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Effects of Anxiety and Depression on Positioning Error of Radiotherapy

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Abstract: *To evaluate the relationship between depression level, anxiety level and positioning error in cancer patients during radiotherapy. 40 cancer patients (6 cases of nasopharyngeal carcinoma, 14 cases of breast cancer, 2 cases of liver cancer, 10 cases of lung cancer and 8 cases of esophageal cancer) were selected for the first radiotherapy.Self rating Anxiety Scale (SAS) was used to measure anxiety level, self rating Depression Scale (SDS) was used to measure depression level, and Yida XVI software was used to measure linear positioning error (mm) and rotational positioning error (°). Anxiety and depression were assessed three times and positioning error was measured six times before radiotherapy in the early stage (T1), middle stage (T2) and late stage (T3). the scores of SDS and SAS in the early stage were higher than those in the middle and late stage ($P < 0.05$). During T1 and T2, the placement error of patients with moderate and high depression was greater than the average value of placement error of patients with non depression , and the placement error of patients with moderate and high anxiety was greater than that of patients with non anxiety ($P < 0.05$). There was no significant difference dbetween K1 and K2 and between B1 and B2 in T3 ($P > 0.05$). The level of depression and anxiety is the highest in tumor patients before the first radiotherapy. High level of depression and anxiety may be related to positioning error.*

Keywords: *Anxiety; depression; positioning error; radiotherapy*

1. Introduction

With the development of radiotherapy technology, radiotherapy plays a more and more important role in the field of tumor therapy. Intensity modulated radiation therapy (IMRT) is a high-precision radiotherapy technique, which can improve the target dose rate and local control rate of tumor and reduce the dose of surrounding normal tissues[1,2]. The positioning error of radiotherapy is one of the most critical factors affecting the high accuracy of IMRT. There are many factors affecting the positioning error, including machine factors,positioning process factors, positioning operator factors and patient factors. Research by Nixon[3]found that 14% to 58% of patients with head and neck tumors feel anxious and afraid of the thermoplastic film on the face. In the past studies, the psychological problems of anxiety or depression of radiotherapy patients or the accuracy of radiotherapy alone were generally focused, but few studies have shown that the two are related.The purpose of this study is to explore the relationship between the two.

2. Data and methods

2.1 Object

Tumor patients who underwent image guided radiotherapy (IGRT) inour department from August 2021 to January 2022 were selected.Selection criteria: 1 Patients exposed to radiotherapy for the first time; 2 Patients with normal intelligence, who can fully understand the contents of SAS and SDS; 3 Age >18 years, meeting the age requirement for filling the scale. Exclusion criteria: 1 Patients with mental disorders who are unable to cooperate with the scale; 2Patients who are unwilling to complete the scale; 3 Patients who are in extremely poor physical condition and unable to cooperate with the scale. A total of 40 cancer patients, including the nose.There were 6 cases of pharyngeal cancer, 14 cases of breast cancer, 2 cases of liver cancer, 10 cases of lung cancer and 8 cases of esophageal cancer.Patient age 38-78Years old, 18 male patients and 22 female patients.

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2.2 Tools

2.2.1 Equipment

Elekta Image-guided Volume rotation intensity modulated radiotherapy system (Elekta Synergy): The linear acceleratorincludes Synergy XVI system, which can be used for conventional radiotherapy and 3-D conformal radiotherapy3D-CRT, IMRT, VMAT and IGRT. The positioning errors calculated by the XVI software are three linear errors and three rotational errors,which are convenient for this study

2.2.2 Anxiety Assessment Tool

Self-Rating Anxiety Scale (SAS) is a self-measuring scale developed by William Zhuang, a professor of psychology at Duke University, to assess the level of anxiety symptoms in adults. There are 4 frequencies in the scale, which represent the frequency of corresponding symptoms. Grade 1 represents no or little timeoccurrence; Grade 2 represents occurrence in a small part of time;Grade 3 represents occurrence in a considerable amount of time; Grade 4 represents occurrence in most or all of the time. There are 20 items in the scale. The final reference statistic for SAS is the total score.After the completion of the self-assessment by the person filling in the self-assessment scale, the final standard score can be obtained by adding the scores of the 20 items and then multiplying the scores by 1.25 to obtain a whole. We can also query the Rough Score Standard Score Conversion Table for similar standard score conversion. The higher the final standard score, the more severe the anxiety symptoms.Generally, if the standard score is less than 50, it is normal; If the standard score is 50-60, it is a mild anxiety patient; if the standard score is 61-70, it is a moderate anxiety patient; if the standard score is more than 70, it is a severe anxiety patient. The form of the SAS scale is shown in Table 1.

Table 1: Self-Measurement of Anxiety (SAS)

Performance	none or very little	sometimes	Most of the time	Most or all of the time
I'm scared for no reason				
I tend to get upset or panic				
I think I might be going crazy				
I am distressed by headaches, neck pain and back pain				
I think my heart is beating fast.				

2.2.3 Depression Assessment Tool

The Self-rating Depression Scale (SDS) is also a self- measure scale developed by Prof (Table 2). William Trang from 1965 to 1966 to evaluate the degree of adult depression. Consistent with SAS, it also includes 20 items, including eight items for depressive disorder, eight items for somatic disorder, two items for psychomotor disorder, and two items for psychotic-emotional symptoms. The form of the scale is simple and convenient for patients to understand and study. Most importantly, it can directly reflect the subjective psychological feelings of the patients with depression. This scale is indicated for adults with depressive symptoms. Like SAS, the scale has 4 frequencies, representing the frequency of occurrence of the corresponding symptoms, “1” for no or very little time, and “2” for a small proportion of the time: Grade “3” represents that it occurs in a considerable amount of time; grade “4” represents that most or all of the time will occur. After the assessment of the scale, add the scores of each of the 20 items to obtain the total crude score (X), then multiply the crude score by 1.25 and take an integer to obtain the standard score (Y)[5-6].

Table 2: The form of SDS table

Performance	none or very little	sometimes	Most of the time	Most or all of the time
I don't sleep well at night				
I suffer from constipation				
Ithink mornings are the best in the day				
I think I'm a useful person. Someone needs me				
I'm still interested in things I'm usually interested in				

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2.2.4 Evaluation of positioning error in radiotherapy

A cone - beam computed tomography (CBCT) scan was performed before treatment, and the scanned CBCT image was registered with the planned CT. Registration rules: The selection range of the clipbox of tumor patients will adopt the IGRT cooperative group standard of Yikda, and the upper and lower PTVs are 2cm of upper and lower extension respectively; The left and right PTVs were left and right dilated by 2cm respectively; The anterior border and posterior border should be 2cm for PTV, but the posterior border should include the vertebral body and spinous process. The XVI system will automatically calculate the linear and rotational setup errors in X-axis (leftright), Y-axis (head-to-foot) and Z-axis (front-rear).

3. Method

3.1 SAS and SDS Filling

Patients were instructed to complete SAS and SDS scales before the first radiotherapy (T1); before interim treatment (T2) (before the thirteenth treatment for 25 times and before the 15th or 16th treatment for 30 times); and before the last treatment (T3). The two questionnaires were anonymously numbered and distributed by the investigators on site to instruct the patients to fill out the questionnaires and retrieve the questionnaires in real time.

3.2 Acquisition of setting error

All the patients were in supine position, and then fixed with thermoplastic film and headrest. 6 positioning errors were obtained by XVI software. Taking 25 times of radiotherapy as an example, the positioning errors were recorded after the first and second radiotherapy CBCT scans were completed, and the average positioning errors were taken as the initial (T1) positioning errors (K1). After the 12th and 13th radiotherapy CBCT scans were completed, the positioning errors were recorded twice, and the average positioning errors were taken as the positioning errors (K2) in the middle stage of radiotherapy. After completing the CBCT scan of 24 and 25 times of radiotherapy, the positioning errors were recorded again, and the average value of positioning errors was taken as the positioning error (K3) in the later stage of treatment (T3).

3.3 Statistical Methods

SPSS25.0 was used for statistical analysis. The scores and positioning errors of anxiety self-scale and depression self-scale were analyzed descriptively. The variance of repeated measures was used to explore the change trend of anxiety and depression grades. For those with statistically significant differences, LSD method was used for statistical analysis. Wilcoxon rank sum test was used to compare the positioning errors of patients with high anxiety (SAS score > 59) and non-anxiety patients (SAS score < 50).

4. Results

4.1 Results of Anxiety Assessment

4.1.1 T1 period

The total score of SAS in 40 patients was 28-79 and the average score was (52.5±8.0). There were 20 non-anxiety patients(score<50),12 mild anxiety patients(score 50-59),6 moderate anxiety patients(score 60-69), and 2 severe anxiety patients(score 70-100).

4.1.2 T2 period

The total score of SAS in T2 of 40 patients ranged from 26 to 72 and the average score was 47.8±8.4. There were 29 non-anxiety patients (score <50), 7 mild anxiety patients (score 50-59), 3 moderate anxiety patients (score 60-69), and 1 severe anxiety patient (score 70-100). Anxiety symptoms decreased significantly during T2 as patients became more knowledgeable about radiation therapy.

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4.1.3 T3 period

The total SAS score of 40 patients with T3 was 280.79, with an average score of 46.8 ±8.0. there were 31 non-anxiety patients (score-lt;50), 6 mild anxiety patients (50-59), 2 moderate anxiety patients (60-69) and 1 severe anxiety patient (70-100). The results are shown in Table 3.

Table 3 Anxiety assessment in three periods (number of people)

Performance	Non-anxious patients	Mild anxiety	Moderate anxiety	Severe anxiety
T1	20	12	6	2
T2	28	8	3	1
T3	31	6	2	1

4.2 Depression Assessment Results

4.2.1 Depression Assessment in T1

The total score of T1 in 40 patients ranged from 32 to 80, with an average score of (51.6±7.5). There were 24 non-depressed patients (score <53), 10 mild depressed patients (score 53-62), 5 moderate depressed patients (score 63-72), and 1 major depressed patient (score 73-100).

4.2.2 T2 period

The total scores of T2 in 40 patients ranged from 28 to 78, with an average score of 48.4±8.0. There were 30 non-depressed patients (score <53), 6 patients with mild anxiety (scores of 53-62), 3 patients with moderate depression (scores of 63-72), and 1 patient with severe anxiety (scores of 73-100). As with SAS, depressive symptoms were significantly reduced during T2 as patients became more knowledgeable about radiation therapy.

4.2.3 Period T3

The total scores of T3 in 40 patients ranged from 26 to 76 and the average score was (48.1±8.2). There were 31 non-depressed patients(score<53), 6 mild depressed patients(score 53 - 62), 2 moderate depressed patients(score 63 - 73) and 1 severely depressed patient(score 73-100).

The results are shown in Table 4.

Table 4: Depression assessment in three periods(number of people)

	Non-depressive patients	Mild depression	Moderate depression	Severe depression
T1	24	10	5	1
T2	30	6	3	1
T3	31	6	2	1

4.3 Results of analysis of variance for repetitive measures of anxiety and depression scores

The difference of SAS scores in T1, T2 and T3 was statistically significant(F=11.22, P<0.001). The results of LSD comparison showed that the SAS score of T1 period was higher than that of T2 period (P=0.008) and T3 period (P=0.012). There was no significant difference between T2 period and T3 period. The difference of SDS scores in T1, T2 and T3 was statistically significant(F=14.22, P<0.001). The results of LSD comparison showed that SDS scores in T1 period were higher than those in T2 period (P=0.008) and T3 period (P=0.012). There was no significant difference between T2 period and T3 period.

4.4 Analysis of Positioning Error Results

4.4.1 linear setting error

The mean positioning error of T 1 was 3.0±0.1mm in left and right, 3.5±0.1mm in head-foot direction and 2.8±0.1mm in front-back direction.The average positioning error in left-right direction, head-foot direction and front-back direction was 2.9±0.1mm, 3.3±0.1mm and 2.8±0.1mm respectively. At T3 The average positioning error in the left-right direction was 2.9±0.1mm, the average positioning error in the head-foot direction was 3.4±0.1mm, and the positioning error in the anterior-posterior direction was 2.9±0.1mm. The results are shown in Table 5.

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Table 5: Linear Setting Error in Different Periods (mm)

	X-axis (left and right)	Y Axis (Head to Foot)	Z-axis (A/P)
T1	3.0±0.1	3.5±0.1	2.8±0.1
T2	2.9±0.1	3.3±0.1	2.8±0.1
T3	2.9±0.1	3.4±0.1	2.9±0.1

4.4.2 Rotation setting error

In T1, the average rotation setting error in left-right direction is 1.5±0.1°, the average rotation setting error in head-foot direction is 1.2±0.1° and the setting error in front-rear direction is 0.6±0.1°; in T2, the average rotation setting error in left-right direction is 1.4±0.1°, the average rotation setting error in headfoot direction is 1.1±0.1° and the setting error in front-back direction is 0.5±0.1°; in T3, the average rotation setting error in left-right direction is 1.6±0.1°, the average rotation setting error in head-foot direction is 1.5±0.1°, and the rotation setting error in front-back direction is 0.6±0.1°. The results are shown in Table 6 .

Table 6: Rotation Setting Error in Different Periods (°)

	X-axis (left and right)	Y Axis (Head to Foot)	Z-axis (A/P)
T1	1.5±0.1	1.2±0.1	0.6±0.1
T2	1.4±0.1	1.1±0.1	0.5±0.1
T3	1.6±0.1	1.5±0.1	0.6±0.1

4.5 Comparison of Positioning Errors in Different Depression and Anxiety

4.5.1 Anxiety

The SAS scores of patients at T1, T2 and T3 were ranked respectively. Patients with moderate-to-high anxiety scores greater than 60 were classified as K1 group, and non-anxiety patients with scores less than 50 were classified as K2 group. By Wilcoxon ranksum test, the average values of linear positioning error and rotational positioning error of K1 group were greater than those of K2 group at T1 and T2 [(3.6±0.1)mm vs (2.5±0.1)mm, (1.4±0.1)mm 1)°VS (1.1 ± 0. 1), Z=-2.10, -1.96, *P*=0.035, 0.037] At T3, there was no statistically significant difference in positioning error between patients in K1 group and K2 group [(2. 9±0. 1) mmVS. (3. 0±0. 1) mm, (1.3±0.1)°VS (1.2±0.1)°Z= -0. 35, -0.40, *P*=0.745, 0.750] There was no significant difference in positioning error between patients in K1 and K2 groups in the three periods according to the ranking of SAI scores [(2. 9 ±0. 1) VS (2. 3±0. 1) ,(2. 9±0. 1) VS. (2. 5±0. 1), (2. 8±0. 1) VS. (3. 0±0. 1) (Z=-1. 34,-0. 87,-0. 73, *P*=0. 180, 0.383,0.468].

4.5.2 Depression

In accordance with the above method, we sorted the SDS scores of patients in T1, T2, and T3 respectively, and classified the patients with moderate and high depression score greater than 62 as group B1, and the non-depressed patients with score less than 53 as group B2. Similarly, by Wilcoxon rank sum test, the linear positioning error and rotational positioning error of group B1 at T1 and T2 were also larger than those of group B2 [(3.5±0.1)mm vs (2.6±0.1)mm, (1.4±0.1)mm and (1.4±0.1)mm, respectively. 1)°VS. (1.2±0. 1), Z = -2. 04, -1.98, *P*=0. 034, 0. 036] at T3, there was no statistically significant difference in positioning error between patients in group B1 and group B2 [(2. 8 ±0. 1) mmVS(2. 9±0. 1) mm, (1.2±0.1)° VS (1.3±0.1)°Z = -0. 36, -0.41, *P*=0. 751, 0.755] according to SAI There was no significant difference in positioning error between patients in B1 and B2 groups in the three periods [(2. 7±0. 1) VS (2. 3±0. 1) (3.0±0. 1) VS (2. 6±0. 1), (2.9±0. 1) VS. (2.9±0. 1) (Z=-1. 36. -0. 84. -0. 70, *P*=0. 185, 0. 392, 0. 476], Preliminary, it was found that the effects of positioning error caused by anxiety and depression were highly similar.

5. Conclusions

The results of this study showed that the anxiety level assessed by SAS was the highest at the initial stage, and the focus rate level of patients decreased significantly with the progress of radiotherapy. Due to the lack of understanding of the side effects of radiotherapy such as skin injury, visceral injury, pain, loss of appetite and so on, as well as the unfamiliarity of radiotherapy itself, coupled with the lack of contact with radiotherapy professionals before starting radiotherapy, it is easy for tumor patients to worry about radiotherapy[7] the first radiotherapy is similar to the waiting room. Some characteristics in

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the treatment environment such as linear accelerator may also aggravate anxiety [8]. Therefore, with the progress of radiotherapy, the decrease of anxiety level shows that patients have an understanding of radiotherapy technology itself, in-depth understanding of radiotherapy side effects, and adaptation to the radiotherapy environment. Colleagues may also be related to the support provided by the radiotherapy team after treatment, such as humanistic care. However, the anxiety level of patients will not change significantly in the later stage [9].Memory loss, slow thinking, loss of interest, emptiness in life, difficulty in decision-making and feeling useless, worthless, etc. These symptoms will slowly appear after the patient's illness, and these depressive symptoms will in turn aggravate the difficulty in decision-making.[10] After the illness, patients' living habits change greatly, and their emotions are easy to collapse. once they know their illness, they are depressed, and it is extremely easy to produce a desolate state of mind, which may eventually lead to the most desperate choice of suicide. Patients often feel that life is very boring, frequent negative treatment of life, seriously affect their own mental health, cancer patients in the end of depression, helplessness, hope to die early [11], depression can be used as a predictor of suicidal tendency. Henderson JM et al [12] have also shown that despair and pain are the most important factors for suicide. Pain constitutes a physical and psychological stressor, which is likely to induce and aggravate mental pain. Some literatures have also reported that depression is the consequence of chronic pain [13] and physical health is getting worse and worse with age. Some studies have shown that the level of depression increases with age [4]. This study found that there was a significant difference in the setting error of radiotherapy with different anxiety or depression levels of cancer patients, which roughly accorded with the basic model that the higher the anxiety level, the greater the positioning error and the higher the depression grade, the greater the positioning error. and we found that the effects of anxiety and depression on positioning errors were highly similar. However, at present, there are few studies on the relationship between anxiety and positioning error or between depression and positioning error, so the influence of anxiety on positioning error or the mechanism of depression on positioning error is still unclear. More in-depth research is needed.

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