The Glasgow Prognostic Score. An useful tool to predict survival in patients with advanced esophageal squamous cell carcinoma

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DOI: http://dx.doi.org/10.1590/S0102-8650201500800000010

ABSTRACT

PURPOSE: To evaluate the usefulness of the Glasgow Prognostic Score (GPS) in patients with esophageal carcinoma (EC).

METHODS: A total of 50 patients with EC were analyzed for GPS, nutritional and clinicopathologic parameters. Patients with CRP ≤ 1.0mg/L and albumin ≥ 3.5mg/L were considered as GPS=0. Patients with only CRP increased or albumin decreased were classified as GPS=1 and patients with CRP > 1.0mg/L and albumin < 3.5mg/L were considered as GPS=2.

RESULTS: GPS of 0, 1 and 2 were observed in seven, 23 and 20 patients, respectively. A significant inverse relationship was observed between GPS scores and the survival rate. The survival rate was greatest in patients with GPS= 0 and significantly higher than those from patients with GPS=1 and GPS=2. Minimum 12-month survival was observed in 71% patients with GPS=0 and in 30% patients with GPS=1. None of the patients with GPS=2 survived for 12 months. A significant relationship between CRP or albumin individually and the survival rate was observed. No significant relationship among nutritional, clinic pathological parameters and survival was found.

CONCLUSION: Glasgow Prognostic Score is an useful tool to predict survival in patients with esophageal carcinoma.

Key words: Esophageal Neoplasms. Neplasms, Squamous Cell. Glasgow Outcome Scale.
Introduction

Esophageal cancer is the fourth leading cause of cancer-related mortality in Brazil. The main histological type is squamous cell carcinoma, comprising about 90% of all esophageal carcinomas in our country. The diagnosis is usually made at advanced stages, which explains the high mortality rate.

The survival of patients with esophageal cancer submitted to surgery has been widely evaluated, but few studies have investigated the clinical evolution of patients with advanced esophageal cancer.

Recent reports have demonstrated that systemic inflammation, expressed by high levels of serum-C reactive protein, can predict the survival of patients with cancer. The Glasgow Prognostic Score is an inflammation-based prognostic score used as a predictive index of survival for patients with advanced cancer, including gastrointestinal carcinomas. It is a simple prognostic indicator based on the serum levels of albumin and C reactive protein. It is calculated as follows: a score of 0 for normal C reactive protein and albumin levels, score 1 for either an abnormal C reactive protein or abnormal albumin level and score 2 for both abnormal C reactive protein and abnormal albumin levels.

The aim of this retrospective study was to evaluate the usefulness of the Glasgow Prognostic Score as a predictive factor of survival in a cohort of patients with advanced esophageal squamous cell carcinoma under palliative clinical care.

Methods

This study was approved by the Research Ethics Committee of Botucatu Medical School, UNESP.

In this retrospective study, medical records of 50 patients with esophageal cancer, referred to the Botucatu University Hospital (BUH), UNESP, from January 2010 to December 2013, were analysed. Patient inclusion criteria were: esophageal squamous cell carcinoma stages III or IV (TNM classification) of either sex and any age. Exclusion criteria were: squamous cell carcinoma stages I and II, esophageal adenocarcinoma, occurrence of infection or inflammatory disease. The analysis of the patients’ medical records allowed the evaluation of the following parameters:

1. Demographics: age, sex, race.
2. Nutritional condition: Body Mass Index (BMI, kg/m²), calculated from the weight and height using Cronk & Roche's formula: BMI = weight divided by the squared height in meters. The collected data were compared to reference values.
3. Percent weight loss (%WL) was calculated from the usual body weight reported by the patient and the actual body weight using the formula: %WL = (usual body weight – actual body weight x 100) divided by the actual body weight. A weight loss over 10% was considered severe according to the criteria proposed by Blackburn.
4. Biochemical Evaluation: Serum albumin and C reactive protein levels were determined by automatic methods in the Biochemistry Laboratory of the BUH, Clinical Analysis Sector. The obtained values were compared to the reference data.
5. The Glasgow Prognosis Score (GPS) was based on the serum levels of albumin and C-reactive protein (CRP). It was calculated as follows: Patients with both normal CRP (≤1.0mg/dL) and albumin (≥3.5mg/dL) levels were allocated a score of 0. Patients with either an abnormal C reactive protein or abnormal albumin level were allocated a score of 1 and patients with both an elevated CRP (>1.0 mg/dL) and hypoalbuminemia (<3.5mg/dL) were allocated a score of 2.
6. Tumor site and histopathology were determined by endoscopic evaluation and biopsy reports.
7. Clinical Tumor Staging was performed based on tomographic exams of the thorax and abdomen (TNM/ UICC classification – National Cancer Institute, 2012).
8. Survival rate was evaluated considering the time between endoscopic diagnosis and patient death or last interview.

Results

Demographics

The study included 50 patients with advanced esophageal squamous cell carcinoma stages III and IV, under palliative clinical care. The demographics are summarized on Table 1. Forty eight patients were male (96%) and 2 female, aged 38-81 years (median age 60.9 years). 56% of the studied population was older than 60.

Nutritional condition

A) Body Mass Index: BMI of the study population ranged from 14.1 to 37.3 kg/m² with a mean body surface of 20.02 ± 4.74 kg/m² (Table 1). Twenty two patients (44%) were undernourished and had BMI lower than 18.5 kg/m². Eutrophic patients (56%, IMC ≥ 18.5 kg/m²) had a 12-month survival of 28.57% and in undernourished patients it was 13.6% in relation to the study population. The Spearman correlation test did not show a significant correlation between BMI and survival (Table 2, p<0.3).
B) The percent weight loss: %WL mean value was 18.4 ± 9.1%, with extremes of zero and 37.5%. There was no significant relationship between %WL and the survival rate. The percent weight loss was greater than 10% (undernourished) in 82% patients, 19.5% of which had minimal survival of 12 months. Thirty three percent of the patients were eutrophic (%WL<10%) and all had 12-month survival (p<0.6).

The Glasgow Prognosis Score (GPS)

GPS of 0, 1 and 2 were observed in seven, 23 and 20 patients, respectively (Table 1). A significant inverse relationship was observed between GPS scores and the survival rate (p<0.001, Table 3). The survival rate was greatest in patients with GPS= 0 (20.5 ± 8.8 months) and significantly higher (p<0.001) than those from patients with GPS=1 (8.8 ± 5.5 months) and GPS=2 (3.2± 2.5).

Minimum 12-month survival was observed in 71% patients with GPS=0 and in 30% patients with GPS=1. None of the patients with GPS=2 survived for 12 months (p<0.001, Table 4).

Serum albumin

Serum albumin levels ranged from 1.6 to 4.8 mg/dL, with a mean of 3.4 ± 0.7 mg/dL (Table 1). Fifty percent of the patients presented normal serum albumin levels. A significant relationship was observed between serum albumin levels and the survival rate (p<0.001, Table 2). Forty percent of the patients with normal albumin levels survived for at least 12 months, while only 4% of the patients with low albumin levels survived for 12 months (p<0.006, Table 4).

C Reactive Protein (CRP)

Serum-C reactive protein levels ranged from 0.2 to 40.3 mg/dL with a mean of 7.8 ±10.2 mg/dL (Table 1). A significant relationship was observed between CRP levels and the survival rate (p<0.001, Table 2). Most patients (n=41) presented high CRP values and only five patients (12%) with high CRP levels survived for at least 12 months. From the nine patients with normal CRP levels, five (55.5%) survived for at least 12 months (p<0.01, Table 4).

Tumor site

Endoscopically, the tumor was located in the middle third of the esophagus in the majority of patients (n=30). Tumor was in the upper (n=10) or at the distal third of the esophagus in 10 patients (p<0.0001). Survival rate did not differ significantly in relation to tumor site (Table 4).

Staging

Most patients (n=35) were in stage IV (T_N_M) and 15 patients were in stage III (T_N_M) (p<0.0001). There were no significant differences on the 12-month survival rates between patients in stages III and IV (Table 4).

| TABLE 1 - Clinicopathological features of patients with advanced esophageal squamous cell carcinoma (n=50). |
|----------------------------------------|----------------------------------------|
| **Sex ratio, male/female** | 48/2 |
| **Median age (range), years** | 60.92 ± 10.04 (38 - 81) |
| **Median BMI (range), (kg/m²)** | 20.02 ± 4.74 (14.1 – 37.3) |
| **Median WL (range), %** | 18.47 ± 9.17 (0 – 37.5) |
| **Median Albumin (range), mg/dL** | 3.46 ± 0.74 (1.6 – 4.8) |
| **Median CRP (range), mg/dL** | 7.80 ± 10.25 (0.20 – 40.30) |
| **Glasgow Prognostic Score (GPS)** | 7 23 20  |
| **Tumor Site** | Upper | 10 | Middle | 30 | Lower | 10 |
| **Tumor Stage** | III | 15 | IV | 35 |
| **Global Survival (months)** | 8.26 ± 7.62 (1 - 38) |

BMI=Body Mass Index, WL=Light Loss, CRP=C Reactive Protein.

| TABLE 2 – Correlation among survival, Glasgow Prognostic Score, Albumin, CRP and nutritional variables. |
|-------------------------------------------------|-----------------|
| **Survival vs GPS** | 0.0001 |
| **Survival vs Albumin** | 0.0010 |
| **Survival vs CRP** | 0.0011 |
| **Survival vs BMI** | 0.3676 |
| **Survival vs % WL** | 0.1961 |

Spearman Correlation.
The Glasgow Prognostic Score. An useful tool to predict survival in patients with advanced esophageal squamous cell carcinoma

Discussion

This study investigated the usefulness of the Glasgow Prognostic Score, which is an inflammation-based prognostic score, to predict survival in a cohort of patients with advanced esophageal squamous cell carcinoma under palliative clinical care.

The high incidence of advanced esophageal cancer in male patients (96%) observed in our study has been reported in other studies.3,15,16 Patient mean age (60 ± 10 years old) in our series of cases was lower than that reported by Ando et al.7 and Eloubeidi et al.17.

Anthropometric nutritional evaluation revealed a mean BMI of 20.2 ± 4.7 kg/m² body surface. However, 22 patients (44%) were protein-energy undernourished and presented a BMI lower than 18.5 kg/m² due to the tumor and the ensuing esophageal obstruction and alimentary alteration. In this group, only three patients (13.6%) survived 12 months or longer. In eutrophic patients 8 (28%) presented 12-month survival. No correlation was found between BMI and survival rate by the Spearman test.

The mean involuntary percent weight loss in the period of six months before diagnosis was 18.4 ± 9.1%. Severe undernourishment (%WL>10%) was diagnosed in 41 patients (82%). Although no correlation has been found between severe undernourishment and survival rate, undernourished patients had a survival rate of 12 months of 19.5%. In eutrophic patients, the minimal survival rate of 12 months was 33.3% of the study population. Our results are in agreement with recent studies on patients with esophageal and stomach cancer, that revealed no correlation between nutritional condition and survival18, but are in contrast to reports of poorer chemotherapy response and shorter survival in patients with weight loss19.

Considering that cancer patients are in a chronic inflammation condition20, the Glasgow Prognostic Score has been used to classify the degree of inflammation based on the serum levels of C reactive protein and albumin10-12,18.

In the present study we have evaluated the Glasgow Prognostic Score (GPS) in a homogeneous population of fifty patients with advanced esophageal squamous cell carcinoma submitted only to palliative clinical treatment, gastrostomy or jejunostomy, in association with chemotherapy and radiotherapy.

Global patient survival in our study was 8.2 ± 7.6 months. It is similar to that reported in patients with advanced esophageal cancer submitted to two types of palliative treatment, self expandable metallic stent or isoperistaltic gastric tube21. However, when the GPS score was considered, a significant inverse relationship was observed between GPS scores and the survival rate (p< 0.001). The survival rate was greatest in patients with GPS= 0 (20.5 ± 8.8 months) and significantly higher (< 0.001) than those from patients with GPS= 1 (8.8 ± 5.5 months) and GPS=2 (3.2± 2.5 months). We have observed that 71% patients with GPS = 0 survived for at least 12 months, while 30% of patients with GPS=1 and none of the patients with GPS=2 survived for 12 months (p<0.001, Table 4). Our results on patient survival are higher than those reported by Crumley22 and Silva et al.18.

In our study, the majority of patients (n=43) had a GPS of 1 and 2 than a GPS = 0 (n=7), which matches with the advanced

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**TABLE 3** - Survival rate (months) in patients with Glasgow Prognostic Score 0, 1 and 2.

<table>
<thead>
<tr>
<th>GPS</th>
<th>n</th>
<th>Survival rate (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7</td>
<td>20.57 ± 8.84 a</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>8.86 ± 5.56 b</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>3.25 ± 2.55 c</td>
</tr>
</tbody>
</table>

p=0.00001.

**TABLE 4** - Correlation among 12-month survival, GPS and clinicopathological features in patients with advanced esophageal cancer (n=50).

<table>
<thead>
<tr>
<th>Variable</th>
<th>12-month survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glasgow Prognostic Score(GPS)</td>
<td>71%</td>
</tr>
<tr>
<td>GPS= 0</td>
<td></td>
</tr>
<tr>
<td>GPS= 1</td>
<td>30%</td>
</tr>
<tr>
<td>GPS= 2</td>
<td>0%</td>
</tr>
<tr>
<td>Hypoalbuminaemia</td>
<td>4%</td>
</tr>
<tr>
<td>Normalalbuminaemia</td>
<td>40%</td>
</tr>
<tr>
<td>BMI &lt; 18.5</td>
<td>13.6%</td>
</tr>
<tr>
<td>BMI &gt; 18.5</td>
<td>28.0%</td>
</tr>
<tr>
<td>% WL ≥ 10</td>
<td>19.5%</td>
</tr>
<tr>
<td>% WL &lt; 10</td>
<td>33.3%</td>
</tr>
<tr>
<td>CRP ≤ 1</td>
<td>55.5%</td>
</tr>
<tr>
<td>CRP &gt; 1</td>
<td>12.1%</td>
</tr>
<tr>
<td>Stage III</td>
<td>26.6%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>20.0%</td>
</tr>
<tr>
<td>Tumor Site</td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>10%</td>
</tr>
<tr>
<td>Middle</td>
<td>20%</td>
</tr>
<tr>
<td>Lower</td>
<td>40%</td>
</tr>
</tbody>
</table>

p indicates significance according to chi-square test.
stage of the disease in this cohort of patients analysed. Similar results were reported by Wang et al.\(^\text{15}\).

Out of the 50 patients analyzed, 30 had the tumor in the middle third of the esophagus, 10 in the upper and 10 in the lower third of the esophagus. The preferential tumor site observed in our study is similar to the reported by most authors.\(^{3,5,7}\) As expected, there were no relationship between tumor site and patient survival.

As to staging, most patients in this series (70%) were in stage IV and the others were in stage III (30%). The 12-month patient survival of the two groups did not differ significantly (p=0.7). This result was not surprising since both groups were in advanced stages of the disease.

In the present study most patients (n=41) presented high values of C reactive protein and from these only five patients survived for at least 12 months (p<0.001, Table 2). This finding highlights the sensitivity of this biomarker of inflammation to predict survival in patients with cancer, as previously reported.\(^{6,15,23}\)

Interestingly, half of the patients (n=25) with advanced esophageal cancer presented normal albumin levels and from these, 40% patients survived for at least 12 months, while only 4% of the patients with low albumin levels survived for 12 months (p=0.006, Table 4). These results emphasize that albumin concentrations on its own are associated with survival in cancer patients\(^{24}\).

**Conclusion**

The Glasgow Prognostic Score (GPS), which is based on the serum levels of C reactive protein (CRP) and albumin, is an useful prognostic factor of survival for patients with advanced esophageal squamous cell carcinoma. Considering the low cost and the availability of C reactive protein and albumin testing, we recommend the use of the GPS score as a routine evaluation procedure to predict survival in patients with advanced esophageal cancer.

**References**

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Received: Apr 10, 2015
Review: June 13, 2015
Accepted: July 12 2015
Conflict of interest: none
Financial source: none

1Research performed at Department of Surgery, Gastroenterology Surgery Division and Department of Pathology, Investigative Pathology Division, Botucatu Medical School, Universidade Estadual Paulista (UNESP), Brazil.