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Accuracy of anxiety and depression screening tools in heart transplant recipients

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Abstract

Purpose

The aim of this study was to assess the validity and reliability of psychological screening tools in outpatient heart transplant recipients.

Methods

Forty-eight heart transplant recipients completed the Patient Health Questionnaire 9-item scale (PHQ-9), Generalized Anxiety Disorder 7-item Scale (GAD-7), Kessler Psychological Distress 10-item Scale (K-10) and Medical Outcomes Short Form 36-item Health Survey. A structured psychological interview (Mini International Neuropsychiatric Interview Version 6) was conducted after completion of the questionnaires. Internal consistency, criterion validity and construct validity of the PHQ-9, GAD-7 and K-10 were evaluated.

Results

Internal consistency supported the reliability of the screening tools. The optimal cut-off on the PHQ-9 for depression was 10 (sensitivity=0.86; specificity=0.93). A score of 6 on the GAD-7 maximised sensitivity (0.75) and specificity (0.89) for anxiety. A score of 17 on the K-10 was the optimal cut-off for diagnosis of either anxiety or depression (sensitivity=0.83; specificity=0.84). Increasing scores on the screening tools were associated with lower health-related quality of life.

Conclusion

Psychometric analyses support the reliability and validity of the PHQ-9, GAD-7 and K-10 as screening tools for detection of anxiety and depression in heart transplant recipients.

Keywords

Heart transplant, depression, anxiety, quality of life

Psychological disorders, such as anxiety and depression, are common after heart transplantation.[1-4] A recent study reported that the risk for post heart transplant major depression was 41% and post-traumatic stress disorder (PTSD) 13%.[5] Post-transplant anxiety and depression requires treatment because of the negative impact of these disorders on quality of life and association with increased morbidity and mortality.[6, 7] Although strong evidence regarding the effectiveness of interventions for post-transplant depression and anxiety is lacking,[8] specialized treatment from a multidisciplinary team is recommended by the International Society for Heart and Lung Transplantation (ISHLT).[9]

To deliver specialized treatment for psychological disorders, heart transplant recipients affected by anxiety or depression must first be identified. In most circumstances, routine psychological evaluation for all recipients by a specialist is not feasible in clinical practice. Moreover, self-reporting of psychological distress is not common.[10] Identification of psychological disorders can be aided with screening tools that identify patients who have a likelihood of a psychological disorder. In this regard, the ISHLT[9] recommends that depressive symptoms should be regularly evaluated during follow-up with user-friendly, validated screening instruments. Although the ISHLT guidelines focus on recognition and referral for treatment of depression specifically, we propose that screening for anxiety disorders would also be worthwhile in clinical practice due to the considerable prevalence and negative consequences of these disorders in heart transplant recipients.[1]

Despite the potential benefits of routine evaluation of the presence of psychological distress for heart transplant recipients, the psychometric properties of screening tools for the detection of depression and anxiety have not been evaluated in this population. To assist implementation of screening and referral for specialist treatment of post-transplant psychological disorders, the aim of this analysis was to assess the validity and reliability of

self-administered questionnaires to screen for post heart transplant anxiety and depression in heart transplant recipients.

Patients and Methods

A single-site, cross-sectional study was conducted to assess the psychometric properties of screening tools for the detection of anxiety and depression in heart transplant recipients. Human research ethics committee and institutional approval was granted for the study and it was registered prospectively with the Australian New Zealand Clinical Trials Registry (ACTRN12613000740796). Internal consistency was used to test the reliability of the screening tools. Criterion validity was assessed by comparing results from the screening tools with a standard diagnostic tool for detection of psychological disorders. Construct validity was evaluated by testing hypotheses derived from previous research regarding the associations between psychopathology and quality of life. It was hypothesised that the heart transplant recipients who reported greater severity of psychological symptoms on the screening tools would also report lower health-related quality of life.

Patients

Heart transplant recipients over 18 years of age who attended the outpatient clinic at a major metropolitan hospital in Australia were eligible to participate in the study. Patients who were less than three months post-transplant as well as those who were cognitively impaired (as confirmed by a treating clinician), unable to understand and speak English, had a diagnosed major psychiatric comorbidity (schizophrenia, bipolar disorder, dementia) or terminal illness were excluded.

Data collection

Data concerning demographics and clinical characteristics were collected from medical records. Psychological symptom experience and quality of life data were collected from

participants using self-report questionnaires. Questionnaires were completed by participants while waiting for their appointment at the outpatient clinic. A research assistant was available to provide clarification about any of the items contained within the questionnaire. A structured psychological interview was conducted over the phone by a provisional psychologist undertaking a Doctor of Clinical Psychology degree after the initial screening. The psychologist was blinded to the results of the screening questionnaires.

Measures

Mini International Neuropsychiatric Interview version 6.0 (MINI 6.0)

The MINI 6.0 is a short structured diagnostic interview for psychiatric disorders as included in the 4th version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the 10th version of the International Classification of Diseases (ICD-10).[11] It consists of 120 questions and screens 17 axis I disorders for 24 current and lifetime diagnoses. Current is defined as experiencing symptoms associated with the disorder within the past month for all disorders except generalized anxiety disorder and substance abuse disorders. In a validation study, which enrolled 370 participants, sensitivity of the MINI was 0.7 and specificity was 0.85 with the Structured Clinical Interview for DSM-III (SCID-P).[12] Inter-rater reliability between interviewers was excellent in this study, with the kappa score for the majority (16/23) of modules being over 0.9.[12]

Patient Health Questionnaire 9-item scale

The Patient Health Questionnaire 9-item scale (PHQ-9) is a brief self-report measure of depression.[13] Participants were asked to consider the preceding two weeks and rate symptom frequency as not at all (0), several days (1), more than half of all days (2) or nearly all days (3).

Generalized Anxiety Disorder 7-item scale

The Generalized Anxiety Disorder 7-item scale (GAD-7) is a self-reported measure of anxiety. Higher scores indicate higher levels of anxiety. Participants were asked to consider the preceding two weeks and rate symptom frequency as not at all (0), several days (1), more than half of all days (2) or nearly all days (3). The GAD-7 has high internal consistency ($\alpha=0.92$) and is strongly correlated with the Beck Anxiety Inventory (Spearman's correlation coefficient=0.72).[14]

Kessler Psychological Distress Scale (K-10)

The Kessler Psychological Distress Scale (K-10) is a brief self-report measure of psychological distress, which is used frequently in research and clinical practice to screen for psychological disorders. This 10-item scale measures severity of anxiety and depression symptoms using a 5-point Likert type scale. It has been shown to strongly discriminate between community cases and non-cases of DSM-IV psychological disorders.[15]

Medical Outcomes Short Form-36 Health Survey

The Medical Outcomes Short Form-36 Health Survey (SF-36) yields an 8-scale profile of self-reported functional health and well-being. Higher scores indicate a better health status. [16] The domains of quality of life measured by the SF-36 are physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain and general health.

Statistical analysis

Formal sample size calculation was not conducted. Descriptive statistics were generated using STATA version 13 (Statacorp, Texas, USA). Frequencies, means and standard deviations (SD) were used to describe demographic, clinical and symptom characteristics. Reliability was measured as internal consistency using Cronbach's alpha. Receiver Operating

Characteristics with the MINI as the criterion were calculated to assess criterion validity of GAD-7, PHQ-9 and K-10 results. MINI diagnoses of ‘major depression (current or recurrent)’, ‘major depression with melancholic features’ and ‘dysthymia’ were used as the criterion standard for evaluation of the validity of the PHQ-9. For the GAD-7, MINI diagnoses of ‘panic disorder’, ‘agoraphobia’, ‘panic disorder with agoraphobia’, ‘agoraphobia without a history of a panic disorder’, ‘social disorder (generalised or non-generalised)’, ‘post-traumatic stress disorder’ and ‘generalised anxiety disorder’ were used. As the K-10 is a non-specific measure of psychological distress, the presence of either anxiety or depression MINI diagnoses was used as the criterion. The Liu method was used to identify the optimal cut-point that maximised the sensitivity and specificity of the screening tools in the detection of psychopathology. Hierarchical regression (controlling for demographic and clinical characteristics) was used to assess whether the severity of psychological symptoms, as measured by the screening tools, was associated with quality of life. A Bonferroni correction was applied to account for multiple comparisons made from the same dataset. A p -value of <0.002 ($0.05/24$) was considered statistically significant.

Results

From January to September 2014, 48 participants completed the screening questionnaires (PHQ-9, GAD-7 and K-10) as well as the structured psychological interview (MINI). The sample comprised mostly of long-term survivors of heart transplantation (median 9 years post-transplant) who were predominantly male ($n=37$; 76%). An overview of demographic and clinical characteristics for the overall sample and those participants who completed the structured psychological interview (MINI) is presented in Table 1. A moderate prevalence of both depression ($n=7$; 14%) and anxiety disorders ($n=8$; 16%) was identified.

Reliability

The Cronbach's alpha for each of the screening tools indicated that internal consistency was adequate (0.88 for PHQ-9, 0.86 for K-10 and 0.91 for GAD-7).

Criterion validity

The optimal cut-off point on the PHQ-9 that maximised the sensitivity (0.86) and specificity (0.93) for diagnosis of depression was a score of 10 (Area under Receiver Operating Characteristic Curve [AUC] = 0.89). A score of 6 on the GAD-7 maximised the sensitivity (0.75) and specificity (0.89) for diagnosis of an anxiety disorder (AUROC=0.82). For the K-10, which non-specifically measures psychological distress, a score of 17 maximised the sensitivity (0.83) and specificity (0.84) for diagnosis of either anxiety or depression (AUROC=0.84).

Construct validity

Quality of life

Associations between the screening tools and health-related quality of life were investigated using hierarchical regression, accounting for age, gender, number of years post-transplant, number of medical comorbidities, presence of chronic allograft vasculopathy and presence of an oncology illness (Table 2). Increasing scores on the PHQ-9 were associated with lower quality of life in the role limitations due to physical health, role limitations due to emotional problems, energy/fatigue and emotional wellbeing domains of the SF-36. The GAD-7 was associated with lower quality of life in the emotional well-being domain of the SF-36. Participants' quality of life ratings in the role limitations due to emotional problems, energy/fatigue and emotional well-being domains of the SF-36 also decreased with increasing scores on the K-10.

Discussion

Results of our psychometric analyses supported the reliability and validity of the PHQ-9, GAD-7 and K-10 as screening tools for detection of anxiety and depression in a sample comprised predominantly of male long-term survivors of heart transplantation. The prevalence of depression in our study was consistent with previous research, which supports the generalizability of our results. Previous reports identified prevalence of depression from 15.8% to 41% in heart transplant recipients.[5, 6] In contrast, the prevalence of PTSD in our sample (2%; $n=1$) was not as high as it has been previously reported. The most recent study reported a prevalence of PTSD in a sample of 107 heart transplant recipients at 13%.[5] This estimate is consistent with previous literature.[6, 17] Due to the low prevalence of this specific anxiety disorder in our sample, further studies utilising larger sample sizes should be undertaken to confirm the validity of the GAD-7 or K-10 in detecting PTSD in heart transplant recipients. Nevertheless, it should be noted that studies conducted with other populations have confirmed that both of these tools have a high sensitivity and specificity for detection of PTSD.[18-20] For this reason, results of the current study that demonstrated the GAD-7 and K-10 have a high sensitivity and specificity for the detection of various anxiety disorders in a sample of heart transplant recipients should not be disregarded solely due to the low prevalence of PTSD that was observed.

A higher score was required on the PHQ-9 to maximise the sensitivity and specificity of this tool in the detection of depression compared with some other populations that have been studied. For example, a score of more than 4 on the PHQ-9 was deemed to be the optimal cut-off to identify major depression in a sample of in-patients diagnosed with acute coronary syndrome.[21] Potentially, greater severity of somatic symptoms contained within the PHQ-9 not caused by depression, such as fatigue and sleep disturbance, was present in the heart transplant recipients included in our sample compared with a typical ACS population. It has

been identified previously that PHQ-9 scores may include a small amount of variance from somatic symptoms not related to depression.[22]

Our hypothesis that greater severity of psychological symptoms measured by the PHQ-9, GAD-7 and K-10 would be associated with lower quality of life was supported. Lower scores in various quality of life domains relevant to psychological symptoms measured by the SF-36, such as role limitations due to emotional problems and emotional well-being, were significantly associated with increasing scores on the screening tools. This finding was aligned with previous population-based studies that identified significant associations between psychological symptom severity (measured by the screening tools evaluated in our study) and all domains of the SF-36 using Pearson correlation.[23] Using hierarchical multivariate linear regression to adjust for demographic and clinical variables was a strength of our study. By controlling for these variables, we were able to identify the specific domains of quality of life that were more strongly influenced by psychological symptoms.

Larger multi-centre studies would be required to increase confidence in our results, as the analyses were conducted with a small number of heart transplant recipients from one transplantation centre. Employing a longitudinal design in future studies would facilitate evaluation of the sensitivity to change of the screening tools. As heart transplant recipients suffering from anxiety or depression might be less inclined to participate in research,^[24] selection bias might have impacted the prevalence of anxiety and depression in our study. There was not an exact overlap between the recall periods for the GAD-7 (two weeks) and the time frame for anxiety disorders assessed by the MINI (one month). However, psychological distress associated with chronic conditions such as heart transplantation would not likely change over this short period of time.^[17] As such, it is unlikely that the slightly different recall periods would have significantly influenced the validation of the GAD-7. It should also be noted that as the screening tools were presented to participants in the same

order, there was the potential for bias related to a sequential priming effect. As such, future studies focused on validation of anxiety and depression screening tools for heart transplant recipients should consider presenting the tools to participants in a random order. It should also be noted that other aspects of the validity and reliability of the screening tools, such as test-retest reliability for example, could be assessed in future studies.

In conclusion, consistent with previous studies undertaken with other populations, results of our psychometric analyses supported the reliability and validity of the PHQ-9, GAD-7 and K-10 in a sample of heart transplant recipients. For this reason, nurses and other clinicians who apply the ISHLT recommendations regarding screening for psychological disorders during routine follow-up of heart transplant recipients of a similar profile to participants included in our study can be confident that these tools will identify cases with a high degree of accuracy. However, further larger-scale studies investigating the clinical and cost-effectiveness of screening and referral for psychological treatment in heart transplant recipients should also be considered.

Disclosures

None

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Table 1 Demographic and clinical characteristics

Variable	Mean (SD), Median (IQR) or Count (%) Total n=48
Age	63 (55,67)
Male	37 (76)
Time since transplant	9(2.5, 18)
Ischaemic aetiology of heart failure	15 (31)
Cancer (including skin cancer)	19 (39)
Chronic allograft vasculopathy	3 (6)
Current acute rejection	0 (0)
Taking anti-depressants	9 (18)
Fit criteria for any current depressive disorder	7(14) ^a
Major depression (current)	5(10)
Major depression (recurrent)	3(6)
Major depression with melancholic features	2(4)
Dysthymia	1(2)
Fit criteria for any current anxiety disorder	8 (16)
Current panic disorder	0(0)
Current agoraphobia	3(6)
Panic disorder without agoraphobia	0(0)
Panic disorder with agoraphobia	0(0)

Social anxiety disorder	1(2)
(generalized)	
Social anxiety disorder (non-	0(0)
generalized)	
Generalized anxiety disorder	4(8)
Post traumatic disorder	1(2)

MINI=Mini International Neuropsychiatric Interview; SD=Standard deviation.

Table 2 Associations between psychological symptoms and health-related quality of life by hierarchical multiple regression

SF-36 domains	PHQ-9					GAD-7					K-10				
	β	95% CI	R ²	R ² Change _a	p-value	β	95% CI	R ²	R ² Change _a	p-value	β	95% CI	R ²	R ² Change _a	p-value
Physical functioning	-1.79	-3.46 to -0.12	0.25	0.08	.04	0.73	-1.65 to 3.11	0.18	0.01	0.54	-1.00	-2.59 to 0.57	0.20	0.03	0.21
Role limitations due to physical health	-4.26	-6.6 to -1.94	0.34	0.21	.00*	-2.62	-6.17 to 0.92	0.17	0.04	0.14	-3.48	-5.67 to -1.29	0.30	0.17	0.003
Role limitations due to emotional problems	-4.8	-7.05 to -2.55	0.36	0.27	.00*	-5.11	-8.42 to -1.8	0.26	0.17	0.003	-4.6	-6.61 to -2.59	0.39	0.30	0.00*
Energy/fatigue	-2.79	-3.83 to -1.73	0.46	0.36	.00*	-1.86	-3.62 to -0.10	0.18	0.09	0.04	-2.24	-3.27 to -1.21	0.38	0.28	0.00*
Emotional well-being	-2.55	-3.26 to -1.84	0.59	0.50	.00*	-3.0	-4.11 to -1.89	0.46	0.37	0.00*	-2.32	-2.97 to -1.67	0.59	0.49	0.00*
Social functioning	-0.07	-0.8 to 0.65	0.13	0.00	0.84	-0.02	-1.0 to 0.97	0.13	0.00	0.97	0.08	-0.58 to 0.74	0.13	0.00	0.81
Pain	0.52	0.03 to 1.01	0.16	0.09	0.04	0.41	-0.28 to 1.1	0.10	0.03	0.24	0.29	-0.175 to 0.75	0.10	0.03	0.22
General health	0.21	-0.40 to 0.82	0.24	0.01	0.50	0.22	-2.53 to 1.05	0.23	0.01	0.60	0.22	-0.34 to 0.77	0.24	0.01	0.44

^aAdjusting for age, gender, number of years post-transplant, number of medical comorbidities, presence of chronic allograft vasculopathy and presence of an oncology illness; * $p < 0.002$ (Bonferroni correction); SF-36 = Medical Outcomes Short Form-36 Health Survey; PHQ-9=Patient Health Questionnaire 9-item scale; GAD-7=Generalized Anxiety Disorder 7-item scale; K-10=Kessler Psychological Distress Scale.