HHS Public Access

Author manuscript

Psychosom Med. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

Psychosom Med. 2016 ; 78(6): 667–676. doi:10.1097/PSY.0000000000000316.

A pilot randomized study of a gratitude journaling intervention on HRV and inflammatory biomarkers in Stage B heart failure patients

Laura Redwine, Ph.D.[1], **Brook L. Henry, Ph.D.**[1], **Meredith A. Pung, Ph.D.**[2], **Kathleen Wilson, M.S.**[2], **Kelly Chinh, B.S.**[1], **Brian Knight, B.S.**[3], **Shamini Jain, Ph.D.**[1], **Thomas Rutledge, Ph.D.**[1], **Barry Greenberg, M.D.**[3], **Alan Maisel, M.D.**[3], and **Paul J Mills, Ph.D.**[2]

[1]Department of Psychiatry, University of California, San Diego, CA

[2]Department of Family Medicine and Public Health, University of California, San Diego, CA.

[3]Department of Medicine, University of California, San Diego, CA

Abstract

Objective—Stage B, asymptomatic heart failure (HF) presents a therapeutic window for attenuating disease progression and development of HF symptoms, and improving quality of life. Gratitude, the practice of appreciating positive life features, is highly related to quality of life, leading to development of promising clinical interventions. However, few gratitude studies have investigated objective measures of physical health; most relied on self-report measures. We conducted a pilot study in Stage B HF patients to examine whether gratitude journaling improved biomarkers related to HF prognosis.

Methods—Patients (N = 70; mean age = 66.2 years, SD = 7.6) were randomized to an 8-week gratitude journaling intervention or treatment as usual (TAU). Baseline (T1) assessments included 6-item Gratitude Questionnaire (GQ-6), resting heart rate variability (HRV), and an inflammatory biomarker index. At T2 (mid-intervention) GQ6 was measured. At T3 (post-intervention), T1 measures were repeated but also included a gratitude journaling task.

Results—The gratitude intervention was associated with improved trait gratitude scores ($F = 6.0$, $p = .017$, $\eta^2 = .10$), reduced inflammatory biomarker index score over time ($F = 9.7$, $p = .004$, $\eta^2 = .21$) and increased parasympathetic HRV responses during the gratitude journaling task ($F = 4.2$, $p = .036$, $\eta^2 = .15$), compared with TAU. However, there were no resting pre- to post-intervention group differences in HRV (p's > .10).

Conclusions—Gratitude journaling may improve biomarkers related to HF morbidity, such as reduced inflammation; large-scale studies with active control conditions are needed to confirm these findings.

Correspondence concerning this article should be addressed to: Laura Redwine, Department of Psychiatry, University of California, 9500 Gilman Dr. San Diego, CA. 92093. Mail Code 0804, lredwine@ucsd.edu.

Trial Registration: Clinicaltrials.gov identifier: NCT01615094

There were no conflicts of interest to disclose by any of the authors.

Keywords

heart failure; heart rate variability; inflammatory; gratitude; intervention

Heart Failure (HF) is the end stage of most cardiac anomalies, affecting over 5 million Americans, with rates expected to triple over the next thirty years as the population ages (1). The yearly number of hospitalizations for HF exceeds one million in the U.S., and medical costs are over $40 billion per year (2, 3). A staging system developed by the American College of Cardiology (ACC) in cooperation with the American Heart Association (AHA) emphasizes the evolution and progression of chronic HF and the need for early intervention to prevent disease advancement and ultimately to diminish morbidity and mortality (4). In this staging system, patients with “Stage A” are at high risk for developing HF but do not have a structural disorder of the heart. Patients with “Stage B” have a structural abnormality of the heart but are asymptomatic, and are at high risk for developing symptomatic (“Stage C”) HF. “Stage D” consists of advanced structural heart disease and symptoms even at rest. Progression from Stage B asymptomatic HF to Stage C symptomatic HF is associated with a 5-fold increase in mortality risk (5). Thus, the Stage B level of disease presents an important therapeutic window for potentially halting disease progression, forestalling the development of HF symptoms and maintaining quality of life.

In the area of behavioral cardiology (6), there is increasing focus on relationships among positive psychological attributes such as gratitude, the potential mechanisms of action, and associated clinical outcomes (7-9). Gratitude is suggested to be an aspect of a broader life orientation toward noticing and appreciating the positive features of life (10). A body of evidence has emerged suggesting that gratitude is strongly related to well-being (e.g. mood, satisfaction with life, and health-related quality of life), leading to the development of promising clinical interventions (e.g. (11, 12). A number of studies have examined gratitude interventions using a variety of approaches. Much of the existing research on gratitude has focused primarily on outcomes associated with psychological factors and social interactions. Emmons and McCullough (2003) originally proposed gratitude diaries as a useful intervention for well-being enhancement. More recent work suggests it to be as effective as cognitive behavioral techniques used in clinical therapies for improving psychological well-being (12, 13). Few studies have investigated the relationship between gratitude and physical health, particularly in clinical populations, and most have relied on self-report rather than objective measures of physical health. For example, a cross-sectional study from a non-clinical population of 962 individuals ranging in age from 19 to 84 found that gratitude scores positively related with self-reported physical health. However, in a cross-sectional investigation of asymptomatic patients with HF we found a relationship between gratitude levels and an index of inflammatory biomarkers known to be associated with adverse cardiac remodeling and progression to HF (14). There have been even fewer intervention studies examining the effects of increased gratitude on physical health. Emmons & McCullough (2003) found that people who were requested to list items for which they were grateful over a 10-week period reported fewer symptoms of physical illness than controls. Further investigations using objective measures of physical health in randomized controlled trials are necessary to understand the potential disease-buffering effects of gratitude.

Research evidence suggests that psychological factors such as chronic stress and depression are related to alterations in autonomic nervous system (ANS) function (15). In turn, it has long been known that dysregulation of ANS function is a predictor of worse CVD outcomes (16). Heart rate variability (HRV) is used to quantitatively assess variation in heartbeat intervals and is often used to detect changes in autonomic function (17). Healthy individuals exhibit a high level of HRV while decreased HRV is implicated in cardiovascular disease (CVD) pathophysiology (18). In particular, reduced parasympathetic tone is a predictor of HF and is related to increased mortality in men and women at risk for CVD, as well as in patients who suffered a myocardial infarction (19-21).

Inflammation is also implicated in the pathogenesis and prognosis of HF (22). As suggested by Torre Amione (2005), HF is a systemic illness where deleterious processes can occur in response to cardiac injury regardless of the initial insult (23). Pro-inflammatory factors such as CRP, IL-6, TNF-α and sTNFr1 are activated beginning even at asymptomatic stages, and continue to increase in relation to worsening HF (24). While a vast amount of evidence links inflammation processes to CVD and HF, the efficacy of pharmacological interventions to reduce inflammation remains uncertain (25). Therefore, there is a significant need to develop novel therapeutic methods to address this critical problem.

In light of the evidence discussed above, in Stage B HF patients we performed a pilot randomized controlled trial (RCT) examining the effects of an 8-week gratitude journaling intervention as compared to individuals receiving treatment as usual (TAU) on HRV and markers of inflammation. We hypothesized that the intervention would increase gratitude, elevate parasympathetic cardiac tone, and reduce inflammatory biomakers. In addition, we conducted exploratory analyses to examine the relationships between gratitude and biomarkers of inflammation and parasympathetic activity.

METHODS

Participants

This is a sub-study of a larger observational study examining the relationship among trait gratitude and biological factors linked with HF (14). Participants had a diagnosis of AHA/ACC classification Stage B HF for at least 3 months, were 18 years of age or older and were recruited from the University of California, San Diego (UCSD) Medical Center Cardiology Programs and the Veterans Affairs San Diego Healthcare System (VASDHS). Data were collected from April 2013 – June 2014. The sample consisted of 70 men and women (mean age = 66.2 years, SD = 7.58) who were randomly assigned according to a computer algorithm to an intervention of either 8-weeks of gratitude journaling (n = 34) or TAU (n = 36). Allocation of group assignment was concealed until after baseline testing. Participants were assessed at pre-, mid-, and post-intervention (Figure 1). Both groups were under the care of their primary care physician and cardiologist and but were restricted from participation in other intervention studies during this period.

Presence of Stage B HF was defined as structural heart disease based on the American Society of Echocardiography guidelines (26). Criteria include left ventricular (LV) hypertrophy (mean LV wall thickness of septum and posterior wall ≥ 12mm), LV

enlargement (at least moderate in severity, with LV end diastolic diameter ≥ 64 mm in men or ≥ 58 mm in women, or LV mass index ≥ 132 in men or ≥ 109 in women), LV systolic dysfunction (LV ejection fraction <55% or wall motion abnormality), LV diastolic dysfunction, asymptomatic valvular heart disease of at least moderate severity, or previous myocardial infarction but without symptoms of HF. Measurements were made by sonographers naive to participant's other study characteristics. An important distinction of Stage B HF is the lack of symptoms such as shortness of breath during mild exercise, compared with Stage C HF which exhibits symptoms.

Procedures overview

This study was approved by the UCSD and VASDHS Institutional Review Boards, and participants gave written informed consent. It was carried out in accordance with the Declaration of Helsinki principles. Testing occurred at baseline (T1), 4 weeks (T2: mid-intervention; gratitude assessment only) and 8 weeks (T3: post-intervention) visits. At T1 testing, participants arrived at the laboratory at various times of the day between 0800 and 1500 hrs and were given a brief overview of the study and then were asked to sit quietly for 10 minutes and subsequently were administered a blood draw while in a seated upright position. Following the blood draw, seated basal HRV data were recorded after a 5-minute acclimation interval. Participants filled out a gratitude and an exercise activities questionnaire and then participants who were randomized to the gratitude journaling condition were given instructions for the 8-week intervention. Compliance in the gratitude journaling group was assessed by examining the number of journal entries per week and numbers of words written per journal entry. Both groups were told to continue their healthcare as usual. After 4 weeks (T2) participants in both conditions were mailed a gratitude questionnaire (GQ-6) and pre-addressed envelope, which they were told to complete and mail back. After the 8-week intervention period, the T3 visit was similar to the T1 visit where participants in both groups received a blood draw, filled out the GQ-6, and had a basal HRV assessment. Additionally, participants in both groups were assessed for HRV responses to a gratitude journaling task. Participants were paid and thanked.

Gratitude

At T1 (baseline), T2 (mid-intervention) and T3 (post-intervention) visits, gratitude was measured with the 6-item Gratitude Questionnaire (GQ-6) (27) where the frequency and intensity are assessed with six items in which grateful affect are experienced. Items are rated with a Likert-type scale: 1 (strongly disagree) to 7 (strongly agree). The GQ-6 produces a single-factor score, and has convergent validity with other gratitude measures (27). The GQ-6 was chosen since it is most often used in gratitude intervention studies (e.g. Emmons & Mccullough) as well as in larger cross-sectional studies measuring physical health (28) including in patients with asymptomatic HF (14). In the present study, the Cronbach's alpha for baseline GQ6 = .83.

Leisure-Time Exercise Questionnaire the (LTEQ)

As a manipulation check to determine whether the control group differed at baseline or in changes in exercise activities the LTEQ (29) was administered at T1 and T3 in both groups (see Table 1 and Table 2).

HRV

At both T1 (baseline) and T3 (post-intervention) assessments, participants were fitted with the Equivital™ EQ-02 LifeMonitor (Hidalgo, UK). After an initial 5-minute acclimation interval, basal HRV data were recorded during the subsequent 5-minute period. At T3, following basal HRV recording participants in both groups performed a gratitude journaling task where they were asked to write for 5 minutes about things for which they were grateful; HRV responsiveness to gratitude journaling was determined by measuring changes in HRV from rest to the journaling task period. Digitized electrocardiogram (ECG) data were analyzed to detect the R-wave peaks of the QRS complex and R-R interval artifacts were manually removed using linear interpolation. Ectopic beats were identified and removed using VivoSense® software (Vivonoetics, Inc., San Diego, CA) automated ectopic beat detection algorithm.

The Equivital™ EQ-02 LifeMonitor (Hidalgo, UK) is a multi-parameter system that includes a two-lead ECG sensor belt and an ambulatory Sensor Electronics Module (SEM) for recording ECG data. Cardiac data are sampled at 256 Hz and were analyzed with the VivoSense® software platform (Vivonoetics, Inc., San Diego, CA). The accuracy and reliability of EQ-02 heart rate and R-R interval collection during rest and exercise has previously been validated (30-32). The objective was to quantify HRV indices of parasympathetic cardiac control using measures from time, frequency and non-linear domains during the 5-minute periods of rest and gratitude journaling. In the time domain, the root mean square of successive differences (RMSSD) was determined, which has been shown to reflect vagal activity (15). In the frequency domain, high frequency (HF: 0.15–0.40 Hz) power spectral density was measured, which has also been used as an index of vagal activity and reflects primarily parasympathetic influences (15). Since the ANS is not a linear system, it has been argued that non-linear analysis would be informative for HRV (33) and nonlinear measures have also been proposed to be more accurate at predicting cardiac dysfunction, including ventricular tachycardia and sudden cardiac death (34, 35) when compared to traditional time and frequency domain analyses. Poincare analyses are commonly used as a nonlinear measures of HRV (36), including SD1, which represents a measure of rapid changes in R–R intervals. Because vagal effects on the sinus node are known to develop faster than sympathetically mediated effects, it is considered a parasympathetic index of sinus node control (37, 38). SD1 was calculated by determining the standard deviations of the distances of the RRi to the slope of the line x = y, where x = RR (i +1) and y = (RRi).

Inflammatory Biomarkers

Inflammation is implicated in the pathogenesis of HF and inflammatory biomarkers are used for risk stratification and prognosis (22). Therefore, we assessed an index of relevant inflammatory biomarkers known to be involved in adverse remodeling of the heart and the progression to heart failure, which included CRP, TNF-α, IL-6, and sTNFr1 (Huang, Yang, Xiang, & Wang, 2014; Sun et al., 2014) at both T1 (baseline) and T3 (post-intervention). After a ten-minute rest period, whole blood was drawn into a 10 ml vacutainer tube preserved with EDTA while participants were in an upright sitting position. Blood samples were immediately placed on ice, centrifugation was performed within 30 minutes, plasma

was aliquoted and immediately stored at −80° C until assay. Circulating levels of these biomarkers were determined by commercial high sensitivity ELISA (Meso Scale Discovery, Rockville, MD) and performed in duplicate. Median lower limit of detection for CRP = 1.33 pg/mL, IL-6 = 0.06 pg/mL, TNF-α = 0.04 pg/mL, and minimum detectable dose for sTNF RI= 0.77 pg/mL. Intra- and inter-assay coefficients were < 7%.

Journaling Intervention

At the T1 visit, participants were provided written and oral instructions for keeping a daily gratitude journal diary. To aid comparison with previous work, journaling instructions were modeled after Emmons and McCullough (2003) and read, “For the next eight weeks you will be asked to record 3-5 things for which you are grateful on a daily basis. Think back over your day and include anything, however small or great, that was a source of gratitude that day. Make the list personal, and try to think of different things each day (12).” In accordance with existing protocols, we did not set any specific requirements for the length of the text (how many words or lines written), time spent journaling (minutes per day), or set a daily schedule (e.g., having entries occur in morning or evening). The first journal was mailed back at 4 weeks (T2) and the second journal was returned during the post-intervention (T3) testing visit.

Statistical analyses

Analyses were performed using IBM SPSS Statistics for Windows Version 23.0 (IBM Corp, Armonk, NY). In order to maximize statistical power, imputations were performed for missing GQ-6 data using a multiple regression approach. Age, gender and race were each used as predictor variables. Reported analyses for GQ-6 were conducted using imputed data. Initial power analyses focused on the anticipated change in gratitude score from baseline to immediate post-intervention for the journaling and TAU groups: the primary endpoint being the difference between gratitude at baseline and the end of the 8-week intervention. Assuming a standard deviation of approximately 4 units for both the baseline and 8 week measurements of gratitude and a 20% dropout rate, an initial sample size of 80 subjects per treatment group was expected to provide approximately 80% power to detect a difference of approximately 3 units in mean change in gratitude scores between groups, with a two sided significant level of 0.05. Additional analyses examining biomarkers (HRV and inflammatory factor) were considered exploratory given the nature of this pilot study and the fact that few, if any, other studies have examined these in response to a gratitude journaling intervention. Consequently, sample size calculations did not consider these planned but exploratory analyses, as one aim of this pilot study was to generate effect sizes for these biomarkers to inform future, larger scale studies. Skewed data distribution was determined by the Kolmogorov-Smirnov test, and variables not normally distributed were log transformed to more closely approximate normality. HRV and inflammation biomarkers were log transformed and achieved normal distribution. Group differences in sociodemographic and medical characteristics (Table 1) were computed using independent t-tests, or for categorical data, Kruskal-Wallis tests. In order to reduce the number of repeated measures tests and risk of type I error, a factor analysis was used to calculate a composite inflammatory index score comprised of circulating levels of CRP, TNF-α, IL-6, and sTNFrI. The resultant factor score Eigenvalue was 1.8, accounting for 45.2% of inflammatory variance. To measure differences

between groups for changes in gratitude levels (GQ-6) a repeated measures analyses of aovariance (ANCOVA) was performed using a 2 × 3 design (two groups: gratitude journaling and TAU; three time points: T1, pre-intervention; T2, mid-intervention; T3, post-intervention). Repeated measures ANCOVAs were performed to examine changes over time for basal HRV and inflammatory biomarkers utilizing a 2 × 2 design (two groups: gratitude journaling and TAU; two time points: T1 and T3. Group differences in HRV responses to the T3 post-intervention gratitude journaling task was examined by measuring changes in HRV during the task from resting HRV, utilizing a repeated-measures ANCOVA 2 × 2 design (two groups: gratitude journaling and TAU; two time points: T3, post-intervention basal HRV and T3 post-intervention HRV during the gratitude journaling task). Percentage of left ventricular ejection fraction (% LVEF) and Stage B HF etiology (myocarditis, hypertension, MI, hypertrophy, valvular, ischemic, idiopathic, or other) was adjusted during all analyses, and body mass index (BMI) was used as an additional covariate for analyses including pro-inflammatory biomarkers. The effect sizes for repeated measures ANCOVAs are reported as Partial Eta Squared (η^2). Cohen (1988), p. 283 suggests for η^2 where 0.010 constitutes a small effect, 0.059 a medium effect and 0.138 a large effect (39). In order to determine whether alterations in gratitude levels were related to changes in biomarkers, partial correlations of GQ-6 (mid- and post-intervention) were conducted in relation to HRV responses and basal inflammatory biomarker levels (post-intervention), while adjusting for baseline (T1) values.

RESULTS

Table 1 presents baseline characteristics of the study sample. Baseline subject characteristics revealed statistical differences for inflammation biomarker IL-6 ($p < .05$). From the original 70 participants, 21% (n = 7) of those randomized to the journaling intervention dropped-out prior to beginning the intervention. Of the 26 subjects who began the journaling intervention, 89% completed the study. The total gratitude intervention completion rate was 71%. Of the 36 participants allocated to the TAU group, 94% of the participants completed the study. HRV biomarker data were analyzed from a subsample of 34 participants. Inflammatory biomarker data were analyzed from 43 participants.

Participants in the gratitude journaling condition that completed the study averaged 5.29 days per week (s.d. = 1.98) of journaling and averaged 1482.82 words (s.d. = 819.78) over the 8-week period. Although there were reductions, there were not significant differences between the first 4-weeks and the last 4-weeks of the intervention for average numbers of journaling days per week (5.46, s.d. = 1.99 versus 5.05, s.d. = 2.31) or numbers of words journaled (766.12, s.d. = 418.75 versus 716.71, s.d. = 538.38) (p's > .10). There were no group differences in exercise activities over time measured with the LTEQ ($p > .10$). There were no differences in age, %LVEF, Stage B HF etiology, education, BMI, baseline gratitude levels, LTEQ levels, inflammation biomarkers, or HRV biomarkers between those who dropped out from those who remained in the study (all p's > .05).

Gratitude

Missing GQ-6 values (9.6%) at one of the three time-points were replaced with imputed values. Adjusting for % LVEF and etiology, a repeated measures ANCOVA of GQ-6 scores, at T1 (pre-intervention), T2 (mid-intervention) and T3 (post-intervention) revealed a quadratic group × time interaction ($F = 6.0$, $p = .017$, $\eta^2 = .10$) with a medium effect size (see Table 2). Pair-wise comparisons revealed significant differences between groups across time from T1 to T2, with the gratitude journaling group increasing in gratitude scores from pre- to mid- intervention to a greater degree than the TAU group ($p = .038$). Also, there were group differences across time from T1 to T3 ($p = .044$) with the gratitude journaling group increasing in gratitude scores from pre- to post-intervention to a greater extent than the TAU group. Table S1, Supplemental Digital Content 1, contains partial correlations among GQ6 gratitude scores (mid- and post-intervention), and basal inflammatory biomarker levels and journaling task HRV responses (post-intervention), while adjusting for respective baseline (T1) levels.

Basal HRV

repeated measures ANCOVAs revealed that there were no group × time interactions for basal HRV in time (RMSSD), frequency (HF power), and non-linear (SD1) domains, adjusting for %LVEF and etiology (all p's > .10).

HRV response to gratitude task

A repeated measures ANCOVA revealed significant T3 (post-intervention) group × time effects for the gratitude journaling task for parasympathetic HRV measures, RMSSD ($F = 4.5$, $p = .049$, $\eta^2 = .14$) and SD1, ($F=4.2$, $p = .036$, $\eta^2 = .15$) and a trend for HF power ($F = 3.2$, $p = .084$, $\eta^2 = .12$), while adjusting for %LVEF and etiology. Medium to large effect sizes were revealed for all three analyses. At post-intervention, HRV increased in the gratitude intervention group in response to the journaling task while there were lower HRV responses during the task in the TAU group (see Table 2).

Inflammatory Index

Repeated measures ANCOVA revealed significant group × time interactions for the composite inflammatory index score derived from CRP, IL-6, sTNFrI and TNF-α, adjusting for %LVEF, etiology, and BMI ($F = 9.7$, $p = .004$, $\eta^2 = .21$).

Post-hoc analyses

Partial correlation analyses, adjusting for baseline values did not find significant relationships between mid- or post-intervention (T3) GQ6 scores and HRV (RMSSD, HF and SD1) journaling task responses ($p > .10$) or basal inflammatory biomarker index scores ($p > .10$).

DISCUSSION

There is a need for early employment of interventions to prevent disease advancement and ultimately to diminish morbidity and mortality for patients with HF (40). Transition from

asymptomatic Stage B to symptomatic Stage C HF is related to a large increase in mortality risk (5), and thus finding a means to protect against HF progression at early stages of the disease are vital. The current pilot study of patients with asymptomatic Stage B HF found that in response to the gratitude intervention there were potential improvements in objective measures of physical health that have been associated with HF prognosis. These biomarker improvements paralleled increases in gratitude levels across the intervention period. While these findings are encouraging, definitive conclusions cannot be made due to the modest sample size. However, the present pilot study suggests that large scale RCTs with active control conditions are warranted to ascertain whether improvements in physiologically relevant biomarkers associated with gratitude interventions can be achieved.

In the present study gratitude levels increased to a greater extent in the journaling intervention group after the first 4-weeks of the intervention compared with TAU, and although dipping by the end of the 8-week gratitude journaling intervention, still showed a significant improvement from baseline compared with TAU. Heightened gratitude levels at 4 weeks may result from the new practice of identifying or noticing areas in life to be grateful for, which may then lead to a new set-point (a “new normal”) at 8-weeks. However, caution should be taken in interpreting our findings since there were no significant differences in gratitude levels post-intervention suggesting the possibility of a regression to the mean. Future large-scale studies are needed to confirm our findings and to determine whether elevated gratitude levels are maintained for a prolonged period.

The present investigation saw no resting HRV differences from pre- to post-gratitude journaling compared with TAU, but group differences in post-intervention responses to the laboratory-based gratitude journaling task were observed. Parasympathetic HRV measures within time (RMSSD), non-linear (SD1) and a trend for frequency (HF power) domains appeared to increase in response to the gratitude journaling task following the 8-week gratitude journaling intervention compared with TAU. Acute challenges create a window into complicated physiological processes and can reveal alterations in physiological regulation that may be masked under resting conditions (41). Moreover, increases in parasympathetic cardiac tone during the laboratory-based journaling task may reflect state changes that occur while contemplating items or feelings of gratitude during daily life. On the other hand, since we did not perform a gratitude journaling task at baseline we cannot rule out whether group differences were present pre-intervention and carried forward to post-intervention. Rash et al (2011), the only other gratitude study that we are aware of that examined HRV (HF, LF (low frequency) and VLF (very low frequency) power) albeit in healthy young adults also observed increases in HRV with a gratitude induction task when compared with a memorable event induction task. However, their study differed from ours in that both groups were naive to journaling about these topics when participants performed the tasks (42).

Exercise training intervention studies that assess changes in HRV are more widely investigated in patients with CVD. Oliveira and colleagues (2013) suggests that despite conflicting findings, exercise training appears to improve autonomic function in patients with CVD, and to have prognostic implications (43). However, among patients with CVD, only 14-35% of eligible patients who suffer an MI participate in exercise training through

cardiac rehabilitation (44, 45). In patients with HF, aerobic exercise therapy has even lower adherence rates (46). Gratitude journaling requires little equipment, can be performed safely at home, and can be conducted by adult patients of any age with most co-morbidities. In addition, gratitude interventions may complement treatment regimens, which could potentially make up for shortfalls in exercise compliance, although further research on this is needed.

To our knowledge, there are no other gratitude intervention studies measuring inflammatory biomarkers. HF is characterized by chronic inflammation, with elevated circulating inflammatory cytokines associated with ventricular remodeling by inducing ventricular hypertrophy, fibrosis and apoptosis (25). A specific panel of inflammatory markers, CRP, IL-6, TNF-α and sTNFr1, was chosen to form an inflammatory biomarker index for the present study that are associated in patients with HF with both worse self-reported health status (47) and disease progression and mortality (48, 49). We found that patients with Stage B HF in the gratitude journaling group had a reduction of the basal plasma inflammatory index compared with TAU controls. These results are consistent with our recent naturalistic study (n = 186) that found patients expressing more gratitude also had lower levels of an inflammatory biomarker index (14). However, in the current pilot study IL-6 levels included in the inflammatory biomarker index differed at baseline, and thus caution should be taken in interpreting the results and further research is clearly needed to make definitive conclusions about the effects of gratitude journaling on inflammatory biomarker alterations.

There were no relationships found between gratitude levels at mid- and post-intervention and HRV responses to the gratitude induction task post-intervention or with post-intervention basal inflammatory biomarker index scores. Since biomarkers were not measured at mid-intervention it is unknown whether there was a correspondence with gratitude levels at mid-intervention. Future larger-scale studies with added biomarker time-points during the gratitude intervention will help to determine relationships between changes in gratitude levels and physiological outcomes. Thus, it is not clear from our study by what mechanism gratitude journaling affects HRV and inflammation. Other psychological or behavioral factors may be mediating the changes observed in HRV and inflammatory biomarkers in response to the intervention. Wood et al (2010) suggest that gratitude interventions potentially operate through other mechanisms (10) such as engaging in protective health behaviors such as regular exercise, a healthy diet, and seeking regular health care (50). The identification of other potential mediating factors that affect biological changes associated with the practice of gratitude will enable the determination of the mechanisms of action. Changes in symptoms of depression as a mediating factor would be of particular interest in future investigations, since various studies have associated depression with inflammation, as well as HRV e.g. (51, 52).

Limitations of the current study that should be addressed in a larger scale RCT

This pilot study was composed of a modest sample size. In addition, the optimal dose of journaling frequency and duration for patients with asymptomatic HF is not yet known. A follow up study is needed examining various doses of the journaling intervention. We chose an 8-week intervention duration since Emmons and McCullough (2003) found reductions in

self-reported health related complaints with a longer intervention time, but not at shorter intervals of two or three weeks. Although we found improvements in gratitude levels at mid-intervention, we did not assess physiological measures at that time point and so it is unknown whether physiological effects may have occurred earlier than 8-weeks.

In spite of randomization there was a significant pre-intervention (baseline) group difference in IL-6 (see Table 1). Generalizability of inflammatory biomarker findings may be limited since there may have been systemic differences between the two groups. Changes over time for both groups could have resulted from a regression to the mean. It is suggested that a potential limitation of small clinical trials ($n < 100$) is that simple randomization methods may result in imbalanced baseline characteristics among treatment and control groups (53, 54). Also a limitation was the lack of standardization of baseline and post-treatment times of lab visits which could have affected our results, since many inflammatory factors are characterized by diurnal variation (55). Other factors might have confounded the results, including depressive symptoms and medication use. Another limitation was the absence of an HRV gratitude journaling task at baseline to determine whether the associations found post- intervention were not due to individual differences present at baseline. Also, the decrease in parasympathetic HRV signal in the control group may have been the result of a cognitive task in which they were unfamiliar.

This pilot study lacked an active control condition, therefore it is unknown whether participant expectations affected outcome measures. In addition, since the TAU group was not restricted in their activities other than participation in outside studies, it is unknown whether they participated in healthy lifestyle changes during the study period that affected results. However, the LTEQ was administered at baseline and post-intervention and there were no group differences in leisure time exercises, suggesting that the TAU group did not add physical activities during participation in the study.

Finally, there were differences in attrition between the groups, with reasons reported for dropping-out by those who could be contacted being time constraints and loss of interest in participation. However, by not having a matching journaling control group we are unable to determine whether greater attrition in the gratitude journaling group was due to differences in propensity for journaling, resulting in a selection bias that could have affected outcomes of the study. However, there were no differences in those who dropped out in age, education, health related factors such as %LVEF and etiology. As a pilot study, our aim was to preliminarily explore intervention related changes and thus we did not perform an intent-to-treat analysis, and thus did not include participants that did not participate in the gratitude journaling intervention. Future studies should consider including interviews and focus groups, which may provide additional information to better determine for whom gratitude journaling is an appropriate intervention.

Conclusions

The results of the present pilot study suggest that a future large scale clinical trial with an active control group is warranted to further examine autonomic and inflammatory biomarkers in response to a gratitude journaling intervention. Research suggests HRV levels are associated with CVD prognosis. Also, it is known that circulating levels of inflammatory

biomarkers are related to morbidity and mortality in patients with HF (22-24). Our preliminary results show a potential for the gratitude journaling intervention as a novel tool for improving physiological factors associated with CVD prognosis. Future larger scale studies are necessary to confirm the benefits of gratitude journaling on physiological alterations, and to determine potential clinical relevance for CVD outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by the John Templeton Foundation, Grant no. 15627, Expanding the Science and Practice of Gratitude and NIH R01 HL07355.

Abbreviations

TAU	treatment as usual
HF	heart failure
GQ6	6-item Gratitude Questionnaire
LTEQ	Leisure-time Exercise Questionnaire
HRV	heart rate variability
ANS	autonomic nervous system
CVD	cardiovascular disease
AHA	American Heart Association
ACC	American College of Cardiology
LV	left ventricular
EF	ejection fraction
ECG	electrocardiogram
CRP	c-reactive protein
TNF-α	tumor necrosis factor-alpha
IL-6	interleukin −6
sTNFr1	soluble tumor necrosis factor-alpha receptor 1
ANCOVA	analysis of co-variance
ELISA	enzyme-linked immunosorbent assay
BMI	body mass index

MI	myocardial infarction
RMSSD	root mean square successive differences
SDNN	standard deviation of the N-N
SD1	standard deviation of the distances of the RRi to the slope of the line
HF	high frequency
LF	low frequency
VLF	very low frequency

References

1. Krum H, Stewart S. Chronic heart failure: time to recognize this major public health problem. The Medical journal of Australia. 2006; 184:147–8. [PubMed: 16489893]
2. Desai AS, Stevenson LW. Rehospitalization for heart failure: predict or prevent? Circulation. 2012; 126:501–6. [PubMed: 22825412]
3. Wang G, Zhang Z, Ayala C, Wall HK, Fang J. Costs of heart failure-related hospitalizations in patients aged 18 to 64 years. Am J Manag Care. 2010; 16:769–76. [PubMed: 20964473]
4. Hunt SA, American College of C, American Heart Association Task Force on Practice G. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol. 2005; 46:e1–82. [PubMed: 16168273]
5. Ammar KA, Jacobsen SJ, Mahoney DW, Kors JA, Redfield MM, Burnett JC Jr. Rodeheffer RJ. Prevalence and prognostic significance of heart failure stages: application of the American College of Cardiology/American Heart Association heart failure staging criteria in the community. Circulation. 2007; 115:1563–70. [PubMed: 17353436]
6. Rozanski A. Behavioral cardiology: current advances and future directions. Journal of the American College of Cardiology. 2014; 64:100–10. [PubMed: 24998134]
7. Dubois CM, Beach SR, Kashdan TB, Nyer MB, Park ER, Celano CM, Huffman JC. Positive psychological attributes and cardiac outcomes: associations, mechanisms, and interventions. Psychosomatics. 2012; 53:303–18. [PubMed: 22748749]
8. Huffman JC, Mastromauro CA, Boehm JK, Seabrook R, Fricchione GL, Denninger JW, Lyubomirsky S. Development of a positive psychology intervention for patients with acute cardiovascular disease. Heart international. 2011; 6:e14. [PubMed: 23825741]
9. Sacco SJ, Park CL, Suresh DP, Bliss D. Living with heart failure: psychosocial resources, meaning, gratitude and well-being. Heart & lung : the journal of critical care. 2014; 43:213–8. [PubMed: 24661743]
10. Wood AM, Froh JJ, Geraghty AW. Gratitude and well-being: a review and theoretical integration. Clin Psychol Rev. 2010; 30:890–905. [PubMed: 20451313]
11. Bono, G.; Emmons, RA.; McCullough, ME. Gratitude in practice and the practice of gratitude. Linley SJ, PA., editor. John Wiley & Sons, Inc.; Hoboken, NJ, US: 2004.
12. Emmons RA, McCullough ME. Counting blessings versus burdens: an experimental investigation of gratitude and subjective well-being in daily life. J Pers Soc Psychol. 2003; 84:377–89. [PubMed: 12585811]
13. Geraghty AW, Wood AM, Hyland ME. Attrition from self-directed interventions: investigating the relationship between psychological predictors, intervention content and dropout from a body dissatisfaction intervention. Soc Sci Med. 2010; 71:30–7. [PubMed: 20400220]
14. Mills PJ, Redwine L, Wilson K, Pung MA, Chinh K, Greenberg BH, Lunde O, Maisel A, Raisinghani A, Wood A, Chopra D. The Role of Gratitude in Spiritual Well-Being in

Asymptomatic Heart Failure Patients. Spirituality in Clinical Practice. 2015; 2:5–17. [PubMed: 26203459]

15. Thayer JF, Yamamoto SS, Brosschot JF. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. Int J Cardiol. 2010; 141:122–31. [PubMed: 19910061]
16. Kleiger RE, Miller JP, Bigger JT, Moss AJ. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. Am J Cardiol. 1987; 59:256–62. [PubMed: 3812275]
17. Bilchick KC, Berger RD. Heart rate variability. J Cardiovasc Electrophysiol. 2006; 17:691–4. [PubMed: 16836727]
18. Billman GE. Cardiac autonomic neural remodeling and susceptibility to sudden cardiac death: effect of endurance exercise training. Am J Physiol Heart Circ Physiol. 2009; 297:H1171–93. [PubMed: 19684184]
19. Machado DB, Crow RS, Boland LL, Hannan PJ, Taylor HA, Folsom AR. Electrocardiographic findings and incident coronary heart disease among participants in the Atherosclerosis Risk in Communities (ARIC) study. Am J Cardiol. 2006; 97:1176–81. [PubMed: 16616022]
20. La Rovere MT, Bigger JT, Marcus FI, Mortara A, Schwartz PJ. Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators. Lancet. 1998; 351:478–84. [PubMed: 9482439]
21. Shah SA, Kambur T, Chan C, Herrington DM, Liu K, Shah SJ. Relation of short-term heart rate variability to incident heart failure (from the Multi-Ethnic Study of Atherosclerosis). The American journal of cardiology. 2013; 112:533–40. [PubMed: 23683953]
22. Bouras G, Giannopoulos G, Hatzis G, Alexopoulos D, Leventopoulos G, Deftereos S. Inflammation and Chronic Heart Failure: From Biomarkers to Novel Anti-inflammatory Therapeutic Strategies. Medicinal chemistry. 2014
23. Torre-Amione G. Immune activation in chronic heart failure. Am J Cardiol. 2005; 95:3C–8C. discussion 38C-40C.
24. Bozkurt B, Mann DL, Deswal A. Biomarkers of inflammation in heart failure. Heart Fail Rev. 2010; 15:331–41. [PubMed: 19363700]
25. Gullestad L, Aukrust P. Review of trials in chronic heart failure showing broad-spectrum anti-inflammatory approaches. Am J Cardiol. 2005; 95:17C–23C.
26. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ, Chamber Quantification Writing G, American Society of Echocardiography's G, Standards C, European Association of E. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005; 18:1440–63. [PubMed: 16376782]
27. Mccullough ME, Emmons RA, Tsang JA. The grateful disposition: a conceptual and empirical topography. J Pers Soc Psychol. 2002; 82:112–27. [PubMed: 11811629]
28. Hill PL, Allemand M, Roberts BW. Examining the Pathways between Gratitude and Self-Rated Physical Health across Adulthood. Pers Individ Dif. 2013; 54:92–6. [PubMed: 23139438]
29. Godin G, Shephard RJ. A simple method to assess exercise behavior in the community. Can J Appl Sport Sci. 1985; 10:141–6. [PubMed: 4053261]
30. Liu Y, Zhu SH, Wang GH, Ye F, Li PZ. Validity and reliability of multiparameter physiological measurements recorded by the Equivital LifeMonitor during activities of various intensities. Journal of occupational and environmental hygiene. 2013; 10:78–85. [PubMed: 23259751]
31. Heilman KJ, Porges SW. Accuracy of the LifeShirt (Vivometrics) in the detection of cardiac rhythms. Biological psychology. 2007; 75:300–5. [PubMed: 17540493]
32. Kent L, O'Neill B, Davison G, Nevill A, Elborn JS, Bradley JM. Validity and reliability of cardiorespiratory measurements recorded by the LifeShirt during exercise tests. Respiratory physiology & neurobiology. 2009; 167:162–7. [PubMed: 19505672]

33. Korhonen, I.; Mainardi, L.; Yppärilä, H.; Musialowicz, T., editors. Comparison of linear and non-linear analysis of heart rate variability in sedated cardiac surgery patients.. 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society; Istanbul, Turkey. 2001.
34. Baumert M, Baier V, Haueisen J, Wessel N, Meyerfeldt U, Schirdewan A, Voss A. Forecasting of life threatening arrhythmias using the compression entropy of heart rate. Methods of information in medicine. 2004; 43:202–6. [PubMed: 15136870]
35. Hoyer D, Friedrich H, Zwiener U, Pompe B, Baranowski R, Werdan K, Muller-Werdan U, Schmidt H. Prognostic impact of autonomic information flow in multiple organ dysfunction syndrome patients. International journal of cardiology. 2006; 108:359–69. [PubMed: 15979171]
36. Hoshi RA, Pastre CM, Vanderlei LC, Godoy MF. Poincare plot indexes of heart rate variability: relationships with other nonlinear variables. Auton Neurosci. 2013; 177:271–4. [PubMed: 23755947]
37. Mourot L, Bouhaddi M, Perrey S, Cappelle S, Henriet MT, Wolf JP, Rouillon JD, Regnard J. Decrease in heart rate variability with overtraining: assessment by the Poincare plot analysis. Clinical physiology and functional imaging. 2004; 24:10–8. [PubMed: 14717743]
38. Mourot L, Bouhaddi M, Perrey S, Rouillon JD, Regnard J. Quantitative Poincare plot analysis of heart rate variability: effect of endurance training. European journal of applied physiology. 2004; 91:79–87. [PubMed: 12955518]
39. Cohen, J. Statistical power analysis for the behavior sciences. 2nd ed.. Lawrence Erlbaum Association, Inc.; Hillsdale, New Jersey: 1988.
40. Hunt SA. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol. 2005; 46:e1–82. [PubMed: 16168273]
41. Linden W, Gerin W, Davidson K. Cardiovascular reactivity: status quo and a research agenda for the new millennium. Psychosom Med. 2003; 65:5–8. [PubMed: 12554811]
42. Rash J, Matsuba M, Prkachin K. Gratitude and Well-Being: Who Benefits the Most from a Gratitude Intervention? Applied Psychology: Health and Well-Being. 2011; 3:350–69.
43. Oliveira NL, Ribeiro F, Alves AJ, Teixeira M, Miranda F, Oliveira J. Heart rate variability in myocardial infarction patients: effects of exercise training. Rev Port Cardiol. 2013; 32:687–700. [PubMed: 23993292]
44. Lavie C, Milani R, Ventura H. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. J Am Coll Cardiol. 2009; 53:1925–32. [PubMed: 19460605]
45. Balady GJ, Ades PA, Bittner VA, Franklin BA, Gordon NF, Thomas RJ, Tomaselli GF, Yancy CW. Referral, enrollment, and delivery of cardiac rehabilitation/secondary prevention programs at clinical centers and beyond: a presidential advisory from the american heart association. Circulation. 2011; 124:2951–60. [PubMed: 22082676]
46. Barbour K, Miller N. Adherence to exercise training in heart failure: a review. Heart Fail Rev. 2008; 13:81–9. [PubMed: 18008161]
47. Mommersteeg PM, Kupper N, Schoormans D, Emons W, Pedersen SS. Health-related quality of life is related to cytokine levels at 12 months in patients with chronic heart failure. Brain Behav Immun. 2010; 24:615–22. [PubMed: 20074634]
48. Araújo J, Lourenço P, Azevedo A, Friões F, Rocha-Gonçalves F, Ferreira A, Bettencourt P. Prognostic value of high-sensitivity C-reactive protein in heart failure: a systematic review. J Card Fail. 2009; 15:256–66. [PubMed: 19327628]
49. Deswal A, Petersen NJ, Feldman AM, Young JB, White BG, Mann DL. Cytokines and cytokine receptors in advanced heart failure: an analysis of the cytokine database from the Vesnarinone trial (VEST). Circulation. 2001; 103:2055–9. [PubMed: 11319194]
50. Alspach G. Extending the tradition of giving thanks recognizing the health benefits of gratitude. Crit Care Nurse. 2009; 29:12–8.
51. Taylor CB. Depression, heart rate related variables and cardiovascular disease. Int J Psychophysiol. 2010; 78:80–8. [PubMed: 20420861]

52. Raison CL, Capuron L, Miller AH. Cytokines sing the blues: inflammation and the pathogenesis of depression. Trends Immunol. 2006; 27:24–31. [PubMed: 16316783]

53. Lachin JM, Matts JP, Wei LJ. Randomization in clinical trials: conclusions and recommendations. Control Clin Trials. 1988; 9:365–74. [PubMed: 3203526]

54. Lachin JM. Statistical properties of randomization in clinical trials. Control Clin Trials. 1988; 9:289–311. [PubMed: 3060315]

55. Keller M, Mazuch J, Abraham U, Eom GD, Herzog ED, Volk HD, Kramer A, Maier B. A circadian clock in macrophages controls inflammatory immune responses. Proc Natl Acad Sci U S A. 2009; 106:21407–12. [PubMed: 19955445]

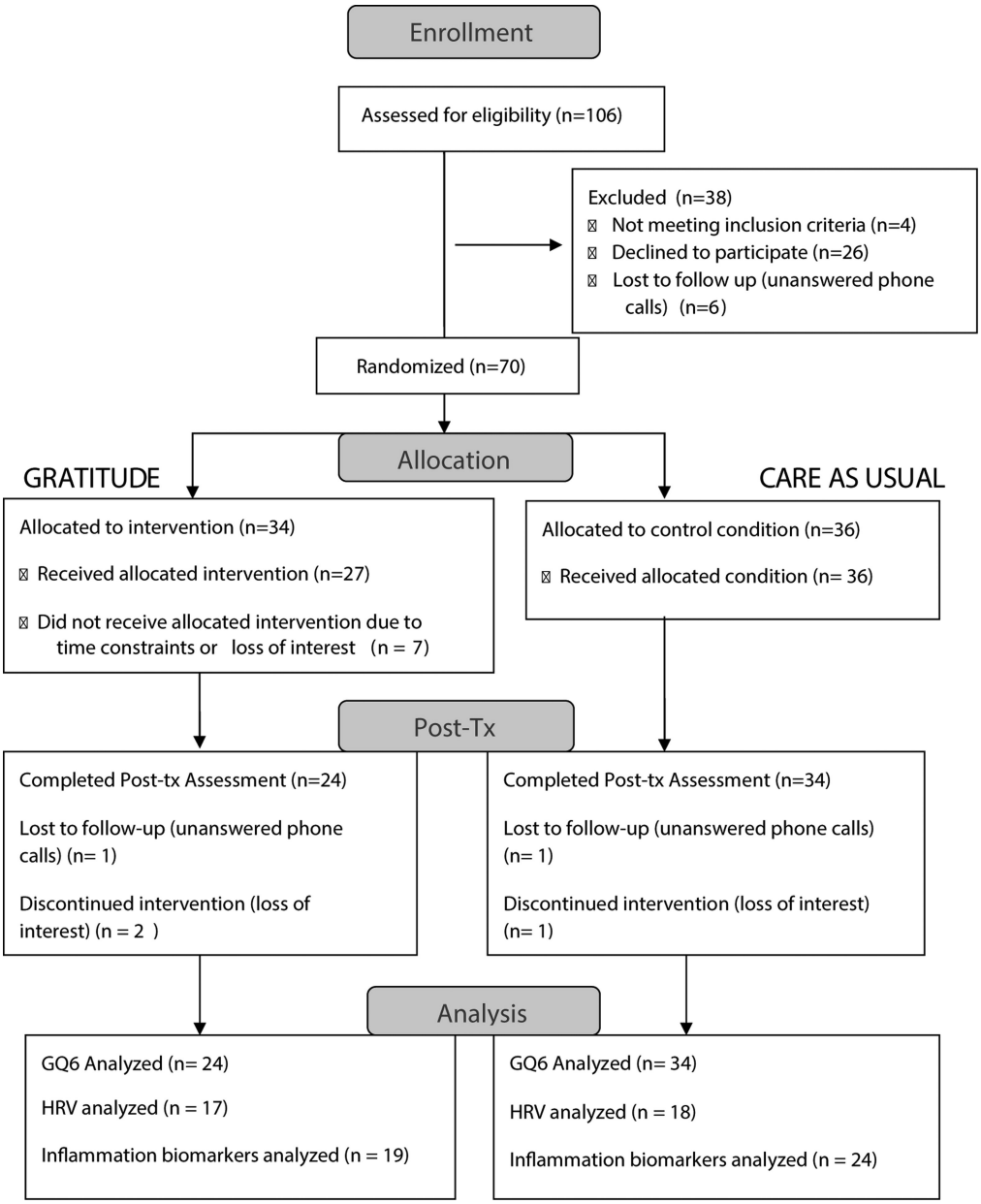

Figure 1.
CONSORT diagram.

Table 1

Sociodemographic, Medical, Behavioral, and Inflammatory Biomarker Characteristics of Study Participants.

	Journal Group	N	TAU	N	p value
Age years (mean, s.d.)	66.43 (8.4)	24	66.0 (7.1)	34	.87
Sex (% male)	95.2	24	86.4	34	.32
Race (% white)	73.7	24	63.6	34	.27
College Degree (%)	38.5	24	29.2	34	.50
LVEF (%, s.d.)	62.9 (9.4)	24	62.9 (5.7)	34	.99
BMI kg/meter (mean, s.d.)	29.6 (5.5)	24	29.8 (4.2)	34	.87
GQ6 (mean, s.d.)	32.0 (9.01)	24	33.6 (6.96)	34	.60
Marital (% married)	55.0	24	47.4	34	.63
LTEQ (mean, s.d.)	32.04 (30.14)	24	36.59 (26.89)	34	.67
Diabetes (%)	36.8	24	27.8	34	.56
Etiology (%)		24		34	.51
Myocarditis	0		3.0		
Hypertrophic	13.6		15.2		
MI	13.6		18.2		
Idiopathic	4.5		0		
Ischemic	18.2		0		
Hypertension	31.8		42.4		
Valvular	4.5		6.1		
Other	13.6		15.2		
Inflamm Factor	0.18 (0.82)	19	−0.26 (1.13)	24	.19
log sTNFr1 (pg/ml)	7.03 (0.40)		7.04 (0.49)		.98
log CRP (mg/dl)	.82 (1.26)		.92 (1.66)		.84
log TNF alpha (pg/ml)	1.06 (0.28)		0.94 (0.30)		.51
log IL-6 (pg/ml)*	0.87 (0.61)		0.34 (0.55)		.010
log RMSSD	3.53 (0.87)	17	3.41 (0.71)	18	.89
log HF power	5.31 (2.13)	15	5.57 (0.86)	16	.78
log SD1	3.09 (0.84)	17	3.05 (0.70)	18	.92

Independent t-tests and Kruskal-Wallis tests were used to determine significant group differences. s.d. = standard deviation; LVEF = left ventricular ejection fraction; BMI = body mass index; GQ6 = gratitude questionnaire – 6 item; LTEQ = Leisure-Time Exercise Questionnaire; MI = myocardial infarction; sTNFr1 = soluble tumor necrosis factor receptor 1; IL-6 = interleukin 6; RMSSD = root mean square successive differences; HF power = high frequency power; SD1 = standard deviation of the distances of the RRi to the slope of the line

* $p < .05$

Table 2

Group resting levels across time.

	Gratitude Journaling Group			Treatment as Usual					
	Pre-	**Mid-**	**Post-**	**Pre-**	**Mid-**	**Post-**	**η^2**	**Observed Power**	**P**
GQ6 mean (SD)	31.7	35.04	33.48	33.6	33.60	34.86	.10	.67	.017
	(9.01)	(7.86)	(8.10)	(6.96)	(5.52)	(6.06)			
log RMSSD mean (SD)	3.53	-	3.60	3.41	-	3.59	< .001	.05	.99
	(0.87)	-	(0.67)	(0.71)	-	(0.80)			
log HFp mean (SD)	5.31	-	5.42	5.57	-	5.14	.04	.15	.35
	(2.13)	-	(1.66)	(0.86)	-	(1.41)			
log SD1 mean (SD)	3.09	-	3.23	3.05	-	3.22	.002	.06	.81
	(0.84)	-	(0.67)	(0.70)	-	(0.80)			
Infamm. factor mean (SD)	0.16	-	−0.33	−0.25	-	−0.05	.21	.86	.004
	(0.82)	-	(0.91)	(1.13)	-	(0.97)			
Log CRP (mg/dl)	.82	-	.09	.92	-	.61			
	(1.26)	-	(0.91)	(1.66)	-	(1.23)			
Log IL-6 (pg/ml)	.87	-	.59	.34	-	.49			
	(.61)	-	(.54)	(.55)	-	(.54)			
Log TNFa (pg/ml)	1.06	-	1.09	.94	-	1.06			
	(.28)	-	(.35)	(.30)	-	(.38)			
Log sTNFrl (pg/ml)	7.03	-	6.82	7.04	-	6.95			
	(.40)	-	(.52)	(.49)	-	(.44)			
LTEQ mean (SD)	32.04	-	36.31	36.59	-	37.56	.003	.06	.84
	(30.14)		(28.62)	(26.89		(27.81)			

Data were analyzed with repeated measures ANCOVAs, adjusting for %LVEF, Stage B etiology in all analyses plus BMI (kg/meter) for inflammation biomarkers. P values represent group x time interactions. ANCOVA = analysis of co-variance; LVEF = left ventricular ejection fraction; BMI = body mass index; SD = standard deviation; LVEF = left ventricular ejection fraction; BMI = body mass index; GQ6 = gratitude questionnaire – 6 item; LTEQ = Leisure-Time Exercise Questionnaire; sTNFr1 = soluble tumor necrosis factor receptor 1; IL-6 = interleukin 6; RMSSD = root mean square successive differences; HF power = high frequency power; SD1 = standard deviation of the distances of the RRi to the slope of the line.

Table 3

Group responses to the journaling task post- intervention.

	Gratitude Journaling		Treatment as Usual		η^2	Observed Power	P
	Rest	**Journaling**	**Rest**	**Journaling**			
log RMSSD mean (SD)	3.68	3.85	3.56	3.32	.14	.51	.049
	(0.75)	(0.80)	(0.80)	(0.81)			
log HF power mean (SD)	5.60	5.91	5.51	4.88	.12	.41	.084
	(1.89)	(1.72)	(1.52)	(1.45)			
log SD1 mean (SD)	3.31	3.48	3.19	2.98	.15	.57	.036
	(0.75)	(0.78)	(0.80)	(0.79)			

Group differences were determined using repeated measures ANCOVAs, adjusting for %LVEF and Stage B etiology. P values represent group x time interactions. ANCOVA = analysis of co-variance; LVEF= left ventricular ejection fraction; SD= standard deviation; η^2 = partial eta squared; RMSSD = root mean square successive differences; HF power = high frequency power; SD1 = standard deviation of the distances of the RRi to the slope of the line.