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Research Article

Prognostic Value Of PET/CT Determined Sarcopenia in Patients with Resected Ampullary Carcinoma

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Abstract

Objectives: Our aim is to investigate the prognostic value and effect on chemotherapy toxicity of pre-treatment sarcopenia determined with positron emission tomography/computerized tomography(PET/CT) in patients with ampullary carcinoma.

Methods: Characteristics of patients retrieved retrospectively. Skeletal muscle area(SMA) measurement of the muscle at L3 vertebra level was evaluated for each patient from their PET/CT scan taken at the time of diagnosis. The sex-specific cut-off levels for determining sarcopenia were <38.5 cm2/m2 for females and <52.4 cm2/m2 for males. Association between oncological and radiological data was analyzed.

Results: A total of 90 patients included in the study. Median age at diagnosis was 62(range: 44-77). Half of the patients were sarcopenic. Pre-treatment sarcopenia was determined as an independent variable predicting survival for both disease-free-survival(DFS) and overall survival(OS). Sarcopenic patients had statistically significant shorter OS(67.2 months for non-sarcopenic patients vs 53.2 months for sarcopenic patients, 95%CI:63.6-70.9, p<0.001), and a trend for shorter DFS(48 months for non-sarcopenic patients vs 36.8 months for sarcopenic patients, 95%CI:20.3-53.4, p=0.95) was also determined. On the other hand, chemotherapy related toxicity has also seen more in sarcopenic patients.

Conclusion: Detecting the presence of pre-treatment sarcopenia may enable clinicians to predict the patient group with low survival and high probability of treatment toxicity. In order to protect this group of patients from toxicity, pre-treatment sarcopenia measurement should be applied in routine practice and should guide treatment plan.

Keywords: Ampullary carcinoma, sarcopenia, toxicity, survival

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Ampullary carcinomas are rare, accounting for only 0.2% of gastrointestinal cancers and 7% of all periampullary cancers.[1]

The patients with ampullary carcinomas are usually diagnosed at earlier stages due to the symptoms related to biliary obstruction. Ampullary cancer must be treated

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with multidisciplinary approach (surgery, chemotherapy, radiotherapy) as in pancreatic cancer. Surgery is the only curative treatment method. Curative surgery is possible in approximately 50% of ampullary cancers compared to that of less than 10% in pancreatic adenocarcinoma,[2] which reflects to better survival outcomes in ampullary cancers.

Ampullary carcinomas have two histological subtypes: intestinal and pancreatobiliary; notably intestinal type is more common and has a better prognosis than the pancreatobiliary type [median overall survival (OS) of 115.5 vs. 16 months, respectively; p<0.001].[3]

Recently, it has been understood that clinical outcomes are not only affected by tumor related factors, but also by patient-related factors. Sarcopenia, which is defined as progressive loss in muscle mass and function in recent studies, has been found as the one of the most important factors affecting survival.[4] Sarcopenia is associated with increased morbidity and mortality for many cancer types such as pancreatic cancer, breast cancer, hepatocellular cancer, and renal cell carcinoma.[5-8] In the literature, up to %65 of pancreatic cancer cases, in particular, have been found associated with sarcopenia.[5, 9, 10] Moreover, presence of sarcopenia was shown to be associated with increased chemotherapy toxicity.[8, 11-13] Recently, there has been an increasing interest in sarcopenia in the field of oncology. In the literature, different technological methods such as computer tomography (CT), magnetic resonance imaging (MRI) and lately fluorodeoxyglucose (FDG)- positron emission tomography/ computerized tomography (PET/CT) has been used to measure sarcopenia.[14-16]

CT can be considered as a good choice for the assessment of body composition since it allows a distinction of different tissues with regards to the attenuation of the X-ray beam.[17] Thus, CT enables the analysis of fat distribution within muscles by distinguishing fat around the muscle and interstitial adipose tissue. Therefore, it provides a qualitative and quantitative characterisation to detect sarcopenia.[18] Sarcopenia measurement using PET/CT can technically be defined as low-dose CT evaluation.

Any method (X-Ray, CT, PET/CT or MRG) to measure patients' skeletal muscle area (SMA) has been acknowledged as one of the fundamental tools in the literature.[19, 20] Most commonly used landmark for SMA measurement is the cross-sectional area of muscle at the L3 vertebra which has been shown to reflect the whole-body muscle mass in the best way.[21, 22]

In this study, we investigated the prognostic significance of the presence of sarcopenia during the diagnosis of patients with resected ampullary carcinoma.

Methods

Study Design and Patient Selection

Files of patients diagnosed with ampullary cancer who were followed up in our oncology clinic between January 2012 and June 2019 were retrospectively reviewed. Inclusion criteria were: Patients over 18 years of age, resected and pathologically confirmed as pure ampullary cancer, had complete follow oncological files and had tumor stagigng PET/CT scan in our center. We reviewed 272 patients record, of which 90 met inclusion criteria (Fig. 1).

The pathological examination of the resection specimens was performed by the specialist pathologist of our center, in alignment with N. Volkan Adsay et al's definition of ampullary tumors.[23]

SMA measurement of the muscle at L3 vertebra level was evaluated for each patient in the Nuclear Medicine Department. The sex-specific cut-off levels for determining sarcopenia were <38.5 cm^2/m^2 for females and <52.4 cm^2/m^2 for males.[24] Patients were classified on the basis of their body mass index(BMI) as follows: underweight <18.5 kg/m^2, normal 18.5-24.9 kg/m^2, overweight 25-29.9 kg/m^2, obese>30 kg/m^2. We preferred to classify as overweight (BMI≥25) vs non-overweight (BMI<25) in our manuscript.

Demographic data, clinical follow-up parameters, treatment responses and toxicities, survival outcomes were recorded. Association between the oncological and radiological data was analysed. Chemotherapy related toxicities were graded in line with Common Terminology Criteria for Adverse Event Version 4.03.

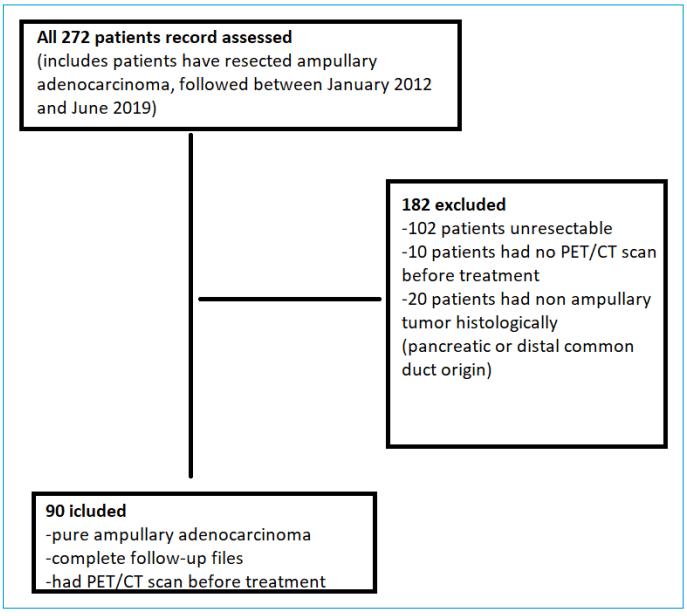

Figure 1. Flow-chart of inclusion and exclusion criteria.

PET/CT Protocol and Evaluation

All patients underwent FDG-PET/CT to stage the primary malignancy. PET/CT scans were performed after at least 6 hours fasting, and all patients were hydrated with iodinated oral contrast (Omnipaque; GE Healthcare) water. No intravenous iodinated contrast was administered to patients. All patient's blood glucose levels were <150 mg/dLprior to administering the radiotracer. 5 Mbq/kg body weight of radiotracer was injected, and PET/CT (Discovery STE; GE Medical Systems, Milwaukee, WI) scan was performed approximately 60 minutes after tracer administration. A low-dose multislice CT scan was collected from the base of the skull to mid-thighs (parameters: 80 mA, 140 kV, table speed 27 mm/rotation, and slice thickness 3 mm). PET compartment of PET/CT scan of the same areas was performed three-dimensional mode in 5-7 bed positions for 2.5 minutes. The obtained 3D PET data was reconstructed accurately using an iterative algorithm and CT-based attenuation correction is used. Next, the acquisition data were transferred to a workstation (Advantage Windows Server 4.5; GE Healthcare) for segmentation and interpretation. PET, CT, and PET/CT images were examined into trans-axial, coronal, and sagittal views, and evaluated by two experienced nuclear medicine physicians.

Skeletal Muscle Mass Measurement

Having a staging PET/CT scans was collected before enrolment in the present study. The CT compartment of the PET/CT imaging was used for the evaluation of SMA. To measure the cross-sectional areas of SMA, L3 vertebra was set as a landmark point.[25] For each patient, a region of interest was drawn on the psoas and paraspinal muscles at the level of the spinous process of the L3 vertebra, and single-slice muscle volume was calculated in cm^2. SMA was quantified based on the calculation of the average Hounsfield Unit (HU) value of the muscle area within the range of -29 and +150 to distinguish it from other tissues.[26]

Statistical Analysis

Descriptive statistics were given as numbers and percentages for categorical variables, averages, minimums, and maximums for numeric variables. In our study, we preferred to report medians and quartiles instead of mean and stadart deviation due to data were not normally distributed. Two independent group comparisons of numerical variables were performed with Mann–Whitney U Test when normal distribution conditions were not achieved. More than two independent group comparisons were done with Kruskal–Wallis Test. To identify factors predicting survival, categorical variables were individually included in the univariate analysis with using cox regression model. Significant or close to significant variables in the univariate analysis were included in the multivariate analysis with cox regression model. Variables that were statistically significant ($p<0.05$) were found to be predictors of survival. Independent factors that predict sarcopenia was assessed through Logistic Regression analyses. Confidence interval (CI) was selected as 95% and a two-sided p-value less than 0.05 was accepted as statistically significant. Median disease-free survival (DFS) and overall survival (OS) were estimated with Kaplan–Meier method and log-rank test. All statistical analysis were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Forty-six (51.1%) of 90 patients included in the study were male. Median age at diagnosis was 62 (range: 44-77). Pathological diagnosis of all patients was adenocarcinoma, and 70% had intestinal histology.

Approximately 50% of the patients were sarcopenic. There was no difference in the distribution of sarcopenia based on the demographic characteristics of the patients and tumors, except for perineural invasion and histological subtype.

The majority of the patients (62.2%) have normal weight, whilst the rest were overweight (11.1% were obese). Although the rate of sarcopenia among obese patients was 60%, no statistically significant relationship was found between obesity and sarcopenia (p=0.14).

Descriptive characteristics are shown in Table 1.

Six of all operated patients could not receive adjuvant chemotherapy for various reasons (poor performance, delayed wound healing etc.). These patients were also sarcopenic.

It was observed that the whole patient cohort received median of one lines of chemotherapy (range: 0-3 line) during the follow-up period. Gemcitabine (78.4% in sarcopenic patients, 86.4% in non-sarcopenic patients) was the most commonly used chemotherapy regimen in the whole group, while the 5-fluorouracil, oxaliplatin, and irinotecan regimen (FOLFIRINOX) was used only for four non-sarcopenic patients. Dose modification or discontinuation due to chemotherapy toxicity was done in 24.4% of all patients, and this rate was 39.2% in sarcopenic and 9.1% in non-sarcopenic patients (p=0.001). Details of chemotherapy related toxicity presented in Table 2.

Table 1. Descriptive Characteristics

Descriptives	All patients n(%)	Sarcopenia		p
		Yes, n=46 (%)	No, n=44 (%)	
Gender				
Male	46(51.1)	26(56.5)	18(40.9)	0.14
Female	44(48.9)	20(43.5)	26(59.1)	
Diagnostic Age				
< 60 years	34(37.8)	14(30.4)	20(45.5)	0.19
≥ 60 years	56(62.2)	32(69.6)	24(54.5)	
Diabetus Mellitus				
Yes	26(28.9)	14(30.4)	12(27.3)	0.74
No	64(71.1)	32(69.6)	32(72.7)	
Smoking History				
Current/Past	42(46.7)	20(43.5)	22(50)	0.53
Never	48(53.3)	26(56.5)	22(50)	
ECOG PS				
PS 0-1	76(84.4)	38(82.6)	38(86.4)	0.77
PS 2-3	14(15.6)	8(17.4)	6(13.6)	
Histological Subtype				
Pancreatobiliary	27(30)	20(43.5)	7(15.9)	0.004
Intestinal	63(70)	26(56.5)	37(84.1)	
Grade groups				
Grade<3	74(82.2)	38(82.6)	36(81.8)	0.92
Grade≥3	16(18.7)	8(17.4)	8(18.2)	
T stage				
T1-2	32(35.6)	16(34.8)	16(36.4)	0.87
T3-4	58(64.4)	30(65.2)	28(63.6)	
N stage				
Positive	36(40)	16(34.8)	20(45.5)	0.30
Negative	54(60)	30(65.2)	24(54.5)	
Stage groups				
Stage I-II	74(82.2)	36(78.3)	38(86.4)	0.31
Stage III	16(17.8)	10(21.7)	6(13.6)	
PNI				
Yes	66(73.3)	40(87)	26(59.1)	0.003
No	24(26.7)	6(13)	18(40.9)	
LVI				
Yes	72(80)	40(87)	32(72.7)	0.09
No	18(20)	6(13)	12(27.3)	
Surgical margin				
Negative	48(53.3)	24(52.2)	24(54.5)	0.82
Positive	42 (46.7)	22(47.8)	20(45.5)	
Body Mass Index				
Non-overweight	56(62.2)	32(69.6)	24(54.5)	0.14
Overweight	34(37.8)	14(30.4)	20(44.5)	

ECOG PS: Eastern Cooperative Oncology Group Performance Status, PNI: perineural invasion, LVI:lyphovascular invasion.

Survival Analysis

The median follow-up period was 17.8 months, estimated OS was 64 months (range: 3-75.7 months), and estimated DFS was 12 months (range: 2.1-68.4 months). Estimated one and two-year OS rate were 95% and 85%, respectively. Sarcopenic patients had statistically significantly shorter OS and DFS than non-sarcopenic patients (OS was 53.2 months vs. 67.2 months, HR:1.8, 95%CI:63.6-70.9, p<0.001 and DFS was 8 months vs. 20 months, HR:1.5, 95%CI:11.4-29.0, p<0.001). Kaplan-Meier curves were given in Figure 2 and 3. When sur-

Table 2. Chemotherapy Related Toxicity According To Sarcopenia

Categorical variables	Sarcopenic patients n=46 (%)	Non-sarcopenic patients n=44(%)	p
CT related toxicity (any grade)	32(69.6)	16(36.4)	0.002
Delay or interrupted CT			
Yes	18 (39.2)	4(9.1)	0.001
No	28 (60.9)	40(90.9)	
Most common			
CT related toxicity	15(32.6)	13(29.5)	

CT: chemotherapy.

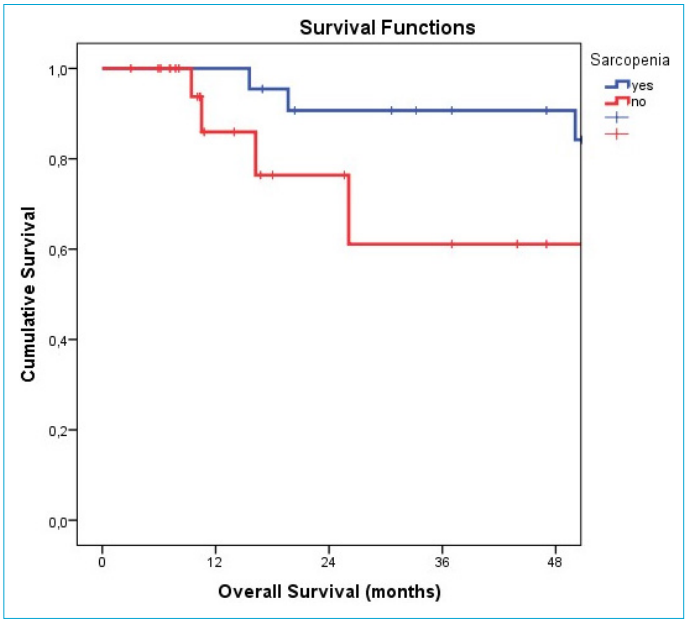

Figure 2. Kaplan-Meier Curve for Sarcopenia Predicting Overall Survival.

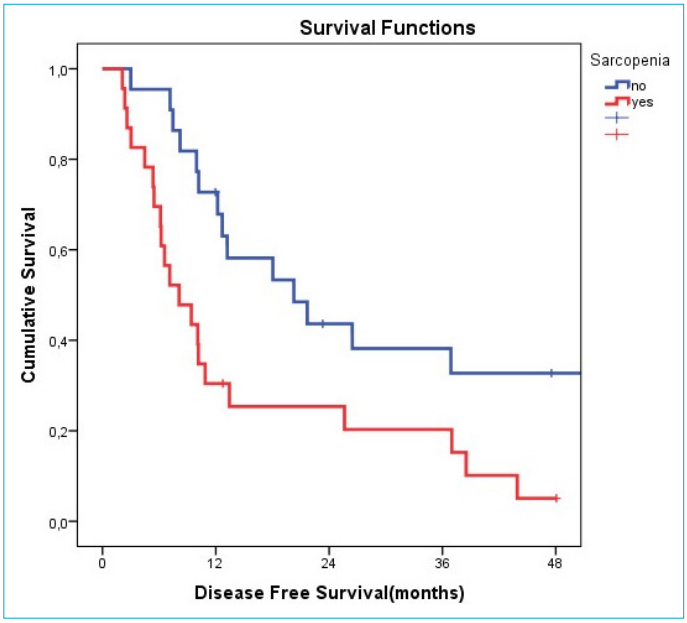

Figure 3. Kaplan-Meier Curve for Sarcopenia Predicting Disease Free Survival.

vival analysis was performed in regards with sarcopenia status of patients receiving gemcitabine, which is the most frequently applied chemotherapy regimen (82.2%), estimated OS and DFS were shorter for sarcopenic patients than non-sarcopenic patients (sarcopenic vs non-sarcopenic patients: OS was 53 months vs 64 months, HR:2.4, 95% CI:59.3-68.7, p=0.027 and DFS was 9 months vs 21 months, HR:2.2, 95% CI:5.0-13.7, p=0.001).

Sarcopenia was considered as an independent variable predicting survival for both DFS and OS. Univariate and multivariate analysis results are presented in Table 3A and 3B.

As shown in Table 4, independent variables considering sarcopenia in the logistic regression analysis were histological subtype, diagnosed over 60 years old, obesity, and presence of perineural invasion.

Discussion

In this study, we investigated the effect of pre-treatment sarcopenia PET/CT on chemotherapy side effects and survival outcome of patients with resected primary ampullary adenocarcinoma. Best of our knowledge, this is the first study of sarcopenia in patients with resected pure ampullary adenocarcinoma. This research seeks to address the following two questions: 1. Why is it important to detect sarcopenia before treatment in these selected patients group? 2. Why is it valuable to evaluate sarcopenia with PET/CT?

In the literature, sarcopenia has been defined as one of the factors predicting poor survival for many tumors and specifically in pancreatic cancers.[27, 28] We were also found worse OS in sarcopenic patients consistent with the literature.

These poor survival outcomes related to sarcopenia can be associated with many factors. Firstly, it is known that low lean mass may carry a higher risk of mortality, both cachexia-dependent and independent manners. Animal studies have showed that reversal of muscle wasting led to prolonged survival in a cancer cachexia model.[29] Therefore, knowing the muscle mass of patients before treatment will be useful in cancer management. We believe that BMI or body surface area (BSA) used to calculate the treatment dose are not adequate methods today because it is not considered as the features of body composition and BSA can not reflect an exact lean mass. For this reason, sarcopenic patients may be receiving inappropriate doses of treatment and therefore they have lower tolerance to aggresive chemotherapy, which often interupts the therapy. Taken together, the evidence from this study suggests that lean body mass should be taken into account when planning treatment.

Table 3a. Univariate and Multivariate Analysis Predicting Overall Survival

	Univariate Analysis			Multivariate Analysis		
Categorical Variables	**p**	**HR**	**CI 95%**	**p**	**HR**	**CI 95%**
Gender						
Female vs Male	0.36	1.36	0.70-2.65			
Smoking History						
Yes vs No	0.14	0.60	0.30-1.19			
Diagnostic Age						
≥60 vs <60	0.03	2.22	1.05-4.69	0.002	3.87	1.65-9.06
ECOG						
≥2 vs <2	0.19	2.05	0.69-6.08			
Histological Subtype						
Pancreatobiliary vs Intestinal	0.005	5.27	0.05-0.61	0.13	2.49	0.75-8.26
Grade groups						
≥3 vs <3	0.37	1.43	0.64-3.19			
Tumor Diameter Groups						
≥2cm vs <2cm	0.44	0.74	0.35-1.58			
Stage Groups						
Stage 3 vs Stage1-2	0.03	2.45	1.07-5.58	0.01	3.33	1.25-8.89
PNI						
Yes vs No	0.04	2.28	1.03-5.05	0.04	2.59	1.00-6.66
LVI						
Yes vs No	0.40	1.37	0.64-2.91			
Surgical Margin						
Positive vs. Negative	0.16	1.62	0.82-3.21			
BMI						
Oweweight vs Non-overweight	0.24	1.49	0.76-2.89			
Sarcopenia						
Yes vs No	0.001	5.21	1.90-14.26	0.002	6.33	2.00-19.97

ECOG PS: Eastern Cooperative Oncology Group Performance Status, PNI: perineural invasion, LVI: lyphovascular invasion BMI: Body Mass Index, HR: Hazard Ratio, CI: Confidence Interval.

Furthermore, one of the reasons why more chemotherapy toxicity is seen in sarcopenic patients may be the fact that these patients are generally elderly and more fragile. These group of patients have frequently comorbidities and hepatic and/or urinary disorders. Therefore, It may have an effect on the metabolism of chemotherapeutics and increasing the toxicity.

In addition, Mir et al. suggested another hypotheses that systemic inflammation underlies sarcopenia, and might play a role in the occurrence of toxicities.[30]

In our cohort, toxicity and treatment delay and/or discontinuation due to chemotherapy-related side effects were more common in the sarcopenic group($p<0.05$) than non-sarcopenic group.

As a result, this study has shown that patients with sarcopenia or lower SMA before treatment, should be considered for prevention and aggressive management of chemotherapy toxicity.

Secondly, the present study is set out to investigate value of PET/CT on detecting sarcopenia. Although various measurements have been used to examine sarcopenia in the literature, CT is considered to be a highly precise tool for assessing body composition because it can distinguish different tissues.[31] PET/CT has been started to preferred more in recent studies.[14] One of the most important reasons for this is low-dose radiation exposure. A recent study by Albano D et al. demonstrated that smooth muscle area, visceral adipose tissue, and subcutaneous adipose tissue measurements obtained with PET/CT (known as low-dose CT) imaging are similar to those of the high-dose CT imaging.[32] In view of all that has been mentioned so far, it can be interpreted that not exposing the patient to unnecessary radiation can be considered as one of the advantages of PET/CT imaging.

Moreover, PET/CT is performed routinely for the staging of

Table 3b. Univariate and Multivariate Analysis Predicting Disease Free Survival

	Univariate Analysis			Multivariate Analysis		
Categorical Variables	**p**	**HR**	**CI 95%**	**p**	**HR**	**CI 95%**
Gender						
Female vs Male	0.68	1.10	0.69-1.75			
Smoking History						
Yes vs No	0.03	1.64	1.02-2.63	0.01	0.53	0.32-0.89
Diagnostic Age						
≥60 vs <60	0.06	1.57	0.97-2.55			
ECOG						
≥2 vs <2	0.19	2.05	0.69-6.08			
Histological Subtype						
Pancreatobiliary vs Intestinal	<0.001	3.74	2.17-6.43	0.005	2.27	1.28-4.03
Grade Groups						
≥3 vs <3	<0.001	3.36	1.86-6.08	<0.001	3.47	1.89-8.29
Tumor Diameter Groups						
≥2cm vs <2cm	0.008	1.89	1.18-3.05	0.69	1.12	0.62-1.99
Stage Groups						
Stage 3 vs Stage1-2	0.01	2.27	1.16-4.45	0.02	2.33	1.12-3.34
PNI						
Yes vs No	<0.001	3.54	1.85-677	0.02	2.32	1.12-4.83
LVI						
Yes vs No	0.10	1.63	0.90-2.96			
Surgical Margin						
Positive vs. Negative	0.02	1.69	1.05-2.73	0.98	1.00	0.56-1.77
BMI						
Oweweight vs Non-overweight	0.10	1.49	0.91-242			
Sarcopenia						
Yes vs No	<0.001	2.46	1.52-3.98	0.01	1.93	1.12-3.34

ECOG PS: Eastern Cooperative Oncology Group Performance Status, PNI: perineural invasion, LVI: lyphovascular invasion BMI: Body Mass Index, HR: Hazard Ratio, CI: Confidence Interval.

many malignancies including ampullary carcinoma. In accordance with the design of our study, while PET/CT was already taken, sarcopenia was also evaluated on these images. It has conclusively seen that taking additional scans increases the cost and brings unnecessary workload.

Although we have not evaluated metabolic indices of PET/CT (such as mtv, tlg) because it was not the aim of our study, it has been found that adding metabolic indices to volumetric indices (SUVmax) for detecting sarcopenia provides a better prediction on survival in the literature.[33] This could be determined as one of the advantages of PET/CT over CT.

Another issue is that although L3 cross-sectional area has become standardized in the literature,[34] the cut off value to define sarcopenia has not yet been standardized.

Since sarcopenia can be defined according to many factors such as age, sex, ethnicity, many different cut-offs have been described in the literature.

We reviewed the literature to investigate the most appropriate cut-off value for our study. Based on our studies, we rejected the frequently used consensus report of Asian Working Group for Sarcopenia (AWGS)[35] and The European Working Group on Sarcopenia in Older People (EWGSOP)[36] because they defined sarcopenia for geriatric population.

In another sarcopenia study conducted by Ufuk et al., sex-specific cut-offs were determined as 36 cm^2/m^2 for females, 44 cm^2/m^2 for males in our country; however, this study was conducted in healthy adults, not in cancer patients.[37]

Due to lack of standardization for determining optimal cut-off values for sarcopenia, we accepted the cut-off values obtained from a metanalysis for gastrointestinal cancer outcomes based on CT-assessed sarcopenia.[24] According to this metanalysis, sarcopenia was defined as SMA< 52.4 cm^2/m^2 for males and SMI < 38.5 cm^2/m^2 for females and it was used in 20 studies across 10 countries.[24]

Table 4. Univariate And Multivariate Analysis Predicting Sarcopenia

	Univariate Analysis			Multivariate Analysis		
Categorical Variables	**p**	**HR**	**CI 95%**	**p**	**HR**	**CI 95%**
Gender						
Female vs Male	0.14	1.87	0.81-4.33			
Smoking History						
Yes vs No	0.53	1.30	0.56-2.98			
Diabetus Mellitus						
Yes vs. No	0.03	1.16	0.46-2.90	0.38	1.59	0.55-4.59
Diagnostic Age						
≥60 vs <60	0.02	1.33	0.22-1.24	0.03	2.91	1.07-7.96
ECOG						
≥2 vs <2	0.62	1.33	0.42-4.21			
Histological Subtype						
Pancreatobiliary vs Intestinal	0.006	4.06	1.50-11.0	0.006	5.20	1.61-16.72
Grade Groups						
≥3 vs <3	0.92	1.05	0.35-3.11			
Tumor Diameter Groups						
≥2cm vs <2cm	0.05	2.33	0.99-5.51			
Stage Groups						
Stage 3 vs Stage1-2	0.52	1.11	0.25-2.02			
PNI						
Yes vs No	0.004	1.53	0.07-1.61	0.001	2.4	0.42-1.21
LVI						
Yes vs No	0.09	1.25	0.13-1.18			
Surgical Margin						
Positive vs. Negative	0.82	1.10	0.48-2.51			
BMI						
Overweight vs Non-overweight	0.02	1.33	0.22-1.24	0.01	1.3	0.10-1.81

ECOG PS: Eastern Cooperative Oncology Group Performance Status, PNI: perineural invasion, LVI: lyphovascular invasion BMI: Body Mass Index, HR: Hazard Ratio, CI: Confidence Interval.

Limitations of our study are retrospective design, shorter follow-up period and lack of specific cut-off values for our country when determining sarcopenia. Additionally, many patients were excluded from the study even though they had CT due to inclusion criteria.

In conclusion, pre-treatment evaluation of sarcopenia plays a crucial role in cancer management. Knowing the sarcopenic patient group in advance means knowing the patient group with poor survival and a high probability of experiencing treatment-related toxicity. In order to protect this group of patients from toxicity, we believe that new indicators should be created to consider sarcopenic measurements when assessing routine treatment. However, furtherer prospective trials with larger number of patients to substantiate our findings are required.

Disclosures

Ethics Committee Approval: All procedures performed were in accordance with ethical standards of institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The study has been approved by our University Ethical Committee with a number of 09.2020.1109.

Peer-review: Externally peer-reviewed.

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