Positive and Negative Affect Is Related to Experiencing Chest Pain During Exercise-Induced Myocardial Ischemia

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ABSTRACT

Objective: Silent myocardial ischemia is thought to be associated with worse cardiovascular outcomes due to a lack of perception of pain cues that initiate treatment seeking. Negative affect (NA) has been associated with increased pain reporting and positive affect (PA) with decreased pain reporting, but these psychological factors have not been examined within the context of myocardial ischemia. This study evaluated the associations between PA, NA, and chest pain reporting in patients with and without ischemia during exercise testing.
Methods: A total of 246 patients referred for myocardial perfusion single-photon emission computed tomography exercise stress testing completed the positive and negative affect schedule-expanded version, a measure of PA and NA. Presence of chest pain and myocardial ischemia were evaluated using standardized protocols.
Results: Logistic regression analyses revealed that for every 1-point increase in NA, there was a 13% higher chance for ischemic patients (odds ratio [OR] = 1.13; 95% confidence interval [CI] = 1.02 to 1.26) and an 11% higher chance in nonischemic patients (OR = 1.11; 95% CI = 1.03 to 1.19) to report chest pain. A significant interaction of PA and NA on chest pain reporting ($\beta = 0.02$; 95% CI = 0.002 to 0.031) was also observed; nonischemic patients with high NA and PA reported more chest pain (57%) versus patients with low NA and low PA (13%), with high NA and low PA (17%), and with high PA and low NA (7%).
Conclusions: Patients who experience higher NA are more likely to report experiencing chest pain. In patients without ischemia, high NA and PA was also associated with a higher likelihood of reporting chest pain. Results suggest that high levels of PA as well as NA may increase the experience and/or reporting of chest pain.
Key words: chest pain, coronary heart disease, positive affect, negative affect, silent ischemia.

INTRODUCTION

According to the World Health Organization, cardiovascular disease (CVD) is the number one cause of mortality worldwide (1). Of all forms of CVD, coronary artery disease (CAD) is responsible for most morbidity and mortality (2). The American Heart Association reported that 15.5 million persons in the United States have CHD, including 8.2 million with angina pectoris (2). Myocardial ischemia is a condition triggered by an imbalance between myocardial oxygen supply and demand (3,4) and is a key predictor of future CVD events and outcomes (5–7).

Importantly, myocardial ischemia may or may not be accompanied by chest pain (3,4). However, most ischemic episodes (i.e., 70%–75%) occur in the absence of chest pain, a condition known as "silent ischemia" (4,8–10). The occurrence and detection of chest pain during an ischemic episode may be critical for self-initiation of treatment (e.g., taking vasodilators) or timely presentation to the emergency department, both of which may reduce cardiac morbidity and mortality (11). Delays in treatments or presentation for assessment are likely the reasons why patients with silent ischemia are at increased risk for cardiac events and mortality (8,10). Accurate chest pain perception during episodes of ischemia may be even more critical for patients with previously undiagnosed CAD, because of lack of awareness of a pre-existing cardiac condition. The American Heart Association estimates that approximately two thirds of women and half of men who died suddenly of CAD had no CAD history (2). Therefore, determining factors associated with accurate chest pain perception in the context of ischemia represents an important clinical research goal. In addition to the links between CVD outcomes and ischemia, there is also a

CAD = coronary artery disease, **CI** = confidence interval, **CVD** = cardiovascular disease, **DBP** = diastolic blood pressure, **HR** = heart rate, **METs** = metabolic equivalents, **MHI** = Montreal Heart Institute, **MOSMI** = cross-sectional Mechanisms and Longitudinal Outcomes of Silent Myocardial Ischemia, **MPHR** = maximum predicted heart rate, **NA** = negative affect, **OR** = odds ratio, **PA** = positive affect, **PANAS-X** = Positive And Negative Affect Schedule-Expanded Version, **SBP** = systolic blood pressure, **SPECT** = single-photon emission computed tomography

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documented link between psychiatric disorders and CVD development and outcomes (12,13). Negative affect (NA; e.g., depressed mood and anxiety) is a strong predictor of future CVD events and outcomes (12,13) and has been linked to clinical markers of CVD such as exercise-induced ischemia (14,15) as well as poor pain perception (16,17).

Pain perception is a multidimensional experience involving physical pain sensitivity and accurate interpretation of pain sensations (18). Accurate pain perception may be influenced by NA and positive affect (PA). Collectively, the general affect-pain literature suggests that NA (e.g., anxiety, anger) may increase and PA (e.g., happiness, joy) may decrease pain perception or sensitivity (19). For example, patients exposed to high situational anxiety tend to report higher levels of pain intensity in response to the cold pressor test (20), with trait anger positively correlated with pain perception (21). Also, patients with higher levels of anger and frustration are more likely to experience cancer-related pain at greater intensity levels and for longer durations compared with patients with lower levels of anger and frustration (22). Previous studies have demonstrated that measures of NA, such as depression, are generally associated with greater pain symptom reporting in patients with and without CVD (16,17), as well as higher reported pain intensity in postsurgical patients (23). However, higher general NA has also been shown to predict the presence of exercise-induced angina (24). Anxiety, another measure of NA, has been linked to higher reports of chest pain among cardiac and noncardiac populations (25,26). In contrast, patients with silent ischemia (no chest pain) seem to have lower levels of depression and anxiety (27).

Little is known as to whether NA can influence the reporting and presence of chest pain when myocardial ischemia is also present nor whether NA can lead to increases in chest pain reporting when there is no other physiological symptom of disease such as myocardial ischemia. Untangling whether NA can lead to the reporting of chest pain, which may be "phantom pain" or psychosomatic in nature, is clinically important, because accurate pain perception may be critical for timely and potentially life-saving intervention (20,28–31).

Studies in chronic disease populations (e.g., rheumatoid arthritis, fibromyalgia, and sickle-cell disease), have shown that higher levels of PA are associated with reduced pain perception (29–31), lower pain intensity (29,30), and reduced perceptions of pain intensity (19,31). In the context of CVD, increased PA has been linked with a reduced risk of stroke, decreased hospital readmission after a cardiac events, and lower mortality in cardiac patients (32–34). However, there is minimal information on the role of PA on chest pain perception in the context of CVD.

In most CVD literature, studies have focused on either NA or PA and few have assessed both in the same study. This limitation is notable given that the dynamic model of affect suggests that in a chronic, stressful situation (e.g., chronic pain), a high level of NA could suppress the capacity of PA to compensate by becoming the only information that is processed by the brain (35). This model also suggests that under normal circumstances, PA and NA are processed by distinct neural process and they can be manipulated independently (35). Thus, examining the role of NA and PA concurrently is important, particularly in the context of detecting chest pain and ischemia, to examine whether NA or PA plays a buffering role on chest pain reporting and whether this could mask clinically important factors such as ischemia and chest pain.

Thus, the objective of the present study was to assess associations between PA and NA and chest pain perception among patients who presented for diagnostic exercise stress testing. We hypothesized that patients with higher levels of NA would be more likely to report experiencing chest pain during exercise compared with patients with lower levels of NA and that patients with higher levels of PA would be less likely to report chest pain during exercise compared with patients with lower levels of PA, particularly among patients in whom ischemia is not induced during exercise testing.

METHODS

Participants

This study was a substudy of the cross-sectional Mechanisms and Longitudinal Outcomes of Silent Myocardial Ischemia (MOSMI) study, a prospective study designed to examine the impact of blood pressure and pain on myocardial ischemia. Participants presenting to the Montreal Heart Institute (MHI) for single-photon emission computed tomography (SPECT) exercise stress testing were recruited between May 2005 and December 2006. Exclusion criteria were the following: (1) already participating in another study at the MHI; (2) pregnant or nursing; (3) taking nonsteroid anti-inflammatory drugs in 7 days before stress test; (4) taking an analgesic the day of the stress test; (5) having a major medical condition other than CAD (e.g., cancer, acquired immunodeficiency syndrome); (6) having any severe mental disorder (e.g., schizophrenia) or evidence of current substance abuse; (7) younger than 18 years; (8) unable to speak/understand English or French; or (9) having a pain disorder other than angina. Our definition of a pain disorder was based on the DSM-IV definition of pain disorder that included chronic pain in one or more areas thought to have psychogenic origin and related neurologic conditions (phantom pain, hyperalgesia, hypoalgesia) but did not include musculoskeletal pain or back/pelvic pain.

A total of 2138 participants presented to the Nuclear Medicine Department of the MHI for an exercise stress test prescribed by their doctor during the recruitment period, of which 1174 patients (55%) were approached to participate. Because of a lack of personnel, some patients were not approached if they presented simultaneously for their stress test. As shown in Figure 1, 124 patients were excluded, resulting in 1050 eligible participants. Only 143 participants declined to participate, yielding a final sample of 907 participants (86% participation rate). Late introduction of this substudy in the larger MOSMI study (after the 582th patient), missing data, and participant attrition, left a final participating sample of 246 participants for this substudy. There were no significant differences between this subgroup and the remaining MOSMI sample (i.e., the 661 individuals not included in this substudy) in demographic or clinical data (i.e., age, sex, presence of clinical pain, ischemia, silent ischemia, or previous cardiac diseases). The MHI scientific and ethics committees approved this study, and all patients provided written informed consent.

Procedure

Patients were informed of the study procedures, and a trained clinical research assistant obtained informed consent. Eligible and consenting patients underwent a standard treadmill exercise stress test (modified Bruce protocol). The stress test was followed by SPECT imaging under the supervision of a nuclear medicine physician according to standard procedure (36,37). Patients were maintained on their usual medication throughout the protocol. Participants were then asked to complete a sociodemographic and medical history questionnaire, followed by the self-report Positive and Negative Affect Schedule-Expanded Version (PANAS-X; 38).

Measures

PA and NA Schedule Expanded

PA and NA were evaluated using the PANAS-X, which measures state and trait constructs of PA and NA experienced in the last few weeks (38). The PANAS has 60 items, rated on a scale from 1 to 5 (1 = very slightly or not at all; 5 = extremely) to yield overall PA and NA scores as well as scores on subscales of negative (fear, sadness, guilt, hostility, shyness, fatigue) and positive (surprise, joviality, self-assurance, attentiveness, and serenity) affect. NA was calculated by summing the scores for the following constructs:

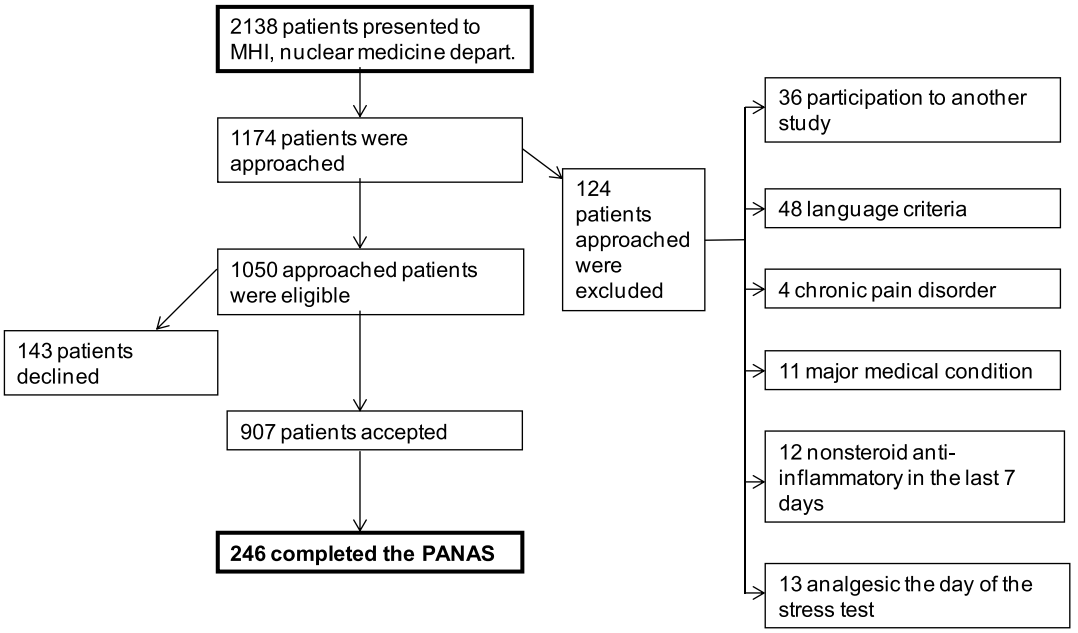

FIGURE 1. Recruitment of participants.

afraid, scared, nervous, jittery, guilty, ashamed, irritable, hostile, upset, and distressed. PA was calculated as the sum of the following constructs: active, alert, attentive, enthusiastic, excited, inspired, interested, proud, strong, and determined. This is in line with the PANAS-X scoring manual (38). Conceptually, the PA and NA scales are independent dimensions, such that patients can score anywhere along the continuum of each scale (i.e., patients can score high on both PA and NA; 38,39). The mean of each scale is calculated for each patient to determine overall PA and NA levels. Internal reliability ranges from 0.85 to 0.90 for the NA scale and from 0.83 to 0.90 for the PA scale (38). The PANAS-X subscales have demonstrated excellent psychometric properties, including excellent convergent validity (r = 0.85–0.91) with the profile of mood states and good and moderate correlations, respectively, for the PA and NA subscales of the global mood scale (PA = 0.79 and NA = 0.56; 38,40,41). Both PA and NA scales have good stability for 2 months (test-retest correlations of 0.71 and 0.70, respectively; 38). A standard forward-backward translation of the PANAS-X was performed to translate the PANAS-X into French. The internal reliability ranges were from 0.81 to 0.86 for the individual constructs of the NA scale and from 0.81 to 0.89 for the individual constructs of the PA scale for the whole sample; specifically, the internal reliability coefficients were 0.87 for PA and 0.81 for NA both English version and 0.87 for PA and 0.86 for NA for the translated French version of the PANAS-X.

Chest Pain Assessment

Chest pain perception during treadmill exercise stress testing was evaluated by a trained exercise stress test technician and overseen by a cardiologist, who asked patients to self-report the presence and intensity of any chest pain occurring during the test using a 10-point rating scale (42). Patients with a score of higher than 0 were considered to be experiencing chest pain. Ultimately, the cardiologist determined whether the pain was related to an underlying cardiac or noncardiac condition (e.g., back pain) according to standard procedure (43). Patients who had confirmed exercise-induced chest pain were classified as having angina-related chest pain; those without were classified as having no chest pain.

Ischemia Assessment

SPECT assessments of reversible myocardial perfusion defects at peak exercise were evaluated by experienced nuclear medicine physicians according to the standard procedure (36,37) using an Irix-3 model camera (Philips, Cleveland, Ohio). The objective of the visual assessment of SPECT myocardial perfusion images was to determine whether there were defects on stress images and whether these defects were reversible on the rest SPECT images (44). A total of 21 segments were analyzed for each patient, with at least 2 reversible defects needed to classify the patient as having ischemia. Patients were determined to have had silent ischemia if they had evidence of ischemia on the SPECT scan but reported no chest pain, discomfort, or other angina equivalent during their treadmill test (44).

Statistical Analyses

Primary Analyses

Baseline variables are presented as means(standard deviation [SD]) and proportions (*n*) for continuous and categorical variables, respectively. General linear models were used to determine baseline variable differences as a function of group. These groups were the following: (1) no chest pain, no ischemia, (2) ischemia, no chest pain ("silent ischemia"), (3) chest pain, no ischemia, and (4) ischemia with chest pain. Correlations (or χ^2 analyses, where appropriate) were used to determine relationships between NA, PA, ischemia, and chest pain. A series of logistic regressions analyses adjusting for age, sex, total exercise metabolic equivalents (METs), prescription of anti-ischemic medications, and analgesic medication use (not initially reported during recruitment) on the day of the test were used to assess main and interaction effects of PA and NA on chest pain perception. Identical analyses also investigated the 3-way interaction between PA, NA, and ischemia, with further examination of the interaction between PA and NA completed for patients with and without ischemia, separately. For the analyses, PA and NA were used continuously. Estimates from the multiple imputation analysis for the main and interaction effects are reported in tables. Corresponding odds ratios for the main effects are reported in the text. As per previous examples (45), upper and lower quartiles of NA and PA were used to graphically represent the nature of any statistically significant interactions. All covariates were determined a priori on the basis of previously established associations with the dependent variables (14).

Imputation of Missing Data

Using Rubin rules (46), our missing data analysis procedures used multiple imputations (47) with missing-at-random assumptions. There were no systematic differences in the amount of missing data across groups. Using the PROC MI method of multiple multivariate imputations in SAS, we independently analyzed 20 copies of the data. PROC MIANALYZE was used according to Harrell guidelines (48). Details of the amount of missing data per variables are included in Table 1. All analyses were 2-tailed and

TABLE 1. Participant Sociodemographic Characteristics

	No Chest Pain, No Ischemia (n = 145)	Silent Ischemia (n = 55)	Chest Pain, No Ischemia (n = 23)	Ischemia With Chest Pain (n = 23)	No. Missing Data	F/χ^2	P
Sociodemographics							
Age, M (SD)	58.3(11)	63.7(9.7)[a]	59.7(11.3)	58.7(7)	0	3.57	.015
Sex (% female)	66 (46)	4 (7)[a]	11 (48)[b]	4 (17)[ac]	0	11.46	<.001
White	140 (97)	51 (94)	21 (91)	23 (100)	1	0.89	.45
Living with a partner	115 (69)	42 (78)	17 (74)	19 (83)	1	0.95	.42
Years of education, M (SD)	14.1(4.4)	13.83(3.7)	13.3(3.6)	11.4(3.7)[ab]	16	2.81	.040
Medical history characteristics							
BMI, M (SD)	27.5(4.7)	29.3(3.9)	27.6(4.6)	29.3(3.8)	3	1.32	.27
Hypertension	77 (53)	39 (72)[a]	15 (65)	19 (83)[a]	1	3.91	.009
Hyperlipidemia	78 (54)	42 (78)[a]	16 (69)	20 (87)[a]	1	5.51	.001
Current smoker	18 (9)	8 (4)	2 (4)	3 (7)	6	3.79	.15
Former smoker	70 (36)	32 (16)	11 (24)	14 (30)	6	1.56	.46
Diabetes	15 (10)	7 (16)[a]	0[b]	5 (22)[c]	1	4.49	.004
Cardiac history							
Any CHD	41 (28)	30 (55)[a]	6 (26)[b]	15 (65)[ac]	9	7.5	<.001
Previous MI	22 (16)	19 (40)[a]	4 (20)	10 (48)[ac]	21	6.14	<.001
Previous CABG	12 (9)	5 (11)	1 (5)	6 (32)[abc]	29	3.25	.023
Previous PCI	22 (16)	16 (36)[a]	4 (19)	10 (53)[ac]	25	6.20	<.001
Medications							
ACE inhibitors	19 (13)	13 (24) [a]	4 (17)	9 (39)[ac]	2	3.87	.010
β-Blockers	40 (28)	17 (31)	7 (30)	13 (57)[abc]	2	2.57	.055
Any anti blood pressure	61 (42)	37 (69) [a]	10 (43)	18 (78)[ac]	2	6.76	<.001
ARB	16 (11)	13 (24) [a]	1 (4) [b]	4 (17)	2	2.56	.055
Diuretics	16 (11)	8 (15)	9 (4)	4 (17)	2	0.81	.49
Ca-Channel blockers	19 (13)	12 (22)	3 (13)	9 (39)[ac]	2	3.86	.010
Vasodilators	4 (3)	2 (4)	2 (9)	3 (13)[a]	2	1.99	.12
Any anti-ischemic	52 (36)	27 (50)	9 (39)	17 (74)[abc]	2	4.49	.004
Lipid lowering	55 (38)	37 (69)[a]	10 (43)[b]	16 (70)[a]	2	6.80	<.001
Affect scale scores, M (SD)							
NA	16.8(5.9)	15.6(4.7)	19.8(6.7)[ab]	20.0(8.7)[ab]	2	4.44	.004
PA	29.1(7.0)	28.8(6.4)	30.6(7.1)	28.6(7.8)	1	0.41	.74

M (SD) = mean (standard deviation); BMI = body mass Index; CHD = coronary heart disease; MI = myocardial infarction; CABG = coronary artery bypass graft surgery; PCI = Percutaneous coronary intervention; ACE = angiotensin converting enzyme; ARB = angiotensin II receptor blockers; Ca-channel = calcium channel; NA = negative affect; PA = positive affect.

Data are presented as n (%), unless otherwise indicated.

[a] Indicates significantly different from no chest pain; no ischemia ($p < .05$).

[b] Indicates significantly different from silent ischemia ($p < .05$).

[c] Indicates significantly different from chest pain, no ischemia group ($p < .05$).

[d] Indicates significantly different from ischemia with chest pain ($p < .05$).

significance was set at a p value of less than.05. All statistical analyses were conducted using SAS V. 9.3 (SAS Institute, Cary, NC).

RESULTS

Participant Characteristics

Most patients were men (65%) with a mean (SD) age of 59.9 (10.57) years (range age, 27–83 years). Ninety-five percent were white, 73% were cohabitating with a partner, and the mean (SD) number of years of education was 13.7 (4.1) years. The participants' mean (SD) body mass index (BMI) was 27.8 (4.5) kg/m^2 (overweight range) and 13% were current smokers. A total of 24% of the sample had a previous myocardial infarction, 61% were hypertensive, and 14% had diabetes. Comparisons of sociodemographics and clinical characteristics as a function of chest pain and ischemia status are presented in Tables 1 and 2. The analyses showed significant differences between the two ischemia groups (with and without chest pain) and the nonischemia groups (with and without chest pain) on BMI, hypertension, cholesterol, any coronary heart disease, previous myocardial infarction, and diabetes, with higher prevalence seen in the ischemia groups. Similarly, the analyses also showed that the ischemia groups were prescribed more medication than the nonischemia groups.

TABLE 2. Exercise Stress Test Characteristics as Related to Ischemia and Chest Pain

Stress Test Results	No Chest Pain, No Ischemia (n = 145)	Silent Ischemia (n = 55)	Chest Pain, No Ischemia (n = 23)	Ischemia With Chest Pain (n = 23)	No. Missing Data	F/χ^2	P
Duration, s	458(108)	471(93)	456(90)	432(90)	1	0.81	.49
METs (3.5 ml/kg/0_2/min)	8.24(1.8)	8.25(1.7)	8.11(1.7)	7.46(1.8)	0	1.42	.24
% MPHR	90.74(12.9)	87.47(13.3)	86.22(12.7)	80.30(15.4)[ab]	0	4.65	.004
Baseline SBP, mm Hg	130.65(16.6)	133.64(17.2)	131.85(17.2)	130.46(17.3)	2	0.44	.72
Baseline DBP, mm Hg	81.89(10.9)	81.07(8.4)	81.74(8.1)	83.04(12.9)	2	0.20	.89
Baseline HR, beats per minute	73.62(14.8)	71.20(14.9)	68.13(9.1)	69.46(13.8)	2	1.45	.23
Peak SBP, mm Hg	164.66(27.7)	163.74(23)	163.13(24.5)	159.73(24.7)	3	26	.86
Peak DBP, mm Hg	83.22(11.2)	83.29(8.9)	83.74(9.7)	84.39(13.8)	3	0.08	.97
Peak HR, beats per minute	137.53(24.7)	129.63(21.1)[a]	129.48(26.3)	125.57(28.2)[a]	3	2.75	.044
Self-reported chest pain score (0–10)	0.10(0.61)	0	4.30(2.93)[a]	4.09(2.92)[a]	0	119.27	<.001

METs = metabolic equivalents; MPHR = maximum predicted heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

Data are presented as M (SD), unless otherwise indicated.

[a] Indicates significantly different from no chest pain, no ischemia ($p < .05$).

[b] Indicates significantly different from silent ischemia ($p < .05$).

Among the 246 patients, 78 (31.7%) developed exercise-induced ischemia. Exercise-induced ischemia with chest pain was observed in 23 patients (9.35%), 55 (22.4%) had ischemia without chest pain (silent ischemia), and 23 (9.35%) had no ischemia but nonetheless reported chest pain. Patients with inducible ischemia had more often chest pain during exercise (29.5% versus 13.7%, $\chi^2 = 8.74$, $p = .003$) and a higher pain severity score (1.19[2.43] versus 0.72[1.92]) compared with patients without ischemia. Eight (9.1%) of 85 women developed ischemia, compared with 71 (43.6%) of 163 men ($p < .001$), whereas no sex differences were found in reported chest pain (20.0% [M] versus 17.7% [W], $p = .65$).

PA, NA, and the Relationships to Chest Pain and Ischemia

The mean (SD) PA and NA scores were 29.3(6.9) and 17.2(6.2), respectively. There was a negative correlation between NA and PA ($r = -0.34$, $p < .001$), indicating that patients with higher NA reported lower levels of PA. Furthermore, chest pain was correlated with NA ($r = 0.23$, $p < .001$) but not PA ($r = 0.04$, $p = .55$). Ischemia was not associated with NA ($r = -0.01$, $p = .88$) nor PA ($r = -0.04$, $p = .51$). Analysis of differences in NA and PA by group (no ischemia, no chest pain; silent ischemia; chest pain, no ischemia; chest pain and ischemia) revealed an effect of group for NA ($F = 4.44$, $p = .004$). Post hoc analysis revealed the highest levels of NA in the group with chest pain and ischemia and the lowest NA in the no–chest pain nonischemia group. These differences are displayed in Table 1.

Regarding exercise stress test characteristics (Table 2), there were no significant main effects of group for test duration, METs, baseline systolic blood pressure (SBP), baseline diastolic blood pressure (DBP), or baseline heart rate (HR; all $p > .05$). Although there were no main effects of group for peak SBP or peak DBP, there was a main effect of peak HR ($F = 2.75$, $p = .044$). Post hoc analyses revealed patients who experienced ischemia with chest pain or silent ischemia had significantly lower peak HR's compared with patients with no chest pain and no ischemia (both $p < .05$). There were no post hoc differences in peak HR between patients with chest pain but no ischemia and patients with no chest pain and no ischemia. There was also a main effect of group for patients who achieved their maximum predicted heart rate (MPHR; $F = 4.65$, $p = .004$). Post hoc analyses revealed that patients with ischemia and chest pain had a lower number of patients who did not reach their MPHR compared with patients with no ischemia and no chest pain and compared with patients who had silent ischemia ($p < .05$). There were no other group differences. Unsurprisingly, there were also group differences for self-reported chest pain ($F = 119.27$, $p < .001$), where patients with chest pain and no ischemia and patients with ischemia and chest pain had higher self-reported chest pain than the patients with silent ischemia and patients with no chest pain and no ischemia (*all p's* < .05).

Associations Between PA, NA, and Ischemia on Chest Pain

A series of logistic regressions examined the associations between PA, NA, and ischemia on chest pain (Table 3). Across the whole sample, we saw associations between PA (odds ratio [OR] = 1.01, 95% confidence interval [CI] = 1.00 to 1.02, $p = .038$), NA

TABLE 3. Logistic Regressions to Examine the Association Between the Presence of Pain Across the Whole Sample and Examine a Three-Way Interaction Between PA, NA, and ISCHEMIA

	Model 1			Model 2[a]			Model 3			Model 4[a]		
	β	95% CI	*P*	β	95% CI	*P*	β	95% CI	*P*	β	95% CI	*P*
PA	0.007	0.00 to 0.01	.048	0.01	0.00 to 0.02	.038	−0.02	−0.05 to 0.00	.06	−0.03	−0.05 to −0.00	.02
NA	0.02	0.01 to 0.02	<.001	0.02	0.01 to 0.02	<.001	−0.03	−0.07 to 0.00	.06	−0.04	−0.07 to −0.01	.02
Ischemia	0.16	0.06 to 0.27	.002	0.16	0.04 to 0.27	.007	−1.10	−2.36 to 0.17	.09	−1.17	−2.43 to 0.09	.07
PA × NA	—	—	—	—	—	—	−0.00	−0.00 to 0.00	.09	−0.00	−0.00 to 0.00	.07
PA × ischemia	—	—	—	—	—	—	0.04	−0.01 to 0.08	.10	0.04	−0.00 to 0.08	.08
NA × ischemia	—	—	—	—	—	—	0.07	0.01 to 0.13	.03	0.07	0.01 to 0.13	.02
PA × NA × ischemia	—	—	—	—	—	—	−0.00	−0.00 to 0.00	.09	−0.00	−0.00 to 0.00	.07

β = beta estimate; 95% CI = 95% confidence interval; PA = positive affect; NA = negative affect.

[a] Adjusted for age, sex, total exercise METs, prescription of anti-ischemic medications, and analgesic medication use.

(OR = 1.02, 95% CI = 1.01 to 1.02, $p < .001$), and ischemia (OR = 1.17, 95% CI = 1.04 to 1.31, $p = .007$) on chest pain, which were significant having adjusted for age, sex, total exercise METs, prescription of anti-ischemic medications, and analgesic medication use. Furthermore, across the whole sample, we also saw trends for an interaction between PA and NA (β = −0.001, 95% CI = −0.00 to 0.00, $p = .07$), after adjusting for covariates, including ischemia. In addition, there was a trend for an interaction between PA and ischemia (β = 0.04, 95% CI = −0.005 to 0.08, $p = .079$), a significant interaction between NA and ischemia (β = 0.07, 95% CI = 0.01 to 0.13, $p = .02$), and a trend for a 3-way interaction between PA, NA, and ischemia (β = −0.002, 95% CI = −0.004 to 0.00, $p = .069$) in the association with pain.

Interrogation of the 3-way interaction was undertaken, stratifying patients by ischemia status. As detailed in Table 4, the analysis revealed that in patients *with ischemia*, there was a significant effect of NA (OR = 1.13, 95% CI = 1.02 to 1.26) but not for PA (OR = 1.06, 95% CI = 0.96 to 1.12) for the association between reporting chest pain, indicating that patients with higher levels of NA were more likely to report experiencing chest pain during exercise. In the interaction model, there was no interaction effect of PA and NA. In patients *without ischemia*, higher levels of NA were also associated with an increased frequency of reporting chest pain during the stress test. As detailed in Table 4, the main effects analysis in patients without ischemia mirrored that of the ischemia patients with a statistically significant association between for NA (OR = 1.11, 95% CI = 1.03 to 1.19) but not PA (OR = 1.07, 95% CI = 0.99 to 1.15). Among patients without ischemia, there was also a significant interaction between PA and NA on chest pain reporting where patients with higher levels of both NA and PA were more likely to report chest pain (β = 0.02, 95% CI = 0.002 to 0.03) compared with patients with low levels of NA and PA (Fig. 2).

DISCUSSION

The objective of the present study was to examine relationships between PA/NA and chest pain perception in the context of ischemia in patients undergoing exercise stress tests. We expected that patients with higher levels of NA would be more likely to report chest pain and patients with higher levels of PA would be less likely to report chest pain, particularly among those with ischemia (silent ischemia). Our hypotheses were only partially supported, with higher levels of NA being associated with an increased frequency of reporting chest pain in both ischemia and nonischemia patients. However, higher levels of PA alone were not associated with a reduction in chest pain reporting; higher NA was associated with an increased chance of chest pain reporting, irrespective of ischemic status. Interestingly, we observed an interaction between PA and

TABLE 4. Logistic Regressions to Examine the Association Between the Presence of Pain in Ischemic and Nonischemic Patients

	Model 1				Model 2[a]				Model 3[a]			Model 4[a]		
	β	OR	95% CI	*p*	β	OR	95% CI	*p*	β	95% CI	*p*	β	95% CI	*p*
Nonischemic patients only														
PA	0.06	1.07	0.99 to 1.14	.075	0.07	1.07	1.00 to 1.15	.070	−0.21	−0.46 to 0.04	.096	−0.23	−0.51 to 0.02	.081
NA	0.09	1.10	1.02 to 1.18	.010	0.10	1.11	1.03 to 1.20	.007	−0.32	−0.71 to 0.07	.110	−0.35	−0.79 to 0.04	.098
PA × NA	—	—	—	—	—	—	—	—	0.01	0.00 to 0.03	.036	0.02	0.00 to 0.03	.031
Ischemic patients only														
PA	0.04	1.04	0.96 to 1.14	.31	0.06	1.07	0.96 to 1.18	.22	0.09	−0.16 to 0.34	.48	0.04	−0.26 to 0.29	.79
NA	0.13	1.14	1.03 to 1.25	.008	0.13	1.13	1.02 to 1.27	.026	0.19	−0.14 to 0.52	.26	0.09	−0.32 to 0.43	.63
PA × NA	—	—	—	—	—	—	—	—	−0.00	−0.01 to 0.01	.69	0.00	−0.01 to 0.02	.84

β = beta-estimate; OR = odds ratio; 95% CI = 95% confidence interval; PA = positive affect; NA = negative affect.

[a] Adjusted for age, sex, total exercise METs, prescription of anti-ischemic medications, and analgesic medication use. Sample sizes: ischemic patients only ($n = 78$) and nonischemic patients only ($n = 172$).

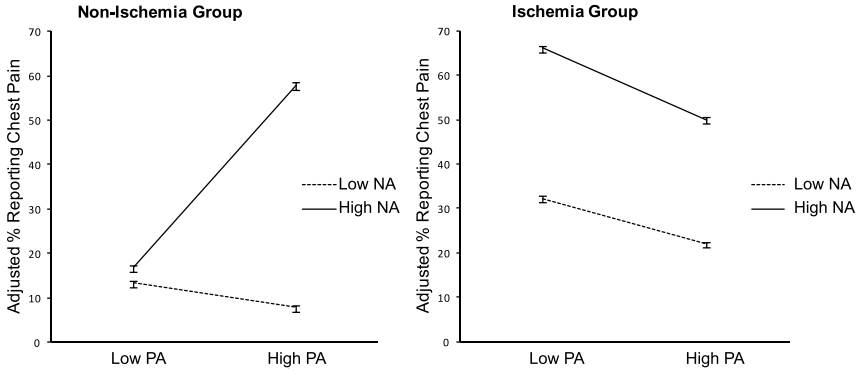

FIGURE 2. Chest pain reporting by PA in patients without ischemia (left) and patients with ischemia (right). Dashed line indicates low NA; solid line, high NA.

NA on chest pain reporting in the nonischemic patients only, such that patients with higher levels of both PA and NA had a greater probability of reporting chest pain. This suggests that patients with overall higher levels of both NA and PA are more likely to report experiencing chest pain during exercise stress tests, especially in the absence of ischemia. However, ischemia was not associated with NA or PA. Our study uniquely presents evidence of the interactive and dynamic associations of both NA and PA in the context of ischemia and chest pain reporting, particularly the unique association of elevated affect in those who do not have ischemia.

In terms of the magnitude of our associations, our findings suggest that every 1-point increase in NA was associated with a 13% and 11% greater chance of reporting chest pain during exercise in patients with and without ischemia, respectively. These results are generally consistent with previous reports (24). Previous studies have demonstrated that NA measures, such as depression, are associated with greater symptom reporting in patients with and without CVD (16,17). Another study demonstrated that higher levels of anxiety and depression, evaluated by the Hospital Anxiety and Depression Scale, were associated with higher reported pain intensity in postsurgical patients (23). Anxiety, another measure of NA, has also been linked to higher reports of chest pain among cardiac and noncardiac populations (25,26). It is thought that these relationships may be due to changes in a combination of physiological systems such as the autonomic nervous system and coronary vasculature system including increased microvascular resistance (26), and possibly due to fears associated with having cardiac events (49,50). Patients with a high level of anxiety have a greater tendency to catastrophize somatic symptoms, which has been related to increase pain reporting (51). Patients with anxiety may also be hypervigilant to chest pain and report more chest pain during a stress test (52). Our findings are also consistent with a study reporting that most patients seeking emergency care for noncardiac chest pain report higher levels of NA (e.g., depression and history of panic; 49). Similarly, patients with a high level of neuroticism (a personality trait where individuals are more likely to experience anger, anxiety, and depression) report more chest pain or discomfort than patients with a lower level of neuroticism (17,53). Although the mechanisms linking negative affective states and pain perception have not been fully delineated, one possibility is impairments of the endogenous opioid system in the anterior cingulated cortex, which is involved in pain regulation (54). When impaired, this system is associated with a reduced ability to modulate negative emotions as well as elevated pain sensitivity (54).

Contrary to our hypotheses, we did not observe any associations between higher levels of PA alone and reduced pain reporting, irrespective of ischemia. Rather, we observed that PA was related to increased chest pain reporting and demonstrated a significant interaction between PA and NA and reports of chest pain in nonischemic patients. In this group, patients with higher levels of both PA and NA reported more chest pain compared with other patients. This is particularly interesting, given that patients with high NA and low PA did not report the same prevalence of the presence of chest pain compared with high NA/high PA patients. A previous study demonstrated that patients with higher levels of "emotionality" reported more incongruent lower back pain (inappropriate symptomatic complaints or nonorganic physical signs; 55), which parallels our findings. Although we did not directly assess emotionality, it is possible that scoring high on both PA and NA may reflect the same construct. In contrast to our findings, it has been observed that anhedonic patients have a tendency to report more somatic symptoms (56). An alternative hypothesis is that patients with high levels of PA, including feelings of assertiveness and self-assurance, could also be displaying proactive health behaviors by reporting that they are experiencing chest pain. Others have shown that PA is related to internal components of the multicomponent health locus of control (57). However, because we did not assess multicomponent health locus of control in our sample, this must remain speculative. To our knowledge, this is the first study to specifically assess the association between PA and pain reporting in the context of ischemia. Although our findings did not support an association, they do add to the extant literature on the psychological factors that may (or may not) be involved in chest pain in cardiac patients.

Results of the present study should be interpreted in light of some limitations. First, patient selection was not random and participants were predominantly male and white, so results may not generalize to women or a nonwhite population. Second, although the sex ratio in our study is consistent with that seen in a clinical setting, because of the uneven proportions of men and women and low absolute numbers of women, we were not able to examine sex differences in chest pain reporting and ischemia as a function of PA and NA. Many studies report that women are more likely to exhibit lower pain thresholds, have a lower tolerance to noxious stimuli, and report more somatic complaints compared with men (58). Women also describe their chest pain differently than men and report greater pain intensity relative to men (59). Although we adjusted for sex in our analyses, future studies should aim to

examine sex differences in these associations. Also, the pain measure used in this study was dichotomous (presence or absence of chest pain). This does not allow us to assess potential differences in pain quality as a function of PA or NA. Furthermore, it should be noted that this is a population who were undergoing exercise stress testing and, as such, individuals with conditions that interfered with their ability to exercise (e.g., severe musculoskeletal pain) would have been ineligible for such a test, and our findings should be viewed in light of this. One important consideration is the broader role of psychological characteristics, which may influence chest pain and reporting of chest pain (50,60). Furthermore, patients with CAD are more likely to underreport their emotional distress compared with patients with less severe cardiac conditions (61). This may have disproportionally influenced the chest pain reported in the ischemia group. Furthermore, patients with CHD (or more severe CHD) may be more likely to under-report emotional distress relative to patients with less severe CHD symptom. This disparity could have influenced the NA-PA reporting in the ischemia group and should be considered in light of our findings.

Despite some limitations, this study also has several important strengths. To our knowledge, this study is the first to investigate the relationship between PA and NA and their interaction on chest pain reporting among patients with and without ischemia, adding critical new information. Second, compared with pain perception studies in general, our sample size is relatively large at 246. Although we had uneven proportions of men and women in the study, the percentage of men (65%) in our sample reflects the disproportionately male cardiac population referred for an exercise SPECT tests and is thus highly representative of this population. Third, experienced cardiologists conducted the chest pain and ischemia assessments according to standard procedures. Fourth, PA and NA were assessed using the PANAS-X, which is an excellent assessment of affect with very good psychometric properties.

Our results indicate that irrespective of ischemia, patients who experience greater levels of NA or PA are more likely to report experiencing chest pain. However, among patients without ischemia, those reporting generally high levels of both NA and PA are also more likely to report chest pain. Given that patients with high NA have higher odds to report chest pain, whether or not they have ischemia, practitioners should be vigilant if patients exhibit or report symptoms of negative mood, because this may influence the perception and experience of chest pain among patients undergoing diagnostic exercise stress testing, which may affect clinical findings. They should also consider that the pain reported in those patients may or may not be related to underlying ischemia (28). Given that both high PA and NA seem to be important, more studies are needed to further disentangle the relationship between positive and negative emotions and pain perception in the context of ischemic heart disease.

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