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Death anxiety among caregivers of patients with advanced cancer: a cross-sectional survey

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Received: 18 January 2024 / Accepted: 1 July 2024 / Published online: 13 July 2024 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2024

Abstract

Purpose This study aimed to investigate death anxiety (DA) in caregivers of patients with advanced cancer and identify associated factors in the context of Chinese culture.

Methods Caregivers (N=588) of advanced cancer patients in a tertiary cancer hospital completed anonymous questionnaire surveys. Measures included the Chinese version of the Templer Death Anxiety Scale (C-T-DAS), the Quality-of-Life Scale, the State–Trait Anxiety Scale, and the Social Support Rating Scale. Data were analyzed in SPSS (IBM Corp, Armonk, NY, USA) using descriptive statistics, Pearson's correlation test, and linear regression.

Results Respondents returned 588 (93.03%) of the 632 questionnaires. The total C-T-DAS score was 7.92 ± 2.68 points. The top-scoring dimension was "Stress and pain" (3.19 \pm 1.29 points), followed by "Emotion" (2.28 \pm 1.31 points) and "Cognition" (1.40 \pm 0.94 points). In contrast, the lowest-scoring dimension was "Time" (1.06 \pm 0.77 points). Factors associated with DA ($R^2 = 0.274$, F = 13.348, p < 0.001) included quality of life (QoL), trait anxious personality, social support, caregiver length of care, caregiver gender, and patients' level of activities of daily living (ADL).

Conclusions Our results demonstrated high levels of DA in caregivers of patients with advanced cancer. Generally, female caregivers and those with low social support had high DA. Caregivers caring for patients with low ADL levels or with a low QoL and trait anxious personality reported high DA. Certain associated factors help to reduce caregivers DA. Social interventions are recommended to improve the end-of-life transition and trait anxious personality as well as quality of life for caregivers.

Keywords Caregivers · Death anxiety · Quality of life · Trait anxious personality · Social support

Background

In 2020, the number of new cancer cases worldwide totaled 19.29 million, and cancer was responsible for 9.96 million deaths. Cases in China account for about 23.7% and 30% of

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these numbers, respectively [1, 2]. The late stage of cancer is a strong reminder of death. Long-term care of dying patients causes caregivers to think about death and feel anxious and fearful, a phenomenon defined as death anxiety (DA) [3, 4]. Previous studies [5, 6] found that being exposed to frequent death reminders was associated with greater DA in caregivers than in cancer patients. Some studies [7–9] suggested that caregivers of cancer patients have a high level of DA. In China, as a result of differences in socio-economic culture and lifestyle, there are few studies on DA.

Some studies have concluded that an abnormally high level of DA may lead to maladaptation, anxiety, and other psychological disorders, reducing the perception of happiness and QoL [10, 11]. DA among caregivers of advanced cancer patients reduces the quality of care and leads to reduced communication on end-of-life care [12, 13] and medical decision-making [14] between caregivers and advanced cancer patients. Therefore, studies on the



association of DA and QoL among caregivers of patients with advanced cancer are needed.

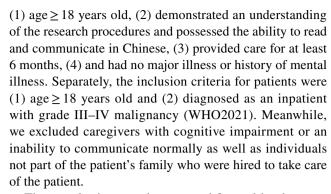
In addition, personality characteristics are classified as inner characteristics of a person, forming a stable and uniform mental structure that governs individual behavior in different spatio-temporal situations [15]. According to previous research [16], trait anxious personality was positively correlated with DA, while an open personality was negatively correlated with DA. An abnormally high level of trait anxious personality might lead to tension and anxiety, and long-term accumulation of negative mental states can easily facilitate fear and unease about death. Social support [17] is the connection between an individual and the outside world; it is the outside help, including spiritual, economic, and other aspects of understanding and support. Accordingly, the presence of social support may reduce or prevent the emergence of psychological distress, and some studies have reported its alleviating effect on DA [7, 9]. When confronted with the prospect of death, the greater the perceived social support, the less the amount of DA. Clarify the effect of trait anxious personality, social support and DA among caregivers of patients with advanced cancer can also help medical staff better cope with death, and take interventions to improve the QoL for caregivers.

With the evolution of hospice and palliative care during the past few decades in China, DA is gaining more and more attention. However, there have been many studies of DA in college students, the elderly, medical staff, and patients with advanced cancer [6–8, 18, 19]. In traditional Chinese culture, there is a strong taboo surrounding discussions of death. It is common for people to avoid speaking about death or end-of-life matters due to the belief that such conversations can bring about bad luck and adverse outcomes. Consequently, there is a lack of understanding about caregivers' DA. This quantitative study therefore sought to describe the status of DA among Chinese caregivers of patients with advanced cancer and explore factors associated with DA to improve the quality of both care and life for patients and caregivers alike. During this study, nursing staff identified the characteristics of high-risk individuals with DA and evaluated and intervened in DA cases among family caregivers, focusing particularly on the impact of the patient's dying state on the caregivers' DA.

Methods

Participants and procedures

The study population included caregivers of advanced cancer patients diagnosed in the inpatient department of Sun Yat-sen University Cancer Center from August 2022 to November 2022. The inclusion criteria for caregivers were:



The sample size equation we used for multivariate correlation was $N = (U\alpha/2S/\delta)2$, with $\alpha = 0.05$ and $U\alpha/2 = 1.96$. Upon consulting medical statistics, nursing studies, and literature related to sample size calculation formulas on DA [20], we identified the maximum value of the standard deviation of DA score S = 3.2 points [21], with an allowable error $\delta = 0.44$, which was n = 299. Considering that 10%-20% of questionnaires will be invalid [20], the required sample size was determined to be 329-359 cases. The final sample size was 588 cases.

Measurements

Sociodemographic characteristics included: (1) individual factors like age, gender, education, monthly income, relationship with patient, marital status, comorbidities (e.g., hypertension, diabetes, cardiopathy), religious beliefs, and length of care; (2) interpersonal factors like patient age, gender, having received treatment to improve physical health (e.g., operation, radiotherapy, chemotherapy, or targeted therapy), relapse, and physical symptoms; (3) and ADL level. The ADL level was identified using the Barthel index [22], which included 10 items (self-feeding, self-bathing, grooming, getting dressed); the total score ranges from 0~100 points, The cutoff point is 5, with scores above 5 indicating ADL. Higher scores suggest a better level of ADL.

Templer's death anxiety scale

In 1970, American psychologist Templer [23] developed and published Templer's Death Anxiety Scale (T-DAS) with 15 items. The 3-week test–retest reliability of the English original version was 0.83, and the internal consistency coefficient KR20 was 0.76. T-DAS is a multidimensional scale with a total possible score ranging from 0–15 points. The cutoff point is 7, with scores above 7 indicating DA. Higher scores suggest greater DA. Scholars from many countries have used this scale to measure the DA levels of patients and their caregivers. It has high reliability and validity and has been used as the gold standard for detecting DA [24].



Yang [21] introduced the T-DAS scale to China in 2012. The Cronbach's α of the Chinese version of T-DAS (C-T-DAS) was 0.71, the test–retest reliability was 0.831, and it has good criterion and construct validity. C-T-DAS includes four dimensions: stress and pain (items 4–6, 9, and 11), emotion (items 1, 3, 10, 13, and 14), cognition (items 2, 7, and 15), and time (items 8 and 12). Nine items are positively scored and six items (items 2, 3, 5–7, and 16) are reverse-scored. The total score ranges from 0–15 points, the cutoff point is 7, with scores above 7 indicating DA. Similar to with the original version, higher scores suggest greater DA. The Cronbach's α of the scale in this study was 0.71, and the test–retest reliability was 0.831.

Quality of life scale

The World Health Organization Quality-of-Life Brief Scale (WHOQOL-BREF) is a simplified scale based on WHOQOL-100 [25]. It includes 26 items and can be divided into four dimensions: physical health, mental health, social relationships, and social environment. Items 3, 4, and 26 are reverse-scored. The total score ranges from 12–130 points, the cutoff point is 60, with scores under 60 indicating worse QoL. Higher scores suggest better QoL. The Cronbach's α of the scale is 0.90, and the test–retest reliability is 0.86, both of which have good reliability and validity [26].

Social support revalued scale

The Social Support Revalued Scale(SSRS) was compiled by Xiao [27] in 1986 and contains 10 items divided into three dimensions: subjective support (items 1–3 and 5), objective support (items 6, 7, and 10), and social support (items 4, 8, and 9). The total score ranges from 12–66 points, the cutoff point of 22, with scores above indicating social support, higher scores suggest more social support. The Cronbach's α of the overall scale is 0.80 [28].

Trait-state anxiety inventory

Spielberger [29] compiled the State—Trait Anxiety Scale in 1970. The Chinese version of the State—Trait Anxiety Inventory (STAI) was subsequently developed in 1980. STAI contains the state anxiety subscale and the trait anxiety subscale. Its total score ranges from 0–54 points, the cutoff point of 40, with scores above indicating trait anxious personality and higher scores suggesting more trait anxious personality. The scale had an internal consistency reliability of 0.90 and a test—retest reliability of 0.86.

Statistical analysis

SPSS version 21.0 (IBM Corp., Armonk, NY, USA) was used for data input and statistical analyses. Caregivers' characteristics were summarized using descriptive statistics. The total C-T-DAS scores were tested by normality plots with tests and showed normal distribution. Pearson's correlation, the independent-samples t test, and one-way analysis of variance were used to explore factors associated with DA. Multiple regression analyses were then performed. Taking DA as the dependent variable, the stepwise variable selection method was adopted. Significance was accepted as p < 0.05.

Results

Caregivers' characteristics

Participants' sociodemographic characteristics are presented in Table 1.

Patients' disease-specific characteristics

Patients' disease-specific characteristics are presented in Table 2.

Death anxiety level

This study showed that 428 (76.3%) participants had high levels of DA (C-T-DAS cutoff point scores above 7). The total C-T-DAS score was 7.92 ± 2.68 points. The top-scoring dimension was "Stress and pain" (3.19 ± 1.29 points), followed by "Emotion" (2.28 ± 1.31 points), and "Cognition" (1.40 ± 0.94 points), while the lowest-scoring dimension was "Time" (1.06 ± 0.77 points). 509 (86.6%) participants had low levels of QoL (WHOQOL-BREF cutoff point scores under 60). 256 (43.9%) participants had high levels of trait anxiety personality (STAI cutoff point scores above 40). 213 (36.2%) participants had low levels of social support (SSRS cutoff point scores above 22).

Factors related to death anxiety

We analyzed the relationships between DA and individual variables, respectively (Table 3). DA was negatively correlated with quality of life (r = -0.666, p < 0.01) and social support (r = -0.672, p < 0.01) but positively correlated with trait anxious personality (r = 0.622, p < 0.01).

Factors associated with DA included caregiver gender, length of care, religious beliefs, patients' level of ADL, actively receiving treatment, and physical symptoms, which



Table 1 Study caregivers' characteristics (N = 588)

Characteristics	Group	n (%)	Mean ± SD		F/t	p
Gender	Male	291 (49.5)	7.20 ± 2.85	-6.756		0.008**
	Female	297 (50.5)	8.64 ± 2.29			
Education	Primary school	38 (6.5)	8.34 ± 2.69	0.445		0.721
	Junior high school	171 (29.1)	7.99 ± 2.50			
	High school or technical Secondary school	167 (28.4)	7.85 ± 2.76			
	College degree or above	212 (36.1)	7.85 ± 2.75			
Monthly income	< 5000	194 (33.0)	7.78 ± 2.54	0.767		0.465
(RMB)	5000-10000	187 (31.8)	8.11 ± 2.85			
	> 10000	207 (35.2)	7.89 ± 2.64			
Relationship with patient	Spouse	231 (39.3)	8.26 ± 2.76	2.051		0.070
	Child	215 (36.6)	7.85 ± 2.73			
	Brother/sister	75 (12.8)	7.43 ± 2.41			
	Other relative	40 (6.8)	7.15 ± 2.49			
	Friend	3 (0.5)	8.67 ± 1.53			
	Parent	24 (4.1)	8.08 ± 2.22			
Age (years)	18-29	98 (16.7)	8.05 ± 2.58	0.300		0.826
	30–45	255 (43.4)	7.99 ± 2.74			
	46–60	189 (32.1)	7.81 ± 2.72			
	≥61	46 (7.8)	7.74 ± 2.37			
Marital status	Unmarried	88 (15.0)	7.39 ± 2.81	2.164		0.091
	Married	490 (83.3)	8.01 ± 2.66			
	Divorced	6 (1.0)	7.17 ± 1.94			
	Widowed	4 (0.7)	9.75 ± 0.50			
Length of care (months)	≤12	191 (32.5)	6.57 ± 2.56	7.650		0.006**
	12-24	143 (24.3)	7.17 ± 2.82			
	25–36	153 (26.0)	9.25 ± 1.92			
	≥37	101 (17.2)	9.53 ± 1.76			
Comorbidity	None	559 (95.1)	7.94 ± 2.68	0.767		0.443
	Hypertension	12 (2.0)	6.78 ± 1.95			
	Diabetes	10 (1.7)	7.98 ± 1.90			
	Cardiopathy	7 (1.1)	8.09 ± 2.16			
Religious beliefs	None	407 (69.2)	8.91 ± 2.01	4.590		0.009**
-	Have	181 (30.8)	5.70 ± 2.65			

^{**}p < 0.01, SD standard deviation, RMB renminbi, t t-test the statistic value, F variance test, p p value

showed statistical significance (Tables 1 and 2). We also found that the variables of QoL, social support, and trait anxious personality were related to DA (p < 0.01) (Table 3).

The results from the stepwise multiple regression analysis showed that QoL, social support, trait anxious personality, caregiver gender, caregiver length of care, and patients' level of ADL were associated with DA ($R^2 = 0.274$, F = 13.348, p < 0.001) (Table 4).

Discussion

Death anxiety among caregivers of patients with advanced cancer

All caregivers of patients with advanced cancer experience some degree of DA. Our result is similar to those



Table 2 Study patients' disease-specific characteristics (N = 588)

Characteristics	Croun	n (01)	Mean ± SD	F/t	
Characteristics	Group	n (%)	Mean ± SD	F/l	p
Gender	Male	295 (50.2)	8.07 ± 2.52	1.343	0.180
	Female	293 (49.8)	7.77 ± 2.82		
Age (years)	18–29	36 (6.1)	8.14 ± 2.62	1.625	0.182
	30–45	178 (30.3)	8.10 ± 2.81		
	46–60	220 (37.4)	8.03 ± 2.66		
	61–75	154 (26.2)	7.52 ± 2.54		
ADL	Complete self-care	127 (21.6)	5.71 ± 2.78	9.123	0.007**
	Mild dependence	166 (28.2)	6.83 ± 2.11		
	Moderate dependence	232 (39.5)	9.61 ± 1.79		
	Heavy dependence	63 (10.7)	9.05 ± 1.76		
Cancer relapse	Have	345 (58.7)	7.66 ± 1.70	1.420	0.156
	None	243 (41.3)	7.29 ± 2.79		
Physical symptoms	Cancer pain	199 (33.8)	8.22 ± 3.04	1.646	0.006**
	Vomiting	89 (15.1)	7.68 ± 2.68		
	Sleep disorder	31 (5.3)	7.54 ± 2.43		
	Fatigue	29 (4.9)	7.65 ± 2.14		
	Other	11 (1.8)	7.32 ± 2.19		
	None	229 (38.9)	5.71 ± 2.45		
Treatment	Operation	204 (24.7)	6.79 ± 2.16	2.669	0.008**
	Radiotherapy and Chemotherapy	189 (32.1)	7.01 ± 2.19		
	Targeted therapy	43 (7.3)	7.21 ± 2.23		
	None	152 (25.9)	8.82 ± 2.55		

^{**}p<0.01, ADL activity of daily living, SD standard deviation, t t-test the statistic value, F variance test, p p value

Table 3 Descriptive statistics and inter-correlations of all variables

	Mean	SD	r	p
QoL	63.76	14.10	-0.666**	0.004
Physical health	51.63	11.86	-0.485**	0.005
Mental health	56.67	13.78	-0.472**	0.006
Social relationships	51.58	17.39	-0.507**	0.002
Social environment	51.68	13.62	-0.472**	0.026
Social Support	36.12	2.68	-0.672**	0.005
Subjective support	20.06	4.46	-0.612**	0.001
Objective support	9.84	3.45	-0.589**	0.004
Use of support	6.22	2.64	-0.547**	0.016
Trait Anxious Personality	64.10	12.94	0.622**	0.019

^{***}p<0.01, QoL=quality of life, SD=standard deviation, r=correlation coefficient p=p value

reported by Alkan et al. [8] and Soleimani et al. [9] among caregivers of patients with advanced cancer. Patients are on the verge of death, making caregivers more aware of death. The top-scoring C-T-DAS dimension was "Stress and pain" $(3.19 \pm 1.29 \text{ points})$, which includes statements like "I fear dying a painful death," "I dread to think about

having to have an operation," and "I am really scared of having a heart attack."

Patients with advanced cancer suffer from physical symptoms like pain, nausea, and vomiting as well as various side effects of treatment like myelosuppression, hair loss, and radiodermatitis, leading caregivers to worry and fear for their own health and comfort. On the other hand, in Chinese traditional culture, people avoid the topic of death, and death education is seriously lacking as a result, so caregivers are afraid to mention and discuss death with medical workers, increasing their levels of DA [30]. Caregivers hold a denial and avoidance attitude toward hospice and death, and they lack a scientific and correct view of life and death. According to the Quality of Death Index report for 80 countries or territories, Chinese residents rank 71st in the Quality of Death Index [31]. Cancer diagnoses are a highly visible reminder of death; as a result, caregivers are threatened with death, and DA occurs. Therefore, nursing staff should strengthen the death education of caregivers, helping them to understand the patient's condition, establish a correct view of life and death, and ultimately reduce the level of DA in caregivers.



Table 4 Multiple regression analysis

Variable	Partial Regression Coefficient	Standard error	Standardized regression coefficient	t	p	95% CL
Constant	52.082	9.062		2.451	0.001**	48.667~59.348
Caregiver QoL	-2.451	0.868	-0.906	-1.250	0.006**	$-2.894 \sim -1.652$
Caregiver social support	-6.523	1.352	-1.467	-4.530	0.004**	$-7.324 \sim -5.876$
Caregiver trait anxiety personality	1.247	0.232	0.337	3.170	0.001**	0.873~1.876
Caregiver religious beliefs	-0.246	0.057	-0.124	-0.398	0.089	$-0.947 \sim 0.125$
Caregiver length of care	1.236	0.721	0.842	0.003	0.010**	$0.817 \sim 1.658$
Caregiver gender	0.159	0.054	0.137	0.039	0.024*	$0.021 \sim 1.275$
Patient ADL	1.652	0.626	0.765	0.043	0.035*	1.093~2.076
Patient somatic symptoms	3.214	1.214	1.298	0.659	0.899	2.765~3.593
Patient treatment	-1.425	0.849	-0.917	-0.379	0.187	$-2.086 \sim -0.892$

p < 0.05, **p < 0.01, QoL quality of life, ADL activity of daily living, CL confidence interval, t t-test the statistic value, p p value

Factors related to death anxiety among caregivers of patients with advanced cancer

QoL

Our findings indicated a significant negative correlation between QoL and DA. Researchers confirm that QoL is negatively correlated with DA, and good QoL can alleviate DA [17, 32]. Similarly, previous studies [32, 33] have shown that reduced QoL can lead to death anxiety.

Reduced QoL in caregivers can lead to sleep disturbances, loss of appetite, changes in social functioning, and negative coping with death, which can trigger death anxiety [24, 34]. In addition, a patient's physical symptoms and heavy care burden reduce the caregiver's QoL and increase DA [7, 17, 24, 34]. Improving the QoL in caregivers can lessen the burden of care, improve the quality of care, help actively cope with death, and reduce death anxiety. Therefore, interventions to promote QoL should be available for caregivers of patients with advanced cancer to help them cope with the patient's impending death.

Trait anxious personality

Our study showed that trait anxious personality was positively correlated with DA. Research confirms that caregivers with lower trait anxious personality reported less DA [23, 35, 36]. Conversely, caregivers with high trait anxiety personality were affected by the progression of patients' disease and emotions, so they showed a higher level of DA.

A cross-sectional study [35] of 4,070 male and female participants found that individuals with anxious personality traits had higher levels of perceived DA. Previous studies [37, 38] have documented significant positive correlations between neuroticism and DA. Neurotic individuals are more likely to react negatively to stressful situations as a result of

their worry and helplessness, as they are more prepared to experience emotions and express negative behaviors. However, trait anxiety personality positively correlates with neuroticism. According to the effect of neuroticism on DA, trait anxiety personality triggers DA. A study [39] found that life stress, negative automatic thoughts, and dysfunctional attitudes cause psychological distress. Long-term accumulation of negative mental states can easily trigger fear and unease about death. Trait anxiety personality triggers negative thinking and dysfunction, which leads to DA.

Therefore, nursing staff should treat caregivers as unique individuals, consider the impact of caregivers' personality traits on their mental health, and develop individualized DA interventions.

Social support

Our findings indicated that social support negatively correlated with DA. Researchers confirm that social support could reduce anxiety, depression, and DA in caregivers [15, 16]. Multiple studies [40–42] concluded that social support can buffer DA. Adequate social support for caregivers is conducive to rebuilding the cognition of illness and death, regulating negative emotions, and actively coping with death [41, 42]. Greater social support can improve the self-efficacy of caregivers and thus reduce the negative impact of life, leading to less DA among caregivers [24].

According to the buffer model theory of social support [40], relatives, friends, neighbors, work partners, and medical staff can provide an individual with spiritual or material care and help, which enables the individual to better cope with stress and recover from fear of death [41, 43, 44]. Therefore, social support should be made available to caregivers of patients with advanced cancer to help them deal with the impending death and QoL.



Demographic and patients' disease-specific characteristics

We found that DA among female caregivers was significantly higher than that among male caregivers, consistent with the findings of previous research [8]. Women typically bear greater social responsibilities than men, such as being mothers to children, homemakers, and emotional support providers [8, 45]. Female caregivers often experience empathetic responses to death but frequently neglect their own emotions, leading to psychological distress and depression, which leads to DA.

As the duration of care increases, caregivers experienced more DA, contradicting Beydag's [45] research findings. Beydag suggested that the relatives of diagnosed patients might find it challenging to adapt to the progression of the illness. Caregivers cycle through various negative emotions, including fear, despair, guilt, and helplessness, during the caregiving process. Consequently, a longer time from diagnosis to death was associated with higher DA in patients. Therefore, further research on the impact of caregiving duration on DA is still needed.

We also explored the influence of patient ADL on caregiver DA. In the context of caring for patients, caregivers' burden increases as patients' ADL levels diminish. Providing care and companionship to patients leads to heightened levels of anxiety about one's own QoL, which leads to DA [33].

Therefore, medical workers should give female caregivers, longer-term caregivers, and caregivers caring for patients with worse ADL more attention and help.

Study limitations

The present study had several limitations. First, the participants were recruited from a single cancer center, so the sample representation had certain limitations. We should collect samples in different regions and hospitals of different levels in future research efforts. Second, our study only investigated the DA of caregivers at a certain point in time, and it does not reflect the dynamic change of DA. Despite our efforts, the causal relationships among trait anxiety personality, social support, QoL, and DA remain inadequately demonstrated. A longitudinal study is necessary to explore the changing trajectory of caregivers' DA. Finally, our study did not test additional models that predict C-T-DAS subscores in depth, so mediating and regulating models should be integrated for further research in this area.

Clinical implications

Our study revealed possible factors related to DA among Chinese caregivers of patients with advanced cancer. Our findings suggest that medical staff should pay attention to DA. The analysis of influencing factors showed the need to provide more social support to female, extended-care caregivers and those caring for patients with low ADL levels to reduce care distress in the face of painful death.

In addition, further correlational and regression studies aimed to examine in depth the predictive role of DA on positive constructs, such as the meaning of life [46] and coping mode. Additionally, interventional studies on this topic should take into account death education [46, 47], mindfulness-based intervention [48] (such as meditation, laughter yoga), rational emotive hospice care therapy [6, 49], and spirituality support [50] as the main strategies to help caregivers find their meaning in life and improve their trait anxious personality and QoL to better deal with impending death.

Conclusions

Our results demonstrate that most caregivers of patients with advanced cancer experience some degree of DA. Female caregivers and those with low social support had greater DA. Also, Caregivers caring for patients with low ADL levels or with a low QoL and trait anxious personality reported high DA. This study offers a framework for mental health professionals to methodically evaluate and address DA in caregivers. Enhancing the QoL and support system, as well as mitigating the DA experienced by caregivers, is of paramount importance.

Author contribution Z. Zhou and Y. Li contributed to the study conception and design. Material preparation, data collection and analysis were performed by Y. Duan, Q. Zhao, Y. Yang, Q. Niu and Y. Li. The first draft of the manuscript was written by Y. Li. Z. Zhou and Y. Duan, Q. Zhao commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding This research was supported by the Young Talents Training Foundation in Nursing of Sun Yat-sen University, China (grant no. N2022Y05).

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval The study was approved by the Medical Ethics Committee of Sun Yat-sen University Cancer Center, Guang Zhou, China (no. SL-B2022-416–02). We certify that the study was performed in accordance with the 1964 Declaration of Helsinki and later amendments.

Informed consent This study strictly follows the principle of informed consent of research subjects. We explained the purpose, significance, benefits, and risks of the study in detail to the subjects, informing them of the principle of voluntariness and confidentiality, The study was conducted after subject consent was obtained and the informed consent form was signed.



Competing interests The authors declare no competing interests.

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