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A Comparison of Pre-Operative Nutritional Status with Post-Operative Morbidity and Mortality in Obese Esophageal Surgery Patients*

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Objectives. The nutrition state of obese patients scheduled to undergo esophageal surgery was evaluated using two nutritional score systems: the mini nutritional assessment (MNA) and the prognostic and nutritional index (PINI). A further comparison of various proteins, lymphocytes and cholesterol was performed using biochemical tests. These factors were compared with post-operative morbidity and mortality in a prospective, descriptive clinical study.

Material and Methods. The study included 34 obese patients undergoing esophagus resection due to cancer, who were examined over four years using both scoring systems to analyze whether nutritional status influences the outcome of surgery. The patients were divided into four groups based on the severity of the outcome and their MNA and PINI scores were analyzed.

Results. There were no significant differences between the nutritional status of survivors and deceased patients. The European Society for Parenteral and Enteral Nutrition (ESPEN) nutritional risk score was 1.35 ± 0.47 for Group I and 1.47 ± 0.58 for Group II (p = 0.62). With respect to severe morbidity there was no significant difference between Group III and Group IV: 2.01 ± 2.28 vs. 1.02 ± 3.67 (p = 0.54). Although there were minor differences, there were no major variations seen in the MNA or PINI scores comparing the four examined groups. No significant changes were observed in the biochemical parameters.

Conclusions. The study found no differences between post-operative morbidity or mortality and the pre-operative nutrition status of obese patients who underwent surgery due to esophageal cancer (**Adv Clin Exp Med 2014, 23, 5, 763–768**).

Key words: morbidity, mortality, nutrition, obesity, esophagectomy.

Evidence from animal and clinical experiments shows that malnutrition increases post-operative morbidity and mortality following elective surgery [1, 2]. However, many clinical studies have failed to show that pre-operative nutrition improves clinical outcome. Nutritional support has the potential for both risks and benefits, depending upon the type of therapy and the patient selection [3, 4]. If the therapy is used on patients who have a low risk of malnutrition-related complications, the results may reflect complications resulting from the therapy itself. If patients at risk for malnutrition-related complications receive nutritional support, then the benefits from the therapy may outweigh the risks and the post-operative outcome may be improved. Although malnutrition

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contributes to morbidity, studies of pre-operative nutrition often include well-nourished patients unlikely to benefit from therapy [5]. The situation is further complicated in cases of obesity. A recent meta-analysis on patients undergoing esophagectomy for cancer showed that on the one hand conditions like diabetes have a significant impact on the risk of anastomotic leakage and atrial fibrillation in obese patients, and on the other hand obese patients had significantly better long term survival than non-obese patients [6].

Extensive surgical intervention performed on cancer patients with malnutrition is accompanied by chronic fasting that can result in increased morbidity and mortality during the post-operative period. Verification of a direct correlation is complicated, but in patients with malnutrition, impaired wound healing and decreased immune responses can lead to damaged cardiac or skeletal muscle function and an increase in post-operative complications, which may be accompanied by increased mortality, prolonged hospitalization and elevated healthcare costs [7, 8].

Malnutrition affects all the organs except for the brain. The cells of the renal tubule suffer atrophy; the composition of the intestinal bacterial flora shifts towards a dominance of pathogenic bacteria; and intestinal cells suffer atrophy due to decreased protein intake that favors bacterial translocation. The causes for malnutrition are multifactorial and range from physiological to iatrogenic. As a rapid response to the hypermetabolism associated with critical illness, adequate nutritional support must be delivered promptly [9, 10]. According to a study by Larrea et al., the incidence of malnutrition is 79% higher in patients with esophageal cancer than in patients with other types of gastrointestinal tumors [11].

The evaluation of pre-operative nutrition status includes the patient's nutritional history, anthropometric examinations and laboratory tests. Tissue injury influences plasma protein concentrations, causing a rapid decrease in albumin, transferrin, pre-albumin and retinol binding protein levels, while the concentration of acute phase proteins increases. The prognostic inflammatory and nutritional index (PINI) was developed by Ingenbleek and Carpentier to evaluate the nutritional and inflammatory status of critically ill patients. The PINI scoring system is based on albumin, glycoprotein acid and C-reactive protein levels [12]. It has been found to be a sensitive parameter for patients with physical trauma, burn injuries, infection or cardiac diseases [13]. Since most traditional nutritional assessment methods for advanced cancer patients are difficult to complete due to high costs and inaccuracy, Nelson et al. evaluated the PINI in advanced disease. The results of the study showed significantly elevated PINI scores in patients with advanced cancer, anorexia and weight loss. These scores were higher in critically ill intensive care patients [14].

The aim of the present study was to evaluate the nutritional status of morbidly obese patients using nutritional histories based on questionnaires recommended by the European Society for Parenteral and Enteral Nutrition (ESPEN), the Mini Nutritional Assessment (MNA) scoring system, regular biochemical parameters and the PINI score. These factors were compared with post-operative morbidity and mortality in a prospective, descriptive clinical study.

Material and Methods

The study included 34 obese patients (BMI ≥ 30) scheduled for esophagus resection due to cancer over a period of 4 years. Following approval from the regional ethics committee, all the patients were informed about the study in detail and informed consent was obtained.

All the patients underwent transhiatal esophagectomy, during which none of the groups were exposed to transfusion. A jejunostomy tube was put in place during the operation and used for rehydration, administering isotonic sodium chloride 0.9% solution at the rate of 10 mL/h. Following that, on the first post-operative day, rehydration was given at 15 kcal/kg of body weight; on the second post-operative day at 20 kcal/kg; on the third day at 25 kcal/kg; and starting from the fourth post-operative day patients received enteral nutrition (Fresubin, Fresenius) at 30 kcal/kg until oral nutrition was resumed. The patients were not given any additional parenteral nutrition as supplements.

Each patient's nutritional history was evaluated in accordance with ESPEN and MNA guidelines prior to surgery. The ESPEN evaluation of nutritional history consists of 2 parts: an initial evaluation and a final summary. If the score is 3 or more, that means surgery puts the patient at high risk [15].

After the ESPEN nutritional history, the MNA was performed [16]. The MNA was developed primarily for the evaluation of surgical risks in senior patients, but (unlike the ESPEN score) the nutritional history is complemented by anthropometric examinations.

The two scoring systems were used to investigate whether there was a difference in pre-operative nutritional status between the deceased patients (Group I, n = 7) and the survivors (Group II, n = 27), or between those who recovered without complications (Group III, n = 24) and those with severe complications like pneumonia, artificial respiration, inotropic therapy, anti-arrhythmia treatment (Group IV, n = 10). Along with pre-operative body mass index, blood samples were taken 24 h prior to surgery to determine the biochemical parameters of the patients' nutritional status, such as total protein, albumin, retinol binding protein, pre-albumin, transferrin, transferrin-saturation lymphocyte count and cholesterol levels.

Statistical Analysis

The data are shown as mean values and standard deviations. The statistical analysis was carried out using the Statistical Program for Social Sciences for Windows (SPSS), using Mann-Whitney and Kolmogorov-Smirnov tests and an analysis of variance (ANOVA). Statistical significance was set at $p < 0.05$.

Results

No differences in nutritional status was found between the survivors and the deceased patients. The ESPEN score was 1.35 ± 0.47 for Group I and 1.47 ± 0.58 for Group II ($p = 0.62$). With respect to severe morbidity, there was no difference between Groups III and IV: 2.01 ± 2.28 vs. 1.02 ± 3.67, $p = 0.54$. There was no variation seen in the pre-operative MNA score when comparing the deceased patients (Group I) and those recovering with severe complications (Group IV, Fig. 1c). The comparison of the MNA scores of Groups I and II is shown in Fig. 1a, and between Groups III and IV in Fig. 1b.

Nutritional Status Parameters in Relation to Morbidity and Mortality

Table 1 summarizes the BMI and biochemical parameters for Group I (the deceased patients) and Group II (the survivors); Table 2 presents the data for Group III (those recovering without complications) and Group IV (survivors with severe complications). Table 3 shows a comparison of the demographic data of the patients studied and the cancer stages of the survivors and the deceased patients; no statistically significant differences were found between the groups in any of these parameters. The cause of death in Group I patients was septic shock leading to multiple organ dysfunction syndrome. Post-operative pulmonary complications were diagnosed using radiological, clinical and microbiological features. Respiratory failure was diagnosed by arterial blood gas analysis with or without ventilatory support. Besides respiratory complications, other complications included cardiac, renal and hepatic failure as well as stroke. Surgical complications included anastomotic leakage, chylothorax, hemorrhage and gastric outlet obstruction. The 30-day mortality was defined as death within 30 days of the esophageal resection, whereas any death in the hospital after surgery was recorded as a hospital death.

PINI Scores in Relation to Mortality and Morbidity

No statistically significant differences were observed between pre-operatively evaluated PINI scores and post-operative mortality or morbidity

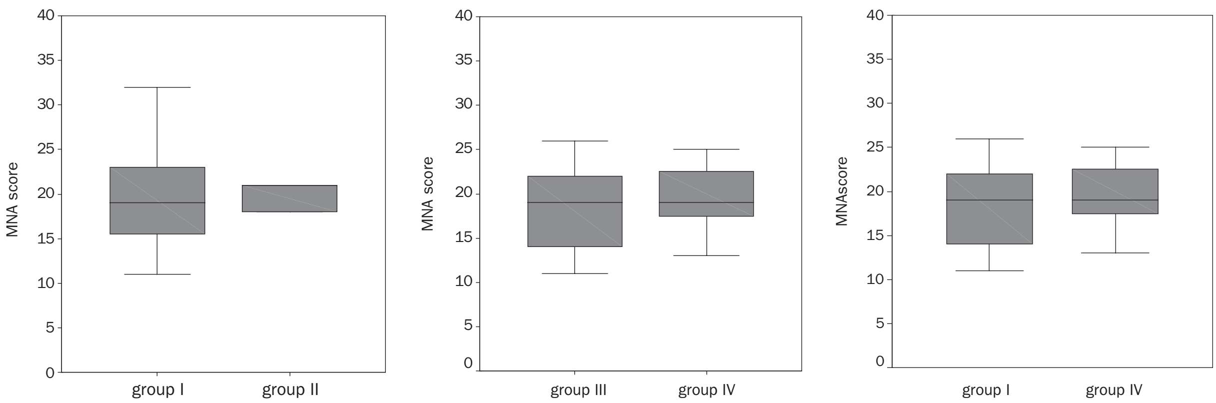

Fig. 1. Differences in the patients' morbidity and mortality in relation to their nutritional history evaluated using the MNA scoring system. A – shows the comparison between Group I (deceased patients) and Group II (survivors). B – is a comparison between patients recovering with no complications (Group III) and those with severe complications (Group IV). C – shows a comparison of Group I and Group IV. The data are represented in "box-plot" format, with minimum-maximum, median and inter-quartile range values are shown. Differences between the groups were verified by ANOVA analysis

Table 1. Comparison of biochemical parameters of nutritional status and post-operative mortality in Group II (survivors) and Group I (deceased patients)

	Group II (survivors) n = 27	**Group I (deceased) n = 7**	**p**
BMI	33.00 ± 4.37	30.00 ± 3.29	0.53
Protein (g/L)	60.5 ± 8.10	63.60 ± 6.15	0.90
Albumin (g/L)	34.60 ± 4.16	32.40 ± 3.59	0.42
Pre-albumin (g/L)	0.20 ± 0.07	0.19 ± 0.08	0.90
Retinol binding protein (g/L)	0.03 ± 0.01	0.02 ± 0.01	0.44
Lymphocyte (%)	15.10 ± 8.29	17.30 ± 5.37	0.42
Cholesterol (mmol/L)	4.30 ± 1.02	3.77 ± 1.07	0.34
Transferrin (g/L)	1.89 ± 0.39	1.9 ± 0.37	0.90
Transferrin saturation %	22.4 ± 9.32	26.7 ± 11.14	0.34

The data are shown as mean values and standard deviations. The Mann-Whitney *U* test was used for the statistical analysis.

Table 2. Comparison of biochemical parameters of nutritional status and post-operative morbidity in patients who recovered without severe complications (Group III) and those who recovered with severe complications (Group IV)

	Group III recovered without severe complications n = 20	**Group IV recovered with severe complications n = 7**	**p**
BMI	31.0 ± 5.2	32.5 ± 3.6	0.53
Protein (g/L)	56.80 ± 6.95	66.35 ± 5.75	0.68
Albumin (g/L)	34.30 ± 1.66	35.70 ± 4.37	0.77
Pre-albumin (g/L)	0.14 ± 0.02	0.19 ± 0.08	0.52
Retinol binding protein (g/L)	0.03 ± 0.01	0.03 ± 0.01	0.50
Lymphocyte (%)	16.30 ± 4.33	14.4 ± 6.5	0.37
Cholesterol (mmol/L)	3.75 ± 1.03	4.66 ± 0.68	0.38
Transferrin (g/L)	1.78 ± 0.45	1.73 ± 0.44	0.53
Transferrin saturation %	18.90 ± 1.64	11.60 ± 8.82	0.89

The data are shown as mean values and standard deviations. The Mann-Whitney *U* test was used for the statistical analysis.

Table 3. Comparison of demographic data and cancer staging of Group II (survivors) and Group I (deceased patients)

	Group II (survivors) n = 27	**Group I (deceased) n = 7**	**SD**
Age (years)	54.15	57.33	5.39
Gender (M/F)	60.5 ± 8.10	63.60 ± 6.15	
Height (cm)	165	167	4.22
Weight (kg)	86	69	3.33
Stage of the cancer	T3	T3	0.44

The data are shown as mean values and standard deviations. The Mann-Whitney *U* test was used for the statistical analysis.

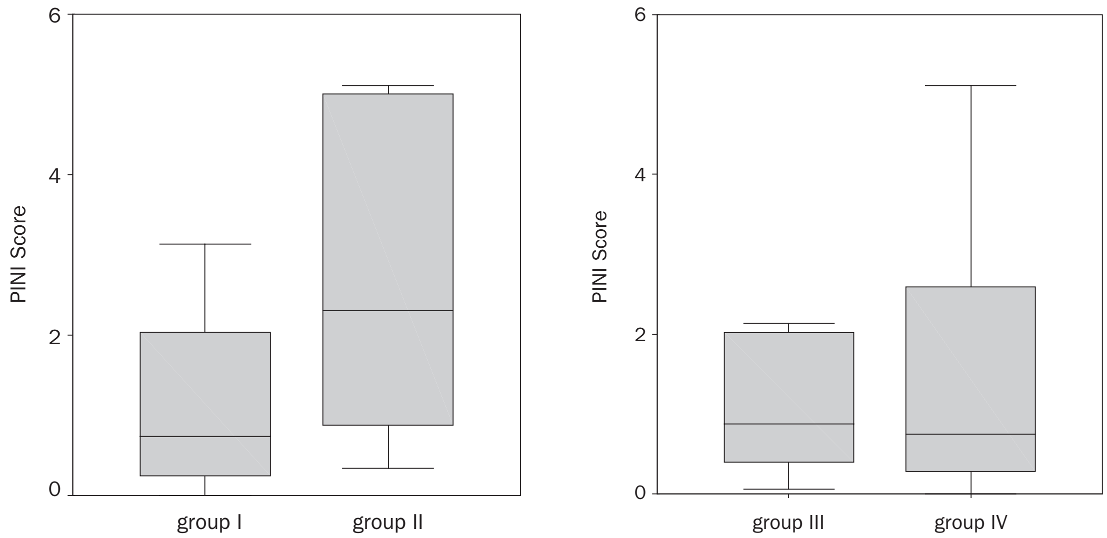

Fig. 2. Differences between pre-operative PINI scores and post-operative morbidity or mortality. A – shows the comparison between Group I (deceased patients) and Group II (survivors). B – between patients recovering with no complications (Group III) and those with severe complications (Group IV). The data are represented in "box-plot" format, with minimum-maximum, median and inter-quartile range values are shown. Differences between the groups were verified by ANOVA analysis

(Fig. 2). The comparison of Groups I and II is presented in Fig. 2a; the comparison between Groups III and IV is shown in Fig. 2b.

Discussion

According to the literature, it is of vital importance to evaluate patients' pre-operative nutritional status and identify those suffering from severe malnutrition, because it influences the development of post-operative complications and concomitant expenditures. Clinical malnutrition has been shown to have serious implications for recovery from disease, trauma and surgery. It is generally associated with increased morbidity and mortality in both acute and chronic conditions. As a result of this, the duration of hospital treatment is significantly longer in malnourished patients and is associated with higher costs [17, 18].

The current study addressed the question of whether the evaluation of pre-operative nutritional status in patients with esophagal cancer has any predictive value for post-operative morbidity and mortality. The evaluation of the patients' nutritional status was performed using the ESPEN and MNA score systems. Neither of the two score systems indicated any difference in the patients' postoperative morbidity or mortality.

Total Protein and Albumin

A decrease in classical nutritional status parameters increases the incidence of post-operative infectious complications [19]. Although albumin is a good indicator of chronic malnutrition, it is not a sensitive indicator of either malnutrition or the efficiency of nutritive therapy due to its relatively long half-life. Also, the serum level of albumin can decrease during various inflammatory responses. In the present study, preoperative mean values of patients for total protein and albumin were within the normal range and malnutrition could not be confirmed on the basis of their values. A possible explanation is that the body decomposes skeletal muscle to maintain albumin and total protein levels. This could be supported by the patients' insignificant drop in BMI during the preparations for surgery and their stay in the hospital, as all preoperative samples were taken 24 h before the procedure, and were in parallel with normal albumin and total protein values. It probably would have been more appropriate to determine the patients' 3-methyl-histidin levels, which are a sensitive indicator of protein loss, but unfortunately those data were not available.

Retinol Binding Protein and Pre-Albumin

Several studies have shown that the two most sensitive biochemical parameters for predicting post-operative morbidity and mortality are pre-albumin and retinol binding protein [20]. However, this was not confirmed in the current study. It is conceivable that the liquid intake of patients with esophagus cancer had decreased, and that the subsequent exsiccation led to a relative increase in the concentration of these negative acute-phase proteins.

In summary, using a prospective, descriptive clinical study and evaluating the pre-operative nutritional status of obese patients with esophagal cancer, no differences were found to correlate with post-operative morbidity or mortality. However, one of the major drawbacks of the current study was the small number of patients, which makes statistical analysis very difficult. It is very rare to see obese patients with esophageal cancer and as current evidence is seen only in the early stage of cancer [21], this would suggest that more research is needed in this area. Considering the importance of nutrition in obese cancer patients undergoing surgery, the current results suggest that further investigation in the form of a multicenter study would be appropriate.

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