



Comparison of anxiety and depressive symptoms of head and neck cancer patients in a closed-loop management system before and during the 2019 coronavirus pandemic: a comparative study

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Background: The coronavirus disease of 2019 (COVID-19) poses an unprecedented challenge to health and the financial system, especially the healthcare of patients with cancer. However, the research on the negative effect of the pandemic on the anxiety and depressive symptoms of cancer patients in closed-loop is rarely reported at present. In view of the limitations of previous studies. In this study, we compared the anxiety and depressive symptoms of head and neck cancer patients in the closed-loop management system before and during the 2019 coronavirus pandemic.

Methods: In this comparative study, a total of 526 head and neck cancer patients (269 and 257 patients before and during the COVID-19 pandemic) were enrolled in the present study. The two groups of patients' median age (53 years, 52 years), female distribution (70.26%, 66.15%) and male distribution (29.74%, 33.85%) were analyzed before and after the COVID-19 epidemic. They received questionnaires using the standardized data forms of Self-Rating Anxiety Scale (SAS) and the Self-Rating Depression Scale (SDS) to collect the relevant data of patients for retrospective investigation. For data analysis, either the chi-squared test or Fisher's exact test was employed for categorical variables, and we described the time trend of psychological states before and after the outbreak with Cochran-Armitage trend (CAT) test.

Results: A total of 526 head and neck cancer patients were included in the final analysis; 26.85% and 50.19% of cases experienced anxiety and depression during the COVID-19 epidemic. In contrast, 18.22% and 33.46% of cases had experienced anxiety and depression before the pandemic. According to the statistical results, the prevalence of anxiety and depression in patients during the COVID-19 epidemic was higher compared to that of patients prior to the pandemic ($P=0.018$). More importantly, both anxiety and depression incidence trends increased significantly before and after the outbreak of COVID-19 ($P=0.000$).

Conclusions: The present study demonstrates the significant impact of COVID-19 on the psychological states of cancer patients in the case of closed-loop management system, effectively indicating the need for appropriate changes in treatment decisions, enhanced psychotherapy, and interventions to reduce the incidence of anxiety, depression, and even suicide during this pandemic.

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Introduction

We have experienced an outbreak of the coronavirus disease of 2019 (COVID-19), which has spread rapidly across the country (1,2). The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 days (3,4). Prevention entails home isolation of suspected cases and those with mild illnesses and strict infection control measures at hospitals that include contact and droplet precautions (5). In the context of the novel coronavirus pneumonia epidemic period, hospital is a special place wherein the prevention and control management are particularly important. As the only designated hospital for COVID-19 treatment in Zhuhai, the Fifth Affiliated Hospital of Sun Yat-sen University has 1,650 open beds. As a designated hospital for international medical rescue, the Hospital is also a medical treatment unit in Zhuhai designated by foreign embassies and consulates, serving 2,023,700 residents of Zhuhai. The Cancer Center has 300 beds. Even during a pandemic, cancer patients require timely diagnosis, evaluation, and treatment (6). As a cancer center of a large university hospital, despite the severity of the situation, the treatment of cancer patients continued as usual during the outbreak of COVID-19 due to the urgency and continuity of treatment for cancer patients. However, it is important to consider that cancer patients are immunocompromised and at increased risk of COVID-19-related serious events in comparison to the general population. Cancer patients are the most susceptible group among novel coronavirus patients under the current COVID-19 epidemic due to reasons such as low immunity and poor nutrition (7). In addition, head and neck oncological diseases are associated with high psychosocial distress (8,9). Hospitals around the world have issued internal guidelines for oncologists, aiming to decrease patient exposure to COVID-19. Given the immunocompromised nature of the patient population, cancer centers have been adhering to strict infection control guidelines, in inpatient and outpatient settings (10). To prevent the spread of COVID-19 without delaying anti-tumor treatment, our head and neck tumor ward has

implemented a completely closed-loop management system since 31 January, 2020. According to the prevention and control requirements, all patients admitted for antitumor therapy must obtain negative novel coronavirus nucleic acid test results and normal chest computed tomography (CT) results before entering the ward for treatment. In addition, the ward shall be completely closed. Patients are forbidden to leave the ward except for in-hospital examination and radiotherapy. Relatives who usually accompany patients for diagnosis, treatment, and palliative care are discouraged from visiting patients in hospitals. Patients are prohibited from contact with any member of the public other than hospital staff.

Considering the high degree of specialization required from professionals for cancer care, it is highly advisable to take protective measures to ensure the safety of caregivers and maintain an efficient staff (11). Preventive barriers (facial masks, hydroalcoholic hand wash solutions, disposable overalls, etc.) are mandatory for all professionals who are in contact with cancer patients. Our medical staff keep up to date with the latest version of the novel coronavirus pneumonia diagnosis and treatment scheme guidelines. In addition to the diagnosis and treatment of cancer patients, efforts should be made to prevent and control the epidemic. Although our cancer treatment was very efficient, in our contact with patients, we found that the majority were experiencing mental disorders.

The incidence of anxiety and depression in cancer patients is high (12,13). Among cancer patients, psychiatric disorders such as maladjustment, anxiety, depressive disorders, and neuropsychiatric disorders such as post-treatment cognitive impairment have been shown to affect about one third to half of patients, depending on the stage and type of cancer (14-16). Literature shows that patients' negative emotions will lead to a decline in their quality of life and a shorter survival period, which is not conducive to the prognosis of the patients (17). Cancer patients mostly desire companionship from their caregivers (18). During the outbreak, cancer patients become susceptible to COVID-19 due to their lowered immunity and come to the

hospital for fear of COVID-19 infection. Anxiety rates may be higher in cancer patients during COVID-19. There is a study on the psychosocial status of cancer patients, and that of cancer patients during the COVID-19 epidemic period has recently also been reported. A meta-analysis included 27,590 participants evaluated the psychological disorders of cancer patients during the COVID-19 outbreak. The results showed that the prevalence rate of clinically significant depression, anxiety among cancer patients were 32.5% and 31.3%. In addition, head and neck cancer patients had the highest prevalence of clinically significant depression (74.6%) and anxiety (92.3%) symptoms in the subgroup analysis (9). However, study on the psychological disorders of cancer patients under the completely closed-loop management system during the epidemic of COVID-19 has not yet been reported. The condition of the patients in our study is very rare. In closed-loop management, the psychological condition of head and neck cancer patients may face very dangerous and worse conditions. It is of great practical significance to study the psychological state of cancer patients under the closed-loop management during the COVID-19 epidemic and take timely measures to improve this situation. If our results reveal that such patients experience amplification of psychiatric distress, it will be necessary to take aggressive measures to improve the situation.

To gain insight into the psychological state of the cancer patients during COVID-19 in the closed-loop management, we initiated a retrospective study to analyze the impact of the closed management of the tumor ward on the patients' psychological status during the epidemic of COVID-19. We present the following article in accordance with the STROBE reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-1013/rc>).

Methods

Patient enrollment and exclusion criteria

We retrospectively analyzed the anxiety and depression scale of 257 patients who experienced the closed-loop management system of the tumor ward during the epidemic. From 1 March, 2020 to 31 July, 2020, inpatients receiving antitumor therapy, symptomatic, or palliative care therapy under the closed-loop management system of our oncology department were enrolled. Another 269 cancer patients prior to the outbreak of COVID-19 were included in the control group from 1 February, 2019 to 30 June, 2019.

- (I) The inclusion criteria (only if all the following criteria are met) were as follows:
 - (i) Age: 18–75 years;
 - (ii) Mentally clear and able to complete the scale;
 - (iii) Voluntary participation in the study and provision of written informed consent.
- (II) The exclusion criteria (patients were not admitted to the study if they met any of the following criteria) were as follows:
 - (i) Previously diagnosed mental illness;
 - (ii) Lack of comprehension or inability to cooperate with the completion of the scale;
 - (iii) Extreme treatment failure with an expected survival time of less than 1 month.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the Fifth Affiliated Hospital of Sun Yat-sen University (No. ZDWY. TJZLK.001. V 2.0) and informed consent was taken from all the patients.

Survey protocol and variables factors

The patients received questionnaires using the Self-rating Anxiety Scale (SAS) and the Self-rating Depression Scale (SDS) prospectively and consecutively. Standardized data forms were used for collecting patient-related data. We scored and created statistics according to the contents of the scale. The SAS was developed by William Zung in 1971 to assess the subjective feelings of anxious patients (19). The SDS was compiled by Zung in 1965 (20); it is a self-rating scale, which is used to measure the severity of depression and its change in treatment. The specific contents of SAS and SDS are listed in the articles mentioned above.

The anxiety and depression scales were assessed by at least two psychiatrists in accordance with the latest guidelines and rated for anxiety and depression. Assessment criteria for anxiety and depression: add the scores of 20 items, multiply the total score by 1.25 and take the integer part to get the standard score. The lower the score, the better. Cumulative points ≥ 50 indicate symptoms of anxiety or depression. Cut-off points of the standard score: (I) mild anxiety/depression: 53–62 points; (II) moderate anxiety/depression: 63–72 points; (III) severe anxiety/depression: >72 points.

We used univariate and multivariate regression analysis to study the differences in SAS and SDS of patients in the general ward before the epidemic of COVID and those in

Table 1 Clinical characteristics of 526 cancer patients

Characteristics	Before the outbreak of COVID-19 (n=269)	Epidemic period of COVID-19 (n=257)	χ^2/t	P value
Gender, n (%)			1.026	0.311
Male	189 (70.26)	170 (66.15)		
Female	80 (29.74)	87 (33.85)		
Age, median, year [range]	53 [19–83]	52 [22–83]	0.943	0.346
Marital status			0.092	0.761
Married	256	246		
Unmarried	13	11		
Economic status			5.059	0.08
Good	139	131		
Ordinary	86	66		
Bad	44	60		
Medical insurance			1.591	0.207
Yes	231	230		
No	38	27		

COVID-19, coronavirus disease of 2019.

the closed-loop management system after the epidemic and further studied the other factors that may affect patients' mental status, such as gender, age, clinical stage, therapeutic aims, financial situation, marital status, level of education, social support, occupational stability, smoking, drinking, complicated with other diseases, hemoglobin (Hb), white blood cells (WBC), and platelet (PLT).

Statistical analysis

The software SPSS 21.0 (IBM Corp., Armonk, NY, USA) and R language (The R Foundation for Statistical Computing, Vienna, Austria) were used for statistical processing. Chi-squared test or Fisher's exact test was employed for categorical variables, we described the time trend of psychological states before and after the outbreak with Cochran-Armitage trend (CAT) test. The level of significance was $\alpha=0.05$, and the difference was statistically significant at $P<0.05$.

Results

Study population and baseline features

A total of 526 cases of head and neck tumors in our center

were included. The clinical characteristics of cases are shown in *Table 1*. The median age was 53 years (range, 19 to 83 years), and 52 years (range, 22 to 83 years) before and after the COVID-19 epidemic, respectively. A total of 189 (70.26%) cases were females and 80 (29.74%) cases were males before the COVID-19 epidemic and 170 (66.15%) cases were females and 87 (33.85%) cases were males after the COVID-19 epidemic. The gender ratio and age distribution of the two groups were basically the same. There was no significant difference in marital status between married and spousal, and no significant difference was found between levels of financial status and medical insurance coverage.

Analysis of the relationship between psychological status of cancer patients and COVID-19 epidemic

The evaluation results of anxiety and depression are shown in *Table 2*. It shows that 26.85% had anxiety and 50.19% had depression during the COVID-19 epidemic. Before the COVID-19 pandemic, 18.22% had anxiety and 33.46% had depression. Anxiety and depression incidences in patients in the group during the COVID-19 epidemic were higher than that in the group before the COVID-19 pandemic ($P<0.05$). The results also showed that after the occurrence

Table 2 The impact of the closed management of the tumor ward on the patients' psychological status during the epidemic of COVID-19

Psychological states	Anxiety	Normal	Depression	Normal
Before the outbreak of COVID-19 (n=269, %)	49 (18.22)	220 (81.78)	90 (33.46)	179 (66.54)
Epidemic period of COVID-19 (n=257, %)	69 (26.85)	188 (73.15)	129 (50.19)	128 (49.81)
χ^2		5.629		15.152
P value		0.018		<0.01

COVID-19, coronavirus disease of 2019.

Table 3 The time trend of psychological states before and after the outbreak with CAT test

Psychological states	Before the outbreak of COVID-19 (n=269, %)	Epidemic period of COVID-19 (n=257, %)	χ^2	P value
Anxiety			247.6	<0.01
Normal	220 (81.78)	188 (73.15)		
Mild	30 (11.15)	43 (16.73)		
Moderate	17 (6.32)	22 (8.56)		
Severe	2 (0.74)	4 (1.56)		
Depression			711.35	<0.01
Normal	179 (66.54)	128 (45.55)		
Mild	61 (22.68)	86 (30.61)		
Moderate	27 (10.04)	36 (12.81)		
Severe	2 (0.74)	7 (2.72)		

CAT, Cochran-Armitage trend; COVID-19, coronavirus disease of 2019.

Table 4 Univariate analysis of the patients' psychological status during the epidemic versus before the epidemic of COVID-19

	HR	95% CI	P value
SAS	0.547	0.354–0.843	0.006
SDS	0.517	0.364–0.734	0.000

COVID-19, coronavirus disease of 2019; HR, hazard ratio; CI, confidence interval; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale.

of the COVID-19 epidemic, there was a correlation between closed-loop management and the severity of anxiety and depression ($P<0.01$) (Table 3).

Analysis of related factors of anxiety and depression

The results of univariate and multivariate regression analysis showed that there were significant differences in SAS and SDS between patients in the general ward before

the epidemic of COVID-19 and patients in the closed-loop management system after the epidemic (Tables 4,5). Cox regression analysis demonstrated that the other factors such as gender [hazard ratio (HR) 3.275, 95% confidence interval (CI): 1.915–5.602], age (HR 1.029, 95% CI: 1.007–1.051) may affect patients SAS score. And therapeutic aims (HR 0.599, 95% CI: 0.416–0.863) (HR 0.565, 95% CI: 0.416–0.768), social support (HR 5.112, 95% CI: 2.334–11.198) (HR 3.493, 95% CI: 1.545–7.896), complicated with other diseases (HR 2.898, 95% CI: 1.706–4.923) (HR 2.938, 95% CI: 1.859–4.643) were positively associated with both SAS and SDS score ($P<0.05$) (Table 5).

Discussion

The COVID-19 outbreak is generating significant traumatic psychological consequences in the general population (21). Patients with cancer and healthcare providers are exposed to similar stresses, with the addition of facing the diagnosis

Table 5 Multivariate analysis of other influence factors of the patients' psychological status during the epidemic versus before the epidemic of COVID-19

Variables	SAS			SDS		
	HR	95% CI	P	HR	95% CI	P
Gender (male versus female)	3.275	1.915–5.602	0.000	1.545	1.001–2.385	0.050
Age	1.029	1.007–1.051	0.009	0.996	0.979–1.013	0.635
Clinical stage (I–IV TNM stage)	1.414	0.920–2.175	0.115	1.230	0.887–1.704	0.215
Therapy aims (radiotherapy, chemotherapy, targeted or immunotherapy, palliative symptomatic treatment)	0.599	0.416–0.863	0.006	0.565	0.416–0.768	0.000
Financial situation (with health insurance versus without health insurance)	0.910	0.409–2.024	0.817	0.686	0.362–1.300	0.248
Marriage status (married, unmarried or divorced)	1.381	0.683–2.792	0.369	0.629	0.323–1.227	0.174
Level of education (primary school, middle school, high school, college or above)	1.126	0.585–2.166	0.722	0.707	0.420–1.192	0.193
Social support (poor, average, good)	5.112	2.334–11.198	0.000	3.493	1.545–7.896	0.003
Occupational stability (regular jobs versus unstable jobs)	1.748	1.023–2.986	0.041	0.862	0.572–1.297	0.475
Smoking	1.313	0.575–2.994	0.518	1.097	0.558–2.156	0.787
Drinking	1.862	0.652–5.315	0.245	2.158	0.810–5.750	0.124
Complicated with other diseases	2.898	1.706–4.923	0.000	2.938	1.859–4.643	0.000
Hb	0.993	0.981–1.004	0.212	0.998	0.989–1.008	0.747
WBC	1.111	1.026–1.202	0.010	1.030	0.966–1.099	0.364
PLT	1.000	0.997–1.003	0.934	1.001	0.998–1.004	0.499

COVID-19, coronavirus disease of 2019; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale; HR, hazard ratio; CI, confidence interval; TNM, tumor-node-metastasis; Hb, hemoglobin; WBC, baseline white blood cell; PLT, platelet.

and treatment of a dreadful disease (11). In our study, a significant increase in anxiety and depression was observed after the COVID-19 epidemic. To assess the impact of the epidemic on cancer treatment, de Joode *et al.* conducted a national survey of 5,302 cancer patients in the Netherlands. Their study demonstrated the significant impact of the COVID-19 crisis on oncological care, indicating the need for psycho-oncological support during this pandemic. Oncology physicians are very concerned about the impact of the COVID-19 pandemic on oncological care (22).

In addition to concerns about treatment delays and disease progression, another very prominent issue is the psychological condition of cancer patients. Experts have focused too much on the effects of cancer on patients and neglected another very important aspect. There has been a lack of research on the psychological impact of these patients. Especially regarding the treatment of the tumor, there is also a lot of psychological pressure, such as fear

of being infected by the virus, and fear of the COVID-19 epidemic affecting the treatment process. In our tumor ward, a fully closed-loop management system was adopted. Although the risk of infection was partly reduced and anti-tumor treatment was given to the patients as scheduled, the cost was increased psychological pressure on patients, as well as the risk of increased anxiety and depression. Our results further indicate that the following factors can indeed increase the incidence of anxiety and depression in patients: therapeutic aims, social support, and complicated with other diseases. Furthermore, the gender, age, occupational stability, and WBC factors were associated with the onset of anxiety. In addition to patients' concerns about the deterioration of their cancer treatment, due to the lack of family company, lack of proper social activities and recreation, the mundane atmosphere of ward life does not facilitate overcoming their depressed mood.

For certain diseases, telemedicine can be used (23).

Rodler *et al.*, for example, are trialing telemedicine for their patients. Their research showed that anxiety about cancer had replaced anxiety about COVID-19, with patients objecting to a temporary interruption of treatment. In the future, patients would prefer to maintain in-person appointments as opposed to complete remote care, but will accept remote care during the pandemic. Patients are more likely to be treated in person than remotely (24).

During the COVID-19 epidemic, to address the challenge of in-person treatment, our ward began to provide patients with nonstop antitumor therapy, including radiotherapy, chemotherapy, immunotherapy, and targeted therapy, starting from 31 January 2020. Most of the patients who had been scheduled for antitumor therapy returned on schedule. For them, anxiety about cancer replaces anxiety about COVID-19, and they are more concerned about the adverse effects of tumor progression. How to minimize the risk of infection during this phase of the COVID-19 epidemic poses a major challenge to our tumor ward. To address this problem, our ward employed a completely closed-loop management system. Patients are not allowed to leave the ward except for inpatient examinations and radiotherapy. Family members or others are denied visitation and entry to the tumor ward. Patients are prohibited from physical contact with any member of the public except staff. With well-organized management, our anti-tumor treatment proceeded as scheduled. However, we found that in conducting our work under this system, a very big problem arose. Most patients developed psychological disorders. We gave each patient an anxiety and depression rating scale and found that anxiety and depression increased significantly under this system, which caused an elevation of stress in our work. To relieve the psychological pressure of these patients, our ward studied and carried out some intervention measures, including music and meditation interventions. For example, we selected some soothing music for patients to listen to every day, and often held some entertainment activities, such as playing movies in the activity room and holding some interesting lectures. These measures have also had good results in helping these patients through this difficult time.

Clinical implications

These findings highlight that personal experience related to the diagnosis of COVID-19, mortality in acquaintances, and COVID-19-associated stress is associated with a greatly elevated risk of emotional disorder symptomatology and

that the COVID-19 pandemic may result in increased demand for mental health services.

Gallagher *et al.*'s study examined how experiences related to COVID-19 and associated stress impact, anxiety, depression, and functional impairment in a convenience sample of 565 American adults. These findings reveal that COVID-19 experiences were consistently associated with higher odds of probable anxiety and depression diagnoses. Stress associated with COVID-19 also predicted large proportions of variance in anxiety, depression, health anxiety, and functional impairment. The COVID-19 pandemic may result in increased demand for mental health services (25). The incidence of anxiety and depression were also increased because of cancer (26). During the COVID-19 epidemic, anxiety and depression were more severe in the closed-loop oncology wards. In oncology wards, reinforcement should be made in terms of identifying professional teams that comprise mental health personnel as a basic tenet in dealing with emotional distress for patients with cancer and healthcare providers (11,27). It is of great significance to deeply understand and analyze the psychological status of this group of people and implement active intervention measures.

Study limitations

Our study was a monocenter study, which limited the generalizability of the data. Moreover, the tumor types included in the study were limited to head and neck tumors, which was not universal for other tumor types. Our scoring scale is mainly conducted in China, and people in different countries have different cultural differences, which may lead to different statistical results in the scoring of the scale. The result is not representative of the broad population.

Conclusions

The mental health status of cancer patients is a problem worthy of worldwide attention. During the COVID-19 pandemic period, in order not to delay the treatment, we adopted the fully enclosed loop to reduce the chance of viral transmission. In this period, although the cancer patient's condition is under control, the resulting mental problems are also very prominent. The system increases the risk of anxiety and depression and could even cause serious adverse events. How to strike a balance between treatment decision and mental health, and how to implement some effective measures to improve this situation in unaccompanied wards are worthy of further exploration.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://apm.amegroupp.com/article/view/10.21037/apm-22-1013/rc>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroupp.com/article/view/10.21037/apm-22-1013/coif>). The authors have no conflicts of interest to declare.

Ethics Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the Fifth Affiliated Hospital of Sun Yat-sen University (No. ZDWY.TJZLK.001. V 2.0) and informed consent was taken from all the patients.

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