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.
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.
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®)

Figure 2. Kaplan-Meyer survival curves in patients with and without gastrointestinal (GI) bleeding in 3 acute coronary syndrome trials (p < 0.03). (Adapted from J Am Coll Cardiol®)
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.

**Figure 1: Study Cohort Assembly**

- Patients undergoing PCI, index hospitalization data available January 1998 to December 2008, n = 33,393
- Death During Index Hospitalization, n = 487
- Patients who survived to discharge from index hospitalization, n = 32,906

**Predictors of Interest: Events occurring from 7 to 365 days after discharge from index hospitalization**

- MI Only, n = 952, 2.9%
- Bleeding Only, n = 491, 1.5%
- Both MI and Bleeding, n = 39, 0.1%
- Neither MI nor Bleeding, n = 31,424, 95.5%

**Outcome of Interest**

- Death, n = 294, 30.9%
- Death, n = 143, 29.1%
- Death, n = 21, 53.8%
- Death, n = 3,590, 11.4%

**Central Illustration: Spontaneous Bleed Versus MI After PCI: Potential Pathogenetic Mechanisms**

- **Index PCI**
  - **Survival to Discharge**
    - Spontaneous Bleed
    - Spontaneous MI
    - Neither Event

**Potential Mechanisms for Spontaneous Bleed**

- Activation of coagulation cascade
- Increased prothrombotic cytokines
- Hypovolemia
- Anemia (compromised oxygen delivery)
- Reflex tachycardia (increased myocardial oxygen demand)
- Transfusion of blood products
- Cessation of antplatelet and anticoagulant therapy

**Potential Mechanisms for Spontaneous MI**

- Arrhythmias
- Cardiogenic shock
- Heart failure

**Increased Mortality**

Case Study

Male patient aged 58 years.

Not hypertensive nor diabetic.

Chronic liver disease, HCV +ve.

Past history of an attack of hematemesis 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 = severely 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.
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 continues on Rivaroxaban 10mg daily & **plavix** 75mg EOD

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

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

<table>
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<th>Score</th>
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<th>1</th>
<th>2</th>
<th>3</th>
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<tr>
<td>Age (years)</td>
<td>&lt;60</td>
<td>60–79</td>
<td>&gt;80</td>
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<tr>
<td>Shock</td>
<td>No shock</td>
<td>Tachycardia</td>
<td>Hypotension</td>
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<tr>
<td></td>
<td>Systolic</td>
<td>HR&gt;100 bpm</td>
<td>Systolic</td>
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<tr>
<td></td>
<td>BP&gt;100 mmHg</td>
<td>Systolic</td>
<td>BP&lt;100 mmHg</td>
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<tr>
<td></td>
<td>HR&lt;100 bpm</td>
<td>BP&gt;100 mmHg</td>
<td>HR&gt;100 bpm</td>
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<tr>
<td>Comorbidty</td>
<td>Nil major</td>
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<td>Cardiac failure</td>
<td>Renal failure</td>
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<td></td>
<td>Ischemic heart disease</td>
<td>Liver failure</td>
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<tr>
<td>Endoscopic finding</td>
<td>No lesion</td>
<td>All other diagnosis</td>
<td>Malignancy of UGI tract</td>
<td>Disseminated malignancy</td>
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<tr>
<td></td>
<td>Mallory-Weiss tear with no SRH</td>
<td>All other diagnosis</td>
<td>Malignancy of UGI tract</td>
<td>Disseminated malignancy</td>
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<tr>
<td>Major SRH</td>
<td>None or dark spot</td>
<td></td>
<td>Adherent clot</td>
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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

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
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<tr>
<td>Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>A PPI in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>In patients with an indication for oral anticoagulation, oral anticoagulants are indicated in addition to antiplatelet therapy.</td>
<td>I</td>
<td>C</td>
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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.