

Prescreening of Patient-reported Symptoms using the Edmonton Symptom Assessment System (ESAS) in Outpatient Palliative Cancer Care

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Abstract

Background: Although early palliative care is associated with a better quality of life and improved outcomes in end-of-life cancer care, the criteria of palliative care referral are still elusive.

Methods: We collected patient-reported symptoms using the Edmonton Symptom Assessment System (ESAS) at the baseline, first, and second follow-up visit. The ESAS evaluates ten symptoms: pain, fatigue, nausea, depression, anxiety, drowsiness, dyspnea, sleep disorder, appetite, and wellbeing. A total of 71 patients were evaluable, with a median age of 65 years, male (62%), and the Eastern Cooperative Oncology Group (ECOG) performance status distribution of 1/2/3 (28%/39%/33%), respectively. **Results:** Twenty (28%) patients had moderate/severe symptom burden with the mean ESAS ≥ 5 . Interestingly, most of the patients with moderate/severe symptom burdens (ESAS ≥ 5) had globally elevated symptom expression. While the mean ESAS score was maintained in patients with mild symptom burden (ESAS<5; 2.7 at the baseline; 3.4 at the first follow-up; 3.0 at the second follow-up; P =0.117), there was significant symptom improvement in patients with moderate/severe symptom burden (ESAS ≥ 5 ; 6.5 at the baseline; 4.5 at the first follow-up; 3.6 at the second follow-up; P <0.001).

Conclusions: Advanced cancer patients with ESAS ≥ 5 may benefit from outpatient palliative cancer care. Prescreening of patient-reported symptoms using ESAS can be useful for identifying unmet palliative care needs in advanced cancer patients.

Background

Integration of early palliative care into standard oncology care in patients with advanced cancer improves quality of life (QoL), reduces depression and symptom burden, and leads to survival benefit [1–5]. Although early palliative care involvement is increasingly recommended in patients with cancer [6], palliative care was delivered to only 50–65% of cancer patients with a median time of 20 days before death in real-world practice [7, 8]. To overcome barriers to palliative care integration, systematic symptom assessment and the optimal timing for referral to outpatient palliative care need to be addressed [9].

To facilitate improved patient-centered care, patient-reported outcomes measure (PROM) was advocated using a self-reported measure [10]. The Edmonton Symptom Assessment System (ESAS) is a validated PROM that systematically and efficiently evaluates 10 physical and/or emotional symptoms in patients with advanced cancer [11–13]. The ability of ESAS to quantify multiple symptoms rapidly with easy-to-interpret scores has been proved in both clinical practice and research over the past 25 years [14]. Of note, ESAS is efficacious for symptom screening and longitudinal monitoring to identify patients' unmet needs for outpatient palliative care [15, 16].

Currently, the optimal timing and criteria of palliative care referral is still elusive [17]. Six major reasons for palliative care referral include advanced cancer diagnosis, physical symptom management, prognostication, poor performance status, psychosocial distress, and end-of-life care planning [18, 19]. Although ESAS can be a useful prescreening tool for palliative care referral, a clear cutoff for symptom severity before initiating a palliative care referral was not well characterized.

The current study evaluated patient-reported symptoms using ESAS in patients with advanced cancer referred to an outpatient palliative care clinic at the baseline and the follow-up. The aim of this study is to identify an optimal ESAS score indicating a need for palliative care referral. Identification of patients who would benefit (e.g., symptom improvement) from palliative care services can enhance the integration of palliative care into standard oncology.

Methods

Patient selection

A total of 212 patients with advanced cancer that were referred to the outpatient palliative care clinic at Yonsei Cancer Center from April 2014 to December 2014. Eligible patients were at least 18 years old, were diagnosed with advanced cancer, and had to have completed the ESAS questionnaire at both the initial visit and a follow-up visit within a month. We retrospectively identified 71 eligible patients. The ESAS questionnaires were collected at the initial visit and a follow-up visit, respectively. The study protocol was approved by the Institutional Review Board of Severance Hospital (4–2019–0276).

Outcome Measures

The ESAS is a validated assessment tool to measure symptom severity in cancer patients [12]. The Korean version of the ESAS (K-ESAS) was used in this study and was further validated by Korean patients with cancer [13]. ESAS scores at the baseline, first, and second follow-up visit at 4 week intervals were obtained. All questionnaires were completed by the patients or read to them by a nurse or caregiver. If patients had difficulties in understanding the meaning of the question, a palliative care-trained nurse explained it in a simple way. Patients' average symptom over a 24 hour period was assessed using the ESAS. The ESAS is a 0 to 10 numerical scale (0, no symptom; 10, worst possible) to rate severity of the following 10 individual symptoms: pain, fatigue, nausea, depression, anxiety, drowsiness, dyspnea, sleep disorder, anorexia, and well-being. All instruments were completed using paper forms and then entered into an electronic database for analysis. Patient demographics and clinical factors were also collected.

Outpatient Palliative Care

Yonsei Cancer Center established palliative care center with a hospice referral system for terminally ill cancer patients [20]. Briefly, if a patient with advanced cancer have a life expectancy no more than 6 months, the patient is guided to the hospice counseling of palliative care center to request for a referral. Palliative care center is staffed by a board certified palliative care physicians, nurses, social workers, spiritual care professionals, music therapists, and art therapists to provides comprehensive care for advanced cancer patients as previously described [21].

Statistical Analysis

Baseline demographic characteristics were summarized using descriptive statistics. Continuous variables are expressed as the median and interquartile range and were compared using the Mann-Whitney U test. Categorical variables are expressed as a number (%) and were compared using the chi-square test or Fisher's exact test. Linear mixed models were used to assure that there is a significant trend of the ESAS score over time within each group. All statistical tests were 2-sided, and *P* values less than .05 were considered statistically significant. Analyses were performed using R statistical software version 3.5.0 (www.r-project.org) or SAS, version 9.4 (SAS Institute Inc).

Results

Patient Characteristics

Patient demographics are listed in Table 1 at the first palliative care consultation. The median age was 65 years old. The ECOG performance status distribution was 1/2/3 (28%/39%/33%), respectively. Median overall survival (OS) was 4.4 months (95% confidence interval [CI], 2.7–6.2). The majority of patients received ongoing treatment at the time of the palliative care referral. The most prevalent malignant diagnoses were lung (37%), pancreaticobiliary (17%), and colorectal (15%) cancers.

To analyze the effect of outpatient palliative care on symptom improvement, we classified the patients according to the mean ESAS score at the cut-off of 5 as previously described [22]. Among the 71 patients, 20 (28%) had moderate/severe symptom burden with the mean ESAS ≥ 5 (Table 1). The average ESAS symptom intensity was 2.7 for the mild symptom group and 6.3 for the moderate/severe symptom group, respectively. No significant differences in OS was observed between the two groups (4.4 vs 3.6 months with mean ESAS ≥ 5 ; log-rank *P* = .09; Table 1).

Baseline Symptom Intensity

Approximately 30% of patients had moderate/severe symptom burdens (ESAS ≥ 5 ; pain, 24%; fatigue, 26%; nausea, 24%; depression, 25%; anxiety, 25%; drowsiness, 26%; dyspnea, 25%; sleep disorder, 27%; loss of appetite 28%; sensation of well-being, 27%; Figure 1A). To illustrate the ESAS symptoms for all patients at the same time, we generated a heatmap in which each row represents an individual patient and each column represents one ESAS symptom (Figure 1B). The color represents symptom intensity (blue, none; red, worst). Interestingly, most of the patients with moderate/severe symptom burdens (ESAS ≥ 5) had globally elevated symptom expression (Figure 1B). Solitary dyspnea (n = 2) or loss of appetite (n = 3) was observed in atypical patients.

Next, we calculated the Pearson correlation co-efficient to evaluate any potential association between ESAS symptoms (Figure 1C). Ten ESAS symptoms were classified into three clusters: Six symptoms such as depression, anxiety, fatigue, drowsiness, pain, and sleep

disorder are clustered, suggesting that each symptom may affect the severity of another symptom. Likewise, two related symptoms such as loss of appetite and nausea or dyspnea and sensation of well-being were clustered together, respectively (Figure 1C).

Symptom changes

Next, the first and second follow-up ESAS scores were compared with the respective patient's baseline score, and symptoms were examined to determine whether symptom burden had improved or deteriorated (Figure 2). The physical score is an average of six physical symptoms such as pain, fatigue, nausea, drowsiness, dyspnea, and loss of appetite. The emotional score is the average of anxiety and depression. Interestingly, the mean total ESAS score was maintained in patients with mild symptom burden (ESAS <5; 2.7 at the baseline; 3.4 at the first follow-up; 3.0 at the second follow-up) while there was significant symptom improvement in patients with moderate/severe symptom burden (ESAS ≥5; 6.5 at the baseline; 4.5 at the first follow-up; 3.6 at the second follow-up; $P < 0.001$), suggesting that patients with ESAS ≥5 can benefit from palliative care (Figure 1A). Furthermore, both the ESAS physical score and the emotional score were significantly improved at both the first- and second follow-up in patients with a moderate/severe symptom burden (ESAS ≥5; physical score, 6.3 at the baseline, 4.5 at the first follow-up, and 3.6 at the second follow-up, $P < 0.001$; emotional score, 7.1 at the baseline, 4.4 at the first follow-up, and 3.2 at the second follow-up, $P < 0.001$; Figure 2B and 2C). In patients with mild symptom burden (ESAS <5), both the physical score and emotional score were maintained at the second follow-up, compared to symptom scores at the baseline.

Finally, individual symptom changes from the baseline, first follow-up, and second follow-up were evaluated (Figure 3 and Table 2). As shown in Figure 3A and Table 2, most symptom scores were maintained during outpatient palliative care in patients with mild symptom burden (ESAS <5). Fatigue was slightly worse from 3.3 at the baseline to 4.7 at the first follow-up and to 4.0 at the second follow-up, respectively. However, in patients with moderate/severe symptom burden (ESAS ≥5), the majority of symptoms were significantly improved at the first and second follow-up, compared to the baseline (Figure 3B and Table 2). In addition, nausea and dyspnea scores showed a trend toward improvement (nausea, 3.9 at the baseline, 3.2 at the first follow-up, and 2.9 at the second follow-up, $P = 0.555$; dyspnea, 4.8 at the baseline, 2.9 at the first follow-up, and 3.1 at the second follow-up, $P = 0.145$; Figure 3B).

To sum up, most of the patients with ESAS ≥5 had globally elevated symptom burden and showed significant symptom improvement after palliative care referral, suggesting that prescreening of ESAS can help to identify patients who can benefit from outpatient palliative care.

Discussion

Although the early integration of palliative care is increasingly recommended in advanced cancer care planning, systematic and/or active symptom assessment is still rarely performed, resulting in low referral rates of palliative care services in a real world setting [6, 9]. In our study, we showed that ESAS is an easy-to-use systematic screening tool in longitudinal symptom monitoring. Furthermore, a baseline ESAS score can help to identify advanced cancer patients who may benefit from palliative care. Although our findings need to be validated in future prospective trials, our study demonstrated the applicability of ESAS as the criteria for palliative care referral.

Symptom management is one of the main reasons for palliative care referral [19]. However, a validated tool in an oncology setting and the cutoff point for palliative care referral are still elusive. Previous reports suggested ESAS can be used as a prescreening tool, but the recommended cutoff was not well-specified [14, 19]. In this study, most of the patients with moderate/severe symptom burden (ESAS ≥5) showed globally elevated symptom scores (Figure 1), indicating that patients with a mean ESAS score of 5 or more had physical distress, which may improve from palliative care. Previously, a retrospective analysis reported that ambulatory palliative care cancer patients had a distressful symptom burden with an average ESAS score of 5.1 [23], suggesting the referral ESAS criteria of ≥5 is reasonable.

Our data indicate that palliative care is presumably associated with significant symptom improvement in patients with moderate/severe symptom burden (ESAS ≥5). Previously, a single cutoff point of 4 or 5 was suggested as moderate/severe symptom burden, with a better sensitivity using 4 and increased specificity using 5 as a cutoff point [22]. In our study, the symptom pattern in patients with an ESAS of 4 ($n = 9$) was comparable to those with patients with mild symptom burden (ESAS <4), suggesting that a single cutoff point of 5 is a better indicator for moderate/severe symptoms. Previous reports also suggested a cutoff point of 5 for defining moderate/severe symptoms such as pain, anxiety, and depression [24–26], supporting our results.

Still, the proportion of patients referred to an outpatient palliative care team is small, and the referral usually occurs very late in the disease trajectory [27]. For a future study, we plan to collect ESAS using mobile devices for all possible advanced cancer patients. Electronic data capture reduced missing data and enabled rapid data interpretation, resulting in improvement of symptom control in a randomized controlled trial [28]. Likewise, longitudinal symptom monitoring using ESAS will facilitate the identification of patients with palliative care needs in an outpatient setting.

This study has several limitations. First, this study retrospectively reviewed the ESAS questionnaire. Second, a sample size of 71 can be used for hypothesis generation, but may not be enough to draw a concrete conclusion. Third, long-term follow-up of patients visiting three or more times was not available. Although a future prospective trial is warranted, we believe that our result supports the importance of ESAS as a useful prescreening tool in outpatient palliative cancer care.

Conclusions

We found that patients with moderate/severe symptom burden (ESAS ≥ 5) showed significant symptom improvement after palliative care referral at follow-up visits. Prescreening of ESAS will help to identify advanced cancer patients who would benefit from palliative care services, thereby enhancing the integration of palliative care into standard oncology.

Abbreviations

ESAS: Edmonton Symptom Assessment System; K-ESAS: Korean version of the ESAS; QoL: quality of life; PROM: patient-reported outcomes measure; ECOG: Eastern Cooperative Oncology Group; OS: overall survival; CI: confidence interval; LMM: Linear mixed model

Declarations

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None.

Author's contributions

G. L. and H. S. K. wrote the manuscript. S. W.L, M. J.K, B.L, and Y. J.H collected the data. G. L. and H. S.K analyzed the results. E. H.K performed statistical analysis. H. C. designed the study. All authors reviewed the manuscript.

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Availability of data and materials

Please contact the author Hye Jin Choi (choihj@yuhs.ac) upon reasonable requests.

Ethics approval and consent to participate

This study protocol was approved by the Institutional Review Board of Severance Hospital (4–2019–0276). The requirement for obtaining informed consent was waived due to the retrospective nature of the study.

Consent for publication

Not Applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Characteristic	ESAS <5 (n=51)	ESAS ≥5 (n=20)	Total (n=71)	P value
Age, years				0.004
Median	67	59	65	
Range	31-91	40-78	31-91	
Sex				0.383
Male	30 (59%)	14 (70%)	44	
Female	21 (41%)	6 (30%)	27	
ECOG score				0.008
1	17 (33%)	3 (15%)	20	
2	23 (45%)	5 (25%)	28	
3	11 (22%)	12 (60%)	23	
Median overall survival (month)	4.4	3.6	4.4	0.090
95% CI	2.2-6.6	0.2-7.0	2.7-6.2	
Primary cancer				0.094
Lung	10 (20%)	8 (40%)	18	
Pancreaticobiliary	12 (24%)	0 (0)	12	
Colorectal	9 (18%)	2 (10%)	11	
Gynecology	7 (14%)	2 (10%)	9	
Genitourinary	5 (10%)	0 (0)	5	
Stomach	3 (6%)	1 (5%)	4	
Liver	2 (4%)	2 (10%)	4	
Bone and Spine	2 (4%)	3 (15%)	5	
Head and Neck	1 (2%)	2 (10%)	3	
Ongoing treatment				0.998
Chemotherapy	16 (31%)	10 (50%)	26	
Radiotherapy	10 (20%)	6 (30%)	16	
Surgery	3 (6%)	1 (5%)	4	
Gamma Knife Surgery	1 (2%)	2 (10%)	3	
No further treatment	14 (27%)	8 (40%)	22	
Mean ESAS total score	2.7 (± 1.2)	6.3 (± 1.3)	3.9 (± 3.0)	<0.001
Mean ESAS physical score	2.6 (± 1.2)	6.2 (± 1.2)	3.8 (± 3.1)	<0.001
Mean ESAS emotional score	2.6 (± 2.0)	6.7 (± 2.3)	3.8 (± 2.9)	<0.001

Abbreviations: CI, confidence interval; ESAS, Edmonton Symptom Assessment System; ECOG, Eastern Cooperative Oncology Group

Table 1. Patient characteristics at the baseline. The mean ESAS physical score is the average of six physical symptoms (pain, fatigue, nausea, drowsiness, dyspnea, and appetite). The mean ESAS emotional score is the average of two emotional symptoms (anxiety and depression).

Symptom	Mean ESAS total score at the baseline < 5 (n=51)				Mean ESAS total score ≥ 5 at the baseline (n=20)									
	Baseline		1st follow-up		2nd follow-up	P value ^a	Baseline		1st follow-up		2nd follow-up	P value ^a		
	Mean	SD	Mean	SD			Mean	SD	Mean	SD				
Pain	3.0	2.1	3.4	2.6	3.1	2.1	0.660	6.3	2.8	4.8	2.9	3.1	2.0	0.006
Fatigue	3.3	2.2	4.7	2.7	4.0	2.8	0.033	8.2	1.5	5.4	2.4	4.2	2.6	<0.001
Nausea	1.1	1.6	2.0	2.2	1.0	1.3	0.427	3.9	2.7	3.3	3.2	2.9	2.7	0.555
Depression	2.8	2.4	3.4	3.0	2.8	2.3	0.425	6.7	1.8	4.1	2.7	4.0	3.0	0.009
Anxiety	2.5	1.9	3.5	2.8	3.3	2.5	0.307	7.5	1.6	4.8	3.4	2.5	2.5	<0.001
Drowsiness	2.6	2.6	3.4	2.5	3.7	2.7	0.077	6.7	2.8	5.5	3.0	4.5	2.6	0.004
Dyspnea	2.3	2.2	2.9	2.3	2.7	1.9	0.214	4.8	3.4	2.9	2.7	3.1	3.1	0.145
Sleep disorder	2.7	2.6	3.3	2.8	3.0	2.4	0.342	6.9	2.8	4.9	2.8	3.5	2.9	0.001
Appetite	3.6	2.9	4.1	3.1	3.3	2.8	0.877	7.5	2.1	4.9	3.1	4.3	2.6	0.001
Well-being	4.2	2.4	4.5	2.7	4.2	2.1	0.940	6.8	2.9	4.5	2.8	4.9	3.7	0.032
mean ESAS physical score	2.6	1.2	3.3	1.6	2.9	1.5	0.145	6.3	1.2	4.5	2.4	3.6	1.9	<0.001
mean ESAS emotional score	2.6	2.0	3.4	2.6	3.1	2.3	0.080	7.1	1.6	4.4	2.9	3.2	2.0	<0.001
mean ESAS total score	2.7	1.2	3.4	1.6	3.0	1.5	0.117	6.5	1.2	4.5	2.3	3.6	2.0	<0.001

Abbreviations: ESAS, Edmonton Symptom Assessment System; SD, standard deviation

Table 2. ESAS scores at the baseline, 1st follow-up (4-week), and 2nd follow-up visits. The ^aLinear mixed model (LMM) was used to compare ESAS scores at the baseline, 1st follow-up, and 2nd follow-up visits. The mean ESAS physical score is the average of six physical symptoms (pain, fatigue, nausea, drowsiness, dyspnea, and appetite). The mean ESAS emotional score is the average of two emotional symptoms (anxiety and depression).

Figures

Figure 1

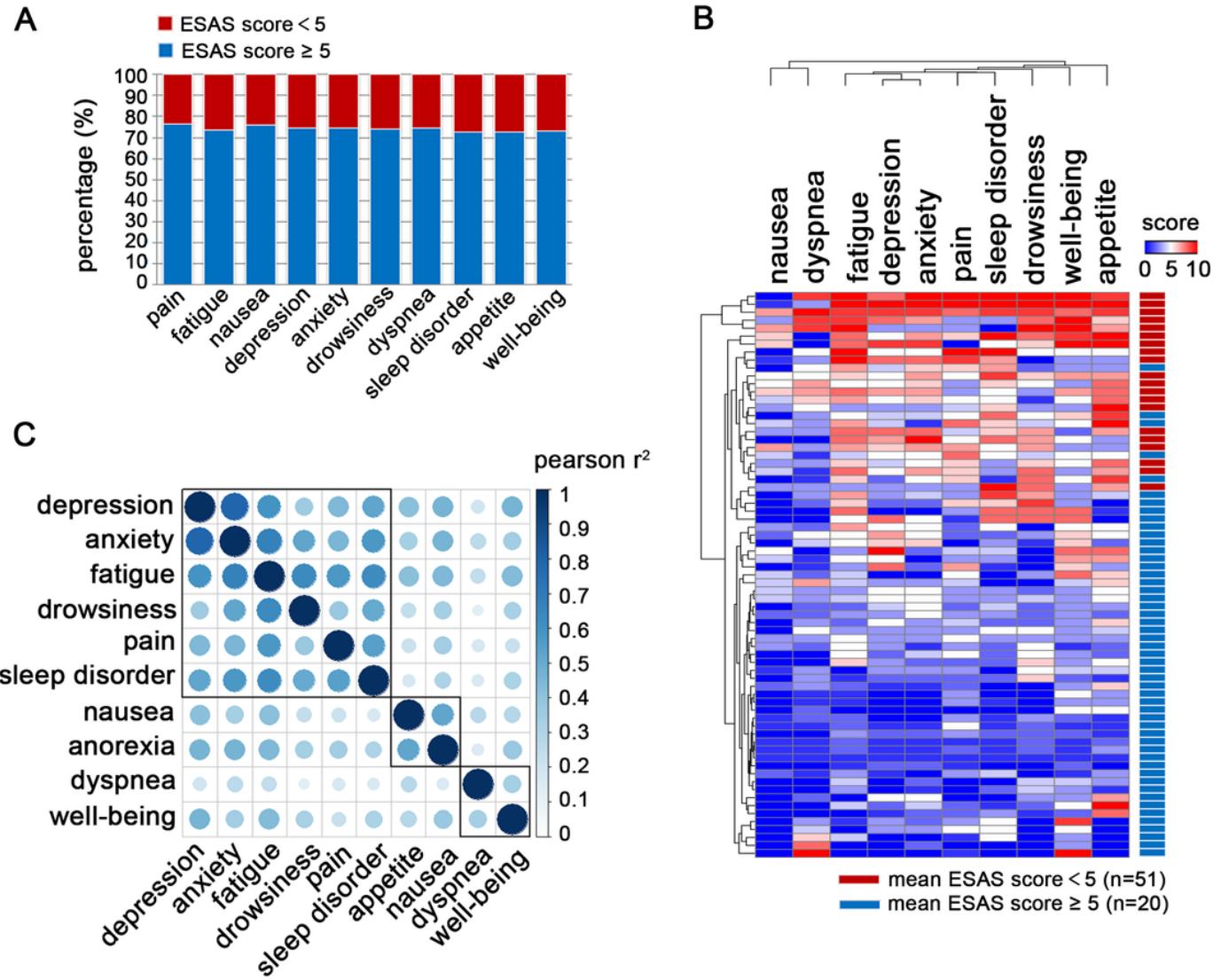


Figure 1

ESAS score distribution. (A) All ten ESAS items were illustrated according to symptom severity (B) A heatmap represents ten ESAS items in all patients at the same time. (C) A correlation matrix classified ten ESAS symptoms into three clusters.

Figure 2

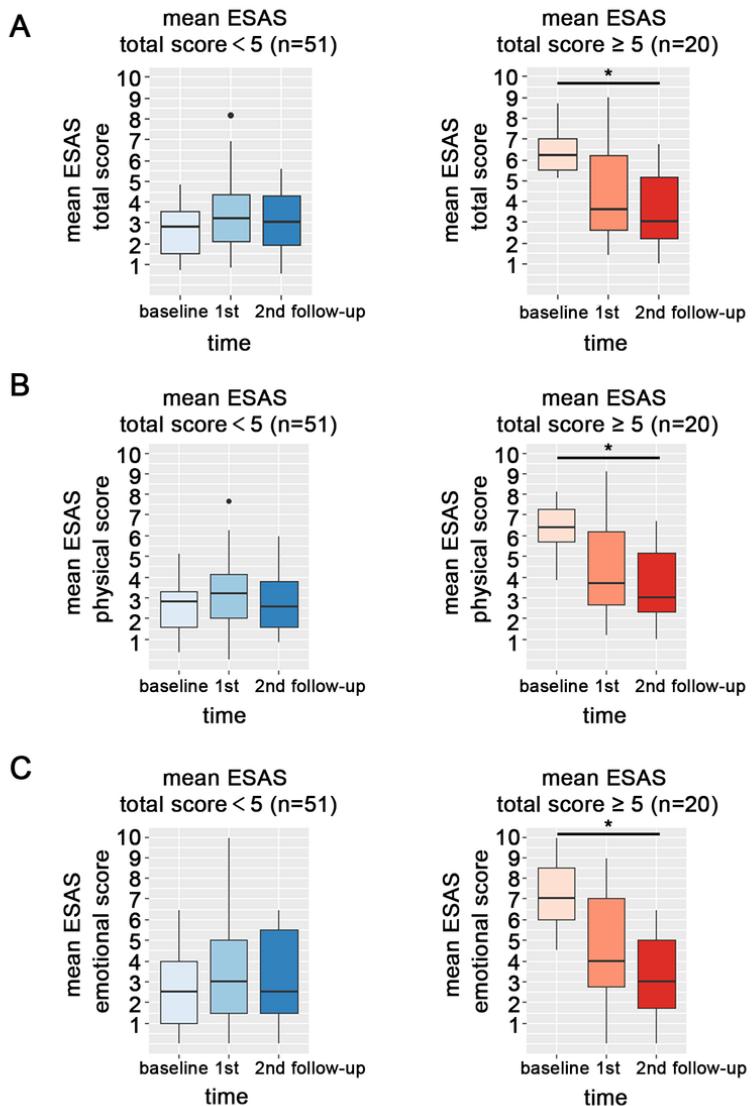


Figure 2

Mean (A) total ESAS score, (B) physical ESAS score, and (C) emotional ESAS score at the baseline, 1st follow-up, and 2nd follow-up in patients with mild symptoms (ESAS<5) or moderate/severe symptoms (ESAS ≥ 5). The ESAS physical score is the average of six physical symptoms (pain, fatigue, nausea, drowsiness, dyspnea, and appetite). The mean ESAS emotional score is the average of two emotional symptoms (anxiety and depression). *P < 0.05

Figure 3

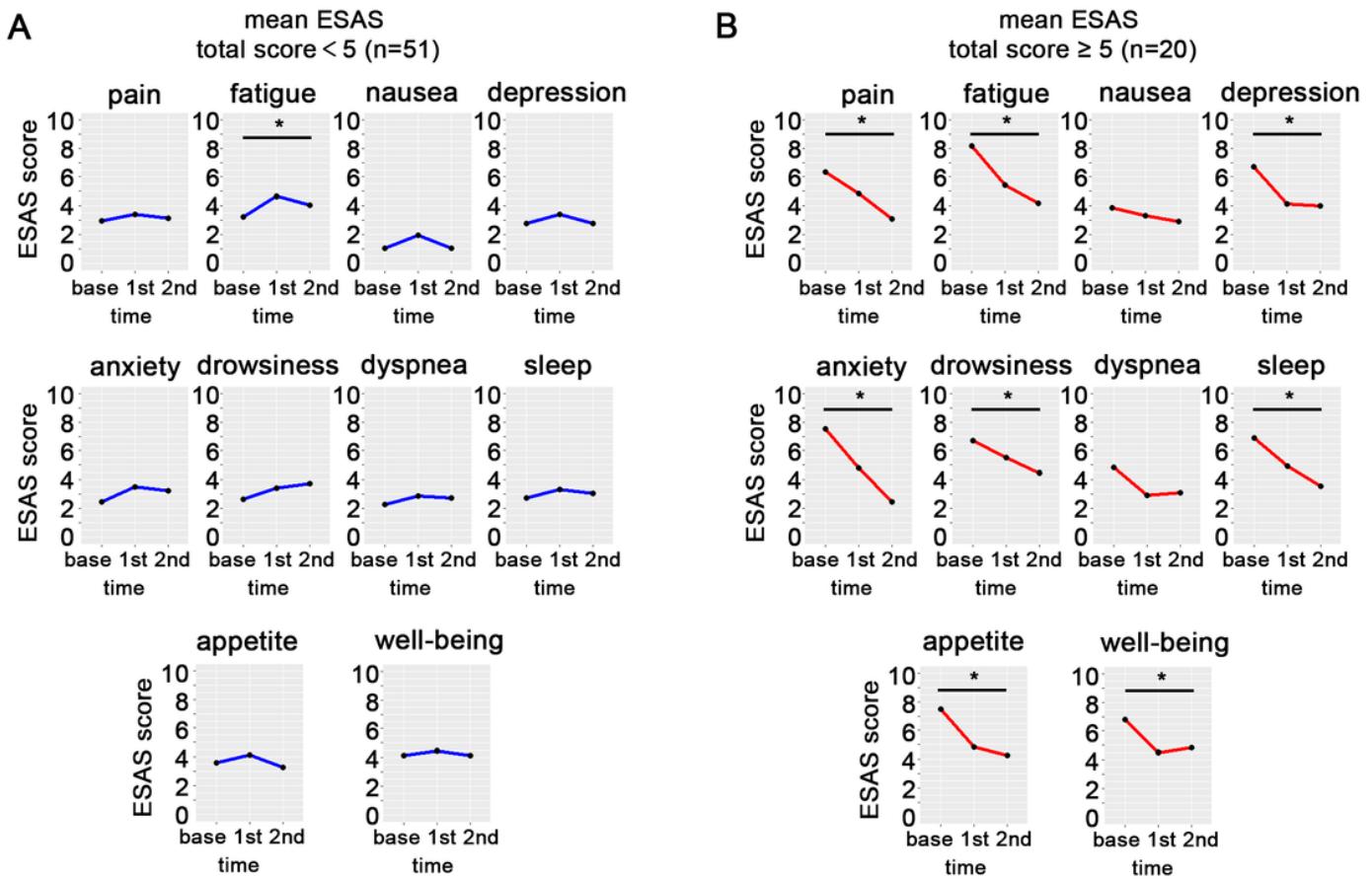


Figure 3

Time trends of all ten ESAS items at the baseline, 1st follow-up, and 2nd follow-up in patients with mild symptoms (ESAS<5) or moderate/severe symptoms (ESAS ≥5). *P < 0.05