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CLINICAL RESEARCH

Factors Related to the Selection of Surgical Versus Percutaneous Revascularization in Diabetic Patients With Multivessel Coronary Artery Disease in the BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes) Trial

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Objectives We evaluated demographic, clinical, and angiographic factors influencing the selection of coronary artery bypass graft (CABG) surgery versus percutaneous coronary intervention (PCI) in diabetic patients with multivessel coronary artery disease (CAD) in the BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes) trial.

Background Factors guiding selection of mode of revascularization for patients with diabetes mellitus and multivessel CAD are not clearly defined.

Methods In the BARI 2D trial, the selected revascularization strategy, CABG or PCI, was based on physician discretion, declared independent of randomization to either immediate or deferred revascularization if clinically warranted. We analyzed factors favoring selection of CABG versus PCI in 1,593 diabetic patients with multivessel CAD enrolled between 2001 and 2005.

Results Selection of CABG over PCI was declared in 44% of patients and was driven by angiographic factors including triple vessel disease (odds ratio [OR]: 4.43), left anterior descending stenosis ≥70% (OR: 2.86), proximal left anterior descending stenosis ≥50% (OR: 1.78), total occlusion (OR: 2.35), and multiple class C lesions (OR: 2.06) (all $p < 0.005$). Nonangiographic predictors of CABG included age ≥65 years (OR: 1.43, $p = 0.011$) and non-U.S. region (OR: 2.89, $p = 0.017$). Absence of prior PCI (OR: 0.45, $p < 0.001$) and the availability of drug-eluting stents conferred a lower probability of choosing CABG (OR: 0.60, $p = 0.003$).

Conclusions The majority of diabetic patients with multivessel disease were selected for PCI rather than CABG. Preference for CABG over PCI was largely based on angiographic features related to the extent, location, and nature of CAD, as well as geographic, demographic, and clinical factors. (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes [BARI 2D]; NCT00006305) (J Am Coll Cardiol Intv 2009;2:384–92) © 2009 by the American College of Cardiology Foundation

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Patients with diabetes mellitus (DM) who comprise approximately 25% of the 1.5 million undergoing coronary revascularizations annually in the U.S. experience worse outcomes after both coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) than those without DM (1–4). Determination of the appropriate revascularization strategy for an individual patient is a complex issue that is of great importance, considering the growing number of patients with DM and coronary artery disease (CAD). In the original BARI (Bypass Angioplasty Revascularization Investigation) trial, patients with medically treated DM and multivessel disease randomized to CABG versus PCI, limited to balloon angioplasty, had a significantly lower long-term mortality, which prompted the National Heart, Lung, and Blood Institute to issue a Clinical Alert recommending CABG over angioplasty in this high-risk subset (5,6). However, findings from the BARI registry, in which selection of revascularization strategy was at the discretion of the treating physician, showed nearly identical 7-year survival with PCI or CABG in patients with diabetes, even when the data were adjusted for covariates (7).

In the years since the BARI trial results were first reported, advances in PCI technology and adjunctive therapies have significantly improved clinical outcomes. In particular, the use of stents, glycoprotein IIb/IIIa receptor inhibitors, and the direct thrombin inhibitor bivalirudin have substantially lowered restenosis and acute ischemic and/or bleeding complication rates (1,8–13). Furthermore, a growing appreciation for the critical role of intensive medical management and attention to cardiovascular risk factors has led to the widespread use of statins, beta-blockers, and angiotensin-converting enzyme inhibitors (14–16). These improvements in therapy have not changed American College of Cardiology/American Heart Association practice guidelines, which recommend that, in general, patients with less extensive CAD be treated with PCI, while those with more extensive and severe disease be referred for CABG (17,18). In addition, regional differences in the treatment of ischemic heart disease have been previously described (19,20). Therefore, we evaluated demographic, clinical, geographic, and angiographic factors that influenced the selection of CABG versus PCI in patients with DM and multivessel CAD with stable symptoms enrolled in the BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes) trial.

Methods

Study design. The BARI 2D trial has a randomized 2 × 2 factorial design to compare treatment strategies in patients with DM and CAD with stable symptoms: 1) immediate coronary revascularization plus intensive medical therapy versus intensive medical therapy alone with deferred revascularization, as needed, for treatment of CAD; and 2) an insulin-providing strategy versus insulin-sensitizing strategy for treatment of DM. After angiographic evaluation, and before randomization to immediate versus deferred revascularization, the mode of revascularization with either CABG or PCI was selected and declared by the clinical site study physicians. Patient preference was not recorded. A detailed description of the protocol has been published (21). In brief, eligibility criteria required angiographically documented CAD involving at least 1 coronary artery (≥50% stenosis) suitable for treatment with either medical therapy alone or elective revascularization with CABG or PCI, and documented myocardial ischemia or at least 1 >70% stenosis with stable angina. Exclusion criteria included left main stenosis ≥50%, any prior CABG or PCI in the past 12 months. A total of 2,368 participants enrolled from 49 clinical sites in the U.S., Brazil, Canada, Mexico, the Czech Republic, and Austria between January 1, 2001, and March 31, 2005, have been described (22).

In the present analysis, we excluded patients with single-vessel disease (n = 611), those who had previously undergone CABG (n = 152), and those with <80% complete baseline data or without clinical site evaluation of the baseline angiogram (n = 35). Thus, the study population included 1,593 patients with multivessel CAD from U.S. (n = 910) and non-U.S. (n = 683) sites.

Angiographic characteristics were assessed at the clinical sites and by a core laboratory (Stanford University). For this analysis, site-determined angiographic variables are reported since they were utilized to determine the mode of revascularization. However, myocardial jeopardy index (MJI),

Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery

CAD = coronary artery disease

CI = confidence interval

DES = drug-eluting stent(s)

DM = diabetes mellitus

MJI = myocardial jeopardy index

OR = odds ratio

PCI = percutaneous coronary intervention

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which reflects the percentage of jeopardized myocardium, was determined by the core lab (23). Because MJI does not account for territories previously revascularized by either CABG or PCI, patients with prior PCI (n = 285) were excluded from the presentation of MJI data.

Statistical methods. Demographic, clinical, and angiographic characteristics related to the choice of CABG versus PCI were compared, using the chi-square test for categorical variables and the Cochran-Armitage trend test for ordinal variables, for the overall cohort and stratified by region (U.S. and non-U.S.). We examined the choice of revascularization procedure by MJI, and compared the U.S. versus the non-U.S. clinical centers.

Multivariable analysis of the "CABG selection" outcome was performed using a nonlinear mixed model that included a random-effect intercept term for each clinical site (24). These models incorporate the multilevel nature of treatment selection, based both on physician judgment and patient-level characteristics, and account for the correlation between observations within a site. The odds ratio (OR) for a patient-level factor (e.g., age) in a mixed model is interpreted as the estimated effect of the factor on the decision to choose CABG *within* an individual site, while the OR for a site-level factor such as geographic region is interpreted as the estimated odds of choosing CABG among sites in 1 region versus another region adjusting for population differences between sites. Variable selection was accomplished using standard logistic regression (25). Forward stepwise variable-selection methods were used to construct separate multivariable models for: 1) demographic and clinical characteristics; 2) cardiovascular medications; 3) site angiographic measurements; and 4) core lab angiographic measurements. In addition to the variables listed in Tables 1 to 3, candidate variables included angina status, history of hypercholesterolemia, renal dysfunction, chronic obstructive pulmonary disease, pulmonary edema, history of malignancy, smoking status, body mass index, glycosylated hemoglobin, presence of Q waves, ST-segment depression, ST-segment elevation, inverted T waves, or any major electrocardiographic abnormality, left ventricular ejection fraction <50%, serum creatinine, as well as right coronary artery and circumflex variables similar to the left anterior descending coronary artery (LAD) variables presented in Table 3. Factors identified from these models were combined, and geographic region (non-U.S. vs. U.S.) and time of randomization (before vs. after April 25, 2003, when DES became available at U.S. and non-U.S. sites) were added to the model. Covariates with a value of $p > 0.05$ were subsequently removed using backward selection. Statistical interactions between geographic region and main effects variables were tested, and interaction terms with a value of $p < 0.01$ were retained. Each of the interaction terms involving geographic region and the other explanatory variables had a p value >0.01 when added to the multivariable model; as a result, the final model does not include any interaction terms. Finally, a mixed model with random intercepts was created using the selected variables. The model intraclass correlation, representing the proportion of the total unexplained variability in treatment selection accounted for by clinical site, is reported (25). Estimates for ORs, 95% confidence intervals (CIs), and p values are presented, and a value of $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SAS version 9.1 (SAS Inc., Cary, North Carolina).

Results

Variation in treatment selection by region and time. Among the 1,593 diabetic patients with multivessel coronary disease, the decision to select CABG and PCI was declared in

Table 1. Intended Revascularization Strategy by Geographic Region and Time Among Patients With Diabetes and Multivessel CAD in the BARI 2D Trial

	No. of Clinical Sites	No. of Patients	Intended Procedure		p Value
			CABG	PCI	
Total	49	1,593	44%	56%	
By region					
U.S.	40	910	31%	69%	<0.001*
Non-U.S.	9	683	61%	39%	
Brazil (Sao Paulo)	1	293	73%	27%	<0.001†
Canada	5	271	47%	53%	
Mexico (Mexico City)	1	62	76%	24%	
Europe‡	2	57	56%	44%	
By date of randomization§					
U.S./Canada on or before April 25, 2003	39	656	39%	61%	0.0025
U.S./Canada after April 25, 2003	39	473	30%	70%	

Row percentages are presented. *Comparison of U.S. vs. non-U.S. regions using chi-square test; †comparison across the 5 regions using chi-square test; ‡Czech Republic and Austria; §includes only sites that randomized patients before April 25, 2003. Drug-eluting stents became available on April 25, 2003 in the U.S.

BARI 2D = Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes trial; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; PCI = percutaneous coronary intervention.

Table 2. Demographic and Clinical Characteristics Associated With the Selection of CABG and PCI

		All Patients (N = 1,593)				U.S. (n = 910)				Non-U.S. (n = 683)			
			Intended Procedure				Intended Procedure				Intended Procedure		
		n	CABG	PCI	p Value	n	CABG	PCI	p Value	n	CABG	PCI	p Value
Demographic profile													
Sex	Men	1,149	46%	54%	0.002	640	34%	66%	0.002	509	62%	38%	0.70
	Women	444	38%	62%		270	24%	76%		174	60%	40%	
Age ≥65 yrs	No	949	42%	58%	0.05	514	27%	73%	0.003	435	60%	40%	0.29
	Yes	644	47%	53%		396	36%	64%		248	64%	36%	
Race	White (NH)	1,055	47%	53%	<0.001	533	33%	67%	0.04	522	61%	39%	0.003
	Black (NH)	251	31%	69%		208	24%	76%		43	67%	33%	
	Hispanic	198	48%	52%		134	36%	64%		64	75%	25%	
	Other	89	36%	64%		35	26%	74%		54	43%	57%	
≥HS education	No	620	55%	45%	<0.001	224	31%	69%	0.90	396	68%	32%	<0.001
	Yes	968	37%	63%		682	31%	69%		286	52%	48%	
Health insurance	Public	1,156	49%	51%	<0.001	519	33%	67%	0.26	637	61%	39%	—
	Private	368	32%	68%		330	28%	72%		38	68%	32%	
	None/self-pay	67	27%	73%		60	28%	72%		7	14%	86%	
Clinical profile													
History of MI	No	1,066	41%	59%	0.001	641	30%	70%	0.35	425	59%	41%	0.02
	Yes	501	50%	50%		255	33%	67%		246	67%	33%	
Prior PCI	No	1,308	47%	53%	<0.001	714	34%	66%	<0.001	594	63%	37%	0.006
	Yes	285	29%	71%		196	20%	80%		89	48%	52%	
CHF	No	1,500	45%	55%	0.12	834	31%	69%	0.66	666	62%	38%	0.37
	Yes	86	36%	64%		72	33%	67%		14	50%	50%	
Angina class	No angina	309	42%	58%	0.09	177	29%	71%	0.50	132	59%	41%	0.16
	Atypical	329	42%	58%		220	35%	65%		109	57%	43%	
	Stable 1/2	684	46%	54%		336	32%	68%		348	61%	39%	
	Stable 3/4	139	50%	50%		69	29%	71%		70	70%	30%	
	Unstable	132	36%	64%		108	26%	74%		24	79%	21%	
Hypertension	No	271	41%	59%	0.25	139	31%	69%	0.97	132	52%	48%	0.007
	Yes	1,301	45%	55%		766	31%	69%		535	64%	36%	
Stroke/TIA	No	1,426	45%	55%	0.008	794	32%	68%	0.02	632	61%	39%	0.65
	Yes	160	34%	66%		112	21%	79%		48	65%	35%	
Diabetes duration (yrs)*	<5	499	43%	57%	0.5	278	27%	73%	0.07	221	62%	38%	0.99
	5–10	395	45%	55%		209	31%	69%		186	61%	39%	
	>10	695	45%	55%		420	34%	66%		275	61%	39%	
Insulin use	No	1,171	47%	53%	<0.001	617	33%	67%	0.06	554	62%	38%	0.64
	Yes	422	37%	63%		293	27%	73%		129	60%	40%	

Row percentages are presented. *Cochran-Armitage trend test $p < 0.05$.
CHF = congestive heart failure; HS = high school; MI = myocardial infarction; NH = non-Hispanic; TIA = transient ischemic attack; other abbreviations as in Table 1.

44% (n = 703) and 56% (n = 890), respectively. Of 890 patients in whom PCI was declared, 434 (49%) were deemed suitable for CABG; of 703 patients intended for CABG, 79 (11%) were deemed suitable for PCI. The main reasons that investigators preferred CABG among CABG-intended patients were the likelihood of success and safety, cited in 97% and 46% of patients, respectively, while the main reasons for preferring PCI among PCI-intended patients were the likelihood of success and physician preference cited in 66% and 26% of patients. Selection of CABG rather than PCI was significantly lower in the U.S. compared with non-U.S. sites (31% vs. 61%, $p < 0.001$) (Table 1). Outside of the U.S., selection of CABG ranged from 47% in Canada, 56% in Europe, 73% in Brazil, to 76% in Mexico ($p < 0.001$ for trend). Substantial variability in the selection of revascularization strategy existed among participating sites within the U.S. as well as outside of the U.S. (Fig. 1). In both U.S. and non-U.S. regions, the decision to select CABG increased as disease burden increased, but within each MJI quartile, patients in the U.S. were significantly less likely to be selected for CABG than those in other countries ($p < 0.001$) (Fig. 2). The date of

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Table 3. Angiographic Characteristics Associated With the Selection of CABG and PCI

		All Patients (N = 1,593)				U.S. (n = 910)				Non-U.S. (n = 683)			
			Intended Procedure				Intended Procedure				Intended Procedure		
		n	CABG	PCI	p Value*	n	CABG	PCI	p Value*	n	CABG	PCI	p Value*
Clinical site measurements													
Vessel disease	Double	746	25%	75%	<0.001	453	16%	84%	<0.001	293	40%	60%	<0.001
	Triple	847	61%	39%		457	46%	54%		390	77%	23%	
Number of vessels ≥70%†	0	44	11%	89%	<0.001	32	0%	100%	<0.001	12	42%	58%	<0.001
	1	366	22%	78%		242	14%	86%		124	40%	60%	
	2	713	39%	61%		408	28%	72%		305	53%	47%	
	3	470	72%	28%		228	59%	41%		242	85%	15%	
Proximal LAD ≥50%	No	202	17%	83%	<0.001	130	11%	89%	<0.001	72	29%	71%	<0.001
	Yes	1,391	48%	52%		780	34%	66%		611	65%	35%	
Any LAD ≥70%	No	510	24%	76%	<0.001	334	16%	84%	<0.001	176	39%	61%	<0.001
	Yes	1,083	54%	46%		576	40%	60%		507	69%	31%	
Maximum stenosis in any vessel (%)†	50–69	44	11%	89%	<0.001	32	0%	100%	<0.001	12	42%	58%	<0.001
	70–89	477	26%	74%		342	18%	82%		135	46%	54%	
	90–99	495	43%	57%		258	32%	68%		237	56%	44%	
	100	577	62%	38%		278	49%	51%		299	74%	26%	
Any total occlusions	No	1,016	34%	66%	<0.001	632	23%	77%	<0.001	384	52%	48%	<0.001
	Yes	577	62%	38%		278	49%	51%		299	74%	26%	
Ejection fraction <40%‡	No	1,425	45%	55%	0.47	794	30%	70%	<0.01	631	63%	37%	0.54
	Yes	82	49%	51%		64	47%	53%		18	56%	44%	
Core lab measurements													
MJI (%)†§	≤25	158	18%	82%	<0.001	109	11%	89%	<0.001	49	35%	65%	<0.001
	26–50	445	33%	67%		264	22%	78%		181	51%	49%	
	51–75	467	58%	42%		241	46%	54%		226	71%	29%	
	76–100	238	72%	28%		100	64%	36%		138	78%	22%	
Proximal LAD ≥50%	No	1,378	41%	59%	<0.001	805	28%	72%	<0.001	573	60%	40%	0.03
	Yes	214	62%	38%		104	52%	48%		110	71%	29%	
Total number of lesions†	≤3	313	25%	75%	<0.001	183	12%	88%	<0.001	130	43%	57%	<0.001
	4	331	39%	61%		186	24%	76%		145	58%	42%	
	5	300	46%	54%		173	32%	68%		127	65%	35%	
	6	239	50%	50%		132	39%	61%		107	64%	36%	
	≥7	409	59%	41%		235	47%	53%		174	75%	25%	
Number of lesions ≥50%†	≤1	273	17%	83%	<0.001	191	8%	92%	<0.001	82	38%	62%	<0.001
	2	401	33%	67%		224	25%	75%		177	44%	66%	
	3	377	49%	51%		213	34%	66%		164	68%	32%	
	≥4	541	62%	38%		281	49%	51%		260	77%	23%	
Number of class C lesions†	0	698	28%	72%	<0.001	451	19%	81%	<0.001	247	45%	55%	<0.001
	1	567	50%	50%		305	39%	61%		262	64%	36%	
	2	221	63%	37%		109	50%	50%		112	77%	23%	
	3+	106	76%	24%		44	59%	41%		62	89%	11%	
Any nondiscrete lesions	No	612	38%	62%	<0.001	358	25%	75%	<0.001	254	58%	42%	0.72
	Yes	980	48%	52%		551	38%	62%		429	65%	35%	

Row percentages are presented. *Chi-square p values compare percentage of CABG-intended patients for groups defined by variables listed; †Cochran-Armitage trend test $p < 0.05$; ‡ejection fraction missing for 86 patients; §excludes patients with prior PCI (n = 285).
LAD = left anterior descending coronary artery; MJI = myocardial jeopardy index; other abbreviations as in Table 1.

randomization was also a factor that influenced the revascularization treatment decision. Among the 39 sites that enrolled patients before April 25, 2003, the availability of drug-eluting stents (DES) was associated with an increased selection of PCI ($p = 0.0025$) (Table 1).

Patient characteristics associated with the selection of CABG. Demographic and clinical factors associated with revascularization selection for the entire group and stratified by region are presented in Table 2. Overall, the recommendation for CABG was more common in patients who were

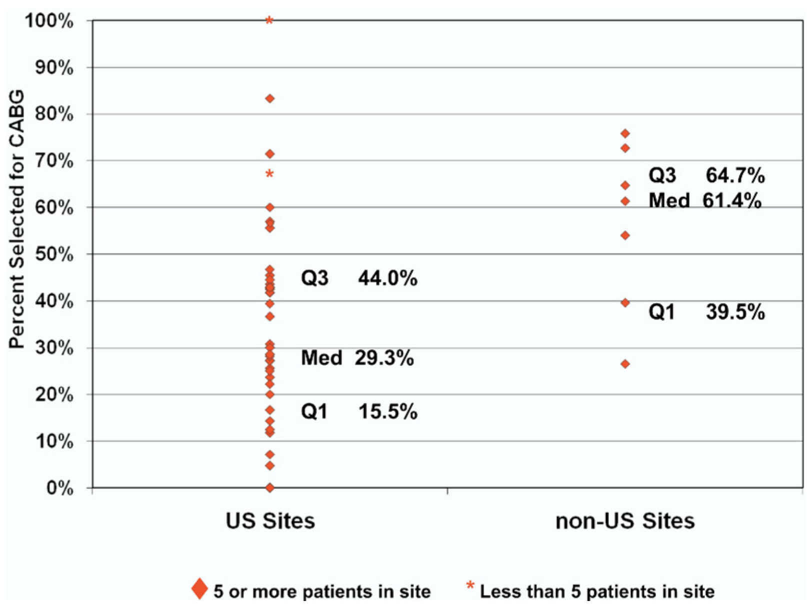

Figure 1. Multivessel CAD Patients Selected for CABG Within Clinical Site by Region

Percentage of coronary artery bypass graft surgery (CABG)-intended patients per site for U.S. sites versus non-U.S. sites. CAD = coronary artery disease; Med = median; Q1 = first quartile; Q3 = third quartile.

white or Hispanic and had not undergone a prior PCI. In the U.S., patients who were male, age 65 years and older, and without a history of cerebrovascular events were more likely to be selected for CABG. Outside the U.S., less formal education, prior MI, and history of hypertension were associated with the selection of CABG.

Angiographic characteristics associated with the selection of revascularization strategy were consistent across U.S. and non-U.S. regions (Table 3). Patients with more severe and extensive CAD, as indicated by triple- versus double-vessel disease and extent of jeopardized myocardium, were more likely to be selected for CABG (both $p < 0.001$). Other angiographic features related to the selection of CABG over PCI included number of vessels with ≥70% stenosis; LAD stenosis ≥70%; number of lesions ≥50% stenosis; and total number of lesions, irrespective of severity (all $p < 0.001$). In addition, the choice of CABG was more common in patients with complex lesions, particularly total occlusions, class C lesions, and nondiscrete lesions (all $p < 0.001$). An ejection fraction <40% was related to the selection of CABG among patients in the U.S. ($p < 0.01$).

Independent predictors of the selection of CABG. The multivariable mixed model analysis indicated that after adjusting for patient characteristics, the odds of selecting CABG was higher among participants enrolled outside of the U.S. compared with those enrolled in the U.S. (OR: 2.89, 95% CI: 1.22 to 6.83, $p = 0.017$) (Fig. 3). Selection of CABG versus PCI within clinical sites was driven largely by angiographic characteristics related to severity of CAD including presence of triple-vessel disease (OR: 4.43, 95% CI: 3.35 to 5.85, $p < 0.001$), proximal LAD stenosis ≥50% (OR: 1.78, 95% CI: 1.20 to 2.64, $p = 0.005$), any LAD stenosis ≥70% (OR: 2.86, 95% CI: 2.11 to 3.88, $p < 0.001$), total occlusion (OR: 2.35, 95% CI: 1.76 to 3.13, $p < 0.001$), and 2 or more class C lesions (OR: 2.06, 95% CI: 1.44 to 2.95, $p \leq 0.001$). Age ≥65 years was also significantly associated with a preference for CABG (OR: 1.43, 95% CI: 1.09 to 1.88, $p = 0.011$). Conversely, CABG was less likely to be selected in patients who had previously undergone PCI (OR: 0.45, 95% CI: 0.31 to 0.64, $p < 0.001$) and those randomized after April 25, 2003 (OR: 0.60, 95% CI: 0.43 to 0.83, $p = 0.003$). The "intrasite" correlation estimated from the mixed model was intraclass correlation = 0.25 ($p < 0.001$) indicating that the decision to select CABG versus PCI is strongly correlated with clinical site, although substantial within-site variability exists.

Discussion

In this analysis of the predictors of the selection of revascularization strategy in patients from the BARI 2D trial with DM, multivessel CAD, and stable symptoms, we found that the choice of CABG rather than PCI was: 1) based largely on angiographic features related to a greater extent, severity, and complexity of CAD; 2) more likely in patients >65 years of age and less likely in those who had undergone a prior PCI; 3) more likely in non-U.S. than

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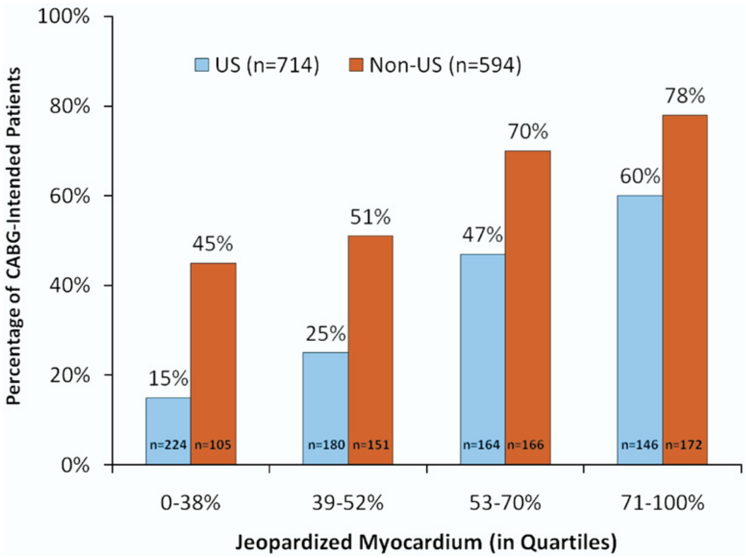

Figure 2. Likelihood of Intended CABG by MJI in U.S. and non-U.S. Sites

Percentage of coronary artery bypass grafting (CABG)-intended patients by myocardial jeopardy index (MJI) quartiles in U.S. and non-U.S. regions, among patients without prior percutaneous coronary intervention (n = 1,308). Note that for each quartile of MJI, non-U.S. patients were more likely to be selected for CABG.

U.S. centers, with significant site-specific preferences within the U.S.; and 4) less likely after the introduction of DES.

The multivariable analysis indicated that the angiographic findings that resulted in the selection of CABG, including chronic total occlusions, triple-vessel disease, significant left anterior descending coronary artery disease, presence of type C lesions, and extent of myocardial jeopardy, reflects existing technical limitations and evidence-based long-term outcomes of PCI under specific anatomic circumstances (1,4–7,26). Among demographic and clinical factors, only older age (directly) and prior PCI (inversely) were associated with the selection of revascularization strategy. Older age was associated with a greater probability of selecting CABG. This finding may be due partially to the trial design. Since study inclusion criteria require a minimum 5-year expected survival and stable presenting clinical status, elderly patients in the BARI 2D trial were, in general, likely to be in better health than elderly patients seen in routine practice.

Substantial regional and temporal variations in the selection of mode of revascularization were detected. Practice patterns in the U.S. were notable for lesser likelihood of CABG as 54% of diabetic patients with triple-vessel disease were selected for PCI. The preference for surgical revascularization outside of the U.S. was demonstrated at every level of myocardial disease burden, and this regional discrepancy remained significant after adjusting for differences in clinical profiles and severity of CAD. The temporal shift towards a preference for PCI in the BARI 2D trial after the availability of DES is consistent with the very rapid implementation of this technology that occurred for both approved and off-label indications. There are several possible explanations for the regional variation in selection of CABG versus PCI. First, key high-level factors associated with the public health care systems in Brazil, Canada, Mexico, and Europe may result in a preference for surgical revascularization in these regions. Conversely, the greater use of PCI in the U.S. may reflect an underlying philosophy that physicians and patients favor the less invasive strategy whenever technically and clinically feasible.

Impact of the original BARI study results. Because the original BARI trial pre-dated the use of stents or any device other than a balloon, its finding regarding the superiority of CABG over conventional balloon angioplasty in diabetic patients with multivessel CAD may have limited applicability in contemporary practice. McGuire et al. (27) reported that 2 years after the Clinical Alert was issued, BARI study results did not impact practice patterns in the U.S., which varied markedly throughout the country. This is not surprising given the findings of nearly identical long-term survival in diabetic patients receiving PTCA versus CABG by physician selection in the original BARI registry (7). Remarkably, there has been little change in the angiographic predictors that drive a selection of CABG rather than PCI in patients with multivessel CAD, from the era when only balloon angioplasty was available. Data from the BARI registry, gathered between 1988 and 1991, indicated that just as in the BARI 2D trial, the selection of CABG rather than PCI was driven by triple- versus double-vessel disease, the number of significant lesions, and the presence

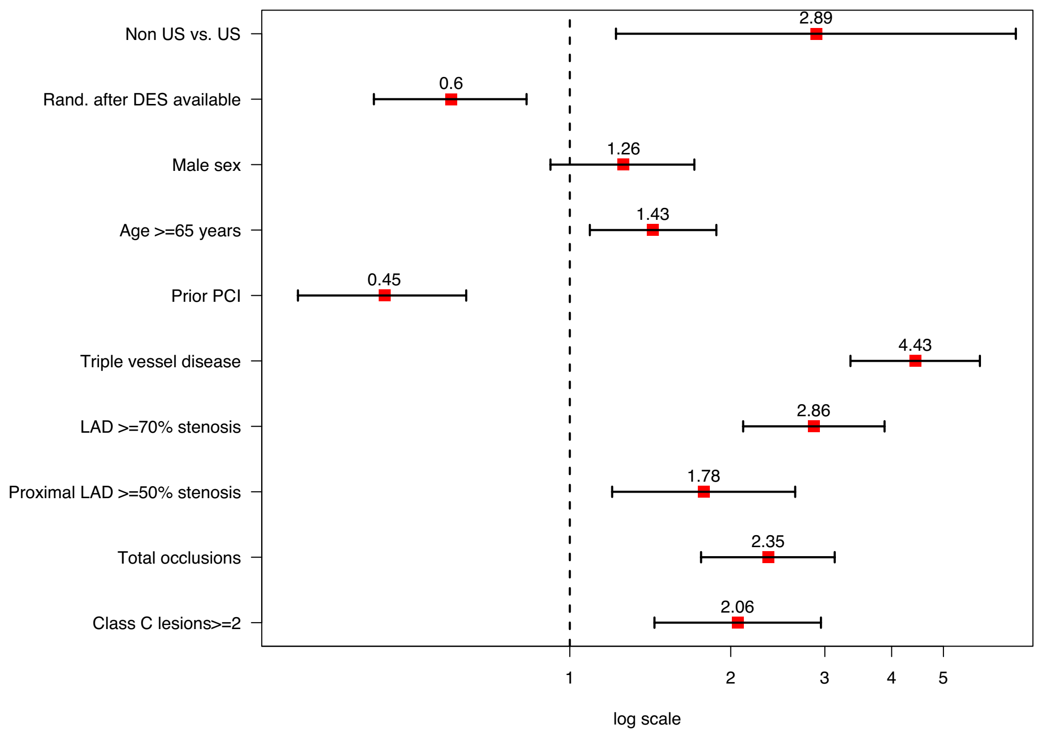

Figure 3. Adjusted Odds Ratio of CABG Selection

Plot of independent predictors of the selection of coronary artery bypass grafting (CABG) over percutaneous coronary intervention (PCI) in diabetic patients with stable multivessel coronary disease. The **red squares** depict adjusted odds ratios; the **horizontal lines** depict the 95% confidence interval. DES = drug-eluting stent(s); LAD = left anterior descending coronary artery; Rand. = Randomized.

of a proximal left anterior descending coronary artery lesion, type C lesion(s), or diffuse disease (7).

Study limitations. Several issues may limit the application of our findings. First, practice patterns in sites participating in the BARI 2D trial may not reflect general practice. Specifically, study investigators and patients from Brazil, Mexico, Czech Republic, and Austria were each from a single center, and it is not clear that selection criteria at these sites represent those of their respective countries or regions. However, since treatment selection was at the discretion of local physicians, practice patterns in all participating sites likely reflect the community standards of their respective centers. Second, study enrollment occurred as the first generation of DES were introduced, which decreased the percentage of patients selected for CABG. Newer generations of DES may have already resulted in more patients being selected for PCI. Third, a factor that did not predict selection of CABG rather than PCI in this model, such as a left ventricular ejection fraction <40% may have resulted from the relatively low number of patients with that finding enrolled in the BARI 2D trial. Despite these limitations, the data presented were prospectively gathered on more than 1,500 patients across a broad spectrum of clinical sites and analyzed by an independent data center. Furthermore, this analysis of the selection of revascularization strategy will be critical to the analysis of the primary study results and subsequent comparisons of those patients undergoing CABG versus PCI.

Conclusions

Among patients with diabetes and multivessel CAD with stable symptoms in the BARI 2D trial, the decision to select CABG over PCI was driven largely by angiographic features associated with extent, location, and nature of CAD. Geographic region also played an important role, as a greater preference for surgical revascularization was demonstrated in countries outside of the U.S. irrespective of other factors. Moreover, treatment selection varied substantially across geographic regions and across clinical sites within regions, reflecting a lack of consensus regarding optimal therapy in contemporary practice. Finally, the introduction of the first generation DES decreased the likelihood of the selection of CABG.

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Key Words: revascularization selection ■ diabetes ■ percutaneous coronary intervention ■ coronary artery bypass graft surgery.