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Received: 10 December 2019 | Revised: 4 February 2020 | Accepted: 16 April 2020

DOI: 10.1111/ecc.13249

ORIGINAL ARTICLE

European Journal of Cancer Care WILEY

Stress-reducing effects of a brief mindfulness intervention in palliative care: Results from a randomised, crossover study

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Funding information
This study received funding by the Medical Faculty at Heidelberg University. The academic positions of MW and FK are currently funded by the "H.W. & J. Hector Stiftung" and by "Sonnen-Blau. Gemeinnützige Morgott-Schupp-Stiftung für frühkindliche Erziehung und Palliativversorgung."

Abstract

Objective: Mindfulness-based interventions are a widely used and highly accepted adjunct treatment in oncology. Due to a paucity of research in advanced cancer and other terminal illnesses, we aimed to evaluate the stress-reducing effects of a brief, standardised mindfulness intervention for use in palliative care.

Methods: This study was a randomised, crossover trial where patients participated in both a single mindfulness intervention and a resting state control condition. The order of the conditions was randomised. Study outcomes encompassed self-report data on stress and well-being and measures of heart rate variability. All outcome data were measured at four times per day.

Results: Forty-two patients participated in this study. We found significantly stronger reductions in self-rated stress and mean heart rate as well as an increase in heart rate variability after the mindfulness intervention. Psychophysiological effects were strongest in the immediate pre- to post-intervention comparison, while the effect on subjective stress persisted after 20 to 40 min. No significant differences were found for self-rated well-being.

Conclusions: Despite the rather small magnitude of effects, the brief mindfulness intervention showed to be effective and accepted by patients in very advanced stages of a disease and could be offered by trained healthcare professionals in palliative care.

KEYWORDS

cancer, heart rate variability, mindfulness, oncology, Palliative care, stress

1 | INTRODUCTION

The World Health Organization defines palliative care as an approach that "improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the [...] treatment of pain and other problems, physical, psychosocial and spiritual" (World Health Organization, 2015). This definition hints at both the holistic tradition that palliative care derived from (Mount, 1976) and the nowadays multiprofessional team composition in palliative care wards or hospices.

Trial Registration: German Clinical Trials Registry (DRKS00013135).

Physicians, specialised nurses, clinical psychologist, social workers, physiotherapists, creative-arts therapists and others jointly aim at providing accurate diagnoses and effective integrated treatment (Hearn & Higginson, 1998).

Palliative care literature shows a vast increase in the emergence of non-pharmacological interventions to specifically address psychosocial and spiritual needs of terminally ill patients (Warth, Kessler, et al., 2019). Facing the specific requirements of palliative care, these approaches have several factors in common, such as short duration, high flexibility and a biographical focus (von Blanckenburg & Leppin, 2018). Among others, psychosocial palliative care interventions encompass dignity therapy (Chochinov et al., 2011), life review techniques (Kwan, Chan, & Choi, 2019;Wang, Chow, & Chan, 2017), meaning-based interventions (Breitbart et al., 2010) and music therapy techniques (Warth, Koehler, et al., 2019).

Additionally, mindfulness has been proposed as a promising mechanism in the psychological coping with advanced or terminal illnesses. Mindfulness is a complex construct that involves deliberately binding of attention to the present moment of experience, accompanied by a non-judgmental, accepting attitude (Kabat-Zinn, 1994). Attention can either be focused on a specific object, for example the breath, (i.e. *focused attention*), or it remains at the current moment-to-moment experience (i.e. *open awareness* or *open monitoring*). The latter comprises the attitude to openly perceive external or internal stimuli without following the impulse to react or to judge (Lutz, Slagter, Dunne, & Davidson, 2008).

Mindfulness originally derives from Buddhist tradition. However, due to its seamless integration into the fields of health psychology and medicine and its solid efficacy (Gu, Strauss, Bond, & Cavanagh, 2015;Khoury et al., 2013), mindfulness is now widely accepted in various areas of modern health care as a secular training program. Prominent and well-studied variants are mindfulness-based stress reduction (MBSR) (Grossman, Niemann, Schmidt, & Walach, 2004) and the group-based therapy for relapse prevention in depression, mindfulness-based cognitive therapy (MBCT) (Segal & Walsh, 2016).

The eight-week MBSR program showed convincing effects in patients with chronic pain (P. Grossman, Tiefenthaler-Gilmer, Raysz, & Kesper, 2007;Khoo et al., 2019), and MBCT showed to improve symptoms of anxiety and depression in psychiatric patients (Chiesa & Serretti, 2011;Klainin-Yobas, Cho, & Creedy, 2012). Recently, a growing body of research has emerged on the potential benefits of mindfulness interventions in cancer patients, indicating that mindfulness can facilitate psychological adjustment (Ledesma & Kumano, 2009;Tate, Newbury-Birch, & McGeechan, 2018). Mindfulness-based interventions led to improvements regarding subjective stress, anxiety, depression and sexual dysfunctions (Shennan, Payne, & Fenlon, 2011). Evidence is particularly broad in breast cancer patients, with MBSR showing beneficial effects on quality of life, anxiety, depression, sleep quality, stress, fatigue, physiological and cognitive functioning (Schell, Monsef, Wockel, & Skoetz, 2019;Zhang, Zhao, & Zheng, 2019). Improvements in anxiety and depression were persistent after 6–12 months (Haller et al., 2017) and were also reported in breast cancer survivors (Huang, He, Wang, & Zhou, 2016). In addition, biomarker studies found first evidence for a possible association between mindfulness practices and improved immune functioning in breast cancer patients (Sanada et al., 2017).

Despite the promising potential of this rapidly growing field, some critical concerns are now present in the literature. Among other aspects, these refer to the small magnitude and short endurance of effects on quality of life (Schell et al., 2019) and other clinically relevant outcomes (Shaw, Sekelja, Frasca, Dhillon, & Price, 2018), to inconsistent results with regard to cancer pain reduction (Ngamkham, Holden, & Smith, 2019;Zhang, Xu, Wang, & Wang, 2016), and to the problem of adherence to treatment manuals (Cillessen, Johannsen, Speckens, & Zachariae, 2019;Shaw et al., 2018).

Moreover, only few studies have yet evaluated the effectiveness of mindfulness interventions for patients with advanced or terminal cancer or other severe illnesses requiring specialised palliative care. Due to limited time and both fragile and rapidly changing physical states in palliative care, interventions need to be brief and flexible (von Blanckenburg & Leppin, 2018;Zimmermann, Burrell, & Jordan, 2018). A recent review identified eight studies using various methodologies to investigate the effects of mindfulness interventions in advanced cancer populations, hinting at generally high acceptance and potential effects with regard to quality of life, anxiety and depression (Zimmermann et al., 2018). One large RCT found a significant reduction of distress in men diagnosed with advanced prostate cancer who participated in MBCT (Chambers et al., 2017). In women with advanced breast cancer, participation in MBSR promoted psychological adaption in a preliminary study (Eyles et al., 2015). A mindful body scan meditation including additional practices at home facilitated outcomes of mental and physical health in end-stage cancer patients (Tsang, Mok, Lam, & Lee, 2012). In a couple-based intervention, MBSR significantly reduced caregiver burden, but did not improve advanced lung cancer patients' distress (van den Hurk, Schellekens, Molema, Speckens, & van der Drift, 2015).

For patients receiving palliative care, a recent review found only limited evidence regarding the reduction of stress (Latorraca, Martimbianco, Pachito, Pacheco, & Riera, 2017). One group of researchers conducted the only two published RCTs on brief mindful breathing interventions (5 and 20 min, respectively) for inpatient palliative care patients and found significant reductions in perceived distress, the bispectral index score, and improvements in several psychophysiological parameters including heart and breathing rate (Beng et al., 2019;Ng, Lai, Tan, Sulaiman, & Zainal, 2016).

Based on these limited—albeit promising—research results, we developed a brief, standardised mindfulness intervention that could be applied to palliative care patients by various healthcare professionals including physicians, psychologists, nurses and therapists, and aimed to evaluate its potential to psychologically and physically reduce stress.

2 | METHODS

2.1 | Study design and ethics

We designed a randomised, crossover trial, in which all included patients participated in both the mindfulness intervention (MI) and a resting state control condition (CC) on two consecutive days. The order of the experimental condition was randomised with a computer-based block randomisation method by the primary researcher. We used the SNOSE method for allocation concealment (Scales & Adhikari, 2005). No blinding procedures were feasible in this study.

The present clinical trial originally included an exploratory assessment and analysis of salivary cortisol and α-amylase as novel, potential biomarker of stress in palliative care. Facing high drop-out rates and unclear interpretability in terminally ill patients, we intended to present our learnings on the feasibility and validity of these markers in a "proof-of-concept"-approach, separate from the present effectiveness evaluation. The idea to additionally evaluate the feasibility of novel stress markers also influenced the decision to choose a randomised, crossover trial rather than a classical parallel RCT, as crossover trials offer the advantage to use the individual as its own control (Quintana & Heathers, 2014;Wellek & Blettner, 2012).

The study was entered into the German Clinical Trials Registry (DRKS00013135) and received ethical approval by the Ethics Committee of the Medical Faculty at Heidelberg University (S-435/2017). All procedures in this study were carried out in accordance with the Declaration of Helsinki.

2.2 | Patients and procedures

All participants were recruited from the University Palliative Care Unit at St. Vincentius Hospital, Heidelberg, Germany. Based on an initial patient contact and the medical record, possible participants were screened for eligibility. Patients were included if they (a) received inpatient palliative treatment according to the German procedure classification (Operationen- und Prozedurenschlüssel—OPS 8–982 or OPS 8-98e), (b) were not in a final phase of the disease (assessed by the treating physician), (c) had no cognitive or hearing impairment, (d) had no primary psychiatric diagnosis (based on the medical record) and (e) had sufficient understanding of German language.

Patients were informed about the study goals, benefits, and potential risks and were asked to sign the informed consent sheet if they were interested to participate. Afterwards, we opened a sealed envelope containing the randomised order of experimental conditions. Appointments were made for two sessions, preferably on the afternoons of the two following days. In the first session, the facilitator (a research assistant with a bachelor degree in psychology) started the baseline assessment of the McGill Quality of Life Questionnaire—Revised (MQOL-R) (Cohen et al., 2017), followed by placement of a photoplethysmography (PPG) sensor on the index finger of the patient's non-dominant hand (blood volume pulse sensor, biosignalsplux, Lisbon, Portugal). We then assessed self-rated stress and well-being at four measuring times (T0 – T3) every 20 min. Psychobiological data were continuously recorded throughout the first 20 min, where the MI or CC took place. During that time, the facilitator remained present in the patient's room. Additional HRV recordings of 5-min duration were taken at T2 and T3 (see Figure 1 for an overview of the assessment plan).

2.3 | Intervention

The MI was a brief, standardised and pre-recorded excerpt from the mindfulness-based stress reduction program carried out at bedside (Kabat-Zinn & Kesper-Grossman, 1999). It consisted of a short breathing exercise and guided body scan meditation for supine positions and lasted 20 min. The purpose of the MI was to defocus the patient's attention from symptom burden by focusing on the breath, the bodily sensations and the present moment. The primary goal of this MI was an increase of the attentional inhibition ability to align oneself internally and hence, to improve self-regulatory processes. From a previous study, we learned that this kind of MI was feasible due to its brief duration and simple instructions, and that it can potentially reduce stress in patients with terminal diseases (Warth, Kessler, Hillecke, & Bardenheuer, 2015). After completion of the MI, patients were asked to remain in a

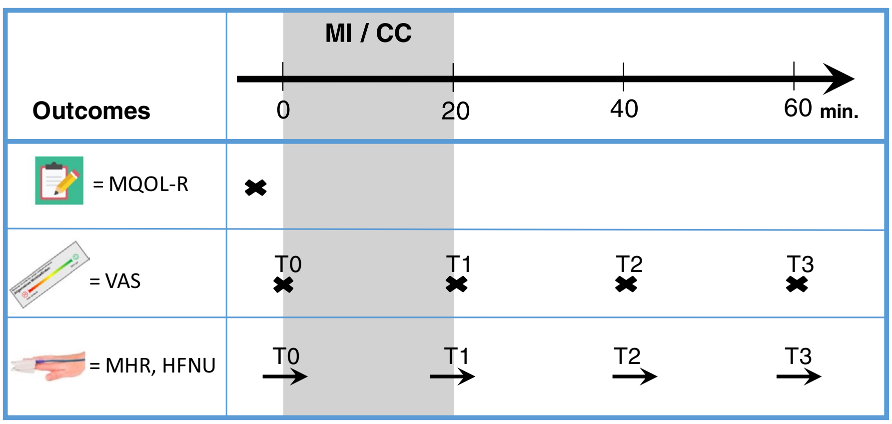

FIGURE 1 Assessments. Notes: MI, mindfulness intervention; CC, control condition; MQOL-R, McGill Quality of Life Questionnaire—Revised (assessed only once at baseline); VAS, visual analogue scale; MHR, mean heart rate; HFNU, high-frequency spectrum in normalised units

comfortable resting state position in their beds for another 40 min. All assessments and procedures were identical for the CC, except that patients remained in their resting position for the entire 60 min and did not listen to the MI.

2.4 | OUTCOMES

2.4.1 | Self-ratings

As in previous clinical trials in palliative care, we used visual analogue scales (VAS) for a brief and economic assessment of acute psychological states (Caraceni et al., 2002;Stiel et al., 2011;Warth et al., 2015). The scales contained a colour code from red to green and smileys at the poles. Both subjective stress level and well-being were coded from 0 to 10 with ten indicating the highest score on the construct (high stress or high well-being). As Figure 1 shows, VAS was assessed four times every 20 min (before the MI, after the MI, + 20 min, + 40 min).

2.4.2 | Photoplethysmography

The PPG sensor continuously recorded relative changes in peripheral blood flow. Pulse wave peaks were treated as estimates for the beat-to-beat variation in heart rate, that is heart rate variability (HRV) (Schafer & Vagedes, 2013). We extracted HRV parameters for four 5-min segments, according to the VAS assessments (T0-T3, see Figure 1) and chose to look both at the mean heart rate (MHR) and at the high-frequency power band in normalised units (HFNU). MHR was regarded as a general marker of the autonomic nervous system with a reduction in heart rate indicating a shift towards more parasympathetic-dominated regulation (Singh, Moneghetti, Christle, Hadley, Froelicher, et al., 2018). HFNU is a frequency-domain HRV index being described as a measure of relative vagal cardiac outflow that was shown to increase in response to mindfulness or meditation-based interventions in previous studies (Krygier et al., 2013;Tang et al., 2009;Wu & Lo, 2008). Data cleaning and HRV analysis were performed with Kubios HRV Premium Version 3.3.0 (Tarvainen, Niskanen, Lipponen, Ranta-Aho, & Karjalainen, 2014).

2.5 | Sample size, missing data and statistical analyses

We used data from a previous study on mindfulness in palliative care (Warth et al., 2015;Warth, Kessler, Hillecke, & Bardenheuer, 2016) to gather an effect size estimate which was then entered into G*Power (Faul, Erdfelder, & Buchner, 2007). The software suggested *N* = 32 as an optimal sample size for 4 (measurements) * 2 (conditions) within-subjects comparisons (f = 0.25, α = 0.05, (1-β) = 0.85). We intended to include approximately 4042 patients in this study as we expected drop-out rates to be up to 30%.

Overall, we tested the hypothesis that the MI would have a short-term stress-reducing effect and expected this relaxation response (Dusek & Benson, 2009) to be observable in a significantly stronger (a) increase in self-rated well-being, (b) decrease in self-rated stress, (c) decrease in MHR and (d) increase in HFNU, all compared to the CC. In the course of an intention-to-treat approach and after exclusion of outliers, we replaced missing values with both the last observation carried forward (LOCF) method and with multiple imputations. The latter were created with the R package Amelia II (Zhang, 2016), and then pooled into one single dataset (MULT). The LOCF method appeared plausible from a theoretical point of view due to the close time distances between measurements in our study, while multiple imputation generally produces less statistically biased estimates. Both datasets were compared within sensitivity analyses.

Descriptive statistics and baseline comparisons with paired-samples *t* tests were conducted with IBM SPSS Version 24. Effect sizes for selected within-subjects differences (Morris & DeShon, 2002) and their confidence intervals (Viechtbauer, 2007) were calculated as standardised mean changes (SMC, i.e. mean change divided by standard deviation of change scores). SMCs can be interpreted according to Cohen's *d*, as small (SMC = 0.2 – 0.5), medium (SMC = 0.5–0.8) or large effects (SMC > 0.8) (J. Cohen, 1992).

The T-statistic described in Wellek and Blettner (2012) was used for preliminary testing of possible carryover-effects (T0-T1) due to the crossover design of this study. If carryover effects could be ruled out, the subsequent statistical effect modelling was performed with the student version of HLM7 (Raudenbush, Bryk, & Congdon, 2011). Multilevel analysis was chosen as multiple observations were nested within individuals. For all outcomes, we tested the significance of the cross-level interaction between time (linear, quadratic and cubic) and condition (MI vs. CC), with the linear interaction being crucial for the hypothesis tests. Details on the model specification process can be found in a previous publication with comparable statistical procedures (Warth, Kessler, et al., 2016). Age and gender (Lutfi & Sukkar, 2011;Voss, Schroeder, Heitmann, Peters, & Perz, 2015) as well as the order of the experimental conditions were statistically controlled for if they contributed to the explanation of variation in the intercepts or slopes. As we did not a priori define one primary outcome and expected all four measures to be related to stress and thus to intercorrelate, we chose an uncorrected type-I error probability of α = 0.05 for all hypothesis tests.

3 | RESULTS

Between April and November 2018, *N* = 42 patients were included in this study. Figure 2 shows a patient flow chart with reasons for decline or drop-out. *N* = 36 patients completed both sessions as intended. The drop-out-rate, however, was higher in the psychophysiological recordings due to measurement artefacts (19% missing data in total).

The mean age of the sample was *M* = 65.88 years (*SD* = 13.02), and 69% (*N* = 29) were female. Almost all patients were diagnosed with

FIGURE 2 Patient flow chart

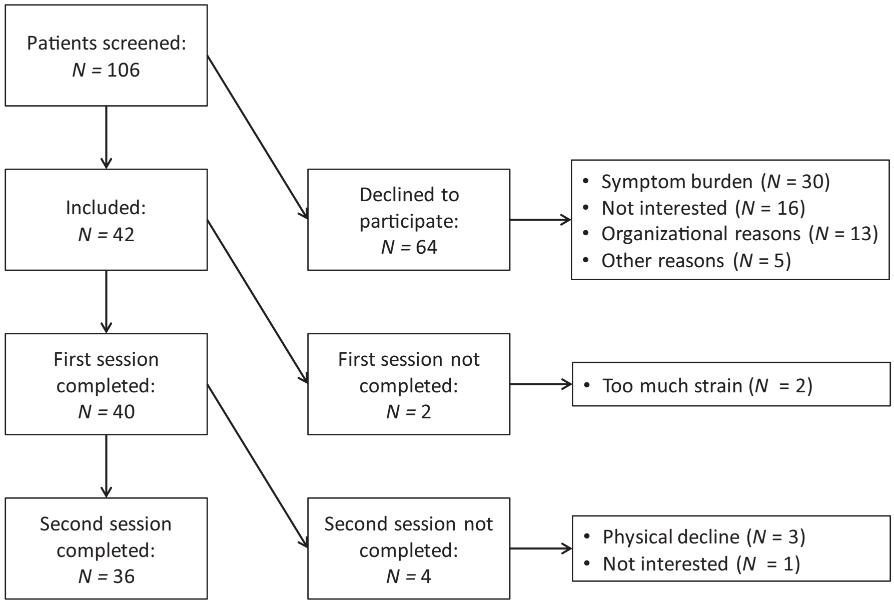

TABLE 1 Unadjusted means (standard deviations), baseline comparisons and final model estimations ($N = 42$)

		T0[a]	T1	T2	T3	Final model estimation (TIME x GROUP)
VAS_WELL	MI	5.82 (2.01)	6.40 (1.96)	6.52 (2.19)	6.39 (2.08)	Linear: β = 0.49, *SE* = 0.35, *p* = 0.18 Quadratic: β = −0.15, *SE* = 0.11, *p* = 0.20
	CC	6.21 (1.90) *p* = 0.19	6.30 (2.05)	6.59 (1.75)	6.56 (1.83)	
VAS_STRESS	MI	4.17 (2.04)	3.54 (2.18)	3.20 (2.11)	3.51 (2.18)	Linear: β = −1.00, *SE* = 0.43, *p* = 0.03* Quadratic: β = 0.29, *SE* = 0.12, *p* = 0.02*
	CC	3.71 (2.31) *p* = 0.21	3.78 (2.06)	3.59 (2.02)	3.45 (2.15)	
MHR	MI	85.97 (13.82)	82.77 (14.03)	84.44 (13.95)	84.25 (14.22)	Linear: β = −6.68, *SE* = 2.15, *p* < 0.01* Quadratic: β = 4.74, *SE* = 1.83, *p* = 0.01* Cubic: β = −0.92, *SE* = 0.40, *p* = 0.03*
	CC	86.70 (15.53) *p* = 0.74	86.37 (15.24)	86.93 (14.90)	87.19 (15.35)	
HFNU	MI	40.21 (20.31)	47.47 (23.98)	43.26 (21.06)	40.81 (24.16)	Linear: β = 20.01, *SE* = 9.70, *p* = 0.05* Quadratic: β = −16.94, *SE* = 8.36, *p* = 0.05 Cubic: β = 3.56, *SE* = 1.83, *p* = 0.06
	CC	37.92 (16.51) *p* = 0.48	38.55 (17.32)	40.23 (16.87)	34.8 (16.54)	

Abbreviations: CC, control condition; HFNU, high-frequency spectrum in normalised units; MHR, mean heart rate; MI, mindfulness intervention; VAS_STRESS, visual analogue scale stress; VAS_WELL, visual analogue scale well-being.

[a]including *p*-values for baseline comparisons with paired-samples *t* tests,

*statistically significant

advanced cancer (95%, $N = 40$), with gynaecological ($N = 11$), pancreatic ($N = 6$), gastrointestinal ($N = 5$), thoracic ($N = 3$) and prostate cancer ($N = 2$) being the most frequent categories. $N = 13$ suffered from other tumour entities, and $N = 2$ patients had non-oncological primary diagnoses. Baseline analysis of the MQOL-R subscales revealed that the patients' quality of life was rather low in the physical domain ($M = 4.11$, $SD = 1.85$), while the psychological ($M = 5.93$, $SD = 2.68$), spiritual ($M = 6.55$, $SD = 1.98$) and social domain ($M = 8.53$ $SD = 2.25$) received relatively high ratings. The baseline values of all study outcomes did not differ significantly between the two study conditions (all $p > 0.05$, see Table 1). Statistical tests did not show any evidence for the presence of potential carryover effects in any of the four study outcomes regarding the T0-T1 comparisons (all $p > 0.05$). Age as a control variable significantly explained differences in the baseline intercepts for well-being, MHR and HFNU. On average, older patients showed higher well-being ($\beta = 0.05$, $p = 0.02$) and HFNU ($\beta = 0.33$, $p = 0.47$), and a lower MHR ($\beta = -0.50$), $p < 0.01$). The subsequent models were adjusted, accordingly. Gender did not significantly explain any differences between intercepts or slopes on any outcome.

Figure 3 shows the predicted values of the final model estimates for the self-reported and psychobiological study outcomes over time. Regarding subjective well-being (Figure 3a) and stress (Figure 3b), both self-report VAS showed the expected U- (or inversely U-) shaped trajectories over time in the mindfulness condition, indicating that the intervention initially had a beneficial effect which attenuated towards the end of the recording (T3). The linear (p = 0.03) and quadratic effects (p = 0.02) for stress differed significantly from the CC, while the improvements in well-being were not statistically superior (linear: p = 0.18; quadratic: p = 0.20). The strongest within-subjects improvements on the 0 to 10 VAS were observed between T0 and T2 (i.e. 20 min. after the MI) with a reduction in stress from 4.17 to 3.20 (SMC = −0.46, CI = −0.78 to −0.14) and an increase in well-being from 5.82 to 6.52 (SMC = 0.42, CI = 0.10 to 0.74).

Regarding psychobiological change over time, the trajectories of MHR and HFNU were best described by cubic trends. As Figure 3c shows, MHR was significantly reduced after the MI and remained on a lower level compared with the relatively steady CC trajectory (linear: p < 0.01; quadratic: p = 0.01, cubic: p = 0.03). The strongest decline was observed in the pre-MI (T0) to post-MI (T1) comparison, where MHR dropped from 85.97 to 82.77 beats per minute on average (SMC = −0.66, CI = −1.02 to −0.34).

The relative percentage of high-frequent oscillation in heart rate (HFNU) rose in response to the MI from 40.21% (T0) to 47.47% (T1, SMC = 0.35, CI = 0.03 to 0.66). The linear increase over time was statistically significant (p = 0.05), and the convergence of trajectories represented in the higher-order polynomials showed statistical trends (quadratic: p = 0.05, cubic: p = 0.06).

Sensitivity analysis with the multiply imputed dataset (MULT) revealed that the hypothesis decisions for well-being, stress and HFNU were robust with regard to the handling of missing values. Only the result for MHR differed between the two data handling strategies, as the linear TIME*CONDITION interaction slightly failed to reach significance in the MULT data (β = −7.56, SE = 4.02, p = 0.07).

4 | DISCUSSION

The present study reports the effects of a MI in palliative care using a combination of self-report data and psychobiological measures of autonomic functioning. Overall, findings indicate that the brief and standardised MI had a stress-reducing effect, visible in both the subjective experience and cardiovascular regulation.

4.1 | Summary and interpretation of findings

Beneficial effects on heart rate and HRV were most pronounced in the immediate response from T0 (pre-MI) to T1 (post-MI), with small to medium-sized effects. The reduction in self-rated stress was even stronger at T2, that is 20 min after completion of the MI. Both results are consistent with previous findings showing immediate effects of a 5-min mindful breathing exercise on both distress and heart rate (Ng et al., 2016). While the positive effect on distress was persistent 10 min after the breathing intervention, the reduction in heart rate no longer differed to the control condition at that time. Taken together, these results suggest that MIs can exert a short-term, both

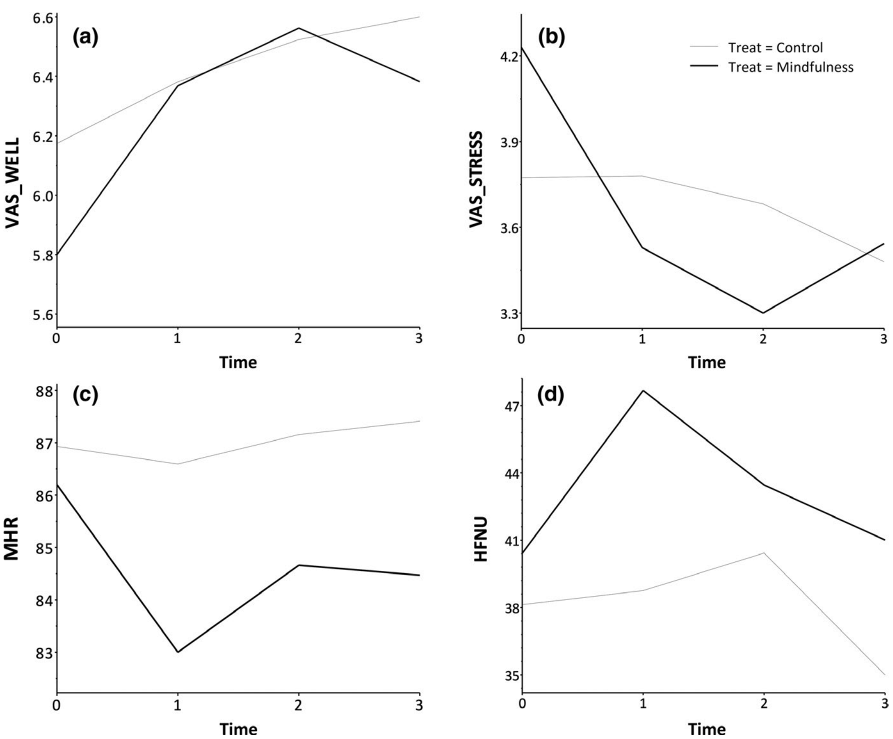

FIGURE 3 Predicted values by treatment conditions. **Notes:** (a) VAS_WELL = visual analogue scale for well-being (Range: 0–10), (b) VAS_STRESS = visual analogue scale for stress (Range: 0–10), (c) MHR = mean heart rate, (d) HFNU = high frequency spectrum in normalised units; time points: T0 = before the intervention, T1 = after the intervention, T2 = plus 20 min after the intervention, T3 = plus 40 min after the intervention

physiologically and psychologically stress-reducing effect, which may persist up to 20–30 min in the subjective domain only.

The reported increase in high-frequent HRV (HFNU) at T1 could be interpreted as a shift towards increased vagal tone or more parasympathetic activity in response to the MI. While straightforward and in line with previous research (Tang et al., 2009;Wu & Lo, 2008), recent methodological reviews, however, recommend interpreting normalised and ratio values jointly with the absolute power in the frequency band (Heathers, 2014). An exploratory inspection of our data revealed that the absolute high-frequency power initially decreased from pre-MI to post-MI (and later increased again), indicating that the increase in HFNU was mainly driven by a very pronounced decrease in the low-frequency band. While this does not generally contradict the interpretation of a shift towards relatively more parasympathetic control over the heart, Krygier et al. proposed an interesting alternative explanation for this pattern of HRV change (Krygier et al., 2013): that is the loss of power in the low-frequency band could be associated with mental effort according to focused, pleasurable attention or flow experience, which is one of the proposed mechanisms of mindfulness (Lutz et al., 2008).

We could not find any between-groups effect for self-rated well-being in our study, which may be attributable to the rather small magnitude of effects in this study. While changes in well-being were in the expected direction, the maximum mean improvement of 0.7 points on a VAS may have been too small regarding the limited statistical power. Additionally, a single mindfulness intervention might not be sufficient for a notable effect on such a broad outcome as well-being. While patients' assessment of distress might specifically refer to their acute state of being, their assessment of well-being might include more general cognitive evaluations. Moreover, mindfulness is generally seen as a skill to be learned in long-term practice (Kabat-Zinn, 2003), and measurable effects on well-being may only occur after a higher number of training sessions. However, even small changes in well-being could still cause clinically relevant and meaningful change in patients facing a terminal disease, and the very brief MI in this study can be applied cost-efficiently and with low risks by various healthcare professionals.

Only one patient cancelled the mindfulness session due to high symptom burden, which is consistent with the low occurrence of adverse effects in other studies (Wong, Chan, Zhang, Lee, & Tsoi, 2018). Other instances where MIs may not be feasible or indicated in palliative care are rapidly declining or very unsteady physical states, final stages of a disease or cognitive impairments. The facilitator's introduction should address acute pain sensations particularly in body scan meditations and give some ideas on how to deal with the possible risk of focusing attention on painful body parts (e.g. to remain open and non-judgmental with regard to any changes that may occur). The facilitator should remain physically and mentally present to anticipate, contain or, if necessary, react flexibly to any sign of increased symptom burden that may occur during the session. As the present study applied a pre-recorded mindfulness intervention, future research might therefore examine live mindfulness exercises by trained practitioners in palliative care which might even increase the beneficial effects of mindfulness found in this study.

4.2 | Limitations

This study faced a number of limitations. First, the interpretation of results from crossover trials is only valid, if no carryover effects are present in the data (Wellek & Blettner, 2012), which was the case in our study. While advantageous from a statistical point of view, the absence of carryover effects also confirms the limited endurance of effects. If not adequately addressed, carryover effects can lead to biased results in crossover-trials. However, we initially chose to use a crossover design rather than a parallel RCT in this study, as within-subject comparisons were reported to provide better experimental control in psychobiological data (Quintana & Heathers, 2014). Moreover, crossover designs require a lower total number of subjects as they offer more statistical power than parallel RCTs, which is an enormous advantage in palliative care research (Wellek & Blettner, 2012). Second, the use of a PPG sensor for the physiological recordings led to a higher number of movement artefacts and lower precision than the use of electrocardiogram (Singh, Moneghetti, Christle, Hadley, Plews, et al., 2018). However, PPG recordings showed to produce valid estimates particularly in resting state positions (Heathers, Fink, Kuhnert, & de Rosnay, 2014;Schafer & Vagedes, 2013) and are preferable with regard to measurement distress in vulnerable patient populations such as in palliative care (Warth, Kessler, Hillecke, & Bardenheuer, 2016). Third, missing data are a frequent methodological challenge in palliative care research (Preston et al., 2013). In the present study, we used two data imputation methods to investigate the robustness of results. While statistical decisions were equal for three of four reported outcomes, the deviating findings on MHR emphasise that conclusions need to be drawn cautiously.

5 | CONCLUSIONS

The present study found evidence for a stress-reducing effect of a brief and standardised MI for use in palliative care, both on a psychological and physiological level. Although the magnitude of effects was rather small, offering mindfulness-based interventions might be a useful and effective adjunct treatment not only for early-stage cancer patients, but also for advanced and terminal illnesses. Future studies may overcome the reported limitations of a single mindfulness intervention by testing whether higher doses (e.g. three or four sessions on consecutive days) might be able to improve patient well-being. Considering the high acceptance, low risk and ease of use, the present intervention can be applied by various healthcare professionals, including palliative care nurses, clinical psychologists or psychotherapists, and other therapists that are experienced in providing psychosocial palliative care and that received training in the principles of mindfulness.

ACKNOWLEDGEMENTS

We would like to thank Jana Hillie, B.Sc., and Natalie Hess, B.Sc., who supported this study in the acquisition and management of data and in the review of literature.

CONFLICT OF INTEREST

None.

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How to cite this article: Warth M, Koehler F, Aguilar-Raab C, Bardenheuer HJ, Ditzen B, Kessler J. Stress-reducing effects of a brief mindfulness intervention in palliative care: Results from a randomised, crossover study. *Eur J Cancer Care*. 2020;29:e13249. https://doi.org/10.1111/ecc.13249