Aim of the study: To assess nausea and vomiting in cancer patients during two cycles of chemotherapy, and the impact on their quality of life.
Material and methods: A longitudinal study was conducted in an oncology department of a large general public hospital in Northern Greece. The sample consisted of 200 cancer patients. Data were collected with the MASCC-Antiemesis Tool and FACT-G questionnaire and specific demographic and clinical characteristics.
Results: In cycle 2, acute vomiting was experienced by 16% of the patients and delayed vomiting by 14%; acute nausea was experienced by 27.5% and delayed nausea by 38%. In cycle 3, acute and delayed vomiting were experienced by 17.5% and 15% of the patients, respectively, acute nausea by 29.5%, and delayed nausea by 36.5%. The comparison of severity in acute vomiting between cycle 2 and cycle 3 yielded a statistically significant ($p = 0.003$) difference; similar results were obtained in the comparison of severity of acute nausea ($p < 0.001$). The correlation of severity of acute nausea with physical, emotional, and functional well-being as well as the total score of quality of life in two measurement points was statistically significant ($p < 0.005$). Multiple forward linear regression analysis showed that the total score of quality of life was significantly associated with age, gender, educational status, occupational status, type of cancer, family status, and diet.
Conclusions: Our study confirms that nausea and vomiting are significant clinical problems that influence quality of life. Further research is needed to evaluate the predictors of acute and delayed nausea and vomiting during chemotherapy.

Key words: nausea, vomiting, chemotherapy, quality of life, Northern Greece.

The incidence of nausea and vomiting in cancer patients in Greek clinical practice: A longitudinal study

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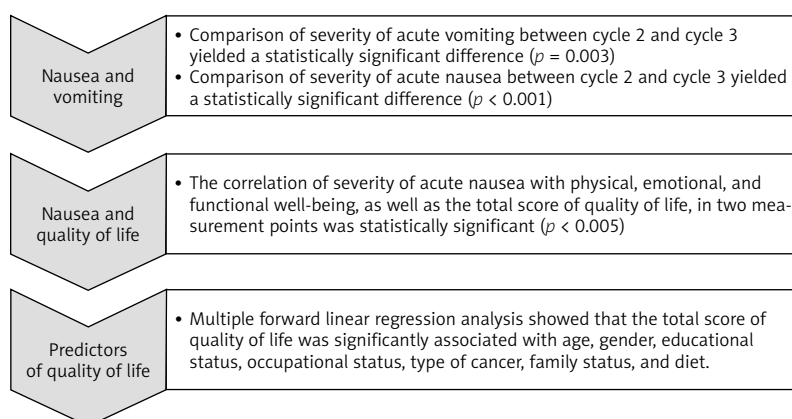[2]Nursing Department, University of West Attica, Athens, Greece
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Nausea and vomiting	• Comparison of severity of acute vomiting between cycle 2 and cycle 3 yielded a statistically significant difference ($p = 0.003$) • Comparison of severity of acute nausea between cycle 2 and cycle 3 yielded a statistically significant difference ($p < 0.001$)
Nausea and quality of life	• The correlation of severity of acute nausea with physical, emotional, and functional well-being, as well as the total score of quality of life, in two measurement points was statistically significant ($p < 0.005$)
Predictors of quality of life	• Multiple forward linear regression analysis showed that the total score of quality of life was significantly associated with age, gender, educational status, occupational status, type of cancer, family status, and diet.

Introduction

Chemotherapy-induced nausea and vomiting (CINV) is a significant problem in cancer patients [1–3]. It is estimated that approximately 45–65% of patients experience nausea and 15–25% vomiting [3]. Although the use of effective antiemetic treatment and antiemetic prophylaxis in recent years have alleviated the symptoms in a daily clinical setting [3], CINV still affects patients' daily functioning and their quality of life [1–3].

Previous studies have assessed the incidence of acute and delayed CINV and how it changes during chemotherapy [4, 5] or on pretreatment, treatment, and post-treatment measurement points in patients subjected to concurrent antineoplastic therapy [6]. Two studies found that acute and delayed vomiting was experienced by a significant percentage of cancer patients, which increased during chemotherapy cycles [4, 5]. It has been reported that nausea is affected by age, gender, and emetogenicity chemotherapy [5]. In other recent studies, nausea and vomiting were examined as one of the symptoms of symptom clusters. It was found that nausea is more severe when combined with other symptoms [6, 7] and impairs quality of life [6]. Another study conducted in oesophageal cancer patients found that delayed nausea occurs more frequently than acute nausea and vomiting [8],

and a more recent study has shown that a higher percentage of patients who received highly and moderate emetogenic therapy experienced delayed nausea and vomiting than acute [9].

Several studies have examined the impact of nausea and vomiting on quality of life during chemotherapy [1, 2, 10, 11]. They found that nausea and vomiting affected patients' quality of life [1, 2, 12] and daily activities [10]. These studies performed data collection during chemotherapy [1]; a day before chemotherapy and for the next five days [2]; before and on day 5 of chemotherapy [11]; or within the first 24 hours and on third to fifth days of chemotherapy [12]. Moreover, different questionnaires were used, such as the MASCC Antiemesis Tool [1], a daily diary for recording nausea and vomiting [2, 11], and the Morrow Assessment of Nausea and Emesis (MANE) [12]. For assessing quality of life Functional Living Index-Emesis [2, 10], EORTC QLQ-C30, SF-36 [11] and FACT-G [1] were used. More recent studies have examined the efficacy of newer antiemetics in controlling chemotherapy-induced nausea and vomiting and their impact on quality of life [13, 14].

Undoubtedly, there is growing interest in nausea and vomiting and their impact on quality of life. In Greece, to the best of our knowledge, no research in this field has been conducted. The purpose of the present study was to perform the longitudinal assessment of nausea and vomiting in cancer patients undergoing chemotherapy and their impact on quality of life. Specifically, we aimed to assess the following research questions:

- Is there a difference in frequencies of nausea and vomiting between cycle 2 and cycle 3 of chemotherapy?
- Is there an impact of CINV on quality of life?
- What are the demographic and clinical characteristics that affect quality of life during chemotherapy?

Material and methods

Study design and sample

This longitudinal study was conducted in the oncology department of a large general public hospital in Northern Greece between March 2016 and March 2017. The sample was convenience and consisted of 200 cancer patients. The inclusion criteria were age over 18 years, histologically documented diagnosis of cancer, willingness to participate in the study, mental ability to complete the questionnaire, and ability to speak and write in the Greek language. Patients who were undergoing concomitant chemotherapy and radiotherapy or experienced nausea or vomiting because of reasons other than chemotherapy (e.g. pregnancy, other medications) were excluded from the study. Out of 206 patients, 200 agreed to participate in the study (response rate: 97.08).

Data were collected at two points in time during chemotherapy: during the second and third chemotherapy cycle. All eligible participants provided written, informed consent before completing a structured questionnaire. Patients and treatment characteristics were collected from patients' records. Chemotherapy programs divided into subtypes according to MASCC and ESMO guidelines [15].

The study was approved by the hospital's Research Committee.

Instruments

Quality of life was measured with the Functional Assessment of Cancer Therapy – General (FACT-G). It consists of 27 items that measure the four dimensions of quality of life: physical well-being, social/family well-being, emotional well-being, and functional well-being. Each question of the scale uses a five-point scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much). The scores of all items in the subscales were added, and the possible scores ranged from 0–108, with higher scores indicating better quality of life. The FACT-G was translated into the Greek language by the FACIT Translation Project. The reliability of the questionnaire has been established in patients with cancer in previous studies [16]. In the present study, the Cronbach's alpha ranged from 0.70 to 0.85. Nausea and vomiting presence and severity were measured with the MASCC Antiemesis Tool (MAT). This eight-item scale assesses the presence (yes/no) and severity (frequency; 0–10) of acute and delayed nausea as well as that of vomiting. The severity of nausea was calculated based on the MAT visual analogue scale score of 6–10 in the respective items. The scores of the items were not added. The scale reliability has been validated in patients with cancer by previous studies [8]. Demographic characteristics and clinical variables were obtained from patients' medical records.

Data analysis

The statistical software SPSS 25 was used to analyse the data. Descriptive statistics were used for demographic characteristics. For data that were not normally distributed, nonparametric tests (Mann-Whitney U test, Kruskal-Wallis test, and Spearman correlation coefficient) were used. Correlations were calculated using the Spearman correlation coefficient. To perform multiple forward linear regression analysis, we used Levene's test to achieve homogeneity of variances, Kolmogorov-Smirnov for the normality of variances, and Run's test for the independence of variances. A lack of homoscedasticity or normality of the errors in a linear regression was observed in some cases. In such instances, we used a Box–Cox transformation of the response variable in order to fit a linear regression model [17].

Results

Demographic characteristics of patients are shown in Table 1. The mean age of the participants was 58.95 ±9.95 years (range 38–76 years). Most of the patients were married (n = 159, 79.5%), male (n = 122, 61%), retired (n = 126, 63%), had primary school education (n = 79, 39.5%), and had lung cancer (n = 98, 48%). More than a half of patients received moderately emetogenic chemotherapy (n = 117, 58.5%). The clinical characteristics of patients are shown in Table 2.

In cycle 2, acute vomiting was experienced by 16% (n = 32) of the patients and delayed vomiting by 14% (n = 28).

Table 1. Demographic characteristics of participants

Variables	n	Percentage
Gender		
Male	122	61
Female	78	39
Family status		
Single	14	7
Married	159	79.5
Divorced	10	5
Widowed	17	8.5
Educational status		
Primary school	79	40.5
Middle school	16	8.2
High school	60	30.8
Technological education	8	4.1
University	24	12.3
PhD	8	4.1
Occupational status		
Unemployed	18	9
Private-sector employees	18	9
Civil servants	11	5.5
Housekeepers	14	7
Retired	126	63
Other	13	6.5

Table 2. Clinical characteristics of participants

Type of cancer	n	Percentage
Lung	96	48
Stomach	5	2.5
Colon	84	42
Pancreas	15	7.5
Emetogenicity of chemotherapy		
High emetogenic chemotherapy	19	9.5
Moderate emetogenic chemotherapy	117	58.5
Low emetogenic chemotherapy	51	25.5
Minimal emetogenic chemotherapy	13	6.5

Table 3. Means and standards deviations of FACT-G subscales in two measurement points

FACT-G subscales scores	Cycle 2 Mean ±SD	Cycle 3 Mean ±SD	p
Physical wellbeing	22.13 ±4.57	22.04 ±4.96	0.810
Social/family wellbeing	21.87 ±4.03	21.72 ±4.47	0.469
Emotional wellbeing	18.75 ±3.84	18.55 ±3.24	0.568
Functional wellbeing	16.29 ±6.71	15.85 ±7.06	0.352
Total scores	78.97 ±12.71	78.16 ±14.58	< 0.001

Table 4. Comparisons between total score of FACT-G and demographic and clinical characteristics

Variables	Cycle 2	Sig	Cycle 3	Sig
Gender	U = 3244	0.002	U = 3323	0.003
Occupational status	H = 31.136	< 0.001	H = 25.815	< 0.001
Educational status	H = 19.301	0.002	H = 28.822	< 0.001
Diet	H = 19.301	0.002	H = 28.822	< 0.001
Cancer type	H = 17.909	0.001	–	–
Family status	H = 20.677	< 0.001		
Acute nausea	U = 2282	< 0.001	U = 2348.500	< 0.001
Delayed nausea	U = 2163.500	< 0.001	U = 2140	< 0.001

Acute nausea was experienced by 27.5% (n = 55) and delayed nausea by 38% (n = 68). In the second measurement time, at cycle 3, acute and delayed vomiting were slightly increased and were experienced by 17.5% (n = 35) and 15% (n = 30) of the patients, respectively. At cycle 3, acute nausea was experienced by 29.5% (n = 59) and delayed nausea by 36.5% (n = 73); thus, an increasing trend was observed over the cycles.

The difference in severity of acute vomiting between cycle 2 (3.12 ±1.58) and cycle 3 (3.31 ±1.72) was statistically significant (p = 0.003); this was similar for the difference in severity of acute nausea (p < 0.001) (cycle 2 [4.72 ±2.04] and cycle 3 [5.16 ±2.11]). In the comparisons of the subscales of FACT-G and the total score over two cycles, a statistically significant difference was only observed for the total score p < 0.001 (Table 3). Table 4 presents the comparison across demographics, clinical characteristics, variables of antiemesis tool, and the total score of the FACT-G scale. As can be seen in cycle 2, statistically significant differences were found between total score and gender, occupational status, educational status, diet, type of cancer, family status, acute nausea, and delayed nausea. In cycle 3, the variables that had statistically significant differences were gender, occupational status, educational status, diet, acute nausea, and delayed nausea.

Correlations of the variables are shown in Table 5 and Table 6. Age had a negative correlation with all subscales of the FACT-G scale except physical wellbeing in cycle 2 and cycle 3. Severity of acute nausea had a negative correlation with physical wellbeing at the two measurement points. The severity of delayed nausea correlated negatively with physical wellbeing in cycle 2. This means that more severe acute and delayed nausea were associated with worse physical wellbeing. Additionally, in cycle 2, emotional wellbeing correlated positively with the severity of delayed vomiting. The functional wellbeing and total score of FACT-G scale had a positive correlation with the severity (number of times) of acute and delayed vomiting in cycle 2 and 3. Also, this means that more severe delayed vomiting and delayed nausea correlated with increased emotional and functional wellbeing, respectively. Finally, functional wellbeing correlated positively with the severity of acute and delayed nausea and the severity (number of times) of acute and delayed vomiting in the two measurement points, indicating that more

Table 5. Correlations among the FACT-G Scale and demographics and MAT for cycle 2

Variables	Physical wellbeing r	p	Social/family wellbeing r	p	Emotional wellbeing r	p	Functional wellbeing r	p	Total score r	p
Age	−0.273	< 0.001	−0.155	0.030	−0.161	0.023			−0.287	< 0.001
Severity of acute nausea	−0.289	0.003					0.649	< 0.001	0.461	< 0.001
Severity of delayed nausea	−0.361	0.032			0.377	0.48			0.481	0.010
Severity (number of times) of acute vomiting							0.839	< 0.001		
Severity (number of times) of delayed vomiting							0.779	< 0.001		

Table 6. Correlations among the FACT-G Scale and demographics and MAT for cycle 3

Variables	Physical wellbeing r	p	Social/family wellbeing r	p	Emotional wellbeing r	p	Functional wellbeing r	p	Total score r	p
Age	−0.265	< 0.001	−0.166	0.018	−0.386	< 0.001			−0.316	< 0.001
Severity of acute nausea	−0.336	0.004					0.572	< 0.001		
Severity of delayed nausea							0.541	< 0.001		
Severity (number of times) of acute vomiting							0.815	< 0.001	0.621	< 0.001
Severity (number of times) of delayed vomiting							0.794	< 0.001	0.679	< 0.001

Table 7. Predicting factors for quality of life in cycle 2

Model	Unstandardised coefficients		Standardised coefficients			Collinearity statistics	
	B	Std. error	Beta	t	Sig	Tolerance	VIF
(Constant)	107.784	4.682		23.021	0.000		
Age	−0.311	0.076	−0.240	−4.066	0.000	0.927	1.078
Gender	−8.497	1.615	−0.324	−5.263	0.000	0.852	1.174
Occupational status	−9.096	2.546	−0.208	−3.573	0.000	0.958	1.044
Educational status	10.927	3.935	0.171	2.777	0.006	0.854	1.172
Diet	−10.694	1.563	−0.406	−6.841	0.000	0.919	1.088

Table 8. Predicting factors for quality of life in cycle 3

Model	Unstandardised coefficients		Standardised coefficients			Collinearity statistics	
	B	Std. error	Beta	t	Sig	Tolerance	VIF
(Constant)	105.880	6.391		16.568	0.000		
Age	−0.494	0.090	−0.332	−5.468	0.000	0.835	1.198
Gender	−9.429	2.008	−0.313	−4.696	0.000	0.693	1.443
Diet	−8.228	2.272	−0.271	−3.622	0.000	0.548	1.826
Family status	−9.708	4.275	−0.140	−2.271	0.024	0.813	1.229
Lung cancer	9.922	3.011	0.339	3.296	0.001	0.290	3.448
Colon cancer	14.775	3.034	0.502	4.869	0.000	0.290	3.450
Occupational status	−9.875	3.147	−0.196	−3.137	0.002	0.788	1.268
Educational status	14.785	4.889	0.201	3.024	0.003	0.696	1.437

severe were the symptoms the functional wellbeing was increased.

Multiple forward linear regression analysis was conducted to identify the predictors of total score of FACT-G in cycle 2 and 3 (Table 7 and Table 8). In cycle 2, the results

indicated that the total score of quality of life was significantly associated with age, gender, educational status, occupational status, and diet. Furthermore, in cycle 3, the quality of life was associated with all the aforementioned variables and with the type of cancer (lung or colon cancer), family status, and the kind of diet.

Discussion

This study investigated the incidence of nausea and vomiting in Greek cancer patients undergoing chemotherapy, and its impact on their quality of life. It contributes to the growing body of evidence regarding these symptoms and provides important information for Greek oncology nurses.

In this study, we found a moderate incidence of acute and delayed vomiting in cycles 2 and 3 of chemotherapy. This is consistent with the results of other studies [1, 4]. This is an expected outcome that reflects the fact that vomiting has been well controlled in recent years [1]. The occurrence of acute and delayed nausea amounted to about 27.5–38% over the two cycles of chemotherapy. This is in line with the results reported by existing literature [1, 2, 4]. Also, this finding forced us to hypothesise that although healthcare professionals tend to pay more attention to vomiting than nausea, the latter is a distressing problem in clinical practice. It is worthwhile to mention that the participants experienced a higher percentage of acute and delayed nausea than acute and delayed vomiting. This finding is consistent with the findings of other studies [1, 7, 18]. The above findings suggest that although nausea is a significant symptom in a clinical setting, its clinical impact may be underestimated if a symptom is seen in isolation rather than as part of a symptom cluster [7]. Moreover, this finding demonstrated that in the present study, nausea is the main symptom faced by patients.

The statistically significant difference in acute nausea and vomiting over the two cycles of chemotherapy has stressed once again the fact that cancer patients experience these symptoms despite receiving antiemetics [18], with most of them receiving moderate emetogenic chemotherapy.

From the comparison analysis between the demographic variables and the total score of quality of life over the two cycles of chemotherapy, it was found that gender, occupational status, educational status, and cancer type influence nausea and vomiting. This result could be explained by the findings of other studies that have shown that quality of life is affected by these factors [19].

Furthermore, the total score of quality of life is affected by the existence of delayed nausea and vomiting in cycle 2 and cycle 3. This finding is in line with those of other studies [1, 2, 10].

Acute and delayed nausea has an impact on quality of life (especially with regard to physical, emotional, and functional wellbeing), and it had a greater impact on it than acute and delayed vomiting in cycle 2. This is in accordance with the results of other studies [2, 3, 12]. This needs to be further ascertained in future research with the use of a larger and more heterogeneous sample.

In cycle 3, acute and delayed nausea as well as acute and delayed vomiting have approximately the same impact on quality of life. This finding might be explained by the assumption that antiemetic therapy produced better results as chemotherapy cycles progressed, patients were compliant to antiemetic prophylaxis, or physicians were more aggressive in prescribing antiemetics [18]. There is a need for further research to clarify this issue. Moreover, we can observe that the overall CINV has a greater impact on quality of life. This is consistent with the findings of other studies, which have shown nausea as one symptom of a symptom cluster that has a greater impact on quality of life than a single symptom in isolation [6, 7].

We also found that the more severe were the symptoms of nausea and vomiting, the better were the emotional and functional wellbeing. This finding is surprising and paradoxical for us. It is inconsistent with the findings of another study [1]. It might be explained by the fact that in the present study a few patients experienced the symptoms. Further study is needed to make clear the effect of these symptoms in emotional and functional wellbeing in cancer patients in Greece.

According to the results of multiple forward linear regression analysis, the factors that influenced the quality of life in cycles 2 and 3 have also been reported by other studies [19], but the result that surprised us is that CINV was not included among the predictor factors, even though the kind of diet was included. There is a great need for further research in order to clarify this issue.

This study has some limitations. It was conducted in one hospital located in a major Greek city, so the results cannot be generalised to the entire Greek population. Another limitation is that although the study is longitudinal, we could not assess the trajectory of the symptoms at the end of chemotherapy. A future study in Greece employing a longitudinal design at every cycle of chemotherapy could provide clearer conclusions. Although we studied how nausea and vomiting changed during chemotherapy, the present study did not investigate some other important clinical characteristics, such as the type of chemotherapy regimen and the effect of antiemetics on symptoms, among others. However, the results provide valuable information for the issue at hand and illustrate the great need for further longitudinal studies in order to draw reliable conclusions. Despite these limitations, our study has one significant strength: To our knowledge, this is the first population-based study to investigate the incidence of nausea and vomiting, the pattern of them, as well as the impact of the symptoms on quality of life in cancer patients in Greece, where the culture and lifestyle are significantly different from those in western populations.

Conclusions

Our study confirms that nausea and vomiting is a significant clinical problem in Greece. These symptoms influence quality of life and its various domains. Careful assessment of the patients and patients' education about compliance with antiemetic therapy are necessary to reduce the incidence of these two symptoms. Further re-

search is needed to evaluate the predictor factors of acute and delayed nausea and vomiting during chemotherapy. The results of the present study should help healthcare professionals arrange appropriate healthcare plans to alleviate these symptoms and improve patients' quality of life.

The authors declare no conflict of interest.

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