Bridging Therapy in the Perioperative Management of Patients With Drug-Eluting Stents

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Patients with drug-eluting stents appear to be at increased risk of thrombosis beyond 30 days (late) or even 1 year (very late) after stent placement. Patients with recent placement of drug-eluting stents who are receiving dual-antiplatelet therapy pose a challenge in the perioperative period. Current guidelines recommend discontinuation of clopidogrel 5 to 7 days prior to surgery or invasive procedures to prevent bleeding complications. When a patient with a drug-eluting stent is off of clopidogrel, he or she is at risk of stent thrombosis, even during treatment with anticoagulants, such as intravenous heparin. There are currently no universal recommendations for decreasing the risk of stent thrombosis. We herein outline a strategy involving the use of glycoprotein IIb/IIIa inhibitors as "bridging therapy" during the high-risk perioperative period and report on 8 patients who successfully underwent bridging therapy with no adverse cardiac outcomes (death, myocardial infarction, or stent thrombosis) or bleeding complications.
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Since the advent of percutaneous transluminal coronary angioplasty in 1977, major advances have been made in percutaneous coronary intervention, culminating in the introduction of drug-eluting stents (DES) in 2001. These polymer-coated stents contain antiproliferative agents that elute locally to prevent neointimal proliferation, the major cause of in-stent restenosis. DES replaced the non–drug-coated bare-metal stents (BMS) in the majority of patients because DES reduced coronary artery restenosis by 60% to 70%.[1] However, recent observations have revealed an increased risk of late stent thrombosis with DES,[2,3] resulting in a decline in their use. The peak use of DES in the

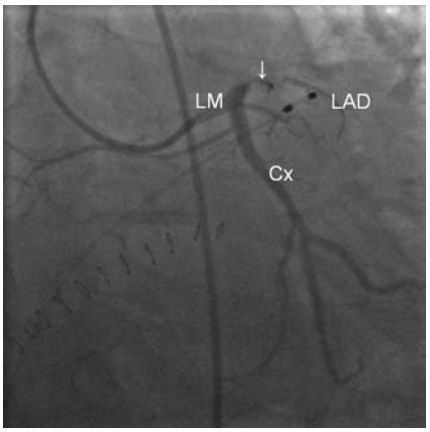

Figure 1. *Right anterior oblique caudal view of an angiogram in a patient with stent thrombosis (arrow). LM, left main coronary artery; LAD, left anterior descending artery; Cx, circumflex artery.*

United States occurred in January 2006, when they represented 90% of all coronary stents used; they currently represent 60% of coronary stents used. The longer duration of dual-antiplatelet therapy (DAT) that is required following DES implantation can impact plans for elective and semielective procedures and surgeries. Stopping either DAT agent during the first year following DES implantation can expose the patient to a risk of life-threatening stent thrombosis (Figure 1).

Stent Thrombosis

Stent thrombosis is an uncommon but serious complication of coronary stents that presents as an ST-elevation myocardial infarction in more than 70% of cases and carries a mortality rate of up to 45%.[4,5] In patients with ST-elevation myocardial infarctions, stent thrombosis represents a subgroup with poor angiographic results and 2.8 times the risk of in-hospital major adverse cardiovascular outcomes compared with de novo infarctions.[6] Exposure of blood to nonendothelialized stent struts is the key mechanistic trigger for stent thrombosis. Clinically, most cases of stent thrombosis occur within the first 24 hours (acute) or within the first month (subacute). With BMS, thrombosis is rarely seen after 1 month (late).[7-13] In contrast, patients with DES appear to be at increased risk of thrombosis beyond 30 days (late) or even 1 year (very late) after stent placement.[2,3] Contributing to the increased risk of late thrombosis is delayed reendothelialization caused by the antiproliferative drug (sirolimus, paclitaxel, zotarolimus, everolimus, or tacrolimus) that is eluted by the stent. Animal studies have shown complete reendothelialization by 28 days with BMS, whereas DES can have incomplete healing even at 180 days.[14] In one human study, angioscopic evaluation at 6 months demonstrated complete endothelialization in 100% of BMS but in only a striking 13.3% of DES.[15] Similar findings were documented via optical coherence tomography[16] and postmortem examination.[5,17] For this reason, the 2007 American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI)[18] focused update of the 2005 guidelines recommended that patients with BMS be on DAT for a minimum of 1 month (Class I A) after BMS placement and, ideally, up to 1 year in patients who are not at high risk for bleeding (Class I B). For DES, the guidelines recommend DAT for at least 12 months (Class IIa B). However, the ideal duration of therapy is still unclear and may exceed 12 months in patients who are at lower bleeding risk. Table 1 summarizes clinical and angiographic risk factors for stent thrombosis.

Coronary Stents and Interim Invasive Procedures or Surgeries

Patients with coronary stents pose a challenge in the perioperative period for invasive procedures and surgeries. The current ACC/AHA guidelines[19] recommend discontinuation of clopidogrel 5 to 7 days prior to surgery to prevent bleeding complications. Patients with recent (< 1 year) coronary stent implants are at risk of stent thrombosis when they are not taking clopidogrel. Furthermore, surgery itself induces a state of heightened platelet reactivity, placing these patients at an even greater

Table 1
Risk Factors for Stent Thrombosis

Clinical	Angiographic
Advanced age	Long stents*
Acute coronary syndrome	Multiple lesions
Diabetes	Overlapping stents
Low ejection fraction	Ostial or bifurcation lesions
Prior brachytherapy	Small vessels†
Renal failure	Suboptimal stent results
Previous history of stent thrombosis	

*No specific numerical length cutoff for stent thrombosis risk, but the longer the stent, the greater the risk.
†No specific numerical size cutoff for stent thrombosis risk, but the smaller the vessel, the greater the risk.
Adapted from Fleisher LA et al.[19]

risk for stent thrombosis. The Science Advisory issued by 5 professional societies advocates postponement of elective surgery for at least 1 year after DES placement, if possible.[20] Although this approach would be preferred, it is not always possible, particularly with DES, which require a much longer duration of DAT. Moreover, the ideal length of therapy with DES is still unknown, and patients may be at risk even beyond 12 months after stent placement.

Bridging Therapy With Glycoprotein IIb/IIIa Inhibitors

One approach to surgical patients with coronary stents on DAT involves the use of short-acting platelet glycoprotein (GP) IIb/IIIa inhibitors as "bridging antiplatelet therapy" during the high-risk perioperative period.[21] The empirical use of these agents is based on theory, and there are currently minimal data in the literature on their use for this purpose.[22,23] We herein report on our initial experiences with GP IIb/IIIa inhibitor bridging therapy.

Methods

Between January 2007 and July 2008, 8 patients underwent bridging therapy with a GP IIb/IIIa inhibitor at Cedars-Sinai Medical Center (Los Angeles, CA). All patients had previously been treated with DAT (aspirin and clopidogrel) after placement of DES but had clopidogrel discontinued secondary to surgical procedures. Aspirin was continued in all patients.

A retrospective chart review was performed in these 8 patients. The type of GP IIb/IIIa inhibitor (eptifibatide or tirofiban) and the timing and duration of therapy were examined. The patient's age, types and locations of stents, duration since stent placement, type of surgical procedure, coagulation function, preoperative and postoperative hemoglobin and hematocrit, and number of blood products transfused within 24 hours of the procedure were evaluated. Postoperative troponins were not routinely checked unless clinically indicated. Whenever available, risk factors for stent thrombosis, including prior acute coronary syndrome, diabetes mellitus, renal failure, heart failure, prior brachytherapy, and stent-specific risk factors (long stents or overlapping stents), were also noted.

Results

The baseline clinical and angiographic characteristics of all patients are summarized in Table 2 and Table 3, respectively. Age of the patients ranged from 69 to 81 years. The duration of time from placement of the stent to the surgical procedure ranged from 1 month to 3 years, with the average being 13 months. Four patients had no clinical risk factors for stent thrombosis, 1 patient had diabetes only, 1 patient had heart failure only, and 2 patients had 4 risk factors (prior acute coronary syndrome, diabetes mellitus, renal failure, and heart failure). One patient had overlapping stents. None of the patients had received prior brachytherapy.

Details on the bridging therapy regimens are shown in Table 4. Three patients received eptifibatide, and

Table 2
Baseline Clinical Characteristics of the Patients

			Stent Thrombosis Risk Factors			
Patient	Age (y)	Sex	ACS	Diabetes Mellitus	Renal Failure	Heart Failure
1	69	M	0	0	0	0
2	72	M	0	0	0	0
3	77	M	0	+	0	0
4	75	F	+	+	Stage 3*	NYHA class II
5	78	M	+	+	Stage 5†	NYHA class IV
6	81	F	0	0	0	0
7	73	M	0	0	0	NYHA class II
8	75	F	0	0	0	0

*Stage 3: GFR 30-59 mL/min/1.73 m^2.
†Stage 5: GFR < 15 mL/min/1.73 m^2 or permanent renal replacement therapy.
ACS, acute coronary syndrome; F, female; GFR, glomerular filtration rate; M, male; NYHA, New York Heart Association.

Table 3
Baseline Angiographic Characteristics of the Patients

	Most Recent PCI							
Patient	Stent	Number of Stents	Size	Location	Lesion Before PCI	Lesion After PCI	Time Since (mo)	Prior Stents
1	Cypher*	1	3.0 × 18 mm	Proximal LAD	80% Stenosis	0% Stenosis	9	0
2	Cypher	1	3.0 × 13 mm	RCA	85% Stenosis	0% Stenosis	1	BMS × 2 (RCA, first OM)
3	DES (type unknown)	1	Unknown	RCA	Unknown	Unknown	2	Unknown
4	Cypher	1	2.5 × 18 mm	LCx	"Severe" stenosis	0% Stenosis	22	0
5	TAXUS†	1	3.0 × 12 mm	RCA	90% Stenosis	0% Stenosis	6	DES × 2 (LAD)
6	BMS	2 (overlap)	2.5 × 12 mm 2.5 × 15 mm	Proximal LAD	90% Stenosis	0% Stenosis	14	DES × 1 (RCA)
7	DES (type unknown)	Unknown	Unknown	Unknown	Unknown	Unknown	3 years	Unknown
8	Cypher	1	2.5 × 23 mm	Proximal LAD	90% Stenosis	"Excellent results"	16	DES × 1 (mid LAD)

*The Cypher® stent is manufactured by Cordis Corp., Bridgewater, NJ.
†The TAXUS® stent is manufactured by Boston Scientific Corp., Natick, MA.
DES, drug-eluting stent; BMS, bare-metal stent; LAD, left anterior descending artery; RCA, right coronary artery; OM, obtuse marginal artery; LCx, left circumflex artery.

Table 4
Bridging Therapy Summary

	Clopidogrel			Glycoprotein IIb/IIIa Inhibitor			
Patient	Discontinued (days preoperative)	Restarted (days postoperative)	Loading Dose	Drug	Started (days preoperative)	Discontinued (hours preoperative)	Continued Aspirin, 325 mg
1	5	0	0	Eptifibatide	3	12	+
2	5	1	300 mg	Eptifibatide	5	12	+
3	5	1	0	Eptifibatide	1	12	+
4	5	1	600 mg	Tirofiban	2	12	+
5	7	1	0	Tirofiban	6	12	+
6	6	1	0	Tirofiban	3	12	+
7	6	1	0	Tirofiban	4	12	+
8	5	1	0	Tirofiban	2	12	+

5 patients received tirofiban. Clopidogrel was discontinued between 5 to 7 days prior to surgery and restarted within 1 day after surgery in all patients. A loading dose of clopidogrel was used in 2 patients when it was restarted after surgery, 1 with 600 mg and the other with 300 mg. GP IIb/IIIa inhibitor therapy was started between 1 to 6 days prior to surgery (range: from 4 days after discontinuation of clopidogrel to the same day after discontinuation of clopidogrel) and discontinued 12 hours prior to the procedure. The range of starting times for the GP IIb/IIIa inhibitor was due to logistical reasons. All patients received aspirin 325 mg/d during the perioperative period.

Table 5 summarizes pertinent data from the hospital course. Four

Table 5
Perioperative Characteristics of the Patients

		Preoperative*					Postoperative					
Patient	Type of Procedure	Platelets (× 1000/μL)	INR	aPTT (sec)	Hgb (g/dL)	Hct (%)	Platelets (× 1000/μL)	INR	aPTT (sec)	Hgb (g/dL)	Hct (%)	Transfused
1	Left lower lung lobectomy	129	1.3	29	13.6	40.1	154	—	—	14.1	41.9	0
2	VATS left upper lobe wedge resection	204	1.2	29	13.2	38.7	217	—	—	12.8	37.3	0
3	L3 laminectomy, intrathecal catheter revision	182	1.1	28	13.1	39.9	151	—	—	12.0	36.4	0
4	Anterior radical hemivulvectomy	379	1.0	28	11.5	35.0	315	—	—	10.6	32.3	0
5	AVR, 1-vessel CABG	122	1.7	31	8.6	26.8	83	1.8	34	9.2	27.2	3 units pRBC 1 unit platelets
6	AVR	236	0.9	32	11.0	33.1	203	1.4	32	11.0	33.5	3 units pRBC 1 unit platelets
7	AVR, CryoMaze†	318	1.2	13.4	13.4	40.7	220	1.4	14.7	9.8	29.1	1 unit platelets
8	2-Vessel CABG	189	1.1	31	12.8	36.8	137	1.5	30	14.4	41.7	3 units pRBC 1 unit platelets

*Normal ranges: platelets 150,000-450,000/μL; INR 0.8-1.3; aPTT 22-37; Hgb 13.0-17.0 g/dL (men), 11.6-15.4 g/dL (women); Hct 37.5% to 49.9% (men), 34.3% to 45.4% (women).
†The CryoMaze™ Surgical Ablation System is manufactured by ATS Medical Inc., Minneapolis, MN.
aPTT, activated partial thromboplastin time; AVR, aortic valve replacement; CABG, coronary artery bypass graft; Hct, hematocrit; Hgb, hemoglobin; INR, international normalized ratio; pRBC, packed red blood cells; VATS, video-assisted thoracoscopic surgery.

patients underwent cardiac surgery. The other 4 patients had noncardiac surgery: lobectomy, a lung wedge resection via video-assisted thoracoscopic surgery, a spinal surgery, and an anterior radical hemivulvectomy.

One patient had a mildly elevated international normalized ratio of 1.7 prior to surgery. The maximum drop in hemoglobin was 3.6 g/dL (range: 3.6 to 1.6 g/dL, mean −0.4 g/DL). Only the 4 patients who underwent cardiac surgeries required transfusion of blood products. There were no incidences of stent thrombosis or adverse cardiac outcomes such as mortality or clinically evident myocardial infarction.

Discussion

Advances in science and technology have brought about marked improvements in the field of medicine, from the development of sophisticated imaging modalities to the creation of new drugs and devices. These gains, though, have also led to new challenges. With the advent of organ transplantation came the problem of organ rejection and graft versus host disease. Decline in mortality from myocardial infarctions has been offset by the rise in heart failure. Although advances in coronary stents have resulted in decreased rates of restenosis and a subsequent need for repeat interventions, they too have been accompanied by their own set of challenges. One such dilemma is the perioperative management of antiplatelet therapy in patients with coronary stents. DAT combined with aspirin and clopidogrel is associated with higher risks of perioperative bleeding, but discontinuation of therapy places patients at increased risk for stent thrombosis. Ideally, surgery should be delayed until the course of DAT has been completed. However, this approach is not always feasible or practical, and patients with DES are likely at risk for stent thrombosis even after a 12-month course of therapy. In patients who are likely to undergo surgery or an invasive procedure within a year of stenting, a BMS or balloon angioplasty should be considered instead of a DES.

Aspirin in the Perioperative Period

Aspirin acts by irreversibly blocking platelet cyclo-oxygenase 1 (COX-1), thereby inhibiting aggregation in affected platelets for the remainder of their lifespan. Platelet function is partially restored within 4 to 5 days after aspirin is stopped. Although there are concerns about increased perioperative bleeding with aspirin, discontinuation of aspirin is usually not required for most procedures. One large meta-analysis of 474 studies showed a 1.5 times increase in intraoperative bleeding risk in patients taking aspirin, but no increase in surgical mortality or morbidity.[24] There was no difference in surgical complications or outcome related to bleeding in most procedures, including biopsies, endoscopies, dental procedures, and ophthalmologic, visceral, and general surgeries. In cataract surgery, patients taking aspirin had a similarly low risk of ocular hemorrhage as patients not taking aspirin.[25] The data for orthopedic surgeries are less clear, showing an increased rate of bleeding in hip arthroplasty,[26] but not in osteosynthesis of femoral neck fractures[27] or in spinal fusion or instrumentation surgery.[28] In intracranial neurosurgery, aspirin has been associated with increased postoperative intracranial bleeding and has contributed to fatal outcomes in some cases.[29]

The increased risk of perioperative bleeding must be weighed against the harm of discontinuing aspirin. In observational studies, preoperative withdrawal of aspirin has been associated with increased in-hospital mortality in patients undergoing coronary artery bypass graft surgery and peripheral vascular disease surgery.[30-32] For all types of surgeries, patients with underlying cardiovascular disease may have an increased risk of acute coronary syndromes or stroke if aspirin is stopped.[33,34] In particular, patients with coronary stents have an even higher risk of adverse cardiac events when aspirin is discontinued (odds ratio, 89.78),[35] and an increased risk exists even beyond 1 year after implantation.

For patients with DES undergoing bridging therapy, we recommend that aspirin be continued at a dose of 325 mg/d during the perioperative period unless there is a prohibitive bleeding risk (as in "high-risk" procedures in which perioperative hemorrhage could be catastrophic or adversely impact surgical outcome). Table 6 presents guidelines used at our institution for bleeding risk assessment of common procedures. Ultimately, the risk-benefit profile of continuing aspirin will need to be determined individually in each patient via collaboration among the surgeon, cardiologist, and anesthesiologist.

Clopidogrel in the Perioperative Period

Clopidogrel acts by irreversibly modifying the platelet adenosine diphosphate receptor, consequently impairing affected platelets for the rest of their lifespan. Unlike aspirin, it is generally considered unsafe to continue clopidogrel prior to elective surgery. After discontinuation, it takes approximately 5 to 7 days for new platelets to repopulate the circulating blood and for platelet function to return to baseline.

Currently, the ACC/AHA guidelines[19] recommend discontinuation of clopidogrel 5 to 7 days prior to

Table 6
Procedures With Low, Intermediate, and High Bleeding Risk

Low Risk	Intermediate Risk	High Risk
Anterior chamber eye surgery	Cardiac surgery	Intracranial neurosurgery
Biopsy	Ear, nose, and throat surgery	Posterior chamber eye surgery
Dental extraction	Major orthopedic surgery	Spinal cord surgery
Endoscopy	Prostate surgery	
Minor orthopedic surgery	Reconstructive surgery	
Spinal anesthesia	Vascular surgery	
	Visceral surgery	

surgery to prevent bleeding complications. However, there are no universal recommendations for decreasing the risk of stent thrombosis. One proposed approach is the use of short-acting platelet GP IIb/IIIa inhibitors as "bridging therapy" during the high-risk perioperative period. This approach is only meant for patients undergoing elective surgery, as patients requiring emergent surgeries are taken directly to the operating room even while on DAT. Recent guidelines from the American College of Chest Physicians recommend against the routine use of bridging therapy (Class II C), but these recommendations are not based on empirical evidence and the guidelines acknowledge the need for studies to assess the efficacy and safety of this approach.[36] To our knowledge, other specialty societies have issued no official recommendations on this issue.

Use of GP IIb/IIIa Inhibitors as Bridging Therapy

GP IIb/IIIa inhibitors reversibly inhibit platelet aggregation by preventing binding to the IIb/IIIa receptor. Currently, 3 GP IIb/IIIa inhibitors are available for use in the United States: eptifibatide, tirofiban, and abciximab. All 3 drugs have rapid onsets of action of less than 15 minutes. After discontinuation of eptifibatide and tirofiban, platelet function returns to baseline within 4 to 8 hours, making these drugs ideal candidates for bridging therapy. These agents can be continued up until shortly before surgery, providing patients with protection against stent thrombosis during the preoperative period while they are off of clopidogrel. In contrast, abciximab is not a suitable option for bridging therapy because platelet function takes 24 to 48 hours to return to normal after discontinuation of this drug.

Other agents have also been suggested for bridging therapy, including heparin, low molecular weight heparin, bivalirudin, and fondaparinux. These agents all act via an antithrombin-mediated mechanism. Stent thrombosis is thought to be a predominantly platelet-mediated phenomenon, so antithrombins, including unfractionated and low molecular weight heparins, are unlikely to be effective. Although these agents have not been specifically studied for this purpose, several studies indirectly suggest that antithrombins are ineffective in preventing stent thrombosis and are associated with increased perioperative bleeding risk.[37-39]

In our initial experience with the GP IIb/IIIa inhibitor bridging therapy reported here, all patients had uncomplicated surgical interventions and uneventful hospital courses. A particular concern with bridging therapy is bleeding complications secondary to incomplete reversal of platelet inhibition before surgery. Of the 4 patients who underwent noncardiac surgery, none were reported to have clinically significant bleeding and none required transfusion of blood products. With the exception of 1 patient who underwent cardiac surgery without receiving any transfusion of packed red blood cells, postoperative drops in hemoglobin were 1.1 gm/dL or less, below the cutoff for Thrombolysis In Myocardial Infarction (TIMI) minimal bleeding criteria. The other 3 patients who underwent cardiac surgeries received transfusions of 3 units of packed red blood cells and 1 unit of platelets or less, which is consistent with typical transfusion requirements for cardiac surgery.[40,41] Based on these results, it can be concluded that these patients did not experience greater than usual bleeding complications. Also, in the limited number of cases evaluated, none of the patients experienced stent thrombosis.

Table 7
Bridging Therapy Protocol

1. Discontinue clopidogrel 5 days prior to procedure
2. Continue or increase aspirin to 325 mg, unless prohibitive bleeding risk
3. Two days prior to the procedure, start
   - Tirofiban 0.1 μg/kg/min if patient has normal renal function, or
   - Tirofiban 0.05 μg/kg/min if CrCl < 30 mL/min, or
   - Eptifibatide 2.0 μg/kg/min if patient has normal renal function, or
   - Eptifibatide 1.0 μg/kg/min if CrCl < 50 mL/min
4. Monitor CBC daily
5. Hold tirofiban or eptifibatide 12 hours prior to procedure
6. Check platelet count and/or function 2 hours prior to procedure
7. Restart clopidogrel > 24 hours postoperative
   - Loading dose: clopidogrel 300 mg or 600 mg × 1
   - Maintenance dose: clopidogrel 75 mg/d
8. Reduce aspirin to preprocedure dose

CBC, complete blood count; CrCl, creatinine clearance.

At our institution, we have developed a clopidogrel hotline in conjunction with the department of pharmacy and a clopidogrel bridging protocol (Table 7) to raise awareness of this issue and to ease the process of perioperative risk assessment and bridging therapy. Additional recommendations on clopidogrel bridging are outlined in Table 8. The key step is a formal preoperative evaluation with the involvement of the surgeon, cardiologist, and anesthesiologist in a comprehensive risk-benefit analysis of surgical bleeding versus stent thrombosis. The focus is on discontinuing clopidogrel, continuing aspirin therapy, and bridging infusion of the GP IIb/IIIa inhibitor. It should be noted that GP IIb/IIIa

Table 8
Bridging Therapy Recommendations

Dos	Don't knows	Don'ts
Communication among the surgeon, cardiologist, and anesthesiologist is key	Adjunctive use of heparin with GP IIb/IIIa inhibitor infusion not clear	Don't use abciximab (long half-life)
Formal preoperative evaluation at least 1 week prior	Antithrombin agents such as unfractionated heparin, low-molecular weight heparin, bivalirudin, and fondaparinux have not been studied	Don't replace the use of intravenous GP IIb/IIIa inhibitors with heparins (including low-molecular-weight heparin) or other anticoagulants
Hold clopidogrel at least 5 days prior	Platelet function assay to guide and titrate treatment is currently investigational	Routine use of prophylactic platelet or erythrocyte transfusions not helpful
Continue aspirin and increase dose to 325 mg unless prohibitive bleeding risk	Role of apheresis platelets unclear	
Admit patient 2-3 days prior to procedure	Antiplatelet agents such as dipyridamole or aspirin/extended-release dipyridamole have not been studied	
Initiate intravenous short-acting GP IIb/IIIa inhibitor (eptifibatide or tirofiban) with or without loading dose	The ADP antagonist intravenous cangrelor is currently investigational	
Monitor CBC daily for platelet count	How long after stent placement should any degree of concern persist and require strict assessments?	
Stop GP IIb/IIIa inhibitor 10-12 hours (5-6 half-lives) prior to procedure		
Check platelet count 2 hours prior to procedure		
Surveillance for stent thrombosis and bleeding should continue in early postoperative period (telemetry monitoring is suggested)		
Restart clopidogrel ≥ 24 hours postprocedure with or without loading dose (300 or 600 mg) after evaluating risk-benefit		
Reduce aspirin to preprocedure dose		

ADP, adenosine diphosphate; CBC, complete blood count; GP, glycoprotein.

inhibitor bridging therapy does not offer protection during the intraoperative and postoperative period (when stent thrombosis risk is the highest), so it is important to continue surveillance for stent thrombosis (and bleeding) in the early postoperative period and restart clopidogrel as soon as possible.

Even though aspirin and clopidogrel have elimination half-lives of 2 to 3 hours and 7.5 hours, respectively, drug-exposed platelets are typically irreversibly affected, causing platelet inhibition until new, unaffected thrombocytes are produced by the bone marrow. It is likely that perioperative administration of a titrated platelet transfusion (preferably ABO compatible) or of apheresis platelets would correct drug-induced thrombasthenia caused by these agents in patients who do not discontinue DAT prior to surgery and who then actively display a need for functional platelets intraoperatively. However, routine prophylactic platelet transfusions should be avoided.

Conclusions

The perioperative management of patients with coronary stents is a relatively new dilemma, and it is important to raise awareness of this issue among health care providers. Although there are currently no "evidence-based" recommendations on how to manage these patients, our limited series reported here demonstrates that short-acting GP IIb/IIIa inhibitor bridging therapy is a feasible approach that appears to be safe. Further experience is required to confirm the safety and efficacy of bridging therapy. Finally, problems are best anticipated and avoided, not solved. Accordingly, given our limited understanding of the exact mechanism and incidence of stent thrombosis, our inability to accurately identify at-risk patients, and the lack of effective and safe therapies to mitigate this risk, the most prudent strategy to limit this rare but potentially life-threatening complication at the current time is a selective, thoughtful, and evidence-based application of DES in clinical practice. ■

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Main Points

- The longer duration of dual-antiplatelet therapy (DAT) that is required following drug-eluting stent (DES) implantation can impact plans for elective and semielective procedures and surgeries. Stopping either DAT agent during the first year following DES implantation can expose the patient to a risk of life-threatening stent thrombosis.
- Patients with DES appear to be at increased risk of thrombosis beyond 30 days (late) or even 1 year (very late) after stent placement.
- One approach to surgical patients with coronary stents on DAT involves the use of short-acting platelet glycoprotein (GP) IIb/IIIa inhibitors as "bridging antiplatelet therapy" during the high-risk perioperative period.
- GP IIb/IIIa inhibitors reversibly inhibit platelet aggregation by preventing binding to the IIb/IIIa receptor.
- In our initial experience with the GP IIb/IIIa inhibitor bridging therapy, all patients had uncomplicated surgical interventions and uneventful hospital courses.
- GP IIb/IIIa inhibitor bridging therapy does not offer protection during the intraoperative and postoperative period (when stent thrombosis risk is the highest), so it is important to continue surveillance for stent thrombosis (and bleeding) in the early postoperative period and restart clopidogrel as soon as possible.

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