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**MANIFESTATIONS OF HEALTH ANXIETY IN PATIENTS WITH HEART
TRANSPLANT**

Running head: Health anxiety in heart transplantation

Abstract

Background: Health anxiety is an important component of psychological adjustment to chronic medical conditions. However, it has been overlooked after heart transplantation.

Objectives: To examine demographic, clinical, and psychological correlates of health anxiety in heart transplanted patients and to compare health anxiety between patients and a sample of matched controls from the general population.

Methods: The study design was observational. Seventy-three cardiac recipients and 73 controls completed the Illness Attitude Scales and the Symptom Questionnaire. Patients' clinical parameters were collected.

Results: Health anxiety was significantly associated with clinical variables suggesting a worse outcome, especially a higher NYHA class and occurrence of cancer. Compared to controls, patients had significantly more "hypochondriacal responses" (32.9% vs 16.4%), an index of clinically significant health anxiety.

Conclusions: Health anxiety affects a significant subset of heart transplanted patients and deserves a thorough assessment. Cardiologists' and nurses' specific communication skills and psychological treatment strategies may be necessary.

Keywords: health anxiety; heart transplantation; hypochondriasis; Illness Attitude Scales; psychological distress.

Abbreviations: IAS, Illness Attitude Scales; NYHA, New York Heart Association; SQ, Symptom Questionnaire; VIF, Variance Inflation Factor.

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Introduction

Heart transplantation is a life-saving and widespread procedure for advanced heart failure and it is associated with an ever-increasing length of survival.¹ Although heart transplantation leads to a significant improvement in functional status, different complications may occur and many cardiac recipients have high levels of psychological distress.¹⁻⁴ The waiting list period is a very distressing stage of the transplantation program and, even after transplantation, sense of uncertainty often remains, since patients have still to cope with several sources of distress.⁵ Therefore, anxiety may be one of the most frequent emotional correlates of the transplantation program. Anxiety is a psychological state characterized by apprehension about the occurrence of some negative events. Anxiety encompasses cognitive (e.g., preoccupation about future troubles), emotional (e.g., worry about some life issues, such as work or family), and physiological (e.g., increased heart rate or sweating) symptoms. Anxiety disorders, such as generalized anxiety disorder and panic disorder, are characterized by excessive, enduring, and disabling anxiety symptoms. Both self-reported anxiety symptoms and anxiety disorders are worthy of attention in the field of cardiovascular disease, since they have been significantly associated with increased cardiovascular risk.^{6,7} The term health anxiety refers to the presence of anxiety focused on one's health status. Health anxiety frequently manifests itself as fear of developing a life-threatening illness. People with high levels of health anxiety have significant impairment and healthcare-related expenditures due to repeated medical visits.^{8,9}

Health anxiety also occurs in people with an existing medical condition, often leading to concerns about complications and recurrences. A certain degree of health anxiety is a normal response to a severe medical condition and it may promote regular attendance to follow-up visits and adherence to pharmacological treatments and lifestyle modification programs. However, health anxiety may also play a detrimental role in the adjustment to illness, especially for two reasons. First, health anxiety, when overwhelming, significantly impairs psychological quality of life, with patients having to cope with constant concerns. The second reason regards the most frequent behavioral

response to anxiety, namely avoidance. In the setting of medical disease, the mechanism of avoidance may lead to poor treatment adherence and low attendance to follow-up visits, since they remind the idea of one's illness. The presence of a medical condition is a frequent trigger for excessive health anxiety,^{8,10} which had a prevalence of about 20% in a sample of nearly 29,000 patients attending various outpatient clinics.¹¹

Therefore, health anxiety is an important issue to consider when examining psychological adjustment to a medical condition. In the field of heart disease, two independent studies documented a prospective association between untreated health anxiety and worse cardiac outcomes.^{12,13} Health anxiety significantly predicted an increased risk of ischemic heart disease in a large, community-based sample, independently of cardiovascular risk factors.¹² Furthermore, survivors to myocardial infarction with higher levels of cardiac anxiety had a significantly higher risk of major adverse cardiac events at a four-month follow-up.¹³

However, determining when health anxiety becomes "excessive" in response to an illness remains a challenge for psychological assessment in medical settings and detailed information about illness course and prognosis is necessary.

After heart transplantation, different factors may increase patients' health anxiety, especially the awareness of being at risk of both acute rejection and several complications (e.g., infections). Furthermore, the need to engage in a continuous clinical monitoring and the occurrence of new somatic symptoms, induced by the immunosuppressive treatment, may result in hypervigilance to bodily symptoms.^{14,15} Although after heart transplantation high levels of health anxiety may be understandable, they may negatively affect patients' quality of life and their adjustment to the new condition of cardiac recipients. However, there is a dearth of knowledge of health anxiety in the field of heart transplantation.

The aim of this study was to explore the manifestations of health anxiety in heart transplanted patients. In particular, we examined whether health anxiety significantly varies according to demographic characteristics as well as measures of clinical status and psychological adjustment to

heart transplantation. We also compared levels of health anxiety between patients and a sample of matched controls from the general population.

Methods

Participants and procedures

The clinical sample was recruited among the heart transplanted outpatients consecutively referred to the Cardiovascular Department of the [removed for anonymity] for routine follow-up. Patients were eligible for study inclusion if they (a) were more than 18-year old, (b) had been transplanted since at least six months, and (c) had adequate understanding of the Italian language. According to these inclusion criteria, 117 patients were eligible for the study and 95 of them agreed to participate in the study. Patients were invited by their cardiologists to participate in a study about psychological adjustment to heart transplantation. A sample of control subjects, matched for sex and age in decades with the cardiac recipients, was recruited from the general population. All the participants provided written informed consent after complete description of the study.

Measures

Health anxiety was assessed by means of the Italian version of Kellner's Illness Attitude Scales (IAS), a self-report questionnaire made of nine scales, assessing distinct attitudes, fears, and beliefs: *worry about illness, concerns about pain, health habits, hypochondriacal beliefs, thanatophobia, disease phobia, bodily preoccupations, treatment experience, and effects of symptoms*.¹⁶ Higher scores on the first seven scales, except for *health habits*, indicate more severe health anxiety. The *health habits* scale assesses the tendency to avoid smoking and unhealthy foods and to examine one's body to find something wrong. A high score on this scale does not necessarily correspond to greater severity of health anxiety. *Health habits* was the only IAS scale that did not significantly discriminate patients with a diagnosis of hypochondriasis from control subjects.¹⁷ The last two

scales were included to gather information about frequency of medical visits and treatments and the degree of impairment due to bodily symptoms.

Each scale is made of three items rated on a 5-point Likert scale ranging from “no” (scored 0) to “most of the time” (scored 4), with the score of each scale ranging between 0 and 12. Kellner also identified a “hypochondriacal response” pattern, characterized by a response “often” or “most of the time” on at least one of the items of the *hypochondriacal beliefs* and *disease phobia* scales.¹⁶ This response pattern has been used as a proxy for the hypochondriacal syndrome.¹⁷ The IAS have been used in several clinical settings and they sensitively discriminated hypochondriacal patients from normal controls, but also from populations sharing some clinical characteristics, such as non-somatizing psychiatric patients and non-hypochondriacal somatizers.¹⁷⁻¹⁹ The IAS total score showed a high test-retest reliability (~ 0.80). Furthermore, the IAS scores sensitively detected treatment-related changes in health anxiety.¹⁷⁻¹⁹

The Italian version of the Symptom Questionnaire (SQ) was administered to measure psychological distress.²⁰ The SQ contains four 23-item, self-report scales assessing anxiety, depressive, somatization, and hostility symptoms. Each item is made of an adjective or a very brief statement that can be rated as “yes/true” or “no/false”. In each scale 17 items describe symptoms of psychological distress and six items concern well-being.²⁰ The score of each scale may range from 0 to 23 and the higher is the score the more is the distress. The four SQ scales significantly discriminated between patients with psychiatric disorders and normal controls.^{20,21} Test-retest reliability of the SQ scores ranged between 0.71 and 0.95 and sensitivity to changes after treatment has also been proved.²⁰

The following clinical parameters were obtained by reviewing patients’ medical records: distance from transplantation, waiting list duration, functional status according to the New York Heart Association (NYHA) classification, and occurrence of cancer, diabetes, at least one acute rejection episode (graded as 2R or higher by endomyocardial biopsy), infectious events, re-hospitalization,

chronic renal insufficiency, and osteoporosis. Matched controls were asked to indicate in a demographic form whether they had some medical condition and to describe it, if any.

Statistical analyses

Analyses were performed with the SPSS statistical package 23.0 version (SPSS Inc., Chicago, Illinois). Categorical data are reported as percentages and dimensional data as means (standard deviation). The association between the IAS scores and age, distance from transplantation, waiting list duration, and the four SQ scores was examined by means of Pearson's product-moment correlation. Independent-samples t-test was used to assess whether the IAS scores significantly differed according to gender, NYHA class (I vs II or III), and occurrence of at least one acute rejection episode, diabetes, cancer, re-hospitalization, at least one infection, and chronic renal insufficiency. Eta squared values were calculated as measures of effect size for independent-samples t-test. The demographic, clinical, and psychological characteristics significantly associated with at least one of the IAS were then entered as the independent variables in a series of standard multiple regression analyses to identify their relative contribution to the variance in the IAS scores. Multicollinearity between the independent variables was examined by means of Tolerance and Variance Inflation Factor (VIF) values.

Significant differences between patients and matched controls on the IAS scores were assessed through independent-samples t-test. The two samples were also compared according to prevalence of the "hypochondriacal response" pattern on the IAS by means of chi-square test.

A p value ≤ 0.05 was considered significant. No adjustment for multiple comparisons was performed because of the exploratory nature of the study.

Results

Participants' characteristics

Scores on the IAS and the SQ were available for 73 out of the 95 patients who agreed to participate in the study. The remaining 22 patients were excluded from analyses since they did not complete both the questionnaires. Cardiomyopathy leading to heart transplantation was nonischemic for 49 patients (67.1%) and ischemic for the remaining 24 (32.9%). Table 1 shows participants' demographic and clinical characteristics. Twenty-seven matched controls (37%) reported at least one medical condition at the time of assessment, including hypertension, prostatitis, and allergy.

Association between IAS scores and demographic, clinical, and psychological characteristics in heart transplanted patients

Waiting list duration was inversely associated with the *health habits* scale, suggesting a greater tendency to avoid unhealthy lifestyles and to check one's body for something wrong in patients with a shorter waiting list ($r(64) = -0.30, p = 0.015$). Scores on the *health habits* scale were also significantly higher in patients without acute rejection episodes than those who had at least one acute rejection episode (9.67 ± 1.91 vs $8.20 \pm 2.45, t(69) = -2.15, p = 0.035, \eta^2 = 0.06$).

Patients with NYHA class II or III scored significantly higher on the *hypochondriacal beliefs* (2.50 ± 2.28 vs $0.96 \pm 1.77, t(69) = -3.04, p = 0.003, \eta^2 = 0.12$), *disease phobia* (4.00 ± 2.22 vs $2.26 \pm 2.86, t(69) = -2.45, p = 0.017, \eta^2 = 0.08$), and *effects of symptoms* (4.90 ± 2.96 vs $2.60 \pm 3.11, t(65) = -2.76, p = 0.008, \eta^2 = 0.10$) scales than patients with NYHA class I. Occurrence of cancer was significantly related to higher scores on the *bodily preoccupations* scale (7.00 ± 3.61 vs $3.38 \pm 2.27, t(69) = 2.64, p = 0.010, \eta^2 = 0.09$). Scores on the *treatment experience* scale were positively associated with age ($r(66) = 0.26, p = 0.032$) and inversely with distance from transplantation ($r(66) = -0.25, p = 0.039$). No significant difference was found on the IAS scores according to gender, re-hospitalization, occurrence of at least one infectious event, chronic renal insufficiency, and diabetes.

Except for the *health habits* and *treatment experience* scales, all the IAS scores were significantly associated with most of the SQ scales (Table 2).

In a series of standard multiple regression analyses each of the IAS scores was entered as the dependent variable. In all the analyses, the following demographic, clinical, and psychological characteristics were entered as the independent variables: age, distance from transplantation, waiting list duration, NYHA class, occurrence of at least one acute rejection episode, occurrence of cancer, and the four SQ scores. Variance in the IAS scores explained by these independent variables was as follows: 31.2% for *worry about illness* ($R^2=0.31$, adjusted $R^2=0.18$), 33.3% for *concerns about pain* ($R^2=0.33$, adjusted $R^2=0.21$), 21.4% for *health habits* ($R^2=0.21$, adjusted $R^2=0.07$), 33.4% for *hypochondriacal beliefs* ($R^2=0.33$, adjusted $R^2=0.21$), 39.6% for *thanatophobia* ($R^2=0.40$, adjusted $R^2=0.28$), 51.1% for *disease phobia* ($R^2=0.51$, adjusted $R^2=0.42$), 38.4% for *bodily preoccupations* ($R^2=0.38$, adjusted $R^2=0.27$), 24.0% for *treatment experience* ($R^2=0.24$, adjusted $R^2=0.09$), and 43.9% for *effects of symptoms* ($R^2=0.44$, adjusted $R^2=0.33$). Tolerance and VIF values excluded multicollinearity between the independent variables, with the former ranging between 0.267 and 0.916 and the latter between 1.092 and 3.747.

Significant correlates of the IAS scores were as follows: a shorter waiting list duration (standardized Beta= -0.34, $t= -2.52$, $p=0.015$) and absence of acute rejection episodes (standardized Beta=0.27, $t=2.10$, $p=0.040$) for *health habits*, occurrence of cancer (standardized Beta= -0.28, $t= -2.37$, $p=0.022$) and NYHA class II or III (standardized Beta=0.28, $t=2.18$, $p=0.034$) for *hypochondriacal beliefs*, higher levels of anxiety (standardized Beta=0.63, $t=3.10$, $p=0.003$) for *thanatophobia*, a longer distance from transplantation (standardized Beta=0.25, $t=2.45$, $p=0.018$) and higher levels of depressive symptoms (standardized Beta=0.36, $t=2.06$, $p=0.045$) for *disease phobia*, occurrence of cancer (standardized Beta= -0.25, $t= -2.20$, $p=0.032$) for *bodily preoccupations*, and older age (standardized Beta=0.35, $t=2.54$, $p=0.014$) and a shorter distance from transplantation (standardized Beta= -0.29, $t= -2.17$, $p=0.035$) for *treatment experience*.

Comparison of the IAS scores between heart transplanted patients and matched controls

Heart transplanted patients scored significantly higher than controls on the *health habits, treatment experience, and effects of symptoms* scales (Table 3). Effect sizes, expressed as eta squared values, for the three scales were: 0.08, 0.26, and 0.05. No significant difference was found on the other IAS scores.

Prevalence of subjects with at least one “hypochondriacal response” was significantly higher in cardiac recipients than matched controls (n=24, 32.9% vs n=12, 16.4%, $X^2=4.46$, $p=0.035$). Patients and controls provided a total of 35 and 22 “hypochondriacal responses”. Most of the patients’ “hypochondriacal responses” concerned the *disease phobia* scale: 17 regarded fear of heart disease, five fear of cancer, and four fear of another serious illness.

Discussion

To our knowledge, this is the first study specifically looking at the manifestations and correlates of health anxiety in heart transplanted patients. In multiple regression analyses, health anxiety was more likely to be associated with clinical variables than with psychological distress. Therefore, the presence of excessive health anxiety after heart transplantation should be carefully assessed, even when other psychopathological manifestations do not occur. This finding also confirms the high content validity of the IAS, whose scores are not affected by other psychological symptoms frequently associated with health anxiety, such as depressive and anxiety symptoms.^{17,18}

The significant association between the IAS scores and a worse functional status and the occurrence of cancer is consistent with a recent study, where cancer and a higher NYHA class were significantly related to cardiac recipients’ depression and psychological distress.⁴

The relationship between NYHA class and health anxiety may be mediated by patients’ symptom reporting. NYHA classification is based on the degree of functional limitation due to cardiovascular symptoms as reported by the patient. Health anxiety is often characterized by hypervigilance to physical symptoms, which may result in the amplification of even mild bodily sensations and a

higher likelihood to perceive them as bothersome.^{14,15} As a result, those heart transplanted patients who are more worried about their health may be more likely to report physical symptoms and thus to be classified in a higher NYHA class. In keeping with this hypothesis, in previous studies, symptom burden was positively associated with health anxiety in the general population²² and with depressive and anxiety symptoms in heart failure patients.^{23,24} However, the correlational design of our study does not allow firm conclusions about the direction of the relationship between functional status and health anxiety. It may also be that the more severe functional limitations make patients with a higher NYHA class more worried about their health.

The increased levels of health anxiety in patients who had to cope with cancer after heart transplantation seem to reflect the detrimental effect of cancer diagnosis on psychological well-being.²⁵

Patients with no acute rejection episodes and those with a shorter waiting list were more likely to engage in adaptive health-related behaviors, as assessed by the *health habits* scale. The waiting list period is a very distressing stage of the heart transplantation process, since advanced heart failure tends to worsen and availability of a suitable organ is not guaranteed. Thus, patients who had a shorter waiting list may be less psychologically distressed and more optimistic about their new condition of cardiac recipients, with positive effects on their adjustment to heart transplantation. In keeping with this hypothesis, a significant association between stress and maladaptive health-related behaviors has been documented,²⁶ while optimism is positively associated with the engagement in healthier cardiovascular-related behaviors.²⁷ Similarly, patients with no acute rejection episodes may be more likely to engage in adaptive health-related lifestyles because of higher optimism about the clinical course and confidence in the possibility to control their health.

The positive association between older age and higher *treatment experience* scores may reflect the relationship between aging and morbidity, leading to a greater healthcare utilization.²⁸ Although some gender-related differences in psychological adjustment to heart transplantation have been

reported,²⁹ in our study health anxiety did not vary according to gender. However, replication in larger samples is necessary.

Several explanations may be provided for the lack of significant group differences in most of the IAS scores. First, in our sample a good functional status (e.g., seven out of ten patients were in NYHA class I) and a low rate of major comorbidities (e.g., occurrence of cancer was 4%) could have reduced the risk of excessive health anxiety. Another explanation comes from Kellner et al.'s observation of less health anxiety in patients with chronic airflow obstruction than matched family practice patients.³⁰ According to Kellner and colleagues, the provision of continuous medical care, promoted by the physicians rather than asked by the patients, may play a reassurance role and prevent excessive health anxiety.³⁰ Patients attending the Cardiovascular Department after heart transplantation regularly undergo medical visits as part of their routine clinical monitoring and prompt treatments are provided in case of complications. Furthermore, the awareness of having successfully overcome a life-threatening condition (i.e., heart failure), a distressing waiting list period, and a transplantation procedure may have strengthened patients' resilience against health anxiety. Finally, despite the paucity of significant differences between groups, overall heart transplanted patients tended to score higher than controls. Therefore, it could be hypothesized that also the small sample size may partly explain the few significant differences.

The use of the "hypochondriacal response" pattern provided clinical information that would not have been detected by only comparing the IAS mean scores. An important percentage of patients had significant fears of heart disease, cancer or another serious illness. In the long run, these fears may lead to more severe manifestations of abnormal illness behavior and negatively affect the doctor-patient relationship. We did not evaluate whether patients with a "hypochondriacal response" pattern had a formal diagnosis of hypochondriasis, which is currently classified as somatic symptom disorder or illness anxiety disorder.³¹ However, it is unlikely that illness-related fears, as those identified by this response pattern, have spontaneous remission.³² Treatment of excessive health anxiety requires specific strategies and skills,^{33,34} and management of health

anxiety in patients with a medical condition may be very difficult, especially because reassurance may be useless. For instance, some kinds of reassurance were found to be detrimental in cancer patients in remission, especially in those with the highest levels of general anxiety.³⁵ Effectiveness of psychological interventions for health anxiety in patients from different medical settings has been demonstrated,³⁶ with benefits of cognitive-behavioral therapy lasting up to a five-year follow-up.³⁷ In the setting of heart transplantation, the use of interventions focused on meditation and promotion of well-being is particularly worthy of further research. Both a mindfulness-based stress reduction program and a mindfulness-based resilience training resulted in a significant decrease of psychological distress in solid organ transplant recipients.^{38,39} Meditation and mindfulness-based interventions also significantly improved physical and psychological quality of life in heart failure patients.⁴⁰⁻⁴²

Further studies should also examine whether health anxiety after heart transplantation may result from inadequate health literacy, which has been found in one third of cardiac recipients.⁴³ If so, the strengthening of cardiologists' and nurses' patient-centered communication and education strategies may be beneficial for the prevention and management of health anxiety during the heart transplantation program.^{43,44}

Limitations

Some limitations may reduce the generalizability of our findings. The first one is the small sample size. Further studies on this topic should involve larger samples to confirm our results. Second, the cross-sectional design did not allow to examine the course of health anxiety dimensions (e.g., whether they significantly vary over time according to changes in clinical status). Furthermore, patients who were too ill to attend the follow-up visit at the Cardiovascular Department cannot be included in the study. Levels of health anxiety found in our sample may be thus representative of the subset of heart transplanted patients with a better clinical outcome. Finally, despite the IAS are a valid and sensitive instrument, they do not examine health anxiety specifically related to heart

transplantation (e.g., fear of rejection or complications). Therefore, a certain underestimation of some transplantation-related worries cannot be excluded.

Conclusions

Overall, our study suggests that heart transplanted patients with a worse clinical outcome are at significantly increased risk of health anxiety. Health anxiety seems to be relatively independent of psychological distress and an important subset of cardiac recipients displayed significant fear of specific disease, identified by the IAS “hypochondriacal response” pattern. Therefore, health anxiety should be carefully examined during the psychosocial assessment of heart transplanted patients. Our findings highlight the need for further research on psychological treatments for excessive health anxiety in patients involved in the heart transplantation program. In particular, the application of meditation and mindfulness-based interventions would be worthy of further research.

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Table 1. Clinical and demographic characteristics

Characteristics	Patients (n = 73) Mean (SD) or %	Controls (n = 73) Mean (SD) or %
Gender (male)	83.6%	83.6%
Age (years)	55.9 (9.6)	56.5 ± 9.9
Marital status		
<i>Married or living as married</i>	80.8%	84.9%
<i>Single</i>	19.2%	15.1%
Educational status		
<i>Primary school</i>	42.5%	12.3%
<i>Lower secondary school or high school</i>	49.3%	79.5%
<i>University</i>	8.2%	8.2%
Employment status		
<i>Employed</i>	30.1%	46.6%
<i>Retired/Unemployed</i>	69.9%	53.4%
Distance from transplant (years)	4.4 (3.3)	
Waiting list duration (days)	101.4 (97.7)	
At least one acute rejection episode \geq 2R	78.9%	
NYHA classification		
<i>Class I</i>	70.8%	
<i>Class II</i>	27.8%	
<i>Class III</i>	1.4%	
Diabetes	12.5%	
Cancer	4.2%	
At least one re-hospitalization	43.8%	
At least one infection	39.7%	
Chronic renal insufficiency	5.5%	
Osteoporosis	2.7%	

Table 2. Correlations between the Illness Attitude Scales and the Symptom Questionnaire in heart transplanted patients

	Anxiety	Depression	Somatization	Hostility
Worry about illness	0.47***	0.40***	0.16	0.42***
Concerns about pain	0.53***	0.47***	0.22	0.42***
Health habits	0.10	0.08	-0.00	0.07
Hypochondriacal beliefs	0.26*	0.29*	0.36**	0.32**
Thanatophobia	0.56***	0.38***	0.28*	0.47***
Disease phobia	0.54***	0.55***	0.22	0.59***
Bodily preoccupations	0.53***	0.44***	0.32**	0.52***
Treatment experience	0.12	0.09	0.07	0.09
Effects of symptoms	0.53***	0.55***	0.40***	0.51***

* $p \leq 0.05$

** $p \leq 0.01$

*** $p \leq 0.001$

Table 3. Comparison between heart transplanted patients and matched controls on the Illness Attitude Scales

	Heart transplanted patients n = 73	Matched control subjects n = 73	<i>t</i>	<i>p</i>
Worry about illness	6.40 ± 3.20	5.89 ± 3.08	0.98	0.33
Concerns about pain	5.63 ± 2.58	5.11 ± 2.69	1.19	0.24
Health habits	8.51 ± 2.38	7.00 ± 2.91	3.43	0.001
Hypochondriacal beliefs	1.38 ± 2.02	0.89 ± 1.45	1.66	0.10
Thanatophobia	3.78 ± 3.86	3.53 ± 3.24	0.41	0.68
Disease phobia	2.71 ± 2.80	2.27 ± 2.91	0.92	0.36
Bodily preoccupations	3.49 ± 2.44	3.49 ± 2.30	-0.02	0.99
Treatment experience	7.15 ± 2.74	4.11 ± 2.35	7.08	<0.001
Effects of symptoms	3.21 ± 3.22	1.93 ± 2.58	2.58	0.01

Bold values indicate *p* values ≤0.05