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Original article

Comparison of the prognostic value of MUST, ECOG-PS, mGPS and CT derived body composition analysis in patients with advanced lung cancer

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SUMMARY

Background: Assessment of malnutrition, performance status and systemic inflammation are routine aspects of clinical assessment in patients with advanced cancer. There is increasing evidence that body composition measurements from routine staging CT also have prognostic value. To date the relative prognostic value of Malnutrition Universal Screening Tool (MUST), Eastern Cooperative Oncology Group Performance Status (ECOG-PS), modified Glasgow Prognostic score (mGPS) and CT derived body composition analysis in patients with advanced lung cancer has not been examined. The aim of the present study was to examine this relationship.

Methods: Clinicopathological characteristics including MUST, ECOG-PS, mGPS and body composition data were collected pre-radiotherapy from a prospectively maintained database of patients with advanced lung cancer (n = 643). Using the MUST score, patients were classified into low (MUST = 0, n = 189), medium (MUST = 1, n = 341) and high (MUST ≥ 2, n = 113) malnutrition risk and their relationship to systemic inflammatory response (SIR) and body composition with clinical outcomes were examined using univariate and multivariate analyses. Primary outcome of the study was overall survival.

Results: Compared with the patients at low nutrition risk (MUST = 0), patients at moderate to high risk (MUST 1−≥2) had poorer ECOG-PS > 1 ($p < 0.01$), elevated modified frailty index (mFI) ($p < 0.001$), elevated mGPS ($p < 0.001$), lower skeletal muscle index (SMI, $p < 0.01$) but not lower skeletal muscle density (SMD, $p = 0.115$). MUST was an important prognostic marker of 12 months overall survival ($p = 0.001$). On multivariate analysis, higher MUST (HR 1.16, 95% CI 1.03−1.31, $p < 0.05$), ECOG-PS > 1 (HR 1.23, 95% CI 1.10−1.39, $p < 0.001$), elevated mGPS (HR 1.20, 95% CI 1.09−1.33, $p < 0.001$) were independently associated with overall survival.

Conclusion: A large proportion of patients (71%) with advanced lung cancer were at moderate to high nutrition risk. Higher malnutrition risk and elevated inflammatory status were independently associated with poor overall survival. MUST, ECOG-PS and mGPS all had independent prognostic value and may form an important prognostic framework in treatment decision making and resource utilization

1. Introduction

Although the treatment options for patients with advanced lung cancer have increased over the last decade, prognosis remains relatively poor compared with other advanced cancers, in part due to the presence of cachexia. The definition of cancer cachexia has been the subject of ongoing discussion and there have been considerable efforts to rationalize its definition. The starting point for much of this work was an international consensus in 2011 [1] and cancer cachexia was defined as "a multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and

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leads to progressive functional impairment." In the intervening years the importance of systemic inflammatory responses in the progressive nutritional and functional decline of patients with cancer has been increasingly recognized and is now integral to the definition and treatment of cancer cachexia [2–6]. This more nuanced definition reflects the evolution of criteria in the definition of malnutrition in which cancer cachexia is considered as part of disease related malnutrition with inflammation [7,8].

The Global Leadership Initiative on Malnutrition [8] has proposed that malnutrition be defined by using at least one phenotypic criteria (weight loss, low BMI or low muscle mass) and at least one aetiologic criteria (low food intake or assimilation and inflammation or disease burden). With reference to such work there are established clinical tools that include such phenotypic and aetiologic criteria. For example, the malnutrition universal screening tool (MUST) includes weight loss, BMI and nutritional intake (Fig. 2), ECOG-performance status includes muscle mass and function and the modified Glasgow Prognostic Score (mGPS) includes systemic inflammation. More recently, CT derived body composition analyses have enabled accurate determination of muscle mass [9]. To date, data on the interaction between these tools and their comparative use to predict clinical outcome in patients with cancer has been limited. Recently, in patients with operable colorectal cancer, approximately 20% of patients were considered at medium or high nutritional risk by MUST and of these approximately 40% also had evidence of systemic inflammation (CRP > 10 mg/L) and both had independent prognostic value [10]. Therefore, the aim of the present study was to examine the relationship between MUST, ECOG, SIR and body composition in patients with advanced lung cancer.

2. Patients and methods

Clinicopathological characteristics including MUST, ECOG-PS, mGPS and body composition data were collected prior to radiotherapy into a prospectively maintained database of patients with advanced lung cancer undergoing radiotherapy at The Beatson West of Scotland Cancer Institute from Jan 2009 to Feb 2017 (n = 643). This included patients with available pre-treatment MUST, systemic inflammatory scores and cross-sectional CT with available L3 image. Only patients with TNM stage III/IV disease were included in the analysis and 19 patients with TNM stage II were excluded. This study was approved by Health Research Authority Ethics Committee (17/NW/0190) of Greater Glasgow and Clyde NHS Health Board.

Malnutrition Universal Screening Tool (MUST) is included as a part of admission checklist prior to commencing oncology treatment and is performed by admitting nursing staff. MUST is a bed side assessment of patient weight loss, BMI and nutritional intake as shown in Fig. 2 [11]. Using MUST, patients were classified into low (MUST = 0, n = 189), medium (MUST = 1, n = 341) and high malnutrition risk (MUST ≥ 2, n = 113) as shown in Fig. 1.

Performance status was measured according to the Eastern Cooperative Oncology Group (ECOG) classification which ranges from grade 0 (fully active) to grade 5 (dead). ECOG grades 0 and 1 were grouped into one category as this has been standard practice in the majority of prospective phase III trials in lung cancer.

Plasma CRP and albumin values were used to calculate the mGPS score for each patient. The limit of detection for CRP was 5 mg/L and all samples were processed according to standardized laboratory procedures. The mGPS was calculated as follows:

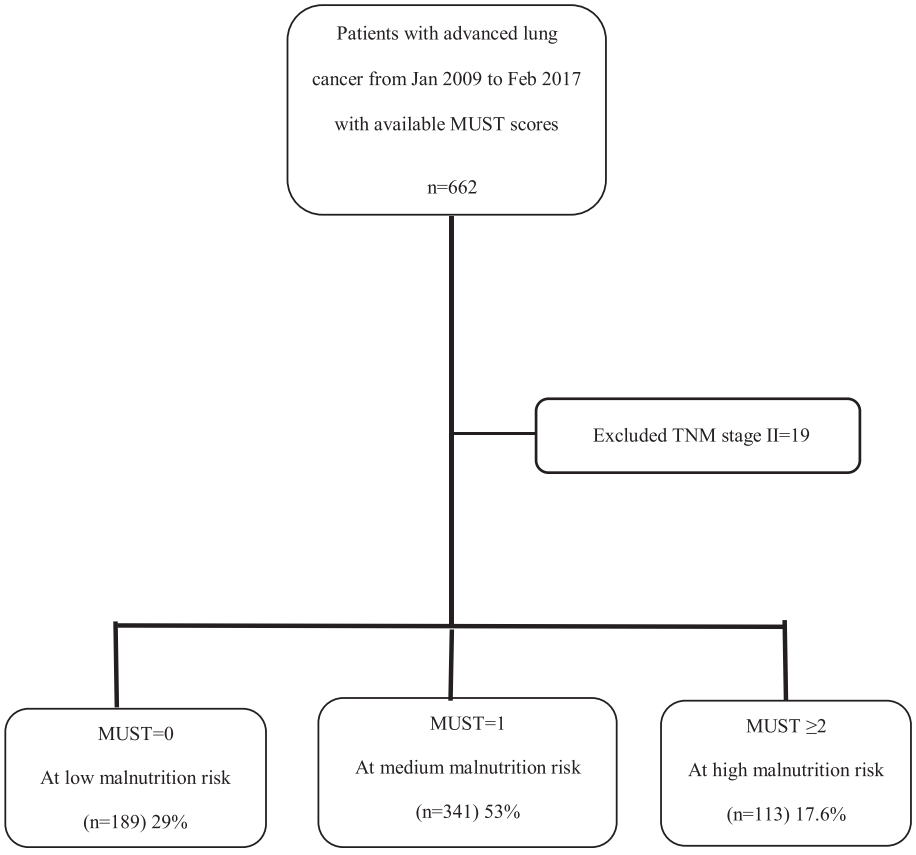

Fig. 1. Flow diagram of included patients with advanced lung cancer. MUST = Malnutrition Universal Screening Tool.

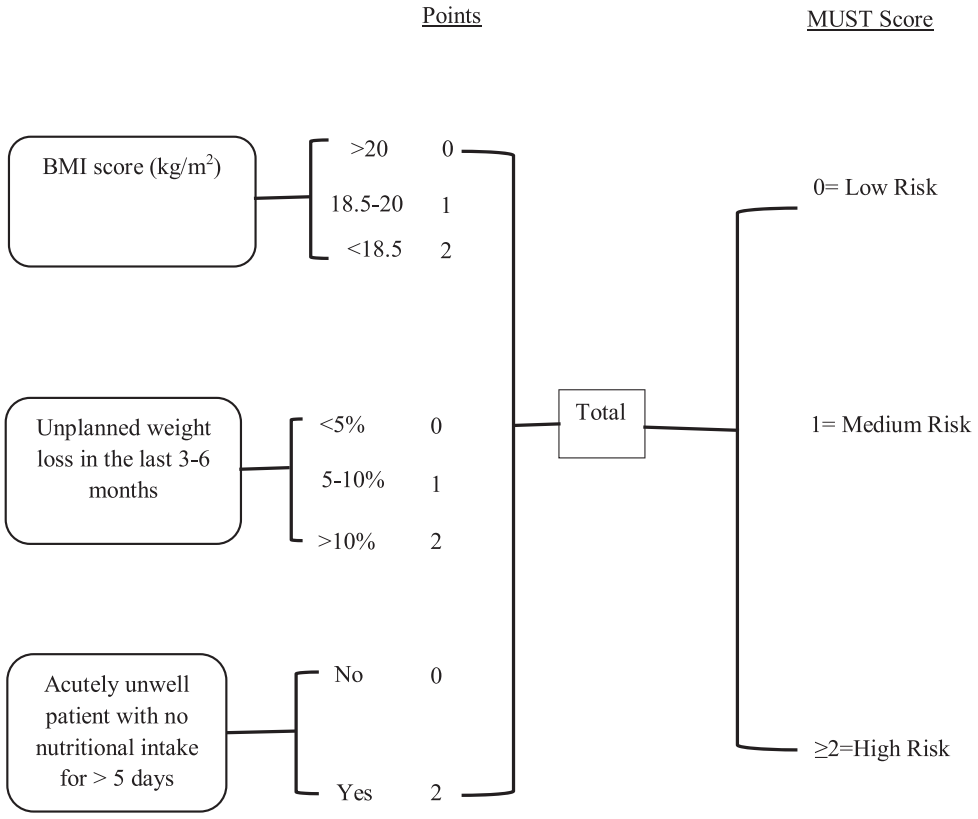

Fig. 2. The Malnutrition Universal Screening Tool (Elia et al., 2003) [11].

CRP ≤ 10 mg/L = 0, CRP > 10 mg/L = 1, CRP > 10 mg/L and albumin < 35 g/L = 2.

Body composition was assessed from the pre-radiotherapy CT scans using image J software (https://imagej.nih.gov/ij/). The CT scan L3 DICOM image was analysed for total fat area (TFA), visceral fat area (VFA), subcutaneous fat area (SFA), skeletal muscle area (SMA) and skeletal muscle density (SMD). Measurements were performed by two individuals (TA and RD) blinded to the patients' clinical data on a sample of 40 patients to reduce the risk of observer bias and ensure accuracy. The interrater reliability was assessed using inter-class correlation coefficients (ICCs). The ICCC values were as follows; TFA and VFA = 0.999; SMA = 0.996 and SMD = 0.993. The cross-sectional area of fat and muscles was normalized for height (m^2) to calculate fat and skeletal muscle indices. The thresholds used for subcutaneous adiposity [12], visceral obesity [13], low SMI and low SMD [14] were shown in Table 1.

The relationship between the MUST score (Fig. 2) and its relationship with clinicopathological factors including ECOG-PS, mGPS and body composition analysis (in particular SMI) and survival was examined using univariate and multivariate analyses. χ^2 test was used for analysis of categorical variables.

Overall survival was calculated in months and defined as the time from study entry until death or censored if alive at follow-up date (1st October 2019). Median duration of follow up was 10 months. Cox proportional hazard model was used to calculate HR and 95% CI for overall survival. Significant variables identified on univariate analysis ($p < 0.1$) were entered into multivariate analysis in backward conditional manner and adjustment was performed for patient age and sex. Survival curves were obtained using Kaplan Meier analysis and 3-year survival rates were calculated by life table analysis. P-value of <0.05 was considered significant. The statistical analysis was performed using SPSS version 25 (IBM Corporation, 2017, Armonk, NY).

The study has been conducted and adheres to the Reporting Recommendations for Tumor Marker Prognostic Studies (REMARK) guidelines [15].

3. Results

All patients included in this study were discussed in multidisciplinary meeting (MDM) and an informed decision was made by considering tumour and patient characteristics and patient wishes. All patients received radiotherapy. 54% of patients in this

Table 1
Body composition thresholds used in patients with advanced lung cancer.

CT derived body composition measurement
Subcutaneous adiposity
Increased Subcutaneous fat index (Ebadi threshold) [12]
Males: SFI > 50 cm^2 m^2
Females: SFI > 42 cm^2 m^2
Visceral Obesity
Increased visceral obesity (Doyle threshold) [13]
Males: VFA > 160 cm^2
Females: VFA > 80 cm^2
Sarcopenia
Low SMI (Martin) (Martin, Birdsell et al. 2013) [14]
Males: BMI < 25 kg/m^2 and SMI < 43 cm^2 m^2 or BMI ≥ 25 kg/m^2 and SMI < 53 cm^2 m^2
Females: BMI < 25 kg/m^2 and SMI < 41 cm^2 m^2 or BMI ≥ 25 kg/m^2 and SMI < 41 cm^2 m^2
Myosteatosis
Low SMD (Martin) (Martin, Birdsell et al. 2013) [14]
BMI < 25 kg/m^2 and SMD < 41 HU or BMI > 25 kg/m^2 and SMD < 33HU

cohort also received concurrent systemic chemotherapy. Platinum compounds (cisplatin and carboplatin) being the first line chemotherapeutic agents. 8 (1.2%) patients also received immunotherapy with programmed cell death (PD-1) inhibitors e.g. Nivolumab. Patients with high malnutrition risk received less chemotherapy (see Table 2).

Nutritional status was determined using MUST score prior to commencing radiotherapy. 640 (99.5%) patients received radiotherapy to the chest. Careful marking of the patients receiving radiotherapy was carried out prior to treatment to limit toxicity to the surrounding structures. Because of advanced stage of these patients, various other regions of body were also radiated, brain n = 31 (4.8%), spinal n = 18 (2.8%), bone n = 16 (2.5%) n = neck n = 3 (0.5%). Distant metastases were common. Common regions of metastases were skeletal (109, 17%), liver (83, 13%), adrenal (68, 11%), brain (64, 10%), spine (34, 5%), pancreas (7, 1%) and kidneys (7, 1%). Patients were discussed in MDM. Patients with symptomatic brain metastases (n = 16) and those with advanced stage small cell lung cancer (n = 15) received cranial radiotherapy.

Only patients receiving radiotherapy as principal mode of treatment were included in the study. However, 12 of these patients (2%) had prior lobectomy and 1 had previous pneumonectomy, these patients developed post-operative recurrence and had advanced lung cancer.

Comorbidities were assessed systematically and were documented using body systems as shown (Supplementary Table 1a). These were grouped into 11 point scoring system called as modified frailty index which is validated screening tool in oncological and geriatric population [16–18]. These comorbidities scores were added and classified into 4 groups (Supplementary Table 1b). Relationship of the MUST and mFI was examined in Table 2. Comorbidities were strongly associated with MUST categories and this was independent of ASA class ($p < 0.001$).

Table 2
The relationship between MUST, clinicopathological characteristics, CT derived body composition and overall survival in patients with advanced lung cancer (n = 643).

Characteristics	Total n = 643	MUST = 0 n = 189 (29%)	MUST = 1 n = 341 (53%)	MUST = 2 n = 113 (18%)	p-value
Age, y					
<65	195 (30.3)	57 (30.2)	107 (31.4)	31 (27.4)	0.854
65–74	249 (38.7)	78 (41.3)	119 (34.9)	52 (46.0)	
>74	199 (30.9)	54 (28.6)	115 (33.7)	30 (26.5)	
Sex					
Male	330 (51.3)	94 (49.7)	179 (52.5)	57 (50.4)	0.815
Female	313 (48.7)	95 (50.3)	162 (47.5)	56 (49.6)	
ASA					
II	60 (9.3)	23 (12.2)	26 (7.6)	11 (9.7)	0.125
III	434 (67.5)	127 (67.2)	236 (69.2)	71 (62.8)	
IV	149 (23.2)	39 (20.6)	79 (23.2)	31 (27.4)	
mFI					
Group I	31 (4.8)	19 (10.1)	10 (2.9)	2 (1.8)	<0.001
Group II	122 (19)	50 (26.5)	58 (17)	14 (12.4)	
Group III	237 (36.9)	51 (27)	138 (40.5)	48 (42.5)	
Group IV	253 (39.3)	69 (36.5)	135 (39.6)	49 (43.4)	
Cancer type					
NSCLC	521 (81)	148 (78.3)	283 (83)	90 (79.6)	0.386
SCLC	122 (19)	41 (21.7)	58 (17)	23 (20.4)	
TNM					
3	240 (37.3)	64 (33.9)	137 (40.2)	39 (34.5)	0.684
4	403 (62.7)	125 (66.1)	204 (59.8)	74 (65.5)	
ECOG					
0–1	402 (62.5)	131 (69.3)	213 (62.5)	58 (51.3)	0.001
2	174 (27.1)	45 (23.8)	92 (27)	37 (32.7)	
3	67 (10.4)	13 (6.9)	36 (10.6)	18 (15.9)	
mGPS					
0	169 (26.3)	82 (43.4)	65 (19.1)	22 (19.5)	<0.001
1	175 (27.2)	51 (27)	104 (30.5)	20 (17.7)	
2	299 (46.5)	56 (29.6)	172 (50.4)	71 (62.8)	
Body composition					
Subcutaneous adiposity (Ebadi threshold) [12]					
No	140 (22.2)	30 (16.9)	73 (21.5)	37 (32.7)	0.002
Yes	490 (77.8)	148 (83.1)	266 (78.5)	76 (67.3)	
Visceral obesity (Doyle threshold) [13]					
No	154 (24.4)	36 (20.2)	79 (23.3)	39 (34.5)	0.009
Yes	476 (75.6)	142 (79.8)	260 (76.7)	74 (65.5)	
Low SMI (Martin threshold) [14]					
No	374 (58.2)	128 (67.7)	194 (56.9)	52 (46)	<0.001
Yes	269 (41.8)	61 (32.3)	147 (43.1)	61 (54)	
Low SMD (Martin threshold) [14]					
No	213 (33.1)	71 (37.6)	110 (32.3)	32 (28.3)	0.086
Yes	430 (66.9)	118 (62.4)	231 (67.7)	81 (71.7)	
Concurrent chemotherapy					
Yes	344 (53.5)	114 (60.3)	179 (52.5)	51 (45)	0.009
No	299 (46.5)	75 (39.7)	162 (47.5)	62 (55)	
Radiotherapy intent					
Radical	117 (18.2)	31 (16.4)	70 (20.5)	16 (14.2)	0.236
Palliative	526 (81.8)	158 (83.6)	271 (79.5)	97 (85.8)	
Survival					
12 months survival % (SE)	45 (2)	57 (4)	43 (3)	34 (4)	0.001

Of the 643 lung cancer patients studied, the majority of patients were >65 years old (70%), had ASA III (67%), had NSCLC (81%), had TNM stage IV (63%), had ECOG 0–1 (62%), had systemic inflammation (mGPS > 0, 74%) and had MUST ≥1 (71%). The majority of patients had subcutaneous adiposity (78%), visceral obesity (76%), had normal SMI (58%) and had low SMD (67%). The majority of patients received radiotherapy with palliative intent (82%). On follow-up 593 died (95% cancer related and 5% of non-cancerous causes).

The relationship between MUST, clinicopathological characteristics and body composition is shown in Table 2. A higher MUST was significantly associated with elevated mFI ($p < 0.001$), poorer ECOG-PS ($p = 0.001$), elevated mGPS ($p < 0.001$), less subcutaneous adiposity ($p < 0.01$), less visceral obesity ($p < 0.01$), low SMI ($p < 0.001$) and poorer 12-month survival rate ($p = 0.001$).

The relationship between clinicopathological characteristics, body composition and overall survival is shown in Table 3. On univariate analysis, higher TNM stage ($p < 0.001$), MUST ($p < 0.001$), ECOG-PS ($p < 0.001$), mGPS ($p < 0.001$) and low SMI ($p < 0.05$) were significantly associated with poorer overall survival. On multivariate analysis, TNM stage (HR 1.64, 95% CI 1.38–1.94, $p < 0.001$), MUST (HR 1.16, 95% CI 1.03–1.31, $p < 0.05$), ECOG-PS (HR 1.23, 95% CI 1.10–1.39, $p < 0.001$) and mGPS (HR 1.20, 95% CI 1.09–1.33, $p < 0.001$) were independently associated with overall survival. The relationship between MUST, ECOG-PS, mGPS and overall survival is shown in Fig. 3.1, 3.2 and 3.3 respectively.

The relationship between TNM stage, MUST, ECOG-PS, mGPS and overall survival in patients with advanced lung cancer (stage III–IV) was shown in Tables 4a, 4b, 4c and 4d. In all patients (Table 4a, n = 643) on multivariate cox regression analysis, TNM stage (HR 1.70, 95% CI 1.43–2.01, $p < 0.001$), MUST (HR 1.17, 95% CI 1.04–1.31, $p = 0.011$), ECOG-PS (HR 1.25, 95% CI 1.11–1.40, $p < 0.001$) and mGPS (HR 1.24, 95% CI 1.13–1.37, $p < 0.001$) were independently associated with overall survival.

In patients with MUST = 0, the relationship between TNM stage, ECOG-PS, mGPS and overall survival was shown in Table 4b (n = 189). On multivariate cox regression analysis, TNM stage (HR 2.49, 95% CI 1.74–3.58, $p < 0.001$) and ECOG-PS (HR 1.22, 95% CI 0.94–1.57, $p = 0.013$) were independently associated with overall survival.

In patients with MUST = 1, the relationship between ECOG-PS, mGPS and overall survival was shown in Table 4c (n = 341). On multivariate cox regression analysis, TNM stage (HR 1.67, 95% CI 1.33–2.09, $p < 0.001$), ECOG-PS (HR 1.17, 95% CI 0.99–1.37, $p = 0.060$) and mGPS (HR 1.25, 95% CI 1.08–1.45, $p = 0.002$) were independently associated with overall survival.

In patients with MUST > 2, the relationship between TNM stage, ECOG-PS, mGPS and overall survival was shown in Table 4d (n = 113). On multivariate cox regression analysis, ECOG-PS (HR 1.32, 95% CI 1.02–1.71, $p = 0.033$) and mGPS (HR 1.61, 95% CI 1.24–2.09, $p < 0.001$) were independently associated with overall survival.

Therefore, TNM stage had independent prognostic value in low and medium risk MUST which was maintained after adjustment for age and sex. Tumour characteristics and host phenotype both were important for lung cancer treatment.

The relationship between MUST, ECOG-PS, mGPS and overall survival in patients with TNM stage IV disease was examined (n = 403). In these patients, MUST and ECOG-PS were not independently associated with overall survival ($p = 0.343$ and $p = 0.057$), while mGPS had independent prognostic value (HR 1.26, 95% CI 1.10–1.43, $p = 0.003$).

4. Discussion

The results of the present study show that, in patients with advanced lung cancer, nutritional risk (MUST) was associated with poor performance status (ECOG-PS), systemic inflammation and lower fat (SFI and VFA) and muscle mass (SMI). Moreover, together with performance status and systemic inflammation, MUST had independent prognostic value whereas body composition measures did not. Taken together, the present study shows, for the first time, the optimal combination of routine clinical phenotypic and aetiologic criteria of malnutrition to predict survival in patients with advanced lung cancer.

Antoun and coworkers (2019) reported that, in 531 patients with non-small cell lung cancer, higher cachexia stage as defined by the original criteria of Fearon and coworkers [1,19] was associated with poorer functional items of quality of life and activity levels but not low SMI. In this study, approximately 70% of patients were defined at nutritional risk and none of these parameters was examined in relation to survival [20]. Also, Daly and coworkers (2020) in 1027 patients with advanced cancer and using Fearon criteria to define BMI adjusted weight loss grading system (WLGS; Martin et al., 2015 [19]), reported that higher WLGS was associated with poorer functional and symptom scales of quality of life questionnaires. Furthermore, higher WLGS (grade 4) was associated with poorer overall survival. In this study approximately 40% of

Table 3
The relationship between clinicopathological characteristics and overall survival in patients with advanced lung cancer: univariate and multivariate analysis (n = 643).

Variables	Univariate analysis	p-value	Multivariate analysis	p-value
	HR (95% CI)		HR (95% CI)	
Clinico-pathological				
Age (<65/65–74/>74)	0.93 (0.84–1.03)	0.147		
Sex (male/female)	0.97 (0.83–1.14)	0.710		
ASA (II–IV)	0.96 (0.83–1.11)	0.541		
TNM stage (III–IV)	1.65 (1.40–1.95)	<0.001	1.64 (1.38–1.94)	<0.001
MUST (0/1/≥2)	1.25 (1.11–1.40)	<0.001	1.16 (1.03–1.31)	0.012
ECOG-PS (0–1/2/3)	1.29 (1.15–1.45)	<0.001	1.23 (1.10–1.39)	<0.001
mGPS (0/1/2)	1.28 (1.16–1.41)	<0.001	1.20 (1.09–1.33)	<0.001
Body composition				
Subcutaneous adiposity (Ebadi threshold) [12]	0.98 (0.81–1.19)	0.856	–	–
Visceral adiposity (Doyle threshold) [13]	0.98 (0.82–1.18)	0.838	–	–
Low SMI (Martin threshold) [14]	1.22 (1.04–1.43)	0.014	1.17 (1.00–1.38)	0.055
Low SMD (Martin threshold) [14]	1.11 (0.94–1.31)	0.217		

Cox regression analysis, variables with $p < 0.1$ on univariate analysis were entered into backward conditional multi variate analysis. p-value <0.05 was considered significant. ASA, American Society of Anaesthesiologists score; TNM, tumour, node, metastasis.; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil lymphocyte ratio; SMI, skeletal muscle index; SMD, skeletal muscle radiodensity.

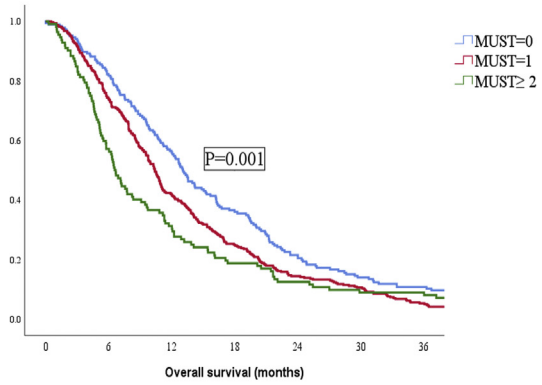

Figure 3.1: The relationship between the MUST and OS in patients with advanced lung cancer.

(Median Survival in months: MUST 0: 13, MUST 1: 10, MUST ≥ 2: 6.0)

MUST=0	186	153	105	68	40	26	20
MUST=1	340	252	143	85	49	36	18
MUST≥2	112	64	35	21	14	10	10

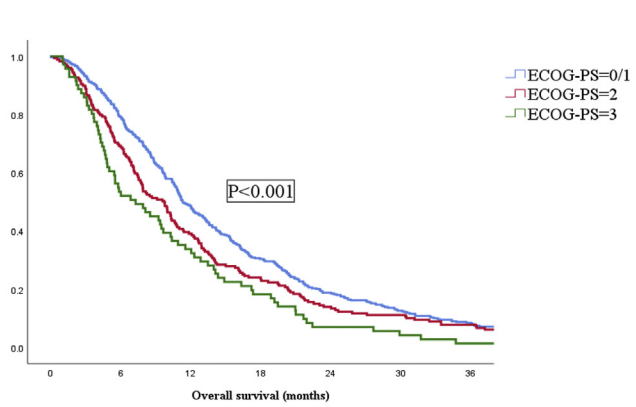

Figure 3.2: The relationship between the ECOG-PS and OS in patients with advanced lung cancer.

(Median Survival in months ECOG-PS 0-1: 11, ECOG-PS 2: 10 ECOG-PS 3: 7)

ECOG=0/1	388	307	189	118	73	49	33
ECOG =2	179	124	70	43	25	20	14
ECOG =3	71	38	24	13	5	3	1

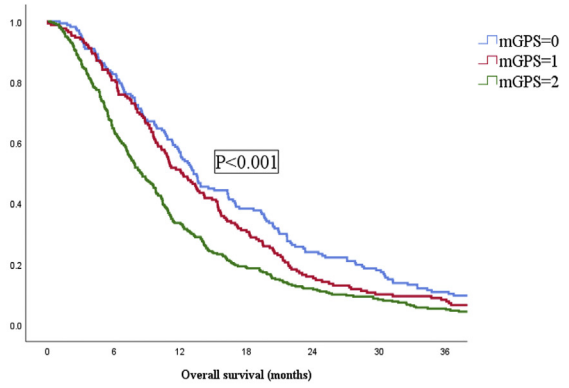

Figure 3.3: The relationship between the mGPS and OS in patients with advanced lung cancer.

(Median Survival in months: mGPS 0: 13, mGPS 1: 12, mGPS 2: 8)

mGPS=0	167	138	95	64	40	30	18
mGPS=1	170	137	87	53	27	17	14
mGPS=2	301	194	101	57	36	25	16

Fig. 3. 1: The relationship between the MUST and OS in patients with advanced lung cancer. (Median Survival in months: MUST 0: 13, MUST 1: 10, MUST ≥ 2: 6.0). 2: The relationship between the ECOG-PS and OS in patients with advanced lung cancer. (Median Survival in months ECOG-PS 0–1: 11, ECOG-PS 2: 10 ECOG-PS 3: 7). 3: The relationship between the mGPS and OS in patients with advanced lung cancer. (Median Survival in months: mGPS 0: 13, mGPS 1: 12, mGPS 2: 8).

patients were defined at nutritional risk [21]. Recently, Dolan and coworkers reported that, in 730 patients with advanced cancer, when WLGS was directly compared with ECOG-PS and mGPS all 3 were independently associated with overall survival. In this study 40% of patients were defined at nutritional risk. In those patients not at nutritional risk (WLGS 0/1), ECOG-PS and mGPS retained prognostic value [22]. In the present study, using MUST, approximately 70% of patients were considered at nutritional risk and of these approximately 80% also had evidence of systemic inflammation (CRP > 10 mg/L) and both had independent prognostic

Table 4
The relationship between TNM stage, MUST, ECOG-PS, mGPS and overall survival in patients with advanced cancer (n = 643).

Characteristics **Table 4a**	Univariate	p-value	Multivariate	p-value	Multivariate Adjusted for Age and Sex	p-value
TNM (III–IV)	1.74 (1.47–2.06)	<0.001	1.70 (1.43–2.01)	<0.001	1.70 (1.44–2.02)	<0.001
MUST 0–≥2	1.25 (1.11–1.40)	<0.001	1.17 (1.04–1.31)	0.011	1.17 (1.04–1.32)	0.008
ECOG-PS (0–1/2/3)	1.29 (1.15–1.45)	<0.001	1.25 (1.11–1.40)	<0.001	1.28 (1.14–1.44)	<0.001
mGPS (0/1/2)	1.28 (1.16–1.41)	<0.001	1.24 (1.13–1.37)	<0.001	1.25 (1.13–1.38)	<0.001
Table 4b MUST = 0	**n = 189**					
TNM (III–IV)	2.35 (1.65–3.35)	<0.001	2.49 (1.74–3.58)	<0.001	2.35 (1.65–3.35)	<0.001
ECOG-PS	1.29 (1.01–1.67)	0.045	1.22 (0.94–1.57)	0.013	1.24 (0.96–1.60)	0.098
mGPS	1.10 (0.92–1.30)	0.294				
Table 4c MUST = 1	**n = 341**					
TNM (III–IV)	1.77 (1.42–2.22)	<0.001	1.67 (1.33–2.09)	<0.001	1.70 (1.35–2.14)	<0.001
ECOG-PS	1.22 (1.04–1.43)	0.015	1.17 (0.99–1.37)	0.060	1.19 (1.02–1.40)	0.031
mGPS	1.27 (1.10–1.46)	0.001	1.25 (1.08–1.45)	0.002	1.26 (1.09–1.45)	0.002
Table 4d MUST = ≥2	**n = 113**					
TNM (III–IV)	1.35 (0.91–2.00)	0.140				
ECOG-PS	1.33 (1.03–1.71)	0.029	1.32 (1.02–1.71)	0.033	1.40 (1.08–1.83)	0.012
mGPS	1.62 (1.24–2.10)	<0.001	1.61 (1.24–2.09)	<0.001	1.60 (1.24–2.08)	<0.001

value. Therefore, given the present and these previous results MUST and WLGS are useful prognostic adjuncts to the ECOG-PS/mGPS framework. It remains to be determined whether existing measures of nutritional risk such as MUST or new measures such as WLGS have most clinical utility in patients with advanced cancer.

In Europe, Malnutrition Universal Screening Tool (MUST) developed by task force established by BAPEN [11] is commonly used and medical and nursing staff are familiar with its use and clinical applicability. MUST reliably assesses host factors (BMI), weight loss and food intake and has been shown to provide a validated scoring system to reliably assess nutritional status [23]. Therefore, since MUST is already part of routine clinical assessment, WLGS would have to be shown to be superior to MUST to enter routine clinical practice. Similarly, globally where other nutritional risk screening tools are used in clinical practice [24], WLGS would have to show superior prognostic value.

It has now been established that the systemic inflammatory response has prognostic value in localised and advanced cancer patients. In the present study the mGPS was used to assess the systemic inflammatory response as it is routinely clinically available, has standardised thresholds and has been extensively validated [25].

The results of the present study clearly support the GLIM recommendations on the assessment of disease related malnutrition and multimodal approach to the treatment of cancer cachexia such as the MENAC trials [26]. Moreover, given the simplicity of MUST, ECOG-PS and mGPS assessments, this framework should be applied to existing advanced cancer datasets and clinical trials to identify important patient subgroups amenable to targeted treatment.

In the present study validated prognostic tools were compared to examine whether they had complementary value in patients with advanced lung cancer and the combination of MUST, ECOG-PS and mGPS provided a routine clinically available assessment that is compatible with GLIM guidelines and predicts overall survival. Indeed, some the components of MUST and the mGPS are captured in the new GLIM criteria. These include the phenotypic criteria such as weight loss and low BMI and etiologic criteria such as compromised dietary intake and inflammation. Therefore, in the present analysis it would appear that some of the GLIM criteria do indeed have complementary prognostic value. However, in contrast to the validated prognostic tools used in the present study, it remains to be established how the GLIM criteria are to be measured and combined for optimal prognostic value. Furthermore, the GLIM criteria do not include a measure of physical activity and performance status was shown to have independent prognostic value in the present study.

A number of studies have shown that approximately 50% of patients with terminal lung cancer did not have a discussion of hospice and end of life care, two months before death [27]. By taking into consideration objective tumour and host characteristics it may be possible to have such discussions on an evidence based basis and therefore better palliation of symptoms and end of life care.

The present study has some limitations. This is a retrospective cohort study and has limitations seen with this study design. However, data were collected using a prospective proforma and thus the study had well documented clinicopathological data reducing the risk of bias. Further prospective and longitudinal studies on examining relationship between MUST, ECOG-PS, SIR and body composition in patients with advanced cancer are warranted.

In summary, there was a strong association between MUST, ECOG-PS, mGPS and low SMI in patients with advanced lung cancer. However, only MUST, ECOG-PS and mGPS were independently associated with overall survival. The combination of MUST, ECOG-PS and mGPS provides a routine clinically available assessment that is compatible with GLIM guidelines and predicts overall survival.

Author contributions

Tanvir Abbass: Data collection, scan analysis, data interpretation and writing of the manuscript. Ross D Dolan: Scan analysis and reviewed the final manuscript. Nicholas MacLeod: Provided data and reviewed the final manuscript. Paul G Horgan: Supervision and reviewed the final manuscript. Barry J Laird: Supervision and reviewed the final manuscript. Donald C McMillan: Senior author who assisted with the manuscript and data interpretation.

Declaration of competing interest

All contributing authors declare no conflicts of interests to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2020.08.003.

References

[1] Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011;12(5):489–95.
[2] Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. Lancet Oncol 2014;15(11):e493–503.
[3] Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. Clin Nutr 2017;36(5):1187–96.
[4] Simmons CPL, McMillan DC, McWilliams K, Sande TA, Fearon KC, Tuck S, et al. Prognostic tools in patients with advanced cancer: a systematic review. J Pain Symptom Manag 2017;53(5). 962–970.e10.
[5] Laird BJ, Kaasa S, McMillan DC, Fallon MT, Hjermstad MJ, Fayers P, et al. Prognostic factors in patients with advanced cancer: a comparison of clinicopathological factors and the development of an inflammation-based prognostic system. Clin Canc Res 2013;19(19):5456–64.
[6] Baracos VE. Cancer-associated malnutrition. Eur J Clin Nutr 2018;72(9):1255–9.
[7] Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017;36(1):49–64.
[8] Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition – a consensus report from the global clinical nutrition community. Clin Nutr 2019;38(1):1–9.
[9] Daly LE, Prado CM, Ryan AM. A window beneath the skin: how computed tomography assessment of body composition can assist in the identification of hidden wasting conditions in oncology that profoundly impact outcomes. Proc Nutr Soc 2018;77(2):135–51.
[10] Almasaudi AS, McSorley ST, Dolan RD, Edwards CA, McMillan DC. The relation between Malnutrition Universal Screening Tool (MUST), computed tomography-derived body composition, systemic inflammation, and clinical outcomes in patients undergoing surgery for colorectal cancer. Am J Clin Nutr 2019;110(6):1327–34.
[11] Elia M. Screening for malnutrition: a multidisciplinary responsibility. development and use of the 'malnutrition universal screening tool' ('MUST') for adults. 2003. Report No.: ISBN 1-899467-70X.
[12] Ebadi M, Martin L, Ghosh S, Field CJ, Lehner R, Baracos VE, et al. Subcutaneous adiposity is an independent predictor of mortality in cancer patients. Br J Cancer 2017;117(1):148–55.
[13] Doyle SL, Bennett AM, Donohoe CL, Mongan AM, Howard JM, Lithander FE, et al. Establishing computed tomography-defined visceral fat area thresholds for use in obesity-related cancer research. Nutr Res 2013;33(3):171–9.
[14] Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol 2013;31(12):1539–47.
[15] McShane LM, Altman DG, Sauerbrei W, Taube SE, Gion M, Clark GM. Reporting recommendations for tumor marker prognostic studies (REMARK). J Natl Cancer Inst 2005;97(16):1180–4.
[16] Ehlert BA, Najafian A, Orion KC, Malas MB, Black JH, Abularrage CJ. Validation of a modified Frailty Index to predict mortality in vascular surgery patients. J Vasc Surg 2016;63(6). 1595–1601.e2.
[17] Al-Khamis A, Warner C, Park J, Marecik S, Davis N, Mellgren A, et al. Modified frailty index predicts early outcomes after colorectal surgery: an ACS-NSQIP study. Colorectal Dis 2019;21(10):1192–205.
[18] Shahrokni A, Vishnevsky BM, Jang B, Sarraf S, Alexander K, Kim SJ, et al. Geriatric assessment, not ASA physical status, is associated with 6-month postoperative survival in patients with cancer aged ≥75 years. J Natl Compr Cancer Netw 2019;17(6):687–94.
[19] Martin L, Senesse P, Gioulbasanis I, Antoun S, Bozzetti F, Deans C, et al. Diagnostic criteria for the classification of cancer-associated weight loss. J Clin Oncol 2015;33(1):90–9.
[20] Antoun S, Morel H, Souquet PJ, Surmont V, Planchard D, Bonnetain F, et al. Staging of nutrition disorders in non-small-cell lung cancer patients: utility of skeletal muscle mass assessment. J Cachexia Sarcopenia Muscle 2019;10(4):782–93.
[21] Daly LE, Dolan RD, Power DG, Ni Bhuachalla E, Sim W, Cushen SJ, et al. Determinants of quality of life in patients with incurable cancer. Cancer; 2020.
[22] Dolan RD, Daly L, Sim WMJ, Fallon M, Ryan A, McMillan DC, et al. Comparison of the prognostic value of ECOG-PS, mGPS and BMI/WL: implications for a clinically important framework in the assessment and treatment of advanced cancer. Clin Nutr 2019.
[23] Boleo-Tome C, Monteiro-Grillo I, Camilo M, Ravasco P. Validation of the malnutrition universal screening tool (MUST) in cancer. Br J Nutr 2012;108(2):343–8.
[24] Chen X-Y, Zhang X-Z, Ma B-W, Li B, Zhou D-L, Liu Z-C, et al. A comparison of four common malnutrition risk screening tools for detecting cachexia in patients with curable gastric cancer. Nutrition 2020;70:110498.
[25] Dupre A, Malik HZ. Inflammation and cancer: what a surgical oncologist should know. Eur J Surg Oncol 2018;44(5):566–70.
[26] Solheim TS, Laird BJA, Balstad TR, Bye A, Stene G, Baracos V, et al. Cancer cachexia: rationale for the MENAC (multimodal-exercise, nutrition and anti-inflammatory medication for cachexia) trial. BMJ Support Palliat Care 2018;8(3):258–65.
[27] Huskamp HA, Keating NL, Malin JL, Zaslavsky AM, Weeks JC, Earle CC, et al. Discussions with physicians about hospice among patients with metastatic lung cancer. Arch Intern Med 2009;169(10):954–62.