

# Low thoracic muscle radiation attenuation is associated with postoperative pneumonia following partial hepatectomy for colorectal metastasis

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ORIGINAL ARTICLE

# Low thoracic muscle radiation attenuation is associated with postoperative pneumonia following partial hepatectomy for colorectal metastasis

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## Abstract

**Background:** Low skeletal muscle radiation attenuation (SM-RA) is indicative of myosteosis and diminished muscle function. It is predictive of poor outcome following oncological surgery in several cancer types. Postoperative pneumonia is a known risk factor for increased postoperative mortality. We hypothesized that low SM-RA of the respiratory muscles at the 4th thoracic-vertebra (T4) is associated with postoperative pneumonia following liver surgery.

**Methods:** Postoperative pneumonia was identified using prospective infection control data. Computed tomography body composition analysis was performed at the L3- and T4 level to determine SM-RA. Body composition variables were corrected for confounders and related to postoperative pneumonia and admission time by multivariable logistic regression.

**Results:** Body composition analysis of 180 patients was performed. Twenty-one patients developed postoperative pneumonia (11.6%). Multivariable analysis showed that low T4 SM-RA as well as low L3 SM-RA were significantly associated with postoperative pneumonia (OR 3.65, 95% CI 1.41–9.49,  $p < 0.01$ ) and (OR 3.22, 95% CI 1.20–8.61,  $p = 0.02$ , respectively).

**Conclusion:** Low SM-RA at either the L3- or T4-level is associated with a higher risk of postoperative pneumonia following CLRM resection.

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## Introduction

The impact of sarcopenia and muscle wasting on the efficacy of treatment and outcome following oncological surgery has been widely established.<sup>1–4</sup> Sarcopenia has been shown to be associated with reduced pulmonary function in healthy adults, as well as with increased pulmonary complications following oncological esophageal resection.<sup>5–9</sup> In addition, skeletal muscle

radiation attenuation (SM-RA) has emerged as a radiological marker indicative of myosteosis, which has been shown to be predictive of poor outcome following oncological surgery.<sup>2,10,11,48</sup> Myosteosis is characterized by increased inter- and intra-myocellular fat stores, which can be influenced by dietary pattern and activity changes. This is related to reduced physical fitness and reduced muscle function.<sup>12–16</sup>

Postoperative pneumonia has been shown to increase postoperative morbidity, prolong hospital admission, and increase in-hospital mortality following a range of surgical interventions, most notably after major abdominal and upper gastro-intestinal surgery.<sup>17–21</sup> More specifically, patients undergoing partial hepatectomy frequently develop reactive pleural effusion, which increases the risk of post-operative pneumonia to incidences above 10%.<sup>17,19–24</sup> Besides the medical implications, pulmonary complications constitute a significant burden to healthcare systems by increasing healthcare costs.<sup>19,22</sup>

Recent developments in perioperative patient conditioning have suggested that prehabilitation training can increase preoperative aerobic condition, thereby reducing postoperative pneumonia following major abdominal surgery.<sup>25</sup> To that end, identifying patients at risk for postoperative pneumonia is of paramount importance.

Bearing in mind that SM-RA is indicative of muscle function, we hypothesized that low SM-RA is indicative of increased risk of postoperative pneumonia, and that SM-RA predicts postoperative pneumonia better than muscle mass. Furthermore, we hypothesized that SM-RA assessed at the 4th thoracic vertebra (T4) predicts postoperative pneumonia better than SM-RA measurements at the 3rd lumbar vertebra (L3), when assuming that it reflects thoracic muscle myosteatosis.

Thus, the aims of this study were 1) to assess whether reduced SM-RA is associated with increased postoperative pneumonia, and 2) to investigate whether T4 SM-RA has a stronger association with postoperative pneumonia than L3 SM-RA.

## Materials and methods

### Study design

Prospective infection control data of a cohort of patients aged 18 years and older who underwent elective CRLM resection between January 2008 and December 2013 at Maastricht University Medical Center were collected. Exclusion criteria included American Society of Anesthesiology (ASA)-classification V, severe liver cirrhosis (Child grade C), end-stage renal disease requiring dialysis, severe heart disease (New York Heart Association class IV) and chronic obstructive pulmonary disease (COPD) requiring (home)oxygen therapy. Furthermore, patients were excluded from analysis if their CT scans did not show the thoracic or abdominal wall or displayed large radiation artifacts, if they had a time interval greater than three months between the time of the scan and surgery, and if the thoracic and abdominal scans were not performed at the same time.

Besides body composition data, sex, age, ASA-classification (<3 and  $\geq 3$ ), smoking, planned type of procedure (laparoscopic or open), comorbidities, and body mass index (BMI), Portal Vein Embolization (PVE), neoadjuvant chemotherapy, tumor stage (1–2 versus 3–4), duration of surgery, minor versus major liver resection (<3 and  $\geq 3$  liver segments), and left-versus right-sided liver resections were considered potential

confounders.<sup>26,27</sup> Right-sided resections were hypothesized to have an increased risk of pleural effusion and thus an increased risk of pneumonia.<sup>24</sup>

The primary endpoint was the occurrence of postoperative pneumonia as defined below. The secondary outcomes were length of hospital stay, in hospital mortality, and 30-day mortality. In addition, we evaluated the association with major abdominal complications rather than selectively evaluating postoperative pneumonia, to explore whether pneumonia was a surrogate for major abdominal complications, and whether reduced SM-RA was associated with major complications. Data was reported in accordance with STROBE guidelines for reporting of observational COHORT studies.<sup>28</sup>

### Defining postoperative pneumonia

Pulmonary infection data were prospectively acquired by a study nurse in collaboration with clinicians and infection specialists in the context of compliance to national quality control guidelines. The criteria for respiratory infection were set as a fever greater than 38 °C, chest pain, dyspnea and cough including expectoration developing within 30 days of surgery in addition to an infiltration visible on the chest x-ray, regardless of the presence or absence of bacteria in the sputum.<sup>29</sup> Because these data were ascertained in the context of a quality control evaluation, no blinding was performed. Clinical evaluation was performed by the treating surgeon and the evaluation of the chest x-ray was performed by the on-duty radiologist.

### Defining major abdominal complications

We used the liver surgery-specific composite endpoint (LSSCEP) composed of postoperative liver failure, bile leakage, intra-abdominal hemorrhage, intra-abdominal abscess, and mortality to assess liver surgery-specific complications.<sup>30</sup> Liver failure was defined according to the peak bilirubin criterion of Mullen *et al.*<sup>31</sup> Patients were defined as having suffered a major abdominal complication if at least one LSSCEP event had occurred.

### CT body composition analysis

Muscle mass was assessed by analyses of electronically stored CT images; these CT scans were part of routine clinical work. Body composition analysis of abdominal and thoracic CT scans was performed. CT scans were selected and analyzed blindly by a single investigator using Slice-O-matic software, version 5.0 (Tomovision, Montreal, QC, Canada).

### Abdominal body composition measurements

L3 was used as a standard landmark to measure tissue cross-sectional area in cm<sup>2</sup> as previously reported.<sup>2</sup> In short, skeletal muscle (SM), visceral adipose tissue (VAT), and subcutaneous adipose tissue (SAT) were identified and quantified on CT images using predefined Hounsfield unit (HU) ranges (SM: -29 to 150 HU, VAT: -150 to -50 HU, and SAT: -190 to -30 HU).<sup>32</sup>

**Table 1** Treatment and Disease characteristics

	Pneumonia		P Value	Percent of total
	no	yes		
Duration of surgery (minutes) (Mean 215) <sup>a</sup>	(OR 1.00, 95% CI 0.99–1.01)		0.12	
Type of Resection <sup>a</sup>			0.16	
minor	97	9		53.3%
major	62	12		46.7%
T-Stage			0.30	
1–2	21	3		13.3%
3–4	137	19		86.7%
Neoadjuvant chemotherapy			0.32	
no	51	4		30.5%
yes	108	17		69.5%
Right sided resection <sup>b</sup>			0.55	
other	138	18		86.7%
right sides resection	21	3		13.3%
PVE (portal vein embolization) <sup>c</sup>			0.60	
no	155	21		97.8%
yes	4	0		2.2%

Table showing treatment and disease characteristics as well as their association with the primary outcome using univariate binary logistic regression analysis.

<sup>a</sup> Type of resection defined as minor when  $2 \leq$  segments resected, major when  $\geq$  segments resected.

<sup>b</sup> Right sided resection includes right sides hemi-hepatectomy and extended right resection.

<sup>c</sup> Portal vein embolization is performed to promote liver regeneration prior to surgery, ensure adequate functional liver remnant after resection. P-value calculated through Chi-square or fisher exact testing.

SMA, VAT, and SAT were corrected for stature to calculate the L3-muscle index, L3-VAT index, and L3-SAT index in  $\text{cm}^2/\text{m}^2$ , providing good estimates of total body SM, VAT, and SAT mass.<sup>32</sup> Cut offs were established based on tertiles (see statistical analysis) (Table 2).

#### Thoracic body composition measurements

T4 was used as a standard landmark to measure tissue cross-sectional area in  $\text{cm}^2$ . SMA and SAT were identified and quantified on CT images using the same predefined Hounsfield unit (HU) ranges as in the abdominal scans (Fig. 1). The total areas of SMA and SAT were corrected for stature to calculate the T4-muscle index (T4-muscle-index and T4-SAT-index).

#### Muscle radiation attenuation

The radiation attenuation for skeletal muscle (SM-RA) at L3 and T4 level was assessed by calculating the average HU value of the total muscle area within the specified range of -29 to 150 HU (excluding intramuscular adipose tissue).

#### Statistical analyses

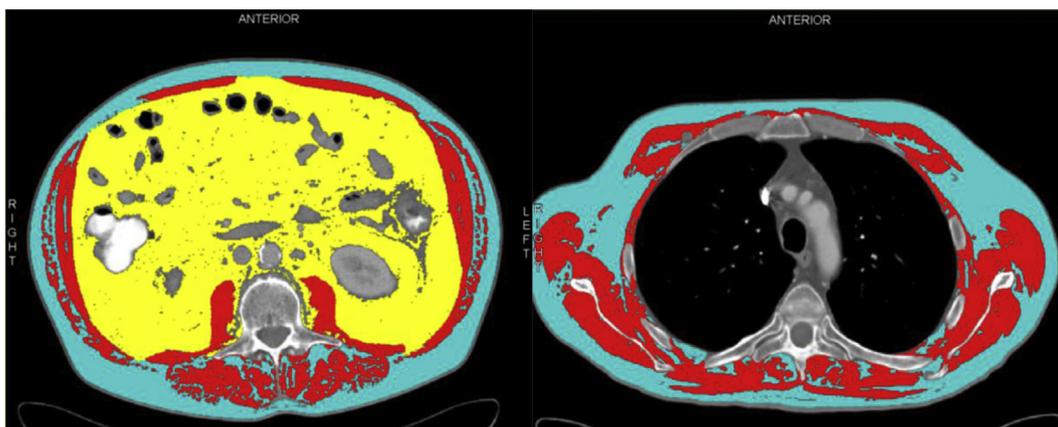
##### Cut-offs

Previously published cut-off values for L3-muscle-index were established in cohorts of patients with different demographics and ethnicities, and may not be comparable with the present Dutch cohort of patients with CRLM.<sup>26,33–35</sup> Therefore, we decided to determine our own cut-offs for L3-muscle-index, as

**Table 2** Calculated sex-specific cut-offs for body composition variables used in this study

	Units	Female cut off (mean - SD)	Male cut off (mean - SD)	Mean Cohort
L3-muscle-index	$\text{cm}^2/\text{m}^2$	36.8 (40.3–5.9)	46.6 (50.1–7.9)	46.5
L3-SM-RA	HU	29.4 (32.9–9.0)	31.0 (34.8–8.2)	34.1
L3-VAT-index	$\text{cm}^2/\text{m}^2$	23.9 (39.7–23.9)	46.7 (60.9–28.7)	53.0
L3-SAT-index	$\text{cm}^2/\text{m}^2$	69.9 (84.5–34.7)	43.9 (55.2–24.9)	66.1
T4-muscle-index	$\text{cm}^2/\text{m}^2$	51.9 (58.4–13.0)	65.2 (71.0–14.3)	66.3
T4-muscle-attenuation	HU	36.2 (38.6–6.9)	(48) (39.7–6.0)	39.2
T4-SAT-index	$\text{cm}^2/\text{m}^2$	61.4 (76.4–32.2)	42.1 (53.0–21.0)	66.1

Sex-specific cut-offs and mean value based on tertiles of our cohort for each body composition variable.



**Figure 1** Body composition segmentation. CT image of one patient suffering from myosteatorsis at the L3 (left) and T4 (right) level, with muscle groups and fat segmentation: red (muscle), blue (subcutaneous fat) and yellow (visceral fat)

performed by other studies with similar population sizes.<sup>2,36</sup> Due to the fact that no consensus cut-offs exist for thoracic muscle mass, abdominal SM-RA, and thoracic SM-RA, we also stratified these parameters using cut-offs based on the current cohort.

We considered our cohort too small for cut-point analysis by optimal stratification, and therefore determined cut-off values based on tertiles stratified by sex.<sup>37</sup> Determining the cut-off at a tertile enables comparison between groups with a relatively low/high value to be compared with the rest of the group while not forcing subjects with a value around the cut-off value in a low or high category. Cut-off values were set at the lowest tertile for all body composition variables (Table 2).

#### Univariable analysis

Univariable logistic regression analyses were used to determine the association between each individual variable and the occurrence of postoperative pneumonia and 30-day mortality. For patient characteristics, Student's t-test was used for continuous variables, with or without equal variances assumed based on Levene's test. For categorical variables, the Chi-square test was used; Fisher's exact test was used when necessary. The correlation between two continuous variables was examined with a Pearson's correlation coefficient. A p-value of <0.05 was considered significant. For the outcome of length of hospital stay, the log rank test and the cox regression model were used to determine the association between each variable and length of hospital stay. Patients that died during their hospital stay were censored.

#### Multivariable analysis

Variables with a p-value <0.10 in univariable analyses were included in multivariable analysis. Multivariable logistic regression analysis was used to assess the association between our study variables and the occurrence of post-operative pneumonia. Due to the limited number of events, there was limited power to perform multivariable analysis. Therefore, we opted to use

stepwise backward elimination regression, with elimination set at a p-value >0.1. Multivariable cox regression analysis was used to assess the association between the study variables and length of hospital stay in which patients that died during hospital admission were censored. All statistical analyses were performed using IBM SPSS version 24.0.

## Results

### Patient cohort

A total of 250 patients were included in the cohort. Body composition analysis of 180 patients could be performed. Fourteen patients were excluded on the basis of poor quality of CT scans, 21 were excluded due to scans not showing the thoracic or abdominal wall, and 20 patients were excluded due to an interval greater than three months between the time of the scan and surgery. Fifteen patients were excluded due to the abdominal and thoracic CT scans not being performed at the same time. Twenty-one patients suffered from postoperative pneumonia. In total 36 Patients suffered at least one LSSCEP event constituting a positive LSSCEP (Appendix 3). The median hospital stay was 8 days (SD 14.8). Five patients (2,7%) died during admission, or within 30 days of surgery. Sixty-three percent of patients were male, with a mean age of 64.3 and a mean BMI of 26.3 kg/m<sup>2</sup>. Eleven percent of resections were performed laparoscopically. The treatment and disease characteristics of the patients are listed in Table 1. No significant association between treatment or disease characteristics and the occurrence of pneumonia was observed. SM-RA was comparable between patients receiving and not receiving preoperative chemotherapy at T4 level (mean 39.4 HU (SD 6.4 HU)) and (mean 38.9 HU (6.3 HU)), and L3 level (mean 34.1 HU (SD 8.3 HU)) and (mean 34.2 HU(SD 8.9 HU)). Mean and sex-specific cut-off values for all CT-derived body composition parameters are shown in Table 2. There was no missing data, all patients were included in the multivariable models.

## Thoracic and abdominal body composition imaging methods

L3 and T4 measurements of both SMA and SM-RA showed significant correlations, with T4 and L3 SMA showing a stronger correlation ( $r = 0.78$ ,  $p < 0.001$ ,  $r^2 = 0.60$ ) than T4 and L3 SM-RA ( $r = 0.43$ ,  $p < 0.001$ ,  $r^2 = 0.18$ ) (Fig. 2). Intra-observer reliability was ascertained by performing blinded re-segmentation of a subset of L3 and T4 scans ( $N = 25$ ). Intra-observer reliability was similar in both groups with correlation coefficient of 0.98 (95% CI 0.95–0.99) for T4 SM-RA and 0.99 (95% CI 0.98–0.99) for L3 SM-RA.

## Univariable analysis

Univariable analysis (Appendix 1) indicated that low T4 SM-RA was associated with a high risk of postoperative pneumonia (OR 2.74, 95% CI 1.22–6.12,  $p = 0.01$ ). Low L3 SM-RA (OR 2.20, 95% CI 0.99–4.89,  $p = 0.05$ ), increased BMI (OR 0.89, 95% CI 0.78–1.02,  $p = 0.09$ ), and increased age (OR 1.04, 95% CI 0.99–1.09,  $p = 0.09$ ) were not significant, however were included in multivariable analysis. Low L3 SM-RA (HR 1.45, 95% CI 1.05–2.01,  $p = 0.03$ ), low T4 SM-RA (HR 1.40, 95% CI 1.01–1.94,  $p = 0.04$ ), increased age (HR 0.98, 95% CI 0.97–0.99,  $p = 0.03$ ), as well as open procedure (HR 3.16, 95% CI 1.92–5.21,  $p < 0.01$ ) were associated with hospital stay in univariable cox-regression analysis (Appendix 2). Postoperative pneumonia and a positive LSSCEP were significantly associated ( $p < 0.01$ ). 62% of patients with postoperative pneumonia also had positive LSSCEP ( $n = 13$ ). However, no significant association was found between any of our study variables and a positive LSSCEP.

## Multivariable analysis

Due to co-linearity between L3 and T4 SMA and SM-RA, we created two multivariable models for the occurrence of postoperative pneumonia and increased length of hospital stay containing 1) L3 SM-RA and 2) T4 SM-RA. In both L3 and T4 multivariable models, low SM-RA remained associated with

increased risk of postoperative pneumonia, when corrected for BMI and age (Fig. 3 & Appendix 1). T4 SM-RA showed a similar odds ratio (OR 3.65, 95% CI 1.41–9.49,  $p < 0.01$ ) compared to L3 SM-RA (OR 3.22, 95% CI 1.20–8.61,  $p = 0.02$ ). To evaluate the effect of SM-RA as a continuous variable rather than a binary variable we inserted SM-RA as a continuous variable into our multivariable analysis and observed no change in our conclusion. In both multivariable analyses T4 SM-RA and L3 SM-RA remained significantly associated with postoperative pneumonia OR 0.91 (95% CI 0.84–0.99,  $P=0.02$ ) and OR 0.92 (95% CI 0.87–0.98,  $P=0.01$ ) respectively. Multivariable analysis for hospital admission showed that in both L3 and T4 models, open versus laparoscopic procedure (HR 3.43, 95% CI 2.07–5.70,  $p < 0.01$  in both models) and increased age (HR 0.98, 95% CI 0.96–0.99,  $p = 0.01$  in both models) were associated with hospital stay. In contrast, L3 and T4 SM-RA were not (HR 1.33, 95% CI 0.94–1.88,  $p = 0.11$ ; HR 1.32, 95% CI 0.94–1.86,  $p = 0.11$ , respectively) (Fig. 3, Appendix 2).

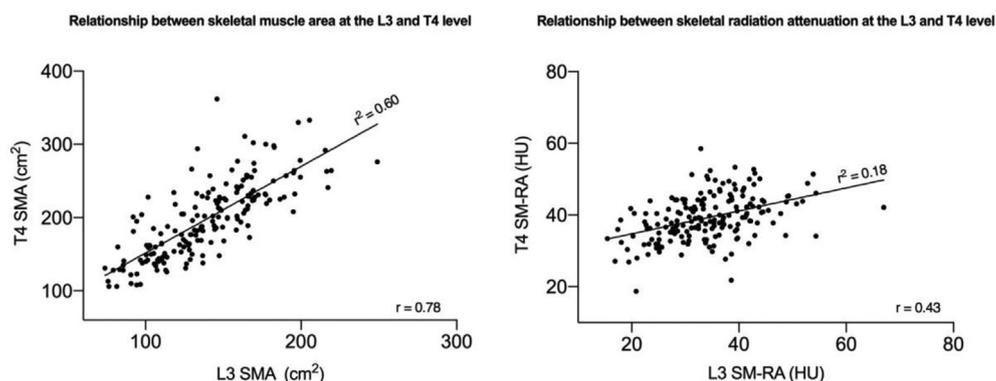
## Mortality

Five patients (3%) died within the same admission or within 30 days of surgery. Due to this limited number of events, we could not perform multivariable analysis. We did, however, observe a higher postoperative mortality in patients suffering from postoperative pneumonia (4/21 vs 1/159,  $p = 0.001$ ).

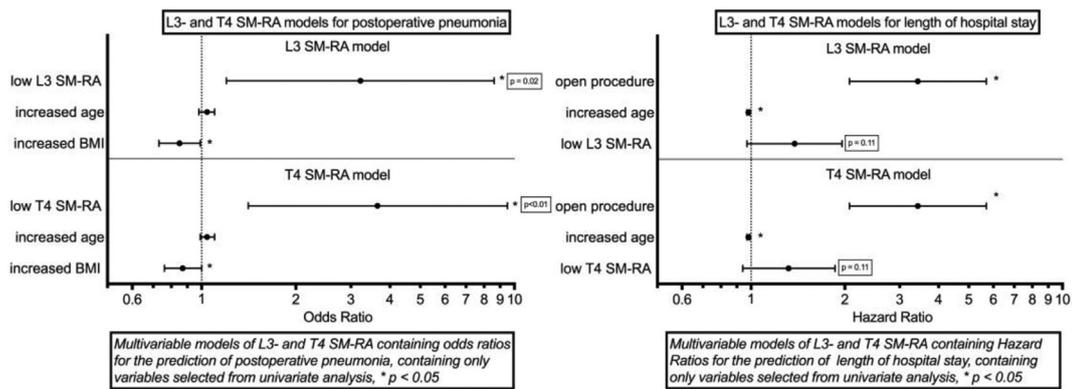
## Discussion

Our data suggest that low SM-RA as assessed at both the L3 and T4 level is associated with an increased risk of occurrence of postoperative pneumonia.

The impact of sarcopenia as a risk factor for pulmonary complications has previously been described in studies investigating the association between L3 muscle mass and outcome following esophageal resection.<sup>6,8,9</sup> Low appendicular muscle



**Figure 2** Relationship between skeletal muscle area (SMA) and skeletal muscle radiation attenuation (SM-RA) at the L3 and T4 level. Scatter plots for the correlation between L3- and T4 SMA ( $r = 0.78$ ,  $p < 0.01$ ) and L3 and T4 SM-RA ( $r = 0.43$ ,  $p < 0.01$ ). Correlation measured with Pearson correlation testing



**Figure 3** L3 and T4 multivariable models for the occurrence of postoperative pneumonia and length of hospital stay

mass has also been associated with a higher risk of aspiration pneumonia and 90 day mortality in older patients.<sup>7</sup> Moon *et al.* performed a population wide study in a large cohort of patients aged 65 years and over, and showed that low appendicular muscle mass was independently associated with decreased forced expiratory value and forced vital capacity, which are clinical indicators of pulmonary function.<sup>5</sup> Recently, Rozenberg *et al.* demonstrated that thoracic muscle cross-sectional area was associated with longer hospital stay following lung transplantation.<sup>38</sup> In their study, however, cross-sectional thoracic muscle area was not corrected for patient stature, and therefore did not reflect whole body muscle mass. Furthermore, no comparison between thoracic muscle mass and validated L3 measurements for total body muscle mass measurements or SM-RA were performed.

In the clinical setting, CT scans are not performed for the purpose of body composition imaging, but rather to perform tumor staging or assess oncological dissemination. As a consequence, CT scans made in the context of non-abdominal oncological pathologies often do not extend to the L3 level. We therefore argue that T4 SM-RA reflecting thoracic myosteatosis may be a valuable body composition parameter, in particular when no recent abdominal scan is available. The current study therefore holds clinical relevance for cohorts where patients only receive thoracic CT imaging, or in cohorts where only upper abdominal scans are performed, such as in head/neck, lung or upper abdominal cancers like primary liver cancer.

Skeletal muscle radiation attenuation (SM-RA) is a radiological marker of myosteatosis, which is characterized by an increase in intra- and extramyocellular fat deposits, and is highly variable amongst cancer patients.<sup>13,39</sup> Sarcopenia is characterized by a loss of muscle mass. Both sarcopenia and myosteatosis have been found to be independent prognostic factors of reduced survival and poor outcome after surgery or neoadjuvant treatments in various cancer types. A recent study (West MA *et al.*) has shown that reduced SM-RA is associated with a reduction in cardio-pulmonary fitness in a HPB population, whereas sarcopenia is not.<sup>40</sup> It can therefore be argued that, although sarcopenia and

myosteatosis are both associated with poor outcome, they may not be surrogates of the same thing, but rather, that myosteatosis is associated with muscle function, and sarcopenia is associated with muscle mass. This however remains a topic of ongoing research, in which the pathophysiological mechanisms are yet to be clearly defined. In our cohort we found low correlation between SMA and SMRA at the L3 and T4 level ( $r = 0.21$ ,  $p < 0.05$  and  $r = 0.15$ ,  $p = 0.05$ ) respectively.

The pathophysiological mechanism which may underlie the association between myosteatosis in the thoracic compartment and pneumonia is not clear. It is known that coughing is the most immediate protective mechanism from aspiration, requiring the coordinated activation of inspiratory, expiratory, and intrinsic laryngeal muscles.<sup>41,42</sup> Sillanpaa *et al.* investigated interdependency between muscle strength and spirometric pulmonary functions in healthy older men and women and observed that reduced muscle strength was associated with reduced pulmonary function.<sup>43</sup> It can be hypothesized that a muscle wasting or myosteatosis associated decline of thoracic muscle function reduces this functional protection mechanisms against pneumonia, thus increasing the risk of postoperative pneumonia. Our study suggests that both reduced thoracic and lumbar SM-RA show a significant association with postoperative pneumonia.

Although CT scans were evaluated retrospectively, pneumonia data were collected prospectively by an independent infection registration nurse for quality control purposes. Nevertheless, the use of unvalidated body composition imaging techniques warrants caution and can lead to false premises.<sup>44</sup> The limitations of this study must therefore be mentioned. Of the 250 potential cases, 23 were excluded because the thoracic wall was not completely shown. This is a problem seen more often in thoracic scans and related to the fact that thoracic circumference is usually larger than abdominal circumference. Furthermore, subcutaneous thoracic tissue is often segmented out by technicians editing the images because it is traditionally not considered to hold clinical relevance. Our secondary endpoint - length of hospital stay, did not show any association with body composition parameters in multivariable analysis. It must be noted that the

retrospectively acquired data regarding discharge generally do not accurately represent the time at which the patient is ready for discharge.<sup>45</sup> This means that social or other non-medical reasons for a prolonged hospital stay were not considered in the current study. It must also be noted that the plots showing the correlation between L3 and T4 measurements are notably scattered (Fig. 2). This may be caused by biological variation as well as measurement error. In our experience T4 segmentation was slightly more difficult to perform as bone structure needs to be more diligently segmented out of the bodycomposition analysis. We therefore performed an inter-observer analysis which observed similar correlation between L3 and T4 images segmentations. Another explanation for the notable scatter could be a skewed distribution of SM-RA and SMA variables. To better visualize the distribution of T4 and L3 values, we created Z-values by subtracting the mean from each value and dividing it by the standard deviation. Visually, the distribution for SM-RA at L3 and T4 level seem similar. However, L3 measurements were notably skewed (L3 skewness 0.4, T4 Skewness 0.03). To normalize skew, we performed a log normal transformation on L3 and T4 SM-RA, as well as L3 and T4 SMA and found that this did not correct the skew. We subsequently re-plotted the corresponding scatter plots and did not see an improvement in the variation seen in the scatter plots. It may therefore be argued that the scatter seen is indeed a result of biological variation. Another possible reason for variation in measurements could be due to patient-to-patient differences in the axial orientation in the CT scanner, which could lead to variation in segmentation measurements. It is, in the clinical setting, unrealistic to expect an absolutely perfect patient orientation in the CT-scanner. It could be argued that variations in measurements due to imperfect patient orientation may lead to statistical ‘noise’ in our results. However, we expect variations in measurements due to differences in patient orientation to be minimal.

We neither used previously published cutpoints for SM-RA in our cohort, nor did we create our own stratified cutpoints. In our opinion both the use of previously established cut-offs and establishing of new cut-offs should be approached with caution because it insinuates what should be considered “normal” or “abnormal” bodycomposition values. Body composition varies greatly among regions and ethnicities as illustrated by the large Japanese cohort study of Fujiwara *et al.*, which found highly different cut-offs compared with the study of Martin (e.g. female cut-off for L3-muscle index at 29.6 in the Japanese cohort versus 41 in the Canadian cohort).<sup>26,33</sup> Further-more optimum stratification for establishing cutoffs works well for large cohorts in which the lowest P-value will be used to set the cut-off.<sup>46</sup> However, in smaller cohorts, the P-value is too unstable to use optimum stratification to find a reliable cut-off. We considered our cohort too small for cut-point analysis by optimal stratification, we therefore determined cut-off values for our cohort based on tertiles.<sup>46</sup> The discussion regarding the use of cutpoint was brought to life in a recently published editorial in the Journal

of Cachexia, Sarcopenia and Muscle, which proposes that unanticipated differences in bodycomposition across international populations also highlight the importance of examining bodycomposition data in the context of the local geographical and ethnic norms, and they strongly support the aim of current multicentre strategies to generate international, disease-specific bodycomposition cutpoints.<sup>47</sup>

In conclusion, this study shows that low SM-RA assessed at both the L3 and the T4 level is associated with a higher risk of post-operative pneumonia following CRLM resection. We therefore argue that T4 SM-RA reflecting thoracic myosteotosis may be a valuable body composition parameter, in particular when no recent abdominal scan is available, and thus holds clinical relevance.

#### Conflicts of interest

None to declare.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpb.2019.10.1532>.