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Endoscopic findings of non-variceal upper gastrointestinal system bleeding and the relationship to rebleeding

Varise bağlı olmayan üst gastrointestinal sistem kanamasında endoskopik bulgular ve kanamayla ilişkileri

Emrah ALPER[1], Behlül BAYDAR[2], Cem ÇEKİÇ[1], Fatih ASLAN[1], Serdar AKÇA[2], Belkıs ÜNSAL[1]

[1]*Atatürk Training and Research Hospital, Izmir*
[2]*Memorial Antalya Hastanesi, Antalya*

Background and Aims: *Non-variceal upper gastrointestinal system bleeding is among the common reasons for urgent hospitalization worldwide and still causes high rates of mortality. In the present study, the lesions causing upper gastrointestinal bleeding were evaluated according to Forrest classification and the relationship between these lesions and rebleeding was elucidated.* ***Materials and methods:*** *The present study is a retrospective study conducted in a tertiary training and research hospital. Patients who were admitted between November 2005 and May 2009 with upper gastrointestinal bleeding developed within the previous 24 hours were included in the study. The data of 1647 patients were analyzed, and of those, the data of 1342 were evaluated and the results are reported herein.* ***Results:*** *Distribution of the lesions was as follows: 96 (7.15%) esophagus, 552 (41.13%) stomach, 523 (38.97%) duodenum, and 171 (12.74%) in multiple areas. It was also demonstrated that 34 (2.53%) of the lesions were classified as Forrest Ia, 192 (14.31%) as Forrest Ib, 85 (6.33%) as Forrest IIa, 121 (9.02%) as Forrest IIb, 210 (15.65%) as Forrest IIc, and 700 (52.16%) as Forrest III.* ***Conclusion:*** *In conclusion, evaluation of non-variceal upper gastrointestinal bleeding according to the Forrest classification demonstrated that the rate of rebleeding in the Forrest Ia, Ib and IIa groups was higher when compared to the others. It is suggested that endoscopic evaluation within the first 12 hours should be performed according to the Forrest classification in order to determine the risk of rebleeding.*

Key words: *Rebleeding, upper gastrointestinal bleeding, Forrest classification*

Amaç: *Non variseal üst gastrointestinal sistem kanaması dünyada acil hastaneye yatış nedenleri arasında yaygındır ve hala yüksek mortalite oranlarına neden olur. Bu çalışmada, üst gastrointestinal sistem kanamasına neden olan lezyonlar Forrest sınıflamasına gore değerlendirildi ve bu lezyonlarla tekrar kanama arası ilişki açıklandı.* ***Yöntem ve Gereç:*** *Bu çalışma, tersiyer eğitim ve araştırma hastanesinde retrospektif olarak yapılmıştır. Kasım 2005 ile Mayıs 2009 arasında, son 24 saatte üst gastrointestinal sistem kanaması gelişen ve hastaneye başvuran hastalar çalışmaya alındı. Binaltıyüzkırkyedi hastanın verileri analiz edildi ve 1342 hastanın verileri değerlendirildi.* ***Bulgular:*** *Lezyonların dağılımı: 96'sı (%7.15) özofagusta, 552'si (%41.13) midede, 523'ü (%38.97) duodenumda ve 171'i (%12.74) birden çok bölgede yerleşmiştir. Ayrıca 34 (%2.53) lezyon Forrest Ia, 192'si (%14.31) Forrest Ib, 85'i (%6.33) Forrest IIa, 121'i (%9.02) Forrest IIb, 210'u (%15.65) Forrest IIc ve 700'ü (%52.16) Forrest III olarak sınıflanmıştır.* ***Sonuç:*** *Sonuç olarak, non-variseal üst gastrointestinal sistem kanamalarının Forrest sınıflamasına göre değerlendirilmesinde, Forrest Ia, Ib ve IIa gruplarında tekrar kanama oranı, diğerleriyle kıyaslandığında daha yüksekti. Tekrar kanama riskini belirlemek için endoskopik değerlendirmenin ilk 12 saat içinde Forrest sınıflamasına göre yapılmasını önerebiliriz.*

Anahtar Kelimeler: *Tekrar kanama, üst gastrointestinal kanama, Forrest sınıflaması*

INTRODUCTION

Non-variceal upper gastrointestinal (GI) system bleeding is among the common reasons for urgent hospitalization worldwide and still causes high rates of mortality (1-7). The incidence of this category of bleeding ranges between 50/100,000 and 150/100,000 (8). While the bleeding ceases spontaneously in 80% of the patients, endoscopic treatment is required for the remaining 20%. Even though endoscopic treatment methods are effective in 90% of patients (9), bleeding after endoscopic treatment accounts for mortality in 20% of patients.

A hemoglobin level <6 g/dl at the time of first admission, the location of ulcer at the bulbus (10, 11), a large-sized ulcer (11-14), hemodynamic instability, coexisting illnesses (13-15), and active bleeding or signs of bleeding on endoscopy (11, 13, 16-19) determine the risk of rebleeding. The continuation of medical treatment with proton pump inhibitors (PPIs) after endoscopic treatment lowers the risk of rebleeding considerably (18, 20-24).

In the present study, the lesions causing upper GI bleeding were evaluated according to Forrest classification (25), and the relationship between these lesions and rebleeding was elucidated.

MATERIALS AND METHODS

The present study was a retrospective study conducted at the Izmir Ataturk Training and Research Hospital, a tertiary training and research hospital, involving patients with non-variceal upper GI bleeding who had undergone upper GI endoscopy and were being treated with medical and endoscopic techniques. Patients who were admitted to the outpatient clinic and emergency units of the hospital between November

İletişim: Behlül BAYDAR
Memorial Antalya Hastanesi, Genel Cerrahi Kliniği Zafer Mah. Yıldırım Beyazıd Cad. No: 91 Kepez, Antalya, Türkiye • Phone: + 90 242 314 66 66-4115
Fax: + 90 242 344 16 78 • E-mail: behlulbaydar@hotmail.com

2005 and May 2009 with upper GI bleeding developed within the last 24 hours were included in the study. Upper GI endoscopy was performed in all patients within 12 hours of admission and the non-variceal causes of bleeding were identified. All patients (except for mortalities) were hospitalized and followed for at least 5 days and treated with 80 mg pantoprazole intravenous (i.v.) push, followed by an i.v. infusion at 8 mg/hour for at least 72 hours. Data were obtained through evaluation of records of the endoscopy laboratory and investigation of patient documents from the hospital database. Biopsies were obtained for histologic sampling from patients with a single gastric ulcer and from patients in whom the endoscopic evaluation demonstrated lesions in the esophagus and stomach suggestive of malignancy with no contraindication for biopsy. Patients with variceal bleeding, cirrhotic patients with non-variceal bleeding, patients whose lesions could not be evaluated due to excessive bleeding, patients with bleeding following a recent GI surgical procedure, and patients with histologically detected malignancies were excluded from the study. Demographic data, patient history and treatments, and findings of biochemical and hematology laboratories were obtained from patient records; localization of lesions, endoscopic levels of lesions according to the Forrest classification, and endoscopic treatment and their types were analyzed from endoscopy laboratory files.

Bleeding was considered as rebleeding or continuous bleeding when it could not be stopped by endoscopic or medical treatment, and in cases of recurrence of bleeding, death due to bleeding or bleeding requiring surgical intervention, hematemesis following endoscopic or medical treatment, fresh bleeding from a nasogastric tube, a decrease in the hemoglobin level >2 g/dl within 24 hours, hypotension (<90/60 mmHg), tachycardia (>130/min), and the development of signs of shock. Signs of active bleeding were observed in this group of patients following a second upper GI endoscopy or operations for surgical treatment. Attempts were made to treat patients with rebleeding endoscopically or surgically. Statistical analyses were performed using SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA). Patient characteristics and variables were analyzed by chi-square test and Student's t test. Odds ratios were also calculated.

RESULTS

The data of 1647 patients fulfilling the study criteria, who were admitted with complaints of upper GI bleeding within 24 hours and who underwent upper GI endoscopy, were analyzed. Three hundred five patients were excluded from the study according to the exclusion criteria; thus, the data for 1342 patients were evaluated. The mean age of the patients was 61 years (range, 17-91 years); 755 females (56.26%) and 587 males (43.74%) were evaluated. Seven hundred twenty (53.2%) of the patients had a history of non-steroidal anti-inflammatory drug (aspirin; Bayer AG, Leverkusen, Germany) use within the past 7 days, while 52 (3.9%) of the patients had a history of anticoagulant drug use. Ninety-six of the patients had a history of upper GI bleeding. The mean hemoglobin level during the first admission was 10.1 g/dl (Table 1).

Endoscopic evaluation was performed on 242 (18.03%) and 1100 (81.07%) patients before and after PPI treatment, respectively. In the 265 patients with lesions classified as Forrest Ia, Ib and IIa, sclerotherapy with 1/10,000 adrenalin was performed, while endoscopic therapy with sclerotherapy and clips was performed in 5 patients (Table 1). All patients, except the ones who died or underwent surgery, received medical treatment with a pantoprazole infusion (8 mg/hour) for at least 3 days.

No significant difference was found between patients with rebleeding and patients without bleeding with respect to age, gender and the etiology of bleeding ($p<0.05$). The mean hemoglobin level of patients with bleeding was 9.2 g/dl on admission, whereas it was 10.6 g/dl in those without bleeding. The difference between the two groups was statistically significant ($p>0.05$).

Tablo 1. Characteristics of the patients with non-variceal upper gastrointestinal bleeding

Characteristics of the patients	
Number of upper GI endoscopies	1647
Number of patients evaluated	1342
Gender (Male/Female), n (%)	587 (48.74)/755 (56.26)
Mean age of patients (years) (min-max)	61 years (17-91)
Previous upper GI bleeding, n (%)	96 (7.15)
Medical history, n (%)	
NSAID (aspirin)	720 (53.20)
Anticoagulants	52 (3.90)
Location of bleeding, n (%)	
Esophagus	96 (7.15)
Stomach	552 (41.13)
Duodenum	523 (38.97)
Multiple	171 (12.74)
Forrest classification, n (%)	
Ia (spurting blood)	34 (2.53)
Ib (oozing blood)	192 (14.31)
IIa (non-bleeding visible vessel)	85 (6.33)
IIb (adherent blood clot)	121 (9.02)
IIc (black base)	210 (15.65)
III (lesion without stigmata of recent hemorrhage)	700 (52.16)
Endoscopic treatment, n	242
Pre-endoscopic treatment, n	1100
Sclerotherapy, n	265
Sclerotherapy and clips, n	5
Rebleeding, n (%)	92 (6.86)
Number of mortalities, n (%)	6 (0.45)

GI: Gastrointestinal. NSAID: Non-steroidal anti-inflammatory drug.

Tablo 2. Number and rate of rebleeding in patients with bleeding according to the Forrest classification

Forrest classification	Bleeding at admission Number of patients n (%)	Patients with rebleeding Number of patients n (%)	OR
Ia	34 (2.53)	14 (41.18)	11.03
Ib	192 (14.31)	44 (22.92)	6.82
IIa	85 (6.33)	11 (12.94)	2.15
IIb	121 (9.02)	7 (5.79)	0.82
IIc	210 (15.65)	4 (1.91)	0.23
III	700 (52.16)	12 (1.71)	0.12
Total	1342	92 (6.86)	

OR: Odds ratio

Distribution of the lesions was as follows: 96 (7.15%) esophagus, 552 (41.13%) stomach, 523 (38.97%) duodenum, and 171 (12.74%) in multiple areas. It was also demonstrated that 34 (2.53%) of the lesions were classified as Forrest Ia, 192 (14.31%) as Forrest Ib, 85 (6.33%) as Forrest IIa, 121 (9.02%) as Forrest IIb, 210 (15.65%) as Forrest IIc, and 700 (52.16%) as Forrest III (Table 2).

No rebleeding was observed in 1250 (93.14%) of the patients who underwent medical and endoscopic therapy during the 5-day follow-up and treatment period. Rebleeding and mortality associated with rebleeding was observed in 92 (6.86%) of the patients. Mortality occurred in 6 (0.45%) patients; 3 of the patients died before surgery -- 1 during surgery and 2 during the postoperative period. Rebleeding and mortality was observed in 85 (92.3%) of the patients within the first 48 hours. Of the lesions causing rebleeding and mortality, 14 (15.21%) were classified as Forrest Ia, 44 (47.83%) as Forrest Ib, 11 (11.96%) as Forrest IIa, 7 (7.61%) as Forrest IIb, 4 (4.35%) as Forrest IIc, and 12 (13.04%) as Forrest III (Table 3).

Evaluation according to endoscopic severity demonstrated that the rates of rebleeding were 41.18%, 22.92%, 12.94%, 5.79%, 1.91% and 1.71% in Forrest class Ia, Ib IIa, IIb, IIc, and III lesions, respectively. Odds ratios were 11.03, 6.82, 2.15, 0.82, 0.23 and 0.12 in Forrest class Ia, Ib, IIa, IIb, IIc, and III lesions, respectively (Table 2).

DISCUSSION

In the present study, a significant increase in the risk of rebleeding in lesions with active bleeding or visible vessels according to the Forrest classification was shown in the patients with upper GI bleeding,

In the literature, the rates of rebleeding and mortality have been reported to be 12-39% and 3.5-35.7% following treatment, respectively, whereas the number of cases requiring surgery has been reported to be 2.8-14.2% (1, 2, 7, 12, 14, 21, 26-28). In the present study, the rate of rebleeding and mortality was 6.86%. This is lower than the rates reported in other studies. (2-7, 14, 15) It has been suggested that this is due to the inability to identify the bleeding site in cases of excessive bleeding, exclusion of patients from the study who could not be categorized according to the Forrest classification, performing endoscopic intervention in patients in Forrest class IIa, the presence of variability in distribution according to the Forrest classification, and intensive PPI infusion therapy.

The endoscopic classification of upper GI bleeding was first reported by Forrest et al. in 1974 (25). The risk determination based on the Forrest classification is currently one of the most commonly used methods of evaluation. Methods evaluating clinical findings and laboratory parameters of patients have also been used. In the prospective study by Kim et al. (7) comparing five different scoring systems in patients with non-variceal bleeding, it was demonstrated that the Forrest classification was more specific and had a higher positive predicti-

Tablo 3. The number of patients with bleeding and non-bleeding according to Forrest classification and location of the lesion

Site of bleeding	Number of patients	Presence of bleeding	Forrest classification						Total
			Ia	Ib	IIa	IIb	IIc	III	
Esophagus	96	+	3	7	2	1	0	1	**14**
		-	1	11	5	14	20	31	**82**
Stomach	552	+	3	15	5	2	1	5	**31**
		-	8	47	37	47	77	304	**521**
Duodenum	523	+	5	16	3	2	2	3	**31**
		-	5	66	22	43	81	275	**492**
Multiple	171	+	3	6	1	2	1	3	**16**
		-	6	24	9	10	28	78	**155**
		Total +	14	44	11	7	4	12	**92**
		Total -	20	148	74	114	206	688	**1250**
	Total		**34**	**192**	**85**	**121**	**210**	**700**	**1342**

"+": Bleeding. "-": Non-bleeding.

ve value when compared to the other scoring systems with respect to rebleeding and mortality risk determination (7). In a study involving 239 patients, the rate of bleeding was 14.6%, whereas the mortality rate was 8.4%, and it was reported that endoscopic evaluation was necessary for risk determination in patients with upper GI bleeding (7). In the same study, the sensitivity of Forrest classification was found to be 71.4% for rebleeding and 85% for mortality. In a study conducted by Manguso et al. (1), analysis of endoscopic findings of 142 patients with Forrest class Ia and Ib showed that rebleeding occurred in 12% of patients, mortality throughout the hospitalization was 5.6%, and the rate of patients who underwent surgery due to inability to stop bleeding was 2.8%. In upper GI bleeding associated with peptic ulcers, despite the importance of clinical factors, certain studies have reported that the Forrest classification was the principal determining factor (17). In the present study, it was determined that as the severity of factors of active bleeding increased, the risk of rebleeding also increased according to the Forrest classification. It was observed that rebleeding developed in 41.1%, 22.9% and 12.9% of the patients classified as Forrest Ia, Ib and Ic, respectively. On the other hand, the rate of rebleeding in Forrest class III was 1.7%.

In a study conducted by Chung et al. (12), the Forrest classification and location and size of the lesion were evaluated together. Based on univariate analyses, rebleeding was found to be associated with Forrest class Ia, ulcer sizes >2 cm and lesions located in the stomach (12). In a study involving 738 patients who had been evaluated for rebleeding and mortality using multivariate analyses, liver cirrhosis, recent surgery, low systolic blood pressure, hematemesis, Forrest classification, and localization and size of the ulcer were investigated. According to the data, four classes were determined, and the Forrest classification was reported to be the best indicator for early rebleeding (within the first 48 hours). The sensitivity in the first 48 hours was 90%, whereas it was 65% after 48 hours (3). In the present study, the risk of rebleeding was higher in ulcers located in the esophagus and duodenum, and in ulcers classified as Forrest Ia, Ib and IIa, and it was determined that rebleeding and mortality occurred in 92.3% of the patients during the first 48 hours.

In conclusion, evaluation of non-variceal upper GI bleeding according to the Forrest classification demonstrated that the rate of rebleeding in the Forrest Ia, Ib and IIa groups was higher when compared to the others. It is suggested that endoscopic evaluation within the first 12 hours should be performed according to the Forrest classification in order to determine the risk of rebleeding.

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