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Perioperative Inotrope Therapy and Atrial Fibrillation Following Coronary Artery Bypass Graft Surgery: Evidence of a Racial Disparity

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Abstract

Background and Objective—Following coronary artery bypass graft (CABG) surgery, mortality rates are significantly higher among black patients who experience postoperative atrial fibrillation (POAF). Perioperative inotropic therapy (PINOT) was associated with POAF in previous reports, but the extent to which race influences this association is unknown. In the present study, the relationship between PINOT, race, and POAF was examined in patients undergoing CABG surgery.

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Methods and Setting—Clinical records were examined from a prospectively maintained cohort of 11,855 patients (median age 64 yrs; 70% male; 16% black) undergoing primary isolated CABG at a large cardiovascular institute in the southeastern region of the United States. Relative risk (RR) and 95% confidence intervals (CIs) were computed using log-binomial regression.

Main Results—The association between PINOT and POAF was significantly increased among black patients (adjusted RR 1.7, CI 1.4–2.0) compared with white patients (adjusted RR 1.3, CI 1.2–1.4) ($p_{\text{interaction}} = 0.013$).

Conclusions—These findings suggest that PINOT may be disproportionately associated with POAF among black patients undergoing CABG surgery. Additional studies are needed to examine further the potential underlying mechanisms of this association.

Keywords

coronary artery bypass graft; inotrope; postoperative atrial fibrillation; race

Inotropes are used to augment cardiac output, increase renal perfusion, and stabilize hemodynamics in patients during and immediately following coronary artery bypass graft (CABG) surgery (Figure 1). Their use, however, may lead to potential complications including myocardial ischemia, atrial fibrillation (AF), tachycardia, and renal dysfunction.^{1, 2} Inotrope therapy has also been associated with an increase in both short-term and long-term mortality, especially among black patients undergoing cardiac surgery.^{3, 4} Although several reports have focused on the association between inotropes and postoperative atrial fibrillation (POAF), none have examined the influence of race on this relationship.^{1, 5}

Our objective was to determine if POAF was differentially associated with perioperative inotropic therapy (PINOT) among black patients undergoing CABG surgery.

Methods

Study Design and Setting

Details of data collection and management were previously described.⁶ Clinical information was prospectively entered into the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database at East Carolina Heart Institute (ECHI). Patients undergoing primary isolated CABG from 1992–2007 were included in this analysis. PINOT was not collected in our data-base after 2007. The study was approved by the institutional review board at Brody School of Medicine. Comorbidities, demographic data, preoperative medications, and surgical details were obtained at the time of surgery. Race was self-identified. Patients with a history of preoperative paroxysmal, persistent, or permanent AF/atrial flutter and preoperative inotrope use were excluded from the study (~2.4%).

ECHI provides comprehensive cardiovascular care to patients of eastern North Carolina, a rural region with nearly 1.5 million people across 29 counties. The institute is the largest stand-alone cardiovascular facility in the state of North Carolina and has a three-star rating from STS for quality heart surgery. Most patients receiving care at ECHI live and remain within a 150-mile radius of the medical center.

Inotropes

PINOT was defined as any inotropes administered during the intra/postoperative period. These included sympathomimetics (dobutamine, dopamine, epinephrine, isoprenaline, norepinephrine) and phosphodiesterase-3 (PDE-3) inhibitors (amrinone, milrinone). Both classes improve cardiac output and renal perfusion by increasing myocardial contractility, vasodilation, or both. Sympathomimetics improve myocardial contractility by increasing calcium influx into the cell through cyclic adenosine monophosphate (cAMP)-mediated mechanisms.⁷ PDE-3 inhibitors similarly increase intracellular cAMP (by decreasing cAMP degradation) and calcium influx while additionally increasing cyclic guanosine monophosphate in the vasculature. They also selectively reduce left ventricular end diastolic pressure and B-type natriuretic peptide concentrations.^{1, 8, 9}

Definitions

Standard definitions from STS were used to define POAF and comorbidities such as diabetes mellitus (DM), hypertension (HTN), left main coronary artery disease, peripheral artery disease (PAD), prior myocardial infarction, three-vessel coronary disease, and unstable heart failure (HF). This was done using hospital notes, medication reports, outpatient medical records, physician documentation, and radiology readings. Furthermore, patients' cardiac rhythm and rate were continuously monitored by electrocardiogram during and following surgery, until discharge from hospital.

Statistical Analysis

Categorical variables were expressed as frequency and percentage; continuous variables were reported as median and interquartile range (IQR). Statistical significance ($p < 0.05$) for categorical variables was determined using the Fisher exact test and the Deuchler-Wilcoxon procedure for continuous variables. An iterative expectation-maximization algorithm was used to account for missing body mass index values (lower than 0.01%; imputation efficiency more than 99.9%).

Log-binomial regression was used to compute relative risk (RR) and 95% confidence intervals (CIs) for POAF.¹⁰ In this k -factor model, the logarithm of p_i is expressed as $\beta_0 + \beta_1 x_1 + \dots + \beta_i x_i \dots + \beta_k x_k$, where p_i denotes the probability of POAF if exposed to risk factor x_i (i.e., $x_i = 1$). Accordingly, the logarithm of p_i/p'_i equals β_i , where p'_i denotes the probability of POAF if not exposed to risk factor x_i (i.e., $x_i = 0$). Exponentiation of this expression gives the RR corresponding to x_i . Goodness of fit was assessed by examining Akaike information criterion and leverage/casewise diagnostic statistics, generalized to log-binomial regression. All models achieved convergence and satisfied admissibility criteria (i.e., linear predictor constrained to be negative).

Multivariable models included variables in our data set that have been associated with POAF in prior reports, regardless of their statistical significance in the current analysis.^{11, 12} These included patient age, DM, HTN, inotropes, sex, PAD, and three-vessel coronary disease. The post hoc inclusion of other variables into the model was performed in a pairwise fashion. The p values for point estimates were computed assuming asymptotic normality. A

likelihood ratio test was used to examine the two-way interaction between inotrope use and race.

Rounding was performed using a method documented previously.¹³ SAS v.9.4 (Cary, NC) was used for all analyses.

Results

A total of 11,855 patients were included in our study (median age 64 yrs [IQR 15 yrs]; 70% male; 16% black). Comorbidities included DM (33%), HTN (70%), PAD (11%), and three-vessel coronary disease (66%; Table 1). Commonly used preoperative medications were aspirin (68%), antiplatelets (56%), and β -blockers (53%). Approximately 92% of patients underwent CABG surgery with cardiopulmonary bypass (i.e., on pump). The use of lipid-lowering agents was increased among black versus white patients receiving PINOT ($p=0.010$), in contrast to those not receiving PINOT ($p=0.50$). On average, hospital stays as well as aortic cross-clamp, perfusion, and intensive care unit (ICU) times differed among patients who did or did not receive inotropes in both black and white patients ($p<0.0001$). Independent of race, a greater percentage of patients who received PINOT experienced in-hospital complications (pneumonia, renal failure, POAF, and operative mortality) ($p<0.0001$; not shown in tables).

PINOT was greater in black patients (Figure 2). Regardless of their rhythm after surgery, they also received more perioperative dopamine ($p<0.0001$; Table 2). Use of sympathomimetic agents ($p<0.0001$) and PDE-3 inhibitors ($p=0.018$) was associated with a higher incidence of POAF in black compared with white patients (Table 2). Regardless of the agent, POAF was associated with PINOT in both black (adjusted RR 1.7, CI 1.4–2.0) and white (adjusted RR 1.3, CI 1.2–1.4) CABG patients. However, the magnitude of the effect was greater among black patients ($p_{\text{interaction}}=0.013$) (Table 3).

Neither the pairwise addition of variables listed in Table 1 (demographics, prior medical history, preoperative medications) nor the exclusion of PDE-3 inhibitors from the analysis substantively changed our results. Adjusting for year period of surgery (prior to 2000 vs 2000 or later) also had little effect.

Discussion

Nearly 400,000 CABG procedures are performed annually in the United States with costs per disability-adjusted life-years ranging from \$24,000–\$72,000.^{14, 15} AF is the most common complication following CABG surgery. Patients who develop POAF have significantly longer hospital stays and ICU times, adding more than \$9000 per patient in health care costs.¹⁶ These high rates and associated costs have prompted interest in identifying modifiable risk factors of POAF (e.g., pharmacologic therapies, surgical techniques, comorbidities, biomarkers).^{16, 17}

There is a paucity of evidence regarding POAF risk and potential effect modifiers in different races. Although an increased risk for POAF has been noted following inotrope use, to our knowledge no research examining the impact of race on this association has been

published.^{1, 5} In our study, 45% of patients undergoing primary isolated CABG received PINOT, of whom ~18% were black. The proportion of POAF cases attributable to PINOT was 26% for black versus 12% for white patients.

Black patients present with coronary artery disease at an earlier age than white patients and have an increased burden of cardiovascular risk factors.¹⁸ Racial/ethnic differences also exist in response to several cardiovascular drugs (e.g., β -blockers, angiotensin-converting enzyme inhibitors [ACEIs] and/or angiotensin receptor blockers, hydrochlorothiazide, isosorbide dinitrate, and hydralazine), which have translated into mainstay therapy. Findings from the Veterans Affairs Vasodilator-Heart Failure Trial (V-HeFT I) and African-American Heart Failure Trial (A-HeFT) suggest that black patients receiving a combination of hydralazine and isosorbide dinitrate experience greater benefit than their white counterparts and decreased mortality compared with placebo.^{19–22} Black patients are also known to have a less favorable antihypertensive response to β -blockers and ACEIs.^{23–27} An analogous differential response by race may exist for inotropes, as our study suggests.

Genetic polymorphisms in the β -adrenergic signaling pathway were associated with increased mortality and diminished responsiveness to β -blocker therapy in patients with HF and coronary disease.^{28, 29} The magnitude of these adverse outcomes is greater in black patients carrying the polymorphisms. Conceivably, race-specific variations in adrenergic signaling may underlie the differences in POAF incidence that we observed in this study. Furthermore, data suggest that β -receptor sensitivity and density are higher in hypertensive black patients, perhaps underlying the increased POAF risk that we observed for black patients receiving inotropes (~84% of black patients in our study were hypertensive).³⁰

In a study of 131 CABG patients who did not receive inotropes, increased norepinephrine levels in the right atrium were independently associated with POAF ($p=0.02$).³¹ This effect is consistent with several studies that also observed a greater POAF risk among patients receiving inotropes.^{1, 5} The action of inotropic agents is well known to be affected by nitric oxide (NO), an important vasodilating agent.^{32–35} Inherent differences in NO bioavailability between black and white patients have been shown to play a role in several cardiac comorbidities of vascular origin. Black patients with DM, HTN, obesity, and renal insufficiency have been reported to have less NO bioavailability.³⁶ Furthermore, black HF patients with polymorphisms in the G-protein β -3 subunit and endothelial NO synthase (NOS3) receiving isosorbide dinitrate and hydralazine had greater therapeutic outcomes than white patients.^{37, 38} Although the role of the coronary vasculature in POAF is uncertain, it is plausible that the inotrope findings in the present study may be explained by similar “responsive” genotype differences between black and white patients.³⁹ Further research is needed to better understand the interplay between race and genetics on inotrope pharmacology in patients undergoing CABG surgery.

Strengths and Limitations

Our study is strengthened by its large sample size, a racially dichotomous population, few missing values, and the systematic collection of exposure and event information using standard STS definitions. Furthermore, our institution implemented special fields to collect

information on perioperative inotrope use that is not recorded in the national STS database. Nonetheless, a few limitations should be noted when interpreting our results.

In some cases, patients with advanced systolic dysfunction may not have clinically presented with symptoms of, received treatment for, or been classified as having HF. Although this may have slightly affected frequency counts, the impact on our results likely was nominal given that our analysis was stratified by race and inotrope use.

Although the use of inotropes was collected in our data set, the dose, duration, and reason for their use were not available. Standard protocol was followed for their administration, reducing the likelihood of differential bias. In addition, perioperative inotrope information was not collected in our database after 2007, and accordingly, it is not possible to reflect on how current practices may influence our findings.

Our definition of POAF did not include duration of the episodes (e.g., lasting 7 or fewer days or more than 7 days, or ongoing long term). However, all these episodes have similar initial treatment and required additional days in the hospital.

Enlarged left atrial size and hypertrophic left ventricular septum are known risk factors for POAF and are associated with HTN.^{40, 41} However, they were not routinely collected in our database. To minimize the confounding effect of these factors, we excluded patients with preoperative AF and adjusted our multivariable models for HTN. Although we adjusted for several factors in our multivariable analyses, we cannot completely rule out bias owing to residual confounding.

Causal inference vis-à-vis the temporal relationship between perioperative inotrope administration and POAF was difficult to establish in our analysis given the unavailability of exact drug-event-time information. Because inotropes are often given to enhance renal perfusion, it is difficult to ascertain the extent to which fluid reabsorption may be involved. Once the effect of anesthesia tapered off, fluid reabsorption and consequent atrial stretching may have contributed to the induction of POAF, with the time to maximum fluid reabsorption taking place over a few days. Conceivably, such an explanation coincides with the brief 4- to 10-minute half-life for dopamine and the occurrence of most POAF beyond the first 48 hours of surgery. However, we were unable to assess whether or not the onset of POAF was shorter among patients receiving perioperative inotropic agents to stabilize renal function. In future studies, we hope to ascertain if fluid retention is an intermediate variable or a descending proxy for an intermediate variable on the causal pathway between inotrope exposure and POAF.⁴² Nonetheless, the fact remains that black patients in our study more frequently received inotropic agents, and the multivariable adjustment for confounders of renal impairment did not change our differential findings.

Race was self-reported and could have been misclassified in some cases. Boundaries defining race are often poorly delineated and may vary widely between and within groups in the United States.⁴³ However, the racial makeup of eastern North Carolina is historically black and white, with little ambiguity in identifying race in this region. Our study was from a single institution with a unique population (e.g., rural, low socioeconomic status, relatively nontransient, and high percentage of black patients) and may not generalize to other areas of

the country. However, because data were collected from one health system, this might have partially controlled for other health care–related factors (e.g., interinstitutional variation in comorbidity classification, clinical management, geography, and health care coverage).

Conclusion

Our findings suggest that the perioperative administration of inotrope therapy is disproportionately associated with POAF among black patients undergoing CABG surgery. These results are particularly interesting given that the incidence of POAF in the general population is historically higher among white patients. Future studies of genetic and/or other biological variables that underlie arrhythmogenesis are needed to better understand the association between POAF and inotrope therapy, especially with respect to race. Additional research is needed to determine if more aggressive management of comorbidities prior to surgery, through public health directives, will reduce the need for PINOT.

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Favorable Effects

- ↑ Cardiac contractility
- ↑ Heart rate
- ↑ Cardiac output
- ↑ MAP
- ↑ Renal perfusion/GFR

Unfavorable Effects

- ↑ Cardiac O₂ demand/ischemia
- ↑ Arrhythmogenesis
- ↑ Peripheral ischemia (limb and splanchnic tissues)
- ↑ Risk of stroke and mortality

Figure 1.

Clinical outcomes mediated by perioperative inotropic therapy (PINOT) and catecholamine pharmacology in myocardium. Major favorable and unfavorable clinical outcomes of PINOT are shown. In the box is a simplified overview of major pathways of norepinephrine (NE), epinephrine, and dopamine (DA) pharmacology in cardiomyocytes. In addition to the well-known inotropic effect of these catecholamines mediated by increased cytosolic Ca^{2+} , there also is catecholamine uptake by the organic cation transporter isoform 3 (OCT3) and extraneuronal monoamine transporters (ENMT). Following uptake, the enzyme monoamine oxidase (MAO), tethered to the outer mitochondrial membrane, metabolizes DA and NE to form the highly reactive aldehydes Dopal and Dopegal, respectively, along with hydrogen peroxide (H_2O_2) and ammonium (NH_4^+). These catechol aldehydes must then be further metabolized by either aldehyde dehydrogenases or aldose reductase into their corresponding alcohol or acid metabolites. ANT = adenine nucleotide transporter; ATP = adenosine triphosphate; cAMP = cyclic adenosine monophosphate; CAT = catalase; GFR = glomerular filtration rate; HNE = 4-hydroxynonenal; MAP = mean arterial pressure; MnSOD = manganese superoxide dismutase; PKA = cAMP-dependent protein kinase.

Figure 2.

Use of perioperative inotropic therapy and postoperative rhythm status grouped by race. Represents the total number of black and white patients who remained in sinus rhythm (A) and those who developed postoperative atrial fibrillation (POAF) (B) following coronary artery bypass graft surgery. Color-filled portions represent those patients who received perioperative inotropes, along with corresponding percentage. * $p < 0.0001$.

Table 1Patient Characteristics (N=11,855)^a

Patient characteristics ^b	Inotrope ^c				No inotrope ^c			
	Black n (%) Q ₂ [IQR]	White n (%) Q ₂ [IQR]	p value ^d		Black n (%) Q ₂ [IQR]	White n (%) Q ₂ [IQR]	p value ^d	
Overall	987 (18)	4377 (82)	–		943 (15)	5548 (85)	–	
Demographics								
Age 65 yrs	492 (50)	2581 (59)	<0.0001		336 (36)	2359 (43)	<0.0001	
Male	514 (52)	2982 (68)	<0.0001		584 (62)	4217 (76)	<0.0001	
Obesity, BMI 30	499 (51)	1741 (40)	<0.0001		444 (47)	2090 (38)	<0.0001	
Prior medical history								
Diabetes	531 (54)	1578 (36)	<0.0001		370 (39)	1466 (26)	<0.0001	
Dialysis	62 (6)	48 (1)	<0.0001		39 (4)	23 (<1)	<0.0001	
Elective CABG	351 (36)	1497 (34)	0.42		428 (45)	2511 (45)	0.94	
Hypertension	856 (87)	3110 (71)	<0.0001		765 (81)	3566 (64)	<0.0001	
LMCA disease	216 (22)	943 (22)	0.83		168 (18)	1019 (18)	0.72	
LVEF, %	47 [25]	50 [25]	0.038		55 [15]	55 [15]	0.014	
Peripheral artery disease	148 (15)	616 (14)	0.45		109 (12)	421 (8)	<0.0001	
Prior myocardial infarction	440 (45)	1885 (43)	0.39		339 (36)	1756 (32)	0.010	
Recent smoker	192 (19)	874 (20)	0.76		242 (26)	1411 (25)	0.87	
Three-vessel coronary disease	727 (74)	3221 (74)	1.0		575 (61)	3300 (59)	0.41	
Unstable heart failure	259 (26)	714 (16)	<0.0001		97 (10)	372 (7)	0.0002	
Preoperative medications								
ACEIs/ARBs	401 (41)	1329 (30)	<0.0001		300 (32)	1279 (23)	<0.0001	
Anticoagulants	310 (31)	1499 (34)	0.094		273 (29)	1568 (28)	0.67	
Antiplatelet agents	524 (53)	2515 (57)	0.013		493 (52)	3142 (57)	0.013	
Aspirin	651 (66)	2915 (67)	0.39		645 (68)	3835 (69)	0.68	
β-blockers	554 (56)	2267 (52)	0.015		554 (59)	2866 (52)	<0.0001	
Calcium channel blockers	364 (37)	1452 (33)	0.028		316 (34)	1799 (32)	0.52	
Digoxin	89 (9)	412 (9)	0.76		30 (3)	255 (5)	0.048	

Patient characteristics ^b	Inotrope ^c			No inotrope ^c			p value ^d
	Black n (%) Q ₂ [IQR]	White n (%) Q ₂ [IQR]	p value ^d	Black n (%) Q ₂ [IQR]	White n (%) Q ₂ [IQR]	p value ^d	
Diuretics	360 (36)	1151 (26)	<0.0001	226 (24)	820 (15)	<0.0001	
Lipid-lowering agents	374 (38)	1468 (34)	0.010	333 (35)	1895 (34)	0.50	
Nitrates	169 (17)	897 (20)	0.017	116 (12)	816 (15)	0.056	
Perioperative variables							
Cardiopulmonary bypass	939 (95)	4217 (96)	0.083	801 (85)	4912 (89)	0.0023	
Colloid cardioplegia	194 (20)	776 (18)	0.16	138 (15)	715 (13)	0.14	
Crystalloid cardioplegia	221 (22)	1078 (25)	0.15	205 (22)	1525 (27)	0.0002	
Crystalloid + O ₂ cardioplegia	523 (53)	2380 (54)	0.44	448 (48)	2671 (48)	0.72	
Cross-clamp time, min ^e	58 [27]	62 [30]	<0.0001	55 [25]	56 [25]	0.064	
Hospital LOS, days	6 [3]	6 [3]	0.0001	5 [2]	5 [2]	0.042	
Intra-aortic balloon pump ^f	89 (9)	608 (14)	<0.0001	19 (2)	273 (5)	<0.0001	
Perfusion time, min	94 [41]	103 [44]	<0.0001	84 [38]	89 [40]	0.0014	
Total ICU time, hrs	29 [28]	26 [28]	0.0020	23 [8]	22 [8]	0.087	

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers; BMI = body mass index; CABG = coronary artery bypass graft; ICU = intensive care unit; IQR = interquartile range; LMCA = left main coronary artery; LOS = length of stay; LVEF = left ventricular ejection fraction; Q₂ = median.

^aIsolated primary CABG, 1992–2007.

^bComparison group was the complement.

^cPerioperative inotropes.

^dThe p values were computed using the Fisher exact test or the Deuchler-Wilcoxon test.

^eExcludes patients with poor condition of aorta, left ventricular weakness, and other contraindicated conditions (< 0.5%).

^fPre- and intraoperative balloon pump placement only.

Inotropic Support and Postoperative Atrial Fibrillation by Operative Status and Cardiac Rhythm (N=11,855)^a

Table 2

Inotropic agent	Sinus rhythm ^b			POAF ^b		
	Black n (%)	White n (%)	p value ^c	Black n (%)	White n (%)	p value ^c
Overall	1623 (17)	7697 (83)	—	307 (12)	2228 (88)	—
Sympathomimetics						
Dobutamine	54 (3)	178 (2)	0.022	29 (9)	86 (4)	<0.0001
Dopamine	737 (45)	2975 (39)	<0.0001	189 (62)	1081 (49)	<0.0001
Epinephrine	95 (6)	481 (6)	0.57	40 (13)	198 (9)	0.028
Isoprenaline	3 (< 1)	27 (< 1)	0.47	5 (2)	10 (< 1)	0.027
Norepinephrine	54 (3)	226 (3)	0.42	22 (7)	78 (4)	0.0043
Total	775 (48)	3145 (41)	<0.0001	203 (66)	1178 (53)	<0.0001
PDE-3 inhibitors						
Anrinone	29 (2)	127 (2)	0.67	13 (4)	50 (2)	0.048
Milrinone	36 (2)	118 (2)	0.054	15 (5)	59 (3)	0.044
Total	64 (4)	243 (3)	0.11	25 (8)	105 (5)	0.018

PDE = phosphodiesterase enzyme; POAF = postoperative atrial fibrillation.

^aIsolated primary coronary artery bypass grafting procedures from 1992–2007.^bColumn percentages may add up to > 100% owing to some patients receiving more than one inotrope.^cThe p value was computed using the Fisher exact test.

Table 3Univariable and Multivariable Relative Risk for Postoperative Atrial Fibrillation (N=11,855)^a

Characteristic ^b	Black		White	
	Univariable RR (95% CI) ^c	Multivariable ^d RR (95% CI) ^c	Univariable RR (95% CI) ^c	Multivariable ^d RR (95% CI) ^c
Age 65 yrs	2.0 (1.7–2.5)	1.9 (1.5–2.3)	1.9 (1.8–2.1)	1.8 (1.7–1.9)
Diabetes	1.1 (0.91–1.4)	1.0 (0.83–1.3)	1.1 (0.99–1.2)	1.0 (0.93–1.1)
Hypertension	1.5 (1.1–2.1)	1.3 (0.94–1.8)	1.3 (1.2–1.4)	1.2 (1.1–1.4)
Inotrope ^e	1.9 (1.5–2.4)	1.7 (1.4–2.0)	1.5 (1.4–1.6)	1.3 (1.2–1.4)
Male	1.0 (0.82–1.2)	1.2 (0.95–1.4)	1.1 (0.996–1.2)	1.2 (1.1–1.3)
Peripheral arterial disease	1.3 (0.99–1.7)	1.2 (0.91–1.5)	1.4 (1.3–1.6)	1.2 (1.1–1.3)
Three-vessel coronary disease	1.0 (0.84–1.3)	0.91 (0.73–1.1)	1.2 (1.1–1.3)	1.1 (1.02–1.2)

CI = confidence interval; RR = relative risk.

^aIsolated primary coronary artery bypass grafting procedures from 1992–2007.^bComparison group was the absence of the characteristic.^cRR and 95% CI were computed using maximum likelihood log-binomial regression.^dModel adjusted for characteristics shown in column 1.^eLikelihood ratio test for interaction of Black × Inotrope (univariable p=0.024; multivariable p=0.013).