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PRE-INFARCT HEALTH STATUS AND THE USE OF EARLY INVASIVE VERSUS ISCHEMIA-GUIDED MANAGEMENT IN NON-ST-ELEVATION ACUTE CORONARY SYNDROME

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Abstract

Early invasive management improves outcomes in non-ST-elevation myocardial infarction (NSTEMI). The association between pre-infarct health status and the selecting patients for early invasive management is unknown. PREMIER and TRIUMPH are consecutive U.S. multi-center registries, in which the associations between pre-infarct angina frequency and quality of life (both assessed by the Seattle Angina Questionnaire on admission) and the GRACE risk score and referral to early invasive management (coronary angiography within 48 hours) were evaluated using Poisson regression, after adjusting for site, demographics, and clinical and psychosocial variables. Of 3,768 NSTEMI patients, 2182 (57.9%) patients were referred for early invasive treatment. Patients with excellent, good, or very good baseline angina-specific quality of life, respectively, were more likely to receive early angiography, even after adjustment, as compared with patients reporting poor baseline quality of life due to angina (62.1.0%, 60.9%, 59.6%, vs. 51.2%; adjusted RR=1.09, 95% CI: 1.04–1.16; RR=1.13, 95% CI: 1.01–1.27; RR 1.14, 95% CI: 0.99–1.31, respectively). Finally, patients with a GRACE score in the highest risk decile (199.5–<321.4) had significantly lower rates of early invasive treatment (42.7%) as compared with patients with patients in the lowest decile of risk (67.6%; adjusted RR for continuous GRACE score per SD [1 SD=40 points], 0.96, 95% CI: 0.92–0.99, P.019). In conclusion, this real-world NSTEMI cohort, patients with the highest mortality risk and worst health status were less likely to be referred for early invasive management. Further work is needed to understand the role of pre-infarct health status and in-hospital treatment strategy.

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Keywords

Non-ST elevation myocardial infarction; pre-infarct angina; pre-infarct quality of life; GRACE risk score; early invasive management; ischemia-guided management

INTRODUCTION

Despite evidence that patients with non-ST elevation myocardial infarction (NSTEMI) with the greatest mortality risk benefit most from an invasive strategy,¹ many studies have documented that higher-risk patients are less often managed invasively.^{2–5} Given that patients' with significant angina prior to a NSTEMI also have more angina afterwards,⁶ it would be clinically logical to pursue a more aggressive treatment strategy in those with worse pre-infarct angina and angina-related quality of life. In fact, pre-infarct angina, i.e. angina episodes preceding the onset of acute myocardial infarction (AMI), occurs in almost half of patients presenting with NSTEMI^{7,8} and a prior study have suggested that it is associated with higher rates of significant coronary artery disease (CAD).⁸ Moreover, recent data suggest that an invasive strategy for NSTEMI was associated with significantly better 30-day health status among patients with pre-infarct angina (PIA).⁹ However, no data currently exist to describe the patterns of selecting patients for an invasive treatment strategy in the setting of NSTEMI as a function of their pre-infarct health status. To address this gap in knowledge, we leveraged 2 sequential, prospective, multi-center, post-acute myocardial infarction registries in the U.S. to examine the association of pre-infarct angina, quality of life and mortality risk with treatment strategy for patient presenting with NSTEMI.

METHODS

We leveraged 2 consecutive, multi-center, prospective acute myocardial infarction (AMI) registries in the U.S. – PREMIER and TRIUMPH – that consecutively enrolled patients between 2003 and 2008 from 32 academic and non-academic centers (Figure 1 and Appendix I for List of Sites). The design of both studies has been previously described.^{10,11} In both registries, patients were enrolled if they were aged 18 years or older, had biomarker evidence of myocardial injury, and presented with supporting evidence of an AMI, including prolonged ischemic symptoms or electrocardiographic ST changes. Patients that were incarcerated, who refused participation, were unable to provide informed consent, did not speak English or Spanish, and those that expired during hospitalization before they could consent to participate in the study were excluded. All participants provided written informed consent and the study protocols were approved by the institutional review board at each enrolling center.

A total of 3853 NSTEMI patients (1409 from PREMIER, 2444 from TRIUMPH) were identified; patients who died in hospital were excluded (Figure 1), leaving a final study cohort of 3819 patients.

In both the PREMIER and TRIUMPH studies, patients' medical history, clinical characteristics of their index AMI admission, in-hospital treatment, laboratory results, use and timing of catheterization, and discharge diagnoses were collected through chart

abstraction by trained study coordinators. Patient-centered information (demographics, tobacco use, socio-economic factors, health status, and psychosocial factors) was obtained through standardized in-depth interviews performed by trained research staff within 24–72 hours of admission. Patient data included demographics (age, sex, race [black race, other race, vs. white race]), socio-economic factors (marital status [married vs. not], education [completed high school education or higher vs. not], employment status [working part- or full-time vs. not], health insurance information [insurance vs. no insurance], avoidance of care due to cost),¹² medical history (hypercholesterolemia, hypertension, peripheral arterial disease, diabetes mellitus, prior AMI, PCI, coronary artery bypass grafting [CABG], stroke, chronic kidney disease, chronic lung disease, chronic heart failure, current smoking, body mass index [BMI, defined as weight in kilogram/squared height in meter], cancer, family history of coronary artery disease [CAD]), and clinical characteristics of AMI admission (left ventricular function [mild, moderate, severe left ventricular dysfunction vs. normal left ventricular function], Killip class, acute heart rate [beats per minute], acute systolic and diastolic blood pressure [mmHg], initial hematocrit [%], platelet count [$\times 10^3/\mu\text{L}$], creatinine [mg/dL], maximum troponin [$\mu\text{g/L}$], the presence of an ST segment depression as obtained from the initial electrocardiogram). Additionally, information on whether the patient was transferred to the enrolling facility or not, the presence of a cardiac arrest within the past 6 hours of admission or other concomitant acute non-cardiac conditions warranting admission (i.e. gastrointestinal bleeding or pneumonia),¹³ and whether the patient presented at the hospital during a weeknight or weekend as opposed to a weekday (off-hours presentation) were collected.

The primary outcome was whether or not patients were referred to an early invasive management strategy. This was defined as referral for coronary angiography followed by revascularization, if possible, within 48 hours following index AMI admission without having had a prior stress test. The reference group of ischemia-guided strategy (conservatively managed) was defined by those patients were initially treated with pharmacological therapy and angiography/revascularization was used only for those with recurrent symptoms or evidence of inducible ischemia on noninvasive testing (>48 hours following admission). If patients had a non-invasive stress test prior to their angiogram, even if catheterization was performed within 48 hours, patients were also categorized as ischemia-guided strategy. The treating physician made decisions regarding the referral for invasive management or not.

On admission to the hospital, patients' disease-specific health status (angina frequency and quality of life) was assessed with the Seattle Angina Questionnaire (SAQ).^{14–18} The SAQ angina frequency and quality of life scales range from 0 to 100, where higher scores represent a better health status (i.e., less angina or better quality of life). Consistent with prior work¹⁹, patients' angina frequency scores were classified into the following 4 clinical categories: daily (scores of 0–30), weekly (scores 31–60), monthly (scores 61–99) and no angina (score of 100). The scores on the SAQ quality of life domain were categorized into poor (scores 0–<50), good (scores 50–<75), very good (scores 75–99), and excellent (score of 100) quality of life.

Patients were stratified according to their 6-month mortality risk using the Global Registry of Acute Coronary Events (GRACE) risk model.²⁰ This model generates a highly discriminative cumulative risk score from patients' admission until 6 months after discharge based on patients' age, heart rate, systolic blood pressure, initial serum creatinine, Killip class, cardiac arrest on presentation, initial positive cardiac enzymes, and ST segment deviation.²⁰ For descriptive purposes only, patients' risk scores were divided into deciles, with lower scores representing lower risk. To facilitate the interpretation of the risk estimates in our main analyses, GRACE scores were standardized by dividing their scores by 1 standard deviation (40 points) of the observed distribution.

To adjust for relevant confounders in our models, both registries collected information on patients' depressive symptoms, and social support. The 9-item Patient Health Questionnaire was administered to assess patients' depressive symptoms over the prior 2 weeks. The instrument incorporates the 9 criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition and quantifies each symptom on a 4-item Likert scales to obtain a sum score between 0 and 27. Patients' depressive symptoms were classified as moderate to severe (scores of 10–27), mild (scores of 5–9), and no/minimal (scores of 0–4) depressive symptoms. Perceived levels of social support were quantified by the 7-item Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Social Support Inventory.²¹ Consistent with prior work, patients were considered to have low social support when they had scores equal or greater than 3 on 2 or more items (excluding items on instrumental social support and marital status) and a sum score of 18 or greater on the remaining 5 items.

Patient characteristics were compared by the management strategy received (invasive vs. conservative) using Student t tests and the Wilcoxon rank sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables. Referral rates for invasive management were compared according to the magnitude of patients' symptom burden in the 4 weeks preceding their AMI including their angina frequency (daily angina [scores 0–30], weekly [scores 31–60], monthly [scores 61–99], or no angina [score of 100]) and quality of life (poor [scores 0–<50], good [scores 50–<75], very good [scores 75–100], and excellent [score of 100]) using analyses of variance. The GRACE risk score was used to compare patients' risks for 6-month mortality.

A set of hierarchical modified Poisson regression models were constructed to evaluate the association between the angina frequency (daily angina was defined as the reference category), quality of life (poor quality of life was defined as reference category), and the continuous standardized GRACE risk scores [model 1], sequentially adjusting for demographics (sex, race) and socio-economic factors (marital status, education, work status, insurance status, avoidance of care due to cost) [model 2], medical history (diabetes mellitus, prior AMI, PCI, stroke, chronic lung disease, BMI), clinical characteristics of the AMI admission (left ventricular systolic function, initial hematocrit values, presented at enrolling facility, off hours presentation, and presence of other acute non-cardiac conditions at presentation) [model 3], and psychosocial factors (depressive symptoms, social support) [model 4].

Model covariates for PREMIER were missing for at least 1 study covariate in 22.4% of patients and the average missing number of missing data fields per patient was 0.5. At least 1 study covariate was missing in 22.6% of patients for TRIUMPH with the average number of missing data fields per patient not exceeding 0.4. Missing covariate data were imputed using IVEware software version 2.0 (University of Michigan Survey Research Center, Institute for Social Research, Ann Arbor). Patients who had missing information on use and/or timing of initial management strategy (n=58) during follow-up did not differ on their SAQ angina frequency (P=0.11) or quality of life scores (P=0.85), nor their GRACE risk scores (P=0.18). A set of sensitivity analyses was performed wherein we changed the definition of invasive management from undergoing catheterization within the hospital admission to invasive management within 48 and 72 hours following index AMI admission.

All statistical analyses were conducted with SAS software version 9.2 (SAS Institute Inc, Cary, North Carolina), IVEware, and R software version 2.6.0 (Free Software Foundation, Boston, Massachusetts). All statistical tests were 2-tailed and P-values <.05 were considered as statistically significant. Drs. Smolderen and Spertus had full access to the data and take full responsibility for the integrity of the data and the accuracy of the analysis. Mrs. Gosch performed the statistical analysis.

RESULTS

A comparison of patient characteristics by the receipt of early invasive management is presented in Table 1. A total of 2182 (57.9%) NSTEMIs were referred for an invasive management strategy within 48 hours. As compared with those in whom an ischemia-guided strategy was adopted, patients managed invasively were more likely to be younger, male, and white. They were also more likely to be married, to have completed high school, and to have been working at the time of their AMI. Patients referred for an early invasive management strategy were less likely to have a history of prior cardiovascular disease (peripheral arterial disease, prior AMI, PCI, CABG, stroke) and were less likely to have comorbidities, including hypertension, diabetes, chronic kidney disease, and chronic lung disease. In addition, they were more likely to present with less severe disease (e.g. more likely to present with a normal left ventricular systolic function and a lower Killip class), were more likely to be transferred, were less likely to have other acute non-cardiac conditions upon arrival, and to report clinically significant depressive symptoms.

Unadjusted proportions of patients undergoing an early invasive management strategy during their index NSTEMI admission by indices of their disease burden – their angina frequency, quality of life, and mortality risk – are depicted in Figure 2. There was an inverse relationship between the frequency of patients' pre-procedural angina and the early invasive strategy, implying that patients with more frequent and severe angina prior to their AMI were less likely to undergo an early invasive strategy. For example, only 48.5% of patients who reported daily angina underwent an early invasive strategy, as compared with 59.3% of those without angina prior to their event (P<0.0001). Likewise, when looking at patients' quality of life, a similar inverse relationship was observed: patients presenting with an excellent quality of life had the highest proportion of early invasive management rates,

whereas those with the worst quality of life had the lowest rates (62.1% vs. 51.9%; $P<0.0001$). These associations were paralleled by patients' GRACE mortality risk: low-risk patients had the highest rates and the highest risk patients had the lowest (67.6% vs. 42.7%; $P<0.0001$).

When including angina frequency, quality of life, and the GRACE risk score in the modified Poisson regression that was only adjusted for site, both angina-specific quality of life (e.g., RR for poor vs. excellent quality of life =1.21, 95% CI [1.04–1.40]) and lower GRACE risk score (RR per SD increase =0.96, 95% CI [0.92–0.99]) were independently associated with an early invasive strategy (Model 1; Table 2). These associations persisted following sequential adjustment for demographics and socio-economic factors (Model 2), medical history and clinical characteristics of the AMI admission (Model 3) [except for poor vs excellent quality of life, $p=0.074$], and psychosocial factors (Model 4) [except for poor vs excellent quality of life, $p=0.06$]. Angina frequency was not independently associated with the receipt of an early invasive strategy (P -values $>.05$ for all models). The final model results with an overview of risk estimates associated with the main variables of interest as well as covariates' risk estimates are presented in Figure 3. Similar associations were observed when the definition of early invasive management was relaxed from 48 hours of admission to 72 hours of admission (Results available from the authors).

DISCUSSION

In the era of value-based medicine, understanding factors associated with invasive treatment referral in NSTEMI patients is essential to improve patients' selection and outcomes. We report an inverse association between mortality risk (as determined by GRACE score) and referral for invasive treatment. Moreover, the novel finding of our study is the inverse association between pre-infarct angina and angina-related quality of life and referral for invasive treatment, the latter of which persisted after extensive adjustment for demographics, socio-economic factors, patients' medical history, clinical characteristics of the AMI admission, and psychosocial status.

Our findings of an inverse association between mortality risk and invasive treatment are congruent with prior work. For example, a study by Yan and colleagues documented the Canadian experience before and after the updated 2007 ACC/AHA guidelines on management of NSTEMI patients and found that while there was a trend for increasing use of invasive treatments with publication of these guidelines, the disparity in treating the sickest less often worsened.² The current study not only confirms the Canadian experience in the US, but also demonstrates the persistence of this treatment pattern after adjusting for multiple clinical and patient factors that might confound these observations. For example, we found these patterns to exist even after accounting for other conditions that could be present on admission that might warrant a delay in treatment (i.e. adjusting for other life-threatening conditions being present at the time of admission) or the potential pre-existing knowledge of patients' coronary anatomy (i.e. adjusting for prior MI, PCI and CABG).

Importantly, we expand these observations to show a similar pattern with respect to patients pre-infarct angina and worse angina-related QoL prior to admission. However, it is less clear

if this inverse association represents a risk-treatment paradox like the one found with mortality risk. Prior literature suggests that NSTEMI patients with higher angina burden are more likely to have recurrent angina at follow up and it might seem clinically logical to offer invasive treatment for those with the highest potential of recurrent angina. Moreover, data suggest that an invasive strategy for NSTEMI was associated with significantly better 30-day health status among patients with pre-infarct angina (PIA).⁹ However, only limited data exist to support long-term health status benefits from an invasive strategy in those with worse baseline health status, underscoring the need for future research in this area to better guide patient selection.

The explanations for our findings are not entirely clear. Previous work found that the under-prescription of statins in high-risk coronary artery disease patients was attributed to patients' factors such as patients' depressive symptoms and low functional status.^{22,23} It is certainly possible that those with the worst health status prior to their AMI might have worse comorbidities and peri-procedural risks that preclude an invasive strategy, but even after adjusting for many such factors we found that those with the worst angina-related quality of life prior to their AMI were still less likely to be treated invasively.

Our findings should be interpreted in the context of the following potential limitations. First, it is possible that we were not able to document important contra-indications to an invasive strategy or unmeasured confounders (e.g., frailty) that both prevented clinicians from offering an invasive approach and were associated with patients' baseline health status. Although such confounding is impossible to exclude in observational studies, we were able to control for many clinical and non-clinical patient characteristics in our multivariable models. Second, we used the baseline SAQ scores to document patients' baseline angina and quality of life. Although the SAQ has a 4-week recall period, it is not possible to know whether patients preferentially weighted their experiences immediately prior to, or during, their NSTEMI. Even if this occurred, however, it would remain potentially counter-intuitive to preferentially treat asymptomatic and patients reporting excellent quality of life more aggressively than those reporting more severe impairments. Third, TRIUMPH and PREMIER registries were conducted many years ago (2004–2008). Although revascularization patterns might have changed in response to new data after 2008, the 2002 and the 2007 NSTEMI management guidelines were greatly similar in selecting patients for invasive management. The only appreciable difference was the timing of the invasive management (72 vs 48 hours) and our sensitivity analyses showed no difference in results when taking the timing into consideration.

In conclusion, we found that an invasive strategy for NSTEMI management was preferentially offered to patients with the lowest mortality risk and to patients with less pre-infarct angina and better angina-related quality of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Flowchart of Study Population Consisting of NSTEMIs Enrolled From the Observational, Multi-Center, Prospective PREMIER and TRIUMPH Registries
Abbreviations: NSTEMI, non-ST-elevation myocardial infarction; PREMIER, Prospective Registry Evaluating outcomes after Myocardial Infarctions: Events and Recovery; STEMI, ST-elevation myocardial infarction; TRIUMPH, Translational Research Investigating Underlying disparities in acute Myocardial infarction Patients' Health status.

Figure 2. (a) SAQ Angina Frequency, (b) SAQ Quality of Life, (c) GRACE Risk Scores by the Proportion of Patients Receiving an Early Invasive Management Strategy During Index NSTEMI admission

Abbreviations: GRACE, Global Registry of Acute Coronary Events; NSTEMI, non-ST-elevation myocardial infarction; SAQ, Seattle angina questionnaire.

Figure 3. Multivariable Predictors (RR, 95% CI) for Undergoing Early Invasive Management During Index NSTEMI admission

Abbreviations: LV, left ventricular; PCI, percutaneous coronary interventions; CABG, coronary artery bypass grafting; MI, myocardial infarction; CVA, cerebrovascular accident; BMI, body mass index; PHQ, Patient Health Questionnaire; ESSI, Enrichd Social Support Inventory; SAQ, Seattle Angina Questionnaire; GRACE, Global Registry of Acute Coronary Events.; SD, standard deviation. Error bars indicate 95% CI

Table 1

Baseline Characteristics by Referral For Early Invasive Management.

	Invasive Management 48 Hours		P Value
	Yes (n=2182, 57.9%)	No (n=1586, 42.1%)	
Variables:			
Age, mean (SD), (years)	60.1 ± 12.3	62.3 ± 13.4	<.001
Men	1453 (66.6%)	932 (58.8%)	<.001
White	1548 (71.2%)	835 (52.8%)	<.001
Black	493 (22.7%)	661 (41.8%)	
Other	134 (6.2%)	85 (5.4%)	
Married	1204 (55.5%)	687 (43.9%)	<.001
High school education or higher	1710 (79.0%)	1113 (71.6%)	<.001
Working full or part time	1041 (48.1%)	412 (26.4%)	<.001
No medical insurance	378 (17.8%)	299 (19.4%)	.23
Avoid care due to cost	481 (22.5%)	362 (23.4%)	.52
Hypercholesterolemia	1146 (52.5%)	815 (51.4%)	.49
Hypertension	1495 (68.5%)	1237 (78.0%)	<.001
Peripheral arterial disease	141 (6.5%)	145 (9.1%)	<.001
Diabetes mellitus	663 (30.4%)	685 (43.2%)	<.001
Prior myocardial infarction	494 (22.6%)	502 (31.7%)	<.001
Prior percutaneous coronary intervention	484 (22.2%)	359 (22.6%)	.74
Prior coronary bypass graft surgery	302 (13.2%)	321 (20.2%)	<.001
Prior stroke	115 (5.3%)	138 (8.7%)	<.001
Chronic lung disease	178 (8.2%)	264 (16.6%)	<.001
Chronic heart failure	181 (8.3%)	379 (23.9%)	<.001
Smoked within last 30 days	732 (33.8%)	479 (30.5%)	.04
Body mass index (kg/m ²)	29.7 ± 6.7	29.4 ± 7.1	.21
Cancer (other than skin)	173 (7.9%)	152 (9.6%)	.07
Family history of coronary artery disease	1352 (62.4%)	819 (51.9%)	< 0.001
Left ventricular systolic function			<.001
Normal left ventricular systolic function	1439 (66.0%)	933 (59.0%)	
Mild left ventricular systolic dysfunction	373 (17.1%)	254 (16.1%)	
Moderate left ventricular systolic dysfunction	218 (10.0%)	179 (11.3%)	
Severe left ventricular systolic dysfunction	149 (6.8%)	216 (13.7%)	
Killip class			
I	1949 (90.0%)	1223 (77.6%)	<.001
II	174 (8.0%)	277 (17.6%)	
III	29 (1.3%)	61 (3.9%)	
IV	13 (0.6%)	16 (1.0%)	
Acute heart rate, mean (SD), (beats per minute)	82.3 ± 22.0	87.6 ± 23.3	<.001
Acute systolic blood pressure, mean (SD), (mmHg)	144.8 ± 29.7	144.4 ± 32.6	.67

	Invasive Management 48 Hours		P Value
	Yes (n=2182, 57.9%)	No (n=1586, 42.1%)	
Acute diastolic blood pressure, mean (SD), (mmHg)	82.4 ± 18.0	80.3 ± 20.6	<.001
Initial hematocrit, mean (SD), (%)	41.0 ± 5.4	38.3 ± 6.6	<.001
Initial creatinine, mean (SD), (mg/dL)	1.2 ± 1.1	1.8 ± 2.0	<.001
Glomerular filtration rate, (mL/min per 1.73 m ²)	77.0 ± 27.9	64.5 ± 33.2	< 0.001
Maximum troponin, mean (SD), (µg/L)	19.7 ± 68.6	12.9 ± 61.5	.002
GRACE mortality risk score			
Mean ± SD	141.5 ± 38.6	152.8 ± 42.2	
Median (IQR)	138.3 (114.5, 164.7)	149.5 (121.0, 179.9)	< 0.001
Initial electrocardiogram			
ST Segment depression	635 (29.9%)	424 (27.7%)	.14
Transferred from other hospital	82 (3.7%)	218 (14.0%)	<.001
Cardiac arrest within past 6 hours	25 (1.2%)	20 (1.3%)	.74
Off-hours presentation	1355 (64.4%)	999 (65.3%)	.55
Other acute non-cardiac condition	49 (2.3%)	130 (8.3%)	<.001
Psychosocial factors			
PHQ Depressive symptoms			.007
Not clinically depressed	1130 (55.2%)	747 (49.8%)	
Mild	500 (24.4%)	409 (27.3%)	
Moderate	418 (20.4%)	343 (22.9%)	
Moderate to severe	418 (20.4%)	343 (22.9%)	
Low social support	121 (16.6%)	123 (20.4%)	.08

Table 2
Association Between Angina Frequency, Quality of Life, GRACE Risk Scores and Receiving an Early Invasive Management Strategy

The effect of sequential adjustments for demographic, socio-economic, medical history, clinical characteristics, and psycho-social factors on the relationship between patients' angina frequency, quality of life, and GRACE mortality risk scores with the receipt of early invasive treatment is depicted.

Adjusted for	Model 1		Model 2		Model 3		Model 4	
	Adjusted Only for Site		Model 1 + Demographics, Socio-Economic Factors		Model 2 + Medical History, and Clinical Characteristics of AMI Admission		Model 3 + Psychosocial Factors	
	RR (95% CI)	P Value	RR (95% CI)	P Value	RR (95% CI)	P Value	RR (95% CI)	P Value
Angina Frequency								
Daily	[reference]		[reference]		[reference]		[reference]	
Weekly	1.12 (0.95–1.32)	.19	1.11 (0.94–1.32)	.23	1.07 (0.90–1.26)	.44	1.07 (0.91–1.26)	.42
Monthly	1.13 (0.93–1.37)	.20	1.11 (0.91–1.35)	.32	1.04 (0.86–1.27)	.66	1.04 (0.86–1.26)	.66
None	1.11 (0.92–1.36)	.27	1.10 (0.89–1.36)	.37	1.02 (0.84–1.25)	.82	1.02 (0.84–1.24)	.84
SAQ Quality of Life								
Poor	[reference]		[reference]		[reference]		[reference]	
Good	1.13 (1.07–1.20)	<.0001	1.12 (1.05–1.19)	.0002	1.10 (1.04–1.16)	.0013	1.09 (1.04–1.16)	.001
Very Good	1.18 (1.04–1.33)	.008	1.17 (1.03–1.31)	.011	1.13 (1.01–1.26)	.029	1.13 (1.01–1.27)	.032
Excellent	1.21 (1.04–1.40)	.01	1.19 (1.03–1.38)	.021	1.14 (0.98–1.32)	.074	1.14 (0.99–1.31)	.06
GRACE Risk Score (per SD change)	0.87 (0.84–0.91)	<.0001	0.91 (0.87–0.94)	<.0001	0.96 (0.92–0.99)	.027	0.96 (0.92–0.99)	.019