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Dyspnea in Cancer Patients Undergoing Chemotherapy and Its Impact on Quality of Life in Northern Greece

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Abstract **Objective:** The purpose of this study was to assess dyspnea in cancer patients undergoing chemotherapy and to determine whether dyspnea affects patients' quality of life. **Method:** This study was descriptive and non-experimental. Two scales were used for the selection of the sample. Subjects were assessed for their dyspnea based on the Memorial Symptom Assessment Scale (MSAS) and for quality of life using the Functional Assessment of Cancer Therapy-General (FACT-G). Data collection was carried out during the third cycle of chemotherapy. **Results:** The mean age of patients was 58.95 ± 9.95 years. The majority of patients were male and married. 30% of patients belonging to the sample examined suffered from dyspnea. A percentage of 33.3% frequently experienced shortness of breath. With respect to severity, 31.7% replied that the symptom was severe; it was quite distressing for 21.7% of the sample and somewhat distressing for 18.5% of all patients. Logistic regression analysis showed that the statistically significant factors influencing dyspnea are age ($p = 0.004$) and gender ($p = 0.030$). **Conclusions:** Dyspnea is a symptom appearing in cancer patients during chemotherapy and it affects patients' quality of life. This finding is very significant for Greek nurses seeking to recognize and assess this symptom in clinical settings. The recognition and evaluation of the symptom by nurses can lead to increased continuity in nursing care and to planned interventions to alleviate it.

Keywords: *dyspnea, cancer, chemotherapy, quality of life, Greece*

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1. Introduction

Cancer is a leading cause of death: in 2012, there were 14.1 million new cases worldwide, 8.2 million cancer deaths and 32.6 million people living with cancer. [1] In Greece, cancer is the second most frequent cause of death after cardiovascular disease [2].

The symptoms experienced by patients varied according to the type of cancer involved. [3] Dyspnea (shortness of breath) is reported as one of the most common symptoms of distress in persons with cancer.[4] It has many definitions, but according to the American Thoracic Society, this is "a subjective experience of breathing discomfort that varies in intensity. The experience derives from interactions among multiple physiological, social, and environmental factors and may induce second physiological and behavioral responses" [5]. The frequency of dyspnea in cancer patients depends on the location and extent of the disease. [6] It is reported that 49% of general cancer patients experienced breathlessness and 20% rated it as moderate to severe [5]. There are many causes of dyspnea in cancer patients and some of them are directly or indirectly caused by cancer or are a result of cancer treatment [7].

Chemotherapy is a systemic therapy and it is reported that it can decrease the incidence of both local and systemic recurrence as well as improve overall survival of patients [8]. Chemotherapy induces many symptoms regarded as side effects thereof [9].

Cancer and its treatment have an impact on the quality of life of patients [10]. The World Health Organization gives a broad definition and defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [11]. It is reported that dyspnea can impact patients' physical, social and psychological well-being [12].

Dyspnea is well-documented symptom in advanced cancer patients and in palliative care settings [13,14]. Many studies have examined dyspnea and other symptoms in advanced cancer patients [13,15,16]. One study has documented that hospitalized advanced cancer patients have dyspnea which is assessed differentially by patients, caregivers and nurses [13]. In another study, it was found that dyspnea was one of the main symptoms of

gynecological cancer patients who were treated in a palliative care unit. The prevalence of the symptoms was 46% in this group of patients [15].

A recent study showed that advanced cancer patients near the end of their lives experienced many physical symptoms, dyspnea being one of the most frequent. The researchers also examined quality of life and found that factors such as "sex, educational level, number of children, disclosure of the disease and hospital size were associated with it" [16].

There are few studies about dyspnea in cancer patients undergoing chemotherapy. It was found that dyspnea is one of the symptoms experienced by elderly cancer patients undergoing chemotherapy and suffering from anemia and neutropenia. Dyspnea and other anemia-related symptoms have a profound effect on quality of life [17]. In one qualitative study, the views of lung cancer patients and informal caregivers were examined with respect to non-pharmacological interventions aiming at the management of the following symptoms: cough, breathlessness and fatigue [18,19]. In this study, it was found that older lung cancer patients receiving chemotherapy experienced high levels of dyspnea and fatigue.

Despite the fact that dyspnea reduces the health-related quality of life [20], only very few studies have been published on dyspnea and its impact on the quality of life of patients undergoing chemotherapy. In one study examining the quality of life in non-small-cell lung cancer patients before and after chemotherapy treatment, an improvement in general quality of life was found with respect to various symptoms such as dyspnea, coughing, hemoptysis, thoracic pain, etc. Hallqvist et al, 2012, investigated non-small- cell lung cancer patients undergoing concurrent radiotherapy and chemotherapy, or cetuximab, showed deterioration in functioning and dyspnea which worsened gradually after the completion of treatment [21].

There are several studies regarding symptoms (dyspnea) and quality of life in connection with chemotherapy drugs [22,23,24].

Although the body of evidence is growing with respect to dyspnea and quality of life - above all in advanced cancer patients - little is known about this issue in Greece. Greek nurses show an increasing interest for symptoms experienced during chemotherapy, but some of the symptoms are often underestimated and thus remain unrecognized in clinical practice. The purpose of this study was to assess dyspnea in cancer patients undergoing chemotherapy and to determine whether dyspnea affects patients' quality of life.

2. Materials and Methods

2.1. Sample and Setting

This study was descriptive and non-experimental, and it was carried out during the third cycle of chemotherapy. It was conducted in a large hospital in a major Greek city. The sample consisted of patients diagnosed with cancer who were receiving chemotherapy on an outpatient basis. A convenience sample of 200 patients undergoing the third cycle of chemotherapy was recruited. The inclusion criteria were: age over 18 years old, receiving third cycle of chemotherapy as outpatients, being willing to participate in the study, being mentally able to complete the questionnaire and capable of reading and speaking English.

2.2. Procedure

Data collection was carried out from December 2012 until December 2013. The hospital's Research Committee gave its approval for the study. All potential participants who met the inclusion criteria were approached by a member of a research team and introduced to the aim of the study. A confidential letter was distributed to these potential participants to inform them about the study and participants' rights. Confidential statements were then collected from the patients who agreed to participate, following which they were given the questionnaire. A total of 220 patients were invited to participate in the study, and 200 agreed to do so (90%).

2.3. Instruments

Subjects were assessed for their dyspnea using the Memorial Symptom Assessment Scale and their quality of life using the FACT-G scale. The Memorial Symptom Assessment Scale (MSAS) is an instrument for the assessment of prevalence, severity, and distress of symptoms related to cancer during the past week. Twenty-four symptoms are evaluated with regard to frequency, intensity and distress, and eight symptoms are evaluated with respect to severity and distress. Each symptom is recorded as present or absent. If the symptom is present, it is rated using a four or five point scale for each of the characteristics mentioned. Higher scores indicate greater frequency, more severity and higher distress. The symptom score is an average score of three dimensions. Each dimension is scored as 0 if a symptom is absent [25,26]. The MSAS consists of four psychological symptoms (feeling sad, worrying, feeling irritable and feeling nervous) and the distress associated with six physical symptoms (lack of appetite, lack of energy, pain, feeling drowsy, constipation and dry mouth). The PHYS-scale consists of 12 symptoms: lack of appetite, lack of energy, pain, feeling drowsy, nausea, vomiting, change in taste, weight loss, feeling bloated and dizziness. The PSYCH –scale is the average of the score for the six symptoms: worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable and difficulty concentrating [25,26,27].

The scale was translated into the Greek language using a back translation technique. The content validity of the questionnaire was determined by a panel consisting of one oncology physician, two oncology nurses and one nursing professional. Before the completion of questionnaire, a pilot study was conducted in a convenience sample of 40 cancer patients. All patients were asked to complete the MSAS scale and were interviewed to determine whether or not they had problems understanding the questions. Cronbach a in the present sample is 0.86, i.e. consistent with other studies [25,27].

Functional Assessment of Cancer Therapy-General (FACT-G) is a 27-item questionnaire for evaluating quality of life. It is divided into four domains: physical well-being (seven items), social/family well-being (seven

items), emotional well-being (six items) and functional well-being (seven items). The items are rated on a 5-point Likert scale ranging from 0 = "not at all" to 5 = "very much". The questionnaire is scored by summing the individual scale scores indicating better quality of life. Permission to use the FACT-G was obtained from FACIT.org in 2012 as a result of personal correspondence. Cronbach a in the present sample is 0.71, i.e. consistent with other studies [28].

2.4. Data Analysis

The data analysis was performed using the statistical software package SPSS 21.0 for Windows. Descriptive statistics were used in order to analyze the demographic data. The variables are not normally distributed, so non-parametric tests were used. In addition a logistic regression analysis was used. All p-values reported are two-tailed, with the statistical significance set at 0.05.

3. Results

The mean age of patients was 58.95 ± 9.95 years. The majority of the patients were men (n = 127, 63.5%) and 79.5% were married. A percentage of 62% (n=124) were retired and seventy-nine patients (39.5%) were primary school graduates. Almost half of the sample (n = 98, 48%) were lung cancer patients. The demographic and clinical characteristics of the patients are presented in Table 1.

Table 1. Patients' Demographic Characteristics

Gender	N	%
Male	127	63.5
Female	73	36.5
Marital status		
Single	14	7
Married	159	79.5
Divorced	10	5
Windowed	17	8.5
Educational status		
Primary School	79	39.5
Middle School	16	8
High School	60	30
Secondary School	5	2.5
Technical Training	8	4
University	24	12
Doctorate	8	4
Type of Cancer		
Lung	96	48
Stomach	5	2.5
Colon	84	42
Pancreas	15	7.5

Table 2. The Prevalence of Symptoms

Symptoms	N	%
Difficulty Concentrating	36	18
Pain	59	29.5
Lack of Energy	92	46
Coughing	64	32
Feeling Nervous	104	52
Dry Mouth	78	39
Nausea	62	31
Feeling Drowsy	52	26
Numbness/Tingling in Hands/Feet	108	54
Difficulty Sleeping	82	41
Feeling Bloated	25	12.5
Problems with urination	39	19.5
Vomiting	44	22
Shortness of breath	60	30
Diarrhea	92	46
Feeling Sad	94	47
Sweats	64	32
Worrying	55	27.5
Problems with Sexual Interest or Activity	17	8.5
Itching	56	26
Lack of Appetite	73	36.5
Dizziness	27	13.5
Difficulty Swallowing	25	12.5
Feeling Irritable	23	11.5
Mouth Sores	37	18.5
Change in the way food tastes	136	68
Weight Loss	104	52
Hair Loss	133	66.5
Constipation	91	45.5
Swelling of Arms or Legs	43	21.5
"I don't look like myself"	23	11.5
Changes in Skin	73	36.6

Table 2 shows the frequencies of symptoms experienced during the past week (frequency, severity, associated distress). The most frequently experienced symptoms are lack of energy (n = 92, 46%), feeling nervous (n = 104, 52%), numbness/tingling in hands/feet (n = 108, 54%), diarrhea (n = 92, 46%) feeling sad (n = 133, 66.5%). The table also shows the frequencies of symptoms experienced during the past week (severity, associated distress). The most frequent symptom is the change in the way food tastes (n = 136.68%), weight loss (n = 104, 52%) and hair loss (n=133, 66.5%).

As can be seen, 30% of the sample suffers from shortness of breath. In Table 3, the characteristics of this symptom are presented. A percentage of 33.3% (n = 20) have frequent difficulty breathing, and 55% (n = 33) rarely experience this symptom. As to severity, 58.3% (n = 35), respond that the symptom is minor while 31.7% (n = 19) report that it is severe. The symptom is considerable for 21.7% (n = 13), is not distressing for 50% (n = 30) of the sample and somewhat noticeable for 18.5% (n = 11) of all patients.

Table 3. The Characteristics of Dyspnea in Cancer Patients

Symptom	Frequency							
	Rarely		Occasionally		Frequently		Almost Constantly	
	N	%	N	%	N	%	N	%
Shortness of Breath	33	55	7	11.7	20	33.3	0	0
	Severity							
	Slight		Moderate		Severe		Very severe	
	N	%	N	%	N	%	N	%
	35	58.3	6	10	19	31.7	0	0
Distress								
Not at all		A little bit		Somewhat		Quite a bit		Very much
N	%	N	%	N	%	N	%	N	%
30	50	5	8.3	11	18.5	13	21.7	1	1.7

Table 4 shows the results of a logistic regression analysis. In order to study the influence of each variable on dyspnea, logistic regression was applied, with the following variables as covariates: age, education, gender, physical well-being, social-family well-being, emotional well-being and general well-being.

Table 4. Logistic regression analysis

							95% C.I. for EXP (B)	
Variables	B	S.E.	Wald	df	sig	Exp (B)	Lower	Upper
Age	-,109	,038	8,257	1	0,004	,898	,832	,966
Gender	-1,116	,513	4,727	1	0,030	,327	,120	,896
Emotional Well-being	,610	,095	41,487	1	0,000	1,840	1,528	2,215
General well-being	,223	,050	19,982	1	0,000	1,249	1,133	1,377
Education			18,572	4	0,001			
Primary school	1,262	,952	1,758	1	,185	3,531	,547	22,797
Middle school	,624	1,362	,210	1	,647	1,866	,129	26,951
High school	-2,063	1,229	2,820	1	,093	,127	,011	1,412
Secondary school	,474	,978	,235	1	,628	1,606	,236	10,932
Constant	-1,590	2,991	,283	1	,595	,204		

As can be seen from the table, the likelihood associated with dyspnea decreases by 10.9% as age increases by one year. For the gender factor, the likelihood for men is -1.116 whereas the likelihood that women will experience dyspnea is 0.327. For the covariates emotional well-being and general well-being, the likelihood of dyspnea increases by 84% and 24.9% respectively as the covariates increase by one unit. With respect of the education factor, we observed that even if each level is not statistically significant, the variable cannot be removed from the model, because if the factor of education is excluded, the Xi^2 value of the model decreases significantly.

The Kolmogorov-Smirnov test rejects the hypothesis of normality for the variables. In order to examine the consequences of dyspnea for the quality of life, the Median and Mann-Whitney U non-parametric tests are performed. These two tests do not reject the hypothesis of equality of medians (p=0.715) and equality of distributions (p=0.069) across the two groups, thus showing that dyspnea did not affect the quality of life.

4. Discussion

This study examines the presence of dyspnea in cancer patients undergoing chemotherapy and its impact on quality of life. It provides important knowledge to Greek nurses assessing dyspnea, allowing them to subsequently intervene appropriately in order to improve patients' quality of life.

The results illustrate that the majority of patients are middle-aged men. Also, the vast majority of patients have lung and colon cancer. This is an expected outcome because the aforementioned types of cancer have a higher incidence in men than in women [28].

In this study, the most frequent symptom experience by patients over the past week was rated with respect to severity, frequency and associated distress. These are: feeling nervous, numbness /tingling in hands/feet, feeling nervous, difficulty sleeping, diarrhea, feeling sad. The symptoms are similar but not exactly the same as those described in other studies [30,31]. This difference is explained by the assertion that the symptoms experienced by patients depending on their type of cancer [3]. Also, it is explained by the fact that studies examined different types of cancer, are based on different sample sizes and, in general, have different research structures and methods. Hence there is a need for further research in order to arrive at a definite conclusion on this particular issue.

In the present study, the prevalence of dyspnea is 30%. This is an expected outcome, because dyspnea affected 10-70% of cancer patients [32] and may be the result of cancer treatment [7].

Members of the sample examined in the present study experience mild levels of dyspnea, as shown by the results. In particular, the characteristics of dyspnea are frequent in 33.5% of patients, severe in 31.7% of participants and induce distress in 21.7%. This is an expected outcome, because dyspnea becomes more frequent in patients as their cancer progresses [6,33], is a subjective experience and is rated by patients to establish a baseline [34]. Let us stress that in our study we did not investigate the stage of cancer in order to precisely determine the severity of dyspnea linked to it. Therefore there is a great need for further research in order to indentify whether Greek cancer patients experience this symptom more frequently in advanced cancer than when the disease is still more limited.

An interesting result of this study is that severity, distress and frequency of dyspnea is influenced by factors such as age and gender. These results are not consistent with other studies which found that dyspnea in advanced cancer patients was associated with fatigue, forced expiratory volume, pain depression [35] and lung involvement, anxiety, fatigue/tiredness and vital capacity [36]. This difference may be attributed to the different study population, the use of different questionnaires and generally to differences in study design. There is a need for further research in Greece, using clinical characteristics for assessing dyspnea and clarifing exactly the factors that contribute to it.

Another interesting result is that dyspnea does not affect significantly the overall quality of life. This is inconsistent with the results of other studies [10,12,17] which highlighted that dyspnea has a profound effect on quality of life. [17] These differences may be related to the size of the sample, to the severity of the disease and to the difficulty of detecting influences on this particular study group. Also, the study sample experienced a mild degree of dyspnea, so that the outcome was according to our expectations. However, the studies are not structured in the same way, and hence the need to investigate the symptoms related to chemotherapy and its influence on patients' quality of life in Greece.

There are some limitations which should be discussed. One of them is the use of a convenience sample, and the fact that the data collection was conducted in one single hospital in a major Greek city. Another significant limitation is the fact that the researchers did not study patients' clinical characteristics (e.g. stage, hematocrit, etc.) and thus it is difficult to correlate dyspnea to them. As a result, there is a need to conduct further research based on larger study populations and using additional

study variables in order to be in a better position to generalize these findings.

5. Conclusions

The results of the present study reveal dyspnea as a symptom occurring in cancer patients during chemotherapy and affecting patients' quality of life. Furthermore, it shows that these factors influence overall quality of life.

The results are very significant for Greek nurses with a view to recognizing and assessing this particular symptom in clinical settings. Recognition and evaluation of this symptom by nurses can lead to increased continuity in nursing care and to planned interventions to alleviate it.

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