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Imaging skeletal muscle volume, density, and FDG uptake before and after induction therapy for non-small cell lung cancer

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Abstract

AIM: To assess whether changes in body composition could be assessed serially using conventional thoracic computed tomography (CT) and positron-emission tomography (PET)/CT imaging in patients receiving induction chemotherapy for non-small cell lung cancer (NSCLC).

MATERIALS AND METHODS: CT-based skeletal muscle volume and density were measured retrospectively from thoracic and lumbar segment CT images from 88 patients with newly diagnosed and untreated NSCLC before and after induction chemotherapy. Skeletal muscle 2-[¹⁸F]-fluoro-2-deoxy-D-glucose (FDG) uptake was measured from PET/CT images from a subset of patients ($n=42$). Comparisons of each metric before and after induction chemotherapy were conducted using the non-parametric Wilcoxon signed-rank test for paired data. The association between clinical factors and percentage change in muscle volume was examined using univariate linear regression models, with adjustment for baseline muscle volume.

RESULTS: Following induction chemotherapy, thoracic (-3.3% , $p=0.0005$) and lumbar (-2.6% , $p=0.0101$) skeletal muscle volume were reduced (adiposity remained unchanged). The proportion of skeletal muscle with a density <0 HU increased (7.9% , $p<0.0001$), reflecting a decrease in skeletal muscle density and skeletal muscle FDG uptake increased (10.4 – 31% , $p<0.05$). No imaging biomarkers were correlated with overall survival.

CONCLUSION: Changes in body composition can be measured from routine thoracic imaging. During chemotherapy skeletal muscle volume and metabolism are altered; however, there was no

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impact on survival in this retrospective series, and further validation in prospective, well-controlled studies is required.

INTRODUCTION

Weight loss is particularly prominent in patients with non-small cell lung cancer (NSCLC): 47% of patients with NSCLC have weight loss at the time of diagnosis, and 74% have weight loss with end-stage advanced disease.^{1, 2} Weight loss increases the risk of death (hazard ratio [HR], 1.64–2.94) in these patients.^{3–6} The composition of the lost weight is not easily measured by clinicians, and the importance of relative losses of skeletal muscle or adipose tissue has not been explored thoroughly. For example, the influence of reduced skeletal muscle on the treatment response or on overall survival in patients with NSCLC has not been clearly established.^{7–13}

Computed tomography (CT) and positron-emission tomography (PET) imaging form the standard of care for staging and assessing response to therapy in patients with NSCLC; these images have been shown to contain information allowing accurate assessments of body composition.^{14–18} For example, skeletal muscle and adipose tissue can be non-invasively assessed using abdominal CT imaging; however, the abdominal levels are not serially imaged in lung cancer patients at Memorial Sloan Kettering Cancer Center.¹⁹ Thoracic muscle volume correlates very well ($R^2=0.78$) with whole-body muscle mass in patients with cancer (unpublished data). If imaging is performed serially, this metric allows for the measurement of changes in body composition in patients with NSCLC even if only the thoracic CT image set is available.

2-[¹⁸F]-fluoro-2-deoxy-D-glucose (FDG) PET can be used to non-invasively quantify the metabolic activity of skeletal muscle, adipose tissue, and other organs of the body, such as the liver, brain, and bowel.^{20–23} The standardised uptake value (SUV) of FDG derived from PET imaging is proportional to the metabolic activity of skeletal muscle and correlates well with whole-body measurements of energy expenditure.^{24–27} In patients with cancer, changes in skeletal muscle SUV have been reported to vary between specific muscle groups and with the type of chemotherapy given.²⁸

The degree to which body composition changes over the course of systemic therapy treatment of patients with NSCLC is not known. In this study, it was hypothesised that cytotoxic chemotherapy causes adverse alterations in body composition, most notably, skeletal muscle, and that these changes reduce overall survival. To test this theory, CT and PET images, obtained in the course of clinical care, were used to quantify changes in adipose tissue and skeletal muscle volume, density, and FDG uptake before and after induction chemotherapy in patients with NSCLC.

MATERIALS AND METHODS

Patients and setting

The Institutional Review Board provided a waiver of authorisation for this study. The study represents a retrospective analysis of clinical data and imaging parameters in a cohort of

patients who underwent induction chemotherapy followed by resection for NSCLC between January 2000 and December 2006. The study population was identified from a prospectively maintained single-institution surgical database.²⁹ Clinical and demographic characteristics were obtained from clinical chart review. Pulmonary comorbidities included asthma and chronic obstructive pulmonary disease. Cardiac comorbidities included hypertension, coronary artery disease (angina, prior percutaneous transluminal coronary angioplasty, prior coronary artery bypass grafting, and prior myocardial infarction), atrial fibrillation, and valvular diseases. Endocrine comorbidities included insulin-dependent and -independent diabetes. Documented glucocorticoid doses were converted to equivalent dexamethasone doses using the following ratios: hydrocortisone 25:1, prednisone 6:1, and methylprednisone 5:1. Bilobectomy, lobectomy, wedge resection, and segmentectomy were classified within a single group as “lobar” procedures; pneumonectomy and exploration without complete resection were analysed separately.

The initial cohort included 545 consecutive patients with NSCLC who underwent induction chemotherapy followed by surgical resection. Of these patients, 184 had thoracic CT images available for analysis from two time points: at diagnosis and following induction chemotherapy. The CT images were acquired at multiple sites using different machines. The images were reviewed on commercially available PACS software (Centricity, GE Healthcare). Images with artefact distortion, variable image thickness, or inconsistent image spacing were excluded from further analysis, resulting in 88 patients with images from both time points appropriate for further analysis.

CT image analysis

CT-based thoracic muscle volume (75 mm³ with a superior level of T10) and lumbar muscle volume (30 mm³ with a superior level of L1) were measured by two readers. These readers were trained and supervised by two consultant radiologists. The intraclass correlation was 0.91 (95% confidence interval [CI]: 0.82–0.96). Using iNtuition software (TeraRecon, Houston, TX, USA), the volumetric slabs were analysed for the presence of skeletal muscle using a semi-automated technique. First, attenuation thresholds of –29 and 150 HU were applied to the entire image volume, as previously described.³⁰ A colour-coded map of voxels with mean attenuation values within the range of –29 and 150 HU was generated. The non-muscular soft tissues (abdominopelvic viscera, large blood vessels, brain, spinal cord, and portions of the bone marrow) were manually excluded by drawing a region of interest around the identified tissue region. Given the significant variation in muscle volume during the cardiac cycle, respiratory cycle, and peristaltic activity of the gut, the heart, diaphragm, and organs containing smooth muscle were excluded. A series of images containing only skeletal muscle was generated, which yielded a volumetric calculation of whole-body skeletal muscle. Fig. 1 shows an example of the three-dimensional volume rendering of thoracic muscle volume (Fig. 1a) and cross-sectional area, highlighted in green (Fig. 1b). The percentage of low-density muscle (attenuation <0 HU) was recorded from each volumetric slab. Subcutaneous and visceral adipose tissue volumes were segmented from the L1 volumetric slab using a similar semi-automated approach with iNtuition.

PET image analysis

PET was performed before induction chemotherapy in 73.9% of patients (403/545), after induction chemotherapy in 51.4% (280/545), and both before and after induction chemotherapy in 42% (229/545). Of these patients, 65 had both pre- and post-induction chemotherapy PET/CT performed at Memorial Hospital. The images were collected from a range of different machines across the centre. Patients were advised (by phone call) to avoid strenuous physical exertion beginning the night before the scan. Patients fasted 6 h before PET/CT, and blood glucose level was confirmed to be <200 mg/dl before radiotracer injection (400–488 MBq FDG). During and after receiving the FDG injection, the patient rested calmly in a comfortable chair for an hour, without speaking. Standard helical CT for localisation was acquired from the skull vertex to the proximal thighs (maximum 85 mA, 120 kVp). PET imaging was conducted after the CT scan, 55–65 minutes after injection of the FDG tracer. Three-dimensional-mode PET data acquisition was performed for 3–5 minutes per bed position, with six to seven bed positions used, depending on the height of the patient. After review for artefact distortion and image accessibility, 42 patients had technically acceptable pairs of PET/CT images. Skeletal muscle FDG uptake was measured using HERMES Hybrid Viewer software (Hermes Medical Solutions, Stockholm, Sweden) by a single reader who was trained and supervised by a consultant radiologist. A 1.75-cm diameter volume of interest (VOI) was placed in the centre of the muscle, and the peak SUV was recorded. The peak SUV is the mean SUV of voxels within a small, fixed-size (1 cm³) region of interest centred on the highest-uptake part of the tissue within the VOI, and is less affected by image noise than SUV_{max}.³¹

In particular, VOIs were placed within muscles bilaterally on transverse sections passing through the following structures, using low-dose CT images for anatomical guidance: (1) the pectoralis major muscles at the levels of the superior manubrium and the sterno-manubrial junction, (2) the erector spinae muscle at the level of the L3 vertebra, (3) the psoas muscles at the level of the L3 vertebra, (4) the gluteus maximus muscles at the level of the iliac crest, and (5–6) the rectus femoris and vastus lateralis muscles at the level of the mid-femur. These muscles were chosen as representative of axial and limb muscles reported as having varied type I fibre content. The target-to-background ratio (TBR) was calculated by normalising the skeletal muscle peak SUV to the peak SUV obtained from the ascending aorta.

Statistical measures

Patient demographic and clinical characteristics were summarised using descriptive statistics. Body composition metrics (thoracic muscle, low muscle density, lumbar muscle, subcutaneous fat, and visceral fat) were summarised by pre- and post-induction chemotherapy and within-patient raw difference and percentage difference. Comparisons of each metric from pre- to post-induction chemotherapy were conducted using the non-parametric Wilcoxon signed-rank test for paired data. The association between clinical factors and percentage change in muscle volume was examined using univariate linear regression models, with adjustment for baseline muscle volume.

Overall survival was defined as the time between the date of surgery and the date of death or last follow-up. Overall survival was estimated by the Kaplan–Meier method and compared

between groups using the log-rank test. If the Kaplan–Meier curves indicate potential crossing of hazards, the usual log-rank test to compare groups may fail to detect the hazard rate difference, owing to its low power of detecting crossing hazards. Instead, Renyi statistics with Gehan weights were used, placing higher weights on earlier events. Of particular interest was the relationship between overall survival and percentile muscle loss. Patients with <8% muscle loss versus patients with ≥8% loss were examined, because this value was associated with survival in a large cohort of patients with lung or gastrointestinal cancer.¹¹ HRs were estimated using the Cox proportional hazards model. The proportional hazards assumptions for the Cox models were assessed using the scaled Schoenfeld residuals. Multivariable regressions were constructed, starting with all variables with $p < 0.10$ in univariate analyses.

All significance tests were two-sided, with a 5% level of significance. Analyses were performed with Stata 13 (StataCorp, College Station, TX, USA), and the Renyi test was performed using the %_Renyi macro³² in SAS 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Patient characteristics and treatment regimen

Eighty-eight patients were identified with paired thoracic CT images at diagnosis and after induction chemotherapy (before surgical resection). Patient demographic and clinical characteristics are summarised in Table 1. Of note, 41% of patients had a cardiac comorbidity, and 83% had an initial assessment of stage II or III disease. Median tumour size was 3 cm, and FDG-PET-derived tumour SUV ranged from 6.5 (25th percentile) to 13.2 (75th percentile). Patients were treated with either a cytoskeletal disruptor (taxane, 52/88, 59%), a nucleotide analogue (gemcitabine, 25/88, 28%), or a kinase inhibitor (bevacizumab, 7/88, 8%). Seventy-eight percent of patients received three or four cycles of chemotherapy. The median interval between the start of chemotherapy and surgery was 3.4 months (range, 2.9 [25th percentile] to 4.1 [75th percentile] months). During this chemotherapy window, patients received a variable amount of glucocorticoids, ranging from 80 mg (25th percentile) to 160 mg (75th percentile) of dexamethasone equivalents. Following chemotherapy, most patients (77%) underwent a lobar procedure.

Changes in body composition metrics

Body composition was altered during induction chemotherapy (Table 2). Skeletal muscle volume decreased at both the thoracic (−3.3%, $p = 0.0005$) and lumbar (−2.6%, $p = 0.0101$) segments measured. The proportion of skeletal muscle with a density <0 HU increased (7.9%, $p < 0.0001$), reflecting a decrease in muscle density. Measurements of volumetric adipose tissue were not significantly changed; however, a trend for visceral fat to increase at the lumbar segment was noted (4.7%, $p = 0.0568$).

To assess changes in skeletal muscle metabolism, existing PET imaging was used to record FDG uptake from six skeletal muscles in a subset of the cohort, before and after induction chemotherapy (Fig. 2). Although there was no significant alteration in FDG uptake in the pectoralis major or psoas, increases in FDG uptake were identified in the erector spinae

(10.4%, $p=0.0415$), gluteus maximus (12.4%, $p=0.0077$), rectus femoris (31%, $p=0.0260$), and vastus lateralis (25%, $p=0.0063$). Univariate linear regression was used to identify clinical factors associated with muscle loss from pre- to post-induction chemotherapy (Table 3). After adjustment for baseline muscle volume, only the presence of a cardiac comorbidity was significantly associated with loss of skeletal muscle (95% CI: -8.60 to -0.28 , $p=0.037$). Other factors, such as clinical stage, histopathological stage, tumour grade, chemotherapy regimen, and cumulative glucocorticoid dose, did not reach statistical significance.

Associations between body composition metrics and overall survival

Sixty-six of the 88 patients (75%) in the cohort died. Median survival was 3.25 years (95% CI: 2.26–4.11 years). The 3-year overall survival was 51.2% (95% CI: 40.2–61.1%). Patients were stratified by loss of skeletal muscle volume $<8\%$ ($n=62$) or $\geq 8\%$ ($n=26$); Kaplan–Meier curves are shown in Fig. 3. Overall survival did not differ significantly between the two groups ($p=0.273$). In univariate Cox models, none of the clinical variables recorded were significantly associated with the hazard of death (data not shown).

DISCUSSION

To the authors' knowledge, this is the first study to use thoracic CT and PET image-derived measurements to identify trends in body composition and metabolic activity over time. Muscle volume was chosen instead of cross-sectional muscle area because the thorax contains a relatively small amount of skeletal muscle area in a given CT section, compared with the lumbar and sacral regions, which results in high variability between patients. In addition, the use of muscle volume in the thorax limited variation from the respiratory cycle, which the use of cross-sectional muscle area would not have achieved. This technique can be used with diagnostic and scout CT images from PET if the image acquisition settings (image thickness and spacing) are constant.

Patients undergoing induction chemotherapy lost skeletal muscle volume, whereas adipose tissue was not significantly altered. This finding is in agreement with those of Stene *et al.*, who reported a loss of skeletal muscle cross-sectional area from the abdomen during palliative chemotherapy in patients with NSCLC⁷; it is also in agreement with published reports on patients with other cancer types.^{33–37}

The mechanism of skeletal muscle loss in patients with cancer and patients who receive chemotherapy is not known but may include factors such as altered energy balance,³⁸ tumour-released factors,^{39, 40} tumour-induced changes in the stromal environment⁴¹, upregulation of inflammatory cytokines,^{42–44} and hormone dysregulation including altered glucocorticoid levels.⁴⁵ In the present study, only the presence of a cardiac comorbidity was correlated with skeletal muscle loss. This finding could be attributable to reduced exercise tolerance in NSCLC patients with a cardiac comorbidity, which is a strong independent predictor of survival in this population.⁴⁶ A study to carefully document the role of improved exercise tolerance in the survival of NSCLC patients is ongoing () and will help to determine whether a causal relationship exists.

In addition to the loss of skeletal muscle volume, a significant decrease in skeletal muscle density following chemotherapy was detected. A decrease in skeletal muscle density is thought to reflect excess fat deposition and is noted in histopathological conditions such as obesity, type II diabetes, myositis, osteoarthritis, spinal stenosis, and cancer.⁴⁷ Previous studies have shown that low skeletal density is an important prognostic factor in patients with melanoma, renal cell carcinoma, follicular lymphoma, and metastatic gastric cancer;^{48–51} however, no such relationship was found in the present population.

Many pathological conditions associated with low skeletal muscle density coincide with reduced FDG uptake.^{52, 53} Interestingly, a significant increase in FDG uptake in the muscles of the back and lower extremity was found following chemotherapy. This phenomenon has also been observed in patients with metastatic melanoma following treatment with the alkylating agent temozolomide.²⁸ Several factors are known to influence skeletal muscle FDG uptake, including muscle fibre composition, muscle activity, plasma glucose levels, insulin concentrations, and the presence of inflammatory cells.^{54–56} Cytotoxic chemotherapy appears to alter skeletal muscle metabolism favouring glucose uptake.

This study did not find a correlation between muscle loss during chemotherapy and overall survival. For this analysis, patients were dichotomised using a cut-off value of 8%, as this value was identified as clinically relevant in a large North American population of patients with lung and gastrointestinal cancers.¹¹ Using a smaller cut-off value of 2%, Stene *et al.* were also unable to demonstrate a significant relationship between muscle loss and survival.⁷ These findings suggest that changes in skeletal muscle mass during chemotherapy do not directly affect overall survival, which should be reassuring for clinicians.

The present study is limited by its retrospective nature, which can lead to a selection bias. A large portion of the cohort had advanced disease and a cardiac comorbidity, both of which are likely to be confounding variables. In addition, there was heterogeneity in the treatment regimen between individuals, which may skew the data. A historic cohort was chosen to allow for at least a decade of long-term follow-up data. There have been significant advancements in CT and PET technology since the time of image acquisition (2000–2006). Although the advancements in data acquisition and processing have not biased the volumetric measures of skeletal muscle or the relative uptake in FDG over time, these hypotheses were not formally tested in the present study, and this is a limitation.

A major source of attrition in the present study was the lack of availability of matched data sets over time. Patients frequently arrive at Memorial Hospital for a transition of care following diagnosis at an outside institution. During this transition, the CT images from diagnosis are commonly lost. Additionally, much of the quantitative information from the scans that are received and successfully uploaded is lost due to change in formatting of the stored images. In the present study, only 34% (184/545) of the patients had matching scans that could be used for volumetric analysis. Upon closer scrutiny of these 184 matched pairs, many cases (96/184) used different image collection parameters between the two time points. For example, a range of image spacing (4, 4.25, 5, 7.5 mm) and thickness (1.25, 5, 7.5, 10 mm) were observed and could not be directly compared with the calculated muscle volume between diagnosis and following chemotherapy. Part of this heterogeneity was due

to the different types of machines used to collect the images, and this is a limitation of the study's design. Similarly, the major cause of loss of PET-CT patients was the lack of matched pairs over time. It is possible, albeit unlikely, that patients with these technical difficulties comprise a unique population that is underrepresented in the present cohort.

Other limitations of the study include the low number of non-white participants in the study, which may limit its applicability to other racial groups. The PET analysis is limited because SUV is a semi-quantitative metric that depends on patient preparation, scanning procedure, image reconstruction, and image analysis procedures. At Memorial Hospital, however, conditions are standardised to limit patient-to-patient variation. There was widespread use of glucocorticoids in the present patient population, which may induce insulin resistance and reduce FDG uptake. Therefore, the present study is limited by the lack of serum inflammatory markers or measures of endogenous muscle altering hormones, such as insulin, insulin-like growth factors, and cortisol.

In conclusion, despite these limitations, this study described the changes that occur in skeletal muscle volume, density, and FDG uptake during chemotherapy treatment. These findings highlight the breadth of information that can be garnered from repurposing diagnostic imaging. Skeletal muscle volume and density are lost during chemotherapy; however, there was no impact on survival in this retrospective series, and further validation in prospective, well-controlled studies is required.

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Highlights

- Weight loss is common and predictive in patients with NSCLC; however, the composition of this lost weight is unknown.
- Conventional thoracic CT and PET/CT imaging can identify changes in skeletal muscle and adipose tissue volume, density, and FDG uptake during cancer therapy.
- Following chemotherapy, skeletal muscle volume and metabolism are altered; however, there was no impact on survival in this retrospective series, and further validation in prospective, well-controlled studies is required.

Figure 1. Segmented thoracic muscle volume. Three-dimensional volume rendering of thoracic muscle volume (a,c) and cross-sectional skeletal muscle contouring, highlighted in green (b,d). (a,b) Images from a patient showing markedly reduced thoracic muscle volume (490 cm³), compared with (c,d) another patient (826 cm³) with the same body mass index (29 kg/m²).

Figure 2.

Change in FDG uptake following induction chemotherapy. Percentage change in the target-to-background ratio of the peak SUV following induction chemotherapy in the pectoralis major (PM), psoas (PS), erector spinae (ES), gluteus maximus (GM), rectus femoris (RF), and vastus lateralis (VL) muscles. * $p < 0.05$, ** $p < 0.01$.

Figure 3.

Kaplan–Meier survival curves according to change in muscle volume. Survival curves for subjects who lost <8% (black) or ≥8% (red) muscle volume during induction chemotherapy.

Table 1.Demographic and Clinical Characteristics of the Study Cohort (*N*=88)

Characteristic	Value
Age	64.7 (54.8, 71.3)
Sex, female	46 (52)
Race	
White	77 (88)
Hispanic	2 (2)
Black	6 (7)
Northern Asian	2 (2)
Unknown	1 (1)
Weight, kg (<i>n</i> =87)	73.8 (62.6, 84)
Height, cm (<i>n</i> =87)	164 (160, 175)
BMI, kg/m ² (<i>n</i> =87)	26.4 (23.2, 29.5)
Comorbidity	
Pulmonary	22 (25)
Cardiac	36 (41)
Endocrine	8 (9)
Other cancer	22 (25)
FEV1, % expected (<i>n</i> =87)	87 (75, 98)
DLC0, % expected (<i>n</i> =87)	71 (60, 85)
Clinical stage	
I	12 (14)
II	15 (17)
III	58 (66)
IV	3 (3)
Initial tumour SUV (<i>n</i> =77)	9 (6.5, 13.2)
Initial tumour size, cm (<i>n</i> =82)	3 (2, 4.5)
Histopathological subtype	
Squamous	15 (17)
Adenocarcinoma	57 (65)
Bronchioloalveolar	1 (1)
Large cell undifferentiated	9 (10)
Large cell neuroendocrine	6 (7)
Poor tumour grade (<i>n</i> =71)	48 (68)
Vascular invasion, present (<i>n</i> =72)	35 (49)
Perineural invasion, present (<i>n</i> =69)	6 (9)
Histopathological stage	
0	5 (6)
I	21 (24)
II	13 (15)
III	41 (47)

Characteristic	Value
IV	8 (9)
Chemotherapy regimen	
Taxane based	52 (59)
Gemcitabine based	25 (28)
Bevacizumab containing	7 (8)
Other	4 (5)
Number of chemotherapy cycles ($n=82$)	
2	12 (15)
3	33 (40)
4	31 (38)
5	3 (4)
6	3 (4)
Cumulative glucocorticoid dose ($n=85$)	104.5 (80, 160)
Procedure	
Lobar	68 (77)
Pneumonectomy	13 (15)
Exploration	7 (8)

Data are no. (%) or median (25th, 75th percentile).

BMI, body mass index; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; SUV, standardised uptake value.

Table 2.

Measurements before and after induction chemotherapy

Measurement	Before induction chemotherapy	After induction chemotherapy	Raw difference (within patient)	Percentage difference (within patient)	<i>p</i> -Value ^a
Thoracic muscle, cm ³	558.5 (474.5, 688.5)	531.5 (462.5, 685)	-18.5 (-53.5, 15)	-3.3 (-9.9, 2.5)	0.0005
Low muscle density, % <0 HU (<i>n</i> =81)	14.3 (11.6, 18.2)	16 (13, 19.9)	1.3 (-0.2, 2.2)	7.9 (-1.3, 18)	<0.0001
Lumbar muscle, cm ³ (<i>n</i> =78)	296.5 (249, 369)	283 (241, 337)	-7 (-24, 4)	-2.6 (-7.7, 1.7)	0.0101
Subcutaneous fat, cm ³ (<i>n</i> =77)	303 (178, 425)	286.5 (189.5, 408)	7 (-20, 33)	1.8 (-7.6, 17.2)	0.4310
Visceral fat, cm ³ (<i>n</i> =77)	272 (162, 504)	308.5 (163.5, 457.5)	12 (-17, 50)	4.7 (-6.3, 29.2)	0.0568

Data are median (25th, 75th percentile).

^aDerived from the Wilcoxon signed-rank test (nonparametric version of the paired *t* test), comparing the pre- and post-induction chemotherapy measurements for each patient. We used the paired test because the pre- and post-induction chemotherapy values are for the same patient, rather than from two independent groups. A significant *p*-value indicates that the pre and post values were significantly different.

Table 3.

Univariate linear regression of percentage change after adjustment for baseline muscle value

Variable	Coefficient	95% CI	p-Value
Age	-0.07	-0.28, 0.14	0.5
Male	1.07	-4.50, 6.64	0.7
Comorbidity			
Pulmonary	-0.86	-5.71, 3.99	0.7
Cardiac	-4.44	-8.60, -0.28	0.037
Endocrine	1.10	-6.42, 8.62	0.8
Other cancer	2.61	-2.20, 7.42	0.3
FEV1, % expected	0.02	-0.10, 0.14	0.7
DLCO, % expected	0.08	-0.05, 0.20	0.2
Initial stage			
II	2.02	-5.71, 9.76	0.6
III	0.55	-5.76, 6.86	0.9
IV	0.10	-12.74, 12.93	1
Initial tumour SUV	0.18	-0.18, 0.54	0.3
Poor tumour grade	4.65	-0.35, 9.66	0.068
Histopathological stage			
0	8.96	-0.67, 18.59	0.068
II	4.14	-2.69, 10.97	0.2
III	3.39	-1.83, 8.60	0.2
IV	-2.01	-10.06, 6.04	0.6
Number of chemotherapy cycles	0.05	-2.43, 2.52	1
Pneumonectomy	-1.09	-7.09, 4.91	0.7
Exploration	0.17	-7.84, 8.18	1
Chemotherapy regimen			0.5
Bevacizumab containing	26.4	-19.6, 72.5	0.3
Gemcitabine based	16.1	-11.7, 44.0	0.3
Other	11.2	-48.1, 70.6	0.7
Cumulative glucocorticoid dose	-0.00	-0.03, 0.02	0.9

CI, confidence interval; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; SUV, standardised uptake value.