Published online 2022 June 20 **Original Article**

Clinical Impact of Sarcopenia on Gastric Cancer and the Effect of Neoadjuvant Chemotherapy on Sarcopenia

Cem Kaan Parsak[1], Serdar Gumus[2,*], Mehmet Onur Gul[2], Merih Altiok[2], Ayse Gizem Unal[2], Orcun Yalav[3] and Cagla Bali[4]

[1]Professor, Head of the Department of Surgical Oncology, Faculty of Medicine, Cukurova University, Sarıçam, Adana, Turkey
[2]MD, Specialist, Department of Surgical Oncology, Faculty of Medicine, Cukurova University, Sarıçam, Adana, Turkey
[3]Associate Professor, Department of Surgical Oncology, Faculty of Medicine, Cukurova University, Sarıçam, Adana, Turkey
[4]Associate Professor, Baskent University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Yuregir, Adana, Turkey

*** *Corresponding author:*** Serdar Gumus, Department of Surgical Oncology, Faculty of Medicine, Cukurova University, Sarıçam, Adana, Turkey. Tel: +905306117003; Email: seredargumus@hotmail.com

Received 2021 December 13; **Revised** 2022 January 17; **Accepted** 2022 February 10.

Abstract

Background: Sarcopenia may adversely affect treatment responses and oncological outcomes in cancer patients. However, the importance of pretreatment nutritional assessment as an indicator of treatment response and outcome in patients with gastric cancer undergoing neoadjuvant chemotherapy remains unclear.

Objectives: This study aims to investigate the clinical impact of sarcopenia on gastric cancer and to determine the effect of neoadjuvant chemotherapy (NC) on sarcopenia, as well as body mass index (BMI), psoas muscle index (PMI), and prognostic nutrition index (PNI).

Methods: A retrospective review was performed on patients with gastric adenocarcinoma who were operated on after the NC therapy between January 2016 and December 2019. Weight, BMI-, PMI-, and PNI-dependent variables were compared before and after the NC treatment. Sarcopenia was defined according to PMI at the level of the third lumbar vertebra based on computed tomography.

Results: Forty-five patients (64.4% women) with a mean age of 56.9±11.2 years were included in the study. After the NC treatment, the mean BMI of the cohort decreased from 26.1±4.3 kg/m^2 to 25.1±4.2 kg/m^2, the mean PMI decreased from 5.69±1.39 cm^2/m^2 to 5.16±1.50 cm^2/m^2, and the mean PNI decreased from 46.6±6.5 to 40.0±7.0 (All, P<0.001). The NC treatment increased the frequency of sarcopenia from 48.9% to 64.5% (P<0.001).

According to the Clavien-Dindo (CD) scoring, grade >3 CD complications were more common in the sarcopenic group (27.2%), compared to the non-sarcopenic group (8.7%) (P=0.049). The one-year and three-years overall survival rates were lower in the sarcopenic group (91.7% and 38.2%, respectively), compared to the non-sarcopenic group (93.8% and 45.8%, respectively). However, it was not statistically significant (P=0.509).

Conclusion: Sarcopenia is associated with severe postoperative complications in gastric cancer. In addition, the NC treatment reduces PMI, BMI, as well as PNI, and increases sarcopenia frequency. Therefore, patients should be examined in terms of sarcopenia at the time of diagnosis.

Keywords: Gastric cancer, Neoadjuvant therapy, Sarcopenia

1. Background

According to the World Health Organization 2020 data, gastric cancer is the sixth most common cancer worldwide and ranks fourth in cancer-related deaths (1). Advanced screening programs in Asian societies allow the early diagnosis of the disease and a longer life expectancy, compared to other eastern societies. On the other hand, life expectancy is still not very long worldwide (2).

The majority of gastric cancer patients are either malnourished or lose more than 10% of their weight in the last six months (3). The current literature accentuates the clinical importance of not only weight loss but also muscle mass loss in patients, namely sarcopenia (4). Principally, sarcopenia, which represents a decrease in skeletal muscle mass and function, is often associated with the aging process (4). Moreover, it may develop in many cancer patients due to mechanisms that have not yet been fully elucidated. The effects of sarcopenia on early postoperative and long-term oncological outcomes in gastric cancer patients are still controversial (5).

Although surgical resection continues to be the best treatment option for gastric cancer, current evidence indicates that neoadjuvant chemotherapy (NC) may increase the rate of resectability in unresectable patients and may lead to better survival rates than primary resection (6). However, a very limited number of articles in the literature have analyzed the issue of whether NC worsens sarcopenia due to the body composition changes it creates (7-10).

2. Objectives

The primary aim of this study was to investigate the clinical significance of sarcopenia in gastric cancer. The secondary aim was to reveal the effect of NC on body composition and clinical parameters. Its

tertiary aim was to investigate the effect of NC on sarcopenia.

3. Methods

3.1. Patients

A retrospective analysis was conducted on patients who had undergone surgery in the Department of Surgical Oncology, Faculty of Medicine, Cukurova University (Sarıçam, Adana, Turkey) between January 2016 and December 2019 with histopathologically confirmed gastric adenocarcinoma.

3.2. Inclusion criteria

Gastric cancer patients who had completed NC and underwent R0 resection were included in the study.

3.3. Exclusion criteria

The following patients were excluded from the study: 1) patients who were metastatic at the time of diagnosis, 2) patients who did not receive NC or those who underwent emergency surgery before completing NC, 3) patients who could not undergo R0 resection after NC, 4) Siewert I and II patients due to being treated similar to esophageal carcinoma, and 5) patients whose preoperative blood parameters and computed tomography (CT) images could not be reached.

3.4. Data collection

Demographic characteristics, such as age, gender, height, and weight, as well as chemotherapy regimens, were determined based on patients' files. Albumin and lymphocyte values were recorded by examining laboratory parameters before NC and the last laboratory parameters before surgery.

The duration of operation and the hospital stay of patients were determined. Postoperative complications were performed according to the Clavien-Dindo (11) classification (CD), and the histopathological features were examined from the pathology results.

3.5. Evaluation of skeletal muscle mass and Sarcopenia

Based on previous studies, the authors used the psoas muscle index (PMI) as an indicator of the amount of skeletal muscle mass (12,13). Cross-sectional areas of bilateral psoas muscles at the level of the third lumbar (L3) vertebra were determined using CT scanning (Figure 1) based on the Hounsfield Unit (HU). Areas corresponding to the cross-sectional areas where the psoas muscle was located in the range of –30 to 110 HU were colored and the psoas area was calculated. The researchers (M.O.G. and O.Y.) double-blind measured the clinical outcomes of the patients. The PMI was calculated by normalizing cross-sectional areas for the height (cm^2/m^2). The sarcopenia cut-off value based on the L3 skeletal muscle index is 6.36 cm^2/m^2 for men and 3.92 cm^2/m^2 for women, based on previous studies (13-15). Patients below these cut-off values were considered sarcopenic.

3.6. Evaluation of the prognostic nutritional index

Prognostic nutritional index (PNI) was calculated based on pre- and post-neoadjuvant treatment admission data as follows: 10×serum albumin (g/dl)+0.005×total lymphocyte count (per mm) (16-17).

3.7. Ethical approval

The Ethics committee approval for this study was received from the Cukurova University Ethics Committee (Date: 21 May 2021, No: 111/33).

3.8. Statistical analysis

Data were analyzed with the SPSS software (version 24.0). Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean±SD, as well as minimum-maximum. The conformity of the variables to the normal distribution was examined using one of the analytical methods. The Chi-square test and the Student t-test were used to compare the groups. Paired sample t-test was utilized to compare the means. Survival analysis was performed using the Kaplan-Meier Log-rank test. Results are reported as mean±SD, median, number (n), and percent (%). A P-value of <0.05 was considered significant.

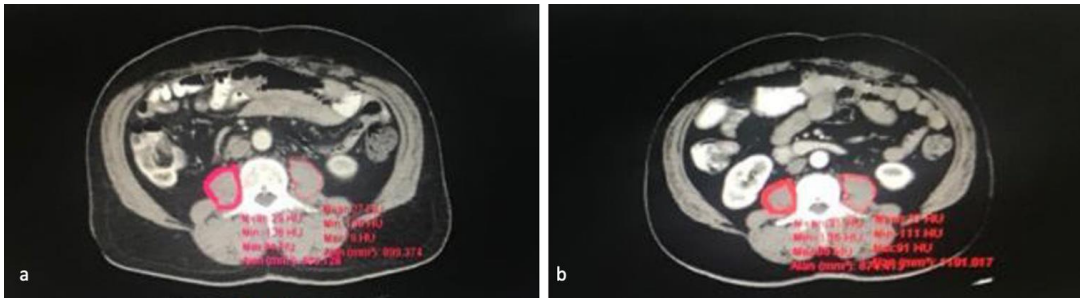

Figure 1. Evaluation of psoas muscle index in the same patient.
a) CT image before neoadjuvant chemotherapy
b) CT image after neoadjuvant chemotherapy (before surgery)

4. Results

4.1. Cohort demographics

Clinical characteristics of patients are given in Table 1. Forty-five patients, 29 (64.4%) of them women, with a mean age of 56.9±11.2 years, were included in the study. The median time between the NC treatment and surgery was 87.3 (range=36.4-201) days. Thirty patients (66.7%) had received Folinic acid, 5-Fluorouracil, Oxaliplatin, and Docetaxel (FLOT) treatment for NC. On the other hand, others were given Docetaxel, Cisplatin, and 5-Fluorouracil (DCF), as well as Epirubicin, Cisplatin, and 5-Fluorouracil (ECF) regimens. Nutrition supplements were given to 10 patients in the non-sarcopenic group and 11 sarcopenic patients according to the Nutritional Risk Screening (NRS). Staging laparoscopy was performed on seven sarcopenic patients and six non-sarcopenic patients. Total gastrectomy was performed on 36 (80%) patients. The operations were more frequently performed with open surgery (75.6%).

According to the pre-NC data, 22 patients were sarcopenic. They were older, and their operative time, as well as hospital stay, were longer; however, none of them were statistically significant (All, P>0.05). Advanced postoperative complications (CD≥3) (stump leak, anastomosis leak, wound dehiscence, and evisceration) were more common in sarcopenic patients (P=0.049).

Table 1. Comparison of clinical and demographic characteristics of sarcopenic and non-sarcopenic patients

Variables		All patients (n=45) N (%)	Non-sarcopenic (n=23) N (%)	Sarcopenic (n=22) N (%)	P-value
Gender	Male	16 (35.6)	10 (43.5)	6 (27.3)	0.256
	Female	29 (64.4)	13 (56.5)	16 (72.7)	
Age (years)		56.9±11.2	53.9±11.0	60.1±10.7	0.061
Interval between NC and surgery		87.3 (36.4-201)	97.5 (64.4-201)	79 (36.4-142)	**0.028**
Nutrition supplement		21 (46.7)	10 (43.5)	11 (50)	0.768
NC regimen	ECF	6 (13.3)	5 (21.7)	1 (4.5)	0.187
	DCF	9 (20)	4 (17.4)	5 (22.7)	0.722
	FLOT	30 (66.7)	14 (60.9)	16 (72.7)	0.530
Resection type	Distal gastrectomy	7 (15.6)	3 (13)	4 (18.2)	0.891
	Proximal gastrectomy	2 (4.4)	1 (4.3)	1 (4.5)	
	Total gastrectomy	36 (80)	19 (82.6)	17 (77.3)	
Operation type	Open	34 (75.6)	18 (78.3)	16 (72.7)	0.738
	Laparoscopic	11 (24.4)	5 (21.7)	6 (27.3)	
Complications (CD)	≤2	37 (82.2)	21 (91.3)	16 (72.8)	**0.049**
	≥3	8 (17.8)	2 (8.7)	6 (27.2)	
Time of operation (minute)		210 (150-500)	200 (150-500)	227.5 (185-480)	0.057
Hospital stays (day)		8 (2-42)	7 (4-42)	9.5 (2-25)	0.345
Histology type	Adenocarcinoma	36 (80)	20 (87)	16 (72.7)	0.426
	Mucinous Adenocarcinoma	2 (4.4)	1 (4.3)	1 (4.5)	
	Ring cell carcinoma	7 (15.6)	2 (8.7)	5 (22.7)	
Histologic grade	Grade 1	8 (17.8)	3 (13)	5 (22.7)	0.816
	Grade 2	10 (22.2)	6 (26.1)	4 (18.2)	
	Grade 3	17 (37.8)	9 (39.1)	8 (36.4)	
	NA	10 (22.2)	5 (21.7)	5 (22.7)	
ypT	T1	9 (20)	4 (17.4)	5 (22.7)	0.068
	T2	4 (8.9)	4 (17.4)	0 (0)	
	T3	3 (6.7)	0 (0)	3 (13.6)	
	T4	29 (64.4)	15 (65.2)	14 (63.6)	
ypN	N0	21 (46.7)	10 (43.5)	11 (50)	0.913
	N1	10 (22.2)	5 (21.7)	5 (22.7)	
	N2	6 (13.3)	3 (13)	3 (13.6)	
	N3	8 (17.8)	5 (21.7)	3 (13.6)	
ypTNM stage	1	11 (24.4)	6 (26.1)	5 (22.7)	0.728
	2	10 (22.2)	4 (17.4)	6 (27.3)	
	3	24 (53.3)	13 (56.5)	11 (50)	
Weight (kg)		71.8±10.2	71.0±10.9	72.7±9.5	0.585
BMI (kg/m²)		26.2±4.3	26.9±4.8	25.4±3.7	0.232
PMI (cm²/m²)		5.69±1.39	6.37±1.28	4.99±1.14	**<0.001**
PNI		46.6±6.5	46.5±6.3	46.7±6.8	0.922
Final status	Alive	20 (44.4)	11 (47.8)	9 (40.9)	0.641
	Dead	25 (55.6)	12 (52.2)	13 (59.1)	

NC: neoadjuvant chemotherapy
FLOT: Folinic acid, 5-Fluorouracil, Oxaliplatin, and Docetaxel
DCF: Docetaxel, Cisplatin, and 5-Fluorouracil
ECF: Epirubicin, Cisplatin, and 5-Fluorouracil
BMI: body mass index
PMI: psoas muscle index
PNI: prognostic nutrition index
NA: not available

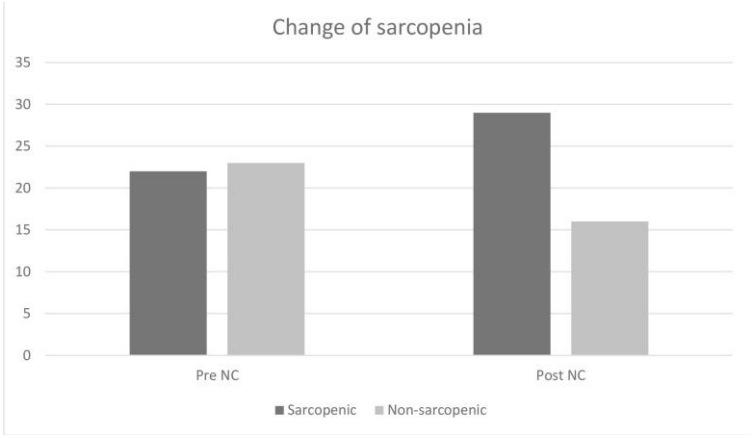

Figure 2. Changes in the frequency of sarcopenia before and after neoadjuvant chemotherapy treatment (P<0.001)

4.2. Effects of neoadjuvant chemotherapy on sarcopenia

While only 48.9% of patients were sarcopenic before NC, the rate of sarcopenia increased to 64.5% after NC (P<0.001) (Figure 2).

4.3. Effects of neoadjuvant chemotherapy on BMI, PNI, and PMI

It was determined that the mean Body Mass Index (BMI) decreased from 26.1±4.3 kg/m² to 25.1±4.2 kg/m², the mean PMI decreased from 5.69±1.39 cm²/m² to 5.16±1.50 cm²/m², and the mean PNI decreased from 46.6±6.5 to 40.0±7.0 after the NC (All, P<0.001) (Table 2).

4.4.The effect of sarcopenia on survival

During the total follow-up period, 26 patients (57.8%) died. The mean overall survival (OS) in the cohort was 40.98±2.76 (95%CI: 35.56-46.4) months. The one-year OS rate of sarcopenic patients (91.7%) was lower than that in non-sarcopenic patients (93.8%) and the three-year OS rate was lower in the sarcopenic group (38.2%), compared to that in the non-sarcopenic group (45.8%); however, these were not statistically significant (P=0.509) (Figure 3).

Table 2. Effect of NC treatment on BMI, PMI, and PNI values

	BMI (kg/m²)	PMI (cm²/m²)	PNI
Pre NC (mean±SD)	26.1±4.3	5.69±1.39	46.6±6.5
Post NC (mean±SD)	25.1±4.2	5.16±1.50	40.0±7.0
P-value	**<0.001**	**<0.001**	**<0.001**
Changes	−1.05±−1.03	−0.52±0.84	−6.52±9.21

NC: neoadjuvant chemotherapy
BMI: body mass index
PMI: psoas muscle index
PNI: prognostic nutrition index

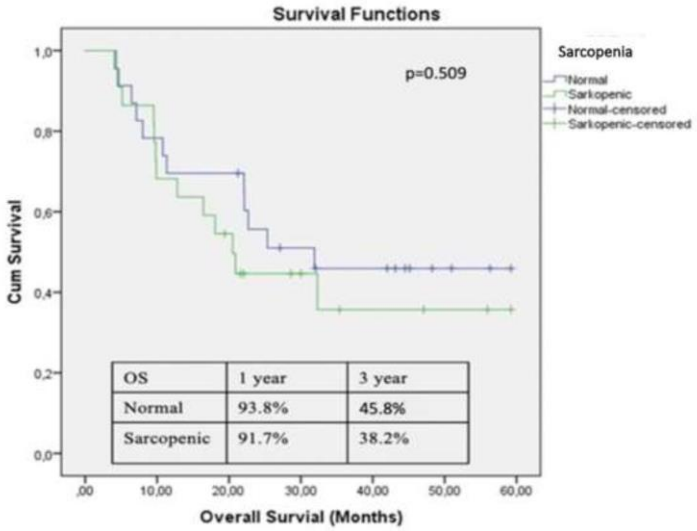

Figure 3. Kaplan-Meier analysis for the effects of sarcopenia on overall survival

5. Discussion

According to the results of the present study, sarcopenia in gastric cancer is associated with advanced postoperative complications. In addition, NC, which is included in the current treatment practice, causes physical and biochemical changes in patients and increases the frequency of sarcopenia. Therefore, it is important to protect patients from sarcopenia as soon as NC starts.

Sarcopenia is traditionally defined as an age-related reduction in muscle mass (4). It is also associated with poor prognosis in a wide range of cancers. It has been reported that sarcopenia is more common in certain cancers, such as lung, pancreatic, esophageal, and gastric cancers, compared to other malignancies (3,5,15,18,19).

The major confusion in the literature in the investigation of sarcopenia is the diversity of parameters being used (CT cross-sectional imaging, a combination of muscle mass using dual-energy X-ray absorptiometry, as well as anthropometric and physical performance measures) (4). This situation makes it difficult to compare a standard definition and the prevalence of sarcopenia among studies. Additionally, comparing the standard cut-off values for sarcopenia is another challenge due to differences in body compositions of societies and races (4).

The PMI is one of the frequently used methods in the evaluation of muscle mass. Since it is based on CT imaging, which is frequently used in the preoperative evaluation of patients, it provides data that can be easily obtained in retrospective scans (12-15). In the present study, PMI was used to evaluate muscle mass change by examining CT images before and after NC treatment.

Studies have begun suggesting that sarcopenia may also be caused by therapeutic protocols regardless of cancer and its stage (20, 21). The NC regimens, which have become an essential component of the treatment algorithm for gastric cancer in the past decade, may also cause various toxicities. Due to these toxicities, it has been demonstrated in various studies that NC can trigger or worsen sarcopenia (10). Rinninella et al. ascertained that there was a statistically significant loss of muscle mass in gastric cancer patients treated with the NC (FLOT type) (7). Matsuura et al., in their study, defined sarcopenia by examining PMI (as in this study) and emphasized that the mean PMI values decreased statistically significantly from 4.77±1.11 before NC treatment to 4.50±1.20 after NC treatment (21). The present study shows that NC treatment caused a statistically significant decrease in PMI, which is consistent with the literature.

Mirkin et al. demonstrated that preoperative chemotherapy increased the prevalence of sarcopenia and significantly increased perioperative complications (10). Awad et al. reported similar results showing that the prevalence of sarcopenia increased with NC administered for esophagogastric cancer (22). The present study also revealed that NC treatment increased the prevalence of sarcopenia in gastric cancer patients.

It is pinpointed that PNI has prognostic importance in cancer patients (23). Zhang et al. emphasized that low PNI is a strong indicator of aggressive biology and poor prognosis for patients with esophageal cancer (24). Xishan et al. found that a low PNI value was associated with lower survival rates for gastric cancer patients (25). The present study examined PNI levels and the findings confirmed that NC treatment significantly decreased PNI value.

Another parameter examined in the present study was BMI. It has long been used to diagnose malnutrition. Low BMI is generally accepted as an indicator of malnutrition (26). However, in cancer patients, weight gain or loss are not reliable indicators of body composition changes due to ascites or fluid retention, such as body edema. In addition, people tend to lose muscle mass and gain fat as they age. Therefore, patients with similar BMI may have different nutritional statuses. Nonetheless, in a study on sarcopenia, BMI examination is inevitable. This study deduced that NC treatment caused a statistically significant decrease in BMI. Similar to this study, Awad et al. revealed that NC caused a decrease in the BMI of patients and a decrease in their muscle mass (22).

The effects of sarcopenia on early postoperative outcomes are disputable. Tegels et al. accentuated that sarcopenia did not have a negative effect on early postoperative outcomes in gastric cancer (27). However, Beuran et al. found in their study that sarcopenia increased the overall postoperative morbidity in gastric cancer patients (2). According to the findings of the present study, surgery time and hospital stay were longer and advanced postoperative complication rates were higher in sarcopenic patients, compared to the non- sarcopenic ones.

With regards to the results of this study, OS was not statistically different in sarcopenic patients, compared to non-sarcopenic patients. However, one-year and three-year OS were lower in sarcopenic patients than in non-sarcopenic ones. This situation has drawn attention in various studies in the literature, as well. Voisinet et al. highlighted that sarcopenic patients in esophageal gastric cancers were not different from non-sarcopenic patients in terms of OS (28). According to Palmela et al., sarcopenia did not affect OS in gastric cancer (29). The findings of the present study were compatible with the literature on this issue.

5.1. Limitations

The present study has some limitations: retrospective design, small sample size, the fact that patients included in the analysis might have had

different supportive treatments, and different chemotherapy regimens (FLOT, DCF, and ECF) and cycles, which could have affected their immune and nutritional status differently.

6. Conclusion

Sarcopenia is associated with advanced postoperative complications in gastric cancer patients. In addition, NC treatment increases the frequency of sarcopenia and reduces BMI, PNI, as well as PMI. Therefore, it is important to examine patients for sarcopenia as soon as NC therapy starts, and nutritional support should be provided if necessary.

Acknowledgments

The authors thank all colleagues who provided patient care.

Footnotes

Conflicts of Interest: The authors have no conflict of interest to declare.
Authors' Contribution: Conceptualization: S.G., M.O.G., and O.Y.
Formal Analysis: M.O.G. and O.Y.
Investigation: All authors
Methodology: C.K.P., S.G., and M.A.
Project Administration: All authors
Writing – Original Draft: S.G., M.O.G., O.Y., and C.K.P.
Writing – Review & Editing: S.G., A.G.U., and C.K.P.
Financial Disclosure: The authors declared that this study had received no financial support.
Ethics Committee Approval: This study was approved by the Institutional Review Board of the Faculty of Medicine, Cukurova University, Sarıçam, Adana, Turkey (Date: 21 May 2021, IRB No: 111/33).
Patient Consent: Patients' informed consent was obtained at the time of surgery with surgical consent for general use of data in future studies.

References

1. World Health Organization (WHO). Global Health Estimates 2020: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2019. WHO; 2020. Accessed December 11, 2020. who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
2. Rahman R, Asombang AW, Ibdah JA. Characteristics of gastric cancer in Asia. *World J Gastroenterol.* 2014;**20**(16):4483-90. doi:10.3748/wjg.v20.i16.4483. [PubMed: 24782601].
3. Beuran M, Tache C, Ciubotaru C, Vartic M, Hostiuc S, Prodan A, et al. Sarcopenia is a predictive factor for postoperative morbidity and mortality in patients having radical gastrectomy for cancer. *Chirurgia*. 2018;**113**(5):678-86. doi: 10.21614/chirurgia.113.5.678. [PubMed: 30383994].
4. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: european consensus on definition and diagnosis: report of the european working group on sarcopenia in older people. *Age Ageing*. 2010;**39**(4):412-23. doi:10.1093/ageing/afq034. [PubMed: 20392703].
5. Kuwada K, Kuroda S, Kikuchi S, Yoshida R, Nishizaki M, Kagawa S, et al. Clinical impact of sarcopenia on gastric cancer. *Anticancer Res.* 2019;**39**(5):2241-9. doi: 10.21873/anticanres.13340. [PubMed: 31092415].
6. Schuhmacher C, Gretschel S, Lordick F, Reichardt P, Hohenberger W, Eisenberger CF, et al. Neoadjuvant chemotherapy compared with surgery alone for locally advanced cancer of the stomach and cardia: european organisation for research and treatment of cancer randomized trial 40954. *J Clin Oncol.* 2010;**28**(35):5210-18. doi: 10.1200/JCO.2009.26.6114. [PubMed: 21060024].
7. Rinninella E, Strippoli A, Cintoni M, Raoul P, Vivolo R, Di Salvatore M, et al. Body composition changes in gastric cancer patients during preoperative flot therapy: preliminary results of an italian cohort study. *Nutrients*. 2021;**13**(3):1-13. doi: 10.3390/nu13030960. [PubMed: 33809587].
8. Horii N, Kosaka T, Fujiwara R, Sato S, Akiyama H, Kunisaki C, et al. Psoas muscle depletion during preoperative chemotherapy for advanced gastric cancer has a negative impact on long-term outcomes after gastrectomy. *Asia Pac J Clin Oncol.* 2022;**18**(1):61-9. doi: 10.1111/ajco.13514. [PubMed: 33644991].
9. Voisinet M, Venkatasamy A, Alratrout H, Delhorme JB, Brigand C, Rohr S, et al. How to Prevent Sarcopenia Occurrence during Neoadjuvant Chemotherapy for Oesogastric Adenocarcinoma? *Nutr Cancer*. 2021;**73**(5):802-8. doi: 10.1080/01635581.2020.1770813. [PubMed: 32449415].
10. Mirkin KA, Luke FE, Gangi A, Pimiento JM, Jeong D, Hollenbeak CS, et al. Sarcopenia related to neoadjuvant chemotherapy and perioperative outcomes in resected gastric cancer: a multi-institutional analysis. *J Gastrointest Oncol.* 2017;**8**(3):589-95. doi: 10.21037/jgo.2017.03.02. [PubMed: 28736646].
11. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;**240**(2):205-13. doi:10.1097/01.sla.0000133083.54934.ae. [PubMed: 15273542].
12. Prashanthi PL, Ramachandran R, Radhan P, Sai V. Standardization of PSOAS muscle index measurements using computed tomography. *Int J Contemp Med*. 2020;**5**(1):169-72. doi:10.21276/ijcmsr.2020.5.1.38.
13. Hamaguchi Y, Kaido T, Okumura S, Kobayashi A, Hammad A, Tamai Y, et al. Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. *Nutrition*. 2016;**32**(11-12):1200-5. doi: 10.1016/j.nut.2016.04.003. [PubMed: 27292773].
14. Ishida T, Makino T, Yamasaki M, Tanaka K, Miyazaki Y, Takahashi T, et al. Impact of measurement of skeletal muscle mass on clinical outcomes in patients with esophageal cancer undergoing esophagectomy after neoadjuvant chemotherapy. *Surgery*. 2019;**166**(6):1041-7. doi: 10.1016/j.surg.2019.07.033. [PubMed: 31607486].
15. Zhang Y, Liu J, Li F, Cao F, Li A. Contrast-enhanced computed tomography does not provide more information about sarcopenia than unenhanced computed tomography in patients with pancreatic cancer. *Contrast Media Mol Imaging.* 2021;**2021**:1-8. doi:10.1155/2021/5546030. [PubMed: 33976592].
16. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Working group. nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr*. 2003;**22**(3):321-36. doi: 10.1016/s0261-5614(02)00214-5. [PubMed: 12765673].
17. Abe A, Kurita K, Hayashi H, Ishihama T, Ueda A. Correlation between prognostic nutritional index and occlusal status in gastric cancer. *Oral Dis.* 2020;**26**(2):465-72. doi: 10.1111/odi.13242. [PubMed: 31758866].
18. Deng HY, Zha P, Peng L, Hou L, Huang KL, Li XY. Preoperative sarcopenia is a predictor of poor prognosis of esophageal cancer after esophagectomy: a comprehensive systematic review and meta-analysis. *Dis Esophagus*. 2019;**32**(3):115. doi: 10.1093/dote/doy115. [PubMed: 30496385].
19. Yang M, Shen Y, Tan L, Li W. Prognostic value of sarcopenia in

lung cancer: a systematic review and meta-analysis. *Chest.* 2019;**156**(1):101-11. doi: 10.1016/j.chest.2019.04.115. [PubMed: 31128115].
20. Levolger S, van Vugt JL, de Bruin RW, IJzermans JN. Systematic review of sarcopenia in patients operated on for gastrointestinal and hepatopancreatobiliary malignancies. *Br J Surg.* 2015;**102**(12):1448-58. doi: 10.1002/bjs.9893. [PubMed: 26375617].
21. Matsuura N, Motoori M, Fujitani K, Nishizawa Y, Komatsu H, Miyazaki Y, et al. Correlation between skeletal muscle mass and adverse events of neoadjuvant chemotherapy in patients with gastric cancer. *Oncology,* 2020;**98**:29-34. doi: 10.1159/000502613.
22. Awad S, Tan BH, Cui H, Bhalla A, Fearon KC, Parsons SL, et al. Marked changes in body composition following neoadjuvant chemotherapy for oesophagogastric cancer. *Clin Nutr*. 2012;**31**(1):74-77. doi: 10.1016/j.clnu.2011.08.008. [PubMed: 21875767].
23. Migita K, Takayama T, Saeki K, Matsumoto S, Wakatsuki K, Enomoto K, et al. The prognostic nutritional index predicts long-term outcomes of gastric cancer patients independent of tumor stage. *Ann Surg Oncol*. 2013;**20**(8):2647-54. doi: 10.1245/s10434-013-2926-5. [PubMed: 23463091].
24. Zhang H, Shang X, Ren P, Gong L, Ahmed A, Ma Z, et al. The predictive value of a preoperative systemic immune-inflammation index and prognostic nutritional index in patients with esophageal squamous cell carcinoma. *J Cell Physiol.* 2019;**234**(2):1794-1802. doi: 10.1002/jcp.27052.
25. Xishan Z, Ye Z, Feiyan M, Liang X, Shikai W. The role of prognostic nutritional index for clinical outcomes of gastric cancer after total gastrectomy. *Sci Rep*. 2020;**10**:1-10. doi: 10.1038/s41598-020-74525-8. [PubMed: 32258526].
26. Nishigori T, Obama K, Sakai Y. Assessment of body composition and impact of sarcopenia and sarcopenic obesity in patients with gastric cancer. *Transl Gastroenterol Hepatol*. 2020;**5**:1-9. doi:10.21037/tgh.2019.10.13. [PubMed: 32258526].
27. Tegels JJ, van Vugt JL, Reisinger KW, Hulsewé KW, Hoofwijk AG, Derikx JP, et al. Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes. *J Surg Oncol*. 2015;**112**(4):403-7. doi: 10.1002/jso.24015. [PubMed: 26331988].
28. Voisinet M, Venkatasamy A, Alratrout H, Delhorme JB, Brigand C, Rohr S, et al. How to prevent sarcopenia occurrence during neoadjuvant chemotherapy for oesogastric adenocarcinoma? *Nutr Cancer*. 2021;**73**(5):802-8. doi: 10.1080/01635581.2020.1770813.
29. Palmela C, Velho S, Agostinho L, Branco F, Santos M, Santos MP, et al. Body composition as a prognostic factor of neoadjuvant chemotherapy toxicity and outcome in patients with locally advanced gastric cancer.*J Gastric Cancer*. 2017;**17**(1):74-87. doi:10.5230/jgc.2017.17.e8. [PubMed: 28337365].