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Symptom Frequency and Distress from 5 to 10 years after Heart Transplantation

Kathleen L. Grady, PhD, APN, FAAN,
Northwestern Memorial Hospital, Chicago, IL

Edward Wang, PhD,
Northwestern Memorial Hospital, Chicago, IL

Robert Higgins, MD,
Rush University Medical Center, Chicago, IL

Alain Heroux, MD,
Loyola University Medical Center, Maywood, IL

Bruce Rybarczyk, PhD,
Virginia Commonwealth University, Richmond, VA

James B. Young, MD,
The Cleveland Clinic, Cleveland, OH

Dave Pelegrin, RN, PA,
The Cleveland Clinic, Cleveland, OH

Jennifer Czerr, RN, BSN,
The Cleveland Clinic, Cleveland, OH

Jon Kobashigawa, MD,
UCLA Medical Center, Los Angeles, CA

Julie Chait, RN, BSN,
UCLA Medical Center, Los Angeles, CA

David C. Naftel, PhD,
University of Alabama, Birmingham, Birmingham, AL

Connie White Williams, MSN, FNP, FAAN,
University of Alabama, Birmingham, Birmingham, AL

Susan Myers, BA, and
University of Alabama, Birmingham, Birmingham, AL

James K. Kirklin, MD
University of Alabama, Birmingham, Birmingham, AL

Abstract

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Correspondence and reprint requests: Kathleen L. Grady, PhD, APN, Bluhm Cardiovascular Institute, Division of Cardiac Surgery, 201 E. Huron Street, Galter Pavilion, 11-140, Chicago, IL 60611, Telephone (312) 695-4860, Fax (312) 695-4860, e-mail kgrady@nmh.org.

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Background—Patterns of symptom frequency and distress have not been examined long-term after heart transplantation, nor have predictors of long-term symptom frequency and distress. This report identified the most commonly reported and distressful symptoms long-term after transplant, described patterns of symptom frequency and distress over time, and examined predictors of symptom frequency and distress at both 5 and 10 years after heart transplantation.

Methods—The sample included participants from a prospective, multi-site, longitudinal study of quality of life outcomes (n=555, 78% male, 88% white, 79% married, and mean age = 54 years at time of heart transplant). Data were collected using patient self-report and medical records review. Statistical analyses included descriptive statistics, Pearson correlations, t tests, and generalized linear models.

Results—Significant predictors of lower symptom frequency after heart transplantation were not having psychological problems and not having cardiac allograft vasculopathy at 5 years and not having psychological problems and not having infection at 10 years. Significant predictors of less symptom distress were having more than a high school education, having no psychological problems, and having gout at 5 years and being married at 10 years.

Conclusions—Symptom frequency is low, and symptom distress is moderate long-term after heart transplantation. Significant relationships exist between both demographic and clinical variables and symptom frequency and distress. Identification of the most common and bothersome symptoms after heart transplantation provides clinicians with important information from which to develop a plan of care.

After heart transplantation, heart failure symptoms are replaced by symptoms related to surgery, complications of transplant, and immunosuppression. The literature contains reports of symptom frequency and distress within the first 5 years post transplant,^{1–5} with some additional reports after 5 years post transplant.^{6–8} Jalowiec et al.¹ identified a decrease in heart failure related symptom distress and increase in symptom distress related to immunosuppression from before to early after heart transplantation. Other researchers have described transplant-related symptoms in long-term survivors of surgery.^{6–8}

Patterns of symptom frequency and distress have not been examined long-term after transplant, nor have predictors of long-term symptom frequency and distress. Therefore, the purposes of this report were to (1) identify the most commonly reported and most distressful symptoms at 5 and 10 years after heart transplantation, (2) describe patterns of symptom frequency and distress from 5 to 10 years after transplant, (3) describe differences in symptom frequency and distress by demographic and clinical variables at 5 and 10 years after transplant, and (4) identify predictors of symptom frequency and distress at both 5 and 10 years after heart transplantation.

Our exploration of symptoms in long-term heart transplant recipients was guided by Spilker and Revicki's⁹ model of quality of life, which demonstrates relationships among disease, treatments, and symptoms, and how they can influence domains of quality of life. Disease causes clinical symptoms, and treatment is directed at the underlying disease and symptom relief, recognizing that symptoms may also result from the treatment. Symptoms influence quality of life. We define a symptom as “a patient's perception of an abnormal physical, emotional, or cognitive state”.¹⁰

METHODS

Sample

Our sample includes participants from a prospective, multi-site, longitudinal study of quality of life. Patients who participated in our study were drawn from a pool of heart transplant recipients (n=1,437) (transplanted between July 1, 1990 and June 30, 1999) at 4 medical centers

across the U.S. We have previously described our inclusion criteria, sample size (including characteristics of enrolled versus non-enrolled patients), and reasons for non-enrollment.¹¹ Our final sample size was 555 heart transplant recipients who were between 5 and 10 years post transplant and completed our booklet of self-report instruments at one or more time periods.

Instruments and Procedures

For this report, we used the Heart Transplant Symptom Checklist.¹ This instrument was selected because our focus was on symptoms and their relationship with clinical variables. The 91-item instrument measures symptom frequency (yes/no) and symptom distress (0=not bothered at all and 3=very bothered). This tool has six subscales: cardiopulmonary, gastrointestinal, genitourinary, neurological, dermatologic/soft tissue, and psychological. The psychometric strength of this instrument has been previously reported.^{1, 12} The instrument demonstrated excellent validity (both content and construct validity) and reliability (internal consistency reliability), and is acceptable for use in the heart transplant population.

Additional data were collected from the patient and medical records. Demographic data (age, gender, race, marital status, and education) were recorded via patient self-report. Clinical data were collected from the patient's medical records and the Cardiac Transplant Research Database (CTRD), a voluntary heart transplant database in Birmingham, AL. Clinical data gathered included etiology of heart failure, United Network for Organ Sharing (UNOS) status at time of transplant, post transplant New York Heart Association (NYHA) class, co-morbidities and complications of immunosuppression (cardiovascular problems, diabetes, renal problems, gout, orthopedic problems, gastrointestinal problems, infection, malignancy, and psychological problems), complications of transplant (acute rejection and coronary allograft vasculopathy), post transplant medications, and hospital readmissions.

Each of the four medical centers received separate Institutional Review Board (IRB) approvals for conduct of our study and participation in the CTRD. Patients who agreed to join our study were given booklets of questionnaires every 6 months (based on the anniversary of their transplant) between 5 and 10 years post transplantation. Clinical data were also collected every 6 months.

Statistics

Before final statistical analysis, preliminary data were analyzed using univariate and graphical methods to facilitate inspection and interpretation of data. Data error due to data entry oversight was appropriately corrected. Each year's data were summarized using descriptive statistics and plotted over time. The degree of association between post transplant symptom frequency and distress was examined using Pearson correlations. Paired t-tests were conducted to assess change in symptom frequency and distress scores between 5 and 10 years post transplantation. Differences in symptom frequency and distress by demographics and clinical characteristics at 5 and 10 years were examined using 2-sample t-tests. Finally, generalized linear models (GLMs) were used to identify predictors of symptom frequency and distress at 5 and 10 years after heart transplantation. Significance was established at an alpha level of 0.05. All statistical analyses were performed using SAS 9.1 statistical software (SAS Inc., Cary, NC).

RESULTS

Descriptive Analyses

Demographic and clinical characteristics—Demographic and clinical characteristics of patients (n=555) are listed in table 1. Immunosuppressive medications were cyclosporine (84%) or tacrolimus (16%), mycophenolate mofetil (52%) or azathioprine (48%), and steroids, reflecting the state-of-the-art for immunosuppression when these patients were transplanted.

Cumulative 5 – 10 year rates of acute rejection and infection were 2.2 ± 2.0 and 0.8 ± 1.3 events per patient, respectively. Forty two percent of patients demonstrated evidence of cardiac allograft vasculopathy, as diagnosed by coronary angiography (between 5 and 10 years after transplant). Hospital re-admissions were uncommon with relatively short hospital lengths of stay (0.2 readmissions / patient and 2.7 days / admission, respectively).

Symptom frequency at 5 and 10 years after heart transplantation—The 30 most common symptoms at 5 and 10 years post transplant are listed in Table 2. Four of the five most frequent symptoms at 5 and 10 years after heart transplantation were memory problems, fatigue, easy bruising, cramps in the extremities, and difficulty in sexual performance. Over time, the mean scores for symptom frequency (overall and by subscale) declined then remained stable after 7 years post transplant (Figure 1). Overall mean symptom scores, gastrointestinal symptom scores, and psychological – emotional symptom scores were significantly lower at 10 years as compared to 5 years after heart transplantation (0.20 versus 0.23, $p = 0.03$; 0.19 versus 0.24, $p = 0.03$; and 0.16 versus 0.25, $p = 0.0007$, respectively) (range = 0 [no symptoms] to 1 [most symptoms]).

Differences in overall mean scores for symptom frequency were also analyzed by demographic and clinical characteristics (Table 3). At 5 and 10 years after transplant, women experienced significantly more overall symptoms than men (0.27 versus 0.22, $p = 0.04$ and 0.26 versus 0.18, $p = 0.03$, respectively). Further subscale analysis indicated that the differences were significant for only physical symptoms at 5 years (0.27 versus 0.22, $p = 0.04$) and for both physical and psychological symptoms at 10 years (0.26 versus 0.19, $p = 0.05$ and 0.25 versus 0.14, $p = 0.01$, respectively).

Differences in mean scores for symptom frequency were also detected by clinical characteristics of patients at both 5 and 10 years after transplant (Table 4). Patients who had psychological problems reported having more overall symptoms than patients who reported no psychological problems at both 5 and 10 years after transplant (0.30 versus 0.21, $p < 0.0001$ and 0.26 versus 0.18, $p = 0.04$, respectively). In addition, at 5 years after transplant, patients having gastrointestinal problems and acute rejection reported having more overall symptoms as compared to patients without these problems (0.27 versus 0.22, $p = 0.03$ and 0.25 versus 0.20, $p = 0.02$, respectively), while at 10 years, patients having infection reported higher symptom frequency scores than patients who did not (0.24 versus 0.16, $p = 0.009$).

Symptom distress at 5 and 10 years after heart transplantation—The 30 most distressful symptoms at 5 and 10 years post transplant are listed in Table 5. Similar to the most frequent symptoms, memory problems, fatigue, easy bruising, cramps in the extremities, and difficulty in sexual performance were the most distressful symptoms at both 5 and 10 year after heart transplantation. Over time, there was a steady decline in symptom distress (Figure 2). Overall symptom distress, overall physical distress, and distress related to gastrointestinal symptoms and psychological symptoms were significantly less at 10 years versus 5 years post transplant (0.51 versus 0.46, $p = 0.02$; 0.51 versus 0.47, $p = 0.04$; 0.53 versus 0.46, $p = 0.01$, and 0.50 versus 0.41, $p = 0.002$, respectively) (range = 0 [no symptom distress] to 1 [most symptom distress]).

Differences in symptom distress were also revealed by demographic and clinical characteristics (Table 3). Overall symptom distress was higher in younger versus older patients and less versus more educated patients at 5 years after transplant (0.54 versus 0.46, $p < 0.002$; 0.56 versus 0.48, $p = 0.0005$, respectively). At 10 years after transplant, differences in overall symptom distress were detected by race (Caucasian versus non-Caucasian) (0.54 versus 0.45, $p = 0.05$) and marital status (not married versus married) (0.54 versus 0.44, $p = 0.008$). Regarding clinical characteristics, patients who had no gout and had psychological problems reported more overall

symptom distress than patients who had gout and had no psychological problems at 5 years after transplant (0.52 versus 0.45, $p = 0.02$ and 0.57 versus 0.49, $p = 0.001$, respectively) (Table 4).

Correlations between symptom frequency and distress at 5 and 10 years after heart transplantation—Correlations between symptom frequency and symptom distress were determined at both 5 and 10 years after transplant (Table 6). At 5 years after transplant, all correlations were significant and ranged from 0.16 – 0.36. All 10 year post transplant correlations were significant except for genito-urinary symptoms. Significant correlations at 10 years after transplant were somewhat stronger and ranged from 0.26 – 0.44.

Multivariate analyses

Four separate GLMs were used to identify predictors of symptom frequency and distress at 5 and 10 years after heart transplantation. Sixteen independent variables including five demographic characteristics, nine comorbidities and complications of immunosuppression, and two complications of transplant were entered into each model. Significant predictors of lower symptom frequency at 5 years after heart transplantation were not having psychological problems and not having cardiac allograft vasculopathy and together with all variables in the model, accounted for 17% variance in symptom frequency (Table 7). At 10 years after transplant, not having psychological problems and not having infection were significant predictors of lower symptom frequency and together with all variables in the model, explained 23% of variance (Table 7).

Significant predictors of less symptom distress at 5 years after transplantation were having more than a high school education, having no psychological problems, and having gout which along with all variables in the model accounted for 20% of symptom distress (Table 8). Twenty three percent of symptom distress at 10 years after heart transplantation was explained by all variables in the model, with only marriage being significantly related to decreased symptom distress (Table 8).

DISCUSSION

The most frequently reported symptoms long-term after heart transplantation (at moderate rates of 50–65%) were fatigue, sexual dysfunction, memory problems, bruising, and cramps. They were also most frequently reported as distressful symptoms, but at significantly lower rates (16–22%). However, the mean symptom distress scores were higher than the mean symptom frequency scores. Our findings are influenced by demographic and clinical factors, as revealed by univariate and multivariate analyses at different times long-term after transplant. The rates of symptom frequency between 5 and 10 years after heart transplantation are fairly similar to rates of symptom frequency reported by other researchers.^{4, 5, 7, 8, 13} Regarding short and long-term symptom distress, our rates are also similar to those reported by others in the literature.^{3–5} The prevalence of symptom frequency and distress suggests that clinicians need to assess for frequently occurring and bothersome symptoms short and long-term in order to provide targeted treatment strategies. Furthermore, our previous finding of a significant relationship between less overall symptom distress and better quality of life supports the importance of symptom management after transplant.¹⁴

Two of the most frequently reported and most distressful symptoms, fatigue and sexual dysfunction, merit further discussion. We have previously reported the relationship between fatigue and lower quality of life.¹¹ Reyes et al⁶ reported high levels of fatigue in older post heart transplant women, also noting that mean fatigue scores were higher in depressed versus non-depressed women. Fatigue was associated with anemia and renal insufficiency in their study. These findings provide evidence regarding the importance of assessing fatigue long-

term after transplant and incorporating both physiological and psychological treatments, which may contribute to enhanced quality of life.

Sexual dysfunction may also have both physiological and psychological components. Similar to our findings, other researchers reported impairment in sexual function after transplant.^{4, 13, 15, 16} Medications, depression, body image, and changes in roles may contribute to sexual dysfunction after transplant.¹⁶ A majority of reports also identified decreased libido after transplant, similar to our results.^{4, 13, 16} Our findings of sexual dysfunction, reported almost two decades after some of these articles,^{4, 15, 16} suggest that this problem is still prevalent long-term after transplant and requires follow-up.

In our multivariable models, only two of the demographic variables, marital status and educational level, achieved significance and were related to symptom distress. Marriage after heart transplantation has been previously reported as being associated with better quality of life^{11, 13} and decreased mortality.¹⁷ To our knowledge, the relationship between having a spouse and decreased symptom distress has not been reported before. The association between being married and having lower symptom distress suggests that marriage may be a proxy for social support and/or social interaction and may moderate the symptom experience. Regarding education, perhaps having more education contributes to greater understanding of symptom occurrence and treatment, resulting in less symptom distress. Having more education is also related to being more satisfied with health and functioning between 5 and 10 years after heart transplantation.¹¹ However, we only measured level of overall education and not health-related education, which are different constructs. Understanding the relationships of marriage and education with symptom distress requires further exploration.

Clinical variables were also associated with symptom frequency and distress. The relationship between psychological problems and symptom frequency and distress long-term after heart transplantation is notable. We have previously described the relationship of depression with quality of life¹¹ and physical functional disability¹⁸ at 5 to 10 years post heart transplantation. Researchers have also reported that psychological distress may continue or increase at > 5 years after heart transplantation.^{19–22} Thus, long-term after heart transplant, psychological counseling remains an important therapeutic intervention. Gout was also a significant predictor in our multivariable model for symptom distress 5 years after heart transplantation, but the relationship was not in the expected direction, i.e., having more gout predicted less symptom distress. The direction of this relationship may have been influenced by other confounding factors and its fairly low incidence. In our previous reports, the relationship between gout and disability in ambulation approached significance at 5 years post transplant,²³ and gout was a significant predictor of satisfaction with health and functioning at 5–10 years after transplant.¹¹ Treatment of gout and control of symptoms may explain the unanticipated direction of the relationship in our model. More research is needed.

Limitations of our study include our survey of long-term survivors of heart transplantation who volunteered to participate in our study which may have contributed to underestimation of symptom frequency and distress. Fourteen percent of patients who did not join our study indicated they were too sick to participate (and perhaps had higher rates of symptoms and symptom distress). However, 12% of patients did not enroll in our study because they were too busy (and may have had lower rates of symptoms and symptom distress). These limitations may be attenuated by the fact that our sample was robust, drawn from four distinct geographical regions in the U.S. Our questionnaire completion rate was approximately 70%. In addition, our comparisons of symptom frequency and distress at 5 and 10 years after heart transplantation were from two mostly independent, pooled samples (only 11% of patients completed both 5 and 10 year surveys) which may have influenced our findings. However, we didn't find any significant differences in demographic and clinical characteristics between the two cohorts of

patients at 5 and 10 years post transplant. Another limitation of our study is that we may not have listed all relevant post-transplant symptoms in our questionnaire. However, we included open-ended questions regarding other symptoms, which had low reported frequencies.

CONCLUSIONS

We conclude that overall symptom frequency is low, and symptom distress is moderate long-term after heart transplantation. Furthermore, significant relationships exist between both demographic and clinical variables and symptom frequency and distress. Identification of the most common and bothersome symptoms after heart transplantation provides clinicians with important information on which to base development of a plan of care.

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Figure 1.
Symptom Frequency at 5 to 10 Years after Heart Transplantation

Figure 2.
Symptom Distress at 5 to 10 Years after Heart Transplantation

Table 1
Characteristics of Enrolled Patients

Characteristics	Enrolled in study (n = 555)
<i>Demographic characteristics</i>	
Age at transplant, years (mean $\pm$ SD)	53.8 $\pm$ 9.9
Gender (%)	
Male	78
Female	22
Race/ethnicity (%)	
White	88
Black	9
Hispanic	1
Other	2
Marital status (%)	
Married	79
Divorced/separated	11
Single	6
Widowed	4
Education	
High school (%)	59
Mean level of education (yrs)	14 $\pm$ 2.9
<i>Clinical characteristics</i>	
Etiology of heart failure (%)	
Ischemic cardiomyopathy	56
Dilated cardiomyopathy	32
Other	12
UNOS status 1A or 1B at time of transplant (%)	61
NYHA Class (between 5–10 years after transplant) (mean)	1.3
Comorbidities (%)	
Hypertension	87
Hyperlipidemia	78
Renal dysfunction	37
Cancer (including skin cancer)	27
Diabetes	27
Orthopedic problems	26
Psychological problems	23
Gastrointestinal problems	22
Gout	18
Genitourinary problems	12

UNOS, United Network for Organ Sharing

NYHA, New York Heart Association

Table 2
Most Commonly Reported Symptoms at 5 and 10 Years Post HT

5 Years Post HT		10 Years Post HT	
Symptom	Percent	Symptom	Percent
trouble remembering	64.2%	tiredness	59.1%
tiredness	62.1%	cramps hands feet legs	59.1%
easy bruising	59.0%	easy bruising	52.7%
cramps hands feet legs	58.6%	swelling legs / feet	50.0%
irritability	51.4%	trouble remembering	49.1%
difficulty in sexual performance	50.7%	difficulty in sexual performance	47.3%
sensitive or fragile skin	49.8%	sensitive or fragile skin	47.3%
weight gain	43.4%	difficulty sleeping	40.9%
mood swings	42.0%	sleepiness	38.2%
swelling legs / feet	41.5%	tremors shaking hands / body	38.2%
difficulty sleeping	41.0%	diff breathing when walking doing	36.4%
decreased sexual desire	40.8%	weakness whole body	35.5%
incision pain	40.6%	incision pain	34.5%
weakness legs	40.1%	coughing	32.7%
tremors shaking hands / body	38.7%	decreased sexual desire	32.7%
sleepiness	37.3%	nervousness	32.7%
nervousness	37.3%	irritability	30.9%
feeling depressed	37.3%	bloated feeling	30.0%
bloated feeling	35.8%	weight gain	30.0%
weakness whole body	35.5%	weakness legs	30.0%
excessive hairiness	35.4%	dizziness	29.1%
trouble concentrating	34.9%	overeating	28.2%
blurred or unclear sight	34.4%	mood swings	27.3%
diff breathing when walking doing	34.0%	cold feeling hands / feet	26.4%
overeating	34.0%	headache	26.4%
cold feeling hands/feet	32.5%	feeling depressed	26.4%
burning throbbing numb	32.1%	constipation	25.5%
feeling sad	32.1%	excessive hairiness	25.5%
diarrhea or loose bowels	31.6%	acne	25.5%
feeling anxious or apprehensive	31.6%	fast heart rate	24.5%

HT = heart transplantation

Table 3
Symptom Frequency and Distress by Demographic Characteristics at 5 and 10 Years Post HT

	5 Year Total Symptom Frequency	5 Year Total Symptom Distress	10 Year Total Symptom Frequency	10 Year Total Symptom Distress
Age				
< 60 (n=130)	0.25	0.54	0.20	0.47
≥ 60 (n=80)	0.21	0.46	0.19	0.43
p value ^a	0.061	0.002	0.574	0.254
Gender				
Male (n=168)	0.22	0.50	0.18	0.46
Female (n=42)	0.27	0.55	0.26	0.48
p value	0.038	0.077	0.029	0.628
Race				
Caucasian (n=193)	0.24	0.51	0.19	0.45
Non-Caucasian (N=17)	0.21	0.48	0.24	0.54
p value	0.621	0.640	0.192	0.047
Marital status				
Married (n=162)	0.23	0.52	0.18	0.44
Not married (n=48)	0.24	0.48	0.25	0.54
p value	0.884	0.220	0.074	0.008
Education				
≤ high school (n=83)	0.24	0.56	0.21	0.48
> high school (n=127)	0.23	0.48	0.19	0.45
p value	0.411	0.001	0.550	0.257

^aTwo sample t-test

Table 4
Symptom Frequency and Distress by Clinical Characteristics at 5 and 10 Years Post HT

	5 Year Total Symptom Frequency	5 Year Total Symptom Distress	10 Year Total Symptom Frequency	10 Year Total Symptom Distress
Diabetes				
Yes (n=65)	0.25	0.53	0.20	0.43
No (n=143)	0.23	0.50	0.19	0.47
p value ^a	0.270	0.202	0.775	0.302
Orthopedic problems				
Yes (n=43)	0.24	0.53	0.22	0.50
No (n=165)	0.23	0.50	0.18	0.45
p value	0.962	0.430	0.203	0.110
Gout				
Yes (n=37)	0.25	0.45	0.18	0.43
No (n=171)	0.23	0.52	0.20	0.47
p value	0.555	0.019	0.703	0.274
Cardiovascular problems				
Yes (n=39)	0.25	0.51	0.20	0.49
No (n=169)	0.23	0.51	0.19	0.46
p value	0.454	0.903	0.819	0.42
Oncologic problems				
Yes (n=47)	0.25	0.49	0.19	0.45
No (n=161)	0.23	0.52	0.20	0.47
p value	0.281	0.308	0.714	0.430
Gastrointestinal problems				
Yes (n=47)	0.27	0.54	0.23	0.47
No (n=161)	0.22	0.50	0.19	0.46
p value	0.034	0.202	0.271	0.936
Renal problems				
Yes (n=79)	0.25	0.51	0.21	0.47
No (n=129)	0.23	0.51	0.18	0.46
p value	0.315	0.815	0.413	0.680
Psychological problems				
Yes (n=52)	0.30	0.57	0.26	0.53
No (n=156)	0.21	0.49	0.18	0.45
p value	<.0001	0.001	0.041	0.053
Rejection				
Yes (n=153)	0.25	0.52	0.20	0.47
No (n=57)	0.20	0.49	0.20	0.44
p value	0.023	0.295	0.993	0.423
Infection				
Yes (n=92)	0.23	0.53	0.24	0.47
No (n=118)	0.24	0.49	0.16	0.45
p value	0.808	0.075	0.009	0.480
CAD				
Yes (n=74)	0.26	0.51	0.21	0.49
No (n=136)	0.22	0.51	0.18	0.43
p value	0.074	0.794	0.383	0.073

^aTwo sample t-test

Table 5
Most Symptoms Reported as Distressful at 5 and 10 Years Post HT

5 Years Post HT		10 Years Post HT	
Symptom Distress	Percent	Symptom Distress	Percent
trouble remembering	21.8%	tiredness	22.4%
tiredness	20.8%	Cramps hands feet legs	21.0%
cramps hands feet legs	19.5%	trouble remembering	17.1%
easy bruising	18.3%	difficulty sexual perform	16.4%
irritability	17.3%	swelling legs / feet	16.4%
difficulty sexual perform	17.0%	easy bruising	16.4%
sensitive or fragile skin	16.3%	sensitive or fragile skin	16.1%
with weight gain	15.0%	difficulty sleeping	15.7%
difficulty sleeping	14.5%	sleepiness	14.3%
mood swings	14.5%	breathing when walking doing	13.3%
weakness legs	14.0%	weakness whole body	13.3%
pain incision site	13.8%	tremors shaking hands / body	12.6%
swelling legs / feet	13.6%	pain incision site	12.6%
decreased sexual desire	13.1%	degree of coughing	11.9%
nervousness	13.0%	decreased sexual desire	11.5%
tremors shaking hands / body	12.8%	with bloated feeling	11.2%
feeling depressed	12.5%	nervousness	10.8%
with bloated feeling	12.3%	weakness legs	10.5%
weakness whole body	12.3%	irritability	10.5%
sleepiness	12.3%	mood swings	10.5%
trouble concentrating	12.1%	with weight gain	10.1%
breathing when walking doing	12.0%	dizziness	10.1%
blurred or unclear sight	12.0%	with overeating	9.8%
with overeating	11.0%	cold feeling hands / feet	9.8%
feeling anxious or apprehens	10.8%	headache	9.4%
feeling sad	10.8%	acne	9.4%
cold feeling hands / feet	10.5%	feeling anxious or apprehens	9.1%
with diarrhea loose bowel	10.3%	with constipation	8.7%
burning throbbing numb	10.3%	feeling depressed	8.7%
feeling restless passing out	9.8%	feeling restless passing out	8.4%

HT = heart transplantation

Table 6
Correlations Between Symptom Frequency and Symptom Distress at 5 and 10 Years Post HT

Symptom Distress	Symptom Frequency					
	5 Years Post HT					
	Total symptoms	Overall physical symptoms	Cardio-pulmonary symptoms	Gastro-intestinal symptoms	Genito-urinary symptoms	Sens-cog-neur-musc symptoms
Total symptoms	0.36					
Overall physical symptoms		0.35				
Cardiopulmonary symptoms			0.21			
Gastrointestinal symptoms				0.16		
Genito-urinary symptoms					0.29	
Sen-cog-neur-musc symptoms						0.35
Derm-soft tissue symptoms						0.31
10 Years Post HT						
Total symptoms	0.44					
Overall physical symptoms		0.42				
Cardiopulmonary symptoms			0.43			
Gastrointestinal symptoms				0.36		
Genito-urinary symptoms					0.11	
Sen-cog-neur-musc symptoms						0.39
Derm-soft tissue symptoms						0.26

Correlations bolded are significant (p<0.05)
HT = heart transplantation

Table 7
Generalized Linear Model of Symptom Frequency at 5 and 10 Years post HT

	Total symptom frequency at 5 years		Total symptom frequency at 10 years	
	Standardized coefficient	p value	Standardized coefficient	p value
Age	-1.718	0.087	-0.744	0.459
Gender (Female)	1.840	0.067	1.256	0.212
Race (Non-white)	-0.685	0.494	0.695	0.489
Marital status (Married)	0.599	0.550	-1.907	0.060
Education (< High school)	0.798	0.426	0.931	0.354
Diabetes (No)	-1.251	0.213	-0.245	0.807
Orthopedic problems (No)	-0.416	0.678	-0.576	0.566
Gout (No)	-0.168	0.867	0.541	0.590
Cardiovascular problems (No)	0.075	0.940	0.715	0.477
Oncologic problems (No)	-1.134	0.258	-0.435	0.664
Gastrointestinal problems (No)	-1.009	0.314	-1.382	0.170
Renal problems (No)	-1.339	0.182	-1.234	0.221
Psychological problems (No)	-3.623	<0.001	-2.074	0.041
Rejection (No)	-0.711	0.478	0.344	0.732
Infection (No)	0.805	0.422	-2.695	0.008
CAD (No)	-2.053	0.041	-0.977	0.331
R ²	0.1732		0.2340	

Table 8
Generalized Linear Model of Symptom Distress at 5 and 10 Years post HT

	Total symptom distress at 5 years		Total symptom distress at 10 years	
	Standardized coefficient	p value	Standardized coefficient	p value
Age	-1.683	0.094	-0.282	0.779
Gender (Female)	1.472	0.143	-0.934	0.353
Race (Non-white)	-0.635	0.526	1.771	0.080
Marital status (Married)	1.880	0.062	-2.380	0.019
Education (< High school)	3.452	0.001	1.224	0.224
Diabetes (No)	-0.967	0.335	0.885	0.379
Orthopedic problems (No)	-0.775	0.439	-1.555	0.123
Gout (No)	2.065	0.040	1.058	0.293
Cardiovascular problems (No)	0.203	0.839	-0.975	0.332
Oncologic problems (No)	1.063	0.289	-0.145	0.885
Gastrointestinal problems (No)	-0.661	0.509	0.191	0.849
Renal problems (No)	-0.447	0.655	-0.994	0.323
Psychological problems (No)	-2.751	0.007	-1.923	0.058
Rejection (No)	0.119	0.906	0.011	0.991
Infection (No)	-1.773	0.078	-1.120	0.266
CAD (No)	-0.947	0.345	-1.514	0.134
R ²	0.1963		0.2341	