

Outcome of non-variceal acute upper gastrointestinal bleeding in relation to the time of endoscopy and the experience of the endoscopist: A two-year survey

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Abstract

AIM: To prospectively assess the impact of time of endoscopy and endoscopist's experience on the outcome of non-variceal acute upper gastrointestinal (GI) bleeding patients in a large teaching hospital.

METHODS: All patients admitted for non-variceal acute upper GI bleeding for over a 2-year period were potentially eligible for this study. They were managed by a team of seven endoscopists on 24-h call whose experience was categorized into two levels (high and low) according to the number of endoscopic hemostatic procedures undertaken before the study. Endoscopic treatment was standardized according to Forrest classification of lesions as well as the subsequent medical therapy. Time of endoscopy was subdivided into two time periods: routine (8 a.m.-5 p.m.) and on-call (5 p.m.-8 a.m.). For each category of experience and time periods rebleeding rate, transfusion requirement, need for surgery, length of hospital stay and mortality were compared. Multivariate analysis was used to discriminate the impact of different variables on the outcomes that were considered.

RESULTS: Study population consisted of 272 patients (mean age 67.3 years) with endoscopic stigmata of hemorrhage. The patients were equally distributed among the endoscopists, whereas only 19% of

procedures were done out of working hours. Rockall score and Forrest classification at admission did not differ between time periods and degree of experience. Univariate analysis showed that higher endoscopist's experience was associated with significant reduction in rebleeding rate (14% vs 37%), transfusion requirements (1.8 ± 0.6 vs 3.0 ± 1.7 units) as well as surgery (4% vs 10%), but not associated with the length of hospital stay nor mortality. By contrast, outcomes did not significantly differ between the two time periods of endoscopy. On multivariate analysis, endoscopist's experience was independently associated with rebleeding rate and transfusion requirements. Odds ratios for low experienced endoscopist were 4.47 for rebleeding and 6.90 for need of transfusion after the endoscopy.

CONCLUSION: Endoscopist's experience is an important independent prognostic factor for non-variceal acute upper GI bleeding. Urgent endoscopy should be undertaken preferentially by a skilled endoscopist as less expert staff tends to underestimate some risk lesions with a negative influence on hemostasis.

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Key words: Non-variceal acute GI bleeding; Time of endoscopy; Surgeon's experience; Endoscopic hemostasis

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INTRODUCTION

Acute upper gastrointestinal bleeding (AUGB) is the most common emergency managed by gastroenterologists, with an incidence ranging from approximately 50 to 150 per 100 000 per year in the Western population^[1,2]. The treatment of this condition has made important progress since the introduction of emergency endoscopy and endoscopic techniques for hemostasis along with

the application of specific post-endoscopic protocols, significantly decreases rebleeding and the need for surgery^[3-7], whereas mortality rates associated with AUGB still range as 5-15%^[8,9].

Several clinical and endoscopic score systems have been proposed to risk-stratify patients with AUGB in order to predict outcome and several factors such as age, shock and tachycardia at presentation, the presence of severe medical comorbidity and the lesion's appearance at endoscopy have been shown to be associated with adverse prognosis^[10-13]. In particular, Forrest's classification of endoscopic findings closely associated with peptic ulcer disease but sometimes seen with other causes of AUGB is associated with specific recurrent bleeding rates and is commonly used to assess the need for endoscopic therapy^[14].

As far as the effectiveness of various endoscopic therapies for AUGB is concerned, a recent review indicates that differences in terms of hemostatic results using the same treatment modality, exist between research studies and clinical practice as well as among various randomized clinical trials and are probably related to surgeon-dependent factors^[15]. Surprisingly, the experience of surgeons in achieving endoscopic hemostasis has not yet been examined, whereas the time of endoscopy has received so far little attention as a possible variable influencing the outcome of AUGB^[16-19].

We therefore undertook a 2-year survey in order to assess prospectively the impact of surgeon's experience and time of endoscopy on the outcome of acute non-variceal upper gastrointestinal (GI) bleeding patients in a large tertiary referral center of western Milan.

MATERIALS AND METHODS

Patients

Two hundred and seventy-two (mean age 67.3 years) patients who presented with AUGB to L. Sacco University Hospital, Milan, between June 2001 and July 2003 were included in this study. L. Sacco Hospital is a large teaching hospital located in western Milan with a catchment area of nearly 250,000 inhabitants and provides 24 h emergency endoscopy for two district neighboring hospitals serving an additional population of approximately 200 000 inhabitants.

The treatment protocol for patients with AUGB did not change during the study period and could be summarized in short as follows. All patients who arrived or were referred from a district hospital to the Accident and Emergency Department of our hospital with clinical manifestations of AUGB were managed according to a three-stage scheme: stage I: initial clinical and laboratory evaluation in the Emergency Department including placement of a double-bore nasogastric tube; stage II: hemodynamic stabilization including infusion of crystalloid fluids to maintain adequate blood pressure; stage III: urgent endoscopy within 12 h from presentation in patients who had at least one of the following presenting features: hematemesis with red blood or coffee

grounds, passage of melena and a hematocrit below the normal range with a nasogastric aspirate demonstrating red blood or coffee ground material. Recommendations regarding admission to the various hospital departments were made to the attending physicians by the endoscopist mainly based on the assessment of clinical and endoscopic criteria.

We used the Forrest's classification^[14] for endoscopic grading of bleeding lesions as follows: class 1A: active ulcer bleeding presenting as arterial spurting or pulsatile bleeding from the ulcer base; class 1B: milder forms present as continuous oozing either from a visible vessel or from underneath an adherent clot; class 2A: in the absence of active bleeding, the stigmata of recent hemorrhage including a non-bleeding visible vessel seen as a red or whitish-gray elevated lesion at the base of the ulcer; class 2B: an adherent clot covering the base of an ulcer; class 2C: a flat pigmented spot or a black membrane covering the ulcer base; class 3: a clean ulcer bottom (i.e., without vessel nor clot).

Patients with endoscopic stigmata of recent hemorrhage, regardless of whether they received endoscopic hemostasis or not were usually admitted to the surgical or gastroenterological ward. The allocation choice was mainly based on the presence of additional medical comorbidity (such as diabetes mellitus, renal failure, etc.) and available space at the different services. Patients with hemodynamic instability after the endoscopic procedure were usually admitted to the intensive care unit (ICU).

Study population

All patients aged 16-95 years undergoing urgent endoscopy (within 12 h after admission) for non-variceal AUGB and those who presented endoscopic stigmata of recent hemorrhage were potentially eligible for this study. Patients were excluded if they had variceal bleeding (both from esophagus and stomach), those who bled from an evident digestive tumor and other non-ulcer lesions such as Dieulafoy's lesions and Mallory-Weiss tears. In particular, Mallory-Weiss tears could not be enrolled since they have a low risk of recurrent bleeding^[20]. Dieulafoy's lesions were excluded since we preferred to treat these lesions by mechanical methods (such as banding or clipping) or APC rather than by epinephrine injection plus heat probe as in this study. Even patients with clearly malignant ulcers at endoscopy (i.e., patients with large flat, plaque-like, ulcerated tumors) were excluded due to the difficulty of standardizing the endoscopic hemostatic maneuvers under these circumstances. Finally, patients with ASA grade 5 were not enrolled in the study due to their severe clinical conditions as defined in this category.

Patients were evaluated at the time of admission using an extensive standardized-item list. The medical history (including concomitant disease, smoking habit, previous peptic disorders) and complaints (melena, hematemesis, hematochezia, dyspeptic complaints, syncope) were recorded. Concomitant diseases were categorized into six main classes (Table 1). The findings on physical examination were also recorded. Hemodynamic instability

Table 1 Distribution of 272 patients with acute non-variceal upper GI bleeding according to age, sex, and other selected covariates

Covariates	n (%)
Sex, male	186 (68.4)
Mean age (yr)	67.4±15.8
<40	19 (7.0)
40-49	24 (8.8)
50-59	26 (9.6)
60-69	51 (18.8)
70-79	88 (32.4)
≥ 80	64 (23.5)
Shock grade ¹ : 0	213 (78.3)
1	35 (12.8)
2	24 (8.8)
Comorbidities: cardiovascular	73 (26.8)
Neoplastic	30 (11.0)
Hepatic	26 (9.5)
Nephropathic	17 (6.2)
Multiple	48 (17.6)
Others	37 (13.3)
Main symptom at presentation ² : hematemesis	114 (42.0)
Melena	89 (33.0)
Anemia	69 (25.0)
Epigastric pain	19 (7.0)
Time of endoscopy: 8.00 a.m.-5.00 a.m.	221 (81.0)
5.00 p.m.-8.00 a.m.	51 (19.0)
Rockall score: 1-3	58 (21.3)
4-6	146 (53.7)
>6	68 (25.0)
Ulcer location: esophagus	21 (7.7)
Stomach	121 (44.5)
Duodenum	130 (47.8)
Ulcer size ³ : <20 mm	152 (68.5)
≥20 mm	70 (31.5)
Forrest classification: 1A	6 (2.2)
1B	59 (21.7)
2A	19 (7.0)
2B	63 (23.2)
2C	125 (45.9)
Transfusion requirements before endoscopy: (number of blood units)	
0	229 (84.2)
1-4	37 (13.6)
≥5	6 (2.2)

¹Shock grade: grade 0 = no shock signs (systolic BP >100, pulse <100), grade 1 = tachycardia (systolic BP >100, pulse >100), grade 2 = hypotension (systolic BP <100, pulse >100). ²The sum of main symptoms is higher than the number of patients as some patients had more than one main symptom at presentation. ³The sum does not add up to the total because of some missing values.

was defined as a systolic blood pressure <100×0.133 kpa or a heart rate >100 r/mm.

The Rockall score was calculated from age, hemodynamic characteristics, endoscopic findings, and comorbidity as previously described^[21].

Medications before and during the hospital stay [apart from intravenous proton pump inhibitors (PPIs) used for the bleeding episode] as well as the number of units of blood transfused before and after endoscopy were specifically noted.

Endoscopists and endoscopic procedures

We limited the endoscopists to seven gastroenterologists who were on a 24-h call for emergency endoscopy and whose experience was arbitrarily categorized into two levels according to the number of hemostatic endoscopic procedures done at the time of study. Five endoscopists (three consultant gastroenterologists and two senior registrars) had high experience (each one had performed more than 3 000 upper GI endoscopies and more than 100 emergency procedures). The three consultants had been in practice for more than 8 years, whereas the two senior registrars had completed 6 years of training in general gastroenterology and gastrointestinal endoscopy. The other endoscopists (young senior registrars in gastroenterology) had less experience as they had just completed only 4 years of training in general gastroenterology and had performed less than 1 000 upper GI endoscopies and 40-70 emergency procedures, as a principal surgeon before participating in this study. All emergency endoscopies were undertaken by the gastroenterologists on call in a separate endoscopic suite. Endoscopies performed between 8 am and 5 pm from Monday to Friday were defined as done within working hours (routine), whereas those performed at other time points were classified as done out of working hours (on call).

The endoscope employed was a Pentax EG 3440 video endoscope with a large operative channel (3.5 mm, Pentax, GmbH, Hamburg, Germany).

To improve the visual field, gastric lavage with a broad double-bore nasogastric tube was used and continuous normal saline infusion was carried out before endoscopy. Ulcers with bleeding stigmata were cleaned by water irrigation through the biopsy channel. Adherent clots were washed with a jet of water delivered through a catheter passed through the endoscope.

Only ulcerative lesions with endoscopic stigmata of acute bleeding, visible vessels or adherent clot (Forrest Ia-IIc) were included in the present study. Since previous studies have shown medium to poor inter observer variability in assessing endoscopic stigmata of bleeding^[21], we attempted at reducing interobserver bias on the grading of endoscopic stigmata by reviewing the video records of 20 explicative cases at a pre-study meeting.

Endoscopic therapy was standardized as follows: initial injection of 1:10 000 adrenaline around the bleeding lesion (up to a maximum of 20 mL) to achieve a tamponade effect, followed by application of a 3.2-mm heater probe

(Olympus, CD-120 U, Tokyo, Japan) at settings of 30 J per goal until the achievement of a coaptive effect^[22]. This method was used whenever endoscopic stigmata of hemorrhage such as acute spurting, oozing, visible vessel or adherent clots were present. Written guidelines containing the above mentioned recommendations concerning the hemostatic maneuvers to be undertaken were circulated among the endoscopists participating in this survey before the study.

The success of endoscopic hemostasis was defined as the cessation of bleeding together with the achievement of cavitation over the lesion after the application of the heater probe.

After endoscopy, the surgeon filled in a specific form with all the details concerning the procedure with specific reference to the appearance of bleeding lesions (according to the Forrest's classification) and the hemostatic maneuvers that were undertaken. Epinephrine solution injected and the number of pulses with the heater probe whenever employed were recorded. The time of endoscopy after admission was also recorded.

No patient was initially treated either with endoscopic band ligation or with hemoclippping, whereas these therapies were occasionally used by a senior endoscopist to obtain hemostasis in case of recurrent bleeding.

All patients received high dose intravenous PPIs: omeprazole or pantoprazole, 80 mg bolus within 12 h of endoscopy followed by 8 mg/h for 3 d^[23] and then an oral PPI, 40 mg once daily for the remainder of their hospital stay. Patients were closely monitored and underwent clinical reviews with their blood pressure, pulse, respiratory rate, and urine output measured hourly for the first 24 h followed by close observation for symptoms and signs of recurrent bleeding throughout their stay in the hospital. Subsequent management decision was made by the attending physician. No attempt was made to persuade the attending physician to follow a specific course of action beyond the recommendations quoted above and to determine the length of hospital stay.

Outcome measures

The major outcome parameters were rebleeding, surgical intervention, and mortality. Rebleeding was defined as repeated melena, hematemesis or a drop in hemoglobin concentration (>2 g/dL in 24 h) after a period of stabilization and unexplained by fluid replacement within 28 d of the initial bleeding episode. We performed a second endoscopy to confirm clinical recurrent bleeding which was defined as persistent endoscopic stigmata of acute spurting or oozing, visible vessels or adherent clots with the appearance of blood clots or coffee ground material in the stomach or duodenum. Our study had a result greater than 95% to reject the null hypothesis that the proportion of rebleeding patients was the same in endoscopists with high and low experience.

Surgery was performed in those patients whose bleeding could not be stopped by primary endoscopic hemostasis or by a second or third endoscopic therapy. Interventional radiology was not available for patients who did not

respond to endoscopic therapy when the study started. The choice of surgery was left to the individual surgeon though gastrectomy was the most preferred operation for the control of ulcer bleeding. The mortality was defined as death within 28 d of the bleeding episode.

Secondary outcome measures included the number of packed red cell units transfused after endoscopy and the length of hospital stay.

Appropriateness of endoscopic hemostatic maneuvers

The appropriateness of each endoscopic procedure was evaluated jointly by the two consultant gastroenterologists who did not participate in the procedures and were blinded to the outcome of patients and name of the endoscopist. Treatment in accordance with the implemented guidelines^[6] was classified as appropriate, treatment in disagreement as inappropriate. In many instances video taping of the cases was also used with regard to the appropriateness.

Statistical analysis

Univariate analysis was performed by the χ^2 test for frequencies and by the Man-Whitney rank sum test for means.

Odds ratios (OR) and corresponding 95% confidence intervals (CI) were estimated by unconditional multiple logistic regression models^[24] after adjustment for age (<40/40-49/50-59/60-69/70-79/ \geq 80 years), sex, Rockall (<6/ \geq 6) and Forrest's score (IA,IB/2A-2C), blood transfusion (no/yes), endoscopist's experience (high/low), and time of endoscopy (routine/on-call). Moreover, we estimated ORs after a further adjustment for appropriateness of treatment (appropriate/inappropriate).

The significance of OR estimates was represented by the corresponding 95%CI. If OR did not include unity, the estimate was statistically significant.

RESULTS

Overall results

Between June 2001 and July 2003, we recruited 272 patients (mean age 67.3 years, 186 males, 94% Caucasians) who presented to the A&E, Department of Luigi, Sacco University Hospital for non-variceal AUGB and underwent upper GI endoscopy within 12 h after admission with the presence of endoscopic stigmata of hemorrhage. They satisfied all the inclusion criteria of the study. Table 1 describes the distribution of these patients according to sex, age, and other selected covariates.

Overall, the rebleeding, surgical intervention, and mortality rates were 18.7%, 5.5%, and 13.2%, respectively. Initial endoscopic hemostasis was achieved in 268 of the 272 patients (98.5%) and four patients required immediate surgery for failure of primary endoscopic hemostasis. Fifty-one patients had at least a rebleeding episode after initial hemostasis (Figure 1). Thirty-six patients died within 28 d from the initial episode of bleeding. Their ultimate causes of death were cardiac failure (15), pulmonary failure (9), liver failure (4), multi organ failure (2), renal failure (4), and cerebral edema (2).

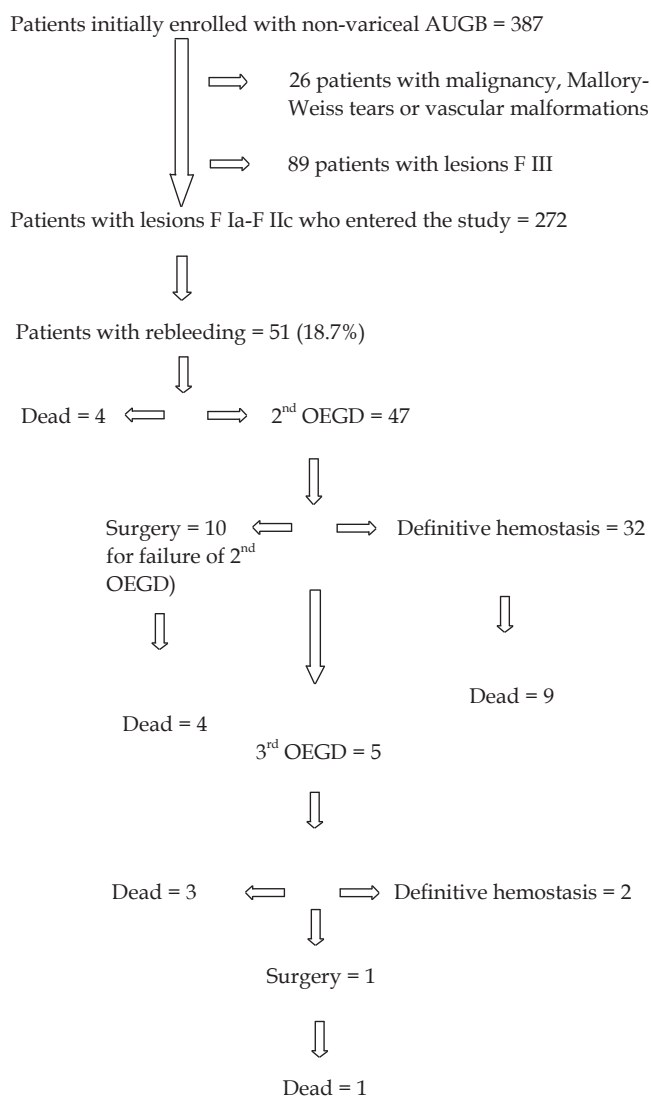


Figure 1 Flow chart illustrates the study design and how the 51 patients who had at least one rebleeding episode were managed and their clinical outcomes.

Outcome of patients

Eighty-one percent of the emergency procedures were performed between 8 a.m. and 5 p.m. whereas only 19% were done out of working hours.

Forrest's classification of lesions at admission did not significantly differ between the two endoscopist categories, though no significant trend towards a higher mean Rockall's score was found in patients undergoing endoscopy out of working hours.

Univariate analysis showed that higher endoscopist's experience was associated with significant reduction in rebleeding rate (14% *vs* 37%), transfusion requirements (1.8 ± 0.6 *vs* 3.0 ± 1.7 units) as well as the need for surgery (4% *vs* 10%), but not associated with the length of hospital stay and mortality (Table 2). In contrast, outcomes did not significantly differ between the two time periods of endoscopy.

Table 3 shows the distribution of patients according to the experience of endoscopists and the time of

Table 2 Rebleeding rate according to age, sex, Rockall score, Forrest's classification, ulcer size, operator's experience, and time of endoscopy

	Total NO. of patients	Rebleeding rate	<i>P</i>	
Age (yr)				
<65	88	8 9.1% (A)	0.046	A <i>vs</i> B
65-74	75	15 20.0% (B)	0.370	B <i>vs</i> C
> 74	109	28 25.7% (C)	0.003	A <i>vs</i> C
Sex				
Males	186	36 19.4%	0.707	
Females	86	15 17.4%		
Rockall score				
1-4	92	6 6.5% (A)	0.016	A <i>vs</i> B
5-6	112	20 17.8% (B)	0.005	B <i>vs</i> C
>6	68	25 36.7% (C)	<0.001	A <i>vs</i> C
Forrest's classification				
I A- I B	65	9 13.8% (A)	0.001	A <i>vs</i> B
II A- II B	82	33 40.2% (B)	<0.001	B <i>vs</i> C
III C	125	9 7.2% (C)	0.138	A <i>vs</i> C
Ulcer size ^a				
< 20 mm	152	24 15.8%	0.079	
≥ 20 mm	70	18 25.7%		
Surgeon's experience				
High	214	29 13.6%	< 0.001	
Low	58	22 37.9%		
Time of endoscopy				
Working hours	221	41 18.5%	0.862	
Out of working hours	51	10 19.6%		

¹ The sum does not add up to the total because of some missing values.

endoscopy. Univariate (Table 3) and multivariate (Table 4) analyses showed that low endoscopist's experience was associated with the higher rebleeding rate and transfusion requirements, but not significantly associated with the need for surgery, the length of hospital stay, and higher mortality rate. After adjustment for age, sex, and other selected covariates, the OR of low experienced endoscopist was 4.47 for rebleeding, 6.90 for need of transfusion after endoscopy, 2.36 for need of surgery, 0.47 for mortality, and 0.88 for length of hospital stay, respectively (Table 4). The estimates were statistically significant for rebleeding and need of blood transfusions. However, after further adjustment for appropriateness, the association with rebleeding disappeared (OR = 1.33), whereas it was still significant with the need of transfusion (OR = 5.07). The OR of making endoscopy in non-ordinary time period was 0.94 for rebleeding, 0.89 for need of transfusion after endoscopy, 1.85 for need of surgery, 1.96 for mortality, and 1.51 for length of hospital stay, respectively. None of the estimates were statistically significant even after further adjustment for appropriateness.

Table 5 shows the effect of an inappropriate endoscopic treatment on the occurrence of events of interest. A direct association was found between inappropriateness of treatment and risk of subsequent rebleeding (OR = 43.49),

Table 3 Distribution of patients by experience of endoscopists and time period of treatment, according to selected outcomes. Univariate analysis.

	Experience of endoscopist			Time period		P
	High n (%)	Low n (%)	P	8AM-5PM n (%)	5PM-8AM n (%)	
				n	n	
Rebleeding						
Yes	29 (58.9)	22 (43.1)	< 0.001	41 (80.4)	10 (19.6)	0.862
No	185 (83.7)	36 (16.3)		180 (81.5)	41 (18.6)	
N. of blood units transfused after endoscopy						
≥ 3	14 (48.3)	15 (51.7)	< 0.001	23 (79.3)	6 (20.7)	0.777
< 3	200 (82.3)	43 (17.7)		198 (81.5)	45 (18.5)	
Need for Surgery						
Yes	9 (60.0)	6 (40.0)	0.069	10 (66.7)	5 (33.3)	0.137
No	205 (79.8)	52 (20.2)		211 (82.1)	46 (17.9)	
Mortality						
Death	31 (86.1)	5 (13.9)	0.242	26 (72.2)	10 (27.8)	0.136
Alive	183 (77.5)	53 (22.5)		195 (82.6)	41 (17.4)	
Length of hospital staying						
≥ 13 d	107 (75.9)	34 (24.1)	0.244	120 (85.1)	21 (14.9)	0.091
< 13 d	107 (81.7)	24 (18.3)		101 (77.1)	30 (22.9)	
Rockall score						
< 6	111 (83.5)	22 (16.5)	0.06	108 (81.2)	25 (18.8)	0.985
≥ 6	103 (74.1)	36 (25.9)		113 (81.3)	26 (18.7)	
Forrest's classification						

Table 4 OR and corresponding 95%CI for patients treated by less vs well experienced endoscopists and for patients treated between 5 p.m. and 8 a.m. compared to those treated between 8 a.m. and 5 p.m. according to selected outcomes

	Low vs high experience of endoscopist		8 a.m.-5 p.m. vs 5 p.m.-8 a.m. time period	OR ⁴ (95%CI)
	OR ¹ (95%CI)	OR ² (95%CI)		
Rebleeding				
Yes	4.47	1.33	0.94	1.40
No	(2.11-9.47)	(0.46-3.83)	(0.38-2.30)	(0.51-3.83)
Number of blood units transfused after endoscopy				
≥ 3	6.90	5.07	0.89	0.92
< 3	(2.80-16.98)	(1.89-13.61)	(0.31-2.56)	(0.32-2.70)
Need for surgery				
Yes	2.36	1.67	1.85	1.99
No	(0.74-7.50)	(0.43-6.41)	(0.54-6.37)	(0.56-7.04)
Mortality				
Dead	0.47	0.64	1.96	1.92
Alive	(0.17-1.34)	(0.20-2.11)	(0.80-4.78)	(0.79-4.69)
Length of hospital stay				
≥ 13 d	0.88	1.66	1.51	0.52
< 13 d	(0.51-1.53)	(0.85-3.28)	(0.84-2.72)	(0.27-1.01)

¹Estimates from multiple logistic regression after adjustment for age, sex, Rockall and Forrest score, blood transfusion, and time period. Reference category is highly experienced endoscopists. ²As in 1 after further adjustment for appropriateness. Reference category is highly experienced endoscopists. ³Estimates from multiple logistic regression after adjustment for age, sex, Rockall and Forrest score, blood transfusion, and experience of endoscopists. Reference category is 5 p.m.-8 a.m. ⁴As in 3 after further adjustment for appropriateness. Reference category is 5 p.m.-8 a.m.

whereas no significant association was found between inappropriateness and need of transfusion after endoscopy (OR = 2.98), need of surgery (OR = 2.62), mortality (OR = 0.47), and length of hospital stay (OR = 0.60). The latter findings showed that appropriateness of endoscopic therapy rather than the endoscopist experience was the main variable associated with rebleeding. Of course,

the lower the endoscopist's experience, the higher the inappropriateness in hemostatic maneuvers. Again, the two time periods of endoscopy were not associated with any of the variables evaluated.

When considering subjects with lesions 2A and 2B of the Forrest's classification, we found a stronger association between low endoscopist's experience and rebleeding, the

Table 5 OR and corresponding 95%CI for patients cured with inappropriate and appropriate treatment according to selected outcomes

	Treatment used		OR ¹ (95%CI)
	Appropriate n (%)	Inappropriate n (%)	
Rebleeding			
Yes	27 (52.9)	24 (47.1)	43.49
No	216 (97.7)	5 (2.3)	(11.29-167.60)
Number of blood units transfused after endoscopy			
≥3	21 (72.4)	8 (27.6)	2.98
<3	222 (91.4)	21 (8.6)	(0.82-10.78)
Need for surgery			
Yes	11 (73.3)	4 (26.7)	2.62
No	232 (90.3)	25 (9.7)	(0.46-14.94)
Mortality			
Dead	33 (91.7)	3 (8.3)	0.47
Alive	210 (88.9)	26 (11.0)	(0.10-2.25)
Length of hospital stay			
≥13 d	125 (88.7)	16 (11.4)	0.60
<13 d	118 (90.1)	13 (9.9)	(0.24-1.54)

¹Estimates from multiple logistic regression after adjustment for age, sex, Rockall and Forrest score, blood transfusion, time period, and experience of endoscopists. Reference category is appropriate endoscopic treatment.

multivariate OR being 9.82 (95%CI: 2.62-36.89).

Finally, there was a trend towards more adrenaline injected and a significant difference in the number of heater probe pulses used by endoscopists with high and low experience, respectively. The mean adrenaline injected was 9.4 and 8.6 mL, whereas the median number of heater probe pulses was 7 (range 0-15) *vs* 4 (range 0-10) for high- and low-experienced endoscopists, respectively.

DISCUSSION

Over the past two decades, advances have been made in the management of non-variceal AUGB^[5]. Various endoscopic single-modality treatments including epinephrine injection, thermal therapy (heater probe, electrocoagulation, laser, etc.) and their combination are efficacious in achieving hemostasis in clinical trials^[7]. These endoscopic procedures can control active bleeding in 85-90% of patients with a significant decrease in the rate of recurrent bleeding and need for surgery^[6,7,25]. Therefore, the management decision for preventing recurrent bleeding is a rapid endoscopic diagnosis with adequate hemostasis. Recent data demonstrate that the best predictor of recurrent bleeding is the endoscopic finding of ulcer since the presence of a visible vessel or sentinel clot in the ulcer base indicates a high likelihood of rebleeding (43% and 22%, respectively), whereas ulcers with a clean base have a recurrent bleeding risk that is negligible^[25]. The above rebleeding rates can be lowered by 60-80% by the application of aggressive endoscopic therapeutic modalities (such as a combined injection/thermal therapy^[26]). However, one should keep in mind that these results are obtained in centers of

excellence, often known internationally for their expertise in the treatment of peptic ulcer bleeding. Whether the aforementioned results are reproducible in centers with less endoscopic expertise is currently a matter of debate^[15].

The influence of endoscopy time on the outcome of patients with non-variceal AUGB remains a subject of debate as very few studies have addressed the question so far. Adler *et al*^[17] showed that complications are significantly more frequent after emergency endoscopy between 7 p.m. and 11 p.m. as compared to regular working hours, which may be due to the fact that during non-working hours endoscopy is performed by more fatigued personnel. Choudari *et al*^[16] and Ramage *et al*^[18] found that there is no difference in the outcome of patients with non-variceal AUGB who had undergone endoscopy during working or non-working hours and weekdays *vs* weekends, respectively.

The present survey aimed at evaluating the impact of these two single factors (endoscopist's experience and time of endoscopy) on the outcome of patients with non-variceal AUGB presenting at a single large tertiary referral center. We did not include in our study inpatient referrals in order to deal with similar patients and to reduce as much as possible the severe comorbidities usually present in patients during their hospital stay. upper GI haemorrhage while hospitalized for another reason (so-called secondary bleeding) has been associated with an increased risk of rebleeding and death^[26].

Findings from our study showed that the endoscopist's experience was an important independent prognostic factor for the outcome of non-variceal AUGB. Indeed, less experienced surgeon resulted in a significantly higher recurrent bleeding rate and transfusion requirement than highly experienced endoscopists, whereas mortality was not influenced probably due to comorbidities.

We found a direct significant association between low experience endoscopists and risk of rebleeding (multivariate OR = 4.47). After a further adjustment for appropriateness, the association disappeared (OR = 1.33), suggesting that if surgeons with lower experience have a rate of appropriateness of treatment similar to that of high experience endoscopists, we could not obtain any significant difference in terms of rebleeding rate between low and high experience endoscopists.

Moreover, the recurrent bleeding of F2A and F2B ulcers was significantly higher among the less experienced endoscopists as compared to the rate of highly skilled surgeons as well as the value reported in the literature^[27]. The evaluation of appropriateness of endoscopic therapy by the two consultants who blindly examined the endoscopic reports might help understand the discrepancy. Planned guidelines of hemostasis were not followed entirely by less experienced staff in 36% of cases, particularly in patients with F2B ulcers, where the most frequent protocol violation was the non removal of an adherent clot. The fear of removing an apparently stable clot adherent to the ulcer base as well as the hypothetical difficulties in managing the subsequent hemorrhage under unfavorable circumstances (i.e, without any supervision) is the most frequently reported explanation by the youngest

endoscopists to justify guideline violations. Independently by the experience of endoscopists, fewer protocol violations have been done for patients with lesions classified as both F1A, F1B, and F2C, which might explain at least in part the lower rebleeding rate in these subjects (13.8% and 7.2%, respectively) as compared to those classified as F2A and F2B (40.2%).

Our findings also add some useful information to a still intricate problem that is the optimum treatment for ulcers with no hemorrhage at the time of endoscopy but present with the stigmata of hemorrhage. While there is no doubt that ulcers with actively bleeding vessels are treated immediately with injection and thermocoagulation by both highly experienced and less expert endoscopists, is the management strategy for intermediate findings (Forrest IIa & IIb) which remains less certain, especially when considering the great benefit of acid suppression in this group^[28]. If aggressive endoscopic therapy (clot removal + epinephrine injection and thermal therapy) is superior to non endoscopic intervention in patients with adherent clots receiving oral PPI^[29], profound in acid suppression without clot removal is more effective than endoscopic intervention alone^[30]. A supplemental jog to this matter was provided by our current survey during which all bleeding patients received the same PPI scheme after endoscopy. We adjusted the paradigm to study the value of high dose in PPI alone over endoscopic therapy + of PPI in F2A and 2B ulcers, showing that combination of appropriate endoscopic therapy with profound acid suppression is better than PPI alone (or PPI plus endoscopic under treatment)^[31].

As far as the time of endoscopy is concerned, our findings suggest that emergency endoscopy out of working hours is as safe and effective as endoscopy performed during working hours provided that it is done under optimal conditions as during working hours. The success of procedures out of hours in this study may be related to the existence of a specific bleeding team composed of the endoscopist and two well-trained specialized nurses. It is conceivable that the same results cannot be obtained in other institutions with less endoscopic facilities and untrained assistants (i.e. non-specialized nurses), where examinations may perhaps be delayed by a few hours in order to perform endoscopy more safely during working hours.

In conclusion, endoscopist's experience is an important independent predicting variable for the outcome of non-variceal AUGB, whereas time of endoscopy (working *vs* non working hours) does not make any difference in terms of patients' prognosis. Urgent endoscopy for AUGB should be undertaken by experienced endoscopists because less experienced staff may not achieve hemostasis.

REFERENCES

- 1 **Non-variceal upper gastrointestinal haemorrhage: guidelines.** *Gut* 2002; 51 Suppl 4: iv1-iv6
- 2 **Longstreth GF Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study.** *Am J Gastroenterol* 1995; 90: 206-210
- 3 **Sacks HS,** Chalmers TC, Blum AL, Berrier J, Pagano D. Endoscopic hemostasis. An effective therapy for bleeding peptic ulcers. *JAMA* 1990; 264: 494-499
- 4 **Sanderson JD,** Taylor RF, Pugh S, Vicary FR. Specialized gastrointestinal units for the management of upper gastrointestinal haemorrhage. *Postgrad Med J* 1990; 66: 654-656
- 5 **Cook DJ,** Guyatt GH, Salena BJ, Laine LA. Endoscopic therapy for acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. *Gastroenterology* 1992; 102: 139-148
- 6 **Adler DG,** Leighton JA, Davila RE, Hirota WK, Jacobson BC, Qureshi WA, Rajan E, Zuckerman MJ, Fanelli RD, Hambrick RD, Baron T, Faigel DO. ASGE guideline: The role of endoscopy in acute non-variceal upper-GI hemorrhage. *Gastrointest Endosc* 2004; 60: 497-504
- 7 **Rollhauser C,** Fleischer DE. Nonvariceal upper gastrointestinal bleeding: an update. *Endoscopy* 1997; 29: 91-105
- 8 **Rockall TA,** Logan RF, Devlin HB, Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering Committee and members of the National Audit of Acute Upper Gastrointestinal Haemorrhage. *BMJ* 1995; 311: 222-226
- 9 **Skok P.** Does endoscopic hemostasis effect the reduction of mortality in patients with hemorrhage from the digestive tract? *Hepatogastroenterology* 1998; 45: 123-127
- 10 **Bullet E,** Calvet X, Campo R, Rue M, Catot L, Donoso L. Factors predicting failure of endoscopic injection therapy in bleeding duodenal ulcer. *Gastrointest Endosc* 1996; 43: 111-116
- 11 **Bullet E,** Campo R, Calvet X, Coroleu D, Rivero E, Simó Deu J. Factors related to the failure of endoscopic injection therapy for bleeding gastric ulcer. *Gut* 1996; 39: 155-158
- 12 **Saeed ZA,** Ramirez FC, Hepps KS, Cole RA, Graham DY. Prospective validation of the Baylor bleeding score for predicting the likelihood of rebleeding after endoscopic hemostasis of peptic ulcers. *Gastrointest Endosc* 1995; 41: 561-565
- 13 **Saeed ZA,** Ramirez FC, Hepps KS, Cole RA, Graham DY. Prospective validation of the Baylor bleeding score for predicting the likelihood of rebleeding after endoscopic hemostasis of peptic ulcers. *Gastrointest Endosc* 1995; 41: 561-565
- 14 **Forrest JA,** Finlayson ND, Shearman DJ. Endoscopy in gastrointestinal bleeding. *Lancet* 1974; 2: 394-397
- 15 **Rollhauser C,** Fleischer DE. Current status of endoscopic therapy for ulcer bleeding. *Baillieres Best Pract Res Clin Gastroenterol* 2000; 14: 391-410
- 16 **Choudari CP,** Rajgopal C, Elton RA, Palmer KR. Failures of endoscopic therapy for bleeding peptic ulcer: an analysis of risk factors. *Am J Gastroenterol* 1994; 89: 1968-1972
- 17 **Adler DG,** Adler AL, Nolte T, Hermans J, Gostout CJ, Baron TH. Complications of urgent and emergency endoscopy in patients with GI bleeding as a function of time. *Am J Gastroenterol* 2001; 96: 3452-3454
- 18 **Ramage J,** Harewood G, Gostout C. Effect of a dedicated GI bleed team on emergent upper endoscopy outcome: weekday versus weekend. *Gastrointest Endosc* 2003; 57: AB148
- 19 **Bjorkman DJ,** Zaman A, Fennerty MB, Lieberman D, Disario JA, Guest-Warnick G. Urgent vs. elective endoscopy for acute non-variceal upper-GI bleeding: an effectiveness study. *Gastrointest Endosc* 2004; 60: 1-8
- 20 **Laine L,** Cohen H, Brodhead J, Cantor D, Garcia F, Mosquera M. Prospective evaluation of immediate versus delayed refeeding and prognostic value of endoscopy in patients with upper gastrointestinal hemorrhage. *Gastroenterology* 1992; 102: 314-316
- 21 **Rockall TA,** Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. *Gut* 1996; 38: 316-321
- 22 **Fullarton GM,** Birnie GG, Macdonald A, Murray WR. Controlled trial of heater probe treatment in bleeding peptic ulcers. *Br J Surg* 1989; 76: 541-544
- 23 **Lau JY,** Sung JJ, Lee KK, Yung MY, Wong SK, Wu JC, Chan FK, Ng EK, You JH, Lee CW, Chan AC, Chung SC. Effect of intravenous omeprazole on recurrent bleeding after endoscopic

- treatment of bleeding peptic ulcers. *N Engl J Med* 2000; **343**: 310-316
- 24 Breslow NE, Day NE. Statistical methods in cancer research. Volume I - The analysis of case-control studies. *IARC Sci Publ* 1980; 5-338
- 25 Laine L, Peterson WL. Bleeding peptic ulcer. *N Engl J Med* 1994; **331**: 717-727
- 26 Lau JY, Sung JJ, Lam YH, Chan AC, Ng EK, Lee DW, Chan FK, Suen RC, Chung SC. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. *N Engl J Med* 1999; **340**: 751-756
- 27 Das A, Wong RC. Prediction of outcome of acute GI hemorrhage: a review of risk scores and predictive models. *Gastrointest Endosc* 2004; **60**: 85-93
- 28 Khuroo MS, Yattoo GN, Javid G, Khan BA, Shah AA, Gulzar GM, Sodi JS. A comparison of omeprazole and placebo for bleeding peptic ulcer. *N Engl J Med* 1997; **336**: 1054-1058
- 29 Bleau BL, Gostout MJ, Shaw RF. Final results : rebleeding from peptic ulcers associated with adherent clots : a prospective randomized controlled study comparing endoscopic therapy with medical therapy. *Gastrointest Endosc* 1997; **45**: AB87
- 30 Jensen DM, Kovacs T, Jutabha GM. Final results and cost assessment of endoscopic vs medical therapies for prevention of recurrent ulcer hemorrhage from adherent clots in a randomized controlled trial. *Gastrointest Endosc* 1995; **41**: AB365
- 31 Sung JJ, Chan FK, Lau JY, Yung MY, Leung WK, Wu JC, Ng EK, Chung SC. The effect of endoscopic therapy in patients receiving omeprazole for bleeding ulcers with nonbleeding visible vessels or adherent clots: a randomized comparison. *Ann Intern Med* 2003; **139**: 237-243

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