Factors Associated with the Quality of Life of Patients with Cancer Undergoing Radiotherapy

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Abstract
Background: Nearly half of cancer patients have comorbidities such as adjustment disorder, major depressive disorder, and delirium. Radiotherapy can cause psychological problems, e.g., the fear of treatment and its side effects, anxiety, depression, and social isolation. Determining health-related quality of life (QoL) is crucial for evaluating cancer treatment effectiveness. We analyzed the clinical, psychological, and sociodemographic factors influencing QoL in cancer patients undergoing radiotherapy.

Methods: Twenty-six patients undergoing radiotherapy (10 male, 16 female) were included. Sociodemographic and clinical data were collected prior to radiotherapy. Psychosocial factors were assessed by self-reported questionnaires before, immediately after, and 3 months after radiotherapy. Multiple regression analysis identified factors affecting QoL at each time point.

Results: Patients’ diagnoses were breast, cervical, prostate, endometrial, rectal, hypopharyngeal, laryngeal, liver, gallbladder, esophageal, ovarian, lung, and skin cancers. Before radiotherapy, better resilience was significantly associated with a higher QoL score ($R^2=0.199$, $p=0.033$). Immediately after radiotherapy, financial difficulty was significantly associated with a lower QoL score ($R^2=0.274$, $p=0.010$). Three months after radiotherapy, the presence of chronic disease ($R^2=0.398$, $p=0.002$) and the severity of nausea and vomiting were significantly associated with a lower QoL score ($R^2=0.278$, $p=0.014$).

Conclusions: Resilience, financial difficulty, the presence of chronic diseases, and the severity of nausea and vomiting significantly influenced QoL in cancer patients undergoing radiotherapy. Factors affecting QoL varied at each time point. Thus, cancer patients should undergo regular mental health assessments, including QoL. Multidimensional (physical, psychological, and social) approaches and individualized time-based interventions are needed to improve the QoL of cancer patients undergoing radiotherapy.

Background
Cancer is a major health problem and one of the leading causes of death in Korea. According to the annual report of the Korea Central Cancer Registry, 214,701 patients were newly diagnosed with
cancer, and 76,855 died due to cancer [1]. According to the 2017 Statistics Korea information regarding the causes of death, the most common cause of death in Korea was cancer, accounting for 27.6% of all deaths [2]. Cancer affects not only physical health but also mental health, and being diagnosed with cancer causes severe stress in patients. The psychological response to a cancer diagnosis involves the fear of losing independence, the fear of losing one’s role in society and economic power, and the fear of premature death, and the patients can experience emotions such as denial, anxiety, anger, or guilt [3–5]. Some cancer patients have severe symptoms of anxiety and depression as a result of the cancer diagnosis and treatment [6, 7], and approximately half are known to have mental disorders such as adjustment disorder, depressive disorder, and delirium [8].

Most cancer patients are treated with surgery, chemotherapy, and radiotherapy. Among these treatments, compared to the other treatment modalities, radiotherapy is relatively less well known with regard to the treatment method, mechanism, and side effects [9]. Although radiotherapy is a type of therapy that can result in the maintenance of a relatively high quality of life (QoL) [10], receiving radiotherapy also causes stress in patients and is known to be associated with the development of psychiatric symptoms in cancer patients [11]. Radiotherapy can cause various side effects according to the treatment method and site of irradiation. Some patients may experience psychological problems such as anxiety, depression, and social isolation due to the fear of radiotherapy itself or its side effects [9, 11, 12]. In addition, by being reminded of the cancer diagnosis at each treatment session, the patients’ mental distress can be exacerbated [13].

The level of interest in the long-term treatment of chronic diseases has increased because of the longer life expectancy of patients. The survival rate of cancer patients has also increased compared to what it was in the past. The cancer mortality rate in Korea has decreased 2.7% annually since 2002, and the 5-year survival rate of cancer patients between 2011 and 2015 was 70.7%, which was increased from 41.2% between 1993 and 1995 [1]. According to the National Cancer Information Center’s 2016 cancer prevalence statistics in Korea, 3.4% (1,739,951) of Korean nationals (51,112,980) were undergoing cancer treatment or had survived treatment, and among elderly people aged 65 years or older, 11.0% (747,898) were undergoing cancer treatment or had survived
As the difference in the survival rates between chronic disease patients and the general population has decreased, QoL has been recognized as an important factor in judging the effects of treatment in the clinical setting [15].

Health-related QoL is a subjective and multidimensional concept defined as a ‘patient’s perception of the functional effect of the disease or disease treatment’ [16], and it is considered one of the important treatment results in oncology [17]. In several previous studies with cancer patients, QoL was related to survival [18] and affected the decisions made by the medical staff regarding the method of treatment and patients’ evaluation of and compliance with treatment [17]. In previous studies, the QoL of cancer patients was associated with race, cancer type, combination therapy, fatigue, performance status, satisfaction with the explanation provided by the medical staff, and depressive mood [19–21]. However, the overall health status, psychological state, and social environment can change over time in the course of cancer treatment, including treatment with radiotherapy, and the factors affecting the QoL may vary depending on the time point in the course of treatment. Identifying the differences in factors affecting the QoL before and after radiotherapy in cancer patients may help researchers understand what factors are important for patients over time, which may facilitate an improvement in the QoL of this population. Thus, in this study, we investigated the sociodemographic and clinical data of cancer patients who were treated with radiotherapy and evaluated their QoL and psychosocial factors before and after radiotherapy. We aimed to analyze the factors that influence QoL in patients with cancer undergoing radiotherapy at each time point before and after radiotherapy.

Methods
Subjects
This study was conducted at the outpatient clinic of the Radiation Oncology Department, Daegu Catholic University Hospital, in 2018. Twenty-six cancer patients (10 male and 16 female) voluntarily agreed to participate after receiving an explanation of the purpose and methodology of the study, the expected benefits and risks, and confidentiality. The sociodemographic and clinical data of the participants were acquired before the initiation of radiotherapy. Sociodemographic data and medical
history were recorded directly by the participants, and clinical data about cancer were obtained by a radiation oncologist from medical records. To evaluate the psychosocial factors, including the QoL among participants, self-reported questionnaires were administered before, immediately after, and 3 months after the completion of radiotherapy. This study was approved by the Institutional Review Board of Daegu Catholic University Hospital (Study No. CR-17-136).

Study tools
1) The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (EORTC-QLQ-C30)

This questionnaire was designed to assess health-related QoL in cancer patients, and it consists of 28 items rated on a scale from 1 to 4 and 2 items rated on a scale from 1 to 7 [22]. It consists of five functional subscales (physical, role, cognitive, emotional, and social), three symptom subscales (fatigue, pain, and nausea/vomiting), six single items (dyspnea, appetite loss, insomnia, constipation, diarrhea, and financial difficulty), a global health scale, and a QoL scale. Each subscale and single item score is expressed in terms of the proportion of the total score. A higher functional scale score indicates better function, and higher symptom scale and single item scores indicate more severe symptoms. A higher global health and QoL scale scores indicate better global health and QoL. In this study, we used the Korean version, which was translated from the EORTC (version 3.0, 1995), after approval from the EORTC website (URL: https://qol.eortc.org/questionnaires/).

2) Beck Depression Inventory-II (BDI-II)

This questionnaire was designed by Beck to measure the degree of clinical depression symptoms [23]. It consists of 21 items scored on scales from 0 to 3; these items include cognitive, emotional, motivational, and somatic symptoms. The total score ranges from 0 to 63, and a higher total score means more severe depressive symptoms. In this study, we used the scale validated by Sung et al. [24].

3) Beck Anxiety Inventory (BAI)

This questionnaire was developed by Beck to measure the degree of anxiety and to distinguish between anxiety and depression [25]. It consists of 21 items scored on a scale from 0 to 3; these
items include cognitive, emotional, and somatic symptoms of anxiety. The total score ranges from 0 to 63, and a higher total score means more severe anxiety symptoms. In this study, we used the scale translated by Kwon [26].

4) Perceived Stress Scale (PSS)
This questionnaire was developed by Cohen et al. to evaluate the degree of stress felt by an individual [27]. It consists of 5 positive and 5 negative stress perception questions scored from 0 to 4; these questions ask about feelings and thoughts during the last month. The total score is obtained by summing the scores of the 5 negative items and the inverse of the scores of the 5 positive items. The total score ranges from 0 to 40, and a higher score indicates a more severe degree of subjectively perceived stress. In this study, we used the scale translated and validated by Park and Seo [28].

5) Rosenberg Self Esteem Scale (RSES)
This questionnaire was developed by Rosenberg to measure self-esteem and self-acceptance. It consists of 5 positive and 5 negative self-esteem items scored from 1 to 4. The total score is obtained by summing the scores of the 5 positive items and the inverse of the scores of the 5 negative items, and the total ranges from 10 to 40, with a higher score indicating better self-esteem. In this study, we used the scale translated by Jeon [29].

6) Conner-Davidson Resilience Scale (CD-RISC)
This questionnaire was developed by Conner and Davidson to measure resilience, defined as the ability to successfully cope with stress [30]. It consists of 25 items scored from 0 to 4, and the total score is ranges from 0 to 100. A higher total score indicates better resilience. In this study, we used the scale validated by Jung et al. [31].

7) Lubben Social Network Scale (LSNS)
This questionnaire was developed by Lubben to evaluate the level of social support [32]. The short version used in our study consists of 6 items scored from 0 to 5; these items inquire about the family network and the friends network. The total score ranges from 0 to 30, and a higher total score indicates a better social network. In this study, we used the scale translated by Lee et al. [33].

Statistical analysis
All data were analyzed using SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL, USA), and statistical significance was defined as p < 0.05. The demographics, clinical characteristics and self-reported results were analyzed with descriptive statistics. Multiple regression analysis was performed to identify factors that affected the participants’ QoL at each time point. One of the EORTC-QLQ-C30 subscales, the QoL subscale, was used as a dependent variable. Sociodemographic and clinical data and all the other self-reported results except the EORTC-QLQ-C30 global health subscale and QoL subscale were used as independent variables.

Results

Sociodemographic characteristics
The mean age of the participants was 56.15 (± 10.40) years. Thirteen (50%) had graduated from high school, and 13 (50%) had a monthly income of less than 2 million won. At the time of radiotherapy initiation, 9 (34.6%) consumed alcohol, and 6 (23.1%) were smokers (Table 1).

Clinical characteristics
The diagnoses received by the subjects were as follows: breast cancer in 7 (26.9%), cervical cancer in 4 (15.4%), prostate cancer in 3 (11.5%), endometrial cancer in 2 (7.7%), rectal cancer in 2 (7.7%), hypopharyngeal cancer in 1 (3.8%), laryngeal cancer in 1 (3.8%), liver cancer in 1 (3.8%), ovarian cancer in 1 (3.8%), gallbladder cancer in 1 (3.8%), esophageal cancer in 1 (3.8%), lung cancer in 1 (3.8%), and skin cancer in 1 (3.8%) (Table 2). The most frequent stage of cancer in the participants was stage III (10, 38.5%); 25 participants (96.2%) were diagnosed for the first time at the time of enrolment, and 24 (92.3%) participants had no metastasis. Eleven (42.3%) participants underwent chemotherapy, 10 (38.5%) participants underwent surgical treatment, and 5 (19.2%) participants underwent both chemotherapy and surgical treatment. Nine (34.6%) participants experienced pain, and 20 (76.9%) participants experienced side effects from radiotherapy. Two (7.7%) participants had a history of mental disorders, and 11 (42.3%) participants had other chronic illnesses (Table 3).

Factors associated with QoL before and after radiotherapy
The mean QoL scores of participants before, immediately after, and 3 months after the completion of radiotherapy as evaluated by the EORTC-QLQ-C-30 QoL scale were 67.31 (± 20.26), 66.67 (± 17.63),
and 69.44 (± 21.79), respectively (Figure 1). Before initiating radiotherapy, better resilience, as evaluated by the CD-RISC, was significantly associated with a higher QoL score (β = 0.447, p = 0.033), and it accounted for 19.9% of the QoL. Immediately after radiotherapy, financial difficulty, as evaluated by the EORTC-QLQ-C30 single item, was significantly associated with a lower QoL score (β = -0.524, p = 0.010), and it accounted for 27.4% of the QoL. Three months after the end of radiotherapy, the presence of other chronic diseases (β = -0.549, p = 0.002) and the severity of nausea and vomiting symptoms evaluated via the EROTC-QLQ-C30 symptom scale (β = -0.419, p = 0.014) were significantly associated with lower QoL score, and they accounted for 55.9% of the QoL (Table 4). The relationships between other factors and QoL were not statistically significant.

Discussion

As the survival rate of cancer patients has increased, the importance of QoL when setting treatment goals has been increasingly emphasized. The purpose of this study was to identify the factors that influence the QoL before and after radiotherapy of cancer patients who visited the outpatient clinic of the Radiation Oncology Department of Daegu Catholic University Hospital for radiotherapy. The main findings of this study were as follows. First, before the initiation of radiotherapy, better resilience was associated with a higher QoL score. Second, immediately after the end of radiotherapy, financial difficulty was associated with a lower QoL score. Third, 3 months after the end of radiotherapy, the presence of chronic disease and the severity of nausea and vomiting symptoms were associated with a lower QoL score.

The results of this study showed that before the initiation of radiotherapy, better resilience was associated with better QoL. Resilience refers to the ability to maintain or recover a healthy state by coping effectively when encountering adversity [34]. Emotional distress, such as depression and anxiety, experienced by cancer patients because of the diagnosis and treatment of cancer lowers their QoL and interferes with adherence to treatment [17]. Previous studies with cancer patients have shown that resilience contributes to decreasing emotional distress [35] and may ameliorate the decrease in QoL due to emotional distress [36]. In addition, a high degree of resilience could help improve QoL by alleviating the emotional distress experienced by patients with newly diagnosed
cancer and facilitating the use of better coping strategies [37]. All of the participants in this study, except one, were diagnosed with cancer for the first time, not a relapse. The participants with good resilience might not have experienced a decrease in their QoL because they were better able to cope with the life crisis of a cancer diagnosis, and their better resilience ameliorated the emotional distress resulting from the cancer diagnosis. Thus, it may be helpful to screen patients for low resilience in addition to significant emotional distress such as depression and anxiety immediately after a cancer diagnosis is made. Along with appropriate interventions, this screening may contribute to improving the QoL of cancer patients by enhancing their resilience and alleviating negative emotions caused by the cancer diagnosis. However, the time elapsed from the time of first cancer diagnosis to enrolment in the study varied from at least 1 month to at most 8 months for each participant. After receiving a diagnosis, patients have time to accept cancer as part of their lives and develop resistance to other stressors related to cancer [36]. Thus, the effect of the cancer diagnosis on the QoL of the participant might vary depending on the time elapsed since the cancer diagnosis, but we did not consider that as a variable in this study.

Immediately after radiotherapy, financial difficulty due to poor health and cancer treatment was associated with a worse QoL. This was consistent with the findings of previous studies that showed an association between financial difficulty and poor QoL in cancer patients [38–40]. Cancer patients can experience financial burdens due to the cost of treatments such as radiotherapy, chemotherapy, and surgery [41]; a decrease in productivity at the workplace or unemployment [42]; and decrease in the family income because of the costs of caring for the patients [43]. The financial burden on cancer patients can lower their QoL by increasing their risk of using their savings, reducing the money available for groceries, delaying vacations, and necessitating longer work hours [44]. The financial burden on cancer patients is known to increase the mortality rate because it negatively affects their well-being and health-related QoL, and the attempt to reduce the financial burden interferes with treatment compliance and the quality of care [45]. In a previous study in Korea, it was found that the incidence of overspending, defined as an annual household medical expenditure of more than 10% of the total annual household income, was the highest during the first year after a cancer diagnosis [46].
All of the participants in this study received combination therapy including chemotherapy, surgical treatment, or both. At the time point immediately after the completion of radiotherapy, the duration of cancer had been relatively short, from 3 months to 10 months. From these results, we supposed that cancer patients experience financial burdens starting from the beginning of treatment. Immediately after completing radiotherapy, participants who started cancer therapy for the first time or who started radiotherapy as a new therapy seemed to experience a relatively large impact of the financial burden on their quality of life. Therefore, when administering radiotherapy to cancer patients, clinicians should consider that the household income and financial burden can greatly influence the patients’ QoL.

Three months after radiotherapy, the presence of chronic disease and the severity of nausea and vomiting symptoms were associated with worse quality of life. Three of the participants in this study had diabetes, 3 had hypertension, 3 had both diabetes and hypertension, 1 had arthritis, and 1 had prostate disease. Studies have shown that diabetes can negatively affect QoL depending on the type and use of medication and comorbidities [47], and hypertension is also associated with worse QoL [47, 48]. Cancer patients often experience nausea and vomiting because of direct or indirect complications of cancer and the toxicity of the chemotherapy or radiotherapy [49]. These symptoms can adversely affect QoL by deteriorating the nutritional status of the patient and interfering with their pleasure in eating [49, 50]. In particular, patients with head and neck cancer and gastrointestinal cancer are more likely to experience nausea or develop malnutrition after radiotherapy compared to other cancer patients [51, 52]. Patients with head and neck cancer have worse QoL before and after radiotherapy compared to those with other cancers [51]. In the same study mentioned above, increased nutritional intake after radiotherapy was associated with improved QoL in head and neck cancer patients [51]. Three months after the completion of radiotherapy, the impact of the cancer diagnosis on QoL may be reduced, and QoL is affected by coexisting chronic diseases and nausea and vomiting that occur as a result of the cancer or its treatment. Therefore, after the completion of radiotherapy, there is a need to pay attention to patients’ overall mental health, including QoL, in those with chronic diseases and severe side effects such as nausea and
vomiting caused by the cancer treatment. In addition, efforts by clinicians to effectively control side effects such as nausea and vomiting are needed.

The limitations of this study were as follows. First, it is difficult to generalize the results of this study because all of the participants were recruited from one hospital outpatient clinic, and the number of participants was relatively small. Second, the participants had several types of cancer, but the types of cancer were not considered in the analysis. Therefore, the differences in the symptoms and side effects that might occur depending on the cancer type and the irradiation site were not reflected in the results. Third, the frequency and dose of radiotherapy were not considered in the analysis. Fourth, follow-up was terminated 3 months after the completion of radiotherapy. Therefore, the results do not reflect the effects of late-onset side effects of radiotherapy, which may have appeared after the end of this follow-up period. Fifth, in the analysis, the EORTC-QLQ-C30 overall QoL was used as a dependent variable. Thus, the results do not reflect the multidimensional aspects of health-related QoL. Sixth, the cancer disease process occurs over a long period, but the period of study participation was as short as 4–7 months at the initial stage of diagnosis. However, this study was meaningful in that we tried to analyze the factors associated with the QoL of cancer patients, both before and after radiotherapy. In the future, it will be necessary to study the long-term QoL and associated factors over the entire cancer disease process.

Conclusions
This study found that in cancer patients undergoing radiotherapy, the factors associated with QoL varied based on whether it was before or after radiotherapy. Resilience influenced QoL before the initiation of radiotherapy, financial difficulty influenced QoL immediately after radiotherapy, and chronic disease and nausea and vomiting affected QoL 3 months after radiotherapy. Thus, regular assessments of mental health, including QoL, should be considered in cancer patients undergoing radiotherapy. Multidimensional approaches that consider physical, psychological, and social factors and individualized interventions designed for each time point are needed to improve the QoL of patients with cancer undergoing radiotherapy.

Declarations
Abbreviations

BAI: Beck Anxiety Inventory; BDI-II: Beck Depression Inventory-II; CD-RISC: Conner-Davidson Resilience Scale; EORTC: European Organization for Research and Treatment of Cancer; EORTC-QLQ-C30: The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; LSNS: Lubben Social Network Scale; PSS: Perceived Stress Scale; RSES: Rosenberg Self Esteem Scale; QoL: Quality of life

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Authors’ contributions

JWK : Study design, writing the paper, data acquisition, statistical analysis. DHK and SHB : Data acquisition and analysis, performing experiment, helped to write the paper. KHS : Study concept, data acquisition, performing radiotherapy, helped to write the paper. All authors read and approved the final manuscript.

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Availability of data and materials

The data supporting our findings are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Daegu Catholic University Hospital (Study No. CR-17-136). Written informed consent was received from the patients before the study.

Conent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

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Tables

Table 1. Sociodemographic characteristics of participants

| Characteristics                             | Mean ± SD or N (%) |
|--------------------------------------------|--------------------|
| Age                                        | 56.15 ± 10.40      |
| Sex                                         |                    |
| Male                                       | 10 (38.5)          |
| Female                                     | 16 (61.5)          |
| Education                                  |                    |
| Elementary school education or lower       | 4 (15.4)           |
| Middle school education                    | 3 (11.5)           |
| High school education                      | 13 (50.0)          |
| College degree or higher                   | 6 (23.1)           |
| Monthly income                             |                    |
| < 2,000,000,000 won                        | 13 (50.0)          |
| 2,000,000,000 won - 3,999,999 won           | 5 (19.2)           |
| 4,000,000,000 won - 5,999,999 won           | 4 (15.4)           |
| ≥ 6,000,000,000 won                        | 2 (7.7)            |
| Alcohol use                                |                    |
| Yes                                        | 9 (34.6)           |
| No                                         | 17 (63.4)          |
| Tobacco use                                |                    |
| Yes                                        | 6 (23.1)           |
| No                                         | 20 (76.9)          |

SD : standard deviation, N : number of patients

Table 2. Tumor sites in participants

| Site of tumors | N (%) |
|----------------|-------|
| Breast         | 7 (26.9) |
| Cervix         | 4 (15.4) |
| Prostate       | 3 (11.5) |
| Endometrium    | 2 (7.7)  |
| Rectum         | 2 (7.7)  |
| Hypopharynx    | 1 (3.8)  |
| Larynx         | 1 (3.8)  |
| Liver          | 1 (3.8)  |
| Gall bladder   | 1 (3.8)  |
| Esophagus      | 1 (3.8)  |
| Ovary          | 1 (3.8)  |
| Lung           | 1 (3.8)  |
| Skin           | 1 (3.8)  |

N : number of patients
| Characteristics                  | N (%) |
|---------------------------------|-------|
| **Stage of disease**            |       |
| O                               | 2 (7.7)|
| I                               | 4 (15.4)|
| II                              | 7 (26.9)|
| III                             | 10 (38.5)|
| IV                              | 3 (11.5)|
| **Relapse**                     |       |
| Yes                             | 1 (3.8)|
| No                              | 25 (96.2)|
| **Metastases**                  |       |
| Yes                             | 2 (7.7)|
| No                              | 24 (92.3)|
| **Chemotherapy**                |       |
| Yes                             | 16 (61.5)|
| No                              | 10 (38.5)|
| **Surgery**                     |       |
| Yes                             | 15 (57.7)|
| No                              | 11 (42.3)|
| **Pain**                        |       |
| Yes                             | 9 (34.6)|
| No                              | 17 (63.4)|
| **Adverse effects of radiotherapy**|     |
| No                              | 6 (23.1)|
| G1-2                            | 19 (73.1)|
| G3-4                            | 1 (3.8)|
| **History of mental disorders** |       |
| Yes                             | 2 (7.7)|
| No                              | 24 (92.3)|
| **History of chronic diseases** |       |
| Yes                             | 11 (42.3)|
| No                              | 15 (57.7)|

N: number of patients, *Based on common terminology criteria for adverse events 4.0
Table 4. Associations of quality of life with variables by multiple regression analysis

| Before initiating radiotherapy | Beta   | t     | R^2  | Adjusted R^2 |
|-------------------------------|--------|-------|------|--------------|
| Resilience immediately after radiotherapy | 0.447  | 2.288 | 0.199 | 0.161 |
| Financial difficulty 3 months after radiotherapy | -0.524 | -2.816 | 0.274 | 0.239 |
| Presence of chronic diseases | -0.549 | -3.547 | 0.559 | 0.513 |
| Nausea and vomiting           | -0.419 | -2.705 |      |              |

Figures
Figure 1

Quality of life of participants