Journal of Internal Medicine and Emergency Research

ISSN: 2582-7367
Forțofoiu MC, et al., 2022-Intern Med Emerg Res
Research Article

Nutrition Impact on the Prognosis of Patients with Esophageal Cancer

Mircea-Cătălin Forțofoiu[1,6], Adrian Mită[1,6], Elena Simona Micu[1,6], Anca Maria Amzolini[1,6], Anca Barău Abu-Alhija[1,6], Sorin Berbecaru[1,6], Maria Monalisa Filip[2,6], Ion-Cristian Efrem[3,6], Adina Mitrea[4,6], Diana Clenciu[4,6], Ionela Mihaela Vladu[4,9], Maria Forțofoiu[5,8], Aurelian Dobrinescu[6], Delia Cîțu[6] and Simona Munteanu[6]

Abstract

Obesity is one of the most important risk factors for esophageal cancer. Case-control studies performed in people with body mass index (BMI) over 30 kg/m2 have statistically favorable results for the occurrence of esophageal adenocarcinoma. The purpose of this study is to analyze the role of obesity in the prognosis of patients with squamous cell carcinoma and esophageal adenocarcinoma. The results of the study showed a similar profile of survival curves in patients with squamous cell carcinoma, regardless of the BMI. For patients with esophageal adenocarcinoma, there were statistically significant differences between the BMI value and their survival.

Keywords: Body mass index (BMI); Esophageal cancer; Survival rate.

Introduction

Esophageal cancer is a poor prognosis disease due to diagnoses in advanced stages of evolution. Early detection of patients with esophageal cancer and the management of the risk factors may improve the prognosis and increase the survival rate. Multiple epidemiological studies have confirmed that the obesity, especially the abdominal and visceral one, is an important consequence for the esophageal adenocarcinoma, through the sequence obesity-gastroesophageal reflux-Barett metaplasia-

[1]Department of Medical Semiology, Faculty of Medicine, University of Medicine and Pharmacy of Craiova, Romania

[2]Department of Medical Semiology, Faculty of Nursing and Midwives, University of Medicine and Pharmacy of Craiova, Romania

[3]Department of Medical Semiology, Faculty of Dentistry, University of Medicine and Pharmacy of Craiova, Romania

[4]Department of Diabetes, Nutrition and Metabolic Diseases, Faculty of Medicine, University of Medicine and Pharmacy of Craiova, Romania

[5]Department of Emergency, Faculty of Medicine, University of Medicine and Pharmacy of Craiova, Romania

[6]Internal Medicine Clinic with Gastroenterology Compartment;" Philanthropy" Clinical Municipal Hospital Craiova, Romania

[7]Endocrinology–Diabetes Clinic;" Philanthropy" Clinical Municipal Hospital Craiova, Romania

[8]Emergency Department;" Philanthropy" Clinical Municipal Hospital Craiova, Romania

[9]Diabetes and Nutrition Diseases Clinic; Clinical County Emergency Hospital of Craiova, Romania

[*]**Corresponding Author:** Mircea-Cătălin Forțofoiu, Department of Medical Semiology, Faculty of Medicine, University of Medicine and Pharmacy of Craiova, Romania and 6Internal Medicine Clinic with Gastroenterology Compartment;" Philanthropy" Clinical Municipal Hospital Craiova, Romania.

Received Date: 05-28-2022

Accepted Date: 06-15-2022

Published Date: 06-21-2022

dysplasia-esophageal adenocarcinoma [1-7]. In the last three decades, esophageal adenocarcinoma incidence has increased by more than 300% among women and by 500% among men, especially in the countries of America, Western Europe, and Australia, showing a 3-7-fold increased risk of developing esophageal adenocarcinoma in people with a BMI beyond 30 kg/m2 [8,9]. World health organization data about worldwide obesity rate, shows that over 12% of adults over the age of 20 are obese, representing about 500 million people [10].

People with a BMI over 30 kg/m2 have a 16 times higher risk of developing esophageal neoplasia compared to the normal weight population. The weight excess has also been associated with other types of cancers, the risk for developing gastric and kidney cancer is higher in people with a BMI over 35 kg/m2, compared to individuals with normal weight [11]. A series of cumulative results from observational studies demonstrate that the risk of developing esophageal cancer is associated with both BMI over 30 kg/m2 and increased abdominal circumference (AC).

Epidemiological studies show that the prevalence of gastroesophageal reflux disease is significantly higher in obese people than in the general population, with an almost linear increase of symptomatology severity for each degree of the BMI. It is interesting how, even for those with a BMI between 22.5-24.9 kg/m2, the risk was increased compared to a control group, which showed a BMI in the 20-22.4 kg/m2 range. The link between obesity, gastroesophageal reflux disease, and carcinogenesis has been explained by several processes [12]. There is a higher prevalence of esophageal motility abnormalities, lower esophageal sphincter pressure is lower, hiatal hernia is more common, and intragastric pressure is higher (especially in people with central obesity). Furthermore, visceral fat is metabolically active and produces cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-), both of which might impair the function of the lower esophageal sphincter. Obesity is associated with elevated serum levels of pro-proliferative hormones, such as insulin-like growth factor I (IGF I) and leptin, but also with low levels of adiponectin (as antiproliferative hormone), factors that may contribute to carcinogenesis of Barrett's esophagus [13-15].

Patients with esophageal adenocarcinoma had a higher incidence of visceral obesity than those with squamous cell cancer. Comparative studies performed in patients with both types of esophageal cancer, showed a statistically significant value in patients with adenocarcinoma [16,17]. Although obesity is recognized as a risk factor for esophageal cancer and especially for esophageal adenocarcinoma, the prognosis of this neoplasm does not appear to be influenced by the presence of this factor [18].

Material and method

The current study comprised 143 individuals who were diagnosed with esophageal cancer endoscopically and histopathologically and monitored for 5 years. BMI was calculated in all patients and survival curves were determined statistically according to the degree of obesity. Body mass index was calculated after measuring height and determining body weight by weighing each participant with a standardized scale. According to the International Diabetes

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Federation (IDF), the abdominal circumference was measured with a metric tape in a horizontal plane, passing through the intermediate distance between the lower edge of the ribs and the iliac crest. Abdominal circumference values greater than 94 cm in men and 80 cm in women are considered to be risk factors for the sequence obesity–gastroesophageal reflux disease–esophageal adenocarcinoma.

The generalized Wilcoxon test and the log-rank test are two tests widely used to compare survival curves. The Wilcoxon test is more sensitive for differences in survival between groups that occur later in time, while the log-rank test is more sensitive for differences that occur earlier in time, in the first few months.

Results and discussions

The demographic study of the patients showed 115 men and 28 women, with ages between 29 and 87 years. The largest group of patients was between 50-59 years old, but over half of the patients (56%) were over 60 years old, which made the average age of patients to be 61.7 years (Figure 1).

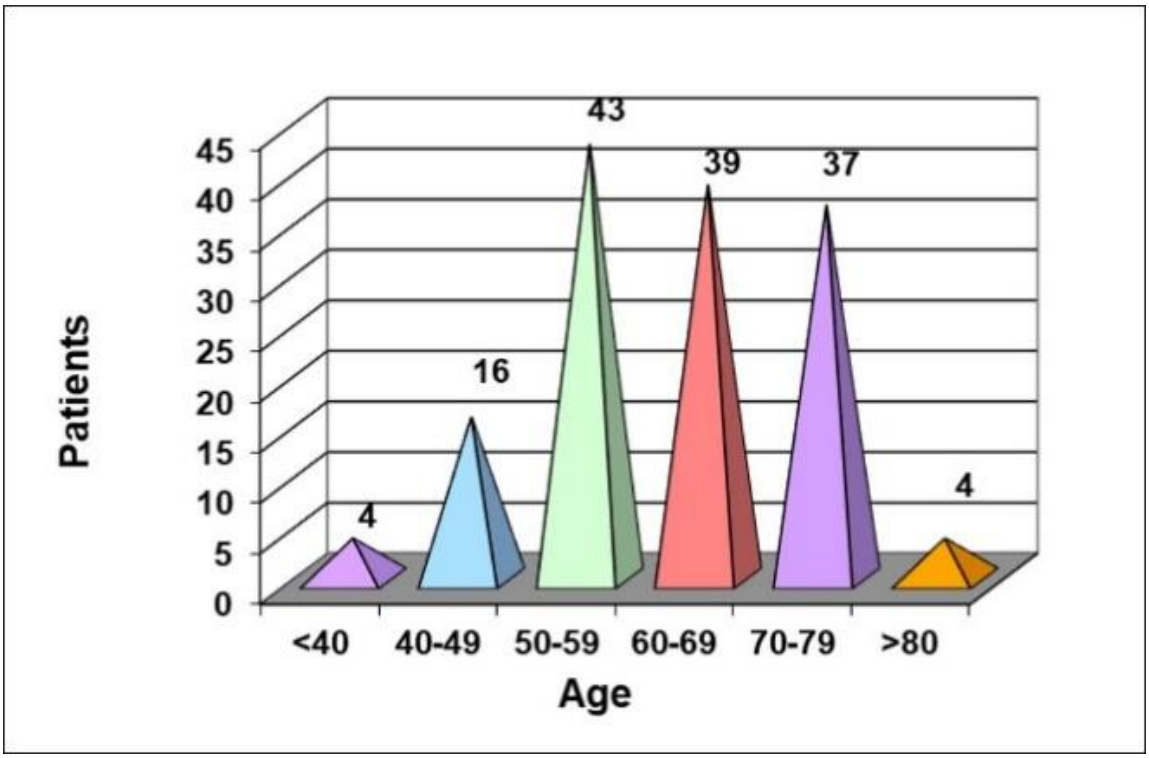

Figure 1: Patients distribution by age.

According with the histological type, the patients were divided into two subgroups: subgroup I-85 patients with esophageal squamous cell carcinoma (68 patients were men and 17 were women) and subgroup II - 58 patients with esophageal adenocarcinoma (47 patients were men and 11 were women). The body mass index of patients with esophageal squamous cell carcinoma revealed that 50 patients (39 men and 11 women) had a BMI less than 25 kg/m2, 28 patients (22 men and 6 women) were overweight with a BMI between 25 and 30 kg/m2, and 7 men had a BMI greater than 30 kg/m2 (Figure 2).

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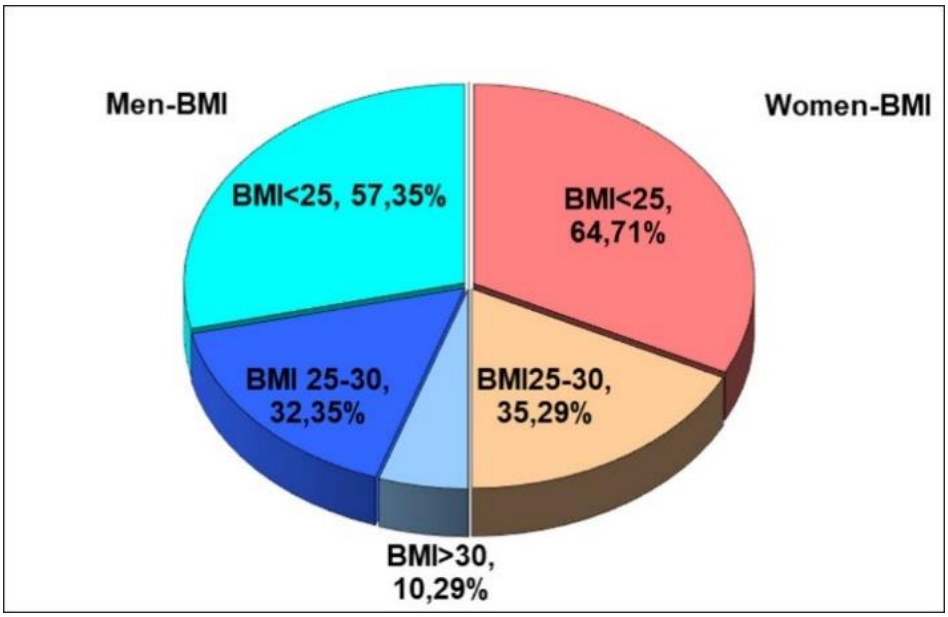

Figure 2: Distribution of patients with esophageal adenocarcinoma by sex and BMI.

The patients with esophageal squamous cell carcinoma and BMI over than 30 kg/m2 were distributed as follows: There were four patients aged 50 to 59, two patients aged 60 to 69, and one patient aged 78 (Figure 3).

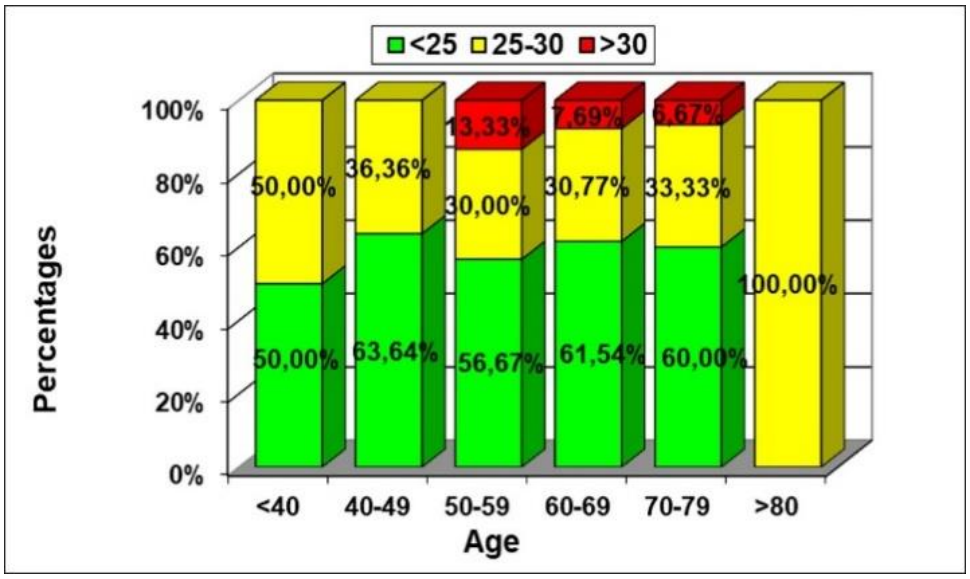

Figure 3: Distribution of patients with esophageal adenocarcinoma by BMI and age.

The abdominal circumference measurements revealed that 23 of the 68 men had values greater than 94 cm, while 10 of the women had values greater than 80 cm (Figure 4).

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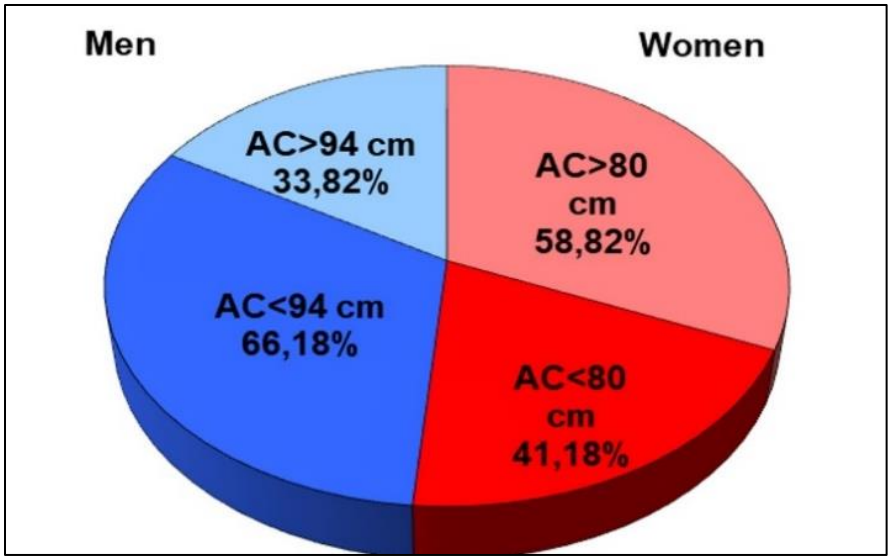

Figure 4: Distribution of patients with esophageal adenocarcinoma by sex and abdominal circumference (AC).

Correlating the BMI with the abdominal circumference resulted that out of the 23 men with AC>94 cm, 13 had a BMI between 25-29,9 kg/m2, 7 had a BMI>30 kg/m2, and 3 patients had a BMI equal to 24 kg/m2. In women group, 5 patients with AC>80 cm had a BMI between 25-29,9 kg/m2, falling into the overweight class. The body mass index of the patients in subgroup II revealed that 18 patients (12 men and 6 women) had a BMI less than 25 kg/m2, 24 patients (20 men and 4 women) were overweight with a BMI between 25 and 30 kg/m2, and 16 patients had a BMI greater than 30 kg/m2 (15 men and 1 woman) (Figure 5).

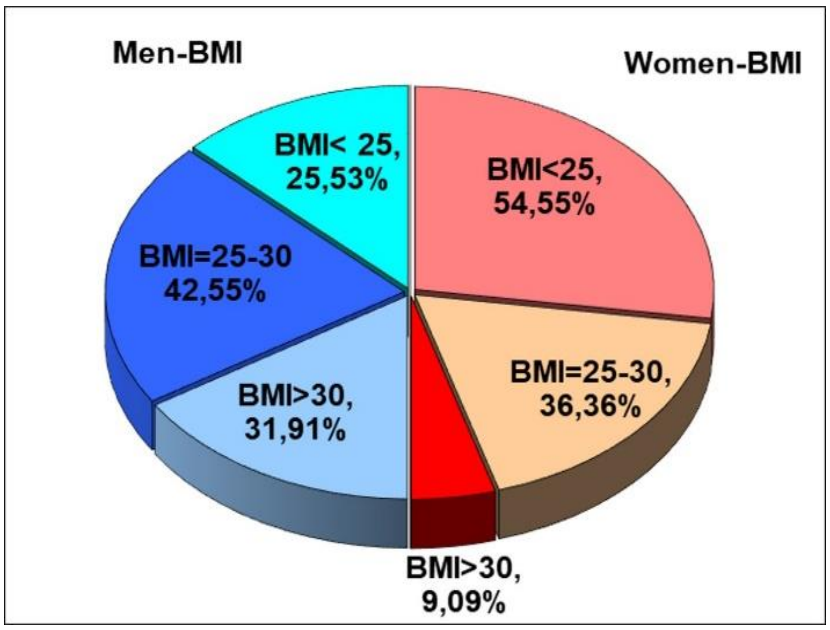

Figure 5: Distribution of patients with esophageal adenocarcinoma by sex and BMI.

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The obesity predominated in patients aged 40-49 years followed by a gradual decrease in the number of obese patients with age (Figure 6).

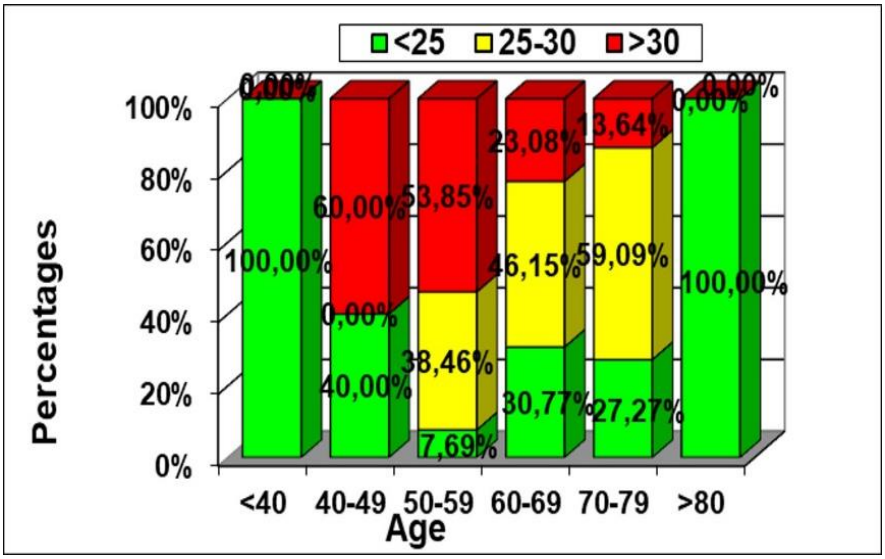

Figure 6: Distribution of patients with esophageal adenocarcinoma by BMI and age.

The abdominal circumference of the 47 men with esophageal adenocarcinoma was measured, and 31 of them had values more than 94 cm at the waist level. Among women, 9 exceeded the value of 80 cm at the waist level (Figure 7).

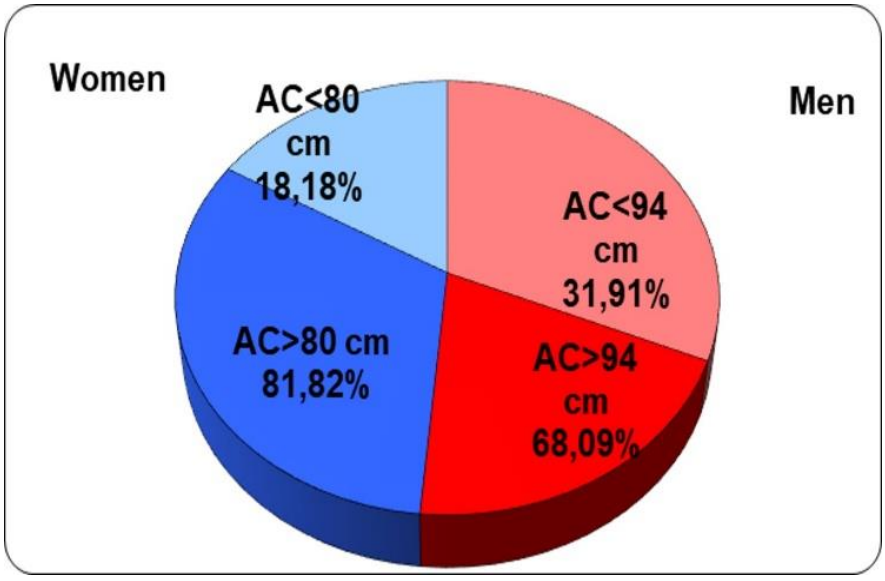

Figure 7: Distribution of patients with esophageal adenocarcinoma by sex and abdominal circumference.

Correlating the BMI with the abdominal circumference resulted in the fact that out of the 31 men with AC>94 cm, only 15 men had a BMI>30 kg/m2. A single woman patient had a BMI>30 kg/m2. Comparing the two groups, Obesity and overweight were shown to be

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more prevalent in patients with esophageal adenocarcinoma, with over 70% of patients in subgroup II having a BMI of greater than 25 kg/m2 (Figure 8).

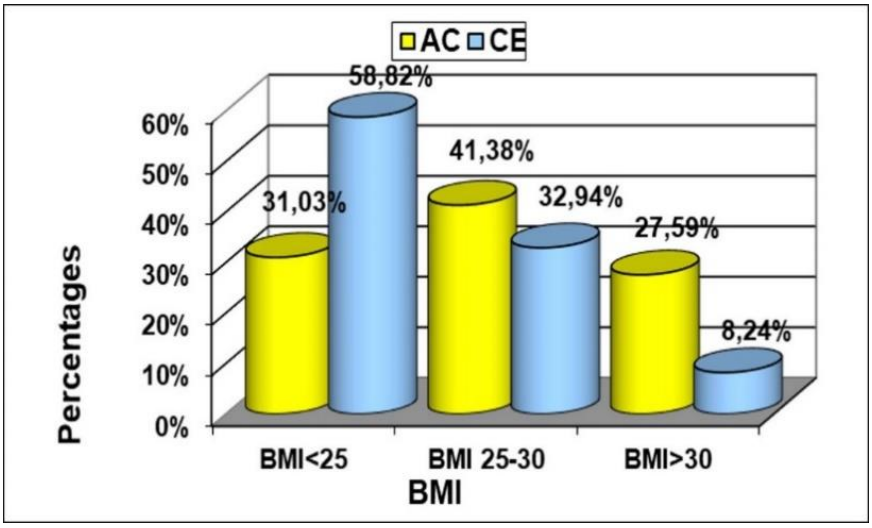

Figure 8: Patients' distribution by BMI and histopathological forms.

Subgroup II had a higher proportion of patients with increased abdominal circumference values, with over 70% of patients with esophageal adenocarcinoma having increased abdominal circumference compared to only 40% of patients with esophageal squamous cell carcinoma (Figure 9).

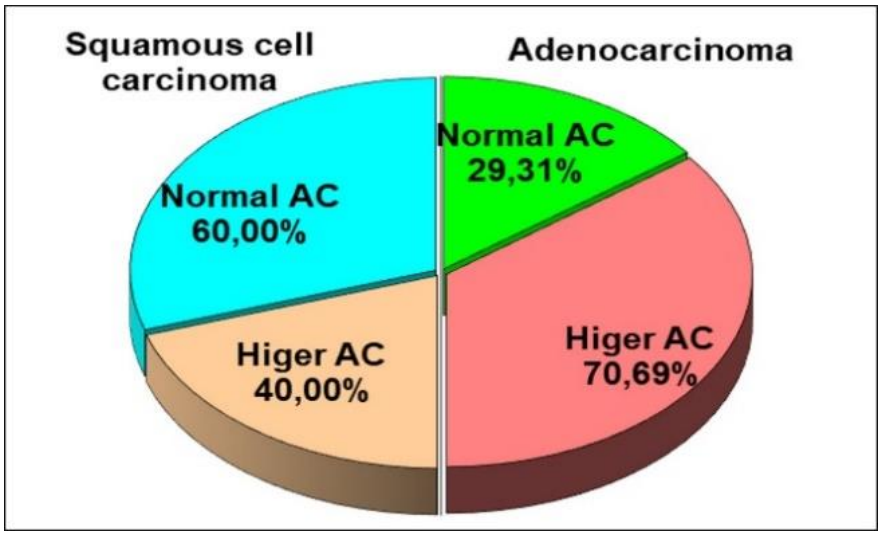

Figure 9: Patients' distribution by abdominal circumference and histopathological forms.

By comparing the two subgroups in term of the BMI and the abdominal circumference, statistically significant differences were found. Only 34 patients were still alive at the end of the trial, indicating that the average survival span was 14 months. There was a low percentage of survivors at 12 months after diagnosis, which demonstrates the extremely aggressive nature of this neoplasm (Figure 10).

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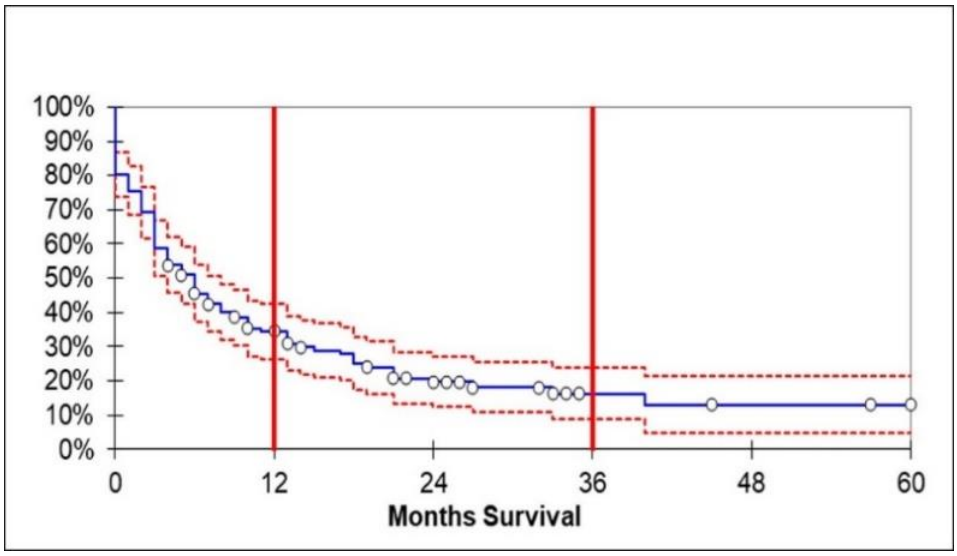

Figure 10: Survival curves for the entire study lot.

The Kaplan-Meier curves for estimating the survival of patients according to their nutritional status revealed a similar aspect for overweight and obese patients, with statistically significant differences between BMI values and patient's survival with esophageal cancer. Patients with a BMI greater than 30 kg/m2 had the longest survival, with an average survival time of 15 months (p = 0,012) (Figure 11).

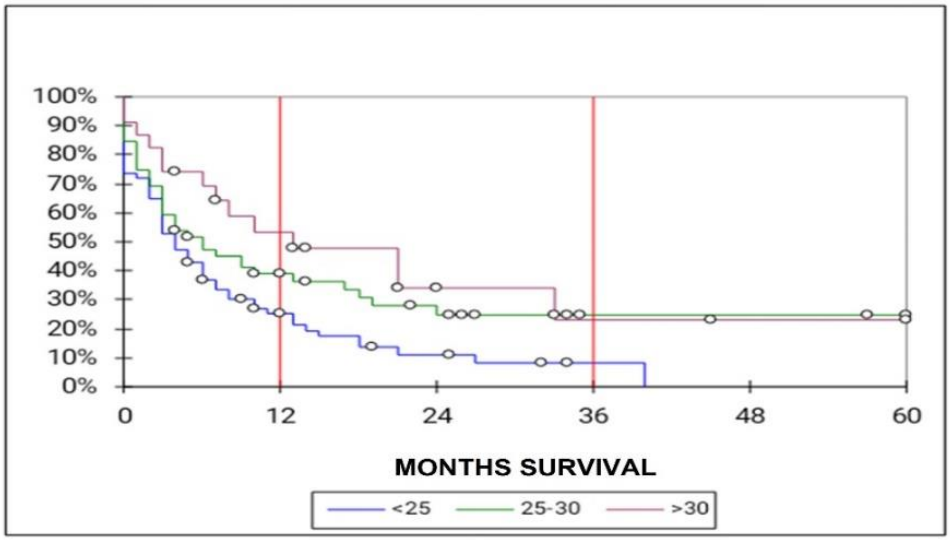

Figure 11: Survival curves in relation to the BMI value.

Comparing the two subgroups, we found similarity of the survival curves in patients with squamous cell carcinoma regardless of the BMI values. For the patients with esophageal adenocarcinoma, we found significant statistically differences between the BMI values and the survival rate (p=0,012), those patients with BMI greater than 30 kg/m2 have had the longest survival, with an average of 15 months (Figure 12,13).

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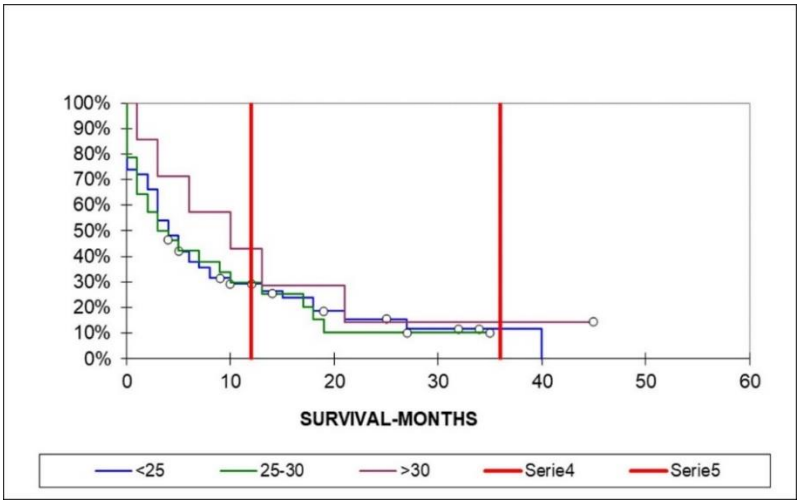

Figure 12. Survival curves for patients with squamous cell carcinoma in relation to their BMI.

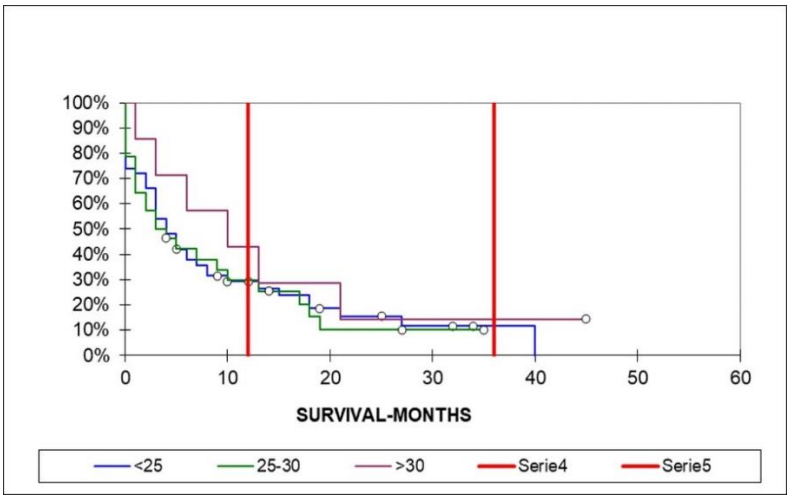

Figure 13. In patients with esophageal cancer, survival curves in response to BMI value.

Conclusions

- The male/female ratio in both histological classifications was 4/1, indicating an elevated incidence of esophageal cancer in male patients.
- For man, in esophageal squamous cell adenocarcinoma cases, the age groups 50–59 years and 60–69 years predominated, while in esophageal adenocarcinoma cases, the age group 70–79 years predominated.
- For woman, in esophageal squamous cell adenocarcinoma cases, the age groups 50–59 years and 60–69 years were equally represented, as were the 60–69 years and 70–79 years groups in esophageal adenocarcinoma cases.
- The majority of the patients in the study had a short survival time, with a median of 14 months.
- Similar appearance of survival curves was discovered in squamous cell carcinoma group regardless BMI. Statistically significant differences between the BMI values and the survival of patients with esophageal

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adenocarcinoma were found. Patients with a BMI of more than 30 kg/m2 have had the best survival rates (15 months).

- The diagnosis of esophageal cancer in advanced, often terminal stages, is a red flag for the detection time, requiring screening programs development and implementation.

Conflict of interest

The authors have no conflict to disclose

Author Contributions

Conceptualization, E.S.M., A.M.A., I.M.V., D.C.; methodology, A.M., M.C.F, A.D., D.C.; software, A.B.A., A.M.; validation, M.I.V., M.F., M.M.F.; formal analysis, S.B.I, I.C.E., S.M.; investigation, A.D.; resources, M.C.F, A.D., D.C; data curation, E.S.M., A.M.A., I.M.V., D.C.; writing-original draft preparation, A.P., S.D.P., M.I.V.; writing-review and editing, M.I.V., M.F., M.M.F.; visualization, S.B.I, I.C.E., S.M.; supervision, M.M.F., M.F., S.B.I., I.C.E.; project administration, E.S.M., A.M.A. M.C.F. All authors have read and agreed to the published version of the manuscript and share first authorship.

Funding

This research received no external funding.

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