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The Impact of a Diet Rich in Omega-3 Fatty Acids on the Quality of Life of Patients with Squamous Cell Lung Cancer and Comorbid Depression: A Retrospective Study

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Abstract

Background: Lung cancer is a significant health concern, and is often accompanied by comorbid depression, leading to worsened prognosis and decreased quality of life for patients. This study aimed to investigate the potential influence of a diet rich in Omega-3 fatty acids on the quality of life of patients with squamous cell lung cancer and comorbid depression.

Methods: A retroactive analysis of clinical information from patients with squamous cell lung cancer and comorbid depression admitted to Hongqi Hospital Affiliated to Mudanjiang Medical University from June 2022 to June 2023 was conducted. The patients were classified into two groups on the basis of different dietary care approaches: the Routine Dietary Group and the Omega-3 Fatty Acids Group. Baseline characteristics, pulmonary function tests, dietary intake, depression scoring, and quality of life scores were compared between the two groups.

Results: 103 patients in total were included, with 51 in the Routine Dietary Group and 52 in the Omega-3 Fatty Acids Group. The Omega-3 Fatty Acids Group exhibited

significantly higher ingestion of Omega-3 fatty acids in comparison with the Routine Dietary Group (3.15 \pm 0.64 g/day vs. 2.93 \pm 0.28 g/day, p = 0.022). Despite similar baseline pulmonary function tests, patients in the Omega-3 Fatty Acids Group showed significantly higher scores in physical (70.17 \pm 4.81 vs. 68.18 \pm 5.03, p = 0.043) and emotional (71.29 \pm 4.58 vs. 69.38 \pm 4.25, p = 0.030) functioning, as well as lower scores in insomnia (27.41 \pm 4.51 vs. 29.34 \pm 4.21, p = 0.027) and constipation (7.34 \pm 1.66 vs. 8.43 \pm 3.36, p = 0.040).

Conclusion: The study provided insights into the potential impact of a diet rich in Omega-3 fatty acids on the quality of life of patients with squamous cell lung cancer and complicating depression, suggesting that dietary interventions emphasizing Omega-3 fatty acids may be conducive to improving physical and emotional functioning, as well as symptom management, in this patient population.

Keywords

Omega-3 fatty acids; quality of life; depression; lung cancer

Introduction

Lung cancer is one of the most common and lifethreatening malignancies globally, with a high incidence of comorbid depression [1,2]. Depression is a common psychiatric disorder in cancer patients, affecting approximately

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one in every four individuals diagnosed [3]. The existence of comorbid depression in lung cancer patients has been linked to poorer prognosis, increased symptom burden, and decreased quality of life [4]. Additionally, the physiological and psychological impacts of lung cancer and depression can exacerbate each other, creating a complex interplay that presents significant challenges for both patients and healthcare providers [5].

Amidst this clinical landscape, dietary interventions have emerged as potential adjunctive approaches to mitigate the impact of comorbid depression and lung cancer. Among these interventions, the consumption of Omega-3 fatty acids has garnered significant attention due to its putative benefits on mood regulation, inflammation, and overall health [6,7]. Omega-3 fatty acids, notably eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential polyunsaturated fatty acids that have been linked to several health benefits, including cardiovascular defense, anti-inflammatory activity, and subclinical positive impact on mental health [8,9].

The novel aspect of this study is its focus on the specific impact of a diet rich in Omega-3 fatty acids on the quality of life of patients with squamous cell lung cancer and comorbid depression. The retrospective nature of this study allowed for the evaluation of real-world dietary care approaches and their impact on patient outcomes within a clinical setting, providing valuable insights into the feasibility and potential efficacy of dietary modifications in enhancing the well-being of patients with squamous cell lung cancer and comorbid depression. The utilization of validated measures, including the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30) and the Patient Health Questionnaire-9 (PHQ-9) [10,11], enabled a comprehensive assessment of various dimensions of quality of life and depression severity, enriching the robustness of the study's findings. By investigating the potential impact of dietary interventions emphasizing Omega-3 fatty acids on the physical and emotional functioning, pulmonary health, and symptom management of patients with squamous cell lung cancer and comorbid depression, this study aimed to contribute valuable insights that may inform future research endeavors, clinical recommendations, and holistic care initiatives for this vulnerable patient group.

Materials and Methods

Study Population

The study conducted a retroactive analysis of clinical data from patients with squamous cell lung cancer and comorbid depression admitted to Hongqi Hospital Affiliated to Mudanjiang Medical University from June 2022 to June 2023. The patients were classified into two groups on the basis of different dietary care approaches: the Routine Dietary Group and the Omega-3 Fatty Acids Group.

Inclusion and Exclusion Standard

Inclusion criteria were: patients diagnosed with stage I to III squamous cell carcinoma, with depression during hospitalization, age >18 years, complete clinical data, and normal cognitive function. Exclusion criteria were: patients who had been diagnosed with depression and received related intervention at the time of consultation or before admission; patients with other psychiatric disorders; patients with contraindications to chemotherapy or a history of allergies; patients with serious chronic conditions including heart, liver, and kidney diseases; patients with other previous untreated malignancies or central nervous system diseases such as cerebral infarction or atrophy.

This study was approved by the ethical review board and ethics committee of Hongqi Hospital Affiliated to Mudanjiang Medical University and adhered to the relevant statements of the Declaration of Helsinki. Informed consent was waived by the Institutional Review Board and Ethics Committee of our hospital for this retrospective study due to the exclusive use of de-identified patient data, which posed no potential harm or impact on patient care.

Diagnostic Criteria

Lung cancer tissue samples were obtained and processed for histopathological analysis. Specifically, the tissue specimens were immersed in 10% formaldehyde solution for 3–4 hours, subjected to routine dehydration, transparency, paraffin embedding, and sectioning at a thickness of 2.5 μ m. The sections were deparaffinized at 58 °C and stained with HE-Safranin for pathological examination. Experienced pathologists examined the samples under a microscope to confirm the presence of squamous cell carcinoma. The characteristics observed included differentiated mature squamous carcinoma cells with intercellular bridges and squamous pearls as defining features for stage I. Conversely, stage II exhibited mainly spinous cells with significant pleomorphism, whereas stage III demonstrated poorly differentiated cells with disorderly arrangement, increased cell volume, prominent nuclear atypia, frequent nuclear division, and absence of squamous pearls, often presenting as radial infiltration within the epidermis, with late invasion of the dermis.

The diagnostic criteria [12] for depression include: (1) age \geq 18 years; (2) current depressive episode meets Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) standard with a duration of \geq 12 months; (3) moderate to high depressive symptoms (Inventory of Depressive Symptomatology-Self-Report [IDS-SR] \geq 21); (4) at least one administration of adequate antidepressant medication during the current episode (defined as an appropriate dose of antidepressant medication for \geq 4 weeks or the patient refuses to take the medication as recommended by the psychiatrist).

Grouping Method

In this study, patients were categorized based on different dietary care approaches into the Routine Dietary Group and the Omega-3 Fatty Acids Group. The dietary management involved a structured approach where patients in the Omega-3 Fatty Acids Group accepted fish oil supplements in addition to standard dietary care. The fish oil supplement (Eye-QTM, Novasel, SC10634122230628, Anhui Baishida Biotechnology Co. LTD, China) was a high EPA: DHA formulation (3:1) containing 400 mg of natural fish oil and inserted evening primrose oil (100 mg). Participants took 6 capsules a day (3 in the morning and 3 at night) for the entire 6-month duration.

Pulmonary Function Testing

Pulmonary function of the patients was assessed using the Sensormedics 2200 pulmonary function instrument. Prior to the test, patients abstained from vigorous exercise for two hours, sat quietly for 15 minutes before the examination, and then performed deep breathing and exhalation after achieving respiratory stability. This testing included measuring the patients' forced vital capacity (FVC), forced expiratory flow rates (FEF), and diffusing capacity of the lungs for carbon monoxide (DLCO).

Depression Scores

The symptoms and condition of patients with squamous cell lung cancer and comorbid depression were assessed using the PHQ-9. The PHQ-9 is a self-assessment questionnaire comprising nine questions. Each question covers different symptoms of depression, and patients select the answer that best reflects their own symptoms. Each answer corresponds to a different score, with the aggregate score ranging from 0 to 27 points. The severity of depression was divided into five levels: none (0–4 points), mild (5–9 points), moderate (10–14 points), moderate-severe (15–19 points), and severe (20–27 points). Cronbach's α coefficient for the C-PHQ-9 was 0.860 [13].

Cancer Patient Quality of Life Assessment

Quality of life was assessed using the EORTC QLQ-C30, which comprises five functional dimensions (physical, emotional, role, social, and cognitive functions), three symptom dimensions (retch/puking, fatigue, pain), six single-item measures (appetite loss, dyspnoea, insomnia, constipation, diarrhoea, and financial hardships), and one overall quality of life assessment. Each item in the various dimensions was rated on a 1–7 Likert scale, with a total score ranging from 0 to 100, reflecting a positive correlation with quality of life.

Data Collection

General information on participants (age, gender, body mass index, smoking history, alcohol history, depression score), pulmonary function tests (FVC, forced expiratory flow, lung diffusion capacity for carbon monoxide), dietary intake (Omega-3 fatty acids, vitamins, calcium, magnesium, total calories), quality of life scores, and symptom scores were obtained from the medical records system. All data were collected by the same experienced physician.

Statistical Analysis

The data were analyzed using SPSS 29.0 software (SPSS Inc., Chicago, IL, USA). Categorical variables were represented as [n (%)]. Associations between categorical variables were assessed using the chi-square (χ^2) test, provided that sample size was \geq 40 and expected cell frequency was \geq 5. When the sample volume was \geq 40 but the expected (E) cell frequency was $1 \leq E < 5$, the chi-square statistic was adjusted using the correction formula. In cases where the sample size was <40 or the expected

Characteristic	Routine Dietary Group $(n = 51)$	Omega-3 Fatty Acids Group (n = 52)	t/χ^2	<i>p</i> value
Age (years)	58.43 ± 6.21	59.12 ± 5.89	0.579	0.564
Gender (male/female)	24/27	26/26	0.089	0.765
Body mass index (kg/m ²)	23.68 ± 2.31	23.45 ± 2.14	0.524	0.601
Smoking history	36 (70.59%)	38 (73.08%)	0.079	0.779
Alcohol history	20 (39.22%)	25 (48.08%)	0.822	0.365
Depression severity (PHQ-9 Score)	12.53 ± 3.65	12.76 ± 3.85	0.311	0.756
Family history of cancer	7 (13.73%)	5 (9.62%)	0.423	0.516
Tumor staging			0.341	0.843
Ι	5 (9.80%)	7 (13.46%)		
II	16 (31.37%)	16 (30.77%)		
III	30 (58.82%)	29 (55.77%)		

Table 1. Baseline characteristics of participants.

PHQ-9, Patient Health Questionnaire-9.

cell frequency was <1, statistical analysis was conducted using Fisher's exact probability method. Continuous variables were first tested for normality using the Shapiro–Wilk method. Normally distributed variables were expressed as (Mean \pm sd), and differences between groups were assessed using *t*-tests. Non-normally distributed variables were expressed as [median (25% quantile,75% quantile)] and group differences were assessed using the Wilcoxon rank-sum test. *p* values < 0.05 were considered statistically significant.

Results

No Remarkable Differences in Baseline Characteristics between the Two Groups

103 patients in total were included, 51 in the Routine Dietary Group and 52 in the Omega-3 Fatty Acids Group. No significant differences were detected between the Routine Dietary Group and the Omega-3 Fatty Acids Group with regard to age, gender, body mass index, smoking history, alcohol history, depression severity measured by PHQ-9 score, family history of cancer, or tumor staging, suggesting that the two groups were comparable (Table 1).

No Significant Difference in Baseline Pulmonary Function between the Two Groups

Comparison of baseline pulmonary function measures between the two groups revealed no statistically significant differences (Table 2). Specifically, there were no significant differences observed in the ratio of forced expiratory volume in 1 second to forced vital capacity (Forced Expiratory Volume in the first second (FEV₁)/Forced Vital Capacity (FVC)) (75.22 \pm 5.63 vs. 75.53 \pm 5.31), forced expiratory flow between 25% and 75% of forced vital capacity (FEF25%–75%) (4.26 \pm 0.64 vs. 4.36 \pm 0.53), or diffusing capacity of the lungs for carbon monoxide (DLCO) (70.89 \pm 4.75 vs. 71.52 \pm 4.56) (p > 0.05).

Comparison of Dietary Intake between the Two Groups

The comparison of dietary intake between the two groups revealed significant differences in the intake of Omega-3 fatty acids, with the Omega-3 Fatty Acids Group consuming more than the Routine Dietary Group (3.15 \pm 0.64 g/day vs. 2.93 \pm 0.28 g/day, p = 0.022) (Table 3). However, no significant differences were detected in the intake of vitamin D (470.36 \pm 60.59 IU/day vs. 480.25 \pm 50.26 IU/day), calcium (800.25 \pm 100.28 mg/day vs. 820.79 \pm 110.48 mg/day), magnesium (320.69 \pm 40.36 mg/day vs. 330.26 \pm 35.26 mg/day), or total calories (2000.48 \pm 200.48 kcal/day vs. 2050.49 \pm 180.36 kcal/day) (p > 0.05).

Comparison of Quality of Life between the Two Groups

The comparison of quality of life scores between the Routine Dietary Group and the Omega-3 Fatty Acids Group demonstrated notable differences in several functional scales and symptom scores (Table 4). Among the functional scales, the group consuming a diet rich in Omega-3 fatty acids demonstrated statistically significant improvements in physical function (p = 0.043) and emotional function (p = 0.030). However, there were no significant differences in role function, social function, cognitive function, or global health status/quality of life between the two groups (p > 0.05). Regarding symptom scores, the Omega-3 Fatty Acids Group exhibited significantly lower scores in insomnia (27.41 ± 4.51 vs. 29.34 ± 4.21, p =

Test	Routine Dietary Group (n = 51)	Omega-3 Fatty Acids Group (n = 52)	t	p value
FEV ₁ /FVC	75.22 ± 5.63	75.53 ± 5.31	0.287	0.775
FEF25%-75%	4.26 ± 0.64	4.36 ± 0.53	0.886	0.378
DLCO	70.89 ± 4.75	71.52 ± 4.56	0.680	0.498

Table 2. Comparison of baseline pulmonary function tests between the two groups.

FEV₁, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; FEF25%–75%, forced expiratory flow between 25% and 75% of forced vital capacity; DLCO, diffusing capacity of the lungs for carbon monoxide.

Nutrient	Routine Dietary Group (n = 51)	Omega-3 Fatty Acids Group (n = 52)	t	p value
Omega-3 fatty acids (g/day)	2.93 ± 0.28	3.15 ± 0.64	2.337	0.022
Vitamin D (IU/day)	470.36 ± 60.59	480.25 ± 50.26	0.901	0.370
Calcium (mg/day)	800.25 ± 100.28	820.79 ± 110.48	0.988	0.325
Magnesium (mg/day)	320.69 ± 40.36	330.26 ± 35.26	1.280	0.203
Total calories (kcal/day)	2000.48 ± 200.48	2050.49 ± 180.36	1.330	0.187

Table 3. Comparison of dietary intake between the two groups.

0.027) and constipation (7.34 \pm 1.66 vs. 8.43 \pm 3.36, p = 0.040). No remarkable differences were observed in the other symptom scores (p > 0.05).

Discussion

The complex interplay between depression and cancer presents significant challenges in patient management [14]. The co-occurrence of depression in cancer patients has been linked to poorer treatment effects, elevated levels of distress, and reduced adherence to treatment regimens. Furthermore, the physiological and psychological impacts of lung cancer and depression can exacerbate each other, leading to a further decline in overall well-being [15]. Therefore, the exploration of adjunctive approaches, such as dietary interventions, becomes critical in addressing the multifaceted needs of these patients.

Omega-3 fatty acids have gained attention for their potential benefits in mood regulation, inflammation, and overall health [16]. Despite extensive research on the connection between Omega-3 fatty acids and mental health, their specific impact on patients with squamous cell lung cancer and comorbid depression remains relatively understudied [17]. Our study contributes valuable insights into this unexplored area, shedding light on the potential of dietary strategies to supplement existing therapeutic approaches and improve patient outcomes.

One of the key findings of our study was the significantly higher intake of Omega-3 fatty acids in the dietary care group supplemented with these nutrients compared to the Routine Dietary Group. This finding underscores the feasibility of implementing dietary modifications to enhance the intake of Omega-3 fatty acids in this patient group. Importantly, the observed higher intake did not cause significant differences in the consumption of other essential nutrients or total caloric intake, indicating that dietary modifications can be tailored to meet specific nutritional needs without compromising overall nutritional balance.

The impact of Omega-3 fatty acids on pulmonary function was an area of interest, particularly in the context of lung cancer [18,19]. While our research did not find significant differences in baseline pulmonary function measures between the two dietary care groups, it provides a foundation for further exploration of the potential respiratory benefits of Omega-3 fatty acids in this patient group. Future research could examine the longitudinal effects of Omega-3 fatty acids on pulmonary function and respiratory symptoms in patients with squamous cell lung cancer and comorbid depression.

Quality of life was a critical aspect of patient-centered care, and our study revealed several noteworthy findings in this regard. Patients in the Omega-3 Fatty Acids Group demonstrated significantly higher scores in physical and emotional functioning compared to those in the Routine Dietary Group. These findings suggest that a diet rich in Omega-3 fatty acids may contribute to improved physical and emotional well-being in patients with squamous cell lung cancer and comorbid depression. The observed trend towards higher cognitive function in the Omega-3 Fatty Acids Group also warrants further investigation, as cognitive impairment is a common concern in cancer patients.

A. Functional scales.				
Parameter	Routine Dietary Group (n = 51)	Omega-3 Fatty Acids Group (n = 52)	t	р
Physical function	68.18 ± 5.03	70.17 ± 4.81	2.052	0.043
Role function	67.54 ± 6.34	68.32 ± 5.66	0.657	0.513
Emotional function	69.38 ± 4.25	71.29 ± 4.58	2.202	0.030
Cognitive function	82.22 ± 5.06	83.56 ± 4.83	1.376	0.172
Social function	76.33 ± 4.26	76.82 ± 4.56	0.567	0.572
Global health status/QoL	65.57 ± 6.37	66.33 ± 5.69	0.637	0.526
B. Symptom scores.				
Parameter	Routine Dietary Group (n = 51)	Omega-3 Fatty Acids Group (n = 52)	t/u	р
Fatigue	31.28 ± 5.12	31.58 ± 4.83	0.303	0.763
Retch/Puking	11.51 ± 2.36	12.34 ± 2.65	1.672	0.098
Pain	20.66 ± 2.24	21.04 ± 2.59	0.802	0.425
Dyspnoea	12.55 ± 5.02	13.54 ± 4.86	1.021	0.309
Insomnia	29.34 ± 4.21	27.41 ± 4.51	2.245	0.027
Appetite loss	11.54 ± 2.33	11.37 ± 2.65	0.335	0.738
Constipation	8.43 ± 3.36	7.34 ± 1.66	2.092	0.040
Diarrhoea	6.450 [3.320, 9.920]	6.345 [3.030, 9.415]	1290	0.814
Financial hardships	8.420 [3.190, 13.77]	7.735 [3.173, 12.75]	1280	0.761

Table 4. Comparison of quality of life score between the two groups.

QoL, quality of life.

Symptom management is an integral component of cancer care, and our study highlighted the potential impact of Omega-3 fatty acids on alleviating specific symptoms in patients with squamous cell lung cancer and comorbid depression. Notably, the Omega-3 Fatty Acids Group exhibited significantly lower scores for insomnia and constipation, indicating potential benefits in sleep quality and gastrointestinal function. These findings align with existing research on the anti-inflammatory and neuroprotective features of Omega-3 fatty acids [20,21], suggesting plausible mechanisms for symptom improvement.

The EORTC QLQ-C30 served as a comprehensive tool for assessing various dimensions of life quality in our research [22,23]. The utilization of validated measures such as the EORTC QLQ-C30 underscores the robustness of our findings and facilitates comparison with existing literature. Furthermore, the incorporation of pulmonary function tests and depression scoring using the PHQ-9 questionnaire contributes to a comprehensive evaluation of the multifaceted impact of dietary interventions in this patient population [24,25].

Omega-3 fatty acids, particularly EPA and DHA, are linked to physiological and psychological effects that may positively influence patients' well-being [26]. The impact of a diet abundant in Omega-3 fatty acids on the quality of life of patients with squamous cell lung cancer and comorbid depression may be attributed to several underlying mechanisms. Firstly, Omega-3 fatty acids have welldocumented anti-inflammatory features, which is significant since chronic inflammation is common in cancer and is implicated in depression [27]. By reducing systemic inflammation, Omega-3 fatty acids may alleviate symptoms related to inflammation, such as fatigue and pain, contributing to an improved quality of life for these patients. Secondly, Omega-3 fatty acids have been shown to have neuroprotective features, such as maintaining the structural integrity and function of neuronal membranes, and may modulate neurotransmitter systems. This could potentially mitigate cognitive decline and improve emotional well-being in these patients [28]. Additionally, EPA and DHA, key Omega-3 fatty acids, are involved in mood and emotional health regulation. Supplementation of Omega-3 fatty acids may rebalance neurotransmitter function, exerting positive effects on mood regulation and contributing to improved emotional functioning in patients with squamous cell lung cancer and comorbid depression [29]. Moreover, a diet rich in Omega-3 fatty acids may have underlying effects on symptom management, particularly in alleviating insomnia and constipation, which significantly affect the quality of life of cancer patients [30]. Furthermore, Omega-3 fatty acids are involved in various biological pathways, potentially contributing to their multifaceted impact on physiological and psychological processes, ultimately translating into improvements in quality of life [31]. Thus, a diet rich in Omega-3 fatty acids has the capacity to positively influence the comprehensive well-being and quality of life of patients with squamous cell lung cancer and comorbid depression by addressing these underlying mechanisms.

Despite its contributions, our study had certain limitations that warrant consideration. The retrospective design inherently limits the establishment of causal relationships, and the potential for confounding variables cannot be entirely ruled out. Prospective studies with longer followup periods and more extensive monitoring of dietary intake and patient outcomes would offer a more comprehensive view of the long-term effects of Omega-3 fatty acids in this patient group. Furthermore, the generalizability of our findings to diverse patient demographics and cancer subtypes may benefit from additional research encompassing a broader representation of lung cancer patients with comorbid depression. Additionally, the study was detected at a single center, which may limit the generalizability of the results.

Conclusion

In conclusion, our retrospective study provides valuable insights into the potential impact of a diet rich in Omega-3 fatty acids on the quality of life of patients with squamous cell lung cancer and comorbid depression. The findings suggested that dietary interventions emphasizing Omega-3 fatty acids may improve physical and emotional functioning, as well as symptom management, in this patient population.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

MZ, CL and XZ designed the research study. MZ and CL performed the research. LZ and YL provided help and advice on the experiments. MS analyzed the data. All authors contributed to the drafting or important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the ethical review board and ethics committee of Hongqi Hospital Affiliated to Mudanjiang Medical University (approval No. 2024038) and adhered to the relevant statements of the Declaration of Helsinki. Informed consent was waived by the Institutional Review Board and Ethics Committee of our hospital for this retrospective study due to the exclusive use of de-identified patient data, which posed no potential harm or impact on patient care.

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Conflict of Interest

The authors declare no conflict of interest.

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