

# Quality of life of esophagectomized patients: adenocarcinoma versus squamous cell carcinoma

## *Qualidade de vida de doentes esofagectomizados: adenocarcinoma versus carcinoma epidermoide*

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### A B S T R A C T

**Objective:** To evaluate and compare the quality of life (QOL) of patients undergoing esophagectomy for treatment of adenocarcinoma of the esophagogastric junction and squamous cell carcinoma. **Methods:** We conducted a cross-sectional study in postoperative patients submitted to esophagectomy for adenocarcinoma of the esophagogastric junction (ACA) and squamous cell carcinoma (SCC), using the SF-36 questionnaire applied in 24 patients (10 ACAs and 14 SCCs), from the 5th months postoperatively, including clinical symptoms and weight change. **Results:** The assessment of QOL showed the best functional capacity ( $p = 0.018$ ) in the ACA group. There was a correlation between the domains "mental health" and "Role of Emotions" ( $p = 0.003$ ) and between "pain" and "physical aspects limitation" ( $p = 0.003$ ) in both histological types. Weight loss was greater in ACA (45.9 kg), with no significant difference between current BMI ( $p > 0.66$ ). Dysphagia was reported by 83.3% of patients, anorexia by 58.3%, chewing difficulty by 42%, nausea and vomiting by 41.7% and diarrhea by 29.2%, with no correlation with QOL reported ( $p > 0.05$ ). **Conclusion:** The highest score for functional capacity indicates that ACA patients were able to perform all types of physical activity, including the more demanding, at a higher level than patients with SCC. Some symptoms persisted postoperatively, but did not affect the quality of life of patients.

**Key words:** Adenocarcinoma. Carcinoma, squamous cell. Quality of life. Esophagectomy. Deglutition disorders.

### INTRODUCTION

Squamous cell carcinoma (SCC) used to be the main focus of attention of the studies on esophageal cancer<sup>1</sup>. However, increased incidence of adenocarcinoma of the esophagogastric junction (Adenoca) has been reported in the last four decades<sup>2</sup>.

The SCC is strongly correlated with smoking and alcohol consumption, and the adenocarcinoma of the esophagogastric junction is associated with Barrett's esophagus and gastroesophageal reflux<sup>3</sup>. Evidence suggests that obesity is positively associated with risk of developing esophageal Adenoca, while malnutrition has been linked to SCC<sup>4</sup>.

There are comparative analysis of the quality of life of patients submitted to esophagectomy according to some surgical aspects, such as comparing the limited trans-hiatal resection to extensive transthoracic resection<sup>5</sup>; between reconstruction with gastric tube and interposing the colon<sup>6</sup>; comparison between curative esophagectomy

and palliation<sup>7,8</sup>; or even the comparison between the domains of quality of life with symptoms (physical and emotional) and factors related to illness and operation<sup>9</sup>. We did not find in the literature the possible differences between the quality of life of patients submitted to esophagectomy for Adenoca of the esophagogastric junction and the one of those submitted to esophagectomy by SCC.

De Boer et al. compared the quality of life of patients undergoing esophagectomy for Adenoca three years after trans-hiatal or transthoracic resection<sup>5</sup>. Moreover, Rosmolen *et al.*, in a longitudinal study, analyzed the quality of life among survivors of long periods<sup>8</sup> (minimum two years) after resection and reconstruction with transmediastinal gastric tube in 100 patients, also in patients with Adenoca. De Boer et al., in another longitudinal study, included 67% of Adenoca in the total sample studied and 28% of SCC<sup>9</sup>.

In the first six months after surgery, during a variable period of time the patient experiences undesirable

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symptoms, such as low food intake, nausea, ongoing weight loss, feeling of weakness, diarrhea, dysphagia and pain<sup>10</sup>, and a quality of life that can be greatly impaired, returning to preoperative levels<sup>7,11</sup>. Thus, once it is possible to better evaluate and investigate these symptoms, they can certainly be minimized through guidelines and treatments, improving the quality of life of the patient.

The objective of this study was to evaluate and compare the quality of life of patients submitted to esophagectomy for adenocarcinoma of the esophagogastric junction and squamous cell carcinoma, from the fifth month postoperatively, using the generic SF-36, and to investigate weight variations, the presence of dysphagia, anorexia, nausea, vomiting, diarrhea and constipation and relate them to quality of life.

## METHODS

We performed transversal analyses of 24 patients undergoing esophagectomy from September 2004 to August 2008, due to cancer of the esophagus or cardia, from the fifth postoperative month. The operations were performed by the Group of Esophagus, Stomach and Duodenum Surgery of the Clinics Hospital of the Faculty of Medical Sciences, University of Campinas (UNICAMP), according to the standardized transmediastinal technique, followed by esophagogastroplasty with gastric tube, cervical esophagogastric anastomosis, pyloromyotomy and feeding jejunostomy in all cases.

This research was developed to meet the requirements of Resolution MS/CNS No 196 of October 10<sup>th</sup>, 1996, and was approved by the Ethics and Research Committee of FCM-UNICAMP, with Protocol 505/2003 on 20/07/2004.

As inclusion criteria, we selected patients who were not undergoing chemo or radiotherapy and had no metastasis at the time of the study. No patient had verbalizing or memory difficulty to answer questions and all agreed to sign an Informed Consent Informed.

We did not include patients submitted to esophagectomy for benign disease, in the immediate postoperative period or in less than five months, bedridden and those who could not attend the clinic for evaluations.

Patients were asked, via social worker, to attend to the clinic on the date established to respond to the SF-36 questionnaire and physical examination, and recording of medical history, socio-economic and cultural data and clinical symptoms.

The data analyzed were age, sex, marital status, race, education, histological type, time elapsed between the operation and the interview, weight and height to calculate body mass index (BMI) obtained in balance platform, with the individual barefoot and wearing light clothing. The results of BMI were assessed according to the World Health Organization<sup>12</sup> for adults and to Lipschitz<sup>13</sup> for elders.

Weight loss was calculated by analyzing the percentage of adequacy between the regular or usual weight of the patient before the operation and the current. The presence of dysphagia, difficulty chewing, anorexia, nausea, vomiting, diarrhea and constipation were investigated during the interview with the patient.

The quality of life was assessed by the questionnaire "Medical Outcomes Study 36-Item Short Form Health Survey" (SF-36) used in clinical practice in general, in research, evaluation of health policies and population analyzes to measure general quality of life. This questionnaire was developed by Ware and Sherbourne<sup>14</sup> and translated into Portuguese and validated by Ciconelli *et al.*<sup>15</sup>.

The SF-36 consists of 11 sections with sub-items totaling 36 questions spread across eight domains. These areas are grouped into two major components: physical and mental.

The physical component involves the domains functional capacity, role physical aspects, pain and general health, while the mental component comprises the domains mental health, vitality, emotional and social aspects. The results obtained are compared with those of Aaronson *et al.*<sup>16</sup>.

The results from the SF-36 questionnaire of quality of life indicate better results when closer to 100 and worse outcomes when closer to zero.

Due to the characteristics of the disease, the sample size was established according to the availability of patients in the period studied, the occurrence of death, loss to follow-up and reflection on the practical aspects, such as time constraints and statistical issues. We used the absolute (n) and relative (%) frequencies for nominal qualitative variables, and the mean and standard deviation for quantitative variables and to describe the values found.

The Student t test was applied to the study of mean BMI of each histological type and to comparisons of the results obtained in the domains "Pain", "General Health" and "Mental Health", and the Mann-Whitney test for domains "Functional Capacity", "Limitation due to physical aspects", "vitality", "Social Aspects" and "Limitation due to Emotional Aspects".

The search for association between the time elapsed after the operation until the interview and the results of the assessment of quality of life was performed by Pearson correlation test. Furthermore, it was assessed whether the time elapsed from operation until the interview influenced the results of the quality of life of patients interviewed. The comparison between the mean obtained for each histological type was performed by the Mann-Whitney test.

The testes of association of anorexia, dysphagia, nausea/vomiting, bowel habits and the histological type were performed by Fisher's test. Significance was considered if "p" was less than 0.05.

## RESULTS

The 24 study participants were mostly men (91.7%), Caucasian (70.8%), married (83.3%), mean age 58.8 years, minimum 44 and maximum 83 years. It is worth noting that 37.5% were elderly, or older than 60 years. Regarding education, the mean for this sample was 4.9 years studied (Table 1).

Patients eligible for the study were divided into two groups according to histological type: Adenoca (n = 10) and SCC (n = 14). All patients were evaluated with a minimum of five months postoperatively and a maximum of eight years, 11 months and four days. The mean postoperative time for survey participants was two years, four months and 26 days and, according to histological type, in cases of Adenoca the average time was one year, eight months and five days, and for SCC, two years, ten months and 31 days. However, this difference in time between the two histological types was not significant (p = 0.8168).

The distribution of variables "quality of life" and "time elapsed from operation" can be seen in figure 1.

Table 2 shows the values of the components of the SF-36 scores obtained and related to the time elapsed from operation.

The average percentage of weight loss (Table 3) was higher among patients with Adenoca (16.84%). However, the mean current BMI for the Adenoca group

was 21.5 (SD 2.7) and in the SCC group it was 21.0 (SD-2, 8), without significant difference between the results (p = 0, 6602).

When comparing the quality of life of both histological types of esophageal cancer, there was no significant difference in the domain "Functional Capacity", and all other areas were equal.

By analyzing the responses collected in the eight components of the SF-36 that were presented in Table 4, it can be said that there is a difference between the two histological types for the domain "Functional Capacity" (p = 0.017) and that for all other domains, equality cannot be rejected, and in the domains "Pain", "vitality", "Mental Health" and "Limitation due to Emotional Aspects", there is strong evidence for equality between the histological types.

The result obtained in the domain "Social Aspects" shows an average slightly different between the two histological types, but not considered significant (p = 0.2570), the same happening to "General Health" (p = 0.3591), "Limitation due to Physical Aspects" (p = 0.3614) and "Limitation due to Emotional Aspects" (p = 0.7317).

The domains "Limitations by Emotional Aspects" and "Limitation due to Physical Aspects" have the highest standard deviation among all categories, with the average component "Limitation due to Emotional Aspects" 20 points higher than the average of the variable "Limitation due to Physical Aspects".

Correlation analysis between the variable "Mental Health" and "Limitation due to Emotional Aspects" has resulted in  $r = 0.587$ , with a p-value of 0.003, and a strong evidence that there is a relationship between the two variables. Similar results were obtained in the variables "Limitation due to Physical Aspects" and "Pain", ( $r = 0.586$ ,  $p = 0.003$ ). In addition, when analyzing the correlation of these variables between patients with Adenoca and SCC separately, the correlation was even greater.

The results obtained from the 24 patients studied after administration of the SF-36 are included in Table 4. Statistical analysis using the Fisher exact test showed no statistically significant differences in the pain domain (p = 0.032) for the group Adenoca and functional capacity (p = 0.003), Limitation due to physical aspects (p = 0.027) and in social aspects (p = 0.0468) for the SCC group.

The analysis of clinical data shows that there was no association between dysphagia, anorexia, nausea, vomiting, diarrhea and constipation and histological type (Table 5). Dysphagia was reported by 83.3% of patients and remains a major postoperative symptom, followed by anorexia (58.3%), nausea and vomiting (41.7%) and diarrhea (29.2%).

Other symptoms not related to postoperative esophagectomy were investigated and displayed percentages close to 42% for difficulty chewing and 25% for constipation.

**Table 1 -** Characteristics of the sample of patients studied.

Characteristics	N (%)
<b>Gender</b>	
M	22 (91.6)
F	2 (8.4)
<b>Age (years)</b>	
< 60	15 (62.5)
60 - 69	4 (16.7)
70 a 83	5 (20.8)
<b>Race</b>	
Caucasian	17 (70.8)
Non-caucasian	7 (29.2)
<b>Tumor Histological Type</b>	
Adenocarcinoma of Esophagus or Cardia	10 (41.7)
Squamous Cell Carcinoma	14 (58.3)
<b>Marital Status</b>	
Married	20 (83.4)
Single/ divorced	4 (16.6)
<b>Education</b>	
Illiterate	2 (8.3)
Up to 4 years	11 (45.8)
Up to 7 years	3 (12.5)
More than 7 years	1 (4.17)
College graduation	1 (4.17)
Not informed	6 (25)

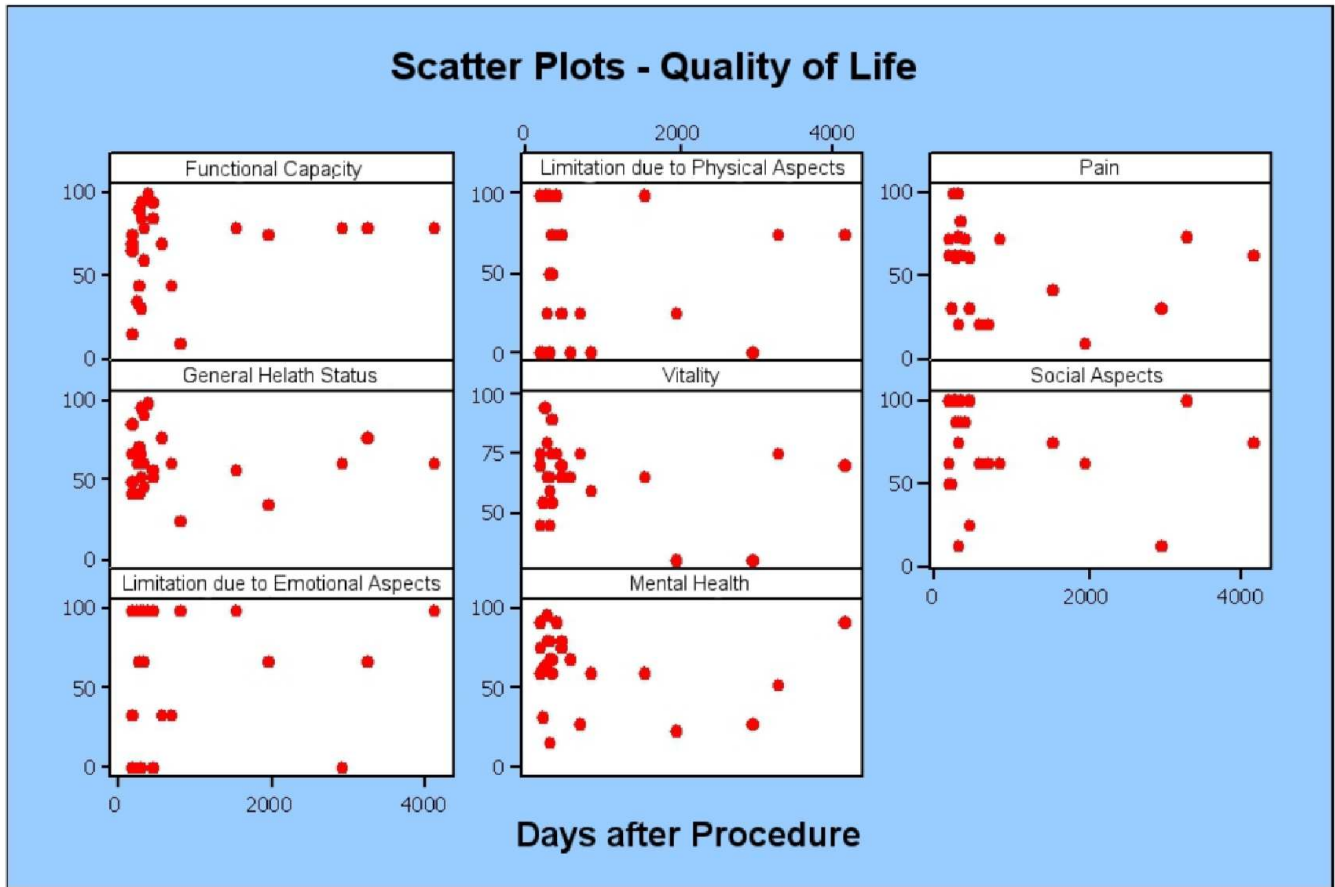


Figure 1 - Correlation between the variables of quality of life and time elapsed from the operation until the interview.

## DISCUSSION

The focus of this study was to compare the quality of life of patients submitted to esophagectomy for two histological types of esophageal cancer: the Adenoca of esophagus or cardia and SCC. The increasing frequency of

Adenoca justifies this concern<sup>17-20</sup>. Another issue to consider is the most pronounced increase in survival of patients with esophageal Adenoca when compared to patients with SCC, according to a study conducted in Sweden in the nineties<sup>21</sup>.

The SF-36 has been validated and used worldwide to evaluate patients with benign and malignant diseases, pre and

Table 2 - Mean, standard deviation, minimum and maximum values of the results of the SF-36 scores according to the histological type and the elapsed time from the operation.

Domain	Adenocarcinoma (n = 10)					Squamous Cell Carcinoma (n = 14)					p value
	mean	standard deviation	median	minimum	maximum	mean	standard deviation	median	minimum	maximum	
Functional Capacity	80.5	11.9	80.0	60.0	100.0	58.6	28.1	67.5	10.0	95.0	0.017
Limitation due to Physical Aspects	57.5	39.2	62.5	0.0	100.0	41.1	41.2	25.0	0.0	100.0	0.3614
Pain	54.5	21.6	61.5	10.0	84.0	57.1	28.1	62.0	20.0	100.0	0.8056*
General Health Status	58.4	21.5	53.5	35.0	100.0	65.8	17.1	64.5	25.0	97.0	0.3591*
Vitality	64.0	17.9	67.5	30.0	90.0	65.4	15.0	65.0	30.0	95.0	1.0000
Social Aspects	81.3	17.9	87.5	50.0	100.0	65.2	30.7	68.8	12.5	100.0	0.2570
Limitation due to Emotional Aspects	73.4	34.4	83.4	0.0	100.0	64.3	42.3	83.4	0.0	100.0	0.7317
Mental Health	61.6	20.9	60.0	24.0	92.0	64.0	25.2	68.0	16.0	96.0	0.8076*
Time after operation in months	19.2	20.4	10.4	5.6	64.0	33.4	43.6	11.9	5.0	132.0	0.8168

Mann-Whitney test/ \* Student's t test.

**Table 3** - Changes in weight after esophagectomy.

	Percentage Mean	Minimum (Kg)	Maximum (Kg)
Adenoca	16.84%	-0.7	45.9
SCC	8.54%	-2	22.9
Total	12.00%	-2	45.9

**Table 4** - SF-36 of 24 patients (58.8 years) compared to those of Aaronson et al.<sup>16</sup> in a healthy population (41-60 years).

Variable	Total sample study	p value	Adeno-carcinoma	p value	Ca epidermoid	p value	Aaronson et al. <sup>16</sup> sample
Functional Capacity	67.71 (sd 24.98)	0.003	80.5 (sd 11.89)	0.473	58.57 (sd 28.11)	0.0033	84.0 (sd 19.6)
Limitation due to Physical Aspects	47.92 (sd 40.32)	0.023	57.5 (39.2)	0.5430	41.1 (sd 41.1)	0.0270	74.5 (sd 36.8)
Pain*	56.04 (sd 25.10)	0.005	54.5 (21.58)	0.0320	57.14 (28.09)	0.0728	71.8 (sd 24.1)
General Health Status	62.71 (sd 19.00)	0.046	58.4 (sd 21.51)	0.188	65.79 (sd 17.14)	0.2329	69.7 (sd 20.6)
Vitality	64.79 (sd 15.91)	0.371	64 (sd 17.92)	0.5410	65.36 (sd 15)	0.4517	68.6 (sd 20.2)
Social Aspects	71.88 (sd 26.90)	0.056	81.25 (sd 17.92)	0.731	65.18 (sd 15)	0.0468	83.5 (sd 22.1)
Limitation due to Emotional Aspects	68.07 (sd 38.66)	0.735	73.4 (sd 34.4)	0.844	64.3 (sd 42.3)	0.5161	81.6 (sd 33.2)
Mental Health*	63 (sd 23.03)	0.013	61.6 (sd 20.93)	0.064	64 (sd 25.15)	0.1081	75.6 (sd 18.5)

Mann-Whitney test/ \* Student's t test

**Table 5** - Association of anorexia, dysphagia, nausea / vomiting and bowel habits with histological type.

	TOTAL		Adenocarcinoma		Squamous Cell Carcinoma		p value
	n	%	n	%	n	%	
<b>Anorexia</b>							0.6785
absent	10	<b>41.7</b>	5	<b>50.0</b>	5	<b>35.7</b>	
present	14	<b>58.3</b>	5	<b>50.0</b>	9	<b>64.3</b>	
<b>Dysphagia</b>							0.2721
absent	4	<b>16.7</b>	3	<b>30.0</b>	1	<b>7.1</b>	
present	20	<b>83.3</b>	7	<b>70.0</b>	13	<b>92.9</b>	
<b>Chewing</b>							0.2112
Good	14	<b>58.3</b>	4	<b>40.0</b>	10	<b>71.4</b>	
Bad	10	<b>41.7</b>	6	<b>60.0</b>	4	<b>28.6</b>	
<b>Nausea/Vomiting</b>							0.2112
absent	14	<b>58.3</b>	4	<b>40.0</b>	10	<b>71.4</b>	
present	10	<b>41.7</b>	6	<b>60.0</b>	4	<b>28.6</b>	
<b>Bowel Habit</b>							0.0713
constipation	6	<b>25.0</b>	5	<b>50.0</b>	1	<b>7.1</b>	
diarrhea	7	<b>29.2</b>	2	<b>20.0</b>	5	<b>35.7</b>	
normal	11	<b>45.8</b>	3	<b>30.0</b>	8	<b>57.1</b>	

Fisher's exact test (p> 0.05)

postoperatively<sup>14,15,22</sup>. And it was very useful in this population, since 79% of interviewed patients had some degree of functional illiteracy. The use of a visual scale that could be used in these situations to corroborate the results presented would contribute to obtain information more easily. Moreover, since it is a transversal study, during the research inevitable deaths occurred; this difficulty was also reported by other authors<sup>8</sup>.

The strong point of this study was to compare our results with the data presented by Aaronson et al.<sup>16</sup> for a healthy Netherlands population, demonstrating significant differences in the pain domain (p = 0.032) for the Adenoca group, and functional capacity (p = 0.003), Limitation due to physical aspects (p = 0.027) and social aspects (p = 0.0468) for the SCC group.

The quality of life of patients with Adenoca showed similar results with the healthy population, according to research from De Boer *et al.*<sup>9</sup>, with the exception of pain domain, which differed from the healthy population. Zieren *et al.*<sup>23</sup> demonstrated that the quality of life of patients undergoing esophagectomy for SCC proved to be hampered by physical limitations.

In this research, the lowest scores were found in "Limitation due to Physical Aspects" and "Limitation due to Emotional Aspects". The lowest scores in these areas mean that the patients had problems with work or other daily activity depending on their physical and emotional health. These considerations were confirmed by the correlation found between the domains "Mental Health" and "Limitation due to Emotional Aspects" and "Limitation due to Physical Aspects" and "Pain" for all patients in general and also according to the histological type. And the best result for the histological type Adenoca in the domain "Functional Capacity" suggests that these patients are more likely than the others to perform all kinds of physical activities, including the most vigorous ones. Moreover, considering that the average of component "Limitation due to Emotional Aspects" was 20 points higher than the average of the variable "Limitation due to Physical Aspects", we can conclude that, after esophagectomy, the patient's physical condition is a greater difficulty than the psychological one.

The analysis of quality of life of patients in this study, in different transversal points (from five months to more than eight years after surgery) did not show to have been influenced by time, ie there was not a relationship of dependence between them. These results are in agreement with the prospective study of Djärv *et al.*, who included patients submitted to esophagectomy between six months and three years, with no difference in quality of life related to health after the operation<sup>24</sup>.

The dispersion analysis (Figure 1) between the variables quality of life and the elapsed time after surgery until the time of the interview also showed no statistical difference ( $p > 0.05$ ), therefore not influencing the final results of the research. However, we believe that this result

should be interpreted with caution due to the small sample and because quality of life is a subjective and multidimensional measure, results needing to be validated in a larger sample.

No association was found between quality of life and dysphagia, difficulty in chewing, anorexia, nausea, vomiting, diarrhea and constipation, although these data have been reported in both histological types. The difficulty in chewing reported by 42% of patients may be due to the presence of elderly in 37% of the sample, for whom the adequacy of dental prostheses and oral health could minimize the problems reported.

Although esophagectomy for esophageal cancer has a high operative morbidity, it is considered the standard treatment for patients with resectable tumors without clinical contraindications<sup>3,25</sup>. Knowing the quality of life of the patient and the points at which it can be improved will certainly help the patient and the healthcare team to decide the best treatment and how to face this new phase of life.

It is essential that patients undergoing esophagectomy receive postoperative behavioral and dietary counseling as part of their overall treatment. In this sense, the participation of a multidisciplinary team composed of nutritionists, physiotherapists and psychologists can help patients in their recovery. The role of the family in this confrontation contributed greatly according to the observations of Steinglass *et al.*<sup>26</sup> in their survey on quality of life in oncology, emphasizing the need to develop tools for family assessment.

In conclusion, this study showed better functional capacity in the Adenoca group when compared to the SCC group and equality between them in the other areas of assessment of quality of life. A comparison of these groups with a healthy population showed equality of life between healthy people and the Adenoca group, except for pain and worse outcomes for functional capacity when the healthy group is compared to the SCC group. Patients in both groups suffered from dysphagia, anorexia, difficulty chewing, nausea, vomiting, diarrhea and constipation, which were not related to quality of life.

## R E S U M O

**Objetivo:** Avaliar e comparar a qualidade de vida de pacientes esofagectomizados para tratamento de adenocarcinoma da junção esofagogástrica e de carcinoma epidermoide. **Métodos:** estudo transversal no pós-operatório de doentes esofagectomizados por adenocarcinoma da junção esofagogástrica (Adenoca) e carcinoma epidermoide (CEC), empregando o questionário SF-36 aplicado em 24 pacientes (10 por Adenoca e 14 por CEC), a partir do 5º mês de pós-operatório, incluindo os sintomas clínicos e a variação de peso. **Resultados:** A avaliação da QV mostrou melhor resultado de capacidade funcional ( $p=0,018$ ) para o grupo Adenoca. Houve correlação entre os domínios "saúde mental" e "limitação por aspectos emocionais" ( $p=0,003$ ) e entre "dor" e "limitação por aspectos físicos" ( $p=0,003$ ) nos dois tipos histológicos. A perda de peso foi maior nos esofagectomizados por Adenoca (45,9Kg), sem diferença significativa entre o IMC atual ( $p>0,66$ ). A disfagia foi relatada por 83,3% dos pacientes, a anorexia por 58,3%, a dificuldade de mastigação por 42%, a náuseas e os vômitos por 41,7% e a diarreia por 29,2%, sem correlação com a QV relatada ( $p>0,05$ ). **Conclusão:** O escore mais alto para capacidade funcional indica que o paciente com Adenoca foi capaz de realizar todo tipo de atividade física, incluindo as mais vigorosas em um nível maior que o paciente com CEC. Alguns sintomas persistiram no pós-operatório, porém não interferiram na qualidade de vida dos pacientes.

**Descritores:** Adenocarcinoma. Carcinoma de células escamosas. Qualidade de vida. Esofagectomia. Transtornos de deglutição.

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