GASTROINTESTINAL BLEEDING AND ACS

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Incidence: IN ***J-AMI*** prospective multicenter registry: incidence of bleeding was 1.58%, with gastrointestinal bleeding accounting for about 30% of all bleeding complications.

In the ***ACUITY trial*** GIB within 30 days occurred in 178 patients (1.3%).

In the ***CURE study***: patients with ACS the incidence of GI bleeding was 1.33% in the dual antiplatelet group compared with 0.75% in the aspirin group.

Risk factors for upper GIB:

Increasing age
Female sex
Major organ dysfunction (cardiac, respiratory, or hepatic),
Diabetes
Hypertension
Positive results for *Helicobacter pylori* infection
Hemostatic disorders
LDA use.

Table 2 Multivariable Predictors of GIB in the Entire ACUITY Population and in Patients Triaged to PCI, CABG, or Medical Management

Multivariable Predictors	Coefficient	Standard Error	Odds Ratio	95% Confidence Interval	p Value
All patients					
Age (per 10-yr increase)	0.4739	0.0897	1.61	1.35–1.92	<0.0001
Baseline anemia	0.7182	0.1884	2.05	1.42–2.97	0.0001
Time from study drug administration to angiogram (per 10-h increase)	0.1311	0.0405	1.14	1.05–1.23	0.0012
ST-segment deviation >1 mm	0.5809	0.2378	1.79	1.12–2.85	0.015
Current smoker	0.5500	0.2154	1.73	1.14–2.64	0.011
Diabetes mellitus	0.3747	0.1863	1.46	1.01–2.10	0.044
Randomization to bivalirudin monotherapy (versus heparin + glycoprotein IIb/IIIa)	−0.3290	0.1992	0.72	0.49–1.06	0.098
Patients triaged to PCI					
Age (per 10-yr increase)	0.4161	0.1123	1.52	1.22–1.89	0.0002
Baseline anemia	0.7488	0.2362	2.12	1.33–3.36	0.002
Diabetes mellitus	0.6232	0.2283	1.87	1.19–2.92	0.006
Current smoker	0.5620	0.2691	1.75	1.04–2.97	0.037
Time from study drug administration to angiogram (per 10-h increase)	0.1120	0.0540	1.12	1.01–1.24	0.0038
Randomization to bivalirudin + glycoprotein IIb/IIIa (vs. heparin + glycoprotein IIb/IIIa)	0.4094	0.2227	1.51	0.97–2.33	0.066
Patients triaged to CABG					
Age (per 10-yr increase)	0.6854	0.2206	1.99	1.29–3.06	0.002
Patients triaged to medical management					
Renal insufficiency	1.1490	0.4377	3.16	1.34–7.44	0.009
Baseline anemia	0.9973	0.4422	2.71	1.14–6.45	0.024
Time from study drug administration to angiogram (per 10-h increase)	0.2754	0.0748	1.32	1.14–1.53	0.0002

ACUITY = Acute Catheterization and Urgent Intervention Triage Strategy; other abbreviations as in Table 1.

Outcomes of GIB

Risk of bleeding : major bleeding has been reported as an independent risk factor for mortality after acute myocardial infarctions (AMIs)

Outcomes of GIB

30-d mortality rates were as high as 20.5% in patients with GIB, compared to 2.4% in those without GIB.

In the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial, 13,819 patients with moderate- and high-risk ACS, enrolled at 450 centers in 17 countries between August 2003 and December 2005

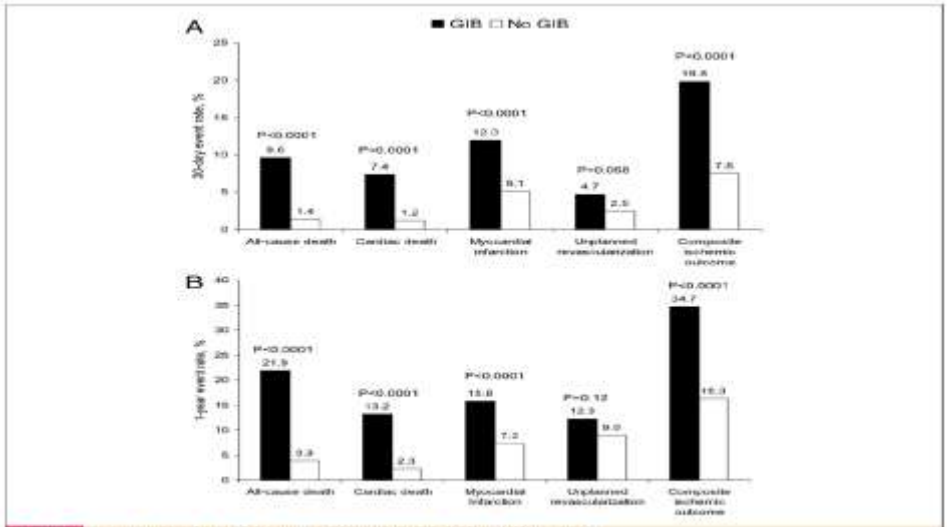


Figure 1 Ischemic Events at 30 Days and 1 Year in Patients With and Without GIB

Patients with versus without gastrointestinal bleeding (GIB) have significantly increased 30-day (**A**) and 1-year (**B**) rates of cardiac and all-cause mortality, myocardial infarction, and composite ischemic outcome.

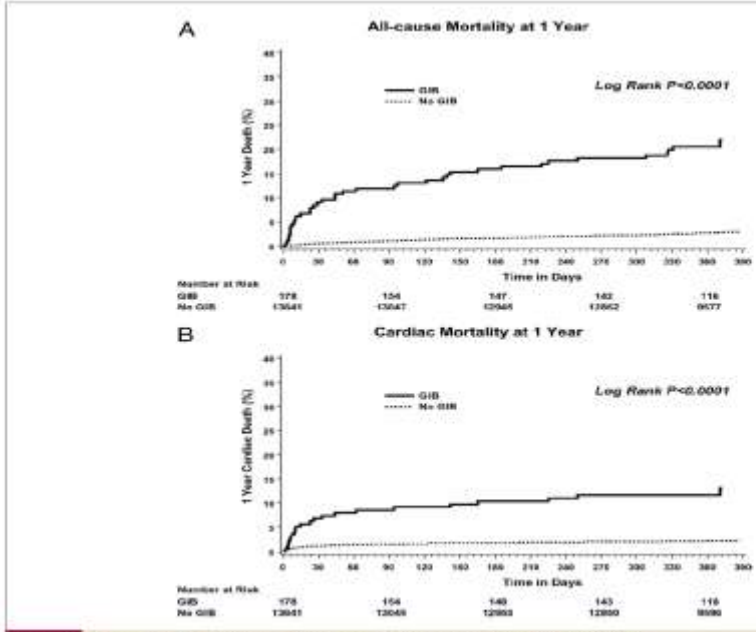


Figure 2 Cumulative Risk of All-Cause and Cardiac Death in Patients With and Without GIB

By Kaplan-Meier estimates, patients with versus without gastrointestinal bleeding (GIB) had significantly higher all-cause (**A**) and cardiac (**B**) death at 1 year.

Retrospective study of 1023 patients hospitalized with ACS at the American University of Beirut Medical Center from September 2001 to November 2005

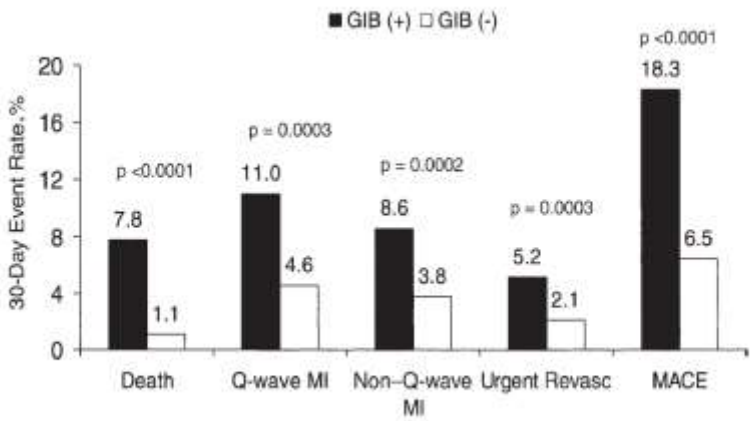
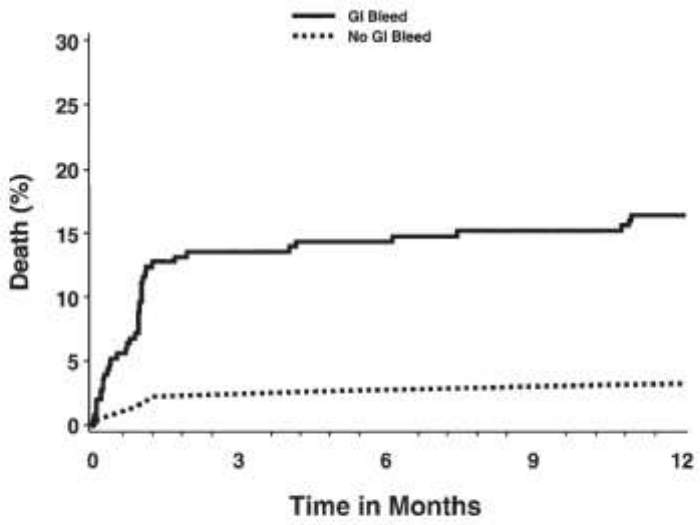


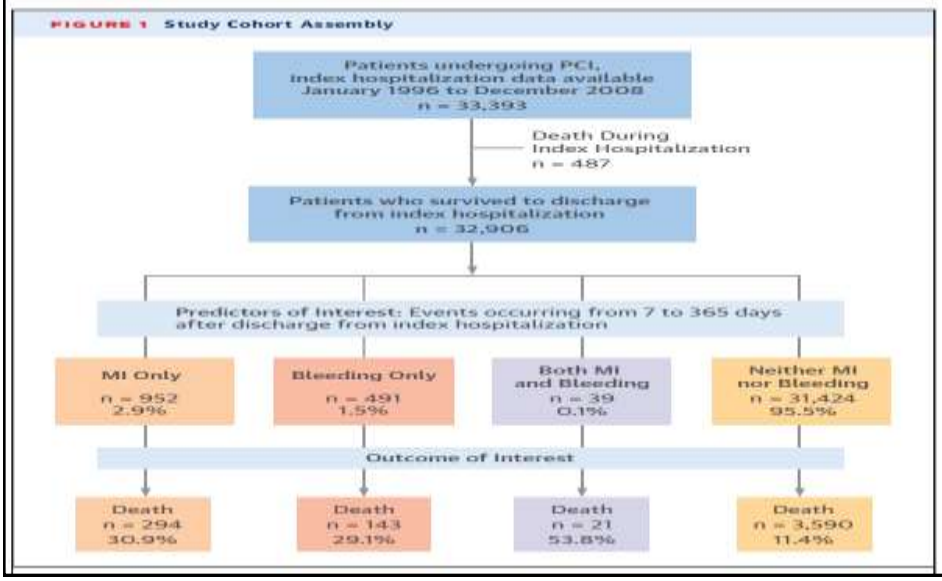
Figure 1. The 30-day clinical outcomes in patients with and without gastrointestinal bleeding in 3 acute coronary syndrome trials. GIB = gastrointestinal bleeding; MACE = major adverse cardiac events; MI = myocardial infarction; Revasc = revascularization. (Adapted from *J Am Coll Cardiol.*[4])

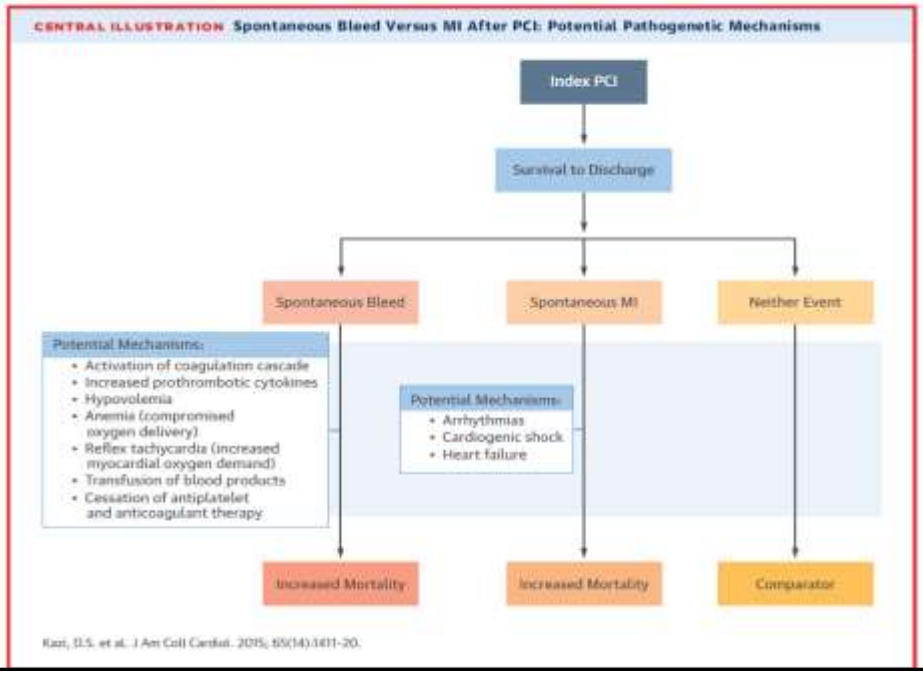


Number at risk					
GI Bleed	253	213	211	206	136
No GI Bleed	23,170	22,108	21,981	21,860	14,568

Figure 2. Kaplan-Meyer survival curves in patients with and without gastrointestinal (GI) bleeding in 3 acute coronary syndrome trials ($p < 0.01$). (Adapted from *J Am Coll Cardiol.*[4])

32,906 patients who had a PCI and survived the index hospitalization, 530 had bleeds and 991 had MIs between 7 and 365 days post-discharge.





Case Study

Male patient aged 58 years.

Not hypertensive nor diabetic.

Chronic liver disease, HCV +ve.

Past history of an attack of hematemsis and melena on 2008 and 2 setting of injection sclerotherapy.
Band ligation for gastric varices on Jan. 2014.

Patient had thrombocytopenia 25000.

On July 2014 patient had chest pain and diagnosed as UA.

CA= was done revealed coronary ectasia
LAD: mid non significant stenosis

Patient received marevan with INR target = 2-3

One year later, patient started oral anti HCV therapy (ribavirin & sovaldi) for 6 months during this period patient stopped marevan.

2 months later after this anti-viral course, patient developed ACS & admitted to CCU diagnosed as UA
Platelet count was 20000 and to be prepared to upper endoscopy he received 6 packs platelets.

On January 2016, patient developed typical chest pain admitted to CCU and diagnosed as inferior MI.

ECG= inferior STEMI
Echo= EF=59%, resting SWMA in inf wall
Lab. = Platelet = 27000, INR =2.4 Scr. = 1.2

Patient received clexan 60ml, plavix 4 tab

Coronary angio: was done 7 hs after onset of chest pain revealed
left main = normal
LAD= ectatic with mid subtotal occlusion with ?thrombus containing lesion.
LCX= fill of thrombi on the wall of the artery with TIMI II flow.
RCA= severly ectatic, proximal total occlusion with thrombus.

We have 3 challenges here

1- Thrombocytopenia
2- Previous bleeding gastric varices
3- High thrombus burden

Decision PCI of totally occluded RCA
PCI was done with thrombus suction of RCA.

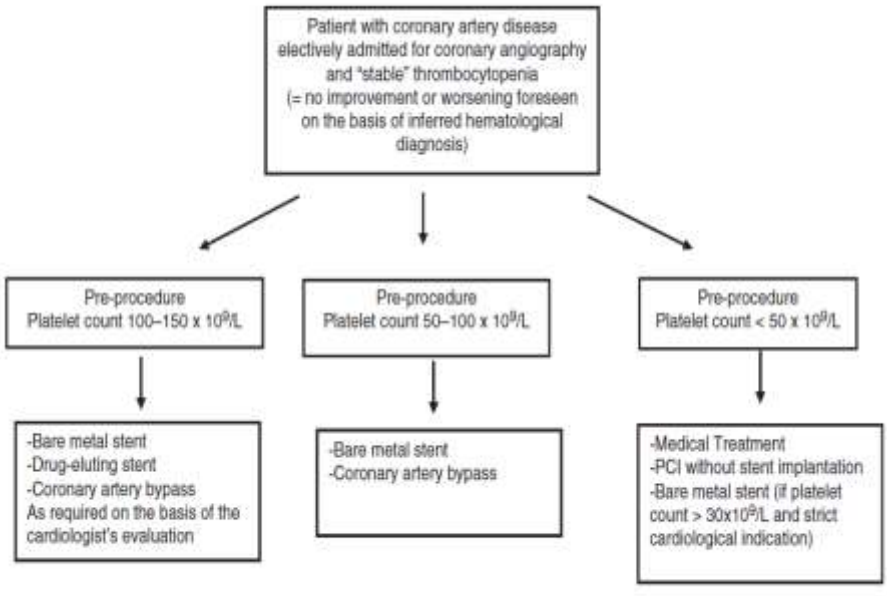


Figure 1. Management of patients with elective indication to coronary angiography and "stable" thrombocytopenia.

What will you do?

1- Continue suction
2- Stenting with BMS
3- Deferred stenting for few days

Patient continued on **plavix** 75mg once daily and **clexan** 60ml twice daily. Pantoprazol 40mg & H2 blocker.

Prepared for deferred PCI.

CA was done after 9 days:

Patient contiues on Rivaroxaban 10mg daily & plavix 75mg EOD

After 45 days patient consulted his gastroentrogist and adviced upper GI endoscopy

Patient needs IST and withhold antithrombotic one weak before and one week after this procedure.

Maintenance antithrombotic strategy after ST-elevation myocardial infarction *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
In high ischaemic risk patients who have tolerated DAPT without a bleeding complication, treatment with DAPT in the form of ticagrelor 60 mg twice a day on top of aspirin for longer than 12 months may be considered for up to 3 years.	IIb	B
In low bleeding risk patients who receive aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered.	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and oral anticoagulation.	III	C

Regarding use of **rivaroxaban** in this patient

All antiplatelet agents are associated with an increased risk of bleeding and are susceptible to being withheld in patients who have or develop TP.

ATLAS ACS 2–TIMI 51 a placebo-controlled trial that randomly assigned 15,526 patients with recent ACS to receive twice-daily doses of either 2.5 mg or 5 mg of rivaroxaban or placebo for a mean of 13 months and up to 31 months.

The primary objective was to demonstrate superiority of rivaroxaban compared with placebo in reducing the major adverse cardiac events (MACE).

Treatment with rivaroxaban, combined doses as well as the 2.5-mg dose, significantly reduced MACE.

Management of GIB in Patients with ACS

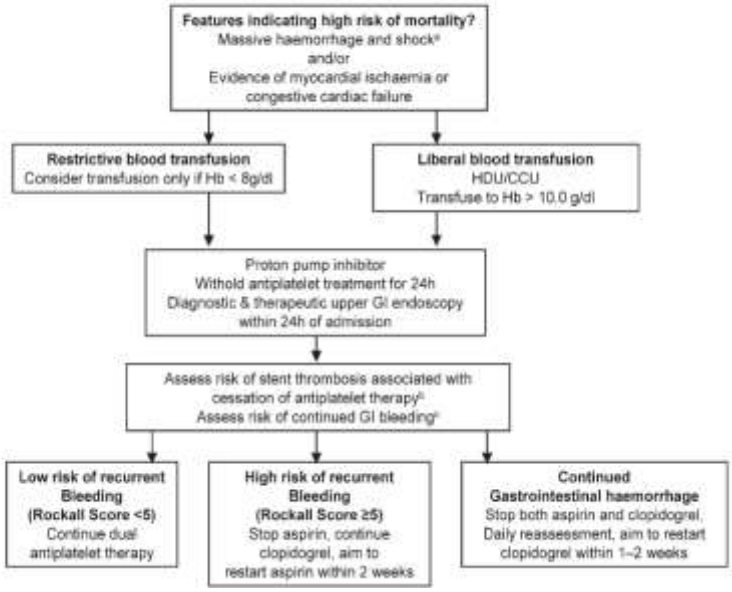
Management of GIB:

1- PPI should be started.
2- Discontinuation of ASA and clopidogrel during the first 24 hours of bleeding
3- endoscopic evaluation performed as early as possible to provide definitive treatment and achieving hemostasis whenever possible.
4- fluid resuscitation and blood transfusion for patients with unstable hemodynamic condition.
5- Assess risk of recurrent bleeding and death, by the Rockall score[35] by combining esophagogastroduodenoscopy (EGD) data with clinical parameters.

Rockall scoring system for risk of rebleeding and death after admission to hospital with acute gastrointestinal bleeding

Score	0	1	2	3
Age (years)	<60	60–79	>80	
Shock	No shock Systolic BP>100 mmHg HR<100 bpm	Tachycardia HR>100 bpm Systolic BP>100 mmHg	Hypotension Systolic BP<100 mmHg HR>100 bpm	
Comorbidity	Nil major		Cardiac failure Ischemic heart disease	Renal failure Liver failure Disseminated malignancy
Endoscopic finding	No lesion Mallory–Weiss tear with no SRH	All other diagnosis	Malignancy of UGI tract Adherent clot Visible or spurting vessel	
Major SRH	None or dark spot			

SRH, stigmata of recent hemorrhage.



PRIMARY PREVENTION OF GIB IN PATIENTS TREATED WITH ANTIPLATELET MEDICATIONS:

WIDESPREAD USE OF PROTEIN PUMP INHIBITORS (PPIS) IN

Maintenance antithrombotic strategy after ST-elevation myocardial infarction

ESC European Society of Cardiology

Recommendations	Class	Level
Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.	I	A
DAPT in the form of aspirin plus ticagrelor or prasugrel (or clopidogrel if ticagrelor or prasugrel is not available or is contra-indicated) is recommended for 12 months after PCI unless there are contra-indications such as excessive risk of bleeding.	I	A
A PPI in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.	I	B
In patients with an indication for oral anticoagulation, oral anti-coagulants are indicated in addition to antiplatelet therapy.	I	C

Debates

1- *Can clopidogrel and proton pump inhibitors be used together to reduce the risk of bleeding?*

2- *Continuation of antiplatelet therapy?*

3- *How soon should upper gastrointestinal endoscopy take place?*

4- *Impact of blood transfusion on mortality after PCI?*

Can clopidogrel and proton pump inhibitors be used together to reduce the risk of bleeding?

The majority of data on the clinical significance of the PPI-clopidogrel interaction derive from observational studies and the results have been conflicting.
Two randomised controlled trials (RCTs) have failed to show an increased incidence of ischaemic CV outcomes in patients on concomitant use of clopidogrel and a PPI.

Retrospective studies: showed that such treatment might reduce the cardiovascular efficacy of clopidogrel, this observation could be prone to biases.

So PPI should be given for prevention of bleeding in high risk groups or for treatment of acute bleeding.

Should antiplatelet agents be withheld in a major bleed?

Discontinuation of ASA confers a 1.8-fold increase in the risk of stent thrombosis. The discontinuation of clopidogrel and ASA in patients with drug-eluting stents within the first 30 days of follow-up carries a 29% risk of thrombosis.

1- Antiplatelet therapy and PPI cotherapy should be resumed immediately after the successful endoscopic control of ulcer bleeding to avoid further ischemic events.

2- Aspirin is stopped acutely in an upper gastrointestinal bleed.

3- In patients with coronary artery stents, especially if bleeding occurs more than a month after coronary intervention continuation of one antiplatelet drug (potentially with gastroprotectant cover) after adequate haemostasis.

4- Withholding aspirin and using clopidogrel in some settings, because of clopidogrel's relatively safer gastrointestinal profile.

Impact of blood transfusion on mortality after PCI?

Blood transfusion: should be given for hemodynamically significant blood loss.

In patients hemodynamically stable, RBC transfusion is considered when the hemoglobin concentration falls below 7.0 g/dL in patients with stable angina and is 8-10 g/dL in those with ACS.

In stored RBCs, hemoglobin tend not to release oxygen to the tissues. Banked blood, predisposing to vasoconstriction and ischemic insult. Therefore, blood transfusion does not always provide beneficial effects in ACS patients.

How soon should upper gastrointestinal endoscopy take place?

Endoscopy is safe after acute coronary syndromes, although its timing should be considered on a case-by-case basis.

The major risk from this procedure is cardiorespiratory depression associated with sedation.

Early endoscopy (within 24 h) is recommended for significant UGI hemorrhage for risk stratification and therapeutic interventions.

The **British Society of Gastroenterology** recommends that all patients with suspected upper gastrointestinal bleeding should undergo upper gastrointestinal endoscopy within 24 hours of presentation, early hours with risk of haemodynamic compromise.

Endoscopic hemostasis: with a combination of *epinephrine injection* therapy and *electrical coagulation* or *use of endoclips* is also effective to achieve better outcomes.

Conclusions:

GIB, in the setting of ACS, is a devastating condition and is associated with high rates of mortality, nonfatal MI, stent thrombosis, and prolonged hospitalization.

Physicians should be aware of GIB in high-risk populations, including the elderly, smokers, and patients with anemia.

Given the adverse prognostic significance of GIB, it should be reported in any trial assessing the safety of new antithrombotic agents and regimens.