Management of Proton Pump Inhibitors and Antiplatelet Agents

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Learning Objectives

1. To critically assess the evidence regarding PPI use and the:
   - Interaction with clopidogrel therapy
   - Risk of bone fractures
   - Risk of hypomagnesemia
   - Risk of Clostridium difficile infections

2. To review best-practice recommendations for management of antiplatelets in the peri-endoscopic period.
PPI Use

- ~119 million prescriptions filled each year in U.S.
- Common clinical use*:
  - Treatment of GERD/esophagitis
  - Hypersecretory state
  - Previous or active upper GI event
  - Dyspepsia
  - ICU prophylaxis (intubation, coagulopathy or renal failure)
  - *H. pylori* infection
  - Zollinger-Ellison syndrome
  - Gastroprotection in high-risk patients**

*Dries, Abraham et al. Aliment Pharmacol Ther. 2009;

Interaction with Clopidogrel
### The Cardiac Patient: Indications for Dual Antiplatelet Therapy

**Acute Coronary Syndrome (ACS)**
- Up to 12 months following unstable angina or NSTEMI managed without PCI
- At least 14 days (12 months in some) following STEMI

**Post-Stent**
- Up to 12 months after bare metal stent (BMS) placement
- At least 12 months after DES placement

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### Dual Antiplatelet Therapy

#### THIENOPYRIDINES
- **Clopidogrel**
- **Prasugrel**
- **Ticagrelor**

#### Arachidonic Acid
- **COX-1** (constitutive)
- **COX-2** (inducible)

#### ASA
- **Thromboxane A2 (TXA2)**
- **Prostacyclin (PGI2)**

#### Platelet Aggregation

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**Required Time to Recover Adequate Platelet Function:**
- **ASA:** 7 days
- **Clopidogrel:** 5-7 days
- **Prasugrel:** 7-9 days
- **Ticagrelor:** 3 days
### GI Bleeding with Dual Antiplatelet Therapy: Evidence from Cardiovascular RCTs

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient Population</th>
<th>Treatment Arms</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURE (2001)</td>
<td>12,562 NSTEMI-ACS</td>
<td>Clopidogrel + ASA vs. ASA alone</td>
<td>1.78 (1.25-2.54)</td>
</tr>
<tr>
<td>ACTIVE (2009)</td>
<td>7,554 Afib</td>
<td>Clopidogrel + ASA vs. ASA alone</td>
<td>1.96 (1.46-2.63)</td>
</tr>
</tbody>
</table>
## Recommendations of ACCF/ACG/AHA 2008

**Expert Consensus Document**

<table>
<thead>
<tr>
<th>Clinical Issue</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| GI Complications of ASA and Non-ASA NSAIDs | • NSAIDs + cardiac-dose ASA ↑ UGIE risk.  
• *H. pylori* should be eradicated if found  
• Gastroprotection should be prescribed. |
| GI Effects of ASA | • Low-dose ASA ↑ UGIE risk.  
• Gastroprotection should be prescribed. |
| GI Effects of Clopidogrel | • Substitution of clopidogrel for ASA is not recommended to reduce the risk of recurrent ulcer bleeding in high-risk patients.  
• Clopidogrel is inferior to the combination of ASA + PPI.  
• Gastroprotection should be prescribed to patients taking dual antiplatelet therapy. |
Hypothesis: PPIs reduce the biological action of clopidogrel through competitive inhibition of CYP2C19.
Do PPIs Inhibit Clopidogrel Activity?: Observational Studies and RCT Post-Hoc Analyses

No Association

Observational:

Post-Hoc:

Significant Association

Observational:
- Pezalla et al. *JACC* 2008 → *significant comorbidity differences between groups*
- Juurlink et al. *CMAJ* 2009 → *significant comorbidity differences between groups*


Confounding by indication:
- More PPI use in “sicker” patients; “prescription channeling”

COGENT Trial (N=3,627)

*Composite of overt or occult bleeding, symptomatic duodenal ulcers or erosions, obstructions, or perforation*

**Why the COGENT Trial is Important:**
- Significant reduction in GI events with DAPT + omeprazole
  - No difference in CV events between arms over 180 days of observation (55 events in PPI vs. 54 in placebo)
- COGENT not powered for secondary CV outcomes
  - CV events LESS than anticipated; wide confidence intervals (0.68-1.44)
  - REASSURING!
Clopidogrel Metabolism: Hypothesis II

**Inactive metabolite**

Liver Cell

- **CYP3A4**
- **CYP3A5**
- **CYP2C9**
- **CYP2C19**
- **CYP1A2**
- **CYP2B6**

**ADP**

Platelet

**P2Y12**

**Reduced-Function CYP2C19 Genetic Polymorphism**

- Less active metabolite of clopidogrel
- **CYP2C19*2** carriers have higher CV rate than non-carriers
  \[ \text{RRs} = 1.5-3.7^* \]
- Meta-analysis of 10 studies: OR 1.29 (1.12-1.49)**

**Prevalence of 1 CYP2C19*2 Allele: U.S. Data**

- **African Americans** 33%
- **Caucasians** 24%
- **Mexican Americans** 18%
- **Asians** 51%

**Reduction in clopidogrel efficacy associated with CYP2C19*2:**

- 1 copy of allele = 47% reduction
- 2 copies = 65% reduction

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**References:**

- Takakubo et al. Pharmacogen 1996.
Independent Genetic Risk Factors Associated with Early Stent Thrombosis (0-30 Days Post-PCI)

Genotypes associated with impaired clopidogrel metabolism and platelet function

CYP2C19 Metabolic Status (rapid, extensive, intermediate or poor)
- OR (95% CI): 1.99 (1.47-2.69)

ABCB1 3435 TT Genotype
- OR (95% CI): 2.16 (1.21-3.88)

Prevalence of Genotypes and 1-Year Risk of Death, Stroke or MI: FAST-MI Trial (N=2208 French Patients)

**ABCB1 Alleles**
- 1 variant allele: 26.2%
- 2 variant alleles: 25.8%
- No variant alleles: 48.0%

**CYP2C19 Loss-of-Function Alleles**
- (*2, *3, *4, and *5)
- 1 variant allele: 26.1%
- 2 variant alleles: 28.7%
- No variant alleles: 71.2%

**ABCB1 Alleles**
- 1 variant allele: 51% ↑ risk
- 2 variant alleles: 72% ↑ risk

**CYP2C19 Loss-of-Function Alleles**
- 1 variant allele: 98% ↑ risk
- 2 variant alleles: 98% ↑ risk
- Post-PCI: HR 3.6 (1.7-7.5)
3rd-Generation Thienopyridines

- Includes prasugrel (Effient®) and ticagrelor (Brilinta®)

- Higher levels of platelet inhibition than clopidogrel

- Prasugrel and ticagrelor unaffected by variants of the \textit{CYP2C19} genotype

- Prasugrel unaffected by variants of the \textit{ABCB1} genotype

Rates of Bleeding Events in Antiplatelet Drug Trials for ACS

- **TRITON-TIMI 38 Trial**
  - Prasugrel: 2.4% (HR 1.32 (1.03-1.68))
  - Clopidogrel: 1.8%

- **PLATO Trial**
  - Ticagrelor: 2.8% (HR 1.19 (1.02-1.38))
  - Clopidogrel: 2.2%

Most common bleeding location = Gastrointestinal
Interaction with Clopidogrel: Summary

Evidence Summary

• Inconsistent study results
• Low magnitude of association in observational studies
• RCTs (COGENT, PLATO) showed no significant association between omeprazole and CV events
• Genetic polymorphisms and baseline CV risk may be a primary cause for impaired clopidogrel activity

Recommendations

• Gastroprotection with PPI should be reserved for patients at high-risk for GI bleeding*
• Embrace risk stratification and modification principles
• Consider risk versus benefit of PPI therapy on a case-by-case basis

*High-risk= History of GI bleeding OR multiple risk factors-- Hx PUD (bleeding or non-bleeding), advanced age, concomitant anticoagulants, steroids, or NSAID/ASA, H. pylori infection


Other PPI-Associated Adverse Effects

• Bone-fracture
• Hypomagnesemia
• Respiratory infection
• Clostridium difficile
PPI and Bone Strength

Long-Term PPI Therapy

Profound acid suppression

↓ Vitamin B12 absorption

Hypergastrinemia

↓ Calcium absorption

Vitamin B12 deficiency

Parathyroid hyperplasia

(+) Calcium balance

↑ Homocysteine

↓ Osteoblastic activity

↑ PTH

↓ Bone formation

↑ Bone absorption

Abnormal collagen cross-linking

↓ BMD

↓ Cortical BMD and dimensions

↓ Bone Strength

PTH= parathyroid hormone
vBMD= volumetric bone mineral density

PPI Use and Risk of Fracture: Meta-Analysis

OR (95% CI)

Corey et al. 2010  1.3 (1.2-1.4)
De Vries et al. 2009  1.2 (1.1-1.4)
Gray et al. 2010  1.0 (0.7-1.4)
Kaye et al. 2008  0.9 (0.7-1.1)
Pouwels et al. 2010  1.2 (1.0-1.4)
Targownik et al. 2008  1.6 (1.0-2.6)
Vetgeraad et al. 2005  1.5 (1.3-1.7)
Yang et al. 2006  1.4 (1.3-1.6)
Yu et al. MrOS 2008  0.6 (0.3-1.5)
Yu et al. SOF 2008  1.2 (0.8-1.7)
POOLED OR (95% CI)  1.3 (1.1-1.4)
PPI Use and Risk of Fracture: Meta-Analysis

Who is Most at Risk?

- Corley et al. 2010: Excess fracture risk with PPI use among persons with $\geq 1$ risk factor
  - OR 1.3 (1.2-1.4)

- Other risk factors: alcohol abuse, arthritis, diabetes, kidney disease, glucocorticoids, cerebrovascular disease, dementia, epilepsy, visual impairment, anxiolytics, pre-existing osteoporosis

PPI and Longitudinal Changes in BMD

- Absence of an association between PPI and BMD change over time*
  - Continuous PPI use for 5-10 years not associated with significant deleterious change in BMD

- Association between PPI and fractures may reflect baseline differences in fracture risk between PPI users and non-users (unrelated to the actual use of medication)
  - Supports Corley et al. (2010) hypothesis**

Association with Bone Fractures: Summary

**Evidence Summary**
- Inconsistent study results
- Low magnitude of association in observational studies
- PPI does not increase risk of fractures among patients with no pre-existing risk factors
- Excess fracture risk seen only among those with non-PPI risk factors
  - Confounding cannot be excluded
- Long-term PPI use (5-10 yrs) not associated with accelerated BMD loss

**Recommendations**
- Evidence does not justify routine pharmacologic prophylaxis
- Consider risk versus benefit of PPI therapy on an individual basis
- Be aware of other risk factors for fracture risk that identify high-risk patients

PPI and Hypomagnesemia

- PPIs may cause low serum magnesium levels if taken for prolonged periods of time (i.e., > 1 year)
- ~50 cases of hypomagnesemia reported since 2006
  - Under-recognized and under-reported → insufficient data to quantify an incidence rate with PPI therapy
- Severe hypomagnesemia: 0.05-0.35 mmol/L
  - Often secondary to hypokalemia and hypocalcemia
- Symptoms → fatigue, ataxia, paresthesias, tetany, seizures, confusion, bowel symptoms requiring inpatient care

Potential mechanism: Impaired intestinal absorption of magnesium; mechanism unknown

Association with Hypomagnesemia: Summary

Evidence Summary
- Very rare (~50 cases reported since 2006)
- Biologic mechanism unknown

Recommendations
- Remain vigilant for unexplained hypomagnesemia
- Hypomagnesemia in PPI users require discontinuation of PPI in addition to magnesium replacement
  - Magnesium levels normalize in 1 week after discontinuation

PPI and Susceptibility to Infection

- Gastric acidity: a major defense mechanism
  - Sterilizes contents entering digestive tract
  - Prevents bacterial colonization
  - Influences composition of intestinal normal flora
- PPIs ↑ gastric pH
  - ↓ in acidity associated with ↑ bacterial colonization of stomach*
- PPIs impair leukocyte function**
  - ↑ basal cytosolic Ca2++ concentrations in neutrophils
  - ↓ intra- and extracellular reactive oxygen production
  - ↓ bactericidal activity

### PPI and Respiratory Infection Risk: Meta-Analysis of Observational Studies

<table>
<thead>
<tr>
<th>Analysis (no. of studies)</th>
<th>Pooled Adjusted OR (95% CI)</th>
<th>Heterogeneity (I²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n=8)</td>
<td>1.27 (1.11-1.46)</td>
<td>90.5%</td>
</tr>
<tr>
<td>Subgroup Analysis: Study Design</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case-control (n=5)</td>
<td>1.44 (1.09-1.91)</td>
<td>93.7%</td>
</tr>
<tr>
<td>Cohort (n=3)</td>
<td>1.14 (0.96-1.36)</td>
<td>79.1%</td>
</tr>
<tr>
<td>Subgroup Analysis: Type of Pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital-acquired (n=3)</td>
<td>1.04 (0.58-1.88)</td>
<td>76.9%</td>
</tr>
<tr>
<td>Community-acquired (n=5)</td>
<td>1.34 (1.14-1.57)</td>
<td>93.6%</td>
</tr>
<tr>
<td>Subgroup Analysis: Duration of exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7 days (n=2)</td>
<td>3.95 (2.86-5.45)</td>
<td>0.0</td>
</tr>
<tr>
<td>&lt;30 days (n=4)</td>
<td>1.61 (1.46-1.78)</td>
<td>30.6%</td>
</tr>
<tr>
<td>30-180 days (n=4)</td>
<td>1.36 (1.05-1.78)</td>
<td>84.3%</td>
</tr>
</tbody>
</table>

Results suggest increase in risk associated with PPI use

- **High degree of heterogeneity (90.5%)**

Inverse relationship between magnitude of association and chronicity of PPI use ➔ Weakest association with longest duration of time

- Highlighting likely residual confounding caused by higher comorbidity among pneumonia patients prescribed a PPI
PPI and Respiratory Infection Risk: Meta-Analysis of RCTs

- No significant association between PPIs and respiratory infection
  - Even among ventilator-assisted patients on chronic PPI where abnormal gastric colonization exists (↑ risk of microaspiration or translocation)

Association with Respiratory Infection Risk: Summary

**Evidence Summary**
- Minimal increase in theoretical risk
  - Not substantiated after controlling for confounders
- Meta-analysis of RCTs fail to show a significant association between PPI and respiratory infections

**Recommendations**
- PPIs should not be withheld from patients with pulmonary disease
- Recommend annual influenza vaccination in patients who are*:  
  - Immunocompromised
  - Elderly
  - Smokers
  - COPD
  - Other risk factors for community-acquired pneumonia

PPI and *Clostridium difficile* Infection Risk: Meta-Analysis of Observational Studies

**2012 Update**

<table>
<thead>
<tr>
<th>Analysis (no. of studies)</th>
<th>Events</th>
<th>Pooled OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPI</td>
<td>No PPI</td>
</tr>
<tr>
<td>Overall Analysis (n=29)</td>
<td>3441</td>
<td>5383</td>
</tr>
<tr>
<td><strong>Subgroup Analyses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort studies (n=5)</td>
<td>367</td>
<td>279</td>
</tr>
<tr>
<td>Case-control studies (n=25)</td>
<td>3074</td>
<td>5104</td>
</tr>
<tr>
<td>Antibiotic use &gt;80% (n= 9)</td>
<td>1378</td>
<td>1836</td>
</tr>
<tr>
<td>Antibiotic use &lt;80% (n= 9)</td>
<td>1070</td>
<td>2232</td>
</tr>
</tbody>
</table>

Compared to nonusers, PPI users have twice the risk of developing *Clostridium difficile* infection.


**Recurrent *Clostridium difficile* Infection Risk: Retrospective Cohort Study**

<table>
<thead>
<tr>
<th>Recurrent CDI within 90 days</th>
<th>HR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (N=527)</td>
<td>1.4 (1.1-1.8)</td>
</tr>
<tr>
<td>Antibiotic use* (n=426)</td>
<td>1.7 (1.1-1.6)</td>
</tr>
<tr>
<td>Age&lt;60 (n=189)</td>
<td>1.2 (0.6-2.5)</td>
</tr>
<tr>
<td>Age 60-80 (n=593)</td>
<td>1.3 (0.9-1.8)</td>
</tr>
<tr>
<td>Age&gt;80 (n=384)</td>
<td>1.9 (1.1-3.0)</td>
</tr>
</tbody>
</table>

*Antibiotic exposure not targeted to *Clostridium difficile* infection

Risk highest among those older than 80 years and receiving antibiotics.

Association with *Clostridium difficile* Infections: Summary

**Evidence Summary**

- Acid suppression from PPI increases the risk of infection
  - Observational data & meta-analyses
- Excess infection risk with PPI seen in patients with other infection risk factors
  - Elderly, hospitalized
- Limited data regarding risk and PPI dose or duration

**Recommendations**

- *Clostridium difficile*-associated diarrhea should be considered in PPI users who develop diarrhea that does not improve
- Consider risk versus benefit of PPI therapy in:
  - Hospitalized patients on antibiotics or during institutionalized outbreaks
  - The elderly
  - Patients embarking on travel to endemic areas

Association with *Clostridium difficile* Infections: Summary

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- Consider risk versus benefit of PPI therapy in:
  - Hospitalized patients on antibiotics or during institutionalized outbreaks
  - The elderly
  - Patients embarking on travel to endemic areas
Managing Antiplatelet Agents in Peri-Endoscopic Period

Case

• 65-year-old man with a family history of colorectal cancer
• STEMI with PCI and drug-eluting stent (DES) 13 months ago with history of stent occlusion
• Dual antiplatelet therapy: ASA + clopidogrel (Plavix®)
• Asthma—Rx: Inhalers
• No other comorbidities/medications
• Normal labs
• PLAN: Elective screening colonoscopy

How should you manage his antiplatelet therapy?
Thromboembolic Risk
Probability of event depends on 3 factors

Indication for antiplatelet therapy

Consequence of thromboembolic event

Presence of additional thromboembolic risk factors

Low- vs. High-Risk Thromboembolic Conditions

<table>
<thead>
<tr>
<th>Low-Risk</th>
<th>High-Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated or paroxysmal nonvalvular atrial fibrillation</td>
<td>Atrial fibrillation associated with:</td>
</tr>
<tr>
<td>Bioprosthesis valve</td>
<td>- Valvular heart disease</td>
</tr>
<tr>
<td>Mechanical valve in the aortic position</td>
<td>- Prosthetic valves</td>
</tr>
<tr>
<td>Deep-vein thrombosis</td>
<td>- Active CHF</td>
</tr>
<tr>
<td></td>
<td>- LVEF &lt;35%</td>
</tr>
<tr>
<td></td>
<td>- History of thromboembolic event</td>
</tr>
<tr>
<td></td>
<td>- Mechanical valve in any position and previous thromboembolic event</td>
</tr>
<tr>
<td></td>
<td>- Prior stent occlusion</td>
</tr>
<tr>
<td></td>
<td>- Recently (~1 yr) placed coronary stent</td>
</tr>
<tr>
<td></td>
<td>- Acute coronary syndrome</td>
</tr>
<tr>
<td></td>
<td>- Non-stented PCI after MI</td>
</tr>
</tbody>
</table>


Endoscopy-Related GI Bleeding Risks

**Bleeding risk varies with procedure type and presence/absence of therapeutic interventions.**

<table>
<thead>
<tr>
<th>Low Risk (&lt;1%)</th>
<th>High Risk (&gt;1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diagnostic + biopsy:</td>
<td>• Polypectomy:</td>
</tr>
<tr>
<td>♦ EGD (0.1%)</td>
<td>♦ Gastric (7.2%)</td>
</tr>
<tr>
<td>♦ Double balloon enteroscopy (0.1%)</td>
<td>♦ Duodenal/ampullary</td>
</tr>
<tr>
<td>♦ Colonoscopy (0-0.02%)</td>
<td>• 1-3 cm (4.5%)</td>
</tr>
<tr>
<td>• Biliary/pancreatic stent without sphincterotomy (0.3%)</td>
<td>• &gt;3 cm (10.3%)</td>
</tr>
<tr>
<td>• ERCP without sphincterotomy*</td>
<td>• Colonic (0.7-3.3%)</td>
</tr>
<tr>
<td>• EUS without FNA</td>
<td>• Endoscopic mucosal resection (22%)</td>
</tr>
<tr>
<td>• Flexible sphincterotomy + biopsy*</td>
<td>• Biliary sphincterotomy (2.0-3.2%)</td>
</tr>
<tr>
<td>• Endosonography without FNA</td>
<td>• Pneumatic or bougie dilation (1.7%)</td>
</tr>
<tr>
<td>• Wireless capsule endoscopy*</td>
<td>• PEG placement (0.2-2.5%)</td>
</tr>
<tr>
<td>*Limited data, presumed negligible</td>
<td>• Endosonography-guided FNA (0.5-2.9%)</td>
</tr>
<tr>
<td></td>
<td>• Laser ablation and coagulation (1.1%)</td>
</tr>
<tr>
<td></td>
<td>• Treatment of varices (2.4-25.4%)</td>
</tr>
</tbody>
</table>

**Risk ↑ 2-12x:**
- ↑ Age
- Cautery use
- >1 polyp removed
- Pre-procedural warfarin


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Post-Polypectomy Bleeding With and Without Clopidogrel Therapy

*Single-site (VAMC), retrospective case-control*

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel (n=142)</th>
<th>No Clopidogrel (n=1243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>5.6%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Immediate (at endoscopy)</td>
<td>2.1%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Delayed (&lt; 4 weeks)</td>
<td>100% on ASA</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Avoiding the Post-Polypectomy Bleed

- Consider saline/epi lifts to prevent excessive bleeding during hot snare procedures

- Consider prophylactic mechanical hemostasis following polypectomy of large polyps with broad based stalks.
  - Avoid cautery as prone to bleeding with eschar sloughing

*Anecdotal evidence

Continuation of ASA After Endoscopic Control of Peptic Ulcer Bleeding

<table>
<thead>
<tr>
<th></th>
<th>Low-dose ASA (n=78)</th>
<th>Placebo (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day Recurrent Bleeding</td>
<td>10.3% (3.4-17.2%)</td>
<td>5.4% (0.3-10.5%)</td>
</tr>
<tr>
<td></td>
<td>ARR 4.9% (NNT= 20)</td>
<td></td>
</tr>
<tr>
<td>30-day All-Cause Mortality</td>
<td>9.0% (2.7-15.3%)</td>
<td>1.3% (0-3.8%)</td>
</tr>
<tr>
<td></td>
<td>ARI 7.7% (NNH= 13)</td>
<td></td>
</tr>
</tbody>
</table>


0.0% 5.0% 10.0% 15.0% 20.0%
Event Rate (%)
Current Best-Practice Recommendations for Secondary Prevention

1. Avoid cessation of all antiplatelet therapies after PCI with stent placement, continue ASA.
2. Avoid cessation of clopidogrel (even when ASA is continued) within the first 30 days of PCI and DES or BMS placement.
3. Defer elective endoscopic procedures, possibly up to 12 months following PCI and DES placement.
4. Perform high-bleeding risk endoscopic procedures 5-7 days after thienopyridine drug cessation.
   ▶ In patients on dual therapy, ASA should be continued.
5. Resume thienopyridine and ASA once hemostasis is achieved.
6. Continue platelet-directed therapy during elective endoscopy with low risk for bleeding.
Conclusions

- PPI prescription must be tailored, limiting use to robust indications

- Antiplatelet therapy management requires an individualized approach considering both the cardiovascular risk of antiplatelet discontinuation and the risk of GI bleeding
  - Discuss your recommendations with your patient
  - Consult cardiologist
  - Document carefully the rationale of your approach