Research Paper

Quality of Life Breast Cancer Survivors: Compassion and Cognitive Flexibility Mediated by Mental Distress

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ABSTRACT

Background: Breast cancer is the most common cancer among women and the second leading cause of death after lung cancer. Although the number of recovered patients has increased, the treatment's side effects still affect them. This study aimed to investigate the mediating role of mental distress in the relationship between self-compassion, cognitive flexibility, and quality of life (QoL).

Methods: The descriptive method used correlation and structural equations. The population consisted of women referred to Iranmehr Hospital in Birjand City, Iran, between 2016 and March 2022, diagnosed with breast cancer. Of these, 202 participants were selected through convenience sampling. The patients were administered quality-of-life questionnaires, the psychological impact of cancer scale for measuring mental distress, the cognitive flexibility questionnaire, and the self-compassion questionnaire. SPSS software, version 25, LISREL software, version 8.8, Pearson correlation methods, and structural equation modeling analysis were used.

Results: All goodness-of-fit indices for the model fell within an acceptable range, indicating that the hypothesized model was a good fit for the sample. The significance level for the Sobel test was considered to be <0.05. Thus, self-compassion had a significant positive effect on QoL through mental distress (β=0.52, P<0.05), but cognitive flexibility did not (β=0.14, P>0.05).

Conclusion: The findings support the mediating role of mental distress in the relationship between self-compassion and QoL; therefore, therapeutic interventions based on self-compassion can be helpful in improving the QoL of women who have recovered from breast cancer.

Keywords: Breast cancer, Quality of life (QoL), Psychological distress, Cognitive flexibility, Self-compassion

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Introduction

Breast cancer, the most common cancer in women, is a crucial public health problem. This chronic disease is associated with several psychological problems [1]. According to available evidence, more than 1.6 million cases of breast cancer are reported worldwide annually, and this number is increasing. Survival rates for breast cancer patients vary widely worldwide, ranging from 80% in developed countries to less than 40% in low-income countries. Although clinical methods, surgery, chemotherapy, and radiation therapy increase the survival rate of these patients and reduce their pain and suffering, these patients also face psychological complications related to breast cancer after treatment [2]. Breast cancer affects patients' quality of life (QoL) [3]. According to the Nilsson model, four factors affect the QoL of cancer patients: biological function, symptoms, functional status, and perceived general health (GH). Additionally, individual characteristics and environmental attributes are two factors that influence not only the QoL but also these four dimensions [4]. According to the World Health Organization (WHO), QoL depends on people's understanding of their situation in life, including the cultural aspects and value systems in which they live.

In addition, being aware of a cancer diagnosis brings much fear and often causes psychological distress [5]. It encompasses adverse states of depression, anxiety, and stress, accompanied by mood and physical symptoms [6]. Surgery and long-term treatments may cause symptoms, such as anxiety, fear, and depression. Cognitive flexibility, which is one of the factors that enables a person to cope with challenging life situations, is also one of the variables associated with psychopathology [7]. Cognitive flexibility refers to the ability to modify cognitive elements to adapt to environmental changes. In such situations, a person who faces them with gentleness and awareness can use this opportunity for growth and development and exhibit the desired behavior [8]. Improving psychological flexibility can reduce distress in cancer patients and enhance their QoL. Self-compassion and psychological flexibility are associated with mental health and QoL in both general and clinical populations [9]. Self-compassion has been described as a three-component construct that includes self-kindness versus self-judgment, human commonality versus isolation, and mindfulness versus over-identification. The combination of three elements of self-compassion is a personal trait that practices kindness toward oneself [10]. Self-compassion, characterized by kind behavior in adverse situations, the understanding that hardships and suffering are part of the human experience, and the acknowledgment of thoughts and feelings without judgment, helps patients accept difficulties, manage negative emotions, and respond to physical changes with awareness and self-kindness [11]. Confronting cancer not only has physical and psychological consequences but is also intertwined with specific cultural and social experiences that can influence coping mechanisms. Cultural attitudes related to catastrophe and death can increase the stress burden on patients, leading individuals and their surroundings to believe that no effort will be beneficial in coping with the illness, equating a cancer diagnosis with death [12]. The significance of this issue lies in the fact that QoL revolves around the patient's health status, social relationships, environment, and psychological condition. Therefore, cultural attitudes that increase the stress burden on cancer patients can impact their QoL [13].

In the present study, the mediating role of mental distress in the relationship between self-compassion, psychological flexibility, and QoL was investigated. This study seeks to clarify the relationship between self-compassion, an emotional component, and cognitive flexibility, a cognitive component, in the presence of mental distress. During the research, the following question was raised: Can mental distress mediate the relationship between self-compassion and cognitive flexibility, simultaneously with QoL?

Methods

This study employed a descriptive–correlational research design and utilized structural equation modeling to achieve its fundamental goal. Structural equation modeling was employed to simultaneously test hypotheses related to the relationships between latent variables and their indicators. In this study, the statistical population consisted of all women aged 25-85 with breast cancer who were referred to Iranmehr Hospital in Birjand City, Iran, from the beginning of 2016 to March 2022. The hospital provided a list of 330 patients along with their contact numbers. Deceased individuals and those whose contact information was unavailable or who did not consent to participate were excluded. All individuals were contacted, and consent for participation in the study was obtained via telephone. Questionnaires were administered in person to those who were able to attend, and to individuals outside Birjand City, they were completed over the phone. A structured clinical interview was conducted to ensure the absence of psychotic disorders and intellectual disabilities. Ultimately, 202 individuals participated in the study. In this research, the questionnaires of demographic information, the 36-question (SF-

36) QoL by Ware and Sherbourne [14], the scale of the psychological impact of cancer by Hulbert-Williams et al. [15], the cognitive flexibility questionnaire by Dennis and Vander Wal [16], and the self-compassion questionnaire by Raes et al. [17] were used. The inclusion criteria included age between 25-85 years, at least 2 months since cancer diagnosis, absence of accompanying psychotic disorders or mental retardation, and satisfaction with participating in the research. According to Klein, the sample size should be approximately between 5-20 times the number of observable variables. Given that 24 indicators were considered in this study, a sample size of 202 was deemed sufficient [18].

Study instruments

QoL questionnaire (SF-36)

The 36-item short form health survey (SF-36) consists of 36 items. This quality-of-life questionnaire contains 36 questions and eight subscales, each comprising two to ten items. The eight subscales of this questionnaire are physical functioning (PF), role limitations due to physical health (PH), role limitations due to emotional problems (EP), energy/fatigue (EF), emotional well-being (EW), social functioning (SF), pain (P), and GH. Additionally, by combining these subscales, two comprehensive summary measures are derived: PH and mental health. In this questionnaire, lower scores indicate poorer QoL and vice versa. In this study, QoL refers to the scores respondents obtained on the 36-item QoL questionnaire. This questionnaire has two main summary measures: The PH component, which aggregates the subscales of PF, role limitations due to PH, P, and GH; and the mental health component, which combines the subscales of role limitations due to EP, EF, EW, and SF. In one study, the cronbach's α coefficient for this questionnaire was estimated at 0.78 [18]. In the current study, confirmatory factor analysis was used to examine the validity of the QoL questionnaire. The fit indices goodness of fit index (GFI), comparative fit index (CFI), and normed fit index (NFI) were above 0.9, the root mean square error of approximation (RMSEA) index was 0.022 (<0.1), and the P=0.35802 (>0.05), confirming model fit. Furthermore, the chi-square to degrees of freedom ratio was less than 3, indicating optimal model fit. The best-fitting model was achieved using eight factors. The validity and reliability of this questionnaire have been confirmed in the Iranian population, with internal consistency coefficients for the eight subscales ranging between 0.7 and 0.85, and test-re-test reliability coefficients (with a one-week interval) ranging from 0.43 to 0.79 [18]. In the study, cronbach's α coefficients for the eight dimensions in the healthy group ranged from 0.68 to 0.90, indicating the scale's acceptable reliability [19]. In the chronic patient group, these coefficients ranged from 0.66 to 0.91.

Cancer psychological impact scale

The scale of the psychological impact of cancer by Hulbert-Williams et al. (2019) [15], with 12 items, measures four factors: Cognitive distress, cognitive avoidance, emotional distress, and fighting spirit. The internal validity of all indicators and the concurrent validity compared with the longer versions were >0.62. The reliability of the mental distress questionnaire was confirmed by the test-re-test method with a correlation coefficient of 0.95 [19]. The reliability of the mental distress questionnaire subscales was confirmed by the internal consistency method with cronbach's α (α=0.88). Also, the reliability of the mental distress subscales was examined by the internal consistency method, with cronbach's α for cognitive distress (α=0.73), cognitive avoidance (α=0.83), emotional distress (α=0.80), and fighting spirit (α=0.93). Analyses and assessment results showed that the content validity index of the scale was 0.96. In the exploratory factor analysis of the Turkish adaptation study, the total variance explained was 84.98. The factor loading of all items ranged from 0.82 to 0.94. Cronbach's α values ranged from 0.860 to 0.930, and the total-scale Cronbach α was 0.844 [20]. Confirmatory factor analysis was employed in the current study to examine the validity of the psychological distress questionnaire. Cronbach's α coefficients for all four factors exceeded 0.7, and the fit indices (GFI, CFI, and NFI) were above 0.9. The model fit was confirmed based on the RMSEA index (0.042, <0.1 threshold) and P (0.05474, >0.05). Additionally, the chi-square to degrees of freedom ratio was <3, indicating optimal model fit. The best-fitting model was achieved using four factors.

Cognitive flexibility inventory, Dennis et al. (2010) [16]

The cognitive flexibility inventory was created as a concise self-report tool to assess the cognitive flexibility required for individuals to effectively challenge and replace maladaptive thoughts with more balanced and adaptive ones. It evaluates three key aspects of cognitive flexibility: a) the perception of difficult situations as controllable; b) the ability to see multiple alternative explanations for life events and human behavior; and c) the capacity to generate multiple alternative solutions to challenging situations.

Researchers presented two studies: The initial development of the CFI (time 1) and a 7-week longitudinal study (time 2). Findings from these studies show that the CFI has a reliable two-factor structure, excellent internal consistency, and high 7-week test-re-test reliability. Preliminary evidence for the CFI's convergent construct validity was obtained through its correlations with other measures of cognitive flexibility (cognitive flexibility scale [CFS]) and coping (ways of coping checklist-revised). Additionally, the CFI's concurrent construct validity was supported by its correlation with the Beck's Depression Inventory (BDI)-II. Therefore, greater cognitive rigidity on the CFI was associated with increasing depressive symptomatology on the BDI-II. A fundamental principle of CBT is that depression is most effectively treated with interventions geared toward breaking down automatic maladaptive cognitions and replacing them with more realistic, adaptive cognitions [21]. The correlations between the BDI-II and the CFI's alternatives subscale at time 1 (r=-0.19, P<0.01) and Time 2 (r=-0.20, P<0.01) and the CFI's control subscale at time 1 (r=-0.50, P<0.001) and Time 2 (r=-0.44, P<0.001) provided further support for the concurrent criterion validity of these subscales. Martin and Rubin's CFS, a 12-item self-report measure of cognitive flexibility, was developed to measure aspects of cognitive flexibility considered necessary for effective communication. Research found concurrent validity of 0.75 with the CFS scale. For comparison, the BDI-II was significantly correlated with the CFS at time 1 (r=-0.42, P<0.001) and time 2 (r=-0.34, P<0.001). The CFI and CFS shared approximately 56% of their variance. Additionally, research has indicated that the CFI has significantly stronger internal consistency compared to the CFS [16].

CFI has been validated in Iran, and one of the questions has been removed from its Persian version due to its low factor loading [12]. The CFI has 19 questions and two components: The perception of controllability and problem-solving processing. In Iran, the re-test coefficient of the whole scale was reported as 0.71 and cronbach's α coefficient was reported as 0.9 [22]. The cronbach's α coefficients of the subscales were 0.72, 0.77, and 0.63, and for the whole scale, 0.84. In this study, the cronbach's α coefficient was 0.88. The cronbach's α coefficient for this questionnaire was estimated to be 0.893 [23]. In the present study, cronbach's α coefficients for both factors exceeded 0.7. The fit indices (GFI, CFI, and NFI) were all >0.9, with RMSEA=0.068 (<0.1 threshold), and P=0.09235 >0.05). Furthermore, the chi-square to degrees of freedom ratio was <3, indicating optimal model fit for the two-factor structure.

The standard questionnaire of self-compassion, Raes et al. (2011) [17], short form

The self-compassion questionnaire by Raes et al. (2011) [17], measures the three components of self-compassion: Self-kindness versus self-judgment, common humanity versus isolation, and mindfulness versus over-identification. This questionnaire has 12 questions and six subscales.

The cronbach's α coefficient calculated for this questionnaire was estimated to be 0.91 [24]. In the study by Raes et al. the validity of the short form of this scale was confirmed (internal consistency=0.86). In Iranian studies, the cronbach's α for the short form of this scale was 0.68 [25]. The short form of the scale had a high correlation (0.97) with the long form, and a test-re-test reliability of 0.92 was reported. The internal consistency reliability of the short form was 0.86. Additionally, cronbach's α coefficients for the short form and its subscales ranged from 0.55 to 0.81. Studies have shown that concurrent validity of the GH questionnaire was 0.45 (P<0.001), and for the six subscales, it ranged from 0.28 (P<0.036) to 0.48 (P<0.001) [26]. Furthermore, these researchers reported cronbach's α coefficients for the subscales of self-kindness, self-judgment, common humanity, isolation, mindfulness, and over-identification as 0.83, 0.87, 0.88, 0.92, and 0.77, respectively [27]. In the current study, cronbach's α for all six factors was >0.7. The fit indices GFI, CFI, and NFI were above 0.9, the chi-square to degrees of freedom ratio was 1.24 (<3), RMSEA was 0.034 (<0.1), and P=0.015236 (>0.05), confirming optimal model fit for the six-factor structure.

Results

The results showed that 37.4% of the sample was 25-45, 54% was 45-65, and 11.4% were 65-85 years old. For 11.8% of the sample, three months had passed since their last chemotherapy, for 14.87% it was 6 months, for 36.77% it was one year, for 27.2% it was more than two years, for 6.4% it was >5 years, and for 1% it was more than ten years. A total of 53% had less than a high school diploma, 26% held a high school diploma, 10% had a bachelor's degree, and 11% possessed a master's or doctoral degree. Thirteen percent were household heads while 87% were not.

The results show that the tolerance coefficient values of all predictor variables are >0.1 and their variance inflation factor values are smaller than 10. The tolerance coefficients for self-compassion, mental distress, cognitive flexibility, and QoL are 0.791, 0.787, 0.913, and 0.842,

Table 1. Correlation coefficients between research variables (n=202)

Variables	Self-Compassion	Mental Distress	Cognitive Flexibility	Spiritual Distress	QoL
Self-compassion	1	-	-	-	-
Mental distress	r=–0.435, P<0.01	1	-	-	-
Cognitive flexibility	r=0.191, P<0.01	r=–0.044, P>0.05	1	-	-
Spiritual distress	r=–0.591, P<0.01	r=–0.627, P<0.01	r=–0.322, P<0.05	1	-
QoL	r=0.487, P<0.01	r=–0.428, P<0.01	r=0.255, P<0.01	r=–0.506, P<0.01	1

*P<0.05, **P<0.01.

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respectively. The variance inflation factors are 1.264, 1.271, 1.095, and 1.188, respectively. Therefore, it can be said that the assumption of non-collinearity among the research data is valid. To evaluate the establishment or non-establishment of the assumption of normality of the multivariate distribution, the analysis of information related to "Mahalanobis distance" and the drawing of its distribution diagram were used. The Mahalanobis distance, considering relationships between variables, indicates how far each data point is from the data center and was thus used to assess multivariate normality. The skewness and kurtosis of the Mahalanobis distance scores are 1.62 and 1.27, respectively, which shows that the kurtosis of the Mahalanobis data is ±2, and the assumption of the normality of the multivariate distribution among the data is established.

To evaluate whether error distributions were equal across all data levels (homoscedasticity assessment), scatter plots of standardized residuals were examined. The random dispersion of points without specific patterns in the scatter plots confirmed the assumption of homoscedasticity for the study data. Since correlations exceeding 0.8 between exogenous variables indicate multicollinearity, the correlation coefficients between study variables presented in Table 1 confirmed the absence of multicollinearity.

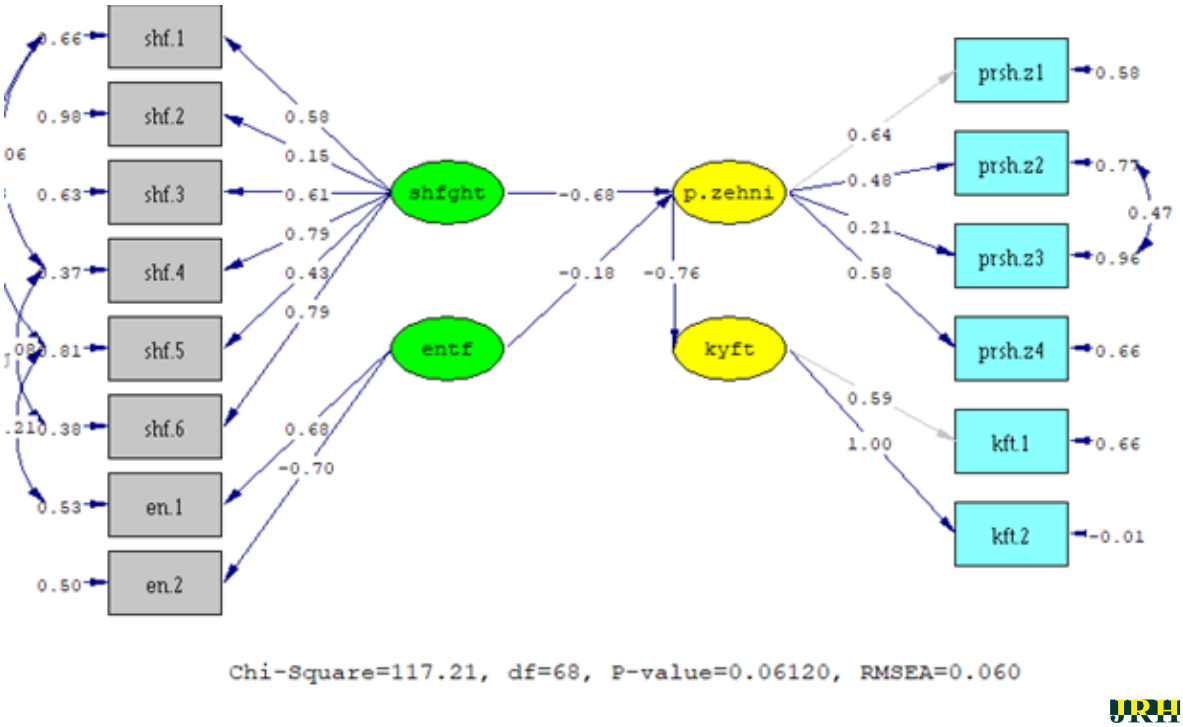

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Figure 1. Factor loading coefficients of the conceptual model of the relationship between self-compassion and cognitive flexibility with quality of life through mental distress

Table 2. Fit indices of the structural equation model of the research

Index	Adequate Fit	Desirability
Quadratic to degrees of freedom	1.72	1-5
RMSEA	0.06	<0.1
NFI	0.94	>0.9
CFI	0.97	>0.9
GFI	0.92	>0.9

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Table 3. Estimation of the standardized coefficients of the research model based on the first question with the ML method

Routes	Product of Direct Betas	The Coefficient of Determining	The Sobel Statistic	The Significance Level
Self-compassion⟶mental distress⟶QoL	0.52	0.58	2.43	<0.05
Cognitive flexibility⟶mental distress⟶QoL	0.14		0.70	>0.05

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Based on the theoretical foundations and the conducted research, a hypothetical model was developed that includes the variables of self-compassion, cognitive flexibility, mental distress, and QoL. The results of structural equation modeling in Figure 1 show the fit of the conceptual model of the relationship between self-compassion and cognitive flexibility with QoL through mental distress. After modifying the model, the covariance between errors was established, and the model was presented.

Table 2 presents several indices of absolute and comparative fit. The absolute fit indices indicate how well the proposed hypothetical model matches the observed data. RMSEA, GFI, and chi-square are examples of absolute fit indices. Comparative fit indices show the model's relative fit, ranging from worst fit (zero) to best fit (one). The acceptance threshold for a good fit in this group of indices is 0.9. NFI is an example of a CFI. Parsimonious fit indices are used to compare different models with varying parameters. When the values of at least three fit indices fall within the acceptable range, we can claim that the model fit is good and acceptable.

The ratio of the chi-square to the number of degrees of freedom was 1.72, which is between 1 and 5. At the same time, the RMSEA was 0.06, below the threshold of 0.1, indicating that it fell within the acceptable range. The GFI, CFI, and NFI were 0.92, 0.97, and 0.94, respectively, within the acceptable range. Therefore, since at least three fit indices fell within the acceptable range, we can claim that the model fit is good and acceptable. According to the results of the figure and the P obtained, which was 0.0612 and >0.05, it can be concluded that the fit of the conceptual model of the relationship between self-compassion and cognitive flexibility with QoL through mental distress was confirmed with the data, and the results obtained from the fitting of this model were reliable. The results of examining the coefficients related to the direct paths of the model showed that the relationship between self-compassion and mental distress (β=-0.69), the relationship between self-compassion and QoL (β=0.67), the relationship between cognitive flexibility and mental distress (β=-0.53), the relationship between cognitive flexibility and QoL (β=0.59) and the relationship between mental distress and QoL (β=-0.71) were significant at the significance level of 0.05.

The results of the Sobel test in Table 3 to investigate the mediating role of mental distress in the relationship between self-compassion and cognitive flexibility with QoL show that at a significance level of <0.05, self-compassion has a significant effect on the QoL through mental distress (P<0.05, β=0.52); however, cognitive flexibility does not have a significant effect on the QoL through mental distress (P>0.05, β=0.14).

Discussion

This study aimed to determine whether self-compassion (an emotional factor) or cognitive flexibility (a cognitive factor) has a greater impact on the QoL in breast

cancer survivors, considering the mediating role of mental distress. This study also explored whether mental distress can simultaneously mediate the relationship between self-compassion, cognitive flexibility, and QoL. The findings indicated that self-compassion showed a significant negative relationship with mental distress and self-compassion significantly predicted mental distress in the direct path. The proposed model of this study was well-suited to the sample analyzed. Consequently, self-compassion significantly influenced the QoL by reducing mental distress (β=-0.52, P<0.05). However, cognitive flexibility did not significantly impact QoL through mental distress (β=-0.14, P<0.05). These results can serve as a foundation for future research. Given that self-compassion, through the reduction of psychological distress, may be more effective in enhancing the QoL compared to cognitive flexibility via the same pathway, the question arises: Will the application of self-compassion therapy yield better outcomes in improving the QoL for breast cancer survivors compared to acceptance and commitment therapy? A review of the research literature in this context revealed that lower self-compassion was associated with higher emotional distress [28]. The reduction of self-compassion in the form of an ineffective strategy causes the patient's emotional distress to intensify [29]. Self-compassion is less associated with increased psychological distress among breast cancer survivors. Self-compassion was found to mediate the relationship between body image disorders and psychological distress [30]. Higher self-compassion scores are associated with lower psychological distress [31]. However, researchers also mentioned that self-compassion and mindfulness reduce psychological distress [32].

In the present study on breast cancer survivors, cognitive flexibility had a significant negative relationship with mental distress. Cognitive flexibility also significantly predicted mental distress in the direct path. Researchers showed that psychological flexibility is directly related to the psychological distress of mothers with children with leukemia [33]. In this regard, it was shown that treatment based on increasing psychological flexibility leads to a significant reduction of psychological distress and an increase in QoL in women with multiple sclerosis [34]. Consistent with previous findings, the studies showed that treatment based on acceptance and commitment can reduce psychological distress in women with breast cancer [35]. Researchers have found a negative and significant relationship between the psychological distress of female cancer patients and their QoL [5]. Depression can have a significant effect on the QoL of cancer patients, which is consistent with some research by Bektas and Demir, So et al. Celik et al. Zenger et al. and Hutter et al. [36-40]. Researchers have shown a significant negative correlation between self-compassion and psychological inflexibility, and psychological inflexibility significantly predicts depression [41]. Self-compassion significantly influences cognitive flexibility in cancer patients by facilitating emotional regulation and reducing negative self-criticism. This capacity enables patients to adopt more adaptive coping strategies and positively reframe their experiences, ultimately enhancing their psychological well-being and QoL [42]. Self-compassion and psychological inflexibility both showed a strong and significant relationship with distress, but not with QoL. Research in psychological inflexibility showed a significant moderating effect on the relationship between the QoL of breast cancer patients with depression, anxiety, fatigue, and functional status [43]. Therefore, by reducing anxiety, depression, fatigue, and functional problems, the psychologically flexible participants reported a better QoL [42]. In the present study, the mediating role of mental distress in predicting the QoL within an endogenous variable has been investigated using cognitive flexibility as an exogenous variable. This study had several limitations. Patients residing outside Birjand City, as well as those within the city who were unwilling to complete the questionnaire in person, were administered the questions via telephone. Also, the situational, family, financial, emotional, and spiritual contexts of the patient on the day of filling out the questionnaire were not considered. Future research should consider economic problems, emotional support from spouses, and experiences of trauma in addition to the cancer diagnosis. This model was only applied to breast cancer in women; however, more comprehensive studies could be conducted on various types of cancer in men. Given the transdiagnostic nature of personality traits in most disorders, this study could be extended to examine different personality traits. The effectiveness of an integrated intervention combining acceptance and commitment therapy (focusing on cognitive flexibility) and compassion-focused therapy (emphasizing self-compassion) was investigated for enhancing QoL among patients with, or recovering from, breast cancer. Research has explored the effectiveness of integrating compassion-focused therapy with spiritual therapy in improving the QoL of individuals undergoing treatment for, or recovering from, breast cancer. Furthermore, efforts have been directed toward developing communication protocols informed by the specific components of mental distress, intended to guide oncology healthcare personnel in enhancing the QoL of cancer patients. Synchronizing the administration of medical and psychological treatment protocols for patients with various cancer diagnoses in oncology centers can be

beneficial. Self-compassion integration strategies in cancer patient care include mindfulness exercises and daily writing to enhance compassion skills and reduce self-criticism. Compassion-focused practices encourage patients to develop a compassionate mindset toward themselves and others by decreasing self-judgment. Group interventions that facilitate shared experiences and the practice of collective self-compassion contribute to the development of a supportive environment, ultimately leading to reductions in psychological distress and improvements in overall QoL [43].

Conclusion

The present study showed that the role of mental distress as a mediator in the relationship between self-compassion and QoL is significant, and psychological flexibility in the presence of the relationship between self-compassion and the mediation of mental distress with QoL cannot increase the QoL through mental distress. This shows that self-compassion (an emotional component) plays a stronger role than cognitive flexibility (a cognitive component) in predicting QoL via the indirect path of mental distress.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Birjand University of Medical Sciences, Birjand, Iran (Code: IR.BUMS.REC.1402.035). Informed consent was obtained via telephone, with research objectives explained to the participants. Participants were assured of no harm from participation and guaranteed complete confidentiality-no personal identifiers were collected on questionnaires. Additionally, to encourage participation, free psychotherapy interventions were offered outside the study framework.

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Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interpretation of the results, and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflict of interest

The authors declared no conflicts of interest.

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