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Presentation in Patients with Angiographically Documented Coronary Artery Disease and Type II Diabetes Mellitus (From the BARI 2D Clinical Trial)

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Abstract

Clinically stable patients with type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) are not often thought to present with the symptom of typical angina. We sought to enumerate the proportion of patients presenting with typical angina or other cardiac symptoms and to elucidate what important clinical variables are associated with the presence of typical angina in patients with T2DM and angiographically documented CAD. Symptoms of angina, anginal equivalents or an absence of symptoms were obtained utilizing baseline data from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial (n=2319). A bivariate analysis stratified by the presence or absence of prior revascularization and logistic regression modeling with a stepwise covariate selection was used. Our results noted that 82% of patients had symptoms while 18 % presented asymptomatically. This was further divided approximately into typical angina ($1/5^{th}$); anginal equivalents ($1/5^{th}$); combination ($2/5^{th}$); asymptomatic ($1/5^{th}$). A history of prior revascularization was a determinant of the type of symptom presentation in regards to the variables sex, age, current insulin use, myocardial jeopardy index score and use of beta-blockers. In the multivariable logistic regression analysis, of the available candidate variables only a history of beta-blocker use (OR=1.53, 95% CI 1.24–194, p<0.0001 and prior percutaneous coronary intervention (OR=1.55, 95% CI 1.24–1.94, p<0.0001) had a higher odds of an association with typical angina. In conclusion, a large proportion of patients with T2DM and CAD indeed have symptoms. Future studies of long term outcomes associated with these symptoms are needed.

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Keywords

symptoms; chest pain; diabetes mellitus; coronary artery disease

Introduction

In order to gain an appreciation of symptom presentation in a select group of patients with type 2 diabetes mellitus (T2DM) and angiographically documented coronary artery disease (CAD) we sought to: a) enumerate the proportion of each symptom noted. b) elucidate the important demographic and clinical variables independently associated with the presence of typical angina pectoris. c) assess the association of fibrinolytic variables plasminogen activator inhibitor-1 (PAI-1) antigen, PAI-1 activity and tissue plasminogen activator (t-PA) to the symptom typical angina pectoris.

Methods

To meet the aims as noted above, a cross-sectional analysis was designed utilizing baseline data at the time of initial patient entry into the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial (BARI 2D). The study design, patient characteristics and primary outcomes of the primary BARI 2D trial have been published[1–4]. In brief, the BARI 2D study was a multi-center National Institutes of Health trial that tested two simultaneous hypotheses in a 2×2 factorial design (immediate versus delayed or no revascularization and insulin sensitizing agents versus insulin providing agents) in patients with T2DM and angiographically documented stable CAD who all received optimal intensive medical therapy to control risk factors.

To obtain entry into the trial every patient had to have a coronary angiogram documenting ≥ 1 vessel with a ≥ 50% stenosis that was suitable for revascularization by either percutaneous coronary intervention (PCI) or by coronary artery bypass grafting surgery (CABG) with either objective documentation of ischemia or subjective documentation of angina with a ≥ 70% stenosis. Major exclusion criteria included a definite need for revascularization as judged by the attending cardiologist, left main coronary artery stenosis, planned intervention on a bypass graft, advanced congestive heart failure, elevated creatinine and poorly controlled diabetes mellitus (HgbA1c >13%).

Patients were questioned regarding their symptoms at the time of their initial baseline visit. The symptoms that were reported were within 6 weeks prior to this baseline visit. The symptoms reported were then categorized by clinical site staff as typical angina pectoris, anginal equivalent (shortness of breath, dyspnea on exertion, exertional fatigue, nausea, unexplained diaphoresis, other) or asymptomatic (no angina or anginal equivalents). Typical angina pectoris was defined as a discomfort or pain located in the chest or upper epigastrium described as a pressure, heaviness, tightness, squeezing, burning, or choking sensation that suggested an ischemic heart disease diagnosis. Patients that had symptoms of both typical angina pectoris and anginal equivalents were categorized as typical angina.

The fibrinolytic variables used were PAI-1 antigen, PAI-1 activity and t-PA. The biological basis for this addition was felt to be that elevated PAI-1 is likely to be associated with impaired fibrinolysis and promote a procoagulatory milieu that may contribute to acceleration of coronary artery disease with precipitation of events including angina or anginal equivalents. Tissue plasminogen activator is known to track with PAI-1. This tracking reflects a complexing of t-PA with PAI-1 with a consequent diminished clearance of complexed t-PA that is biochemically inactive.

Of the 2368 patients enrolled in the BARI 2D study, 2321 had 80% of their baseline data available for analysis. Of these, 2 patients did not report angina status within 6 weeks prior to randomization. This report includes the data from 2319 patients. Coronary revascularization was noted as the presence or absence of either PCI or CABG. An initial unadjusted and subsequent bivariate analysis stratified by revascularization method was performed. A p-value of < 0.05 was used to determine statistical significance. The p-values in the baseline table refer to Cochran-Mantel-Haenszel tests of general association among the three symptom groups after controlling for cardiac revascularization status. Differences among the symptoms groups for continuous variables were tested using ANOVA stratified by revascularization status. Multivariable stepwise logistic regression analysis was used to determine independent associations between baseline demographic, clinical and angiographic variables and typical angina. The model was built using stepwise regression of the candidate variables with a p-value of 0.1 to enter the model and 0.05 to be included (stay) in the model. The candidate variables were: age, sex, smoking status, exercise status, duration of diabetes mellitus, body mass index, systolic blood pressure, diastolic blood pressure, hemoglobin A1C level, LDL-cholesterol, HDL-cholesterol, total cholesterol, triglycerides, ankle-brachial index, history of lung disease, myocardial infarction, stroke, hypertension, non-coronary artery disease, PCI, stent, CABG, myocardial jeopardy index score[5], coronary artery stenosis > 70%, current beta blocker, calcium channel blocker, statin, thiazolidinedione and insulin use. Left ventricular ejection fraction was not placed in the regression model due to the exclusion of advanced congestive heart failure patients in the main trial. Myocardial jeopardy index was defined as the percentage of left ventricular myocardium jeopardized by ≥ 50% stenosis[5]. Once the demographic and clinical variables having independent associations with typical angina were determined, baseline fibrinolysis measures of PAI-1 antigen, PAI-1 activity and t-PA were added to the final typical angina model to determine if they added any more information to the model. Since PAI-1 antigen and activity measures were skewed, they were transformed using the natural log. Two further similar logistic regression analyses were performed in patients with and without prior revascularization. SAS v.9.2 software was used for all statistical analysis.

Results

The distribution of symptoms reported were typical angina (n=437, 19%), anginal equivalents (n=493, 21%), combination of typical angina and anginal equivalents (n=971, 42%) and asymptomatic (n=418, 18%). Baseline left ventricular ejection fraction was 57.2 ± 10.9% (SD) in the entire cohort, 57.1 ± 11.0 % in the PCI stratum and 57.5 ± 10.8% in the CABG stratum. A history of prior coronary revascularization as well as the type of revascularization (PCI or CABG) was a determinant of symptom presentation (table 1).

Regardless of prior revascularization status, males presented asymptomatically more often than females; females presented with typical angina more often; and older individuals presented less often with typical angina. The variations across symptoms stratified by revascularization in the baseline characteristics are noted in table 2. As noted in table 3, all three fibrinolytic variables (PAI-1 activity, PAI-1 antigen and t-PA) varied significantly across the groups (p=0.0071, p=0.0058, p=0.0003 respectively) after adjustment for prior revascularization status.

In the multivariable logistic regression analysis utilizing the entire cohort, only participants with a history of beta-blocker use (OR=1.53, 95% CI 1.24–1.94, p<0.0001) and prior percutaneous coronary intervention (OR=1.55, 95% CI 1.24–1.94, p<0.0001) were more likely to report typical angina. Participants that were male gender, older than 60 years, current exercisers, and had a history of thiazolidinedione use were less likely to report typical angina (Figure 1). PAI-1 antigen and PAI-1 activity were not significantly associated (p> 0.08) with typical angina. However, higher t-PA levels were independently associated with higher odds of typical angina (OR 1.03 for every one unit of increase in t-PA level, 95% CI 1.01 –1.06, p=0.008). In table 4, the adjusted covariates that were statistically significant are shown stratified by presence or absence of prior revascularization. In patients with prior revascularization, PAI-1 antigen, PAI-1 activity and t-PA were not significantly associated with typical angina. In those who did not undergo prior revascularization, t-PA continued to be independently associated with a higher odds of typical angina (OR 1.03, 1.01 –1.06, p=0.02).

Discussion

This analysis brings to the forefront a few important points which will be individually dealt with in the following paragraphs. First, a large proportion of patients with T2DM and documented stable CAD do indeed have symptoms. Second, prior coronary revascularization in general and particularly the type of prior revascularization, is associated with the type of symptom presentation. Third, future studies will need to assess the prognostic implications of typical angina or dyspnea[6] (or other anginal equivalents) in this or a similar cohort which was not addressed in the current baseline analysis.

We were able to demonstrate that in a population of patients with T2DM and angiographically proven CAD, a large proportion (82%) have symptoms; only 18 % had no symptoms. Symptom status in the present study can be divided approximately into typical angina (1/5th); anginal equivalents (1/5th); combination of typical angina and anginal equivalents (2/5th); no angina or anginal equivalents (1/5th). Typical angina pectoris as the sole symptom was noted in 19% in our study compared with 28% of diabetic patients in a very early study utilizing thallium scintigraphy. The variations between the two studies are probably a result of different study designs[7].

We felt that the type of symptoms that patients present with may vary with whether they have had prior revascularization or not and also with the type of prior coronary revascularization i.e., PCI or CABG. A paucity of data exists on this topic. In the current study typical angina was noted more often (26.2%, p<0.0001) compared to the other

symptoms in patients with a history of any prior coronary revascularization. Comparing the two revascularization techniques, typical angina was noted in 22.0 % (p<0.0001) of patients with a history of prior PCI but only 7.0% (p=0.09) in those who had prior CABG suggesting variations in symptom presentation by mode of revascularization. This was validated in the initial multivariable logistic regression analysis when participants with a history of percutaneous coronary intervention had 55% higher odds of reporting typical angina (p<0.0001). Slight variations in the covariates that were significantly associated with typical angina were also noted between those who had prior revascularization and those who did not have prior revascularization. Further work needs to be done to explore the interaction between the type of prior revascularization and symptom presentation using multivariable analysis techniques on a hard outcome such as all-cause mortality.

Dyspnea is a well established symptom of cardiorespiratory illness and is usually "applied to sensations experienced by individuals who complain of unpleasant or uncomfortable respiratory sensations"[8]. The etiology of dyspnea in cardiac diseases is quite often related to the underlying left ventricular function[9–10]. In the present study, overall left ventricular ejection fraction was > 45% so it is less likely that the shortness of breath is related to underlying left ventricular systolic dysfunction. Thiazolidinedione use in patients with T2DM has been reported to cause or exacerbate edema in 2.5%–16.2% of patients and approximately 0.25–0.45%/year may experience symptoms of volume overload or heart failure[11–12]. Based on our analysis, thiazolidinedione use was associated with 39% lower odds of presenting with typical angina (p<0.0001) i.e., more likely presenting with anginal equivalents or asymptomatically. Dyspnea can also be a manifestation of pulmonary disease. However, only 4–6 % of the total cohort in this study had a diagnosis of chronic obstructive pulmonary disease or asthma and this covariate was not statistically significant in the multivariable analysis. Therefore, dyspnea in this study probably represents manifestations of varying degrees of obstructive coronary artery disease primarily or through a combination of other mechanisms leading to decreased left ventricular compliance (i.e., diastolic dysfunction) that was not evaluated in the present study.

The overall prognosis in patients with T2DM and CAD is thought to vary by the type of symptom presentation. Prior studies have suggested a poorer prognosis in patients presenting with dyspnea[6, 13]. Zellweger et al[13], using a Cox proportional hazards model noted an adjusted hazard ratio of 2.1, 95% CI 1.24–3.42, (p=0.005) in patients with shortness of breath for the composite outcome of myocardial infarction or cardiac death. They also noted that in patients with shortness of breath event rates were significantly greater in those with abnormal myocardial perfusion SPECT imaging (13.2%), compared to normal myocardial perfusion SPECT imaging (3.3%), p=0.001. In a very well done epidemiological study Abidov et al[6], described the annual mortality rate based on symptom presentation and the presence or absence of coronary artery disease. It was noted that in patients with no known coronary artery disease presenting with dyspnea the annual all-cause mortality rate was 6.2 %/year compared with typical angina, atypical angina, nonanginal chest pain or asymptomatic (p<0.001 for the difference across the other four groups.). In those patients with known coronary artery disease and presenting with dyspnea, the annual all-cause mortality rate was even higher at 11.7%/year (p<0.001 for the difference across the other four groups.). This suggests that the assessment of symptoms is of paramount importance

for future prognostic implications. The present study examined data at baseline from the BARI 2D clinical trial. Further studies from this cohort will need to be undertaken to assess prognosis based on the presence or absence of typical angina or anginal equivalents.

A final intriguing question is whether underlying fibrinolytic biomarkers are associated with symptom development in patients with T2DM and stable CAD? Our initial analysis noted that values of fibrinolytic factors varied significantly with symptom presentation. However, in the multivariable model, only t-PA was significantly associated with typical angina in the entire cohort as well as in those who had no prior revascularization. Although, t-PA has been noted to predict future cardiovascular events in patients with established CAD[14–15] there have been no prior studies that have assessed symptom presentation with underlying fibrinolytic activity. Further work is needed to better understand how symptoms correlate with the underlying fibrinolytic status[16].

The limitation of this study is that it is cross-sectional in nature which reveals certain associations of interest but do not establish causal relationships. Also, the BARI 2D patient cohort is a highly select group of patients chosen on very strict inclusion and exclusion criteria. Therefore, due to entry bias our results may not be representative of those in the general patient population with CAD and T2DM. An important strength is that symptom ascertainment in a cohort of patients with T2DM and documented CAD have not been established and this study thus adds to the literature in this aspect.

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References:

1. Frye RL, August P, Brooks MM, Hardison RM, Kelsey SF, MacGregor JM, Orchard TJ, Chaitman BR, Genuth SM, Goldberg SH, Hlatky MA, Jones TL, Molitch ME, Nesto RW, Sako EY, Sobel BE. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med 2009;24:2503–2515.
2. Baseline characteristics of patients with diabetes and coronary artery disease enrolled in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial. Am Heart J 2008;3:528–53636 e1–5.

3. Magee MF, Isley WL. Rationale, design, and methods for glycemic control in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial. Am J Cardiol 2006;97:20G–30G.

4. Barsness GW, Gersh BJ, Brooks MM, Frye RL. Rationale for the revascularization arm of the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial. Am J Cardiol 2006;97:31G–40G.

5. Alderman EL SM. The angiographic definitions of the Bypass Angioplasty Revascularization Investigation. Coronary Artery Disease 1992;3:1189–1207

6. Abidov A, Rozanski A, Hachamovitch R, Hayes SW, Aboul-Enein F, Cohen I, Friedman JD, Germano G, Berman DS. Prognostic significance of dyspnea in patients referred for cardiac stress testing. N Engl J Med 200518:1889–1898.

7. Nesto RW, Phillips RT, Kett KG, Hill T, Perper E, Young E, Leland OS, Jr. Angina and exertional myocardial ischemia in diabetic and nondiabetic patients: assessment by exercise thallium scintigraphy. Ann Intern Med 1988;2:170–175.

8. Dyspnea. Mechanisms, assessment, and management: a consensus statement. American Thoracic Society. Am J Respir Crit Care Med 1999;1:321–340.

9. ADHERE Scientific Advisory Committee:Acute Decompensated Heart Failure National Registry (ADHERE©) Core Module Q1 2006 Final Cumulative National Benchmark Report.: Scios, Inc. July 2006.

10. O'Connor CM, Stough WG, Gallup DS, Hasselblad V, Gheorghiade M. Demographics, clinical characteristics, and outcomes of patients hospitalized for decompensated heart failure: observations from the IMPACT-HF registry. J Card Fail 2005;3:200–205.

11. Thiazolidinediones Yki-Jarvinen H.. N Engl J Med 2004;11:1106–1118.

12. Nesto RW, Bell D, Bonow RO, Fonseca V, Grundy SM, Horton ES, Le Winter M, Porte D, Semenkovich CF, Smith S, Young LH, Kahn R. Thiazolidinedione use, fluid retention, and congestive heart failure: a consensus statement from the American Heart Association and American Diabetes Association. October 7, 2003. Circulation 2003;23:2941–2948.

13. Zellweger MJ, Hachamovitch R, Kang X, Hayes SW, Friedman JD, Germano G, Pfisterer ME, Berman DS. Prognostic relevance of symptoms versus objective evidence of coronary artery disease in diabetic patients. Eur Heart J 2004;7:543–550.

14. Gorog DA. Prognostic value of plasma fibrinolysis activation markers in cardiovascular disease. J Am Coll Cardiol 2010;24:2701–2709.

15. Smith FB, Fowkes FG, Rumley A, Lee AJ, Lowe GD, Hau CM. Tissue plasminogen activator and leucocyte elastase as predictors of cardiovascular events in subjects with angina pectoris: Edinburgh Artery Study. Eur Heart J 2000;19:1607–1613.

16. Sobel BE. Ancillary studies in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial: Synergies and opportunities. Am J Cardiol 2006;12A:53G–8G.

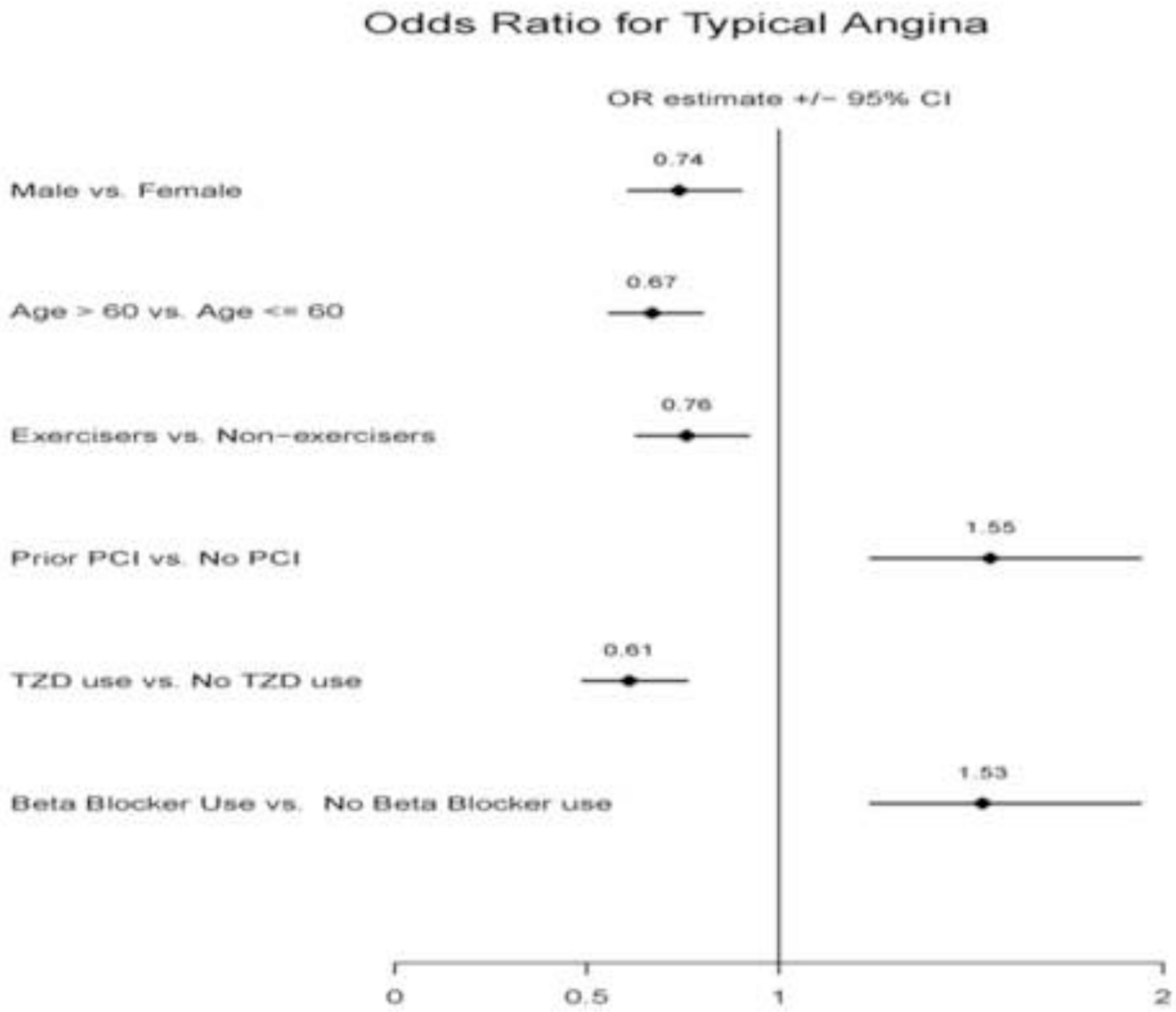

Figure 1.

Multivariable logistic regression analysis showing independent adjusted odds ratios for typical angina within 6 weeks prior to the baseline visit in the BARI 2D clinical trial (n=2311 for final model). Age in years, PCI = percutaneous coronary intervention, TZD= thiazolidinedione. The diamond represents the odds ratio estimate and the line shows the 95% CI.

Table 1.

Symptom presentation by the presence and type of prior coronary revascularization. PCI=percutaneous coronary intervention, CABG=coronary artery bypass grafting. Nominal p-values shown in the table refer to global tests of equality among symptom groups.

Variable	Total	Typical Angina	Anginal Equivalent	Asymptomatic	p-value
	(N= 2319)	(N=1408)	(N=493)	(N=418)	
Any prior coronary revascularization	23.5%	26.2%	22.1%	16.0%	<0.0001
Prior PCI	19.6%	22.2%	17.2%	13.4%	<0.0001
Prior CABG	6.4%	7.0%	6.9%	4.1%	0.09

Table 2.

A comparison of baseline demographics, clinical, laboratory and angiographic variables shown by symptom presentation stratified by presence or absence of prior coronary revascularization. SD= standard deviation, DM =diabetes mellitus, TZD= Thiazolidinedione, Lung disease=chronic obstructive pulmonary disease & asthma, HbA1c = glycated hemoglobin, LDLc=low density lipoprotein cholesterol. Nominal p-values shown in the table refer to global tests of equality among symptom groups.

	No History of Prior Revascularization			History of Prior Revascularization			
Characteristic	**Typical Angina (N=1039)**	**Anginal Equivalent (N=384)**	**Asymptomatic (N=351)**	**Typical Angina (N=369)**	**Anginal Equivalent (N=109)**	**Asymptomatic (N=67)**	**p-value**
Male	66.6%	71.1%	78.6%	71.0%	71.6%	79.1%	<.0001
Age at study entry, mean, SD (years)	61.6, 8.9	63.1, 8.7	63.1, 8.9	61.8, 8.8	64.6, 9.6	65.5, 7.3	<.0001
Current smoker	11.9%	14.9%	11.7%	14.1%	7.3%	6.0%	0.49
Regular exercise	22.9%	24.0%	34.2%	25.0%	23.9%	43.3%	<.0001
Age at DM diagnosis, mean, SD (years)	51.0, 10.9	51.7, 10.9	52.7, 11.3	50.6, 10.9	52.1, 11.3	54.6, 8.6	0.094
Duration of DM, mean, SD (years)	10.2, 8.4	10.9, 9.1	9.8, 8.6	10.8, 9.2	11.8, 8.3	10.4, 7.6	0.2036
Currently taking insulin	26.9%	30.7%	21.1%	33.1%	31.2%	25.4%	0.0092
Currently taking TZD	15.0%	21.6%	21.4%	18.2%	28.4%	34.3%	<0.0001
HbA1c %, mean, SD	7.68, 1.61	7.65, 1.61	7.57, 1.68	7.71, 1.62	7.74, 1.62	7.54, 1.38	0.19
History of lung disease	10.6%	11.2%	5.1%	13.6%	12.0%	9.0%	0.0043
Sitting systolic blood pressure, mean, SD (mmHg)	132.2, 20.7	132.9, 20.6	131.9, 19.6	129.2, 19.2	129.8, 16.3	134.2, 17.8	0.74
Myocardial Jeopardy score, mean, SD (%)	46.9, 24.2	42.9, 25.1	48.2, 24.1	38.3, 22.1	36.8, 24.5	44.4, 23.7	0.0015
Coronary Stenosis > 70%	62.6%	59.6%	66.9%	64.0%	73.1%	67.2%	0.25
LDL-c (mg/dl) median, Q1-Q3	92.0 (72.0–116.0)	96.0 (77.0–118.0)	90.5 (74.0–111.0)	89.0 (72.0–109.0)	92.0 (69.0–115.0)	93.6 (80.0–113.0)	0.45
Beta blocker	74.7%	64.8%	64.4%	82.3%	74.3%	80.6%	<.0001
Calcium Channel Blocker	30.3%	30.5%	28.2%	37.0%	35.8%	32.8%	0.63
Any Nitrates	55.3%	25.8%	27.1%	63.6%	45.9%	32.8%	<.0001
Statin	71.8%	71.0%	68.9%	85.9%	86.2%	92.5%	0.88

Table 3.

Fibrinolytic variables shown by symptom presentation stratified by presence or absence of prior revascularization status. PAI-1 = plasminogen activator inhibitor, t-PA= tissue plasminogen activator. Nominal p-values shown in the table refer to global tests of equality among symptom groups.

	No history of prior revascularization			History of prior revascularization			
Variable	**Typical Angina (N=1039)**	**Anginal Equivalent (N=384)**	**Asymptomatic (N=351)**	**Typical Angina (N=369)**	**Anginal Equivalent (N=109)**	**Asymptomatic (N=67)**	**p-value**
PAI-1 Activity (AU/ml) median, Q1-Q3	16 10.0 – 26.0	18 11.0 – 28.0	15 9.3 – 25.0	17 9.9–28.0	13 9.0–23.0	17 9.0 – 27.0	0.007
PAI-1 Antigen (ng/ml) median, Q1-Q3	23 16.0 – 35.0	24 16.0 – 36.0	22 14.0 – 33.0	24 15.0 – 36.0	21.5 13.0 – 33.0	23 14.0 – 35.0	0.006
t-PA(ng/ml) mean, SD	10.36, 4.05	10.49, 3.97	9.69, 3.71	10.29, 4.52	9.59, 3.88	9.56, 3.47	0.0003

Table 4.

Independent adjusted odds ratio of covariates in patients with and without a history of prior revascularization in a multivariable logistic regression analysis for typical angina within 6 weeks prior to the baseline visit in the BARI 2D clinical trial. TZD= thiazolidinedione.

	No history of prior revascularization (N=1748)		History of prior revascularization (n=544)	
Variable	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**
Male	0.70 (0.57 – 0.87)	<0.002		
Age >60 years	0.68 (0.55 – 0.83)	<0.0001	0.54 (0.36 – 0.72)	0.002
Regular Exercise	0.77 (0.61 – 0.96)	0.018		
History of hypertension	1.43 (1.11 – 1.83)	0.006		
Use of TZD	0.65 (0.51 – 0.84)	0.001	0.52 (0.34 –0.79)	0.002
Beta-blocker use	1.56 (1.26 – 1.93)	<0.0001		