, 33], Karnofsky performance status and Eastern Cooperative Oncology Group (ECOG) score were both investigated in only one study, concluding a statistically significant deterioration [27] and a deterioration without a specified p-value [33] respectively.

In summary, 100% (13/13) of the results indicate a deterioration of participation outcomes, with 38% (5/13 results) demonstrating significant deteriorations.

### After treatment

Seven studies focused on participation outcomes, ranging from post-operative day 1 up to 3 months post-treatment. Within research on objectively measured physical activity (n=5) [89–93], a limitation was found in moderate-to-vigorous physical activity (n=4) [89–92], total activity (n=1) [89] and sedentary time (n=4) [89–92]. Of the five studies investigating daily total steps [89–93], four studies showed a low physical activity [89, 91–93]. Light-intensity physical activity is investigated in four studies [89–92], of which three found a limitation [89, 90, 92].

Within research on performance status (n=2) [32, 33], Karnofsky performance status and ECOG were both investigated in one study, showing an impairment [32] and no impairment [33].

In summary, 85% (17/20) of the results found an impairment of participation outcomes.

#### Surgery with (neo-)adjuvant therapy

# Before versus after treatment

One study focused on participation outcomes, 1 month post-treatment, in objectively measured physical activity [82]. This study found a statistically significant deterioration in light-intensity physical activity, moderate-to-vigorous-intensity physical activity, total activity and sedentary behaviour.

#### After treatment

No studies focusing on participation outcomes were found.

#### Discussion

This scoping review summarises the scientific literature investigating the impact of lung surgery with or without (neo-)adjuvant therapy on PF in patients with NSCLC.

The PF of patients with NSCLC tends to deteriorate following lung surgery, whether or not (neo-) adjuvant treatment is administered. The vast majority of studies showed a decline in many of the reported outcomes, across several ICF domains, from immediately post-operative up to 1 year after treatment.

Body weight is the only component showing a significant increase following surgery. However, this increase might be a sign of the development of oedema [28]. Weight gain due to oedema is a known complication of major surgical procedures, with an incidence rate as high as 40% [28]. However, with the recent advances in endoscopic instruments and operative techniques, lung resection surgery has become less invasive and oedema is less likely to occur [28].

The timing of assessment varied substantially among the different papers. As time emerges as a crucial factor, an attempt was made to standardise the timing of assessment by selecting and representing the earliest measurement moment from each paper. While there is likely spontaneous recovery over time, uncertainty remains regarding the extent of this recovery [18]. For instance, EDVARDSEN *et al.* [39] noted an improvement in lean mass, handgrip strength, stair climb test and 30-s chair–stand test 25–27 weeks after lung surgery, compared to pre-surgery values.

In addition to the substantial variation in assessment timing, most studies focus on assessments that fall within one single subcategory of the ICF classification, complicating the assessment of the overall impact of surgery with or without (neo-)adjuvant treatment on total PF. Within assessments classified under the subcategory "body function", a differentiation can be made between body composition and muscle function. While body composition results remain unclear, both peripheral muscle function and respiratory muscle function demonstrate a decline following surgery with or without (neo-)adjuvant therapy. Assessments categorised in the subcategory of "activity" are predominant indicating a consistent negative impact of surgery with or without (neo-)adjuvant treatment on functional and maximal exercise capacity. There is a notable absence of objectively measured physical activity, falling under the subcategory of "participation". This gap hinders our ability to gain insight into the impact of treatment on the daily activities of patients and their involvement in life situations.

Similarly, only few studies have examined objectively measured physical activity levels after breast cancer surgery, concluding significantly decreased physical activity post-surgery [94]. Interestingly, based on self-report, patients with breast cancer had significantly lower total physical activity levels in the year prior to surgery compared to a reference population [95]. In addition, about 25% of colorectal cancer patients managed to increase their physical activity levels from diagnosis to 6 months post-surgery [96].

Additionally, few studies in this review investigate the potential additional impact of (neo-)adjuvant therapies on the PF of patients, as the majority of studies recruited patients undergoing surgery without (neo-)adjuvant therapy. However, adjuvant treatment has been recommended for patients in order to minimise the chance of postoperative recurrence and adjuvant chemotherapy has been associated with better overall survival [97]. The potential added burden of adjuvant treatment on PF requires further insight to guide physicians in making informed decisions regarding adjuvant therapies. In other cancer populations, the extent of change in PF varies depending on the treatment modalities used for (neo-)adjuvant therapy [98]. However, more high-quality studies are needed to further understand the impact of (neo-)adjuvant therapies [99].

A key limitation of this review is its broad and generic scope. First, several factors likely influence the impact of surgical procedures on PF, including the degree of surgery (pneumonectomy, lobectomy, segmentectomy and atypical resection), the extent of resection, time since the resection, age and comorbidities. A subgroup analysis was conducted based on the type of surgery (minimally invasive VATS or RATS), or more invasive (traditional thoracotomy), showing a similar impact on PF. In many results, statistical data is unavailable because these analyses were not performed in the original studies. It is also important to note that 98% of the findings point to a deterioration in PF, though not all are statistically significant. Therefore, the lack of statistical analyses or significance levels means this subgroup analysis does not alter the conclusions of the manuscript, as no additional details on the magnitude or significance of this deterioration can be provided. Further subanalyses could not be performed, largely due to the absence of detailed subgroup analyses and the heterogeneity of the included patient populations

Certain limitations also persist regarding the role of time since surgery. Time frames used to assess outcomes varied significantly across studies, with some assessing outcomes days post-surgery, while others spanned weeks, months or even up to a year. An attempt was made to standardise timing by selecting the earliest measurement moment from each paper, but the substantial heterogeneity and lack of detailed subsample data prevented a more detailed analysis based on time frames.

# Recommendations for clinical practice and future research

The impact of lung surgery, with or without (neo-)adjuvant therapy, on PF in patients with NSCLC is a complex interplay of surgical and medical interventions. While these treatments significantly improve

survival rates, they also pose challenges to physical well-being. In light of these challenges, there is a clear need for focus on nonmedical treatment of these patients. This scoping review reveals that 98% of the results demonstrate a decline over time and 71% show an impairment compared to reference values in PF following surgery, with or without (neo-)adjuvant therapy. This finding underscores the need for comprehensive rehabilitation strategies to optimise patient outcomes [100]. Pulmonary rehabilitation is imperative and plays a crucial role in restoring and maintaining PF [100]. Effective rehabilitation strategies are vital to mitigate the impact of surgery and (neo-)adjuvant therapy, enabling patients to regain and maintain optimal PF throughout their cancer journey [101]. Tailored rehabilitation plans should be designed to address the unique needs of each patient, considering the extent of surgery, the type of (neo-)adjuvant therapy and individual health status, as PF among NSCLC survivors is influenced by these factors.

Future research should focus on insights into the impact of lung surgery on the ICF subcategory "participation" and the additional impact of (neo-)adjuvant therapies on PF.

# Methodological considerations

A thorough systematic search and screening was performed, and the most well-established guideline for the conductance of scoping reviews (PRISMA-ScR) was followed. Nevertheless, several concepts have been used to define PF and numerous tools were designed to assess the different aspects of this comprehensive measure. To ensure clarity, this work followed a previously published assessment framework for PF [12].

The literature on this topic is markedly heterogeneous. The lack of detailed characteristics of the studied population is a challenge. Often, results are not presented separated when (neo-)adjuvant therapy is used, making it difficult to distinguish the specific effects of surgery and the effects of (neo-)adjuvant therapy on PF. As a result, there are only few findings available in this category "surgery with (neo-)adjuvant therapy". Also, there is no continuity in the timing of assessment, making comparisons of results challenging. There is a lack of consensus on outcome measures and measurement tools used for assessing PF. Therefore, to structure the results, they are organised according to the ICF classification and in case of multiple post-treatment assessments, only the earliest assessment has been extracted and described. However, as a consequence, the analysis of the effects of different NSCLC treatments on PF was found to be challenging due to this diversity. All these aspects have hampered results synthesis and the draw of more definitive conclusions.

Several of the included studies are randomised controlled trials, providing data for a control group receiving standard care. However, this setup posed challenges in relevant data extraction, as these studies primarily focused on within-group results. Furthermore, sample size is low in many studies.

# Conclusion

The PF of patients with NSCLC tends to deteriorate following lung surgery, whether or not (neo-)adjuvant treatment is administered, from immediately post-operative up to 1 year after treatment. While the negative impact of lung surgery on ICF categories of "body function" and "activity" have been described to some depth, insights into the impact on the "participation" subcategory are lacking.

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