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RESEARCH PAPER

A dynamic view of comorbid depression and generalized anxiety disorder symptom change in chronic heart failure: the discrete effects of cognitive behavioral therapy, exercise, and psychotropic medication

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Abstract

Purpose: No previous study has reported upon comorbid depression and anxiety disorders and their treatment in heart failure (HF), which the current study has sought to document. *Materials and methods*: Total 29 HF patients under psychiatric management underwent primary depression cognitive behavioral therapy (CBT; $n = 15$) or primary generalized anxiety disorder (GAD) CBT ($n = 14$), and participated in a community exercise program and standard physician care. Repeated measures analysis of variance assessed Patient Health Questionnaire (PHQ-9) and GAD-7 symptom change pre- and post-CBT treatment, and assessed the interaction effects of treatment type, exercise, anti-depressant and anxiolytic. *Results*: There was a significant time and treatment interaction effect that favored the primary GAD CBT group for reduction in PHQ symptoms ($F(1, 24) = 4.52$, $p = 0.04$). Analysis of PHQ-somatic symptoms also showed a significant main effect for participation in the exercise program ($F(1, 24) = 4.21$, $p = 0.05$) and a significant time and anxiolytic interaction ($F(1, 24) = 3.98$, $p = 0.05$). The average number of cardiac hospital readmissions favored the primary GAD CBT group ($p = 0.05$). *Conclusion*: The findings support the use of multifaceted interventions in the rehabilitation of HF patients with comorbid psychiatric needs.

➤ Implications for Rehabilitation

- Comorbid depression and anxiety disorders are a clinical and research focus that deserves more attention in the treatment of heart failure patients.
- Cognitive behavioral therapy, exercise, and anxiolytic use was associated with significant changes in depression and anxiety though discrete effects were evident.
- Multifaceted interventions are most likely to be successful in the rehabilitation of HF patients with psychiatric needs.

Keywords

Anti-depressant, anxiolytic, cognitive behavioral therapy, exercise major depression disorder, generalized anxiety disorder, heart failure

History

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Introduction

The end stage of all cardiovascular diseases (CVD) is heart failure (HF), a complex clinical syndrome characterized by dyspnea and fatigue, and objective evidence of underlying structural abnormality or cardiac dysfunction [1]. HF is a chronic and disabling condition and survival rates are approximately 25%, five years after the first HF hospitalization [2]. Given the chronic and disabling nature of HF psychological adjustment difficulties are common. For example, a meta-analysis by Rutledge et al. [3] reported a 22% prevalence of depression determined by structured psychiatric interview in the HF population. Moreover, previous studies consistently support that depression doubles the risk of major cardiac events and death in patients with documented HF [3,4], is associated with higher healthcare costs [5], significantly impairs quality of life [6], impacts upon participation in HF disease-management strategies [7] and is associated with lower physical functioning targets in cardiac rehabilitation [8]. Indeed, with nearly 6 million cases of HF in the Unites States alone [9], combined with 22% depression prevalence in HF [3,10], it is timely to evaluate the efficacy of various treatments in clinical settings for psychiatric comorbidities in this burgeoning population.

In CVDs, depression is a condition with a number of effective treatments including anti-depressants, psychotherapy, exercise (e.g. behavioral activation), and cardiac rehabilitation [11–16]. Recent systematic reviews suggest that overall, mental health interventions were associated with small changes in depression symptoms (range of Standardized Mean Differences (SMD) 0.15 to 0.34 [17,18]. Comparable findings have been reported for cardiac rehabilitation (Cohen's $d = 0.23$) [19] and the selective

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serotonin reuptake inhibitor class of anti-depressant (SMD 0.41) [12]. Together the results highlight the importance of identifying specific components of depression interventions that work most effectively [17].

By contrast to randomized controlled trials (RCTs) in clinical settings it may not be desirable from the perspective of the patient, pragmatic, nor ethical to provide a single mode of psychiatric care. As such, clinical care may involve a number of treatments and thus better reflects real-world practices than does the exclusion criteria imposed by RCTs [20]. To guide clinicians on depression management in CVDs, several international consensus statements have been published [21,22]. However, Hasnain et al. [23] critiqued the dearth of guidance for individualized depression treatment plans when a comorbid anxiety disorder was present. In fact, to date, only one collaborative care trial reported on management strategies for either depressive or anxious symptoms [24]. Notably, the sample was not restricted to HF and a structured interview was not performed to determine anxiety or depression disorder status. Otherwise focus to date has been almost exclusively on depression. Consideration of anxiety disorder treatment is imperative in HF due to high prevalence of these disorders [25], and the fact that HF symptoms and dyspnea is exacerbated by anxiety [26–28]. To date, it is unknown whether CBT, exercise, and psychotropic management is effective for anxiety disorders in HF [29] as has been established in non-CVD populations [30,31].

Among the anxiety disorders generalized anxiety disorder (GAD) is the most commonly comorbid disorder with major depression in CVD [32,33]. Recent research shows that GAD increases the risk for CVD morbidity and portends poorer prognosis [34–36]. Indeed, GAD and major depression share some cognitive processes such as rumination and worry [37–39], with worry an established correlate of hypertension, diminished heart rate variability, and poorer CVD prognosis [40].

Here, the authors report on a consecutive series of HF patients with comorbid depression and GAD who underwent cognitive behavioral therapy (CBT) for either disorder, in addition to HF self-management, cardiac rehabilitation, and psychotropic medication management. The objective of this study was to document the change in depression and GAD symptoms and assess the effects of CBT, cardiac rehabilitation, anti-depressant and anxiolytic use on symptom change.

Methods

This study received ethics approval and all participants provided written and informed consent (Human Research Ethics Committee of The Queen Elizabeth Hospital and Lyell McEwin Hospital #HREC/12/TQEHLMH/188). Between April 2011 and June 2012 patients with verified HF admission were managed by specialist nurses in a HF self-management program (HFSMP) at three South Australian hospitals (Queen Elizabeth Hospital, Royal Adelaide Hospital, Lyell McEwin Hospital). Recruitment did not extend after June 2012 as one of the hospitals was no longer funded for HFSMP psychologist services or patient transportation if required to exercise rehabilitation classes. During this period nurses referred patients to the HFSMP psychologist when either of the following criteria were met; (a) depression symptoms were in the clinically significant range (Patient Health Questionnaire (PHQ-9) $\geq$10); (b) anxiety symptoms were in the clinically significant range (GAD-7 $\geq$7); (c) patients had evidence of panic attack. (d) There was evidence of suicidality on PHQ or from nurse interview.

Patients excluded from these analyses had a primary diagnosis other than major depression and GAD, alcohol or illicit substance abuse, Axis-II personality disorder that impacted upon treatments, and cognitive impairment (medical records or Mini Mental State Examination <24). Ineligibility criteria for psychologist referral was not having cardiologist-verified HF or currently receiving psychology and/or psychiatrist support elsewhere. A flow chart of participants through the study is shown in Figure 1.

Exercise program

The gymnasium-based exercise programs were prescribed and delivered by qualified exercise physiologists accredited in chronic disease self-management, a full overview is described elsewhere [41]. The exercise sessions were funded by the State Government once per week and of 1 h duration (approximately 15-min aerobic training, 40-min resistance training and 5-min flexibility and/or balance exercises) and were held within the gymnasium at a central location (the Centre for Physical Activity in Ageing) for a period of 12 weeks. Transport was provided to and from exercise sessions for patients at no cost. Programs were progressive in intensity and based on safe intensities rather than optimum fitness to ensure maintenance after discharge from the rehabilitation program. Programs were individually prescribed and adapted as necessary [42]. In addition to the weekly exercise, clients were provided with a home exercise program and/or encouraged to walk between 3 and 5 times per week depending on HF patients' access to gymnasium equipment, their mobility restrictions and the severity of HF.

Psychological assessment

Patients completed depression and anxiety questionnaires at the intake assessment and again post-discharge. The PHQ-9 [43] is a 9-item depression questionnaire covering major depression disorder criteria demarcated by DSM-IV [44]. PHQ scores $\geq$10 warrant further evaluation according to guidelines [22]. Patients also completed an 8-item questionnaire regarding anxiety (GAD-7, 7 items (GAD-7); and a 1-item panic screener *In the last 4 weeks, have you had an anxiety attack – suddenly feeling fear or panic*?) [43,45]. The GAD-7 is a 7-item anxiety questionnaire covering GAD criteria [44] and GAD-7 scores $\geq$7 warrant further evaluation [43]. Patients were assessed with the Structured Clinical Interview for DSM-IV Axis-I and AXIS-II disorders [46,47]. The SCID is a widely validated interview with favorable psychometric properties. Diagnoses and CBT progress was verified by two senior clinical psychologists once per month.

CBT intervention

Psychologist delivered CBT consisted of 1-h sessions and was provided once per week for 12 weeks. After SCID assessment corroborating the comorbid depression and GAD diagnoses, patients were given psycho-education about each disorder and asked to indicate preference for treatment. The treatment focus of CBT was determined in collaboration with the psychologist and determined by patient preference, similar to recent studies among acute coronary syndrome patients [48].

Manualized clinical guides were adopted for standardization primary depression treatment [49] and primary GAD treatment [50]. Depression CBT treatment targeted depressogenic cognitions, negative beliefs, automatic thoughts and related schema [49]. By contrast, GAD CBT treatment targeted worry frequency, positive and negative worry meta-beliefs, and challenging worry cognitions [50].

Psychotropic medication

Psychotropic medication use was managed by the primary care physician. Physicians received a letter outlining the psychologists' assessment and relevant diagnoses though no recommendation

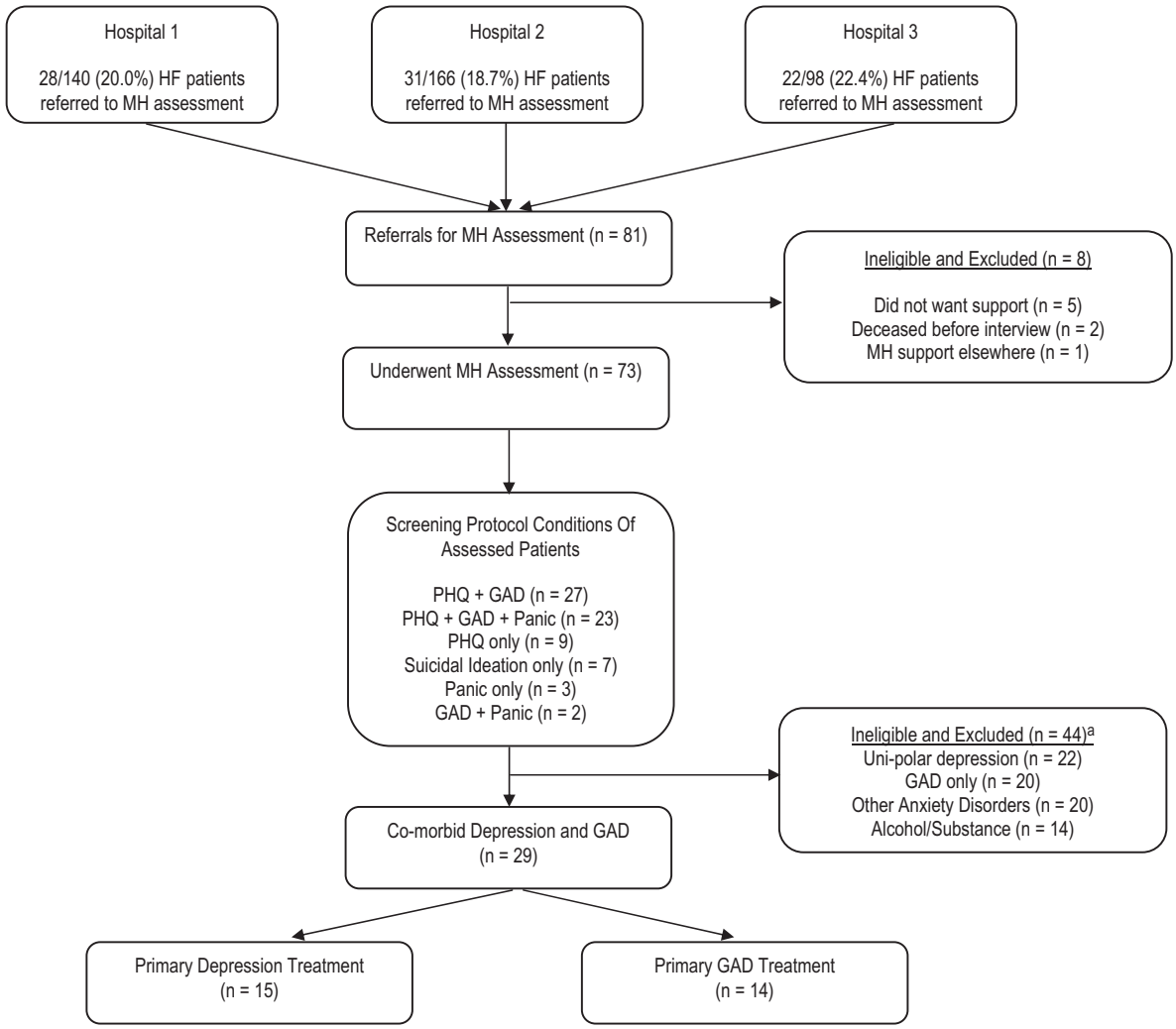

Figure 1. Flow chart of patients through the study. (a) Numbers do not equal 44 due to multiple psychiatric exclusions. HF, heart failure; GAD, generalized anxiety disorder; MH, mental health; PHQ, Patient Health Questionnaire.

was given pertaining to medication classes. For these analyses, psychotropic medications were classified into anti-depressants or anxiolytics. In the primary depression group, six patients were receiving anti-depressant medications (paroxetine $n = 3$, citalopram $n = 1$, venlafaxine $n = 1$, mirtazapine $n = 1$) and six were receiving anxiolytic (temazepam $n = 4$, alprazolam $n = 2$). In the primary GAD group, nine patients were receiving anti-depressant (citalopram $n = 4$, fluoxetine $n = 1$, amitriptyline $n = 1$, sertraline $n = 1$, dothiepin $n = 1$, mirtazapine $n = 1$), and 5 were receiving anxiolytic (temazepam $n = 5$).

Unplanned hospital admissions

Six-month follow-up for unplanned hospital admissions was collated by HFSMP nurses at each hospital site. Readmission data was confirmed via an electronic database that links 15 South Australian hospitals. Electronic readmission data were verified using the principal diagnosis at readmission according to International Classification of Disease (ICD) criteria. Fatal and non-fatal major adverse cardiovascular events were recorded for ICD codes I00-I99. A psychiatric readmission was recorded for fatal and non-fatal event codes ICD F00-F99.

Statistical analysis

Statistical analyses were performed with SPSS® 20.0 (IBM Corp., Armonk, NY, 2011). Analyses were undertaken with a dataset consisting of numerical code and the statistician was blinded to treatment condition. Descriptive comparisons were made with the General Linear Model and chi-square statistic with Fisher's exact test as appropriate. Change in depression and anxiety symptoms conformed to the intention-to-treat principle and there was no cross-over. Independent samples *t*-test was utilized to analyze Δ (calculated separately as Discharge $\text{Score}_{\text{Time 2}} - \text{Baseline Score}_{\text{Time 1}}$) for the PHQ-9 and GAD-7 scores; Cohen's d was used as an estimate of effect size. Sensitivity analysis utilized a full-factorial repeated measures analysis of variance model and treatment group was specified as a random variable, η_p^2 values provided estimate of effect sizes. Sensitivity analyses adjusted for main and interaction effects for covariates; exercise rehabilitation, anxiolytic use, and anti-depressant use. Analysis of unplanned CVD hospital admission (binary) utilized the chi-square statistic with Fisher's exact test, mean number of CVD admissions utilized the General Linear Model. Given the exploratory nature of the study and the restricted recruitment dates no *a priori* power calculation was performed and no adjustment was made for multiple comparisons [51]. In all analyses $p \leq 0.05$ was considered statistically significant.

Results

From the first 81 consecutive HF patients with psychiatric needs, 73 underwent assessment and management. For these analyses, total 29 patients met criteria for current depression and comorbid

Table 1. Comparisons between treatment groups.

	Primary depression treatment, $n = 15$	Primary GAD treatment, $n = 14$	p
Age, yrs M (SD)	61.1 ± 17.4	57.6 ± 13.2	0.56
Female	9 (60.0)	6 (42.9)	0.36
Disability pension	4 (26.7)	4 (28.6)	1.0
Current employment	1 (6.7)	2 (14.3)	0.60
Left ventricular ejection fraction, M (SD)	34.5 ± 15.6	31.6 ± 11.1	0.57
Previous myocardial infarction	8 (53.3)	4 (28.6)	0.18
Atrial fibrillation	6 (40.0)	5 (35.7)	0.81
Implantable cardioverter defibrillator	3 (20.0)	5 (35.7)	0.43
Coronary artery bypass surgery	5 (33.3)	1 (7.1)	0.17
Valve surgery	5 (33.3)	3 (21.4)	0.68
Hypertension	8 (53.3)	10 (71.4)	0.32
Hypercholesterolemia	4 (26.7)	8 (57.1)	0.10
Diabetes	7 (46.7)	6 (42.9)	0.84
Renal disease	6 (40.0)	4 (28.6)	0.70
Cerebrovascular disease	2 (13.3)	1 (7.1)	1.0
Chronic obstructive pulmonary disease	3 (20.0)	3 (21.4)	1.0
Sleep apnea	3 (20.0)	3 (21.4)	1.0
Obesity, body mass index ≥30	7 (46.7)	5 (35.7)	0.55
Current tobacco use	4 (26.7)	5 (35.7)	0.70
Rehabilitation exercise	6 (40.0)	3 (21.4)	0.43
Anti-depressant	6 (40.0)	9 (64.3)	0.19
Anxiolytic	5 (33.3)	5 (35.7)	0.89
Median depression onset, years (IQR)	11.7 (5.0–14.0)	11.9 (10.1–16.3)	0.46
Median GAD onset, years (IQR)	15.0 (3.0–25.0)	11.0 (6.3–19.3)	0.46

GAD and completed treatment and follow-up measures. Patient selection was MDD-focused treatment ($n = 15$) and GAD-focused treatment ($n = 14$) and a comparison of the groups showed no significant differences in demographics, comorbid medical conditions, or pharmacological management with anti-depressants or anxiolytics (Table 1).

Depression and anxiety change scores

From pre-treatment to discharge, there were no significant between-treatment group differences in PHQ-9 change scores for depression versus GAD CBT (-7.33 ± 8.24 versus -11.00 ± 6.53, $p = 0.20$, Cohen's d = 0.51). There were also no significant between-treatment group differences in PHQ-cognitive change scores (-4.87 ± 5.08 versus -6.36 ± 3.61, $p = 0.37$, Cohen's d = 0.35) or PHQ-somatic change scores (-2.47 ± 4.29 versus 4.64 ± 4.22, $p = 0.18$, Cohen's d = 0.53). There was no significant between-treatment group differences in GAD-7 change scores (-10.60 ± 7.52 versus -9.86 ± 6.04, $p = 0.77$, Cohen's d = 0.11; Table 2).

Table 2. Between-treatment group change scores for depression and anxiety symptoms pre and post treatment.

	Primary depression treatment M ± SD	Primary GAD treatment M ± SD	Cohen's d	p
PHQ-9				
Pre treatment	12.87 ± 6.41	15.93 ± 4.48	0.51	0.20
Post treatment	5.53 ± 4.55	4.93 ± 4.38		
Δ Change	−7.33 ± 8.24	−11.00 ± 6.53		
PHQ cognitive				
Pre treatment	7.20 ± 4.11	8.29 ± 3.05	0.35	0.37
Post treatment	2.33 ± 2.31	1.93 ± 1.90		
Δ Change	−4.87 ± 5.08	−6.36 ± 3.61		
PHQ somatic				
Pre treatment	5.67 ± 3.11	7.64 ± 2.44	0.53	0.18
Post treatment	3.20 ± 2.88	3.00 ± 2.83		
Δ Change	−2.47 ± 4.29	−4.64 ± 4.22		
GAD-7				
Pre treatment	14.33 ± 6.34	14.00 ± 4.25	0.11	0.77
Post treatment	3.73 ± 3.13	4.14 ± 4.09		
Δ Change	−10.60 ± 7.52	−9.86 ± 6.04		

Sensitivity analysis: depression symptom response

The main effects and interaction effects with time are shown in Table 3 for depression and anxiety symptom change. With respect to PHQ total scores, none of the main effects were significant (CBT treatment type $p = 0.19$, exercise rehabilitation $p = 0.20$, anti-depressants $p = 0.46$, anxiolytics $p = 0.80$). There was however a significant time and treatment interaction effect showing greater reduction in depression symptoms that favored the GAD CBT group ($F(1, 24) = 4.52$, $p = 0.04$, partial $\eta_p^2 = 0.16$).

For change in PHQ-somatic symptoms, the main effect for participation in cardiac rehabilitation was significant ($F(1, 24) = 4.21$, $p = 0.05$, $\eta_p^2 = 0.15$). With respect to the interaction terms, it was found that significantly more PHQ-somatic change was observed with use of anxiolytic medication ($F(1, 24) = 3.98$, $p = 0.05$, $\eta_p^2 = 0.14$).

For change in PHQ-cognitive symptoms, there was no main effect for CBT treatment group ($F(1, 24) = 0.47$, $p = 0.50$). All other main effects were also not significant as was the case for interaction effects with time.

Sensitivity analysis: generalized anxiety disorder symptom response

Analysis of GAD-7 suggested no main effects for CBT treatment group in GAD-7 symptom change over time ($F(1, 24) = 0.09$, $p = 0.77$). However, the time by anxiolytic interaction effect was significant, suggesting greater GAD symptom reduction for patients prescribed anxiolytic medications ($F(1, 24) = 5.43$, $p = 0.03$, $\eta_p^2 = 0.19$). No other interactions terms were significant.

Ancillary analysis

Given the significant effects for primary GAD treatment on total depression symptoms and PHQ-somatic symptoms, ancillary analysis tested for changes in depression symptoms and specified

Table 3. Sensitivity analysis for change in depression and anxiety over time.

	Main effects			Interaction effects		
	ANOVA F (df = 1, 24)	p	η_p^2	ANOVA F (df = 1, 24)	Interaction × time p	η_p^2
PHQ-9						
Treatment	1.82	0.19	0.07	4.52	0.04*	0.16
Rehabilitation	1.78	0.20	0.07	3.38	0.08	0.12
Anti-depressant	0.56	0.46	0.02	2.00	0.17	0.08
Anxiolytic	0.07	0.80	0.01	2.84	0.11	0.11
PHQ-cognitive						
Treatment	0.47	0.50	0.02	2.40	0.13	0.09
Rehabilitation	0.17	0.69	0.01	2.47	0.13	0.09
Anti-depressant	0.68	0.42	0.03	1.82	0.19	0.07
Anxiolytic	0.30	0.59	0.01	0.71	0.41	0.03
PHQ-somatic						
Treatment	3.11	0.09	0.12	3.94	0.06	0.14
Rehabilitation	4.21	0.05*	0.15	2.15	0.16	0.08
Anti-depressant	0.23	0.64	0.01	0.96	0.34	0.04
Anxiolytic	0.02	0.90	0.01	3.98	0.05*	0.14
GAD-7						
Treatment	0.09	0.77	0.01	0.09	0.77	0.01
Rehabilitation	0.11	0.75	0.01	2.85	0.10	0.11
Anti-depressant	0.74	0.40	0.03	0.78	0.39	0.03
Anxiolytic	0.11	0.75	0.01	5.43	0.03*	0.19

*$p \leq 0.05$.

contemporaneous change in GAD symptoms (Δ change score) as a covariate. Change in total depression symptoms showed a significant main effect for Δ GAD-7 ($F(1, 26) = 4.81$, $p = 0.04$, $\eta_p^2 = 0.16$). The interaction effect for time by Δ GAD-7 was also significant ($F(1, 26) = 28.02$, $p =< 0.001$, $\eta_p^2 = 0.51$). The main effect for CBT treatment was not significant ($p = 0.26$) but the treatment by time interaction was significant ($F(1, 26) = 4.68$, $p = 0.04$, $\eta_p^2 = 0.15$).

For change in PHQ-somatic symptoms, there was no main effect for Δ GAD-7 ($p = 0.12$) though there was a significant interaction effect for time by Δ GAD-7 ($F(1, 26) = 8.20$, $p = 0.008$, $\eta_p^2 = 0.24$). The main effect for CBT treatment ($p = 0.17$) and the treatment by time interaction were not significant ($p = 0.10$). With respect to change in PHQ-cognitive symptoms, there was a main effect for Δ GAD-7 ($F(1, 26) = 4.80$, $p = 0.04$, $\eta_p^2 = 0.16$) and also a significant interaction effect between time and Δ GAD-7 ($F(1, 26) = 32.02$, $p < 0.001$, $\eta_p^2 = 0.55$). The main effect for CBT treatment ($p = 0.55$) and the treatment by time interaction was not significant ($p = 0.11$).

Cardiac hospital readmissions

When analyzed as a binary outcome the unplanned hospital readmission rate was 20.7% by 6-month follow-up and no significant difference was evident between the depression and GAD CBT treatment groups (33.3% versus 7.1%, χ^2 (1) = 3.03, $p = 0.17$). However, some patients had multiple hospital readmissions and a significant difference was evident between groups in total number of hospital admissions per person favoring the GAD CBT group by comparison to the depression CBT group (0.1 ± 0.27 versus 0.80 ± 1.32, $p = 0.05$). For psychiatric admissions, there were two readmissions in the primary depression group (13.3% versus 0%, $p = 0.48$).

Discussion

To the best of the author's knowledge, this study was the first to report on comorbid depression and GAD disorder treatment and characteristic symptom change in any heart disease population. Findings indicated that comorbid depression and GAD were generally effectively treated regardless of the primary treatment modality. In fact CBT, exercise, and anxiolytic were associated with significant changes in depression and anxiety though discrete effects were evident. The most important findings were that primary GAD treatment led to significant change in depression symptoms and ancillary analyses highlight this effect was potentially driven by changes in somatic depression symptoms. Notably, it was found that participation in the exercise program was associated with significant reduction in somatic depression symptoms. Primary GAD treatment in HF patients also led to a reduction in average number of hospital readmissions at 6-month follow-up, consistent with depression interventions reported elsewhere [52,53].

These data provide insight into depression and anxiety symptom changes for comorbid major depression and GAD in a clinical treatment sample of ambulatory HF patients. Significant reductions in depression and anxiety symptoms were achieved for comorbid depression-GAD regardless of the patient selected treatment focus. Significant changes in somatic and cognitive depression symptoms were achieved with both CBT treatments. The current findings can be interpreted alongside a number of prior depression RCTs in HF [52,54,55] and also general CVD [56,57]. Indeed, a number of depression interventions in CVD have reported contemporaneous reductions in anxiety symptoms [56] suggesting that broader psychological processes are at play [58,59].

Previous intervention studies in CVD have been almost exclusively limited to major depression, neglecting the complexity of comorbid anxiety that is observed among heart disease patients [24]. Underestimation of comorbidity and the inherent complexity of the requisite treatments may hamper efforts to implement depression screening guidelines into clinical practice [1,22]. Notwithstanding the dearth of clinical guidance on depression treatment plans when comorbid anxiety is present [23], there is a paucity of evidence-based treatments for anxiety disorders in CVD. Shemesh et al. [60] reported a brief imaginal exposure and CBT intervention for post-traumatic stress disorder after a CVD event and found no marked increase in blood pressure, pulse and mean arterial pressure. More recently, Huffman et al. [61] outlined a collaborative care model for the treatment of either depression, GAD or panic symptoms in

hospitalised CVD patients, and showed that 53% of GAD patients had this disorder for more than 1 year. Previously, Pedersen [62] questioned whether anxiety interventions were redundant in light of the immense funding, research and intervention efforts invested for depression among CVD populations. The paucity of prior anxiety studies by comparison to depression in CVDs suggests that further work is required to explicate potential gains in mental health, CVD related outcomes [63], and cost-effectiveness by treating anxiety disorders.

The findings here that an exercise program, and GAD focused CBT, had significant clinical impact on somatic and cognitive depression symptoms, the latter also affected cardiac readmissions. A potential explanation is that primary intervention for GAD and worry might lead to a reduction in somatic and heart focused worry [40], potentially altering illness perceptions [58]. That said the main effect for exercise program and change in somatic depression symptoms could also be contextualized as graded behavioral exposure for cardiovascular symptoms over 12 weeks. For example, the authors of a recent systematic review hypothesized that exercise induction of bodily sensations mimic those homeostatic changes associated with anxiety, and thus may alleviate anxiety sensitivity [30]. Strategies that alter somatic depression symptoms in particular might be important as accumulating findings suggest that the somatic, and not cognitive-affective, depression symptoms portend poorer cardiovascular prognosis [64]. Indeed, other primarily cognitive depression interventions have also reported a material impact upon CVD prognosis [52].

Like earlier studies of post-traumatic stress disorder after myocardial infarction [65], this study is an exploratory investigation and was not designed as proof of treatment efficacy. This study is presented with several limitations including that the use of anxiety questionnaires may have elicited more referrals for patients with comorbid GAD and depression. Also, GAD and other anxiety disorders, including sub-threshold disorders, are known to increase in prevalence with age and CVDs [66]. As such this study may not reflect comorbidity rates in other earlier stage CVD populations [33]. Other potential sampling limitations include that depression and anxiety disorders are frequently under-recognized [67]. For example, as many as 27% of cardiac patients are not assessed by routine screening protocols [68] and severely depressed patients are less likely to prefer counselling than anti-depressants [48]. Treatment was not allocated according to a randomization process, but rather, based on consultation and patient preference. Patients participated in multifaceted HFSM strategies collaboratively with other staff and improvements in depression and anxiety could not be attributed to CBT, exercise or psychotropic management alone, consistent with collaborative care intervention strategies [61]. Also, briefer psychiatric interventions of shorter duration may be equally effective to promote the rehabilitation of patients with chronic conditions [69]. Exercise with greater frequency on the other hand would likely achieve stronger effect sizes. Notably, the current HFSMP was only government funded for one session per week. Importantly, patients were excluded from these analyses if meeting criteria for alcohol of substance abuse, or personality disorders which indeed form suitable reasons for psychologist or psychiatrist intervention [70]. Finally, the sample size, low statistical power, width of standard deviations, and number of statistical analyses should be considered when interpreting the findings of this exploratory study. Given the potential for Type I errors the findings require confirmation in independent cohorts.

Despite these limitations, the strength of this study was that a single therapist delivered the CBT intervention therefore permitting a level of control and homogeneity that is uncommon in psychological interventions, consistent with a recent depression RCT [71]. Also, allocation of depression treatment was based on patient preferences which have been shown to be effective in cardiovascular populations [56] and might be particularly important due to perceptions of not being psychiatric patients *per se* [60,65].

In conclusion, HF patients with comorbid depression and GAD achieved significant symptom reduction that was associated with multifaceted treatment modalities. The findings support the use of multifaceted interventions in rehabilitation of HF patients with psychiatric needs. Further research could examine the effects of these treatments upon somatic and heart focused worry and unplanned hospital admissions.

Declaration of interest

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