Original Article

Outcome of Acute Upper Gastrointestinal Bleeding in Patients with Coronary Artery Disease: A Matched Case–control Study

Kessarin Thanapirom, Wiriyaporn Ridtitid, Rungsun Rerknimitr, Rattikorn Thungsuk[1], Phadet Noophun[2], Chatchawan Wongjitrat[3], Somchai Luangjaru[4], Padet Vedkijkul[5], Comson Lertkupinit[6], Swangphong Poonsab[7], Thawee Ratanachu-ek[8], Piyathida Hansomburana[9], Bubpha Pornthisarn[10], Thirada Thongbai[11], Varocha Mahachai, Sombat Treeprasertsuk

Division of Gastroenterology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, [1]Division of Gastroenterology, Sawanpracharak Hospital, Nakhon Sawan, [2]Division of Gastroenterology, Surin Hospital, Surin, [3]Division of Gastroenterology, HRH Princess MahaChakriSirindhorn Medical Center-MSMC Hospital, Bangkok, [4]Division of Gastroenterology, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, [5]Division of Gastroenterology, Maharaj Nakhonsithammarat Hospital, Nakhonsithammarat, [6]Division of Gastroenterology, Chonburi Hospital, Chonburi, [7]Division of Gastroenterology, Bangkok Hospital, Bangkok, [8]Department of Surgery, Rajavithi Hospital, Bangkok, [9]Division of Gastroenterology, Rajavithi Hospital, Bangkok, [10]Division of Gastroenterology, Department of Medicine, Faculty of Medicine, Thammasat University Hospital, Pathum Thani, [11]Division of Gastroenterology, Bangkok Metropolitan Administration General Hospital, Bangkok, Thailand

Address for correspondence:
Dr. Sombat Treeprasertsuk, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Rama 4 Road, Pathumwan District, Bangkok- 10330, Thailand.
E-mail: battan5410@gmail.com

Access this article online

Quick Response Code:

Website: www.saudijgastro.com

DOI: 10.4103/1319-3767.182452

ABSTRACT

Background/Aim: The risk of upper gastrointestinal bleeding (UGIB) increases in patients with coronary artery disease (CAD) due to the frequent use of antiplatelets. There is some data reporting on treatment outcomes in CAD patients presenting with UGIB. We aim to determine the clinical characteristics and outcomes of UGIB in patients with CAD, compared with non-CAD patients. **Patients and Methods:** We conducted a prospective multi-center cohort study (THAI UGIB-2010) that enrolled 981 consecutive hospitalized patients with acute UGIB. A matched case–control analysis using this database, which was collected from 11 tertiary referral hospitals in Thailand between January 2010 and September 2011, was performed. **Result:** Of 981 hospitalized patients with UGIB, there were 61 CAD patients and 244 gender-matched non-CAD patients (ratio 1:4). UGIB patients with CAD were significantly older, and had more frequently used antiplatelets and warfarin than in non-CAD patients. Compared with non-CAD, the CAD patients had significantly higher Glasgow–Blatchford score, full and pre-endoscopic Rockall score and full. Peptic ulcer in CAD patients was identified more often than in non-CAD patients. UGIB patients with CAD and non-CAD had similar outcomes with regard to mortality rate, re-bleeding, surgery, embolization, and packed erythrocyte transfusion. However, CAD patients had longer duration of hospital stays than non-CAD patients. Two CAD patients died from cardiac arrest after endoscopy, whereas three non-CAD patients died from pneumonia and acute renal failure during their hospitalization. **Conclusion:** In Thailand, patients presenting with UGIB, concomitant CAD did not affect clinical outcome of treatment, compared with non-CAD patients, except for longer hospital stay.

Key Words: Coronary artery disease, outcome, upper gastrointestinal bleeding

Received: 08.07.2015, Accepted: 17.10.2015

How to cite this article: Thanapirom K, Ridtitid W, Rerknimitr R, Thungsuk R, Noophun P, Wongjitrat C, *et al*. Outcome of acute upper gastrointestinal bleeding in patients with coronary artery disease: A matched case–control study. Saudi J Gastroenterol 2016;22:203-7.

Acute upper gastrointestinal bleeding (UGIB) is a common cause of hospital admissions with a mortality rate ranging from 4% to 14%.[1,2] The burden of comorbidity, including coronary artery disease (CAD) is greater among older patients. The risk of UGIB increases in patients with CAD due to frequent use of antiplatelets, including aspirin and/or clopidogrel with an overall prevalence of 1.2%–1.5% per year.[3,4] History of UGIB or peptic ulcer without concomitant antisecretory drugs such as proton-pump inhibitors (PPIs) or H2 receptor antagonists is an independent risk factor for UGIB in patients with CAD.[4,5]

Performing upper gastrointestinal (GI) endoscopy has many adverse effects on cardiopulmonary functions and can precipitate cardiovascular events, for example, cardiac arrhythmias, myocardial infarction, and ischemia, especially in patients with heart disease.[6,7] The incidence of GI endoscopy-related myocardial ischemia occurs in 16% of hospitalized patients with severe CAD.[8] In addition, preprocedure and postprocedure myocardial infarction occurs in 9.2% of high-risk CAD patients undergoing emergency GI endoscopy for UGIB.[9] Only a few studies have reported on the outcomes of treatment in patients with CAD presenting with acute UGIB. Several risk score systems are widely used for risk stratification of UGIB. The Glasgow–Blatchford score (GBS) identifies patients who need clinical intervention.[10] The pre-endoscopic Rockall score (RS) and full RS (including endoscopic findings) predict mortality or rebleeding in patients presenting with UGIB.[11,12]

This study aims to determine the clinical characteristics, risk scores, treatment outcomes, including rebleeding, mortality, length of hospital stay, need for endoscopic interventions, surgery, and embolization in patients with known CAD who present with acute UGIB compared with patients without CAD.

PATIENTS AND METHODS

Data sources

We conducted a prospective multicentered study using the THAI UGIB-2010 database, collected in 11 tertiary referral hospitals in Thailand between January 1, 2010, and September 30, 2011. A matched case–control analysis was performed using the THAI UGIB-2010 database including 981 consecutive hospitalized patients managed for UGIB, enrolled from King Chulalongkorn Memorial Hospital, Chulalongkorn University (Bangkok), MaharatNakhonratchasima Hospital (NakhonRatchasima), Sawanpracharak Hospital (NakhonSawan), Surin hospital (Surin), MaharajNakhonsithammarat Hospital (NakhonSithammarat), HRH Princess MahaChakriSirindhorn Medical Center (Bangkok), Chonburi hospital (Chonburi), Bangkok Metropolitan Administration General hospital (Bangkok), Bangkok hospital (Bangkok), Rajavithi hospital (Bangkok), and Thammasat University hospital (PathumThani). Management of UGIB was based on the Consensus for Clinical Practice Guideline for the management of UGIB from the Thai Association for Gastrointestinal Endoscopy (TAGE). All patients admitted to the hospital underwent EGD according to a standardized examination protocol. If endoscopy was not available, patient referral for angiography or surgery was considered. Clinical management, treatment with PPI pre-endoscopy, blood transfusion, timing of endoscopy, and type of endoscopic therapy were determined by each gastroenterologist, although the majority were in accordance with the TAGE guideline.

Data collection was performed by the Clinical Research Collaboration Network (CRCN, Nonthaburi, Thailand) using standardized case record forms. Relevant demographic data were collected, including age, gender, presenting symptoms, history of alcohol consumption, comorbidities, history of NSAIDs/anticoagulant usage, hemodynamic status, laboratory parameters, and time to EGD. The following variables were recorded: Endoscopic findings, need for treatment (endoscopic therapy, packed erythrocyte transfusion, surgery, and embolization), and clinical outcomes (rebleeding and death).

The study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (IRB number 480/51).

Case definition and identification of controls

Cases were patients who were 25 years or older, and were previously diagnosed with CAD with or without current angina symptoms. The diagnosis of CAD was based on criteria including more than 50% stenosis in the lumen of at least one coronary artery on prior coronary angiography, positive treadmill (exercise) stress test, or a history of myocardial infarction. Matched controls (non-CAD) were randomly selected from the remaining patients by the best match of 4:1 with cases based on gender. Patients qualifying in the control group were those declared without CAD history or any other comorbidity such as hypertension, diabetes, or chronic kidney disease.

Definitions

UGIB was defined as hematemesis (including coffee-ground vomiting), melena, or hematochezia.

Findings on gastroscopy that were considered *high-risk features (stigmata)* of upper GI bleeding included adherent clot, nonbleeding or bleeding visible vessel and varices with red color or white nipple sign.

Data analysis

We described categorical variables using number and percentage and compared groups using Pearson Chi-square test. We described continuous variables using means ± standard deviation (SD) and compared groups using the independent *t*-test (for normally distributed data) and Mann–Whitney test (for non-normally distributed data). Univariate and multivariate regression analyses were performed to identify prognostic factor for poor clinical outcomes. A $P < 0.05$ was considered statistically significant. Statistical analysis was performed using SPSS version 20.0 (IBM, NY, USA).

RESULTS

Patient characteristics

Among a total of 981 patients who presented with UGIB, 61 patients were known to have CAD (12 women, mean ± SD age = 68.9 ± 11.5 years) and 244 patients did not have CAD (50 women, mean ± SD = 55.7 ± 14.9 years). The demographic data, medical history, laboratory parameters, timing of EGD, GBS, full and pre-endoscopic RS between CAD patients compared with non-CAD are shown in Table 1. Patients with CAD were older, had more chronic kidney disease, frequently used antiplatelets and warfarin than patients without CAD. The mean GBS, full RS, and pre-endoscopic RS were significantly higher in patients with CAD than in non-CAD patients.

Causes of gastrointestinal bleeding and endoscopic findings

Endoscopic findings and treatments are shown in Table 2. Peptic ulcer bleeding was the main etiology in both groups of patients. In addition, peptic ulcers (75.4% vs 57.4%, respectively; $P < 0.01$), especially gastric ulcers (57.4% vs 36.1%, respectively) were more frequently found in CAD patients than in non-CAD patients. In contrast, esophageal varices were identified more in non-CAD patients than in CAD patients. High-risk stigmata on endoscopy did not significantly differ between the two groups. Requirement of endoscopic therapy was not statistically different between CAD ($n = 12$, 19.7%) and non-CAD groups ($n = 72$, 29.5%) ($P > 0.05$). Heater probe coagulation (9.8%) and adrenaline injection (9.8%) were the most commonly used methods for bleeding control in patients with CAD.

Treatment outcome

Performing early endoscopy within 24 h was not different between patients with CAD ($n = 40$, 65.6%) and without CAD ($n = 166$, 68%) ($P > 0.05$). A comparison of clinical outcomes between CAD and non-CAD patients with UGIB is presented in Table 3. Rebleeding did not occur during admission or within one month in both groups of patients. Two CAD patients (3.3%) and three non-CAD patients (1.2%) died during hospitalization. The cause of death in the two patients with CAD was cardiac arrest after endoscopic therapy, whereas in non-CAD group it was pneumonia ($n = 2$) and acute renal failure ($n = 1$). Mortality rate within one month was 4.9% ($n = 3$) in patients with CAD and 1.6% ($n = 4$) in patients without CAD ($P = 0.12$). The length of hospital stay was significantly longer in patients with CAD (13.2 ± 48.7 days) than in non-CAD (4.4 ± 5.5 days) ($P < 0.01$). In addition, surgery, embolization, and mean number of units of packed erythrocyte transfused did not differ between the two.

Table 1: Comparison of patient characteristics and clinical outcomes between acute UGIB patients with and without CAD

Parameters	Non-CAD (*n*=244)	CAD (*n*=61)	*P*
Age (years)	55.7±14.9	68.9±11.5	<0.001
Female	50 (20.5)	12 (19.7)	0.79
Alcohol drinking	116 (47.5)	9 (14.8)	<0.001
Comorbidity			
Chronic kidney disease	0	8 (13.1)	<0.001
Cirrhosis	0	1 (1.6)	0.56
Medication			
NSAIDs	42 (17.2)	7 (11.5)	0.28
Aspirin/Clopidogrel	0	42 (68.9)	<0.001
Warfarin	0	8 (13.1)	<0.001
Presentation			
Hematemesis	164 (67.2)	21 (34.4)	<0.001
Melena	148 (60.7)	48 (78.7)	<0.01
Hematochezia	20 (8.2)	6 (9.8)	0.68
Hemodynamic instability	35 (14.3)	7 (11.5)	0.56
Use of PPI infusion	226 (92.6)	56 (91.8)	0.83
Hemoglobin (g/dL)	9.4±4.0	8.4±2.2	0.08
Serum creatinine (mg/dL)	1.3±1.5	1.6±1.1	<0.001
INR	1.2±1.3	1.4±1.4	0.07
Glasgow–Blatchford score	6.6±3.5	8.5±3.2	<0.001
Full Rockall score	1.9±1.6	4.5±1.2	<0.001
Pre-endoscopic Rockall score	0.9±1.1	3.3±1.0	<0.001

CAD: Coronary artery disease, NSAIDs: Nonsteroidal anti-inflammatory drugs, PPI: Proton-pump inhibitor, INR: International normalized ratio

Table 2: Endoscopic findings and hemostasis between acute UGIB patients with and without CAD

Parameters	Non-CAD (*n*=244)	CAD (*n*=61)	*P*
Peptic ulcer	140 (57.4)	46 (75.4)	<0.05
Gastric ulcer	88 (36.1)	35 (57.4)	<0.05
Duodenal ulcer	36 (14.8)	6 (9.8)	0.32
Gastric and duodenal ulcer	16 (6.6)	5 (8.2)	0.65
Esophagitis	7 (2.9)	0	0.18
Gastritis	56 (23)	16 (26.2)	0.59
Duodenitis	13 (5.3)	5 (8.2)	0.40
Mallory–Weiss tear	12 (4.9)	1 (1.6)	0.26
Neoplasm of stomach	3 (1.2)	1 (1.6)	0.80
Varices			
Esophageal varices	37 (15.2)	3 (4.9)	<0.05
Gastric varices	0	0	-
Esophageal and gastric varices	2 (0.8)	1 (1.6)	0.56
High risk endoscopic lesions	54 (22.1)	12 (19.7)	0.68
Endoscopic hemostasis	72 (29.5)	12 (19.7)	0.12
Heater probe	22 (9)	6 (9.8)	0.84
Adrenaline injection	45 (18.4)	6 (9.8)	0.11
Variceal band ligation	23 (9.4)	3 (4.9)	0.26
Hemo-clipping	12 (4.9)	3 (4.9)	1.00
Glue injection	1 (0.4)	1 (1.6)	0.29

CAD: Coronary artery disease

Table 3: Outcome of treatment between acute UGIB patients with and without CAD

Outcome	Non-CAD (*n*=244)	CAD (*n*=61)	*P*
Rebleeding			
In hospital	0	0	-
Within 30 days	0	0	-
Death			
In hospital	3 (1.2)	2 (3.3)	0.26
Within 30 days	4 (1.6)	3 (4.9)	0.13
Surgery or embolization	8 (3.3)	2 (3.3)	0.98
Length of hospital stay (days)	4.4±5.5	13.2±48.7	<0.05
Need of packed erythrocyte transfusion (units)	3.0±3.6	2.3±1.3	0.15

CAD: Coronary artery disease

Prognostic factors for poor clinical outcomes

Factors that predicted poor clinical outcomes during admission, including surgery, embolization, rebleeding, and death during admission were assessed. Multivariate analysis revealed baseline hemoglobin <7 g/dL (OR = 5.0, 95%CI: 2.7–9.3, $P < 0.01$), hemodynamic instability (OR = 3.1, 95%CI: 1.5–6.5, $P < 0.01$) and high-risk stigmata on endoscopy (OR = 2.0, 95%CI: 1.0–4.0, $P < 0.05$) were associated with poor outcomes. CAD did not predict poor outcomes. However, CAD patients had a higher risk for hospital stays ≥5 days (OR = 2.6, 95%CI: 1.4–5.0, $P < 0.01$). Other factors, associated with a duration of hospital stay ≥5 days were surgery and therapeutic interventions (OR = 5.6, 95%CI: 1.3–24.4, $P < 0.05$), hemodynamic instability (OR = 3.3, 95%CI: 1.6–6.7, $P < 0.01$) and high-risk stigmata from endoscopy (OR = 2.8, 95%CI: 1.5–5.3, $P < 0.01$). Stepwise logistic regression analysis was performed to identify risk factors for duration of hospital stay ≥5 days in CAD patients (shown in Supplement Table 1) and found that nonpeptic ulcer bleeding (OR = 8.27, 95%CI = 2.0–33.8, $P = 0.001$) was an independent predictor for longer hospital stay. Half of the patients with nonpeptic ulcer bleeding had esophageal variceal bleeding. In addition, CAD patients who had high-risk endoscopic lesions, tended to have a higher risk for this outcome ($P = 0.08$). Early endoscopy or medications could not decrease the risk of longer hospital stay.

DISCUSSION

The main findings of our study are: (1) In Thailand, 6.2% of patients presenting with acute UGIB had concomitant CAD; (2) Compared with non-CAD, UGIB patients with CAD had more advanced age, comorbidity, antiplatelet, and warfarin usage; (3) Peptic ulcer especially gastric ulcer was the main etiology of patients with CAD. The prevalence of peptic ulcer bleeding was significantly higher in patients with CAD than without CAD; (4) In-hospital rebleeding, mortality, surgery, embolization, and mean number of packed erythrocyte transfusion requirement were not different between UGIB patients with CAD and without CAD. However, patients with CAD were at a risk for longer hospital stay ≥5 days.

Patients with acute UGIB are more likely to be of advanced age, with 63%–65% of these patients aged ≥60 years,[1,13] and to have multiple comorbidities. For example, patients with CAD are at a risk for UGIB due to the frequent use of antiplatelet drugs. A multicenter survey from the United Kingdom found that 20% of patients had concomitant ischemic heart disease.[13] Our data showed a lower prevalence of CAD in Thai patients presenting with UGIB (6%). One potential difference, however, is the use of a different definition for CAD, as our current study used coronary stenosis ≥50% for the diagnosis of CAD,[14] whereas in the UK study, the definition was not documented.

Acute UGIB affects cardiac function and may precipitate myocardial infarction from hypovolemia, hemodynamic compromise, myocardial hypoperfusion, and compensated reflex tachycardia.[15] Besides, upper GI endoscopy has many adverse effects on cardiopulmonary function in patients with heart disease such as cardiac arrhythmias.[6,16,17] In high-risk patients for CAD presenting with UGIB undergoing upper GI endoscopy, 4.6% had myocardial infarction pre-endoscopy and 4.6% postendoscopy.[9] Underlying heart disease, low blood pressure, low hemoglobin level, and persistent shock were predictors of procedure-related myocardial infarction.[9] Although both UGIB and upper GI endoscopy may contribute to cardiac events in patients with CAD, a previous study showed that clinical outcomes were not different from non-CAD. According to Tseng *et al.*'s .study,[18] inhospital rebleeding, mortality, surgery, embolization, and mean number of packed erythrocyte transfusion were not distinct between UGIB patients with and without CAD, consistent with results of our current study. However, our study found that patients with CAD had longer hospital stay (≥5 days) and had a higher mortality rate than non-CAD patients. Mean GBS, pre-endoscopic and full RS were higher in CAD patients when compared with non-CAD patients. Theoretically, the reason might be that CAD patients had more advanced age, and comorbidities. In CAD patients, nonpeptic ulcer bleeding, especially variceal bleeding was a predictor for longer hospital stay. The current study provided additional information about causes of death in UGIB patients with CAD, which were mainly cardiac complications. Conversely, deaths in patients without CAD were related to noncardiac organ failure or infection. Another difference between the two studies is that CAD in our study was matched with controls at a ratio of 1:4, whereas a ratio of

1:1 was used in the Tseng *et al*.'s study. Controls, or non-CAD patients in this study included patients without a history of CAD or other comorbidities, such as hypertension, diabetes, chronic kidney disease to exclude high-risk patients for CAD, but Tseng *et al*.'s included these comorbidities.

There are some limitations in this study. First, we did not evaluate ECG changes or cardiac enzyme levels before and after performing EGDs, thus the incidence of myocardial infarction or ischemia related to procedures is unknown and precluded us from calculating risk stratification scores for these cardiac events. Additionally, we could not conclude that the cause of death was associated with performing endoscopy. However, the main outcome of this study was to determine clinical outcomes of UGIB patients with a known history of CAD compared with patients without CAD. Second, the sample size was relatively small, which might lead to a statistical type 2 error and prevents us from identifying all significant differences. Third, most patients in this patient population (92.4%) received PPI infusion, which could have influenced endoscopic findings and clinical outcomes. Finally, the decision making regarding the selected endoscopic therapy and need for blood transfusions in the THAI UGIB study 2010 was subjective and varied between individual gastroenterologists.

CONCLUSIONS

This study demonstrates that clinical outcomes, including mortality, rebleeding, surgery, embolization, and packed erythrocyte transfusion requirements, are not different between UGIB patients with concomitant CAD and those without CAD. However, CAD patients had longer duration of hospital stays (≥5 days) compared with those without CAD.

Acknowledgments
Research reported in this publication was supported by the National Research Council of Thailand (NRCT) and the Clinical Research Collaboration Network, Thailand (CRCN-2553-n-03).

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Halland M, Young M, Fitzgerald MN, Inder K, Duggan JM, Duggan A. Characteristics and outcomes of upper gastrointestinal hemorrhage in a tertiary referral hospital. Dig Dis Sci 2010;55:3430-5.
2. Nahon S, Hagège H, Latrive JP, Rosa I, Nalet B, Bour B, *et al*.; Groupe des Hémorragies Digestives Hautes de l'ANGH. Epidemiological and prognostic factors involved in upper gastrointestinal bleeding: Results of a French prospective multicenter study. Endoscopy 2012;44:998-1008.
3. Bhatt DL, Cryer BL, Contant CF, Cohen M, Lanas A, Schnitzer TJ, *et al*. COGENT Investigators. Clopidogrel with or without omeprazole in coronary artery disease. N Engl J Med 2010;363:1909-17.
4. Ng W, Wong WM, Chen WH, Tse HF, Lee PY, Lai KC, *et al*. Incidence and predictors of upper gastrointestinal bleeding in patients receiving low-dose aspirin for secondary prevention of cardiovascular events in patients with coronary artery disease. World J Gastroenterol 2006;12:2923-7.
5. Yasuda H, Yamada M, Sawada S, Endo Y, Inoue K, Asano F, *et al*. Upper gastrointestinal bleeding in patients receiving dual antiplatelet therapy after coronary stenting. Intern Med 2009;48:1725-30.
6. Yazawa K, Adachi W, Koide N, Watanabe H, Koike S, Hanazaki K. Changes in cardiopulmonary parameters during upper gastrointestinal endoscopy in patients with heart disease: Towards safer endoscopy. Endoscopy 2000;32:287-93.
7. Gangi S, Saidi F, Patel K, Johnstone B, Jaeger J, Shine D. Cardiovascular complications after GI endoscopy: Occurrence and risks in a large hospital system. GastrointestEndosc 2004;60:679-85.
8. Lee JG, Krucoff MW, Brazer SR. Periprocedural myocardial ischemia in patients with severe symptomatic coronary artery disease undergoing endoscopy: Prevalence and risk factors. Am J Med 1995;99:270-5.
9. Lee CT, Huang SP, Cheng TY, Chiang TH, Tai CM, Su WC, *et al*. Factors associated with myocardial infarction after emergency endoscopy for upper gastrointestinal bleeding in high-risk patients: A prospective observational study. Am J Emerg Med 2007;25:49-52.
10. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet 2000;356:1318-21.
11. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996;38:316-21.
12. Rockall TA, Logan RF, Devlin HB, Northfield TC. Selection of patients for early discharge or outpatient care after acute upper gastrointestinal haemorrhage. National audit of acute upper gastrointestinal haemorrhage. Lancet 1996;347:1138-40.
13. Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Acute upper gastrointestinal bleeding in the UK: Patient characteristics, diagnoses and outcomes in the 2007 UK audit. Gut 2011;60:1327-35.
14. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, *et al*. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation 2014;130:1749-67.
15. Cappell MS. Gastrointestinal bleeding associated with myocardial infarction. GastroenterolClin North Am 2000;29:423-44, vi.
16. Lieberman DA, Wuerker CK, Katon RM. Cardiopulmonary risk of esophagogastroduodenoscopy. Role of endoscope diameter and systemic sedation. Gastroenterology 1985;88:468-72.
17. Schenck J, Müller CH, Lübbers H, Mahlke R, Lehnick D, Lankisch PG. Does gastroscopy induce myocardial ischemia in patients with coronary heart disease? Endoscopy 2000;32:373-6.
18. Tseng PH, Liou JM, Lee YC, Lin LY, Yan-Zhen Liu A, Chang DC, *et al*. Emergency endoscopy for upper gastrointestinal bleeding in patients with coronary artery disease. Am J Emerg Med 2009;27:802-9.