Prevalence, Severity, and Self-Reported Characteristics of Taste Alterations in Patients Receiving Chemotherapy

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OBJECTIVES: To describe the prevalence, severity, and self-reported characteristics of taste alterations (TAs) induced by chemotherapy and to investigate TAs across chemotherapy regimens.

SAMPLE & SETTING: 243 adult patients from five outpatient practices in Northern Italy.

METHODS & VARIABLES: Correlation, univariate, and multivariate linear regression analyses. Variables include TAs, symptoms reported by patients, and the effect of TAs on quality of life.

RESULTS: A majority of the study sample reported TAs. Difficulty in tasting saltiness was most common, followed by difficulty in tasting umami and sweetness. The severity and characteristics of TAs changed across chemotherapy regimens. TAs correlated with quality of life and were significantly associated with patient's age and a 21-day chemotherapy schedule.

IMPLICATIONS FOR NURSING: TAs are a frequent side effect of chemotherapy, with varying characteristics that have a negative effect on quality of life. Healthcare professionals should routinely assess for TAs and provide patients with specific management strategies depending on the nature of TAs.

KEYWORDS taste alterations; antineoplastic agents; dysgeusia; quality of life; taste disorders

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Advances in antineoplastic therapy, particularly in chemotherapy, have improved survival among patients with cancer (Ribrag et al., 2016). However, chemotherapeutic agents can cause a wide range of side effects, including taste alterations (TAs) (Bolukbas & Kutluturkan, 2014; Gift, Jablonski, Stommel, & Given, 2004). Although the prevalence, severity, and clinical course of TAs may depend on disease stage, combinations of chemotherapeutic agents, and dose intensities (Ravasco, 2005), more than 75% of patients receiving chemotherapy report that food tastes like metal, cardboard, or sandpaper; is too salty, sweet, sour, or bitter; or is simply tasteless (Bernhardson, Tishelman, & Rutqvist, 2008; Hutton, Baracos, & Wismer, 2007; Jensen et al., 2008; Rehwaldt et al., 2009). TAs have been a neglected side effect of chemotherapy, and healthcare professionals continue to overlook chemotherapy-related TAs, possibly because they are not considered life-threatening, unlike vomiting and diarrhea (Zabernigg et al., 2010). However, moderate to severe TAs affect more than half of all patients who receive chemotherapy (Brisbois, de Kock, Watanabe, Baracos, & Wismer, 2011; Hutton et al., 2007).

Impaired gustatory function can have a negative effect on clinical outcomes and reduce food enjoyment (Boltong, Keast, & Aranda, 2012), leading to malnutrition and weight loss, which, in turn, may prolong the side effects of treatment or even reduce treatment response (Bressan et al., 2016; Brisbois et al., 2011; Kubrak et al., 2013; Sánchez-Lara et al., 2010). TAs can also affect the social and emotional aspects of quality of life (QOL) by causing a loss of enjoyment of food, which can lead patients to withdraw from social situations and recreational activities that may involve food (Alvarez-Camacho et al., 2016). The

greater intensity or frequency of the TA, the lower the food enjoyment (Goebell et al., 2016) (see Figure 1).

Patients have frequently ranked TAs as one of the most distressing side effects of chemotherapy (Alvarez-Camacho et al., 2016; Bolukbas & Kutluturkan, 2014; Jensen et al., 2008; Molassiotis & Rogers, 2012). In a cross-sectional study by Bolukbas and Kutluturkan (2014), 110 patients with lymphoma who were receiving chemotherapy reported that TAs were the most distressing side effect. In the same study, TAs were the third-most prevalent side effect, and they were among the three most severe symptoms reported. A cross-sectional study by Goebell et al. (2016) compared questionnaires completed by 63 patients receiving first-line systemic treatment for renal carcinoma, with matching questionnaires completed by their physicians. They found that patients reported significantly more frequent and severe TAs than physicians. In addition, patients do not always communicate TAs to their healthcare providers, even when TAs become a source of great distress and affect daily life (Bernhardson, Tishelman, & Rutqvist, 2009). Many possible explanations exist for this underreporting. Patients may not immediately recognize this side effect or it may be difficult for them to describe, suggesting that healthcare providers should elicit this information and assess TAs as part of routine clinical practice.

Most previous research explored TAs in limited cancer populations, such as patients with head and neck cancer who were treated with radiation therapy (Baharvand, ShoalehSaadi, Barakian, & Moghaddam, 2013; McLaughlin, 2013; Riva et al., 2015), and patients with renal cancer (Goebell et al., 2016), lung cancer (Belqaid et al., 2016), or gynecologic cancers (Gamper et al., 2012; Nishijima, Yanase, Tsuneki, Tamura, & Kurabayashi, 2013; Steinbach et al., 2009). In addition, these studies often used psychophysical tests, which evaluate dimensions of taste perception, instead of self-reported TAs, as detection or recognition thresholds (Baharvand et al., 2013; Imai, Soeda, Komine, Otsuka, & Shibata, 2013; Nishijima et al., 2013; Riva et al., 2015). Self-reported TAs are considered the best way to capture dimensions such as flavor, food enjoyment, and distortions of normal perception (Alvarez-Camacho et al., 2016; Bernhardson et al., 2009; Brisbois et al., 2011). However, only a few studies have explored self-reported TAs in a heterogeneous outpatient population receiving chemotherapy (Brisbois et al., 2011; Wickham et al., 1999).

The current study aimed to describe the prevalence, severity, and self-reported characteristics of TAs induced by chemotherapy and to investigate TAs across chemotherapy regimens in an outpatient setting in Italy. The study also aimed to describe the effect of TAs on QOL and to determine factors affecting TAs.

Methods

Design and Sample

This cross-sectional study included consecutive outpatients with cancer who received chemotherapy at five different hospitals in Northern Italy from April to June 2014. To be eligible, patients had to (a) be aged 18 years or older, (b) be attending at least their second chemotherapy session, (c) understand and speak Italian, (d) have an Eastern Cooperative Oncology Group (ECOG) performance status of 2 or lower (0 = no symptoms, 1 = mild symptoms, 2 = bedridden for 50% or less of waking hours), and (e) have no cognitive impairments.

Procedures

A researcher approached eligible patients before their chemotherapy session, and informed them about the study and its aims. The researcher then screened

FIGURE 1. Definition of Terms

Ageusia
Absence of taste perception

Hypergeusia
Increased sensitivity to taste perception

Hypogeusia
Decreased sensitivity to taste perception

Parageusia
Unpleasant perception of taste with an external stimulus

Phantageusia
Unpleasant perception of taste (often described as metallic or salty) without an external stimulus

Taste Alteration
Abnormal or impaired sense of taste, unpleasant alteration of taste sensation, or a distortion or perversion of the sense of taste

Umami
Known also as savory taste, it is one of the five basic tastes (together with sweetness, sourness, bitterness, and saltiness). It has been described as brothy or meaty.

Note. Based on information from Hong et al., 2009; Hovan et al., 2010.

consenting patients for chemotherapy-related TAs using the TA Scale (Gamper et al., 2012; Zabernigg et al., 2010), which consists of two items: "Have you had problems with your sense of taste?" and "Does food or drink taste different from usual?" To be enrolled in the study, patients had to provide at least one affirmative answer, and the problem had to have arisen after the initiation of chemotherapy. The screening test and the following assessments took place during the same outpatient visit for chemotherapy administration. The study was approved by the hospital review board of each participating center, and all participating patients provided written informed consent.

Enrolled participants were asked to self-report the duration of their TAs and to rate the effect of TAs on their QOL in the previous week from 0 (no impact) to 100 (maximum impact) using a numeric rating scale (NRS). They were then asked to self-report their TAs in the previous week using the Italian version of the Chemotherapy-induced TA Scale (CiTAS) (Campagna et al., 2016). The CiTAS contains 18 items that explore four dimensions: decline in basic taste (five items), discomfort (six items), phantageusia and parageusia (four items), and general TAs (three items). Answers are given on a five-point Likert-type scale ranging from 1 (no disorder) to 5 (maximum disorder). Responses to items in each dimension are summed and then divided by the number of items to estimate the mean score. The overall CiTAS score was obtained by summing the mean scores of all four dimensions and ranged from 4 (no TAs) to 20 (maximum severity of TAs). CiTAS has demonstrated good validity (Cronbach $\alpha = 0.82$) and moderate test-retest reliability ($r = 0.41$, $p < 0.003$) (Campagna et al., 2016).

Sociodemographic and clinical information was collected using clinical records and included gender, age, cancer site, presence and site of metastasis, number of chemotherapy cycles administered at enrollment, chemotherapy schedule, chemotherapy regimen, type of chemotherapy (adjuvant, neoadjuvant, or palliative), and ECOG performance status.

Data Analysis

Analyses were carried out using R, version 3.3. Continuous variables were expressed as averages and 95% confidence intervals or standard deviations, or as median and interquartile ranges. The categorical variables were computed as sums and percentages.

Correlation between overall CiTAS score and QOL was assessed using the Kendall tau coefficient, and breaks rounded to the closer integer were identified to categorize overall CiTAS scores into four classes (less

TABLE 1. Sample Characteristics (N = 243)

Characteristic	$\bar{X}$	SD
Age (years)	60.4	11.7
Characteristic	**n**	**%**
Gender		
Female	150	62
Male	93	38
Cancer site		
Breast	88	36
Colon or rectum	49	20
Lung	36	15
Stomach	10	4
Oral cavity	10	4
Ovary	9	4
Pancreas	8	3
Liver, gallbladder, or bile ducts	7	3
Prostate	7	3
Other	19	8
Site of metastasis[a]		
Lung	73	30
Bone	36	15
Liver	34	14
Peritoneum	20	8
Brain	3	1
Other	21	9
Chemotherapy cycles already administered at enrollment		
1–5	166	68
6–10	62	26
11–15	15	6
Chemotherapy schedule		
Every 7 days	52	21
Every 15 days	63	26
Every 21 days	119	49
Every 30 days	9	4
Chemotherapy regimen		
FOLFOX	42	17
Paclitaxel	40	16
Docetaxel	22	9
Cisplatin plus pemetrexed	15	6
FEC	12	5
EC	11	5
FOLFRI	9	4
Gemcitabine	9	4
TJ	7	3
TPF	6	2

Continued on the next page

TABLE 1. Sample Characteristics (N = 243) *(Continued)*

Characteristic	n	%
Chemotherapy regimen *(continued)*		
GEMCARBO	6	2
CISGEM	6	2
Docetaxel plus EC	5	2
GEMOX	5	2
Other[b]	48	20

[a] Patients could report more than one site of metastasis.
[b] Chemotherapy regimens occurring fewer than five times
CISGEM—cisplatin, gemcitabine; EC—epirubicin, cyclophosphamide; FEC—epirubicin, fluorouracil, cyclophosphamide; FOLFOX—folinic acid, fluorouracil, oxaliplatin; FOLFRI—folinic acid, fluorouracil, irinotecan; GEMCARBO—gemcitabine, carboplatin; GEMOX—gemcitabine, oxaliplatin; TJ—carboplatin, paclitaxel; TPF—docetaxel, cisplatin, fluorouracil
Note. Because of rounding, percentages may not total 100.

than 6 is insignificant, 6–10 is mild, 10–14 is moderate, and 15–20 is severe) using a LOESS smoother. The correlation between the NRS and CiTAS scores was assessed using the Pearson correlation (r). Correlation was considered very weak for $0 < r \leq 0.2$, weak for $0.2 < r \leq 0.4$, moderate for $0.4 < r \leq 0.6$, strong for $0.6 < r \leq 0.8$, and very strong for absolute values > 0.8 (Evans, 1996).

Association between overall CiTAS score and gender, age, cancer site, presence and site of metastasis, number of chemotherapy cycles administered at enrollment, chemotherapy schedule, type of chemotherapy, and ECOG performance status was assessed using univariate linear regression models. A multivariate linear regression analysis, including all variables and then selecting the final model on the basis of AIC (Akaike information criterion) rule, was also performed.

Results

Sample Characteristics

Of the 370 patients who met the inclusion criteria, 243 (66%) gave at least one positive answer to the TA Scale and were enrolled in the study (see Table 1). Participants had received from 1–15 cycles of chemotherapy; 68% (n = 166) were interviewed at the time of their 2–3 cycle, and 25% (n = 62) were interviewed at the time of their 6–10 cycle. Almost half of the participants (n = 119, 49%) were on a 21-day chemotherapy schedule. Sixty-two percent (n = 150) of participants were women, and the mean age was 60.4 years (range = 29–84). The majority of patients had ECOG performance status of 0 (n = 158, 65%) or 1 (n = 78, 32%); only 7 (3%) had an ECOG performance status of 2. Breast cancer was the most common diagnosis (n = 88, 36%), followed by cancer of the colon or rectum (n = 49, 20%). Metastasis of the lung affected 73 participants (30%), followed by bone (n = 36, 15%) and/or liver metastases (n = 34, 14%). Of the 125 participants with metastasis, about 70% (n = 87) received neoadjuvant chemotherapy before undergoing surgery, and 38 (30%) were on adjuvant or palliative chemotherapy. In the entire sample, 29% (n = 71) received adjuvant chemotherapy.

Prevalence, Onset, and Severity of Taste Alterations

The proportion of participants reporting TAs ranged from 51%–86% across the five hospitals, with an overall prevalence of 66%. Forty-three percent of participants (n = 105) complained of TAs with the start of chemotherapy, and 75% (n = 182) reported TAs within the fourth week of treatment. The mean overall CiTAS score was 8.5 of 20 (SD = 2.3; min = 4.3, max = 16.9). Only 30 (12%) patients reported insignificant TAs, whereas 156 (64%) reported mild, 51 (21%) reported moderate, and 6 (3%) reported severe TAs.

Self-Reported Characteristics of Taste Alterations

Fifty-five percent of participants (n = 134) reported some difficulties in tasting food. Tasting saltiness was the most affected ability, with 84 participants (35%) reporting that saltiness was somewhat or quite difficult to taste, and 12 (5%) reporting that they were unable to taste saltiness at all. In addition, 35% (n = 83) and 30% (n = 74) of participants reported that umami and sweetness, respectively, were either somewhat or quite difficult to taste or that they were unable to taste them at all (see Table 2). Of the 225 patients (93%) who complained that food did not taste as it should, 66 (29%) rated the experience as very unpleasant. Of the 153 (63%) reporting to have a bad taste in their mouth, 45 (19%) perceived the change as very unpleasant.

Feeling nauseated (n = 153, 63%), having a reduced appetite (n = 148, 61%), and having difficulty eating meat (n = 124, 51%) were the most frequent and distressing problems, rated as quite or very unpleasant by 41 (17%), 54 (22%), and 47 (19%) patients, respectively.

Chemotherapy Regimen and Taste Alterations

Gemcitabine ($\bar{X}$ CiTAS score = 9.7, SD = 1.8), cisplatin plus pemetrexed ($\bar{X}$ = 9.6, SD = 3.8), and epirubicin plus cyclophosphamide (EC) ($\bar{X}$ = 9.6, SD = 2.8) caused the most severe TAs, whereas low levels of TAs were found among participants receiving gemcitabine and

carboplatin (GEMCARBO) ($\bar{X}$ = 7.7, SD = 2.2) and cisplatin and gemcitabine (CISGEM) ($\bar{X}$ = 7.2, SD = 1.7) (see Table 3). General TAs ($\bar{X}$ = 2.4, SD = 0.8) was the dimension most affected, followed by parageusia and phantageusia ($\bar{X}$ = 2.1, SD = 1), decline in basic taste ($\bar{X}$ = 2, SD = 0.8), and discomfort ($\bar{X}$ = 1.9, SD = 0.7). Specifically, the highest scores for general TAs were found for gemcitabine ($\bar{X}$ = 2.9, SD = 0.7) and docetaxel ($\bar{X}$ = 2.8, SD = 0.9), whereas the highest levels of parageusia and phantageusia were associated with EC ($\bar{X}$ = 2.8, SD = 1) and cisplatin plus pemetrexed ($\bar{X}$ = 2.7, SD = 1.3). Docetaxel ($\bar{X}$ = 2.6, SD = 0.9) and cisplatin

TABLE 2. Difficulty in Tasting and Unpleasant Symptoms as Reported by Patients (N = 243)

	Tastes Normal or Slightly Difficult to Taste		Somewhat or Quite Difficult to Taste		Unable to Taste at All	
Change in Sense of Taste[a]	**n**	**%**	**n**	**%**	**n**	**%**
Have difficulty tasting food	109	45	120	49	14	6
Have difficulty tasting saltiness	147	61	84	35	12	5
Have difficulty tasting umami	160	66	74	31	9	4
Have difficulty tasting sweetness	169	70	63	26	11	5
Have difficulty tasting bitterness	178	73	55	23	10	4
Have difficulty tasting sourness	193	79	42	17	8	3
	No Taste Change		**Slightly or Somewhat**		**Quite or Very**	
Unpleasant Taste Change[b]	**n**	**%**	**n**	**%**	**n**	**%**
Food does not taste as it should.	18	7	159	65	66	27
Have a bad taste in the mouth	90	37	108	45	45	19
Have a bitter taste in the mouth	95	39	110	45	38	16
Everything tastes bad.	105	43	113	47	25	10
Everything tastes bitter.	129	53	89	37	25	10
Unable to perceive the smell or flavor	133	55	82	34	28	12
	No Symptoms or Problems		**Slightly or Somewhat**		**Quite or Very**	
Unpleasant Symptom or Problem[b]	**n**	**%**	**n**	**%**	**n**	**%**
Feel nauseated or queasy	90	37	112	46	41	17
Have a reduced appetite	95	39	94	39	54	22
Have difficulty eating meat	119	49	77	32	47	19
Bothered by the smell of food	125	51	84	35	34	14
Have difficulty eating oily food	141	58	77	32	25	10
Have difficulty eating hot food	179	74	53	22	11	5

[a] 1—tastes normal; 2—slightly difficult to taste; 3—somewhat difficult to taste; 4—quite difficult to taste; 5—unable to taste at all. Three groups were created: taste normally or slightly difficult to taste (patients scoring 1 or 2), somewhat or quite difficult to taste (patients scoring score 3 or 4), and unable to taste at all (patients scoring 5).
[b] 1—no; 2—slightly; 3—somewhat; 4—quite; 5—very. Three groups were created: no taste change/no symptoms or problems (patients scoring 1), slightly or somewhat (patients scoring 2 or 3), and quite or very (patients scoring 4 or 5).
Note. Because of rounding, percentages may not total 100.

TABLE 3. Overall CiTAS Score, General TAs, Decline in Basic Taste, Discomfort, and Parageusia and Phantageusia for Each Chemotherapy Regimen (N = 243)

	Overall CiTAS Score		General TAs		Decline in Basic Taste		Discomfort		Parageusia and Phantageusia	
Chemotherapy	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
Gemcitabine	9.67	1.78	2.89	0.71	1.93	0.6	2.33	0.42	2.52	0.8
Cisplatin/pemetrexed	9.64	3.75	2.68	1.25	2.25	1.21	2.02	0.68	2.69	1.31
EC	9.61	2.77	2.66	0.56	2.2	0.95	1.96	0.95	2.79	0.95
Docetaxel	9.12	2.29	2.78	0.86	2.55	0.85	1.83	0.63	1.95	1.06
FEC	8.98	2.42	2.17	0.66	2.1	0.72	2.24	0.91	2.47	1.09
TJ	8.71	1.68	2.25	0.72	1.71	0.56	2.22	0.56	2.52	1.36
FOLFOX	8.4	2.19	2.29	0.68	2.01	0.79	2.09	0.73	2.01	0.87
GEMOX	8.31	1.99	2.45	0.33	1.96	0.5	2.03	0.85	1.87	0.73
Other[a]	8.14	2.05	2.32	0.67	1.87	0.61	1.85	0.64	2.1	1.03
TPF	8.03	0.83	2.5	0.39	2.17	0.69	1.81	0.41	1.56	0.5
FOLFIRI	7.96	2.95	2.39	0.88	1.93	0.94	1.94	0.7	1.7	1.02
Paclitaxel	7.92	2.24	2.24	0.75	2.03	0.87	1.61	0.57	2.03	0.87
Docetaxel/EC	7.86	0.98	1.95	0.57	2.04	0.09	1.6	0.52	2.27	0.37
GEMCARBO	7.72	2.19	2.42	0.88	1.57	0.53	1.9	0.59	1.83	1.01
CISGEM	7.17	1.7	2	0.59	1.5	0.62	2	0.85	1.67	0.47
Overall	8.46	2.32	2.39	0.76	2.03	0.8	1.92	0.69	2.12	0.99

[a] Chemotherapy regimens occurring fewer than five times
CISGEM—cisplatin, gemcitabine; CiTAS—Chemotherapy-induced Taste-Alteration Scale; EC—epirubicin, cyclophosphamide; FEC—epirubicin, fluorouracil, cyclophosphamide; FOLFIRI—folinic acid, fluorouracil, irinotecan; FOLFOX—folinic acid, fluorouracil, oxaliplatin; GEMCARBO—gemcitabine, carboplatin; GEMOX—gemcitabine, oxaliplatin; TAs—taste alterations; TPF—docetaxel, cisplatin, fluorouracil; TJ—carboplatin, paclitaxel
Note. The overall CiTAS score ranged from 4 (no TAs) to 20 (maximum severity of TAs). The score of general TAs, decline in basic taste, discomfort, and parageusia and phantageusia ranged from 1 (no disorder) to 5 (maximum disorder).

plus pemetrexed ($\bar{X}$ = 2.3, SD = 1.2) mainly affected the perception of basic taste, whereas high discomfort was reported by patients treated with gemcitabine ($\bar{X}$ = 2.3, SD = 0.4) and fluorouracil, epirubicin, and cyclophosphamide (FEC) ($\bar{X}$ = 2.2, SD = 0.9).

Taste Alterations and Quality of Life

A weak correlation between overall CiTAS score and QOL ($r = 0.31$, $p < 0.001$) was found. Patients with an overall CiTAS score of less than 6 also had a better QOL (lower scores), whereas those with overall CiTAS scores greater than 10 reported the worst QOL. For patients with CiTAS scores ranging from 6–10, the pattern was mixed and no clear trend was noted, with QOL scores ranging from the minimum (better) to the maximum (worst) of the scale.

Sociodemographic and Clinical Variables

Univariate linear regression indicated that age and chemotherapy schedule had a significant effect on the severity of TAs (see Table 4). In addition, in the adjusted model, both of these factors were confirmed to be predictors of TAs (see Table 5). For each 10-year age increase, the overall CiTAS score decreased significantly by 0.37 points ($p = 0.002$). A 21-day chemotherapy schedule significantly increased the overall CiTAS score by 1.41 points ($p < 0.001$) compared to a 7-day schedule.

Discussion

The literature on TAs in patients with cancer is limited, as is healthcare professionals' awareness of it. The aim of this study was to contribute to the knowledge about this understudied issue and to explore the prevalence, severity, and self-reported characteristics of TAs in patients with cancer receiving chemotherapy.

TAs were frequent in the current study sample, occurring in 66% of patients receiving chemotherapy for a wide set of malignancies, including gynecologic, gastrointestinal, lung, and prostate cancers. This is supported by previous studies, which found a prevalence of TAs at 67%–70% (Bernhardson et al. 2008; Zabernigg et al., 2010). TAs can occur as a severe side effect of chemotherapy; 24% of the participants (n = 57) in the current study rated their TAs as moderate to severe. By measuring the self-reported affect of TAs on QOL to assess severity, the CiTAS captured the amount of distress perceived by patients.

TABLE 4. Univariate Analysis of Risk Factors for Taste Alterations

Variable	Effect	SE	95% CI	p
Age (years)	–0.61	0.21	[–1.03, –0.19]	0.005
Gender				
Male (yes versus no)	–0.39	0.31	[–1, 0.21]	0.2
Presence of metastasis				
Yes versus no	–0.42	0.3	[–1.01, 0.17]	0.16
ECOG performance status				
0	Ref	–	–	–
1	0.31	0.32	[–0.33, 0.94]	0.34
2	–0.77	0.9	[–2.54, 1]	0.39
Cancer site				
Breast	Ref	–	–	–
Colon or rectum	–0.24	0.42	[–1.07, 0.58]	0.56
Lung	0.56	0.46	[–0.35, 1.48]	0.22
Stomach	0.53	0.78	[–1.01, 2.07]	0.5
Oral cavity	–1.11	0.78	[–2.65, 0.43]	0.16
Ovarian	0.16	0.82	[–1.45, 1.78]	0.84
Pancreatic	–0.1	0.86	[–1.8, 1.61]	0.91
Liver, gallbladder, bile duct	0.16	0.92	[–1.65, 1.97]	0.86
Prostate	–0.45	0.92	[–2.26, 1.37]	0.63
Other	–0.16	0.59	[–1.33, 1.01]	0.79
Therapy				
Adjuvant	0.18	0.33	[–0.47, 0.83]	0.58
Chemotherapy schedule				
Every 7 days	Ref	–	–	–
Every 15 days	0.53	0.43	[–0.31, 1.37]	0.21
Every 21 days	1.41	0.38	[0.66, 2.15]	< 0.001
Every 30 days	0.39	0.78	[–1.15, 1.93]	0.62
Chemotherapy cycles already administered at enrollment				
2–5	Ref	–	–	–
6–10	–0.23	0.35	[–0.91, 0.46]	0.55
11–15	–0.62	0.63	[–1.86, 0.61]	0.32

CI—confidence interval; ECOG—Eastern Cooperative Oncology Group; Ref—reference; SE—standard error

The current findings confirmed a significant correlation between overall CiTAS score and QOL. The mechanisms by which TAs affect QOL have been previously investigated. TAs correlate with reduced appetite, fatigue, nausea and vomiting, and loss of the social enjoyment of food (Alvarez-Camacho et al., 2016; Hutton et al., 2007; Kano & Kanda, 2013; Zabernigg et al., 2010). In the current study's sample, feeling nauseated, having a reduced appetite, being bothered by the smell of food, and having difficulties with eating meat were the most distressing problems experienced by participants.

General TAs, as well as parageusia and phantageusia, were the most affected dimensions. Subjective data confirmed major difficulties in tasting saltiness (Bernhardson et al., 2008; Steinbach et al., 2009), whereas the ability to taste sourness was least affected (Wickham et al., 1999). Only a few study participants were unable to perceive one or more taste sensations at all, which correlated with previous findings (Brisbois et al., 2011). Sixty-one percent of the patients (n = 148) complained of a persistent bitter taste in the mouth, which may have contributed to nausea (Peyrot des Gachons, Beauchamp, Stern, Koch, & Breslin, 2011).

Unfortunately, the current study did not provide a comprehensive picture of TAs in patients with cancer who are receiving chemotherapy. The CiTAS does not investigate the metallic taste, which occurs in as many as 78% of patients with cancer who receive chemotherapy (Ijpma, Renken, Ter Horst, & Reyners, 2015); therefore, the relationship between metallic taste and difficulty in eating meat, which half of the current participants reported as an unpleasant problem, could not be tested. The metallic taste, also referred to as phantageusia, causes an aversion to red meat and, therefore, limits its consumption among patients. The taste is likely related to the iron-containing compounds in meat (Boltong & Keast, 2012; Ijpma et al., 2015).

The current study highlighted the risk of TAs related to different chemotherapy regimens and the dimension of taste that each regimen is more likely to affect. Similar to previous research (Rehwaldt et al., 2009; Steinbach et al., 2009), TAs were found to be common in patients receiving cisplatin, cyclophosfamide, and taxane-based chemotherapy. Unexpectedly, the current authors observed the most severe TAs with gemcitabine monotherapy. In addition, gemcitabine scored the worst not only in the overall CiTAS score, but also in the dimension of general TAs and discomfort, and was ranked third for parageusia and phantageusia. Gemcitabine is generally considered to have a favorable toxicity profile (Karampeazis et al., 2016), and previous studies (Bernhardson et al., 2008; Gamper et al., 2012; Kano & Kanda, 2013; Zabernigg et al., 2010) showed low levels of TAs in patients receiving gemcitabine as monotherapy. However, the current study's findings should be confirmed by a larger sample size because only nine participants in the current sample received gemcitabine monotherapy. Conversely, the findings related to the EC regimen were consistent with those from a previous study by Gamper et al. (2012) of 109 patients with breast and gynecologic cancer. High parageusia and phantageusia scores were associated with a combined regimen of EC and cisplatin/pemetrexed, which are used to treat breast and lung cancer, respectively. Patients treated with docetaxel, which is used in breast cancer, were also at high risk for TAs in the current study, which is in line with previous research (Kano & Kanda, 2013; Steinbach et al., 2009). Docetaxel affected the dimension of basic taste and general TAs. Therefore, the current data suggest that chemotherapy regimens used in breast cancer are likely to affect taste perception, particularly on basic perception, parageusia, and phantageusia symptoms.

Older adult patients reported fewer TAs than other patient populations. It has been largely documented that older adult patients tend to have higher taste thresholds for detection and recognition (Feng, Huang, & Wang, 2014); therefore, they might perceive TAs later or less intensely (Bernhardson et al., 2008; Gamper et al., 2012; Zabernigg et al., 2010).

No previous studies have looked at the chemotherapy schedule as a factor in this regard. Of note, the authors of the current study found that patients who received chemotherapy every 21 days, compared to every 7 days, were more likely to report a higher severity of TAs. Because they are primary cells, taste

TABLE 5. Multivariate Linear Regression Model of Risk Factors for Taste Alterations

Variable	Effect	SE	95% CI	p
Age (years)	−0.37[a]	0.12	[−0.61, −0.13]	0.002
Chemotherapy				
Every 7 days	Ref	–	–	–
Every 15 days	0.58	0.42	[−0.25, 1.41]	0.17
Every 21 days	1.45	0.37	[0.71, 2.18]	< 0.001
Every 30 days	0.51	0.77	[−1.01, 2.02]	0.51

[a] The effect of age is estimated on a difference of 10 years.
CI—confidence interval; Ref—reference; SE—standard error

cells are able to regenerate and have a half-life of about 15 days (Hummel, Landis, & Hüttenbrink, 2011). Taste cells usually degenerate in the first week after chemotherapy and recover by about day 20 (Feng et al., 2014). Therefore, it may be hypothesized that taste cells in patients receiving chemotherapy every 21 days have just started to recover by the time these patients have their next chemotherapy session, which repeats the apoptosis cycle in these cells. These patients experienced marked changes. However, taste cells in patients receiving treatments every seven days never recover; therefore, the patient gets used to the taste change without experiencing a fluctuating pattern of taste perception.

This study has some limitations. Information on potential taste-influencing factors, such as nicotine abuse, severe mucositis, medications, and other treatments that can affect taste, were not collected. Second, the study does not provide information on smell changes, which are closely connected with altered taste perception through the retronasal perception of odors (Wrobel & Leopold, 2005). However, the CiTAS scale is not time-consuming, and it is an easy tool to screen for TAs among patients undergoing chemotherapy regardless of the type of TA. In addition, the CiTAS scale provides information on different taste qualities and unpleasant symptoms that may occur. Similar to other studies (Gamper et al., 2012; Zabernigg et al., 2010), the current authors assessed the effect of chemotherapy on TAs by comparing chemotherapy regimens actually administered in clinical practice instead of splitting them into polychemotherapies or categorizing them by antineoplastic category. In this way, the authors were able to convey information about chemotherapy regimens rather than on single agents or categories.

Implications for Nursing

The results of this study have several implications for nursing practice. Nurses should routinely assess changes in chemosensory perception to identify TAs in a timely manner and offer patients dietary and behavioral advice to cope with them and to prevent a negative impact on nutrition and QOL. The CiTAS is a useful self-report instrument that allows nurses to recognize different TAs (e.g., saltiness, sweetness, sourness, bitterness). Based on the chemotherapy regimen, nurses can identify patients who are more likely to experience severe TAs and the most affected dimensions of taste (i.e., general TAs, decline in basic taste, discomfort, and parageusia and phantageusia) and inform patients about the possible taste changes that they could experience. Patient distress is possibly worsened if TAs are unexpected. By providing information on taste changes that may occur during chemotherapy, nurses can help patients to better cope with TAs (Ravasco, 2005).

KNOWLEDGE TRANSLATION

- Taste alterations are often associated with unpleasant symptoms, such as nausea, loss of appetite, or difficulty eating meat.
- Chemotherapy regimens used in breast cancer are likely to provoke taste alterations.
- Older age and chemotherapy schedule are independent predictors of taste alterations.

Similar to other distressing symptoms of cancer that can affect QOL, such as pain (Kwon, 2014; Prandi et al., 2015), TAs are often overlooked in assessment and intervention. A review of the management and treatment of TAs and smell alterations in patients with cancer by Thorne, Olson, and Wismer (2015) found that there appears to be no effective approach to managing TAs in patients with cancer.

Barriers in the management of the subjective side effects of cancer could be healthcare professional–, patient-, and systems-related (Borneman et al., 2010; Kwon, 2014). Although different reasons may exist, healthcare professional–related barriers frequently include poor TA assessment, lack of knowledge, and tendency to consider TAs as non–life-threatening problems (Zabernigg et al., 2010). Professional education may improve these aspects so that healthcare professionals can better identify TAs, assess their nature and severity, and provide patients with personalized dietary and behavioral advice according to taste change. To date, no study has assessed the effect of such educational programs on healthcare professionals' knowledge and management of TAs. This may be an important field for future research aimed at testing interventions to overcame barriers in the management of TAs. In addition, in Italy, no dedicated services are in place where patients are screened for TAs. Consequently, during the 15- to 20-minute visit, doctors have to address several issues and may not have enough time to thoroughly investigate all the side effects, such as TAs, that patients may have. It would be desirable for nurses to dedicate time to collaborate with doctors in systematically investigating patients' reported outcomes. TAs may even become a field of nursing competence; a trained nurse can use validated tools, such as the CiTAS, for screening and

monitoring TAs across the course of treatment and provide patients with first-line dietary and behavioral advice to cope with their disorder according to local protocols and guidelines. Nurses may further personalize strategies by providing patients with dietary diaries to register food reactions and factors that influence appetite (Ravasco, 2005).

From the patient perspective, potential barriers may include fatalistic beliefs that TAs are an inevitable side effect of chemotherapy or that patients underreport TAs because they do not recognize the symptoms, have difficulties describing the problem, or do not want to distract doctors from providing cancer treatment. Nurses may overcome these barriers by informing patients and their family members about how to alleviate TAs, explaining that their management will not affect the disease treatment, and eliciting information with a standard set of questions.

Additional longitudinal studies are needed to investigate TAs over time across different chemotherapy regimens and to provide patients with specific information about the characteristics, clinical course, and symptoms of TAs. In addition, although CiTAS is a useful assessment tool, future studies are needed to improve its clinical benefits by adding items that explore metallic taste, which is a major taste dysfunction in patients with cancer, and quantitative alterations of taste perception, such as decreased sensitivity to taste perception (hypogeusia), increased sensitivity to taste perception (hypergeusia), or absence of taste perception (ageusia). Currently, this scale is mainly aimed at a qualitative evaluation and only marginally addresses the quantitative aspect (Gonella, 2013).

Conclusion

TAs are a frequent side effect of chemotherapy, and 24% of the patients (n = 57) in the current study complained of moderate to severe symptoms, causing a negative impact on QOL. The data suggest that TAs are still a neglected side effect of chemotherapy and deserve more attention in daily clinical practice.

Chemotherapy was shown to affect all the tasting qualities, with tasting saltiness going through the greatest change. In addition, the severity of TAs and the dimensions of taste were affected to a different extent according to chemotherapy regimen. This study showed that TAs were often associated with unpleasant symptoms, such as nausea and loss of appetite, or problems, such as difficulty in consuming meat, prompting a relationship with nutrition.

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