# Safety of "Bridging" With *Eptifibatide* for Patients With Coronary Stents Before Cardiac and Non-Cardiac Surgery

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**Patients with previously implanted coronary stents are at risk for stent thrombosis if dual-antiplatelet therapy is prematurely discontinued. Bridging with a glycoprotein IIb/IIIa inhibitor has been advocated as an alternative, with few supporting data. The aim of this study was to determine the safety of such a strategy by retrospectively analyzing bleeding in 100 consecutive patients with previously implanted coronary stents who were bridged to surgery with eptifibatide after discontinuing thienopyridine therapy. A propensity-matched control comparison was performed for a subgroup of 71 patients who underwent cardiovascular surgery. Blood transfusions were required in 65% in the bridged group versus 66% in the control group ($p = 0.86$). The mean numbers of units transfused were $4.84 \pm 6.93$ and $3.65 \pm 7.46$, respectively ($p > 0.25$). Rates of return to the operating room for bleeding or tamponade were 10% and 2.9%, respectively ($p = 0.085$). Increased rates of transfusion were noted for patients who received concomitant aspirin and/or intravenous heparin infusion. In conclusion, there does not appear to be any increase in the need for blood transfusions or rate of return to the operating room for patients being bridged with eptifibatide when thienopyridines are discontinued in the perioperative period, but concomitant use of additional antiplatelet or anticoagulant agents may increase transfusions and delays to surgery. Clinicians who are considering this strategy must weigh the risks of stent thrombosis versus bleeding.** **© 2012 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2012;110:485–490)**

Stent thrombosis (ST) is a rare but catastrophic event that usually occurs <30 days after stent implantation and is associated with a mortality rate of 9% to 45%.[1–5] Cases of late and very late ST have been described, particularly in the era of drug-eluting stents (DES).[6–9] The most important predictor of ST is premature cessation of dual-antiplatelet therapy (DAT).[1,9,10] Current guidelines recommend 12 months of DAT for DES and ≥1 month for bare-metal stents. Additionally, elective surgeries should be postponed until DAT is complete, and aspirin therapy should be continued throughout surgery when possible.[11,12] Despite these recommendations, 4% to 5% of patients who have DES undergo noncardiac surgery in the first year after stent implantation.[13] Case reports and anecdotal evidence suggest that the risk for ST can be minimized through the use of glycoprotein IIb/IIIa inhibitors while thienopyridine therapy is discontinued in the perioperative period.[1,14–17] We sought to evaluate the safety of this strategy with respect to bleeding outcomes given the paucity of data available.

## Methods

Two groups of patients were included in this study. The first group was identified retrospectively using our pharmacy database and consisted of 100 consecutive patients at Cleveland Clinic from January 2008 to August 2010 who had previously implanted coronary stents and were bridged to surgery using eptifibatide, a glycoprotein IIb/IIIa inhibitor, after discontinuation of thienopyridine therapy. Patients who were bridged to cardiovascular surgery were included in a model to create a propensity-matched analysis. The second group consisted of 492 potential controls identified from the Cleveland Clinic Cardiovascular Information Registry, a prospectively collected registry of all cardiovascular surgeries at Cleveland Clinic. Potential controls underwent cardiac surgery from January 2008 to December 2010, discontinued thienopyridine therapy >5 days before surgery, did not receive perioperative glycoprotein IIb/IIIa inhibitors, and had previously implanted coronary stents. Electronic and paper charts were reviewed for each of the 100 subjects in the bridging group by 2 independent reviewers. Reporting discrepancies were reviewed and adjudicated by a third reviewer. Similar data were obtained for the control group by extracting information from the Cardiovascular Information Registry database. The 2 matched groups were compared to evaluate outcomes. The Cleveland Clinic institutional review board approved the study.

Patients in the bridged group discontinued thienopyridine therapy (either clopidogrel or prasugrel) before surgery. An infusion of eptifibatide was used to provide platelet

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inhibition while patients were not receiving thienopyridine therapy, which was stopped 6 to 12 hours before surgery. After surgery, patients were either restarted on thienopyridines or temporarily placed back on eptifibatide infusion, with eventual thienopyridine resumption. Decisions regarding the timing of thienopyridine discontinuation before surgery, initiation of the eptifibatide infusion and admission for bridging, and how to restart thienopyridine therapy after surgery were determined by the individual practices of the patient's physicians. Patients in the matched control cohort did not receive any thienopyridine therapy within ≥5 days of surgery. All continued to receive aspirin therapy (dose determined by treating physician) through surgery and received similar preoperative and postoperative care, with the exception that they did not receive any perioperative eptifibatide. For patients in the 2 groups, all concomitant medications, including anticoagulants, were determined by the treating physicians' discretion and were often influenced by co-morbidities such as atrial fibrillation and mechanical valves.

The primary end point was the transfusion of units of blood during the hospital admission. Secondary outcomes included transfusion of units of platelets or fresh frozen plasma and major adverse cardiac events such as death, myocardial infarction, urgent revascularization, and ischemic stroke. Deaths were classified as cardiac (including death from undetermined cause) and noncardiac. Myocardial infarction was defined as a clinical event consistent with myocardial ischemia with an increase in serum troponin T or creatine kinase-MB concentration >2 times the upper limit of normal with or without ST-segment deviation ≥1 mm or T-wave flattening or inversion on electrocardiography. Urgent revascularization was defined as the need for coronary intervention or bypass surgery on the basis of evidence of myocardial ischemia. Ischemic stroke was defined by the presence of a neurologic deficit secondary to infarction of central nervous system tissue with or without radiographic confirmation. Secondary bleeding end points included the presence of a bleeding complication such as intracranial hemorrhage (neurologic deficit with radiographic evidence of hemorrhage), intraocular hemorrhage, gastrointestinal bleeding (defined by clinical or endoscopic evidence), bleeding requiring return to the operating room (defined by the need to keep the wound open after surgery or the presence of bleeding on reexploration), severe epistaxis (defined by bleeding requiring a blood transfusion, resulting in a surgical delay, requiring a specialized intervention to treat, or requiring discontinuation or decreased dose of eptifibatide; minor epistaxis cases were excluded), surgical wound bleeding or hematoma (defined by bleeding requiring a blood transfusion, requiring discontinuation or decreased dose of eptifibatide or access site hematomas resulting in a delay of surgery). Our study was not powered to detect a statistical significant difference in secondary end points (bleeding or ischemic); therefore, secondary end points were collected only for descriptive analysis of the unmatched 100 bridged patients.

All continuous variables were summarized as means and standard deviations or medians and interquartile ranges. All categorical data were summarized by the percentage of nonmissing data. Multivariate logistic regression was performed to develop a parsimonious model identifying factors that were associated using eptifibatide as a bridging strategy. This model was augmented with additional patient factors to form the propensity model and calculate propensity scores. Patients were then matched on the basis of the propensity score to form a matched subgroup for analyses. The greedy matching algorithm was used to match a case with a control with the nearest propensity score. The largest distance to be considered as a valid match was 0.1. Distance was calculated as the absolute case minus the control difference in propensity score. Group comparisons for categorical variables were made using chi-square tests. Continuous variables were compared between groups using Wilcoxon's rank-sum test.

Table 1
Baseline characteristics of the unmatched bridged group (n = 100)

| Variable | Value |
|---|---|
| Age (years) | 63.2 ± 10.58 |
| Body mass index (kg/m$^2$) | 30 ± 6.64 |
| Men | 77 (77%) |
| White | 88 (88%) |
| Active smoker | 20 (20%) |
| Hypertension | 95 (95%) |
| Hyperlipidemia | 96 (96%) |
| Diabetes mellitus | 36 (36%) |
| Previous myocardial infarction | 55 (55%) |
| Peripheral arterial disease | 11 (11%) |
| Previous stroke or transient ischemic attack | 8 (8%) |
| Previous open-heart surgery | 45 (45%) |
| Serum creatinine (mg/dl) | 1.0 ± 0.37 |
| Hemoglobin (g/dl) | 12.9 ± 3.26 |
| Platelets (g/dl) | 212.7 ± 65.68 |
| Ejection fraction (%) | 49.7 ± 11.67 |
| Bare-metal stent | 11 (11%) |
| DES | 89 (89)% |
| Noncardiovascular surgery | 22 (22%) |
| Cardiovascular surgery | 71 (71%) |
| CABG | 43% (43%) |
| CABG and valve surgery | 14% (14%) |
| Valve surgery | 9% (9%) |
| Myectomy and valve surgery | 2% (2%) |
| Left ventricular assist device surgery | 2% (2%) |
| Heart transplantation | 1% (1%) |
| Time from PCI to surgery (days) | |
| Median | 118 |
| Mean | 156.8 ± 154.1 |
| Range | 7–906 |
| IQR | 62–196 |
| Days off thienopyridine (days) | |
| Median | 6 |
| Mean | 7.4 ± 3.4 |
| Range | 2–18 |
| IQR | 5–9 |
| Duration of eptifibatide therapy (days) | |
| Median | 5 |
| Mean | 5.3 ± 2.7 |
| Range | 0.5–16 |
| IQR | 3–6 |

Data are expressed as mean ± SD or as number (percentage), except as indicated.

IQR = interquartile range.

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