

## Time and Cardiac Risk of Surgery after Bare-metal Stent Percutaneous Coronary Intervention

Gregory A. Nuttall, M.D.,\* Michael J. Brown, M.D.,† John W. Stombaugh, C.R.N.A., M.N.A.,‡ Peter B. Michon, C.R.N.A., M.N.A.,‡ Matthew F. Hathaway, C.R.N.A., M.N.A.,‡ Kevin C. Lindén, C.R.N.A., M.N.A.,‡ Andrew C. Hanson, B.S.,§ Darrell R. Schroeder, M.S.,|| William C. Oliver, M.D.,\* David R. Holmes, M.D.,# Charanjit S. Rihal, M.D.#

**Background:** The duration of time that elective noncardiac surgery (NCS) should be delayed after percutaneous coronary intervention (PCI) with bare metal stents (BMSs) is unknown.

**Methods:** This large, single-center, retrospective study examined the relation between complication rate in patients with BMSs undergoing NCS and the duration of time between PCI and NCS. Primary endpoints included in-hospital major adverse cardiac events (death, myocardial infarction, stent thrombosis, or repeat revascularization with either coronary artery bypass grafting or PCI of the target vessel) and bleeding events. The relation between the events and the timing of noncardiac surgery after PCI with BMS was assessed using univariate analysis and multiple logistic regression.

**Results:** From January 1, 1990, to January 1, 2005, a total of 899 patients were identified. The frequency of major adverse cardiac events was 10.5% when NCS was performed less than 30 days after PCI with BMS, 3.8% when NCS was performed between 31 and 90 days after PCI with BMS, and 2.8% when NCS was performed more than 90 days after PCI with BMS. In univariate and multivariate analyses, a shorter time interval between PCI with BMS and noncardiac surgery was significantly associated with increased incidence of major adverse cardiac events (univariate:  $P < 0.001$ ; odds ratio = 4.0; 95% confidence interval, 2.0–8.3; multivariate:  $P = 0.006$ ; odds ratio = 3.2; 95% confidence interval, 1.5–6.9). Bleeding events were not associated with time between PCI with BMS and NCS or with the use of antiplatelet therapy in the week before NCS.

**Conclusions:** The incidence of major adverse cardiac events is lowest when NCS is performed at least 90 days after PCI with BMS.

PERCUTANEOUS coronary intervention (PCI) with stenting<sup>1</sup> is the most common method of myocardial revascularization. Coronary stents have been shown to provide better short- and long-term outcome when compared with balloon angioplasty alone.<sup>2</sup> Both bare-metal stents (BMSs) and drug-eluting stents are used in clinical practice, the former for more than 10 yr, whereas drug-eluting stents have been commercially available since 2003 in the United States.<sup>3</sup> Although drug-eluting stents are now used in the majority of procedures, BMSs are still indicated for a variety of patients based on individual clinical situations.<sup>4</sup>

Thrombosis of a stent is associated with major morbidity and mortality.<sup>5</sup> Antiplatelet therapy is routinely administered to prevent stent thrombosis after PCI with BMS.<sup>6</sup> Current oral pharmacotherapy includes aspirin and clopidogrel. Bare metal stent thrombosis with this regimen occurs in less than 0.5% of patients at 30 days after PCI with BMS.<sup>7</sup>

Approximately 5% of patients who receive a coronary stent will require noncardiac surgery (NCS) within 1 yr after PCI.<sup>8</sup> If surgery is required, the risk of bleeding while on dual antiplatelet therapy is increased.<sup>9</sup> The risk of perioperative bleeding must be balanced by the risk of stent thrombosis induced by the procoagulant state associated with surgery. The American College of Cardiology–American Heart Association practice guidelines recommend delaying NCS for at least 6 weeks after PCI with BMS.<sup>10,11</sup> This recommendation is based on several studies with small sample sizes and varying durations of delay before surgery.<sup>12–16</sup> To address the hypothesis that the risk of major adverse cardiac events (MACEs) and bleeding events is related to the time interval between PCI with BMS and NCS, we undertook a comprehensive evaluation of all patients undergoing NCS after PCI with BMS during a 15-yr period at our institution.

### Materials and Methods

After institutional review board approval, we performed a retrospective analysis of 899 patients who underwent NCS within 1 yr after PCI with BMS at Mayo Clinic (Rochester, Minnesota) between January 1, 1990, and January 1, 2005. Patients were identified using the Mayo Clinic PCI registry and the Mayo Clinic Surgical database. This article includes the 207 patients previ-

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\* Professor of Anesthesiology, † Assistant Professor of Anesthesiology, ‡ Student in Nurse Anesthesia, Department of Anesthesiology, # Professor of Medicine, Department of Medicine, Cardiovascular Diseases, || Assistant Professor of Biostatistics, College of Medicine, § Statistical Programmer Analyst, Division of Biostatistics, Mayo Clinic.

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Address correspondence to Dr. Nuttall: Mayo Clinic, 200 First Street Southwest, Rochester, Minnesota 55905. nuttall.gregory@mayo.edu. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

ously described by Wilson *et al.*<sup>17</sup> The complete medical records of identified patients were reviewed individually. Patient demographic data included risk factors for coronary artery disease, presenting condition at time of PCI (PCI performed on an elective basis or urgently for acute coronary syndrome, as well as pre-PCI cardiogenic shock), angiographic data (including number of stents placed, percent residual stenosis, residual dissection, postprocedural TIMI [Thrombolysis in Myocardial Infarction trial] flow, and successful PCI in all lesions stented), maintenance antiplatelet therapy (none, aspirin, thienopyridine, or both), antiplatelet therapy before NCS (none within 30 days, used within 7 days of NCS, or stopped > 7 days before NCS), type of NCS (categorized according to American College of Cardiology–American Heart Association classification),<sup>10</sup> urgency of NCS (non-emergent or emergent), and use of general anesthesia. Patients on long-term warfarin therapy were excluded from the study.

Coronary angiography and intracoronary stent implantation were performed using standard percutaneous techniques as previously described.<sup>18</sup> Patients were prescribed long-term therapy with 325 mg aspirin daily, while ticlopidine or clopidogrel was administered for 4 weeks after the time of the index PCI. All patients undergoing PCI at the Mayo Clinic have been prospectively followed up in a registry since 1979. Demographic, clinical, and angiographic data are recorded by trained data technicians, and 10% of records are audited by the supervisor for quality control. Patients are prospectively contacted at 6 and 12 months and annually thereafter, and follow-up events are recorded.

### Definitions

In-hospital MACEs associated with NCS included death, Q-wave myocardial infarction (MI), non-Q-wave MI, stent thrombosis, and repeat PCI of the target coronary stenosis or coronary artery bypass grafting.

Perioperative MI was defined according to World Health Organization criteria for MI,<sup>19</sup> including the presence of at least two of the following three criteria: (1) chest pain persistent for more than 30 min, (2) electrocardiographic changes consistent with MI or ischemia, and (3) elevation in creatine kinase-MB isoform greater than two times the upper limit of institutional reference range. Serum troponin was not routinely available in the early 1990s, and for consistency throughout the study interval, only creatine kinase-MB concentrations were analyzed. Q-wave MI was defined as two of the above three criteria along with presence of pathologic Q waves on electrocardiographic analysis.

Stent thrombosis was defined as the angiographic appearance of one or more luminal filling defects in a stented coronary artery, or pathologic Q waves in the coronary distribution of the stented artery along with

two of the three determinants for diagnosis of myocardial infarction.

Successful PCI was defined for each patient as final residual stenosis within all stents less than 50% by visual estimation.

Bleeding was defined as intraoperative and postoperative bleeding necessitating the transfusion of nonerythrocyte clotting factors (including platelets, fresh frozen plasma, or cryoprecipitate).

### Statistical Analysis

All analyses were performed using SAS version 8 (SAS Institute Inc., Cary, NC). To assess whether the risk for complications after NCS is associated with the duration of time from PCI to surgery, the time from PCI to NCS was assessed as both a continuous variable and also categorically ( $\leq 30$ , 31–90, and  $\geq 91$  days). These time categories were chosen *a priori* based on published retrospective studies.<sup>8,12,14,20,21</sup> Patient and procedural characteristics were summarized and compared across timing groups using the chi-square test for discrete variables and the Kruskal-Wallis test for continuous and ordinal variables. Logistic regression analyses were performed to assess characteristics potentially associated with the development of MACEs or bleeding complications. Given the duration of the study period, initial logistic regression analyses were performed to verify that the frequency of these events did not change significantly over calendar time. The risk factor of specific interest was the time from PCI to surgery. However, because the time from PCI to surgery was not randomly assigned, any observed relation between the timing of procedures and the frequency of complications could be due to imbalances in other prognostic factors. To control for this possibility, two sets of adjusted analyses were performed. One adjusted analysis was performed using multiple logistic regression with standard covariate adjustment. Given the limited number of complications observed in the current study, all possible covariates were not included in this adjusted analysis. To determine a set of covariates to include in the adjusted analyses, a preliminary multivariable analysis was performed for each endpoint using multiple logistic regression. All potential covariates (*i.e.*, variables other than the time from PCI to surgery) were included in the initial step, and a backward elimination algorithm was used to eliminate those that were nonsignificant. The potential covariates that were considered included all of the variables listed in table 1, with the exception of a history of cholesterol 240 mg/dl or greater and the type of maintenance antiplatelet agent used after PCI. Cholesterol information was excluded because it was missing for 88 patients. The type of maintenance antiplatelet agent used after PCI was excluded because it was missing for 13 patients, the majority of whom underwent surgery within 30 days after PCI, and because it was thought to be less impor-

**Table 1. Patient Characteristics**

Variable	Time from PCI to Noncardiac Surgery						P Value*
	0–30 Days		31–90 Days		91 or More Days		
	n	%	n	%	n	%	
Overall	248	100	260	100	391	100	
Age group							0.908
≤ 55 yr	32	12.9	33	12.7	49	12.5	
56–65 yr	56	22.6	62	23.8	88	22.5	
66–75 yr	105	42.3	93	35.8	144	36.8	
≥ 76 yr	55	22.2	72	27.7	110	28.1	
Sex							0.891
Female	90	36.3	93	35.8	135	34.5	
Male	158	63.7	167	64.2	256	65.5	
Current/former smoker							0.244
No	91	37.1	78	30.5	138	35.7	
Yes	154	62.9	178	69.5	249	64.3	
History of cholesterol ≥ 240 mg/dl							< 0.001
No	85	39.2	52	21.7	83	23.4	
Yes	132	60.8	188	78.3	271	76.6	
Diabetes							0.721
No	183	73.8	187	71.9	277	70.8	
Yes	65	26.2	73	28.1	114	29.2	
Hypertension							0.398
No	88	35.5	78	30.0	124	31.7	
Yes	160	64.5	182	70.0	267	68.3	
Previous MI							0.153
No	117	47.2	141	54.2	184	47.1	
Yes	131	52.8	119	45.8	207	52.9	
Previous CABG							0.373
No	197	79.4	203	78.1	322	82.4	
Yes	51	20.6	57	21.9	69	17.6	
Preprocedural shock							< 0.001
No	221	89.1	255	98.1	380	97.2	
Yes	27	10.9	5	1.9	11	2.8	
Indication for PCI							< 0.001
Elective	99	39.9	146	56.6	165	42.3	
Acute coronary syndrome	149	60.1	112	43.4	225	57.7	
Residual dissection							< 0.001
No	148	59.7	191	73.5	290	74.2	
Yes	100	40.3	69	26.5	101	25.8	
Residual stenosis							< 0.001
≤ 5%	136	54.8	189	72.7	276	70.6	
6–49%	93	37.5	64	24.6	99	25.3	
≥ 50%	19	7.7	7	2.7	16	4.1	
Number of stents placed							0.671
1	148	59.7	159	61.2	230	58.8	
2	65	26.2	76	29.2	111	28.4	
3	26	10.5	19	7.3	34	8.7	
4	9	3.6	6	2.3	16	4.1	
Postprocedure TIMI flow grade							0.347
0	5	2.2	0	0.0	4	1.1	
1	2	0.9	0	0.0	0	0.0	
2	6	2.6	8	3.1	15	4.0	
3	217	94.3	248	96.9	360	95.0	
Successful PCI in all lesions							0.023
No	19	7.7	7	2.7	16	4.1	
Yes	229	92.3	253	97.3	375	95.9	
Maintenance anticoagulant after PCI							< 0.001
None	18	7.6	2	0.8	0	0	
Aspirin	50	21.1	8	3.1	21	5.4	
Thienopyridine	8	3.4	13	5.0	14	3.6	
Aspirin and thienopyridine	161	67.9	236	91.1	355	91.0	
Anticoagulant use before surgery							0.030
Used within 7 days	180	72.6	162	62.3	238	60.9	
Stopped > 7 days	48	19.3	73	28.1	106	27.1	
No use within 30 days	20	8.1	25	9.6	47	12.0	

(continued)

Table 1. Continued

Variable	Time from PCI to Noncardiac Surgery						P Value*
	0–30 Days		31–90 Days		91 or More Days		
	n	%	n	%	n	%	
Surgical risk group							< 0.001
Low	35	14.1	61	23.5	87	22.2	
Intermediate	85	34.3	106	40.8	220	56.3	
High	128	51.6	93	35.8	84	21.5	
General anesthesia							0.275
Yes	158	63.7	183	70.4	264	67.5	
No	90	36.3	77	29.6	127	32.5	

\* P values are from Kruskal–Wallis test for age, residual percent stenosis, number of stents placed, and postprocedure TIMI (Thrombolysis in Myocardial Infarction trial) flow. All other P values are from chi-square test.

CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

tant than the covariate summarizing the use of antiplatelet medications in the 30 days before the subsequent NCS. A second adjusted analysis was performed using propensity scores to adjust for characteristics potentially associated with the time between PCI and surgery.<sup>22</sup> There were three propensity scores included as adjustor variables in this multivariable analysis. These propensity scores were determined from separate binary logistic regression models assessing differences between timing groups ( $\leq 30$  days *vs.* 31–90 days,  $c = 0.71$ ; 31–90 days *vs.*  $\geq 91$  days,  $c = 0.65$ ; and  $\leq 30$  days *vs.*  $\geq 91$  days,  $c = 0.73$ ). In all cases, two-tailed tests were performed with  $P \leq 0.05$  used to denote statistical significance.

## Results

### Clinical Characteristics

During the study period, a total of 899 patients (318 female, 581 male) were identified who underwent NCS within 1 yr after PCI with BMS. The median time from PCI to NCS was 64 days (interquartile range, 27–182 days). Patient demographic data, risk factors for coronary artery disease, condition at time of PCI, angiographic data, maintenance antiplatelet therapy, and antiplatelet therapy within 7 days of NCS are delineated in table 1 according to the time between PCI with BMS and NCS ( $\leq 30$ , 31–90, or  $\geq 91$  days). A number of these characteristics were found to differ significantly across timing groups. In general, patients who underwent NCS sooner after PCI with BMS tended to have more acute symptoms at the time of the PCI (*e.g.*, more preprocedural shock) and less successful PCI (*e.g.*, higher residual stenosis) and were more likely to undergo high-risk NCS. Surgical procedures and their associated risk classification are presented in table 2.

### Risk of Perioperative MACEs

Of the 899 patients in the study population, 47 (5.2%; 95% confidence interval [CI], 3.8–6.7%) experienced

one or more in-hospital MACEs (31 deaths, 12 Q-wave MIs, 6 non-Q-wave MIs, 9 stent thromboses, and 12 repeat revascularizations) when NCS was performed within 1 yr of PCI with BMS. The frequency of MACEs did not change significantly over the calendar time of the study ( $P = 0.403$ ). Characteristics found to be associated with MACEs by univariate analysis are presented in table 3. These included PCI with BMS performed for acute coronary syndrome ( $P = 0.013$ ), pre-PCI cardiogenic shock ( $P < 0.001$ ), unsuccessful PCI in a coronary lesion ( $P = 0.002$ ), absence of either aspirin or a thienopyridine as maintenance antiplatelet therapy after PCI with BMS ( $P = 0.017$ ), American College of Cardiology–American Heart Association risk classification of surgery ( $P = 0.136$ ), emergent nature of surgery ( $P = 0.003$ ), use of general anesthesia ( $P = 0.046$ ), and days from stent placement to surgery ( $P = 0.003$ ) (table 3).

The analyses assessing the association of time between PCI with BMS and NCS with MACEs are summarized in

Table 2. Types of Noncardiac Surgery as Categorized According to American College of Cardiology–American Heart Association Classification

Surgical Group	n (%)
High risk	
Vascular	202 (22)
Any emergency	103 (11)
Intermediate risk	
Nose, mouth, and pharynx	15 (2)
Digestive system	127 (14)
Musculoskeletal system	159 (18)
Respiratory system	63 (7)
Nervous system	34 (4)
Endocrine system	13 (1)
Low risk	
Ear	6 (1)
Hemi and lymphatic system	14 (2)
Urinary system	99 (11)
Male genital	26 (3)
Female genital	15 (2)
Integumentary system	22 (2)
Miscellaneous	1 (0)

**Table 3. Univariate Analysis of Characteristics Potentially Associated with MACEs or Bleeding Events**

Characteristic	Total n	MACEs			Bleeding Events		
		n	%	P Value*	n	%	P Value*
Overall	899	47	5.2		43	4.8	
Age group				0.068			0.131
≤ 55 yr	114	5	4.4		4	3.5	
56–65 yr	206	10	4.9		7	3.4	
66–75 yr	342	11	3.2		17	5.0	
≥ 76 yr	237	21	8.9		15	6.3	
Sex				0.457			0.363
Female	318	19	6.0		18	5.7	
Male	581	28	4.8		25	4.3	
Current/former smoker				0.479			0.693
No	307	14	4.6		13	4.2	
Yes	581	33	5.7		28	4.8	
History of cholesterol ≥ 240 mg/dl				0.317			0.393
No	220	13	5.9		12	5.5	
Yes	591	25	4.2		24	4.1	
Diabetes				0.292			0.291
No	647	37	5.7		34	5.3	
Yes	252	10	4.0		9	3.6	
Hypertension				0.788			0.771
No	290	16	5.5		13	4.5	
Yes	609	31	5.1		30	4.9	
Previous MI				0.070			0.016
No	442	17	3.8		29	6.6	
Yes	457	30	6.6		14	3.1	
Previous CABG				0.161			0.855
No	722	34	4.7		35	4.8	
Yes	177	13	7.3		8	4.5	
Shock before PCI procedure				< .001			0.450
No	856	36	4.2		42	4.9	
Yes	43	11	25.6		1	2.3	
Indication for PCI				0.013			0.178
Elective	410	13	3.2		24	5.9	
Acute coronary syndrome	486	34	7.0		19	3.9	
Residual dissection				0.207			0.167
No	629	29	4.6		26	4.1	
Yes	270	18	6.7		17	6.3	
Residual stenosis				0.073			0.229
≤ 5%	601	28	4.7		26	4.3	
6–49%	256	12	4.7		13	5.1	
≥ 50%	42	7	16.7		4	9.5	
Number of stents placed				0.237			0.078
1	537	31	5.8		30	5.6	
2	252	13	5.2		11	4.4	
3	79	2	2.5		2	2.5	
4	31	1	3.2		0	0.0	
Postprocedure TIMI flow grade				0.194			0.969
0	9	1	11.1		0	0.0	
1	2	0	0.0		1	50.0	
2	29	3	10.3		1	3.4	
3	825	38	4.6		40	4.8	
Successful PCI in all lesions				0.002			0.150
No	42	7	16.7		4	9.5	
Yes	857	40	4.7		39	4.6	
Maintenance antiplatelet after PCI				0.017			0.258
None	20	4	20.0		3	15.0	
Aspirin	79	3	3.8		3	3.8	
Thienopyridine	35	1	2.9		0	0.0	
Aspirin and thienopyridine	752	28	3.7		36	4.8	
Days from stent to surgery				0.003			0.046
≤ 30	248	26	10.5		17	6.9	
31–90	260	10	3.8		12	4.6	
91–180	165	5	3.0		7	4.2	
181–270	114	3	2.6		3	2.6	
271–365	112	3	2.7		4	3.6	

(continued)

Table 3. Continued

Characteristic	Total n	MACEs			Bleeding Events		
		n	%	P Value*	n	%	P Value*
Anticoagulant use before surgery				0.956			0.788
Used within 7 days	580	31	5.3		29	5.0	
Stopped > 7 days	227	11	4.8		9	4.0	
No previous use within 30 days	92	5	5.4		5	5.4	
Emergent surgery				0.003			0.016
Yes	103	12	11.7		10	9.7	
No	796	35	4.4		33	4.1	
Surgical risk group				0.136			< 0.001
Low	183	4	2.2		3	1.6	
Intermediate	411	24	5.8		9	2.2	
High	305	19	6.2		31	10.2	
General anesthesia				0.046			0.002
Yes	605	38	6.3		39	6.4	
No	294	9	3.1		4	1.4	

\* P values presented are from logistic regression. For these analyses, age, residual percent stenosis, and days from stent to surgery were analyzed as continuous variables, and all other variables were analyzed as categorical variables using the categories specified.

CABG = coronary artery bypass grafting; MACE = major adverse cardiac event; MI = myocardial infarction; PCI = percutaneous coronary intervention; TIMI = Thrombolysis in Myocardial Infarction trial.

table 4. The frequency of MACEs was 10.5% (95% CI, 6.7–14.3%) when NCS was performed 30 or fewer days after PCI with BMS, 3.8% (95% CI, 1.5–6.2%) when NCS was 31–90 days after PCI with BMS, and 2.8% (95% CI, 1.2–4.5%) when NCS was 91 or more days after PCI with BMS. From univariate analysis, a shorter time interval between PCI with BMS and surgery was found to be associated with an increased likelihood of MACEs ( $P < 0.001$ ; odds ratios [ORs] = 4.0 and 1.4 for NCS performed 0–30 days and 31–90 days after PCI compared with  $\geq 91$  days after PCI). When time was treated as a continuous variable, the risk of MACEs significantly decreased for each 30-day increment between PCI with BMS and NCS ( $P = 0.003$ ; OR = 0.84 per 30-day increase in time between PCI with BMS and surgery). From multivariable analysis controlling for age, use of general anesthesia, cardiogenic shock before PCI with BMS, and successful PCI in all vessels, the adjusted ORs for MACEs

were 3.2 and 1.4 for NCS performed 0–30 days and 31–90 days after PCI with BMS ( $P = 0.006$ ). Similar findings were obtained when the adjusted analysis was performed using propensity scores (ORs = 3.6 and 1.6;  $P = 0.003$ ) (table 5).

#### Risk of Perioperative Bleeding Events

Surgical bleeding events necessitating the transfusion of any nonerythrocyte clotting factors occurred in 43 patients (4.8%; 95% CI, 3.4–6.2%). Thirty-three required platelet transfusion, 29 required perioperative fresh frozen plasma transfusion, and 5 required perioperative cryoprecipitate transfusion. The frequency of bleeding events did not change significantly over the calendar time of the study ( $P = 0.544$ ). The analyses assessing the association of time between PCI with BMS and NCS with bleeding events are summarized in tables 5 and 6. The frequency of bleeding events was 6.9% (95% CI, 3.7–10.0%) when NCS was performed 30 or fewer days after PCI with BMS, 4.6% (95% CI, 2.1–7.2%) when NCS was 31–90 days after PCI with BMS, and 3.6% (95% CI, 1.7–5.4%) when NCS was 91 or more days after PCI with BMS. From univariate analysis, there was some evidence suggesting that a longer time interval between PCI with BMS and surgery was associated with a reduced likelihood of bleeding events ( $P = 0.046$ ; OR = 0.90 per 30 days) (table 6). However, the frequency of bleeding events did not differ significantly ( $P = 0.174$ ) across time period groups (table 5). Other characteristics found to be associated with bleeding events included previous MI ( $P = 0.016$ ), emergency surgery ( $P = 0.016$ ), risk classification of surgery ( $P < 0.001$ ), and use of GA ( $P = 0.002$ ) (table 3). In multivariable analysis controlling simultaneously for previous MI and risk classification of surgery, and from a propensity score adjusted analysis,

Table 4. Association of Time from PCI to Surgery with MACEs

	OR	95% CI	P Value
Unadjusted			
Time from PCI to surgery, per 30 days	0.84	0.74–0.94	0.003
Adjusted			
Time from PCI to surgery, per 30 days	0.87	0.77–0.97	0.016
Age, per decade	1.41	1.03–1.93	0.030
Shock before PCI	8.06	3.53–18.41	< 0.001
General anesthesia	2.79	1.27–6.13	0.011
Successful PCI	0.22	0.09–0.56	0.001

Analyses were performed using logistic regression with time from percutaneous coronary intervention (PCI) to surgery treated as a continuous variable. The process used to select the covariates for the adjusted analysis is described in the Materials and Methods.

CI = confidence interval; MACE = major adverse cardiac event; OR = odds ratio.

**Table 5. Frequency of MACEs and Bleeding Events in Patients Undergoing Noncardiac Surgery after PCI with BMS\***

	MACEs				Bleeding Events			
	Days from PCI to Surgery			P Value*	Days from PCI to Surgery			P Value*
	≤ 30	31–90	≥ 91		≤ 30	31–90	≥ 91	
Surgeries, n	248	260	391		248	260	391	
Events, n (%)	26 (10.5)	10 (3.8)	11 (2.8)		17 (6.9)	12 (4.6)	14 (3.6)	
Unadjusted								
OR	4.0	1.4	1.0	< 0.001	2.0	1.3	1.0	0.174
95% CI	2.0–8.3	0.6–3.3			1.0–4.1	0.6–2.9		
Covariate adjusted†								
OR	3.2	1.4	1.0	0.006	1.2	0.9	1.0	0.857
95% CI	1.5–6.9	0.6–3.4			0.5–2.5	0.4–2.1		
Propensity score adjusted‡								
OR	3.6	1.6	1.0	0.003	1.3	0.7	1.0	0.457
95% CI	1.7–7.9	0.6–3.8			0.6–2.9	0.3–1.7		

\* Logistic regression was used to assess whether the likelihood of the given event differed across timing groups. For the logistic regression analyses, the *P* value presented corresponds to the 2 *df* test comparing all three timing groups simultaneously. In addition, the odds ratio (OR) and corresponding 95% confidence interval (CI) are presented for the two shorter interval groups (≤ 30 days and 31–90 days) with the largest interval group (≥ 91 days) as the reference. Both unadjusted and adjusted logistic regression analyses are presented. † For ischemic events, the covariates included age, shock before percutaneous coronary intervention (PCI), general anesthesia, and successful PCI. For surgical bleed events, the covariates included surgical risk group and previous myocardial infarction. The methods used to select these covariates are described in the text. ‡ Three propensity scores, calculated from binary logistic regression models assessing differences between timing groups, were included as covariates.

BMS = bare metal stent; MACE = major adverse cardiac event.

the frequency of bleeding events was not found to be significantly associated with duration of time between PCI with BMS and NCS (tables 5 and 6).

## Discussion

Practice guidelines recommend delaying elective NCS for at least 6 weeks after PCI with BMS. This is based on the assumption that a delay of 6 weeks will allow for a complete course of antiplatelet therapy and facilitating reendothelialization of the BMS, decreasing the likelihood of potentially catastrophic stent thrombosis. This recommendation is based on a number of retrospective evaluations that provided various durations of delay of

timing of NCS after PCI with BMS.<sup>8,12,14,17,20,21</sup> The current evaluation is the largest study to date addressing perioperative MACEs and bleeding events in noncardiac surgical patients after recent PCI with BMS. Our study demonstrates a clear association between the duration of time between PCI and NCS and ischemic cardiac events. We found that NCS performed more than 90 days after PCI with BMS was associated with the lowest risk of in-hospital MACEs (2.8%). The risk of MACEs decreased from 10.5% to 2.8% if NCS was delayed until 90 days after PCI with BMS. Bleeding events were not associated with duration of time between PCI with BMS and NCS.

The common practice of withdrawal of antiplatelet therapy in surgical patients with recently placed BMSs to decrease bleeding events has been associated with perioperative stent thrombosis.<sup>21</sup> The average duration of dual antiplatelet therapy after PCI with BMS is 4 weeks.<sup>23</sup> Although we did not find a significant association between antiplatelet therapy before NCS and risk of either ischemic or bleeding events, delaying elective NCS for at least 90 days after PCI with BMS would allow a complete course of dual antiplatelet therapy and allow for complete reendothelialization of the stent.

The American College of Cardiology–American Heart Association guidelines on perioperative cardiac risk reduction identify type of surgery as a specific risk factor for perioperative ischemic events. Most of the studies referred to above did not control for the type of surgical procedure when delineating MACEs and bleeding risk in surgical patients soon after PCI with BMS. Although many surgical procedures performed in a nonurgent setting may be classified as low or intermediate risk, if

**Table 6. Association of Time from PCI to Surgery with Bleeding Events**

	OR	95% CI	P Value
Unadjusted			
Time from PCI to surgery, per 30 days	0.90	0.81–1.00	0.046
Adjusted			
Time from PCI to surgery, per 30 days	0.96	0.86–1.06	0.425
Previous MI	0.40	0.21–0.78	0.007
Surgical risk group			< 0.001
Low	1.0		
Medium	1.39	0.37–5.21	
High	6.90	2.06–23.17	

Analyses were performed using logistic regression, with time from percutaneous coronary intervention (PCI) to surgery treated as a continuous variable. The process used to select the covariates for the adjusted analysis is described in the Materials and Methods.

CI = confidence interval; MI = myocardial infarction; OR = odds ratio.

those same procedures are performed in an emergency setting, they are reclassified as high risk.<sup>10</sup> All emergent surgical procedures performed during the study period were therefore defined as high risk in our analysis. Emergent surgery was independently associated with both MACEs and bleeding events.

Our study was not designed to determine the optimal perioperative antiplatelet regimen in patients who require NCS after recent PCI with BMS. If emergency or urgent surgery is required during the time period of dual antiplatelet therapy or within 90 days of PCI with BMS, perioperative caregivers should have a high index of suspicion for ischemic events, be prepared for surgical bleeding, and seek consultation regarding postoperative antiplatelet therapy regimens.

### Limitations

This study has the inherent limitations of a retrospective study. A limitation of our study is that we did not collect information on  $\beta$ -blocker and statin use. Patient care was not controlled by a study protocol. It is possible that patients discharged from our institution experienced an ischemic or bleeding event and were admitted to a facility other than our own. In addition, the more sensitive cardiac biomarkers available today may have captured additional MACEs and bleeding events. A large portion of the cohort likely had both electrocardiographic and creatine kinase levels drawn immediately after their NCS, but use of these tests was not standardized by a protocol, and therefore not every patient had this done. There is potential survival bias because patients in the current study needed to survive the PCI long enough to have a subsequent surgery. It could be that the most ill patients either have surgery soon after their PCI or die without having a subsequent surgery. If we assume that these patients would be at high risk for perioperative complications, this might partially explain why we found that patients who have surgery within the first 30 days are found to be at higher risk.

### Conclusions

The risk of ischemic events after NCS is greatest within 30 days of PCI with BMS and lowest after 90 days. When possible, NCS should be delayed at least 90 days after PCI with BMS. Bleeding events were not associated with time between PCI with BMS and NCS, or the use of antiplatelet therapy in the week before NCS.

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