Nonvariceal upper gastrointestinal tract bleeding – risk factors and the value of emergency endoscopy

Pawel Wierzchowski[1], Stanislaw Dabrowiecki[1], Wojciech Szczesny[2], Jakub Szmytkowski[1]

[1]Department of General and Endocrine Surgery, University Hospital No. 1, Bydgoszcz, Poland
[2]Department of Nutrition and Dietetics, Nicolaus Copernicus University, *Collegium Medicum*, Bydgoszcz, Poland

Submitted: 18 November 2011
Accepted: 11 May 2012

Arch Med Sci 2013; 9, 5: 843–848
DOI: 10.5114/aoms.2013.36911

Corresponding author:
Pawel Wierzchowski MD, PhD
Department of General and Endocrine Surgery
University Hospital No. 1
9 Sklodowskiej St
85-737 Bydgoszcz, Poland
Phone: +48 52 585 46 30
Fax: +48 52 585 40 16
E-mail: pawel.wierzchowski@gmail.com

Abstract

Introduction: Upper gastrointestinal tract bleeding (UGIB) remains a valid issue of modern medicine. The mortality and recurrence rates remain high and have not decreased as expected over the past decades. Aim of the study: to assess the treatment outcomes of nonvariceal UGIB depending on the timing of endoscopy (urgent vs. elective) and to perform an analysis of risk factors for death in patients with nonvariceal UGIB.

Material and methods: Comparative evaluation of treatment outcomes in two groups of patients. Group A consisted of patients undergoing elective endoscopy (n = 187). Group B consisted of patients undergoing emergency endoscopy (n = 295). Moreover, the influence of selected factors on the risk of death and bleeding recurrence was analyzed in the combined population of the two groups. This was done by constructing a logistic regression model and testing dependence hypotheses.

Results: In group A the mortality rate was 9.1%, and the recurrence rate was 18.2%. In group B the values were 6.8% and 12.2%, respectively. No statistically significant difference was found (p = NS). In group B the number of surgical interventions, blood transfusions and intensive care admissions was significantly lower ($p < 0.05$). An analysis of the combined material showed that the factors which correlated with an elevated risk of death included: old age, hemodynamic state (shock), elevated Charlson Comorbidity Index score, hemoglobin concentration, bleeding from a malignant lesion, recurrent bleeding and the need for surgery ($p < 0.05$).

Conclusions: The use of emergency endoscopy improves the treatment outcomes in patients with UGIB, although no statistically significant decrease in the mortality and recurrence rates could be observed.

Key words: emergency endoscopy, intestinal tract bleeding, risk factors.

Introduction

Upper gastrointestinal tract bleeding (UGIB) is a frequently encountered acute surgical emergency and the most frequent complication of peptic ulcer disease. It is estimated to occur in 50–172/100 000 people annually. The incidence of UGIB increases in populations with the lowest socioeconomic status [1, 2]. Despite the developments in endoscopy, *Helicobacter pylori* eradication schemes and the widespread use of proton pump inhibitors (PPIs), the problem of UGIB remains. Even though in 70–80% the bleeding is self-limiting, the mortality rate in the remainder of cases is high at approximately 7–11% [3, 4].

The current therapeutic model calls for early endoscopy and bleeding control regardless of the causative factor of the UGIB. Intensive treatment within the initial 24 h of hospital stay significantly increases chances of survival [5–8]. Such a course of treatment has both medical and economical implications. The high cost of maintaining an endoscopic team with 24-hour availability and the high mortality of patients with UGIB necessitate discussion and search for the best therapeutic options.

In the authors' center, the management of UGIB in the past decade was dependent on the organizational structure of the hospital. In the first 5 years of this century, endoscopy was performed within normal working hours only, i.e. usually the next working day after admission. The establishment of a dedicated endoscopy division has made 24-hour on-call endoscopy available. These changes in the management options available for UGIB patients have given us the opportunity and clinical material to inquire whether the new model of treatment does indeed decrease the mortality and complication rates.

The goal of this study was to compare the treatment outcomes of patients with nonvariceal UGIB in two periods differing by the timing of endoscopy (elective vs. urgent), and also to evaluate the influence of selected parameters on the risk of death and bleeding recurrence in patients with nonvariceal UGIB.

Material and methods

The study population consisted of patients with nonvariceal UGIB treated at the Department of General, Vascular and Endocrine Surgery. Two patient groups were created, based on the type of therapy:

- group A – elective endoscopy (years: January 2003 –May 2005),
- group B – emergency endoscopy (years: June 2005 –December 2008).

During the first analyzed period (group A, retrospective data) the endoscopies were performed within the working hours of the Department of Gastroenterological Endoscopy (8.00 AM to 3.00 PM). In practice, a patient with UGIB admitted after 3:00 PM would wait for an endoscopy until the next morning. In the second period (group B, prospective data) the endoscopy was performed on the day of admission, usually within 2–3 h, by the on-call endoscopy team.

The gathered clinical material was analyzed twofold. Firstly, groups A and B were compared with respect to the type of intervention performed and the outcome thereof. Secondly, the relationship was investigated between selected parameters and the recurrence of bleeding or patient death; this analysis was performed on all of the material, without dividing it into groups.

The homogeneity of the groups was assessed considering the time from the onset of the symptoms, history of UGIB, hemodynamic condition upon admission, the Charlson Comorbidity Index (CCI) [9], initial hemoglobin concentration, cause of bleeding and type of endoscopic intervention.

Groups A and B were compared primarily with respect to the number of deaths and bleeding recurrences. The patients were followed until discharge from hospital. The following events were considered as bleeding recurrence:

- confirmed recurrent UGIB upon endoscopy,
- a decrease in hemoglobin concentration > 2 g/dl during 24 h despite transfusion,
- a recurrence, after a period of stabilization, of one or more of the following: hemodynamic abnormalities, hematemesis, tarry stools.

The following were adopted as secondary indicators of therapeutic failure and analyzed in both groups: number of surgical interventions, duration of hospital stay, number of red blood cell concentrate (RCC) units administered, the need for ICU treatment.

Statistical analysis

The influence of selected parameters on the risk of death and bleeding recurrence was evaluated in the combined population of the two study groups. To this end, dependence hypotheses were evaluated using the *t* test for independent samples, Pearson's χ^2 and an independently constructed logistic regression model. The influence of the following was evaluated: age, hemoglobin concentration upon admission, CCI score, hemodynamic state, pathology diagnosed, need for surgical intervention and duration thereof.

Results

In the period 2003–2008, 482 patients with UGIB were treated at the authors' center (285 males, 197 females): group A (2003–2005) – 187 cases and group B (2005–2008) – 295 cases.

Epidemiology and patient condition

The mean age of the patients was 62.7 ±15.6 years, and group A patients were significantly older (65 years vs. 61 years, $p < 0.02$). The patients were admitted to the hospital after a mean period of 1.66 days from the onset of the first signs of UGIB. For 353 patients (73%) this was their first episode of UGIB. Most of the patients were admitted with no hemodynamic abnormalities (49%). Tachycardia was observed in 32%, and shock was diagnosed in 19% of the patients. Mean hemoglobin concentration was 9.2 g/dl. The mean CCI value of the patients was 4.3 points. The differences in these parameters between the two groups are shown in Table I.

Table I. Evaluation of patients upon admission to hospital

Parameter	Group A	Group B	Value of *p*
Duration of the sequelae [days]	1.65	1.67	NS
CCI	3.98	4.56	0.02
Hemoglobin [g/dl]	9.35	9.16	NS
History of bleeding [%]:			NS
First	81.6	78.3	
Second	7.6	12.2	
Multiple	3.2	3.5	
Another episode within 1 year	7.6	5.9	
Hemodynamic state [%]:			< 0.02
Normal	58.3	43.4	
Tachycardia	22.5	37.3	
Shock	19.2	19.3	

The type and location of the pathology were established from the endoscopy reports or surgical records. The distribution of UGIB causes was similar in both groups. In the whole population, gastric and duodenal ulcers were the most frequently diagnosed conditions (respectively: 26.6% and 26.4% patients), followed by: inflammatory lesions and erosions (19.6%), neoplasms (8.5%) and Mallory-Weiss syndrome (7.4%). Other pathologies (Dieulafoy lesion, angiodysplasia, polyp, diverticulum, iatrogenic lesion) were found in 5.9% of the patients. The cause of the bleeding could not be established in 5.5% of patients.

Therapeutic interventions and outcomes

Endoscopy was performed in 453 (94%) of the 482 patients hospitalized for UGIB. In 79 cases two, and in 5 cases multiple endoscopic interventions were performed. In group A the endoscopy was performed as an elective procedure 1 day after admission or later (161 patients, mean delay 1.1 days after admission). All endoscopies in group B were emergency procedures, performed on the day of admission (292 patients).

Table II. Number and type of endoscopic hemostatic procedures

Hemostatic procedure	Group A	Group B
Injection, *n* (%)	25 (33.3)	174 (66.7)
APC, *n* (%)	28 (37.3)	41 (15.7)
Clip, *n* (%)	4 (5.3)	15 (5.7)
Combination of two methods, *n* (%)	18 (24.0)	31 (11.9)
Total, *n* (%)	75 (100.0)	261 (100.0)

APC – argon plasma coagulation

Endoscopic hemostasis was performed during 336 endoscopies – by default in Forrest IA–IIB patients. The most frequently utilized technique was adrenalin injection (Table II).

The treatment outcomes in both groups are compared in Table III. The overall mortality rate was 7.7%, and the number of bleeding recurrences was 14.5%. The mortality rate was lower in group B, but the difference failed to reach significance (9.1% vs. 6.8%). Similar results were obtained by comparing the recurrence rates in both groups (18.2% vs. 12.2%). In this instance, the difference between the

Table III. Comparison of treatment outcomes between groups

Parameter	Group A (*n* = 187)	Group B (*n* = 295)	Value of *p*
Death	17 (9.09)	20 (6.78)	0.353
Bleeding recurrence	34 (18.2)	36 (12.2)	0.069
Surgery for UGIB	12 (6.42)	7 (2.37)	0.026
Duration of surgery [min]	87.1	103.6	0.516
Hospital stay [days]	4.79	4.30	0.127
Blood transfusions [RCC units]	2.94	2.35	0.042
Admission to ICU	10 (5.35)	5 (1.7)	0.024

Table IV. Parametric variables in deceased and successfully treated UGIB patients

Variable	Death				Value of *p*
	No		Yes		
	Mean	SD	Mean	SD	
Age	61.8	15.5	73.7	13.2	< 0.001*
CCI	4.17	2.73	6.38	2.51	< 0.001*
Duration of sequelae [days]	1.68	1.12	1.459	0.900	0.25
Hemoglobin [g/dl]	9.32	2.60	8.09	2.28	0.01*
Duration of surgery [min]	85.5	45.7	103.8	60.1	0.46

**Statistically significant value*

Table V. Nonparametric variables influencing the risk of death and recurrence of UGIB in the study population

Variable	Death			UGIB recurrence		
	OR (95% CI)	NNT < 0; NNH > 0	ARR < 0; ARI > 0	OR (95% CI)	NNT < 0; NNH > 0	ARR < 0; ARI > 0
Surgery	10.9* (4.06–29.16)	2.79	35.84%	40.4* (11.39–143.2)	1.38	72.55%
Shock	11.5* (5.37–24.09)	4.20	23.80%	3.3* (1.9–5.7)	5.56	17.98%
Neoplasm	3.7* (1.55–8.74)	7.16	13.97%	1.3 (0.55–3.11)	26.82	3.73%

**Value significant at p < 0.01, OR – odds ratio, NNT – number needed to treat, NNH – number needed to harm, ARR – absolute risk reduction, ARI – absolute risk increase*

groups was on the borderline of statistical significance.

The mean percentage of surgical interventions in our material was 3.94 and was significantly lower in group B. At the same time, the mortality rate among the patients undergoing surgery was high at 42%.

In group B, fewer patients required admission to the ICU ($p < 0.03$). The patients received a mean amount of 2.58 RCC units – this parameter was again significantly lower in group B ($p < 0.05$). The mean hospital stay was 4.49 ±3.2 days and was comparable in both groups.

Analysis of risk factors for death and bleeding recurrence

The influence of the parameters measured upon admission and the therapeutic interventions performed on the number of deaths and bleeding recurrences during the hospital stay was assessed. Old age, higher CCI score and lower hemoglobin level upon admission were all found to be risk factors for death due to UGIB (Table IV).

The number of deaths was significantly higher among the patients with hemodynamic shock upon admission, bleeding from a neoplasm and those undergoing surgery (Table V). Patients with recurrent bleeding more frequently displayed lower hemoglobin levels upon admission; the difference was statistically significant (8.19 g/dl vs. 9.4 g/dl; $p = 0.001$). Moreover, in patients with recurrent UGIB the incidence of hemodynamic shock and the need for surgery were greater (Table V).

An analysis using a logistic regression model mostly confirmed the earlier results (Table VI). The following have been shown to have a significant influence on the mortality rate: patient age, hemodynamic state upon admission, recurrence of bleeding, need for surgical intervention and bleeding from a neoplasm.

Table VI. Logistic regression model for dependent variable: death

Stepwise regression ($n = 333$)	F(6.326) = 18.990; $p < 0.001$	
	Value of *t*	Value of *p*
Bleeding recurrence	4.77003	< 0.001
Shock	5.40871	< 0.001
Age	4.28963	< 0.001
Neoplasm	3.14597	0.002
Surgery	2.41673	0.016
Hemoglobin level	1.64543	0.1

Discussion

An analysis of the treatment outcomes of patients with upper gastrointestinal bleeding has shown that the introduction of emergency endoscopy has significantly influenced the decrease in the number of surgical procedures, blood transfusions and intensive care referrals. Despite the advances of UGIB therapy, it is still a condition with significant mortality. With the availability of emergency endoscopy, performed within 2–3 h of admis-

sion, a decrease in mortality was observed when compared to a group of patients in whom endoscopy was performed 1 day after admission (6.8% vs. 9.1%; $p = 0.35$). The methodology the authors have adopted for this study does not allow them to verify whether this is a stable trend. A drop in the recurrence rates has also been observed; however, this phenomenon was on the borderline of statistical significance. Patient age, hemodynamic state, CCI score, hemoglobin concentration, malignant disease and the need for surgical intervention were all correlated with an increased risk of death in UGIB patients.

The analysis summarizes the effects of the development of an endoscopy center at the authors' institution. The intensification of endoscopic interventions has visibly influenced the overall outcomes of treatment of patients with UGIB. Changes similar to those observed by the authors at their center have been taking place worldwide throughout the past two decades. Introducing techniques for endoscopic hemostasis has decreased the invasiveness of UGIB management and decreased the number of patients referred for emergent surgery [7, 10]. This analysis also confirms the hypothesis of the role of surgery in the treatment of UGIB becoming marginal. The number of surgical interventions for UGIB has decreased and – as may be expected – so has the number of people requiring ICU treatment. Those patients who did require surgery were admitted in poor overall condition, and the perioperative mortality rate was high. Even though statistics show that performing a surgical intervention in a UGIB patient is a risk factor for death, the decision to perform surgery is influenced by the patient's critical condition, the failure of other treatment options or insufficient time to adopt a different course of treatment.

The resulting opinion of the advantages of emergency endoscopy in all of the patients presenting with UGIB is often disputed, and economic data clearly indicate that the cost of keeping an endoscopic team on call is high. Despite that fact, certain measurable advantages of early endoscopic treatment can be observed [6, 11]. Our analysis has shown that the patients undergoing emergency endoscopy needed fewer blood transfusions. Earlier endoscopy allows for early identification of the source of the active bleeding and successful hemostasis, effectively reducing the need for transfusion. The reduced number of operations, ICU stays, transfused blood and blood-related products all serve to significantly decrease treatment cost.

Another aspect is the technique used to achieve hemostasis. The most efficient option is considered to be a combination of two hemostatic techniques, one of them being hemostatic clips, if possible [8, 12, 13]. In our material the type of hemostatic intervention was not standardized. In group A the use of two techniques prevailed, while in group B adrenaline injection was the dominant method. These parameters also could have had some influence on the results.

In our study, the parameters most important from the viewpoint of treatment effectiveness – the mortality and recurrence rates – did not differ by a statistically significant value between the groups. The recurrence and mortality rates were lower in patients after emergency endoscopy. Considering the worse hemodynamic state of group B patients and their higher comorbidity, one might venture to state that the availability of on-call endoscopy did have a significant impact in this aspect. The need for such indirect reasoning might result from the imperfect methodology the authors have chosen for their study. A randomized trial would show significant differences between the study groups; it is, however, difficult to conceive of a contemporary study based on such methodology.

Developing a perfect therapeutic model for UGIB management requires a careful assessment of risk factors. Based on this, risk scores are created, which evaluate the probability of an undesirable occurrence. For UGIB, the most widely recognized and used scores include Rockall, Baylor, Cedars-Sinai Medical Center Predictive Index, and Glasgow-Blatchford [14–19]. A statistical analysis performed by the authors has shown that the risk of death increased with patient age and CCI score. Important predictive factors were the hemodynamic state and hemoglobin concentration upon admission. If the bleeding was due to a malignant tumor or if it recurred, the mortality rate was significantly higher. These observations are in agreement with published results of other series. Numerous publications indicate that the aggravating factors include age > 65 years, hemodynamic shock, and the presence of fresh blood upon digital rectal examination or in the nasogastric tube. Higher comorbidity, low hemoglobin concentration and the need for transfusion also negatively influence the prognosis. The risk of death is also higher if the bleeding recurs or if it affects a patient hospitalized for another condition [12, 16, 19, 20]. In addition, our study has shown that the CCI score may be a useful addition to the initial assessment of an UGIB patient. Other authors have published reports proving the usefulness of the CCI scale to evaluate the risk of death in many medical conditions and long-term outcomes of UGIB treatment [21, 22]. This analysis serves to complement those studies in this aspect.

The population of patients treated for UGIB in recent years has been significantly changing: the patients are older, more frequently use NSAIDs, more often present in shock and show more severe comorbidities. Antihemorrhagic agents are more

frequently used. A similar trend is visible in our analysis. In effect – even though the mortality and recurrence rates are similar in both groups – if we consider the overall condition of the patients we may find out that emergency treatment of UGIB is more effective than we think.

References

1. Blatchford O, Davidson LA, Murray WR, Blatchford M, Pell J. Acute upper gastrointestinal haemorrhage in west of Scotland: case ascertainment study. BMJ 1997; 315: 510-4.
2. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol 2008; 22: 209-24.
3. Yavorski RT, Wong RK, Maydonovitch C, Battin LS, Furnia A, Amundson DE. Analysis of 3,294 cases of upper gastrointestinal bleeding in military medical facilities. Am J Gastroenterol 1995; 90: 568-73.
4. Di Fiore F, Lecleire S, Merle V, et al. Changes in characteristics and outcome of acute upper gastrointestinal haemorrhage: a comparison of epidemiology and practices between 1996 and 2000 in a multicentre French study. Eur J Gastroenterol Hepatol 2005; 17: 641-7.
5. Cook DJ, Guyatt GH, Salena BJ, Laine LA. Endoscopic therapy for acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Gastroenterology 1992; 102: 139-48.
6. Barkun A, Fallone CA, Chiba N, et al. A Canadian clinical practice algorithm for the management of patients with nonvariceal upper gastrointestinal bleeding. Can J Gastroenterol 2004; 18: 605-9.
7. Adler DG, Leighton JA, Davila RE, et al. ASGE guideline: The role of endoscopy in acute non-variceal upper-GI hemorrhage. Gastrointest Endosc 2004; 60: 497-504.
8. Kujawski K, Stasiak M, Stepien M, Rysz J. Effectiveness comparison of endoscopic methods of non-varicose upper gastrointestinal bleeding treatment. Arch Med Sci 2010; 6: 599-604.
9. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994; 47: 1245-51.
10. Lau JY, Sung JJ, Lam YH, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. N Engl J Med 1999; 340: 751-6.
11. Wallner G, Skoczylas T, Lundell L. Management of patients with upper gastrointestinal bleeding. Pol Przegl Chir 2007; 79: (1).
12. Barkun AN, Martel M, Toubouti Y, Rahme E, Bardou M. Endoscopic hemostasis in peptic ulcer bleeding for patients with high-risk lesions: a series of meta-analyses. Gastrointest Endosc 2009; 69: 786-99.
13. Marek T, Baniukiewicz A, Wallner G, Rydzewska G, Dąbrowski A. Wytyczne w postępowaniu w krwawieniu z górnego odcinka przewodu pokarmowego pochodzenia nieżylakowego. Grupa Robocza Konsultanta Krajowego w Dziedzinie Gastroenetrologii [Polish]. Prz Gastroenterol 2008; 3: 1-22.
14. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996; 38: 316-21.
15. Saeed ZA, Winchester CB, Michaletz PA, Woods KL, Graham DY. A scoring system to predict rebleeding after endoscopic therapy of nonvariceal upper gastrointestinal haemorrhage with a comparison of heat probe and ethanol injection. Am J Gastroenterol 1993; 88: 1842-9.
16. Hay JA, Lyubashevsky E, Elashoff J, Maldonado L, Weingarten SR, Ellrodt AG. Upper gastrointestinal hemorrhage clinical guideline: determining the optimal hospital length of stay. Am J Med 1996; 100: 313-22.
17. Blatchford O, Murray WR, Blatchford MA. A risk score to predict need for treatment for upper gastrointestinal haemorrhage. Lancet 2000; 356: 1318-21.
18. Das A, Wong K. Prediction of outcome of acute GI hemorrhage: a review of risk scores and predictive models. Gastrointest Endosc 2000; 60: 85-93.
19. Camellini L, Merighi A, Pagnini C, et al. Comparison of three different risk scoring systems in non-variceal upper gastrointestinal bleeding. Dig Liver Dis 2004; 36: 271-7.
20. Barkun A, Bardou M, Marshall JK; Nonvariceal Upper GI Bleeding Consensus Conference Group. Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2003; 139: 843-57.
21. Gopalswamy N, Malhotra V, Reddy N, et al. Long-term mortality of patients admitted to the intensive care unit for gastrointestinal bleeding. South Med J 2004; 97: 955-8.
22. Wolf AT, Wasan SK, Saltzman JR. Impact of anticoagulation on rebleeding following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage. Am J Gastroenterol 2007; 102: 290-6.