Published in final edited form as:

Am Heart J. 2013 September ; 166(3): . doi:10.1016/j.ahj.2013.05.017.

Change in enrollment patterns, patient selection, and clinical outcomes with the availability of drug-eluting stents in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial

Binita Shah, MD, MS^{a,i}, Vankeepuram S. Srinivas, MBBS, MS^{b,i}, Jiang Lu, MS^{c,i}, Maria M. Brooks, PhD^{c,i}, Eric R. Bates, MD^{d,i}, Zoran S. Nedeljkovic, MD^{e,i}, Jorge Escobedo, MD^{f,i}, Gladwin S. Das, MD^{g,i}, John J. Lopez, MD^{h,i}, and Frederick Feit, MD^{a,i}

^aNew York University School of Medicine, New York, NY

^bMontefiore Medical Center, New York, NY

^cUniversity of Pittsburgh, Pittsburgh, PA

^dUniversity of Michigan, Ann Arbor, MI

^eBoston University School of Medicine, Boston Medical Center, Boston, MA

^fMexican Institute of Social Security, Mexico City, Mexico

^gUniversity of Minnesota, Minneapolis, MN

^hLoyola University Medical Center, Maywood, IL

Abstract

Background—In the BARI 2D trial, patients with type 2 diabetes and stable coronary artery disease were randomized to prompt revascularization versus intensive medical therapy (IMT). This analysis sought to evaluate how the availability of drug-eluting stents (DESs) has changed practice and outcomes.

Methods—In BARI 2D, 1,605 patients were in the percutaneous coronary intervention (PCI)–intended stratum. As DES became available midway through recruitment, we report clinical outcomes among patients who underwent IMT versus prompt PCI with bare-metal stents (BMSs) or DES up to 4 years.

Results—In North America, after DES became available, selection for the PCI-intended stratum increased from 73% to 79% ($P = .003$). Fewer BMS than DES patients had total occlusions treated or underwent rotational atherectomy (5.6% vs 9.7%, $P = .02$, and 1.2% vs 3.7%, $P < .01$, respectively). Subsequent revascularization (IMT 39%, BMS 29%, DES 21%, $P < .01$) and target vessel revascularization (BMS 16.1% vs DES 9.6%, $P = .03$) were lower with DES. Angina at 2 years tended to be less common with DES (IMT 39%, BMS 37%, DES 29%, $P = .04$, for 3 groups, $P = .07$ for DES vs BMS). The composite of death, myocardial infarction, or stroke was IMT 16.0%, BMS 20.5%, DES 17.5%; $P = .80$.

Conclusions—When DES became available in North America, patients were more likely to be selected into the PCI-intended stratum. Compared with patients receiving BMS, those receiving DES tended to have less target vessel revascularization and angina.

One-third of patients undergoing elective percutaneous coronary intervention (PCI) have diabetes mellitus (DM).¹ These patients represent a population at high risk for adverse cardiovascular outcomes related to their glycemic status, comorbid diseases, and associated risk factors.² Furthermore, the treatment of diabetic patients remains a challenge given the greater burden and more diffuse pattern of atherosclerosis as well as more rapid rates of restenosis.^{3,4} Percutaneous coronary intervention with bare-metal stent (BMS) is associated with significantly higher rates of target vessel revascularization (TVR) in patients with compared to those without DM.⁵ Although drug-eluting stents (DESs) have significantly reduced restenosis and TVR rates in the short term, long-term outcomes with DES compared with BMS on a background of intensive medical therapy (IMT) have not been fully defined.^{6,7}

The strategy of prompt revascularization on a background of intensive risk factor modification was compared with a strategy of initial IMT with revascularization if clinically indicated by the progression of angina, the development of an acute coronary syndrome, or severe ischemia in diabetic patients with stable coronary artery disease in the BARI 2D trial.⁸ With the availability of DES for clinical use midway through patient recruitment in North America, the PCI stratum of BARI 2D offers a unique opportunity to examine changes in enrollment pattern, patient selection, and outcomes between patients who received IMT only (with revascularization as needed to relieve symptoms) and those who received IMT plus prompt PCI with either BMS or DES.

Methods

Study design

The design of the BARI 2D trial, including inclusion and exclusion criteria, has been described in detail.^{8–11} Briefly, 2,368 patients with type 2 DM and stable coronary artery disease amenable to elective revascularization (either surgical or catheter based) were enrolled between January 1, 2001, and March 31, 2005, at 49 clinical sites in the United States, Canada, Brazil, Mexico, the Czech Republic, and Austria. Patients were stratified according to the method of revascularization determined a priori by the responsible physician and then randomized to undergo either prompt coronary revascularization or medical therapy. Finally, all-cause mortality and the composite of death, nonfatal myocardial infarction (MI), and stroke were compared between patients who underwent prompt revascularization with either PCI or coronary artery bypass graft (CABG) versus initial medical therapy strategies, and no significant difference was noted between the 2 groups.

Percutaneous coronary intervention stratum

Physicians at clinical sites predetermined PCI rather than CABG to be the more appropriate revascularization treatment modality in 1,605 of the total 2,368 patients. These patients were then randomized to receive either IMT (n = 807) (with revascularization only if clinically indicated by the progression of angina or the development of an acute coronary syndrome or severe ischemia) or IMT plus prompt PCI (n = 798) within 4 weeks after randomization. Of the 798 patients randomized to prompt PCI, 424 received BMS only, and 245 received DES only; 15 who received both BMS and DES were excluded from the current analysis. In addition, 114 were excluded from this treatment-based analysis because PCI did not involve the use of a stent or stent type was not specified or the initial PCI was done after 3 months of

randomization. All baseline angiograms were reviewed in an angiographic core laboratory, details of which have been described earlier.⁹ A myocardial jeopardy index (MJI) was calculated for all patients based on initial angiography.¹²

Outcomes

All patients were followed up monthly for the first 6 months and quarterly thereafter with assessment of risk factors and symptoms. *Subsequent revascularization during follow-up* was defined as the first revascularization in the IMT group or the second revascularization in the BMS and DES groups (planned staged intervention was not treated as a subsequent PCI). Target vessel revascularization was defined in the BMS and DES groups as subsequent revascularization (PCI or CABG) to the same vessels that were attempted during the initial procedure.

Angina status was a repeated measure outcome, with data collected at each of the scheduled follow-up visits. The annual prevalence of angina represented the proportion of patients who experienced angina symptoms during each year of follow-up. Myocardial infarction was defined based on BARI 2D core laboratory evaluation of cardiac biomarkers, symptoms, and electrocardiographic results. The diagnosis of spontaneous MI and periprocedural MI has been described in detail.^{8–11} Creatine kinase-MB was the biomarker of choice after revascularization, but troponin was used if creatine kinase-MB was not available.

Statistical analysis

Because DES became widely available for clinical use midstream in the enrollment of BARI 2D in the United States and Canada, the average follow-up time for patients who underwent prompt PCI with DES was 4 years. Therefore, we compare 4-year clinical outcomes in patients within the PCI stratum of BARI 2D who received initial IMT or prompt PCI with BMS or DES. Drug-eluting stent was available throughout the entire enrollment period in Brazil, Mexico, the Czech Republic, and Austria, and therefore, enrollment patterns before and after the availability of DES were only studied in North America. April 25, 2003, and November 30, 2002, were the dates when DES became available in the United States and Canada, respectively. Baseline variables included demographics, clinical history, angina symptoms within 6 weeks before randomization, laboratory measures, and angiographic characteristics. Related risk factors and pharmacologic therapy were compared among the 4-year survivors at baseline and 4-year follow-up. Analysis of variance and the χ^2 test was performed for continuous and categorical variables, respectively. The annual prevalence of angina symptoms was compared using χ^2 test. The Kaplan-Meier estimator was computed for subsequent revascularization rates, TVR rates, and safety outcomes. Log-rank test was performed for the comparison of cumulative event curves over the 4-year follow-up. Cox regression models were used to obtain hazard ratio estimates, unadjusted and adjusted for country and time of enrollment, with 95% CIs. Because comparisons were made among 3 groups (IMT vs BMS vs DES) for multiple outcomes, the statistical significance level was set at 0.01 after application of the Bonferroni correction. The statistical software SAS 9.2 (Cary, NC) was used to analyze data.

Dr Shah was funded by the American College of Cardiology Foundation/Merck Research Fellowship Award (2011–2012) and the National Institutes of Health/National Heart, Lung and Blood Institute (T32HL098129) (2012–2013). The BARI 2D trial was sponsored by the National Heart, Lung and Blood Institute and received funding from the NIDDK (U01 HL061744, U01 HL061746, U01 HL061748, U01 HL063804); GlaxoSmithKline; Lantheus Medical Imaging, Inc; AstellasPharma US, Inc; Merck & Co, Inc; Abbott Laboratories, Inc; Pfizer, Inc; Abbott Laboratories Ltd; MediSense Products; Bayer Diagnostics; Becton Dickinson and Company; J. R. Carlson Laboratories, Inc; Centocor, Inc; Eli Lilly and

Company; LipoScience, Inc; Merck Sante; Novartis Pharmaceuticals Corporation; and Novo Nordisk, Inc. The BARI 2D trial was coordinated by the Epidemiology Data Center at the University of Pittsburgh, Graduate School of Public Health. The authors are solely responsible for the study design and analyses and drafting and editing of the manuscript and its final contents.

Results

Enrollment patterns and baseline characteristics

Before DES became available in North America, 691 (73%) of 949 patients were selected for the PCI stratum, whereas after their availability, 711 (79%) of 903 patients were selected for the PCI stratum ($P = .003$). In addition, before DES became available in North America, 282 patients received BMS only, whereas after their availability, 80 patients received BMS only, and 214 patients received DES only.

Baseline demographic and clinical characteristics for the IMT alone and BMS and DES groups are shown in Table I. The pattern of stent use differed significantly by country of enrollment, largely due to the relatively low use of DES in Brazil. Baseline angiographic characteristics and PCI procedural data are shown in Tables II and III. The treatment of total occlusions and use of rotational atherectomy were more frequent in patients receiving DES compared with patients receiving BMS (Table III). Furthermore, direct thrombin-inhibitor use was significantly more frequent, and heparin/glycoprotein IIb/IIIa receptor blocker use was significantly less frequent in patients receiving DES (Table III). Thienopyridine use was 21% in the IMT group and 25% in the BMS group compared with 68% in the DES group at 1-year follow-up. Overall, the angiographic and procedure-related adverse events were low and similar between BMS and DES (online Appendix Supplementary Table I).

Subsequent revascularization, angina status, and medication use

Adjunctive medical therapy for lipid, blood pressure, and DM were similar in the 3 groups with approximately 1 in 5 patients meeting all the prespecified blood pressure, low-density lipoprotein (LDL) cholesterol, triglyceride, and hemoglobin A1c goals at 4 years (online Appendix Supplementary Table II).

Overall, 39.3% in the IMT group, 28.9% in the BMS group, and 20.8% in the DES group required subsequent revascularization during the 4-year follow-up ($P < .01$ 3-group comparison, IMT vs BMS $P < .001$, IMT vs DES $P < .001$, BMS vs DES $P = .84$) (Figure 1A). Similar results were observed in rates of subsequent PCI (IMT 32.4%, BMS 23.9%, DES 18.1%, $P < .01$ 3-group comparison, IMT vs BMS $P < .001$, IMT vs DES $P < .001$, BMS vs DES $P = .97$) (Figure 1B). Among patients who underwent a prompt PCI procedure at entry, 16.1% in the BMS group and 9.6% in the DES group underwent TVR ($P = .03$) (Figure 1C).

Compared with the IMT and BMS groups, self-reported angina at 2 years tended to be less common in patients in the DES group (IMT 39%, BMS 37%, DES 29%, $P = .04$ for 3-group comparison, IMT vs BMS $P = .45$, IMT vs DES $P = .01$, BMS vs DES, $P = .07$) (Figure 2). However, the prevalence of self-reported angina was not significantly different across the 3 groups at 4 years (IMT 28%, BMS 24%, DES 21%, $P = .18$) (Figure 2). Long-acting nitrate therapy at 4 years was lower in patients randomized to prompt PCI (IMT 26.3%, BMS 18.7%, DES 19.2%, $P = .02$) (online Appendix Supplementary Table II).

Safety outcomes

At 4 years, the rate of mortality and the composite of mortality, MI, and stroke did not differ significantly among the groups (Table IV).

Discussion

In this well-defined population of diabetic patients with stable coronary artery disease, we found that after DES became widely available for clinical use in the North American population, enrollment patterns changed resulting in a greater proportion of patients being selected for the PCI stratum relative to the CABG stratum. Furthermore, in the overall trial, DES was used more widely in patients whose angiographic profiles included total occlusions and those undergoing rotational atherectomy. Within BARI 2D, patients receiving DES only had lower rates of TVR than those receiving BMS only.

This is the first time a large prospective multicenter randomized clinical trial with adjudicated clinical end points has allowed the substitution of a significant new technology involving one of the primary treatment strategies midway through enrollment. As such, BARI 2D offers insight into the impact of the availability of a technological or pharmacologic breakthrough during the recruitment phase of a randomized trial. When a significant new relevant therapy arises during the enrollment of a large clinical trial, there are only 3 options in proceeding. The first is to complete the trial without incorporating the new therapy, as was done in the original BARI trial.¹³ Directional coronary atherectomy (DCA) was thought to represent a breakthrough technology when it first became available for clinical use in 1990. However, at that time, the BARI trial had already reached approximately 90% of target enrollment, and therefore, it was considered ethical to continue enrollment without allowing inclusion of DCA. This proved to be a wise decision as the evidence for the superiority of DCA using the device and techniques available at that time was weak and the initial randomized clinical trial, CAVEAT, showed no advantage for DCA.¹⁴ In fact, CAVEAT demonstrated a higher rate of death or MI in the DCA group.¹⁴ The second option is to start the trial over, which is usually not appropriate once substantial enrollment has occurred. The third option is to include the new therapy in the protocol and proceed despite potential changes in recruitment practice and outcomes. In the ACUTY trial, the original active control group was enoxaparin plus a glycoprotein IIb/IIIa inhibitor because this was the preferred guideline-based strategy for patients presenting with an acute coronary syndrome.¹⁵ However, following the presentation of the SYNERGY trial, which demonstrated that unfractionated heparin resulted in similar rates of ischemic outcomes but less bleeding than enoxaparin in patients with acute coronary syndrome, the ACUTY trial design allowed each site to choose either enoxaparin or unfractionated heparin with a glycoprotein IIb/IIIa inhibitor, creating a hybrid control group but allowing for continued ethical recruitment in the trial.^{15,16}

As DESs were considered to be superior to BMS for preventing restenosis, particularly in patients with DM and that the BARI 2D trial was midway in its recruitment phase, the decision was made to allow the use of DES. This did result in a change in revascularization strategy; following the availability of DES in North America, a higher proportion of patients enrolled were selected for the PCI stratum. Furthermore, DES was used far more often than BMS after its availability in North America, given the perception of improved outcomes with DES versus BMS in patients with DM.⁶ The increased use of rotational atherectomy and treatment of patients with total occlusions indicates a more aggressive approach to percutaneous revascularization with the availability of DES. However, despite the use of DES in more complex anatomy, there were no significant differences noted in procedure-related adverse events or major adverse cardiovascular events.

The current analysis demonstrates that PCI with DES is associated with lower rates of subsequent revascularization. Furthermore, the prevalence of self-reported angina was reduced with stenting versus IMT at both 1 and 2 years with an advantage of DES over BMS compared with IMT at both time points. Although relief was maximal in the first year after PCI with DES, there was subsequent attenuation of this advantage, such that by 4 years, the prevalence of angina was not significantly different in patients who received IMT and those who had prompt PCI. However, rates of self-reported angina did improve in all groups over time, and the loss of statistical significance at 4 years may have resulted in part from the high rate of revascularization (39%) in the IMT group. Despite the significant improvement in risk factors between baseline and 4-year follow-up with aggressive medical and lifestyle intervention, only 20% of patients in the PCI stratum of BARI 2D met risk factor goals at 4 years of follow-up, highlighting the potential of disease progression in all 3 groups. In addition, some data suggest attenuation of benefit in patients with insulin-treated DM compared with patients treated with oral hypoglycemic agents,¹⁷ and the patients in the current cohort demonstrated a considerable increase in the use of insulin at 4-year follow-up.

When specifically comparing BMS with DES, studies have consistently demonstrated significantly lower TVR rates in patients treated with DES up to 1 year post-PCI.^{18,19} In a recent large meta-analysis comparing outcomes with various DES or BMS in patients with DM, we reported significant benefit with sirolimus- and everolimus-eluting stents in reduction of MI and stent thrombosis as well as a significant reduction in rates of TVR with all the currently used DES compared with BMS.²⁰ Thus, it is reasonable to speculate that these outcomes might have been better in our analysis had DES been available for the entire duration of the study. In BARI-2D, we did demonstrate a lower rate of TVR in patients receiving DES versus BMS over 4-year follow-up. A significant difference in rate of subsequent revascularization and self-reported angina during the first 2 years was noted across the 3 groups. When the BMS group was compared with the DES group, there were 28% and 22% relative risk reductions in the rates of subsequent revascularization and prevalence of self-reported angina at 2 years, respectively, with DES. Although these results were not statistically significant, this analysis is underpowered to detect differences of this magnitude that may be clinically relevant.

There are several limitations to this analysis given that the selection of BMS or DES was not randomized. As DES became available during study recruitment, the outcome data might be subject to temporal bias. Patients who received DES had significantly higher use of a direct-thrombin inhibitor as adjunctive pharmacotherapy. This is likely due to a parallel temporal increase in published data reflecting net clinical benefit with bivalirudin over heparin and a glycoprotein IIb/IIIa inhibitor in patients undergoing PCI.^{21,22} However, for the most part, patients who received DES versus BMS had similar baseline characteristics, with patients receiving DES having, if anything, more complex anatomical features. Furthermore, although patients who received DES had a more prolonged thienopyridine use after PCI, there is no conclusive benefit for dual-antiplatelet therapy use for more than 6 months after PCI with DES in patients without acute coronary syndrome.²³ This analysis does not adjust for all known predictors of DES use including small reference vessel diameter and greater lesion length, both of which independently predict target lesion revascularization after stenting.²⁴ Finally, there is the limitation inherent to randomized clinical trials where only patients with true clinical equipoise are selected for inclusion, and without an accompanying registry, it is difficult to state that the results apply to all patients with DM and stable coronary artery disease.²⁵ Despite these limitations, BARI 2D offers a unique opportunity to present outcome data in a population where 1 arm is offered a significant new technology midway through enrollment.

Conclusions

When DES became available in the BARI 2D trial, they were used in a significant majority of patients and resulted in several favorable outcomes, including a reduction in TVR and self-reported angina at 2 years, relative to BMS and IMT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We dedicate this article to the memory of Katherine M. Detre, MD, PhD, who initiated and led the study to enhance the care of patients through the rigorous analysis of clinical evidence.

References

1. Percutaneous coronary interventions in New York state 2006–2008. New York State Department of Health; 2010 Dec.
2. [Accessed August 2, 2012] National diabetes statistics, 2011. National Diabetes Information Clearinghouse. <http://diabetes.niddk.nih.gov/dm/pubs/statistics/#Deaths>
3. Goraya TY, Leibson CL, Palumbo PJ, et al. Coronary atherosclerosis in diabetes mellitus: a population-based autopsy study. *J Am Coll Cardiol.* 2002; 40:946–953. [PubMed: 12225721]
4. Luscher TF, Creager MA, Beckman JA, Cosentino F. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part II. *Circulation.* 2003; 108:1655–1661. [PubMed: 14517152]
5. Elezi S, Kastrati A, Pache J, et al. Diabetes mellitus and the clinical and angiographic outcome after coronary stent placement. *J Am Coll Cardiol.* 1998; 32:1866–1873. [PubMed: 9857865]
6. Hermiller JB, Raizner A, Cannon L, et al. Outcomes with the polymer-based paclitaxel-eluting TAXUS stent in patients with diabetes mellitus: the TAXUS-IV trial. *J Am Coll Cardiol.* 2005; 45:1172–1179. [PubMed: 15837245]
7. De Waha A, Dibra A, Kufner S, et al. Long-term outcome after sirolimus-eluting stent versus bare metal stents in patients with diabetes mellitus: a patient-level meta-analysis of randomized trials. *Clin Res Cardiol.* 2011; 100:561–570. [PubMed: 21221607]
8. The BARI 2D Study Group. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med.* 2009; 360:2503–2515. [PubMed: 19502645]
9. Brooks MM, Frye RL, Genuth S, et al. Hypothesis, design and methods for the Bypass Angioplasty Revascularization Investigation 2 Diabetes Trial. *Am J Cardiol.* 2006; 97(Suppl):9G–19G.
10. Barsness GW, Gersh BJ, Brooks MM, Frye RL. Rationale for the revascularization arm of the Bypass Angioplasty Revascularization Investigation 2 Diabetes Trial. *Am J Cardiol.* 2006; 97 suppl(12A):31G–40G.
11. Bypass Angioplasty Revascularization Investigation 2 Diabetes Study Group. Baseline characteristics of patients with diabetes and coronary artery disease enrolled in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. *Am Heart J.* 2008; 156:528–536,536.e1–e5. [PubMed: 18760137]
12. Schwartz L, Kip KE, Alderman E, et al. Baseline coronary angiographic findings in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. *Am J Cardiol.* 2009; 103:632–638. [PubMed: 19231325]
13. The Bypass Angioplasty Revascularization Investigation Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. *N Engl J Med.* 1996; 335:217–225. [PubMed: 8657237]
14. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of coronary angioplasty with directional atherectomy in patients with coronary artery disease. *N Engl J Med.* 1993; 329:221–227. [PubMed: 8316266]

15. Stone GW, Bertrand M, Colombo A, et al. Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial: study design and rationale. *Am Heart J*. 2004; 148:764–775. [PubMed: 15523305]
16. Ferguson JJ, Califf RM, Antman EM, et al. Enoxaparin vs unfractionated heparin in high-risk patients with non-ST-segment elevation acute coronary syndromes managed with an intended early invasive strategy: primary results of the SYNERGY randomized trial. *JAMA*. 2004; 292:45–54. [PubMed: 15238590]
17. Flaherty JD, Davidson CJ. Diabetes and coronary revascularization. *JAMA*. 2005; 293:1501–1508. [PubMed: 15784875]
18. Moussa I, Leon MB, Baim DS. Impact of sirolimus-eluting stents on outcome in diabetic patients: a SIRIUS substudy. *Circulation*. 2004; 109:2273–2278. [PubMed: 15123524]
19. Sabaté M, Jiménez-Quevedo P, Angiolillo DJ, et al. Randomized comparison of sirolimus-eluting stent versus standard stent for percutaneous coronary revascularization in diabetic patients: the diabetes and sirolimus-eluting stent trial. *Circulation*. 2005; 112:2175–2183. [PubMed: 16203930]
20. Bangalore S, Kumar S, Fusaro M, et al. Outcomes with various drug eluting or bare metal stents in patients with diabetes mellitus: mixed treatment comparison analysis of 22 844 patient years of follow-up from randomised trials. *BMJ*. 2012; 345:e5170. [PubMed: 22885395]
21. Gurm HS, Sarembock IJ, Keriakes DJ, et al. Use of bivalirudin during percutaneous coronary artery intervention in patients with diabetes mellitus: a report from the randomized evaluation in percutaneous coronary intervention linking angiogram to reduced clinical events-2 trial. *J Am Coll Cardiol*. 2005; 45:1932–1938. [PubMed: 15963389]
22. Feit F, Manoukian SV, Ebrahimi R, et al. Safety and efficacy of bivalirudin monotherapy in patients with diabetes mellitus and acute coronary syndromes: a report from the ACUITY trial. *J Am Coll Cardiol*. 2008; 51:1645–1652. [PubMed: 18436116]
23. Valgimigli M, Campo G, Monti M, et al. Short- versus long-term duration of dual antiplatelet therapy after coronary stenting: a randomized multicentre trial. *Circulation*. 2012; 125:2015–2026. [PubMed: 22438530]
24. Stone GW, Parise H, Witzenbichler B, et al. Selection criteria for drug-eluting versus bare-metal stents and the impact of routine angiographic follow-up: 2-year insights from the HORIZONS-AMI trial. *J Am Coll Cardiol*. 2010; 56:1597–1604. [PubMed: 20888162]
25. Feit F, Brooks MM, Sopko G, et al. Long-term clinical outcome in the Bypass Angioplasty Revascularization Investigation Registry: comparison with the randomized trial. BARI Investigators. *Circulation*. 2000; 101:2795–2802. [PubMed: 10859284]

Figure 1.
Subsequent revascularization, subsequent PCI, and TVR rates.

* 1 year IMT vs BMS $P = .03$, IMT vs DES $P < .01$; ** 2 year IMT vs DES $P < 0.01$

Figure 2.

Self-reported angina by revascularization type.

* 1 year IMT vs BMS $P = .03$, IMT vs DES $P < .01$; ** 2 year IMT vs DES $P < 0.01$

Table I

Baseline characteristics in the PCI-intended stratum

	PCI + medical therapy			<i>P</i>
	IMT (n = 807)	BMS (n = 424)	DES (n = 245)	
Demographics				
Age, y	61.9 ± 9.3	61.4 ± 8.9	62.4 ± 9.2	.33
Female sex, %	33.0	31.6	31.4	.84
Race, %				.23
White	68.0	68.2	68.6	
Black	20.2	21.5	15.9	
Asian	4.1	4.2	4.1	
Ethnicity, %				
Hispanic	18.8	22.9	18.4	.19
Country of enrollment, %				<.01
United States	73.7	71.2	73.1	
Canada	13.6	14.2	14.3	
Brazil	7.9	13.2	1.2	
Mexico	2.0	0.7	4.9	
Czech Republic/Austria	2.7	0.7	6.5	
Stent use after DES availability, n (%)				<.01
United States		54 (23)	179 (77)	
Canada		26 (43)	35 (57)	
Brazil		56 (95)	3 (5)	
Mexico		3 (20)	12 (80)	
Czech Republic/Austria		3 (16)	16 (84)	
Medical history, %				
MI	29.5	30.5	31.7	.79
PCI	22.5	21.0	24.5	.58
Coronary artery bypass surgery	9.9	6.1	8.6	.08
Congestive heart failure	7.2	7.6	8.6	.76
Renal insufficiency	3.5	4.0	2.1	.40
Stroke or transient ischemic attack	11.3	10.7	9.0	.59
Peripheral artery disease	24.2	24.3	20.4	.44
PCI	22.5	21.0	24.5	.58
Diabetes characteristics				
Duration of diabetes, y	10.5 ± 8.9	10.6 ± 8.8	9.6 ± 8.1	.31
Neuropathy (MNSI >2), %	50.3	50.2	46.1	.50
Angina status, %				
Stable class I/II	42.3	39.6	42.0	.46
Stable class III/IV	7.8	8.7	8.6	
Unstable	9.3	12.3	9.0	

	PCI + medical therapy			<i>P</i>
	IMT (n = 807)	BMS (n = 424)	DES (n = 245)	
Anginal equivalents	21.8	24.8	21.6	

MNSI, Michigan Neuropathy Screening Instrument.

Table II

Angiographic characteristics in the PCI-intended stratum

	IMT (n = 807)	PCI + medical therapy		<i>P</i>
		BMS (n = 424)	DES (n = 245)	
Distribution of coronary artery disease, %				.62
Single-vessel	43.8	45.0	47.4	
Double-vessel	35.7	34.9	34.7	
Triple-vessel	20.5	20.0	18.0	
MJI	36.5 ± 21.4	38.7 ± 21.9	36.4 ± 22.5	.20
Categorical MJI, %				.44
25%	35.7	29.7	35.1	
26%–50%	39.9	44.8	40.0	
51%–75%	19.3	18.9	19.6	
76%–100%	5.2	6.6	5.3	
No. of lesions 50% diameter stenosis/patient, %				.89
0	9.2	9.5	12.7	
1	31.2	22.9	29.0	
2	23.5	25.3	22.9	
3	16.1	16.1	15.1	
4	20.0	18.9	20.4	
No. of lesions 70% diameter stenosis/patient, %				.50
0	45.6	45.6	51.4	
1	31.1	33.1	29.0	
2	11.4	12.1	10.6	
3	11.9	9.2	9.0	
Proximal LAD disease (50%), %	10.2	11.6	10.2	.73
Among lesions 50% diameter stenosis	Lesion n = 1842	Lesion n = 932	Lesion n = 587	
Class B/C lesion, %	71.2	71.7	74.1	.42
Proximal, %	26.4	27.5	29.6	.33
Midvessel, %	41.5	39.3	41.0	.52
Distal, %	29.8	32.2	28.1	.22

LAD, Left anterior descending artery.

Table III

Procedural characteristics in patients who underwent PCI with BMS or DES

	PCI + medical therapy		<i>P</i>
	BMS (n = 424)	DES (n = 245)	
Revascularization priority, %			
Elective	98.3	97.7	.47
No. of treated vessels/patient, %			.59
1	81.1	78.0	
2	17.2	20.4	
3	1.7	1.6	
No. of treated lesions/patient, %			.24
1	61.1	64.5	
2	28.1	22.4	
3	10.8	13.1	
Multivessel PCI, %	18.9	22.0	.32
Vessel treated, %			
Left main artery	0.5	0.8	.58
LAD	47.9	49.4	.71
Left circumflex artery	33.0	40.0	.07
Right coronary artery	39.6	34.3	.17
Adjunctive pharmacotherapy, %			
Unfractionated heparin	80.2	59.2	<.01
Glycoprotein IIb/IIIa receptor inhibitor	68.9	47.3	<.01
Planned	98.6	98.3	.78
Bail-out	1.4	1.7	
Direct thrombin-inhibitor	3.3	13.9	<.01
Thrombolytic therapy <48 h before PCI	0.7	0.0	.19
Among treated lesions	Lesion n = 656	Lesion n = 376	
Site of lesion treated, %			
Proximal	30.2	29.8	.91
Midvessel	43.3	44.9	.63
Distal	26.4	25.3	.71
Characteristic of lesion treated, %			
Complex lesions (B2/C)	58.5	59.9	.65
Moderate/severe calcification	3.3	2.1	.29
Moderate/severe tortuosity	17.9	19.5	.59
Total occlusions	5.6	9.7	.02
Diameter stenosis (by visual assessment),%			
Preprocedure	61.6 ± 16.6	61.0 ± 17.3	.61
Postprocedure	8.3 ± 15.5	8.7 ± 17.0	.70
Postprocedural TIMI flow grade, %			.34

	PCI + medical therapy		<i>P</i>
	BMS (n = 424)	DES (n = 245)	
0/1	1.6	2.4	
2/3	98.4	97.6	
Rotational atherectomy, %	1.2	3.7	<.01
Unsuccessful PCI of intended lesion, %	2.5	2.1	.75

TIMI, Thrombolysis in myocardial infarction.

Table IV
Association between type of therapy and 4-year major cardiovascular events in the PCI-intended stratum

	Unadjusted event rates			Unadjusted models			Adjusted models*		
	IMT (n = 807)	BMS (n = 424)	DES (n = 245)	BMS vs IMT, HR (95% CI)	DES vs IMT, HR (95% CI)	P	BMS vs IMT, HR (95% CI)	DES vs IMT, HR (95% CI)	P
Death, %	7.0	8.8	7.8	0.97 (0.70–1.36)	0.99 (0.62–1.61)	.99	0.94 (0.67–1.32)	1.12 (0.66–1.89)	.84
MI, %	10.0	12.0	9.1	1.16 (0.83–1.62)	0.90 (0.56–1.46)	.55	1.20 (0.85–1.69)	0.86 (0.52–1.42)	.43
Stroke, %	2.7	2.6	1.4	0.94 (0.47–1.89)	0.48 (0.14–1.60)	.49	0.92 (0.45–1.89)	0.52 (0.15–1.85)	.59
Death/MI/stroke, %	16.0	20.5	17.5	1.09 (0.85–1.39)	1.04 (0.74–1.46)	.80	1.10 (0.86–1.42)	1.03 (0.71–1.49)	.73
Subsequent revascularization, %	39.3	28.9	20.8	0.68 (0.55–0.83)	0.47 (0.35–0.64)	<.001	0.69 (0.56–0.85)	0.46 (0.33–0.63)	<.001
Subsequent PCI, %	32.4	23.9	18.1	0.68 (0.54–0.85)	0.51 (0.37–0.71)	<.001	0.70 (0.55–0.88)	0.49 (0.35–0.69)	<.001
Subsequent CABG, %	9.9	8.1	4.6	0.86 (0.58–1.26)	0.56 (0.23–0.87)	.054	0.82 (0.55–1.21)	0.51 (2.54–1.01)	.11

HR, Hazard ratio.

* Adjusting for country (United States vs Canada vs Mexico/Brazil/Czech Republic/Austria) and enrollment period (January 1, 2001–December 31, 2002, vs January 1, 2003–March 31, 2004, vs April 1, 2004–March 31, 2005).