Original Article

Residual Angina After Elective Percutaneous Coronary Intervention in Patients With Diabetes Mellitus

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Background—Previous studies suggest that among patients with stable coronary artery disease, patients with diabetes mellitus (DM) have less angina and more silent ischemia when compared with those without DM. However, the burden of angina in diabetic versus nondiabetic patients after elective percutaneous coronary intervention (PCI) has not been recently examined.

Methods and Results—In a 10-site US PCI registry, we assessed angina before and at 1, 6, and 12 months after elective PCI with the Seattle Angina Questionnaire angina frequency score (range, 0–100, higher=better). We also examined the rates of antianginal medication prescriptions at discharge. A multivariable, repeated-measures Poisson model was used to examine the independent association of DM with angina over the year after treatment. Among 1080 elective PCI patients (mean age, 65 years; 74.7% men), 34.0% had DM. At baseline and at each follow-up, patients with DM had similar angina prevalence and severity as those without DM. Patients with DM were more commonly prescribed calcium channel blockers and long-acting nitrates at discharge (DM versus not: 27.9% versus 20.9% [*P*=0.01] and 32.8% versus 25.5% [*P*=0.01], respectively), whereas β-blockers and ranolazine were prescribed at similar rates. In the multivariable, repeated-measures model, the risk of angina was similar over the year after PCI in patients with versus without DM (relative risk, 1.04; range, 0.80–1.36).

Conclusions—Patients with stable coronary artery disease and DM exhibit a burden of angina that is at least as high as those without DM despite more antianginal prescriptions at discharge. These findings contradict the conventional teachings that patients with DM experience less angina because of silent ischemia. **(*Circ Cardiovasc Qual Outcomes*. 2017;10:e003553. DOI: 10.1161/CIRCOUTCOMES.117.003553.)**

Key Words: coronary artery disease ■ diabetes mellitus ■ myocardial ischemia ■ percutaneous coronary intervention ■ risk

Patients with diabetes mellitus (DM) generally have more diffuse coronary artery disease (CAD) than patients without DM,[1], greater progression of CAD,[2] and a higher risk of restenosis after percutaneous coronary intervention (PCI).[3] However, the degree to which these anatomic differences translate into differences in ischemic symptoms is not clear. Previous studies comparing the burden of angina by DM status in patients with CAD have yielded contradictory results. Earlier studies suggested that patients with DM experienced less angina than those without DM[4,5], theoretically because of silent ischemia as a consequence of autonomic neuropathy.[5,6] Conversely, more recent study has shown more angina in patients with DM, both before and after acute myocardial infarction.[7] However, the prevalence of residual angina after PCI in patients with DM and stable CAD has not been examined.

This is particularly relevant as the primary benefit of PCI in patients with stable ischemic heart disease is amelioration of angina. Residual angina after PCI is associated with impaired quality of life[8] and is associated with repeat hospitalizations.[9] As such, a better understanding of the burden of residual angina is needed among patients with DM and stable ischemic heart disease—patients who are often challenging to treat interventionally because of the diffuse nature of their atherosclerosis and increased risk of restenosis after successful PCI.[1] To address this gap in knowledge, we compared angina

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WHAT IS KNOWN

- The prevailing wisdom has been that patients with diabetes mellitus (DM) and coronary artery disease primarily experience myocardial ischemia silently and therefore have less angina as compared coronary artery disease patients without DM.
- However, more contemporary work investigating the rates of symptomatic myocardial ischemia in patients with and without DM demonstrated that patients with DM experience angina at similar or even higher rates as patients without DM.

WHAT THE STUDY ADDS

- We found that angina burden was similar between those with and without DM, both at the time of elective PCI and over the following year.
- Residual angina after PCI was associated with an increased risk of rehospitalization—a risk that was similar among patients with and without DM—highlighting the clinical importance of residual angina.
- Our findings support recent studies demonstrating that patients with DM have a high burden of symptomatic chest pain as opposed to only silent ischemia. Continued efforts to reduce the burden of angina in patients with DM, including novel interventional and surgical techniques and antianginal medications, are needed.

over the year after elective PCI among patients with and without DM in a large, multicenter US PCI registry.

Methods

Study Design and Participants

Our analytic population was derived from the OPS (Outcomes of PCI Study)/PRISM (Personalized Risk Information Services Manager) prospective study of patients undergoing PCI.[10–12] Briefly, from May 26, 2009, to October 21, 2011, consecutive patients undergoing PCI for all indications at 10 US hospitals were invited to participate in OPS/PRISM at the time of PCI. Baseline data were obtained through a combination of chart abstraction and a detailed interview performed by trained study coordinators at each site. For the purposes of this analysis, only patients who underwent PCI electively for stable angina were included. Detailed telephone follow-up interviews were attempted on all surviving patients at 1, 6, and 12 months after index PCI by a specialized team at the coordinating center. If patients were unavailable by phone, follow-up interviews were mailed to the patients with a prepaid return envelope. During follow-up interviews, patients were asked to report interval hospitalizations since their last study contact, which were confirmed with hospitalization records review. Each participating site obtained institutional research board approval, and all patients provided informed consent for baseline and follow-up assessments.

Definition of DM and Angina

DM was defined as a chart-derived diagnosis of either type 1 or type 2 DM. Angina was assessed during the PCI hospitalization and at each follow-up interview using the Seattle Angina Questionnaire (SAQ).[13] The SAQ is a reliable, responsive, and valid 19-item questionnaire with a 4-week recall that assesses 5 clinically important domains of health in patients with CAD: angina frequency, angina stability, quality of life, physical limitations, and treatment satisfaction. The scores for each of the SAQ domains are transformed, with a range from 0 to 100, with higher scores indicating less angina and better health status. For this study, we focused on the SAQ angina frequency domain (SAQ AF), which has been shown to correlate well with patient-reported daily diaries of angina.[14] To facilitate interpretation of the SAQ AF scores, we mirrored previous work by categorizing scores into daily (SAQ AF score of 0–30), weekly (SAQ AF score of 31–60), monthly (SAQ score of 61–99), and no angina (SAQ AF score of 100).[15]

Statistical Analysis

Baseline characteristics were compared between patients with and without DM using χ^2 tests for categorical variables and *t* test for continuous variables. The prevalence (SAQ AF score of <100 versus 100) and severity of angina (category of SAQ AF [daily, weekly, monthly, and none]) were compared between groups at each follow-up time point using χ^2 tests. Mean scores on all SAQ domains were compared at baseline and at 12 months between groups using *t* tests. A hierarchical, multivariable repeated-measures Poisson model was then used to assess the independent association between DM and angina over the year after index PCI. This allowed us to integrate multiple follow-up time points into a single estimation of risk over time and also to estimate relative risks directly, to avoid overestimating the effect size.[16,17] Covariates for the model were selected a priori based on literature review and clinical judgment, balancing adjustment with overfitting, and included age, sex, race, current smoking, dyslipidemia, hypertension, history of myocardial infarction, history of PCI, history of coronary artery bypass grafting, and multivessel disease on the current angiogram (defined as ≥70% stenosis in ≥2 major epicardial coronary arteries or ≥50% stenosis of the left main coronary artery). Hospital was entered in the model as a random effect to adjust for patient clustering by site.

The association of residual angina at 1 month post-PCI with subsequent all-cause rehospitalizations was examined in patients with and without DM using Kaplan–Meier methods. A Cox proportional hazards model was used to examine whether the association of residual angina (yes/no), DM, and the interaction of DM×1-month angina.

Baseline data were generally complete, with a mean number of missing items per patient of 0.03. Table I in the online-only Data Supplement describes baseline characteristics of patients missing from analytic cohort (n=42) compared with patients included in overall cohort. These data were estimated with a single imputation data set using IVEware (University of Michigan's Survey Research Center, Institute for Social Research, Ann Arbor, MI). All remaining analyses were conducted using SAS v9.3 (SAS Institute, Inc., Cary, NC), and statistical significance was determined by a 2-sided $P<0.05$.

Results

Study Population

From 2009 to 2011, 3299 patients who underwent PCI at 10 US sites were enrolled in OPS/PRISM. We excluded 1230 patients who underwent PCI for an acute coronary syndrome, 947 patients whose PCI was performed urgently or emergently, and 42 (3.7%) patients who were missing either baseline or follow-up angina assessments (Figure 1). Our final analytic cohort thus consisted of 1080 patients who underwent PCI for stable ischemic heart disease, of whom 367 (34.0%) had DM. The mean age of the cohort was 65 years, 74.7% were men, 93.8% were of white race, and 92.6% had at least a high-school education (Table 1). An established diagnosis of CAD was common, with 23.2% having a history of MI, 41.8% with a history of PCI, and 19.0% with a history of CABG.

Patients with DM (versus those without) were less likely to be white (89.8% versus 95.9%; $P<0.001$; Table 1) and were

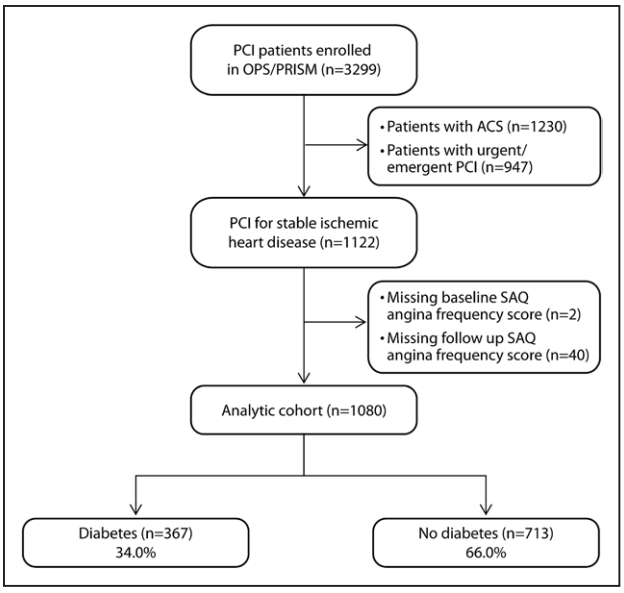

Figure 1. Flow chart of the analytic cohort. ACS indicates acute coronary syndrome; OPS, outcomes of PCI study; PCI, percutaneous coronary intervention; PRISM, Personalized Risk Information Services Manager; and SAQ, Seattle Angina Questionnaire.

more likely to report avoiding care because of costs (11.5% versus 7.0%; *P*=0.013). They had a higher mean body mass index (32.9 versus 29.4; *P*<0.001), had more frequent clinical diagnosis of heart failure (12.3% versus 5.3%; *P*<0.001), and had a prior PCI (48.5% versus 38.3%; *P*=0.001) more often than patients without DM. Angiographic findings, however, were comparable between patients with and without DM (no difference in number of patients with multivessel disease, and no numeric difference in number of diseased vessels [neither ≥50% nor ≥70% stenoses, nor number of vessels with chronic total occlusion]). There was, however, a nonsignificant trend toward more obstructive CAD among patients with DM.

Burden of Angina

Over the 4 weeks before PCI, patients with and without DM reported similarly high angina burden (Table 2), with over one third of patients reporting daily or weekly angina (DM versus non-DM, 37.1% versus 36.2%; *P*=0.952; Figure 2). Patients with DM were more commonly discharged on antianginal medication as compared with patients without DM (81.6% versus 74.7%; *P*=0.011; Table 2) and were more likely to be discharged on ≥2 antianginal medications (31.2% versus 23.1%; *P*=0.004). These differences were primarily driven by increased use of calcium channel blockers and long-acting nitrates in patients with DM, as β-blocker and ranolazine prescription rates were similar between groups. There was no significant difference in the number of antianginals in those with and without HF.

Over the 12 months after PCI, patients with DM reported nominally higher but statistically similar rates of angina when compared with patients without DM, both in prevalence of angina and severity of angina (Figure 2). One year after PCI, 17.4% of patients with DM reported residual angina versus 16.0% of patients without DM (*P*=0.577). Other SAQ domains were also similar between those with and without DM with the exception of SAQ physical limitations scores, which were statistically lower (worse) at 12 months in patients with DM (DM versus non-DM, 95.1 versus 96.5; *P*=0.047) although this mean difference is not generally considered clinically important. After adjusting for demographic and clinical characteristics, including multivessel disease, patients with DM had a similar risk of residual angina over the year after PCI (relative risk, 1.04; range, 0.80–1.36).

Rehospitalization

At 1 month after PCI, 24.0% of patients reported residual angina (DM, 27.7%; no DM, 21.9%). Residual angina was associated with a greater risk of rehospitalization after PCI in both patients with and without DM (Figure 3). In the Cox model that included DM, residual angina was associated with a 1.74-increased hazard of rehospitalization (95% confidence interval, 1.23–2.47; *P*=0.002). However, this increased hazard did not vary by DM status (DM×angina interaction, *P*=0.808). As patients with DM were more likely to have HF and rehospitalizations were not restricted to those for angina, we also examined whether a diagnosis of HF impacted the association between residual angina and risk of rehospitalization. The addition of HF to the model did not impact the HR for residual angina (HR, 1.37; 95% CI, 0.74–2.56).

Discussion

In a large, contemporary multicenter US PCI registry, we found that angina burden was similar between those with and without DM, both at the time of elective PCI and over the following year despite more aggressive treatment of diabetic patients with antianginal medications. Furthermore, we found that residual angina after PCI was associated with an increased risk of rehospitalization—a risk that was similar among patients with and without DM—highlighting the clinical importance of residual angina. These findings support results from recent studies demonstrating that patients with DM and CAD (stable or unstable) frequently experience symptomatic ischemia by extending these observations to a post-PCI population.

Earlier studies suggested that patients with DM incur a large burden of silent ischemia because of autonomic neuropathy.[18–20] As such, the prevailing wisdom has been that patients with DM and CAD primarily experience myocardial ischemia silently and therefore have less angina when compared CAD patients without DM. However, more contemporary work explicitly investigating the rates of symptomatic myocardial ischemia in patients with and without DM demonstrated consistent results to ours, namely, that patients with DM experience angina at similar or even higher rates as patients without DM.[21–24]

Furthermore, the concept that patients with DM and CAD have autonomic dysfunction and therefore more silent ischemia than patients without DM has also been challenged. In the ACIP study (Asymptomatic Cardiac Ischemia Pilot) of patients with stable ischemic heart disease, patients with DM had a similar prevalence of asymptomatic ischemia during exercise treadmill testing as compared with patients without DM.[21] Our results therefore add to a growing body of studies demonstrating that patients with DM and CAD may

Table 1. Baseline Characteristics of Analytic Cohort From the OPS/PRISM Registry

	Overall (n=1080)	Diabetes Mellitus (n=367)	No Diabetes Mellitus (n=713)	*P* Value
Sociodemographics				
Age, y	65.1±10.4	65.3±9.9	65.0±10.6	0.692
Male sex, %	74.7	71.7	76.3	0.097
White race, %	93.8	89.8	95.9	<0.001
High-school education, %	92.6	90.9	93.4	0.143
Insurance for medications, %	95.5	97.0	94.7	0.084
Self-reported avoidance of care because of cost, %	8.6	11.5	7.0	0.013
Clinical characteristics				
Body mass index, kg/m^2	30.6±6.1	32.9±6.6	29.4±5.5	<0.001
History of MI, %	23.2	26.4	21.6	0.075
History of PCI, %	41.8	48.5	38.3	0.001
History of CABG, %	19.0	18.8	19.1	0.914
Chronic heart failure, %	7.7	12.3	5.3	<0.001
Peripheral artery disease, %	8.7	10.9	7.6	0.066
Chronic lung disease, %	9.4	11.2	8.4	0.141
Depression, %	6.9	6.2	6.9	0.217
Angiographic characteristics				
Multivessel disease,* %	39.4	42.7	37.7	0.112
No. of patients with diffuse disease, %	9.3	11.5	8.1	0.073
Residual no. of diseased vessels post PCI†	0.4±0.7	0.4±0.6	0.4±0.7	0.206
Vessels with ≥50% stenoses, %				0.053
0	2.5	3.9	1.8	
1	57.9	53.2	60.3	
2	27.8	30.3	26.6	
3	11.7	12.7	11.3	
Vessels with ≥70% stenoses,‡ %				0.056
0	2.5	3.9	1.8	
1	58.1	53.4	60.5	
2	27.7	30.3	26.4	
3	11.6	12.4	11.3	
Vessels with chronic total occlusions, %				0.538
0	84.9	83.9	85.4	
1	12.0	12.6	11.8	
2	2.5	3.3	2.1	
3	0.6	0.3	0.7	

Data are presented as mean±SD of %. CABG indicates coronary artery bypass graft surgery; LM, left main coronary artery; MI, myocardial infarction; OPS, Outcomes of PCI Study; PCI, percutaneous coronary intervention; and PRISM, Personalized Risk Information Services Manager.

*Defined as ≥70% stenosis in ≥2 major epicardial coronary arteries or ≥50% stenosis of the left main coronary artery.

†Defined as number of vessels with ≥70% stenosis (including LM≥50%) minus number of vessels with successful PCI.

‡Includes left main stenosis ≥50%.

experience myocardial ischemia symptomatically, and not just silently, and that angina (and mechanisms to treat angina) remains a substantial clinical concern in this population. In fact, a recent large clinical trial of an antianginal medication focused specifically on patients with DM, with the idea that these patients are particularly challenging to treat.[25] Further defining the high burden of angina among patients with DM and CAD should encourage continued efforts to identify

Table 2. Health Status and Antianginal Medication Use, Stratified by DM Status

	Diabetes Mellitus (n=367)	No Diabetes Mellitus (n=713)	*P* Value
SAQ domain scores			
Baseline			
Angina frequency	73.2±24.8	73.8±24.6	0.718
Quality of life	58.4±24.3	60.1±25.9	0.278
Physical limitation	77.1±23.1	78.4±23.3	0.396
Treatment satisfaction	94.3±9.7	94.1±9.9	0.720
12 mo			
Angina frequency	94.9±13.2	95.2±13.6	0.754
Quality of life	81.8±18.3	83.7±16.7	0.106
Physical limitation	95.1±13.0	96.5±10.5	0.047
Treatment satisfaction	94.4±9.8	93.7±11.7	0.333
Antianginal medications at discharge, %			
No. of medications			
0	11.5	16.1	0.040
1	51.4	59.7	0.008
≥2	37.2	24.1	<0.001
Class of medications			
β-blocker	81.1	76.4	0.077
Calcium channel blocker	27.9	20.9	0.010
Long-acting nitrate	32.8	25.5	0.012
Ranolazine	3.8	3.0	0.233

DM indicates diabetes mellitus; and SAQ, Seattle Angina Questionnaire.

mechanisms by which to treat these symptoms of ischemia, particularly given the implications of this angina in terms of rehospitalizations and quality of life. Furthermore, these data should encourage clinicians to continue to probe about the presence of angina (or anginal equivalent) in their patients with DM.

Limitations

Our findings should be considered in the context of the following potential limitations. First, while the severity of anatomic CAD was similar between groups, we did not have functional assessments of ischemia at baseline or at follow-up. These would have allowed us to determine the proportion of ischemia over follow-up that was experienced as angina (versus silent ischemia). Although this could be an interesting future study, our study was designed to compare the prevalence and burden of angina after PCI between patients with and without DM—not to compare the amount of residual ischemia. Angina, as assessed with the SAQ, is associated with lower quality of life[26], an increased risk of hospitalization, and higher healthcare costs,[27] and as such, we believe that it is an important patient-centered outcome. Second, our population included only patients who presented for PCI, most of whom had some degree of symptomatic ischemia on presentation. As such, we cannot generalize our results to the general population of patients with CAD. Third, DM classification was based only on chart-derived diagnosis. This potentially misses a healthy minority of patients who may have previously undiagnosed DM as studies have shown that a substantial amount of patients presenting with coronary disease

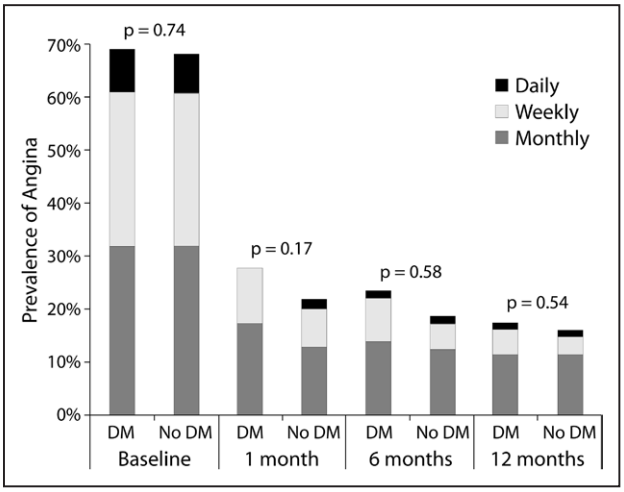

Figure 2. Angina burden at baseline and over the year after percutaneous coronary intervention in patients with and without diabetes mellitus (DM). As assessed with the Seattle Angina Questionnaire angina frequency domain. Scores of 0 to 30 indicate daily angina; 31 to 60 indicate weekly angina; 61 to 99 indicate monthly angina.

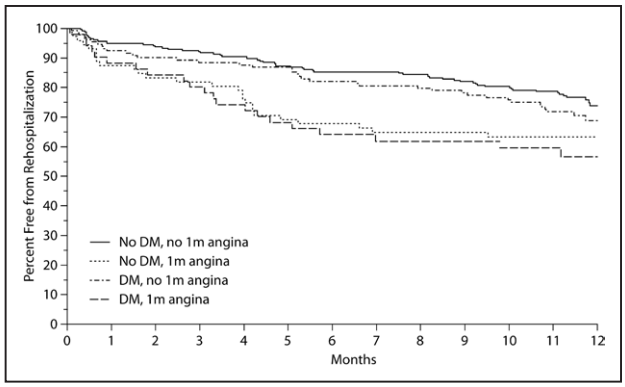

Figure 3. Kaplan–Meier curve depicting rehospitalization after percutaneous coronary intervention (PCI) in patients with and without diabetes mellitus (DM) stratified by the presence or absence of residual angina at 1 mo following index PCI.

become newly diagnosed with DM.[28] Another consideration is that HF was more common in patients with DM, and some antianginal medications are not recommended in heart failure with reduced ejection fraction (eg, verapamil, diltiazem, propranolol, and nebivolol). As such, there is a possibility that differences in antianginal medications may have been influenced by the differing rates of HF between groups. However, all 4 classes of antianginal medications have options that are safe and effective even in heart failure with reduced ejection fraction, and so it is unlikely that this was a major contributor to the observed differences in use in antianginal medications between groups. Finally, although we adjusted for many demographic and clinical characteristics, as an observational analysis, residual confounding is possible

Conclusions

Among patients undergoing PCI for stable CAD, patients with DM report a burden of angina that is at least as high as those without DM—both before and up to 1 year after PCI—despite more aggressive antianginal prescription. These findings lend support to recent studies demonstrating that patients with DM have a high burden of symptomatic chest pain as opposed to only silent ischemia. Continued efforts to reduce the burden of angina in patients with DM, including novel interventional and surgical techniques and antianginal medications, are needed.

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References

1. Lüscher TF, Creager MA, Beckman JA, Cosentino F. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part II. *Circulation*. 2003;108:1655–1661. doi: 10.1161/01.CIR.0000089189.70578.E2.
2. Tousek P, Pavei A, Oreglia J, Martin G, Sharif F, Fajadet J, Farah B. Impact of atherosclerotic disease progression on mid-term clinical outcome in diabetic patients in the drug-eluting stent era. *EuroIntervention*. 2009;4:588–592.
3. Tu JV, Bowen J, Chiu M, Ko DT, Austin PC, He Y, Hopkins R, Tarride JE, Blackhouse G, Lazzam C, Cohen EA, Goeree R. Effectiveness and safety of drug-eluting stents in Ontario. *N Engl J Med*. 2007;357:1393–1402. doi: 10.1056/NEJMoa071076.
4. Rutter MK, McComb JM, Brady S, Marshall SM. Silent myocardial ischemia and microalbuminuria in asymptomatic subjects with non-insulin-dependent diabetes mellitus. *Am J Cardiol*. 1999;83:27–31.
5. Chiariello M, Indolfi C. Silent myocardial ischemia in patients with diabetes mellitus. *Circulation*. 1996;93:2089–2091.
6. Zarich S, Waxman S, Freeman RT, Mittleman M, Hegarty P, Nesto RW. Effect of autonomic nervous system dysfunction on the circadian pattern of myocardial ischemia in diabetes mellitus. *J Am Coll Cardiol*. 1994;24:956–962.
7. Arnold SV, Spertus JA, Lipska KJ, Tang F, Goyal A, McGuire DK, Cresci S, Maddox TM, Kosiborod M. Association between diabetes mellitus and angina after acute myocardial infarction: analysis of the TRIUMPH prospective cohort study. *Eur J Prev Cardiol*. 2015;22:779–787. doi: 10.1177/2047487314533622.
8. Pocock SJ, Henderson RA, Clayton T, Lyman GH, Chamberlain DA. Quality of life after coronary angioplasty or continued medical treatment for angina: three-year follow-up in the RITA-2 trial. Randomized Intervention Treatment of Angina. *J Am Coll Cardiol*. 2000;35:907–914.
9. Khawaja FJ, Shah ND, Lennon RJ, Slusser JP, Alkatib AA, Rihal CS, Gersh BJ, Montori VM, Holmes DR, Bell MR, Curtis JP, Krumholz HM, Ting HH. Factors associated with 30-day readmission rates after percutaneous coronary intervention. *Arch Intern Med*. 2012;172:112–117. doi: 10.1001/archinternmed.2011.569.
10. Kureshi F, Jones PG, Buchanan DM, Abdallah MS, Spertus JA. Variation in patients' perceptions of elective percutaneous coronary intervention in stable coronary artery disease: cross sectional study. *BMJ*. 2014;349:g5309.
11. Spertus JA, Decker C, Gialde E, Jones PG, McNulty EJ, Bach R, Chhatriwalla AK. Precision medicine to improve use of bleeding avoidance strategies and reduce bleeding in patients undergoing percutaneous coronary intervention: prospective cohort study before and after implementation of personalized bleeding risks. *BMJ*. 2015;350:h1302.
12. Spertus JA, Bach R, Bethea C, Chhatriwalla A, Curtis JP, Gialde E, Guerrero M, Gosch K, Jones PG, Kugelmass A, Leonard BM, McNulty EJ, Shelton M, Ting HH, Decker C. Improving the process of informed consent for percutaneous coronary intervention: patient outcomes from the Patient Risk Information Services Manager (ePRISM) study. *Am Heart J*. 2015;169:234–241.e1. doi: 10.1016/j.ahj.2014.11.008.
13. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonell M, Fihn SD. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. *J Am Coll Cardiol*. 1995;25:333–341.

14. Arnold SV, Kosiborod M, Li Y, Jones PG, Yue P, Belardinelli L, Spertus JA. Comparison of the Seattle Angina Questionnaire with daily angina diary in the TERISA Clinical Trial. *Circ Cardiovasc Qual Outcomes*. 2014;7:844–850. doi: 10.1161/CIRCOUTCOMES.113.000752.
15. Spertus JA, Salisbury AC, Jones PG, Conaway DG, Thompson RC. Predictors of quality-of-life benefit after percutaneous coronary intervention. *Circulation*. 2004;110:3789–3794. doi: 10.1161/01.CIR.0000150392.70749.C7.
16. Greenland S. Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. *Am J Epidemiol*. 2004;160:301–305. doi: 10.1093/aje/kwh221.
17. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159:702–706.
18. Marchant B, Umachandran V, Stevenson R, Kopelman PG, Timmis AD. Silent myocardial ischemia: role of subclinical neuropathy in patients with and without diabetes. *J Am Coll Cardiol*. 1993;22:1433–1437.
19. Sukhija R, Dhanwal D, Gambhir DS, Dewan R. Silent myocardial ischaemia in patients with type II diabetes mellitus and its relation with autonomic dysfunction. *Indian Heart J*. 2000;52:540–546.
20. Wackers FJ, Young LH, Inzucchi SE, Chyun DA, Davey JA, Barrett EJ, Taillefer R, Wittlin SD, Heller GV, Filipchuk N, Engel S, Ratner RE, Iskandrian AE; Detection of Ischemia in Asymptomatic Diabetics Investigators. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. *Diabetes Care*. 2004;27:1954–1961.
21. Caracciolo EA, Chaitman BR, Forman SA, Stone PH, Bourassa MG, Sopko G, Geller NL, Conti CR. Diabetics with coronary disease have a prevalence of asymptomatic ischemia during exercise treadmill testing and ambulatory ischemia monitoring similar to that of nondiabetic patients. An ACIP database study. ACIP Investigators. Asymptomatic Cardiac Ischemia Pilot Investigators. *Circulation*. 1996;93:2097–2105.
22. Arnold S, Spertus J, Lipska K, Tang F, Goyal A, McGuire D, Cresci S, Maddox T, Kosiborod M. Association of diabetes mellitus with post-myocardial infarction angina: analysis of the TRIUMPH prospective cohort study. *J Am Coll Cardiol*. 2013;61:10.
23. Peterson PN, Spertus JA, Magid DJ, Masoudi FA, Reid K, Hamman RF, Rumsfeld JS. The impact of diabetes on one-year health status outcomes following acute coronary syndromes. *BMC Cardiovasc Disord*. 2006;6:41. doi: 10.1186/1471-2261-6-41.
24. Morrow DA, Scirica BM, Chaitman BR, McGuire DK, Murphy SA, Karwatowska-Prokopczuk E, McCabe CH, Braunwald E; MERLIN-TIMI 36 Investigators. Evaluation of the glycometabolic effects of ranolazine in patients with and without diabetes mellitus in the MERLIN-TIMI 36 randomized controlled trial. *Circulation*. 2009;119:2032–2039. doi: 10.1161/CIRCULATIONAHA.107.763912.
25. Kosiborod M, Arnold SV, Spertus JA, McGuire DK, Li Y, Yue P, Ben-Yehuda O, Katz A, Jones PG, Olmsted A, Belardinelli L, Chaitman BR. Evaluation of ranolazine in patients with type 2 diabetes mellitus and chronic stable angina: results from the TERISA randomized clinical trial (Type 2 Diabetes Evaluation of Ranolazine in Subjects With Chronic Stable Angina). *J Am Coll Cardiol*. 2013;61:2038–2045. doi: 10.1016/j.jacc.2013.02.011.
26. Brorsson B, Bernstein SJ, Brook RH, Werkö L. Quality of life of patients with chronic stable angina before and four years after coronary revascularisation compared with a normal population. *Heart*. 2002;87:140–145.
27. Arnold SV, Morrow DA, Lei Y, Cohen DJ, Mahoney EM, Braunwald E, Chan PS. Economic impact of angina after an acute coronary syndrome: insights from the MERLIN-TIMI 36 trial. *Circ Cardiovasc Qual Outcomes*. 2009;2:344–353. doi: 10.1161/CIRCOUTCOMES.108.829523.
28. Arnold SV, Stolker JM, Lipska KJ, Jones PG, Spertus JA, McGuire DK, Inzucchi SE, Goyal A, Maddox TM, Lind M, Gumber D, Shore S, Kosiborod M. Recognition of incident diabetes mellitus during an acute myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2015;8:260–267. doi: 10.1161/CIRCOUTCOMES.114.001452.

Residual Angina After Elective Percutaneous Coronary Intervention in Patients With Diabetes Mellitus

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Supplemental Table 1. Characteristics of patients with missing data compared with the from analytic cohort

	Missing data n=42	Analytic cohort n=1080	p-value
Age (years)	60.2 ± 14.1	65.1 ± 10.4	0.003
Male sex	76.2%	74.7%	0.830
White race	85.4%	93.8%	0.045
High school education	90.0%	92.6%	0.536
Insurance for medications	95.0%	95.5%	0.704
Avoid care due to cost	20.0%	8.6%	0.021
Body mass index (kg/m^2)	31.4 ± 6.7	30.6 ± 6.1	0.390
Prior MI	33.3%	23.2%	0.131
Prior PCI	52.4%	41.8%	0.171
Peripheral artery disease	14.3%	8.7%	0.261
Chronic lung disease	11.9%	9.4%	0.587
Depression	14.3%	6.9%	0.114
Current Smoker	40.5%	10.4%	<0.001
Multivessel disease	47.6%	39.4%	0.285
Highest CCS class in past 2 weeks			0.623
(0) No symptoms	28.6%	32.0%	
(1) I	14.3%	9.3%	
(2) II	25.0%	31.5%	
(3) III	14.3%	16.0%	
(4) IV	17.9%	11.2%	
# of antianginals medications			0.355
0	12.2%	14.6%	
1	53.7%	56.9%	
2+	34.1%	28.6%	