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Impact of Anxiety and Perceived Control on In-Hospital Complications After Acute Myocardial Infarction

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Abstract

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Background: Anxiety is common among patients with AMI, but whether it is associated with poorer outcomes is controversial. Conflicting findings about the relationship of anxiety with cardiac morbidity and mortality may result from failure to consider the moderating effect of perceived control.

Methods: This was a prospective examination of the association among anxiety, perceived control, and subsequent in-hospital complications among patients (N = 536) hospitalized for AMI.

Results: Patients' mean anxiety level was double that of the published mean norm. Patients with higher levels of perceived control had substantially lower anxiety (p = .001). A total of 145 (27%) patients experienced one or more in-hospital complications. Patients with higher levels of anxiety had significantly more episodes of ventricular tachycardia, ventricular fibrillation, and reinfarction and ischemia (p < .01 for all). In a multivariate hierarchical logistic regression model, left ventricular ejection fraction, history of myocardial infarction, anxiety score, and the interaction of anxiety and perceived control were significant predictors of complications.

Conclusion: Anxiety during the in-hospital phase of AMI is associated with increased risk for in-hospital arrhythmic and ischemic complications that is independent of traditional sociodemographic and clinical risk factors. This relationship is moderated by level of perceived control such that the combination of high anxiety and low perceived control is associated with the highest risk of complications.

AMI = acute myocardial infarction; CHD = coronary heart disease; BSI = Brief Symptom Inventory; CAS = Control Attitudes Scale.

Keywords
anxiety, psychological factors, acute myocardial infarction

Disciplines
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Abstract

Objectives: We tested the hypothesis that perception of control moderates any relationship between anxiety and in-hospital complications (i.e., recurrent ischemia, reinfarction, sustained ventricular tachycardia or fibrillation, and cardiac death) in acute myocardial infarction (AMI) patients.

Background: Anxiety is common among AMI patients, but whether it is associated with poorer outcomes is controversial. Conflicting findings about the relationship of anxiety with cardiac morbidity and mortality may result from failure to consider the moderating effect of perceived control.

Methods: This was a prospective examination of the association between anxiety, perceived control, and subsequent in-hospital complications among patients (N= 536) hospitalized for AMI.

Results: Patients' mean anxiety level was double that of the published mean norm. Patients with higher levels of perceived control had substantially lower anxiety ($p < 0.01$). A total of 145 (27%) patients experienced one or more in-hospital complications that comprised the combined end-point. Patients with higher levels of anxiety had significantly more episodes of ventricular tachycardia, ventricular fibrillation, and reinfarction and ischemia ($p < 0.01$ for all). In a multivariate hierarchical logistic regression model left ventricular ejection fraction, history of previous myocardial infarction, anxiety score and the interaction of anxiety and perceived control were significant predictors of complications.

Conclusion: Anxiety during the in-hospital phase of AMI is associated with increased risk for in-hospital arrhythmic and ischemic complications that is independent of traditional sociodemographic and clinical risk factors. This relationship is moderated by level of perceived control such that the combination of high anxiety and low perceived control is associated with the highest risk of complications.

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Acute myocardial infarction = AMI

Coronary heart disease = CHD

Accumulating evidence strongly suggests that psychological and social factors affect morbidity and mortality among individuals with coronary heart disease (CHD).(1-5) In particular, depression (6-12) and lack of social support (13-16) have been shown convincingly to contribute to development of acute cardiac events and CHD mortality. Anxiety is common and levels are high in persons hospitalized with acute cardiac events (4,17,18), but the influence of anxiety on subsequent cardiac events and mortality, particularly in the acute phase of a cardiac event, has not been well characterized.(19-21)

In a small sample, we demonstrated previously that acute myocardial infarction (AMI) patients with high anxiety had 4.9 times greater risk than patients with lower anxiety of developing recurrent ischemia, reinfarction, ventricular tachycardia or ventricular fibrillation during hospitalization.(17) Others have demonstrated that anxiety is an independent predictor for CHD events,(22-24) and mortality months to years after AMI, (25,26) although some investigators have reported that anxiety is unrelated to morbidity or mortality.(21,27-28) Most notably lacking in this area of research is evidence on the impact of anxiety in the acute (i.e., during hospitalization) stages of myocardial infarction. Attention to the effect of anxiety within the early hours and days after AMI could yield substantial early benefits as monitoring and intervention are readily available during hospitalization.

There are several possible reasons for the disparate findings seen, including inadequate sample size in some studies, varying conceptual and operational definitions of anxiety, and use of homogeneous samples within studies, which decreases statistical power. Another reason may be failure to consider the role of moderators of anxiety in these studies. That is, there may be important factors that, when present, change the manner in which anxiety affects outcomes. Identification of factors that moderate any association between anxiety and poor outcomes is important as such factors are targets for intervention.

One potential moderating factor is perceived control.(29-31) Perceived control is associated with anxiety level.(29,32,33) In a variety of cardiac patients, including heart failure, AMI, and recovering myocardial infarction and cardiac bypass patients, patients with higher levels of perceived control compared to those with lower levels have substantially lower levels of anxiety and other negative emotions.(29-33) Patients with higher perceived control have a better course after diagnosis of a variety of chronic and/or life-threatening illnesses.(32,34,35) In addition, investigators have demonstrated that perceived control can be modified by simple interventions, and that increases in perceived control predict improved emotional state, including lower anxiety levels. (31)

Accordingly, we tested the hypothesis that level of perceived control moderated the relationship between anxiety and the development of in-hospital complications in patients hospitalized for AMI. To overcome limitations of previous studies, we used a large, heterogeneous sample.

Methods

The investigation was a prospective, comparative examination of the association between early anxiety, perceived control, and subsequent in-hospital complications. Patients were enrolled from the cardiac care units of 6 diverse hospitals that included 4 large urban university medical centers and 2 large urban community hospitals in the United States and Australia.

Patients

Institutional review board approval was obtained at all sites, and all patients gave signed, informed consent. From January 2001 through December 2002, consecutive patients were identified by the cardiac care unit manager, educator, or clinical specialist who briefly explained the study and informed patients that a member of the research team would explain the study in full, obtain consent and then conduct an interview. Cardiac care unit patients who met the following criteria were eligible for the study: 1) diagnosis of AMI

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confirmed by elevated cardiac enzymes and typical ECG changes; 2) pain-free and hemodynamically stable at the time they were approached for inclusion in the study; 3) free of cognitive impairment that could interfere with ability to provide informed consent and participate in a short interview; 5) free of noncardiac serious or life-threatening co-morbidities such as sepsis, shock, stroke, or acute renal failure.

Protocol and Measurement

Sociodemographic and clinical data (Table 1) were obtained by patient interview and medical record review. Within 72 hours (median 28 hours) of arrival at the hospital, patients were interviewed regarding anxiety (36) and perceived control,(30,37) as described below. Questionnaires were read to them and they were provided with laminated sheets that contained the possible responses for each questionnaire in very large type to improve ease of answering. Although patients may have been admitted with or had hemodynamic compromise after admission, they were pain-free and hemodynamically stable when interviewed. Complications that occurred subsequent in time to the interview were abstracted from the medical record by registered nurses who were cardiac care specialists and who were extensively trained in data collection and interview techniques. Data extraction included review of every page of each patients' medical record to determine complications, instead of relying on physician or nurse documentation of the complication. Patients with complications before the interview were excluded as the occurrence of complications likely increases anxiety. Nurses collecting complication data were blinded to the anxiety level of the patient.

Anxiety Measurement

Anxiety was defined conceptually as a feeling of foreboding, dread or threat, elicited by a real or imagined threat.(38) The anxiety subscale of the Brief Symptom Inventory (BSI) was used to measure anxiety.(36) The anxiety subscale measures state (as opposed to trait) anxiety and symptom refers to psychological and not physical

manifestations. The BSI anxiety subscale was chosen for its brevity, reliability and validity in medical clinical populations, and its demonstrated sensitivity to anxiety. Construct, convergent, discriminant, and predictive validity of the BSI have been established in a series of studies. Internal consistency coefficients for the anxiety subscale are consistently reported to be higher than 0.80;(17,36,39) in this study, Cronbach's alpha was 0.87. The anxiety subscale of the BSI has the additional advantage of not using physical indicators of emotional states that often over-estimate the level of mood states in patients with physical disease. Each item on the BSI is rated by the patient on a 5-point scale (0-4) of distress ranging from "not at all" to "extremely". Item scores are summed and the mean obtained. Thus, the possible range of scores for the anxiety scale is 0 to 4, with higher scores indicative of higher levels of anxiety. Norm referenced data are available for comparison.(36)

In order to further validate the use of the BSI in acutely ill patients, we conducted a psychometric study comparing the reliability and validity of the anxiety subscale of the BSI with the more established Spielberger State Anxiety Index.(40) We found that the BSI demonstrated equal or greater reliability and validity in AMI patients than the Spielberger State Anxiety Index. Patients found the BSI less conceptually challenging than the longer Spielberger State Anxiety Index and thus easier to understand.

Perceived Control Measurement

Control was defined as the perception or belief that individual's have a coping response that can positively influence adverse events or circumstances. Importantly, control does not need to be exerted and the belief does not need to be realistic. The Control Attitudes Scale (CAS),(30,37) used to measure perceived control, consists of 4 belief statements measuring perceived control and lack of control, in the context of cardiac disease. Patients rate their level of agreement with the statements on the CAS using a 7-point Likert–type scale. Responses for each item are summed to arrive at a total score,

which can range from 4 to 28. Instrument reliability as assessed by internal consistency was high, with a Cronbach's alpha of 0.89. Content, construct, and predictive validity of the instrument have been demonstrated.(30,31)

Complications

In-hospital complications were defined as the composite endpoint of one or more of the following: 1) acute recurrent ischemia as evidenced by new onset chest pain with a) ST segment elevation on bedside ST segment monitor or 12-lead ECG, and/or b) hemodynamic compromise evidenced by blood pressure or pulse changes from baseline, and/or c) nitrates and/or intravenous pain medication given for chest pain relief; 2) reinfarction as evidenced by recurrent positive CK-MB that occurs after an episode of recurrent chest pain or hemodynamic compromise and after CK-MB or troponin levels have stopped rising from the initial infarct; 3) sustained ventricular tachycardia (> 15 sec) or any ventricular tachycardia requiring pharmacologic or electrical intervention due to hemodynamic compromise and/or chest pain; 4) ventricular fibrillation; or 5) in-hospital death. These complications were chosen because they are the complications consistent with the theory that increased anxiety produces enhanced sympathetic nervous system arousal.

Data Analysis

Data are presented as means ± standard deviations or frequencies and percentages. To reduce the possibility that any demonstrated association between increased anxiety level and complications could be explained by severity of myocardial infarction, or differences in treatment or sociodemographics, differences in baseline characteristics between higher and lower anxiety patients were examined using Chi-square for categorical variables, Student's t-tests or Mann-Whitney U for continuous variables. For these analyses only, patients were split into two groups based on the median split of anxiety score. In all subsequent analyses, anxiety score was used in its

raw form. Baseline variables upon which the groups differed were controlled in subsequent analyses. Mann-Whitney U was used to compare anxiety level between high control and low control patients.

To explore the association of anxiety, the interaction between anxiety and perceived control, and other potential covariates with the outcome variable of complications we used multiple logistic regression. The odds ratios and 95% confidence intervals for the occurrence of complications in relation to the baseline sociodemographic (i.e. age, gender), clinical (i.e. history of hypertension, diabetes or previous AMI, type of infarction, aspirin or beta-blocker administration in the emergency department, anxiolytic use during hospitalization, left ventricular ejection fraction, admission Killip classification, peak chest pain level), and psychological (i.e. anxiety score, perceived control) variables were assessed. To evaluate the prognostic importance of anxiety in relation to other established measures of risk, we determined the degree to which anxiety score and perceived control level improved a predictive model of the other significant predictors of complications. These predictors were entered first into the model followed by the anxiety-control interaction term.

Results

A total of 540 patients were recruited for the study. Four patients failed to complete the anxiety assessment instrument and thus the total final sample size was 536 (Table 1). The only baseline sociodemographic variable that differentiated between patients in the low and high anxiety groups was age (Table 1). Younger patients reported higher anxiety. Although there were more women in the high anxiety group compared to the low anxiety group, this difference did not reach statistical significance. Three clinical variables differed between the two groups. Patients in the high versus low anxiety group received a beta-adrenergic blocking agent, aspirin, or anxiolytic in the emergency department more often than did those in the low anxiety group (Table 2). There were no differences in treatment

after the emergency department and during the remainder of the hospitalization between the two groups with the exception that more patients in the high anxiety group received an anxiolytic during their hospital stay.

Anxiety and perceived control

The mean anxiety level of patients in this sample (0.66 ± 0.79) was double that of the published mean from the norm reference group.(36) Nineteen percent of patients expressed anxiety levels that were at or above those referenced for psychiatric in-patients.(36) The level of perceived control ranged from a low of 4 to a high of 28 (mean 18 ± 5). Although there are no published norms, levels below 16 reflect a low level of perceived control(30,37) and 41% of patients in this sample had levels lower than 16. Patients with higher levels of perceived control had substantially lower anxiety than those with lower levels of perceived control (0.48 ± 0.75 vs 0.79 ± 0.73 p < 0.01).

Anxiety, Perceived Control and Complications.

A total of 145 (27%) patients experienced one or more of the in-hospital complications that comprised the combined end-point. These complications included 64 unique episodes of ventricular tachycardia, 13 cases of multiple episodes of ventricular tachycardia, 26 instances of ventricular fibrillation, 110 of recurrent ischemia, 12 reinfarctions, and 7 cardiac deaths. In bivariate analyses, patients with higher levels of anxiety had significantly more episodes of the combined end-point, and of the following individual end-points: ventricular tachycardia, ventricular fibrillation, and reinfarction or ischemia (Figure 1). There were no differences in number of cardiac deaths between the two groups.

We also stratified the sample by presence of ST segment elevation myocardial infarction and non ST segment elevation myocardial infarction, and examined the association between anxiety and in-hospital complications. Patients with higher levels of

anxiety had more complications than those with lower levels of anxiety regardless of type of AMI. A total of 31% of ST segment elevation myocardial infarction patients versus 23% of non ST segment elevation myocardial infarction patients had any in-hospital complication (p = 0.01). In-hospital complication rates for patients with ST segment elevation myocardial infarction were 36% for high anxiety patients versus 23% for low anxiety patients (p = 0.01). Rates for patients with non ST segment elevation myocardial infarction were 26% for high anxiety patients versus 15% for low anxiety patients (p = 0.04).

Of the variables tested in the multivariate hierarchical logistic regression model (i.e. age, gender, left ventricular ejection fraction, type of myocardial infarction, peak chest pain level, history of hypertension, diabetes or previous AMI, admission Killip classification, aspirin or beta-blocker administration in the emergency department, anxiolytic use during hospitalization, anxiety score, and level of perceived control), left ventricular ejection fraction, history of previous myocardial infarction, anxiety score and the interaction of anxiety and perceived control were significant predictors of complications (Table 3). Patients with a lower ejection fraction, a history of previous AMI, and a higher level of anxiety had significantly more occurrences of the combined end-point. In addition, the interaction of anxiety and perceived control was a significant predictor of complications, indicating that perceived control moderated the relationship between anxiety and complications. Patients with high anxiety and low perceived control had the highest occurrence of complications (Figure 2).

Discussion

Results of this multicenter study contribute to the body of literature implicating anxiety as a risk factor for short- and long-term physical complications after AMI.(25,41) It is one of the few investigations of the impact of anxiety very early after AMI on in-

hospital complications. Both ischemic and arrhythmic complications were predicted by the presence of higher anxiety. Importantly, this relationship was independent of the risk conferred by a number of traditional clinical factors. Risk stratification after AMI continues to be driven by clinical variables alone. Results from this study and from others demonstrating the long-term cardiovascular risks of negative affective states and social isolation provide further evidence that psychological and social factors should be considered when assessing risk after AMI and that interventions to decrease anxiety need to be investigated and applied widely.(5)

Conflicting findings to date about the relationship between anxiety and outcomes in CHD patients are thought primarily to be the result of two major factors: failure to consider moderators of anxiety and anxiety measurement ambiguities. Our findings further the research regarding the role of anxiety in morbidity and mortality outcomes among those with heart disease by demonstrating the moderating effect of perceived control on the association between anxiety and in-hospital outcomes. Patients with high levels of anxiety had significantly more complications than those with low anxiety, but those with the greatest occurrence of complications were patients with both high anxiety and low perceived control.

Perceived control is modifiable by a number of simple, but well-timed, well-constructed, systematically delivered interventions.(31) Such interventions include education and counseling to reframe an acute cardiac event from an out of control crisis to the herald of a chronic condition that can be controlled with adherence to recommended therapy and lifestyle changes.(42,43) Given that the over-riding threat for most individuals after an acute cardiac event is the perception of a loss of control(44) (45) plus the strong inverse association between perceived control and anxiety,(29,30,33) aggressive development and testing of specific intervention approaches targeted at increasing the perception of control among AMI patients appears warranted.

With regard to measurement ambiguities that may have clouded the accurate assessment of the relationship between anxiety and outcomes, the major controversy has centered around the measurement of clinical anxiety syndromes such as phobic anxiety versus symptoms of anxiety. Some researchers have contended that it is only clinically diagnosed anxiety syndromes that are associated with morbidity and mortality outcomes. However, our previous work(17), the results presented in this study, and the work of others who have measured anxiety symptoms, but not anxiety syndromes(25,46) and demonstrated a strong independent association between anxiety and patient outcomes argues against this stance.

Patients in this study expressed a mean anxiety level that was 50% greater than the norm reference figure and almost a quarter of patients reported anxiety levels that exceed those reported by psychiatric in-patients. This was despite the finding that patients in the higher anxiety group tended to receive an anxiolytic more often in the emergency department and during hospitalization. These findings highlight the persistent problem of inadequate assessment and management of anxiety and other psychological problems in cardiac patients.(47,48) Anxiety can not be treated unless it is first recognized. Without a formal screening instrument, clinicians are not able to accurately identify psychological distress in their patients.(47,48) Routine use of a short, simple anxiety assessment appears warranted in the hospital setting for patients suffering acute cardiac events. A number of such instruments exist and have been shown to be valid for screening in clinical settings.(49) The instrument used in this study assesses anxiety using 6 items and has been shown to perform well in a variety of clinical cardiac settings.(17,50)

The mechanisms whereby anxiety could be associated with morbidity and mortality outcomes in AMI patients remain unclear. The major theories are that both physiological and behavioral mechanisms contribute to poor physical outcomes in anxious cardiac patients.(5) Although behavioral mechanisms (e.g. nonadherence to medications or

lifestyle change recommendations, adoption or maintenance of risky behaviors such as smoking or sedentary life-style) likely are important factors that contribute to the relationship between psychological distress and physical outcomes seen on long-term follow-up, it is unlikely that they play a major role in precipitating acute cardiac events in the short-term among AMI patients. A more plausible mechanism linking anxiety with in-hospital complications in AMI patients is a physiologic one wherein excess activation of the sympathetic nervous system results in decreased heart rate variability, increased platelet aggregation and other changes in coagulation, alterations in fibrillation threshold, and endothelial dysfunction.(5) Although we did not test mechanisms in this study, the increased incidence of ischemic and arrhythmic complications seen in patients with higher anxiety supports the theory that anxiety is associated with excess sympathetic nervous system activation.

Study Limitations. A potential limitation in this study relates to concerns about generalizability. The incidence of ST segment elevation myocardial infarction was higher in this sample than seen in large registries of acute myocardial infarction patients, suggesting that this sample does not completely reflect the typical proportions of ST segment elevation myocardial infarction and non-ST segment elevation myocardial infarction. Our higher proportion of ST segment elevation myocardial infarction is likely due to our inclusion criteria and the need to identify patients very early in the course of hospitalization. Nonetheless, our large sample size provided a sufficient number of non ST segment elevation myocardial infarction patients to allow generalizability to both types of AMI patients.

Conclusion.

Anxiety during the in-hospital phase of AMI care is associated with an increased risk for in-hospital arrhythmic and ischemic complications that is independent of a number of traditional sociodemographic and clinical risk factors. This relationship is moderated by

level of perceived control such that the combination of high anxiety and low perceived control is associated with the highest risk. These findings provide specific targets for intervention to sever the link between anxiety and poor physical outcomes in hospitalized AMI patients. Assessment for anxiety in hospitalized AMI patients is warranted given the high levels that exist in this patient population and the potential for adverse outcomes associated with anxiety.

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Figure Legends

Figure 1. Comparison of in-hospital complication rates by high and low anxiety groups.

Figure 2. The moderating impact of perceived control on the relationship between anxiety and complications. Comparison of percentage of patients out of the entire sample who had complications based on anxiety and perceived control.

Table 1. Characteristics of the sample of 536 acute myocardial infarction patients

	Entire Sample	High Anxiety	Low Anxiety
	N = 536	n = 262	n = 274
Sex[c]			
Male	354 (66)	165 (63)	189 (70)
Female	180 (34)	97 (37)	83 (30)
Marital status[c]			
Married/cohabitate	369 (69)	182 (70)	187 (69)
Single/divorced/ widowed	164 (31)	79 (30)	85 (31)
Age, years[b,*]	62 ± 14	60 ± 13	64 ± 13
Education, years[b]	13 ± 3	13 ± 3	13 ± 3
Peak chest pain, scale 0 to 10, 10 = worst[d]	7 ± 3	7 ± 3	7 ± 3
Peak CK-MB, ng/ml[d]	148 ± 167	151 ± 175	145 ± 160
ST segment elevation myocardial infarction[c]	330 (64)	162 (64)	168 (63)
Left ventricular ejection fraction, %[b]	50 ± 13	51 ± 14	49 ± 13
Admission Killip class[c]			
I/II	485 (92)	234 (91)	251 (92)
III/IV	45 (9)	23 (9)	22 (8)

Diabetes[c]	116 (22)	57 (22)	59 (22)
Hypertension[c]	301 (57)	147 (57)	154 (57)
Previous myocardial infarction[c]	144 (27)	66 (25)	78 (29)
Admission systolic blood pressure, mmHg[b]	141 ± 28	141 ± 28	142 ± 29
Admission diastolic blood pressure, mmHg[b]	81 ± 18	81 ± 18	81 ± 18
Admission pulse, beats/min[b]	79 ± 21	79 ± 19	79 ± 22

Values are n (%) or mean $\pm$ SD; * $p < 0.05$ for comparison between high and low anxiety groups; statistical tests used to compare high vs low anxiety patients were chi-square,[c] Student's t-test,[b] or Mann-Whitney U[d]

Table 2. Treatments Received in the Emergency Department and Hospital (n=536)

	Entire Sample N = 536	High Anxiety n = 262	Low Anxiety n = 274	P*
Fibrinolysis in ED	163 (31)	86 (34)	77 (28)	.22
Beta-adrenergic blocking agent in ED	237 (46)	126 (50)	111 (41)	.04
Aspirin in ED	421 (80)	214 (84)	207 (76)	.03
Anxiolytic in ED	168 (32)	92 (37)	76 (28)	.05
Coronary artery bypass grafting	62 (12)	23 (9)	39 (14)	.06
Angioplasty	337 (64)	166 (65)	171 (63)	.65
ACEI during hospitalization	313 (60)	146 (58)	167 (61)	.38
Beta-adrenergic blocking agent during hospitalization	450 (85)	218 (84)	232 (85)	.81
As needed anxiolytic during hospitalization	247 (47)	135 (53)	112 (42)	.01

* p value for comparison between high and low anxiety groups; chi-square used for comparisons; ACEI = Angiotensin converting enzyme inhibitor; ED = emergency department

Table 3: Multivariate Hierarchical Logistic Regression for Prediction of In-hospital Complications

Predictor	Odds Ratio	CI	P
Previous myocardial infarction	1.9	1.1 - 3.3	<0.01
Left ventricular ejection fraction	.97	.96 - .99	<0.01
Anxiety score	1.5	1.1 – 2.0	<0.01
Anxiety score * perceived control	1.3	1.1 – 1.8	<0.01

In a test of the following model: age, sex, hypertension, diabetes, previous myocardial infarction, left ventricular ejection fraction, type of myocardial infarction, peak pain level, admission Killip class, aspirin administration in the emergency department, beta-blocker administration in the emergency department, anxiolytic given during hospitalization, total anxiety score, perceived control and the interaction of anxiety score and perceived control
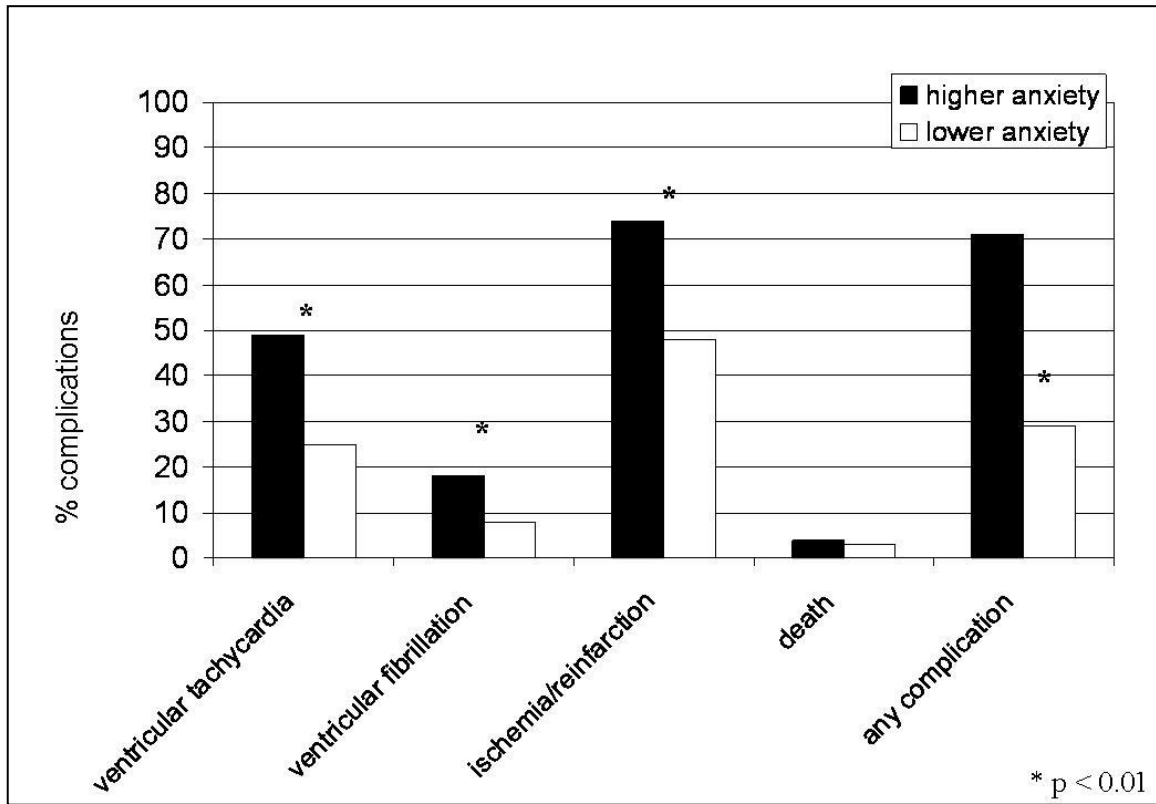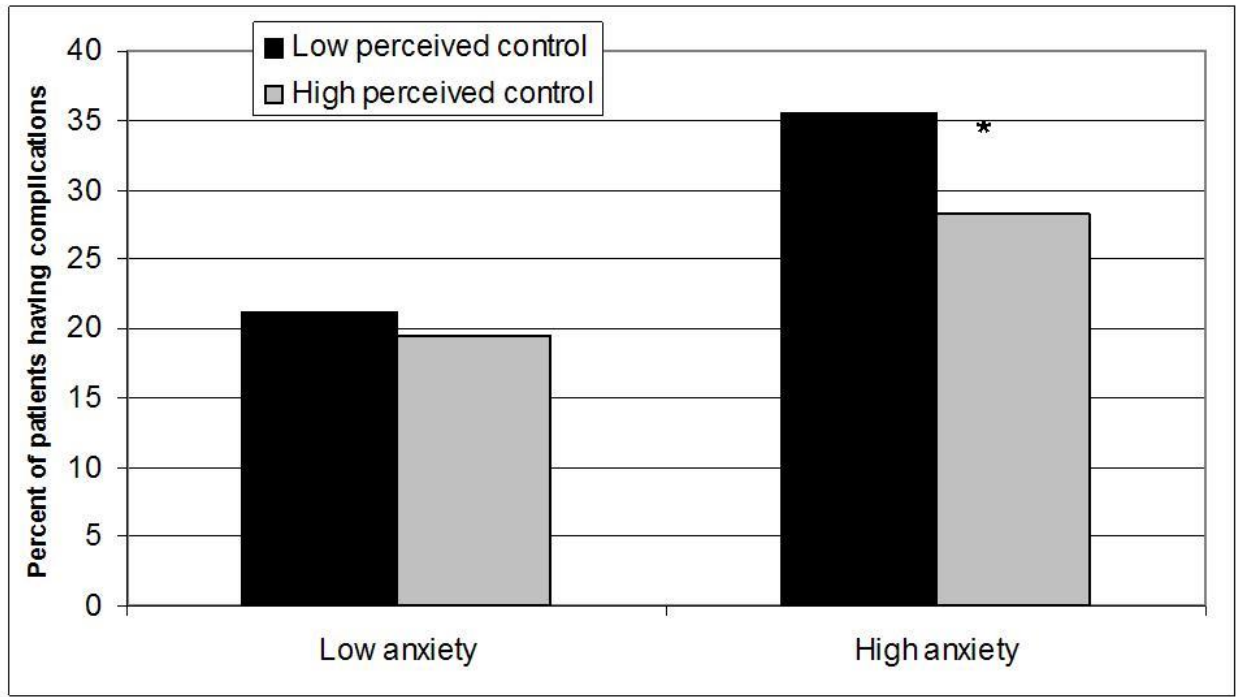
Figure 1.

Figure 2.

* p<0.01