Results of Surgical Treatment of Uncontrollable Upper Gastrointestinal Hemorrhage Using Endoscopy

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ABSTRACT

Background/Aims: Acute hemorrhage of the upper gastrointestinal tract occurs at a rate of 50 to 100 per 100,000 annually in the Western adult population. With the increased use of therapeutic endoscopy, the role of surgery is decreasing; surgical intervention is now only used in cases of failure of endoscopic hemostasis. The goal of this study is to determine whether there are predictive factors associated with high-risk post-operative mortality.
Methodology: This retrospective study included 30 patients treated from March 1996 to September 2008 at Brugmann Hospital. These patients presented with upper gastrointestinal non-variceal hemorrhage that was treated first endoscopically then surgically for recurrent hemorrhage. Multiple risk factors (variable and fixed) and parameters were evaluated to determine their influence on mortality.
Results: Of 30 patients, 10 (33%) developed recurrent hemorrhage following surgical treatment. A total of 8 (26.6%) deaths occurred of which 4 were related to hemorrhage. Three deaths occurred after the first intervention and 5 occurred after a second intervention. Logistic regression analysis revealed that the total number of blood units transfused and the presence of at least one surgical reintervention both significantly increased mortality rate (p=0.0426 and p=0.0068). Other parameters were not significant. However, there is a lack of power due to the small sample size.
Conclusion: For recurrent massive upper gastrointestinal hemorrhage following endoscopic treatment and necessitating more than 19 blood transfusions, early surgical intervention is recommended and surgical reintervention should be avoided. If reintervention is necessary, radical surgery is recommended. However, the small number of patients treated over a 12-year period limits the results of this study, and these results may represent simple coincidences.

KEY WORDS: Digestive hemorrhage; Endoscopy; Surgery; Morbidity; Mortality

ABBREVIATIONS: American Society of Anesthesiologists (ASA); Body Mass Index (BMI)

INTRODUCTION

With an overall incidence of 50 to 100 per 100,000 per year in the Western adult population, acute upper gastrointestinal hemorrhages are emergencies frequently encountered by gastroenterologists. In three-quarters of cases, peptic ulcers are the underlying cause of bleeding (1-2). Currently, surgical intervention is less frequently required due to improvements in endoscopic hemostasis and medical treatment (3). However, a number of patients are seen by gastrointestinal surgeons following failure of endoscopic treatment or in life threatening emergencies. These patients carry a high risk of morbidity and mortality.

The current study includes patients with non-variceal upper gastrointestinal hemorrhages that, for various reasons, could not be controlled endoscopically and required surgical intervention. The risk factors predictive of post-operative mortality were evaluated in order to improve patient planning and management.

METHODOLOGY

Among the patients hospitalized at Brugmann for endoscopic treatment of non-variceal upper gastrointestinal hemorrhage, only those requiring surgical intervention to treat hemorrhage refractory to endoscopic treatment were included. Thirty patients were identified from retrospective review of surgery and intensive care department records for March 1996 through September 2008. Multiple different parameters were collected in order to assess their impact on post-operative mortality.

1) Variable and fixed risk factors

Fixed risk factors include gender, age, ulcer history, and hemorrhage history. Variable risk factors

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TABLE 1 Individual Risk Factors

FIXED	n	%	Ave.	SD	Range	Median
Gender (male)	17	56.6 (N=30)				
Age	30	100 (N=30)	66.6	16.95	24-96	71.5
ASA Score*	30	100 (N=30)	2.53	0.73	1-4	3
BMI*	12	100 (N=12)	29	10.18	22.8-50	24.25
History includes ulcer	7	24 (N=29)				
History includes digestive hemorrhage	5	16.6 (N=30)				

*ASA=American Society of Anesthesiologists; BMI=Body Mass Index

VARIABLE	n	%
Tobacco	3	11.1 (N=27)
Alcohol	3	11.1 (N=27)
Arterial hypertension	11	36.6 (N=30)
Diabetes	5	16.6 (N=30)
Cardiovascular disease	12	40 (N=30)
Arrhythmia	8	26.6 (N=30)
Renal insufficiency	10	33.3 (N=30)
Respiratory insufficiency	8	26.6 (N=30)
Cirrhosis	1	3 (N=30)
Neoplasm	2	6 (N=30)

TABLE 2 Origin of Hemorrhage

1) Nature of bleeding	n	% (N=30)
Mallory-Weiss	4	13.3
Ulcer(s)	26	86.6
2) Location of ulcer	**n**	**% (N=34*)**
Esophagus	0	0
Cardia	2	5.8
Fundus	1	2.9
Lesser curvature	3	8.8
Antrum	2	5.8
Pylorus	1	2.9
Bulb	18	52.9
Posterior duodenum	7	20.5

*N>30 due to multiple ulcers in some patients

are body mass index (BMI), American Society of Anesthesiologists (ASA) score, arterial hypertension, diabetes, cardiovascular disease, arrhythmia, cirrhosis, cancer, renal insufficiency, respiratory insufficiency, tobacco smoking, alcohol consumption, and treatment with aspirin, non-steroidal anti-inflammatories, and anticoagulants.

2) Other data

The following symptoms were recorded: hematemesis, hematochezia, melena, arterial hypotension, tachycardia, origin of bleeding (esophagus, Mallory-Weiss, cardia, fundus, lesser curvature, antrum, pylorus, bulb, posterior duodenum), number of endoscopies performed, type of endoscopic technique (clip, thermo-coagulation, adrenalin injection, aethoxysclerol injection), hemoglobin rate before endoscopy and surgery, time between appearance of symptoms and endoscopy, time between first therapeutic endoscopy and surgical intervention, type of surgical interventions, number of recurrent hemorrhages after surgery, and the type of surgical re-intervention (iterative raphe versus iterative raphe with ligation of the gastroduodenal artery), number of units of blood transfused, stay in intensive care, duration of hospitalization, rate of local and general morbidity, and etiology of death (multisystem failure, recurrent hemorrhage, septic shock, acute renal insufficiency, purulent bronchiolitis, mesenteric infarct, etc).

Statistical analysis

Logistic regression analysis was performed using the program Statistix 9.0. Mortality rate was defined as the dependent variable and each factor likely to influence mortality rate as the independent variable.

RESULTS

Of the 30 patients, there were 17 men and 13 women (gender ratio of 1.3); average age was 66.7±16.9 years old (range 24-96) and average ASA score was 2.5±0.73 (range 1-4). There were 5 cases of hypovolemic shock on admission, 7 patients with history of ulcer, and 5 patients with history of gastrointestinal hemorrhage. Other individual risk factors are shown in **Table 1**.

The origin of hemorrhage was ulcer in 26 cases (86%) including 1 Dieulafoy lesion of the cardia. There were 4 cases of Mallory-Weiss tears (13.3%). Some patients had multiple concomitant lesions. In total, there were 34 ulcerous lesions of which the bulb form was most frequent (18 out of 34, 52.9%). **Table 2** illustrates these results.

Average time from development of symptoms to first therapeutic endoscopy was 1.6±3.09 days

(range 0-11). Average time between the first endoscopic hemostasis and surgical treatment was 2.7±4.56 days (range 0-19). Average hemoglobin was 8.62±2.43 mg/dl (range 4.5-15.4) prior to first endoscopy.

Sixty-one endoscopies were performed therapeutically; 8 of these (13.1%) were observational only either because the source of hemorrhaging could not be visualized, bleeding prevented further treatment, or because the object viewed with the endoscope (clot) suggested the need for surgery rather than endoscopic care. Among the various endoscopic treatments (hemostatic clip or hemoclip, thermo-coagulation using Bicap, adrenalin injection, aethoxysclerol injection), Bicap thermo-coagulation was most frequent (23 of 61 endoscopic procedures performed, 37%) whether used alone or combined with other techniques, followed by sclerotherapy by aethoxysclerol injection (14 of 61 endoscopic procedures, 22%).

Average hemoglobin was 6.97±2.37mg/dl (range 3-13.2) prior to the first surgical intervention; average value was 6.94±1.7mg/dl (range 5-8.9) before surgical reintervention.

Table 3 provides details on the different surgical techniques used. All were conducted via laparotomy. Of the initial interventions, 28 were conservative (93%). Two were radical (6.6%) with one Thal procedure for Mallory-Weiss and one subtotal gastrectomy for a hemorrhaging gastric ulcer of the lesser curvature perforating the pancreas. For conservative interventions, an ulcer raphe was always used, alone or in combination with other procedures. For surgical reinterventions following recurrent hemorrhage, 5 iterative raphes for ulcer with or without ligation of the gastroduodenal artery were performed. One post-operative hemostasis splenectomy and one post-operative evisceration were necessary (**Table 3**).

Ten recurrent hemorrhages (33.3%) after surgery occurred, of which 7 required reoperated (23.3%). Among the 7 reinterventions, one patient had recurrent hemorrhage and died of apparent hypovolemic shock. A total of 8 deaths, with 3 following the first surgical procedure (10%) and 5 after reintervention (71%), occurred (**Figure 1**). Causes of death were 4 massive hemorrhages including 2 with septic shock, 2 cases of multisystem failure, 1 mesenteric infarct, and 1 respiratory infection.

Two patients had local complications (recurrent hemorrhage, wound infection, wound dehiscence, collection at the sutures, wall abscess, mesenteric infarct, splenic breach, evisceration, or pancreatitis) and 18 had general complications (multisystem failure, disseminated intravascular coagulation, sepsis, renal insufficiency, pulmonary complication, auricular fibrillation, deep venous thrombosis, encephalopathy, or urinary infection). Five patients had both local and general complications and five had no complication.

Of all results, only the total number of transfused blood units and the requirement of a second surgical intervention significantly influenced mortality (**Table 4**). The total number of transfused blood units in all 30 patients was 378 (per-patient range 0-40; average 12.6; median 9.5) compared to 152 units of blood transfused in the 8 patients who died (per-patient range 7-33; average 19; median 20). Consequently, when greater than 19 units of blood were transfused, we observe a significantly higher mortality with a p-value of 0.0426 (OR=1.11 [1-1.23]). Likewise, mortality significantly increased following a second surgery. Overall mortality was 26.6% (8 deaths among 30 patients) but mortality after a second surgical intervention was 71.4% (5 deaths out of 7 reoperated patients) with a p-value of 0.0068 (OR=16.67 [2.17-127.93]). No link was found between the number of units of blood transfused and the necessity of surgical intervention.

TABLE 3 Surgical Interventions

1) First procedure

Radical	**n**	**% (N=30)**
Subtotal gastrectomy	1	3.3
Total	*1*	*3.3*
Conservative	**n**	**% (N=30)**
Raphe of ulcer	12	40
Raphe of ulcer+gastroduodenal artery ligation	9	30
Raphe of ulcer+ligation of the duodenal-pancreatic artery	1	3.3
Raphe of ulcer+biopsy	1	3.3
Raphe of ulcer+gastroduodenal artery ligation +biopsy	1	3.3
Raphe of ulcer+gastroduodenal artery ligation+epiploplasty	2	6.6
Raphe of ulcer+ vagotomy+pyloroplasty	2	6.6
Thal procedure	1	3.3
Total	*28*	*96.6*

2) Second procedure

For recurrent hemorrhage	**n**	**% (N=7)**
Raphe of iterative ulcer	2	28.5
Raphe of iterative ulcer+gastroduodenal artery ligation	3	42.8
Total	*5*	*71.4*
For post-operative complication	**n**	**% (N=7)**
Splenectomy	1	14.2
Evisceration	1	14.2
Total	*2*	*28.5*

DISCUSSION

Studies on upper gastrointestinal hemorrhages unresponsive to endoscopic treatment are rare in the medical literature. In this review, we included all cases of upper gastrointestinal hemorrhages without distinction. However, no cases of hemorrhage related to esophageal varices were encountered during the study period. The majority of pa-

TABLE 4 Application of a Logistic regression Analysis with Mortality as the Dependent Variable

INDEPENDENT FACTOR	*p*	CI 95%	OR
Fixed risk factors			
Age	0.1587	0.98-1.11	1.04
Male	0.6573	0.14-3.51	0.69
ASA Score*	0.4702	0.22-2.01	0.67
BMI*	0.3481	0.93-1.22	1.07
History of ulcer	0.3076	0.42-15.40	2.55
History of gastrointestinal hemorrhage	0.7134	0.06-6.79	0.64
*ASA=American Society of Anesthesiologists); BMI=Body Mass Index			
Variable risk factors			
Arterial hypertension	0.4291	0.08-2.95	0.48
Diabetes	0.5681	0.00-*	0
Cardiovascular disease	0.8661	0.16-4.57	0.87
Arrhythmia	0.4229	0.36-11.67	2.04
Renal insufficiency	0.2506	0.50-14.21	2.67
Respiratory insufficiency	0.3079	0.03-2.98	0.31
Cirrhosis	0.6339	0.00-*	2228.25
Neoplasm	0.6218	0.00-*	0
Aspirin	0.229	0.03-2.39	0.25
Non-steroidal anti-inflammatory	0.5418	0.05-4.94	0.49
Anti-coagulant	0.4579	0.16-54.56	3
Tobacco	0.6022	0.26-10.09	1.63
Symptoms on admission			
Hematemesis	0.7704	0.14-4.21	0.78
Melena	0.9009	0.18-7.18	1.12
Hematochezia	0.9009	0.14-5.67	0.89
Symptoms on admission			
Average arterial pressure <100mmHg	0.3491	0.42-11.82	2.22
Cardiac rhythm >100 per minute	0.5697	0.10-3.49	0.6
Shock on admission	0.8506	0.07-26.6	1.33
Parameters linked to endoscopic treatment			
Pre-endoscopic hemoglobin	0.4214	0.59-1.24	0.86
Symptom times-1st endoscopy	0.6916	0.82-1.35	1.05
Number of endoscopies	0.8164	0.58-1.97	1.07
Active hemorrhage on endoscopy	0.137	0.01-1.86	0.14
Visible vessels on endoscopy	0.7704	0.24-6.95	1.29
Presence of clot on endoscopy	0.1213	0.63-54.24	5.83
Hemoclip	0.6329	0.00-*	0
Bicap	0.1681	0.36-11.67	2.04
Adrenalin injection	0.4229	0.51-45.69	4.85
Aethoxysclerol injection	0.1213	0.02-1.6	0.17
Characteristic of the hemorrhage			
Mallory-Weiss	0.275	0.38-28.95	3.33
Cardia	0.6218	0.00-*	0
Fundus	0.7294	0.00-*	0
Lesser curvature	0.6126	0.00-*	0
Antrum	0.6218	0.00-*	0
Pylorus	0.6339	0.00-*	2228.25
Bulb	0.0857	0.76-64.27	6.99
Duodenum	0.4098	0.04-3.78	0.38
Parameters linked to surgical treatment			
Pre-operative hemoglobin	0.2442	0.52-1.18	0.78
Time 1st endoscopy-surgery	0.6878	0.87-1.23	1.04
Thal procedure	0.7294	0.00-*	0

TABLE 4 Application of a Logistic regression Analysis with Mortality as the Dependent Variable			
Gastrectomy	0.7294	0.00-*	0
Raphe of ulcer	0.4291	0.08-2.95	0.48
" +gastroduodenal artery ligation	0.0938	0.77-26.13	4.5
" +ligation of duodeno-pancreatic artery	0.7294	0.00-*	0
" +biopsy	0.7294	0.00-*	0
" +gastroduodenal artery ligation+biopsy	0.6218	0.00-*	0
" +gastroduodenal artery ligation+epiplopasty	0.7294	0.00-*	0
" +vagotomy+pyloroplasty	0.4579	0.16-54.56	3
Parameters linked to reintervention			
Post-operative recurrent hemorrhage	0.4996	0.00-*	57082.45
Pre-reintervention hemoglobin	0.5197	0.00-*	0
Surgical reintervention	0.0068	2.17-127.93	16.67
Iterative raphe	0.6218	0.00-*	0
" +gastroduodenal artery ligation	0.557	0.00-*	8491.78
Complications			
Only local complications	0.2781	0.45-16.25	2.7
Only general complications	0.8964	0.13-5.81	0.88
Local and general complications	0.1637	0.58-24.88	3.8
Units of blood transfused			
Total number	0.0426	1.00-1.23	1.11
Pre-operative	0.1718	0.94-1.37	1.14
1 Per-operative	0.0793	0.97-1.66	1.27
Pre-reintervention	0.2463	0.42-1.25	0.72
2 Per-operative	0.5325	0.23-2.12	0.7
Post-operative	0.9943	0.81-1.23	1
Intensive care unit (ICU)			
Duration	0.8837	0.97-1.04	1
Pre-operative ICU	0.4693	0.76-1.82	1.18
1 Post-operative ICU	0.8599	0.88-1.17	1.01
Post-reintervention ICU	0.2744	0.88-1.04	0.95
Hospitalization			
Duration	0.451	0.91-1.04	0.97

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tients were found to have hemorrhage due to peptic ulcers (86%); there was one case of Dieulafoy lesion and four cases of Mallory-Weiss tear.

With respect to the Dieulafoy lesions, a retrospective study by Katsinelos *et al* (4) showed that the best management of Dieulafoy lesions is endoscopic treatment by hemoclips. Clips are significantly more effective ($p<0.01$) than injections in terms of permanent hemostasis (78% in this study), recurrent hemorrhage, and recourse to surgery for therapeutic failure. In our case of gastrointestinal bleeding from a Dieulafoy lesion, endoscopic treatment, in particular by clipping, was not adequate.

For peptic ulcer hemorrhages, several studies are found in the literature. The study by Garripoli *et al* (2) reports the utility of clinical scores classifying patients according to their risk of recurrent hemorrhage following endoscopic treatment. The Cedar Sinai Medical Center predictive index is reliable in particular for determining the risk hemorrhagic recurrence ($p=0.004$) because of its sensitivity; however, it suffers from weak specificity and predictability.

An older prospective study by Choudari *et al* (5) attempts to define at-risk peptic ulcer patients who would benefit from early surgical intervention, similar to the subject of our study. Hypovolemic shock on admission ($p<0.001$), lower hemoglobin than in the group with successful endoscopic hemostasis ($p<0.001$), active hemorrhage on endoscopy ($p<0.001$), and posterior or anterior duodenal ulcer ($p=0.02$ and 0.004) were significantly linked to a greater rate of failure by endoscopic treatment. This failure is observed even more frequently when the duodenal ulcers are posterior rather than anterior (51% compared to 9%). These statistically significant results are not precise, in particular the lower hemoglobin associated with endoscopic failure.

Another randomized, controlled study by Lau *et al* (6) evaluating recurrent peptic ulcer hemorrhages following endoscopic treatment compared endoscopic retreatment with surgery. The study shows that hypotension ($p=0.01$) and an ulcer larger than 2 centimeters ($p=0.03$) are predictive factors for failure of endoscopic treatment; results

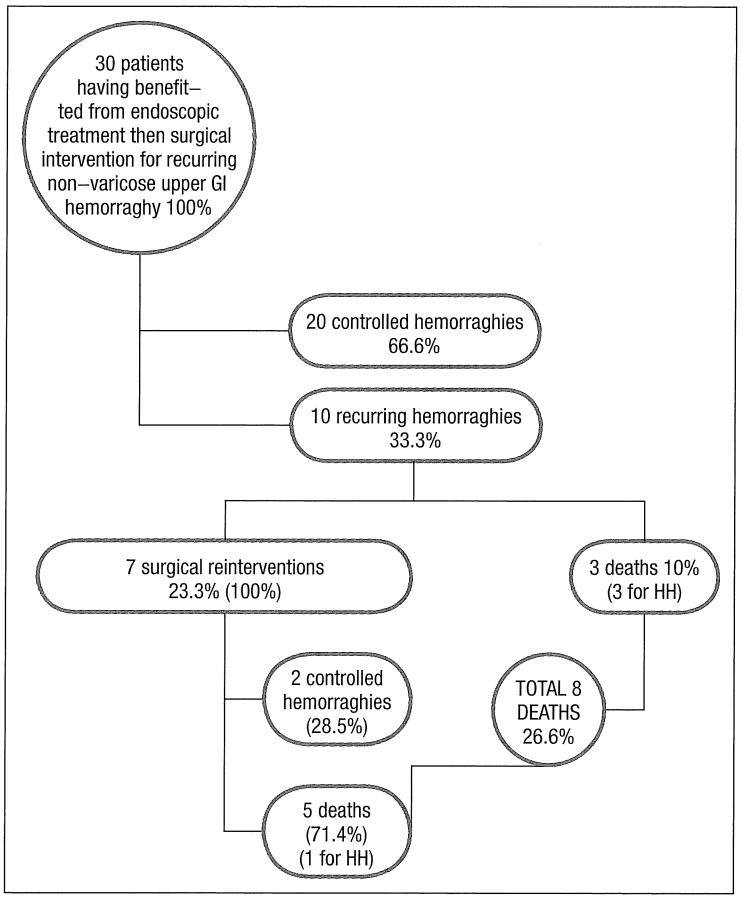

FIGURE 1 Recurrent Hemorrhage (RH) and Mortality

also showed that endoscopic retreatment was associated with fewer complications (p=0.03) than surgical treatment. The authors of this study thus favor a surgical approach only for large ulcers and before such ulcers begin rebleeding, because they showed that postoperative mortality increased with the number of endoscopies conducted both post-operatively and in emergency situations. In our study, we did not demonstrate a link between the number of endoscopies conducted pre-operatively and mortality rate.

On the other hand, Chiu *et al* (7) showed that a planned second therapeutic endoscopy within 24 hours after the success of a first endoscopy for hemorrhagic peptic ulcer significantly reduces the number of hemorrhagic recurrence (p=0.027 on day 7 and 0.034 on day 30); this treatment also had a tendency to reduce the need for surgery and mortality although this result was not statistically significant (p=0.05).

Brehant *et al* (3) conducted a prospective study on recurrent hemorrhagic duodenal ulcers with erosion of the gastroduodenal artery after endoscopic hemostasis. Single ligation of the gastroduodenal artery was compared to double ligation; intermittent versus continuous use of intravenous (IV) proton-pump inhibitor (PPI) was also compared. Double ligation of the gastroduodenal artery combined with continuous intravenous administration of a PPI reduced the risk of rebleeding, but no difference in mortality was demonstrated. It should be noted that this study does not mention any statistical analysis of results.

Finally, we did not take into consideration either the experience of the endoscopist or the time of the endoscopy (between 8:00 am and 5:00 pm or 5:00 pm and 8:00 am); a prospective study by Parente *et al* (1) explored these variables. The authors included 272 patients with acute non-variceal upper gastrointestinal hemorrhage; they did not demonstrate any influence of time of endoscopy on outcome for these patients. A significant difference was found based on the experience of the endoscopist and the number of transfusions required (p<0.001).

From 1996 to 2008, there has been progress in endoscopic treatments performed at Brugmann Hospital. In this study more treatments with bicap, thermo-coagulation, and injections initially were noted; their use declines with the increased popularity of hemoclips beginning in the late 1990s.

In view of the statistically significantly results obtained in this retrospective study, as conclusion it is preferable to operate early on non-variceal upper gastrointestinal hemorrhages that necessitate more than 19 blood transfusion units. Also it is imperative to ensure that the first surgical intervention is the most optimal possible with strict control of the hemorrhage, due to the increased risk of mortality with surgical reintervention. Moreover, if a second surgical procedure is required, it could be suggested that radical surgery, such as a gastrectomy or antrectomy with vagotomy, rather than conservative intervention, to be considered, based on the results obtained with the majority of conservative treatments. However, the fact that our results could represent mere coincidences and require further investigation cannot be denied.

Concerning results that are not statistically significant, it is necessary to complete this study in upcoming years and/or combining various gastrointestinal surgery departments in order to include more staff and a larger patient population. The current study lacks sufficient power in spite of the 12-year data collection. A randomized, prospective study would be ideal, but the rareness of these cases makes it difficult to conduct.

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