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Psychosocial Predictors of Health-Related Quality of Life in Lymphoma: A Multiple Mediation Model

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Abstract

Objective: To identify predictors of poorer Health-Related Quality of Life (HRQoL) in lymphoma, focusing on socio-demographic, clinical, and psychosocial variables.

Methods: One hundred twenty-six patients with Hodgkin lymphoma or non-Hodgkin lymphoma completed the EORTC QLQ-C30, Hospital Anxiety and Depression Scale, and Multidimensional Scale of Perceived Social Support.

Results: Depressive symptoms were significantly associated with poorer HRQoL ($\beta = -0.54$, $p<0.001$). Perceived social support was associated with lower depression and anxiety ($\beta = -0.34$, $p<0.001$; $\beta = -0.19$, $p<0.01$, respectively). Mediation analysis indicated that social support was indirectly associated with HRQoL, through depressive symptoms ($\beta = 0.30$, $p<0.001$).

Conclusion: Depressive symptoms showed a significant association with poorer HRQoL in lymphoma. Perceived Social support was associated with better HRQoL through its association with lower depressive symptoms. Identifying individuals at risk can inform targeted, timely psychosocial interventions to reduce distress and improve overall well-being. Findings support routine screening and monitoring in hematology care.

Keywords: Quality of life; Lymphoma; Social support; Mediation model; Depression symptoms

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Introduction

Improving Health-Related Quality of Life (HRQoL) is a central objective in modern oncological care [1]. In the context of lymphoma, encompassing both Non-Hodgkin Lymphoma (NHL) and Hodgkin Lymphoma (HL), HRQoL assumes a critical role due to the unique challenges these malignancies present. Lymphomas are heterogeneous hematologic cancers that differ in epidemiology, clinical course, and treatment trajectories [2]. According to the Global Cancer Observatory (GLOBOCAN), non-Hodgkin lymphoma accounts for more than 540,000 new cases and approximately 260,000 deaths worldwide each year, whereas Hodgkin lymphoma accounts for approximately 83,000 new cases annually and shows a distinct epidemiological distribution with higher incidence among adolescents and young adults [3]. Advances in oncological treatments have markedly improved survival among lymphoma patients. As survival rates increase, greater attention has been directed toward patient-reported outcomes and the broader psychosocial impact of cancer and its treatment [4]. Patients face physical and emotional challenges, including psychological factors such as anxiety and depression, which are highly prevalent in this population. Studies indicate that 15% to 47% of patients with hematologic malignancies report depressive symptoms, while 22% to 47% experience anxiety symptoms during the course of their illness [5-8]. Psychological distress may be particularly pronounced during the early phases following diagnosis. In a large cohort study, Odejide and colleagues reported that more than half of patients newly diagnosed with lymphoma or myeloma experienced clinically significant symptoms of anxiety or depression, and depressive symptoms were strongly associated with poorer HRQoL [9]. Anxiety symptoms may include restlessness and sleep disorders, while depressive symptoms can manifest as loss of interest and social withdrawal [10,11]. If persistent, these symptoms may negatively affect multiple domains of functioning and have been associated with poorer HRQoL and increased mortality risk in cancer populations [12,13]. Population-based evidence further suggests that a proportion of individuals with hematologic malignancies receive a formal diagnosis of anxiety or depression following cancer diagnosis [14]. These psychological conditions may substantially affect patients' overall well-being and have been associated with poorer HRQoL [12-14]. Beyond psychological symptoms, psychosocial resources may play an important role in patients' adjustment to cancer. Perceived social support from family members, friends, and healthcare professionals has been associated with lower levels of psychological distress and better psychosocial adaptation among oncology patients [15]. In lymphoma populations specifically, higher perceived social support has been linked to improved mental health outcomes and better overall adjustment to illness. For example, Caviness-Ashe and colleagues reported that lymphoma survivors who perceived greater levels of social support also reported better mental health and psychosocial functioning [16]. Recent psychosocial oncology research suggests that relationships among psychosocial variables influencing patient outcomes may involve complex and indirect pathways rather than simple linear associations. In lymphoma patients, perceived social support has been shown to mediate the relationship between illness perception and feelings of powerlessness [17]. Similarly, studies, applying structural equation modelling in patients with hematologic malignancies have suggested that social support, anxiety, and depression may interact through mediated pathways influencing psychological adjustment and quality of life outcomes [18]. Taken together, these findings suggest that anxiety, depression, and perceived social support represent psychosocial dimensions potentially associated with variations in HRQoL among patients with lymphoma. Psychological responses to cancer may also reflect mechanisms such as uncertainty about the future, perceived loss of control, and fear of disease progression [19]. Kanellopoulos and colleagues reported that 32% of long-term survivors of leukemia and pediatric lymphoma experienced poor HRQoL compared with 19% of the general population [20]. Despite the growing literature examining HRQoL in oncology, relatively few studies have specifically investigated psychosocial predictors of HRQoL in adult patients with lymphoma within an integrated explanatory framework.

Therefore, the aim of this study is to investigate psychosocial predictors of HRQoL in patients with lymphoma by examining the association between depressive symptoms, anxiety symptoms, and perceived social support. Specifically: (a) to assess the association between depressive and anxiety symptoms and HRQoL; (b) to examine whether perceived social support is associated with HRQoL directly or indirectly through psychological symptoms; (c) to explore the potential mediating role of depressive symptoms in the relationship between perceived social support and HRQoL.

Materials and Methods

Participants

A consecutive sample of 126 patients was recruited from the Department of Oncology-Hematology, UOC Clinical Hematology, General Hospital of Pescara (Italy). The sample included both women and men with a medically documented diagnosis of Non-Hodgkin Lymphoma (NHL) or Hodgkin Lymphoma (HL), in accordance with World Health Organization diagnostic criteria. Participants were outpatients and they were contacted by clinical psychologists in collaboration with medical hematologists. All participants were undergoing first-line chemotherapy treatment, and the psychological assessment was conducted between the first and third month of treatment. Data collection took place between [January 2024] and [December 2024] as part of routine clinical evaluation procedures. Inclusion criteria for the study were as follows: a) adult patients aged 18 to 65 years; and b) patients undergoing chemotherapy treatment. Conversely, patients younger than 18 years, older than 65, or those with severe addictions, neurological or psychiatric disorders, were excluded from the study. The study was approved by the Ethical Committee under the title "Observational study on the quality of life of hematologic patients" (Prot. n. 260168/25) at the General Hospital in Pescara, Italy. All recruited participants were informed about the scientific purpose of the study and provided their written informed consent. The evaluation was conducted as part of the routine clinical assessment of patients. All participants underwent a clinical assessment conducted by certified clinical psychologists. The research was conducted with respect for the rights of all participants, and the data were analyzed anonymously. Participation was voluntary; all participants completed questionnaires and engaged in clinical interviews in a confidential setting.

Study measures

Demographic data, including age, gender, education level, and marital status were collected at baseline, specifically at the time of diagnosis. Clinical variables including lymphoma diagnosis and cancer stage were obtained from the patients' medical records.

Multidimensional Scale of Perceived Social Support (MSPSS)

The Multidimensional Scale of Perceived Social Support (MSPSS) developed by Zimet G. (1988) [21], is a 12-item self-reported instrument designed to assess perceived social support from three sources: family, friends, and significant others. Participants rated each item on a seven-point Likert scale, where 1 indicates "strongly disagree" and 7 indicates "strongly agree". Each source of support is represented by four items (family, friends, significant others), and sub-dimensional scores are calculated as the mean score of the corresponding four items. The overall MSPSS score is derived from the mean score of all 12 items, with higher scores reflecting higher levels of perceived social support. The MSPSS demonstrates high internal consistency, with Cronbach's alpha values ranging from 0.85 to 0.91, and it exhibits good test-retest reliability [21,22].

Hospital Anxiety and Depression Scale (HADS)

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) [23], which consists of two subscales of seven items each, measuring symptoms of anxiety and depression respectively. A score greater than 8 on either subscale indicates a potential concern for an anxiety or depressive disorder; while a score exceeding 11 suggests a probable case. For the purposes of this study, a score greater than 8 was used as the cut-off value for defining cases of anxiety or depression, as this threshold provides an optimal balance between sensitivity and specificity [23-25].

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) is a health-related QoL questionnaire developed by the European Organization for Research and Treatment of Cancer [26,27]. The validity and reliability of this questionnaire have been established in multiple studies [28,29], and it is available in several languages [30]. The questionnaire consists of 15 scales encompassing a total of 30 questions in total, including physical, emotional, cognitive, social and role functioning, fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties and global health status. Responses to the items are rated on a scale from 1 to 4, with scores corresponding to “not at all” to “very much.” Items 29 and 30 are rated on a scale from 1 to 7, ranging from very poor to excellent [26]. Each scale is scored according to the scoring manual by Fayers, et al. [30], resulting in scores that range from 0 to 100. In our study, Cronbach’s α of the GHS/QoL and FS scale was 0.86 and 0.85, respectively.

Statistical Analysis

Characteristics of the respondents and non-respondents; Statistical analysis was conducted using STATA 18 (StataCorp. LLC, College Station, TX, USA) A three-step strategy was employed for data analysis. First, socio-demographic and clinical variables between the two groups (Low QoL and High QoL) were compared using Student’s t-test or χ^2. The standardized mean difference was utilized as a measure of effect size. The standardized mean difference was used as a measure of effect size, with Cohen’s d interpreted as follows: 0.20-0.50 indicates a small effect, 0.50-0.80 a moderate effect, and greater than 0.80 a large effect [31].

Second, binary logistic regression analysis was performed to identify the major determinants that best predict QoL. GHS/QoL was considered as a dependent variable, and using the median as a cut-off. The independent variables included social support, age, education, marital status, gender, cancer stage and symptoms of anxiety and depression. Three regression models were developed: the first model included the four socio-demographic variables (age, gender, education, and marital status) to describe participant characteristics, the second model included the clinical variable cancer stage, and the third model incorporated psychological variables (total social support score, depression, and anxiety symptom subscales). This approach allowed us to assess the contribution of each factor to the explained variance in the final QoL model.

Third, Structural Equation Model (SEM) was employed to evaluate the effect of the latent dimension of social support on QoL mediated by symptoms of anxiety and depression. Our model included one exogenous latent trait (social support), one endogenous latent factor for the HRQoL items treated as measurements loadings, and two continuous mediator variables (anxiety and depression symptoms). SEM can be conceptualized as a combination of factor analysis and regression, or path analysis. Latent factors represent theoretical constructs that can be considered latent traits or “true” variables underlying the measured items.

The primary focus of the investigation is on the relationships among factors or between factors and observed variables (the structural part of the model) [32-34]. Using maximum likelihood estimation, SEM was applied to evaluate the fit of the hypothesized model based on several criteria: a chi-squared (χ^2) p-value greater than 0.05, a Standardized Root Mean Square Residual (SRMR) value less than 0.08 (considered a good fit) [35], and Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI) values near or greater than 0.90 [36]. Hypotheses regarding the structural relationships among the

Table 1: Socio-demographic and clinical characteristics between patients with lower and higher QoL.

		Total sample	**Low QoL**	**High QoL**	**t /χ^2**	***p***	***d***
		(N = 126)	**(N =87)**	**(N = 39)**			
			(69.05%)	**(30.95%)**			
Age (Mean and SD)		50.23 (13.55)	51.4 (13.6)	47.63(13.27)	1.43	0.15	0.27
Gender	Male	59 (46.83%)	40 (45.98%)	19 (48.72%)	0.28	0.77	0.05
	Female	67 (53.17%)	47(54.02%)	20 (51.28%)			
Education	Primary	8 (6.45%)	7 (8.14%)	1 (2.63%)	0.36	0.71	0.07
	Secondary	45 (36.29%)	30 (34.88%)	15 (39.47%)			
	High	54 (43.55%)	37 (43.02%)	17 (44.74%)			
	University	17 (13.71%)	12 (13.95%)	5 (13.16%)			
Marital status	Unmarried	10 (8.26%)	9 (10.71%)	1 (2.70%)	1.45	0.13	0.29
	Currently married	111 (91.74%)	75 (89.29%)	36 (97.30%)			
Disease	HL	51 (40.48%)	37 (42.53%)	14 (35.90%)	-	-	-
	NHL	75 (59.52%)	50 (57.47%)	25 (64.10%)			
	I	11 (8.73%)	7 (8.05%)	4 (10.26%)	0.49	0.63	0.10
Cancer stage	II	37(29.37%)	28 (32.18%)	9 (23.08%)			
	III	43 (34.13%)	29 (33.33%)	14 (35.90%)			
	IV	35 (27.78%)	23 (26.44%)	12 (30.77%)			
MSPSS family		26.14 (4.89)	26 (4.89)	26.46 (4.95)	0.48	0.62	0.09
MSPSS friends		22.98 (7.11)	22.41 (7.29)	24.25 (6.62)	1.34	0.18	0.25
MSPSS others		25.46 (5.55)	25.39 (5.56)	25.64 (5.59)	0.23	0.81	0.04
MSPSS total score		74.11 (14.44)	73.83(13.75)	74.71 (16.05)	0.31	0.75	0.06
HADS-D		7.19 (4.32)	8.21 (4.37)	4.89 (3.21)	4.25	<.001	0.59
HADS-A		8.26 (4.67)	9.10 (4.76)	6.41 (3.91)	3.09	<.001	0.81

Abbreviations: MSPSS: Multidimensional Scale of Perceived Social Support; HADS-A: Hospital Anxiety and Depression Scale-anxiety subscale; HADS-D: Hospital Anxiety and Depression Scale-depression subscale; NHL: non-Hodgkin lymphoma; LH: Hodgkin lymphoma constructs in the final model were evaluated using the magnitude of path coefficients (standardized coefficient) and their significance [37].

Results

The findings indicate significant correlations between psychological variables and perceived QoL. Notably, emotional well-being and social support were identified as critical factors.

Socio demographic and clinical data

Of the 127 patients recruited, 126 (99.19%) were successfully enrolled. The majority of the patients were female (53.17%), with a mean age of 50.23 years. Most participants had high level of education (43.55%) and were currently married (91.74%). The sample included 51 patients with Hodgkin's Lymphoma and 75 with Non-Hodgkin's Lymphoma, with 69.05% of the participants reporting a low QoL.

Between group comparisons QoL

No socio-demographic differences were observed between the two groups, and there are no missing data. QoL dimensions, including physical, emotional, cognitive, social and role functioning, as well as fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties and global health status, showed significant differences between the groups, with effect sizes falling within the small to moderate range. Notably, patients exhibiting symptoms of anxiety and depression reported lower QoL scores (d = .59, d = .81; respectively) compared to those with high QoL (Table 1). These differences are consistent with the distribution of EORTC QLQ-C30 domain score (Table 2).

Health-related quality of life (EORTC QLQ-C30)

Descriptive statistics for the EORTC QLQ-C30 scales are presented in Table 2. Overall, functional domains showed moderate levels, while symptom burden was present across multiple domains. (Means and standard deviations of all QoL domains and symptoms scales for the total sample).

Table 2: The Health-Related Quality of Life scores (EORTC QLQ-C30).

Scales	Mean	SD	Minimum	Maximum
Global health status/Quality of life	51.87	25.37	0	100
Functioning scale	64.88	20.69	14.2	100
Physical functioning	70.33	28.99	0	100
Role functioning	55.08	37.65	0	100
Cognitive functioning	81.45	21.98	16	100
Emotional functioning	61.07	27.47	0	100
Social functioning	56.25	33.73	0	100
Symptom scale	29.72	22.12	0	94.33
Fatigue	44.98	29.47	0	100
Insomnia	42.99	36.12	0	100
Appetite loss	27.45	36.55	0	100
Pain	27.74	29.36	0	100
Nausea and vomiting	16.67	28.2	0	100
Constipation	20.13	29.77	0	100
Dyspnea	22	31.81	0	100
Diarrhea	13.13	25.21	0	100
Financial	22.62	32.73	0	100

Abbreviations: EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30

Table 3: Predictors of worsening QoL. Results of binary regression models (N=126).

	β	OR (95% C.I.)	p_value	R^2
Model 1				0.03
Age	0.02	0.97 (0.94-1.01)	0.21	
Gender	0.07	1.95 (0.72-2.25)	0.18	
Education	0.16	0.84 (0.48-1.24)	0.56	
Marital Status	1.04	1.04 (0.48-1.26)	0.72	
Model 2				
Cancer Stage	0.23	1.15 (0.81-1.88)	0.28	0.04
Model 3				0.17
+MSPSS family	0.1	0.89 (0.80-1.01)	0.09	
+MSPSS friends	0.04	1.04 (0.96-1.12)	0.26	
+MSPSS others	0.08	1.00 (0.90-1.08)	0.85	
+HADS-D	0.24	0.94 (0.82-1.08)	<0.001	
+HADS-A	0.05	0.78 (0.66-0.93)	0.39	

Abbreviations: MSPSS: Multidimensional Scale of Perceived Social Support; HADS-A: Hospital Anxiety and Depression Scale-anxiety subscale; HADS-D: Hospital Anxiety and Depression Scale-depression subscale

Predictors of poorer QoL

Table 3 presents three regression models predicting QoL, including socio-demographic, clinical and psychological variables, with the GHS/QoL score as a binary outcome criterion (dummy coded 0-1 low and high, respectively). In the first model, socio-demographic characteristics (age, gender, education and marital status) accounted for 3% in worsening QoL. In model 2, the clinical variable cancer stage (OR = 1.15, 95% CI [0.81-1.88]) was included but did not show a significant contribution to QoL variance. Finally, the social support dimension, family (OR = 0.89, 95% CI [0.80-1.01]), friends (OR = 1.04, 95% CI [0.96-1.12]) and others (OR = 1.00, 95% CI [0.90-1.08]); anxiety (OR = 0.78, 95% CI [0.66-0.93]), and depression (OR = 0.94, 95% CI [0.82-1.08]), were included in Model 3, they significantly contributed an additional 17% to the variance in QoL.

Structural equation model

To complement the binary logistic regression analysis, SEM was conducted to test the direct and indirect effects within a multiple mediation model of latent dimension of social support on QoL through symptoms of depression and anxiety. The structural components of the model included one exogenous latent trait (social support), one endogenous latent factor representing HRQoL, two continuous mediator variables (depression and anxiety symptoms) and one covariate (age).

The latent HRQoL construct was operationalized using two indicators from the EORTC QLQ-C30: global health status and functioning subscales total score (physical, role, cognitive, emotional, social factors). The eight symptom scales were retained as separate measured variables but not included as direct indicators of the latent construct, reflecting the distinction between positive functioning and disease burden. The measurement model was evaluated for factorial validity by examining factor loadings, standardized residuals, and model fit indices.

Figure 1, show path analysis and parameter estimates. All observed variables were appropriately loaded onto their corresponding latent constructs, thereby supporting the validity of each latent construct, and standardized residuals were normally distributed. The parameter

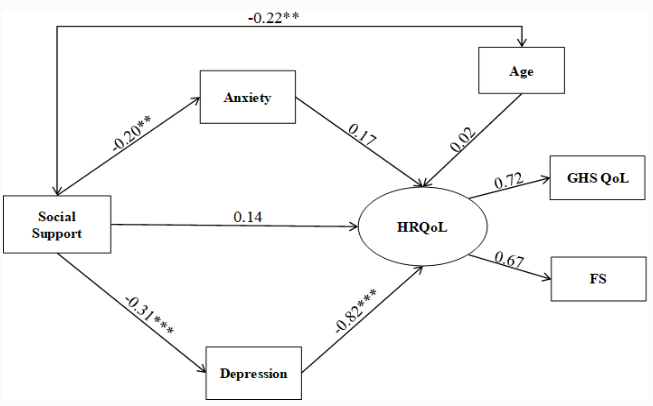

Figure 1: Multiple Mediation Model.

Table 4: Indirect effects on QoL (N=126).

	B	SE	p	z
HRQoL	-	-	-	-
Social Support	0.30	0.07	<0.001	3.71

model estimates indicated that social support has a negative correlation with symptoms of anxiety (β = -0.20, $p < 0.01$) and depression (β = -0.31, $p < 0.001$). However, no significant direct effect of social support on HRQoL (β = .14) was observed, and similarly, anxiety did not significantly demonstrate a direct effect on QoL. In contrast, depressive symptoms demonstrated a negative significant impact on HRQoL (β = -.82, $p<0.001$), suggesting that higher levels of perceived social support are associated with reduced symptoms of anxiety and depression, while the presence of depressive symptoms contributes to a decline in perceived HRQoL. Finally, no significant effects age on HRQol, but there is a significant correlation between the age variable and social support (β = -.22, $p<0.01$). The significant indirect effects are summarized in Table 4. The SEM analysis revealed an indirect effect of social support on HRQoL, mediated by depressive symptoms (β indirect =.30, $p<0.001$), indicating that perceived social support significantly influences QoL exclusively through the mediating role of depression. Fit indices for the proposed model indicated an acceptable fit data, (χ^2=73.651, df = 6, $p <0.000$, TLI = 0.89, CFI = 0.90, and RMSEA = 0.07). In summary, the SEM analysis demonstrated that the dimensions of social support affect QoL through various pathways.

Discussion

The present study suggests the critical role of depressive and anxious symptoms in the lower levels of HRQoL among patients with lymphoma. The findings indicate that depression directly and negatively relates to HRQoL, while social support is a protective factor that is linked to lower levels of psychological distress and indirectly contributes to improved QoL. Importantly, the present findings clarify that perceived social support appears to operate as a distal resource, reaching HRQoL only through its capacity to reduce depressive symptoms. The mediation model suggests that social support is associated with lower depressive symptoms, which in turn supports psychological adaptation and improved HRQoL. These findings are consistent with evidence indicating that a substantial proportion of lymphoma patients experience clinically relevant symptoms of anxiety and depression, which significantly affect quality of life outcomes [9]. Depressive symptoms not only compromise patients' subjective well-being but are also associated with increased morbidity and lower adherence to oncological treatments [12]. The significance of psychological dimension is further supported by qualitative literature on the lived experiences of lymphoma patients. Studies by Chircop et al. [40] and Ruan, et al. [39] reveal that a lymphoma diagnosis is often accompanied by shock, fear, and disorientation, profoundly affecting emotional well-being. Additionally, hematological treatments are a period characterized by intense emotional fluctuations between hope and fear, significantly influencing patients' QoL. These results support a model in which psychosocial resources influence HRQoL through affective processes rather than direct effects, consistent with evidence of mediated pathways between social support, psychological distress, and quality of life in cancer populations [18]. From a clinical perspective, this suggests that interventions aimed solely at increasing social support may be insufficient unless they also effectively target depressive symptoms. Our findings underscore the need for multidisciplinary intervention strategies that integrate psychological support and social care networks to mitigate declines in HRQoL and optimize clinical outcomes. Furthermore, recent evidence highlights the role of additional factors such as sleep quality and lifestyle behaviors in modulating depressive symptoms among hematologic patients, suggesting the need for targeted and integrative interventions aimed at preventing psychological deterioration [38]. Qualitative research also suggests that patients engage in adaptive processes aimed at maintaining a sense of control and continuity in the face of illness, often supported by relational and cognitive resources [39], which may represent complementary targets for psychosocial care without constituting primary mechanisms within the present model. Despite the significance of the findings, several limitations should be acknowledged. The cross-sectional design of the study limits the possibility of establishing causal relationships among variables. Future research should adopt longitudinal designs to explore the temporal dynamics between psychosocial factors and HRQoL across different phases of hematological treatment [38-40]. Additionally, although validated self-report measures were used, they may be subject to response biases, including social desirability and recall bias. Future studies should incorporate multimodal assessments, including clinician-rated measures and biological indicators of psychological distress. Another limitation concerns the sample size and its recruitment from a single clinical setting, which may limit generalizability. Multicentric studies involving larger and more diverse populations are warranted. Finally, HRQoL is a multidimensional construct that cannot be fully understood without considering additional clinical and socio-economic factors.

Conclusion

The present findings indicate that depressive symptoms represent a central factor associated with lower HRQoL in lymphoma patients. Routine psychological screening within hematological care pathways may therefore be warranted. The absence of a direct effect of social support on HRQoL suggests that supportive interventions should be specifically designed to target depressive symptoms and emotional regulation processes.

Anxiety and depression represent related but distinct components of psychological distress, highlighting the importance of differentiated and symptom-specific assessment. The mediation model proposed in this study provides an empirically grounded framework for developing integrated psychosocial interventions, in which social support is conceptualized as a resource acting through affective mechanisms. Finally, embedding psychosocial variables into routine outcome monitoring may facilitate the early identification of patients at risk of HRQoL deterioration and support a more preventive and personalized approach in psychosocial oncology.

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