

Influence of an elevated nutrition risk score in patients suffering from esophageal cancer following tumor resection

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ABSTRACT

Background: Patients who suffer from malignant tumors of the esophagus and esophagogastric junction have 5-year survival rates of up to 83%, something that is documented in the early stages of cancer. Too often, weight loss is an underestimated sign for patients suffering from cancer on the upper gastrointestinal tract. Weight loss is associated with different adverse outcomes. Even after tumor resection, malnutrition remains a severe problem that still affects long-term disease free survivors.

Material and methods: This study included the clinical courses of 205 patients suffering from cancer of the esophagus or the esophagogastric junction who were operated on between July 2007 and December 2009. On admission, the nutrition risk score was evaluated. Follow-up data were collected routinely. The aim of the underlying study was to show the prevalence of an elevated nutrition risk score (NRS) and to demonstrate its influence on perioperative mortality and morbidity. Furthermore, the relevance of an elevated nutrition risk score on the postoperative survival was analyzed.

Results: More than a third (35.8%) of the patients included in this study had a nutrition risk score of at least three. A preoperative elevated nutrition risk score did not have a significant influence on perioperative morbidity or on 30-days mortality rate. In patients with early tumor stage UICC stage I a/b, an elevated risk score of 3 or more had a significant influence on postoperative survival.

In contrast, in advanced tumor stages an increased NRS did not have a significant negative influence on survival within both UICC II a/b and UICC III a/b.

Conclusion: Further studies are required to demonstrate whether a nutritional intervention can improve the survival rates of patients suffering from malignant tumors within the esophagus and in whom an operation has to be performed.

Keywords: Weight loss, esophageal cancer, NRS

INTRODUCTION

Cancer of the esophagus and the esophagogastric junction

In the United States in the year 2016, there were over 16000 new esophageal cancer cases and cancers of the esophagogastric junction estimated, with over 15000 estimated deaths [1]. The survival of patients suffering from malignant tumors within the esophagus and esophagogastric junction depends on the stage of the tumors; there are 5-year survival rates of 83% documented in the early stages [2], and 5-year survival rates of up to 20% in all stages [1], with survival rates increasing in the last few decades. The perioperative morbidity depends on the comorbidity, in addition to the operative procedure: transthoracic approaches lead to more respiratory complications compared to a transhiatal approach. Moreover, a high volume of surgeons seem to lower the risk of anastomotic leakage [3, 4]. Weight loss induced by different changes like stenosis of the esophagus, nausea and vomiting, and malabsorption syndromes is often an existing and underestimated sign in patients suffering from cancer of the upper gastrointestinal tract [5]. However, this did not only reduce energy intake but also elevated resting energy expenditure, which is responsible for weight loss in cancer patients [6].

Weight loss is associated with different adverse outcomes [7]. After tumor resection, malnutrition often remains a severe problem, even within long-term disease free survivors [8]. For example, it has been demonstrated that in over 3000 patients who received chemotherapy, weight loss is associated with a shorter survival [9]. Fat malabsorption and reduced caloric intake have been shown to occur in patients after gastrectomy [5, 10].

In patients with pancreatic cancer, weight loss exceeding 10% of the stable body weight had a significant influence in survival, regardless of the tumor stage [11, 12]. On the other hand, weight stabilization in pancreatic cancer patients without tumor resection has been associated with improved survival rates and an overall better quality of life [13]. The nutritional risk score was established in 2003 in order to have a screening tool capable of detecting patients at risk before undertaking any kind of anticancer treatment [14]. Malnutrition in a cancer patient is a risk that will worsen the future condition of affected patients [15]. An elevated NRS has influence on infectious complications [16]. Moreover, it has been shown that in patients with an elevated NRS, the toxicity of anti-cancer treatment results in a reduction of the therapy [17].

The aim of the underlying study was to show the prevalence of an elevated nutrition risk score (NRS) in patients suffering from cancer in the esophagus and the esophagogastric junction and to demonstrate its influence on perioperative mortality and morbidity. Additionally, the relevance of an elevated nutrition risk score on the postoperative survival was analyzed

PATIENTS AND METHODS

This study included 205 patients who were operated on in the Department of Surgery, University of Munich between July 2007 and December 2009. From these patients, 32 patients were suffering from squamous cell cancer of the esophagus (SCC) and the remaining 173 patients were suffering from cancer of the esophagogastric junction (AEG). Patients in whom UICC IV was diagnosed were excluded from further analyses. In 63 patients, a primary surgical resection was performed, while in 138 patients a preoperative chemotherapy with or without radiation was conducted, followed by surgical resection.

On admission for operation, the nutrition risk score according to the definition given by J. Kondrup [14] and the ESPEN working group was evaluated. The value of the score consists of the sum of three parameters: 1st nutritional status, 2nd severity of the disease, and 3rd age. First, the data of the nutritional status was collected. To calculate the body mass index, the actual weight and height of the patient was asked for. Additionally, the patients were asked if weight loss had occurred, in addition to the amount of weight loss as well as the corresponding time period (1, 2, or 3 months) in which the weight loss had occurred. According to the scale, one point is given if the weight loss exceeds 5% within the last 3 months. Two points are given if weight loss exceeds 5% within the last 2 months and/or the BMI is between 18.5 and 20.5. Three points are given if the weight loss exceeds 5% within only one month and/or the BMI is less than 18.5. To classify the severity of the disease according to the nutrition risk score, one point is added. If the patient is suffering from a malignant disease, two points are added if abdominal surgery is planned. In patients aged 70 years or older, one additional point is added. The sum of the results was calculated. See table 1 for results.

Table 1. Evaluation of the nutrition risk score

parameter	severity	points	result
nutritional status	<ul style="list-style-type: none"> • Loss of weight > 5% in 3 months 	1	
	<ul style="list-style-type: none"> • Loss of weight > 5% in 2 months or • BMI >18.5/<20.5 	2	
	<ul style="list-style-type: none"> • Loss of weight > 5% in 3 months or • BMI <18.5 	3	
severity of the disease	oncology patients	1	
	abdominal surgery	2	
age	> 70	1	
sum			

In every patient the three parameters nutritional status, severity of the disease and age are evaluated and the points are summated

In 69 patients, a gastrectomy was done with a Roux-Y-esophagojejunostomy and in 132 patients an esophagectomy was performed, with a gastric tube being used for reconstruction. Table 2 shows the patients' characteristics in detail.

Table 2. Characteristics of 201 patients suffering from esophageal cancer

all patients N= 205		AEG (N=169) N [%]	SCC (N=32) N [%]	P value
gender	male	154 [91.1]	24 [75]	
	female	15 [8.9]	8 [25]	
age	median [lq/uq]	63 [56/72]	63 [56/67]	> 0.05
30-days mortality rate		7 [4.2]	1 [3.1]	> 0.05
morbidity		51 [46.4]	15 [62.5]	> 0.05
operation	gastrectomy	69 [40.9]	0 [0]	
	esophagectomy	100 [59.1]	32 [100]	
UICC	No visible tumor	14 [8.3]	4 [12.5]	
	UICC I a/b	62 [36.7]	16 [50]	
	UICC II a/b	37 [21.9]	9 [28.1]	
	UICC III a/b	56 [33.1]	3 [9.4]	
NRS	<3	107 [63.3]	22 [68.8]	
	>=3	62 [36.7]	10 [31.3]	> 0.05

Two independent pathologists from the Department of Pathology at the University of Munich confirmed the diagnosis of the resected tissue. The prevalence of wound infection, postoperative bleeding, anastomotic leakage, intraabdominal fluid collection, pneumonia, urinary tract infection, myocardial infarction, and pulmonary embolism were evaluated. After being discharged, the patients were presented routinely every 3 months within the first 12 months in our outpatient department. After the first year, they were presented every 6 months until the routinely performed follow up concluded 60 months after the operation. If a patient was presented in hospital after the routine follow up, we collected the survival data and included these into our analysis. Every included patient gave written informed consent for data collection. The study was performed according to the guidelines of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using the following software: IBM Corp. Released 2014. IBM SPSS statistics for Mac, Version 24.0. Armonk, NY: IBM Corp. Survival curves were calculated using Kaplan–Meier analysis and the log rank test. Results are displayed in median [with lower and upper quartile]. For testing significant differences between the examined groups, we used Student’s t-test and the Mann-Whitney U-test. A significance level < 0.05 was used. Results are reported as median and lower and upper quartiles.

RESULTS

Between July 2007 and December 2009, two hundred and five consecutive patients with esophageal cancer were presented in the department of surgery for tumor resection. Afterwards, 4 of these patients were diagnosed with UICC IV after tumor resection and were excluded from further analyses. 72 patients (35.8%) had a nutrition risk score of three or more: 62 (36.7%) of the patients were suffering from an adenocarcinoma of the esophagus and 10 (31.3%) of the patients were suffering with a squamous cell cancer of the esophagus respectively. A preoperative elevated nutrition risk score of three or more did not have a significant influence on perioperative morbidity ($P > 0.05$) or on the 30-days mortality rate ($P > 0.05$). The survival rate was significantly reduced in patients with advanced tumor stages ($P < 0.001$, figure 1). Figure 2 shows that in patients with an early tumor stage, UICC stage I a/b an elevated risk score of 3 or more has a significant influence on postoperative survival ($P = 0.006$); the mean survival is 5.6 years in patients with a NRS of less than three, while the mean survival is reduced to 3.8 years if the NRS is three or more.

In contrast, in advanced tumor stages, an increased NRS did not have a significant negative influence on survival in either UICC II a/b ($P = 0.971$) or in UICC III a/b ($P = 0.389$, figure 3).

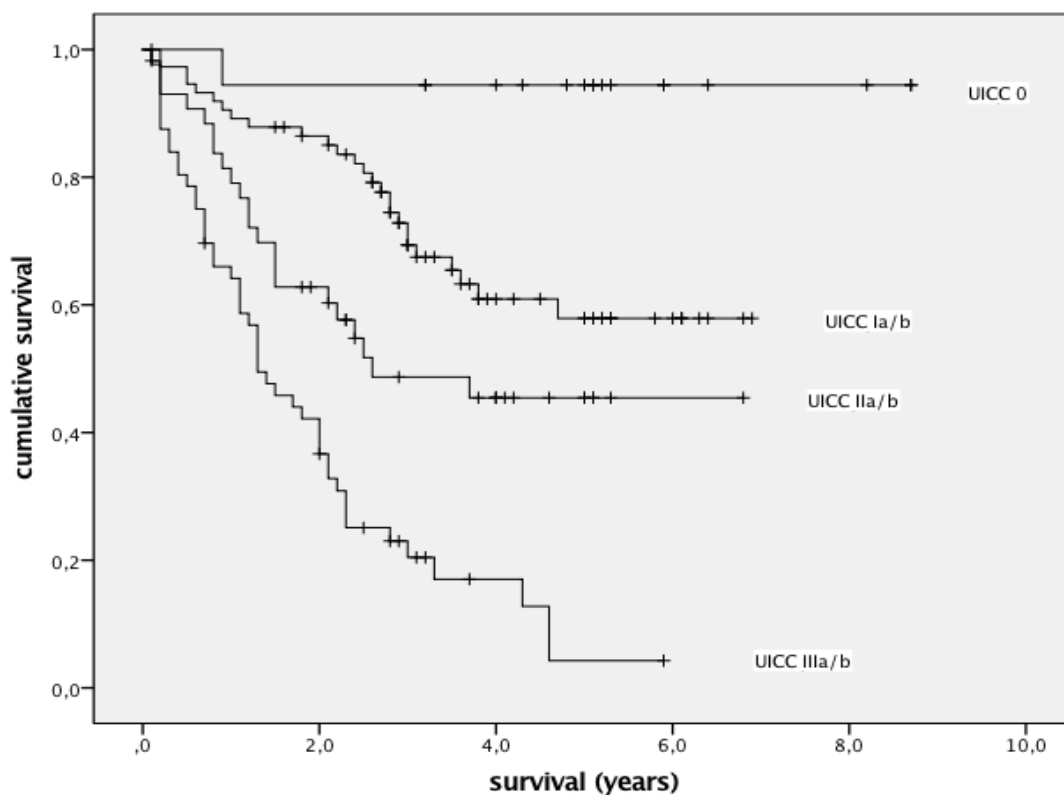


Figure 1. Kaplan- Meier survival curve in patients with an esophageal cancer with UICC stage 0 (N= 18), UICC stage I a/b (N= 78), UICC II a/b (N= 46) and UICC III a/b (N= 59) $P < 0.001$

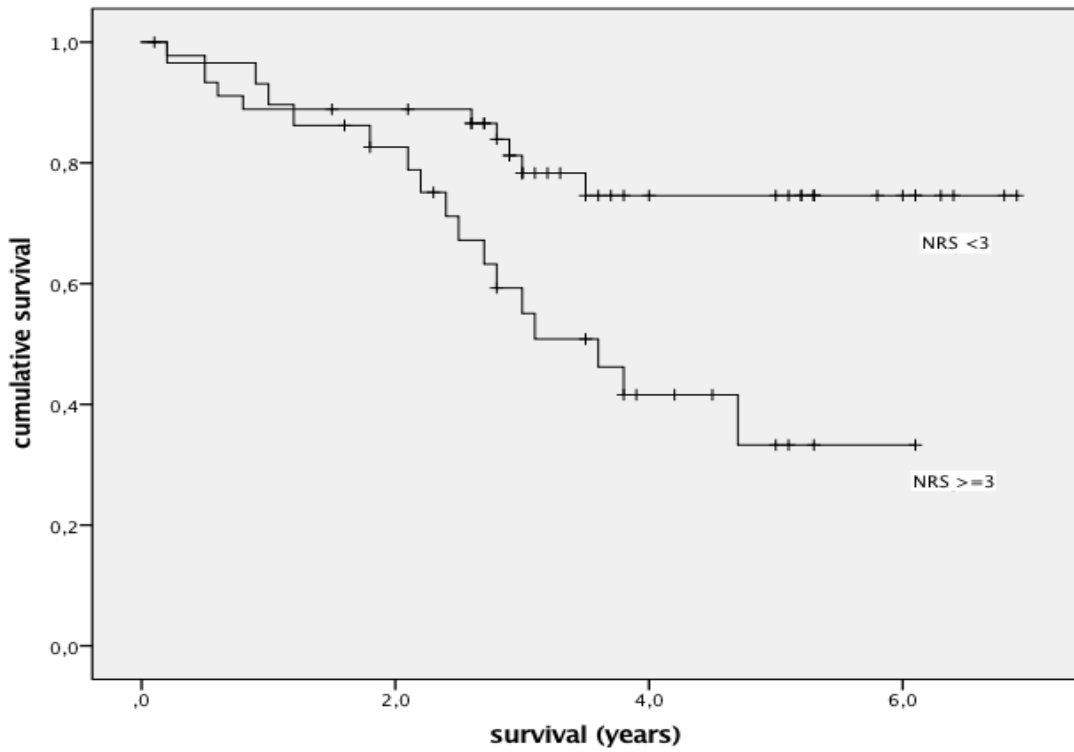


Figure 2. Kaplan- Meier survival curve in patients with an esophageal cancer with UICC stage I a/b showing the influence of the nutrition risk score

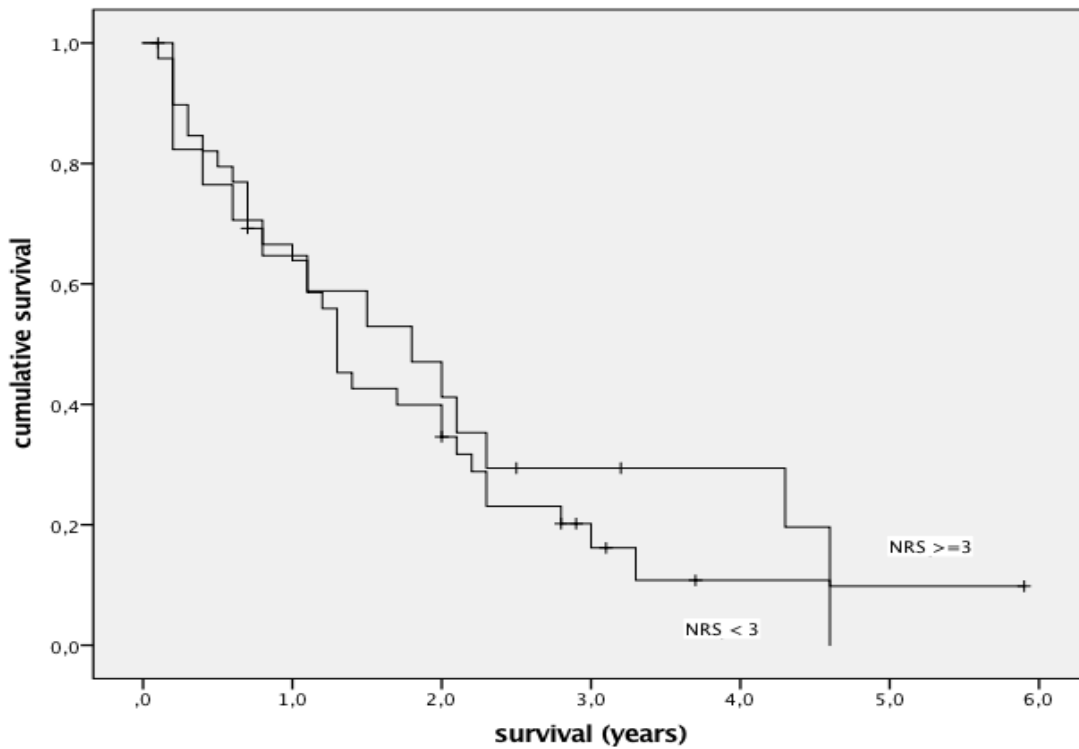


Figure 3. Kaplan- Meier survival curve in 59 patients with an esophageal cancer stage UICC III a/b (P= 0.389)

DISCUSSION

Weight loss in patients with malignant tumors of the gastrointestinal tract system is common. In a large series of over 3000 patients, it has been shown that weight loss is associated with significantly reduced survival in patients receiving chemotherapy [9].

More than every third patient (35.8%) who was presented for tumor resection because of a malignant tumor of the esophagus or esophagogastric junction had an elevated nutritional risk score at least three. This has also been shown by Bozetti et al, who evaluated the prevalence of an elevated nutrition risk score in unselected cancer patients [18]. The underlying data reveals that the prevalence of an elevated NRS did not have a significant influence on morbidity in the perioperative period ($P > 0.05$) or on the 30-days mortality rate ($P > 0.05$). With progression of tumor stage the survival was significantly reduced (see figure 1). These results have also been shown by others [2]. In patients suffering from a malignant tumor of the esophagus or esophagogastric junction with an early tumor stage (UICC I a/b), an elevated nutrition risk score (NRS ≥ 3) significantly reduced postoperative survival ($P = 0.006$).

In contrast, in advanced stages (UICC II a/b, UICC III a/b) the influence of an increased nutrition risk score did not have a significant influence on postoperative survival ($P = 0.971$, $P = 0.389$ respectively).

CONCLUSION

Further studies are required to demonstrate whether an intervention to improve the nutrition risk score (either by additional feeding or prolonged postoperative feeding) can improve survival in patients suffering from esophageal cancer in the postoperative period, especially in early tumor stages. The traditional care of “nil by mouth” has to be changed to early enteral nutrition (i.e. using feeding tubes) in order to reduce the time period in which the patient is not fed after major abdominal surgery [19].

List of Abbreviations: UICC, Union internationale contre le cancer; NRS, nutrition risk score.

Competing Interests: None of the authors has a competing interest to declare.

Authors' Contributions: J. Bachmann designed the study. Kristina Schultheiß, Olga Prokopchuk and Carina Riediger performed the practical part of the study, in addition to the statistical analysis of the data together with Marc Martignoni, Marcus Feith and JB. J Bachmann drafted the manuscript and all authors were engaged in the manuscript work. JB, MME and HF have primary responsibility for the final content. All authors have read and approved the final manuscript.

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