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The Impact of Sarcopenia on the Early Mortality and Survival of Patients Undergoing Primary Repair for Perforated Peptic Ulcer

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ABSTRACT

Introduction: Sarcopenia is a significant prognostic factor that influences morbidity and mortality, particularly in patients with cancer. The current study aimed to investigate the impact of sarcopenia on early mortality and survival among patients undergoing surgery for perforated peptic ulcers at our clinic.

Methods: This retrospective study was conducted at the Mersin University Faculty of Medicine, Department of General Surgery between January 1st 2010 and December 31st 2021. The study included adult patients aged >18 years who were diagnosed with peptic ulcus perforation and underwent Graham patch repair (primary closure + omental patch). Sarcopenia was assessed based on the patients' demographic data, nutritional status, and preoperative computed tomography scans, and mortality and survival analyses were performed to compare patients with and without sarcopenia.

Results: A total of 238 patients were included in the study. Of these, 165 were male (69.3%) and 73 were female (30.7%). Mean age was 50.7±16.9. The median age of the non-survivors was 63.6 years, compared to 48.4 years in those with prolonged survival ($p<0.001$), whereas the median survival of the entire sample was 84.45%, specifically 64.41% for the patients with sarcopenia and 91.06% for those without sarcopenia ($p<0.001$).

Conclusion: This study identified advanced age and sarcopenia as factors that independently decreased survival among patients undergoing primary repair for perforated peptic ulcers.

Keywords: Peptic ulcer perforation, sarcopenia, mortality, survival

Introduction

Sarcopenia is typically considered a geriatric condition that is characterized by low muscle mass and diminished muscle function (strength or performance) (1). The reported prevalence rates around the globe range from 3% to 30% in the elderly population (2). Unlike cachexia, sarcopenia does not necessitate the presence of an underlying condition, and so many cases of sarcopenia do not have cachexia. Several authors have used the term secondary sarcopenia to describe sarcopenic conditions associated with diseases such as organ failure, inflammatory diseases, malignancies, and endocrine disorders (3-5).

Sarcopenia can be characterized as 2 standard deviation (SD) points below the mean appendicular muscle mass in healthy young adults. Sarcopenia and body composition are often assessed using dual-energy X-ray absorptiometry, bioelectrical impedance analysis, and imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (6).

There have been numerous studies in the literature investigating sarcopenia and cachexia, and its prevalence in oncological patients in particular, reporting it to be a significant prognostic factor affecting morbidity and mortality (7). Although it is believed that there may be a higher risk of sarcopenia in cases with gastrointestinal tract disorders resulting from inadequate nutrition following dyspepsia and malabsorption, very few studies to date have addressed this issue. To date, studies have tended to focus on patients with inflammatory bowel disease and hepatopancreaticobiliary diseases (8), reporting a prevalence of sarcopenia of 32.0% in those with gastrointestinal tract disorders (8),

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whereas studies of patients with peptic ulcers and perforated peptic ulcers are relatively more scarce (9). Most studies of sarcopenia report a close relationship with mortality (10).

The current study aimed to investigate the effect of sarcopenia on early mortality and survival among patients undergoing surgery for peptic ulcer perforation in our clinic.

Methods

This retrospective study was conducted at the Mersin University Faculty of Medicine, Department of General Surgery between January 1st 2010 and December 31st 2021. The study included adult patients aged >18 years who were diagnosed with peptic ulcus perforation and underwent Graham patch repair (primary closure + omental patch) (Figure 1). Information on 238 patients who met the study criteria was obtained from the hospital archives. On September 2nd, 2022, the study was approved by the Mersin University Faculty of Medicine Ethics Committee (approval number 2022/610, date: 31.08.2022). Consent forms were obtained from all patients. Patients under the age of 18, those without preoperative CT imaging, those who were preoperatively-postoperatively diagnosed with malignancy, and those who underwent other surgical procedures were excluded from the study. Patients with unreliable data and for whom we were not able to follow-up were also excluded.

The patient demographics, including age, sex, weight, and height, were recorded, and body mass index (BMI) was calculated. Based on the BMI, patients were categorized as underweight, normal weight, overweight, or obese. For the calculation of the average hounsfield unit (AHU), validated sarcopenia indicators and measurements of the area and density of the right and left psoas muscles at the L3 vertebral level were performed by a single radiologist at our hospital, following the appropriate guidelines in literature (Figure 2) (11-13). For the area and density calculations, the psoas muscle was examined through axial sections at the level of the L3 vertebra. After outlining the psoas muscle and calculating the Hounsfield units and psoas area, the AHU was calculated using the following formula:

Left AHU = (Left Hounsfield Unit × Left Psoas Area)/Total Psoas Area;

Right AHU = (Right Hounsfield Unit × Right Psoas Area)/Total Psoas Area;

AHU = (Left AHU + Right AHU) / 2

Patients were categorized as sarcopenic or non-sarcopenic based on the sex-specific lower quartile thresholds defined by the AHU calculation and were assigned to separate groups. The pathological threshold value for females is <20.3 HU, for males is <18.8 HU.

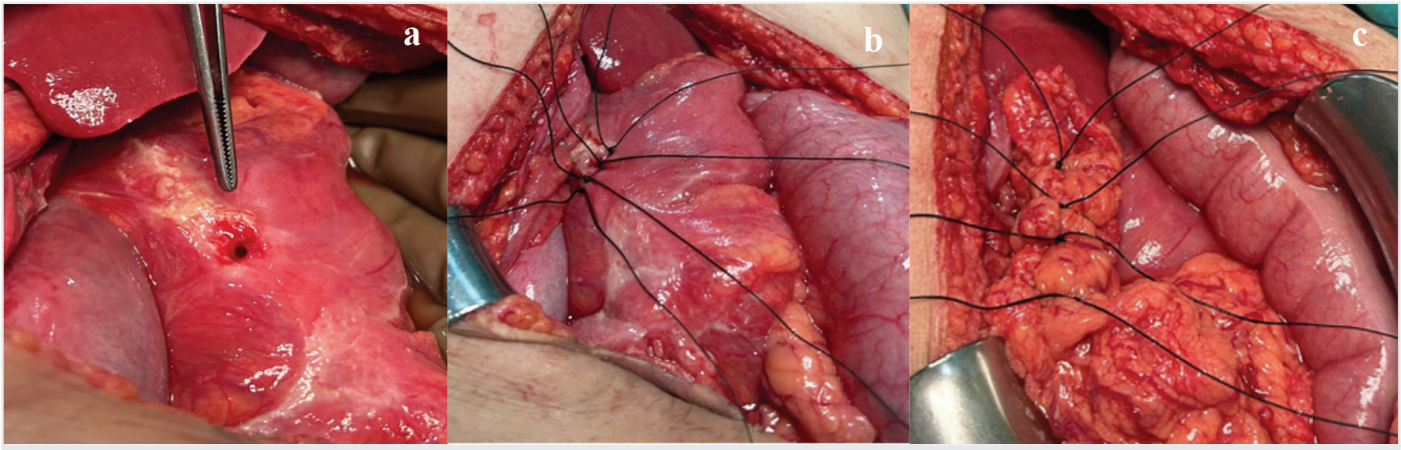

Figure 1. Graham rafi (primary repair + omental patch procedure). (a) Perforated area, (b) primary repair, (c) omental patch procedure. Informed consent was obtained from the patient to use the images for scientific purposes

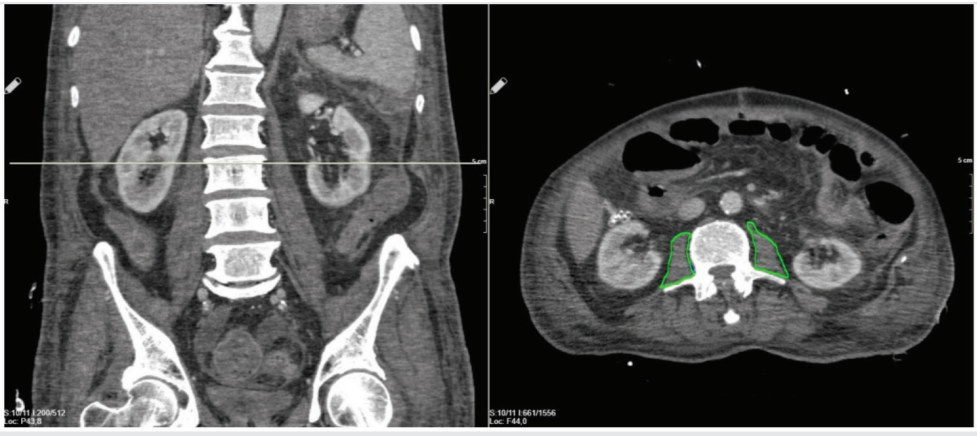

Figure 2. Hounsfield unit average calculation and psoas muscle size measurement

The non-survivors were considered a separate group, and the survival duration from the time of surgery was calculated. The patients were subsequently divided into survivors and non-survivors. The survival time of both groups was calculated in days, and mortality within the first 30 days (first month) was defined as early mortality.

Statistical Analysis

The data were analyzed using the www.e-picos.com software and the MedCalc statistical package program. For data analysis, continuous variables were presented as mean and SD and minimum and maximum values, while categorical variables were represented as frequencies and percentages. The Student's t-test was used to compare the means of the independent groups, and the chi-square test was used to evaluate the relationship between categorical variables. The odds ratio for the sarcopenia variable, which is hypothesized to be associated with early mortality/survival, was calculated at a 95% confidence interval (CI). Total survival curves were generated using the Kaplan-Meier method, and differences based on risk factors were identified using the log-rank test, with hazard ratios and corresponding 95% CIs reported. Statistical significance was determined using a p-value 0.05.

Results

Two hundred thirty-eight patients were included in the study. Of these, 165 were male (69.3%) and 73 were female (30.7%). Mean age was 50.7±16.9. Considering patient's BMI; 75 of the patients were underweight (31.5%), 131 were normal weight (55%), 27 were overweight (11.35%), and 5 were obese (2.1%). According to AHU measures, 59 of the patients were sarcopenic and 179 were not sarcopenic. The median age of mortality was 65.5. The median age of survival was 49.2. Patient age and early mortality rates were highly correlated, and a significant statistical difference was found.

No significant relationship was identified between early mortality and sex or BMI ($p>0.05$). A significant relationship was identified between the presence of sarcopenia and early mortality ($p<0.05$), with sarcopenia identified in 54.5% of the patients who died and 21.8% of the survivors (Table 1).

A survival analysis revealed that the median age of patients who died during the follow-up period was 63.6 years, compared with 48.4 years among the survivors. No significant relationship was identified between survival and gender or BMI ($p>0.05$). A significant relationship was noted between the presence of sarcopenia and survival ($p<0.05$), with a sarcopenia rate of 56.8% recorded among those who died in the long term compared with 18.9% among the survivors (Table 2).

The number of patients with sarcopenic who experienced early mortality was 4.32 times greater than that of patients who did not experience early mortality ($p<0.05$) (Table 3).

In the survival analysis, the number of sarcopenic patients who died was 5.63 times higher than the number of patients who did not die ($p<0.05$).

In the comparison of the survival curves in Table 4, the median survival is presented with a 95% CI, and the overall survival among those who underwent surgery for a perforated peptic ulcer was 84.45%. In the log-rank test comparing the two survival curves, mortality was noted in 21 of the 59 patients with and 16 of the 179 patients without sarcopenia. The chi-square statistic for this case was 25.33, with a p-value 0.05 (<0.001).

The study was concluded on day 4,134, and as can be seen in Figure 3, the probability (%) of survival decreased over time. The number of at-

Table 1. Relationship of demographics and characteristics with early mortality

	Total, (n=238)	EM (-), (n=216)	EM (4), (n=22)	p
Age	50.7	49.2	65.5	**<0.001**
	n (%)	**n (%)**	**n (%)**	
Sex				
Male	165 (69.3)	151 (69.9)	14 (63.6)	0.54
Female	73 (30.7)	65 (30.1)	8 (36.4)	
BMI				
Underweight	75 (31.5)	65 (30.1)	10 (45.5)	0.29
Normal	131 (55)	121 (56)	10 (45.5)	
Overweight	27 (11.3)	26 (12)	1 (4.5)	
Obesity	5 (2.1)	4 (1.9)	1 (4.5)	
Sarcopenia				
(-)	179 (75.2)	169 (78.2)	10 (45.5)	**0.001**
(+)	59 (24.8)	47 (21.8)	12 (54.5)	

BMI: Body mass index, EM: Early mortality

Table 2. Evaluation of socio-demographic and clinical characteristics in relationship with survival

(n=238)	Survival, (n=201)	Ex, (n=37)	p
Age	48.4	63.6	**<0.001**
	n (%)	**n (%)**	
Sex			
Male	144 (71.6)	21 (56.8)	0.07
Female	57 (28.4)	16 (43.2)	
BMI			
Undeweight	59 (29.4)	16 (43.2)	0.37
Normal	115 (57.2)	16 (43.2)	
Overweight	23 (11.4)	4 (10.8)	
Obesity	4 (2)	1 (2.7)	
Sarcopenia			
(-)	163 (81.1)	16 (43.2)	**<0.001**
(+)	38 (18.9)	21 (56.8)	

BMI: Body mass index

Table 3. Evaluation of early mortality/survival status in relation to sarcopenia

Variable	OR	Lower (95% CI)	Upper (95% CI)	p
Early mortality				
Sarcopenia	4.32	1.76	10.61	**p<0.05**
Survival				
Sarcopenia	5.63	2.69	11.81	**p<0.05**

OR: Odds ratio, CI: Confidence interval

risk patients indicates the number of patients who are at risk of an event at each time point (day).

Among the patients with sarcopenia, 59 were considered at risk at the outset of the study (day 0), and by day 1,000, the number of patients considered at risk was 38. Throughout the period from day 0 to day 1,000, mortality or censored data (no mortality) were observed in 21 patients. Among the non-sarcopenic patients, 179 were considered at risk at the outset of the study (day 0). By day 1,000, 147 patients were considered at risk was 147. Throughout the period from day 0 to day 1,000, mortality or censored data were observed in 32 patients.

Discussion

In the present study, advanced age and sarcopenia were identified as significant factors influencing early mortality and survival among patients with perforated peptic ulcers, and the inclusion of such a wide age range in the study adds significance to its findings. In a study investigating mortality and sarcopenia in patients aged 65 years and over (6), sarcopenia, like other prognostic factors, was found to be valuable in predicting mortality in elderly patients with perforated peptic ulcers. However, in patients older than 65 years, the direct influence of sarcopenia may be masked by advanced age and the presence of multiple comorbidities. In the present study, the median age of the patients who died was 63.6 years, and 48.4 years among the survivors.

Perforated peptic ulcers have been reported in the range of 3.8-14 per 100,000 (14), with a mortality rate of 8-27% that increases with age (15-18). Several studies have investigated the prognostic factors that influence mortality (16-18), and those identifying the factors that contribute to perforation and mortality, especially in patients with peptic ulcers, can be considered of critical importance. In the present study, sarcopenic patients were found to have a 7.32-fold greater risk of mortality than non-sarcopenic patients. Therefore, sarcopenia directly influences mortality. The median age was 63.6 years among the non-survivors, 48.4 years among those with prolonged survival, 65.5 years among patients who experienced early mortality, and 49.2 years among the survivors. It is necessary to consider how sarcopenia can be prevented in patients with peptic ulcers, especially the elderly, and how mortality can be reduced in the event of ulcer perforations.

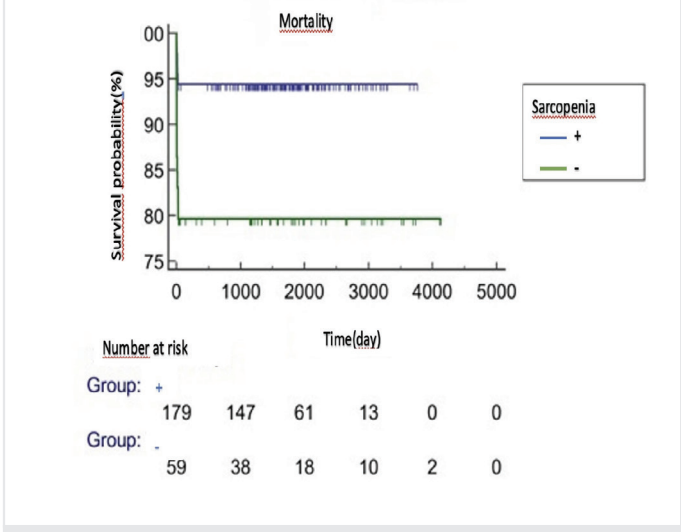

Figure 3. Sarcopenia mortality relationship

Peptic ulcers and perforations are characterized by inflammation and damage starting from the mucosa and extending to greater depths. It is believed that mechanisms involving proteins and amino acids that begin in the mucosa and contribute to the healing process may be inadequate in patients with sarcopenia (19). The defects in the protective and reparative mechanisms caused by sarcopenia can lead to acute abdominal conditions such as hollow organ perforation and mesenteric ischemia (20). In the early stages of peptic ulcer, the provision of protein-rich supplements for sarcopenia, alongside proton pump inhibitors and the standard medications used for *Helicobacter pylori* eradication, appears reasonable (21). There is little evidence supporting an increase in muscle mass in older adults taking nutritional supplements, although sarcopenia can be found in all inadequately nourished patients (22), highlighting the need for further prospective studies involving patient populations with peptic ulcers in particular.

The pathophysiology of sarcopenia involves factors such as neuromuscular aging, sarcopenia as a component of cachexia, inflammation, advanced age, immobility and confinement to bed, and sarcopenic obesity (22). For instance, in SO, not only low muscle mass but also the combination of low muscle and high fat mass has been identified as influential. In a study by Choi et al. (23), sarcopenic obesity was found to be associated with a greater prevalence of peptic ulcer disease, with an increased risk of developing idiopathic peptic ulcer disease in patients with low muscle and high fat mass. This indicates that not only sarcopenia but also various conditions related to malnutrition is contributing factors to the disease.

Study Limitations

This study has some limitations, including its retrospective nature, limited opportunity for postoperative follow-up, and the disregard for morbidities due to the lack of data.

Table 4. Comparison of survival curves (log-rank test) and HRs with 95% CI

	Long term mortalityn (%)	Survival, n (%)	Mean survival days (95% CI)	HR, (95% CI)	Log-rank (p)
Sarcopenia					
(-) (<32.65)	16 (8.94)	163 (91.06)	3424.8 (3265.1-3584.5)	7.32 (3.37-18.89)	<0.001
(+) (≥32.65)	21 (35.59)	38 (64.41)	2707.1 (2216.3-3197.9)		
Total	37 (15.55)	201 (84.45)	3496.8 (3307.1-3686.2)		

CI: Confidence interval, HR: Hazard ratios

Conclusion

In conclusion, advanced age and sarcopenia are factors that can independently decrease survival in patients undergoing primary repair for perforated peptic ulcers. Determining the risk of sarcopenia among patients with peptic ulcers is particularly important for screening and preventive measures.

Ethics

Ethics Committee Approval: This study was approved by the Mersin University Faculty of Medicine Ethics Committee (approval number 2022/610, date: 31.08.2022).

Informed Consent: Consent forms were obtained from all patients.

Footnotes

Authorship Contributions: Surgical and Medical Practices - Ö.Ö., E.R., H.B.; Concept - Ö.Ö., E.R., H.B., D.T.; Design - Ö.Ö., E.R., H.B., D.T.; Data Collection or Processing - H.B., S.E., E.E.; Analysis or Interpretation - Ö.Ö., E.R., H.B., E.E.; Literature Search - Ö.Ö.; Writing - E.R., H.B., D.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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