Clinical presentations and outcomes of patients with non-variceal upper gastrointestinal bleeding requiring endoscopic therapy

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Abstract

Gastrointestinal bleeding is a common medical emergency that requires urgent endoscopy and treatment. Rebleeding is an important complication that can lead to death. Scoring systems such as the Rockall score and Forrest endoscopic criteria can predict rebleed and poor outcomes. We investigated the clinical presentation and outcome of patients with non-variceal upper gastrointestinal (GI) bleeding who required endoscopic therapy. Patients presenting with non variceal upper GI bleed over a one year period (Jan to Dec 2004) were identified from the endoscopy register and retrospectively reviewed. There were 61 patients (male 77%) with a mean age of 54.6 years (range 3-92). The commonest presentation was with melena (77%). 49.2% were on medications associated with increased risk for GI bleed and 46% had significant comorbid illnesses. Peptic ulcer was the most common cause of bleeding (78.7%). The prevalence of *Helicobacter pylori* was 31%. Blood transfusion was required in 44 patients (72.1%) with a mean requirement of 3.3 units per patient (range 0-21). Rebleeding occurred in 25% and 3.3% were referred for surgery. The overall mortality was 18%. However, majority died from other significant illnesses. Two deaths (3.3%) occurred as result of bleeding. Older age ($p < 0.05$), higher admission INR ($p < 0.05$), longer hospital stay ($p < 0.05$) and higher blood transfusion requirements ($p < 0.05$) were predictive of mortality. The Rockall score correlated with rebleed and death but not the Forrest endoscopic criteria. In conclusion, ulcer disease account for the major proportion of non-variceal upper GI bleed and half of these patients were taking medications associated with increased risk for bleeding. Certain factors are predictive of mortality.

Introduction

Upper gastrointestinal (GI) bleed is defined as GI blood loss proximal to the ligament of Treitz. [1] It may be variceal or non-variceal. Acute non-variceal upper GI bleed is a common emergency with a reported incidence of 50-100 cases/100,000 population/year [2, 3] and a mortality of 5-14% [3, 4] Peptic ulcer is the most common cause of acute non-variceal upper GI bleed [4] Over the past three decades there have been advances in the management of this condition. Endoscopy has become an important tool and has changed from a purely diagnostic procedure to a first line therapeutic tool in the management of GI bleeding. In additions, prognostic scores such as the endoscopic Forrest criteria and Rockall score [5, 6] have been developed to predict risk of rebleed and poor outcomes. This study aimed to evaluate the clinical, endoscopic features and outcome of our patients in Brunei Darussalam undergoing endoscopic therapy for non-variceal upper GI bleeding

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Methods

All patients admitted with suspected upper GI bleeding had full blood count, urea and electrolytes, clotting and cross match done. Liver function test was done if underlying liver disease was suspected. All patients were assessed for severity of blood loss and resuscitated with volume expander. Patients were monitored closely and kept nil per orally until bleeding settled. They were given acid suppression with either omeprazole or ranitidine. Patients who developed GI bleeding as in-patient were routinely referred to the gastroenterologist on duty. Decision for either urgent or elective endoscopy depends on the time of admission or referral. Generally, cases referred during office hours have their endoscopy done during the same day. Otherwise, patients have their endoscopy in the next available endoscopy list.

There are five endoscopists working in the unit during the period of the study, consisting of three specialists and two senior medical officers. Overall four endoscopists had experience with over 1,000 procedures and one trainee with less than 1,000 procedures carrying out procedures under supervision. Treatment modalities available for treatment of bleeding lesions included; i) adrenaline injection mono-therapy (1 mg in 1/10,000 dilution with water); b) heater probe coagulation mono-therapy; c) combination of adrenaline and heater probe coagulation; d) haemoclip. Treatment modalities used were at the discretion of the endoscopists.

Rebleeding was defined as new onset of hematemesis, coffee ground vomitus, malena and drop in hemoglobin level of 2 or more grams after a successful initial endoscopic treatment over the next 48 to 72 hours. Failure of treatment is defined as failed endoscopic therapy to achieve haemostasis or ongoing evidence of blood loss with 24 hours of first endoscopy. Repeat endoscopies with further attempt at achieving haemostasis were often carried out before considering alternative interventions. The modalities available for repeat endoscopic therapies were the same as the index endoscopy. Decisions for surgical intervention were made if there was failure to achieve haemostasis at the index endoscopy or if there was rebleed after two previous endoscopic interventions.

Patients with non-variceal upper GI bleed requiring endoscopic therapy over a one year period (Jan-Dec 2004) were identified from the endoscopy register. Their charts were reviewed retrospectively. Clinical data, endoscopic findings, laboratory data & outcome measures (blood transfusion requirements, rebleed, surgery and death) were retrieved and coded in preset proforma. The endoscopic findings for the bleeding lesions were extracted from the endoscopic record and the Forrest grade and Rockall scores of patients were assigned as per criteria given in Tables 1 and 2. The data was entered into the SPSS program (SPSS, Version 10.0, Chicago, IL, USA) for analysis. The Mann-Whitney U test was used for continuous variables and the Fischer's Exact or Chi-squared tests were used for categorical variables. Significance was taken when $p < 0.05$.

Table 1: Forrest classification of bleeding peptic ulcers

Results

Forrest classification	Endoscopic findings
1a	Spurting
1b	Oozing
2a	Non-bleeding vessel
2b	Ulcer with surface clot
2c	Ulcer with haematenic spot at base (Red spot, blue or black spot)
3	Ulcer with clean base

Risk of rebleed: 100%, 50% and <3% (for types 1a, 2a & 3 ulcers respectively) [1]
Risk of death: 11%, 11% and 2% (for types1a, 2a & 3 ulcers respectively) [7]

Table 2: Rockall risk scoring system [6]

Variables	0	1	2	3
Age (yrs)	< 60	60 to 80	> 80	
Shock	Systolic BP >100 mmHg Pulse rate <100 No Major comorbidity	SBP > 100 mmHg Pulse rate > 100	SBP < 100 mmHg Pulse rate > 100	Renal failure Liver disease Disseminated malignancy
Co morbidity			Cardiac failure Ischemic heart disease Any major co-morbidity	
Diagnosis	Mallory-weiss tear No lesion identified No SRH*	All other diagnosis	Malignancy of upper gastrointestinal tract	
Major SRH	None Dark spot sign		Blood in upper GI tract Adherent clot Visible or spurting vessel	

SRH: Stigmata of recent haemorrhage
Risk of rebleed: 5% (if score is ≤2) and 40% (if score ≥ 8)
Risk of death: <1% (if score is ≤2) and 41% (if score ≥ 8)

RESULTS

There were a total of 61 patients identified and their demographic is shown in Table 3. Forty one patients (67.2%) presented with GI bleed and in the remainder (32.8%) bleed occurred when hospitalized for other illnesses. The most common presentation was malena (77%) followed by haemetemesis (47.5% - fresh blood 26.2% and coffee ground 21.3%). Haemotochezia occurred in 6.6%. 37.7% presented with various combinations of the above symptoms. Bleeding following endoscopic procedures occurred in 8.2%. Fifty-eight patients (95.1%) received medical treatment in addition to endoscopic treatment. Omeprazole was used intravenously in 49 (80.3%) patients and orally in 7 (11.5%). Two patients (3.3%) were treated with intravenous ranitidine.

Table 3: Patients demographic, co-morbidities and medications used

Mean age (yrs)	54.6 (range, 3-92)
Genders (male / female)	47 (77%)/ 14 (23%)
Race	
Malay	47 (77%)
Chinese	5 (8.2%)
Indigenous	6 (9.8%)
Others	3 (4.9%)
Co morbidities	
Renal disease	12 (19.7%)
Gastrointestinal disease	12 (19.7%)
Cardiovascular disease	12 (19.7%)
Malignancy	4 (6.6%)
Cerebrovascular disease	3 (4.9%)
Respiratory	6 (9.8%)
Medications associated with GI bleeding	30 (49.2%)
NSAIDs	14 (23%)
Aspirin	13 (21.3%)
Clopidogrel	9 (14.8%)
Warfarin	3 (5%)
Heparin	2 (3.3%)
History of dyspepsia	25 (41%)
History of previous upper GI bleeds	21 (34.4%)

NSAIDs: non-steroidal anti-inflammatory drugs
GI: gastrointestinal

Endoscopy was carried out as emergency procedure (≤ 24 hrs) in 16 patients (26.2%) and as elective procedure (> 24 hrs) in the remaining 45 (73.8%).Endoscopy was carried out as emergency procedure (≤ 24 hrs) in 42 patients (85.7%) and as elective procedure (> 24 hrs) in the remaining 7 (14.3%). Findings at endoscopy are shown in Table 4. All patients were treated with submucosal adrenaline injection. Heater probe coagulation was used in 15 patients (25%) in addition to the adrenaline injection. *H. pylori* was tested in 29 patients (47.5%) and was positive in 9, giving a prevalence of 31%. The mean duration of hospital stay was 13.8 days (range 1-92).

Table 4: Causes of GI bleed at endoscopy

Findings	n (%)
Oesophagus	
Oesophageal ulcer	2 (3.3)
Mallory Weiss tear	1 (1.6)
Stomach	
Gastric ulcers (GU)	18 (29.5)
Malignancy	2 (3.3)
Haemorrhagic gastritis	2 (3.3)
Post procedure bleeding	
Biopsy	2 (3.3)
Polypectomy	2 (3.3)
Duodenum	
Duodenal ulcers (DU)	30 (49.2)
Malignancy	1 (1.6)
Post sphincterotomy	1 (1.6)

Multiple GUs: 5(8.2%); Multiple DUs: 4(6.6%); Combined GU and DU: 5(8.2%)

Outcome measures are summarized in Table 5. Forty-four patients (72.1%) needed blood transfusion. The bulk of the patients who rebled were old (age ≥ 60 - 86.7%) and had significant comorbidities (93.3%). Rebleed occurred early in 46.7% of patients (within 24 hrs in 20% and between 24 to 72 hrs in 26.7%) and was delayed beyond 72 hours in the remainder. Nine (60%) patients' rebleeding settled, five spontaneously and four after a second endoscopic therapy session. The overall mortality rate was 18% (n = 11). Eight of the patients who had rebleeding died giving mortality among rebleeders of 53.3%. However, in 7 of the 11 patients who died in this series, GI bleed had already settled and the patients died as results of severe underlying illness. In the remaining 4 patients, there was evidence of

on going bleeding; metastatic gastric carcinoma (n = 1), carcinoma of the gallbladder with biliary/systemic sepsis (n = 1), proximal oesophageal ulcer/hepatobiliary tuberculosis and polyarthritis/PUD (n = 1). Both patients with malignancies were at terminal stages. When deaths due to severe underlying illnesses and malignancies were excluded, there were only two deaths (3.3%) directly attributable to bleeding. One patient had an oesophageal ulcer that was believed to be an aortoesophageal fistula. The other patients had significant com morbid conditions. Older age ($p < 0.05$), higher admission INR ($p < 0.05$), longer hospital stay ($p < 0.05$) & higher blood transfusion requirements ($p < 0.05$) were predictors of mortality.

Table 5: Outcome measures

Mean blood transfusion requirement (range 0-21)	3.3 units
Incidence of rebleeding	15 (24.6%)
Number referred for surgery	2 (3.3%)
Overall mortality	11 (18%)

The Rockall score (Fig. 1) correlated with risk of rebleed and mortality ($p < 0.05$). However, there was no correlation with the Forrest grade [Fig. 2: risk of rebleed ($p = 0.59$) and mortality ($p = 0.83$)].

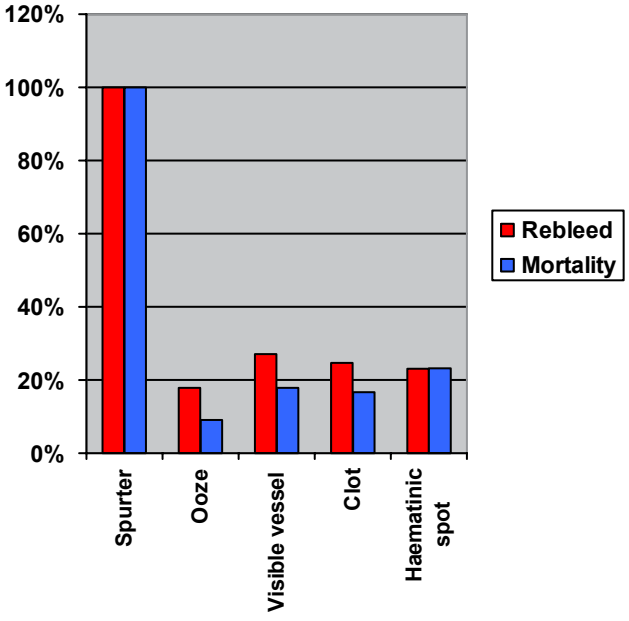

Figure 1: Correlation of the Forrest grade with rebleed and mortality

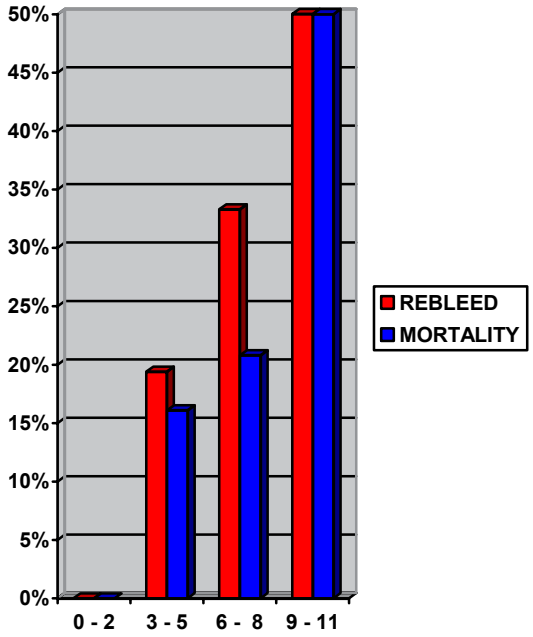

Figure 2: Correlation of the Rockall score with rebleeding and mortality.

Discussion

Our study shows that patients undergoing endoscopic therapy for non-variceal upper GI bleeding were elderly, predominantly male with malena as their most common presenting symptom. They have a high prevalence of co-morbid illnesses and a large proportion were taking medications associated with increased risk for bleeding. This is consistent with published findings reporting older age and male gender to be at higher risk. [3, 8] However, our patients were slightly younger with a mean age of 54.6 years compared to 66 years reported in the West. [9] Male preponderance in our series is higher than corresponding figures from the West [9] (M: F ratio of 3:1 vs. 1.6:1). Medications especially non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin are well known risk factors for the development of peptic ulcer and bleeding. [10, 11] Nearly 44% of patients in our series were on either aspirin or NSAIDs which could have contributed to ulcer formation and bleeding in this group. Up to a third of our patients had history of upper GI bleed and this may be accounted by the higher prevalence of use of medications associated with risk of bleeding. As reported in other studies, peptic ulcer was the most common cause of bleeding in our series. [4, 12]

It is interesting to note that there were five patients (8.2%) with endoscopic procedure related bleeding that required endoscopic therapy in our study. Two were post polypectomy, two post biopsy and one post sphincterotomy bleed after endoscopic retrograde cholangiopancreatograpy. Bleeding post sphincterotomy and polypectomy are well recognized complications with prevalence of 1-2% and 5-6% respectively. [13, 14] Biopsy related bleeding is less common but have also been reported. [14] This probably reflects the growing role of endoscopy in management of various GI illnesses. Most of our patients had endoscopy within 24 hours of admission. There were some delay with the remaining patients for reasons that included; late referral, delay in patients or family giving consent for endoscopy or admission over weekend with patients being hemodynamically stable.

H. pylori is an important association with PUD. In our series, only 47.5% of patients were tested for *H. pylori* and approximately a third tested were positive. Despite lower than expected, this is still higher than the overall prevalence of *H. pylori* among patients referred for endoscopy in our local setting (25%). [16] The low number of patients tested is due to the fact that in the setting of GI bleeding the main goal of endoscopy is to control bleeding. Callicutt *et al.* reported that only 2 out of their 42 patients had assessment for *H. pylori* prior to undergoing surgery for acute non-variceal upper GI bleeding although all of them had upper GI endoscopy. [17] Prevalence of *H. pylori* in their series was 68.7% for duodenal ulcer and 39.1% for gastric ulcer. Prevalence was reduced in those over 60 years of age (28.6%). In our study, *H. pylori* was assessed mainly by rapid urease test. Our previous finding showed that rapid urease test has a low sensitivity (57.1%) when compared to histology. [18] Therefore, the prevalence rate may be higher if histology was used instead of rapid urease test. More diligent testing for *H. pylori* will increase the detection and subsequent eradication rate and hence the risk of rebleeding.

Mean blood transfusion requirement in our series (3.3 units) was slightly higher than that reported by Barkun *et. al* (2.9 units). [4] The rebleeding rate in our study was 24.6%. This is in agreement with other studies which reported rebleeding rates varying from 14.1% to 36%. [4, 19] Our surgical referral rate (3.3%) was comparable to other studies (4.5 to 6.5%). [2, 4] The low surgical referral rate is probably due to the increasingly successful use of endoscopy as a first line tool in the management of this condition. The overall mortality in our study was 18%. This is higher than the 5-14% reported in literature. [3, 9] However, majority of our patients who died had significant illnesses and did not have bleeding as cause of death. This is in agreement with a study done in Singapore. Most of patients who died were due to worsening of co morbid conditions and none of the patients who had rebleed died. [20] Only two deaths (3.3%) were directly attributable to bleeding. These two patients also had significant co illness and had evidence of on going blood loss when these patients died. Older age, higher admission INR, longer hospital stay and higher blood transfusion requirements were predictive of mortality in our series. This is also comparable to published data. [1]

In our study, the Forrest Criteria did not correlate with either rebleeding rates or mortality. However, the Rockall scores showed good correlations. Forrest Criteria is widely accepted to be predictive of rebleed based on the endoscopic findings. The discrepancy of the Forrest Criteria in our study is probably due to the overall small number of patients in our study. In fact, there was only one patient with Forrest type 1a ulcer. This patient had a poor outcome. Moreover our study is a retrospective and factors like inter-observer disagreement on Forrest classification [21], endoscopic technique used to treat different Forrest class ulcers [22] were not controlled for and these could account for the observed discrepancy. However in our unit, the endoscopic findings were routinely recorded down with any assignment of any criteria. The Forrest criteria were retrospectively assigned based on the most advanced lesions recorded. In contrast, the Rockall score correlated well with outcome of patients as assessed both in terms of rebleed and mortality rates. The risk of rebleed and death increased as the scores increased. Rockall *et al*. in their original study [6] had suggested that patients with a low score could be candidates for early discharge with considerable savings to the health care system. Our study is in agreement with theirs. Patients with Rockall score of equal or less than 2 had no rebleed and mortality rates in our study could possibly be considered for early discharge.

There are few limitations with our study. Firstly, this is a retrospective study and this is inherently associated with limitations such as incomplete data and lack of essential data. Secondly, the sample size is small and results obtained may not be very accurate. Thirdly, the reporting and the criteria for choosing the type of endoscopic treatment were not standardized and depended on the individual endoscopists. However, almost all endoscopists are experienced and have been involved with therapeutic works. The modalities available in our centre are standard and comparable what is commonly used in many endoscopic centers, internationally and regionally. [12] Overall, our results are comparable to published reports.

In conclusion, the findings in our study are generally in agreement with that reported in literature with some exceptions as discussed above. Ulcer disease accounted for the major proportion of non-variceal upper GI bleed. Importantly, almost half of our patients were taking medications associated with increased risk for bleeding. Certain factors are predictive of mortality. Despite the small sample size, our study provides useful information on clinical and endoscopic features and outcomes of patients undergoing endoscopic therapy in our local setting. These findings however need to be validated by bigger sample in a prospective study. In the meantime the findings reported could serve as a benchmark for audit purposes in future.

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