RESEARCH ARTICLE

Changes in Psychological Condition during Cancer Chemotherapy

Kensuke Kamimura[1,2]*, Hiroaki Haga[1], Tomomi Wada[1], Masato Aoyama[1], Rui Ito[1], Juri Minami[3], Takatoshi Uchitsubo[1], Yasuo Saijo[2]

Abstract

Background: Psychological disorders are prevalent in cancer patients and their psychological condition can change during cancer chemotherapy and influence their quality of life and adherence to treatment. **Patients and methods:** This prospective observational study enrolled cancer patients undergoing chemotherapy. The enrolled patients were assessed at the start of chemotherapy, after the first course of chemotherapy, and more than 2 months later by themselves and by medical staff using four different items. The cancer patients assessed themselves using the Numerical Rating Scale for Anxiety (NRS-A), Hospital Anxiety and Depression Scale subscale for anxiety (HADS-A) and subscale for depression (HADS-D), and patient-reported outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). A pharmacist or nurse assessed them using Common Terminology Criteria for Adverse Events (CTCAE) v5.0. **Results:** This study enrolled 109 patients. The anxiety and depression scores were highest at the start of chemotherapy and declined thereafter. Patients with history of psychiatric disorders or taking psychotropic drugs had higher scores than those without such disorders or treatments (P < 0.05), and tended to maintain these high scores at the second and third HADS-A and -D assessments. The scores assessed by the patients themselves were higher than those assessed by the medical staff. **Conclusion:** Psychiatric distress scores were highest when commencing chemotherapy and declined thereafter. The patients with history of psychiatric disorders or taking psychotropic drugs kept higher scores of HADS-A and -D during whole chemotherapy courses.

Keywords: Anxiety- depression- psycho-oncology- psychological distress- antineoplastic agents

Introduction

Cancer has been a leading cause of death in Japan for 40 years. Although cancer treatment outcomes are improving, cancer is still life-threatening. After being diagnosed with cancer, patients usually experience disbelief or denial as the initial response in phase I; this is followed by anxiety or a depressed mood as a dysphoria in phase II; and finally they adapt after about 2 weeks (phase III) [1]. Therefore, cancer patients suffer from psychological distress. Psychiatric disorders were found in 47% of cancer patients, of whom 68% were adjustment disorders and 13% were major depression [2]. Among cancer patients referred for psychiatric consultations, adjustment disorder was the most common (34%), followed by delirium (17%), and major depression (14%) [3].

The psychological condition of cancer patients includes not only their reaction to a diagnosis of cancer but is also affected by the cancer stage, treatment modality, prognosis, and patient's education and economic status. Since cancer chemotherapy can have severe adverse effects, patients are often anxious before initiating chemotherapy, which may cause psychiatric distress. The Hospital Anxiety and Depression Scale (HADS) found a high prevalence of anxiety (45%) and depression (25%) in patients commencing cancer chemotherapy, even for potentially curable cancers [4]. The psychological condition of the cancer patients changes after experiencing chemotherapy [5, 6].

Although 44% of cancer patients in Japan were concerned about the adverse effects of outpatient cancer chemotherapy [7], no report has evaluated chronological changes in the psychological condition of cancer patients in Japan treated with chemotherapy. Awareness of the psychological condition of cancer patients by medical staff can lead to a better quality of life and, ultimately, better adherence to cancer treatment. In this study, we evaluated changes in the psychological condition of cancer patients during cancer chemotherapy using different assessment methods by both patients and medical staff.

[1]Department of Pharmacy, Saiseikai Niigata Hospital, 280-7 Teraji, Nishi-ku, Niigata 950-1104, Japan. [2]Department of Medical Oncology, Niigata University, Graduate School of Medical and Dental Sciences, Niigata, Japan. [3]Department of Nursing, Saiseikai Niigata Hospital, Niigata, Japan. *For Correspondence: kamimurakensuke@ngt.saiseikai.or.jp

Materials and Methods

Patients and data collection

This prospective observational study was approved by the Ethics Review Committees of Saiseikai Niigata Hospital (no. E20-22) and Niigata University School of Medicine (no. 2020-0421). Patients aged 20 years and above who initially undergo cancer chemotherapy containing anticancer drug injection in Saiseikai Niigata Hospital were eligible for this study. The study also included patients who underwent surgery including endoscopic resection, radiotherapy including interventional radiology (e.g., transcatheter arterial chemoembolization), or hormone therapy (e.g., aromatase inhibitors, antiestrogens, or gonadotropin-releasing hormone analogues) before the cancer chemotherapy. Informed consent was obtained from all patients, who were registered from April 2021 to May 2022. Baseline data collected included patient age and sex, type and stage of cancer, types of medical treatment, days from cancer notification to the first assessment, and history of psychiatric disorders or psychotropic drug use. Cancer notifications included notification of recurrence. Psychiatric disorders included anxiety neurosis, anxiety disorder, depression, and insomnia. Psychotropic drugs included anti-anxiety (e.g., etizolam), antidepressant (e.g., duloxetine), and hypnotic (e.g., triazolam) drugs.

Assessment methods

Patients completed questionnaires three times: at the beginning of chemotherapy, after the first course, and more than 2 months later. The questionnaires included four different assessment items. The cancer patients assessed themselves using the Numerical Rating Scale for Anxiety (NRS-A), Hospital Anxiety and Depression Scale (HADS), and patient-reported outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). A pharmacist or nurse assessed the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 at the same time as the patients.

Numerical Rating Scale for Anxiety

The NRS-A was used to measure anxiety about cancer chemotherapy directly. This 11-point numeric scale ranges from 0 (absolutely no anxiety) to 10 (the worst anxiety imaginable) [8].

Hospital Anxiety and Depression Scale

The HADS was used to assess anxiety and depression [9]. The HADS is a 14 item self-rating scale, with seven items each for anxiety (HADS-A) and depression (HADS-D). We used the Japanese version of the HADS [10, 11].

NCI-PRO-CTCAE ITEMS-JAPANESE v1.0

The PRO-CTCAE was used to assess symptomatic adverse events in cancer clinical trials [12]. We used the Japanese version of PRO-CTCAE [13, 14]. Anxious, discouraged, and sad items in the PRO-CTCAE were evaluated as frequency, severity, and interference, and scored from 0 to 4 (e.g., never = 0, rarely = 1, occasionally

= 2, frequently = 3, and almost constantly = 4) [15].

Common Terminology Criteria for Adverse Events v5.0

We used the Japanese version of the CTCAE v5.0 – JCOG [16]. Among the CTCAE items, we assess psychiatric condition using anxiety (G0 to G4) and depression (G0 to G5).

Statistical analysis

To analyze the NRS-A and HADS data, we used the Friedman and Wilcoxon signed-rank tests. The PRO-CTCAE and CTCAE data were analyzed using Spearman's rank correlation coefficient. Subgroup analyses were performed using the Mann–Whitney U-test. $P < 0.05$ was considered significant. For multiple comparisons, the Bonferroni correction was used. The statistical analyses were performed using EZR ver. 1.61 [17] and IBM SPSS Statistics, ver. 22.0.

Results

Patient characteristics

This study enrolled 109 patients (52 men, 57 women) who completed the questionnaires three times before finishing chemotherapy. Table 1 summarizes the patient characteristics. Seventy patients were 65 years old or older. Gastrointestinal cancer accounted for 61.5%, followed by breast cancer (22.0%), and hematological malignancies (11.9%). Median days after cancer notification was 33 days. Eighteen (16.5%) patients had history of psychiatric disorders or were taking psychotropic drugs. All five patients with history of psychiatric disorders were taking psychotropic drugs.

Changes in the NRS-A, HADS-A and HADS-D

The NRS-A, HADS-A, and HADS-D scores were all highest at the first assessment and declined at the second and third (Figure 1). There were significant differences between the first and second or third scores for all three items ($P < 0.01$). Only the NRS-A about cancer chemotherapy differed significantly between the second and third scores ($P < 0.05$).

Changes in the NCI-PRO-CTCAE ITEMS-JAPANESE v1.0 and CTACEv5.0

Figure 2 shows changes in the frequency (Figure 2A), severity (Figure 2B), and interference (Figure 2C) of anxious, discouraged, and sad in the NCI-PRO-CTCAE, as assessed by the patients. The frequency, severity, and interference scores for anxious, discouraged, and sad were all negatively correlated with the number of ratings ($P < 0.01$). Although the assessment methods differed, CTCAE showed a significant negative correlation between anxiety grades and the number of ratings ($P < 0.001$), but not depression grades (Figure 2D). Although the scoring methods of the PRO-CTCAE and CTCAE differ, grades scored by medical staff were lower than those by patients themselves. In the first assessment, there were few instances of none for severity in the PRO-CTCAE assessed by patients themselves (anxious 14.7%, discouraged 28.4%, and sad 33.9%), whereas

Table 1. Patient Characteristics

	Total (n=109)
Age	
< 65 years	39 (35.8%)
≥ 65 years	70 (64.2%)
Median (interquartile range)	66 (60-74)
Sex	
Male	52 (47.7%)
Female	57 (52.3%)
Types of cancer	
Gastrointestinal cancer	67 (61.5%)
Breast cancer	24 (22.0%)
Hematological malignancies	13 (11.9%)
Lung cancer	5 (4.6%)
Stage	
II	27 (24.8%)
III	29 (26.6%)
IV	30 (27.5%)
Recurrence	6 (5.5%)
Hematological malignancies	13 (11.9%)
Unknown	4 (3.7%)
Types of medical treatment	
Adjuvant chemotherapy	42 (38.5%)
Neoadjuvant chemotherapy	14 (12.8%)
Advenced and Recurrent	40 (36.7%)
Hematological malignancies	13 (11.9%)
Days from cancer notification to the first assessment	
< 14 days	36 (33.0%)
≥ 14 days	73 (67.0%)
Median (interquartile range)	33 (8-59)
Psychiatric disorders or taking psychotropic drugs	
Positive	18 (16.5%)
Negative	91 (83.5%)

there were many instances of G0 in the CTCAE assessed by the medical staff (anxiety 35.8%, depression 73.4%) (Figs. 2B and 2D).

Subgroup analyses

Subgroup analyses were performed for the NRS-A and HADS-A and -D (Table 2). The subgroups with history of psychiatric disorders or taking psychotropic drugs and those with less than 14 days since cancer notification had higher initial scores in all three assessments (NRS-A, HADS-A, and HADS-D). Only the subgroups with history of psychiatric disorders or taking psychotropic drugs had significantly higher HADS-A scores than the negative group at all three assessments. The group with advanced and recurrent/hematological malignancies had significantly higher scores in the first NRS-A and HADS-D than the adjuvant chemotherapy/neoadjuvant chemotherapy group, but not for the first HADS-A.
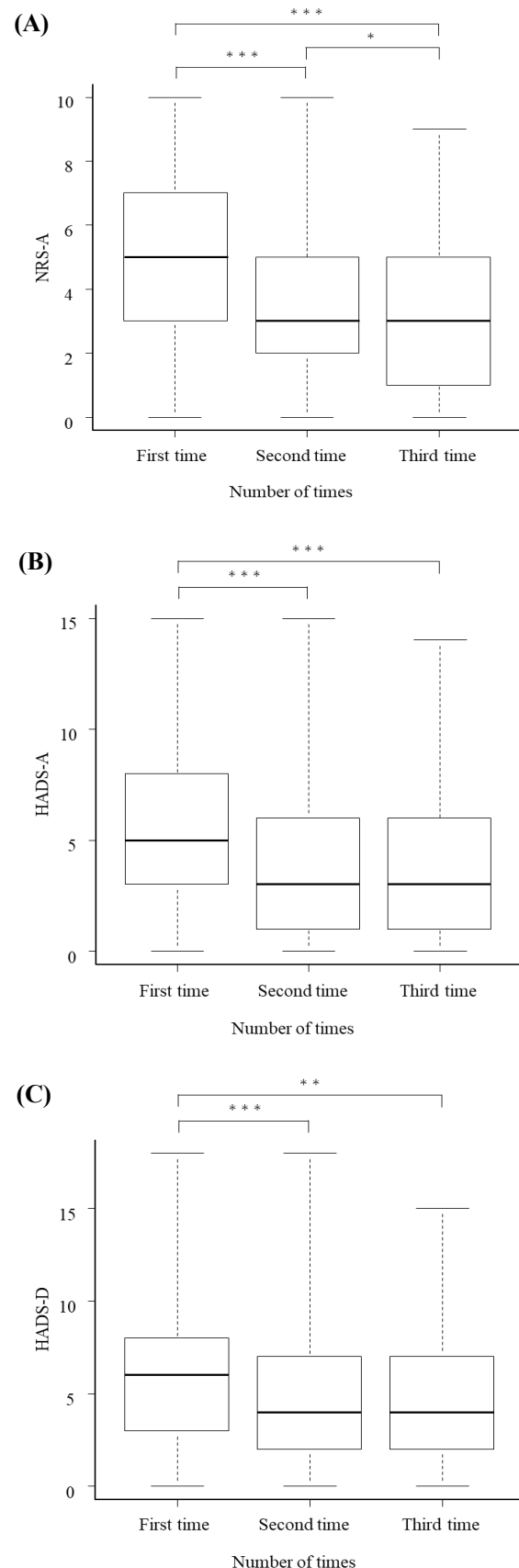

Figure 1. Changes in the NRS-A about cancer chemotherapy and HADS-A and HADS-D. (A) The Numerical Rating Scale for Anxiety (NRS-A) about cancer chemotherapy. *** P < 0.001, * P < 0.05; (B) HADS subscale for anxiety (HADS-A); *** P < 0.001; (C) HADS subscale for depression (HADS-D); *** P < 0.001, ** P < 0.01

Table 2. Subgroup analyses for the NRS-A, HADS-A and HADS-D

	NRS-A about cancer chemotherapy			HADS-A			HADS-D		
	Median (interquartile range)			Median (interquartile range)			Median (interquartile range)		
	First time	Second time	Third time	First time	Second time	Third time	First time	Second time	Third time
Age									
< 65 years	5 (2.5-7)	3 (2-5)	3 (2-5)	4 (2-9)	3 (1.5-6)	2 (1-6)	6 (3-9)	4 (2-7)	5 (2-7)
≥ 65 years	5 (3-7.75)	3 (2-5)	3 (1-4.75)	5 (3-8)	3 (1-6)	3 (1-5)	6 (3-8)	4 (2-7)	4 (1.25-7)
P-value	0.66	0.992	0.152	0.692	0.975	0.577	0.937	0.942	0.546
Sex									
Male	5 (3-7)	3 (1.75-5)	2.5 (1-5)	4.5 (3-7)	3 (1-6)	3 (1-5)	6 (2.75-8.25)	4 (2-7)	4 (1-7.25)
Female	5 (3-7)	3 (2-5)	3 (2-5)	5 (3-9)	3 (1-6)	4 (1-6)	6 (3-8)	4 (2-7)	4 (2-7)
P-value	0.741	0.66	0.062	0.237	0.541	0.432	0.905	0.913	0.48
Types of medical treatment									
Adjuvant chemotherapy / Neoadjuvant chemotherapy	3.5 (2-6)	3 (2-5)	3 (1.75-4)	4 (2-8)	4 (1.75-6)	3 (1-6)	5 (2-8)	4 (2-7)	5 (2-7)
Advanced and Recurrent / Hematological malignancies	6 (4-8)	3 (2-5)	3 (1-5)	5 (3-9)	3 (1-6)	3 (1-5)	7 (4-9)	4 (2-7)	4 (2-7)
P-value	< 0.01	0.521	0.847	0.129	0.309	0.932	< 0.05	0.905	0.465
Days from cancer notification to the first assessment									
< 14 days	6 (4-8)	3.5 (2-5)	3 (1-4.25)	6 (4-10.25)	3 (1.75-6.25)	4 (1-6)	7 (5.5-10)	3 (3-7.25)	5 (2.75-8)
≥ 14 days	5 (2-6)	3 (2-5)	3 (1-5)	4 (2-7)	3 (1-6)	3 (1-5)	5 (3-8)	4 (2-6)	4 (2-7)
P-value	< 0.05	0.137	0.896	< 0.05	0.76	0.459	< 0.05	0.615	0.227
Psychiatric disorders or taking psychotropic drugs									
Positive	7 (3.5-8)	3 (2-5)	3 (2-5)	7 (5.25-10.75)	5 (2.25-8)	4.5 (3.25-7)	7.5 (4.5-10)	7 (2.25-10)	6.5 (4-8.5)
Negative	5 (3-6)	3 (2-5)	3 (1-4.5)	4 (3-8)	3 (1-5)	2 (1-5)	6 (3-8)	4 (2-6)	4 (1.5-7)
P-value	< 0.05	0.655	0.188	< 0.05	< 0.05	< 0.05	< 0.05	0.0635	0.0567

NRS-A, Numerical Rating Scale for Anxiety; HADS-A, Hospital Anxiety and Depression Scale subscale for anxiety; HADS-D, Hospital Anxiety and Depression Scale subscale for depression

Discussion

This prospective observational study compared the psychological condition of cancer patients at different time points during chemotherapy using different methods. We found that the psychological condition scores were highest on commencing chemotherapy and declined thereafter. Furthermore, the NRS-A about cancer chemotherapy declined significantly between the second and third assessments.

The patients with history of psychiatric disorders or taking psychotropic drugs had higher scores than those without history of psychiatric disorders or taking psychotropic drugs (P < 0.05), and tended keep these high scores at the second and third assessments with the HADS-A and -D, although the p-value was not significant for the HADS-D. The patient-assessed scores were higher than the scores assessed by medical staff. These results suggest that medical staff need to focus on the patients when they commence chemotherapy and on the patients with history of psychiatric disorders or those taking psychotropic drugs.

Several studies have reported changes in the psychological condition of patients during chemotherapy. HADS showed that breast cancer patients had moderate anxiety and depression predominantly after treatment, although the treatment modalities included surgery, radiotherapy, and chemotherapy [18]. In bladder cancer patients, the HADS-A and -D scores were elevated after adjuvant chemotherapy [19]. In these studies, the patients' psychological condition tended to deteriorate after chemotherapy, while our study found that the scores improved. This discrepancy might be due to the different time points or periods of assessment. We assessed patients at the commencement of chemotherapy and at early time points, whereas the previous studies assessed them before and after completing chemotherapy. On the other hand, chemotherapy could be a potential protector against cancer and thus reduced distress in cancer patients [20]. In this study, patients completed the questionnaires before finishing chemotherapy, which may have reduced distress. The psychological distress of cancer patients decreases quality of life. Anxiety and depression symptoms were significantly associated with worsening quality of life among breast cancer patients [21]. In our study, psychological distress scores were highest on commencing chemotherapy and declined thereafter. Therefore, the decreasing quality of life due to psychological distress may not occurred in the assessment period after initiating chemotherapy.

The patients adapt to crises generally two weeks after being diagnosed as cancer [1]. The subgroup with shorter periods (< 14 days) after cancer notification had higher initial scores in all three assessments (NRS-A, HADS-A,

(A) PRO-CTCAE Frequency

(B) PRO-CTCAE Severity
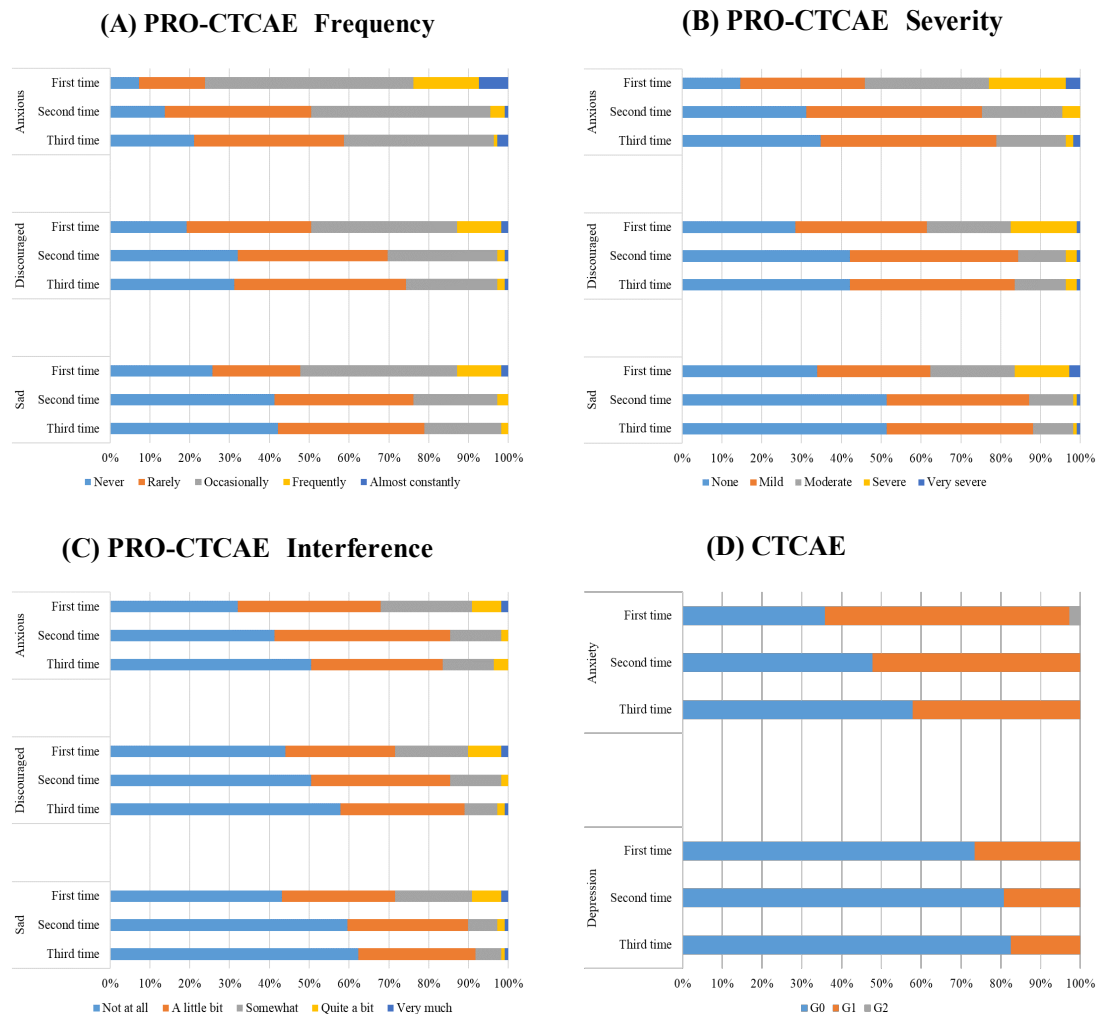

(C) PRO-CTCAE Interference

(D) CTCAE

Figure 2. Changes in the PRO-CTCAE (anxious, discouraged, sad) and CTCAE (anxiety, depression). (A) PRO-CTCAE (anxious, discouraged, sad) frequency. Anxious, P < 0.001, rs = –0.35; discouraged, P < 0.001, rs = –0.329; sad, P < 0.001, rs = –0.276. (B) PRO-CTCAE (anxious, discouraged, sad) severity. Anxious, P < 0.001, rs = –0.206; discouraged, P < 0.01, rs = –0.179; sad, P < 0.001, rs = –0.227. (C) PRO-CTCAE (anxious, discouraged, sad) interference. Anxious, P < 0.01, rs = –0.181; discouraged, P < 0.01, rs = –0.17; sad, P < 0.001, rs = –0.182. (D) CTCAE (anxiety, depression). Anxiety, P < 0.001, rs = –0.189; depression, P=0.0975, rs = –0.0918.

and HADS-D), but not second and third assessments. These results suggested that patients adapted to cancer notification after initiating chemotherapy also in this study. We found that the patients with history of psychiatric disorders or taking psychotropic drugs had higher scores at three assessments (NRS-A, HADS-A, and HADS-D) initially, whereas patients with advanced and recurrent/ hematological malignancies had higher initial NRS-A and HADS-D scores, but not HADS-A. Those with history of psychiatric disorders or taking psychotropic drugs kept higher HADS-A and -D scores at the second and third assessments, but NRS-A did not. Because the NRS-A mainly assesses anxiety about cancer chemotherapy, the NRS-A scores declined at the second assessment. The patients often complaint anxiety about cancer chemotherapy before treatment begins, although this study suggested that anxiety about cancer chemotherapy decline over time. Medical staff should explain and reassure patients at the start of chemotherapy that their anxiety about chemotherapy will decline.

Several studies have reported risk factors for depression and anxiety in cancer patients; these include being a rural resident, non-orthodox Christian, and experiencing extended symptoms [22]. Common mental disorders in cancer patients were associated with gender, education, family income, psychotropic use, and cancer surgery [23]. The influence of prior psychiatric disorders on cancer treatment has been studied [24, 25]. Colon cancer patients with serious psychiatric disorders presented at more advanced cancer stages and received less adjuvant chemotherapy [24], although pre-existing psychiatric disorders did not influence the cancer treatments [25]. Although the risk factors for depression and anxiety in cancer patients differ across studies, medical staff need to focus on cancer patients with these risk factors because psychiatric disorders in cancer patients may influence their choice of cancer treatment. This study has several limitations. First, relatively few cancer patients were enrolled (n = 109) and they had different types of cancer and at different stages. Second, the observation period was

short. Future studies should include more cancer patients and longer observation periods.

In conclusion, psychiatric distress scores were highest when commencing chemotherapy and declined thereafter. Cancer patients with history of psychiatric disorders or taking psychotropic drugs kept higher scores after initiating chemotherapy. We need to be aware of the psychological condition of patients during chemotherapy.

Author Contribution Statement

KK, YS, and TU planned this study. KK and YS drafted the manuscript. KK, HH, TW, MA, RI, JM, and TU collected and analyzed the data. KK and YS designed the study and edited the manuscript. All authors approved the final manuscript.

Acknowledgements

References

1. Holland JC, Rowland JH. Handbook of psychooncology: Psychological care of the patient with cancer. New york: Oxford university press; 1989.
2. Derogatis LR, Morrow GR, Fetting J, Penman D, Piasetsky S, Schmale AM, et al. The prevalence of psychiatric disorders among cancer patients. Jama. 1983;249(6):751-7. https://doi.org/10.1001/jama.249.6.751.
3. Akechi T, Nakano T, Okamura H, Ueda S, Akizuki N, Nakanishi T, et al. Psychiatric disorders in cancer patients: Descriptive analysis of 1721 psychiatric referrals at two japanese cancer center hospitals. Jpn J Clin Oncol. 2001;31(5):188-94. https://doi.org/10.1093/jjco/hye039.
4. Breen SJ, Baravelli CM, Schofield PE, Jefford M, Yates PM, Aranda SK. Is symptom burden a predictor of anxiety and depression in patients with cancer about to commence chemotherapy? Med J Aust. 2009;190(S7):S99-104. https://doi.org/10.5694/j.1326-5377.2009.tb02480.x.
5. Liu H, Yang L. Dynamic change of depression and anxiety after chemotherapy among patients with ovarian cancer. Medicine (Baltimore). 2019;98(31):e16620. https://doi.org/10.1097/md.0000000000016620.
6. Hormozi M, Hashemi SM, Shahraki S. Investigating relationship between pre- and post- chemotherapy cognitive

7. Uramoto H, Kabashima M, Yamazaki K, Kadota T, Narimatsu M, Iwashige A, et al. [what do cancer chemotherapy outpatients want?--results of a questionnaire survey]. Gan To Kagaku Ryoho. 2006;33(11):1681-3.
8. Walawender I, Roczniak W, Nowak D, Skowron M, Waliczek M, Rogalska A, et al. Applicability of the numeric scale for anxiety evaluation in patients undergoing dental treatment. Dent Med Probl. 2015;52:205-14.
9. Zigmond AS, snaith RP. The hospital anxiety and depression scale. Acta psychiatr scand. 1983;67(6):361–70.
10. Zigmond AS, snaith RP (translated to japanese by kitamura t). Hospital anxiety and depression scale. Seishinka shindangaku. 1993;4:371–2.
11. Kugaya A, Akechi T, Okuyama T, Okamura H, Uchitomi Y. Screening for psychological distress in japanese cancer patients. Jpn J Clin Oncol. 1998;28(5):333-8. https://doi.org/10.1093/jjco/28.5.333.
12. Basch E, Reeve BB, Mitchell SA, Clauser SB, Minasian LM, Dueck AC, et al. Development of the national cancer institute's patient-reported outcomes version of the common terminology criteria for adverse events (pro-ctcae). J Natl Cancer Inst. 2014;106(9). https://doi.org/10.1093/jnci/dju244.
13. Japan clinical oncology group. Nci- pro-ctcae® items-japanese item library version 1[internet]. Jco; 2017 [cited 2024 jan 18]. Available from: https://jcog.jp/assets/pro-ctcae_japanese.pdf.
14. Kawaguchi T, Azuma K, Sano M, Kim S, Kawahara Y, Sano Y, et al. The japanese version of the national cancer institute's patient-reported outcomes version of the common terminology criteria for adverse events (pro-ctcae): Psychometric validation and discordance between clinician and patient assessments of adverse events. J Patient Rep Outcomes. 2017;2(1):2. https://doi.org/10.1186/s41687-017-0022-5.
15. National cancer institute. Frequently asked questions; how is pro-ctcae scored? [internet]. Nci [cited 2024 jan 18]. Available from: https://healthcaredelivery.cancer.gov/pro-ctcae/faqs.html.
16. Japan clinical oncology group. Common terminology criteria for adverse events (ctcae) ver. 5.0 [internet]. Jco; 2017 [cited 2024 jan 18]. Available from: https://jcog.jp/assets/CTCAEv5J_20220901_v25_1.pdf.
17. Kanda Y. Investigation of the freely available easy-to-use software 'ezr' for medical statistics. Bone Marrow Transplant. 2013;48(3):452-8. https://doi.org/10.1038/bmt.2012.244.
18. Grusdat NP, Stäuber A, Tolkmitt M, Schnabel J, Schubotz B, Wright PR, et al. Routine cancer treatments and their impact on physical function, symptoms of cancer-related fatigue, anxiety, and depression. Support Care Cancer. 2022;30(5):3733-44. https://doi.org/10.1007/s00520-021-06787-5.
19. Zhang Y, Wang Y, Song B, Li H. Patients' self-report anxiety, depression and quality of life and their predictive factors in muscle invasive bladder cancer patients receiving adjuvant chemotherapy. Psychol Health Med. 2020;25(2):190-200. https://doi.org/10.1080/13548506.2019.1687912.
20. Gil F, Costa G, Pérez FJ. Does chemotherapy reduce stress? Palliat Support Care. 2010;8(4):455-60. https://doi.org/10.1017/s1478951510000337.
21. Daldoul A, Khechine W, Bhiri H, Ammar N, Bouriga R, Krir MW, et al. Factors predictive of quality of life among breast

cancer patients. Asian Pac J Cancer Prev. 2018;19(6):1671-5. https://doi.org/10.22034/apjcp.2018.19.6.1671.

22. Tsaras K, Papathanasiou IV, Mitsi D, Veneti A, Kelesi M, Zyga S, et al. Assessment of depression and anxiety in breast cancer patients: Prevalence and associated factors. Asian Pac J Cancer Prev. 2018;19(6):1661-9. https://doi.org/10.22034/apjcp.2018.19.6.1661.

23. Shirama FH, Silva TB, Dos Santos JC, de Oliveira PA, de Oliveira JI, Borges TL, et al. Factors associated with common mental disorders and use of psychiatric drugs in cancer outpatients. Arch Psychiatr Nurs. 2019;33(5):88-93. https://doi.org/10.1016/j.apnu.2019.06.001.

24. Kaerlev L, Iachina M, Trosko O, Qvist N, Ljungdalh PM, Nørgård BM. Colon cancer patients with a serious psychiatric disorder present with a more advanced cancer stage and receive less adjuvant chemotherapy - a nationwide danish cohort study. BMC Cancer. 2018;18(1):1050. https://doi.org/10.1186/s12885-018-4879-3.

25. Iachina M, Ljungdalh PM, Sørensen RG, Kaerlev L, Blaakær J, Trosko O, et al. Influence of prior psychiatric disorders on the treatment course of gynaecological cancer - a nationwide cohort study. Clin Oncol (R Coll Radiol). 2019;31(2):115-23. https://doi.org/10.1016/j.clon.2018.11.006.