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Psychological adjustment and heart rate variability in ovarian cancer survivors

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Abstract

Introduction: Body image, posttraumatic growth, quality of life, coping, and social support are relevant concepts to ovarian cancer survivors. This study aimed to examine the associations among these concepts as well as their relationships with heart rate variability (HRV), which is an index of vagal tone.

Methods: an exploratory and correlational study was conducted on 25 ovarian cancer survivors. We used self-report measures to assess psychological variables. HRV parameters recorded for this study were analyzed in the time domain and in the frequency domain. Spearman correlations were *performed.*

Results: Positive attitude coping strategy was associated with psychological and physical distress related to problems of appearance (Rho = -.57, $p < .01$), emotional functioning (Rho = .53, $p < .01$), and global health (Rho = .47, $p < .05$). Problem solving coping strategy was correlated with a higher posttraumatic growth, namely greater personal strength (Rho = .44, $p < .05$) and better relationships with others (Rho = .40, $p < .05$). Seeking social support was associated with growth in relationships with others (Rho = .40, $p < .05$). Higher HRV parameters were associated with higher physical functioning (SDNN: Rho = .59, $p < .01$; RMSSD: Rho = .54; $p < .01$; pNN50: Rho = .56, $p < .01$; HF: Rho = .58, $p < .01$). The ratio of low-frequency to high-frequency power (LF/HF) was negatively associated with posttraumatic growth (i.e., personal strength: Rho = .51, $p < .05$; new possibilities: Rho = -.54, $p < .01$).

Discussion: Positive attitude and problem solving coping strategies may facilitate psychological adjustment to ovarian cancer. The strong association between markers of vagal tone and physical functioning offers insights on the possible role of vagus nerve in ovarian cancer survivors. These findings should be further investigated by future studies with larger samples and longitudinal designs.

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1. Introduction

Ovarian cancer treatment often includes a combination of surgery and chemotherapy, determining a wide range of physical and psychological symptoms (Stavraka et al., 2012). The long-term treatment sequelae and quality of life during remission have been less studied than the active disease phase (Ahmed-Lecheheb & Joly, 2016; Puppo et al., 2020). In this context, specific quality of life domains were found to be clinically significant in ovarian cancer survivors, including sexual symptoms, body image concerns and psychological distress (Ahmed-Lecheheb & Joly, 2016; Cosentino & Pruneti, 2015; Logue et al., 2020; Matulonis et al., 2008; Puppo et al., 2020; Roland et al., 2013). Although surviving ovarian cancer could reduce well-being or increase distress, many ovarian cancer survivors also reported good quality of life (Ahmed-Lecheheb & Joly, 2016; Roland et al., 2013) and personal growth in the aftermath of illness, despite disease and treatment challenges (Puppo et al., 2020; Roland et al., 2013) and the negative impact of ovarian cancer on women's body image (Puppo et al., 2020).

The experience of posttraumatic growth refers to a positive change which originates from a person's struggle with the new reality imposed by highly negative circumstances, as they challenge pre-existing assumptions about the self and the world (Cafaro et al., 2019; Joseph et al., 2012; Tedeschi & Calhoun, 2004). Manifestations of posttraumatic growth include greater appreciation of life, new priorities, better relations with others, higher sense of personal strength, and a deeper existential and spiritual life (Tedeschi & Calhoun, 2004). Studies with cancer survivors found a positive association between posttraumatic growth and health-related quality of life, which may have a positive effect on patients' prognosis (Liu et al., 2020). Few studies investigated posttraumatic growth in ovarian cancer patients (Hill & Watkins, 2017; Shand et al., 2018) and only one focused on ovarian cancer survivors (Oh et al., 2021). Being religious and cancer coping strategies predicted posttraumatic growth in ovarian cancer survivors and the main strategy used by these patients was positive reframing (i.e., reappraisal of life and finding new meaning in life; Oh et al., 2021). Coping strategies and social support are essential for ovarian cancer survivors as they may influence both adjustment to cancer (Cosentino & Pruneti, 2015; Fasano et al., 2020; Roland et al., 2013) and posttraumatic growth (Prati & Pietrantoni, 2009; Rajandram et al., 2019). In this vein, low posttraumatic growth was associated with high avoidance coping and low levels of quality of life, meaning centered-coping, and social support (Shand et al., 2018). Furthermore, both perceived social support and seeking social support were correlated with growth in relationships with others (Hill & Watkins, 2017; Shand et al., 2018).

Heart rate variability (HRV), as a marker of disease and adaptability, is an index of cardiac function and interdependent regulatory processes which help individuals to adapt to psychological and environmental challenges (Shaffer & Ginsberg, 2017). HRV may reflect a bodily state of balance (i.e., coherence), which is physiologically related to the synchronization of both higher-level brain systems and autonomic nervous system branches; psychologically, coherence is related to higher cognitive and emotional stability (McCraty & Childre, 2010). Experiencing positive emotions, such as appreciation, caring, or compassion, leads to a more coherent heart rhythm (i.e., sine-wave like and more ordered pattern; McCraty & Zayas, 2014). Instead, when experiencing negative emotions, such as anger or anxiety, an incoherent heart rhythm is produced (McCraty & Childre, 2010). Some HRV parameters provide an index of vagal tone (Laborde et al., 2017), which has been associated with several physiological processes. For example, healthy males with low baseline vagal tone exhibited an impaired post-stress recovery in markers of cardiovascular (i.e., blood pressure), endocrine (i.e., cortisol), and immune (i.e., tumor necrosis factor-alpha) systems compared to those with higher vagal tone (Weber et al., 2010). In this vein, a recent meta-analysis found an overall negative association between HRV (including vagally-mediated HRV) and markers of inflammation (Williams et al., 2019). Moreover, optimal levels of vagal tone were found to predict a better cancer prognosis (i.e., high survival rates and low tumor markers) independently from other prognostic factors (e.g., age, stage of disease), suggesting that possible mechanisms include the reduction of oxidative stress, and the inhibition of inflammation and sympathetic activity (De Couck et al., 2018). Interestingly, HRV was recently found to be associated with posttraumatic growth (Wei et al., 2017). The authors found that low and high frequency parameters of HRV were higher in the posttraumatic growth group compared to the control group during a stimulation with positive affective pictures; nevertheless, the same result was not obtained during the presentation of negative or neutral affective pictures. Wey et al. concluded that posttraumatic growth and vagal function may contribute to more efficient processing of emotional stimuli. However, studies examining vagally-mediated HRV in ovarian cancer survivors are sparse (Cosentino et al., 2018; Pruneti et al., 2020). Ovarian cancer survivors reported lower levels of standard deviation of NN intervals (SDNN) and similar levels of the ratio of low-frequency power to high-frequency power (LF/HF) compared to normative values (Cosentino et al., 2018); moreover, social support from friends, avoidance coping, and body image explained 38% of SDNN variance (Pruneti et al., 2020).

1.1 The current study

According to clinical guidelines, a person-centered and holistic care is important to maximize quality of life because of the increasing number of persons who survive cancer (Davies & Gracey, 2020). Therefore, the identification of psychological risk and protective factors, as well as mind-body interactions, could inform future research and clinical practice towards a comprehensive care of ovarian cancer survivors. In line with the biopsychosocial model (Engel, 1979) and drawing from previous research, we selected quality of life, posttraumatic growth, appearance concerns, coping, social support, and HRV as characteristics of psychological and psychophysiological adjustment to ovarian cancer. However, little is known about their mutual relationships in ovarian cancer survivors. Moreover, although research suggests to use specific methods to assess vagal tone (i.e., root mean square of successive RR interval differences: RMSSD; percentage of successive RR intervals that differ by more than 50 ms: pNN50; and Absolute power of the high-frequency band: HF power; Laborde et al., 2017), only SDNN was used in previous research with ovarian cancer survivors (Cosentino et al., 2018; Pruneti et al., 2020). Thus, the present study aims to examine the relationships between positive psychological functioning, quality of life, and HRV in ovarian cancer survivors.

2. Method

2.1 Study Design

The study design was exploratory and cross-sectional.

2.2 Participants

Ovarian cancer survivors undergoing a follow-up program at the Oncological Clinic, Gynecological ward, University-Hospital of Parma (Italy), were asked to participate in the study if they met the following inclusion criteria: (1) ovarian cancer diagnosed since at least six months; (2) no surgery in the previous two months; (2) no ongoing chemotherapy; (3) ability to understand and speak Italian; (4) aged 18 or older; (5) reading and signing informed consent. Exclusion criteria included: (1) current or past diagnosis of psychiatric disorder; (2) psychopharmacological treatment before cancer onset; (3) pharmacological treatment directly affecting heart rate (i.e., beta-blockers). Twenty-five women agreed to participate in the study and completed the questionnaires. The study was approved by the Institutional Review Board of Parma University (n. 0033/2017).

2.3 Procedure

Recruitment was done during routine follow-up visits, which were made one day per week and lasted one year. After the follow-up visit, patients were taken to a quiet room and were informed by a research assistant about the study procedures, the right to decline to participate or withdraw from the study at any time without penalty, and the anonymity of data. After providing informed consent, patients completed the questionnaires and were familiarized with the equipment (e.g., cables) and the procedure of HRV recording. Patients were then invited to sit and keep the knees at an angle of 90°, the hands on thighs with palms facing upward, and eyes closed. Disposable surface electrodes were placed on the internal area of both wrists, after cleaning the skin with an alcohol wipe. Recording of HRV started after a rest period of 5 minutes.

2.4 Measures

Quality of life, as a state of well-being reflecting the ability to perform everyday activities in the physical, psychological, and social domains, as well as satisfaction with levels of functioning and disease control, was measured with the EORTC Quality of Life Questionnaire-C30 (EORTC-QLQ-C30; Aaronson et al., 1993; Apolone et al., 1998). It is a cancer-specific questionnaire containing nine multi-item scales: five functioning scales (Physical: alpha = .77; Role: alpha = .52; Emotional: alpha = .85; Cognitive: alpha = .73; and Social: alpha = .81), three symptoms scales (Fatigue: alpha = .07; Nausea and vomiting: alpha = .00; and Pain: alpha = .39), and one Global health scale (alpha = .82). Additional six single-item scales measure cancer-specific symptoms (i.e., dyspnea, loss of appetite, insomnia, constipation, and diarrhea) and financial difficulties. Higher scores indicate greater quality of life except for the symptoms scales. Single items were not used in this study.

The Posttraumatic Growth Inventory (PTGI; Prati & Pietrantoni, 2014; Tedeschi & Calhoun, 1996) was used to measure posttraumatic growth. It is composed by five subscales: New possibilities (alpha = .89), Relating to others (alpha = .89), Change in spirituality (alpha = .86), Appreciation of life (alpha = .86), and Personal strength (alpha = .90). Higher scores indicate greater posttraumatic growth.

Social support, referred to the perceived adequacy of support received from different sources, was measured with the Multidimensional Scale of Perceived Social Support (MSPSS; Prezza & Pacilli, 2002; Zimet et al., 1988). It includes three sources of social support: Family (alpha = .93), Friends (alpha = .96), and Significant others (alpha = .77). Higher scores indicate greater social support.

The Coping Orientation to Problems Experienced – New Italian Version – 25 (COPE-NVI-25; Carver et al., 1989; Foà et al., 2015) was used to assess coping strategies, that is cognitive and behavioral efforts adopted by individuals facing a stressor that reflect a wide range of self-regulatory functions. Items are grouped into five scales: Avoidance strategies (alpha = .02), Turning to religion (alpha = .95), Positive attitude (alpha = .82), Social support (alpha = .71), Problem solving (alpha = .77). Higher scores indicate higher levels of coping.

The Derriford Appearance Scale-59 (DAS-59; Carr et al., 2000; Moss et al., 2013) was used to assess typical responses to living with problems of appearance, which may be visible to others or apparent only to the person concerned. Responses to problems of appearance may include emotional distress, disruption to everyday living, and lowered self-esteem. It is composed by five subscales: General self-consciousness (alpha = .94), Social self-consciousness (alpha = .92), Sexual and bodily self-consciousness (alpha = .76), Facial self-consciousness (alpha = .64) of appearance, Negative self-concept (alpha = .76), and Physical distress and dysfunction (alpha = .90). Higher scores indicate greater distress and dysfunction related to problems of appearance.

Short-term HRV (5 min.) was measured using the hardware PsychoLab VD13SV-Satem, which was interfaced online with a PC. The software PC Soft (Satem) was used to record and score Interbeat Interval (IBI), which was derived from the electrocardiographic (ECG) signal. An internal command of PC Soft (i.e., Stapik) automatically detects R wave peaks and estimate HRV parameters in both time and frequency domains. The following HRV parameters were used: SDNN, pNN50, RMSSD (time domain), HF power, and LF/HF (frequency domain; Shaffer & Ginsberg, 2017). Outliers were detected through Stapik command and deleted. Stapik uses Fast Fourier Transformation to break HRV down into its components operating in different frequency ranges.

2.5 Data analysis

In the present study, Cronbach's alpha was used to assess the internal consistency of each scale. Variables with a low internal consistency (alpha <.60) were excluded from the analyses. Tests for skewness, kurtosis, and Kolmogorov-Smirnov were used to determine normality of distribution. As data were not normally distributed, we used Spearman correlations with a significance level of $p < .05$. All statistical analyses were performed using IBM SPSS for Windows (version 22).

3. Results

Two participants were excluded from the HRV analysis due to technical issues during data collection. Demographic and disease-related characteristics are shown in Table 1.

Table 1. Demographic and disease-related characteristics

Age (years), *M* (*SD*)	55.08 (14.86)
Time since diagnosis (years), *M* (*SD*)	2.96 (2.26)
Marital status, *N* (%)	
Married/cohabitant	17 (68)
Unmarried	5 (20)
Separated/divorced	2 (8)
Widowed	1 (4)
Children, *N* (%)	
Yes	17 (68)
No	8 (32)
Education Level, *N* (%)	
Elementary school	3 (12)
Middle school	8 (32)
High school	14 (56)
Inherited predisposition to cancer, *N* (%)	
Yes	14 (56)
No	11 (44)
Type of ovarian cancer, *N* (%)	
Malignant	17 (68)
Borderline	8 (32)
Stage of disease, *N* (%)	
Missing	4 (16)
I	13 (52)
II	0 (0)
III	8 (32)
IV	0 (0)
Previous chemotherapy, *N* (%)	
Yes	12 (48)
No	13 (52)

The mean age of participants was 55.08 years and most of them were married/cohabitant, had children, and completed high school. The mean time since diagnosis was 2.96 years and most women received a diagnosis of malignant ovarian cancer. According to the International Federation of Gynecology and Obstetrics (FIGO) criteria, the more frequent stages of disease were I (52%) and III (32%).

With regards to demographic characteristics (see Table S1), only marital status was not associated with any psychological variables or HRV parameters. Age was negatively associated with all HRV parameters but LF/HF (SDNN: Rho = -.66, p = .001; RMSSD: Rho = -.59, p = .003; pNN50: Rho = -.56, p = .005; LF/HF: Rho = -.02, p = .922; HF: Rho = -.58; p = .004). Moreover, younger women reported higher scores in General self-consciousness of appearance (Rho = -.42; p = .034) and Physical distress and dysfunction (Rho = -.47; p = .018) subscales, as well as lower scores in Turning to religion (Rho = .58; p = .003), Positive attitude (Rho = -41; p = .041), and Emotional functioning (Rho = .50; p = .012) subscales. Having children was negatively associated with all HRV parameters but LF/HF (SDNN: Rho = -.50, p = .015; RMSSD: Rho = -.44, p = .035; pNN50: Rho = -.53, p = .009; LF/HF: Rho = -.19, p = .362; HF: Rho = -.46; p = .029). Education level was not associated with any HRV parameters and was negatively associated with Facial self-consciousness of appearance (Rho = -.59; p = .002) and Turning to religion (Rho = -.43; p = .032), and positively associated with Social support from friends (Rho = .70; p = .000).

Regarding disease-related characteristics (see Table S1), Inherited predisposition to cancer was positively associated with social support. In particular, women with predisposition reported higher support from family (Rho = .55; p = .004) and from friends (Rho = .48; p = .015). Time since diagnosis was negatively associated with social support coping strategy (Rho = -.43; p = .032), whereas stage of disease was positively correlated with personal strength (Rho = .47; p = .018) and appreciation of life (Rho = .40; p = .048) PTGI subscales. Stage of disease was negatively associated with Social self-consciousness (Rho = -.56; p = .009) and Sexual and bodily self-consciousness (Rho = -.50; p = .021). Finally, women who underwent chemotherapy reported higher appreciation of life (Rho = .45; p = .023) and higher personal strength (Rho = .45; p = .023).

3.3 Associations between coping strategies, posttraumatic growth, body image, and quality of life

Table 2 shows the relationships between coping strategies and different psychological variables (further relationships are provided in Table S1).

Table 2. Associations between coping, posttraumatic growth, body image, and quality of life

	Turning to religion (COPE)	Positive attitude (COPE)	Social Support (COPE)	Problem solving (COPE)
Relating to others (PTGI)	.195	-.246	.403*	.403*
Personal Strength (PTGI)	.153	.038	.042	.444*
Change in spirituality (PTGI)	.108	-.524**	-.001	-.271
Global self-consciousness (DAS)	-.146	-.575**	.055	-.306
Social self-consciousness (DAS)	-.130	-.444*	-.009	-.302
Sexual and bodily self-consciousness (DAS)	-.258	-.681***	.091	-.355
Negative self-concept (DAS)	-.137	-.670***	.007	-.507**
Facial self-consciousness (DAS)	.069	-.487*	-.084	-.335
Physical Distress and Dysfunction (DAS)	-.195	-.402*	.025	-.328
Emotional functioning (EORTC)	.253	.529**	-.031	.255
Global Health (EORTC)	.224	.473*	-.118	.041

Note. COPE = The Coping Orientation to Problems Experienced – New Italian Version – 25; PTGI = The Posttraumatic Growth Inventory; DAS = The Derriford Appearance Scale-59; EORTC = The European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire-C30.
* $p < .05$; ** $p < .01$; *** $p < .001$. Only significant associations were reported.

Positive attitude was the coping strategy more strongly associated with DAS, PTGI, and EORTC subscales. Specifically, Positive attitude was negatively associated with all DAS subscales and with Change in spirituality, and positively associated with Emotional functioning and Global health.

Problem solving was negatively associated with Negative self-concept and positively associated with Relating to others and Personal strength. Finally, high Social support was positively associated with high Relating to others, whereas Turning to religion was the only coping strategy which was not associated with any psychological variables.

3.2 Associations of quality of life with posttraumatic growth and body image

Table 3 shows the relationships of quality of life with posttraumatic growth and body image (further relationships are provided in Table S1).

Table 3. Associations of quality of life with posttraumatic growth and body image

	Emotional functioning (EORTC)	Physical functioning (EORTC)	Cognitive functioning (EORTC)
Personal strength (PTGI)	-.122	-.482*	-.208
Change in spirituality (PTGI)	-.276	-.015	-.485*
Negative self-concept (DAS)	-.482*	.043	-.238

Note. EORTC = The European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire-C30; PTGI = The Posttraumatic Growth Inventory; DAS = The Derriford Appearance Scale-59.

* $p < .05$. Only significant associations were reported.

Negative and moderate to large associations were found between Emotional functioning and Negative self-concept, between Physical functioning and Personal strength, and between Cognitive functioning and Change in spirituality. Social functioning, Role functioning, and Global health were not associated with any psychological variables.

Associations between HRV parameters and psychological variables

Table 4 shows the correlations between HRV parameters and psychological variables (further relationships are provided in Table S1).

Table 4. Associations between HRV and psychological variables

	SDNN	LF/HF	RMSSD	pNN50	HF Power
New possibilities (PTGI)	-.178	-.539**	-.045	.042	-.062
Personal Strength (PTGI)	-.360	-.509*	-.259	-.209	-.253
Turning to religion (COPE)	-.391	-.108	-.316	-.289	-.429*
Physical functioning (EORTC)	.588**	-.084	.537**	.565**	.579**

Note. HRV = Heart Rate Variability; SDNN = standard deviation of NN intervals (ms); LF/HF = Ratio of low-frequency power to high-frequency power (%); RMSSD = root mean square of successive RR interval differences (ms); pNN50 = percentage of successive RR intervals that differ by more than 50 ms (%); HF Power = Absolute power of the high-frequency band (ms^2); PTGI = The Posttraumatic Growth Inventory; COPE = The Coping Orientation to Problems Experienced – New Italian Version – 25; EORTC = The European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire-C30.

* $p < .05$; ** $p < .01$. Only significant associations were reported.

LF/HF was negatively associated with Personal strength and New possibilities. HF was negatively and positively associated with Turning to religion and Physical functioning, respectively. Finally, SDNN, RMSSD, pNN50, and HF were positively and strongly associated with Physical functioning.

4. Discussion

The aim of this study was to examine the relationships between positive psychological functioning, quality of life, and HRV in ovarian cancer survivors. Our findings show a strong negative association between Positive attitude and appearance-related distress and dysfunction. Women adopting a Positive attitude reported less concerns about their facial, social, sexual, and bodily appearance as well as better self-concept and lower physical distress. Positive attitude involves acceptance and reappraisal of the event (Carver et al., 1989; Foà et al., 2015). We hypothesize that this coping strategy may promote an adaptation to physical and psychological long-term effects of ovarian cancer and its treatment on appearance. Although no study investigated this association in ovarian cancer patients (including survivors), similar results were found in breast cancer patients. For instance, women using strategies focused on accepting the challenging event and on positive self-care or positive and constructive thoughts about one's appearance were more likely to report a better body image (Yamani Ardakani et al., 2020). Moreover, women who reported worst body image had lower acceptance of cancer or positive attitude (Pikler & Winterowd, 2009). In our study, women high in Positive attitude also reported to feel less tense, worried, depressed, and irritable (i.e., high emotional functioning) and to perceive a high global health. This finding is consistent with that of a previous study showing that ovarian cancer survivors high in taking action and positive framing reported less depression (Beesley et al., 2018). Interestingly, older ovarian cancer survivors were more likely to adopt a Positive attitude. This result parallels previous findings on age differences in coping strategies among healthy individuals, showing that older people reported greater use of coping strategies involving cognitive reinterpretation of situations (Carver & Connor-Smith, 2010; Diehl et al., 1996). These studies suggested that age differences may be explained by accumulated life experiences, such as confronting with losses and changes due to aging. Accordingly, we hypothesize that the accumulated experience of older ovarian cancer women facilitates the acknowledgment that certain situations cannot be controlled (the acceptance of such situations) as well as their "ability to repaint a dark picture in more positive colours" (Diehl et al., 1996, p. 134).

Problem solving involves active coping, planning, and suppression of competing activities (Carver et al., 1989; Foà et al., 2015). In our study, women low in Problem solving were more likely to feel less confident, secure, cheerful, normal, feminine (i.e., negative self-concept), and to report low levels of personal strength and growth in relationships with others in the aftermath of ovarian cancer. This result is consistent with that of a previous study in which posttraumatic growth was associated with problem solving in cancer patients (Widows et al., 2005).

Seeking social support, but not perceived social support, was associated with growth in relationships with others. Previous studies found similar results for seeking social support, although perceived social support was also associated with growth in relationships with others (Hill & Watkins, 2017; Shand et al., 2018). Both these constructs may be considered as positive psychological factors as they are associated with higher posttraumatic growth (Joseph et al., 2012; Rajandram et al., 2011; Tedeschi & Calhoun, 2004). It is possible that perceiving social support is not important to experience growth in interpersonal relationships for ovarian cancer survivors in our sample. Rather, seeking social support to cope with stress is an active behavior that, being likely related to expressing and reframing traumatic events (e.g., cancer diagnosis), may be a step towards experiencing growth in relationships (Tedeschi & Calhoun, 2004). On the other hand, the nonsignificant result with regard to perceived social support may be due to the type of instrument used to measure social support. As suggested by previous research, using an assessment of social support that is specific to ovarian cancer could reveal significant relationships between this construct and posttraumatic growth (Hill & Watkins, 2017). According to the affective-cognitive processing model (Joseph et al., 2012), posttraumatic growth is related to post-traumatic stress symptoms because the latter indicate the person's struggle of "working through the implications of the stressor" (Helgeson et al., 2006, p. 810). The results of the present study seem to be in line with such theoretical model as ovarian cancer survivors who underwent chemotherapy, and were diagnosed with advanced stage ovarian cancer, were also more likely to experience higher personal strength and appreciation of life. We hypothesize that women with more adverse clinical status had a higher chance to perceive discrepancies between pre-trauma assumptions and new trauma-related information, and to trigger emotional-cognitive processing, thus leading to posttraumatic growth.

We also investigated the associations between heart rate variability and psychological variables to examine mind-body interactions. Indeed, ovarian cancer affects the mind as well as mind can affect the course of cancer (Spiegel, 2012). Our findings show a strong association between physical functioning and heart rate variability parameters reflecting vagal tone (RMSSD, pNN50, HF) as well as SDNN (Laborde et al., 2017). According to previous studies, vagal tone may inhibit oxidative stress, inflammation, and excessive sympathetic activity, which contribute to onset and progression of tumorigenesis (De Couck et al., 2018). We hypothesize that a higher vagal tone may contribute to a better physical functioning in ovarian cancer patients by inhibiting maladaptive physiological responses (e.g., inflammation). As an alternative explanation, experiencing physical functioning limitations may be distressing or hinder physical activity, both of which may in turn decrease vagal tone. Finally, ovarian cancer patients

perceiving new possibilities and a higher personal strength in the aftermath of ovarian cancer show lower LF/HF. Thus, it is possible that ovarian cancer patients in our study show higher parasympathetic activity when experiencing posttraumatic growth. However, this result should be interpreted with caution. Traditionally, LF/HF is meant to reflect sympatho-vagal balance but there is consensus that underlying mechanisms are unclear (Laborde et al., 2017; Shaffer & Ginsberg, 2017). Surprisingly, our results are not consistent with those of a study with ovarian cancer patients showing that SDNN was associated with high appearance distress (Pruneti et al., 2020). These inconsistent results may be due to the assessment of heart rate variability. Since short-term SDNN reflects all cyclic components of heart rate variability and is primarily determined by parasympathetically-mediated respiratory sinus-arrhythmia (Shaffer & Ginsberg, 2017), respiratory influences may mask the variance attributed to vagal tone. This is why recommendations suggest to use multiple heart rate variability parameters including RMSSD, which is relatively free of respiratory influences (Laborde et al., 2017).

5. Conclusions, strengths, and limitations

The present study has several limitations. First, the small sample size reduced statistical power and the generalizability of the results. Indeed, our study did not include each stage of disease. Furthermore, the small sample size prevented controlling for socio-demographic and disease-related variables (e.g., time since diagnosis). Second, the effects of different variables on HRV were not considered as time recording across days was not fix (circadian effects) and respiratory parameters were not measured (respiration effects). Nevertheless, according to Laborde et al. (2017), respiration influences on parasympathetic parameters of HRV are minimal during resting state conditions, and spontaneous breathing allows a better recording of HRV at rest. Moreover, we also measured RMSSD which is less affected by respiration (Laborde et al., 2017). Third, causal relationships cannot be established due to the cross-sectional nature of the study. Indeed, in our study data were collected from single participants at a single point in time. Fourth, as this was an exploratory study, we did not correct for multiple testing, leading to potential false positive results. Thus, results must be interpreted with caution. Notwithstanding these limitations, this study showed an important role of positive attitude and problem solving for appearance distress and posttraumatic growth in ovarian cancer patients. However, our findings should be further investigated by future studies with larger samples and longitudinal designs. If confirmed by further studies, these associations may pave the way for clinical trials. For example, interventions that promote a positive attitude may exert beneficial effects on psychological and physical distress related to appearance. Moreover, these interventions may be more beneficial for younger ovarian cancer patients, who less frequently use this coping strategy. Finally, future

studies could also investigate whether HRV would predict worst physical functioning or vice versa. In the former case, HRV may be used to identify vulnerable women.

Ethical approval: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Research data are available under request to corresponding authors.

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Author Contributions: FDV drafted the manuscript, collected the data, and analyzed the data. CP and CC conceived the study and analyzed the data. All authors revised the manuscript.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any potential conflict of interest.

Supplementary Materials: TABLE S1 (see supplementary file)

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