The Role of Cognitive Dysfunction and Health Literacy on the Quality of Life in Cancer Survivors

Fatemeh Keshmiri Nasrabadi 1, Susan Rahimzadeh 1, * and Mohammad Esmaeil Akbari 2

1 South Tehran Branch, Islamic Azad University, Tehran, Iran
2 Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
* Corresponding author: South Tehran Branch, Islamic Azad University, Tehran, Iran. Email: susan-r@azad.ac.ir

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Abstract

Background: Cancer disease is considered one of the basic health problems in the world, which threatens the health of human life. It causes numerous personal, family and social damages in physical, psychological, and social dimensions.

Objectives: The present study aimed at investigating health literacy and cognitive dysfunction on the quality of life of cancer survivors to make better decisions for the daily functioning, quality of life, and work capacity of cancer survivors so that their lives can be spent with more peace and less stress.

Methods: With a descriptive correlational design, 350 cancer survivors of the Cancer Research Cancer, Shahid Beheshti University of Medical Sciences (Shohadasy Tajrish Hospital) from September 2021 to November 2021, who had been treated for at least one year, volunteered online and in person. The questionnaires were the Cognitive Failure Questionnaire, Cancer Health Literacy Test, and Quality of Life in Adult Cancer Survivors questionnaire.

Results: Pearson correlation showed a negative relationship between cognitive dysfunction and quality of life; so, path analysis showed that 25% of the quality of life is predicted by cognitive dysfunction, but cancer health literacy was not correlated with the quality of life of cancer survivors.

Conclusions: According to the findings, the optimization of cognitive functions after treatment was emphasized to increase the quality of life of cancer survivors.

Keywords: Health Literacy, Cognitive Dysfunction, Quality of Life, Cancer Survivors

1. Background

Cancer is a major health problem and one of the leading causes of death worldwide. By 2020, 10 million people will be victims and it is predicted that 19.3 million new cases will be identified, and by 2040, the incidence of cancer will increase by 47% (1). From the end of the 20th century, the death rate from cancer in 2018 has decreased by 33%. In the United States in 2021, out of 1.2 million new cases of cancer, 1.2 million have survived (2). In Iran, 131 000 people have been diagnosed with cancer, of whom 79 000 have died of cancer and 52 000 have survived (3). The number of cancer survivors seems to have increased due to the continuous improvement in screening and treatment. Despite these improvements, many of them suffer from therapeutic side effects. There are 3 types of complications, including acute (occurring during treatment and lasting for a short time), chronic (occurring during treatment, lasting months and years), and delayed (occurring months, even years after treatment). Cancer treatment includes surgery, chemotherapy, radiation therapy, hormone therapy, or a combination of these methods. These therapies have many physical and psychological side effects that reduce the abilities and activities of the patient’s daily life (4). The most important side effects are psychological problems such as stress, anxiety, depression, fear of recurrence, cognitive problems, sleep and sex; physiological problems such as hair loss, appearance and body image concerns, pain, fatigue, nausea, difficulty breathing, vomiting; social problems such as social isolation, loss of social role and performance, intellectual concerns about the family, and financial problems (5-7) have all been pointed out, which ultimately worsen the quality of life (8). According to the World Health Organization (WHO), quality of life is a person’s perception of his or her position...
in life in terms of culture, the value system in which he or she lives, and goals, expectations, standards, and priorities. So, it is a completely subjective issue and is based on people's understanding of different aspects of life. In other words, high quality of life increases patients' adaptation and desire for complete treatment with minimal harm, and controls and overcomes the experienced symptoms (9). Research shows that one of the determining factors in the quality of life is the patient's level of cognition, which plays an important role in patients' decision-making and behavior. Cognition is defined as any type of information processing, mental function, or thought activity such as thinking, reasoning, remembering, imagining, or learning (10). However, drug therapies for cancer can have acute and long-term effects on cognitive function (11). Cognitive failure is the failure of a person to do things that he or she would normally be able to do. In other words, cognitive dysfunctions are a set of cognitive errors that occur when performing tasks that a person usually accomplishes (12). Cognitive dysfunctions can be a worrying side effect of cancer and their treatment that seriously affect the quality of life and productivity at work. Studies show that about 30% of patients with breast cancer develop cognitive dysfunction before chemotherapy and up to 75% after chemotherapy (13). Cancer and its therapies (chemotherapy) mainly affect the areas of attention, concentration, executive function, processing speed (14), and visual, verbal and linguistic memory (15), which can persist for years after treatment and ultimately worsen the overall quality of life as well as the recovery of patients is compromised (16-19). A study by Crouch et al. (20) found that cognitive impairment in survivors was associated with age, sleep, receiving chemotherapy, neuropsychological symptoms, and poor quality of life. Recent studies show that along with cognitive dysfunction, patients' health literacy levels can also be decisive (21).

In the meantime, behavioral changes through health literacy to play an active role in medical decision-making are a prerequisite for informed healthcare decision-making. The WHO considers health literacy to be one of the most important determinants of health, which is related to a wide range of health findings (22). The medical institute defines health literacy as the ability of individuals to access, process, and understand the basic information and services needed to make appropriate health decisions (23). This concept is of particular importance in the health system, especially in the community of people with cancer. Because they have to make important decisions that ultimately have a major impact on treatment and their future. Since health literacy covers all aspects of health care such as prevention, screening, and diagnosis, it is considered the basis for the health care delivery system (24, 25). Patients and survivors can differ in health literacy, which refers to their ability to understand health information. Patients with high health literacy can easily understand written medical information and hospital forms (26). Research by Song et al. (27) has shown that reading drug labels and understanding prescription guidelines explain the paths that health literacy takes to adherence to medication and quality of life. Health literacy predicts quality of life-related to physical and mental health (28). Studies have shown that health literacy factors reflect social support, the guidance of health systems, understanding of health information, and active interaction with providers who have little or no relationship with the mental health base and little or no relationship with the physical health base (17, 29). Several factors that act as mediators influence the relationship between health literacy and quality of life. We can mention cultural characteristics, geographical location, self-efficacy, perceived social support, age, level of education, and health skills (30-34). As a result, it may affect the relationship between health literacy and quality of life (35). Age has a negative effect on 3 dimensions of health literacy: Health care system, health promotion, and disease prevention. As a result, it can be found that older patients have more difficulty finding information about mental health management (36). Poor health literacy can affect the function of cancer patients: Poor health, limited access to health care, reduced understanding of medical information, lack of interaction with physicians and health care personnel, and inconsistencies with treatment plans (37). They have a higher risk of hospitalization and increased mortality than people with higher health literacy (38). However, little is known about the relationship between health literacy and quality of life. Reading pen-paper and computer questionnaires is difficult to identify in clinical settings; so, literacy screening is not routinely performed and illiterate people tend to hide their reading problems and may even avoid medical care (39). Regarding colon cancer, Halverson et al. (21) believe that low health literacy is associated with low physical activity, increased smoking, lower quality of life, and higher mental distress. In another study, health literacy was not recognized as a risk factor for poorer quality of life (35, 39, 40). Thus, the quality of life of cancer survivors, on the one hand, is a function of cognitive activism, which is associated with numerous deficiencies after treatment, and on the other hand, adequate health literacy, which also facilitates the treatment process. Therefore, this study will try to answer the question: What is the role of cognitive dysfunction and health literacy on the quality of life of cancer survivors?
2. Objectives

Studies showed that cognitive functions and health literacy are two important factors in the quality of life of people and cancer and its treatment can cause many psychological problems in the quality of life of survivors. Therefore, the study of these two structures to improve and increase the quality of life of cancer survivors leads to better knowledge, more appropriate decisions, and the creation of a comprehensive care plan.

3. Methods

This research was conducted with a descriptive correlational design on cancer survivors from the Cancer Research Center of Shahid Beheshti University (Shodai Djirish Hospital) in 1400. The inclusion criteria for the research sample were: (1) having at least 18 years of age; (2) having at least general literacy (reading and writing, etc.); (3) at least 1 year after their last treatment without relapse; and (4) completing a written consent form. The exclusion criteria included: (1) being under 18 years of age; (2) people who relapsed after several years of recovery; and (3) recovering people who did not answer the questions completely were excluded from the present study (Table 1).

### Table 1. Demographic Information

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>59 (16.9)</td>
</tr>
<tr>
<td>Diploma</td>
<td>104 (29.7)</td>
</tr>
<tr>
<td>Associate degree</td>
<td>26 (7.4)</td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>102 (29.1)</td>
</tr>
<tr>
<td>Master’s degree</td>
<td>52 (14.9)</td>
</tr>
<tr>
<td>PhD</td>
<td>7 (2)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>36 (10.3)</td>
</tr>
<tr>
<td>Married</td>
<td>281 (80.3)</td>
</tr>
<tr>
<td>Divorced</td>
<td>20 (5.7)</td>
</tr>
<tr>
<td>Widow</td>
<td>13 (3.7)</td>
</tr>
</tbody>
</table>

3.1. Determine Sample Size and Method

Using Kline (41) in correlation schemes, the sample population can be considered 2.5 to 5 times the number of females, resulting in 350 cancer survivors non-random, voluntarily (in person, online) from 1 October to 30 December 1400 participated. The age range of survivors in the sample group was 29 to 74 years with an average of 46 years and a standard deviation of 10.75 years.

3.2. Measuring Tools

In this study, a Cognitive Failure Questionnaire (12), Cancer Health Literacy Test (22), and the Quality of Life of Adults surviving Cancer (5) were used.

3.2.1. Cognitive Failure Questionnaire

This questionnaire is one of the tools that is widely used in the evaluation of cognitive processes, from the age of 18 to 85 years (12). This questionnaire has 25 items with 3 subscales of distractibility (9 items), forgetfulness (8 items), and false triggering (8 items). In this questionnaire, participants are asked to indicate with a 5-point Likert scale how many of the errors described in the questionnaire have been experienced. The scores obtained are among the correct answers with a range of zero to 100 and are scored from the absence of error to the highest level of error. Scores are zero (never), 1 (very rarely), 2 (occasionally), 3 (quite often), and 4 (very often). Broadbent et al. (12), obtained Cronbach’s alpha coefficient of the Cognitive Failure Questionnaire 0.96. In their research, Zanesco et al. (42), obtained the Cronbach’s alpha coefficient of this questionnaire between 0.91 and 0.94 with high internal coordination. In an internal study, the retest validity of this questionnaire with a 1-month interval of 0.77 and Cronbach’s alpha coefficient of 0.83 was reported (43). In this study, Cronbach’s alpha coefficient was 0.77.

3.2.2. Cancer Health Literacy Test

The Cancer Health Literacy Test is one of the tools used to assess the health literacy of patients with cancer ranging in age from 18 to 93 years. The 30-item test, which deals with cancer treatment, drug side effects, and other related topics, was conducted in 2011 and 2013 at the University of Virginia and oncology clinics. This one-dimensional test includes knowledge (a survey of cancer knowledge and feedback on cancer), skills (for example, the ability to read medication labels, appointment cards, and insurance forms), and items that require a combination of knowledge and skills. The cancer health literacy test is provided to the subject to choose the correct answer to each material from the options provided. Scoring is based on the number of correct answers ranging from 0 to 30. The higher the number of correct answers, the higher the score and the higher the literacy level. Response to the materials takes between 10 and 15 minutes (22). In the study of Echeverri et al. (44), the validity of the health literacy test in the Spanish version was estimated to be 0.88. In this study, Cronbach’s alpha coefficient was 0.71.
3.2.3. Quality of Life in Adult Cancer Survivors

Avis et al. (5) designed this tool for adult cancer survivors, who have been diagnosed with cancer for at least 1 to 5 years, ranging in age from 29 to 92 years, with 47 items and 12 domains (7 are considered generic and 5 cancer-specific). The general dimension covers areas that are not necessarily related to cancer: Physical pain, positive feelings, negative feelings, cognitive problems, sexual problems, social avoidance, and fatigue. The cancer-specific dimension includes cancer-related areas: Financial problems caused by cancer, family-related distress, distress over recurrence, apparent concerns, and the benefits of cancer (for example, article 32: You found that cancer helped you better deal with problems). Answers are scored on a 7-point Likert from 1 (never), 2 (seldom), 3 (sometimes), 4 (about as often as not), 5 (frequently), 6 (very often), 7 (always)). Scoring is the realm of inverse positive emotions. In the general dimension, the range of each domain is from 4 to 28, and by adding the scores of each of the 7 domains, the total score is obtained with the range of 28 to 196. In the cancer-specific dimension, cancer benefit scores are reported separately, and the sum of the scores of the 4 areas (excluding the cancer benefit area) is shown in the range of 16 to 112 (three items multiply the family-related helplessness score by 1.33). The lower the score, the higher the quality of life and higher scores indicate more problems or lower quality of life (5). In Avis et al.’s study (5), Cronbach’s alpha coefficient was 0.72 and the retest was 0.72. In another study by Sohl et al. (45), Cronbach’s alpha coefficients for 12 domains were reported to be 0.70 to 0.91 with good convergent and divergent validity and retest higher than 0.70 with high internal coordination. In Iran, Cronbach’s alpha range for the 2 dimensions of the questionnaire was 0.74 and 0.93 with internal coordination of 0.99 (46). In the present study, Cronbach’s alpha coefficient was calculated for the general dimension of 0.92 and the specific dimension of 0.81.

4. Results

The statistical characteristics (such as the lowest, the highest, dispersion indices, and indices of the tendency to the center, etc.) of the measurements obtained from the research questionnaires, separated by three variables, are shown in Table 2.

As can be seen in the table above, the skewness values of all variables are negative, which shows that most of the people in the sample group have scored higher than the average in these variables.

To analyze the data, firstly, the relationship between the research variables is used through the Pearson torque correlation method, and its results are shown separately in the total scores of each variable in Table 3.

As can be seen in the table above, there is a significant but weak correlation between cognitive dysfunction with quality of life (r = -0.237) and a positive but weak correlation with cancer health literacy (r = 0.193). In other words, with increasing cognitive dysfunction, the quality of life in the sample group decreases, while increasing cognitive dysfunction is associated with increased cancer health literacy. Quality of life has no significant relationship with cancer health literacy.

According to the results of the assumption of linearity, to test the research hypotheses, 2 models of linear and nonlinear regression (curves) are used and the results are shown in Table 4.

As can be seen in Tables 2 - 4, the regression coefficient in the linear model is statistically significant for cognitive dysfunctional variables (F = 20.75, P < 0.01) at a level of less than 0.01 and the quality of life can be measured. It predicted the basis of this variable; but cancer health literacy (F = 0.63, P < 0.183) has no statistically significant relationship with quality of life. The value of R2 for this model and the dysfunctional variable is 0.112. Thus, it can be concluded that about 11% of the quality of life is explained by the variable of cognitive dysfunction.

On the other hand, regression coefficients for the cognitive dysfunction variable in the nonlinear model (F = 21.82, P < 0.01) are also significant at a level less than 0.01. Thus, coefficient 1 b (6-11-11) is negative and significant and coefficient 2 b (0.034) is positive and significant. The R2 value for this model is 0.25. Thus, it can be concluded that about 25% of the quality of life of adults surviving cancer is explained by the variable of cognitive dysfunction.

5. Discussion

In the present study, it has been shown that cognitive dysfunction with a high correlation explains 25% of the quality of life in adult cancer survivors, and cancer health literacy without correlation with the quality of life cannot predict it. The role of cognitive dysfunction on the quality of life has been aligned according to the results of many research (13-18, 20). Evidence shows that cognitive domains such as memory, processing speed, attention, and executive and motor function are damaged after chemotherapy, radiation therapy, and hormone therapy. Cognitive changes create unique challenges for individual recognition and management. Firstly, cognitive changes may not be obvious and these deficits and disorders may not be assessable by standard objective neuropsychological assessments. Secondly, cognitive changes may be compounded by other problems that
Table 2. Characteristics of Descriptive Statistics of Research Variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD</th>
<th>Crookedness</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cognitive dysfunction</td>
<td>82.64 ± 14.41</td>
<td>-0.44</td>
<td>37</td>
<td>115</td>
</tr>
<tr>
<td>2. Quality of life</td>
<td>207.69 ± 40.07</td>
<td>-0.19</td>
<td>107</td>
<td>313</td>
</tr>
<tr>
<td>3. Health literacy</td>
<td>20.39 ± 4.05</td>
<td>-0.45</td>
<td>7</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 3. Correlation Coefficients Between Research Variables

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Quality of life</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2. Cognitive dysfunction</td>
<td>-0.237 *</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3. Cancer health literacy</td>
<td>0.19 *</td>
<td>0.041</td>
<td>-</td>
</tr>
</tbody>
</table>

* P < 0.01.

are commonly associated with cancer and its treatment, such as depression. Thus, the use of both objective and subjective assessments may help to describe cognitive dysfunction (20).

Chemotherapy disrupts cellular processes and cell division and can lead to increased levels of inflammatory components during and after treatment, especially cytokine receptors (15). Elevated levels of proinflammatory cytokines and white matter damage may contribute to cognitive dysfunction and the decreased hypothalamic-pituitary-adrenal axis activity may be associated with exposure to higher doses of chemotherapy (intra-arterial and intrathecal methods) (14).

In addition, people undergoing chemotherapy constantly show white and gray matter changes in their brains that are associated with cognitive dysfunction (20). In longitudinal studies, patients receiving chemotherapy show a reduction in gray matter mainly in the bilateral areas of the forehead and hippocampus and have only a slight improvement in the gray matter within 1 year after chemotherapy compared to patients, who do not receive chemotherapy. For example, in a study, changes in total gray matter volume were observed in breast cancer survivors after 20 years (16).

Furthermore, people who have undergone radiation therapy in addition to chemotherapy have impaired verbal memory, attention, and motor function due to changes in white matter, which may lead to white matter repair and recovery in the years after radiation therapy. Numerous factors such as age, dosage, shorter treatment, concomitant treatment or immediately after chemotherapy, and larger amounts of radiation therapy are involved in cognitive dysfunction that can lead to severe and even irreversible memory loss years after treatment is completed. As a result, monitoring the cognitive and daily functioning of patients undergoing radiation therapy is essential. Cognitive changes and the resulting impairments can be related to cancer itself, such as the posterior glands, which lead to vision impairment. The location and movement of the lesion (the rate at which the gland grows that can lead to destruction, displacement, and penetration into brain tissue) affect the presence, severity, and pattern of cognitive changes in patients with the gland (14). However, to reduce cognitive dysfunction and increase the quality of life of cancer survivors, research shows that non-pharmacological interventions may improve cognitive function in these individuals. Interventions such as cognitive education, physical activity, yoga, meditation, imagery, mindfulness, music, mindfulness-based therapy, and cognitive-behavioral therapy can be effective through various mechanisms such as immunity enhancement, neurological correction, stress reduction, cognitive training, and restoring attention function (47).

Another finding of the research on the role of quality of life on the health literacy of cancer survivors showed that cancer health literacy is not an independent risk factor for the quality of life in cancer survivors, which is consistent with previous studies (27, 30, 35, 38, 40). The lack of a relationship between cancer health literacy and the quality of life of cancer survivors does not mean that there is no relationship between health literacy and quality of life in general. As mentioned in the research background, health literacy studies with different qualities of life show different results. For example, Panagioti et al. (28) examined the role of health literacy in 4 dimensions of quality of life, only 2 of which were predictable and unrelated to the other 2 (especially the social dimension). Or in the research of Couture et al. (30), no relationship was found between health literacy and physical and psychological dimensions of quality of life.

In their research, Nilsen et al. (38) concluded that health literacy after controlling the socio-psychological dimension and age is not related to the quality of life. Song et al. (29) found that health literacy was positively related to the psychological dimension of quality of life in patients with prostate cancer, while it was unrelated to the physical dimension of quality of life. Some studies show that quality of life varies depending on high or low...
levels of health literacy (31). For example, people with low health literacy but a coordinated care system (inpatient, outpatient, and home care) improve their quality of life after treatment, while people with moderate to high health literacy have no change in their quality of life (26). In another study, there was a direct relationship between low health literacy and academic achievement with a physical dimension, but there was no relationship between high health literacy (37).

The findings of a study by Hahn et al. (40) showed that education level, gender, and the presence of chronic disease are not good predictors of health literacy and are not related to the quality of life, while in another study (32), education was the main factor related to health literacy. This meant that people with higher levels of education had a better ability to find and understand health problems, signs, and symptoms. In addition, some other studies have shown that age has been identified as a good predictor of health literacy and quality of life. In other words, inadequate literacy among the elderly reduces their quality of life. Another study showed that older age, lower level of education, and living in rural areas are associated with lower health literacy (36). The results can be explained from another angle. The findings indicate that the quality of life in cancer patients and patients after treatment is affected by mental and physical health and high levels of anxiety and depression, which are important factors in facilitating and adapting to daily life after treatment. Depression and anxiety play a key role in the relationship between health literacy and quality of life. Studies show that people who experience short-term and long-term negative consequences of depression and anxiety after treatment eventually experience a lower quality of life. As a result, it can be said that by reducing depression and anxiety, health literacy has an indirect effect on the quality of life, which indicates that health literacy alone cannot predict the quality of life of patients with cancer (21). One of these structures is perceived social support, which can play a mediating role between health literacy and quality of life. Research has shown that people with high social support (especially the elderly) also have a better quality of life (33). Other factors include the mediating role of geographical location and culture. For some of the findings, researchers should always consider the cultural, social, and geographical location of the participants as a latent explanation (30). Another structure is self-efficacy, which is related to the quality of life. Researchers have found that by increasing self-efficacy, individuals may engage in behaviors such as weight loss, smoking cessation, and adhesion to exercise programs that ultimately improve their satisfactory health. Differences in these mediating factors may lead to different roles of health literacy in improving quality of life (34).

The lack of a relationship between cancer health literacy and the quality of life of cancer survivors in the present study was not consistent with some studies (17, 21, 26, 33). Perhaps this contradiction can be explained by the fact that the findings of some studies use only 1 dimension of general health status to measure comprehensive areas of quality of life. In this research, the quality of life has been studied from 2 dimensions with 12 different domains. Another possibility is that the different measures taken to assess and classify health literacy may lead to different interpretations of the impact of health literacy on quality of life. Answers to questions about cancer health literacy and quality of life are based on a personal report that may indicate bias (39). Finally, the lack of a relationship between cancer health literacy and the quality of life of cancer survivors needs further investigation (30).

### 5.1. Research Limitations

Caution should be exercised in generalizing the results to men due to being in the Covid 19 condition and its impact on quality of life, and given that most volunteers were female.

### 5.2. Suggestions

#### 5.2.1. Research Suggestions

- The research has been done in Covid 19 conditions. For better generalization of the results, it is suggested to repeat the research in normal conditions.
- In examining the relationship between cancer health literacy and the quality of life of cancer survivors, the mediating role of other variables (such as gender, age, perceived social support, self-efficacy, cultural differences, different geographical areas, and socio-economic status) should also be examined.
- To have a clearer understanding of cognitive dysfunctions, and the side effects of therapies and to
provide appropriate coping strategies, it is necessary to do more research in this area.

5.2.2. Practical Suggestions

Physicians, nurses, and health care providers should pay attention to the cognitive dysfunction reported by the patient, even when objective assessments do not indicate deficiencies. To improve the quality of life and reduce cognitive dysfunction, cognitive-behavioral training, mindfulness, music therapy, yoga, exercise, and regular physical activity should be included in the rehabilitation of the recovered. Providing patients with information related to cognitive dysfunctions after treatment and ways to deal with them by preparing brochures and simple booklets should be considered as well.

5.3. Conclusions

Evidence shows that cognitive domains such as memory, processing speed, attention, and executive and motor function are damaged after chemotherapy, radiation therapy, and hormone therapy.

Another finding of this study showed that cancer health literacy is not an independent risk factor for cancer survivors’ quality of life, which is consistent with research because other mediating variables such as perceived social support, education, self-efficacy, social status, culture, and other variables are involved. Studies show that cognitive behaviors and health literacy are two important factors in the quality of life of people and cancer, and its treatment can cause many psychological problems in the quality of life of survivors.

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Footnotes

Authors’ Contribution: S. R., F. K. N. and M. E. A. conceived and designed the evaluation and drafted the manuscript. M. E. A. participated in designing the evaluation, performed parts of the statistical analysis, and helped to draft the manuscript. S. R. re-evaluated the clinical data, revised the manuscript and performed the statistical analysis, and revised the manuscript. S. R. collected the clinical data, interpreted them, and revised the manuscript. S. R. re-analyzed the clinical and statistical data and revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interests: The authors declare no conflict of interest.

Ethical Approval: The current experimental research has been confirmed and registered at the Ethics Committee of the Cancer Research Center, Shahid Beheshti University of Medical Sciences with the ethical code of IR.SBMU.CRC.REC.1400.034.

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Informed Consent: Written informed consent was obtained.

References


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