Original Article

The validity of ASMI, RASM, and L3 SMI in assessing skeletal muscle mass in patients with lung cancer

Chunhua Bian MD[1,2†], Liting Li MD[3†], Ying Xie MD[1,2], Hongzhen Du PhD[1,2], Zengning Li PhD[1,2]

[1]*Department of Nutrition, the First Hospital of Hebei Medical University, Shijiazhuang, Hebei, China*
[2]*Hebei Province Key Laboratory of Nutrition and Health, Shijiazhuang, Hebei, China*
[3]*Department of Radiology, the First Hospital of Hebei Medical University, Shijiazhuang, Hebei, China*
[†]*Both authors contributed equally to this manuscript*

Background and Objectives: Both bioelectrical impedance analysis (BIA) and electron computed tomography (CT) can be used as tools for assessing skeletal muscle mass. In order to find a more suitable method for assessing skeletal muscle mass in lung cancer patients, this study conducted a comprehensive comparative analysis of the two methods. **Methods and Study Design:** We collected baseline data from patients admitted to the oncology department of the First Hospital of Hebei Medical University from October 2017 to December 2021, and collected data through physical examination, body composition analysis measurements and CT examinations. Then we calculated skeletal muscle mass index (ASMI), relative skeletal muscle index (RASM), and third lumbar spine skeletal muscle index (L3 SMI), respectively. Finally we analyzed the correlation between the three methods and body composition and biochemical indicators and the validity of the three methods. **Results:** A total of 63 patients, 41 males and 22 females, were screened and eligible for enrollment, and the validity of RASM and ASMI was analyzed using L3 SMI as the diagnostic criteria: the sensitivity of RASM and ASMI were 66.67% and 13.33%, respectively, and the specificity was 70.83% and 39.58%, respectively, and the AUC of ROC was 0.736 (p<0.05), 0.264 (p<0.05). **Conclusions:** In this study, L3 SMI was used as the diagnostic criterion and after calculating and comparing the valid parameters of RASM and ASMI, RASM was recommended as the assessment criterion for skeletal muscle mass in Chinese lung cancer patients.

Key Words: lung cancer, skeletal muscle mass, ASMI, RASM, L3 SMI

INTRODUCTION

Sarcopenia was first named by Rosenberg in 1989.[1,2] The European Working Groupon Sarcopenia in Older People (EWGSOP) classified sarcopenia into primary and secondary sarcopenia and stated that tumors are the main cause of secondary sarcopenia.[3,4]

It has been shown that the prevalence of sarcopenia ranges from 15% to 74% in adult oncology patients and is higher in elderly oncology patients.[5] The incidence of tumor-associated sarcopenia reported in different literature varies and may be related to tumor type, tumor stage and diagnostic criteria.[5,6] Less attention has been paid to sarcopenia in oncology patients in China, and screening for sarcopenia has not been routinely assessed clinically as a preoperative or pre-chemotherapy procedure.[7,8] In 2019 the AWGS first suggested that 'sarcopenia is possible': a decline in muscle strength and/or a decline in somatic function. It also suggests that this stage may be reversible,[8] indicating its critical nature. If lifestyle or health education interventions are made at this stage, they can be crucial for later development.

The International Consensus on the Definition and Classification of Cachexia in Cancer, published in 2010, first included X-ray computed tomography (CT) assessment of muscle mass in the assessment system of cachexia, and low muscle mass is considered an independent prognostic indicator of morbidity and mortality in oncology patients.[9,10] CT is the gold standard for assessing skeletal muscle mass.[10,11] CT measurements are performed at the abdomen, thighs and upper arms, and most commonly at the level of the 3rd lumbar vertebra, including measurement of cross sectional area (CSA) and skeletal muscle index (L3 SMI),[12,13] which is the square of the CSA to height ratio.[14] Semi-automatic contouring can be performed by third-party software based on CT values, with the skeletal muscle edges being manually trimmed by the investigator and the area within the contour calculated by the software.[2,11]

The L3 SMI is commonly used abroad as a criterion for assessing skeletal muscle mass in patients with tumours, while it is less used in China. Some studies have also shown that different tumour types have different diag-

Corresponding Author: Dr Zengning Li, Department of Nutrition, The First Hospital of Hebei Medical University Donggang Road 89 Shijiazhuang, Hebei province, 050031, China.
Tel: 0311-85917290
Email: lizengning@126.com
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nostic thresholds, and not all lung cancer patients undergo abdominal CT, and about 1/3 of lung cancer patients could not be included in studies related to sarcopenia due to lack of abdominal CT in retrospective studies,[15-18] so finding a simpler and more economical method for assessing muscle mass in lung cancer patients is of great importance to improve patient prognosis.

In this study, the validity of the ASMI, RASM and L3 SMI in assessing skeletal muscle mass in lung cancer patients and their correlation with body composition and biochemical indicators were investigated to explore the advantages and disadvantages of the three methods in order to provide a basis for finding a suitable method for assessing skeletal muscle mass in lung cancer patients in China.

METHODS

Patients

Patients admitted to the Department of Oncology of The First Hospital of Hebei Medical University from October 2017 to December 2021 were included in this study. The survey was approved by the Ethics Committee of the First Hospital of Hebei Medical University (approval number 20210722), and all subjects participated voluntarily. Inclusion criteria: (1) Patients with pathological and/or cytological diagnosis of lung cancer; (2) Voluntary participation and written signed informed consent; (3) No restriction on gender; (4) Expected survival ≥3 months; (5) General physical condition (ECOG) score of 0-2. Exclusion criteria: (1) clinically significant cardiovascular disease such as heart failure (NYHA class III-IV), uncontrolled coronary artery disease, cardiomyopathy, uncontrolled arrhythmias, uncontrolled hypertension or history of myocardial infarction within 1 year previously; (2) neurological or psychiatric abnormalities affecting cognitive ability, including central nervous system metastases; (3) pacemaker in vivo with varying degrees of ascites and oedema of the extremities.

Research methodology

Physical examination

Height (m) and weight (kg) were measured using the Inbody height and weight machine (BSM370). Test requirements: The subject should empty the urine and faeces, wear light clothing, remove the shoes, stand with his feet together, hands hanging naturally, and stand with his eyes forward on the height and weight meter.

Body composition analysis

The Korean Inbody S10 body composition analyser was used to carry out the body composition analysis of the subject population. Measurement requirements: Empty bladder after 2 hours of fasting or eating, no metal objects on the body, rest quietly for more than 5 minutes, and adopt a lying or sitting position to test the subject population.[19,20] The testers were professionally trained and the test was performed by one person to reduce errors. Appendicular skeletal muscle mass (ASM) is the sum of the skeletal muscle mass of both upper and lower limbs.

CT scan analysis of the third lumbar spine

CT scan analysis of the skeletal muscle of the third lumbar spine was performed using Slice Omatic software, and the cross sectional area (CSA) of the skeletal muscle of the third lumbar spine was plotted (Figure 1).

Diagnostic criteria

Body mass index (BMI) = body mass (kg)/height $(m)^2$. The Chinese standard for low weight: BMI <18.5 kg/m^2; normal weight: 18.5 $kg/m^2 \leq$BMI<23.9 kg/m^2; overweight: 24.0 $kg/m^2 \leq$BMI<27.9 kg/m^2; obesity: BMI ≥28.0 kg/m^2.[21]

The relative appendicular skeletal muscle index (RASM) = limb muscle mass (kg)/body mass (kg) × 100%. Due to various differences in geography, diet and genetics, muscle mass assessment and cut-off values vary from country to country. Skeletal muscle reduction was defined as more than 2 standard deviations from the mean of the population, and the RASM cut-off point in this study was <29.53% in men and <23.20% in women.[22]

Appendicular skeletal muscle mass index (ASMI) = limb muscle mass (kg)/height $(m)^2$. In this study, skeletal muscle reduction was defined as <7.0 kg/m^2 in males and <5.7 kg/m^2 in females, using the diagnostic criteria of the Asian Working Group on Sarcopenia.[22]

The skeletal muscle index (L3 SMI) of the third lumbar spine = skeletal muscle cross-sectional area (cm^2)/height $(m)^2$. In this paper, we used the skeletal muscle quality assessment criteria obtained by Shi Hanping et al[17] using a large sample cohort study, which are suitable for Chi-

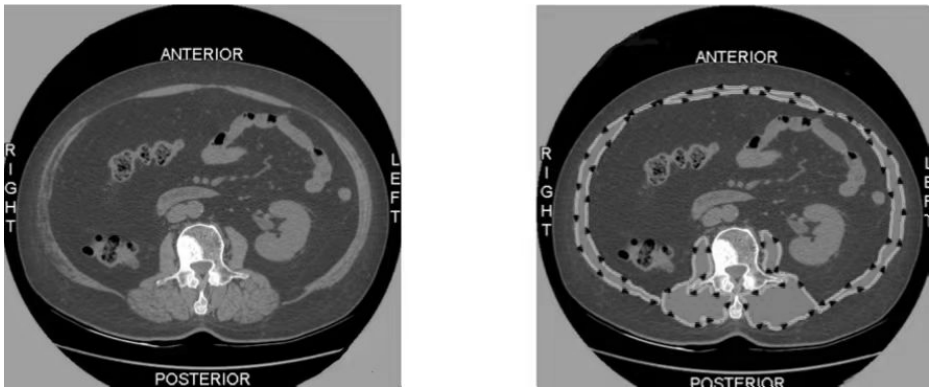

Figure 1. Graphing process using slice Omatic software. Original diagram (DCM file format†) (LEFT). Muscle tissue part drawn out in dotted lines (RIGHT). †DCM file format is a type of software that follows the Digital and Communications in Medicine (DCTM) standard.

nese people: L3 SMI ≤40.8 cm^2/m^2 in male and L3 SMI≤34.9 cm^2/m^2 in female was defined as skeletal muscle reduction.

Statistical analysis

SPSS 25.0 software was used to create the database and analysis the statistical data. Measures were statistically described as mean ± standard deviation ($\bar{X}$±SD) if the data from independent samples met normality, otherwise they were expressed as median (interquartile range) [M(QR)]. Comparisons between groups were made using ANOVA if the variances were equal, and Kruskal-Wallis rank sum test if the variances were not equal. Count data were expressed as frequencies and their composition ratios. The Kappa test was used to analyse diagnostic consistency.[23] Pearson and Spearman correlation analysis was used to describe the relationship between RASM, ASMI, L3 SMI and other indicators. $P < 0.05$ for statistically significant difference.

RESULTS

Baseline information of the study population

A total of 63 patients with malignant tumours were included in this study, including 41 males and 22 females. According to the Chinese BMI standard: 3 cases (4.76%) were low weight patients, 23 cases (36.51%) were normal weight patients, 19 cases (30.16%) were overweight patients and 18 cases (28.57%) were obese patients. The body composition results showed that the obese patients had higher body weight, body fat percentage and L3 SMI than the other groups of study subjects, all with statistically significant differences (p<0.05). The skeletal muscle mass, fat free mass, appendicular skeletal muscle mass, fat free mass of right arm, fat free mass of left arm, fat free mass of right leg, fat free mass of left arm, ASM, ASMI and RASM of the overweight patients were all higher than those of the other groups studied, and the differences were all statistically significant (p<0.05), and the results are shown in Table 1. The results of the biochemical index analysis showed that the patients in the obese group had higher triglycerides, haemoglobin and red blood cell count were all higher in the obese group than in the other groups, and the differences were all statistically significant (p<0.05), and the results are shown in Table 2.

Correlation analysis between ASMI, RASM, L3 SMI and other indicators

Skeletal muscle mass, fat free mass, fat free mass of right arm, fat free mass of left arm, fat free mass of right leg, fat free mass of left leg and appendicular skeletal muscle mass were correlated strongly and positively with ASMI (r>0.75, p<0.001), results in Table 3.

Consistency and validity analysis of RASM and ASMI using L3 SMI as the diagnostic criterion

Kappa test consistency analysis results: Kappa value of L3 SMI and ASMI was -0.345 (p=0.001), Kappa value of L3 SMI and RASM was 0.311 (p=0.009), using L3 SMI as the diagnostic criterion, RASM and Validity analysis of ASMI: the sensitivity of RASM and ASMI were 66.67% and 13.33%, the specificity was 70.83% and 39.58%, respectively, and the area under the ROC curve was 0.736 (p=0.006) and 0.264 (p=0.006), respectively. The results are shown in Tables 4, 5 and Figure 2.

DISCUSSION

At present, a large number of studies have shown a significant correlation between skeletal muscle mass reduction and poor prognosis in lung cancer patients.[24] In this study, we conducted correlation analysis between body mass index grouping and body composition and biochemical indexes in patients with lung cancer, and the results showed that the biochemical indexes of patients with different BMI groups did not change significantly, but the body composition changed significantly. This may suggest that early measurement of body composition in lung cancer patients may have predictive value in the assessment of patients' health status and condition. However, there is no reliable measure of muscle mass in lung cancer patients in China. Lung cancer patients as a special population may assess skeletal muscle mass differently from other populations. Therefore, this study was conducted to investigate the application of three measures, ASMI, RASM and L3 SMI, in assessing skeletal muscle mass in lung cancer patients.

In this study, we analyzed the correlation between ASMI, RASM and L3 SMI and patients' basic information, body composition, hospitalization times, total length of stay and biochemical indices. The three methods correlate significantly better with body composition (skeletal muscle mass, fat free mass, fat free mass of right arm, fat free mass of left arm, fat free mass of right leg, fat free mass of left leg and appendicular skeletal muscle mass) than biochemical indicators. The results may indicate that lung cancer patients do not have significant changes in the corresponding biochemical parameters in the early stages of skeletal muscle mass reduction. This further suggests that if skeletal muscle mass is assessed early in lung cancer patients it may be a better measure of their nutritional status, thus reducing the irreversible damage caused by sarcopenia leading to cachexia in order to slow down the progression of the disease, improve survival and reduce morbidity and mortality in patients with malignancy.

Skeletal muscle mass in lung cancer patients was assessed by three methods, ASMI, RASM and L3 SMI, and the Kappa test showed differences between the three diagnostic methods, which is consistent with the findings of Zhou Ruifen[25] et al Further using L3 SMI as a diagnostic criterion, the RASM had a sensitivity of 66.67, a specificity of 70.8% and a positive predictive value of 41.7%. This suggests that RASM is better than ASMI at assessing skeletal muscle mass in lung cancer, which is consistent with the Brazilian community as well as the Korean criteria for defining reduced skeletal muscle mass by RASM in the diagnosis of sarcopenia.[26,27] Mallick I et al reported that patients with malignancy, as a special group, tend to be low weight people.[28] Therefore, RASM uses body weight as corrective index to calculate skeletal muscle mass index, which may be more suitable for evaluating skeletal muscle mass in oncology patients.

Table 1. Results of body composition analysis of lung cancer patients with different BMI [$\bar{x}$ ± s/M (QR)]

Indicators	Low weight (n/%) (3/4.76)	Normal weight (n/%) (23/36.51)	Overweight (n/%) (19/30.16)	Obesity (n/%) (18/28.57)	F/H (K)	*p* value
Age (y)	69.33±5.13	62.08±11.72	63.00±9.89	65.06±8.86	0.61	0.61
Height (cm)	160.70±9.07	164.07±6.09	163.26±6.23	158.62±5.74	2.76	0.50
Body weight (kg)	42.27±9.71	57.89±6.09	69.55±6.70	75.03±5.47	39.71	<0.001
SMM (kg)	17.23±5.15	22.97±3.88	25.70±4.31	23.71±2.60	5.07	0.003
FFM (kg)	32.50±9.11	42.80±6.47	47.25±7.30	44.03±4.21	5.30	<0.001
PBF (%)	23.63±3.62	26.09±7.63	32.23±6.67	41.26±4.69	18.58	<0.001
FRA (kg)	1.43±0.68	2.22±0.49	2.65 (0.50)	2.49±0.32	7.72†	<0.001
FLA (kg)	1.34±0.65	2.19±0.48	2.60±0.44	2.53±0.34	9.17	<0.001
FRL (kg)	5.33±1.70	6.36±1.16	7.07±1.41	6.25±0.85	2.90	0.048
FLL (kg)	5.42±1.72	6.39±1.12	7.04±1.36	6.44±0.75	2.42	0.075
ASM (kg)	13.52±4.50	17.16±3.18	19.36±3.65	17.70±2.09	3.81	0.001
ASMI (%)	31.63±6.18	29.55±3.70	27.68±3.49	23.58±3.49	11.30	<0.001
RASM (kg/m^2)	5.14±1.22	6.33±0.78	7.21±0.94	7.01±0.45	9.15	<0.001
L3 SMI (cm^2/m^2)	31.47±5.32	40.60±7.19	48.51±8.22	52.30±9.23	10.64	<0.001

SMM: Skeletal Muscle Mass; FFM: Fat Free Mass; PBF: Percent Body Fat; FRA: FFM of Right Arm; FLA: FFM of Left Arm; FRL: FFM of Right Leg; FLL: FFM of Left Leg; ASM: Appendicular skeletal muscle mass.
†Data do not conform to normal distribution, *p* values were estimated by Kruskal-Wallis rank sum test.

Table 2. Results of biochemical index analysis of lung cancer patients with different BMI [$\bar{x}$ ± s/M (QR)]

Indicators	Low weight (n/%) (3/4.76)	Normal weight (n/%) (23/36.51)	Overweight (n/%) (19/30.16)	Obesity (n/%) (18/28.57)	F/H (K)	*p* value
Total protein	64.60±2.69	67.14±5.70	65.87±5.14	66.84±5.56	0.349	0.790
Creatinine	56.13±8.55	64.00±15.42	66.34±13.40	74.92±18.04	2.233	0.094
Creatine kinase	48.00(/)	45.00(60.50)	49.90±28.45	71.19±34.41	1.424†	0.301
Creatine kinase isoenzyme	9.33±3.05	16.65±11.70	12.52±8.42	20.13±17.67	1.436	0.241
Albumin	35.93±3.59	38.57±5.17	36.10±4.89	36.08±3.59	0.056	0.982
Urea	3.50±0.82	4.64±2.25	5.37±2.02	5.16±1.69	1.065	0.3711
Total bilirubin	13.17±9.22	13.63±4.85	12.68±5.30	13.48±8.07	0.098	0.961
Total Cholesterol	4.92±0.84	4.98±1.35	10.40±25.81	5.02±1.00	0.601	0.617
Blood glucose	4.49±0.15	5.09±1.73	5.23±1.06	5.06±1.29	0.257	0.856
Triglycerides	3.17±1.45	1.31±0.69	1.50±0.87	1.63±0.53	5.360	0.002
High-density lipoprotein	0.87±0.11	1.60±2.29	1.12±0.28	1.12±0.20	0.631	0.598
Low-density lipoprotein	2.89(/)	3.71±2.75	2.93±0.57	2.80±0.56	0.915†	0.465
Haemoglobin	89.00(/)	113.26±18.46	115.57±28.35	121.25±17.25	4.109†	0.034
Platelets	140.33±5.51	206.83±116.08	213.22±97.54	236.06±101.25	0.775	0.513
Red blood cell count	2.62±0.92	3.07±1.30	3.85±0.88	3.86 (0.30)	4.113*	0.041

†Data do not conform to normal distribution, *p* values were estimated by Kruskal-Wallis rank sum test.

Table 3. Correlation analysis between ASMI, RASM, L3 SMI and other indicators (r/*p*)

Indicators	ASMI		RASM		L3 SMI	
	r	*p*	r	*p*	r	*p*
Age (y)	0.130	0.312	0.012	0.923	0.218	0.086
Height (cm)	0.501	<0.001	0.673	<0.001	-0.125	0.328
Body weight (kg)	0.746	<0.001	-0.291	0.021	0.561	<0.001
SMM (kg)	0.935	<0.001	0.491	<0.001	0.349	0.005
FFM (kg)	0.932	<0.001	0.475	<0.001	0.355	0.004
PBF (%)	-0.165	0.196	-0.932	<0.001	0.294	0.004
FRA (kg)	0.934	<0.001	0.324	0.010	0.471	<0.001
FLA (kg)	0.932	<0.001	0.259	0.040	0.501	<0.001
FRL (kg)	0.878	<0.001	0.629	<0.001	0.186	0.143
FLL (kg)	0.880	<0.001	0.529	<0.001	0.166	0.193
ASM (kg)	0.930	<0.001	0.534	<0.001	0.280	0.026
BMI (kg/m^2)	0.513	<0.001	-0.613	<0.001	0.622	<0.001
Whole Body Phase Angle	0.318	0.011	0.296	0.019	0.128	0.317
Karnofsky score	0.272	0.031	0.058	0.652	0.515	<0.001
Number of hospital admissions	-0.032	0.813	-0.233	0.066	0.064	0.618
Total number of days in hospital	0.000	0.998	-0.170	0.182	0.014	0.092
Total protein	0.045	0.726	0.073	0.570	0.607	0.601
Creatinine	0.240	0.258	-0.041	0.155	0.384	0.002
Creatine kinase	0.050	0.696	0.049	0.705	0.092	0.475
Creatine kinase isoenzyme	-0.023	0.058	-0.132	0.303	-0.050	0.699
Albumin	-0.237	0.041	-0.150	0.240	-0.106	0.047
Urea	0.231	0.069	-0.030	0.814	0.222	0.080
Total bilirubin	-0.167	0.192	-0.166	0.193	0.008	0.949
Total Cholesterol	0.144	0.259	0.082	0.522	-0.004	0.975
Blood glucose	0.224	0.078	0.087	0.497	0.034	0.789
Triglycerides	-0.145	0.257	-0.085	0.507	0.132	0.302
High-density lipoprotein	-0.013	0.920	0.116	0.365	-0.023	0.860
Low-density lipoprotein	-0.156	0.220	-0.170	0.183	-0.038	0.765
Haemoglobin	0.226	0.075	0.060	0.640	0.386	0.035
Platelets	0.074	0.566	-0.170	0.182	0.182	0.153
Red blood cell count	0.388	0.005	-0.030	0.818	0.378	0.003

SMM: Skeletal Muscle Mass; FFM: Fat Free Mass; PBF: Percent Body Fat; FRA: FFM of Right Arm; FLA: FFM of Left Arm; FRL: FFM of Right Leg; FLL: FFM of Left Leg; ASM: Appendicular skeletal muscle mass; BMI: Body Mass Index

Table 4. L3 SMI and RASM diagnostic concordance

	L3 SMI				
	+	-	Total	χ^2/*p*	Kappa/*p*
RASM					
+	10	14	24	6.815/0.009	0.311/0.009
-	5	34	39		
Total	15	48	63		
ASMI					
+	2	29	31	10.137/0.001	-0.345/0.001
-	13	19	32		
Total	15	48	63		

ASMI: Appendicular Skeletal Muscle Mass Index; RASM: Relative Appendicular Skeletal Muscle Index; L3 SMI: Skeletal Muscle Index of the Third Lumbar Spine.
+: skeletal muscle reduction; -: no reduction in skeletal muscle.

Table 5. Valid parameters for the calculation of RASM and ASMI using L3 SMI as diagnostic criteria

Indicator	RASM	ASMI
Sensitivity (%)	66.7	13.3
Specificity (%)	70.8	39.6
Positive predictive value (%)	41.7	6.45
Negative predictive value (%)	40.6	40.6
Positive Likelihood Ratio (LR+)	2.29	0.22
Negative Likelihood Ratio (LR-)	0.47	2.19
Youden's index	0.38	-0.47
Area under the ROC curve (*p*)	0.74 (*p*=0.006)	0.26 (*p*=0.006)

ASMI: Appendicular Skeletal Muscle Mass Index; RASM: Relative Appendicular Skeletal Muscle Index.

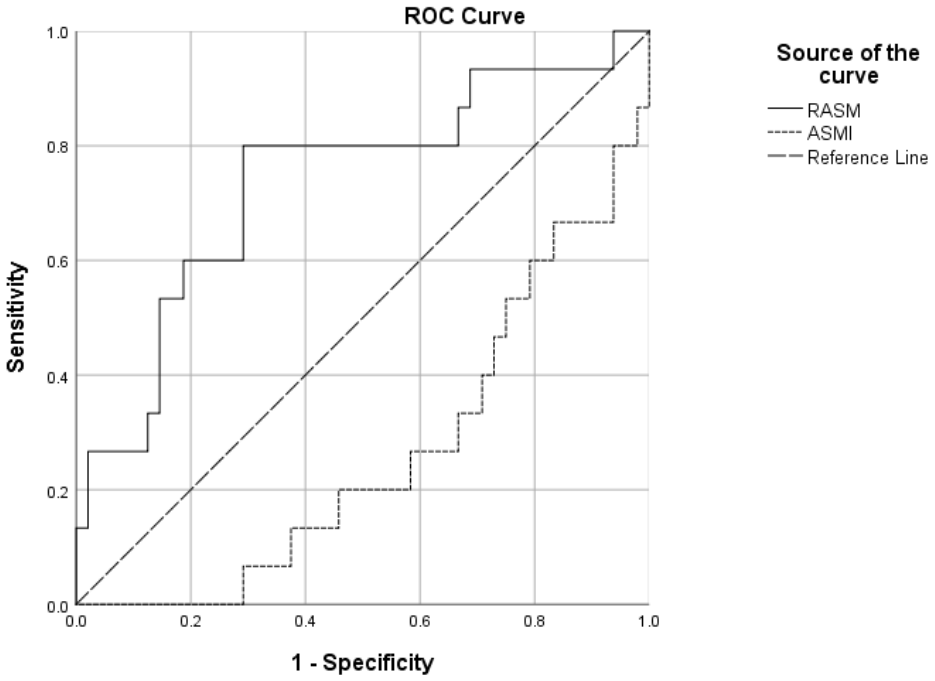

Figure 2. ROC plot of RASM and ASMI using L3 SMI as diagnostic criteria.

Conclusions

The GLIM consensus proposed the BIA method as the standard for assessing skeletal muscle mass in China and CT as the gold standard for assessing skeletal muscle mass abroad, with L3 SMI as the common index.29 However, due to the location of the tumour, routine CT scans do not always include the third lumbar spine. If an additional CT scan of the abdomen is performed just to check for sarcopenia, it will not only increase radiation exposure but also increase the financial burden on the patient. In this study, the concordance results of assessing skeletal muscle mass in lung cancer patients by ASMI, RASM and L3 SMI showed that L3 SMI was in better agreement with RASM. Moreover, RASM, compared to L3 SMI, has the advantages of being simple, economical and non-invasive, which makes it more acceptable to patients and more valuable for promotion. Therefore, this study recommends RASM as the standard for skeletal muscle mass assessment criteria in China.

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AUTHOR DISCLOSURES

All of the authors declare that they have no conflicts of interest.

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