

Evaluation of the relationship between D-dimer levels and endoscopic findings of patients with upper gastrointestinal hemorrhage

Relationship between D-dimer levels and endoscopic findings of upper gastrointestinal hemorrhage

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Abstract

Aim: Gastrointestinal (GI) bleeding is the most common reason for admission to the emergency department, and, despite technological advances, mortality is still high. The aim of our study was to evaluate the relationship between endoscopic findings and D-Dimer in patients presenting with suspected upper GI bleeding.

Materials and Methods: This retrospective, cross-sectional descriptive study included all patients who met the inclusion criteria for patients with GI bleeding who applied to the Department of Emergency Medicine between August 15, 2016 and February 15, 2017. Demographic characteristics, history, D-dimer and endoscopy were evaluated. Significance was evaluated at $p < 0.05$.

Results: Among the 90 patients included in the study, 61.1% were male ($n=55$) and 38.9% were female ($n=35$). While there was a statistically significant difference between the systolic blood pressure measurements and the stages according to the Forrest classification ($p=0.020$); no difference was found between the other vital findings and the stages. There was no statistically significant difference in mean D-Dimer levels or D-Dimer limit values between the patients with and without a history of GI hemorrhage or hospital admission ($p > 0.05$). No statistical difference was found between D-Dimer mean values and limit values and the stages according to Forrest classification ($p > 0.05$).

Discussion: In the study, there was no relationship between the endoscopic findings (Forrest classification stage I, II, III) and the increased D-Dimer levels.

Keywords

D-dimer; Endoscopy; GI hemorrhage

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Introduction

Gastrointestinal system (GI) bleeding is one of the most common reasons for admission to the emergency department; it is a clinical picture that draws attention with its high mortality, diagnosis, and treatment costs, often requiring hospitalization and even intensive care, as well as the need for follow-up with a multidisciplinary study. GI bleeding is seen in 1-2 out of 1000 people in the community and its mortality varies between 6-10% [1]. Through using flexible endoscopy in 1957, a radical change occurred in the diagnosis and treatment approaches of upper GI bleeding. Surgical procedures previously performed before the use of endoscopy in diagnosis and treatments have now been replaced by endoscopy [2]. D-Dimer is a product of the enzymatic degradation of cross-linked fibrin by plasmin. Fibrin is the main component of the thrombus and is formed by the activation of the coagulation system. Fibrin formation and plasmin mediated destruction of fibrin are in equilibrium under normal physiological conditions and play a key role in hemostasis. In the study conducted by Akbaş et al., D-Dimer levels were found to be increased approximately 3-4 times the normal in patients with extravascular fibrin formation (traumatic hematoma, gastrointestinal bleeding) or liver failure [3]. Our study aims to correlate endoscopy findings with laboratory values in patients with GIS bleeding and to retrospectively evaluate the guidance of these findings in terms of re-application.

Material and Methods

This retrospective, cross-sectional descriptive study was performed in the Emergency Medicine Department of Health Sciences University Kanuni Sultan Süleyman Training and Research Hospital from 15 August 2016 to 15 February 2017. Ethic committee approval was obtained (Number 2017-09-12). The study included patients who presented with signs of upper GI bleeding such as melena, syncope, hematemesis or prediagnosed with upper GI bleeding and had undergone emergency endoscopy for upper GI bleeding. Patients with active bleeding other than the GI, a history of recent surgery and embolic diseases, and patients with GIS bleeding without endoscopy were excluded from the study.

In 2017, it was determined that the number of patients in ED was 694000 and 528 of these patients were diagnosed with GI bleeding. The number of patients diagnosed with upper GI bleeding between August 15, 2016, and February 15, 2017; was reported as 210. By analyzing the accessed files, patient gender, age, admission time, admission outpatient clinic number, systolic and diastolic blood pressure, pulse rate, fingertip saturation, respiratory rate, presence of re-admission in history, presence of syncope before admission, presence of liver disease and heart failure, the presence of melena at patient's arrival, history of acetylsalicylic acid (ASA) and nonsteroidal anti-inflammatory drug (NSAID) use, history of previous GI bleeding, hemoglobin, hematocrit, BUN, D-Dimer and INR results and endoscopy reports were obtained. The study was approved by the Local Ethics Committee. All included patients gave informed consent.

We used NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program for statistical analysis. While evaluating the study data, besides descriptive statistical

methods (Average, Standard Deviation, Median, Frequency, Ratio, Minimum, Maximum), the Kolmogorov-Smirnov test, and box plot graphs were used for the conformity of numerical data to a normal distribution. While the One-way Anova Test was used for comparing numerical data with normal distribution, the Kruskal Wallis test is used for comparisons of three or more groups that do not show a normal distribution; the Mann-Whitney U test was used in the evaluation of two groups. The Pearson Chi-Square test and the Fisher-Freeman-Halton test were used for comparison of non-numerical data. Significance was evaluated at the $p < 0.05$ level.

Results

The study was carried out with 90 cases; 61.1% (n=55) were males and 38.9% (n=35) were females. The ages of the cases ranged from 19 to 96, with a mean of 61 ± 22 years. The vital signs and histories of the cases are summarized in Table 1. Re-application rate was 21.1% (n=19). Pre-admission syncope was observed in 11.1% (n=10) of the patients, liver disease in 8.9% (n=8), congestive heart disease in 17.8% (n=16) and melena on rectal examination in 68.9% (n = 62). The rate of using ASA was 27.8% (n=25), the rate of NSAID use was 34.4% (n=31), the rate of Coumadin use was 13.3% (n=12), and 21.1% (n=19) of the patients had a history of gastrointestinal bleeding.

The diagnostic examination findings, intervention, and examination values of the cases are also summarized in Table 1. Bleeding was detected in nasogastric lavage in 32.2% (n=29) of the cases. Hemoglobin measurements ranged from 3.3 to 18.5, with a mean of 9.03 ± 3.26 ; Hematocrit measurements ranged from 4.6 to 53, with a mean of 27.49 ± 9.66 ; BUN measurements ranged from 9.4 to 411.1, with a mean of 44.84 ± 49.44 and INR measurements from 0.8 to 12, with a mean of 1.50 ± 1.55 .

D-Dimer measurements ranged from 0 to 23.8, with a mean of 1.25 ± 2.75 ; It is less than 0.50 in 44.4% of the cases (n=40), and greater than 0.50 in 55.6% (n=50).

The distribution of the patients based on the Forrest classification is shown in Table 2. Based on the Forrest classification, the differences between the groups in terms of age and gender are summarized in Table 3.

Based on the Forrest classification, the differences between the groups with previous GI bleeding or history of hospital admission, pre-admission syncope, liver disease, congestive heart disease, use of ASA, and NSAID, history of GI bleeding are summarized in Table 3. According to the Forrest classification, the rate of heart disease in grade I cases was significantly higher than in grade III cases ($p=0.006$). According to the Forrest classification, the rate of using NSAIDs in grade I ($p=0.007$) and grade II ($p=0.012$) cases was significantly higher than in grade III cases ($p=0.01$).

There was no statistically significant difference ($p > 0.05$) between the D-Dimer mean values, cut-off values (0.50), and the stages according to the Forrest classification (Stage I, II, III) (Table 3).

No statistically significant difference was found in terms of mean D-Dimer levels and D-Dimer cut-off values between the patients with previous GI bleeding or a history of hospital admission and the patients without these histories ($p=0,774$ and 0,453, respectively).

Table 1. Distribution of Demographic Features, Test Results and Patient Histories Characteristics

| | Minimum | Maximum | Value Range (Mean±SD) |
|--|----------------------|---------------------|-----------------------|
| Age (year) | 19 | 96 | 64 (61±22) |
| Systolic blood pressure | 75 | 180 | 120(119,31±20,69) |
| Diastolic blood pressure | 43 | 120 | 70 (70,48±12,80) |
| Heart rate | 54 | 140 | 85 (87,31±16,91) |
| Respiratory rate | 12 | 34 | 18 (18,14±3,91) |
| Oxygen Saturation | 90 | 100 | 98 (97,43±2,07) |
| | Value Range (Median) | | (Mean±SD) |
| Hematocrit | 4,6-53 (26,8) | | 27,49±9,66 |
| D-Dimer | 0-23,8 (0,6) | | 1,25±2,75 |
| | D dimer <0,50; n(%) | D dimer >0,50; n(%) | |
| | 40 (44,4) | 50 (55,6) | |
| | Yes | No | |
| Syncope before admission; n (%) | 10 (11,1) | 80 (88,9) | |
| Liver disease; n (%) | 8 (8,9) | 82 (91,1) | |
| Congestive heart disease; n (%) | 16 (17,8) | 74 (82,2) | |
| ASA use; n (%) | 25 (27,8) | 65 (72,2) | |
| NSAIDs use; n (%) | 31 (34,4) | 59 (65,6) | |
| Previous GI bleeding or hospital admissions; n (%) | 19 (21,1) | 71 (78,9) | |
| Hemorrhagic fluid from nasogastric catheter; n (%) | 29 (32,2) | 61 (67,8) | |
| Melena on rectal examination; n (%) | 62 (68,9) | 28 (31,1) | |

Table 2. Distribution of Demographic Features, Test Results and Patient Histories Characteristics

| | n | % |
|--|----|------|
| Grade Ia: Active, Spurting hemorrhage | 5 | 5,6 |
| Grade Ib: Active Oozing hemorrhage | 19 | 21,1 |
| Grade IIa: Non-bleeding Visible vessel | 6 | 6,6 |
| Grade IIb: Adherent clot | 10 | 11,1 |
| Grade IIc: Flat pigmented lesion on ulcer base | 7 | 7,8 |
| Grade III: Clean, non-bleeding ulcer base | 43 | 47,8 |
| Grade I | 24 | 26,7 |
| Grade II | 23 | 25,6 |
| Grade III | 43 | 47,8 |

Table 3. Evaluation of Demographic Characteristics and Admission Features Based on the Forrest Classification

| | | Forrest classification | | | | | | P |
|--------------------------|----------------------|------------------------|----------|-----------------|----------|------------------|----------|--------|
| | | Grade I (n=24) | | Grade II (n=23) | | Grade III (n=43) | | |
| | Yes | No | Yes | No | Yes | No | | |
| Age (year) | Mean±SD | 63±20 | | 58±25 | | 61±22 | | *0,730 |
| Gender; n (%) | Male | 11 (45,8) | | 17 (73,9) | | 27 (62,8) | | *0,136 |
| | Female | 13 (54,2) | | 6 (26,1) | | 16 (37,2) | | |
| D-Dimer | Value Range (Median) | 0-2,8 (0,4) | | 0,1-3,6 (1) | | 0,1-23,8 (0,6) | | *0,268 |
| | <0,50 | 13 (54,2) | | 8 (34,8) | | 19 (44,2) | | *0,409 |
| | >0,50 | 11 (45,8) | | 15 (65,2) | | 24 (55,8) | | |
| Syncope before admission | | 5(20,8) | 19(79,2) | 2(8,7) | 21(91,3) | 3(7,0) | 40(93,0) | *0,246 |
| Liver disease | | 1(4,2) | 23(95,8) | 4(17,4) | 19(82,6) | 3(7,0) | 40(93,0) | *0,307 |
| Congestive heart disease | | 9(37,5) | 15(62,5) | 4(17,4) | 19(82,6) | 3(7,0) | 40(93,0) | *0,009 |
| ASA use | | 4(16,7) | 20(83,3) | 5(21,7) | 18(78,3) | 16(37,2) | 27(62,8) | *0,149 |
| NSAID use | | 12(50,0) | 12(50,0) | 11(47,8) | 12(52,2) | 8(18,6) | 35(81,4) | *0,010 |
| Previous GI bleeding | | 5(20,8) | 19(79,2) | 3(13) | 20(87) | 11(25,6) | 32(74,4) | *0,543 |

*One-way ANOVA Test, *Pearson Chi-Square Test, *Kruskall-Wallis Test, *Fisher-Freeman Halton Test

Discussion

Our study was conducted on the patients with a diagnosis of GI bleeding undergoing endoscopy and included 90 cases; 61.1% (n=55) of cases were males and 38.9% (n=35) were females. Olt et al. also found a high rate of male patients (72%) [4]. In our study, the ages of the patients ranged from 19 to 96, and the mean was found to be 61±22 years. In other studies, the mean age was found to be 57±21 and 57±17 years, respectively [5,6]. Our study is similar to previous studies in terms of both age and gender distribution.

When the vital signs of the cases were evaluated, the mean systolic blood pressure was 119.31±20.69; the mean diastolic blood pressure 70.48±12.80; the mean heart rate was measured as 87.31±16.91 and these findings were found to be close to the results of the study conducted by Çete et al, in Turkey. In the mentioned study, the mean systolic blood pressure was measured as 129.5; the mean diastolic blood pressure was measured as 70.71, and the mean pulse rate was measured as 100.7 [7]. The rate of previous GI bleeding or hospital admission history was 21.1% (n=19). In the study conducted by Bayır et al. in 2003, it was found to be 59%, unlike this study [8]. We think that the reason for this difference in two different studies conducted in our country may be the widespread use of endoscopic procedures in our country in the last 14 years and the development of early diagnosis and treatment methods.

When the patients were evaluated in terms of other accompanying diseases, liver disease was detected in 8.9% (n=8) and congestive heart disease in 17.8% (n=16) of the patients.

In the study of Gürel et al., 58.4% of the patients had comorbid diseases and comorbidity was found as a risk factor for mortality in varicose veins and upper GI bleeding other than malignancy [9]. We think that the reason for the lower rate of comorbid diseases in our study is that only patients who underwent endoscopy were included in the study.

In 68.9% of the study cases (n=62), melena was observed on rectal examination and it was observed that hemorrhagic fluid came from the nasogastric catheter in 32.2% (n=29) of the cases.

In the study by Lewis et al., melena was found in 48% of the patients [10]. In the study by Adamopoulos et al., melena was found in 66.3% of the patients [11]. In the study conducted by Chassaignon et al in France, hematemesis was found to be the most frequent complaint with 39%, and it was observed that the melena accounted for 28% [12]. In our study, we found compatible results with other studies in the literature.

NSAIDs and acetylsalicylic acid, which are used frequently worldwide, have an important place in the etiology of upper gastrointestinal bleeding [13]. In our study, we found that the rate of ASA use was 27.8% (n=25), while the rate of NSAID use was 34.4% (n=31). In a study conducted in our country by Coşar et al. , it was seen that the use of ASA was more frequent in cases with GI bleeding (NSAID, n=35 (40%); ASA, n=51 (60%)) [14]. We think that the reason for the lower rate of ASA use in our study is due to the lower GI side effect profile of new antiplatelet drugs.

In our study, D-Dimer was less than 0.50 in 44.4% (n=40) of the cases, and greater than 0.50 in 55.6% (n=50). A study showed that patients with high plasma D-Dimer levels had a 7.5 times worse prognosis than the group without high D-Dimer levels and had a positive predictive value of 20.5% in terms of outcomes such as death or re-admission. In this study, the increase in D-dimer levels in patients with upper gastrointestinal bleeding is consistent with local fibrinolysis, suggesting that plasma fibrinolytic tests may be a suitable prognostic marker for upper GI bleeding [15]. In another study, upper GI bleeding was observed in 30% (n=34) of patients with high D-Dimer levels, who were followed up for liver cirrhosis [16]. In our study, we found no statistically significant difference between D-Dimer levels and previous GI bleeding or hospital admission history. As a reason for this; we think that the D-Dimer level may vary depending on the bleeding time, the interaction of other drugs used by the patients, and comorbid diseases.

In our study, based on the Forrest classification, the most seen stage was stage 3 (47.8%, n=43). In two separate studies conducted in our country where cases were classified according to the Forrest classification, class III cases were more common, as in our study [4,17].

Gastric ulcer develops in 10% of chronic NSAID users. The risk of developing peptic ulcer is 5-10 times higher in chronic NSAID users than in those who do not take NSAIDs [18]. In studies conducted by Unsal, Çetinkaya, Kaplan, and Shafi et al., it was found that NSAID use was observed in patients with peptic ulcer (42%, 32.2%, 80%, and 38.4%, respectively) [19-22]. In our study, NSAID use was found in 35.3% of the patients with peptic ulcer which is consistent with the literature.

In our study, no statistically significant difference was found between the groups according to the presence of a history of melena on rectal examination and ASA use ($p > 0.05$). In the study conducted by Okutur et al., the number of patients who were admitted with only melena symptoms was significantly higher in the group without recurrent bleeding ($p < 0.01$) [4]. In another study in patients with upper GI bleeding, the most common etiology was peptic ulcer, 48% of the cases had comorbid diseases, the bleeding was found to be due to the use of ASA or NSAIDs in 19.1% [4]. In our study, a statistically significant difference was found between the groups according

to NSAID use ($p = 0.010$). As a result of paired comparisons made to identify the group that creates difference, the rate of NSAID use in grade I ($p = 0.007$) and grade II ($p = 0.012$) cases was significantly higher than in grade III cases ($p = 0.01$).

In this study, which investigated the relationship between D-Dimer and upper GI bleeding, no statistically significant difference was found between D-Dimer levels according to GI bleeding history ($p > 0.05$). In the study by Primignani et al., the basic measurements of coagulation activation and fibrinolysis of cases were measured as more impaired in those with bleeding. High D-Dimer levels were found to be significant as a marker of poor prognosis in upper GI bleeding [23]. In the study conducted by Junquera et al. in patients with upper GI bleeding due to angiodysplasia, D-Dimer levels were found to be higher in patients who had upper GI bleeding due to angiodysplasia than control groups, and it was concluded that high D-Dimer levels may be an indicator of bleeding from angiodysplasia [24]. In the study by Gutiérrez et al. on 84 patients, in which the prognostic values of fibrinolytic tests in terms of discharge were investigated in patients with upper GI bleeding, surgical or D-Dimer plasma levels were found to be significantly higher than those who had positive results. ($p = 0.01$) [25].

Conclusion

No relationship was found between endoscopic findings (Forrest classification) and D-Dimer elevation in patients who underwent emergency endoscopy for upper GI bleeding. Consistent with the literature, the most common causes of GI bleeding were peptic ulcer and NSAID use. We believe that rational drug use and preventive medicine should be developed to prevent GI bleeding, and further studies on this subject are needed.

Limitations

As limitations of our study, we can mention the inclusion of only patients who can undergo endoscopy, not including all the patients with a diagnosis of GI bleeding, and a small number of patients who were admitted for 6 months

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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