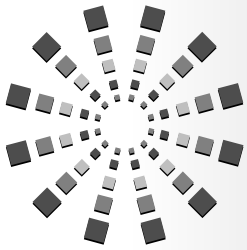

Valentina E. Di Mattei, PhD
Letizia Carnelli, PsyD
Lisa Carrara, PsyD
Martina Bernardi, PsyD
Giulia Crespi, PsyD
Paola M.V. Rancoita, PhD
Alice Bergamini, MD
Micaela Petrone, MD
Chiara Ritella, DNP
Emanuela Rabaiotti, MD
Giorgia Mangili, MD

Chemotherapy-Induced Nausea and Vomiting in Women With Gynecological Cancer

A Preliminary Single-Center Study Investigating Medical and Psychosocial Risk Factors

KEY WORDS
Chemotherapy-induced nausea
Chemotherapy-induced vomiting
Gynecological cancer
Palliative care
Risk factors

Background: Chemotherapy is the treatment of choice for many gynecological tumors, but cytotoxic drugs lead to a wide range of stressful side effects; nausea and vomiting are 2 of the most common and distressing consequences of many chemotherapy regimens. **Objective:** The aim of this study is to investigate various risk factors that could influence the experience of nausea and vomiting after the first chemotherapeutic infusion. **Methods:** Women treated for various gynecological cancers (n = 94) took part in the study. Pharmacological and personal risk factors in the development of chemotherapy-induced nausea and vomiting (CINV) were assessed with the use of the State-Trait Anxiety Inventory and a self-report questionnaire. Regression analyses (both univariate and multiple) were performed to establish risk factors associated with CINV. **Results:** The study highlights the importance of working status (being involved in a working activity during treatment) as a protective factor for developing chemotherapy-induced nausea. Furthermore,

Author Affiliations: Faculty of Psychology, Vita-Salute San Raffaele University (Dr Di Mattei); Clinical and Health Psychology Unit, Department of Clinical Neurosciences, IRCCS San Raffaele Hospital (Drs Carnelli, Carrara, Bernardi, and Crespi); University Centre of Statistics in the Biomedical Sciences (CUSSB), Vita-Salute San Raffaele University (Dr Rancoita); Department of Obstetrics and Gynecology, IRCCS San Raffaele Hospital, Milan, Italy (Drs Bergamini, Petrone, Ritella, Rabaiotti, and Mangili).

The authors have no funding or conflicts of interest to disclose.

Correspondence: Letizia Carnelli, PsyD, Clinical and Health Psychology Unit, Department of Clinical Neurosciences, IRCCS San Raffaele Hospital, Via Olgettina 58, Milan 20132, Italy (carnelli.letizia@hsr.it).

Accepted for publication December 1, 2015.
DOI: 10.1097/NCC.0000000000000342

younger age, levels of state anxiety, chemotherapy-induced nausea in previous treatments, and alcohol intake were found to have an effect on CINV, increasing its risk. Emetogenic potential was associated only with the presence of delayed vomiting. **Conclusions:** Although this is a preliminary study into the risk factors of CINV in gynecological tumors, these findings offer support that personal risk factors contribute to individual differences in the frequency and severity of CINV. **Implications for Practice:** Personal factors should be taken into consideration by the multidisciplinary treating team in gynecology.

Almost 1 250 000 women in Italy have cancer; of these women, 182 830 are affected by a gynecological cancer (ovary, cervix uteri, and corpus uteri).[1] Along with surgery, chemotherapy (with various regimens) is generally used in the treatment of these tumors. The administration of cytotoxic drugs leads to a wide range of side effects that negatively affect patients' quality of life.[2,3] Nausea and vomiting are 2 of the most common and distressing consequences of many chemotherapy regimens.[4] Vomiting (described as the vigorous emptying of gastric contents by the action of abdominal muscles and the opening of the gastric cardia[5]) can be objectively measured. Nausea is a more subjective, disagreeable sensation that may indicate imminent vomiting[6] and requires different measurement tools.[4] Both symptoms are unpleasant and can reduce quality of life.[7] Despite significant improvements in antiemetic control achieved with serotonin ($5\text{-}HT_3$) and neurokinin-1 antagonists, approximately 50% of cancer patients still experience chemotherapy-induced nausea and vomiting (CINV) during treatment.[8–11] Moreover, nausea and vomiting have been repeatedly ranked as 2 of the most debilitating and feared side effects of chemotherapy treatment.[12] Nausea ranks first as the adverse event of chemotherapy that most concerns patients; vomiting ranks as the third most adverse event and the fifth most distressing symptom.[13,14] Inadequate control of CINV is associated with complications such as nutritional depletion, anorexia, metabolite imbalances, and a deterioration of general physical and mental status, which could increase the likelihood of patient dropout from a potentially useful and curative treatment.[15] Chemotherapy-induced nausea and vomiting are characterized as either postchemotherapy nausea, which occurs after a chemotherapy infusion, or anticipatory nausea, which is experienced by approximately 25% of patients in anticipation of receiving chemotherapy.[10] The Multinational Association of Supportive Care in Cancer (MASCC) and the European Society of Medical Oncology widely agree in classifying postchemotherapy nausea into either acute nausea, occurring within 18 to 24 hours after the infusion, or delayed nausea, occurring 24 hours to several days after chemotherapy treatment.[4] Delayed and acute nausea may involve different central nervous system processes,[10] and antiemetic drugs seem to be less effective in controlling delayed rather than acute nausea.[7]

Antineoplastic drugs differ quantitatively and qualitatively in their emetogenic potential; on this basis, the international guidelines classify chemotherapeutic agents into 4 groups: high (>90%), moderate (30%–90%), low (10%–30%) and minimal (<10%) emetogenic potential.[4,16] The type of chemotherapeutic agent used is the main risk factor for CINV.[15,17,18] However, different studies have reported great variation in the frequency and severity of CINV that cannot be explained by the emetogenic potential of antineoplastic drugs alone[19]; indeed, even among patients receiving the same agents at equivalent doses, different levels of CINV have been reported.[20]

Consequently, numerous other risk factors for CINV have been identified.[10,17] The strongest of these are generally assumed to be female gender,[11,17,21,22] younger age,[17,21,23] experience of nausea and emesis during pregnancy,[17,24] susceptibility to motion sickness,[17,25] anxiety,[17,26–29] and patient expectations.[30,31] For patients who have already experienced a chemotherapy treatment, the presence of CINV in the previous cycles represents the strongest predictor of CINV in the current one.[17,32] Having a history of alcohol intake (more than 100 g/d) can be considered a protective factor of CINV as long-term alcohol exposure seems to decrease the sensitivity of the chemoreceptor trigger zone.[21,23,33,34]

The aim of the present prospective study was to evaluate the predictive power of personal risk factors in the development of CINV, using a heterogeneous group of gynecological cancer patients receiving routine chemotherapy. On the basis of this literature, we focused our attention on the following risk factors: type of chemotherapy,[17,18] age (younger patients should experience more CINV[32,35–38]), anxiety,[26–28] CINV in previous chemotherapy treatment,[4,34,39] motion sickness,[7] nausea or vomiting during pregnancy (hyperemesis gravidarum),[4,24] and alcohol intake.[33,34,40] We also investigated the role of working status; we hypothesized that women who were involved in a working activity (both part-time and full-time) during chemotherapy treatments may experience less CINV.

■ Materials and Methods

Sample Selection and Recruitment

Patients treated with chemotherapy for gynecological cancer (ovary, cervix uteri, and corpus uteri) in a hospital in Northern Italy were invited to take part in the research project. Eligible women had to be older than 18 years, Italian-speaking, and with at least an elementary school certificate. Following these criteria, 94 women were invited to take part in the study; none declined participation. Fifty-seven patients were chemotherapy-naïve (had not received chemotherapy treatment previously), whereas the other 37 had been treated with chemotherapy antecedently. Data collection began in September 2014 and concluded in June 2015.

The Medical Ethical Committee approved the study. Written informed consent was obtained from all the participants before data collection.

Participants received different chemotherapeutic regimens, classified according to the MASCC–European Society of Medical Oncology Perugia Consensus Conference into high, moderate, low, and minimal emetogenic potential. All were given ondansetron (a serotonin 5-HT_3 receptor antagonist used to prevent nausea and vomiting during chemotherapy) and corticosteroid therapy at the initial infusion and were counseled about antiemetic therapy for the following days. Participants with high emetogenic potential treatments were also given the antiemetic compound aprepitant.

Measures and Procedure

After patients provided informed consent but before receiving the first chemotherapy treatment, participant demographic and clinical information was collected, including date of birth, working status, date and type of diagnosis, primary or recurrent disease, type of chemotherapy regimen, and the emetogenic potential of the chemotherapy agents used. Participants' risk factors were assessed by both validated instruments and a self-report questionnaire. Personal risk factors in the development of CINV were evaluated before chemotherapy through specific questions about hyperemesis gravidarum, susceptibility to motion sickness, presence of CINV in previous chemotherapy cycles (if patients were not chemotherapy-naïve), and alcohol intake.

Levels of anxiety were assessed prior to chemotherapy using the State-Trait Anxiety Inventory (STAI),[41] a widely used measure of anxiety in clinical contexts, including assessments of cancer patients.[42,43] The STAI consists of 2 subscales of 20 items each: The state subscale measures anxiety related to a specific situation or period (at the moment of questionnaire completion), whereas the trait subscale measures relatively stable anxiety (how one feels on a day-to-day basis). Responses are given on a 4-point Likert scale (from 1 to 4), with total scores range from 20 to 80 for each subscale. Scores are grouped into 3 categories: low anxiety (scores of 20–39), medium anxiety (scores of 40–59), and high anxiety (scores of 60–80). The STAI has good reliability (Cronbach's α of .85–.95) and convergent and discriminant validity.[44] In this study, we used the Italian version of the STAI.[45]

Participants were to complete the MASCC Antiemesis Tool (MAT)[46] at 24 hours and at 4 days after their first infusion and to return it at the time of their next infusion. The MAT is an easy-to-use and easy-to-evaluate tool used to assess if patients receiving chemotherapy are experiencing any CINV. It was developed by members of the MASCC to assist patients and oncology professionals in communicating accurately about the prevention and control of CINV. The questionnaire is divided into 2 sections. The first part assesses the presence (0 = no; 1 = yes), the frequency, and the intensity (range from 0 to 10) of acute nausea and vomiting, respectively, and is to be completed 24 hours after receiving chemotherapy. In the second part of the questionnaire, the same questions are used to evaluate delayed vomiting and nausea, but it refers to a period from 24 hours to 4 days after chemotherapy and should be completed at the very end of this period. The MAT has acceptable internal consistency, with a Cronbach's α of .77.[46]

Statistical Analysis

Logistic regression analyses (both univariate and multiple) were performed to identify possible risk or protective factors predicting the experience of CINV. Separate analyses were performed for delayed and acute nausea and vomiting. The following factors were evaluated: age at diagnosis, previous chemotherapy treatments and the experience of CINV during these treatments, motion sickness, hyperemesis gravidarum, alcohol intake, working status, emetogenic potential of chemotherapy (categorized as high vs low-medium levels), and trait and state STAI scores (not categorized). Possible factors predicting nausea intensity were assessed using a multiple linear regression analysis, considering only those patients who experienced the symptom. In all analyses, P values less than .05 were considered significant. All statistical analyses were performed using SPSS 22.0 software (SPSS Inc, Chicago, Illinois).

■ Results

Sample Characteristics

Complete data were available for 94 patients. Sixty-three participants were being treated for ovarian cancer, and 31 patients, for uterine cancer. The mean (SD) age of the entire cohort was 58.93 (12.65) years (range, 35–84 years). Fifty-seven patients (60.6%) received their first course of chemotherapy treatment; 17 patients, (18.1%) their second; 12 patients (12.8%), their third; and 8 patients (8.5%), their fourth or more courses.

Chemotherapeutic regimens classified according to emetogenic potential MASCC score were as follows: 12 patients (12.8%) were treated with low emetogenic potential regimens; 69 (73.4%), with moderate emetogenic potential drugs; and 13 (13.8%), with high emetogenic potential drugs. No patients were treated with a minimal emetogenic potential chemotherapeutic regimen.

Thirty-six patients (38.3%) experienced acute nausea; the mean intensity was 4.31 (of 10). Delayed nausea was reported by 43 patients (45.7%), with an intensity of 4.6 on average. With regard to chemotherapy-induced vomiting, only 6 patients (6.4%) reported acute vomiting, whereas 16 (17.0%) reported delayed vomiting.

Past motion sickness was reported by 35 patients (37.2%), and hyperemesis gravidarum was recorded in 35 women (42.7%) out of the 82 who had been pregnant. Alcohol intake was registered in 14 patients (14.9%); 24 patients (25.5%) were working during the chemotherapy treatment. In patients who had already received chemotherapy (n = 37; 39.4%), nausea in previous cycles was registered in 23 women (62.2%) and vomiting was reported in 17 (45.9%) (Tables 1 and 2).

The study sample had slightly higher state scale scores (mean [SD], 46.81 [12.33]) compared with the trait scale ones (mean [SD], 37.76 [10.25]). The mean state score falls within the medium anxiety range of the STAI questionnaire (scores of 40–59), whereas the mean trait score is in the low range (scores of 20–39). Sixteen patients (17%) presented high levels of state anxiety (scores $\geq$ 60), and 5 (5.3%) obtained high scores on the trait scale.

Table 1 • Descriptive Statistics of the Numeric Risk Factors and CINV Variables for the Study Population

Variable	Min	Max	Mean	Median	SD
Age	35	84	58.93	59	12.65
Time since diagnosis	1	180	17.71	4	33.75
Acute nausea intensity[a]	0	10	4.31	0	2.57
Delayed nausea intensity[a]	0	10	4.60	0	2.91
Number of times—acute vomiting[b]	0	3	1.5	0	0.42
Number of times—delayed vomiting[b]	0	3	1.2	0	0.50

Abbreviation: CINV, chemotherapy-induced nausea and vomiting.
[a]Only in women who experienced nausea.
[b]Only in women who experienced vomiting.

Regression Analyses

Acute vomiting was excluded from the analyses because it was reported in only 6 of 94 women in our sample (6.38%).

ACUTE NAUSEA REGRESSION ANALYSES

The univariate regression analyses (Table 3) conducted on acute nausea (nausea within the first 24 hours) highlighted working status as a predictor of the experience of acute chemotherapy-induced nausea (CIN) ($P = .016$): Women who were able to keep working after diagnosis and during treatment reported less acute nausea ($B = -1.438$) than did those who did not work. The women who did not work during treatment were 4 times at greater risk of developing CIN (odds ratio, 0.238). Age was also significantly associated with acute nausea ($P = .023$), whereby older age was a protective factor for the development of CIN ($B = -0.040$).

Furthermore, women who had already experienced chemotherapy treatment and who had symptoms of nausea in previous chemotherapy cycles reported more acute nausea ($B = 2.094$, $P = .018$); these patients were at 8 times more risk of experiencing acute nausea (odds ratio, 7.800) than women who had not experienced nausea in previous treatments. Having experienced vomiting in previous chemotherapy cycles was also significantly associated to acute nausea in the present treatment regime ($B = 1.455$, $P = .041$); for these patients, the risk of experiencing acute nausea in the present treatment plan was 4 times greater (odds ratio, 4.286).

From the multiple regression analyses (Table 4), we found that only working status ($B = -2.430$, $P = .002$) and older age ($B = -0.073$, $P = .001$) maintained their role as protective factors against acute CIN. In particular, women who were not working during chemotherapy treatment were 11 times at greater risk of presenting acute nausea (odds ratio, 0.088). Moreover, having had nausea in previous treatments (but not vomiting) was associated with more acute nausea in present chemotherapy regimens ($B = 1.385$, $P = .020$). These women were at a 4 times greater risk of developing acute CIN in following treatment cycles (odds ratio, 3.997). Alcohol, which in the univariate analysis did not reveal any association to acute nausea, emerged as a risk factor for CIN in the multiple analyses ($B = 1.384$, $P = .047$). Thus, women who drank more alcohol had a 3-old risk of developing acute nausea (odds ratio, 3.991).

In the multiple regression analysis for nausea intensity, no variable analyzed had a significant effect on the intensity experienced by participants. This could be because of a small number of patients reporting acute nausea (36/94) and/or to the medium-low intensity of nausea detected (mean intensity, 4.31).

DELAYED NAUSEA REGRESSION ANALYSES

Having had nausea in previous chemotherapy treatment cycles was associated with delayed nausea (nausea experienced 3 to 5 days after the treatment infusion) ($B = 1.545$, $P = .036$). These patients were 5 times at greater risk of developing delayed nausea during present chemotherapy treatments (odds ratio, 4.687) (Table 3).

Nausea in previous cycles was confirmed as a risk factor for delayed nausea ($B = 1.260$, $P = .019$) (Table 5). Furthermore, working status was found to be a protective factor for developing delayed nausea ($B = -1.106$, $P = .045$). State anxiety also emerged as a risk factor ($B = 0.049$, $P = .029$). It is interesting to

Table 2 • Descriptive Statistics of the Categorical Risk Factors and CINV Variables for the Study Population

Variable		Frequency	Relative Frequency, %
Status of illness	Primary	64	68.1%
	Relapse	30	31.9%
Emotogenic potential	Low	12	12.8%
	Medium	69	73.4%
	High	13	13.8%
Working status	No	70	74.5%
	Yes	24	25.5%
Alcohol	No	80	85.1%
	Yes	14	14.9%
Pregnancy	No	12	12.8%
	Yes	82	87.2%
Hyperemesis gravidarum[a]	No	47	57.3%
	Yes	35	42.7%
Motion sickness	No	59	62.8%
	Yes	35	37.2%
Previous chemotherapy treatment	No	57	60.6%
	Yes	37	39.4%
Nausea previous treatment[b]	No	14	37.8%
	Yes	23	62.2%
Vomiting previous treatment[b]	No	20	54.1%
	Yes	17	45.9%
Acute vomiting	No	88	93.6%
	Yes	6	6.4%
Acute nausea	No	58	61.7%
	Yes	36	38.3%
Delayed vomiting	No	78	83.0%
	Yes	16	17.0%
Delayed nausea	No	51	54.3%
	Yes	43	45.7%

Abbreviation: CINV, chemotherapy-induced nausea and vomiting.
[a]Only in women who had been pregnant.
[b]Only in women who had previously undergone chemotherapeutic treatment.

Table 3 • Univariate Logistic Analysis of Acute Nausea and Delayed Nausea

	Acute Nausea			Delayed Nausea		
Variable	Coefficient (*B*)	Odds Ratio	*P*	Coefficient (*B*)	Odds Ratio	*P*
Motion sickness	0.687	1.988	.117	0.365	1.440	.395
Alcohol	0.907	2.476	.124	0.890	2.435	.139
Working status	−1.438	0.238	.016[a]	−0.693	0.500	.161
Previous chemotherapy	0.156	1.169	.719	0.373	1.451	.380
Hyperemesis gravidarum[b]	0.490	1.632	.285	0.156	1.169	.727
Nausea previous treatment[c]	2.054	7.800	.018[a]	1.545	4.687	.036[a]
Vomiting previous treatment[c]	1.455	4.286	.041[a]	1.012	2.750	.138
Age	−0.040	0.961	.023[a]	−0.029	0.971	.082
Time since diagnosis	0.002	1.002	.802	0.001	1.001	.889
State Anxiety (STAI)	0.013	1.013	.459	0.034	1.035	.052
Trait Anxiety (STAI)	0.014	1.014	.496	0.029	1.029	.163
Emetogenic potential (high vs medium and low)	0.008	1.008	.990	0.377	1.458	.529

Abbreviation: STAI, State-Trait Anxiety Inventory.
[a]$P < .05$.
[b]Only in women who had been pregnant.
[c]Only in women who had previously undergone chemotherapeutic treatment.

note that only the multiple regressions highlighted state anxiety's association with CIN; in the univariate analyses, the value was slightly above the statistical level of significance ($P = .052$), but only in the presence of other variables (working status and nausea in previous treatments) did it become significant in predicting delayed nausea. No variable analyzed had an effect on delayed nausea intensity (mean intensity, 4.6).

DELAYED VOMITING REGRESSION ANALYSES

From the univariate and multiple analyses, emetogenic potential was the only risk factor that emerged ($B = 1.381$, $P = .035$). Women who received high emetogenic potential chemotherapy regimens were at 4 times (odds ratio, 3.977) more risk of experiencing delayed vomiting after a treatment infusion. Delayed vomiting analyses were limited by the small number of women who experienced vomiting on the third to fifth day after a treatment infusion (17.02%) in our sample. Results are summarized in Tables 6 and 7.

■ Discussion

Chemotherapy is the treatment of choice for thousands of patients with gynecological cancer. The administration of cytotoxic drugs leads to a wide range of side effects that can vary widely among patients receiving identical chemotherapeutic therapies.[19,20] The lack of an adequate pharmacological explanation for this variation suggests that personal and psychological factors may contribute to observed differences.

In this preliminary single-center study, we focused our attention on the predictive power of personal risk factors in the development of CINV, which is experienced by approximately 50% of cancer patients[8–11] during treatment (despite the introduction of new antiemetic drugs). All patients involved in our study did in fact share one of the strongest risk factors for CINV, that is, female gender.[11,17,21,22]

According to the literature, emesis is a common side effect of chemotherapy, and we found this also within our sample, where CIN represented a more relevant problem than vomiting. In our analysis of CINV risk factors, we considered nausea and vomiting separately to better characterize the risk of emesis. Furthermore, we differentiated between acute and delayed nausea and vomiting, as we found that in the literature, they could differ in their predictors.[22] Delayed nausea, in particular, was reported by 45.7% of women (vs 38.3% who experienced acute nausea), confirming the fact that antiemetic drugs seem to

Table 4 • Multiple Logistic Analysis: Acute Nausea

	Acute Nausea		
Variable	Coefficient (*B*)	Odds Ratio	*P*
Age	−0.073	0.930	.001[a]
Alcohol	1.384	3.991	.047[a]
Working status	−2.430	0.088	.002[a]
Nausea previous treatment (if the woman had previously undergone chemotherapeutic treatment)	1.385	3.997	.020[a]

[a]$P < .05$.

Table 5 • Multiple Logistic Analysis: Delayed Nausea

	Delayed Nausea		
Variable	Coefficient (*B*)	Odds Ratio	*P*
Working status	−1.106	0.331	.045[a]
State Anxiety (STAI)	0.042	1.043	.029[a]
Nausea previous treatment (if the woman had previously undergone chemotherapeutic treatment)	1.260	3.525	.019[a]

Abbreviation: STAI, State-Trait Anxiety Inventory.
[a]$P < .05$.

Table 6 • Univariate Logistic Analysis: Delayed Vomiting

	Delayed Vomiting		
Variable	Coefficient (*B*)	Odds Ratio	*P*
Motion sickness	0.944	2.571	.091
Alcohol	0.340	1.406	.636
Working status	−0034	0.967	.957
Previous chemotherapy	0.525	1.690	.342
Hyperemesis gravidarum[a]	0.198	1.219	.730
Nausea previous treatment[b]	0.018	1.019	.982
Vomiting previous treatment[b]	0.208	1.231	.795
Age	−0.008	0.714	.714
Time since diagnosis	0.003	1.003	.668
State anxiety (STAI)	0.032	1.033	.151
Trait anxiety (STAI)	0.035	1.036	.169
Emetogenic potential (high vs low and medium)	1.381	3.977	.035[c]

Abbreviation: STAI, State-Trait Anxiety Inventory.
[a]Only in women who had been pregnant.
[b]Only in women who had previously undergone chemotherapeutic treatment.
[c]$P < .05$.

be less effective in controlling delayed compared with acute-onset CINV.[47]

The literature describes CINV as one of the most debilitating side effects of chemotherapy treatment,[12] and despite its pervasiveness, the nausea intensity in our sample was not as severe as expected. For both acute and delayed nausea, mean values of intensity were around 4 (4.31 and 4.6, respectively) in a range from 0 to 10. The relatively low intensity of this symptom could be one of the reasons why patients in our sample generally do not report CINV as a relevant consequence of chemotherapy when they are asked about it by medical staff during routine appointments, preceding any treatment infusion.

With respect to our first hypothesis regarding the emetogenic potential of the chemotherapy treatment, this variable emerged as a risk factor only for delayed vomiting: The higher the emetogenic potential of the chemotherapy treatment is, the higher the probability of reporting delayed vomiting. This result is confirmed by the literature: Antiemetic drugs are less effective in controlling delayed symptoms, particularly those associated with the administration of cisplatin and ciclophosphamide (high emetogenic potential).[47,48] Moreover, vomiting is a more objective symptom, compared with nausea, which can be described as a subjective sensation: that is why it could be affected by treatment-related risk factors (ie, emetogenic potential of antineoplastic drugs) more than by patients' personal characteristics.[15]

Our study confirmed the role of younger age as a risk factor for the development of CIN, but not for vomiting: Patients who experienced acute nausea were significantly younger than those who did not. The regression analysis highlighted age as an independent predictor of CIN, confirming what Roila and colleagues[4] reported in their study. These data reflect previous studies[35–38] that found that younger patients are more demanding during chemotherapy and report greater difficulty in adjusting to treatments than older patients.

In line with previous research,[26–28] higher levels of state anxiety may indicate a higher probability of delayed nausea reported, which points to the role of anxiety as a predictor of emesis in patients receiving chemotherapy. Specifically, state anxiety seems to affect CIN, which occurs 3 to 5 days after the treatment infusion. This finding is in accordance with previous studies; for example, Molassiotis and colleagues[29] also found that women with higher state anxiety scale scores experienced a higher incidence of CINV in the delayed phase after chemotherapy treatment. This may be because of the fact that delayed side effects are less controlled by antiemetics and they appear when patients are at home, away from the supportive hospital environment; far from the protective hospital surroundings, patient anxiety may reinforce its role and emerge as an independent risk factor in delayed CIN.[32] Thus, the psychological state of the patient can influence how the side effects of treatment are experienced.

We noted that 17% of our sample reported high state anxiety; this could indicate that some patients were particularly anxious about a situation that they perceived as dangerous at the time of questionnaire completion in hospital. This is probably because of the fear of beginning a new chemotherapy treatment and of its possible side effects.[49]

Within the sample of women who had previously undergone chemotherapeutic treatment, more than half (62.2%) experienced nausea in previous cycles and 45% had experienced vomiting. In our analyses, having had nausea previously emerged as a risk factor for both acute and delayed nausea (in present treatment), increasing the risk of CIN by 4 times. This is in line with previous research, which suggests that patients who had poorly controlled emesis in previous cycles of treatment could be subject to inadequate antiemetic results in later treatments.[29,30] This may occur as a result of the diminishing efficacy of antiemetics as the cycles of chemotherapy progress[32] or this may also be connected to anticipatory emesis. Anticipatory emesis (nausea before the start of an infusion) is a serious effect of chemotherapy that can lead cancer patients to suspend treatment.[50] The most widely held explanation for experiencing nausea before treatment is Pavlovian conditioning: The administration of chemotherapeutic drugs can act as an unconditioned stimulus with consequent CINV (unconditioned response). Through association with the clinical environment during the infusion session (conditioned stimulus), these effects are consequently elicited as a conditioned response (anticipatory emesis) in future infusions.[50] However, alternative explanations have been posited.[50] The risk of anticipatory nausea tends to increase with the number of treatment infusions received and symptoms may endure for a while after the completion of chemotherapy.[4]

Table 7 • Multiple Logistic Analysis: Delayed Vomiting

	Delayed Vomiting		
Variable	Coefficient (*B*)	Odds Ratio	*P*
Emetogenic potential: high vs low and medium	1.381	3.977	.035[a]

[a]$P < .05$.

With respect to alcohol intake, contrary to our hypothesis, we found that women who stated that they consumed alcohol frequently were more at risk of developing acute nausea (only in the multiple regression analysis). The reason for this discrepancy could be that the women in our study were frequent drinkers, but not chronic, heavy drinkers. Previous research highlights that patients with a history of chronic heavy alcohol intake experienced less CINV than did those who were not heavy drinkers.[33,40] However, these studies present some limitations: They had a selection bias related to gender and age of heavy drinkers (older men with head and neck cancer).[40]

A variable that has not, to our knowledge, been discussed in the literature previously is working status. We found that women who worked before their diagnosis and then continued to work during treatment (part-time or full-time) had a different experience of side effects during chemotherapy treatment. Specifically, they had 11 times less risk of experiencing acute nausea (odds ratio, 0.088) and 3 times less risk of developing delayed nausea (odds ratio, 0.331) after chemotherapy treatment. We hypothesize that women with a job have a different disease outlook and that working is a different way of coping with cancer. For a patient, working signifies continuing on with daily, routine activities, which may remind the cancer sufferer of the healthier aspects of one's life and allow him/her to imagine the more salubrious representations of one's self. Conceivably, working may help a cancer sufferer feel less like a patient and more like "everyone else." They are probably busier, more engrossed in their daily assignments, and therefore more distracted when it comes to experiencing treatment side effects (especially as nausea seems to be a more subjective sensation of unease). More studies are needed to support this finding. In the future, we hope to study this variable in more detail and try to understand why women who work during chemotherapy treatment experience less nausea (acute and delayed).

■ Limitations

The limitations of this study must also be addressed: this is a preliminary single-center study conducted on a relatively small sample size; this could have affected the significance and generalizability of the results. Although our study focused on a relatively homogenous group of patients who all had gynecological cancer, future research could also focus on investigating different gynecological diagnoses and different treatment protocols separately. Notwithstanding these limitations, our assessment was performed during the peak period of CINV, avoiding any retrospective inaccuracies.

■ Conclusion

Chemotherapy-induced nausea and vomiting represent a significant problem for patients with cancer. Our findings support the view that, along with emetogenic potential, nonpharmacological factors contribute to individual differences in gastrointestinal responses to chemotherapy, especially age, working status, anxiety levels, alcohol intake, and CINV in previous infusions. The clinical implications of this research are that all these factors should be kept in mind by the treating team to minimize the side effects brought on by chemotherapy treatments. Considering that anxiety and working status may be of a more psychological nature, the presence of a psychologist on the gynecology ward may help patients adapt better to treatment and therefore experience less nausea and vomiting.

ACKNOWLEDGMENTS

We thank all the doctors and the nurses of the department of Obstetrics and Gynecology, IRCCS San Raffaele Hospital, for their contribution in subject recruitment and all patients who took part in the study for their collaboration.

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