The effect of treatment timing on repeat revascularization in patients with stable ischemic heart disease

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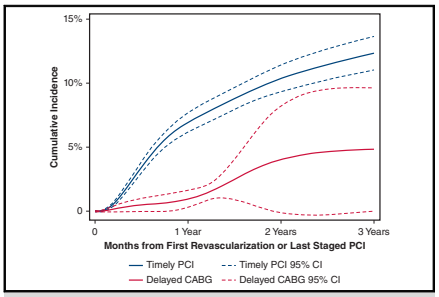
ABSTRACT

Objectives: In patients with stable ischemic heart disease, there is no evidence for the effect of revascularization treatment timing on the need for repeat procedures. We aimed to determine if repeat revascularizations differed among patients who received coronary artery bypass graft surgery after the time recommended by physicians compared with those who had timely percutaneous coronary intervention.

Methods: We identified 25,520 British Columbia residents 60 years or older who underwent first-time nonemergency revascularization for angiographically proven, stable left main or multivessel ischemic heart disease between January 1, 2001, and December 31, 2016. We estimated unadjusted and adjusted cumulative incidence functions for repeat revascularization, in the presence of death as a competing risk, after index revascularization or last staged percutaneous coronary intervention for patients undergoing delayed coronary artery bypass grafting compared with timely percutaneous coronary intervention.

Results: After adjustment with inverse probability of treatment weights, at 3 years, patients who underwent delayed coronary artery bypass grafting had a statistically significant lower cumulative incidence of a repeat revascularization compared with patients who received timely percutaneous coronary intervention (4.84% delayed coronary artery bypass grafting, 12.32% timely percutaneous coronary intervention; subdistribution hazard ratio, 0.16, 95% CI, 0.04-0.65).

Conclusions: Patients who undergo delayed coronary artery bypass grafting have a lower cumulative incidence of repeat revascularization than patients who undergo timely percutaneous coronary intervention. Patients who want to wait to receive coronary artery bypass grafting will see the benefit of lower repeat revascularization over percutaneous coronary intervention unaffected by a delay in treatment. (JTCVS Open 2024;19:164-74)



Adjusted cumulative incidence functions of repeat revascularization in the delayed CABG and timely PCI populations. Timely PCI (*red*); delayed CABG (*blue*).

CENTRAL MESSAGE

Patients with stable ischemic heart disease who want revascularization with CABG but cannot receive it in the time recommended by doctors will experience fewer repeat revascularizations than if they chose PCI as an alternative.

PERSPECTIVE

It is unknown if patients who receive delayed CABG have a different frequency of repeat revascularization than patients who have timely PCI. We found that patients who underwent delayed CABG had fewer repeat revascularizations compared with patients who had timely PCI. Physicians can now know that a delay in CABG treatment does not attenuate the benefits of CABG over PCI on repeat revascularization.

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Access to data provided by the Data Stewards is subject to approval but can be requested for research projects through the Data Stewards or their designated service providers. All inferences, opinions, and conclusions drawn in this publication are those of the author(s) and do not reflect the opinions or policies of the Data Stewards. Data in this analysis are limited by the terms of the Data Application Request to only those patients who have already undergone revascularization.

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Abbreviations and Acronyms

BMS = bare metal stent
CABG = coronary artery bypass grafting
CIF = cumulative incidence function
CSBC = Cardiac Services BC
DES = drug-eluting stent
HR = hazard ratio
MVD = multivessel disease
PCI = percutaneous coronary intervention
SVG = saphenous vein graft

Clinical need, patient demand, and resource allocations contribute to the timing of coronary artery disease treatment in Canada. In British Columbia (BC), regional health authorities use a global budget funding model[1] that creates a ceiling for the number of procedures a hospital can perform. Thus, patients with stable ischemic heart disease in whom nonemergency coronary revascularization is required, either by coronary artery bypass grafting (CABG) surgery or percutaneous coronary intervention (PCI), can experience delays during times of greater demand or reduced supply.[2]

Randomized controlled trials have shown that patients undergoing CABG have a lower rate of repeat revascularization compared with PCI, contributing to guideline recommendations that advise CABG over PCI in patients with complex stable ischemic heart disease.[3] However, these trials included repeat revascularization as a component in a composite end point, instead of as an independent end point, yet were not sized or powered to do so.[4]

Using published guidance,[5] we established our research question: Is there is a difference in repeat revascularizations in patients treated with delayed CABG compared with timely PCI? This article has 2 objectives: estimate the cumulative incidence of repeat revascularization, in the presence of death as a competing risk, in patients with stable multivessel or left main ischemic heart disease after CABG with delay and PCI within appropriate time, (1) without adjustment and (2) adjusting for patient, disease, and treatment characteristics. We hypothesized that the disease progression enabled by delay may compromise the benefits of CABG over PCI on repeat revascularization.

BC's population-based clinical registries and administrative databases have been used to achieve these objectives and answer our research question. This linked data set creates a picture of the coronary revascularization system for the population over the study period. Although treatment bias is generally controlled for through the execution of randomized trials, such methods offer limited insight into the real-world experience of patients, clinicians, and health systems, where the complexities of organizing and delivering resource-intensive procedural care must be managed. Our approach combines population-based data with robust statistical methods to answer our research question.

MATERIAL AND METHODS

This study follows the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for the reporting of observational cohort studies.[6] The University of British Columbia's Clinical Research Ethics Board provided ethical approval of this research (Certificate Number H17-00505) on May 17, 2017. The data stewards for this research provided their consent for publication.

Study Design

We conducted a retrospective cohort study of prospectively collected data among all patients in the province of BC, Canada, who underwent isolated CABG surgery or PCI for the treatment of stable ischemic heart disease.

Data Sources

We obtained diagnostic catheterization, PCI, and isolated CABG records from the provincial registries maintained by Cardiac Services BC (CSBC), a program of the Provincial Health Services Authority (Vancouver, BC, Canada). We used CSBC's registry data to construct an episode of care, which contains all events occurring from diagnostic catheterization through to revascularization. We linked these care episodes to the BC Ministry of Health's Discharge Abstract Database, which contains hospitalization records, and the BC Vital Statistics Deaths File, which contains deaths data. Finally, we linked this data set to Population Data BC's Central Demographics File, which contains demographic data for all study participants. We compared the data contained in the constructed episodes of care with that in hospitalization records to confirm information on dates of procedures, identify comorbidities, derive complications, and ascertain care outcomes (Online Data Supplement). In BC, cardiac catheterization is limited to tertiary centers where both diagnostic cardiac catheterization and interventional cardiology services were provided. Interventional cardiologists provided most diagnostic cardiac catheterizations during the study period.

Setting and Participants

The study cohort consists of patients aged 60 years or older who underwent nonemergency first-time revascularization for angiographically proven, stable left main or multivessel ischemic heart disease in British Columbia, between January 1, 2001, and December 31, 2016 (Figure 1). The criteria adopted by the ASCERT[7] investigators were used as the foundation for our patient selection. We selected an age cutoff that approximated the time when CABG or PCI became more evenly distributed in the study population, recognizing that in BC, younger patients were more likely to undergo PC than CABG. We defined revascularization as a PCI or an isolated CABG surgery. Patient age, extent of disease, and nonemergency status were identified using the CSBC cardiac surgery and PCI registry data. Stable disease was identified using atherosclerotic heart disease code (International Classification of Diseases, 10th Revision, Canada I25.0, I25.1, I25.10; International Classification of Diseases ninth Revision 429.2 414.0) logged as type M (most responsible), type 1 (preadmit comorbidity), type 2 (postadmit comorbidity), type 6 (proxy most responsible diagnosis), or types W, X, or Y (first, second, or third service transfers) in the Discharge Abstract Database. The index event in this study is first-ever revascularization, by either PCI or CABG, within the study period of January 1, 2001, and December 31, 2016.

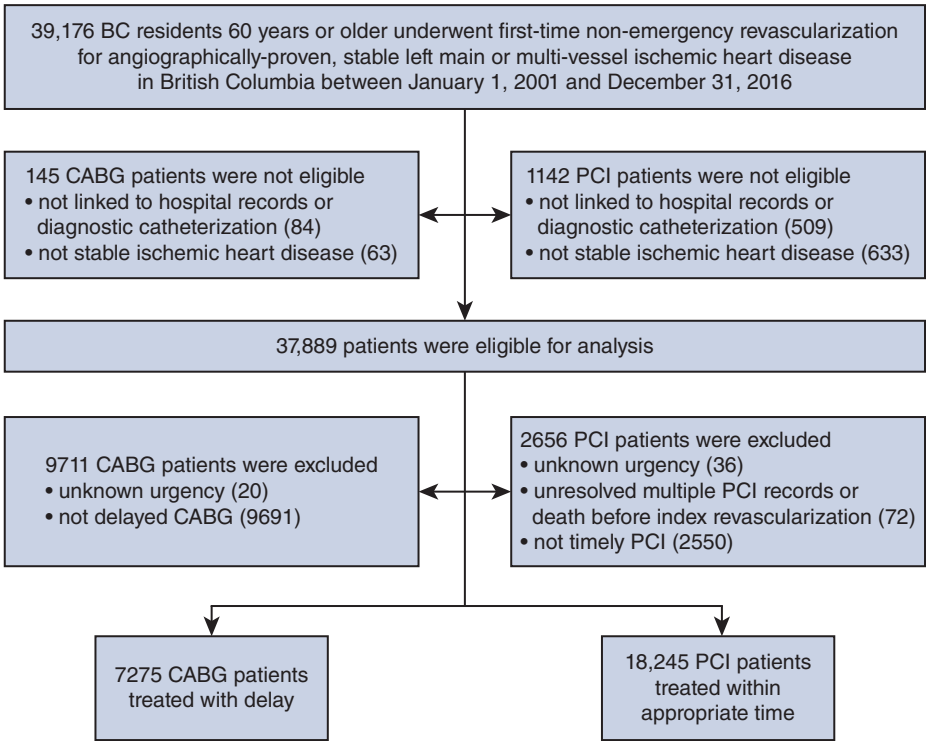

FIGURE 1. Flow diagram for the study population selection. *CABG*, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention.

Variables

Study variable. The study variable is treatment timing, operationalized as the time to coronary revascularization treatment and computed in calendar days. On the basis of treatment timing and the type of revascularization procedure received, patients were assigned to 1 of 2 study groups: delayed CABG or timely PCI. The time to treatment starts on the date when the need for revascularization is clinically established and the patient is ready, willing, and able to undergo revascularization. The time to treatment ends on the date the index revascularization procedure was performed. To establish intervals defining timely and delayed treatment, we used the Canadian Cardiovascular Society Access to Care recommended times[8] to define delayed CABG and timely PCI for semi-urgent and elective patients undergoing CABG and PCI, the First Minsters' Meeting benchmarks[9] for urgent CABG, and CSBC benchmarks for patients undergoing urgent PCI (Table 1). Dates were collected from CSBC registries for CABG and PCI, where triage coordinators recorded the date that the patient was booked for their procedure and the date their procedure occurred.

Outcome variable. The outcome variable is the occurrence of the first repeat revascularization or death after index revascularization or, in the case of patients with multiple PCI records, after the last staged PCI. We followed patients until the occurrence of an outcome, study end, or 3 years' time. We selected 3 years given the frequency of 3-year reports in the randomized controlled trial literature, specifically in the SYNTAX, FREEDOM, NOBLE, and EXCEL trials. CSBC records do not identify repeat revascularization as an outcome and provided data for staged PCI were inconsistent over the course of our study period. Therefore, we developed a rule to identify repeat revascularization using Spitzer and colleagues' criteria[10] for staged PCI procedures (Online Data Supplement). A repeat revascularization was identified from CSBC records as the first CABG or PCI occurring after index revascularization, when the diagnostic catheterization date preceding the procedure differs from the diagnostic catheterization date that preceded the index revascularization. In the case of patients with multiple PCI records, repeat revascularization also must have followed the index PCI after 60 days or staged PCI after 30 days, based on the literature. All nonemergency patients can choose to have planned or unplanned PCI as the time exists for a discussion of options. We used the date of death from any cause recorded in the BC Vital Statistics Deaths File. We measured time to a repeat revascularization or death from the date of revascularization for patients who received CABG or a single PCI procedure, and last staged PCI for those patients with multiple PCI records.

Additional variables. We used variables in the form in which they were received from the data stewards. Some concepts, such as comorbidities and clearance time, were operationalized by the study team from data already in the data set (Online Data Supplement). Comorbidities were identified from diagnosis codes in the Discharge Abstract Database, using work completed in previous research by the study investigators[11] as a foundation, and informed by clinical advisor feedback and the Canadian Institute for Health Information/Canadian Cardiovascular Society Cardiac Care Quality Initiative's comorbidity methodology.[12]

Statistical Methods

We estimated the frequency and percentage of patients by characteristics and by treatment group. Groups were compared using a chi-square test for categorical variables with *P* values for between group differences reported. We modeled the cumulative incidence function (CIF) of repeat revascularization, in the presence of death as a competing risk, for each treatment group over 3 years using with a flexible parametric approach using restricted cubic spline functions.[13] We reported the unadjusted cumulative incidence at 3 years and the unadjusted subdistribution hazard ratio (HR) of repeat revascularization, in the presence of death as a competing risk, at 3 years, for each study group.[14] The subdistribution HR for repeat revascularization gives the association between treatment received and the repeat revascularization-specific CIF.

TABLE 1. Study group assignments by procedure type and urgency and treatment delay in days

Procedure	Urgency	Timely treatment		Delayed treatment
		Interval start	Interval end	Interval start
CABG	Priority I	1 d	7 d	8+ d
	Priority II	1 d	14 d	15+ d
	Priority III	1 d	42 d	43+ d
PCI	Urgent inpatient	1 d	5 d	6+ d
	Urgent outpatient	1 d	14 d	15+ d
	Elective	1 d	42 d	43+ d

CABG, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention.

A subdistribution HR of less than 1 means the delayed CABG group had a lower subdistribution hazard of a repeat revascularization outcome at 3 years compared with the timely PCI group, in the presence of death as a competing risk. A hazard greater than 1 means the delayed CABG group had a higher subdistribution hazard of a repeat revascularization at 3 years compared with the timely PCI group, in the presence of death as a competing risk.

We then estimated propensity scores for the probability of belonging to each study group using logistic regression and used those scores to calculate inverse probability of treatment weights with the goal of achieving balance between the 2 groups.[15] Propensity score model variables were selected through a multistep iterative process starting with those used by the ASCERT investigators,[7] informed by a scoping review of the structures, processes, and patient factors of mortality after CABG,[16] and feedback from the study clinical and scientific advisors. Each patient was weighted by the inverse of the probability of being assigned to their treatment group to adjust for differences between the 2 treatment groups. Inverse probability of treatment weighting (IPTW) creates a synthetic cohort that establishes balance between the groups based on the covariates used in the propensity score model and may increase the study group size to ensure balance is achieved. We assessed the performance of the propensity score model by comparing the distribution of covariates, propensity scores, and standardized differences, before and after inverse probability weighting. Adjusted CIFs and subdistribution hazard estimates were obtained using an inverse probability weighted flexible parametric approach. Statistical analyses were performed using Stata 17 (StataCorp). Flexible parametric models for competing risks were constructed using *stpm2cr*, a Stata software package.[17]

Patient and Public Involvement

We consulted a cardiac surgery peer support group in Vancouver, BC, the Pacific Open-Heart Association, to inform our research inquiry. They told us that patients frequently waited for CABG and that they had concerns about the effects of delay on their health including death, heart attacks, and the need for repeat procedures. Identification of repeat revascularization by this group is consistent with the work of the International Consortium for Health Outcomes Measurement, which also identifies repeat revascularization as a patient-oriented outcome that should be measured.[18]

RESULTS

Participants

We identified 39,176 patients who met the selection criteria for our study (Figure 1). We did not select patients for the analytical cohort if their revascularization record could not be linked to hospital records or their PCI record was for ad hoc PCI, but the procedure could not be linked to a diagnostic catheterization (n = 591), or their hospital records did not contain diagnosis codes indicative of stable ischemic heart disease (n = 696). A total of 37,889 patients were eligible for analysis.

We set aside patients if their procedure urgency could not be determined (n = 56), if patients with multiple PCI records were not resolved after applying the repeat revascularization rule or if there were errors in the administrative data set where date of death preceded the date of revascularization (n = 72), if the patient received delayed PCI (n = 2550), or if the patient received timely CABG (n = 9711). A total of 25,520 patients were available to be analyzed (Figure 1).

Descriptive Data

The baseline characteristics of the patients in the analytical cohort are shown in Table 2. Before adjustment with inverse probability of treatment weights and compared with patients undergoing timely PCI, the patients undergoing delayed CABG had higher proportions of triple vessel disease, left main disease, male sex, a body mass index more than 30, and an ejection fraction 50% or less. The delayed CABG group also had higher proportions of atrial fibrillation or atrial flutter, congestive heart failure, diabetes, hypertension, and renal disease compared with timely PCI. The timely PCI group had higher proportions of double-vessel disease and Canadian Cardiovascular Society Angina Class 4. Patients were treated primarily in metropolitan hospitals, regardless of study group. Clearance time was shorter among patients treated with timely PCI compared with delayed CABG. Proportions of neighborhood income decile were similar throughout the study cohort. Of the patients who underwent delayed CABG, 8.5% received only a saphenous vein graft (SVG), 71.6% received a single arterial graft, 16.3% received a double arterial graft, and 3.4% received a triple arterial graft. More than half of patients who received only an SVG did so during the first 5 years of the study period. SVG rates were higher during the first 3 years of the study period, then decreased significantly and are consistent with the range reported by the SYNTAX investigators.[19] Of the patients who underwent timely PCI, 48.1% received

TABLE 2. Baseline characteristics of the patients

Characteristic	Unadjusted data					Data adjusted with inverse probability weighting				
	Timely PCI (n = 18,245)		Delayed CABG (n = 7275)		*P* value	Timely PCI (n = 26,376)		Delayed CABG (n = 22,813)		*P* value
	N	%	N	%		N	%	N	%	
Age, y*										
60-64	3594	19.7%	1609	22.1%	<.001	5150	19.5%	4556	20.0%	.17
65-69	3849	21.1%	1868	25.7%		5862	22.2%	4760	20.9%	
70-74	3635	19.9%	1827	25.1%		5811	22.0%	5950	26.1%	
75-79	3361	18.4%	1355	18.6%		4791	18.2%	4225	18.5%	
≥80	3806	20.9%	616	8.5%		4762	18.1%	3322	14.6%	
Sex										
Male	12,718	69.7%	5994	82.4%	<.001	19,389	73.5%	16,323	71.6%	.49
Female	5527	30.1%	1281	17.6%		6987	26.4%	6489	28.4%	
Body mass index*										
<18.5	237	1.3%	43	0.6%	<.001	298	1.1%	130	0.6%	.52
≥18.5 and <25	5380	29.5%	1897	26.1%		7583	28.8%	6718	29.4%	
≥25 and <30	7886	43.2%	3173	43.6%		11,452	43.4%	9983	43.8%	
>30	4625	25.3%	2046	28.1%		6857	26.0%	5777	25.3%	
Missing	117	0.6%	116	1.6%		186	0.7%	205	0.9%	
Extent of disease										
Double-vessel disease	10,076	55.2%	543	7.5%	<.001	10,575	40.1%	8350	36.6%	.18
Triple-vessel disease	7290	40.0%	4587	63.1%		11,643	44.1%	11,151	48.9%	
Left main disease	879	4.8%	2145	29.5%		4158	15.8%	3311	14.5%	
Ejection fraction†										
EF <30%	697	3.8%	268	3.7%	<.001	984	3.7%	830	3.6%	.70
EF ≥30% and ≤50%	3389	18.6%	1965	27.0%		5765	21.9%	4550	19.9%	
EF >50%	10,410	57.1%	4496	61.8%		15,244	57.8%	13,385	58.7%	
Missing	3749	20.5%	546	7.5%		4383	16.6%	4047	17.7%	
Serum creatinine (μmol/L)*										
<60	775	4.2%	219	3.0%	<.001	977	3.7%	1281	5.6%	.47
60≥ and <80	4380	24.0%	1525	21.0%		6149	23.3%	5308	23.3%	
80≥ and <100	6400	35.1%	2470	34.0%		9332	35.4%	8134	35.7%	
≥100	6024	33.0%	2320	31.9%		8562	32.5%	6813	29.9%	
Unknown	666	3.7%	741	10.2%		1355	5.1%	1276	5.6%	
Canadian Cardiovascular Society Angina Class*										
None	715	3.9%	389	5.3%	<.001	1082	4.1%	1161	5.1%	.12
Class 1	661	3.6%	347	4.8%		970	3.7%	1020	4.5%	
Class 2	2882	15.8%	1785	24.5%		4872	18.5%	4473	19.6%	
Class 3	1452	8.0%	2730	37.5%		4724	17.9%	4030	17.7%	
Class 4	11,450	62.8%	1494	20.5%		12,821	48.6%	10,113	44.3%	
Atypical	314	1.7%	68	0.9%		377	1.4%	208	0.9%	
Missing	771	4.2%	462	6.4%		1529	5.8%	1807	7.9%	
Prior acute myocardial infarction*										
Yes	3479	19.1%	2516	34.6%	<.001	6843	25.9%	5993	26.3%	.98
Unknown	4385	24.0%	2109	29.0%		6616	25.1%	5654	24.8%	
Smoking status*										
Never	7094	38.9%	2626	36.1%	<.001	9620	36.5%	8798	38.6%	.34
Current/now	2283	12.5%	621	8.5%		2979	11.3%	2181	9.6%	
Former/quit	8226	45.1%	3086	42.4%		12,129	46.0%	10,054	44.1%	
Unknown	642	3.5%	942	12.9%		1648	6.2%	1780	7.8%	
Comorbidities										
Atrial fibrillation or atrial flutter	1421	7.8%	2051	28.2%	<.001	3210	12.2%	3236	14.2%	.14
Cardiac dysrhythmias‡	728	4.0%	351	4.8%	<.001	1083	4.1%	1477	6.5%	.05
Cerebrovascular disease	428	2.3%	379	5.2%	<.001	906	3.4%	1251	5.5%	.27

(Continued)

TABLE 2. Continued

Characteristic	Unadjusted data					Data adjusted with inverse probability weighting				
	Timely PCI (n = 18,245)		Delayed CABG (n = 7275)		*P* value	Timely PCI (n = 26,376)		Delayed CABG (n = 22,813)		*P* value
	N	%	N	%		N	%	N	%	
Chronic pulmonary disease	911	5.0%	341	4.7%	.31	1465	5.6%	982	4.3%	.23
Congestive heart failure	2109	11.6%	958	13.2%	<.001	3474	13.2%	2496	10.9%	.09
Connective tissue disease	238	1.3%	93	1.3%	.87	356	1.3%	280	1.2%	.78
Diabetes	4986	27.3%	2908	40.0%	<.001	8484	32.2%	7416	32.5%	.88
Hypertension	9102	49.9%	4450	61.2%	<.001	14,237	54.0%	11,814	51.8%	.39
Hypertensive heart disease	35	0.2%	18	0.2%	.38	149	0.6%	48	0.2%	.21
Liver disease	53	0.3%	19	0.3%	.69	105	0.4%	72	0.3%	.67
Metastatic cancer	496	2.7%	168	2.3%	.06	662	2.5%	662	2.9%	.67
Peripheral vascular disease	715	3.9%	460	6.3%	<.001	1404	5.3%	1064	4.7%	.55
Pneumonia	522	2.9%	287	3.9%	<.001	1088	4.1%	776	3.4%	.50
Renal disease	1240	6.8%	711	9.8%	<.001	1895	7.2%	1770	7.8%	.59
Ulcer disease	104	0.6%	104	1.4%	<.001	179	0.7%	494	2.2%	.01
Calendar period of index revascularization										
2001	949	5.2%	484	6.7%	<.001	1532	5.8%	1901	8.3%	.26
2002	1101	6.0%	684	9.4%		1766	6.7%	2088	9.2%	
2003	1210	6.6%	714	9.8%		2023	7.7%	2180	9.6%	
2004	1224	6.7%	544	7.5%		1826	6.9%	1612	7.1%	
2005	1166	6.4%	503	6.9%		1844	7.0%	1499	6.6%	
2006	1100	6.0%	512	7.0%		1688	6.4%	1260	5.5%	
2007	1252	6.9%	485	6.7%		1690	6.4%	1353	5.9%	
2008	1266	6.9%	373	5.1%		1797	6.8%	1256	5.5%	
2009	1342	7.4%	238	3.3%		1790	6.8%	1592	7.0%	
2010	1387	7.6%	263	3.6%		1639	6.2%	945	4.1%	
2011	1325	7.3%	250	3.4%		1576	6.0%	1084	4.8%	
2012	1122	6.1%	347	4.8%		1467	5.6%	1094	4.8%	
2013	897	4.9%	467	6.4%		1470	5.6%	1373	6.0%	
2014	939	5.1%	455	6.3%		1434	5.4%	1295	5.7%	
2015	905	5.0%	421	5.8%		1296	4.9%	940	4.1%	
2016	1060	5.8%	535	7.4%		1537	5.8%	1339	5.9%	
Hospital type										
Metropolitan	14,197	77.8%	5396	74.2%	<.001	20,531	77.8%	16,981	74.4%	.17
Urban	4048	22.2%	1879	25.8%		5845	22.2%	5831	25.6%	
Clearance time category§										
1 wk	14,410	79.0%	3052	42.0%	<.001	17,410	66.0%	14,689	64.4%	.66
2 wk	2387	13.1%	1910	26.3%		4836	18.3%	4332	19.0%	
≥3 wk	1448	7.9%	2313	31.8%		4130	15.7%	3791	16.6%	
Neighborhood income decile										
Lowest decile	1956	10.7%	707	9.7%	.22	2664	10.1%	2417	10.6%	.87
2nd decile	1925	10.6%	756	10.4%		2814	10.7%	2089	9.2%	
3rd decile	1822	10.0%	742	10.2%		2742	10.4%	2427	10.6%	
4th decile	1907	10.5%	784	10.8%		2934	11.1%	2790	12.2%	
5th decile	1778	9.7%	759	10.4%		2374	9.0%	2030	8.9%	
6th decile	1760	9.6%	645	8.9%		2392	9.1%	2249	9.9%	
7th decile	1699	9.3%	694	9.5%		2459	9.3%	2097	9.2%	
8th decile	1755	9.6%	708	9.7%		2774	10.5%	2131	9.3%	
9th decile	1698	9.3%	706	9.7%		2421	9.2%	1957	8.6%	
Highest decile	1679	9.2%	673	9.3%		2346	8.9%	2360	10.3%	
Unknown	266	1.5%	101	1.4%		457	1.7%	265	1.2%	

PCI, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *EF*, ejection fraction. *At the time of revascularization. †Ejection fraction at the time of revascularization; if missing, at the time of diagnostic catheterization. ‡Excluding atrial fibrillation and atrial flutter. §Clearance time is the hypothetical time within which the wait list would be cleared at maximum weekly service capacity if there were no new arrivals.

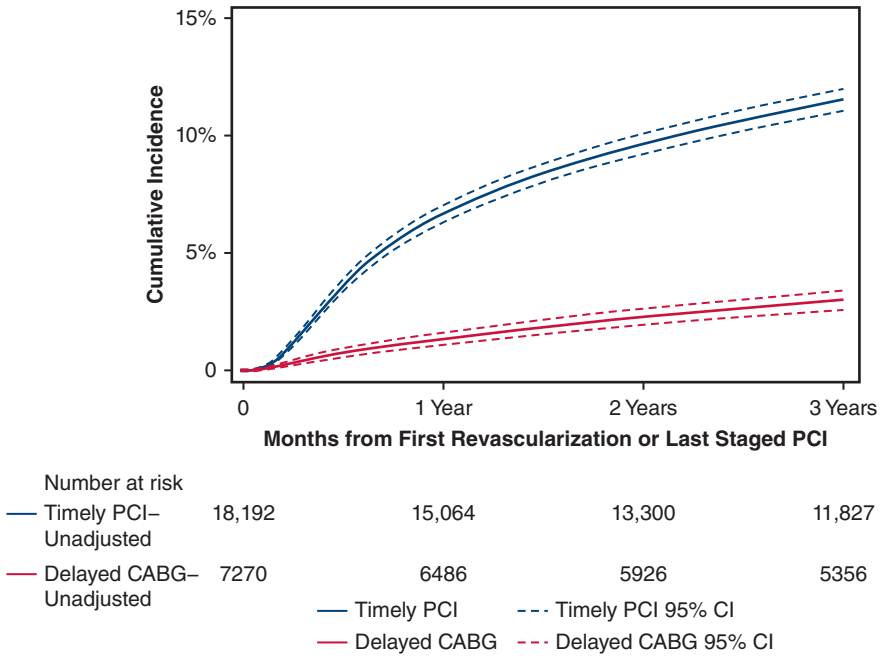

FIGURE 2. Unadjusted cumulative incidence functions for repeat revascularization in the delayed CABG and timely PCI populations. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting.

bare-metal stents (BMS), 4.5% received a combination of BMS and drug-eluting stents (DES), and 42.8% received only DES.

Patients in the timely PCI group had a lower probability of being selected for delayed CABG than did those in the CABG group (Online Data Supplement), an expected finding in this population and consistent with other similarly designed studies.[7] Patients had a positive probability of being assigned to CABG or PCI, meeting the assumptions of the propensity score model. All factors listed in Table 2 were included in the final propensity score model.

Outcome Data and Main Results

Unadjusted and adjusted CIF plots for repeat revascularization, adjusted using inverse probability of treatment weighting, are shown in Figures 2 and 3; unadjusted and adjusted cumulative repeat revascularization point estimates and CIs are reported in Table 3.

The median wait time for CABG was 45 days. The 3-year unadjusted cumulative incidence of repeat revascularization was lower in the delayed CABG group than in the timely PCI group, before (2.99% vs 11.54%) and after (4.84% vs 12.32%) adjustment. The unadjusted subdistribution HR of repeat revascularization for delayed CABG compared with timely PCI at 3 years was 0.36 (95% CI, 0.25-0.53); the adjusted subdistribution HR was 0.16 (95% CI, 0.04-0.65).

The 3-year adjusted cumulative incidence of mortality as a competing risk was lower in the delayed CABG group than in the timely PCI group (4.32% vs 12.49%). The adjusted subdistribution HR for mortality as a competing risk at 3 years was 0.47 (95% CI, 0.31-0.74). These estimates should be interpreted within their context as a competing risk to avoid the Table 2 fallacy,[20] and given that in a competing risks analysis, the primary outcome is the only one powered for reporting.[20]

DISCUSSION

Key Results

We used data from BC's population-based registries and databases to evaluate the effectiveness of delayed CABG compared with timely PCI on the cumulative incidence of repeat revascularization in the presence of death as a competing risk. We found that among BC patients 60 aged years or older, who underwent nonemergency first-time revascularization for angiographically proven, stable left main or multivessel ischemic heart disease in BC, between January 1, 2001, and December 31, 2016, there was a significant difference in repeat revascularization favoring CABG both before and after adjustment with inverse probability of treatment weights at 3 years. We also found a statistically significant difference between the 2 study groups favoring CABG in the cumulative incidence of mortality as a competing risk. This difference was also established at 1 year and sustained over the duration of the study period.

Our findings should be considered in the context of results from other studies. There are 10 randomized

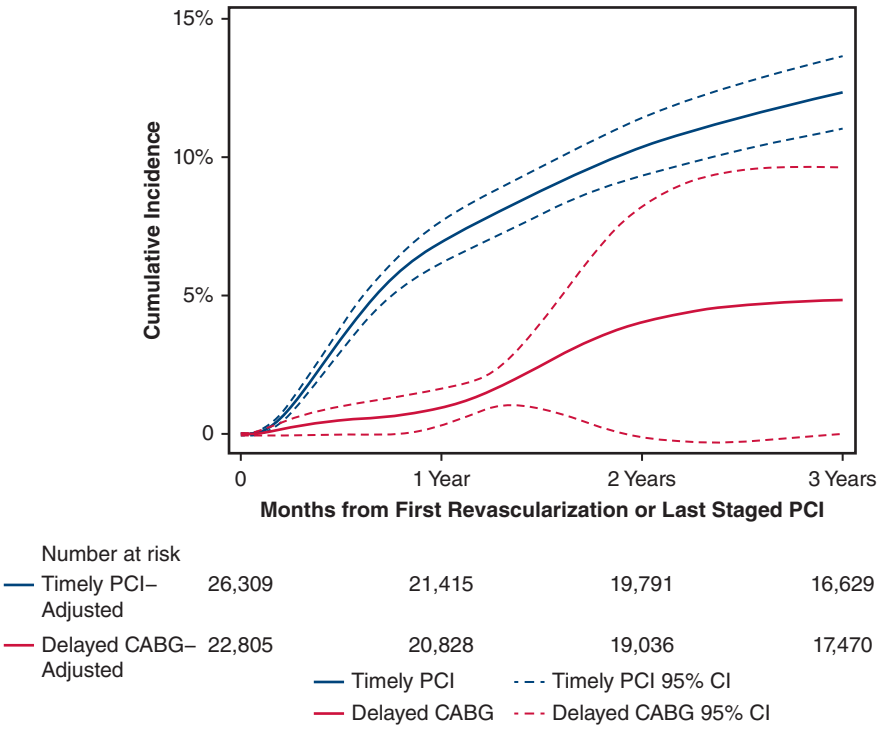

FIGURE 3. Adjusted cumulative incidence functions for repeat revascularization in the delayed CABG and timely PCI populations. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; .

controlled trials comparing CABG with PCI and stenting in patients with multivessel disease (MVD) and 6 in patients with left-main disease. Of these, 7 MVD trials reported on repeat revascularization as an outcome, with all 6 left-main trials reporting repeat revascularization rates.

Of the 7 MVD trials, 5 reported[21-25] statistically significantly lower rates of repeat revascularization among patients who underwent CABG compared with PCI. Of the remaining 2, the ARTS II trial[26] did not report statistical significance tests, although the rate of repeat revascularization for PCI was double that for CABG at 3 years, whereas the SYNTAX II study,[27] a comparison of CABG with modern DES reported no significant difference, although a modest trend to higher rates of repeat revascularization was observed. All 6 randomized controlled trials that compared CABG with PCI in patients with left main disease[28-33] included repeat revascularization in their analysis. Each found statistically significant differences favoring CABG over PCI. Among the larger studies in the population with left main disease, SYNTAX,[29] EXCEL,[32] and NOBLE,[33] each found significantly higher proportions of repeat revascularizations among PCI recipients compared with CABG recipients.

Recognizing that PCI with BMS is no longer contemporary care, we performed a sensitivity analysis comparing patients undergoing delayed CABG with timely PCI who received DES during the study period. Patients who underwent delayed CABG had a lower adjusted cumulative incidence of repeat revascularization in the presence of death as a competing risk (3.68%, 95% CI, 1.28-6.09 vs 10.9%, 95% CI, 8.6-13.7) (Online Data Supplement).

Study Limitations

There are limitations to this study. First, unmeasured confounders could have affected our results. Although the use of inverse probability of treatment weights to balance differences in patient and health system factors in study groups is an accepted method, it remains possible that unmeasured confounders could have affected our results. Second, our study period included patients who underwent revascularization between 2001 and 2016. During that time, stent technology evolved significantly as did the use of antiplatelet therapy, both contributing to improvements in outcomes from PCI. Factors selected for the adjustment model must have a nonzero probability of occurring in both study groups; therefore, it was not possible to directly adjust for stent type or any other factor that might occur only in one study group. Instead, we attempted to account for this by adjusting for calendar year of revascularization. It is possible that this approach may have been insufficient, and thus our findings may not be completely representative of contemporary PCI approaches. Third, the CSBC clinical registries provide limited data on the extent of coronary artery disease. Revascularization appropriate use criteria[34] suggest

TABLE 3. Cumulative incidence (percent) and 95% CIs for repeat revascularization in the delayed coronary artery bypass grafting and timely percutaneous coronary intervention populations, from unadjusted and adjusted analyses

Treatment group	1 y	2 y	3 y
Unadjusted			
Delayed CABG	1.33 (1.07-1.60)	2.28 (1.93-2.62)	2.99 (2.58-3.40)
Timely PCI	6.65 (6.29-7.01)	9.67 (9.28-10.10)	11.54 (11.06-12.02)
Adjusted*			
Delayed CABG	0.97 (0.31-1.63)	4.04 (0.00-8.14)	4.84 (0.00-9.65)
Timely PCI	6.75 (4.80-8.70)	10.36 (9.31-11.41)	12.32 (11.03-13.62)

CABG, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention. *Adjusted with inverse probability of treatment weights.

that SYNTAX scores be used to differentiate eligibility for CABG and PCI, but this level of data is not available in BC. The absence of these scores, or indeed, any greater level of extent of disease data, precluded us from enhancing the extent of disease stratification to a greater level of detail. Fourth, our study cohort only includes patients who experience an outcome in BC, and outcomes that occur outside the province are not captured in our data. However, given age

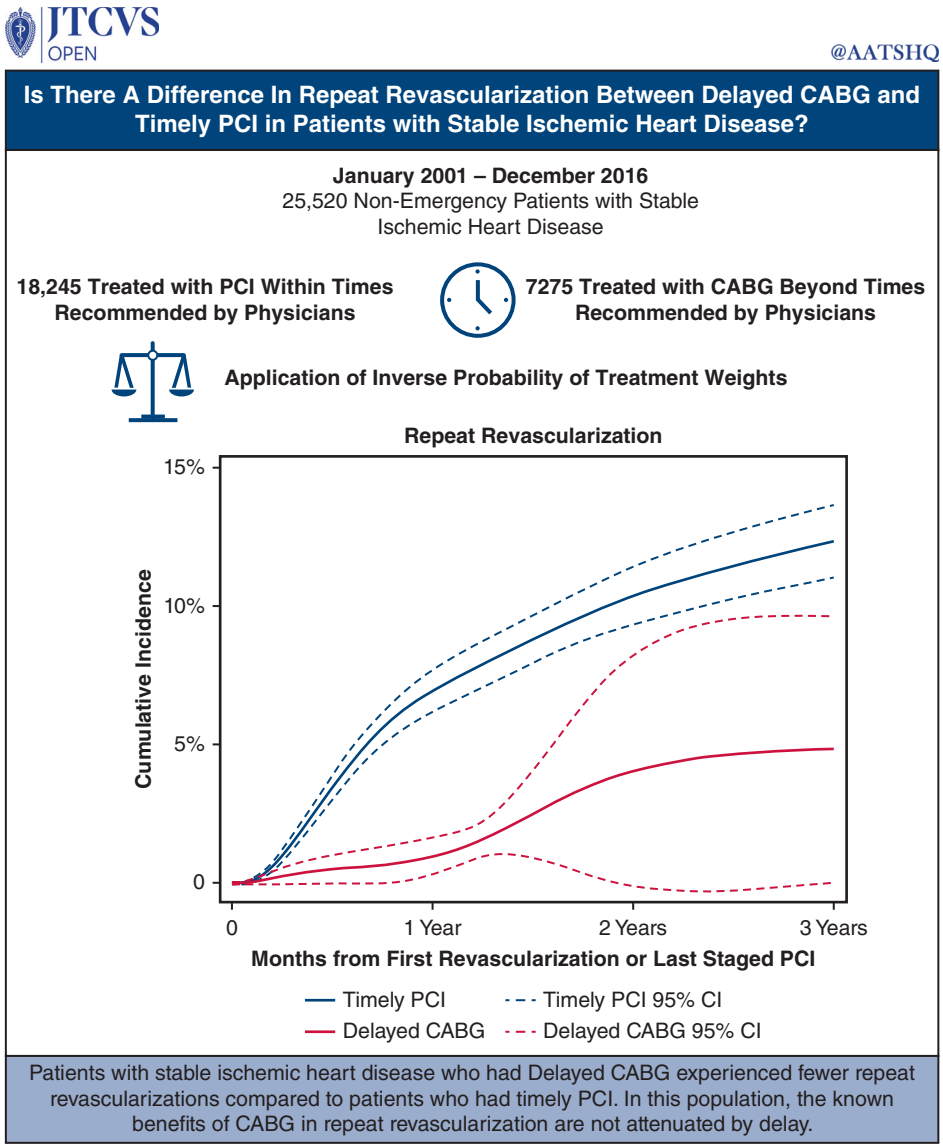

FIGURE 4. Graphical Abstract. *CABG*, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention.

and health concerns for patients in our study cohort, it is not expected that many patients would be lost to follow-up due to migration outside the province. Fifth, we note that more patients than expected with Canadian Cardiovascular Society Class 4 angina were present in the timely PCI study group. Although the propensity score model and treatment weighting procedure effectively balanced out any difference between groups, it is possible that a residual effect on outcomes for PCI recipients may persist. Sixth, we used Spitzer's criteria to differentiate staged PCI from repeat revascularization, resulting in possible misclassification bias. Although we applied our developed rules judiciously, the potential for bias remains. A final limitation is the absence of data on the completeness of revascularization for CABG or PCI. As a result, we are unable to definitively establish that complete revascularization was achieved at the conclusion of each CABG or after single-session or staged PCI.

Interpretation

Our results suggest there is evidence that the treatment benefit of CABG surgery on repeat revascularization compared with PCI may not be extinguished by delay.

Generalizability

These results can be generalized to populations the same or similar to those selected for this study and to health care systems similar to those that are found in socialized health care systems where timely access to CABG is not always assured. Caution should be used in applying these results to other patient populations or health care systems that do not share common attributes with the BC system.

CONCLUSIONS

We wanted to see if there was any effect of treatment timing on the cumulative incidence of repeat revascularization, knowing *a priori* that CABG has lower rates of reintervention. We found that in patients 60 years of age and older with stable, multivessel, or left-main ischemic heart disease who did not require emergency treatment experienced fewer repeat revascularizations when they received delayed CABG compared with timely PCI, suggesting that the benefits of CABG on repeat revascularization are not extinguished by delay (Figure 4). Patients who face a delay in receiving their CABG surgery and are considering PCI as an alternative may want to consider these findings with their physicians as they make their treatment decision.

Conflict of Interest Statement

The authors reported no conflicts of interest. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: comparative effectiveness, coronary artery bypass graft, percutaneous coronary intervention, repeat revascularization, treatment timing