

# Effect of Psychological Intervention on Differentiated Thyroid Cancer Patients in the Treatment with Radioactive Iodine

Yan-Bin Liu<sup>1</sup>, Li-Juan Zuo<sup>2</sup>, Ya-Chao Liu<sup>1</sup>, Yan-Ping Li<sup>1</sup>, Yun-Chao Xin<sup>1</sup>, Hong-Yan Zhang<sup>3</sup>, Li-Yuan Hou<sup>4</sup>

<sup>1</sup>Department of ENT & HN Surgery, The First Affiliated Hospital of Hebei North University, Zhangjiakou City, Hebei, 075000, People's Republic of China;

<sup>2</sup>Department of Endocrine, The First Affiliated Hospital of Hebei North University, Zhangjiakou City, Hebei, 075000, People's Republic of China;

<sup>3</sup>Department of Psychiatry, The First Affiliated Hospital of Hebei North University, Zhangjiakou City, Hebei, 075000, People's Republic of China; <sup>4</sup>Department of Nuclear Medicine, The First Affiliated Hospital of Hebei North University, Zhangjiakou City, Hebei, 075000, People's Republic of China

Correspondence: Yan-Bin Liu, Department of ENT & HN Surgery, The First Affiliated Hospital of Hebei North University, No. 12, Changqing Street, Qiaoxi District, Zhangjiakou, Hebei, 075000, People's Republic of China, Email liuyanbin19830524@163.com

**Objective:** This study aimed to design a standard method of psychological intervention and evaluate the effect of such psychological intervention against the psychological distress of differentiated thyroid cancer (DTC) patients in the treatment with radioactive iodine.

**Methods:** The enrolled patients were randomly divided into the intervention group and the control group. Both the patients in the 2 groups received the routine nursing care, while the patients in the intervention group also received the additional standard psychological interventions. The questionnaires including patient health questionnaire-9 (PHQ-9), generalized anxiety disorder 7-item (GAD-7), cancer fatigue scale (CFS) and positive and negative affect schedule (PANAS) were used to assess psychological status. These questionnaires were performed at week 0 (T0), week 8 (T1, immediately after the last time of intervention) and week 24 (T2, 16 weeks after the intervention).

**Results:** PHQ-9, GAD-7, CFS and Negative Affect (NA) scores measured at T1 and T2 in the intervention group were significantly lower than those in the control group ( $P < 0.001$ ). And intervention group also had higher positive affect (PA) scores at T1 and T2 ( $P < 0.001$ ). Furthermore, the changes of PHQ-9, GAD-7, CFS, PA and NA scores from T0 to T1 and T0 to T2 were more evident in the intervention group than in the control group.

**Conclusion:** Psychological intervention could significantly improve psychological distress of DTC patients in the treatment with radioactive iodine.

**Keywords:** differentiated thyroid cancer, radioactive iodine, psychological intervention, psychological distress, mood

## Introduction

Differentiated thyroid cancer (DTC), arising from thyroid follicular cells that include both papillary and follicular types, is the most common endocrine malignancy with increasing incidence rates.<sup>1,2</sup> The thyroid gland, consisting of two connected lobes, is one of the largest endocrine glands in the human body, weighing 20–30 g in adults. Thyroid lesions are often found on the gland, with a prevalence of 4–7%. Most of them are asymptomatic, and thyroid hormone secretion is normal.<sup>3</sup> Generally, DTC has a very good prognosis after standard treatments, resulting in a high prevalence of survivors.<sup>4</sup> Surgery and radioactive iodine are the two major therapeutic options for DTC. But both of the treatments will result in a lifelong dependence on substitution therapy with levothyroxine.<sup>5</sup>

Although patients with DTC have excellent disease prognosis, they still complain about poor quality of life (QoL), especially psychological distress.<sup>2,5</sup> Previous studies suggests that DTC patients had greater levels of anxious and depressive symptoms than normal populations.<sup>6</sup> And these psychological symptoms will persist throughout the long-term survivorship.<sup>6</sup> Furthermore, patients with DTC have been reported to have a similar or greater psychological burden than patients with other cancers.<sup>7</sup> Psychological distress increases the risk of progression, recurrence, and metastasis of cancer. DTC patients with

psychological distress have poorer clinical outcomes than the patients without psychosocial disorder.<sup>8</sup> Thus, it is necessary to manage DTC patients' psychological distress during their long-term survivorships.

Psychological intervention refers to the planned implementation of psychological counseling for patients in order to help them reduce psychological pressure and complete the predetermined goal.<sup>9</sup> Previous studies have reported that psychological intervention could help improve DTC patients' QoL. In 2016, Wu et al<sup>10</sup> reported that a 1-year psychological and behavioral intervention could improve functional capacities and QoL, alone with reducing depression and anxiety in patients with DTC who treated with postoperative radioactive iodine. In 2020, Wang et al<sup>11</sup> found that a four-week psychological nursing intervention, including the processes such as improving patient's care environment, enhancing patient's understanding of the disease and reducing patient's fear and tension, could reduce psychological distress and enhance the QoL of thyroid cancer patients. Similarly, He et al<sup>12</sup> reported in 2021 that WeChat app-based perioperative nursing interventions could reduce disease stress and improve positive attitudes and self-management efficacy in patients with thyroid cancer. However, due to the small number of published articles, the effect of psychological intervention in patients with DTC and the standard intervention procedures still remain controversial.

Thus, in the present study, we aimed to design a standard method of psychological intervention, and evaluate the effect of such psychological intervention against the psychological distress of DTC patients in the treatment with radioactive iodine.

## Methods

### Patients

This prospective study was approved by the Ethics Committee of the First Affiliated Hospital of Hebei North University in accordance with the Declaration of Helsinki. The ethical committee protocol number was K2020210. All participants written provided informed consent for publishing the data.

The inclusion criteria were as followed: (1) patients were pathologically diagnosed with DTC or Well Differentiated Thyroid Carcinoma (WDTC) following surgical treatment; (2) patients were over the age of 18; (3) patients were treated with radioactive iodine. The exclusion criteria included as followed: (1) patients were diagnosed with other type of thyroid cancer; (2) patients were unable to complete the questionnaires; (3) patients were diagnosed with dementia or mental illness.

### Randomization and Interventions

The enrolled patients were randomly divided into the intervention group and the control group, according to the random number table. Both the patients in intervention group and control group received the routine nursing care including the isolation protection education, the medication guide and the discharge guidance, while the intervention group also received the additional standard psychological interventions. Each patient in intervention group received 6 times of psychological therapies. Each therapy was 60–120 min in duration through face to face communication. The details of the psychological intervention are illustrated in Table 1. Total thyroidectomy and cervical lymph node dissection were performed when patients had distal metastasis (eg lung metastasis). Subtotal thyroidectomy and cervical lymph node dissection were performed when patients did not have distal metastasis of cancer cells, but cancer cells involved nerves and invaded trachea, which could not be completely removed by surgery, and tumors remained.

### Tools

The patient health questionnaire-9 (PHQ-9) is a 9-item questionnaire designed to screen for depression. The PHQ-9 evaluates the presence of depression symptoms over the previous two-week period. Response options for each item range from “not at all” (0-point) to “nearly every day” (3-point).<sup>13</sup> Thus, the depression severity score can be summarized with a range from 0 (no depression) to 27 (maximum).<sup>14</sup> The 10 point was often used as cut off value to identify depression symptoms.<sup>15</sup>

The generalized anxiety disorder 7-item (GAD-7) Scale is a self-rating measure tool to assess general anxiety disorder. Each item was ranged from “not at all” (0-point) to “nearly every day” (3-point) in relation to the past two

**Table 1** Contents of the Psychological Intervention

Time	Methods	Contents
Week 0 (before radioactive iodine treatment)	Face-to-face counseling	1. Help patients know the disease. 2. Help patients better understand their inner feelings and nature of their psychological reaction to the treatment. 3. Know the patients' educational level and condition.
Week 1	Face-to-face counseling	1. Guide patients on valuing themselves, developing a positive self-concept. 2. Encourage patients to express their stressful and illness. 3. Encourage patients to cooperate with medical staffs
Week 2	Face-to-face counseling	1. Help patients find the appropriate ways (eg music and videos) to relax themselves. 2. Share the experiences of other patients. 3. Encourage patients to talk about their negative emotions.
Week 4	Face-to-face counseling	1. Improve patients' social identity and sense of belonging. 2. Help patients to develop their own interests.
Week 6	Face-to-face counseling	1. Encourage patients to share their emotional changes during the treatment. 2. Encourage patients to chat with each other.
Week 8	Face-to-face counseling	1. Conclude methods to alleviate negative emotions 2. Emphasis on what to be cautious of at a later stage

**Note:** The details of the psychological intervention.

weeks. The GAD-7 severity score ranged from 0 (no depression) to 21 (maximum).<sup>15</sup> The 10 point was often used as cut off value to identify anxiety symptoms.<sup>15</sup>

The cancer fatigue scale (CFS) is a 15-item scale used to assess fatigue in cancer patients with a total score ranging from 0 (no fatigue) to 60 (maximum).<sup>16</sup> The scale has 3 subscales including physical (maximum score of 28), affective (maximum score of 16), and cognitive (maximum score of 16). The scale has a high sensitivity and specificity and usually set a cut-off value of 19 to identify fatigue in cancer patients.<sup>16</sup>

Positive and negative affect schedule (PANAS) is a scale composed of 20 items to measure positive (PA, 10 items) and negative affect (NA, 10 items). Response options for each item range from “very slightly or not at all” (0-point) to “extremely” (5-point). Total scores of PA and NA were calculated, where a higher score was indicative of higher PA or NA.<sup>17</sup>

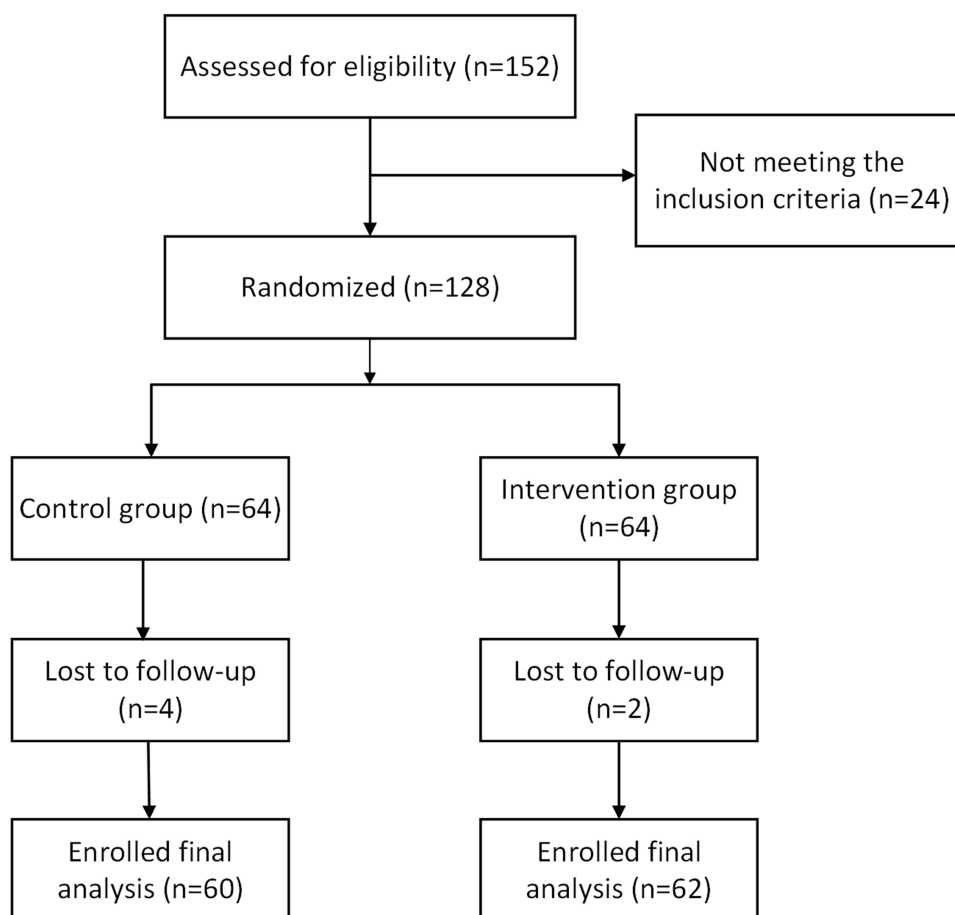
The above questionnaires/scales were performed at week 0 (T0), week 8 (T1, immediately after the last time of intervention) and week 24 (T2, 16 weeks after the intervention). All questionnaires and scales were completed by patients themselves independently or with the assistance of their caregivers. All medical staff conducting psychological intervention for patients were trained uniformly to ensure uniform standards. When carrying out psychological intervention on patients, we use fixed mode and unified treatment group to deal with it, so as to avoid the influence of different treatment groups on the results.

## Statistical Methods

The data in this study were analyzed by the SPSS (version 22.0). The categorical data were described as numbers (percentages) and compared using the  $\chi^2$  test or Fisher's exact test. The quantitative data were described as mean  $\pm$  standard deviation (SD) and compared by *t*-test. Linear mixed models were used to evaluate the differences in PHQ-9, GAD-7, CFS, PA and NA scores. A *P* value < 0.05 considered as statistically significant.

## Results

From January 2021 to March 2022, 152 patients with DTC were screened in this study. 24 patients were excluded because of not meeting the inclusion criteria. The remaining 128 patients were divided randomly and equally into the control (n=64) and intervention (n=64) groups. Six patients were lost to the follow-up during the study period, leaving a final sample of 60 in the control group and 62 in the intervention group. The flow diagram of the study is shown in Figure 1. There were 12 males and 48 females in the control group, with the mean age of (54.32  $\pm$  8.78) years. There were 15 males and 47 females in the intervention group, with the mean age of (56.21  $\pm$  9.09) years. The baseline



**Figure 1** Flow diagram of the study.

characteristics of the 2 groups are shown in [Table 2](#). All characteristics did not differ different between the 2 groups ( $P > 0.05$ ).

At the baseline evaluation, 10/60 patients in the control group (16.67%) showed symptoms of depression (PHQ-9 score  $> 10$ ), the number increased to 13/60 (21.67%) at T1 and 24/60 (40.00%) at T2, respectively. In the intervention group, 11/62 (17.74%) patients showed symptoms of depression at baseline (T0), the number decreased to 4/62 (6.67%) at T1 and 6/62 (9.68%) at T2, respectively. Analysis of means comparison ([Table 3](#)) showed that PHQ-9 scores measured at T1 and T2 in the intervention group were significantly lower than those in the control group ( $P < 0.001$ ), respectively.

As for anxiety evaluation, 13/60 (21.67%) patients in the control group and 10/62 (16.13%) patients in the intervention group showed symptoms of anxiety (GAD-7 score  $> 10$ ). The 2 groups of patients had similar GAD-7 scores at T0 ( $p = 0.314$ , [Table 3](#)). The number of patients with anxiety symptoms increased to 26/60 (43.33%) at T1 and 35/60 (58.33%) at T2 in the control group, while decreased to 6/62 (9.68%) at T1 and 9/62 (14.52%) at T2 in the intervention group. The GAD-7 scores measured at T1 and T2 in the intervention group were significantly lower than those in the control group ( $P < 0.001$ , [Table 3](#)), respectively.

At the baseline evaluation, patients in the control group had similar CFS scores comparing to the intervention group ( $p = 0.985$ , [Table 3](#)). However, the CFS scores measured at T1 and T2 in the intervention group were significantly lower than those in the control group ( $P < 0.001$ , [Table 3](#)), indicating patients with DTC had decreased cancer fatigue after psychological intervention. Comparing to the control group, the intervention group also had higher PA scores and lower NA scores at T1 and T2 ( $P < 0.001$ , [Table 3](#)), respectively.

**Table 2** Baseline Characteristics of the Intervention Group and the Control Group

	Intervention Group (n=62)	Control Group (n=60)	P value
Age, mean $\pm$ SD, years	58.24 $\pm$ 7.44	56.21 $\pm$ 9.09	0.245
Gender, n (%)			0.577
Male	15 (24.19)	12 (20.00)	
Female	47 (75.81)	48 (80.00)	
Educational level, n (%)			0.747
Middle or high school	41 (66.13)	38 (63.33)	
$\geq$ College	21 (33.87)	22 (36.67)	
Histological type, n (%)			0.411
Follicular	14 (22.58)	10 (16.67)	
Papillary	48 (77.42)	50 (83.33)	
Comorbidities, n (%)	30 (48.39)	28 (46.67)	0.849
Current occupation, n (%)			0.217
Employed	39 (62.90)	44 (73.33)	
Unemployed	23 (37.10)	16 (26.67)	
Family history with cancer, n (%)	15 (24.19)	18 (30.00)	0.470

**Note:** There was no significant difference in general information between the two groups.

**Abbreviation:** SD, standard deviation.

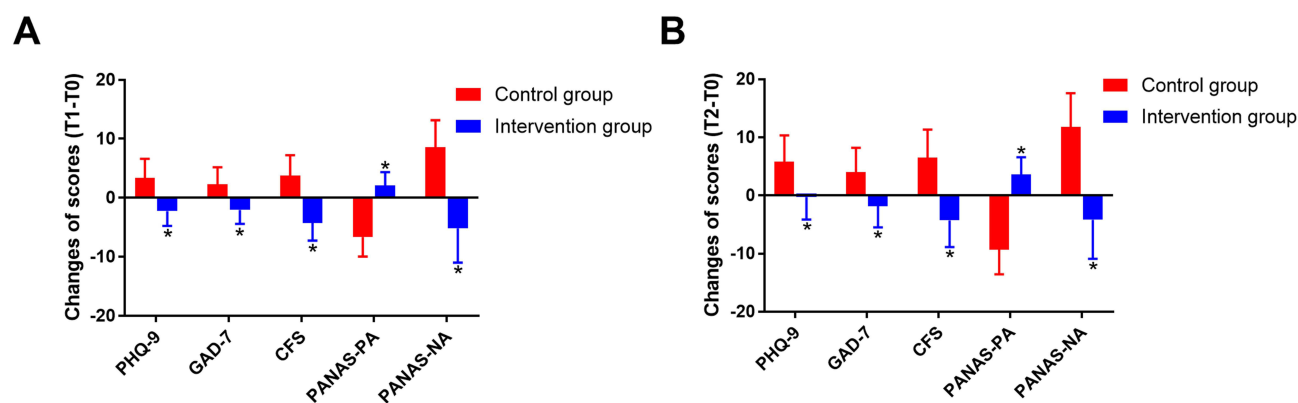
**Table 3** Changes in Psychological Distress Over Time

Questionnaires	Intervention Group (n=62)	Control Group (n=60)	P value
PHQ-9			
T0	5.32 $\pm$ 4.06	5.48 $\pm$ 4.55	0.837
T1	3.06 $\pm$ 3.15	8.83 $\pm$ 4.40	< 0.001
T2	5.08 $\pm$ 4.02	11.27 $\pm$ 5.00	< 0.001
GAD-7			
T0	7.26 $\pm$ 3.76	7.97 $\pm$ 3.34	0.314
T1	5.21 $\pm$ 3.19	10.28 $\pm$ 3.92	< 0.001
T2	5.45 $\pm$ 3.18	11.98 $\pm$ 4.76	< 0.001
CFS			
T0	17.55 $\pm$ 4.53	17.57 $\pm$ 6.03	0.985
T1	13.29 $\pm$ 4.46	21.32 $\pm$ 5.34	< 0.001
T2	13.24 $\pm$ 5.22	24.03 $\pm$ 5.34	< 0.001
PANAS-PA			
T0	30.81 $\pm$ 3.58	31.40 $\pm$ 4.31	0.409
T1	32.89 $\pm$ 4.21	24.75 $\pm$ 4.15	< 0.001
T2	34.43 $\pm$ 3.82	22.08 $\pm$ 4.38	< 0.001
PANAS-NA			
T0	22.43 $\pm$ 4.82	21.30 $\pm$ 5.12	0.210
T1	17.26 $\pm$ 4.48	29.87 $\pm$ 4.51	< 0.001
T2	18.26 $\pm$ 4.58	33.10 $\pm$ 4.46	< 0.001

**Notes:** The above data were assessment scores of patients. T0: week 0. T1: week 8, immediately after the last time of intervention. T2: week 24, 16 weeks after the intervention.

**Abbreviations:** PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized anxiety disorder 7-item; CFS, Cancer Fatigue Scale; PANAS, Positive and Negative Affect Schedule; PA, Positive Affect; NA, Negative Affect.

Furthermore, the changes of PHQ-9, GAD-7, CFS, PA and NA scores from T0 to T1 were more evident in the intervention group than in the control group (Figure 2A). Similarly, we also observed more evident score changes from T0 to T2 in the intervention group (Figure 2B).



**Figure 2** Changes in psychological distress over time. (A) The changes of scores from T0 to T1; (B) The changes of scores from T0 to T2. \* $P < 0.05$ .

## Discussion

In the present study, we aimed to design a standard method of psychological intervention, and evaluate the effect of such psychological intervention against the psychological distress of DTC patients. We found that psychological intervention could significantly improve psychological distress (including depression, anxiety, cancer fatigue and negative mood) of DTC patients in the treatment with radioactive iodine.

The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) uses six categories for thyroid cytology reporting (I-nondiagnostic, II-benign, III-atypia of undetermined significance (AUS)/ follicular lesion of undetermined significance (FLUS), IV-follicular neoplasm/suspicious for follicular neoplasm (SFN), V-suspicious for malignancy, and VI-malignant).<sup>18</sup> Thyroid nodules that fall within Bethesda categories III–IV have an overall risk of malignancy of between 15 and 40%.<sup>19</sup> Surgery combined with radioactive iodine is the main treatment choice for DTC. The benefits of this combination include lower recurrence rates and higher survival rates.<sup>20</sup> However, the treatment for DTC may cause psychological distress despite increased therapeutic efficiency. Studies have shown the adverse reactions during the DTC treatments can increase the psychological suffering of patients and affect their physical and mental health.<sup>21,22</sup> Especially for patients who receive the treatment of radioactive iodine, large radioactive iodine doses result in the need of special protection and the fear of radiation exposure, which may cause the negative moods such as loneliness, anxiety and pessimism, affecting the treatment adherence of patients.<sup>10</sup>

Psychological intervention plays an important role in improving the QoL among patients with DTC.<sup>11</sup> Wu et al<sup>10</sup> enrolled 60 patients with DTC who were treated with radioactive iodine to examine the effects of psychological and behavioral intervention. They provided a psychological and behavioral intervention for DTC patients before and after the treatment of radioactive iodine, and found that this intervention was effective in alleviating depressive and anxiety symptoms.<sup>10</sup> Javaloyes et al<sup>20</sup> evaluated the effectiveness of a psycho-oncological intervention based on counseling in patients with DTC in treatment with radioactive iodine. They found that the psycho-oncological intervention could significantly improve anxiety, depression and QoL.<sup>20</sup> However, it is a non-randomized controlled study with small sample size, which limits its clinical value.<sup>20</sup>

In the present study, we conducted a randomized controlled study to evaluate the effect of psychological intervention in DTC patients treated with radioactive iodine. We randomly assigned the enrolled patients into the intervention and the control groups. In the intervention group, patients received the standard psychological interventions for 6 times. The intervention strategies included helping patients know the disease, developing a positive self-concept, finding the appropriate ways to relax the patients, improving patients' social identity and sense of belonging, and developing methods to alleviate negative emotions. These strategies have been demonstrated as the efficient ways to alleviate depressive and anxiety symptoms in cancer patients previously.<sup>11,23,24</sup> We adopted one-to-one communication to give the psychological intervention. It has been reported that one-to-one communication with patients could help encourage patients to express their negative emotions and transfer any positive energy.<sup>10</sup>



In the present study, we showed the advantages of a psychological intervention via one-to-one communication for the remission of psychological distress in DTC patients who received radioactive iodine therapy. The symptoms of depression, anxiety, cancer fatigue and negative moods at T1 (week 8, immediately after the last time of intervention) were significantly improved in the intervention group compared with the control group. And the benefits of psychological intervention on mood disturbance could be maintained to T2 (week 24, 16 weeks after the intervention). These results indicated that the mood disturbance was indeed alleviated by the psychological intervention. However, in the intervention group, the scores of questionnaires measured at T2 were not significantly different from those measured at T1. These results suggested that psychological interventions should be given for a longer period to achieve better results.

The present study has several limitations. First, it is a single-center study with limited sample size. This may cause participant selection bias. Second, the duration of this study was only 24 weeks. Long-term efficacy of psychological intervention has not been observed. Third, this study did not evaluate QoL of DTC patients after psychological interventions using questionnaires such as QLQ-C30.<sup>11</sup> Thus, our encouraging findings should be confirmed in further multicentric studies with longer term follow-ups and larger sample size. In addition, endocrine and phonological status of patients were not collected. Besides, due to the diagnosis and treatment mechanism of Chinese hospitals, we could not obtain the assessment status of patients 1 year ago and 5 years ago, the family status, and the condition of patients who did not receive treatment.

## Conclusion

In conclusion, psychological intervention could significantly improve psychological distress of DTC patients in the treatment with radioactive iodine. This method is worth being used widely in clinic.

## Data Sharing Statement

Data not directly reported in this publication can be obtained from the corresponding author upon reasonable request.

## Ethical Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the First Affiliated Hospital of Hebei North University. Written informed consent was obtained from all participants. The ethical committee protocol number was K2020210.

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## Disclosure

The authors declare no conflicts of interest in this work.

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