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Upper Gastrointestinal Bleeding: Do Emergency Endoscopic Evaluations Affect Clinical Outcomes?

Osman Inan[1(ID)], Muhammed Fatih Acehan[1(ID)], Karsavuranoğlu Buket[2(ID)], Enes Seyda Sahiner[1(ID)], Meryem Aslan[1(ID)], Ihsan Ates[1(ID)]

[1]Department of Internal Medicine, Ankara City Hospital, Ankara, Turkey
[2]Department of Internal Medicine, İnebolu City Hospital, Kastamonu, Turkey

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Abstract

Objective: We aimed to reveal the effect of time from admission to endoscopy on clinical outcomes such as mortality, rebleeding, and prolonged hospitalization among patients with acute upper gastrointestinal bleeding.

Methods: Patients aged ≥18 years with acute upper gastrointestinal bleeding were enrolled in the study. Those who had variceal bleeding during endoscopy, those whose hospital stay was shorter than 24 hours, those who did not undergo endoscopy, and those who underwent endoscopy after 24 hours were excluded from the study. Clinical findings, routine laboratory test results, and imaging findings of the patients were retrospectively reviewed through the hospital's records system.

Results: A total of 252 patients were enrolled in the study. At admission, 30.2% (76) of patients were at clinically high risk of death or rebleeding, 71.8% had melena, and 51.2% had hematemesis. While 72 (28.6%) of the patients had high-risk endoscopic stigmata, 89 (35.3%) had low-risk endoscopic stigmata. The median hospital stay was 6 (1-91) days. In-hospital mortality occurred in 8 (3.2%) cases, rebleeding developed in 16 (6.3%) cases, endoscopic intervention was required in 103 (40.9%) cases, and prolonged hospital stay was required in 43 (17.1%) cases. High-risk endoscopic stigmata were identified in 63 (34.1%) cases in the urgent group and in 9 (13.4%) in the early group (p=0.001). Endoscopic intervention was required in 47.0% cases in the urgent group, while the incidence was 23.9% in the early group (p=0.001).

Conclusion: While no significant difference was found between the urgent and early groups in terms of mortality and re-bleeding, the need for endoscopic intervention and the incidence of high-risk endoscopic stigmata were found to be significantly higher in the urgent group.

Key words: Endoscopy, Outcome, Upper gastrointestinal bleeding

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Address for correspondence/reprints: **Telephone number:** +905054643065

Osman İnan **E-mail:** drosmaninan@gmail.com

INTRODUCTION

When upper gastrointestinal bleeding (UGIB) is mentioned, bleeding from the mouth to the Treitz ligament in the proximal duodenum comes to mind (1). UGIB, one of the common reasons for admission to the emergency department, may result in serious morbidity and mortality. Despite advancements in medical and endoscopic treatments, the death rate from UGIB remains high (2-4). Scoring systems intended to identify the risk status of patients with UGIB have been developed, among which the Glasgow-Blatchford score (GBS) and Rockall score are commonly used (5, 6). Patients with a GBS of 2 or lower are considered to be at low risk and they are suitable candidates for outpatient treatment (7). On the other hand, the lower limit of the GBS for high-risk patients is not clear, but patients with a GBS of higher than 2 have been shown to have a higher risk of rebleeding and increased mortality (8). Many studies have shown mortality rates of up to 25% among high-risk patients (2, 9).

Endoscopy is the primary technique used in diagnosis and treatment to determine the focus of bleeding and to perform hemostatic treatment in cases of actively bleeding lesions (10, 11). Several randomized clinical studies and two meta-analyses conducted in recent years have revealed the beneficial effects of endoscopic therapy in reducing the incidence of rebleeding, the need for surgical interventions, and mortality rates among patients with UGIB (12-14). Time from admission to endoscopy after UGIB has been accepted as a quality standard for both patients and the endoscopy unit by the National Institute for Health and Clinical Excellence (NICE) (11), the European Society of Gastrointestinal Endoscopy (ESGE) (15), and the Joint Advisory Group on Gastrointestinal Endoscopy (JAG) (16).

Recently, studies on times from admission to endoscopy and clinical outcomes have intensified, but the results of various studies evaluating the relationship between times from admission to endoscopy and mortality differ (17-28). In the present study, we aim to reveal the effect of times from admission to endoscopy on clinical outcomes such as mortality, intensive care stay, and prolonged hospitalization among patients with UGIB with the intention of adding our results to the current body of literature.

METHODS

Study Area

This study included patients ≥18 years of age who were diagnosed with acute UGIB between 2019 and 2020. Those who had variceal bleeding during endoscopy, those whose hospital stay was shorter than 24 hours, those who did not undergo endoscopy, those who underwent endoscopy after 24 hours, and those diagnosed with lower gastrointestinal bleeding by colonoscopy were excluded from the study (figure1). Among the patients enrolled in the study, those who underwent endoscopy less than 12 hours after admission to the hospital were assigned to the urgent group, while those who underwent endoscopy after 12 to 24 hours were assigned to the early group.

Data collection and definitions

Age, gender, compliance at admission, heart rate at admission, mean blood pressure, major comorbidities, medications associated with bleeding, endoscopic bleeding etiologies, endoscopic Forrest classification, need for endoscopic intervention, length of hospital stay, and presence of rebleeding and mortality were clinically obtained from patient

files and recorded. Patients' laboratory parameters at admission were collected from electronic medical records, including data on white blood cell count, neutrophils, lymphocytes, hemoglobin, hematocrit, platelets, blood urea nitrogen, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transpeptidase, lactate dehydrogenase, amylase, albumin, activated partial thromboplastin time, international normalized ratio, and lactate.

Patients with any of the symptoms of hematemesis, melena, or hematochezia at presentation and no lower gastrointestinal bleeding were considered to have UGIB. Patients who were of clinically high risk at admission were defined as those having a GBS of ≥12. Cases of high-risk endoscopic stigmata were assigned to Forrest classes 1A, 1B, and 2A. Hospital stays of 14 days or longer were defined as prolonged hospitalization.

Clinical outcomes

The primary endpoints of this study were determined to be in-hospital mortality, rebleeding rates, and the primary composite outcome including them, while secondary endpoints were the need for endoscopic intervention and prolonged hospitalization.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics 26.0 for Windows (IBM Corp., Armonk, NY, USA). The frequency of the variables was expressed as number (n) and percentage (%). Data were evaluated for normality by performing the Shapiro-Wilk test. Continuous variables with normal distribution were presented as mean ± standard deviation, while those with non-normal distribution were presented as median (interquartile range). Pairwise comparisons of continuous variables with normal distribution were performed with Student t-tests, while pairwise comparisons of data with non-normal distribution were performed with Mann-Whitney U tests. Categorical variables were compared with Pearson chi-square tests. Univariate logistic regression analysis was performed using the appropriate parameters thought to be associated with the primary composite outcome. Parameters with a significance value of $p<0.1$ according to univariate analysis were included in the stepwise multivariate logistic regression analysis. Odds ratios (ORs) were calculated with 95% confidence intervals. In all analyses, $p<0.05$ was consider ed to be statistically significant.

RESULTS

Baseline patient characteristics at admission

Of the 252 patients enrolled in this study, 170 (67.5%) were men and 82 (32.5%) were women. The mean age of the overall population was 64.8±18.4 years. Of the patients, 71.8% had melena and 51.2% had hematemesis at admission. No accompanying comorbidity was observed in 69 (27.4%) cases, while 130 (51.6%) patients had hypertension, 60 (23.8%) had diabetes mellitus, and 97 (38.5%) had ischemic heart disease. One hundred patients did not use any drugs associated with bleeding, while 49 (19.4%) patients used anticoagulants, 80 (31.7%) used antiplatelets, and 54 (21.4%) used nonsteroidal anti-inflammatory drugs. Table 1 shows the baseline clinical features at admission.

Clinical characteristics of patients during follow-up Of the 252 patients, 30.2% (n=76) were at clinically high risk of death or rebleeding. Urgent endoscopy was performed for 27% (n=50) of the high-risk patients. The etiology of UGIB primarily

included duodenal ulcer (31.3%), gastric ulcer (18.7%), malignant ulcer (9.5%), and esophagitis (7.1%), while the etiology could not be specified in 9.1% of cases. While 72 (28.6%) of patients had high-risk endoscopic stigmata, 89 (35.3) had low-risk endoscopic stigmata. The median hospital stay was 6 (1-91) days. In-hospital mortality occurred in 8 (3.2%) cases, rebleeding developed in 16 (6.3%) cases, endoscopic intervention was required in 103 (40.9%) cases, and prolonged hospital stay was required in 43 (17.1%) cases (figure 2). Clinical characteristics during follow-up are summarized in Table 2.

Table 1. Baseline clinical features of patients at admission

Variable	n (%)
Overall	252 (100)
Age, years (mean ± SD)	64.8±18.4
Male	170 (67.5)
Main complaint on admission	
Melena	181 (71.8)
Hematemesis	129 (51.2)
Hematochezia	19 (7.5)
Syncope	26 (10.3)
Major comorbidities	
None	69 (27.4)
Hypertension	130 (51.6)
Diabetes mellitus	60 (23.8)
Cerebrovascular disease	24 (9.5)
Liver disease	2 (0.8)
Chronic renal impairment	27 (10.7)
Ischemic heart disease	97 (38.5)
Congestive cardiac failure	31 (12.3)
Arrhythmia	51 (20.2)
Chronic obstructive airways disease	22 (8.7)
Malignancy	33 (13.1)
Bleeding risk medications	
None	100 (39.7)
Anticoagulant drug	49 (19.4)
Warfarin	19 (7.5)
Heparin/low-molecular-weight heparin	8 (3.2)
Direct oral anticoagulant	23 (9.1)
Antiplatelet drug	80 (31.7)
Nonsteroidal anti-inflammatory drugs	54 (21.4)

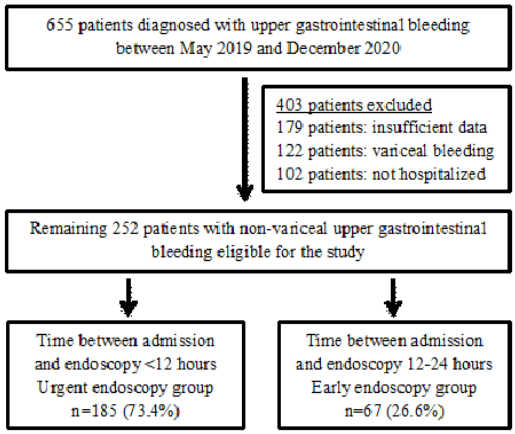

Figure 1. A flowchart showing patient selection

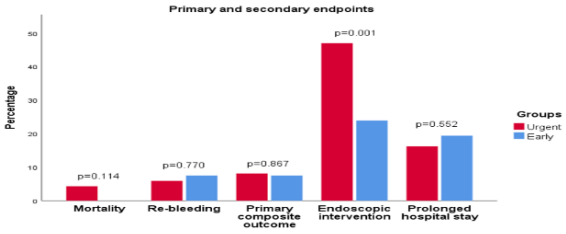

Figure 2. Comparison of urgent and early groups for primary and secondary endpoints

Clinical characteristics of patients during follow-up

Of the 252 patients, 30.2% (n=76) were at clinically high risk of death or rebleeding. Urgent endoscopy was performed for 27% (n=50) of the high-risk patients. The etiology of UGIB primarily included duodenal ulcer (31.3%), gastric ulcer (18.7%), malignant ulcer (9.5%), and esophagitis (7.1%), while the etiology could not be specified in 9.1% of cases. While 72 (28.6%) of patients had high-risk endoscopic stigmata, 89 (35.3) had low-risk endoscopic stigmata. The median hospital stay was 6 (1-91) days. In-hospital mortality occurred in 8 (3.2%) cases, rebleeding developed in 16 (6.3%) cases, endoscopic intervention was required in 103 (40.9%) cases, and prolonged hospital stay was required in 43 (17.1%) cases (figure 2). Clinical characteristics during follow-up are summarized in Table 2.

Clinical and laboratory differences between the urgent and early groups

High-risk endoscopic stigmata were observed in 63 (34.1%) cases in the urgent group and in 9 (13.4%)

in the early group (p=0.001). Endoscopic intervention was required in 47.0% cases in the urgent group and 23.9% in the early group (p=0.001). In terms of other clinical parameters, there were no significant differences between the urgent group and early group. The hemoglobin level at admission was found to be 9.98±2.62 g/dL in the urgent group and 8.64±2.95 g/dL in the early group, being statistically significantly lower in the early group. No significant differences were found for other laboratory parameters (Table 3).

Table 2. Clinical characteristics of patients during follow-up

Variable	n (%)
Clinical high risk at admission (death or rebleeding)*	**76 (30.2)**
Urgent endoscopy	50 (65.8)
Early endoscopy	26 (34.2)
Time to endoscopy	
<12 hours	**185 (73.4)**
12-24 hours	**67 (26.6)**
Etiology	
Unspecified	23 (9.1)
Duodenal ulcer	79 (31.3)
Gastric ulcer	47 (18.7)
Gastroduodenal ulcer	10 (4.0)
Esophageal ulcer	10 (4.0)
Esophagitis	18 (7.1)
Mallory-Weiss	7 (2.8)
Malignant ulcer	24 (9.5)
Angiodysplasia	8 (3.2)
Dieulafoy's lesion	3 (1.2)
Erosive gastritis/bulbitis	13 (5.2)
Other	10 (4.0)
Forrest classification	
Not reported	**91 (36.1)**
High-risk endoscopic stigmata	**72 (28.6**)
IA	1 (0.4)
IB	44 (17.5)
IIA	27 (10.7)
Low-risk endoscopic stigmata	89 (35.3)
IIB	12 (4.8)
IIC	18 (7.1)
III	59 (23.4)
Length of hospital stay, days, median (min-max)	**6** (1-94)
Primary endpoint	
In-hospital mortality	**8 (3.2)**
Rebleeding	**16 (6.3)**
Primary composite outcome**	**20 (7.9)**
Secondary endpoints	
Endoscopic intervention	**103 (40.9)**
Prolonged hospital stay	**43 (17.1)**

*Includes patients with a Glasgow-Blatchford score of 12 or higher at admission
**Primary composite outcome includes in-hospital mortality and rebleeding
IQR: Interquartile range

Predictors of primary composite outcome.

Univariate and multivariate regression analyses were conducted for the primary composite outcome. Accordingly, in univariate analysis, diabetes mellitus (OR: 2.904; 95% CI: 1.141-7.390; p=0.025), heart rate (OR: 1.028, 95% CI: 1.005-1.051; p=0.015), and high-risk endoscopic stigmata (OR: 2.742; 95% CI: 1.089-6.904; p=0.032) were significantly associated with primary composite outcome. In multivariate analysis, male gender (OR: 5.656; 95% CI: 1.333-23.998; p=0.019), diabetes mellitus (OR: 2.941; 95% CI: 1.073-8.064; p=0.036), congestive heart failure (OR: 5.813; 95% CI: 1.560-21.656; p=0.009), heart rate (OR: 1.030; 95% CI: 1.005-1.055; p=0.017), and high-risk endoscopic stigmata (OR: 3.450; 95% CI: 1.246-9.551; p=0.017) were found to be significantly associated with primary composite outcome. Other clinical and laboratory parameters were not significantly associated with primary composite outcome (Table 4).

DISCUSSION

In terms of primary endpoints (in-hospital mortality and rebleeding), statistical analyses revealed no significant differences between patients who underwent urgent endoscopy and those who underwent early endoscopy. No significant differences were found in terms of length of hospital stay as a secondary endpoint, while the need for endoscopic intervention was found to be statistically significantly different for the patients who underwent emergency endoscopy.

An international consensus report recommended performing endoscopy within the first 24 hours for patients presenting with UGIB, while it offered no recommendations in support of or against endoscopy

within 12 hours for patients at high risk of bleeding and death (17). Three recent randomized controlled trials (18-20) and two systemic compilations (21, 22) reported that endoscopy performed between 2 hours and 12 hours for patients with upper gastrointestinal bleeding did not reduce mortality. Randomized controlled studies showed that the risk status of patients was not taken into account during the planning of endoscopy. In a recent study conducted by James et al. (23), endoscopy performed within 6 hours after gastroenterology consultation for patients with UGIB who were at high risk of bleeding and death (GBS of >12) was not found to be associated with lower mortality compared to endoscopy performed between the 6th and 24th hours. In that study, randomization was performed approximately 7 to 8 hours after patients presented with bleeding (23).

Table 3. Comparison of clinical and laboratory parameters between urgent and early endoscopy groups

Variable	Urgent group (n=185)	Early group (n=67)	p
Clinical parameters			
Main complaint on admission			
Melena	135 (73.0%)	46 (68.7%)	0.501
Hematemesis	99 (53.5%)	30 (44.8%)	0.220
Hematochezia	14 (7.6%)	5 (7.5%)	0.978
Syncope	18 (9.7%)	8 (11.9%)	0.610
Heart rate, per minute (mean ± SD)	91.96±18.11	87.96±17.62	0.120
Mean blood pressure, mmHg (mean ± SD)	80.93±14.38	79.42±12.74	0.450
Clinical high risk at admission (death or rebleeding)	50 (27.0%)	26 (38.8%)	0.072
High-risk endoscopic stigmata	63 (34.1%)	9 (13.4%)	0.001
Length of hospital stay, days, median (min-max)	6 (1-94)	7 (1-32)	0.905
Primary endpoint			
In-hospital mortality	8 (4.3%)	0 (0.0%)	0.114
Rebleeding	11 (5.9%)	5 (7.5%)	0.770
Primary composite outcome	15 (8.1%)	5 (7.5%)	0.867
Secondary endpoints			
Endoscopic intervention	87 (47.0%)	16 (23.9%)	0.001
Prolonged hospital stay	30 (16.2%)	13 (19.4%)	0.552
Laboratory parameters*			
White blood cells (10^3/µL)	9.6 (7.3-13.6)	9.4 (6.7-11.8)	0.258
Neutrophils (10^3/µL)	7.2 (5.3-10.8)	7.6 (4.9-10.2)	0.441
Lymphocytes (10^3/µL)	1.41 (0.96-1.96)	1.22 (0.88-1.93)	0.132
Hemoglobin (g/dL)	9.98±2.62	8.64±2.95	0.001
Hematocrit (%)	30.34±7.45	26.80±8.47	0.002
Platelets (10^3/µL)	256 (199-340)	263 (205-333)	0.840
Blood urea nitrogen (mg/dL)	36.9 (25.7-56.0)	35.9 (23.8-56.0)	0.587
Alanine aminotransferase (U/L)	16 (12-24)	15 (11-26)	0.727
Aspartate aminotransferase (U/L)	19 (15-25)	19 (14-26)	0.973
Gamma-glutamyl transpeptidase (U/L)	23 (14-40)	18.5 (13-43)	0.266
Lactate dehydrogenase (U/L)	198 (160-249)	195 (151-234)	0.327
Amylase (U/L)	55 (40-76)	52 (35-85)	0.636
Albumin (g/dL)	3.49±0.63	3.44±0.60	0.525
aPTT, seconds	24.0 (21.6-27.3)	24.1 (21.3-30.7)	0.964
INR	1.14 (1.06-1.29)	1.16 (1.06-1.34)	0.433
Lactate (mmol/L)	1.73 (1.17-2.39)	1.79 (1.25-3.04)	0.174

*Normally distributed parameters are expressed as mean ± SD, non-normally distributed parameters are expressed as median (IQR)
IQR: Interquartile range, aPTT: activated partial thromboplastin time, INR: international normalized ratio

Table 4. Univariate and multivariate analyses of predictors of primary composite outcome

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Clinical parameters				
Age	1.019 (0.991-1.048)	0.191		
Male gender	2.926 (0.832-10.285)	0.094	5.656 (1.333-23.998)	0.019
Diabetes mellitus	2.904 (1.141-7.390)	0.025	2.941 (1.073-8.064)	0.036
Ischemic heart disease	2.075 (0.827-5.208)	0.120		
Congestive cardiac failure	2.641 (0.887-7.865)	0.081	5.813 (1.560-21.656)	0.009
Arrhythmia	2.301 (0.867-6.104)	0.094		
Chronic obstructive airway disease	2.972 (0.898-9.835)	0.074		
Heart rate	1.028 (1.005-1.051)	0.015	1.030 (1.005-1.055)	0.017
Mean blood pressure	0.993 (0.960-1.026)	0.657		
Clinical high risk at admission (death or rebleeding)	2.015 (0.799-5.084)	0.138		
High-risk endoscopic stigmata	2.742 (1.089-6.904)	0.032	3.450 (1.246-9.551)	0.017
Laboratory parameters				
Hemoglobin	0.927 (0.784-1.096)	0.375		
Platelets	1.001 (0.998-1.003)	0.584		
Blood urea nitrogen	1.005 (0.990-1.020)	0.553		
Aspartate aminotransferase	1.005 (1.000-1.011)	0.054		
Gamma-glutamyl transpeptidase	1.002 (0.999-1.006)	0.164		
Albumin	0.943 (0.879-1.011)	0.099		
aPTT	1.003 (0.970-1.037)	0.849		
INR	1.041 (0.750-1.446)	0.810		

aPTT: Activated partial thromboplastin time, INR: international normalized ratio

In our study, no significant relationship was found between times from admission to endoscopy and rates of mortality or rebleeding. We think this was because there was no relationship between risk planning at admission and urgent or early endoscopy planning. Likewise, 27% of the patients who underwent emergency endoscopy were found to be at high risk at the time of admission. In studies where endoscopy planning was performed according to risk classifications at the time of admission (24, 25), a correlation was found between mortality and time from admission to endoscopy. In a cohort study conducted by Cho et al. with a large number of participants, times between 6 and 24 hours from admission to endoscopy were compared among patients with UGIB (24) who had no high-risk varicose veins and endoscopy performed within 6 hours was found to be an independent predictor of lower mortality but was not associated with rebleeding. In another study conducted by Laursen et al. (25), endoscopy performed within 6 to 24 hours from admission was found to be associated with lower in-hospital mortality among hemodynamically stable patients, while the times from admission to endoscopy associated with the lowest mortality were between 6 and 24 hours among hemodynamically unstable patients.

The study conducted by James et al. showed that high-risk stigmata on endoscopy were more common in patients undergoing urgent endoscopy. Acid suppression treatment was administered for patients in the early endoscopy group and signs of active bleeding and major bleeding were observed to decrease among patients who received acid suppression treatment for longer periods until endoscopy (23). In our study, high-risk findings on endoscopy and the need for endoscopic treatment were observed to be statistically significantly more common in the urgent endoscopy group than the early endoscopy group. This supports findings achieved

with high-dose acid suppression treatment before endoscopy (26). Based on these findings, we can say that urgent endoscopy has a positive effect on mortality in patients found to be at high risk at the time of admission. Furthermore, we found that acid suppression treatment performed before endoscopy for stable low-risk patients reduced the signs of major bleeding and the need for endoscopic treatment. We accordingly suggest that the duration of internal medicine/gastroenterological evaluations and risk analyses of patients presenting with UGIB after admission to the emergency department were closely associated with the clinical outcomes of urgent/early endoscopy.

Limitations

The retrospective design of this study was its main limitation. Another limitation was the lack of data on vital conditions and detailed anamneses of patients due to the retrospective design.

CONCLUSION

In conclusion, in our study, there was no significant difference in mortality or rebleeding rates among patients who underwent urgent endoscopy, and we found both the need for endoscopic treatment and the rate of high risk endoscopic stigmata on to be statistically significantly higher in this group. Prospective studies involving larger numbers of cases are needed to allow for the use of our results in clinical practice.

Ethics Committee Approval: It was approved by the Ethics Committee of the Health Sciences University Ankara City Hospital with decision no. E2-21-1000, dated 10/11/2021.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: O.I, M.F.A, K.B, E.S.S, M.A, I.A. Design: O.I, M.F.A, K.B, E.S.S, M.A, I.A. Data Collection/Processing: O.I, M.F.A, K.B, E.S.S, M.A, Analysis/Interpretation: O.I, M.F.A, K.B, E.S.S, M.A, I.A. Literature Review: M.F.A, Drafting/Writing: O.I, M.F.A, I.A, Critical Review: O.I, M.F.A, I.A.

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