# One-Year Survival is Not Affected by Gastrointestinal Bleeding After Percutaneous Coronary Interventions

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## ABSTRACT

**Background:** Percutaneous coronary intervention (PCI) has been the main therapy in acute coronary syndromes, and early antithrombotic agents as well as 1-year dual antiplatelet therapy are required for adjuvant therapy. However, the development of post-PCI gastrointestinal (GI) bleeding may increase all-cause mortality. We compared the characteristics and outcomes of patients with GI bleeding within 1 year after PCI to those who did not develop bleeding.

**Methods:** A retrospective cohort study was conducted using data from 384 PCI procedures performed between January 2011 and December 2013 at our hospital. End points were identified after 30 days, 90 days and 1 year postprocedure for evidence of GI bleeding or new onset anemia. Variables were compared between patients with and without GI bleeding using *t* test and Fisher exact test. Kaplan-Meier curve was constructed for estimating bleeding-free survival probability.

**Results:** In a more than 1-year follow-up period, there were 39 cases (10.2%, 95% CI: 0.073-0.136) of documented GI bleeds. Females were found to have a significantly higher frequency of GI bleeding than males (16.8% vs. 8.0%, $P = 0.018$), and Hispanics more than non-Hispanics (11.7% vs. 1.7%, $P = 0.017$). All patients with GI bleeding survived at 1 year.

**Conclusion:** In our study of a predominantly Hispanic population, a high incidence of GI bleeding after PCI occurred. However, there was no association between the incidence of GI bleeding and all-cause mortality, whether PCI was performed in the setting of acute coronary syndrome or as an elective procedure. There is a need to conduct a larger prospective study to validate the findings of our study.

**Key Indexing Terms:** Gastrointestinal bleeding; Percutaneous coronary intervention; Dual Antiplatelet therapy. **[Am J Med Sci 2017;353(4):381–386.]**

## INTRODUCTION

The advent of potent antiplatelet and antithrombotic medications has led to a substantial improvement of ischemic outcomes among patients with coronary artery disease (CAD) undergoing percutaneous coronary interventions (PCIs).[1-4] However, gastrointestinal (GI) bleeding has become an important concern, because it represents the most frequent noncardiac long-term complication after PCI with an adverse prognostic effect comparable with ischemic events.[5-8] Randomized trials reported a 2- to 3-fold increased risk of GI bleeding associated with dual antiplatelet therapy (DAPT) compared with aspirin alone, but the absolute risk increase was between the ranges of 0.6% and 2.0%.[9-12] Ng et al[13] and Ibanez et al[14] reported a relative risk of 1.78 (95% CI: 1.25-2.54; number needed to harm = 130) and 1.96 (95% CI: 1.46-2.63; number needed to harm = 167) of GI bleeding risk associated with DAPT.

Although previous studies identified patient- and medication-related factors predisposing to GI bleeding after PCI, several of these studies were restricted to GI bleeding occurring during the in-hospital period[15-17] or within 30 days of the procedure.[18] Although 12 months duration of DAPT is the current standard of care after PCI, the time course, predictors and prognostic implications of GI bleeding occurring late after PCI have not been systematically assessed, especially in the Hispanic population.[19]

In this context, we estimated incidence of GI bleeding and analyzed the patient characteristics and outcomes of GI bleeding within 1 year in patients undergoing PCI and 12 months of DAPT therapy.

## METHODS

### Patient Population

This was a retrospective cohort study using the National Cardiovascular Data Registry (NCDR) database at University Medical Center in El Paso, TX. This database was queried, and all patients who underwent PCI between January 2011 and December 2013 were identified. Using the hospital's electronic medical records (EMR), patients were followed for an average of 1 year. Baseline demographic and clinical characteristics,

including age, sex, ethnicity, smoking history, alcohol and intravenous drug use, presence of systemic disease (such as hypertension, diabetes mellitus, atrial fibrillation, heart failure, CAD, dyslipidemia or stroke [cerebrovascular accident]), information on performed interventions and hospital outcome data were systematically collected. Laboratory values during hospitalization were retrieved from the EMR. All PCI patients who presented with endoscopy-documented upper or lower GI bleed or new onset anemia within the first year of their index PCI were identified. There were no formal exclusion criteria, and all-comers of either sex were included in this registry. The institutional review board approved and waived informed consent due to the retrospective nature of the study.

### Procedures

PCI and endoscopy were performed in accordance with current practice guidelines.[19,20] PCI consisted of drug eluting stent (DES), bare metal stent or balloon angioplasty without stent placement. Endoscopy procedure variables included esophagogastroduodenoscopy (EGD), colonoscopy and capsule endoscopy when indicated. Unfractionated heparin (UFH) was started immediately at diagnosis and periprocedural use of glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors was left to the discretion of the operator. Anticoagulants were discontinued immediately after stent placement. DAPT consisting of aspirin (ASA) and a $P2Y_{12}$ inhibitor was initiated before or at the time of procedure, and ASA was continued indefinitely. The duration of DAPT was typically 12 months after the index PCI. For the patients diagnosed with acute GI bleeding, DAPT therapy was generally discontinued or clopidogrel alone was discontinued until hemostasis was achieved.

### Patient Follow-Up

A total of 384 patients underwent PCI. Among these patients, we identified the patients with clinically significant GI bleed at 30 and 90 days, and within 1 year of the index PCI. Survival data were obtained from the EMR. For patients treated for adverse events at other medical institutions, external medical records, discharge letters and coronary angiography documentation were requested and reviewed when available. Information on medical treatment during index PCI, at 30 and 90 days, and at 1 year was available for all patients; in addition, medical treatment and endoscopic findings were assessed at the time point of the bleeding event for patients who developed GI bleeding.

### Clinical End Points and Definitions

For this analysis, only single bleeding events in each patient were considered. GI bleeding was defined as new onset or worsening anemia with heme-positive stool test, a significant drop in hemoglobin with a heme-positive stool test, coffee-ground emesis, hematemesis, melena or hematochezia documented by a treating physician with or without endoscopic evidence of an upper or lower GI bleeding site. Acute coronary syndrome (ACS) consisted of ST-elevation myocardial infarction, non–ST elevation myocardial infarction or unstable angina. The primary outcome was GI bleeding more than a year after the index PCI. Secondary outcome was all-cause mortality.

### Statistical Analysis

Data were summarized as per the type of variables. Continuous data were compared as per the bleeding status using unpaired *t* test, whereas categorical variables were compared using Fisher exact test. Overall survival was defined as date of index PCI to date of last visit or date of mortality while bleeding-free survival was defined as date of index PCI to date of last visit or date of bleeding. Nonbleeding cases were considered as censored event. Kaplan-Meier method was used to calculate overall survival and bleeding-free survival over the follow-up. Cox proportional hazards regression was used to determine the effect of baseline cofactors on bleeding-free survival. The results of Cox analysis were presented using hazard ratio along with 95% CI and *P*-value. All the statistical analyses were conducted using STATA 13. *P*-values less than 5% were regarded as significant results.

## RESULTS

Table 1 presents the summary of considered variables and unadjusted association of considered risk factors with GI bleeding. The average age of subjects was 59.9 (standard deviation [SD] = 10.6) years, 25% were women and most patients were Hispanic (84.9%). Of all the patients, 83.8% presented with ACS, and 62% had a troponin peak $<10$. Only 14% of the patients had a proton pump inhibitor (PPI) prescribed and 10% had a history of peptic ulcer disease/gastritis. DES was placed in 57.38% of the subjects.

A total of 39 subjects (10.2%, 95% CI: 0. 073-0.136) had bleeding over the 1 year of follow-up. The estimated rates of bleeding at 30 days, 90 days, and 180 days were 4.5% (95% CI: 0.03-0.07), 6.3% (95% CI: 0.04-0.10) and 7.8% (95% CI: 0.05-0.11), respectively. Of the 39 bleeders, 19 (49%) patients had occult bleeding (acute anemia with heme-positive stool), whereas 20 (51%) had frank GI bleed (melena [5], hematemesis [6] and hematochezia [9]). Of those who had occult bleeding ($n = 19$), the average hemoglobin drop was 3.69 g/dL (SD = 1.47), whereas average hemoglobin drop in the patients with frank GI bleeding ($n = 20$) was 4.1 g/dL (SD = 1.91).

Of these 39 subjects, 31 (79.5%) had endoscopic evaluation: 25 patients had an EGD and 18 patients had colonoscopy (12 patients had both EGD and colonoscopy, 13 patients had only EGD and 6 patients had only colonoscopy). Of the 25 patients who had EGD, 17 (60%) were tested by biopsy for *Helicobacter pylori*. Four patients tested positive. One patient had a capsule endoscopy. Eighteen patients (58.1%) had endoscopic