Frequency of Symptoms in Patients With Cancer Receiving Chemotherapy, According to Gender and the Primary Site of the Cancer in Kashan, Iran, 2017

Fereshteh Jalili[1], Negin Masoudi Alavi[2,*], Masoumeh Abedzadeh Kalahroudi[2]

[1] *Medical Surgical Nursing Department, Faculty of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran*
[2] *Trauma Nursing Research Center, Faculty of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, Iran*

*Corresponding author: Negin Masoudi Alavi, Trauma Nursing Research Center, Faculty of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, IR Iran. Tel: +98315550021; Fax: +983155546633; E-mail: alavi.negin@yahoo.com, masudialavi_n@kaums.ac.ir

Abstract

Introduction: Patients with cancer under chemotherapy usually manifest a wide range of symptoms. The frequency of these symptoms is reported differently. The current study aimed at addressing the common symptoms of cancer, according to gender and primary site of cancer in patients receiving chemotherapy in Kashan, Iran, in 2017.

Methods: The current cross-sectional study was conducted on 186 patients with cancer. The frequency of 14 common symptoms in cancer was evaluated with interviewing the patients. The data were analyzed with SPSS version 13 using descriptive statistics, chi-square, the Mann-Whitney U, and the Kruskal-Wallis tests.

Results: About half of the subjects were female, and 58.1% aged above 50 years. The common primary sites of cancer were breast (23.1%), colon (21%), bone (11.3%), and lung (7%). The most common symptoms were fatigue (86.6%), followed by dry mouth, insomnia, anorexia, and pain. The subjects reported 6.672.63± symptoms in average. The patients with the history of surgery reported significantly more symptoms. The symptoms of insomnia, nausea, and diarrhea were significantly higher in female patients, while anorexia was significantly higher in male ones. Dry mouth, diarrhea, and total number of symptoms were significantly associated with the primary site of the cancer.

Conclusions: Patients with cancer experience various symptoms that are different based on the primary site of the cancer and the gender of patients. Any effective actions in palliative care should be based on the accurate assessment of the symptoms.

INTRODUCTION

Cancer is the second cause of death in the world [1], and the third in Iran [2]. The five-year global prevalence for all cancers was estimated 28.8 million [3]. The incidence of cancer is 20% higher in males compare with females [4]. Stomach cancer in males and breast cancer in females are the most common cancers in Iran [5]. Cancer and its treatments such as chemotherapy induce different complications. Cancer is associated with malnutrition following metabolic changes, and proteolysis and lipolysis effects of cytotoxic chemotherapies are an example of interrelated

symptoms [6]. Cancer and chemotherapy-induced nausea and vomiting are another example [7]. The symptoms such as lack of energy, dry mouth, and weight-loss can indistinguishably occur due to cancer or chemotherapy [8]. Patients with cancer experience 11 to 13 symptoms in average [9]. Fatigue, pain, nausea, vomiting, constipation, and depression are the common ones [10]. Symptoms of cancer change over the course of the disease. Progression of disease is accompanied by the development of new symptoms or the exacerbation of chronic symptoms [11].

The patients reporting more symptoms tend to have a poorer quality of life [12]. Uncontrolled symptoms are associated with increased emotional distress, decreased physical and social function, reduction in the compatibility, and even death of patients [11, 13, 14]. Studies show that caring needs of patients with cancer are considerably neglected [15-17]. Chan et al., reported nausea as the most common symptom of cancer [18]. While in another study, fatigue was the most common problem in such patients [19]. In a systematic review, the prevalence of fatigue was reported 23%-100%, and the nausea was 2%-78% [20]. These wide ranges of reported symptoms make the data unreliable for clinicians.

The way people experience symptoms has impacts on their healthcare seeking behaviors [21], and give helpful information to health personnel. Gender and primary site of cancer are two variables that might influence the perception of cancer symptoms. Vainio et al., found that the pain was more prevalent in females, and the primary site of the cancer was related to the reported symptoms [22]. An accurate assessment of the symptoms is necessary before any actions [23]. After extensive literature review, the studies on the symptoms of cancer according to the gender of patients and the primary site of the cancer in Iran were not found; therefore, the current study aimed at addressing the issue in Kashan in 2017.

METHODS
Study Design and Sampling
The current cross sectional study was conducted in health care centers of Kashan, Iran from May to November 2017. All the patients diagnosed with cancer by an oncologist and receiving chemotherapy were included in the study; sampling was continued sequentially for six months and 186 patients were enrolled in the study. The inclusion

criteria were definite diagnosis of cancer, age above 18, and having psychological, mental, and physical readiness to respond to the questions.

Instrument
The assessment tool had two parts: The first part included questions about demographic and clinical characteristics, i e, age, gender, health insurance, disease awareness, current and previous treatments, marital status, and the site of primary cancer. The second part consisted of 14 common symptoms in cancer derived from Edmonton symptom assessment system and the Assessment Symptoms Palliative Elderly [23, 24]. The presence of symptoms in previous week was specified with the Yes or No option. Pain, dry mouth, mouth ulcer, dyspnea, cough, nausea, vomiting, constipation, diarrhea, urinary problems, fatigue, insomnia, anorexia, helplessness, and depression were the 14 recorded symptoms. To determine the scientific validity of the instrument, the questionnaire was distributed among 11 nursing faculty members of Kashan University of Medical Sciences, and content validity ratio (CVR) and content validity index (CVI) were calculated 0.63 and 0.81, respectively. The test-retest reliability was 0.87.

Data Gathering
First author attended the chemotherapy centers and questionnaires were completed through interview in the waiting rooms before starting the chemotherapy sessions.

Ethical Considerations
The current study was approved by the Ethics Committee of Kashan University of Medical Sciences (ethical code: IR.KAUMS.NUHEPM. REC.1396.02). The objectives of the study were explained to the patients, and written consent was obtained. The patients were assured that their personal information would remain confidential. The study was conducted according to the Declaration of Helsinki.

Data Analysis
Data were analyzed with SPSS version 13. Descriptive statistics were used to express data. The chi-square test was used to analyze the symptoms according to the site of primary cancer, and gender of the patients. The sum of the symptoms was considered as a variable and the Kolmogorov–

Smirnov test showed non-normal distribution of variables. The Mann-Whitney U and the Kruskal-Wallis tests were used to examine the relationship between the number of symptoms and gender, and the primary site of cancer.

RESULTS

The current study was conducted on 186 patients with cancer that 51.1% were female, and 58.1% aged above 50. The demographic and clinical characteristics of patients are provided in Table 1. The frequency of primary site of cancer was as follows: breast (n=43; 23.1%), colon (n=39; 21%), bone (n=21; 11.3%), lung (n=13; 7%), prostate (n=7; 3.8%), cervix (n=7; 3.8%), liver (n=6; 3.2%), lymphoma (n=5; 2.7%) and others or not-specified cases (n=45; 24.2%). The most common symptom was fatigue (86.6%), followed by dry mouth, insomnia, anorexia, and pain (Table 2). The subjects reported 6.67±2.63 symptoms in average. The patients with the history of surgery reported significantly more symptoms (Table 1).

The most prevalent symptoms among male patients were fatigue (83.5%), anorexia (64.8%), and dry mouth (59.3%), while in female patients there were fatigue (89.5%), insomnia (68.4%), and pain (66.3%). The symptoms of insomnia, nausea, and diarrhea were significantly higher in female patients, while anorexia was significantly higher in male ones (Table 2).

Dry mouth, diarrhea, and total number of symptoms were significantly associated with the primary site of the cancer (Table 3).

DISCUSSION

In the current study, breast and colon were the most frequent primary sites of cancer. Common symptoms were fatigue, dry mouth, insomnia, anorexia, and pain. Insomnia, nausea, and diarrhea were higher in female patients and anorexia was higher in male ones. Symptoms were significantly associated with the primary site of the cancer. Fatigue was the most

Table 1: Demographic and Clinical Information of Patients and Their Relationship With Symptoms

	Patients, No. (%)	Number of Symptoms, mean ± SD	P Value
Gender			0.12
Male	91 (48.9)	6.36 ± 2.7	
Female	95 (51.1)	7 ± 2.5	
Age, y			0.36
<50	78 (41.9)	6.4 ± 2.7	
>50	108 (58.1)	6.8 ± 2.5	
Healthcare Insurance			0.99
Yes	177 (95.2)	6.6 ± 2.6	
No	9 (4.8)	7 ± 2.8	
Aware of Illness			0.76
Yes	140 (75.3)	6.6 ± 2.7	
No	46 (24.7)	6.6 ± 2.1	
Chemotherapy History			0.90
Yes	72 (38.7)	6.7 ± 2.5	
No	114 (61.3)	6.6 ± 2.7	
Surgical History			0.007
Yes	106 (57)	7 ± 2.6	
No	80 (43)	6.2 ± 2.5	
Radiotherapy History			0.22
Yes	71 (38.2)	7 ± 2.5	
No	115 (61.8)	6.5 ± 2.7	
The Session of Chemotherapy			0.11
<5	75 (40.4)	6.1 ± 2.4	
5-10	65 (34.9)	6.9 ± 2.9	
>10	46 (24.7)	7.1 ± 2.3	

Table 2: The Frequency of Symptoms by Gender in Patients With Cancer

	Frequency	Male	Female	P Value
Fatigue, No. (%)	161 (86.6)	76 (83.5)	85 (89.5)	0.16
Dry Mouth, No. (%)	117 (62.9)	54 (59.3)	63 (66.3)	0.20
Insomnia, No. (%)	116 (62.4)	51 (56)	65 (68.4)	0.05
Anorexia, No. (%)	115 (61.8)	59 (64.8)	56 (58.9)	0.05
Pain, No. (%)	114 (61.3)	51 (56)	63 (66.3)	0.09
Constipation, No. (%)	99 (53.32)	52 (57.1)	47 (49.5)	0.18
Hopelessness and Depression, No. (%)	98 (52.7)	50 (51)	48 (50.5)	0.32
Nausea, No. (%)	87 (46.8)	33 (36.3)	54 (56.8)	0.004
Urinary Problems, No. (%)	66 (35.5)	37 (40.7)	29 (30.5)	0.09
Oral Ulcer, No. (%)	61 (32.8)	27 (29.7)	34 (35.8)	0.23
Dyspnea, No. (%)	60 (32.3)	26 (28.6)	34 (35.8)	0.18
Cough, No. (%)	52 (28)	24 (26.4)	28 (29.5)	0.38
Diarrhea, No. (%)	51 (27.4)	19 (20.9)	32 (33.7)	0.03
Vomiting, No. (%)	45 (24.2)	20 (22)	25 (26.3)	0.30
The Total Number of Symptoms, mean ± SD	6.67 ± 2.63	6.3 ± 2.7	6.9 ± 2.5	0.11

common reported symptom in both genders. In a meta-analysis by Van Lancker et al., fatigue was reported as the most common symptom in patients with cancer [25]. Riechelmann et al., also reported fatigue as the most common symptom [26]. Lack of energy and weakness can lead to various problems such as frustration, anxiety, and depression [27].

Dry mouth was the second prevalent symptom. Dry mouth can reduce nutrition, and quality of life. In the study by Mercadent et al., the frequency of dry mouth was 40.4% [28] that was less than that of the current study. In Jordanian patients with cancer, dry mouth was 82.9% [12]. Dry mouth was also more common in patients with breast and liver cancers. The least common symptom in current study was vomiting that was consistent with the findings of Van Lancker et al. [25], but the frequency of vomiting was more in the study by Okuyama [17]. This discrepancy could be due to differences in chemotherapy regimen, tolerance, and type of anti-nausea drugs. Nausea was more common in the current study. Studies by Ware showed that more than half of the patients undergoing chemotherapy experience nausea or vomiting, either due to cancer or due to its complications and treatments [29]. This rate was comparable with that of the current study. The nausea was significantly higher in female patients.

Oral ulcer was reported by 61 (32.8%) patients. According to the study by Naidu et al., oral ulcers are adverse effects of radiation therapy and chemotherapy, which changes the nutritional status

of the patients. This symptom was experienced by 40% of patients [30] that was somewhat consistent with that of the current study. Insomnia was the third reported problem in the studied patients. In the study by Moustian et al., the incidence of insomnia was up to 90%. Insomnia symptoms include daily sleepiness, difficulty in falling asleep, difficulty in sleeping, and early waking trouble, which can increase mortality and morbidity in such patients [31]. Insomnia was significantly higher in females compare with males in present study. A meta-analysis suggested a female predisposition to insomnia. The risk ratio of insomnia was 1.41 (95% confidence interval (CI): 1.28-1.55) for female versus male patients [32].

Pain was the fifth prevalent symptom in the current study. Pain was higher in other studies [12, 22]. But the finding of the current study was comparable with that of the meta-analysis by Van Lancker [25]. Pain was more common in females than males, although the difference was insignificant. A meta-analysis showed that the prevalence of pain in the patients under anticancer therapies was 59%, [33]. Pain is a common and disturbing problem and despite the provided suggestions to control it, pain still is a major problem in such patients. Anorexia with the frequency of 115 (61.8%) was significantly higher in male patients. Anorexia, cachexia, and loss of adipose and muscle tissue are reported in half of all patients with cancer. Cachexia can have a profound impact on quality of life. Weight loss in patients with cancer is associated with higher chemotherapy-related side effects, which decreases survival rate [34].

Table 3: The Prevalence of Symptoms by the Primary Site of Cancer

	The Primary Site of Cancer, No. (%)									P Value
	Breast (n=43)	Lung (n=13)	Cervix (n=7)	Prostate (n=7)	Lymphoma (n=5)	Liver (n=6)	Bone (n=21)	Colon (n=39)	Other (n=45)	
Pain, No. (%)	30 (69.8)	6 (46.2)	4 (57.1)	4 (57.1)	1 (20)	5 (83.3)	11 (52.4)	26 (66.7)	27 (60)	0.36
Dry mouth, No. (%)	32 (74.4)	3 (23.1)	4 (57.1)	3 (42.9)	4 (80)	5 (83.3)	14 (66.7)	31 (79.5)	21 (46.7)	0.002
Dyspnea, No. (%)	14 (32.6)	6 (46.2)	1 (14.3)	1 (14.3)	2 (40)	3 (50)	8 (38.1)	9 (23.1)	16 (35.6)	0.61
Cough, No. (%)	14 (32.6)	6 (46.2)	0 (0)	1 (14.3)	2 (40)	1 (16.7)	10 (47.6)	9 (23.1)	9 (20)	0.12
Nausea, No. (%)	25 (58.1)	5 (38.5)	4 (57.1)	0 (0)	2 (40)	3 (50)	6 (28.6)	19 (48.7)	23 (51.1)	0.13
Vomiting, No. (%)	13 (30.2)	4 (30.8)	2 (28.6)	0 (0)	0 (0)	1 (16.7)	2 (9.5)	12 (30.8)	11 (24.4)	0.37
Constipation, No. (%)	22 (51.2)	8 (61.5)	4 (57.1)	5 (71.4)	1 (20)	2 (33.3)	15 (71.4)	8 (46.2)	24 (53.3)	0.41
Diarrhea, No. (%)	15 (34.9)	2 (15.4)	2 (28.6)	0 (0)	0 (0)	2 (33.3)	2 (9.5)	18 (46.2)	10 (22.2)	0.02
Fatigue, No. (%)	39 (90.7)	10 (76.9)	6 (85.7)	5 (71.4)	4 (80)	6 (100)	18 (85.7)	36 (92.3)	37 (82.2)	0.64
Anorexia, No. (%)	29 (67.4)	6 (46.2)	5 (71.4)	2 (28.6)	1 (20)	3 (50)	14 (66.7)	25 (64.1)	30 (66.7)	0.24
Depression, No. (%)	23 (53.5)	5 (38.5)	5 (71.4)	2 (28.6)	2 (40)	4 (66.7)	10 (47.6)	22 (56.4)	25 (55.6)	0.75
Urinary Tract Problem, No. (%)	15 (34.9)	3 (23.1)	1 (14.3)	4 (57.1)	1 (20)	1 (16.7)	11 (52.4)	16 (41)	14 (31.1)	0.37
Insomnia, No. (%)	30 (69.8)	9 (69.2)	6 (85.7)	4 (57.1)	3 (60)	1 (16.7)	13 (61.9)	24 (61.5)	26 (57.8)	0.36
Oral Ulcer, No. (%)	18 (41.9)	2 (15.4)	2 (28.6)	2 (28.6)	2 (40)	1(16.7)	8 (38.1)	12 (30.8)	14 (31.1)	0.78
Number of symptoms, mean ± SD	7.4 ± 2.5	5.7 ± 3.7	6.6 ± 2.2	4.7 ± 1.8	5 ± 3.1	6.3 ± 2.8	6.7 ± 2.6	7.1 ± 2	7.4 ± 2.7	0.02

Constipation was reported by 99 (53.32%) patients. Diarrhea was less common than constipation and it was significantly more prevalent in females in current study. According to Stein, diarrhea was one of the most common problems associated with chemotherapy, especially in patients with advanced cancer, and its prevalence was 50%-80%, which was not consistent with the results of the current study [35]. The frequency of depression in the current study was 98 (52.7%). In a meta-analysis, the prevalence of major depressive disorders in patients with cancer was 3% to 40%, and the average was approximately 11% that was twice compared with that of the general population [36].

The current study findings showed that the primary site of the cancer might be related to the type and number of symptoms, which was consistent with the study by McPherson et al., [37]. A survey of Canadian oncology nurses revealed that the most common identified symptoms were fatigue, pain, nausea, constipation, and anxiety. Frequent symptoms, which nurses felt low confidence in managing them were anxiety, neuropathy, depression, anorexia, and skin alterations [38]. It shows that nurses have a clear view of cancer symptoms and limitations to management them. Many times, there are concurrent symptoms such as pain, fatigue, and sleep disturbances, or nausea, vomiting, and poor appetite that are related to each other and are called a symptom cluster. Some believe that it is quite better to look at the cluster of symptoms or nested structure of symptoms since their management is interrelated [9]. Some believe it is better to focus on core symptoms that means the symptoms that remain consistent over time [11].

The current study had some strength. First, it was about the symptoms of cancer considering gender and primary site of cancer in Iran. This view to the cancer symptom is new. Many believe that cancer is not a single disease, but a group of hundreds of illnesses sharing common biological features [13]; therefore, it might be beneficial to evaluate the symptoms in different types of the disease separately. This might provide more helpful data to clinicians in palliative care settings. Second, the data was completed with interviewing the patients that may reduce the reporting errors. The current study had some limitations. First, the sample size was small; this reduces the reliability of the results. Second, the patients were recruited from limited health care centers in one city; this non-representative sample of the study affects the generalizability of the results. For example, the frequency of bone cancer was much higher in the current study compared with that of the literature; therefore the findings must be considered with caution. Patients diagnosed with cancer receive many curative or palliative treatments. Surgery, radiotherapy, and chemotherapy are common treatments for cancer [39]. These treatments have their own complications and symptoms. In the current study, along with many other studies mentioned here, it was not possible to attribute the symptoms to the treatments or the cancer itself. It was a limitation of the current study that should be considered when referring to the data. Further studies with the same objectives in a larger population of patients with cancer are recommended.

It seems that the primary site of cancer and gender of patients can influence the perception of symptoms. Patients and their families have uncontrolled symptoms, and this imposes additional costs on the health system. The assessment of cancer symptoms is the first step in symptom management; therefore, it is a crucial issue and needs more studies.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The authors declared no conflict of interest.

ETHICS APPROVAL

The current study was approved by the Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.NUHEPM.REC.1396.02).

REFERENCES

1. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1459-544. DOI: 10.1016/s0140-6736(16)31012-1 PMID: 27733281

2. Saadat S, Yousefifard M, Asady H, Moghadas Jafari A, Fayaz M, Hosseini M. The Most Important Causes of Death in Iranian Population; a Retrospective Cohort Study. Emergency. 2015;3(1):16-21. PMID: 26512364

3. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of

cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer. 2013;132(5):1133-45. DOI: 10.1002/ijc.27711 PMID: 22752881

4. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30. DOI: 10.3322/caac.21387 PMID: 28055103

5. Amirkhah R, Naderi-Meshkin H, Mirahmadi M, Allahyari A, Reza Sharifi H. Cancer statistics in Iran: Towards finding priority for prevention and treatment. Cancer Press. 2017;3(2):27-38. DOI: 10.15562/tcp.42

6. Schiessel DL, Baracos VE. Barriers to cancer nutrition therapy: excess catabolism of muscle and adipose tissues induced by tumour products and chemotherapy. Proc Nutr Soc. 2018;77(4):394-402. DOI: 10.1017/s0029665118000186 PMID: 29708079

7. Bosnjak SM, Dimitrijevic J, Djordjevic F. Cancer and chemotherapy-induced nausea and vomiting: a focus on olanzapine. Curr Opin Support Palliat Care. 2016;10(2):180-8. DOI: 10.1097/spc.0000000000000206 PMID: 27028050

8. Yahaya NA, Subramanian P, Bustam AZ, Taib NA. Symptom experiences and coping strategies among multi- ethnic solid tumor patients undergoing chemotherapy in Malaysia. Asian Pac J Cancer Prev. 2015;16(2):723-30. PMID: 25684515

9. Bhavnani SK, Bellala G, Ganesan A, Krishna R, Saxman P, Scott C, et al. The nested structure of cancer symptoms. Implications for analyzing co-occurrence and managing symptoms. Methods Inf Med. 2010;49(6):581-91. DOI: 10.3414/me09-01-0083 PMID: 21085743

10. Hui D, Bruera E. Integrating palliative care into the trajectory of cancer care. Nature reviews Clinical oncology. 2016;13(3):159-71. DOI: 10.1038/nrclinonc.2015.201 PMID: 26598947

11. Cooley ME, Siefert ML. Assessment of Multiple Co-Occurring Cancer Symptoms in the Clinical Setting. Semin Oncol Nurs. 2016;32(4):361-72. DOI: 10.1016/j.soncn.2016.08.003 PMID: 27776830

12. Al Qadire M, Al Khalaileh M. Prevalence of Symptoms and Quality of Life Among Jordanian Cancer Patients. Clin Nurs Res. 2016;25(2):174-91. DOI: 10.1177/1054773814564212 PMID: 25550305

13. Benz EJ, Jr. The Jeremiah Metzger Lecture Cancer in the Twenty-First Century: An Inside View from an Outsider. Trans Am Clin Climatol Assoc. 2017;128:275-97. PMID: 28790513

14. Rome RB, Luminais HH, Bourgeois DA, Blais CM. The role of palliative care at the end of life. Ochsner J. 2011;11(4):348-52. PMID: 22190887

15. Chen SC, Lai YH, Liao CT, Chang JT, Lin CY, Fan KH, et al. Supportive care needs in newly diagnosed oral cavity cancer patients receiving radiation therapy. Psychooncology. 2013;22(6):1220-8. DOI: 10.1002/pon.3126 PMID: 22730021

16. Lam WW, Au AH, Wong JH, Lehmann C, Koch U, Fielding R, et al. Unmet supportive care needs: a cross-cultural comparison between Hong Kong Chinese and German Caucasian women with breast cancer. Breast Cancer Res Treat. 2011;130(2):531-41. DOI: 10.1007/s10549-011-1592-1 PMID: 21617919

17. Okuyama T, Akechi T, Yamashita H, Toyama T, Nakaguchi T, Uchida M, et al. Oncologists' recognition of supportive care needs and symptoms of their patients in a breast cancer outpatient consultation. Jpn J Clin Oncol. 2011;41(11):1251-8. DOI: 10.1093/jjco/hyr146 PMID: 22003206

18. Chan HK, Ismail S. Side effects of chemotherapy among cancer patients in a Malaysian General Hospital: experiences, perceptions and informational needs from clinical pharmacists. Asian Pac J Cancer Prev. 2014;15(13):5305-9. PMID: 25040993

19. Rainbird K, Perkins J, Sanson-Fisher R, Rolfe I, Anseline P. The needs of patients with advanced, incurable cancer. Br J Cancer. 2009;101(5):759-64. DOI: 10.1038/sj.bjc.6605235 PMID: 19654579

20. Moens K, Higginson IJ, Harding R. Are there differences in the prevalence of palliative care-related problems in people living with advanced cancer and eight non-cancer conditions? A systematic review. J Pain Symptom Manage. 2014;48(4):660-77. DOI: 10.1016/j.jpainsymman.2013.11.009 PMID: 24801658

21. Hvidberg L, Jensen LF, Pedersen AF, Aro AR, Vedsted P. Measurement properties of the Danish version of the Illness Perception Questionnaire-Revised for patients with colorectal cancer symptoms. J Health Psychol. 2014;19(10):1279-90. DOI: 10.1177/1359105313488978 PMID: 23818508

22. Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. Symptom Prevalence Group. J Pain Symptom Manage. 1996;12(1):3-10. PMID: 8718910

23. Van Lancker A, Beeckman D, Verhaeghe S, Van Den Noortgate N, Grypdonck M, Van Hecke A. An instrument to collect data on frequency and intensity of symptoms in older palliative cancer patients: A development and validation study. Eur J Oncol Nurs. 2016;21:38-47. DOI: 10.1016/j.ejon.2015.11.003 PMID: 26952677

24. Diplock BD, McGarragle KMC, Mueller WA, Haddad S, Ehrlich R, Yoon DA, et al. The impact of automated screening with Edmonton Symptom Assessment System (ESAS) on health-related quality of life, supportive care needs, and patient satisfaction with care in 268 ambulatory cancer patients. Support Care Cancer. 2019;27(1):209–18. DOI: 10.1007/s00520-018-4304-0 PMID: 29931490

25. Van Lancker A, Velghe A, Van Hecke A, Verbrugghe M, Van Den Noortgate N, Grypdonck M, et al. Prevalence of symptoms in older cancer patients receiving palliative care: a systematic review and meta-analysis. J Pain Symptom Manage. 2014;47(1):90-104. DOI: 10.1016/j.jpainsymman.2013.02.016 PMID: 23764109

26. Riechelmann RP, Krzyzanowska MK, O'Carroll A, Zimmermann C. Symptom and medication profiles among cancer patients attending a palliative care clinic. Support Care Cancer. 2007;15(12):1407-12. DOI: 10.1007/s00520-007-0253-8 PMID: 17429699

27. Wu C-h, Yao G. Relations among self-certainty, sense of control and quality of life. International Journal of Psychology. 2007;42(5):342-52. DOI:

doi:10.1080/00207590701264831

28. Mercadante S, Aielli F, Adile C, Ferrera P, Valle A, Fusco F, et al. Prevalence of oral mucositis, dry mouth, and dysphagia in advanced cancer patients. Support Care Cancer. 2015;23(11):3249-55. DOI: 10.1007/s00520-015-2720-y PMID: 25832897

29. Warr DG. Chemotherapy-and cancer-related nausea and vomiting. Curr Oncol. 2008;15(Suppl 1):S4-9. PMID: 18231647

30. Naidu MU, Ramana GV, Rani PU, Mohan IK, Suman A, Roy P. Chemotherapy-induced and/or radiation therapy-induced oral mucositis--complicating the treatment of cancer. Neoplasia. 2004;6(5):423-31. DOI: 10.1593/neo.04169 PMID: 15548350

31. Mustian KM, Janelsins M, Peppone LJ, Kamen C. Yoga for the Treatment of Insomnia among Cancer Patients: Evidence, Mechanisms of Action, and Clinical Recommendations. Oncol Hematol Rev. 2014;10(2):164-8. PMID: 25861453

32. Zhang B, Wing YK. Sex differences in insomnia: a meta-analysis. Sleep. 2006;29(1):85-93. PMID: 16453985

33. van den Beuken-van Everdingen MHJ, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol. 2007;18(9):1437-49. DOI: 10.1093/annonc/mdm056

34. Suzuki H, Asakawa A, Amitani H, Nakamura N, Inui A. Cancer cachexia—pathophysiology and management. J Gastroenterol. 2013;48(5):574-94. DOI: 10.1007/s00535-013-0787-0 PMID: 23512346

35. Stein A, Voigt W, Jordan K. Chemotherapy-induced diarrhea: pathophysiology, frequency and guideline-based management. Ther Adv Med Oncol. 2010;2(1):51-63. DOI: 10.1177/1758834009355164 PMID: 21789126

36. Meijer A, Roseman M, Milette K, Coyne JC, Stefanek ME, Ziegelstein RC, et al. Depression Screening and Patient Outcomes in Cancer: A Systematic Review. PLoS ONE. 2011;6(11):e27181. DOI: 10.1371/journal.pone.0027181 PMID: 22110613

37. McPherson K, Steel CM, Dixon JM. Breast cancer—epidemiology, risk factors, and genetics. BMJ : British Medical Journal. 2000;321(7261):624-8. PMID: 10977847

38. Macartney G, Stacey D, Carley M, Harrison MB. Priorities, barriers and facilitators for remote support of cancer symptoms: a survey of Canadian oncology nurses. Can Oncol Nurs J. 2012;22(4):235-47. PMID: 23362657

39. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin. 2016;66(4):271-89. DOI:10.3322/caac.21349