




Mind-Body and Psychosocial Interventions May Similarly Affect Heart Rate Variability Patterns in Cancer Recovery: Implications for a Mechanism of Symptom Improvement

Integrative Cancer Therapies
Volume 19: 1–10
© The Author(s) 2020
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/1534735420949677
journals.sagepub.com/home/ict


Linda Larkey, PhD¹ , Wonsun Kim, PhD¹ , Dara James, PhD¹,
Moé Kishida, PhD¹, Maricarmen Vizcaino, PhD², Jennifer Huberty, PhD²,
and Narayanan Krishnamurthi, PhD¹

Abstract

Background: Advancements in early detection and treatment of cancer have led to increased survival rates and greater need to identify effective supportive care options for resolving symptoms of survivorship. Many non-pharmacological approaches to symptom management during and after cancer treatment involve emotional self-regulation as a central strategy for improving well-being. Identifying commonalities among these strategies' mechanisms of action may facilitate understanding of what might be useful for optimizing intervention effects. Heart rate variability (HRV) parameters are indicative of improved autonomic nervous system (ANS) balance and resiliency and reduced emotional distress and are thus identified as a mechanism to discuss as a marker of potential for intervention efficacy and a target for optimization.

Methods: HRV data from 2 studies, 1 examining a mind-body intervention and 1 examining a psychosocial intervention, are presented as a point of discussion about preliminary associations between the interventions, change in HRV, and emotional distress reduction.

Results: HRV significantly decreased in sympathetic activity in response to a mind-body intervention (Qigong/Tai Chi), and increased vagal tone in response to a psychosocial (storytelling) intervention. In both, these changes in HRV parameters were associated with improved emotional states.

Conclusion: Our preliminary data suggest that HRV may serve as an important marker of underlying changes that mediate emotional regulation; this observation deserves further investigation. If identified as a worthy target, focusing on interventions that improve HRV within the context of interventions for cancer patients may be important to key outcomes and clinical practice.

Keywords

heart rate variability, mind-body, Qigong, Tai Chi Easy, cancer survivorship, cancer supportive care, psychosocial intervention, storytelling

Submitted November 7, 2019; revised July 16, 2020; accepted July 23, 2020

Introduction

Improvements in early detection and treatment of cancer have resulted in declining cancer incidence and mortality rates and increasing survival rates. In the US, cancer survivors are expected to exceed 20.3 million by 2026.¹ With continued incidence and a growing population of cancer survivors, there is an ongoing need to identify supportive care options beyond pharmacologic interventions for resolving symptoms such as fatigue, cognitive impairment, sleep disturbance, and emotional distress during and after treatment.^{2,3}

Our focus in this paper is to discuss 2 non-pharmacological types of interventions; mind-body and psychosocial, and to

¹Edson College of Nursing and Health Innovation, Arizona State University, Phoenix, AZ, USA

²College of Health Solutions, Arizona State University, Phoenix, AZ, USA

Corresponding Author:

Linda Larkey, Center for Health Promotion and Disease Prevention, Edson College of Nursing and Health Innovation, Arizona State University, 500 N 3rd St, Phoenix, AZ 85004, USA.
Email: linda.larkey@asu.edu



identify overlapping components that may explain the potential mechanism(s) underlying the benefits commonly found in response to these interventions.⁴⁻⁷ Each of these 2 intervention types requires an individual's investment of time and effort in changing one's emotions and responses to life challenges. Mind-body practices are defined as a combination of "mental focus, controlled breathing, and body movements to help relax the body and mind,"⁸ while psychosocial interventions generally include emotional appraisal and strategies for active, cognitive coping often guided by a professional interventionist.⁹ As such, in both interventions, the cancer patient or survivor engages one's own inner resources to manage emotional responses¹⁰⁻¹² in contrast to those practices in which the focus is receiving treatment at the hands of a massage therapist or acupuncturist.

In the current paper, we suggest there is value in examining and promoting underlying mechanisms that are activated by the individual to cope with emotional distress when engaging in mind-body and psychosocial interventions, and to further examine the degree to which these interventions may activate such mechanisms. In particular, although there may be a number of physiological mechanisms that explain changes in cancer-related symptoms over time (eg, reductions in biomarkers of inflammation associated with decreased fatigue),¹³ we will closely examine heart rate variability (HRV) as a factor over which individuals have direct influence in the short term, and may affect set-point changes long term, as well as the link between HRV to emotional self-regulation,¹⁴ stress, and anxiety.¹⁵ Recent studies have implicated HRV as a predictor of longer survival after cancer diagnosis,¹⁶ further suggesting the value of examining the effects of interventions on HRV. By first recognizing a possible underlying factor (ie, HRV), and attempting to find ways to optimize such a factor, we introduce a potential strategy to obtain increased benefits from engaging in these practices. This review of HRV as a potential mechanism through which change might occur via both mind-body and psychosocial practices, relative to the effort on the part of the patient, will be followed by 2 small datasets from our research that provide examples of the proposed mechanism.

HRV: What Is It and How Is It Reported?

HRV is a measure of the variation in beat-to-beat time intervals of the heartbeat (ie, variability in the time series containing the time intervals between 2 successive "R" peaks of the QRS pattern on an electrocardiogram). The parameters derived from assessing these interval patterns are thought to represent (among other psychophysiological inputs) the interaction between the 2 branches of the ANS, sympathetic, and parasympathetic. In general, the variability in R-R intervals is calculated in 2 domains, namely, time and frequency domains.¹⁷ The time-domain represents the amount of variation in the R-R intervals by computing

indices such as the standard deviation of the intervals (SDNN) or root mean square of successive heartbeat interval differences (RMSSD). Higher values in time-domain measures are considered indicative of overall heart function resilience in adults¹⁸ and are commonly used parameters reported in personal heart rate monitors designed to track fitness progress.¹⁹

The frequency domain is based on a power spectrum analysis that examines R-R interval time series to provide a portion of the time series' power falling within given frequency spans, including the very low, low, and high-frequency spectra. Greater representation of high frequency (HF) power in the heart rhythm spectra (0.15-0.4 Hz) is consistently considered to be a marker of vagal dominance or vagal "tone," a factor often associated with reduced physiological stress reactivity and/or improved emotional self-regulation.^{20,21} Low frequency power (LF) is considered to be oscillations in the 0.04 to 0.15 Hz range. Also derived from these frequency data is a unique signature pattern called resonance frequency (RF). The RF is tied to a complex set of psychophysiological interacting influences including the baroreflex (arising from responses from stretch receptors in the arterial trunk and aorta, blood pressure, and respiratory rate) and reflects an optimum state of function for oxygen uptake as well as emotional self-regulation.²² The RF parallels an HRV pattern also called "coherence"; the rhythm pattern of RF/coherence is considered to be a marker of vagal tone, although the frequency range that characterizes this pattern is lower than the more commonly agreed upon HF range for vagal tone.²³ RF or coherence are thought to be somewhat lower due to a slower respiratory rate exhibited when the state of focused awareness on breathing is part of the instruction for achieving this rhythm or pattern resulting in a high amplitude peak in the HRV power spectrum near 0.1 Hz (usually with a range of 0.09-0.14 Hz).^{22,24-30} This 0.1 Hz near the higher end of LF, and associated with coherence, is thought to represent vagal tone in the lower respiratory rate ranges, and thus is also one of the targets we examine in looking for potential beneficial effects of a stress-reducing intervention.

Why Might HRV Be an Important Indicator of an Active Mechanism for Health Improvement/Symptom Reduction?

It has been consistently observed that overall HRV declines as a function of age which may indicate decreased adaptability or responsiveness of cardiac function to physiological changes.^{31,32} Poor outcomes after myocardial infarction (MI) or a diagnosis of chronic heart failure are also known to be predicted by lower time domain HRV (eg, reduced SDNN or RMSSD)^{33,34}. Further, low HRV in the time domain has been shown to be associated with increased

all-cause mortality^{35,36} and associated with stress,³⁷ and poor sleep.³⁸ In the power domain, reduced vagal activity, considered to be represented by decreased high frequency (HF) or, in some cases, increased low (LF) or very low-frequency (VLF) power, is associated with many stress-related disease risks, including cardiometabolic risk factors (eg, hypertension,²⁶ elevated lipids,³⁹ poor glucose metabolism,⁴⁰⁻⁴⁴ and increased body fat⁴⁵). For example, in a sample of breast cancer patients, poor vagal tone was an indicator of prospective anxiety over time.⁴⁶

On the other hand, improved vagal tone (indicated by increased HF power or, at slower breathing rates, LF power or RF/coherence) is considered to represent improved resiliency and reduced adverse response to stress.⁴⁷ Further, there are indications that emotional self-regulation and positive emotions may be associated with vagal tone HRV indicators,⁴⁸ but it is not well established in research that improving emotional state or interventions designed to assist participants to self-regulate consistently increases HRV. There is substantial evidence, however, suggesting HRV biofeedback directly impacts HRV parameters; thereby improving emotional status and mental health sequelae (eg, reduced PTSD symptoms, depression, stress, anxiety, insomnia⁴⁹⁻⁵¹), symptoms (eg, pain, inflammation⁵²), and addictive behaviors.⁵³⁻⁵⁵

Given these associations among HRV parameters and symptoms and/or emotional states, it appears there may be added potential for interventions that increase HRV to facilitate improvements for a range of physical, mental, and behavioral indicators. We therefore explore the types of interventions that are known to affect HRV, and as an example present 2 sets of data from our research in the specific arena of mind-body and psychosocial cancer supportive care interventions which demonstrated positive changes in HRV. In the end, it is suggested that HRV parameters indicative of vagal tone may serve as a target mechanism by which emotional self-regulation improvements and symptom and inflammation reduction are achieved.

Interventions Known to Affect HRV Parameters

In the existing literature, physical activity (PA) is the most well-known and tested intervention used to improve HRV (time-domain and frequency-domain indices). Levels of moderate to vigorous PA (eg, PA \geq 3 METS such as brisk walking and jogging) are generally found to be correlated with improved HRV (more time domain variability or greater HF power). These improved HRV parameters are considered to be markers for fitness among various populations and age groups, including cancer patients.⁵⁶⁻⁶¹ A recent study observed that cancer patients in recovery from treatment exhibited increased HRV with PA compared to those without PA; however, no effect was found for those in the midst of acute treatment.⁶⁰

Another category of interventions known to affect HRV includes mind-body practices, including meditation or mindfulness, and a category of PA called “Meditative Movement” (MM).⁶² Studies of breath-focused or meditation practices show increases in time domain HRV,^{63,64} an increase in HRV amplitude (during resting meditation post qigong and yoga),⁶⁵ and improvements in vagal tone (mostly indicated by HF power)⁶⁶⁻⁶⁹ from pre- to post-intervention.

MM, defined as practices that incorporate a focus on the body postures or movements, and a simultaneous focus on the breath to achieve a meditative state (eg, yoga, or qigong or tai chi),⁶² have been shown to be associated with improvements in HRV. A meta-analytic review of both Tai Chi and yoga combined found a significant effect for LF and HF power increases.⁷⁰ For some studies testing effects of MM on HRV, the target outcome was increased vagal tone at post-intervention assessed via either increased HF power or reduced low frequency/high frequency (LF/HF) ratio, but similarly interpreted as increased vagal tone, showing both significant⁷¹⁻⁷⁴ and non-significant changes⁷⁵ in one or more of the predicted HRV parameters.⁷⁶⁻⁷⁸ For other MM studies, overall levels of variability in beat-to-beat intervals (eg, SDNN) or baroreflex sensitivity were changed, but not the HF or LF/HF parameters.^{79,80} Overall, the evidence is mixed regarding associations of specific HRV parameters with MM practices, unlike the more consistent findings on HRV during stationary meditative or paced breathing practices.

Although it is commonly observed that HRV is affected by, or correlated with psychological and physiological stress,⁸¹⁻⁸⁵ there are only a few studies that have examined the effects of psychosocial interventions on emotional distress concurrent with evaluating improvements in HRV. However, the results for those intervention studies are reasonably consistent irrespective of the type of interventions and population such as art-making among distressed college students,⁸⁶ counseling and psychosocial support to veterans with PTSD,³² and promoting physical and psychological rehabilitation for cancer survivors.⁸⁷ These psychosocial interventions designed to reduce emotional distress typically result in improvements in one or more of the HRV parameters.

In our work with cancer survivors testing these 2 types of interventions, mind-body (primarily Qigong and Tai Chi) and psychosocial (using narratives as therapeutic intervention), we have examined effects on a range of symptoms including fatigue, sleep, emotional distress (anxiety/depression), and cognitive function. While we report a variety of changes in emotional and physical symptoms,⁸⁸⁻⁹⁰ we have noted some form of emotional processing resulting in emotional self-regulation to be a common experience of participants, either through recognition and validation of emotion identified in narratives or through relaxation prompted by the combination of rhythmic movements synchronized with deep breathing in mind-body experiences. To examine how

this common factor, emotional self-regulation may underlie these processes, we have systematically begun to investigate if and how these interventions may impact HRV. The HRV parameters we review (eg, coherence, HF power) are considered psychophysiological representations of emotional responses such as emotional self-regulation of feelings related to social safety,⁹¹ or mitigation of anxiety.^{32,86} Thus, HRV provides a window to examine this common factor and the opportunity to assess if it contributes to observed outcomes. Here we present 2 examples of data collected within the context of larger, parent studies (either published⁹⁰ or to be published later) to illustrate the potential of HRV as a psychophysiological marker associated with desired emotional self-regulation outcomes.

In both of the following brief study reports, HRV assessments were conducted using equipment designed to capture inter-beat intervals of the heart beat⁹² using pulse sensors attached to the participants' earlobe. Participants were asked to sit quietly while recording a 3-minute session of their pulse.²⁹ The *EmWave Pro* (HeartMath[®]) software displays HRV in real time with visual representation of coherence level at each moment and accumulated coherence over time. Accumulated scores for time in coherence at the end of the session and the proportions of high, medium and low coherence are reported as percentages. Also, raw inter-beat interval data are captured and converted using internal system software to examine time domain and frequency domain HRV parameters.

Example 1: Qigong/Tai Chi and HRV. In one avenue of our research, we have explicitly focused on a set of MM forms sharing similar principles arising from the practices of Qigong, and the later evolution of Qigong inspired by martial arts, Tai Chi, to explore effects on cancer survivors and other populations. Tai Chi shows evidence for reducing psychological stress⁷⁰ and improving sleep⁹³ in systematic reviews and meta-analyses, with growing but still limited evidence for these outcomes for Qigong.^{94,95} While we acknowledge that Tai Chi and Qigong are different practices, they share similar roots, principles of practice, and are both designed to combine movement with a focus on the breath and a meditative state to achieve results (ie, MM practices).⁶² These 2 practices are sometimes combined in interventions for research.^{96,97} A number of reviews examining evidence of the effects of these practices combine them due to the classification as mind-body interventions⁹⁸⁻¹⁰¹ based on Traditional Chinese Medicine and the focus on cultivating “qi.” For example, meta-analytic reviews have demonstrated significant effects for anxiety, depression, fatigue, and sleep among those recovering from cancer/cancer treatment have been found for Qigong, Tai Chi or these practices combined.^{100,102}

The Qigong/Tai Chi (QTC) protocol tested in our research is standardized, manualized and called “Tai Chi

Easy™”¹⁰³ and includes a number of Qigong and Tai Chi moves that are taught as individual, repeated movements, straightforward to learn so that there is less cognitive “work,” easily adopted, and with an emphasis on a rhythmic, moving meditative state. In our prior research, and the currently reported studies, we have incorporated intervention fidelity strategies to assure the QTC was implemented with the appropriate components of movement, breath practices and meditative focus, and have developed and applied an instrument to assess the breath and meditative aspects to assure fidelity.¹⁰⁴ For purposes of demonstration of the proposed HRV-as-mechanism, we first sought to establish that HRV parameters change in response to QTC, and then examined how that change may impact an emotion-based outcome, depression.

In our study of female breast cancer survivors (published without HRV data), we randomized participants to either QTC or a sham Qigong (SQG) control intervention (low-intensity, low-impact movements as QTC but without the focus on the breath or meditative state).⁹⁰ The purpose of the study was to test effects of the QTC compared to SQG on fatigue (primary outcome), depression and sleep (secondary outcomes). Of the 101 women randomized, 87 (mean age 58.8, SD=8.94) completed the study with QTC showing significant effects on improved fatigue compared to SQG, and within group changes for QTC for improved sleep and decreased depression (but not for SQG) (details reported in Larkey et al⁹⁰).

The 3-minute sessions of HRV recordings provided percentages of time in low, medium, and high coherence. The QTC group (n=37) showed a mean low coherence (an indicator of sympathetic activity) of 75.69% (SD=19.62) at baseline, reduced to 52.53% (SD=32.54) after a 12-week intervention ($t=3.821$; $df=31$, $P=.001$). Reduction in low coherence values indicates lower sympathetic activation in the ANS relative to parasympathetic, also associated with the relaxation response. Although the mean drop in low coherence was smaller for participants in the SQG compared to QTC, this difference was not significant (QTC mean change=-23.16, SD=34.28; SQG mean change=-15.94, SD=31.65; $t=.370$; $df=66$, $P=.688$). The within-group reduction of coherence in SQG was not significant, which suggests that only the QTC intervention produced significant lowering of sympathetic activation. Furthermore, differences in percentage of high coherence HRV in pre- to post-QTC intervention readings were positively, significantly correlated with improvements in depression (Pearson correlation .367, $P=.042$).

While corroborating research is warranted, these preliminary results demonstrate HRV parameter improvements in coherence (earlier also described as resonance frequency, considered a vagally-mediated state associated with reduced sympathetic activation) among breast cancer survivors practicing QTC. This suggests that the practice of QTC may

reset the ANS to respond to emotional self-regulatory attempts to reduce emotional distress.

Example 2: A storytelling intervention addressing psychosocial distress with patients undergoing hematopoietic cell transplantation and HRV. Patients undergoing hematopoietic cell transplantation (HCT) and their caregivers are at risk for high levels of psychosocial distress.^{105,106} Treatment requires lengthy hospitalizations, possible relocation close to the treatment center, mandatory employment cessation for at least 6 months, isolation in a germ-free environment, and possibility of re-occurrence and death. Previous studies indicate that 25% to 50% of HCT survivors and caregivers report psychosocial distress, including depression, anxiety, and social isolation.^{105,107,108} Very few studies have explored the potential for psychosocial interventions to reduce emotional distress for patients and/or caregivers after HCT. Intervention types have included telephone-based cognitive behavior therapy,¹⁰⁹ and psychoeducation.^{107,110}

Narrative-based (storytelling) interventions have been used to understand patients' experiences of illness, to improve health communication and engagement, and to ameliorate distress as a therapeutic intervention in cancer care.¹¹¹⁻¹¹⁵ In our model of narratives as therapeutic intervention, we suggest a set of narrative elements considered essential to engage interest in and connection to a story and its characters for emotional acceptance effect.¹¹⁶ Narratives with likeable narrators who are similar to the viewers, generate empathy and have an appealing, relatable storyline with dramatic sequencing are more likely to generate the experience of transportation into the story (ie, getting "carried away" by the story), and identification (with characters and the story).¹¹⁷ Viewers of such engaging stories that address a difficult life event to be encountered are expected, then, to vicariously experience emotional processing and expression, leading to emotional acceptance, emotional self-regulation, and reduced anxiety.

In an ongoing pilot study, we are testing the use of digital stories (DS) developed in a group-based 3-day DS workshop conducted with survivors who had undergone HCT within the past 2 years. The digital stories, produced by the individuals attending the workshop, are short, first-person visual narratives that synthesize digital images, audio recording, music, and text to document personal experiences. The digital storytelling workshop is described in detail elsewhere.¹¹⁸

A set of digital stories from these patients/survivors, are being used to present as interventional content to new patients/caregivers in the current pilot study reported. The primary purpose of this pilot study is to examine the feasibility of a DS intervention using stories shared by those who already experienced HCT and to evaluate its preliminary effects on psychosocial distress among current HCT patients and their caregivers. A total of 20 HCT patient-caregiver

dyads (n=40, patient mean age=58.9 years old [SD=9.66], and caregiver mean age=59.5 years old [SD=8.57]) recruited to date were randomized to 4 weeks of a weekly DS-viewing intervention compared to an information-only control (IC) condition. Data were collected at baseline (T1), and immediately at post-intervention (4-weeks, T2) for the psychosocial distress related variables (depression, anxiety, social support), and included HRV assessments at these time points. Because the main aim of this pilot study was to establish feasibility of the protocol rather than formal hypothesis testing, we focused our presentation on estimates of standardized between-group (DS vs IC) differences (Cohen's *d*) in Δ s when describing intervention effects on outcomes.

Scores for depression and anxiety decreased from pre- to post-intervention, for both conditions indicating that DS and IC were effective in reducing distress. On average, ratings of perception of social support increased for the DS group ($\Delta=0.07$, SD=0.15) but decreased for the IC group ($\Delta=-0.05$, SD=0.12).

The HRV findings drawn from analyses of the inter-beat interval data from the 3-minute session of participants at T1 and T2 revealed that the frequency domain values for HRV indicated by high frequency (HF) power increased in the DS group ($\Delta=2.23$, SD=0.12) and IC group ($\Delta=0.8$, SD=0.13) from pre- to post-intervention. Furthermore, those changes in HF power HRV patterns were correlated with improved emotional coping (Pearson correlation $r=.62$, $P<.05$) and emotional expression ($r=.57$, $P<.05$).

These preliminary results showed that viewing digital stories, with content evoking emotional contexts similar to one's own health challenges, may facilitate emotional expression and emotional processing, which may contribute to improvements in psychosocial well-being. These changes are associated with a shift to HRV patterns associated with vagal control, or coherence, and parasympathetic dominance. It is possible that accessing appropriate information could help patients and caregivers to reduce treatment-related information needs, which could have an influence on reducing emotional distress and improving HRV parameter in the IC group.

A larger clinical trial is needed to examine the associations between the DS intervention and the improvement of HRV parameters among HCT patients and caregivers relative to the IC condition to help explain our preliminary results. Although we have presented the preliminary findings from the DS and IC interventions in this paper, our next steps are to examine the effects of DS compared to IC on HRV with more robust implementation when the study is completed with a larger sample. A full paper is under construction which includes a consort flow chart and more detailed information about recruitment, data collection procedures, and data analyses that will represent the final study.

Discussion

In this article, we sought to examine heart rate variability (HRV) as a potential mechanism and its association with emotional self-regulatory effects in 2 specific intervention types (mind-body and psychosocial interventions) through a preliminary presentation of results from a prior (published) and an ongoing study. There are a limited number of published studies examining changes in HRV in cancer patients in response to non-pharmacological interventions designed to reduce symptoms, emotional distress, and inflammation. As noted above, numerous studies have examined the effects of meditation and MM practices on HRV parameters in non-cancer contexts. To date, other than our own preliminary findings with breast cancer survivors, only 2 other recent publications show work on this cancer track, 1 showing increases in SDNN, and total power in response to Qigong and mindfulness,¹¹⁹ and 1 in which a sleep intervention increased HF power.¹²⁰ No published study thus far has examined HRV responses to storytelling interventions.

Implications of our modest findings may lead to new considerations for future directions. First, we suggest that assessments of HRV parameters be routinely added to studies that examine non-pharmacologic interventions for cancer patients and survivors so that a body of knowledge may accumulate. If a variety of stress-reducing, emotion regulating practices are examined for this common denominator, a pattern of HRV as a potential mechanism may emerge. Gathering measures of HRV is a non-invasive data collection method; moreover, it is reasonably inexpensive (eg, the cost of the device for the data collection at the pre and post-intervention and/or follow up period and software to analyze, can be obtained for less than \$600, compared to the higher costs required to gather and analyze blood or saliva biomarker data).

Our research strategies have mostly involved sampling HRV during brief episodes of non-engaged sitting to capture HRV parameters associated with ANS changes from pre- to post-intervention. However; there are many approaches detailed in consortium-developed HRV measurement guidelines to steer design decisions based on the goals of one's study (eg, examining stress reactivity and recovery) that may be considered.²⁹

Secondly, although we have only skimmed the surface by presenting these 2 study reports, there is a large body of literature outside of oncology that suggests strong associations with HRV parameters thought to represent vagal dominance and/or parasympathetic activity and factors such as patient reported symptoms, emotional distress, sleep disturbances, and even inflammation. These studies test interventions that are non-pharmacological, mostly mind-body or psychosocial in nature. If HRV parameters indicative of vagal tone are consistently shown to be related to achieving results such as reducing emotional distress,

improving emotional self-regulation, and any number of symptom-related outcome, this would be important information for future research. Indeed, if HRV is a shared mechanism (across mind-body and psychosocial interventions) by which improved health outcomes may be attained, HRV may be a promising mediator to examine in future cancer supportive care research.^{120,121}

As such, we are exploring whether testing this objective psychophysiological measure, HRV, can be used to characterize the experience (quality control) and/or provide a correlative or mediative indicator (mechanism) showing how targeted symptoms improve over time. Interventions as disparate in their theories of effects and proposed mechanisms of action as MM, storytelling, various forms of meditation, and psychosocial support are all promising ways to intervene. If it is found that each of these appears to shift participants' psychophysiology through balancing the ANS as indicated by the HRV parameters of coherence/resonant frequency, or high-frequency power, then there may be a clear target for theoretically choosing interventions for cancer patients and survivors.

Finally, our interests for future work also examine the potential of directly manipulating HRV through biofeedback. HRV biofeedback (HRVB) with emotional self-regulation goals designed to provide signals to "learn" to shift HRV is demonstrated to be an effective way to bring HRV back into more normal ranges,³² or improve relative to age-adjusted levels. For example, in a study conducted with veterans with PTSD (who show significantly lower HRV than veterans without PTSD) an intervention adding HRVB to usual care (counseling and psychosocial support) showed a 9% improvement relative to a usual care group. Similarly, there may be an advantage to coupling HRVB with current evidence-based practices in treating emotional distress, sleep disturbance, and mood disorders, perhaps as a way to "prime" the ANS to shift toward vagal dominance, allowing the intervention to move more quickly through the barriers of initial stress reactivity.

Conclusion

We have discussed the potential for HRV to be a target of continued research as a potential mediator of mind-body and psychosocial intervention effects on outcomes for cancer patients/survivors. Current preliminary data suggests a trend that these types of interventions may make changes in HRV parameters associated with improved ANS balance. The modest sample sizes and lack of assessing potential mediators and moderators limit an empirical understanding of how both mind-body and psychosocial interventions may impact HRV in the 2 studies we have described. Despite limitations, the presentation and discussion of our studies and preliminary findings add meaningful contribution to the

current growing literature in HRV as a marker of underlying changes in the stress response among cancer survivors. Larger clinical trials are needed to tease out the underlying mechanisms of HRV changes in both interventions. Focusing on HRV is worthwhile since HRV information is easy to obtain and is relatively low cost. Providing HRV biofeedback may be a more effective way of increasing the benefits related to mitigating emotional distress and improving emotional self-regulation among cancer survivors.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the NIH National Center for Complementary and Integrative Health (formerly NCCAM) [U01 AT002706-03]; and the NIH National Cancer Institute [R15CA213035-01A1].

ORCID iDs

Linda Larkey  <https://orcid.org/0000-0001-7681-6813>

Wonsun Kim  <https://orcid.org/0000-0002-2926-2712>

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69:7-34.
2. Antoni MH, Dhabhar FS. The impact of psychosocial stress and stress management on immune responses in patients with cancer. *Cancer*. 2019;125:1417-1431.
3. Chan RJ, McCarthy AL, Devenish J, Sullivan KA, Chan A. Systematic review of pharmacologic and non-pharmacologic interventions to manage cognitive alterations after chemotherapy for breast cancer. *Eur J Cancer*. 2015;51:437-450.
4. Buffart LM, van Uffelen JG, Riphagen II, et al. Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. *BMC Cancer*. 2012;12:559.
5. Duijts SF, Faber MM, Oldenburg HS, van Beurden M, Aaronson NK. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors—a meta-analysis. *Psychooncology*. 2011;20:115-126.
6. Goldstein KM, Shepherd-Banigan M, Coeytaux RR, et al. Use of mindfulness, meditation and relaxation to treat vasomotor symptoms. *Climacteric*. 2017;20:178-182.
7. Kellar I, Budworth L, Fadli F, Nash H, Weighall A. A systematic review of nonpharmacological interventions for improving, and reducing disturbances of sleep, for patients with non-remissive cancer. *PROSPERO*. 2015:CRD42015025204.
8. National Cancer Institute. NCI dictionary of cancer terms—mind-body practice, 2020. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/mind-body-practice>. Accessed June 18, 2020.
9. Galway K, Black A, Cantwell M, Cardwell CR, Mills M, Donnelly M. Psychosocial interventions to improve quality of life and emotional wellbeing for recently diagnosed cancer patients. *Cochrane Database Syst Rev*. 2012;11:CD007064.
10. CancerCare. Relaxation techniques and mind/body practices: how they can help you cope with cancer, 2020. https://www.cancercare.org/publications/54-relaxation_techniques_and_mind_body_practices_how_they_can_help_you_cope_with_cancer. Accessed June 18, 2020.
11. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. *Support Care Cancer*. 2009;17:1117-1128.
12. Teo I, Krishnan A, Lee GL. Psychosocial interventions for advanced cancer patients: a systematic review. *Psychooncology*. 2019;28:1394-1407.
13. Bower JE, Ganz PA, Tao ML, et al. Inflammatory biomarkers and fatigue during radiation therapy for breast and prostate cancer. *Clin Cancer Res*. 2009;15:5534-5540.
14. McCraty R, Shaffer F. Heart rate variability: new perspectives on physiological mechanisms, assessment of self-regulatory capacity, and health risk. *Glob Adv Health Med*. 2015;4:46-61.
15. Goessl VC, Curtiss JE, Hofmann SG. The effect of heart rate variability biofeedback training on stress and anxiety: a meta-analysis. *Psychol Med*. 2017;47:2578-2586.
16. Adegoke VF, Chen D, Banissi E, Barsikzai S. Improving prediction accuracy of breast cancer survivability and diabetes diagnosis via RBF networks trained with EKF models. *Int J Comput Inf Syst Ind Manag Appl*. 2019;11:82-100.
17. Cowan MJ. Measurement of heart rate variability. *West J Nurs Res*. 1995;17:32-48; discussion 101-111.
18. Chen CK, Lin SL, Huang CY, Wang TC, Yao TY, Wu CL. Analysis of dynamic cardiopulmonary signals and heart rate variability for distinct cardiopulmonary fitness norms under graded exercise and recovery periods. Paper presented at: 2019 IEEE Eurasia Conference on Biomedical Engineering, Healthcare and Sustainability (ECBIOS); May 31-June 3, 2019; Okinawa, Japan.
19. Aslani A, Aslani A, Kheirkhah J, Sobhani V. Cardiopulmonary fitness test by ultra-short heart rate variability. *J Cardiovasc Dis Res*. 2011;2:233-236.
20. Geisler FCM, Vennwald N, Kubiak T, Weber H. The impact of heart rate variability on subjective well-being is mediated by emotion regulation. *Pers Individ Differ*. 2010;49:723-728.
21. Williams DP, Cash C, Rankin C, Bernardi A, Koenig J, Thayer JF. Resting heart rate variability predicts self-reported difficulties in emotion regulation: a focus on different facets of emotion regulation. *Front Psychol*. 2015;6:261.
22. Gunneson LA, Davenport RS, Gevirtz RN. Establishing a resonance frequency breathing rate: a comparison of MyCalmBeat to HRV biofeedback. *Appl Psychophys Biof*. 2014;39:307.
23. Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Front Psychol*. 2014;5:1040.
24. Lehrer PM, Vaschillo E, Vaschillo B, et al. Heart rate variability biofeedback increases baroreflex gain and peak expiratory flow. *Psychosom Med*. 2003;65:796-805.

25. Lin IM, Tai LY, Fan SY. Breathing at a rate of 5.5 breaths per minute with equal inhalation-to-exhalation ratio increases heart rate variability. *Int J Psychophysiol.* 2014;91:206-211.
26. Steffen PR, Austin T, DeBarros A, Brown T. The impact of resonance frequency breathing on measures of heart rate variability, blood pressure, and mood. *Front Public Health.* 2017;5:222.
27. Porges SW. The polyvagal perspective. *Biol Psychol.* 2007;74:116-143.
28. Porges SW. *The Polyvagal Theory: Neurophysiological Foundations of Emotions, Attachment, Communication, and Self-Regulation.* 1st ed. New York: W. W. Norton; 2011.
29. Laborde S, Mosley E, Thayer JF. Heart rate variability and cardiac vagal tone in psychophysiological research—recommendations for experiment planning, data analysis, and data reporting. *Front Psychol.* 2017;8:213.
30. Appel ML, Berger RD, Saul JP, Smith JM, Cohen RJ. Beat to beat variability in cardiovascular variables: noise or music? *J Am Coll Cardiol.* 1989;14:1139-1148.
31. Melo RC, Santos MD, Silva E, et al. Effects of age and physical activity on the autonomic control of heart rate in healthy men. *Braz J Med Biol Res.* 2005;38:1331-1338.
32. Tan G, Dao TK, Farmer L, Sutherland RJ, Gevirtz R. Heart rate variability (HRV) and posttraumatic stress disorder (PTSD): a pilot study. *Appl Psychophysiol Biofeedback.* 2011;36:27-35.
33. La Rovere MT, Bigger JT Jr, 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;351:478-484.
34. Nolan J, Batin PD, Andrews R, et al. Prospective study of heart rate variability and mortality in chronic heart failure: results of the United Kingdom heart failure evaluation and assessment of risk trial (UK-heart). *Circulation.* 1998;98:1510-1516.
35. Dekker JM, Schouten EG, Klootwijk P, Pool J, Swenne CA, Kromhout D. Heart rate variability from short electrocardiographic recordings predicts mortality from all causes in middle-aged and elderly men. The Zutphen Study. *Am J Epidemiol.* 1997;145:899-908.
36. Tsuji H, Venditti FJ Jr, Manders ES, et al. Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham Heart Study. *Circulation.* 1994;90:878-883.
37. Kim HG, Cheon EJ, Bai DS, Lee YH, Koo BH. Stress and heart rate variability: a meta-analysis and review of the literature. *Psychiatry Investig.* 2018;15:235-245.
38. Hall M, Vasko R, Buysse D, et al. Acute stress affects heart rate variability during sleep. *Psychosom Med.* 2004;66:56-62.
39. Pistorio E, Luca M, Luca A, Messina V, Calandra C. Autonomic nervous system and lipid metabolism: findings in anxious-depressive spectrum and eating disorders. *Lipids Health Dis.* 2011;10:192.
40. Liao D, Cai J, Brancati FL, et al. Association of vagal tone with serum insulin, glucose, and diabetes mellitus—The ARIC Study. *Diabetes Res Clin Pract.* 1995;30:211-221.
41. Singh JP, Larson MG, O'Donnell CJ, et al. Association of hyperglycemia with reduced heart rate variability (The Framingham Heart Study). *Am J Cardiol.* 2000;86:309-312.
42. Stamatakis KA, Punjabi NM. Effects of sleep fragmentation on glucose metabolism in normal subjects. *Chest.* 2010;137:95-101.
43. Schroeder EB, Chambless LE, Liao D, et al. Diabetes, glucose, insulin, and heart rate variability: the Atherosclerosis Risk in Communities (ARIC) study. *Diabetes Care.* 2005;28:668-674.
44. Prinsloo GE, Rauch HG, Derman WE. A brief review and clinical application of heart rate variability biofeedback in sports, exercise, and rehabilitation medicine. *Phys Sportsmed.* 2014;42:88-99.
45. Chintala KK, Krishna BH, Reddy MN. Heart rate variability in overweight health care students: correlation with visceral fat. *J Clin Diagn Res.* 2015;9:CC06-08.
46. Kogan AV, Allen JJ, Weihs KL. Cardiac vagal control as a prospective predictor of anxiety in women diagnosed with breast cancer. *Biol Psychol.* 2012;90:105-111.
47. Souza GG, Mendonca-de-Souza AC, Barros EM, et al. Resilience and vagal tone predict cardiac recovery from acute social stress. *Stress.* 2007;10:368-374.
48. Geisler FC, Kubiak T, Siewert K, Weber H. Cardiac vagal tone is associated with social engagement and self-regulation. *Biol Psychol.* 2013;93:279-286.
49. Blase KL, van Dijke A, Cluitmans PJ, Vermetten E. [Efficacy of HRV-biofeedback as additional treatment of depression and PTSD]. *Tijdschr Psychiatr.* 2016;58:292-300.
50. Karavidas MK, Lehrer PM, Vaschillo E, et al. Preliminary results of an open label study of heart rate variability biofeedback for the treatment of major depression. *Appl Psychophysiol Biofeedback.* 2007;32:19-30.
51. Hongyu LU, Song L, Hongyu LI, Shu XU, Wang M. Comparison of heart rate variability biofeedback intervention for different types of insomnia disorder. *Chinese J Rehab Theor Pract.* 2017;23:720-724.
52. Rådmark L, Sidorchuk A, Osika W, Niemi M. A systematic review and meta-analysis of the impact of mindfulness based interventions on heart rate variability and inflammatory markers. *J Clin Med.* 2019;8:1638.
53. Hallman DM, Olsson EM, von Scheele B, Melin L, Lyskov E. Effects of heart rate variability biofeedback in subjects with stress-related chronic neck pain: a pilot study. *Appl Psychophysiol Biofeedback.* 2011;36:71-80.
54. Hassett AL, Radvanski DC, Vaschillo EG, et al. A pilot study of the efficacy of heart rate variability (HRV) biofeedback in patients with fibromyalgia. *Appl Psychophysiol Biofeedback.* 2007;32:1-10.
55. Stern MJ, Guiles RA, Gevirtz R. HRV biofeedback for pediatric irritable bowel syndrome and functional abdominal pain: a clinical replication series. *Appl Psychophysiol Biofeedback.* 2014;39:287-291.
56. Buchheit M, Simon C, Charloux A, Doutreleau S, Piquard F, Brandenberger G. Heart rate variability and intensity of habitual physical activity in middle-aged persons. *Med Sci Sports Exerc.* 2005;37:1530-1534.
57. Buchheit M, Simon C, Viola AU, Doutreleau S, Piquard F, Brandenberger G. Heart rate variability in sportive elderly: relationship with daily physical activity. *Med Sci Sports Exerc.* 2004;36:601-605.

58. Rennie KL, Hemingway H, Kumari M, Brunner E, Malik M, Marmot M. Effects of moderate and vigorous physical activity on heart rate variability in a British study of civil servants. *Am J Epidemiol*. 2003;158:135-143.
59. Jurca R, Church TS, Morss GM, Jordan AN, Earnest CP. Eight weeks of moderate-intensity exercise training increases heart rate variability in sedentary postmenopausal women. *Am Heart J*. 2004;147:e21.
60. Niederer D, Vogt L, Thiel C, et al. Exercise effects on HRV in cancer patients. *Int J Sports Med*. 2013;34:68-73.
61. Voulgari C, Pagoni S, Vinik A, Poirier P. Exercise improves cardiac autonomic function in obesity and diabetes. *Metabolism*. 2013;62:609-621.
62. Larkey L, Jahnke R, Etnier J, Gonzalez J. Meditative movement as a category of exercise: implications for research. *J Phys Act Health*. 2009;6:230-238.
63. Tsai HJ, Kuo TB, Lee GS, Yang CC. Efficacy of paced breathing for insomnia: enhances vagal activity and improves sleep quality. *Psychophysiology*. 2015;52:388-396.
64. Cysarz D, Bussing A. Cardiorespiratory synchronization during Zen meditation. *Eur J Appl Physiol*. 2005;95:88-95.
65. Peng CK, Mietus JE, Liu Y, et al. Exaggerated heart rate oscillations during two meditation techniques. *Int J Cardiol*. 1999;70:101-107.
66. Libby DJ, Worhunsky PD, Pilver CE, Brewer JA. Meditation-induced changes in high-frequency heart rate variability predict smoking outcomes. *Front Hum Neurosci*. 2012;6:54.
67. Howorka K, Pumprla J, Tamm J, et al. Effects of guided breathing on blood pressure and heart rate variability in hypertensive diabetic patients. *Auton Neurosci*. 2013;179:131-137.
68. May RW, Bamber M, Seibert GS, et al. Understanding the physiology of mindfulness: aortic hemodynamics and heart rate variability. *Stress*. 2016;19:168-174.
69. Bernardi L, Sleight P, Bandinelli G, et al. Effect of rosary prayer and yoga mantras on autonomic cardiovascular rhythms: comparative study. *BMJ*. 2001;323:1446-1449.
70. Zou L, Sasaki JE, Wei GX, et al. Effects of mind-body exercises (Tai Chi/Yoga) on heart rate variability parameters and perceived stress: a systematic review with meta-analysis of randomized controlled trials. *J Clin Med*. 2018;7:404.
71. Lee MS, Huh HJ, Kim BG, et al. Effects of Qi-training on heart rate variability. *Am J Chin Med*. 2002;30:463-470.
72. Chang MY. Qigong effects on heart rate variability and peripheral vasomotor responses. *West J Nurs Res*. 2015;37:1383-1403.
73. Kalsaria P, Li H, Waite GN, Moga MM, Kingsley DJ, Geib RW. Acute effects of tai chi exercise on cardiac autonomic function in healthy adults with tai chi experience. *Biomed Sci Instrum*. 2012;48:226-231.
74. Audette JF, Jin YS, Newcomer R, Stein L, Duncan G, Frontera WR. Tai Chi versus brisk walking in elderly women. *Age Ageing*. 2006;35:388-393.
75. Li R, Jin L, Hong P, et al. The effect of baduanjin on promoting the physical fitness and health of adults. *Evid Based Complement Alternat Med*. 2014;2014:784059.
76. Chang C, Tsai G, Hsieh CJ. Psychological, immunological and physiological effects of a Laughing Qigong Program (LQP) on adolescents. *Complement Ther Med*. 2013;21:660-668.
77. Lu WA, Kuo CD. The effect of Tai Chi Chuan on the autonomic nervous modulation in older persons. *Med Sci Sports Exerc*. 2003;35:1972-1976.
78. Fong SS, Wong JY, Chung LM, et al. Changes in heart-rate variability of survivors of nasopharyngeal cancer during Tai Chi Qigong practice. *J Phys Ther Sci*. 2015;27:1577-1579.
79. Sato S, Makita S, Uchida R, Ishihara S, Masuda M. Effect of Tai Chi training on baroreflex sensitivity and heart rate variability in patients with coronary heart disease. *Int Heart J*. 2010;51:238-241.
80. Motivala SJ, Sollers J, Thayer J, Irwin MR. Tai Chi Chih acutely decreases sympathetic nervous system activity in older adults. *J Gerontol A Biol Sci Med Sci*. 2006;61:1177-1180.
81. Hattori K, Asamoto M, Otsuji M, et al. Quantitative evaluation of stress in Japanese anesthesiology residents based on heart rate variability and psychological testing. *J Clin Monit Comput*. 2020;34:371-377.
82. Lee JH, Yu J, Ryu SH, Ha JH, Jeon HJ, Park DH. Change of heart rate variability in depressive disorder after physical or psychological stress. *Sleep Med Psychophysiol*. 2018;25:15.
83. Salmoirago-Blotcher E, Hovey KM, Andrews CA, et al. Psychological traits, heart rate variability, and risk of coronary heart disease in healthy aging women-The Women's Health Initiative. *Psychosom Med*. 2019;81:256-264.
84. Santiago TL, Peixoto D, Costa C, Silva JAPd. AB0930 Cross-sectional analysis of the autonomic nervous system (heart rate variability): correlations with psychological dimensions in women with fibromyalgia, rheumatoid arthritis and healthy controls. *Ann Rheum Dis*. 2017;76:1381.
85. Verkuil B, Brosschot JF, Tollenaar MS, Lane RD, Thayer JF. Prolonged non-metabolic heart rate variability reduction as a physiological marker of psychological stress in daily life. *Ann Behav Med*. 2016;50:704-714.
86. Sandmire DA, Rankin NE, Gorham SR, et al. Psychological and autonomic effects of art making in college-aged students. *Anxiety Stress Coping*. 2016;29:561-569.
87. Lee YH, Lai GM, Lee DC, Tsai Lai LJ, Chang YP. Promoting physical and psychological rehabilitation activities and evaluating potential links among cancer-related fatigue, fear of recurrence, quality of life, and physiological indicators in cancer survivors. *Integr Cancer Ther*. 2018;17:1183-1194.
88. Kim S, Khera N, McNulty J, Larkey L, Thakur R. Creating a digital storytelling intervention: a workshop with hematopoietic cell transplant survivors. *Psychooncology*. 2016;25:108-109.
89. Larkey LK, Roe DJ, Smith L, Millstine D. Exploratory outcome assessment of Qigong/Tai Chi Easy on breast cancer survivors. *Complement Ther Med*. 2016;29:196-203.
90. Larkey LK, Roe DJ, Weihs KL, et al. Randomized controlled trial of Qigong/Tai Chi Easy on cancer-related fatigue in breast cancer survivors. *Ann Behav Med*. 2015;49:165-176.
91. Porges SW, Carter CS. Polyvagal theory and the social engagement system. In: Gerbarg PL, Muskin PR, Brown RP, eds. *Complementary and Integrative Treatments in Psychiatric Practice*. Washington, DC: American Psychiatric Association Publishing; 2017:221-241.
92. HeartMath Institute. HeartMath® Institute: expanding heart connections. <https://www.heartmath.org/science>. Accessed August 3, 2020.

93. Du S, Dong J, Zhang H, et al. Taichi exercise for self-rated sleep quality in older people: a systematic review and meta-analysis. *Int J Nurs Stud*. 2015;52:368-379.
94. Wang CW, Chan CH, Ho RT, Chan JS, Ng SM, Chan CL. Managing stress and anxiety through qigong exercise in healthy adults: a systematic review and meta-analysis of randomized controlled trials. *BMC Complement Altern Med*. 2014;14:8.
95. Zou L, SasaKi JE, Wang H, Xiao Z, Fang Q, Zhang M. A systematic review and meta-analysis Baduanjin Qigong for health benefits: randomized controlled trials. *Evid Based Complement Alternat Med*. 2017;2017:4548706.
96. Chan AW, Lee A, Suen LK, Tam WW. Tai chi Qigong improves lung functions and activity tolerance in COPD clients: a single blind, randomized controlled trial. *Complement Ther Med*. 2011;19:3-11.
97. McQuade JL, Prinsloo S, Chang DZ, et al. Qigong/tai chi for sleep and fatigue in prostate cancer patients undergoing radiotherapy: a randomized controlled trial. *Psychooncology*. 2017;26:1936-1943.
98. Jahnke R, Larkey L, Rogers C, Etnier J, Lin F. A comprehensive review of health benefits of qigong and tai chi. *Am J Health Promot*. 2010;24:e1-e25.
99. Song R, Grabowska W, Park M, et al. The impact of Tai Chi and Qigong mind-body exercises on motor and non-motor function and quality of life in Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism Relat Disord*. 2017;41:3-13.
100. Wayne PM, Lee MS, Novakowski J, et al. Tai Chi and Qigong for cancer-related symptoms and quality of life: a systematic review and meta-analysis. *J Cancer Surviv*. 2018;12:256-267.
101. Yin J, Dishman RK. The effect of Tai Chi and Qigong practice on depression and anxiety symptoms: a systematic review and meta-regression analysis of randomized controlled trials. *Ment Health Phys Act*. 2014;7:135-146.
102. Zeng Y, Xie X, Cheng ASK. Qigong or Tai Chi in cancer care: an updated systematic review and meta-analysis. *Curr Oncol Rep*. 2019;21:48.
103. Jahnke RA, Larkey LK, Rogers C. Dissemination and benefits of a replicable Tai Chi and Qigong program for older adults. *Geriatr Nurs*. 2010;31:272-280.
104. Larkey L, Szalacha L, Rogers C, Jahnke R, Ainsworth B. Measurement pilot study of the Meditative Movement Inventory (MMI). *J Nurs Meas*. 2012;20:230-243.
105. Mosher CE, Redd WH, Rini CM, Burkhalter JE, DuHamel KN. Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: a review of the literature. *Psychooncology*. 2009;18:113-127.
106. Sun CL, Francisco L, Baker KS, Weisdorf DJ, Forman SJ, Bhatia S. Adverse psychological outcomes in long-term survivors of hematopoietic cell transplantation: a report from the Bone Marrow Transplant Survivor Study (BMTSS). *Blood*. 2011;118:4723-4731.
107. Bevans M, Castro K, Prince P, et al. An individualized dyadic problem-solving education intervention for patients and family caregivers during allogeneic hematopoietic stem cell transplantation: a feasibility study. *Cancer Nurs*. 2010;33:E24-E32.
108. Pasquini MC, Wang Z, Horowitz MM, Gale RP. 2010 report from the Center for International Blood and Marrow Transplant Research (CIBMTR): current uses and outcomes of hematopoietic cell transplants for blood and bone marrow disorders. *Clin Transpl*. 2010:87-105.
109. DuHamel KN, Mosher CE, Winkel G, et al. Randomized clinical trial of telephone-administered cognitive-behavioral therapy to reduce post-traumatic stress disorder and distress symptoms after hematopoietic stem-cell transplantation. *J Clin Oncol*. 2010;28:3754-3761.
110. Laudenslager ML, Simoneau TL, Kilbourn K, et al. A randomized control trial of a psychosocial intervention for caregivers of allogeneic hematopoietic stem cell transplant patients: effects on distress. *Bone Marrow Transplant*. 2015;50:1110-1118.
111. Hinyard LJ, Kreuter MW. Using narrative communication as a tool for health behavior change: a conceptual, theoretical, and empirical overview. *Health Educ Behav*. 2007;34:777-792.
112. Larkey LK, McClain D, Roe DJ, et al. Randomized controlled trial of storytelling compared to a personal risk tool intervention on colorectal cancer screening in low-income patients. *Am J Health Promot*. 2015;30:e59.
113. Bae HS, Kang S. The influence of viewing an entertainment-education program on cornea donation intention: a test of the theory of planned behavior. *Health Commun*. 2008;23:87-95.
114. Houston TK, Cherrington A, Coley HL, et al. The art and science of patient storytelling-harnessing narrative communication for behavioral interventions: the ACCE project. *J Health Commun*. 2011;16:686-697.
115. Larkey LK, Gonzalez J. Storytelling for promoting colorectal cancer prevention and early detection among Latinos. *Patient Educ Couns*. 2007;67:272-278.
116. Fiddian-Green A, Kim S, Gubrium AC, Larkey LK, Peterson JC. Restor(y)ing health: a conceptual model of the effects of digital storytelling. *Health Promot Pract*. 2019;20:502-512.
117. Larkey LK, Hecht M. A model of effects of narrative as culture-centric health promotion. *J Health Commun*. 2010;15:114-135.
118. Kim W, Bangerter LR, Jo S, et al. Feasibility and acceptability of a 3-day group-based digital storytelling workshop among caregivers of allogeneic hematopoietic cell transplantation patients: a mixed-methods approach. *Biol Blood Marrow Transplant*. 2019;25:2228-2233.
119. Cheng TC, Lee YH, Mar CL, Huang WT, Chang YP. The health promoting mindfulness or Qigong educational programs for beneficial lifestyle changes of cancer survivors. *J Cancer Educ*. 2020;35:743-750.
120. Palesh O, Scheiber C, Kesler S, et al. Secondary outcomes of a behavioral sleep intervention: a randomized clinical trial. *Health Psychol*. 2019;38:196-205.
121. Chen SC, Yeh ML, Chang HJ, Lin MF. Music, heart rate variability, and symptom clusters: a comparative study. *Support Care Cancer*. 2020;28:351-360.