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Intravenous Antiplatelet Therapy Bridging in Patients Undergoing Cardiac or Non-Cardiac Surgery Following Percutaneous Coronary Intervention☆

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ABSTRACT

Background: The effect of perioperative bridging therapy on risks of ischemic cardiac events and major bleeding complications in patients on dual antiplatelet therapy (DAPT) following percutaneous coronary intervention (PCI) remains undefined.
Methods: We report on 60 consecutive patients between 2010 and 2017 who required cardiac (CS; n = 15) or non-cardiac (NCS; n = 45) surgeries following PCI at our institution. Short-acting intravenous (IV) antiplatelet (APT) bridging with eptifibatide, tirofiban and cangrelor were instituted after DAPT interruption.
Results: All patients were men with multiple atherosclerosis risk factors. An acute coronary syndrome indication (56.7%) was the most common PCI indication in the CS and NCS groups. Drug-eluting stents were used in 93.33% and 95.56% of the above groups, respectively. The median duration from PCI to CS and NCS were 11.17 and 18.25 months, respectively and 38.33% of all surgeries were performed within 6 months of the index PCI. Most patients were on background aspirin (83.33%) and clopidogrel (81.67%) and median duration of DAPT interruption was 7 days. Median duration of perioperative IV APT bridging was 3 days for CS and 5 days for NCS groups. In the CS group, two patients (13.33%) had non-fata myocardial infarction (MI), and four (26.67%) had clinically significant bleeding. No patients had perioperative stent thrombosis. In the NCS group, one patient (2.22%) had stent thrombosis; four (6.67%) had myocardial infarction, and five (11.11%) clinically significant bleeding.
Conclusions: Despite using IV APT as bridging therapy during perioperative DAPT interruption in post-PCI patients, postoperative cardiac events and bleeding complications can still occur.

1. Introduction

Patients on dual antiplatelet therapy (DAPT) post-percutaneous coronary intervention (PCI) who subsequently undergo surgery and require DAPT interruption pose a serious clinical dilemma. DAPT interruption increases the risk of perioperative cardiac events including non-fatal myocardial infarction (MI) and/or stent thrombosis (ST) in patients with drug eluting stent (DES) implantation [1], while continuing DAPT increases the risk of bleeding complications. These risks could be affected by several factors including urgency of surgery, time from PCI to surgery, PCI indication and stent type [2,3].

The most recent American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend that elective non-cardiac surgeries (NCS) should be delayed 30 days after bare metal stent (BMS) implantation and 6 months after DES implantation. It is also recommended to continue aspirin perioperatively (Class I recommendation) and resume interrupted P2Y12 receptor inhibitors as soon as feasible after surgery [4]. However, in some patients, surgery cannot be delayed and DAPT interruption is required earlier than the recommended time interval. Additionally, several patients, including those in our study require DAPT for more than 6 months after PCI for different reasons such as a prior complex PCI, left main PCI, history of stent thrombosis, etc. Bridging therapy, which depends on discontinuation of DAPT and introducing short acting intravenous (IV) anti-platelet therapy (APT) preoperatively has been suggested, but there is insufficient evidence to support this strategy.

In this article, we describe the clinical outcomes of 60 patients who required cardiac (CS) or non-cardiac (NCS) surgery post PCI and underwent DAPT interruption and bridging therapy with IV APT (Fig. 1).

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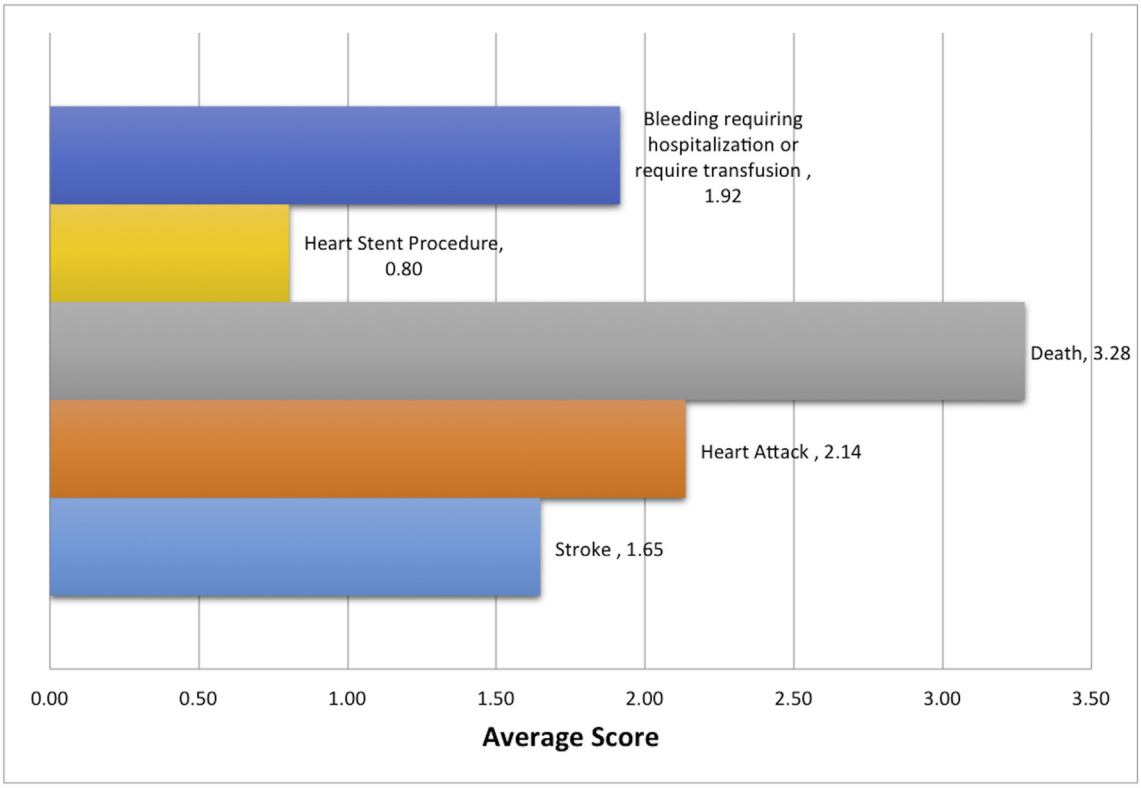


Fig. 1. Median duration of IV APT infusion in patients undergoing cardiac and non-cardiac surgery

2. Materials and methods

2.1. Patients

We retrospectively reviewed the medical records of 60 consecutive patients who required surgery (15 patients who underwent CS and 45 patients who underwent NCS) after PCI at our institution between 2010 and 2017 and underwent bridging with IV APT after DAPT interruption. This study is a follow-up on our prior report of 67 patients who underwent NCS (n = 51) or CS (n = 16) after DES implantation at our institution between 2008 and 2010 and underwent preoperative bridging with glycoprotein IIb/IIIa inhibitors.

2.2. Bridging protocol

Bridging was performed using the following protocol: clopidogrel and ticagrelor were discontinued 5 days prior to planned surgery. Prasugrel was discontinued 7 days prior to surgery. Aspirin was continued preoperatively. Patients were admitted to the hospital and started on intravenous IV APT ≤3 days till 6 ± 2 h prior to surgery. The type of IV APT used was at the discretion of the treating physician. Glycoprotein IIb/IIIa inhibitors infusions were used at doses described in our previous report, however without administration of a bolus dose. In addition, in our current study IV cangrelor was infused without bolus dosing. Table 1 depicts the doses of IV APTs used in this study. Postoperatively, a 600 mg loading dose of clopidogrel was given 6–24 h after surgery and then continued at a once-daily dose of 75 mg. If clopidogrel could not be resumed, a recommendation was made to restart the IV APT infusion two hours after the end of surgery and to continue it for up to 6 h after the resumption of clopidogrel treatment.

2.3. Patient monitoring

During the intra- and post-operative period, patients underwent continuous cardiac and hemodynamic monitoring. Electrocardiograms

Table 1
Short acting intravenous anti-platelet agents.

	Tirofiban	Eptifibatide	Cangrelor
Mechanism	Glycoprotein IIb/IIIa Inhibitor	Glycoprotein IIb/IIIa Inhibitor	Targeted $P2Y_{12}$ Inhibitor
Onset of action	Immediate	Immediate	Immediate
Potent platelet inhibition	Yes	Yes	Yes
Plasma half life	2 h	2.5 h	3–5 min
Offset of action	4–6 h	4–8 h	1 h
P2Y12 specific	No	No	Yes
Dose (no bolus required)	0.1 μg/kg/min (0.05 μg/kg/min for creatinine clearance <50 ml/min)	2.0 μg/kg/min (1.0 μg/kg/min for creatinine clearance <50 ml/min)	0.75 μg/kg/min (does not require dose adjustment with impaired renal function)
Average cost per person per day[a]	786.92 $/2611.44 $	515.48 $/1242.74 $	5770.32 $/10785.60 $

[a] Cost of a 24 h infusion for a 100 kg person at North Texas VA Healthcare System and the average wholesale cost outside the VA (not including a bolus dose).

were obtained in patients who had clinical suspicion for cardiac events and cardiac biomarkers were measured at 12-hour intervals, or earlier if clinically indicated. Stent thrombosis was defined using the Academic Research Consortium criteria [5], and significant bleeding was defined using the bleeding academic research consortium (BARC classification) [6]. Clinically significant bleeding was defined as BARC ≥ 2.

2.4. Statistical analyses

Continuous variables were reported as mean ± SD or median (inter-quartile range) and categorical variables were reported as frequencies. A $p < 0.05$ was considered statistically significant. All statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary NC).

3. Results

3.1. Patient characteristics

Patients' baseline characteristics are presented in Table 2. All patients were men with a mean age of 65.87 ± 0.96 and high prevalence of atherosclerotic risk factors. No significant differences except for age were noted in baseline characteristics between the CS and the NCS groups. Patients in the NCS group were significantly older than the CS group (67.33 ± 6.82 vs. 61.47 ± 7.55; $p = 0.0050$).

Table 2
Baseline characteristics and PCI information of the study population.

	Cardiac surgery (n = 15)	Non-cardiac surgery (n = 45)	p-Value
General demographics			
Age (years)	61.47 ± 7.55	67.33 ± 6.82	0.0050
Men, n (%)	15 (100%)	45 (100%)	–
Hypertension, n (%)	14 (93.33%)	39 (86.67%)	0.4897
Hyperlipidemia, n (%)	10 (66.67%)	36 (80.00%)	0.2944
Diabetes mellitus, n (%)	10 (66.67%)	28 (62.22%)	0.7590
Prior coronary artery bypass graft surgery, n (%)	1 (6.67%)	10 (21.74%)	0.1690
Congestive heart failure, n (%)	5 (33.33%)	14 (31.11%)	0.8735
Chronic kidney disease, n (%)	3 (20.00%)	7 (15.56%)	0.6916
Peripheral arterial disease, n (%)	1 (6.67%)	8 (17.78%)	0.3007
PCI information			
Indication for PCI			0.3708
Stable angina, n (%)	5 (33.33%)	21 (46.67%)	–
Acute coronary syndrome, n (%)	10 (66.67%)	24 (53.33%)	–
PCI target vessel			
Left anterior descending artery, n (%)	4 (26.67%)	21 (46.67%)	0.1772
Circumflex, n (%)	4 (26.67%)	13 (28.89%)	0.8697
Right coronary artery, n (%)	7 (46.67%)	15 (33.33%)	0.3574
Left main, n (%)	0 (0%)	2 (4.44%)	0.4102
Saphenous vein graft, n (%)	1 (6.67%)	2 (4.44%)	0.7345
Other, n (%)	5 (33.33%)	1 (2.22%)	0.0006
Number of vessels treated per patient			0.0010
One vessel, n (%)	4 (26.67%)	32 (71.11%)	–
Two vessels, n (%)	5 (33.33%)	11 (24.44%)	–
Three, n (%)	1 (6.67%)	1 (2.22%)	–
Unknown, n (%)	5 (33.33%)	1 (2.22%)	–
Number of stents implanted per patient[a]	2.36 ± 1.43	2.07 ± 1.26	0.4154
BMS	0 (0%)	1 (2.22%)	0.5637
DES	14 (93.33%)	43 (95.56%)	0.7345
Everolimus-eluting, n (%)	6 (40.00%)	26 (57.78%)	0.2359
Paclitaxel-eluting, n (%)	0 (0%)	6 (13.33%)	0.1393
Zotarolimus-eluting, n (%)	1 (6.67%)	7 (15.56%)	0.3845
Sirolimus-eluting, n (%)	0 (0%)	3 (6.67%)	0.3090
DES of unknown type n (%)	7 (46.67%)	5 (11.11%)	0.0031
Balloon angioplasty	1 (6.67%)	1 (2.22%)	0.4102
Mean time interval between PCI and surgery (months)[a]	12.87 ± 13.25	19.80 ± 15.23	0.1490
Time interval between PCI and surgery			0.9249
<6 months, n (%)	8 (53.33%)	15 (33.33%)	–
6–12 months, n (%)	3 (20.00%)	14 (31.11%)	–
>12 months, n (%)	4 (26.67%)	16 (35.56%)	–
Surgery urgency			0.2249
Elective, n (%)	17 (100%)	39 (90.70%)	–
Urgent, n (%)	0 (0%)	4 (6.90%)	–
Surgery type			
Abdominal, n (%)	0 (0%)	12 (26.67%)	–
Genitourinary, n (%)	0 (0%)	8 (17.78%)	–
Vascular, n (%)	0 (0%)	4 (8.89%)	–
Orthopedic, n (%)	0 (0%)	5 (11.11%)	–
Head & neck, n (%)	0 (0%)	8 (17.78%)	–
Cardiac, n (%)	15 (100%)	0 (0%)	–
Thoracic, n (%)	0 (0%)	3 (6.67%)	–
Other, n (%)	0 (0%)	5 (8.33%)	–

PCI: Percutaneous Coronary Intervention; DES: Drug Eluting Stent; BMS: Bare Metal Stent.
[a] Mean ± standard deviation.

3.2. PCI information

The indication for PCI was acute coronary syndrome (ACS) for the majority of CS (66.67%) and NCS (53.33%) groups, that may have contributed to the prolonged use of DAPT beyond 6 months in some of the patients and the need for bridging therapy prior to surgery. Most patients in the CS group had prior PCI of two or more vessels (40%) whereas NCS patients had majority of interventions on one vessel (71.11%). In the CS group, one patient (6.67%) had balloon angioplasty only and the rest were treated with DES. One patient (2.22%) had balloon angioplasty in the NCS group, and only one patient (2.22%) had PCI with BMS. All others had DES implantations. Most DES was everolimus-eluting stents in both CS (41.18%) and NCS (58.69%) groups. There was no significant difference in PCI treatment modality or type of DES stents used between both groups (Table 2).

3.3. Surgery and preoperative management

The mean and median times between PCI and NCS were 19.80 ± 15.23 and 18.25 (interquartile range 6.92–26.67) months, respectively. The mean and median times between PCI and CS were 12.87 ± 13.25 and 11.17 (interquartile range 1.58–18.08) months respectively (Table 2). Most NCS procedures included abdominal (26.67%), genitourinary (17.78%) and head and neck (17.78%) surgeries. Aspirin was continued in most patients in both groups (80% of CS patients vs. 82.22% of NCS patients; Table 3). Mean and median duration of DAPT interruption were 8.10 ± 3.14 and 7 (Interquartile range 6–10.25) days respectively for the CS group, and 7.13 ± 2.17 and 7 (Interquartile range 6–8) days respectively for the NCS group. There was no significant difference in the duration of bridging with IV APT between both groups (4.13 ± 2.95 for CS group vs. 4.52 ± 2.91 for NCS group; $p = 0.43$). However, median duration of preoperative IV APT (cangrelor, epitifibatide, tirofiban) infusion varied according to the type of surgery performed (Fig. 1). Eptifibitide was the major IV APT used in bridging therapy in the CS (86.67%) and NCS (73.33%) groups. Cangrelor use, however, has dominated (88.89%) since its institutional availability in March 2017.

Table 3
Perioperative management and 30-day outcomes of the study population.

Perioperative management			
Mean duration of bridging with a glycoprotein IIb/IIIa inhibitor (days)[a]	4.13 ± 2.95	4.52 ± 2.91	0.4260
Glycoprotein IIb/IIIa type, n (%)			0.1251
Eptifibatide	13 (86.67 %)	33 (73.33%)	–
Tirofiban	2 (13.33%)	2 (13.33%)	–
Cangrelor	0 (0.00%)	8 (17.78%)	–
Duration of Clopidogrel interruption (days)[a]	8.10 ± 3.14	7.13 ± 2.17	0.5047
Aspirin continued perioperatively, n (%)	12 (80.00%)	37 (82.22%)	0.8485
30-Day outcomes			
Stent thrombosis n (%)	0 (0%)	1 (2.22%)	0.5637
Bleeding n (%)	4 (26.67%)	5 (11.11%)	0.1473
Mean blood loss (ml)[a]	1000 ± 500	168.75 ± 151.68	0.0233
Units of pRBCs transfused	6.75 ± 4.57	3.4 ± 2.61	0.2060
Thrombocytopenia n (%)	0 (0%)	0 (0%)	–
Mean hemoglobin drop[a]	3.47 ± 1.90	1.40 ± 1.09	0.0006
Myocardial Infarction n (%)	2 (13.33%)	3 (6.67%)	0.2067
Urgent coronary revascularization n (%)	2 (13.33%)	1 (2.22%)	0.0900
In-hospital mortality n (%)	2 (13.33%)	5 (11.11%)	0.5660
Mean time to hospital discharge[a]	10.77 ± 12.14	5.05 ± 7.71	0.0013

[a] Mean ± standard deviation.

3.4. Perioperative outcomes in the non-cardiac surgery group

In the NCS group, three patients (6.67%) had an MI one of whom had an urgent coronary revascularization. Five patients (11.11%) died within the first 30 days post-operatively. Five patients (11.11%) had bleeding complications post-operatively. Their cases are described in Table 4a.

One patient (2.22%) had angiographically confirmed acute stent thrombosis in the immediate postoperative period compared to none in the CS group. The patient had a sirolimus-eluting stent placed in the distal right coronary artery 19 months prior to pancreatectomy. Six hours after surgery, he developed inferior ST-segment elevation acute myocardial infarction (STEMI). Emergency coronary angiography revealed thrombosis of the distal right coronary artery stent and this was managed with placement of a bare metal stent.

3.5. Perioperative outcomes in the cardiac surgery group

None of the patients in the CS group had acute ST in the immediate post-operative period (within 30 days of the procedure). Two patients (13.33%) had an MI and urgent coronary revascularization and another two patients (13.33%) died post-operatively. Four patients had bleeding complications (26.67%). Their cases details are described in Table 4b.

The current guidelines suggest delaying surgery till 3–6 months after DES placement. However, there is not enough clinical evidence demonstrating the efficacy of bridging in such situations [7]. For that reason, we analyzed our data for two additional subgroups: patients with a PCI to surgery duration of less than 6 months, and patients with a PCI to surgery duration of more than or equal to 6 months. Supplemental table 1 shows baseline characteristics of both subgroups. Supplemental table 2 shows perioperative management and 30-day outcomes in the two subgroups. A higher percentage of patients who underwent bridging in less than 6 months after PCI had a history of peripheral vascular disease (26.09% vs. 8.11%; $p = 0.03$). No other differences in baseline characteristics were noted between the two subgroups. Thirty days after the procedure, patients who underwent bridging in less than 6 months after PCI had a higher percentage of MI, although not significant. Both groups had a high percentage of bleeding post-operatively.

3.6. Patient determined post-surgical event scores

Our team took the extra step of investigating patients' concerns about post-surgical events, mainly stroke, heart attack, heart stent procedures, bleeding complications, and death. Patients were asked to rank these events based on the significance assigned by them and the final score was computed to a total of 10. The average scores for each event are shown in Fig. 2. Patients' main concern was death (average score 3.28/10) followed by heart attack (2.14/10) and bleeding complications (1.92/10). To further investigate patients' ranking of ischemic versus bleeding events, we grouped ischemic events (a composite of heart attack, stroke, heart stent procedures, and death) and compared them to bleeding complications using the Lickert scale test. There was no significant difference between the mean scores of both groups (1.92 ± 2.55 for bleeding complication vs. 1.96 ± 0.7 for ischemic events; $p = 0.885$) showing that patients are equally concerned about both outcomes.

4. Discussion

This study shows that, in patients undergoing cardiac or non-cardiac surgery post PCI, DAPT interruption and preoperative administration of IV APT may not prevent post-operative cardiac events, including stent thrombosis and MI. IV APT bridging can also be associated with a risk of clinically significant bleeding complications. Perioperative bleeding accounts for almost half of the reported complications.

The vast majority of patients in our study had a DES implantation prior to surgery, heightening provider concern for perioperative stent

Table 4a
Description of bleeding complications post non-cardiac surgery by patient.

Patient ID	Type of surgery	Bleeding event	Hgb drop (g/dl)	Units of pRBC transfused	BARC classificati-on	Time between PCI and surgery	Preoperative bridging therapy	Duration of therapy (days)
1	Above knee amputation	Hematochezia	2.8	7	3a	8 months	Eptifibatide	4
2	Transurethral resection of bladder cancer	Hematuria	2.4	NA	2	4 months	Eptifibatide	6
3	ERCP	Melena	2.8	4	3a	5 months	Eptifibatide	6
4	Total knee arthroplasty	Hemarthrosis	3.9	4	3a	5 years	Eptifibatide	6
5	Excision of nasopharyngeal mass	Epistaxis	1.3	2	3a	9 months	Eptifibatide	6

BARC: Bleeding Academic Research Consortium; Hgb: Hemoglobin; pRBC: packed red blood cells; ERCP: endoscopic retrograde cholangio-pancreatography.

thrombosis. DAPT interruption after stent implantation is one of the strongest predictors of stent thrombosis [8]. This risk is inversely proportional to the time duration between PCI and surgery [8–13]. A recent study by Hawn et al. showed that major adverse cardiac events (MACE) were observed following surgery only within the first 6 months of stent placement [9]. Another study by Egholm et al. showed that this risk is only significant within the first month after stent implantation [10]. Results from the Surgery after stent (SAS) registry by Rossini et al. supported the latter by showing that the risk of 30-day MACE is not significantly higher when surgery is performed within 6 months from previous PCI (OR: 1.70; 95% CI (0.68–4.29); P = 0.26), and the incidence of MACE is highest in the first month after PCI [7]. Moreover, the 2016 ACC/AHA update on duration of DAPT recommends delaying an elective non-cardiac surgery for at least six months after coronary DES implantation [4].

In our study, 39% of surgeries (CS and NCS) were performed within six months post PCI. Although DAPT continuation is recommended to minimize the risk of stent thrombosis, surgeons frequently request discontinuation of at least P2Y12 receptor inhibitors prior to surgery to minimize risk of bleeding. In such cases, a short acting IV APT has been suggested as a bridging therapy [1,14–16].

Glycoprotein IIb/IIIa receptor inhibitors (e.g. eptifibatide and tirofiban) have short half-lives, making them an appealing option for IV APT bridging during the perioperative period. In a study published in 2010 by Savonitto et al., 30 patients with a recently implanted DES underwent tirofiban "bridging" for 4 days until 4 h prior to urgent major surgery. There were no cases of stent thrombosis, MI, death, or surgical re-exploration due to bleeding [14]. A meta-analysis published by Warshauer et al. included a pooled analysis of eight studies that reported the outcomes of 280 patients undergoing bridging therapy with tirofiban or eptifibatide prior to surgery [13]. In this study, the pooled estimate of outcomes included in-hospital mortality 3.5% (95% confidence interval [CI] 1.7–5.9%), stent thrombosis 1.3% (95% CI 0.3–3.0%) and major bleeding 7.4% (95% CI 2.8–14.1%) showing that the risk of perioperative bleeding and cardiac events is still present despite bridging.

Cangrelor, is a potent IV antagonist of P2Y12 receptor with immediate onset of action and a rapid offset [17,18], making it a potential candidate for bridging therapy. The BRIDGE trial, a prospective, randomized, double blinded multicenter trial included 210 patients treated with a coronary stent who received cangrelor or placebo prior to CABG [16]. In this study, patients treated with cangrelor had a significantly lower level of platelet reactivity throughout the procedure compared to placebo, but there were no significant differences in major bleeding events between both groups. This shows that cangrelor can, theoretically, prevent thrombosis without increasing perioperative bleeding. However, the BRIDGE study did not focus on the perioperative ischemic outcomes. Cangrelor has been approved as an adjunct to PCI to reduce risk of perioperative MI, sent thrombosis, and repeat coronary revascularization in the phase 3 CHAMPION trials [18], but conclusive studies for its use as a bridging therapy are lacking.

In our study, one case of angiographically documented stent thrombosis was reported in the NCS group compared to none in the CS group. The time interval between PCI and surgery was more than 12 months in this case. In two out of three cases of perioperative MI in the NCS group, the PCI-to-surgery interval was also more than 12 months. Moreover, when we compared 30-day outcomes between patients who underwent surgery in less than 6 months after PCI to those who underwent surgery after 6 months, we had similarly high rates of perioperative ischemic events and bleeding complications. Our cases demonstrate that postponing surgery for at least 6 months after DES implantation may not necessarily be enough to exclude the risk of perioperative cardiac ischemic events. Additionally, thrombolytics, for the treatment of stent thrombosis, may carry a higher risk of bleeding in the postoperative period, and PCI is the treatment of choice to minimize bleeding complications [19]. Therefore, patients with prior DES implantation should be considered to undergo surgery at centers that are able to perform PCI to treat perioperative stent thrombosis or MI, should they occur [7,15,20].

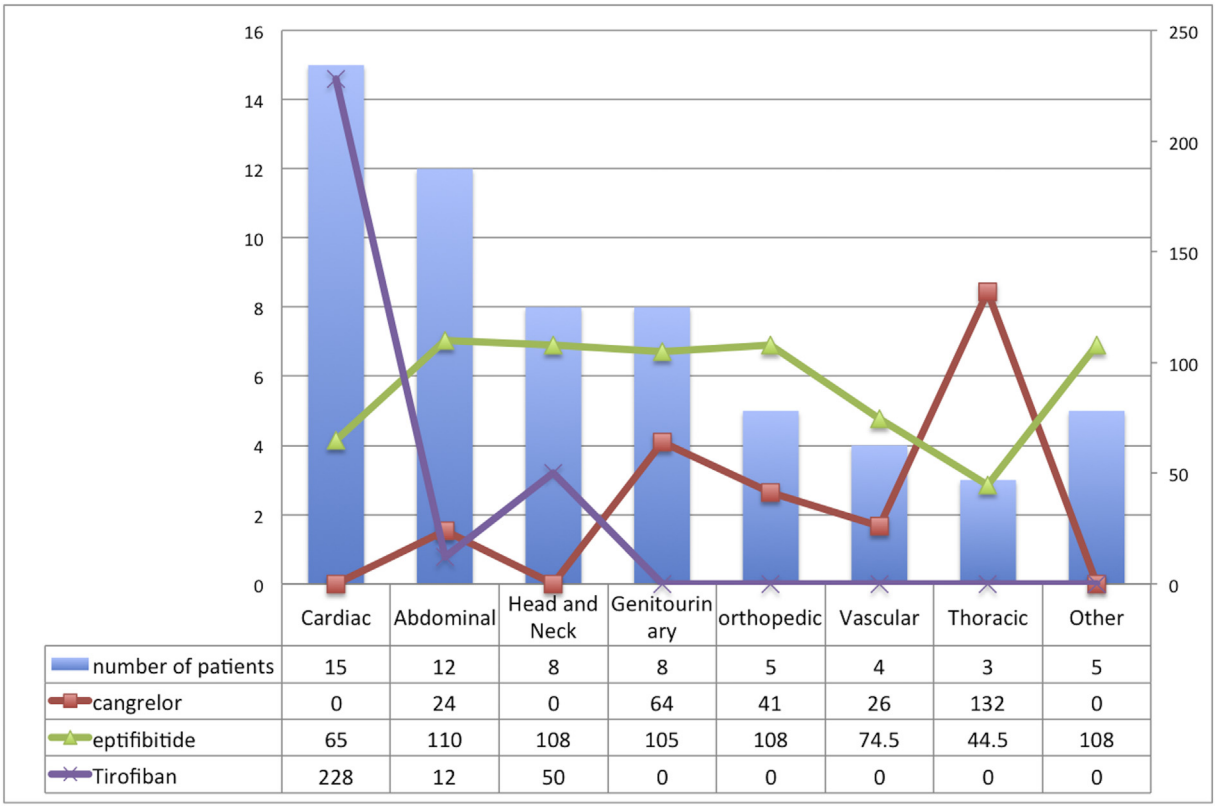
In the absence of clear guidelines that highlight the adequate perioperative antiplatelet therapy, devised strategies are at the discretion of the operators. The decision should be tailored to the patient's baseline comorbidities, lesion characteristics of the initial PCI, perioperative risk of bleeding, and type of surgery performed. Armstrong et al. identified several predictors for major cardiac risk events among patients with prior PCI who underwent NCS including age ≥60 years, revised cardiac risk index ≥2, history of congestive heart failure, chronic kidney disease, diabetes, ACS with MI for PCI indication, and specific lesion characteristics (ostial and distal lesion locations, calcified lesions) [21]. All the cases of stent thrombosis and MI reported in our study had an ACS indication for PCI and at least 2 of the aforementioned risk factors.

The type of procedure performed plays a major role in choosing the best perioperative APT strategy. In patients undergoing minor surgical procedures that do not require major surgical incisions (i.e. eye surgery, endovascular, dermatological procedures etc.), the risk of bleeding is

Table 4b
Description of bleeding complications post cardiac surgery by patient.

Patient ID	Type of surgery	Bleeding event	Hgb drop (g/dl)	Units of pRBC transfused	BARC classification	Time between PCI and surgery	Preoperative bridging therapy	Duration of therapy (days)
1	CABG	Upper GI bleed	3.9	2	3a	2 weeks	Eptifibatide	5
2	CABG	Mediastinal hematoma	5.4	6	4	10 months	Eptifibatide	7
3	CABG	Mediastinal hematoma	4.7	6	4	8 months	Eptifibatide	2
4	CABG	Bleeding from chest tube	2.8	13	4	2 months	Eptifibatide	2

BARC: Bleeding Academic Research Consortium; Hgb: Hemoglobin; pRBC: packed red blood cells; CABG: coronary artery bypass grafting.



	Cardiac	Abdominal	Head and Neck	Genitourinary	orthopedic	Vascular	Thoracic	Other
number of patients	15	12	8	8	5	4	3	5
cangrelor	0	24	0	64	41	26	132	0
eptifibitide	65	110	108	105	108	74.5	44.5	108
Tirofiban	228	12	50	0	0	0	0	0

Fig. 2. Patient determined post-surgical event scores based on importance.

low and continuing DAPT is preferred [22]. In major surgical procedures, continuing DAPT perioperatively may reduce the risk of stent thrombosis and MI, but may also increase the risk of bleeding. In such cases, preoperative bridging with short acting IV APT should theoretically protect patients from postoperative cardiac events without risking major bleeding complications. However, the reported cases in our study population highlight the limitations of preoperative bridging with any short acting APT agent. Surgical interventions result in sympathetic activation, vasospasms, and platelet activation contributing to the hypercoagulable state during the perioperative period [23]. Moreover, the rapid offset of IV APT agents after discontinuation results in minimal postoperative platelet inhibition, leaving patients prone to stent thrombosis and cardiac events. Therefore, meaningful bridging protocols should include early initiation of P2Y12 following surgery or continued IV APT.

Additionally, preoperative bridging requires discontinuation of oral DAPT 5-7 days before the procedure and admitting the patient to the hospital to receive IV APT infusions and be closely monitored for any signs of bleeding or thrombocytopenia. Bridging requires prolonged hospitalization, which is costly and exposes patients to the risk of nosocomial infection. The average cost per person per day is included in Table 1. Hence, several factors should be taken into account before choosing the appropriate antiplatelet therapy.

Critical evaluation of the current evidence shows that the approach to preoperative bridging should be individualized and tailored to every patient's baseline medical comorbidities and type of surgery performed. The patient survey that we previously mentioned shows that patients have equal concerns about post-surgical ischemic and bleeding complications, and any approach should aim at minimizing both outcomes.

To that effect, a consensus document published in 2014 [24] provided a scheme to stratify patients' thrombotic risk after PCI and bleeding risk associated with cardiac and non-cardiac surgery. This scheme was intended to help physicians establish an individualized risk assessment based on patients' baseline characteristics and adopt the appropriate perioperative antiplatelet management strategy. The feasibility of complying with the consensus recommendations in a real world surgery setting was further assessed in the "Stent after Surgery" Registry [7]. 1082 patients from 19 different hospitals were enrolled, and the consensus recommendations were applied to 85% of the cases. The rate of 30-day MACE was low and similar (3.5%) in patients undergoing cardiac and non-cardiac surgery. BARC 3-5 bleeding events were significantly higher in patients undergoing cardiac surgery (36.3% VS. 5.6%; $P < 0.01$). However, the rate of both MACE and BARC 3–5 bleeding events fall within acceptable surgical standards [25], supporting a favorable safety profile. This study sets the stage for individualized perioperative treatment strategies that minimize the rate of ischemic and bleeding events in patients undergoing surgery after PCI.

4.1. Limitations

Our study has several limitations. The main limitation is the absence of a control group that would allow us to compare the perioperative outcomes after following a preoperative bridging strategy to a strategy of antiplatelet therapy discontinuation without bridging. The study included a small number of patients who were all men. Hence our results may not be extrapolated to the female population, although gender-based differences may not exist in the risk of stent thrombosis or bleeding.

5. Conclusion

In summary, patients on DAPT undergoing surgery after PCI and DES stent implantation are at high risk of perioperative stent thrombosis and ischemic events even after receiving IV APT. Despite discounting DAPT and receiving short acting IV APT bridging, there was a high rate of bleeding complications, most of which required transfusions. Novel strategies are needed to maintain platelet inhibition and prevent

thrombotic events in the perioperative period while minimizing the risk of bleeding.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2018.11.018.

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