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***Case Control Study***

**Risk factors for post-traumatic stress disorder among young and middle-aged cancer patients in the intensive care unit: A case-control study**

Chen L *et al*. Risk factors for post-traumatic stress disorder

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**Author contributions:** Chen L designed the study; Chen L and Wang GZ analyzed the data and wrote the manuscript; Chi YY and Wang GZ performed the research; Zhao J supervised the study. All authors have read and approved the final manuscript.

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**Abstract**

BACKGROUND

Young and middle-aged cancer patients in intensive care unit (ICU) often suffer from stress and pressure, causing huge physical and mental damage. Currently, there is few research on post-traumatic stress disorder (PTSD) among young and middle-aged cancer patients in ICU in China, and the psychological status of patients who have experienced both cancer development and ICU stay is still unclear.

AIM

To explore the risk factors for PTSD in young and middle-aged patients with cancer in ICU.

METHODS

Using convenient sampling method, we enrolled 150 young and middle-aged patients with cancer who were admitted to the ICU of our center during the period from July to December 2020. The general data of the patients and PTSD-related indicators were collected. The Impact of Event Scale-Revised (IES-R) was used for assessing PTSD one month after the discharge from the ICU. Binary Logistic regression analysis was performed to assess the independent risk factors for PTSD in these patients.

RESULTS

Among these 150 patients, 32 (21.33%) were found to be with PTSD. Binary Logistic regression analysis revealed that factors significantly associated with PTSD among young and middle-aged patients with cancer in ICU included monthly income (OR = 0.24, *P* = 0.02), planned transfers (OR = 0.208, *P* = 0.019), and Acute Physiology and Chronic Health Evaluation (APACHE II) score (OR = 1.171, *P* = 0.003).

CONCLUSION

The low monthly income, unplanned transfers, and increased APACHE II score are the risk factors for PTSD in young and middle-aged patients with cancer in ICU.

**Key Words:** Post-traumatic stress disorder; Cancer; Intensive care unit; Risk factors

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**Core Tip:** In this study, we investigated and analyzed the incidence of post-traumatic stress disorder (PTSD) and related risk factors in young and middle-aged cancer patients in intensive care unit. We found that young and middle-aged cancer patients are prone to suffer from more serious psychological pain and often bear greater psychological burdens, which cause additional damage to patients' physical and mental health. Therefore, understanding the occurrence and influencing factors for PTSD is crucial for these patients.

**INTRODUCTION**

Malignant tumors have become major causes of harm to the health the Chinese residents. In 2015, there were approximately 3.93 million new cancer cases across China, with a significant increase in the incidence rate among individuals aged > 40 years, and with a highest number of cases in those aged 60-64[1]. The diagnosis of a malignant tumor and the accompanying physical and psychological symptoms bring both physical and mental pain to the patients, which may ultimately result in post-traumatic stress disorder (PTSD)[2-4]. PTSD is a long-lasting psychiatric disorder that occurs or is delayed after an individual experiences or witnesses an unusually catastrophic or threatening event[5]. Several studies[6-8] have shown that tumors have been identified as a source of traumatic stress, and the prevalence of cancer-related PTSD is estimated to range from 7.3% to 15.3%[9]. As young and middle-aged people play crucial roles in families and society, once diagnosed with cancer, they often have to face stress from a variety of aspects including illness, family, work place, and financial burden[10,11]. Research indicates that young and middle-aged cancer patients suffer more serious emotional pain and often bear greater psychological burden, which leads to increased medical costs[12] and, even worse, risk of suicide[13]. Evidence has shown that cancer patients in intensive care unit (ICU) have more serious mental problems such as anxiety, fear, and loneliness, and the prevalence of PTSD among survivors within the first 6 mo after discharge was 25%[14-16]. Unfortunately, few literatures in China have described PTSD in young and middle-aged patients who have experienced both malignancy development and ICU admission. Here we investigated the occurrence of PTSD and its relevant risk factors in young and middle-aged cancer patients in the ICU, in an attempt to provide new evidence for the development of effective prevention and treatment strategies.

**MATERIALS AND METHODS**

***Study design and setting***

A case-control study was conducted from July 2020 to December 2020, at the Department of Intensive Care Unit of Tianjin Medical University Cancer Institute and Hospital.

***Subjects***

Using convenient sampling method, we enrolled young and middle-aged patients with cancer who were admitted to the ICU of our center. The inclusion criteria were: (1) Aged 18-65 years; (2) with a diagnosis of cancer confirmed by clinical, imaging, and pathological examinations; (3) with the ability to communicate; and (4) signed informed consent documents and participated in the study voluntarily. The exclusion criteria were: (1) Patients with severe mental illness or cognitive impairment; (2) those with drop-out, withdrawal, or loss to the follow-up; and (3) recent sufferings from other major life events or traumatic events.

***Determination of sample size***

Kendall’s statistic[17] was applied for sample size estimation in this observational study. The sample size was set to be 5-10 times greater than the number of variables. Since patients might fail to respond to the survey or get lost during follow-up, an additional 20% of the sample size was added. Thus, the final sample size of this study was determined to be 167 cases.

***Research tools***

**General information questionnaire:** This self-designed questionnaire covers data including patients' age, gender, marital status, education level, disease diagnosed, disease treatments, and psychosocial factors.

**Impact of Event Scale-Revised:** The Impact of Event Scale—Revised (IES-R) was developed by Weiss and Marmar in 1997 based on the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) criteria and the Horowitz's Impact of Event Scale (IES)[18]. It is mostly used to assess the symptoms and severity of PTSD in survivors after critical care[13]. Bienvenu *et al*[19]*.* Validated the performance of IES-R and concluded that IES-R was a useful tool in detecting PTSD symptoms in patients discharged from the ICU. The Chinese version of the IES-R was revised by Guo *et al*[20], and has a Cronbach's α coefficient of 0.89. This 22-item scale is divided into three dimensions including intrusion, avoidance, and hyperarousal. For each item, participants respond on a 5-point Likert scale ranging from point 0 “Never” to point 4 “Always”, and a higher score indicates more severe PTSD symptoms. It has a cut-off score of 33: A total score of ≥ 33 denotes positive PTSD symptoms, whereas a total score of < 33 indicates negative PTSD symptoms[21].

***Data collection***

According to the literature review[9], a diagnosis of PTSD can be made if the relevant symptoms last more than one month. In the present study, patients who met the inclusion criteria were surveyed by the investigators *via* telephone one month after ICU discharge. The surveys typically lasted 10–15 min. All the investigators had passed China’s national counselor level-3 examination and had certain clinical experience and good communication skills. Researchers collected general information about patients from the Hospital Information System and established good patient-consultant relationships during the patient's stay in the ICU. The surveys were conducted after informing the patients of the purpose and values of this survey and obtaining their content. Double data entry was applied to ensure the quality of the responses.

***Statistical analysis***

All the statistical analyses were performed using the SPSS 19.0 software package (IBM Corporation, Somers, NY, United States). All tests were two-sided, and a *P* value of < 0.05 was considered statistically significant. The measurement data are expressed as mean ± standard deviation (mean ± SD) or medians/quartiles. The independent *t* test for two samples was used for the comparisons of normally distributed measurement data, and the rank sum test was used for non-normally distributed ones. Count data are described by frequency and rate, and intergroup comparisons were performed by chi-square test or Fisher's exact test. Risk factors for PTSD in young and middle-aged cancer patients in the ICU were firstly screened using univariate analysis, and then the significant variables were included in a binary Logistic regression model for further analysis. The forest plots were created using GraphPad Prism 8.0 software (GraphPad Software Inc., San Diego, CA, United States).

**RESULTS**

***Subjects enrolled***

A total of 169 patients were included in this study, among whom 150 patients entered the final analysis. Nineteen patients were ruled out due to the following reasons: loss to telephone follow-up (*n* = 6); died after discharge (*n* = 6); lost after transfer to other hospitals (*n* = 4); and withdrew voluntarily during the study period (*n* = 3).

***Univariate analysis of PTSD and its risk factors in young and middle-aged cancer patients in the ICU 1 mo after discharge from ICU***

PTSD occurred in 32 of the 150 included patients, yielding an incidence rate of 21.33%, which was consistent with the results reported in a previous study[22]. Nine influencing factors were statistically significant: gender, monthly income, use of analgesics, physical restraint, APACHEII score, family burden, unplanned transfers, tracheal intubation, and duration of ICU admission (Table 1).

***Multivariate Logistic regression analysis of risk factors for PTSD in young and middle-aged cancer patients in the ICU***

With the occurrence of PTSD as the dependent variable, the factors that were statistically significant in the univariate analysis were assigned as independent variables. An unconditional binary multivariate Logistic regression analysis was performed, as shown in Table 2.

Binary Logistic regression analysis showed that monthly income, APACHEII score, and planned transfers were risk factors for PTSD in young and middle-aged cancer patients in the ICU. Hosmer-Lemeshow test for the PTSD risks in the ICU patients showed a *P* value of 0.265, suggesting that the binary Logistic regression model established in the present study fit well with the real-world data and could reliably reflect the relationship among the variables (Figure 1).

**DISCUSSION**

In the present study, patients with an unplanned transfer to the ICU were those who experienced unexpected acute deterioration of their condition during the treatment process. As shown by Logistic regression analysis, the incidence of PTSD in the planned transfer subgroup was 0.208 times that of the incidence in the unplanned transfer subgroup, suggesting that PTSD is more likely to occur after unplanned transfers. It may be explained that the planned ICU patients have been informed about their admissions in advance and therefore have milder stress response. Evidence shows that patients who were unfamiliar with their surroundings and had more fear memories, also had higher PTSD scores[23]. In the present study, patients in the unplanned transfer subgroup felt lonely and panic when they suddenly came to an unfamiliar environment and were not accompanied by their families; meanwhile, the individual psychological response to ICU admission due to disease deterioration can also aggravate their PTSD symptoms. Therefore, adequate psychological care should be offered to unplanned ICU patients to alleviate their anxiety.

Young and middle-aged adults are in the prime of their lives, and they are often the primary breadwinners of their families. In our present study, regression analysis showed that low monthly income was a risk factor for the occurrence of PTSD in young and middle-aged cancer patients in the ICU, as already suggested by Liu *et al*[24]. Treatment expenditure is a major concern among cancer patients. Young and middle-aged cancer patients with low monthly family income typically play the most important roles in their families, and the cost of ICU admission is often much higher than that of a general ward. Thus, the dual economic and psychological pressure can be even more torturous. Patients may feel guilty and self-blaming to their family members, and some even lose confidence in the future and request to give up the treatment; suicidal behaviors may occur[25,26]. These negative emotions make it difficult for patients to adjust their psychological stress levels, and patients become more susceptible to emotional disorders that can lead to PTSD. Therefore, it is important to carefully observe the body language and facial expressions of these patients and learn their innermost thoughts in a timely manner. Efforts should be made to encourage the patients and stop their worries, helping them to regain confidence in their future life and thus reduce the occurrence of PTSD after discharge.

The APACHEII score is calculated within 24 h after ICU admission and is used to for assess disease severity and predict treatment outcomes[27]. In the present study, cancer patients in the ICU with higher APACHEII scores were more likely to have PTSD-positive symptoms, which was consistent with the findings of Ye *et al*[28]. In fact, patients with advanced cancer are at higher risk of disease deterioration or even life-threatening events at any time during a specific treatment process, which will aggravate their anxiety, depression, and other disturbing emotions. Research has shown that negative emotions such as anxiety and depression were positively correlated with the occurrence of PTSD[29]. Therefore, early interventions targeting the psychological problems of critically ill patients should be offered to reduce the risk of long-term PTSD[30].

There are some limitations in this study. First, as a single-center study, its findings may not represent the clinical characteristics of the cancer patients in ICUs at hospitals of different levels in different regions. Second, long-term follow-up was not carried out due to the limited study period, and some risk factors were not analyzed. Third, limited by the budget, we followed up our patients only *via* telephone, and no customized clinical interviews on PTSD diagnosis by clinical professionals were arranged. In future, we will further screen PTSD patients by this method in multi-center large-sample studies.

**CONCLUSION**

PTSD in young and middle-aged cancer patients in the ICU can lead to varying degrees of psychological distress and mental disorders, which can seriously reduce patients' quality of life after hospital discharge. Without timely diagnosis and management, these problems can further affect the long-term prognosis of the patients. It was found in our study that low monthly income, unplanned transfers, and increased APACHE II score were the risk factors for PTSD in young and middle-aged cancer patients in the ICU. Early identification and effective preventive interventions may help to reduce the occurrence of PTSD and improve the quality of life in this population.

**ARTICLE HIGHLIGHTS**

***Research background***

Young and middle-aged cancer patients in intensive care unit (ICU) often suffer from stress and pressure from many aspects, causing huge physical and mental damage. Currently, there is few research on post-traumatic stress disorder (PTSD) among young and middle-aged cancer patients in ICU in China, and the psychological status of patients who have experienced both cancer development and ICU stay is still unclear.

***Research motivation***

Few literatures in China have described PTSD in young and middle-aged patients who have experienced both malignancy development and ICU admission. Here we investigated the occurrence of PTSD and its relevant risk factors in young and middle-aged cancer patients in the ICU, in an attempt to provide new evidence for the development of effective prevention and treatment strategies.

***Research objectives***

To explore the risk factors for PTSD in young and middle-aged patients with cancer in ICU.

***Research methods***

Using convenient sampling method, we enrolled 150 young and middle-aged patients with cancer who were admitted to the ICU of our center during the period from July to December 2020. The general data of the patients and PTSD-related indicators were collected. The Impact of Event Scale-Revised (IES-R) was used for assessing PTSD one month after the discharge from the ICU. Binary Logistic regression analysis was performed to assess the independent risk factors for PTSD in these patients.

***Research results***

Among these 150 patients, 32 (21.33%) were found to have PTSD. Binary Logistic regression analysis revealed that factors significantly associated with PTSD among young and middle-aged patients with cancer in ICU included monthly income (OR = 0.24, *P* = 0.02), planned transfers (OR = 0.208, *P* = 0.019), and Acute Physiology and Chronic Health Evaluation (APACHE II) score (OR = 1.171, *P* = 0.003).

***Research conclusions***

PTSD in young and middle-aged cancer patients in the ICU can lead to varying degrees of psychological distress and mental disorders, which can seriously reduce patients' quality of life after hospital discharge. Without timely diagnosis and management, these problems can further affect the long-term prognosis of the patients. It was found in our study that low monthly income, unplanned transfers, and increased APACHE II score were the risk factors for PTSD in young and middle-aged cancer patients in the ICU.

***Research perspectives***

Young and middle-aged cancer patients suffer from more serious psychological pain and often bear greater psychological burdens, which cause additional damage to patients' physical and mental health. Therefore, understanding the occurrence and influencing factors of PTSD is crucial for these patients.

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**Footnotes**

**Institutional review board statement:** The study was reviewed and approved by the Medical Ethics Committee of Tianjin Medical University Cancer Institute and Hospital (Approval No. bc2023050).

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** No conflict of interest has been declared by the authors.

**Data sharing statement:** No additional data are available.

**STROBE statement:** The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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**Figure Legends**



**Figure 1 A forest plot based on the Logistic regression analysis of factors associated with the occurrence of post-traumatic stress disorder.** APACHE II: Acute Physiology and Chronic Health Evaluation.

**Table 1 Univariate analysis of independent variables between post-traumatic stress disorder (PTSD)-positive and PTSD-negative patients**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Patient information** | 　 | **PTSD-positive group** | **PTSD-negative group** | ***χ*2/*Z*** | ***P* value** |
| Gender | Males | 11 | 64 | 3.972a | 0.046 |
| Females | 21 | 54 |
| Age (yr) |  | 58 (53.25, 61) | 59 (54, 62) | -1.306b | 0.192 |
| Marital status | Unmarried | 1 | 31 |  | 0.213c |
| Married | 0 | 118 |
| Place of residence | Rural | 11 | 39 | 0.153a | 0.927 |
|  | Suburban | 4 | 18 |
|  | Urban | 17 | 61 |
| Education level | Elementary school and below | 4 | 21 | 0.554a | 0.799 |
| Middle or high school | 17 | 61 |
| College and above | 11 | 36 |
| Monthly income | ≤ 3000 *yuan* | 0 | 9 | 7.537a | 0.024 |
| 3000-6000 *yuan* | 14 | 71 |
| > 6000 *yuan* | 18 | 38 |
| History of trauma | Yes | 6 | 29 | 0.478a | 0.639 |
| None | 26 | 89 |
| Hypertension | Yes | 10 | 44 | 0.398a | 0.544 |
| None | 22 | 74 |
| Diabetes | Yes | 7 | 20 | 0.414a | 0.604 |
| None | 25 | 98 |
| Smoking |  | 16 | 41 | 2.486a | 0.15 |
| Yes |
| None | 16 | 77 |
| Alcohol consumption | Yes | 12 | 25 | 3.605a | 0.067 |
| None | 20 | 93 |
| Fertility | With children | 29 | 116 |  | 0.065c |
| Without children | 3 | 2 |
| Use of sedatives | Yes | 29 | 98 |  | 0.41c |
| None | 3 | 20 |
| Use of analgesics | Yes | 28 | 67 | 10.23a | 0.002 |
| None | 4 | 51 |
| Physical restraint | Yes | 23 | 42 | 13.495a | < 0.001 |
| None | 9 | 76 |
| Sputum suctioning | Yes | 18 | 45 | 3.391a | 0.073 |
| None | 14 | 73 |
| Use of glucocorticoids | Yes | 3 | 29 | 3.466a | 0.087 |
| None | 29 | 89 |
| APACHE II score |  | 16.5 (13.25, 21) | 9 (6.75, 14) | -5.38b | < 0.001 |
| Family burden | Yes | 25 | 67 | 4.836a | 0.04 |
| None | 7 | 51 |
| Family breadwinner | Yes | 6 | 13 |  | 0.243c |
| No | 26 | 105 |  |
| Planned transfers | Yes | 6 | 72 | 18.018a | < 0.001 |
| No | 26 | 46 |
| Tracheal intubation | Yes | 24 | 64 | 4.475a | 0.043 |
| No | 8 | 54 |
| Length of ICU stay |  | 147 (115.375, 205.25) | 67 | -5.366b | < 0.001 |
| (42.875, 114.25) |

aChi-square test.

b*Z* value.

cFisher's exact test. APACHE II: Acute Physiology and Chronic Health Evaluation; ICU: Intensive care unit; PTSD: Post-traumatic stress disorder.

**Table 2 Value assignment for factors potentially related to post-traumatic stress disorder**

|  |  |  |
| --- | --- | --- |
| **Factors** | **Variables** | **Assignment methods** |
| Occurrence of PTSD | *Y* | PTSD-negative = 0, PTSD-positive = 1 |
| Gender | *X*1 | Male = 0, Female = 1 |
| Monthly income, | *X*2 | ≤ 3000 = 0, 3000 – 6000 = 1, > 6000 = 2 |
| Use of analgesics | *X*3 | No = 0, Yes = 1 |
| Physical restraint | *X*4 | No =0, Yes= 1 |
| APACHE II score | *X*5 | Actual measurement value |
| Family burden | *X*6 | No = 0, Yes = 1 |
| Planned transfers | *X*7 | No = 0, Yes = 1 |
| Tracheal intubation | *X*8 | No = 0, Yes = 1 |
| Length of ICU stay | *X*9 | Actual measurement value |

APACHE II: Acute Physiology and Chronic Health Evaluation; ICU: Intensive care unit; PTSD: Post-traumatic stress disorder.



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