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ORIGINAL ARTICLE

The value of physical performance measurements alongside assessment of sarcopenia in predicting receipt and completion of planned treatment in non-small cell lung cancer: an observational exploratory study

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Abstract

Introduction The presence of muscle mass depletion is associated with poor outcomes and survival in cancer. Alongside muscle mass, assessment of muscle strength or physical performance is essential for the diagnosis of sarcopenia. Non-small cell lung cancer (NSCLC) is a prevalent form of cancer with high mortality, and Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) is commonly used to assess patients' suitability for treatment. However, a significant proportion of patients with good PS are unable to complete multidisciplinary team (MDT)-planned treatment. Little is known about the ability of objective measurements of physical performance in predicting patients' ability to complete MDT-planned treatment and outcomes in NSCLC.

Objectives We sought to establish whether physical performance, utilising the short physical performance battery (SPPB), alongside muscle mass measurements, was able to predict receipt and completion of MDT-planned treatment, with a focus on chemotherapy in NSCLC.

Materials and methods Participants with NSCLC treated through a single lung cancer MDT and ECOG PS 0–2 were recruited and the following assessed: body composition [bioelectrical impedance (BIA) and whole body dual-energy X-ray absorptiometry (DXA) in a subset], physical performance (SPPB), PS and nutritional status. We recorded receipt and completion of chemotherapy, as well as any adverse effects, hospitalisations, and treatment delays.

Results We included a total of 62 participants with NSCLC, and in 26 of these, the MDT-planned treatment was chemotherapy. Participants with earlier stage disease and weight loss of <10% were more likely to complete MDT-planned treatment ($p < 0.001$ and $p < 0.05$). Patients with a higher total SPPB score were more likely to complete more cycles of chemotherapy as well as the full course. Quicker gait speeds and sit-to-stand times were associated with completion of three or more cycles of chemotherapy (all $p < 0.05$). For every unit increase in SPPB score, there was a 28.2% decrease in adverse events, hospitalisations and delays of chemotherapy (incidence rate ratio 0.718, $p = 0.001$), whilst ECOG PS showed no correlation with these outcomes.

Conclusion Assessing physical performance by SPPB is quick and simple to do in clinical settings and may give better indication of likely chemotherapy treatment course completion than muscle mass alone and ECOG PS. In turn, this may identify specific targets for early functional intervention and impact on MDT decision-making and prudent use of resources.

Keywords Sarcopenia · Non-small cell lung cancer · Short physical performance battery

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Introduction

The depletion of muscle mass, which is also known as sarcopenia, is now an integral component of the diagnosis of cancer cachexia [1]. Its presence in the cancer patient is associated with increased length of hospital stay and symptom burden, as well as being an independent factor for poor survival [2–4]. It may also contribute to chemotherapy toxicity by altering drug pharmacokinetics and metabolism [5, 6].

Sarcopenia was first established as a predictor of poor prognosis in older people, being prevalent in this population due to age-related changes in muscle mass, causing significant morbidity, hospitalisation, loss of independence, and physical frailty—a hallmark of the ageing process [7–10]. The reduction in physical function seen in frailty is linked to muscle mass, where an established non-linear relationship between skeletal muscle mass and function exists [11], an association which is also noted in advanced cancer [12]. Whilst loss of function can sometimes outpace loss of mass [13], greater emphasis has been placed on the clinical assessment of physical function alongside muscle mass [14]. Sarcopenia is therefore better defined as a state in which there is a dual loss: both of muscle mass, as well as muscle function [15].

Older frail patients with cancer have an increased risk of treatment intolerance, increased post-operative complication rate and increased mortality compared to their non-frail counterparts [16–18]. Currently, the subjective measure of Eastern Cooperative Oncology Group (ECOG) performance status (PS) score [19] is used to help distinguish between patients at the same disease stage who may have potentially curative treatment and those for whom palliative treatment options should be considered. While PS is a prognostic factor for survival, less is known about its ability to predict tolerance of anti-cancer treatment accurately. Previous reports suggest that a significant proportion of patients with lung cancer do not go on to commence planned treatment, despite a reasonable initial PS score, with functional reasons predominating [20, 21].

A more objective evaluation of physical performance or muscle strength is therefore warranted, which may complement or even outperform PS scoring [22]. The short physical performance battery (SPPB) is a valid, reliable and feasible measure of physical performance in older people [23, 24]. Together with measurement of muscle mass, a functional assessment of physical performance such as SPPB may prove a better measure of ability to tolerate a whole course of chemotherapy, compared to PS. We therefore undertook an exploratory study to evaluate the predictive utility of SPPB and muscle mass for the completion of treatment, particularly chemotherapy, in non-small cell lung cancer (NSCLC) patients.

Participants

We chose to undertake the study in NSCLC patients, since it is a common cancer which frequently presents in advanced stages. Despite advances in anti-cancer treatment in the last 3 decades, corresponding increases in survival have been relatively small, compared to other cancers such as breast, colorectal and prostate cancers [25]. Furthermore, NSCLC has a particularly strong association with muscle depletion [4, 26], with early evidence that reduced physical tolerance could precede muscle loss in early-stage disease [27].

Adult participants were recruited from a Rapid Access Lung Cancer Clinic (RALCC). Inclusion criteria were (i) high clinical suspicion of NSCLC, (ii) ECOG PS 0–2, (iii) no physical or neurological impediment precluding the ability to complete study assessments and (iv) no implantable cardiac devices such as pacemakers which are contraindicated in bioelectrical impedance analysis (BIA). Besides evaluating whether body composition and physical performance parameters were predictive of receipt and completion of chemotherapy, we were also interested in the predictive value of other parameters such as weight loss and PS. As the endpoints of interest were receipt and completion of multidisciplinary team (MDT)-planned treatment, a cut-off of PS 2 was set, as those with poorer PS were less likely to be planned for active treatment. Initially, 86 participants were recruited and 24 were excluded from follow-up due to subsequent diagnoses other than NSCLC. Sixty-two participants with varying stages of NSCLC were included for analysis, with a focus on those planned for chemotherapy (n = 26) (Fig. 1).

Methods

This was an exploratory study, conducted in order to inform the design and recruitment feasibility to a definitive, adequately powered large-scale multicentre study. The primary and main secondary outcomes were binary (commencement and completion of chemotherapy). As such, it was not possible to establish a figure for minimal detectable difference; a target recruitment of 75–100 patients over 18 months was agreed. Due to the relatively small numbers, it was acknowledged that potentially important associations could be missed.

We conducted this prospective, single-centre study between February 2014 and June 2015 in a university hospital setting in South Wales in the UK. A favourable ethical opinion was granted in November 2013 by the South East Wales Research Ethics Committee. All recruited participants had baseline study tests performed on the day of attendance at the RALCC. These consisted of body mass index (BMI) calculation, body composition analysis by BIA (Tanita BC-418) and physical performance testing with the SPPB. Height was measured using a wall-mounted stadiometer and recorded to

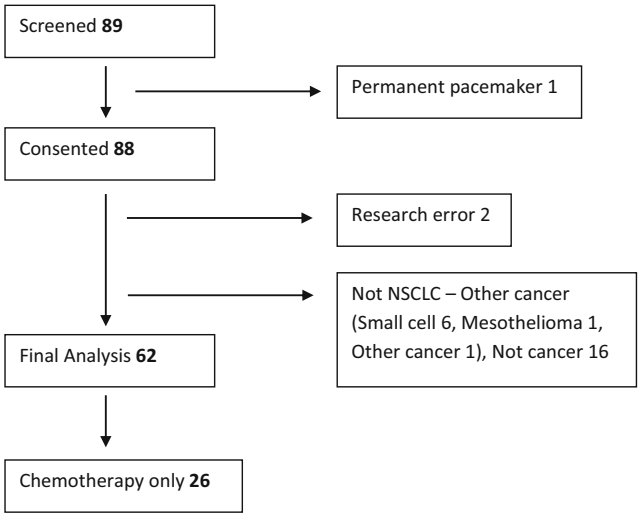

Fig. 1 Consort diagram of all participants

the nearest 0.1 cm. Body composition measurement comprised body weight, fat mass, fat-free mass, estimated total and segmental muscle mass that were recorded in grammes. In order to assess the accuracy of muscle mass, we compared BIA measurements to those made by whole-body dual-energy X-ray absorptiometry (DXA) (Hologic Discovery A) within 3 days of BIA in a subgroup of 16 participants. In our analysis, we used both the continuous variables of appendicular skeletal muscle index (ASMI) and cutoffs for sarcopenia: ASMI <7.26 kg/m^2 for men and <5.45 kg/m^2 for women, based on BIA derived values, assuming that these were comparable to DXA values [1]. BMI was calculated according to the equation weight in kilogrammes / (height in metres)^2.

SPPB is a reliable and feasible method of assessing physical performance and has been validated and recommended for use in older people [28, 29]. It is quick to perform, easily reproducible, requires little additional equipment and with basic training can be performed by most healthcare personnel. It measures balance, gait speed and five times sit-to-stand on a 12-point scale, where 12 and 0 respectively are the best and worst possible scores. In the elderly, those with SPPB score 4–6 had the greatest relative risk of disability related to mobility or activities of daily living, compared with SPPB score 10–12 [30]. For exploratory purposes in this study, we divided SPPB into categories of 11–12, 9–10, 7–8 and <6. For gait speed alone, we used both continuous data as well as a 0.8 m/s cutoff which is associated with reduced leg strength in the elderly [31]. We recorded CTCAE grade 3 or 4 adverse events, number of hospitalisations and delays of treatment during the chemotherapy course (collectively reported as 'adverse events'), where CTCAE is the common terminology criteria for adverse event reporting, grade 1 indicating a mild and grade 4 a life-threatening event [32]. Weight loss in the last 6 months was documented, and nutrition status screening with the Malnutrition Universal Screening Tool (MUST) was recorded. Both physician- and patient-rated ECOG and Karnofsky PS were collected. We noted co-morbidities and presence of chronic obstructive pulmonary disease and its severity to account for potential confounders.

For outcome measures, receipt of treatment was defined as commencement of chemotherapy only. Successful completion of treatment was defined as completion of planned chemotherapy course, which is defined as at least three planned cycles at oncologist-determined full dose. Completion of both whole course of treatment and at least 3 cycles (yes/no, in each case) was determined a priori by an oncologist and palliative care physician, without knowledge of participants' PS. In keeping with the exploratory nature of this study, we captured only baseline data, in order to record function at a pre-MDT discussion stage. The entire study protocol has been published elsewhere [33].

Statistical analyses

Descriptive statistics were employed for demographics, tumour-node-metastasis (TNM) stage and histological diagnosis. Each categorical predictive factor was tested against binary outcomes of receipt and successful completion of MDT-planned treatment with logistic regression, chi-squared test or Fisher's exact test, where appropriate. We reported odds ratios where possible. We also considered numbers of cycles of chemotherapy as an outcome measure, and for this, we utilised linear regression and reported the unstandardised regression coefficient, *B* together with 95% confidence intervals. With regard to the association between SPPB values and adverse events, we employed Poisson regression analysis, which is a generalised linear model form of regression analysis utilised to model count data, and reported the incidence rate ratio (IRR). All analyses were performed using SPSS (SPSS for Windows, version 20, IBM).

Results

All participants

A total of 86 participants were included into the study, and 62 of these participants had a confirmed diagnosis of NSCLC; these are presented descriptively in Table 1. The mean age and SD were 68.2 ± 9.6 years. There were 38 men and 24 women. In terms of histology, adenocarcinoma was the most prevalent (43.5%), followed by squamous cell carcinoma (38.7%), other NSCLC (6.5%) and radiological diagnosis only (11.3%). TNM stage ranged from early stage to advanced disseminated disease (Table 1).

In terms of those who had NSCLC, 12 patients had a low muscle mass (19.4%) according to BIA-derived cutoffs of

Table 1 Descriptive analysis of all participants with NSCLC, *n* (%), with subset of those planned for chemotherapy only

	Men	Women	All participants with NSCLC	Chemotherapy only
N	55	31	62	26
Age, year	68.7 ± 8.5	65.3 ± 10.8	68.2 ± 9.6	64.4 ± 9.4
Weight loss, % over last 6 months	4.6 ± 6.7	7.2 ± 7.9	6.5 ± 7.6	9.5 ± 8.5
Histology, *n* (%)				
Squamous cell	14 (25.4)	10 (32.2)	24 (38.7)	9 (34.6)
Adenocarcinoma	18 (32.7)	9 (29)	27 (43.5)	14 (53.8)
NSCLC other	4 (7.2)	0 (0)	4 (6.5)	3 (11.5)
No tissue diagnosis[a]	2 (3.6)	5 (16.1)	7 (11.3)	0
Comorbidities[b], *n* (%)				
<2	13 (34.2)	8 (33.3)	21 (33.9)	15 (57.7)
≥2	25 (65.8)	16 (66.6)	41 (66.1)	11 (42.3)
COPD, *n* (%)				
Nil	26 (68.4)	18 (75)	44 (71.0)	22 (84.6)
Mild	2 (5.3)	1 (4.2)	3 (4.8)	1 (3.8)
Mod	9 (23.7)	3 (12.5)	12 (19.4)	3 (11.5)
Severe	1 (2.6)	2 (8.3)	3 (4.8)	0
TNM stage, *n* (%)				
I	9 (23.7)	9 (37.5)	18 (29)	0
II	5 (13.2)	4 (16.7)	9 (14.5)	2 (7.7)
III	12 (31.6)	6 (25)	18 (29)	9 (34.6)
IV	12 (31.6)	4 (16.7)	16 (25.8)	15 (57.7)
Staging unavailable	0	1 (4.2)	1 (1.6)	0
Planned treatment, *n* (%)				
Surgery	9 (23.7)	8 (33.3)	17 (27.4)	0
Radical radiotherapy	5 (13.2)	4 (16.7)	9 (14.5)	0
Palliative radiotherapy	5 (13.2)	5 (20.8)	10 (16.1)	0
Chemotherapy	17 (44.7)	7 (29.2)	24 (38.7)	24 (92.3)
Chemo-radiotherapy	2 (5.3)	0	2 (3.2)	2 (7.7)

[a] Radiological diagnosis of NSCLC only

[b] Comorbidities at time of diagnosis. Common diagnoses include hypertension, ischaemic heart disease, diabetes mellitus and obstructive airways disease

Table 2 Regression analyses expressed as odds ratios (OR) or B (unstandardised regression coefficient) with *p* values and 95% confidence intervals of total and component SPPB scores, and associations with receipt and completion of cycles of chemotherapy

Predictor variables	Receipt of chemotherapy		Receipt and completion of chemotherapy course		Completion of three or more cycles of chemotherapy		Completion of number of cycles of chemotherapy	
	OR (*p* value)	95% CI	OR (*p* value)	95% CI	OR (*p* value)	95% CI	*B* (*p* value)	95% CI
Total SPPB score	1.282 (0.272)	0.82 to 2.00	1.903 (0.047)*	1.01 to 3.60	1.849 (0.043)*	1.02 to 3.36	0.351 (0.023)*	0.05 to 0.65
Gait speed <0.8/s vs ≥0.8 m/s	4.200 (0.227)	0.41 to 43.04	4.333 (0.124)	0.67 to 28.12	7.222 (0.042)*	1.08 to 48.48	1.313 (0.055)	−0.03 to 2.66
Gait speed (m/s)	20.5 (0.349)	[b]	473.9 (0.106)	[b]	959.5 (0.076)	[b]	3.913 (0.077)	−0.46 to 8.29
Five times sit-to-stand categories 0–2 vs 3–4	1.905 (0.478)	0.32 to 11.31	8.571 (0.070)	0.84 to 87.83	11.667 (0.039)*	1.14 to 119.54	1.552 (0.014)	0.35 to 2.76
Five times sit-to-stand (s)	0.962 (0.698)	0.79 to 1.17	1.00 (0.682)	0.99 to 1.02	1.00 (0.658)	0.99 to 1.02	0.001 (0.665)	−0.00 to 0.00
Balance categories[a]	(0.076)[a]		(1.000)[a]		(1.000)[a]		1.826 (0.272)	−1.53 to 5.19

B is the unstandardised regression coefficient

*Statistical significance at the 95% confidence level

[a] Calculations of odds ratios failed to converge; therefore, only *p* values for Fisher's exact test or chi-squared test were reported, where applicable

[b] Error in calculation of confidence intervals

ASMI for defining sarcopenia. There were 24 participants planned for chemotherapy, 2 planned for chemo-radiotherapy, 17 participants planned for surgery and a total of 19 planned for radical and palliative radiotherapy. TNM stage was associated with completion of MDT-planned treatment ($p < 0.001$), with those with earlier stages being more likely to complete the treatment course. Collectively, there were no associations between SPPB scores and receipt and completion of MDT-planned treatment. With regard to body composition, muscle mass, the presence of sarcopenia and BMI had no bearing on receipt and completion of MDT-planned treatment. However, those with less than 10% weight loss at diagnosis were more likely to successfully complete all modes of MDT-planned treatment ($p = 0.035$).

Participants planned for chemotherapy

Participants in the subset planned for palliative chemotherapy were more likely to have stage III and IV disease, and greater weight loss at presentation compared to all participants (Table 1). The individual components of the SPPB—five times sit-to-stand, balance and gait speed—were considered separately and as a whole, in order to gauge whether any one component had a greater predictive effect than another.

Physical performance

The higher the SPPB score, the more likely one was to complete more cycles of chemotherapy ($B = 0.351$, $p = 0.023$). The odds of receiving three or more cycles of chemotherapy was increased by around 85%, for each unit increase in SPPB score (OR 1.849, $p = 0.043$), and the odds of completing the full course of chemotherapy was increased by 90% (OR 1.903, $p = 0.047$), for each unit increase in SPPB score. The collated results for the total and components of the SPPB, as predictors for chemotherapy outcomes, are shown in Table 2.

The five times sit-to-stand (STS) test was not discriminatory for receipt of chemotherapy. However, the odds of completing three or more cycles of chemotherapy were 11 times higher in those with quicker STS speeds (categories 3–4 on the SPPB component score) than slower STS speeds (categories 0–2) (OR = 11.667, $p = 0.039$). In terms of gait speed, the odds of completing three or more cycles of chemotherapy were seven times greater in those with gait speeds of 0.8 m/s or more, than those with gait speeds of less than 0.8 m/s (OR = 7.22, $p = 0.042$). Balance was not found to be associated with either receipt or completion of chemotherapy.

With regard to adverse events, an association was seen between this and SPPB scores (IRR = 0.718, $p = 0.001$), where for every unit increase in SPPB score, there was a 28.2% decrease in adverse events (Fig. 2).

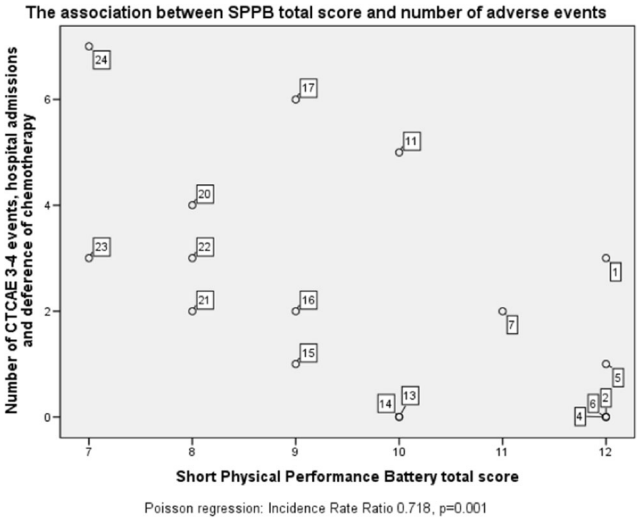

Fig. 2 Poisson regression showing the association between SPPB score and development of adverse events during chemotherapy, IRR 0.718, $p = 0.001$

Body composition

In terms of body composition, BMI, fat mass and muscle mass as determined by BIA were significantly predictive neither of adverse chemotherapy-related events nor of receipt and successful completion of chemotherapy. With DXA as the gold standard investigation, BIA consistently overestimated ASMI in a subset of 16 participants from the main initial cohort (mean difference of ASMI 0.546, 95% CI −0.312, 1.404; $p < 0.001$), which may compromise the overall reliability of BIA-derived muscle mass values.

Nutrition parameters and performance status

Weight loss of <10% was associated with being more likely to receive chemotherapy, but not with completion of chemotherapy, compared to those with losses of ≥10%. Furthermore, weight loss ≥10% was associated with completion of less cycles of chemotherapy (both $p < 0.05$). Greater BMI was also significantly associated with completion of more cycles of chemotherapy ($p < 0.05$), but not receipt or completion of the chemotherapy course, whereas nutrition status and physician-assessed PS at baseline were not significantly associated with receipt or successful completion of chemotherapy (Table 3).

Discussion

Patients with cancer sarcopenia tend to have poorer physical status, increased fatigue levels, impaired quality of life and reduced survival. Perhaps worse still is the fact that loss of muscle mass tends to be occult, a fact that makes its easy

Table 3 Regression analyses expressed as odds ratios (OR) and B (unstandardised regression coefficient) and p values of parameters commonly used to describe nutrition status, and association with receipt and completion of cycles of chemotherapy

Predictor variables	Receipt of chemotherapy		Successful completion of chemotherapy course		Completion of three or more cycles of chemotherapy		Completion of number of cycles of chemotherapy	
	OR (p value)	95% CI	OR (p value)	95% CI	OR (p value)	95% CI	B (p value)	95% CI
Weight loss %	0.908 (0.102)	0.81 to 1.02	0.913 (0.159)	0.81 to 1.04	0.920 (0.164)	0.82 to 1.04	−0.064 (0.101)	−0.14 to 0.01
Weight loss <10% vs ≥10%	0.091 (0.045)*	0.01 to 0.94	0.280 (0.190)	0.04 to 1.88	0.200 (0.096)	0.03 to 1.33	−1.333 (0.037)*	−2.58 to −0.09
BMI (kg/m^2)	1.127 (0.198)	0.94 to 1.35	1.212 (0.065)	0.99 to 1.49	1.221 (0.060)	0.99 to 1.50	0.106 (0.019)*	0.02 to 0.19
MUST 0, 1, ≥2	0.378 (0.117)	0.11 to 1.28	0.440 (0.107)	0.16 to 1.20	0.459 (0.107)	0.18 to 1.18	−0.625 (0.064)	−1.3 to 0.04
Physician ECOG[a]	0.100		0.446		0.741			
Physician Karnofsky[a]	1.000		0.316		0.400			

*Statistical significance at the 95% confidence level

[a] Calculations of odds ratios failed to converge; therefore, only p values for Fisher's exact test or chi-squared test were reported, where applicable

identification challenging. In keeping with the new diagnostic criteria of sarcopenia, which is low muscle mass as well as low observed physical performance [34], we explored the utility of physical performance measurements in identifying and predicting treatment outcomes in cancer, where sarcopenia tends to be described in terms of low muscle mass alone. In performing this study in NSCLC patients, we were able to explore the value of these measurements in a high-incidence, high-mortality cancer-specific group where many present with advanced disease.

Important prognostic factors in NSCLC include advanced stage, PS and weight loss. Current estimates of 5-year survival are 73% for stage 1A and 13% for stage IV [35]. While current advances in NSCLC, and the wider cancer community, tend to focus efforts on improving survival, our study takes a step back to consider the factors that may contribute to barriers to treatment receipt and completion. Multiple phase III clinical trials have demonstrated that receiving palliative systemic treatment results in prolonged survival [36–38]. However, a significant proportion of advanced NSCLC patients do not receive treatment at all, many due to poor PS [39, 40]. Our study suggests that PS is not the best marker of fitness for treatment, as even in those with good or borderline PS, treatment is not always tolerated, let alone begun. Non-receipt of treatment would subsequently result in poorer overall survival, as previously reported [40].

We found that higher TNM stage and greater weight loss showed associations with non-completion of all modes of MDT-planned treatment. This was in keeping with previous data in lung cancer [20] where these parameters were also associated with non-receipt of treatment. Furthermore, 10% or more weight loss and low BMI were associated with completion of less cycles of chemotherapy—factors which are also well-known to be poor prognostic markers in lung cancer [41, 42].

More significantly, we found that the SPPB was able to predict completion of more cycles of chemotherapy and also completion of the full course of chemotherapy. In particular, the sit-to-stand and gait speed components identified associations between these parameters and successful completion of three or more cycles of chemotherapy. This may suggest a link between observed task performance and an underlying physical resilience to withstand treatment. A recently published study of older cancer survivors also used SPPB to assess outcomes over time. It found that older cancer survivors with low total SPPB and gait speed scores had increased all-cause mortality relative to their counterparts with high scores. Furthermore, each unit increase in SPPB score predicted a 12% reduction in mortality [43]. Our smaller study in a population receiving palliative chemotherapy had complementary findings, where for every 1 unit increase in SPPB score, there was a 28% decrease in adverse events, hospitalisations and delays of chemotherapy. We found that the highest score category was significantly predictive of fewer adverse events including hospitalisation, delays of chemotherapy and associated toxicities.

The fact that physician-rated ECOG performance status (PS), the currently used gold standard marker of fitness for withstanding treatment, was not predictive of completion of treatment or adverse events was in contrast to the positive association between high SPPB score and completion of more cycles of chemotherapy, as well as fewer adverse events. This, again, highlights the potential of the SPPB as a clinical tool in the pre-treatment evaluation of patients with NSCLC and suggests the need for a larger study with appropriate power to validate these findings.

Although the SPPB seems to be a promising test in terms of completing chemotherapy, when tested against all MDT-planned treatment types including surgery with curative intent and radical radiotherapy, it failed to show any association with treatment receipt or completion. It may be that the SPPB is better suited to patients with more advanced disease being treated with palliative intent. More traditional prognostic markers such as weight loss and ECOG PS were also not predictive of chemotherapy completion and adverse events in our small cohort. Overall, the SPPB, as an easily applied clinical measure, appears to be a better indicator of tolerance of palliative chemotherapy than body composition parameters alone and may highlight targets for functional intervention earlier than weight loss alone.

In contrast to physical performance values, low muscle mass in our group neither was significantly predictive of receipt of and successful completion of chemotherapy nor was it associated with adverse events. Several similar-sized studies in other cancer-specific groups have suggested an increased incidence of adverse events in patients with low muscle mass [44–46], but we found this not to be the case. In addition to our small sample size, one important reason for this negative finding may be the use of bioelectrical impedance in this study, in contrast to more commonly used DXA or computed tomography (CT). BIA is used to determine muscle mass and body composition in lung cancer patients [47], despite a previous report that BIA overestimates muscle mass in this group [48]. Given its ease of use in busy clinical settings, we felt that it was important to assess whether this overestimate was clinically relevant, and whether BIA-derived muscle mass was able to predict treatment-related outcomes with adequate certainty. We found that BIA-derived muscle mass consistently overestimated DXA-derived values and was not significantly predictive of treatment-related outcomes. This needs to be borne in mind when interpreting BIA-derived results of body composition and limits its utility in clinical decision making.

Our study had several limitations. This was an observational exploratory study, with a small sample size. Furthermore, the ‘real-time’ prospective enrolment of patients, recruited at the time of initial presentation to the RALCC, led to an

inevitable loss of participants who were subsequently found not to have NSCLC. The consistent overestimation of muscle mass values by BIA compared to DXA made correlation of mass and function difficult to assess. Finally, we did not sequentially assess participants' body composition and physical performance—this should be included in further validation studies to enable analysis of changes over time and the response of these parameters to systemic treatment.

Our exploratory study highlights the fact that the current focus on survival must be broadened to incorporate reasons for non-receipt and non-completion of systemic treatment, and include predictive factors for the same. Going forward, our results show that SPPB has promise as a pre-diagnostic test in the work-up to treatment in NSCLC. This finding is similar to that seen with other elderly care tests such as the Comprehensive Geriatric Assessment (CGA). It has been shown in Phase III trials in NSCLC to have superior predictive value of chemotherapy toxicity, compared with PS and age alone [49]. Other assessments in cancer patients in general, including assessment of activities of daily living and frailty, have also been found to be predictive of completion of chemotherapy and mortality, regardless of PS [50, 51]. While a case can be made for utilising many tests in this setting, important test characteristics should be ease of use and validity for important outcomes.

The SPPB is much shorter a test than the CGA and warrants testing in a similar vein to prove its worth. The SPPB is reported to be predictive of survival in other cancer groups [52–54], but not specifically in NSCLC. Understanding any associations between SPPB at baseline and prognosis will be of benefit whilst making treatment decisions within the MDT. This test needs to be validated in a larger cohort, with sequential measurements taken over time to enable longitudinal analysis. Evaluating its worth in terms of prognosis is also desirable; therefore, future work should include whether there is any relationship between this test and survival.

Conclusion

In conclusion, our exploratory study highlights that SPPB may be a better tool than ECOG-PS at predicting the likelihood of patients with advanced NSCLC completing a course of chemotherapy. Furthermore, it may enable early detection of deficits in task performance, identifying the group of patients who may struggle through chemotherapy. This, in turn, may ascertain specific targets for early functional intervention and impact on MDT decision-making and prudent use of resources. Whilst demonstrating the feasibility of recruiting into such a study and the usability of SPPB within the NSCLC population, these promising results warrant further study with a larger, appropriately powered study.

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Authors' contributions JCo, HED and AB devised the study concept and design. JCo, HED, DP, WDE, RP, JL and AB contributed to the study protocol. JCo and DF statistically analysed the data. JCo, SN and AB wrote the manuscript, with contributions from all other authors. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

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