



Effects of Self-compassion on Diurnal Cortisol Pattern via Positive Affect in Colorectal Cancer Survivors

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Abstract

Objectives Colorectal cancer survivors are at risks of emotional distress and dysregulated diurnal cortisol rhythms. Dispositional self-compassion has been linked with better psychological adjustment and greater positive affect. This study evaluated the associations between self-compassion and the diurnal cortisol pattern, and the role of positive affect and emotional distress in mediating this association, in cancer patients.

Methods This longitudinal study recruited 127 Chinese colorectal cancer survivors, who completed assessments for self-compassion, positive affect, emotional distress, and naturalistic salivary cortisol at baseline. The participants completed follow-up assessments for affect and emotional distress after 2 months (time 2) and the diurnal cortisol pattern after 8 months (time 3). Bootstrapped mediation analysis analyzed the direct and indirect effects of self-compassion on the diurnal cortisol pattern via positive affect and emotional distress.

Results A structural equation model with latent factors of self-compassion, self-criticism, and emotional distress provided an adequate fit to the data. The direct effects of self-compassion and self-criticism on the diurnal cortisol pattern were not significant ($p = 0.11–0.50$). Positive affect, but not emotional distress, at time 2 significantly predicted steeper diurnal cortisol slopes at time 3 ($\beta = -0.22$, $SE = 0.08$, $p < 0.01$). Self-compassion and self-criticism showed significant negative and positive indirect effects on time 3 diurnal cortisol slopes via time 2 positive affect, respectively.

Conclusions Our findings support indirect linkages between self-compassion and steeper diurnal cortisol slopes via positive affect. Positive affect may mediate temporal relationships between self-compassion and neuroendocrine functioning in colorectal cancer survivors.

Keywords Emotional distress · Flattened cortisol slopes · Indirect effects · Mediation · Psycho-oncology · Self-criticism

Increased early screening and medical advances have improved the 5-year survival rate for colorectal cancer, which is the second most prevalent cancer in Hong Kong (Zhang et al., 2018). Surgical treatment followed by adjuvant chemotherapy and radiotherapy leave colorectal cancer patients prone to various symptoms such as fatigue (Ho et al., 2014), sleep disturbance (Ho & Fong, 2014), and

emotional distress (Fong & Ho, 2020). Patients are exposed to stressors that disrupt neuroendocrine functioning during the treatment and survivorship stages (Pyter, 2016). The hypothalamic–pituitary–adrenal (HPA) axis is a major neuroendocrine system that controls stress responses via corticosteroids. The HPA axis plays a role in regulating the immune system via downregulation of interleukin-2 production and inhibition of phagocytosis by macrophages. Salivary cortisol is an established stress biomarker that follows a typical diurnal rhythm, showing an initial increase upon awakening that declines gradually during the day (Hellhammer et al., 2009). Dysregulation of the HPA axis, often seen in the form of flattened diurnal cortisol slopes, has been associated with undesirable physical and mental health outcomes (Adam et al., 2017).

Cancer patients are prone to blunted cortisol reactivity (Black et al., 2017) and disruptions of circadian rhythms

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(Sephton & Spiegel, 2003) which could have adverse implications for cancer prognosis. Flattened diurnal cortisol rhythms have been associated with greater negative affect (Castonguay et al., 2017), anxiety (Armer et al., 2018), perceived stress (Ho et al., 2018), and depression (Sharpley et al., 2017) among cancer patients. Previous longitudinal studies (Cuneo et al., 2017; Garland et al., 2015) indicate a potential role for the diurnal cortisol pattern in psychological adjustment during the survivorship process. Abnormal diurnal circadian cortisol rhythms have been linked with tumor progression (Cash et al., 2015) and decreased survival (Cohen et al., 2012; Schrepf et al., 2015; Sephton et al., 2000) in cancer patients. It is clinically important to investigate the behavioral and emotional factors that affect diurnal cortisol rhythms in cancer survivors.

Apart from the conventional psychopathological perspective, recent studies have investigated stress outcomes from a positive psychology perspective. Self-compassion is a holistic construct that refers to being kind and understanding toward oneself when dealing with pain and failure, as opposed to being overly self-critical (Neff, 2003b). It involves the perception of suffering as part of a whole experience rather than as an isolated incident, and approaching painful feelings with mindful awareness rather than over-identifying with them (Neff, 2003a). Dispositional self-compassion has been linked to better psychological adjustment, more effective stress-coping mechanisms (Arambasic et al., 2019), and lower emotional distress in cancer patients (Lennon et al., 2018; Zhu et al., 2019). A recent meta-analysis of 26 studies (Sirois, 2020) found self-compassion to be associated with greater positive affect and lower negative affect and both affect accounted for half of the effects of self-compassion on self-rated health. Positive affect has been linked to steeper diurnal cortisol slopes in healthy adults (Hoyt et al., 2015; Human et al., 2015) and cancer patients (Wang & Hoyt, 2018).

Positive psychological changes have been theorized to predict enhanced allostasis (Bower et al., 2008), which may buffer the adverse effects of stress and improve physical health. Self-compassion has been associated with lower daily cortisol levels in older adults with various physical health problems (Herriot et al., 2018). From a theoretical perspective, self-compassion may facilitate adaptive psychological responses and ameliorate the biological disturbances that arise as a response to unavoidable stressors. A randomized controlled trial (Kirschner et al., 2019) found that self-compassion was correlated with improvements in positive affect, reduced arousal (lower heart rate), and increased parasympathetic activation (higher heart rate variability). The links between affect and diurnal cortisol pattern in cancer patients (Castonguay et al., 2017; Wang & Hoyt, 2018) suggest a potential mediating role for affect between self-compassion and diurnal cortisol pattern. A recent study

(Chan et al., 2021) has found moderating effects of self-compassion against anxiety symptoms but not physiological stress in cancer caregivers.

Given the importance of cortisol in regulation of metabolism and inflammation, it is of practical interests to examine the protective effects of self-compassion on diurnal cortisol pattern in cancer survivors. There were two study objectives for the present study. The first objective was to examine the temporal effects of self-compassion on psychological functioning (positive affect and emotional distress) and diurnal cortisol pattern in colorectal cancer survivors during the survivorship stage. Our second objective was to explore the indirect effects of self-compassion on the diurnal cortisol pattern via positive affect and emotional distress. Such an examination on the physiological effect of self-compassion would contribute to the field in understanding the potential mind–body connection, which could facilitate formulation of clinical interventions for better prognosis of the cancer survivors. This study has several hypotheses: (1) self-compassion has significant effects on positive affect and emotional distress; (2) self-compassion has significant direct effects on the diurnal cortisol pattern; (3) positive affect and emotional distress has significant effects on the diurnal cortisol pattern; and (4) positive affect and emotional distress mediate the relationship between self-compassion and the diurnal cortisol pattern.

Method

Participants

The present study comprised a sample of 127 eligible colorectal cancer patients. The majority of the participants were female (58.3%) and had received at least 10 years of education (64.6%). The mean age of the participants was 63.8 years ($SD = 8.9$, range = 40–85) and the average BMI was 22.5 ($SD = 3.4$). Most of the participants (38.7%) were diagnosed with stage III colorectal cancer, followed by stage I (31.5%) and stage II (29.7%). Almost all participants (96%) had completed surgical treatment. Around half of the sample (44%) had received chemotherapy and around one-tenth of the sample had received radiotherapy (9.5%), and complementary and alternative medicine (13.5%) such as acupuncture, massage, and tai chi that were not part of the standard treatment. The mean number of completed treatments was 1.73 ($SD = 0.95$) and the average time elapsed since the last cancer treatment was 1.62 years ($SD = 1.28$). Less than half of the sample (41.6%) reported current use of Western or Chinese medication. Twenty-one participants were lost to follow-up, giving a drop-out rate of 16.5% for the study over the 8-month study period. The study dropouts ($N = 21$) did not differ significantly from those who completed the study

($N=106$) in terms of demographic characteristics and baseline measures ($p > 0.10$).

Power analysis was conducted using Monte Carlo simulation techniques to determine the sample size requirements for mediation analysis (Wolf et al., 2013). A structural equation model was specified with three observed indicators, with each indicator measuring the predictor, mediator, and outcome variables as latent factors ($\lambda = 0.8$). Standardized path coefficients of 0.14 and 0.39 corresponded to small (2% of the variance) and moderate (13% of the variance) effect sizes (Miočević et al., 2018). The sample ($N=127$) showed adequate statistical power (88.3–91.8%) for detecting indirect effects with moderate magnitudes ($a=b=0.39$). For indirect effects with small to moderate magnitudes ($a=0.39$, $b=0.14$ or $a=0.14$, $b=0.39$), the statistical power dropped to 21.0–26.7%.

Procedure

Study participants were colorectal cancer survivors recruited by convenience sampling through doctor referrals at local hospitals and newsletter advertisements placed at patient resource centers in Hong Kong. Two trained research assistants conducted eligibility screening for 284 patients using the following inclusion criteria: (1) diagnosis of stage I–III colorectal cancer; (2) age 18 years or higher; (3) Cantonese-speaking; (4) expected survival period of ≥ 12 months; and (5) completion of main cancer treatment (surgery and adjuvant chemotherapy) within 5 years of time of recruitment. A total of 123 patients did not meet the inclusion criteria or were excluded based on the following criteria: (1) presence of severe cachexia, dizziness, or nausea, any of which would prevent moderate physical exertion; (2) diagnosis of medical and mental disorders such as cardiovascular disease, epilepsy, major depressive disorder, generalized anxiety disorder, or schizophrenia; and (3) relapses or metastases of colorectal cancer. Thirty-four patients refused to join the study because of time constraints. Ethical approval was obtained from the Human Research Ethics Committee of the University of Hong Kong (IRB Reference Number: UW 15–115).

This study adopted an 8-month, 3-wave longitudinal study design. At baseline (time 1), the participants provided written informed consent; completed a self-report questionnaire on self-compassion, affect, and emotional distress; and provided salivary cortisol samples. Follow-up assessments were performed on affect and emotional distress 2 months later (time 2) and salivary cortisol samples for the diurnal cortisol pattern 8 months later (time 3). Participants who underwent chemotherapy were prone to various side effects and symptoms throughout the treatment trajectory (Röhl et al., 2019). Moreover, long-term changes in immune functions (lymphocytes) have been found in cancer survivors 9 months after chemotherapy

completion (Verma et al., 2016). Given the likely linkages between immune and endocrine parameters, the present study specified a longer time lag of 6 months between time 2 and time 3 to avoid conflation with the long-term side effects of chemotherapy and investigate the longer-term prognosis of the cancer survivors.

Measures

Self-compassion The respondents completed the 26-item Self-Compassion Scale (Williams et al., 2014) at time 1. This instrument computes 6 subscale scores as the average of items scored on a 5-point Likert scale (1 = never, 5 = very often). Although the original developer (Neff, 2003a) advocated the use of a total score for self-compassion, recent psychometric findings (Brenner et al., 2017; López et al., 2015) support the use of two aggregate scores for self-compassion and self-criticism. In this study, the model with two second-order factors provided a significantly better fit ($\Delta\chi^2 = 95.8$, $\Delta df = 1$, $p < 0.01$) than the model with one second-order factor. This study posited self-compassion as a latent factor measured by the three subscales of self-kindness, common humanity, and mindfulness, and self-criticism as a latent factor measured by the three subscales of self-judgment, isolation, and over-identification. Compared to the widely used Cronbach's alpha (α), McDonald's omega (ω) is a more general indicator of scale reliability (Hayes & Coutts, 2020). Satisfactory and good reliability was found for the six subscales ($\omega = 0.71$ – 0.82) and two aggregate scores of self-compassion and self-criticism ($\omega = 0.91$ – 0.92) in the present study, respectively.

Positive Affect and Emotional Distress The participants completed the Chinese version of the 20-item Positive and Negative Affect Schedule (PANAS) and the 14-item Hospital Anxiety and Depression Scale (Fong & Ho, 2014) at times 1 and 2. The PANAS assesses positive affect and negative affect during the 2 weeks preceding the assessment as the sum of 10 items on a 5-point Likert scale (1 = never, 5 = very often). The Hospital Anxiety and Depression Scale measures anxiety and depression by summing the 7-item scores using a 4-point format (0 = almost never, 3 = very often). The total scores for positive affect and negative affect range from 10 to 50 and those for anxiety and depression range from 0 to 21, with higher scores indicating greater distress. In the present study, the continuous score from the PANAS subscale was the observed indicator of positive affect. Emotional distress was posited as a latent variable measured by the continuous scores of anxiety, depression, and negative affect subscales. Good levels of reliability were found for positive affect and negative affect ($\omega = 0.88$ – 0.89) and anxiety and depressive symptoms ($\omega = 0.80$ – 0.86) in the present study.

Diurnal Cortisol Pattern At time 1 and time 3, salivary cortisol samples were collected from the participants using Salivette tubes at 4 different time points during a normal weekday: upon waking, noon (1200 h), late afternoon (1700 h), and evening (2100 h). The current 1-day, 4-sample cortisol sampling method was adopted in a previous study (Ho et al., 2016). The diurnal cortisol pattern recorded at the 8-month follow-up was regarded as the distal outcome of self-compassion at time 1 and affect at time 2. Participants were instructed to collect the first sample immediately upon waking and to avoid consumption of food and coffee/caffeine drinks (de Haan et al., 2020), smoking, and strenuous exercise for an hour prior to saliva collection at the later time points. Instruction sheets were provided to help the participants collect saliva at the specified times. They were asked to record the collection time of each sample in a daily log. Reminder messages were sent via WhatsApp to improve adherence to the collection protocol. The collected Salivette tubes were maintained in a freezer in the stress laboratory of the university. To determine the cortisol concentrations, the tubes were first thawed and then centrifuged at 3000 rpm for 15 min. An ELISA kit (Salimetrics, USA) was then used to process the samples and calculate the cortisol concentrations. The intra-assay and inter-assay coefficients of variation were 3% and 10%, respectively.

At time 1, 127 participants provided 508 saliva samples, 485 (95.5%) of which provided valid cortisol concentrations. At time 3, 424 saliva samples were collected from 106 participants, 401 (94.6%) of which provided valid cortisol concentrations. After preliminary screening, 9 and 14 outliers (> 3 standard deviations [SD] from the mean) were removed from samples obtained at times 1 and 3, respectively. The diurnal cortisol pattern was summarized using the mean cortisol concentration and diurnal cortisol slope. The mean cortisol concentration was derived by dividing the area under the curve with respect to the baseline by the total elapsed time. The diurnal cortisol slope was calculated as the hourly change in cortisol concentration by regressing the four cortisol concentration values on the collection time. Lower (more negative) diurnal slopes indicated a more rapid decline in cortisol levels and slope values closer to zero denoted flatter diurnal rhythms. Previous studies in Chinese samples (Ho et al., 2013; Lai et al., 2005) did not find any significant differences in the diurnal rhythms of cortisol secretion across 2 days of measurement, suggesting acceptable intra-individual stability for the cortisol measures.

Data Analyses

Structural equation modeling was performed using the robust maximum likelihood estimator in Mplus 8.2 (Muthén & Muthén, 2017) to estimate the direct and indirect effects

of self-compassion and self-criticism on the diurnal cortisol pattern via affect. All of the psychological measures followed a normal distribution with a skewness of < 1. The latent factors of self-compassion and self-criticism at time 1 were proposed to be predictors of the diurnal cortisol pattern (mean cortisol concentration and diurnal cortisol slope) at time 3. The observed variables of positive affect and the latent factor of emotional distress at time 2 were hypothesized to be mediator variables. The model included time 1 assessments of affect and the diurnal cortisol pattern to account for autoregressive effects, which describe the stability of individual differences over time. Demographic and clinical characteristics (gender, age, body mass index [BMI], cancer stage, number of treatments completed, time elapsed since last treatment, use of medication) were included as potential confounding variables in the model.

The model fit was assessed using the χ^2 test and cutoff criteria for the following approximate fit indices: $p > 0.05$ for the χ^2 test, comparative fit index (CFI) ≥ 0.95 , and root mean square error of approximation (RMSEA) ≤ 0.06 . To account for the likely skewed distribution, the indirect effects of self-compassion and self-criticism (time 1) on the diurnal cortisol pattern (time 3) via affect (time 2) were estimated using 10,000 bootstrap draws. The estimated indirect effects were considered statistically significant if the 95% confidence interval (CI) excluded zero. Missing data were handled using full information maximum likelihood under the missing-at-random assumption (Little & Rubin, 2019).

Results

Table 1 displays the descriptive statistics and bivariate correlations of the study measures from times 1 to 3. With reference to the theoretical range of the measurement scales, the sample showed moderate levels of self-compassion and positive affect and low levels of self-criticism, negative affect, anxiety, and depression. We found overall stable levels of positive affect (Cohen $d = 0.02$, $p = 0.87$) and a significant and small decrease in negative affect, anxiety, and depression ($d = 0.21$ – 0.25 , $p = 0.01$) across the 2-month period. The participants showed similar cortisol concentrations (in nmol/L) of 8.04 (SD = 5.48)/8.74 (SD = 5.66) in sample 1, 3.96 (SD = 1.99)/3.97 (SD = 1.89) in sample 2, 2.47 (SD = 1.31)/2.40 (SD = 1.25) in sample 3, and 1.58 (SD = 0.81)/1.50 (SD = 0.77) in sample 4 across times 1 and 3. The sample reported consistent saliva collection time across time 1 and time 3 for all of the 4 samples: sample 1 (mean collection time = 0654 h and 0656 h), sample 2 (1205 h and 1211 h), sample 3 (1709 h and 1714 h), and sample 4 (2115 h and 2118 h). The sample displayed overall stability of the diurnal cortisol

Table 1 Descriptive statistics and bivariate correlations of the predictors, mediators, and outcome measures from Time 1 and Time 3

	M (SD)	Theoretical range	1	2	3	4	5	6	7	8	9	10	11	12	13
1. T1 self-compassion	3.08 (0.80)	1–5	<i>0.92</i>												
2. T1 self-criticism	2.35 (0.71)	1–5	0.21	<i>0.91</i>											
3. T1 positive affect	28.5 (6.68)	10–50	0.30	–0.09	<i>0.88</i>										
4. T2 positive affect	28.4 (6.29)	10–50	0.31	–0.16	0.71	<i>0.89</i>									
5. T1 negative affect	19.1 (6.20)	10–50	0.07	0.65	–0.05	–0.07	<i>0.89</i>								
6. T2 negative affect	17.7 (6.11)	10–50	–0.03	0.48	–0.07	–0.05	0.58	<i>0.90</i>							
7. T1 anxiety	5.53 (3.98)	0–21	0.13	0.61	–0.15	–0.05	0.72	0.55	<i>0.86</i>						
8. T2 anxiety	4.73 (3.79)	0–21	0.02	0.45	–0.07	–0.07	0.52	0.79	0.65	<i>0.88</i>					
9. T1 depression	5.31 (3.63)	0–21	0.05	0.52	–0.42	–0.37	0.54	0.42	0.68	0.47	<i>0.80</i>				
10. T2 depression	4.48 (3.50)	0–21	–0.11	0.42	–0.29	–0.35	0.40	0.55	0.36	0.62	0.57	<i>0.78</i>			
11. T1 Mean cortisol	3.69 (1.87)	/	0.07	0.07	0.01	0.09	0.04	0.17	0.16	0.08	–0.04	–0.03	/		
12. T3 Mean cortisol	3.70 (1.72)	/	–0.01	–0.02	0.05	0.11	–0.02	–0.01	–0.04	–0.10	–0.08	–0.08	0.42	/	
13. T1 Diurnal slope	–0.43 (0.33)	/	–0.06	–0.03	0.02	–0.13	–0.02	–0.26	–0.13	–0.10	0.05	0.02	–0.73	–0.36	/
14. T3 Diurnal slope	–0.50 (0.48)	/	0.01	–0.09	–0.08	–0.17	–0.06	–0.13	–0.06	–0.03	0.01	0.05	–0.36	–0.69	0.39

McDonald's omega are presented in italic at the diagonal; correlations with magnitude greater than 0.19 were significant at 0.05 level; lagged correlations are in bold

slope and mean cortisol concentration ($d = 0.03–0.18$, $p = 0.07–0.85$) across the 8-month period.

The proposed structural equation model fitted the observed data adequately with $\chi^2(132) = 159.1$, $p = 0.054$, CFI = 0.972, and RMSEA = 0.044. Figure 1 displays the standardized path estimates of the mediation model. In the figure, the control variables, baseline measures of the stress outcomes, and the direct effects of the time 1 predictors on the time 3 outcomes are omitted for ease of presentation. Gender, BMI, number of treatments completed, time elapsed since last treatment, and use of medication did not show any significant associations ($p > 0.05$) with the study variables in the model. Younger participants and those at more advanced stages of cancer showed greater levels of self-compassion and emotional distress. Substantial factor loading was found for self-compassion ($\lambda = 0.83–0.91$), self-criticism ($\lambda = 0.73–0.82$), and emotional distress ($\lambda = 0.71–0.90$). We found strong autoregressive effects ($\beta = 0.56–0.60$, standard error [SE] = 0.06–0.13, $p < 0.01$) for positive affect and emotional distress from time 1 to time 2 and moderate autoregressive effects ($\beta = 0.31–0.33$, SE = 0.07–0.09, $p < 0.01$) for the diurnal cortisol pattern from time 1 to time 3.

After controlling for covariates and the baseline affect, self-compassion significantly predicted both positive affect ($\beta = 0.20$, SE = 0.08, $p = 0.02$) and emotional distress ($\beta = -0.19$, SE = 0.09, $p = 0.03$) at time 2. Self-criticism had a significant negative effect ($\beta = -0.16$, SE = 0.08, $p = 0.04$) on positive affect at time 2. The time 2 positive affect had a significant negative effect ($\beta = -0.22$, SE = 0.08, $p < 0.01$) on the diurnal cortisol slope but not on the mean cortisol concentration ($\beta = 0.13$, SE = 0.09, $p = 0.15$) at time 3. Time 2 emotional distress did not have any significant effects on the diurnal cortisol pattern ($p = 0.19–0.64$) at time 3. The model explained over half of the variance in time 2 positive affect and emotional distress ($R^2 = 50.3–53.2\%$). The amount of explained variance in the time 3 mean cortisol concentration and the diurnal cortisol slope was 15.3% and 16.5%, respectively.

Self-compassion did not have any significant direct effects on the diurnal cortisol slope ($\beta = 0.17$, SE = 0.11, $p = 0.11$) and mean cortisol concentration ($\beta = -0.14$, SE = 0.11, $p = 0.19$). Similarly, the direct effects of self-criticism on the diurnal cortisol slope ($\beta = -0.20$, SE = 0.14, $p = 0.15$) and mean cortisol concentration ($\beta = 0.10$, SE = 0.14, $p = 0.50$) were not significant. As shown in Table 2, time 1 self-compassion showed a significant and negative indirect effect ($\alpha\beta = -0.043$, 95% CI = -0.126 to -0.005) on the time 3 diurnal cortisol slope via time 2 positive affect. There was a significant positive indirect effect ($\alpha\beta = 0.036$, 95% CI = $0.003–0.108$) of time 1 self-criticism on the time 3 diurnal cortisol slope via time 2 positive affect. None of the indirect effects via emotional distress on mean cortisol

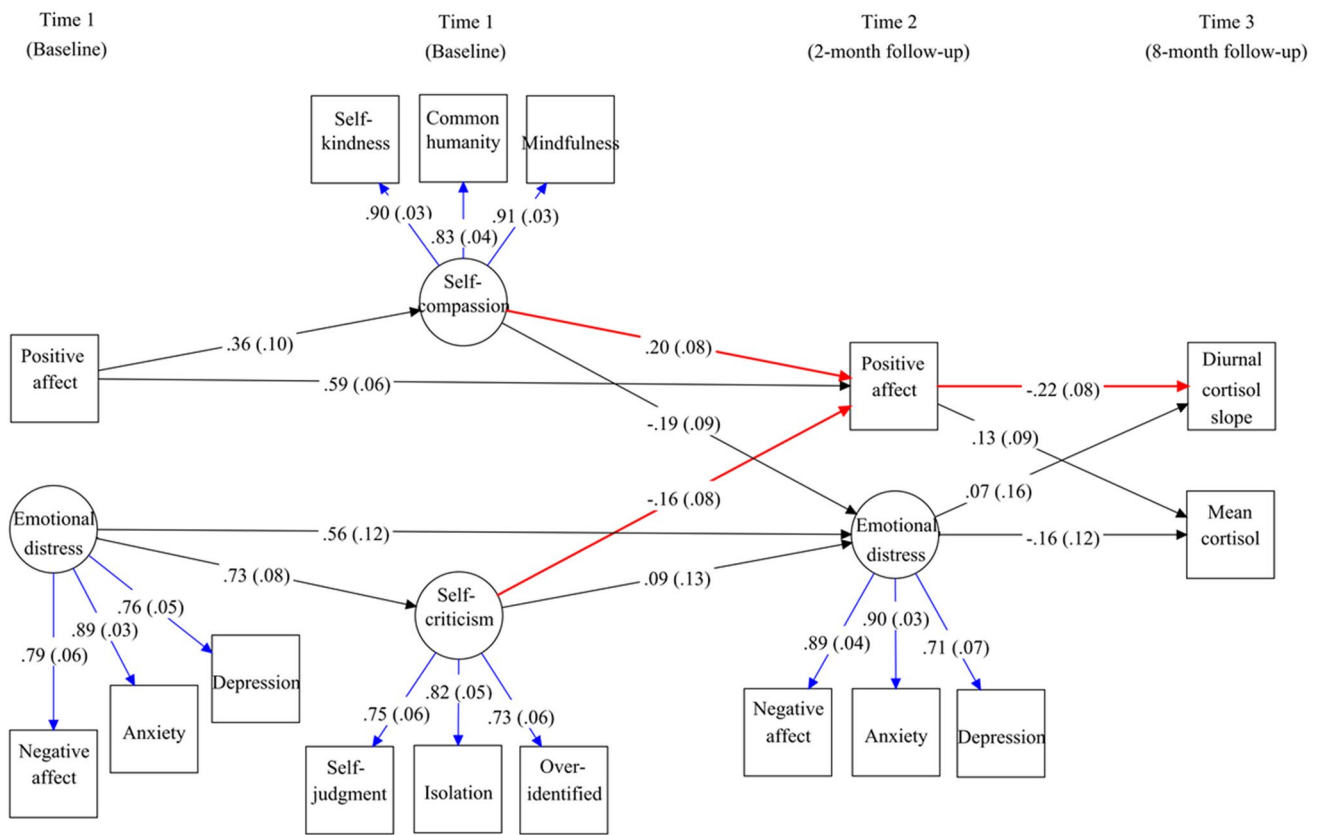


Fig. 1 Standardized path coefficients from self-compassion and self-criticism at time 1 to the diurnal cortisol pattern at time 3 via positive affect and emotional distress at time 2. The factor loading of the measurement model is marked in blue and the significant paths of the main study variables are highlighted in bold and red. Standard

errors are shown in parentheses. The baseline measures of the stress outcomes, residual co-variances among the dependent variables, and direct effects of the time 1 predictors on the time 3 outcomes are not shown

Table 2 Standardized indirect effects from self-compassion/self-criticism to stress outcomes via mediating variables

Time 1 predictor	Time 2 mediator	Time 3 outcome	Indirect effect	95% confidence interval
Self-compassion	Positive affect	Diurnal cortisol slope	-0.043*	-0.126 to -0.005
	Emotional distress		-0.014	-0.113 to 0.040
Self-criticism	Positive affect	Diurnal cortisol slope	0.036*	0.003 to 0.108
	Emotional distress		0.007	-0.030 to 0.118
Self-compassion	Positive affect	Mean cortisol	0.025	-0.005 to 0.096
	Emotional distress		0.030	-0.009 to 0.129
Self-criticism	Positive affect	Mean cortisol	-0.021	-0.087 to 0.004
	Emotional distress		-0.015	-0.136 to 0.025

* $p < 0.05$ with 95% bootstrapped confidence intervals excluding 0

concentration were statistically significant ($\alpha\beta < 0.03$), with the 95% bootstrapped CIs including 0.

Discussion

This study evaluated the longitudinal associations and contributed to a better understanding between self-compassion and the diurnal cortisol pattern in colorectal cancer survivors. Self-compassion at time 1 significantly predicted greater positive affect and lower emotional distress at time 2, which lends support to our first hypothesis. The moderate

correlations found between self-criticism and the components of time 2 emotional distress were consistent with previous studies (Brenner et al., 2017; López et al., 2015). After controlling for baseline emotional distress, self-criticism did not significantly predict time 2 emotional distress. In line with previous findings (Arambasic et al., 2019; Zhu et al., 2019), these results suggest that self-compassion can foster positive affect and ameliorate emotional distress in cancer survivors. Neither self-compassion nor self-criticism had significant direct effects on the diurnal cortisol pattern, which does not support our second hypothesis. The length of time lag (8 months) between time 1 and time 3 assessments could undermine the associations between self-compassion and cortisol responses which were acute biomarkers. Indeed, a recent meta-analysis (Phillips & Hine, 2021) only found a weak correlation ($r=0.14$) between self-compassion and stress hormones.

This study observed a change in emotional distress but not in positive affect between times 1 and 2. Positive affect at time 2 was found to significantly predict steeper diurnal cortisol slopes 6 months later. The present study used structural equation modeling to model self-compassion, self-criticism, and emotional distress as latent factors and account for the associated measurement errors. Both self-compassion and self-criticism showed significant indirect effects on the diurnal cortisol slope via positive affect but the corresponding indirect effects via emotional distress were not statistically significant. These results provide partial support to the third and fourth hypotheses and suggest that positive affect mediated the link between self-compassion and steeper diurnal cortisol slopes in cancer survivors over an 8-month period. Positive affect has shown a similar mediating role between benefit-finding and diurnal cortisol slopes in prostate cancer patients (Wang & Hoyt, 2018). Though previous studies (Armer et al., 2018; Castonguay et al., 2017; Pauly et al., 2019) found significant associations between negative affect and the diurnal cortisol pattern, they have not properly accounted for the role of positive affect. Our results lend support to the linkages between diurnal cortisol slopes and positive affect rather than emotional distress (Hoyt et al., 2015; Nater et al., 2010; Wang & Hoyt, 2018).

One possible explanation for the lack of significant findings between emotional distress measures and the cortisol outcomes could be that the sample was not distressed enough. The mean HADS scores were in the non-clinical range and the relatively low variance in the distress measures could have masked any significance. Future research could test the relationships in a more distressed sample or at a more critical time point in the cancer trajectory. The independent predictive role of positive affect on the diurnal cortisol slope can also be understood from a cultural perspective.

Findings of a recent study (Park et al., 2020) suggest a moderating role for cultural difference, where the association between negative affect and flattened diurnal cortisol slopes was only significant in an American sample but not in a Japanese sample. The discrepancy could reflect divergent cultural beliefs about negative affect being viewed as a threat to self-image in the West, as opposed to being viewed as a natural and integral element of life in the East. The sample of older Chinese individuals in this study likely aligned with Eastern cultural views as they experienced emotions in a dialectic manner (Bagozzi et al., 1999). The stronger emphasis of Chinese culture on feelings of appreciative joy and contentment than Western culture (Zeng et al., 2020) could contribute to a salient role of positive affect in mediating the link between self-compassion and cortisol outcomes.

Our findings on the indirect effects of self-compassion and self-criticism on diurnal cortisol slopes via positive affect integrated multidisciplinary knowledge from positive psychology, neuroendocrinology, and psycho-oncology. Positive affect is a potential pathway by which self-compassion and self-criticism exert their influences on the activities of the HPA axis in cancer survivors. A qualitative study (Goei et al., 2021) reported experiences of increased self-awareness, pleasant body experiences, positive thinking and emotions, and relaxation in adult cancer survivors following mindfulness intervention. Developing self-compassionate attitudes and reducing self-critical attitudes might facilitate positive thinking and overall emotional well-being. Besides, dispositional mindfulness has been found to predict favorable diurnal cortisol pattern in cancer survivors (Garland et al., 2015). Mindfulness-based interventions have shown beneficial effects on the diurnal cortisol pattern in breast cancer survivors (Boyle et al., 2017; Hsiao et al., 2016). Given the potential connections between the endocrine, immune, and metabolic systems (Antoni & Dhabhar, 2019), a recent pilot randomized controlled trial (Ng et al., 2020) on the effectiveness of mindfulness interventions found improvements in the concentrations of C-reactive protein in 55 older adults with mild cognitive impairment. Comparative effectiveness research could highlight the utility of compassion-based and mindfulness-based interventions in modulating physiological stress responses and inform future clinical practice (Conversano et al., 2020).

Limitations and Future Research

This study is subject to a number of limitations. First, methodological literature (Segerstrom et al., 2014) has suggested the use of multiple (≥ 3) days of saliva assessment to derive reliable estimates for the diurnal cortisol

pattern. For budgetary reasons, the present study only estimated the mean cortisol and diurnal cortisol slope based on one day of saliva assessment. This casts doubts over the reliability of the cortisol parameters and robustness of the present results. Since diurnal cortisol slopes could alternatively be calculated from only waking and bedtime cortisol as a prognostic marker in cancer samples, further studies could collect fewer cortisol samples per day over more days to obtain more reliable estimates of the diurnal cortisol pattern. Second, though the present study controlled for the general use of medication in the analyses, we did not differentiate between different types of pharmacologic drugs. As a result, we did not specifically measure and control for the use of corticosteroid, which could have potential interference with neuroendocrine functioning in the current results.

Third, the standardized indirect effects obtained in the present study did not reach moderate magnitudes. The small effect sizes imply that this study was likely underpowered when testing these modest indirect effects. Simulation analysis suggests that future studies will require a larger sample size ($N=280$) to achieve an adequate power of 80% to analyze modest indirect effects. Fourth, the non-randomized sampling design might result in sampling and self-selection biases. There could be potential recall bias over the past 2 weeks for the questionnaire data collection of the study participants. Our mediation model examined the effects of affect on the diurnal cortisol pattern based on previous literature and did not explore the possible reciprocal effects of diurnal cortisol pattern on affect. We recommend caution in interpreting the temporal ordering of these effects before replication in future longitudinal studies. Fifth, moderator variables were not taken into account given the relatively modest sample size. Future larger-scale studies should consider measuring cancer coping strategies using the Mini-Mental Adjustment to Cancer Scale (Fong & Ho, 2015) and test for non-linear effects of self-compassion and self-criticism via moderated mediation analysis.

Based on the present results, future research could test whether self-compassion would be associated with better cancer coping in terms of lower helplessness and anxious preoccupation and higher fighting spirit and explore the potential moderating role of self-compassion on the relationship between cancer coping and psychophysiological functioning in the cancer survivors. Given the prognostic value of cortisol slopes in metastatic populations, future studies should attempt to replicate the present findings in samples of metastatic cancer patients. Randomized clinical trials should be conducted to examine whether compassion-based interventions could foster self-compassion and improve well-being of cancer survivors in both the psychological and physiological domains.

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Author Contribution R. T. H. H.: designed the study, supervised study implementation, acquired funding for the present research, and wrote the paper. T. C. T. F. designed the study, conducted literature review, analyzed the data, interpreted the results, and wrote the paper. A. H. Y. W. collaborated with the study design and editing of the final manuscript.

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Data Availability The raw dataset analyzed in this study is available in the form of a supplementary file.

Declarations

Ethical Approval. The study was conducted in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments. The study was approved by the ethical review board of the University of Hong Kong (IRB Reference Number: UW 15–115).

Conflict of Interest The authors declare no competing interests.

Informed Consent Informed consent was obtained from all individual participants.

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