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Original article

Associations between pretreatment nutritional assessments and treatment complications in patients with stage I-III non-small cell lung cancer: A systematic review

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SUMMARY

Background: Patients with stage I-III non-small cell lung cancer (NSCLC) are often nutritionally depleted and therefore at high-risk for treatment complications. Identifying these patients before the start of treatment is important to initiate preventive interventions for better treatment outcomes. This study aimed to evaluate which outcome variables of pretreatment nutritional assessments are associated with posttreatment complications in patients with stage I-III NSCLC, as well as to identify cut-off values for clinical risk stratification.

Methods: In this systematic review, PubMed, Embase, and Cinahl databases were searched for eligible studies published up to March 2021. Studies describing the association between pretreatment nutritional assessment and treatment complications in patients with NSCLC were included. Methodological quality of the included studies was assessed using the Newcastle–Ottawa Scale for cohort studies.

Results: A total of 23 studies were included, which merely focused on surgical treatment for NSCLC. Methodological quality was poor in thirteen studies (57%). Poor outcomes of body mass index, sarcopenia, serum albumin, controlling nutritional status, prognostic nutrition index, nutrition risk score, and (geriatric) nutrition risk index were associated with a higher risk for treatment complications. Cut-off values for pretreatment nutritional assessment were reported in a limited number of studies and were inconsistent.

Conclusion: Poor outcomes of pretreatment nutritional assessments are associated with a higher risk for posttreatment complications. Further research is needed on the ability of easy-to-use pretreatment nutritional assessments to accurately identify patients who are at high risk for treatment complications, as high-risk patients may benefit from pretreatment interventions to improve their nutritional status.

Abbreviations: **NSCLC**, Non-small cell lung cancer; **SBRT**, Stereotactic body radiation therapy; **PRISMA**, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **NOS**, Newcastle–Ottawa scale; **ROC**, Receiver operating characteristic; **AUC**, Area under the curve; **BMI**, Body mass index; **FFMI**, Fat free mass index; **NRS**, Nutrition risk screening; **CRP**, C-reactive protein; **PS-SGA**, Patient-generated subjective global assessment.

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1. Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide. Non-small cell lung cancer (NSCLC) constitutes the majority (85%) of lung cancers [1]. Surgery remains the best (curative) option for patients with stage I and II NSCLC and for selected patients with locally-advanced disease (stage IIIA). For inoperable patients with early-stage disease, stereotactic body radiation therapy (SBRT) is the advised treatment [2]. For patients with locally advanced stage NSCLC (40%), chemoradiotherapy is the standard treatment [2]. Despite the fact that generally the physically fit patients with a good performance status are advised for surgery, almost 40% of these surgical patients develop postoperative complications [3,4]. Patients with a higher risk for treatment-related complications are often characterized as aged ≥70 years, having tobacco-related comorbidity and/or cognitive impairment, being physically inactive and/or malnourished, and especially as having a low physiological reserve capacity (low aerobic fitness) [5,6].

The importance of an adequate nutritional status has been established in patients with cancer. It has been reported that malnutrition may decrease the response to cancer treatment [7], as well as that malnutrition is associated with poor quality of life and higher rates of treatment intolerance in patients with lung, esophagus, colon, liver, or pancreas cancer [8–11]. Patients with NSCLC are often nutritionally depleted and therefore at high risk for treatment complications [12]. Identification of malnutrition as soon as possible after diagnosis is recommended to identify patients who are at high risk for treatment complications and who therefore might benefit from pretreatment nutrition interventions. Nutritional screening is the process of assessing characteristics and risk factors that predispose a patient to malnourishment [13]. Many tools can be used to evaluate nutritional status. For example, a recent systematic review showed that the prognostic significance of nutritional status, measured with the mini nutritional assessment, was associated with treatment complications in patients with various types of cancer [14]. However, the large heterogeneity of included studies with respect to various types and stages of cancer, differences in anticancer therapy (chemotherapy and/or surgery), and differences in outcome measurements should be noticed when interpreting results [14]. Systematic evidence for the associations between outcomes of various nutritional assessments and treatment complications in patients with NSCLC is lacking. The aim of this systematic review was therefore to evaluate which outcome variables of pretreatment nutritional screening or nutritional assessments are associated with treatment complications in patients with stage I-III NSCLC, as well as to identify cut-off values for clinical risk stratification.

2. Methods

The Cochrane guidelines for systematic reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15] were followed. The study protocol was registered at PROSPERO (CRD42020220639).

2.1. Literature search

PubMed, Embase, and Cinahl databases were searched for eligible studies published up to March 2021. In addition, references from retrieved studies were screened. The search strategy contained a combination of controlled vocabulary (e.g., MeSH, EMTREE) and key word terms and phrases searched in titles, abstracts, and key word fields, as appropriate. Key terms included in the search strategy are non-small cell lung cancer combined with the various treatment options, pretreatment nutritional assessment, treatment complications, overall treatment time, and treatment mortality. Combinations of text words of the literature search are shown in Table 1.

2.2. Study selection

Prospective and retrospective cohort studies with adult patients undergoing treatment for stage I-III NSCLC who completed a pretreatment nutritional assessment and of whom treatment-related complications were recorded were included. All types of assessment methods for nutritional status (e.g., functional or biochemical tests, anthropometric measurements, questionnaires) were included. Studies primarily investigating the impact of prehabilitation or any structured exercise program on physical fitness before treatment, and studies describing long-term survival as outcome measure were excluded. Postoperative mortality (within 90 days) was included as an outcome measure. Conference papers, case series, case reports, opinion studies (non-original research), systematic reviews, and studies not published in English were also excluded. Two reviewers (M.V. and K.B.) independently screened titles and abstracts of studies obtained by the literature search. Assessment of full texts according to eligibility criteria was performed independently by these two reviewers. Any disagreements between reviewers were resolved through discussion and consensus. When no consensus was reached, a third party acted as an adjudicator (M.J).

2.3. Data extraction

Two authors (M.V. and K.B.) independently extracted data from each of the included studies by using a standardized extraction form. Information collected included the name of the first author, year of publication, type of cohort, sample size, age and sex of participants, used pretreatment nutritional screening and/or assessment, preselection method, follow-up period, outcome variables of treatment complications, measures for associations between outcomes of pretreatment nutritional screening and/or assessments and treatment complications, and cut-off values of pretreatment nutritional assessments. Outcome variables of treatment complications were categorized as overall complications of treatment, cardiac complications and pulmonary complications, length of hospital stay and unplanned hospital stay, or as mortality when mortality was separately identified as a complication. The classification used for treatment complications was reported when described in the included studies.

2.4. Quality assessment

The quality of the included studies was assessed using the Newcastle–Ottawa scale (NOS) [15]. Studies scoring 3 or 4 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome/exposure domain were defined as good-quality studies. Studies scoring 2 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome/exposure domain were defined as fair-quality studies. Studies scoring 0 or 1 stars in the selection domain, or scoring 0 stars in the comparability domain, or 0 or 1 stars in the outcome/exposure domain, were defined as low-quality studies [16]. Two investigators (M.V. and K.B.) independently assessed the quality of included studies. Discrepancies were resolved by consensus. When consensus was not reached, a third person acted as an adjudicator (M.J).

2.5. Data analyses

Associations between pretreatment nutritional assessment and treatment complications were interpreted as statistically significant

Table 1
Combinations of text words of the literature search according to the PECO-structure.

Databases[a]	Population	Exposure/comparator	Outcome
Embase, PubMed, Cinahl,	"Chemoradiotherapy"[Mesh] OR "Radiotherapy"[MeSH] OR radiation[tiab] OR radiotherap*[tiab] OR chemotherap*[tiab] OR radiochemotherap*[tiab] OR radio-chemotherap*[tiab] OR CHRT[tiab] OR chemoradiation[tiab] OR chemo-radiation[tiab] chemoradiotherapy[tiab] OR radiochemotherapy[tiab] OR radiochemotherapies[tiab] OR CHRT[tiab] OR "Pulmonary Surgical Procedures"[MeSH] OR "Pneumonectomy"[Mesh] OR "Thoracic Surgical Procedures"[MeSH] OR pulmonary-surgical-procedure*[tiab] OR lung-operation*[tiab] OR lung-resection*[tiab] OR lobectomy[tiab] OR lobectomies[tiab] OR segmentectomy[tiab] OR segmentectomies[tiab] OR resection*[tiab] OR surgery[tiab] OR surgic*[tiab] OR pneumonectomy[tiab] OR thoracic-surgical-procedure*[tiab] OR operable[tiab] AND "lung neoplasms"[MeSH Terms:NoExp] OR "Carcinoma, Non-Small-Cell Lung"[Mesh] OR lung-neoplasm*[tiab] OR lung-cancer*[tiab] OR pulmonary-cancer*[tiab] OR pulmonary-neoplasm*[tiab] OR cancer-of-the-lung*[tiab] OR cancers-of-the-lung*[tiab] OR non-small-cell-lung-carcinoma*[tiab] OR NSCLC[tiab] OR non-small-cell-lung-cancer*[tiab] OR lung-tum*[tiab] OR lung-malignanc*[tiab] OR lung-tumor[tiab] OR lung-tumour[tiab]	"Nutrition Assessment"[Mesh] OR nutrition-assessment*[tiab] OR nutritional-screening [tiab] OR nutritional-status[tiab] OR nutrition-disorders[tiab] OR PG-SGA[tiab] OR Patient-Generated-Subjective-Global-Assessment-Short-Form[tiab] OR nutriscore[tiab] OR malnutrition-screening-tool[tiab] OR nutritional-risk-screening[tiab] OR NRS-2002 [tiab] OR nutritional-risk-index[tiab] OR prognostic-inflammatory-and-nutritional-index[tiab] OR prognostic-nutritional-ind* [tiab] OR PNI[tiab] OR short-nutritional-assessment-questionnaire[tiab] OR SNAQ[tiab] OR general-nutritional-status-score[tiab] OR malnutritional-universal-screening-tool[tiab] OR MUST[tiab] OR Nottingham-screening-tool [tiab] OR malnutrition-screening-tool*[tiab] OR nutritional-screening-questionnaire[tiab] OR subjective-global-assessment[tiab] OR SGA [tiab] OR Nutritional-Appetite-Questionnaire [tiab] OR mini-nutritional-assessment[tiab] OR MNA[tiab] OR albumin[tiab] OR CRP-albumin-ratio[tiab] OR C-reactive-protein-albumin-ratio [tiab] OR CRP/ALB[tiab] OR CRP/ALB-ratio[tiab] OR serum-albumin[tiab] OR sarcopenia[tiab] OR CT-defined-sarcopenia[tiab] OR Nutrition*-Ind* [tiab] OR malnutrition-screening[tiab] OR "nutrition surveys"[MeSH Terms] OR ("nutrition"[tiab] OR "surveys"[tiab]) OR ("nutrition"[tiab] OR "survey"[tiab]) OR Nutrition-survey[tiab] OR nutrition-survey* [tiab]	"complications"[MeSH Subheading] OR complication*[tiab] OR associated-conditions [tiab] OR coexistent-disease[tiab] OR toxicit* [tiab] OR adverse-effects[tiab] OR side-effects [tiab] OR "mortality"[MeSH Terms] OR mortality[tiab] OR mortalities[tiab] OR "mortality"[MeSH Subheading] OR "death"[MeSH Terms] OR death*[tiab] OR fatal* [tiab] OR "hospitalization"[MeSH Terms] OR hospitalization[tiab] OR hospitalisation[tiab] OR "length of stay"[MeSH Terms] OR length-of-stay [tiab] OR length-of-hospital-stay[tiab] OR "patient discharge"[MeSH Terms] OR patient-discharge[tiab] OR dose-reduction[tiab] OR dose-modification*[tiab] OR "time to treatment"[MeSH Terms] OR time-to-treatment [tiab] OR treatment-delay[tiab] OR completion-of-treatment[tiab] OR early-termination[tiab] OR withdraw*[tiab] OR health-outcomes[tiab] OR risk-stratification[tiab] OR stratifications [tiab] OR risk-stratification[tiab] OR pulmonary-function[tiab]

[a] Search presented for PubMed only: the search strategy has been adjusted for searching in the other databases.

when p-values were <0.05. Cut-off values for outcomes of pretreatment nutritional assessments for an increased risk for treatment complications were presented. Receiver operating characteristic (ROC) curves, including area under the curve (AUC), sensitivity and specificity, and/or odds ratios were also determined in the included studies.

3. Results

3.1. Study characteristics

3.1.1. Study selection

Initially, the literature search identified 1485 studies, of which 23 were eventually included. A flow diagram for the selection of studies is shown in Fig. 1. An overview of the characteristics of the 23 studies is shown in Table 2. Seventeen (73%) were retrospective observational studies [17–33] and six (26%) had a prospective observational design [34–39]. The oldest publication dated from 2001 [36] and the most recent publications from 2020 [21,22,26,29]. Median sample size was 228 patients (ranging from 52 to 1011, with a total of 7522) and the mean age of the included patients ranged between 56 and 79 years. In all studies, the intention was to include only curative patients. Ultimately, ten studies (43%) included patients with stage I-IV NSCLC [17–21,34–38], nine studies (39%) stage I-III NSCLC [22–28,32,33], two studies (9%) stage I-II NSCLC [29,30], one study (4%) stage I NSCLC [31], and in one study (4%) the included NSCLC stage was unclear [39]. With the exception of one study [30], cancer treatment consisted at least of surgery (96%). In one of these studies [35], adjuvant chemotherapy and chemoradiotherapy was applied, and in one study [24] patients also underwent adjuvant chemotherapy. In one study [30], cancer treatment consisted of SBRT. One or more of the following surgical techniques were used in 22 of the included studies [17–29,31–39]: pneumonectomy, lobectomy, segmentectomy, bilobectomy, wedge resection, and thoracotomy. Preselection of participants by means of forced expiratory volume in 1 s, carbon monoxide lung diffusion capacity, or oxygen uptake at peak exercise was used in two studies [21,37] (9%) and preselection of participants by means of age in three studies [17,32,33] (13%).

3.1.2. Classification of treatment complications

An association between poorer outcomes of pretreatment nutrition tests and a higher risk for treatment complications and/or treatment mortality was found in all studies. The included studies did not provide information about which complications occurred most frequently stratified by type of surgery. The most frequently reported overall complications were pneumonia (in 65% of the studies), lobar atelectasis (bronchoscopy required) (57%), myocardial infarction (57%), wound infection (52%), air leak (52%), bronchopleural fistula (52%), acute respiratory distress syndrome (43%), acute renal failure (43%), and mortality (26%). In three studies (13%), treatment complications were graded on severity using the Clavien-Dindo classification system [40]. In the other studies, no classification of complications was described, and in three studies [17,34,36] (13%), treatment mortality was reported separately.

3.1.3. Quality assessment

The results of the quality assessment are depicted in Table 3. In two studies there was no consensus, because the assessment of outcome domain was interpreted differently between the reviewers. These discrepancies were resolved by discussion with the adjudicator. In thirteen studies (57%), there was a poor methodological quality, whereas ten studies (43%) were ranked as having a good methodological quality. A poor score on the NOS was often the

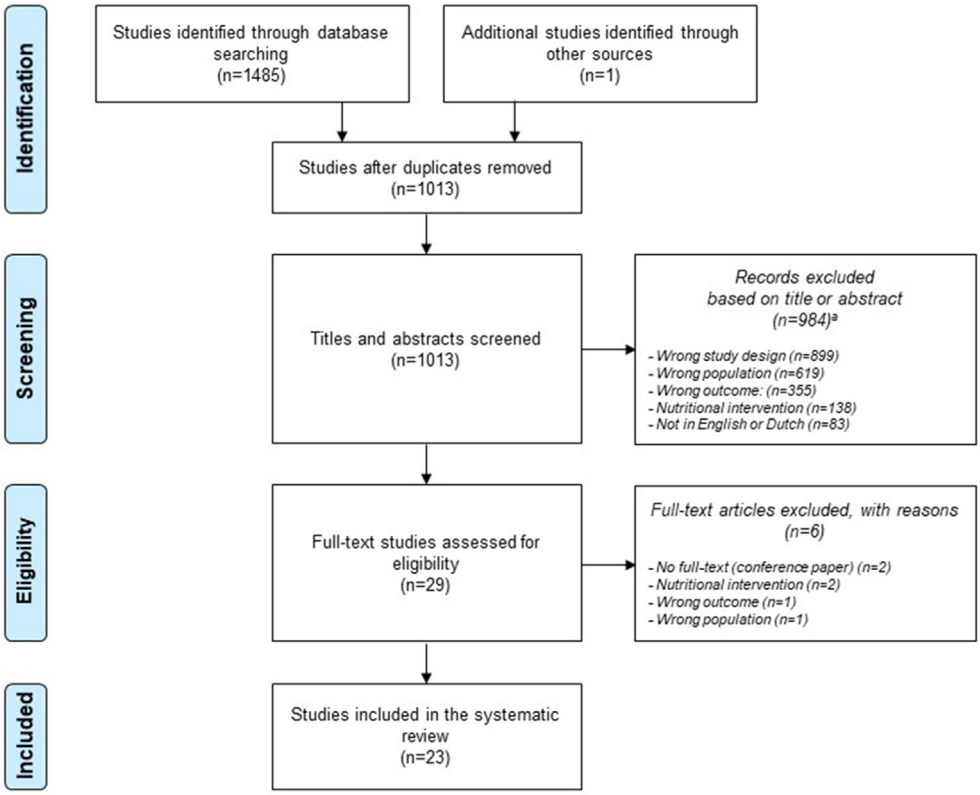

Fig. 1. PRISMA flow diagram displaying the selection of studies and reasons for exclusion. [a]: multiple reasons are possible.

result of the lack of a clear description of the outcome of interest at the start of the study (13/23, 57%) and an unclear description on the comparability of cases in the cohorts (12/23, 52%).

3.2. Associations between pretreatment nutritional assessments and treatment complications

Associations between pretreatment nutritional assessments and treatment complications and treatment mortality are presented in Table 4. When comparing results from univariable analyses and multivariable analyses: although some effect sizes were somewhat larger in univariable analyses compared to multivariable analyses, no clear differences in effect sizes or significance were seen.

3.2.1. Pretreatment assessment of anthropometry and body composition tests

Seven studies [17,20,21,26,33,36,37] (30%) assessed the ability of pretreatment anthropometry and body composition to predict the risk for treatment complications, and in two studies [17,36] the risk for treatment mortality was evaluated as well. A body mass index (BMI) <18.5 kg/m^2 was associated with a higher risk for treatment complications in two of seven studies [17,26] and a lower BMI in another two studies [33,36] (25%) and with a higher risk for pretreatment mortality in two of two studies [17,36] (100%). In the only study that looked at fat free mass index (FFMI), a lower FFMI was associated with a higher risk for treatment complications [36].

3.2.2. Pretreatment assessment of sarcopenia

Pretreatment assessment of sarcopenia was performed in seven studies [18,21,23,27,31,32,36] (30%), in which different protocols were used. The third lumbar vertebra muscle mass index, psoas muscle mass index, thoracic skeletal muscle area, bone-free midarm muscle area, subscapular skinfold thickness, and triceps skinfold thickness were used to assess the presence of sarcopenia. A low psoas muscle mass index (males: <3.70 cm^2/m^2, females: <2.50 cm^2/m^2 [32] and males: <6.36 cm^2/m^2, females: <3.92 cm^2/m^2 [23]) in two of three studies (66.7%), a lower thoracic skeletal muscle area and a lower bone-free midarm muscle area in one study [21] (100%), and a lower subscapular skinfold thickness and a lower triceps skinfold thickness in one study [36] (100%) were associated with a higher risk of treatment complications.

3.2.3. Pretreatment assessment of a combination of multiple nutritional parameters

All five studies [26,34,35,37,38] (22%) reported an association between the ability of a combination of multiple nutritional parameters and the risk for treatment complications, whereas the risk for treatment mortality was also evaluated in one study [34]. The nutrition risk screening (NRS) 2002 is a malnutrition risk assessment tool that evaluates common signs of nutritional status (weight loss, body mass index, and dietary intake) and a score >2 was found to be associated with treatment complications in the only study that looked at the NRS [35]. In the only study that looked a combination of BMI, serum albumin, and transthyretin; a low BMI, high serum albumin, and high transthyretin was associated with a higher risk for treatment complications and treatment mortality [34]. In another study [38], the combination of low BMI, high serum albumin, and weight loss was associated with a high risk for treatment complications. In the only study that looked at the geriatric nutritional risk index, a score $\leq$101 was associated with a higher risk of treatment complications [26]. In the only study that looked at the nutritional risk index, a score <100 and a higher score on the NRI were associated with a higher risk for treatment complications [37].

Table 2
Characteristics of included studies that evaluated the association between pretreatment nutritional assessments and posttreatment complications and posttreatment mortality.

First author	Year of publication	Country	Type of observational cohort	Stage of disease	Sample size (n)	Age (years) mean (range)	Male %	Pretreatment nutritional assessments[a]	Type of treatment
Bagan [34]	2013	France	Prospective	I-IV	86	62	86	BMI, serum albumin, transthyretin	P
Bianchi [39]	2006	Brazil	Prospective	NR	71	56 (19–77)	70	BMI, serum albumin	B, L, P, S, WR
Fiorelli [17]	2014	Italy	Retrospective	I-IV	117	75	80	BMI, serum albumin, serum transferrin	P
Illa [35]	2015	Czech	Prospective	I-IV	188	65	70	NRS 2002	S, aCT, aRT, CT, CHRT
Jagoe [36]	2001	UK	Prospective	I-IV	52	64	67	BMI, FFMI, sarcopenia, serum albumin	B, L, P, S
Kawaguchi [32]	2019	Japan	Retrospective	I-III	173	79	70	PNI	L
Kim [18]	2018	Korea	Retrospective	I-IV	272	63 (33–81)	60	Sarcopenia	B, L, P, T
Lee [22]	2019	Korea	Retrospective	I-II	236	66	42	Sarcopenia, Sarcopenia	L, S
Lee [29]	2020	Korea	Retrospective	I-III	922	64	57	CONUT	L, S, WR, B, P
Li [19]	2018	China	Retrospective	I-IV	533	62	58	Serum albumin	L, S
Madariaga [21]	2020	USA	Retrospective	I-IV	130	61	57	BMI, sarcopenia	P
Nakada [31]	2019	Japan	Retrospective	I	173	68	57	Sarcopenia, PNI, serum albumin	L
Nakamura [23]	2018	Japan	Retrospective	I-III	228	70	86	Sarcopenia	L
Okada [24]	2017	Japan	Retrospective	I-III	248	67	64	PNI	L, aCT
Okada [20]	2018	Japan	Retrospective	I-IV	515	71	63	BMI, PNI	L
Park [25]	2019	Korea	Retrospective	I-III	1011	NR	91	PNI	T
Ramos [37]	2018	Spain	Prospective	I-IV	219	62	81	BMI, NRI	L, P
Shaverdian [30]	2016	USA	Retrospective	I-II	118	NR	NR	Serum albumin	SBRT
Shoji [33]	2017	Japan	Retrospective	I-III	272	70[b] (75–91)	57	BMI, PNI, CONUT, GNRI	P, L
Takahashi [26]	2020	Japan	Retrospective	I-III	475	70[b] (64–75)	62	PNI, CONUT, GNRI	L
Tewari [38]	2007	UK	Prospective	I-IV	642	66[b] (32–89)	62	BMI, weight loss, serum albumin	T, L
Tsukioka [27]	2017	Japan	Retrospective	I-III	215	68 (46–93)	100	Sarcopenia	L, S
Zhang [28]	2019	Germany	Retrospective	I-III	626	67[b]	54	Serum albumin, C-reactive protein	L, S

Abbreviations: B = bilobectomy resection; BMI = body mass index (kg/m^2); CHRT = chemoradiotherapy; CONUT; controlling nutritional status; CT = chemotherapy; FFMI = fat free mass index; GNRI = geriatric nutritional risk index; L = lobectomy; nCT = neoadjuvant chemotherapy; NR = not reported; NRI = nutritional risk index; nRT = neoadjuvant radiotherapy; P = pneumonectomy; PNI = prognostic nutritional index; RT = radiotherapy; S = segmentectomy; SBRT = stereotactic body radiation therapy; T = thoracotomy; WR = wedge resection.
[a] Protocols used for nutritional assessments are shown in supplementary file 1.
[b] Median (interquartile range).

3.2.4. Pretreatment assessment of nutritional biomarkers

In 13 of the 23 studies (57%) in which pretreatment outcomes of biomarkers were collected, one or more biomarkers were significantly associated with treatment complications or treatment mortality. Biomarker serum albumin was used in eight studies [17,19,22,26,28,30,36,39] (35%), of which in three of eight studies (37%) a pretreatment high serum albumin (>15.86 ml/dl [39], ≥35 g/L [17], ≥14.97% [19]) and in two studies [22,30] (25%) higher pretreatment serum albumin was associated with a higher risk for treatment complications. In the only study (13%) that looked at serum albumin, a score of ≥35 g/L was associated [17] with treatment mortality. In the only study [17] were the biomarker transferrin was appraised, and in the two studies [22,28] were the biomarker C-reactive protein was evaluated, there was no association with treatment complications or treatment mortality. In four of five studies (80%), a low score on the prognostic nutritional index (<48 [24], <45 [20], <50 [25], and ≤47 [26]) and a lower score on the prognostic nutritional index in one of five studies [24] (20%) were associated with a higher risk for treatment complications. A high score (>1 [29] and ≥2 [26]) (9%) on the controlling nutritional status in both studies in which was looked at de controlling nutritional status was associated with a higher risk for treatment complications.

3.2.5. Cut-off values

Cut-off values of outcomes of pretreatment nutritional assessments associated with an increased risk for treatment complications and treatment mortality are presented in Table 5. A limited number of studies reported a predetermined cut-off value of outcomes of pretreatment nutritional assessment to indicate a higher risk for postoperative complications; however, the accuracy of these cut-off values was usually moderate. One study reported a BMI <18.5 kg/min^2 as optimal cut-off value for a higher risk for treatment complications [37]. In the same study, an optimal cut-off value indicating a higher risk for pulmonary complications was a score <100 on the nutritional risk index [37]. In another study, a cut-off value for sarcopenia on the psoas muscle mass index of ≤3.70 cm^2/m^2 in male and ≤2.50 cm^2/m^2 in female was reported to indicate a higher risk for treatment complications [32]. The most optimal cut-off value for the geriatric nutritional risk index for predicting a higher risk for treatment complications was a score ≤101 [26]. A score ≥1 on the controlling nutritional status was used as a cut-off value in two studies [26,33]. In another study, the most optimal prognostic nutritional index cut-off value for an higher risk for treatment complications was ≤49.6 [33], while a prognostic nutritional index score ≤47 was reported as a cut-off value for an higher risk for treatment complications [26].

4. Discussion

The aim of this systematic review was to evaluate which outcome variables of pretreatment nutritional assessments are associated with treatment complications in patients with stage I-III NSCLC, as well as to identify cut-off values that can be used for preoperative risk assessment. Results demonstrated that a wide variety of variables of pretreatment nutritional assessments seem to be associated with posttreatment complications and/or posttreatment mortality. A good comparison between studies is hampered due to a large variation in the used outcome criteria between studies. When similar outcomes or criteria were used, studies used a different definition of the outcome or criterion. In addition, only a limited number of cut-off values were provided, all with a poor accuracy. Studies on other treatment strategies than surgery or SBRT were lacking.

Seven included studies investigated the predictive value of BMI in NSCLC, in which two different protocols were used. Being

Table 3
Quality assessment based on the Newcastle–Ottawa scale for cohort studies.

First author	Representativeness exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest present at start of the study	Comparability of cohorts on the basis of the design of analysis	Assessment of outcome	Follow-up time	Adequacy of follow-up of cohort	Quality
Bagan [34]	B☆	A☆	A☆	A☆	A☆	A☆	A☆	A☆	Good
Bianchi [39]	D	A☆	A☆	A☆	A☆	A☆	B	D	Poor
Fiorelli [17]	B☆	A☆	A☆	B	A☆	A☆	B	A☆	Good
Illa [35]	A☆	A☆	A☆	B	NR	A☆	B	A☆	Poor
Jagoe [36]	B☆	A☆	A☆	B	A☆	A☆	A☆	A☆	Poor
Kawaguchi [32]	B☆	A☆	A☆	B	A☆	A☆	A☆	A☆	Good
Kim [18]	B☆	A☆	A☆	A☆	B☆	A☆	A☆	A☆	Good
Lee [22]	B☆	A☆	A☆	A☆	A☆	A☆	A☆	A☆	Good
Lee [29]	B☆	A☆	A☆	A☆	A☆	A☆	B	A☆	Poor
Li [19]	B☆	A☆	A☆	A☆	A☆	A☆	A☆	A☆	Good
Madariaga [21]	B☆	A☆	A☆	B	A☆	A☆	A☆	A☆	Good
Nakada [31]	B☆	A☆	A☆	B	A☆	A☆	B	A☆	Poor
Nakamura [23]	B☆	A☆	A☆	B	A☆	A☆	B	A☆	Poor
Okada [24]	B☆	A☆	A☆	B	A☆	A☆	A☆	A☆	Good
Okada [20]	B☆	A☆	A☆	A☆	A☆	A☆	B	A☆	Poor
Park [25]	B☆	A☆	A☆	A☆	A☆	A☆	B	A☆	Poor
Ramos [37]	B☆	A☆	A☆	A☆	A☆	A☆	A☆	A☆	Good
Shaverdian [30]	C	A☆	A☆	B	A☆	A☆	A☆	C	Poor
Shoji [33]	B☆	A☆	A☆	B	B☆	A☆	B	A☆	Poor
Takahashi [26]	B☆	A☆	A☆	B	A☆	A☆	A☆	A☆	Good
Tewari [38]	D	A☆	A☆	B	NR	A☆	B	A☆	Poor
Tsukioka [27]	B☆	A☆	A☆	B	NR	A☆	B	A☆	Poor
Zhang [28]	B☆	A☆	A☆	A☆	A☆	A☆	B	A☆	Poor

Abbreviations: NR = not reported.
[a]: stars (☆) are awarded on the basis of answers (A, B, C, or D) provided for each item.
[b]: thresholds for converting the Newcastle–Ottawa scale scores to the Agency for Healthcare Research and Quality standards (good, fair, and poor): good quality = 3 or 4 stars in the selection domain AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome/exposure domain; fair quality = 2 stars in the selection domain AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome/exposure domain; poor quality = 0 or 1 star in the selection domain OR 0 stars in the comparability domain OR 0 or 1 stars in the outcome/exposure domain.

underweight (BMI $\leq$18.5 kg/m^2) was associated with treatment complications in two studies [17,26]. In addition, three of five studies [21,33,36] that examined BMI as a continuous variable, found a significant association between a lower BMI and a higher risk for posttreatment complications. A previous study among patients with bladder cancer [41] has shown that it is difficult to use BMI to predict treatment mortality, probably because it is not an adequate indicator of body composition. Patients with less muscle mass may have the same BMI as patients with higher muscle mass and therefore BMI provides insufficient insight into the patient's fitness [41]. When interpreting BMI outcomes, it is important to keep in mind that BMI has its limitations. First, the measurement of BMI includes both fat and fat free mass, both of which are known to be influenced by age and sex [42]. Second, many studies used weight loss expressed in percentages and calculated from the previous six months based on memory recall, so the risk of recall bias should be noted [43]. It is therefore recommended not to use BMI as the only measurement to assess nutritional status.

Seven included studies investigated the predictive value of sarcopenia in NSCLC, in which six different protocols were used. Four of these seven studies found a significant association between sarcopenia and a higher risk for posttreatment complications and/or treatment mortality. Sarcopenia is a commonly used method to predict postoperative complications in esophagus, bladder, urologic, and head and neck cancer [41,44–46]. It therefore seems to be an important predictor for cancer treatment complications. Since a computed tomography scan is standard care for diagnosing NSCLC [47], it can be easily applied to measure sarcopenia for predicting treatment complications in this patient group.

In five of the included articles, a combination of assessments was used to evaluate pretreatment nutritional status. In all of these studies [26,34,35,37,38] a significant association was found between worse nutritional status and the occurrence of posttreatment complications. Furthermore, biomarkers, especially serum albumin, were examined in eight included articles, which found that higher serum albumin was significantly associated with a higher risk for posttreatment complications and/or treatment mortality in five articles [17,19,22,30,39]. Blood tests are usually taken in the diagnostic phase of lung cancer and are easy to acquire in the clinic. In the current review, included articles using a combination of biomarkers such as a low score on the prognostic nutritional index in four studies [20,24–26] and a high score on the controlling nutritional status in two studies [26,29] showed an association between pretreatment higher nutritional biomarkers and a higher risk for posttreatment complications and/or treatment mortality. Other biomarkers, such as the modified Glasgow prognostic score, can reflect inflammatory status and are recognized as predictive factors for survival in NSCLC [48] and renal cell cancer [49] but no articles were found in this systematic review that used the modified Glasgow prognostic score as a predictive variable for treatment complications or treatment mortality. Although the measurement of serum albumin is simple and relatively inexpensive, the biochemical relevance of this assessment in patients with cancer is questionable and difficult, because underlying disease may interfere with albumin synthesis [50]. Due to high physiological stress with local tissue damage (tumor hypoxia and/or necrosis), a systemic release of pro-inflammatory cytokines and growth factors will occur before hypoalbuminemia. This leads both to the production of C-reactive protein (CRP), as well as to a decrease in the production of albumin [51]. Therefore, the use of a combination of different biomarkers such as the prognostic nutritional index might be a better a predictor of malnutrition and ultimately the risk for posttreatment complications.

This review provides a good overview of studies supporting pretreatment risk assessment using nutritional assessments in patients with operable NSCLC, as well as in the single included

Table 4
Association between pretreatment nutritional assessments and posttreatment complications and posttreatment mortality.

Author	Pretreatment nutritional assessments	Posttreatment complications/mortality				
Pretreatment assessment of anthropometry and body composition			**P-value**	**OR**	**95% CI**	
Fiorelli [17]	BMI <18.5 kg/m^2	90-day postoperative complications	**<0.01**	**5.4**	**5.78–6.23**	Univariable
		90-day postoperative mortality	**0.02**	**3.8**	**1.72–6.53**	Multivariable
	BMI ≥18.5 km/m^2			*Reference*		
Takahashi [26]	BMI <18.5 kg/m^2	Postoperative complications[a]	**0.06**	**1.84**	**0.98–3.46**	Univariable
	BMI ≥18.5 km/m^2			*Reference*		
Okada [20]	BMI (kg/m^2) *median IQR*	30-day postoperative complications	0.47	1.02	0.97–1.08	Univariable
Shoji [33]	BMI (kg/m^2) *median IQR*	Postoperative complications[a]	**0.02**			Univariable
Jagoe [36]	BMI (kg/m^2) *continuous*	30-day postoperative pulmonary complications	**<0.01**			Univariable
		30-day postoperative mortality	**0.02**			Univariable
Madariaga [21]	BMI (kg/m^2) *continuous*	90-day postoperative complications	0.32	1.04	0.97–1.11	Multivariable
		90-day postoperative cardiopulmonary complications	**0.09**[b]	**1.07**	**0.99–1.16**	Multivariable
		Length of hospital stay	0.10	0.97	0.93–1.01	Multivariable
Ramos [37]	BMI (kg/m^2) *continuous*	Postoperative complications	0.85			Univariable
Fiorelli [17]	Weight loss ≥5% *continuous*	90-day postoperative complications	0.80	0.80	0.09–6.86	Univariable
Jagoe [36]	FFMI (kg/m^2) *continuous*	30-day postoperative complications	**0.02**			Univariable
Pretreatment assessment of sarcopenia			**P-value**	**OR**	**95% CI**	
Kim [18]	L3 muscle mass index <55 cm^2/m^2[c], <39 cm^2/m^2[d]	30-day postoperative complications	0.16	1.59	0.84–3.02	Univariable
	L3 muscle mass index ≥55 cm^2/m^2[c], ≥39 cm^2/m^2[d]			*Reference*		
Tsukioka [27]	L3 muscle mass index <49 cm^2/m^2	Postoperative complications[a]	0.34			Univariable
	L3 muscle mass index ≥49 cm^2/m^2			*Reference*		
Kawaguchi [32]	Psoas muscle mass index <3.70 cm^2/m^2[d], <2.50 cm^2/m^2[e]	30-day postoperative complications Clavien-Dindo classification grade ≥2	**<0.01**			Univariable
Nakada [31]	Psoas muscle mass index cm^2/m^2 <4.61 cm^2/m^2[c], <3.26 cm^2/m^2[d]	Postoperative complications[a]	0.38	1.50	0.69–3.70	Multivariable
Nakamura [23]	Psoas muscle mass index <6.36 cm^2/m^2[c], <3.92 cm^2/m^2[d]	Postoperative complications Clavien-Dindo classification grade ≥3[a]	**<0.01**			Univariable
Madariaga [21]	Thoracic skeletal muscle area cm^2/m^2 *continuous*	90-day postoperative complications	**0.04**	**0.87**[e]	**0.75–0.99**	Multivariable
		90-day postoperative cardiopulmonary complications	**0.04**	**0.86**[e]	**0.74–0.99**	Multivariable
	Thoracic skeletal muscle area cm^2/m^2 *continuous*	Length of hospital stay	0.18	1.05	0.98–1.12	Multivariable
Jagoe [36]	Bone-free midarm muscle area (%) *continuous*	30-day postoperative pulmonary complications	**0.03**			Univariable
	Subscapular skinfold thickness (%) *continuous*	30-day postoperative pulmonary complications	**<0.01**			Univariable
	Triceps skinfold thickness (%) *continuous*	30-day postoperative pulmonary complications	**<0.01**			Univariable
Pretreatment assessment of a combination of multiple nutritional parameters			**P-value**	**OR**	**95% CI**	
Illa [35]	NRS 2002 >2	Postoperative complications[a]	**0.04**	**2.71**		Univariable
	NRS 2002 ≤2			*Reference*		
Bagan [34]	BMI <18.5 kg/m^2, serum albumin <35 g/dL, transthyretin <0.16 g/L	30-day postoperative complications	**0.03**	**1.76**	**1.1–2.43**	Univariable
		90-day operative mortality	**<0.01**	**6.50**	**9.11–4.14**	Univariable
	BMI ≥18.5 kg/m^2, serum albumin ≥35 g/dL, transthyretin ≥0.16 g/L			*Reference*		
Tewari [38]	BMI <18.5 kg/m^2, serum albumin <30 g/L, weight loss	Postoperative pulmonary complications[a]	**0.02**			Chi^2
Takahashi [26]	GNRI ≤101	Postoperative complications[a]	**<0.01**	**2.41**	**1.52–3.79**	Multivariable
		Postoperative complications[a]	**<0.01**	**2.58**	**1.70–3.94**	Univariable
		Air leakage	**<0.01**	**3.52**	**1.98–6.44**	Univariable
		Pneumonia	**<0.01**	**2.55**	**1.31–5.08**	Univariable
		Atrial fibrillation	0.22	1.92	0.65–6.07	Univariable
	GNRI >101			*Reference*		
Ramos [37]	NRI <100	30-day postoperative complications	**0.05**	**2.38**	**1.02–5.58**	Multivariable
	NRI ≥100			*Reference*		
	NRI *continuous*	30-day postoperative complications	**<0.01**	**0.96**[c]	**0.94–0.99**	Univariable
Pretreatment assessment of nutritional biomarkers			**P-value**	**OR**	**95% CI**	
Bianchi [39]	Serum albumin *IQR >15.*86 ml/dl	Postoperative complications[a]	**0.01**	**0.80**[c]	**0.68–0.95**	Univariable
				Reference		
Fiorelli [17]	Serum albumin (mg/dl) ≥35 g/L	Postoperative complications	**0.02**	**2.3**	**1.43–2.01**	Univariable
		Operative mortality	**0.05**	**3.3**	**0.99–1.14**	Univariable
	Serum albumin (mg/dl) < 35 g/L			***Reference***		
Li [19]	Serum albumin ≥14.97%	30-day postoperative pulmonary complications	**<0.01**	**3.13**	**1.75–5.61**	Univariable
			0.02	**2.27**	**1.15–4.46**	Multivariable
	Serum albumin <14.97%			*Reference*		
Takahashi [26]	Serum albumin >40 g/dl	Postoperative complications[a]	0.61	0.99	0.95–1.04	Univariable
	Serum albumin ≤40 g/dl			*Reference*		
Shaverdian [30]	Serum albumin (mg/dl) *median IQR*	Posttreatment complications after SBRT[a]	0.29	3.09		Multivariable
	Serum albumin (mg/dl) *median IQR*	Posttreatment pulmonary complications after SBRT[a]	**0.05**	**26.87**		Multivariable

Table 4 (*continued*)

Author	Pretreatment nutritional assessments	Posttreatment complications/mortality				
Jagoe [36]	Serum albumin (mg/dl) *continuous*	30-day postoperative complications	0.91			Univariable
Lee [22]	Serum albumin (mg/dl) *continuous*	90-day postoperative complications	**0.03**	**0.40**[c]	**0.18–0.91**	Univariable
	Serum albumin (mg/dl) *continuous*	90-day postoperative pulmonary complications	0.15	0.53	0.22–1.27	Univariable
Zhang [28]	Serum albumin (mg/dl) *continuous*	90-day postoperative cardiopulmonary complications	0.61	0.80	0.34–1.88	Univariable
Fiorelli [17]	Transferrin >1.7 g/L	90-day postoperative complications	0.8	0.8	0.10–3.48	Univariable
		90-day operative mortality	0.9	1.1	0.13–6.58	Univariable
	Transferrin ≤1.7 g/L			*Reference*		
Zhang [28]	C-reactive protein <35 mg/L	90-day postoperative cardiopulmonary complications	0.78	0.99	0.95–1.04	Univariable
	C-reactive protein ≥35 mg/L			*Reference*		
Lee [22]	C-reactive protein *continuous*	30-day postoperative complications	0.65	1.06	0.82–1.37	Univariable
	C-reactive protein *continuous*	30-day postoperative pulmonary complications	0.54	1.09	0.84–1.41	Univariable
Lee [29]	CONUT >1	Postoperative pulmonary complications[a]	**<0.01**	**1.91**	**1.17–3.10**	Univariable
	CONUT 0			*Reference*		
Takahashi [26]	CONUT ≥2	Postoperative pulmonary complications[a]	**0.02**	**1.63**	**1.07–2.51**	Multivariable
		Postoperative pulmonary complications[a]	**<0.01**	**1.88**	**1.22–2.80**	Univariable
		Air leakage	**0.04**	**1.01**	**1.73–3.01**	Univariable
		Pneumonia	0.44	1.28	0.67–2.46	Univariable
		Atrial fibrillation	**0.02**	**1.63**	**1.07–2.51**	Univariable
	CONUT <1			*Reference*		
Okada [24]	PNI <48	Postoperative complications[a]	**<0.01**	**1.08**[f]	**1.02–1.14**	Univariable
		Postoperative pulmonary complications[a]	0.2	1.11[f]	0.94–1.28	Univariable
	PNI ≥48			*Reference*		
Okada [20]	PNI <45	30-day postoperative complications Clavien-Dindo classification grade ≥2	**<0.01**	**2.55**	**1.40–4.57**	Univariable
		30-day postoperative complications Clavien-Dindo classification grade ≥3	**<0.01**	**3.87**	**1.79–8.10**	Univariable
		Air leak	**<0.01**	**4.38**	**1.18–10.2**	Univariable
		Pneumonia	**0.04**	**6.04**	**1.39–26.2**	Univariable
		Atrial fibrillation	0.06	0.62	0.18–1.64	Univariable
		Pulmonary infection	**<0.01**	**8.08**	**1.73–42.0**	Univariable
	PNI ≥45			*Reference*		
Park [25]	PNI <50	Postoperative pulmonary complications[a]	**<0.01**	**1.7**	**1.3–2.3**	Multivariable
		Postoperative pulmonary complications[a]	**<0.01**	**1.7**	**1.1–2.6**	Univariable
		Atrial fibrillation[a]	**0.05**	**1.4**	**1.0–2.1**	Univariable
		Postoperative complications[a]	**0.02**	**1.6**	**1.2–2.2**	Univariable
	PNI ≥50			*Reference*		
Takahashi [26]	PNI ≤47	Postoperative complications[a]	**0.03**	**1.64**	**1.05–2.55**	Multivariable
		Postoperative complications	**<0.01**	**2.09**	**1.38–3.17**	Univariable
		Air leakage	0.06	1.67	0.96–2.90	
		Pneumonia	**0.02**	**2.13**	**1.11–4.14**	
		Atrial fibrillation	0.32	1.67	0.56–5.08	
	PNI >47			*Reference*		
Okada [20]	PNI per unit decrease *continuous*	30-day postoperative complications Clavien-Dindo classification grade ≥2	**<0.01**	**1.08**	**1.04–1.12**	Univariable
	PNI per unit decrease *continuous*	30-day postoperative complications	**0.01**	**1.06**[f]	**1.01–1.11**	Multivariable

Abbreviations: BMI = body mass index; CI = confidence interval; cm = centimeter; CONUT; controlling nutritional status; dl = deciliter; FFMI = fat free mass index; GNRI = geriatric nutritional risk index; kg = kilogram; l = liter; l3 = the third lumbar vertebra; m = meter; mg = milligram; NRI = nutritional risk index; NRS 2002 = nutrition risk screening 2002; OR = odds ratio; PNI = prognostic nutritional index; SBRT = stereotactic body radiation therapy.

[a] Follow-up was not described.
[b] Due to the small population in this study, a p-value of 0.10 was significant.
[c] Males.
[d] Females.
[e] Analysis focused on the non-occurrence of postoperative complications.
[f] Adjusted for smoking status and COPD.

study in patients undergoing SBRT. These results can be used as a basis for further research to timely identify malnourished patients who are at high risk for treatment complications and mortality. There are some limitations in this systematic review. First, when choosing a nutritional assessment tool to identify individuals at risk for malnutrition, it is important to ensure that the nutritional assessment tool accurately identifies individual patients at risk for, or with, malnutrition. However, one of the major limitations is that there is no “gold standard” to diagnose malnutrition, leading to heterogeneity in the included studies. Moreover, it was difficult to evaluate the effect of confounding in multivariable analysis reported in the included studies, due to heterogeneity in the selection of confounders, the definition of outcome of nutritional assessments, and the used posttreatment outcomes. Second, various ways of examining nutritional status are applied in patients with NSCLC. Although this systematic review includes articles that have investigated anthropometry and body composition parameters, sarcopenia, a combination of BMI, serum albumin and weight loss parameters, and biomarkers, no studies have been found that have investigated the association between nutritional assessment questionnaires or surveys and treatment complications in patients with NSCLC. Easy-to-administer nutritional assessments to identify patients with NSCLC who are at high risk for treatment complications are useful in daily practice [52,53]. As a recommendation, tools such as the mini nutritional assessment [54,55], the malnutrition universal

Table 5
Cut-off values at pretreatment nutritional assessments and posttreatment complications and posttreatment mortality.

Author	Pretreatment nutritional assessments	Posttreatment complications/mortality	
Pretreatment assessment of anthropometry and body composition			
Ramos [37]	BMI 18.5 kg/m^2	Postoperative complications	AUC 0.56 (95% CI 0.47–0.65)
Pretreatment assessment of sarcopenia			
Kawaguchi [32]	Psoas muscle index 3.70 cm^2/m^2[a]	30-day postoperative complications Clavien-Dindo classification grade ≥2	AUC 0.63, Sensitivity 86.4%, specificity 65.0%
	Psoas muscle index 2.50 cm^2/m^2[b]	30-day postoperative complications Clavien-Dindo classification grade ≥2	AUC 0.59 Sensitivity 97.5%, specificity 58.3%
Pretreatment assessment of a combination of multiple nutritional parameters			
Takahashi [26]	GNRI 101	Postoperative complications[c]	AUC 0.64 (95% CI 0.58–0.69)
Ramos [37]	NRI 100	30-day postoperative complications	AUC 0.64 (95% CI 0.55–0.72)
Pretreatment assessment of serum albumin			
Li [19]	Serum albumin 14.97%	30-day postoperative pulmonary complications	AUC 0.66 (95% CI 0.58–0.73), sensitivity 57.7%, specificity 69.6%
Pretreatment assessment of CONUT			
Shoji [33]	CONUT 1	Postoperative complications[c]	AUC 0.56, sensitivity 34.69%, specificity 73.98%
Takahashi [26]	CONUT 1	Postoperative complications[c]	AUC 0.61 (95% CI 0.55–0.67), sensitivity 63.3%, specificity 51.7%
Pretreatment assessment of PNI			
Shoji [33]	PNI 49.6	Postoperative complications[c]	AUC 0.53, sensitivity 50.3%, specificity 58.5%
Takahashi [26]	PNI 47	Postoperative complications[c]	AUC 0.62 (95% CI 0.56–0.68), sensitivity 53.1%, specificity 65.2%

Abbreviations: AUC = area under the curve; BMI = body mass index; CI = confidence interval; cm = centimeter; CONUT; controlling nutritional status; dl = deciliter; FFMI = fat free mass index; GNRI = geriatric nutritional risk index; kg = kilogram; l = liter; m = meter; mg = milligram; NRI = nutritional risk index; NRS 2002 = nutrition risk screening 2002; OR = odds ratio; PNI = prognostic nutritional index.
[a] Males.
[b] Females.
[c] Follow-up was not described.

screening tool [56], and the short nutritional assessment questionnaire [57] are practical and inexpensive to apply and can predict clinical outcomes in elderly patients [53]. Nutritional assessments, such as the patient-generated subjective global assessment (PS-SGA) and the mini nutritional assessment, as well as the assessment of biochemical and laboratory parameters and clinical and dietetically factors [52,53] allow for a targeted nutritional intervention to replenish nutritional deficits before surgery, eventually as part of a prehabilitation program. Moreover, previous research among patients with cancer has shown that these nutritional assessments best covered the breadth of the definitions of nutritional status [58] and were classified with the highest content validity [59]. Third, a poor score on the NOS was particularly found in almost half of the included articles. This is mainly due to the non-description of the outcome of interest present at start of the study or incomplete description of the follow-up. Fourth, there was considerable variation between the studies in type of treatment, used nutritional assessment, definitions and cut-off values of nutritional assessments, and there was incomplete description of posttreatment complications in several studies. This variation could have influenced the associations between the outcome of the pretreatment nutritional assessment, and posttreatment complications or mortality. Moreover, no information was found about the association between different types of surgery and postoperative complications and mortality, while the physiological impact and risks of a segmentectomy are expected to be less than those of a pneumonectomy. Therefore, in different surgical procedures different outcomes on the nutritional assessment would intuitively be expected [42]. Fifth, confounding by smoking and chronic obstructive pulmonary disease may play a role in the association between the outcomes of nutritional assessment and postoperative complications (63). Only two studies [22,26] adjusted for smoking and COPD; they reported that associations between outcomes of nutritional assessment and postoperative complications were independent of smoking status and COPD.

Although studies have shown that worse outcomes of pretreatment nutritional assessments are associated with a higher risk for posttreatment complications, the nutritional biomarkers and a computed tomography scan may not always be available, making nutritional assessment questionnaires an attractive alternative. However, there is only limited evidence to justify their use in the preoperative setting in patients with cancer and no evidence in patients with NSCLC. Therefore, research on the predictive value of nutritional assessment questionnaires is recommended. Consideration should be given to which outcome variables and cut-off values are easy-to-use to identify patients who are at high-risk for complications so that nutritional interventions can be applied to the individual patient, as well as to the possibility to perform a pretreatment nutritional assessment, after which the nutrition performance status might be improved by prehabilitation to reduce a patient's risk for complications during and/or after treatment [60].

Almost all articles included surgical patients in this systematic review. More attention should be paid to the potential of nutritional assessments to predict treatment complications in patients with NSCLC who undergo other intensive treatments, such as chemoradiotherapy and radical radiotherapy. Efforts should be made to standardize easy-to-administer pretreatment nutritional assessment with accurate cut-off values in pretreatment risk stratification. In future studies, the description of posttreatment complications and posttreatment mortality should be used according to a standardized protocol, and consensus should be reached to use the appropriate follow-up time regarding complications and mortality to enable pooling of study results.

5. Conclusion

A poor outcome on pretreatment nutritional assessment is associated with a higher risk for posttreatment complications and posttreatment mortality. However, providing specific recommendations for the use of nutritional assessments is difficult due to the heterogeneity in test protocols and used outcome measures in the current literature. Therefore, standardization of the use of pretreatment nutritional assessments is recommended. In addition, more research is needed regarding the ability of easy-to-use pretreatment nutritional assessments, such as nutritional assessment questionnaires, to accurately identify patients who have a high-risk for treatment complications across all curative treatment options for NSCLC. This is important because particularly these high-risk patients may benefit from interventions to improve their physical performance before starting treatment, thereby improving treatment outcomes.

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Credit statement

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Declaration of competing interest

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

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Appendix A. Supplementary data

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