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Changes in patients' quality of life during radiotherapy and 1 month after treatment

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Summary
Background The EORTC QLQ-C30 quality of life (QOL) questionnaire is designed to measure cancer patients' physical, psychological, and social functions. There are few reports on the impact of radiotherapy (RT) on QOL; thus, we investigated QOL changes during the RT period and 1 month after RT.
Methods We scored EORTC QLQ-C30 (version 3.0) questionnaires from 66 patients. The questionnaire contained 30 items, including 1 item on financial concerns, a global health domain, 5 functional domains, 3 symptom domains, and 5 single-symptom items. Assessments were performed before RT, at the end of the day after RT, and 1 month after RT. Correlations between the patients' characteristics (e.g., age, sex, organ, RT response) and QOL change were evaluated.
Results No specific patient characteristic significantly correlated with a QOL change during RT. In 15 QLQ-C30 items, those items in which the change in score achieved statistical significance ($P < 0.05$) were the following: physical function was improved from the end of RT to 1 month after RT; role function worsened from the end of RT to 1 month after RT; and emotional function worsened from the start of RT to 1 month after RT.
Conclusions The QOL was poorest at the end of RT. If treatment was completed, physical function improved, but role function and emotional function worsened just 1 month after treatment. For role and emotional function, observation by medical staff is necessary.

Keywords Radiotherapy · Quality of life · Cancer · Patient-reported outcome · Emotional function

Introduction

The EORTC QLQ-30 quality of life (QOL) questionnaire is designed to measure cancer patients' physical, psychological, and social functions [1–8]. Cancer therapy can be of long duration, and QOL often decreases during this time period. Because radiotherapy (RT) is administered daily, QOL can diminish during treatment. A late effect might occur after RT, and this effect appears to be typical in cancer treatment. Investigations of QOL before and after treatments such as chemotherapy and surgery for various carcinomas have been reported [9–13]. Some studies reported QOL of head and neck cancer after radiotherapy [14–16]. However, there have been few studies focused on total QOL before and after RT; therefore, we investigated QOL change during RT treatment and 1 month after RT.

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Materials and methods

Our study was approved by the Institutional Review Board, and the UMIN-National Clinical Trial Registered number is UMIN000034390. From November 2016 to September 2017, 94 patients were enrolled in the study. All the patients provided written informed consent. We ultimately scored questionnaires from 66 out of 94 patients who completed the questionnaire 3 times. The patients who did not submit a questionnaire 1 month after the RT were excluded from the analysis (28 of 94 patients). The characteristics of the patients are shown in Table 1.

QOL assessment

The EORTC QLQ-C30 (version 3.0) was used for every patient (Fig. 1). This questionnaire assesses patient-reported outcomes and was developed for use with patients with cancer. The questionnaire contained 30 items, including 1 item dealing with financial concerns, a global health domain, 5 functional domains (physical, role, cognitive, emotional, and social), 3 symptom domains (fatigue, pain, nausea and vomiting), and 5 single-symptom items (dyspnea, insomnia, anorexia, diarrhea, and constipation). The questionnaire employs 2 questions on a 7-point scale (for the global health and QOL domains) and 28 questions on a 4-point scale (not at all, a little, quite a bit, very much). In accordance with the EORTC QLQ-C30 scoring manual, all the scores were linearly transformed into a numerical scale with values from 0–100 (see Fig. 2). For scales related to function, a higher score was regarded as a higher level of functioning. For items related to symptoms, a higher score was regarded as an indicator of more severe symptoms [2].

The assessment was performed before RT, at the end of each day of RT, and 1 month after the end of RT. The statistical analysis was performed using a one-way analysis of variance (ANOVA) and Bonferroni comparison. We used a multivariable and a univariate analysis for the correlation of patients' characteristics with changes in QOL. $P < 0.05$ was considered a statistically significant difference between 2 or 3 time points. The statistical software used was BellCurve for Excel (Social Survey Research Information Co. Ltd., Japan).

Table 1 Patient characteristics and impact on global health and quality of life (QOL)

Characteristics			*p* value
Age	Mean ± SD (range)	66 ± 12 (45–84)	0.45
Sex	Male	30	0.61
	Female	36	
Stage	I	19	0.32
	II	21	
	III	16	
	IV	10	
PS	0	22	0.14
	1	29	
	2	11	
	3	3	
	4	1	
Total dose (Gy)	Mean ± SD (range)	47 ± 14 (8–78)	0.22
Number of fraction	Mean ± SD (range)	21 ± 10 (1–39)	0.13
Chemotherapy	Yes	42	0.52
	No	24	
Operation	Yes	25	0.34
	No	41	
Purpose	Radical	24	0.55
	Palliative	28	
	Post Op	14	
Response	CR&PR	36	0.47
	SD&PD	16	
	Post Op	14	
Primary site		–	0.51
Brain (metastasis)		4	–
Head & Neck		3	–
Lung		8	–
Upper GI		4	–
Lower GI		3	–
Breast		18	–
Liver		5	–
Prostate		6	–
Bone (metastasis)		10	–
Lymphoma		2	–
Others		3	–

Multivariable analysis of patients' characteristics and changes in QOL
A *p*-value of 0.05 or less was considered significant
There was no significant correlation between QOL and any patient characteristic
GI gastro-intestinal, *SD* Standard deviation, *PS* Performance Status, *CR&PR* Complete response & Partial response, *SD&PD* Stable disease & Progressive disease, *Op* Operation

Results

The average time taken to complete the questionnaires was 57 (range 31–86) days. No patient characteristic significantly correlated with a QOL change during RT (Table 1). In 15 QLQ-C30 items, those items in which the change in score achieved statistical significance ($P < 0.05$) were the following: physical function was improved from the end of RT to 1 month after RT; role function worsened from the end of RT to 1 month after RT; and emotional function worsened from the start of RT to 1 month after RT.

Discussion

The EORTC QLQ-C30 questionnaire was found to be useful for detecting the effect of palliative radiotherapy over time. It was determined to be practical and

Fig. 1 Questionnaire for individual patients (question 1–16) (actual version is written in Japanese)

EORTC QLQ-C30 (version 3.0)

We are interested in learning about you and your health. Please answer all of the questions by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide to us will remain strictly confidential

Please fill in your initials:_____

Your birthdate (Day, Month, Year): _____

Today's date (Day, Month, Year): _____

1. Do you have any trouble doing strenuous activities, such as carrying a heavy shopping bag or a suitcase?	**Not at All** 1	**A Little** 2	**Quite a Bit** 3	**Very Much** 4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
6. Were you limited in performing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

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valid in measuring QOL in patients with advanced disease [1]. No association was found between patient characteristics and a change in QOL. RT was not compared in terms of the number of fractions because there is a difference in therapeutic intensity. For example, there is a difference in intensity between 25 fractions in breast-conserving therapy and 25 fractions of prophylactic pelvic irradiation for postoperative cervical cancer. In our series, there were 11 irradiate sites and fraction varied (i.e., 8 Gy single dose for bone metastasis—78 Gy/39 fraction for prostate cancer). The radiotherapy is performed for the following three purposes; radical, palliative, and post-operation. Radiotherapy can be adjuvant and prophylactic; for cervical cancer and breast cancer, adjuvant therapy is administered to prevent a postoperative recurrence. Prophylactic radiation is conducted to prevent brain metastasis from small cell lung cancer.

QOL changes with adverse events (AEs). Intensity of treatment increases when we administer a dosage to achieve the greatest effect by radical irradiation; then, the QOL decreases with AEs. Continuation of RT leads to increased AEs; radical chemoradiotherapy for patients with head and neck cancer suffering

Fig. 1 (continued)

During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, such as reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions, please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

from stomatitis and dermatitis leads to appetite loss and pain. Patients with prostate cancer suffer from increasing frequency of urination during RT. In contrast, the pain caused by bone metastasis generally improves within 2 or 4 weeks of administering radiotherapy, leading to improved QOL. In our series, two patients received 8 Gy single fraction radiotherapy and had the same scores at the beginning and at the end of the study. However, their pain subsided after one month and QOL improved. There was no change of QOL start to 1 month later RT in three patients with small lung cancer treated using stereotactic body radiotherapy (SBRT). However, five patients were administered with concurrent 60 Gy radical chemoradiotherapy and suffered with esophagitis similar to that in head and neck cancer. Three patients with esophageal cancer developed esophagitis and suffered from painful swallowing which was relieved one month after RT. One patient with an inoperable gastric cancer with bleeding received 20 Gy/5 fractions hemostatic radiotherapy, and suffered from nausea during RT, which was relieved one week after RT.

In general, QOL is restored when RT is completed. QOL is poorest at the point when RT is completed, due to associated AEs. As organ specific QOL, Trotti et al. reviewed the existing head and neck QOL instruments and found them to be inadequate in addressing important radiation related side effects. Therefore, they developed the QOL-RTI (Radiation Therapy Instrument) which is a valid and reliable tool and is responsive to changes in QOL during a course of H&N radiation therapy [14–16].

In a study by Cameran et al., symptoms were scored by study physicians, with QOL and site-specific modules assessed prior to start of radiation and at 6 and 12 weeks after its completion. Some 21 patients had valid responses within all the EORTC QLQ C-30 scales at baseline, 20/20 at the 6-week follow-up, and at the 12-week follow-up, 17/18 patients remaining in the study had valid responses within all scales [11]. However, their study cohort was small and limited

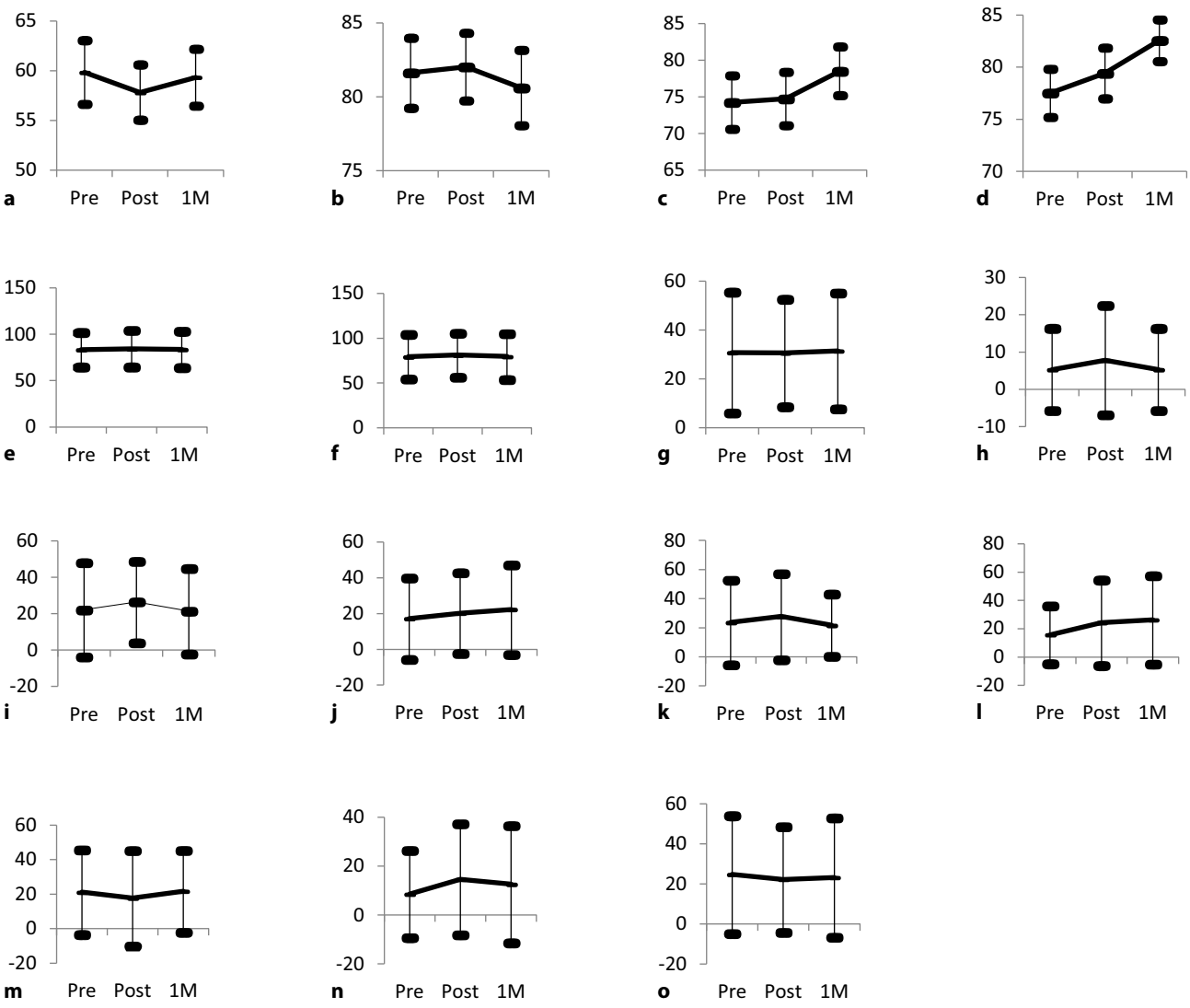

Fig. 2 QLQ-C30 score (European Organization for Research and Treatment Cancer). **a** Global health and quality of life. **b** Physical function. **c** Role function. **d** Emotional function. **e** Cognitive function. **f** Social function. **g** Fatigue. **h** Nausea and vomiting. **i** Pain. **j** Dyspnea. **k** Sleep disturbance. **l** Appetite loss. **m** Constipation. **n** Diarrhea. **o** Financial impact. All scores shown were linearly transformed into a 0–100 scale from the questionnaire responses. The one-way analysis of variance (ANOVA) and Bonferroni's correction were used for the statistical analysis (*The black dot in the center* represents the average value. *The black dot at the top and bottom* points represents the standard error value (mean ± standard error)). *Pre* at the start of day of RT, *Post* at the end of day of RT, *1M* 1 month after the end of RT

to pelvic malignancy. In a study by King-Kallimanis et al. assessing functional QOL, older patients reported poorer physical functioning, and patients who had received treatment prior to RT reported poorer emotional functioning [13]. Emotional function after RT also worsened in our series, which could be associated with AEs (late toxicity).

Physical function was improved 1 month after RT. Tasks such as visiting the hospital require both mental and physical strength in order to be performed day after day. Finishing RT leads to improvements in physical function. However, as the treatment accumulated, role function and emotional function worsened. During the RT period, we expected role function and emotional function to be exacerbated by treatment continuation, but we found that the exacerbation continued after RT ended. The AEs were thought to continue to affect emotional function even after RT.

We have conducted a QOL investigation into long-term RT; however, the number of cases ($n=66$) was small and included a wide range of cancer therapy. For example, even if the irradiated site is liver, results differ from those of SBRT by the normal fractionated irradiation for the portal vein tumor invasion.

If the questionnaires were limited to a specific disease, such as lung cancer or breast cancer, QOL might be not evaluated correctly. RT is employed for patients with all types of carcinomas. It is important that we understand the changes in QOL after a period of RT. This questionnaire is intended to be used only during

the RT period and 1 month after the RT. Late AEs from the RT can appear 6 months and 1 year later. Therefore, a longer-term survey is needed in the future. In addition, medical staff should consider the patient's mental status after RT. Intensive care provided by the medical staff is of utmost importance and should be reflected in the daily appointment calendar for at least one month after RT. To establish more detailed assessment of QOL of RT, the following factors must be considered: (1) organ specific, (2) intention to treatment, and (3) techniques of therapy (conventional RT, intensity modulated RT, brachytherapy and SBRT) in large number of patients.

Conclusion

QOL was poorest at the end of RT. If treatment was completed, physical function was improved, but role function and emotional function worsened even 1 month after treatment. The change in QOL varies depending on the type of cancer. With respect to emotional and role function, observation by medical staff is necessary after treatment and preferably for longer than 1 month post-RT.

Conflict of interest O. Tanaka, Y. Kunishima, T. Taniguchi, K. Ono, and M. Matsuo declare that they have no competing interests.

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