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Autonomic Specificity Associated with Participation in the Mindfulness And Tai chi for Cancer Health (MATCH) Study

by

Kirsti Toivonen

A THESIS

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Abstract

Mindfulness-Based Cancer Recovery (MBCR) and Tai Chi/Qigong (TCQ) are two therapies used by cancer survivors to help alleviate side effects of cancer and its treatment, but have never been directly compared in this population. The present study assessed the autonomic specificity (indexed by blood pressure, heart rate variability, and baroreflex sensitivity) associated with participating in MBCR or TCQ among cancer survivors. Secondary analyses examined associations between changes in distress, quality of life, sleep, and pain and changes in autonomic functioning. Results suggest participation in MBCR, but not TCQ, may be associated with a degree of change in baroreflex sensitivity and blood pressure. Further, increased low-frequency heart rate variability was associated with a pattern of improvements (e.g., decreased fatigue, depression, and mood disturbance). Results may lead to a better understanding of mechanisms involved in symptom improvement as well as a better rationale for selection of complementary therapies.

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List of Symbols, Abbreviations, & Nomenclature

ANOVA	Analysis of variance
BPI	Brief Pain Inventory
BRS	Baroreflex sensitivity
Δ	Change
d	Cohen's d (between-subjects effect size)
d_z	Cohen's d_z (within-subjects effect size)
DBP	Diastolic blood pressure
FACT-G	Functional Assessment of Cancer Therapy – General
HF	High frequency
HRV	Heart rate variability
LF	Low frequency
LMM	Linear mixed modeling
$_{ln}ms^2$	Natural logarithm transformed milliseconds squared
MBCR	Mindfulness-Based Cancer Recovery
MBSR	Mindfulness-Based Stress Reduction
nu	Normalized units
POMS	Profile of Mood States
PSQI	Pittsburgh Sleep Quality Index
RCT	Randomized controlled trial
RMSSD	Root mean square of successive differences
SBP	Systolic blood pressure
TCQ	Tai Chi/Qigong

Chapter 1: Introduction

An estimated 196,900 new cases of cancer were diagnosed in Canada in 2015 (Canadian Cancer Society, 2016). While the prevalence of cancer is rising due to aging of the population and behavioural risk factors such as physical inactivity, smoking, and high body mass index (BMI; World Health Organization, 2015), advances in early detection and treatment have resulted in decreased mortality rates (Kaplan, Malmgren, Atwood, & Calip, 2015; Siegel, Miller, & Jemal, 2015). For example, survival rates in Canada for all cancers combined have increased from 56% in 1992-1994 to 63% in 2006-2008 (Canadian Cancer Society, 2016). Consequently, there is a growing number of survivors (herein defined as anyone who has received a diagnosis of cancer) who experience adverse side effects such as distress, fatigue, insomnia symptoms, and pain associated with cancer and its treatment.

Studies representing cancer survivors across the trajectory of illness (i.e., newly diagnosed to years post-treatment) with different types of cancer report approximately 35 to 38% experience clinically significant distress (Carlson et al., 2004; Ploos van Amstel et al., 2013; Zabora, Brintzenhofeszoc, Curbow, Hooker, & Piantadosi, 2001). Cancer-related fatigue is experienced by 50% to 90% of survivors, the latter number reported by studies of those undergoing active treatment (Campos, Hassan, Riechelmann, & Del Giglio, 2011). Insomnia symptoms affect 30 to 50% of those newly diagnosed/recently treated and 23 to 44% of survivors years after treatment (Savard & Morin, 2001). Finally, it is estimated that 25 to 60% of breast cancer survivors experience post-treatment pain (Andersen & Kehlet, 2011), and 5 to 10% have chronic severe pain (Glare et al., 2014). Distress, fatigue, sleep disturbance, and pain can significantly impair daily functioning, psychological/emotional well-being, and ability to work (Duijts et al., 2014; Gupta, Lis, & Grutsch, 2007; Spelten et al., 2003; Wildgaard et al., 2011);

can affect immune functioning (Theobald, 2004); and can persist for months or years beyond treatment.

Although the mechanisms remain unclear, adverse cancer-related symptoms may directly or indirectly impact other health behaviours and biological stress response systems, which can in turn contribute to further health issues. In addition, such symptoms typically co-occur and can be precipitating or perpetuating factors for each other (Theobald, 2004). Given the significant symptom burden experienced by cancer survivors, improvements in psychosocial and functional well-being after cancer have not paralleled improvements in treatment and outcomes. Increasing rates of cancer coupled with decreasing mortality rates have led to a growing population of survivors and thus an increased need for symptom relief. Psychosocial interventions are often used in integrative oncology in attempt to help alleviate this symptom burden.

1.1 Complementary Therapies for Cancer-Related Distress and Symptom Management

Complementary therapies refer to diverse medical and health care systems, practices, and products used in conjunction with conventional medicine (National Centre for Complementary and Integrative Health; NCCIH). Nearly half (47%) of cancer survivors in Calgary report using a complementary therapy since their diagnosis, typically to improve their quality of life (King et al., 2015). Mindfulness meditation, a mind-body practice, and Tai Chi and/or Qigong, an energy therapy, are two complementary therapies used in integrative oncology.

1.1.1 Mindfulness meditation.

Mindfulness refers to moment to moment non-judgemental awareness (Kabat-Zinn, 1990). Kabat-Zinn adapted mindfulness practice into a secular 8-week group program incorporating mindfulness meditation training, gentle Hatha yoga, group reflection, and education about the mind-body connection; called mindfulness-based stress reduction (MBSR; Kabat-Zinn, 1990). Several systematic reviews support small-medium to

medium-large effect sizes of MBSR for improving mood (d = 0.42), distress (d = 0.48), stress (d = 0.71), anxiety (d = 0.51 – 0.73), and depression (d = 0.37 – 0.42) in cancer survivors (Cramer, Lauche, Paul, & Dobos, 2012; Musial, Büssing, Heusser, Choi, & Ostermann, 2011; Piet, Würtzen, & Zachariae, 2012; Zainal, Booth, & Huppert, 2013).

MBSR has been adapted by Carlson and Speca into Mindfulness-Based Cancer Recovery (MBCR), a group intervention tailored for cancer survivors (Carlson & Speca, 2010). MBCR incorporates the same essential components as MBSR, as well as cognitive coping strategies based on principles of cognitive-behavioural therapy and material specific to living with cancer such as sleep problems, pain, and fear of cancer recurrence (Carlson & Speca, 2010). Recently, MBCR was reported to be superior to supportive-expressive group therapy in a randomized controlled trial (RCT) of 271 breast cancer survivors; resulting in small to medium effect size improvements in quality of life, mood disturbance, stress symptoms, social support, spirituality, and post-traumatic growth that were maintained after 12 months (Carlson et al., 2013; Carlson et al., 2016).

1.1.2 Tai Chi/Qigong. Tai Chi and/or Qigong-based interventions have not been standardized to the degree of MBSR/MBCR. Tai Chi involves slow, intentional movements, incorporating active relaxation of the body and mind and focused attention (Wayne et al., 2013). There is evidence that Tai Chi is helpful for fall prevention, improved balance and mobility, and generally improving health among older adults (Hackney & Wolf, 2014; Lee & Ernst, 2011). Qigong programs involve body movements done in a meditative fashion meant to focus and balance qi (chi, or life energy; Wang et al., 2014); and typically include components such as exercise, breath regulation, and relaxation (Klein, Schneider, & Rhoads, 2016). A review of 11

RCTs supported decreased fatigue and increased quality of life following Qigong participation in cancer survivors (Klein et al., 2016).

Combined Tai Chi and Qigong (TCQ) programs have also been studied in the context of integrative oncology. A review of 13 RCTs of TCQ for cancer survivors reported large effect size improvements in cancer-related quality of life and fatigue, and small effect size reductions in cortisol (Zeng, Luo, Xie, Huang, & Cheng, 2014). However, several studies had high risk of bias due to factors such as lack of allocation concealment or outcome assessor blinding (Zeng et al., 2014). Other RCTs of TCQ have showed decreases in sleep disturbance that were maintained at a 6-month follow-up in 52 nasopharyngeal cancer survivors (Fong, Ng, et al., 2015); and improvements in fatigue among breast cancer survivors over a "sham Qigong" condition (meant to parallel the physical components but exclude breathing and meditative components; Larkey et al., 2014).

1.2 Mindfulness and Tai Chi/Qigong Interventions and Stress Response Systems

There has been a recent effort to demonstrate the effects of participation in mindfulness meditation and Tai Chi/qigong on indices of broad, complimentary stress response systems among cancer survivors, particularly of the hypothalamic-pituitary-adrenal (HPA) axis and immune system (Ledesma & Kumano, 2009; Matchim, Armer, & Stewart, 2011a; Zeng et al., 2014). Indexing changes in biological markers following complementary therapy use is important as they may represent a treatment response, and may underlie mechanisms through which psychosocial functioning could impact health (Rouleau, Garland, & Carlson, 2015). The present study is focused on indices of the autonomic nervous system, particularly blood pressure, heart rate variability (HRV), and baroreflex sensitivity (BRS).

It is important to consider patterns of autonomic activity among cancer survivors because (1) the experience of cancer and particularly cancer treatment can adversely impact autonomic functioning and overall cardiovascular health (Scott et al., 2014; Vigo et al., 2015), (2) impairments in autonomic functioning and reduced cardiovascular health can place cancer survivors at increased risk for all-cause and cardiovascular mortality (Hooning et al., 2007; Gerritsen et al., 2001), and (3) altered patterns of autonomic functioning may be associated with the adverse symptoms typically experienced in this population such as mood disturbance, fatigue, sleep disturbance, and pain. For example, mood and anxiety disorders are associated with reduced HRV, which may in turn perpetuate mood problems through effects on social engagement, self-regulation, and psychological flexibility to stressors (Kemp & Quintana, 2013). Lower HRV has also been associated with greater self-reported fatigue severity in breast cancer survivors (Crosswell, Lockwood, Ganz, & Bower, 2014). Heightened autonomic arousal is typically viewed as a contributor to insomnia, as those with insomnia are physiologically hyper-aroused both nocturnally and in the daytime, and autonomic arousal interferes with the onset and maintenance of sleep (Miglis, 2016; Morin, 1993). Finally, chronic pain is associated with impaired autonomic activity (Woda, Picard, & Dutheil, 2016), which can in turn contribute to amplification of pain and the development of pain-related anxiety (Schlereth & Birklein, 2008).

1.2.1 Mindfulness interventions. Mindfulness interventions have been associated with changes in indices of autonomic functioning in cancer survivors, particularly blood pressure. An uncontrolled study of MBCR with 59 breast and prostate cancer patients resulted in small effect size decreases in systolic (SBP) and diastolic blood pressure (DBP) that were maintained after 12 months (Carlson, Speca, Faris, & Patel, 2007). A waitlist controlled study of MBSR for 76 women with cancer reported that those with higher blood pressure at baseline at baseline in the

MBSR group had lower SBP at week 8 relative to the control group (Campbell, Labelle, Bacon, Faris, & Carlson, 2012). An investigation of MBSR for 32 breast cancer survivors reported no group differences post-intervention, but at 1-month follow-up the MBSR had on average 10.63 mmHg lower SBP and 10.74 mmHg lower DBP than a control group at another cancer centre who received no intervention (Matchim, Armer, & Stewart, 2011b). Heart rate and respiration rate were similarly lower at 1-month follow up (Matchim et al., 2011b). Bauer-Wu and colleagues describe a mindfulness intervention lasting approximately 3 weeks that resulted in decreases in respiration rate of approximately two breaths per minute and decreases in heart rate of approximately six beats per minute in a pre-post design of 20 cancer survivors (Bauer-Wu et al., 2008). A 2015 review posited that mindfulness may improve cardiovascular disease rick factors such as hypertension through potential mechanisms such as improved attention control (e.g., ability to sustain attention on health behaviours), emotion regulation, and self-awareness (e.g., to physical sensations related to risk factors; Loucks et al., 2015).

Very little research has examined changes in HRV following participation in mindfulness meditation in cancer populations. Changes in HRV that reflect increased parasympathetic influence have been found in healthy individuals following participation in MBSR (Nijjar et al., 2014) and use of a digital mindfulness application (Zhu, Hedman, Feng, Li, Osika, 2017). Krygier and colleagues studied the effects of 10-day intensive Vipassana meditation on HRV and baroreflex outflow in healthy individuals; reporting that meditation lowered baroreflex outflow, and interpreting this as a function of greater attentional load (Krygier et al., 2013). One RCT compared the effects of a pre-recorded mindfulness exercise (including a body scan and meditation) and music therapy on HRV in terminally ill inpatients (98% diagnosed with cancer), concluding music therapy lead to relatively greater reductions in sympathetic tone (Warth,

Kessler, Hillecke, & Bardenheuer, 2016). No studies were identified that have examined baroreflex sensitivity (BRS) after a mindfulness intervention in cancer survivors.

1.2.2 Tai Chi/Qigong interventions. One RCT of 63 female cancer survivors who participated in Tai Chi or health education control classes for 12 weeks reported an approximate 10% reduction in SBP, but no changes in DBP (Campo et al., 2015). A 2016 review suggests that both brief and long-term Tai Chi interventions can influence parameters of HRV in participants with cardiovascular disease (Cole, Wijarnpreecha, Chattipakorn, & Chattipakorn, 2016), but less is known about the effect of TCQ on HRV in cancer survivors. One uncontrolled trial reported that participation in 5 minutes of TCQ by 11 survivors of nasopharyngeal cancer resulted in acute HRV changes representing reduced sympathetic activity and increased parasympathetic activity (during the 4th and 5th minute of exercise) but effects were attenuated post-intervention (Fong, Wong, et al., 2015). No studies were identified that examined the effect of participation in a multi-week TCQ intervention on HRV in cancer populations specifically. While research suggests long-term practice of Tai Chi can improve BRS in patients with coronary heart disease (Sato, Makita, Uchida, Ishihara, & Masuda, 2010), no prior studies appear to have examined the effects of Tai Chi on BRS in cancer survivors.

1.3 The Present Study

While MBCR and TCQ have both been researched as complementary therapies in integrative oncology, they are typically studied in isolation, and delivery of interventions (particularly TCQ) has not been standardized. Thus, little is known about the potential relative benefits associated with one type of therapy over another. In addition, little has been done to characterize the effects of mindfulness meditation and TCQ on indices of autonomic functioning, only select few indices have been examined, and measures have not been standardized. In the

absence of comparative trials, these therapies may currently be included in comprehensive cancer care options arbitrarily. It is important to explore which interventions are optimal for symptom reduction – which will ultimately improve the overall quality of life of cancer survivors – and may also support other health behaviours that can contribute to wellness. Therefore, the objectives of the present study are as follows:

Objective 1: To examine the patterns of autonomic functioning (indexed by changes in HRV, BRS, and blood pressure) associated with participation in MBCR and TCQ in post-treatment cancer survivors.

Objective 2: To examine differential changes in mood disturbance, health-related quality of life, sleep quality, and pain associated with participation in MBCR or TCQ

Objective 3: To examine whether changes in HRV, BRS, and blood pressure are associated with changes in mood disturbance, health-related quality of life, sleep disturbance, and pain

Investigating whether there is autonomic specificity (indexed by specific changes in HRV, BRS, and blood pressure) associated with participation in MBCR or TCQ, or whether non-specific changes occur may help inform complementary therapy selection in treatment planning. Furthermore, delineating the autonomic specificity associated with participation in MBCR and TCQ might lead to better understandings of mechanisms associated with symptom improvement, and may provide a better rationale for treatment selection based on specific symptom presentation.

Chapter 2: Methods

2.1 Participants

2.1.1 Recruitment. Participants were recruited through a network of patients in and around Calgary, through advertising, referrals from cancer treatment centres, conventional and social media outreach, and invitation letters sent through the Alberta Cancer Registry.

2.1.2 Inclusion/exclusion criteria. Men and women over age 18 with any type of cancer (stage I-III) who have completed active treatment (e.g., surgery, chemotherapy) at least 4 months previously were recruited. Participants were screened with the Distress Thermometer to ensure recruitment of those experiencing clinically significant distress (score ≥4; National Comprehensive Cancer Network). Other inclusion criteria were: the ability to attend MBCR or TCQ classes at scheduled times, the functional capacity to participate in the interventions, and the ability to speak and write English sufficiently for questionnaire completion and group participation.

Exclusion criteria included: a diagnosis of head, neck or brain cancer; metastatic cancer; and cognitive impairment or current psychiatric disorders that would interfere with participation in questionnaires or interventions. Participants were also excluded if they already practiced mindfulness meditation, Tai Chi, or Qigong >1 time per week, or if they had previously participated in the MBCR program.

2.2 Procedure

2.2.1 Study design. The present study is part of a larger study: Mindfulness And Tai chi for Caner Health (the MATCH study), a preference-based comparative effectiveness trial (Carlson et al., 2017). Participants who had a preference for an intervention received their preference, and those without a preference were randomized, thus embedding an RCT within a

larger, real-world trial. In the preference arm, participants were randomly assorted to immediate or waitlist groups in a 2:1 ratio; and in the no-preference arm, participants were randomized to MBCR (immediate or delayed in a 2:1 ratio) or TCQ (immediate or delayed in a 2:1 ratio). The waitlist groups for each of the interventions served as control groups. Physiological and psychosocial measures were obtained following an intake appointment before randomization (if the participant did not have a preference) and re-obtained following program completion.

2.2.2 Baseline laboratory session. See Figure 1 for the order and timing of data acquisition during the laboratory sessions. Participants were asked to avoid ingesting caffeine and alcohol, smoking cigarettes, or exercising prior to the testing session (Allen, Chambers, & Towers, 2007). They were also asked to sit quietly for at least 5 minutes immediately before recording. Participants completed task one (sitting during free breathing), task two (sitting while breathing to a metronome), task three (laying in supine position while breathing to a metronome), task four (standing while breathing to a metronome), and task five (sitting while actively trying to relax) consecutively. Blood pressure was recorded concurrently with task one and inter-beat interval was recorded continuously throughout all five tasks. Participants were instructed to breathe with a metronome at a pace of 0.2 Hz during tasks two, three, and four to control for potential effects of respiration (Berntson et al., 1997; Grossman & Taylor, 2007). Total testing duration was approximately 30 minutes. Participants received questionnaires via email following the baseline testing session, and prior to the post-intervention testing session.

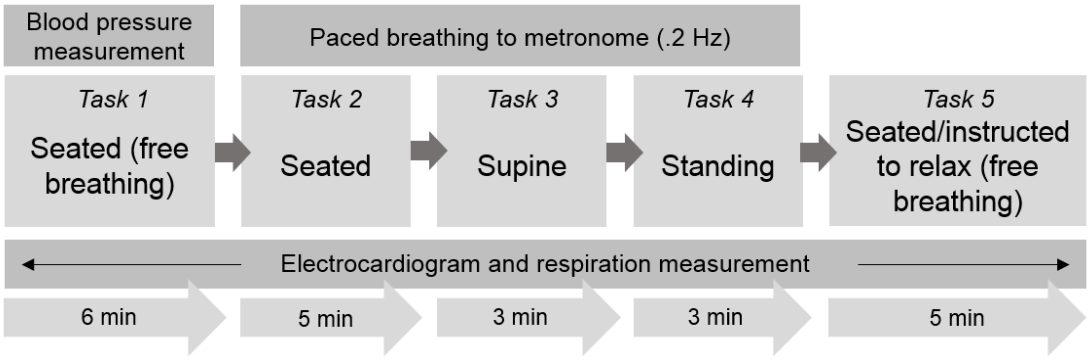

Figure 1. Order of tasks and measurement acquisition during the psychophysiology testing session

2.3 Interventions

2.3.1 Mindfulness-Based Cancer Recovery. The standardized 9-week MBCR program developed by Carlson & Speca (2010) was used. The program consisted of weekly meetings 1.5 to 2 hours alongside daily home practice of 45 minutes (15 minutes yoga, 30 minutes meditation) and a 6-hour weekend retreat. Training includes mindfulness meditation, Hatha yoga, group reflection and problem-solving, and skillful inquiry. Different forms of meditation (e.g. body scan, sitting and walking meditations) and gentle Hatha yoga were incorporated throughout the program. Material specific to cancer survivors (e.g., sleep problems, pain, and fear of cancer recurrence) was included.

2.3.2 Tai Chi Qigong. The TCQ intervention in the present study was based on elements common to both Tai Chi and Qigong: meditative postures, flowing movements, breath awareness, body awareness, focused attention, and imagery (Wayne et al., 2013). TCQ consisted of weekly 1.5-hour group sessions supplemented by home practice and a 4-hour weekend retreat, and had the same contact time at MBCR. A variant of the schedule (45-minute meetings twice weekly) was initially piloted but changed due to participant preference and to more closely resemble the MBCR group (Carlson et al., 2017).

2.4 Measures

2.4.1 Psychophysiological

2.4.1.1 Heart rate variability. Inter-beat intervals were measured via EKG electrodes in a standard 3-lead configuration and recorded on a Biopac MP36 data acquisition device (Biopac Systems Inc.; Goleta, California). Sampling frequency was set to 2000 Hz, above the minimum suggested sampling frequency of 500 Hz (Task Force, 1996). Raw ECG data was visually inspected for errors, which were removed. All segments analyzed were 2 minutes in length: two-minute segments were extracted from 3-minute recordings and averages of two 2-minute segments were extracted from 5-minute recordings. HRV parameters were derived using the Fast-Fourier Transform spectral decomposition method in Kubios HRV v2.2 software (Tarvainen, Niskanen, Lipponen, Ranta-Aho, & Karjalainen, 2014). Regarding frequency domain measures, high frequency HRV (HF-HRV; .15 to .4 Hz) and low frequency HRV (LF-HRV; .04 to .15 Hz) were examined, in both milliseconds squared (ms^2; the absolute power within the band) and normalized units (nu; a ratio of the power in a band over total power, removing the very low frequency component [0 to 0.04 Hz]). The time-domain parameter root mean square of successive differences (RMSSD), also an index of parasympathetic activity, was extracted for comparison to ms^2 HF-HRV (Laborde, Mosley, & Thayer, 2017). The HF-HRV and LF-HRV variables measured in ms^2 were positively skewed, thus a natural logarithm ($_{ln}$) transformation was applied to these variables to approximate a normal distribution. A respiration band attached to the BioPac MP36 device recorded respiration rate throughout the testing session.

2.4.1.2 Blood pressure. Automated office blood pressure was measured in accordance with Hypertension Canada Guidelines (2015). A BpTRU device (BpTRU Medical Devices;

Coquitlam, British Columbia) was used in the testing room alone with the participant. The BpTRU obtained 6 measurements separated by 1-minute intervals and recorded the average of the last 5 (e.g., Greiver et al., 2012).

2.4.1.3 Baroreflex sensitivity. BRS was inferred from the change in HF-HRV in response to the supine to stand challenge (task three to task four). BRS was calculated for all HF-HRV indices as the value from task three (supine) subtracted from task four (standing), such that a greater negative value represents greater sensitivity. BRS change scores were calculated as BRS pre-intervention subtracted from BRS post-intervention, such that a negative change score represents a greater change in sensitivity.

2.4.2 Subjective symptoms

2.4.2.1 Psychological distress. The 37-item Profile of Mood States (POMS-37) is a self-report measure of six dimensions of mood (anxiety, depression, anger, vigor, fatigue, and confusion) that can be summed to create a total mood disturbance score, and has been widely used in clinical populations, including cancer survivors (McNair, Lorr, & Droppleman, 1992). The POMS-37 has been reported to have good internal consistency, convergent validity, and construct validity in a sample of cancer survivors (Baker, Denniston, Zabora, Polland, & Dudley, 2002).

2.4.2.2 Health-related quality of life. The Functional Assessment of Cancer Therapy – General (FACT-G) is a 27-item measure of four domains of health-related quality of life: physical, social, emotional, and functional well-being (Cella et al., 1993). The FACT-G has been shown to have good internal consistency across different cancer groups and across translations to different languages (Victorson, Barocas, Song, & Cella, 2008).

2.4.2.3 Sleep. The Pittsburgh Sleep Quality Index is a self-report measure of several components of sleep quality including subjective quality, sleep latency, sleep efficiency, sleep disturbance, and daytime functioning (Buysse, Reynolds, Monk, & Berman, 1989). The PSQI has been shown to have good internal consistency and construct validity in cancer survivors (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004).

2.4.2.4 Pain. The Brief Pain Inventory is a self-report measure of pain across dimensions of pain severity and interference with daily functioning (Cleeland & Ryan, 1994). It was initially developed for use in cancer survivors; and has been shown to have good internal consistency, test-retest reliability, and construct validity (Cleeland, 2009).

2.5 Analysis Plan

Objective 1: Linear mixed modeling (LMM) was used to examine changes in autonomic indices, where group and time were included as fixed factors in a series of models examining each dependent variable and each task separately. Pairwise comparisons were specifically of interest to examine (1) whether indices changed from pre- to post after participating in MBCR and/or TCQ, (2) whether indices differed at post between MBCR and waitlist, or TCQ and waitlist, and (3) whether indices differed at post between MBCR and TCQ. To curb type I error potential, all pairwise comparisons were Bonferroni corrected through syntax. HF-HRV and LF-HRV were examined in tasks one, two, and five, and BRS was inferred from change in HF-HRV from task three to four. Effect sizes for between-group differences were calculated as the difference between groups at post (Lakens, 2013; McGough & Faraone, 2009). In all LMM analyses outlined in Objective 1 and 2, baseline measures were examined as covariates and included in the models as appropriate (i.e., covariates were only included in models when they did not interact with fixed factors).

LMM was used to assess differential changes in SBP, DBP, and heart rate, including group and time as fixed factors. Use of antihypertensive medication and use of beta-blockers were also examined as covariates for blood pressure and heart rate, respectively, and included in the models as appropriate. Bonferroni corrected pairwise comparisons were of interest specifically to examine the same patterns as outlined previously.

Objective 2: LMM was used to examine differential changes in mood disturbance, sleep disturbance, health-related quality of life, and pain, including group and time as fixed factors. Bonferroni corrected pairwise comparisons were of interest specifically to examine the same patterns as outlined in objective 1. Use of sedative medication was examined as a covariate for sleep disturbance scores and use of antidepressant medication was examined as a covariate for depressive symptoms and emotional well-being scores. Covariates were included in the models as appropriate.

Objective 3: Correlations were used to examine associations between changes in indices of autonomic functioning (HRV, BRS blood pressure, heart rate) and changes in symptoms (mood, sleep, health-related quality of life, pain).

Chapter 3: Results

3.1 Demographics

A total of 25 participants were recruited to the MBCR (*n*=11), TCQ (*n*=7), and waitlist (*n*=7) groups. Two participants were identified during data processing as having arrhythmias and had several HRV measurement points exceeding 3 SDs from the mean. These participants (both in the TCQ group) were excluded from analyses as outliers, for a final sample of 23. On average, participants were 63 years old, female (87%), married (56.5%), had been diagnosed with breast (34.8%) or gastrointestinal (30.4%) cancer, were 28 months post-treatment, had 15 years of education, and had a mean BMI in the overweight range (27.18). Table 1 presents demographic characteristics by group measured at baseline, among which no differences were observed. There were no differences between any of the outcome variables at baseline. There was a near-significant difference between groups in $_{ln}ms^2$ HF-HRV during task four (standing with metronome) ($F(2,20)=3.46$, $p=.05$), driven by a difference between TCQ and waitlist groups ($M_{diff}=1.51$, $SE=.58$ $p=.02$).

3.2 Consideration of Respiration

Respiration was not associated with RMSSD or $_{ln}ms^2$ HF-HRV, at baseline or at post-intervention. However, $_{ln}ms^2$ LF-HRV was negatively associated with respiration during all free breathing tasks at baseline and post-intervention (*r*s=-.54-[-.69], *p*s< .01). The mean respiration rate among all groups during paced breathing tasks was .2 Hz (*SD*s=.00-.02), verifying that the participants breathed in time with the metronome. Respiration rates during free breathing tasks (one and five) at baseline and post intervention were similar (*M*s=.19-.22, *SD*s=.07).

A series of repeated-measures ANOVAs confirmed that there were significant effects of task on all HRV parameters (*F*s=8.66-21.69, all *p*s<.01), confirming that the different tasks

generally elicited different responses. There were no differences in $_{ln}ms^2$ HF-HRV during task one (seated free breathing) or two (seated metronome), either at baseline or post-intervention. However, $_{ln}ms^2$ LF-HRV was significantly higher during task one seated than task two at baseline (M_{diff}=1.04, *SE*=.19 *p*<.001) and post-intervention (M_{diff}=.91, *SE*=.26 *p*<.01), further supporting an influence of respiration on LF-HRV but not HF-HRV in the present study.

3.3 Objective 1: Changes in Indices of Autonomic Functioning

3.3.1 Heart rate variability and baroreflex sensitivity. RMSSD and $_{ln}ms^2$ HF-HRV were significantly correlated among all tasks at baseline and post-intervention (*r*s=.80-.92, all *p*s< .001), indicating consistency between time-domain and frequency-domain indices of parasympathetic activity (Laborde et al., 2017). Table 2 displays the means of all HRV parameters by group at baseline and post-intervention. Pairwise comparisons were examined as outlined in the analysis plan, though it should be noted that there were no overall effects of task, no overall effects of group, and no interaction effects on any of the HRV parameters (see Table 4).

Table 4 indicates when baseline measures were included as covariates in models. There were no differences in any groups from pre- to post or between any groups at post for the indices $_{ln}ms^2$ HF-HRV, nu HF-HRV, $_{ln}ms^2$ LF-HRV, or nu LF-HRV during tasks one, two, or five. BRS (inferred from greater change in RMSSD from supine to standing) improved from pre- to post in the MBCR group (M_{diff}=5.89, *SE*=2.67, *p*=.04, d_z=-.74) and was greater in the MBCR group than TCQ at post (M_{diff}=9.34, *SE*=3.26, *p*=.02, *d*=1.17), though it was not greater in the MBCR group than waitlist at post. Similarly, there was a trend for improvement in BRS (derived from $_{ln}ms^2$ HF-HRV) in the MBCR group from pre-to post (M_{diff}=.86, *SE*=.45, *p*=.07, d_z=-.79) though there were no differences between any groups at post.

3.3.2 Blood pressure. Use of antihypertensive medications did not interact with group or time, thus it was included as a covariate in the models assessing SBP and DBP. There were no differences in SBP or DBP from pre- to post, and neither MBCR or TCQ improved more than waitlist. However, MBCR had significantly lower SBP (M_{diff}=23.72, *SE*=7.37, *p*=.01, *d*=2.05) and DBP (M_{diff}=8.79, *SE*=3.39, *p*=.04, *d*=1.47) than TCQ at post. There was a significant interaction between use of beta-blockers and group ($F(2,17)=3.63$, $p=.05$), thus it could not be included as a covariate when assessing heart rate. Heart rate did not differ from pre- to post, and did not differ between any groups at post.

3.4 Objective 2: Changes in Subjective Symptoms

See Table 3 for mean symptom scores by group at baseline and post-intervention. Only 18 participants completed the follow-up questionnaires. Sedative use did not interact with fixed factors group or time, thus it was included as a covariate when examining sleep disturbance scores. There was a significant group*time interaction ($F(2,14.20)=4.39$, $p=.03$), characterized by an improvement in sleep disturbance in the TCQ group from pre- to post (M_{diff}=3.53, *SE*=1.27, *p*=.02, d_z=-.87) and no change in MBCR or waitlist from pre- to post, however examination of changes in individual participants suggests that a 47% reduction in sleep disturbance reported by one individual in the TCQ group may have driven this finding (see Figure 2).

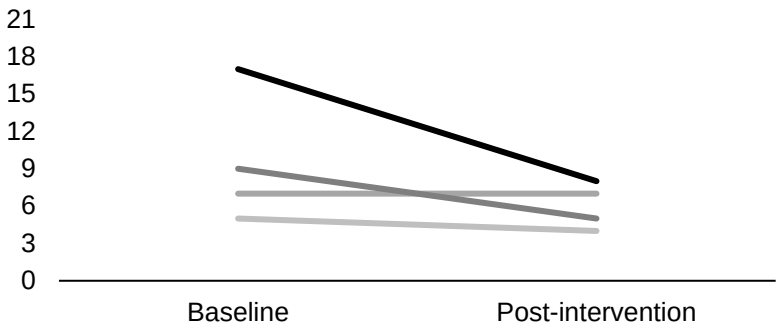

Figure 2. Individual sleep disturbance scores at baseline and post-intervention in the Tai Chi/Qigong group. Sleep disturbance was measured with the Pittsburgh Sleep Quality Index, where higher values (of a total possible 21 points) denote greater disturbance. One participant in TCQ did not complete the follow-up questionnaire.

Antidepressant use did not interact with fixed factors group or time, thus it was included as a covariate when examining emotional well-being scores and depressive symptoms. There were no differences from pre- to post or between any groups at post on physical well-being, social well-being, emotional well-being, functional well-being, total mood disturbance, depressive symptoms, vigor, anger, tension, confusion, or fatigue. There were too few people who experienced pain post-intervention to conduct statistical analyses. Nine of 23 participants (39.1%) experienced pain at baseline; and of the 18 participants who completed the BPI post-intervention, three (16.7%) experienced pain.

3.5 Objective 3: Associations between Changes in Autonomic Indices and Changes in Subjective Symptoms

See Table 4 for correlations between changes in HRV parameters and changes in symptoms. There was a pattern of changes associated with physical well-being, such that increased physical well-being was associated with decreased $_{ln}ms^2$ HF-HRV during tasks one and two, decreased HF-HRV (nu) during task two (*r*s=-.52-[-.66], *p*s<.05), and increased LF-

HRV (nu) during task two ($r(16)=.60$, $p<.01$). Increased physical well-being was also associated with increased heart rate ($r(8)=.58$, $p=.04$). Decreased fatigue was associated with increased $_{ln}ms^2$ HF-HRV ($r(16)=-.60$, $p<.01$) as well as increased $_{ln}ms^2$ LF-HRV during task five ($r(16)=-.48$, $p=.04$). Further, increased vigor was associated with increased $_{ln}ms^2$ LF-HRV during task one ($r(16)=.48$, $p<.05$). Weaker BRS (characterized by a smaller change in HF-HRV [nu] from supine to stand at post than at pre-intervention) was associated with increased anger ($r(16)=.48$, $p=.04$) and increased depressive symptoms ($r(13)=.55$, $p=.04$). Finally, increased LF-HRV (nu) during task one was associated with decreased mood disturbance ($r(16)=-.50$, $p=.04$) and decreased depressive symptoms ($r(13)=-.55$, $p=.04$).

Chapter 4: Discussion

4.1 Objective 1: Changes in Indices of Autonomic Functioning

The present study reports increased BRS (characterized by greater change in RMSSD from supine to stand at post than pre-intervention) following participation in MBCR, and lower SBP and DBP in MBCR relative to TCQ at post-intervention. Although these findings are based on a priori pairwise comparisons, omnibus tests were non-significant and the results should be interpreted with caution. Prior studies have reported moderate effect size reductions in SBP and DBP following mindfulness-based interventions for people with vascular disease (Abbott et al., 2014), reductions in blood pressure following meditation and yoga among those with hypertension (Park & Han, 2017), and reductions in blood pressure following MBCR among cancer survivors (Campbell et al., 2012; Carlson et al., 2007). While the present study is inconsistent with prior reviews supporting reductions in blood pressure following Tai Chi (Yeh, Wang, Wayne, & Phillips, 2008) and Qigong interventions (Xiong, Wang, & Zhang 2015), the reviewed studies had methodological issues, such as lack of allocation concealment, lack of blinding of outcome assessors, lack of adequate sequence generation, and incomplete outcome reporting. Very few studies appear to have examined BRS following a mindfulness or Tai Chi and/or Qigong intervention. While Krygier et al. reported reduced baroreflex activity after meditation training, they interpreted LF-HRV between .06 and .10 Hz as baroreflex influence (Krygier et al., 2013) rather than HF-HRV response to posture change. Despite the differences in methodology, both Krygier et al. and the present study support the notion that mindfulness training may influence baroreflex activity in some way. The present findings are contrary to those of Sato et al., who reported improved BRS following Tai Chi training relative to a control

group; however, they examined a population with coronary heart disease and employed a year-long intervention (Sato et al., 2010).

Although exercise can improve BRS (La Rovere & Pinna, 2014) and reduce blood pressure (Cornelissen & Smart, 2013), any findings related to BRS, SBP, and DBP in the present study should not be attributed to the effects of exercise as it was deliberately slow-paced and may not have been vigorous enough to elicit physical changes. One potential factor contributing to the results of the present study may be a general reduction in psychological distress, considering the inverse association between psychological distress and cardiovascular health (Bunker et al., 2003; Strike & Steptoe, 2004), and prior associations of perseverative cognition with higher blood pressure and decreased HRV (Ottaviani et al., 2016). MBCR may be indirectly associated with change in autonomic indices through decreased psychological distress and perseverative cognition, given its acceptance-based approach that specifically targets maladaptive cognitions and promotes present awareness (Carlson & Speca, 2010), and decreased rumination being a mediator of the effects of MBCR on depressive symptoms (Labelle, Campbell, & Carlson, 2010). Consistent with this explanation, decreased rumination has been associated with decreased SBP in another study of cancer survivors following MBCR (Campbell et al., 2012).

4.2 Objective 2: Changes in Subjective Symptoms

The present study reported a greater decrease in sleep disturbance following participation in TCQ relative to MBCR. Reviews support improvements in subjective sleep quality following Tai Chi and/or Qigong among both older adults (Du et al., 2015; Wu, Kwong, Lan, & Jiang, 2015) and cancer survivors specifically (Tao et al., 2016); though the included studies typically have methodological issues such as lack of allocation concealment. Examination of Figure 3

suggests that the improvement in sleep disturbance scores in the TCQ group are likely driven by one participant, therefore stating any conclusions on the effectiveness of TCQ for reducing sleep disturbance in the present study would be premature. The observed increase in sleep disturbance following participation in MBCR is inconsistent with prior reviews that report the effectiveness of mindfulness-based interventions for sleep problems in adults (Garland, Zhou, Gonzalez, & Rodriguez, 2016) and cancer survivors specifically (Christodoulou & Black, 2017).

4.3 Objective 3: Associations between Changes in Autonomic Indices and Changes in Subjective Symptoms

Increased LF-HRV was associated with a pattern of improvements: increased physical well-being, increased vigor, decreased fatigue, decreased depressive symptoms, and decreased mood disturbance. What LF-HRV represents remains contentious. One interpretation is that LF-HRV represents sympathetic activity or sympathetic/parasympathetic balance (e.g., studies have found reduced LF-HRV with pharmacological blockers of sympathetic synapses, or increased LF-HRV corresponding with sympathetic activation during tasks such as a tilt; Berntson et al., 1997). This interpretation has been challenged, based on several lines of evidence (e.g., LF-HRV does not correspond to other known measures of sympathetic activity, drugs/experimental manipulations known to impact sympathetic outflow do not consistently correspond to changes in LF power; Goldstein, Bentho, Park, & Sharabi, 2011; Reyes del Paso, Langewitz, Mulder, Van Roon, & Duschek, 2013). It has been instead posited that LF-HRV may represent modulation of cardiac autonomic activity by baroreflexes, based on observed decreases in LF-HRV in people with baroreflex failure, and decreases in LF-HRV after experimental baroreflex alteration in animals (Goldstein et al., 2011; Reyes del Paso et al., 2013). Further, increased LF-HRV is not necessarily a marker of negative health outcomes – studies have reported lower LF-

HRV in individuals with cardiovascular disease and higher LF-HRV among regular exercisers (Reyes del Paso et al., 2013). The pattern of associations between increased LF-HRV and improved physical well-being, vigor, fatigue, depressive symptoms, and mood disturbance in the present study further suggests LF-HRV may be a positive indicator of symptom change.

An index of parasympathetic activity, HF-HRV is influenced by the vagus nerve, which innervates the sinoatrial node of the heart and slows the rate of depolarization through release of acetylcholine (Berntson et al., 1997, Laborde et al., 2017). Increased HF-HRV is associated with positive functional and psychological states such as increased sleep quality, decreased fatigue, increased calmness, and increased satisfaction with life (Crosswell et al., 2014; Geisler, Vennewald, Kubiak, & Weber, 2010; Kageyama et al., 1998). Accordingly, the present study reported an inverse association between HF-HRV and fatigue severity. The present study also reported that attenuated BRS (characterized by decreased change in HF-HRV from supine to standing from pre- to post-intervention) was associated with increased anger and increased depressive symptoms. This is consistent with prior studies linking negative psychological states such as anger, anxiety, and depression to negative cardiovascular health in general (Chaddha, Robinson, Rogers, Alexandris-Souphis, & Rubenfire, 2016), and impaired BRS specifically (Davydov, Shapiro, Cook, & Goldstein, 2007; Virtanen et al., 2003). Unexpectedly, increased HF-HRV was associated with decreased in physical well-being in the present study. However, the overall reduction in physical well-being amounted to less than 1% change in score, thus unlikely to translate to meaningful reductions. A larger sample with greater range in physical well-being change scores may have resulted in a positive relationship between changes in HF-HRV and physical well-being, consistent with the literature (Kemp & Quintana, 2013).

4.4 Conclusion

The present study suggests that participation in MBCR may be associated with some degree of change in indices of autonomic functioning among post-treatment cancer survivors while TCQ may not. Additionally, results support a pattern of relationships between increased LF-HRV and increased physical well-being, increased vigor, decreased fatigue, decreased depressive symptoms, and decreased mood disturbance; which may point towards underlying mechanisms involved in symptom improvement. This study adds to a sparse literature examining the effects of mindfulness, Tai Chi, or Qigong interventions on HRV and BRS; and appears to be the first to directly compare the effects of a mindfulness intervention to a Tai Chi and/or Qigong intervention on any index of autonomic activity. The main strength of this study is that multiple indices of autonomic function were examined, which allowed for a more nuanced examination of changes and corroboration between multiple indices of change. Further strengths include a reasonably homogeneous sample of distressed cancer survivors, and the ecological validity of a preference-based design.

4.5 Limitations and Future Directions

The present study has several limitations, primarily (1) small sample size and (2) unequal sample distribution between groups. The small sample size may have reduced the power to detect differences, particularly between groups. (3) There was a lack of available information about attendance or homework completion, as home practice was a component of both interventions. Without information describing comparable amount of home practice between groups, differential improvements relating to differential practice between groups cannot be ruled out. (4) The method used to infer BRS may limit comparisons between the present study and other studies that have calculated BRS differently (e.g., Krygier). (5) The known adverse

impact of cancer treatment on the cardiovascular system (Curigliano et al., 2012) may limit the generalizability of the findings to other populations. (6) There was a lack of information about other interpersonal or behavioural factors that could have contributed to the observed results, such as sources of social support or diet. (7) There was no follow-up information, thus it is unclear whether results would be sustained over time. (8) Finally, the list of outcome questionnaires was not fully comprehensive. For example, there was no information about rumination; and potentially important outcomes such as fatigue and depression may have been better represented with their own specific measure rather than a subscale of the POMS-37.

Future directions include examining the replicability of the results in a larger sample, examining whether MBCR or TCQ might differentially impact other indices of stress response such as cortisol or inflammation, and examining the generalizability of the findings to different populations.

Table 1. Demographic characteristics and tests of differences in demographics at baseline

Demographics	Group			Difference test (*df*)	*p*
	MBCR (*n*=11)	TCQ (*n*=5)	Waitlist (*n*=7)		
Age in years *M* (*SD*)	62.89 (11.92)	63.75 (6.99)	63.14 (8.23)	*F*(2,17)=.01	.99
Sex					
Males % (*n*)	9.10 (1)	20.00 (1)	14.30 (1)	χ^2(2)=.37	.83
Females % (*n*)	90.90 (10)	80.00 (4)	85.70 (6)		
Years of education *M* (*SD*)	13.18 (5.72)	18.00 (3.94)	15.14 (4.98)	*F*(2,20)=1.50	.25
Body Mass Index *M* (*SD*)	27.80 (4.30)	26.74 (3.26)	26.52 (3.24)	*F*(2,20)=.29	.75
Marital status					
Single % (*n*)	36.40 (4)	40.00 (2)	0 (0)	χ^2(6)=6.34	.39
Cohabiting % (*n*)	0 (0)	0 (0)	0 (0)		
Married % (*n*)	45.50 (5)	60.00 (3)	71.4 (5)		
Divorced % (*n*)	0 (0)	0 (0)	14.3 (1)		
Widowed % (*n*)	18.20 (2)	0 (0)	14.3 (1)		
Cancer type					
Breast % (*n*)	45.5 (5)	20.00 (1)	28.6 (2)	χ^2(12)=11.13	.52
Gastrointestinal % (*n*)	27.3 (3)	40.00 (2)	28.6 (2)		
Gynecological% (*n*)	9.1 (1)	40.00 (2)	-		
Lymphoma % (*n*)	9.1 (1)	-	28.6 (2)[1]		
Thyroid % (*n*)	9.1 (1)	-	-		
Ovarian % (*n*)	-	-	14.3 (1)		
Months since last treatment *M* (*SD*)	27.31 (12.89)	31.41 (9.41)	26.37 (15.67)	*F*(2,19)=.23	.80
Minutes of physical activity per day *M* (*SD*)	24.09 (19.85)	19.00 (19.49)	27.14 (13.18)	*F*(2,20)=.30	.75
Alcoholic drinks per week *M* (*SD*)	.36 (.50)	.40 (.55)	1.71 (2.50)	*F*(2,20)=2.12	.15
Caffeinated drinks per week *M* (*SD*)	2.27 (1.33)	3.00 (1.73)	1.21 (.81)	*F*(2,20)=2.94	.08
Uses of nicotine per day *M* (*SD*)	0 (0)	2.40 (5.37)	0 (0)	*F*(2,20)=1.96	.17
Antihypertensive use					
Yes % (*n*)	36.40 (4)	60.00 (3)	42.90 (3)	χ^2(2)=.78	.68
No % (*n*)	63.60 (7)	40.00 (2)	57.10 (4)		
Sedative use					
Yes % (*n*)	0 (0)	20.00 (1)	42.90 (3)	χ^2(2) =5.50	.06
No % (*n*)	100 (11)	80.00 (4)	57.10 (4)		
Antidepressant use					
Yes % (*n*)	9.10 (1)	20.00 (1)	14.30 (1)	χ^2(2)=.37	.83
No % (*n*)	90.90 (10)	80.00 (4)	85.70 (6)		

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Demographics	Group			Difference test (*df*)	*p*
	MBCR (*n*=11)	TCQ (*n*=5)	Waitlist (*n*=7)		
Steroid use					
Yes % (*n*)	9.10 (1)	0 (0)	16.70 (1)	$\chi^2(2)=.92$	.63
No % (*n*)	90.90 (10)	100 (5)	83.30 (5)		

Note. Percentages represent percentages within each group, MBCR = Mindfulness-Based Cancer Recovery, TCQ = Tai Chi/Qigong. [1]Note one of the participants was diagnosed with Hodgkin's lymphoma, one with non-Hodgkin's lymphoma

Table 2. Pre- and post-intervention means and standard deviations of heart rate variability (HRV) parameters by group and task

Parameter	Task	Group					
		MBCR *M* (*SD*)		TCQ *M* (*SD*)		Waitlist *M* (*SD*)	
		Pre	Post	Pre	Post	Pre	Post
High frequency HRV ($_{ln}ms^2$)	1	4.33 (.92)	4.09 (1.54)	4.21 (1.00)	3.87 (1.13)	4.75 (1.37)	4.36 (1.16)
	2	4.50 (1.24)	4.29 (1.49)	4.25 (.82)	4.04 (.88)	5.08 (1.00)	4.81 (1.35)
	3	5.25 (1.01)	5.57 (1.00)	5.46 (.78)	4.76 (.64)	5.79 (.66)	5.45 (1.08)
	4	4.36 (1.07)	3.82 (1.27)	3.68 (.65)	3.95 (.76)	5.19 (1.06)	4.20 (.94)
	5	4.71 (1.26)	4.87 (1.16)	4.53 (1.11)	4.00 (.75)	5.17 (.87)	4.65 (1.05)
High frequency HRV (nu)	1	32.40 (15.08)	32.88 (21.84)	39.53 (22.25)	30.31 (21.34)	35.96 (30.70)	38.12 (24.14)
	2	56.95 (21.72)	57.90 (20.52)	55.95 (23.60)	54.14 (22.84)	65.19 (17.80)	54.74 (21.94)
	3	64.79 (20.74)	70.06 (16.28)	66.49 (18.26)	58.88 (30.02)	71.33 (15.40)	63.03 (8.86)
	4	52.49 (19.38)	50.79 (21.42)	43.92 (17.89)	35.80 (22.50)	63.75 (26.72)	44.41 (20.00)
	5	36.29 (21.30)	36.92 (21.15)	28.38 (21.95)	25.09 (20.51)	34.12 (23.15)	37.59 (25.67)
Low frequency HRV ($_{ln}ms^2$)	1	5.31 (.94)	5.06 (1.64)	4.86 (.68)	5.01 (.88)	5.50 (1.48)	5.02 (1.00)
	2	4.18 (1.09)	3.98 (1.10)	4.10 (.92)	3.84 (.97)	4.40 (.44)	4.55 (1.31)
	3	4.51 (.91)	4.63 (.95)	4.68 (1.10)	4.42 (1.55)	4.75 (1.10)	4.90 (.85)
	4	4.14 (1.27)	3.78 (1.17)	3.96 (.27)	4.67 (1.35)	4.50 (1.03)	4.42 (.35)
	5	5.58 (1.27)	5.60 (1.36)	5.76 (.54)	5.33 (1.02)	6.04 (.95)	5.34 (.99)
Low frequency HRV (nu)	1	67.54 (15.11)	70.52 (24.00)	60.41 (22.26)	69.59 (21.35)	63.99 (30.70)	61.85 (24.15)
	2	42.79 (21.74)	41.71 (20.61)	43.88 (23.68)	45.65 (22.97)	34.63 (17.85)	44.83 (22.02)
	3	35.01 (20.70)	29.80 (16.27)	33.37 (18.37)	41.07 (30.04)	28.49 (15.32)	36.72 (8.85)
	4	47.10 (19.54)	48.92 (21.55)	55.92 (17.96)	64.02 (22.67)	35.99 (26.82)	55.35 (20.19)
	5	63.65 (21.34)	63.00 (21.21)	71.56 (21.99)	74.85 (20.57)	65.86 (23.16)	62.39 (25.68)

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Parameter	Task	Group					
		MBCR *M* (*SD*)		TCQ *M* (*SD*)		Waitlist *M* (*SD*)	
		Pre	Post	Pre	Post	Pre	Post
RMSSD	1	15.65 (5.80)	16.27 (8.57)	16.25 (6.43)	13.44 (5.67)	23.82 (13.97)	15.90 (6.78)
	2	13.81 (7.18)	14.41 (9.05)	13.02 (4.56)	11.66 (4.60)	18.38 (9.70)	16.68 (6.97)
	3	21.40 (8.47)	23.01 (12.35)	23.15 (9.53)	19.39 (8.42)	28.38 (13.03)	25.47 (13.12)
	4	15.21 (6.59)	11.76 (7.66)	12.17 (4.11)	12.86 (6.32)	20.70 (8.33)	15.20 (7.50)
	5	19.97 (9.67)	21.37 (13.53)	20.39 (6.98)	15.66 (4.03)	25.74 (9.51)	19.94 (9.90)

Note. MBCR (*n*=11), TCQ (*n*=5), waitlist (*n*=7).
Task 1 = seated (free breathing), task 2 = seated (metronome), task 3 = supine (metronome), task 4 = standing (metronome), task 5 = directed relaxation (free breathing).
$_{ln}ms^2$ = natural log transformed milliseconds squared, MBCR = Mindfulness-Based Cancer Recovery, nu = normalized units, RMSSD = root mean square of successive differences, TCQ = Tai Chi/Qigong

Table 3. Pre- and post-intervention means and standard deviations of blood pressure, mood disturbance, health-related quality of life, sleep disturbance, and pain by group

Outcome	Group					
	MBCR *M* (*SD*)		TCQ *M* (*SD*)		Waitlist *M* (*SD*)	
	Pre	Post	Pre	Post	Pre	Post
SBP	118.82 (12.02)	112.18 (12.49)	127.60 (17.59)	136.40 (8.91)	123.14 (13.74)	117.14 (15.26)
DBP	75.36 (7.38)	72.73 (5.93)	75.40 (5.22)	81.40 (6.11)	79.00 (2.94)	78.29 (6.85)
Heart rate	77.09 (9.85)	81.18 (13.43)	63.80 (4.82)	65.80 (4.32)	66.14 (15.70)	70.14 (13.64)
Sleep disturbance	9.25 (4.68)	10.13 (4.05)	9.50 (4.26)	6.00 (1.83)	5.50 (5.45)	5.67 (4.27)
Total mood disturbance	31.00 (29.33)	26.75 (18.42)	15.75 (24.96)	8.50 (12.29)	19.17 (37.08)	25.00 (36.17)
Depression	7.38 (9.46)	8.13 (7.97)	5.00 (8.12)	4.00 (3.56)	5.83 (8.61)	7.67 (7.84)
Vigor	7.63 (5.55)	7.13 (2.75)	7.00 (5.35)	10.50 (4.80)	11.83 (4.71)	11.33 (6.50)
Anger	6.88 (5.36)	4.63 (3.62)	2.75 (1.26)	3.75 (4.35)	7.17 (7.08)	9.33 (7.12)
Tension	9.38 (6.30)	8.63 (5.07)	4.75 (5.25)	4.25 (1.71)	8.17 (7.96)	8.67 (7.63)
Confusion	5.75 (4.40)	4.63 (2.92)	4.00 (3.92)	1.75 (2.22)	5.17 (6.55)	5.50 (4.97)
Fatigue	9.25 (5.28)	7.88 (4.91)	6.25 (6.24)	5.25 (5.97)	4.67 (5.43)	5.17 (5.19)
Physical well-being	23.85 (2.44)	23.63 (3.02)	24.25 (3.86)	24.00 (5.48)	24.17 (4.12)	24.17 (3.25)
Social well-being	17.02 (6.86)	16.98 (5.59)	20.71 (5.90)	15.96 (1.46)	19.53 (4.98)	17.53 (2.32)
Emotional well-being	20.71 (3.51)	19.25 (4.14)	18.38 (11.49)	21.58 (4.42)	22.17 (7.23)	21.97 (5.13)
Functional well-being	18.63 (5.37)	18.25 (3.01)	18.50 (8.85)	20.75 (6.34)	23.00 (4.82)	21.83 (5.46)
[1]Pain severity	4.08 (.95)	4.00 (.71)	1.75 (N/A)	-	2.88 (3.01)	5.00 (N/A)
[1]Pain interference	.41 (.36)	.94 (1.34)	.89 (N/A)	-	2.17 (3.06)	5.56 (N/A)

Note. MBCR (*n*=11), TCQ (*n*=5), waitlist (*n*=7). Means for symptom inventories based on those in MBCR (*n*=8), TCQ (*n*=4), and waitlist (*n*=6) who completed both time points. [1]Pain severity and interference scores only calculated for those who endorsed pain at pre- (*n*=6) and post (*n*=3). Only one in TCQ endorsed pain at baseline, one in waitlist endorsed pain post-intervention, and none in TCQ endorsed pain post-intervention. DBP = diastolic blood pressure, MBCR = Mindfulness-Based Cancer Recovery, SBP = systolic blood pressure, TCQ = Tai Chi/Qigong

Table 4. Linear mixed model main effects of group, time, and group by time interactions for autonomic indices and subjective symptom outcomes

Outcome	Main effect		Interaction
	Group	Time	Group*Time
[1]T1 HF HRV ($_{ln}ms^2$)	$F(2,19.00)=.03$, $p=.97$	$F(1,20.00)=1.40$, $p=.25$	$F(2,20.00)=.03$, $p=.97$
[1]T2 HF HRV ($_{ln}ms^2$)	$F(2,19.00)=.05$, $p=.95$	$F(1,20.00)=.77$, $p=.39$	$F(2,20.00)=.01$, $p=.99$
T3-4Δ HF HRV ($_{ln}ms^2$)	$F(2,20.00)=.58$, $p=.57$	$F(1,20.00)=.31$, $p=.59$	$F(2,20.00)=2.81$, $p=.08$
T5 HF HRV ($_{ln}ms^2$)	$F(2,20.00)=,64$, $p=.54$	$F(1,20.00)=2.80$, $p=.11$	$F(2,20.00)=2.01$, $p=.16$
T1 HF HRV (nu)	$F(2,20.00)=.11$, $p=.90$	$F(1,20.00)=.23$, $p=.64$	$F(2,20.00)=.49$, $p=.62$
T2 HF HRV (nu)	$F(2,20.00)=.13$, $p=.88$	$F(1,20.00)=.43$, $p=.52$	$F(2,20.00)=.41$, $p=.67$
T3-4Δ HF HRV (nu)	$F(2,20.00)=.46$, $p=.64$	$F(1,20.00)=.60$, $p=.45$	$F(2,20.00)=.12$, $p=.89$
[1]T5 HF HRV (nu)	$F(2,19.00)=.42$, $p=.66$	$F(1,20.00)=.01$, $p=.94$	$F(2,20.00)=.27$, $p=.76$
[1]T1 LF HRV ($_{ln}ms^2$)	$F(2,19.00)=.16$, $p=.85$	$F(1,20.00)=.54$, $p=.47$	$F(2,20.00)=.40$, $p=.68$
[1]T2 LF HRV ($_{ln}ms^2$)	$F(2,19.00)=.51$, $p=.61$	$F(1,20.00)=.17$, $p=.68$	$F(2,20.00)=.25$, $p=.78$
[1]T5 LF HRV ($_{ln}ms^2$)	$F(2,19.00)=1.05$, $p=.37$	$F(1,20.00)=3.53$, $p=.08$	$F(2,20.00)=1.45$, $p=.26$
T1 LF HRV (nu)	$F(2,20.13)=.12$, $p=.89$	$F(1,19.54)=.25$, $p=.62$	$F(2,19.57)=.45$, $p=.65$
T2 LF HRV (nu)	$F(2,20.00)=.13$, $p=.88$	$F(1,20.00)=.40$, $p=.54$	$F(2,20.00)=.40$, $p=.68$
[1]T5 LF HRV (nu)	$F(2,19.00)=.42$, $p=.66$	$F(1,20.00)=.01$, $p=.94$	$F(2,20.00)=.27$, $p=.76$
T1 RMSSD	$F(2,20.00)=.87$, $p=.43$	$F(1,20.00)=3.39$, $p=.08$	$F(2,20.00)=2.24$, $p=.13$
T2 RMSSD	$F(2,20.00)=.98$, $p=.39$	$F(1,20.00)=.25$, $p=.62$	$F(2,20.00)=.24$, $p=.79$
[1]T3-4Δ RMSSD	$F(2,18.00)=1.65$, $p=.22$	$F(1,19.00)=.52$, $p=.48$	$F(2,19.00)=2.50$, $p=.11$
[1]T5 RMSSD	$F(2,19.00)=1.72$, $p=.21$	$F(1,20.00)=3.01$, $p=.09$	$F(2,20.00)=2.14$, $p=.14$
[2]SBP	$F(2,19.00)=3.32$, $p=.06$	$F(1,20.00)=.16$, $p=.70$	$F(2,20.00)=2.08$, $p=.15$
[2]DBP	$F(2,19.00)=2.15$, $p=.14$	$F(1,20.00)=.36$, $p=.55$	$F(2,20.00)=2.91$, $p=.08$

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Outcome	Main effect		Interaction
	Group	Time	Group*Time
[1]HR	$F(2,18.00)=.54$, $p=.59$	$F(1,20.00)=2.58$, $p=.12$	$F(2,20.00)=.09$, $p=.91$
[3]Sleep disturbance	$F(2,18.98)=2.54$, $p=.11$	$F(1,14.19)=3.44$, $p=.09$	$F(2,14.20)=4.39$, $p=.03$*
[4]Depression	$F(2,19.32)=.08$, $p=.93$	$F(1,16.59)=.06$, $p=.81$	$F(2,16.63)=.41$, $p=.67$
Vigor	$F(2,18.40)=.36$, $p=.71$	$F(1,14.72)=.34$, $p=.57$	$F(2,14.73)=.14$, $p=.27$
Anger	$F(2,19.62)=1.54$, $p=.24$	$F(1,16.43)=.00$, $p=.97$	$F(2,16.44)=.95$, $p=.41$
Tension	$F(2,20.05)=.24$, $p=.79$	$F(1,15.65)=.07$, $p=.79$	$F(2,15.65)=.19$, $p=.83$
Confusion	$F(2,20.30)=.45$, $p=.65$	$F(1,16.18)=2.03$, $p=.17$	$F(2,16.19)=1.00$, $p=.39$
Fatigue	$F(2,19.85)=.55$, $p=.59$	$F(1,15.89)=.51$, $p=.49$	$F(2,15.90)=.35$, $p=.71$
Total mood disturbance	$F(2,19.81)=.05$, $p=.95$	$F(1,15.73)=.17$, $p=.69$	$F(2,15.74)=.63$, $p=.55$
[1]Physical well-being	$F(2,19.60)=.03$, $p=.97$	$F(1,20.58)=.09$, $p=.77$	$F(2,20.60)=.02$, $p=.98$
Social well-being	$F(2,20.29)=.30$, $p=.74$	$F(1,16.70)=3.48$, $p=.08$	$F(2,16.72)=1.60$, $p=.23$
[4]Emotional well-being	$F(2,19.49)=.18$, $p=.84$	$F(1,16.63)=.16$, $p=.70$	$F(2,16.67)=1.50$, $p=.25$
Functional well-being	$F(2,20.06)=.61$, $p=.55$	$F(1,15.72)=1.41$, $p=.27$	$F(2,15.72)=1.41$, $p=.27$

Note. *$p<.05$. T1 = seated (free breathing), T2 = seated (metronome), T3-4Δ = change from supine to stand, T5 = directed relaxation. DBP = diastolic blood pressure, HF = high frequency, HR = heart rate, HRV = heart rate variability, LF = low frequency, $_{ln}ms^2$ = natural log transformed milliseconds squared, nu = normalized units, RMSSD = root mean square of successive differences, SBP = systolic blood pressure. Analyses adjusted for [1]baseline, [2]antihypertensives, [3]sedatives, or [4]antidepressives as indicated by superscript

Table 5. Correlations between changes in autonomic indices and changes in subjective symptoms across all groups

Parameter	[3]Depression Δ	Vigor Δ	Anger Δ	Tension Δ	Confusion Δ	Fatigue Δ	Total mood disturbance Δ	[4]Sleep disturbance Δ	Physical wellbeing Δ	Social wellbeing Δ	[3]Emotional wellbeing Δ	Functional wellbeing Δ
T1 HF HRV ($_{ln}ms^2$) Δ	.25	.25	-.04	.19	.36	-.06	.07	-.04	-.52*	.11	-.31	-.13
T2 HF HRV ($_{ln}ms^2$) Δ	.46	.05	.10	.38	.40	.16	.30	-.15	-.66**	-.10	-.41	-.31
T3-4Δ HF HRV ($_{ln}ms^2$) Δ	.34	-.02	.25	.26	.12	.27	.27	-.12	-.36	-.35	.03	.03
T5 HF HRV ($_{ln}ms^2$) Δ	-.46	-.02	-.33	-.08	-.38	-.60**	-.38	.31	.18	.27	.10	.43
T1 HF HRV (nu) Δ	.36	-.34	.08	.35	.28	.15	.32	.23	-.31	-.24	-.47	-.31
T2 HF HRV (nu) Δ	-.00	.03	-.01	.21	.13	.18	.14	-.16	-.60**	-.09	-.40	-.26
T3-4Δ HF HRV (nu) Δ	.55*	-.21	.48*	.37	.32	.24	.43	-.16	-.36	-.42	-.15	-.02
T5 HF HRV (nu) Δ	-.22	-.45	-.03	-.22	-.32	-.06	-.07	.08	.46	.03	-.03	.07
T1 LF HRV ($_{ln}ms^2$) Δ	-.17	.48*	-.16	-.08	-.00	-.29	-.27	-.14	-.21	.34	.17	.25
T2 LF HRV ($_{ln}ms^2$) Δ	.31	.02	.07	.14	.26	-.07	.13	.08	-.06	.03	.06	-.05
T5 LF HRV ($_{ln}ms^2$) Δ	-.27	.37	-.18	.08	.01	-.48*	-.24	-.00	-.30	.23	.03	.28
T1 LF HRV (nu) Δ	-.55*	.42	-.24	-.38	-.40	-.40	-.50*	-.35	.34	.37	.39	.44
T2 LF HRV (nu) Δ	.01	-.03	.01	-.20	-.13	-.18	-.14	.16	.60**	.09	.40	.27
T5 LF HRV (nu) Δ	.22	.45	.03	.22	.32	.06	.07	-.08	-.46	-.03	.03	-.07
T1 RMSSD Δ	-.10	.21	-.11	.02	.02	-.32	-.15	.12	-.22	.18	-.09	.21
T2 RMSSD Δ	.19	.02	.04	.12	.19	-.01	.13	-.05	-.41	.11	-.22	-.15
T3-4Δ RMSSD Δ	.22	-.01	.10	.09	-.02	.39	.16	.01	.03	-.24	.05	.03
T5 RMSSD Δ	-.18	.06	-.14	-.02	-.05	-.45	-.18	-.05	.12	.26	.01	.22
[1]SBP Δ	.14	.09	.38	-.02	.00	-.41	-.06	-.53	-.22	-.36	.07	.18
[1]DBP Δ	.06	.16	.39	-.06	-.01	-.51	-.15	-.24	-.06	-.11	.13	.27
[2]HR Δ	-.03	-.17	.16	.15	.09	.17	.12	.51	.58*	-.23	-.07	.06

Note. *p<.05 **p<.01. T1 = seated (free breathing), T2 = seated (metronome), T3-4Δ = change from supine to stand, T5 = directed relaxation. DBP = diastolic blood pressure, HF = high frequency, HR = heart rate, HRV = heart rate variability, LF = low frequency, $_{ln}ms^2$ = natural log transformed milliseconds squared, nu = normalized units, RMSSD = root mean square of successive differences, SBP = systolic blood pressure. Individuals taking [1]antihypertensives, [2]beta-blockers, [3]antidepressants, or [4]sedatives at any point were excluded from analyses as indicated by superscript

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