Biological Stress Indicators based on Perceived Stress mediated by Emotional Regulation among Patients with Gastrointestinal Cancer: A Structural Equation Modeling

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Abstract

Background: Cancer is a disorder in the rate of cell proliferation and differentiation that can occur in any tissue of the body and at any age, and attacking healthy tissues of the body causes severe disease and consequently death.

Objective: This study aimed to analyze biological indicators of stress based on perceived stress mediated by emotional regulation among patients with gastrointestinal cancer using structural equation modeling.

Methods: This descriptive-correlational research was conducted based on a structural equation modeling approach. The statistical population of the present study included all patients with gastrointestinal cancer referred to Reza-Mashhad medical center and Avicenna Hospital, Tehran, Iran, and diagnosed with this disease based on the patient's medical record. The sample of this study included 250 cases selected using non-random and available sampling methods. The required data in this study were obtained using the questionnaires, namely the Perceived Stress Scale, Cognitive Emotion Regulation Questionnaire, and Biological Indicators of Stress. The collected data were analyzed in SPSS software (version 22) and AMOS software (version 22) using structural equation modeling and Pearson correlation coefficient.

Results: The results showed that perceived stress (β=-0.37, P<0.001) directly affected emotional regulation. Moreover, emotional regulation (β=0.54, P<0.001) had a direct effect on biological stress indices. Emotional regulation played a mediating role in the relationship between perceived stress and biological stress indices (root mean square error of approximation:0.001; adjusted goodness of fit: 0.93).

Conclusion: It can be concluded that the biological indicators of stress in patients with gastrointestinal cancer based on perceived stress mediated by emotional regulation using structural equation modeling had a good fit.

Keywords: Gastrointestinal cancer, Biological indicators of stress, Emotion regulation

1. Introduction

Cancer is one of the leading causes of death after cardiovascular disease in most countries worldwide. Among cancers, gastrointestinal cancer is one of the leading causes of cancer mortality (1). In terms of incidence, gastric cancer is the fourth most common cancer and the second leading death cancer in the world; however, the incidence of this cancer (especially in developed countries) is decreasing in the world. In the United States, the incidence of this cancer has been declining in recent decades (2). In Iran, this cancer is of particular importance and is considered one of the major health problems. According to the latest researches in Iran, gastric cancer, with a frequency percentage of 9.3%, is the third most common cancer in the country in general, both in men and women. Considering the prevalence of gastric cancer and its high mortality rate in the country, it is necessary to investigate the causes and factors affecting the incidence of this disease (3).

Perceived stress is a psychological variable that can affect the biological index of stress. For a person who is under stressful conditions, it is important to assess stress levels and coping strategies. High, persistent, and prolonged stress can lead to inconsistencies in the individual and cause physical and emotional problems, such as dissatisfaction, anxiety, severe stress, frustration, defensive behaviors, and depression, as well as feeling of failure and undesirable quality of life (4). There is

strong evidence that stress can lead to different negative outcomes, including physical illness, mental disorders, or feelings of burnout (5).

On the other hand, emotion regulation is defined as the process of adjusting one or more aspects of experiences or emotional responses (6). Cognitive emotion regulation involves negative (maladaptive) and positive (adaptive) strategies. In relation to negative strategies, individuals blame and criticize themselves or others in confrontation with a terrible event. They always think about it as an uncomfortable incidence (rumination) and consider it more terrifying than what it really is (angst). On the other hand, in relation to positive strategies, one may look at positive events instead of negative events (positive re-focus), give that event a positive meaning (positive reassessment of the individual), consider it relative, and believe that it is relative compared to other events. It has not been (development of perspective), it is possible to plan for a proper encounter with that event (positive re-focus on planning), or accept that event and act to deal with it (acceptance) (7-8). Therefore, it seems necessary to evaluate the health status and factors affecting it among patients with this chronic disease.

A cancer diagnosis is a very unpleasant and unbelievable experience for every individual. Cancer causes impairments in the job, socioeconomic status, and family life, leading to the devastation of a patient's life. These issues affect especially different aspects of the quality of life of a patient, including mental, social, economic, and sexual function, and increase stress levels among such cases. Considering the relatively high prevalence of cancer types in Iran and psychosocial and familial-social complications of this disease, it is necessary to identify psychological and intra-psychological factors affecting the psychological well-being of these patients. Accordingly, this study was conducted to analyze the biological indicators of stress in patients with gastrointestinal cancer based on perceived stress mediated by emotional regulation using structural equation modeling.

2. Methods

This descriptive-correlational research was conducted based on a structural equation modeling approach. The statistical population of this study consisted of all patients with gastrointestinal cancer referred to Reza-Mashhad medical center and Avicenna Hospital in Tehran, Iran, 2019, The sample (n=205) consisted of patients being diagnosed with this disease according to their medical record and were selected using the convenience sampling method. According to Klein, if structural equation modeling is used, about 20 samples are required for each factor (latent variable), and the minimum sample size of

200 is defensible (9). In this study, five main variables (i.e., five independent variables and one dependent variable with an average of two components for each variable) were investigated. According to Klein's theoretical foundations for selecting the sample, 20 samples for each component are required. However, the final sample number was determined as 250 cases to control the probability of drop-out rate and achieve more validity. In the present study, first, the researchers negotiated with educational and therapeutic centers affiliated to Tehran University of Medical Sciences, Tehran, Iran. Subsequently, the researchers obtained the approval of authorities in these centers, received the necessary permission, and signed the ethical contract, and selected the members of the sample group. The overall research procedures were explained to all participants, and if they agreed to participate in the research, the research plan questionnaires were distributed among them to complete.

Regarding the ethical considerations of the present study, the research objectives and procedures were explained to all individuals in written form, and they were informed of the right to leave the study at any time. Moreover, all participants were assured of anonymity and confidentiality in this study.

The inclusion criteria were having gastrointestinal cancer, having consent to participate in the study, lacking serious medical disease other than cancer, lacking major psychiatric disorder, and having substance dependency. On the other hand, the patients who had psychiatric disorders and substance abuse and those who did not respond to the questionnaires completely were excluded from the study. The collective analysis of the information was also discussed in this study. In the end, the contact number was provided to get informed of the results of the questionnaires if they wished.

Perceived Stress Scale: This 14-item scale, developed by Cohen et al. (2004) consists of two subscales and is scored on a 5-point Likert scale (0=none, 1=low, 2=medium, 3=high, and 4=very high). The internal consistency coefficients of this scale were obtained using Cronbach's alpha coefficient in a range of 0.84-0.86 in two groups of students and a group of smokers in the Leave program. In a study performed on Japanese students, Cronbach's alpha coefficient of the original revised Japanese scale was obtained at 0.81 (10). In this study, Cronbach's alpha coefficients for positive and negative perceived stress were calculated at 0.78 and 0.72, respectively.

Cognitive Emotion Regulation Questionnaire: This 36-item self-report instrument was designed by Garnefski et al. (2006) to identify cognitive coping strategies.
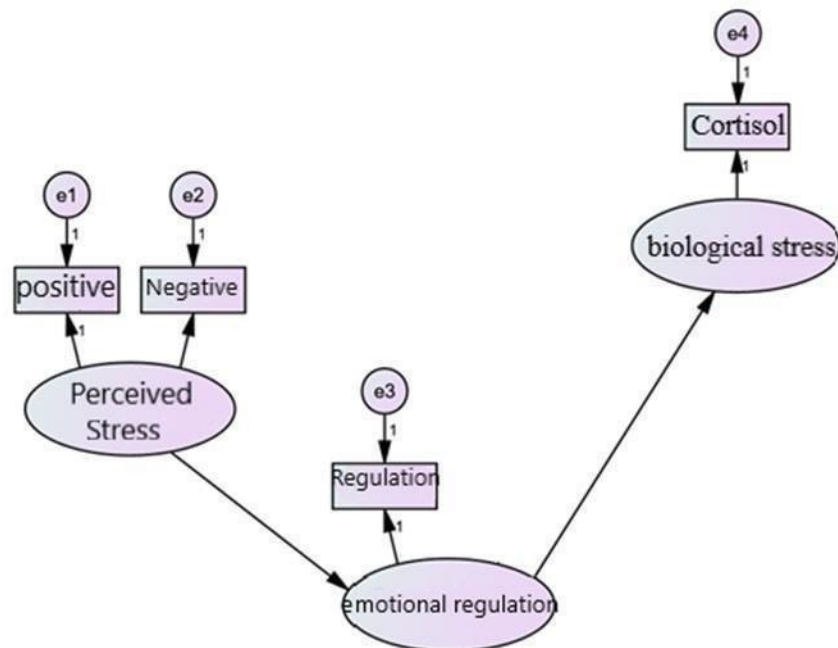
Figure 1. Conceptual model ofresearch

This questionnaire evaluates nine subscales of nine cognitive strategies of self-blame, acceptance, emotional regulation, positive refocusing, refocusing on planning, positive reappraisal, putting into perspective, catastrophizing, and blaming others. This instrument is rated on a 5-point Likert scale ranging from 1=almost never to 5=almost always. The score of each strategy is obtained through the sum of the scores given to each of the phrases that constitute that strategy resulting in the range of 4-20, with the total range score of 36-180. High scores in each subscale indicate that the strategy is more used against stressful and negative events. Garnefski et al calculated Cronbach's alpha coefficient for the nine subscales and reported a range of 0.62-0.80 (11). The internal consistency coefficient of this questionnaire was obtained at 0.83 by Cronbach's alpha coefficient.
Biological Stress Indices: Glucocorticoids play a complex role in response to stress, including mediation in response to current stress, inhibition of response to present stress, and body preparation for later stress. Glucocorticoid receptors are present in all tissues of the body and play a role in the volume of body fluids, cardiovascular system, inflammation and immune system, metabolism, sugar displacement, appetite, cognition, and fertility. Glucocorticoids can be measured in serum, urine, nails, and hair. Biological stress indicators include catecholamines, epinephrine and norepinephrine, dopamine, and inflammatory cytokines.

In descriptive statistics, mean and standard deviation indices were used to organize, summarize, and describe information about the characteristics of subjects and variables. Inferential statistics, structural equation modeling, and Pearson correlation coefficient methods were used to analyze the data.

Table 1. Descriptive statistics of research variables

Variables		M	SD	Min.	Max.	Skewness	Kurtosis
Perceived stress	Positive perception	15.51	2.84	5	23	0.74	0.18
	Negative perception	17.22	5.53	8	25	0.04	0.18
Emotional regulation		109.13	17.60	47	150	0.47	0.18
Biological Stress Indicators (Cortisol)		26.81	32.94	1.80	149	0.14	0.18

Table 2. Coefficients and significant direct effect of exogenous variables of perceived stress on emotional regulation (middle dependent) and biological stress indicators variable (main dependent)

Predicting variable	Criterion variable	B	β	T	P
Perceived stress	Emotional regulation	-0.45	-0.37	3.04	0.002
Emotional regulation	Biological stress indicators	0.57	0.54	2.49	0.001

The above statistical analyses were performed in SPSS software (version 22) and AMOS software (version22).

3. Results

The mean age of the participants was estimated at 57.17±13.39 years. The maximum and minimum age scores were obtained at 83 and 32 years, respectively.

Since path analysis is the correlation matrix among the variables, in this section, the correlation matrix is first reported in this section. Correlation coefficients between perceived stress, emotional regulation, and biological stress indicators were statistically significant (P<0.05). The coefficients of skewness and kurtosis related to the distribution of the scores of research variables showed that due to normality, the research variables all had the absolute magnitude of the crooked coefficient less than three, and the absolute value of the elongation coefficient was less than one. Therefore, the violation of the normality of the data was not visible. As a result, it can be said that the

distribution of research variables was normal. The obtained tolerance values for variables were above 0.10, which indicated the absence of multiple linear regression values between variables. Moreover, the amount of variance inflation factor obtained for variables was smaller than ten, showing that there were no multiple linear regression values between the variables. The results of implementing the initial model in standard mode, along with some of the most important indicators of model grace, are presented in Figure 1 and Table 2. Table 2 tabulates their structural patterns, pathways, and standard coefficients in the final model of the present study.

According to Table 2, perceived stress had a direct effect on emotional regulation and biological stress indicators; therefore, the hypothesis about the relationship among perceived stress and emotional regulation and biological stress indices was confirmed with 95% confidence (P<0.01). Bootstrap instructions were used to

Table 3. Estimation of indirect paths in the model using bootstrap

Variables			B	β	Upper limit	Low limit	P
Perceived stress	Emotional regulation	Biological Stress Indicators	0.097	0.080	0.078	0.006	0.049

Table 4. Model fit index

Index	Fit Indices	
	Value	Limit
$\square\square\square\square^{\square\square\square\square}$ (df)	0.11	Less than 3
RMSEA	0.001	Less than 0.1
CFI	0.97	More than 0.9
NFI	0.97	More than 0.9
GFI	0.92	More than 0.9
AGFI	0.93	More than 0.9
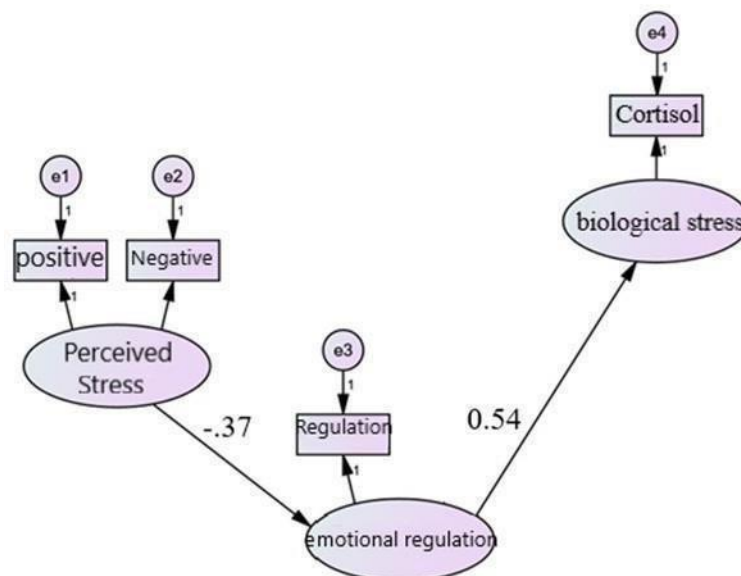
Figure 2. Final fitted model ofresearch

investigate the mediating role of emotional regulation in the relationship between perceived stress and biological stress indices (Table 4).

As Table 3 shows, the indirect effect of perceived stress on biological stress indices is obtained at 0.08 (P=0.049). The results of Table 4 obtained for these indicators show that, in general, the model has a good status to explain and fit.

Discussion

This study aimed to analyze the biological indicators of stress based on perceived stress mediated by emotional regulation among patients with gastrointestinal cancer using structural equation modeling. According to the results, perceived stress had a negative and inverse effect on emotion regulation. It was also revealed that emotion regulation had a positive and direct effect on biological stress indices. The results were in line with those of the studies performed by Song et al. (12) and Levy-Gigi et al. (13).

To explain this finding, it can be said that the nature of cancer makes the patient face many ambiguities due to the difficult conditions of the disease and even the treatment and its side effects. Meanwhile, the patient is unaware of how the disease would respond to the treatment or he/she may think that not only the treatment is inefficient but also the disease spreads to other parts of the body. In this regard, the presence of such ambiguities and the patient's reaction to cancer lead to a high level of perceived stress in such patients and keep the negative mood and stress modes active in the defective cognitive cycle.

Psychological and biological stress activates the sympathetic system, and arterial pressure is determined by two factors, namely cardiac exogenous and blood vessel resistance. Sympathetic system stimulation increases the number and strength of heart rate and vascular resistance at the same time and has a significant and acute increase in arterial pressure (14). The sweat glands also secrete a lot of sweat by sympathetic stimulation, which moisturizes the skin. Some cancer patients have negative beliefs about their emotions, such as their emotions are meaningless, a source of shame, and exclusive to them, cannot be expressed, will never be validated, and the disease will continue forever and kill them. Such individuals may most likely use troublesome methods to cope (e.g., emotional regulation, worry, and avoidance) (15). Others benefit from more positive or adaptive views of emotion and can be more valid. The emotions of such individuals are meaningful and acceptable to them, not embarrassing, not self-exclusive, and not long-term; however, they are considered transient. As a result, these individuals may be less likely to use troublesome coping strategies (15).

In explaining this multifaceted interaction, it should be noted that the hypothalamus-hippophysic-adrenal axis affects energy metabolism, immune system function, and mood. On the other hand, emotional states and personality traits may affect intestinal physiology and play a role in the experience and interpretation of symptoms. The brain is associated with the intestine through the autonomic nervous system. The vagus nerve and pelvic nerves send information about muscle movements and intestinal contents to the brain. On the other hand, the brain also sends signals through the autonomic nervous system to the intestines, and there is a bilateral relationship between the brain and the intestines. Additionally, the brain can regulate intestinal activity in other ways. For example, corticotropin hormone, which is released from the brain during perceived stress, can change intestinal activity. These mechanisms are the evidence that cancer is severely affected by psychological factors (16). According to recent studies, 50-90% of patients with gastrointestinal cancer have a history of a psychological condition, such as major depressive disorder, body disorder, and post-traumatic stress disorder throughout their lives. More than 50% of axis 1 and 100% of axis 2 disorders are associated with emotion regulation deficits, which is in line with the results of this study. Consequently, the researchers witnessed the potential of mutual dependence in different methods of emotional processing and the decisive role of stress in changing brain-intestinal functions mediated by emotion regulation mechanisms. In general, there is a complex pattern that researchers have not yet fully understand or described.

It can also be stated that the lack of acceptance of emotional responses reflects the tendency to have negative secondary responses to negative emotions or non-acceptance of reactions to distress. The difficulty in handling targeted behavior reflects the difficulties of focusing and finishing tasks when experiencing negative emotions, which can be performed to regulate their emotions and emotional transparency, indicating the individual's awareness of his emotions and the clarity of these emotions for him (17). Considering that each component of difficulty in emotion regulation was presented, it is obvious that these components have a relationship with the experience of perceived stress caused by the disease since life-related stress considers living conditions as a source of perceived stress. When a person is unable to adjust his emotions, accept reactions to them, control his behaviors when experiencing negative emotions, focus on life affairs when experiencing negative emotions, and believe that he cannot do much and carry out effective work to regulate his emotions during turmoil, he will reciprocate to experience perceived stress to a

greater extent from the source of life. According to the above, perceived stress had a negative effect on emotion regulation, which in turn, had an effect on biological stress indices.

The limitation of this study was the use of the correlation method, which limited causal inference about the resulting relationships. The other limitation was related to the population of this study, which was conducted only on the patients with gastrointestinal cancer in Tehran. Therefore, caution should be taken in generalizing the results of the present research to other regions and cities. It is suggested that this study be conducted in another sample group, and the results be evaluated and compared with those of this study. It is also recommended that the present study be implemented in the form of an experimental study, in which the effect of teaching different methods are investigated on the biological indicators of stress, perceived stress, and emotional regulation of patients with gastrointestinal cancer. Moreover, this study should be conducted in other cities, and its results should be evaluated. A larger community of patients with gastrointestinal cancer increases generalization to improve biological indicators of stress, perceived stress, resilience, hardiness, emotional regulation, and rumination. In case that several types of research are conducted in different centers, a suitable platform will be provided for comparing the results and better application of these pieces of research. Considering the role of resilience, hardiness, and emotional regulation in the relationship between perceived stress and rumination among patients with gastrointestinal cancer, it is suggested that educational programs and courses be held to promote the mentioned skills in such patients. It is also recommended specialists be trained by relevant organizations to improve the biological indicators of stress, perceived stress, and emotional regulation in patients with gastrointestinal cancer.

Conclusion

It can be concluded that the structural model of biological indicators of stress in patients with gastrointestinal cancer based on perceived stress mediated by emotional regulation had a good fit.

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