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

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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 resilience 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

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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. 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

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identify overlapping components that may explain the potential mechanism(s) underlying the benefits commonly found in response to these interventions. 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,” while psychosocial interventions generally include emotional appraisal and strategies for active, cognitive coping often guided by a professional interventionist. As such, in both interventions, the cancer patient or survivor engages one’s own inner resources to manage emotional responses 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), 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, stress, and anxiety. Recent studies have implicated HRV as a predictor of longer survival after cancer diagnosis, 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. The time-domain represents the ability (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, stress, and anxiety. Recent studies have implicated HRV as a predictor of longer survival after cancer diagnosis, 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.

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. 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). Further, low HRV in the time domain has been shown to be associated with increased
all-cause mortality\textsuperscript{35, 36} and associated with stress,\textsuperscript{37} and poor sleep.\textsuperscript{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,\textsuperscript{26} elevated lipids,\textsuperscript{39} poor glucose metabolism,\textsuperscript{40-44} and increased body fat\textsuperscript{15}). For example, in a sample of breast cancer patients, poor vagal tone was an indicator of prospective anxiety over time.\textsuperscript{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.\textsuperscript{47} Further, there are indications that emotional self-regulation and positive emotions may be associated with vagal tone HRV indicators,\textsuperscript{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, insomnia\textsuperscript{49-51}) , symptoms (eg, pain, inflammation\textsuperscript{52}), and addictive behaviors.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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).\textsuperscript{62} Studies of breath-focused or meditation practices show increases in time domain HRV,\textsuperscript{63, 64} an increase in HRV amplitude (during resting meditation post qigong and yoga),\textsuperscript{65} and improvements in vagal tone (mostly indicated by HF power)\textsuperscript{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),\textsuperscript{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.\textsuperscript{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 significant\textsuperscript{71-74} and non-significant changes\textsuperscript{75} in one or more of the predicted HRV parameters.\textsuperscript{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.\textsuperscript{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,\textsuperscript{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,\textsuperscript{86} counseling and psychosocial support to veterans with PTSD,\textsuperscript{32} and promoting physical and psychological rehabilitation for cancer survivors.\textsuperscript{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,\textsuperscript{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, or mitigation of anxiety. 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 published 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 beat using pulse sensors attached to the participants’ earlobe. Participants were asked to sit quietly while recording a 3-minute session of their pulse. 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 stress and improving sleep in systematic reviews and meta-analyses, with growing but still limited evidence for these outcomes for Qigong.34,95 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 meditative state to achieve results (ie, MM practices).62 These 2 practices are sometimes combined in interventions for research. A number of reviews examining evidence of the effects of these practices combine them due to the classification as mind-body interventions 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™” 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). 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 al). 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, indicating that 25% to 50% of HCT survivors and caregivers report psychosocial distress, including depression, anxiety, and social isolation. 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, and psychoeducation. 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. 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. 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). 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.

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 $\Delta$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 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 interbeat 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, and 1 in which a sleep intervention increased HF power. 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.

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.

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, 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.

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