Chirurgia (2013) 108: 312-318
No. 3, May - June


# Mortality and Need of Surgical Treatment in Acute Upper Gastrointestinal Bleeding: A One Year Study in a Tertiary Center with a 24 Hours / Day-7 Days / Week Endoscopy Call. Has Anything Changed?

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**Rezumat**

***Mortalitatea și necesarul de tratament chirurgical în hemoragia digestivă superioară acută: un studiu pe o perioadă de un an într-un centru terțiar cu gardă permanentă de endoscopie. S-a schimbat ceva?"***

*Introducere:* Deşi în trecut o frecventă urgență chirurgicală, hemoragia digestivă superioară constituie la ora actuală cea mai frecventă urgență gastroenterologică.
*Scop:* Evaluarea situației actuale privind mortalitatea şi necesarul de tratament chirurgical în hemoragia digestivă superioară.
*Material şi metodă:* Studiu clinic retrospectiv nerandomizat desfăşurat la Institutul Regional de Gastroenterologie şi Hepatologie "Profesor Dr. Octavian Fodor" din Cluj Napoca. 757 de pacienți cu hemoragie digestivă superioară au fost examinați endoscopic în primele 24 de ore de la prezentare. Datele au fost colectate din foile de observație şi programul Hospital Manager. Pentru analiza statistică, am efectuat testele: chi pătrat, Spearman, Kruskall-Wallis, Mann-Whitney, AUROC (area under receiver operating curve).
*Rezultate:* A predominat etiologia non-variceală, etiologia principală fiind cea ulceroasă. Mortalitatea intraspitalicească globală a fost de 10.43%, rata de resângerare de 12.02%, tratamentul chirurgical fiind efectuat în 7.66% din cazuri. 3.68% din cazurile de hemoragie nonvariceală au necesitat hemostază chirurgicală de urgență. Necesarul de tratament chirurgical s-a corelat cu scorul Rockall complet (p=0.0425). Pentru ulcerul peptic, necesarul chirurgical nu a fost influențat de momentul endoscopiei sau tipul de tratament efectuat (p=0.1452). Prezentarea în cursul weekendului (p=0.996) sau a nopții (p=0.5414) nu s-a corelat cu un necesar mai mare de intervenție chirurgicală.
*Concluzii:* În ultimul deceniu, necesarul de tratament chirurgical de urgență în hemoragia superioară digestivă s-a redus cu 50% dar mortalitatea a rămas constantă.

**Cuvinte cheie:** hemoragie digestivă superioară, hemostază endoscopică, tratament chirurgical, mortalitate

**Abstract**

*Background:* Acute upper gastrointestinal bleeding, previously often a surgical problem, is now the most common gastroenterological emergency.
*Aim:* To evaluate the current situation in terms of mortality and need of surgery.
*Subjects and methods:* Retrospective non-randomised clinical study performed between 1st January-31st December 2011, at "Professor Dr. Octavian Fodor" Regional Institute of Gastroenterology and Hepatology in Cluj Napoca. 757 patients with upper gastrointestinal bleeding were endoscopically examined within 24 hours from presentation in the emergency unit. Data were collected from admission charts and Hospital Manager

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programme. Statistical analysis was performed with GraphPad 2004, using the following tests: chi square, Spearman, Kruskall –Wallis, Mann-Whitney, area under receiver operating curve.
*Results:* Non-variceal etiology was predominant, the main cause was bleeding being peptic ulcer. In hospital global mortality was of 10.43%, global rebleeding rate was 12.02%, surgery was performed in 7.66% of patients. Urgent haemostatic surgery was needed in 3.68% of patients with nonvariceal bleeding. The need for surgery correlated with the postendoscopic Rockall score (p=0.0425). In peptic ulcer, the need for surgery was not influenced by time to endoscopy or type of treatment (p=0.1452). Weekend (p=0.996) or night (p=0.5414) admission were not correlated with a higher need for surgery.
*Conclusions:* Over the last decade, the need for urgent surgery in upper gastrointestinal bleeding has decreased by half, but mortality has remained unchanged.

**Key words:** upper digestive bleeding, endoscopic hemostasis, surgery, mortality

## Introduction

Formerly a mainly surgical problem, acute upper gastrointestinal bleeding has become the most common gastroenterological life-threatening emergency. Management strategies have changed dramatically over the last 20 years due to the introduction of acid suppressive therapy as well as endoscopic haemostasis, with a decrease in surgical need, but relatively unchanged mortality rates of 6-13% in most studies. Mortality can reach higher values in variceal bleeding (1-4). The majority of deaths do not result from failure of haemostasis, either medical or surgical, but mainly from comorbidities, poorly tolerated blood loss and resultant complications (3,4). Management strategies are clearly defined by national and international guidelines (5-12), but treatment varies according to local experience and medical resources, especially the availability of permanent endoscopic diagnosis and haemostasis. Currently, international guidelines (5-11) support the use of upper endoscopy within 24 hours for patients presenting with upper gastrointestinal bleeding. The guideline of The Romanian Society of Gastroenterology and Hepatology and The Romanian Society of Endoscopy reduces timing recommendations to 16 hours from presentation (12). In high risk patients presenting with haematemesis/haematochezia or hemodynamic instability, endoscopy is recommended as soon as possible. Despite a rich international literature-on risk factors and outcome in acute upper gastrointestinal bleeding, in our country there are relatively few recent data on outcome, including the need for surgery.

The aim of the present study was to obtain actual data on acute upper gastrointestinal bleeding regarding etiology and outcome, as well as to study the factors correlated with mortality, rebleeding and need of surgical treatment in a tertiary specialized center, with a permanent endoscopy call (24 hours/day, 7 days/week).

## Materials and Methods

This is a retrospective non-randomised clinical study performed on the patients evaluated between 1st of January - 31st of December 2011. The study took place at the 3rd Medical Clinic, "Professor Octavian Fodor" Regional Institute of Gastro-enterology and Hepatology in Cluj Napoca. Patients were considered for the study if they had evidence of overt gastro-intestinal bleeding on admission or a recent history of hematemesis/ground vomiting, melena, haematochezia or a combination of any of the above. All patients were endoscopically examined within 24 hours from presentation to the emergency unit. In hospital bleedings were also included in our study. Data collected from admission charts and Hospital Manager programme included: age and sex, etiology, previously validated prognostic scores (pre- and post-endoscopic Rockall score, Glasgow-Blatchford score), endoscopic data (Forrest classification for non-variceal bleeding, the presence of ongoing/stopped bleeding), use of antiplatelet/anticoagulant medication, time to endoscopy from admission to the emergency unit, time of emergency unit presentation (night/day, weekend/weekday), treatment. Outcome was analysed in terms of in hospital death and need of surgical therapy. Statistical analysis was performed with GraphPad 2004, using the following tests: chi square, Spearman, Mann-Whitney, area under receiver operating curve.

## Results

During the mentioned period, 757 endoscopies were performed for the diagnosis of acute upper gastrointestinal bleeding. Patient characteristics are given in *Table 1* and *2*.

Non-variceal etiology was dominant; the main cause of upper gastrointestinal bleeding was gastric and duodenal ulcer. The second most frequent cause was variceal etiology, mainly esophageal and rarely gastric location. The following cause was neoplasia of the upper gastrointestinal tract, especially ulcerated lesions with oozing or adherent clot, and gastric

***Table 1.*** *Clinical characteristics of the patients with upper digestive bleeding*

| |
|---|
| Age : 62.11±13.37 years<br>Gender: 413 (54.42%) males: 345 (45.57%) females |
| *High risk patients according to prognostic scores* |
| Postendoscopic Rockall score: 461 patients.<br>Glasgow-Blatchford score: 432 patients. |
| *Medication and alcohol use* |
| Anticoagulation: n=53 (7%)<br>NSAID : n=130 (17.17%)<br>Aspirin: n=65 (8.58%)<br>Clopidogrel : n=7 (0.92%)<br>Alcohol: n=288 (38.04%) |
| *Mode of presentation* |
| Hematemesis: n=380 (50.19%)<br>Melena: n=750 (99.07%)<br>Hematochesia: n=35 (4.62%) |

***Table 2.*** *Endoscopic characteristics of the 757 patients*

| |
|---|
| *Etiology* |
| Variceal bleeding-n=184 (24.30%) |
| Portal congestive gastropathy-n=10 (1.32%) |
| Peptic ulcer- n=308 (40.68%) |
| Gastric ulcer- n=143 (18.89%) |
| Duodenal ulcer- n=134 (17.70%) |
| Recurrent anastomosis ulcer-n=28 (3.69%) |
| D2 duodenal ulcer-n=3 (0.39%) |
| Angiodysplasia-n=14(1.84%) |
| Erosive bulbitis-n=7 (0.92%) |
| Erosive gastritis-n=55 (7.26%) |
| Oesophagitis- n=20 (2.64%) |
| Esophageal ulcer- n=16 (2.11%) |
| Dieulafoy lesion- n=12 (1.58%) |
| Cameron lesion- n=4 (0.52%) |
| Mallory-Weiss syndrome-n=38 (5.01%) |
| Source of bleeding not identified- n=3 (0.39%) |
| Aorto-duodenal fistula- n=3 (0.39%) |
| Posttherapeutic- n=8 (1.05%) |
| Neoplasia: n=70p (9.24%). |
| Esophageal- n=6 (0.79%) |
| Eso-cardio-tuberositary location- n=9 (1.18%) |
| Stomach- n=50 (6.60%) |
| Vaterian ampuloma (exulcerated)-n=3 (0.39%) |
| Extrinsec tumoral invasion-n=2 (0.26%) |
| Other: 5 (0.66%) |
| *Activity during the first endoscopy* |
| Stopped bleeding: n=554p. (73.18%) |
| Ongoing bleeding: n=203p.(26.81%) |
| *Stigmata of recent haemorrhage* |
| *Nonvariceal (n= 563p.). Forrest classification* |
| IA: n=28 (4.97%). |
| B: n= 109 (19.36%)p. |
| IIA: n= 88 (15.63%) |
| B: n= 97 (17.22%) |
| C: n= 33 (5.86%) |
| III: n=208 (36.94%) |
| *Variceal bleeding (n=194p.)* |
| Active bleeding: n =66 (34.02%) |
| Spurting:n=57 (29.38%) |
| Oozing:n=9 (4.63%) |
| Stopped bleeding: n=128 (65.97%) |
| Collapsed varices: n=9 (4.63%) |
| Adherent clot: n=21 (10.82%) |
| Red spots: n=72 (37.11%) |
| Hematocystic dilatations: n=16 (8.24%) |
| Congestive gastropathy: n=10 (5.15%) |

cancer, eso-cardiotuberositary and esophageal location. Other frequent causes included erosive disease (gastritis or duodenitis) and Mallory-Weiss tear. We noticed a very small number of cases in which the source of the bleeding was not localised, stress ulcer, as well as postprocedural bleeding. Bleeding complications of procedures such as gastric polypectomy, endoscopic sphincterotomy with stone extraction or endoscopic biliary prosthesis for cholangiocarcinoma, were present mainly in patients with coagulation impairment (elevated I.N.R., haemophilia).

A significant proportion of the patients included in our study were high risk patients according either to a Glasgow-Blatchford score >=12 points (57.06% of patients) or a postendoscopic Rockall score >=6 points (60.89% of patients). Only 4 patients had a Glasgow-Blatchford score of 0 with a possible indication of outpatient management. Despite high risk scores in over 50% of the patients, most bleedings were not active at the time of endoscopy but high risk bleeding stigmata were dominant, especially visible vessels without active bleeding and lesions with adherent clot.

From the timing point of view, we found that most patients presented during daytime (n=523 patients), most frequently between 9-10 a.m. and that a significant number of cases presented during the weekend (n=225 patients). All endoscopies were performed within 24 hours from presentation, ranging from 1 minute to 1437 minutes, the median time to endoscopy being 306.6 minutes (5 hours and 6 minutes).

The treatment strategy was adapted to the etiology and type of endoscopic lesion. The most used endoscopic haemostasis method was injection therapy, usually 1:10.000 adrenalin injection (n=250 patients, 33.02%). Other techniques included hemoclip placement (n=55 patients, 7.26%), argon plasma coagulation (n=25 patients, 3.3%),variceal band ligation (n=164 patients, 21.66%) and combined therapy, mainly injection therapy associated with hemoclip placement (n=49 patients, 6.47%). Two hundred and seventy eight (36.72%) patients did not require endoscopic or surgical intervention. Surgery was performed in 58 patients, representing 7.66%. Three patients refused surgical intervention with a good short-term outcome, the indication for surgical treatment was decided for in case of malignancy and not failure of medical haemostasis.

In hospital global mortality was 10.43% and global rebleeding rate was 12.02% (91 out of 757 patients).

### *Mortality*

Mortality rate was correlated with all prognostic scores (Mann-Whitney test, $p<0.0001$), the most significant statistical correlation being with the Rockall postendoscopic score (Spearman test, r=0.2879) followed by pre-endoscopic Rockall score (Spearman test, r=0.2791) and Glasgow Blatchford (Spearman test, r=0.2098). For high risk patients according to complete Rockall score, the global mortality rate was 15.58%. For common etiologies, mortality rates did not differ significantly, being similar to overall mortality. Mortality rates according to etiology are given in *Table 3*. Endoscopic aspects were also analysed separately for non-variceal and variceal bleeding: for nonvariceal bleeding, Forrest classification of endoscopic lesions was used and we registered a significant correlation with mortality for Forrest IIB lesions (chi square test, p=0.0360); cases of variceal bleeding, oozing and the presence of collapsed varices were correlated with higher mortality rates (chi square test, p=0.0179). Treatment was based on etiology, type of endoscopic lesion and stigmata of recent haemorrhage. The time of emergency unit admission was not an independent risk factor for mortality as there was

***Table 3.*** *Mortality rates according to etiology and endoscopic lesions*

| *Etiology* |
|---|
| Angiodysplasia: n=2/14p. (14.28%) |
| Dieulafoy lesion: n=0/12p. (0%) |
| Erosive disease: n=4/62p (6.45%) |
| Neoplasia: n=9/70p. (12.85%) |
| Mallory Weiss tear: n=1/38p. (2.63%) |
| *Peptic ulcer: n=29/308p. (9.41%)* |
| *Variceal bleeding: n=26/194p. (13.4%)* |
| Spurting: n=3/57p. (5.26%) |
| Oozing: n=4/9p. (44.4%) |
| Adherent clot: n=4/21p. (19.04%) |
| Hematocystic dilatations: n=1/16p. (6.25%) |
| Red spots: n=10/72p. (13.88%) |
| Collapsed varices: n=4/9p. (44.4%) |
| *Total: n=79/757p. (10.43%)* |
| *Active bleeding: n=19/203p. (9.35%)* |
| *Stopped bleeding: n=60/554p. (10.80%)* |

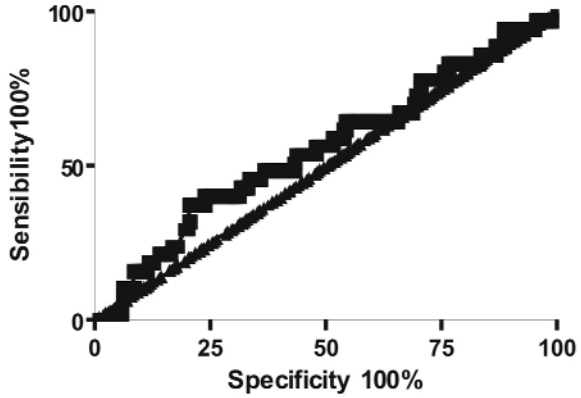


***Figure 1.*** *Area under receiver operator curve, for time to endoscopy in high risk patients according to Glasgow-Blatchford score (>12 points), variceal and nonvariceal etiology*

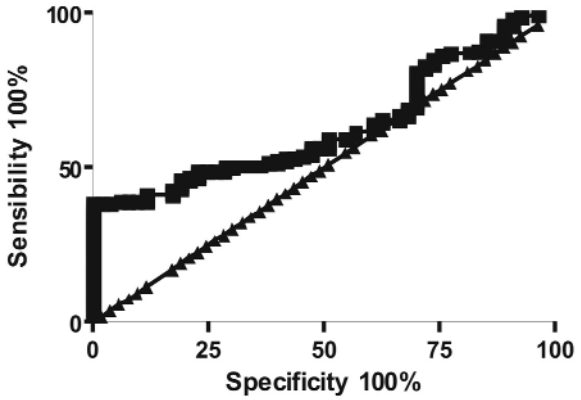


***Figure 2.*** *Area under receiver operator curve, for time to endoscopy in high risk patients according to Glasgow-Blatchford score (>12 points), variceal etiology*

no statistical difference between mortality rates if we compared night versus day admission (p=0.6250) or weekday versus weekend admission (p=0.1152). Time to endoscopy within 24 hours from presentation did not correlate with mortality, on a global analysis. When we analysed the nonvariceal cases based on Forrest classification, we did not find a correlation with time for type IA (p=0.3728) or IIB (p=0.3870) lesions. Within 24 hours of presentation to endoscopy, in patients with gastric or duodenal ulcer, mortality was not influenced by time when analysed according to the type of endoscopic treatment. A time analysis for low risk patients was not possible due to the very low mortality rates. For high risk patients according to complete Rockall score, there was no correlation between time to endoscopy and mortality rates (p=0.8903) within 24 hours from presentation. For the Glasgow-Blatchford score, which is a non-endoscopic one, we found statistically significant mortality rates for a score higher or equal to 12 points. The global analysis for all etiologies of gastrointestinal bleeding revealed an AUROC value of 0.6352, with a cut-off value of 260 minutes, at a 100% sensitivity and a 95 % confidence interval of 0.5689 - 0.7015 (*Fig. 1*). The analysis only for variceal bleedings showed a time cut-off value at 99.03 minutes, with an AUROC value of 0.5595, a sensitivity of 100% and a 95% confidence interval of 0.4572 -0.6618 (*Fig. 2*). For nonvariceal bleedings with a Glasgow-Blatchford score higher or equal to 12 points, the time cut-off value was below 1,435 minutes, close to the upper limit of the time interval.

### *Need for surgery*

Surgical treatment was indicated in 61 patients and performed in 58 (7.66%). For nonvariceal bleedings and the

***Table 4.*** *Relative risk of rebleeding according to type of treatment*

| Type of treatment | Relative risk | Odds ratio | P value, chi square test |
|---|---|---|---|
| Injection therapy | 1.164 | 1.231 | 0.3172 |
| Combined endoscopic therapy | 1.329 | 1.361 | 0.4108 |
| Plasma argon coagulation | 0.4949 | 0.4893 | 0.4807 |
| Acid suppressive therapy | 0.6414 | 0.5665 | 0.0281 |
| Injection versus combined therapy | 0.9813 | 0.9044 | 0.8019 |
| Injection versus plasma argon coagulation | 1.040 | 2.516 | 0.3606 |
| Combined versus argon plasma coagulation | 1.178 | 2.782 | 0.3299 |

indication of urgent haemostasis due to impossibility of endoscopic treatment or rebleeding, surgery was required in 21 patients, i.e. surgery was needed in 3.68% of these patients. Surgery was indicated by several situations, not necessarily failure of endoscopic haemostasis: rebleeding lesions in 9 cases; massive active haemorrhage with impossibility to attempt endoscopic haemostasis in 15 cases (main causes: massive bleedings with poor visualization of the lesion and luminal stenosis with impossibility of reaching the lesions endoscopically). Failure of endoscopic haemostasis did not necessarily mean surgical treatment, which was recommended mainly in case of upper gastrointestinal malignancy. In patients in whom endoscopic haemostasis was achieved, the surgical indication was a diagnosis of malignancy of the upper gastrointestinal tract (18 cases) or complications such as luminal stenosis (duodenal ulcer 2 cases, antral neoplasm 4 cases) or penetration and perforation (gastric ulcer 2 cases).

Surgery was performed in 27 cases of peptic ulcer (14 duodenal and 13 gastric ulcer), 1 case of Dieulafoy lesion, 27 cases of upper gastrointestinal malignancy and 3 cases of aortoduodenal fistula. Surgery was not performed in any of the patients with variceal bleeding.

The need for surgical treatment was correlated with postendoscopic Rockall score ($p=0.0425$), but was not correlated with the pre-endoscopic Rockall score ($p=0.9127$) or Glasgow-Blatchford score ($p=0.1873$). For peptic ulcer, either gastric or duodenal localisations, the need for surgery was not influenced by time to endoscopy or type of treatment, nor endoscopic or acid suppressive therapy ($p=0.1452$). Weekend ($p=0.996$) or night ($p=0.5414$) admission were not correlated with a higher need for surgical intervention.

The global rebleeding rate was 12.02% and was significantly correlated with both pre-endoscopic scores: Rockall pre-endoscopic ($p=0.0008$) and Glasgow-Blatchford score ($p= 0.0002$).The most significant correlation was with complete Rockall score ($p<0.0001$). The etiology of bleeding was not correlated with the rate of rebleeding, although endoscopic aspects of the lesions were: active bleeding (oozing or spurting vessel, $p=0.0144$). Treatment was recommended by the type of stigmata of recent haemorrhage or Forrest type lesion. There was no statistically significant difference between different types of endoscopic methods.

## Discussion

Our study reveals an important decrease in the need for urgent haemostatic surgery despite a relatively constant general mortality rate. Comparing data from 2011 with data from 2002 in the same hospital (14,15), we notice a decrease by half for urgent haemostatic surgery in cases of nonvariceal bleeding. In 2002, the need for urgent haemostatic surgery was 7.9% for nonvariceal bleeding with a drop from 17% in 1989. In 2011, need for urgent surgery was 3.68%. The mortality rate is similar to previously and recent published data (16-22), reaching approximately 10%, but we found the same figures no matter the etiology of gastrointestinal bleeding and lower mortality rates for variceal bleeding. For variceal bleeding, surgical treatment was not performed and treatment consisted mostly in variceal band ligation, mortality rates being similar with those of other etiologies. Our data is concordant with other studies (16-22) in terms of general mortality, recent data indicating variable mortality of 3-14%. Mortality rates as indicated by our study are a little higher for nonvariceal bleeding and lower for variceal bleeding. Differences can be explained by a higher percentage of high risk patients in our group compensated probably by optimal timing and performance of endoscopy within 24 hours. Variceal bleeding mortality rates are lower than previously reported data, ranging from 22.8% in 2000 to 15% in 2010 in several international studies (6,23-27). Other important aspects are the similar mortality rates for surgically, endoscopically or conservatively treated patients, which indicate comorbidities as an important prognostic factor. Previous studies in the same institution (13,14,15,18) revealed higher mortality rates for surgical patients, which indicated endoscopic haemostasis as an important factor in reducing surgical mortality rates by a better control of preoperative risk factors.

Another matter was the optimal timing of endoscopy within 24 hours, still debatable because of risk, etiology and treatment variability. Several recent studies (28-33) show no difference in more urgent timing of endoscopy within 24 hours, but a recent study (34) revealed a higher mortality for delayed endoscopy in high risk patients within 24 hours from presentation. The study analysed only nonvariceal bleeding .We found no difference in mortality regarding time if we analyse nonvariceal bleeding separately but we noticed an increased mortality in high risk patients with variceal bleeding, even within 24 hours from presentation. Though early endoscopy is expected to be associated with better outcomes, there are several factors to be considered. First, if endoscopy is performed while bleeding is ongoing or soon after cessation, the large amount of fresh blood and clots may obscure the bleeding source and make endoscopic haemostasis more difficult or even impossible. On the other hand, time between active bleeding and endoscopy allows the onset of the healing process with possible downstaging of the endoscopic lesion that may not require endoscopic therapy.

Another important factor indicated by our study is the lack of difference between weekend and weekday as well as for night versus day admission in terms of mortality. This supports the importance of permanent endoscopy call for the optimal management of these patients. Several studies which included hospitals without permanent endoscopy call indicated higher mortality rates for weekend admission, though delayed endoscopy was not necessarily incriminated (16,31,35).

## Conclusions

Over the last decade, progress in diagnosis and therapeutic endoscopy has reduced approximately by half the need for urgent surgical haemostasis in acute upper nonvariceal bleeding. Despite this, overall mortality rates are relatively

constant. Mortality was not influenced by etiology or type of treatment as dictated by the type of endoscopic lesion in our patients, but mostly by comorbidities and risk factors as included in validated prognostic scores. Endoscopy performed within 24 hours from presentation is an important factor in optimising the management of patients with upper gastrointestinal bleeding but timing of urgent endoscopy may still be debatable.

### *Conflicts of interests*

None to declare.

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