Cancer pain: Physical Factors affecting Pain Experience

Mahnoosh Khosravi[1], Sanambar Sadighi[1, *], Kazem Zendehdel[1, 3],
Shaghayegh Moradi[2], Fatemeh Sadeghi[1]

A B S T R A C T

Background: Pain adversely affects cancer patients' quality of life. Knowing different sources of pain helps physicians and patients to manage it. The aim of this study was investigating physical factors affecting pain in Iranian cancer patients.

Methods: This cross-sectional study randomly enrolled cancer patients who were newly admitted to the Medical Oncology Department of Cancer Institute of Iran in 2013. Patients were divided into two groups by asking whether they had any pain. The demographic information of the patients were collected from medical records. Multivariate logistic regression was used to analyze the data.

Results: A total of 269 participants were included. 52.78% patients suffered from pain. 69.72% of the pain group and 54.33% of the no-pain group were female, and the average age for the pain group was 49.59±13.57. There was a significant difference in the pain control of patients who were "capable to work but with misery" and those who were "able to conduct personal affairs" (OR: 9.60, 95% CI: 2.38-38.71 P=0.00). Cancer treatment was a protective factor from pain experience (OR: 0.87, 95% CI: 0.37-2.05 P=0.76). 62.70% of the pain group were in the advanced stage and had a 2.18-fold higher risk of pain compared to patients who were in the primary stage (CI: 1.02-4.65). Patients who took more painkillers had less pain control (54.41%) ($OR_{analgesic}$: 3.07, OR_{opium}: 12.11 and $OR_{multiple drugs}$: 8.97).

Conclusion: Although pain could be relieved in most cancer cases, more than 50% of patients showed uncontrolled pain. Understanding patients' desires and past experiences of disease and the collaboration of medical, radiation and surgical oncologists with palliative care nursing and psychological specialties in multidisciplinary teams is urgent to solve the miss-treatment of cancer pain.

Keywords: Cancer pain, Physical factor, Protective, Adverse effect

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1. Cancer Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran.
2. School of Medicine, Tehran University of Medical Sciences.
3. Department of Medical Epidemiology and Biostatistics, Karolinska-Institute, Stockholm, Sweden.

*Corresponding Author:
Sanambar Sadighi
M D , Hematologist-Medical Oncologist Group, Cancer Research Center, Cancer Institute of Iran, Tehran University of Medical Sciences, Tehran, Iran.
Phone: 9821-66581638
Email: s.sadighi@hotmail.com

Introduction

Cancer is a leading cause of death worldwide, accounting for 8.2 million deaths in 2012[1]. In developed countries, one in three people will develop cancer in their lifetimes[2]. In developing countries, the incidence of common malignant tumors is rising with the change in life style. The age standardized incidence rate (ASR) of different types of cancer in Iran (excluding non-melanoma skin cancer) was estimated to be about 134.7/100,000 in men and 120.1/100,000 in women[3]. Moreover, cancer patients face a variety of problems, from physical to socio-ecconomic.

Patients with cancer suffer from a multitude of symptoms that adversely affect their quality of life. Pain is one of the most dreaded and burdensome symptoms in cancer patients[4,5]. It is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[6]. The prevalence of pain ranges from 24% to 60% in patients on active anticancer treatment and 62%–86% in patients on palliative therapy; regrettably, it is often under-treated[7,8]. The World Health Organization (WHO) estimates that 25% of all cancer patients die with unrelieved pain[9]. Cancer pain syndromes are categorized as acute and chronic based on their onset and duration[4]. Dame Cicely Saunders suggested that pain has psychological, social, physical, and spiritual components that make up the "total pain" experience[10,11]. Physical pain may be caused by 1) direct tumor effects, 2) treatment, 3) general debility, and 4) unrelated co-morbidities[11]. Cancer treatments such as chemotherapy, radiation therapy, and surgery are potential sources of cancer pain. Surgery can be painful, and healing may take time. Radiation may leave behind a burning sensation or painful ulcers and scars, and chemotherapy can cause many potentially painful side-effects including mouth sores, diarrhea, and nerve damage[12].

Controlling pain is an important part of coping with recovery and long-term healing[13, 14]. Although WHO and other guidelines have been developed at both national and international levels for assisting the management of cancer pain[7], guidelines have not been universally applied and, as a result, there is considerable gap in the treatment of pain[4]. Accurate assessment and identification of causes of pain is the first major step for optimal pain management. In this way, we can use guidelines properly, narrow the gaps in the treatment of pain, and help patients to live better and longer.

Studies have shown that the rate of prevalence of pain in cancer patients is high and often under-treated. However, there are a few studies that have specifically surveyed the prevalence of pain in cancer patients based on its sources. In this study, we evaluated the prevalence of physical factors as one of the sources affecting pain[11] in Iranian cancer patients. We believe this study can be used in pain control, especially in palliative care services which are expanding these days in our country.

Methods

This is a cross-sectional study, based upon the main hypothesis that physical factors are one of the sources of pain in cancer patients[11]. It was conducted in 2013 in the Medical Oncology Department of Cancer Institute of Iran, the national referral center for cancer patients. The study population included patients who were newly admitted to the Medical Oncology Department. They were randomly selected by trained medical student interviewers. Patients willing to participate proactively approached the researchers to register their interest to be included, and there was no restriction for sex, age, and type or stage of cancer. Patients were questioned as to whether they had pain, and the demographic data including age, educational level, co-morbidity, stage of tumor, recurrence, type of treatments, and drugs

were collected from patients' medical records. Patients were excluded if their medical documentations were incomplete or the reviewer was unable to use them.

Ethics consideration

The present study was conducted according to the guidelines for human studies determined by the National Ethics Committee, Ministry of Health and Medical Education in Iran, and was approved by the Medical Review Board of Tehran University of Medical Sciences. Each patient who participated in this study signed a written informed consent form.

Statistical analysis

We used multivariate logistic regression models to estimate odds ratios, and Wald $\chi 2$ statistics were used to test the significance of individual odds ratios in the model. All significant levels were set to $\alpha=0.05$. Also, we used post-estimation tests including collinearity between independent variables, and model specification and Hosmer–Lemeshow test for selecting appropriate the independent variable and making sure the function of multivariate logistic regression was correctly specified and the data fit the logistic model. Statistical analyses were carried out using STATA 11.1.

Results

We initially recruited 390 patients, although we excluded 121 patients whose medical documentations were incomplete or the reviewer was unable to use them. Results of statistical analyses for 269 patients are presented in **Table 3**. As depicted in **Table 3**, 142 (52.78%) patients suffered from pain and 127 (47.21%) patients reported no pain.

According to model specification results (coefficient: 0.07, 95% CI: -0.11-0.26 P=0.45) we had specified our model correctly and the effect of variables had been estimated without bias. The multi-collinearity results in **Table 1** show that there is no linear correlation between independent variables in the model. The Hosmer–Lemeshow test results ($\chi2=10.04$, 8 degrees of freedom, P = 0.26) indicate that the overall, model is fit. The Nagelkerke R2 value was 0.43, suggesting that the model is quite capable in predicting pain (**Table 2**).

Based on the multivariate model, we found that the patients who were able to work but with misery had a 9.37-fold higher risk of pain experience (OR: 9.37, 95% CI: 2.34-37.52 P=0.00) and the patients who were able to conduct personal affairs had a 2.88-fold higher risk of pain (OR: 2.90, 95% CI: 1.06-7.92 P=0.03) compared to other patients. Patients who

Table 1: Collinearity Diagnostics				
Variable	VIF	Tolerance	Eigenvalue	Cond Index
Sex	1.35	0.74	7.92	1.0
Age	1.22	0.82	0.83	3.07
Education	1.17	0.85	0.79	3.16
Performance status	1.15	1.07	0.54	3.81
Comorbidity	1.27	0.78	0.32	4.94
Recurrence	1.04	0.95	0.23	5.85
Stage of tumor	1.08	0.92	0.14	7.26
Drugs	1.21	0.82	0.07	10.06
Treatment	1.14	0.87	0.06	10.88

Table 2: Results of overall goodness of fit				
Specification error	p-value	Hosmer–Lemeshow	p-value	Nagelkerke R 2
0.07	0.45	10.04	0.26	0.43

had a recurrent disease showed a 5.02-fold higher risk of pain compared to patients with primary cancer (OR: 5.02, 95% CI: 1.72-14.62 P=0.00). Patients with an advanced disease had a higher risk of pain experience compared to patients with a localized disease (OR: 2.18, 95%CI: 1.02-4.65). Patients who reported using analgesics, opium, or other painkillers had 3.02 (95% CI: 1.08-8.40), 11.98 (95% CI: 2.26-63.29) and 8.60 (95% CI: 1.60-46.14) folds of pain experience compared to non-users, respectively (**Table 3**).

Discussion

In the present study, we assessed the associations between sex, age, education, performance status, co-morbidity, recurrence, stage of tumor, drugs, and treatment, and pain experience of cancer patients. In our study, 52.78% of the patients had pain and 47.21% had no uncontrolled pain. In 2007, Everdingen et al.[8] aimed to present a systematic review of prevalence of pain in patients with cancer. They evaluated 52 studies and pooled the prevalence rate of pain in four subgroups. Pain was present in 33% of patients after curative treatment, 59% of patients under anticancer treatment, 64% of patients characterized with advanced/metastatic/terminal disease, and 53% of patients at all disease stages. These findings showed that inadequate pain control in cancer patients is a major problem.

A 10 years prospective, validation World Health Organization' (WHO) study showed that more than 70% of cancer patients who used WHO recommendation (3-step analgesic ladder) achieved good pain relief[4]. We found a significant difference between with pain and no-pain groups in taking drugs. Al-

though patients with cancer pain took sedatives, tranquilizers, and opiates, pain was uncontrolled, which may indicate that care takers as well as patients lack adequate knowledge and training about pain management, and there is considerable gap in the proper use of guidelines of pain treatment[4, 8].

According to these data, there was a significant association between pain experience and more advanced stages of tumor (OR: 2.18, 95%CI: 1.02-4.65). These findings are consistent with others in the literature which declare the direct correlation between pain prevalence and stage of cancer. Although severe pain can occur in all cancer stages, cancer patients with an advanced disease are more likely to experience uncontrolled pain[4, 7, 15-17].

Previous studies have reported significantly lower levels of performance status and higher levels of total mood disturbance in cancer patients who experienced pain[18]. However, in this study we found more pain experience in patients with a better performance status. This result shows under-treatment or even miss-treatment of pain in ambulatory patients in comparison with sedentary ones. In fact, the desire of patients to be active as well as free of pain should be considered.

It is hypothesized that cancer treatments such as chemotherapy, radiation and surgery are potential sources of cancer pain[11]; nevertheless, we found cancer treatment as a protective factor in this study, although this association was not statistically significant (OR: 0.87, 95% CI: 0.37-2.05 P=0.76).

This study has several limitations. First of all, pain is a subjective variable related to many aspects of patients' disease and life. It is very difficult to measure controlled and uncontrolled pain. The sec-

	Variables	Events	Wald test (p-value)	OR (95% CI)	Std. Err.
	Pain	No pain			
Sex					
Male	43	58	-	1	-
Female	99	69	2.01 (0.04)	2.26 (1.01- 5.02)	0.92
Age					
<36	27	25	-	1	-
37-61	89	66	0.35 (0.72)	1.18 (0.46-3.02)	0.56
>62	26	36	-1.21 (0.22)	0.46 (0.13-1.59)	0.29
Education					
Illiterate	48	32	-	1	-
School	77	72	-0.87 (0.38)	0.69 (0.30-1.58)	0.29
University	17	14	0.21 (0.83)	1.15 (0.30-4.34)	0.78
Performance status					
Normal	57	88	-	1	-
Capable to work but with misery	25	5	3.16 (0.00)	9.37 (2.34-37.52)	6.63
Able to conduct personal affairs	30	11	2.08 (0.03)	2.90 (1.06-7.92)	1.48
Bedridden>50%	28	16	1.29 (0.19)	1.88 (0.71-4.94)	0.92
Co-morbidity					
None	85	86	-	1	-
One	44	28	0.85 (0.39)	1.48 (0.59-3.65)	0.68
Multiple	1	6	1.26 (0.20)	2.92 (0.55-15.40)	2.47
Recurrence					
No	114	108	-	1	-
Yes	27	13	2.96 (0.00)	5.02 (1.72-14.62)	0.84
Stage of Tumor					
Limited	32	49	-	1	-
Advanced	79/	47	2.03 (0.04)	2.18 (1.02-4.65)	2.73
Drugs					
None	62	104	-	1	-
Analgesics	27	9	2.11 (0.03)	3.02 (1.09-8.40)	1.58
Opium	22	3	2.92 (0.00)	11.98 (2.26-63.29)	10.17
multiple Drugs	18	4	2.51 (0.01)	8.60 (1.60-46.14)	7.37
Others	7	2	1.78 (0.07)	5.31 (0.84 -33.47)	4.99
Treatment					
One	31	27	-	1	-
Multiple	104	91	-0.32 (0.74)	0.87 (0.37- 2.05)	0.37

Table 3: Output from a statistical package for logistic regression on 269 participants in the study ''Cancer pain: Physical factors affecting pain experience''

ond limitation is that we used a simple validated international scoring system of performance status. However, there are different aspects of normal life such as cognition, gait stability, ability to live independently and sharing emotions and feelings with relatives that are very important for patients and their families. Thus, checking the performance of patients using more sophisticated questionnaires is recommended.

In conclusion, although pain is a prevalent symptom causing severe distress in cancer patients, their families and the society, pain control remains inadequate. Patients with cancer take more drugs but experience less pain relief. Despite their pain, many patients want to do their jobs but their pain is uncontrolled and under-treated with painkillers. We believe the concept of cancer pain needs to be revisited. It should be seen as a multidimensional problem in cancer patients as well as their families, and be treated in a process of creating individualized interventional plans.

Acknowledgments

Reference

1. WHO. Cancer. http://www.who.int/mediacentre/fact-sheets/fs297/en/.

2. Rheingold, S.R., Neugut, A.I., Meadows, N.t. (2003) Secondary Cancers: Incidence, Risk Factors, and Management. Holland-Frei Cancer Medicine. 5th edition (Chapter 136). ISBN 1-55009-213-8.

3. Rouhollahi, M.R., Mohagheghi, M.A. et al. (2014) Situation Analysis of the National Comprehensive Cancer Control Program (2013) in the I. R. of Iran; Assessment and Recommendations Based on the IAEA Impact Mission. Archives of Iranian Medicine, 17(4), 222-231.

4. Parala-Metz, A., Davis, M. (2015) Cancer Pain.

5. Breivik, H., Cherny, N. et al. (2009) Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. Annals of Oncology. 20, 1420–1433.

6. Gebhart, GF. (2000) Scientific Issues of Pain and Distress. NCBI Bookshelf. http://www.ncbi.nlm.nih.gov/books/NBK99533/.

7. van den Beuken-van Everdingen, M.H.J., de Rijke, J.M. et al. (2007) Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Annals of Oncology. 18, 1437–1449.

8. Colak, D., Oguz, A. et al. (2014) Morphine: Patient Knowledge and Attitudes in the Central Anatolia Part of Turkey. Asian Pac J Cancer Prev, 15 (12), 4983-4988.

9. Weinstein, S.M., Janjan, N. (2014) Management of Pain. Cancer net work, Home of the Journal Oncology. 1-10.

10. International Association for the Study of Pain(IASP). Classification of chronic pain.Pain .1986;24:s1.

11. Global Year Against Cancer Pain. (2008-2009) Total Cancer Pain.

12. Lapointe, J. cancer-related pain: The Role of Occupational Therapy in Prevention and Management. Occupational Therapy Now. 14.5, 10-12.

13. Brook Off D.Chronic pain.A new disease? Hosp. Pract.2000.35:45.

14. Russell, K., Portenoy, M.D. (1989) Cancer Pain Epidemiology and Syndromes. Cancer. 63(11), 2298-2307.

15. Global Year Against Cancer Pain. (2008-2009) Epidemiology of Cancer Pain.

16. American Cancer Society. (2014) Guide to Controlling Cancer Pain.

17. Raphael, J., Hester, J. et al. (2010) Palliative Care Section, Cancer Pain: Part 2. Pain Medicine. 11, 872–896.

18. Chia-Chin, L., Yuen-Liang, L. et al. (2003) Effect of Cancer Pain on Performance Status, Mood States, and Level of Hope Among Taiwanese Cancer Patients. Journal of Pain and Symptom Management. 25(1), 29-37.