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Effect of symptom clusters on quality of life in patients with head and neck cancer treated with radiotherapy: a cross-sectional study

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Patients with head and neck cancer (HNC) frequently encounter symptom clusters following radiotherapy, which substantially affect their quality of life. This study aims to identify distinct symptom clusters in undergoing radiotherapy HNC patients and examine how self-perceived burden and social support mediate the relationship between symptom clusters and quality of life. A cross-sectional survey of 409 HNC patients (Jun–Dec 2024) was conducted. Symptoms were assessed using the M.D. Anderson Symptom Inventory-Head and Neck, self-perceived burden using the Self-Perceived Burden Scale for Cancer Patients, social support using the Medical Outcomes Study Social Support Survey, and quality of life using the Functional Assessment of Cancer Therapy-General. Exploratory factor analysis identified symptom clusters, structural equation modeling (SEM) tested mediation paths. Four distinct symptom clusters were identified in HNC patients undergoing radiation therapy: oropharyngeal, neurosensory, psychological, and gastrointestinal. Symptom clusters negatively predicted social support (β= − 0.449, $p < 0.05$, explaining 20.2% variance). Symptom clusters and social support jointly predicted self-perceived burden (Symptom clusters:β = 0.490, Social support:β = − 0.131; $p < 0.05$, explaining 31.6% variance). Symptom clusters, social support, and self-perceived burden collectively predicted quality of life (Symptom clusters:β= − 0.396, Social support:β = 0.150, Self-perceived burden:β= − 0.198; $p < 0.05$, explaining 37.9% variance). Self-perceived burden significantly mediated the relationship between symptom clusters and quality of life(indirect effect = − 0.041, 95% CI − 0.256 to − 0.007), social support mediation was non-significant, and no chain mediation existed. It was found that symptom clusters in HNC patients receiving radiation therapy have a direct negative impact on their quality of life. These symptoms also indirectly affect quality of life through self-perceived burden mediation. Future interventions should focus on reducing patient's burden and improving Social support. Additionally, exploring the relationship between symptoms, psychological factors, and social factors, and creating a comprehensive care system that addresses symptom management, psychological empowerment, and social support enhancement could help improve patients' quality of life.

Keywords Head and neck cancer, Symptom clusters, Quality of life, Self-perceived burden, Social support

Abbreviations

QOL	Quality of life
SC	Symptom clusters

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HNC	Head and neck cancer
SS	Social support
SPB	Self-perceived burden
TOUS	The theory of unpleasant symptoms
MDASI-H&N	M.D. Anderson symptom inventory-head and neck
SPBS-CP	Self-perceived burden scale for cancer patients
MOS-SSS	Medical outcomes study social support survey
FACT-G	Functional assessment of cancer therapy-general
KPS	Karnofsky performance status

Head and neck cancer (HNC) ranks as the sixth most prevalent malignant tumors worldwide, impacting different anatomical locations like the nasopharynx, oropharynx, larynx, and thyroid[1]. In 2020, around 878,000 new cases were reported worldwide[2], with higher incidence rates in China compared to Western countries[3]. To date, radiotherapy is the main treatment for HNC, but it also leads to symptoms like fatigue, dry mouth, anorexia, skin pain, dysphagia, and hoarseness, which can impact treatment effectiveness and patients'quality of life (QOL)[4]. QOL is a key outcome indicator in cancer treatment encompassing various dimensions like physiological function, psychological state, social adaptation, and environmental interaction. Moreover, studies have found that symptoms due to shared pathological mechanisms forms various symptom clusters (SC)[5], such as RT-specific SC (pain, dysphagia, mucositis), gastrointestinal SC (nausea, anorexia), and psychosocial SC (depression, anxiety)[6], which have a more significant impact on QOL than individual symptoms in HNC patients receiving radiotherapy[7]. However, while the relationship between HNC's SC and QOL is known, the underlying mechanisms remain unclear, underscoring the importance of further research to establish a theoretical model for clinical intervention.

This study adopted the Theory of Unpleasant Symptoms (TOUS) as the theoretical framework. which includes three core concepts: symptom experience, influencing factors, and functional performance[8]. TOUS has been used in cancer-related studies to explain how multiple co-occurring symptoms interact to affect patients' health outcomes[9]. However, its use in HNC patients during radiotherapy remains limited. HNC patients often experience co-occurring symptoms during radiotherapy, including pain, dysphagia, and fatigue.The complex interactions between these symptoms align with the multidimensional and interactive characteristics emphasized by TOUS, providing a theoretical basis for this study. TOUS posits that physiological, psychological, and situational factors influence symptom experiences, which in turn affect patients' functional performance and overall health[10]. Guided by this theory, this study conceptualizes SC as core symptom experiences, self-perceived burden(SPB) as a psychological factor, and social support (SS) as an environmental factor-elements that contribute to functional outcomes reflected in QOL. Integrating these elements into a unified theoretical model, this study advances evidence-based supportive care strategies combining nursing, psychological, and social interventions to enhance the overall health of head and neck cancer patients during radiotherapy.

Building on theoretical and empirical evidence, we posits the following hypotheses: Hypothesis 1 (H1): SC can significantly and negatively predict QOL in HNC patients undergoing radiotherapy. Although previous studies have demonstrated an inverse association between SC and QOL[11–15], there is limited evidence in patients undergoing radiotherapy for HNC, particularly within the framework of the TOUS. Hypothesis 2 (H2): SS mediates the relationship between SC and QOL. Social support (SS) is an important component of an individual's external resources in the Conservation of Resources (COR) theory[16]. Medical social support involves support from healthcare professionals, family, friends, and other social networks in medical settings. Research has shown that SS can positively impact QOL through resource gain mechanisms[17]. However, it was also reported that SC hinders patients' access to SS[15]. Thus, it is plausible to suggest that SS partially mediates the SC-QOL relationship.Hypothesis 3 (H3): SPB mediates the relationship between SC and QOL. Self-perceived burden (SPB) is defined as "a complex psychological experience characterized by empathic concern for the impact of illness and caregiving demands on others, leading to feelings of guilt, distress, responsibility, and diminished self-awareness"[18]. Studies have shown that SPB is a crucial factor in determining QOL[19,20]. Moreover, research has suggested that reducing SPB can help lessen the effects of SC on QOL[21], suggesting that SPB may partially mediates the SC-QOL relationship. Hypothesis 4 (H4): a chain mediation path via SS and SPB exists between SC and QOL. Studies have shown that SS significantly reduces the perceived burden of patients after lung cancer surgery through multiple mechanisms such as emotional buffering, cognitive reconstruction, behavioral empowerment, and social capital accumulation[22]. Combined with H2 and H3, it suggests that the severity of SC could impact SS acquisition, leading to changes in SPB levels and ultimately affecting QOL.

The objective of this study is to uncover the connection between SC, SS, SPB and QOL in HNC patients. Theoretically, it demonstrated a dual-pathway conceptual model where SC impact QOL through SPB and SS. Practically, it provides insights for creating comprehensive interventions that combine symptom management, psychological support, and social resource integration.

Methods

Study design and participants

A cross-sectional study was carried out to examine how Social Support (SS) and self-perceived burden (SPB) mediate the relationship between symptom clusters (SC) and quality of life (QOL) in head and neck cancer (HNC) patients undergoing radiotherapy.

A cross-sectional survey was carried out from May to December 2024, using convenience sampling at the radiotherapy departments of three tertiary general hospitals in Zhengzhou, Henan Province. Inclusion criteria included: (1) pathologically confirmed HNC; (2) age≥ 18 years; (3) undergoing radiotherapy; (4) awareness of diagnosis and treatment plan; (5) adequate literacy to complete self-reported measures; and (6) provision

of informed consent. Exclusion criteria were: (1) malignant tumors outside the head and neck region; (2) communication or cognitive dysfunction; and (3) poor physical condition with a Karnofsky Performance Status (KPS) score≤ 30. This study was approved by the Institutional Review Board of Henan Cancer Hospital (No. 2021-KY-0165-002) and performed in accordance with the Declaration of Helsinki and relevant institutional guidelines. Written informed consent was obtained from all participants prior to study procedures. With 409 valid questionnaires retained after quality control, the valid response rate was 93.17%. Invalid questionnaires (6.83%) were excluded due to incomplete responses, logical inconsistencies, or failure to meet inclusion criteria (e.g., patients who did not complete radiotherapy or provided duplicate answers).

Measures

Demographic and disease information questionnaire

A researcher-designed data collection form was developed based on relevant literature and clinical experience. It consists of two sections: demographic information (such as gender, age, and educational level) and disease-related information (including type of HNC, disease stage, illness duration, treatment methods, and presence of nasogastric tube).

Independent variable

The M. D. Anderson Symptom Inventory-Head and Neck (MDASI-H&N) was originally developed in 2007[23] and consists of three parts:13 core items, 9 head and neck cancer-specific items, and the 6 interference items, respectively. The scoring scale range is from 0 to 10, with 0, 10 representing no symptoms, and the most severe symptoms, respectively. The scale was translated, culturally adapted, revised, and validated, showing good reliability and validity. The Cronbach's αcoefficient for the symptom distress section is 0.91 for the first 13 items, 0.85 for the last 9 items, and 0.88 for the daily life distress section[24]. In this study, only the symptom distress section was used, with a Cronbach's αcoefficient of 0.894.

Mediating variables

The Self-perceived Burden Scale for Cancer Patients (SPBS-CP) was developed by Ren et al. based on Cousineau et al.'s scale[25], assesses the degree of self-perceived burden among cancer patients. It consists of four dimensions: economic/family burden, psychological/emotional burden, caregiving burden, and treatment burden, with a total of 21 items. Each item is rated on a 5-point Likert scale, resulting in a total score range of 21–105. Scores below 30 indicate no significant burden, 30–49 indicate mild burden, 50–69 indicates moderate burden, and 70 or above indicate severe burden.The SPBS-CP has been shown to possess good reliability and validity in previous studies[26]. In the present study, it exhibited excellent internal consistency (Cronbach's α = 0.946).

Medical Outcomes Study Social Support Survey (MOS-SSS) was originally developed by Sherbourne and Stewart[27] to assess social support in individuals with chronic diseases. It was translated and culturally adapted by Doris et, showing strong reliability and validity[28].The scale consists of 19 items grouped into four dimensions: emotional-informational support, instrumental support, affectionate support, and positive social interaction. Participants rate each item on a 5-point Likert scale, with higher scores indicating higher perceived social support. The Cronbach's αcoefficient for the MOS-SSS in this study was 0.981.

Dependent variable

Cella et al. developed the Functional Assessment of Cancer Therapy-General (FACT-G) to evaluate the functional status of cancer patients[29].Wan et al. translated and evaluated the FACT-G in 2007 for use Chinese cancer populations, demonstrating good reliability, validity, and responsiveness[30].It includes 27 items measuring physical well-being, social/family well-being, emotional well-being, and functional well-being. Patients rate their feelings over the past week on a scale of 0 ~ 4. Higher scores reflect better quality of life (QOL). In this study, the FACT-G demonstrated a Cronbach's αcoefficient of 0.918.

Data collection methods

The first author sought support from the head of the radiotherapy department and the head nurse before the survey. Data collectors were trained on the study objectives, patient consent procedures, questionnaire administration, and related precautions. They recorded general and disease-related information from electronic medical records. During the mid-to-late stages of radiotherapy, when symptoms stabilize and become more pronounced[31]. patients completed the scales themselves, with assistance available for those who needed it. This period was chosen for data collection as it provides a comprehensive reflection of symptom cluster (SC) characteristics and their impact on quality of life (QOL). Patients with severe comorbidities or unstable conditions were excluded to ensure independent questionnaire completion. All participants successfully completed the questionnaires without refusal or interruption due to physical discomfort. Questionnaires were filled out within 20–30 min, checked for accuracy, and promptly collected after completion.

Statistical analysis

Statistical analyses were conducted using SPSS 24.0 and Amos 24.0. Descriptive statistics were used to describe demographic variables and disease characteristics. The factor structure of SC was determined through principal component analysis with varimax rotation. Factors and items were selected based on eigenvalues > 1 and factor loadings>0.5. Pearson correlation analysis was used to examine the relationship between SC, SS, SPB, and QOL. Structural equation modeling (SEM) was applied to assess the model's convergent validity, discriminant validity, overall fit, and to analyze path relationships and mediating effects.The evaluation of the model was based on established SEM guidelines.Convergent validity was examined using factor loadings, composite reliability (CR), and average variance extracted (AVE), following the criterion that standardized loadings should exceed 0.50, CR

> 0.70, and AVE > 0.50[32,33]. Regression analysis based on a path model within a structural equation modeling framework was performed to examine the direct and indirect effects.

Results

Basic demographic and disease information

Among the 409 patients, 71.39% were aged 50 or older, and 77.51% patients were male. Moreover, 57.7% had junior high school education or below. The primary tumor site for most patients was the nasal cavity and paranasal sinuses (38.88%). A majority of patients (52.32%) had a disease duration of 1–3 months since diagnosis (see Table 1).

Symptom clusters

Symptom clusters(SC) were derived from the MDASI-HN using exploratory factor analysis (EFA). The aim of this analysis was to identify groups of co-occurring symptoms that represent distinct but interrelated dimensions of symptom experience among patients receiving radiotherapy. Principal component extraction with varimax rotation was applied to determine the underlying factor structure.Exploratory factor analysis identified four SC in this study: oropharyngeal (eigenvalue = 3.601), neurosensory(eigenvalue = 3.350), psychological state (eigenvalue = 3.321) and the gastrointestinal (eigenvalue = 2.585). These factors explained a total of 58.443% of the variance. In subsequent analyses, these SC scores served as independent variables to examine effects on patients'quality of life(QOL) within the structural equation model.In subsequent analyses, these symptom cluster scores served as independent variables to examine effects on patients'quality of life within the structural equation model. (see Table 2)

Demographic variables	*n* (%)	Patient disease information	*n* (%)
Age		Cancer primary site	
18–35	20(4.89)	Oral cavity	95 (23.23)
36–50	97 (23.72)	Pharynx	130 (31.78)
> 50	292 (71.39)	Nasal cavity and sinuses	159 (38.88)
Gender		Head and neck	25 (6.11)
Male	317 (77.51)	Disease duration	
Female	92 (22.49)	≤ 1 Month	16 (3.91)
Education level		1–3 months	214 (52.32)
Junior high school or below	236 (57.70)	> 3 months	179 (43.77)
High school/technical school	134 (32.76)	Chemotherapy concurrent with radiotherapy	
College or above	39 (9.54)	No	134 (32.76)
Household monthly income		Yes	275 (67.24)
< 3000	152 (37.16)	Comorbidities	
3000–5000	172 (42.05)	No	203 (49.63)
5001–8000	68 (16.63)	Yes	206 (50.37)
> 8000	17 (4.16)	Other diseases	
Caretaker		None	244 (59.66)
Father	16 (3.91)	Yes	165 (40.34)
Partner	223 (54.52)	Nasal tube placement	
Child	104 (25.43)	No	402 (98.29)
Others	66 (16.14)	Yes	7 (1.71)
Insurance type		ECOG-PS	
Self-pay	5 (1.22)	Level 1: Limited, but can care for self	193 (47.19)
Employee insurance	88 (21.52)	Level 2: Can care for self, but cannot work	184 (44.99)
Resident insurance	305 (74.57)	Level 3: Severely limited, needs some assistance	31 (7.58)
Medical insurance/commercial insurance	11 (2.69)	Level 4: Bedridden, cannot care for self	1 (0.24)
Residence		Smoking status	
Urban	114 (27.87)	No	168 (41.08)
Rural	224 (54.77)	Yes	241 (58.92)
City	71 (17.36)	Alcohol consumption	
Marital status		No	170 (41.56)
Married	396 (96.82)	Yes	239 (58.44)
Unmarried or other	13 (3.18)		

Table 1. Descriptive statistical analysis of sample profiles and patient disease information($n = 409$).

Item	Item name	Factor loadings			
		Ropharyngeal symptoms	Neurosensory symptoms	Psychological symptom	Gastrointestinal symptoms
ASHE14	Severity of oral and pharyngeal mucus	0.808			
ASHE10	Severity of dry mouth	0.772			
ASHE21	Severity of oral or pharyngeal pain	0.765			
ASHE15	Severity of swallowing/choking	0.726			
ASHE20	Severity of taste abnormalities	0.611			
ASHE16	Severity of choking on food or drink		0.692		
ASHE18	Severity of skin pain		0.613		
ASHE22	Severity of dental or gum pain		0.611		
ASHE13	Severity of numbness and tingling		0.503		
ASHE05	Most distressing symptom			0.802	
ASHE11	Severity of sorrow/difficulty			0.777	
ASHE04	Severity of sleeplessness			0.620	
ASHE06	Severity of shortness of breath			0.583	
ASHE02	Severity of fatigue (weakness)			0.547	
ASHE03	Severity of nausea				0.840
ASHE12	Severity of vomiting				0.759
ASHE08	Severity of appetite loss				0.582
Eigenvalue		3.601	3.350	3.321	2.585
Explained variance %		16.370	15.226	15.097	11.750
Total explained variance %		58.443			

Table 2. Factor analysis of symptom clusters.

Correlation analysis of study variables

Correlation analyses among the main study variables were conducted using Pearson's correlation coefficients computed in SPSS to examine bivariate associations. A negative correlation was observed between SC and social support(SS) ($r = -0.347$, $P < 0.001$), as well as QOL ($r = -0.349$, $p < 0.001$), while a positive correlation was noted between SC and self-perceived burden (SPB) ($r = 0.453$, $p < 0.001$). SS exhibited a negative correlation with SPB ($r = -0.364$, $p < 0.001$),but a positive correlation with QOL($r = 0.358$, $p < 0.001$). Moreover, SPB showed a negative correlation with QOL($r = -0.457$, $p < 0.001$) (see Table 3).

Measurement model

Maximum likelihood estimation was used to estimate the measurement model, assessing reliability and convergent validity, as well as discriminant validity(See Fig. 1).

Convergent validity

The standardized factor loadings fell between 0.500 and 0.993, with composite reliability ranging from 0.711 to 0.987, and AVE from 0.382 to 0.949, thus satisfying the recommended criteria for reliability and convergent validity (see Fig. 1).Although some AVE values were slightly below the 0.50 threshold, the corresponding CR values all exceeded 0.70, indicating that the constructs still demonstrated adequate internal consistency and convergent validity[32,33]. In such cases, higher CR values can compensate for marginally low AVE, suggesting that the latent constructs explain sufficient shared variance among their indicators to be considered reliable (Fig. 2).

Discriminant validity

This study assessed the measurement model's discriminant validity using the AVE method. A model has discriminant validity when the square root of the AVE for each construct exceeds its correlations with others.In this study, the square roots of the AVE for most constructs exceeded their corresponding correlation coefficients. Specifically, the AVE square roots for SC, SS, SPB, and QOL were 0.572, 0.949, 0.660, and 0.486, respectively.The correlation coefficients between SC and SS, SC and SPB, SC and QOL, SS and SPB, SS and QOL, and SPB and QOL are − 0.449, 0.549, − 0.572, − 0.352, 0.398, and − 0.468, respectively.These results show that each construct in this study has good discriminant validity (See Table 3).

Structural model analysis

This study used the maximum likelihood method for structural equation modeling (SEM) analysis.Following Kenny's recommendationto exclude GFI and AGFI due to sample size sensitivity[34], we assessed the model's fit.The original MLχ^2 was 7235.559, but after using the Bollen-Stine p-value correction method to address potential chi-square inflation from non-multivariate normality, the corrected chi-square value was 3334.345.We recalculated all fit indices.The recalculated indices indicated that, except for SRMR (0.105), which was slightly above the standard, other indices such asχ^2/DF (1.393), RMSEA (0.031), TLI (0.964), and CFI (0.966) met the conventional SEM criteria, indicating acceptable model fit.

Construct	Item	Convergent validity			Discriminant validity				Correlation analysis			
		Std.	CR	AVE	SC	SS	SPB	QOL	SC	SS	SPB	QOL
SC	SCRO	0.500	0.835	0.572	**0.756**				1.000			
	SCNE	0.937										
	SCPS	0.873										
	SCGA	0.631										
SS	SSFL	0.946	0.987	0.949	− 0.449	**0.974**			− 0.347***	1.000		
	SSIN	0.974										
	SSEM	0.984										
	SSSO	0.993										
SPB	SPBCA	0.754	0.850	0.660	0.549	− 0.352	**0.812**		0.453***	− 0.364***	1.000	
	SPBEF	0.988										
	SPBTR	0.660										
QOL	QOLPH	0.630	0.781	0.486	− 0.572	0.398	− 0.468	**0.697**	− 0.349***	0.358***	− 0.457***	1.000
	QOLSO	0.505										
	QOLEM	0.952										
	QOLFU	0.620										

Table 3. Convergent validity discriminant validity and correlation analysis of variables. ***$p < 0.001$. SC, Symptom clusters; SCRO, Symptom clusters-ropharyngeal; SCNE, Symptom Clusters-Neurosensory; SCPS, Symptom Clusters-Psychologica; SCGA, Symptom Clusters-Gastrointestinal. SS, Social Support; SSFL, Social Support-Flexible; SSIN, Social Support-Emotional Information; SSEM, Social Support-Emotiona; SSSO, Social Support-Social Interaction Features. SPB, Self-Perceived Burden; SPBCA, Self-Perceived Burden-Care; SPBEF, Self-Perceived Burden-Economic /Family; SPBTR, Self-Perceived Burden-Treatment. QOL, Quality of Life; QOLPH, Quality of Life-Physica; QOLSO, Quality of Life-Social Family; QOLEM, Quality of Life-Emotiona; QOLFU: Quality of Life-Function.

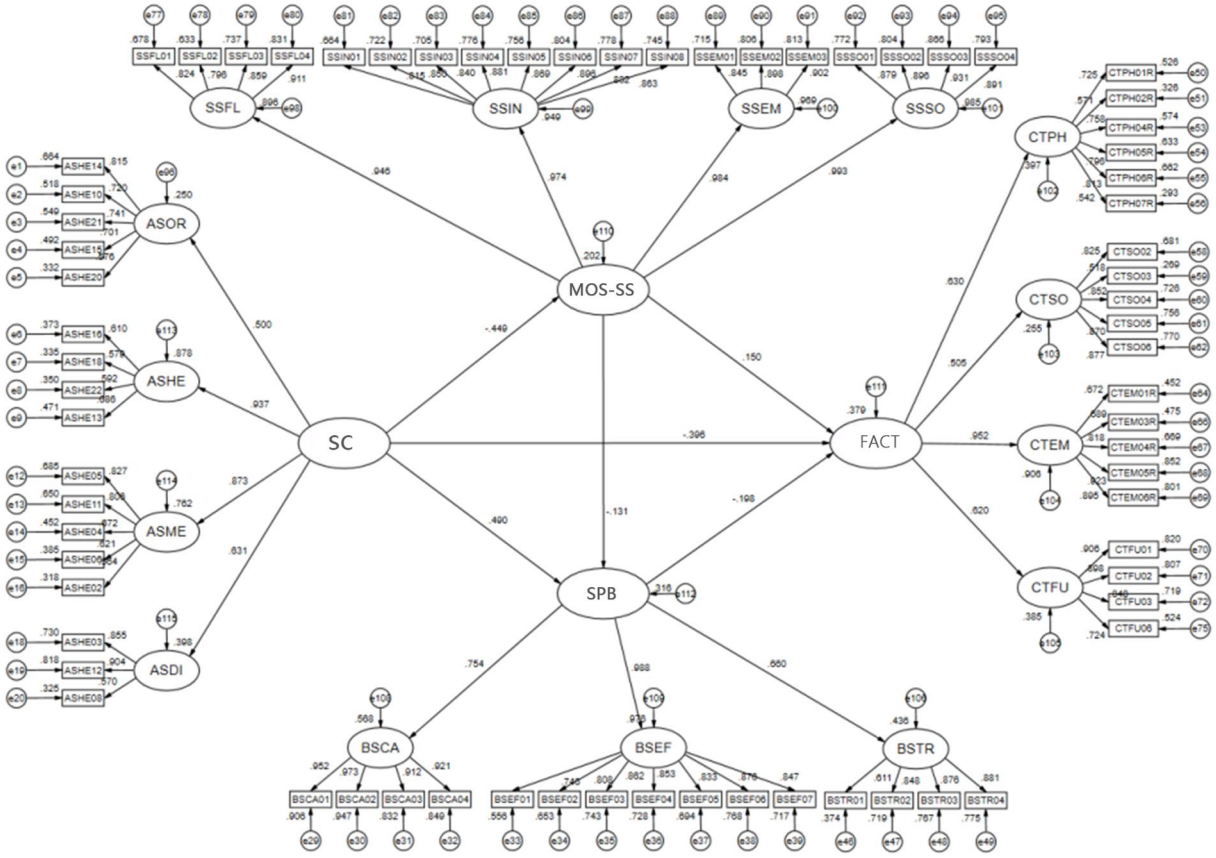

Fig. 1. Structural equation modeling diagram.

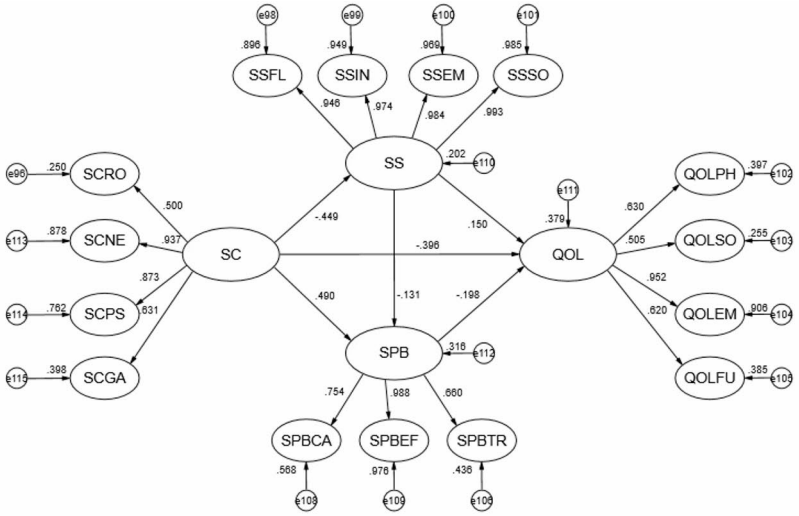

Fig. 2. Structural equation modeling diagram-simple version. SC, Symptom clusters; SCRO, Symptom clusters-ropharyngeal; SCNE, Symptom clusters-neurosensory; SCPS, Symptom clusters-psychological; SCGA, Symptom clusters-gastrointestinal; SS, Social support; SSFL, Social support-flexible; SSIN, Social support-emotional information; SSEM, Social support-emotional; SSSO, Social support-social interaction features; SPB, Self-perceived burden; SPBCA, Self-perceived burden-care; SPBEF, Self-perceived burden-economic/family; SPBTR, Self-perceived burden-treatment; QOL, Quality of life; QOLPH, Quality of life-physical; QOLSO, Quality of life-social family; QOLEM, Quality of life-emotional; QOLFU, Quality of life-function.

DV	IV	Unstd	S.E.	Unstd./S.E.	*p*-value	Std.	R2
MOS-SS	SC	− 0.340	0.055	− 6.186	0.000	− 0.449	0.202
SPB	MOS-SS	− 0.139	0.056	− 2.471	0.013	− 0.131	0.316
	SC	0.392	0.066	5.931	0.000	0.490	
FACT	SC	− 0.166	0.037	− 4.544	0.000	− 0.396	0.379
	MOS-SS	0.083	0.030	2.765	0.006	0.150	
	SPB	− 0.104	0.033	− 3.178	0.001	− 0.198	

Table 4. Regression analysis. SC, Symptom cluster; MOS-SS, Medical outcomes study social support; SPB, Self-perceived burden; FACT, Quality of life.

Regression analysis

SC was found to have a significant negative impact on SS (b = − 0.340, $p < 0.05$), explaining 20.2% of the variance in SS. Both SS (b = − 0.139, $p < 0.05$) and SC (b = 0.392, $p < 0.05$) significantly influenced SPB, explaining 31.6% of the variance in SPB. Furthermore, SC (b = − 0.166, $p < 0.05$), SS (b = 0.083, $p < 0.05$), and SPB (b = − 0.104, $p < 0.05$) were found to significantly impact QOL, explaining 37.9% of the variance in QOL (see Table 4).

Mediation analyses

Bootstrapping is commonly used to test indirect effects of mediating variables by resampling with replacement from the original sample, and bias-corrected bootstrapping is especially powerful for this purpose. The total effect of SC on QOL is significant, with a confidence interval of − 0.384 to − 0.135. The indirect effect of SC on QOL via SS is non-significant, with a confidence interval of − 0.064 to 0.010. By contrast, the indirect effect of SC on QOL via SPB is significant, with a confidence interval of − 0.256 to − 0.007. Additionally, the indirect effect of SC on QOL via SS and SPB together is non-significant, with a confidence interval of − 0.053 to 0.000 (see Table 5).

Effect	Point Estimate	Bootstrap 1000 times	
		Bias-corrected 95%	
		Lower bound	Upper bound
Total effect			
SC→QOL	− 0.240	**− 0.384**	**− 0.135**
Indirect effect			
SC→MOS-SS→QOL	− 0.028	− 0.064	0.010
SC→SPB→QOL	− 0.041	**− 0.256**	**− 0.007**
SC→MOS-SS→SPB→QOL	− 0.005	− 0.053	0.000
Direct effect			
SC→QOL	− 0.166	− 0.341	− 0.007

Table 5. Mediation analysis. SC, Symptom cluster; MOS-SS, Medical outcomes study social support ; SPB, Self-perceived burden; FACT, Quality of life.

Discussion

Symptom clusters in head and neck cancer patients undergoing radiotherapy

Four clinically significant symptom clusters(SC)were identified in this study: the oropharyngeal cluster (oral and pharyngeal mucus, dry mouth, oral or pharyngeal pain, swallowing/choking, taste abnormalities), the neurosensory cluster (choking, skin pain, dental or gum pain, numbness and tingling), the psychological state cluster (distressing, sorrow, sleeplessness, shortness of breath, fatigue), and the gastrointestinal cluster (nausea, vomiting, appetite loss). The SC identified in head and neck cancer (HNC) patients undergoing radiotherapy support the core proposition of the Theory of Unpleasant Symptoms (TOUS), which posits that symptoms often co-occur and share common mechanisms[10]. Among the oropharyngeal cluster, dry mouth was the most prominent symptom, closely associated with radiation-induced salivary gland damage[35]. The neurosensory cluster primarily reflected alterations in sensory function and motor coordination, such as coughing during swallowing. The psychological state cluster was characterized by emotional distress and fatigue, aligning with prior research emphasizing the psychological burden of radiotherapy in HNC patients[36]. The gastrointestinal cluster emerged as an independent cluster, highlighting the close link between treatment toxicity and nutritional status. Notably, oral or pharyngeal pain was classified within thethe oropharyngeal cluster rather than the neurosensory cluster. This may relate to the physiological connections among symptoms such as mucositis, xerostomia, and dysphagia. the oropharyngeal cluster reflects local symptom experiences directly associated with mucosal and glandular damage, rather than systemic neurosensory changes. Overall, these findings shed light on the complex interplay between physical and psychological symptoms in HNC patients undergoing radiotherapy, providing a theoretical foundation for multidisciplinary symptom management.

Correlations among symptom clusters, social support, self-perceived burden, and quality of life

The Pearson correlation analysis revealed strong interrelationships among various variables in HNC patients undergoing radiotherapy. Consistent with previous research[37], SC was to be found positively correlated with self-perceived burden (SPB), indicating that a higher SC burden leads to increased perception of symptom burden. SC was negatively correlated with social support (SS) and quality of life(QOL), suggesting that symptoms may deplete social energy, reduce support resources utilization, and lower QOL[11,15,38]. SPB was negatively correlated with both QOL and SS, in line with prior studies[19,39], indicating a bidirectional weakening effect on QOL and SS through an emotional withdrawal mechanism. In addition, the positive correlation between SS and QOL was also observed in patients with oral cancer[40], highlighting the universal applicability of SS in improving QOL across different cancer types. These findings suggest that symptom burden may impact QOL through direct physical function weakening and indirect effects on SS utilization and SPB.

Mediating role of SPB between SC and QOL

The structural equation model in this study showed a good fit after the Bollen-Stine correction, although the SRMR slightly exceeded the ideal threshold at 0.15.This suggests that the model accurately captured the relationships among variables. Through the mediation analysis, it was found that the SC had both a direct and an indirect effect on QOL, the latter being through SPB. This supports the idea that SC affects QOL in two ways: (1) directly through physiological symptoms like pain and fatigue, which can decrease daily functioning and comfort; (2) indirectly through psychosocial factors such as increased psychological stress from SPB, where more severe SC leads to the higher SPB and a decline QOL. These findings align with the TOUS framework, which highlights the interconnectedness of symptoms, influencing factors, and outcomes in patients'experiences[10]. The bidirectional mechanism suggests that clinical interventions should target both symptom management and psychosocial support. Therefore, recommendations include implementing precision case like wallowing function training and mucosal protection programs[41], and establishing a dyadic intervention model for patients and caregivers to reduce patients' SPB through psychoeducation and family support[42]. This combined strategy offers hope for personalized symptom relief in HNC cancer patients undergoing radiotherapy.

Social support did not mediate between symptom clusters and quality of life, and no chain mediation effect was found

Despite our initial hypothesis, SS did not act as a mediator between SC and QOL in undergoing-radiotherapy patients with HNC cancer. This could be due to the majority of patients being over 50 years old (71.39%), and a significant portion being diagnosed with the disease for only 1 ~ 3 months (52.32%). Older patients may have different needs and perceptions regarding SS[43] and those with shorter disease durations may not have experienced depletion of long-term support[44], explaining why SS did not mediate the association between SC and QOL. The sequential mediation effect of SS and SPB between SC and QOLwas not statistically significant in our study. Two potential explanations for this finding: (1) sample characteristics and data distribution may have contributed to this result. While the Bollen-Stine Bootstrap correction improved model fit indices in our structural equation modeling (SEM) analysis, it's noteworthy that this correction primarily addresses issues of small sample size or violations of multivariate normality assumptions. This methodological consideration may explain the discrepancy between significant individual path coefficients in our regression analyses and non-significant sequential mediation effects in mediation analyses. (2) Second, effect size considerations warrant attention. The current sample size may have been insufficient to achieve adequate statistical power, particularly given the complexity of examining this specific sequential mediation pathway. However, given that no prior studies have reported effect sizes for this particular mediation chain and that the non-significant paths may reflect limited statistical power rather than the true absence of effects[45], a formal post-hoc power analysis is recommended to better evaluate whether sample size constraints influenced these findings[46]. In conclusion, despite the lack of significant sequential mediation in our study, these initial results need to be validated in larger samples. The theoretical framework suggesting that SS could boost coping strategies by providing emotional support, informational guidance, and practical assistance, and potentially leading to improved QOL[47] remains clinically plausible and warrants further investigation with more robust methodologies.

Limitations and future directions

The study found no significant mediating effect of social support (SS) between symptom clusters (SC) and quality of life (QOL) in HNC patients. No chain-mediation was observed where SC influenced QOLthrough SS and SPB. The study has the following limitations: First, the cross-sectional research design restricts causal inferences between SC, SS, SPB, and QOL. Second, the study sample, drawn from three hospitals within the same region, limits the representativeness and generalizability of the findings. Additionally, the small sample size reduces statistical power and weakens the significance of some effects. Future studies should use longitudinal research designs to track the trajectories of SC, SS, SPB, and QOL, thereby deepening understanding of their underlying mechanisms. Multi-center or cross-regional study designs can include more diverse populations and improve the generalizability of the results.Incorporating neurobiological indicators (such as inflammation markers and stress hormones) can uncover the biological mechanisms through which SC affects QOL. These findings support integrating precision strategies for symptom management, psychological interventions, and biomedical measures to optimize individualized clinical decision-making and improve the quality of life for HNC patients.

Clinical implications and innovations

This study introduces a fresh structural equation model to explore the connection between QOL and SC in undergoing radiotherapy patients with HNC cancer, going beyond traditional research methods. The study proposes a dual-intervention approach: (1) incorporating SPB screening tools in regular symptom assessments; and (2) implementing interdisciplinary intervention programs for high-risk patients, such as mindfulness-based stress reduction and cognitive restructuring.

Data availability

The datasets generated and/or analyzed during this study are available from the corresponding author upon reasonable request.

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References

1. Bhat, G. R., Hyole, R. G. & Li, J. Head and neck cancer: current challenges and future perspectives. *Adv. Cancer Res.* **152**, 67–102 (2021).
2. Sung, H. et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **71** (3), 209–249 (2021).
3. Cao, W. et al. Changing profiles of cancer burden worldwide and in china: a secondary analysis of the global cancer statistics 2020. *Chin. Med. J.* **134** (7), 783–791 (2021).
4. Crowder, S. L. et al. Head and neck cancer survivors' experiences with chronic nutrition impact symptom burden after radiation: a qualitative study. *J. Acad. Nutr. Diet.* **120** (10), 1643–1653 (2020).
5. Lopes-Júnior, L. C., Ferrarini, T. F., Pires, L. B. & Pereira-da-Silva, G. Cancer symptom clusters in adult patients undergoing chemotherapy: a systematic review and meta-analysis protocol. *PLOS One.* **17** (7), e0273411 (2022).
6. Wang, Y. et al. Nutrition impact symptom clusters in patients with head and neck cancer receiving concurrent chemoradiotherapy. *J. Pain Symptom Manag.* **62** (2), 277–285 (2021).
7. Lin, Y. et al. A network analysis of self-reported psychoneurological symptoms in patients with head and neck cancer undergoing intensity-modulated radiotherapy. *Cancer* **128** (20), 3734–3743 (2022).
8. Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A. & Suppe, F. The middle-range theory of unpleasant symptoms: an update. *Adv. Nurs. Sci.* **19** (1), 14–27 (1997).

9. Ren, X. et al. The relationships between symptom clusters and contributing factors in patients with esophageal cancer: structural equation modelling based on theory of unpleasant symptoms. *BMC Gastroenterol.* **25** (1), 544 (2025).
10. Lenz, E. R. Application of the theory of unpleasant symptoms in practice: a challenge for nursing. *Investig. Educ. Enferm*. **20** (1), e20 (2018).
11. Li, Y. et al. Symptom clusters in head and neck cancer patients with endotracheal tube: which symptom clusters are independently associated with health-related quality of life. *Eur. J. Oncol. Nurs.* **48**, 101819 (2020).
12. Chen, K. et al. Changes in the symptom clusters of elderly patients with lung cancer over the course of postoperative rehabilitation and their correlation with frailty and quality of life: a longitudinal study. *Eur. J. Oncol. Nurs.* **67**, 102388 (2023).
13. Luo, Y. et al. Symptom clusters and impact on quality of life in lung cancer patients undergoing chemotherapy. *Qual. Life Res.* **33** (12), 3363–3375 (2024).
14. Fei, F. et al. Symptom clusters, associated factors and health-related quality of life in patients with chronic obstructive pulmonary disease: a structural equation modelling analysis. *J. Clin. Nurs.* **32** (1–2), 298–310 (2022).
15. Zhong, Y. Z. *Exploration of Symptom Clusters in Frail Elderly in Nursing Homes and Verification of the Mediating Role of Social Support between Symptom Clusters and Quality of Life* (Chengdu University of Traditional Chinese Medicine, 2021).
16. Egozi, F. H. et al. Conservation of resources, psychological distress, and resilience during the COVID-19 pandemic. *Int. J. Public. Health*. **67**, 1604567 (2022).
17. Chen, Z. et al. Sleep quality mediates the effect of medical social support on depression symptoms in patients with HIV/AIDS. *BMC Public. Health.* **24** (1), 1429 (2024).
18. McPherson, C. J., Wilson, K. G. & Murray, M. A. Feeling like a burden: exploring the perspectives of patients at the end of life. *Soc. Sci. Med.* **64**, 417–427 (2007).
19. Lin, X. et al. Self-perceived burden predicts lower quality of life in advanced cancer patients: the mediating role of existential distress and anxiety. *BMC Geriatr.* **22** (1), 803 (2022).
20. Xu, J. et al. Relationship between psychological resilience and quality of life in cancer patients and the multiple mediating roles of stigma and self perceived burden. *Sci. Rep.* **15** (1), 12375 (2025).
21. Zhang, N. et al. Illness uncertainty, self-perceived burden and quality of life in patients with chronic myeloid leukaemia: a cross-sectional study. *J. Clin. Nurs.* **31** (19–20), 2935–2942 (2021).
22. Ren, N. et al. The relationship between facilitation of patient involvement and self-perceived burden in postoperative lung cancer patients: the mediating role of social support. *Patient Prefer Adherence*. **18**, 1979–1989 (2024).
23. Rosenthal, D. I. et al. Measuring head and neck cancer symptom burden: the development and validation of the M. D. Anderson symptom inventory, head and neck module. *Head Neck*. **29** (10), 923–931 (2007).
24. Xiao, W. et al. Psychometric validation of the Chinese version of the M.D. Anderson symptom Inventory-Head and neck module (MDASI-HN-C) in patients with head and neck cancer. *Support Care Cancer*. **30** (1), 219–229 (2022).
25. Cousineau, N., McDowell, I., Hotz, S. & Hébert, P. Measuring chronic patients' feelings of being a burden to their caregivers: development and preliminary validation of a scale. *Med. Care*. **41** (1), 110–118 (2003).
26. Ren, Y. *Development and Preliminary Clinical Application of the Self-Perceived Burden Scale for Cancer Patients* (Taishan Medical University, 2012).
27. Sherbourne, C. D. & Stewart, A. L. The MOS social support survey. *Soc. Sci. Med.* **32** (5), 705–714 (1991).
28. Doris, S. F., Yu, D. T. F., Lee, D. & Woo, J. Psychometric testing of the Chinese version of the medical outcomes study social support survey (MOS-SSS-C). *Res. Nurs. Health*. **27** (2), 135–143 (2004).
29. Cella, D. F. et al. The functional assessment of cancer therapy scale: development and validation of the general measure. *J. Clin. Oncol.* **11** (3), 570–579 (1993).
30. Wan, C., Meng, Q., Tang, X., Zhang, X. & Yang, Z. A review of the Chinese version of the functional assessment of cancer Therapy-General (FACT-G) scale for cancer patients. *Pract. J. Cancer*. **21** (1), 77–80 (2006).
31. Rocha, P. H. P. et al. Adverse radiation therapy effects in the treatment of head and neck tumors. *Radiographics*. **42** (3), 806–821 (2022).
32. Fornell, C. & Larcker, D. Evaluating structural equation models with unobservable variables and measurement error. *J. Mark. Res.* **18** (1), 39–50 (1981).
33. Hair, J. F., Black, W. C., Babin, B. J. & Anderson, R. E. *Multivariate Data Analysis*, 8th edn (Cengage Learning, 2019).
34. Kenny, D. A. Measuring model fit. http://www.davidakenny.net/cm/fit.htm (accessed 09 Jun 2025).
35. Schulz, R. E. et al. Prevalence of hyposalivation and associated factors in survivors of head and neck cancer treated with radiotherapy. *J. Appl. Oral Sci.* **29**, e20200854 (2021).
36. Bao, R. Z. et al. Analysis of psychological distress status in elderly head and neck malignant tumor patients before and after radiotherapy. *Chin. J. Radiat. Oncol.* **30** (2), 109–113 (2021).
37. Pan, H. Y. *The Mediating Effect of self-perceived Burden between Symptom Clusters and Quality of Life in Patients with Primary Brain Tumors* (North Sichuan Medical College, 2023).
38. Wang, Y. et al. Symptom clusters and impact on quality of life in esophageal cancer patients. *Health Qual. Life Outcomes*. **20** (1), 168 (2022).
39. Chang, Y. et al. Influence of self-perceived burden on quality of life in patients with urostomy based on structural equation model: the mediating effects of resilience and social support. *Biomed. Res. Int.* **2022**, 9724751 (2022).
40. Zhang, Y. et al. Effects of stigma, hope and social support on quality of life among Chinese patients diagnosed with oral cancer: a cross-sectional study. *Health Qual. Life Outcomes*. **18** (1), 112 (2020).
41. Lanzetti, J. et al. Management of oral hygiene in head-neck cancer patients undergoing oncological surgery and radiotherapy: a systematic review. *Dent. J.* **11** (3), 83 (2023).
42. Chen, X. et al. Intervention and coping strategies for self-perceived burden of patients with cancer: a systematic review. *Asia Pac. J. Oncol. Nurs.* **10** (6), 100231 (2023).
43. Won, M. Relationship between perceived social support and physical frailty among older patients with coronary artery disease: a dual mediation model. *J. Clin. Med.* **14** (5), 1744 (2025).
44. Shokrgozar, S., Rouzbehan, V., Zare, R. & Abdollahi, E. Evaluation of patient social support, caregiver burden, and their relationship with the course of the disease in patients with bipolar disorder. *Int. J. Soc. Psychiatry*. **68** (8), 1815–1823 (2022).
45. Kenny, D. A. Mediation. In *The Kenny Handbook of Structural Equation Modeling* (online). (2018).
46. Hayes, A. F. *Introduction To Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach* (Guilford Press, 2013).
47. Ruiz-Rodríguez, I., Hombrados-Mendieta, I., Melguizo-Garín, A. & Martos-Méndez, M. J. The importance of social support, optimism and resilience on the quality of life of cancer patients. *Front. Psychol.* **13**, 833176 (2022).

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Author contributions

R.Z.: Conceptualization, supervision, formal analysis, writing-original draft, writing-review and editing; T.D.,

H.M., Y.M., A.H.: Data curation; J.K.: Supervision, writing-review and editing; Y.Z.: Writing-review and editing, resources.

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Declarations

Competing interests
The authors declare no competing interests.

Ethical approval and consent to participate
The study protocol was approved by the Ethics Committee of Henan Cancer Hospital (Approval No.2021-KY-0165-002). Written informed consent was obtained from all individual participants included in the study.

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