

# Prognostic Factors, Incidence and Management for Acute Variceal Bleeding in the Liver Transplantation Era\*

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## Abstract

**Background:** Gastroesophageal varices are the most common and clinically important part of the portosystemic collaterals due to their tendency to rupture and cause massive gastrointestinal bleeding. **Objective:** The aim of this work was to evaluate retrospectively the incidence and the factors of prediction for the treatment of bleeding by gastroesophageal varices in the patients attended in the Emergency Room of the Hospital State University of Campinas (Brazil) from the last ten years. **Methods:** The method used here consisted of a descriptive and retrospective study carried out from the analyses of the medical records of 769 patients with upper gastrointestinal bleeding of which 220 were admitted because of upper gastrointestinal bleeding caused by gastroesophageal varices during this same period. **Results:** The results showed that the gastroesophageal varices appeared in 28.6% of the patients and they were the second most common cause of upper gastrointestinal bleeding. While evaluating factors such as age, sex and the common individual records, it was proved that this disease occurs mainly among people between the third and the fifth decade of life, with the great majority of cases occurring in the fourth decade (29.2%), of which 76.8% were male. There was an association of hematemesis and melena in the admission of 57.7% of the patients and even ascites was a common diagnosis in 48.2% of them. Most of these patients (40%) were classified as Child class B at admission. The early endoscopic exam was used for 96.8% of them and showed the presence of F3 varices in 38.5%, CB varices in 25.1% and RCS varices in 12.6%. Most of these varices (41.5%) were situated in the distal third of the esophagus. The most used pharmacological treatment was based on octreotide in 45.9% of the patients. They received 0.05 mg of intravenous octreotide and a maintenance dose of 1 mg per day in 98.6% of the cases, with efficacy in 74.2% of the patients. The tamponade with Sengstaken-Blakemore tube was applied in 30.5% of the patients, but it was observed that 69.7% of them did not present any considerable progress and this situation led to their death. The endoscopic treatment was performed in 41.8% of the patients with efficacy in 81.5% of them. The sclerotherapy was used for 60.9% of the studied cases with Ethamolin® being the most used for sclerosing. Emergency surgery was used in just 8.6% of the patients studied and it controlled the bleeding in 78.9% of the cases. **Conclusions:** We concluded that gastroesophageal bleeding was an important cause of upper gastrointestinal hemorrhage, even in the liver transplantation era. Factors of prediction for this bleeding were the endoscopic classification, the presence of ascites and the degree of liver failure, according to the Child-Pugh classification.

**Keywords:** Liver Transplantation, Portal Vein Thrombosis, Surgical Technique

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## 1. Introduction

Bleeding from gastroesophageal varices is still an im-

portant cause of hospital internment all over the world and is also one of the most severe consequences of portal hypertension [1-14]. This specific type of bleeding is an immediate threat to life. The mortality of each bleeding episode varies from 20% to 30%, even increasing from 70% to 90% among patients that are seriously sick [1,7, 11,12,20-32]. However, the cause of rupture of these varices is not totally clear. Many technological advances have taken place in the diagnosis and treatment of portal hypertension. However, it still causes serious complications such as upper gastrointestinal bleeding (caused by gastroesophageal varices) and spontaneous bacterial peritonitis (caused by ascites).

The purpose of this work was to analyze retrospectively the incidence, the factors of prediction, and results after treatment of bleeding caused by gastroesophageal varices.

## 2. Patients and Methods

This research included only those patients who came from the Emergency Room of the Hospital das Clínicas–State University of Campinas (UNICAMP)–SP/Brazil with a diagnosis of upper gastrointestinal bleeding caused by gastroesophageal varices. This retrospective study used information collected from 769 patient medical records of the Emergency Room of the Hospital das Clínicas–State University of Campinas–SP/Brazil from the last ten years.

The data used were: age, gender, type of bleeding, ascites or hepatic encephalopathy presence, portal hypertension etiology, Child-Pugh classification, treatment type and success and evolution during acute phase and one-year after.

The degree of upper gastrointestinal bleeding was classified as mild (little bleeding, without hemodynamics repercussion); moderate (mild clinical manifestation, such as fainting, sweating, cutaneous paleness and stable hemodynamics); and severe (intensive hemodynamics repercussion, such as hemorrhagic shock).

Diagnosis of upper gastrointestinal bleeding and classification of varices were carried out according to the procedure and protocol defined by the endoscopic team at the institution.

Qualitative variables were evaluated with the Chi-square test and Fisher's exact test. Continuous variables were evaluated with the Mann-Whitney and Kruskal-Wallis tests. Categorical variables were evaluated with the Stuart-Maxwell test. Survival analyses employed the Kaplan-Meier method with Log-Rank or Breslow tests. Statistical significance was designated at  $P < 0.05$ .

## 3. Results

Gastroesophageal varices were the second most frequent cause of upper gastrointestinal bleeding in our service representing 220 (28.6%) of the analyzed cases. It was surpassed only by peptic ulcer disease (**Table 1**). One hundred and sixty-nine patients (76.8%) were male. The age of most patients was between the third and the fifth decade of life, with a peak in the fourth decade (29.2% of the cases).

One hundred and twenty patients (57.7%) were admitted with a diagnosis of hematemesis associated with melena, with variceal bleeding at a moderate level in 47.3% of the cases and severe in 14.5%. Thirty-one (14.6%) of them died after admission. Among the symptoms and clinical signs identified in those patients, ascites was present in 106 (48.2%) and liver encephalopathy in 40 (18.2%). Most of them were classified as Child class B at admission (40%). Alcohol was identified as the main cause of portal hypertension in 32.3% of the cases, followed by schistosomiasis (19.1%) and viral hepatitis C in 10% (**Table 2**).

Upper gastrointestinal endoscopy was carried out in 213 (96.8%) patients in the first 24 hours after admission. It showed, according to Osaka's classification (1979), *F3* (38.5%), *CB* (25.1%), *RCS* (12.6%) and *LM* (41.5%) varices.

Most of these patients (45.9%) were submitted to a treatment with octreotide, with good response in 74.2% of the cases. Sengstaken-Blakemore tube was used in 30.5% of the patients admitted with a diagnosis of upper gastrointestinal bleeding due to gastroesophageal varices, controlling the bleeding in 49.3% of the cases. Endoscopic therapy was used in 41.8% of the patients. Elastic

**Table 1. Frequency of the causes of upper gastrointestinal bleeding in the Emergency Room of the Hospital de Clínicas–UNICAMP (Brazil).**

<i>Causes Of Upper Gastrointestinal Bleeding</i>	<i>Frequency (%)</i>
Peptic Ulcer Disease	264 (34.3%)
Esophageal Varices	220 (28.6%)
Acute Gastroduodenal Mucosal Lesions	209 (27.2%)
Gastric Neoplasms	27 (3.5%)
Esophagitis	23 (3.0%)
Mallory-Weiss	13 (1.7%)
Esophageal Neoplasms	10 (1.3%)
Esophageal Ulcers	03 (0.4%)
Total	769

**Table 2. Frequency of portal hypertension causes identified in the patients admitted to the bleeding caused by gastroesophageal varices in the Emergency Room of the Clinical Hospital-UNICAMP (Brazil).**

Portal Hypertension Causes	Frequency
Alcohol	71 (32.3%)
Schistosomiasis	42 (19.1%)
Viral Hepatitis C	22 (10.0%)
Viral Hepatitis B	07 (3.2%)
Idiopathic	34 (15.5%)
HCC and Cirrhosis	05 (2.3%)
Autoimmune hepatitis	04 (1.8%)
Budd-Chiari Syndrome	03 (1.4%)
Others	32 (14.4%)
Total	220 (100.0%)

HCC = hepatocellular carcinoma

band ligation technique was applied in 39.1%. The ethanolamine oleate was the most used sclerotic substance, and in 57.6% of the cases only one session was enough to stop the bleeding that had variceal origin.

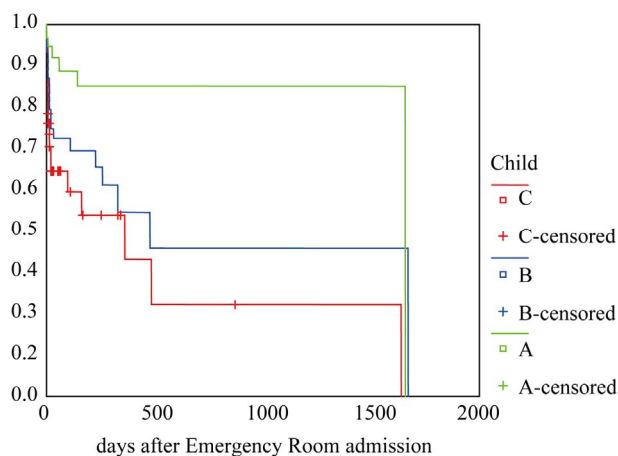
Only nineteen patients (0.6%) were submitted to a surgical treatment during the acute episode of bleeding. In these cases, the procedure of esophagogastric devascularization associated with splenectomy (EGDS) was carried out in 63.2% of the patients. The control of bleeding was successful in 78.9% of the cases.

In the admission period 2.3% of the patients died, and this index went up to 14.6% after hospital internment.

In the one-year follow-up period only two patients (1.1%) were submitted to a liver transplantation. In this period, 20.7% of those who were classified as Child class B at admission changed to Child class A. Survival rate after one-year was higher for Child class A (**Figure 1**).

#### 4. Discussion

Gastroesophageal varices are the most common cause of bleeding and one of the main causes of death among patients admitted with a diagnosis of portal hypertension. These varices are also the most severe complication of portal hypertension that may occur in cirrhotic patients [1,7,20]. This medical condition, with upper gastrointestinal bleeding caused by gastroesophageal varices, indicates in most cases a substantial hematemesis that can be followed by melena or hematochezia. It was discovered that only 14.5% of the analyzed patients were suffering from serious bleeding. Apart from this, there was a tendency of association between the admission data and the



**Figure 1. Comparison of patient survival rate between Child A and Child B and Child C. Patient survival in the Child A was significantly better than in the Child B or C ( $p < 0.001$ )**

patients' evolution. Thus, a higher number of deaths occurred among those patients admitted with a diagnosis of hematemesis or hematemesis and melena (20 and 29.1%, respectively) in comparison to those that were admitted with a diagnosis of only melena (10.8%). This result is probably a result of the poor medical condition.

Gastroesophageal varices are a consequence of portal hypertension, which, in most of the severe cases, are associated with complications such as ascites, liver encephalopathy, flapping, liver failure and even death due to hemorrhagic shock [12,28,31]. During the admission period to the Emergency Room of Clinical Hospital-UNICAMP, a large number of the patients showed ascites (48.2%), although other factors to indicate the level of seriousness of portal hypertension were not found.

The degree of liver encephalopathy is expressed by neuropsychological alterations that have a metabolic origin and are potentially reversible, reflecting the functional aggravation of the liver. In this study 30.8% of admitted patients had degree I, with an equivalent proportion of patients with degree II.

The classification of Child-Turcotte, modified by Pugh, defines three distinct groups (A, B or C) that represent the degree of liver failure. This classification shows an important prognostic value in terms of mortality of these patients [14,16,22]. Most of them were classified as Child class B at admission (40%). However, during one year a significant change was observed in the classification of Child-Turcotte-Pugh in consequence of the applied treatment. After this period, 20.7% of those who were classified as Child class B at admission stayed in Child class A, while 39.3% of those classified as Child class C at admission changed to Child class B. According to the Child-Turcotte-Pugh classification, survival rate after one-year was higher for Child class A, (85%),

followed by Child class B (55%) and Child class C (47%). These data show the necessity of classification of patients according to Child-Pugh due to its great prognostic value.

A variceal hemorrhage, in general, occurs without obvious precipitating factors and without pain. In the admission period 2.3% of the patients died, and this index went up to 14.6% after hospital internment, similar to the results mentioned in the literature [11,12,14,21,27,28].

The endoscopic diagnosis is carried out by observing the right place of the bleeding or viewing varices that have a considerable size varying from moderate to big in those cases where there is no other lesion that could justify the bleeding [1,6]. Early upper gastrointestinal endoscopy (in the first 24 hours after the beginning of bleeding) has been recommended because it allows the application of the adequate therapeutic treatment [14]. Two hundred and thirteen patients (96.8%) were submitted to upper gastrointestinal endoscopy in the first 24 hours after admission to the hospital. According to Osaka's classification (1979), there were *F3* varices in 38.0% of the patients, *CB* varices in 25.1% and *RCS* varices in 12.6%. The highest percentage (41.5%) was situated in the distal esophagus.

Pharmacological treatment in acute bleeding is based on the use of vasoconstrictors (vasopressin or somatostatin and similar,  $\beta$ -adrenergic blockers) and nitrovasodilators [5,10,13,14]. Most of those patients 51 (45.9%) were submitted to a treatment with octreotide, a substance that is similar to somatostatin, with a dose of 0,05mg IV and maintenance of 1mg a day during an average period of four days, succeeding in 74.2% of the cases.

The tamponade of gastroesophageal varices is indicated only in cases of acute bleeding or when the use of vasoconstrictors, sclerotherapy and embolization does not obtain any success. The success of the method varies between 44 to 90% of the cases [14,15,18,23]. The tamponade with a Sengstaken-Blakemore tube was used in 30.5% of the patients admitted with a diagnosis of upper gastrointestinal bleeding by gastroesophageal varices, used during a period of 24 hours in 49.2% of the cases. This treatment had succeeded in controlling bleeding in 49.3% of the cases, confirming the data contained in the literature referred to [14,15,18,23].

Endoscopic intervention (with sclerosis or ligation of varices) could be used as an optional treatment against acute variceal bleeding. A considerable control of the bleeding was reached in cases submitted to this treatment varying from 75 to 90% [2]. Many substances with sclerotic properties can be used. However, if the bleeding persists after the initial sclerotherapy, a second session should be used in a period of 24 hours; if it still persists,

another therapeutic treatment has to be used. During the treatment process, new sessions might be carried out with a view to eradicating the varices and, at the same time, preventing new bleeding [3,8,9,14,15,29-32]. Endoscopic intervention was used in 41.8% of the patients, the elastic band ligation technique was applied to 39.1% of them and sclerotherapy to the others (60.1%). The ethanolamine oleate was the most used sclerotic substance, and in 57.6% of the cases only one session was enough to stop the bleeding that had a variceal origin. During a one-year period, the number of necessary sessions to eradicate the varices varied from three to nine sessions in some cases.

Emergency surgery is usually carried out for only 15 to 25% of the patients that keep on bleeding in spite of treatment with non-surgical therapy [4,13,15]. Some Brazilian authors have demonstrated that it is possible to use the distal splenorenal shunt in the emergency period because of the satisfactory results obtained [19, 24]. Only nineteen patients (8.6%) were submitted to a surgical treatment during the acute episode of bleeding. In this situation the process of esophagogastric devascularization associated with splenectomy (EGDS) was applied to 63.2% of the patients. There was a successful control of bleeding in 78.9% of the cases. In the first following year, 5.2% of the other patients were submitted to surgical treatment after new episodes of upper gastrointestinal bleeding caused by gastroesophageal varices.

A liver transplant is the only procedure that has a great potential to control the bleeding, to correct the portal hypertension and to restore the normal liver function. It is an option for those patients with an advanced liver disease with possible variceal bleeding complications [16,17,24,25]. However, a great percentage of patients with bleeding caused by varices cannot be submitted to a transplant due to factors such as advanced age, drug abuse, non-compliance, active alcoholism or advanced diseases in other organs and long time in waiting list because of the shortage of donor organs [4,16,26]. In this work only two patients (1.1%) were submitted to a liver transplant during a one-year period. Recent reports showed that portal blood flow-preserving procedures performed by a highly skilled surgical team in a well-selected patient population offer excellent results, with very low operative mortality rate (1%), very good 5-year survival, low encephalopathy rate and a low rebleeding rate. No other option can offer such promising results. Therefore, these portal blood flow-preserving procedures have an important role for patients waiting for a liver transplantation [4,16].

In conclusion, the incidence of upper digestive hemorrhage caused by acute variceal bleeding was 28.6% in our Emergency Room with low mortality rate. It is im-

portant to consider that the gastroesophageal varices are still a significant cause of upper gastrointestinal bleeding and may lead to death. Significant prognostic factors were liver failure score, according to Child-Pugh-Turcotte's classification and the efficiency of the applied treatments. We conclude that portal hypertension treatment should be considered again.

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