ORIGINAL ARTICLE

Clinical Profile and Outcome of Non-Variceal Upper Gastrointestinal Bleeding in Relation to Timing of Endoscopic Procedure in Patients Undergoing Elective Endoscopy

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ABSTRACT

Background: *Endoscopy is the most accurate method for diagnosing the source of upper gastrointestinal bleeding.This study was aimed to evaluate the correlation between the timing of elective endoscopy and the length of hospital stay, the amount of transfusion given and incidence of recurrent bleeding or patient mortality.*

Method: *A retrospective study was conducted in all patients with non-variceal upper gastrointestinal bleeding who had experienced elective endoscopy at Cipto Mangunkusumo Hospital between January 2007 and August 2008. Identification of clinical risk using clinical Rockall score was performed at the emergency room. Persistent bleeding, recurrent bleeding, surgical treatment and death were the outcome variables. Statistical analysis was performed using Chi-square/fisher exact test and linear regression.*

Results: *There were 40 eligible cases with mean age of 53 ± 13 years; the greatest occurrence was at the age group of 50-59 years (12%), male (52.5%) and those who had clinical symptom of melena (52.5%). Twenty seven (67.5%) patients had Rockall score of 1-3 points and 13 (32.5%) had 4-6 points. There was only one patient who had adherent clots (Forrest grade II B). Endoscopy results revealed that the most common cause of bleeding was gastric ulcer, which occurred in 12 (30%) patients. There was no correlation between the timing of endoscopic procedures and outcome variable; however the length of hospital stay had a significant correlation with timing of endoscopic procedures.*

Conclusion: *Elective endoscopy does not affect the variables of mortality and recurrent bleeding; however, it affects the length of hospital stay. Further prospective studies are required to find causal relation between them.*

Keywords: non-variceal upper gastrointestinal bleeding, Rockall score, elective endoscopy, outcome variables

ABSTRAK

Latar Belakang*: Endoskopi merupakan metode yang paling akurat dan praktis untuk mendiagnosa sumber perdarahan saluran cerna bagian atas. Tujuan penelitian ini adalah untuk mengevaluasi variabel klinis dan menganalisa hubungan waktu tindakan endoskopi elektif yang dilakukan dengan lama hari perawatan, jumlah transfusi darah yang diberikan serta kejadian pendarahan berulang atau kematian pada pasien.*

Metode*: Studi retrospektif terhadap semua pasien dengan perdarahan saluran cerna bagian atas non varises dilakukan dari bulan Januari 2007 hingga Agustus 2008 di Rumah Sakit Cipto Mangunkusumo yang dilakukan endoskopi elektif. Penilaian risiko klinis dengan skor klinis Rockall dilakukan di ruang gawat darurat. Perdarahan persisten, perdarahan rekuren, adanya tindakan pembedahan dan kematian dikelompokkan sebagai variabel outcome. Analisis data dilakukan dengan uji kai kuadrat atau fisher exact dan uji regresi linear.*

Hasil: *Terdapat 40 kasus yang memenuhi kriteria, dengan rerata umur 53 ± 13 tahun, frekuensi terbanyak pada kelompok umur 50-59 tahun (12%), laki-laki (52,5%) dan gejala klinis melena 52.5%. Penyakit penyerta yang tersering adalah penyakit kardiovaskular (27,5%). Dua puluh tujuh (67,5%) pasien memiliki skor Rockall 1-3 poin dan 13 (32,5%) pasien dengan 4-6 poin. Hanya satu pasien dengan forrest grade IIB (adherent clot). Hasil endoskopi penyebab perdarahan yang terbanyak adalah ulkus gaster pada 12 (30%) pasien. Tidak terdapat hubungan antara waktu tindakan endoskopi dengan variabel outcome, hanya lamanya hari perawatan di rumah sakit yang mempunyai hubungan dengan waktu tindakan endoskopi.*

Kesimpulan: *Tindakan endoskopi elektif tidak mempengaruhi variabel kematian dan perdarahan berulang, akan tetapi berpengaruh pada jumlah hari perawatan. Diperlukan studi prospektif lanjutan agar dapat diketahui hubungan sebab akibat.*

Kata kunci: *perdarahan saluran cerna bagian atas non varises, skor Rockall, endoskopi elektif, variabel outcome*

INTRODUCTION

Upper gastrointestinal bleeding cases are commonly found in the emergency department. The published data reveals 5-10% mortality rate. It also indicates that persistent or recurrent bleeding during hospitalization are the most important predictor for adverse outcome.[1-5] The most common cause for non-variceal upper gastrointestinal bleeding is gastroduodenal ulcer.[1-3] Treatment strategies and management for such condition are extremely required to achieve optimal results. The most common evaluations for early risk stratification Rockall score performed during patient admission to the emergency department are the clinical Rockall score and Blatchford risk score.[6-8] Endoscopy is the most accurate and practical method for diagnosing the source of upper gastrointestinal bleeding.[9] However, it is still a controversy whether urgent endoscopy (within < 24 hours) or emergency endoscopy (within the first 12 hours) compared to elective endoscopy that could reduce the mortality rate.[10-14]

Endoscopic stigmata (Forrest stigmata classification) combined with clinical factors such as Rockall score are the strong predictors to evaluate the outcome in patients with non-variceal upper gastrointestinal bleeding.[11,15] Patients who are classified into the high-risk group may undergo urgent endoscopic hemostasis when the facility and experienced experts are available. Some studies reported that the urgent endoscopic hemostasis may reduce recurrent bleeding, the need of surgical treatment, and mortality rate.[11,16] Other randomized retrospective studies have also reported that those classified as being at low-risk could be discharged after endoscopy procedures depending on the timing time of initial endoscopic procedure.[14,17]

The aim of the study was to evaluate clinical, laboratory and endoscopic variables in hospitalized patients with non-variceal upper gastrointestinal bleeding and to analyze the correlation between timing of endoscopic procedure and the length of hospital stay, the transfusion given and mortality or recurrent bleeding.

METHOD

The study was a retrospective study and the analysis was started from the emergency department for all patients who had non-variceal upper gastrointestinal bleeding with complaints of hematemesis, vomiting of coffee-ground like material and melena at Cipto Mangunkusumo Hospital between January 2007 and August 2008. After the patients had been stabilized, an elective or routine endoscopy was performed at the endoscopy unit. The exclusion criteria were patients with upper gastrointestinal bleeding due to other causes other than non-variceal bleeding and patients who had recurrent bleeding due to other causes.

In this study, we recorded some data of clinical variables, age, sex, chief complaints at the admission in the emergency room (vomiting of coffee-ground like material, melena, or hematemesis), comorbidities such as cardiovascular, pulmonary, neurological, hepatological or rheumatological diseases, diabetes mellitus, active neoplasm, renal failure or other illnesses, history of aspirin medication, non-steroid anti inflammatory drugs (NSAID), corticosteroid, herbal medicines, antiplatelet/anticoagulant drugs, as well as measurement of systolic blood pressure (> 100 mmHg or < 100 mmHg), heart rate (100 times/minute) and blood transfusion. We also recorded the laboratory results of hemoglobin, hematocrit, ureum, creatinine levels and prothrombin time. Clinical evaluation of Rockall score was performed when the patients were admitted to the emergency room.

The Rockall score classification was done based on the Forrest classification, i.e. endoscopic procedures were not performed within 24 hours after bleeding; therefore the bleeding stigmata were only low-risk lesions. Principally, Forrest classification may be divided into 3 grades, i.e. grade I: active ulcer bleeding; grade II: non-active ulcer bleeding; grade III: no signs of recent bleeding.

Outcome variables were divided into some conditions: (1) persistent bleeding within the first 48 hours (hematemesis, melena, unstable hemodynamic and decreased hemoglobin/hematocrit levels in spite of the transfusion); (2) recurrent bleeding or relapse during treatment; (3) requiring surgical treatment; (4) death. When one of the abovementioned outcome variables occurred, it was considered as unfavorable event(s). Univariate data analysis was performed using chi-square or fisher exact test. The analysis was continued with linear regression test to recognize the correlation between the timing of endoscopic procedures and the length of hospital stay. Chi-square test was performed to evaluate the correlation between timing of endoscopic procedure and the amount of transfusion that had been administered, death or rebleeding, with $p < 0.005$ was considered as significant.

RESULTS

This retrospective study found 40 cases that had fulfilled the criteria with mean age of 53 ± 13 years and most subjects were at 50-59 years (12%), mostly were male patients, i.e. 21 (52.5%) subjects; while the most common clinical symptom was melena (52.5%). Cardiovascular disease was comorbidity that was the most frequently found (27.5%). Eighteen (45%) patients had regularly consumed traditional herbs. Evaluation on vital signs was performed at the time the patients were admitted to the emergency room. It revealed 3 patients in shock with systolic pressure < 100 mmHg. Ten patients had pulse rate > 100 times/minute. There was one patient with adherent clot (grade II B) according to Forrest classification. In this study, 27 (67.5%) patients had score of 1-3. The characteristics of clinical variables and laboratory results of the patients are presented in Table 1.

The endoscopic results revealed that gastric ulcer was the most common cause of gastrointestinal bleeding, which was found in 12 (30%) patients. Three (7.5%) patients were dead. Two of them had endoscopic results suggesting erosive gastritis in a patient with peritonitis tuberculosis and myoma uteri;

Table 1. Patient characteristics of clinical variables and laboratory results in patients with upper gastrointestinal bleeding

Variable	n (%)/mean ± SD
Number of patients (person)	40 (100)
Age (years)	55.0 ± 13.0
< 40	5 (12.5)
40-49	7 (17.5)
50-59	12 (30.0)
60-69	11 (27.5)
70-79	4 (10.0)
≥ 80	1 (2.5)
Sex	
Male	21 (52.5)
Female	19 (47.5)
Clinical symptoms	
Hematemesis	19 (47.5)
Melena	21 (52.5)
Comorbid diseases	
Coronary heart disease	11 (27.5)
Kidney disease	8 (20.0)
Drugs consumptiom	
Traditional herbs	18 (45.0)
NSAIDs	5 (12.5)
Anticoagulant	1 (2.5)
Steroid	1 (2.5)
Sistolic blood pressure < 100 (mmHg)	3 (7.5)
Pulse > 100 (times/minute)	10 (25.0)
Shock grade	
Without shock	28 (70.0)
Pre-shock	9 (22.5)
Shock	3 (7.5)
Rockall score	
1-3	27 (67.5)
4-6	13 (32.5)
Hemoglobin (g/dL)	7.0 ± 2.7
Hematocryte (g/dL)	21.9 ± 7.9
Ureum (g/dL)	78.0 ± 79.0
Protrombin time	
Normal	35 (87.5)
Abnormal (increase)	4 (10.0)
Timing of endoscopic procedure	9.0 ± 3.0
Amount of blood transfusion (packs)	4.5 ± 3.6
0	3 (7.5)
1-4	20 (50.0)
5-9	13 (32.5)
≥ 10	4 (10.0)
Length of hospital stay (days)	13.0 ± 5.7
Recurrent bleeding	3 (7.5)
Mortality incidence	3 (7.5)

NSAIDs: non steroidal anti inflammatory drugs

while the other patient had liver cirrhosis, pneumonia and acute renal failure. There was a 76-year-old patient whose endoscopic result indicated gastric ulcer and a mass. The endoscopic results that demonstrate non-variceal upper gastrointestinal bleeding are shown in Table 2.

In this study, we found that 18 patients who had undergone > 5-days endoscopic procedure had received 1-4 blood packs during hospitalization and 12 patients who had undergone > 5-days endoscopic procedure

Table 2. Endoscopic features on non-variceal upper gastrointestinal bleeding

| Endoscopy results	n (%)
Erosive gastritis	11 (27.5)
Gastritis	4 (10.0)
Erosive gastroduodenitis	1 (2.5)
Esophagus candidiasis	1 (2.5)
Duodenal ulcer	4 (10.0)
Duodenal ulcer and mass	1 (2.5)
Gastric ulcer	12 (30.0)
Gastric ulcer and mass in antrum	2 (5.0)
Gastroduodenal ulcer	4 (10.0)
Total	**40 (100.0)**

had received 5-9 blood packs during hospitalization. When we compared the data with < 5 days endoscopic procedure, there were less number of patients who had received blood transfusion during hospitalization; however, it was statistically not significant (p = 0.63) (Table 3).

Table 3. The correlation between the amount of blood transfusion and the timing of endoscopic procedure

Timing of endoscopic procedure (days)	Amount of blood transfusion (packs)				*p
	0	1-4	5-9	≥ 10	
1-5	1	2	1	2	0.63
> 5	2	18	12	2	
Total	**3**	**20**	**13**	**4**	

*Linear regression test

Statistically, there was a significant correlation between the timing of endoscopic procedure and the length of hospital stay with p = 0.00 by using linear regression analysis (Figure 1). In contrast, the correlation between the time of endoscopic procedure and the incidence of recurrent bleeding/death was not significant (p = 0.21) (Table 4).
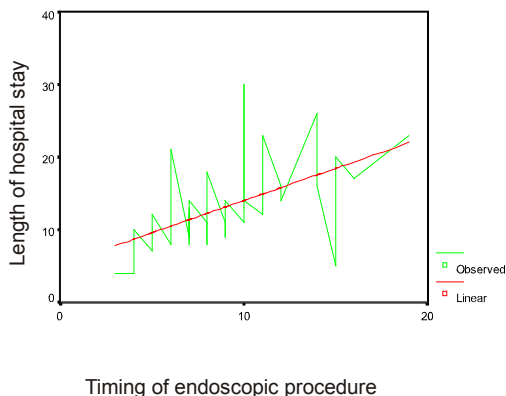
Figure 1. Comparison between the timing of endoscopic procedure and the length of hospital stay

Table 4. Correlation between the timing of endoscopic procedure and the incidence of mortality or recurrent bleeding in the patients

Timing of endoscopic procedure (days)	Outcome		Total	p*
	Alive	Death/ recurrent bleeding		
1-5	4	2	6	
> 5	30	4	34	0.21
Total	**34**	**6**	**40**	

*Chi-square test

DISCUSSION

In this study, patients who had the most frequent upper gastrointestinal bleeding were in 50-69 years age group, the mean ± SD (55 ± 13) and more frequently found in male. The condition was associated with the consumption of analgesics (45% were traditional herbal medicine and 12.5% were NSAIDs). Ohmann et al, reported that the incidence of upper gastrointestinal bleeding due to gastroduodenal ulcer was commonly found, especially in elderly group with approximately 68% were over 60 years and 27% over 80 years.[18] Some studies demonstrated that the increased proportion of upper gastrointestinal bleeding was due to increased consumption of aspirin and NSAID in elderly group.[19] Gisbert et al, found that in addition to the age factor, the use of NSAID and comorbidities are the contributing factors that frequently the leading cause of death for non-variceal upper gastrointestinal bleeding, which was found in 11 patients with comorbidities; moreover, it was more often in male (72%).[6] Parente et al, found that cardiovascular disease (26.8%) was the most commonly found comorbidity.[20] Similar results are also found in this study which demonstrated that cardiovascular disease comorbidity was the most frequently found.

Rockall and Blatchford score are commonly used for initial assessment prior to endoscopic procedure. Early risk stratification combined with therapeutic endoscopy and administration of high-dose intravenous proton pump inhibitors have become the evidence-based optimal approach for non-variceal bleeding (ulcer lesion) of upper gastrointestinal tract. In this study, early risk stratification was performed at the admission to emergency unit and we found 28 (70%) patients without shock, 9 (22.5%) patients in pre-shock condition and 3 (7.5%) patients with shock. Similar condition has also been found in a study conducted by Parente et al revealing 78.3% patients without shock, 12.8% with pre-shock condition and 8.8% experiencing shock.[20] Barkun et al recommended empirical treatment of high-dose pump proton inhibition (PPI) infusion for patients who are waiting

for their endoscopic procedure. However, the treatment could not substitute the role of urgent endoscopy and endoscopic hemostasis.[11]

This study revealed laboratory results of low hemoglobin level with mean value of 7 ± 2.7 mg/dL, hematocrit of $21.9 \pm 7.9\%$. It was much lower compared to the results found in Gisbert et al study, which found mean hemoglobin level of 10 ± 3 mg/dL and mean hematocrit value of $29 \pm 8\%$.[6] The condition may occur since the patients visited the hospital in several days after the bleeding or they had treatment but were not hospitalized and were only admitted to the hospital when there was no improvement. The mean ureum level was increasing to 78 ± 79 mg/dL. The condition is similar to other study result with mean ureum level of 85 ± 44 mg/dL.

The endoscopic evaluation revealed that the most common leading cause of bleeding was gastric ulcer, which occurred in 12 (30%) patients. When it was combined with duodenal ulcer, we found that there were 23 (57.5%) patients with gastroduodenal ulcer. The endoscopic results are similar to data published by Barkun et al, showing that in 50-70% cases, peptic ulcer is the leading cause of non-variceal upper gastrointestinal bleeding.[4]

In this study, early endoscopy was postponed to a time within the first 24 hours after admission to the emergency unit.[11-14] Endoscopic procedure was initiated at the 3rd day and the mean timing of the performed endoscopic procedure was at the 9th ± 3 day. Endoscopic procedure performed in this study was > 72 hours and approximately over 9 days; therefore, the evaluation on endoscopic stigmata according the actual Forrest classification could not be conducted. The endoscopic stigmata found lesions with mild/moderate risk. Endoscopic stigmata (Forrest stigmata classification) or combined with clinical factors such as Rockall or Blatchford score are strong predictors to evaluate the outcome of patients with non-variceal upper gastrointestinal bleeding. Forrest classification of grade 1A (spurting of blood), grade 1B (oozing blood), grade IIA (non-bleeding visible vessel) and grade IIB (adherent clot) indicating high-risk lesions that may cause recurrent bleeding. Low-risk lesions are included as Forrest classification grade IIC (flat, pigmented spot) and grade III (clean-base ulcers).[16] Salztman et al by applying bedside scoring using AIMS65 could measure the mortality rate, length of hospital stay and cost of hospitalization. In their study, there were 5 contributing factors for those measurement including albumin level < 3.0 gr/dl, international normalized ratio (INR) > 1.5,

alteration of mental status, systolic blood pressure 90 mmHg or < 90 mmHg, and age > 65 years. When no risk factor was found, the mortality rate was 0.3% and it was 31.8 % if 5 risk factors were found.[21]

There have been controversies regarding early endoscopic procedure (< 24 hours) on improved outcome variables for patients. A preliminary study, which was a randomized controlled trial by Peterson et al, has demonstrated that early endoscopy has not significantly altered the mortality rate, the incidence of re-bleeding, utilization of blood transfusion and length of hospital stay/cost.[10] Some experts think that it may occur since endoscopic treatment and the knowledge about endoscopic stigmata has not been established. The administered drugs were still antacids combined with histamine-2 receptor antagonists.[22] Marmo et al in their study found that the mortality rate has no effect on endoscopic procedure when the patients had good clinical status; however, if they were high-risk patients at the time of endoscopic procedure (< 12 hours), they will have a very important effect on mortality rate.[13]

A study by Cooper et al, showed that early endoscopy has significantly reduced the incidence of recurrent bleeding, surgical procedures, and the length of hospital stay only in patients who required endoscopic hemostasis procedure.[23] Studies by Lee and Bjorkman et al, demonstrated that urgent endoscopic procedure has not significantly provide different results on patients' outcome (mortality rate, the length of stay in intensive unit and in the ward, as well as the amount of transfusion) compared to elective/routine endoscopy.[14,22]

This evaluation on outcome found that the average length of hospital stay was 13 ± 5.7 days. We found 3 (7.5%) patients with recurrent bleeding with the amount of transfusion > 10 blood packs. Three (7.5%) patients were dead with following endoscopic results: two of them had endoscopic results suggesting erosive gastritis in one patient with peritonitis tuberculosis and myoma uteri as well as in the other patient who had liver cirrhosis, pneumonia and acute renal failure. There was a 76-year-old patient whose endoscopic result indicated gastric ulcer and a mass.

Subsequently, statistic tests were performed in order to recognize any correlation between timing of elective endoscopy procedures (> 3 days) and the length of hospital stay, the incidence of death and the amount of transfusion given. In this study, we found that there is a significant correlation between the timing of endoscopic procedure with the length of hospital stay with p = 0.00. Such condition may occur

since there were longer endoscopic procedures with approximate time of 9 ± 3 days resulting in prolonged length of hospital stay.

This study has statistically found that there was no correlation between the timing of endoscopic procedure and the amount of given transfusion (p = 0.63); also correlation between timing of endoscopic procedure and death and recurrent bleeding using fisher exact test with p = 0.21.

CONCLUSION

The timing of elective endoscopic procedure has no correlation with the incidence and recurrent bleeding in the patients; however, it is correlated to the length of hospital stay. Since the study was a retrospective study with a small number of samples, a larger data and prospective studies are needed to find out the causal relationship.

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