Clinical Impact of Gastrointestinal Bleeding in Patients Undergoing Percutaneous Coronary Interventions

Konstantinos C. Koskinas, MD, MSc*; Lorenz Räber, MD, PhD*; Thomas Zanchin, MD; Peter Wenaweser, MD; Stefan Stortecky, MD; Aris Moschovitis, MD; Ahmed A. Khattab, MD; Thomas Pilgrim, MD; Stefan Blöchlinger, MD; Christina Moro, MSc; Peter Jüni, MD; Bernhard Meier, MD; Dik Heg, PhD; Stephan Windecker, MD

**Background**—The risk factors and clinical sequelae of gastrointestinal bleeding (GIB) in the current era of drug-eluting stents, prolonged dual antiplatelet therapy, and potent P2Y₁₂ inhibitors are not well established. We determined the frequency, predictors, and clinical impact of GIB after percutaneous coronary interventions (PCIs) in a contemporary cohort of consecutive patients treated with unrestricted use of drug-eluting stents.

**Methods and Results**—Between 2009 and 2012, all consecutive patients undergoing PCI were prospectively included in the Bern PCI Registry. Bleeding Academic Research Consortium (BARC) GIB and cardiovascular outcomes were recorded within 1 year of follow-up. Among 6212 patients, 84.1% received new-generation drug-eluting stents and 19.5% received prasugrel. At 1 year, GIB had occurred in 65 patients (1.04%); 70.8% of all events and 84.4% of BARC ≥3B events were recorded >30 days after PCI. The majority of events (64.4%) were related to upper GIB with a more delayed time course compared with lower GIB. Increasing age, previous GIB, history of malignancy, smoking, and triple antithrombotic therapy (ie, oral anticoagulation plus dual antiplatelet therapy) were independent predictors of GIB in multivariable analysis. GIB was associated with increased all-cause mortality (adjusted hazard ratio, 3.40; 95% confidence interval, 1.67–6.92; P=0.001) and the composite of death, myocardial infarction, or stroke (adjusted hazard ratio, 3.75; 95% confidence interval, 1.99–7.07; P<0.001) and was an independent predictor of all-cause mortality during 1 year.

**Conclusions**—Among unselected patients undergoing PCI, GIB has a profound effect on prognosis. Triple antithrombotic therapy emerged as the single drug-related predictor of GIB in addition to patient-related risk factors within 1 year of PCI.

**Clinical Trial Registration**—URL: http://www.clinicaltrials.gov. Unique identifier: NCT02241291.

**Key Words:** antiplatelet drug ■ gastrointestinal hemorrhage ■ percutaneous coronary intervention

The advent of potent antiplatelet and antithrombotic medications has led to a substantial improvement of ischemic outcomes among patients with coronary artery disease undergoing percutaneous coronary interventions (PCIs). However, bleeding has become an important concern because it represents the most frequent noncardiac complication after PCI with an adverse prognostic impact comparable with that of ischemic events. In particular, gastrointestinal bleeding (GIB) is a common source of nonaccess site-related bleeding after PCI and has been associated with an in-hospital mortality of ≤10%. Although previous studies identified patient- and medication-related factors predisposing to GIB after PCI, several issues were raised. First, earlier reports focused on populations with characteristics, which per se portend an increased bleeding risk, including severe heart failure or patients with acute coronary syndromes (ACSs) receiving intensive antithrombotic regimens. Second, previous studies were restricted to GIB occurring during the in-hospital period or within 30 days of the procedure. Although prolonged (12 months) duration of dual antiplatelet therapy (DAPT) is the current standard of care after PCI with drug-eluting stents (DES), the time course, predictors, and prognostic implications of GIB occurring late after PCI have not been systematically assessed. Third, although prasugrel and ticagrelor have been associated with an increased risk of GIB in the setting of randomized trials, the safety profile of these novel P2Y₁₂ inhibitors in unselected patients is not well established.
WHAT IS KNOWN

- Gastrointestinal bleeding is a potential complication in patients undergoing percutaneous coronary interventions.
- Gastrointestinal bleeding after percutaneous coronary intervention has an adverse effect on patient survival.

WHAT THE STUDY ADDS

- Gastrointestinal bleeding is the most common site of bleeding within 1 year after percutaneous coronary intervention.
- Gastrointestinal bleeding has a delayed time course throughout 1 year and primarily affects the upper gastrointestinal tract.
- Triple antithrombotic therapy, that is, the combination of oral anticoagulation and dual antiplatelet therapy, is the single medication-related factor associated with gastrointestinal bleeding after percutaneous coronary intervention.

Finally, considering the differential correlates and prognostic significance of bleeding in the upper versus lower gastrointestinal tract in general populations, the relative frequency and clinical impact of upper versus lower GIB after PCI remain largely unknown.

Against this background, the purpose of this study was to assess the frequency, predictors, and prognostic impact of GIB within 1 year in patients undergoing PCI. Therefore, we analyzed a cohort of 6212 consecutive patients who underwent PCI with the unrestricted use of predominantly new-generation DES, whose management included prolonged DAPT, oral anticoagulation (OAC) where indicated, and novel P2Y12 inhibitors in patients with ACS.

Methods

Patient Population
All patients undergoing PCI at Bern University Hospital, Switzerland, between January 2009 and June 2012 were prospectively entered into the CARDIOBASE Bern PCI Registry (ClinicalTrials.gov. Unique identifier: NCT 02241291). There were no formal exclusion criteria, and all patients who provided informed consent were included in this registry. Demographic and clinical characteristics, information on performed interventions, and hospital outcome data were systematically collected. Laboratory values during hospitalization were retrieved from the central hematology laboratory. The registry was approved by the institutional ethics committee. All patients provided written informed consent for prospective follow-up.

Procedures
PCI was performed in accordance with current practice guidelines. Unfractionated heparin at a dose of at least 5000 IU or 70 to 100 IU/kg was administered during the procedure. The periprocedural use of glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors was left to the discretion of the operator. DAPT consisting of acetylsalicylic acid and a P2Y12 inhibitor was initiated before, at the time, or immediately after the procedure, and acetylsalicylic acid was continued indefinitely. Prasugrel was routinely used in patients presenting with ST-segment-elevation myocardial infarction (STEMI) as of September 2009, and ticagrelor was routinely used in patients with non–ST-segment–elevation ACS as of November 2011. The duration of DAPT was typically 12 months for DES and at least 1 month for bare-metal stent implantation or balloon angioplasty.

Patient Follow-Up
Patients were systematically followed throughout 1 year to assess major adverse cardiac and cerebrovascular events (death, myocardial infarction [MI], stroke), bleeding complications, and medical treatment. Patients were contacted post discharge during any unscheduled hospital visit, during planned hospital visits (eg, staged procedure), and finally at 1 year since index PCI. Survival data were obtained from hospital records and municipal civil registries. A health questionnaire was sent to all living patients with questions on rehospitalization and adverse events, followed by telephone contact in case of missing response. General practitioners and referring cardiologists were contacted as necessary for additional information. For patients treated for adverse events at other medical institutions, external medical records, discharge letters, and coronary angiography documentation were systematically collected and reviewed. Information on medical treatment during index PCI, at discharge, and at 1 year was available for all patients; in addition, medical treatment was assessed at the time point of the bleeding event for patients who developed GIB.

Clinical End Points and Definitions
For this analysis, only first bleeding events in each patient were considered. GIB was defined as clinical event (coffee-ground emesis, hematemesis, melena, or hematochezia) documented by a treating physician or endoscopic evidence of an actively bleeding, upper or lower gastrointestinal site. GIB events within 1 year were categorized according to the Bleeding Academic Research Consortium (BARC), Thrombolysis in Myocardial Infarction (TIMI), and Global Use of Strategies to Open Occluded (GUSTO) Arteries classifications. In an ancillary analysis, we separately assessed early (defined as ≤30 days) versus late (>30 days) GIB to allow for comparisons with previous reports, which focused on in-hospital or 30-day GIB after PCI.

A clinical event committee adjudicated all events using original source documents. MI was defined according to the modified historical definition. Stroke was defined as rapid development of clinical signs of focal or global disturbance of cerebral function lasting >24 hours with imaging evidence of acute, clinically relevant brain lesion.

Statistical Analyses
Statistical analyses were performed with STATA version 13.1 (Stata Corp, College Station, TX). Continuous variables are summarized as mean±SD; categorical ones, as actual numbers and percentages. To assess the association between baseline variables and time to the occurrence of GIB, we used univariable hazard ratios and $P$ values derived from Cox proportional hazard models after multiple imputation of missing baseline data (combined estimate of 10 data sets using Rubin rule). Predictors for GIB were assessed singly for inclusion into a Cox regression model of time to the first GIB, using $P<0.2$ and retained in the final multivariable model with $P<0.1$ (after 10× multiple imputation of missing values using chained equations). The independent association between GIB and subsequent mortality and the composite end point of death, MI, or stroke was examined using Cox proportional hazard models, in which GIB was treated as a time-dependent covariate. All multivariable models controlled for the following baseline covariates: age, sex, diabetic status, renal failure, smoking, history of malignancy, anemia, diagnosis of STEMI, Killip class III–IV at presentation, and use of any DES. Findings were considered statistically significant at the 0.05 level.
Results

Of 6212 consecutive patients enrolled in this observational registry, complete follow-up at 1 year was available for 5848 of patients (94.1%; Figure I in the Data Supplement).

Frequency and Time Course of GIB

GIB occurred in 65 patients during 1 year (1.04%; 95% confidence interval, 0.91–1.47%) and represented the most frequent site of all bleeding events within 1 year (Figure 1). The frequency distribution of GIB according to the BARC, TIMI, and GUSTO classifications is shown in Figure 1C–1E. Mean time of GIB occurrence was 119 days. Figure 2 illustrates the cumulative incidence of GIB over time. The monthly event rate of GIB was highest during the first 30 days (0.3%) and declined thereafter. The proportion of events occurring in-hospital, ≤30 days (early GIB), and >30 days post PCI (late GIB) was 15%, 29%, and 71%, respectively. Late GIB accounted for 84.4% of all BARC ≥3B and for 83.3% of all TIMI major events.

Patient Characteristics and Medications

Of all patients, 45.5% were treated for stable coronary artery disease, 28.8% for non–ST-segment–elevation ACS, and 25.7% for STEMI. Table 1 shows the baseline characteristics of patients. In univariable analyses, we found higher rates of GIB in older patients, current smokers, patients with renal insufficiency, and those with a history of malignancy or previous GIB. Procedural characteristics are summarized in Table 2.

Cardiovascular medications during the intervention and at discharge are summarized in Table 3. In univariable analyses, development of GIB was not associated with the periprocedural use of antiplatelet or antithrombotic medications, including GP IIb/IIIa inhibitors. A landmark analysis set at the time of discharge showed more frequent development of GIB in relation to the use of OAC and triple antithrombotic therapy (ie, a combination of OAC plus DAPT), but no association with the use of DAPT or of different antiplatelet agents at discharge (Table 3). Figure 3 displays the use of DAPT, triple antithrombotic therapy, and proton pump inhibitors (PPIs) at discharge and at 1 year, and also immediately before and after the bleeding event for patients who developed GIB. Among patients who developed GIB, the use of triple therapy and DAPT showed an expected substantial drop after the bleeding event. At 1 year, the use DAPT was lower in patients with as compared with those without GIB (P=0.03). Use of PPIs in patients who developed GIB dropped from 48% at discharge to 28% at the time of the event.

Independent Predictors of GIB

Multivariable predictors of GIB included advanced age, previous GIB, history of malignancy, current smoking, and triple antithrombotic therapy at discharge (Figure 4). Predictors of early GIB were identical and also included Killip class III or IV at presentation.
Upper Versus Lower GIB
Defining the localization of GIB was possible in 59 of 65 patients by means of clinical and endoscopic evaluation. The proportion of classifiable upper versus lower GIB was 64% versus 36%. The proportion of early occurrence (≤30 days) was reduced for upper compared with lower GIB (18% versus 52%; \(P=0.008\)), without differences in 1-year mortality between upper and lower GIB.

Impact of GIB on Clinical Outcomes
Within 1-year follow-up, death occurred in 9 patients who developed GIB (14.0%) versus 377 patients without GIB (6.4%). The composite endpoint of all-cause death, MI, or stroke was observed in 13 patients with GIB (20.2%) versus 596 patients without GIB (10.1%; Table I in the Data Supplement). Multivariable predictors of death and the composite of death, MI or stroke are shown in Figure 5. GIB was associated with increased risk of all-cause mortality (adjusted hazard ratio, 3.40; 95% confidence interval, 1.67–6.92; \(P=0.001\)), and the composite of death, nonfatal MI, or stroke during 1 year (adjusted hazard ratio, 3.75; 95% confidence interval, 1.99–7.07; \(P<0.001\)).

Discussion
The principal findings of this study can be summarized as follows: (1) GIB is the most frequent site of bleeding within
Gastrointestinal Bleeding After PCI

1 year after PCI; (2) GIB that develops >30 days after PCI accounts for the majority (>70%) of overall events and for the vast majority (>80%) of severe bleeding events; (3) independent predictors of 1-year GIB are mostly patient-specific factors, including increasing age, active smoking, and a history of GIB or malignancy; (4) triple antithrombotic therapy, but not the use of DAPT, prasugrel, OAC, or periprocedural anti-thrombotic medications, is the single drug-related predictor of GIB; (5) upper GIB events are twice as frequent, and display a more delayed time course, compared with lower GIB; and (6) GIB is an independent predictor of 1-year mortality.

The present cohort advances our understanding about the role of GIB after PCI in several important ways. Earlier relevant studies included low rates of DES (ranging from none to 6% to about a third of patients in the Acute Catheterization and Urgent Intervention Triage Strategy [ACUITY] analysis) and as a result consistently used regimens of shorter DAPT duration, or they focused specifically on patient subsets with potentially confounding characteristics (eg, ACS or severe heart failure). In contrast, we assessed patients as encountered in routine clinical practice across the entire spectrum of coronary artery disease, including individuals with noncardiac comorbidities (eg, malignancy) or indication for OAC, who were excluded from previous randomized clinical trials assessing GIB. In addition, we addressed the correlates and impact of GIB occurring late (up to 1 year) after the procedure, and we analyzed patients who received treatment according to current practice standards, including implantation of predominantly DES, prolonged DAPT duration, and novel P2Y$_2$ inhibitors. A notable limitation of this analysis is the small number of events in patients with GIB, such that the use of DAPT, prasugrel, OAC, or periprocedural anti-thrombotic medications, is the single drug-related predictor of GIB; (5) upper GIB events are twice as frequent, and display a more delayed time course, compared with lower GIB; and (6) GIB is an independent predictor of 1-year mortality.

The present cohort advances our understanding about the role of GIB after PCI in several important ways. Earlier relevant studies included low rates of DES (ranging from none to 6% to about a third of patients in the Acute Catheterization and Urgent Intervention Triage Strategy [ACUITY] analysis) and as a result consistently used regimens of shorter DAPT duration, or they focused specifically on patient subsets with potentially confounding characteristics (eg, ACS or severe heart failure). In contrast, we assessed patients as encountered in routine clinical practice across the entire spectrum of coronary artery disease, including individuals with noncardiac comorbidities (eg, malignancy) or indication for OAC, who were excluded from previous randomized clinical trials assessing GIB. In addition, we addressed the correlates and impact of GIB occurring late (up to 1 year) after the procedure, and we analyzed patients who received treatment according to current practice standards, including implantation of predominantly DES, prolonged DAPT duration, and novel P2Y$_2$ inhibitors. A notable limitation of this analysis is the small number of events in patients with GIB, such that not the use of DAPT, prasugrel, OAC, or periprocedural anti-thrombotic medications, is the single drug-related predictor of GIB; (5) upper GIB events are twice as frequent, and display a more delayed time course, compared with lower GIB; and (6) GIB is an independent predictor of 1-year mortality.

1 year after PCI; (2) GIB that develops >30 days after PCI accounts for the majority (>70%) of overall events and for the vast majority (>80%) of severe bleeding events; (3) independent predictors of 1-year GIB are mostly patient-specific factors, including increasing age, active smoking, and a history of GIB or malignancy; (4) triple antithrombotic therapy, but not the use of DAPT, prasugrel, OAC, or periprocedural anti-thrombotic medications, is the single drug-related predictor of GIB; (5) upper GIB events are twice as frequent, and display a more delayed time course, compared with lower GIB; and (6) GIB is an independent predictor of 1-year mortality.

The present cohort advances our understanding about the role of GIB after PCI in several important ways. Earlier relevant studies included low rates of DES (ranging from none to 6% to about a third of patients in the Acute Catheterization and Urgent Intervention Triage Strategy [ACUITY] analysis) and as a result consistently used regimens of shorter DAPT duration, or they focused specifically on patient subsets with potentially confounding characteristics (eg, ACS or severe heart failure). In contrast, we assessed patients as encountered in routine clinical practice across the entire spectrum of coronary artery disease, including individuals with noncardiac comorbidities (eg, malignancy) or indication for OAC, who were excluded from previous randomized clinical trials assessing GIB. In addition, we addressed the correlates and impact of GIB occurring late (up to 1 year) after the procedure, and we analyzed patients who received treatment according to current practice standards, including implantation of predominantly DES, prolonged DAPT duration, and novel P2Y$_2$ inhibitors. A notable limitation of this analysis is the small number of events in patients with GIB, such that not the use of DAPT, prasugrel, OAC, or periprocedural anti-thrombotic medications, is the single drug-related predictor of GIB; (5) upper GIB events are twice as frequent, and display a more delayed time course, compared with lower GIB; and (6) GIB is an independent predictor of 1-year mortality.
the estimates of GIB-related risk may not be estimated with adequate precision and thus require cautious interpretation.

In this analysis, GIB occurred in 0.3% of patients within 30 days and in 1% within 1 year after PCI. Previous studies reported a 0.7% incidence of in-hospital GIB; the rate of 30-day GIB was 0.37% in Randomized Evaluation of PCI Linking Angioplasty to Reduced Clinical Events (REPLACE)-2 and 1.3% in the ACUITY trial. Possible reasons for the higher short-term GIB rates in earlier investigations might include the restriction to exclusively patients with ACS, the more frequent use and prolonged, upstream administration of GP IIb/IIIa inhibitors, the higher maintenance dose of acetylsalicylic acid (300 mg versus 100 mg in our study), and the use of thrombolytic therapy in some patients, which has been strongly linked to GIB. Consistent with our findings, rates of GIB after PCI have reportedly declined during the past decade, despite the increasing, prolonged use of more potent antiplatelet and antithrombotic medications. This has been attributed to the implementation of risk-tailored (age-, weight-, and renal function-adjusted) doses of antithrombotic medications and to the prophylactic treatment with PPIs in contemporary practice as compared with earlier reports.

We found that vascular access site was the most frequent bleeding site within 30 days, consistent with previous reports assessing short-term bleeding complication but the gastrointestinal tract represented the most common location of bleeding during 1 year after PCI. This has also been observed in patients with stable coronary artery disease who were free from coronary revascularizations. Although the event rate of GIB was highest during the first month after PCI, late (>30 days) events accounted for the majority of all GIB events throughout 1 year and for the great majority of severe GIB. These findings emphasize the need for prolonged surveillance of patients at risk of GIB after PCI by current standards. It also shows that the majority of GIB is disconnected from the index procedure and is more importantly influenced by underlying patient-related factors.

GIB events were predicted mainly by patient-specific characteristics rather than medication-related factors. In line with earlier reports, we found that increasing age, a history of previous GIB and malignancy, and active smoking—the only modifiable feature—persist as decisive risk factors of GIB in patients treated by contemporary practice.

Triple antithrombotic therapy with OAC plus DAPT at discharge—at a rate that notably remained unchanged until the actual occurrence of bleeding—was the single drug-related factor that independently predicted GIB. This finding complements observations of previous studies, in which OAC use was contraindicated or not reported. Triple therapy has repeatedly been associated with an excess of major bleeding in previous large-scale registries. Our observation of an increased risk of GIB underlines the importance of carefully assessing the risk:benefit ratio of this regimen according to the risk for thromboembolism (ie, CHA₂DS₂-VASc score) and bleeding hazard (HASBLED [hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/ alcohol] score).

The increased risk of non-CABG-related (mainly GIB-driven) bleedings in patients receiving prasugrel or ticagrelor compared with clopidogrel in randomized trials was not confirmed in multivariable analysis in the present cohort, despite the fact that novel P2Y₁₉ inhibitors were administered to >1200 ACS patients with a concurrent loading dose of clopidogrel in >50% of those patients. This may be related to the careful evaluation of relative contraindications to potent P2Y₁₉ inhibitors and the preferential use of prasugrel, in particular, among patients with STEMI in the present cohort. Along this line, no bleeding excess was attributed to prasugrel in The Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY ACS), where contraindications for prasugrel were also applied. Of note, we used prasugrel primarily in patients with STEMI, a subgroup of patients with no increase of bleeding complications in the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel–Thrombolysis in Myocardial Infarction (TRITON-TIMI) 38 trial.

Periprocedural medications were not related to 30-day, or overall 1-year GIB. Notably, because virtually all patients...
received heparin, our results cannot be directly extrapolated to patients receiving bivalirudin, which has been consistently linked to reduced bleeding complications compared with heparin-based regimens. In a landmark analysis of the ACUITY trial, periprocedural administration of GP IIb/IIIa inhibitors was more frequent in patients who experienced GIB within 30 days after an ACS, and heparin plus a GP IIb/IIIa inhibitor showed a trend toward higher risk of GIB in multivariable analysis. In the present registry, a role of GP IIb/IIIa was not confirmed for the development of GIB complications. One can speculate on possible reasons underlying these discordant findings. In ACUITY, half of the patients who received a GP IIb/IIIa inhibitor were allocated toward higher risk of GIB in multivariable analysis. In the present registry, a role of GP IIb/IIIa was not confirmed for the development of GIB complications. One can speculate on possible reasons underlying these discordant findings. In ACUITY, half of the patients who received a GP IIb/IIIa inhibitor were allocated toward higher risk of GIB in multivariable analysis. In the present registry, a role of GP IIb/IIIa was not confirmed for the development of GIB complications. One can speculate on possible reasons underlying these discordant findings. In ACUITY, half of the patients who received a GP IIb/IIIa inhibitor were allocated toward higher risk of GIB in multivariable analysis.

In patients with GIB, the use of DAPT was less frequent at 1 year, despite similarly high rates of DES implantation at the time of the index procedure. Importantly, DAPT was discontinued in almost half of the patients with GIB immediately after the bleeding event, that is, at a mean of 4 months after the intervention. Although the timing of DAPT discontinuation was not consistently available for patients without GIB, it is conceivable that the earlier discontinuation of DAPT in patients who developed GIB might have contributed to the higher incidence of ischemic cardiac and cerebrovascular events; this cannot be further substantiated, however, owing to the nonrandomized nature of this study.

The feasibility of detecting either upper or lower GIB in the acute setting of ACS has been previously demonstrated, yet the relative incidence, time course, and clinical correlates of upper versus lower GIB after PCI have only undergone minimal investigation. The increased rate of upper versus lower GIB in our study is in agreement with findings from unselected, general populations. Upper GIB events predominated and occurred later compared with lower GIB. This observation lends further support to prolonged PPI administration in patients deemed susceptible to GIB after PCI as emphasized by current recommendations. The relatively low proportion (48%) of patients with subsequent GIB who received PPI at discharge, and the substantial drop to only 28% before the GIB event is in line with previous evidence of suboptimal gastrointestinal prophylaxis in patients receiving DAPT. Although this finding does not directly indicate a causal relationship, it is consistent with evidence from randomized trials demonstrating reduced gastrointestinal complications in patients on DAPT who received omeprazole, and emphasizes the need for closer attention to clinical and medication-related risk predictors of GIB.

### Limitations

This study has several limitations owing to its observational, nonrandomized design. First, the registry was not specifically designed to evaluate predictors and clinical outcomes of GIB; however, bleeding outcomes were prospectively defined outcome measures and were specifically evaluated during 1 year follow-up. Second, the single-center nature of the study may limit the external validity of our findings. Third, the association between GIB and clinical outcomes may be confounded by variables that were not recorded (eg, subclinical malignancies). Fourth, atrial fibrillation was not recorded for the purpose of this analysis. However, we previously found a 5.3% prevalence of atrial fibrillation in consecutive patients treated with PCI at our institution; hence, atrial fibrillation most probably reflects favorable outcomes for patients treated by our institution; hence, atrial fibrillation most probably represented the main indication for triple antithrombotic therapy in this study population. Finally, in this sizable cohort of patients receiving contemporary treatment the rate of GIB and the number of events in patients who experienced GIB were low; this probably reflects favorable outcomes for patients treated by current standards, but it may also limit the power of the study and the precision of the analysis of GIB-related risk.

### Conclusions

In this contemporary population of consecutively enrolled patients undergoing PCI, GIB was the most common bleeding complication within 1 year. GIB is predicted mainly by patient-specific rather than drug-related factors, it affects

---

**Figure 4.** Multivariable predictors of 1-year gastrointestinal bleeding (GIB). CI indicates confidence interval; and HR, hazard ratio.

**Figure 5.** Multivariable predictors of all-cause mortality (A) and the composite of death, myocardial infarction (MI) or stroke during 1 year (B). CI indicates confidence interval; DES, drug-eluting stent; HR, hazard ratio; and STEMI, ST-segment-elevation myocardial infarction.
preponderantly the upper gastrointestinal tract—hence, it may largely be amenable to prophylactic use of gastric protection therapies—and appears to have a profound effect on 1-year mortality. These findings indicate the need for thorough assessment of the risk of GIB after PCI, and for prolonged vigilance and implementation of bleeding avoidance strategies (eg, cautious administration of triple antithrombotic therapy) in patients with high-risk characteristics.

Disclosures

None.

References


Clinical Impact of Gastrointestinal Bleeding in Patients Undergoing Percutaneous Coronary Interventions

Konstantinos C. Koskinas, Lorenz Räber, Thomas Zanchin, Peter Wenaweser, Stefan Stortecky, Aris Moschovitis, Ahmed A. Khattab, Thomas Pilgrim, Stefan Blöchlinger, Christina Moro, Peter Jüni, Bernhard Meier, Dik Heg and Stephan Windecker

Circ Cardiovasc Interv. 2015;8:
doi: 10.1161/CIRCINTERVENTIONS.114.002053

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/8/5/e002053

Data Supplement (unedited) at:
http://circinterventions.ahajournals.org/content/suppl/2015/04/28/CIRCINTERVENTIONS.114.002053.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at:
http://circinterventions.ahajournals.org///subscriptions/
Supplemental Material

**Supplemental Table.** Clinical outcomes within one year of follow-up in patients with vs. without GIB.

<table>
<thead>
<tr>
<th>Variable</th>
<th>GIB</th>
<th>No GIB</th>
<th>GIB vs. no GIB*</th>
<th>Number of events before/after GIB*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=65</td>
<td>n=6147</td>
<td></td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P value</td>
</tr>
<tr>
<td>Death</td>
<td>9 (14.0)</td>
<td>377 (6.4)</td>
<td>6.31 (3.12–12.78)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (1.9)</td>
<td>215 (3.7)</td>
<td>1.47 (0.21–10.36)</td>
<td>0.6985</td>
</tr>
<tr>
<td>Revascularization (any)</td>
<td>6 (10.4)</td>
<td>450 (8.0)</td>
<td>2.00 (0.83–4.83)</td>
<td>0.1224</td>
</tr>
<tr>
<td>Death or MI</td>
<td>10 (15.6)</td>
<td>566 (9.6)</td>
<td>4.93 (2.54–9.59)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Death, MI or stroke</td>
<td>13 (20.2)</td>
<td>596 (10.1)</td>
<td>5.38 (2.85–10.15)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Cardiac death, MI or stroke</td>
<td>9 (14.2)</td>
<td>526 (8.9)</td>
<td>4.20 (1.93–9.14)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

GIB indicates gastrointestinal bleeding; MI, myocardial infarction.

*: Hazard ratios (95% confidence intervals) with robust standard errors comparing after GIB vs. before GIB or no GIB, by splitting patient records at the date of GIB (assuming events on the date of GIB are attributed to GIB).
Supplemental Figure. Schematic presentation of study flow.

January 2009 – June 2012
6212 patients underwent PCI and provided written consent

267 (4.3%) lost to follow up at 1 year
97 (1.6%) refused to follow-up

5848 (94.1%) follow-up information available up to 1 year
5462 followed up and alive
386 followed up and died

6212 analysed for clinical endpoints
364 censored at time-point of refusal or loss to follow-up