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Reflection of Pain in Cancer Patients Using a New Screening Tool for Psychological Distress

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ABSTRACT

Objectives : The objective of this study was to investigate the relationship between psychological distress and pain in cancer patients.

Methods : 249 patients with cancer who visited National Health Insurance Service Ilsan Hospital between April 2013 and March 2014 were evaluated with National Cancer Center Psychological Symptom Inventory(NCC-PSI) which consisted of Modified Distress Thermometer(MDT) and Modified Impact Thermometer(MIT). Each scale was divided into 3 subscales targeting separate symptoms: insomnia, anxiety, and depression. Psychological distress was defined as positive for those who scored above the cutoff values in at least one of all six subscales. The Numeric Rating Scale for Pain(NRS-Pain) was used to assess the subjective severity of pain. Logistic regression was performed to investigate the association between psychological distress and pain.

Results : Univariate logistic regression analysis showed that pain, gender, compliance, and two subscale scores of Hospital Anxiety and Depression Scale(HADS) were significantly associated with psychological distress. Multivariate logistic regression analysis showed that pain and HADS anxiety subscale score maintained a statistically significant association with psychological distress adjusted for variables including age, gender, years of education, Eastern Cooperative Oncology Group performance status, cancer stage, Charlson Comorbidity Index, compliance, and HADS depression subscale score. One point increase in pain was 1.31 times more likely to cause psychological distress. In secondary analysis, pain was significantly associated with all subscales of NCC-PSI, except MIT-anxiety subscale.

Conclusions : This study suggests that NCC-PSI, a screening tool for psychological distress, reflects pain. We recommend that physicians who treat cancer patients consider the examination of psychological distress which provides comprehensive evaluation of various factors regarding quality of life.

KEY WORDS : Psychological distress · Pain · Distress thermometer · Impact thermometer · Cancer.

INTRODUCTION

Distress is defined by the National Comprehensive Cancer Network(NCCN) as a "multifactorial unpleasant emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope effectively with can-

cer".[1] Increasing evidence of its association with poor treatment compliance,[2] low quality of life,[3] and high mortality[4] has led to a development of assessment tool that recognizes distress as a independent value.[5] Furthermore, Canadian Strategy for Cancer Control(CSCC) designated emotional distress as the sixth vital sign.[6]

Earlier studies suggested that pain does not only affect the quality of life, but may also be a predictor of survival.[7,8] A recent randomized controlled study reporting the impact of the screening program on distress, anxiety, and depression in lung and breast cancer patients showed that patients showed less improvement in distress while improvements in anxiety and depression were significantly greater.[9] This suggests that there might be other factors contributing to distress besides anxiety and depression, two of which commonly brought up in discussion of distress. Along with the four standard vital signs in medical settings, pain is involved in 50−90% of cancer patients.[10,11] Pain, could be one of the contributing factors since many previous studies showed significant association with depression and anxiety in cancer patients.[12-14]

Growing emphasis on screening for distress and need for brevity of the scale for feasible utilization developed Distress Thermometer(DT), a one-item screening tool introduced by the NCCN.[15] To improve the DT, adding more specific thermometers that enquire about anxiety, depression, anger and desire for help was found effective in British study.[16] The combination method with the Impact Thermometer(IT) which considered the impact that distress is having on the individual was also shown effective in identifying distress.[17] In 2009, as a part of recommendations for distress management to improve quality of life in cancer patients, National Cancer Center(NCC) endorsed by the Ministry of Health and Welfare in South Korea developed NCC Psychological Symptom Inventory(NCC-PSI), a distress screening tool based on DT and IT.[18] The NCC-PSI was validated for screening distress in Korean cancer patients and was developed through literature review, research meetings, and domestic expert consensus which was a multidisciplinary team; psychiatrists, psychologists, social workers, nurses, and health policy experts.[18] As shown in the studies of Europe, anxiety and depression were often included in modified version of distress thermometer to overcome the translation problems of the word "distress".[16,19,20] Insomnia, although not included in routine distress screening tools of other countries, was included in NCC-PSI as supported by Korean experts in various aspects: insomnia is an independent risk factor for depression and anxiety,[21,22] has close relationship with quality of life,[23] and it is appropriate to focus primarily on the patient's complaint in the order of frequency.[18]

To our knowledge, there has been no study that investigated the seemingly close relationship between pain and distress using a screening tool specifically designed for distress. The purpose of this study was to investigate the relationship between pain and distress in Korean cancer patients. The secondary objective was to identify the relationship between pain and each subscale of NCC-PSI.

METHODS

1. Participants

Inpatients and outpatients who were diagnosed with cancer and visited National Health Insurance Service Ilsan Hospital between April 2013 and March 2014 were eligible for this study. Inclusion criteria were age of 20 and more, ability to comprehend the questions and the purpose of the survey, and the written consent of participation in the study. Exclusion criterion was not applied. The survey was performed at the time of visit for all patients. This study was approved by the Institutional Review Board of National Health Insurance Service Ilsan Hospital.

2. Measures

Standardized questions in the survey provided sociodemographic information(e.g. age, gender, marital status, education, and employment status). Clinical information including cancer stage, time since cancer diagnosis, Eastern Cooperative Oncology Group(ECOG) performance status, and Charlson comorbidity index[24] was obtained by medical chart review and physicians' evaluation.

National Cancer Center Psychological Symptom Inventory (NCC-PSI) was used to evaluate patients' distress. The English version of NCC-PSI is shown in the supplementary data. NCC-PSI was developed by the National Cancer Center(NCC) in South Korea and is composed of two parts, Modified Distress Thermometer(MDT) and Modified Impact Thermometer (MIT). Both parts consist of three subscales targeting separate symptoms: insomnia, anxiety, and depression. For each particular symptom, during the past week, patients were instructed to indicate the severity for MDT and the level of impact from the symptom on their daily life activity for MIT. Thus, there are 6 questions in total and patients should choose the number on an 11-point Likert scale with scores ranging from 0(not at all) to 10(extremely). Scores equal to and more than 4 points were considered significant for each question. Psychological distress was defined to be positive for those who scored above the cutoff values in at least one of all six subscales.

The Korean version of Hospital Anxiety and Depression Scale(HADS) was used to measure anxiety and depression in this study.[25] It consists of two subscales, one measuring anxiety (HADS-A), and another measuring depression(HADS-D).

Each subscale comprises of seven items and each item is scored on a 4-point scale(0 to 3). Subscale scores of 8 and more were considered clinical cases.[26] The Numeric Rating Scale for Pain(NRS-Pain) was used to assess the subjective severity of pain with scores from 0(no pain) to 10(highest pain).

3. Statistical analysis

Univariate and multivariate logistic regression was performed to investigate the association between psychological distress and variables including sociodemographic factors, clinical factors, and HADS subscale scores. Psychological distress was fixed as independent variable and other factors were put in as dependent variable in univariate logistic regression analysis. Variables that showed p-value under 0.05 and factors considered clinically important such as age, years of education, ECOG performance status, cancer stage, and Charlson comorbidity index were included in the multivariate logistic regression analysis as covariates. The secondary analysis was performed to find out which subscale of NCC-PSI was related to the pain score. Multivariate logistic regression was used in the secondary analysis with pain fixed as the independent binary variable. Covariates in the secondary analysis included age, gender, years of education, ECOG performance status, cancer stage, Charlson comorbidity index, compliance, HADS-A, HADS-D, and each subscale score of MDT and MIT. P-value below 0.05 was considered statistically significant in all analysis. Statistical Package for Social Sciences(SPSS) version 22.0 by IBM was used for the analysis.

RESULTS

Table 1 provides sociodemographic and clinical characteristics of the 249 participants of this study. There were 123 patients(49.4%) who showed positive in distress screening. The mean age was 61.9 years(S.D.=12.5) and the mean educated year was 11.7 years(S.D.=3.5). More than half of the participants were male(62.2%), and employed(64.7%). The majority of participants were married(74.7%) and living with someone (88.8%). Most of the participants were diagnosed with cancer within 6 months(78.7%), were rated 1 according to the ECOG performance status(62.2%). The mean Charlson comorbidity index was 5.1(S.D.=3.2). Largest portion of participants were in stage 4(43.4%). The mean scores of symptom scales are shown in Table 2. The mean NRS-Pain score was 1.74(S.D.=2.28) and the mean scores of HADS-A and HADS-D were 5.76(S.D.=4.01) and 7.67(S.D.=3.20), respectively.

The association between psychological distress and variables including sociodemographic and clinical factors is shown in Table 3. Univariate logistic regression analysis showed that pain, gender, compliance, HADS-A, and HADS-D were sig-

Table 1. Sociodemographic and clinical characteristics of the study sample

Characteristics	No. of patients(%) (Total N=249)
Distress	
Positive	123(49.4)
Negative	126(50.6)
Age (years), Mean±S.D.	61.9±12.5
Gender	
Male	155(62.2)
Female	94(37.8)
Marital status	
Not married*	63(25.3)
Married	183(74.7)
Education (years), Mean±S.D.	11.7±3.5
Employment status	
Unemployed	88(35.3)
Employed	161(64.7)
Living alone	
Yes	28(11.2)
No	221(88.8)
Alcohol consumption	
No	199(79.9)
Yes	50(20.1)
Smoking	
No	188(75.5)
Yes	61(24.5)
Months since cancer diagnosis	
<6 months	196(78.7)
6-12 months	22(8.8)
> 12 months	31(12.4)
ECOG†	
0	67(26.9)
1	155(62.2)
2	20(8.0)
3	7(2.8)
4	0(0)
Cancer Type	
Breast cancer	36(14.5)
Colorectal cancer	131(52.6)
Hematologic malignancy	47(18.8)
Other Solid cancer	35(14.1)
Cancer Stage	
1	8(3.2)
2	43(17.3)
3	72(28.9)
4	108(43.4)
Missing	18(7.2)
Charlson comorbidity index, Mean±S.D.	5.1±3.2
Compliance	
Good	223(89.6)
Poor	26(10.4)

∗ : single/divorced/widowed, † : Eastern Cooperative Oncology Group performance status

Table 2. The mean scores of symptom scales

Characteristics	Mean(S.D.)
MDT*	
Insomnia	2.59(2.70)
Anxiety	2.77(2.85)
Depression	2.65(2.92)
MIT†	
Insomnia	2.11(2.53)
Anxiety	2.34(2.76)
Depression	2.22(2.72)
NRS-Pain‡	1.74(2.28)
HADS-A§	5.76(4.01)
HADS-D‖	7.67(4.20)

∗ : Modified Distress Thermometer, † : Modified Impact Thermometer, ‡ : Numeric Rating Scale for Pain, § : Hospital Anxiety and Depression Scale-Anxiety, ‖ : Hospital Anxiety and Depression Scale-Depression

nificantly associated with psychological distress. These variables that showed significant association in univariate analysis and other variables that were presumed to be clinically relevant with psychological distress(e.g. education, ECOG performance status, cancer stage, and Charlson comorbidity index) were included in the multivariate analysis. Multivariate logistic regression analysis showed that pain and HADS-A maintained a statistically significant association with psychological distress adjusted for variables mentioned above. One point increase in pain was 1.31 times more likely to cause psychological distress.

To identify the influence of pain on each subscale in NCC-PSI, multivariate analysis was once again performed separately with all six subscales(MDT-insomnia, MIT-insomnia, MDT- anxiety, MIT-anxiety, MDT-depression, and MIT-de-

Table 3. Odds ratios(OR) for psychological distress by patient characteristics

Characteristics		Univariate				Multivariate			
		OR	95% CI* for OR		p-value	OR	95% CI for OR		p-value
			Lower	Upper			Lower	Upper	
Age		0.98	0.96	1.00	0.11	1.00	0.97	1.03	0.99
Gender	Male	1				1			
	Female	1.94	1.15	3.26	0.01	1.57	0.71	3.44	0.26
Education		1.06	0.98	1.14	0.15	1.05	0.94	1.17	0.40
Marital status	Not married	1				−			
	Married	0.85	0.48	1.51	0.58	−			
Employment status	Unemployed	1				−			
	Employed	1.58	0.94	2.67	0.09	−			
Living alone	Yes	1				−			
	No	0.70	0.32	1.56	0.39	−			
NRS-pain†		1.39	1.21	1.60	<0.01	1.31	1.08	1.59	<0.01
Alcohol consumption	No	1				−			
	Yes	1.26	0.68	2.35	0.47	−			
Smoker	No	1				−			
	Yes	1.08	0.61	1.92	0.80	−			
Months since diagnosis	<6 months	1				−			
	6−12 months	0.90	0.37	2.19	0.82	−			
	>12 months	1.72	0.79	3.73	0.17	−			
ECOG‡	0	1				1			
	1	1.13	0.63	2.00	0.68	0.88	0.40	1.93	0.74
	2	2.29	0.81	6.46	0.12	0.52	0.10	2.80	0.45
	3	7.40	0.84	64.88	0.07	0.14	0.01	2.61	0.19
Cancer stage	I	1				1			
	II	1.26	0.28	5.72	0.76	2.62	0.43	16.05	0.30
	III	0.80	0.19	3.45	0.77	2.05	0.36	11.80	0.42
	IV	1.08	0.26	4.53	0.92	1.15	0.05	25.81	0.93
Charlson comorbidity index		1.01	0.94	1.09	0.79	1.06	0.70	1.61	0.80
Compliance	Good	1				1			
	Poor	2.53	1.06	6.06	0.04	2.29	0.59	8.85	0.23
HADS-A§		1.53	1.37	1.72	<0.01	1.51	1.31	1.74	<0.01
HADS-D‖		1.22	1.14	1.32	<0.01	1.02	0.92	1.11	0.67

∗ : Confidence Interval, † : Numeric Rating Scale for Pain, ‡ : Eastern Cooperative Oncology Group performance status, § : Hospital Anxiety and Depression Scale-Anxiety, ‖ : Hospital Anxiety and Depression Scale-Depression

Table 4. Odds ratios for positive screening in each subscale of Modified Distress Thermometer and Modified Impact Thermometer by pain

	NRS-Pain[†]	
	OR[†] (95% CI[§])	p-value
MDT[∥]		
Insomnia	1.27(1.08−1.49)	<0.01*
Anxiety	1.33(1.10−1.60)	<0.01*
Depression	1.36(1.12−1.64)	<0.01*
MIT[¶]		
Insomnia	1.29(1.09−1.52)	<0.01*
Anxiety	1.19(1.00−1.43)	0.06
Depression	1.25(1.03−1.50)	0.02*

Each odds ratio was adjusted for other variables including age, gender, years of education, Eastern Cooperative Oncology Group(ECOG) performance status, cancer stage, Charlson Comorbidity Index, compliance, HADS-A and HADS-D. * : p< 0.05 were considered statistically significant, † : Numeric Rating Scale for Pain, ‡ : Odds Ratio, § : Confidence Interval, ∥ : Modified Distress Thermometer, ¶ : Modified Impact Thermometer

pression). As shown in Table 4, all the subscales, except MIT-anxiety, were significantly associated with pain. MDT-depression subscale showed highest odds ratio with pain(OR=1.36).

DISCUSSION

This was the first study that investigated the relationship between pain and psychological distress, using a distress screening tool based on DT and IT. We found that psychological distress was significantly associated with pain in Korean cancer patients after adjusting for the effects of psychosocial and clinical variables(e.g. age, gender, years of education, ECOG performance status, cancer stage, and Charlson comorbidity index). The secondary analysis revealed that, pain was significantly associated with all subscales of NCC-PSI, except MIT-anxiety subscales.

The primary result of this study shows that NCC-PSI reflects pain in cancer patients effectively. It is consistent with previous report that pain was one of the concerns contributing to distress as shown in the patient self-reports.[27] Close relationship between pain and anxiety was also shown in patients with severe medical illness.[28] NCC-PSI is different from other distress screening tools in that insomnia is included in the subscale and is the first symptom inquired to the patient. During the expert consensus in the development of NCC-PSI, some Korean experts insisted that patients may feel uncomfortable when they face the word "depression" and "anxiety" before "insomnia" and thus, questions are asked in the following order to minimize stigmatization: insomnia, anxiety, and depression.[18] Being more simple and comprehensive than other psychometric scales, NCC-PSI is could be applied easily in the clinical setting.

As much as the distress is sensitive to the pain, relationship between the two is inseparable. In this study, the mean score of pain is low and even lower than each mean score of subscales for distress. Possible reason for underreported pain scores may be that Asians are more hesitant to express pain than they are to express physical and psychological symptoms as shown in previous study.[29] Since there are 6 subscales in NCC-PSI and positive result for distress screening necessitates at least one subscale to be over the cutoff value, further analysis was needed to look for any one-sided scoring of subscale.

In the secondary analysis, pain showed significant association with all subscales of NCC-PSI, except MIT-anxiety. Even MIT-anxiety subscale showed high tendency for association with pain. Thus, screening cancer patients with NCC-PSI for distress would also be helpful for detecting possible pain as all the subscales were shown to be effective, in general, for reflecting pain. MDT-anxiety and MDT-insomnia showing significantly association with pain severity could be the result of the previous reports where pain is a contributing factor for anxiety and insomnia.[30-33] The question of causality between depression and pain is still a debatable issue where one emphasizes that depression amplifies pain in cancer patients[34] and another considers depression as a secondary consequence of chronic pain.[14,35] While further studies are needed to clarify the causality, our results showed that pain has clinically significant influence on all three different aspects of distress as measured by NCC-PSI: insomnia, anxiety, and depression. In other words, distress is one thing that cancer patients with pain are much likely to be associated with. Oncologists should be aware of any distress the patient might have with all the effort including the use of psychiatric consultation.

Apart from pain, multivariate logistic regression showed that psychological distress was associated with HADS-A, but not HADS-D. Considering the result of univariate logistic regression where HADS-A and HADS-D were both associated with psychological distress, anxiety was more significantly and independently associated with distress. Patients might have not expressed depression enough compared to anxiety because of the prejudice that being depressed is same as having incurable mental illness[36] There are two more things that could have affected difference between HADS-A and HADS-D. First, the majority(78.7%) of study population was diagnosed with cancer within 6 months and anxiety might have prevailed in the beginning as similar results were found in previous studies.[37,38] Second, almost half(43.4%) of the patients had stage 4 cancer and there could have been more anxiety about unpredictable future in advanced cancer.[39,40]

There were several limitations in this study. First, the sample size was not large enough to validate the results. Second,

due to the heterogeneity of cancer in current study, both pain and distress could have been affected by certain type of cancer. To overcome the influence of cancer type on the results, other clinical variables such as ECOG performance status, cancer stage, and Charlson comorbidity index were taken into account. Third, there was no clinician rated scale which could have allowed us to compare with self-reported symptom scales and to support the results more strongly. Despite these limitations, this study successfully showed the close relationship between pain and psychological distress in cancer patients using specific screening tool specially designed and standardized for Korean people.

The present study suggests that NCC-PSI, a screening tool for psychological distress, reflects pain. We recommend that oncologists screen cancer patients for any psychological distress which provides comprehensive evaluation of various factors regarding quality of life.

REFERENCES

(1) **Holland J.** NCCN practice guidelines for the management of psychosocial distress. Oncology 1999;13:113-147.

(2) **Colleoni M, Mandala M, Peruzzotti G, Robertson C, Bredart A, Goldhirsch A.** Depression and degree of acceptance of adjuvant cytotoxic drugs. Lancet 2000;356:1326-1327.

(3) **Skarstein J, Aass N, Fossa SD, Skovlund E, Dahl AA.** Anxiety and depression in cancer patients: relation between the Hospital Anxiety and Depression Scale and the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire. J Psychosom Res 2000;49:27-34.

(4) **Prieto JM, Atala J, Blanch J, Carreras E, Rovira M, Cirera E, Espinal A, Gasto C.** Role of depression as a predictor of mortality among cancer patients after stem-cell transplantation. J Clin Oncol 2005;23:6063-6071.

(5) **Roth AJ, Kornblith AB, Batel-Copel L, Peabody E, Scher HI, Holland JC.** Rapid screening for psychologic distress in men with prostate carcinoma. Cancer 1998;82:1904-1908.

(6) **Rebalance Focus Action Group.** A position paper: Screening key indicators in cancer patients-Pain as a 5th vital sign and emotional distress as a 6th vital sign. Canadian Strategy for Cancer Control Bulletin 2005;7:4(suppl).

(7) **Herndon JE, Fleishman S, Kornblith AB, Kosty M, Green MR, Holland J.** Is quality of life predictive of the survival of patients with advanced nonsmall cell lung carcinoma? Cancer 1999;85:333-340.

(8) **Di Maio M, Gridelli C, Gallo C, Manzione L, Brancaccio L, Barbera S, Robbiati S, Ianniello G, Ferrau F, Piazza E.** Prevalence and management of pain in Italian patients with advanced non-small-cell lung cancer. British Journal of Cancer 2004;90:2288-2296.

(9) **Carlson LE, Groff SL, Maciejewski O, Bultz BD.** Screening for distress in lung and breast cancer outpatients: a randomized controlled trial. J Clin Oncol 2010;28:4884-4891.

(10) **Cleeland CS, Gonin R, Hatfield AK, Edmonson JH, Blum RH, Stewart JA, Pandya KJ.** Pain and its treatment in outpatients with metastatic cancer. N Engl J Med 1994;330:592-596.

(11) **Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Coyle N, Smart-Curley T, Kemeny N, Norton L, Hoskins W, Scher H.** Symptom prevalence, characteristics and distress in a cancer population. Qual Life Res 1994;3:183-189.

(12) **Akechi T, Okamura H, Nishiwaki Y, Uchitomi Y.** Psychiatric disorders and associated and predictive factors in patients with unresectable nonsmall cell lung carcinoma: a longitudinal study. Cancer 2001;92:2609-2622.

(13) **Ko HJ, Seo SJ, Youn CH, Kim HM, Chung SE.** The Association between Pain and Depression, Anxiety, and Cognitive Function among Advanced Cancer Patients in the Hospice Ward. Korean J Fam Med 2013;34:347-356.

(14) **Massie MJ, Holland JC.** The cancer patient with pain: psychiatric complications and their management. Med Clin North Am 1987;71:243-258.

(15) **Network NCC.** Distress management. Clinical practice guidelines. Journal of the National Comprehensive Cancer Network: JNCCN 2003;1:344.

(16) **Mitchell AJ, Baker-Glenn EA, Granger L, Symonds P.** Can the Distress Thermometer be improved by additional mood domains? Part I. Initial validation of the Emotion Thermometers tool. Psychooncology 2010;19:125-133.

(17) **Baken DM, Woolley C.** Validation of the Distress Thermometer, Impact Thermometer and combinations of these in screening for distress. Psychooncology 2011;20:609-614.

(18) **Kim J.** Development of recommendation for distress management toward improvement of quality of life in cancer patients. Seoul: Ministry of Health & Welfare 2009.

(19) **Gil F, Grassi L, Travado L, Tomamichel M, Gonzalez JR.** Use of distress and depression thermometers to measure psychosocial morbidity among southern European cancer patients. Support Care Cancer 2005;13:600-606.

(20) **Muszbek K, Balogh E, Molnár M, Rohánszky M, Varga K.** Screening for distress of Hungarian cancer patients, validation study of Hungarian version of HADS. In Psycho-Oncology: JOHN WILEY & SONS LTD THE ATRIUM, SOUTHERN GATE, CHICHESTER PO19 8SQ, W SUSSEX, ENGLAND; 2004.

(21) **Jansson-Frojmark M, Lindblom K.** A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. J Psychosom Res 2008;64:443-449.

(22) **Johnson EO, Roth T, Breslau N.** The association of insomnia with anxiety disorders and depression: exploration of the direction of risk. J Psychiatr Res 2006;40:700-708.

(23) **Walsh JK, Krystal AD, Amato DA, Rubens R, Caron J, Wessel TC, Schaefer K, Roach J, Wallenstein G, Roth T.** Nightly treatment of primary insomnia with eszopiclone for six months: effect on sleep, quality of life, and work limitations. Sleep 2007;30:959-968.

(24) **Kil SR, Lee SI, Khang YH, Lee MS, Kim HJ, Kim SO, Jo**

MW. Development and validation of comorbidity index in South Korea. Int J Qual Health Care 2012;24:391-402.

(25) **Oh SM, Min KJ, Park DB.** A study on the standardization of the hospital anxiety and depression scale for Koreans: a comparison of normal, depressed and anxious groups. Journal of Korean Neuropsychiatric Association 1999;38:289-296.

(26) **Carroll BT, Kathol RG, Noyes R, Wald TG, Clamon GH.** Screening for depression and anxiety in cancer patients using the Hospital Anxiety and Depression Scale. General Hospital Psychiatry 1993;15:69-74.

(27) **Larouche S, Edgar L.** The measure of distress. Oncol Exch 2004;3:34-39.

(28) **Oh J, Sohn JH, Shin CS, Na SH, Yoon HJ, Kim JJ, Park S, Park JY.** Mutual relationship between anxiety and pain in the intensive care unit and its effect on medications. J Crit Care; 2015.

(29) **Im E-O.** Ethnic differences in cancer pain experience. Nursing research 2007;56:296.

(30) **Valentine AD.** Cancer pain and depression: management of the dual-diagnosed patient. Current Pain and Headache Reports 2003;7:262-269.

(31) **Theobald DE.** Cancer pain, fatigue, distress, and insomnia in cancer patients. Clin Cornerstone 2004;6 Suppl 1D:S15-21.

(32) **Velikova G, Selby PJ, Snaith PR, Kirby PG.** The relationship of cancer pain to anxiety. Psychotherapy and Psychoso-matics 1995;63:181-184.

(33) **George M, Elias A, Shafiei M.** Insomnia in Cancer--Associations and Implications. Asian Pac J Cancer Prev 2015;16:6711-6714.

(34) **Spiegel D, Sands S, Koopman C.** Pain and depression in patients with cancer. Cancer 1994;74:2570-2578.

(35) **Hendler N.** Depression caused by chronic pain. Journal of Clinical Psychiatry;1984.

(36) **Cho SJ, Lee JY, Hong JP, Lee HB, Cho MJ, Hahm BJ.** Mental health service use in a nationwide sample of Korean adults. Soc Psychiatry Psychiatr Epidemiol 2009;44:943-951.

(37) **Tan SM, Beck KR, Li H, Lim EC, Krishna LK.** Depression and anxiety in cancer patients in a Tertiary General Hospital in Singapore. Asian J Psychiatr 2014;8:33-37.

(38) **Cardoso G, Graca J, Klut C, Trancas B, Papoila A.** Depression and anxiety symptoms following cancer diagnosis: a cross-sectional study. Psychol Health Med 2015:1-9.

(39) **Johanes C, Monoarfa RA, Ismail RI, Umbas R.** Anxiety level of early- and late-stage prostate cancer patients. Prostate Int 2013;1:177-182.

(40) **Vodermaier A, Linden W, MacKenzie R, Greig D, Marshall C.** Disease stage predicts post-diagnosis anxiety and depression only in some types of cancer. Br J Cancer 2011;105: 1814-1817.