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ABSTRACT

Background: Screening symptoms is important for appropriate symptom management. It remains uncertain which scores on the Edmonton Symptom Assessment System-Revised (ESAS-r) comprise the optimal cut-off points to determine symptom severity for Japanese cancer patients.

Objectives: To investigate optimal cut-off points for individual ESAS-r items for detecting symptom severity and evaluate the screening performance of the ESAS-r depression item, in Japanese cancer patients.

Methods: We recruited palliative care cancer patients from five tertiary acute hospitals in Japan. We asked participants to complete the ESAS-r Japanese version, Verbal Rating Symptom Severity Scale (VRS), and Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR) Japanese version. We calculated sensitivity and specificity for detecting severe and moderate/severe symptoms evaluated by VRS at different cut-off points of ESAS-r. We also calculated sensitivity and specificity for detecting both the presence of depression and moderate/severe depression evaluated by QIDS-SR at various cut-off points of depression item of the ESAS-r Japanese version.

Results: 292 participants completed the questionnaire. For most of ESAS-r symptoms, cut-off points to achieve the best balance between sensitivity and specificity were 5-7 for determining severe intensity, and 3-4 for determining moderate/severe intensity. For the ESAS-r depression item, a cut-off points of 2 achieved the best balance between sensitivity and specificity for detecting both presence of depression and moderate/severe depression.

Conclusions: The ESAS-r Japanese version can accurately represent the severity of many symptoms. The cut-off points established for determining the level of symptom severity using ESAS-r provides a guide for symptom management in Japanese cancer patients.

INTRODUCTION

Cancer patients usually suffer from a wide range of physical and psychological symptoms,[1] and high symptom burden can negatively affect patients' quality of life.[2] Thus, reducing symptom burden is one of the most important roles of palliative care for cancer patients. Routine application of symptom assessment tools such as the widely used Edmonton Symptom Assessment System (ESAS) may help identifying symptom burden.[3-8] After studies showed difficulties in interpreting and completing the original ESAS, a revised version (ESAS-r) was developed.[9] Previous studies in Western countries proposed cut-off points to classify severity of symptoms into mild, moderate, and severe by comparing verbally rated severity scales,[10,11] or functional interference[12], while other studies proposed cut-off points specifically for the ESAS depression item for the diagnosis of depression.[13,14] However, the meaning of a word or the value of a number can be influenced by cultural and linguistic background, so the ESAS cut-off points determined in previous international studies may not be directly applicable to Japanese cancer patients.

We aimed to 1) explore optimal cut-off points for each ESAS-r item to determine symptom severity, and 2) evaluate the screening performance of ESAS-r depression items, in Japanese cancer patients.

METHODS

Patients

This is a prospective cross-sectional study. We recruited palliative care patients from five tertiary-care hospitals (National Cancer Center Hospital East, Japanese Red Cross Medical Center, Okayama University Hospital, St. Luke's International Hospital, Okayama Saiseikai General Hospital) in Japan. All participants had clinically or pathologically diagnosed cancer, were 20 years or older, and were able to understand spoken and written Japanese. We excluded patients with altered mental status or those who were inappropriate to participate due to severe physical or psychological symptoms, as judged by the researchers. We included both ambulatory and hospitalized patients.

Edmonton Symptom Assessment System-Revised (ESAS-r) Japanese Version

ESAS-r is a validated, patient-reported, symptom assessment tool that is widely used in palliative care.[3-5] ESAS-r assesses nine physical and psychological symptoms (pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, well-being) on an 11-point Likert scale (0-10; 0 = no symptom, 10 = worst possible symptom). The Japanese version of ESAS-r has been validated.[15]

Verbal Rating Symptom Severity Scale (VRS)

We also evaluated the severity of all nine symptoms of ESAS-r on a 4-point verbal rating scale (none, mild, moderate, or severe). Although VRS has not been formally validated, we had decided to use VRS to compare the result with previous research.[11]

Quick Inventory of Depressive Symptomatology- Self-Report (QIDS-SR) Japanese version

QIDS-SR is a self-reported depression assessment tool that is widely used in clinical practice.[16] QIDS-SR contains 16 items assessing nine symptom domains that correspond to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-Ⅳ) criteria for major depressive disorder (sad

mood, concentration/decision-making, outlook [self-criticism], suicidal ideation, general interest, energy/fatigability, sleep disturbance, decrease/increase in appetite/weight, psychomotor agitation/retardation). QIDS-SR rates the severity of each item over the preceding seven days on a 4-point Likert scale (0-3: 0 = none, 3 = most severe). The total QIDS-SR score is calculated from the highest score for any one of four items of sleep disturbance, four items of decrease/increase in appetite/weight, two items of psychomotor agitation/retardation, and each item of the other six symptoms (total score range, 0-27). We chose QIDS-SR, because this tool could specifically detect major depression disorder whereas other tools, such as the Patient Health Questionnaire-9 and Hospital Anxiety and Depression Scale, capture not only major depression, but also adjustment disorder or anxiety. Depression is considered as present when the QIDS-SR total score is 6 or higher, and moderate/severe when the total score is 11 or higher. The Japanese version of QIDS-SR has been validated.[17]

Demographic Data

We collected age, gender, primary cancer site, staging of disease, and ECOG performance status (PS) as demographic data.

Procedure

From February 2013 and June 2014, all participants completed a questionnaire covering the ESAS-r Japanese version, VRS, and QIDS-SR Japanese version, immediately after the enrolment. We also collected all demographic data from face-to-face interview and medical records.

Data analyses

We conducted this study as a part of the validation study of ESAS-r Japanese version.[15] Thus, no priori sample size calculation had not been performed for this analysis, and sample sizes were based on available data. We calculated sensitivity and specificity for detecting severe and moderate/severe symptoms

evaluated by VRS at different cut-off points of the ESAS-r Japanese version. We also calculated sensitivity and specificity for detecting presence of depression and moderate/severe depression evaluated by the QIDS-SR Japanese version at various cut-off points of depression item of the ESAS-r Japanese version. Receiver operating characteristic (ROC) curves were used to identify optimal cut-off points for each symptom.[18] We analyzed demographic data descriptively. For all statistical analyses, we used the Japanese version of SPSS for Windows Ver. 19.0 (IBM Japan Institute, Tokyo, Japan).

Ethics

All participants provided written informed consent. The study was approved by the Institutional review board of each participating hospital, and conducted in accordance with the Declaration of Helsinki.

RESULTS

Table 1 shows the participants' demographic data. A total of 320 patients were recruited, of whom 28 were excluded from the analysis because they completed fewer than half of the questionnaire items. Thus, 292 patients completed the questionnaire and data for these patients were analyzed. The mean age of participants was 64.6 ± 12.1 and 64.4% (188/292) of participants were men. The most common primary cancer sites were lung, pancreas, colorectum, liver, and breast; 66.1% (193/292) were in the advanced stage of disease (StageⅣ or recurrent disease); 84.2% (246/292) were ECOG PS 2 or less; and most of participants were inpatients.

Symptom Prevalence in VRS and QIDS

Table 2 shows the prevalence and median score by the ESAS-r Japanese version for each symptom in each severity category rated by VRS. Very few participants had severe symptoms of drowsiness (n = 7), nausea (n = 3), and shortness of breath (n = 9). Although more than 50 participants had moderate/severe intensity for most symptoms, only 15 for nausea and 32 for shortness of breath had moderate/severe symptoms.

The presence of depression as defined by a QIDS score of 6 or more was reported by 70.9% (207/292) of participants, and moderate/severe depression as defined by a QIDS score of 11 or more was reported in 28.8% (84/292).

Optimal Cut-off Points and Screening Performance of the ESAS-r Japanese version for Detecting "Severe" and "Moderate/Severe" Symptoms

For each score rated by the ESAS-r Japanese version, we calculated sensitivity and specificity to determine the best cut-off points to detect severe and moderate/severe symptoms on VRS. The detection of severe symptoms showed variability in the best-fit cut-off points (Table 3): the optimal cut-off point was 5 for 4 symptoms (pain, tiredness, lack of appetite, and depression), and 6 for another two symptoms (anxiety

and well-being). For drowsiness, the optimal cut-off point was 7. Nausea and shortness of breath had optimal cut-off points of 1 and 3, respectively.

There was also variability among the best-fit cut-off points for detecting moderate/severe symptoms (Table 4). The optimal cut-off point was a score of 3 for five symptoms (pain, lack of appetite, shortness of breath, depression, and anxiety), 4 for two symptoms (tiredness, and well-being), 2 for nausea, and 5 for drowsiness.

The area under the ROC curve for all symptoms except for well-being was 0.90 or higher, which indicated excellent agreement between VRS and ESAS-r.

Screening Performance of the ESAS-r Depression Scale for Detecting Presence of Depression and Moderate/Severe Depression

For each ESAS-r depression score, we calculated sensitivity, specificity, and positive and negative predictive values to detect presence of depression and the severity rated as moderate/severe depression evaluated by QIDS (Table 5). The cut-off point of 2 provides the most acceptable balance between sensitivity and specificity for detecting both the presence of depression (sensitivity 0.57, specificity 0.88) and the severity rated as moderate/severe depression (sensitivity 0.81, specificity 0.71). The areas under the ROC curve of the ESAS-r depression score for detecting the presence of depression and the severity rated as moderate/severe depression were 0.74 and 0.79, respectively.

DISCUSSION

To the best of our knowledge, this is the first study to evaluate optimal cut-off points for each ESAS-r item used in assessing symptom severity in Japanese cancer patients. The current study provided two major findings.

First, scores of the ESAS-r Japanese version and verbally rated symptom severity were strongly related for all nine symptoms. For all ESAS-r items except for well-being, and at both severe and moderate/severe symptom ratings by VRS, the area under the ROC curves were greater than 0.90. The area under the ROC curve greater than 0.90 indicate excellent agreement between ESAS-r and VRS.[18,19] Thus, the our result suggested that ESAS-r Japanese version could accurately predict verbally rated severe symptom intensity.

Second, the cut-off point of 2 in the ESAS-r depression item provided the most acceptable balance between sensitivity and specificity for diagnosing both presence of depression and moderate/severe depression, in agreement with previous findings.[13,14] However, for diagnosing presence of depression, the cut-off point of 2 or more showed low sensitivity. In addition, for diagnosing moderate/severe depression, a cut-off point of 2 or more showed fair sensitivity, but low specificity. Thus, the ESAS-r depression item should not be used as a single diagnostic tool for depression, and cancer patients should be assessed more comprehensively following the DSM criteria for major depressive disorder.

This study had several limitations. First, there was a paucity of patients with severe intensity in all nine symptoms. This might be due to good performance status in most participants and affect our results. Second, we enrolled a only small number of participants with moderate/severe symptom intensity of nausea and shortness of breath. For these two symptoms, the cut-off points for severe and moderate/severe symptom intensity were either equal (shortness of breath: the cut-off point of 3 for both severe and moderate/severe) or paradoxical (nausea: the cut-off point of 1 for severe and 2 for moderate/severe). These results may indicate that 15 for nausea and 32 for shortness of breath of 298 participants is not an adequate number for analyzing screening performance for ESAS-r items. Another limitation was the prevalence of depression evaluated by QIDS (70.9%) in current study was much higher than previous studies involving

Japanese cancer patients.[20-25] QIDS contains some items related to physical symptoms such as appetite loss and sleep disturbance. In advance cancer patient, these symptoms are common because of not only disease itself, but also adverse effect of cancer treatment. Thus, it is possible that the participants in our study provided higher score in QIDS due to physical symptoms from disease and cancer treatment. This may explain the reason of high prevalence of severe depression evaluated by QIDS, which might contribute to the low sensitivity of depression item of ESAS-r for screening the presence of depression in our study population. Finally, our study only included cancer patients. Thus, the results may not apply to symptom severity in patients with non-malignant diseases.

In conclusion, the ESAS-r Japanese version can accurately represent the severity of symptoms. Cut-off points presented in our study will provide a guide for symptom management in Japanese cancer patients.

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare

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REFERENCES

1. Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. Support Care Cancer 2000;8:175-9.
2. van den Beuken-van Everdingen MHJ, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Quality of Life and Non-Pain Symptoms in Patients with Cancer. Journal of pain and symptom management 2009;38:216-33.
3. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. Journal of palliative care 1991;7:6-9.
4. Nekolaichuk C, Watanabe S, Beaumont C. The Edmonton Symptom Assessment System: a 15-year retrospective review of validation studies (1991--2006). Palliative medicine 2008;22:111-22.
5. Watanabe SM, Nekolaichuk CL, Beaumont C. The Edmonton Symptom Assessment System, a proposed tool for distress screening in cancer patients: development and refinement. Psycho-oncology 2012;21:977-85.
6. Bruera E, Hui D, Dalal S, et al. Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. J Clin Oncol 2013;31:111-8.
7. Seow H, Barbera L, Sutradhar R, et al. Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. J Clin Oncol 2011;29:1151-8.
8. Yennurajalingam S, Frisbee-Hume S, Palmer JL, et al. Reduction of cancer-related fatigue with dexamethasone: a double-blind, randomized, placebo-controlled trial in patients with advanced cancer. J Clin Oncol 2013;31:3076-82.
9. Watanabe SM, Nekolaichuk C, Beaumont C, Johnson L, Myers J, Strasser F. A Multicenter Study Comparing Two Numerical Versions of the Edmonton Symptom Assessment System in Palliative Care Patients. Journal of pain and symptom management 2011;41:456-68.
10. Gill A, Daines P, Selby D. What do symptom scores mean: observations on discrepancies when defining symptoms using words and numbers. European journal of oncology nursing : the official journal of European Oncology Nursing Society 2010;14:435-8.
11. Selby D, Cascella A, Gardiner K, et al. A single set of numerical cutpoints to define moderate and severe symptoms for the Edmonton Symptom Assessment System. Journal of pain and symptom management 2010;39:241-9.
12. Given B, Given CW, Sikorskii A, et al. Establishing mild, moderate, and severe scores for cancer-related symptoms: how consistent and clinically meaningful are interference-based severity cut-points? Journal of pain and symptom management 2008;35:126-35.
13. Lloyd-Williams M, Dennis M, Taylor F. A prospective study to compare three depression screening tools in patients who are terminally ill. General hospital psychiatry 2004;26:384-9.
14. Vignaroli E, Pace EA, Willey J, Palmer JL, Zhang T, Bruera E. The Edmonton Symptom Assessment System as a screening tool for depression and anxiety. Journal of palliative medicine 2006;9:296-303.
15. Yokomichi N, Morita T, Nitto A, et al. Validation of the Japanese Version of Edmonton Symptom Assessment System-Revised. Journal of pain and symptom management 2015:In Press.
16. Rush AJ, Trivedi MH, Ibrahim HM, et al. The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biological psychiatry 2003;54:573-83.
17. Fujisawa D, Nakagawa A, Tajima M, Sado M, Kikuchi T, Iba M. Cross-cultural adaptation of the Quick inventory of depressive symptomatology, self-report (QIDS-SR). Jpn J Stress Sci 2010;25:43–52. [in Japanese].
18. Akobeng AK. Understanding diagnostic tests 3: Receiver operating characteristic curves. Acta Paediatr 2007;96:644-7.
19. Greiner M, Pfeiffer D, Smith RD. Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. Prev Vet Med 2000;45:23-41.
20. Akechi T. Major Depression, Adjustment Disorders, and Post-Traumatic Stress Disorder in Terminally Ill Cancer Patients: Associated and Predictive Factors. Journal of Clinical Oncology 2004;22:1957-65.
21. 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;92:2609-22.

22. Kugaya A, Akechi T, Okuyama T, et al. Prevalence, predictive factors, and screening for psychologic distress in patients with newly diagnosed head and neck cancer. Cancer 2000;88:2817-23.
23. Minagawa H, Uchitomi Y, Yamawaki S, Ishitani K. Psychiatric morbidity in terminally ill cancer patients. A prospective study. Cancer 1996;78:1131-7.
24. Okamura H, Watanabe T, Narabayashi M, et al. Psychological distress following first recurrence of disease in patients with breast cancer: prevalence and risk factors. Breast Cancer Res Treat 2000;61:131-7.
25. Okamura M. Psychiatric Disorders Following First Breast Cancer Recurrence: Prevalence, Associated Factors and Relationship to Quality of Life. Japanese Journal of Clinical Oncology 2005;35:302-9.

Table 1. Demographic data of all participants (n = 292)

	n (%)
Age (mean ± SD)	64.6 ± 12.1
Sex	
Male	188 (64.4)
Primary Cancer Site	
Lung	77 (26.4)
Pancreas	37 (12.7)
Colon/Rectum	26 (8.9)
Breast	24 (8.1)
Liver	24 (8.1)
Head/Neck	14 (4.8)
Bile duct/Gallbladder	13 (4.5)
Esophagus	12 (4.1)
Urological	12 (4.1)
Other	53 (18.2)
Stage	
Ⅰ	9 (3.1)
Ⅱ	27 (9.2)
Ⅲ	49 (16.8)
Ⅳ	133 (45.5)
Recurrent	60 (20.5)
ECOG Performance Status	
0-2	246 (84.2)
3-4	42 (14.4)
Study Setting	
Outpatient	66 (22.6)
Inpatient	226 (77.4)

SD denotes standard deviation.

Table 2. Prevalence and ESAS-r score for each VRS rating

	None n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Pain	115 (39.4)	123 (42.1)	36 (12.3)	18 (6.2)
Median ESAS-r score	0	2	5	8
Tiredness	101 (34.6)	122 (41.8)	51 (17.5)	18 (6.2)
Median ESAS-r score	0	2	5	8
Drowsiness	131 (44.9)	107 (36.6)	47 (16.1)	7 (2.4)
Median ESAS-r score	0	2	7	9
Nausea	243 (83.2)	34 (11.6)	12 (4.1)	3 (1.0)
Median ESAS-r score	0	2	6	7
Lack of appetite	155 (53.1)	71 (24.3)	44 (15.1)	21 (7.2)
Median ESAS-r score	0	3	5.5	8
Shortness of breath	194 (66.4)	66 (22.6)	23 (7.9)	9 (3.1)
Median ESAS-r score	0	2	6	9
Depression	126 (43.2)	108 (37.0)	44 (15.1)	14 (4.8)
Median ESAS-r score	0	2	5	8
Anxiety	114 (39.0)	111 (38.0)	52 (17.8)	15 (5.1)
Median ESAS-r score	0	2	5	9
Well-being	24 (8.2)	159 (54.5)	91 (31.2)	17 (5.8)
Median ESAS-r score	0	2	5	8

Table 3. Screening Performance of ESAS-r score for Detecting "Severe" Symptoms According to VRS

Symptom	ESAS-r Score	Sensitivity	Specificity	AUC (95% CI)
Pain	**5***	0.94	0.91	0.94 (0.85, 1.00)
	6	0.78	0.96	
Tiredness	4	0.94	0.71	0.93 (0.88, 0.98)
	5*	0.89	0.79	
	6	0.78	0.87	
Drowsiness	**7***	0.86	0.88	0.94 (0.86, 1.00)
	8	0.71	0.94	
Nausea	**1***	1.00	0.76	0.93 (0.83, 1.00)
	2	0.67	0.85	
Lack of appetite	**5***	0.95	0.82	0.96 (0.93, 0.99)
	6	0.86	0.89	
Shortness of breath	**3***	0.89	0.82	0.93 (0.86, 1.00)
	4	0.67	0.89	
Depression	**5***	0.86	0.86	0.90 (0.80, 1.00)
	6	0.64	0.94	
	7	0.64	0.95	
Anxiety	**6***	0.93	0.92	0.93 (0.83, 1.00)
	7	0.87	0.94	
Well-being	5	0.94	0.66	0.89 (0.81, 0.97)
	6*	0.82	0.83	
	7	0.76	0.86	

* Most appropriate balance cut-off point between sensitivity and specificity, according to Youden index[18].

Table 4. Screening Performance of ESAS-r score for Detecting "Moderate/Severe" Symptoms According to VRS

Symptom	ESAS-r Score	Sensitivity	Specificity	AUC (95% CI)
Pain	2	0.98	0.61	0.92 (0.88, 0.96)
	3*	0.87	0.79	
	4*	0.74	0.92	
Tiredness	3	0.90	0.71	0.91 (0.87, 0.95)
	4*	0.86	0.83	
	5	0.75	0.91	
Drowsiness	3	0.93	0.74	0.93 (0.89, 0.97)
	4	0.89	0.85	
	5*	0.85	0.90	
Nausea	1	0.93	0.79	0.93 (0.85, 1.00)
	2*	0.87	0.88	
	3	0.73	0.94	
	4	0.67	0.97	
Lack of appetite	**3***	0.95	0.80	0.95 (0.93, 0.97)
	4	0.85	0.88	
	5	0.78	0.92	
Shortness of breath	2	0.97	0.81	0.97 (0.95, 0.99)
	3*	0.97	0.89	
	4	0.78	0.96	
Depression	**3***	0.88	0.82	0.91 (0.86, 0.95)
	4	0.72	0.92	
	5	0.67	0.95	
Anxiety	**3***	0.90	0.76	0.91 (0.87, 0.95)
	4	0.76	0.88	
	5	0.70	0.92	
Well-being	3	0.94	0.56	0.86 (0.82, 0.90)
	4*	0.80	0.74	
	5	0.71	0.82	

* Most appropriate balance cut-off point between sensitivity and specificity, according to Youden index[18]

Table 5. Screening Performance of Each ESAS-r Depression Score for Detecting Presence and Moderate/Severe Depression According to QIDS-SR

	QIDS-SR-Depression Present				QIDS-SR-Moderate/Severe Depression			
ESAS-r Depression (n)	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
≧1 (159)	0.66	0.74	0.86	0.47	0.87	0.59	0.46	0.92
≧2* (129)	0.57	0.88	0.92	0.46	0.81	0.71	0.53	0.90
≧3 (94)	0.42	0.91	0.91	0.39	0.61	0.79	0.54	0.83
≧4 (61)	0.28	0.95	0.93	0.35	0.42	0.88	0.57	0.79
≧5 (51)	0.23	0.96	0.94	0.34	0.38	0.91	0.63	0.78
≧6 (27)	0.13	1.00	1.00	0.32	0.26	0.98	0.81	0.77
≧7 (22)	0.11	1.00	1.00	0.31	0.21	0.98	0.82	0.76
≧8 (15)	0.07	1.00	1.00	0.31	0.14	0.99	0.80	0.74
≧9 (7)	0.03	1.00	1.00	0.30	0.06	0.99	0.71	0.72
≧10 (4)	0.02	1.00	1.00	0.30	0.05	1.00	1.00	0.72

* Most appropriate balance cut-off point between sensitivity between specificity, according to Youden index[18].