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Predictors of Variceal Cause of Upper Gastrointestinal Tract Hemorrhage

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Abstract

Objective: **To identify significant pre-endoscopic predictors of variceal cause in patients with acute upper gastrointestinal tract (GI) hemorrhage.**

Patients and Methods: **Medical records of 187 patients with primary diagnosis of upper GI hemorrhage treated during the period from May 2003 to July 2004 were reviewed. Predictors studied included age, sex, history of chronic liver disease, physical findings of chronic liver disease, abnormal laboratory findings and blood transfusion requirements prior to endoscopy. The outcome was the presence of variceal cause of upper GI hemorrhage on urgent upper GI endoscopy. Predictors were individually tested for statistical association with endoscopic findings using chi-square, t-test and Wilcoxon rank-sum test, and entered into a multiple logistic regression analysis. The final logistic regression model was tested for discriminatory ability using the Area Under the receiver operating characteristic Curve (AUC) and cross validation was performed using the jackknife method.**

Results: **The prevalence of variceal cause of upper GI hemorrhage was 14% (27/187). Only documented history of chronic liver disease (OR: 51.8, 95% CI: 15.1 to 177.3) and low platelet count (1.9 per 100,000 decrease; 95% CI: 1.0 to 3.3) were significant independent predictors of variceal cause of upper GI hemorrhage. The AUC was 0.921 and the jackknife AUC was 0.892.**

Conclusions: **Documented history of chronic liver disease and low platelet count were independent predictors of variceal cause of upper GI hemorrhage. Patients with bleeding varices can be identified, to a certain extent, prior to upper GI endoscopy.**

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Introduction

Management of acute upper gastrointestinal (GI) variceal hemorrhage differs from that of non-variceal hemorrhage, especially if variceal hemorrhage is associated with significant liver impairment.[1] In particular, a less aggressive surgical approach is recommended for variceal hemorrhage, i.e. surgical management for an acute episode is used only as a last resort since operative outcomes are generally poor in the presence of significant liver disease.[2] Also, certain temporary measures for active upper GI hemorrhage such as balloon tamponade (e.g. Sengstaken-Blakemore tubes) are routinely used only for variceal hemorrhage.[1-3] Because of the emergent nature of the bleeding, these management approaches must often be considered in the absence of endoscopic confirmation of variceal hemorrhage. Alternatively, in certain clinical settings, endoscopist may not be available or at least not available late at night. It would be useful in these instances if, prior to upper GI endoscopy, accurate predictors of variceal cause of upper GI hemorrhage based on easily obtainable clinical and laboratory information can be found. Based on these predictors, treatment specific for variceal hemorrhage can be confidently instituted before endoscopic confirmation. The objective of this study was to identify significant pre-endoscopic predictors of bleeding varices in patients presented with upper GI hemorrhage.

Patients and Methods

Medical records of patients admitted to the Ramathibodi Hospital and Medical School during the period between May 2003 and July 2004 with the primary diagnosis of upper GI hemorrhage of any causes were reviewed. All patients underwent urgent (within 48 hours of admission) esophagogastroduodenoscopy (EGD). Patients were excluded if they had contraindications for EGD, severe hematologic derangement, advanced cancer or if they were hospitalized primarily for other illnesses.

Data on potentially relevant predictors of variceal cause of upper GI hemorrhage were abstracted from the medical records. These included documented history of chronic liver disease (usually cirrhosis of any cause), physical findings compatible with chronic liver disease, complete blood count (CBC), "liver function" test (the transferases, serum alkaline phosphatase, serum bilirubin and serum albumin), International Normalized Ratio (INR) for the prothrombin time and the number of units of packed red cell (PRC) transfused. The liver function test was categorized as being abnormal if the values of any of its components were above the upper normal limit of the hospital's reference range.

The primary outcome was the EGD finding of bleeding esophagogastric varices. This was defined as the finding of any grade of esophagogastric varices in association with evidence of active bleeding, stigmata of recent hemorrhage, or with documentation in the medical records as being the cause of upper GI hemorrhage.

The association between each potential predictor and the finding of bleeding varices was tested using the t-test, Wilcoxon rank-sum test, chi-square test or Fisher's exact test as appropriate. Predictors individually found to be significantly associated with the outcome were entered into a multiple logistic regression model, and only those predictors remaining significant in the logistic model were retained. The final logistic regression model was assessed for the ability to discriminate between patients having variceal cause of upper GI hemorrhage from those having other causes by measuring the Area Under the operating characteristic Curve (AUC), otherwise known as the c-index.[4] The jackknife method was used to assess the cross validity of the model.[5,6] Acceptable AUC was taken to be 0.8 or greater.[7] Statistical significance was defined as a test p-value of 0.05 or less.

Results

Medical charts of 187 patients were reviewed. The mean age for this group of patients was 53.5 years (standard deviation, 17.9 years). There were 118 men (63%) and 69 women (37%). Twenty-seven patients (14%) had variceal cause of upper GI hemorrhage. Predictors of variceal cause of upper GI hemorrhage are displayed in Table 1, along with their values for patients with variceal cause and those with other causes. Table 2 shows the EGD findings in all patients.

As shown in Table 1, predictors significantly associated with the EGD finding of bleeding varices include younger age, history of alcohol abuse, documented history of chronic liver disease, physical

Table 1 Predictors of variceal cause of upper GI hemorrhage

Predictive factors	Total (N = 187)	Variceal cause of bleeding (N = 27)	Other endoscopic findings (N = 160)	p-values
Age (years): mean (sd)	53.5 (17.9)	47.1 (13.2)	54.5 (18.4)	0.047*
Sex (male): number (%)	118/187 (63)	13/27 (48)	105/160 (66)	0.082**
History of alcohol abuse (yes): number (%)	107/187 (57)	25/27 (93)	82/160 (51)	<0.001**
Existing liver disease (yes): number (%)	31/187 (17)	22/27 (81)	9/160 (6)	<0.001**
Signs of chronic liver disease (yes): number (%)	32/187 (17)	22/27 (81)	10/160 (6)	<0.001**
Hemoglobin (gm%): mean (sd)	9.6 (2.7)	9.1 (2.1)	9.6 (2.7)	0.390*
White cell count (per 1000): median (range)	9.92 (1.16 - 28.2)	10.2 (3.2 - 16.0)	9.9 (1.2 - 28.2)	0.470†
Platelet count (per 1000): median (range)	248 (54 - 645)	144 (54 - 377)	258 (56 - 645)	<0.001†
INR: mean (sd)	1.1 (0.4)	1.3 (0.3)	1.1 (0.4)	0.024*
Abnormal LFT (yes): number (%)	150/187 (80)	22/27 (81)	15/160 (9)	<0.001**
PRC infused (U): median (range)	1 (0 - 8)	2 (0 - 8)	1 (0 - 6)	<0.010†

**p-values by independent samples t-test; **p-values by chi-square or Fisher's exact test as appropriate; †p-values by Wilcoxon ranksum test; INR: International Normalized Ratio; LFT: Liver Function Test; PRC: Packed Red Cells.*

Table 2 Frequency of EGD findings

EGD findings	Number (N=187)	Percentage (%)
Normal	14	7
Gastritis	67	38
Esophagogastric varices	27	14
Gastric ulcer	45	24
Duodenal ulcer	21	11
Esophagitis/Mallory-Weiss tear	8	4
Gastric cancer	5	2

Some of the lesions occur together, hence the percentage sums to greater than 100

Table 3 Important predictors of the finding of variceal cause of upper GI hemorrhage in the multiple logistic regression model

Predictor	Odds Ratio (OR)	95% CI for OR
Chronic liver disease	51.8	15.1 to 177.3
Platelet count	1.9 per 100,000 decrease	1.0 to 3.3

signs of chronic liver disease, abnormal liver function test, prolonged INR, lower platelet count and higher number of units of PRC transfused.

After entering all these predictors into a multiple logistic regression model, only documented history of chronic liver disease and lower platelet count remained significant in the model. This was because most of the predictors were highly correlated with one another. The odds ratios of the remaining two predictors are presented in Table 3. The AUC for the model in Table 3 was 0.921. The jackknife AUC was 0.892.

Discussion

Significant predictors of variceal cause of upper GI hemorrhage were related to the presence of liver disease, alcohol abuse, and low platelet counts, as may be expected. Younger patients were more likely to present with bleeding varices, a finding similar to a recent report.[8] However, only a documented history of chronic liver disease and low platelet counts were independently predictive of bleeding varices on multivariable analysis.

Previous studies were mainly concerned with the prediction of existing significant esophagogastric varices in patients with various liver diseases (e.g. cirrhosis or hepatocellular carcinoma) prior to endoscopy.[9-12] The aim was to identify patients most likely to need preventive management of esophagogastric variceal bleeding or rebleeding. Other studies documented the prevalence of various causes of upper GI hemorrhage, not predictors of these causes.[9-14] Thus to the authors' knowledge, no previous reports have attempted to answer the question posed by the current study.

Nonetheless, low platelet counts and severity of liver disease have been found to be predictive of the presence of large, high risk esophagogastric varices.[9-11] It is perhaps not surprising that these two predictors

were also significantly associated with variceal cause of upper GI hemorrhage in this study.

It is notable that a documented history of chronic liver disease, especially that of cirrhosis, was highly predictive of variceal cause of upper GI hemorrhage, confirming an often used rule of thumb in clinical practice. A surprising aspect of the results of the current study was the high discriminatory power of the simple model in Table 3. With only two predictors, namely a history of chronic liver disease and low platelet count, the AUC of the model was a high 0.921, with good cross-validity (jackknife AUC of 0.892).

Translating this finding into a simple clinical rule to help predict the likelihood of variceal cause of upper GI hemorrhage, the sensitivity and specificity of the finding that the patient has a documented history of chronic liver disease and a platelet count of less than 100,000 are 98.8% (158/187) and 22.2% (6/27) respectively. Thus, if the clinical rule is positive (both a positive history and a platelet count less than 100,000), the probability that the patient will have a variceal cause of his/her upper GI hemorrhage is extremely high, and treatment can be initiated. However, if the rule is negative (negative one or both components), then EGD should be performed (cannot rule out variceal cause).

This study was a retrospective analysis of medical records and hence suffered from possible inaccuracies in the data, specifically misclassification. External validation of the results presented has not been done. A future, prospective, independent sample validation study should be performed.

Conclusions

The prevalence of variceal cause of upper GI hemorrhage in the current study was 14%. Independent predictors of bleeding varices included documented history of chronic liver disease and low platelet count. A predictive rule consisting of a documented history of chronic liver disease and a platelet count of less than 100,000 was 22% sensitive and 99% specific in the identification of variceal cause of upper GI hemorrhage. Patients with upper GI hemorrhage having a variceal cause can, to a certain extent, be identified prior to endoscopy.

REFERENCES

1. ASGE. An annotated algorithmic approach to acute gastrointestinal bleeding. Gastrointestinal Endosc 2001; 53: 853-58.
2. Rosemurgy AS, Zervos EE. Management of variceal hemorrhage. Curr Plb Surg 2003; 40: 258-343.
3. Sorbi D, Gostout CJ, Peura D, Johnson D, Lanza F, Foutch PG, et al. An assessment of the management of acute bleeding varices: a multicenter prospective member-based study. Am J Gastroenterol 2003; 98: 2424-34.
4. Agresti A. Categorical data analysis. 2nd ed. New York: John Wiley & Sons; 2002.
5. Fisher LD, van Belle G. Biostatistics: a methodology for health sciences. New York: John Wiley & Sons; 1993.
6. Lang TA, Secic M. How to report statistics in medicine. Philadelphia: American College of Physicians; 1997.
7. Hunt JP, Meyer AA. Predicting survival in the intensive care unit. Curr Plb Surg 1997; 34: 525-600.
8. Segal WN, Cello JP. Hemorrhage in the upper gastrointestinal tract in the older patient. Am J Gastroenterol 1997; 92: 42-6.
9. Madhotra R, Mulcahy HE, Willner I, Reuben A. Prediction of esophageal varices in patients with cirrhosis. J Clin Gastroenterol 2002; 34: 81-5.
10. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Dig Liver Dis 2003; 35: 473-8.
11. Yeh JL, Peng YC, Tung CF, Chen GH, Chow WK, Chang CS, et al. Clinical predictors of large esophagogastric varices in patients with hepatocellular carcinoma. Dig Dis Sci 2002; 47: 723-9.
12. Schepis F, Camma C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, et al. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology 2001; 33: 333-8.
13. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol 1999; 94: 3285-91.
14. Wilcox CM, Alexander LN, Straub RF, Clark WS. A prospective endoscopic evaluation of the causes of upper GI hemorrhage in alcoholics: a focus on alcoholic gastropathy. Am J Gastroenterol 1996; 91: 1343-7.